Regioselective Radical Cyclization & Dicarbofunctionalization of Unsymmetrical Alkynes

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in
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By

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May, 2022

To

My Family

&

Teachers

DECLARATION

I hereby declare that the matter embodied in the thesis entitled **"Regioselective Radical Cyclization & Dicarbofunctionalization of Unsymmetrical Alkynes"** is the result of investigation carried out by me in the School of Chemistry, University of Hyderabad, Hyderabad, India, under the supervision of **Prof. Akhila Kumar Sahoo**.

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CERTIFICATE

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Shubham Dutta

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List of Abbreviations

AcOH	acetic acid
Ac	acetyl
Ar	aryl
α	alpha
aq	aqueous
β	beta
Bn	benzyl
BQ	1,4-benzoquinone
br	broad
Bs	brosyl
^{n}Bu	n-butyl
^{t}Bu	*tert*-butyl
Bz	benzoyl
°C	degree Celsius
cat.	catalyst
calcd	calculated
^{13}C NMR	carbon-13 nuclear magnetic resonance spectroscopy
CH_3CN	acetonitrile
$CHCl_3$	chloroform
m-CPBA	*m*-chloroperbenzoic acid
Cp	cyclopentadienyl
Co	cobalt
d	doublet
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
1,2-DCE	1,2-dichloroethane
DCM	dichloromethane

DMAP	4-dimethylaminopyridine
dd	doublet of doublet
DG	directing group
DMF	*N*,*N*-dimethylformamide
DMSO	dimethyl sulfoxide
dt	doublet of triplet
δ	delta
EDC.HCl	1-ethyl-3-(3-dimethylaminopropyl)carbodiimide
Equiv.	equivalent
Et	ethyl
e.g.	exempli gratia
ESI	electron spray ionization
EWG	electron-withdrawing group
FT-IR	fourier transform infrared spectroscopy
E+	electrophile
g	gram
γ	gamma
h	hour
^{1}H NMR	proton nuclear magnetic resonance spectroscopy
HRMS	high-resolution mass spectroscopy
Hz	hertz
J	coupling constant in hertz
$K_2S_2O_8$	potassium persulfate
mg	milligram
m.p.	melting point
mmol	millimole
mL	milliliter
NHC	N-heterocyclic carbene
N_2	nitrogen

Nu	nucleophile
$PhI(OAc)_2$	phenyl iodo diacetate
P.A	propargyl acetate
Pd	Palladium
^{n}Pr	n-propyl
rt	room temperature
Ru	ruthenium
Rh	rhodium
R_f	retention factor
TBHP	*tert*-butyl hydroperoxide
TEMPO	(2,2,6,6-tetramethylpiperidin-1-yl)oxy
THF	tetrahydrofuran
TLC	thin-layer Chromatography
TM	transition metals
TMS	trimethylsilyl
Ts	tosyl
μm	micromolar

TABLE OF CONTENTS

	Page No.
Declaration	i
Certificate	ii
Acknowledgements	iii
List of Abbreviations	v
Chapter 1A: Reactivity of Electron Rich Alkynes	1
1A.1. Introduction	3
1A.2. Relative Reactivity of Electron Rich Alkynes	3
1A.3. Ynamines and Emergence of ynamides	5
1A.4. Synthesis of Ynamides	6
1A.5. Synthetic Utility of Ynamide	7
1A.5.1. Radical Reactions of Ynamides	8
1A.5.2. Difunctionalization of Ynamides	8
1A.6. Propargyl Acetates and It's Synthetic Utility	10
1A.7. Conclusion	11
Chapter 1B: Unsymmetrical Multicomponent Dicarbofunctionalization of Olefins and Alkynes	12
1B.1. Olefin Dicarbofunctionalization	14
1B.2. Alkyne Dicarbofunctionalization	17
1B.3. Conclusion	19
1.1 Reference	20
Chapter 2A: Alkyne versus Ynamide Reactivity: Regioselective Radical Cyclization of Yne-Ynamides	24
2A.1. Introduction	26
2A.2. Precedents	27
2A.2.1. Nucleophilic Cyclization of Yne-Ynamides	28
2A.2.2. Radical β-Addition to Ynamides	33
2A.3. Motivation and Scheme Design	35
2A.4. Results and Discussion	37
2A.4.1. Reaction Optimization	37

2A.4.2. Synthesis of Ynamides 38
2A.4.3. Substrate Scope 40
2A.4.4. Control Experiments 45
2A.4.5. Synthetic Application 45
2A.4.6. DFT Calculations 47
2A.5. Conclusion 48
2A.6. Experimental Section 50
2A.6.1. General Information 50
2A.6.2. Materials 50
2A.6.3. General Procedure and spectral/analytical data 51
2A.6.3.1. General Procedure for Cyclization 51
2A.6.3.2. Synthesis of (Z)-N-(2-((4-chlorophenyl)thio)-3-phenylallyl)-4-methyl-N-(phenylethynyl)benzenesulfonamide 67
2A.6.3.3. Synthesis of 2-Benzyl-4-(2-methylphenylsulfonimidoyl)-3-phenyl-1-tosyl-1H-pyrrole 68
2A.6.3.4. Synthesis of 2-Benzyl-3-phenyl-4-(o-tolylsulfinyl)-1-tosyl-1H-pyrrole 69
2A.6.3.5. Synthesis of 2-(5-Benzyl-4-phenyl-3-(o-tolylthio)-1-tosyl-1H-pyrrol-2-yl)-1-phenylethanone 69
2A.6.3.6. Synthesis of 5-Benzyl-9-methyl-6-tosyl-6H dibenzo[4,5:6,7]thiepino[2,3-c]pyrrole 8-oxide 70
2A.6.3.7. Synthesis of 2-(5-Benzyl-4-phenyl-3-(o-tolylthio)-1-tosyl-1H-pyrrol-2-yl)-4-(tert-butyl)phenol 70
2A.7. X-ray crystallography 71
2A.8. References 72
2A.9. Spectra 74
Section 2B : An Unconventional Sulfur-to-Selenium-to-Carbon Radical Transfer: Chemo-and Regioselective Cyclization of Yne-Ynamides 85
2B.1. Introduction 87
2B.2. Precedents 87
2B.2.1. Radical reaction of alkynes involving sequential Se• →S• →C• radical transfer 87
2B.2.2. Existing route for selenylated small heterocycles 89
2B.3. Motivation and Scheme Design 91
2B.4. Results and Discussion 92

2B.4.1. Reaction Optimization 92
2B.4.2. Synthesis of Starting Materials 93
2B.4.3. Substrate scope 95
2B.4.4. DFT Studies 99
2B.4.5. HRMS Studies 102
2B.5. Conclusion 102
2B.6. Experimental Section 104
2B.6.1. General Information 104
2B.6.2. Materials 104
2B.6.3. General Procedure and spectral/analytical data 105
2B.6.3.1. General Procedure for selenyl radical cyclization 105
2B.7. X-ray crystallography 117
2B.8. References 118
2B.9. Spectra 120
Chapter 3A: Keteniminium Driven Umpolung Difunctionalization of Ynamides 130
3A.1. Introduction 132
3A.2. Precedents 133
3A.2.1. Umpolung difunctionalization 133
3A.2.2. Keteniminium driven difunctionalization 137
3A.2.3. Via annulation 140
3A.3. Motivation and Scheme Design 141
3A.4. Results and Discussion 142
3A.4.1. Reaction Optimization 142
3A.4.2. Synthesis of Ynamides and aryl diazonium salts 143
3A.4.3. Substrate Scope-I `146
3A.4.4. Substrate Scope-II 148
3A.4.5. Mechanistic Studies 150
3A.4.6. Synthetic Application 151
3A.4.7. DFT Calculations 152
3A.5. Conclusion 154
3A.6. Experimental Section 155
3A.6.1. General Information 155

3A.6.2. Materials 155
3A.6.3. General Procedure and spectral/analytical data 156
3A.6.3.1. General Procedure for diarylatiom 156
3A.6.3.2. Synthesis of 2-Fluoro-1-(4-methoxyphenyl)-2-phenyl-2-(p-tolyl)ethanone 184
3A.6.3.3. Synthesis of N-Benzyl-N-(2-(4-methoxyphenyl)-3-phenyl-3-(p-tolyl)oxiran-2-yl)-4-methylbenzenesulfonamide 185
2A.6.3.4. Synthesis of N-Benzyl-N-(6-methoxy-3-methyl-10-phenylphenanthren-9-yl)-4-methylbenzenesulfonamide 185
3A.6.3.5. Synthesis of (E)-4-(2-(N-Benzyl-4-methylphenylsulfonamido)-2-(4-methoxyphenyl)-1-phenylvinyl)benzoic acid 186
3A.6.3.6. Synthesis of (E)-N-(2-(4-Azidophenyl)-1-(4-methoxyphenyl)-2-phenylvinyl)-N-benzyl-4-methylbenzenesulfonamide 186
3A.6.3.7. Synthesis of (E)-N-Benzyl-N-(1-(4-methoxyphenyl)-2-(4'-methyl-[1,1'-biphenyl]-4-yl)-2-phenylvinyl)-4-methylbenzenesulfonamide `187
3A.7. X-ray crystallography 188
3A.8. References 194
3A.9. Spectra 196
Chapter 3B: Keteniminium Driven Umpolung Difunctionalization of Ynamides 215
3B.1. Introduction 217
3B.2. Precedents 217
3B.2.1. **α-Alkenylation of ynamide** 217
3B.3. Motivation and Scheme Design 219
3B.4. Results and Discussion 220
3B.4.1. Reaction Optimization 220
3B.4.2. Synthesis of Ynamides and aryl diazonium salts 222
3B.4.3. Substrate Scope 224
3B.4.4. Control Experiments 227
3B.4.5. Synthetic Application 228
3B.4.6. DFT Calculations 229
3B.5. Conclusion 230
3B.6. Experimental Section 231
3B.6.1. General Information 231
3B.6.2. Materials 231
3B.6.3. General Procedure and spectral/analytical data 232

3B.6.3.1. General Procedure for aryl-alkenylation 232
3B.6.3.2. 3B.6.3.2. Synthesis of (2E,4Z)-5-(N,4-dimethylphenylsulfonamido)-5-(4-methoxyphenyl)-4-phenylpenta-2,4-dienoic acid 250
3B.6.3.3. N-((1Z,3E)-5-allyl-5-hydroxy-1-(4-methoxyphenyl)-2-phenylocta-1,3,7-trien-1-yl)-N,4-dimethylbenzenesulfonamide 251
3B.6.3.4. N-((1Z,3E)-5-hydroxy-1-(4-methoxyphenyl)-5-methyl-2-phenylhexa-1,3-dien-1-yl)-N,4-dimethylbenzenesulfonamide 251
3B.6.3.5. Synthesis of N-((1Z,3E)-5-hydroxy-1-(4-methoxyphenyl)-5-methyl-2-phenylocta-1,3,7-trien-1-yl)-N,4-dimethylbenzenesulfonamide 252
3B.7. X-ray crystallography 252
3B.8. References 253
3B.9. Spectra 256
Chapter 4A: Cationic-Palladium Catalyzed Regio- and Stereoselective *syn*-1,2-Difunctionalization of Unsymmetrical Internal Alkynes 266
4A.1. Introduction 268
4A.2. Precedents 269
4A.2.1. Transition metal catalyzed diarylaion of unsymmetrical alkynes 270
4A.3. Motivation and Scheme Design 275
4A.4. Results and Discussion 276
4A.4.1. Reaction Optimization 276
4A.4.2. Synthesis of yne-acetates 277
4A.4.3. Substrate Scope-I 280
4A.4.4. Substrate Scope-II 284
4A.4.5. Substrate Scope-III 286
4A.4.6. Synthetic Application 288
4A.4.7. Mechanistic Studies 289
4A.4.8. DFT Calculations 292
4A.5. Conclusion 295
4A.6. Experimental Section 296
4A.6.1. General Information 296
4A.6.2. Materials 296
4A.6.3. General Procedure and spectral/analytical data 297
4A.6.3.1. General procedure for synthesis of biological relevant motif bearing propargyl acetates from alcohol 297
4A.6.3.2. General procedure for the synthesis of biological relevant 298

motif bearing propargyl acetates from carboxylic acid
4A.6.3.3. General procedure for the preparation of aryl diazonium salts 301
4A.6.3.4. General procedure for dicarbofunctionalization 301
4A.6.3.5. General procedure for synthesis of indene derivatives 336
4A.6.3.6. Synthesis of 2-(4-methoxyphenyl)-3-phenyl-1H-inden-1-one 338
4A.6.3.7. General Procedure for synthesis of allylic alcohol derivatives 338
4A.6.3.8. Synthesis of 3-(4-methoxyphenyl)-4,4-diphenylbut-3-en-2-one 339
4A.6.3.9. Synthesis of 2-(4-methoxyphenyl)-3,3-diphenylacrylaldehyde 340
4A.6.3.10. Synthesis of (3Z,5E)-7-Allyl-3-(4-methoxyphenyl)-4-phenyldeca-3,5,9-triene-2,7-diol 340
4A.6.3.11. Synthesis of (2E,4Z)-6-Hydroxy-5-(4-methoxyphenyl)-4-phenylhepta-2,4-dienoic acid 341
4A.7. X-ray crystallography 341
4A.8. References 342
4A.9. Spectra 344
Chapter 4B: Cationic-Palladium Catalyzed Regio- and Stereoselective *syn*-1,2-Difunctionalization of Unsymmetrical Internal Alkynes 359
4B.1. Introduction 361
4B.2. Precedents 362
4B.2.1. Transition Metal Catalyzed Hydro-Arylaion of Activated Alkynes 362
4B.2.2. Directing Group (DG) Assisted Hydro-Arylaion of Unsymmetrical Alkynes 365
4B.3. Motivation and Scheme Design 368
4B.4. Results and Discussion 369
4B.4.1. Reaction Optimization 369
4B.4.2. Synthesis of yne-acetates 371
4B.4.3. Substrate Scope-I 373
4B.4.4. Substrate Scope-II 373
4B.4.5. Substrate Scope-III 376
4B.4.6. Synthetic Application 377
4B.5. Conclusion 377
4B.6. Experimental Section 379
4B.6.1. General Information 379
4B.6.2. Materials 379
4B.6.3. General Procedure and spectral/analytical data 380

4B.6.3.1. General procedure for hydro-arylation 380
4B.6.3.2. Synthesis of 2-(4-Methoxyphenyl)-1-methyl-1H-indene 397
4B.6.3.3. Synthesis of 1-(4-Methoxyphenyl)-1-oxopropan-2-yl acetate 398
4B.6.3.4. Synthesis of (Z)-3-(4-Methoxyphenyl)-4-phenylbut-3-en-2-ol 398
4B.6.3.5. Synthesis of (Z)-3-(4-Methoxyphenyl)-4-phenylbut-3-en-2-one 398
4B.7. X-ray crystallography 399
4B.8. References 400
4B.9. Spectra 402

Chapter 5: Palladium Catalyzed Syn-1,2-Aryl-Methylation of Internal Alkynes 419

5.1. Introduction 421
5.2. Precedents 422
4A.2.1. Hydro-methylation of alkynes 422
5.3. Motivation and Scheme Design 425
5.4. Results and Discussion 426
5.4.1. Reaction Optimization 426
5.4.2. Synthesis of ynamides 428
5.4.3. Substrate Scope-I 430
5.4.4. Substrate Scope-II 431
5.4.5. Substrate Scope-III 433
5.4.6. Gram-scale synthesis and synthetic application 434
5.5. Conclusion 435
5.6. Experimental Section 436
5.6.1. General Information 436
5.6.2. Materials 436
5.6.3. General Procedure and spectral/analytical data 437
5.6.3.1. General procedure for aryl-methylation 437
5.6.3.2. 5.6.3.2. Synthesis of 2-fluoro-1-(4-methoxyphenyl)-2-phenylpropan-1-one 458
5.6.3.3. Synthesis of N-Benzyl-N-(6-methoxy-1-oxo-2-phenyl-1H-inden-3-yl)-4-methylbenzenesulfonamide 459
5.6.3.4. Synthesis of 1-(4-Methoxyphenyl)-1-oxopropan-2-yl acetate 459
5.6.3.5. Synthesis of 2-(4-Methoxyphenyl)-1,3-dimethyl-1H-indene 460
5.6.3.6. Synthesis of (Z)-3-(4-Methoxyphenyl)-4-phenylpent-3-en-2-ol 460

5.6.3.7. Synthesis of (Z)-3-(4-Methoxyphenyl)-4-phenylpent-3-en-2-one 460
5.8. References 461
5.9. Spectra 466
List of Publications 481
Conference Attended 495
Certificates from conference 496
Plagiarism report 501
Biographical Sketch 511

Chapter-1

This Chapter has two sections: Section A enumerates Reactivity of Electron Rich alkynes, and Section B describes Unsymmetrical Multicomponent Dicarbofunctionalization of olefins and alkynes

Section A: Reactivity of Electron Rich alkynes

Abstract

Hetero-atom susbtituted electron-rich alkynes, very unique species with inherited polarization of electronegative hetero-atom lone pair electron to triple bond, has been largely used for the developement of novel synthetic methods and the construction of unusual heteroatom-bearing heterocycles. In this section, especially ynamide synthesis and its reactivity towards the development of novel synthetic transformations are discussed. In addition the reactivity of propargyl acetates is also discussed in brief

.

1A.1. Introduction

The alkyne molecular scaffold and its derivatives have been frequently used for the development of new reactions and peripheral modification. For the art of organic synthesis, terminal alkynes are used very often.[1] Additionally, alkynes have been used experimentally in pharmacology, nanotechnology, and as a starting material for the total synthesis of natural products and biologically active compounds.[2] Terminal alkynes are predominantly employed in various name reactions such as Sonogashira, Glaser reaction, Friedel-Crafts reaction, Castro-Stephens coupling, Huisgen 1.3-dipolar cycloaddtion via Click reaction.[3] In contrast to terminal alkynes, internal dicarbon-substituted alkynes have been used less extensively in annulation, click, difunctionalization reactions because of regioselectivity problems. As a result, electron rich alkynes were emerged. The uneven electron distribution caused by the presence of hetero-electronegative atom near to the carbon helps to program regioselective attachment of functional groups across the triple bond (Figure 1A.1).

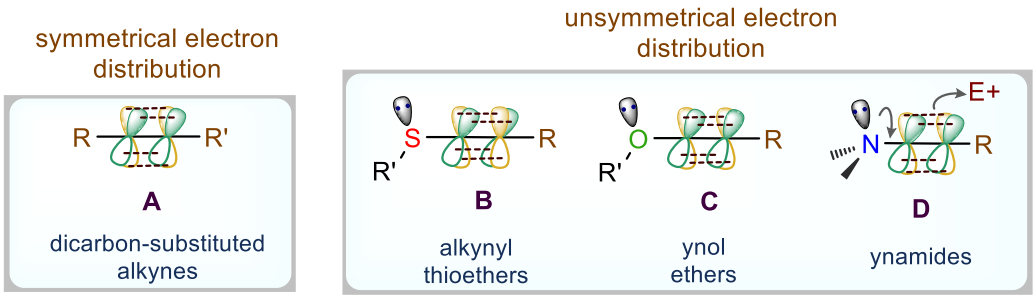


Figure 1A.1. Electron distribution of various alkynes

1A.2. Relative reactivity of electron rich alkynes

In general, all the electron rich alkynes are relatively more reactive as compared to unactivated dicarbon-substuituted alkynes. Nevertheless, the order of reactivity of the electron-rich alkynes can be scaled according to the degree of electron donation from the hetero-electronegative atoms towards the alkyne. As shown in Figure 1A.2, the lone pair of sp^2 hybridized heteroelectronegative atom **X** of **I** is in conjugation with the alkyne triple bond and eventually results in the charged resonating intermediate **II**.

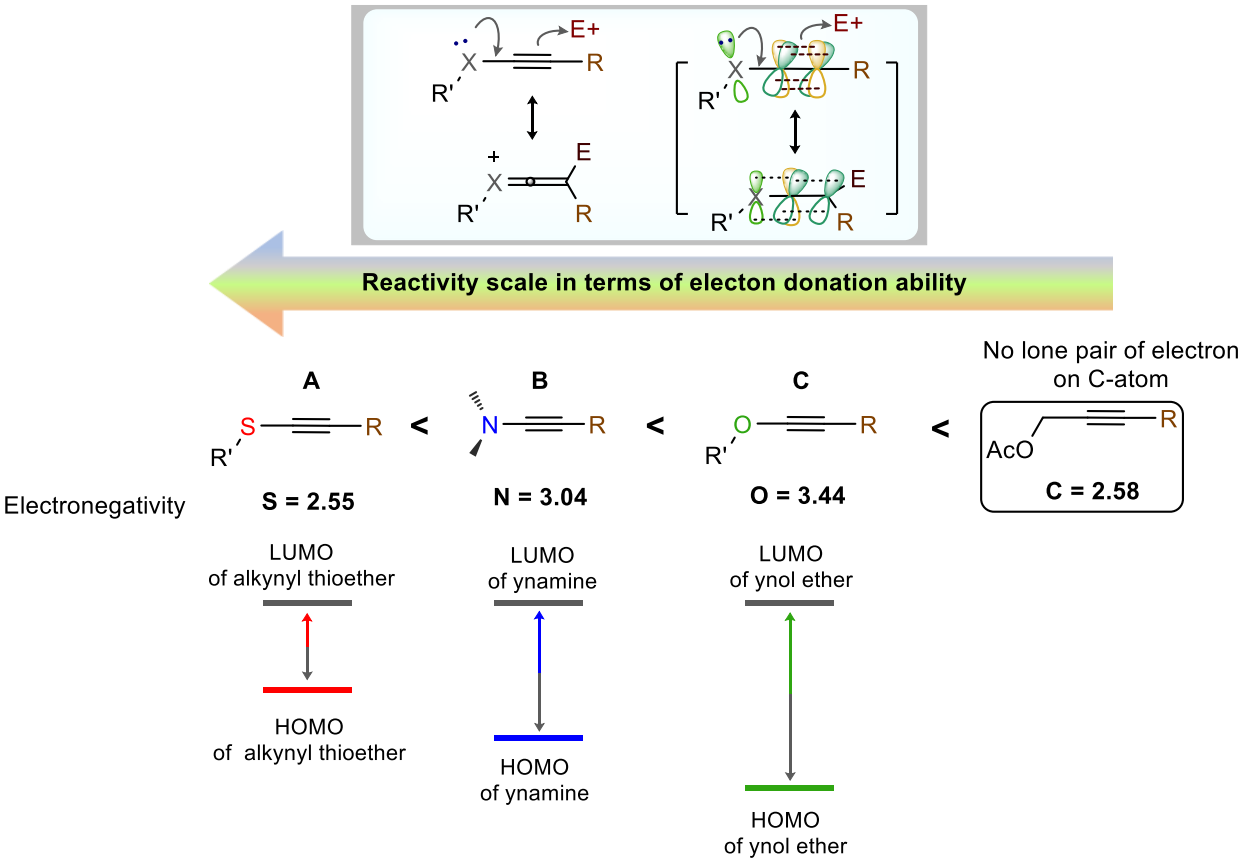


Figure 1A.2. Reactivity of electron rich alkynes

Alkynylthioethers (**A**)[4a], ynamines (**B**)[4b] and ynol ethers (**C**)[4a] are commonly used electron-rich alkynes in organic synthesis. Oxygen being more electronegative than nitrogen and nitrogen being more electronegative than sulfur, the electron donation of O-lone pair to the alkyne in ynol ether would be less than that for ynamines or alkynl thioethers. In the same way, ynamine's ability to donate electron is less compared with alkynylthioethers. Therefore, A > B > C is the order of reactivity.

In addition, this trend can be explained by the energy gap between the HOMO-LUMO of corresponding alkynes.[5] The atomic orbitals of electronegative hetero atom **X** are uniformly lower in energy than the corresponding atomic orbitals of C-atom because of the increased stability of the electrons in electronegative hetero atom. The energies of the bonding molecular orbitals are more similar to those of the atomic orbitals of **X**. Hence

the electron density of bonding electrons is closer to the more electronegative atom X. Therefore, the HOMO of **C** could be located at a lower energy compared to that of **B**, and similarly, the HOMO of **A** could be located at a lower energy compared to that of **B**. Separately, the LUMO of **A**, **B**, and **C** could be located approximately in the same energy. Hence, ynol ether can be considered to be less reactive than its N or S counterparts due to its higher HOMO-LUMO gap (Figure 1A.2).

In this section, the synthesis and reactions of activated ynamides and unactivated propargyl acetates are discussed.

1A.3 Ynamines and Emergence of Ynamides

Ynamines are prominent scaffolds in synthetic chemistry; as the N-lone pair's inherent polarization to the alkyne makes the transformations highly regioselective (**Figure 1A.3**).[6] In consequence, α- and β-carbons of keteniminium species are respectively electrophilic and nucleophilic. However, this uncontrolled polarization makes ynamines sensitive to hydrolysis; since protonation of the electron-rich alkynyl motif leads to reactive keteniminium intermediates which, when trapped in water, produce simple amides (Figure 1A.3). Since ynamines are hydrolytically unstable, they are difficult to prepare during experiments.

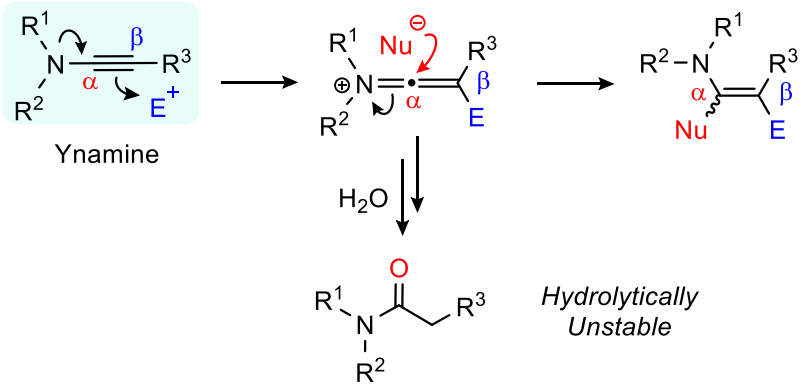


Figure 1A.3. Keteniminium species and hydrolytic instability of ynamines

Adding an electron-withdrawing group to the nitrogen atom will greatly reduce its ability to donate electrons toward the alkynyl motif through resonance delocalization

into the electron-withdrawing group. As a result, ynamide has come into the picture and has served so far as a potential precursor for organic synthesis.[7] Moreover, ynamides have been quite stable to aqueous workup, silica gel chromatography, heating etc. The EWG of ynamides do act as both directing group for regioslective transformation and chiral auxillary for stereoselective transformation. Few examples of EWGs of various analouges of ynamides are shown in **Figure 1A.4**.

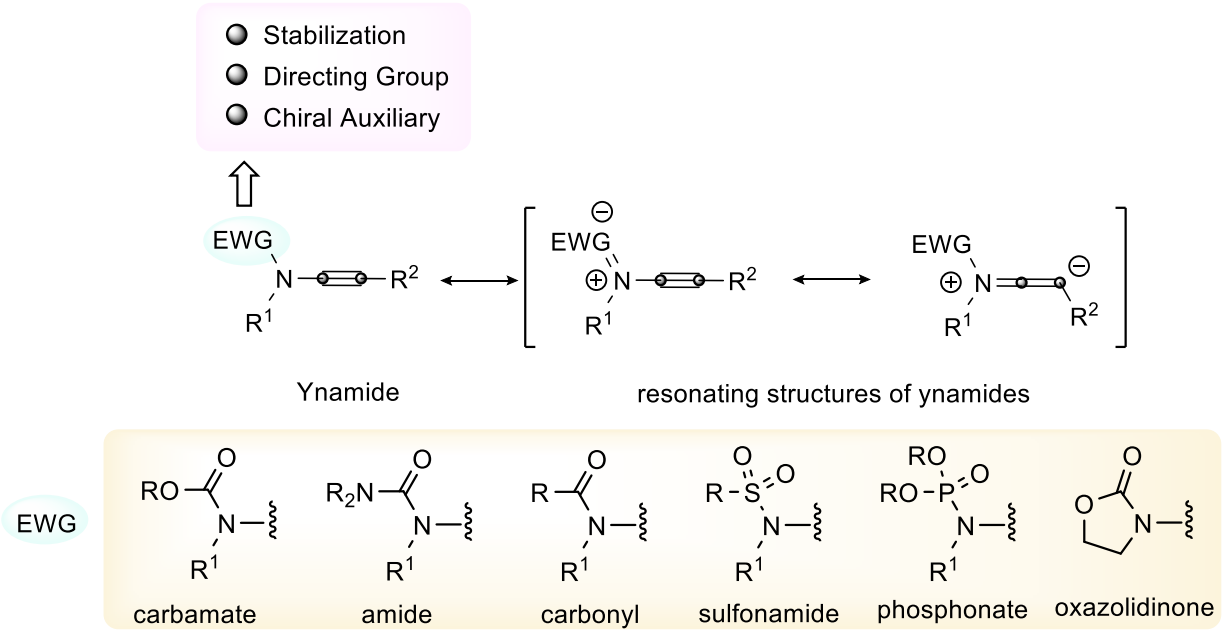


Figure 1A.4. Emergence and various types of ynamides

1A.4. Synthesis of Ynamides

Ynamide was first synthesized in 1972 by Veihe and co-workers. The process involves removal of HCl in presence of strong base KO^{t}Bu from the corresponding α-chloroenamide **1** (**Figure 1A.5**). As of now, numerous synthetic methods have been reported for the synthesis of ynamide, including the amination of alkynylidonium salts, the isomerization of allenamide, copper-catalyzed oxidative amination, and copper-catalyzed cross-coupling reactions (**Figure 1A.5**).[8] Among a variety of synthetic methods, copper-catalyzed amination of bromoalkyne and amide precursors is the most popular techniques to construct ynamide compounds under mild conditions. The copper-

mediated cross-coupling reactions of amide **3** and bromoalkynes **4** led to ynamide derivatives **5** (Hsung method; **Figure 1A.5**).[9]

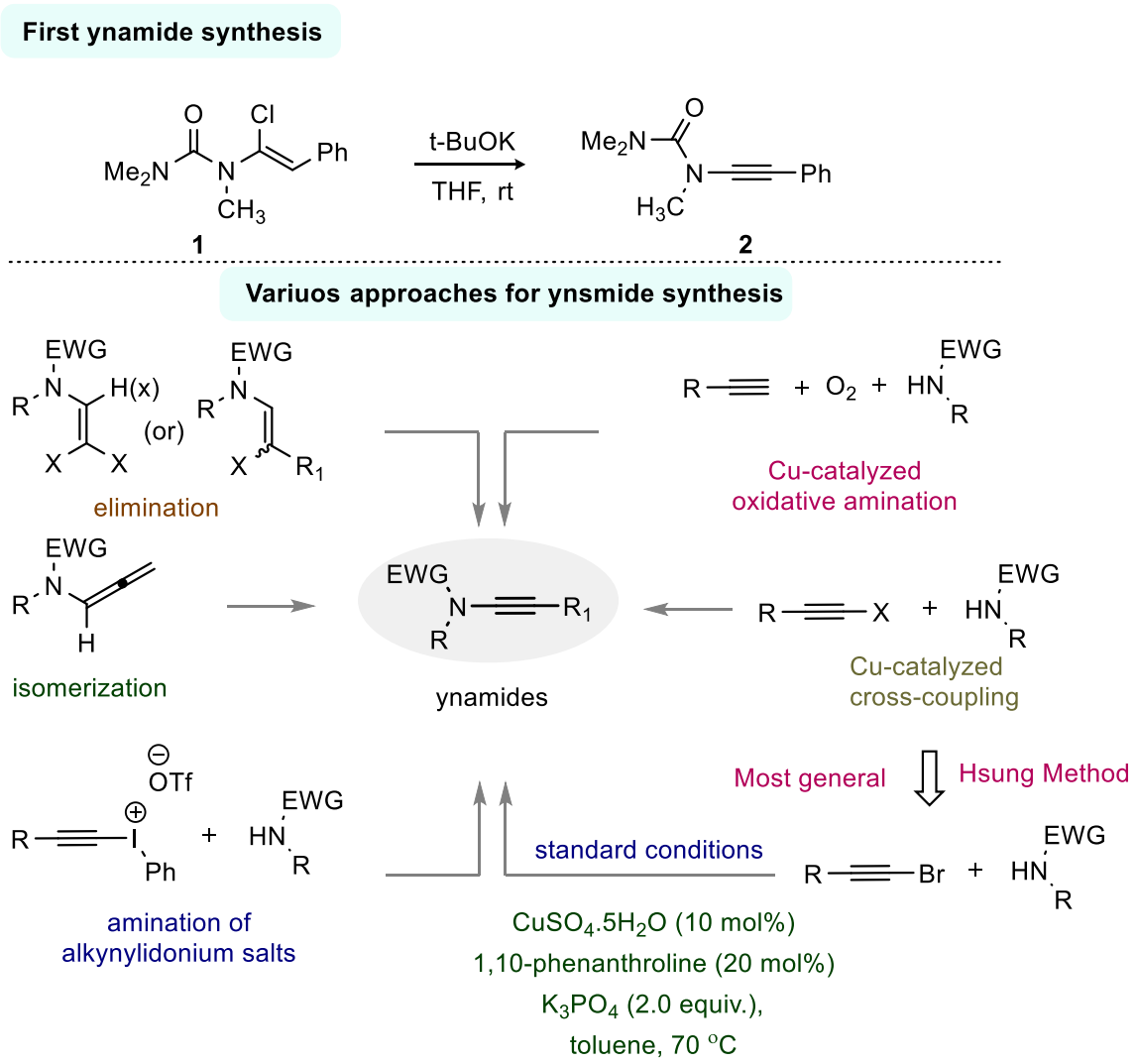
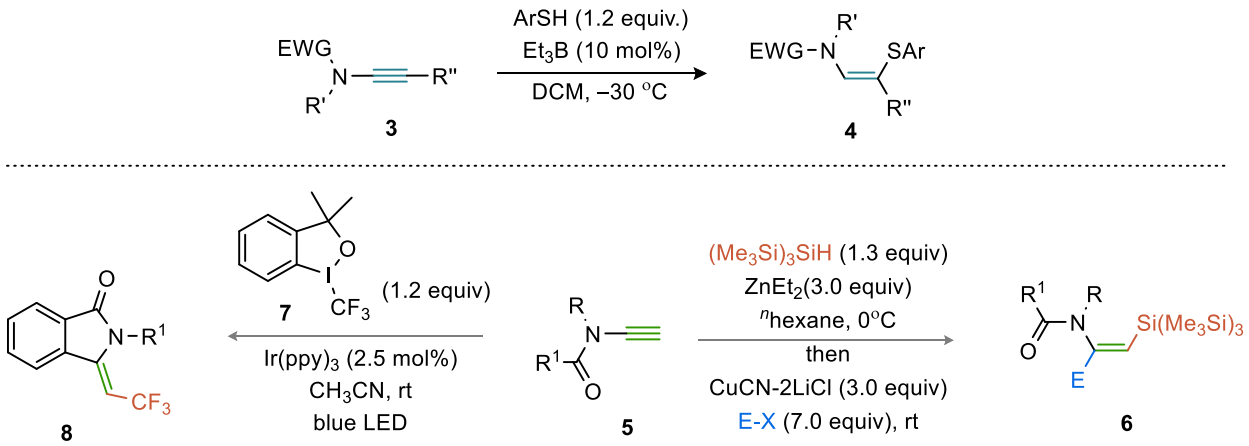


Figure 1A.5. Various approaches towards ynamide synthesis

1A.5. Synthetic Utility of Ynamide

Ynamides have been successfully used in many transformations (such as cycloaddition, cyclization, cycloisomerization, ring-closing metathesis, transition-metal-catalyzed reactions, radical-assisted reactions, and difunctionization). Since this thesis is concerned with radical promoted cyclization and umpolung difunctionalization of ynamides, this section focuses on radical and difunctionalization reactions of ynamides.

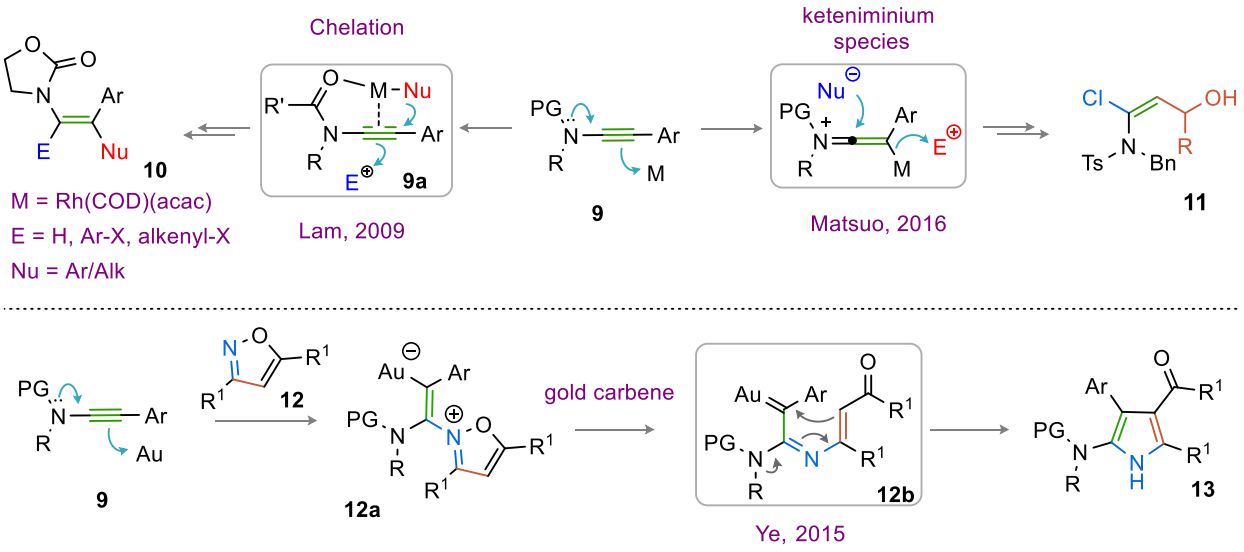
1A.5.1. Radical Reactions of Ynamides



Scheme 1A.1. Selective examples of radical β-addition to ynamide

In 2009, a regio- and stereoselective thiyl radical addition of ynamides in the presence of triethylborane (10 mol%) catalyst was demonstrated by Oshima, Yorimitsu and co-workers (**Scheme 1A.1**).[10] Luna and co-workers in 2014 have shown a *trans*-silyl-zincation of ynamide **5** (**Scheme 1A.1**).[11] The ethyl radical, generated in-situ from $ZnEt_2$ under oxidative condition generates the silyl radical. In 2019, Fensterbank and Olivier elegantly showcased a photocatalytic trifluoromethyl radical triggered cyclization of ynamides (**Scheme 1A.1**). Under visible light irradiation, ynamides **5** are converted into diverse isoindolinones **8** in the presence of 2.5 mol% $Ir(ppy)_3$ as photocatalyst using Togni-I ragent **7** as trifluoromethyl source.[12]

1A.5.2. Difunctionalization of Ynamides



Scheme 1A.2. Selective examples of difunctionalization strategies of ynamide

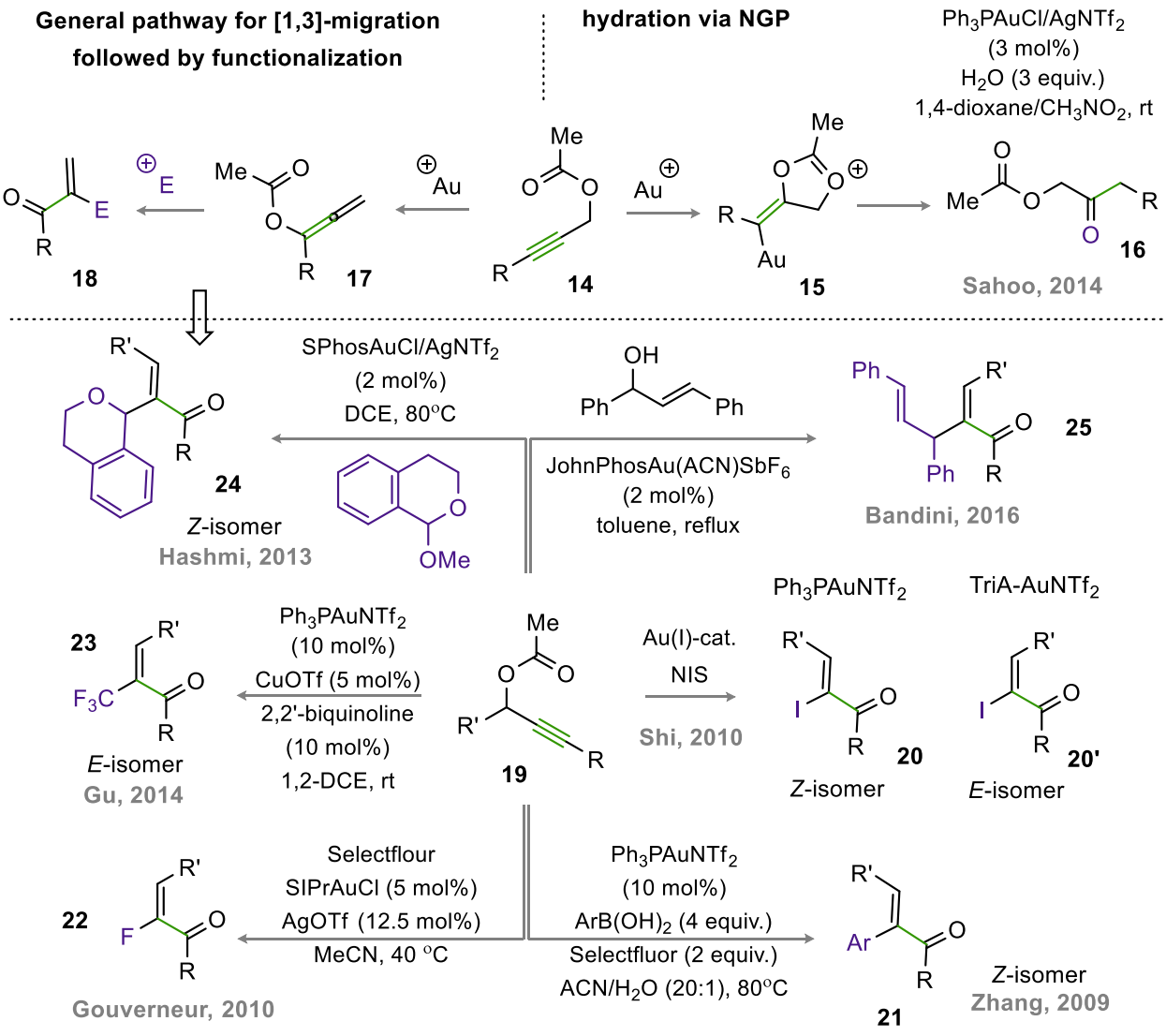
In 2009, the Lam group elegantly adopted a chelation strategy for the regioselective difunctionalization of ynamides (**Scheme 1A.2, left side**).[13] The reaction of ynamide **9** in presence of dialkyl organometallic reagent, Rh(cod)(acac), and electrophile (H^+, aryl, and/or vinyl) furnishes N-enabled tetrasubstituted olefin **10**. Carbometallation of **9a** happens by a regioselective attack of R^2 group at the β-position of ynamide; followed by trap with various electrophiles (H^+, aryl, allyl, vinyl) furnishes **10**.

In 2016, Matsuo and co-workers have showcased a keteniminium species driven addition of terminal-unsubstituted ynamide **9** to carbonyls followed by the attack of chloride to afford 1-Cl-1-amine substituted allylic alcohols **11**.[14]

In 2015, Ye group have developed an atom efficient Au-catalyzed reaction of ynamide 9 with isoxazole to furnish amino-pyrrole derivatives (Scheme 1A.2, below part).[15] The nucleophilic attack of isooxazole at the α-position of Au-keteniminium species generates vinyl-Au species **12a**. Next, the gold back-donation and N–O bond cleavage of intermediate **12a** gives Au-carbene intermediate **12b**. Finally, intramolecular cyclization of **12b** and deauration-isomerization afford amino-substituted pyrrole **13**.

1A.6. Propargyl acetates and its synthetic utility

Propargyl acetates are special calss of alkynes commonly known as α-acylvinyl equivalents. Propargyl acetates are amenable to undergoing rearrangements. In general, the acetate group at the propargyl position assists in neighbouring group participation and undergoes [1,3]/[1,2]-acetate migration or attack in presence of Au-catalyst and Lewis acids. Some of the selected examples of such migration/assistance enabled functionalization of propargyl acetates are narrated below (**Scheme 1A.3**).



Scheme 1A.3. Selected examples of synthetic utility of propargyl acetates

In 2014, our group shown hydration of propargyl acetate **14** via neighbouring group participation of acetate and 1,2-acetate attack to furnish α-acetyl ketones **16**.[16]

Gold catalyzed electrophillic iodination, arylation, fluorination, trifluoromethylation, alkylation and allylation for the synthesis of **20**–**25** from **14** has been demonstrated by Shi (2010)[17], Zhang (2009)[18], Gouverneur (2010)[19], Gu (2014)[20], Hashmi (2013)[21] and Bandini (2016)[22]; these transformations mainly involve 1,3-acetate migration and allene acetate **17** formation stategy (top left side of **Scheme 1A.3).**

1A.7. Conclusion

In summary, the reactivity scale of various electron rich alkynes is briefly discussed. Especially ynamide synthesis and its utility towards radical reactions and difunctionalization of ynamides are highlighted. In addition, typical reactivity of propargyl acetate under gold-catalysis is also shown. Despite wide synthetic manipulations, investigation on difunctionalization of ynamide and propargyl acetate remains to be explored.

Section B: Unsymmetrical Multicomponent Dicarbofunctionalization of Olefins and Alkynes

Abstract

Transition metal (TM)-catalyzed difunctionalization of unactivated olefins/alkynes with two carbon-based entities is a powerful method to construct complex molecular architectures. Over the years, different approaches have been harnessed to either suppress β-H elimination in olefins or resolve regioselectivity issues in unsymmetrical alkynes, which have led to the development of various types of olefins/alkynes dicarbofunctionalization reactions with a wide range of electrophiles and nucleophiles. In this section, historical perspectives on the developments of synthetic methods for the difunctionalization of unsaturated systems is discussed.

1B.1. Olefin Dicarbofunctionalizations

Transition metal (TM)-catalyzed difunctionalization of unactivated olefins installs two carbon-based entities across an olefin to generate two C-C bonds. Thus, dicarbofunctionalization process has gained tremendous interest owing to its ability to assemble complex carbon skeletons. A general approach for the installation of two distinct carbon functionalities (one electrophile and other one nucleophile) across the double bond under transition metal catalysis is shown in Figure 1B.1.

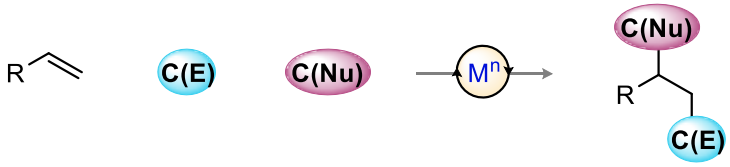


Figure 1B.1. Schematic presentation of dicarbofunctionalization of olefin

Figure 1B.2 shows a general mechanistic pathway for the above mentioned dicarbofunctionalization reaction. At first, electrophillic carbon source C(E) tends to undergo oxidative addition with a low valent transition metal to generate C(E)-metal complex **I**, which undergoes migratory isertion to olefins **II** to give C(sp^3)-[M] complex **III**.

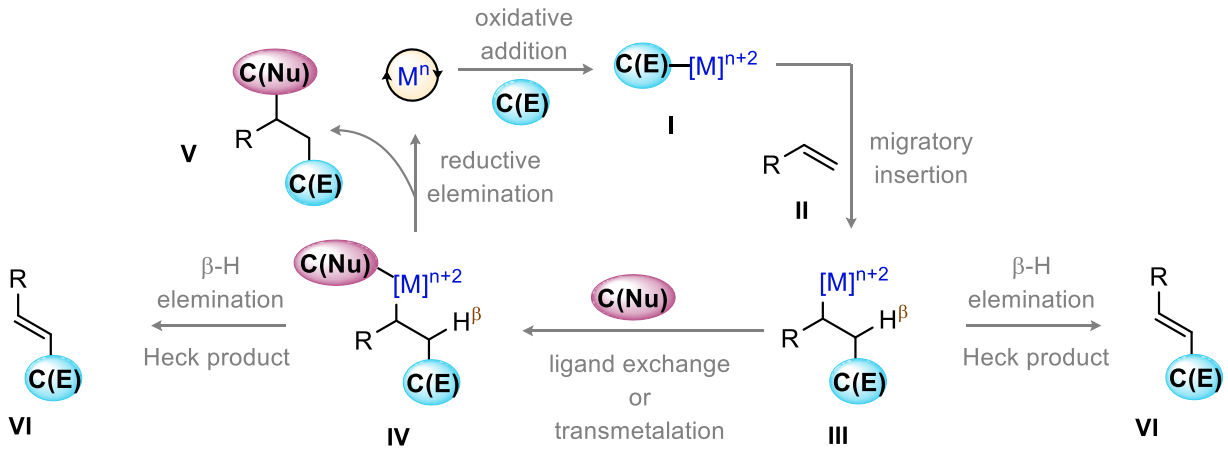


Figure 1B.2. General pathway for unsymmetrical intermolecular dicarbofunctionalization of olefins

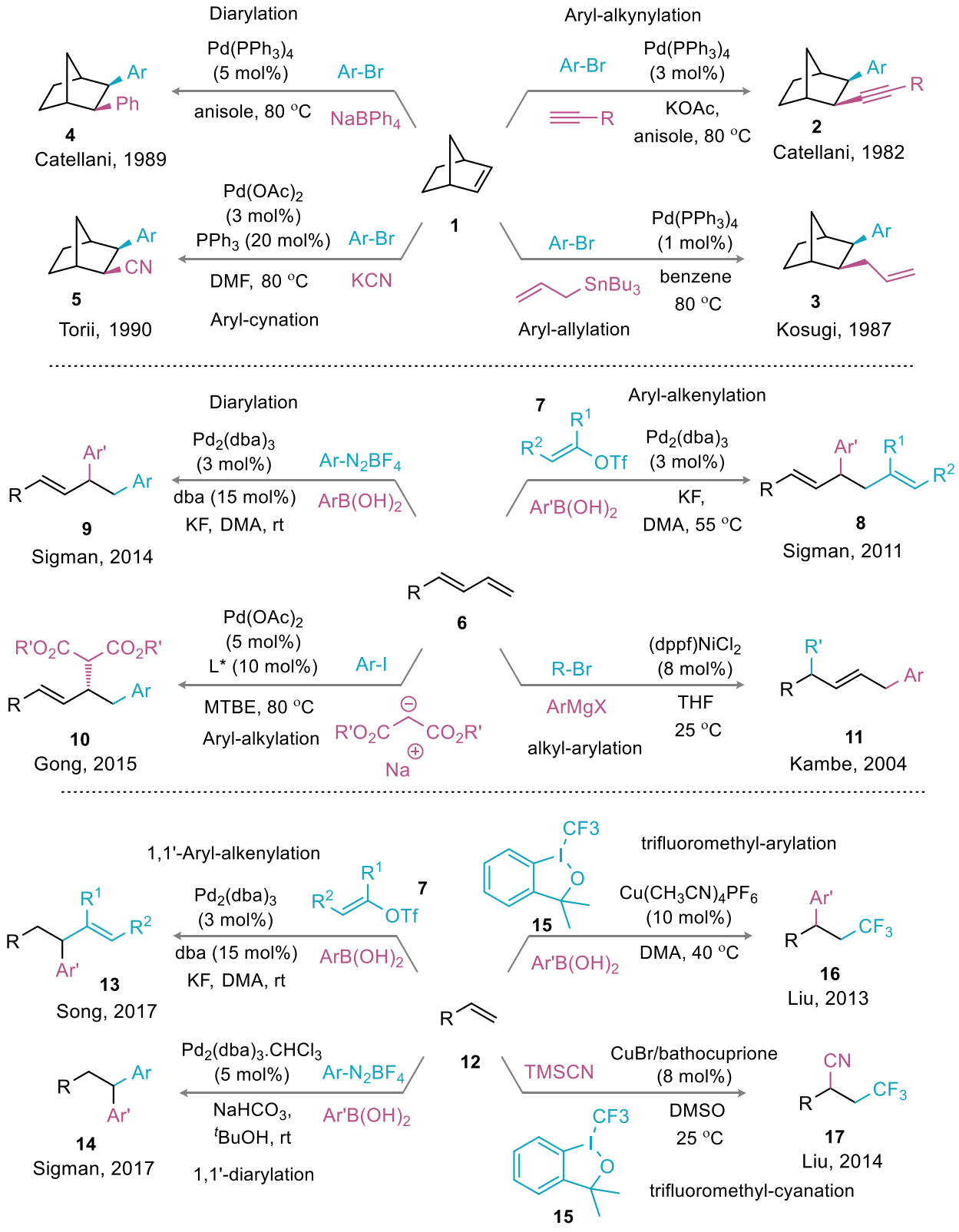
Subsequent ligand exchange or transmetalation of nucleophilic carbon source C(Nu) at C(sp^3)-[M] complex **III** followed by reductive elimination from **IV** constructs the desired difunctionalized product **V**. The formidable challenge is to overcome β-H elimination from the C(sp^3)-[M] intermediate **III** leading to the Heck product **VI**; this path follows a lower energy process than interception by C(Nu) species.

Few examples in the dicarbofunctionalization of olefins are showcased in **Scheme 1B.1**. The use of norbornene **1**, 1,3-diene **6** and styrene **12**, however, overcomes the unformidable β-H elimination of olefins from the C(sp^3)-[M] intermediate.

In 1982, Catellani[23] and co-worker reported aryl-alkynylation of bridged olefins **1**, using aryl bromide and terminal alkynes as coupling partners in presence of $Pd(PPh_3)_4$ catalyst. In a similar manner, allyl-stanous reagent has been used for the aryl-allylation of olefin under Pd-catalysis by Kasugi and coworker in 1987.[24] In 1989, dirylation product **4** from olefin **1** was constructed where aryl-bromides and $NaBPh_4$ were used as two disctinct aryl coupling partners.[25] However, Pd-catalyzed aryl cynation of olefin has been reported by Torii and co-worker in 1990 to make **5**; KCN has been used as cyanating source.[26]

In 2011, Sigman[27] and co-worker showcased 1,2-dicarbofunctionalization of 1,3-diene **6** using cationic Pd-complex generated in-situ from the oxidative addition of vinyl-triflate **7** for the construction of highly densed 1,5-diene **8**. The same group also explored cationic Pd-catalyzed diarylation of **6** using Aryl-diazonium salt and aryl boronic acid as distinct aryl coupling partners. Gong and coworker in 2015 showcased an interesting aryl-alkylation of **6** to give **10** using sodium salt of dialkylmalonate and aryl iodide as alkylating and arylating source, respectively.[28] In 2004, Kambe and co-worker shown 1,4-dicarbofunctionalization of **6** under Ni-catalysis.[29]

By taking the advantage of β-H elimination, sigman an song coworkers disclosed 1,1'-difunctionalization instead of 1,2-difunctionalization **13** and **14** under cationic palladium catalysis.[30-31] Apart from aryl, alkenyl, alkyl, and alkynyl groups functional groups like trifluromethyl (**16**)[32] and cyano (**17**)[33] were also part of the difunctionalization strategies and installed to olefins by Liu and coworkers using togni-II reagent and TMSCN, respectively.



Scheme 1B.1. Few examples of olefin dicarbofunctionalization

1B.2. Alkyne Dicarbofunctionalizations

All carbon tetra-substituted olefins are among the profound skeleton present in leading drugs and biologically important compouds. Transition metal (TM)-catalyzed difunctionalization of alkynes shown great potential towards synthesis of such skeleton in a single step. Shown below is the general scheme involving installation of two distinct carbon functionalities (one electrophile and other one nucleophile) across the symmterical alkyne under transition metal catalyst.

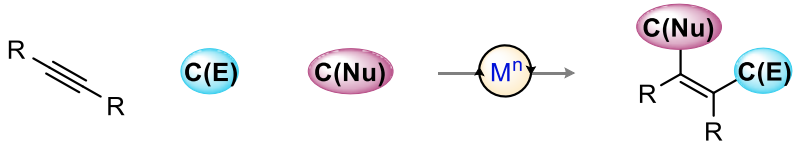


Figure 1B.3. Schematic presentation of dicarbofunctionalization of alkynes

A general mechanistic pathway for the above mentioned dicarbofunctionalization reaction is shown in Figure 1B.4. At first, oxidative addition of electrophillic carbon source C(E) with a low valent transition metal forms C(E)-metal complex **I**. Next, migratory insertion to alkyne **II** gives C(sp^2)-[M] complex **III**. Subsequent ligand exchange or transmetalation of nucleophilic carbon source C(Nu) at C(sp^2)-[M] complex **III** followed by reductive elimination constructs the desired difunctionalized product **IV**. Protodemetalation is the major concern of this difunctionalization process. A trace of water or moisture can readily protodemetalate C(sp^2)-[M] complex **III**; however, fast interception of C(Nu) species could avoid such process.

Whereas it is impossible for the incoming C(E) species to distinguish between the two carbons of unsymmetrical alkyne **IIA**. However, incorporation of directing group (DG) or relatively small group at one of the caron center in the alkyne would make the process regioselective (Figure 1B.4, bottom part).

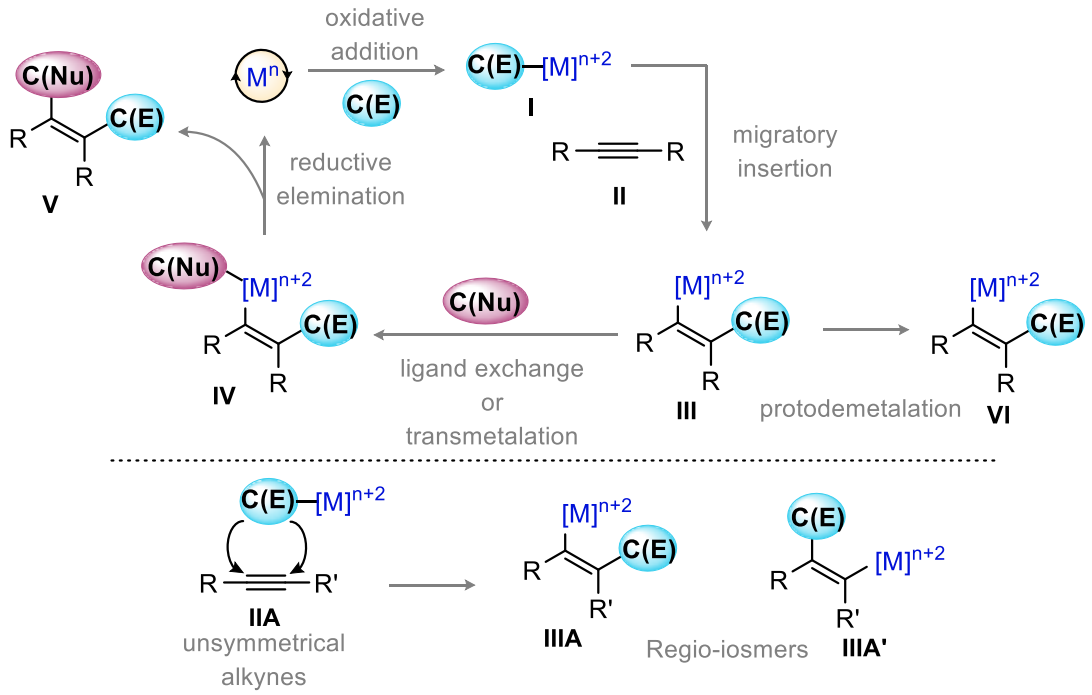
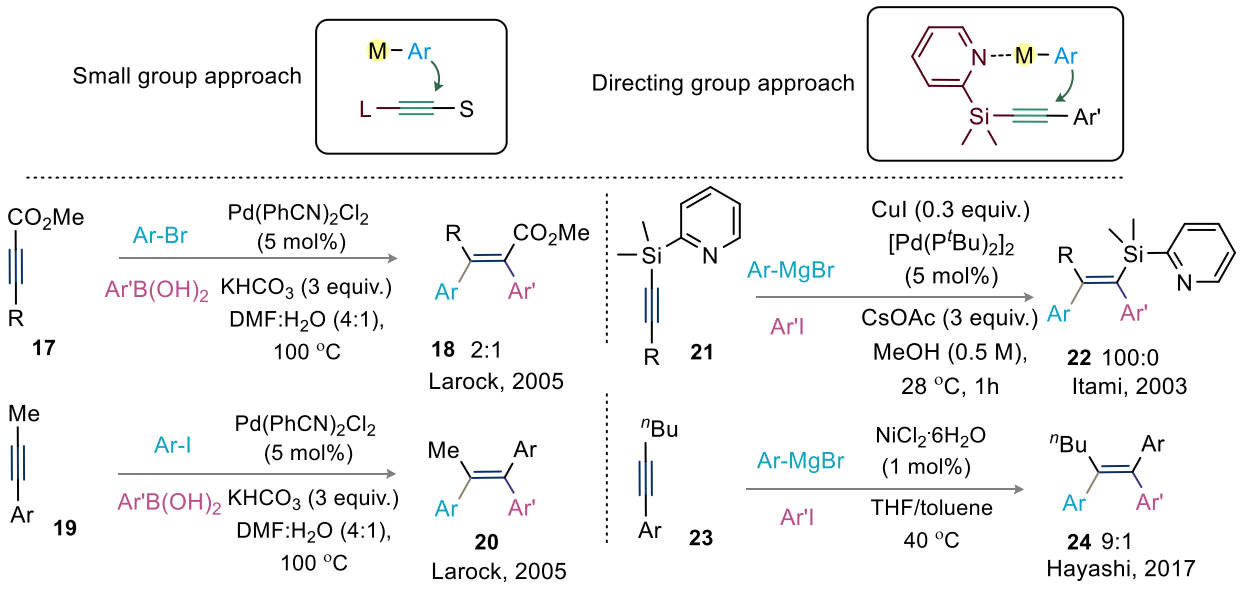


Figure 1B.4. General pathway of dicarbofunctionalization of alkynes

Few examples of dicarbofunctionalization of unsymmetrical alkynes are showcased in **Scheme 1B.2** where regioselectivity is governed by the substituent size or the presence of DG in the alkyne.



Scheme 1B.2. Few examples of alkyne dicarbofunctionalization.

A Pd-catalyzed usymmetrical diarylation of substituted propiolates **17** is described by Larock and co-workers in 2005 to obtain a stereoselective vinyl carboxylate core **18** with moderate regioselectivity (2:1) using aryl-iodide and aryl-boronic acids (**Scheme 1B.2**).[34] Such small group approach of incoming aryl group for the diarylation of simple aryl-methyl/ethyl alkyne **19** has also been shown.[35]

An interesting pyridine directed Pd/Cu-catalyzed regioselective unsymmetrical diarylation of pyridine silyl alkynes **21** for the synthesis of **22** was disclosed by Itami group in 2003. The transformation uses aryl magnesium iodide and aryl iodide.[36]

Under Ni-catalysis in the absence of DG, diarylation of ^{n}Bu substituted alkyne has been successfully performed when reacted with aryl magnesium iodide and aryl iodide; this transformation was emanated from Hayashi group in 2016.[37]

1B.3. Conclusion

This section provides a brief overview of the dicarbofunctionalization of olefins and alkynes catalyzed by transition metals. The strategies that suppress the challenging β-H elimination in the olefin difunctionalization is discussed. Likewise, regioselective difunctionalization process of alkyne is discussed briefly. This thesis aims in the development of novel synthetic methods for the difunctionalization of ynamide and propargyl acetate using Pd-catalyst; the results are discussed in the respective chapters.

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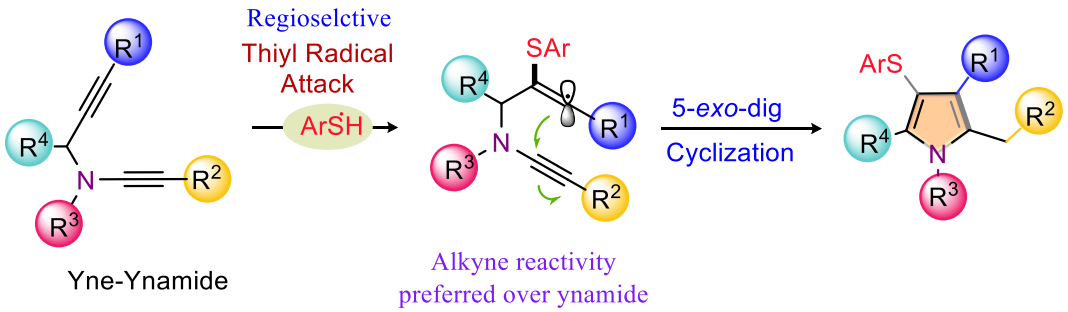
Chapter-2A

Alkyne versus Ynamide Reactivity: Regioselective Radical Cyclization of Yne-Ynamides

Abstract



Ynamides are typically more reactive than simple alkynes and olefins. However, a serendipitous observation revealed a rare case where the reactivity of simple alkynes exceeds that of ynamides. This led to the development of a unique sulfur radical-triggered cyclization of yne-tethered-ynamides, which involves the attack of a thiyl radical to the alkyne and then that of the ynamide. A wide range of novel 4-thioaryl pyrroles that could tolerate common functional moieties and *N*-protecting groups were expediently constructed by this strategy. The current method opposes to the typical cyclization of yne-ynamides, which involves the attack of the ynamide core to the alkyne moiety. Control experiments and DFT calculations supported the participation of the sulfur radical in the reaction and the regioselective cyclization. The synthetic potential of the substituted pyrroles is also discussed.

Publication

S. Dutta, R. K. Mallick, R. Prasad, V. Gandon, and A. K. Sahoo *Angew. Chem. Int. Ed.* ***2019****, 131,* 2311-2316.

2A.1. Introduction

Pyrrole has been largely present in the molecules of natural products and complex N-bearing heterocycles.[1] The combination of pharmacophores with pyrrole ring could enhance phramacokinetic properties of the molecular scaffold. Thus, pyrrole bearing molecules are biologically important. Some of the representative pyrrole bearing marketed drug candidates is shown in **Figure 2A.1**. In addition, pyrrole ring is present in the core motif of molecules showing broad material applications. Pyrrole motifs are successfully used for the construction of porphyrin and poly-pyrroles showing wide application in light emitting diode (LED) and photodynamic therapy (PDT).[1d]

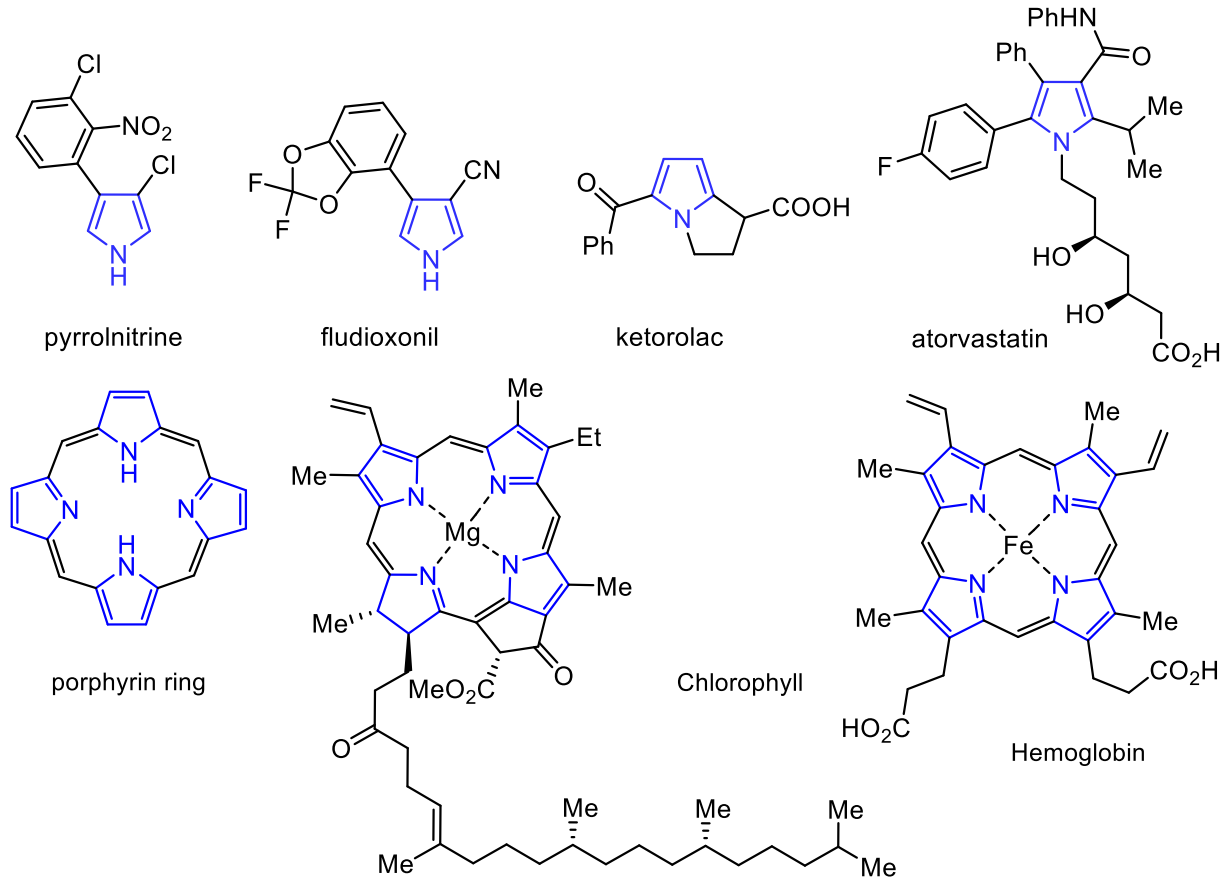


Figure 2A.1. Pyrrole containing pharmaceutically important drugs

Ynamides, a distinct class of *N*-substituted alkynes, have been used for various cyclization/cycloisomerization processes towards the construction of structurally

diverse complex *N*-heterocyclic building blocks.[2] In this context, the transition-metal-catalyzed, *N*-oxide and Brønsted/Lewis acid-triggered cyclizations of yne-tethered-ynamides have shown great potential. Importantly, all these transformations involve nucleophilic attack of the ynamide motif (via oxo-metal carbene/ketene *N*,*O*-acetal) to the alkyne scaffold (**Figure 2A.2**). In contrast, synthetic techniques that are based on reversing the usual reactivity of ynamides over alkynes have been only rarely reported. A worthwhile endeavor is to unravel a radical-mediated cyclization of yne-tethered-ynamides, with the prediction of a preferred radical attack to the alkyne rather than to the inherently polarized ynamide, which, to the best of our knowledged is studied for the firt time.

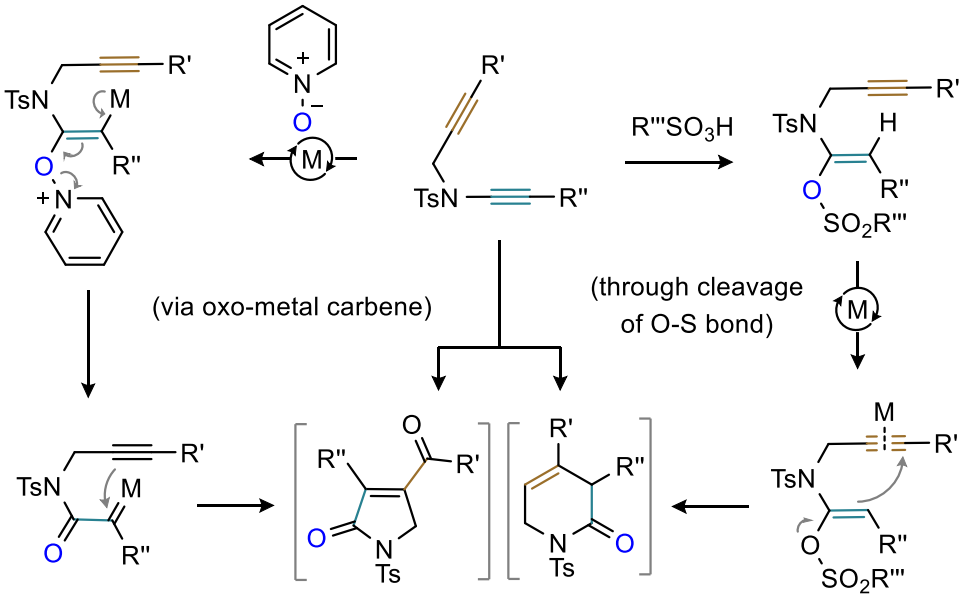


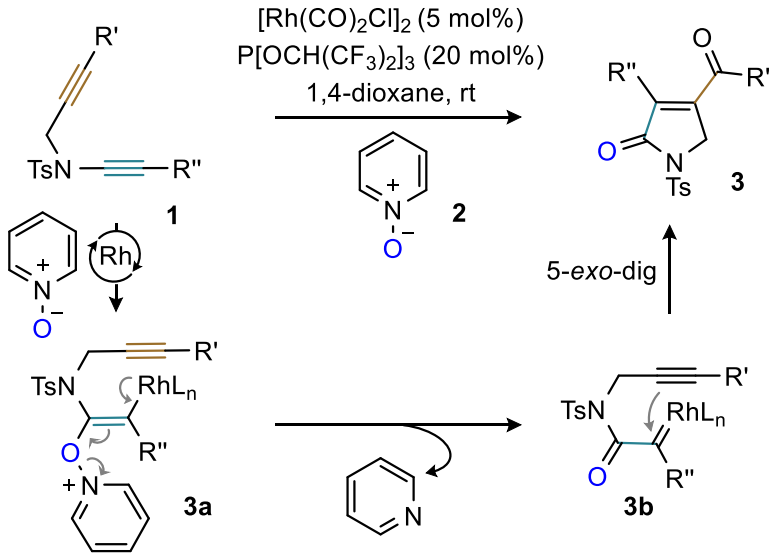
Figure 2A.2. Transition-metal catalyzed cyclization of yneynamides

2A.2. Precedents

The transition-metal catalyzed cyclization and cycloisomerization of yne-tethered ynamides has led to the construction of biologically important N-heterocyclic motifs. Few representative examples of nucleophilic cyclization of yne-ynamides, where ynamide reactivity is preferred over alkyne, are discussed. In many cases mechanistic insights is also shown.

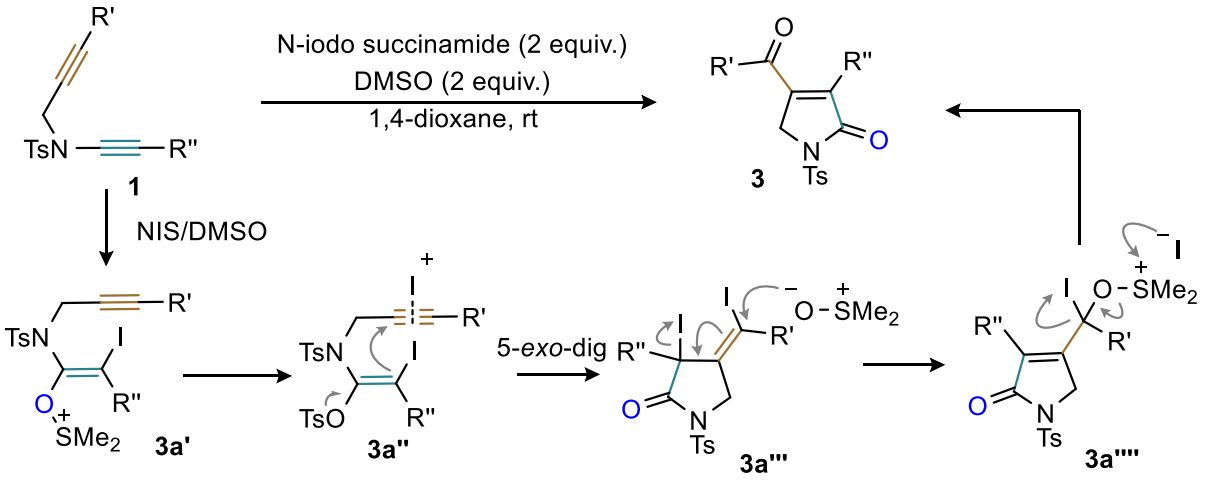
2A.2.1. Nucleophillic Cylization of Yne-Ynamides

In 2013, Tang and coworkers have developed a Rh-catalyzed oxidative cycloisomerization of ynamides **1** to yield pyrrolidones **3**. The transformation initiates with the Rh*carbene intermediate **3b** formation via int-**3a**. Next, metal carbene metathesis with the tethered alkyne and oxidation produces 2-oxopyrrolidines **3** (**Scheme 2A.1**).[3]



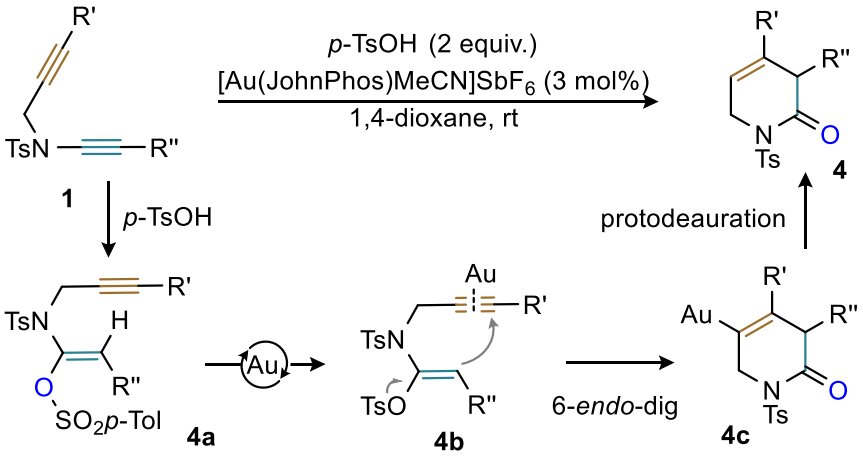
Scheme 2A.1. Rhodium catalyzed oxidative cycloisomerization of yne-ynamide

A metal-free DMSO- and NIS-assisted regioselective 5-*exo*-dig oxidative cyclization of yne-tethered ynamides **1** to functionalized pyrrolidone derivatives **3** was reported by our group in 2016 (**Scheme 2A.2**).[4] The attack of DMSO to the transient ketiniminium species generated via the reaction of ynamide **1** with NIS at first forms ketene N,O-acetal **3a′**. Next, 5-*exo*-dig mode cyclization of acetal to the NIS-activated tethered alkyne makes **3a‴**. Expulsion of allylic iodo group by the DMSO attack to the exocylic double bond of **3a‴** affords **3a⁗**. Finally, iodide triggered displacement of the S and O bond of int-**3a⁗** produces **3**.



Scheme 2A.2. DMSO/NIS-promoted oxidative cyclization of yne-ynamides

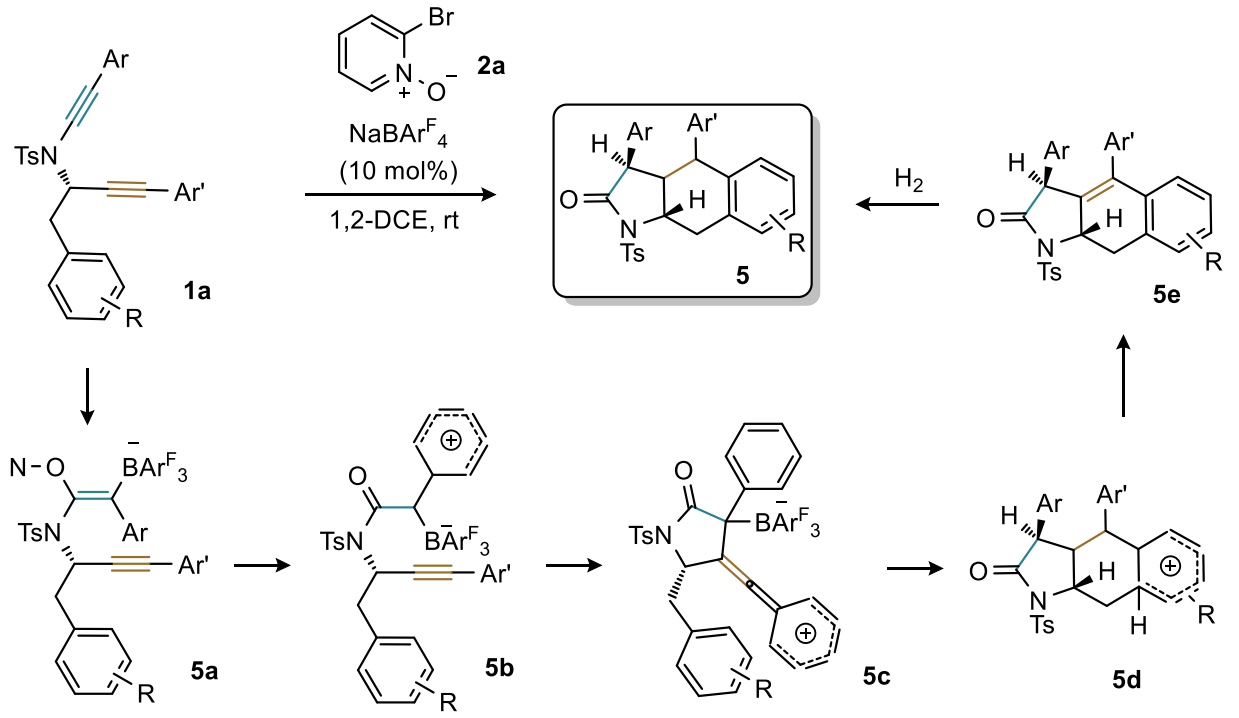
Sahoo goup reported a *p*-TsOH-induced 6-*endo*-dig cyclization of alkyne-linked ynamide **1** to result 1,6-dihydropyridin-2(3H)one **4** (S**cheme 2A.3**).[5] The reaction begins with the formation of highly reactive ketene *N,O*-acetal (a 1,5-ene-yne surrogate) intermediate **4a** by nucleophilic attack of *p*-TsOH on the ynamide **1**. The oxidative intramolecular cyclization of ketene-acetal with the Au-activated yne-motif produces **4b** from **4a**. Finally, protodeauration of **4c** makes **4**.



Scheme 2A.3. *p*-TsOH-promoted Au-catalyzed hydrative cyclization of yne-ynamide

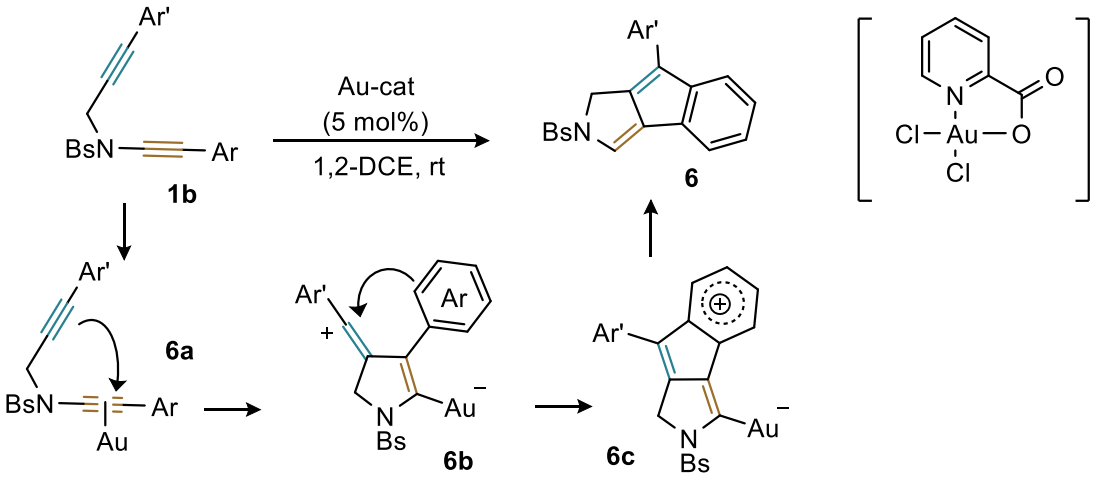
In 2018, a transition-metal-free $NaBAr^{F}_{4}$ promoted oxidative cyclization of *N*-propargyl ynamides was reported by Ye and co-worker for the stereospecific construction of linear

polycyclic N-heterocycles (**Scheme 2A.4**).[6] Initially, the vinyl borate intermediate **5a** was formed by the nucleophilic attack of *N*-oxide **2a** to ynamide **1a** in presence of $NaBAr^F_4$. The N–O bond cleavage of **5a** makes the phenyl-stabilized carbocation **5b**. Next, intramolecular cyclization of **5b** gives the enylium-cationic intermediate **5c**. Intramolecular cyclization of **5c** produces intermediate **5d**. Finally, deprotonation, aromatization, and protonation of **5d** makes **5e**. Further hydrogenation of **5e** affords thermodynamically favoured **5**.



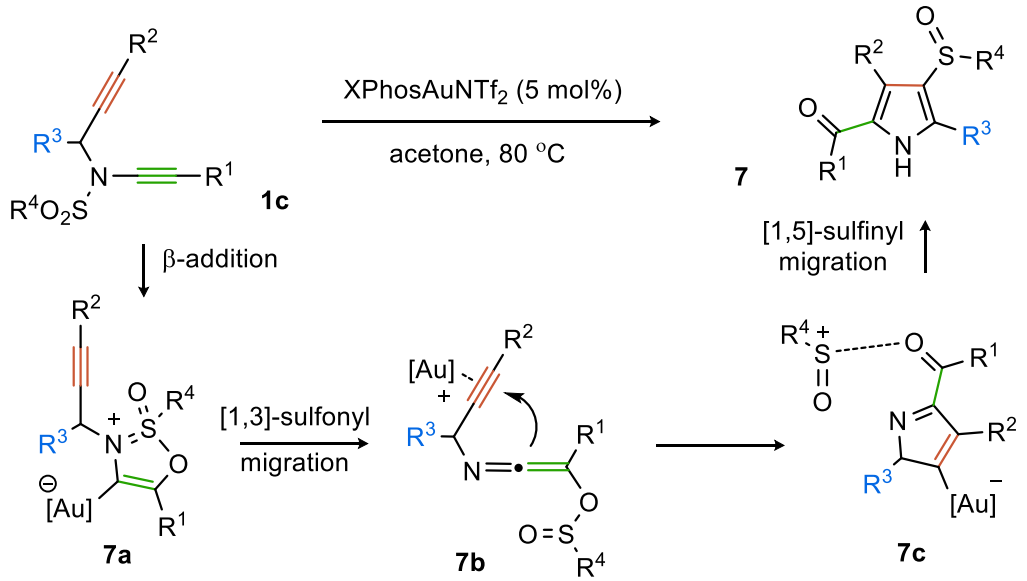
Scheme 2A.4. Metal-free oxidative cycloisomerization of yne-ynamides

A ring strain driven cascade cyclization of *N*-propargyl ynamides **1b** has led to the construction of indeno [1,2-c pyrroles] **6**; the work was emanated from Ye group (**Scheme 2A.5**).[7] The attack of alkyne moiety to the Au-activated ynamide triple bond at first results in the formation of vinyl cation intermediate **6b**. The transformation involves the attack of alkyne to the ynamide β-carbon. Next, intramolecular electrophilic cyclization of the aryl moiety to the vinyl cation generates **6c**. Finally, protodeauration of **6c** and subsequent tautomerisation affords **6**.



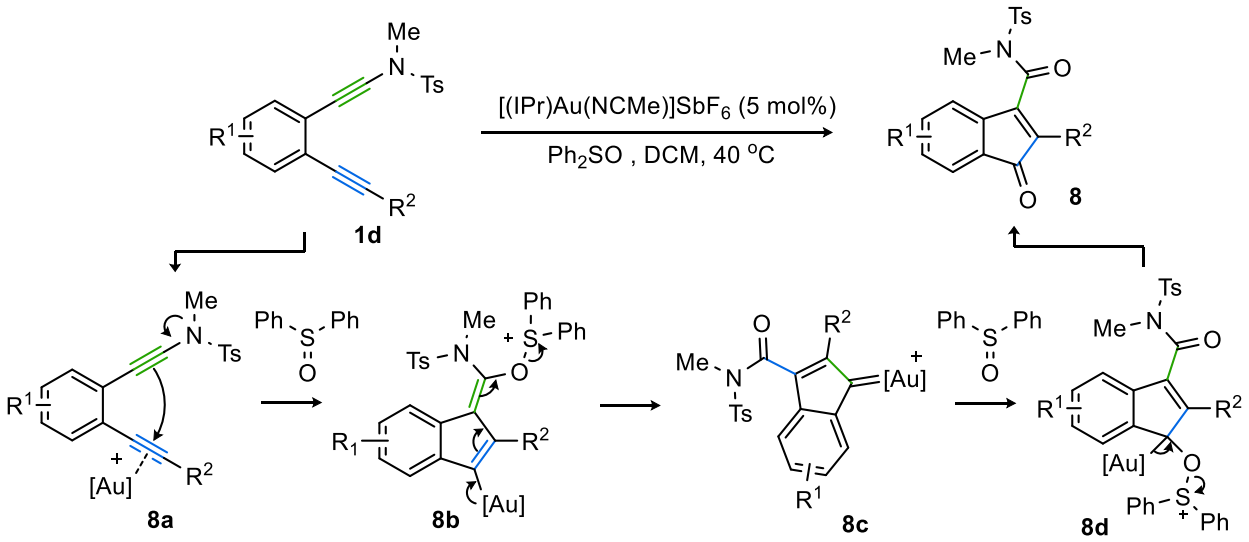
Scheme 2A.5. Gold-catalyzed cascade cyclization of N-propargyl ynamides

In the presence of XPhosAu-catalyst, our group developed an unconventional umpolung approach towards the synthesis of multi-substituted pyyrole. The process involves a regioselective sulfonyl/sulfinyl migration cycloisomerization of yne-ynamide **1c** (**Scheme 2A.6**).[8] The formation of **7b** via **7a** represents the first example of a general migration of [1,3]-sulfonyl from nitrogen center to the ynamide β-carbon. Next, an umpolung 5-*endo*-dig cyclization of ynamide α-carbon to the Au-activated alkyne intermediate **7b** furnishes **7c**. Finally, deaurative [1,5]-sulfinylation of **7c** gives **7**.



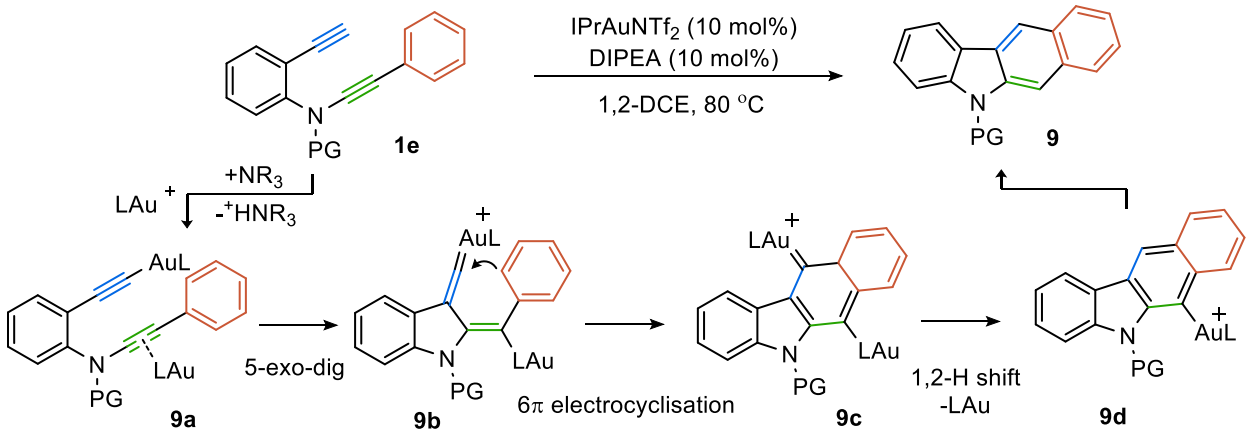
Scheme 2A.6. Gold catalyzed [1,3]-sulfonyl and [1,5]-sulfinyl migration cascade

Hashmi and coworkers reported a cationic Au catalyzed cyclization of amide-substituted diynes **1d** in presence of external nucleophile to result 1-indenones **8** (**Scheme 2A.7**).[9] The keteniminium driven intramolecular 5-*endo*-dig cyclization by the attack of ynamide β-carbon to the Au-π-activated alkyne followed by the attack of diphenyl sulfoxide oxygen to α-carbon of int-**8a** at first forms a cyclized-*N,O*-acetal **8b**. Subsequent release of diphenyl sulfide from 8b produces the gold-carbene intermediate **8c**. Next, addition and elimination of DMSO to the carbene center of **8c** produces the desired indenone product **8**.



Scheme 2A.7. Cationic Au-catalyzed nucleophile promoted cyclization of ynamides

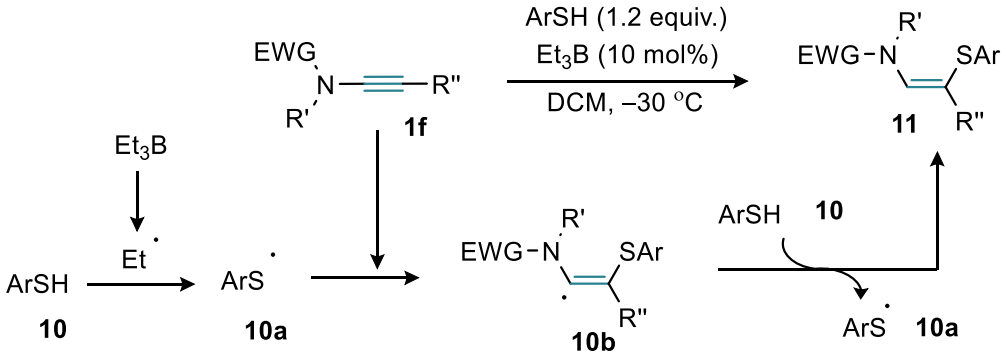
Zi group demonstrated a dual gold catalyzed tetradehydro-Diels-Alder reaction of yne-tethered ynamides for the construction of π-extended indole skeleton (**Scheme 2A.8**).[10] Based on known reports and deuterium labelling experiment, the coordination of cationic Au-species to the alkyne moiety of **1e** at first forms a π,σ-digold complex **9a**. Next, 5-*exo*-dig cyclization of **9a** forms gold vinylidene intermediate **9b**, which immediately undergoes a rapid 6π-electrocyclization to give Au-intermediate **9c.** Next, 1,2-hydrogen shift of **9c** yields aryl gold intermediate **9d**. Finally, protodeauration of **9d** affords p-extended indole-fused heterocycles **9**.



Scheme 2A.8. Cycloisomerization of yne-ynamide via dual Au-catalysis.

2A.2.2. Radical β-Addition to Ynamide

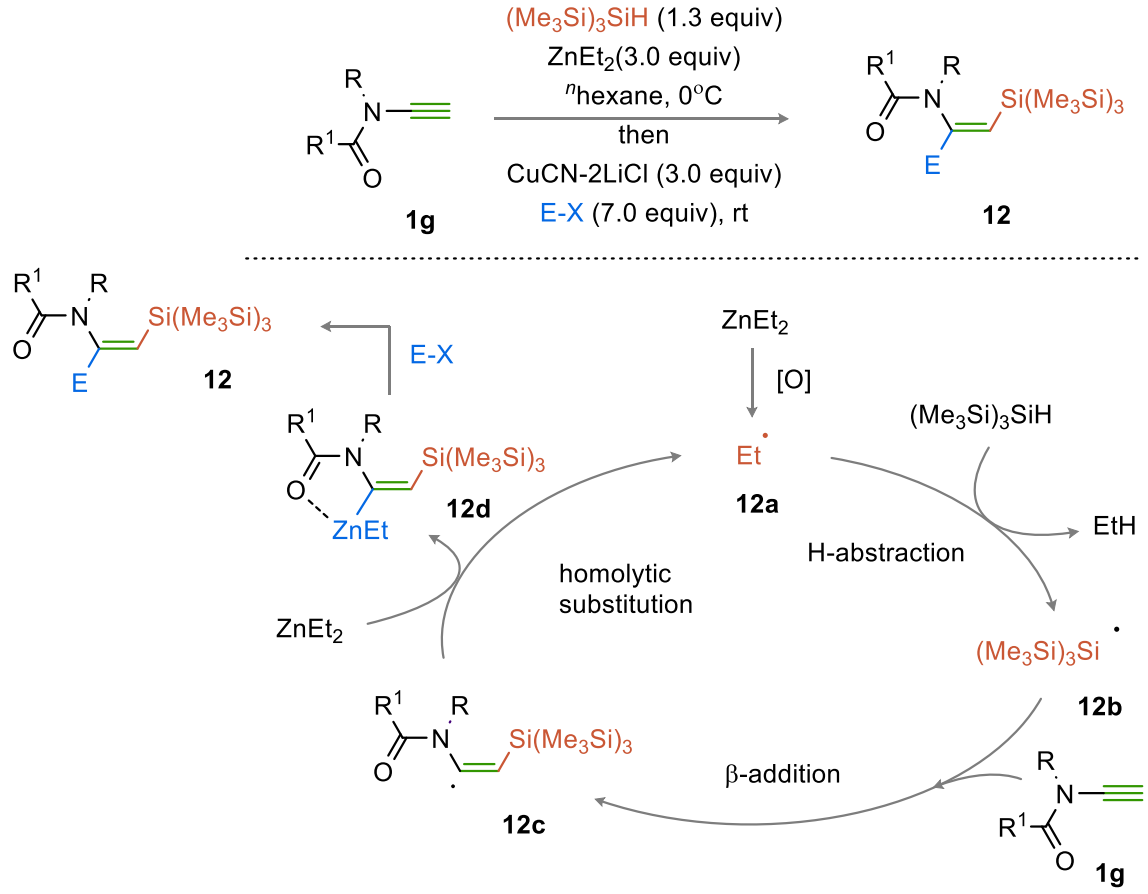
The Oshima, Yorimitsu and co-workers showcased an elegant method for the triethylborane catalyzed regio- and stereoselective thiyl radical addition to ynamides (**Scheme 2A.9**).[11] Triethylborane with molecular oxygen at first releases ethyl radical. Next, reaction of ethyl radical to arenethiols **10** gives thiyl radical **10a**. Next, thiyl radical attack to the β-position of ynamide **1f** gives the Z-vinyl radicals **10b**. Finally, quench of **10b** with H-abstraction of arenethiols generates **11** with the formation of thiyl radical for the next cycle.



Scheme 2A.9. β-Addition of thiol radical to ynamide.

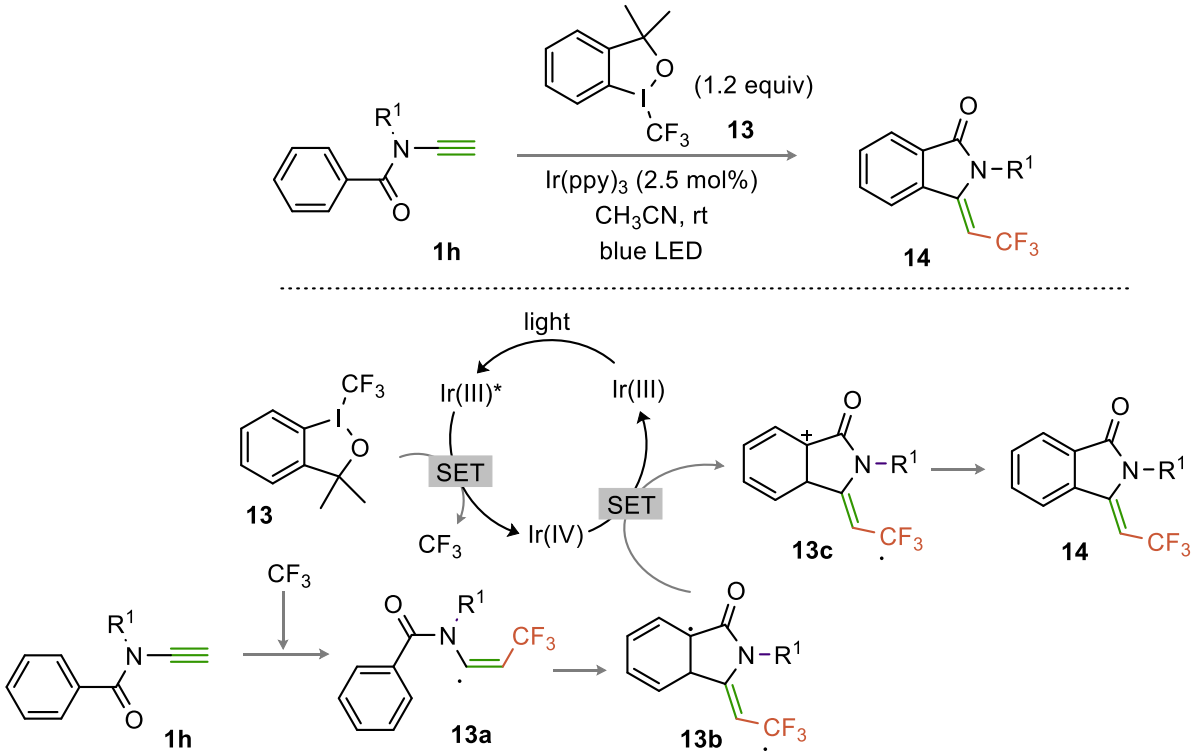
The Luna and co-workers in 2014 have shown a *trans*-silyl-zincation of ynamide **1g** (**Scheme 2A.10**).[12] The ethyl radical **12a**, generated in-situ from $ZnEt_2$ under oxidative condition, mediated abstraction of H-radical from silane at first provides silyl radical **12b**.

Next, regioselective attack of silyl radical to ynamide β-position of ynamide **1g** delivers vinylic radical **12c**. The homolytic substitution of **12c** with $ZnEt_2$ generates vinyl-zinc species **12d**. Finally, trap of electrophiles with **12d** makes β-silylated trisubstituted enamides **12**.



Scheme 2A.10. Silyl-zincation of ynamide.

In 2019, Fensterbank and Olivier elegantly showcased a photocatalytic trifluoromethyl radical triggered radical cyclization of ynamides (**Scheme 2A.11**).[13] Under visible light irradiation, ynamides **1h** in presence of $Ir(ppy)_3$ photocatalyst and trifluoromethyl source Togni-I reagent **13** led to diverse isoindolinones **14**. Under the influence of photocatalyst, Togni-I reagent produces trifluoromethyl (CF_3) radical at first. Next, CF_3 radical attack to ynamide **1h** forms vinylic radicals **13a**, which subsequently undergoes an intramolecular radical addition/oxidation/aromatization sequence to result isoindolinone **14**.



Scheme 2A.11. Ir-catalyzed photo-induced trifluoromethylative cyclization of ynamide.

2A.3. Motivation and Scheme Design

Encouraged by the nucleophillic cyclization and cycloisomerization reactions of yne-ynamides and radical addition reactions of simple ynamides, envisaging a cyclization from ynamide → alkyne to alkyne → ynamide using radical pathway is undoubtedly a worthwhile endeavor. However, a radical-mediated cyclization of yne-ynamides, with the prediction of a preferred radical attack to the alkyne over the inherently polarized ynamide remains challanging. This process could make a large arrays of products due probably to the radical attack is not chemo and regioselective. The possible radical attacks to both ynamide & alkyne as well as respective possible cyclization (for example 5-*exo*/*endo* & 6-*exo*/*endo*) processes are shown in Figure 2A.3 (path I, II, III & IV). As a result, the radical-triggered cyclization of the yne-ynamide would result in the formation of 4-, 6- or 5-membered *N*-heterocycles.

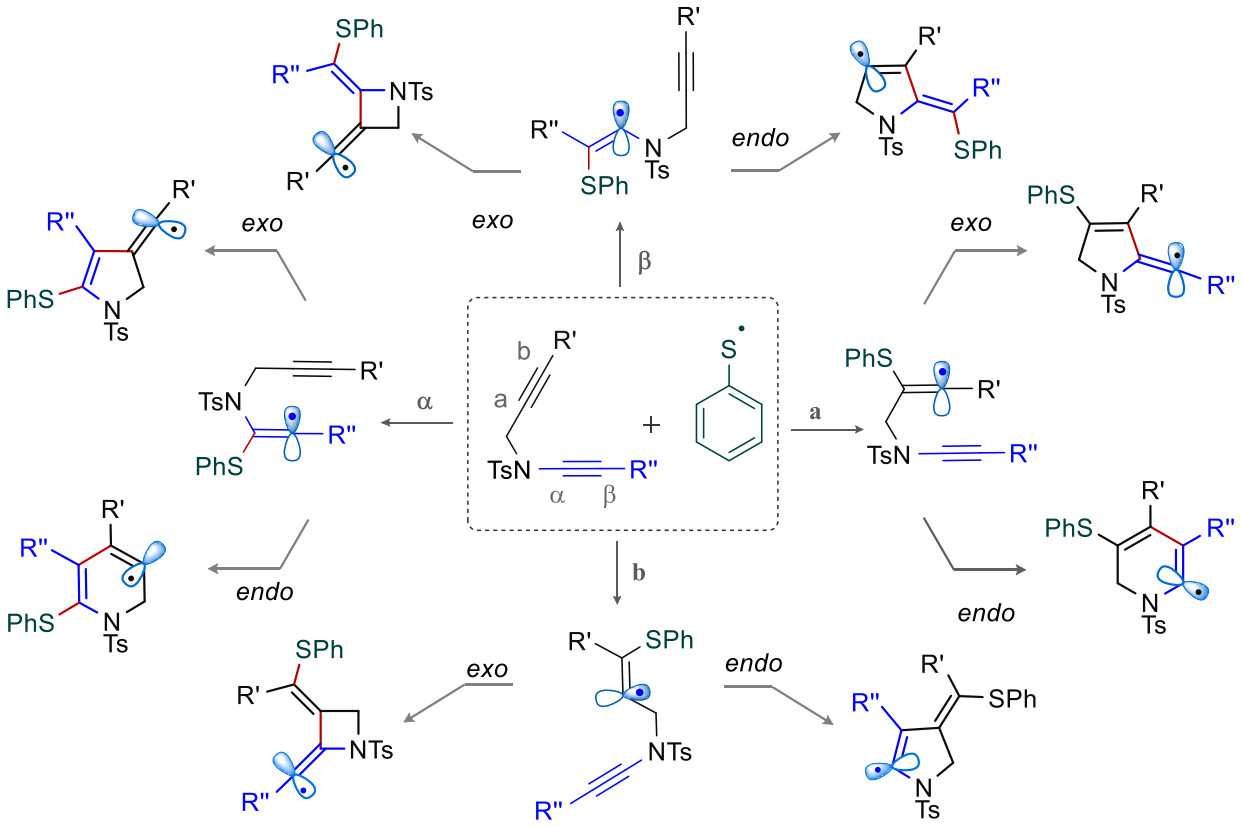


Figure 2A.3. Possible radical attacks and cyclizations

A highly chemoselective as well as regioselective thiyl-radical attack to an alkyne motif, followed by regioselective 5-*exo*-dig intramolecular attack to the ynamide moiety of yne-tethered-ynamides is herein enumerated. This reaction yields novel highly substituted 4-thioaryl-pyrroles (**Figure 2A.4**).

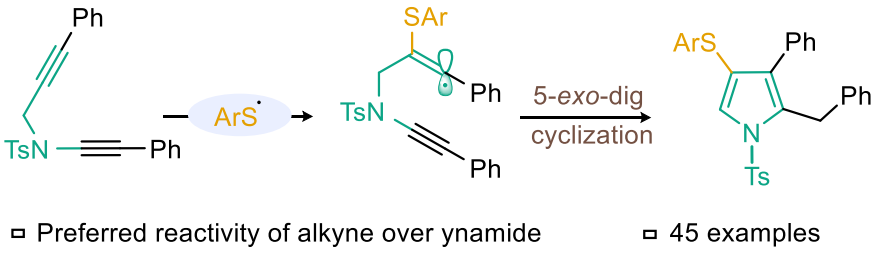


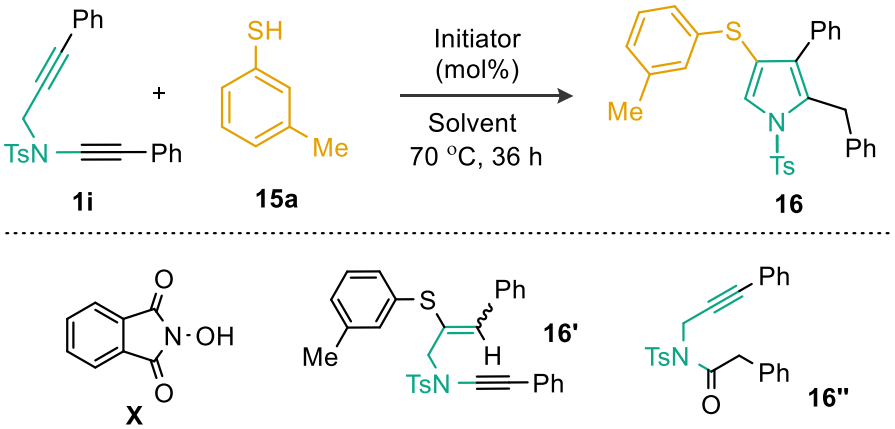
Figure 2A.4. Possible radical attacks and cyclizations

2A.4. Result and Discussion

2A.4.1. Reaction Optimization

The study started by examining the reaction of yne-tethered ynamide **1i** with 3-methylbenzenethiol (**15a**) and a radical initiator. The results are detailed in Table 2A.1. When the reaction was performed in the presence of AIBN (1.5 equiv) in CH_3CN for 24 h at 70 °C, the desired product **16** was isolated in 40% yield along with the alkyne hydrothiolation compound **16'** (15%), and the ynamide hydration product **16''** (30%) (entry 1). This result encouraged us to screen other radical initiators. The oxidant $K_2S_2O_8$ (1.0 equiv) or *N*-hydroxyphthalimide (20 mol %) proved more efficient, affording **16** in 48% and 61% yield, respectively, yet along with substantial amount of **16'** (entries 2 and 3). In air and in the absence of initiator, **16** (30%) was also produced (entry 4). However, the reaction in DMF selectively provided **16'** (entry 5), justifying the attack of the thiyl-radical to the propargyl alkyne moiety over the ynamide motif (DFT studies corroborate this observation, vide infra). The yield of **16** (78%) was enhanced when the reaction was conducted in dichloromethane (DCM) (entry 6). On the other hand, the reaction at 50 °C was less efficient (entry 7). The use of 1,2-dichloroethane (DCE), acetone, or toluene as solvent, or even neat conditions, also resulted in lower yields of **16** (entries 8–11). Only a

Table 2A.1. Optimization of reaction conditions[a,b]



Entry	Initiator	(mol%)	Solvent	Yield (**16'/16"/16**) %
1	AIBN	150	CH_3CN	(15/30/40)
2	$K_2S_2O_8$	100	CH_3CN	(41/––/48)
3	X	20	CH_3CN	(31/––/61)
4	Air	--	CH_3CN	(––/40/30)
5	X	20	DMF	(75/––/10)
6	**X**	**20**	**CH_2Cl_2**	**(––/10/78)**
7	X	20	CH_2Cl_2, 50 °C	(––/10/40)
8	X	20	$ClCH_2CH_2Cl$	(––/25/63)
9	X	20	acetone	(40/––/50)
10	X	20	toluene	(––/25/40)
11	X	20	neat	(––/25/64)
12	--	--	CH_2Cl_2	(––/––/trace)
13[b]	X	20	CH_2Cl_2	(05/––/00)

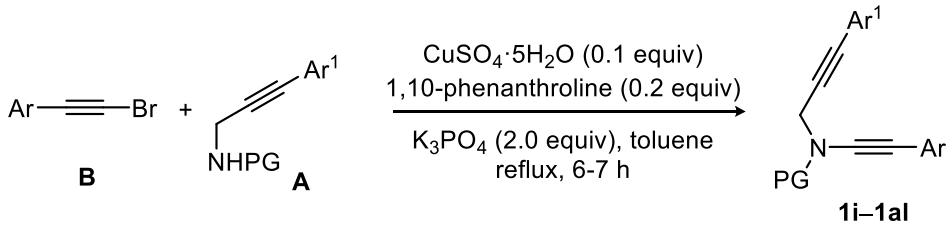
Optimization of the Reaction Conditions[a]. [a]Isolated yield. **1i** (0.2 mmol), **15a** (0.5 mmol),). [b]N_2 atmosphere.

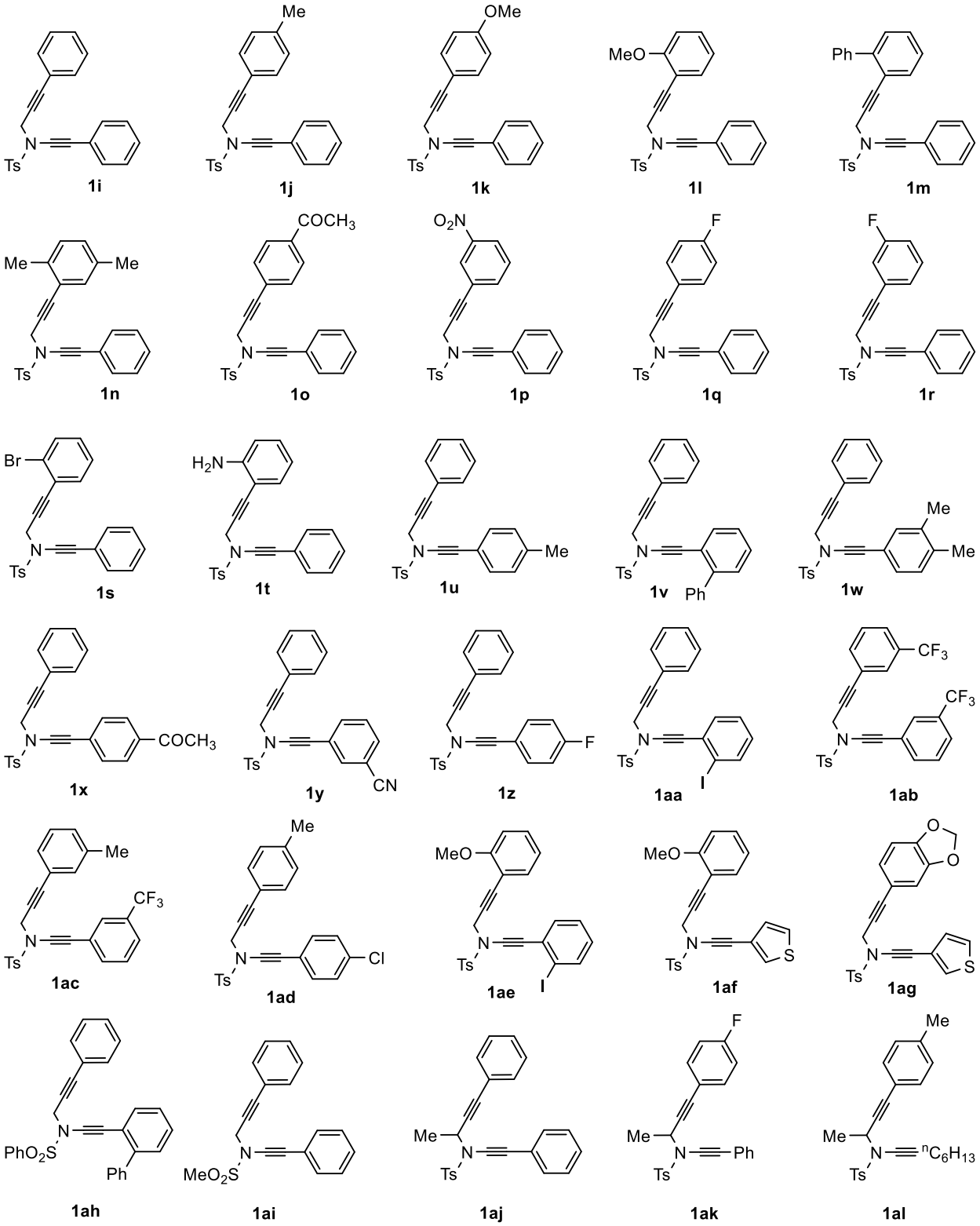
trace of **16** was detected when the reaction was performed under inert atmosphere (entry 12). Use of phenyl disulfide radical source also did not provide the desired product (entry 13).

2A.4.2. Synthesis of Ynamides

Following the known Cu-catalyzed C-N coupling procdure, ynamides **1i-1al** were synthesized from corresponding sulfonamides (A) and bromoalkynes (B) (Table 2A.2).

Table 2A.2. Ynamide chart




1i
1j
1k
1l
1m
1n
1o
1p
1q
1r
1s
1t
1u
1v
1w
1x
1y
1z
1aa
1ab
1ac
1ad
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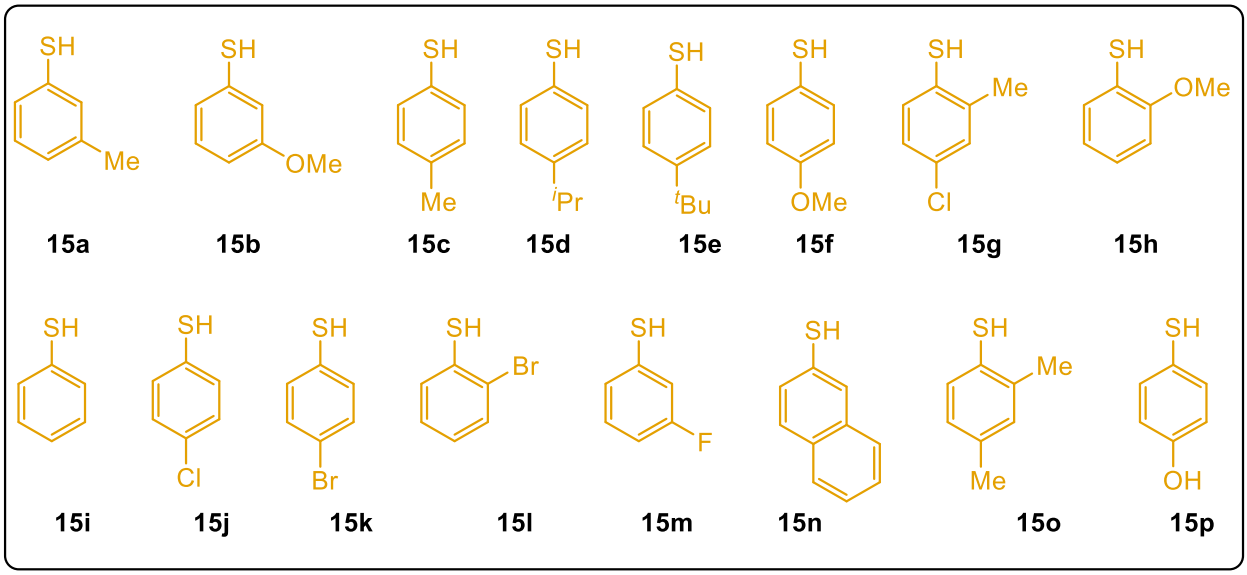
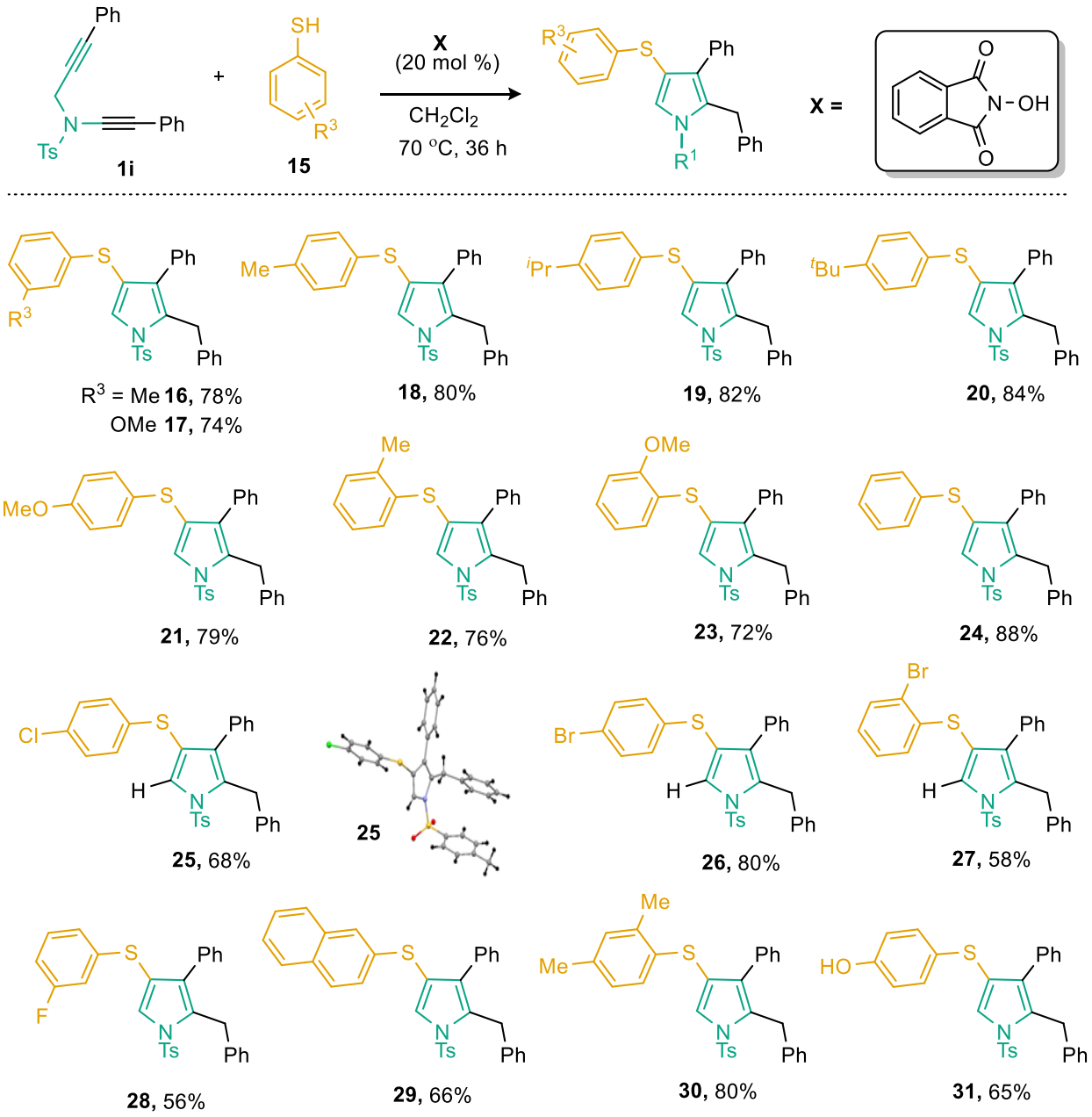
1af
1ag
1ah
1ai
1aj
1ak
1al

Table 2A.3. Aryl thiol Chart

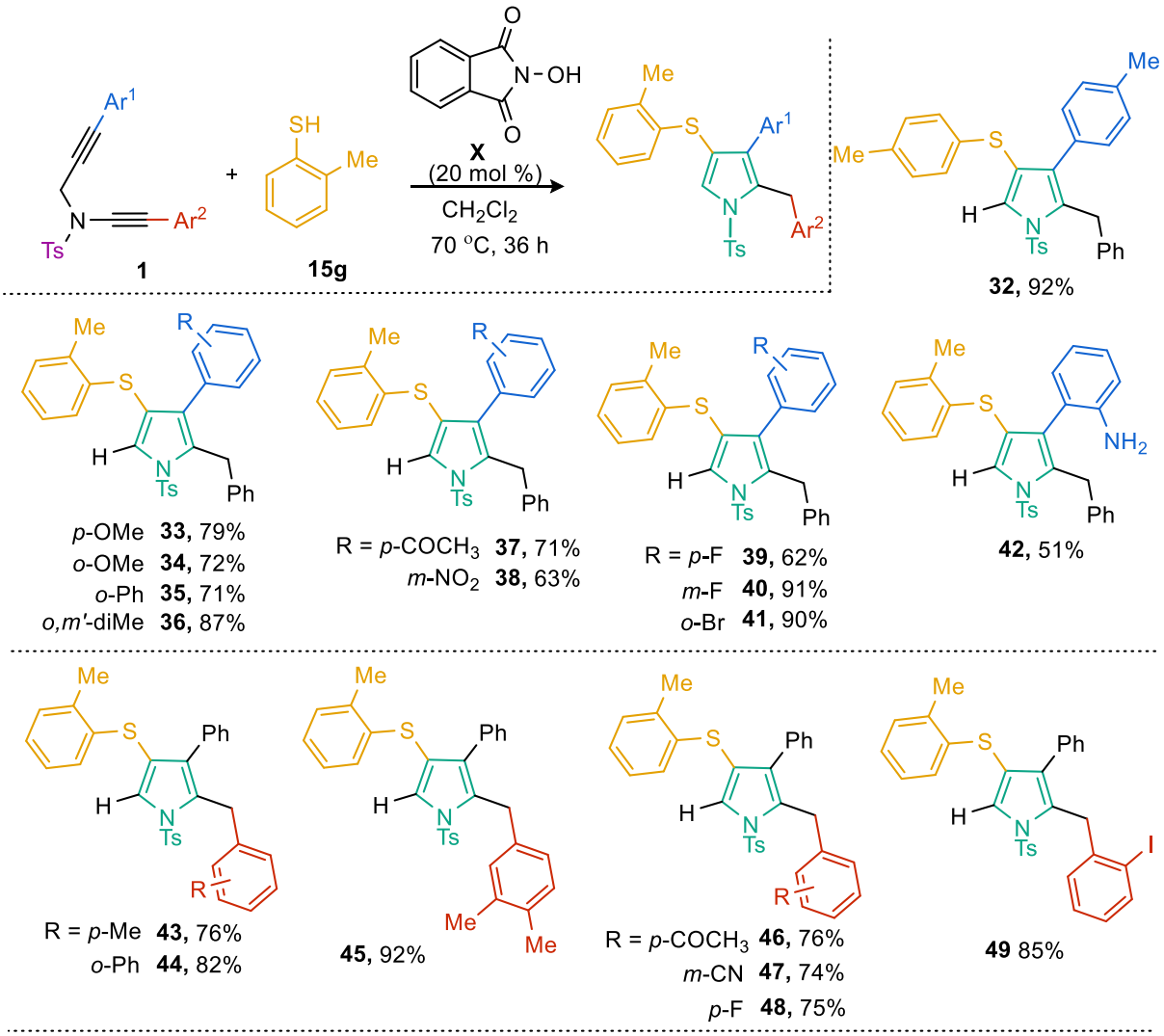


2A.4.3. Substrate Scope

To probe the synthetic generality, reactions between various yne-ynamides (displaying substituents at the alkyne/ynamide terminus and *N*-PG) and thiol derivatives were carried out under the established conditions of Table 2A.1, entry 6. To start with, the aryl thiol derivatives **15a**–**h** [having *m*-Me (**15a**), *m*-OMe (**15b**), *p*-Me (**15c**), *p*-^{i}Pr (**15d**), *p*-^{t}Bu (**15e**), *p*-OMe (**15f**), *o*-Me (**15g**) and *o*-OMe (**15h**) substituents] were reacted with **1a**. The respective 2-benzyl-4-(thioaryl)-3-phenyl-1-tosyl-1*H*-pyrrole **16**–**23** were successfully produced in 72–84% yield (**Scheme 2A.12**). Thiophenol (**15i**) reacted well with **1i** to afford **24** (88%). The halogenated aryl thiols [**15j** (*p*-Cl), **15k** (*p*-Br), **15l** (*o*-Br), **15m** (*m*-F)] did not affect the radical-triggered cyclization, as shown by the efficient formation of **25** (68%), **26** (80%), **27** (58%), and **28** (56%), respectively. Pyrroles **29** (66%) and **30** (80%) were obtained from the reaction of **1i** with sterically hindered β-naphthylthiol (**15n**) and 2,5-dimethyl thiophenol (**15o**). The unprotected OH group containing thiophenol (**15p**) reacted well to provide the desired product **31** (65%). On the other hand, the aliphatic ethanethiol did not react, presumably due to the poor stability of the alkyl thiyl radical.



Scheme 2A.12. Scope of thiophenols [a]Reactions were carried out using **1i** (0.3 mmol), **16** (0.75 mmol) in DCM.



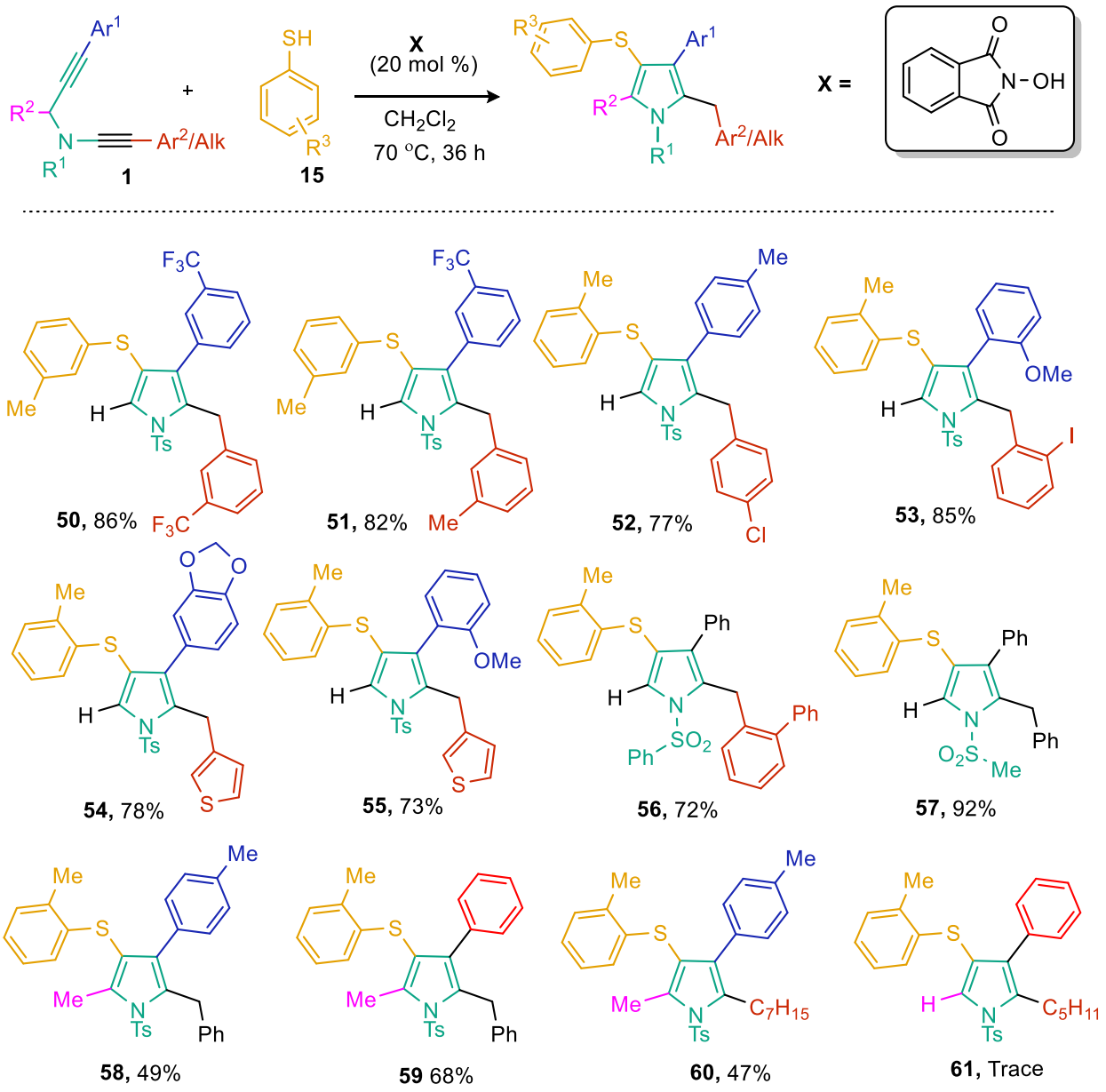
Scheme 2A.13: Scope of yne-ynamides. [a]Reactions were carried out using **1** (0.3 mmol), **15g** (0.9 mmol) in DCM (0.15M).

The thiyl radical-triggered cyclization of yne-ynamides having substitution at the alkyne terminus was next probed (**Scheme 2A.13**). Thus, the cyclization of **1j** [having *p*-Me-aryl motif at the propargyl terminus] with **15b** under the optimized conditions led to **32** (92%) in excellent yield. Likewise, reaction of yne-ynamides possessing electron-rich aryl motifs at the propargyl terminus [*p*-OMe (**1k**), *o*-OMe (**1l**), *o*-Ph (**1m**), and *o*,*m*-*di*Me (**1n**)] with 2-methyl thiophenol (**15g**) delivered **33** (79%), **34** (72%), **35** (71%), and **36** (87%), respectively. The desired pyrrole derivatives **37**–**40** (62–91%) were readily isolated from

the cyclization of **15g** with yne-ynamides having electron-withdrawing aryl groups at the propargyl terminus [*p*-COMe (**1o**), *m*-NO_2 (**1p**), *p*-F (**1q**), and *m*-F (**1r**)]. Besides, yne-ynamides having 2-Br/unprotected 2-NH_2 bearing aryls (**1s**/**1t**) reacted well with **15g**, providing **41** (90%) and **42** (51%), respectively. Thus, electronic and steric effects of the aryl moiety at the propargyl terminus of the yne-ynamides did not affect the reaction outcome. Moreover, electron-withdrawing (possibly radical inhibitors) halo/ester/nitro, and (possibly catalyst inhibitors) amino/hydroxyl groups never obstructed the reaction progress and productivity. Ynamides having alkyl moieties at the alkyne terminus resulted in complex mixtures; presumably due to the less stability of the vinyl radical generated in situ upon attack of thiyl radical to the alkyne.

Owing to the inherent *N*-lone pair polarization of the ynamide, the electron distribution could possibly affect the reaction outcome. To examine this, yne-ynamides having substituents with various steric and electronic properties at the ynamide terminus in the radical-triggered cyclization was used (**Scheme 2A.13**). Thus, electron-rich [*p*-Me (**1u**), *o*-Ph (**1v**), and *m*,*p*-*di*Me (**1w**)], electron-poor [*p*-COMe (**1x**), *m*-CN (**1y**)], and halo-containing [*p*-F (**1z**), *o*-I (**1aa**)] aryl moieties at the ynamide termini underwent cyclizations with **15g** to yield the corresponding 4-thioaryl substituted pyrroles [**43**–**49** (74–92%)]. Once again, the reaction proved successful irrespective of the electronic/steric effects of the functional groups at the periphery of the ynamide scaffold. Despite repeated attempts, the reaction of yne-ynamides having alkyl substituents at the ynamide terminus with **15g** failed to deliver the desired product. Only the hydrothiolation product was observed in such case. We hypothesized that the alkyl moiety inhibited the cyclization of the putative vinyl radical generated in situ upon the addition of the thiyl radical to the alkyne.

Next, the reaction of yne-ynamides (**1ab**–**ac**) with diverse substitutions (arenes bearing electron-withdrawing/electron-donating groups) at both the propargyl and ynamide terminus with **15a**/**15g** in the presence of *N*-hydroxyphthalimide successfully dispensed**50** (86%), **51** (82%), **52** (77%), and **53** (85%) (**Scheme 2A.14**). Similarly, thienyl substituted pyrrole derivatives **54** (78%) and **55** (73%) were synthesized. Yne-ynamides



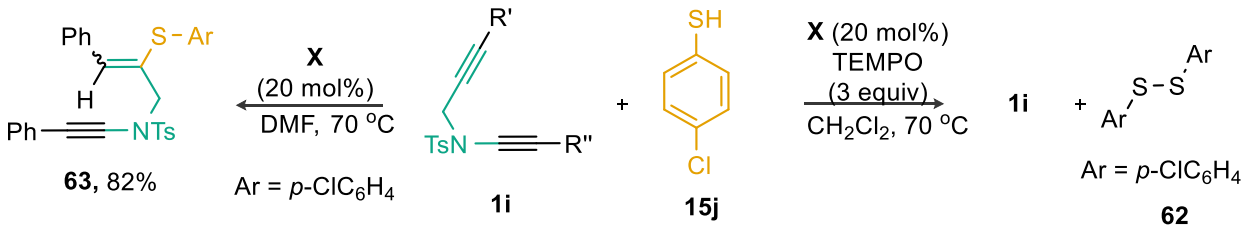
Scheme 2A.14: Scope of yne-ynamides. [a]Reactions were carried out using **1** (0.3 mmol), **15g** (0.9 mmol) in DCM.

1ad and **1ae** with different *N*-protecting groups [*N*-SO_2Ph / *N*-Ms (mesyl)] took part in this thiyl radical-mediated cyclization and delivered the corresponding *N*-SO_2Ph (**56**), *N*-Ms (**57**) derived pyrroles in appreciable yields. Finally, the utility of this thiyl radical-triggered cyclization of yne-ynamides was demonstrated in the synthesis of tetra-substituted pyrrole derivatives. This can be realized from yne-ynamides having alkyl

substituents at the propargyl sp^3-carbon. Gratifyingly, the desired 2-Me substituted pyrrole scaffolds **58/59** were constructed from the cyclization of **1af/1ag** with **15g** under the established conditions. Moreover, the reaction of **15g** with **1ah** (having an alkyl moiety at the ynamide terminus and 2-Me substitution in the propargyl side) produced **60**, albeit in a moderate 47% yield.

2A.4.4. Control experiments

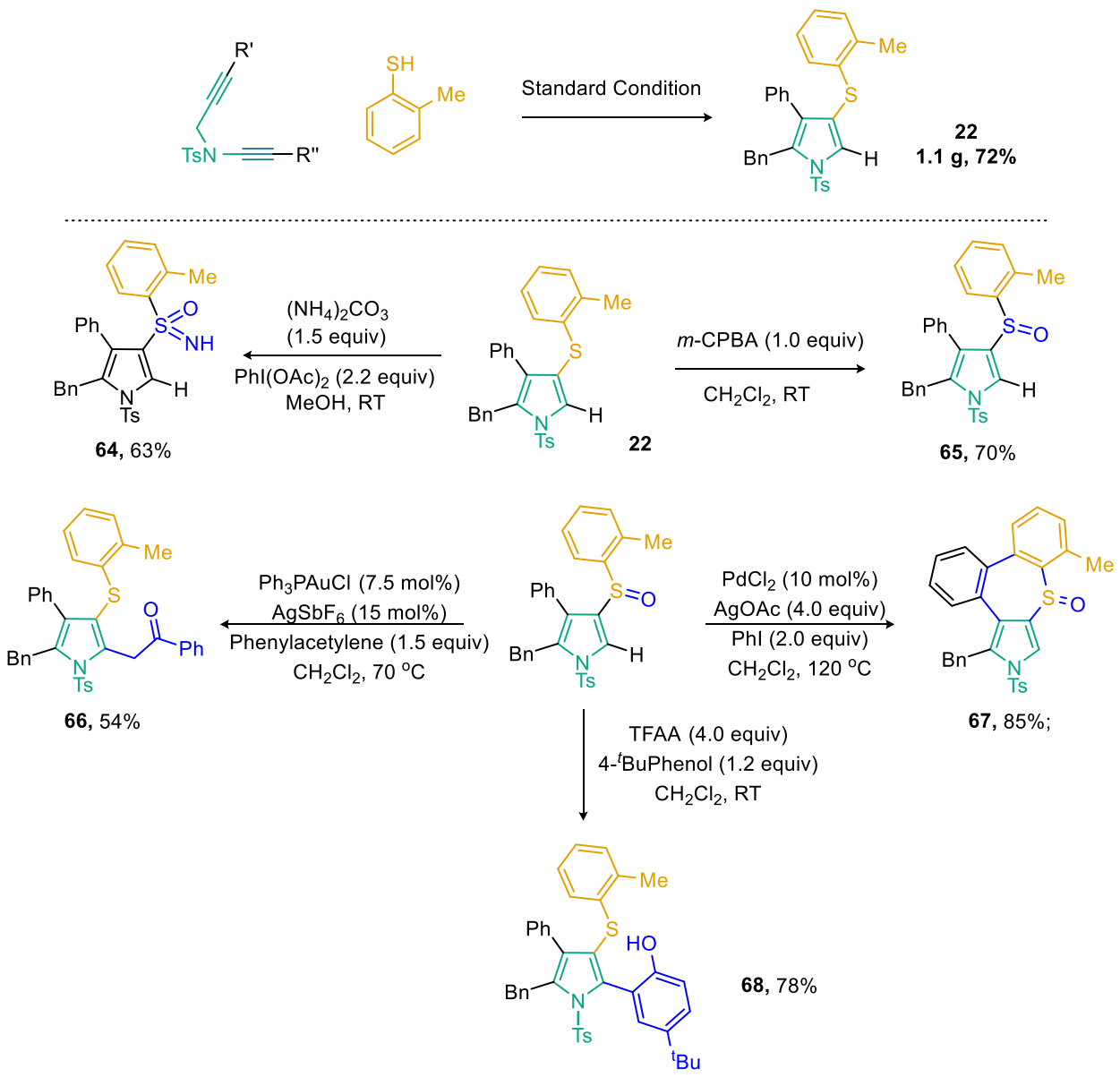
To gain some insights into the reaction mechanism, the reaction between **1a** and *p*-chlorobenzenethiol (**15j**) in the presence of N-hydroxyphthalimide and the radical scavenger TEMPO under the standard reaction conditions was performed. The respective bis(4-chlorophenyl)disulfane **62** was exclusively produced, leaving **1i** untouched (**Scheme 2A.15**). On the other hand, the same reaction in DMF at 70 °C produced the hydroathiolation product **63** (82%). Thus, the attack of the thiyl radical across the alkyne initiates the reaction.



Scheme 2A.15: Control Experiments

2A.4.5. Synthetic application

The robustness of the catalytic system has been tested in the gram scale synthesis of **22** (1.1 g, 72%) from **1i** (1.15 g, 2.2 mmol) and **15g** (6.6 mmol) (**Scheme 2A.16**). The reactivity of **22** was further explored through the direct synthesis of sulfoximine **64** (63%) and *m*-CPBA assisted oxidation of the S-atom to the corresponding sulfoxide **65** (70%).[7] The reaction of sulfoxide **65** with phenyl



Scheme 2A.16: Synthetic Applications.

acetylene in presence of Ph_3PAuCl (7.5 mol%) and $AgSbF_6$ (15 mol%) provided the alkylation product **66**.[8] The cross-dehydrogenative-coupling of **65** led to the unusual [6,7]-fused thiepino-pyrrole **67** in 85% yield.[9] Exposing **65** to *p*-^{t}Bu-phenol in presence of TFAA delivered the arylation product **68** via Pummerer-type transformation.[10]

2A.4.6. DFT Calculations

To validate a radical cyclization pathway and rationalize the selective formation of 4-thioaryl-pyrroles, DFT computations were carried out using the Gaussian 09 software package. In principle, four sites of the two yne units of the yne-ynamide scaffold are available for the attack of the thiyl radical,[13] which would eventually result in eight different products on the basis of specific *exo*/*endo*-mode cyclization. All these possibilities have been investigated and are presented in the reported SI. Only radical additions via 5-*exo*-dig cyclizations, which turn out to be the best computational options, are discussed here. The values are ΔG343 in kcal/mol obtained at the UB3LYP[14]/6-311++G(d,p)[15] level including solvent correction for CH_2Cl_2 (PCM method) (**Figure 2A.5**). The B3LYP functional remains widely used in the computational study of radicals.[17] Starting from system A comprising a model yne-ynamide and the benzothiyl radical, two pathways can provide pyrroles. The radical can attack the internal propargyl alkyne carbon to give B, which then undergoes a 5-*exo*-dig cyclization to yield C. The first step is endergonic by 9.2 kcal/mol, and the second one is exergonic by 17.0 kcal/mol. The corresponding transition states have free energies of 16.9 and 17.5 kcal/mol. Radical C is then likely to abstract a hydrogen atom from thiophenol to give D. The latter should then easily tautomerize to the aromatic 4-thioaryl-pyrrole E, which displays the experimentally observed regiochemistry. If the benzothiyl radical attacks the internal ynamide carbon, vinyl radical H would be formed. Its transformation into the 5-membered ring radical I, which displays an unobserved 2-thio regioselectivity, was then modeled through a 5-*exo*-dig cyclization. Both inter- and intramolecular radical additions leading to I are more difficult to achieve than those providing C. Indeed, the corresponding transition states have free energies of 20.2 and 20.6 kcal/mol. The preference for TSAB over TSAH can be rationalized on the basis of electronic and steric effects. Despite our effort, we could not find an energetically reasonable pathway for the selective formation of 16′ over 16 in DMF.[21] In spite of a good match between our method and the known calculated BDE of thiophenol the computed mechanism remains to be validated.

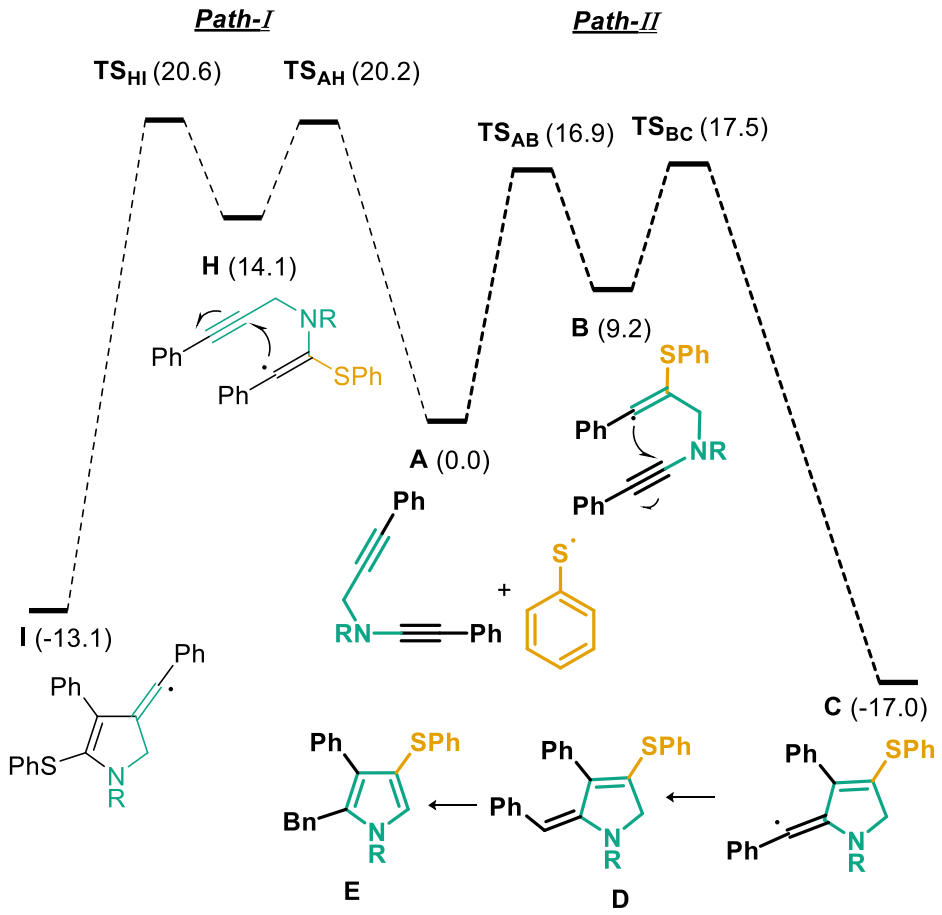


Figure 2A.5: DFT Calculations

2A.5. Conclusion

In summary, a metal-free regioselective radical cyclization of arylthiols with yne-tethered ynamides to fully substituted 4-thioaryl-pyrroles has been developed. The transformation involves an attack of a thiyl radical to the alkyne motif, followed by the cyclization with the ynamide core. The preferred reactivity of an alkyne over an ynamide, although previously observed, remains a rare case. The transformation is general, exhibiting a broad substrate scope and high functional group tolerance (the free NH_2, OH groups and the common radical trap electron-withdrawing groups did not affect the reaction outcome). Control experiments suggest the involvement of radical intermediates. Preliminary DFT calculations support the reaction pathway involving the alkyne moiety as the most reactive part of the yne-ynamide. Implementation of this

method for the synthesis of complex molecules of biological significance and detailed mechanistic studies are currently underway. We believe these findings would open new avenues for discovering novel methods in yne/allene/olefin tethered ynamides.

2A.6. Experimental Section

2A.6.1. General Information

All the reactions were performed in an oven-dried schlenk flask. Commercial grade solvents were distilled prior to use. Column chromatography was performed using silica gel (100–200 Mesh) eluting with hexanes and ethyl acetate mixture. Thin layer chromatography (TLC) was performed on silica gel GF254 plates. Visualization of spots on TLC plate was accomplished with UV light (254 nm) and staining over I_2 chamber. Proton, carbon and fluorine nuclear magnetic resonance spectra (^{1}H NMR, ^{13}C NMR and ^{19}F NMR) were recorded based on 400 MHz (^{1}H NMR, 400 MHz; ^{13}C NMR, 101 MHz; ^{19}F NMR, 376 MHz) spectrometer and 500 MHz (1H NMR, 500 MHz; ^{13}C NMR, 126 MHz; ^{19}F NMR, 470 MHz) spectrometer having solvent resonance as internal standard (^{1}H NMR, $CHCl_3$ at 7.26 ppm; ^{13}C NMR, $CDCl_3$ at 77.0 ppm). Few cases tetramethylsilane (TMS) at 0.00 ppm was used as reference standard. Data for ^{1}H NMR are reported as follows: chemical shift (ppm), the abbreviations were used to explain the multiplicities: s = singlet; d = doublet; t = triplet; q = quartet; dd = doublet of doublet; m = multiplet; quin = quintuplet; sext = sextet, sep = septet; br = broad; coupling constants *J*, in (Hz). ^{13}C NMR, ^{19}F NMR were reported in terms of chemical shift (ppm). IR spectra were recorded on FT/IR spectrometer and reported in cm^{-1}. High resolution mass spectra (HRMS) were obtained in ESI mode. Melting points were determined by electro-thermal heating and are uncorrected. LC-MS spectra were obtained with a Shimadzu 2010A (EI-positive/ negative mode) with ionization voltage of 70ev; data was reported in the form of m/z (intensity relative to base peak = 100). Elemental (C, H, N) analyses were carried out using THERMO FINNIGAN FLASH EA 1112 analyzer. X–ray data was collected at 298K on a Bruker D8 Quest CCD diffractometer using Mo-Kα radiation (0.71073 Å).

2A.6.2. Materials

Unless otherwise noted, all the reagents and intermediates were obtained commercially and used without purification. Toluene, dichloromethane (CH_2Cl_2; DCM), acetone,

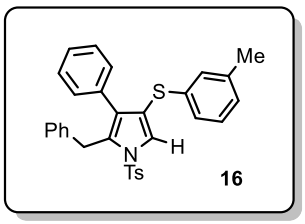
acetonitrile (CH_3CN) and N,N-dimethylformaide (DMF) were distilled over CaH_2.. Catalyst/initiator N-hydroxypthalimde, $K_2S_2O_8$, azobisisobutyronitrile (AIBN) were purchased and used as received. Thiophenols and aryl iodides were purchased and used as received. PTSA·H_2O, PPh_3, DEAD, $CuSO_4$·H_2O, 1.10-phenanthroline, K_3PO_4, Na_2CO_3, $PhB(OH)_2$, and phenyl acetylene were commercially available and used as received. Analytical and spectral data of all those known compounds are exactly matching with the reported values.

2A.6.3. General procedure and spectral/analytical data

2A.6.3.1. General Procedure for Cyclization.

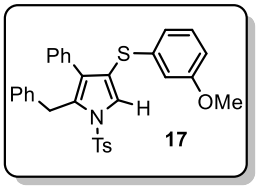
A solution of compound **1i-1al** (0.3 mmol) and N-hydroxypthalimide (0.06 mmol) in dicholoromethane (0.5 mL) was placed in a Schlenk flask under an argon atmosphere. Thiophenol **2** (0.6 mmol) was introduced to the reaction mixture under an argon atmosphere. The reaction mixture was stirred for 36 hours at 70 °C. Progress of the reaction was periodically monitored by TLC. After 36 h, the reaction mixture was diluted with dichloromethane (10 mL). After evaporation of solvent under the reduced pressure, the residue was purified by coloumn chromatography on silica gel (hexane/EtOAc) to afford the expected peripheral substituted pyrroles **16-60**.

2-Benzyl-3-phenyl-4-(*m*-tolylthio)-1-tosyl-1H-pyrrole (16):



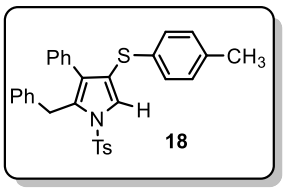
16 (119 mg) was obtained in 78% yield as pale yellow gummy liquid; R_f = 0.46 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (s, 1H), 7.38 (d, J = 8.4 Hz, 2H), 7.25–7.21 (m, 3H), 7.18–7.15 (m, 2H), 7.14–7.10 (m, 3H), 7.10–7.05 (m, 3H), 6.97–6.92 (m, 3H), 6.90 (dd, J = 7.6, 1.6 Hz, 2H), 4.29 (s, 2H), 2.38 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.6, 139.0, 138.4, 137.2, 135.2, 132.5, 131.7, 130.2, 129.8, 129.6, 128.5, 128.1, 127.9, 127.8, 127.2, 126.9, 126.5, 125.6, 124.6, 115.4, 30.9, 21.5, 21.2 ; IR (Neat)ν_{max} 3027, 1593, 1493, 1370, 1189, 1113, 665 cm^{-1}; HRMS (ESI) for $C_{32}H_{30}NO_2S_2$ $(M+CH_3)^+$: calcd 524.1718, found 524.1712.

2-Benzyl-4-((3-methoxyphenyl)thio)-3-phenyl-1-tosyl-1H-pyrrole (17):



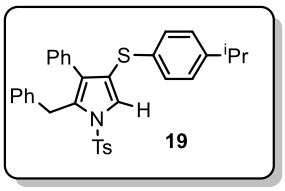
17 (117 mg) was obtained in 74% yield as pale yellow gummy thick liquid; R_f = 0.34 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (s, 1H), 7.35 (d, J = 8.0 Hz, 2H), 7.23–7.18 (m, 3H), 7.16–7.11 (m, 3H), 7.09 (bd, J = 3.2 Hz, 2H), 7.08–7.03 (m, 3H), 6.88–6.83 (m, 2H), 6.70 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 6.67– 6.63 (m, 1H), 6.63–6.60 (m, 1H), 4.24 (s, 2H), 3.69 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.8, 144.7, 139.1, 139.0, 135.3, 132.5, 131.8, 130.4, 129.8, 129.7, 129.5, 128.4, 128.1, 128.0, 127.9, 127.4, 127.3, 127.0, 125.7, 119.7, 114.9, 112.5, 111.7, 55.1, 31.0, 21.5; IR (Neat)ν_{max} 3063, 2835, 1710, 1493, 1282, 1112, 935, 636 cm^{-1}; HRMS (ESI) for $C_{31}H_{28}NO_3S_2$ $(M+H)^+$: calcd 526.1511, found 526.1516.

2-Benzyl-3-phenyl-4-(*p*-tolylthio)-1-tosyl-1H-pyrrole (18):



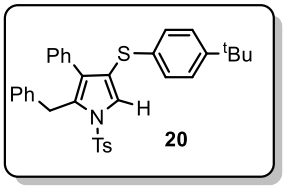
18 (122 mg) was obtained in 80% yield as pale yellow semi solid; R_f = 0.44 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (s, 1H), 7.33 (d, J = 8.0 Hz, 2H), 7.24–7.20 (m, 3H), 7.17–7.12 (m, 2H), 7.11–7.08 (m, 2H), 7.08–7.06 (m, 2H), 7.06–7.02 (m, 5H), 6.88–6.84 (m, 2H), 4.23 (s, 2H), 2.37 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.7, 139.1, 135.9, 135.4, 133.5, 132.7, 131.6, 130.3, 129.9, 129.7, 129.6, 128.5, 128.2, 128.1, 128.0, 127.4, 127.0, 126.2, 125.7, 116.6, 31.0, 21.6, 21.0; IR (Neat)ν_{max} 3027, 1491, 1189, 1113, 1091, 666, 635 cm^{-1}; HRMS (ESI) for $C_{31}H_{28}NO_2S_2$ $(M+H)^+$: calcd 510.1561, found 510.1564.

2-Benzyl-4-((4-*iso*-propylphenyl)thio)-3-phenyl-1-tosyl-1H-pyrrole (19):



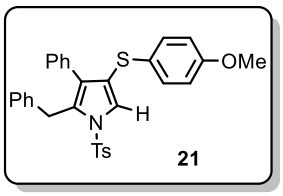
19 (132 mg) was obtained in 82% yield as pale yellow solid; R_f = 0.49 (9.5:0.5 hexane/EtOAc); [Silica, UV and I_2]; mp = 137–139 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.59 (s, 1H), 7.33 (d, J = 8.0 Hz, 2H), 7.22–7.19 (m, 3H), 7.15–7.12 (m, 2H), 7.11–7.04 (m, 9H), 6.87–6.84 (m, 2H), 4.22 (s, 2H), 2.90–2.81 (m, 1H), 2.36 (s, 3H), 1.24 (s, 3H), 1.23 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.9, 144.6, 139.0, 135.4, 133.8, 132.7, 131.6, 130.2, 129.9, 129.6, 128.5, 128.1, 128.0, 127.9, 127.3, 127.0, 126.9, 126.2, 125.7, 116.6, 33.6, 31.0, 23.9, 21.5; IR (Neat)ν_{max} 3021, 1491, 1365, 1158, 665, 590 cm^{-1}; HRMS (ESI) for $C_{33}H_{32}NO_2S_2$ $(M+H)^+$: calcd 538.1874, found 538.1872.

2-Benzyl-4-((4-(*tert*-butyl)phenyl)thio)-3-phenyl-1-tosyl-1H-pyrrole (20):



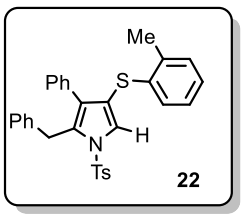
20 (139mg) was obtained in 84% yield as yellowish white solid; mp = 162–163 °C; R_f = 0.51 (9.5:0.5 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60 (bs, 1H), 7.33 (d, J = 8.0 Hz, 2H), 7.23–7.19 (m, 5H), 7.16–7.12 (m, 2H), 7.11–7.03 (m, 7H), 6.88–6.84 (m, 2H), 4.23 (s, 2H), 2.37 (s, 3H), 1.30 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.1, 144.6, 139.1, 135.4, 133.6, 132.7, 131.7, 130.2, 129.9, 129.6, 128.1, 128.0, 127.9, 127.3, 127.0, 126.3, 125.8, 125.7, 116.5, 34.4, 31.3, 31.0, 21.5; IR (Neat)ν_{max} 2960, 1595, 1423, 1169, 1089, 665 cm^{-1}; HRMS (ESI) for $C_{34}H_{33}NO_2S_2Na$ $(M+Na)^+$: calcd 574.1850, found 574.1850

2-Benzyl-4-((4-methoxyphenyl)thio)-3-phenyl-1-tosyl-1H-pyrrole (21):



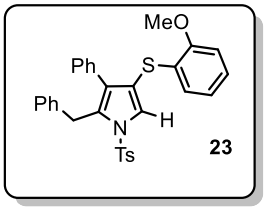
21 (125 mg) was obtained in 79% yield as pale yellow solid; mp = 151–153 °C; R_f = 0.32 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.45 (s, 1H), 7.29 (d, J = 8.5 Hz, 2H), 7.25–7.21 (m, 3H), 7.16–7.12 (m, 3H), 7.12–7.09 (m, 1H), 7.09–7.01 (m, 5H), 6.83 (d, J = 7.0 Hz, 2H), 6.78–6.74 (m, 2H), 4.19 (s, 2H), 3.78 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.7, 144.5, 139.0, 135.4, 132.7, 131.7, 131.0, 129.9, 129.6, 128.1, 128.0, 127.9, 127.3, 126.9, 126.6, 125.6, 124.7, 118.5, 114.5, 55.3, 30.9, 21.5 ; IR (Neat)ν_{max} 2924, 1572, 1492, 1170, 1091, 665 cm^{-1}; HRMS (ESI) for $C_{31}H_{28}NO_3S_2$ $(M+H)^+$: calcd 526.1511, found 526.1515.

2-Benzyl-3-phenyl-4-(*o*-tolylthio)-1-tosyl-1H-pyrrole (22):



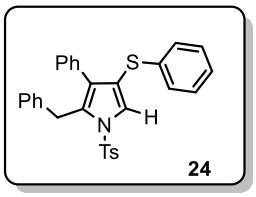
22 (116 mg) was obtained in 76% yield as pale yellow gummy liquid; R_f = 0.44 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (bs, 1H), 7.35 (d, J = 8.4 Hz, 2H), 7.23–7.18 (m, 3H), 7.16–7.12 (m, 2H), 7.12–7.07 (m, 5H), 7.07–7.04 (m, 3H), 7.02–6.98 (m, 1H), 6.90–6.86 (m, 2H), 4.25 (s, 2H), 2.37 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.7, 139.1, 136.5, 136.4, 135.4, 132.6, 131.8, 130.4, 130.0, 129.8, 129.7, 128.2, 128.1, 128.0, 127.4, 127.0, 126.6, 126.4, 125.9, 125.8, 115.8, 31.1, 21.6, 20.1; IR (Neat)ν_{max} 3059, 1493, 1367, 1188, 1169, 1090, 666 cm^{-1}; HRMS (ESI) for $C_{31}H_{28}NO_2S_2$ $(M+H)^+$: calcd 510.1561, found 510.1565.

2-Benzyl-4-((2-methoxyphenyl)thio)-3-phenyl-1-tosyl-1H-pyrrole (23):



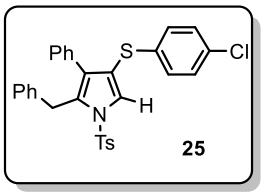
23 (113 mg) was obtained in 72% yield as pale yellow solid; mp = 152–154 °C; R_f = 0.4 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (bs, 1H), 7.34 (d, J = 8.4 Hz, 2H), 7.21–7.14 (m, 5H), 7.12–7.03 (m, 6H), 6.89–6.85 (m, 2H), 6.85–6.82 (m, 1H), 6.82–6.76 (m, 2H), 4.25 (s, 2H), 3.82 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.7, 144.6, 139.1, 135.3, 132.5, 132.2, 130.3, 129.7, 129.6, 128.2, 128.0, 127.9, 127.6, 127.5, 127.3, 127.0, 126.6, 126.4, 125.7, 121.0, 114.0, 110.3, 55.7, 31.0, 21.5 ; IR (Neat)ν_{max} 3060, 1475, 1171, 1114, 1091, 665 cm^{-1}; HRMS (ESI) for $C_{31}H_{28}NO_3S_2$ $(M+H)^+$: calcd 526.1511, found 526.1513.

2-Benzyl-3-phenyl-4-(phenylthio)-1-tosyl-1H-pyrrole (24):



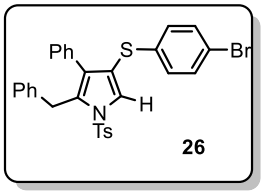
24 (131 mg) was obtained in 88% yield as colourless solid ; mp = 178–180 °C; R_f = 0.41 (9.5:0.5 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (s, 1H), 7.35 (d, J = 8.4 Hz, 2H), 7.23–7.18 (m, 5H), 7.15–7.04 (m, 10H), 6.89–6.84 (m, 2H), 4.26 (s, 2H), 2.37 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.6, 139.0, 137.5, 135.2, 132.5, 131.7, 130.3, 129.8, 129.6, 128.7, 128.1, 128.0, 127.8, 127.6, 127.3, 127.0, 126.9, 125.7, 125.6, 115.3, 31.0, 21.5; IR (Neat)ν_{max} 3145, 1366, 1181, 1166, 664, 577 cm^{-1}; HRMS (ESI) for $C_{30}H_{26}NO_4S$ $(M+H)^+$: calcd 496.1405, found 496.1407.

2-Benzyl-4-((4-chlorophenyl)thio)-3-phenyl-1-tosyl-1H-pyrrole (25):



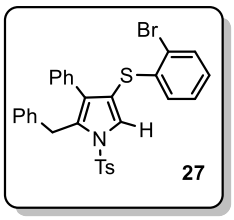
25 (108 mg) was obtained in 68% yield as colourless solid; mp = 153–155 °C; R_f = 0.44 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66 (s, 1H), 7.31 (d, J = 8.5 Hz, 2H), 7.21–7.17 (m, 3H), 7.12 (dt, J = 8.5, 2.0 Hz, 2H), 7.09–7.06 (m, 4H), 7.04 (d, J = 9.0 Hz, 3H), 6.97 (dt, J = 8.5 Hz, 2.0 Hz, 2H), 6.82 (d, J = 6.5 Hz, 2H), 4.22 (s, 2H), 2.36 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.8, 138.9, 136.2, 135.2, 132.4, 131.61, 131.55, 130.7, 129.8, 129.7, 128.9, 128.8, 128.2, 128.1, 127.9, 127.5, 127.14, 127.06, 125.8, 114.9, 31.0, 21.6 ; IR (Neat)ν_{max} 2923, 1452, 1171, 1113, 1090, 665 cm^{-1}; HRMS (ESI) for $C_{30}H_{25}ClNO_2S_2$ $(M+H)^+$: calcd 530.1015, found 530.1016.

2-Benzyl-4-((4-bromophenyl)thio)-3-phenyl-1-tosyl-1H-pyrrole (26):



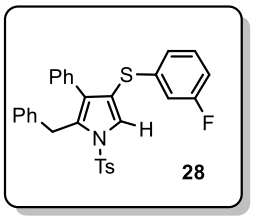
26 (140 mg) was obtained in 80% yield as colourless solid; mp = 164–166 °C; R_f = 0.6 (9.5:0.5 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (s, 1H), 7.34–7.27 (m, 3H), 7.22–7.18 (m, 3H), 7.11–7.02 (m, 8H), 6.91 (dt, J = 8.4, 2.0 Hz, 2H), 6.82 (bd, J = 8.8 Hz, 2H), 4.22 (s, 2H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.8, 138.8, 136.9, 135.1, 132.3, 131.7, 131.6, 130.6, 129.74, 129.67, 128.9, 128.2, 128.1, 127.8, 127.4, 127.3, 127.0, 125.7, 119.3, 114.4, 30.9, 21.6; IR (Neat)ν_{max} 3145, 1370, 1168, 803, 665, 578 cm^{-1}; HRMS (ESI) for $C_{30}H_{25}BrNO_2S_2$ $(M+H)^+$: calcd 574.0510, found 574.0509.

2-Benzyl-4-((2-bromophenyl)thio)-3-phenyl-1-tosyl-1H-pyrrole (27):



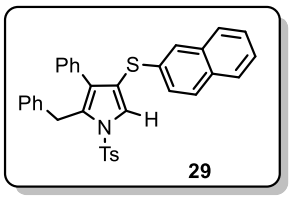
27 (100 mg) was obtained in 58% yield as colourless solid; mp = 186–188 °C; R_f = 0.48 (9.5:0.5 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.67 (s, 1H), 7.41 (dd, J = 8.0, 1.5 Hz, 1H), 7.34 (d, J = 8.5 Hz, 2H), 7.21–7.16 (m, 3H), 7.14–7.04 (m, 8H), 6.93 (td, J = 8.0, 1.5 Hz, 1H), 6.87–6.82 (m, 3H), 4.26 (s, 2H), 2.36 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.8, 139.3, 138.9, 135.2, 132.6, 132.2, 131.9, 130.7, 129.7, 129.6, 128.2, 128.12, 128.08, 127.9, 127.6, 127.5, 127.4, 127.1, 126.3, 125.8, 120.9, 113.9, 31.0, 21.6; IR (Neat)ν_{max} 3156, 1360, 1168, 665, 577 cm^{-1}; HRMS (ESI) for $C_{30}H_{25}BrNO_2S_2$ $(M+H)^+$: calcd 574.0510, found 574.0508.

2-Benzyl-4-((3-fluorophenyl)thio)-3-phenyl-1-tosyl-1H-pyrrole (28):



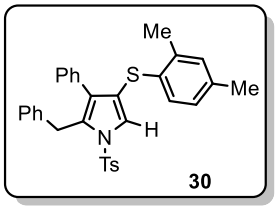
28 (86 mg) was obtained in 56% yield as colourless solid; mp = 160–162 °C; R_f = 0.45 (9.5:0.55 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78–7.74 (m, 1H), 7.41–7.36 (m, 2H), 7.23–7.19 (m, 3H), 7.16–7.07 (m, 8H), 6.90–6.85 (m, 3H), 6.81–6.76 (m, 1H), 6.75–6.70 (m, 1H), 4.27 (s, 2H), 2.38 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.9 (d, J = 248 Hz), 144.8, 140.5 (d, J = 6.3 Hz), 138.8, 135.2, 132.3, 131.8, 130.7, 129.8 (d, J = 8.8 Hz), 129.7 (d, J = 4.0 Hz), 128.2, 128.0, 127.83, 127.75, 127.4, 126.9, 125.7, 122.5, 114.1, 113.7 (d, J = 24 Hz), 112.3 (d, J = 21 Hz), 31.0, 21.5; ^{19}F NMR(471 MHz, $CDCl_3$): δ –112.5 : IR (Neat)ν_{max} 3021, 1366, 1263, 665, 577 cm^{-1}; HRMS (ESI) for $C_{30}H_{25}FNO_2S_2$ $(M+H)^+$: calcd 514.1311, found 514.1312.

2-Benzyl-4-(naphthalen-2-ylthio)-3-phenyl-1-tosyl-1H-pyrrole (29):



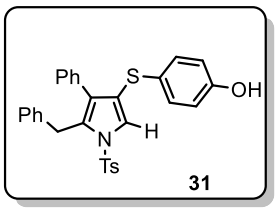
29 (108 mg) was obtained in 66% yield as colourless solid ; mp = 153–155 °C; R_f = 0.48 (9.5:0.5 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, J = 7.6 Hz, 1H), 7.71 (s, 1H), 7.67 (d, J = 8.4 Hz, 1H), 7.60–7.56 (m, 1H), 7.46 (dd, J = 6.8, 1.2 Hz, 1H), 7.44–7.40 (m, 2H), 7.35 (d, J = 8.0 Hz, 2H), 7.24 (dd, J = 8.8, 2.0 Hz, 1H), 7.17–7.14 (m, 3H), 7.14–7.09 (m, 4H), 7.09–7.04 (m, 3H), 6.90–6.85 (m, 2H), 4.26 (s, 2H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.7, 139.0, 135.2, 133.6, 132.5, 131.8, 131.6, 130.5, 129.8, 129.7, 128.7, 128.3, 128.2, 128.0, 127.9, 127.7, 127.4, 127.3, 127.02, 126.99, 126.4, 125.8, 125.7, 125.5, 125.4, 115.0, 31.0, 21.6; IR (Neat)ν_{max} 3023, 1168, 808, 665, 594, 576 cm^{-1}; HRMS (ESI) for $C_{34}H_{28}NO_2S_2$ $(M+H)^+$: calcd 546.1561, found 546.1562.

2-Benzyl-4-((2,4-dimethylphenyl)thio)-3-phenyl-1-tosyl-1H-pyrrole (30):



30 (126 mg) was obtained in 80% yield as pale yellow solid; mp = 155–157 °C; R_f = 0.62 (9.5:0.5 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43 (s, 1H), 7.32 (d, J = 8.0 Hz, 2H), 7.24–7.20 (m, 3H), 7.17–7.13 (m, 2H), 7.11–7.04 (m, 5H), 6.98–6.93 (m, 2H), 6.87 (t, J = 6.0 Hz, 3H), 4.22 (s, 2H), 2.37 (s, 3H), 2.29 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.5, 139.1, 137.1, 136.1, 135.4, 132.7, 132.1, 131.4, 131.0, 130.2, 129.7, 129.6, 129.5, 128.1, 128.0, 127.9, 127.3, 127.1, 126.9, 125.6, 125.4, 117.0, 31.0, 21.5, 20.8, 20.0; IR (Neat)ν_{max} 3028, 1454, 1169, 1088, 665, 578 cm^{-1}; HRMS (ESI) for $C_{32}H_{30}NO_2S_2$ $(M+H)^+$: calcd 524.1718, found 524.1719.

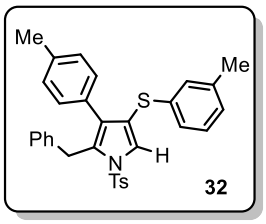
4-((5-Benzyl-4-phenyl-1-tosyl-1H-pyrrol-3-yl)thio)phenol (31):



31 (101 mg) was obtained in 65% yield as pale yellow gummy liquid; R_f = 0.2 (8:2 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.86 (s, 1H), 7.13 (s, 1H), 7.09 (d, J = 8.5 Hz, 2H), 7.06–7.01 (m, 3H), 6.98–6.94 (m, 2H), 6.89–6.83 (m, 7H), 6.62 (d, J = 7.0 Hz, 2H), 6.57–6.52 (m, 2H), 6.56–6.54 (m, 2H), 3.52 (s, 2H), 2.15 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.8, 144.6, 139.0, 135.3, 134.4, 131.9, 130.2, 129.9, 129.6, 128.1, 128.0, 127.9, 127.3, 126.9, 126.6, 125.6, 124.7, 123.6, 118.5, 116.0, 30.9, 21.5; IR (Neat)ν_{max} 3140, 1725, 1169,

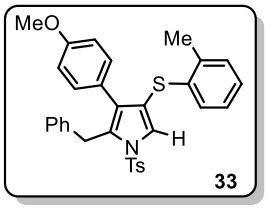
1091, 666, 592 cm^{-1}; HRMS (ESI) for $C_{30}H_{25}NNaO_3S_2$ $(M+Na)^+$: calcd 534.1174, found 534.1212.

2-Benzyl-3-(*p*-tolyl)-4-(*m*-tolylthio)-1-tosyl-1H-pyrrole (32):



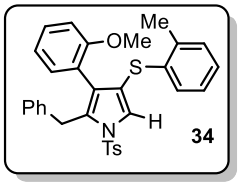
32 (145 mg) was obtained in 92% yield as pale yellow gummy liquid; R_f = 0.4 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (s, 1H), 7.35 (d, J = 8.4 Hz, 2H), 7.16–7.02 (m, 10H), 6.98–6.86 (m, 5H), 4.27 (s, 2H), 2.37 (s, 3H), 2.29 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.6, 139.0, 138.4, 137.4, 136.9, 135.2, 131.7, 130.1, 129.6, 129.5, 128.7, 128.5, 128.1, 128.0, 127.8, 126.9, 126.4, 125.6, 124.5, 115.3, 31.0, 21.5, 21.3, 21.1; IR (Neat)ν_{max} 2919, 1510, 1173, 1090, 668 cm^{-1}; HRMS (ESI) for $C_{32}H_{30}NO_2S_2$ $(M+H)^+$: calcd 524.1718, found 524.1717.

2-Benzyl-3-(4-methoxyphenyl)-4-(*o*-tolylthio)-1-tosyl-1H-pyrrole (33):



33 (128 mg) was obtained in 72% yield as pale yellow gummy liquid; R_f= 0.52 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (bs, 1H), 7.33 (d, J = 8.4 Hz, 2H), 7.13–7.07 (m, 4H), 7.07–7.01 (m, 6H), 7.00–6.93 (m, 1H), 6.87 (d, J = 6.8 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 4.22 (s, 2H), 3.72 (s, 3H), 2.37 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8, 144.6, 139.1, 136.6, 136.2, 135.3, 131.4, 130.8, 130.1, 130.0, 129.6, 128.2, 127.9, 126.9, 126.5, 126.3, 125.7, 124.8, 115.6, 113.5, 55.1, 31.0, 21.5, 20.0; IR (Neat)ν_{max} 2929, 1510, 1175, 1091, 670 cm^{-1}; HRMS (ESI) for $C_{32}H_{30}NO_3S_2$ $(M+H)^+$: calcd 540.1667, found 540.1664.

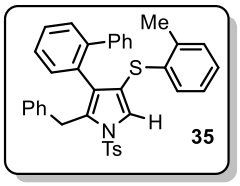
2-Benzyl-3-(2-methoxyphenyl)-4-(*o*-tolylthio)-1-tosyl-1H-pyrrole (34):



34 (117 mg was obtained in 79% yield as pale yellow gummy liquid ; R_f = 0.52 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (s, 1H), 7.30 (d, J = 8.4 Hz, 2H), 7.22–7.16 (m, 1H), 7.09–6.99 (m, 10H), 6.90–6.87 (m, 2H), 6.81 (td, J = 7.6, 0.8 Hz, 1H), 6.76 (d, J = 8.0 Hz, 1H), 4.20 (d, J = 16 Hz, 1H), 4.07 (d, J = 17 Hz, 1H), 3.55 (s, 3H), 2.37 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.3, 144.3, 138.8, 136.40, 136.37, 135.5, 131.9, 131.4, 129.6, 129.5, 129.1, 128.6, 128.1, 127.9, 126.8, 126.0, 125.9, 125.51, 125.45, 121.4, 120.0, 117.0, 110.5, 54.9,

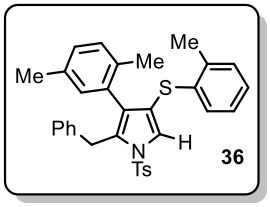
31.3, 21.5, 20.0; IR (Neat)ν_{max} 2835, 1365, 1168, 665, 583 cm^{-1}; HRMS (ESI) for $C_{32}H_{30}NO_3S_2$ $(M+H)^+$: calcd 540.1667, found 540.1666.

3-([1,1'-Biphenyl]-2-yl)-2-benzyl-4-(*o*-tolylthio)-1-tosyl-1H-pyrrole (35):



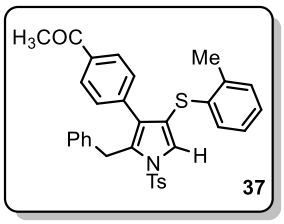
35 (124 mg was obtained in 71% yield as pale yellow solid; mp = 122–124 °C; R_f = 0.5 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40–7.33 (m, 4H), 7.30 (d, J = 13.2 Hz, 2H), 7.23–7.12 (m, 6H), 7.12–7.03 (m, 7H), 6.99 (d, J = 7.6 Hz, 2H), 6.84–6.77 (m, 2H), 3.81 (d, J = 16 Hz, 1H), 3.60 (d, J = 16 Hz, 1H), 2.47 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.4, 142.1, 141.1, 138.7, 138.2, 135.9, 134.9, 132.0, 130.8, 130.7, 130.6, 130.5, 130.1, 129.9, 129.7, 129.0, 128.1, 127.99, 127.95, 127.5, 126.8, 126.7, 126.6, 126.33, 126.28, 125.7, 125.0, 118.5, 31.1, 21.6, 20.1; IR (Neat)ν_{max} 3139, 2925, 1371, 1172, 668 cm^{-1}; HRMS (ESI) for $C_{37}H_{31}NNaO_2S_2$ $(M+Na)^+$: calcd 608.1694, found 608.1697.

2-Benzyl-3-(2,5-dimethylphenyl)-4-(*o*-tolylthio)-1-tosyl-1H-pyrrole (36):



36 (140) mg was obtained in 87% yield as brownish gummy liquid; R_f = 0.5 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55 (bs, 1H), 7.36 (d, J = 8.5 Hz, 2H), 7.13–7.05 (m, 9H), 6.92–6.87 (m, 2H), 6.84 (bs, 1H), 6.67 (bs, 2H), 4.23 (s, 2H), 2.38 (s, 3H), 2.28 (s, 3H), 2.15 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.5, 139.2, 137.2, 136.8, 136.3, 135.4, 132.3, 131.9, 130.3, 129.9, 129.6, 128.92, 128.89, 128.1, 128.0, 127.6, 126.9, 126.23, 126.15, 125.9, 125.6, 116.4, 31.1, 22.6, 21.5, 21.1, 20.1; IR (Neat)ν_{max} 2920, 1599, 1371, 1172, 668, 591 cm^{-1}; HRMS (ESI) for $C_{33}H_{31}NNaO_2S_2$ $(M+Na)^+$: calcd 560.1694, found 560.1692.

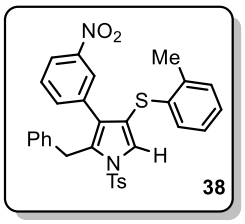
1-(4-(2-Benzyl-4-(*o*-tolylthio)-1-tosyl-1H-pyrrol-3-yl)phenyl)ethanone (37):



37 (118 mg) was obtained in 71% yield as pale yellow gummy liquid; R_f = 0.23 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, J = 8.0 Hz, 2H), 7.60 (s, 1H), 7.35 (d, J = 8.4 Hz, 2H), 7.21 (d, J = 8.4 Hz, 2H), 7.16–7.01 (m, 8H), 6.98–6.91 (m, 1H), 6.82 (bd, J = 6.8 Hz, 2H), 4.24 (s, 2H), 2.51 (s, 3H), 2.37 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.8, 145.0, 138.7, 137.8, 136.2, 135.8, 135.1, 130.73, 130.67, 130.1, 129.9, 129.8, 128.4, 128.1, 127.8, 127.7, 127.2, 127.1, 126.4, 125.9, 115.1, 31.0, 26.6, 21.6, 20.0; IR (Neat)ν_{max} 3058,

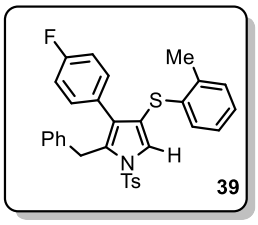
1682, 1265, 782, 643, 589 cm^{-1}; HRMS (ESI) for $C_{33}H_{29}NNaO_3S_2$ $(M+Na)^+$: calcd 574.1487 found 574.1487.

2-Benzyl-3-(3-nitrophenyl)-4-(*o*-tolylthio)-1-tosyl-1H-pyrrole (38):



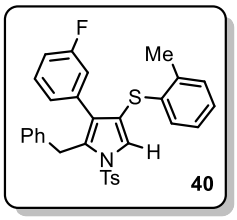
38 (105 mg) was obtained in 63% yield as pale yellow gummy liquid; R_f = 0.35 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.00–7.97 (m, 1H), 7.91 (t, J = 2.0 Hz, 1H), 7.66 (s, 1H), 7.41 (d, J = 8.5 Hz, 2H), 7.34 (dt, J = 8.0, 1.0 Hz, 1H), 7.29 (d, J = 8.0 Hz, 1H), 7.11 (d, J = 7.5 Hz, 2H), 7.09–7.06 (m, 3H), 7.03–7.00 (m, 2H), 7.00–6.98 (m, 1H), 6.91–6.88 (m, 1H), 6.78 (dd, J = 8.0, 1.5 Hz, 2H), 4.21 (s, 2H), 2.39 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.8, 145.1, 138.2, 136.4, 135.7, 135.4, 135.1, 134.4, 131.1, 130.1, 129.9, 129.2, 128.8, 128.7, 128.3, 128.1, 127.7, 127.1, 126.9, 126.3, 126.1, 126.0, 124.8, 115.3, 31.0, 21.6, 19.9; IR (Neat)ν_{max} 3060, 1526, 1347, 1172, 745, 667, 585 cm^{-1}; HRMS (ESI) for $C_{31}H_{26}N_2NaO_4S_2$ $(M+Na)^+$: calcd 577.1232, found 577.1233.

2-Benzyl-3-(4-fluorophenyl)-4-(*o*-tolylthio)-1-tosyl-1H-pyrrole (39):



39 (98 mg) was obtained in 62% yield as pale yellow gummy liquid; R_f = 0.47 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64–7.58 (m, 1H), 7.36 (d, J = 7.2 Hz, 2H), 7.15–7.01 (m, 10H), 6.98-6.92 (m, 1H), 6.91–6.81 (m, 4H), 4.21 (s, 2H), 2.37 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1 (d, J = 247 Hz), 144.8, 138.9, 136.33, 136.27, 135.2, 131.4 (d, J = 8.1 Hz), 130.6 (d, J = 30 Hz), 130.1, 129.7, 128.5 (d, J = 3.0 Hz), 128.3, 128.0, 127.97, 127.85, 127.1, 126.7, 126.4, 125.9, 115.5, 115.1, 114.9, 31.0, 21.6, 20.1; ^{19}F NMR (471 MHz, $CDCl_3$) δ –114.7 ;IR (Neat)ν_{max} 3060, 1507, 1173, 1090, 1057, 670, 578 cm^{-1}; HRMS (ESI) for $C_{31}H_{27}FNO_2S_2$ $(M+H)^+$: calcd 528.1467, found 528.1466.

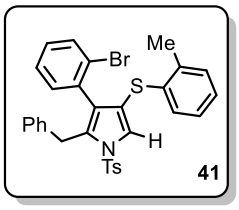
2-Benzyl-3-(3-fluorophenyl)-4-(*o*-tolylthio)-1-tosyl-1H-pyrrole (40):



40 (144 mg) was obtained in 91% yield as brownish solid; mp = 122–124 °C; R_f = 0.41 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (s, 1H), 7.32 (d, J = 8.4 Hz, 2H), 7.16 –7.10 (m, 2H), 7.10 –7.00 (m, 7H), 6.95 –6.91 (m, 1H), 6.89–6.83 (m, 2H), 6.83 –6.77 (m,

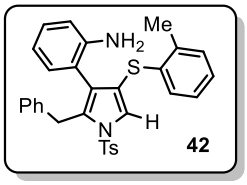
3H), 4.21 (s, 2H), 2.36 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.37 (d, J= 246 Hz), 144.8, 138.6, 135.9, 135.2, 134.7 (d, J= 8.08 Hz), 130.6, 130.4, 130.0, 129.7, 129.4, 129.3, 128.23 (d, J=4.04 Hz), 127.8, 126.9, 126.6, 126.3, 125.9, 125.8, 125.5, 124.3, 116.7 (d, J=22 Hz), 115.6, 114.2 31.0, 21.5, 19.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ –113.5; IR (Neat)ν_{max}: 2922, 1710, 1493, 1173, 665, 589 cm^{-1}; HRMS (ESI) for $C_{31}H_{27}FNO_2S_2$ $(M+H)^+$: calcd 528.1467, found 528.1466.

2-Benzyl-3-(2-bromophenyl)-4-(*o*-tolylthio)-1-tosyl-1H-pyrrole (41):



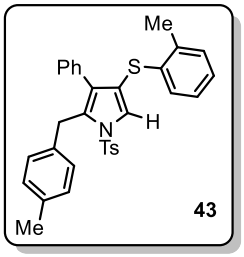
41 (159 mg) was obtained in 90% yield as pale yellow solid; mp = 133–135 °C; R_f = 0.57 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55 (s, 1H), 7.48 (dd, J = 7.5, 1.0 Hz, 1H), 7.38 (d, J = 8.5 Hz, 2H), 7.13–7.09 (m, 3H), 7.08 (d, J = 1.5 Hz, 1H), 7.06–7.01 (m, 5H), 7.01–6.96 (m, 3H), 6.88–6.84 (m, 2H), 4.23 (d, J = 16 Hz, 1H), 3.95 (d, J = 16 Hz, 1H), 2.38 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.7, 138.3, 137.1, 135.6, 135.4, 133.6, 132.5, 132.4, 131.7, 131.1, 129.8, 129.6, 129.5, 129.2, 128.1, 128.0, 126.8, 126.13, 126.08, 126.0, 125.7, 125.3, 117.1, 31.6, 21.5, 20.0 ;IR (Neat)ν_{max} 3061, 1596, 1371, 1172, 1091, 668, 593 cm^{-1}; HRMS (ESI) for $C_{31}H_{26}BrNNaO_2S_2$ $(M+Na)^+$: calcd 610.0486, found 610.0487.

2-(2-Benzyl-4-(*o*-tolylthio)-1-tosyl-1H-pyrrol-3-yl)aniline (42):



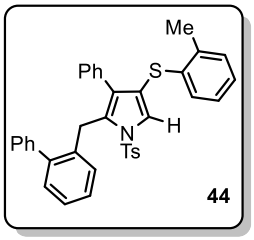
42 (81 mg) was obtained in 51% yield as pale yellow gummy liquid; R_f = 0.3 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (s, 1H), 7.29 (d, J = 8.4 Hz, 2H), 7.09–6.99 (m, 10H), 6.85 (dd, J = 7.6, 1.2 Hz, 2H), 6.81 (dd, J = 8.0, 1.6 Hz, 1H), 6.62–6.56 (m, 2H), 4.20 (d, J = 16 Hz, 1H), 4.00 (d, J = 16 Hz, 1H), 3.31 (bs, 2H), 2.36 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.1, 144.7, 138.6, 138.0, 135.4, 135.3, 132.2, 131.6, 130.13, 130.06, 129.7, 129.1, 128.2, 128.1, 126.9, 126.6, 126.2, 125.9, 125.7, 118.2, 117.88, 117.85, 115.3, 31.3, 21.6, 20.2; IR (Neat)ν_{max} 3379, 2921, 1368, 1091, 666, 596 cm^{-1}; HRMS (ESI) for $C_{31}H_{28}NNaO_2S$ $(M+Na)^+$: calcd 547.1490, found 547.1491.

2-(4-Methylbenzyl)-3-phenyl-4-(*o*-tolylthio)-1-tosyl-1H-pyrrole (43):



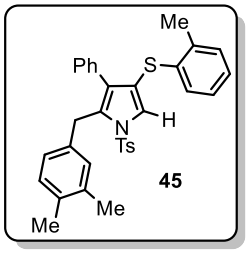
43 (120 mg) was obtained in 76% yield as pale yellow gummy liquid; R_f = 0.64 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (s, 1H), 7.34 (d, J = 8.4 Hz, 2H), 7.24–7.17 (m, 3H), 7.17–7.11 (m, 2H), 7.10–7.03 (m, 5H), 7.02–6.96 (m, 1H), 6.88 (d, J = 8.0 Hz, 2H), 6.74 (d, J = 7.6 Hz, 2H), 4.19 (s, 2H), 2.39 (s, 3H), 2.29 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.5, 136.5, 136.4, 135.9, 135.4, 135.3, 132.7, 131.7, 130.7, 130.0, 129.8, 129.6, 128.9, 128.1, 128.0, 127.8, 127.3, 127.0, 126.7, 126.4, 125.8, 115.6, 30.7, 21.6, 21.0, 20.1; IR (Neat)ν_{max} 2920, 1367, 1170, 1090, 665, 591 cm^{-1}; HRMS (ESI) for $C_{32}H_{30}NO_2S_2$ $(M+H)^+$: calcd 524.1718, found 524.1717.

2-([1,1'-Biphenyl]-2-ylmethyl)-3-phenyl-4-(*o*-tolylthio)-1-tosyl-1H-pyrrole (44):



44 (144 mg) was obtained in 82% yield as pale yellow solid; mp = 141–143 °C : R_f = 0.42 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (s, 1H), 7.53–7.39 (m, 5H), 7.36 (d, J = 8.0 Hz, 2H), 7.32–7.23 (m, 5H), 7.20–7.07 (m, 7H), 7.06–6.99 (m, 2H), 6.78 (d, J = 7.6 Hz, 1H), 4.10 (s, 2H), 2.43 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.8, 141.31, 141.25, 136.7, 136.6, 136.2, 135.2, 132.4, 131.8, 130.1, 129.9, 129.7, 129.6, 129.40, 129.37, 128.1, 128.0, 127.8, 127.4, 127.3, 127.2, 126.93, 126.87, 126.7 126.3, 125.73, 125.65, 115.4, 29.6, 21.5, 20.0; IR (Neat)ν_{max} 2924, 2854, , 1597, 1373, 1172, 1091, 749, 667 cm^{-1}; HRMS (ESI) for $C_{37}H_{32}NO_2S_2$ $(M+H)^+$: calcd 586.1874, found 586.1875.

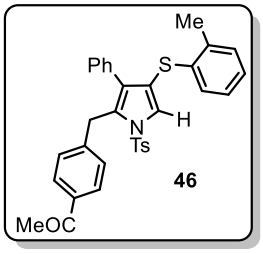
2-(3,4-Dimethylbenzyl)-3-phenyl-4-(*o*-tolylthio)-1-tosyl-1H-pyrrole (45):



45 (148 mg) was obtained in 92% yield as yellow solid; mp = 159–161 °C; R_f = 0.65 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (s, 1H), 7.33 (d, J = 8.4 Hz, 2H), 7.23–7.18 (m, 3H), 7.18–7.13 (m, 2H), 7.12–6.99 (m, 6H), 6.86 (d, J = 7.6 Hz, 1H), 6.65 (d, J = 7.6 Hz, 1H), 6.51 (s, 1H), 4.19 (s, 2H), 2.38 (s, 3H), 2.29 (s, 3H), 2.20 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.3, 136.7, 136.2, 136.0, 135.3, 133.8, 132.61, 131.56, 130.7, 129.9, 129.7, 129.4, 129.3, 129.1, 127.94, 127.85, 127.2, 126.9, 126.7, 126.2, 125.6,

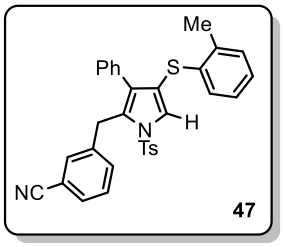
125.4, 115.2, 30.5, 21.5, 20.0, 19.6, 19.2; IR (Neat)ν_{max} 2920, 1367, 1171, 1091, 665, 581 cm^{-1}; HRMS (ESI) for $C_{33}H_{32}NO_2S_2$ $(M+H)^+$: calcd 538.1874, found 538.1873.

1-(4-((3-Phenyl-4-(*o*-tolylthio)-1-tosyl-1H-pyrrol-2-yl)methyl)phenyl)ethanone (46):



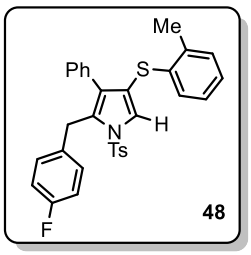
46 (146 mg) was obtained in 76% yield as greenish semi solid; mp = 162–164 °C; R_f = 0.11 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66 (d, J = 8.5 Hz, 2H), 7.55 (s, 1H), 7.37 (d, J = 8.5 Hz, 2H), 7.20–7.17 (m, 3H), 7.09–7.02 (m, 7H), 7.00–6.96 (m, 1H), 6.92 (d, J = 8.0 Hz, 2H), 4.24 (s, 2H), 2.55 (s, 3H), 2.35 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.6, 145.0, 144.7, 136.7, 136.1, 135.4, 135.1, 132.4, 132.2, 130.0, 129.7, 129.6, 129.2, 128.5, 128.3, 128.1, 128.0, 127.5, 126.8, 126.6, 126.3, 126.0, 116.3, 31.2, 26.5, 21.5, 20.0; IR (Neat)ν_{max} 2922, 1681, 1267, 1171, 1091, 752, 666 cm^{-1}; HRMS (ESI) for $C_{33}H_{30}NO_3S_2$ $(M+H)^+$: calcd 552.1667, found 552.1668.

3-((3-Phenyl-4-(*o*-tolylthio)-1-tosyl-1H-pyrrol-2-yl)methyl)benzonitrile (47):



47 (119 mg) was obtained in 74% yield as pale yellow gummy liquid; R_f = 0.33 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.58 (s, 1H), 7.40–7.33 (m, 3H), 7.24–7.17 (m, 5H), 7.13 (d, J = 8.0 Hz, 2H), 7.10–7.02 (m, 5H), 6.99 (bd, J = 3.5 Hz, 1H), 6.84 (s, 1H), 4.23 (s, 2H), 2.42 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.3, 140.4, 136.7, 135.8, 135.2, 132.5, 132.1, 131.0, 130.0, 129.9, 129.54, 129.49, 128.8, 128.6, 128.4, 128.1 127.6, 126.64, 126.60, 126.4, 126.1, 118.5, 116.5, 112.1, 30.5, 21.6, 20.0; IR (Neat)ν_{max} 2922, ,2229, 1369, 1171, 665, 596 cm^{-1}; HRMS (ESI) for $C_{32}H_{27}N_2O_2S_2$ $(M+H)^+$: calcd 535.1514, found 535.1515.

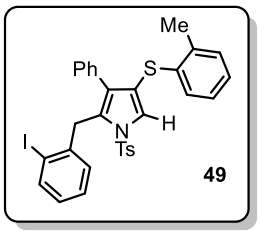
2-(4-Fluorobenzyl)-3-phenyl-4-(*o*-tolylthio)-1-tosyl-1H-pyrrole (48):



48 (119 mg) was obtained in 75% yield as brownish solid; mp = 158–160 °C: R_f = 0.46 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (s, 1H), 7.36 (d, J = 8.0 Hz, 2H), 7.23–7.19 (m, 3H), 7.12–7.07 (m, 5H), 7.07–7.03 (m, 2H), 7.00–6.96 (m, 1H), 6.81–6.71 (m, 4H), 4.18 (s, 2H), 2.39 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ

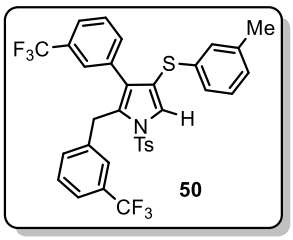
161.5 (d, J = 245 Hz), 145.1, 136.8, 136.4, 135.6, 134.8 (d, J = 3.0 Hz), 132.7, 132.1, 130.4, 130.2, 129.92, 129.88, 129.5 (d, J = 8.1 Hz), 128.5, 128.3, 127.6, 127.1, 126.8, 126.3 (d, J = 41 Hz), 116.2, 115.2, 115.0, 30.4, 21.8, 20.3; ^{19}F NMR (471 MHz, $CDCl_3$) δ −113.5 ; IR (Neat)ν_{max} 2922, 1506, 1170, 665, 636, 579 cm^{-1}; HRMS (ESI) for $C_{31}H_{27}FNO_2S_2$ $(M+H)^+$: calcd 528.1467, found 528.1470.

2-(2-Iodobenzyl)-3-phenyl-4-(*o*-tolylthio)-1-tosyl-1H-pyrrole (49):



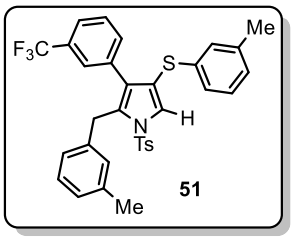
49 (162 mg) was obtained in 85% yield as pale yellow gummy liquid; R_f = 0.59 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (t, J = 3.6 Hz, 2H), 7.60 (d, J = 8.0 Hz, 2H), 7.20 (bt, J = 2.8 Hz, 3H), 7.17–7.09 (m, 5H), 6.99–6.92 (m, 4H), 6.83 (t, J = 7.6 Hz, 1H), 6.50 (d, J = 7.6 Hz, 1H), 4.18 (s, 2H), 2.37 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.0, 141.3, 138.9, 138.4, 137.2, 134.7, 132.13, 132.06, 129.8 ,129.3 128.9, 128.5, 128.1, 128.0, 127.92, 127.89, 127.4, 127.3, 127.1, 126.5, 124.5, 115.0, 100.0, 37.2, 21.5, 21.3; IR (Neat)ν_{max} 3399, 2919, 1170, 1115, 665, 580 cm^{-1}; HRMS (ESI) for $C_{31}H_{26}INNaO_2S_2$ $(M+Na)^+$: calcd 658.0347, found 658.0345.

4-(*m*-tolylthio)-1-tosyl-2-(3-(trifluoromethyl)benzyl)-3-(3-(trifluoromethyl)phenyl)-1H-pyrrole (50):



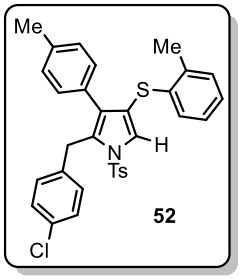
50 (167 mg) was obtained in 86% yield as pale yellow solid; R_f = 0.59 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, $CDCl_3$): δ ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (s, 1H), 7.43 (d, J = 8 Hz, 3H), 7.33 (d, J = 7.5 Hz, 1H), 7.29 (t, J = 7.5 Hz, 1H), 7.20 (t, J = 8 Hz, 2H), 7.13–7.00 (m, 5H), 6.91 (d, J = 7.5 Hz, 1H), 6.89 (s, 1H), 6.86 (d, J = 7 Hz, 2H), 4.28 (s, 2H), 2.35 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.3, 139.4, 138.6, 136.3, 135.0, 133.3, 133.0, 131.3, 130.8, 130.6, 130.5, 130.4, 130.3, 129.9, 129.6, 128.7, 128.6, 128.5, 127.2, 126.9, 126.8, 126.7 (q, J = 5.0 Hz), 125.1, 124.93, 124.87, 124.3–124.1 (m), 122.9 (q, J = 5.0 Hz), 122.8, 122.7, 115.9, 30.6, 21.4, 21.0; ^{19}F NMR (471 MHz, $CDCl_3$) δ −62.8, −62.9; IR (Neat)ν_{max} 2962, 1329, 750, 667, 590 cm^{-1}; HRMS (ESI) for $C_{33}H_{26}F_6NO_2S_2$ $(M+H)^+$: calcd 646.1309, found 646.1308.

2-(3-Methylbenzyl)-4-(*m*-tolylthio)-1-tosyl-3-(3-(trifluoromethyl)phenyl)-1H-pyrrole (51):



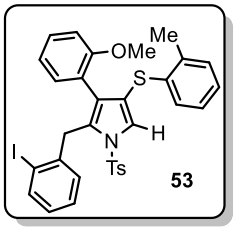
51 (151 mg) was obtained in 82% yield as pale yellow gummy compound; R_f = 0.59 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72 (s, 1H), 7.39 (d, J = 8.5 Hz, 3H), 7.29 (s, 1H), 7.24 (d, J = 7.5 Hz, 1H), 7.22 (d, J = 1.5 Hz, 1H), 7.07 (dd, J = 8.5 Hz, 0.5 Hz, 2H), 7.05 (t, J = 7.5 Hz, 1H), 6.97 (t, J = 7.5 Hz, 1H), 6.91-6.84 (m, 4H), 6.65 (d, J = 8 Hz, 1H), 6.47 (s, 1H), 4.17 (s, 2H), 2.37 (s, 3H), 2.22 (s, 3H), 2.11 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.8, 138.5, 138.3, 137.7, 136.5, 135.1, 133.5, 132.9, 130.9, 130.3, 130.14, 130.06, 129.6, 128.6, 128.5, 128.4, 128.3, 127.13, 127.06, 126.9 (q, J = 5.0 Hz), 126.6, 126.4, 125.0, 123.9 (q, J = 3.8 Hz),122.8, 115.3, 30.8, 21.5, 21.19, 21.16; ^{19}F NMR (471 MHz, $CDCl_3$) δ −62.8 ppm; IR (Neat)ν_{max} 2962, 1371, 1167, 1090, 666, 591 cm^{-1}; HRMS (ESI) for $C_{33}H_{29}F_3NO^2S_2$ $(M+H)^+$: calcd 592.1592, found 592.1590.

2-(4-chlorobenzyl)-3-(*p*-tolyl)-4-(*o*-tolylthio)-1-tosyl-1H-pyrrole (52):



52 (129 mg) was obtained in 77% yield as pale yellow gummy liquid; R_f = 0.6 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52 (s, 1H), 7.30 (dd, J = 6.5, 2.0 Hz, 2H), 7.10–7.03 (m, 5H), 7.01 (bd, J = 8.0 Hz, 2H), 6.99–6.95 (m, 5H), 6.72 (d, J = 8.5 Hz, 2H), 4.16 (s, 2H), 2.40 (s, 3H), 2.28 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.9, 137.4, 137.2, 136.5, 136.4, 135.3, 132.0, 131.7, 130.0, 129.6, 129.54, 129.48, 129.4, 129.2, 128.9, 128.2, 128.1, 126.8, 126.6, 126.3, 125.9, 115.8, 30.4, 21.6, 21.2, 20.0; IR (Neat)ν_{max} 2921, 1170, 1089, 751, 667, 579 cm^{-1}; HRMS (ESI) for $C_{32}H_{28}ClNNaO_2S_2$ $(M+Na)^+$: calcd 580.1148, found 580.1147.

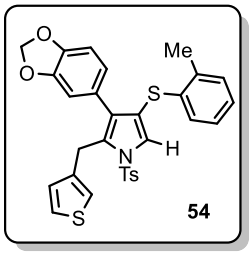
2-(2-Iodobenzyl)-3-(2-methoxyphenyl)-4-(*o*-tolylthio)-1-tosyl-1H-pyrrole (53):



53 (170 mg) was obtained in 85% yield as dark-red solid; mp = 146–148 °C; R_f = 0.29 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (dd, J = 8.0, 1.2 Hz, 1H), 7.65 (s, 1H), 7.54 (d, J = 8.4 Hz, 2H), 7.19–7.13 (m, 1H), 7.10 (d, J = 8.0 Hz, 2H), 7.07–7.01 (m, 4H), 6.95 (dd, 7.2, 1.6 Hz, 1H), 6.86 (td, J = 7.6, 1.2 Hz, 1H), 6.78–6.70 (m, 3H), 6.53

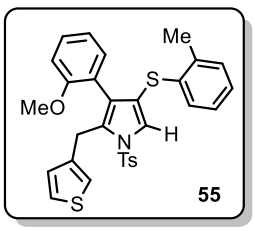
(dd, 8.0, 1.6 Hz, 1H), 4.08 (d, J = 6.4 Hz, 2H), 3.49 (s, 3H), 2.35 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.3, 144.7, 141.2, 138.6, 136.6, 136.3, 135.2, 131.6, 129.9, 129.71, 129.66, 129.4, 129.2, 128.8, 128.7, 127.6, 127.2, 127.1, 126.1, 126.0, 125.7, 121.0, 120.0, 117.1, 110.5, 100.2, 54.8, 37.2, 21.5, 20.0; IR (Neat)ν_{max} 3056, 1367, 1169, 1090, 743, 665 cm^{-1}; HRMS (ESI) for $C_{32}H_{29}INO_3S_2$ $(M+H)^+$: calcd 666.0634, found 666.0639.

3-(Benzo[d][1,3]dioxol-5-yl)-2-(thiophen-3-ylmethyl)-4-(*o*-tolylthio)-1-tosyl-1H-pyrrole (54):



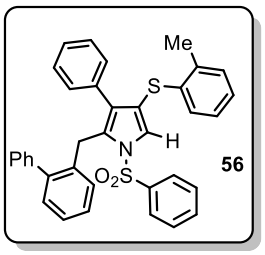
54 (131 mg) was obtained in 78% yield as brownish gummy liquid; R_f = 0.3 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.46 (s, 1H), 7.40 (d, J = 8.5 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 7.10–7.05 (m, 2H), 7.04 (dd, J = 7.0, 2.0 Hz, 1H), 7.01 (dd, J = 7.0, 1.5 Hz, 1H), 6.95–6.91 (m, 1H), 6.68–6.65 (m, 1H), 6.64 (s, 1H), 6.59–6.54 (m, 2H), 6.52–6.49 (m, 1H), 5.88 (s, 2H), 4.17 (s, 2H), 2.39 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.2, 146.9, 144.8, 139.6, 136.5, 136.2, 135.6, 130.8, 130.6, 130.0, 129.7 ,128.3, 127.8, 126.8, 126.3, 126.2, 126.1, 125.9, 125.1, 123.4, 121.1, 116.1, 110.2, 108.0, 100.9, 26.3, 21.6, 20.0; IR (Neat)ν_{max} 2917, 1482, 1172, 750, 667, 594 cm^{-1}; HRMS (ESI) for $C_{30}H_{26}NO_4S_3$ $(M+H)^+$: calcd 560.1024, found 560.1022.

3-(2-Methoxyphenyl)-2-(thiophen-3-ylmethyl)-4-(*o*-tolylthio)-1-tosyl-1H-pyrrole (55):



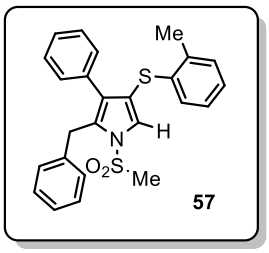
55 (120 mg) was obtained in 73% yield as pale yellow gummy liquid; R_f = 0.51 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (s, 1H), 7.36 (d, J = 8.0 Hz, 2H), 7.23–7.17 (m, 1H), 7.12 (bd, J = 8.4 Hz, 2H), 7.03–6.94 (m, 6H), 6.84–6.74 (m, 2H), 6.68–6.62 (m, 1H), 6.58–6.52 (m, 1H), 4.14 (d, J = 16.4 Hz, 1H), 4.01 (d, J = 16.4 Hz, 1H), 3.54 (s, 3H), 2.39 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.4, 144.5, 139.4, 136.5, 136.4, 135.8, 131.9, 131.7, 129.7, 129.6, 129.2, 128.7, 128.1, 126.8, 126.0, 125.9, 125.6, 124.5, 121.4, 121.1, 120.1, 117.2, 110.6, 55.0, 26.4, 21.6, 20.0; IR (Neat)ν_{max} 2923, 1367, 1170, 750, 665, 593 cm^{-1}; HRMS (ESI) for $C_{30}H_{28}NO_3S_3$ $(M+H)^+$: calcd 546.1231, found 546.1243.

2-([1,1'-Biphenyl]-2-ylmethyl)-3-phenyl-1-(phenylsulfonyl)-4-(*o*-tolylthio)-1H-pyrrole (56):



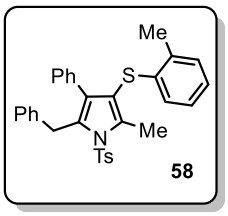
56 (124 mg) was obtained in 72% yield as pale yellow solid; mp = 174–176 °C; R_f = 0.44 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (s, 1H), 7.54–7.49 (m, 1H), 7.47–7.40 (m, 5H), 7.40–7.34 (m, 3H), 7.34–7.28 (m, 3H), 7.25–7.19 (m, 4H), 7.14–7.10 (m, 2H), 7.10–7.07 (m, 1H), 7.07–7.03 (m, 2H), 7.03–7.00 (m, 1H), 7.00–6.96 (m, 1H), 4.06 (s, 2H), 2.29 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.4, 141.3, 138.3, 136.6, 136.4, 133.6, 132.4, 132.0, 130.4, 130.0, 129.7, 129.5, 129.4, 129.1, 128.1, 128.03, 128.0, 127.4, 127.3, 126.91, 126.87, 126.6, 126.3, 125.9, 125.8, 115.9, 29.6, 20.0; IR (Neat)ν_{max} 3059, 1373, 1173, 748, 594 cm^{-1}; HRMS (ESI) for $C_{36}H_{30}NO_2S_2$ $(M+H)^+$: calcd 572.1718, found 572.1722.

2-Benzyl-1-(methylsulfonyl)-3-phenyl-4-(*o*-tolylthio)-1H-pyrrole (57):



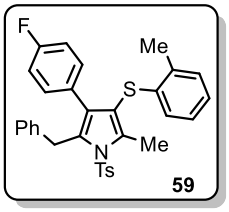
57 (120 mg) was obtained in 92% yield as pale yellow solid; mp = 113–115 °C; R_f = 0.57 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.30 (m, 7H), 7.30–7.24 (m, 2H), 7.21 (bd, J = 7.6 Hz, 2H), 7.10 (bs, 4H), 4.32 (s, 2H), 2.49 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.6, 136.6, 135.9, 132.5, 131.1 131.0, 130.0, 128.7, 128.6, 128.5, 128.1, 127.4, 126.7, 126.3, 125.9, 125.5, 115.6, 42.1, 30.9, 20.0; IR (Neat)ν_{max} 3060, 2926, 1732, 1365, 1168, 1060, 754, 698 cm^{-1}; HRMS (ESI) for $C_{25}H_{24}NO_2S_2$ $(M+H)^+$: calcd 434.1248, found 434.1248.

2-Benzyl-5-methyl-3-phenyl-4-(*o*-tolylthio)-1-tosyl-1H-pyrrole (58):



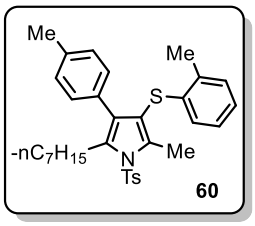
58 (107 mg) was obtained in 68% yield as pale yellow gummy liquid; R_f = 0.51 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, J = 8.4 Hz, 2H), 7.25–7.20 (m, 5H), 7.20–7.14 (m, 5H), 7.13–7.09 (m, 2H), 7.07–7.03 (m, 1H), 7.02–6.94 (m, 2H), 6.63–6.59 (m, 1H), 4.40 (s, 2H), 2.54 (s, 3H), 2.42 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.7, 140.2, 137.7, 137.1, 136.5, 134.9, 133.3, 131.6, 131.5, 130.0, 129.80, 129.7, 128.2, 128.1, 127.9, 127.2, 126.6, 126.1, 125.8, 125.3, 124.6, 113.9, 32.3, 21.5, 19.8, 13.7; IR (Neat)ν_{max} 2925, 1364, 1170, 745, 668, 585 cm^{-1}; HRMS (ESI) for $C_{32}H_{30}NO_2S_2$ $(M+H)^+$: calcd 524.1718, found 524.1718.

2-Benzyl-3-(4-fluorophenyl)-5-methyl-4-(*o*-tolylthio)-1-tosyl-1H-pyrrole (59):



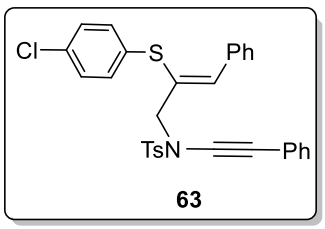
59 (80 mg) was obtained in 49% yield as pale yellow gummy liquid; R_f = 0.52 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (d, J = 8.4 Hz, 2H), 7.22 (d, J = 7.2 Hz, 2H), 7.19–7.14 (m, 3H), 7.08–7.02 (m, 5H), 6.99–6.94 (m, 2H), 6.89 (t, J = 8.8 Hz, 2H), 6.58–6.53 (m, 1H), 4.34 (s, 2H), 2.52 (s, 3H), 2.41 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1 (d, J = 247 Hz), 144.9, 140.1, 137.8, 137.0, 136.4, 135.0, 131.7 (d, J = 8.1 Hz), 131.5, 130.5, 129.9, 129.8, 129.2 (d, J = 3.0 Hz), 128.3, 128.1, 126.8, 126.2, 126.0, 125.3, 124.8, 115.0, 114.83, 113.76, 32.3, 21.6, 19.9, 13.7; ^{19}F NMR (471 MHz, $CDCl_3$) δ –115.0; IR (Neat)ν_{max} 2925, 1364, 1158, 744, 581, 542 cm^{-1}; HRMS (ESI) for $C_{32}H_{28}FNNaO_2S_2$ $(M+Na)^+$: calcd 564.1443, found 564.1444.

2-Heptyl-5-methyl-3-(*p*-tolyl)-4-(*o*-tolylthio)-1-tosyl-1H-pyrrole (60):



60 (63 mg) was obtained in 47% yield as pale yellow gummy liquid; R_f = 0.64 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.61 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 7.05 (d, J = 7.5 Hz, 2H), 7.01 (d, J = 7.0 Hz, 1H), 6.97–6.91 (m, 3H), 6.85 (t, J = 7.5 Hz, 1H), 6.38 (d, J = 7.5 Hz, 1H), 2.83 (t, J = 7.5 Hz, 2H), 2.46 (s, 3H), 2.43 (s, 3H), 2.31 (s, 3H), 2.19 (s, 3H), 1.30–1.15 (m, 10H), 0.85 (t, J = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.3, 137.1, 136.9, 136.8, 136.2, 134.6, 134.4, 130.3, 129.9, 129.7, 129.6, 129.4, 128.2, 125.8, 125.7, 124.6, 124.1, 114.0, 31.4, 28.9, 28.4, 26.8, 22.3, 21.5, 20.9, 19.4, 13.7, 13.5; IR (Neat)ν_{max} 2924, 1366, 1173, 660, 582 cm^{-1}; HRMS (ESI) for $C_{33}H_{39}NNaO_2S_2$ $(M+Na)^+$: calcd 568.2320, found 568.2320.

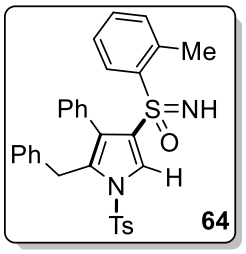
2A.6.3.2. Synthesis of (Z)-N-(2-((4-chlorophenyl)thio)-3-phenylallyl)-4-methyl-N-(phenylethynyl)benzenesulfonamide (63):



A solution of **1i** (115.6 mg, 0.3 mmol) and N-hydroxypthalimide (9.78mg, 0.06 mmol) in N,N-dimethylformamide (0.5 mL) was placed in a Schlenk flask under an argon atmosphere. Next, the compound **15j** (86.7 mg, 0.6 mmol) was added. The resulting mixture was stirred at 70 °C for 36 h. The progress of the reaction was periodically monitored by TLC. The reaction mixture was diluted with ethyl acetate (10 mL) and washed cold

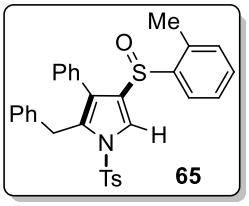
water. The organic layer was dried over Na_2SO_4 and concentrated under the reduced pressure. After evaporation of solvent under the reduced pressure, the residue was purified by coloumn chromatography on silica gel (hexane/EtOAc) to afford product **63** in 88% yield. $R_f = 0.4$ (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, J = 7.6 Hz, 1H), 7.40–7.35 (m, 2H), 7.27–7.13 (m, 8H), 7.06 (d, J = 7.6 Hz, 2H), 7.00 (d, J = 8.8 Hz, 2H), 6.90 (d, J = 8.4 Hz, 2H), 6.59 (s, 1H), 4.77 (s, 2H), 2.31 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.2, 137.3, 135.2, 133.1, 132.8, 132.6, 132.2, 131.5, 131.1, 129.7, 129.5, 129.4, 129.2, 128.7, 128.5, 128.3, 128.2, 128.1, 127.8, 122.1, 85.5, 82.7, 39.3, 21.5; IR (Neat)ν_{max} 2923, 1621, 1452, 1090, 665 cm^{-1}; HRMS (ESI) for $C_{30}H_{25}ClNO_2S_2$ $(M+H)^+$: calcd 530.1015, found 530.1016.

2A.6.3.3. Synthesis of 2-Benzyl-4-(2-methylphenylsulfonimidoyl)-3-phenyl-1-tosyl-1*H*-pyrrole (64):



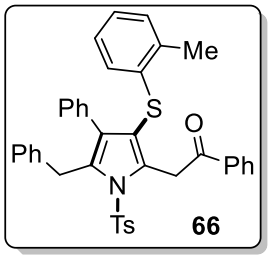
To a solution of **22** (162.5 mg, 0.3 mmol) and $(NH_4)_2CO_3$ (43.2 mg, 0.45 mmol) in MeOH (3.0 mL) was added $PhI(OAc)_2$ (212.5 mg, 0.66 mmol). The resulting mixture was stirred in an open air at room temperature for 30 minutes. The reaction progress was monitored by TLC. Upon completion of the reaction, the crude mixture was concentrated under the reduced pressure. The crude residue was purified using column chromatography on silica gel to afford **64** (103 mg) in 63% yield as yellow gummy liquid; R_f = 0.32 (2:3 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, DMSO-D6): δ 8.23 (s, 1H), 7.55 (d, J = 8.5 Hz, 2H), 7.34–7.30 (m, 2H), 7.26 (d, J = 8.5 Hz, 2H), 7.20 (d, J = 7.5 Hz, 1H), 7.14 (t, J = 7.5 Hz, 1H), 7.08–7.05 (m, 2H), 7.02 (t, J = 8.0 Hz, 2H), 6.95 (t, J = 7.5 Hz, 1H), 6.71 (d, J = 7.0 Hz, 5H), 5.05 (bs, 1H), 3.93 (s, 2H), 2.36 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d6) δ 146.4, 140.3, 138.4, 137.1, 134.3, 132.8, 132.5, 131.5, 130.9, 130.7, 130.6, 130.2, 129.5, 128.6, 127.9, 127.83, 127.78, 127.6, 126.64, 126.56, 126.3, 125.9, 30.3, 21.6, 19.8; IR (Neat)ν_{max} 3317, 2924, 1374, 1173, 756, 666, 589 cm^{-1}; HRMS (ESI) for $C_{31}H_{29}N_2O_3S_2$ $(M+H)^+$: calcd 541.1620, found 541.1632.

2A.6.3.4. Synthesis of 2-Benzyl-3-phenyl-4-(*o*-tolylsulfinyl)-1-tosyl-1*H*-pyrrole (65):



To a solution of **22** (514.6 mg, 0.95 mmol) in CH_2Cl_2 (3.0 mL) was added *m*-CPBA (164 mg, 0.95 mmol) portion wise. The resulting mixture was stirred at room temperature for overnight. The crude reaction mixture was diluted with CH_2Cl_2 (10 mL) and washed with aquous sodium bicarbonate solution (3.0 mL, 2 M). The organic layer was dried over Na_2SO_4 and concentrated under the reduced pressure. The crude residue was purified using column chromatography on silica gel to afford **65** (350 mg) in 70% yield as pale yellow solid; mp = 210–212 °C; R_f = 0.4 (2:3 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (dd, J = 7.6, 1.2 Hz, 1H), 7.51 (s, 1H), 7.30 (td, J = 7.2, 1.2 Hz, 1H), 7.26–7.21 (m, 6H), 7.18–7.13 (m, 2H), 7.08 (d, J = 7.2 Hz, 1H), 7.04 (bd, J = 7.2 Hz, 1H), 7.00 (t, J = 7.2 Hz, 4H), 6.73 (d, J = 7.2 Hz, 2H), 4.13 (s, 2H), 2.32 (s, 3H), 2.06 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.1, 140.5, 138.1, 135.1, 134.3, 131.3, 130.9, 130.6, 130.4, 130.0, 129.6, 128.7, 128.3, 128.2, 128.1, 127.73, 127.70, 127.1, 126.5, 125.7, 124.9, 124.0, 30.1, 21.4, 18.1; IR (Neat)ν_{max} 3060, 1777, 1171, 1028, 749, 665, 586 cm^{-1}; HRMS (ESI) for $C_{31}H_{28}NO_3S_2$ $(M+H)^+$: calcd 526.1511, found 526.1511.

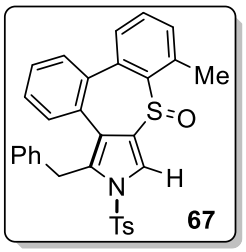
2A.6.3.5. Synthesis of 2-(5-Benzyl-4-phenyl-3-(*o*-tolylthio)-1-tosyl-1H-pyrrol-2-yl)-1-phenylethanone (66):



A mixture of sulfoxide **65** (106 mg, 0.19 mmol), PPh_3AuCl (6.9 mg, 0.014 mmol), and $AgSbF_6$ (9.6 mg, 0.028 mmol) was taken in a Schlenck tube. A solution of phenyl acetylene (0.024 ml, 0.228 mmol) in CH_2Cl_2 (0.5 mL) was next added under N_2 atmosphire. The resulting mixture was stirred at 70 °C for overnight. The reaction progress was monitored by TLC. Upon completion, the crude reaction mixture was concentrated under the reduced pressure. The crude residue was purified using column chromatography on silica gel to afford **66** (65 mg) in 54% yield as red gummy liquid; R_f = 0.5 (7:3 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.99 (d, J = 7.5 Hz, 2H), 7.55 (d, J = 8.0 Hz, 2H), 7.47 (t, J = 8.0 Hz, 3H), 7.17–7.12 (m, 5H), 7.10 (bd, J = 8.0 Hz, 3H), 7.09–7.06 (m, 3H), 6.98 (d, J = 4.5 Hz, 2H), 6.96–6.91 (m, 3H), 4.96 (s, 2H), 4.22 (s, 2H), 2.36 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.8, 144.7, 139.5, 136.8, 136.6, 136.4, 135.3, 135.1, 133.0, 132.97, 131.7, 131.5, 129.8, 129.71, 129.66,

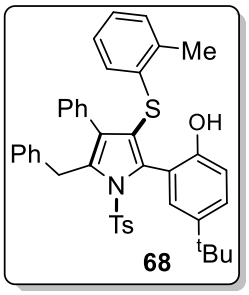
128.5, 128.2, 128.0, 127.8, 127.7, 127.1, 127.0, 126.6, 126.2, 125.5, 117.4, 38.0, 31.8, 21.5, 19.8; IR (Neat)ν_{max} 2924, 1693, 1364, 1178, 747, 699, 589 cm^{-1}; HRMS (ESI) for $C_{39}H_{33}NNaO_3S_2$ $(M+Na)^+$: calcd 650.1800, found 650.1801.

2A.6.3.6. Synthesis of 5-Benzyl-9-methyl-6-tosyl-6H-dibenzo[4,5:6,7]thiepino[2,3-c]pyrrole 8-oxide (67):



To a solution of **65** (111 mg, 0.2 mmol), $PdCl_2$ (3.54 mg, 0.02 mmol) and AgOAc (133.5 mg, 0.8 mmol) in CH_2Cl_2 (0.5 mL) was added iodobenzene (82 mg, 0.4 mmol). The resulting mixture was stirred at 120 °C for 12 h. The reaction progress was monitored by TLC. Upon completion, the solvent was evaporated under the reduced pressure. The crude residue was purified using column chromatography on silica gel to afford **67** (89 mg) was obtained in 85% yield as pale yellow gummy liquid; R_f = 0.3 (7:3 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, $CDCl_3$): 8.13 (s, 1H), δ 7.62 (d, J = 8.0 Hz, 1H), 7.36 (dd, J = 7.5, 1.0 Hz, 1H), 7.28 (dd, J = 8.5 Hz, 1.0 Hz, 1H), 7.23 (tt, J = 7.5, 1.0 Hz, 1H), 7.21–7.12 (m, 6H), 7.04–7.00 (m, 3H), 6.97–6.91 (m, 3H), 4.08 (d, J = 16 Hz, 2H), 4.01 (d, J = 16 Hz, 2H), 2.49 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.2, 139.8, 137.5, 134.8, 134.0, 131.3, 131.0, 130.5, 130.3, 129.9, 129.81, 129.79, 128.5, 128.4, 128.1, 127.9, 126.7, 126.13, 126.10, 125.6, 125.1, 122.2, 121.8, 114.1, 30.3, 22.1, 18.5; IR (Neat)ν_{max} 2924, 1599, 1352, 1187, 754, 666 cm^{-1}; HRMS (ESI) for $C_{31}H_{26}NO_3S_2$ $(M+H)^+$: calcd 524.1354, found 524.1358.

2A.6.3.7. Synthesis of 2-(5-Benzyl-4-phenyl-3-(*o*-tolylthio)-1-tosyl-1H-pyrrol-2-yl)-4-(*tert*-butyl)phenol (68):



To a solution of **65** (111 mg, 0.2 mmol) and 4-^{t}Bu-phenol (36 mg, 0.24 mmol) in CH_2Cl_2 (0.5 mL) was added trifluroacetic anhydride (0.12 ml, 0.8 mmol). The resulting mixture was stirred at room temperature for 4 h. The progress of the reaction was monitored by TLC. Upon completion, the crude reaction mixture was concentrated under the reduced pressure. The crude residue was purified using column chromatography on silica gel to afford **68** (103 mg) in 78% yield as colorless solid; mp = 195–197 °C; R_f = 0.3 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35 (t, J = 7.5 Hz, 2H), 7.30–7.21 (m, 10H), 7.03 (d, J = 8.0 Hz, 2H), 6.94 (dd, J = 7.0, 1.5 Hz, 2H), 6.93–6.91 (m, 1H), 6.91–6.87 (m, 1H),

6.84 (d, J = 8.5 Hz, 1H), 6.74–6.70 (m, 1H), 6.60 (d, J = 2.5 Hz, 1H), 5.15 (bs, 1H), 4.56 (d, J = 16 Hz, 1H), 4.26 (d, J = 16 Hz, 1H), 2.38 (s, 3H), 1.98 (s, 3H), 1.07 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.7, 144.8, 142.1, 140.4, 137.1, 135.9, 135.7, 135.5, 133.9, 133.0, 132.7, 130.2, 129.9, 129.6, 129.4, 128.5, 128.3, 128.04, 127.96, 127.5, 127.4, 126.2, 126.0, 125.1, 119.3, 118.0, 116.1, 33.7, 32.9, 31.1, 21.6, 19.9; IR (Neat)ν_{max} 3461, 2960, 1358, 1173, 746, 589 cm^{-1}; HRMS (ESI) for $C_{41}H_{39}NNaO_3S_2$ $(M+Na)^+$: calcd 680.2269, found 680.2271.

2A.7. X-ray crystallography:

X-ray reflections for **25** were collected on Bruker D8 Quest CCD diffractometer using Mo-Kα, radiation. Data reduction was performed using CrysAlisPro (version 1.171.33.55). Apex 2 and SHELX-TL 97 program were used to solve and refine the data. All non-hydrogen atoms were refined anisotropically and C−H hydrogens were fixed.

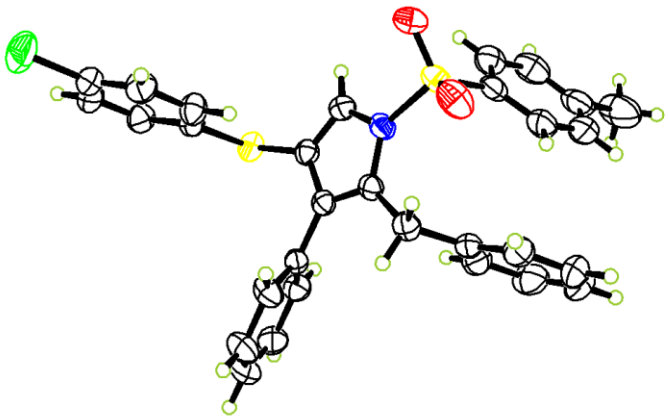


Figure 2A.6. Molecular structures of compounds **25;** thermal ellipsoids are set at 30% probability**.** Oxygen (red), nitrogen (blue), green (chlorine) and sulphur (yellow).

Table 2A.4. Crystallographic Data for Compound **25**

Compound	**25**	V [Å^3]	2586.8 (2)
formula	$C_{30}H_{24}ClNO_2S_2$	Z	4
Formula weight	530.07	ρ_{calcd} [g cm^{-3}]	1.361
crystal system	Monoclinic	μ [mm^{-1}]	0.338
space group	P 21/n	total reflns	69139
T [K]	301 K	unique reflns	4922
a [Å]	6.1673 (3)	observed	4245

b [Å]	19.2105 (10)	R_1[I>2σ(I)]	0.0383 (4245)
c [Å]	21.8486 (13)	wR2 [all]	0.0998 (4922)
α [°]	90	GOF	1.012
β [°]	92.109 (2)	Diffractometer	Bruker D8 Quest CCD
γ [°]	90	CCDC Number	CCDC 1871002

2A.8. References

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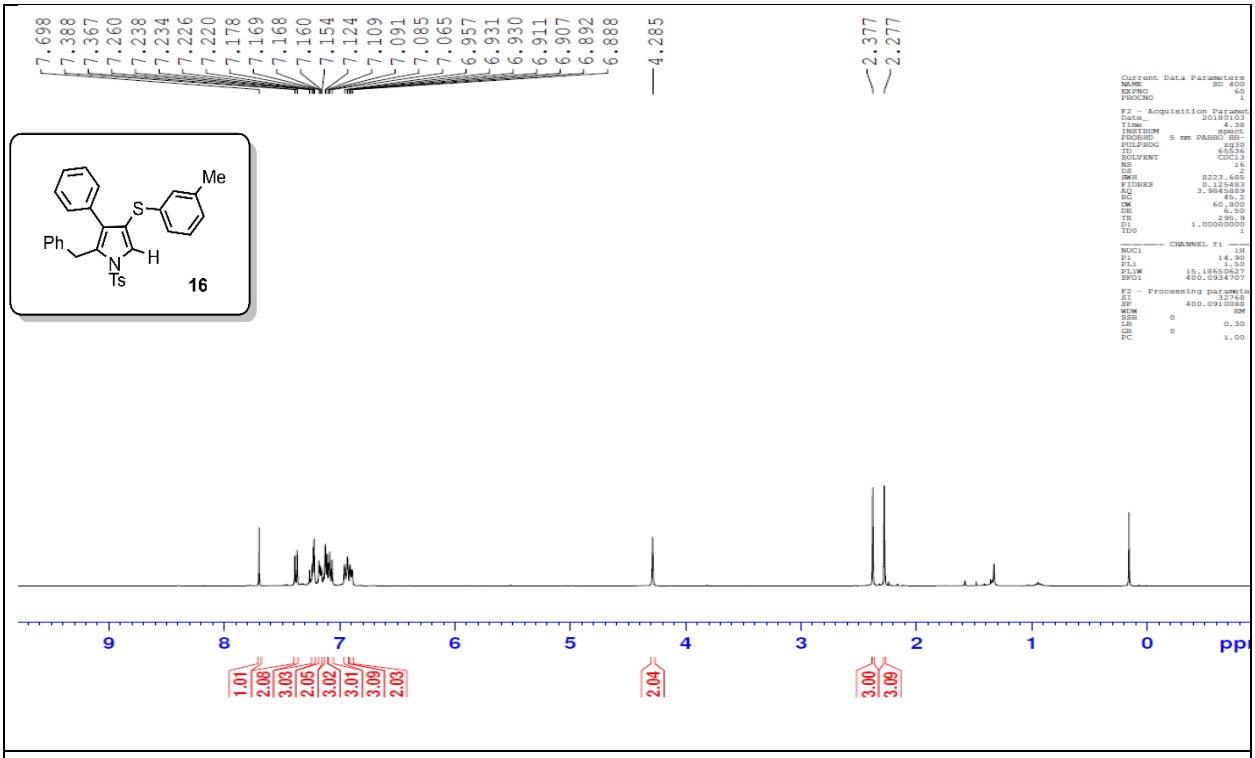
2A.9. Spectra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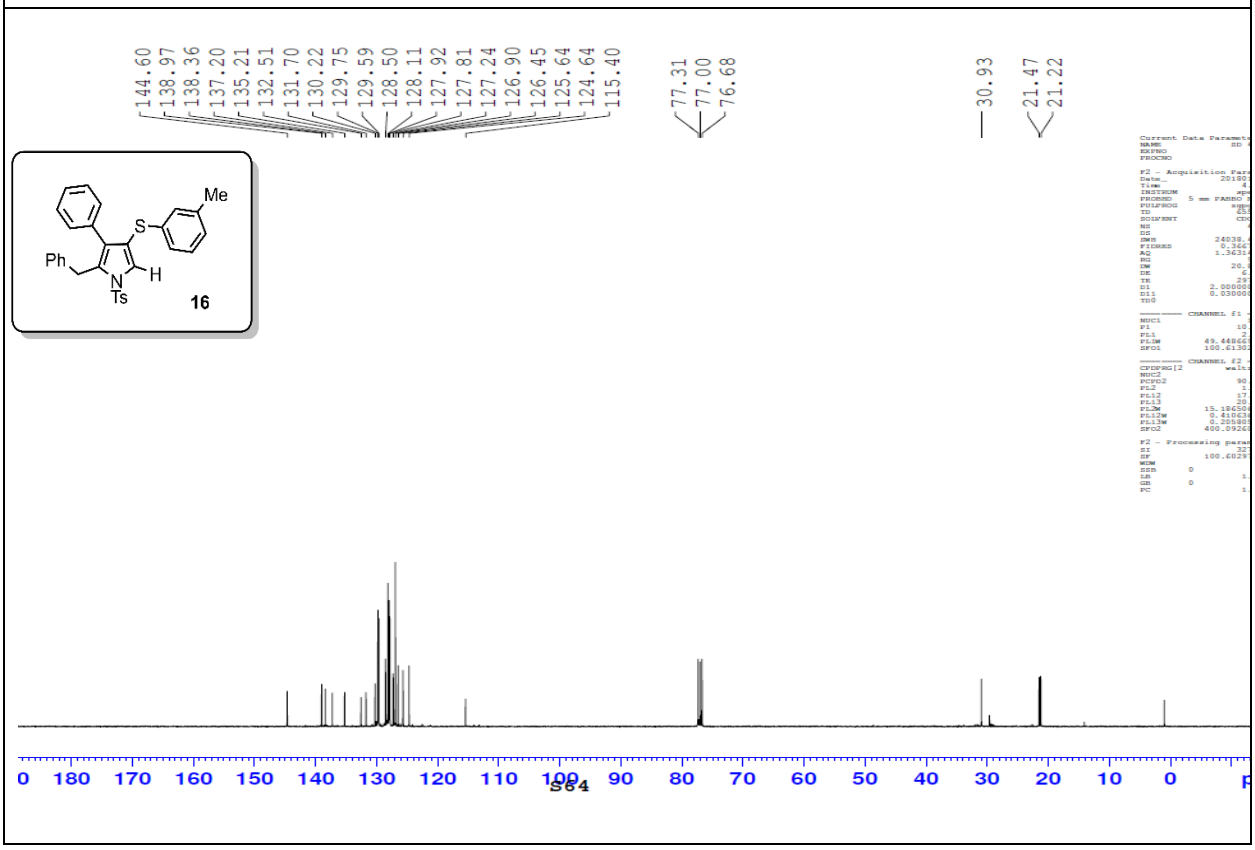
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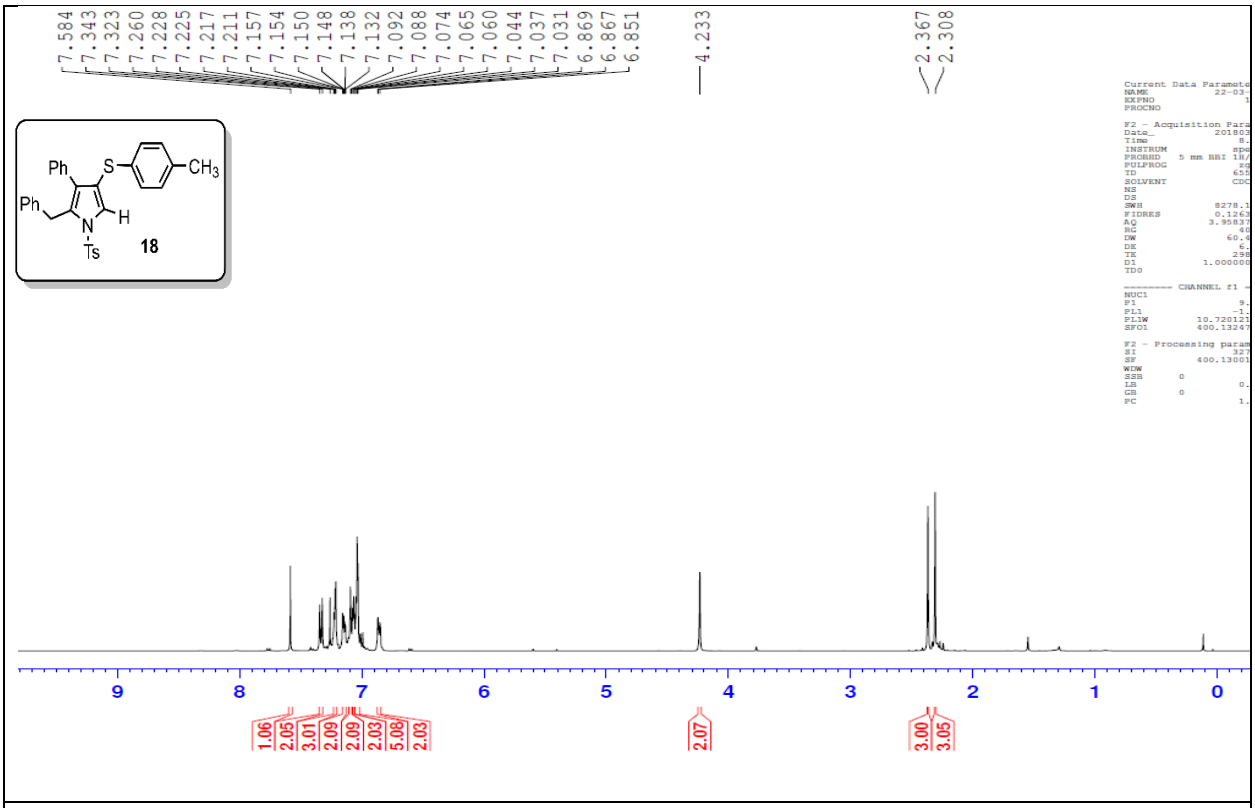
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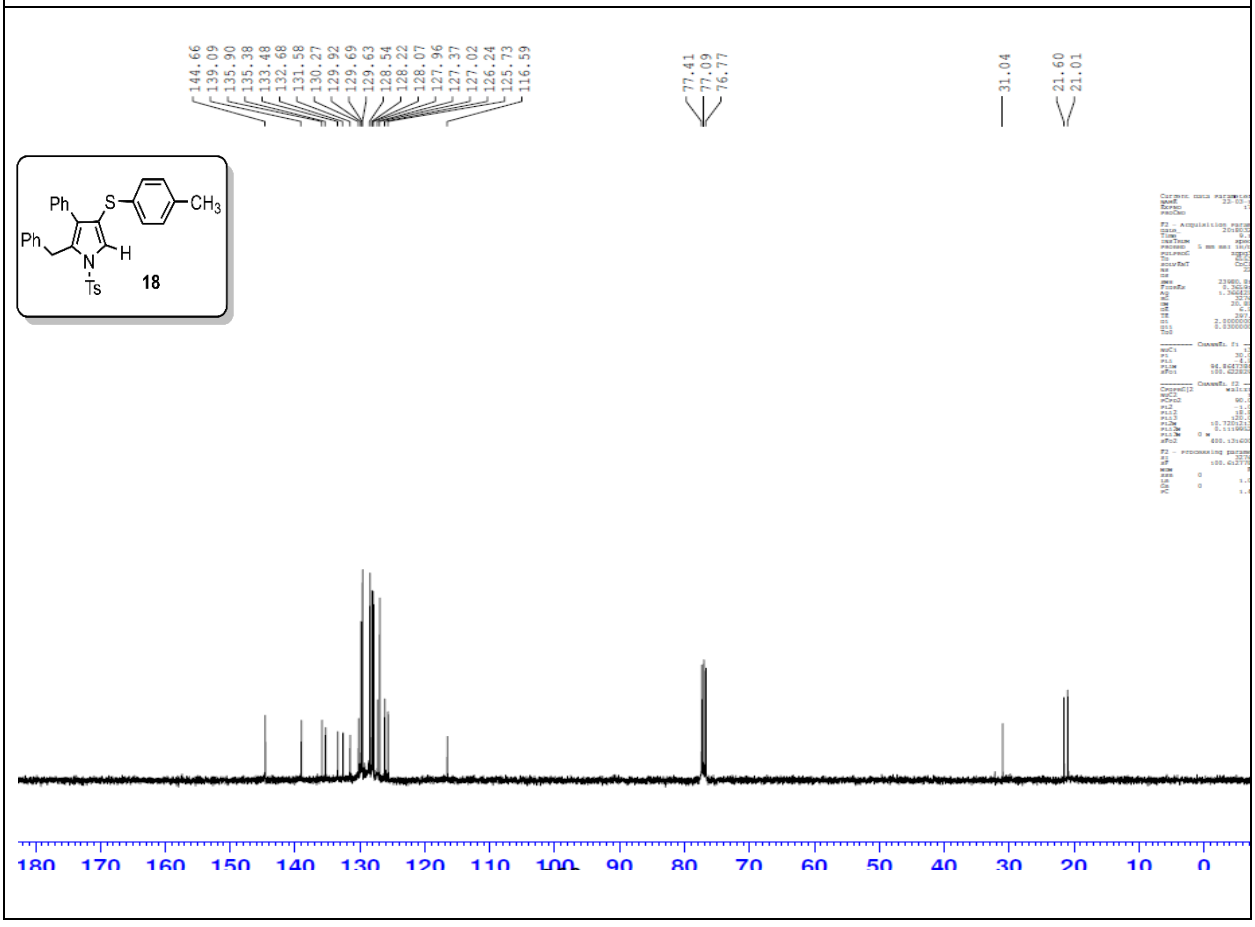
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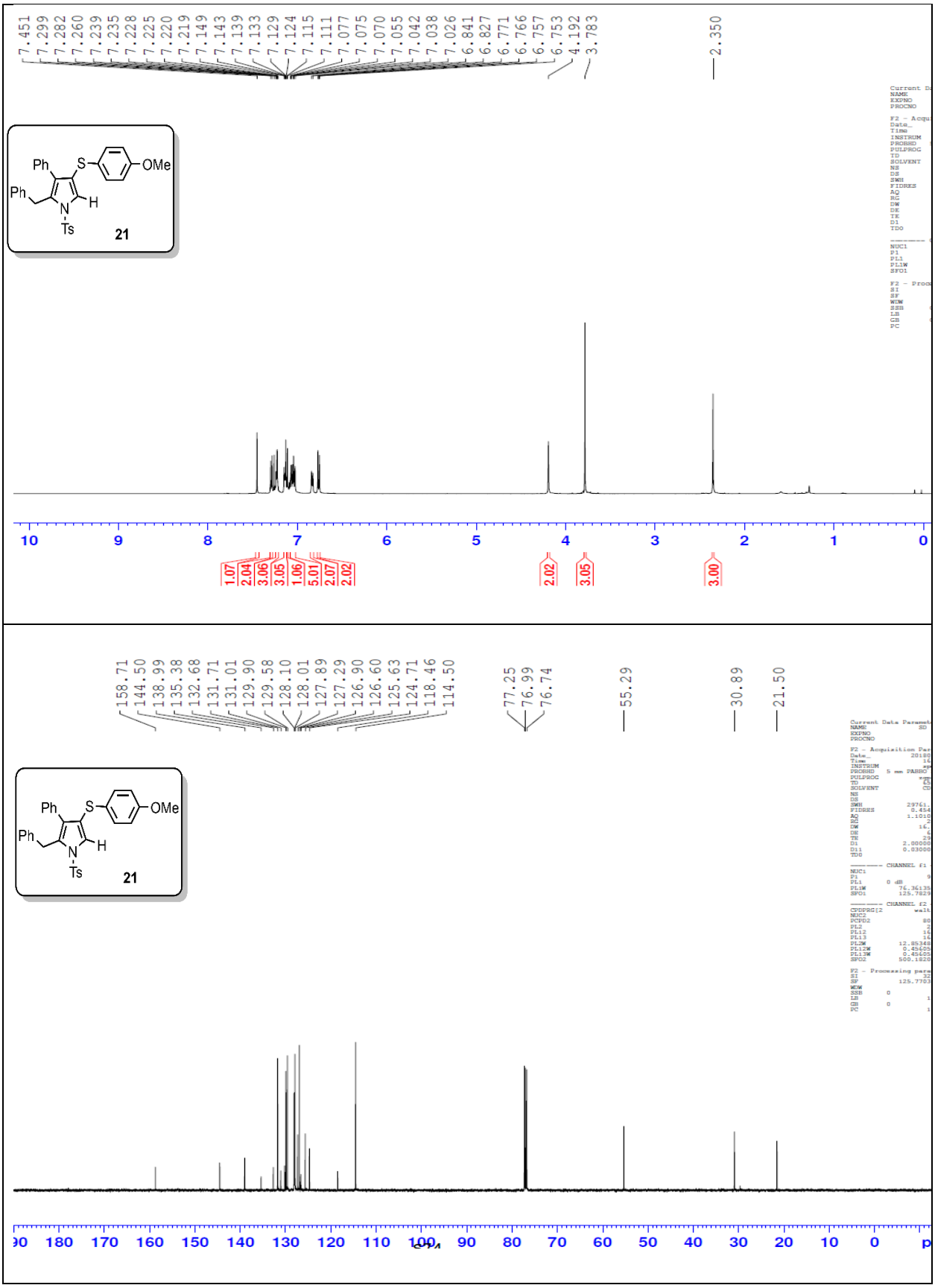
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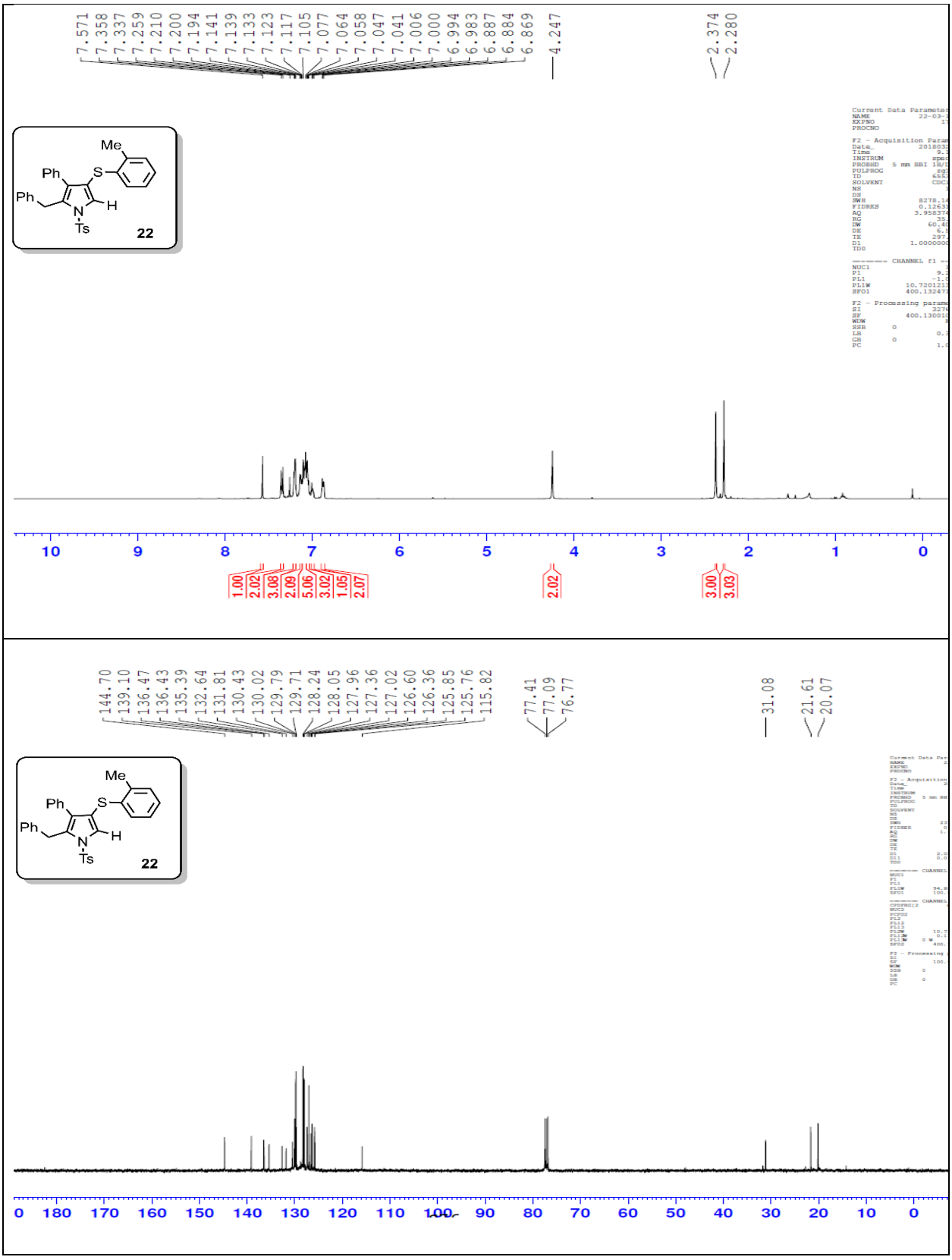
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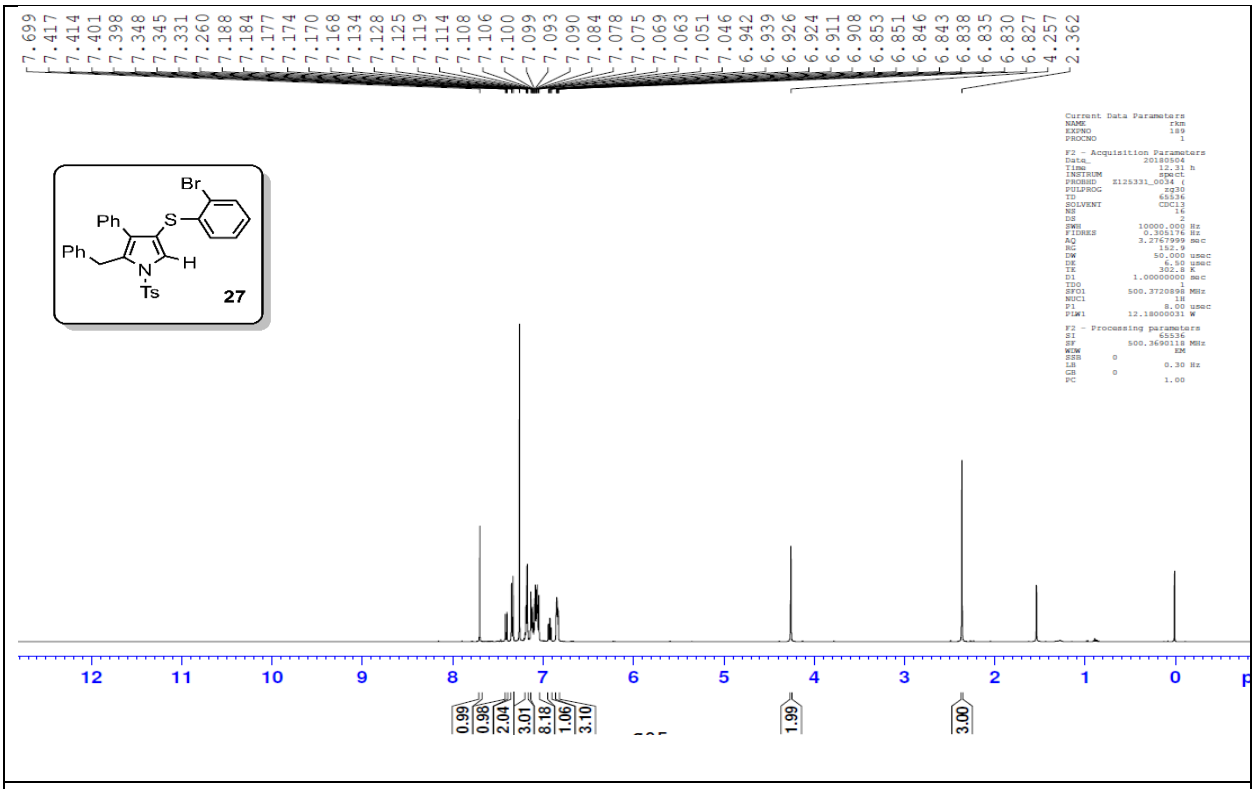
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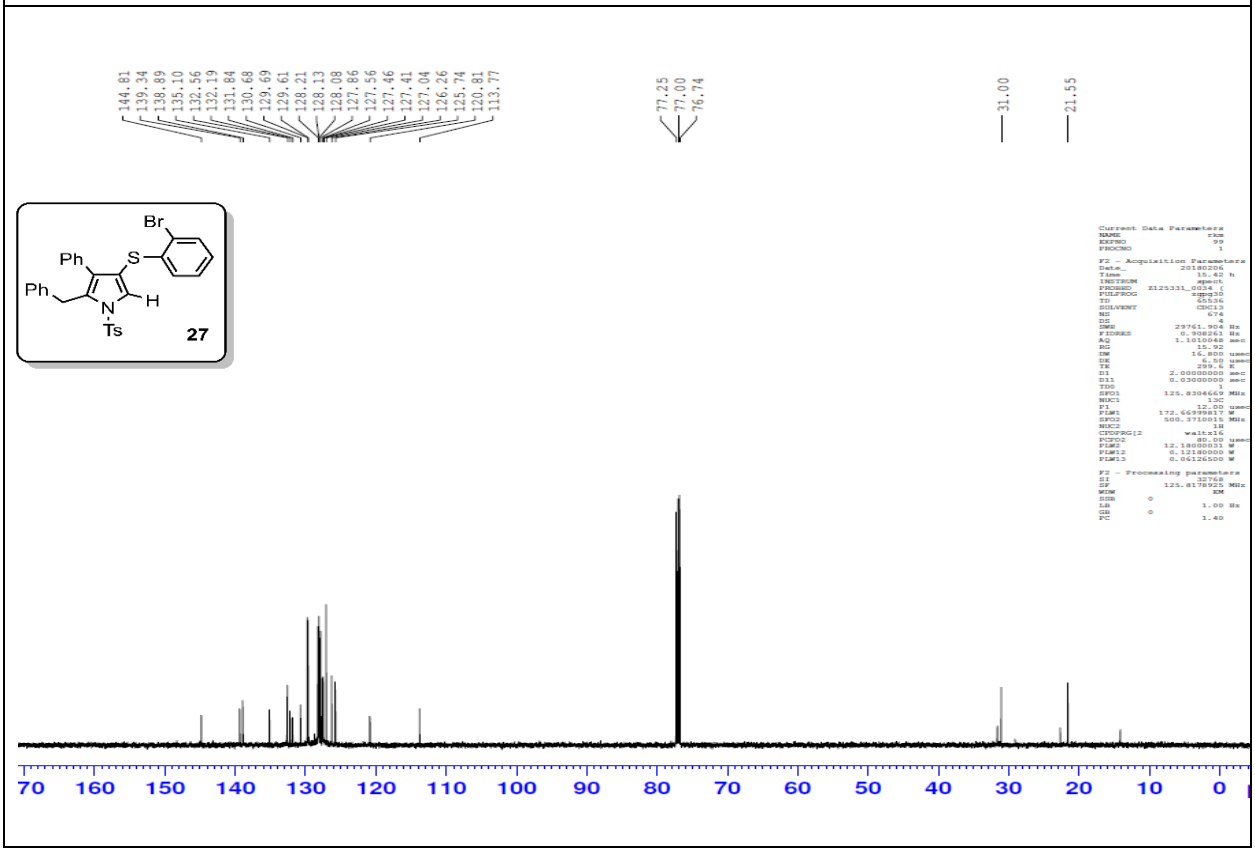
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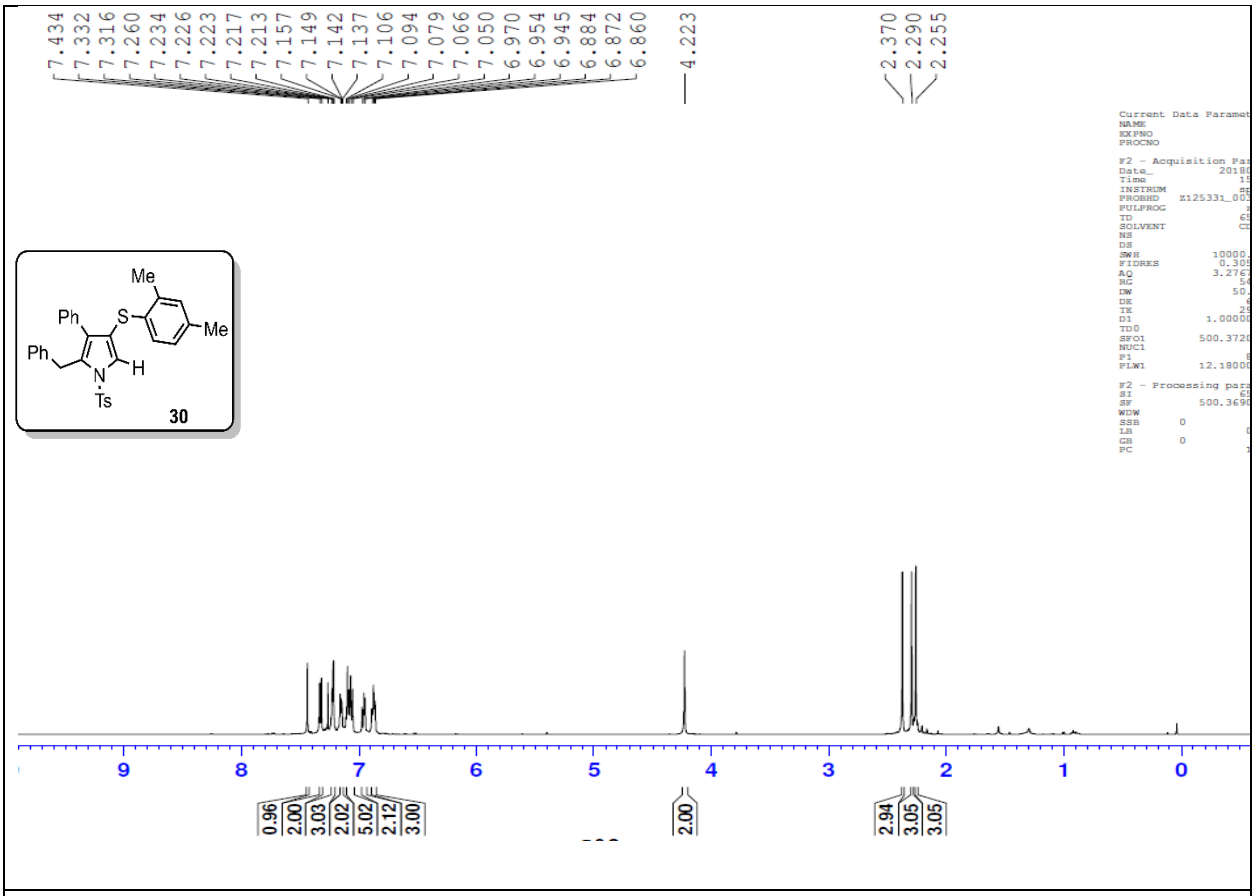
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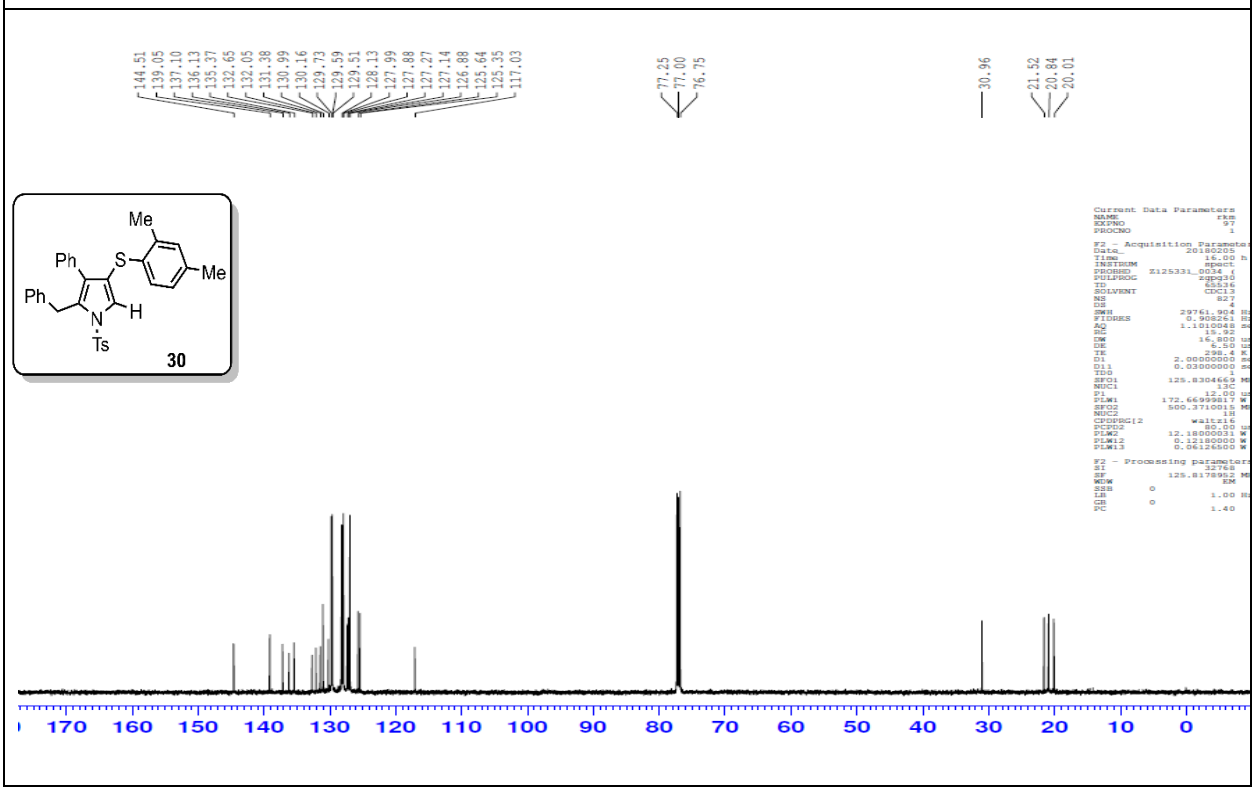
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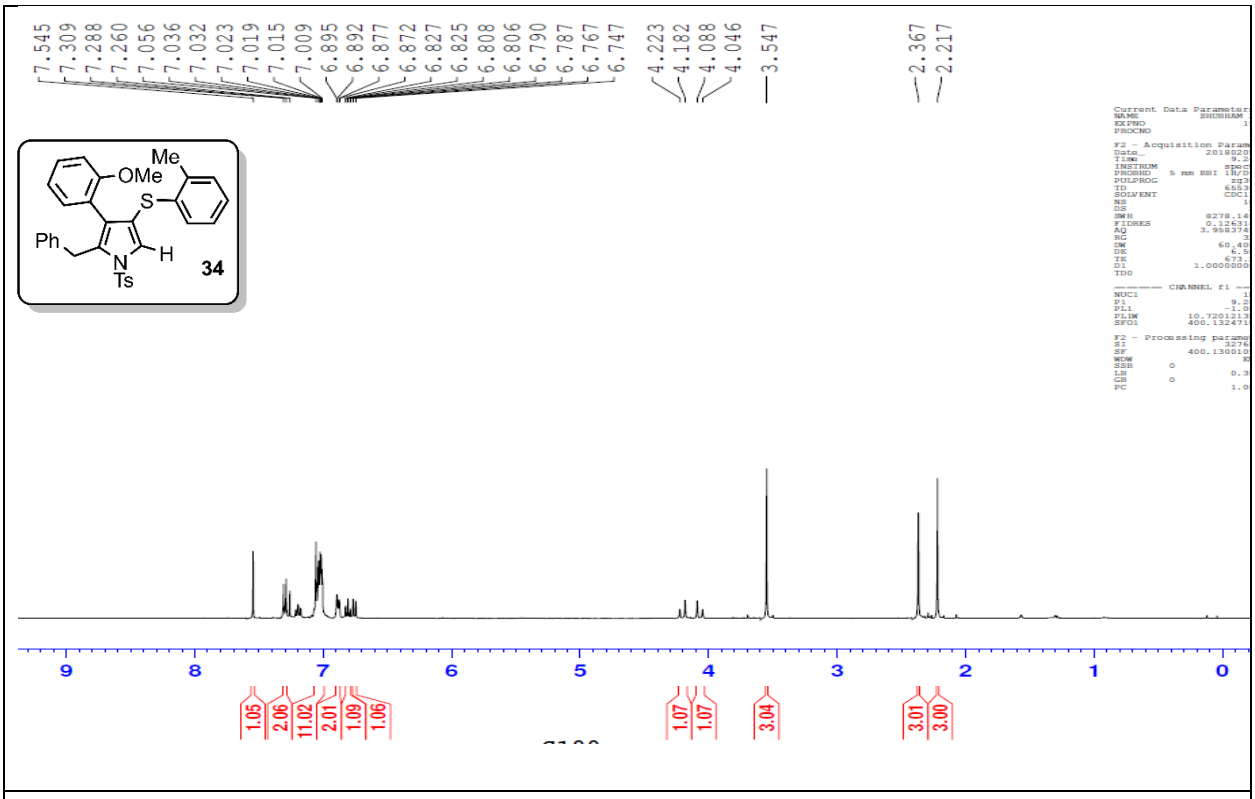
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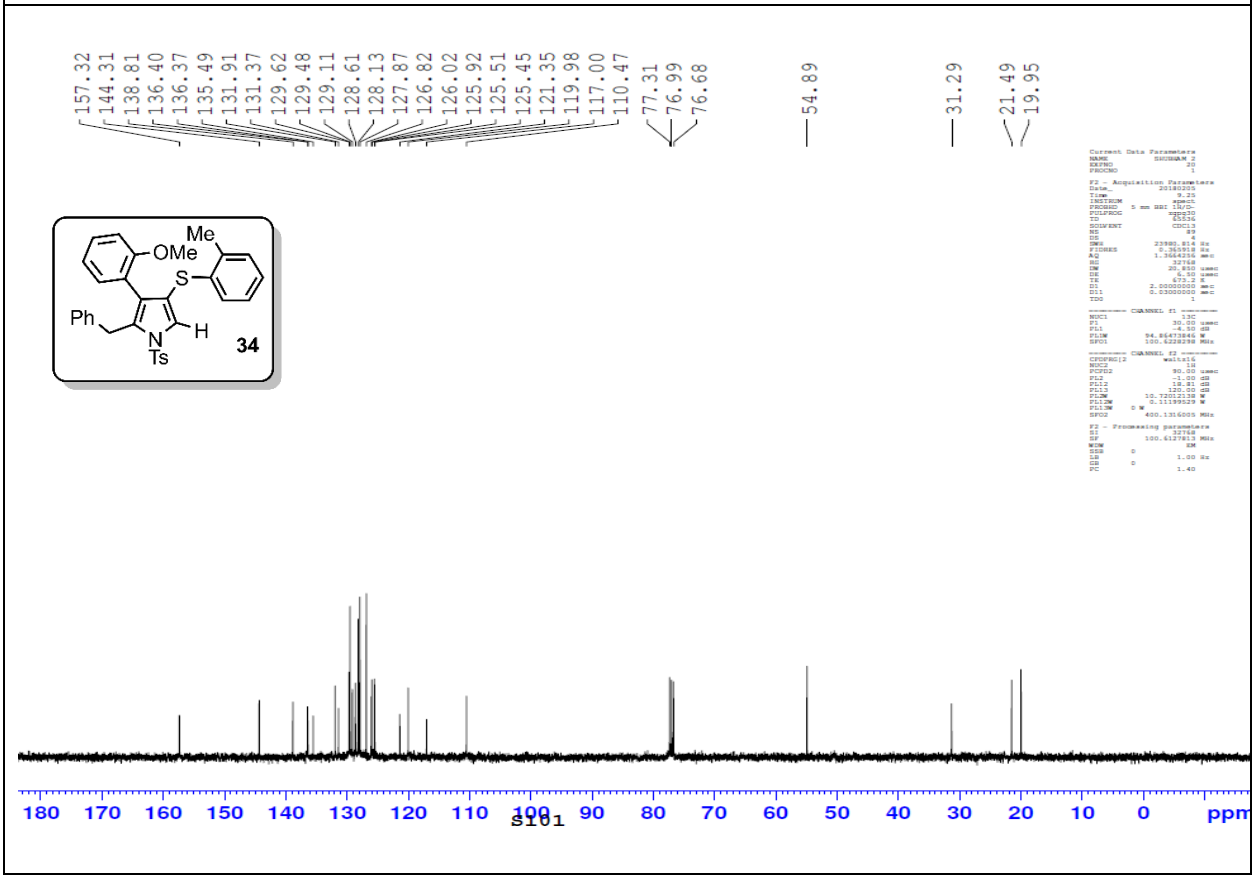
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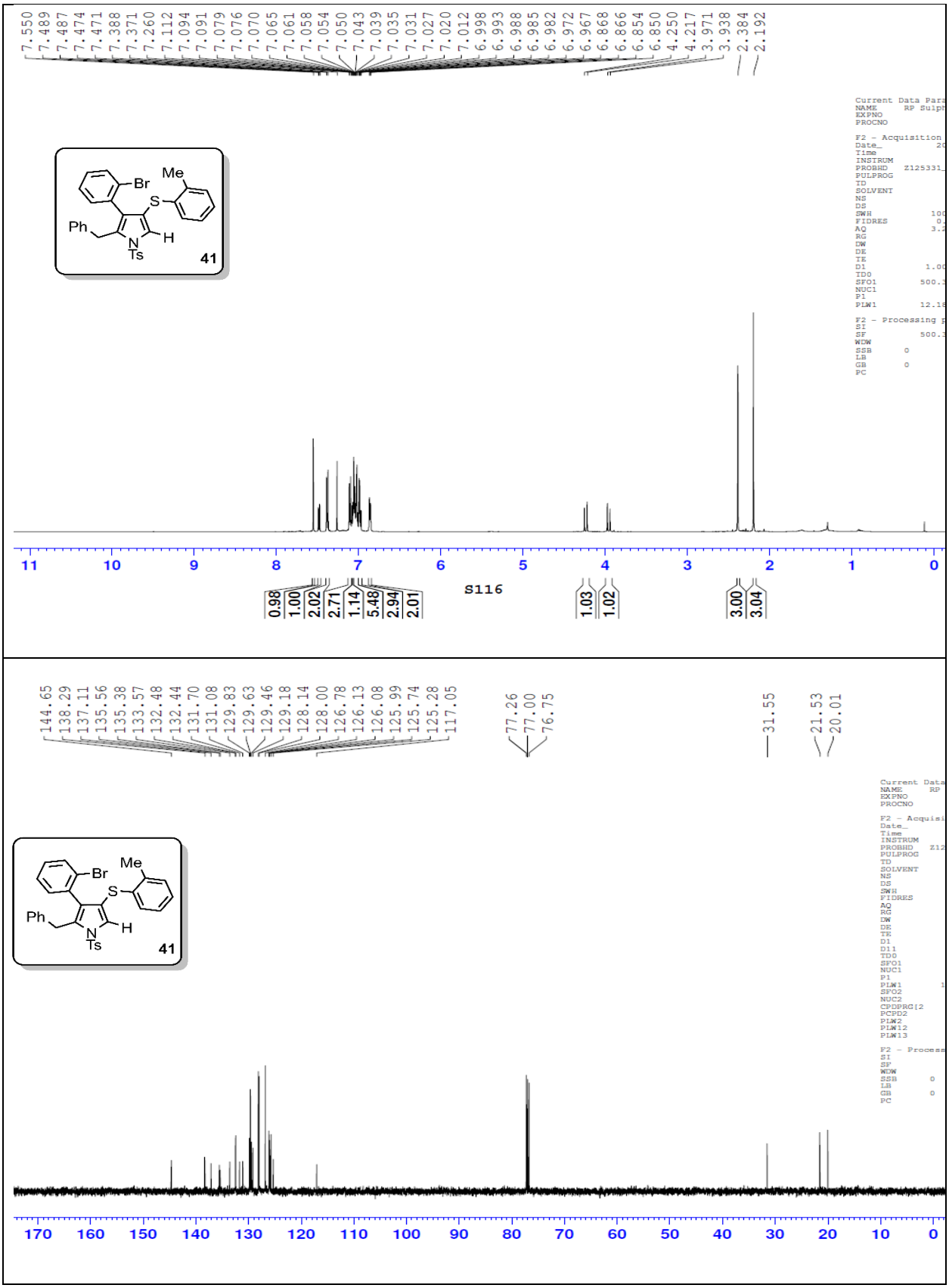
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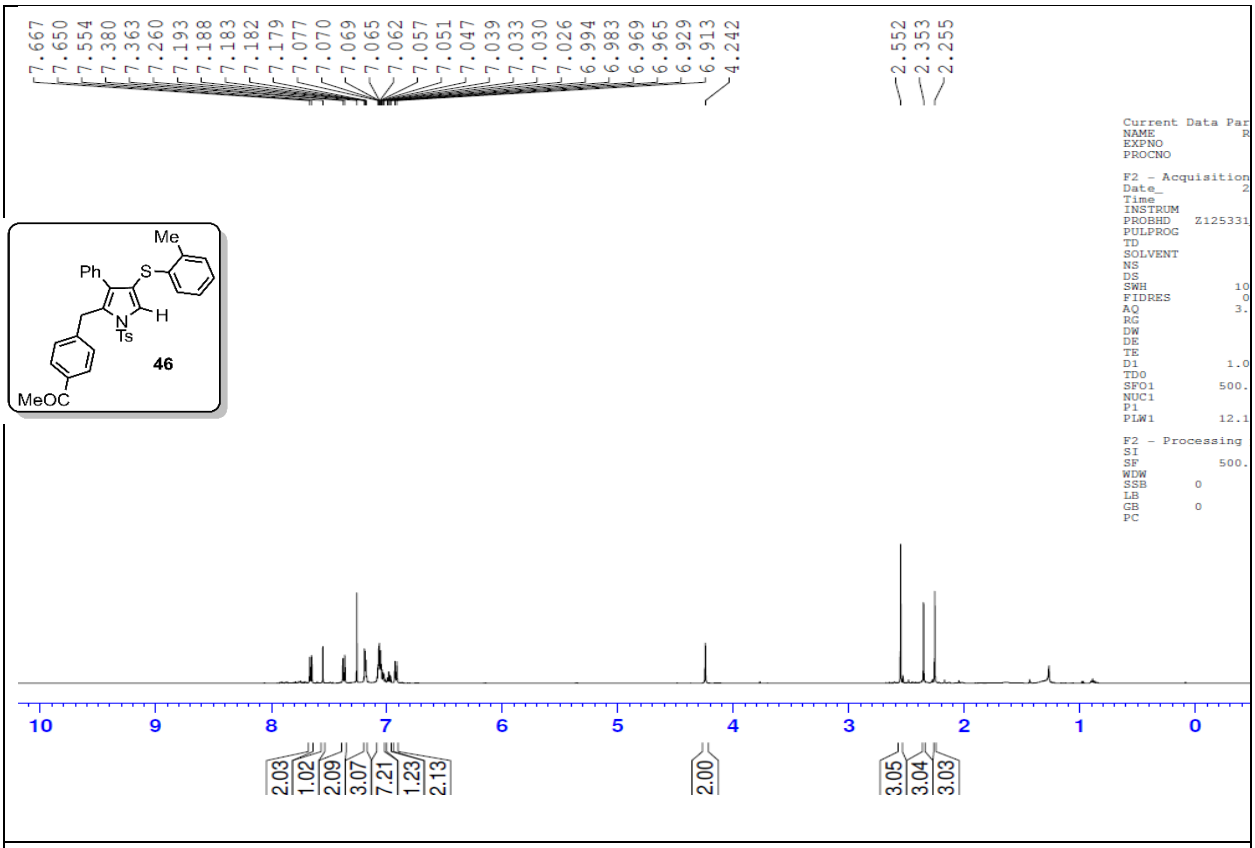
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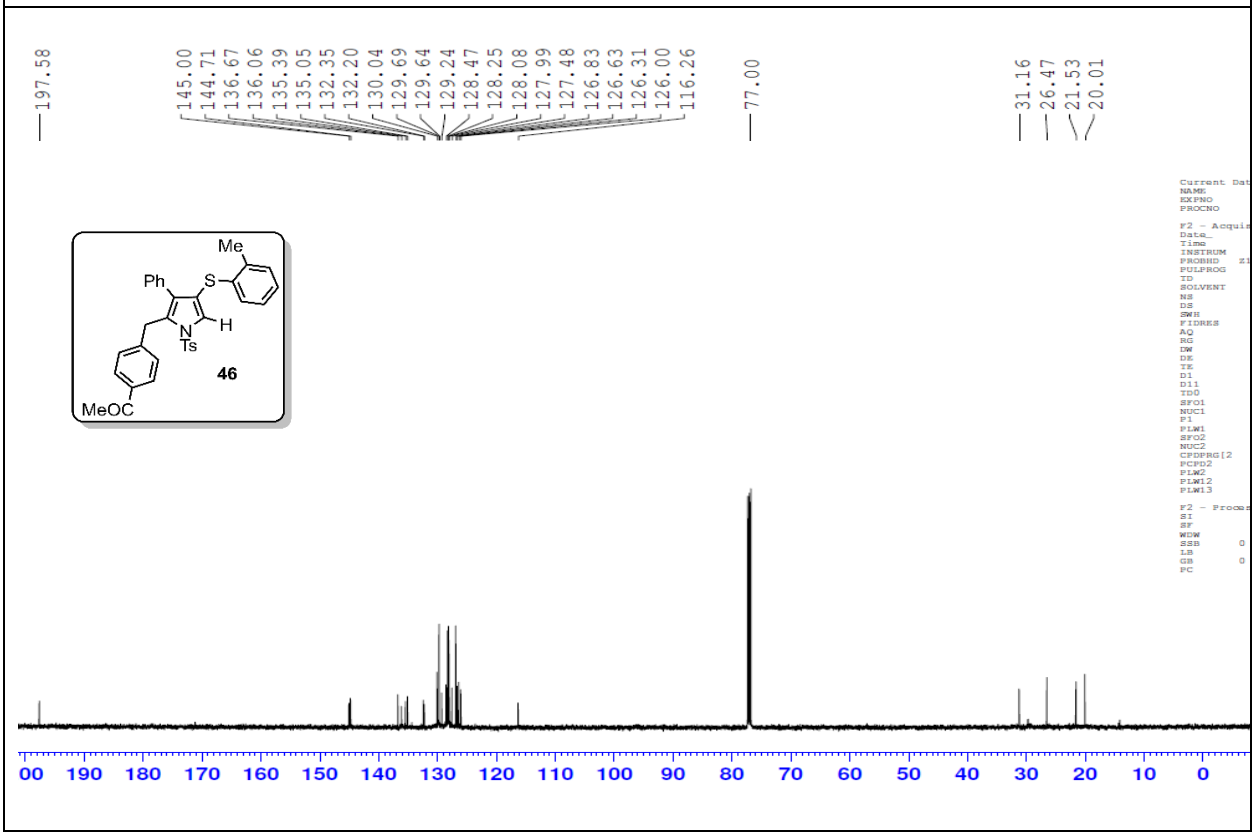
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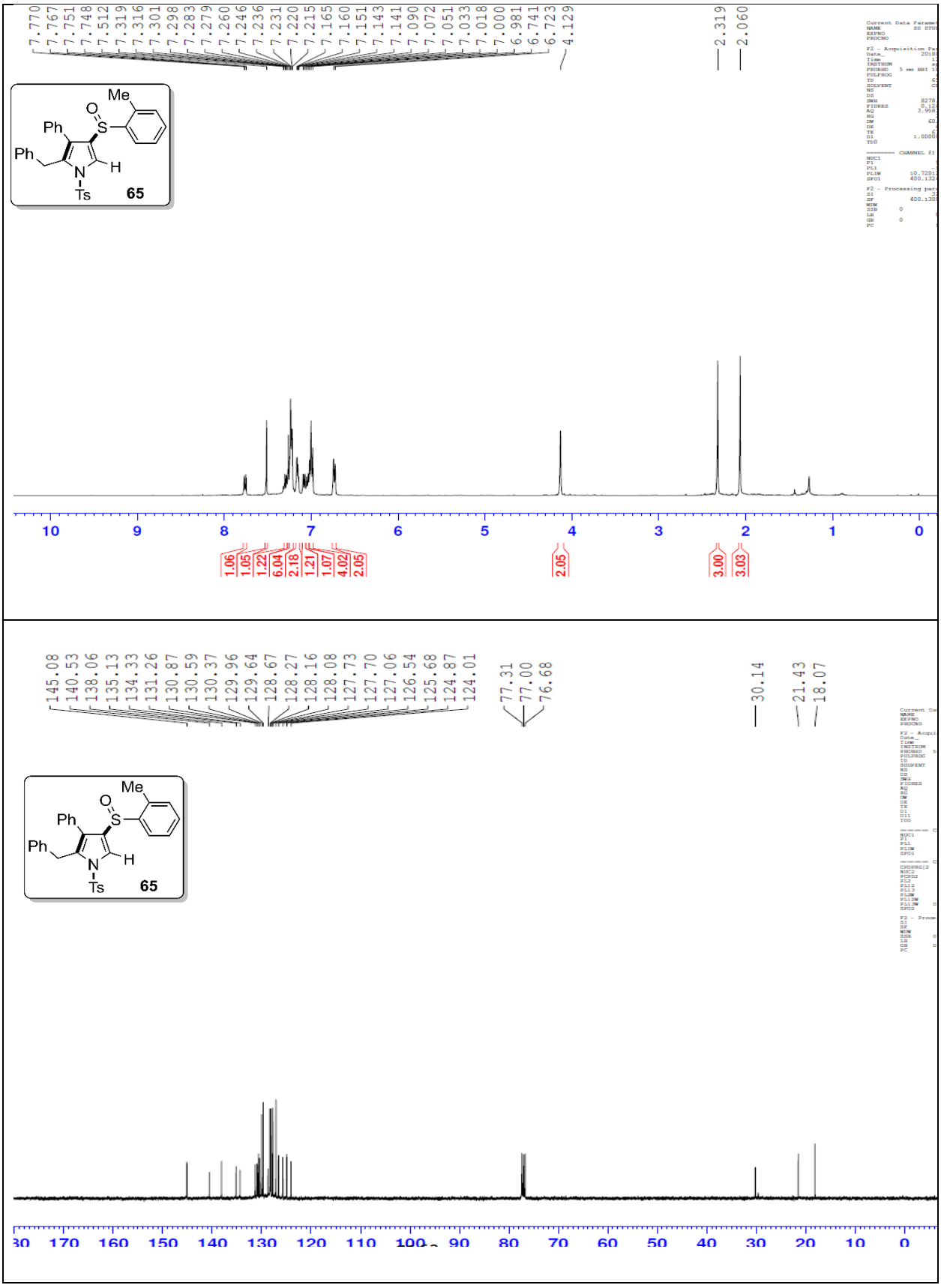
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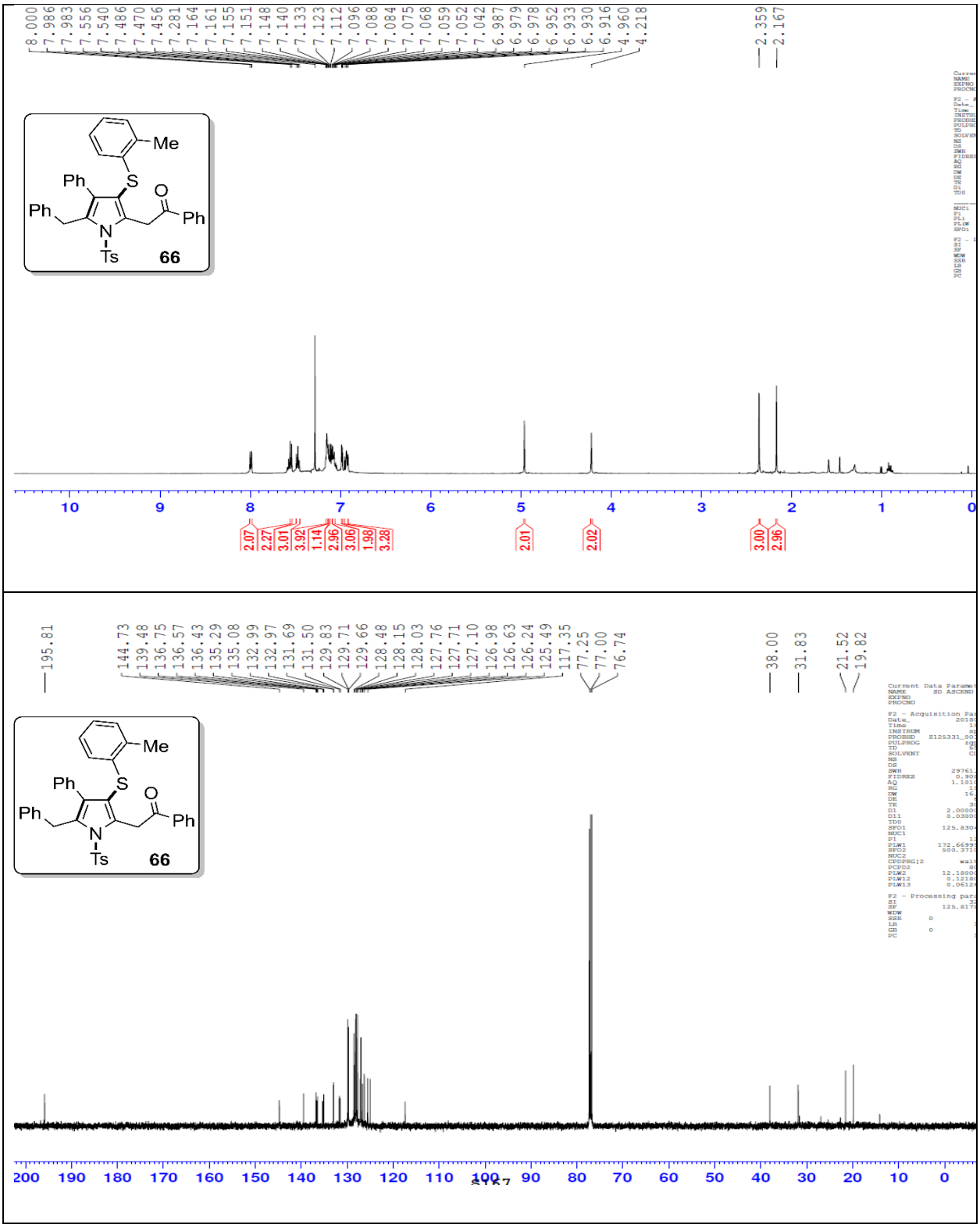
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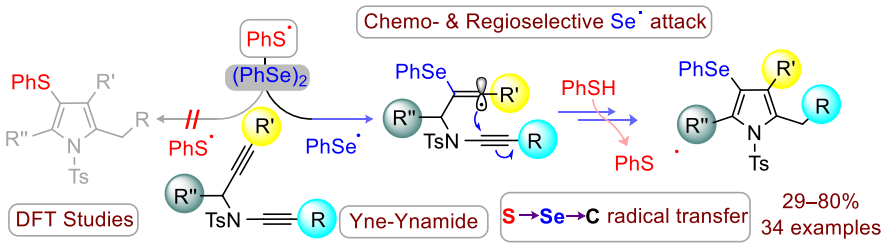
Chapter-2B

An Unconventional Sulfur-to-Selenium-to-Carbon Radical Transfer: Chemo-and Regioselective Cyclization of Yne-Ynamides

Abstract



An uncommon sulfur→selenium→carbon radical transfer process is herein developed to showcasing the unprecedented selenyl radical-mediated regioselective cyclization of yne-tethered-ynamides. Density functional theory studies and HRMS establish the reactivity scale between thiyl and selenyl radicals. The unique features of this transformation include, 1) the chemoselective reactivity of RSe• over RS•, 2) regioselective RSe• attack on alkyne over ynamide, 3) 5-*exo*-dig cyclization of yne-ynamide to unusual 4-selenyl-pyrroles, and 4) green synthetic method. The reaction of methyldiselenide with yne-ynamides to methylselenopyrroles is also described.

Reference

S. Dutta, B. Prabagar, R. Vanjari, V. Gandon, A. Kumar Sahoo. *Green Chem.*, **2020**, *22*, 1113–1118.

2B.1. Introduction

Selenium (Se) is a micronutrient essentially found in natural products, amino acids, and proteins.[1] Se-bearing heteroaryls are invaluable building blocks exhibiting distinct chemical, physical, and biological properties of pharmaceutical relevance.[2] Therefore, green synthetic methods that allow the rapid introduction of Se into heteroaromatic scaffolds are highly desirable.

In this regard, the binary chalcogens $(RS)_2$ and $(RSe)_2$ have been used for diverse synthetic applications, primarily including the homo-difunctionalization of unactivated olefins and alkynes.[3] Another notable application is the hetero-difunctionalization of olefins and alkynes that involves the dominance of two reactive radical species, PhSe• and PhS•, through sequential radical transfer: Se• →S• →C• , via the attack of PhS• to olefin or alkyne (**Figure 2B.1**). These reactions are dependent on the preferential reactivity of PhS•, with the rate constant for the addition to the unsaturated system being 10–50 fold higher than that of PhSe•. Surprisingly, a reverse S• →Se• cross-radical transfer to promote the addition of PhSe• radicals to unsaturated bonds remains unexplored (**Figure 2B.1**).

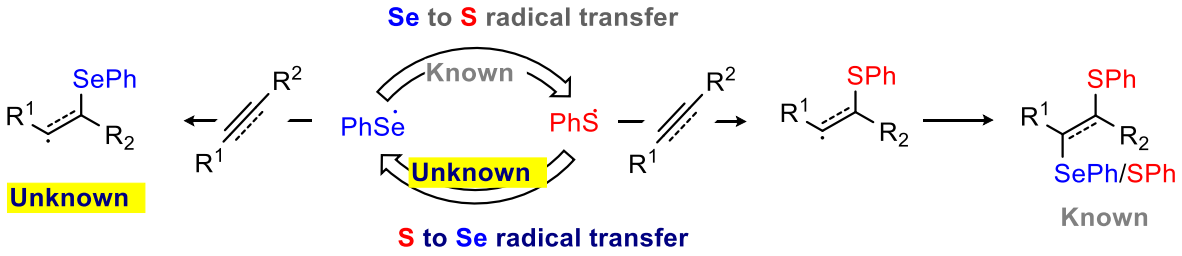


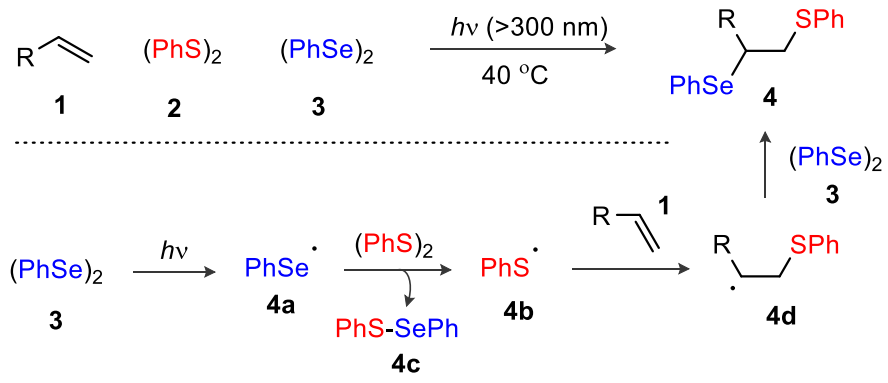
Figure 2B.1. Background of Se to S radical transfer

2B.2. Precedents

2B.2.1. Radical reaction of alkynes involving sequential Se• →S• →C• radical transfer:

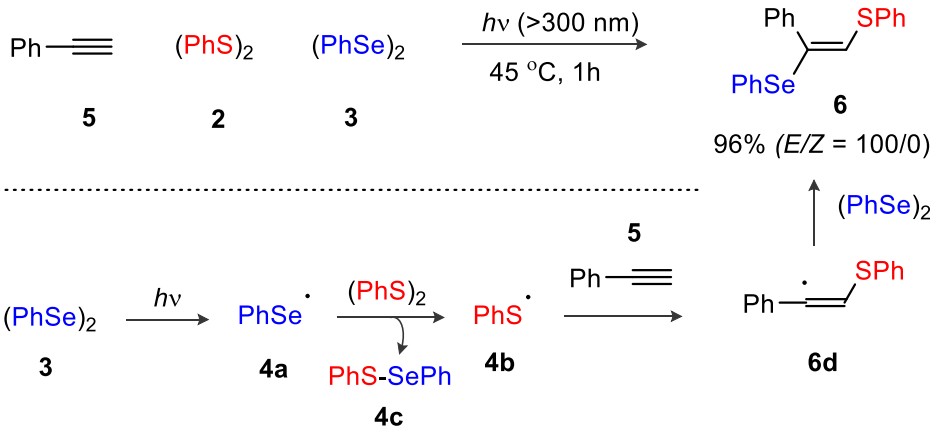
Back in 1992, Sonoda and coworker reported a light mediated thioselenation of olefins **1** when exposed to disulfide-diselenide species (Scheme 2B.1)[2a]; the reaction is highly selective. At first, homolytic cleavage of diphenyldiselenide **3** generates PhSe-radical **4a**, which undergoes radical transfer in presence of diphenyldisulfide **2** to give PhS-radical

4b with the elimination of by-product PhS-SePh **4c**. Next, attack of **4b** to the less hindered side of olefin **1** leads to int-**4d**. Quench of int-**4d** with diphenylselenide **3** yields product **4**; the reaction is highly regioselective.



Scheme 2B.1. Thioselenation of olefins

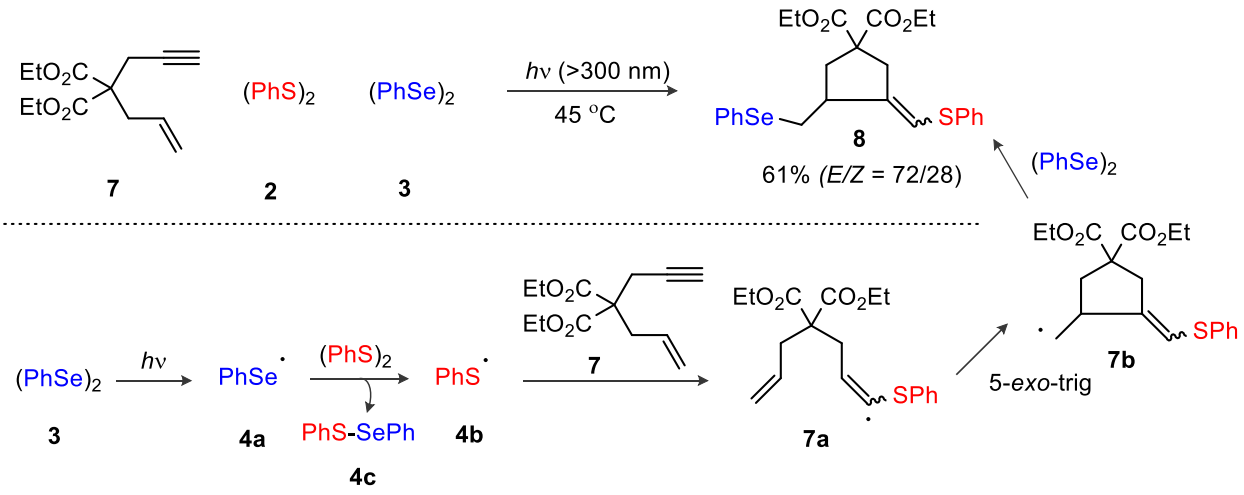
Later in 1998, the Sonoda group used mixed chalcogen for thioselenation of terminal alkynes **5** leading to *E*-thioselenated olefins **6** major product (**Scheme 2B.2**)[2b]. The reaction follows identical pathway shown in Scheme 2B.1. Once again, radical attack to alkyne happens from less crowded side.



Scheme 2B.2. Thioselenation of terminal alkynes

Likewise, a mixed-chalcogen mediated Se-radical triggered cyclization of 1,6-enyne **7** has also been demonstrated (**Scheme 2B.3**)[2b]. As described in Scheme 2B.3, the PhS-radical generated attacks to the alkyne over olefin of 1,6-enyne **7** to provide int-**7a**. Next,

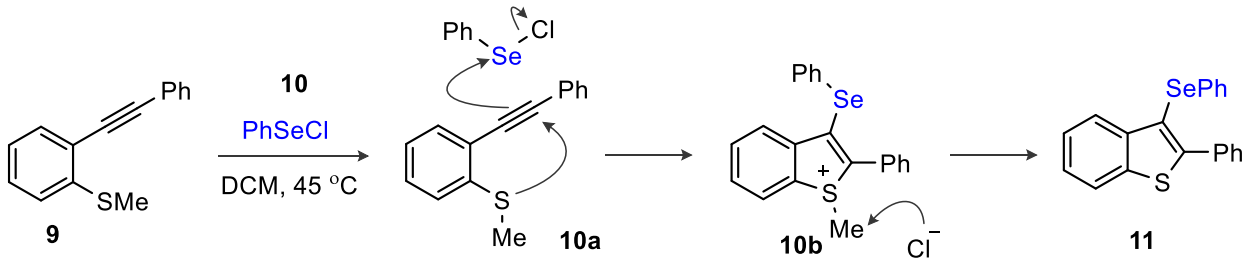
intramolecular 5-*exo*-trig radical cyclization of **7a** with the tethered olefin furnishes the cyclized radical int-**7b**. Finally quench of **7b** with dipheyldiselenide yields the cyclized thio-selenated product **8**.



Scheme 2B.3. Thioselenation of enynes via 5-*exo*-trig radical cyclization

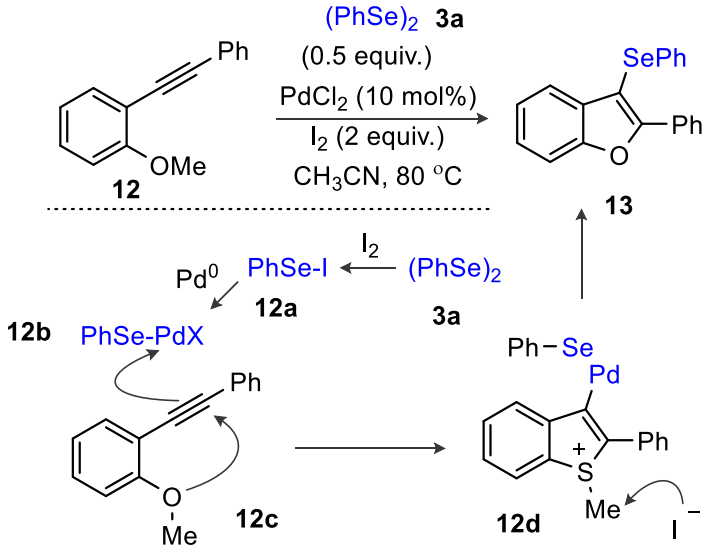
2B.2.2. Existing route for selenylated small heterocycles

An electrophillic cyclization of *o*-thiophenylalkyne moiety **9** in presence of PhSeCl **10** has directly led to selenyl-benzothiophene **11** (**Scheme 2B.4**).[4] Alkyne activation by PhSeCl followed by the intramolecular SMe attack provides **10b** via **10a**. The chloride ion triggered demethylation of **10b** finally produces **11**.



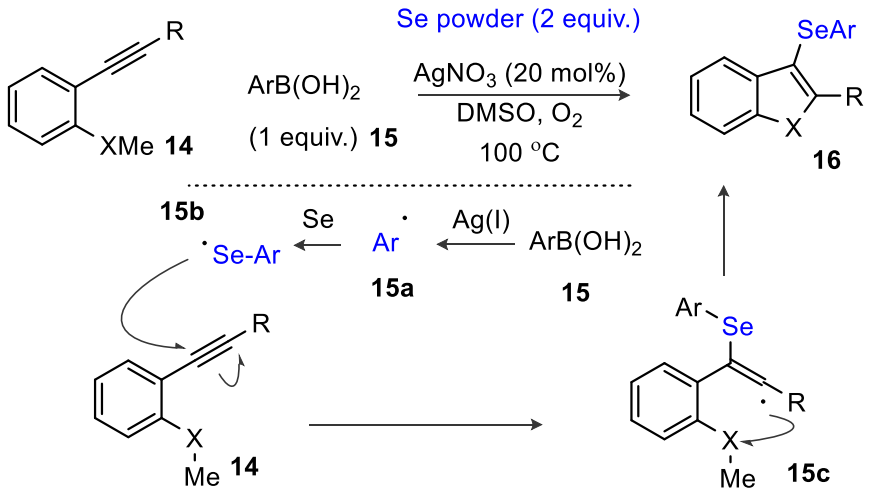
Scheme 2B.4. Synthesis of 2,3-disubstituted benzo[*b*]thiophene via electrophillic cylization

An iodine promoted Pd-catalzed electrophillic annulation of 2-alkynylphenol derivatives **12** was disclosed by Li and coworker in 2009 (**Scheme 2B.5**).[5] Oxidative addtion of PhSe-I, generated in-situ from diphenyldiselenide (**3a**) in presence of iodine, with Pd(0) species at firs give selenyl-Pd complex **12b**. Under the influence of **12b**, electrophillic cyclization of **12** occurs to deliver int-**12d**. Finally, iodide mediated demethylation of **12d** and concomitant reductive elimination yields the β-selenylated benzofuran **13**.



Scheme 2B.5. Iodine promoted electrophilic annulation of 2-alkynylphenol

The Liu group disclosed an elegant strategy for the synthesis of selenylated benzofuran/thiophene derivatives when **14** was exposed to selenium powder (**Scheme 2B.6**).[6] At first, $ArB(OH)_2$ **15** undergoes oxidation in presence of $AgNO_2/O_2$ to give aryl radical **15a**. Next, trap of aryl radical with Se powder generates an aryl selenium radical **15b**. The addition of radical **15b** to 2-alkynylanisole (or 2-alkynylthioanisole) furnishes intermediate **15c**. Finally, cyclization of **15c** produces the desired product **16** along with the oxidative conversion of methyl radical into formaldehyde.



Scheme 2B.6. Selenium radical mediated cascade cyclization; X= O/S

2B.3. Motivation and Scheme Design

A reverse S• →Se• cross-radical transfer to promote the addition of PhSe• radicals to unsaturated bonds remains unexplored. To address this challenge, we intend to examine the selenyl radical triggered cyclization of yne-ynamides. In presence of both diphenyldiselenide and alkyne, an arylthiyl radical generated from aryl-thiol was expected to generate PhSe-radical (Path II, **Figure 2B.2b**) rather than addition to the alkyne species A (Path I, **Figure 2B.2b**). The S• →Se• radical transfer was anticipated through the interaction of PhS• at a low concentration with $(PhSe)_2$; which to our knowledge is revealed for the first time. Moreover, organic solvents and toxic transition-metals are being largely used in the synthetic transformations, which ultimately poses serious concern to the environment as well as the human body. Thus, the development of organic reactions in the absence of these reagents have aroused intensive interest.

Thus, a reverse S• →Se• cross-radical transfer along with chemo- and regioselective cyclization of yne-tethered ynamides, which have been used for diverse cyclization/cycloisomerization processes to construct complex N-heterocycles,[7] is envisioned.

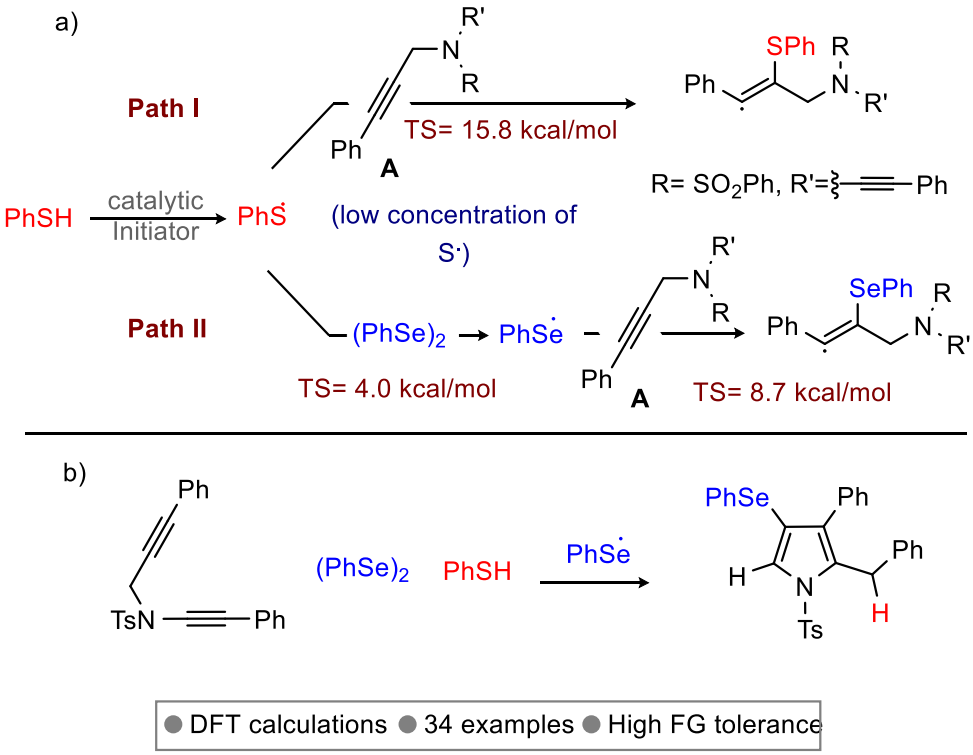


Figure 2B.2. a) Strategy: S to Se radical transfer; b) chemo and regioselective selenyl radical attack to yne-ynamides

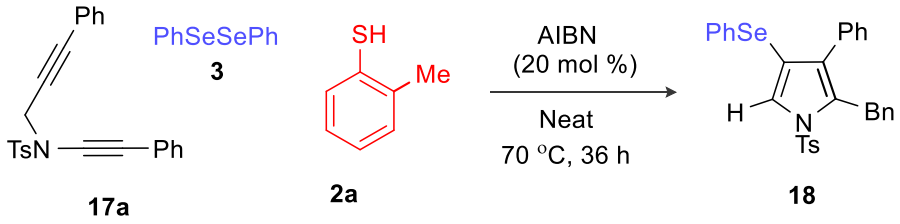
2B.4. Result and Discussion

2B.4.1. Reaction Optimization

To begin with, a reaction between 4-methyl-N-(phenylethynyl)-N-(3-phenylprop-2-yn-1-yl)benzenesulfonamide **17a**, $(PhSe)_2$ **3**, and *o*-tolylthiol **2a** was considered (**Table 2B.1**). Extensive screening of various radical initiators and solvents led us to the optimized conditions [**17a**, **3** (2.5 equiv), **2a** (2.0 equiv), and AIBN (20 mol%) in neat condition at 70 °C] and the cyclized product **18** was isolated in 72% yield (entry 1). The reaction was less effective in DCM solvent (entry 2). The product yield was affected when low amount of **3** and **2a** was used (entries 3 and 4). The initiators like 20 mol% NHPI (N-hydroxy phthalimide), $K_2S_2O_8$ were moderate providing 45% and 67% yield of **18** (entries 5 and 6). The reaction was failed when conducted in the presence of TBHP (entry 7). The use of

catalytic amount **2a** (20 mol%) or in the absence of **2a,** the product was isolated in 12% and trace amount, respectively (entries 8 and 9).

Table 2B.1. Optimization of reaction conditions[a,b]



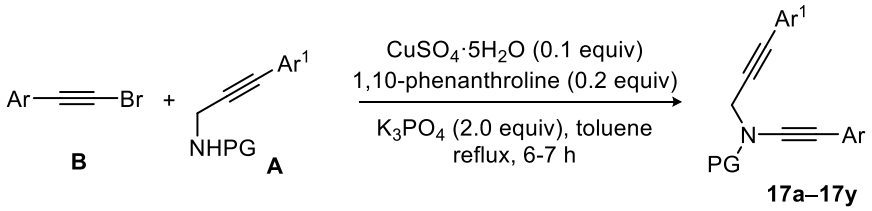
Sl. No	Daviation from standard condition	Yield
1	**None**	**72% (4a)**
2	CH_2Cl_2 as solvent	48% (**4a**)
3	1.2 equiv of **2a** & **3a**	43% (**4a**)
4	1.5 equiv of **2a** & **3a**	56% (**4a**)
5	20 mol% of NHPI instaed AIBN	45% (**4a**)
6	20 mol% of $K_2S_2O_8$ instaed AIBN	67% (**4a**)
7	1.5 equiv of TBHP	00% (**4a**)
8	20 mol% **3a** instead of 2 equiv	12% (**4a**)
9	without **3a**	00% (**4a**)

Optimization of the Reaction Conditions[a]. [a]Isolated yield. **17a** (0.2 mmol), **3** (0.5 mmol), **2a** (0.4 mmol), AIBN (0.01 mmol).

2B.4.2. Synthesis of Starting Materials

Following the known Cu-catalyzed C-N coupling procdure, ynamides **17a-17y** were synthesized from corresponding sulfonamides (A) and bromoalkynes (B) (Table 2B.1).

Table 2B.2. Ynamide chart



17a–17y

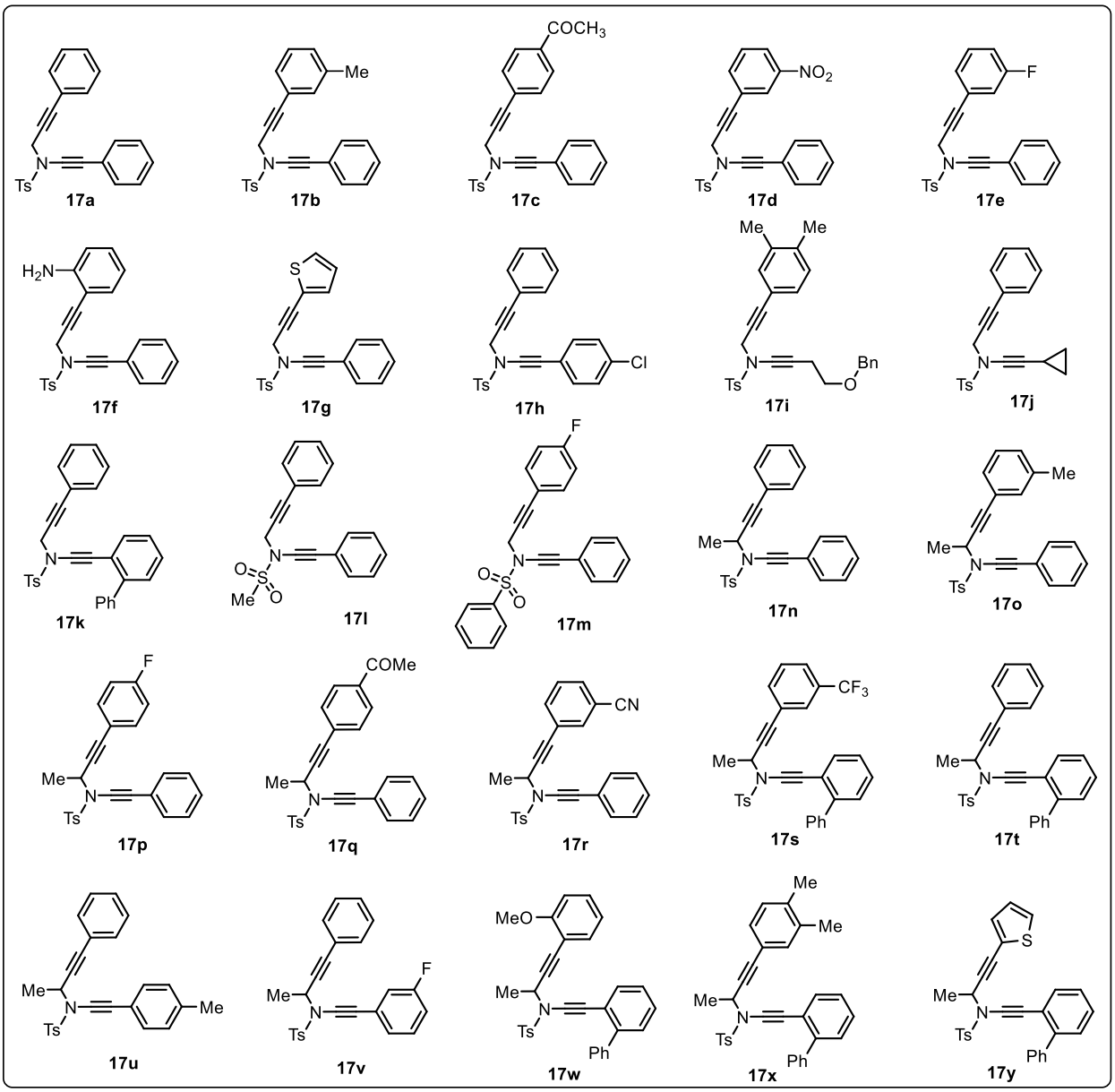
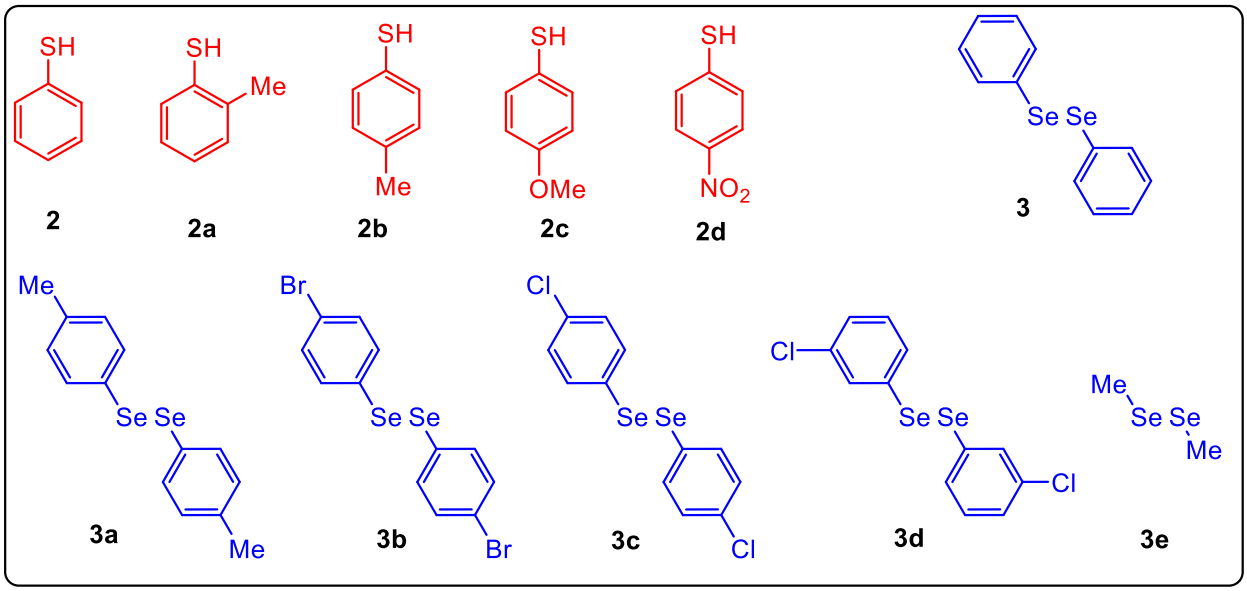
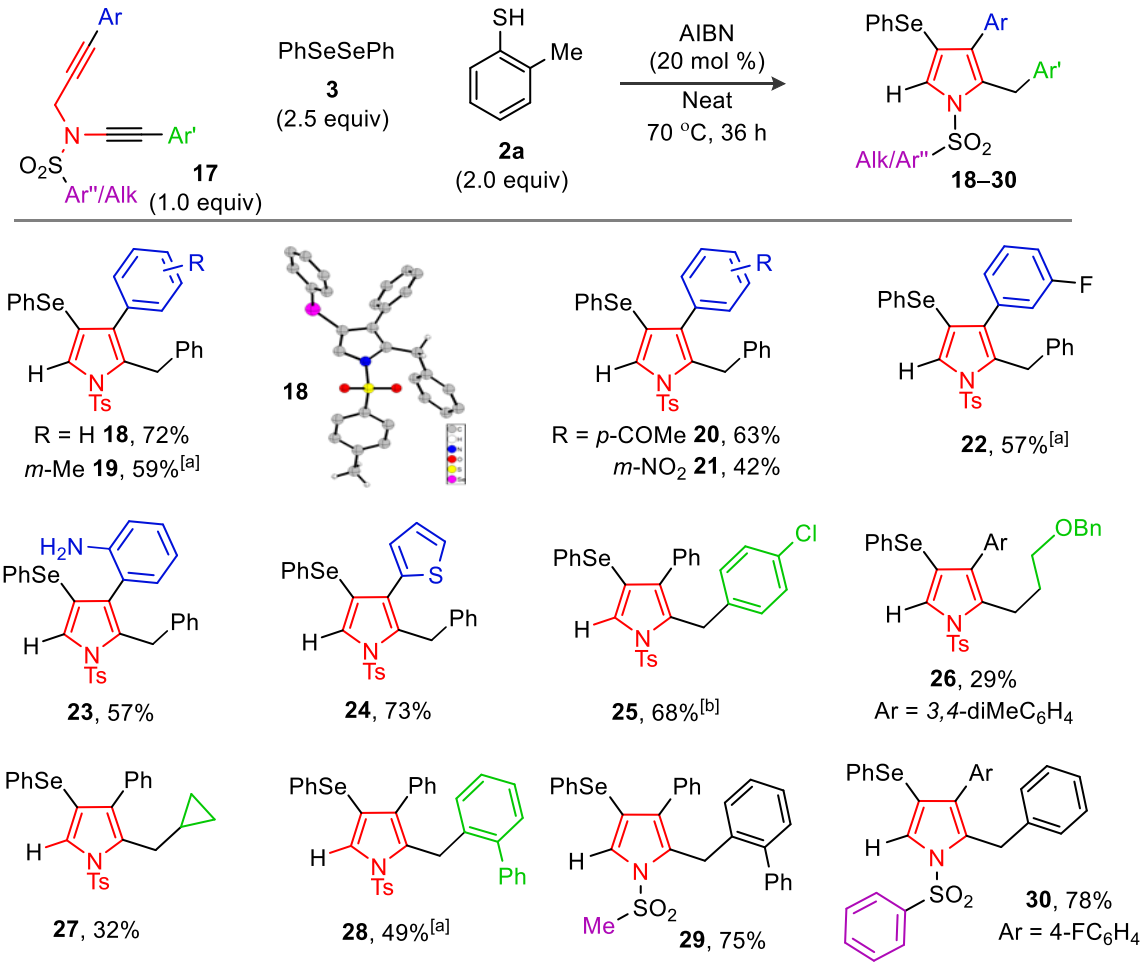


Table 2B.3. Aryl thiol and diselenide chart



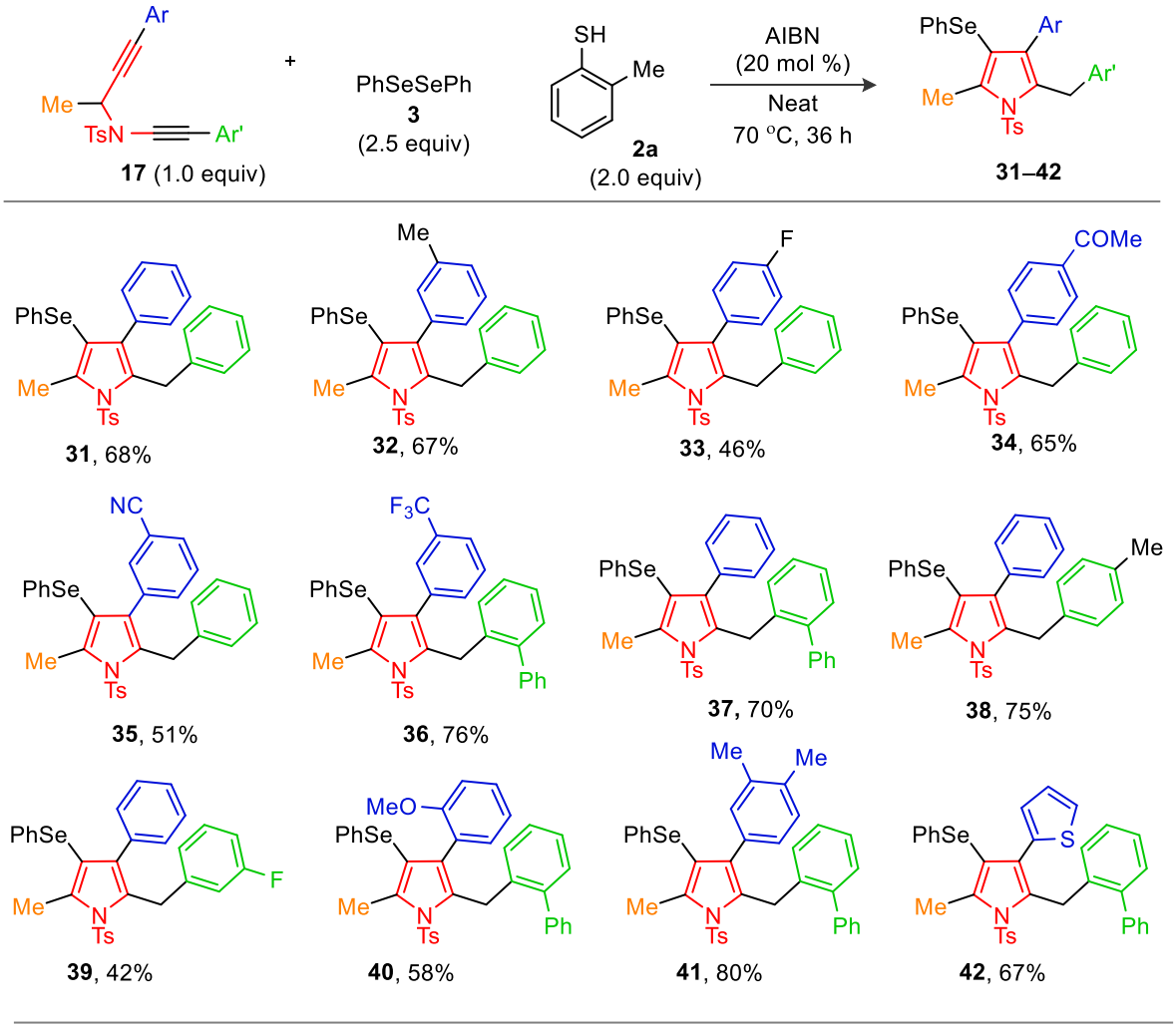
2B.4.3. Substrate Scope

The scope of Se• triggered cyclization of yne-ynamides under the established conditions (entry 1, **Table 2B.1**) for the construction of unusual peripheral substituted 4-selenylated pyrroles was investigated (**Scheme 2B.7**). To start with, the yne-ynamides having aryl substitutions at the propargyl terminus [electron-neutral phenyl, electron-rich (*m*-Me), and electron-poor (*p*-COMe, *m*-NO_2, *m*-F)] provided the desired products **18–22** (42–72%). An aniline substituted product **23** was obtained from **17f**; the free NH_2 group did not obstruct the reaction. Likewise, thienyl-substituted pyrrole **24** was synthesized in 73% yield. The electron distribution via inherent *N*-lone pair polarization of ynamide could possibly affect the reaction outcome. Thus, the Se• triggered cyclization of yne-ynamides having electronic variation of substituents at the ynamide terminus was next investigated (**Scheme 2B.7**). The 4-selenylated pyrrole **25** was fabricated from **17h** having aryl substitutions (*p*-Cl). The cyclization of **17i** with a O-benzyl protected flexible alkyl group at the ynamide terminus afforded **26**, albeit in 29% yield. A noteworthy observation is the synthesis of *N*-Ts-protected pyrrole **27** (32%) with a cyclopropyl motif



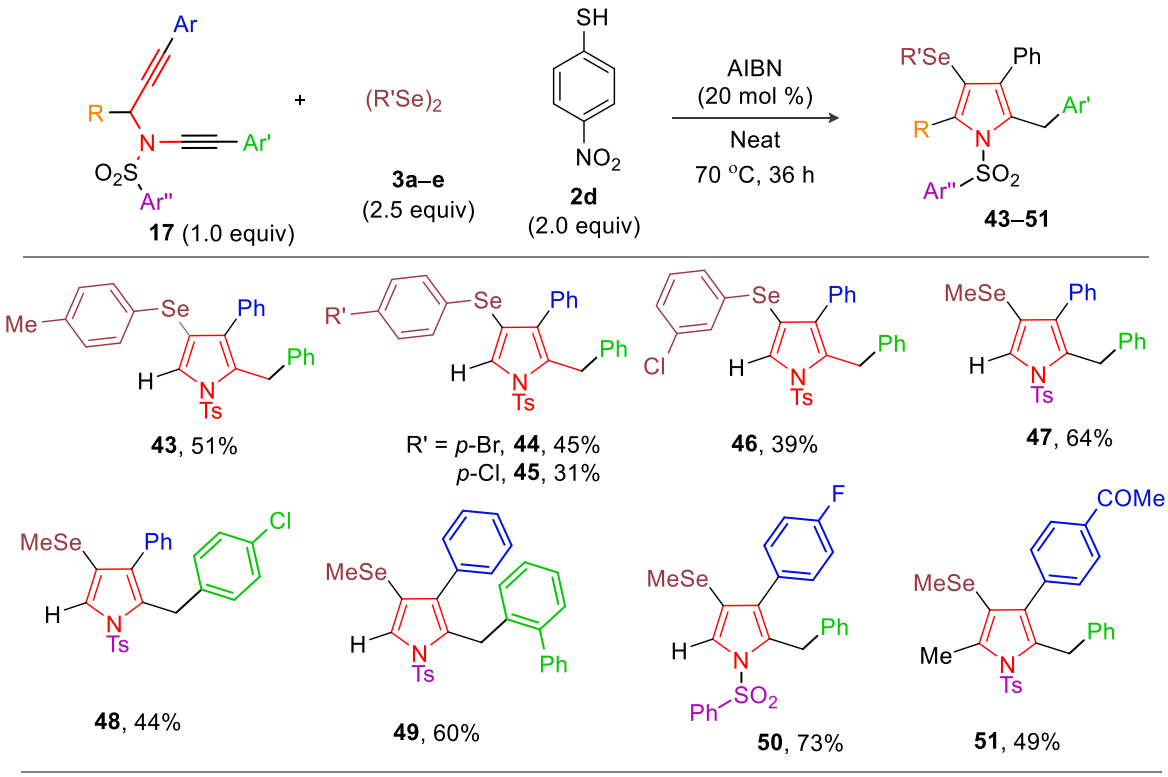
Scheme 2B.7. Scope of yne-ynamides. [a] 50 °C, [b] 60 °C

on the skeleton; cyclopropyl rings are prone to radical clock reactions when located adjacent to a radical (**Scheme 2B.7**). The *ortho*-biphenyl substituted yne-ynamide **17k** provided **28** in moderate yield. To evaluate the electronic properties of N-protecting groups in this cyclization, various N- sulfonyl protected yne-ynamides **17l** and **17m** having different aryl groups at the alkyne terminus (C_6H_5, *p*-FC_6H_4) and at the ynamide terminus (*o*-PhC_6H_4 or C_6H_5,) were subjected to the standard conditions to yield the desired highly substituted 4-selenyl-N-sulfonyl pyrrole derivatives *N*-Ms (**29**), *N*-SO_2Ph (**30**), as shown in **Scheme 2B.7**.



Scheme 2B.8. Scope of tetra-substituted 4-selenylated pyrroles

The PhSe• mediated intramolecular 5-*exo*-trig cyclization of yne-ynamides having a methyl substitution at the propargyl position could furnish fully substituted pyrroles (**Scheme 2B.8**). Hence, the α-methyl substituted propargyl tethered yne-ynamides **17n**–**17y** directly led to peripherally substituted selenylated pyrroles **31**–**42** (42–80%). The steric and electronic effects of the aryl substituents both at the propargyl and ynamide terminus did not prevent the reaction outcome (**Scheme 2B.8**).



Scheme 2B.9. Scope of diselenides

The effect of other diaryl diselenides **3a**–**3e** was next scrutinized (**Scheme 2B.9**). The reaction of **17a** and **3a** (p-$MeC_6H_4Se)_2$ in presence of **2a** led to **43** (27%); however, the identical transformation with p-$O_2NC_6H_4SH$ (**2d**) proved more efficient, delivering **43** in 51% yield. Likewise, the reaction of several diaryl diselenides {[(p-$BrC_6H_4Se)_2$ (**3b**)], [(p-$ClC_6H_4Se)_2$ (**3c**)], [(m-$ClC_6H_4Se)_2$ (**3d**)]} with **17a** in the presence of **2d** yielded the respective products **44**–**46**. Interestingly, the cyclization was compatible with $(MeSe)_2$ to provide 4-methylselenopyrroles **47**–**51**, and is remarkable (**Scheme 2B.9**); as the identical reaction with aliphatic thiyl radicals was not viable. The MeSe$^{\bullet}$ mediated intramolecular 5-*exo*-trig cyclization of yne-ynamides having various substitutions both at the propargyl and ynamide terminus furnished the respective 4-methylselenopyrroles **47**–**49** in moderate to good yield. Other than N-Ts-protected ynamides, the N-benzene sulfonyl protected 4-methylselenopyrrole **50** was constructed in good yield. The fully peripheral substituted selenopyrrole **51** was also synthesized (**Scheme 2B.9**).

2B.4.4. DFT Studies

The envisaged synthetic plan to obtain 4-selenylated pyrroles relies on the following mechanistic hypotheses: *i*) S• →Se• cross-radical transfer; *ii*) chemoselective trapping of RSe• over RS•, *iii*) regioselective RSe• attack to alkyne over ynamide, *iv*) 5-*exo*-dig cyclization, *v*) trapping of the cyclic vinyl radical with H-atom of PhSH.

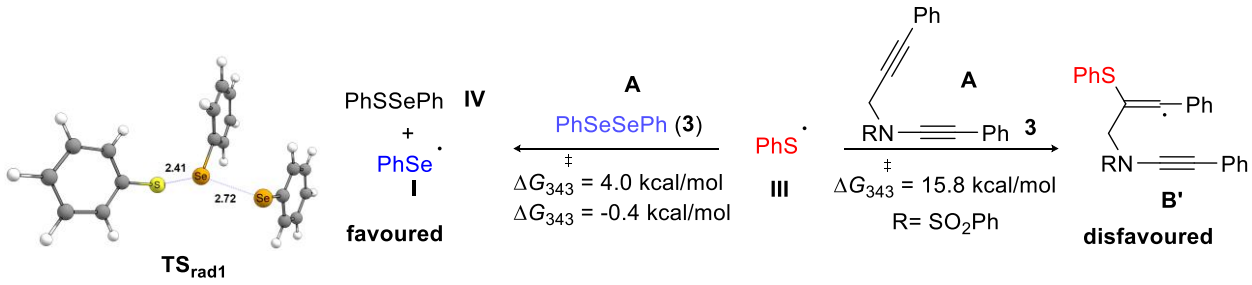
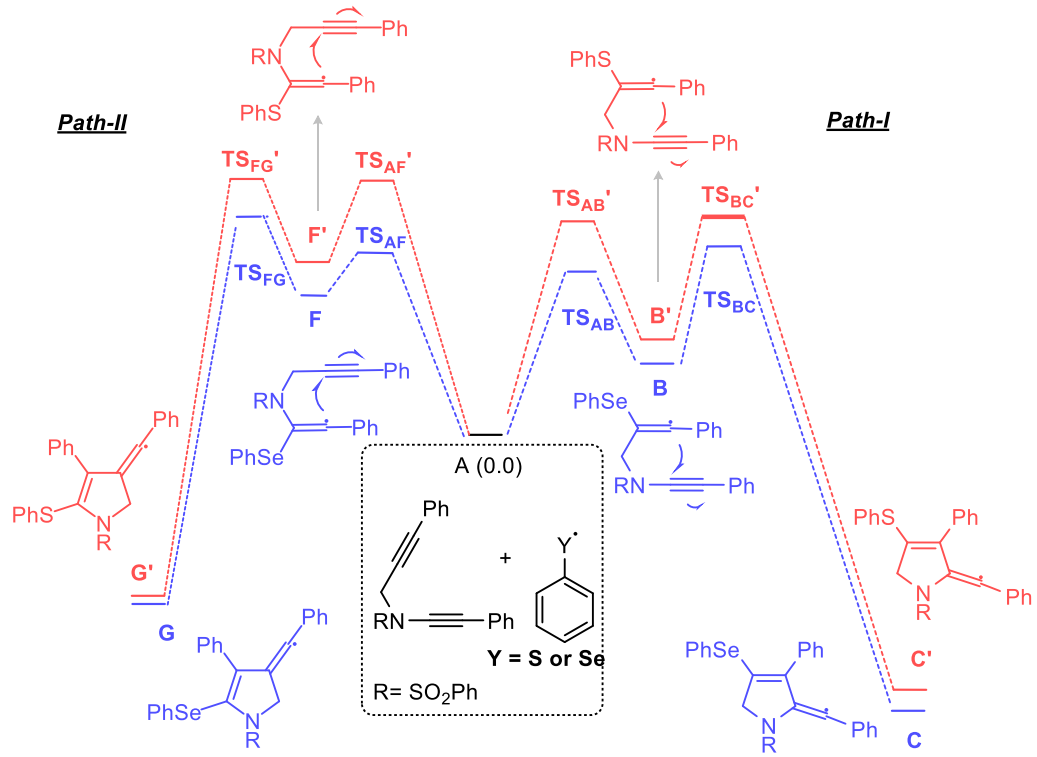


Figure 2B.3. DFT calculation for chemoselctive attack of PhS-radical

DFT computations were carried out to validate the possibility of PhSe• formation by sulfur-to-selenium radical transfer from PhS• and PhSeSePh. The transition state (**TS$_{rad1}$**) for the addition of PhS• (**III**) to PhSeSePh (**2a**) lies 4.0 kcal/mol above the reactants and the step is exergonic by 0.4 kcal/mol (**Figure 2B.3**). On the other hand, the reaction of PhS• to yne-ynamide **A** requires 15.8 kcal/mol of free energy of activation. Thus, attack of PhS• to PhSeSePh seems feasible, even in the presence of yne-ynamide.

We next studied the reactivity and cyclization diversity of PhS• and/or PhSe• with the yne-ynamide (**Figure 2B.4**). The addition of PhS• or PhSe• to one or the other alkyne moiety of **A** would lead to vinyl radicals **B** (PhSe• attack to alkyne), **B′** (PhS• attack to alkyne) (Path-I, **Figure 2B.4**), or **F** (PhSe• attack to ynamide), **F′** (PhS• attack to ynamide) (Path-II, **Figure 2B.4**).[11] Next, intramolecular 5-*exo*-dig radical cyclization of **B/B′** and **F/F′** independently forms **C/C′** and **G/G′**, respectively. The formation of **B/B′** (Y = Se/S) is endergonic by 5.5/7.3 kcal/mol, while formation of **C/C′** is exergonic by 20.9/18.9 kcal/mol. The transition states **TS$_{AB}$** and **TS$_{BC}$** involved in PhSe• attack have free energy 8.7 and 12.2 kcal/mol, respectively, whereas the identical PhS• attack requires free energies of 15.8 kcal/mol for both **TS$_{AB}$′** and **TS$_{BC}$′**.



TS_{AB} (8.7 kcal/mol)	B (5.5)	TS_{BC} (12.2)	C (-20.9)	TS_{AF} (11.0)	F (6.5)	TS_{FG} (15.4)	G (-16.1)
TS_{AB}' (15.8)	B' (7.3)	TS_{BC}' (15.8)	C' (-18.9)	TS_{AF}' (18.4)	F' (11.9)	TS_{FG}' (18.4)	G' (-15.1)

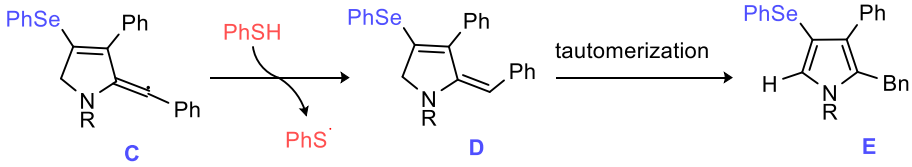
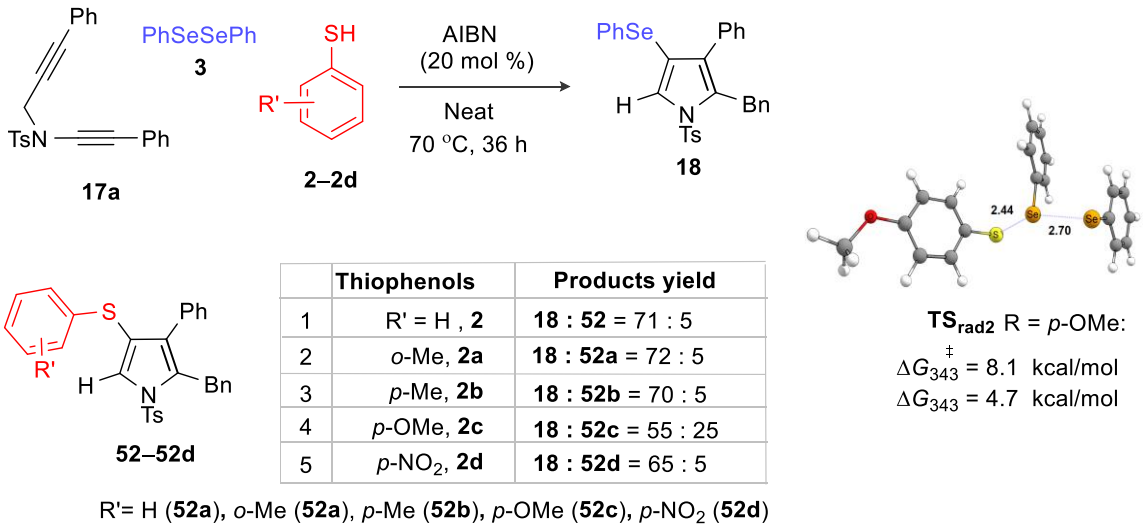


Figure 2B.4. DFT calculation for both S- and Se-triggered cyclizations

Since TS_{AB}' and TS_{BC}' were located at much higher free energies than TS_{AB} and TS_{BC}, formation of **C** (Y = Se) appears facile (Path I).[11] Indeed, TS_{AF} (11.0 kcal/mol) and TS_{FG} (15.4 kcal/mol) involved in the PhSe• attack to ynamide lie 2.3 and 3.2 kcal/mol higher on the free energy surface respective to TS_{AB} and TS_{BC}. Moreover, **G** (Y = Se) is located at –16.1 kcal/mol and is less stable than **C** (Y = Se) by 3.8 kcal/mol. Likewise, the free energy of activation for the attack of PhS• to ynamide through TS_{AF}' (18.4 kcal/mol) or TS_{FG}' (18.4 kcal/mol) is higher. From these pieces of information, ***Path-I*** is found kinetically and thermodynamically favored over ***Path-II***, and the formation of **C** seems



	Thiophenols	Products yield
1	R' = H , **2**	**18 : 52** = 71 : 5
2	*o*-Me, **2a**	**18 : 52a** = 72 : 5
3	*p*-Me, **2b**	**18 : 52b** = 70 : 5
4	*p*-OMe, **2c**	**18 : 52c** = 55 : 25
5	*p*-NO_2, **2d**	**18 : 52d** = 65 : 5

R'= H (**52a**), *o*-Me (**52a**), *p*-Me (**52b**), *p*-OMe (**52c**), *p*-NO_2 (**52d**)

Figure 2B.5. DFT calculation for various thiophenol screening

viable (**Figure 2B.4**).[11] Finally, quenching of **C** by PhSH provides **D** and subsequent tautomerization of **D** affords the desired 4-selenylated pyrrole **E** (**Figure 2B.4**).

These results led us to examine the reaction between **17a** and PhSeSePh (**3**) in the presence of phenylthiol (**2**) and radical initiator. Upon several trials, the expected 4-selenylated pyrrole **18** was obtained in 71% yield along with 4-thiyl pyrrole (**52**; 5%) (entry 1, **Figure 2B.5**), when the reaction conducted with **17a** (1.0 equiv), **3** (2.5 equiv), and **2** (2.0 equiv) in the presence of 20 mol% AIBN under neat condition at 70 °C for 36 h. To increase the reaction selectivity and productivity, various substituted aryl thiols [*o*-MeC_6H_4SH (**2a**), *p*-MeC_6H_4SH (**2b**), *p*-$MeOC_6H_4SH$ (**2c**), *p*-$O_2NC_6H_4SH$ (**2d**)] were screened (**Figure 2B.5**). Compound **18** was isolated as major product in most cases. In contrast, the reaction in presence of **2c** delivered substantial amount of **52c** (4-thio-pyrrole, 25%) and **18** (55%) (entry 4, **Figure 2B.5**). We believe that the radical transfer between *p*-$MeOC_6H_4S^{\bullet}$ and PhSeSePh is inefficient and responsible to this poor product selectivity. A high energy barrier $\mathbf{TS_{rad2}}$ (8.1 kcal/mol) is essential for the addition of *p*-$MeOC_6H_4S^{\bullet}$ to **2c** (a consequence to the formation of electron-rich *p*-$MeOC_6H_4S^{\bullet}$), and the reaction is endergonic by 4.7 kcal/mol (**Figure 2B.5**). This large energy barrier necessary for the radical exchange of **2c** to PhSeSePh (8.1 kcal/mol) in comparison to **2** (4.0 kcal/mol)

validates the observation of entry 4, **Figure 2B.5**. The identical transformation in presence of **2a** afforded **18** in 72% yield (entry 5, **Figure 2B.5**).

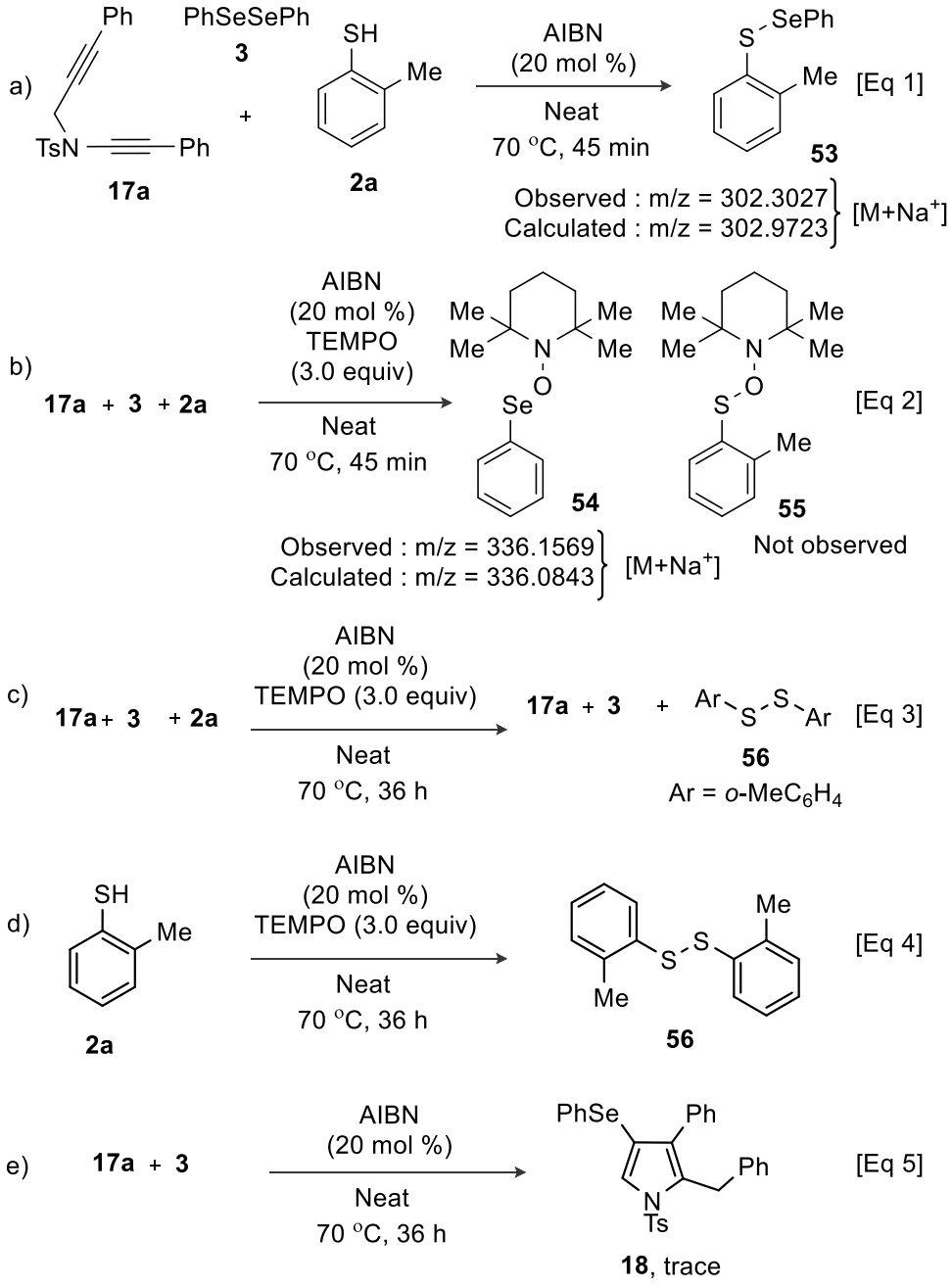
2B.4.5. HRMS Studies

To further investigate the affinity of *o*-$MeC_6H_4S^{\bullet}$ for **2a** to produce $PhSe^{\bullet}$, a few HRMS experiments were conducted. A mass peak at *m/z* 302.3027 [corresponding to (phenylselenyl)(2-tolyl)sulfane (**53**)] was detected from the reaction of **17a**, **3**, and **2a** in presence of AIBN at 70 °C for 45 min [Eq 1, **Scheme 2B.10**]; thus, affinity of *o*-$MeC_6H_4S^{\bullet}$ for **3** is higher than **17a**. Next, radical quenching experiment of **17a**, **3**, **2a**, and TEMPO in presence of AIBN at 70 °C for 45 min produced TEMPO-SePh adduct **54** (*m/z* 336.1569) and not TEMPO-S-*o*-tolyl **55**; the $Se^{\bullet}$ thus seems to be active (Eq 2, **Scheme 2B.10**), whereas the same reaction after 36 h did not provide **54**/**18** but rather the disulfide adduct **56** (Eq 3, **Scheme 2B.10**). Moreover, exposing **2a** with AIBN in presence of TEMPO exclusively provided the disulfide adduct **56** (Eq 4, **Scheme 2B.10**). The reaction in the absence of **2a** did not deliver **18** (Eq 5, **Scheme 2B.10**), thus *o*-$MeC_6H_4S^{\bullet}$ is essential. However, we could not detect the radical through EPR, when the reaction conducted at room temperature.

2B.5. Conclusion

In summary, a chemo and regioselective $RSe^{\bullet}$ radical mediated cyclization of yne-tethered ynamides to fully substituted 4-selenylated pyrroles has been developed. This reaction involves an uncommon $S^{\bullet} \rightarrow Se^{\bullet}$ radical transfer and is contrary to the well-explored radical dominance and reactivity of $S^{\bullet}$ over $Se^{\bullet}$. This green synthetic method does not require transition metal catalyst and solvent and is general exhibiting a broad substrate scope and high functional group tolerance (the free NH_2 and the common radical trap electron-withdrawing groups did not affect the reaction outcome). Computational studies provided mechanistic insights for this transformation. Various control HRMS experiments validated the role of the arylthiol initiator for the in situ

formation PhSe•. We believe these findings will open new avenues in trapping selenium radical for the construction of novel selenylated scaffolds.



Scheme 2B.10. HRMS Experiments

2B.6. Experimental Section

2B.6.1. General Information

All the reactions were performed in an oven-dried schlenk flask. Commercial grade solvents were distilled prior to use. Column chromatography was performed using silica gel (100–200 Mesh) eluting with hexanes and ethyl acetate mixture. Thin layer chromatography (TLC) was performed on silica gel GF254 plates. Visualization of spots on TLC plate was accomplished with UV light (254 nm) and staining over I_2 chamber. Proton, carbon and fluorine nuclear magnetic resonance spectra (^{1}H NMR, ^{13}C NMR and ^{19}F NMR) were recorded based on 400 MHz (^{1}H NMR, 400 MHz; ^{13}C NMR, 101 MHz; ^{19}F NMR, 376 MHz) spectrometer and 500 MHz (1H NMR, 500 MHz; ^{13}C NMR, 126 MHz; ^{19}F NMR, 470 MHz) spectrometer having solvent resonance as internal standard (^{1}H NMR, $CHCl_3$ at 7.26 ppm; ^{13}C NMR, $CDCl_3$ at 77.0 ppm). Few cases tetramethylsilane (TMS) at 0.00 ppm was used as reference standard. Data for ^{1}H NMR are reported as follows: chemical shift (ppm), the abbreviations were used to explain the multiplicities: s = singlet; d = doublet; t = triplet; q = quartet; dd = doublet of doublet; m = multiplet; quin = quintuplet; sext = sextet, sep = septet; br = broad; coupling constants *J*, in (Hz). ^{13}C NMR, ^{19}F NMR were reported in terms of chemical shift (ppm). IR spectra were recorded on FT/IR spectrometer and reported in cm^{-1}. High resolution mass spectra (HRMS) were obtained in ESI mode. Melting points were determined by electro-thermal heating and are uncorrected. LC-MS spectra were obtained with a Shimadzu 2010A (EI-positive/ negative mode) with ionization voltage of 70ev; data was reported in the form of m/z (intensity relative to base peak = 100). Elemental (C, H, N) analyses were carried out using THERMO FINNIGAN FLASH EA 1112 analyzer. X–ray data was collected at 298K on a Bruker D8 Quest CCD diffractometer using Mo-Kα radiation (0.71073 Å).

2B.6.2. Materials

Unless otherwise noted, all the reagents and intermediates were obtained commercially and used without purification. Toluene, dichloromethane (CH_2Cl_2; DCM), acetone,

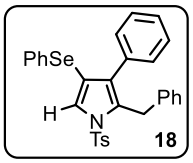
acetonitrile (CH_3CN) and N,N-dimethylformaide (DMF) were distilled over CaH_2.. Catalyst/initiator N-hydroxypthalimde, $K_2S_2O_8$, azobisisobutyronitrile (AIBN) were purchased and used as received. Thiophenols and aryl iodides were purchased and used as received. PTSA·H_2O, PPh_3, DEAD, $CuSO_4$·H_2O, 1.10-phenanthroline, K_3PO_4, Na_2CO_3, $PhB(OH)_2$, and phenyl acetylene were commercially available and used as received. Analytical and spectral data of all those known compounds are exactly matching with the reported values.

2B.6.3. General procedure and spectral/analytical data

2B.6.3.1. General Procedure for selenyl radical cyclization.

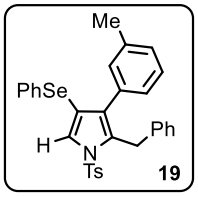
A solution of compound **17a**–**y** (0.3 mmol), diphenyldiselenide **3-3e** (0.75 mmol), and AIBN (0.06 mmol) was placed in a sealed tube. 2-Methyl benzenethiol **3e** (0.6 mmol) was introduced to the reaction mixture. The reaction mixture was stirred for 36 hours at 70 °C. Progress of the reaction was periodically monitored by TLC. After 36 h, the reaction mixture was diluted with dichloromethane (10 mL). After evaporation of solvent under the reduced pressure, the residue was purified by coloumn chromatography on silica gel (hexane/EtOAc) to afford the expected peripheral substituted pyrroles **18-51**.

2-Benzyl-3-phenyl-4-(phenylselanyl)-1-tosyl-1H-pyrrole (18):



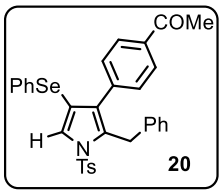
18 (130 mg) was obtained in 72% yield as colorless solid; mp = 162–164 °C; R_f = 0.46 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.74 (s, 1H), 7.48 (d, J = 8.4 Hz, 2H), 7.24–7.16 (m, 8H), 7.14–7.05 (m, 7H), 6.83–6.78 (m, 2H), 4.16 (s, 2H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.6, 139.0, 135.2, 133.3, 130.5, 130.0, 129.9, 129.7, 129.6, 129.0, 128.1, 128.0, 127.9, 127.4, 127.3, 127.0, 126.4, 125.7, 110.6, 31.0, 21.5 ; IR (Neat)ν_{max} 3059, 2923, 1711, 1173, 1091, 665 cm^{-1}; HRMS (ESI) for $C_{30}H_{26}NO_2SSe$ $(M+H)^+$: calcd 544.0844, found 544.0851.

2-Benzyl-4-(phenylselanyl)-3-(*m*-tolyl)-1-tosyl-1H-pyrrole (19):



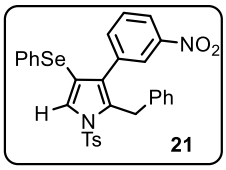
19 (99 mg) was obtained in 59% yield as pale yellow gummy liquid; R_f = 0.71 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, DMSO–d_6): δ 7.79 (s, 1H), 7.56 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 8.4 Hz, 2H), 7.26–7.20 (m, 3H), 7.19–7.09 (m, 6H), 7.03 (br d, J = 7.6 Hz, 1H), 6.88–6.78 (m, 4H), 4.15 (s, 2H), 2.37 (s, 3H), 2.12 (s, 3H); ^{13}C NMR (101 MHz, DMSO–d_6) δ 145.9, 139.4, 137.5, 135.1, 133.2, 132.6, 132.3, 130.9, 130.6, 130.3, 130.0, 129.7, 128.6, 128.52, 128.47, 128.4, 127.9, 127.3, 127.0, 126.3, 110.4, 31.0, 21.5, 21.3; IR (Neat)ν_{max} 1708, 1507, 1362, 1219, 1091, 669 cm^{-1}; HRMS (ESI) for $C_{31}H_{28}NO_2S_2$ $(M+H)^+$: calcd 558.1000, found 558.1004.

1-(4-(2-Benzyl-4-(phenylselanyl)-1-tosyl-1H-pyrrol-3-yl)phenyl)ethanone (20):



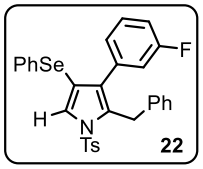
20 (111 mg) was obtained in 63% yield as pale yellow gummy liquid; R_f = 0.49 (9.5:0.5 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, DMSO–d_6): δ 7.89 (s, 1H), 7.81 (d, J = 8.4 Hz, 2H), 7.57 (d, J = 8.4 Hz, 2H), 7.29–7.18 (m, 7H), 7.16–7.10 (m, 5H), 6.81–6.76 (m, 2H), 4.20 (s, 2H), 2.50 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (101 MHz, DMSO–d_6) δ 197.9, 146.0, 139.0, 138.2, 136.1, 134.8, 132.6, 131.4, 130.7, 130.6, 130.4, 129.8, 129.5, 129.2, 128.8, 128.4, 127.8, 127.4, 126.9, 126.4, 109.5, 30.9, 27.2, 21.6; IR (Neat)ν_{max} 2969, 1738, 1434, 1365, 1228, 1216, 670 cm^{-1}; HRMS (ESI) for $C_{32}H_{28}NO_3SSe$ $(M+H)^+$: calcd 586.0950, found 586.0954.

2-Benzyl-3-(3-nitrophenyl)-4-(phenylselanyl)-1-tosyl-1H-pyrrole (21):



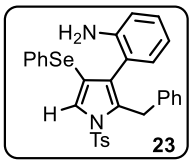
21 (74 mg) was obtained in 42% yield as pale yellow semi solid; R_f = 0.51 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, DMSO–d_6): δ 8.06–8.02 (m, 1H), 7.97 (s, 1H), 7.82–7.79 (m, 1H), 7.62 (d, J = 8.4 Hz, 2H), 7.53–7.48 (m, 2H), 7.29 (d, J = 8.0 Hz, 2H), 7.19–7.14 (m, 3H), 7.13–7.08 (m, 5H), 6.81–6.75 (m, 2H), 4.20 (s, 2H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.7, 145.1, 138.2, 135.9, 135.03, 134.95, 131.4, 130.7, 130.5, 129.9, 129.8, 129.1, 128.8, 128.3, 127.8, 127.7, 127.1, 126.7, 126.0, 125.0, 122.1, 109.9, 30.9, 21.6; IR (Neat)ν_{max} 3060, 1708, 1493, 1361, 1219, 1172, 670 cm^{-1}; HRMS (ESI) for $C_{30}H_{25}N_2O_4SSe$ $(M+H)^+$: calcd 589.0695, found 589.0701.

2-Benzyl-3-(3-fluorophenyl)-4-(phenylselanyl)-1-tosyl-1H-pyrrole (22):



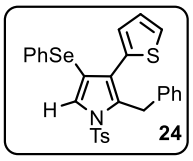
22 (98 mg) was obtained in 57% yield as pale yellow gummy liquid; R_f = 0.32 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, DMSO–d_6): δ 7.86 (s, 1H), 7.59–7.54 (m, 2H), 7.30–7.25 (m, 3H), 7.24–7.18 (m, 3H), 7.15–7.09 (m, 5H), 7.05 (td, J = 8.0, 2.4 Hz, 1H), 6.93–6.89 (m, 1H), 6.88–6.83 (m, 1H), 6.82–6.76 (m, 2H), 4.18 (s, 2H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, DMSO–d_6) δ 162.1 (d, J = 244 Hz, 1C), 146.0, 139.1, 135.7 (d, J = 8.1 Hz, 1C), 135.0, 132.4, 130.9 (d, J = 2.0 Hz, 1C), 130.7, 130.6, 130.5, 130.4 (d, J = 8.1 Hz, 1C), 129.8, 129.7, 128.7, 127.9, 127.4, 126.9, 126.34, 126.28, 126.26, 116.9 (d, J = 21.2 Hz, 1C), 114.7 (d, J = 21.2 Hz, 1C), 109.9, 30.9, 21.5; ^{19}F NMR (376 MHz, DMSO–d_6): δ –113.3; IR (Neat)ν_{max} 2359, 1613, 1581, 1369, 1297, 1172, 1090, 665 cm^{-1}; HRMS (ESI) for $C_{30}H_{24}FNNaO_2SSe$ $(M+Na)^+$: calcd 584.0569, found 584.0575.

2-(2-Benzyl-4-(phenylselanyl)-1-tosyl-1H-pyrrol-3-yl)aniline (23):



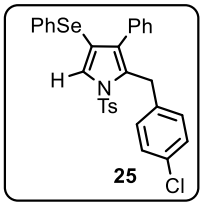
23 (96 mg) was obtained in 57% yield as pale yellow gummy thick liquid; R_f = 0.34 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60 (s, 1H), 7.30 (d, J = 8.0 Hz, 2H), 7.27–7.23 (m, 2H), 7.21–7.13 (m, 2H), 7.08–7.01 (m, 7H), 6.87–6.80 (m, 3H), 6.64–6.58 (m, 2H), 4.22 (d, J = 16.5 Hz, 1H), 4.02 (d, J = 16.5 Hz, 1H), 3.30 (bs, 2H), 2.36 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.0, 144.6, 138.6, 135.5, 131.9, 131.8, 131.7, 131.2, 129.6, 129.0, 128.8, 128.2, 128.0, 126.93, 126.87, 126.8, 125.6, 118.5, 118.0, 115.2, 112.3, 31.2, 21.5; IR (Neat)ν_{max} 3369, 2922, 1708, 1615, 1361, 1172, 664 cm^{-1}; HRMS (ESI) for $C_{30}H_{26}N_2NaO_2SSe$ $(M+Na)^+$: calcd 581.0772, found 581.0775.

2-Benzyl-3-(thienyl)-4-(phenylselanyl)-1-tosyl-1H-pyrrole (24):



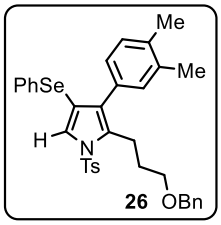
24 (120 mg) was obtained in 73% yield as pale yellow gummy thick liquid; R_f = 0.34 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, DMSO–d_6): δ 7.88 (s, 1H), 7.57 (d, J = 8.4 Hz, 2H), 7.45 (dd, J = 5.2, 1.2 Hz, 1H), 7.28–7.13 (m, 10H), 6.93 (dd, J = 4.8, 3.2 Hz, 1H), 6.88–6.83 (m, 2H), 6.80 (dd, J = 3.6, 1.2 Hz, 1H), 4.29 (s, 2H), 2.33 (s, 3H); ^{13}C NMR (101 MHz, DMSO–d_6) δ 146.1, 138.9, 134.7, 133.5, 132.7, 131.2, 130.6, 129.8, 129.7, 129.0, 128.9, 128.8, 127.9, 127.4, 126.9, 126.4, 125.2, 110.2, 31.1, 21.6; IR (Neat)ν_{max} 3407, 1708, 1595, 1493, 1452, 1365, 1172, 692 cm^{-1}; HRMS (ESI) for $C_{28}H_{23}NNaO_2S_2Se$ $(M+Na)^+$: calcd 572.0228, found 572.0236.

2-(4-Chlorobenzyl)-3-phenyl-4-(phenylselanyl)-1-tosyl-1H-pyrrole (25):



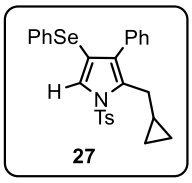
25 (118 mg) was obtained in 68% yield as pale red gummy liquid; R_f = 0.78 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (s, 1H), 7.30 (d, J = 8.4 Hz, 2H), 7.25–7.16 (m, 8H), 7.09–7.04 (m, 4H), 6.98–6.94 (m, 2H), 6.70 (d, J = 8.8 Hz, 2H), 4.16 (s, 2H), 2.40 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.9, 137.3, 135.2, 133.1, 132.5, 132.0, 131.7, 130.6, 129.8, 129.6, 129.3, 129.1, 129.0, 128.1, 128.0, 127.5, 127.4, 126.8, 126.5, 110.6, 30.3, 21.6; IR (Neat)ν_{max} 2920, 1573, 1489, 1364, 1164, 1088, 662 cm^{-1}; HRMS (ESI) for $C_{30}H_{25}ClNO_2SSe$ $(M+H)^+$: calcd 578.0454, found 578.0450.

2-(3-(Benzyloxy)propyl)-3-(3,4-dimethylphenyl)-4-(phenylselanyl)-1-tosyl-1H-pyrrole (26):



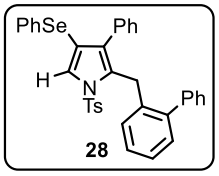
26 (54 mg) was obtained in 29% yield as pale red gummy liquid; R_f = 0.28 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, DMSO–d_6): δ 7.84 (d, J = 8.0 Hz, 2H), 7.63 (s, 1H), 7.48 (d, J = 8.4 Hz, 2H), 7.38–7.27 (m, 4H), 7.24–7.12 (m, 6H), 7.01 (d, J = 7.6 Hz, 1H), 6.81–6.75 (m, 2H), 4.25 (s, 2H), 3.27 (t, J = 6.0 Hz, 2H), 2.73 (br t, J = 7.2 Hz, 2H), 2.42 (s, 3H), 2.14 (s, 3H), 2.04 (s, 3H), 1.72–1.63 (m, 2H); ^{13}C NMR (126 MHz, DMSO–d_6) δ 146.2, 139.0, 136.1, 135.7, 135.6, 132.8, 132.6, 131.3, 131.2, 131.0, 130.9, 130.0, 129.7, 128.6, 127.82, 127.79, 127.68, 127.65, 127.5, 127.3, 126.9, 110.8, 71.9, 69.2, 30.9, 22.9, 21.6, 19.7, 19.5; IR (Neat)ν_{max} 2923, 1358, 1219, 1092, 527, cm^{-1}; HRMS (ESI) for $C_{35}H_{36}NO_3SSe$ $(M+H)^+$: calcd 630.1576, found 630.1575.

2-(Cyclopropylmethyl)-3-phenyl-4-(phenylselanyl)-1-tosyl-1H-pyrrole (27):



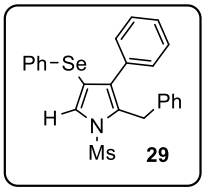
27 (49 mg) was obtained in 32% yield as pale yellow gummy liquid; R_f = 0.63 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72 (d, J = 8.5 Hz, 2H), 7.51 (s, 1H), 7.33 (br d, J = 8.5 Hz, 2H), 7.25–7.22 (m, 3H), 7.18–7.12 (m, 4H), 7.08–7.03 (m, 2H), 6.98–6.95 (m, 1H), 2.63 (d, J = 6.5 Hz, 2H), 2.45 (s, 3H), 0.93–0.86 (m, 1H), 0.25–0.19 (m, 2H), -0.19–-0.25 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.0, 136.4, 133.9, 133.1, 132.2, 131.4, 130.6, 130.4, 130.0, 128.9, 128.7, 127.8, 127.2, 126.8, 126.4, 111.6, 30.0, 21.6, 11.6, 4.8; IR (Neat)ν_{max} 3057, 2921, 1730, 1596, 1369, 1164, 1088, 663 cm^{-1}; HRMS (ESI) for $C_{27}H_{26}NO_2SSe$ $(M+H)^+$: calcd 508.0844, found 508.0844.

2-([1,1'-Biphenyl]-2-ylmethyl)-3-phenyl-4-(phenylselanyl)-1-tosyl-1H-pyrrole (28):



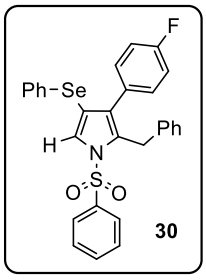
28 (91 mg) was obtained in 49% yield as pale yellow gummy liquid; R_f = 0.48 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, DMSO–d_6): δ 7.81 (s, 1H), 7.50–7.44 (m, 2H), 7.43–7.38 (m, 3H), 7.31–7.14 (m, 14H), 7.07–7.01 (m, 3H), 6.55 (d, J = 7.2 Hz, 1H), 3.95 (s, 2H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, DMSO–d_6) δ 146.0, 141.2, 141.1, 136.4, 134.8, 133.1, 132.7, 132.4, 130.6, 130.0, 129.83, 129.76, 129.62, 129.55, 128.8, 128.6, 128.5, 127.92, 127.87, 127.6, 127.4, 127.1, 126.9, 126.5, 109.8, 29.4, 21.5; IR (Neat)ν_{max} 3056, 1595, 1495, 1436, 1371, 1168, 1090, 662 cm^{-1}; HRMS (ESI) for $C_{36}H_{30}NO_2SSe$ $(M+H)^+$: calcd 620.1157, found 620.1164.

2-Benzyl-1-(methylsulfonyl)-3-phenyl-4-(phenylselanyl)-1H-pyrrole (29):



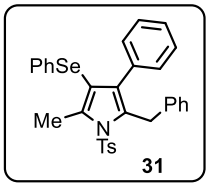
29 (105 mg) was obtained in 75% yield as colorless solid; mp = 157–159 °C; R_f = 0.42 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (s, 1H), 7.34–7.24 (m, 9H), 7.23–7.17 (m, 4H), 7.15 (br d, J = 7.2 Hz, 2H), 4.26 (s, 2H), 2.44 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.7, 133.3, 131.8, 131.7, 131.1, 130.8, 130.2, 129.1, 128.8, 128.6, 128.3, 127.5, 126.8, 126.7, 126.3, 110.7, 42.3, 31.0; IR (Neat)ν_{max} 3055, 1599, 1573, 1493, 1365, 1174, 1157, 688 cm^{-1}; HRMS (ESI) for $C_{24}H_{22}NO_2SSe$ $(M+H)^+$: calcd 468.0536, found 468.0532.

2-Benzyl-3-(4-fluorophenyl)-4-(phenylselanyl)-1-(phenylsulfonyl)-1H-pyrrole (30):



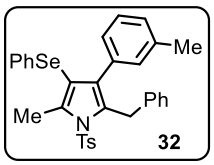
30 (128 mg) was obtained in 78% yield as pale brown gummy liquid; R_f = 0.05 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, DMSO–d_6): δ 7.87 (s, 1H), 7.67 (d, J = 7.5 Hz, 3H), 7.51–7.46 (m, 3H), 7.21–7.16 (m, 2H), 7.14–7.01 (m, 9H), 6.80 (dd, J = 7.5, 3.5 Hz, 2H), 4.17 (s, 2H); ^{13}C NMR (126 MHz, DMSO–d_6) δ 162.0 (d, J = 244 Hz, 1C), 139.1, 137.9, 135.0, 132.4, 132.1 (d, J = 8.8 Hz, 1C), 131.4, 130.7, 130.2, 129.7 (d, J = 11.3 Hz, 1C), 128.7, 127.9, 127.5, 127.2, 126.9, 126.5, 115.4 (d, J = 21 Hz, 1C), 110.5, 31.0; ^{19}F NMR (376 MHz, DMSO–d_6): δ –114.5; IR (Neat)ν_{max} 3059, 1737, 1575, 1505, 1374, 1294, 1163, 754 cm^{-1}; HRMS (ESI) for $C_{29}H_{23}FNO_2SSe$ $(M+H)^+$: calcd 548.0593, found 548.0593.

2-Benzyl-5-methyl-3-phenyl-4-(phenylselanyl)-1-tosyl-1H-pyrrole (31):



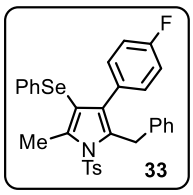
31 (114 mg) was obtained in 68% yield as pale yellow gummy liquid; R_f = 0.73 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35 (br d, J = 8.5 Hz, 2H), 7.29–7.20 (m, 5H), 7.18 (br d, J = 7.5 Hz, 2H), 7.15–7.12 (m, 3H), 7.10 (br d, J = 6.5 Hz, 2H), 7.05–7.00 (m, 2H), 4.39 (s, 2H), 2.62 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.6, 140.2, 137.2, 136.5, 134.1, 133.0, 132.0, 131.4, 130.2, 129.7, 128.9, 128.6, 128.1, 127.8, 127.2, 126.6, 125.8, 125.6, 111.5, 32.4, 21.5, 15.0 ; IR (Neat)ν_{max} 3054, 1721, 1472, 1357, 1167, 1019, 731 cm^{-1}; HRMS (ESI) for $C_{31}H_{28}NO_2SSe$ $(M+H)^+$: calcd 558.1000, found 558.0997.

2-Benzyl-5-methyl-4-(phenylselanyl)-3-(*m*-tolyl)-1-tosyl-1H-pyrrole (32):



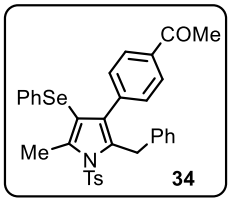
32 (114 mg) was obtained in 67% yield as pale yellow gummy liquid; R_f = 0.41 (9.5:0.5 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, DMSO–d_6): δ 7.57 (d, J = 8.4 Hz, 2H), 7.40 (d, J = 8.0 Hz, 2H), 7.23 (t, J = 7.6 Hz, 2H), 7.19–7.10 (m, 5H), 7.06 (br d, J = 7.6 Hz, 1H), 6.98 (d, J = 6.8 Hz, 2H), 6.93 (d, J = 7.6 Hz, 1H), 6.90 (s, 1H), 6.88–6.84 (m, 2H), 4.30 (s, 2H), 2.47 (s, 3H), 2.40 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (101 MHz, DMSO–d_6) δ 145.9, 140.6, 137.4, 135.9, 134.0, 133.0, 132.6, 131.4, 131.2, 130.8, 129.7, 128.7, 128.5, 128.3, 128.1, 128.0, 127.5, 126.7, 126.3, 111.7, 32.6, 21.6, 21.4, 15.3; IR (Neat)ν_{max} 2969, 1738, 1576, 1493, 1364, 1216, 1104, 718 cm^{-1}; HRMS (ESI) for $C_{32}H_{30}NO_2SSe$ $(M+H)^+$: calcd 594.0982, found 594.0983.

2-Benzyl-3-(4-fluorophenyl)-5-methyl-4-(phenylselanyl)-1-tosyl-1H-pyrrole (33):



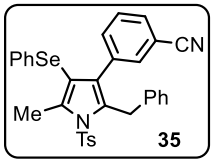
33 (80 mg) was obtained in 46% yield as pale yellow gummy liquid; R_f = 0.56 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, DMSO–d_6): δ 7.55 (d, J = 8.5 Hz, 2H), 7.40 (d, J = 8.0 Hz, 2H), 7.22 (t, J = 7.0 Hz, 2H), 7.19–7.08 (m, 8H), 6.98–6.94 (m, 2H), 6.86–6.82 (m, 2H), 4.28 (s, 2H), 2.46 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (126 MHz, DMSO–d_6) δ 162.0 (d, J = 244 Hz, 1C), 145.9, 140.3, 137.4, 135.9, 132.7, 132.4 (d, J = 7.6 Hz, 2C), 131.7, 131.5, 130.8, 130.41 (d, J = 2.5 Hz, 1C), 129.7, 128.7, 128.2, 128.0, 126.8, 126.4, 126.3, 115.3 (d, J = 21 Hz, 2C), 111.7, 32.5, 21.5, 15.2; ^{19}F NMR (471 MHz, DMSO-d_6): δ –114.6; IR (Neat)ν_{max} 2925, 1737, 1529, 1364, 1169, 1103, 735 cm^{-1}; HRMS (ESI) for $C_{31}H_{27}FNO_2SSe$+ $(M+H)^+$: calcd 576.0906, found 576.0907.

1-(4-(2-Benzyl-5-methyl-4-(phenylselanyl)-1-tosyl-1H-pyrrol-3-yl)phenyl)ethanone (34):



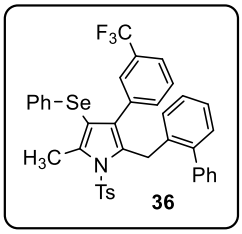
34 (116 mg) was obtained in 65% yield as pale yellow gummy liquid ; R_f = 0.41 (9.5:0.5 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, DMSO–d_6): δ 7.85 (d, J = 8.5 Hz, 2H), 7.57 (d, J = 8.5 Hz, 2H), 7.40 (d, J = 8.5 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 7.22 (t, J = 7.5 Hz, 2H), 7.15 (d, J = 7.5 Hz, 1H), 7.14–7.10 (m, 3H), 6.96 (br d, J = 7.5 Hz, 2H), 6.85 (dd, J = 7.5, 4.0 Hz, 2H), 4.32 (s, 2H), 2.51 (s, 3H), 2.47 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (126 MHz, DMSO–d_6) δ 197.9, 146.0, 140.2, 139.1, 137.8, 136.2, 135.8, 132.7, 131.8, 131.6, 130.8, 129.7, 128.8, 128.3, 128.03, 127.95, 126.8, 126.4, 126.3, 111.0, 32.4, 27.1, 21.6, 15.2; IR (Neat)ν_{max} 2923, 1734, 1679, 1361, 1263, 1166, 683 cm^{-1}; HRMS (ESI) for $C_{33}H_{29}NNaO_3SSe$ $(M+Na)^+$: calcd 622.0926, found 622.0932.

3-(2-Benzyl-5-methyl-4-(phenylselanyl)-1-tosyl-1H-pyrrol-3-yl)benzonitrile (35):



35 (89 mg) was obtained in 51% yield as pale yellow gummy liquid; R_f = 0.33 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, DMSO–d_6): δ 7.73–7.69 (m, 1H), 7.59 (d, J = 8.4 Hz, 2H), 7.57–7.55 (m, 1H), 7.49–7.46 (m, 2H), 7.44 (d, J = 8.4 Hz, 2H), 7.26–7.19 (m, 2H), 7.18–7.10 (m, 4H), 6.94 (d, J = 6.8 Hz, 2H), 6.87–6.82 (m, 2H), 4.30 (s, 2H), 2.48 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (101 MHz, DMSO–d_6) δ 146.0, 140.1, 137.5, 135.8, 135.5, 135.4, 134.0, 132.4, 132.2, 131.6, 130.8, 130.4, 129.7, 128.8, 128.4, 128.0, 126.93, 126.89, 126.5, 119.0, 111.6, 111.3, 32.4, 21.6, 15.2; IR (Neat)ν_{max} 2253, 1657, 1364, 1049, 1023, 1002, 688 cm^{-1}; HRMS (ESI) for $C_{32}H_{27}N_2O_2SSe$ $(M+H)^+$: calcd 583.0953, found 583.0955.

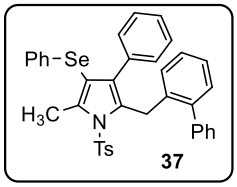
2-([1,1'-Biphenyl]-2-ylmethyl)-5-methyl-4-(phenylselanyl)-1-tosyl-3-(3-(trifluoromethyl) phenyl)-1H-pyrrole (36):



36 (160 mg) was obtained in 76% yield as pale brown semi solid; R_f = 0.6 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, DMSO–d_6): δ 7.56 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 8.5 Hz, 2H), 7.43 (t, J = 8.0 Hz, 1H), 7.41–7.31 (m, 5H), 7.27 (d, J = 7.5 Hz, 1H), 7.25–7.22 (m, 2H), 7.21 (br s, 1H), 7.19–7.09 (m, 6H), 6.89 (dd, J = 8.0, 2.0 Hz, 2H), 6.83–6.78 (m, 1H), 4.07 (s, 2H), 2.54 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (101 MHz, DMSO–d_6) δ 146.1, 141.23, 141.19, 137.7, 137.5, 135.8, 134.9, 134.2–133.8 (m, 1C), 132.6, 131.4, 130.87, 130.85 (q, J = 242 Hz, 1C),

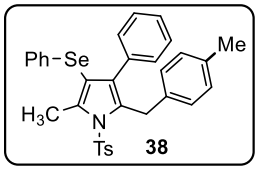
130.6, 130.0, 129.7, 129.4 (q, J = 8.4 Hz, 1C), 128.9, 128.7, 128.2, 128.0, 127.5, 126.7, 126.5, 126.4, 125.7, 124.8–124.4 (m, 1C), 123.0, 111.0, 30.9, 21.5, 15.3; ^{19}F NMR (376 MHz, DMSO–d_6): δ –61.3; IR (Neat)ν_{max} 2925, 1595, 1475, 1366, 1323, 1160, 1071, 673 cm^{-1}; HRMS (ESI) for $C_{38}H_{31}F_3NO_2SSe$ $(M+H)^+$: calcd 702.1193, found 702.1197.

2-([1,1'-Biphenyl]-2-ylmethyl)-5-methyl-3-phenyl-4-(phenylselanyl)-1-tosyl-1H-pyrrole (37):



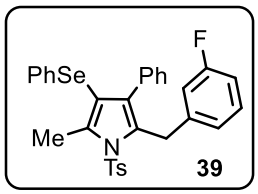
37 (133 mg) was obtained in 70% yield as pale yellow gummy liquid; R_f = 0.57 (9:1 hexane/EtOAc) [Silica, UV and I_2]; ^{1}H NMR (500 MHz, DMSO–d_6): δ 7.44–7.39 (m, 4H), 7.38–7.33 (m, 3H), 7.28–7.19 (m, 7H), 7.18–7.11 (m, 4H), 7.05–7.00 (m, 2H), 6.90 (dd, J = 8.0, 1.5 Hz, 2H), 6.84–6.80 (m, 1H), 4.07 (s, 2H), 2.50 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (126 MHz, DMSO–d_6) δ 145.9, 141.4, 141.2, 137.7, 137.6, 136.0, 133.9, 133.0, 132.5, 130.8, 130.7, 130.1, 130.0, 129.7, 129.4, 128.7, 128.4, 128.1, 127.9, 127.8, 127.43, 127.41, 126.5, 126.4, 126.3, 111.4, 30.8, 21.5, 15.3; IR (Neat)ν_{max} 2924, 1737, 1596, 1366, 1170, 1012, 700; cm^{-1}; HRMS (ESI) for $C_{37}H_{32}NO_2SSe$ $(M+H)^+$: calcd 634.1313, found 634.1314.

2-Methyl-5-(4-methylbenzyl)-4-phenyl-3-(phenylselanyl)-1-tosyl-1H-pyrrole (38):



38 (128 mg) was obtained in 75% yield as pale yellow gummy liquid; R_f = 0.62 (9:1 hexane/EtOAc) [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30–7.24 (m, 2H), 7.24–7.21 (m, 2H), 7.17–7.08 (m, 7H), 7.02–6.96 (m, 5H), 6.95–6.90 (m, 2H), 4.28 (s, 2H), 2.57 (s, 3H), 2.41 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.5, 137.3, 137.2, 136.7, 135.3, 134.2, 133.2, 132.0, 131.7, 130.3, 129.6, 128.9, 128.8, 128.7, 128.0, 127.8, 127.2, 126.6, 125.6, 111.5, 32.0, 21.6, 21.0, 15.1; IR (Neat)ν_{max} 3000, 1709, 1359, 1219, 1169, 1092, 737; cm^{-1}; HRMS (ESI) for $C_{32}H_{30}NO_2SSe$ $(M+H)^+$: calcd 572.1157, found 572.1156.

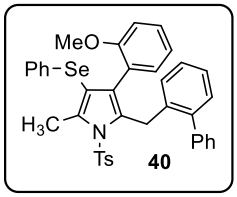
2-(3-Fluorobenzyl)-5-methyl-3-phenyl-4-(phenylselanyl)-1-tosyl-1H-pyrrole (39):



39 (72 mg) was obtained in 42% yield as pale yellow gummy liquid; R_f = 0.32 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, DMSO–d_6): δ 7.61 (d, J = 8.4 Hz, 2H), 7.43 (d, J = 8.0 Hz, 2H), 7.32–7.23 (m, 4H), 7.15–7.09 (m, 5H), 6.97 (td, J = 8.4, 2.4 Hz, 1H), 6.88–6.83 (m, 2H), 6.79 (d, J = 7.6 Hz, 1H), 6.72–6.65 (m, 1H), 4.30 (s, 2H), 2.423 (s, 3H), 2.416 (s, 3H); ^{13}C

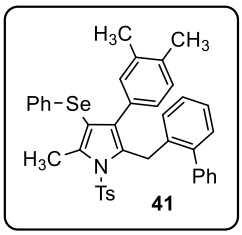
NMR (101 MHz, DMSO–d_6) δ 162.6 (d, J = 244 Hz, 1C), 146.0, 143.3 (d, J = 7.1 Hz, 1C), 137.7, 135.8, 133.9, 132.8 (d, J = 3.0 Hz, 1C), 130.8, 130.58, 130.57 (d, J = 8.1 Hz, 1C), 130.4, 129.7, 128.5, 128.1, 128.0, 126.7, 126.3, 123.98, 123.96, 114.6 (d, J = 22 Hz, 1C), 113.2 (d, J = 21 Hz, 1C), 111.7, 32.2, 21.6, 15.3; ^{19}F NMR (376 MHz, DMSO–d_6): δ –113.7; IR (Neat)ν_{max} 2925, 1613, 1589, 1365, 1192, 1170, 734 cm^{-1}; HRMS (ESI) for $C_{31}H_{26}FNNaO_2SSe$ $(M+Na)^+$: calcd 598.0726, found 598.0725.

2-([1,1'-Biphenyl]-2-ylmethyl)-3-(2-methoxyphenyl)-5-methyl-4-(phenylselanyl)-1-tosyl-1H-pyrrole (40):



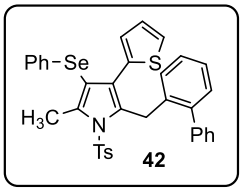
40 (115 mg) was obtained in 58% yield as pale brown solid; mp = 163–165 °C; R_f = 0.42 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, DMSO–d_6): δ 7.46–7.33 (m, 6H), 7.27 (t, J = 8.0 Hz, 2H), 7.20 (br d, J = 5.2 Hz, 4H), 7.15–7.07 (m, 4H), 6.98–6.78 (m, 6H), 4.02 (br s, 2H), 3.51 (s, 3H), 2.42 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (101 MHz, DMSO–d_6) δ 157.7, 145.8, 141.4, 141.2, 137.4, 136.8, 136.0, 132.9, 131.7, 131.3, 130.7, 130.1, 129.9, 129.5, 128.6, 128.1, 127.7, 127.4, 126.4, 126.2, 126.1, 122.6, 120.5, 112.8, 111.6, 55.4, 30.7, 21.5, 15.3; IR (Neat)ν_{max} 2916, 1977, 1596, 1577, 1475, 1365, 1170, 1101; cm^{-1}; HRMS (ESI) for $C_{38}H_{34}NO_3SSe$ $(M+H)^+$: calcd 664.1425, found 664.1431.

2-([1,1'-Biphenyl]-2-ylmethyl)-3-(3,4-dimethylphenyl)-5-methyl-4-(phenylselanyl)-1-tosyl-1H-pyrrole (41):



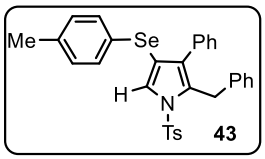
41 (159 mg) was obtained in 80% yield as pale brown solid; mp = 148–150 °C; R_f = 0.52 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, DMSO–d_6): δ 7.44–7.33 (m, 7H), 7.27–7.21 (m, 4H), 7.20–7.11 (m, 4H), 6.97 (d, J = 8.4 Hz, 1H), 6.92 (d, J = 6.8 Hz, 2H), 6.84–6.79 (m, 1H), 6.76–6.71 (m, 2H), 4.07 (s, 2H), 2.51 (s, 3H), 2.37 (s, 3H), 2.12 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (101 MHz, DMSO–d_6) δ 145.9, 141.4, 141.2, 137.8, 137.6, 136.02, 135.95, 135.8, 133.2, 131.3, 130.8, 130.5, 129.7, 129.5, 128.7, 128.0, 127.4, 126.5, 126.4, 126.2, 111.5, 31.0, 21.5, 19.8, 19.5, 15.4; IR (Neat)ν_{max} 2919, 1595, 1474, 1364, 1168, 1101, 730 cm^{-1}; HRMS (ESI) for $C_{39}H_{36}NO_2SSe$ $(M+H)^+$: calcd 662.1626, found 662.1636.

2-([1,1'-Biphenyl]-2-ylmethyl)-5-methyl-4-(phenylselanyl)-3-(thiophen-2-yl)-1-tosyl-1H-pyrrole (42):



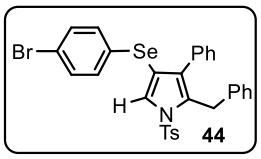
42 (129 mg) was obtained in 67% yield as pale brown semi solid; R_f = 0.42 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, DMSO–d_6): δ 7.54 (d, J = 8.5 Hz, 2H), 7.49 (dd, J = 5.0, 1.0 Hz, 1H), 7.39 (d, J = 8.0 Hz, 3H), 7.25 (t, J = 7.0 Hz, 3H), 7.20–7.12 (m, 5H), 7.01–6.96 (m, 4H), 6.95–6.91 (m, 2H), 6.83 (dd, J = 3.5, 1.0 Hz, 1H), 4.38 (s, 2H), 2.51 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (126 MHz, DMSO–d_6) δ 146.1, 140.1, 137.8, 135.7, 134.2, 132.9, 132.6, 130.8, 130.7, 129.8, 128.8, 128.4, 128.1, 128.0, 127.5, 127.4, 126.9, 126.6, 126.42, 126.36, 125.1, 111.7, 32.6, 21.6, 15.3; IR (Neat)ν_{max} 3029, 1741, 1596, 1493, 1451, 1365, 1098, 733 cm^{-1}; HRMS (ESI) for $C_{35}H_{30}NO_2S_2Se$ $(M+H)^+$: calcd 640.0878, found 640.0883.

2-Benzyl-3-phenyl-4-(*p*-tolylselanyl)-1-tosyl-1H-pyrrole (43):



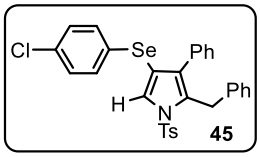
43 (85 mg) was obtained in 51% yield as pale yellow gummy liquid; R_f = 0.70 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (s, 1H), 7.34–7.19 (m, 6H), 7.16 (d, J = 8.0 Hz, 2H), 7.13–6.98 (m, 8H), 6.82 (br d, J = 6.4 Hz, 2H), 4.19 (s, 2H), 2.35 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.5, 139.1, 136.6, 135.4, 133.4, 132.1, 131.2, 129.90, 129.86, 129.6, 128.1, 128.0, 127.9, 127.3, 126.9, 126.7, 126.3, 125.6, 124.4, 111.5, 31.0, 21.6, 21.1; IR (Neat)ν_{max} 2921, 1574, 1338, 1107, 853, 737 cm^{-1}; HRMS (ESI) for $C_{31}H_{28}NO_2SSe$ $(M+H)^+$: calcd 558.1002, found 558.1002.

2-Benzyl-4-((4-bromophenyl)selanyl)-3-phenyl-1-tosyl-1H-pyrrole (44):



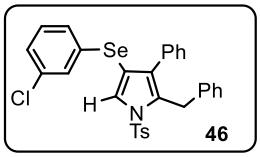
44 (84 mg) was obtained in 45% yield as pale yellow gummy liquid; R_f = 0.55 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, DMSO–d_6): δ 7.87 (s, 1H), 7.54 (d, J = 8.5 Hz, 2H), 7.40–7.35 (m, 2H), 7.26 (d, J = 8.0 Hz, 2H), 7.24–7.21 (m, 3H), 7.13–7.02 (m, 7H), 6.82–6.76 (m, 2H), 4.16 (s, 2H), 2.36 (s, 3H); ^{13}C NMR (126 MHz, DMSO–d_6 + $CDCl_3$) δ 145.9, 139.2, 135.0, 133.2, 132.4, 132.21, 132.19, 131.6, 130.6, 130.5, 130.1, 128.8, 128.7, 128.5, 127.92, 127.86, 127.3, 126.3, 119.9, 109.7, 31.0, 21.5; IR (Neat)ν_{max} 2922, 1727, 1738, 1597, 1338, 1163, 738 cm^{-1}; HRMS (ESI) for $C_{30}H_{25}BrNO_2SSe$ $(M+H)^+$: calcd 621.9949, found 621.9959.

2-Benzyl-4-((4-chlorophenyl)selanyl)-3-phenyl-1-tosyl-1H-pyrrole (45):



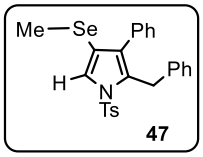
45 (54 mg) was obtained in 31% yield as pale yellow gummy liquid; R_f = 0.71 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (s, 1H), 7.30 (d, J = 8.4 Hz, 2H), 7.23–7.19 (m, 3H), 7.12 (br s, 3H), 7.10–7.02 (m, 8H), 6.81 (br d, J = 6.8 Hz, 2H), 4.21 (s, 2H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.7, 138.9, 135.2, 133.1, 132.5, 132.1, 131.7, 130.2, 129.9, 129.6, 129.0, 128.1, 128.0, 127.8, 127.5, 127.4, 127.0, 125.7, 124.4, 110.2, 31.0, 21.5; IR (Neat)ν_{max} 2923, 1749, 1596, 1493, 1380, 1176, 698 cm^{-1}; HRMS (ESI) for $C_{30}H_{25}ClNO_2SSe$ $(M+H)^+$: calcd 578.0454, found 578.0450.

2-Benzyl-4-((3-chlorophenyl)selanyl)-3-phenyl-1-tosyl-1H-pyrrole (46):



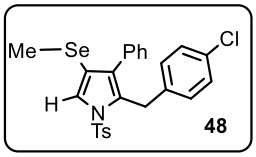
46 (68 mg) was obtained in 39% yield as pale yellow gummy liquid; R_f = 0.71 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, DMSO–d_6): δ 7.96 (s, 1H), 7.58 (d, J = 8.4 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H), 7.24–7.19 (m, 5H), 7.15–7.04 (m, 6H), 7.08 (q, J = 1.2 Hz, 1H), 6.84–6.79 (m, 2H), 4.18 (s, 2H), 2.35 (s, 3H); ^{13}C NMR (101 MHz, DMSO–d_6) δ 145.9, 139.2, 135.5, 134.9, 134.3, 133.1, 132.2, 131.2, 130.6, 130.5, 130.0, 129.5, 128.7, 128.5, 128.2, 128.0, 127.8, 127.7, 127.3, 126.5, 126.3, 109.1, 31.0, 21.6; IR (Neat)ν_{max} 2923, 1749, 1493, 1380, 1176, 1088, 698 cm^{-1}; HRMS (ESI) for $C_{30}H_{25}ClNO_2SSe$ $(M+H)^+$: calcd 578.0454, found 578.0456.

2-Benzyl-4-(methylselanyl)-3-phenyl-1-tosyl-1H-pyrrole (47):



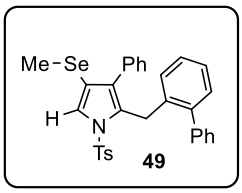
47 (93 mg) was obtained in 64% yield as pale yellow gummy liquid; R_f = 0.44 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, DMSO–d_6): δ 7.52 (d, J = 8.4 Hz, 2H), 7.44 (s, 1H), 7.39–7.27 (m, 3H), 7.26–7.19 (m, 4H), 7.11 (br t, J = 3.2 Hz, 3H), 6.84–6.78 (m, 2H), 4.13 (s, 2H), 2.34 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (101 MHz, DMSO–d_6) δ 145.5, 139.4, 135.3, 133.6, 130.6, 130.5, 129.7, 128.9, 128.7, 128.1, 127.9, 127.2, 126.3, 121.6, 121.5, 113.6, 30.7, 21.5, 7.4; IR (Neat)ν_{max} 3026, 1728, 1596, 1493, 1364, 1169, 1089, 662 cm^{-1}; HRMS (ESI) for $C_{25}H_{24}NO_2SSe$ $(M+H)^+$: calcd 482.0687, found 482.0682.

2-(4-Chlorobenzyl)-4-(methylselanyl)-3-phenyl-1-tosyl-1H-pyrrole (48):



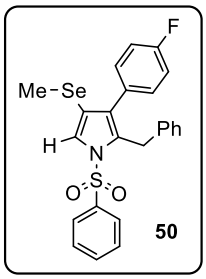
48 (68 mg) was obtained in 44% yield as pale yellow gummy liquid; R_f = 0.44 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (500 MHz, DMSO–d_6): δ 7.54 (d, J = 8.5 Hz, 2H), 7.45 (s, 1H), 7.37–7.28 (m, 3H), 7.24 (d, J = 8.0 Hz, 2H), 7.21–7.17 (m, 2H), 7.11 (d, J = 8.5 Hz, 2H), 6.75 (d, J = 8.5 Hz, 2H), 4.09 (s, 2H), 2.35 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (126 MHz, DMSO–d_6) δ 145.6, 138.2, 135.2, 133.5, 131.1, 130.9, 130.4, 129.7, 129.6, 129.1, 128.9, 128.5, 128.1, 127.2, 121.9, 113.4, 30.1, 21.5, 7.5; IR (Neat)ν_{max} 3026, 1360, 1219, 1092, 666 cm^{-1}; HRMS (ESI) for $C_{25}H_{23}ClNO_2SSe$ $(M+H)^+$: calcd 516.0298, found 516.0298.

2-([1,1'-Biphenyl]-2-ylmethyl)-4-(methylselanyl)-3-phenyl-1-tosyl-1H-pyrrole (49):



49 (101 mg) was obtained in 60% yield as pale yellow gummy liquid; R_f = 0.38 (8:2 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, DMSO–d_6): δ 8.24 (dt, J = 8.8, 3.2 Hz, 1H), 7.80 (dt, J = 9.2, 2.8 Hz, 1H), 7.49–7.40 (m, 4H), 7.38 (d, J = 8.0 Hz, 2H), 7.34–7.27 (m, 4H), 7.22 (br d, J = 8.4 Hz, 2H), 7.19–7.13 (m, 3H), 7.02 (td, J = 7.6, 1.6 Hz, 1H), 6.55 (d, J = 7.6 Hz, 1H), 3.91 (s, 2H), 2.32 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (101 MHz, DMSO–d_6) δ 147.1, 145.6, 144.1, 141.20, 141.17, 136.5, 135.1, 133.5, 130.8, 130.5, 129.9, 129.5, 129.4, 129.3, 128.9, 128.7, 128.0, 127.8, 127.52, 127.50, 127.3, 127.0, 126.4, 125.0, 121.7, 113.3, 29.1, 21.5, 7.5; IR (Neat)ν_{max} 2917, 1596, 1519, 1367, 1264, 1173, 736 cm^{-1}; HRMS (ESI) for $C_{31}H_{27}NNaO_2SSe$ $(M+Na)^+$: calcd 580.0820, found 580.0822.

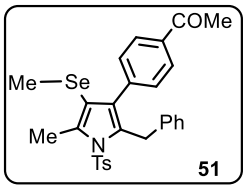
2-Benzyl-3-(4-fluorophenyl)-4-(methylselanyl)-1-(phenylsulfonyl)-1H-pyrrole (50):



50 (104 mg) was obtained in 73% yield as pale brown gummy liquid; R_f = 0.43 (8:2 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, DMSO–d_6): δ 7.66–7.61 (m, 3H), 7.49–7.42 (m, 3H), 7.27–7.15 (m, 4H), 7.12–7.08 (m, 3H), 6.80 (dd, J = 7.2, 3.6 Hz, 2H), 4.12 (s, 2H), 2.15 (s, 3H); ^{13}C NMR (101 MHz, DMSO–d_6) δ 162.1 (d, J= 245 Hz, 1C), 139.2, 138.2, 134.7, 131.8 (d, J= 8.1 Hz, 2C), 130.1, 129.89, 129.85 (d, J= 2.0 Hz, 1C), 128.7, 127.9, 127.1, 126.4, 125.0, 122.0, 115.8 (d, J= 21 Hz, 2C), 113.7, 30.7, 7.6; ^{19}F NMR (376 MHz, DMSO–d_6): δ –114.3; IR (Neat)ν_{max}

2921, 1602, 1508, 1368, 1264, 1153, 1092, 734 cm^{-1}; HRMS (ESI) for $C_{24}H_{20}FNNaO_2SSe^+$ $(M+Na)^+$: calcd 508.0256, found 508.0258.

1-(4-(2-Benzyl-5-methyl-4-(methylselanyl)-1-tosyl-1H-pyrrol-3-yl)phenyl)ethanone (51):



51 (79 mg) was obtained in 49% yield as pale yellow gummy liquid; R_f = 0.18 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, DMSO–d_6): δ 7.96 (d, J = 8.4 Hz, 2H), 7.44 (dd, J = 8.4, 2.4 Hz, 4H), 7.32 (d, J = 8.0 Hz, 2H), 7.23–7.12 (m, 3H), 6.92 (d, J = 6.8 Hz, 2H), 4.22 (s, 2H), 2.57 (s, 3H), 2.55 (s, 3H), 2.36 (s, 3H), 1.77 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 198.0, 145.8, 140.1, 139.6, 136.1, 136.0, 135.2, 130.9, 130.8, 130.7, 128.7, 128.5, 128.0, 126.9, 126.3, 112.4, 32.2, 27.2, 21.5, 15.2, 9.5; IR (Neat)ν_{max} 2923, 1734, 1679, 1361, 1263, 1166, 683 cm^{-1}; HRMS (ESI) for $C_{28}H_{28}NO_3SSe$ $(M+H)^+$: calcd 538.0950, found 538.0951.

2B.7. X-ray crystallography:

X-ray reflections for **18** were collected on Bruker D8 Quest CCD diffractometer using Mo-Kα, radiation. Data reduction was performed using CrysAlisPro (version 1.171.33.55). Apex 2 and SHELX-TL 97 program were used to solve and refine the data. All non-hydrogen atoms were refined anisotropically and C−H hydrogens were fixed.

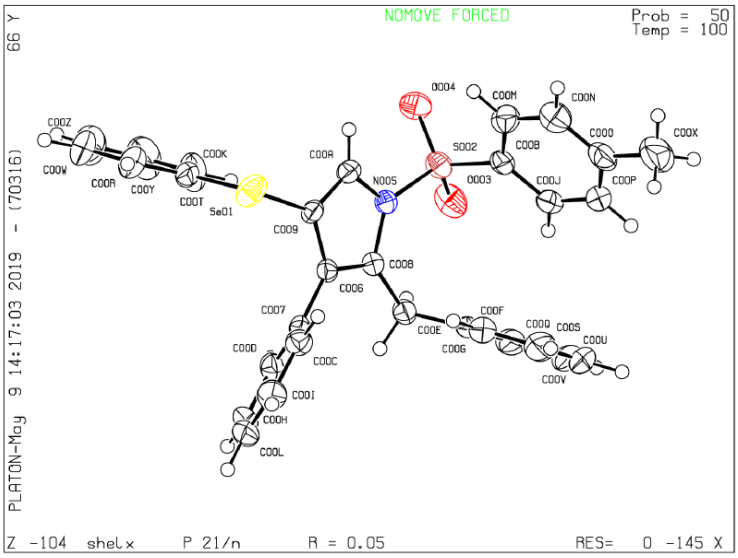


Figure 2B.6. Molecular structures of compounds **18;** thermal ellipsoids are set at 50% probability**.** Oxygen (red), nitrogen (blue), sulphur (maroon) and selenium (yellow).

Table 2B.4. Crystallographic Data for Compound **18**

Compound	**18**	V [Å^3]	2533.7(8)
formula	$C_{30}H_{25}NO_2SSe$	Z	4
Formula weight	542.53	ρ_{calcd} [g cm^{-3}]	1.422
crystal system	Monoclinic	μ [mm^{-1}]	1.592
space group	P 21/n	total reflns	66180
T [K]	100(2) K	unique reflns	5778
a [Å]	6.2629(11)	observed	4250
b [Å]	18.353(3)	R_1[I>2σ(I)]	0.0523(4250)
c [Å]	22.063(5)	wR2 [all]	0.1677(5778)
α [°]	90	GOF	0.909
β [°]	92.471(7)	Diffractometer	Bruker D8 Quest CCD
γ [°]	90	CCDC Number	CCDC 1945002

2B.8. References

(1) (a) Negishi, E. Handbook of Organopalladium Chemistry for Organic Synthesis; *Wiley-Interscience: New York*, **2002**. (b) Fallis, A. G.; Forgione, P. Tetrahedron 2001, 57, 5899. (c) Fagnou, K.; Lautens, M. *Chem. Rev*. **2003**, *103*, 169.

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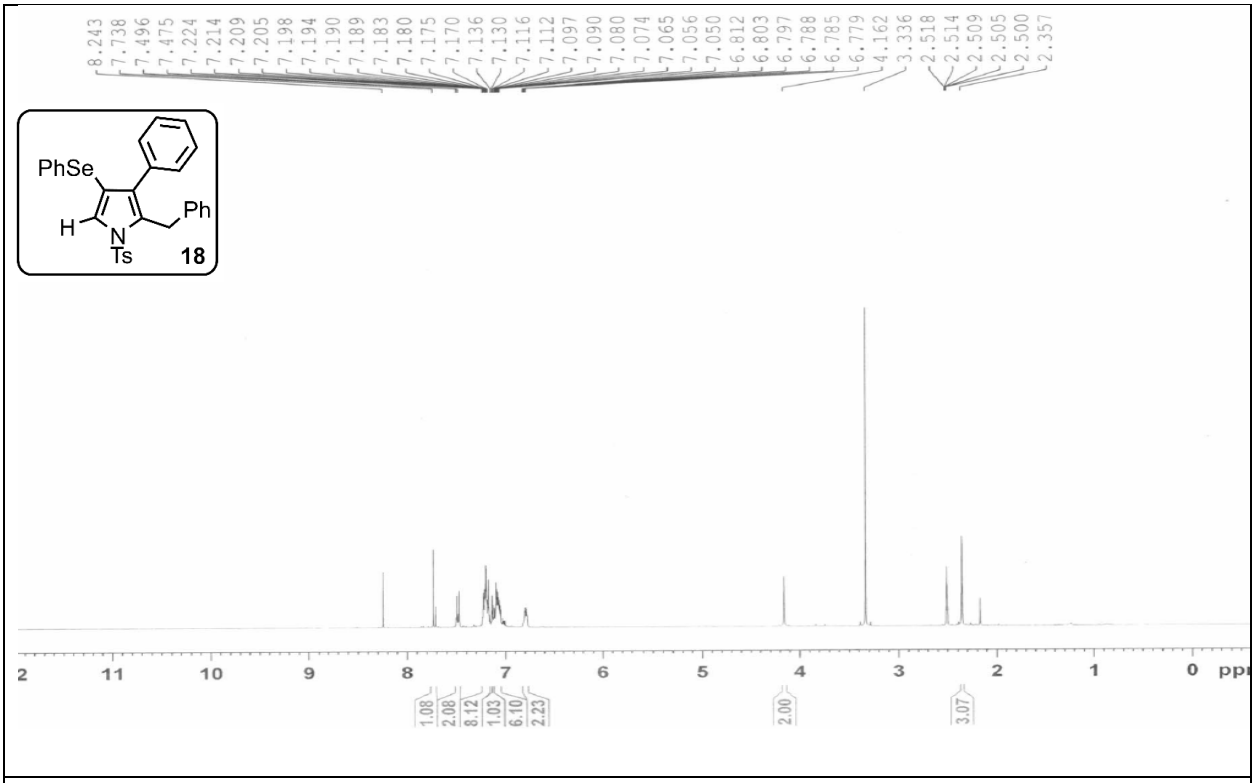
(9) Dutta, S.; Yang, S.; Vanjari, R.; Mallick, R. K.; Gandon, V.; Sahoo, A. K. *Angew. Chem., Int. Ed.* **2020**, *59*, 10785– 10790.

2B.9. Spectra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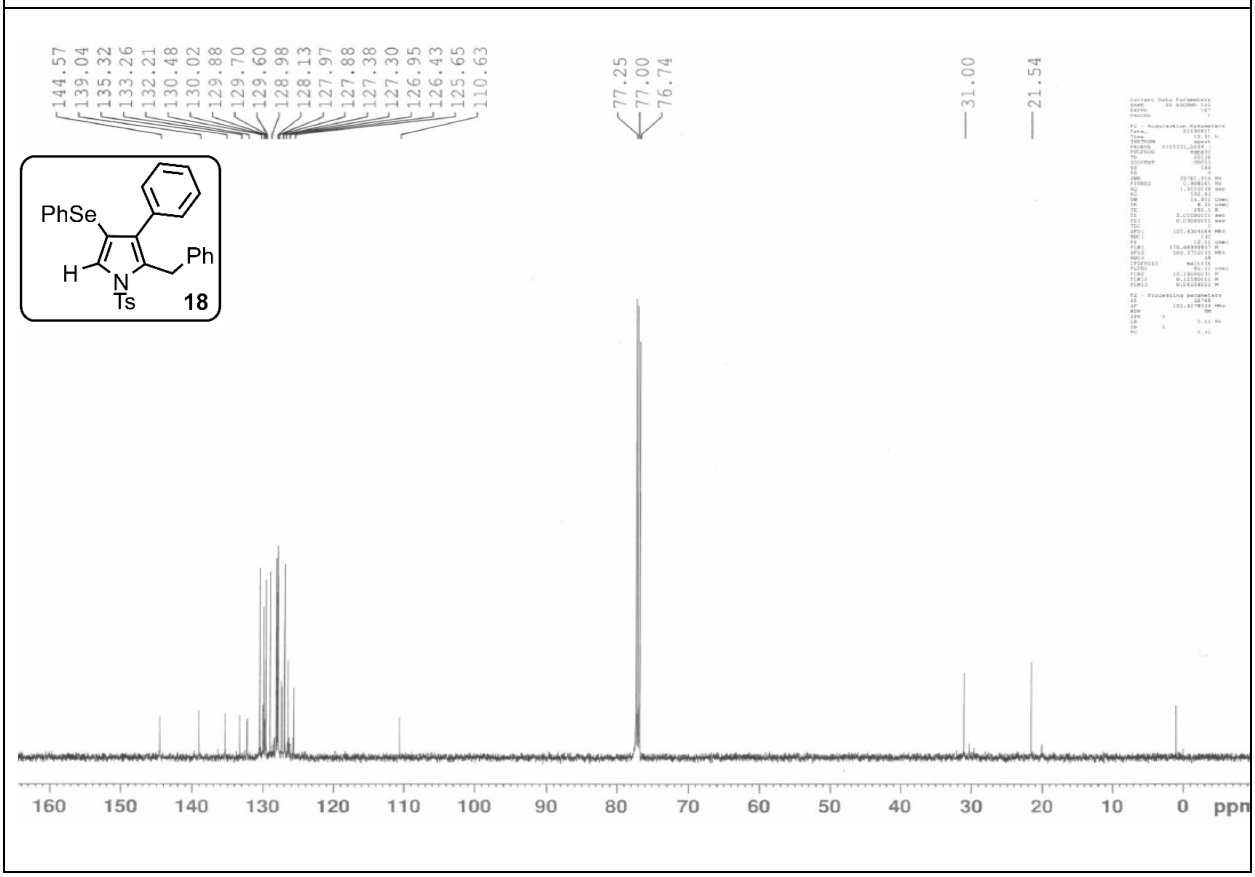
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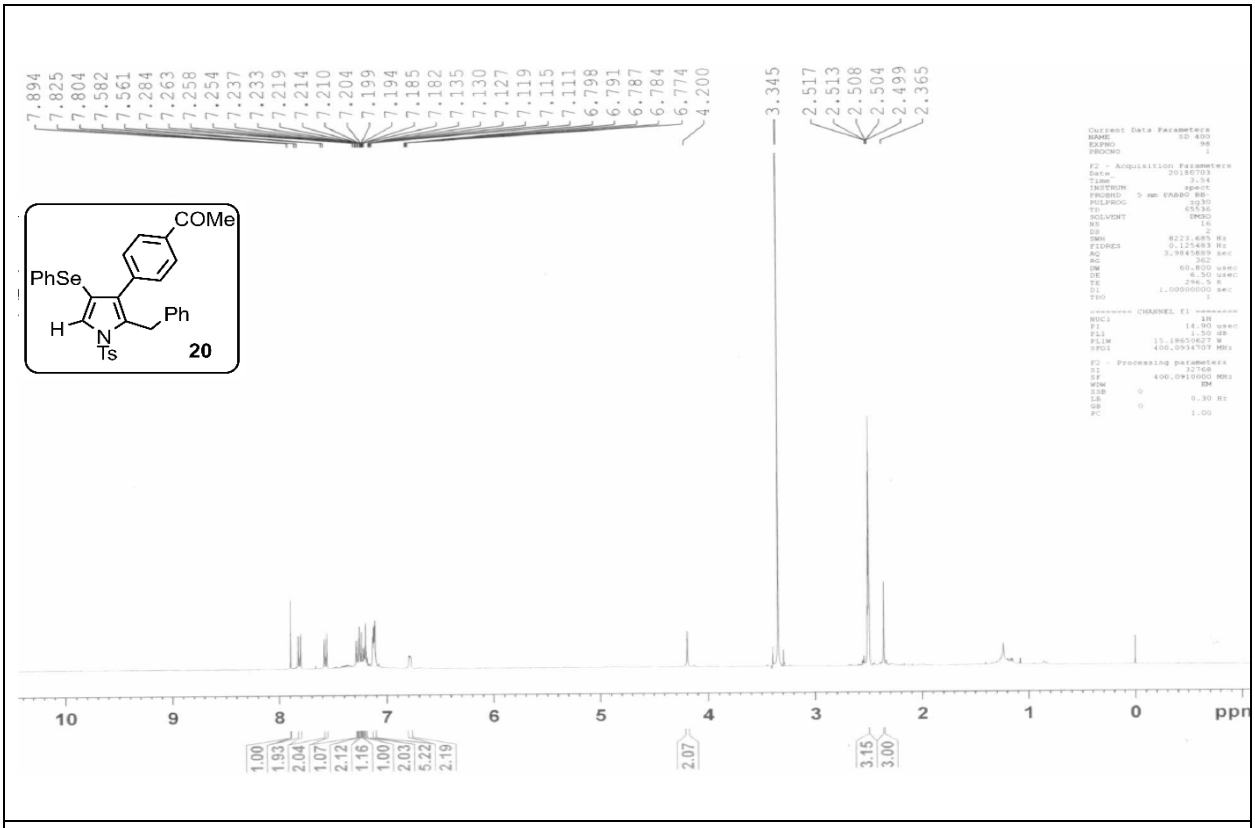
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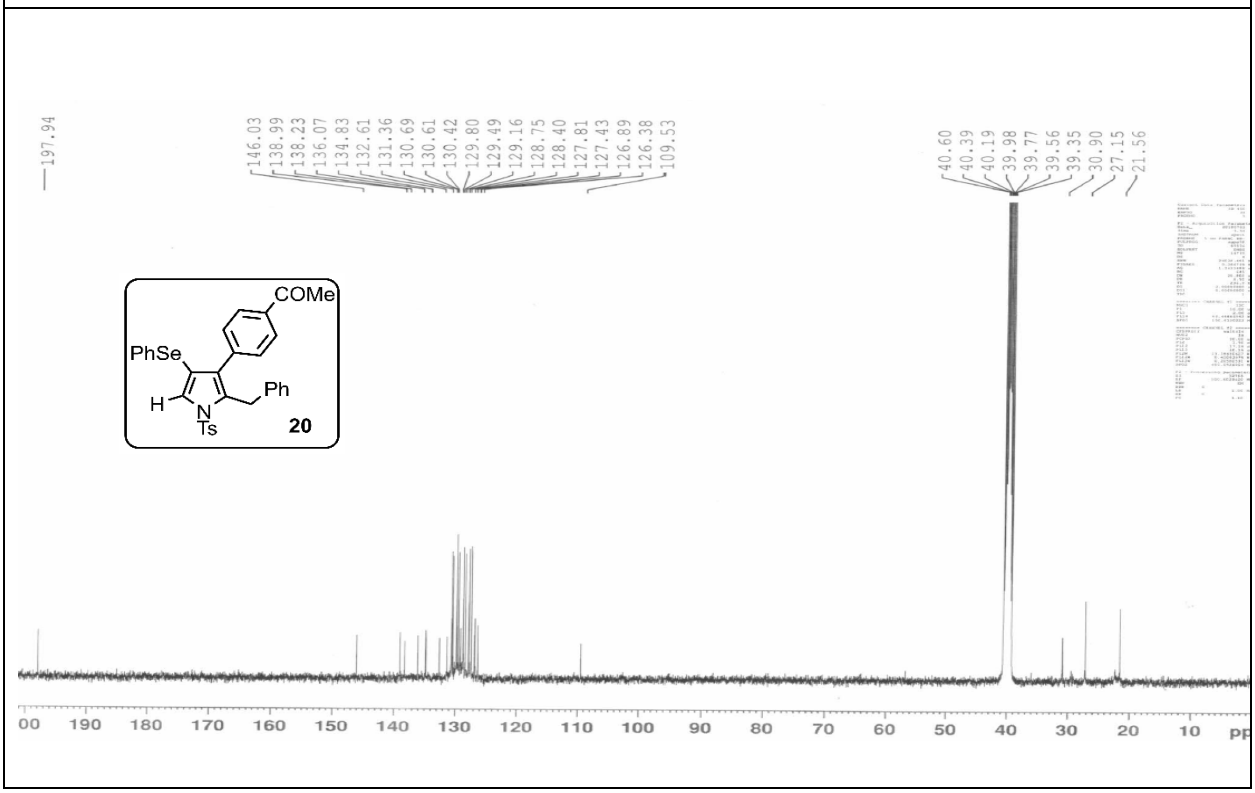
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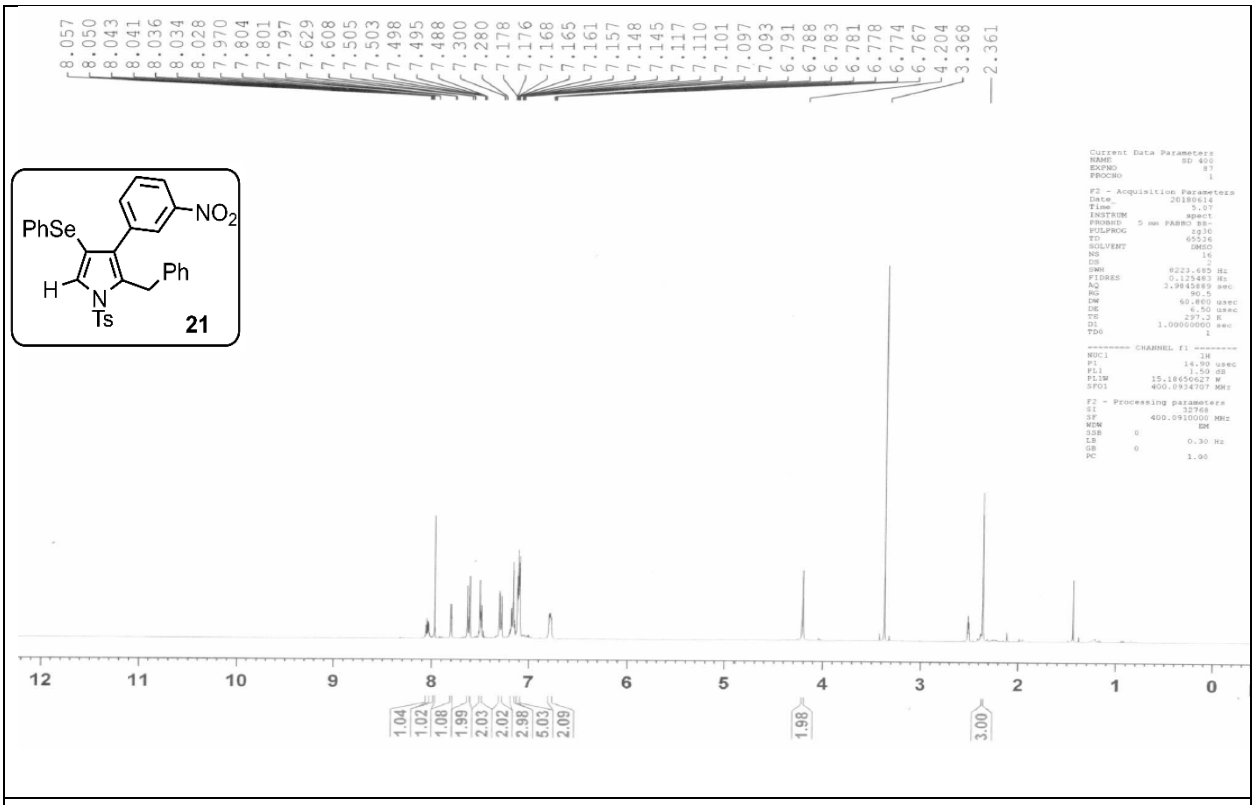
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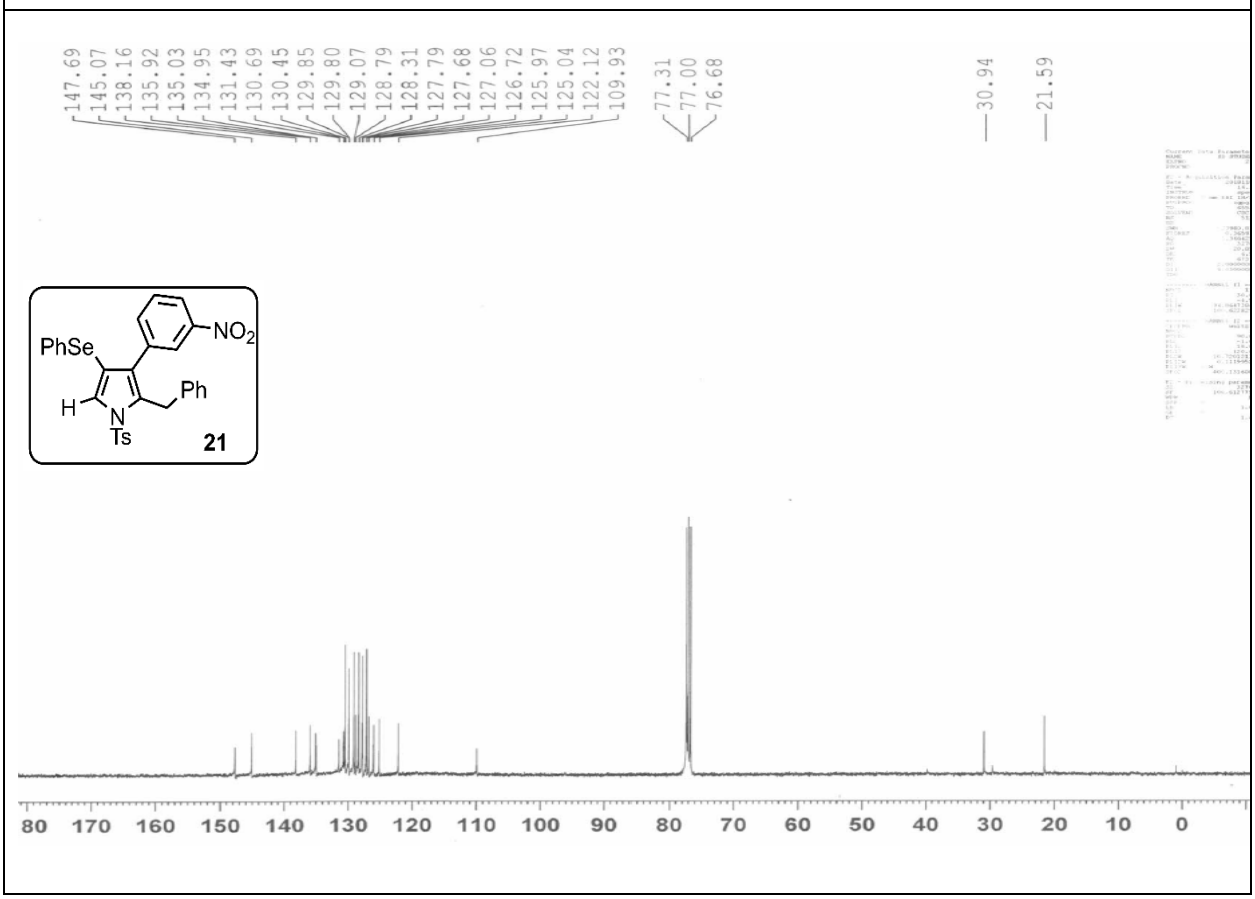
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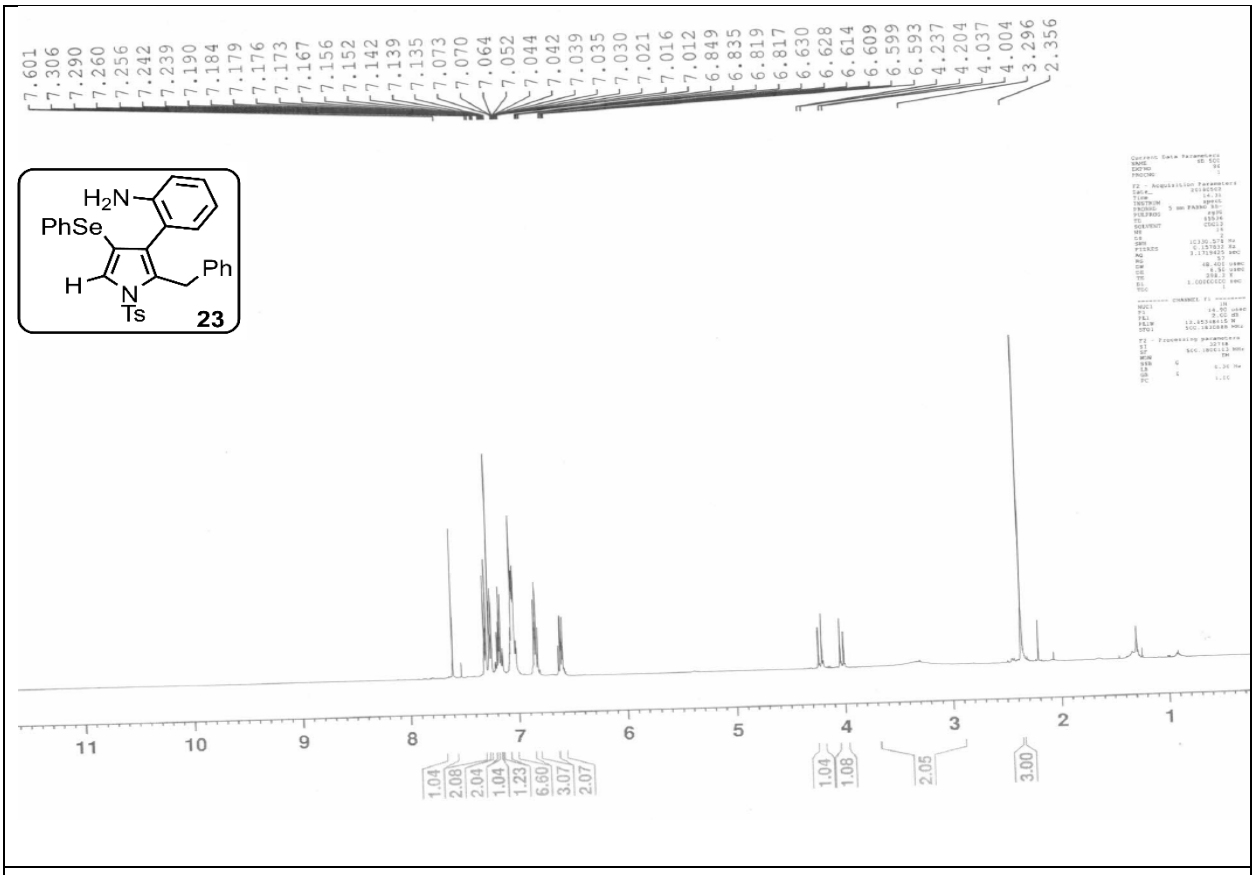
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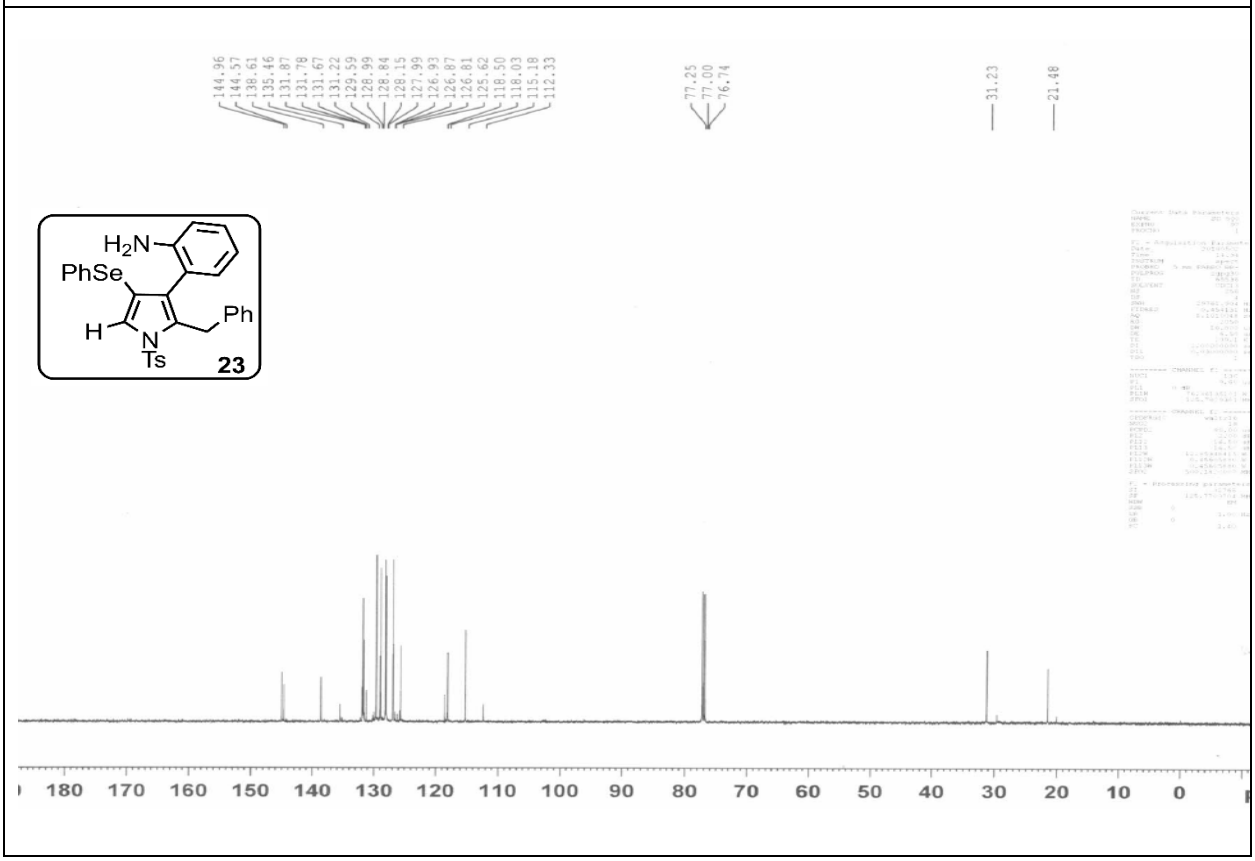
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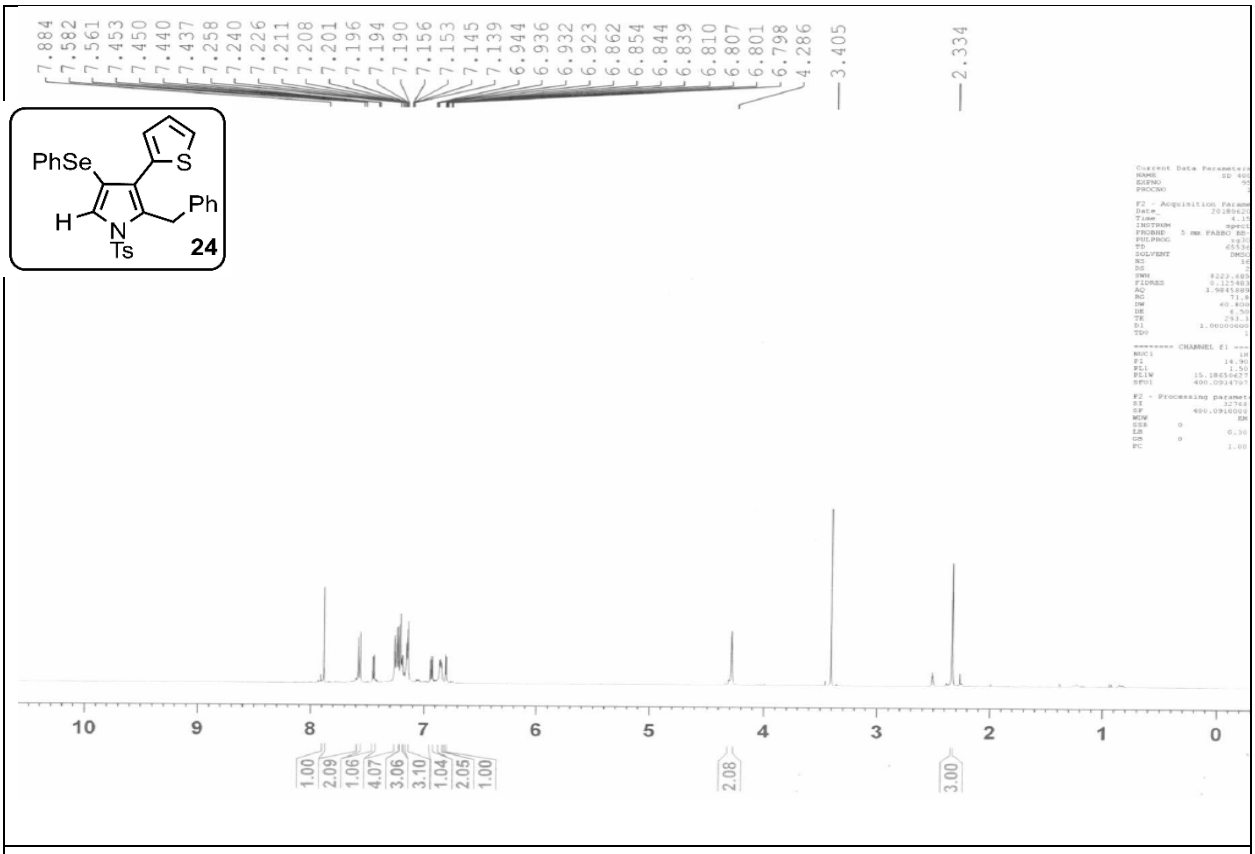
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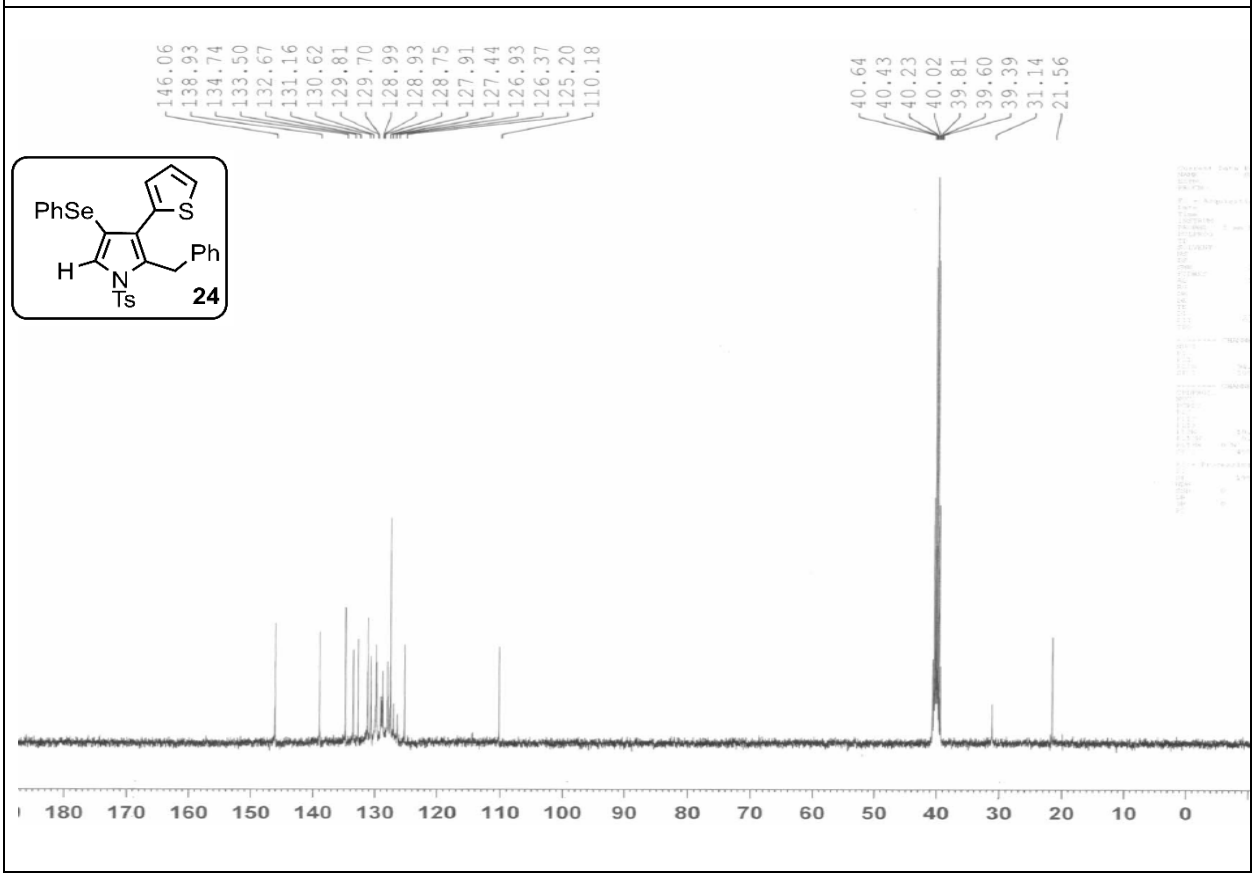
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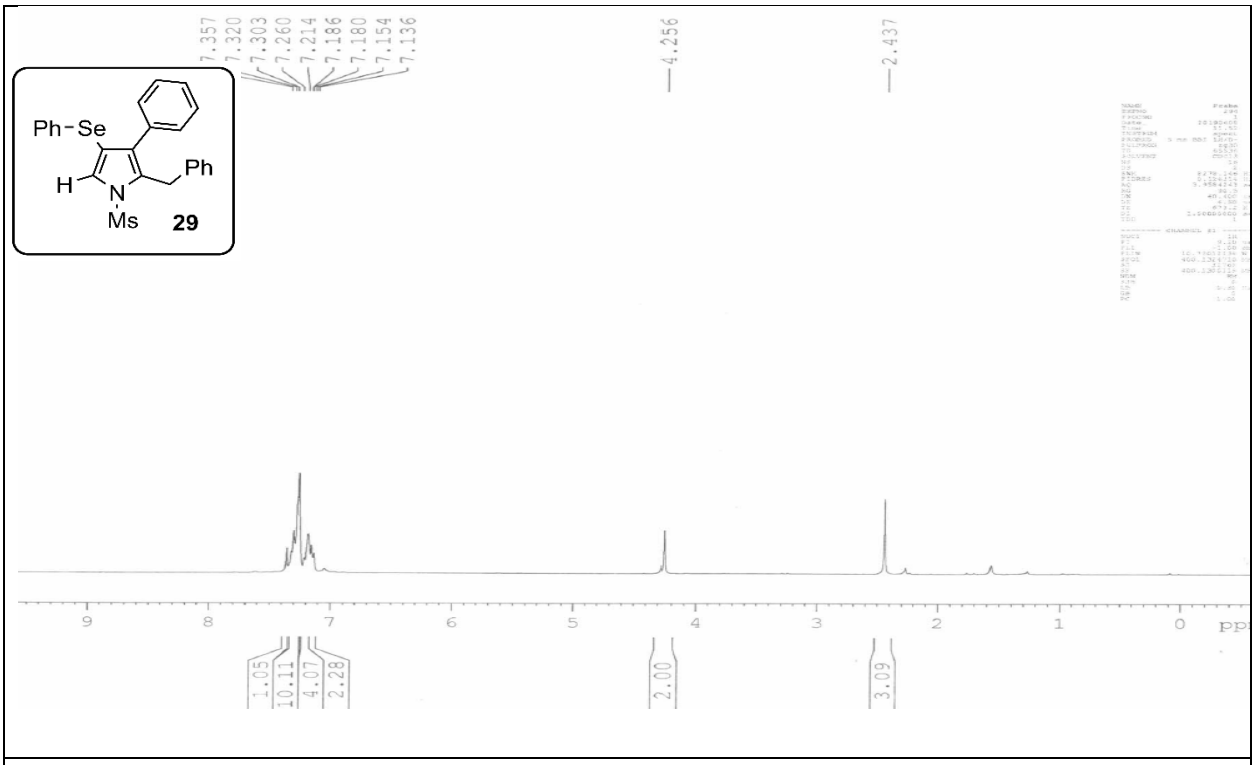
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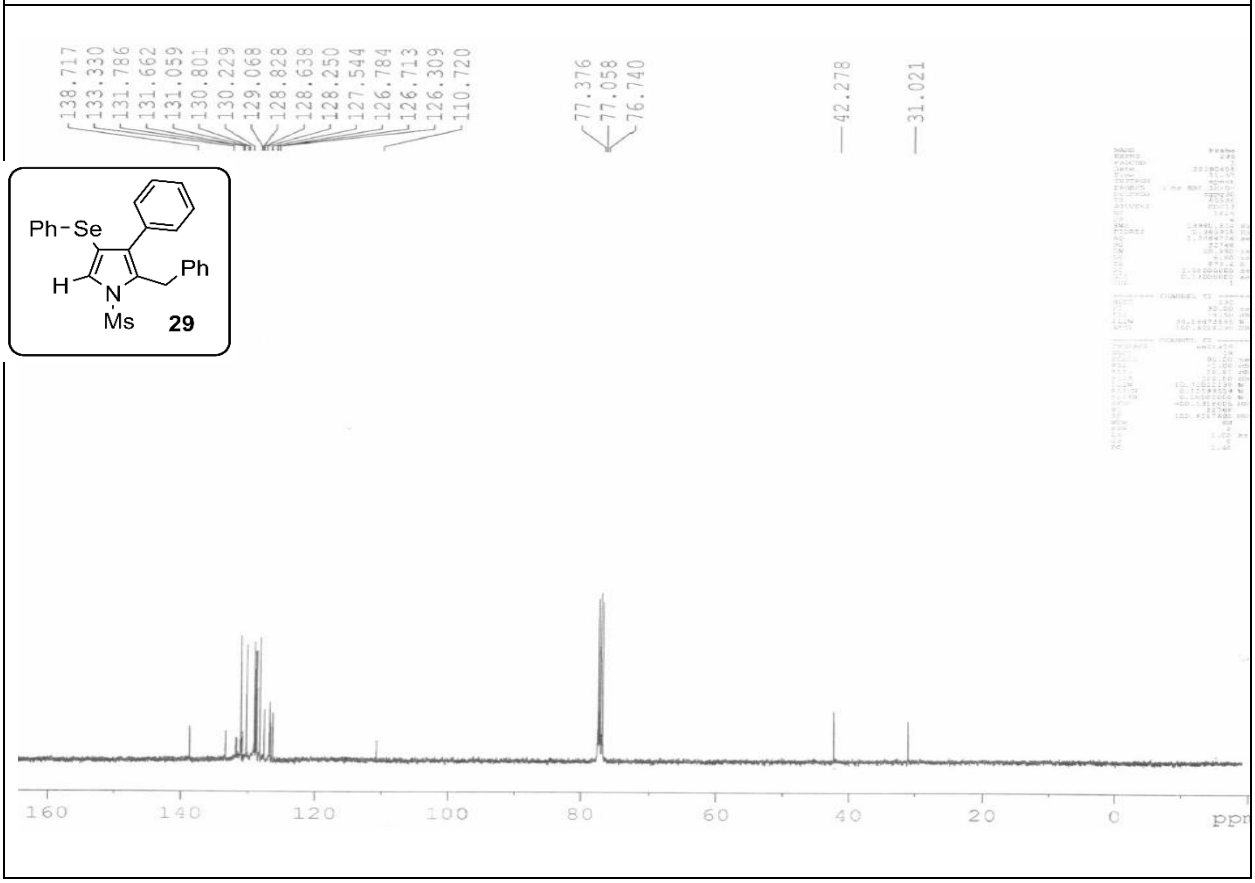
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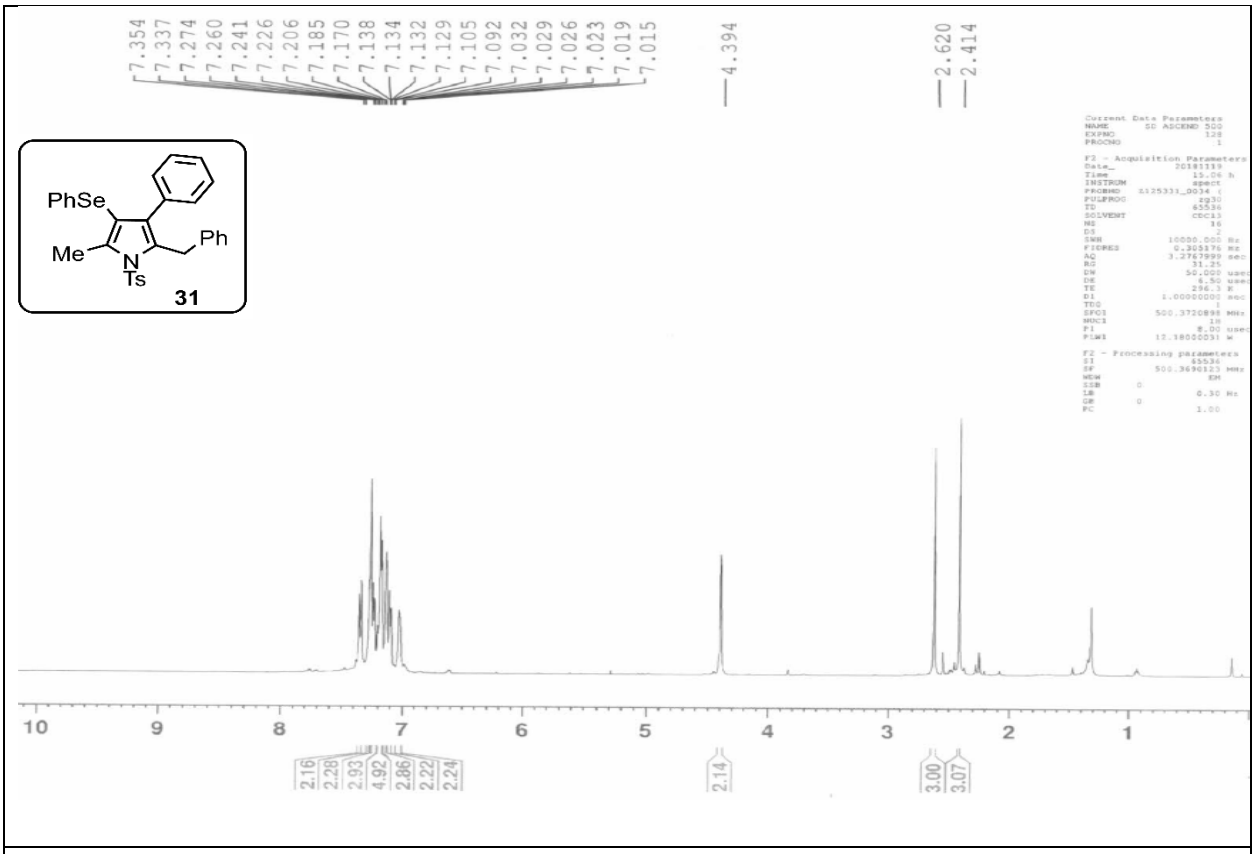
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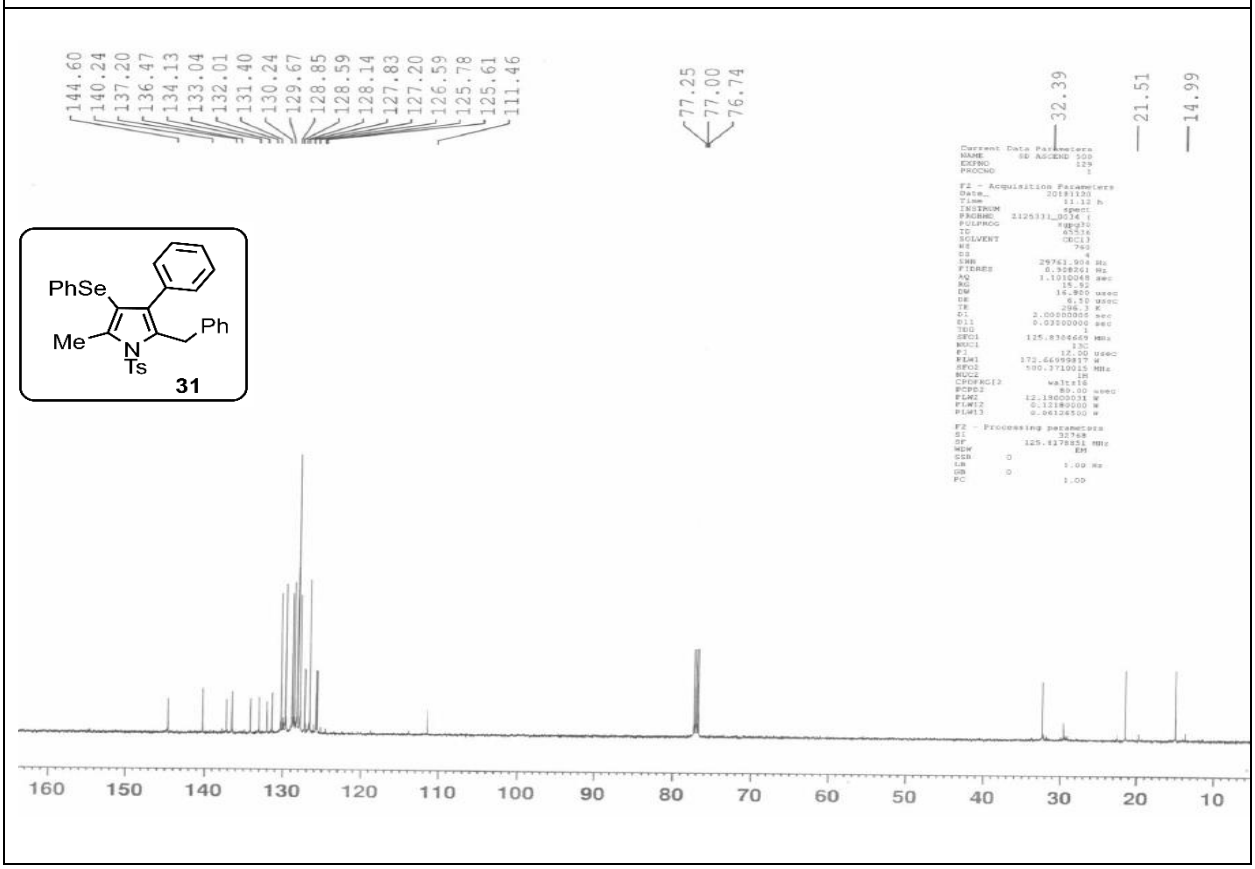
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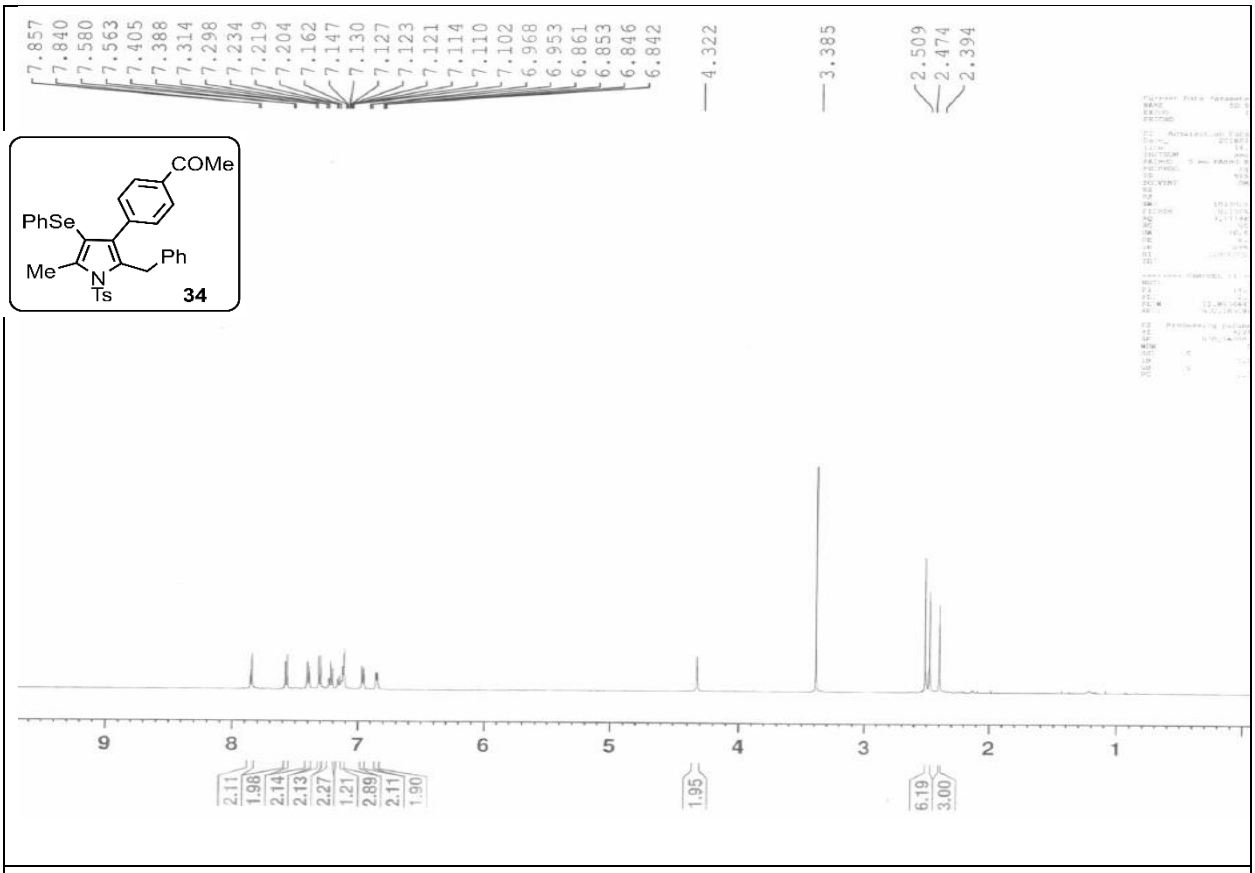
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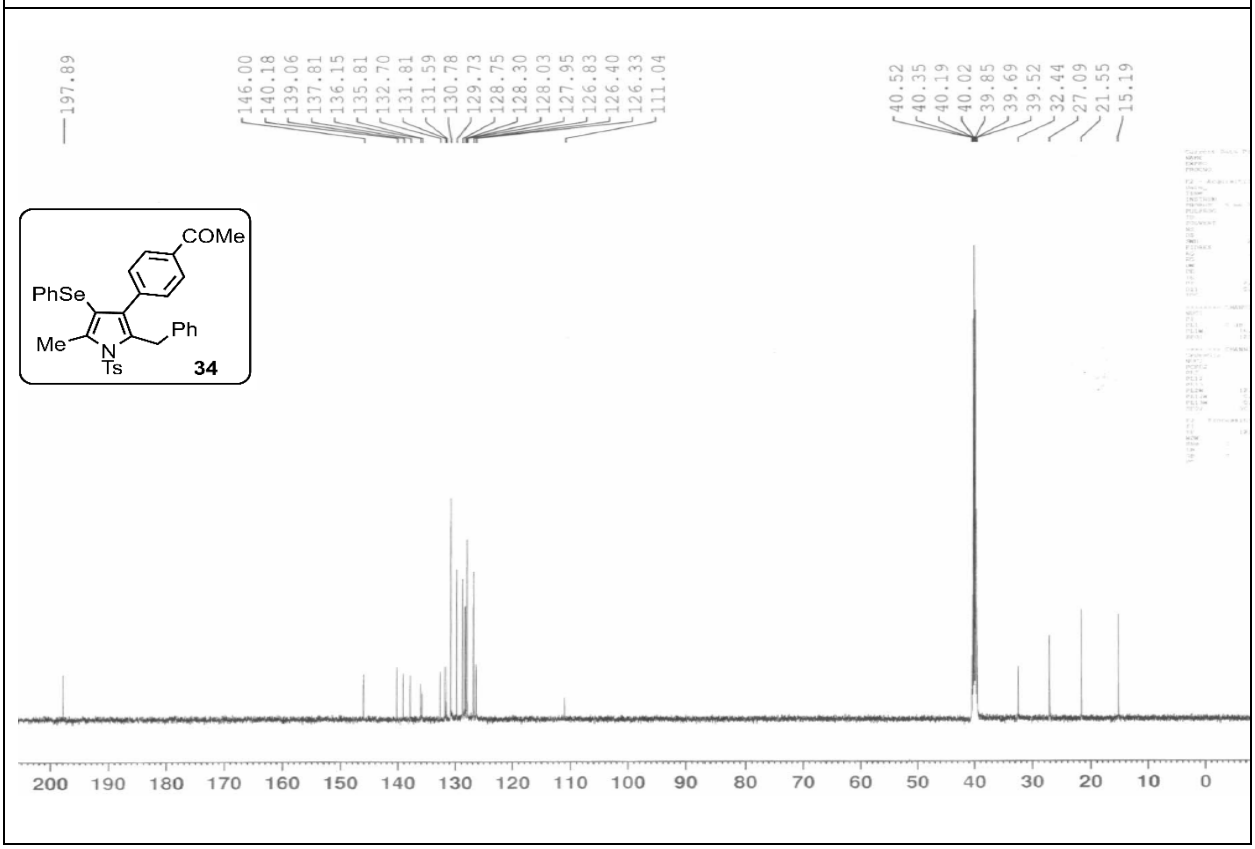
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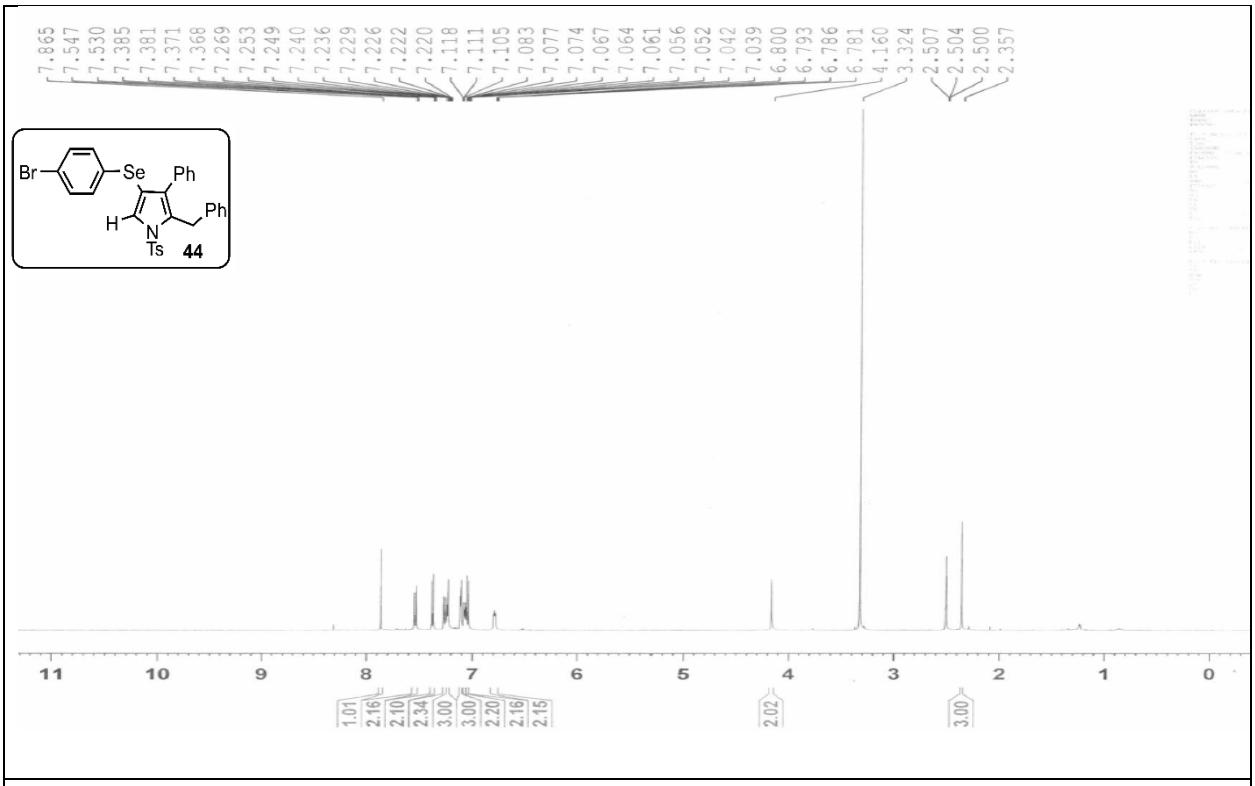
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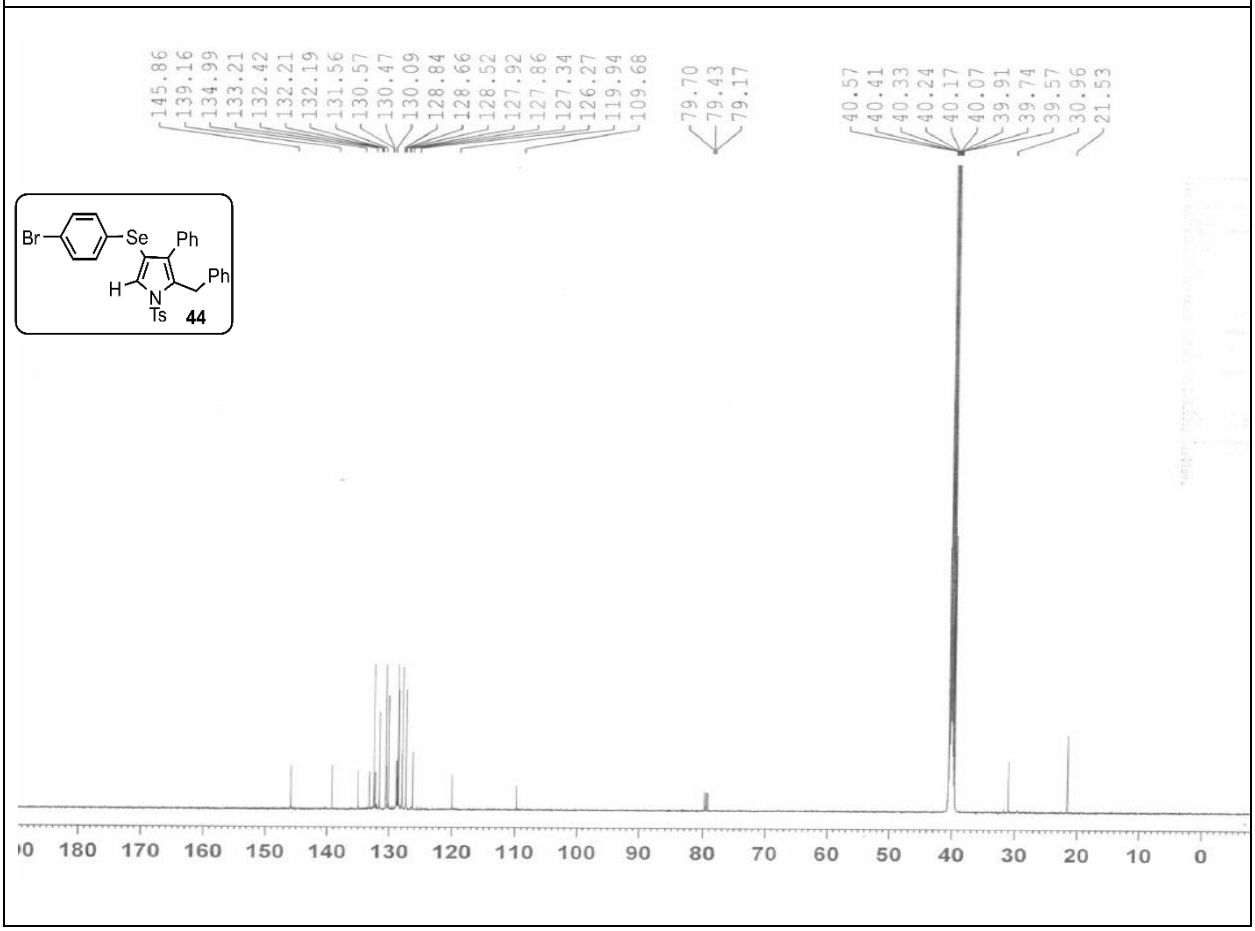
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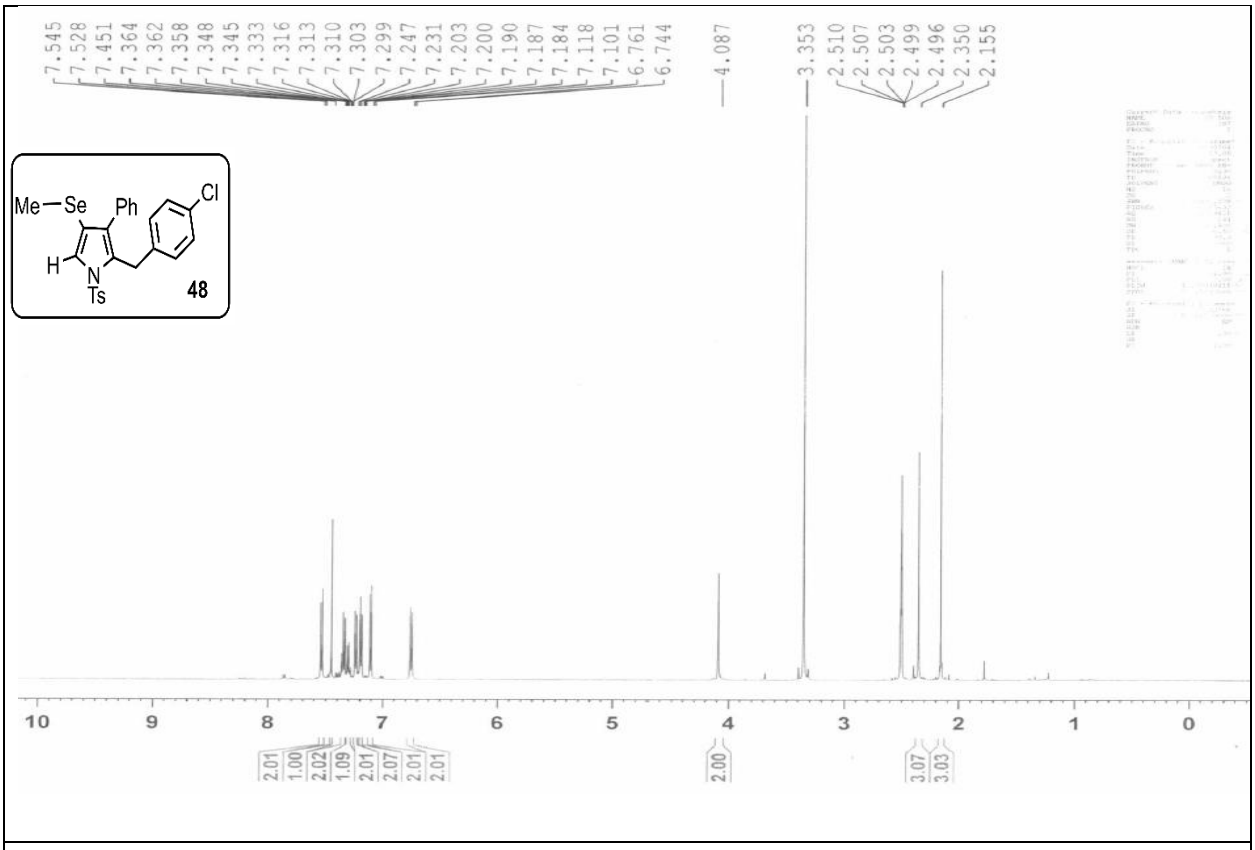
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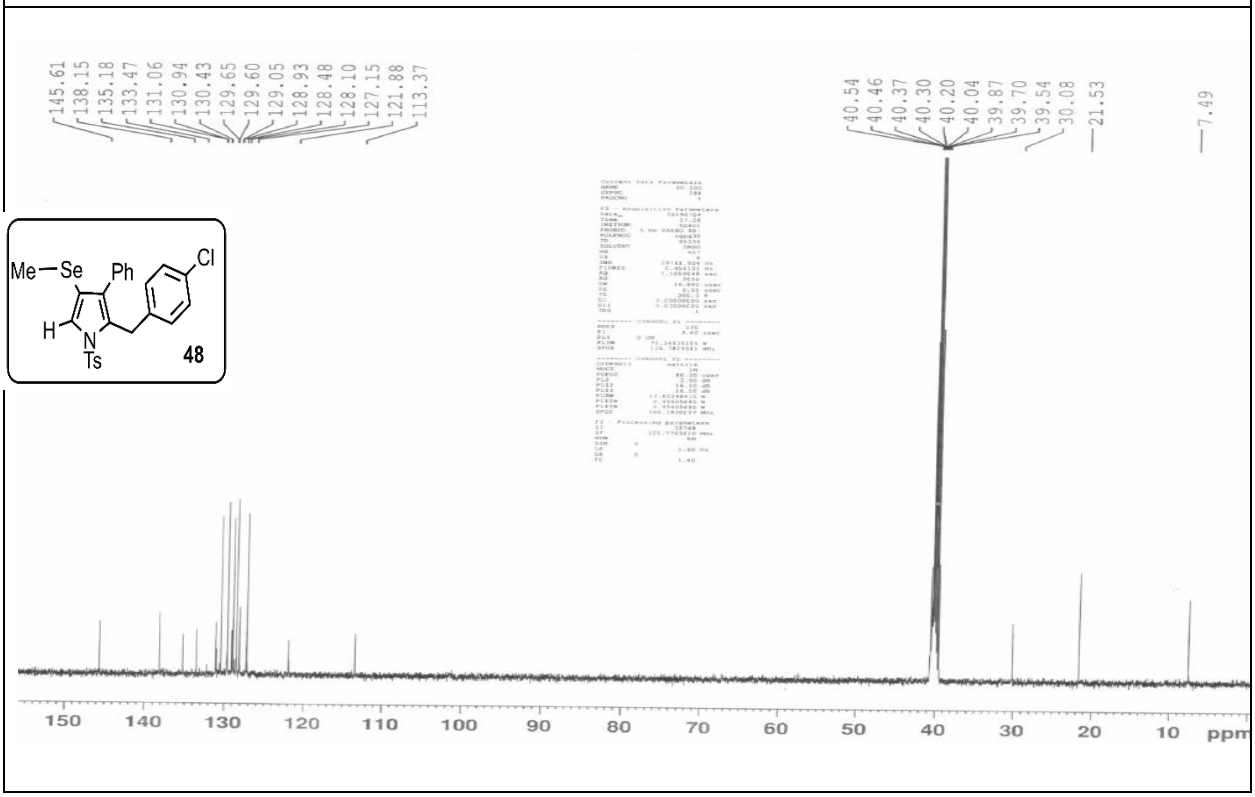
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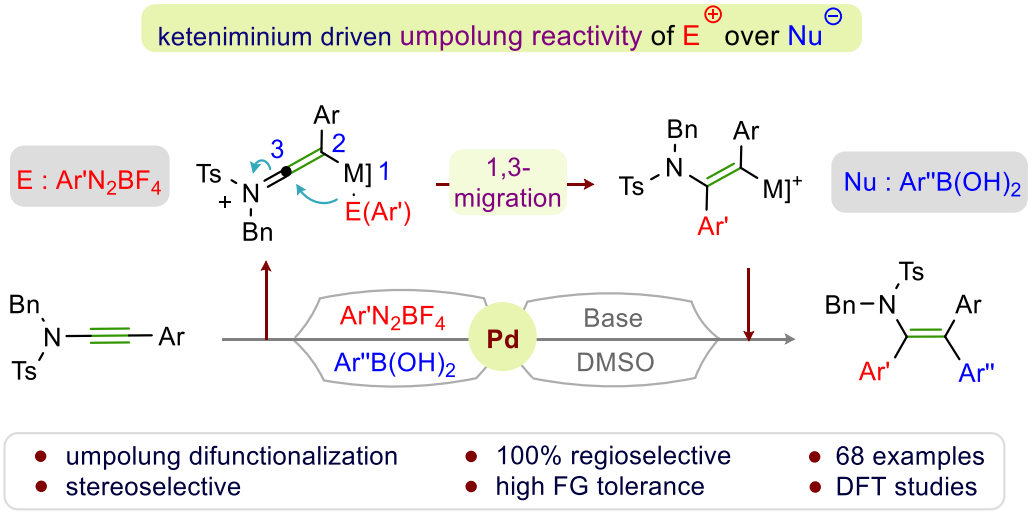
Chapter-3A

Keteniminium Driven Umpolung Difunctionalization of Ynamides

Abstract



A three component Pd-catalyzed coupling of ynamides, aryl diazonium salts, and aryl boronic acids for the synthesis of novel triaryl-substituted enamides is described. This transformation represents the first example of an umpolung regioselective unsymmetrical *syn*-1,2-diarylation/aryl-vinylation of ynamides. The aryl moieties of diazonium salt (electrophile) and boronic acid (nucleophile) are explicitly incorporated in the electrophilic α- and nucleophilic β-position of the ynamide, respectively, resulting in a single isomer of N-bearing tetrasubstituted olefin. The scope is broad (68 examples) showing excellent functional group tolerance. DFT calculations substantiate the rationale of the mechanistic cycle and the regioselectivity. Chemoselectivity and synthetic potential of the enamide products are also studied.

Publication

S. Dutta, S. Yang, R. Vanjari, R. Kumar Mallick, V. Gandon, A. K. Sahoo. *Angew. Chem., Int. Ed.* **2020**, *59,* 10785–10790.

3A.1. Introduction

Tetrasubstituted olefins are integral component in many biologically important scaffolds. A direct alkyne difunctionalization could readily make tetrasubstituted olefins.[1] In this regard, the difunctionalization of ynamide, a versatile N-containing unsymmetrical alkyne, provides an impeccable entry to tetra-substituted enamides. Thus, trapping of a nucleophile and an electrophile at the α and β position of keteniminium species (**II**), generated in-situ via N-lone pair electron polarization to alkyne of ynamide **I**, respectively, provides substituted olefins **III** (Fig. 3A.1a, path-I)].[2] However, on a conceptual note, *umpolung difunctionalization* of ynamides with the incorporation of an electrophiles and nucleophiles at the α- and β-positions, respectively, is significantly challenging although exceedingly valuable (Fig. 3A.1a, path-II). However, such umpolung difunctionalization of ynamides is so far confined to: i) a strain controlled intramolecular trapping of a nucleophile (Fig. 3A.1b, path-I),[3] or ii) a chelation driven

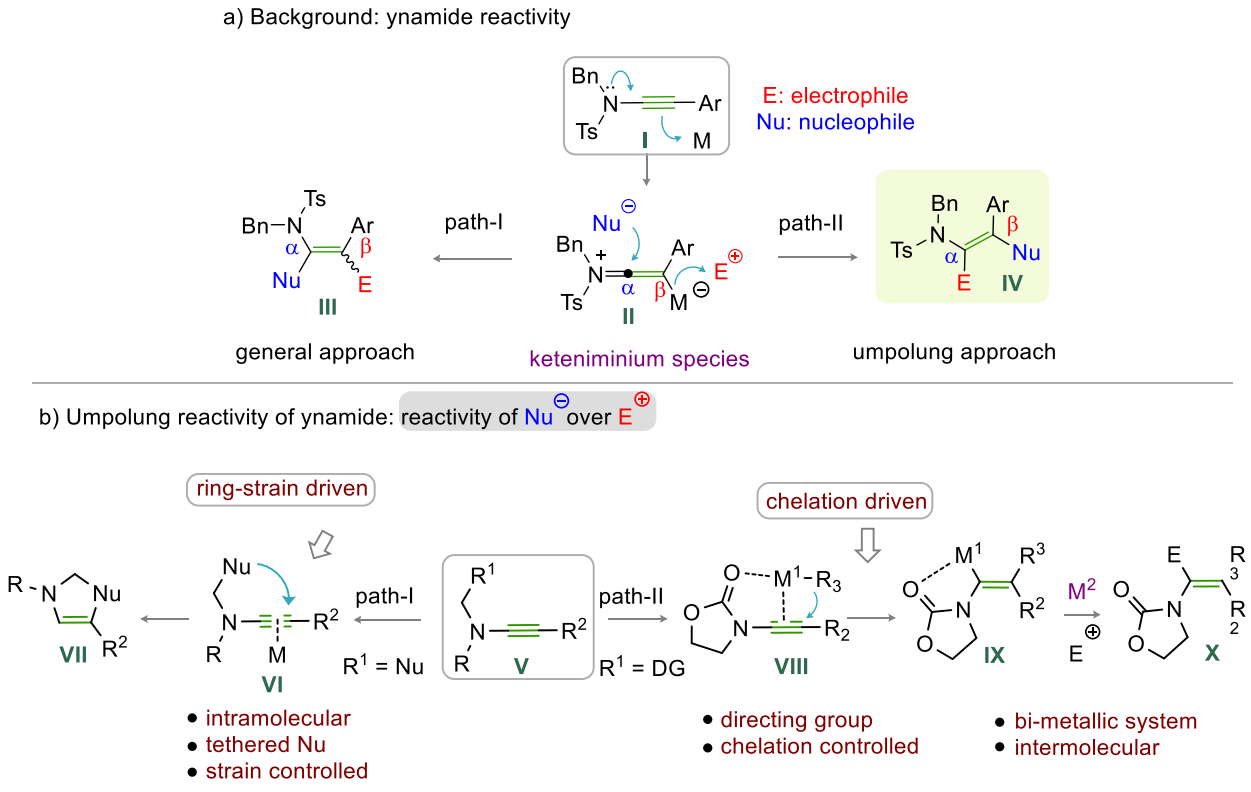


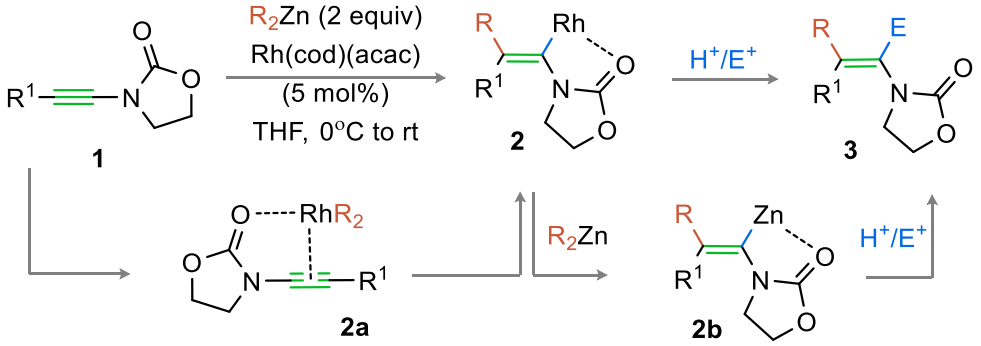
Figure 3A.1. Umpolung reactivity of ynamides

carbometalation and functionalization sequence that primarily requires a bimetallic system (Fig. 3A.1b, path-II).[4] In these approaches, the attack of the nucleophile is pivotal in making such strategies synthetically viable.

3A.2. Precedents

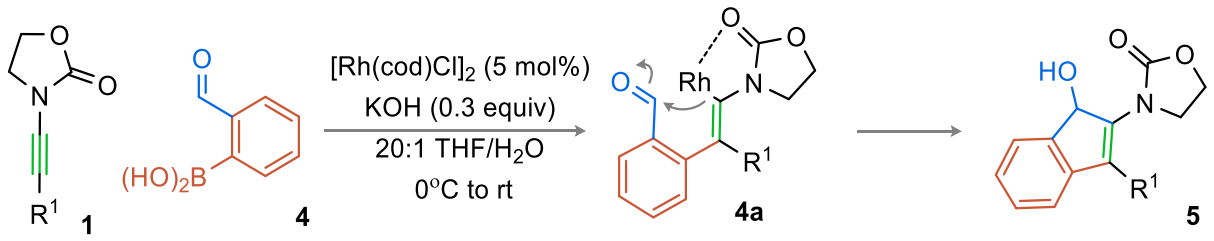
3A.2.1 Umpolung difunctionalization

In 2009, the Lam group elegantly adopted a chelation strategy for the regioselective difunctionalization of ynamides (**Scheme 1**).[4a] The reaction of ynamide **1** in presence of dialkyl zinc (R^2_2Zn), Rh(cod)(acac), and electrophile (H^+, aryl, allyl, and/or vinyl) furnishes N-enabled tetrasubstituted olefin **3**. The transformation initiates a carbamate assisted alkyne activation by a Rh-catalyst to form **2a**. Next, carbozincation of **2a** happens by a regioselective attack of R^2 group at the β-position of ynamide to form **2b**; this process involves the β-alkyl-α-Rh intermediate **2**. Further, trap of alkenyl-zinc species with various electrophiles (H^+, aryl, allyl, vinyl) furnishes **3** (**Scheme 3A.1**).



Scheme 3A.1. Rh-catalyzed carbozincation of ynamide

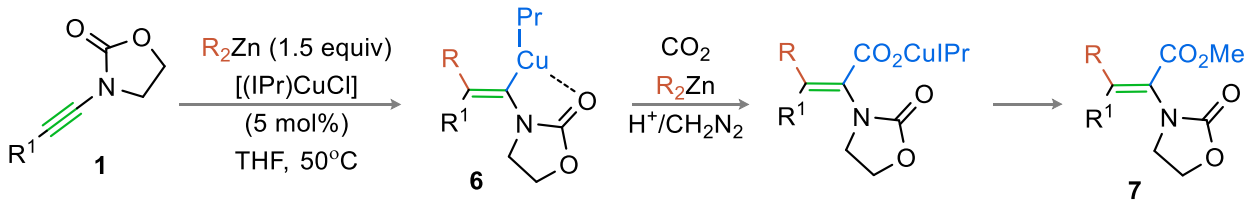
Unlike organo-zinc, organo-boron reagents have also been employed for difunctionalization of ynamide by the same group in 2010 (**Scheme 3A.2**).[4b] The 2-carbonyl substituted aryl boronic acids (**4**) upon oxidative addition of with $[Rh(cod)Cl]_2$, followed by carbometallation with ynamide **1** provides **4a**. Finally,



Scheme 3A.2. Rh-catalyzed intramolecular difunctionalization of ynamide

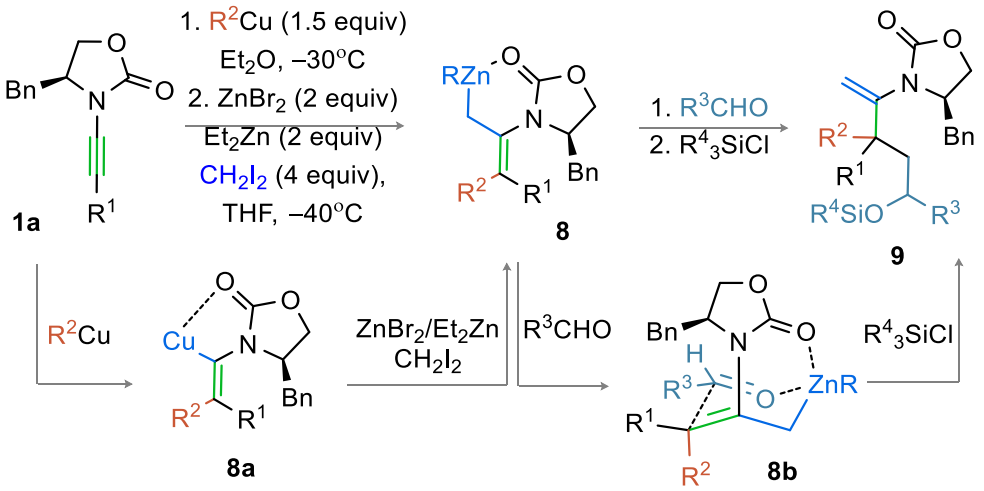
intramolecular cyclization with carbonyl group of **4a** gives the cyclized product **5**.

A seminal work by Hou and co-workers describes Cu-catalyzed alkylative carboxylation of ynamide **1**, when subjected to dialkylzinc, IPrCuCl, CO_2, and diazomethane, to yield **7** (**Scheme 3A.3**).[4c] An umpolung β-alkyl-cupration of ynamide at first generates α-alkenyl-Cu species **6**. Next, CO_2 insertion of **6** and esterification by CH_2N_2 furnishes difunctionalized product **7**.



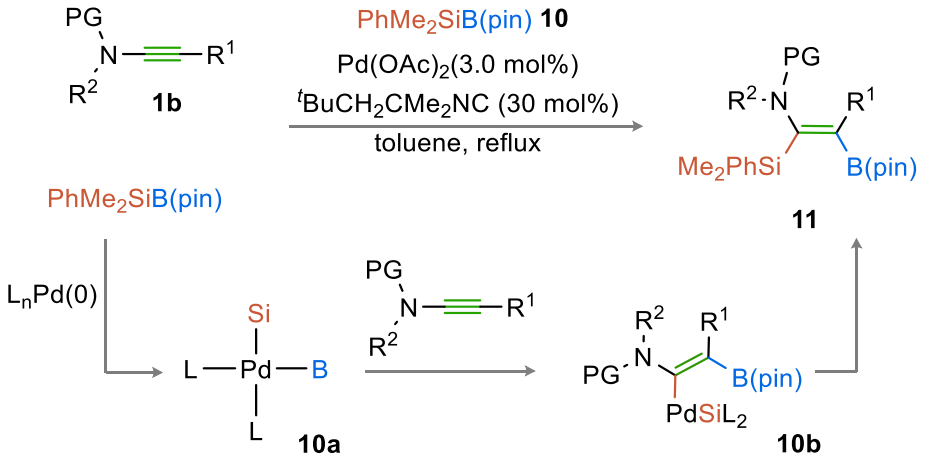
Scheme 3A.3. Cu-catalyzed alkylative-carboxylation of ynamide

In 2009, a remarkable protocol of generating all quaternary carbons via difunctionalization of ynamide under Cu-catalysis has been demonstrated by Marek and coworkers (Scheme 3A.4).[4d] At first, alkyl-cupration of ynamide 1a provides β-alkyl-Cu species 8a, which subsequently undergoes methylation in presence of CH_2I_2 and $ZnBr_2$ to provide Int-8. Next, a stereoselective attack of 8 to aldehyde (involving a chair-like transition state 8b) and O-Si protection yields 9.



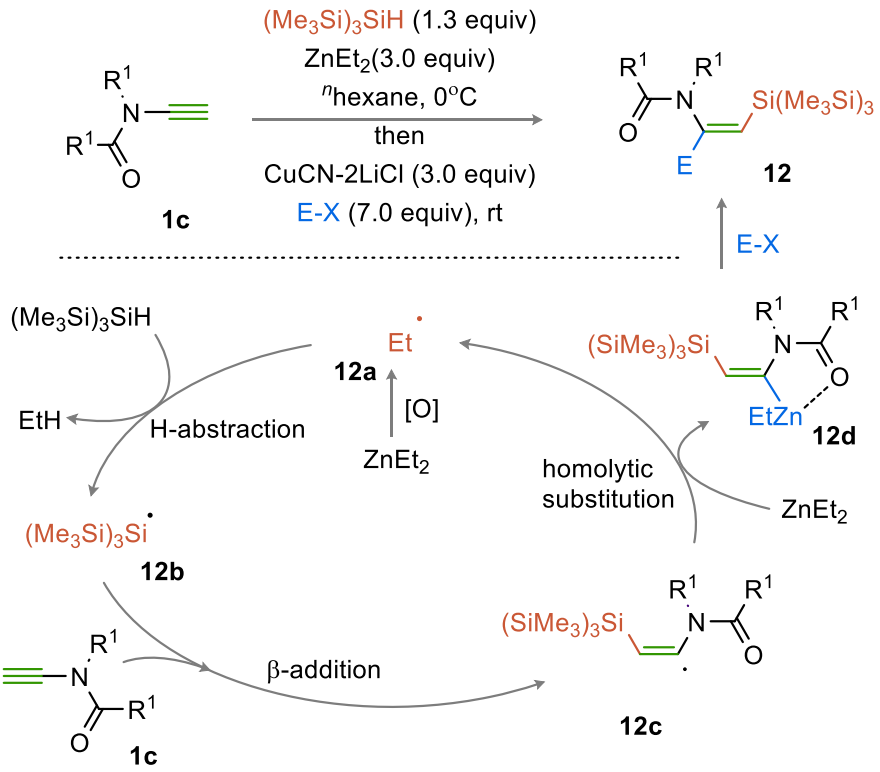
Scheme 3A.4. Alkyl-zincation of ynamides: generation of quaternary center

An interesting breakthrough of Pd-catalyzed *cis*-boryl-silylation of ynamide has been surfaced by Sato and co-workers in 2013 (**Scheme 3A.5**).[5] The mechanism of hetero-difunctionalization of ynamide involves: i) an oxidative addition of boryl-silane reagent **10** to $L_nPd(0)$ to form **10a**, ii) *cis*-boryl-palladation of ynamide (with Pd at α-position of ynamide) to give **10b**, and iii) finally, the reductive elimination of **10b** to afford **11**.



Scheme 3A.5. Pd-catalyzed boryl-silylation of ynamide

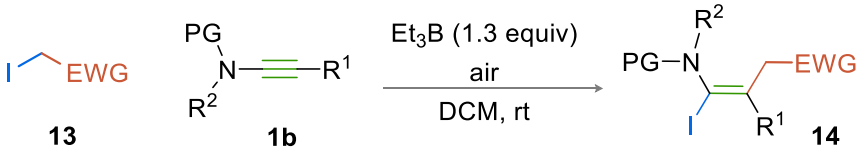
The Luna and co-workers in 2014 have shown a *trans*-silyl-zincation of ynamide (**Scheme 3A.6**).[6] The ethyl radical **12a**, generated in-situ from $ZnEt_2$ under oxidative condition, mediated abstraction of H-radical from silane at first provides silyl radical **12b**. Next, regioselective attack of silyl radical to ynamide β-position delivers vinylic radical **12c**. The homolytic substitution of **12c** with $ZnEt_2$ generates vinyl-zinc species **12d**. Finally, trap of electrophiles with **12d** makes β-silylated trisubstituted enamides **12**.



Scheme 3A.6. Radical mediated *trans*-silyl-zincation of ynamide

Another radical difunctionalization of ynamide with iodoalkanes has been emanated from Feray and co-workers, in 2020 (**Scheme 3A.7**).[7] Exposing ynamide **1c** with triethyl borane (BEt_3) and iodoalkane **13** allows the access of tetrasubstituted iodo-enamide **14**. Accordingly, activation of C-I bond by Lewis acid at first generates the respective carbon radical. Subsequently, a regio and

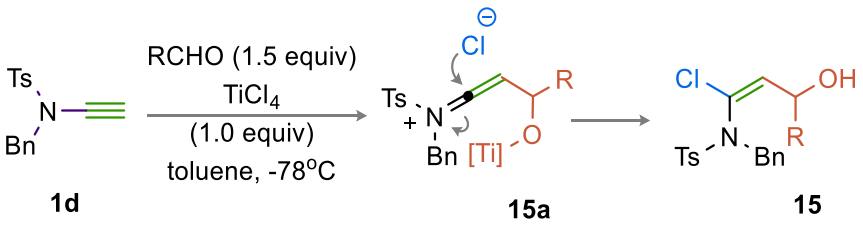
stereoselective attack of carbon radical to β-carbon of ynamide forms the desired product **14**.



Scheme 3A.7. Radical mediated iodo-alkylation of ynamide

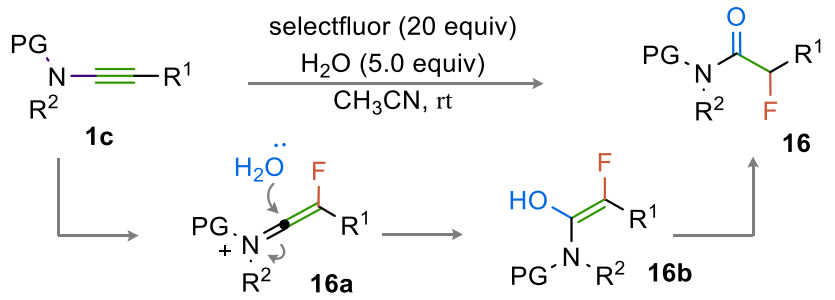
3A.2.2. Keteniminium driven difunctionalization

In 2016, Matsuo and co-workers have showcased a keteniminium species driven addition of terminal-unsubstituted ynamide **1d** to carbonyls followed by the attack of chloride to afford 1-Cl-1-amine substituted allylic alcohols **15** (**Scheme 3A.8**).[8] The reaction initiates the attack of ynamide **1d** to Ti-activated carbonyl compound to yield keteniminium species **15a**. Next, insertion of chloride ion at α-position of **15a** delivers the final product **15**.



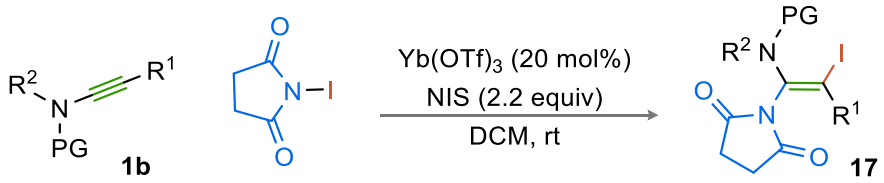
Scheme 3A.8. Addition of halogen and carbonyl compounds to ynamide

Wang and co-worker display a metal-free oxy-fluorination of ynamide in presence of selectfluor and water (Scheme 3A.9).[9] Thus, activation of ynamide 1b with selectfluor in-situ forms fluorinated keteniminium species 16a. The attack of H_2O at the α-position of 16a and then tautomerization delivers the desired product 16.



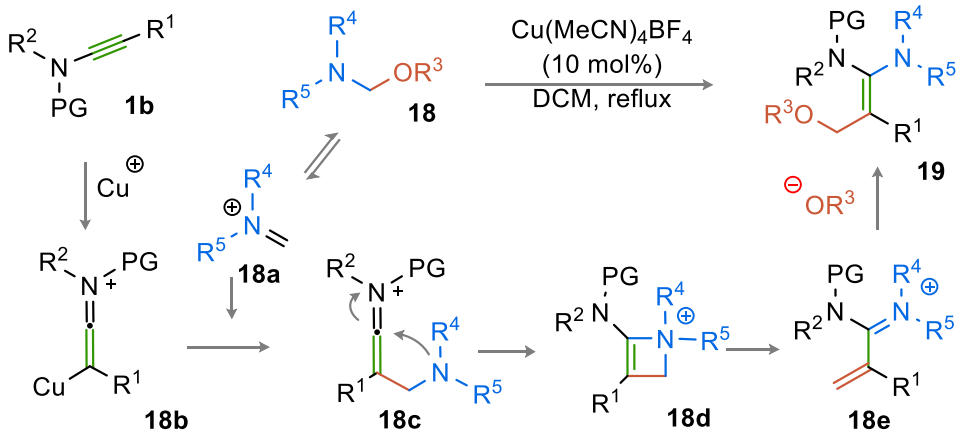
Scheme 3A.9. Keteneiminium driven oxy-fluorination of ynamide

Our group has demonstrated a *trans*-selective iodo-imidation of ynamide to access β-iodo-enamides **17** (**Scheme 3A.10**).[10] In the presence of ytterbium(III) trifluoromethanesulfonate [$Yb(OTf)_3$] and *N*-iodosuccinimide (NIS), ynamide undergoes β-iodination followed by the attack of succinimide at the α–position of ynamide to deliver tetrasubstituted ketene aminals.



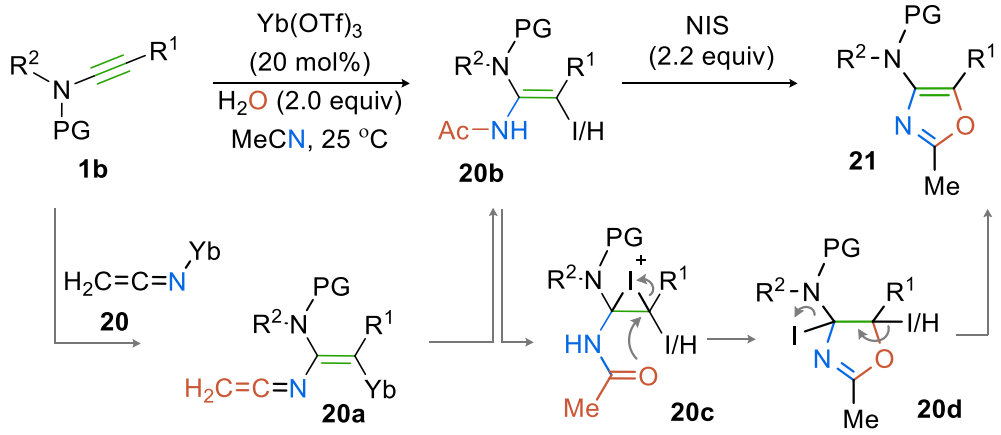
Scheme 3A.10. Yb-catalyzed iodo-imidation of ynamide with NIS

Sun and co-workers have shown a Cu-catalyzed *trans*-amino-oxymethylation of ynamide (**Scheme 3A.11**).[11] The attack of an in-situ generated β–Cu-keteniminium species **18b** to the iminium ion **18a** (obtained from *N*,*O*-acetal **18**) at first generates the intermediate **18c**. Next, the intramolecular nucleophilic attack of N-moiety to α-position of keteniminium species and subsequent ring opening provide intermediates **18d** and **18e**, respectively. Finally, Michael attack of OMe group to **18e** furnishes tetra-substituted dienamide **19**.



Scheme 3A.11. Cu-catalyzed amino-oxymethylation of ynamide

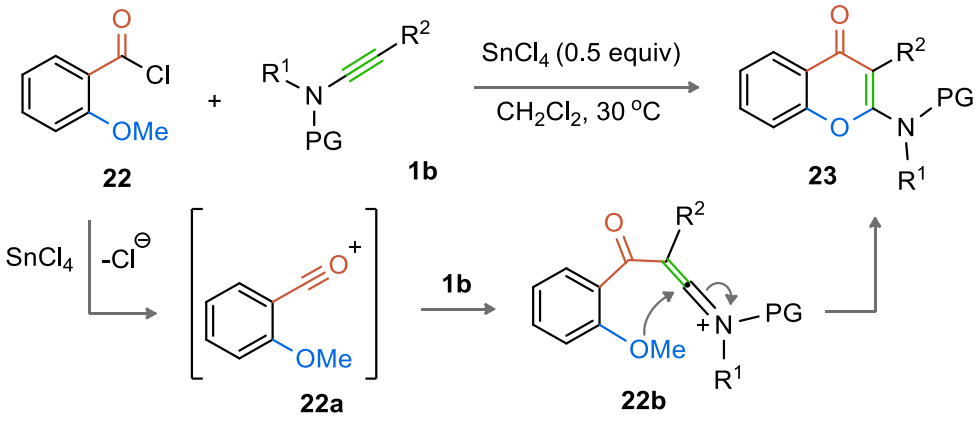
In 2017, our group have developed Yb-catalyzed difunctionalization of ynamide with CH_3CN for the synthesis of 3-amino oxazole derivatives (**Scheme 3A.12**).[10] The mechanism begins with isomerization of CH_3CN in presence of $Yb(OTf)_3$ to Yb-azaketene **20**, followed by attack of ynamide **1b** to give iodo/hydro-amidation intermediate **20b** with the help of H_2O and NIS via **20a**. Later electrophilic activation of **20b** by NIS triggers the attacks of amide O-atom to the terminal carbon to give **20d** via **20c**. Finally, aromatization of **20d** by the elimination of I_2 or HI gives the final product **21**.



Scheme 3A.12. Yb-catalyzed difunctionalization of ynamide with CH_3CN

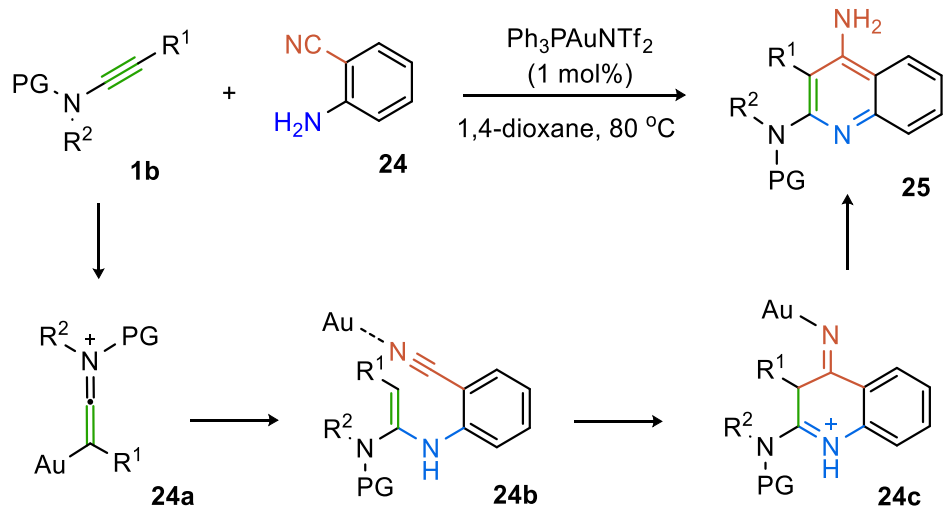
3A.2.3 Via Annulation

In 2015, Chang and co-workers demonstrated a Lewis acid mediated difunctionalization of ynamide **1c** with 2-methoxyaroyl chloride **22** for the synthesis of 3-substituted 2-aminochromones **23** (**Scheme 3A.13**).[12] The nucleophilic addition of **1b** to acylium ion **22a**, generated in-situ from **22** in presence of $SnCl_4$, delivers keteniminium species **22b**. The intramolecular cyclization through the attack of OMe group to the α-position of **22b** provides 2-aminochromone derivatives **23**.



Scheme 3A.13. Reaction of ynamide and 2-methoxyaroyl chloride for the synthesis of 2-aminochromones

In 2018, our group have demonstrated a gold catalyzed 1,2-*syn* di-functionalization of ynamides **1b** with 2-amino benzonitrile **24** for the construction of 2,4-diamino-substituted quinolines **25** (**Scheme 3A.14**).[13] The reaction is regioselective enabling access to the respective quinoline scaffolds in excellent yields. The transformation involves a ketene N,N-acetal **24b** by the attack of $-NH_2$ of benzonitrile **24** to the α–position of keteniminium species **24a**. Next, 6-*exo*-dig cyclization of N,N-acetal **24b** followed by aromatization sequence furnishes the desired product **25**.



Scheme 3A.14. Au-catalyzed *syn*-1,2 difunctionalization of ynamide with 2-cyanoaniline

3A.3. Motivation and Scheme Design

Inspired from the nucleophile initiated umpolung difunctionalization reaction and keteniminium driven general difunctionalization reaction, we hypothesized to develope a non-directed multicomponent keteniminium umpolung difunctionalization of ynamides that is initiated by the attack of an electrophile. Thus, an electrophilic activation of ynamide **I** with aryl metal-complex {generated in-situ from an electrophile $Ar'N_2BF_4$ (E)[14] with a low-valent transition metal species [i.e. Pd(0)]} to a keteniminium species **XI**, regioselective 1,3-aryl (E′) migration to the α-position of **XI** to give the vinylic metal-complex **XII**, and then the trapping of the nucleophile $Ar''B(OH)_2$ with **XII** for the synthesis of tetra substituted N-bearing olefin **XIII** is precisely envisaged (**Fig. 3A.2**).

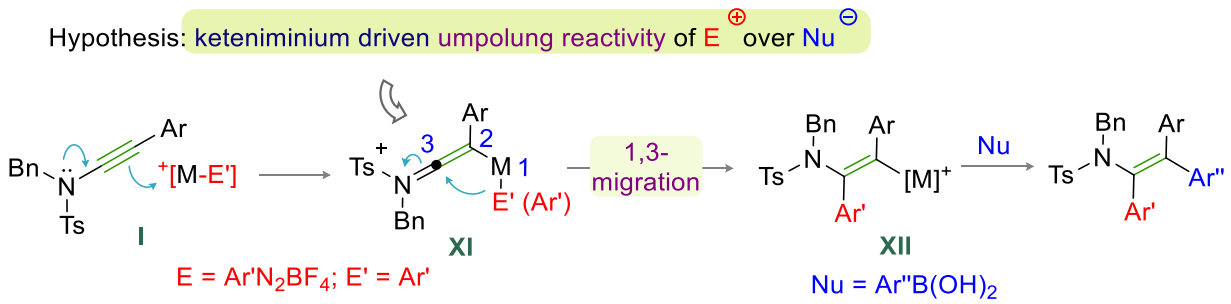


Figure 3A.2. Hypothesis (keteniminium driven umpolung difunctionalization)

Moreover, inspired by the challenges and shortcomings related to regioselectivity and harsh conditions in the unsymmetrical difunctionalization of unsaturated systems for the construction of tetra substituted olefins and tamoxifen analogues,[6] an unsymmetrical diarylation of ynamides with aryl diazonium salts and aryl/vinyl boronic acids in the presence of a Pd(0)-catalyst and a base at room temperature (rt) has been developed.

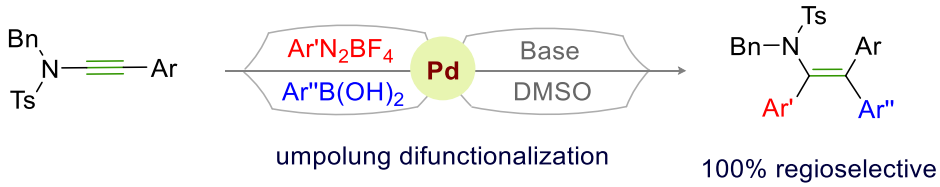
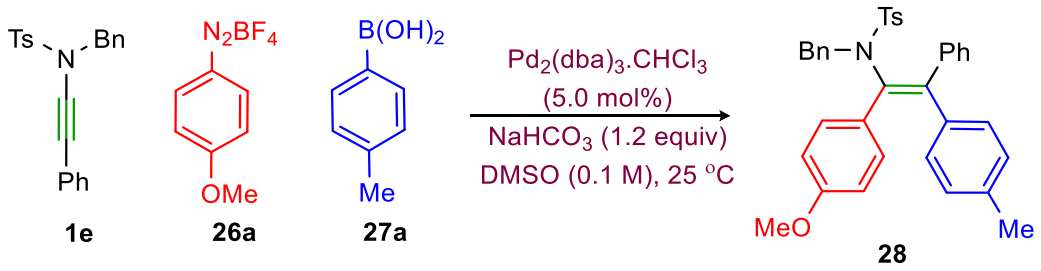


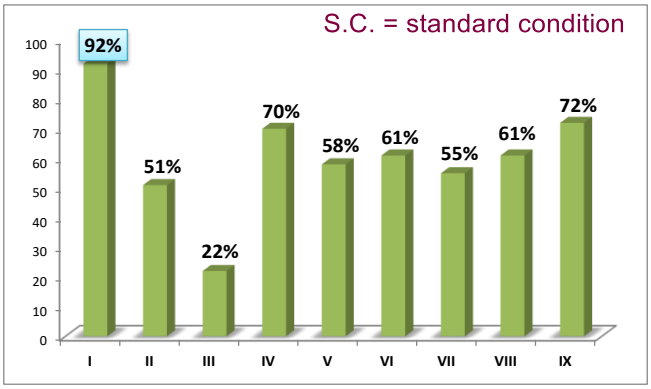
Figure 3A.3. Cationic Pd-catalyzed regioselective syn diarylation

3A.4. Result and Discussion

3A.4.1. Reaction Optimization

The investigation was initiated by examining the reaction of N-benzyl-4-methyl-N-(phenylethynyl)benzenesulfonamide (**1e**) with *p*-methoxybenzene diazonium tetrafluoroborate (**26a**) and *p*-methylbenzene boronic acid (**27a**) using $Pd_2(dba)_3 \cdot CHCl_3$ as catalyst and a base (**Scheme 3A.15**). An extensive screening led to these optimized reaction conditions: [**1a** (1.0 equiv), **2a** (1.5 equiv), **3a** (1.2 equiv), $Pd_2(dba)_3 \cdot CHCl_3$ (5.0 mol%), $NaHCO_3$ (1.2 equiv), DMSO as solvent, at 25 °C, overnight]. With these, the desired diarylation product **28** was isolated in 92% yield (I). K_2CO_3 and LiO^tBu proved to be far less efficient bases (II and III). Comparable results were observed when other Pd(0) catalysts [$Pd_2(dba)_3$, $Pd(dba)_2$, and $Pd(PPh_3)_4$] were used (IV–VI). The use of THF, toluene, and 1,4-dioxane as solvent led to moderate yields (VII–IX).





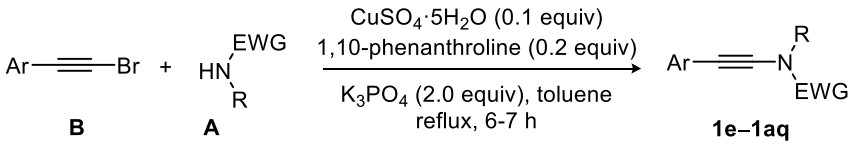
Deviation from S.C.
I) None
II) K_2CO_3 as base
III) LiO^tBu as base
IV) $Pd_2(dba)_3$ as catalyst
V) $Pd(dba)_2$ as catalyst
VI) $Pd(PPh_3)_4$ as catalyst
VII) THF as solvent
VIII) toluene as solvent
IX) 1,4-dioxane as solvent

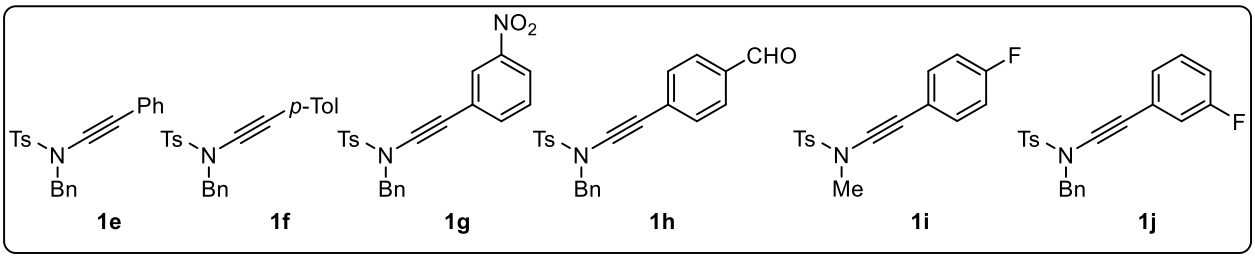
Scheme 3A.15. Optimization Graph[a,b]. [a]Reaction condition: ynamide **1e** (0.15 mmol), diazonium salt **26a** (0.225 mmol), boronic acid **27a** (0.18 mmol) for overnight. All are isolated yield.

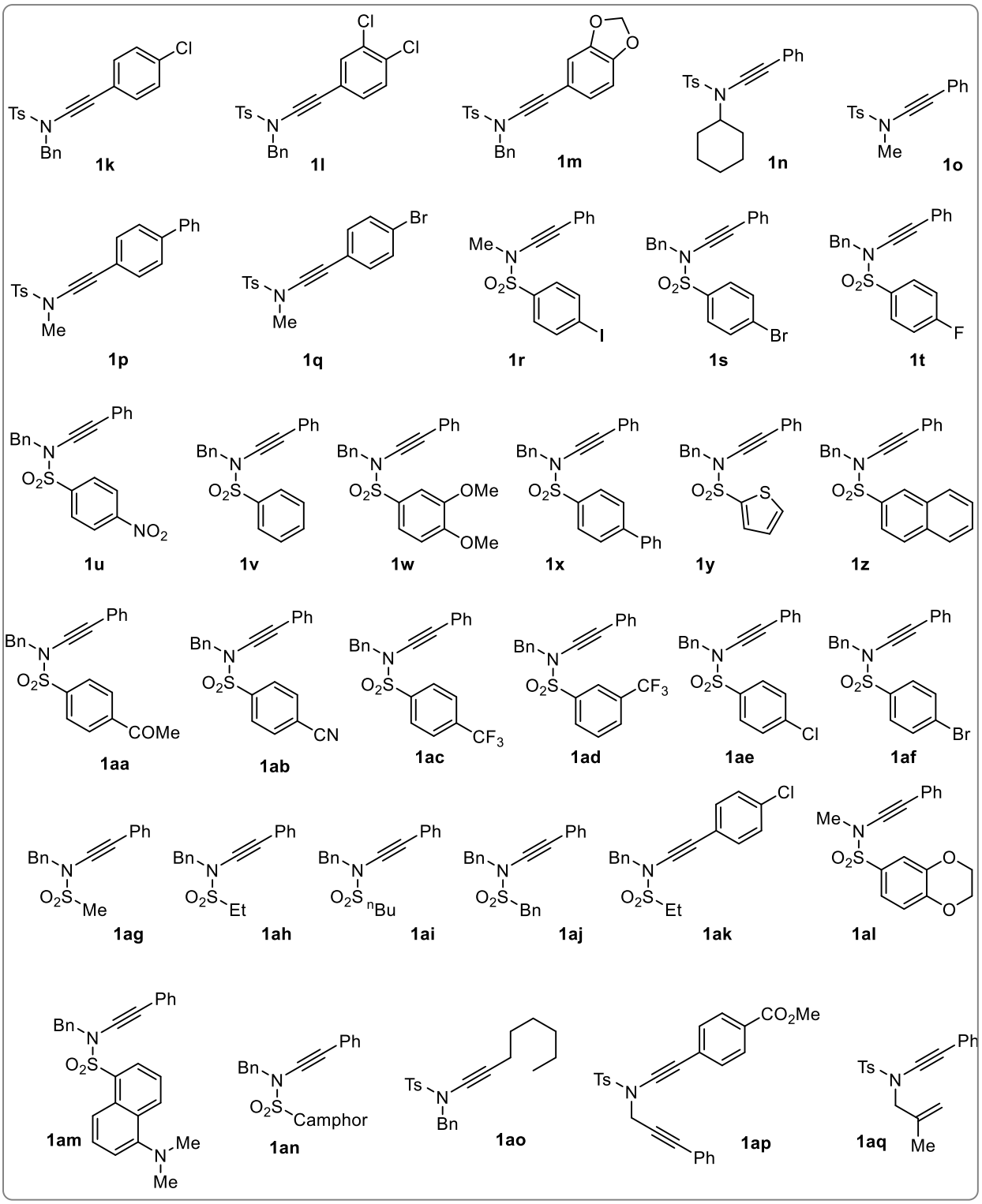
3A.4.2. Synthesis of ynamides, and aryl diazonium salts

Following the known Cu-catalyzed C-N coupling procdure, ynamides **1e-1aq** were synthesized from corresponding sulfonamides (A) and bromoalkynes (B) (Table 3A.1).

Table 3A.1. Ynamide chart






1k
1l
1m
1n
1o
1p
1q
1r
1s
1t
1u
1v
1w
1x
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1aa
1ab
1ac
1ad
1ae
1af
1ag
1ah
1ai
1aj
1ak
1al
1am
1an
1ao
1ap
1aq

Following the known diazodization procdure, aryldiazonium salts **26a-h** were synthesized from corresponding aniline derivatives **C** (Table 3A.2).

Table 3A.2. Aryl diazonium salt chart

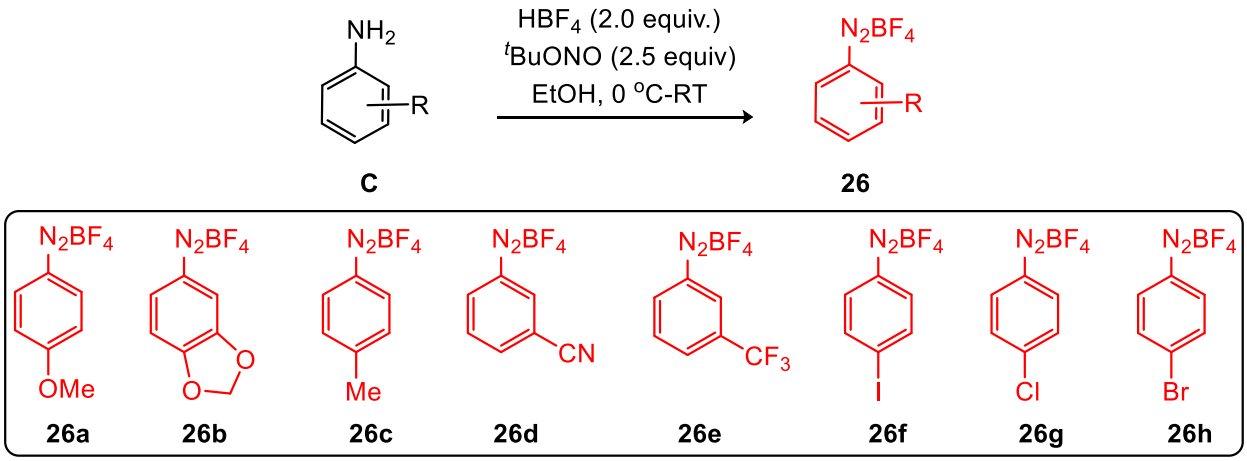
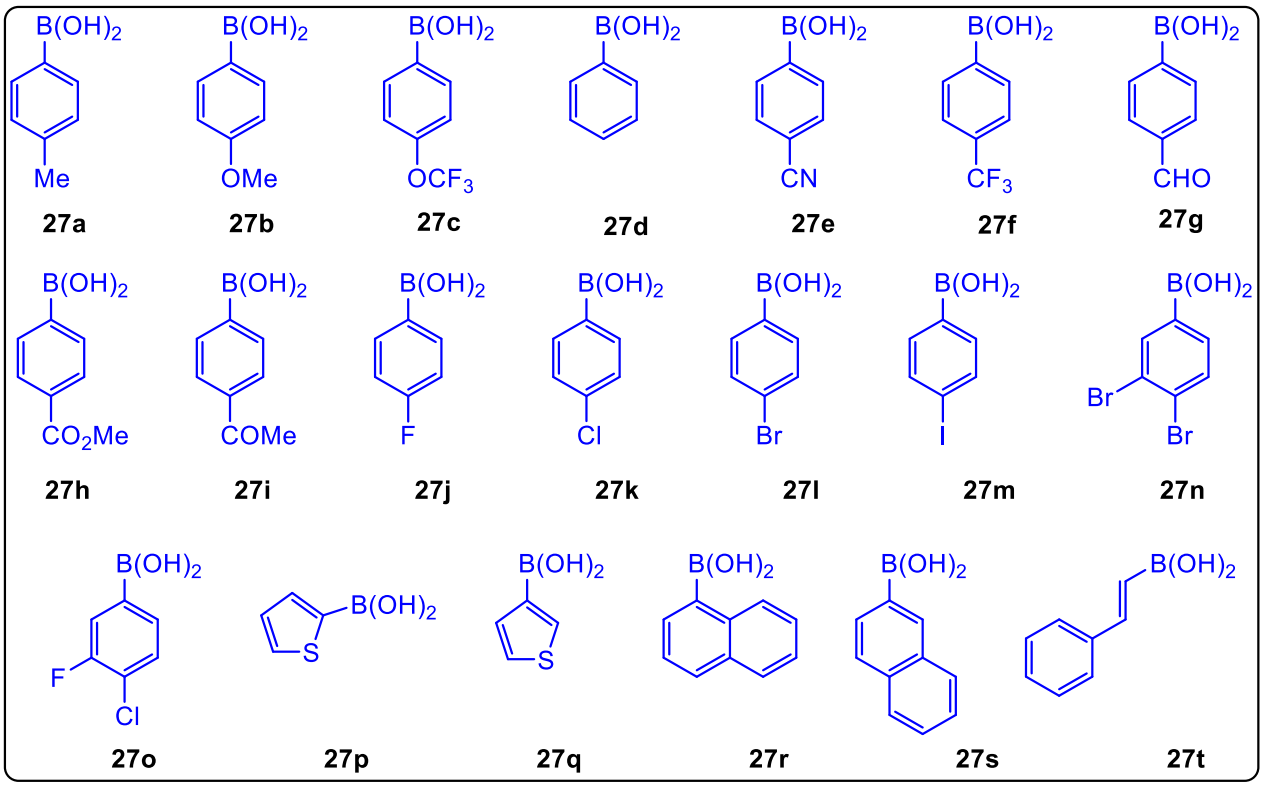


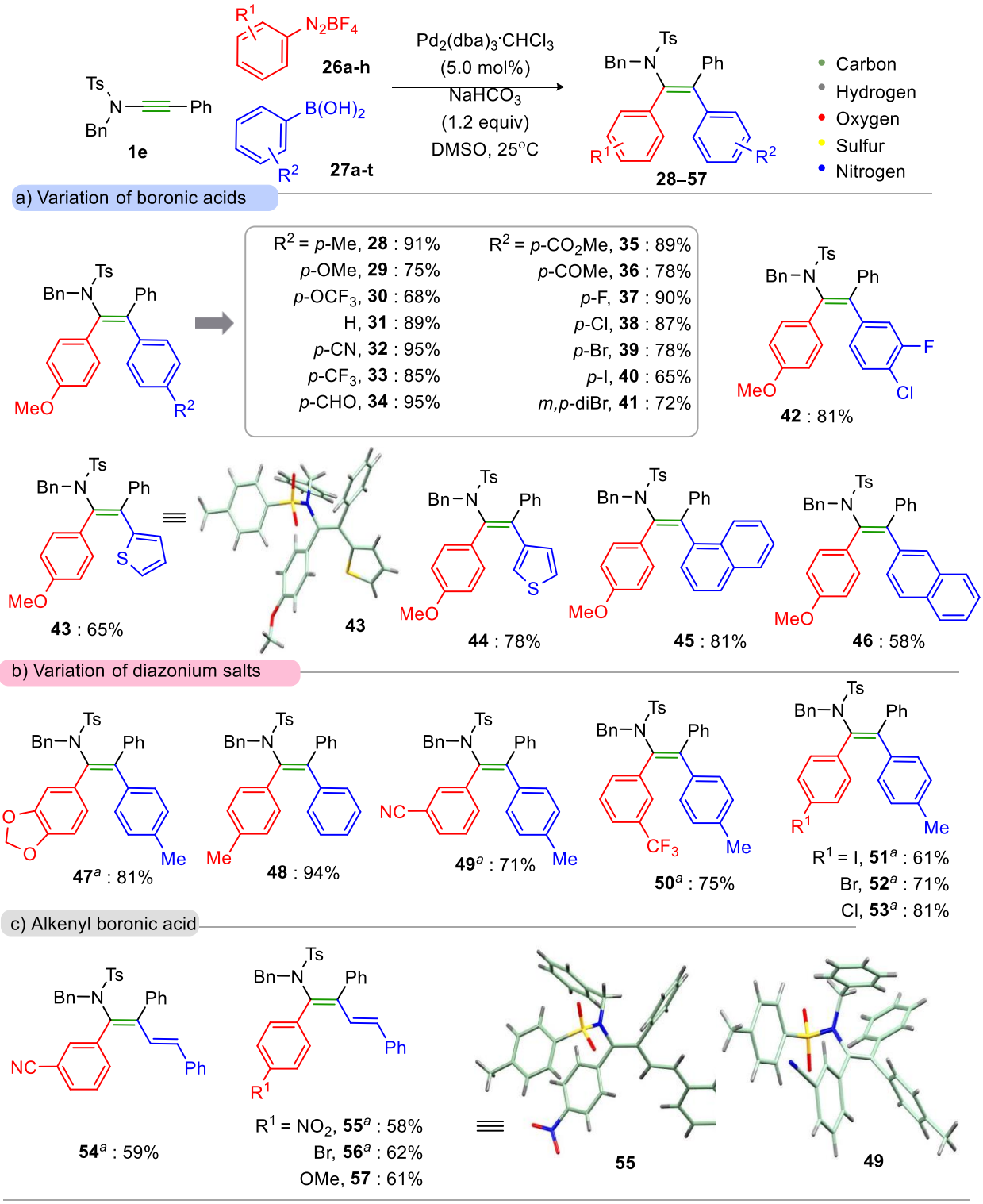
Table 3A.3. Aryl boronic acid chart



3A.4.3. Substrate Scope-I

The optimized catalytic conditions were next probed while examining the scope of this regioselective double arylation of ynamides with distinct coupling partners (**Scheme 3A.16** and **3A.17**). The reactivity of aryl boronic acid coupling partners (**3**) with ynamides **1a** and **2a** was at first surveyed (**Scheme 3A.16**). The reaction of electron-rich *p*-substituted aryl boronic acids [*p*-Me (**27a**), *p*-OMe (**27b**), *p*-OCF_3 (**27c**)] with **1e** and **26a** provided the respective products **28**–**30** in good to excellent yields. Likewise, tetra-substituted enamides **31**–**36** (78–95%) were constructed from the electron-neutral phenyl boronic acid (**27d**) and electron-poor [*p*-CN (**27e**), *p*-CF_3 (**27f**), *p*-CHO (**27g**), *p*-CO_2Me (**27h**), *p*-COMe (**27i**)] substituted aryl boronic acids when exposed independently to **1e** and **26a**. Gratifyingly, the aryl boronic acids having labile halo groups [*p*-F (**27j**), *p*-Cl (**27k**), *p*-Br (**27l**), even the oxidizable *p*-I (**27m**), *m*,*p*-dibromo (**27n**), and *p*-Cl-*m*-F (**27o**)] were tolerated under the Pd-catalysis and the desired products **37**–**42** were isolated in excellent yields. The desired thienyl substituted enamides **43** (65%) and **44** (78%) were accessed from the coupling of 2/3–thienyl boronic acids (**27p** and **27q**) with **1e** and **26a**, respectively. The π-extended 1-naphthyl-(**27r**) and 2-naphthyl boronic acids (**27s**) could also participate in this transformation, delivering **45** (81%) and **46** (58%), respectively.

Next, the scope of aryl diazonium tetrafluoroborates in the coupling of **1a** with **3a**/**3d** was surveyed (**Scheme 3A.16**). The electron-rich [3,4-methylenedioxy (**26b**), *p*-Me (**26c**)] substituted aryl diazonium salts provided a better outcome over the electron-deficient substrates [*m*-CN (**26d**), *m*-CF_3 (**26e**)], furnishing **47** (81%), **48** (94%), **49** (71%), and **50** (75%), respectively. This might be explained by the poor stability of electron-deficient diazonium salts. Once again, the halo groups were well-tolerated under the Pd-catalytic conditions, as the halo-substituted aryl diazonium salts were fruitfully employed in this double arylation of **1e** in the presence of **27a** [*p*-I (**26f**)→**51**, *p*-Br (**26g**)→**52**, and *p*-Cl (**26h**)→**53**]. Unlike aryl boronic acids, the alkenyl boronic acids (generally susceptible to the Heck reaction) were also relevant partners in this three-component coupling transformation, yielding highly substituted 1,3-*trans*-butadienes [**54** (59%), **55** (58%), **56**

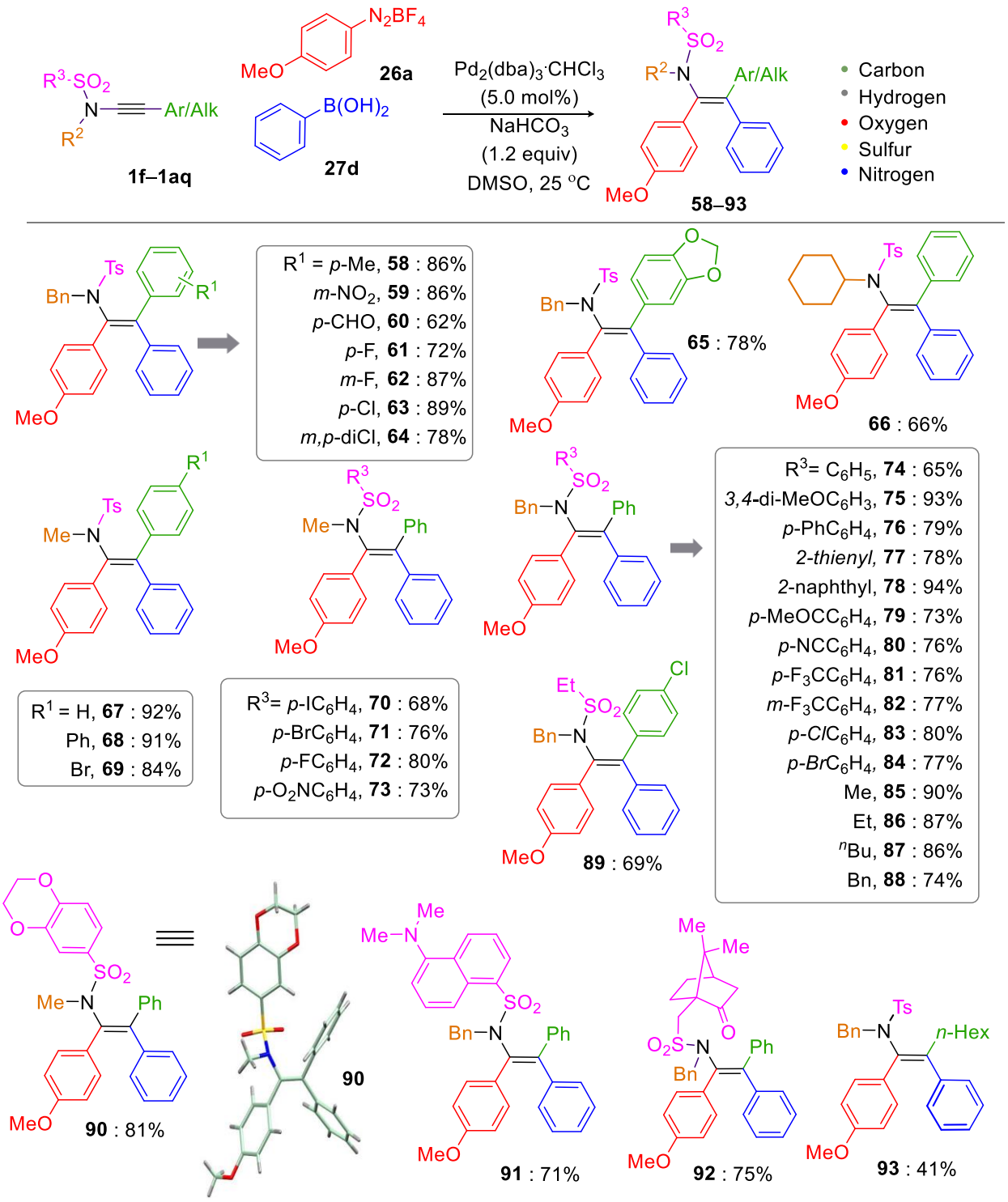


Scheme 3A.16. Scope of aryl boronic and aryl diazonium salts. [a]Reactions were carried out using **1e** (0.3 mmol), **26a-h** (0.45 mmol), **27a-t** (0.36 mmol) in DMSO (0.1M). [a]1,4-dioxane was used at 10 °C.

(62%), and **57** (61%)]. The structures of **43**, **49**, and **55** were confirmed by single crystal X-ray analysis; thus, the electronic factor does not affect the product regioselectivity.[12–14]

3A.4.4. Substrate Scope-II

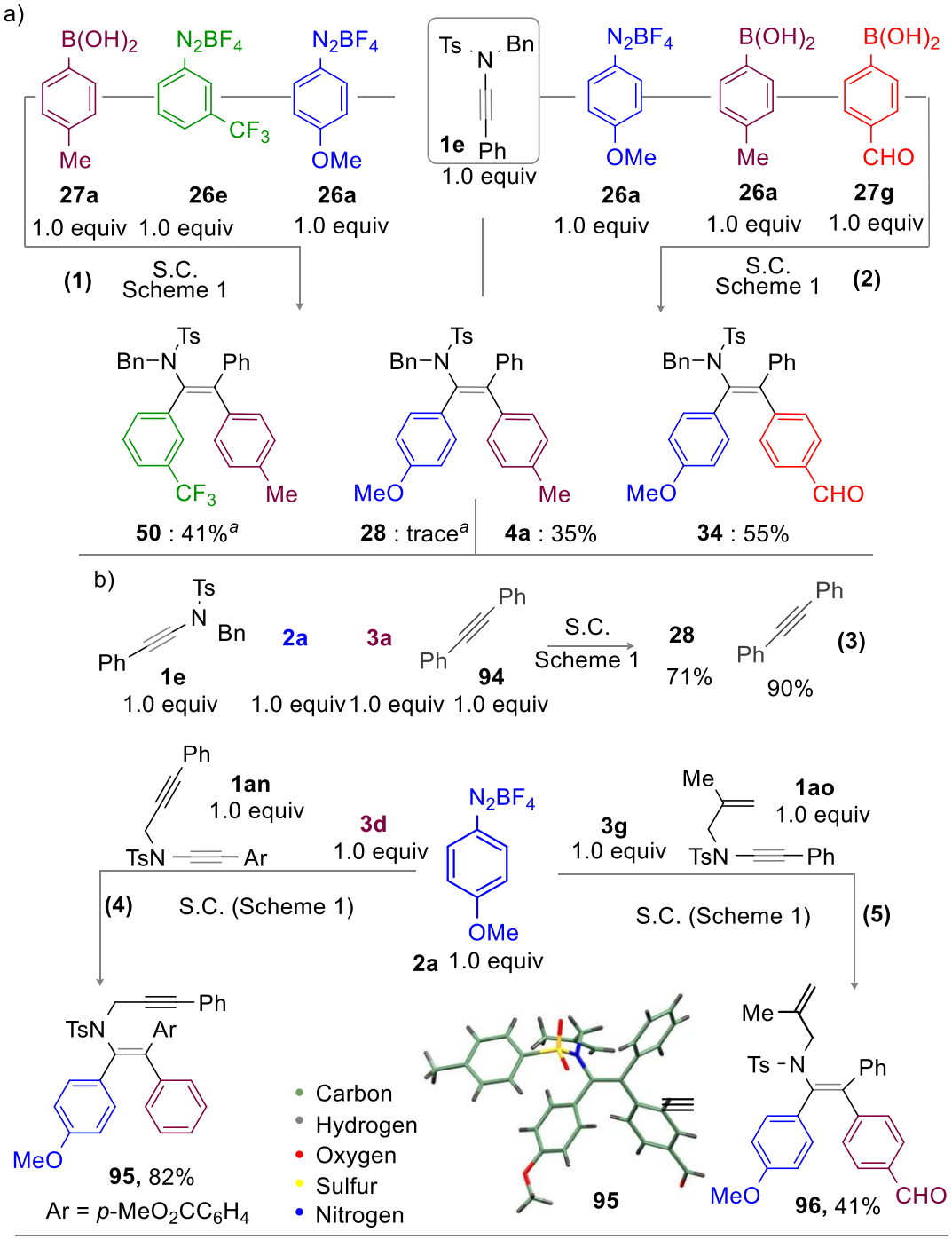
Having demonstrated the synthetic potential of this regioselective double arylation of ynamides with respect to boronic acids and diazonium salts, we next investigated the ynamide scope towards **26a** and **27d** under the optimized conditions (**Scheme 3A.17**). The reaction of respective ynamides {having aryl motifs [electron-rich (*p*-Me), electron-poor (*m*-NO_2, *p*-CHO), labile (*p*-F, *m*-F, *p*-Cl, *m,p*-diCl, *m,p*-methylenedioxy)] at the ynamide terminus} with **26a** and **27d** independently furnished the desired diarylation products **58–65** in good yields. The tetrasubstituted enamide **66** (with a cyclohexyl group on N-atom) was prepared in 66% yield. The N-Me protected ynamides with various aryl substituents at the ynamide terminus effectively participated, affording **67** (92%), **68** (91%), and **69** (84%). Next, *N*- sulfonyl protected diarylated enamides **70**–**73** {having *N*-Me-[$SO_2C_6H_4$-*p*- I/ $SO_2C_6H_4$-*p*-Br/ $SO_2C_6H_4$-*p*-F/ $SO_2C_6H_4$-*p*-NO_2]} were synthesized in good yields. Likewise, several enamides {having *N*-Bn -[$SO_2C_6H_5$ (**74**) / $SO_2C_6H_3$-*m,p*-diOMe (**75**) / SO_2-C_6H_4-*p*-Ph (**76**) /SO_2-2-thienyl (**77**) / SO_2-2-naphthyl (**78**) / $SO_2C_6H_4$-*p*-COMe (**79**) / $SO_2C_6H_4$-*p*-CN (**80**) / $SO_2C_6H_4$-*p*-CF_3 (**81**) / $SO_2C_6H_4$-*m*-CF_3 (**82**) / $SO_2C_6H_4$-*p*-Cl (**83**) / $SO_2C_6H_4$-*p*-Br (**84**) / SO_2Me (**85**) / SO_2Et (**86** and **89**) / $SO_2{}^n$Bu (**87**) / SO_2Bn (**88**)} were accessed. Compound **90** (81%) was obtained from **1ak** and its structure was further confirmed by single crystal X-ray analysis.[15] The N,N-dimethyl group (which easily binds transition metal catalysts) did not prevent the reaction, yielding **91** (71%). The steric demand at the sulfonyl side in the chiral camphor sulfonyl protected ynamide **1al** did not prevent the delivery of **92** (*exo*/*endo* = 58/42) in 75% yield. To our delight, alkyl-substituted ynamide provided the desired product **93** albeit in moderate yield. However, the terminal ynamide led to a complex mixture instead of providing the respective diarylation product.



Scheme 3A.17. Scope of ynamide. [a]Reactions were carried out using **1** (0.3 mmol), **26a** (0.45 mmol), **27d** (0.36 mmol) in DMSO (0.1M).

3A.4.5. Mechanistic Studies

To understand the reactivity of the functionalized arene motifs, a crossover experiment mixing electron-rich *p*-OMe benzenediazonium tetrafluoroborate

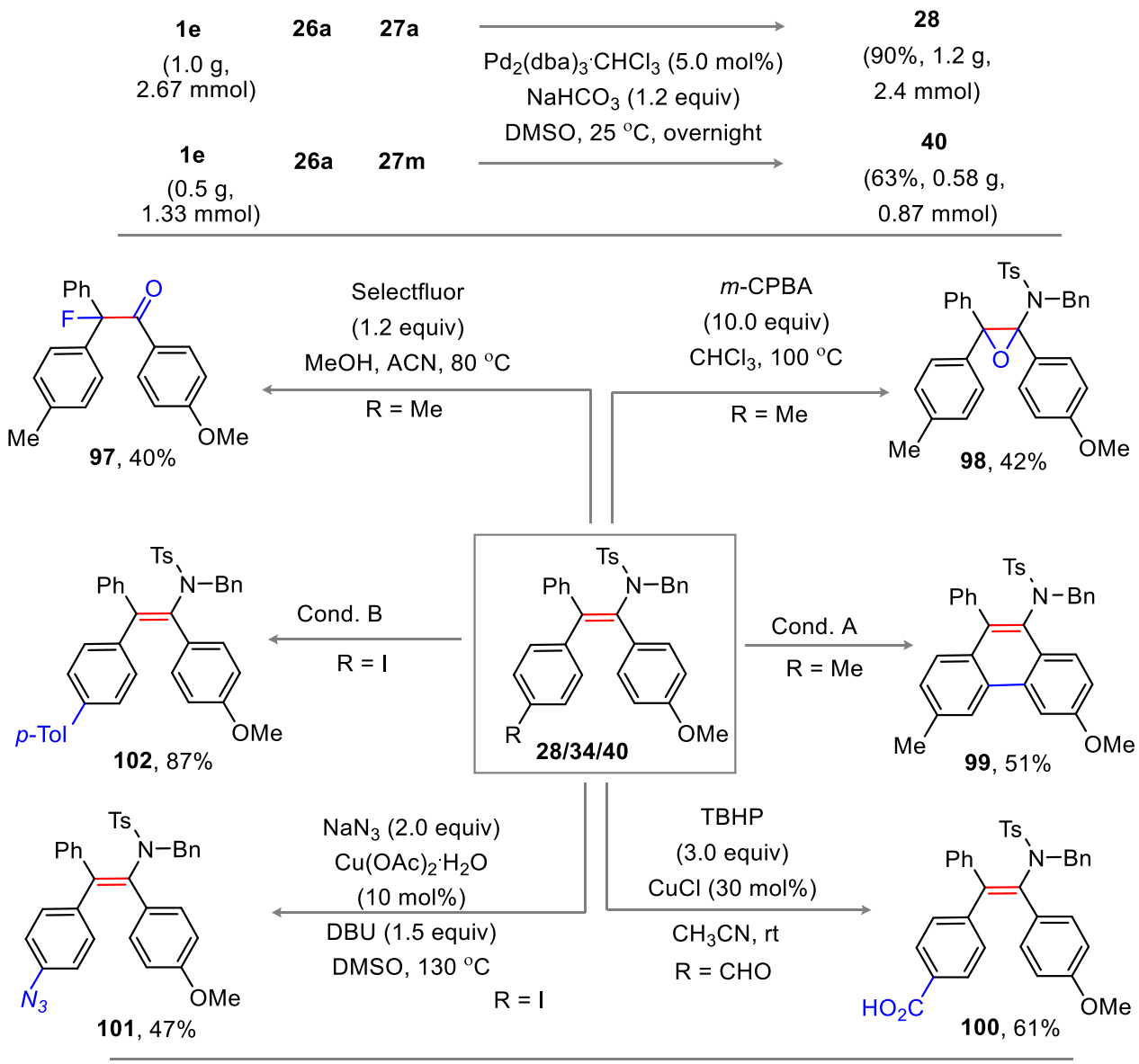


Scheme 3A.18. Competition Experiments.

(**26a**), electron-poor *m*-CF_3 benzenediazonium tetrafluoroborate (**26e**), **1e**, and **27a** under the optimized conditions delivered **50** (41%) and **28** (trace); thus, oxidative addition of Pd(0) is faster with **26e** than with **26a** (eq 1, **Scheme 3A.18**). Probing the reaction of **1e** and **26a** along with *p*-Me-aryl-boronic acid (**27a**) and *p*-CHO-aryl-boronic acid (**27g**) gave **28** (35%) and **34** (55%), respectively; thus, the reaction of **27g** is fast (eq 2, **Scheme 3A.18**).[7] Among the alkyne derivatives, the reaction with ynamide **1e** is preferred over 1,2-diphenylacetylene (**94**) producing **28** (71%) while leaving **94** intact (eq 3, **Scheme 3A.18**). Interestingly, the reaction explicitly occurred with ynamide motifs leaving the yne/ene species completely untouched and finally, provided the respective products **95** and **96** in appreciable yields (eq 4 and 5, **Scheme 3A.18**). Structure of **96** was elucidated by single crystal X-ray analysis.

3A.4.6. Synthetic application

The reaction scalability was validated through the gram-scale preparation **28** (1.2 g, 90%) and **40** (0.58 g, 63%), respectively, from **1e** (1.0 g, 2.67 mmol) and **26a** (1.5 equiv) independently with **27a** (1.2 equiv) or **27m** (1.2 equiv) in $Pd_2(dba)_3 \cdot CHCl_3$ (5.0 mol%) (**Scheme 3A.19**). The synthetic versatility of these newly constructed tetrasubstituted enamides was next probed (**Scheme 3A.19**). The selectfluor assisted oxy-fluorination of **28** provided **97** in 40% yield.[8] An unusual epoxidation product **98** was accessed from **28** when exposed to *m*-CBPA at 100 °C for 3 days.[9] The cross-dehydrogenative coupling of **28** led to 9-amino phenanthrene **99** in 51% yield. The TBHP and CuCl mediated oxidation of **34** (R= CHO) delivered **100** (R = COOH), the enamide motif did not affect this oxidation.[10] Independent coupling of I-moiety in **40** with NaN_3 and *p*-TolB$(OH)_2$ furnished **101** (47%) and **102** (87%), respectively.[11]



Scheme 3A.19: Synthetic versatility.

3A.4.7. DFT Calculations

To gain insight into the reaction mechanism and the stereo/regioselective1,2-diarylation of the ynamide scaffold, DFT calculations were performed (Figure 3A.4). The transformation begins with the barrierless oxidative insertion of $Pd(DMSO)_2$ (**A**) to the C–N bond of *p*-methoxy phenyl diazonium cation **2a** to provide cationic Pd-complex **B**; this process is highly exergonic by 58.4 kcal/mol. Next, coordination of **B** to the ynamide

A' through ligand exchange with N_2 delivers keteniminium complex **C** with a release of 12.8 kcal/mol. A suprafacial 1,3-aryl migration from Pd to the C=N bond of **C** proceeds through transition state $\mathbf{TS_{CD}}$ (found at 0.1 kcal/mol on the free energy surface) and results in Pd-enamide Complex **D** (–24.5 kcal/mol; with *trans* orientation of phenyl and *p*-methoxyphenyl groups). The ligand exchange between **D** and **3a'** is exergonic, leading to complex **E** (–42.7 kcal/mol; with the chelation of borate oxygen and *ipso* aryl carbon to Pd). Transmetalation through $\mathbf{TS_{EF}}$ (4.8 kcal/mol) delivers **F** (–63.0 kcal/mol); the boric

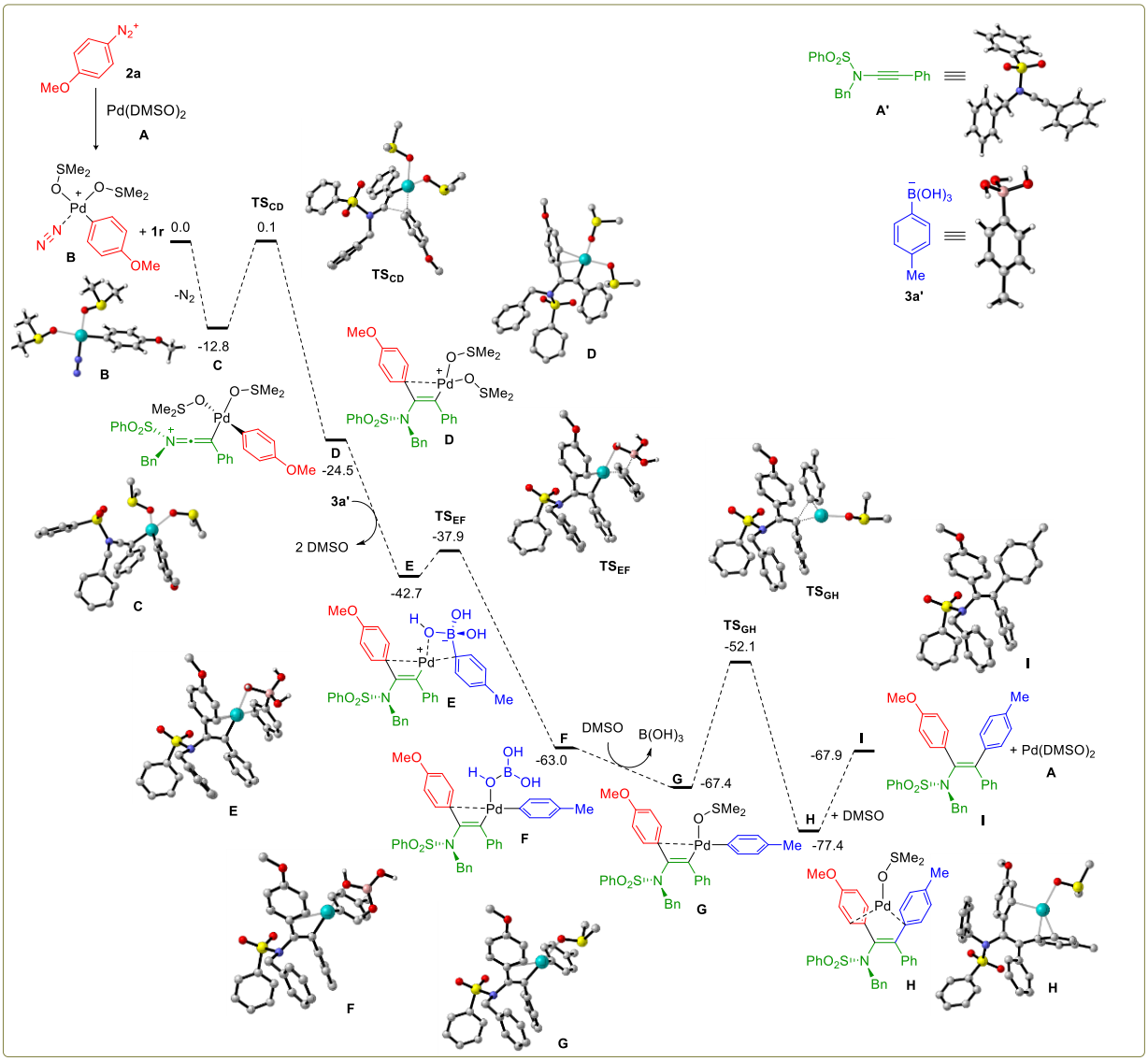


Figure 3A.4: DFT Calculations

acid serves as L-type ligand. The exchange of boric acid ligand by DMSO then dispenses **G** (–67.4 kcal/mol). The reductive elimination of **G** passes through transition state $\mathbf{TS_{GH}}$ (–52.1 kcal/mol, requiring 15.3 kcal/mol from **G**) to provide **H** (–77.4 kcal/mol). Ligation of *ortho*-carbon of *p*-MeOPh and the *ipso*-carbon of *p*-tolyl moieties makes the (DMSO)Pd(0) intermediate **H**. Finally, the desired product **I** is liberated from **H**, which requires 9.5 kcal/mol of free energy, along with the regeneration of the active catalyst species **A** for further use. The DFT studies thus rationalize the reactivity preference of aryl diazonium salts over aryl boronic acid species, as well as the chemo- and regio-selectivity of the reaction.

3A.5. Conclusion

In summary, a base-mediated Pd(0)-catalyzed keteniminium driven umpolung regioselective unsymmetrical diarylation of ynamides with distinct reactive partners aryl-diazonium salts and boronic acids has been revealed for the first time. The transformation proceeds at room temperature and exhibits a broad scope [68 examples; the catalytic system tolerates oxidizable halo-species (I/Br), easily transformable functionalities (CHO, COMe, CO_2Me, CN), and sulfonyl-protecting groups]. This process is thus practical and even successful on a gram-scale. DFT studies support the viability of intramolecular 1,3-aryl migration and the possibility of transmetalation of boronic acid to vinylic Pd-species and makes the transformation explicitly chemo-, regio- and stereoselective. This finding paves the way for a diverse range of unknown difunctionalization of ynamides; the results will be reported in due course.

3A.6. Experimental Section

3A.6.1. General Information

All the reactions were performed in oven-dried sealed tubes. Commercial grade solvents were distilled prior to use. Column chromatography was performed using either 100-200 Mesh or 230-400 Mesh silica gel or neutral alumina. Thin layer chromatography (TLC) was performed on silica gel GF254 plates and alumina plates.

Proton, carbon, and fluorine nuclear magnetic resonance spectra (^{1}H NMR, ^{13}C NMR, and ^{19}F NMR) were recorded based on the resonating frequencies as follows:(^{1}H NMR, 400 MHz; ^{13}C NMR, 101 MHz; ^{19}F NMR, 376 MHz), (^{1}H NMR, 500 MHz; ^{13}C NMR, 126 MHz; ^{19}F NMR, 470 MHz) and (^{1}H NMR, 600 MHz; ^{13}C NMR, 151 MHz) having the solvent resonance as internal standard (^{1}H NMR, $CDCl_3$ at 7.26 ppm; ^{13}C NMR, $CDCl_3$ at 77.0 ppm). Few cases tetramethylsilane (TMS) at 0.00 ppm was used as reference standard. Data for ^{1}H NMR are reported as follows: chemical shift (ppm), multiplicity (s = singlet; br s = broad singlet; d = doublet; br d = broad doublet, t = triplet; br t = broad triplet; q = quartet; m = multiplet; tt = triplet of triplet; dt = doublet of triplet), coupling constant, *J*, in (Hz), and integration. Data for ^{13}C NMR, ^{19}F NMR were reported in terms of chemical shift (ppm). IR spectra were reported in cm^{-1}. High resolution mass spectra were obtained in ESI mode. Melting points were determined by electro-thermal heating and are uncorrected. X-ray data was collected at 293 K using graphite monochromated Mo-Kα radiation (0.71073 Å).

3A.6.2. Materials

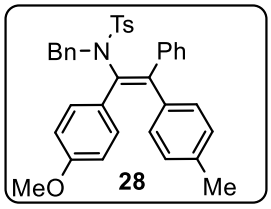
Unless otherwise noted, all the reagents and intermediates were obtained commercially and used without purification. Toluene and 1,4-dioxane were distilled over CaH_2. $Pd_2dba_3.CHCl_3$ and aryl boronic acids were purchased from commercially available source, and used as received. Analytical and spectral data of all the known compounds are exactly matching with the reported values.

3A.6.3. General procedure and spectral/analytical data

3A.6.3.1. General Procedure for diarylation.

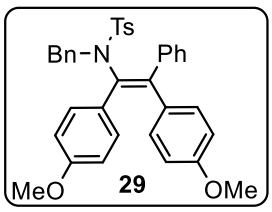
To a mixture of ynamide **1e-aq** (0.3 mmol), aryl diazonium-tetrafluoroborate **26a** (0.45 mmol), aryl boronic acid **27** (0.36 mmol), $Pd_2dba_3 \cdot CHCl_3$ (0.015 mmol), and $NaHCO_3$ (0.36 mmol) was added dimethyl sulfoxide (DMSO; 3.0 mL). The reaction mixture was stirred at 25 °C overnight. After completion of the reaction, DMSO was removed by water workup. The organic layer was extracted in ethyl acetate (3 × 10 mL) and dried over Na_2SO_4. The organic layer was evaporated and purified by column chromatography to afford **28-46**, **48**, **57-93**, **95** and **96**.

(*E*)-N-Benzyl-N-(1-(4-methoxyphenyl)-2-phenyl-2-(p-tolyl)vinyl)-4-methylbenzenesulfonamide (28):



28 (153 mg, 91%) as pale yellow solid. mp = 209–210 °C; R_f = 0.3 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.31 (m, 4H), 7.30–7.25 (m, 2H), 7.16 (br d, J = 6.0 Hz, 2H), 7.08 (d, J = 8.0 Hz, 2H), 6.99 (d, J = 8.5 Hz, 2H), 6.89–6.85 (m, 4H), 6.83 (d, J = 7.0 Hz, 2H), 6.78 (d, J = 8.0 Hz, 2H), 6.58 (d, J = 9.0 Hz, 2H), 4.31 (d, J = 14.5 Hz, 1H), 4.02 (d, J = 14.5 Hz, 1H), 3.76 (s, 3H), 2.41 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.6, 142.9, 142.1, 141.5, 139.5, 137.7, 136.1, 133.4, 132.8, 131.1, 130.1, 130.0, 129.6, 128.9, 128.31, 128.30, 128.2, 128.1, 127.9, 127.2, 113.0, 55.0, 51.0, 21.4, 21.1; IR (Neat) ν_{max} 2939, 2183, 1598, 1508, 1329, 1292, 1247, 1171, 1027, 813 cm^{-1}; **HRMS (ESI)** for $C_{36}H_{33}NNaO_3S$ $(M+Na)^+$: calcd. 582.2073, found 582.2070.

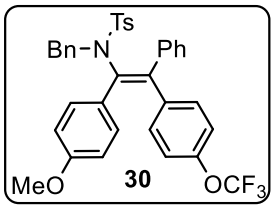
(*E*)-N-Benzyl-N-(1,2-bis(4-methoxyphenyl)-2-phenylvinyl)-4-methylbenzenesulfonamide (29):



29 (129 mg, 75%) as pale yellow solid. mp = 191–192 °C; R_f = 0.24 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33–7.28 (m, 4H), 7.27–7.22 (m, 2H), 7.11 (br d, J = 6.5 Hz, 2H), 7.05 (d, J = 8.0 Hz, 2H), 6.96 (d, J = 8.5 Hz, 2H), 6.85 (d, J = 8.5 Hz, 2H), 6.80–6.75 (m, 4H), 6.57 (dd, J = 8.5, 1.5 Hz, 4H), 4.27 (d, J = 14.5 Hz, 1H), 3.98 (d, J = 14.5 Hz, 1H), 3.74 (s, 3H), 3.69 (s, 3H),

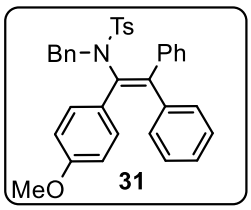
2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.5, 158.0, 142.9, 142.1, 137.6, 136.0, 134.8, 132.80, 132.75, 132.4, 130.12, 130.05, 129.5, 128.9, 128.3, 128.2, 128.1, 127.9, 127.2, 113.1, 113.0, 55.04, 54.95, 50.8, 21.4; IR (Neat) ν_{max} 2183, 1601, 1346, 1245, 1157, 1027, 834 cm^{-1}; **HRMS (ESI)** for $C_{36}H_{33}NNaO_4S$ $(M+Na)^+$: calcd. 598.2023, found 598.2025.

(*E*)-N-Benzyl-N-(1-(4-methoxyphenyl)-2-phenyl-2-(4-(trifluoromethoxy)phenyl)vinyl)-4-methylbenzenesulfonamide (30):



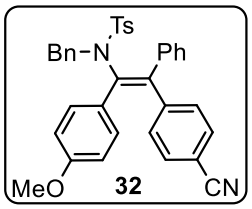
30 (129 mg, 68%) as colorless solid. mp = 190–191 °C; R_f = 0.3 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.27 (m, 6H), 7.12 (br d, J = 6.4 Hz, 2H), 7.08 (br d, J = 8.4 Hz, 2H), 6.99 (d, J = 8.4 Hz, 2H), 6.94–6.89 (m, 4H), 6.86 (br d, J = 8.4 Hz, 2H), 6.80 (d, J = 6.8 Hz, 2H), 6.60 (d, J = 8.8 Hz, 2H), 4.31 (d, J = 14.4 Hz, 1H), 4.02 (d, J = 14.4 Hz, 1H), 3.77 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 147.5, 143.1, 141.4, 141.2, 140.1, 137.4, 135.9, 134.6, 132.9, 132.5, 130.1, 130.03, 128.95, 128.8, 128.4, 128.2, 127.9, 127.5, 120.3 (q, J = 258 Hz, 1C), 119.9, 113.2, 55.1, 50.9, 21.4; ^{19}F NMR (471 MHz) δ –57.8; IR (Neat) ν_{max} 2183, 1601, 1502, 1335, 1249, 1154, 1027, 699 cm^{-1}; **HRMS (ESI)** for $C_{36}H_{30}F_3NNaO_4S$ $(M+Na)^+$: calcd. 652.1740, found 652.1742.

N-Benzyl-N-(1-(4-methoxyphenyl)-2,2-diphenylvinyl)-4-methylbenzenesulfonamide (31):



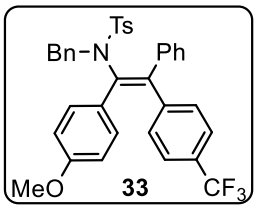
31 (145 mg, 89%) as colorless solid. mp = 203–204 °C; R_f = 0.25 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.30 (m, 4H), 7.29–7.24 (m, 2H), 7.16–7.12 (m, 2H), 7.08–7.02 (m, 5H), 6.97 (d, J = 8.4 Hz, 2H), 6.87 (dd, J = 4.8, 2.4 Hz, 2H), 6.82 (t, J = 9.2 Hz, 4H), 6.54 (d, J = 8.8 Hz, 2H), 4.30 (d, J = 14.4 Hz, 1H), 4.00 (d, J = 14.4 Hz, 1H), 3.73 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.7, 143.0, 142.5, 141.8, 141.5, 137.6, 136.0, 133.8, 132.8, 131.2, 130.1, 130.0, 129.3, 128.9, 128.3, 128.23, 128.15, 127.9, 127.6, 127.3, 126.4, 113.0, 55.1, 51.0, 21.5; IR (Neat) ν_{max} 2185, 1601, 1505, 1337, 1246, 1153, 1088, 1027, 834 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{31}NNaO_3S$ $(M+Na)^+$: calcd. 568.1917, found 568.1919.

(*E*)-N-Benzyl-N-(2-(4-cyanophenyl)-1-(4-methoxyphenyl)-2-phenylvinyl)-4-methylbenzenesulfonamide (32):



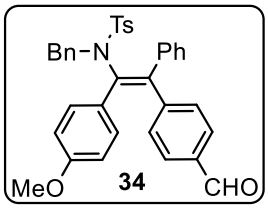
32 (163 mg, 95%) as pale yellow solid. mp = 158–159 °C; R_f = 0.15 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.28 (m, 6H), 7.27–7.22 (m, 2H), 7.09–7.02 (m, 4H), 6.93 (t, J = 9.2 Hz, 4H), 6.82 (d, J = 8.4 Hz, 2H), 6.75 (d, J = 7.2 Hz, 2H), 6.57 (d, J = 8.8 Hz, 2H), 4.28 (d, J = 14.4 Hz, 1H), 4.00 (d, J = 14.4 Hz, 1H), 3.75 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4, 147.8, 143.3, 140.8, 139.7, 137.3, 136.2, 135.8, 133.0, 131.8, 131.4, 130.1, 130.0, 129.0, 128.5, 128.4, 128.3, 127.94, 127.89, 127.8, 118.9, 113.4, 109.8, 55.2, 51.1, 21.5; IR (Neat) ν_{max} 2294, 1601, 1507, 1333, 1293, 1155, 1110, 1026, 836 cm^{-1}; **HRMS (ESI)** for $C_{36}H_{30}N_2NaO_3S$ $(M+Na)^+$: calcd. 593.1869, found 593.1868.

(*E*)-N-Benzyl-N-(1-(4-methoxyphenyl)-2-phenyl-2-(4-(trifluoromethyl)phenyl)vinyl)-4-methylbenzenesulfonamide (33):



33 (156 mg, 85%) as colorless solid. mp = 198–200 °C; R_f = 0.28 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.23 (m, 8H), 7.11–7.04 (m, 4H), 6.96 (dd, J = 8.4, 2.8 Hz, 4H), 6.83 (d, J = 8.4 Hz, 2H), 6.78 (d, J = 7.2 Hz, 2H), 6.57 (d, J = 8.8 Hz, 2H), 4.30 (d, J = 14.4 Hz, 1H), 4.00 (d, J = 14.0 Hz, 1H), 3.74 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) 159.4, 146.4, 143.3, 143.2, 141.2, 140.1, 13.4, 135.9, 135.5, 132.9, 131.5, 130.5, 130.1, 129.0, 128.7, 128.5, 128.40, 128.36, 127.6 (q, J = 268 Hz, 1C), 127.64, 125.4 (q, J = 5.1 Hz, 2C), 124.5 (q, J = 4.0 Hz, 2C), 122.7, 113.3, 55.1, 51.1, 21.5; IR (Neat) ν_{max} 2225, 1601, 1507, 1332, 1247, 1155, 1025, 836 cm^{-1}; ^{19}F NMR (376 MHz) δ –62.5; **HRMS (ESI)** for $C_{36}H_{30}F_3NNaO_3S$ $(M+Na)^+$: calcd. 636.1791, found 636.1795.

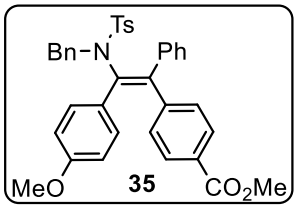
(*E*)-N-Benzyl-N-(2-(4-formylphenyl)-1-(4-methoxyphenyl)-2-phenylvinyl)-4-methylbenzenesulfonamide (34):



34 (163 mg, 95%) as colorless solid. mp = 182–183 °C; R_f = 0.13 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.85 (s, 1H), 7.54 (d, J = 8.5 Hz, 2H), 7.37–7.28 (m, 4H), 7.26 (t, J = 7.5 Hz, 2H), 7.11–7.03 (m, 4H), 7.00 (d, J = 8.5 Hz, 2H), 6.95 (d, J = 8.5 Hz, 2H), 6.83 (d, J = 8.0 Hz, 2H),

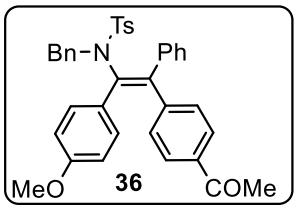
6.77 (d, *J* = 7.0 Hz, 2H), 6.55 (d, *J* = 9.0 Hz, 2H), 4.30 (d, *J* = 14.0 Hz, 1H), 4.00 (d, *J* = 14.5 Hz, 1H), 3.73 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.8, 159.2, 149.4, 143.2, 141.0, 140.3, 137.3, 135.9, 135.8, 134.1, 132.9, 131.8, 130.1, 130.0, 129.1, 129.0, 128.7, 128.5, 128.4, 128.3, 127.9, 127.7, 113.3, 55.1, 51.1, 21.5; IR (Neat) ν_{max} 2834, 1700, 1599, 1507, 1331, 1246, 1025, 835 cm^{-1}; **HRMS (ESI)** for C36H32NO4S $(M+H)^+$: calcd. 574.2047, found 574.2047.

(*E*)-Methyl-4-(2-(N-benzyl-4-methylphenylsulfonamido)-2-(4-methoxyphenyl)-1-phenylvinyl)benzoate (35):



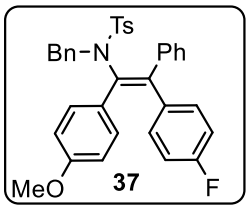
35 (162 mg, 89%) as pale yellow solid. mp = 228–229 °C; R_f = 0.16 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.4 Hz, 2H), 7.35–7.22 (m, 6H), 7.09 (br d, *J* = 6.8 Hz, 2H), 7.05 (d, *J* = 8.0 Hz, 2H), 6.95 (d, *J* = 8.0 Hz, 2H), 6.91 (d, *J* = 8.0 Hz, 2H), 6.82 (d, *J* = 8.0 Hz, 2H), 6.77 (d, *J* = 7.2 Hz, 2H), 6.54 (d, *J* = 8.8 Hz, 2H), 4.29 (d, *J* = 14.8 Hz, 1H), 4.00 (d, *J* = 14.4 Hz, 1H), 3.83 (s, 3H), 3.72 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.9, 159.0, 147.6, 143.1, 141.2, 140.4, 137.4, 135.8, 135.3, 132.9, 131.2, 130.0, 128.94, 128.86, 128.8, 128.4, 128.2, 127.9, 127.8, 127.6, 113.2, 55.1, 51.9, 51.0, 21.5; IR (Neat) ν_{max} 2181, 1728, 1603, 1507, 1334, 1248, 1154, 1090, 1024, 834 cm^{-1}; **HRMS (ESI)** for $C_{37}H_{33}NNaO_5S$ $(M+Na)^+$: calcd. 626.1972, found 626.1975.

(*E*)-N-(2-(4-Acetylphenyl)-1-(4-methoxyphenyl)-2-phenylvinyl)-N-benzyl-4-methylbenzenesulfonamide (36):



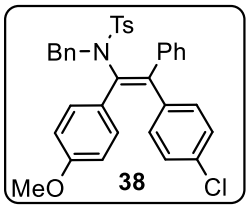
36 (138 mg, 78%) as pale yellow solid. mp = 220–222 °C; R_f = 0.08 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.0 Hz, 2H), 7.39–7.27 (m, 6H), 7.15–7.05 (m, 4H), 7.01–6.93 (m, 4H), 6.85 (d, *J* = 8.4 Hz, 2H), 6.80 (d, *J* = 7.6 Hz, 2H), 6.57 (d, *J* = 8.4 Hz, 2H), 4.32 (d, *J* = 14.4 Hz, 1H), 4.03 (d, *J* = 14.4 Hz, 1H), 3.76 (s, 3H), 2.52 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.7, 159.2, 147.9, 143.2, 141.2, 140.4, 137.5, 135.9, 135.5, 134.8, 132.9, 131.4, 130.1, 129.0, 128.9, 128.43, 128.40, 128.3, 128.0, 127.7, 127.6, 127.4, 113.3, 55.1, 51.1, 26.5, 21.5; IR (Neat) ν_{max} 2178, 1728, 1602, 1507, 1333, 1248, 1153, 1090, 1024, 834 cm^{-1}; **HRMS (ESI)** for $C_{37}H_{33}NNaO_4S$ $(M+Na)^+$: calcd. 610.2023, found 610.2022.

(*E*)-N-Benzyl-N-(2-(4-fluorophenyl)-1-(4-methoxyphenyl)-2-phenylvinyl)-4-methylbenzenesulfonamide (37):



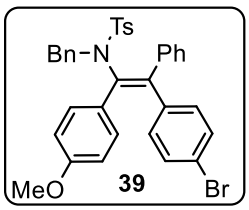
37 (152 mg, 90%) as pale yellow solid. mp = 181–185 °C; R_f = 0.28 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.22 (m, 6H), 7.08 (br d, J = 7.2 Hz, 2H), 7.05 (d, J = 8.4 Hz, 2H), 6.95 (d, J = 7.6 Hz, 2H), 6.86–6.79 (m, 4H), 6.77 (d, J = 8.0 Hz, 2H), 6.72 (t, J = 8.8 Hz, 2H), 6.57 (d, J = 8.0 Hz, 2H), 4.27 (d, J = 14.4 Hz, 1H), 4.00 (d, J = 14.4 Hz, 1H), 3.74 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.3 (d, J = 248 Hz, 1C), 158.9, 143.1, 141.7, 140.6, 138.5 (d, J = 3.0 Hz, 1C), 137.6, 136.0, 134.0, 132.84, 132.77, 130.1 (d, J = 9.1 Hz, 2C), 129.1, 128.9, 128.4, 128.3, 128.2, 128.0, 127.4, 114.6 (d, J = 21 Hz, 2C), 113.2, 55.1, 51.0, 21.5; ^{19}F NMR (376 MHz) δ −115.3; IR (Neat) ν_{max} 2184, 1601, 1504, 1332, 1246, 1153, 1089, 1025 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{30}FNNaO_3S$ $(M+Na)^+$: calcd. 586.1823, found 586.1827.

(*E*)-N-Benzyl-N-(2-(4-chlorophenyl)-1-(4-methoxyphenyl)-2-phenylvinyl)-4-methylbenzenesulfonamide (38):



38 (152 mg, 87%) as colorless solid. mp = 198–199 °C; R_f = 0.28 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.28 (m, 4H), 7.25–7.22 (m, 2H), 7.08 (br d, J = 6.5 Hz, 2H), 7.05 (d, J = 8.0 Hz, 2H), 7.00 (d, J = 8.5 Hz, 2H), 6.95 (d, J = 8.0 Hz, 2H), 6.83 (d, J = 8.0 Hz, 2H), 6.76 (t, J = 8.5 Hz, 4H), 6.57 (d, J = 9.0 Hz, 2H), 4.27 (d, J = 14.0 Hz, 1H), 3.98 (d, J = 14.5 Hz, 1H), 3.75 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.9, 143.1, 141.4, 141.1, 140.3, 137.4, 135.9, 134.4, 132.8, 132.5, 132.2, 130.1, 130.0, 129.0, 128.9, 128.4, 128.3, 128.2, 127.94, 127.85, 127.5, 113.2, 55.1, 50.9, 21.5; IR (Neat) ν_{max} 2182, 1598, 1507, 1490, 1329, 1246, 1152, 1090, 1026 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{30}ClNNaO_3S$ $(M+Na)^+$: calcd. 602.1527, found 602.1526.

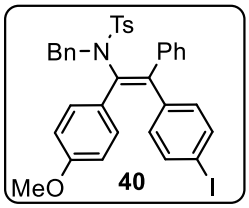
(*E*)-N-Benzyl-N-(2-(4-bromophenyl)-1-(4-methoxyphenyl)-2-phenylvinyl)-4-methylbenzenesulfonamide (39):



39 (146 mg, 78%) as colorless solid. mp = 203–204 °C; R_f = 0.28 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33–7.27 (m, 4H), 7.26–7.22 (m, 2H), 7.15 (d, J = 8.5 Hz, 2H), 7.08 (br d, J = 7.0 Hz, 2H), 7.05 (d, J = 8.0 Hz, 2H), 6.94 (d, J = 8.5 Hz, 2H), 6.83 (d, J = 8.0 Hz, 2H), 6.76 (d, J = 7.0

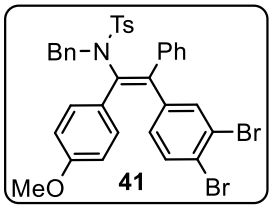
Hz, 2H), 6.71 (d, J = 8.5 Hz, 2H), 6.57 (d, J = 9.0 Hz, 2H), 4.27 (d, J = 14.5 Hz, 1H), 3.98 (d, J = 14.5 Hz, 1H), 3.75 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 143.1, 141.6, 141.4, 140.3, 137.5, 135.9, 134.4, 132.9, 132.8, 130.8, 130.08, 130.06, 129.0, 128.9, 128.4, 128.2, 127.9, 127.5, 120.6, 113.2, 55.1, 51.0, 21.5; IR (Neat) ν_{max} 2185, 1604, 1507, 1328, 1246, 1171, 1027, 902, 831 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{30}BrNNaO_3S$ $(M+Na)^+$: calcd. 646.1022, found 646.1019, 648.1003 (M+2).

(*E*)-N-Benzyl-N-(2-(4-iodophenyl)-1-(4-methoxyphenyl)-2-phenylvinyl)-4-methylbenzenesulfonamide (40):



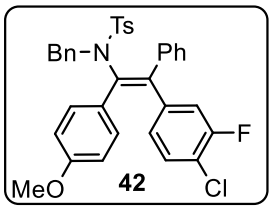
40 (131 mg, 65%) as pale yellow solid. mp = 197–199 °C; R_f = 0.28 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.22 (m, 8H), 7.13–7.01 (m, 4H), 6.95 (d, J = 8.4 Hz, 2H), 6.83 (d, J = 8.4 Hz, 2H), 6.76 (d, J = 7.2 Hz, 2H), 6.63–6.54 (m, 4H), 4.27 (d, J = 14.4 Hz, 1H), 3.98 (d, J = 14.4 Hz, 1H), 3.75 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 143.1, 142.2, 141.3, 140.4, 137.5, 136.8, 135.9, 134.5, 133.1, 132.8, 130.1, 128.94, 128.92, 128.4, 128.2, 127.9, 127.5, 113.3, 92.3, 55.1, 51.0, 21.5; IR (Neat) ν_{max} 2184, 1600, 1507, 1333, 1294, 1246, 1153, 1089, 1024, 900, 835 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{30}INNaO_3S$ $(M+Na)^+$: calcd. 694.0883, found 694.0884.

(*E*)-N-Benzyl-N-(2-(4-iodophenyl)-1-(4-methoxyphenyl)-2-phenylvinyl)-4-methylbenzenesulfonamide (41):



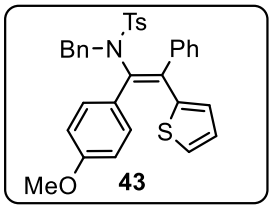
41 (152 mg, 72%) as pale yellow solid. mp = 183–184 °C; R_f = 0.28 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.21 (m, 7H), 7.04 (d, J = 7.5 Hz, 2H), 7.02–6.97 (m, 2H), 6.96–6.86 (m, 6H), 6.70 (br d, J = 7.5 Hz, 2H), 6.63 (d, J = 8.5 Hz, 2H), 4.23 (d, J = 13.0 Hz, 1H), 4.00 (d, J = 13.5 Hz, 1H), 3.76 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4, 146.3, 143.2, 140.6, 138.9, 137.2, 136.0, 135.7, 132.9, 132.7, 132.0, 130.0, 129.0, 128.9, 128.5, 128.4, 128.3, 128.2, 128.0, 127.7, 122.0, 113.5, 55.2, 51.1, 21.5; IR (Neat) ν_{max} 2185, 1598, 1572, 1509, 1332, 1250, 1152, 1088 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{29}Br_2NNaO_3S$ $(M+Na)^+$: calcd. 724.0127, found 724.0125, 726.0108 (M+2).

(*E*)-N-Benzyl-N-(2-(4-chloro-3-fluorophenyl)-1-(4-methoxyphenyl)-2-phenylvinyl)-4-methylbenzenesulfonamide (42):



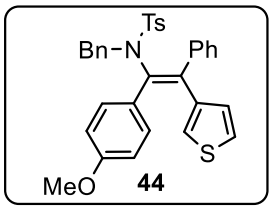
42 (145 mg, 81%) as colorless solid. mp = 178–180 °C; R_f = 0.23 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.27 (m, 4H), 7.24 (t, *J* = 8.0 Hz, 2H), 7.04 (d, *J* = 8.5 Hz, 2H), 7.01 (d, *J* = 7.0 Hz, 2H), 6.91 (d, *J* = 8.5 Hz, 2H), 6.89–6.83 (m, 3H), 6.77 (t, *J* = 9.0 Hz, 1H), 6.73–6.67 (m, 3H), 6.60 (d, *J* = 9.0 Hz, 2H), 4.23 (d, *J* = 14.0 Hz, 1H), 3.98 (d, *J* = 14.5 Hz, 1H), 3.76 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.2, 156.6 (d, *J* = 251 Hz, 1C), 143.2, 141.1, 139.8 (d, *J* = 3.8 Hz, 1C), 139.5, 137.4, 135.8, 135.0, 133.0, 132.9, 131.1 (d, *J* = 7.6 Hz, 1C), 130.1 (d, *J* = 6.3 Hz, 1C), 129.0, 128.7, 128.5, 128.4, 128.3, 128.0, 127.6, 120.2 (d, *J* = 19 Hz, 1C), 115.8 (d, *J* = 20 Hz, 1C), 113.4, 55.2, 51.1, 21.5; ^{19}F NMR (471 MHz) δ –117.7; IR (Neat) ν_{max} 1597, 1493, 1328, 1244, 1153, 1112, 1024, 860, 829 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{29}ClFNNaO_3S$ $(M+Na)^+$: calcd. 620.1433, found 620.1433.

(*E*)-N-Benzyl-N-(1-(4-methoxyphenyl)-2-phenyl-2-(thiophen-2-yl)vinyl)-4-methylbenzenesulfonamide (43):



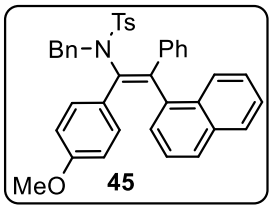
43 (108 mg, 65%) as colourless solid. mp = 171–172 °C; R_f = 0.18 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39–7.28 (m, 4H), 7.26–7.21 (m, 4H), 7.08 (dd, *J* = 5.0, 1.0 Hz, 1H), 7.05 (d, *J* = 8.5 Hz, 2H), 6.99 (d, *J* = 8.0 Hz, 2H), 6.95 (d, *J* = 8.0 Hz, 2H), 6.77 (d, *J* = 7.0 Hz, 2H), 6.73–6.67 (m, 3H), 6.45 (dd, *J* = 3.0, 0.5 Hz, 1H), 4.20 (d, *J* = 14.0 Hz, 1H), 3.97 (d, *J* = 14.0 Hz, 1H), 3.80 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.5, 145.0, 143.0, 141.4, 137.5, 135.9, 135.4, 133.8, 132.8, 130.2, 130.1, 129.8, 129.2, 129.1, 128.9, 128.5, 128.3, 128.1, 128.0, 127.9, 127.7, 126.6, 126.0, 113.5, 55.1, 51.1, 21.4; IR (Neat) ν_{max} 2931, 1599, 1500, 1333, 1240, 1154, 1109, 1026, 840 cm^{-1}; **HRMS (ESI)** for $C_{33}H_{30}NO_3S_2$ $(M+H)^+$: calcd. 552.1662, found 552.1663.

(*E*)-N-Benzyl-N-(1-(4-methoxyphenyl)-2-phenyl-2-(thiophen-3-yl)vinyl)-4-methylbenzenesulfonamide (44):



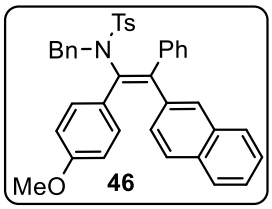
44 (129 mg, 78%) as colorless solid. mp = 183–184 °C; R_f = 0.23 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.27 (m, 4H), 7.24 (t, *J* = 9.5 Hz, 2H), 7.15 (br d, *J* = 6.5 Hz, 2H), 7.04 (d, *J* = 8.5 Hz, 2H), 6.97–6.93 (m, 3H), 6.88 (d, *J* = 8.0 Hz, 2H), 6.76 (d, *J* = 7.0 Hz, 2H), 6.62 (d, *J* = 9.0 Hz, 2H), 6.59 (dd, *J* = 3.0, 1.0 Hz, 1H), 6.42 (dd, *J* = 5.0, 1.0 Hz, 1H), 4.23 (d, *J* = 14.5 Hz, 1H), 3.96 (d, *J* = 14.5 Hz, 1H), 3.77 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.1, 143.0, 142.9, 141.6, 137.7, 136.5, 136.0, 133.6, 132.5, 130.2, 130.0, 129.8, 129.7, 128.9, 128.3, 128.2, 128.1, 128.0, 127.4, 126.1, 123.8, 113.3, 55.1, 51.1, 21.4; IR (Neat) ν_{max} 2929, 1600, 1501, 1333, 1245, 1154, 1087, 1027, 835 cm^{-1}; **HRMS (ESI)** for $C_{33}H_{30}NO_3S_2$ $(M+H)^+$: calcd. 552.1662, found 552.1663.

(*E*)-N-Benzyl-N-(1-(4-methoxyphenyl)-2-(naphthalen-1-yl)-2-phenylvinyl)-4-methylbenzenesulfonamide (45):



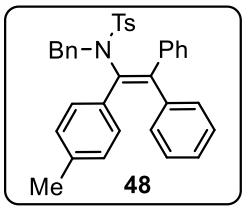
45 (136 mg, 81%) as pale yellow solid. mp = 155–156 °C; R_f = 0.18 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.6 Hz, 1H), 7.55 (d, *J* = 7.6 Hz, 1H), 7.49 (d, *J* = 8.4 Hz, 1H), 7.39–7.26 (m, 9H), 7.15 (br d, *J* = 6.8 Hz, 2H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.99 (d, *J* = 8.0 Hz, 3H), 6.92 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 7.2 Hz, 2H), 6.52 (d, *J* = 8.4 Hz, 2H), 4.33 (d, *J* = 14.4 Hz, 1H), 4.06 (d, *J* = 14.4 Hz, 1H), 3.69 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8, 143.0, 142.0, 141.5, 140.3, 137.6, 136.0, 134.3, 133.0, 132.0, 130.5, 130.22, 130.20, 129.3, 129.2, 128.9, 128.4, 128.3, 128.2, 128.0, 127.9, 127.4, 127.3, 126.9, 125.8, 125.7, 113.2, 55.0, 51.1, 21.5; IR (Neat) ν_{max} 2929, 1600, 1505, 1334, 1245, 1154, 1088, 1026, 835 cm^{-1}; **HRMS (ESI)** for $C_{39}H_{33}NNaO_3S$ $(M+Na)^+$: calcd. 618.2073, found 618.2074.

(*E*)-N-Benzyl-N-(1-(4-methoxyphenyl)-2-(naphthalen-2-yl)-2-phenylvinyl)-4-methylbenzenesulfonamide (46):



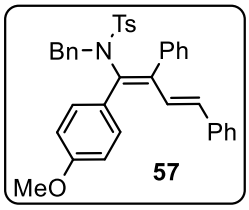
46 (103 mg, 58%) as colorless solid. mp = 217–218 °C; R_f = 0.18 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 7.2 Hz, 1H), 7.55 (d, J = 7.2 Hz, 1H), 7.49 (d, J = 8.4 Hz, 1H), 7.39–7.27 (m, 9H), 7.15 (br d, J = 6.8 Hz, 2H), 7.07 (d, J = 8.0 Hz, 2H), 6.99 (d, J = 6.8 Hz, 3H), 6.92 (d, J = 8.0 Hz, 2H), 6.83 (d, J = 7.2 Hz, 2H), 6.52 (d, J = 8.8 Hz, 2H), 4.33 (d, J = 14.4 Hz, 1H), 4.06 (d, J = 14.4 Hz, 1H), 3.69 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8, 143.0, 142.0, 141.5, 140.3, 137.6, 136.0, 134.3, 133.0, 132.0, 130.5, 130.22, 130.20, 129.3, 129.2, 128.9, 128.7, 128.4, 128.3, 128.2, 128.0, 127.9, 127.4, 127.3, 126.9, 125.8, 125.7, 113.2, 55.0, 51.1, 21.5; IR (Neat) ν_{max} 1596, 1504, 1339, 1289, 1242, 1172, 1026, 839 cm^{-1}; **HRMS (ESI)** for $C_{39}H_{33}NNaO_3S$ $(M+Na)^+$: calcd. 618.2073, found 618.2074.

N-Benzyl-N-(2,2-diphenyl-1-(*p*-tolyl)vinyl)-4-methylbenzenesulfonamide (48):



48 (149 mg, 94%) as colorless solid. mp = 205–207 °C; R_f = 0.41 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.23 (m, 6H), 7.11 (br d, J = 7.5 Hz, 2H), 7.07–7.01 (m, 5H), 6.96 (d, J = 8.0 Hz, 2H), 6.90–6.77 (m, 8H), 4.27 (d, J = 14.5 Hz, 1H), 4.02 (d, J = 14.5 Hz, 1H), 2.40 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.0, 142.5, 142.2, 141.9, 137.5, 137.1, 136.0, 134.1, 134.0, 131.4, 131.2, 130.2, 130.0, 128.9, 128.34, 128.31, 128.2, 128.1, 128.0, 127.5, 127.3, 126.5, 51.0, 21.5, 21.2; IR (Neat) ν_{max} 1596, 1492, 1444, 1330, 1153, 1015, 757 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{31}NNaO_2S$ $(M+Na)^+$: calcd. 552.1968, found 552.1966.

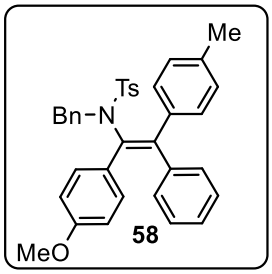
N-Benzyl-N-((1*Z*,3*E*)-1-(4-bromophenyl)-2,4-diphenylbuta-1,3-dien-1-yl)-4-methylbenzenesulfonamide (57):



57 (106 mg, 61%) as pale yellow liquid; R_f = 0.25 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44–7.27 (m, 7H), 7.23–7.18 (m, 5H), 7.17–7.12 (m, 3H), 7.09–7.03 (m, 3H), 6.91 (d, J = 8.5 Hz, 2H), 6.84 (d, J = 8.0 Hz, 2H), 6.61 (d, J = 7.5 Hz, 2H), 6.05 (d, J = 16.0 Hz, 1H), 4.03 (d, J = 7.0 Hz, 2H), 3.89 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.7, 143.2, 141.0, 138.7, 137.4, 137.1, 135.6, 135.3, 133.2, 133.1, 130.9, 130.6, 130.1, 129.0, 128.8, 128.5, 128.3,

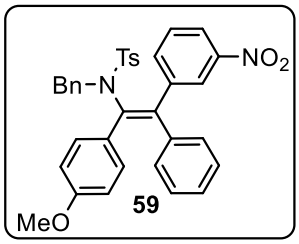
128.2, 128.1, 128.0, 127.4, 127.2, 126.5, 113.5, 55.3, 51.5, 21.5; IR (Neat) ν_{max} 2926, 1736, 1600, 1507, 1443, 1247, 1152, 1087, 1022, 836 cm^{-1}; **HRMS (ESI)** for $C_{37}H_{34}NO_3S$ $(M+H)^+$: calcd. 572.2254, found 572.2255.

(*Z*)-N-Benzyl-N-(1-(4-methoxyphenyl)-2-phenyl-2-(*p*-tolyl)vinyl)-4-methylbenzenesulfonamide (58):



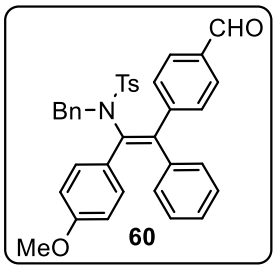
58 (144 mg, 86%) as yellow solid. mp = 205–206 °C; R_f = 0. 41 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.23 (m, 3H), 7.13 (q, *J* = 8.0 Hz, 4H), 7.07–6.99 (m, 7H), 6.89–6.83 (m, 4H), 6.74 (d, *J* = 8.4 Hz, 2H), 6.50 (d, *J* = 8.8 Hz, 2H), 4.34 (d, *J* = 14.4 Hz, 1H), 3.99 (d, *J* = 14.8 Hz, 1H), 3.71 (s, 3H), 2.41 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.6, 142.8, 142.6, 141.1, 138.8, 137.9, 137.2, 136.2, 133.6, 132.7, 131.2, 130.1, 129.8, 129.6, 128.9, 128.8, 128.3, 128.1, 127.8, 127.5, 126.3, 112.9, 55.0, 50.9, 21.5, 21.3; IR (Neat) ν_{max} 2920, 1600, 1510, 1327, 1255, 1155, 1087, 1027, 811 cm^{-1}; **HRMS (ESI)** for $C_{36}H_{34}NO_3S$ $(M+H)^+$: calcd. 560.2254, found 560.2256.

(*Z*)-N-Benzyl-N-(1-(4-methoxyphenyl)-2-(3-nitrophenyl)-2-phenylvinyl)-4-methylbenzenesulfonamide (59):



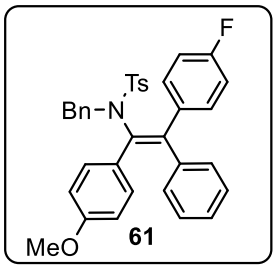
59 (159 mg, 86%) as pale yellow solid. mp = 189–190 °C; R_f = 0.38 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (dq, *J* = 8.0, 1.2 Hz, 1H), 7.68 (s, 1H), 7.51 (d, *J* = 7.6 Hz, 1H), 7.41 (t, *J* = 8.0 Hz, 1H), 7.34–7.23 (m, 3H), 7.09–7.02 (m, 7H), 6.96 (d, *J* = 8.8 Hz, 2H), 6.88–6.83 (m, 2H), 6.81 (d, *J* = 6.8 Hz, 2H), 6.61 (d, *J* = 8.8 Hz, 2H), 4.25 (d, *J* = 3.6 Hz, 2H), 3.75 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 148.2, 143.7, 143.5, 141.4, 140.2, 137.1, 136.7, 135.7, 135.0, 132.9, 131.1, 130.0, 129.1, 128.9, 128.6, 128.4, 128.3, 128.0, 127.6, 127.1, 124.7, 121.9, 113.4, 55.1, 51.9, 21.4; IR (Neat) ν_{max} 2922, 1610, 1524, 1343, 1154, 816 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{34}N_3O_5S$ $(M+NH_4)^+$: calcd. 608.2214, found 608.2225.

(*Z*)-N-Benzyl-N-(2-(4-formylphenyl)-1-(4-methoxyphenyl)-2-phenylvinyl)-4-methylbenzenesulfonamide (60):



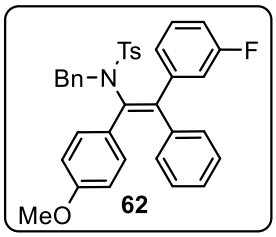
60 (107 mg, 62%) as pale yellow solid. mp = 212–213 °C; R_f = 0.23 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.03 (s, 1H), 7.74 (d, J = 8.5 Hz, 2H), 7.35–7.30 (m, 1H), 7.29–7.25 (m, 2H), 7.12 (d, J = 7.5 Hz, 2H), 7.07–7.01 (m, 5H), 6.98–6.93 (m, 4H), 6.86–6.82 (m, 2H), 6.74 (d, J = 7.5 Hz, 2H), 6.60 (d, J = 8.5 Hz, 2H), 4.24 (d, J = 14.5 Hz, 1H), 4.11 (d, J = 14.0 Hz, 2H), 3.75 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.9, 159.1, 148.6, 143.4, 141.8, 141.0, 137.2, 135.5, 135.3, 135.0, 132.9, 131.2, 130.9, 130.1, 129.5, 129.0, 128.7, 128.5, 128.4, 127.9, 127.2, 126.9, 113.3, 55.1, 51.3, 21.5; IR (Neat) ν_{max} 1690, 1597, 1328, 1250, 1153, 1025, 836 cm^{-1}; **HRMS (ESI)** for $C_{36}H_{32}NO_4S$ $(M+H)^+$: calcd. 574.2047, found 574.2053.

(*Z*)-N-Benzyl-N-(2-(4-fluorophenyl)-1-(4-methoxyphenyl)-2-phenylvinyl)-4-methylbenzenesulfonamide (61):



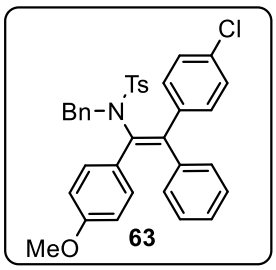
61 (122 mg, 72%) as pale yellow solid. mp = 206–208 °C; R_f = 0.29 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.29 (m, 1H), 7.28–7.23 (m, 2H), 7.10–6.99 (m, 9H), 6.96 (t, J = 8.8 Hz, 2H), 6.87–6.77 (m, 6H), 6.54 (d, J = 8.8 Hz, 2H), 4.29 (d, J = 14.4 Hz, 1H), 4.06 (d, J = 14.4 Hz, 1H), 3.73 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.2 (d, J = 248 Hz, 1C), 158.8, 143.1, 142.4, 140.7, 137.9 (d, J = 4.1 Hz, 1C), 137.6, 135.9, 134.1, 132.8, 131.8 (d, J = 7.1 Hz, 2C), 131.2, 130.1, 129.2, 129.0, 128.4, 128.2, 127.9, 127.7, 126.6, 115.1 (d, J = 21 Hz, 2C), 113.1, 55.1, 51.2, 21.5; ^{19}F NMR (376 MHz) δ −114.7; IR (Neat) ν_{max} 1600, 1506, 1332, 1242, 1156, 1087, 1022, 861, 834 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{31}FNO_3S$ $(M+H)^+$: calcd. 564.2003, found 564.2003.

(*Z*)-N-Benzyl-N-(2-(3-fluorophenyl)-1-(4-methoxyphenyl)-2-phenylvinyl)-4-methylbenzenesulfonamide (62):



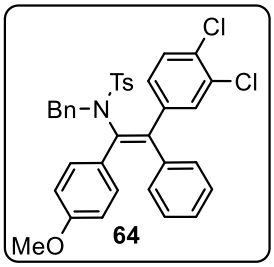
62 (147 mg, 87%) as pale yellow solid. mp = 189–190 °C; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.30 (m, 1H), 7.28–7.23 (m, 5H), 7.07 (d, J = 8.0 Hz, 2H), 7.05–7.03 (m, 3H), 6.99 (d, J =8.5 Hz, 2H), 6.95 (br d, J = 8.0 Hz, 1H), 6.89 (d, J = 8.5 Hz, 2H), 6.86–6.84 (m, 2H), 6.76 (d, J = 7.5 Hz, 2H), 6.57 (d, J = 9.0 Hz, 2H), 4.26 (d, J = 14.5 Hz, 1H), 4.09 (d, J = 14.0 Hz, 1H), 3.74 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.6 (d, J = 247 Hz, 1C), 158.9, 144.0 (d, J = 7.6 Hz, 1C), 143.2, 142.0, 140.7, 137.4, 135.7, 134.5, 132.9, 131.1, 130.1, 129.6 (d, J = 8.8 Hz, 1C), 129.0, 128.9, 128.5, 128.3, 127.9, 127.7, 126.7, 126.0 (d, J = 3.1 Hz, 1C), 116.9 (d, J = 21 Hz, 1C), 114.1 (d, J = 21 Hz, 1C), 113.2, 55.1, 51.1, 21.5; ^{19}F NMR (376 MHz) δ –113.2; IR (Neat) ν_{max} 1690, 1597, 1328, 1250, 1153, 1025, 836 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{30}FNNaO_3S$ $(M+Na)^+$: calcd. 586.1823, found 586.1829.

(*Z*)-N-Benzyl-N-(2-(4-chlorophenyl)-1-(4-methoxyphenyl)-2-phenylvinyl)-4-methylbenzenesulfonamide (63):



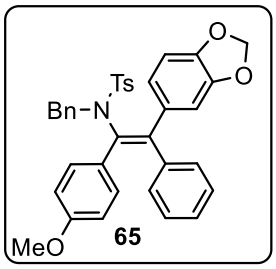
63 (155 mg, 89%) as pale yellow solid. mp = 206–207 °C; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.29 (m, 2H), 7.26–7.23 (m, 1H), 7.20 (d, J = 8.5 Hz, 2H), 7.09 (d, J = 8.0 Hz, 2H), 7.06–7.02 (m, 3H), 6.98 (d, J = 8.0 Hz, 2H), 6.91 (d, J = 8.0 Hz, 4H), 6.86–6.83 (m, 2H), 6.75 (d, J = 7.5 Hz, 2H), 6.58 (d, J = 8.5 Hz, 2H), 4.26 (d, J = 14.5 Hz, 1H), 4.12 (d, J = 14.5 Hz, 1H), 3.74 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 143.2, 142.2, 140.8, 140.5, 137.5, 135.8, 134.4, 133.2, 132.9, 131.5, 131.2, 130.7, 130.1, 129.0, 128.42, 128.35, 128.3, 127.9, 127.7, 126.7, 113.2, 55.1, 51.2, 21.5; IR (Neat) ν_{max} 2929, 1601, 1507, 1332, 1247, 1154, 1026, 835 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{31}ClNO_3S$ $(M+H)^+$: calcd. 580.1708, found 580.1713.

(*Z*)-N-Benzyl-N-(2-(3,4-dichlorophenyl)-1-(4-methoxyphenyl)-2-phenylvinyl)-4-methylbenzenesulfonamide (64):



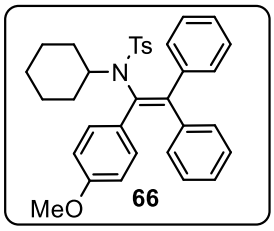
64 (149 mg, 78%) as pale yellow solid. mp = 206–208 °C; R_f = 0.59 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.30 (m, 2H), 7.28–7.26 (m, 2H), 7.10 (d, J = 8.0 Hz, 2H), 7.06–7.01 (m, 6H), 7.00 (s, 1H), 6.87–6.82 (m, 4H), 6.77–6.73 (m, 2H), 6.63 (d, J = 8.8 Hz, 2H), 4.29 (d, J = 14.0 Hz, 1H), 4.21 (d, J = 14.0 Hz, 1H), 3.76 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 143.5, 142.0, 141.7, 140.2, 137.2, 135.3, 135.0, 132.9, 132.0, 131.4, 131.20, 131.15, 130.1, 130.00, 129.96, 129.1, 128.7, 128.4, 128.3, 127.9, 127.7, 126.9, 113.4, 55.2, 51.4, 21.5; IR (Neat) ν_{max} 2920, 1601, 1512, 1436, 1350, 1330, 1156, 1026, 811 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{29}Cl_2NNaO_3S$ $(M+H)^+$: calcd. 636.1137, found 636.1144.

(*Z*)-N-(2-(Benzo[d][1,3]dioxol-5-yl)-1-(4-methoxyphenyl)-2-phenylvinyl)-N-benzyl-4-methylbenzenesulfonamide (65):



65 (134 mg, 78%) as pale yellow solid. mp = 188–190 °C; R_f = 0.16 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33–7.24 (m, 3H), 7.11–7.08 (m, 4H), 7.04–7.02 (m, 3H), 6.91 (d, J = 6.5 Hz, 2H), 6.89–6.85 (m, 2H), 6.80–6.75 (m, 2H), 6.72 (d, J = 8.5 Hz, 2H), 6.66 (s, 1H), 6.49 (d, J = 9.0 Hz, 2H), 5.96 (br d, J = 4.0 Hz, 2H), 4.40 (d, J = 14.5 Hz, 1H), 4.12 (d, J = 14.5 Hz, 1H), 3.70 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.6, 147.4, 146.9, 142.8, 142.5, 140.5, 137.9, 136.1, 135.4, 133.8, 132.7, 131.1, 130.1, 129.6, 128.8, 128.4, 128.1, 127.7, 127.5, 126.4, 123.8, 112.9, 110.4, 108.1, 101.0, 55.0, 51.1, 21.4; IR (Neat) ν_{max} 1598, 1479, 1325, 1241, 1152, 1085, 1030, 811 cm^{-1}; **HRMS (ESI)** for $C_{36}H_{32}NO_5S$ $(M+H)^+$: calcd. 590.1996, found 590.1993.

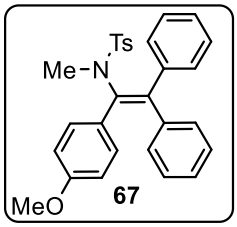
N-Cyclohexyl-N-(1-(4-methoxyphenyl)-2,2-diphenylvinyl)-4-methylbenzenesulfonamide (66):



66 (107 mg, 66%) as pale yellow gummy liquid. R_f = 0.33 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52–7.48 (m, 2H), 7.37–7.28 (m, 4H), 7.07–7.01 (m, 5H), 6.96–6.94 (m, 5H), 6.56–6.48 (m, 2H), 3.73 (s, 3H), 3.30 (tt, J = 11.6, 3.2 Hz, 1H), 2.33 (s, 3H), 2.11–2.01

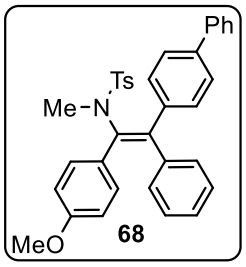
(m, 1H), 1.95–1.85 (m, 1H), 1.69–1.63 (m, 1H), 1.50–1.42 (m, 1H), 1.38–1.23 (m, 2H), 1.16–1.01 (m, 2H), 0.91–0.82 (m, 1H), 0.80–0.68 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.6, 143.2, 142.8, 142.5, 142.2, 138.4, 134.6, 133.0, 131.2, 131.0, 130.6, 128.7, 128.1, 127.7, 127.6, 127.3, 126.3, 112.8, 62.7, 55.1, 33.6, 33.2, 32.3, 26.7, 26.4, 25.3, 21.4; IR (Neat) ν_{max} 2928, 2852, 1737, 1598, 1442, 1243, 1149, 1086, 1030, 833 cm^{-1}; **HRMS (ESI)** for $C_{34}H_{35}NNaO_3S$ $(M+Na)^+$: calcd. 560.2230, found 560.2236.

N-(1-(4-Methoxyphenyl)-2,2-diphenylvinyl)-N,4-dimethylbenzenesulfonamide (67):



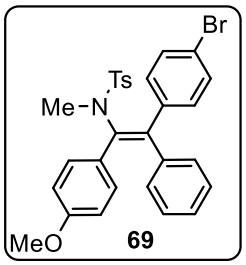
67 (129 mg, 92%) as pale yellow semi-solid. mp = 190–191 °C; R_f = 0.47 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, J = 7.0 Hz, 2H), 7.33–7.27 (m, 3H), 7.10–7.05 (m, 5H), 7.01–6.98 (m, 6H), 6.59 (d, J = 9.0 Hz, 2H), 3.74 (s, 3H), 2.83 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.9, 142.4, 142.1, 141.9, 140.9, 137.0, 136.6, 132.0, 131.1, 129.9, 129.4, 129.3, 128.9, 128.2, 127.7, 127.5, 127.4, 127.2, 126.6, 113.2, 55.1, 37.2, 21.4; IR (Neat) ν_{max} 2890, 1595, 1510, 1364, 1246, 1048, 836 cm^{-1}; **HRMS (ESI)** for $C_{29}H_{28}NO_3S$ $(M+H)^+$: calcd. 470.1784, found 470.1792.

(*Z*)-N-(2-([1,1'-Biphenyl]-4-yl)-1-(4-methoxyphenyl)-2-phenylvinyl)-N,4-dimethylbenzenesulfonamide (68):



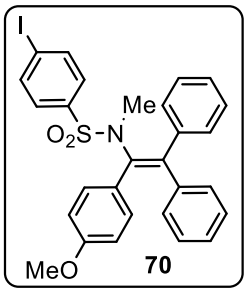
68 (149 mg, 91%) as pale yellow semi-solid. mp = 237–239 °C; R_f = 0.44 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, J = 9.0 Hz, 2H), 7.52–7.45 (m, 4H), 7.39–7.33 (m, 3H), 7.16–7.10 (m, 5H), 7.08–7.03 (m, 4H), 6.94 (d, J = 10.0 Hz, 2H), 6.65–6.61 (m, 2H), 3.76 (s, 3H), 2.90 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 142.4, 141.9, 141.2, 140.52, 140.48, 139.7, 136.9, 136.6, 132.1, 131.3, 130.3, 129.2, 128.9, 128.8, 127.8, 127.3, 127.2, 126.9, 126.7, 113.3, 55.1, 37.1, 21.3; IR (Neat) ν_{max} 2929, 1613, 1515, 1369, 1246, 1148, 825 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{31}NNaO_3S$ $(M+Na)^+$: calcd. 568.1917, found 568.1924.

(*Z*)-N-(2-(4-Bromophenyl)-1-(4-methoxyphenyl)-2-phenylvinyl)-N,4-dimethylbenzenesulfonamide (69):



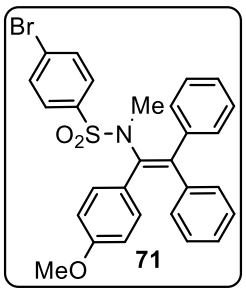
69 (138 mg, 84%) as yellow solid. mp = 165–167 °C; R_f = 0.25 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37–7.31 (m, 2H), 7.17–7.13 (m, 2H), 7.12–7.06 (m, 5H), 7.05–7.02 (m, 4H), 7.00–6.95 (m, 2H), 6.64–6.57 (m, 2H), 3.74 (s, 3H), 2.86 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.9, 142.7, 141.4, 141.0, 139.6, 137.0, 136.8, 132.0, 131.6, 131.3, 131.1, 129.0, 128.9, 127.9, 127.0, 126.9, 121.5, 113.3, 55.1, 37.2, 21.5; IR (Neat) ν_{max} 1559, 1507, 1335, 1243, 1150, 1018, 1003, 927, 822 cm^{-1}; **HRMS (ESI)** for $C_{29}H_{27}BrNO_3S$ $(M+H)^+$: calcd. 548.0890, found 548.0898.

4-Iodo-N-(1-(4-methoxyphenyl)-2,2-diphenylvinyl)-N-methylbenzenesulfonamide (70):



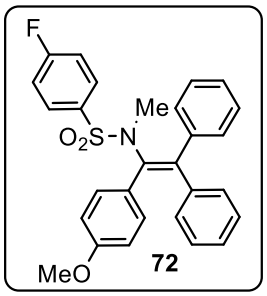
70 (118 mg, 68%) as pale yellow solid. mp = 215–217 °C; R_f = 0.33 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57–7.52 (m, 2H), 7.36–7.27 (m, 5H), 7.11–7.07 (m, 3H), 7.06–7.01 (m, 2H), 7.00–6.95 (m, 2H), 6.85–6.80 (m, 2H), 6.62–6.56 (m, 2H), 3.76 (s, 3H), 2.88 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 141.7, 141.5, 141.0, 139.6, 137.4, 136.1, 131.9, 131.0, 129.8, 129.0, 128.5, 128.3, 127.7, 127.6, 127.4, 126.8, 126.3, 113.3, 99.1, 55.2, 37.5; IR (Neat) ν_{max} 2929, 1603, 1564, 1508, 1440, 1336, 1269, 1153, 1000, 941, 838 cm^{-1}; **HRMS (ESI)** for $C_{28}H_{25}INO_3S$ $(M+H)^+$: calcd. 582.0594, found 582.0594.

4-Bromo-N-(1-(4-methoxyphenyl)-2,2-diphenylvinyl)-N-methylbenzenesulfonamide (71):



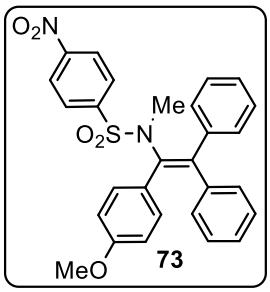
71 (122 mg, 76%) as pale yellow solid. mp = 185–186 °C; R_f = 0.63 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.27 (m, 6H), 7.27–7.26 (m, 1H), 7.11–7.06 (m, 3H), 7.03 (d, J = 8.8 Hz, 2H), 7.00–6.95 (m, 4H), 6.59 (d, J = 8.8 Hz, 2H), 3.76 (s, 3H), 2.87 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 141.8, 141.6, 141.1, 139.0, 136.2, 131.9, 131.5, 131.1, 129.8, 129.1, 128.7, 128.3, 127.8, 127.4, 126.8, 126.7, 113.3, 55.2, 37.5; IR (Neat) ν_{max} 2929, 1613, 1515, 136, 1246, 1148, 825 cm^{-1}; **HRMS (ESI)** for $C_{28}H_{25}BrNO_3S$ $(M+H)^+$: calcd. 534.0733, found 534.0736, 536.0739 (M+2).

4-Fluoro-N-(1-(4-methoxyphenyl)-2,2-diphenylvinyl)-N-methylbenzenesulfonamide (72):



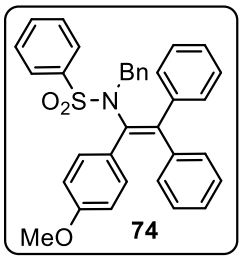
72 (115 mg, 80%) as yellow solid. mp = 170–172 °C; R_f = 0.47 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.27 (m, 5H), 7.13–7.07 (m, 5H), 7.06–7.03 (m, 2H), 7.00–6.95 (m, 2H), 6.89–6.83 (m, 2H), 6.62–6.52 (m, 2H), 3.75 (s, 3H), 2.84 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.5 (d, J = 255 Hz, 1C), 158.9, 141.9, 141.6, 141.1, 136.2, 135.9 (d, J = 2.0 Hz, 1C), 132.0, 131.1, 129.9, 129.8, 129.1, 128.3, 127.8, 127.4, 126.8, 115.4 (d, J = 20 Hz, 2C), 113.3, 55.1, 37.3; ^{19}F NMR (376 MHz) δ −106.5; IR (Neat) ν_{max} 2952, 1591, 1509, 1492, 1342, 1291, 1247, 1148, 829 cm^{-1}; **HRMS (ESI)** for $C_{28}H_{28}FN_2O_3S$ $(M+NH_4)^+$: calcd. 491.1799, found 491.1792.

N-(1-(4-Methoxyphenyl)-2,2-diphenylvinyl)-N-methyl-4-nitrobenzenesulfonamide (73):



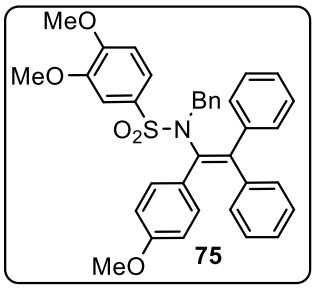
73 (110 mg, 73%) as yellow solid. mp = 173–175 °C; R_f = 0.47 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03–7.97 (m, 2H), 7.33–7.23 (m, 7H), 7.12–7.06 (m, 3H), 7.03–6.99 (m, 2H), 6.98–6.93 (m, 2H), 6.61–6.52 (m, 2H), 3.73 (s, 3H), 2.94 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 149.2, 145.6, 141.47, 141.45, 141.3, 135.7, 131.9, 131.0, 129.7, 128.9, 128.4, 128.1, 127.8, 127.6, 127.0, 123.4, 113.4, 55.2, 37.7; IR (Neat) ν_{max} 2916, 2840, 1597, 1524, 1342, 1245, 1153, 700 cm^{-1}; **HRMS (ESI)** for $C_{28}H_{25}N_2O_5S$ $(M+H)^+$: calcd. 501.1479, found 501.1484.

N-Benzyl-N-(1-(4-methoxyphenyl)-2,2-diphenylvinyl)benzenesulfonamide (74):



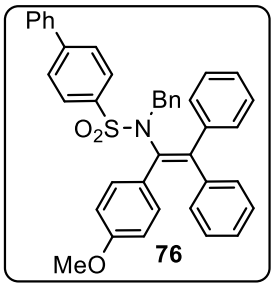
74 (104 mg, 65%) as pale yellow solid. mp = 157–159 °C; R_f = 0.29 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (t, J = 7.2 Hz, 1H), 7.37–7.32 (m, 4H), 7.28 (t, J = 8.0 Hz, 4H), 7.22–7.17 (m, 2H), 7.15–7.10 (m, 2H), 7.07 (br t, J = 3.2 Hz, 3H), 6.92–6.88 (m, 2H), 6.83 (t, J = 7.2 Hz, 4H), 6.56 (d, J = 8.8 Hz, 2H), 4.36 (d, J = 14.4 Hz, 1H), 4.04 (d, J = 14.4 Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.7, 142.4, 141.8, 141.5, 140.6, 135.9, 133.8, 132.8, 132.2, 131.2, 130.1, 130.0, 129.3, 128.4, 128.3, 128.2, 127.8, 127.6, 127.4, 126.4, 113.0, 55.0, 51.1; IR (Neat) ν_{max} 1604, 1445, 1331, 1246, 1154, 1028, 836 cm^{-1}; **HRMS (ESI)** for $C_{34}H_{29}NNaO_3S$ $(M+Na)^+$: calcd. 554.1760, found 554.1757.

N-Benzyl-3,4-dimethoxy-N-(1-(4-methoxyphenyl)-2,2-diphenylvinyl)benzenesulfonamide (75):



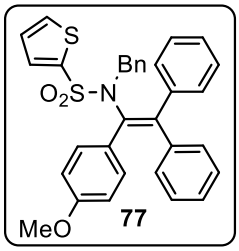
75 (165 mg, 93%) as pale yellow solid. mp = 174–176 °C; R_f = 0.05 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42–7.27 (m, 8H), 7.03–6.99 (m, 5H), 6.90 (dd, J = 8.5, 2.0 Hz, 1H), 6.87–6.81 (m, 2H), 6.71 (d, J = 8.5 Hz, 1H), 6.64 (d, J = 8.5 Hz, 2H), 6.61 (d, J = 2.5 Hz, 1H), 6.43 (d, J = 9.0 Hz, 2H), 4.42 (d, J = 14.5 Hz, 1H), 3.93 (d, J = 15.0 Hz, 1H), 3.90 (s, 3H), 3.66 (s, 3H), 3.63 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4, 152.0, 148.2, 142.3, 141.5, 140.4, 136.4, 134.4, 133.0, 132.7, 131.1, 130.0, 129.9, 129.8, 128.3, 128.2, 127.6, 127.5, 126.3, 121.5, 112.7, 110.1, 109.8, 56.0, 55.8, 54.9, 51.4; IR (Neat) ν_{max} 1587, 1506, 1326, 1236, 1139, 1020, 832 cm^{-1}; **HRMS (ESI)** for $C_{36}H_{33}NNaO_5S$ $(M+Na)^+$: calcd. 614.1972, found 614.1970.

N-Benzyl-N-(1-(4-methoxyphenyl)-2,2-diphenylvinyl)-[1,1'-biphenyl]-4-sulfonamide (76):



76 (144 mg, 79%) as pale yellow solid. mp = 216–218 °C; R_f = 0.29 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63–7.58 (m, 2H), 7.53–7.42 (m, 6H), 7.37–7.31 (m, 4H), 7.31–7.26 (m, 2H), 7.25–7.19 (m, 2H), 7.16 (d, J = 8.5 Hz, 2H), 7.08–7.03 (m, 3H), 6.94–6.88 (m, 3H), 6.83 (br d, J = 8.5 Hz, 2H), 6.54 (d, J = 9.0 Hz, 2H), 4.40 (d, J = 14.0 Hz, 1H), 4.07 (d, J = 14.5 Hz, 1H), 3.71 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.7, 144.9, 142.4, 141.8, 141.4, 139.33, 139.27, 136.0, 133.9, 132.8, 131.2, 130.1, 130.0, 129.3, 129.0, 128.39, 128.35, 128.31, 128.27, 128.2, 127.6, 127.4, 127.2, 126.8, 126.5, 113.0, 55.0, 51.3; IR (Neat) ν_{max} 1591, 1508, 1334, 1246, 1153, 1089, 1021, 894, 829 cm^{-1}; **HRMS (ESI)** for $C_{40}H_{33}NNaO_3S$ $(M+Na)^+$: calcd. 630.2073, found 630.2076.

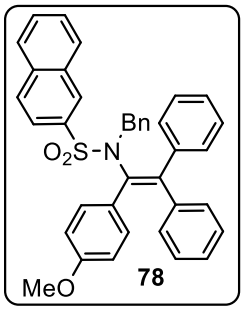
N-Benzyl-N-(1-(4-methoxyphenyl)-2,2-diphenylvinyl)thiophene-2-sulfonamide (77):



77 (126 mg, 78%) as pale yellow solid. mp = 180–182 °C; R_f = 0.21 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (dd, J = 5.2, 1.2 Hz, 1H), 7.38–7.29 (m, 6H), 7.24–7.19 (m, 2H), 7.09–7.03 (m, 3H), 7.01 (d, J = 6.8 Hz, 2H), 6.91–6.82 (m, 3H), 6.76 (d, J = 8.8 Hz, 2H), 6.64 (dd, J = 3.6, 1.2 Hz, 1H), 6.52 (d, J = 8.8 Hz, 2H), 4.43 (d, J = 14.4 Hz, 1H), 4.09 (d, J = 14.4

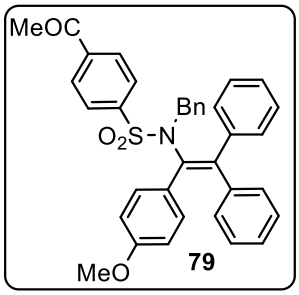
Hz, 1H), 3.71 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.7, 142.3, 141.8, 141.6, 141.4, 135.8, 133.9, 132.7, 132.6, 131.6, 131.1, 130.3, 129.9, 129.2, 128.4, 128.33, 128.29, 127.6, 127.5, 126.9, 126.5, 113.0, 55.0, 51.5; IR (Neat) ν_{max} 1604, 1509, 1336, 1249, 1176, 1150, 1025, 900, 832 cm^{-1}; **HRMS (ESI)** for $C_{32}H_{28}NO_3S_2$ $(M+H)^+$: calcd. 538.1505, found 538.1509.

N-Benzyl-N-(1-(4-methoxyphenyl)-2,2-diphenylvinyl)naphthalene-2-sulfonamide (78):



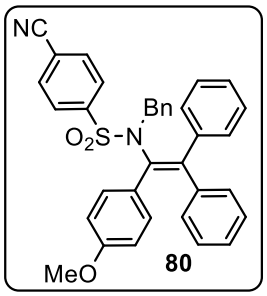
78 (158 mg, 94%) as pale yellow solid. mp = 189–191 °C; R_f = 0.47 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 8.0 Hz, 1H), 7.72 (d, J = 8.4 Hz, 1H), 7.65–7.57 (m, 2H), 7.55–7.49 (m, 2H), 7.40–7.27 (m, 6H), 7.23–7.09 (m, 3H), 7.06–7.01 (m, 3H), 6.92 (d, J = 7.2 Hz, 2H), 6.88–6.84 (m, 2H), 6.67 (d, J = 8.0 Hz, 2H), 6.35 (d, J = 8.8 Hz, 2H), 4.47 (d, J = 14.8 Hz, 1H), 4.02 (d, J = 14.4 Hz, 1H), 3.57 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.6, 142.4, 141.7, 140.8, 137.8, 136.2, 134.4, 134.2, 132.9, 131.8, 131.3, 130.2, 130.0, 129.4, 129.2, 129.1, 128.5, 128.4, 128.3, 128.2, 127.6, 126.9, 126.5, 122.9, 112.9, 54.9, 51.6; IR (Neat) ν_{max} 2930, 1598, 1504, 1441, 1338, 1243, 1149, 1023, 808 cm^{-1}; **HRMS (ESI)** $C_{38}H_{32}NO_3S$ $(M+Na)^+$: calcd. 582.2096, found 582.2097.

4-Acetyl-N-benzyl-N-(1-(4-methoxyphenyl)-2,2-diphenylvinyl)benzenesulfonamide (79):



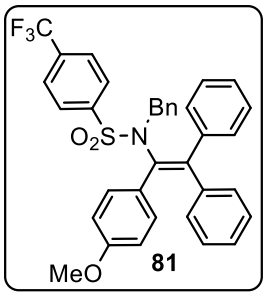
79 (125 mg, 73%) as pale yellow solid. mp = 206–208 °C; R_f = 0.1 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 8.4 Hz, 2H), 7.36–7.28 (m, 6H), 7.25–7.23 (m, 2H), 7.13 (d, J = 8.4 Hz, 2H), 7.06–7.03 (m, 3H), 6.91 (d, J = 7.2 Hz, 2H), 6.87–6.83 (m, 2H), 6.69 (d, J = 8.4 Hz, 2H), 6.46 (d, J = 8.8 Hz, 2H), 4.39 (d, J = 14.4 Hz, 1H), 4.01 (d, J = 14.4 Hz, 1H), 3.70 (s, 3H), 2.61 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.1, 158.8, 144.7, 142.2, 141.5, 141.4, 139.2, 135.8, 133.8, 132.8, 131.1, 130.1, 129.9, 129.2, 128.54, 128.45, 128.1, 127.9, 127.7, 126.6, 113.1, 55.1, 51.7, 26.9; IR (Neat) ν_{max} 1688, 1507, 1341, 1246, 1155, 1091, 1024, 834 cm^{-1}; **HRMS (ESI)** for $C_{36}H_{32}NO_4S$ $(M+H)^+$: calcd. 574.2047, found 574.2048.

N-Benzyl-4-cyano-N-(1-(4-methoxyphenyl)-2,2-diphenylvinyl)benzenesulfonamide (80):



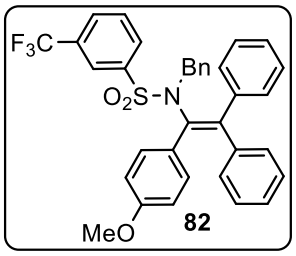
80 (127 mg, 76%) as colorless solid. mp = 206–208 °C; R_f = 0.16 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47–7.43 (m, 2H), 7.37–7.27 (m, 8H), 7.11–7.08 (m, 2H), 7.07–7.03 (m, 3H), 6.99–6.94 (m, 2H), 6.91–6.84 (m, 2H), 6.68 (d, *J* = 8.0 Hz, 2H), 6.47 (d, *J* = 8.5 Hz, 2H), 4.41 (d, *J* = 14.5 Hz, 1H), 4.05 (d, *J* = 14.5 Hz, 1H), 3.71 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 145.0, 142.0, 141.42, 141.36, 135.6, 133.8, 132.7, 131.9, 131.1, 130.1, 129.8, 128.9, 128.59, 128.57, 128.5, 128.1, 127.72, 127.69, 126.7, 117.4, 115.4, 113.1, 55.1, 52.2; IR (Neat) ν_{max} 1603, 1507, 1336, 1288, 1243, 1152, 1024, 908, 834 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{29}N_2O_3S$ $(M+H)^+$: calcd. 557.1893, found 557.1894.

N-Benzyl-N-(1-(4-methoxyphenyl)-2,2-diphenylvinyl)-4-(trifluoromethyl)benzenesulfonamide (81):



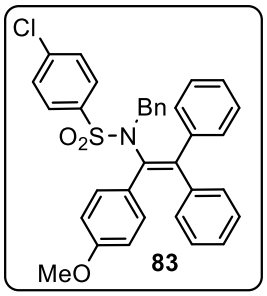
81 (136 mg, 76%) as colorless solid. mp = 174–176 °C; R_f = 0.38 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.0 Hz, 3H), 7.37–7.32 (m, 4H), 7.32–7.27 (m, 3H), 7.14 (d, *J* = 8.4 Hz, 2H), 7.07–7.02 (m, 3H), 6.95 (d, *J* = 6.8 Hz, 2H), 6.90–6.84 (m, 2H), 6.68 (d, *J* = 8.8 Hz, 2H), 6.45 (d, *J* = 8.8 Hz, 2H), 4.41 (d, *J* = 14.4 Hz, 1H), 4.05 (d, *J* = 14.4 Hz, 1H), 3.69 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 144.4, 143.2, 142.1, 141.5, 141.3, 135.7, 133.9, 133.5 (q, J = 33 Hz, 1C), 132.7, 131.1, 130.1, 129.9, 129.0, 128.9, 128.6, 128.5, 128.4, 128.0, 127.7, 126.6, 125.2 (q, J = 4.1 Hz, 1C), 125.0 (q, J = 76 Hz, 1C), 123.2 (q, J = 271 Hz, 1C), 113.0, 55.0, 52.0; ^{19}F NMR (471 MHz) δ –63.0; IR (Neat) ν_{max} 1605, 1508, 1340, 1302, 1142, 1022, 902 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{28}F_3NO_3S$ $(M)^+$: calcd. 599.1742, found 599.1742.

N-Benzyl-N-(1-(4-methoxyphenyl)-2,2-diphenylvinyl)-3-(trifluoromethyl)benzenesulfonamide (82):



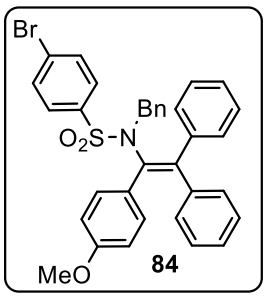
82 (138 mg, 77%) as colorless solid. mp = 174–176 °C; R_f = 0.39 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 7.6 Hz, 1H), 7.46–7.29 (m, 10H), 7.28–7.22 (m, 1H), 7.09–7.01 (m, 5H), 6.90–6.83 (m, 2H), 6.56 (d, J = 8.4 Hz, 2H), 6.40 (d, J = 8.8 Hz, 2H), 4.48 (d, J = 14.8 Hz, 1H), 4.01 (d, J = 14.8 Hz, 1H), 3.68 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 142.5, 142.1, 141.3, 140.7, 136.0, 134.3, 132.6, 131.1, 130.7, 130.1, 129.8, 129.0, 128.9, 128.60, 128.55, 128.5, 127.9, 127.7 (q, J = 264 Hz, 1C), 124.5 (q, J = 4.0, 1C), 121.8, 113.0, 54.9, 52.3; ^{19}F NMR (471 MHz) δ –62.7; IR (Neat) ν_{max} 1605, 1508, 1340, 1302, 1142, 1022, 902 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{28}F_3NO_3S$ $(M)^+$: calcd. 599.1742, found 599.1742.

N-Benzyl-4-chloro-N-(1-(4-methoxyphenyl)-2,2-diphenylvinyl)benzenesulfonamide (83):



83 (136 mg, 80%) as colorless solid. mp = 169–171 °C; R_f = 0.41 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.27 (m, 6H), 7.22–7.15 (m, 4H), 7.07–7.02 (m, 3H), 6.98–6.93 (m, 2H), 6.92–6.84 (m, 4H), 6.76 (d, J = 8.4 Hz, 2H), 6.51 (d, J = 8.8 Hz, 2H), 4.35 (d, J = 14.4 Hz, 1H), 4.02 (d, J = 14.4 Hz, 1H), 3.72 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 142.3, 141.4, 139.4, 138.5, 135.8, 133.9, 132.8, 131.2, 130.1, 129.9, 129.2, 129.1, 128.5, 128.42, 128.39, 127.7, 127.5, 126.6, 113.1, 55.1, 51.6; IR (Neat) ν_{max} 2923, 1600, 1507, 1336, 1245, 1157, 1086, 1025, 835 cm^{-1}; **HRMS (ESI)** for $C_{34}H_{28}ClNNaO_3S$ $(M+Na)^+$: calcd. 588.1371, found 588.1372.

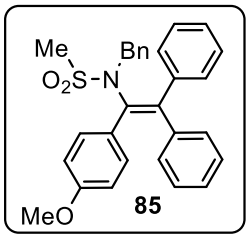
N-Benzyl-4-bromo-N-(1-(4-methoxyphenyl)-2,2-diphenylvinyl)benzenesulfonamide (84):



84 (141 mg, 77%) as yellow semi solid. R_f = 0.35 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37–7.27 (m, 8H), 7.23–7.17 (m, 2H), 7.08–7.01 (m, 3H), 6.94–6.84 (m, 6H), 6.74 (d, J = 8.0 Hz, 2H), 6.50 (d, J = 8.5 Hz, 2H), 4.35 (d, J = 14.5 Hz, 1H), 4.01 (d, J = 14.5 Hz, 1H), 3.72 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.8, 143.3, 142.2, 141.6, 141.4, 139.9, 135.8, 133.8, 132.8, 131.4, 131.2, 130.1, 129.9, 129.2, 128.5, 128.4, 127.6, 127.5, 127.0, 126.6, 125.4, 113.1, 55.1, 51.6; IR (Neat) ν_{max} 1599, 1572, 1505, 1335, 1244,

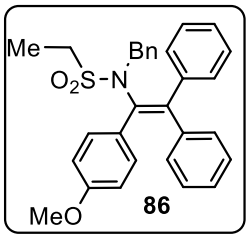
1152, 1024, 823 cm^{-1}; **HRMS (ESI)** for $C_{34}H_{28}BrNNaO_3S$ $(M+Na)^+$: calcd. 632.0865, found 632.0868.

N-Benzyl-N-(1-(4-methoxyphenyl)-2,2-diphenylvinyl)methanesulfonamide (85):



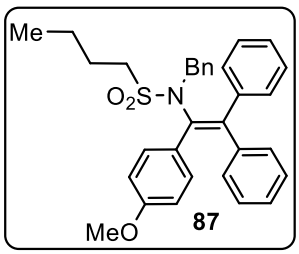
85 (126 mg, 90%) as yellow solid. mp = 164–166 °C; R_f = 0.17 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47–7.42 (m, 3H), 7.30–7.26 (m, 2H), 7.25–7.20 (m, 3H), 7.09–6.96 (m, 7H), 6.96–6.88 (m, 2H), 6.69 (d, J = 8.8 Hz, 2H), 4.32 (d, J = 14.5 Hz, 1H), 4.24 (d, J = 14.5 Hz, 1H), 3.75 (s, 3H), 2.11 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 141.99, 141.96, 140.4, 136.2, 135.0, 132.4, 131.0, 130.3, 129.8, 128.8, 128.4, 128.1, 127.7, 127.3, 126.5, 113.4, 55.1, 52.1, 42.1; IR (Neat) ν_{max} 2921, 1604, 1508, 1440, 1328, 1251, 1174, 1145, 837 cm^{-1}; **HRMS (ESI)** for $C_{29}H_{27}NNaO_3S$ $(M+Na)^+$: calcd. 492.1604, found 492.1604.

N-Benzyl-N-(1-(4-methoxyphenyl)-2,2-diphenylvinyl)ethanesulfonamide (86):



86 (126 mg, 87%) as colorless solid. mp = 166–168 °C; R_f = 0.17 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46–7.42 (m, 3H), 7.29–7.26 (m, 2H), 7.25–7.20 (m, 3H), 7.08–7.00 (m, 7H), 6.95–6.89 (m, 2H), 6.68 (d, J = 9.0 Hz, 2H), 4.26 (s, 2H), 3.74 (s, 3H), 2.41–2.30 (m, 1H), 1.84–1.74 (m, 1H), 1.12 (t, J = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$)δ 158.9, 142.2, 142.0, 140.5, 136.5, 135.1, 132.4, 131.0, 130.3, 129.8, 129.2, 128.7, 128.4, 128.1, 127.6, 127.3, 126.5, 113.4, 55.0, 52.0, 49.4, 7.8 ; IR (Neat) ν_{max} 1605, 1509, 1324, 1250, 1144, 1029, 838 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{30}NO_3S$ $(M+H)^+$: calcd. 484.1941, found 484.1946.

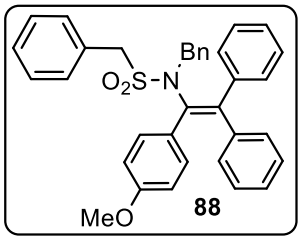
N-Benzyl-N-(1-(4-methoxyphenyl)-2,2-diphenylvinyl)butane-1-sulfonamide (87):



87 (132 mg, 86%) as colorless semisolid. R_f = 0.26 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46–7.42 (m, 3H), 7.28–7.25 (m, 2H), 7.23–7.19 (m, 3H), 7.11–7.03 (m, 5H), 6.98–6.92 (m, 4H), 6.73–6.69 (m, 2H), 4.33 (d, J = 14.4 Hz, 1H), 4.22 (d, J = 14.8 Hz, 1H), 3.75 (s, 3H), 2.40–2.27 (m, 1H), 1.70–1.54 (m, 3H), 1.21–1.11 (m, 2H), 0.79 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 142.2, 142.1, 140.6, 136.3, 135.1, 132.5, 131.0, 131.0, 129.8, 128.9, 128.6, 128.3, 128.0, 127.6, 127.1, 126.4, 113.4, 55.0, 54.7, 51.9, 24.9,

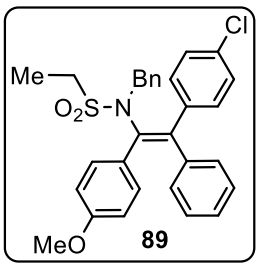
21.4, 13.4; IR (Neat) ν_{max} 1603, 1508, 1341, 1299, 1246, 1173, 1029, 834 cm^{-1}; **HRMS (ESI)** for $C_{32}H_{34}NO_3S$ $(M+H)^+$: calcd. 512.2254, found 512.2252.

N-Benzyl-N-(1-(4-methoxyphenyl)-2,2-diphenylvinyl)-1-phenylmethanesulfonamide (88):



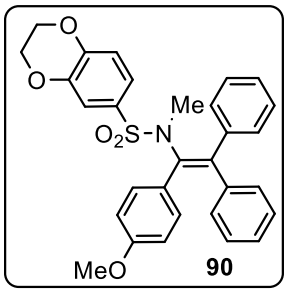
88 (121 mg, 74%) as colorless solid. mp = 190–192 °C; R_f = 0.22 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.41 (m, 3H), 7.34–7.19 (m, 8H), 7.16–7.04 (m, 9H), 7.00–6.91 (m, 2H), 6.77–6.69 (m, 2H), 4.32 (d, J = 14.4 Hz, 1H), 4.21 (d, J = 14.4 Hz, 1H), 3.50 (s, 3H), 3.54 (d, J = 13.2 Hz, 1H), 2.78 (d, J = 13.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$)δ 159.0, 142.12, 142.05, 140.8, 136.1, 135.3, 132.5, 131.0, 130.8, 130.5, 130.0, 128.9, 128.6, 128.4, 128.3, 128.2, 127.7, 127.4, 126.5, 113.5, 60.5, 55.1, 52.4; IR (Neat) ν_{max} 1604, 1508, 1338, 1242, 1142, 1027, 802 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{31}NNaO_3S$ $(M+Na)^+$: calcd. 568.1917, found 568.1919.

(*Z*)-N-Benzyl-N-(2-(4-chlorophenyl)-1-(4-methoxyphenyl)-2-phenylvinyl)ethanesulfonamide (89):



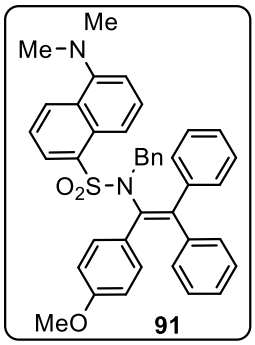
89 (107 mg, 69%) as colorless solid. mp = 181–183 °C; R_f = 0.17 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46–7.42 (m, 3H), 7.27–7.24 (m, 2H), 7.21 (d, J = 8.5 Hz, 2H), 7.08–7.03 (m, 3H), 7.01–6.94 (m, 4H), 6.92–6.86 (m, 2H), 6.67 (d, J = 9.0 Hz, 2H), 4.28 (d, J = 14.5 Hz, 1H), 4.23 (d, J = 14.0 Hz, 1H), 3.74 (s, 3H), 2.50–2.37 (m, 1H), 1.98–1.86 (m, 1H), 1.15 (t, J = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$)δ 159.1, 141.8, 140.4, 139.5, 136.4, 135.6, 133.2, 132.5, 131.2, 131.0, 130.3, 129.0, 128.8, 128.5, 128.3, 127.8, 126.7, 113.5, 55.1, 52.1; IR (Neat) ν_{max} 1601, 1341, 1246, 1173, 1147, 1024, 833 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{29}ClNO_3S$ $(M+H)^+$: calcd. 518.1551, found 518.1554.

N-(1-(4-Methoxyphenyl)-2,2-diphenylvinyl)-N-methyl-2,3-dihydrobenzo[b][1,4]dioxine-6-sulfonamide (90):



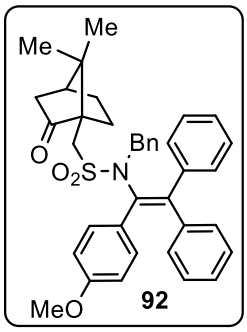
90 (125 mg, 81%) as pale yellow solid. mp = 194–196 °C; R_f = 0.06 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.35 (m, 2H), 7.34–7.26 (m, 3H), 7.10–7.06 (m, 3H), 7.05–7.01 (m, 2H), 7.00–6.95 (m, 2H), 6.69–6.65 (m, 2H), 6.63–6.60 (m, 1H), 6.60–6.55 (m, 2H), 4.25 (dd, J = 6.0, 2.8 Hz, 2H), 4.21 (dd, J = 5.2, 2.0 Hz, 2H), 3.74 (s, 3H), 2.86 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8, 146.7, 142.7, 141.78, 141.75, 140.6, 136.6, 132.6, 131.9, 131.1, 129.8, 129.3, 128.2, 127.7, 127.3, 126.6, 120.7, 117.1, 116.9, 113.1, 64.4, 63.9, 55.0, 37.5; IR (Neat) ν_{max} 2921, 1690, 1507, 1324, 1284, 1247, 1143, 1122, 1029, 824 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{28}NO_5S$ $(M+H)^+$: calcd. 514.1688, found 514.1681.

N-Benzyl-5-(dimethylamino)-N-(1-(4-methoxyphenyl)-2,2-diphenylvinyl)naphthalene-1-sulfonamide (91):



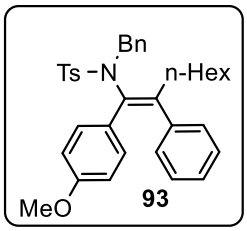
91 (134 mg, 71%) as pale yellow solid. mp = 173–175 °C; R_f = 0.22 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.61 (d, J = 8.5 Hz, 1H), 8.43 (d, J = 8.0 Hz, 1H), 7.47 (dd, J = 9.0, 8.5 Hz, 1H), 7.33–7.21 (m, 9H), 7.19–7.11 (m, 2H), 7.04–7.01 (m, 3H), 6.93 (d, J = 7.0 Hz, 2H), 6.86–6.83 (m, 2H), 6.68 (d, J = 9.0 Hz, 2H), 6.39 (d, J = 9.0 Hz, 2H), 4.65 (br s, 1H), 4.14 (br s, 1H), 3.68 (s, 3H), 2.90 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.6, 151.4, 142.7, 141.7, 140.8, 136.8, 136.2, 134.4, 132.8, 131.2, 130.3, 130.0, 129.9, 129.62, 129.56, 129.5, 128.2, 128.1, 127.9, 127.6, 127.5, 126.3, 123.1, 119.8, 114.8, 112.8, 54.9, 50.9, 45.4; IR (Neat) ν_{max} 1507, 1452, 1326, 1245, 1140, 1059, 831 cm^{-1}; **HRMS (ESI)** for $C_{40}H_{37}N_2O_3S$ $(M+Na)^+$: calcd. 625.2517, found 625.2518.

N-Benzyl-1-((1R,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)-N-(1-(4-methoxyphenyl)-2,2-diphenylvinyl)methanesulfonamide (92, exo/endo = 58/42):



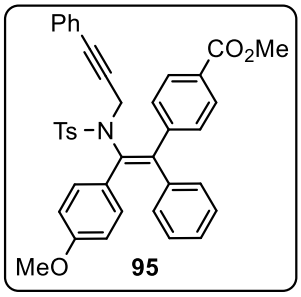
92 (136 mg, 75%) as colorless solid. mp = 155–156 °C; R_f = 0.08 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50–7.39 (m, 7.60H), 7.36–7.28 (m, 5.94H), 7.21 (d, J = 8.5 Hz, 2.15H), 7.16–7.02 (m, 9.22H), 6.95–6.88 (m, 3.94H), 6.76 (t, J = 9.0 Hz, 3.88H), 6.62 (d, J = 7.0 Hz, 2.17 H), 6.58 (d, J = 9.0 Hz, 1.64H), 4.71 (d, J = 14.5 Hz, 1H), 4.44 (d, J = 14.5 Hz, 0.78H), 4.17 (d, J = 14.5 Hz, 1H), 4.05 (d, J = 14.5 Hz, 0.72H), 3.78 (s, 3H), 3.68 (s, 2.16H), 3.00 (d, J = 14.5 Hz, 1H), 2.74 (d, J = 14.5 Hz, 0.74H), 2.38–2.33 (m, 4H), 2.18 (d, J = 14.5 Hz, 0.86H), 2.02–1.82 (m, 6.09H), 1.80–1.71 (m, 1.34H), 1.48–1.29 (m, 3.66H), 0.87 (s, 3H), 0.80 (s, 2.1H), 0.58 (s, 3H), 0.53 (s, 2.3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 214.8, 214.6, 159.0, 158.8, 142.42, 142.38, 142.1, 141.5, 140.2, 136.9, 136.1, 135.0, 134.9, 134.4, 132.7, 132.5, 131.1, 130.6, 130.4, 130.0, 129.8, 128.8, 128.7, 128.4, 128.3, 127.9, 127.7, 127.0, 126.5, 113.6, 113.2, 58.4, 58.0, 55.13, 55.08, 52.03, 51.99, 51.5, 51.3, 47.8, 47.4, 42.8, 42.6, 42.5, 42.4, 26.9, 26.7, 25.9, 24.7, 19.6, 19.5, 19.4, 19.3; IR (Neat) ν_{max} 2954, 1743, 1604, 1508, 1336, 1292, 1246, 1175, 1025, 835 cm^{-1}; **HRMS (ESI)** for $C_{38}H_{40}NO_4S$ $(M+H)^+$: calcd. 606.2673, found 606.2677.

(E)-N-Benzyl-N-(1-(4-methoxyphenyl)-2-phenyloct-1-en-1-yl)-4-methylbenzenesulfonamide (93):



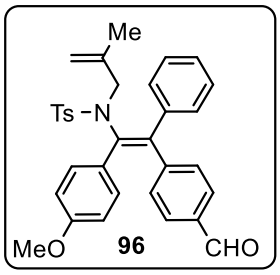
93 (126 mg, 87%) as pale yellow gummy liquid. R_f = 0.39 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, J = 8.5 Hz, 2H), 7.33–7.27 (m, 5H), 7.15–7.01 (m, 5H), 6.92–6.88 (m, 2H), 6.79–6.74 (m, 2H), 6.53–6.47 (m, 2H), 4.65 (d, J = 14.5 Hz, 1H), 4.08 (d, J = 14.5 Hz, 1H), 3.68 (s, 3H), 2.50–2.40 (m, 4H), 2.18–2.09 (m, 1H), 1.17–1.30 (m, 4H), 1.15–1.06 (m, 4H), 0.84 (t, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$)δ 158.1, 146.9, 143.2, 140.9, 138.1, 136.0, 132.3, 131.5, 129.62, 129.60, 129.5, 129.1, 128.2, 12.9, 127.8, 127.7, 126.3, 112.7, 55.0, 52.2, 34.9, 31.6, 29.8, 26.9, 22.7, 21.5, 14.1 ; IR (Neat) ν_{max} 2968, 2927, 2855, 1738, 1508, 1365, 1216, 1157, 734 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{39}NNaO_3S$ $(M+Na)^+$: calcd. 576.2543, found 576.2541.

(*Z*)-Methyl 4-(2-(4-methoxyphenyl)-2-(4-methyl-N-(3-phenylprop-2-yn-1-yl)phenylsulfonamido)-1-phenylvinyl)benzoate (95):



95 (154 mg, 82%) as pale-yellow semisolid. mp = 148–150 °C; R_f = 0.08 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, J = 8.5 Hz, 2H), 7.61 (d, J = 8.0 Hz, 2H), 7.37–7.30 (m, 5H), 7.20 (d, J = 8.5 Hz, 2H), 7.10 (d, J = 8.5 Hz, 2H), 7.09–7.03 (m, 3H), 6.96 (d, J = 8.5 Hz, 4H), 6.56 (d, J = 8.5 Hz, 2H), 4.33 (d, J = 18.0 Hz, 1H), 3.97 (d, J = 17.5 Hz, 1H), 3.94 (s, 3H), 3.74 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 159.1, 146.4, 142.9, 141.3, 139.7, 137.5, 136.2, 132.7, 131.4, 131.2, 130.1, 129.6, 129.0, 128.8, 128.7, 128.6, 128.4, 127.8, 127.3, 126.8, 122.3, 113.1, 85.6, 84.1, 55.1, 52.1, 39.8, 21.4; IR (Neat) ν_{max} 2184, 1718, 1601, 1508, 1342, 1275, 1246, 1155, 1102, 834 cm^{-1}; **HRMS (ESI)** for $C_{39}H_{34}NO_5S$ $(M+H)^+$: calcd. 628.2152, found 628.2153.

(*E*)-N-(2-(4-Formylphenyl)-1-(4-methoxyphenyl)-2-phenylvinyl)-4-methyl-N-(2-methylallyl)benzenesulfonamide (96):



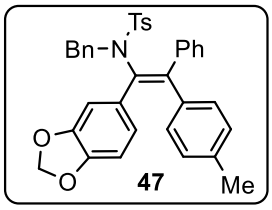
96 (66 mg, 41%) as pale yellow solid. mp = 219–221 °C; R_f = 0.08 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.86 (s, 1H), 7.56 (d, J = 8.0 Hz, 2H), 7.43–7.34 (m, 5H), 7.11 (t, J = 8.8 Hz, 4H), 7.01 (d, J = 8.0 Hz, 2H), 6.92 (d, J = 8.0 Hz, 2H), 6.64 (d, J = 8.8 Hz, 2H), 4.79 (d, J = 98 Hz, 2H), 3.76 (s, 3H), 3.70–3.40 (m, 2H), 2.34 (s, 3H), 1.27 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.9, 159.3, 149.6, 143.2, 141.2, 140.6, 140.5, 137.1, 136.5, 134.1, 133.1, 131.9, 130.2, 129.11, 129.09, 128.9, 128.5, 128.0, 127.7, 117.6, 113.4, 55.2, 53.7, 21.5, 21.4; IR (Neat) ν_{max} 1697, 1599, 1507, 1443, 1335, 1301, 1246, 1210, 1170, 1004, 905, 833 cm^{-1}; **HRMS (ESI)** for $C_{33}H_{32}NO_4S$ $(M+H)^+$: calcd. 538.2047, found 538.2046.

General Procedure for Regioselective Cascade Double arylation of Ynamides (1e) with aryl diazonium salts (26b, 26d-26h) and aryl boronic acids (27a/27d/27t):

To a mixture of **1e** (0.3 mmol), aryl diazonium-tetrafluoroborate **26b, 26d-26h** (0.45 mmol), aryl boronic acid **3** (0.36 mmol), $Pd_2dba_3{\cdot}CHCl_3$ (0.015 mmol) and $NaHCO_3$ (0.36 mmol) was added 1,4-dioxane (3.0 mL). The reaction mixture was stirred at 10 ^{o}C overnight. After completion of

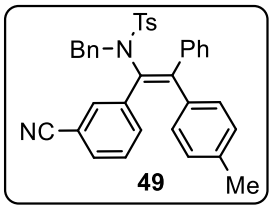
the reaction, the crude reaction mixture after evaporation and column chromatography delivered **47, 49-56**.

(*E*)-N-(1-(Benzo[d][1,3]dioxol-5-yl)-2-phenyl-2-(*p*-tolyl)vinyl)-N-benzyl-4-methylbenzenesulfonamide (47):



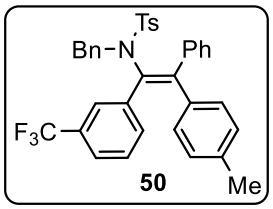
47 (139 mg, 81%) as pale yellow soli. mp = 230–232 °C; R_f = 0.25 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.24 (m, 5H), 7.20–7.15 (m, 2H), 7.10–7.00 (m, 5H), 6.86 (t, *J* = 7.6 Hz, 4H), 6.76 (d, *J* = 7.6 Hz, 2H), 6.49–6.46 (m, 2H), 6.27 (s, 1H), 5.85 (br d, *J* = 5.2 Hz, 2H), 4.33 (d, *J* = 14.4 Hz, 1H), 3.97 (d, *J* = 14.4 Hz, 1H), 2.39 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.9, 146.6, 143.0, 141.8, 141.7, 139.4, 137.6, 136.3, 136.0, 133.1, 131.2, 131.0, 130.1, 130.0, 128.9, 128.4, 128.2, 127.8, 127.4, 126.2, 115.0, 111.3, 107.6, 100.8, 51.0, 21.5, 21.1; IR (Neat) ν_{max} 2184, 1485, 1329, 1246, 1153, 1028, 811 cm^{-1}; **HRMS (ESI)** for $C_{36}H_{31}NNaO_4S$ $(M+Na)^+$: calcd. 596.1866, found 596.1870.

(*E*)-N-Benzyl-N-(1-(3-cyanophenyl)-2-phenyl-2-(*p*-tolyl)vinyl)-4-methylbenzenesulfonamide (49):



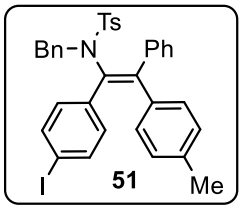
49 (118 mg, 71%) as pale yellow solid; mp = 183–184 °C; R_f = 0.15 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44–7.38 (m, 4H), 7.37–7.34 (m, 1H), 7.30 (t, *J* = 7.5 Hz, 2H), 7.28–7.26 (m, 1H), 7.11 (d, *J* = 7.0 Hz, 3H), 7.07–7.00 (m, 4H), 6.92 (d, *J* = 7.5 Hz, 2H), 6.85 (d, *J* = 8.0 Hz, 2H), 6.65 (d, *J* = 7.5 Hz, 2H), 6.51 (s, 1H), 4.41 (d, *J* = 14.5 Hz, 1H), 3.84 (d, *J* = 14.5 Hz, 1H), 2.42 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.7, 143.4, 140.8, 139.2, 138.0, 137.6, 137.2, 136.2, 135.9, 134.1, 131.6, 131.1, 130.3, 130.0, 129.7, 129.6, 129.2, 128.7, 128.6, 128.3, 127.9, 127.6, 127.3, 118.3, 111.5, 51.2, 21.5, 21.1; IR (Neat) ν_{max} 2227, 1596, 1492, 1443, 1334, 1154, 1089, 1023 cm^{-1}; **HRMS (ESI)** for $C_{36}H_{30}N_2NaO_2S$ $(M+Na)^+$: calcd. 577.1920, found 577.1921.

(*E*)-N-Benzyl-4-methyl-N-(2-phenyl-2-(*p*-tolyl)-1-(3-(trifluoromethyl)phenyl)vinyl) benzenesulfonamide (50):



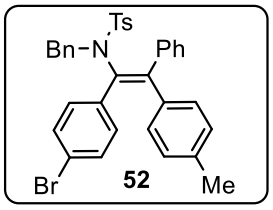
50 (134 mg, 75%) as pale yellow gummy liquid. R_f = 0.30 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (br d, J = 7.0 Hz, 2H), 7.47–7.39 (m, 3H), 7.35–7.31 (m, 1H), 7.29 (d, J = 7.5 Hz, 2H), 7.16 (d, J = 7.5 Hz, 1H), 7.10–7.01 (m, 6H), 6.92 (d, J = 7.0 Hz, 2H), 6.84 (d, J = 8.0 Hz, 2H), 6.67 (d, J = 8.0 Hz, 2H), 6.43 (s, 1H), 4.44 (d, J = 14.5 Hz, 1H), 3.84 (d, J = 14.5 Hz, 1H), 2.38 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.4, 142.9, 141.0, 138.7, 138.4, 137.9, 136.9, 136.1, 135.6, 132.5, 131.1, 130.0, 129.9, 129.1, 128.6, 128.54, 128.52, 128.50, 128.2, 127.9, 127.3, 127.2 (q, J = 6.3 Hz, 1C), 123.7 (q, J = 271 Hz, 1C), 123.6 (q, J = 3.8 Hz, 1C), 122.6, 51.2, 21.4, 21.0; ^{19}F NMR (471 MHz) δ –62.8; IR (Neat) ν_{max} cm^{-1}; **HRMS (ESI)** for $C_{36}H_{30}F_3NNaO_2S$ $(M+Na)^+$: calcd. 620.1842, found 620.1839.

(E)-N-benzyl-N-(1-(4-iodophenyl)-2-phenyl-2-(*p*-tolyl)vinyl)-4-methylbenzenesulfonamide (51):



51 (120 mg, 61%) as pale yellow solid. mp = 196–197 °C; R_f = 0.35 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.29 (m, 4H), 7.27–7.20 (m, 5H), 7.06 (d, J = 8.0 Hz, 2H), 6.97 (d, J = 8.0 Hz, 2H), 6.87–6.80 (m, 5H), 6.70 (d, J = 8.0 Hz, 2H), 6.49 (d, J = 8.0 Hz, 2H), 4.31 (d, J = 14.5 Hz, 1H), 3.91 (d, J = 14.5 Hz, 1H), 2.40 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.2, 142.8, 141.5, 138.8, 137.7, 137.2, 136.8, 136.7, 136.1, 133.3, 132.7, 131.1, 130.1, 129.9, 129.0, 128.6, 128.5, 128.4, 128.3, 127.8, 127.7, 93.1, 51.2, 21.5, 21.2; IR (Neat) ν_{max} 1596, 1443, 1334, 1180, 1153, 1089, 1025, 815 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{30}INNaO_2S$ $(M+Na)^+$: calcd. 678.0934, found 678.0934.

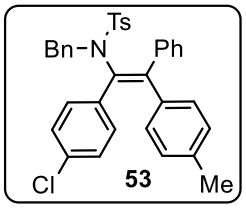
(*E*)-N-Benzyl-N-(1-(4-bromophenyl)-2-phenyl-2-(*p*-tolyl)vinyl)-4-methylbenzenesulfonamide (52):



52 (129 mg, 71%) as pale yellow solid. mp = 181–182 °C; R_f = 0.35 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.29 (m, 6H), 7.09–7.04 (m, 5H), 6.98 (d, J = 8.4 Hz, 2H), 6.86–6.81 (m, 5H), 6.70 (d, J = 8.0 Hz, 2H), 6.64 (d, J = 8.4 Hz, 2H), 4.30 (d, J = 14.8 Hz, 1H), 3.92 (d,

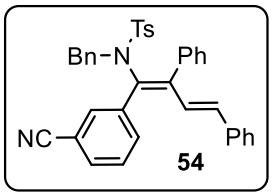
J = 14.4 Hz, 1H), 2.40 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.2, 142.9, 141.5, 138.8, 137.7, 136.8, 136.5, 136.1, 133.1, 132.6, 131.6, 131.1, 130.7, 130.1, 129.9, 129.0, 128.6, 128.5, 128.4, 128.3, 127.8, 121.3, 51.1, 21.5, 21.1; IR (Neat) ν_{max} 2184, 1490, 1335, 1153, 833, 814 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{30}BrNNaO_2S$ $(M+Na)^+$: calcd. 630.1073, found 630.1075.

(*E*)-N-Benzyl-N-(1-(4-chlorophenyl)-2-phenyl-2-(*p*-tolyl)vinyl)-4-methylbenzenesulfonamide (53):



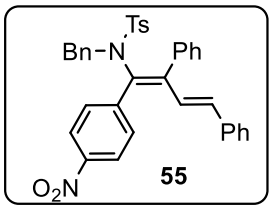
53 (152 mg, 81%) as colorless solid. mp = 194–195 °C; R_f = 0.35 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.27 (m, 6H), 7.10–7.00 (m, 6H), 6.96 (d, *J* = 8.8 Hz, 2H), 6.86 (t, *J* = 7.2 Hz, 4H), 6.80–6.71 (m, 4H), 4.33 (d, *J* = 14.4 Hz, 1H), 3.96 (d, *J* = 14.4 Hz, 1H), 2.41 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.2, 142.9, 141.5, 138.8, 137.6, 136.7, 136.03, 135.97, 132.9, 132.7, 132.5, 131.1, 130.1, 129.9, 129.0, 128.5, 128.4, 128.3, 127.8, 127.7, 127.6, 127.5, 51.0, 21.4, 21.1; IR (Neat) ν_{max} 2185, 1594, 1491, 1336, 1153, 1089, 1014, 834, 814 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{30}ClNNaO_2S$ $(M+Na)^+$: calcd. 586.1578, found 586.1574.

N-Benzyl-N-((1*Z*,3*E*)-1-(3-cyanophenyl)-2,4-diphenylbuta-1,3-dien-1-yl)-4-methylbenzenesulfonamide (54):



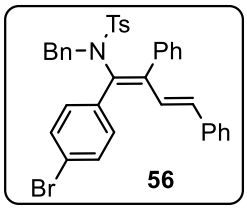
54 (100 mg, 59%) as pale yellow solid. mp = 140–142 °C; R_f = 0.10 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68–7.56 (m, 2H), 7.50–7.42 (m, 4H), 7.36–7.29 (m, 2H), 7.27–7.07 (m, 7H), 7.13 (d, *J* = 7.2 Hz, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 6.92 (d, *J* = 8.0 Hz, 1H), 6.82 (d, *J* = 16.0 Hz, 1H), 6.75 (d, *J* = 7.6 Hz, 2H), 6.24 (d, *J* = 15.6 Hz, 1H), 4.14 (br s, 1H), 3.87 (br s, 1H), 2.41 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.7, 142.4, 138.3, 137.4, 137.1, 136.6, 136.3, 135.5, 135.4, 134.2, 133.1, 131.5, 130.5, 129.8, 129.2, 128.8, 128.64, 128.59, 128.49, 128.46, 128.4, 128.2, 128.1, 127.6, 126.6, 118.2, 112.2, 51.5, 21.5; IR (Neat) ν_{max} 2228, 1596, 1491, 1340, 1154, 1022, 966, 808 cm^{-1}; **HRMS (ESI)** for $C_{37}H_{30}N_2NaO_2S$ $(M+Na)^+$: calcd. 589.1920, found 589.1918.

N-benzyl-4-methyl-N-((1*Z*,3*E*)-1-(4-nitrophenyl)-2,4-diphenylbuta-1,3-dien-1-yl)benzenesulfonamide (55):



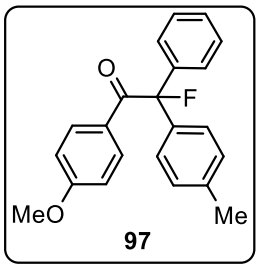
55 (102 mg, 58%) as yellow solid. mp = 217–219 °C; R_f = 0.33 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 8.8 Hz, 2H), 7.49–7.30 (m, 8H), 7.25–7.20 (m, 5H), 7.14 (dd, J = 7.6, 2.0 Hz, 2H), 7.09 (d, J = 8.0 Hz, 2H), 6.97–6.89 (m, 3H), 6.71 (d, J = 7.2 Hz, 2H), 6.23 (d, J = 16.0 Hz, 1H), 4.11 (br s, 1H), 3.93 (br s, 1H), 2.41 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.1, 143.9, 143.8, 143.6, 137.5, 136.7, 136.6, 136.0, 135.3, 132.9, 132.3, 130.6, 129.9, 129.2, 128.7, 128.6, 128.4, 128.3, 128.1, 128.0, 126.7, 123.2, 51.5, 21.5; IR (Neat) ν_{max} 1691, 1598, 1511, 1338, 1152, 1011, 852, 812 cm^{-1}; **HRMS (ESI)** for $C_{36}H_{30}N_2NaO_4S$ $(M+Na)^+$: calcd. 609.1818, found 609.1818.

N-benzyl-N-((1Z,3E)-1-(4-bromophenyl)-2,4-diphenylbuta-1,3-dien-1-yl)-4-methylbenzenesulfonamide (56):



56 (115 mg, 62%) as pale yellow solid. mp = 213–215 °C; R_f = 0.42 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, J = 8.0 Hz, 2H), 7.45 (d, J = 7.5 Hz, 1H), 7.43–7.38 (m, 2H), 7.33–7.28 (m, 2H), 7.27–7.15 (m, 10H), 7.08 (d, J = 7.5 Hz, 2H), 7.00 (d, J = 16.0 Hz, 1H), 6.90 (d, J = 8.0 Hz, 2H), 6.69 (d, J = 7.5 Hz, 2H), 6.16 (d, J = 16.0 Hz, 1H), 4.08 (br s, 1H), 4.01 (br s, 1H), 2.41 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.4, 142.0, 138.0, 136.93, 136.85, 135.5, 135.4, 134.4, 134.1, 133.2, 131.2, 130.7, 130.0, 129.5, 129.1, 128.5, 128.3, 128.19, 128.15, 128.1, 127.8, 127.6, 126.6, 122.6, 51.4, 21.5; IR (Neat) ν_{max} 2183, 1488, 1339, 1150, 1086, 1009, 967, 874, 813 cm^{-1}; **HRMS (ESI)** for $C_{36}H_{30}BrNNaO_2S$ $(M+Na)^+$: calcd. 642.1073, found 642.1074.

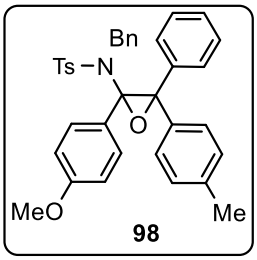
3A.6.3.2. Synthesis of 2-Fluoro-1-(4-methoxyphenyl)-2-phenyl-2-(*p*-tolyl)ethanone (97):



To a solution of **28** (111 mg, 0.2 mmol) in MeOH:CH_3CN (1:9, 2.0 mL) was added selectfluor (0.24 mmol). The resulting mixture was stirred at 80 ^{o}C overnight. The reaction progress was monitored by TLC. Upon completion, the crude mixture was concentrated under the reduced pressure. The crude residue was purified using column chromatography on silica gel to afford **97** (27 mg) in 40% yield as a yellow gummy liquid; R_f = 0.66 (10% EtOAc/Hex); ^{1}H

NMR (400 MHz, $CDCl_3$) δ 7.99 (dd, J = 8.8, 1.6 Hz, 2H), 7.46–7.37 (m, 5H), 7.29 (br d, J = 8.0 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 6.89 (d, J = 8.4 Hz, 2H), 3.86 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.8 (d, J = 29 Hz, 1C), 163.4, 139.6 (d, J = 23 Hz, 1C), 138.5 (d, J = 1.3 Hz, 1C), 136.6 (d, J = 23 Hz, 1C), 133.0 (d, J = 6.2 Hz, 2C), 129.0, 128.5 (d, J = 1.0 Hz, 1C), 128.2, 128.0, 127.8 (d, J = 4.0 Hz, 2C), 126.72 (d, J = 4.0 Hz, 2C), 126.65 (d, J = 3.7 Hz, 1C), 113.4, 103.0 (d, J = 187 Hz, 1C), 55.4, 21.1; ^{19}F NMR (471 MHz) δ −139.0; IR (Neat) ν_{max} 1655, 1595, 1508, 1307, 1244, 1168, 1023, 979, 837 cm^{-1}; **HRMS (ESI)** for $C_{22}H_{19}FKO_2$ $(M+K)^+$: calcd. 373.1001, found 373.0987.

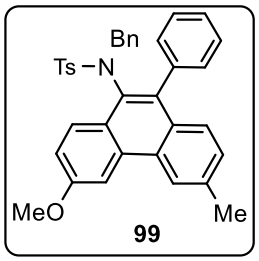
3A.6.3.3. Synthesis of N-Benzyl-N-(2-(4-methoxyphenyl)-3-phenyl-3-(*p*-tolyl)oxiran-2-yl)-4-methylbenzenesulfonamide (98):



98

To a solution of **28** (0.1 mmol) in $CHCl_3$ (1.0 mL) was added *m*-CBPA (1.0 mmol). The resulting mixture was stirred at 100 °C for 3 days. The reaction progress was monitored by TLC. Upon completion of the reaction, the crude mixture was concentrated under the reduced pressure. The crude residue was purified using column chromatography on silica gel to afford **98** (24 mg) in 42% yield as a colorless solid; mp = 154–156 °C; R_f = 0.12 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.4 Hz, 2H), 7.23–7.10 (m, 11H), 7.07–6.93 (m, 5H), 6.70 (d, J = 8.8 Hz, 2H), 6.40 (d, J = 7.6 Hz, 2H), 4.79 (s, 2H), 3.72 (s, 3H), 2.41 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4, 158.2, 144.3, 142.1, 138.3, 136.6, 136.3, 135.8, 133.1, 130.9, 129.59, 129.57, 129.5, 129.0, 128.7, 128.1, 127.5, 126.7, 126.5, 126.4, 113.6, 96.1, 67.7, 55.1, 52.7, 21.6, 20.8; IR (Neat) ν_{max} 2920, 2851, 1687, 1508, 1453, 1351, 1252, 1162, 1107, 1031, 809 cm^{-1}; **HRMS (ESI)** for $C_{36}H_{34}NO_4S$ $(M+H)^+$: calcd. 576.2203, found 576.2204.

3A.6.3.4. Synthesis of N-Benzyl-N-(6-methoxy-3-methyl-10-phenylphenanthren-9-yl)-4-methylbenzenesulfonamide (99):

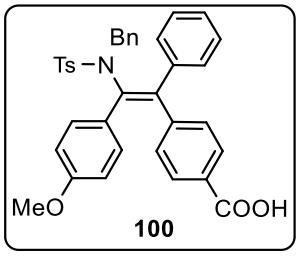


99

To a solution of **28** (0.1 mmol) in toluene (1.0 mL) was added $AlCl_3$ (0.2 mmol). The resulting mixture was stirred at 120 °C for 24 h. The reaction progress was monitored by TLC. Upon completion of the reaction, the crude mixture was concentrated under the reduced pressure. The crude residue was purified using column chromatography on silica gel to afford **99** (29

mg) in 51% yield as a colorless liquid; R_f = 0.40 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.78 (s, 1H), 7.47 (s, 1H), 7.29–7.15 (m, 10H), 7.07 (d, J = 8.0 Hz, 2H), 6.68–6.59 (m, 6H), 5.35 (s, 2H), 3.76 (s, 3H), 2.34 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 159.8, 138.4, 138.3, 137.5, 135.3, 134.90, 134.88, 134.8, 132.6, 130.3, 129.7, 129.0, 128.8, 127.6, 127.5, 126.60, 126.55, 126.3, 126.2, 123.5, 123.4, 114.7, 114.5, 113.0, 55.6, 47.0, 21.4, 20.9; IR (Neat) ν_{max} 2923, 1737, 1609, 1510, 1461, 1263, 1176, 1031, 834 cm^{-1}; **HRMS (ESI)** for $C_{36}H_{32}NO_3S$ $(M+H)^+$: calcd. 558.2097, found 558.2098.

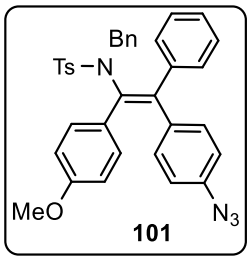
3A.6.3.5. Synthesis of (*E*)-4-(2-(N-Benzyl-4-methylphenylsulfonamido)-2-(4-methoxyphenyl)-1-phenylvinyl)benzoic acid (100):



100

To a solution of **34** (0.1 mmol) and CuCl (0.03 mmol) in CH_3CN (1.0 mL) was added TBHP (0.3 mmol). The resulting mixture was stirred at rt under open air overnight. The reaction progress was monitored by TLC. Upon completion of the reaction, the crude mixture was concentrated under the reduced pressure. The crude residue was purified using column chromatography on silica gel to afford **100** (36 mg) in 61% yield as a colorless semisolid; R_f = 0.22 (20% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.64 (d, J = 8.0 Hz, 2H), 7.38–7.30 (m, 6H), 7.15 (d, J = 8.5 Hz, 2H), 7.08–7.03 (m, 2H), 7.00 (d, J = 8.0 Hz, 2H), 6.87–6.82 (m, 4H), 6.65–6.52 (m, 4H), 4.31 (d, J = 14.5 Hz, 1H), 3.90 (d, J = 14.5 Hz, 1H), 3.76 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 167.4, 159.2, 147.5, 143.8, 141.3, 140.0, 137.7, 136.0, 135.6, 132.8, 131.3, 130.33, 130.27, 129.9, 129.6, 129.3, 129.2, 129.0, 128.9, 128.2, 127.8, 113.6, 55.5, 51.2, 21.4; IR (Neat) ν_{max} 2933, 1737, 1634, 1372, 1241, 1092, 1044, 800 cm^{-1}; **HRMS (ESI)** for $C_{36}H_{32}NO_5S$ $(M+H)^+$: calcd. 590.1996, found 590.1996.

3A.6.3.6. Synthesis of (*E*)-N-(2-(4-Azidophenyl)-1-(4-methoxyphenyl)-2-phenylvinyl)-N-benzyl-4-methylbenzenesulfonamide (101):

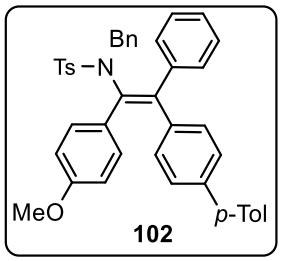


101

To a solution of **40** (0.1 mmol), CuCl (0.03 mmol), and NaN_3 (0.2 mmol) in DMSO (1.0 mL) was added DBU (0.15 mmol). The resulting mixture was stirred at 130 ^{o}C for 1 day. The reaction progress was monitored by TLC. DMSO was removed by water workup and the organic layer was extracted with ethyl acetate (3 × 10 mL) and evaporated under reduced pressure. The

crude residue was next purified using column chromatography on silica gel to afford **13** (28 mg) in 47% yield as a colorless solid; mp = 218–220 °C; R_f = 0.16 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.21 (m, 6H), 7.10 (br d, J = 6.4 Hz, 2H), 7.04 (d, J = 8.0 Hz, 2H), 6.95 (d, J = 8.0 Hz, 2H), 6.89 (d, J = 8.4 Hz, 2H), 6.83 (d, J = 8.4 Hz, 2H), 6.76 (t, J = 7.6 Hz, 4H), 6.56 (d, J = 8.8 Hz, 2H), 4.26 (d, J = 14.4 Hz, 1H), 3.97 (d, J = 14.4 Hz, 1H), 3.74 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8, 143.0, 141.8, 141.0, 139.3, 137.6, 136.6, 136.0, 133.7, 132.8, 131.7, 130.1, 129.3, 128.9, 128.34, 128.25, 128.2, 128.0, 127.4, 125.3, 113.2, 55.1, 51.0, 21.5, 15.3; IR (Neat) ν_{max} 2917, 1593, 1333, 1245, 1153, 1090, 1024, 900, 835 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{30}N_4NaO_3S$ $(M+Na)^+$: calcd. 609.1931, found 609.1935.

3A.6.3.7. Synthesis of (*E*)-N-Benzyl-N-(1-(4-methoxyphenyl)-2-(4'-methyl-[1,1'-biphenyl]-4-yl)-2-phenylvinyl)-4-methylbenzenesulfonamide (102):



102

To a mixture of **40** (0.1 mmol), $Pd(PPh_3)_4$ (0.005 mmol), *p*-$TolB(OH)_2$ (0.12 mmol), and K_3PO_4 (0.3 mmol) was added EtOH (1.0 mL). The resulting mixture was stirred at 90 °C for 24 h. The reaction progress was monitored by TLC. Upon completion of the reaction, the crude mixture was concentrated under the reduced pressure. The crude residue was purified using column chromatography on silica gel to afford **102** (55 mg) in 87% yield as yellow solid; mp = 251–253 °C; R_f = 0.18 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 8.0 Hz, 2H), 7.35–7.24 (m, 8H), 7.22–7.13 (m, 4H), 7.05 (d, J = 8.0 Hz, 2H), 6.97 (d, J = 8.0 Hz, 2H), 6.93–6.85 (m, 4H), 6.80 (d, J = 7.2 Hz, 2H), 6.55 (d, J = 8.8 Hz, 2H), 4.29 (d, J = 14.4 Hz, 1H), 3.99 (d, J = 14.4 Hz, 1H), 3.73 (s, 3H), 2.39 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.8, 143.0, 141.9, 141.3, 138.8, 137.7, 137.6, 136.9, 136.1, 133.9, 132.9, 131.6, 130.2, 129.44, 129.36, 128.9, 128.4, 128.3, 128.2, 128.0, 127.4, 126.6, 125.9, 113.1, 55.1, 51.0, 21.5, 21.0; IR (Neat) ν_{max} 1722, 1601, 1494, 1335, 1249, 1154, 1031, 810 cm^{-1}; **HRMS (ESI)** for $C_{42}H_{38}NO_3S$ $(M+H)^+$: calcd. 636.2567, found 636.2568.

3A.7. X-ray crystallography:

3A.7.1. X-ray reflections for **43** were collected on Bruker D8 Quest CCD diffractometer using Mo-Kα, radiation. Data reduction was performed using CrysAlisPro (version 1.171.33.55). Apex 2 and SHELXL 97 program were used to solve and refine the data. All non-hydrogen atoms were refined anisotropically, and C−H hydrogens were fixed.

Table 3A.4. Crystallographic Data for Compound **43**

Compound	**43**	V [Å^3]	V [Å^3]
formula	$C_{33}H_{29}NO_3S_2$	Z	2858.9(6)
Formula weight	551.69	ρ_{calcd} [g cm^{-3}]	4
crystal system	Monoclinic	μ [mm^{-1}]	1.282
space group	P 1 21/n 1	total reflns	0.221
T [K]	295(2) K	unique reflns	52479
a [Å]	17.254(2)	observed	4432
b [Å]	9.2478(10)	$R_1[I>2\sigma(I)]$	3451
c [Å]	18.199(2)	wR2 [all]	0.0437 (3451)
α [°]	90	GOF	0.1133 (4432)
β [°]	100.101(5)	Diffractometer	1.060
γ [°]	90	CCDC Number	CCDC 1977850

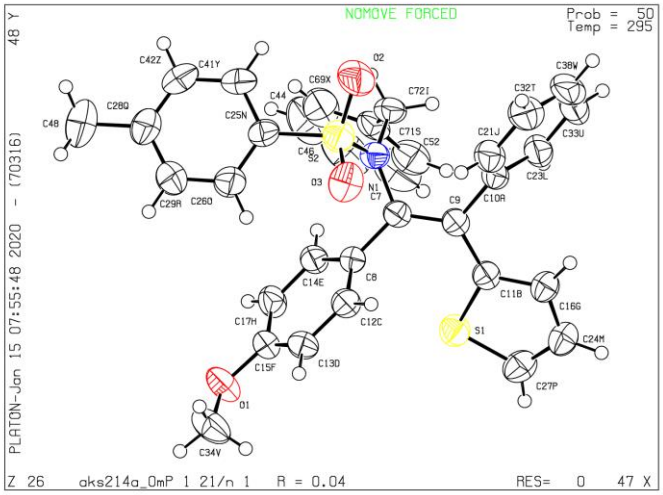


Figure 3A.5. Molecular structure of compound **43**, (Oxygen (red), nitrogen (blue), and sulphur (yellow))

3A.7.2. X-ray reflections for **49** were collected on Bruker D8 Quest CCD diffractometer using Mo-Kα, radiation. Data reduction was performed using CrysAlisPro (version 1.171.33.55). Apex 2 and SHELXL 97 program were used to solve and refine the data. All non-hydrogen atoms were refined anisotropically, and C−H hydrogens were fixed.

Table 3A.5. Crystallographic Data for Compound **49**

Compound	**49**	V [Å^3]	1511.17(15)
formula	$C_{36}H_{30}N2O_2S$	Z	2
Formula weight	554.68	ρ_{calcd} [g cm^{-3}]	1.219
crystal system	Monoclinic	μ [mm^{-1}]	0.141
space group	P 21	total reflns	39927
T [K]	297 K	unique reflns	6900
a [Å]	11.9343(7)	observed	5695
b [Å]	9.7715(6)	$R_1[I>2\sigma(I)]$	0.0382 (5695)
c [Å]	13.0179(7)	wR2 [all]	0.0982 (6900)
α [°]	90	GOF	1.032
β [°]	95.473(2)	Diffractometer	Bruker D8 Quest CCD
γ [°]	90	CCDC Number	CCDC 1977848

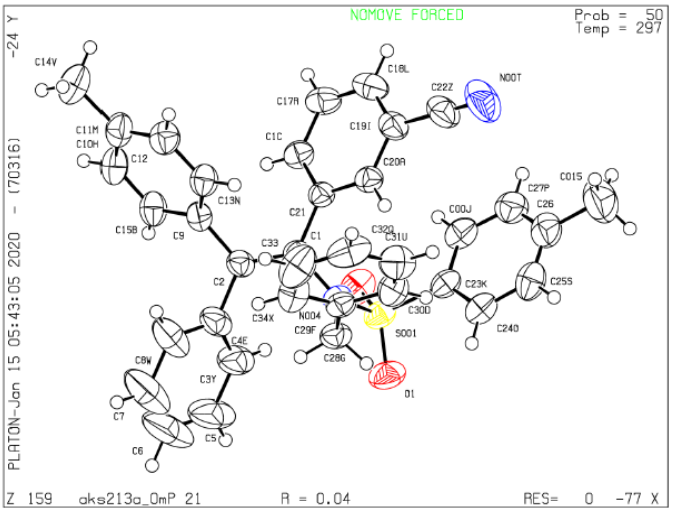


Figure 3A.6. Molecular structure of compound **49**, (Oxygen (red), nitrogen (blue), and sulphur (yellow))

3A.7.3. X-ray reflections for **55** were collected on XT-Lab Synergy Rigaku Oxford diffraction using Mo-Kα, radiation. Data reduction was performed using CrysAlisPro (version 1.171.33.55). Apex 2 and SHELXL 97 program were used to solve and refine the data. All non-hydrogen atoms were refined anisotropically, and C−H hydrogens were fixed.

Table 3A.6. Crystallographic Data for Compound **55**

Compound	**55**
formula	$C_{36}H_{30}N2O_4S$
Formula weight	586.68
crystal system	Monoclinic
space group	P 1 21/c 1
T [K]	293(2) K
a [Å]	10.1018(2)
b [Å]	36.2052(6)
c [Å]	8.4923(2)
α [°]	90
β [°]	107.587(2)
γ [°]	90

V [Å^3]	2960.78(11)
Z	1
ρ_{calcd} [g cm^{-3}]	1.316
μ [mm^{-1}]	0.153
total reflns	16587
unique reflns	6177
observed	5426
R_1[I>2σ(I)]	0.0400 (5425)
wR2 [all]	0.1029 (6177)
GOF	1.056
Diffractometer	Rigaku Ofxord
CCDC Number	CCDC 1977849

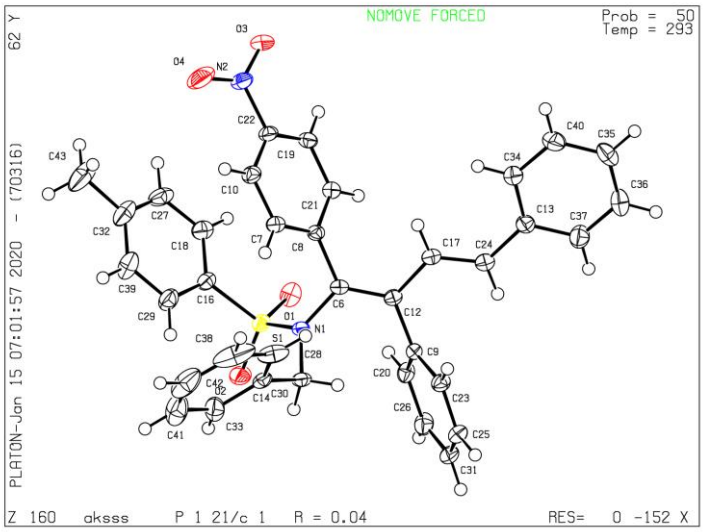


Figure 3A.7. Molecular structure of compound **55**, (Oxygen (red), nitrogen (blue), and sulphur (yellow))

3A.7.4. X-ray reflections for **90** were collected on Bruker D8 Quest CCD diffractometer using Mo-Kα, radiation. Data reduction was performed using CrysAlisPro (version 1.171.33.55). Apex 2 and SHELXL 97 program were used to solve and refine the data. All non-hydrogen atoms were refined anisotropically, and C−H hydrogens were fixed.

Table 3A.7. Crystallographic Data for Compound **90**

Compound	**90**	V [Å^3]	1262.31(12)
formula	$C_{30}H_{27}NO_5S$	Z	2
Formula weight	513.62	ρ_{calcd} [g cm^{-3}]	1.351
crystal system	Monoclinic	μ [mm^{-1}]	0.170
space group	P 1 21 1	total reflns	10668
T [K]	298 K	unique reflns	4735
a [Å]	9.4337(6)	observed	2519
b [Å]	10.3800(5)	R_1[I>2σ(I)]	0.0687 (2519)
c [Å]	13.3587(7)	wR2 [all]	0.1572 (4735)
α [º]	90	GOF	0.944
β [º]	105.206(5)	Diffractometer	Bruker D8 Quest CCD
γ [º]	90	CCDC Number	CCDC 1968461

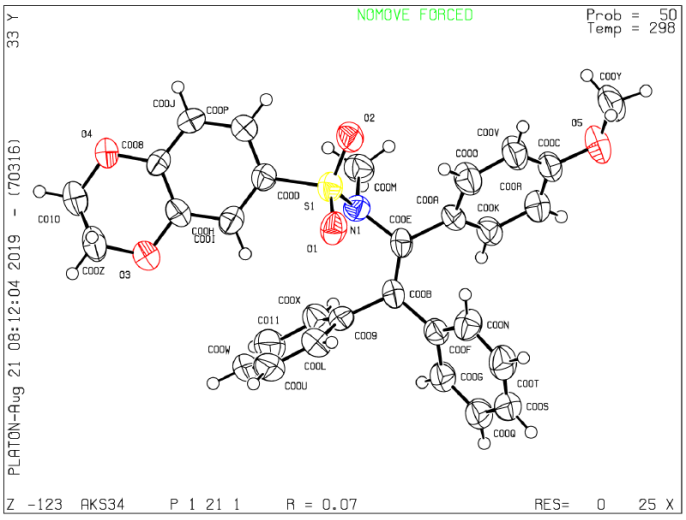


Figure 3A.8. Molecular structure of compound **90**, (Oxygen (red), nitrogen (blue), and sulphur (yellow))

3A.7.5. X-ray reflections for **95** were collected on Bruker D8 Quest CCD diffractometer using Mo-Kα, radiation. Data reduction was performed using CrysAlisPro (version 1.171.33.55). Apex 2 and SHELXL 97 program were used to solve and refine the data. All non-hydrogen atoms were refined anisotropically, and C−H hydrogens were fixed.

Table 3A.8. Crystallographic Data for Compound **95**

Compound	**95**		V [Å^3]	1610.0(4)
formula	$C_{33}H_{31}NO_4S$		Z	2
Formula weight	537.65		ρ_{calcd} [g cm^{-3}]	1.109
crystal system	triclinic		μ [mm^{-1}]	0.134
space group	P -1		total reflns	83087
T [K]	298 K		unique reflns	5883
a [Å]	9.4675(12)		observed	3746
b [Å]	13.459(2)		R_1[I>2σ(I)]	0.0550 (3746)
c [Å]	14.159(3)		wR2 [all]	0.1307 (5883)
α [°]	105.741(9)		GOF	1.016
β [°]	109.391(6)		Diffractometer	Bruker D8 Quest CCD
γ [°]	94.444(6)		CCDC Number	CCDC 1977851

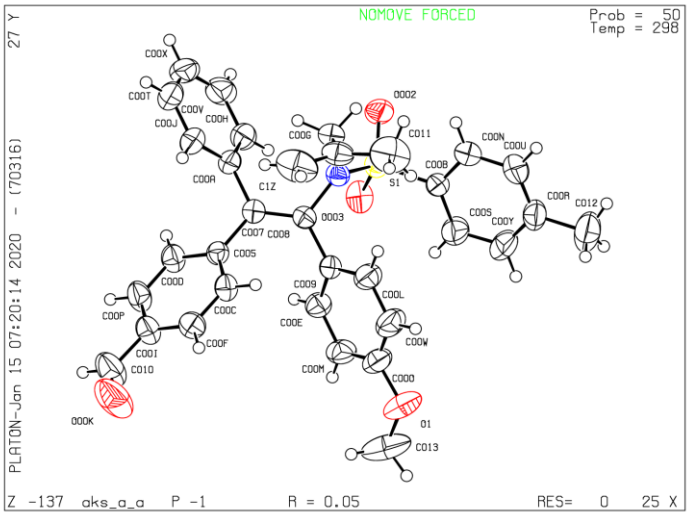


Figure 3A.9. Molecular structure of compound **95**, (Oxygen (red), nitrogen (blue), and sulphur (yellow))

3A.8. References

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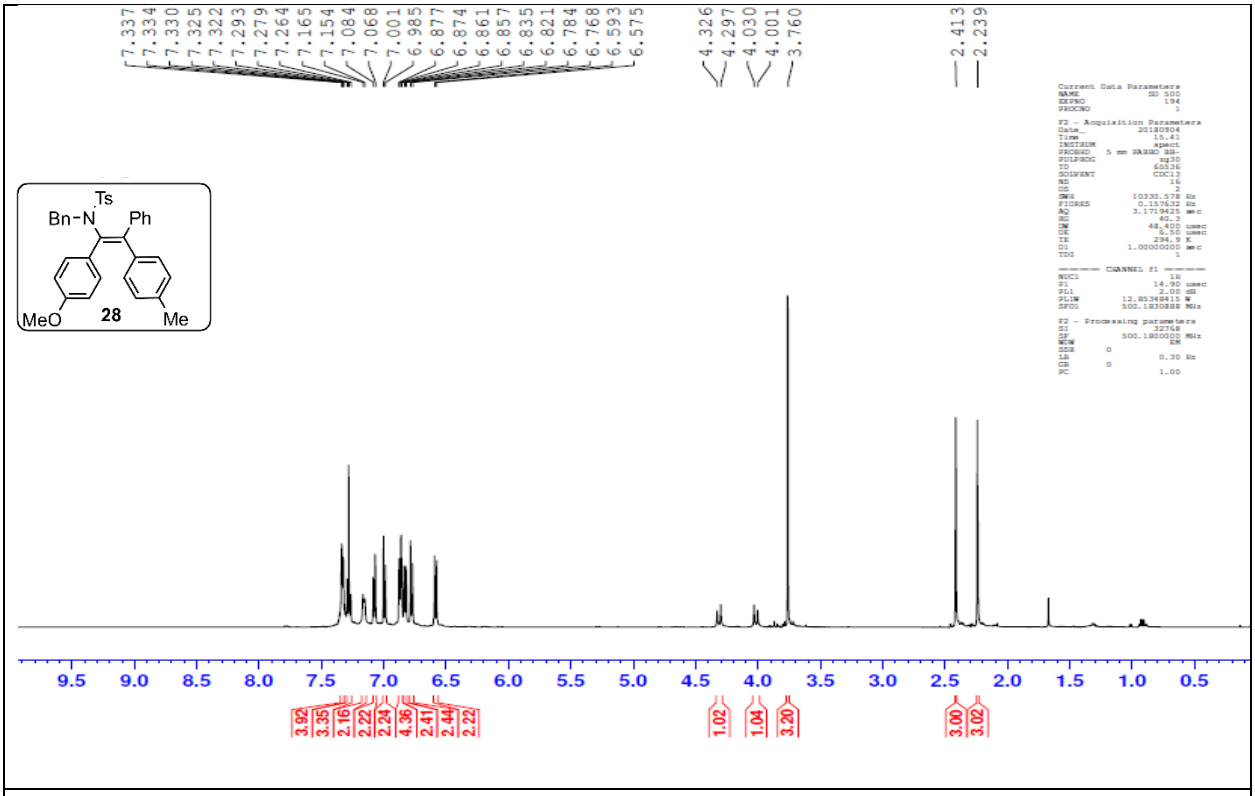
3A.9. Spectra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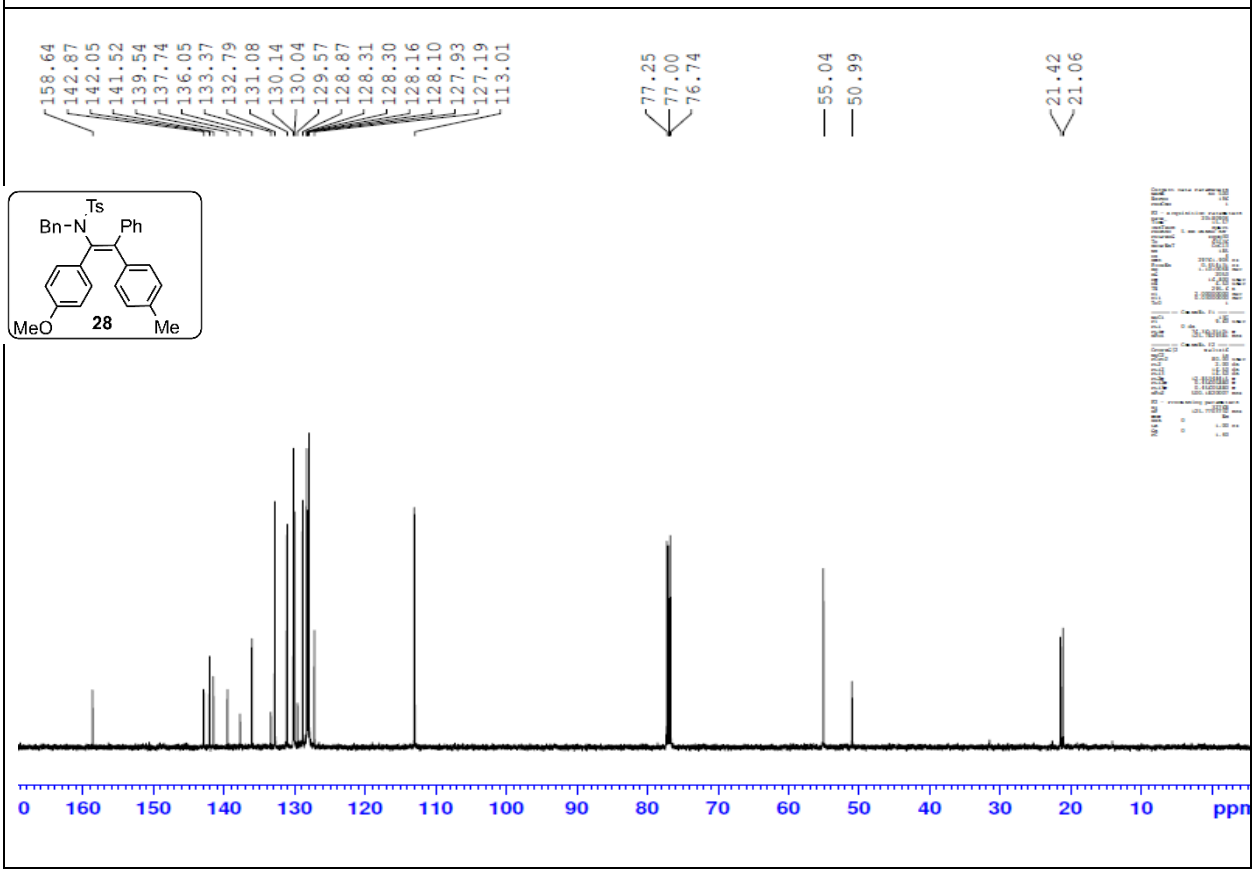
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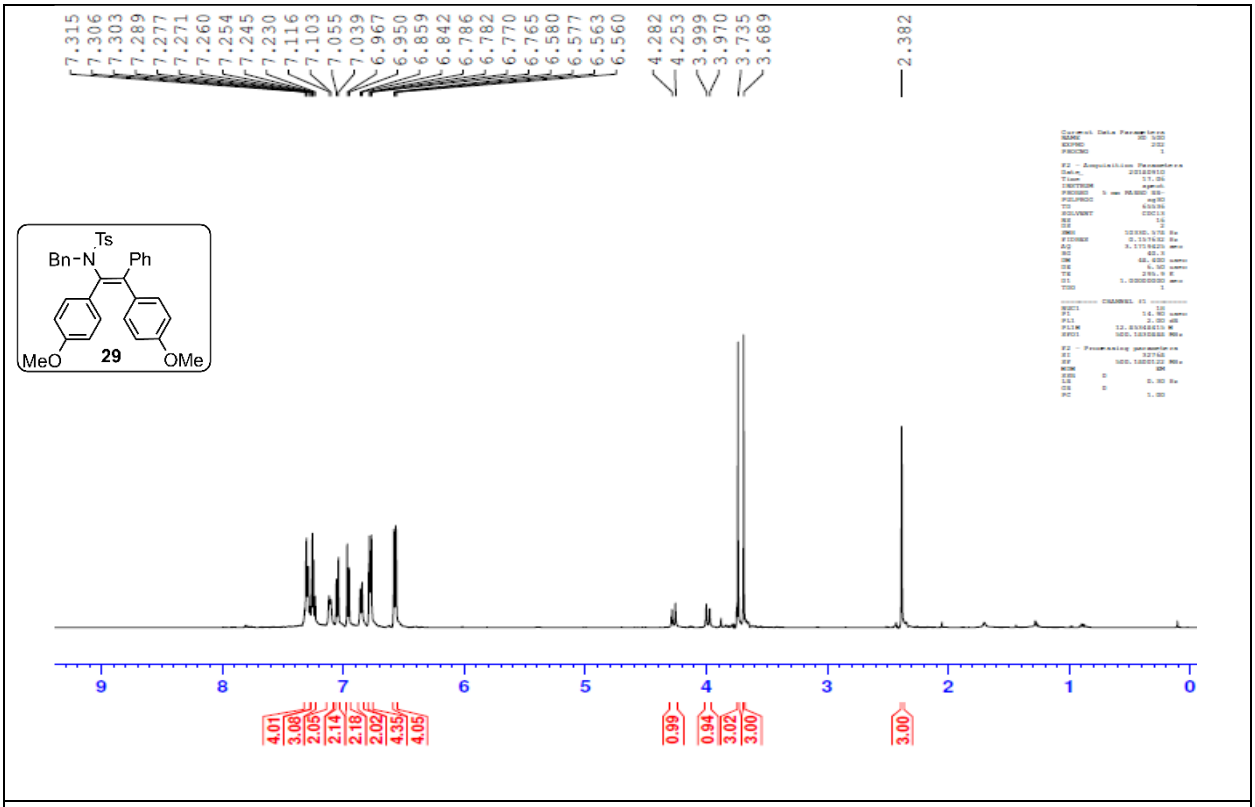
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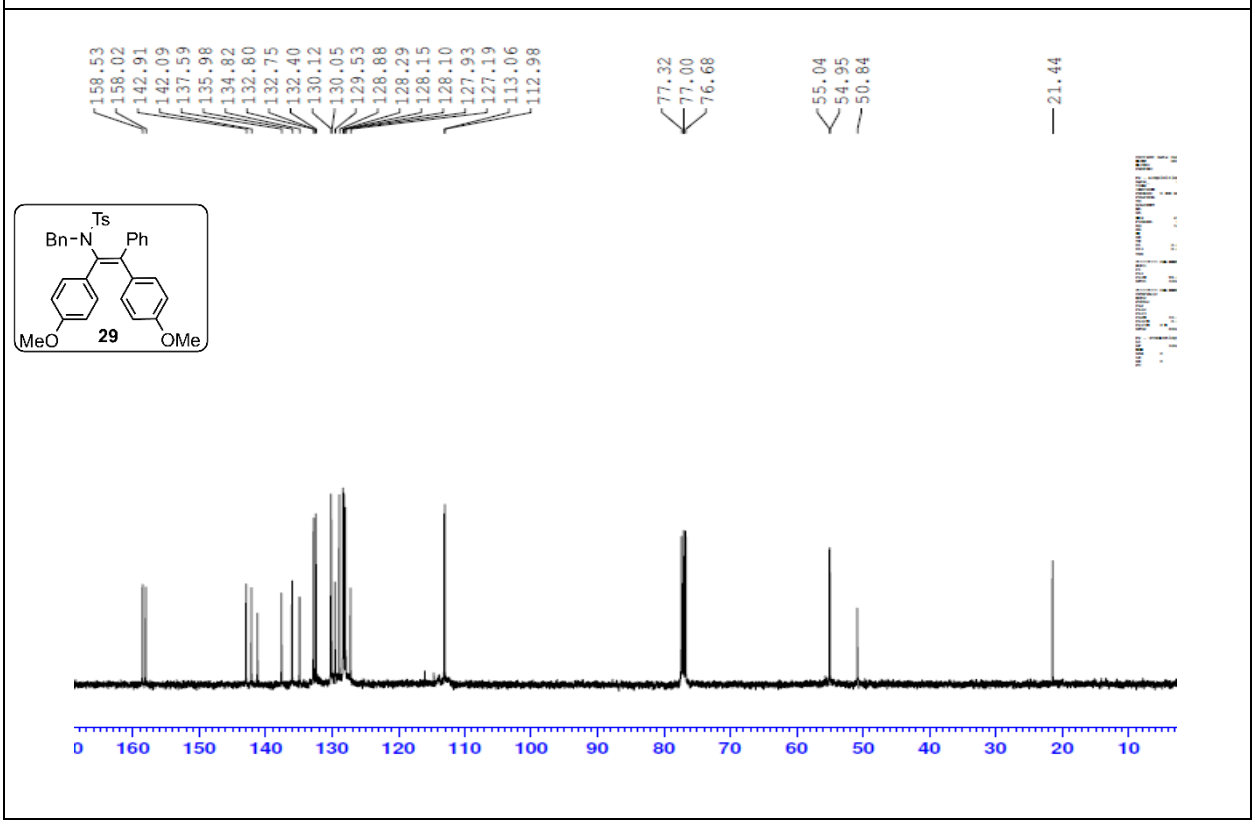
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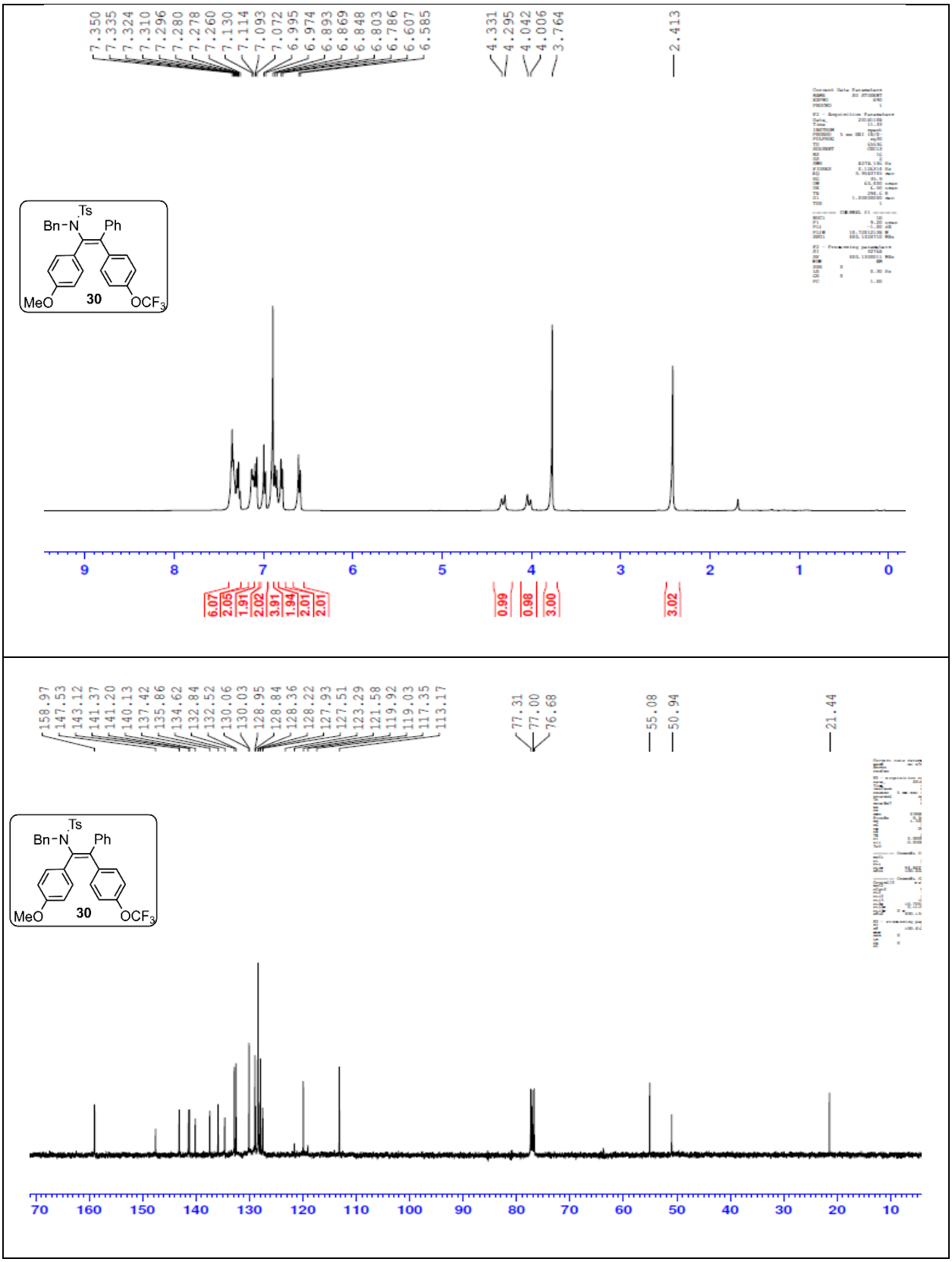
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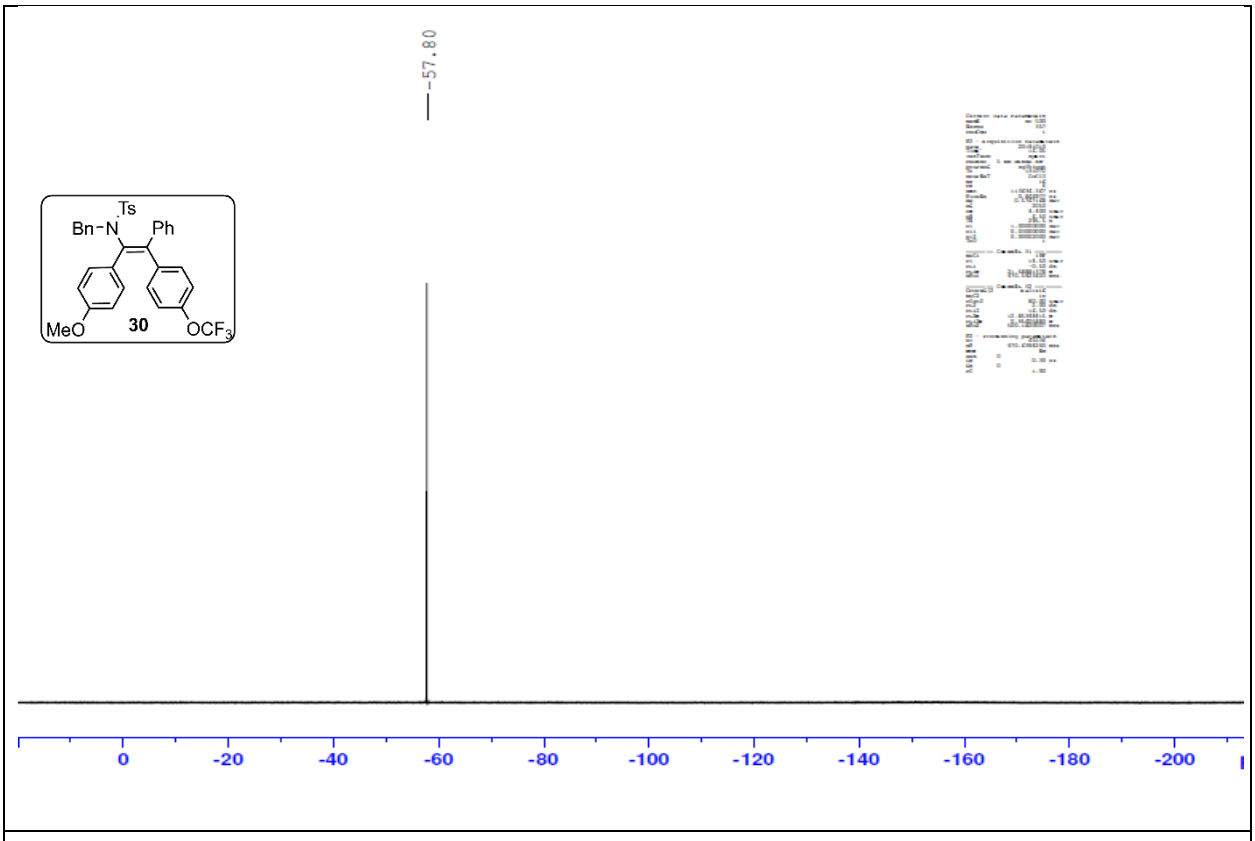
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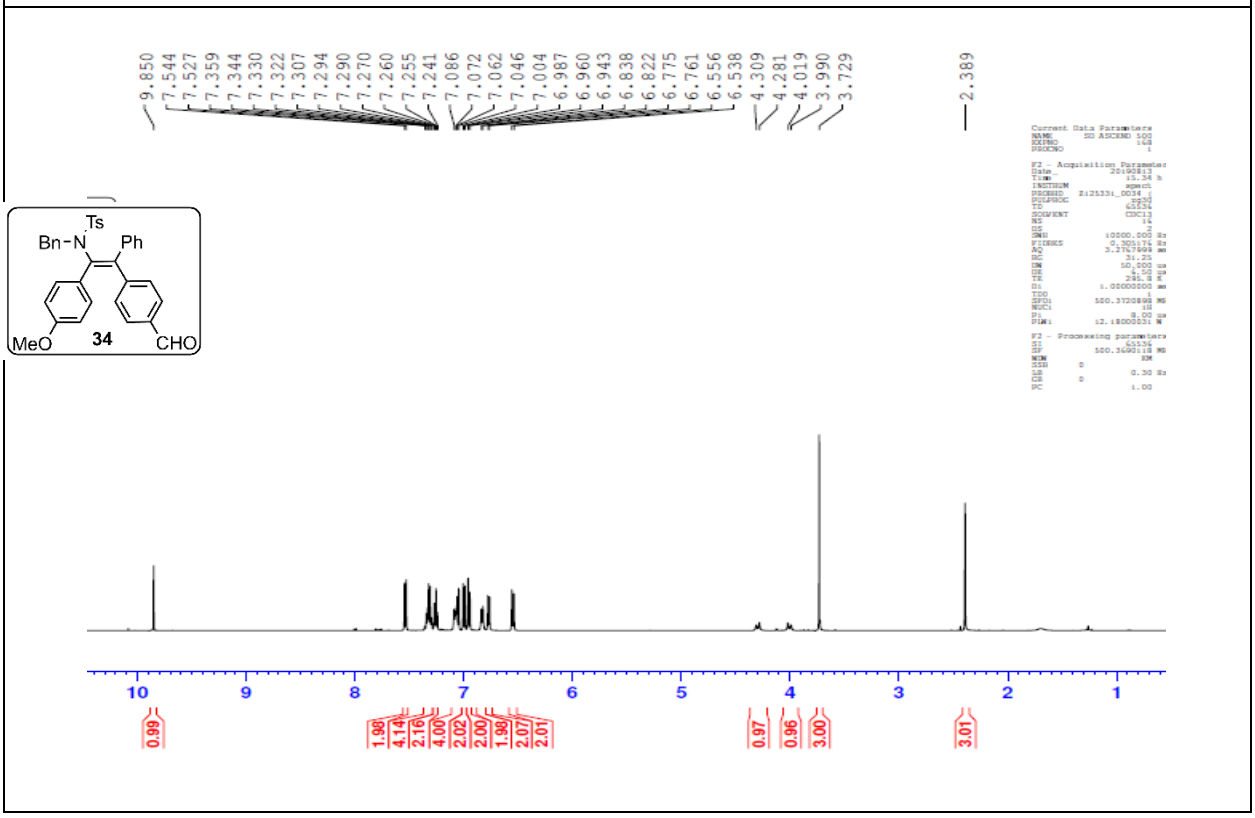
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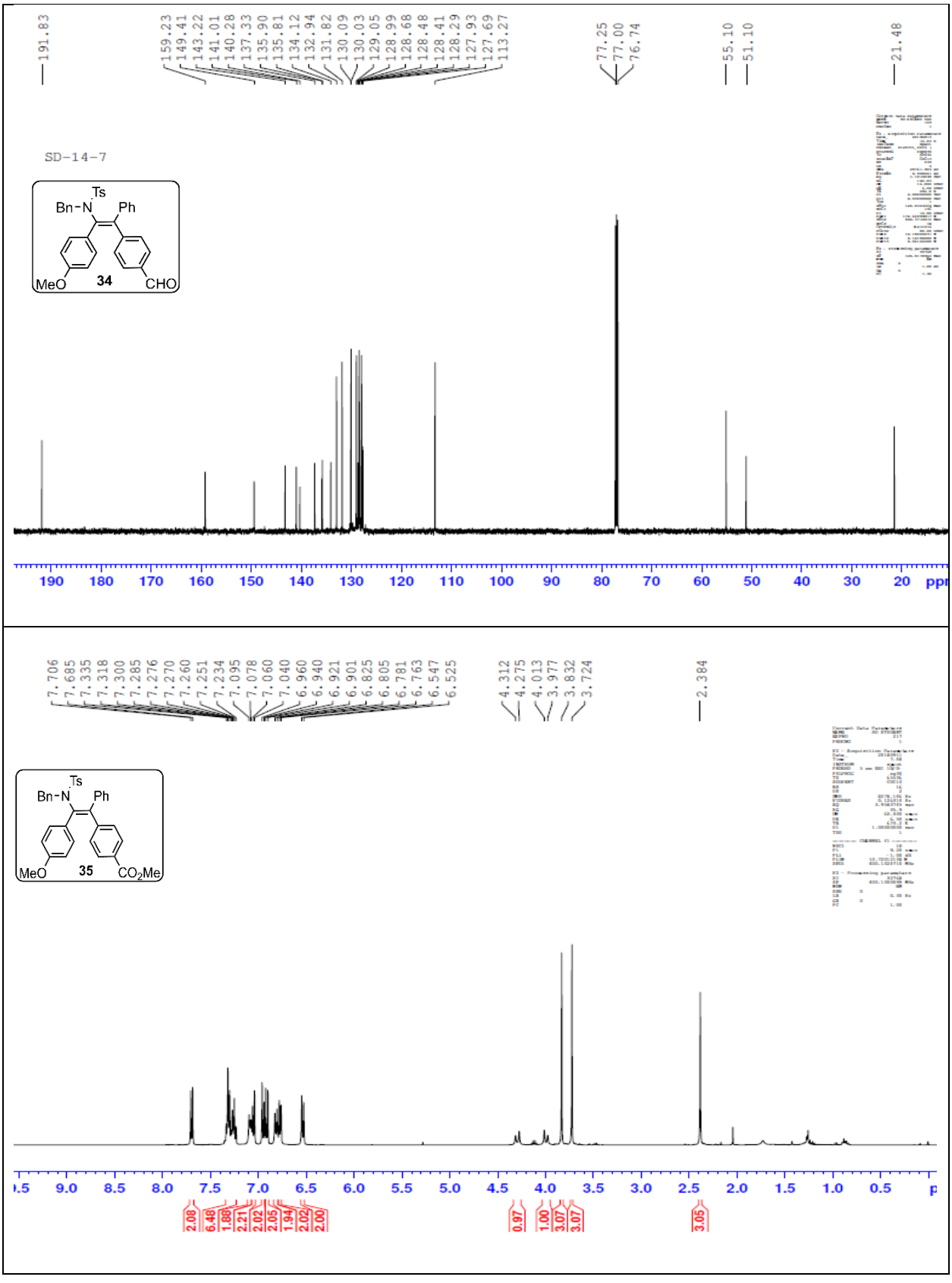
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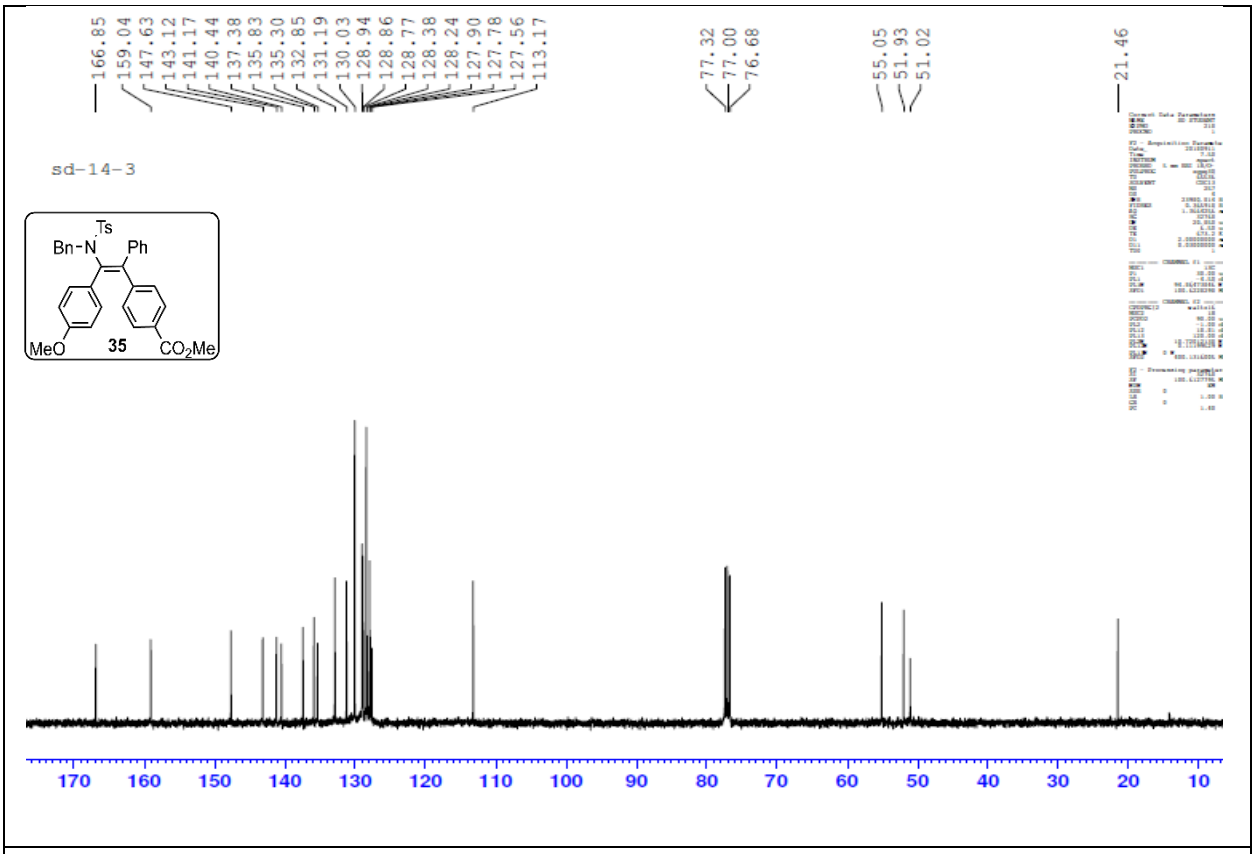
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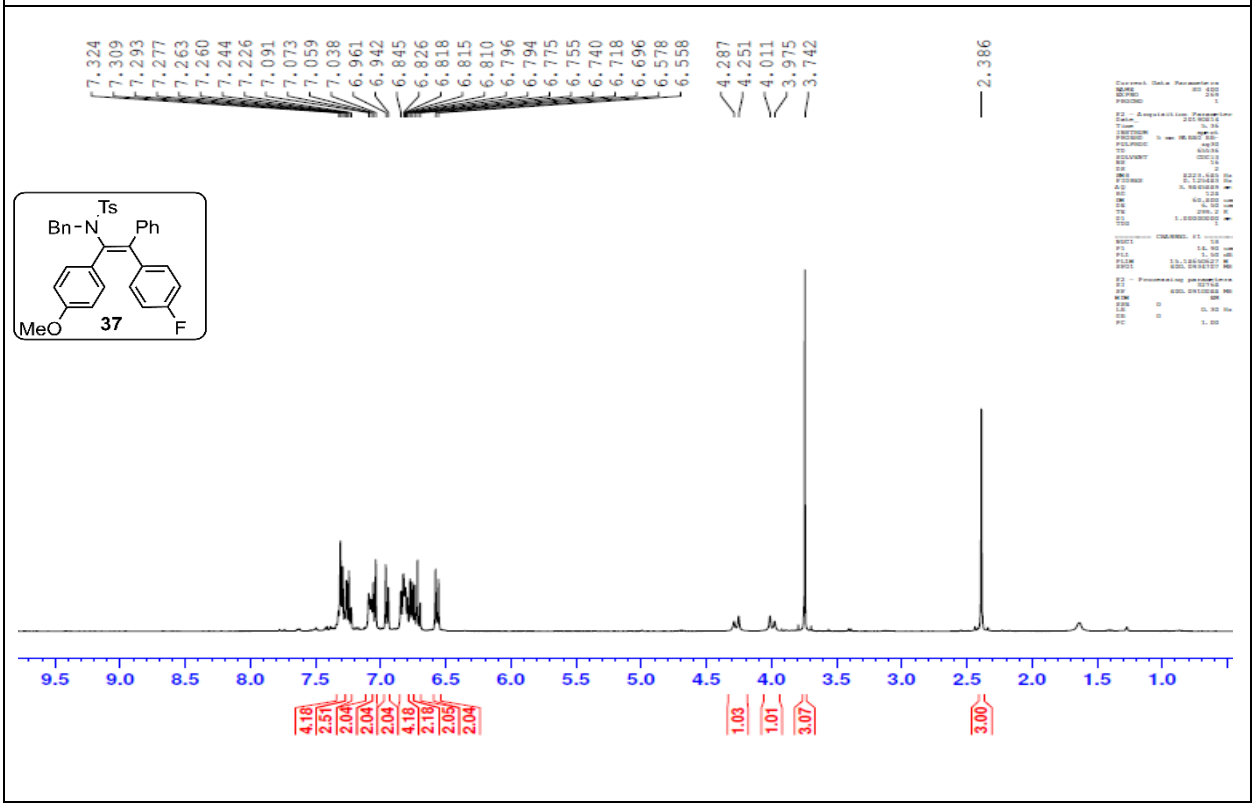
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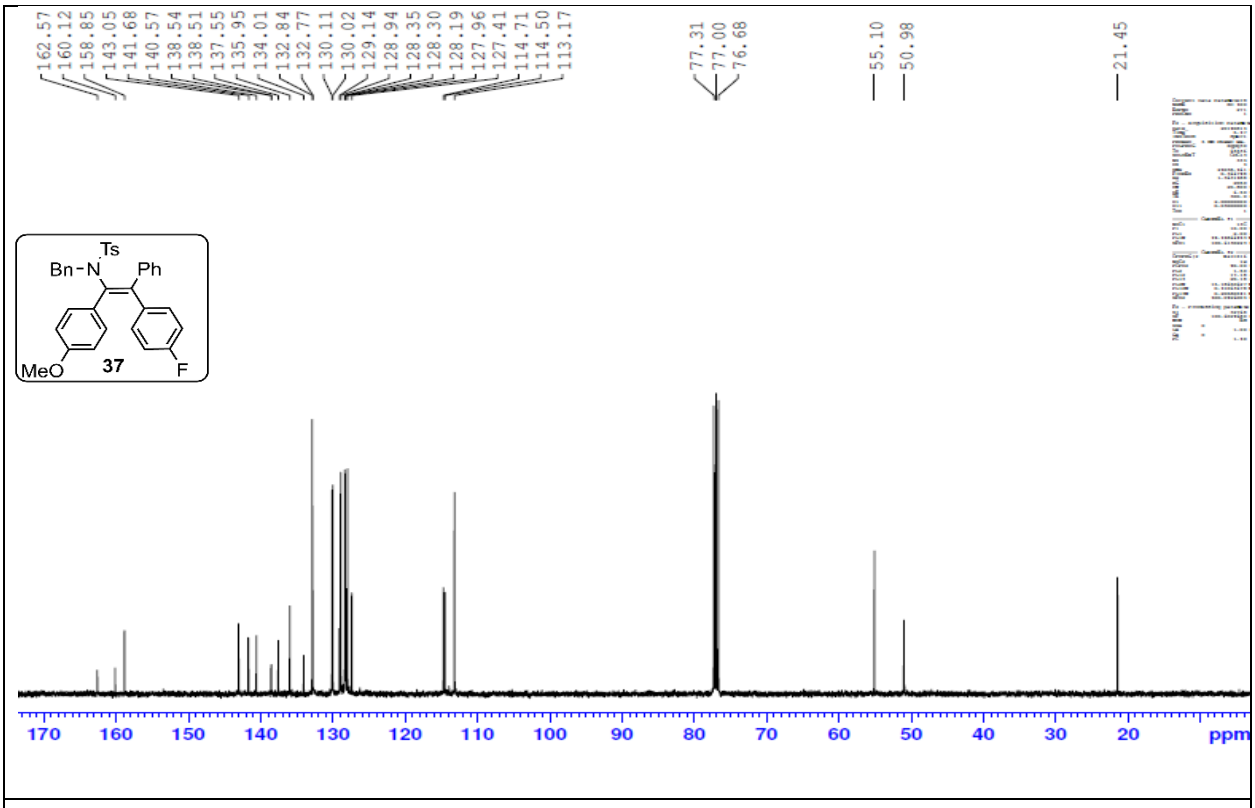
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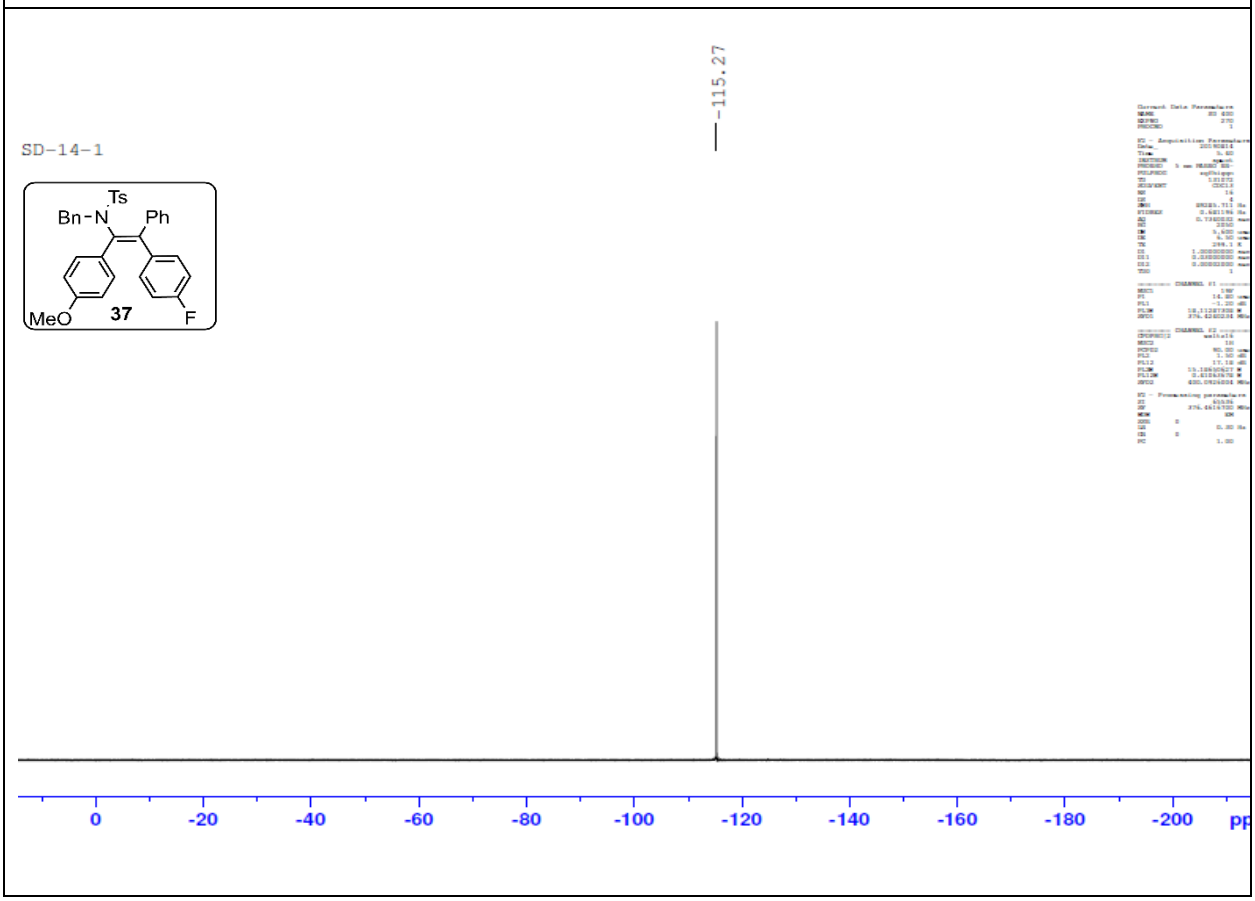
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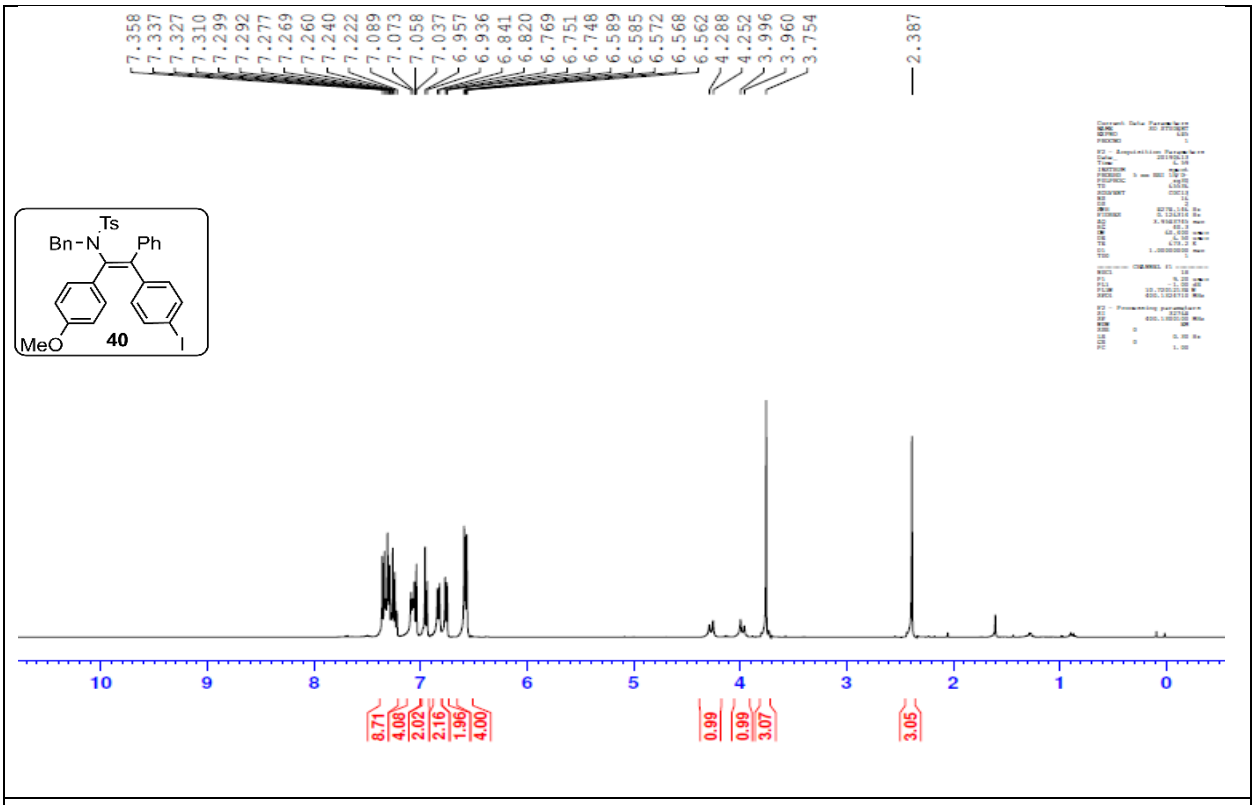
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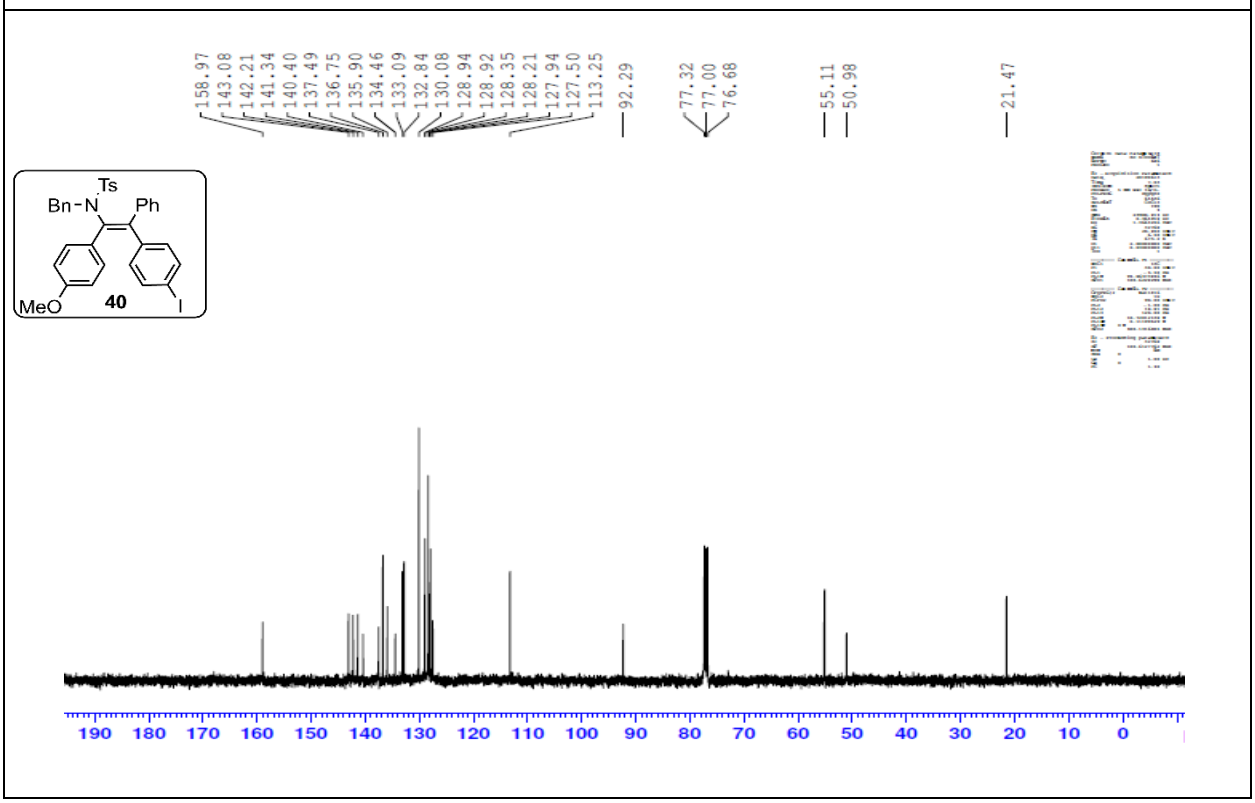
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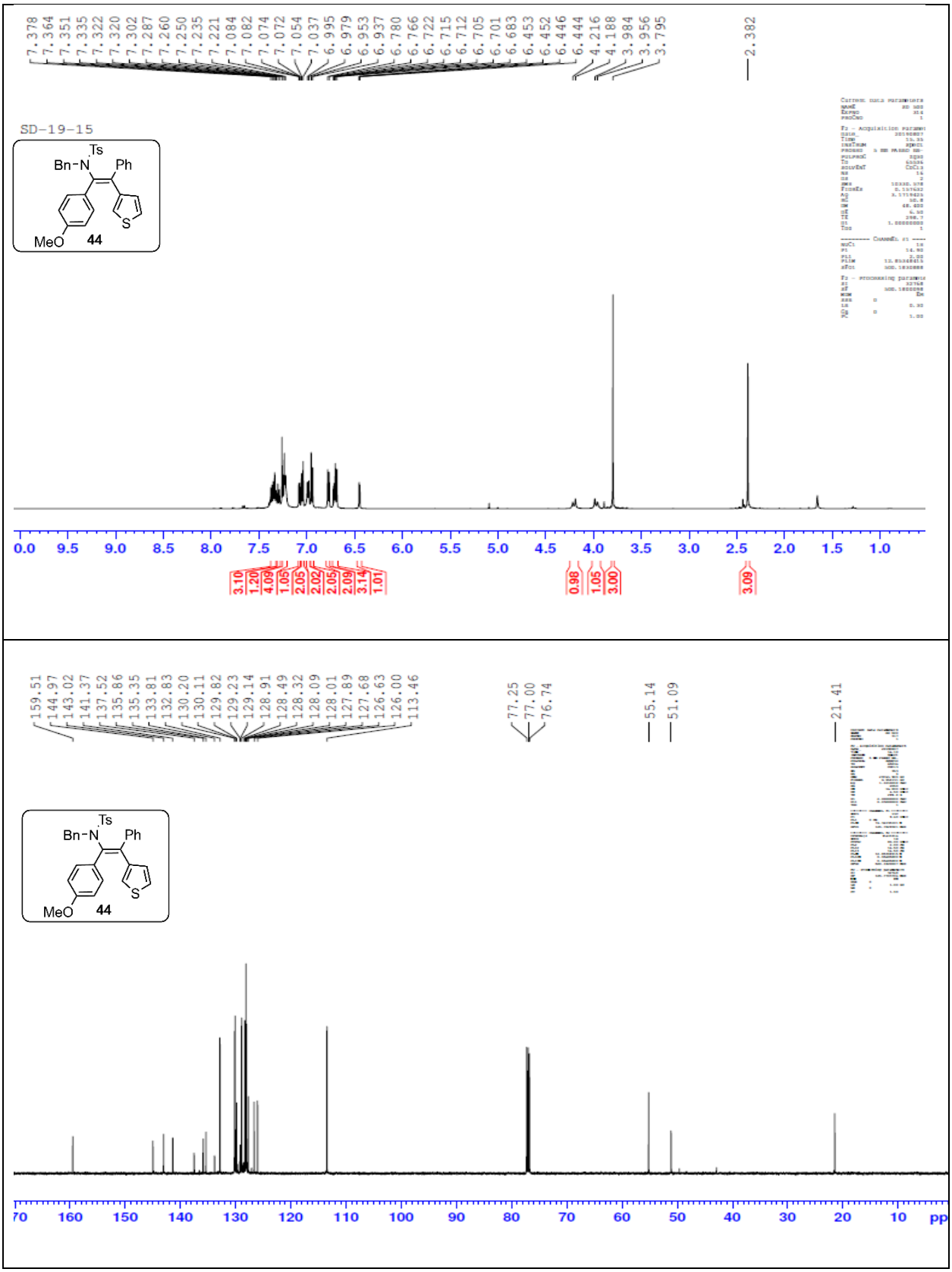
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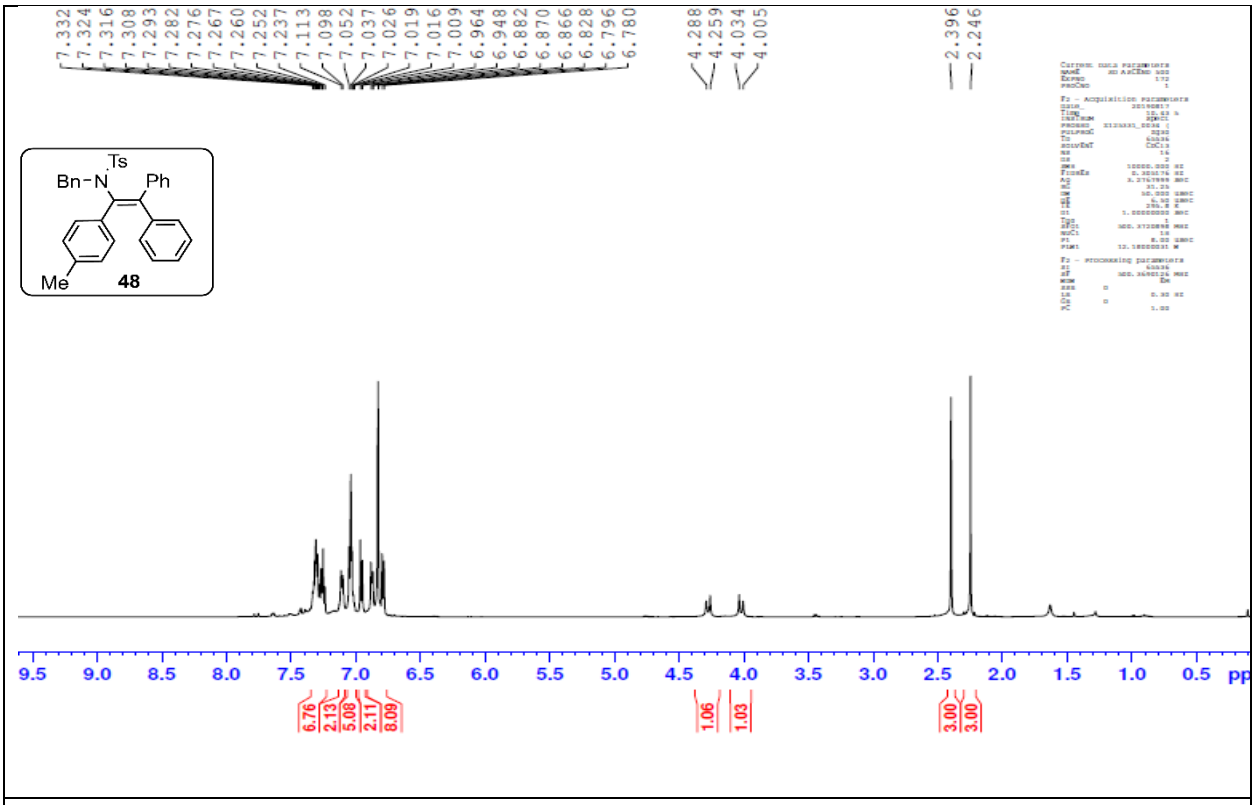
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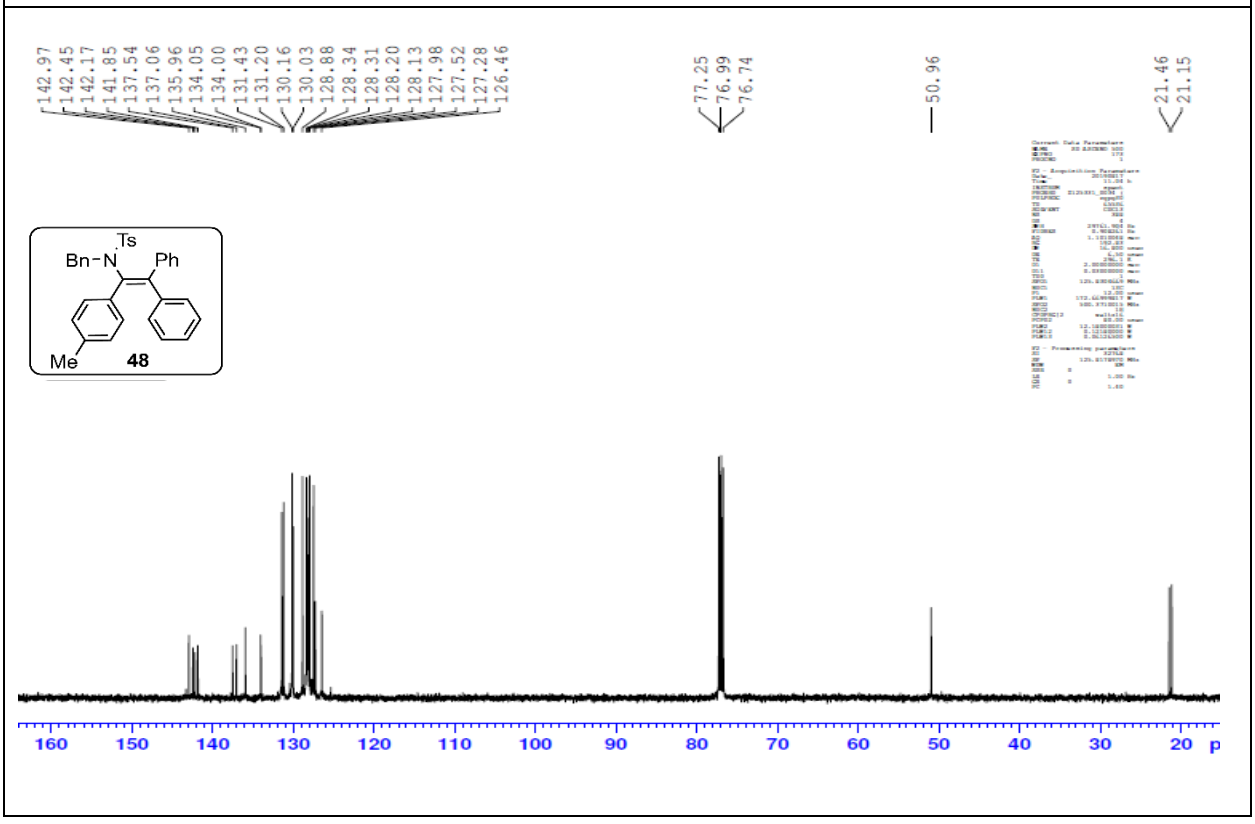
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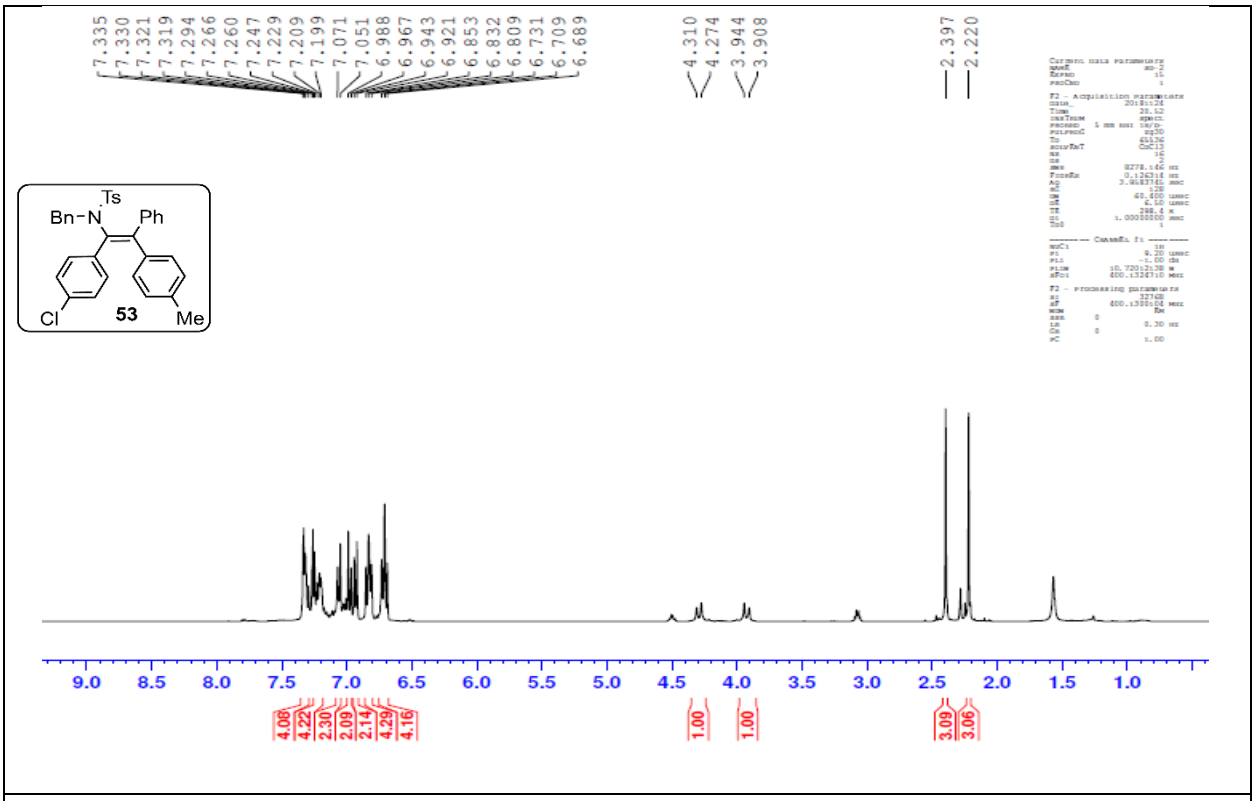
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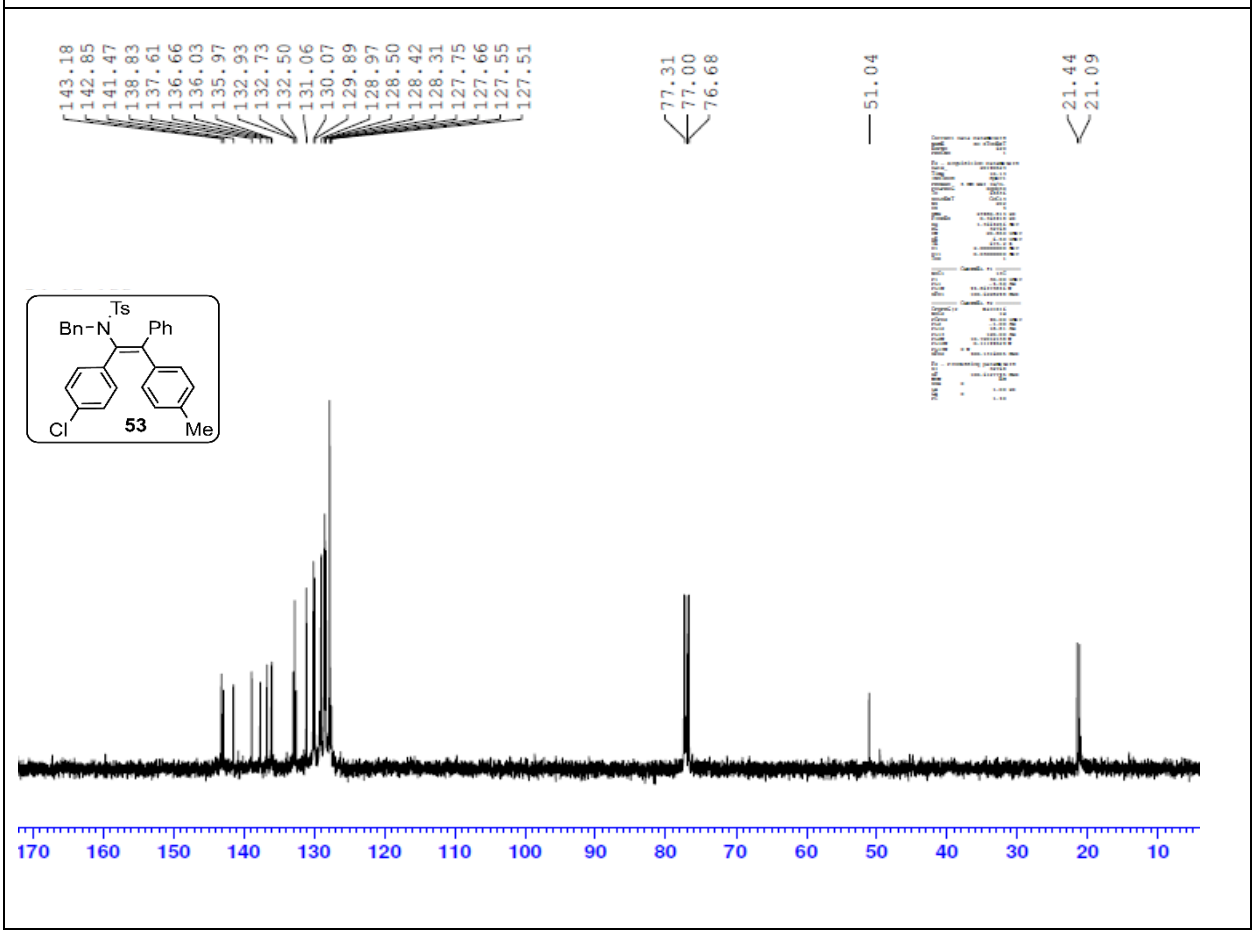
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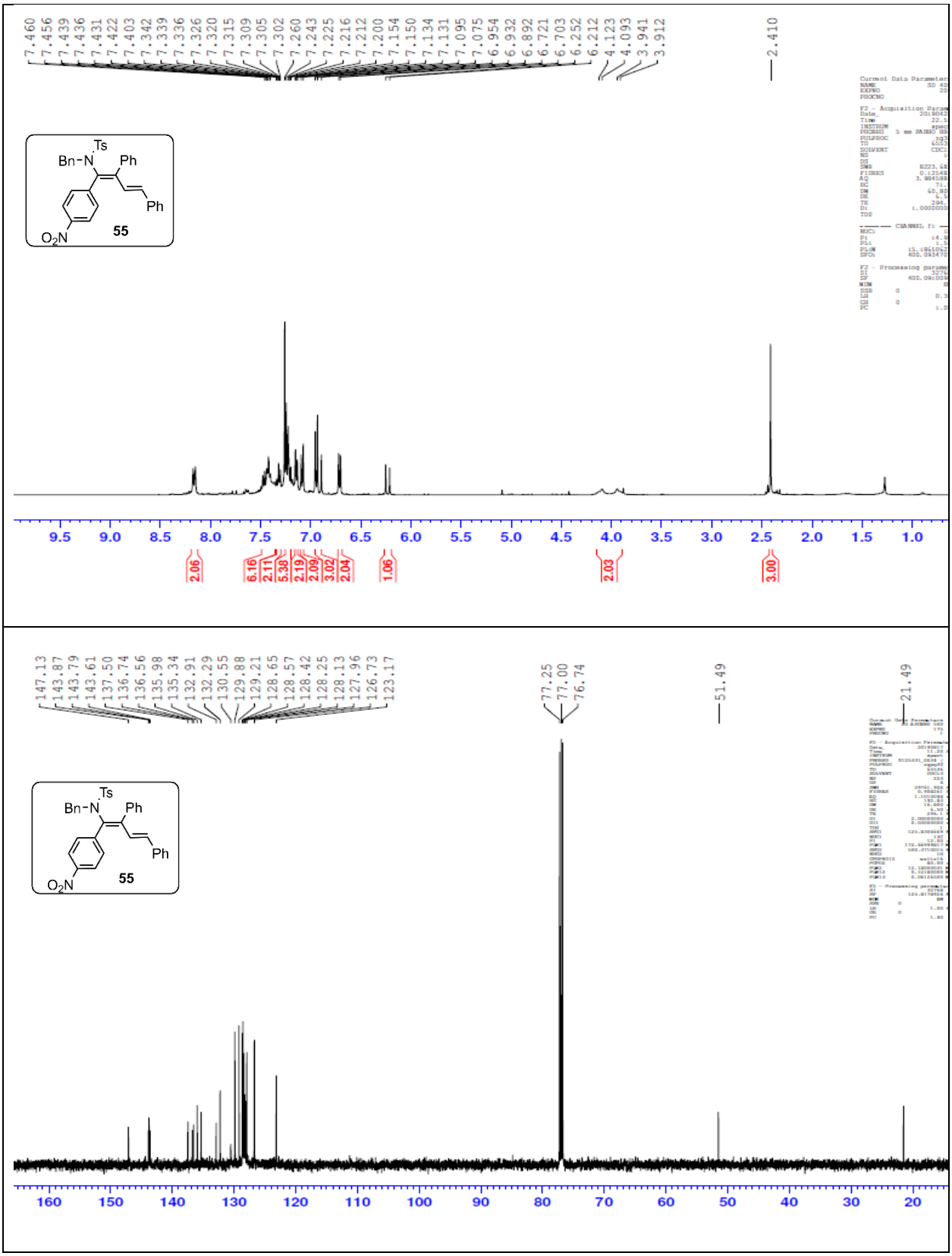
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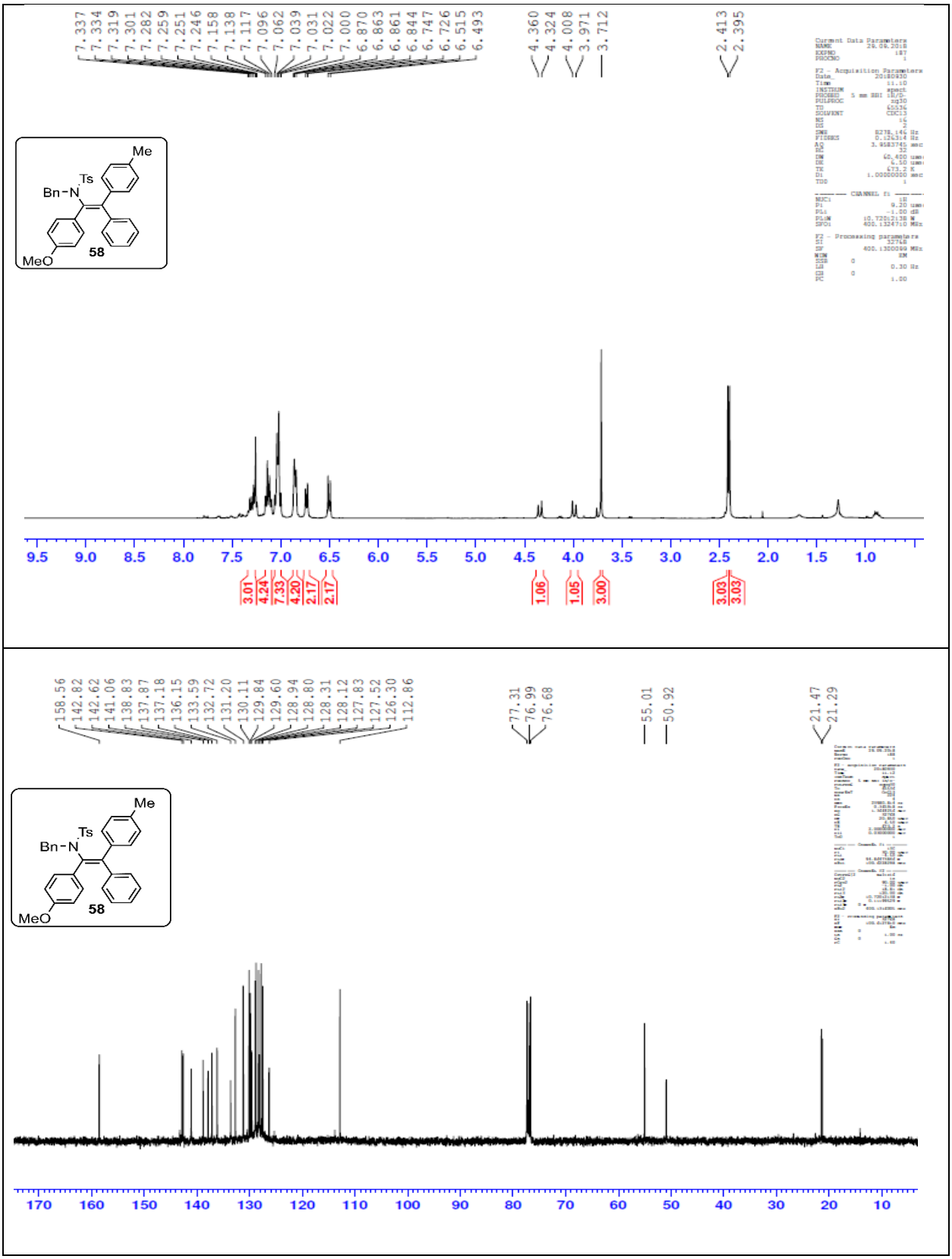
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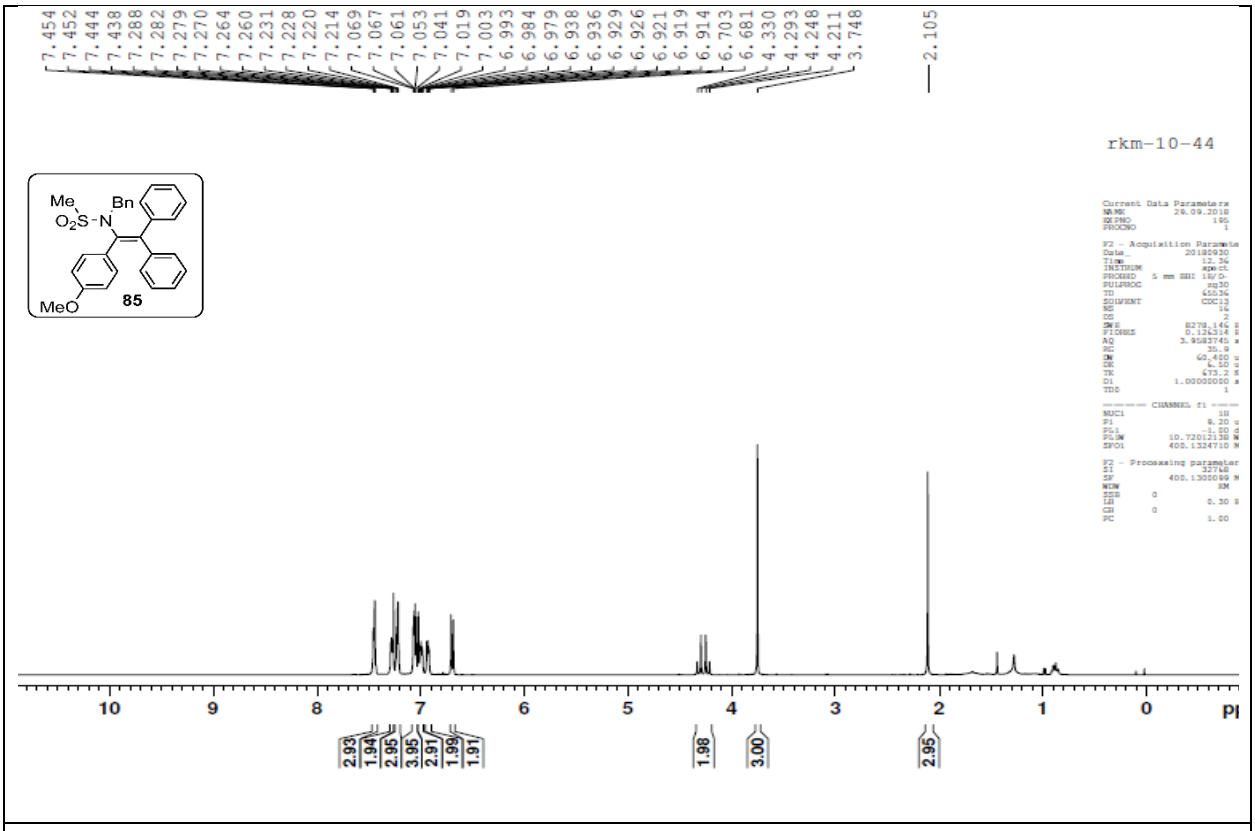
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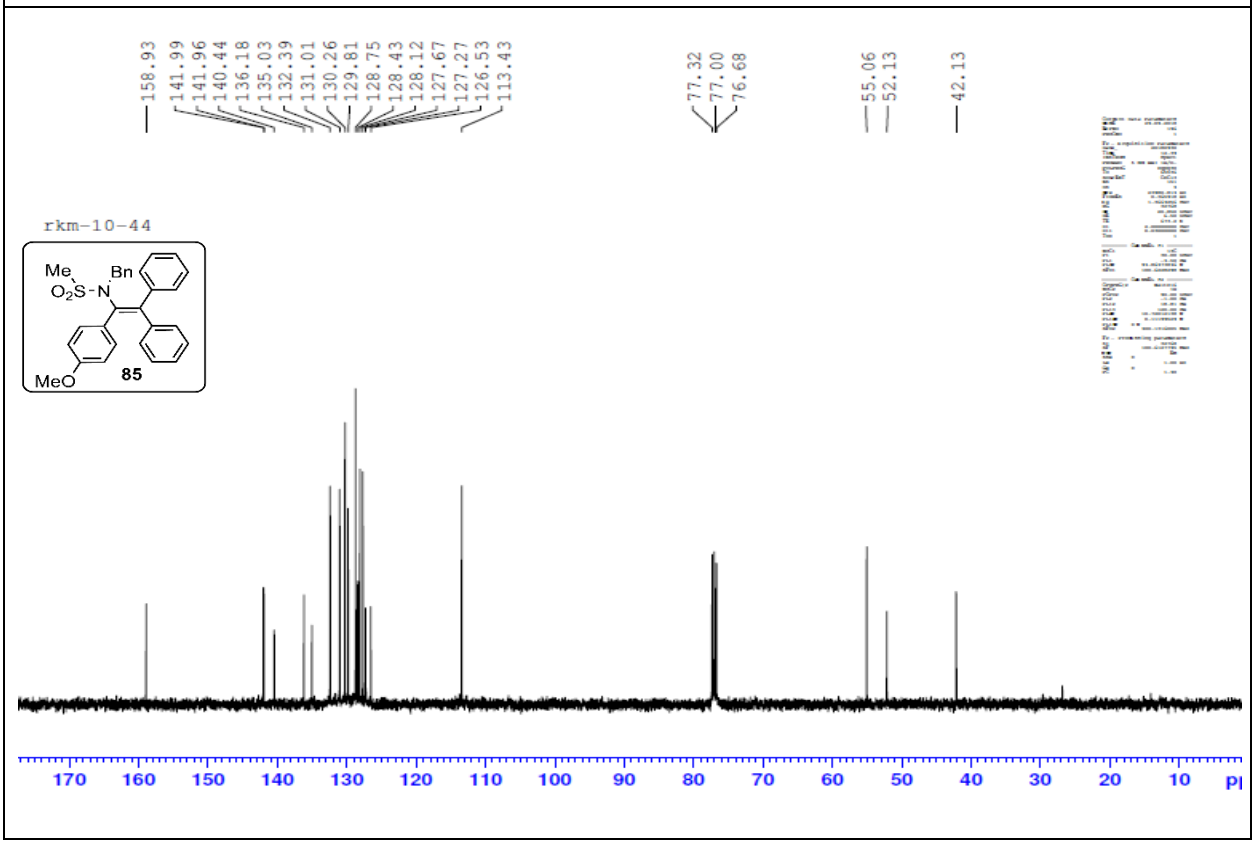
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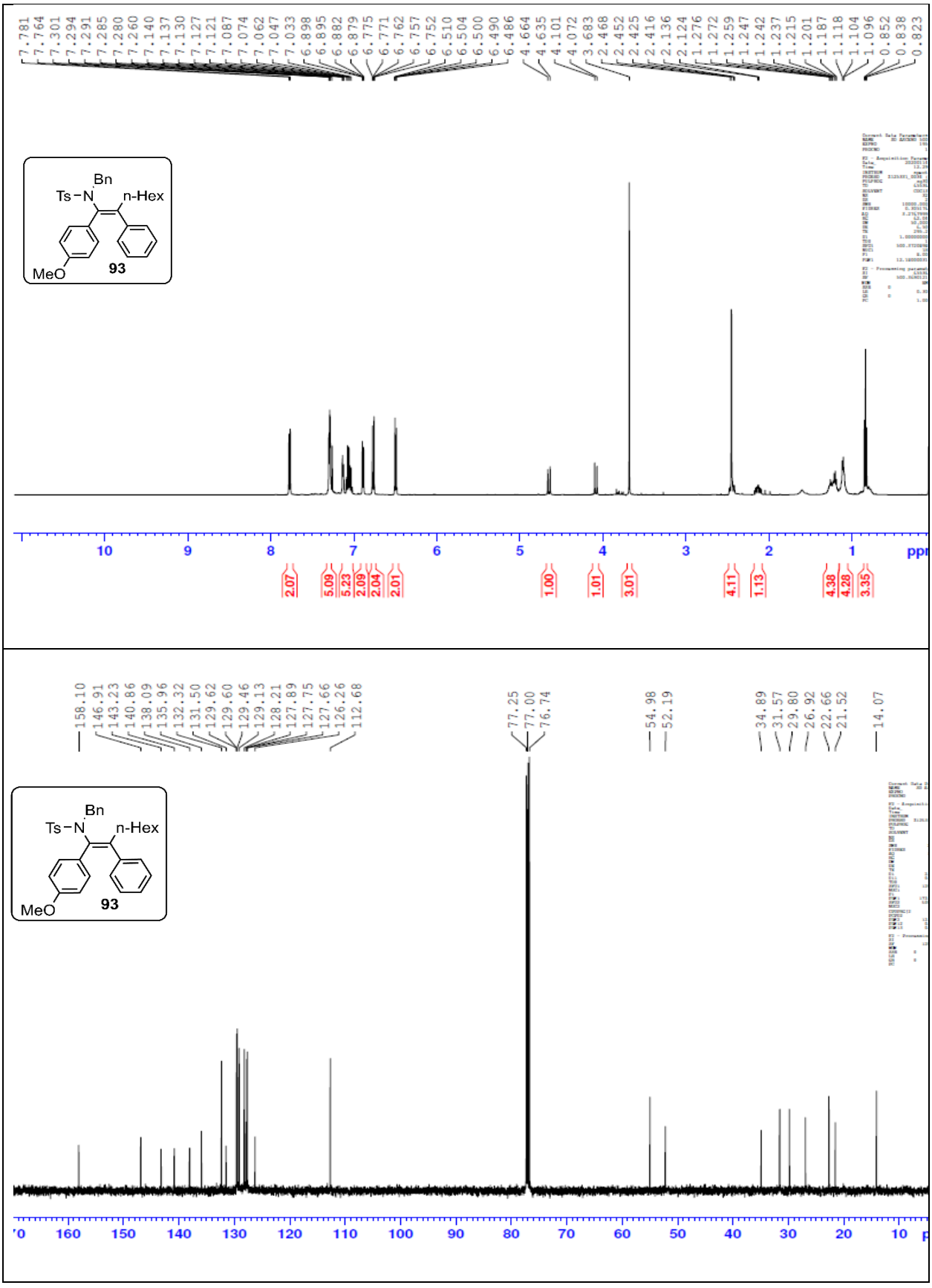
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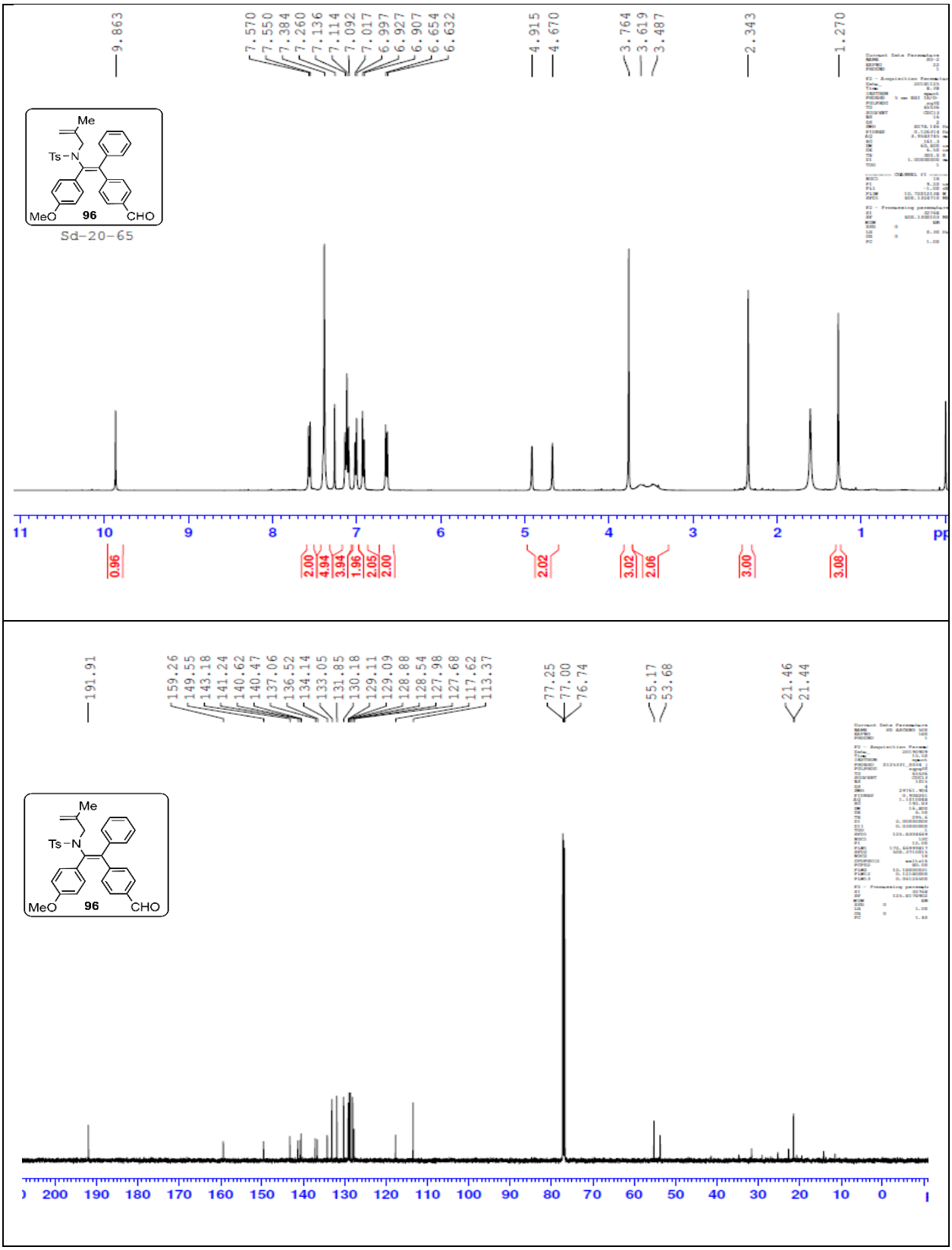
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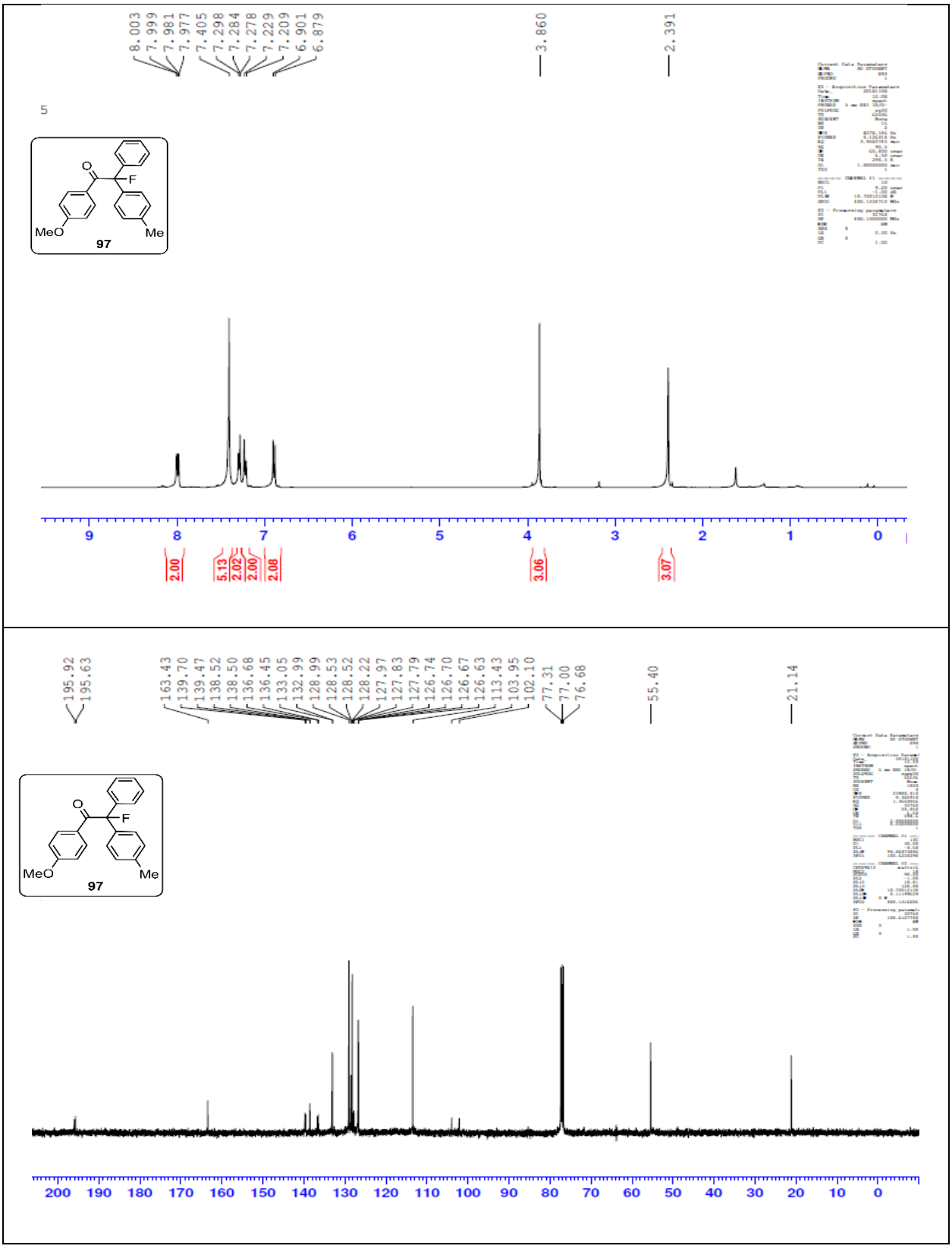
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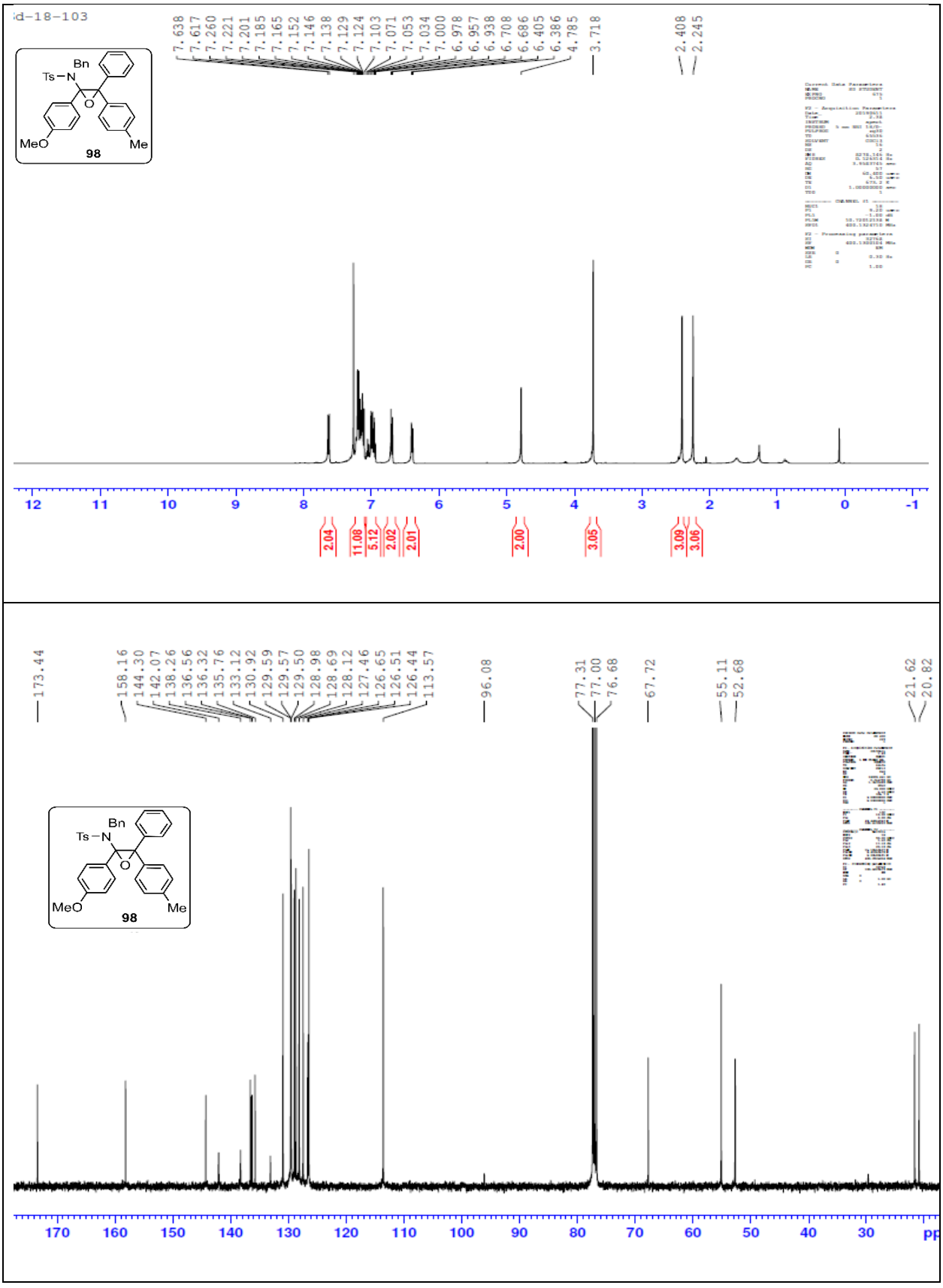
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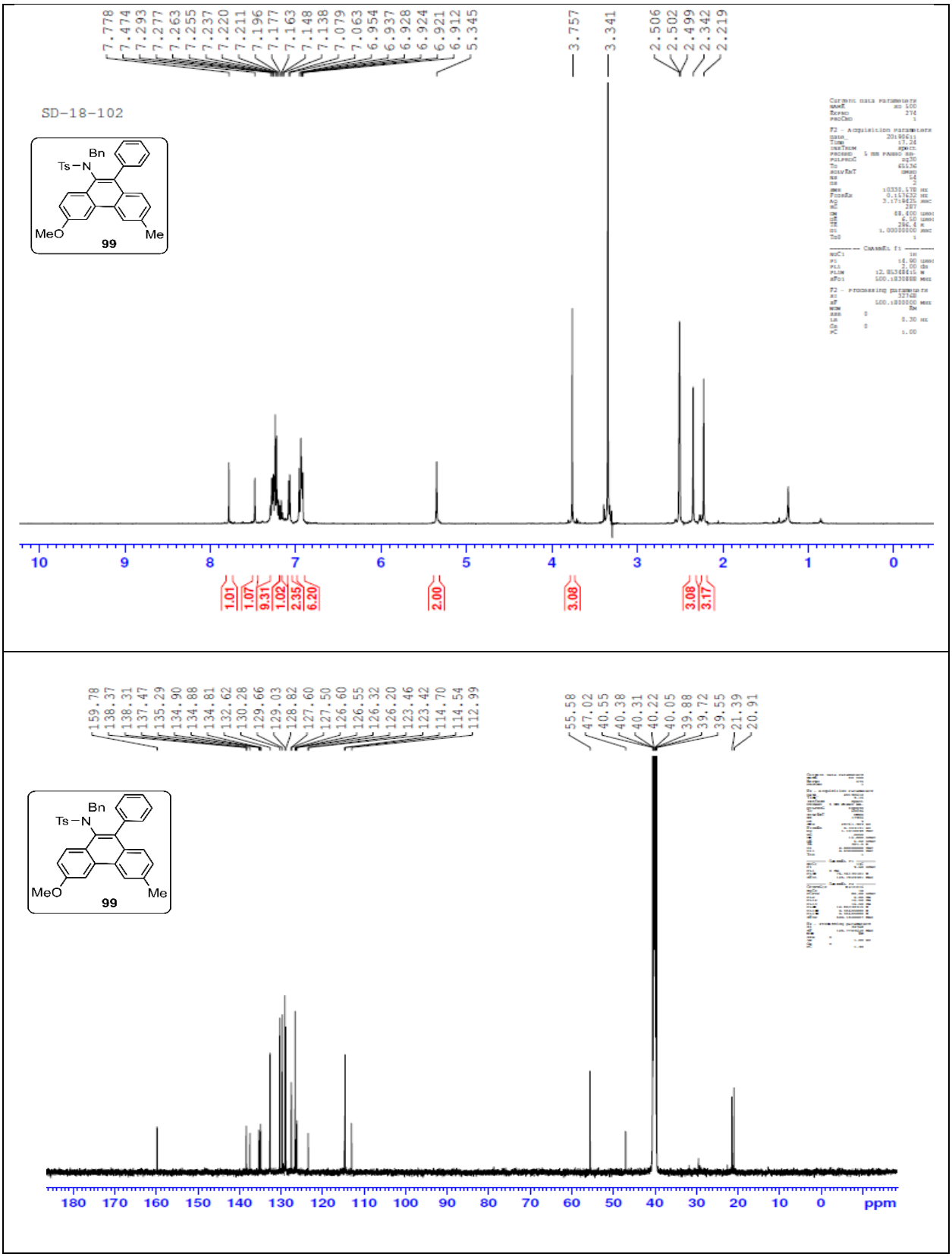
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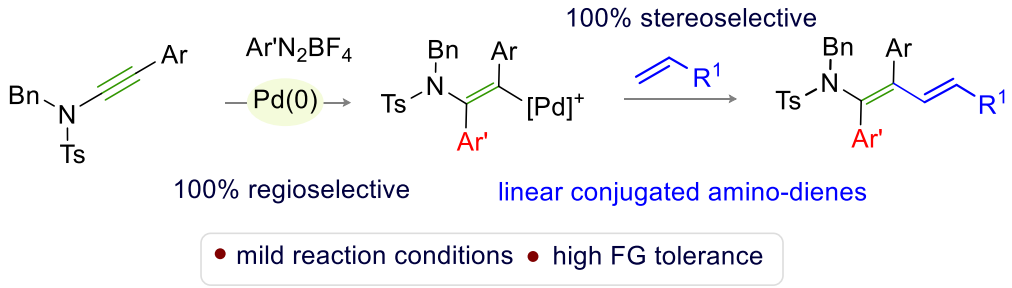
126.32
126.20
123.46
123.42
114.70
114.54
112.99
55.58
47.02
40.55
40.38
40.31
40.22
40.05
39.88
39.72
39.55
21.39
20.91
ppm

Chapter-3B

Palladium-Catalyzed Regioselective Aryl-Alkenylation of Ynamides

Abstract



A cationic palladium-catalyzed aryl-alkenylation of ynamides is presented. The putative keteniminium aryl palladium intermediate likely dictates the regioselective carbopalladation of the ynamide to form a vinyl-Pd species. The capture of this complex by the olefin yields linear conjugated β-alkenyl amino-dienes (especially with *trans*-selectivity). The transformation features broad scope with labile functional group tolerance and makes 42 unusual molecular scaffolds with structural diversity. DFT studies provide valuable insights into the reaction mechanism.

Publication

R. Vanjari,¥ **S. Dutta**,¥ S. Yang, V. Gandon, A. K. Sahoo*. (¥equal contribution). *Org. Lett.* **2022**, *24*, 1524–1529.

3B.1. Introduction

π-Conjugated olefins are versatile synthons in organic chemistry and also found in active pharmaceutical ingredients (API), agrochemicals, and electron-transport materials.[1] While the synthesis of dienes through a three-component arylative dicarbofunctionalization of alkynes is a proven strategy,[2] direct access to aminodienes[3] is not a thoroughly explored domain.[4-6] By analogy, the use of N-substituted alkynes, i.e. ynamides,[7] comes to mind. However, direct olefination of these inherently polarizable compounds has been so far less explored than simple alkynes.[7,8] The known reactions allowing direct alkenylation of ynamides primarily deliver α-alkenylated enamides.[9] For instance, transition-metal catalyzed Heck coupling and hydro-alkenylation introduces an alkenyl group at the α-position (next to the nitrogen) of the ynamide (Figure 3B.1, right side).[4,5] On the otherhand, chelation assisted transition-metal catalyzed *syn*-1,2-difunctionalization of oxazolidinone-derived ynamides with organometallic reagent and halo-alkenyl reagents leads to β–alkyl-α-alkenylation species (Figure 3B.1, left side).[6] *To date, no strategy enables the formation of α-aryl-β-alkenyl enamides by directly introducing two distinct C(sp²) functionalities on ynamides.*

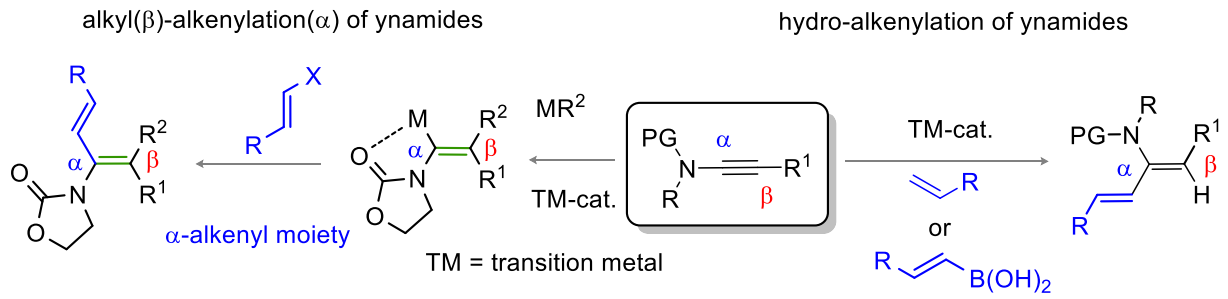


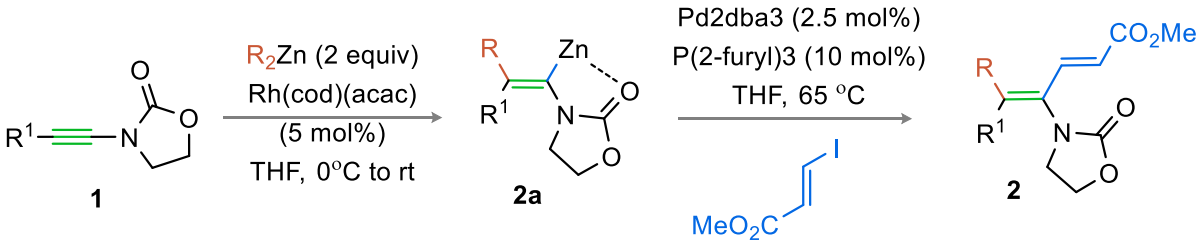
Figure 3B.1. α-alkenylation of ynamide

3B.2. Precedents

3B.2.1 α-Alkenylation of ynamide

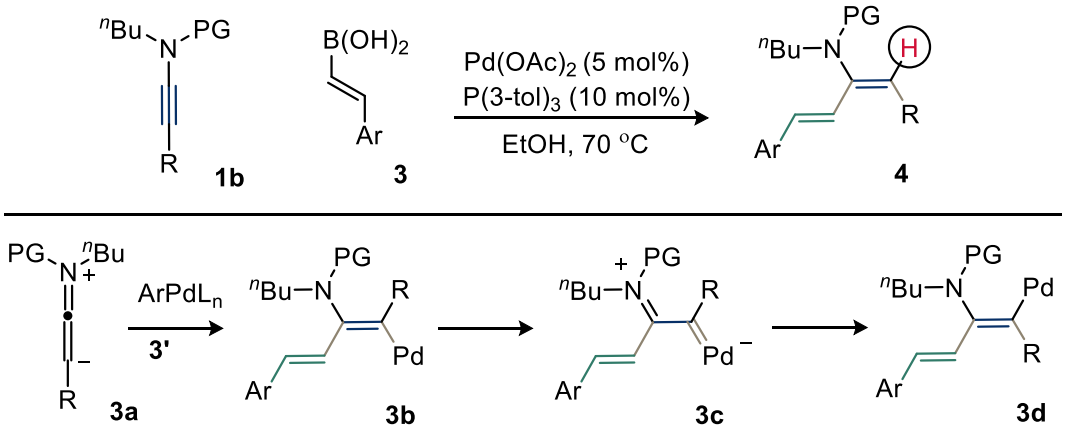
In 2009, the Lam and coworker reported alkyl-alkenylation of oxazolidone ynamides using chelation strategy (**Scheme 3B.1**).[6] The reaction begins with

formation of vinyl-α-zinc intermediate **2a** formed by regioselctive addition of alkyl group to the β-carbon of ynamide (**Scheme 3B.1**). Next Pd-catalyzed cross-coupling with alkenyl-iodo compound yields the α-alkenyl branched amino diene **2**.



Scheme 3B.1. Rh-catalyzed carbozincation of ynamide

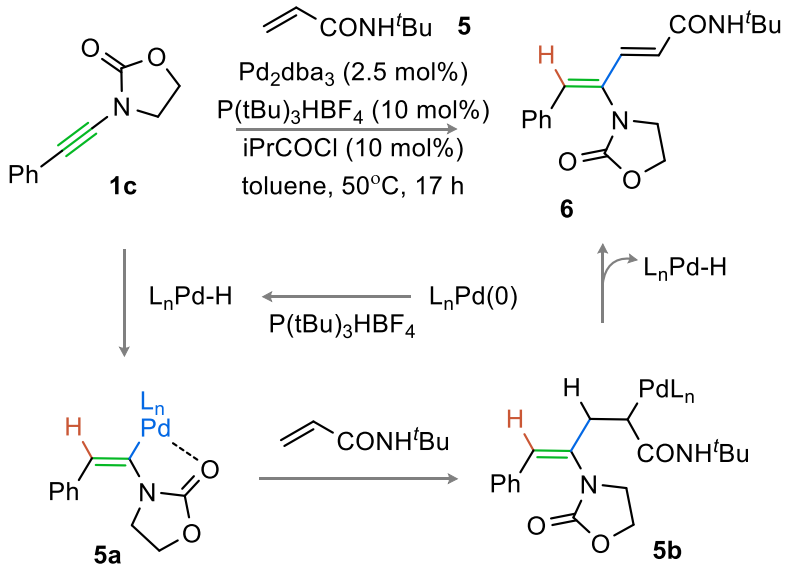
In 2014, Zhu et. al. disclosed a palladium catalyzed *trans*-addition of alkenyl-boronic acid to sulfonyl ynamide **1b** (**Scheme 3B.2**).[4d] The initial step involves the transmetallation of Pd(II) catalyst with alkenyl-boronic acid **3** to form aryl palladium species **3′**. Next, *syn*-addition to keteniminium species **3a** to give vinylic palladium species **3b**. Subsequent isomerization of **3b** to **3d** occurs via **3c**. Finally, protonation of **3d** gives the desired product **4**.



Scheme 3B.2. Pd-catalyzed *trans*-addition of alkenyl-boronic acid to ynamide

The Pd-catalyzed *cis*-hydro-alkenylation of oxazolidinone ynamide **1c** with activated olefin **5** has been demonstrated by Skrydstrup and co-workers (**Scheme**

3B.3).[5] An umpolung hydro-palladation of ynamide **1c** with Pd-H species generated in situ from Pd(0) and P(^{t}Bu)$_3$HBF$_4$ to form **5a**. Next, Heck coupling of vinyl-pd-species **5a** with **5** furnishes the final product **6** and regenerates the active catalyst Pd-H for the next cycle.



Scheme 3B.3. Pd-catalyzed *cis*-hydro-alkenylation of ynamide

3B.3. Motivation and Scheme Design

As highlighted above, synthetic methods are directed for the construction of branched amino-dienes. While synthesis of linear amino-dienes from N-bearing precursors are rare. At this juncture, devising a synthetic plan for linear amino-dienes from readily accessible ynamide is a worthwhile endeavor. Thus, a keteniminium driven aryl-alkenylation of ynamides with olefins in stead of aryl boronic acid is envisioned. The transformation would rely on a β-nucleophilic attack of ynamide **I** to a cationic Pd(II) species, generated in situ by the oxidative addition of an aryl diazonium salt[10b] with Pd(0), to form a keteniminium species **II**. Next, *syn*-1,3-aryl migration from the Pd-center to the α-carbon of **II** results in a cationic vinyl Pd-species **III**. Finally, olefin insertion into the Pd-C bond of **III**, and β-hydride elimination produces linear conjugated

aminodienes. This unsymmetrical dicarbofunctionalization of ynamides through *syn*-aryl-alkenylation is regio- as well stereoselective (**Fig. 3B.2**).

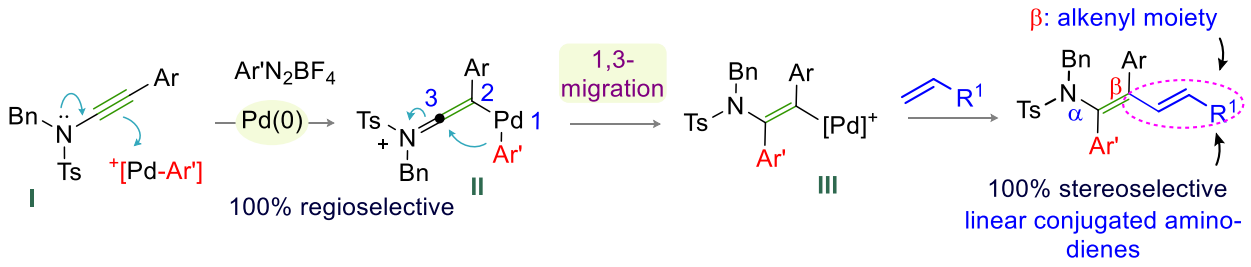


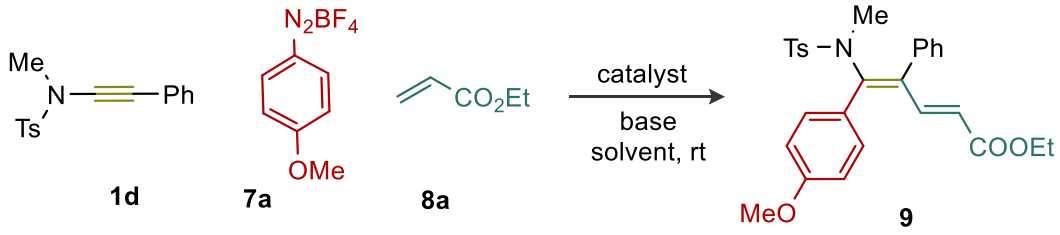
Figure 3B.2. Regio and stereoselective aryl-alkenylation of ynamides

3B.4. Result and Discussion

3B.4.1. Reaction Optimization

To begin with, the aryl-alkenylation of ynamide **1d** was performed with *p*-methoxybenzene diazonium tetrafluoroborate (**7a**) and ethyl acrylate (**8a**) in presence of $Pd(dba)_2$ and $NaHCO_3$ (Table 3B.1). The resulting reaction mixture was intractable in DMSO (entry 1), yet a trace amount of the desired product **9** could be detected when the reaction was conducted in THF (entry 2) or in 1,2-dichloroethane (DCE) (entry 3). When carried out in a 1:1 DMSO/DMF mixture, the reaction led to **9** in an encouraging 19% yield (entry 4). Screening of bases (i.e. K_2CO_3, K_3PO_4, and Cs_2CO_3) under the same catalytic conditions of entry 4, were not successful (entries 5–7). Interestingly, Li_2CO_3 proved effective, **9** being isolated in 61% yield (entry 8). Addition of benzoquinone (BQ) in catalytic amount to the reaction mixture slightly improved the product yield to 67% (entry 9). No significant change in product yield was measured when the reaction was conducted with Na_2HPO_4 (entry 10). However, the reaction in presence of Na_2HPO_4 and BQ provided **9** in 73% yield (entry 11). By contrast, a combination of $Pd(PPh_3)_4$, K_2HPO_4, and BQ was ineffective (entry 12). Other than simple BQ ligand, no susbstituted BQs and phosphine ligands like PPh_3, DPPP, XantPhos did not increase the reaction yield of **9** (entry 13–18).

Table 3B.1. Optimization Table



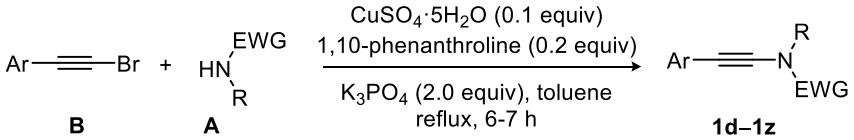
Entry	Catalyst/ligand	Base	Solvent	Yield of **9** (%)[b]
1	$Pd(dba)_2$	$NaHCO_3$	DMSO	N.D
2	$Pd(dba)_2$	$NaHCO_3$	THF	trace
3	$Pd(dba)_2$	$NaHCO_3$	$ClCH_2CH_2Cl$	trace
4	$Pd(dba)_2$	$NaHCO_3$	DMSO:DMF (1:1)	19
5	$Pd(dba)_2$	K_2CO_3	DMSO:DMF (1:1)	trace
6	$Pd(dba)_2$	K_3PO_4	DMSO:DMF (1:1)	trace
7	$Pd(dba)_2$	Cs_2CO_3	DMSO:DMF (1:1)	trace
8	$Pd(dba)_2$	Li_2CO_3	DMSO:DMF (1:1)	61
9	$Pd(dba)_2$/BQ	Li_2CO_3	DMSO:DMF (1:1)	67
10	$Pd(dba)_2$	Na_2HPO_4	DMSO:DMF (1:1)	67
11	$Pd(dba)_2$/BQ	Na_2HPO_4	DMSO:DMF (1:1)	73
12	$Pd(PPh_3)_4$/BQ	K_2HPO_4	DMSO:DMF (1:1)	36
13	$Pd(dba)_2$/2,6-di(Me)BQ	Na_2HPO_4	DMSO:DMF (1:1)	52
14	$Pd(dba)_2$/2,5-di(^{t}Bu)BQ	Na_2HPO_4	DMSO:DMF (1:1)	58
15	$Pd(dba)_2$/2,5-di(Cl)BQ	Na_2HPO_4	DMSO:DMF (1:1)	35
16	$Pd(dba)_2$/PPh_3	Na_2HPO_4	DMSO:DMF (1:1)	23
17	$Pd(dba)_2$/DPPP	Na_2HPO_4	DMSO:DMF (1:1)	29
18	$Pd(dba)_2$/XantPhos	Na_2HPO_4	DMSO:DMF (1:1)	26

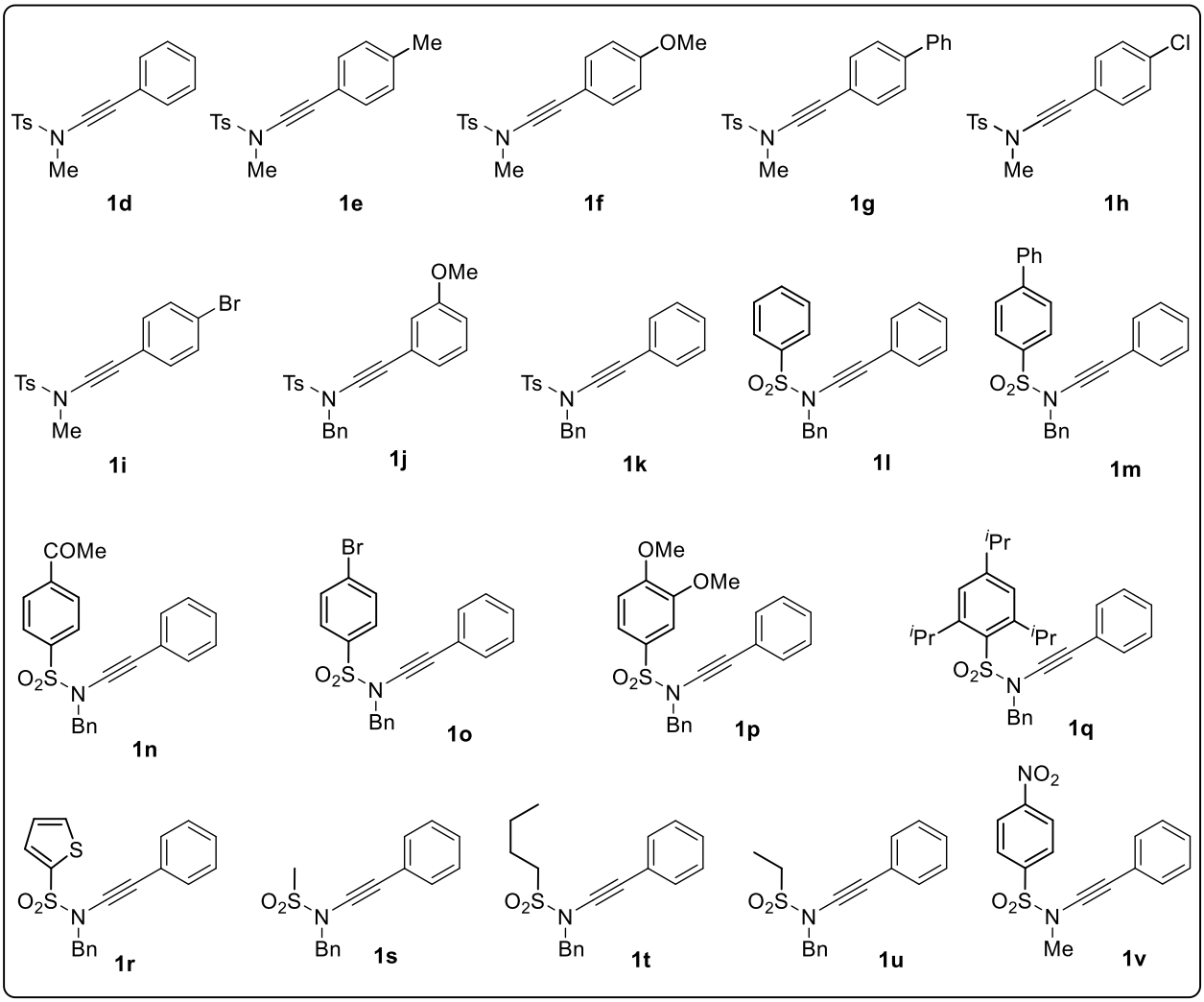
[a]Reaction conditions: **1d** (0.2 mmol, 1.0 equiv), **7a** (0.3 mmol, 1.5 equiv), **8a** (0.4 mmol, 2.0 equiv), catalyst (10 mol%), solvent (0.1M) at rt for 12 h. [b]isolated yield. N.D = not determined.

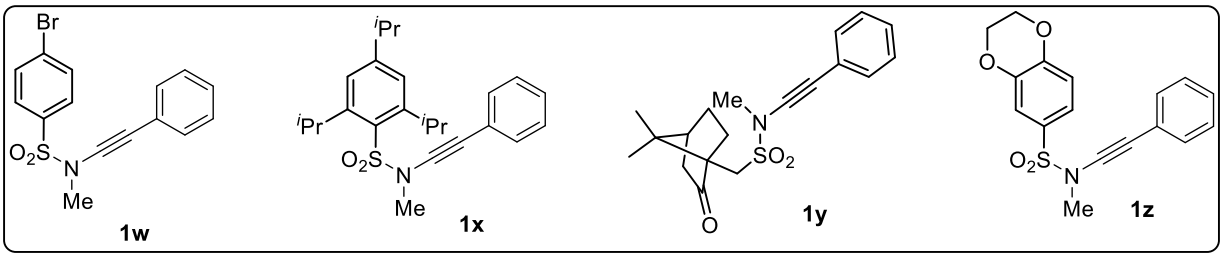
3B.4.2. Synthesis of ynamides, and aryl diazonium salts

Following the known Cu-catalyzed C-N coupling procdure, ynamides **1d-1z** were synthesized from corresponding sulfonamides (A) and bromoalkynes (B) (Table 3B.2).

Table 3B.2. Ynamide chart







Following the known diazodization procdure, aryldiazonium salts **7a-h** were synthesized from corresponding aniline derivatives **C** (Table 3B.3).

Table 3B.3. Aryl diazonium salt chart

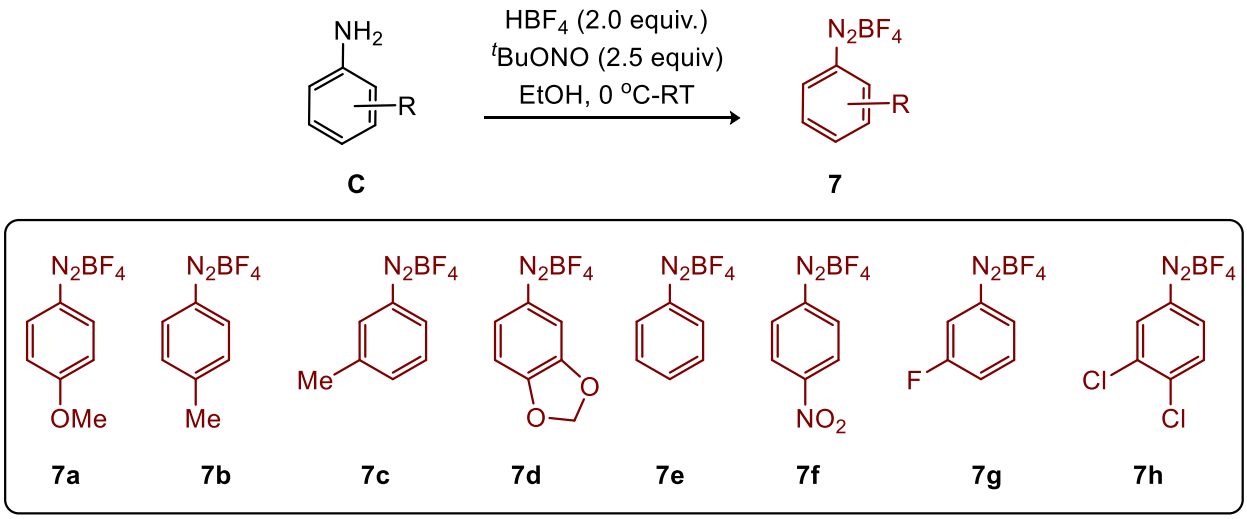
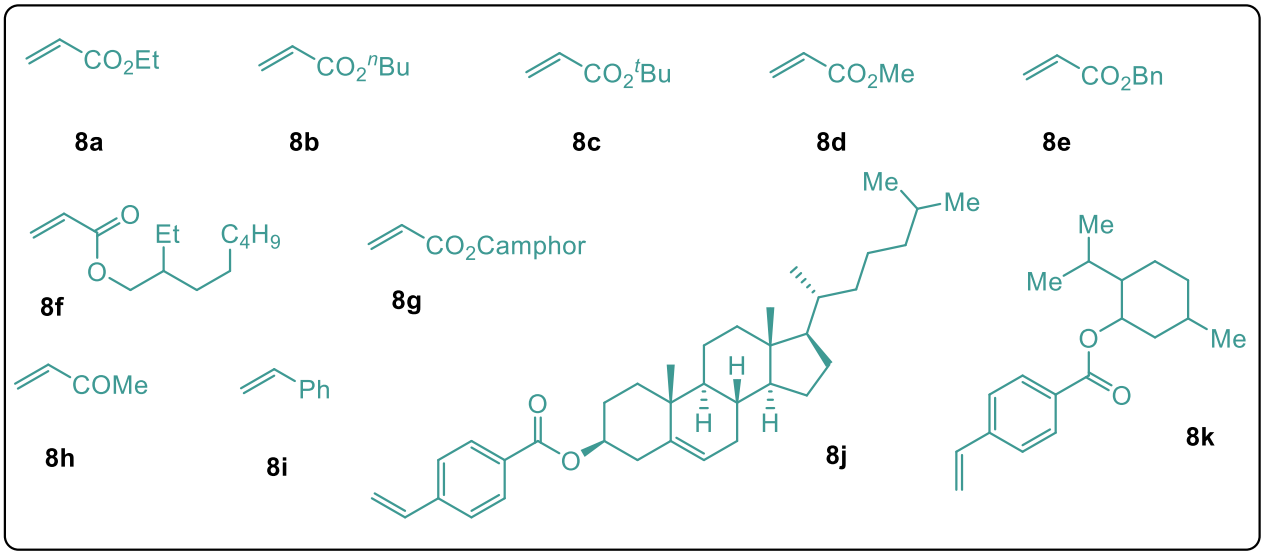


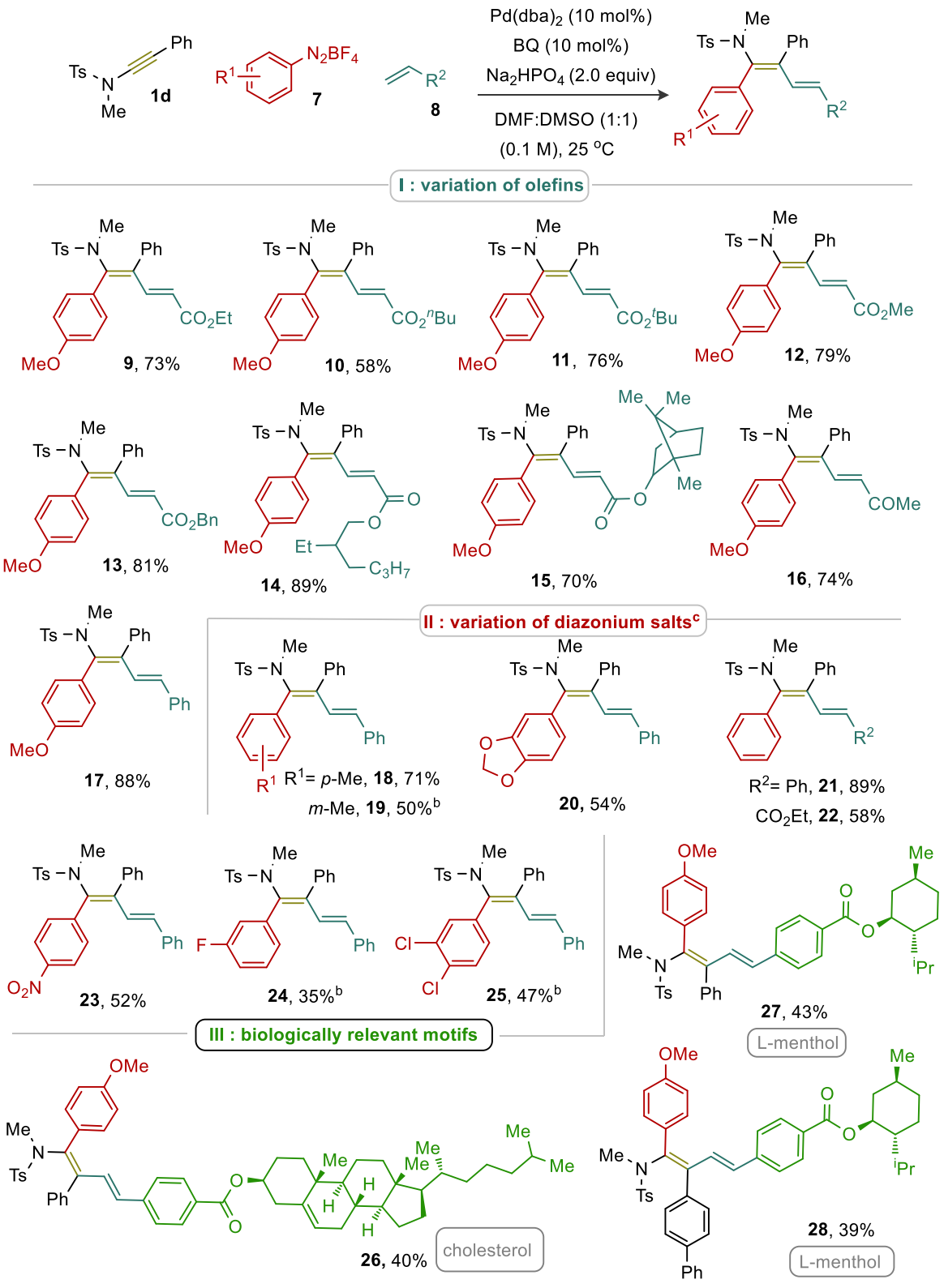
Table 3B.4. Aryl boronic acid chart



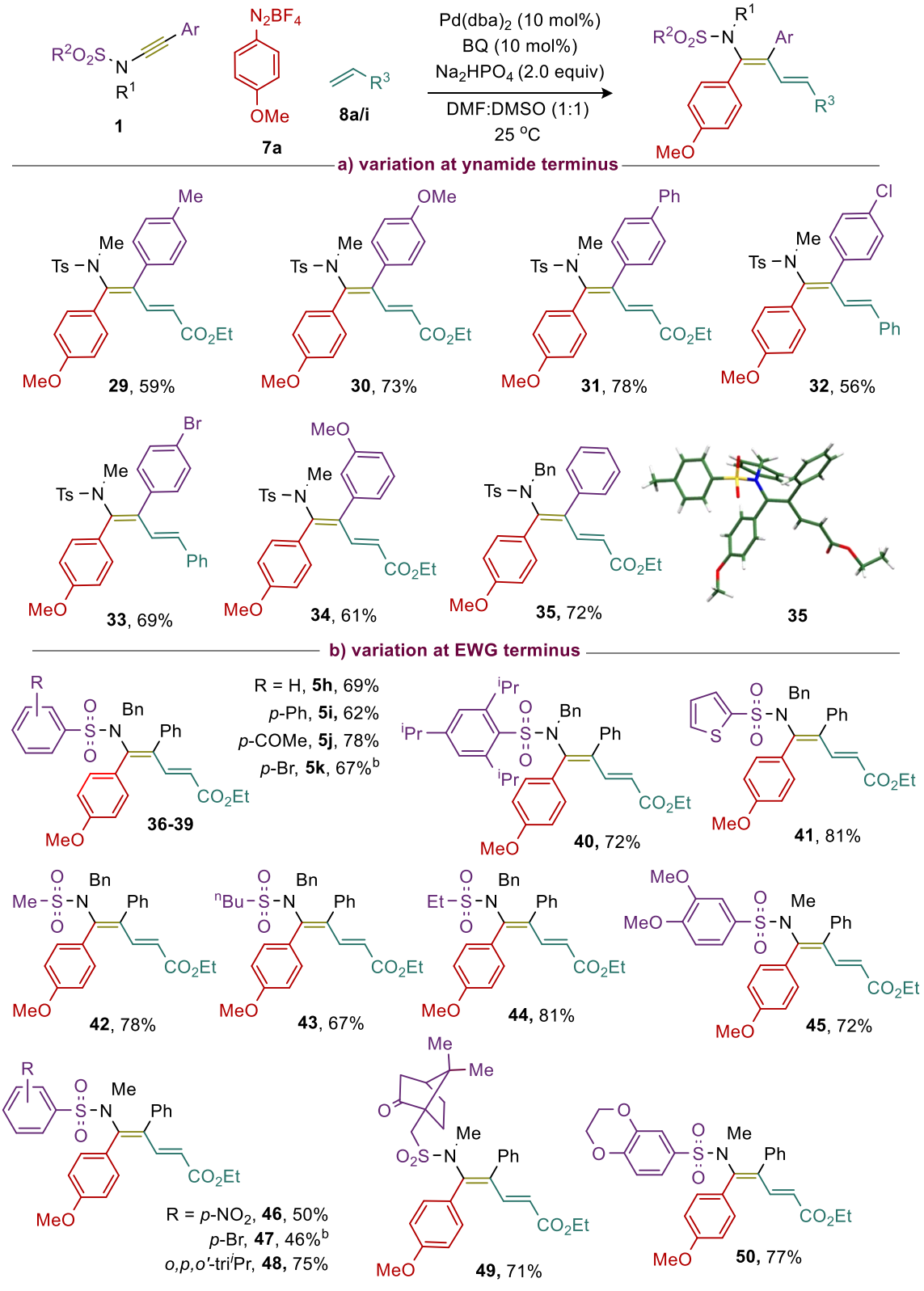
3B.4.3. Substrate Scope

We then probed the compatibility of various olefin partners in this aryl-olefination of ynamides (**Scheme 3B.4-I**). Gratifyingly, the reaction of various [ethyl (**8a**), *n*-butyl (**8b**), *t*-butyl (**8c**), methyl (**8d**), benzyl (**8e**), 2-ethylhexyl (**8f**), isobornyl (**8g**)] substituted acrylates with **1d** and **7a** provided the respective products **9**–**15** in good yields. Although sensitive to polymerization, methyl-vinyl ketone (**8h**) reacted well, delivering **16** in 74% yield. The unactivated styrene (**8i**) was no exception, leading to **17** in 88% yield. Next, we surveyed the scope of aryl diazonium tetrafluoroborates in the coupling of **1d** with ethyl acrylate (**8a**) / styrene (**8i**) (**Scheme 3B.4-II**). The reaction of electron-rich [*p*-Me (**7b**), *m*-Me (**7c**), and 3,4-methylenedioxy (**7d**)] aryl diazonium salts with **1d** and **8i** led to the respective aminodienes **18** (71%), **19** (50%), and **20** (54%). Likewise, the three-component coupling of **1d**, electron-neutral phenyl diazonium salt (**7e**) with **8i** or **8a** resulted in **21** (89%) and **22** (58%). The moderate outcome for **23** and **24** is presumably due to the poor stability of electron-deficient aryl diazonium salts [*p*-NO_2 (**7f**) and *m*-F (**7g**)] in the reaction. The transformable chloro group was tolerated, **25** being isolated in moderate yield (**Scheme 3B.4-II**). Interestingly, biologically relevant cholesterol or menthol molded styrene derivatives were successfully used in this transformation, providing access to **26**–**28** in moderate yields (**Scheme 3B.4-III**).

To broaden the scope of the transformation, the ynamide terminus and N-protected ynamides] was explored (**Scheme 3B.5**). The reaction of ynamides displaying aryl motifs [electron-rich (*p*-Me, *p*-OMe, *p*-Ph, *m*-OMe), labile (*p*-Cl, *p*-Br)] with **7a** and **8a**/**8i** led to the respective highly substituted linear aminodienes **29**–**34** in 56–78% yield (**Scheme 3B.5a**). The *N*-Ts/Bn protected ynamide underwent *syn*-aryl-olefination to furnish **35**; single crystal X-ray analysis confirmed its structure.[11] Next, the coupling of various *N*-sulfonyl protected ynamides **1** with **7a** and **8a** allowed the synthesis of a range of desired aminodienes **5h**–**5v** [N-Bn-{$SO_2C_6H_5$ (**36**) / $SO_2C_6H_4$-*p*-Ph (**37**) / $SO_2C_6H_4$-*p*-COMe (**38**)/ $SO_2C_6H_4$-*p*-Br (**39**) / $SO_2C_6H_2$-*o,p,o'*-triisopropryl (**40**) / SO_2-2-thienyl (**41**) / SO_2Me (**42**) / $SO_2{}^nBu$ (**43**) / SO_2Et (**44**)}] and N-Me-[$SO_2C_6H_3$-*m,p*-diOMe (**45**) / $SO_2C_6H_4$-*p*-NO_2 (**46**)



Scheme 3B.4. Scope of olefins and aryl-diazonium salts.

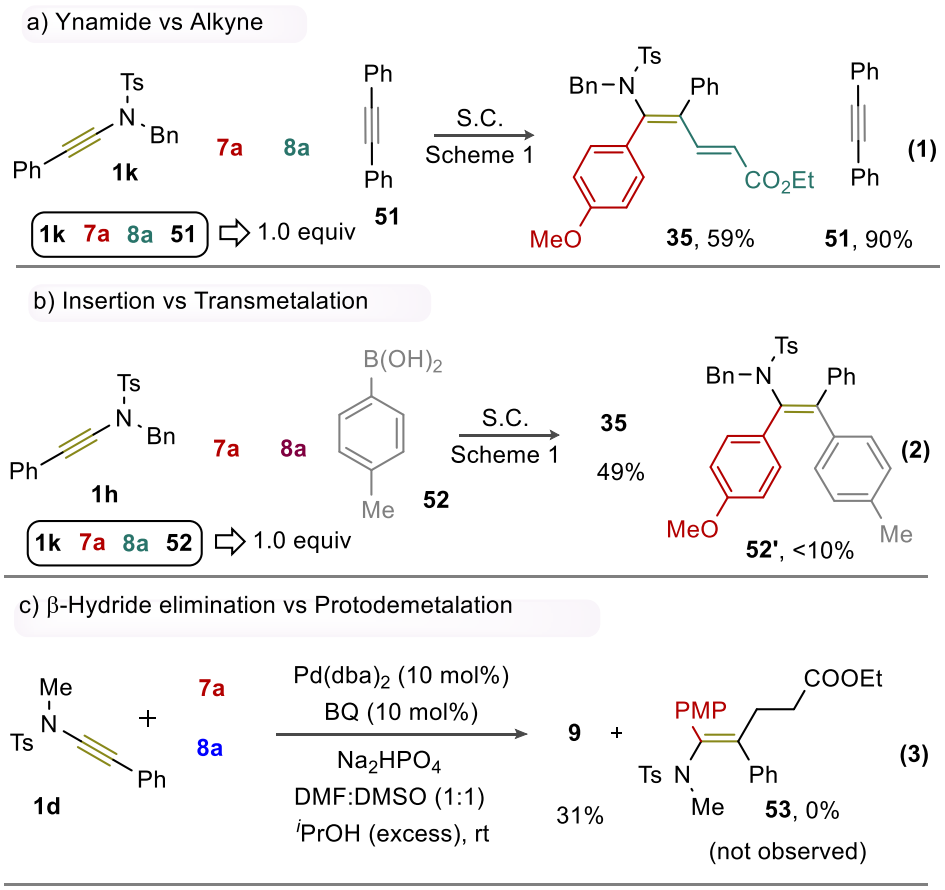


Scheme 3B.5. Scope of ynamides.

/ $SO_2C_6H_4$-*p*-Br (**47**) / $SO_2C_6H_2$-*o,p,o'*-triisopropryl (**48**) / SO_2-camphor (**49**) / $SO_2C_6H_3$-*m,p*-ethylenedioxy (**50**)] in moderate to good yields (**Scheme 3B.5-b**).

3B.4.4. Control Experiments

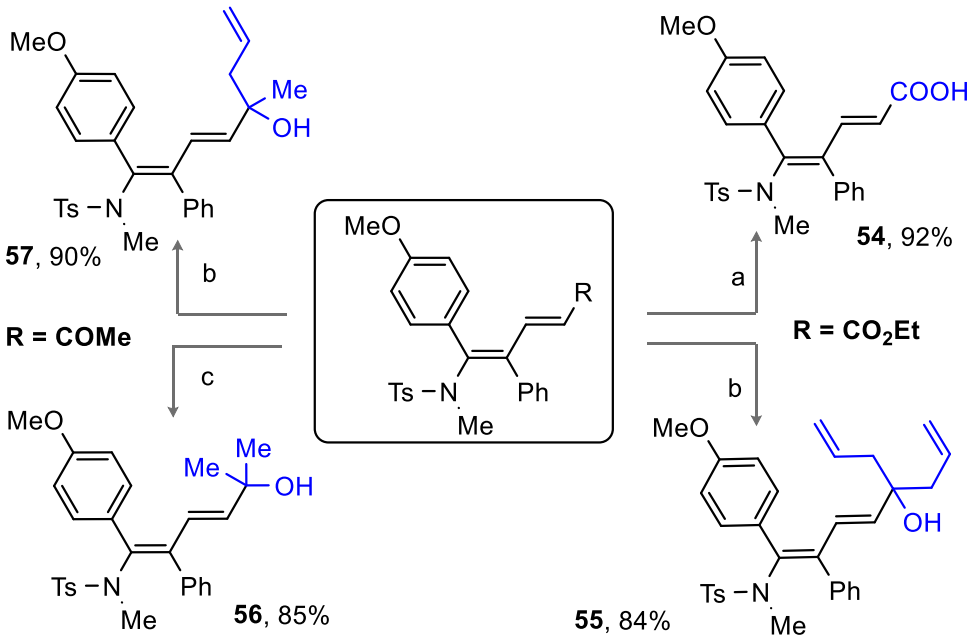
To gain mechanistic insights, a few control experiments were carried out (**Scheme 3B.6**). Among the alkyne derivatives, chemoselectivity of the reaction is in favor of ynamide **1k** over 1,2-diphenylacetylene (**51**), producing **35** (59%) while leaving **51** intact (eq 1). The reaction of **1k**, **7a**, **8a** along with *p*-tolyl boronic acid (**52**) under the standard conditions led to **35** (49%) and **52'** (<10%). This shows that olefin insertion is favored over transmetalation between the aryl boronic acid and the alkenyl-Pd cationic species (eq 2). The absence of protodemetalation product **53** from an identical reaction of **1d**, **7a**, and **8a** performed in isopropanol demonstrates the facile β-hydride elimination (eq 3). This also supports that the carbopalladation of the ynamide by the aryl-Pd moiety is favored over the Heck reaction with the olefin.



Scheme 3B.6. Control experimrnts

3B.4.5. Synthetic Applications

The robustness of this catalytic system has been tested in the gram scale preparation of product **9** (0.95 g, 1.93 mmol, 55%) from **1d** (1.00 g, 3.51 mmol). Further synthetic elaboration of aminodienes was probed and the results are summarized in **Scheme 3B.7**. The base-mediated hydrolysis of the ester led to the respective vinyl-carboxylic acid **54** in 92% yield (conditions a). The respective diallylated 3°-alcohol **55** (84%) was accessed from the allylation of the ester moiety in presence of CuBr (10 mol%) (conditions b). Likewise, Cu-assisted reaction of allyl/methyl-Grignard reagent with the keto moiety of aminodiene **16** afforded the alcohols **56** (85%; conditions c) and **57** (90%; conditions b), respectively.



Scheme 3B.7. Synthetic Applications. [a]Reaction conditions: a) NaOH (10% solution)/MeOH at 120 °C. b) CuBr (10 mol%), allylMgCl (2.0 M in THF, 3.0 equiv), rt. c) CuBr (10 mol%), MeMgBr [1.2 M in THF:toluene (1:3), 3.0 equiv], rt.

3B.4.6. DFT Calculations

To gain insights into the mechanism of the 1,2-*syn*-aryl-alkenylation of ynamides, DFT computations were performed at the M06L/def2-TZVPP//BP86/LANL2DZ(Pd);6-31G(d,p) level of theory. Compounds **1d**, **7a** (cationic part), and ethyl acrylate (**8a**) were used in the calculations of the free energy profile (**Figure 3B.3**). The transformation begins with the interaction of the active catalytic species Pd(dba)(DMSO), **7a**, and benzoquinone. The process is strongly exergonic (–65.2 kcal/mol), providing complex **A**. Next, replacement of dba by ynamide **1d** provides the keteniminium intermediate **B**, with the release of 4.8 kcal/mol of free energy.[R] Subsequent 1,3-migration of the aryl group from Pd to the iminium fragment takes place via transition state **C-ts**, with an energy barrier of 13.4 kcal/mol, and delivers the Pd-enamide complex **D** (–76.6 kcal/mol). This insertion is the rate-determining step of the mechanism. The coordination of **8a** to the Pd-center then generates intermediate **E**, a step which is exergonic by 9.2 kcal/mol. The migratory insertion of the acrylate to Pd-species **E** appears flexible and would possibly provide products with different configu-rations (*Z*,*E*-**9** or *Z*,*Z*-**9**). The free energy profile for the formation of *Z*,*E*-**9** is shown as black lines. The insertion of **8a** into the Pd-C(sp^2) bond faces an energy barrier of 16.8 kcal/mol to reach the four-membered ring transition state ^{Z,E}**F**-ts and generates complex ^{Z,E}**G** with the release of 9.1 kcal/mol of free energy. β-Hydride elimination provides intermediate ^{Z,E}**I** via transition state ^{Z,E}**H**-ts; this step is endergonic by 11.1 kcal/mol, with an energy barrier of 11.2 kcal/mol. Finally, release of Pd-H species **J** from ^{Z,E}**I** provides the expected product ^{Z,E}**9**. The base would then assist the regeneration of active catalyst from **J**. The free energy of ^{Z,E}**9** and **J** may seem quite high compared to ^{Z,E}**G**. However, **J** is an unsaturated species that will be taken care of by the ligands available in the mixture, which should greatly ease the release of ^{Z,E}**9** from the coordination sphere of Pd. Since *Z*,*E*-conjugated dienes are mainly observed experimentally, the formation of *Z*,*Z*-conjugated dienes is expected to be energetically less favorable. The grey profile is consistent with the experimental outcome. The insertion of the acrylate into the Pd–C(sp^2) single bond of intermediate **E** to form complex ^{Z,Z}**G** via transition state ^{Z,Z}**F**-ts requires 17.9 kcal/mol of free energy of activation and is exergonic

by 8.1 kcal/mol. Considering the other steps, this grey pathway is indeed less favorable than the black one towards ^{Z,E}**G**. The stereoselectivity is actually mainly controlled by the steric demand during the acrylate insertion step. There is a significant hindrance between the ethyl group and the benzoquinone ligand in ^{Z,Z}**F**-ts, which is probably the reason for the high activation energy.

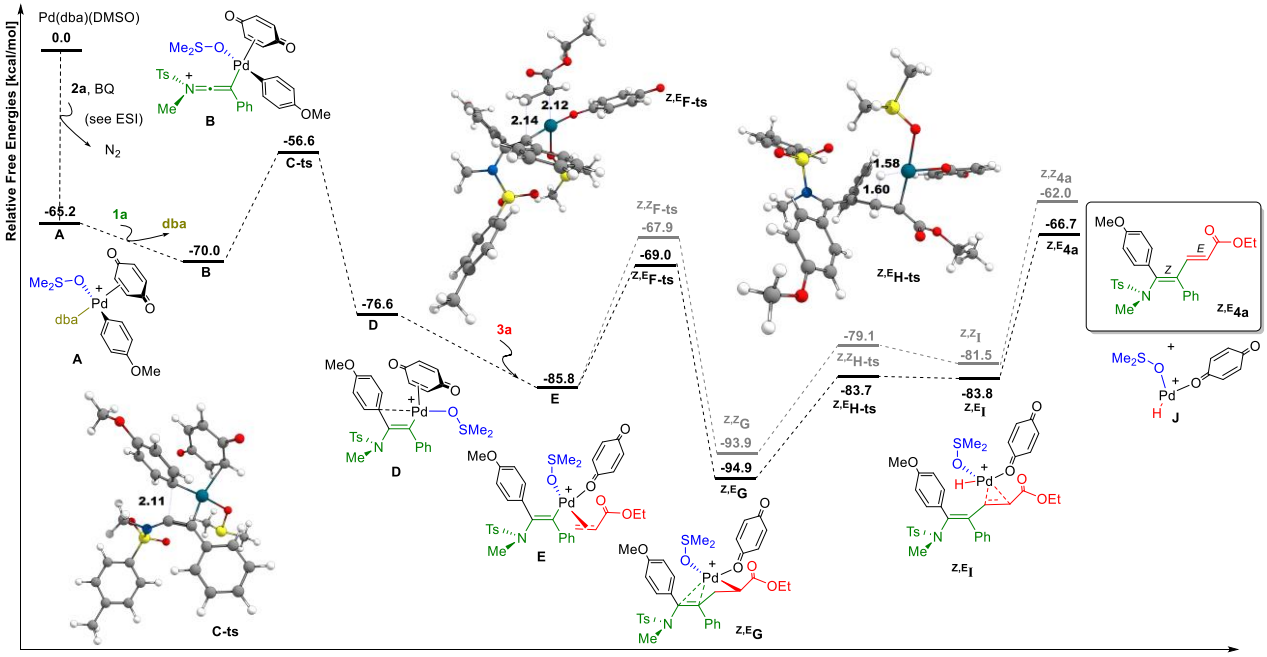


Figure 3B.3: DFT Calculations

3B.5. Conclusion

In summary, a *syn*-1,2-aryl-alkenylation of ynamides has been developed by making two diverse C(sp^2)–C(sp^2) bonds between ynamides, arenes, and olefins. The transformation involves β-nucleophilic attack of the ynamide to a cationic aryl-Pd(II) species, *syn*-1,3-aryl migration, and olefin insertion into the vinyl-Pd-species as main steps. The reaction provides access to β-alkenylated linear conjugated aminodienes, complimentary to the known α-alkenylated enamides. The entire process is regio- as well stereoselective; DFT studies endorse this outcome. This process is even successful on the gram-scale, featuring broad scope with labile functional groups tolerance and making 42 unusual molecular

scaffolds of structural diversity. The current finding is synthetically important and will certainly help to unravel novel difunctionalizations of ynamides.

3B.6. Experimental Section

3B.6.1. General Information

All the reactions were performed in oven-dried Schlenk flasks. Commercial grade solvents were distilled prior to use. Column chromatography was performed using either 100–200 Mesh or 230–400 Mesh silica gel or neutral alumina. Thin layer chromatography (TLC) was performed on silica gel GF254 plates and alumina plates.

Proton, carbon, and fluorine nuclear magnetic resonance spectra (^{1}H NMR, ^{13}C NMR, and ^{19}F NMR) were recorded based on the resonating frequencies as follows: (^{1}H NMR, 400 MHz; ^{13}C NMR, 101 MHz; ^{19}F NMR, 376 MHz) and (^{1}H NMR, 500 MHz; ^{13}C NMR, 126 MHz; ^{19}F NMR, 470 MHz) having the solvent resonance as internal standard (^{1}H NMR, $CDCl_3$ at 7.26 ppm; ^{13}C NMR, $CDCl_3$ at 77.0 ppm). In few cases, tetramethylsilane (TMS) was used as reference standard (at 0.00 ppm). Data for ^{1}H NMR are reported as follows: chemical shift (ppm), multiplicity (s = singlet; bs= broad singlet; d = doublet; bd = broad doublet, t = triplet; bt = broad triplet; q = quartet; m = multiplet), coupling constants, *J*, in (Hz), and integration. Data for ^{13}C NMR, ^{19}F NMR are reported in terms of chemical shift (ppm). IR spectra are reported in cm^{-1}. High resolution mass spectra were obtained in ESI mode. Melting points were determined by electro-thermal heating and are uncorrected. X-ray data was collected at 293 K using graphite monochromated Mo-Kα radiation (0.71073 Å).

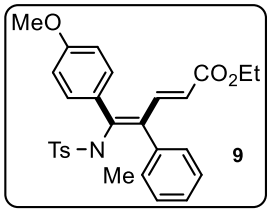
3B.6.2. Materials: Unless otherwise noted, all the reagents and intermediates were obtained commercially and used without purification. 1,2-Dichloroethane ($ClCH_2CH_2Cl$, DCE), acetone, toluene, and 1,4-dioxane were distilled over CaH_2 and THF, DMF, and DMSO were used as received. $Pd(dba)_2$ was purchased from commercially available source, and used as received. Commericially available olefins and other reagents were purchased and directly used without purification. Following a known procedure, ynamides (**1d-1z**) were prepared. Analytical and spectral data of all the known compounds are exactly matching with the reported values.

3B.6.3. General procedure and spectral/analytical data

3B.6.3.1. General Procedure for aryl-alkenylation.

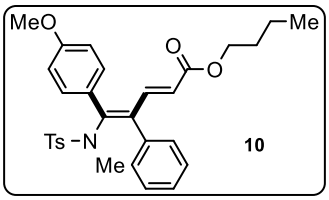
To a solution of ynamide **1d-1z** (0.2 mmol, 1.0 equiv) and aryldiazonium salt **7** (0.30 mmol, 1.5 equiv), and alkene **8** (0.4 mmol, 2.0 equiv) in DMF:DMSO (1:1) or THF (0.1M) was added $Pd(dba)_2$ (10 mol%), benzoquinone (BQ) (10 mol%) and Na_2HPO_4 (2.0 equiv) at 0 °C. The resulting mixture was stirred at rt (25 °C) for 12 h. Progress of the reaction was monitored periodically by TLC. Upon completion, the reaction mixture was diluted with ethyl acetate (10 mL). The crude mixture was filtered through a small pad of Celite and concentrated under reduced pressure. The crude residue was purified through column chromatography on neutral alumina to provide **9-50**. (**Note: The reactions are heat sensitive**)

(2*E*,4*Z*)-Ethyl 5-(*N*,4-dimethylphenylsulfonamido)-5-(4-methoxyphenyl)-4-phenylpenta-2,4-dienoate (9)



9 (107 mg, 73%) as yellow solid. mp = 158–159 °C; R_f = 0.32 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, J = 15.5 Hz, 1H), 7.44–7.33 (m, 5H), 7.17 (d, J = 8.5 Hz, 2H), 7.01 (q, J = 8.5 Hz, 4H), 6.80 (d, J = 9.0 Hz, 2H), 5.59 (d, J = 15.5 Hz, 1H), 4.10 (q, J = 7.0 Hz, 2H), 3.84 (s, 3H), 2.68 (s, 3H), 2.34 (s, 3H), 1.20 (t, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 160.4, 145.2, 145.0, 142.9, 137.3, 136.5, 136.2, 132.2, 130.1, 129.0, 128.6, 128.3, 127.8, 127.3, 121.9, 113.5, 60.2, 55.3, 38.0, 21.4, 14.1; IR (Neat) ν_{max} 2939, 1697, 1611, 1600, 1509, 1342, 1249, 1149 cm^{-1}; **HRMS (ESI)** for $C_{28}H_{30}NO_5S$ $(M+H)^+$: calcd. 492.1845, found 492.1846.

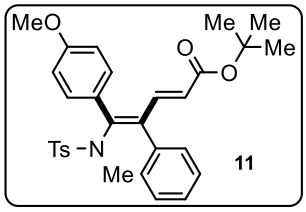
(2*E*,4*Z*)-Butyl 5-(*N*,4-dimethylphenylsulfonamido)-5-(4-methoxyphenyl)-4-phenylpenta-2,4-dienoate (10):



10 (90 mg, 58%) as yellow solid. mp = 158–159 °C; R_f = 0.40 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 15.6 Hz, 1H), 7.44–7.33 (m, 5H), 7.17 (d, J = 8.4 Hz, 2H), 7.01 (q, J = 8.4 Hz, 4H), 6.80 (d, J = 8.8 Hz, 2H), 5.60 (d, J = 15.6 Hz, 1H), 4.05 (t, J = 6.8 Hz, 2H), 3.85 (s, 3H), 2.68 (s, 3H), 2.35 (s, 3H), 1.60–1.50 (m, 2H), 1.34–1.24 (m, 2H), 0.88 (t, J = 7.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 160.4,

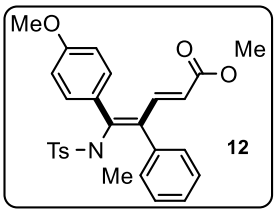
145.2, 145.0, 142.9, 137.3, 136.5, 136.2, 132.2, 130.1, 129.0, 128.6, 128.4, 127.8, 127.3, 121.9, 113.5, 64.1, 55.3, 38.0, 30.6, 21.4, 19.1, 13.6; IR (Neat) ν_{max} 2958, 1703, 1599, 1508, 1247, 1157 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{34}NO_5S$ $(M+H)^+$: calcd. 520.2158, found 520.2157.

(2*E*,4*Z*)-Tert-butyl-5-(*N*,4-dimethylphenylsulfonamido)-5-(4-methoxyphenyl)-4-phenylpenta-2,4-dienoate (11):



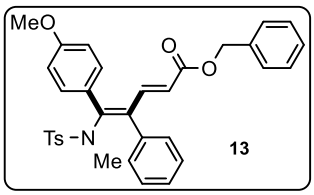
11 (118 mg, 76%) as yellow solid. mp = 177–178 °C; R_f = 0.37 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, J = 15.5 Hz, 1H), 7.44–7.40 (m, 2H), 7.37 (bd, J = 7.0 Hz, 3H), 7.17 (d, J = 8.5 Hz, 2H), 7.00 (q, J = 8.5 Hz, 4H), 6.79 (d, J = 9.0 Hz, 2H), 5.51 (d, J = 15.5 Hz, 1H), 3.84 (s, 3H), 2.67 (s, 3H), 2.34 (s, 3H), 1.39 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4, 160.3, 144.8, 143.9, 142.8, 137.4, 136.6, 136.5, 132.1, 130.1, 129.0, 128.5, 128.5, 128.4, 127.7, 127.3, 123.8, 113.5, 80.1, 55.3, 38.0, 28.1, 21.4; IR (Neat) ν_{max} 2973, 1703, 1604, 1508, 1149 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{34}NO_5S$ $(M+H)^+$: calcd. 520.2158, found 520.2156.

(2*E*,4*Z*)-Methyl 5-(*N*,4-dimethylphenylsulfonamido)-5-(4-methoxyphenyl)-4-phenylpenta-2,4-dienoate (12):



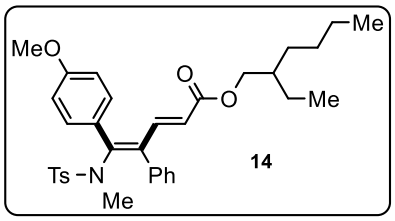
12 (113 mg, 79%) as yellow solid. mp = 186–187 °C; R_f = 0.30 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, J = 15.5 Hz, 1H), 7.43–7.32 (m, 5H), 7.17 (d, J = 8.5 Hz, 2H), 7.01 (q, J = 8.5 Hz, 4H), 6.80 (d, J = 8.5 Hz, 2H), 5.59 (d, J = 15.5 Hz, 1H), 3.84 (s, 3H), 3.64 (s, 3H), 2.68 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.4, 160.4, 145.4, 145.2, 142.9, 137.3, 136.6, 136.2, 132.2, 130.1, 129.0, 128.5, 128.4, 127.8, 127.3, 121.5, 113.6, 55.3, 51.3, 38.0, 21.3; IR (Neat) ν_{max} 2951, 1702, 1600, 1507, 1434, 1343, 1280, 1161 cm^{-1}; **HRMS (ESI)** for $C_{27}H_{28}NO_5S$ $(M+H)^+$: calcd. 478.1688, found 478.1688.

(2*E*,4*Z*)-Benzyl 5-(*N*,4-dimethylphenylsulfonamido)-5-(4-methoxyphenyl)-4-phenylpenta-2,4-dienoate (13):



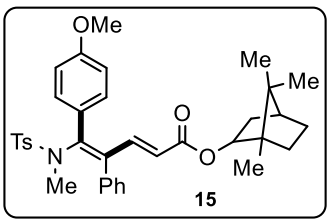
13 (134 mg, 81%) as yellow solid. mp = 138–139 °C; R_f = 0.30 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 15.6 Hz, 1H), 7.44–7.35 (m, 5H), 7.33–7.29 (m, 4H), 7.28–7.26 (m, 1H), 7.19 (d, J = 8.4 Hz, 2H), 7.06–6.99 (m, 4H), 6.81 (d, J = 8.8 Hz, 2H), 5.65 (d, J = 15.6 Hz, 1H), 5.11 (s, 2H), 3.86 (s, 3H), 2.69 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 160.4, 145.7, 145.6, 142.9, 137.2, 136.5, 136.1, 136.0, 132.2, 130.1, 129.0, 128.6, 128.42, 128.35, 128.04, 127.99, 127.8, 127.4, 121.3, 113.5, 66.0, 55.3, 38.0, 21.4; IR (Neat) ν_{max} 2919, 1700, 1601, 1509, 1339, 1251 cm^{-1}; **HRMS (ESI)** for $C_{33}H_{32}NO_5S$ $(M+H)^+$: calcd. 554.2001, found 554.2006.

(2*E*,4*Z*)-2-Ethylhexyl 5-(*N*,4-dimethylphenylsulfonamido)-5-(4-methoxyphenyl)-4-phenylpenta-2,4-dienoate (14):



14 (153 mg, 89%) as yellow solid. mp = 127–128 °C; R_f = 0.50 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, J = 15.5 Hz, 1H), 7.44–7.34 (m, 5H), 7.18 (d, J = 8.5 Hz, 2H), 7.01 (q, J = 8.5 Hz, 4H), 6.79 (d, J = 9.0 Hz, 2H), 5.58 (d, J = 15.5 Hz, 1H), 4.01–3.92 (m, 2H), 3.84 (s, 3H), 2.68 (s, 3H), 2.34 (s, 3H), 1.54–1.46 (m, 1H), 1.31–1.18 (m, 8H), 0.87–0.80 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.1, 160.4, 145.2, 144.91, 142.88, 137.2, 136.6, 136.2, 132.2, 130.1, 129.0, 128.6, 128.4, 127.8, 127.3, 121.9, 113.5, 66.6, 55.3, 38.7, 38.0, 30.3, 28.8, 23.7, 22.8, 21.4, 13.9, 10.9, 0.9; IR (Neat) ν_{max} 2958, 2925, 1702, 1602, 1246,1160 cm^{-1}; **HRMS (ESI)** for $C_{34}H_{42}NO_5S$ $(M+H)^+$: calcd. 576.2784, found 576.2781.

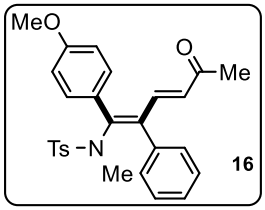
(2*E*,4*Z*)-(1R,4S)-1,7,7-Trimethylbicyclo[2.2.1]heptan-2-yl 5-(*N*,4-dimethylphenylsulfonamido)-5-(4-methoxyphenyl)-4-phenylpenta-2,4-dienoate (15):



15 (126 mg, 70%) as yellow solid. mp = 190–191 °C; R_f = 0.41 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (d, J = 16.0 Hz, 1H), 7.43–7.33 (m, 5H), 7.18 (d, J = 8.5 Hz, 2H), 7.01 (q, J = 8.5 Hz, 4H), 6.79 (d, J = 8.5 Hz, 2H), 5.54 (d, J = 15.5 Hz, 1H), 4.68–4.60

(m, 1H), 3.85 (s, 3H), 2.67 (s, 3H), 2.34 (s, 3H), 1.80–1.61 (m, 3H), 1.54–1.46 (m, 1H), 1.13–1.00 (m, 2H), 0.91–0.80 (m, 1H), 0.77 (s, 3H), 0.74 (s, 3H), 0.72 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.3, 160.3, 144.9, 144.4, 142.9, 137.0, 136.4, 136.3, 132.1, 130.1, 129.0, 128.6, 128.4, 127.8, 127.3, 122.3, 113.5, 80.7, 55.3, 48.7, 46.7, 44.9, 38.7, 37.9, 33.6, 26.9, 21.4, 20.0, 19.8, 11.4; IR (Neat) ν_{max} 2951, 1698, 1603, 1508, 1248, 1159 cm^{-1}; **HRMS (ESI)** for $C_{36}H_{41}NNaO_5S$ $(M+Na)^+$: calcd. 622.2603, found 622.2598.

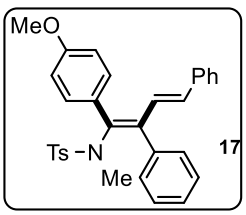
***N*-((1*Z*,3*E*)-1-(4-Methoxyphenyl)-5-oxo-2-phenylhexa-1,3-dien-1-yl)-*N*,4-dimethylbenzenesulfonamide (16):**



16 (102 mg, 74%) as yellow gummy solid; R_f = 0.25 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74–7.71 (m, 1H), 7.46–7.31 (m, 5H), 7.23 (d, J = 8.5 Hz, 2H), 7.04 (q, J = 8.5 Hz, 4H), 6.84 (d, J = 8.5 Hz, 2H), 5.80 (d, J = 16.0 Hz, 1H), 3.87 (s, 3H), 2.70 (s, 3H), 2.37 (s, 3H), 2.13 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.5, 160.5, 145.8, 144.2, 143.0, 137.1, 136.29, 136.27, 132.3, 130.6, 130.1, 129.6, 129.0, 128.6, 128.3, 127.8, 127.3, 127.2, 113.5, 55.3, 37.9, 27.5, 21.4; IR (Neat) ν_{max} 3300, 2921, 1680, 1576, 1250, 1158 cm^{-1}; **HRMS (ESI)** for $C_{27}H_{28}NO_4S$ $(M+H)^+$: calcd. 462.1739, found 462.1739.

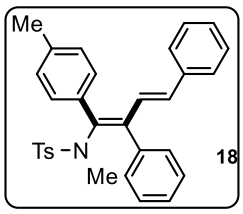
Minor isomer 4h' (inseparable): ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.72 (s, 0.42H), 3.13 (s, 0.35H).

***N*-((1*Z*,3*E*)-1-(4-methoxyphenyl)-2,4-diphenylbuta-1,3-dien-1-yl)-*N*-4-dimethylbenzene-sulfonamide (17):**



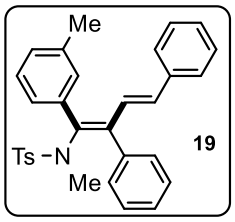
17 (130 mg, 88%) as light-yellow solid. mp = 190–191 °C; R_f = 0.62 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, J = 7.0 Hz, 2H), 7.46 (d, J = 8.0 Hz, 1H), 7.44–7.41 (m, 1H), 7.32 (d, J = 8.5 Hz, 2H), 7.25 (d, J = 7.5 Hz, 2H), 7.21–7.15 (m, 3H), 7.08 (d, J = 16.0 Hz, 1H), 7.02 (q, J = 8.5 Hz, 5H), 6.85 (d, J = 9.0 Hz, 2H), 6.25 (d, J = 16.0 Hz, 1H), 3.88 (s, 3H), 2.73 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.5, 142.5, 139.3, 138.4, 138.3, 137.3, 136.6, 133.3, 132.0, 130.3, 129.3, 129.1, 128.9, 128.4, 128.3, 127.42, 127.38, 127.3, 126.4, 113.3, 55.2, 37.7, 21.3; IR (Neat) ν_{max} 3031, 2931, 1605, 1507, 1333, 1249, 1148 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{30}NO_3S$ $(M+H)^+$: calcd. 496.1946, found 496.1946.

_N_-((1_Z_,3_E_)-2,4-Diphenyl-1-(_p_-tolyl)buta-1,3-dien-1-yl)-_N_,4-dimethylbenzenesulfonamide (18):



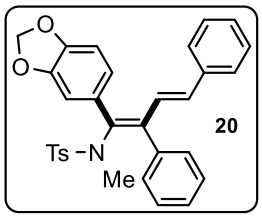
18 (102 mg, 71%) as yellow solid. mp = 214–215 °C; R_f = 0.62 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49–7.44 (m, 4H), 7.43–7.38 (m, 2H), 7.25–7.21 (m, 3H), 7.20–7.16 (m, 3H), 7.11 (d, J = 7.5 Hz, 2H), 7.06 (d, J = 16.0 Hz, 1H), 7.01–6.96 (m, 4H), 6.22 (d, J = 16.0 Hz, 1H), 2.71 (s, 3H), 2.42 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.5, 140.0, 138.7, 138.5, 138.2, 137.4, 136.8, 133.9, 133.6, 130.6, 130.4, 129.4, 128.8, 128.7, 128.5, 128.3, 127.50, 127.45, 126.6, 37.8, 21.4, 21.3; IR (Neat) ν_{max} 3026, 2922, 1507, 1489, 1442, 1337, 1147 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{30}NO_2S$ $(M+H)^+$: calcd. 480.1997, found 480.1998.

N-((1_Z_,3_E_)-2,4-Diphenyl-1-(_m_-tolyl)buta-1,3-dien-1-yl)-_N_,4-dimethylbenzenesulfonamide (19):



19 (72 mg, 50%) as yellow solid. mp = 160–161 °C; R_f = 0.58 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 7.2 Hz, 2H), 7.51 (t, J = 7.2 Hz, 2H), 7.49–7.45 (m, 1H), 7.29–7.26 (m, 4H), 7.24 (s, 1H), 7.23–7.18 (m, 3H), 7.13–7.02 (m, 6H), 6.29 (d, J = 16.0 Hz, 1H), 2.79 (s, 3H), 2.39 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.5, 140.0, 138.8, 138.2, 137.5, 137.3, 136.8, 136.5, 133.6, 130.7, 130.4, 129.1, 129.0, 128.8, 128.5, 128.4, 128.3, 127.9, 127.52, 127.49, 127.2, 126.5, 38.0, 21.3, 21.2; IR (Neat) ν_{max} 3027, 2922, 1598, 1490, 1339, 1152 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{30}NO_2S$ $(M+H)^+$: calcd. 480.1997, found 480.1997.

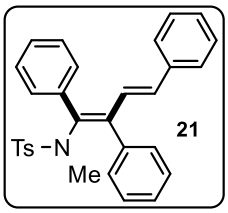
_N_-((1_Z_,3_E_)-1-(Benzo[d][1,3]dioxol-5-yl)-2,4-diphenylbuta-1,3-dien-1-yl)-_N_,4-dimethylbenzenesulfonamide (20):



20 (82 mg, 54%) as yellow solid. mp = 186–187 °C; R_f = 0.50 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49–7.40 (m, 5H), 7.23 (d, J = 7.0 Hz, 2H), 7.19 (t, J = 7.5 Hz, 3H), 7.07–7.02 (m, 5H), 6.91 (dd, J = 8.0 Hz, 1.5 Hz, 1H), 6.80–6.75 (m, 2H), 6.23 (d, J = 16.0 Hz, 1H), 5.99 (s, 2H), 2.72 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.6, 147.4, 142.7, 139.8, 138.3, 138.1, 137.3, 136.8, 133.6, 130.7, 130.4, 129.2, 128.9, 128.5, 128.3, 127.6,

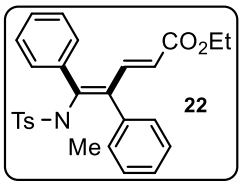
127.5, 127.3, 126.5, 125.5, 110.5, 107.8, 101.2, 37.9, 21.4; IR (Neat) ν_{max} 2897, 1597, 1483, 1434, 1340, 1152 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{27}NNaO_4S$ $(M+Na)^+$: calcd. 532.1558, found 532.1558.

***N*,4-Dimethyl-*N*-((1*Z*,3*E*)-1,2,4-triphenylbuta-1,3-dien-1-yl)benzenesulfonamide (21):**



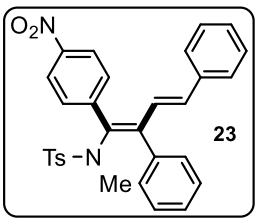
21 (124 mg, 89%) as yellow solid. mp = 215–216 °C; R_f = 0.64 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, J = 16.0 Hz, 1H), 7.67–7.63 (m, 1H), 7.55–7.51 (m, 1H), 7.48 (t, J = 7.0 Hz, 2H), 7.45–7.41 (m, 2H), 7.40–7.37 (m, 2H), 7.35–7.32 (m, 2H), 7.24–7.21 (m, 2H), 7.18 (d, J = 7.0 Hz, 2H), 7.12 (d, J = 16.0 Hz, 1H), 7.06 (dd, J = 16.0 Hz, 2.0 Hz, 1H), 7.01 (d, J = 8.0 Hz, 2H), 6.97 (d, J = 8.5 Hz, 1H), 6.27 (d, J = 16.0 Hz, 1H), 2.74 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.3, 142.6, 140.3, 138.5, 138.2, 137.2, 136.8, 136.6, 133.8, 130.7, 130.3, 129.0, 128.9, 128.5, 128.3, 128.0, 127.6, 127.3, 126.5, 125.4, 37.7, 21.3; IR (Neat) ν_{max} 3025, 2923, 1648, 1592, 1337 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{27}NNaO_2S$ $(M+Na)^+$: calcd. 488.1660, found 488.1661.

(2*E*,4*Z*)-Ethyl 5-(*N*,4-dimethylphenylsulfonamido)-4,5-diphenylpenta-2,4-dienoate (22):



22 (80 mg, 58%) as yellow solid. mp = 201–202 °C; R_f = 0.37 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, J = 15.5 Hz, 1H), 7.46–7.41 (m, 2H), 7.39 (d, J = 7.5 Hz, 3H), 7.37–7.34 (m, 1H), 7.29 (t, J = 8.0 Hz, 2H), 7.25–7.23 (m, 2H), 7.00 (d, J = 8.0 Hz, 2H), 6.95 (d, J = 8.5 Hz, 2H), 5.61 (d, J = 15.5 Hz, 1H), 4.10 (q, J = 7.0 Hz, 2H), 2.70 (s, 3H), 2.34 (s, 3H), 1.19 (t, J = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 145.2, 144.5, 142.9, 137.3, 137.0, 136.3, 135.8, 130.7, 130.1, 129.1, 129.0, 128.6, 128.1, 127.9, 127.3, 122.6, 60.2, 38.0, 21.4, 14.1; IR (Neat) ν_{max} 2922, 1710, 1611, 1491, 1442, 1344, 1275, 1153 cm^{-1}; **HRMS (ESI)** for $C_{27}H_{28}NO_4S$ $(M+H)^+$: calcd. 462.1739, found 462.1731.

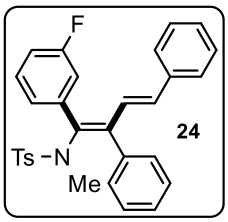
***N*,4-Dimethyl-*N*-((1*Z*,3*E*)-1-(4-nitrophenyl)-2,4-diphenylbuta-1,3-dien-1-yl)benzenesulfonamide (23):**



23 (80 mg, 52%) as yellow solid. mp = 220–221 °C; R_f = 0.62 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, J = 8.5 Hz, 2H), 7.52 (d, J = 8.5 Hz, 2H), 7.45 (s, 5H), 7.25–7.21 (m, 3H), 7.19–7.16 (m, 2H), 7.07–7.00 (m, 4H), 6.93 (d, J = 16.0 Hz, 1H), 6.32 (d, J = 15.5 Hz, 1H),

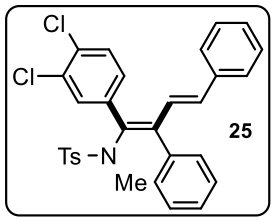
2.73 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.2, 143.9, 143.4, 142.5, 137.4, 136.6, 136.4, 136.2, 135.9, 131.4, 130.2, 129.1, 128.7, 128.5, 128.3, 128.2, 127.7, 127.2, 126.7, 123.3, 38.0, 21.4; IR (Neat) ν_{max} 2922, 1594, 1516, 1443, 1341, 1151 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{27}N_2O_4S$ $(M+H)^+$: calcd. 511.1692, found 511.1688.

***N*-((1*Z*,3*E*)-1-(3-Fluorophenyl)-2,4-diphenylbuta-1,3-dien-1-yl)-*N*,4-dimethylbenzenesulfonamide (24):**



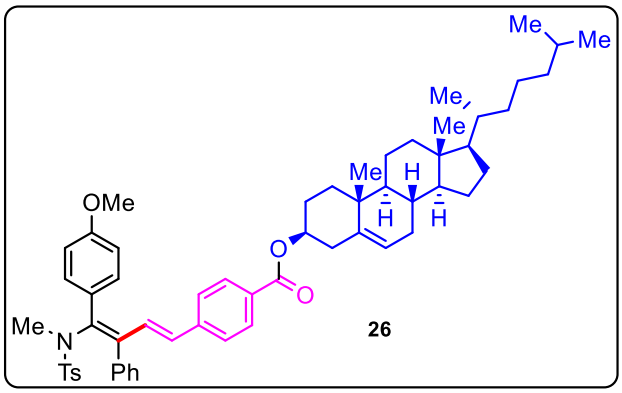
24 (51 mg, 35%) as yellow solid. mp = 201–202 °C; R_f = 0.64 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50–7.41 (m, 5H), 7.34–7.28 (m, 2H), 7.25–7.22 (m, 2H), 7.21–7.18 (m, 2H), 7.17 (s, 1H) 7.07–7.04 (m, 2H), 7.03–7.01 (m, 3H), 7.00–6.96 (m, 2H), 6.28 (d, J = 16.0 Hz, 1H), 2.73 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.5 (d, J = 247 Hz, 1C), 142.9, 141.1, 139.0 (d, J = 7.8 Hz, 1C), 137.9, 137.1, 136.6, 134.7, 130.3, 129.5 (d, J = 7.8 Hz, 1C), 129.0, 128.6, 128.5, 128.4, 127.83, 127.77, 127.2, 126.8 (d, J = 2.5 Hz, 1C), 126.6, 117.2 (d, J = 21 Hz, 1C), 115.2 (d, J = 21 Hz, 1C), 37.8, 21.4; ^{19}F NMR (376 MHz, $CDCl_3$) -113.2; IR (Neat) ν_{max} 2923, 1581, 1482, 1340, 1152 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{27}FNO_2S$ $(M+H)^+$: calcd. 484.1747, found 484.1745.

***N*-((1*Z*,3*E*)-1-(3,4-Dichlorophenyl)-2,4-diphenylbuta-1,3-dien-1-yl)-*N*,4-dimethylbenzenesulfonamide (25):**



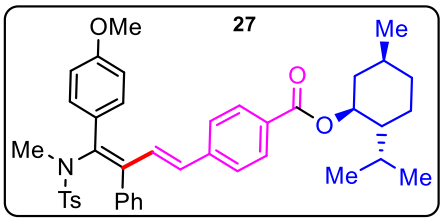
25 (75 mg, 47%) as yellow solid. mp = 190–191 °C; R_f = 0.77 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51–7.42 (m, 5H), 7.41 (d, J = 8.5 Hz, 1H), 7.30–7.26 (m, 2H), 7.24 (s, 1H), 7.21–7.16 (m, 4H), 7.05 (q, J = 8.5 Hz, 4H), 6.94 (d, J = 16.0 Hz, 1H), 6.30 (d, J = 15.5 Hz, 1H), 2.74 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.3, 141.1, 137.5, 136.80, 136.75, 136.6, 135.9, 135.2, 132.3, 131.7, 130.7, 130.2, 129.9, 129.1, 128.6, 128.5, 128.02, 127.96, 127.8, 126.9, 126.7, 38.1, 21.4; IR (Neat) ν_{max} 2923, 1597, 1492, 1344, 1158 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{26}Cl_2NO_2S$ $(M+H)^+$: calcd. 534.1061, found 534.1057.

(3S,8S,9S,10R,13R,14S,17R)-10,13-Dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 4-((1*E*,3*Z*)-4-(N,4-dimethylphenylsulfonamido)-4-(4-methoxyphenyl)-3-phenylbuta-1,3-dien-1-yl)benzoate (26):



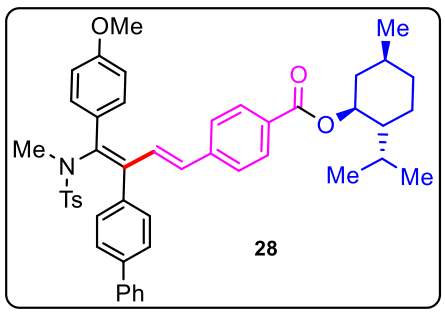
26 (109 mg, 40%) as yellow solid; mp = 213–214 °C; R_f = 0.62 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, J = 8.5 Hz, 1H), 7.85 (d, J = 8.5 Hz, 2H), 7.75 (d, J = 16.0 Hz, 1H), 7.64–7.61 (m, 1H), 7.53 (d, J = 8.5 Hz, 1H), 7.48 (d, J = 9.0 Hz, 1H), 7.44–7.41 (m, 2H), 7.39–7.35 (m, 4H), 7.31–7.28 (m, 2H), 7.17 (d, J = 16.0 Hz, 1H), 7.10 (d, J = 15.5 Hz, 1H), 6.99 (d, J = 16.0 Hz, 1H), 6.91 (d, J = 8.5 Hz, 1H), 5.42 (d, J = 3.5 Hz, 1H), 4.93–4.82 (m, 1H), 3.83 (s, 3H), 3.15 (s, 3H), 2.46 (s, 5H), 2.04–1.96 (m, 3H), 1.95–1.90 (m, 1H), 1.88–1.81 (m, 1H), 1.79–1.70 (m, 1H), 1.64 (s, 1H), 1.61–1.57 (m, 1H), 1.55–1.51 (m, 2H), 1.50–1.44 (m, 2H), 1.41–1.34 (m, 3H), 1.28–1.21 (m, 3H), 1.19–1.11 (m, 5H), 1.08 (s, 3H), 1.05–0.99 (m, 3H), 0.93 (d, J = 6.5 Hz, 3H), 0.89 (d, J = 6.5 Hz, 3H), 0.87 (d, J = 7.0 Hz, 3H), 0.70 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.8, 159.7, 144.8, 143.3, 142.0, 139.7, 134.8, 133.2, 131.4, 130.6, 130.5, 129.9, 129.8, 129.5, 129.1, 129.0, 128.9, 128.8, 128.4, 128.3, 128.2, 128.0, 127.8, 125.9, 125.5, 125.4, 122.7, 122.6, 114.2, 83.9, 74.5, 69.0, 56.7, 56.1, 55.3, 50.0, 42.3, 39.7, 39.5, 39.3, 38.2, 37.0, 36.6, 36.2, 35.8, 31.9, 31.8, 28.2, 28.0, 27.9, 24.3, 23.8, 22.8, 22.5, 21.6, 21.0, 19.4, 18.7, 11.8; IR (Neat) ν_{max} 2933, 2866, 2232, 1704, 1598, 1511, 1448, 1364, 1276, 1165, 1103 cm^{-1}; **HRMS (ESI)** for $C_{59}H_{74}NO_5S$ $(M+H)^+$: calcd. 908.5288, found 908.5148.

(1S,2S,5S)-2-Isopropyl-5-methylcyclohexyl 4-((1*E*,3*Z*)-4-(N,4-dimethylphenylsulfonamido)-4-(4-methoxyphenyl)-3-phenylbuta-1,3-dien-1-yl)benzoate (27):



27 (87 mg, 43%) as yellow gummy liquid; dr = 85:15; R_f = 0.62 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, J = 8.5 Hz, 2H), 7.73–7.62 (m, 1H), 7.46 (d, J = 4.5 Hz, 2H), 7.43–7.39 (m, 1H), 7.29–7.27 (m, 2H), 7.22 (d, J = 8.5 Hz, 2H), 7.15–7.11 (m, 2H), 7.04–6.98 (m, 4H), 6.83 (d, J = 9.0 Hz, 2H), 6.25 (d, J = 15.5 Hz, 1H), 4.95–4.70 (m, 1H), 3.87 (s, 3H), 3.72 (s, 0.52H), 3.28 (s, 0.45H), 2.71 (s, 3H), 2.44 (s, 0.43H), 2.11 (s, 0.55H), 2.35 (s, 3H), 2.12–2.07 (m, 1H), 1.95–1.89 (m, 1H), 1.73–1.69 (m, 2H), 1.56–1.49 (m, 2H), 1.16–1.10 (m, 1H), 1.09–1.01 (m, 1H), 0.91 (d, J = 6.5 Hz, 3H), 0.90 (d, J = 7.0 Hz, 3H), 0.77 (d, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.8, 159.8, 158.9, 143.2, 142.7, 141.7, 139.9, 138.9, 138.2, 136.6, 133.4, 132.1, 132.0, 131.9, 131.7, 130.4, 129.83, 129.79, 129.6, 129.5, 129.3, 129.0, 128.9, 128.5, 128.4, 128.2, 127.6, 127.5, 127.4, 127.1, 126.3, 126.2, 113.4, 55.3, 55.1, 47.2, 40.9, 37.8, 34.3, 33.2, 31.4, 26.4, 23.6, 22.0, 21.6, 21.4, 20.7, 16.5; IR (Neat) ν_{max} 2951, 2861, 2360, 1704, 1599, 1507, 1454, 1434, 1248, 1174, 1157 cm^{-1}; **HRMS (ESI)** for $C_{42}H_{48}NO_5S$ $(M+H)^+$: calcd. 678.3253, found 678.3246.

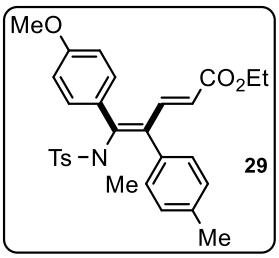
(1S,2S,5S)-2-Isopropyl-5-methylcyclohexyl 4-((1*E*,3*Z*)-3-([1,1'-biphenyl]-4-yl)-4-(N,4-dimethylphenylsulfonamido)-4-(4-methoxyphenyl)buta-1,3-dien-1-yl)benzoate (28):



28 (88 mg, 39%) as yellow offwhite solid; dr = 90:10; mp = 141–142 °C; R_f = 0.50 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, J = 8.5 Hz, 2H), 7.73–7.67 (m, 4H), 7.53–7.49 (m, 4H), 7.43–7.38 (m, 1H), 7.35 (d, J = 8.5 Hz, 2H), 7.26–7.24 (m, 1H), 7.17 (d, J = 16.0 Hz, 1H), 7.14–7.09 (m, 1H), 7.04–6.97 (m, 4H), 6.87 (d, J = 9.0 Hz, 2H), 6.34 (d, J = 16.0 Hz, 1H), 4.95–4.70 (m, 1H), 3.87 (s, 3H), 3.37 (s, 0.33H), 2.78 (s, 3H), 2.29 (s, 3H), 2.12–2.07 (m, 1H), 1.95–1.89 (m, 1H), 1.73–1.65 (m, 3H), 1.56–1.49 (m, 2H), 1.14–1.05 (m, 2H), 0.91 (d, J = 6.5 Hz, 3H), 0.90 (d, J = 7.0 Hz, 3H), 0.77 (d, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.8, 159.8, 142.7, 141.7, 140.5, 140.4, 140.2, 139.8, 138.5, 137.3,

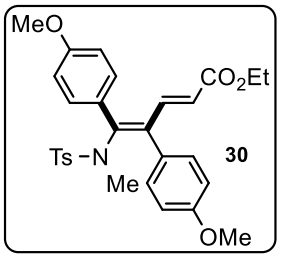
136.6, 132.2, 132.1, 131.9, 131.8, 131.6, 130.8, 129.8, 129.4, 128.9, 128.8, 127.4, 127.3, 127.0, 126.2, 113.5, 74.7, 55.3, 55.1, 47.2, 40.9, 37.8, 34.3, 31.4, 26.4, 23.6, 22.0, 21.4, 20.7, 16.5; IR (Neat) ν_{max} 2951, 2866, 1705, 1599, 1506, 1453, 1453, 1249, 1175, 1157 cm^{-1}; **HRMS (ESI)** for $C_{48}H_{52}NO_5S$ $(M+H)^+$: calcd. 754.3566, found 754.3568.

(2*E*,4*Z*)-Ethyl 5-(*N*,4-dimethylphenylsulfonamido)-5-(4-methoxyphenyl)-4-(p-tolyl)penta-2,4-dienoate (29):



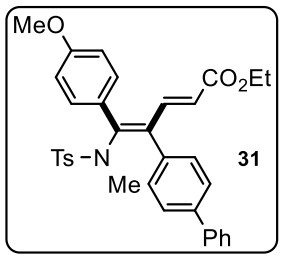
29 (89 mg, 59%) as yellow solid. mp = 166–167 °C; R_f = 0.33 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J = 15.6 Hz, 1H), 7.25–7.18 (m, 4H), 7.15 (d, J = 8.8 Hz, 2H), 7.02 (s, 4H), 6.78 (d, J = 8.8 Hz, 2H), 5.61 (d, J = 15.6 Hz, 1H), 4.10 (q, J = 7.2 Hz, 2H), 3.84 (s, 3H), 2.70 (s, 3H), 2.40 (s, 3H), 2.35 (s, 3H), 1.19 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 160.3, 145.2, 145.0, 142.8, 137.5, 136.7, 136.2, 134.2, 132.1, 130.0, 129.2, 128.9, 128.5, 127.3, 121.8, 113.5, 60.1, 55.3, 38.0, 21.4, 21.3, 14.2; IR (Neat) ν_{max} 2955, 2867, 1700, 1593, 1506, 1467, 1433, 1232, 1161, 1143 cm^{-1}; **HRMS (ESI)** for $C_{29}H_{32}NO_5S$ $(M+H)^+$: calcd. 506.2001, found 506.2002.

(2*E*,4*Z*)-Ethyl 5-(*N*,4-dimethylphenylsulfonamido)-4,5-bis(4-methoxyphenyl)penta-2,4-dienoate (30):



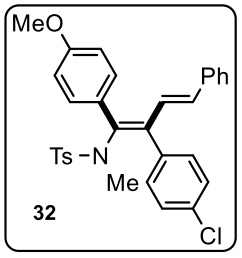
30 (114 mg, 73%) as yellow solid. mp = 168–170 °C; R_f = 0.26 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, J = 15.5 Hz, 1H), 7.29 (d, J = 8.5 Hz, 2H), 7.13 (d, J = 8.5 Hz, 2H), 7.03 (s, 4H), 6.93 (d, J = 8.5 Hz, 2H), 6.78 (d, J = 8.5 Hz, 2H), 5.63 (d, J = 15.5 Hz, 1H), 4.10 (q, J = 7.0 Hz, 2H), 3.85 (s, 3H), 3.84 (s, 3H), 2.72 (s, 3H), 2.35 (s, 3H), 1.20 (t, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.1, 160.3, 159.2, 145.4, 145.0, 142.8, 136.8, 135.7, 132.1, 131.3, 129.3, 128.9, 128.6, 127.2, 121.8, 114.0, 113.5, 60.1, 55.3, 55.2, 38.0, 21.4, 14.2; IR (Neat) ν_{max} 2932, 1698, 1604, 1509, 1364, 1245, 1155 cm^{-1}; **HRMS (ESI)** for $C_{29}H_{32}NO_6S$ $(M+H)^+$: calcd. 522.1950, found 522.1953.

(2*E*,4*Z*)-Ethyl 4-([1,1'-biphenyl]-4-yl)-5-(N,4-dimethylphenylsulfonamido)-5-(4-methoxyphenyl)penta-2,4-dienoate (31):



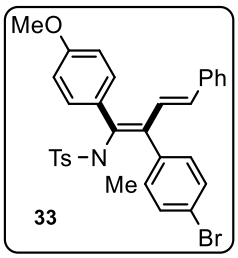
31 (132 mg, 78%) as yellow solid. mp = 181–182 °C; R_f = 0.40 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (t, J = 8.4 Hz, 3H), 7.61 (d, J = 15.6 Hz, 1H), 7.54–7.38 (m, 6H), 7.30–7.24 (m, 2H), 7.04 (q, J = 8.4 Hz, 4H), 6.86 (d, J = 8.8 Hz, 2H), 5.71 (d, J = 15.6 Hz, 1H), 4.15 (q, J = 7.2 Hz, 2H), 3.88 (s, 3H), 2.78 (s, 3H), 2.33 (s, 3H), 1.24 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 160.4, 145.2, 145.1, 142.9, 140.6, 136.5, 136.4, 135.9, 132.2, 130.6, 129.6, 129.0, 128.8, 128.3, 127.4, 127.3, 127.1, 127.0, 122.0, 113.6, 60.2, 55.3, 38.0, 21.3, 14.2; IR (Neat) ν_{max} 2930, 1705, 1602, 1506, 1339, 1245 cm^{-1}; **HRMS (ESI)** for $C_{34}H_{34}NO_5S$ $(M+H)^+$: calcd. 568.2158, found 568.2156.

***N*-((1*Z*,3*E*)-2-(4-chlorophenyl)-1-(4-methoxyphenyl)-4-phenylbuta-1,3-dien-1-yl)-*N*,4-dimethylbenzenesulfonamide (32):**



32 (88 mg, 56%) as yellow solid. mp = 210–211 °C; R_f = 0.50 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (s, 3H), 7.29 (d, J = 8.5 Hz, 2H), 7.23 (d, J = 7.0 Hz, 2H), 7.19 (d, J = 7.5 Hz, 3H), 7.07–7.00 (m, 6H), 6.84 (d, J = 8.5 Hz, 2H), 6.20 (d, J = 16.0 Hz, 1H), 3.87 (s, 3H), 2.76 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.8, 142.7, 138.8, 138.3, 137.2, 137.0, 136.8, 133.48, 133.45, 132.1, 131.8, 129.1, 128.94, 128.87, 128.6, 128.5, 127.7, 127.2, 126.5, 113.5, 55.3, 37.8, 21.4; IR (Neat) ν_{max} 2931, 1700, 1597, 1506,1463, 1345, 1159 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{29}ClNO_3S$ $(M+H)^+$: calcd. 530.1557, found 530.1555.

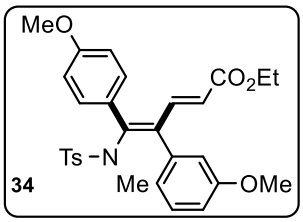
***N*-((1*Z*,3*E*)-2-(4-bromophenyl)-1-(4-methoxyphenyl)-4-phenylbuta-1,3-dien-1-yl)-*N*,4-dimethylbenzenesulfonamide (33):**



33 (118 mg, 69%) as yellow solid. mp = 220–221 °C; R_f = 0.50 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 8.8 Hz, 2H), 7.36–7.32 (m, 2H), 7.31 (d, J = 8.8 Hz, 2H), 7.25–7.22 (m, 2H), 7.21–7.17 (m, 2H), 7.08–7.04 (m, 3H), 7.04–7.00 (m, 3H), 6.84 (d, J = 8.8 Hz, 2H), 6.21 (d, J = 16.0 Hz, 1H), 3.87 (s, 3H), 2.76 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.8 142.8, 138.7, 138.3, 137.6, 137.2, 136.8, 133.5, 132.2, 132.1, 131.6, 129.1, 129.0, 128.8, 128.6, 127.7, 127.2, 126.5, 121.7, 113.5, 55.3, 37.8, 21.4; IR (Neat) ν_{max} 2931,

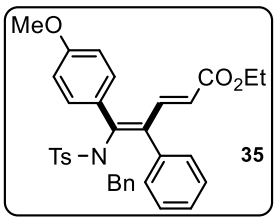
1700, 1597, 1506,1463, 1345, 1159 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{29}BrNO_3S$ $(M+H)^+$: calcd. 574.1052, found 574.1051, 576.1038 (M+2).

(2*E*,4*Z*)-Ethyl 5-(N,4-dimethylphenylsulfonamido)-4-(3-methoxyphenyl)-5-(4-methoxyphenyl)penta-2,4-dienoate (34):



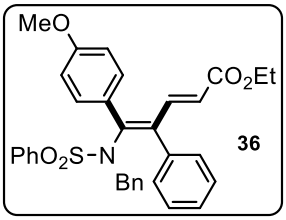
34 (95 mg, 61%) as yellow solid. mp = 147–148 °C; R_f = 0.27 (10% EtOAc/Hex); ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, J = 15.6 Hz, 1H), 7.31 (t, J = 8.0 Hz, 2H), 7.13 (d, J = 8.8 Hz, 2H), 7.02 (s, 4H), 6.91 (dd, J = 8.4 Hz, 2.4 Hz, 2H), 6.77 (d, J = 8.8 Hz, 2H), 5.66 (d, J = 15.6 Hz, 1H), 4.11 (q, J = 7.2 Hz, 2H), 3.85 (s, 3H), 3.84 (s, 3H), 2.73 (s, 3H), 2.35 (s, 3H), 1.20 (t, J = 8.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 160.4, 159.8, 144.8, 142.8, 138.4, 136.8, 136.0, 132.2, 129.7, 129.4, 129.0, 128.4, 127.2, 122.4, 122.0, 115.1, 114.2, 113.5, 60.2, 55.32, 55.30, 38.1, 21.4, 14.2; IR (Neat) ν_{max} 2931, 1700, 1597, 1506,1463, 1345, 1159 cm^{-1}; **HRMS (ESI)** for $C_{29}H_{31}NNaO_6S$ $(M+Na)^+$: calcd. 544.1770, found 544.1770.

(2*E*,4*Z*)-Ethyl 5-(*N*-benzyl-4-methylphenylsulfonamido)-5-(4-methoxyphenyl)-4-phenylpenta-2,4-dienoate (35):



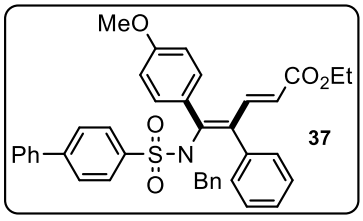
35 (122 mg, 72%) as yellow solid. mp = 185–186 °C; R_f = 0.40 (10% EtOAc/Hex); ^1H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, J = 15.5 Hz, 1H), 7.43–7.27 (m, 7H), 7.21 (t, J = 7.5 Hz, 3H), 7.04 (d, J = 8.0 Hz, 2H), 6.89–6.83 (m, 4H), 6.67 (d, J = 7.5 Hz, 2H), 5.49 (d, J = 15.5 Hz, 1H), 4.11 (q, J = 7.0 Hz, 2H), 4.06 (bs, 2H), 3.87 (s, 3H), 2.39 (s, 3H), 1.21 (t, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.1, 160.4, 146.0, 143.3, 142.3, 137.7, 137.5, 137.0, 135.5, 133.1, 130.6, 129.9, 129.0, 128.4, 128.3, 128.14, 128.09, 127.9, 127.7, 121.8, 113.6, 60.1, 55.3, 51.9, 21.4, 14.2; IR (Neat) ν_{max} 2922, 1711, 1620, 1598, 1507, 1455, 1333, 1249, 1155 cm^{-1}; **HRMS (ESI)** for $C_{34}H_{34}NO_5S$ $(M+H)^+$: calcd. 568.2158, found 568.2156.

(2*E*,4*Z*)-ethyl 5-(N-benzylphenylsulfonamido)-5-(4-methoxyphenyl)-4-phenylpenta-2,4-dienoate (36):



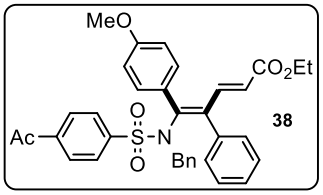
36 (114 mg, 69%) as pale-yellow gummy solid. R_f = 0.41 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 15.6 Hz, 1H), 7.45 (t, J = 7.6 Hz, 1H), 7.42–7.00 (m, 12H), 6.96 (d, J = 7.6 Hz, 2H), 6.83 (bd, J = 8.4 Hz, 2H), 6.66 (d, J = 7.2 Hz, 2H), 5.50 (d, J = 15.6 Hz, 1H), 4.10 (q, J = 7.2 Hz, 2H), 4.07 (bs, 2H), 3.85 (s, 3H), 1.19 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 160.4, 145.9, 142.2, 137.6, 137.4, 135.4, 133.1, 132.5, 130.5, 129.9, 128.5, 128.4, 128.2, 128.0, 127.84, 127.76, 121.9, 113.6, 60.2, 55.3, 52.0, 14.2; IR (Neat) ν_{max} 1710, 1599, 1332, 1249, 1157, 1021, 844 cm^{-1}; **HRMS (ESI)** for $C_{33}H_{32}NO_5S$+ $(M+H)^+$: calcd. 554.2001, found 554.2003.

(2*E*,4*Z*)-ethyl 5-(N-benzyl-[1,1'-biphenyl]-4-ylsulfonamido)-5-(4-methoxyphenyl)-4-phenylpenta-2,4-dienoate (37):



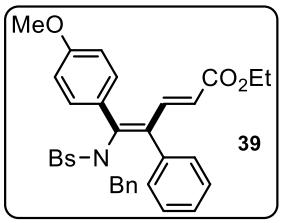
37 (117 mg, 62%) as pale-yellow gummy solid. R_f = 0.39 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67–7.56 (m, 4H), 7.52–7.38 (m, 9H), 7.33–7.15 (m, 5H), 7.04 (d, J = 8.4 Hz, 2H), 6.86 (bd, J = 8.0 Hz, 2H), 6.78 (d, J = 7.6 Hz, 2H), 5.56 (dd, J = 15.6, 2.0 Hz, 1H), 4.13 (q, J = 7.2 Hz, 2H), 4.10 (bs, 2H), 3.84 (s, 3H), 1.21 (t, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 160.4, 145.9, 145.2, 142.3, 139.1, 138.4, 137.41, 137.35, 135.3, 133.0, 130.5, 129.9, 128.9, 128.44, 128.39, 128.36, 128.3, 128.2, 127.7, 127.1, 126.8, 121.8, 113.5, 60.1, 55.2, 52.0, 14.1; IR (Neat) ν_{max} 3492, 3393, 1616, 1565, 1495, 1431, 1332 cm^{-1}; **HRMS (ESI)** for $C_{39}H_{36}NO_5S$ $(M+H)^+$: calcd. 630.2309, found 630.2309.

(2*E*,4*Z*)-Ethyl 5-(4-acetyl-*N*-benzylphenylsulfonamido)-5-(4-methoxyphenyl)-4-phenylpenta-2,4-dienoate (38):



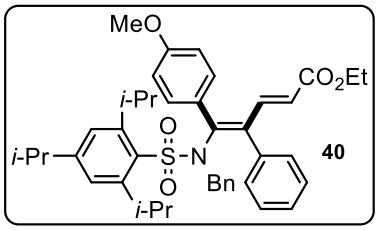
38 (139 mg, 78%) as pale yellow semi solid; R_f = 0.2 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, J = 8.5 Hz, 2H), 7.52 (d, J = 15.5 Hz, 1H), 7.44–7.25 (m, 5H), 7.20 (t, J = 7.5 Hz, 3H), 7.09–7.01 (m, 2H), 6.99 (d, J = 11 Hz, 2H), 6.81–6.72 (m, 4H), 5.52 (d, J = 15.5 Hz, 1H), 4.20–3.91 (m, 4H), 3.82 (s, 3H), 2.59 (s, 3H), 1.18 (t, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.8, 166.9, 160.4, 145.6, 143.9, 142.1, 139.4, 137.4, 137.1, 135.1, 133.0, 130.4, 129.9, 128.6, 128.5, 128.4, 128.0, 127.5, 122.2. 113.5, 60.2, 55.3, 52.5, 26.8, 14.1; IR (Neat) ν_{max} 1689, 1604, 1346, 1246, 1154, 1018, 839 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{33}NNaO_6S$ (M+Na)$^+$: calcd. 618.1921, found 618.1930.

(2*E*,4*Z*)-Ethyl 5-(*N*-benzyl-4-bromophenylsulfonamido)-5-(4-methoxyphenyl)-4-phenylpenta-2,4-dienoate (39):



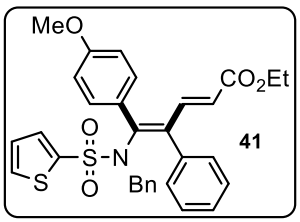
39 (129 mg, 67%) as colorless semi-solid. R_f = 0.38 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 15.6 Hz, 1H), 7.39 (bs, 3H), 7.33–7.28 (m, 3H), 7.27–7.20 (m, 3H), 7.19–6.88 (m, 3H), 6.81 (bd, J = 8.0 Hz, 2H), 6.76 (d, J = 6.8 Hz, 2H), 6.72 (d, J = 8.8 Hz, 2H), 5.51 (d, J = 15.6 Hz, 1H), 4.10 (q, J = 7.2 Hz, 2H), 4.02 (bs, 2H), 3.84 (s, 3H), 1.19 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 160.4, 145.6, 142.3, 139.2, 137.3, 137.2, 135.2, 133.0, 131.5, 130.4, 129.9, 129.3, 128.6, 128.5, 128.3, 127.9, 127.5, 127.3, 122.1, 113.6, 60.2, 55.3, 52.4, 14.1; IR (Neat) ν_{max} 1695, 1604, 1345, 1249, 1020, 1005, 828 cm^{-1}; **HRMS (ESI)** for $C_{33}H_{30}BrNNaO_5S$ (M+2+Na)$^+$: calcd. 656.0926, found 656.0933 (M+2).

(2*E*,4*Z*)-Ethyl 5-(*N*-benzyl-2,4,6-triisopropylphenylsulfonamido)-5-(4-methoxyphenyl)-4-phenylpenta-2,4-dienoate (40):



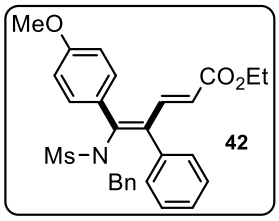
40 (146 mg, 72%) as pale-yellow gummy liquid. The compound is sparingly soluble in $CDCl_3$. R_f = 0.43 (10% EtOAc/Hex); ^1H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, J = 15.5 Hz, 1H), 7.35–7.30 (m, 3H), 7.21–7.11 (m, 7H), 6.92 (d, J = 8.5 Hz, 2H), 6.84 (d, J = 7.5 Hz, 2H), 6.72 (d, J = 9.0 Hz, 2H), 5.38 (d, J = 15.5 Hz, 1H), 4.28 (s, 2H), 4.09 (q, J = 7.0 Hz, 2H), 4.02–3.85 (m, 2H), 3.80 (s, 3H), 2.99–2.78 (m, 1H), 1.29 (d, J = 7.0 Hz, 6H), 1.19 (t, J = 7.0 Hz, 3H), 1.12 (d, J = 6.5 Hz, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2, 160.3, 152.9, 150.6, 147.6, 142.7, 137.7, 136.6, 136.1, 134.4, 133.1, 130.4, 129.8, 128.6, 128.5, 128.2, 128.1, 128.0, 127.8, 124.2, 121.0, 113.0, 60.1, 55.1, 51.2, 34.1, 30.2, 25.1, 23.6, 14.1; IR (Neat) ν_{max} 2956, 1707, 1599, 1251, 1161, 1030, 833 cm^{-1}; **HRMS (ESI)** for $C_{42}H_{49}NNaO_5S+$ $(M+Na)^+$: calcd. 702.3224, found 702.3236.

(2*E*,4*Z*)-Ethyl 5-(*N*-benzylthiophene-2-sulfonamido)-5-(4-methoxyphenyl)-4-phenylpenta-2,4-dienoate (41):



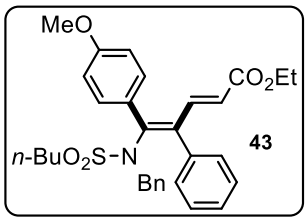
41 (136 mg, 81%) as colorless solid. mp = 190–191 °C; R_f = 0.41 (10% EtOAc/Hex); ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 15.6 Hz, 1H), 7.44 (dd, J = 5.2, 1.2 Hz, 1H), 7.39–7.28 (m, 4H), 7.26–7.21 (m, 2H), 7.18–6.93 (m, 4H), 6.87–6.79 (m, 5H), 6.57 (dd, J = 3.6 Hz, 1.2 Hz, 1H), 5.49 (d, J = 15.6 Hz, 1H), 4.22–4.00 (m, 4H), 3.83 (s, 3H), 1.19 (t, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 160.3, 145.7, 142.2, 141.0, 137.4, 137.2, 135.2, 133.1, 132.8, 132.3, 130.3, 130.0, 128.4, 128.3, 127.9, 127.6, 126.9, 122.0, 113.5, 60.1, 55.2, 52.3, 14.1; IR (Neat) ν_{max} 2969, 1738, 1366, 1215, 835 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{33}N_2O_5S_2$ $(M+NH_4)^+$: calcd. 577.1825, found 577.1830.

(2*E*,4*Z*)-ethyl 5-(*N*-benzylmethylsulfonamido)-5-(4-methoxyphenyl)-4-phenylpenta-2,4-dienoate (42):



42 (115 mg, 78%), pale yellow gummy liquid; R_f = 0.32 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 15.6 Hz, 1H), 7.43–7.25 (m, 9H), 7.15–7.10 (m, 2H), 6.98 (d, J = 8.4 Hz, 3H), 5.45 (d, J = 15.6 Hz, 1H), 4.27 (bs, 2H), 4.09 (q, J = 7.2 Hz, 2H), 3.87 (s, 3H), 1.98 (s, 3H), 1.18 (t, J = 6.8 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 160.7, 145.5, 143.5, 137.7, 136.6, 135.6, 132.6, 130.5, 130.1, 128.7, 128.5, 128.3, 127.8, 127.6, 122.1, 114.1, 60.2, 55.4, 53.2, 41.8, 14.2; IR (Neat) ν_{max} 1738, 1599, 1364, 1231, 1156, 1017, 833 cm^{-1}; **HRMS (ESI)** for $C_{28}H_{30}NO_5S$+ $(M+H)^+$: calcd. 492.1839, found 492.1839.

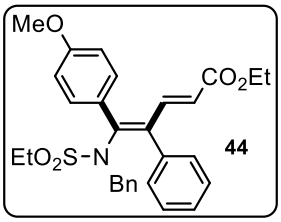
(2*E*,4*Z*)-ethyl 5-(benzyl(butyl)amino)-5-(4-methoxyphenyl)-4-phenylpenta-2,4-dienoate (43):



43 (107 mg, 67%) as yellow semi-solid. R_f = 0.22 (20% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, J = 15.5 Hz, 1H), 7.40–7.27 (m, 8H), 7.22–7.17 (m, 2H), 7.11–7.06 (m, 2H), 6.98 (d, J = 8.5 Hz, 2H), 5.41 (d, J = 15.5 Hz, 1H), 4.23–4.01 (m, 2H), 4.09 (q, J = 7.0 Hz, 2H), 3.88 (s, 3H), 1.55–1.48 (m, 3H), 1.19 (t, J = 7.0 Hz, 3H), 1.16–1.07 (m, 3H), 0.76 (t, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 160.6, 145.7, 143.6, 137.9, 136.7, 135.8, 132.7, 130.5, 130.2, 128.6, 128.4, 128.2, 127.8, 127.7, 122.0, 114.0, 60.2, 55.4, 54.4, 53.00, 24.8, 21.5, 14.2, 13.4; IR (Neat) ν_{max} 2926, 1706, 1602, 1508, 1334, 1252, 1142, 1024, 841 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{35}NNaO_5S$ $(M+Na)^+$: calcd. 556.2128, found 556.2136.

5o'. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.54 (d, J = 12.1 Hz, 0.24H), 5.71 (d, J = 12.2 Hz, 0.23H).

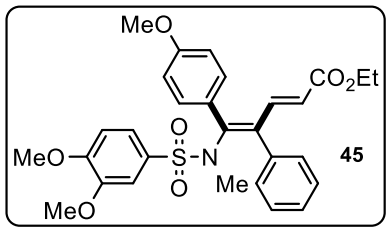
(2*E*,4*Z*)-Ethyl 5-(*N*-benzylethylsulfonamido)-5-(4-methoxyphenyl)-4-phenylpenta-2,4-dienoate (44):



44 (123 mg, 81%) as yellowish semi-solid; R_f = 0.22 (20% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 15.6 Hz, 1H), 7.40–7.24 (m, 10H), 7.14–7.08 (m, 2H), 6.96 (d, J = 8.8 Hz, 2H), 5.44 (d, J = 15.6 Hz, 1H), 4.16 (bs, 2H), 4.11 (d, J = 7.2 Hz, 2H), 3.87 (s, 3H), 1.76–1.26 (m,

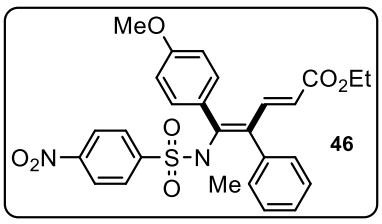
2H), 1.18 (t, J = 7.2 Hz, 3H), 1.06 (t, J = 7.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 160.5, 145.6, 143.5, 137.7, 136.6, 135.8, 132.6, 130.1, 128.6, 128.4, 128.2, 127.8, 127.7, 121.9, 113.9, 60.1, 55.3, 52.9, 49.0, 14.2, 7.5; IR (Neat) ν_{max} 1704, 1600, 1508, 1332, 1250, 1141, 1023, 839 cm^{-1}; **HRMS (ESI)** for $C_{29}H_{31}NNaO_5S$ $(M+Na)^+$: calcd. 528.1815, found 528.1823.

(2*E*,4*Z*)-Ethyl 5-(3,4-dimethoxy-*N*-methylphenylsulfonamido)-5-(4-methoxyphenyl)-4-phenylpenta-2,4-dienoate (45):



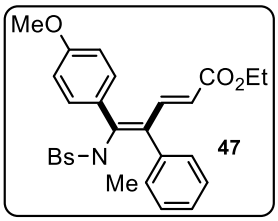
45 (116 mg, 72%) as pale yellow semi solid.; R_f = 0.13 (20% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, J = 15.6 Hz, 1H), 7.46–7.33 (m, 5H), 7.12 (d, J = 8.8 Hz, 2H), 6.90 (dd, J = 8.4 Hz, 2.0 Hz, 1H), 6.78 (d, J = 8.8 Hz, 2H), 6.72 (d, J = 8.8 Hz, 1H), 6.57 (d, J = 2.0 Hz, 1H), 5.60 (d, J = 15.6 Hz, 1H), 4.11 (q, J = 6.8 Hz, 2H), 3.89 (s, 3H), 3.82 (s, 3H), 3.66 (s, 3H), 2.72 (s, 3H), 1.20 (t, J = 6.8 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.1, 160.3, 152.2, 148.4, 145.4, 144.9, 137.1, 136.1, 132.2, 131.8, 130.1, 128.6, 127.9, 122.0, 121.0, 113.4, 110.2, 110.1, 60.2, 56.1, 55.8, 55.3, 38.3, 14.2; IR (Neat) ν_{max} 1707, 1603, 1506, 1346, 1258, 1135, 1020, 836 cm^{-1}; **HRMS (ESI)** for $C_{29}H_{31}NNaO_7S$+ $(M+Na)^+$: calcd. 560.1713, found 560.1757.

(2*E*,4*Z*)-Ethyl- 5-(4-methoxyphenyl)-5-(N-methyl-4-nitrophenylsulfonamido)-4-phenylpenta-2,4-dienoate (46):



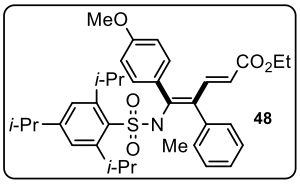
46 (75 mg, 50%) as yellow compound; mp = 150–152 °C; R_f = 0.25 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, J = 8.5 Hz, 2H), 7.52 (d, J = 15.5 Hz, 1H), 7.48–7.39 (m, 5H), 7.30–7.26 (m, 2H), 7.13 (d, J = 8.5 Hz, 2H), 6.78 (d, J = 9.0 Hz, 2H), 5.63 (d, J = 15.5 Hz, 1H), 4.13 (q, J = 7.0 Hz, 2H), 3.85 (s, 3H), 2.81 (s, 3H), 1.22 (t, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.8, 160.6, 149.4, 145.3, 144.2, 143.8, 137.2, 136.8, 132.1, 129.9, 128.8, 128.2, 127.8, 123.5, 123.0, 114.9, 113.7, 60.3, 55.4, 38.4, 14.1; IR (Neat) ν_{max} 2939, 1693, 1601, 1531, 1444, 1347, 1248 cm^{-1}; **HRMS (ESI)** for $C_{27}H_{27}N_2O_7S$ $(M+H)^+$: calcd. 523.1539, found 523.1539.

(2*E*,4*Z*)-ethyl 5-(4-bromo-*N*-methylphenylsulfonamido)-5-(4-methoxyphenyl)-4-phenylpenta-2,4-dienoate (47):



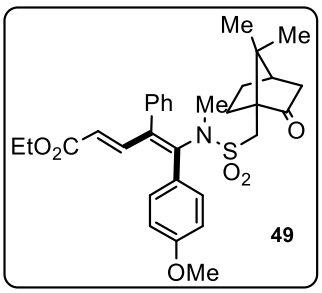
47 (77 mg, 46%) as yellow solid. mp = 147–148 °C; R_f = 0.38 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, J = 15.5 Hz, 1H), 7.45–7.41 (m, 2H), 7.40–7.33 (m, 5H), 7.14 (d, J = 8.5 Hz, 2H), 6.95 (dt, J = 8.5, 1.5 Hz, 2H), 6.79 (d, J = 8.5 Hz, 2H), 5.60 (d, J = 15.5 Hz, 1H), 4.11 (q, J = 7.0 Hz, 2H), 3.86 (s, 3H), 2.73 (s, 3H), 1.20 (t, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 160.5, 144.7, 144.6, 138.7, 137.1, 136.7, 132.1, 131.6, 130.0, 128.7, 127.98, 127.95, 127.1, 122.5, 113.6, 60.3, 55.4, 38.2; IR (Neat) ν_{max} 2989, 1696, 1611, 1600, 1508, 1347, 1248, 1166 cm^{-1}; **HRMS (ESI)** for $C_{27}H_{26}BrNNaO_5S$ $(M+Na)^+$: calcd. 578.0613, 580.0592 (M+2), found 578.0614, 580.0598 (M+2).

(2*E*,4*Z*)-Ethyl 5-(4-methoxyphenyl)-4-phenyl-5-(2,4,6-triisopropyl-*N*-methylphenylsulfonamido)penta-2,4-dienoate (48):



48 (125 mg, 75%) as pale-yellow semi-solid. R_f = 0.4 (20% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 15.6 Hz, 1H), 7.28–7.17 (m, 5H), 7.14 (dd, J = 7.6, 1.2 Hz, 2H), 7.09–7.05 (m, 2H), 6.74 (d, J = 8.8 Hz, 2H), 5.48 (d, J = 15.2 Hz, 1H), 4.10 (q, J = 7.2 Hz, 2H), 3.87–3.78 (m, 5H), 2.92–2.86 (m, 1H), 2.84 (s, 3H), 1.26 (d, J = 6.8 Hz, 6H), 1.19 (t, J = 7.2 Hz, 3H), 1.13 (d, J = 6.4 Hz, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 160.4, 152.7, 150.3, 146.8, 146.3, 137.8, 134.1, 133.7, 132.4, 130.3, 129.5, 128.4, 127.7, 123.8, 120.8, 113.2, 60.1, 55.2, 39.8, 34.1, 29.9, 25.0, 23.7, 14.2; IR (Neat) ν_{max} 2956, 1708, 1599, 1460, 1281, 1247, 1159, 1031, 834 cm^{-1}; **HRMS (ESI)** for $C_{36}H_{46}NO_5S$ $(M+H)^+$: calcd. 604.3091, found 604.3092.

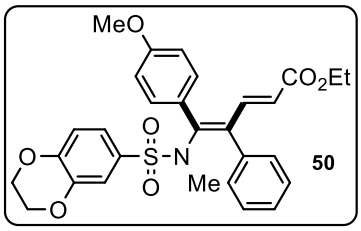
(2*E*,4*Z*)-Ethyl 5-(1-((1R,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)-*N*-methylmethylsulfonamido)-5-(4-methoxyphenyl)-4-phenylpenta-2,4-dienoate (49):



49 (117 mg, 71%) as yellow solid. mp = 215–216 °C; R_f = 0.2 (20% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (bd, J = 16.0 Hz, 1H), 7.45–7.39 (m, 4H), 7.36–7.31 (m, 3H), 6.95 (d, J = 8.5 Hz, 2H), 5.57 (d, J = 15.5 Hz, 1H), 4.11 (q, J = 7.0 Hz, 2H), 3.85 (s, 3H), 2.80 (s, 3H), 2.70 (bs, 1H), 2.30–2.20 (m, 2H), 2.00–1.89 (m, 2H), 1.82 (d, J = 18.5 Hz, 1H), 1.57 (bs, 1H), 1.37–1.23 (m, 2H), 1.19 (t, J = 7.0

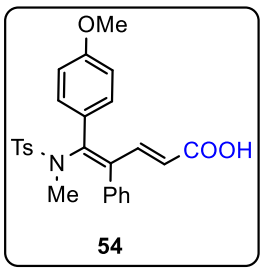
Hz, 3H), 0.89 (s, 3H), 0.60 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 214.6, 166.9, 160.6, 144.9, 144.7, 136.3, 132.1, 130.2, 128.7, 127.9, 127.7, 122.1, 113.9, 60.2, 57.9, 55.3, 48.2, 47.6, 42.6, 42.4, 37.2, 26.7, 19.6, 19.4, 14.1; IR (Neat) ν_{max} 1743, 1707, 1602, 1340, 1279, 1170, 841 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{38}NO_6S$ $(M+H)^+$: calcd. 552.2414, found 552.2413.

((2*E*,4*Z*)-Ethyl 5-(4-methoxyphenyl)-5-(N-methyl-2,3-dihydrobenzo[b][1,4]dioxine-6-sulfonamido)-4-phenylpenta-2,4-dienoate (50):



50 (123 mg, 77%) as yellow solid; mp = 200–201 °C; R_f = 0.62 (20% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, J = 15.5 Hz, 1H), 7.44–7.33 (m, 5H), 7.14 (d, J = 8.5 Hz, 2H), 6.78 (d, J = 8.5 Hz, 2H), 6.71–6.63 (m, 2H), 6.58 (bs, 1H), 5.59 (d, J = 16.0 Hz, 1H), 4.22 (dd, J = 22.5, 3.0 Hz, 2H), 4.10 (q, J = 7.0 Hz, 2H), 3.84 (s, 3H), 2.71 (s, 3H), 1.19 (t, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 160.3, 146.9, 145.3, 144.9, 142.8, 137.0, 135.9, 132.07, 132.05, 130.0, 128.5, 128.1, 127.8, 121.7, 120.5, 117.0, 116.9, 115.9, 113.4, 64.4, 63.9, 60.1, 55.2, 38.2, 14.1; IR (Neat) ν_{max} 3492, 3393, 1616, 1565, 1495,1431, 1332 cm^{-1}; **HRMS (ESI)** for $C_{29}H_{31}NO_7S$ $(M+H)^+$: calcd. 536.1737, found 536.1733.

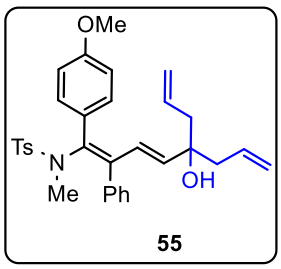
3B.6.3.2. Synthesis of (2*E*,4*Z*)-5-(*N*,4-dimethylphenylsulfonamido)-5-(4-methoxyphenyl)-4-phenylpenta-2,4-dienoic acid (54):



To the solution of **9** (50 mg, 1.0 equiv) in MeOH (2.0 mL) was added NaOH (2.0 mL, 10.0%) in a sealed tube. The resulting mixture was stirred at 120 ^{0}C for 12 h. Upon completion, the reaction mixture was acidified with HCl, extracted with DCM and concentrated under reduced pressure. The product **54** was obtained pure as off white solid; Yield 92%; mp = 212 °C; R_f = 0.20 (30% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$+DMSO D_6) δ 11.25 (bs, 1H), 8.10–8.03 (m, 1H), 7.72 (d, J = 7.5 Hz, 1H), 7.61–7.58 (m, 2H), 7.48–7.44 (m, 2H), 7.39–7.32 (m, 2H), 7.06 (d, J = 8.5 Hz, 1H), 7.00 (bd, J = 7.0 Hz, 1H), 6.91–6.74 (m, 4H), 5.31 (d, J = 15.5 Hz, 1H), 3.75 (s, 3H), 2.60 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$+DMSO D_6) δ 172.5, 169.1, 167.7, 161.8, 160.5, 145.0, 144.4, 143.2, 137.5, 136.7, 136.2, 135.7, 133.3, 132.3, 130.8, 130.6, 130.2, 129.4, 128.7, 128.2, 128.0, 127.2, 122.8, 119.2, 117.3, 113.8, 55.6,

38.2, 21.4; IR (Neat) ν_{max} 3200, 1702, 1600, 1507, 1434, 1343, 1280, 1161 cm^{-1}; **HRMS (ESI)** for $C_{26}H_{25}NNaO_5S$ $(M+Na)^+$: calcd. 486.1351, found 486.1352.

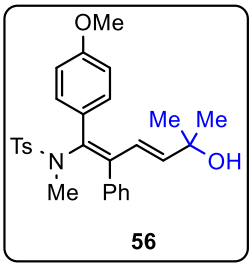
3B.6.3.3. *N*-((1*Z*,3*E*)-5-allyl-5-hydroxy-1-(4-methoxyphenyl)-2-phenylocta-1,3,7-trien-1-yl)-N,4-dimethylbenzenesulfonamide (55):



55

To the solution of **9** (50 mg, 1.0 equiv) in THF (2.0 mL) at 0 ^{0}C was added allylMgCl (2M in THF, 3.0 equiv). The resulting mixture was stirred for 12 h at rt. Upon completion, the reaction mixture was quenched with sat. NH_4Cl solution; extracted with DCM and concentrated under reduced pressure. The product **55** was obtained pure as gummy compound; Yield 84%; R_f = 0.30 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, J = 4.5 Hz, 4H), 7.19 (d, J = 8.5 Hz, 2H), 7.02–6.93 (m, 5H), 6.76 (d, J = 9.0 Hz, 1H), 6.46 (d, J = 15.5 Hz, 1H), 5.74–5.64 (m, 2H), 5.37 (d, J = 15.5 Hz, 1H), 5.13–5.11 (m, 2H), 5.05 (d, J = 17.0 Hz, 2H), 3.83 (s, 3H), 2.66 (s, 3H), 2.21 (s, 3H), 2.20–2.11 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.5, 142.5, 140.3, 138.8, 138.5, 137.6, 136.9, 133.3, 131.8, 130.2, 129.6, 129.4, 129.0, 128.8, 128.2, 127.30, 127.27, 127.2, 118.8, 113.3, 74.0, 55.2, 45.4, 37.6, 21.3; IR (Neat) ν_{max} 3456, 1706, 1607, 1507, 1434, 1343, 1280, 1145 cm^{-1}; **HRMS (ESI)** for $C_{32}H_{36}NO_4S$ $(M+H)^+$: calcd. 530.2365, found 530.2367.

3B.6.3.4. N-((1Z,3E)-5-hydroxy-1-(4-methoxyphenyl)-5-methyl-2-phenylhexa-1,3-dien-1-yl)-N,4-dimethylbenzenesulfonamide (56):

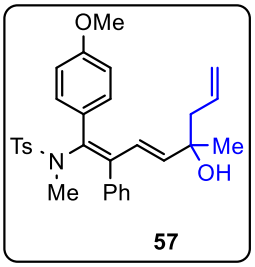


56

To the solution of **16** (50 mg, 1.0 equiv) in THF (2 mL) at 0 ^{0}C was added MeMgBr (1.2M in THF:Toluene (1:3), 3.0 equiv). The resulting mixture was stirred for 12 h at rt. Upon completion, the reaction mixture was quenched with sat. NH_4Cl solution; extracted with DCM and concentrated under the reduced pressure. The product **56** was obtained pure as gummy compound; Yield 85%; R_f = 0.11 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, J = 8.5 Hz, 1H), 7.41–7.31 (m, 3H), 7.23-7.20 (m, 2H), 7.05–6.97 (m, 3H), 6.93 (d, J = 8.5 Hz, 1H), 6.84–6.76 (m, 3H), 6.50 (d, J = 15.5 Hz, 1H), 5.49 (d, J = 16.0 Hz, 1H), 3.84 (s, 3H), 2.33 (s, 3H), 2.21 (s, 1H), 1.25 (s, 3H), 1.21 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.4,

142.6, 138.8, 137.6, 136.7, 132.3, 131.8, 130.2, 129.7, 128.9, 128.3, 127.4, 127.3, 127.2, 127.1, 113.3, 71.1, 55.3, 37.5, 29.7, 29.6, 21.4; IR (Neat) ν_{max} 3460, 1707, 1616, 1555, 1432, 1100cm^{-1}; **HRMS (ESI)** for $C_{28}H_{32}NO_4S$ $(M+H)^+$: calcd. 478.2052, found 478.2054.

3B.6.3.5. Synthesis of *N*-((1*Z*,3*E*)-5-hydroxy-1-(4-methoxyphenyl)-5-methyl-2-phenylocta-1,3,7-trien-1-yl)-N,4-dimethylbenzenesulfonamide (57):



57

To the solution of **16** (50 mg, 1.0 equiv) in THF (2.0 mL) at 0 ^{0}C was added allylMgCl (2M in THF, 3.0 equiv). The resulting mixture was stirred for 12 h at rt. Upon completion, the reaction mixture was quenched with sat. NH_4Cl solution; extracted with DCM and concentrated under reduced pressure. The product **12** was obtained pure as gummy compound; Yield 90%; R_f = 0.11 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, J = 8.0 Hz, 1H), 7.41–7.38 (m, 3H), 7.20 (d, J = 8.5 Hz, 2H), 6.99 (d, J = 8.0 Hz, 2H), 6.94 (d, J = 8.0 Hz, 2H), 6.78 (d, J = 8.5 Hz, 2H), 6.48 (d, J = 16.0 Hz, 1H), 5.74–5.63 (m, 1H), 5.43 (d, J = 15.5 Hz, 1H), 5.12 (dd, J = 10.5, 1.5 Hz, 1H), 5.05 (d, J = 17.0 Hz, 1H), 3.84 (s, 3H), 2.66 (s, 3H), 2.65–2.61 (m, 1H), 2.43 (s, 1H), 2.33 (s, 3H), 2.25–2.13 (m, 2H), 1.18 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.5, 142.5, 141.5, 138.7, 138.6, 137.6, 136.8, 133.5, 131.8, 130.2, 129.7, 128.9, 128.23, 128.15, 127.34, 127.29, 119.1, 113.3, 72.5, 55.3, 47.1, 37.6, 27.7, 21.4; IR (Neat) ν_{max} 3461, 1709, 1619, 1556, 1434, 1343, 1288, 1147; **HRMS (ESI)** for $C_{30}H_{34}NO_4S$ $(M+H)^+$: calcd. 504.2209, found 504.2207.

3B.7. X-ray Crystallography:

X-ray reflections for **35** were collected on Bruker D8 Quest CCD diffractometer using Mo-Kα, radiation. Data reduction was performed using CrysAlisPro (version 1.171.33.55).[2] Apex 2 and SHELXL 97 program were used to solve and refine the data. All non-hydrogen atoms were refined anisotropically, and C−H hydrogens were fixed.

Table 3B.5. Crystallographic Data for Compound **35**

Compound	**35**
formula	C_{34} H_{33} N O_5 S
Mw	567.67

V [Å^3]	2961.2(3)
Z	4
ρ_{calcd} [g cm^{-3}]	1.273

crystal system	monoclinic
space group	P 21/c
T [K]	100 K
a [Å]	10.1538(6)
b [Å]	16.0305(10)
c [Å]	18.1936(11)
α [°]	90
β [°]	90.574(2)
γ [°]	90

μ [mm^{-1}]	0.152
total reflns	9841
unique reflns	6079
observed	4517
R_1[I>2σ(I)]	0.0506
wR2 [all]	0.1354
GOF	1.0783
Diffractometer	Bruker D8 Quest CCD
CCDC No.	2131186

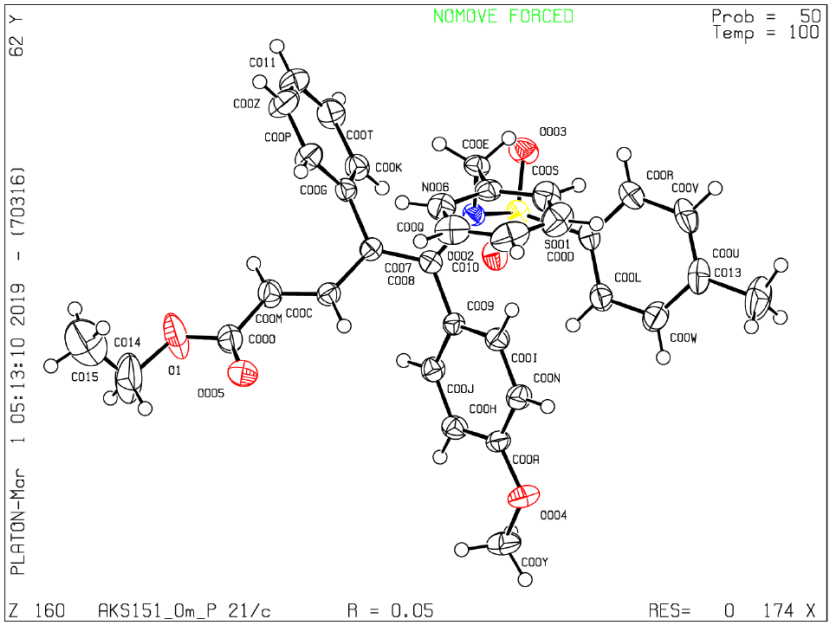


Figure 3B.4. Molecular structure of compound **35**, (Oxygen (red), nitrogen (blue), and sulphur (yellow))

3B.8. References

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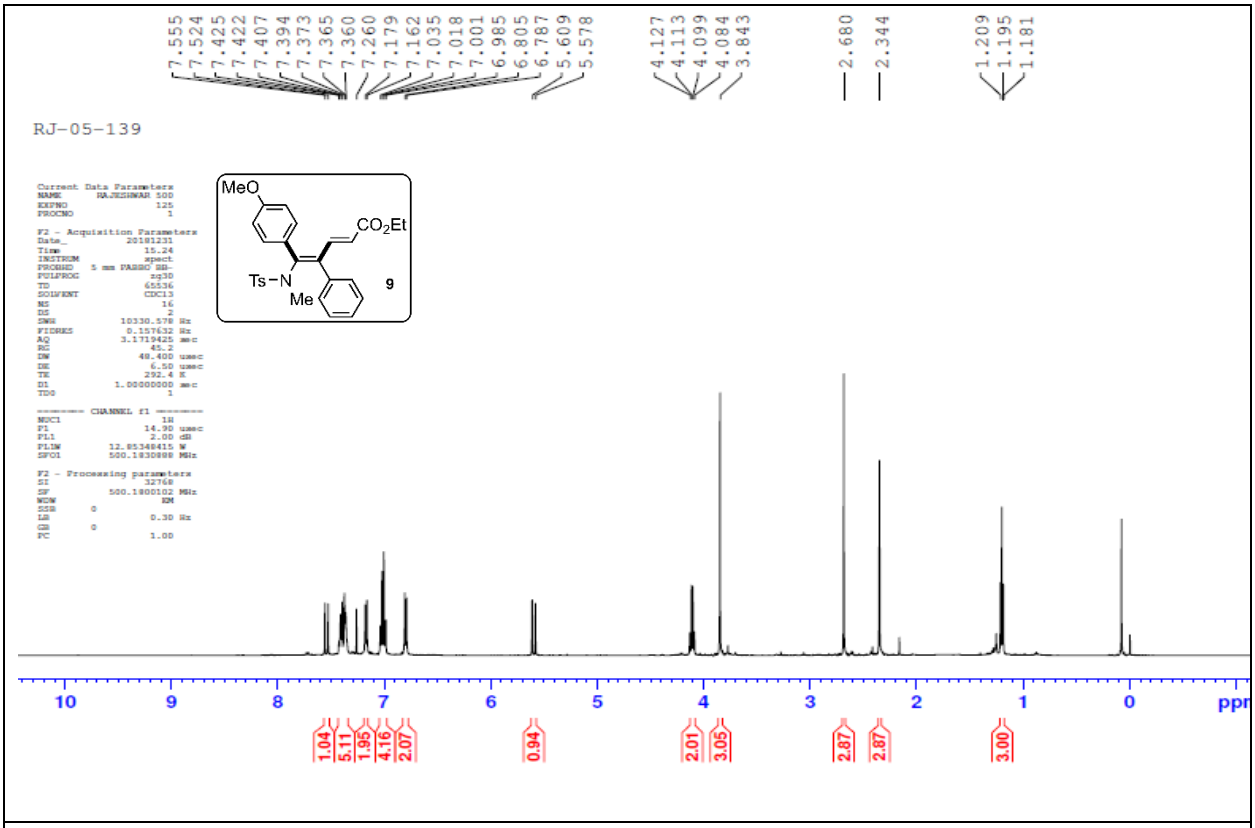
3B.9. Spectra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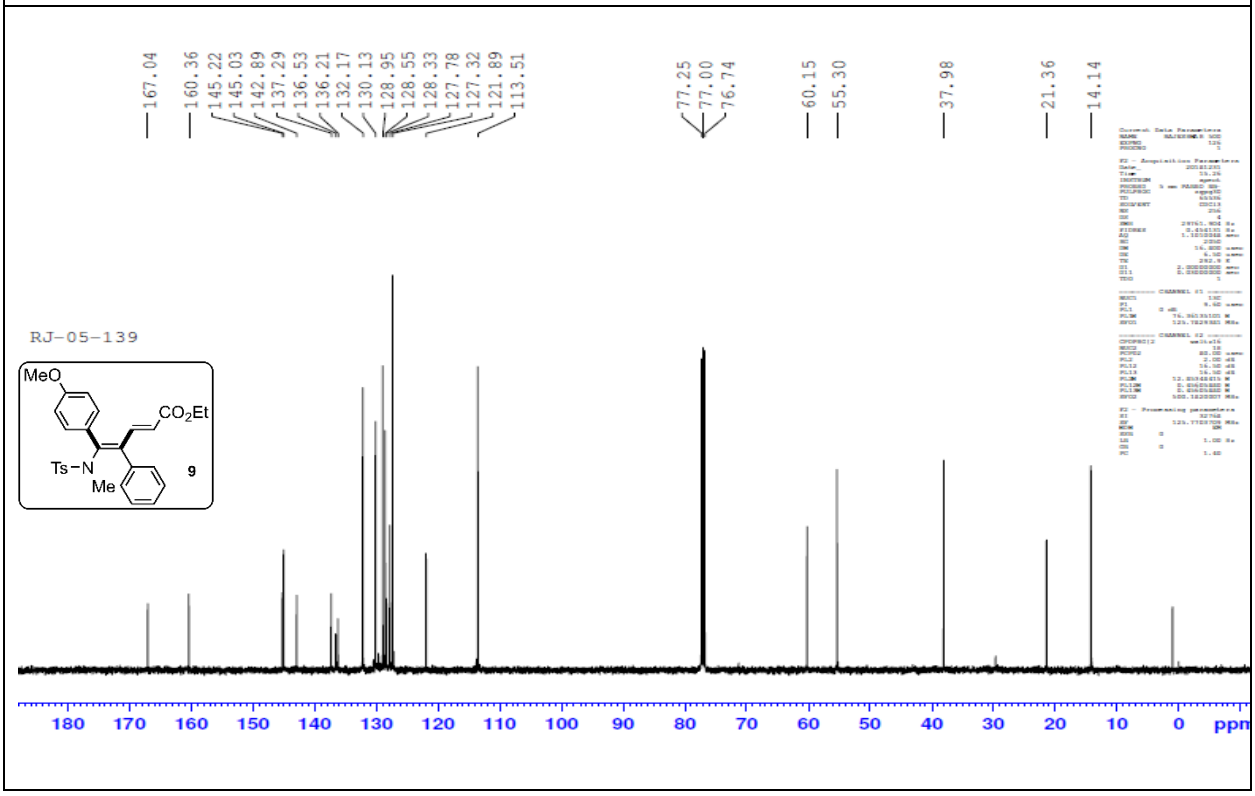
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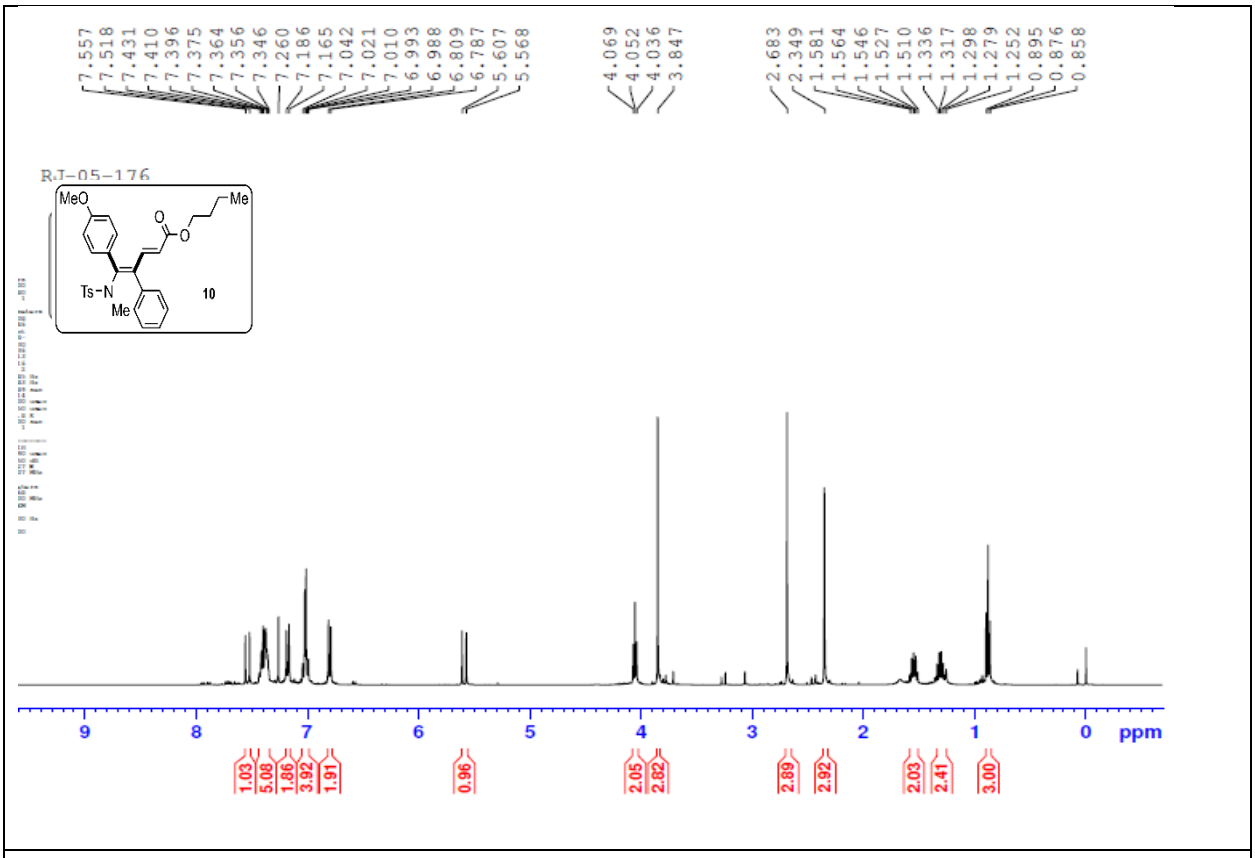
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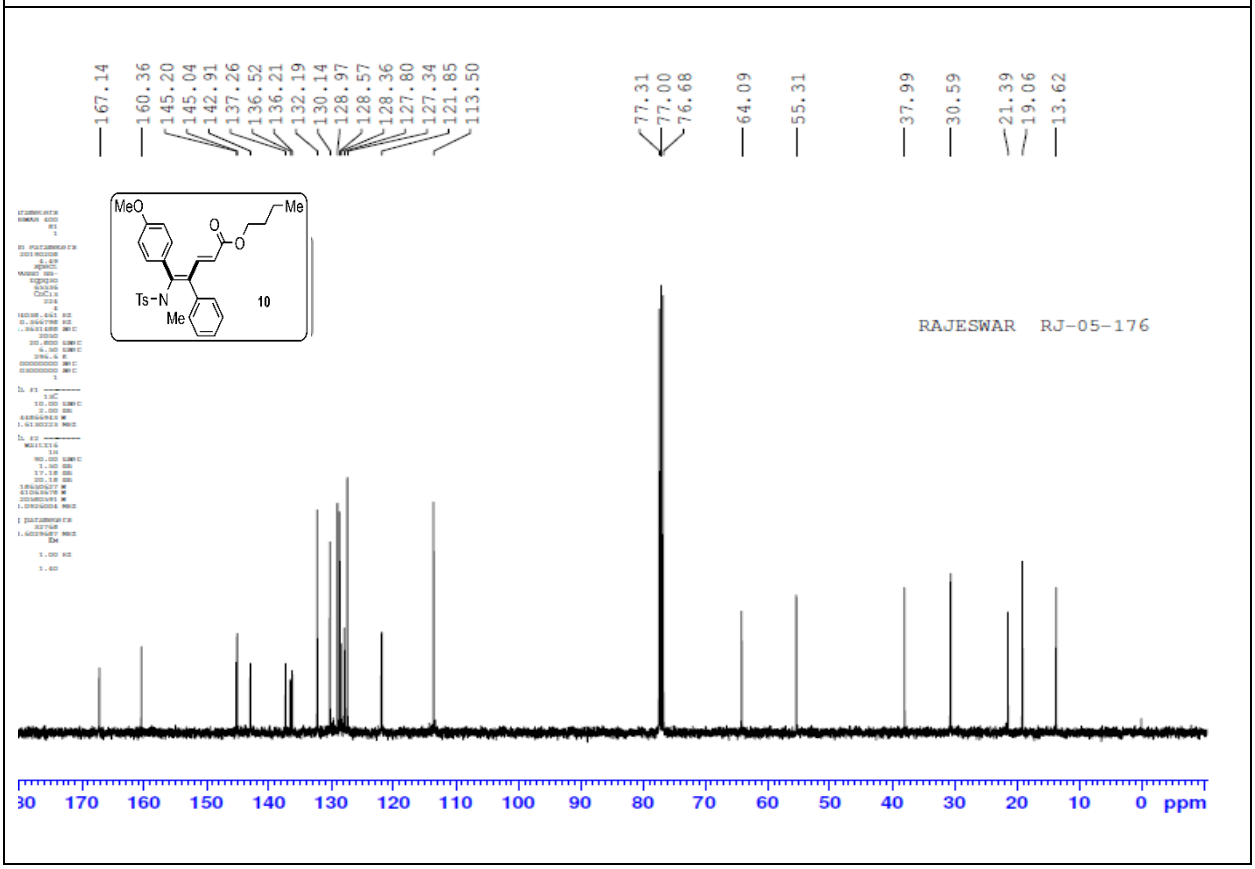
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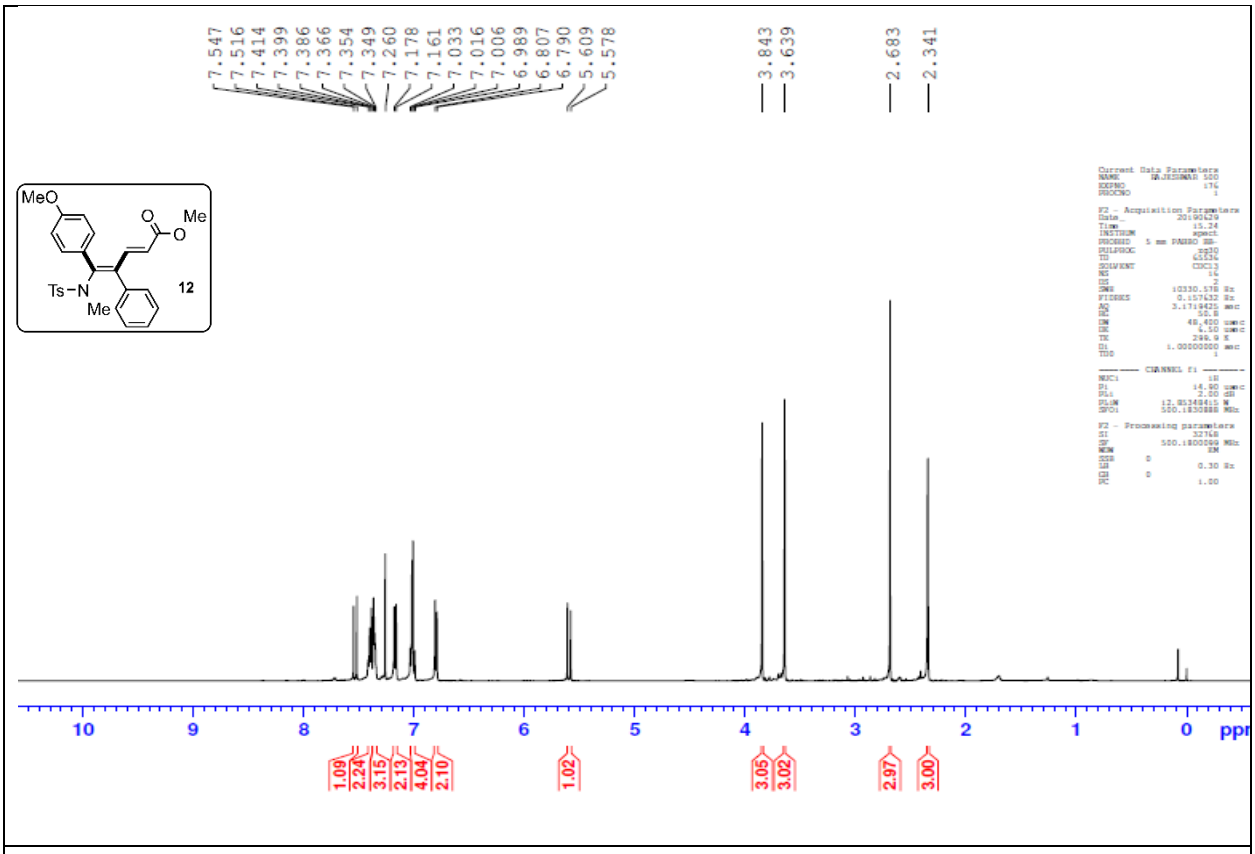
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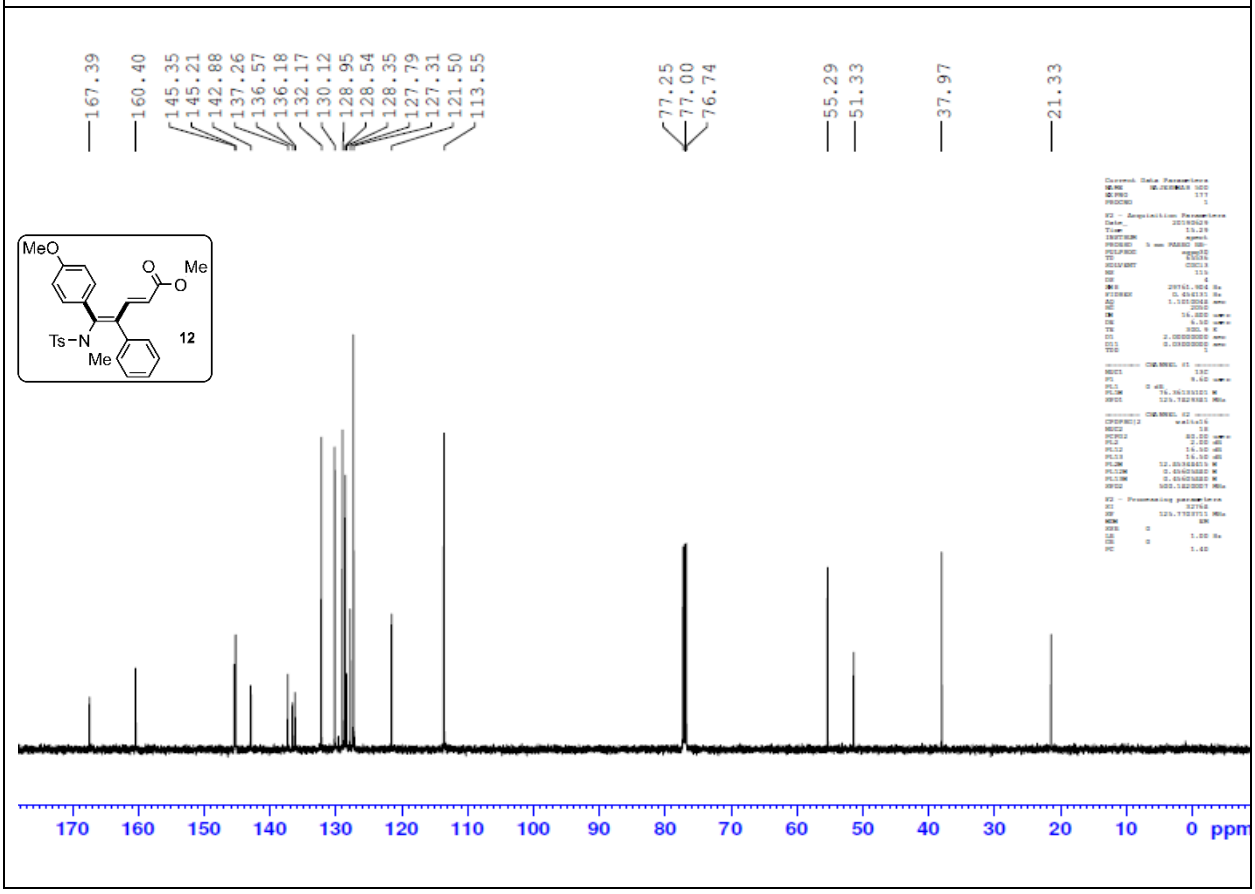
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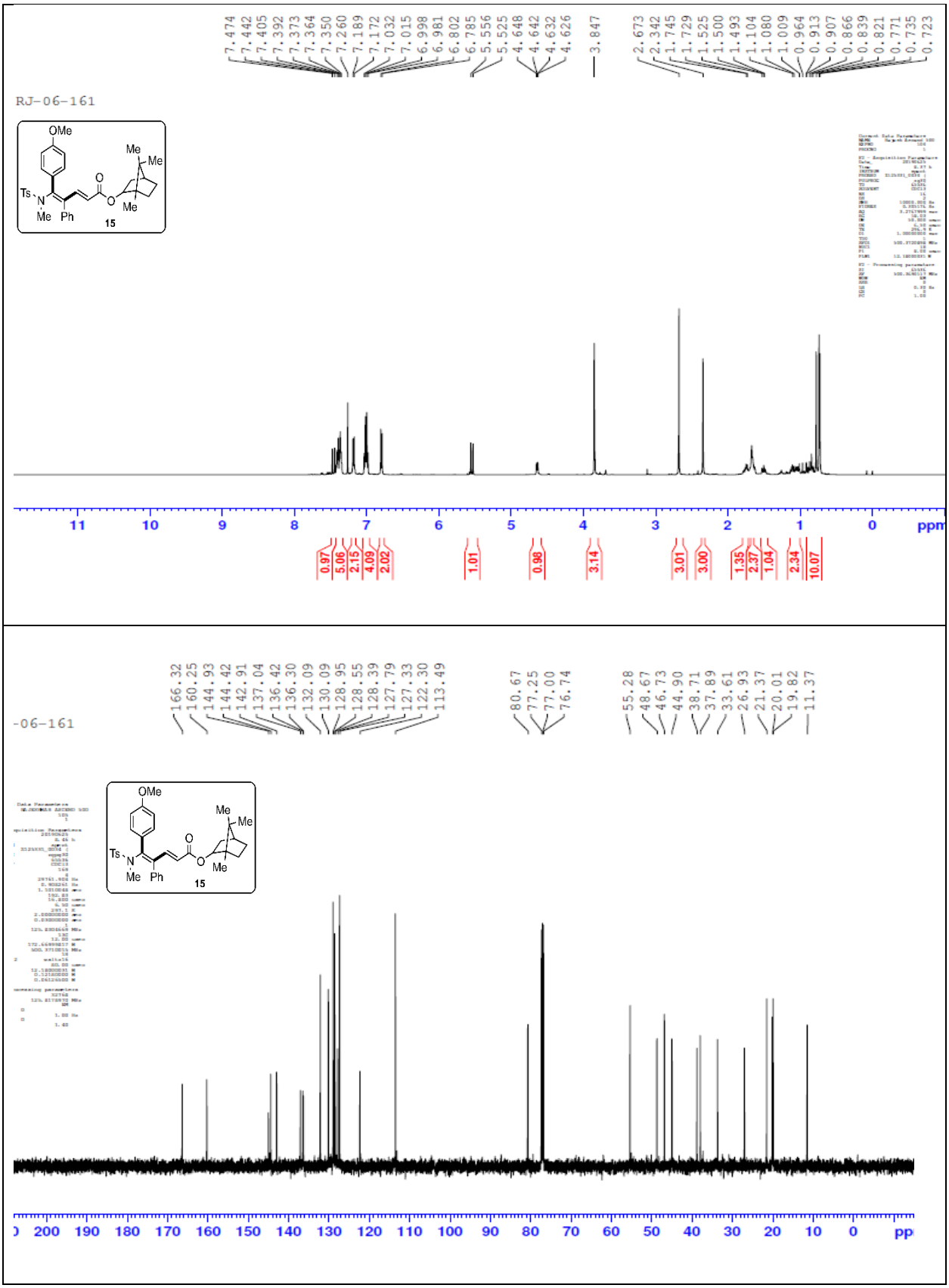
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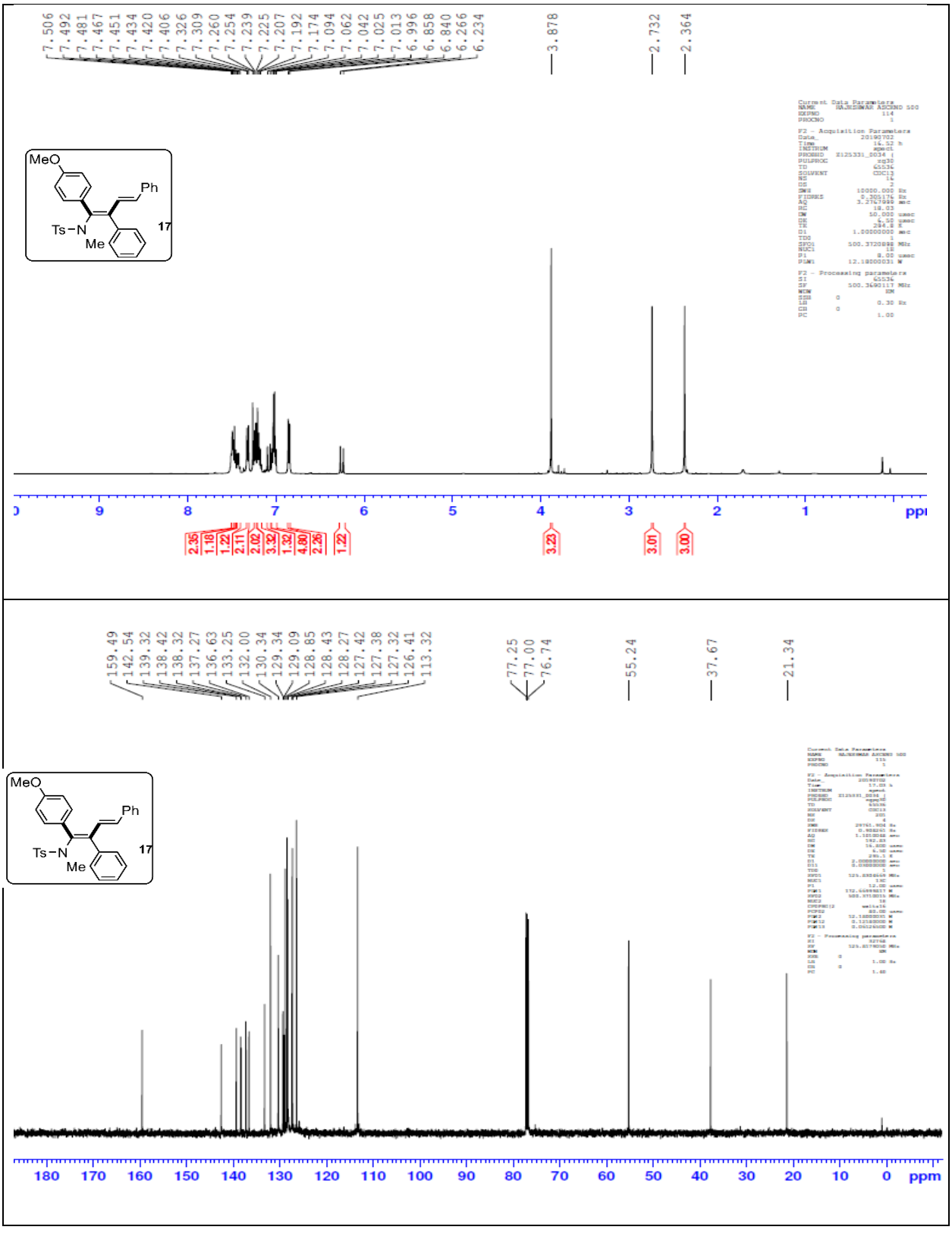
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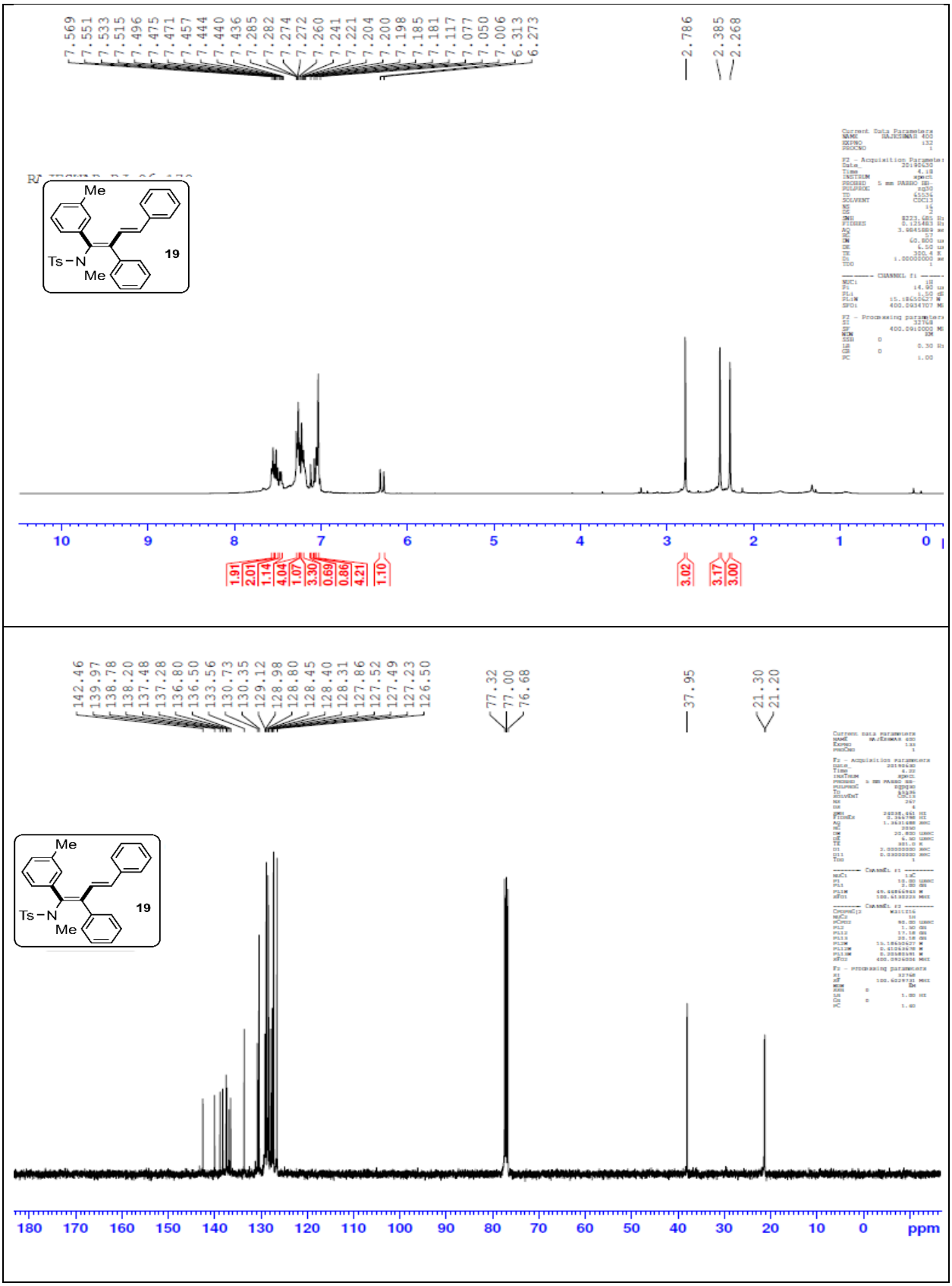
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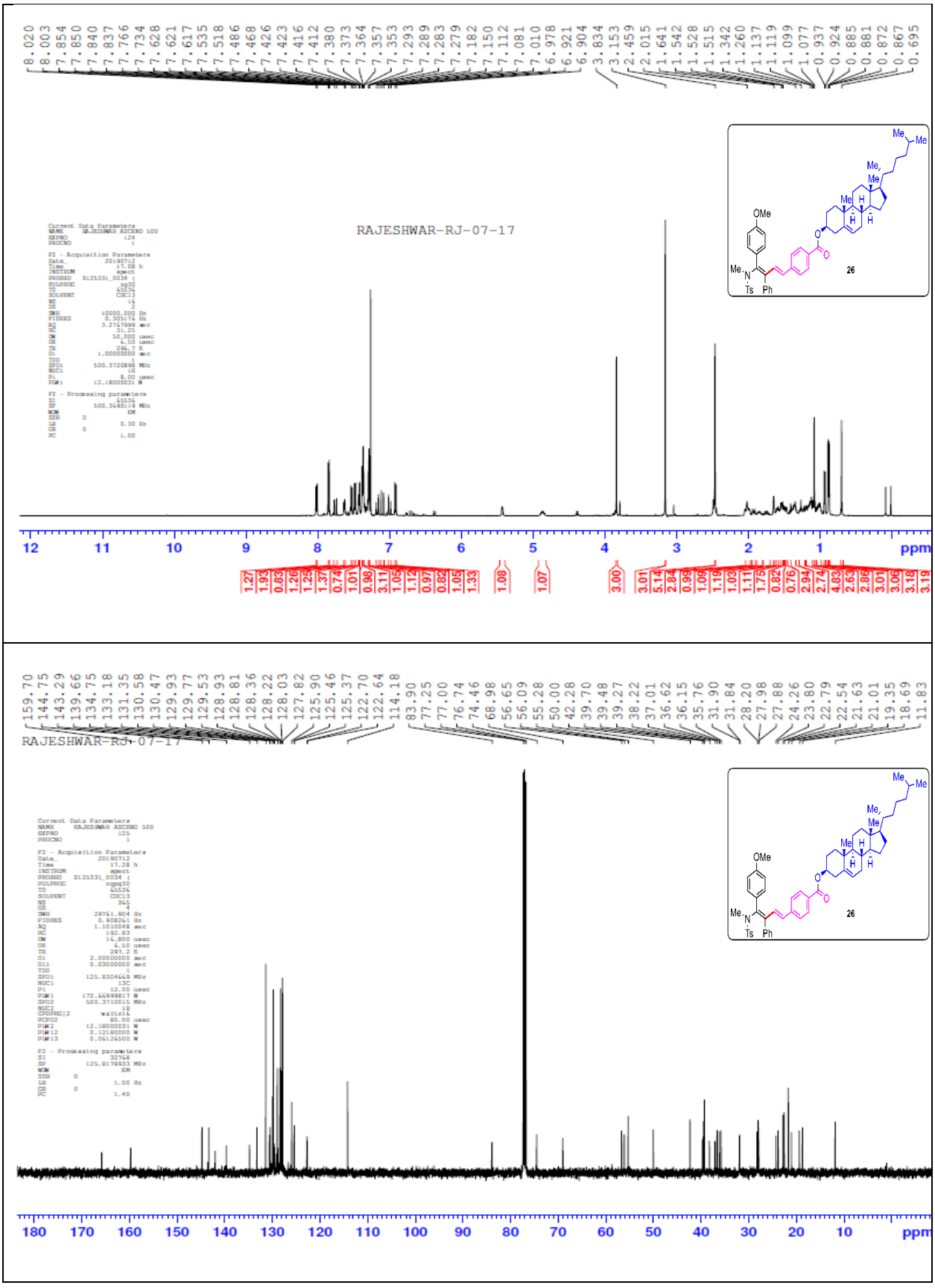
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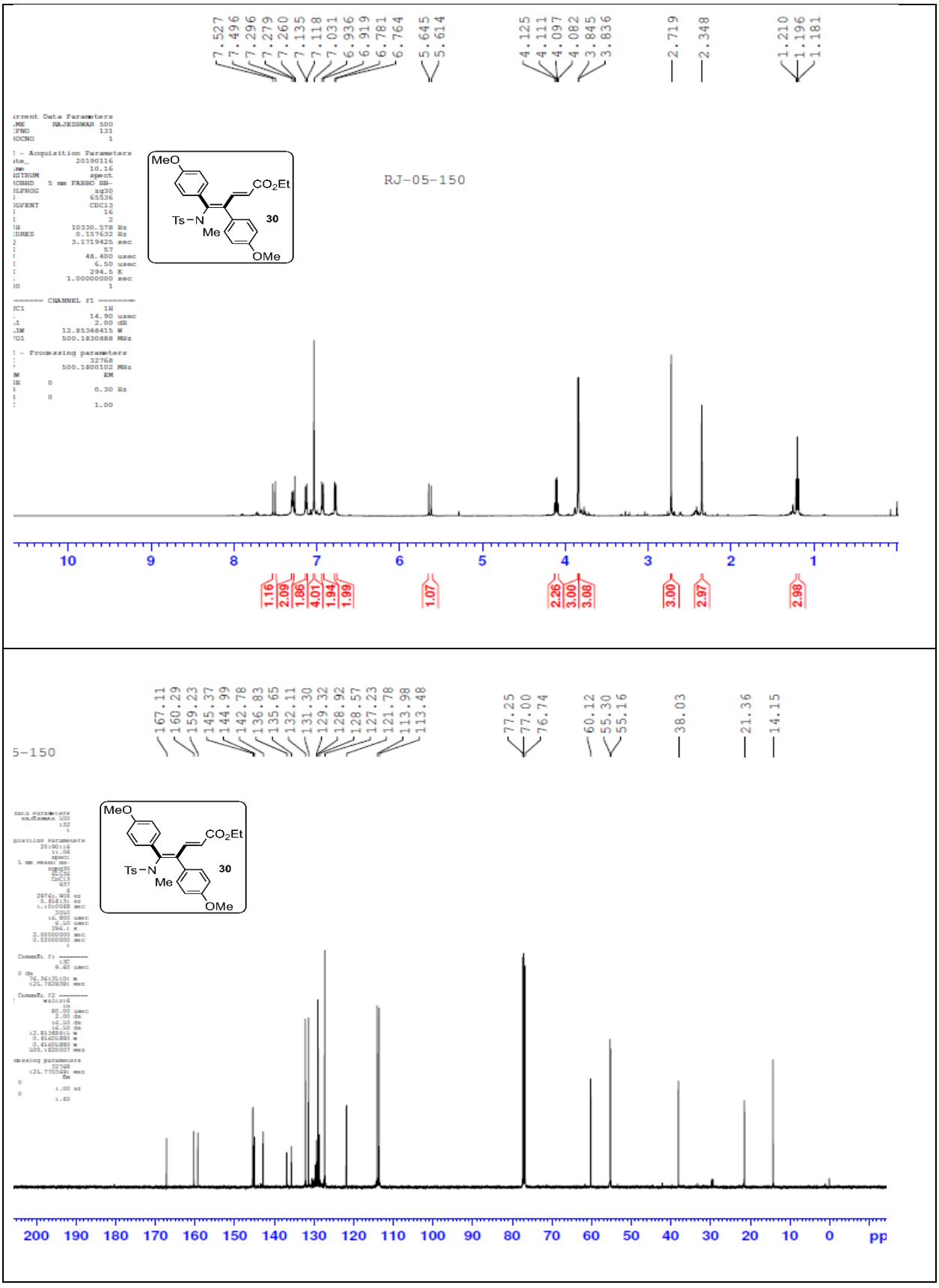
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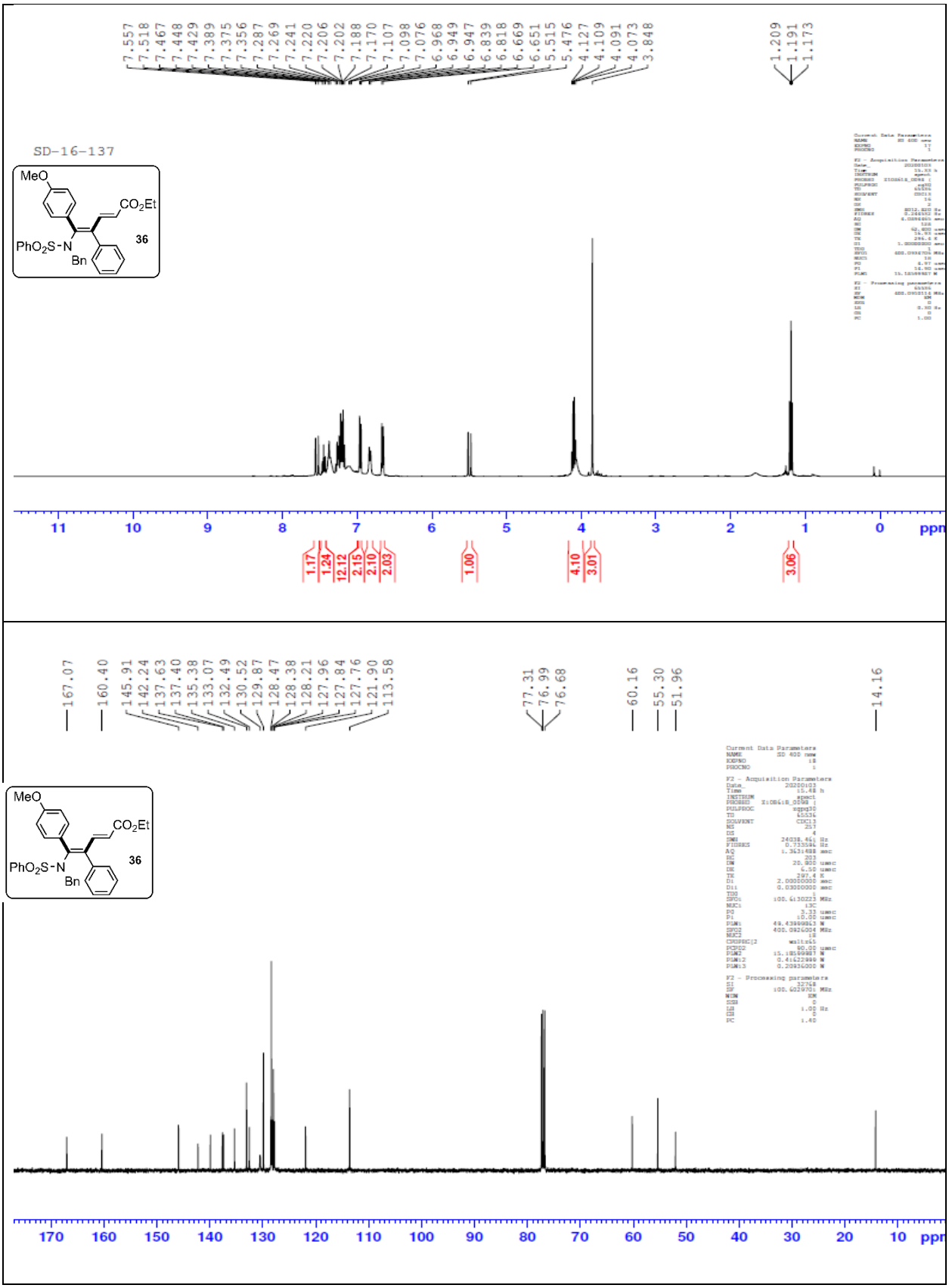
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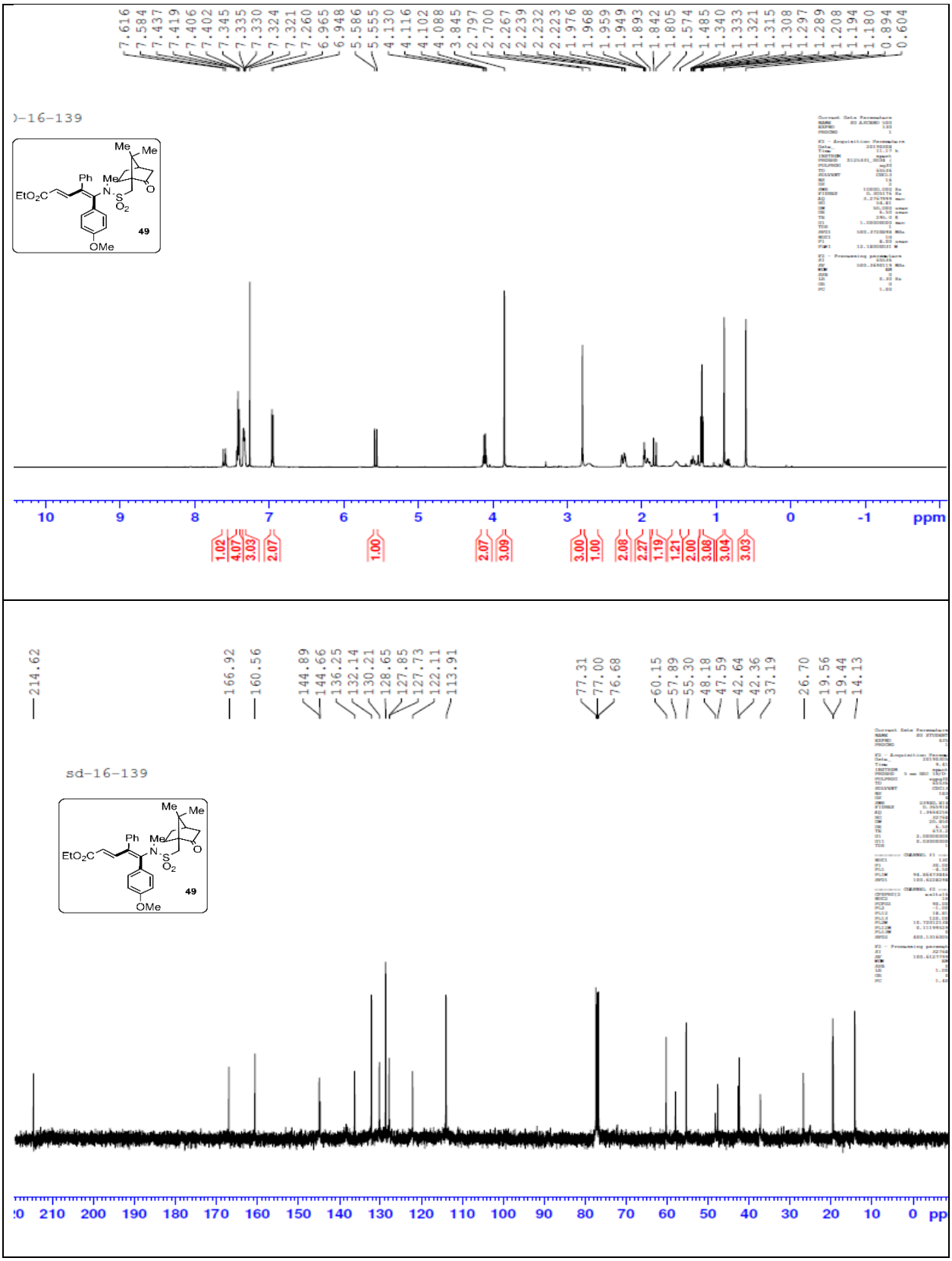
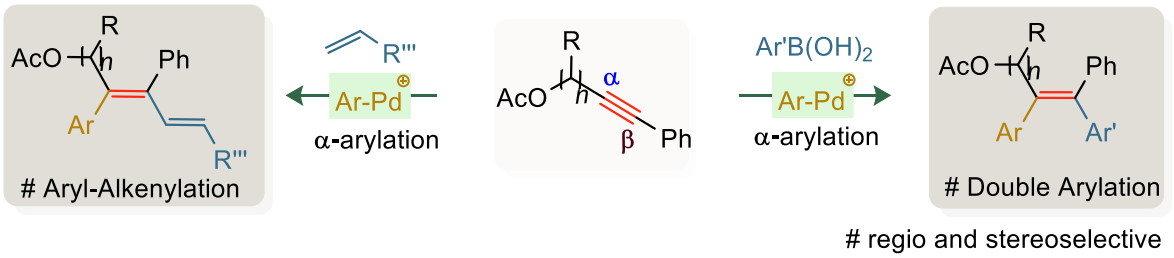
12.12
2.15
2.10
2.03
1.00
4.10
3.01
3.06
167.07
160.40
145.91
142.24
137.63
137.40
135.38
133.07
132.49
130.52
129.87
128.47
128.38
128.21
127.96
127.84
127.76
121.90
113.58
77.31
76.99
76.68
60.16
55.30
51.96
14.16
MeO
CO2Et
PhO2S-N
Bn
36
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.616
7.584
7.437
7.419
7.406
7.402
7.345
7.335
7.330
7.324
7.321
7.260
6.965
6.948
5.586
5.555
4.130
4.116
4.102
4.088
3.845
2.797
2.700
2.267
2.239
2.232
2.223
1.976
1.968
1.959
1.949
1.893
1.842
1.805
1.574
1.485
1.340
1.333
1.321
1.315
1.308
1.297
1.289
1.208
1.194
1.180
0.894
0.604
)-16-139
Me
Me
Ph
Me
N
S
O2
O
EtO2C
OMe
49
10 9 8 7 6 5 4 3 2 1 0 -1 ppm
1.02 4.07 3.03 2.07 1.00 2.07 3.09 3.00 1.00 2.08 2.27 1.19 1.21 2.00 3.08 3.04 3.03
214.62
166.92
160.56
144.89
144.66
136.25
132.14
130.21
128.65
127.85
127.73
122.11
113.91
77.31
77.00
76.68
60.15
57.89
55.30
48.18
47.59
42.64
42.36
37.19
26.70
19.56
19.44
14.13
sd-16-139
Me
Me
Ph
Me
N
S
O2
O
EtO2C
OMe
49
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 pp

Chapter-4A

Cationic-Palladium Catalyzed Regio- and Stereoselective *syn*-1,2-Difunctionalization of Unsymmetrical Internal Alkynes

Abstract



π-Extended tetrasubstituted olefins are widely found motifs in natural products, leading drugs, and agrochemicals. The difunctionalization of unsymmetrical alkynes is an attractive approach but often deals with regioselectivity issues. Here we report the discovery of a regio- and stereoselective *syn*-1,2-dicarbofunctionalization of unsymmetrical internal alkynes. A cationic Pd-catalyzed three-component coupling of aryl diazonium salts, aryl boronic acids (or olefins), and yne-acetates enables access to all-carbon substituted unsymmetrical olefins. The transformation features broad scope with labile functional group tolerance, building broad chemical space of structural diversity. The value of this synthetic method is demonstrated by the direct transformation of natural products and drug candidates containing yne-acetates, to enable highly substituted structurally complex allyl acetate analogues of biologically important compounds. Synthetic versatility of the carboxylate bearing highly-substituted olefins is also presented. The reaction outcome is attributed to the in-situ formation of stabilized cationic aryl-Pd species, which regulates regioselective aryl-palladation of unsymmetrical yne-acetates. Control experiments reveal the synergy between the carboxylate protecting group and the cationic Pd-intermediate in the regioselectivity and reaction productivity; density functional theory (DFT) studies rationalize the selectivity of the reaction.

Publication

S. Dutta, S. Shandilya, S. Yang, M. P. Gogoi, V. Gandon, A. K. Sahoo. *Nature Communications.* **2022**, *13*, 1360.

4A.1. Introduction

Tetrasubstituted and π-extended olefins are widespread in numerous natural products, leading drugs, and agrochemicals. They also hold potential applications in electron-transport materials and light-emitting-diodes (**Figure 4A.1**).[1]

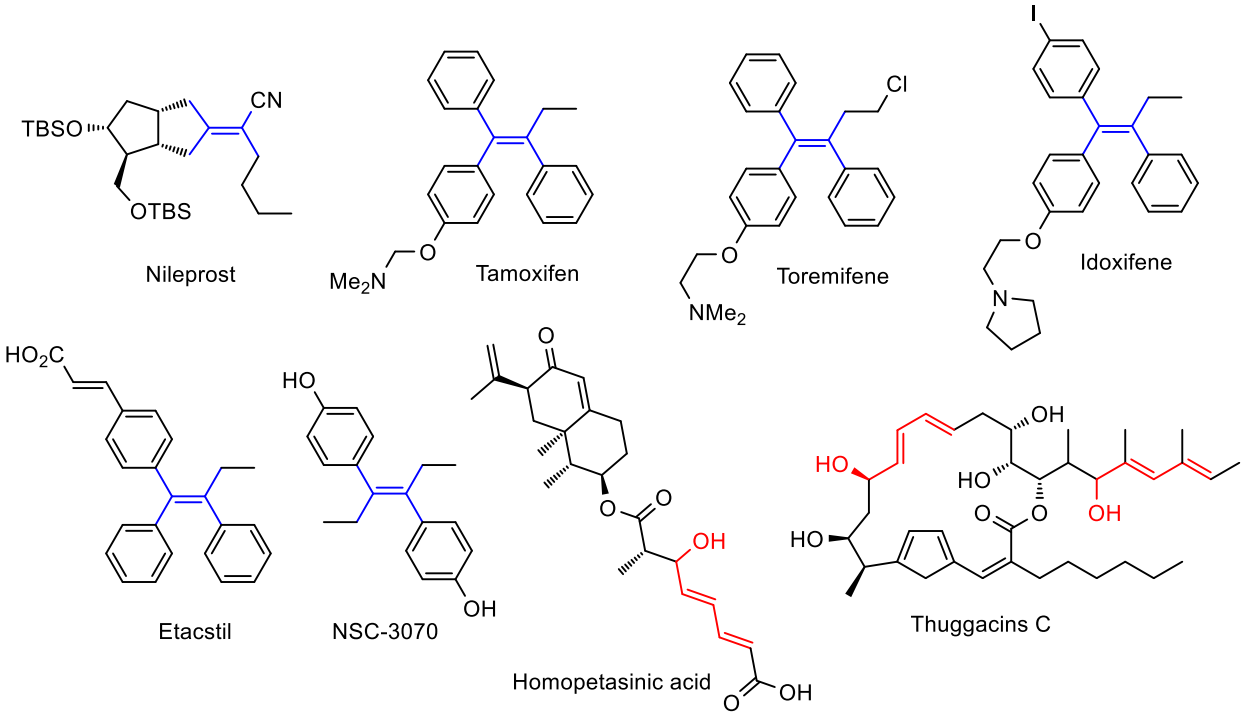


Figure 4A.1. Representative examples of tetrasubstituted and π-extended olefins containing biologically important compounds

The carbometallation of unsaturated C–C bonds has always been a gateway to biologically valuable feedstocks.[2] The transition-metal (TM) catalyzed alkyne dicarbofunctionalization by interrupting two cross-couplings [for example: Suzuki and Heck] offers a potential entry to highly-substituted olefins. However, this approach often suffers from insolvable regioselectivity issues. Mostly, the state-of-the-art regioselective carbometallation of unsymmetrical alkynes is restricted to inherently polarized substrates (**Figure 4A.2**-i), 2-pyridylsilyl alkynes (Itami; **Figure 4A.2**-ii) or sterically hindered borylated alkynes (Wang; **Figure 4A.2**-iii). The Larock's Pd-catalyzed *syn*-1,2-diarylation of unsymmetrical alkynes is also a good strategy to access all-carbon-

substituted olefins (**Figure 4A.2**-iv); however, it suffers from several limitations. For instance, *syn*-1,2-diarylation of diaryl-substituted alkynes occurs at an elevated temperature to deliver a mixture of regioisomers in moderate selectivity (**Figure 4A.2**–iv). In case of aryl-alkyl alkynes, the arylation takes place at the less hindered site of alkyne, resulting in better regioselectivity (**Figure 4A.2**–iv), but only with Me and Et groups. Thus, the *syn*-1,2-diarylation of unsymmetrical alkynes is substrate specific.

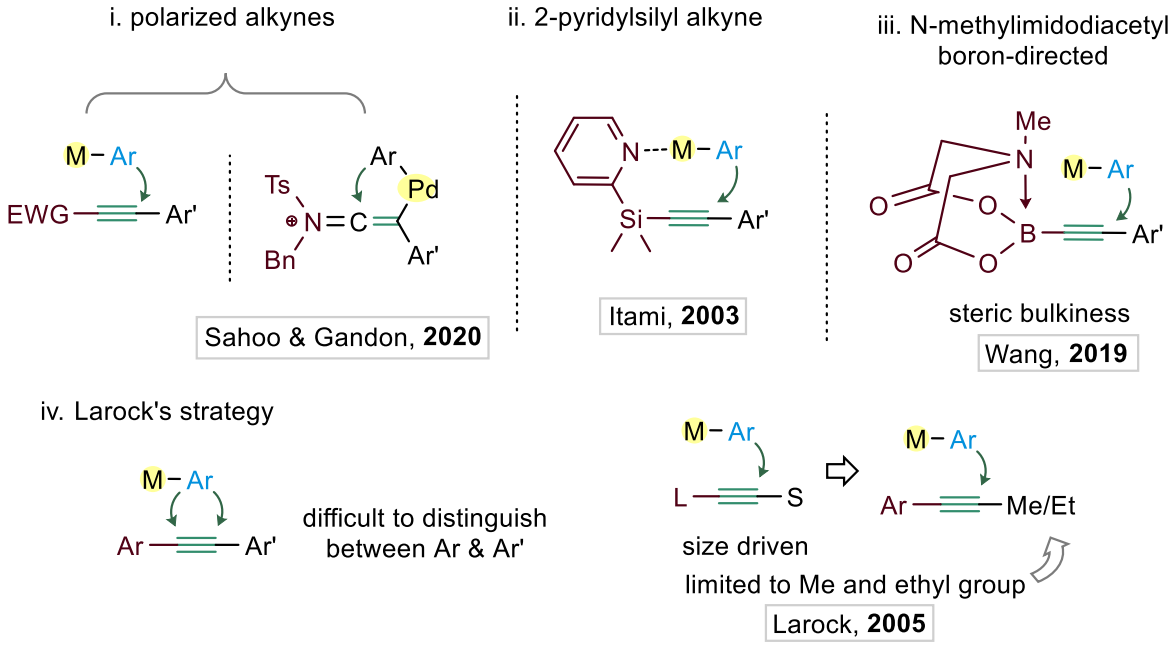


Figure 4A.2. Strategies towards regioselective aryl-metallation of unsymmetrical alkynes

4A.2. Precedents

As enumerated in Figure 4A.2, the diarylation of unsymmtrical alkynes is non-regioselective. A general mechanistic cycle of alkyne difunctionalization is depicted in **Figure 4A.3**. The transformation initiates with the oxidative addition of aryl-electrophile with ML_n (**A**) to give aryl metal species **B**, which upon migratory insertion with alkyne **C** leads to vinylic metal species **D**. Next consecutive transmetalation with $ArB(OH)_2$ and reductive elimination furnishes **F** with regeneration of catalyst for the next cycle.

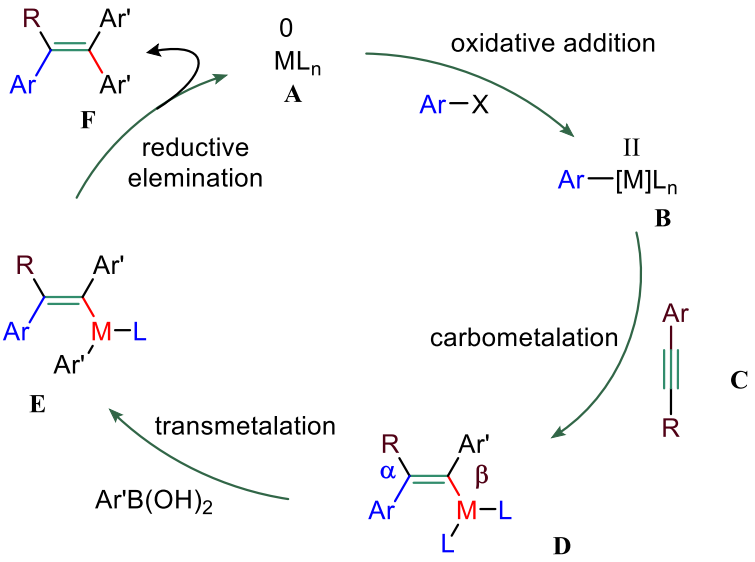
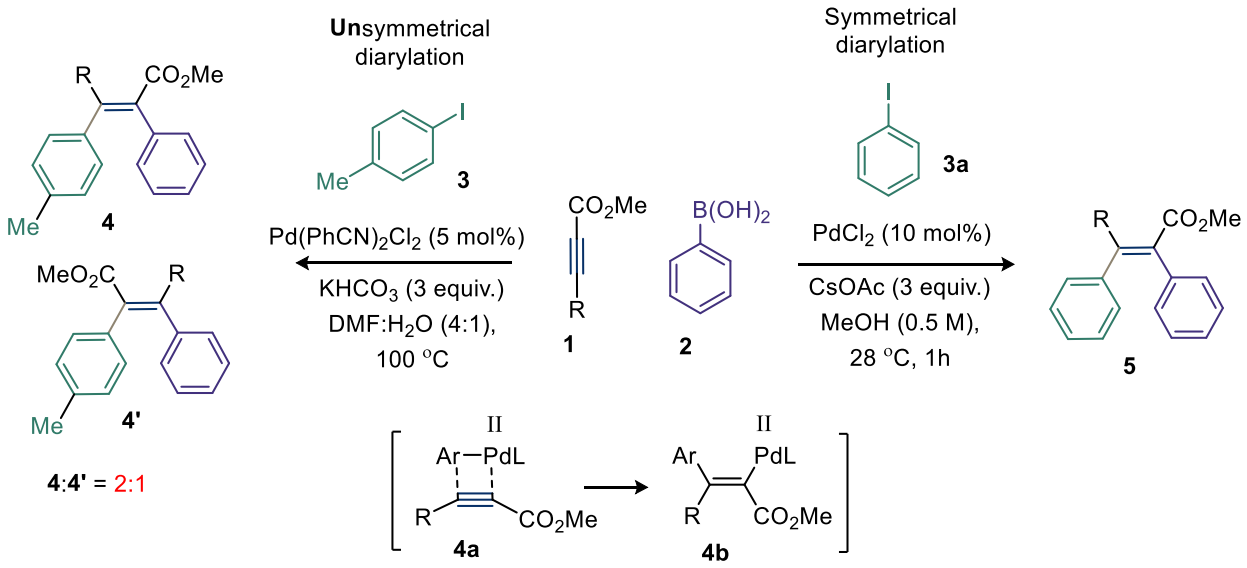


Figure 4A3. General mechanistic cycle in the diarylation of alkynes

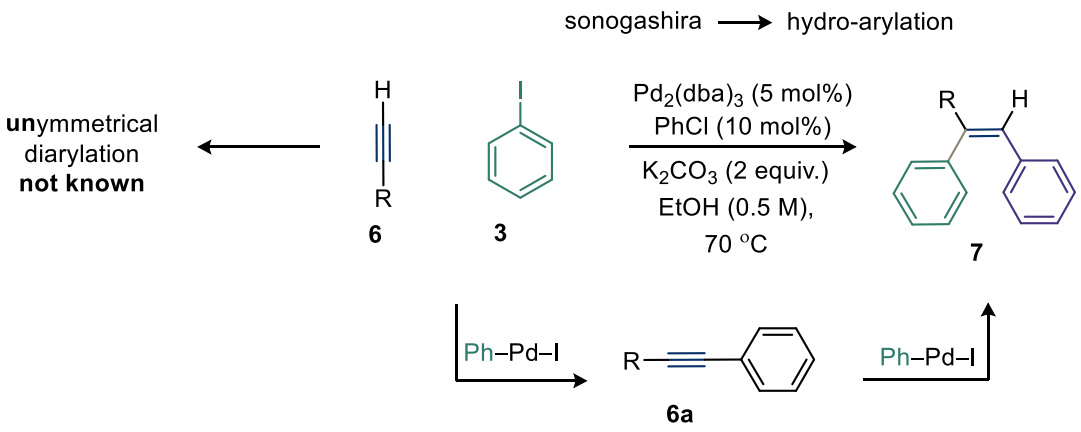
4A.2.1. Transition metal catalyzed diarylaion of unsymmetrical alkynes

A Pd-catalyzed usymmetrical diarylation of substituted propiolates **1** is described by Larock and co-workers in 2003 to obtain a stereoselective vinyl carboxylate core **4** with moderate regioselectivity (2:1) using aryl-iodide **3** and aryl-boronic acids **2** (**Scheme 4A.1**).[3] Slightly improved regioselectivity (2:1) was observed due to the electron baiseness of propiolate making the β-carbon **int-4a** electrophillic. This makes the aryl group attack facile to the β-carbon instead α-carbon to give int-**4b.** Next, transmetalation with aryl boronic acid and reductive elimination gives the desire product. In 2008, Wang and coworker reported symmetrical diarylation of propiolates using Pd-catalysis.



Scheme 4A.1. Palladium catalysed unsymmetrical diarylation of propiolates

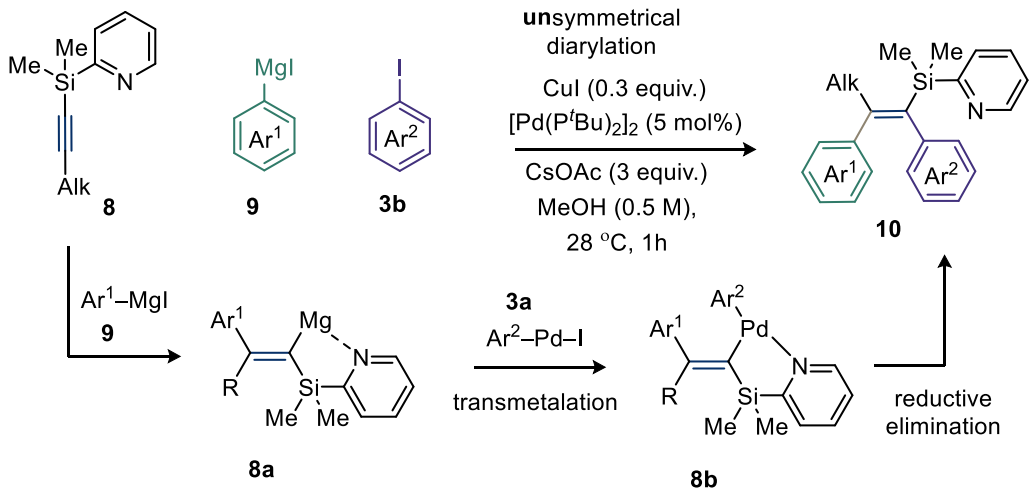
In 2014, Gao group reported a Pd-catalyzed sequential Sonogashira and hydro-arylation of terminal alkyne in presence of aryl-iodides under palladium catalysis (**Scheme 4A.2**).[4] At first, terminal alkyne **6** undergoes sonogashira coupling with aryl iodide **3**. Next, Ar-Pd-I complex undergoes migratory insertion followed by protodemetalation to yield the desired product **7**.



Scheme 4A.2. Palladium catalyzed symmetrical diarylation of terminal alkynes

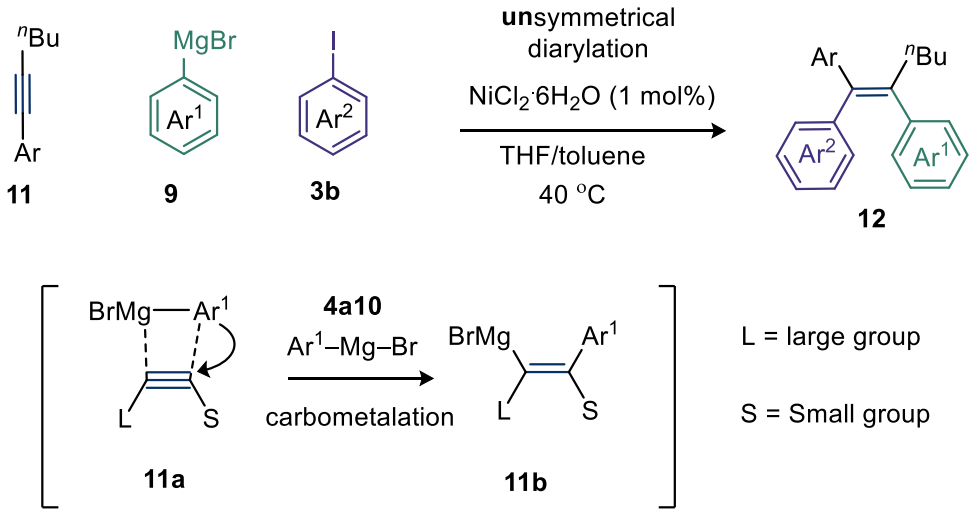
An interesting Pd/Cu-catalyzed regioselective unsymmetrical diarylation of pyridine silyl alkynes **8** using aryl magnesium iodide **9** and aryl iodide **3b** was disclosed by Itami group in 2003 (**Scheme 4A.3**).[5] The reaction begins with the regio- and stereoselective

addition of an aryl-magnesium iodide to (2-pyridyl)silyl alkyne (**8**) to yield a vinyl magnesium iodide compound **8a** (due probably to the complex-induced proximity effect of the pyridyl group on silicon). Next, transmetalation of **8a** with in-situ generated Ar-Pd-I gives **8b**, which upon reductive elimination yields the desired diarylation product **10**.



Scheme 4A.3. Palladium catalyzed unsymmetrical diarylation of 2-pyridyl silyl alkynes

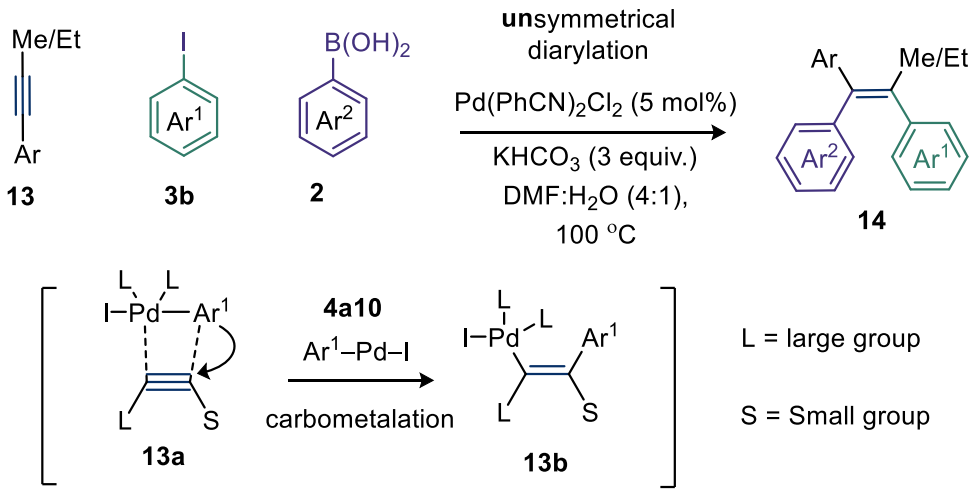
A very similar Ni-catalyzed diarylation of alkyne has been shown by Hayashi group in 2016. The reaction usages an aryl magnesium iodide **9** and aryl iodide **3b** and does not



Scheme 4A.4. Ni-catalyzed addition of aryl Grignard and aryl iodide to alkynes

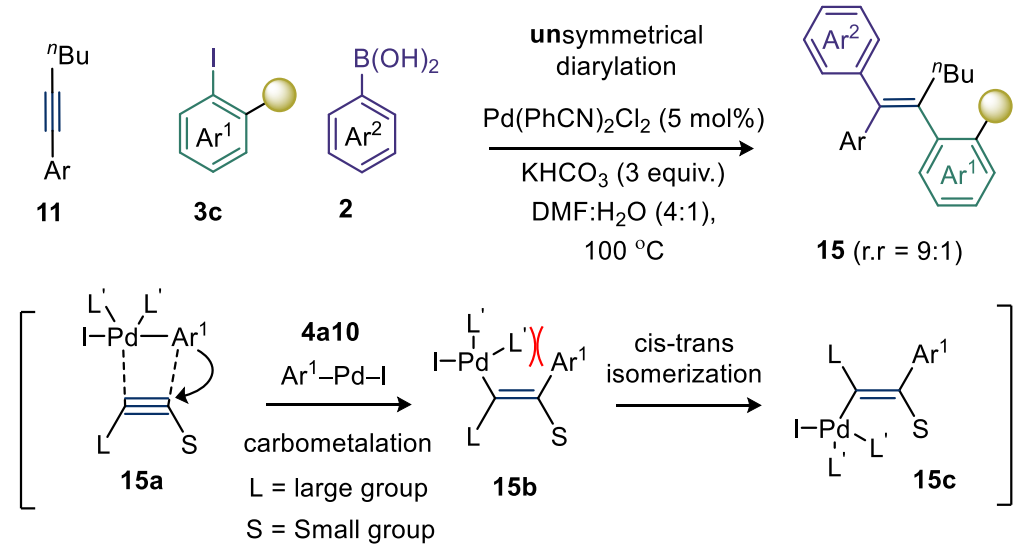
primarily require a directing group (**Scheme 4A.4**).[6] Reaction mechanism is quite similar to the catalytic cycle shown in **Scheme 4A.3**. The incoming aryl group approaches alkyne **11a** from the less hindered side, where a small group is attached on the alkyne. However, the reaction is substrate dependent and limited to alkynes having *n*-Bu group at the terminus.

The reaction regioselectivity is driven by a less-hindered group containing alkynes. Thus, diarylation of simple aryl-methyl/ethyl alkyne **13** was at first shown in 2005 by Larock group, when reacted with aryl-iodides **3b** and aryl boronic acid **2** coupling partners (**Scheme 4A.5**).[7] As the reaction regioselectivity was limited to methyl/ethyl alkynes, hence the reaction is not general with limited scope.



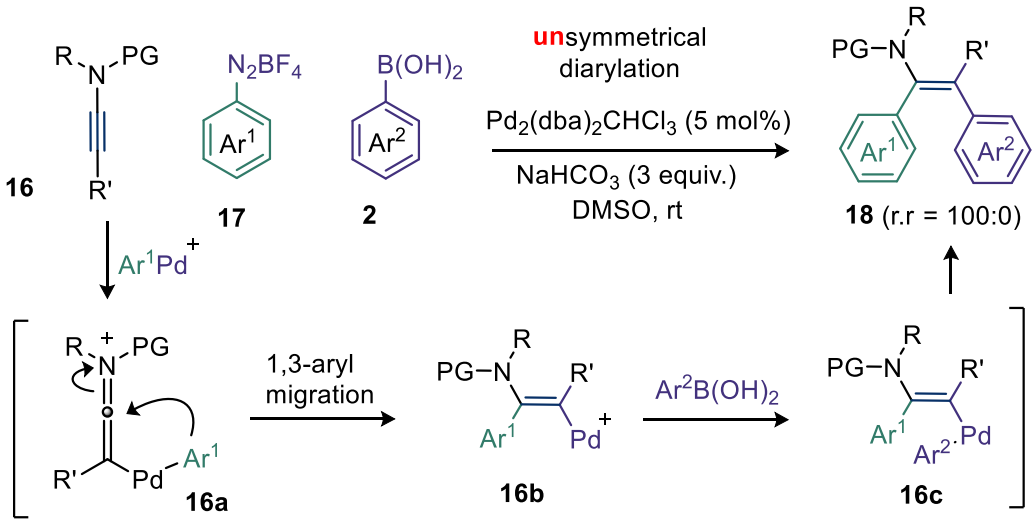
Scheme 4A.5. Pd-catalyzed unsymmetrical diarylation of aryl-methyl/ethyl alkynes

Very recently the Cheng and co-worker reported an anti-diarylation of internal alkyne using exclusively *ortho*-substituted iodo arenes under Pd-catalysis (**Scheme 4A.6**).[8] The reaction takes general approach of *syn*-carbopaladation from small group side of alkyne **15a** and gives **15b**. Next, the steric hindrance between the ligands of Pd-complex and *ortho*-substituent isomerizes *syn* int-**15b** to *anti* int-**15c'''**.



Scheme 4A.6. Palladium catalyzed hydro-arylation of propargyl alcohols

In 2020, our group reported a keteniminium driven highly regioslective unsymmetrical diarylation of ynamide **16** under cationic Pd-catalysis (**Scheme 4A.7**).[9] Aryl diazonium salts **17** and aryl boronic acid **2** have been used as coupling partners. Electrophilic activation of ynamide **16** in presence of aryl cationic Pd species provides keteniminium species **16a**. Next, 1,3-aryl migration from Pd to α-carbon of int-**16a** leads to int-**16b** which upon transmetalation with **2** and reductive elimination of int-**16c** yields the fully substituted enamides **18**.



Scheme 4A.7. Cationic palladium catalyzed diarylation of ynamides

4A.3. Motivation and Scheme Design

Overall, DG and the electron-bias of the alkyne are essential features in regioselective alkyne difunctionalization. In this context, the development of a ligand free regioselective *syn*-1,2-dicarbofunctionalization of unsymmetrical alkynes to build tetrasubstituted olefins appears to be a worthwhile endeavor. We herein showcase a cationic Pd-catalyzed 1,2-dicarbofunctionalization of unsymmetrical alkynes (**Figure 4A.4**). We envisioned that the reaction could rely on a site-selective coordination of a cationic Pd(II) species, generated in situ by the oxidative addition of an aryl diazonium salt[R] to Pd(0), to an yne-acetate (**I**) (**Figure 4A.4**). This would result in a *syn*-α-arylated-Pd intermediate **II**. The lone pair repulsion between the carboxylate moiety and the Pd-complex possibly excludes *syn*-β-arylated-Pd intermediate **III**. Further functionalization of vinyl-Pd(II)-cationic species **II** with aryl boronic acids (or olefins) would deliver highly-substituted olefins (or dienes). This strategy would lead to structurally diverse all-carbon-functionalized olefins in a single step from readily available yne-acetates. The transformation is highly regio- and stereoselective, even in the absence of external ligand and DG.

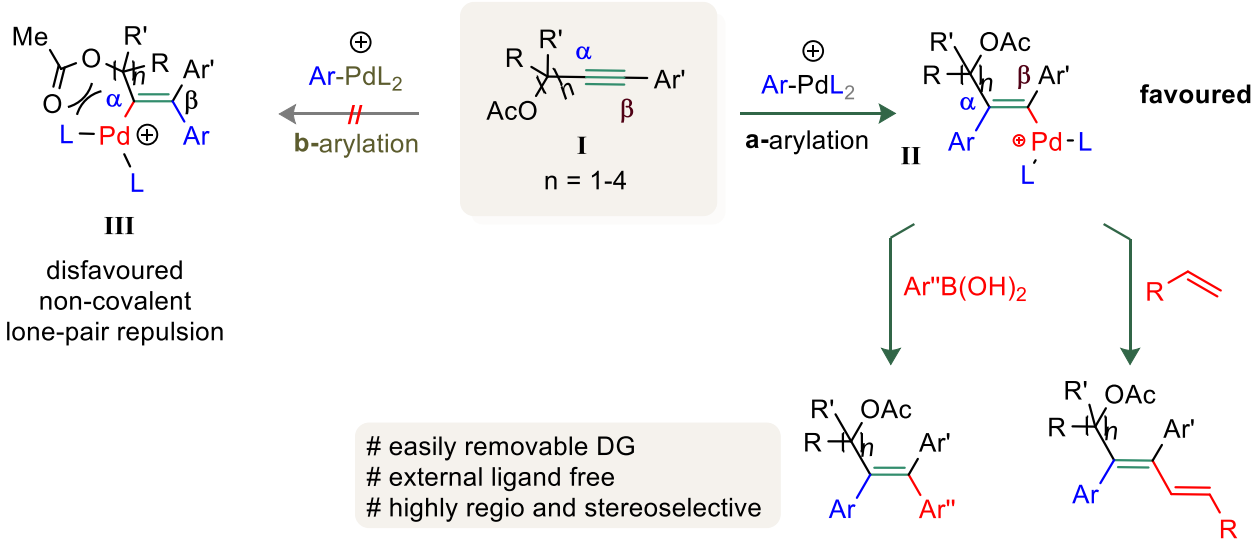
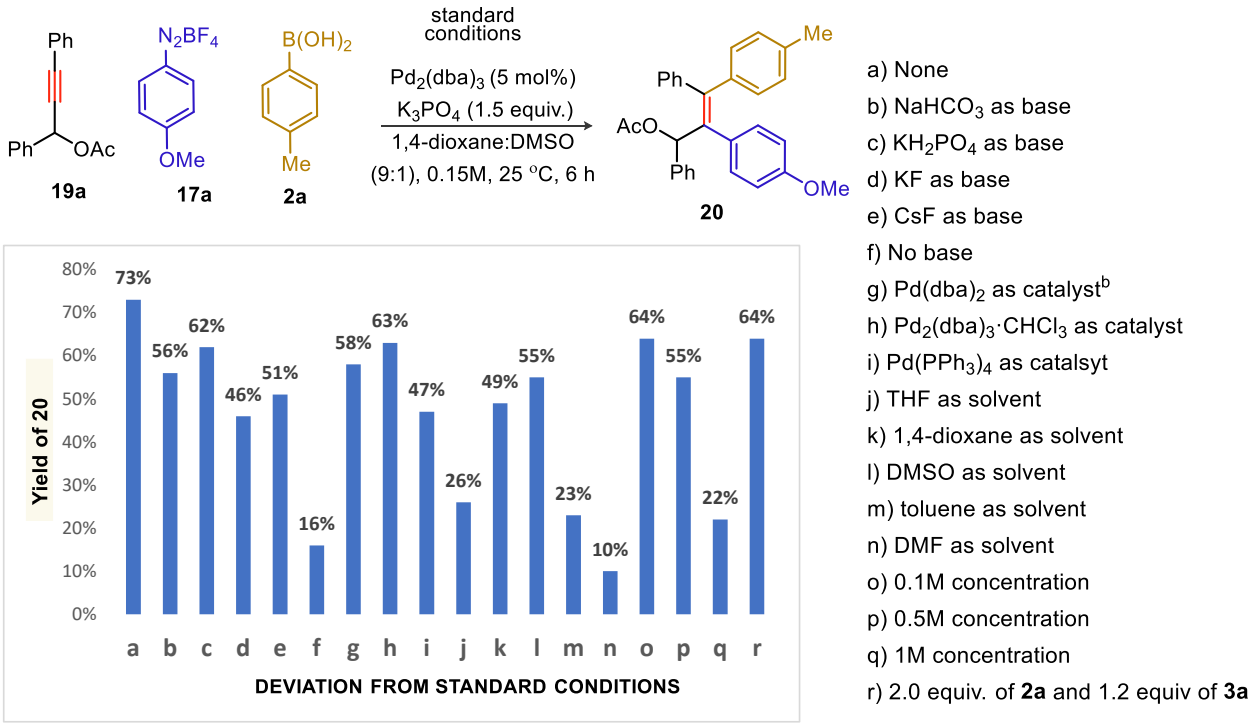


Figure 4A.4. Cationic Pd-catalyzed regioselective *syn*-dicarbofunctionalization of alkynes

4A.4. Result and Discussion

4A.4.1. Reaction Optimization

To investigate the 1,2-diarylation of structurally simple yne-acetates [i.e. propargyl acetates (PAs) to start with], a three-component reaction of 1,3-diphenylprop-2-yn-1-yl acetate (**19a**), *p*–methoxyphenyl diazonium tetrafluoroborate (**17a**), and *p*–tolyl boronic acid (**2a**) in presence of $Pd_2(dba)_3$ as the catalyst and a base was performed (**Figure 4A.5**). An extensive screening led to the optimized reaction conditions: [**19a** (1.0 equiv), **17a** (3.0 equiv), **2a** (1.5 equiv), $Pd_2(dba)_3$ (5.0 mol%) and K_3PO_4 (1.5 equiv) in 1,4-dioxane/DMSO (9:1) at 25 °C, 6 h]. With these, the unsymmetrical *syn*-diarylation product **20** was isolated in 73% yield (**Figure 4A.5**, **a**). $NaHCO_3$, KH_2PO_4, KF and CsF proved to be less efficient bases (**b**–**e**). Compound **20** was isolated in 16% in the absence of base (**f**). Lower yields



a) None
b) $NaHCO_3$ as base
c) KH_2PO_4 as base
d) KF as base
e) CsF as base
f) No base
g) $Pd(dba)_2$ as catalyst[b]
h) $Pd_2(dba)_3{\cdot}CHCl_3$ as catalyst
i) $Pd(PPh_3)_4$ as catalsyt
j) THF as solvent
k) 1,4-dioxane as solvent
l) DMSO as solvent
m) toluene as solvent
n) DMF as solvent
o) 0.1M concentration
p) 0.5M concentration
q) 1M concentration
r) 2.0 equiv. of **2a** and 1.2 equiv of **3a**

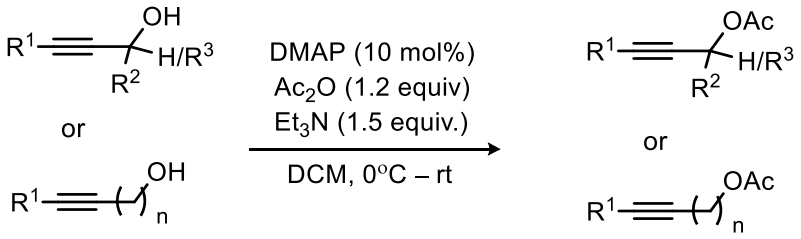
Figure 4A.5. Optimization of reaction conditions. ·All yields are Isolated yield. **19a** (0.2 mmol), **17a** (0.6 mmol), **2a** (0.3 mmol), cat. (0.01 mmol) and base (0.45 mmol). [b]10 mol % cat. was used.

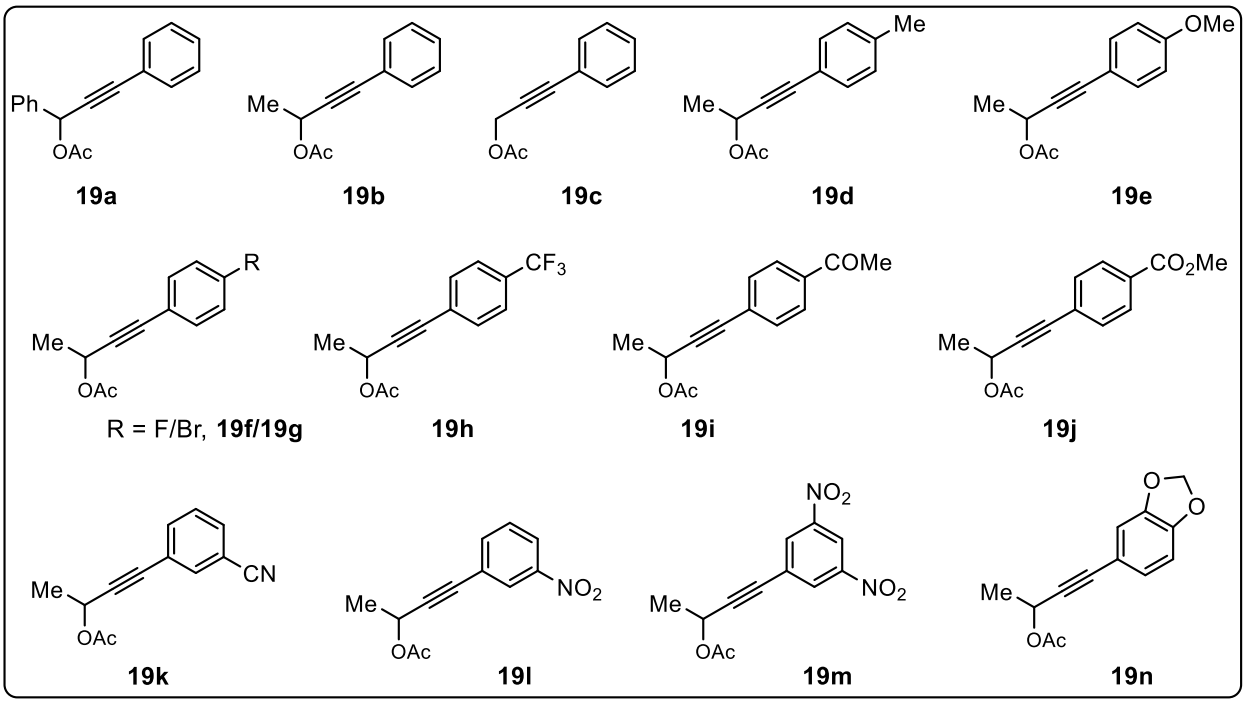
were obtained when other Pd(0) catalysts [$Pd(dba)_2$, $Pd_2(dba)_3{\cdot}CHCl_3$, $Pd(PPh_3)_4$,] were used (**g–i**). The solvents THF, 1,4–dioxane, DMSO, toluene or DMF did not improve the outcome (**j–n**). The reaction concentration did influence the product yield **20** (**o**–**q**). The reaction was less efficient when **17a** (2.0 equiv) and **2a** (1.2 equiv) were used (**r**).

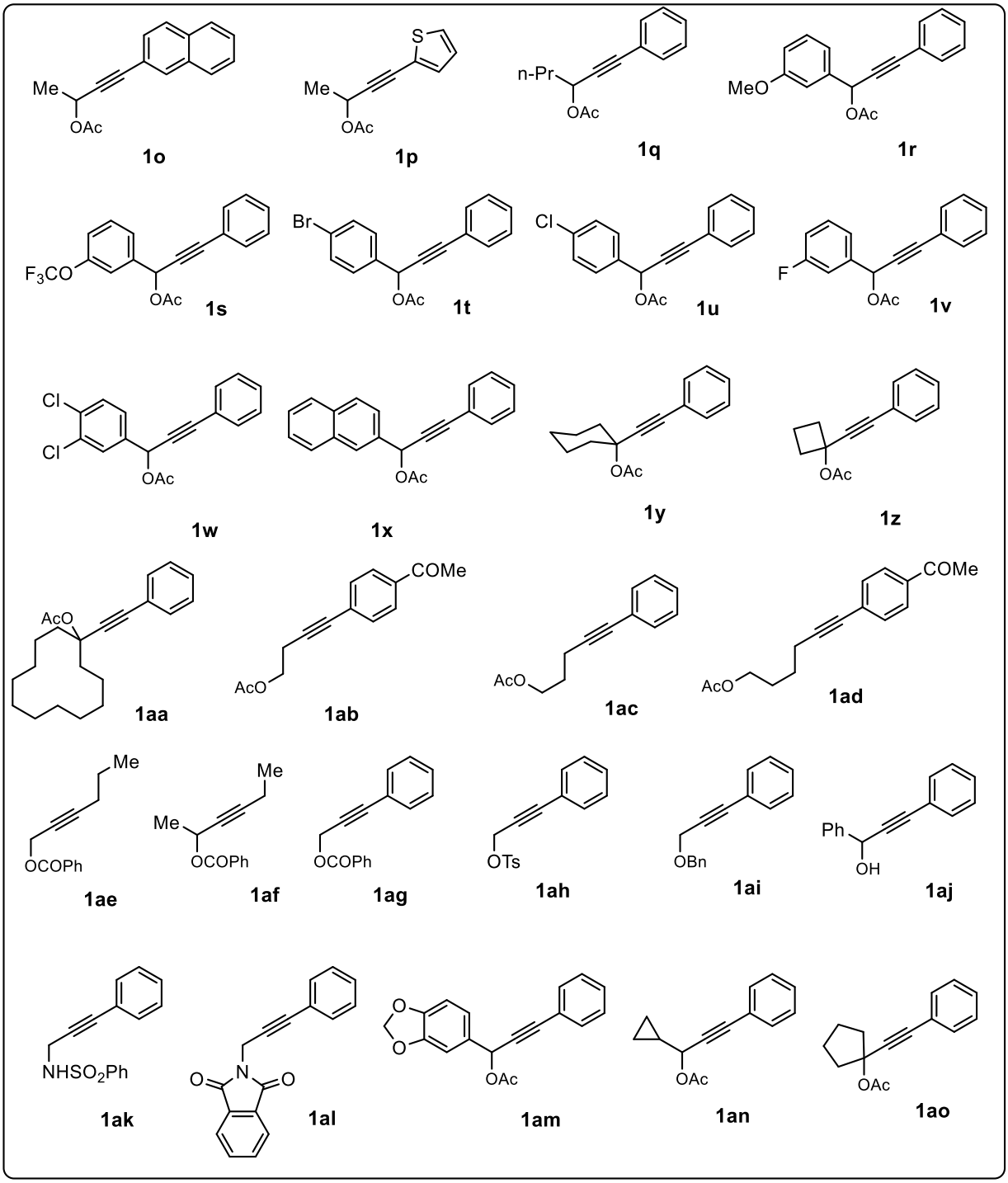
4A.4.2. Synthesis of yne acetates

Following the known Cu-catalyzed C-N coupling procdure, yne-acetaes **19a-1av** were synthesized from corresponding alcohols (Table 4A.1).

Table 4A.1. Propargyl acetate chart






Me
OAc
1o
S
Me
OAc
1p
n-Pr
OAc
1q
MeO
OAc
1r
F3CO
OAc
1s
Br
OAc
1t
Cl
OAc
1u
F
OAc
1v
Cl
Cl
OAc
1w
OAc
1x
OAc
1y
OAc
1z
AcO
1aa
COMe
AcO
1ab
AcO
1ac
COMe
AcO
1ad
Me
OCOPh
1ae
Me
Me
OCOPh
1af
OCOPh
1ag
OTs
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1ai
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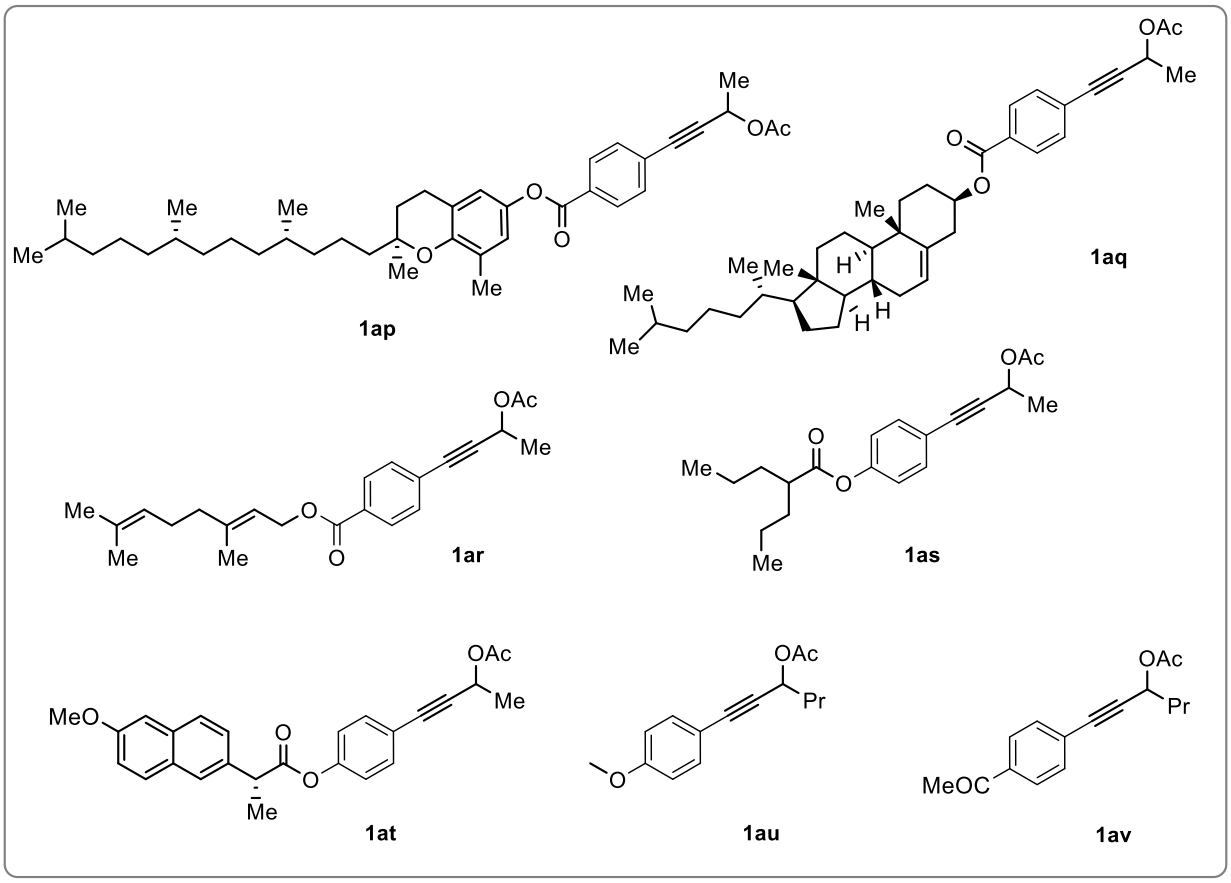


Table 4A.2. Aryl Diazonium Salt chart

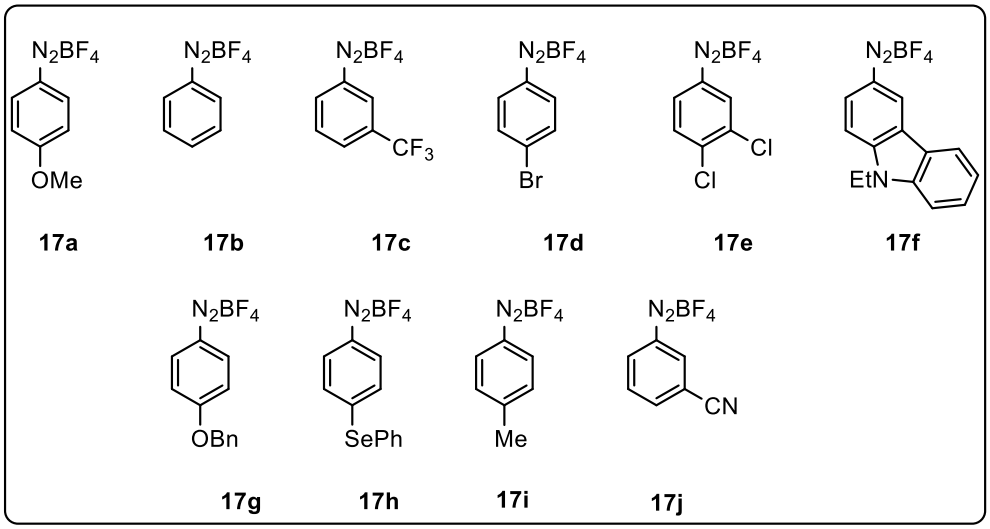
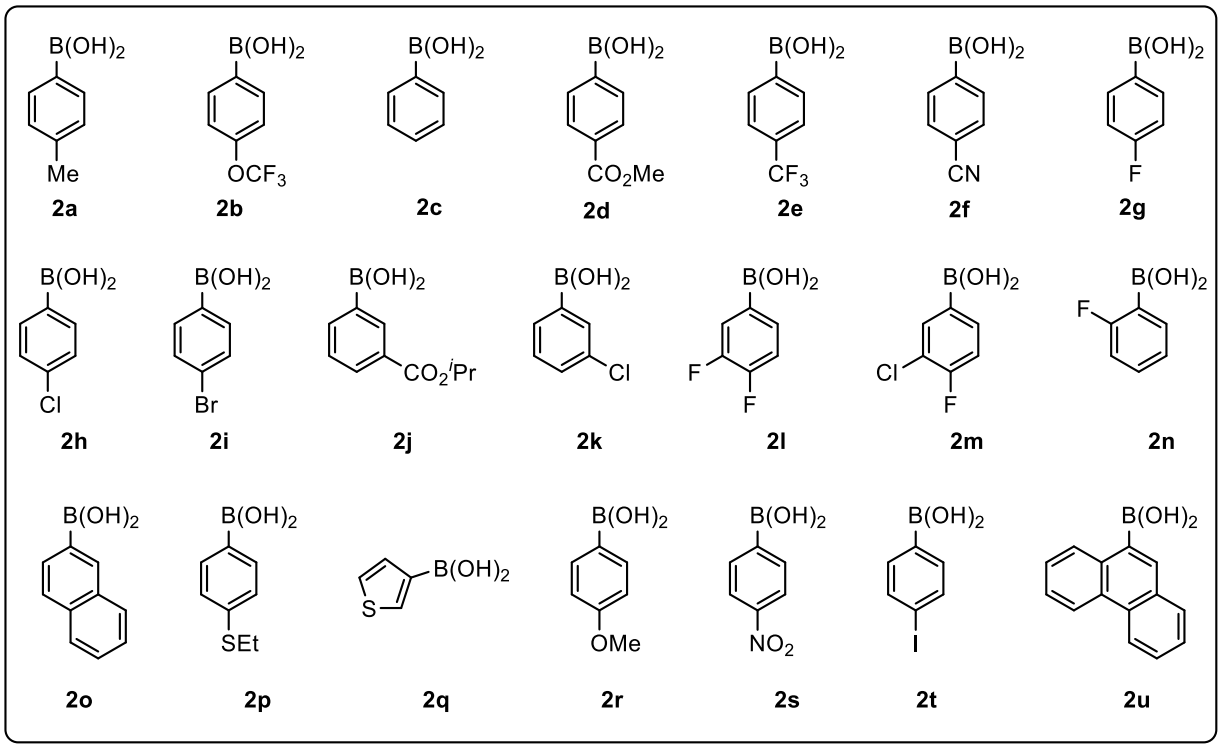
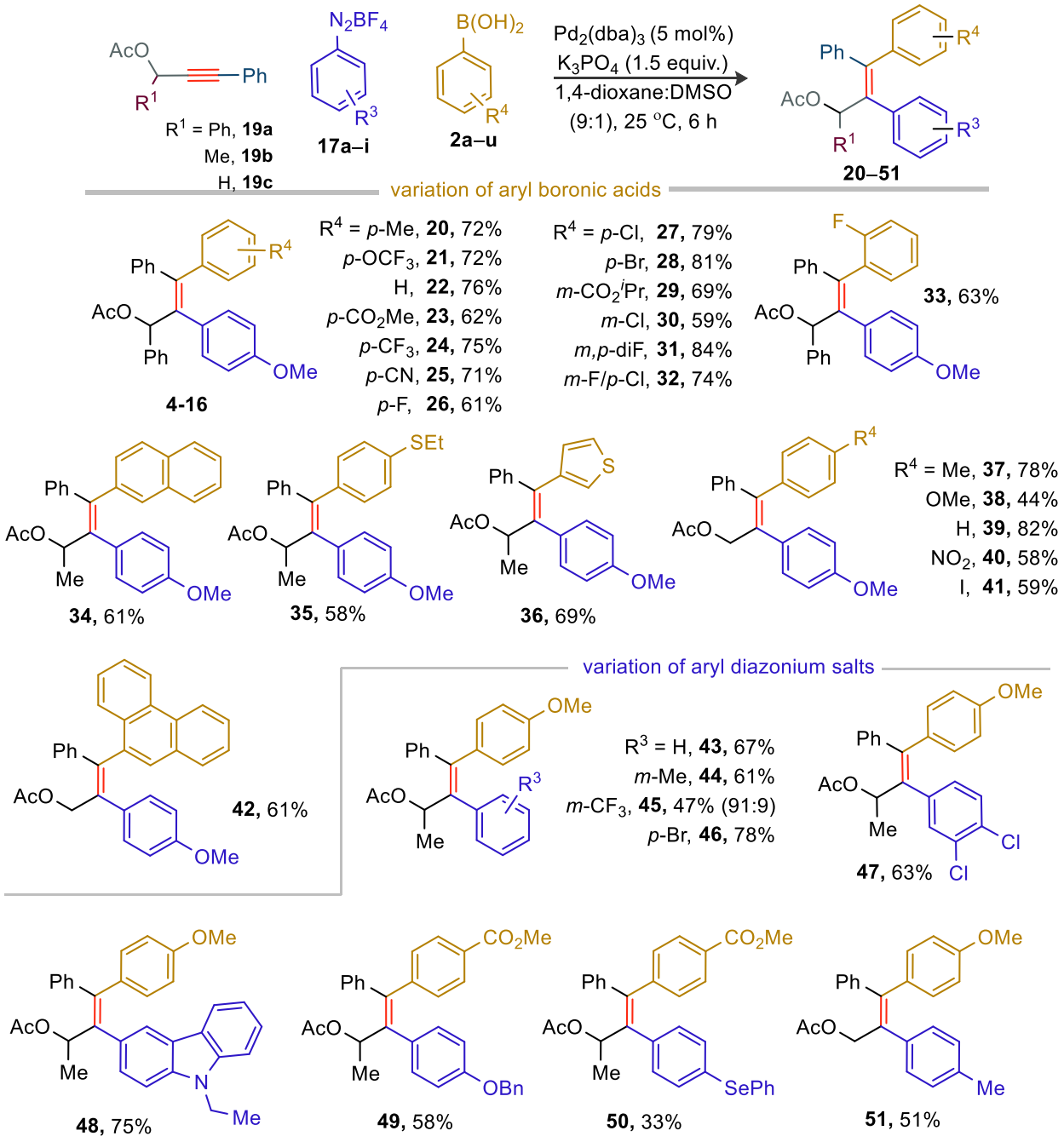


Table 4A.3. Aryl Boronic Acid chart



4A.4.3. Substrate Scope-I

This breakthrough encouraged us to investigate the reaction scope (**Scheme 4A.8-11**). The reactivity of the aryl boronic acid partners were first probed (**Scheme 4A.8**). The reaction of electron-rich *p*-substituted aryl boronic acids [*p*-Me (**2a**), *p*-OCF_3 (**2b**)] with **19** and **17a** provided **20** and **21** in good yields. Likewise, the tetrasubstituted olefins **22–25** (62–76 %) were constructed from phenyl boronic acid (**2c**) and electron-poor aryl boronic acids [*p*-CO_2Me (**2d**), *p*-CF_3 (**2e**), *p*-CN (**2f**)] when exposed to **19a** and **17a**. Although halo groups are usually amenable to cross-couplings under Pd(0)-catalysis, to our delight, the halogen-substituted aryl boronic acids [*p*-F (**2g**), *p*-Cl (**2h**), *p*-Br (**2i**)] proved compatible with the title reaction, leading to **26–28** in good yields. The transformation was compatible with *meta*- and *ortho*-substituted aryl boronic acids as well, leading to the



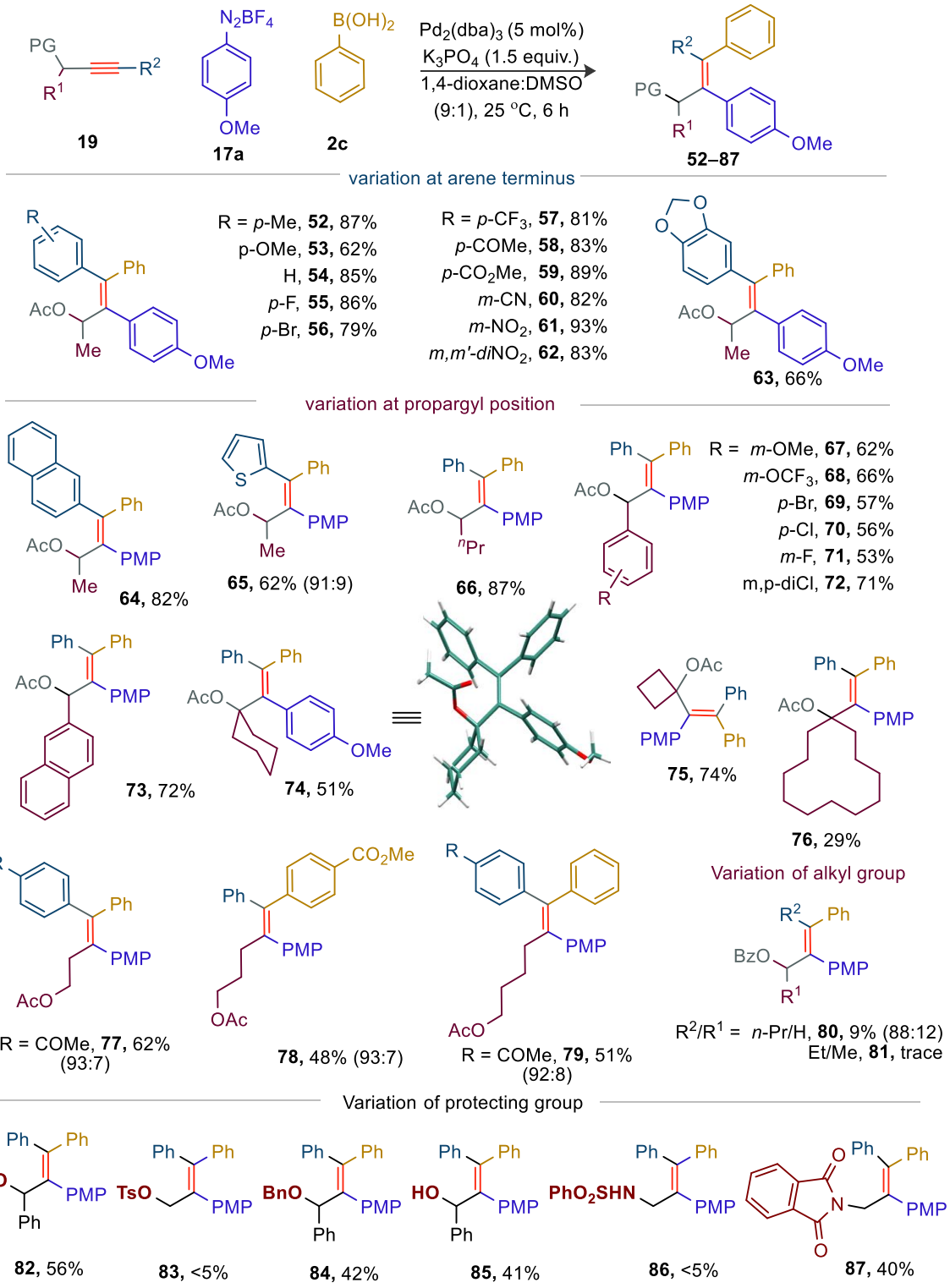
Scheme 4A.8. Scope of aryl-diazonium tetrafluoroborate salts and aryl boronic acids. **19a-c** (0.3 mmol), **17** (0.9 mmol), **2** (0.45 mmol), cat. (0.01 mmol) and base (0.45 mmol).

densely functionalized tetrasubstituted olefins **29–33** (59-84%). The desired 2-naphthyl, 4-ethylthiophenyl, 3-thienyl-bearing allyl-acetates **34-36** (58-69%) were also assembled

from the methyl-substituted yne-acetate **19b**. The unsubstituted propargyl acetate **19c** also proved to be a relevant substrate; various aryl boronic acids [*p*-Me (**2a**), *p*-OMe (**2r**), *p*-H (**2c**), *p*-NO_2 (**2s**), and *p*-I (**2t**)] were coupled to provide **37–41**. The bulky 9-phenanthrene boronic acid was not an exception, providing the π-extended product **42** in 61% yield.

Next, the three-component couplings of aryl diazonium tetrafluoroborates **17** with **19b** and **2r/2d** were surveyed. The reaction of **19b**, **2r** and diverse arene diazonium salts [phenyl (**17b**), electron-rich *m*-Me (**17c**), electron-poor *m*-CF_3 (**17d**), *p*-Br (**17e**), and *m,p*-diCl (**17f**)] provided **43–47** in good yields. The allyl acetate **45** was isolated as regioisomeric mixture (91:9). A carbazole bearing diarylation product **48** was isolated in 75% yield. The OBn protecting group and the oxidizable SePh group were unaffected under this Pd-catalysis, giving access to **49** and **50**. Likewise, **51** (51%) was made from the reaction of **19b** with **17j** and **2r**.

We next scrutinized the reactivity of unsymmetrical alkynes (**Scheme 4A.9**). The reaction of PAs [having aryl motifs: *p*-Me, *p*-OMe, *p*-F, *p*-Br, *p*-CF_3, *p*-COMe, *p*-CO_2Me, *m*-CN, *m*-NO_2, *m,m'*-diNO_2, and *m,p*-methylenedioxy at the alkyne terminus] with **17a** and **2c** independently furnished the desired products **52–63** (62-93%). Likewise, the π-extended 2-naphthyl- and heteroaryl 2-thienyl-enabled tetrasubstituted olefins **64** and **65** were constructed. Irrespective of *n*-propyl and various aryl-moieties at the propargyl position of PAs, the diarylation was equally effective in making **66**–**73**. In general, sterically bulky substituents severely affect cross-couplings. Nevertheless, *syn*-diarylation of cyclohexyl and cyclobutyl tethered PAs with **17a** and **2c** provided all-carbon-substituted olefins **74** and **75**. X-ray analysis confirmed the structure of **74**.[45] A macrocycle dodecane tethered diarylation product **76** was also fabricated. However, the terminal ynamide led to a complex mixture instead of providing the respective diarylation product. The product complexity justifies moderate yields (< 50%); in such cases, the reaction was incomplete with recovery of unreacted PAs. To test the potential coordination ability of the carboxylate group, diarylation of yne-acetates with different tether lengths between the alkyne and the acetate functionalities was probed. Irrespective of the acetate position in

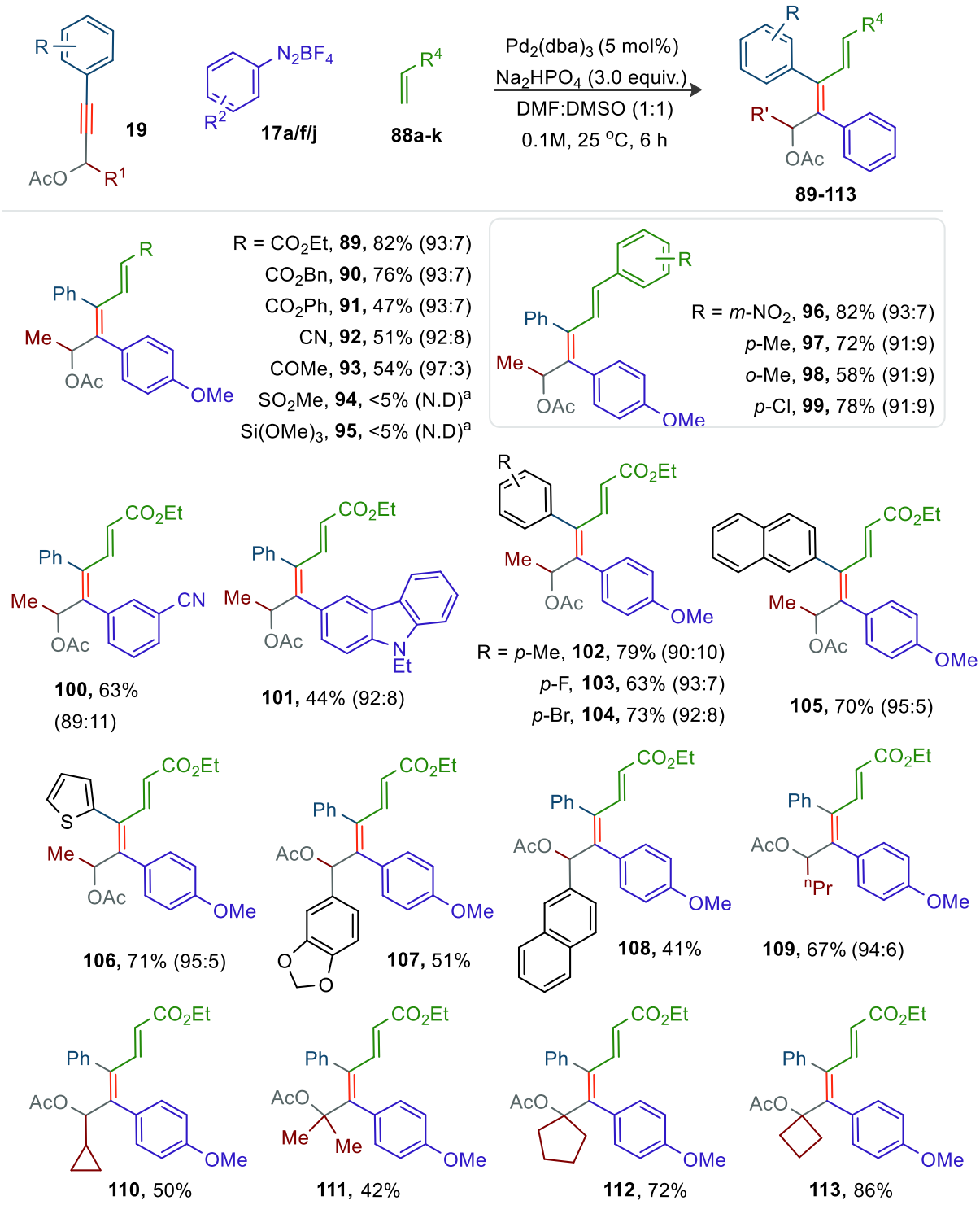


Scheme 4A.9: Scope of propargyl acetates **19** (0.3 mmol), **17a** (0.9 mmol), **2c** (0.45 mmol), cat. (0.015 mmol) and base (0.45 mmol).

yne-acetates, *syn*-diarylation of alkyne motifs was highly regioselective, furnishing **77**–**79** in moderate yields. The diarylation of alkyl-substituted PAs **19ae** / **19af** independently with **17a** and **2c** under the optimized condition has led to **80** (9%) and **81** (trace). In these cases, reaction was complex forming arylative dimerization of alkyne (confirmed by HRMS analysis) along with unreacted precursors. Next, the reaction of O-benzoate and O-benzyl protected propargyl alcohols with **17a** and **2c** afforded **82** (56%) and **83** (42%), respectively. On the other hand, the reaction of O-tosyl protected alkyne led to a complex mixture including a low amount of **84** (<5%); the low yield is possibly due to the facile cleavage of the labile C-OTs bond. The reaction of alkynes having unprotected hydroxy group or phthalimide group at the propargyl position with **16a** and **2c** delivered the desired diarylation products **85** and **87** in moderate yield with good regioselectivity. Unfortunately, the identical transformation of propargyl sulfonamide did not give the desired diarylation product **86**. The reaction is scalable to the gram, as shown by the preparation of **54** (1.2 g, 73 %) from the coupling of **19b** (1.0 g, 2.67 mmol), **16a** (1.77g, 8.01 mmol) and **2c** (0.5g, 4.00 mmol) using $Pd_2(dba)_3$ (3.0 mol %).

4A.4.4. Substrate scope-II

π-Conjugated scaffolds are widely found in molecules of pharmaceutical importance and light-emitting-diode materials.[1] We thus attempted to trap the cationic vinyl palladium species, obtained after aryl-palladation of the alkyne moiety, with olefins for constructing π-conjugated dienes (**Scheme 4A.10**). As envisaged, the reaction of **19b**, **2a** and ethyl acrylate (**88a**) under the optimized conditions of entry 1, **Figure 4A.5**, successfully led to **89** in 66% yield. To enhance the reaction productivity, bases and solvents were further screened. The Na_2HPO_4 base and DMSO:DMF (1:1) solvent combination were found optimum; **89** was isolated in 82% yield. Next, the reaction of wide ranges of acrylates and acrylonitriles with **19b** and **16a** under the adapted catalytic conditions furnished the desired conjugated dienes such as **89** (82%, 93:7), **90** (76%, 93:7), **91** (47%, 93:7) and **92** (51%, 92:8). Methyl vinyl ketone is usually susceptible to polymerization;[46] despite this potential issue, **93** was isolated in 54% yield and 97:3

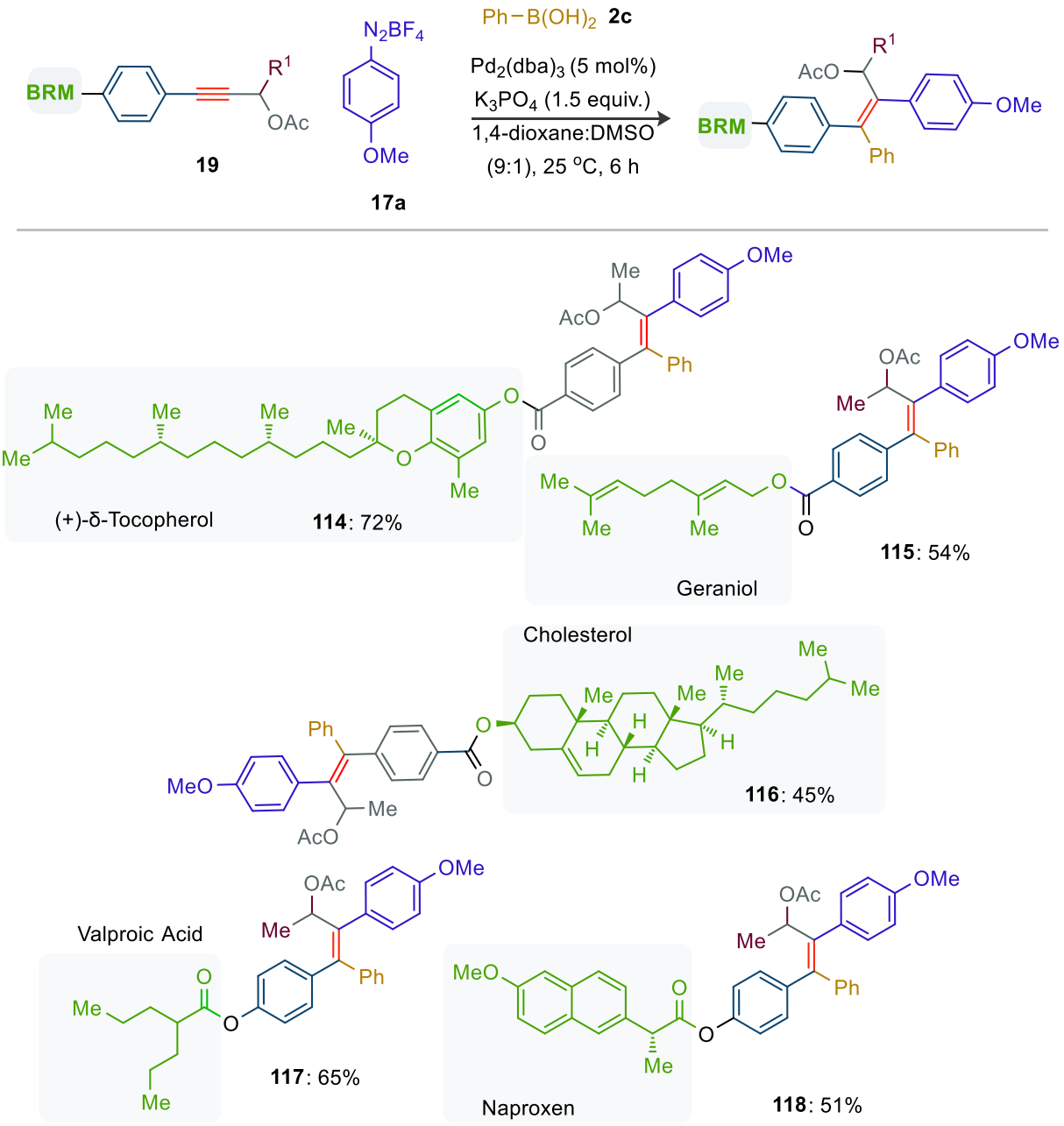


Scheme 4A.10: Scope of aryl-alkenylation[a] **19** (0.3 mmol), **17a/f/j** (0.9 mmol), **88** (0.6 mmol), cat. (0.01 mmol) and base (0.6 mmol).

regioisomeric ratio. However, identical transformations with methyl-vinyl sulfone or vinyl-trimethoxysilane did not provide the desired aryl-alkenylation products **94** and **95**. This difunctionalization even worked with styrenes, affording **96** (93:7), **97** (91:9), **98** (91:9), and **99** (91:9) in 58–82% yield. Rather substantial amount of hydro-arylation product was observed along with unreacted yne-acetate. The products **100** (63%, 89:11) and **101** (44%, 92:8) were made from the couplings of **19b** and **88a** with **17f** and **17j**, respectively. The PAs [having aryl motifs: *p*-Me, *p*-F, *p*-Br, p-extended 2-naphthyl or 2-thienyl at the alkyne terminus)] were independently coupled with **17a** and **88a** to deliver **102**–**106** in good yields along with 5-10% minor isomer. Likewise, **107**–**110** were made, albeit in moderate yield, from the reaction of PAs [with variation of substituents, *m*,*p*-methylenedioxy-phenyl, 2-naphthyl, *n*-Pr, and cyclopropyl at the propargyl position] with **17a** and **88a**. Even the sterically encumbered di-Me, cyclopentyl, and cyclobutyl tethered PAs were successfully converted into unusual π-conjugated dienes **111**–**113** (42-86%). Thus, the cationic Pd-catalytic system did not virtually affect the reaction outcome and the strained cyclopropyl ring, labile halo groups, and easily modifiable functional groups were well tolerated.

4A.4.5. Substrate Scope-III

Late-stage difunctionalization of unsymmetrical alkynes having biologically relevant motifs (BRMs) is invaluable for the sustainable development of complex molecules with enhanced pharmacokinetic properties. However, BRMs with polar groups and unsaturated moieties often cause problems for cross-coupling reactions, as the TM binding ability could lead to substrate decomposition and affect the difunctionalization efficiency. We were therefore intrigued by the viability of the cationic Pd-catalyzed double arylation of pharmacophore-coupled alkynes **19** (**Scheme 4A.11**). Once again, the title reaction proved reliable: tetra-substituted allyl acetates encapsulated fatty alcohol [vitamin-E-tocopherol (**114**)], steroid [cholesterol (**115**)], and terpenoid [geraniol (**116**)] were produced in 45–72% yields from the diarylation of respective BRMs-coupled propargyl acetates with **17a** and **2c**. We further probed the efficacy of the regioselective

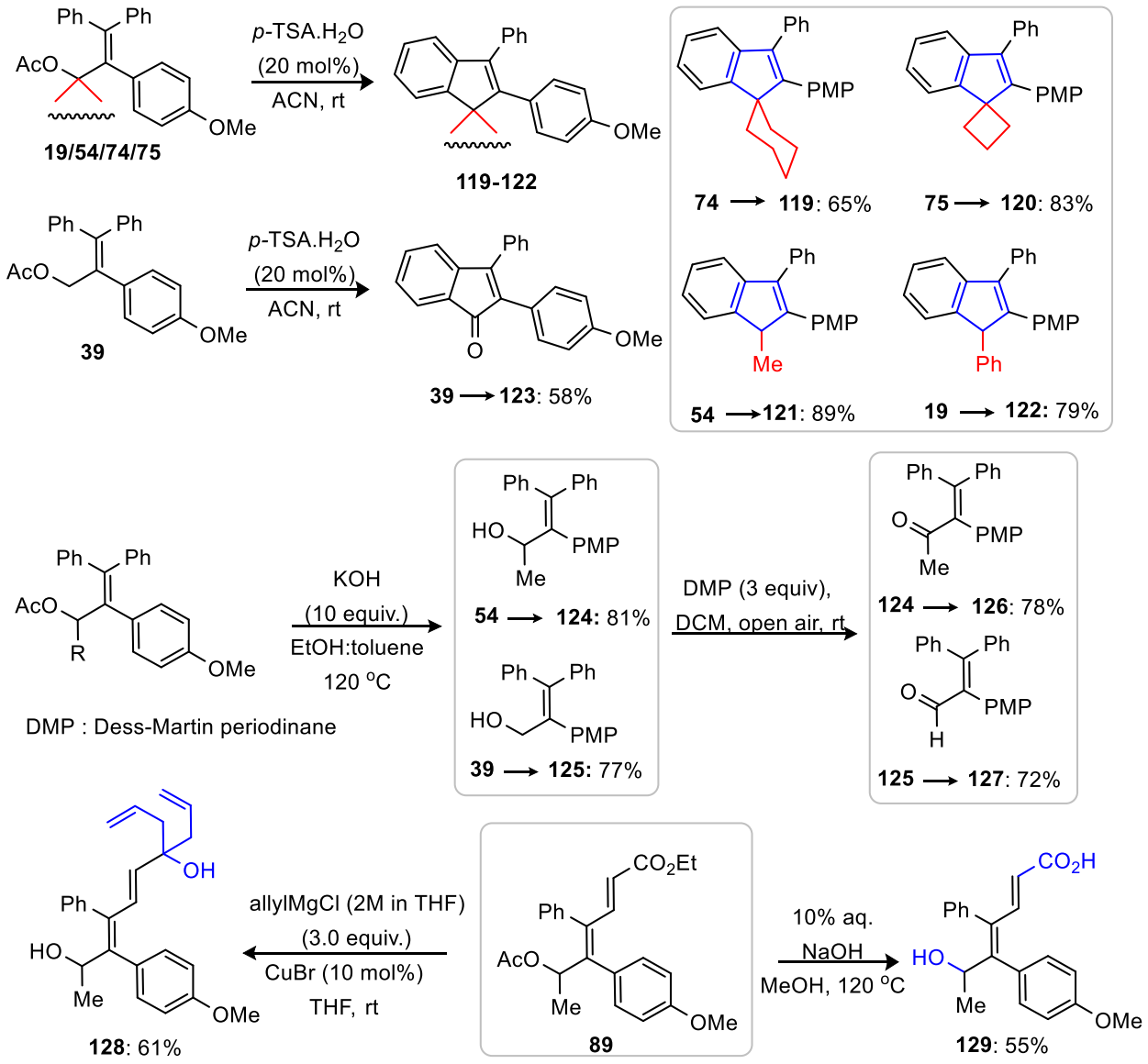


Scheme 4A.11: Scope of diarylation of Biological relevant motif containing alkynes

diarylation using marketed drug molecules containing unsymmetrical alkynes. Thus, reaction of the anti-epileptic drug, bipolar disorder, and migraine preventer valproic acid coupled PA with **17a** and **2c** provided highly substituted allyl acetate **117** in 65% yield. Likewise, nonsteroidal anti-inflammatory drug containing allyl acetate **118** was made in good yield.

4A.4.6. Synthetic application

We next probed the synthetic versatility of the newly constructed tetrasubstituted allyl-acetates (**Scheme 4A.12**). The *p*-TSA driven intramolecular Friedel-Crafts arene cyclization of **74/75** led to unusual cyclohexyl/cyclobutyl spiro-fused indene derivatives **119** (65%) and **120** (83%), respectively, and peripheral-substituted indenes **54**→**121** (89%) and **19**→**122** (79%).



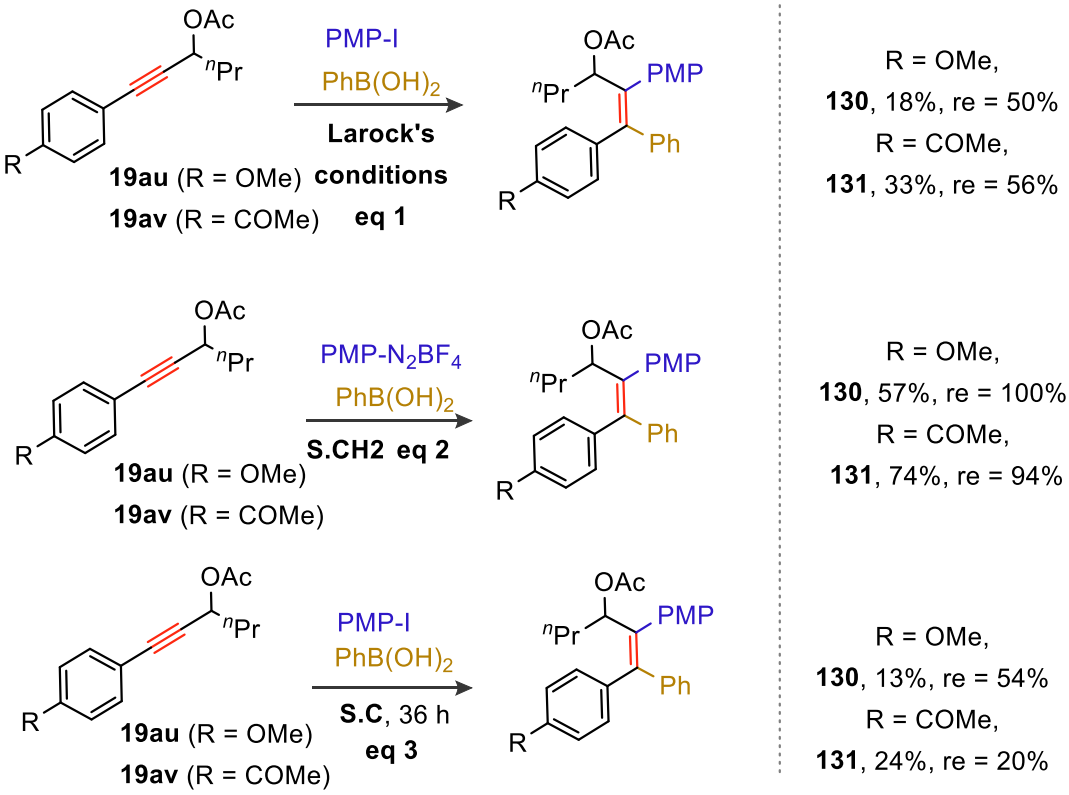
Scheme 4A.12: Synthetic Applications

Likewise, electrophilic cyclization of **39** provided indanone **123** in 58% yield. Fully substituted propargyl alcohols [**54**→**124** (81%); **39**→**125** (77%)] were accessed from the KOH mediated hydrolysis of the acetate motif. Dess-Martin periodinane (DMP)-mediated oxidation of **124** and **125** delivered methyl-vinyl ketone **126** (78%) and acrolein **127** (72%), respectively; further functionalization of carbonyl groups is therefore possible. Allylation and hydrolysis of π-extended ester **89** yielded allylic-3°-alcohol **128** and α,β-unsaturated carboxylic acid **129**.

4A.4.7. Mechanistic Studies

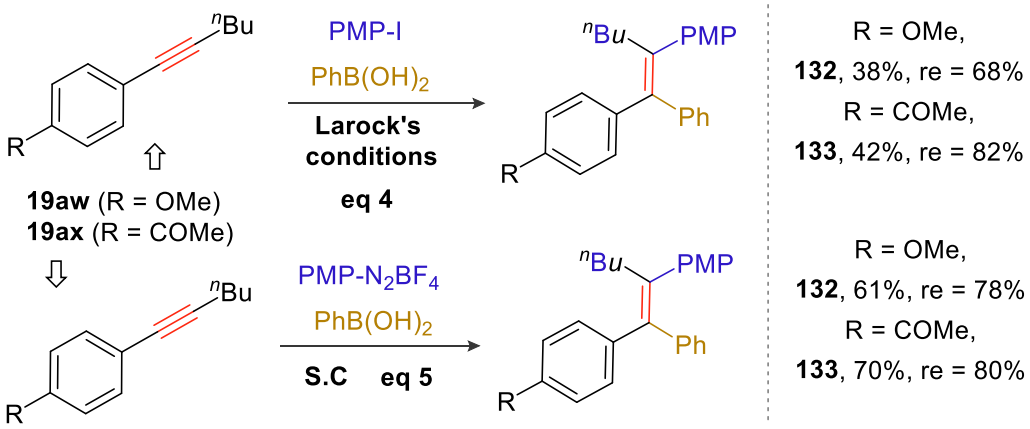
To shed light on the reaction mechanism and importance of ArN_2BF_4, cationic palladium species, and acetate (OAc) group for the notable regioselectivity outcome in the 1,2-diarylation of PAs, a series of experiments was planned (**Scheme 4A.13a-d**). The reaction of electronically diverse PAs (having aryl moiety *p*-OMe (**19au**)/*p*-COMe (**19av**) at the alkyne terminus) were independently subjected to different reaction conditions: {Larock's conditions: eq 1 [*p*-methoxyphenyl (PMP)-I, $PhB(OH)_2$, $Pd(PhCN)_2Cl_2$, K_2CO_3, DMF:H_2O (4:1), rt]}, {standard conditions (SC) of current reaction: eq 2 [PMP-N_2BF_4, $PhB(OH)_2$, $Pd_2(dba)_3$, K_3PO_4, 1,4-dioxane:DMSO (9:1), rt]}, and {SC of current reaction: eq 3 [PMP-I instead PMP-N_2BF_4]}. As anticipated, the diarylation products **130** (57%) and **131** (74%) with regioisomeric excess (*re*) 100% and 94%, respectively, were formed (eq 2, **Scheme 4A.13a**). On the other hand, the identical reaction under Larock's conditions provided poor productivity as well as low *re* **130** (11%, 50% *re*) and **131** (21%, 56% *re*) (eq 1, **Scheme 4A.13a**). In comparison, **130** (13%, 54% *re*) and **131** (24%, 20% *re*) were observed when the reaction was performed with PMP-I instead PMP-N_2BF_4 under the SC (eq 3, **Scheme 4A.13a**). It appears that cationic palladium species [obtained in-situ by the oxidative addition of PMP-N_2BF_4 with Pd(0) catalyst] play a crucial role in the control of the regioselectivity as well as productivity.

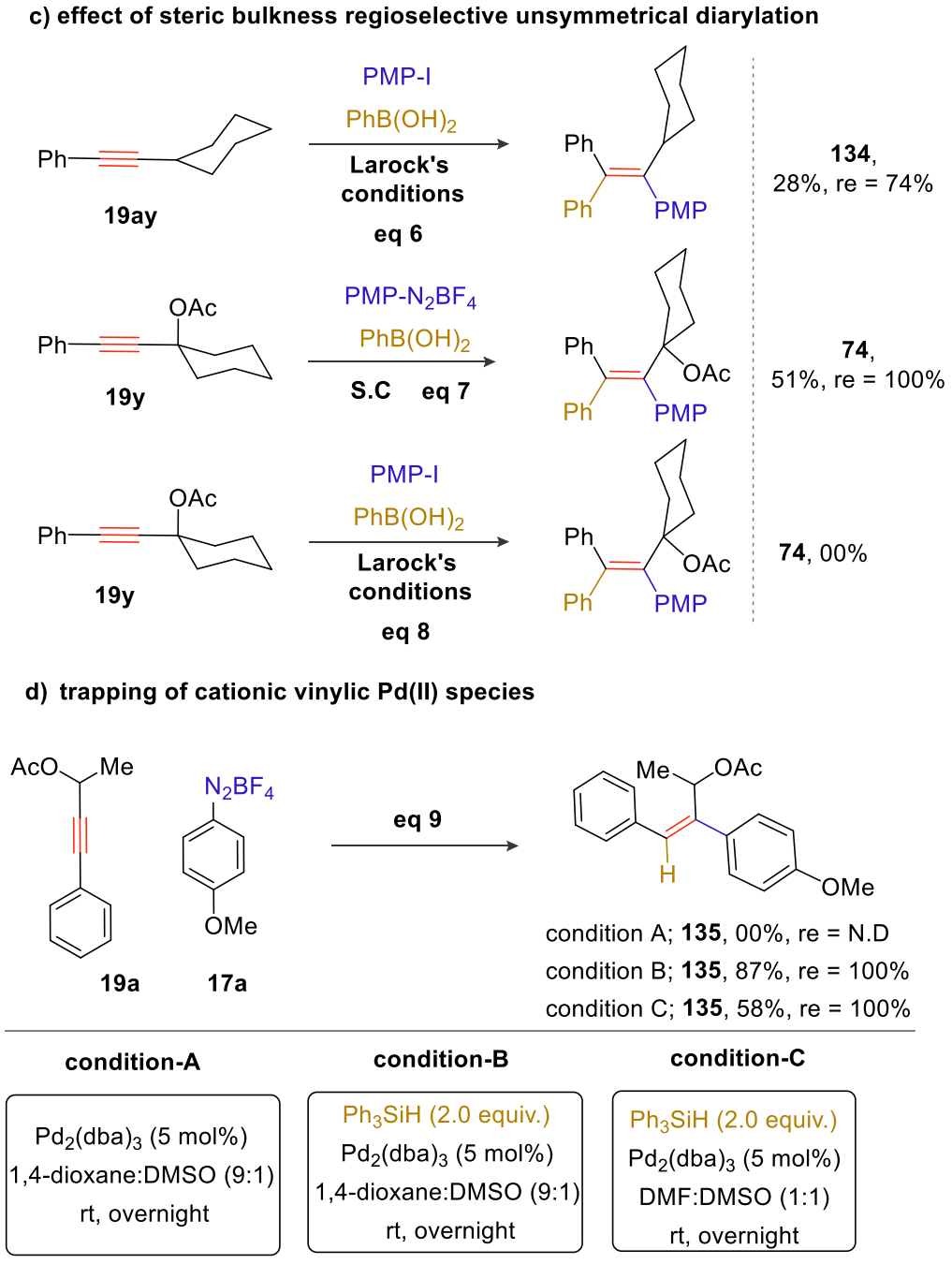
a) Role of ArN_2BF_4 in regioselective unsymmetrical diarylation



Larock's conditions	Standard conditions (S.C)
$Pd(PhCN)_2Cl_2$ (2 mol%) K_2CO_3 (1.5 equiv.) DMF:H_2O (4:1), rt, 36 h	$Pd_2(dba)_3$ (5 mol%) K_3PO_4 (1.5 equiv.) 1,4-dioxane:DMSO (9:1), rt, 6 h

b) Role of OAc group in regioselective unsymmetrical diarylation





Scheme 4A.13: Mechanistic Studies

Likewise, 1,2-diarylation of *p*-MeO-C_6H_4 (**19aw**)/*p*-MeOC-C_6H_4 (**19ax**)-^{n}butyl alkynes with PMP-I/ PMP-N_2BF_4 along with $PhB(OH)_2$ independently led to [**132** (38%, 68% *re*) and **133** (42%, 82% *re*) under Larock's conditions, shown in eq 4, **Scheme 4A.13b**] and [**132** (61%, 78% *re*) and **133** (70%, 80% *re*) under SC, shown in

eq 5, **Scheme 4A.13b**]. Thus, **132** (~70% *re*) and **133** (~80% *re*) with regioisomeric products mixture obtained in the diarylation of **19ar/19as** (with no carboxylate moiety) irrespective of Larock/SC suggests that alkynes with electronic variation marginally affect both selectivity and productivity. On the other hand, diarylation of yne-acetates occurs with excellent regioselectivity (eq 2, **Scheme 4A.13a**); notably, the electronic properties of functional groups did virtually not show any impact.

To further validate the importance of the acetate group, sterically hindered phenyl cyclohexyl alkyne **19ay** was subjected to PMP-I, and $PhB(OH)_2$ under Larock's reaction conditions (eq 6, **Scheme 4A.13c**); the respective product **134** (28%, 74% *re*) was isolated in low yield and moderate regioselectivity (eq 6, **Scheme 4A.13c**). By contrast, reaction of **19y**, exhibiting an acetate group at the propargyl position of **19ay**, with PMP-N_2BF_4 and $PhB(OH)_2$ under the SC furnished **74** (51%) in 100% *re* (eq 7, **Scheme 4A.13c**). Moreover, **19y** failed to give the desired diarylation product **74** under Larock condition, thus, cationic Pd-species is essential (eq 8, **Scheme 4A.13c**). From the mechanistic discussions highlighted in eqs 1-8, **Scheme 4A.13**, we conclude that the outcome and regioselectivity of *syn*-1,2-diarylation of unsymmetrical alkynes are strongly influenced by the carboxylate protecting group and the in-situ formation of a stabilized cationic Pd-intermediate. Trapping of cationic vinylic Pd(II) species in the absence of aryl boronic acid was achieved using triphenyl silane providing **135** in excellent yields in both diarylation and aryl-alkentlation reaction conditions (eq. 9).

4A.4.8. DFT Calculations

To gain insight into the reaction mechanism and notably the stereo/regioselectivity of the 1,2-diarylation of PAs, DFT calculations were performed at the M06L/def2-TZVPP(SMD)//BP86/LANL2DZ(Pd)_6-31G(d,p) level of theory. The transformation begins with the barrierless oxidative addition of $Pd(DMSO)_2$ (**a**) to the phenyl diazonium salt **b** to provide the

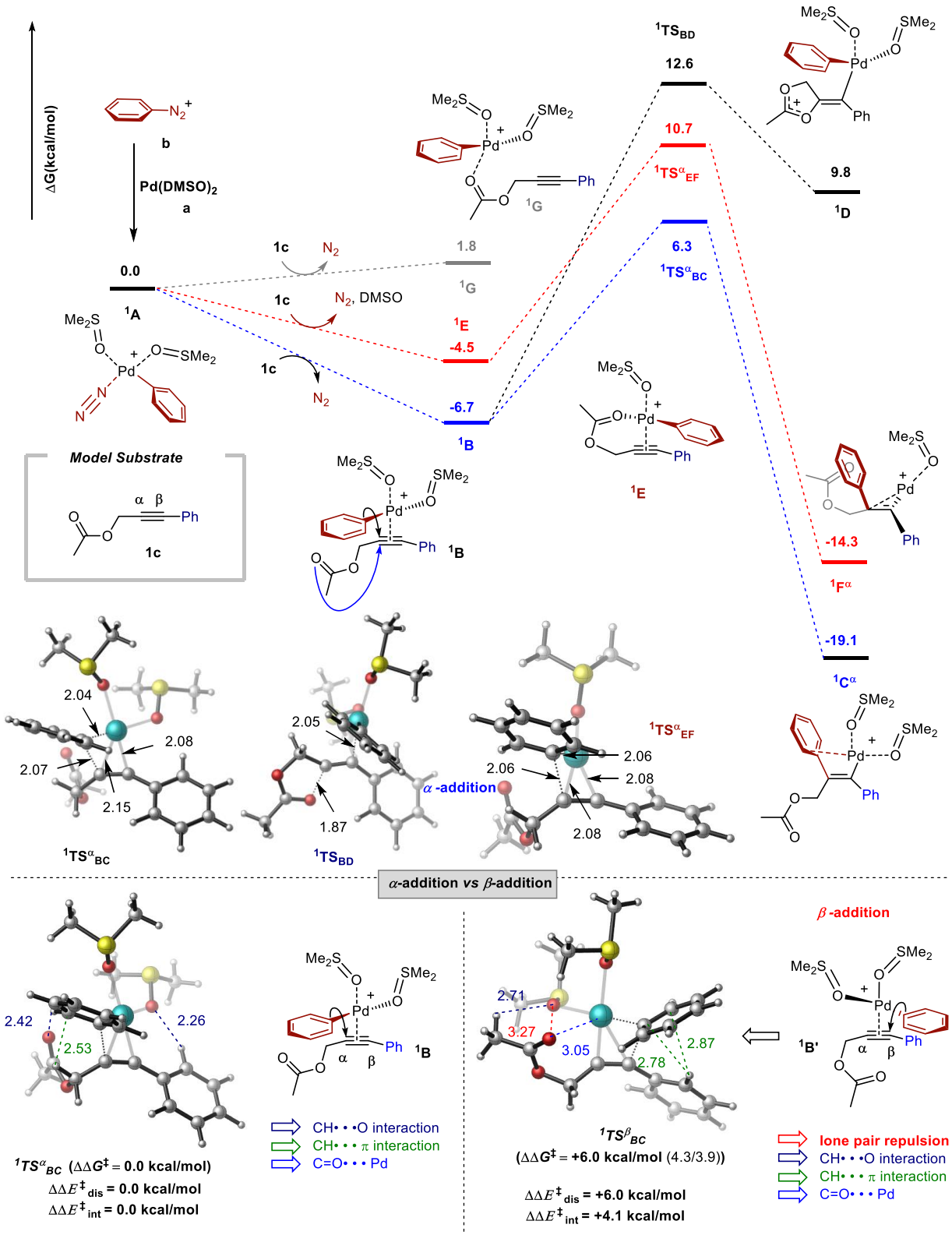


Figure 4A.6: DFT Calculations

cationic Pd-complex **^{1}A**.[6a] Next, coordination of **^{1}A** to propargyl acetate **19b** is possible by substitution of N_2. However, this process could happen in three different ways, via *i*) the coordination of the C≡C bond of **19b** to form complex **^{1}B** by releasing 6.7 kcal/mol of free energy (**Figure 4A.6**; blue) *ii*) the coordination of both the C≡C bond and the ester group in **19b** to provide **^{1}E** with the release of 4.5 kcal/mol of free energy (**Figure 4A.6**; red), and *iii*) the coordination of the ester group in **19b** to generate **^{1}G**, this step being endergonic by 1.8 kcal/mol (**Figure 4A.6**; grey). Thus, the ester group participation for the replacement of N_2 in **^{1}A** is not necessary. Next, a suprafacial α-aryl migration from Pd to the C≡C bond of **^{1}B** (*syn*-insertion) proceeds through transition state **^{1}TS$^a_{BC}$**, found at 6.3 kcal/mol on the free energy surface, and results in the Pd-alkenyl ester complex **^{1}C^a**. This complex lies at -19.1 kcal/mol on the free energy surface with *trans*-relationship of two phenyl groups. Intramolecular neighboring group participation of the ester group at C^α of **^{1}B** can provide the Pd-alkenyl heterocyclic complex **^{1}D** through **^{1}TS$_{BD}$** (12.6 kcal/mol); however, this process needs an additional 6.3 kcal/mol activation energy and is thus ruled out. Alternatively, α-aryl migration of ester chelate **^{1}E** forms intermediate ^{1}F^a (–14.3 kcal/mol) through **^{1}TS$^a_{EF}$** (10.7 kcal/mol). The energy barrier is 4.4 kcal/mol higher than ^{1}TS$^a_{BC}$; this pathway is thus not preferred. A detailed comparison of all the options justifies the feasibility of the bottom pathway **^{1}B→^{1}C^a** (marked in blue). Like normal Suzuki reactions, transmetalation of **^{1}C** with aryl boronic acid followed by reductive elimination gives the final diarylation product. We have studied various tether lengths of the yne-acetate and found that the **C^α**-arylation process is always favored over the **C^β**-arylation. To rationalize this selectivity, a distortion/interaction and non-covalent interactions analysis of the aryl migration transition states **^{1}TS$^\alpha_{BC}$** and **^{1}TS$^b_{BC}$** (that includes substrate fragment and aryl-palladium fragment) was performed. The large rotation angle for β-aryl migration (see the SI: 36.12° for **^{1}TS$^b_{BC}$** and 7.34° for **^{1}TS$^\alpha_{BC}$**) contributes to excess distortion energy [+6.0 kcal/mol; that includes both arylpalladium (+3.68 kcal/mol) and substrate (+2.32 kcal/mol) distortion]. In addition, a large level of non-covalent lone pair repulsion of the carboxylate moiety with ligated DMSO for **^{1}TS$^b_{BC}$** (+4.1 kcal/mol) relative to **^{1}TS$^\alpha_{BC}$** was detected.

4A.5. Conclusion

In summary, a regio- and stereoselective *syn*-1,2-dicarbofunctionalization of unsymmetrical alkynes involving structurally distinct carbon functionalities has been developed. The cationic Pd(II)-catalyst plays an essential role in modulating the regioselective insertion of aryl-diazonium salts and boronic acids/olefins to the unsymmetrical alkynes. The transformation proceeds at room temperature and tolerates oxidizable halo-species (I/Br), easily transformable functionalities (CO_2Me, CN) and strained rings, thus opening a broad chemical space [94 examples]. It is even successful on the gram scale. Carboxylate protecting group and the in-situ for-mation of a stabilized cationic Pd-intermediate solely responsible for the outcome and regioselectivity of *syn*-1,2-diarylation of unsymmetrical alkynes. DFT studies rationalize the α-arylation preference over β-arylation of PAs and discard direct participation of the acetate as a DG. The highly-substituted olefins are subsequently used for the construction of function-alized indene, methyl-vinyl ketone, and acrolein skeletons. The current finding paves the way to the discovery of unknown difunctionalization strategies of unactivated alkynes.

4A.6. Experimental Section

4A.6.1. General Information

All the reactions were performed in oven-dried sealed tubes. Commercial grade solvents were distilled prior to use. Column chromatography was performed using either 100-200 Mesh or 230-400 Mesh silica gel or neutral alumina. Thin layer chromatography (TLC) was performed on silica gel GF254 plates and alumina plates.

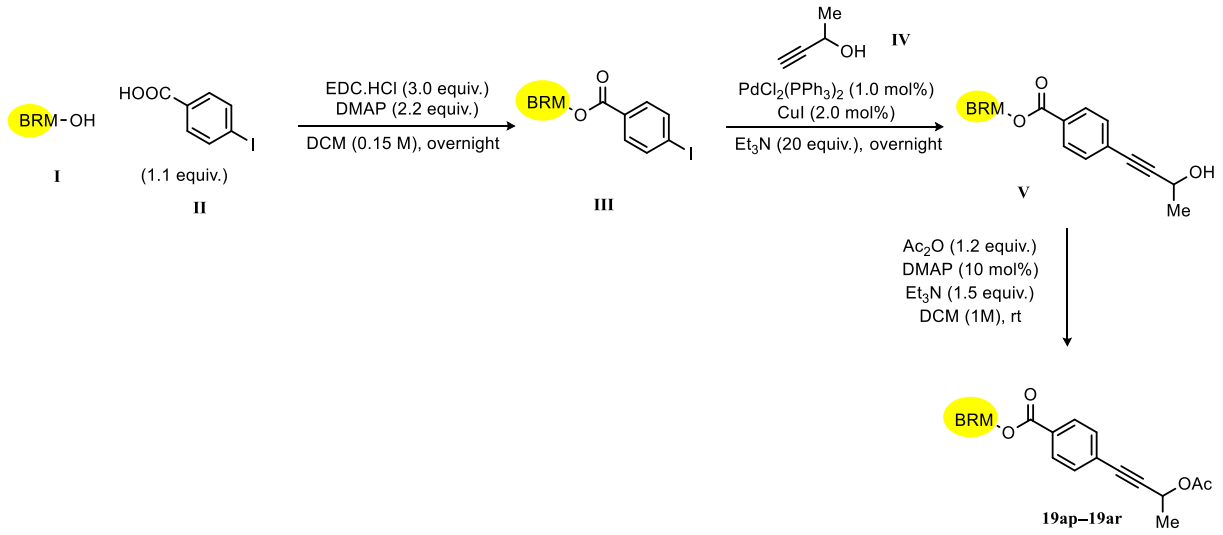
Proton, carbon, and fluorine nuclear magnetic resonance spectra (^{1}H NMR, ^{13}C NMR, and ^{19}F NMR) were recorded based on the resonating frequencies as follows:(^{1}H NMR, 400 MHz; ^{13}C NMR, 101 MHz; ^{19}F NMR, 376 MHz), (^{1}H NMR, 500 MHz; ^{13}C NMR, 126 MHz; ^{19}F NMR, 470 MHz) and (^{1}H NMR, 600 MHz; ^{13}C NMR, 151 MHz) having the solvent resonance as internal standard (^{1}H NMR, $CDCl_3$ at 7.26 ppm; ^{13}C NMR, $CDCl_3$ at 77.0 ppm). Few cases tetramethylsilane (TMS) at 0.00 ppm was used as reference standard. Data for ^{1}H NMR are reported as follows: chemical shift (ppm), multiplicity (s = singlet; br s = broad singlet; d = doublet; br d = broad doublet, t = triplet; br t = broad triplet; q = quartet; m = multiplet; tt = triplet of triplet; dt = doublet of triplet), coupling constant, *J*, in (Hz), and integration. Data for ^{13}C NMR, ^{19}F NMR were reported in terms of chemical shift (ppm). IR spectra were reported in cm^{-1}. High resolution mass spectra were obtained in ESI mode. Melting points were determined by electro-thermal heating and are uncorrected. X-ray data was collected at 293 K using graphite monochromated Mo-Kα radiation (0.71073 Å).

4A.6.2. Materials

Unless otherwise noted, all the reagents and intermediates were obtained commercially and used without purification. Toluene and 1,4-dioxane were distilled over CaH_2. $Pd_2(dba)_3$ and aryl boronic acids were purchased from commercially available source, and used as received. Analytical and spectral data of all the known compounds are exactly matching with the reported values.

4A.6.3. General procedure and spectral/analytical data

4A.6.3.1. General procedure for synthesis of biological relevant motif bearing propargyl acetates from alcohol (19ap, 19aq, and 19ar):



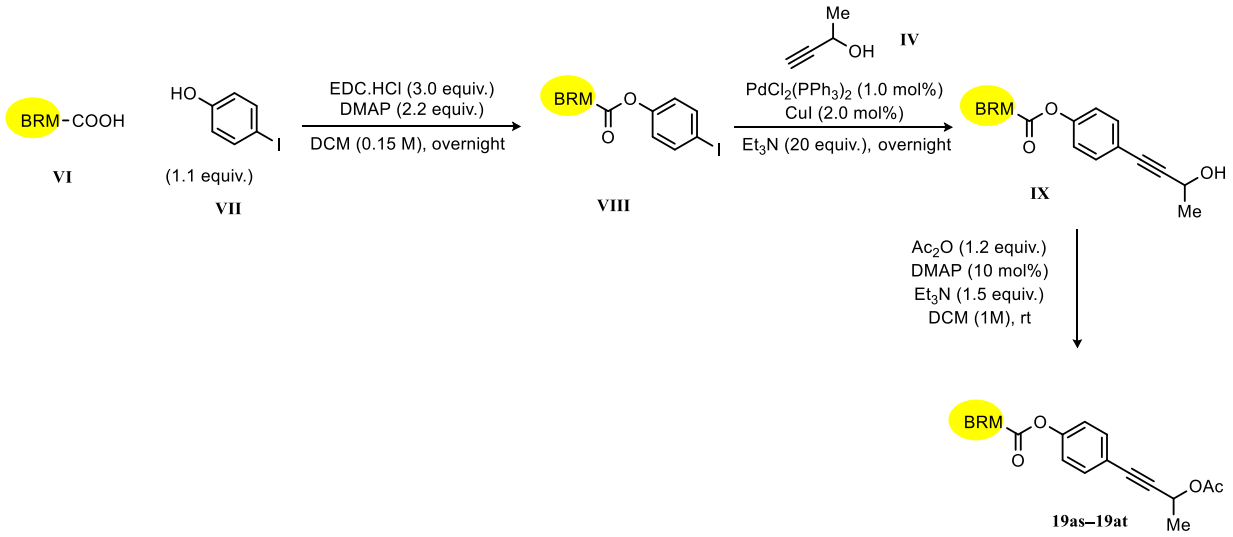
A solution of N'-(3-dimethylaminopropyl)-N-ethylcarbodimide, hydrochloride salt (EDC·HCl) (3.0 equiv), 4-N,N-dimethylaminopyridine (DMAP) (2.2 equiv) and 4-iodobenzoic acids (**II**) (1.1 equiv) in CH_2Cl_2 (0.15M) was stirred under an argon atmosphere. Alcohol (**I**; 1.0 equiv) was introduced dropwise (portion wise if the alcohol is solid) at 0 °C. The resulting reaction mixture was stirred for about 1 h at 0 °C and then 12 h at ambient temperature. Upon complete consumption of alcohol, the solvent was filtered and evaporated under reduced pressure. The crude residue was purified using column chromatography on silica gel using hexane/ethyl acetate to afford **III**.

To a solution of $PdCl_2(PPh_3)_2$ (0.02 mmol) and CuI (0.04 mmol) in Et_3N (20 equiv) were added aryl iodide **III** (2.6 mmol) and substrate **IV** (2.0 mmol) successively under an argon atmosphere. The resulting mixture was stirred at room temperature overnight. The crude reaction mixture was filtered through a small pad of Celite and concentrated under reduced pressure. The crude residue was purified using column chromatography on silica gel to afford the respective ynols **V**.

To a solution of an alcohol (**V**, 1.0 equiv), Et_3N (1.5 equiv) and DMAP (0.1 equiv) in anhydrous CH_2Cl_2 (1M) was added acetic anhydride (1.2 equiv) at 0 °C. The mixture was stirred at room

temperature for 2–3 h. Upon complete consumption of alcohol (monitored by TLC), the mixture was concerted under reduced pressure and purified by column chromatography on silica gel eluting with hexane/EtOAc to give yne-acetates **19ap–19ar**.

4A.6.3.2. General procedure for the synthesis of biological relevant motif bearing propargyl acetates from carboxylic acid (19as and 19at):

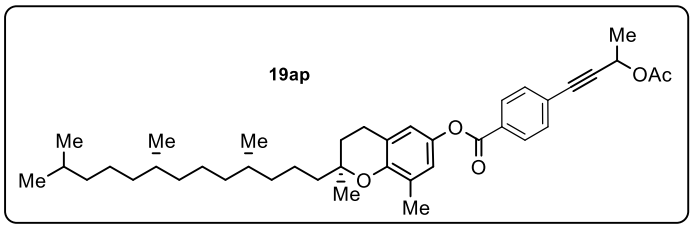


A solution of N'-(3-dimethylaminopropyl)-N-ethylcarbodimide, hydrochloride salt (EDC·HCl) (3.0 equiv), 4-N,N-dimethylaminopyridine (DMAP) (2.2 equiv) and carboxylic acids (**VI**) (1.1 equiv) in CH_2Cl_2 (0.15M) was stirred under an argon atmosphere. Next, 4-iodo phenol (**VII**) (1.0 equiv) was introduced portionwise at 0 °C. The resulting reaction mixture was stirred for about 1 h at 0 °C and then 12 h at ambient temperature. Upon complete consumption of carboxylic acid, the solvent was filtered and evaporated under reduced pressure. The crude residue was purified using column chromatography on silica gel using hexane/ethyl acetate to afford **VIII**.

To a solution of $PdCl_2(PPh_3)_2$ (0.02 mmol) and CuI (0.04 mmol) in Et_3N (20 equiv) were added aryl iodide **VIII** (2.6 mmol) and substrate **IV** (2.0 mmol) successively under an argon atmosphere. The resulting mixture was stirred at room temperature overnight. The crude reaction mixture was filtered through a small pad of Celite and concentrated under reduced pressure. The crude residue was purified using column chromatography on silica gel to afford the respective ynols **IX**.

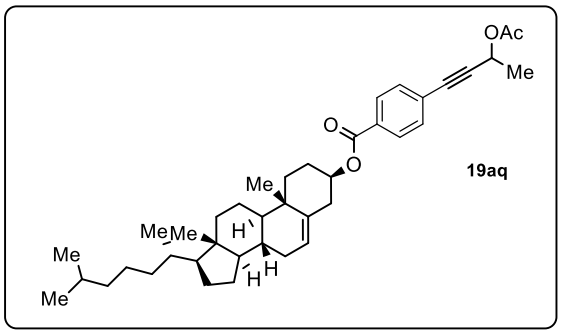
To a solution of an alcohol (**IX**, 1.0 equiv), Et_3N (1.5 equiv) and DMAP (0.1 equiv) in anhydrous CH_2Cl_2 (1M) was added acetic anhydride (1.2 equiv) at 0 °C. The mixture was stirred at room temperature for 2–3 h. Upon complete consumption of alcohol (monitored by TLC), the mixture was concerted under reduced pressure and purified by column chromatography on silica gel eluting with hexane/EtOAc to give yne-acetates **19as–19at**.

(S)-2,8-Dimethyl-2-((4S,8S)-4,8,12-trimethyltridecyl)chroman-6-yl 4-(3-acetoxybut-1-yn-1-yl)benzoate (19ap):



19ap (73%) as pale yellow gummy liquid; R_f = 0.58 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (d, J = 9.0 Hz, 2H), 7.55 (d, J = 8.5 Hz, 2H), 6.77 (dd, J = 25.5, 2.5 Hz, 2H), 5.71 (q, J = 6.5 Hz, 1H), 2.81–2.72 (m, 2H), 2.18 (s, 3H), 2.13 (s, 3H), 1.88–1.73 (m, 2H), 1.64–1.50 (m, 7H), 1.46–1.37 (m, 3H), 1.33–1.25 (m, 10H), 1.18–1.03 (m, 6H), 0.91–0.83 (m, 13H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.8, 165.1, 149.9, 142.5, 131.8, 129.9, 129.7, 127.4, 127.3, 121.1, 121.0, 119.0, 90.6, 83.7, 76.2, 60.6, 40.1, 39.3, 37.42, 37.39, 37.3, 34.6, 32.8, 32.7, 31.6, 31.0, 27.9, 24.8, 24.4, 24.2, 22.7, 22.6, 22.5, 21.3, 21.0, 20.9, 19.7, 16.1; IR (Neat) ν_{max} 1736, 1471, 1370, 1261, 1221, 1072, 1033, 1016 cm^{-1}; **HRMS (ESI)** for $C_{40}H_{57}O_5$ $(M+H)^+$: calcd. 671.4201, found 671.4204.

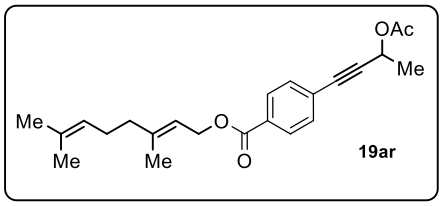
(3R,8R,9R,10S,13S,14R,17S)-10,13-Dimethyl-17-((S)-6-methylheptan-2-yl) 2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 4-(3-acetoxybut-1-yn-1-yl)benzoate (19aq):



19aq (70%) as pale yellow semi-solid; R_f = 0.64 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, J = 8.5 Hz, 2H), 7.48 (d, J = 8.0 Hz, 2H), 5.68 (q, J = 6.5 Hz, 1H), 5.41 (d, J = 4.0 Hz, 1H), 4.89–4.79 (m, 1H), 2.51–2.41 (m, 2H), 2.10 (s, 3H), 2.05–1.94 (m, 4H), 1.93–1.80 (m, 3H), 1.78–1.69 (m, 2H), 1.60–1.43 (m, 10H), 1.39–1.31 (m, 3H), 1.28–1.08 (m, 10H), 0.91 (d, J = 6.5 Hz, 3H), 0.86 (dd, J = 6.5, 2.0 Hz, 6H), 0.68 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.8, 165.3, 139.5, 131.6, 130.6, 129.3, 126.7, 122.8, 90.1, 83.8, 74.8, 60.6, 56.6, 56.1, 50.0, 42.3, 39.7, 39.5, 38.1,

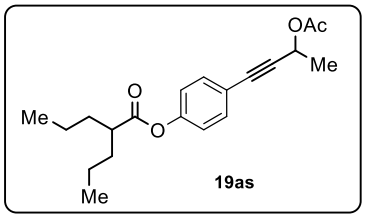
37.0, 36.6, 36.1, 35.8, 31.9, 31.8, 28.2, 28.0, 27.8, 24.2, 23.8, 22.8, 22.5, 21.3, 19.3, 18.7, 11.8; IR (Neat) ν_{max} 1746, 1714, 1369, 1272, 1225, 1106, 1033, 952, 767 cm^{-1}; **HRMS (ESI)** for $C_{40}H_{56}O_4Na$ $(M+Na)^+$: calcd. 623.4071, found 623.4073.

(E)-3,7-Dimethylocta-2,6-dien-1-yl 4-(3-acetoxybut-1-yn-1-yl)benzoate (19ar):



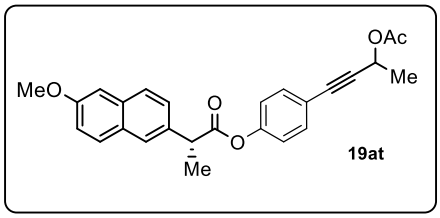
19ar (65%) as pale yellow gummy liquid; R_f = 0.58 (10% EtOAc/Hex); ^1H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J = 8.5 Hz, 2H), 7.48 (d, J = 8.5 Hz, 2H), 5.68 (q, J = 7.0 Hz, 1H), 5.49–5.42 (m, 1H), 5.12–5.05 (m, 1H), 4.83 (d, J = 7.0 Hz, 2H), 2.15–2.04 (m, 7H), 1.75 (m, 3H), 1.66 (m, 3H), 1.61–1.51 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.9, 166.0, 142.6, 131.8, 131.7, 130.3, 129.4, 126.7, 123.7, 118.2, 90.2, 83.8, 62.0, 60.6, 39.5, 26.2, 25.6, 21.3, 21.0, 17.7, 16.5; IR (Neat) ν_{max} 1716, 1371, 1266, 1225, 1084, 1032, 1016, 951, 767 cm^{-1}; **HRMS (ESI)** for $C_{23}H_{29}O_4$ $(M+H)^+$: calcd. 369.2060, found 369.2061.

4-(3-Acetoxybut-1-yn-1-yl)phenyl 2-propylpentanoate (19as):



19as (78%) as pale yellow gummy liquid; R_f = 0.61 (10% EtOAc/Hex); ^1H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, J = 9.0 Hz, 2H), 7.09 (d, J = 9.0 Hz, 2H), 5.67 (q, J = 6.5 Hz, 1H), 2.63–2.56 (m, 1H), 2.10 (m, 3H), 1.78–1.68 (m, 2H), 1.59–1.50 (m, 5H), 1.46–1.37 (m, 4H), 0.95 (q, J = 7.0 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.6, 169.9, 150.9, 133.0, 121.7, 119.7, 87.4, 83.8, 60.7, 45.3, 34.6, 21.4, 21.1, 20.7, 14.0; IR (Neat) ν_{max} 1742, 1503, 1370, 1227, 1199, 1102, 1032, 752 cm^{-1}; **HRMS (ESI)** for $C_{20}H_{26}O_4$ $(M+Na)^+$: calcd. 353.1723, found 353.1724.

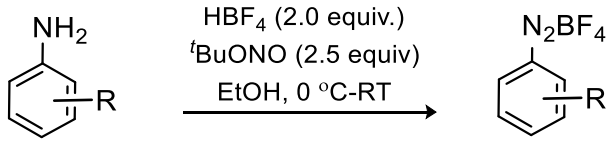
4-(3-Acetoxybut-1-yn-1-yl)phenyl (2R)-2-(6-methoxynaphthalen-2-yl)propanoate (19at):



19at (75%) as pale yellow gummy liquid; R_f = 0.5 (10% EtOAc/Hex); ^1H NMR (500 MHz, $CDCl_3$) δ 7.78–7.72 (m, 3H), 7.44 (dd, J = 8.5, 2.0 Hz, 1H), 7.40 (d, J = 8.5 Hz, 2H), 7.19–7.12 (m, 2H), 6.95 (d, J = 9.0 Hz, 2H), 5.67 (q, J = 6.5 Hz, 1H), 4.08 (q, J = 7.0 Hz, 1H), 3.92 (s, 3H), 2.09 (s, 3H), 1.69 (d, J = 7.5 Hz, 3H), 1.56 (d, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 169.9, 157.8, 1509, 134.9, 133.8, 133.0,

132.9, 129.3, 129.0, 127.4, 126.1, 126.0, 121.6, 121.4, 119.8, 119.1, 105.6, 87.4, 83.7, 60.7, 55.3, 45.5, 21.4, 21.1, 18.4; IR (Neat) ν_{max} 1738, 1631, 1502, 1369, 11226, 1196, 1126, 1029, 848 cm^{-1}; **HRMS (ESI)** for $C_{26}H_{24}O_5Na$ $(M+Na)^+$: calcd. 439.1516, found 439.1514.

4A.6.3.3. General procedure for the preparation of aryl diazonium salts (17):[5]



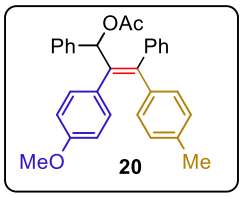
17

To the solution of HBF_4 (1.3 mL) and corresponding aniline (5.0 mmol) in EtOH (5.0 mL) was added ^{t}BuONO (1.4 mL) dropwise at 0 °C. The reaction mixture was stirred for 30 min at room temperature. Upon reaction completion, Et_2O (20 mL) was added to precipitate the diazonium salt. Next, the crude reaction mixture was filtered and the residue was washed with Et_2O (3 × 10 mL).

4A.6.3.4. General Procedure for dicarbofunctionalization.

To a mixture of **19** (0.3 mmol), aryl(hetero) diazonium-tetrafluoroborate **17** (0.9 mmol), aryl(hetero) boronic acid **2** or olefin **88** (0.45 mmol), $Pd_2(dba)_3$ (0.015 mmol), and base (0.45 mmol) was added solvent (2.0 mL). The reaction mixture was stirred at 25 °C for 6 h. The reaction progress was periodically monitored by TLC. The reaction mixture was diluted with EtOAc (20 mL) and washed with water (3 × 10 mL) and brine. The organic layer was dried over Na_2SO_4. The solvent was evaporated and purified by column chromatography over neutral alumina eluting with EtOAc/hexane to afford desired product.

2-(4-Methoxyphenyl)-1,3-diphenyl-3-(*p*-tolyl)propyl acetate (20):

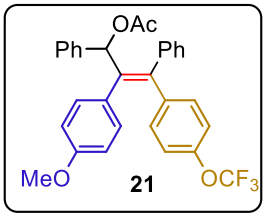


20

20 (98 mg, 73%) as pale yellow gummy liquid; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (600 MHz, DMSO d_6) δ 7.39–7.32 (m, 4H), 7.29–7.22 (m, 3H), 7.19 (t, J = 6.6 Hz, 1H), 7.10 (d, J = 7.8 Hz, 2H), 6.83 (d, J = 7.8 Hz, 2H), 6.77 (d, J = 7.2 Hz, 2H), 6.73 (d, J = 8.4 Hz, 2H), 6.63 (s, 1H), 6.58 (d, J = 8.4 Hz, 2H), 3.58 (s, 3H), 2.08 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (151 MHz, DMSO d_6) δ 169.7, 158.2, 144.3, 142.3, 139.5, 139.2, 136.5, 136.0, 132.3, 130.3, 130.1, 129.4, 129.01, 128.8, 128.7, 127.8,

127.7, 126.4, 113.3, 75.6, 55.3, 21.4, 21.1; IR (Neat) ν_{max} 1736, 1521, 1235, 1179, 1026, 779 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{28}NaO_3$ $(M+Na)^+$: calcd. 471.1931, found 471.1985.

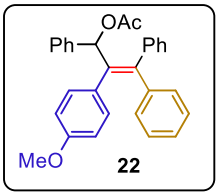
(E)-2-(4-Methoxyphenyl)-1,3-diphenyl-3-(4-(trifluoromethoxy)phenyl)allyl acetate (21):



21

21 (112 mg, 72%) as pale yellow liquid; R_f = 0.5 (10% EtOAc/Hex); ^1H NMR (400 MHz, DMSO d_6) δ 7.48–7.42 (m, 4H), 7.39–7.29 (m, 3H), 7.26 (d, J = 7.2 Hz, 1H), 7.19 (d, J = 7.6 Hz, 2H), 7.11–7.06 (m, 4H), 6.81 (d, J = 8.8 Hz, 2H), 6.70 (s, 1H), 6.65 (d, J = 8.8 Hz, 2H), 3.63 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (101 MHz, DMSO d_6) δ 169.7, 158.4, 147.0, 143.0, 141.6, 141.5, 138.8, 137.9, 132.2, 131.9, 129.7, 129.4, 129.1, 128.7, 128.0, 127.9, 126.4, 120.6, 120.4 (q, J = 261 Hz, 1C), 113.3, 75.4, 55.2, 21.3; ^{19}F NMR (376 MHz) δ –56.8; IR (Neat) ν_{max} 1735, 1597, 1447, 1238, 720 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{25}F_3NaO_4$ $(M+Na)^+$: calcd. 541.1603, found 541.1604.

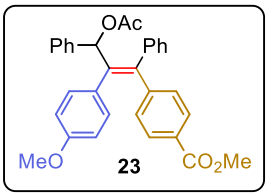
2-(4-Methoxyphenyl)-1,3,3-triphenylallyl acetate (22):



22

22 (94 mg, 72%) as pale yellow liquid; R_f = 0.5 (10% EtOAc/Hex); ^1H NMR (400 MHz, $CDCl_3$) δ 7.54–7.48 (m, 2H), 7.42 (t, J = 7.6 Hz, 2H), 7.36–7.22 (m, 6H), 7.08–6.95 (m, 5H), 6.91 (s, 1H), 6.81 (dt, J = 8.0, 2.8 Hz, 2H), 6.65 (dt, J = 8.8, 2.8 Hz, 2H), 3.71 (s, 3H), 2.02 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.7, 158.1, 143.7, 142.2, 141.8, 138.9, 136.9, 132.0, 130.2, 130.1, 129.4, 128.4, 128.0, 127.4, 127.3, 127.2, 126.3, 126.1, 112.7, 76.1, 54.8, 21.0; IR (Neat) ν_{max} 1740, 1605, 1509, 1442, 1230, 751 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{26}NaO_3$+ $(M+Na)^+$: calcd. 457.1774, found 457.1773.

(E)-Methyl 4-(3-acetoxy-2-(4-methoxyphenyl)-1,3-diphenylprop-1-en-1-yl)benzoate (23):

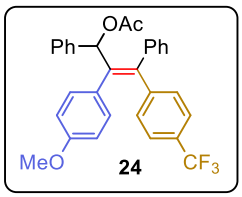


23

23 (92 mg, 62%) as pale yellow liquid; R_f = 0.3 (10% EtOAc/Hex); ^1H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, J = 8.5 Hz, 2H), 7.54–7.48 (m, 2H), 7.44 (t, J = 7.5 Hz, 2H), 7.37–7.23 (m, 6H), 7.08–7.04 (m, 2H), 6.92 (s, 1H), 6.86–6.81 (m, 2H), 6.63 (d, J = 8.5 Hz, 2H), 3.84 (s, 3H), 3.72 (s, 3H), 2.02 (s, 3H); ^{13}C NMR (101 MHz,$CDCl_3$) 169.7, 166.8, 158.3, 147.2, 142.6, 141.0, 138.6, 138.5, 131.9, 130.1, 129.7, 129.5, 128.8, 128.5, 128.1, 127.6, 127.5, 127.4, 126.3, 112.9, 75.9, 54.9, 51.9,

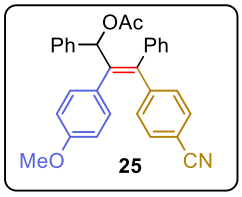
21.0; IR (Neat) ν_{max} 1735, 1603, 1492, 1228, 1029, 695 cm^{-1}; **HRMS (ESI)** for $C_{32}H_{28}NaO_5$+ $(M+Na)^+$: calcd. 515.1829, found 515.1858.

(E)-2-(4-Methoxyphenyl)-1,3-diphenyl-3-(4-(trifluoromethyl)phenyl)allyl acetate (24):



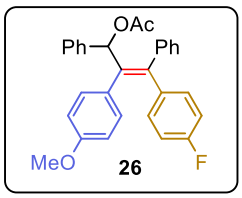
24 (113 mg, 75%) as pale yellow liquid; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, DMSO d_6) δ 7.49–7.42 (m, 6H), 7.39–7.25 (m, 4H), 7.19 (d, *J* = 8.0 Hz, 4H), 6.82 (d, *J* = 8.8 Hz, 2H), 6.72 (s, 1H), 6.65 (d, *J* = 8.8 Hz, 2H), 3.62 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (101 MHz, DMSO d_6) δ 169.7, 158.5, 146.7, 143.0, 141.2, 138.7, 138.5, 132.2, 130.8, 129.50, 129.45, 129.2, 128.7, 128.1, 127.9, 127.2 (q, *J* = 31 Hz, 1C), 126.4, 125.1 (q, *J* = 4.0 Hz, 2C), 124.6 (q, *J* = 273 Hz, 1C), 113.3, 75.3, 55.3, 21.2; ^{19}F NMR (376 MHz) δ –61.0; IR (Neat) ν_{max} 1741, 1509, 1324, 1264, 1123, 1065, 731 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{25}F_3NaO_3$+ $(M+Na)^+$: calcd. 525.1648, found 525.1654.

(E)-3-(4-Cyanophenyl)-2-(4-methoxyphenyl)-1,3-diphenylallyl acetate (25):



25 (98 mg, 71%) as pale yellow semi-solid; R_f = 0.28 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.55 (d, *J* = 8.5 Hz, 2H), 7.44 (d, *J* = 9.0 Hz, 4H), 7.38–7.33 (m, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 7.0 Hz, 1H), 7.18 (br d, *J* = 7.5 Hz, 2H), 7.15 (d, *J* = 8.5 Hz, 2H), 6.80 (d, *J* = 8.5 Hz, 2H), 6.69 (s, 1H), 6.65 (d, *J* = 9.0 Hz, 2H), 3.63 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (101 MHz, DMSO d_6) δ 169.7, 158.5, 147.5, 142.9, 140.9, 138.7, 138.6, 132.2, 132.1, 131.0, 129.5, 129.4, 129.2, 128.8, 128.2, 128.0, 126.4, 119.1, 113.4, 109.4, 75.2, 55.3, 21.3; IR (Neat) ν_{max} 2225, 1739, 1603, 1508, 1369, 1287, 1226, 1028, 698 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{25}NNaO_3$+ $(M+Na)^+$: calcd. 482.1727, found 482.1729.

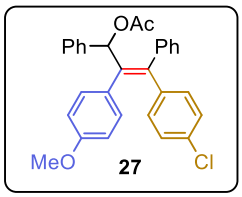
(E)-3-(4-Fluorophenyl)-2-(4-methoxyphenyl)-1,3-diphenylallyl acetate (26):



26 (mg, 61%) as pale yellow liquid; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47–7.41 (m, 4H), 7.38–7.24 (m, 4H), 7.17 (d, *J* = 7.6 Hz, 2H), 7.01–6.88 (m, 4H), 6.79 (d, *J* = 7.6 Hz, 2H), 6.69 (s, 1H), 6.64 (d, *J* = 8.0 Hz, 2H), 3.64 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.7, 161.0 (d, *J* = 246 Hz, 1C), 158.2, 142.5, 141.6, 138.8, 138.2, 137.3, 132.0, 131.8 (d, *J* = 7.6 Hz, 2C), 130.1, 129.4, 128.6, 128.5, 128.1, 127.3 (d, *J* = 1.3 Hz, 1C), 126.3, 114.4 (d, *J*

= 21.4 Hz, 2C), 112.8, 76.1, 54.9, 21.0; ^{19}F NMR (471 MHz) δ −115.6; IR (Neat) ν_{max} 1663, 1597, 1504, 1244, 1175, 1027, 835, 734 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{25}FNaO_3$+ $(M+Na)^+$: calcd. 475.1680, found 475.1684.

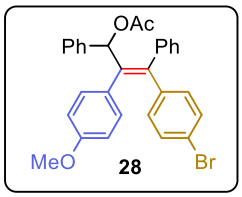
(E)-3-(4-Chlorophenyl)-2-(4-methoxyphenyl)-1,3-diphenylallyl acetate (27):



27

27 (111 mg, 79%) as pale yellow liquid; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.48–7.45 (m, 2H), 7.41 (t, J = 7.2 Hz, 2H), 7.35–7.19 (m, 6H), 6.99 (d, J = 9.0 Hz, 2H), 6.88 (d, J = 9.0 Hz, 3H), 6.81 (d, J = 8.4 Hz, 2H), 6.63 (d, J = 9.0 Hz, 2H), 3.72 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.7, 158.3, 142.3, 141.4, 140.7, 138.7, 137.7, 132.0, 131.5, 129.9, 129.5, 128.5, 128.1, 127.7, 127.4, 126.4, 112.9, 76.0, 54.9, 21.0; IR (Neat) ν_{max} 1739, 1605, 1508, 1227, 1029, 812, 698 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{25}ClO_3Na$+ $(M+Na)^+$: calcd. 491.1384, found 491.1381.

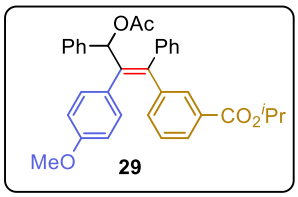
(E)-3-(4-Bromophenyl)-2-(4-methoxyphenyl)-1,3-diphenylallyl acetate (28):



28

28 (125 mg, 81%) as pale yellow semi-solid; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, DMSO d_6) δ 7.41 (d, J = 4.4 Hz, 4H), 7.38–7.24 (m, 6H), 7.19 (br d, J = 7.6 Hz, 2H), 6.91 (d, J = 8.4 Hz, 2H), 6.81 (d, J = 8.8 Hz, 2H), 6.71 (s, 1H), 6.66 (d, J = 8.8 Hz, 2H), 3.64 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (101 MHz, DMSO d_6) δ 169.7, 158.4, 143.1, 141.7, 141.5, 138.8, 137.6, 132.2, 129.8, 129.4, 129.1, 128.7, 127.94, 127.88, 126.4, 120.2, 113.4, 75.4, 55.2, 21.3; IR (Neat) ν_{max} 1736, 1604, 1508, 1483, 1225, 1175, 696 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{25}BrO_3Na$ + $(M+Na)^+$: calcd. 535.0879, found 535.0889.

(E)-Isopropyl 3-(3-acetoxy-2-(4-methoxyphenyl)-1,3-diphenylprop-1-en-1-yl)benzoate (29):

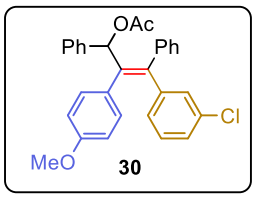


29

29 (108 mg, 69%) as pale yellow liquid; R_f = 0.35 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.63–7.58 (m, 1H), 7.57–7.54 (m, 1H), 7.48–7.41 (m, 4H), 7.38–7.28 (m, 3H), 7.27–7.17 (m, 5H), 6.81 (d, J = 9.0 Hz, 2H), 6.73 (s, 1H), 6.64 (d, J = 9.0 Hz, 2H), 5.07–4.99 (m, 1H), 3.60 (s, 3H), 2.05 (s, 3H), 1.22 (d, J = 6.0 Hz, 6H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.7, 165.3, 158.4, 143.2, 142.6, 141.5, 138.9, 138.0, 134.8, 132.2, 130.8, 130.0, 129.7, 129.5, 129.1, 128.7, 128.5, 128.0, 127.9, 127.6, 126.4, 113.4, 75.4, 68.5, 55.2, 22.0, 21.3; IR (Neat) ν_{max} 1710,

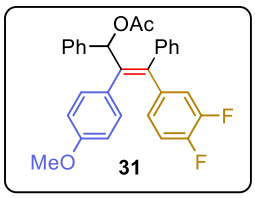
1579, 1275, 1101, 754 cm^{-1}; **HRMS (ESI)** for $C_{34}H_{32}NaO_5$+ $(M+Na)^+$: calcd. 543.2142, found 543.2152.

(E)-3-(3-Chlorophenyl)-2-(4-methoxyphenyl)-1,3-diphenylallyl acetate (30):



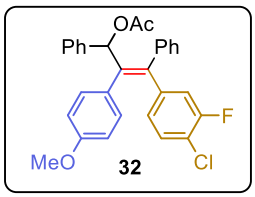
30 (83 mg, 59%) as pale yellow liquid; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.48–7.41 (m, 4H), 7.38–7.28 (m, 3H), 7.28–7.23 (m, 1H), 7.17 (d, J = 8.0 Hz, 2H), 7.13–7.02 (m, 2H), 7.00 (s, 1H), 6.91 (br d, J = 6.5 Hz, 1H), 6.81 (d, J = 8.5 Hz, 2H), 6.67 (d, J = 9.0 Hz, 2H), 6.65 (s, 1H), 3.63 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.9, 158.4, 144.5, 142.9, 141.3, 138.7, 138.0, 132.7, 132.2, 130.0, 129.6, 129.4, 129.1, 128.72, 128.70, 128.0, 127.9, 126.8, 126.4, 113.3, 75.3, 55.3, 21.3; IR (Neat) ν_{max} 1740, 1605, 1508, 1370, 1224, 1164, 1029, 700 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{25}ClO_3Na$+ $(M+Na)^+$: calcd. 491.1384, found 491.1381.

(E)-3-(3,4-Difluorophenyl)-2-(4-methoxyphenyl)-1,3-diphenylallyl acetate (31):



31 (115 mg, 84%) as pale yellow liquid; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.48–7.39 (m, 4H), 7.35–7.22 (m, 4H), 7.18 (d, J = 7.8 Hz, 2H), 6.83 (s, 1H), 6.83–6.72 (m, 4H), 6.68–6.62 (m, 3H), 3.72 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (101 MHz, DMSO d_6) δ 169.7, 158.5, 149.1 (dd, J = 246, 13.1 Hz, 1C), 148.3 (dd, J = 247, 13.1 Hz, 1C), 142.3, 141.2, 140.2–139.7 (m, 1C), 138.7, 138.2, 132.2, 129.6, 129.4, 129.1, 128.7, 128.1, 127.9, 127.0, 126.4, 118.9 (d, J = 17.2 Hz, 1C), 117.3 (d, J = 17.2 Hz, 1C), 113.4, 75.2, 55.3, 21.3; ^{19}F NMR (471 MHz) δ −139.3 (d, J = 22.6 Hz, 1F), −141.1 (d, J = 22.6 Hz, 1F); IR (Neat) ν_{max} 1739, 1603, 1507, 1225, 1027, 698 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{24}F_2NaO_3$ $(M+Na)^+$: calcd. 493.1586, found 493.1587.

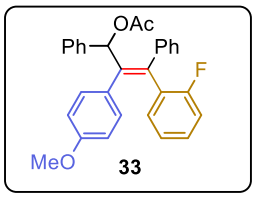
(E)-3-(4-Chloro-3-fluorophenyl)-2-(4-methoxyphenyl)-1,3-diphenylallyl acetate (32):



32 (108 mg, 74%) as pale yellow gummy-liquid; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.49–7.41 (m, 4H), 7.37–7.27 (m, 3H), 7.24 (br d, J = 7.0 Hz, 1H), 7.21–7.09 (m, 4H), 6.98–6.92 (m, 1H), 6.83 (d, J = 8.5 Hz, 2H), 6.67 (d, J = 8.0 Hz, 3H), 3.63 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (101 MHz, DMSO d_6) δ 169.7, 158.5, 156.1 (dd, J = 248 Hz, 1C), 142.1, 141.2, 140.2, 138.7, 138.3, 132.2, 131.9, 130.8, 129.6, 129.4, 129.1, 128.7, 128.1, 127.9, 126.4, 126.4, 119.2 (d,

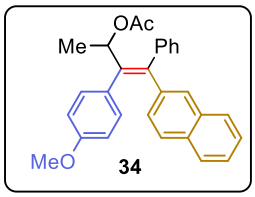
J = 17.2 Hz, 1C), 116.7 (d, J = 21.2 Hz, 1C), 113.4, 75.2, 55.3, 21.3; ^{19}F NMR (471 MHz) δ −118.8; IR (Neat) ν_{max} 1739, 1508, 1228, 1059, 1030, 699 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{24}ClFNaO_3$+ $(M+Na)^+$: calcd. 509.1290, found 509.1292.

(E)-3-(2-Fluorophenyl)-2-(4-methoxyphenyl)-1,3-diphenylallyl acetate (33):



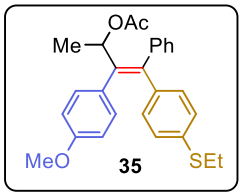
33 (85 mg, 63%) as pale yellow gummy-liquid; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d$_6$) δ 7.48 (d, J = 7.5 Hz, 2H), 7.42 (t, J = 8.0 Hz, 2H), 7.33 (t, J = 7.0 Hz, 2H), 7.28–7.23 (m, 1H), 7.20–7.07 (m, 4H), 6.98–6.91 (m, 2H), 6.78 (s, 3H), 6.77 (d, J = 1.6 Hz, 2H), 6.60 (d, J = 8.5 Hz, 2H), 3.60 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (101 MHz, DMSO d$_6$) δ 169.7, 158.8 (d, J = 245 Hz, 1C), 158.3, 140.7, 139.7, 138.7, 138.4, 131.7 (d, J = 3.0 Hz, 1C), 131.3, 130.3 (d, J = 17.2 Hz, 1C), 129.7, 129.5 (d, J = 8.1 Hz, 1C), 129.02, 128.98, 128.0, 126.3, 124.5 (d, J = 3.0 Hz, 1C), 115.7 (d, J = 22.2 Hz, 1C), 113.1, 74.8, 55.2, 21.3; ^{19}F NMR (471 MHz) δ −109.1; IR (Neat) ν_{max} 1738, 1605, 1509, 1226, 1026, 697 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{25}FNaO_3$+ $(M+Na)^+$: calcd. 475.1680, found 475.1684.

(E)-3-(4-Methoxyphenyl)-4-(naphthalen-2-yl)-4-phenylbut-3-en-2-yl acetate (34):



34 (77 mg, 61%) as pale yellow gummy liquid; R_f = 0.45 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.73–7.68 (m, 1H), 7.66–7.61 (m, 1H), 7.57 (d, J = 8.5 Hz, 1H), 7.44–7.29 (m, 8H), 7.14 (dt, J = 6.5, 2.0 Hz, 2H), 7.09 (dd, J = 8.5, 1.5 Hz, 1H), 6.75 (d, J = 8.5 Hz, 2H), 5.67 (q, J = 6.5 Hz, 1H), 3.63 (s, 3H), 1.92 (s, 3H), 1.24 (d, J = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, DMSO d$_6$) δ 169.8, 158.3, 142.4, 141.9, 140.2, 139.1, 132.9, 132.3, 131.8, 130.3, 129.5, 128.9, 128.8, 128.4, 128.2, 127.8, 127.7, 127.3, 126.5, 126.4, 113.5, 71.0, 55.3, 21.4, 19.9; IR (Neat) ν_{max} 1731, 1507, 1235, 1175, 1029, 700 cm^{-1}; **HRMS (ESI)** for $C_{29}H_{26}O_3Na$ $(M+Na)^+$: calcd. 445.1774, found 445.1784.

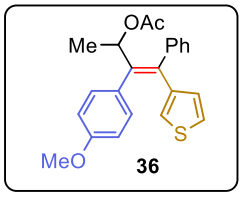
(E)-4-(4-(Ethylthio)phenyl)-3-(4-methoxyphenyl)-4-phenylbut-3-en-2-yl acetate (35):



35 (75 mg, 58%) as pale yellow gummy liquid; R_f = 0.42 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d$_6$) δ 7.40 (t, J = 7.0 Hz, 2H), 7.36–7.24 (m, 3H), 7.08 (d, J = 9.0 Hz, 2H), 6.97 (d, J = 8.5 Hz, 2H), 6.81 (t, J = 8.5 Hz, 4H), 5.57 (q, J = 6.5 Hz, 1H), 3.70 (s, 3H), 2.84 (q, J = 7.5 Hz, 2H), 1.89 (s, 3H),

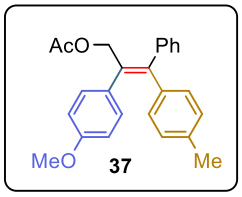
1.19 (d, J = 6.5 Hz, 3H), 1.13 (t, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d$_6$) δ 169.6, 158.4, 141.8, 138.6, 134.8, 132.2, 130.6, 130.3, 129.3, 128.8, 127.6, 127.1, 113.6, 71.0, 55.3, 26.2, 21.4, 19.8, 14.4; IR (Neat) ν_{max} 1731, 1507, 1490, 1367, 1235, 1029, 759 cm^{-1}; **HRMS (ESI)** for $C_{27}H_{28}NaO_3S$+ $(M+Na)^+$: calcd. 455.1651, found 455.1658.

(E)-3-(4-Methoxyphenyl)-4-phenyl-4-(thiophen-3-yl)but-3-en-2-yl acetate (36):



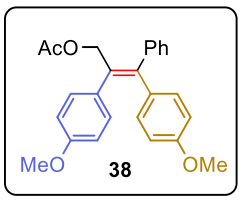
36 (78 mg, 69%) as pale yellow gummy liquid; R$_f$ = 0.4 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d$_6$) δ 7.44 (t, J = 7.5 Hz, 2H), 7.36 (t, J = 7.5 Hz, 1H), 7.28 (d, J = 7.0 Hz, 2H), 7.18–7.10 (m, 3H), 6.92 (d, J = 9.0 Hz, 2H), 6.56 (dd, J = 3.0, 1.5 Hz, 1H), 6.28 (dd, J = 5.0, 1.0 Hz, 1H), 5.44 (q, J = 6.5 Hz, 1H), 3.76 (s, 3H), 1.88 (s, 3H), 1.15 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d$_6$) δ 169.7, 158.0, 142.4, 141.7, 137.6, 136.7, 131.8, 130.5, 129.3, 128.9, 128.8, 127.7, 125.7, 125.1, 114.1, 71.2, 55.4, 21.4, 19.6; IR (Neat) ν_{max} 1731, 1507, 1234, 1174, 1029, 699 cm^{-1}; **HRMS (ESI)** for $C_{23}H_{22}NaO_3S$ $(M+Na)^+$: calcd. 401.1182, found 401.1188.

(E)-2-(4-Methoxyphenyl)-3-phenyl-3-(*p*-tolyl)allyl acetate (37):



37 (87 mg, 78%) as semi-colorless solid; R$_f$ = 0.39 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.36–7.24 (m, 5H), 7.10 (dt, J = 6.5, 2.0 Hz, 2H), 6.88 (d, J = 8.0 Hz, 2H), 6.81 (d, J = 8.0 Hz, 2H), 6.73 (dt, J = 9.0, 2.5 Hz, 2H), 4.88 (s, 2H), 3.77 (s, 3H), 2.22 (s, 3H), 1.95 (s, 3H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 171.0, 158.2, 144.7, 142.3, 139.2, 136.2, 132.9, 132.4, 130.9, 130.5, 129.5, 128.3, 128.2, 127.3, 113.4, 66.7, 55.1, 21.1, 20.9; IR (Neat) ν_{max} 1725, 1508, 1039, 859, 708 cm^{-1}; **HRMS (ESI)** for $C_{25}H_{24}O_3Na$+ $(M+Na)^+$: calcd. 395.1618, found 395.1626.

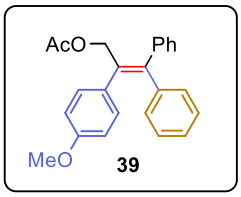
(E)-2,3-Bis(4-Methoxyphenyl)-3-phenylallyl acetate (38):



38 (52 mg, 44%) as pale yellow semi-solid solid; R$_f$ = 0.38 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.38–7.24 (m, 5H), 7.12 (d, J = 8.5 Hz, 2H), 6.85 (d, J = 8.5 Hz, 2H), 6.74 (d, J = 9.0 Hz, 2H), 6.61 (d, J = 9.0 Hz, 2H), 4.88 (s, 2H), 3.77 (s, 3H), 3.71 (s, 3H), 1.95 (s, 3H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 170.9, 158.3, 158.1, 144.2, 142.4, 134.6, 132.5, 131.9, 130.9, 129.6, 128.2,

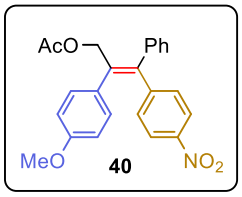
127.3, 113.5, 113.0, 66.7, 55.1, 55.0, 20.9; IR (Neat) ν_{max} 1731, 1605, 1508, 1243, 1023, 700 cm^{-1}; **HRMS (ESI)** for $C_{25}H_{24}O_4Na^+$ $(M+Na)^+$: calcd. 411.1567, found 411.1575.

2-(4-Methoxyphenyl)-3,3-diphenylallyl acetate (39):



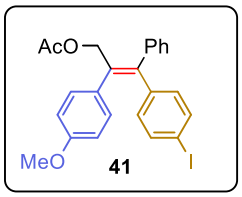
39 (88 mg, 82%) as colorless solid; R_f = 0.39 (10% EtOAc/Hex); M.P (196–198); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38–7.25 (m, 5H), 7.14–7.05 (m, 5H), 6.98–6.93 (m, 2H), 6.72 (d, J = 9.0 Hz, 2H), 4.92 (s, 2H), 3.76 (s, 3H), 1.96 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.9, 158.3, 144.7, 142.2, 142.1, 133.4, 132.1, 130.9, 130.6, 129.5, 128.2, 127.6, 127.3, 126.5, 113.3, 66.6, 55.0, 20.9; IR (Neat) ν_{max} 1731, 1509, 1245, 1224, 1024, 702 cm^{-1}; **HRMS (ESI)** for $C_{24}H_{22}O_3Na^+$ $(M+Na)^+$: calcd. 381.1461, found 381.1469.

(E)-2-(4-Methoxyphenyl)-3-(4-nitrophenyl)-3-phenylallyl acetate (40):



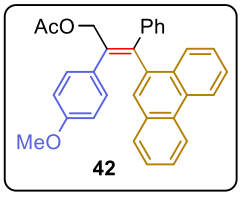
40 (70 mg, 58%) as pale yellow semi-solid; R_f = 0.22 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, J = 9.0 Hz, 2H), 7.43–7.33 (m, 3H), 7.30–7.24 (m, 2H), 7.13–7.06 (m, 4H), 6.75 (dt, J = 7.0, 2.0 Hz, 2H), 4.94 (s, 2H), 3.78 (s, 3H), 1.96 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.7, 158.9, 149.3, 146.0, 142.3, 140.7, 136.7, 131.4, 130.9, 129.5, 128.6, 128.0, 122.9, 113.7, 66.0, 55.1, 20.8; IR (Neat) ν_{max} 1731, 1595, 1506, 1338, 1228, 1081, 700 cm^{-1}; **HRMS (ESI)** for $C_{24}H_{21}NO_5Na^+$ $(M+Na)^+$: calcd. 426.1312, found 426.1320.

(E)-3-(4-Iodophenyl)-2-(4-methoxyphenyl)-3-phenylallyl acetate (41):



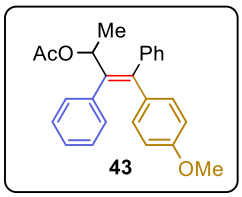
41 (86 mg, 59%) as pale yellow solid; R_f = 0.5 (10% EtOAc/Hex); M.P (210–211 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, J = 8.5 Hz, 2H), 7.37–7.28 (m, 3H), 7.27–7.22 (m, 2H), 7.08 (d, J = 8.5 Hz, 2H), 6.74 (dt, J = 6.5, 2.0 Hz, 2H), 6.67 (dt, J = 6.5, 1.5 Hz, 2H), 4.88 (s, 2H), 3.78 (s, 3H), 1.94 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.8, 158.5, 143.4, 141.8, 141.5, 136.8, 134.2, 132.5, 131.6, 130.8, 129.5, 128.4, 127.6, 113.6, 92.4, 66.4, 55.1, 20.9; IR (Neat) ν_{max} 1730, 1605, 1508, 1229, 1023, 719 cm^{-1}; **HRMS (ESI)** for $C_{24}H_{21}IO_3Na^+$ $(M+Na)^+$: calcd. 507.0428, found 507.0434.

(E)-2-(4-Methoxyphenyl)-3-(phenanthren-9-yl)-3-phenylallyl acetate (42):



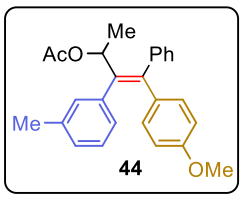
42 (84 mg, 61%) as pale yellow solid; R_f = 0.41 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.67–8.58 (m, 2H), 8.19–8.11 (m, 1H), 7.77 (d, J = 7.5 Hz, 1H), 7.65–7.45 (m, 7H), 7.38–7.13 (m, 5H), 6.51 (d, J = 8.5 Hz, 2H), 5.21 (dd, J = 11.5, 11.5 Hz, 2H), 3.56 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.0, 158.2, 143.4, 141.0, 138.5, 136.1, 132.2, 131.4, 130.9, 130.5, 129.8, 129.5, 128.9, 128.8, 128.6, 128.2, 127.5, 126.9, 126.5, 126.4, 126.1, 122.8, 122.3, 113.1, 66.1, 54.8, 21.0; IR (Neat) ν_{max} 1734, 1603, 1439, 1223, 1018, 699 cm^{-1}; **HRMS (ESI)** for $C_{32}H_{26}O_3Na^+$ $(M+Na)^+$: calcd. 481.1774, found 481.1783.

(E)-4-(4-Methoxyphenyl)-3,4-diphenylbut-3-en-2-yl acetate (43):



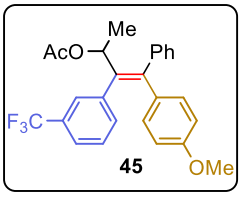
43 (75 mg, 67%) as pale yellow gummy liquid; R_f = 0.45 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.40 (t, J = 7.5 Hz, 2H), 7.34–7.22 (m, 5H), 7.18 (d, J = 7.0 Hz, 3H), 6.80 (dt, J = 7.0, 2.0 Hz, 2H), 6.59 (d, J = 9.0 Hz, 2H), 5.63 (q, J = 6.5 Hz, 1H), 3.59 (s, 3H), 1.88 (s, 3H), 1.20 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.7, 158.0, 142.1, 138.6, 138.0, 134.3, 131.3, 131.2, 129.4, 128.8, 128.1, 127.6, 127.1, 113.4, 71.0, 55.3, 21.4, 19.8; IR (Neat) ν_{max} 1731, 1658, 1508, 1370, 1243, 1001, 704 cm^{-1}; **HRMS (ESI)** for $C_{25}H_{24}O_3Na^+$ $(M+Na)^+$: calcd. 395.1618, found 395.1626.

(E)-4-(4-Methoxyphenyl)-4-phenyl-3-(*m*-tolyl)but-3-en-2-yl acetate (44):



28 (71 mg, 61%) as pale yellow gummy liquid; R_f = 0.45 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.40 (t, J = 7.5 Hz, 2H), 7.31 (t, J = 7.5 Hz, 1H), 7.25 (d, J = 7.0 Hz, 2H), 7.12 (t, J = 7.5 Hz, 1H), 7.02–6.92 (m, 3H), 6.80 (d, J = 8.5 Hz, 2H), 6.59 (d, J = 8.5 Hz, 2H), 5.57 (q, J = 6.5 Hz, 1H), 3.59 (s, 3H), 2.33 (s, 3H), 1.88 (s, 3H), 1.20 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.7, 157.9, 142.2, 141.8, 138.4, 138.0, 136.9, 134.4, 131.6, 131.2, 129.5, 129.3, 129.0, 128.7, 128.4, 127.9, 127.7, 127.5, 126.2, 113.4, 71.0, 55.3, 21.6, 21.4, 19.8; IR (Neat) ν_{max} 1735, 1650, 1244, 1022, 760 cm^{-1}; **HRMS (ESI)** for $C_{26}H_{26}O_3Na$ $(M+Na)^+$: calcd. 409.1774, found 409.1782.

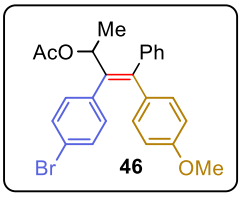
(E)-4-(4-Methoxyphenyl)-4-phenyl-3-(3-(trifluoromethyl)phenyl)but-3-en-2-yl acetate (45/45′ = 90:10)



45 (62 mg, 47%) as pale yellow gummy liquid; R_f = 0.45 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d$_6$) δ 7.52–7.48 (m, 2H), 7.46 (br s, 1H), 7.42 (t, J = 7.0 Hz, 2H), 7.37–7.28 (m, 4H), 6.81 (d, J = 9.0 Hz, 2H), 6.62 (d, J = 9.0 Hz, 2H), 5.64 (q, J = 6.5 Hz, 1H), 3.60 (s, 3H), 1.91 (s, 3H), 1.21 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d$_6$) δ 169.6, 158.2, 143.4, 141.6, 139.6, 136.7, 135.3, 133.8, 131.2, 129.22, 129.15, 128.8, 127.8, 124.6 (q, J = 272 Hz, 1C), 123.8 (q, J = 3.8 Hz, 1C), 113.5, 70.6, 55.3, 21.3, 19.7; ^{19}F NMR (471 MHz) δ –61.2; IR (Neat) ν_{max} 1730, 1605, 1508, 1232, 1114, 1040, 698 cm^{-1}; **HRMS (ESI)** for $C_{26}H_{23}F_3O_3Na$ $(M+Na)^+$: calcd. 463.1492, found 463.1498.

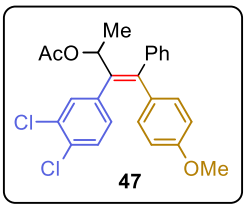
Representative peaks of the inseparable minor regioisomer **45′**: ^{1}H NMR (500 MHz, DMSO d$_6$) δ 3.68 (s, 0.32H).

(E)-3-(4-Bromophenyl)-4-(4-methoxyphenyl)-4-phenylbut-3-en-2-yl acetate (46):



46 (105 mg, 78%) as pale yellow gummy liquid; R_f = 0.46 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.44–7.27 (m, 7H), 7.10 (dd, J = 8.0, 1.5 Hz, 2H), 6.83 (d, J = 8.5 Hz, 2H), 6.59 (d, J = 9.0 Hz, 2H), 5.80 (q, J = 6.5 Hz, 1H), 3.70 (s, 3H), 1.94 (s, 3H), 1.29 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 169.8, 158.0, 142.9, 141.6, 137.8, 136.7, 133.8, 132.6, 131.4, 130.8, 129.1, 128.3, 127.2, 120.7, 112.9, 71.3, 55.0, 21.1, 19.6; IR (Neat) ν_{max} 1731, 1604, 1507, 1231, 1030, 1009, 701 cm^{-1}; **HRMS (ESI)** for $C_{25}H_{23}BrO_3Na$ $(M+Na)^+$: calcd. 473.0723, found 473.0724.

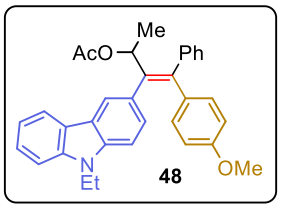
(E)-3-(3,4-Dichlorophenyl)-4-(4-methoxyphenyl)-4-phenylbut-3-en-2-yl acetate (47):



47 (92 mg, 63%) as pale yellow gummy liquid; R_f = 0.46 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d$_6$) δ 7.51 (d, J = 8.5 Hz, 1H), 7.46 (d, J = 1.0 Hz, 1H), 7.40 (d, J = 7.5 Hz, 2H), 7.35–7.29 (m, 1H), 7.26 (dd, J = 8.0, 1.0 Hz, 2H), 7.17 (dd, J = 8.0, 2.0 Hz, 1H), 6.83 (d, J = 9.0 Hz, 2H), 6.66 (d, J = 9.0 Hz, 2H), 5.60 (q, J = 6.5 Hz, 1H), 3.62 (s, 3H), 1.92 (s, 3H), 1.19 (d, J = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 169.6, 158.3, 143.6, 139.5, 135.7, 133.7, 133.0, 131.8, 131.3, 130.7, 130.3, 129.9, 129.5, 129.2, 128.8, 127.8, 113.7, 70.5, 55.4, 21.4, 19.7; IR (Neat) ν_{max} 1734, 1603,

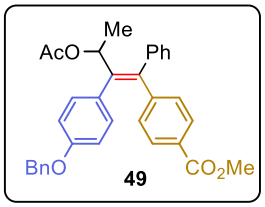
1507, 1369, 1231, 1028, 698 cm^{-1}; **HRMS (ESI)** for $C_{25}H_{22}Cl_2NaO_3$ + $(M+Na)^+$: calcd. 463.0838, found 463.0845.

(E)-3-(9-Ethyl-9H-carbazol-3-yl)-4-(4-methoxyphenyl)-4-phenylbut-3-en-2-yl acetate (48):



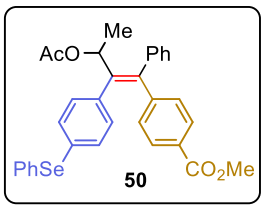
48 (110 mg, 75%) as pale yellow solid; R_f = 0.3 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO d_6) δ 8.11 (d, J = 7.5 Hz, 1H), 7.98 (d, J = 1.5 Hz, 1H), 7.56 (d, J = 8.5 Hz, 1H), 7.47 (d, J = 8.5 Hz, 1H), 7.43 (t, J = 7.5 Hz, 3H), 7.36–7.28 (m, 3H), 7.22 (dd, J = 8.5, 1.5 Hz, 1H), 7.18 (t, J = 7.5 Hz, 1H), 6.84 (d, J = 9.0 Hz, 2H), 6.53 (d, J = 8.5 Hz, 2H), 5.66 (q, J = 6.0 Hz, 1H), 4.39 (q, J = 7.0 Hz, 2H), 3.52 (s, 3H), 1.94 (s, 3H), 1.30 (t, J = 7.5 Hz, 3H), 1.23 (d, J = 7.0 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.1, 157.5, 142.3, 141.9, 140.0, 138.8, 138.2, 134.5, 131.6, 129.4, 129.0, 128.2, 126.9, 125.5, 123.0, 122.4, 120.3, 118.6, 112.7, 108.4, 107.7, 72.1, 54.8, 37.5, 21.3, 19.8, 13.8; IR (Neat) ν_{max} 1728, 1507, 1231, 1034, 700 cm^{-1}; **HRMS (ESI)** for $C_{33}H_{31}NO_3Na$+ $(M+Na)^+$: calcd. 512.2196, found 512.2207.

(E)-Methyl 4-(3-acetoxy-2-(4-(benzyloxy)phenyl)-1-phenylbut-1-en-1-yl)benzoate (49):



49 (88 mg, 58%) as pale yellow liquid; R_f = 0.23 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO d_6) δ 7.65 (d, J = 8.5 Hz, 2H), 7.45–7.28 (m, 10H), 7.08 (d, J = 8.5 Hz, 2H), 7.05 (d, J = 8.5 Hz, 2H), 6.87 (d, J = 8.5 Hz, 2H), 5.60 (q, J = 6.5 Hz, 1H), 5.01 (s, 2H), 3.76 (s, 3H), 1.89 (s, 3H), 1.22 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.7, 166.3, 157.7, 147.5, 141.5, 141.1, 139.9, 137.4, 132.2, 130.3, 130.0, 129.4, 128.9, 128.8, 128.3, 127.8, 127.7, 114.4, 70.8, 69.6, 52.4, 21.3, 19.7; IR (Neat) ν_{max} 1716, 1605, 1506, 1368, 1274, 1232, 1017, 697 cm^{-1}; **HRMS (ESI)** for $C_{33}H_{30}O_5Na$+ $(M+Na)^+$: calcd. 529.1985, found 529.1992.

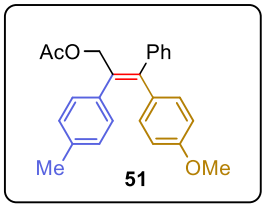
(E)-Methyl 4-(3-acetoxy-1-phenyl-2-(4-(phenylselanyl)phenyl)but-1-en-1-yl)benzoate (50):



50 (55 mg, 33%) as pale yellow liquid; R_f = 0.31 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO d_6) δ 7.67 (d, J = 8.5 Hz, 2H), 7.43 (t, J = 7.0 Hz, 2H), 7.38–7.21 (m, 10H), 7.14 (d, J = 8.5 Hz, 2H), 7.05 (d, J = 8.5 Hz, 2H), 5.63 (q, J = 6.5 Hz, 1H), 3.78 (s, 3H), 1.89 (s, 3H), 1.25 (d, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.8, 166.3, 147.0, 142.1, 140.6, 139.5, 137.7, 133.1, 132.5,

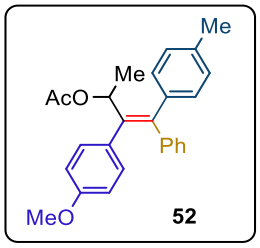
132.1, 131.3, 130.3, 129.3, 129.0, 128.9, 128.7, 128.0, 127.9, 127.7, 70.4, 52.5, 21.3, 19.7; IR (Neat) ν_{max} 1716, 1605, 1476, 1435, 1273, 1231, 1104, 703 cm^{-1}; **HRMS (ESI)** for $C_{32}H_{28}O_4SeNa+$ $(M+Na)^+$: calcd. 579.1045, found 579.1053.

(*E*)-3-(4-Methoxyphenyl)-3-phenyl-2-(*p*-tolyl)allyl acetate (51):



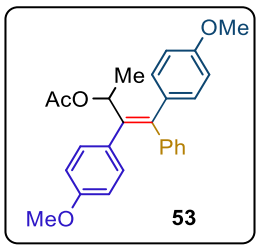
51 (57 mg, 51%) as pale red gummy liquid; R_f = 0.3 (10% EtOAc/Hex); ^1H NMR (400 MHz, Acetone d_6) δ 7.43–7.29 (m, 5H), 7.15 (d, J = 8.0 Hz, 2H), 7.03 (d, J = 7.6 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 6.66 (d, J = 8.4 Hz, 2H), 4.84 (s, 2H), 3.70 (s, 3H), 2.27 (s, 3H), 1.89 (s, 3H); ^{13}C NMR (101 MHz, Acetone d_6) δ 169.9, 158.4, 144.4, 142.5, 137.6, 136.0, 134.5, 133.4, 131.7, 129.7, 129.5, 128.6, 128.2, 127.3, 113.0, 66.4, 54.5, 20.3, 19.9; IR (Neat) ν_{max} 1734, 1508, 1232, 1018, 704 cm^{-1}; **HRMS (ESI)** for $C_{25}H_{24}NaO_3+$ $(M+Na)^+$: calcd. 395.1618, found 395.1626.

(*Z*)-3-(4-Methoxyphenyl)-4-phenyl-4-(*p*-tolyl)but-3-en-2-yl acetate (52):



52 (101 mg, 87%) as pale yellow gummy liquid; R_f = 0.5 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO d_6) δ 7.20 (d, J = 8.0 Hz, 2H), 7.15 (d, J = 8.0 Hz, 2H), 7.10–7.00 (m, 4H), 7.00–6.95 (m, 1H), 6.89 (d, J = 8.5 Hz, 2H), 6.77 (d, J = 9.0 Hz, 2H), 5.63 (q, J = 6.5 Hz, 1H), 3.68 (s, 3H), 2.31 (s, 3H), 1.90 (s, 3H), 1.20 (d, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.7, 158.3, 142.5, 142.4, 139.0, 138.3, 136.7, 132.3, 130.4, 130.0, 129..4, 129.2, 127.9, 126.5, 113.4, 71.0, 55.3, 21.4, 21.2, 19.8; IR (Neat) ν_{max} 1734, 1601, 1508, 1227, 1028, 692 cm^{-1}; **HRMS (ESI)** for $C_{26}H_{26}O_3Na$ $(M+Na)^+$: calcd. 409.1774, found 409.1782.

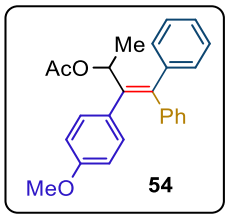
(Z)-3,4-Bis(4-Methoxyphenyl)-4-phenylbut-3-en-2-yl acetate (53):



53 (75 mg, 62%) as pale yellow liquid; R_f = 0.29 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO d_6) δ 7.17 (d, J = 9.0 Hz, 2H), 7.06 (d, J = 8.5 Hz, 2H), 7.03 (d, J = 7.5 Hz, 2H), 7.00–6.93 (m, 3H), 6.89 (d, J = 8.5 Hz, 2H), 6.77 (d, J = 9.0 Hz, 2H), 5.68 (q, J = 6.5 Hz, 1H), 3.77 (s, 3H), 3.68 (s, 3H), 1.91 (s, 3H), 1.20 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.7, 158.7, 158.2, 142.8, 142.2, 138.3, 134.1, 132.3, 130.6, 130.5, 130.1, 127.9, 126.5, 114.2,

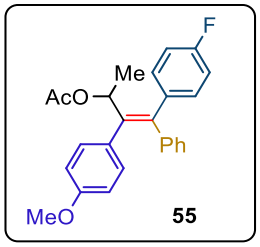
113.4, 71.0, 55.5, 55.3, 21.4, 19.8; IR (Neat) ν_{max} 1730, 1655, 1243, 10001, 822, 760 cm^{-1}; **HRMS (ESI)** for $C_{26}H_{26}O_4Na$ $(M+Na)^+$: calcd. 425.1723, found 425.1733.

3-(4-Methoxyphenyl)-4,4-diphenylbut-3-en-2-yl acetate (54):



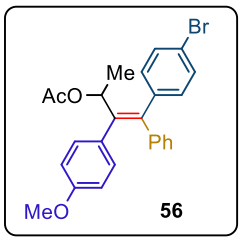
54 (95 mg, 85%) as pale yellow solid; R_f = 0.43 (10% EtOAc/Hex); M.P (147–148 °C); ^1H NMR (500 MHz, DMSO d_6) δ 7.40 (d, J = 7.5 Hz, 2H), 7.34–7.25 (m, 3H), 7.10–7.01 (m, 4H), 7.01–6.95 (m, 1H), 6.91 (d, J = 7.0 Hz, 2H), 6.78 (d, J = 8.5 Hz, 2H), 5.60 (q, J = 6.5 Hz, 1H), 3.68 (s, 3H), 1.89 (s, 3H), 1.20 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.7, 158.3, 142.5, 142.4, 141.9, 138.6, 132.2, 130.3, 129.9, 129.3, 128.8, 128.0, 127.5, 126.6, 113.5, 71.0, 55.3, 21.4, 19.8; IR (Neat) ν_{max} 1725, 1603, 1507, 1441, 1287, 1174, 692 cm^{-1}; **HRMS (ESI)** for $C_{25}H_{24}O_3Na$ $(M+Na)^+$: calcd. 395.1618, found 395.1627.

(Z)-4-(4-Fluorophenyl)-3-(4-methoxyphenyl)-4-phenylbut-3-en-2-yl acetate (55):



55 (101 mg, 86%) as pale yellow liquid; R_f = 0.43 (10% EtOAc/Hex); ^1H NMR (400 MHz, DMSO d_6) δ 7.35–7.29 (m, 2H), 7.28–7.19 (m, 2H), 7.11–6.98 (m, 5H), 6.94–6.88 (m, 2H), 6.78 (d, J = 7.6 Hz, 2H), 5.58 (q, J = 6.4 Hz, 1H), 3.69 (s, 3H), 1.91 (s, 3H), 1.21 (d, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, DMSO d_6) δ 169.8, 161.7 (d, J = 244 Hz, 1C), 158.3, 142.2, 141.4, 139.0, 138.2 (d, J = 3.0 Hz, 1C), 132.2, 131.4 (d, J = 8.1 Hz, 2C), 130.1, 130.0, 128.1, 126.7, 115.7 (d, J = 21.2 Hz, 2C), 113.5, 70.9, 55.3, 21.4, 19.7; ^{19}F NMR (376 MHz) δ −115.3; IR (Neat) ν_{max} 1731, 1373, 1242, 1024, 1005, 757 cm^{-1}; **HRMS (ESI)** for $C_{25}H_{23}FO_3Na$ $(M+Na)^+$: calcd. 413.1523, found 413.1532.

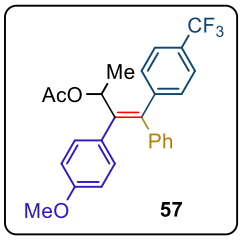
(Z)-4-(4-Fluorophenyl)-3-(4-methoxyphenyl)-4-phenylbut-3-en-2-yl acetate (56):



56 (107 mg, 79%) as pale yellow liquid; R_f = 0.43 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO d_6) δ 7.60 (d, J = 8.5 Hz, 2H), 7.24 (d, J = 8.5 Hz, 2H), 7.09–7.03 (m, 4H), 7.02–6.97 (m, 1H), 6.90 (br d, J = 7.0 Hz, 2H), 6.78 (br d, J = 8.5 Hz, 2H), 5.56 (q, J = 6.5 Hz, 1H), 3.68 (s, 3H), 1.91 (s, 3H), 1.21 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.7, 158.4, 141.9, 141.21, 141.15, 139.1, 132.1, 131.7, 131.6, 130.0, 128.1, 126.8, 120.9, 113.5, 70.9, 55.3,

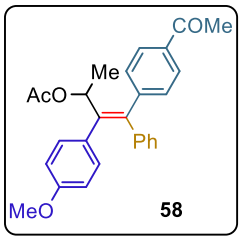
21.4, 19.7; IR (Neat) ν_{max} 1735, 1569, 1325, 1022, 760 cm^{-1}; **HRMS (ESI)** for $C_{25}H_{23}BrO_3Na$ $(M+Na)^+$: calcd. 473.0723, found 473.0729.

(Z)-3-(4-Methoxyphenyl)-4-phenyl-4-(4-(trifluoromethyl)phenyl)but-3-en-2-yl acetate (57):



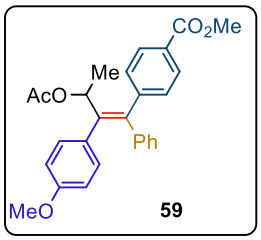
57 (107 mg, 81%) as pale yellow liquid; R_f = 0.39 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO d_6) δ 7.77 (d, J = 8.0 Hz, 2H), 7.52 (d, J = 8.0 Hz, 2H), 7.11–6.98 (m, 5H), 6.92 (d, J = 7.0 Hz, 2H), 6.79 (d, J = 8.5 Hz, 2H), 5.49 (q, J = 6.5 Hz, 1H), 3.68 (s, 3H), 1.89 (s, 3H), 1.21 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.8, 158.5, 146.2, 141.6, 141.0, 139.5, 132.1, 130.2, 130.0, 129.8, 128.2, 127.8 (q, J = 31.1 Hz, 1C), 126.9, 125.7 (q, J = 2.5 Hz, 1C), 124.7 (d, J = 273 Hz, 1C), 113.5, 70.9, 55.3, 21.3, 19.6; ^{19}F NMR (471 MHz) δ –61.0; IR (Neat) ν_{max} 1739, 1568, 1254, 1158, 1025, 701 cm^{-1}; **HRMS (ESI)** for $C_{26}H_{23}F_3O_3Na$ $(M+Na)^+$: calcd. 463.1492, found 463.1498.

(*Z*)-4-(4-Acetylphenyl)-3-(4-methoxyphenyl)-4-phenylbut-3-en-2-yl acetate (58):



58 (104 mg, 83%) as pale yellow liquid; R_f = 0.15 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO d_6) δ 8.00 (d, J = 8.5 Hz, 2H), 7.44 (d, J = 8.5 Hz, 2H), 7.12–6.96 (m, 5H), 6.92 (d, J = 7.0 Hz, 2H), 6.79 (d, J = 8.5 Hz, 2H), 5.55 (q, J = 6.5 Hz, 1H), 3.68 (s, 3H), 2.59 (s, 3H), 1.90 (s, 3H), 1.22 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 197.9, 169.8, 158.4, 146.8, 141.7, 141.5, 139.2, 135.9, 132.2, 130.0, 129.9, 129.7, 128.8, 128.1, 126.9, 113.5, 70.9, 55.3, 27.1, 21.3, 19.7; IR (Neat) ν_{max} 1731, 1680, 1600, 1508, 1235, 1029, 705 cm^{-1}; **HRMS (ESI)** for $C_{27}H_{26}O_4Na$ $(M+Na)^+$: calcd. 437.1723, found 437.1731.

(Z)-Methyl 4-(3-acetoxy-2-(4-methoxyphenyl)-1-phenylbut-1-en-1-yl)benzoate (59):

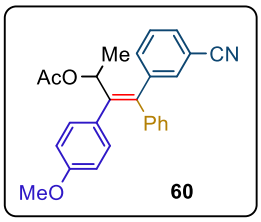


59 (115 mg, 89%) as pale yellow liquid; R_f = 0.23 (10% EtOAc/Hex); ^1H NMR (500 MHz, $CDCl_3$) δ 8.06 (dt, J = 8.5, 2.0 Hz, 2H), 7.39 (d, J = 8.5 Hz, 2H), 7.12–7.06 (m, 2H), 7.05–6.96 (m, 3H), 6.92–6.87 (m, 2H), 6.74 (dt, J = 9.0, 2.0 Hz, 2H), 5.70 (q, J = 6.5 Hz, 1H), 3.91 (s, 3H), 3.74 (s, 3H), 1.90 (s, 3H), 1.30 (d, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.9, 166.8, 158.3, 146.7, 141.34, 141.32, 139.2, 131.8, 130.1, 129.6, 129.4, 128.8, 127.5, 126.3, 113.1,

71.4, 55.0, 52.0, 21.1, 19.6; IR (Neat) ν_{max} 1718, 1603, 1508, 1272, 1234, 1100, 707 cm^{-1}; **HRMS (ESI)** for $C_{27}H_{26}O_5Na$ $(M+Na)^+$: calcd. 453.1672, found 453.1681.

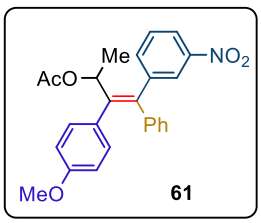
The compound **59** was insoluble in DMSO d_6. Thus, the spectra have been taken in $CDCl_3$. A little amount of cylization indene product **59′** has been observed in ^1H NMR during the recording of spectrum.

(Z)-4-(3-Cyanophenyl)-3-(4-methoxyphenyl)-4-phenylbut-3-en-2-yl acetate (60):



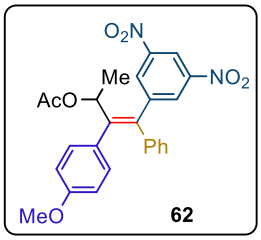
60 (98 mg, 82%) as pale yellow liquid; R_f = 0.19 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO d_6) δ 7.83–7.77 (m, 2H), 7.65–7.59 (m, 2H), 7.10–7.05 (m, 4H), 7.04–6.99 (m, 1H), 6.96–6.91 (m, 2H), 6.79 (d, J = 8.5 Hz, 2H), 5.44 (q, J = 6.5 Hz, 1H), 3.69 (s, 3H), 1.91 (s, 3H), 1.20 (d, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.8, 158.5, 143.2, 141.5, 140.4, 139.9, 134.3, 132.7, 132.1, 131.4, 130.2, 130.0, 129.7, 128.2, 127.0, 119.1, 113.5, 111.9, 70.8, 55.3, 21.3, 19.5; IR (Neat) ν_{max} 1731, 1373, 1242m 1024, 1005, 611 cm^{-1}; **HRMS (ESI)** for $C_{26}H_{23}NO_3Na$ $(M+Na)^+$: calcd. 420.1570, found 420.1579.

(Z)-3-(4-Methoxyphenyl)-4-(3-nitrophenyl)-4-phenylbut-3-en-2-yl acetate (61):



61 (117 mg, 93%) as pale yellow liquid; R_f = 0.18 (10% EtOAc/Hex); ^1H NMR (500 MHz, $CDCl_3$) δ 8.23–8.16 (m, 2H), 7.70 (d, J = 7.5 Hz, 1H), 7.58 (t, J = 7.5 Hz, 1H), 7.12 (d, J = 8.5 Hz, 2H), 7.10–7.01 (m, 3H), 6.96–6.91 (m, 2H), 6.78 (d, J = 9.0 Hz, 2H), 5.68 (q, J = 7.0 Hz, 1H), 3.70 (s, 3H), 1.95 (s, 3H), 1.34 (d, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.9, 158.5, 148.1, 143.4, 140.8, 140.2, 140.1, 135.5, 131.6, 130.0, 129.6, 129.3, 127.7, 126.6, 124.1, 122.1, 113.2, 71.2, 55.0, 21.0, 19.5; IR (Neat) ν_{max} 1732, 1524, 1345, 1029, 701 cm^{-1}; **HRMS (ESI)** for $C_{25}H_{23}NO_5Na$ $(M+Na)^+$: calcd. 440.1468, found 440.1474.

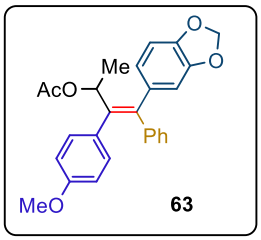
(Z)-4-(3,5-Dinitrophenyl)-3-(4-methoxyphenyl)-4-phenylbut-3-en-2-yl acetate (62):



62 (115 mg, 83%) as pale yellow liquid; R_f = 0.19 (10% EtOAc/Hex); ^1H NMR (500 MHz, $CDCl_3$) δ 8.98 (t, J = 2.5 Hz, 1H), 8.51 (d, J = 2.0 Hz, 2H), 7.11–7.05 (m, 5H), 6.91–6.87 (m, 2H), 6.76 (d, J = 8.5 Hz, 2H), 5.66 (q, J = 6.5 Hz, 1H), 3.76 (s, 3H), 1.94 (s, 3H), 1.33 (d, J = 6.5 Hz, 3H); ^{13}C NMR

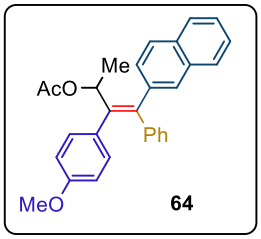
(126 MHz, $CDCl_3$) δ 170.0, 158.8, 148.4, 145.5, 142.0, 139.7, 138.3, 131.5, 130.0, 129.6, 128.9, 128.1, 127.3, 117.4, 113.4, 70.9, 55.0, 20.9, 19.4; IR (Neat) ν_{max} 1731, 1535, 1341, 1234, 700 cm^{-1}; **HRMS (ESI)** for $C_{25}H_{22}N_2O_7Na$ $(M+Na)^+$: calcd. 485.1319, found 485.1327.

(Z)-4-(Benzo[d][1,3]dioxol-5-yl)-3-(4-methoxyphenyl)-4-phenylbut-3-en-2-yl acetate (63):



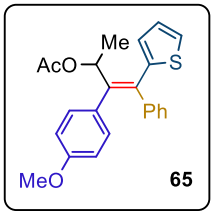
63 (83 mg, 66%) as pale yellow liquid; R_f = 0.21 (10% EtOAc/Hex); ^1H NMR (500 MHz, $CDCl_3$) δ 7.07 (dt, J = 6.5, 2.0 Hz, 2H), 7.05–6.96 (m, 3H), 6.94–6.89 (m, 2H), 6.83 (d, J = 8.0 Hz, 1H), 6.78 (dd, J = 7.5, 3.0 Hz, 1H), 6.75–6.70 (m, 3H), 5.96 (q, J = 1.5 Hz, 2H), 5.85 (q, J = 6.5 Hz, 1H), 3.74 (s, 3H), 1.95 (s, 3H), 1.30 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.0, 158.1, 147.5, 146.6, 142.13, 142.05, 138.4, 135.4, 131.9, 130.5, 130.0, 127.4, 126.1, 122.6, 113.0, 109.8, 108.1, 101.0, 71.5, 55.0, 21.2, 19.6; IR (Neat) ν_{max} 1733, 1604, 1507, 1468, 1240, 1032, 698 cm^{-1}; **HRMS (ESI)** for $C_{26}H_{24}O_5Na$ $(M+Na)^+$: calcd. 439.1516, found 439.1521.

(Z)-3-(4-Methoxyphenyl)-4-(naphthalen-2-yl)-4-phenylbut-3-en-2-yl acetate (64):



64 (104 mg, 82%) as pale yellow liquid; R_f = 0.45 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO d_6) δ 7.99–7.86 (m, 4H), 7.58–7.51 (m, 2H), 7.37 (dd, J = 8.5, 1.5 Hz, 1H), 7.14 (d, J = 9.0 Hz, 2H), 7.05 (t, J = 7.0 Hz, 2H), 7.02–6.95 (m, 3H), 6.82 (dt, J = 7.5, 2.0 Hz, 2H), 5.68 (q, J = 6.5 Hz, 1H), 3.70 (s, 3H), 1.90 (s, 3H), 1.25 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.8, 158.4, 142.4, 142.2, 139.4, 138.9, 133.3, 132.4, 132.3, 130.3, 130.2, 128.4, 128.3, 128.1, 127.9, 127.8, 126.8, 126.7, 126.6, 113.5, 71.1, 55.3, 21.4, 19.8; IR (Neat) ν_{max} 1739, 1604, 1507, 1368, 1232, 1031, 708 cm^{-1}; **HRMS (ESI)** for $C_{29}H_{26}O_3Na$ $(M+Na)^+$: calcd. 445.1774, found 445.1784.

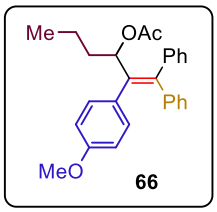
(Z)-3-(4-Methoxyphenyl)-4-phenyl-4-(thiophen-2-yl)but-3-en-2-yl acetate (65):



65 (71 mg, 62%) as pale yellow liquid; R_f = 0.42 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO d_6) δ 7.58 (dd, J = 4.5, 1.5 Hz, 1H), 7.12–7.00 (m, 7H), 6.94 (d, J = 7.0 Hz, 2H), 6.75 (d, J = 8.5 Hz, 2H), 5.96 (q, J = 6.5 Hz, 1H), 3.67 (s, 3H), 1.94 (s, 3H), 1.27 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6)

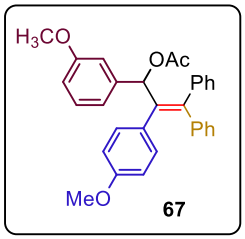
δ 169.8, 158.3, 142.9, 142.3, 141.1, 135.2, 132.1, 130.0, 129.9, 128.1, 127.6, 127.4, 127.0, 113.4, 70.6, 55.3, 21.5, 19.9; IR (Neat) ν_{max} 1731, 1604, 1507, 1236, 1028, 695 cm^{-1}; **HRMS (ESI)** for $C_{23}H_{22}NaO_3S$ $(M+Na)^+$: calcd. 401.1182, found 401.1188.

2-(4-Methoxyphenyl)-1,1-diphenylhex-1-en-3-yl acetate (66):



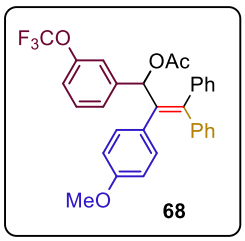
66 (105 mg, 87%) as pale yellow liquid; R_f = 0.43 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.42–7.35 (m, 2H), 7.32–7.26 (m, 3H), 7.07–7.02 (m, 4H), 7.00–6.95 (m, 1H), 6.94–6.89 (m, 2H), 6.76 (d, J = 9.0 Hz, 2H), 5.54 (dd, J = 8.0, 8.0 Hz, 1H), 3.68 (s, 3H), 1.89 (s, 3H), 1.59–1.48 (m, 2H), 1.26–1.11 (m, 2H), 0.69 (t, J = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.8, 158.3, 142.9, 142.5, 141.9, 138.0, 132.0, 130.5, 129.9, 129.3, 128.6, 128.0, 127.4, 126.5, 113.5, 74.2, 55.3, 35.5, 21.3, 18.8, 13.8; IR (Neat) ν_{max} 1731, 1373, 1242, 1023, 1004, 758 cm^{-1}; **HRMS (ESI)** for $C_{27}H_{28}O_3Na$ $(M+Na)^+$: calcd. 423.1931, found 423.1940.

1-(3-Methoxyphenyl)-2-(4-methoxyphenyl)-3,3-diphenylallyl acetate (67):



67 (86 mg, 62%) as pale yellow liquid; R_f = 0.40 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, DMSO d_6) δ 7.43 (d, J = 4.8 Hz, 4H), 7.38–7.29 (m, 1H), 7.24 (t, J = 8.0 Hz, 1H), 7.11–6.94 (m, 5H), 6.85–6.76 (m, 4H), 6.70–6.62 (m, 4H), 3.69 (s, 3H), 3.63 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (101 MHz, DMSO d_6) δ 169.7, 159.5, 158.2, 144.3, 142.4, 142.1, 140.7, 137.0, 132.2, 130.1, 130.0, 129.8, 129.4, 129.0, 128.2, 127.8, 126.8, 118.6, 113.2, 112.1, 75.3, 55.4, 55.2, 21.3; IR (Neat) ν_{max} 1739, 1604, 1508, 1227, 1030, 698 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{25}O_4$ $(M+H)^+$: calcd. 465.2060, found 465.2062.

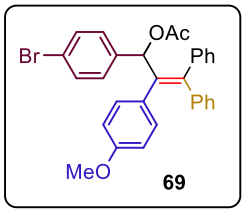
2-(4-Methoxyphenyl)-3,3-diphenyl-1-(3-(trifluoromethoxy)phenyl)allyl acetate (68):



68 (103 mg, 66%) as pale yellow liquid; R_f = 0.45 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, DMSO d_6) δ 7.43 (d, J = 7.6 Hz, 4H), 7.37–7.27 (m, 5H), 7.12–7.05 (m, 2H), 7.04–6.96 (m, 3H), 6.82 (dt, J = 6.8, 2.0 Hz, 2H), 6.69 (s, 1H), 6.64 (dt, J = 6.8, 2.0 Hz, 2H), 3.62 (s, 3H), 2.06 (s, 3H); ^{13}C NMR (101 MHz, DMSO d_6) δ 169.7, 158.3, 147.9, 144.9, 142.2, 141.9, 138.4, 136.5, 132.2, 129.9, 129.8, 129.3, 129.0, 128.4, 128.1, 127.8, 126.9, 121.2, 120.5 (d, J = 257 Hz, 1C),

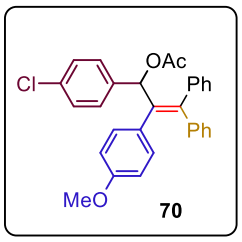
113.3, 74.9, 55.2, 21.2; ^{19}F NMR (376 MHz) δ –56.8; IR (Neat) ν_{max} 1765, 1542, 1489, 1226, 1098, 1008, 698 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{25}F_3NaO_4$ $(M+Na)^+$: calcd. 541.1603, found 541.1604.

1-(4-Bromophenyl)-2-(4-methoxyphenyl)-3,3-diphenylallyl acetate (69):



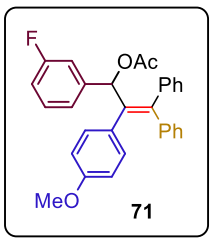
69 (88 mg, 57%) as pale yellow liquid; R_f = 0.45 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, ACETONE d_6) δ 7.52 (d, J = 8.0 Hz, 2H), 7.47 (d, J = 8.5 Hz, 2H), 7.43 (t, J = 7.5 Hz, 2H), 7.38–7.31 (m, 1H), 7.20 (d, J = 8.5 Hz, 2H), 7.09–6.99 (m, 5H), 6.89 (d, J = 8.0 Hz, 2H), 6.80 (s, 1H), 6.65 (d, J = 8.5 Hz, 2H), 3.67 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (126 MHz, ACETONE d_6) δ 169.0, 158.5, 144.6, 142.2, 141.9, 138.7, 136.8, 132.1, 131.1, 129.9, 129.3, 128.5, 128.4, 127.5, 127.3, 126.3, 120.8, 112.7, 75.1, 54.4, 20.1; IR (Neat) ν_{max} 1750, 1510, 1485, 1223, 1067, 1006, 700 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{25}BrO_3Na$ + $(M+Na)^+$: calcd. 535.0879, found 535.0889.

1-(4-Chlorophenyl)-2-(4-methoxyphenyl)-3,3-diphenylallyl acetate (70):



70 (79 mg, 56%) as pale yellow liquid; R_f = 0.45 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.42 (d, J = 4.5 Hz, 4H), 7.38–7.30 (m, 3H), 7.17 (d, J = 8.0 Hz, 2H), 7.10–7.04 (m, 2H), 7.03–6.95 (m, 3H), 6.81 (d, J = 9.0 Hz, 2H), 6.64 (d, J = 9.0 Hz, 3H), 3.62 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.6, 158.3, 144.8, 142.2, 141.9, 138.1, 136.5, 132.4, 132.2, 129.9, 129.8, 129.3, 129.0, 128.7, 128.3, 128.1, 127.8, 126.8, 113.3, 75.0, 55.2, 21.2; IR (Neat) ν_{max} 1734, 1605, 1508, 1368, 1226, 1029, 696 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{25}ClO_3Na$+ $(M+Na)^+$: calcd. 491.1384, found 491.1381.

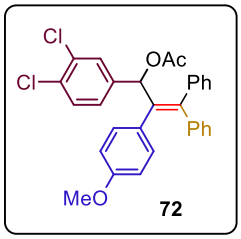
1-(3-Fluorophenyl)-2-(4-methoxyphenyl)-3,3-diphenylallyl acetate (71):



71 (72 mg, 53%) as pale yellow liquid; R_f = 0.45 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, DMSO d_6) δ 7.47–7.41 (m, 4H), 7.39–7.31 (m, 2H), 7.11–6.97 (m, 7H), 6.88 (br d, J = 10.4 Hz, 1H), 6.83 (dt, J = 6.4, 2.0 Hz, 2H), 6.69 (s, 1H), 6.64 (d, J = 8.8 Hz, 2H), 3.62 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (101 MHz, DMSO d_6) δ 169.7, 162.5 (d, J = 244 Hz, 1C), 158.3, 145.0, 142.2, 142.1 (d, J = 7.1 Hz, 1C), 141.9, 136.5, 132.2, 130.8 (d, J = 8.1 Hz, 1C), 130.0, 129.8, 129.3, 129.0, 128.2, 127.8, 126.9,

122.5 (d, J = 3.0 Hz, 1C), 114.7 (d, J = 21.2 Hz, 1C), 113.3, 113.1 (d, J = 23.2 Hz, 1C), 74.8, 55.2, 21.2; ^{19}F NMR (376 MHz) δ −112.8; IR (Neat) ν_{max} 1734, 1677, 1596, 1239, 1064, 703 cm^{-1}; **HRMS (ESI)** $C_{30}H_{25}FNaO_3$+ $(M+Na)^+$: calcd. 475.1680, found 475.1684.

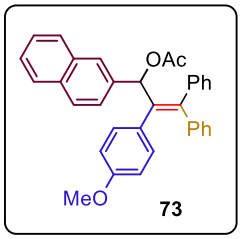
1-(3,4-Dichlorophenyl)-2-(4-methoxyphenyl)-3,3-diphenylallyl acetate (72):



72

72 (107 mg, 71%) as pale yellow liquid; R_f = 0.42 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.56 (d, J = 8.5 Hz, 1H), 7.46–7.40 (m, 4H), 7.36–7.31 (m, 1H), 7.25–7.18 (m, 2H), 7.07 (t, J = 7.0 Hz, 2H), 7.03–6.96 (m, 3H), 6.84 (d, J = 8.5 Hz, 2H), 6.66 (d, J = 8.5 Hz, 2H), 6.62 (s, 1H), 3.62 (s, 3H), 2.06 (s, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.6, 158.4, 145.3, 142.0, 141.7, 140.2, 136.1, 132.2, 131.5, 130.9, 130.6, 129.9, 129.6, 129.2, 129.0, 128.3, 128.1, 127.9, 126.94, 126.91, 113.4, 74.4, 55.3, 21.2, ; IR (Neat) ν_{max} 1690, 1580, 1254, 1005, 968, 705 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{24}Cl_2NaO_3$ $(M+Na)^+$: calcd. 525.0995, found.525.0991.

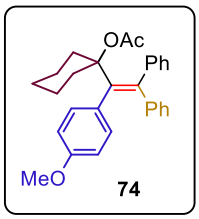
2-(4-Methoxyphenyl)-1-(naphthalen-2-yl)-3,3-diphenylallyl acetate (73):



73

73 (105 mg, 72%) as pale yellow liquid; R_f = 0.41 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, ACETONE d_6) δ 7.90–7.82 (m, 3H), 7.77 (s, 1H), 7.61 (d, J = 8.5 Hz, 2H), 7.52–7.42 (m, 5H), 7.38–7.32 (m, 1H), 7.11–6.99 (m, 6H), 6.91 (d, J = 8.5 Hz, 2H), 6.60 (d, J = 9.0 Hz, 2H), 3.63 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (126 MHz, ACETONE d_6) δ 169.1, 158.4, 144.3, 142.5, 142.2, 137.2, 136.8, 133.2, 132.8, 132.1, 130.2, 130.0, 129.4, 128.5, 128.0, 127.8, 127.6, 127.3, 126.3, 126.2, 126.0, 125.1, 124.5, 112.7, 75.7, 54.4, 20.2; IR (Neat) ν_{max} 1735, 1508, 1224, 1027, 696 cm^{-1}; **HRMS (ESI)** for $C_{34}H_{28}NaO_3$ $(M+Na)^+$: calcd. 507.1931, found. 507.1930.

1-(1-(4-Methoxyphenyl)-2,2-diphenylvinyl)cyclohexyl acetate (74):

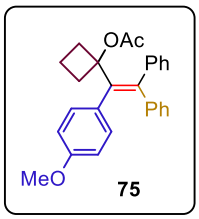


74

74 (65 mg, 51%) as pale yellow solid; R_f = 0.54 (10% EtOAc/Hex); M.P (220–222 ^{o}C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.28 (m, 4H), 7.23–7.13 (m, 3H), 7.00–6.94 (m, 4H), 6.89–6.84 (m, 1H), 6.68 (d, J = 9.0 Hz, 2H), 3.72 (s, 3H), 2.57 (d, J = 10 Hz, 2H), 1.59–1.32 (m, 10H), 1.08–0.07 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.7, 157.7, 144.8, 143.3, 142.8, 140.3, 132.9, 132.0, 129.0, 128.5, 127.8, 127.3, 125.9, 125.1, 112.4, 83.0, 54.9, 35.9, 24.8, 21.7, 21.6; IR (Neat) ν_{max} 1725, 1606, 1507,

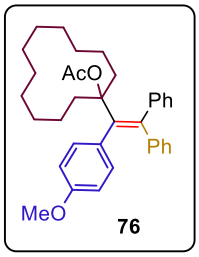
1441, 1235, 1032, 695 cm^{-1}; **HRMS (ESI)** for $C_{29}H_{30}O_3Na$ $(M+Na)^+$: calcd. 449.2087, found 449.2090.

1-(1-(4-Methoxyphenyl)-2,2-diphenylvinyl)cyclobutyl acetate (75):



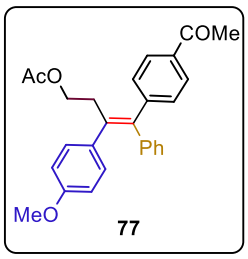
75 (89 mg, 74%) as pale yellow liquid; R_f = 0.54 (10% EtOAc/Hex); ^1H NMR (500 MHz, $CDCl_3$) δ 7.36–7.20 (m, 7H), 7.02–6.90 (m, 5H), 6.75 (d, J = 9.0 Hz, 2H), 3.76 (s, 3H), 2.58–2.49 (m, 2H), 2.36–2.28 (m, 2H), 1.92–1.81 (m, 1H), 1.66 (s, 3H), 1.49–1.38 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.8, 158.0, 143.9, 143.4, 142.3, 139.6, 132.9, 132.2, 130.0, 129.0, 127.6, 127.2, 126.4, 125.4, 112.7, 84.8, 54.9, 36.2, 21.2, 15.6; IR (Neat) ν_{max} 1719, 1606, 1505, 1239, 1028, 698 cm^{-1}; **HRMS (ESI)** for $C_{27}H_{26}O_3Na$ $(M+Na)^+$: calcd. 421.1774, found 421.1780.

1-(1-(4-Methoxyphenyl)-2,2-diphenylvinyl)cyclododecyl acetate (76):



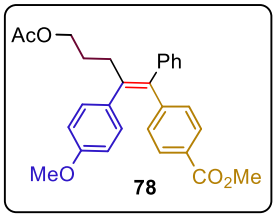
76 (48 mg, 31%) as pale yellow liquid; R_f = 0.54 (10% EtOAc/Hex);the compound is partially soluble in DMSO d_6 and thus ^{13}C NMR was recorded overnight; ^1H NMR (600 MHz, DMSO d_6) δ 7.28 (t, J = 8.4 Hz, 2H), 7.23 (d, J = 7.8 Hz, 2H), 7.18–7.00 (m, 3H), 6.95–6.86 (m, 4H), 6.79 (t, J = 6.6 Hz, 1H), 6.62 (d, J = 7.8 Hz, 2H), 3.58 (s, 3H), 1.94–1.82 (m, 2H), 1.79 (s, 3H), 1.37–1.04 (m, 20H); ^{13}C NMR (101 MHz, DMSO d_6) δ 169.6, 157.5, 145.2, 143.4, 142.7, 141.3, 132.8, 132.5, 128.8, 128.21, 128.16, 127.9, 126.8, 125.6, 112.6, 85.7, 55.1, 32.7, 26.8, 26.2, 22.3, 21.9, 21.8, 19.6; IR (Neat) ν_{max} 1735, 1650, 1594, 1022, 991, 611 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{42}O_3Na$ $(M+Na)^+$: calcd. 533.3026, found 533.3027.

(*E*)-4-(4-Acetylphenyl)-3-(4-methoxyphenyl)-4-phenylbut-3-en-1-yl acetate (77):



77 (77 mg, 62%) as pale yellow liquid; R_f = 0.54 (10% EtOAc/Hex); ^1H NMR (400 MHz, DMSO d_6) δ 8.00 (d, J = 8.4 Hz, 2H), 7.43 (d, J = 8.4 Hz, 2H), 7.12–7.01 (m, 5H), 6.93–6.87 (m, 2H), 6.77 (d, J = 8.8 Hz, 2H), 3.91 (t, J = 6.8 Hz, 2H), 3.69 (s, 3H), 2.72 (t, J = 7.2 Hz, 2H), 2.60 (s, 3H), 1.97 (s, 3H); ^{13}C NMR (101 MHz, DMSO d_6) δ 197.9, 170.6, 158.4, 148.1, 142.5, 140.3, 136.8, 135.7, 132.9, 130.9, 130.5, 129.9, 128.9, 128.3, 113.9, 62.5, 55.4, 34.8, 27.1, 21.1; IR (Neat) ν_{max} 1734, 1679, 1599, 1508, 1359, 1233, 1174, 1028, 699 cm^{-1}; **HRMS (ESI)** for $C_{27}H_{26}NaO_4$+ $(M+Na)^+$: calcd. 437.1723, found 437.1733.

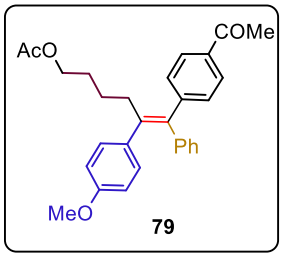
((Z)-Methyl 4-(5-acetoxy-2-(4-methoxyphenyl)-1-phenylpent-1-en-1-yl)benzoate (78/78′ = 93:7)



78 (mg, 48%) as pale yellow liquid; R_f = 0.54 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, DMSO d$_6$) δ 7.66 (d, J = 8.4 Hz, 2H), 7.40 (t, J = 7.2 Hz, 2H), 7.35–7.28 (m, 1H), 7.25–7.20 (m, 2H), 7.05 (d, J = 8.8 Hz, 2H), 7.02 (d, J = 8.4 Hz, 2H), 6.76 (d, J = 8.8 Hz, 2H), 3.87 (t, J = 6.4 Hz, 2H), 3.77 (s, 3H), 3.69 (s, 3H), 2.44–2.40 (m, 2H), 1.90 (s, 3H), 1.61–1.47 (m, 2H); ^{13}C NMR (101 MHz, DMSO d$_6$) δ 170.7, 166.4, 158.4, 148.5, 142.7, 141.1, 138.5, 133.2, 130.9, 129.5, 129.0, 128.9, 127.5, 127.4, 114.0, 63.8, 55.4, 52.4, 32.1, 27.9, 21.1; IR (Neat) ν_{max} 1717, 1605, 1508, 1276, 1242, 1023, 992, 703 cm^{-1}; **HRMS (ESI)** for $C_{28}H_{28}NaO_5$+ $(M+Na)^+$: calcd. 467.1829, found 467.1836.

Representative peaks of the inseparable minor regio-isomer **78′**: ^{1}H NMR (400 MHz, DMSO d$_6$) δ 3.82 (s, 0.23H), 3.62 (s, 0.23H); ^{13}C NMR (101 MHz, DMSO d$_6$) δ 131.8, 128.8, 127.8.

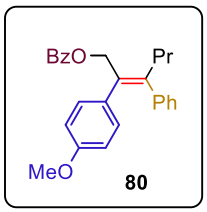
(E)-6-(4-Acetylphenyl)-5-(4-methoxyphenyl)-6-phenylhex-5-en-1-yl acetate (79/79′ = 92:8):



79 (67 mg, 51%) as pale yellow liquid; R_f = 0.54 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, ACETONE d$_6$) δ 8.02 (d, J = 8.0 Hz, 2H), 7.43 (d, J = 8.5 Hz, 2H), 7.12 (d, J = 9.0 Hz, 2H), 7.10–7.00 (m, 3H), 6.99–6.94 (m, 2H), 6.76 (d, J = 9.0 Hz, 2H), 3.91 (t, J = 65 Hz, 2H), 3.73 (s, 3H), 2.60 (s, 3H), 2.49 (t, J = 7.5 Hz, 2H), 1.93 (s, 3H), 1.59–1.51 (m, 2H), 1.49–1.40 (m, 2H); ^{13}C NMR (126 MHz, ACETONE d$_6$) δ 196.6, 170.0, 158.4, 148.5, 142.8, 141.0, 138.3, 135.7, 133.7, 130.6, 130.5, 129.6, 128.3, 127.6, 126.0, 113.3, 63.5, 54.5, 35.1, 25.8, 24.9, 19.9; IR (Neat) ν_{max} 1740, 1636, 1569, 1288, 1189, 1056, 956, 699 cm^{-1}; **HRMS (ESI)** for $C_{29}H_{30}O_4Na$ $(M+Na)^+$: calcd. 465.2036, found. 465.2037.

Representative peaks of the inseparable minor regio-isomer **79′**: ^{1}H NMR (500 MHz, DMSO d$_6$) δ 6.85 (d, J = 8.5 Hz, 0.18H), 6.62 (d, J = 9.0 Hz, 0.19H), 3.66 (s, 0.28H); ^{13}C NMR (126 MHz, DMSO d$_6$) δ 158.1, 142.1, 140.6, 134.6, 131.7, 113.0.

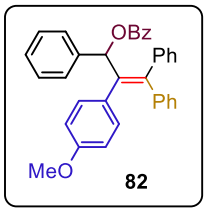
(*E*)-2-(4-Methoxyphenyl)-3-phenylhex-2-en-1-yl benzoate (80/80′ = 88:12):



80 (10 mg, 9%) as pale yellow liquid; R_f = 0.53 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.85–7.79 (m, 2H), 7.65–7.59 (m, 1H), 7.49 (t, J = 8.0 Hz, 2H), 7.14 (t, J = 7.5 Hz, 2H), 7.10–7.05 (m, 1H), 7.04–7.00 (m, 2H), 7.97 (d, J = 8.5 Hz, 2H), 6.65 (d, J = 9.0 Hz, 2H), 5.27 (s, 2H), 3.62 (s, 3H), 2.66 (t, J = 7.5 Hz, 2H), 1.33–1.26 (m, 2H), 0.86 (t, J = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, DMSO d_6) δ 160.0,, 157.8, 144.1, 142.6, 133.8, 133.3, 132.4, 131.0, 130.2, 129.47, 129.45, 129.2, 128.2, 113.5, 65.5, 55.3, 36.6, 21.7, 14.0; IR (Neat) ν_{max} 1718, 159, 1459, 1267, 1246, 711 cm^{-1}; **HRMS (ESI)** for $C_{26}H_{26}O_3Na$ $(M+Na)^+$: calcd. 409.1774, found 409.1777.

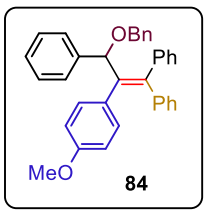
Representative peaks of the inseparable minor regio-isomer **80′**: ^{1}H NMR (500 MHz, DMSO d_6) δ 3.65 (s, 0.43H); ^{13}C NMR (126 MHz, DMSO d_6) δ 158.0, 144.2, 129.4, 128.2, 16.5, 124.6, 115.0, 113.6, 55.3, 21.7.

2-(4-Methoxyphenyl)-1,3,3-triphenylallyl benzoate (82):



82 (83 mg, 56%) as pale yellow liquid; R_f = 0.43 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.89 (d, J = 8.0 Hz, 2H), 7.67 (t, J = 7.5 Hz, 1H), 7.53 (t, J = 8.0 Hz, 2H), 7.50–7.41 (m, 4H), 7.37–7.30 (m, 3H), 7.27 (t, J = 7.0 Hz, 1H), 7.21 (d, J = 7.5 Hz, 2H), 7.08 (t, J = 7.5 Hz, 2H), 7.04–6.96 (m, 4H), 6.83 (dt, J = 7.0, 1.5 Hz, 2H), 6.64 (d, J = 8.5 Hz, 2H), 3.62 (s, 3H); ^{13}C NMR (101 MHz, DMSO d_6) δ 165.0, 158.3, 144.7, 142.3, 142.0, 139.0, 136.7, 134.1, 132.2, 130.0, 129.7, 129.4, 129.1, 128.9, 128.2, 128.0, 127.8, 126.9, 126.3, 113.3, 76.2, 55.3; IR (Neat) ν_{max} 1716, 1604, 1508, 1242, 1174, 1025, 748, 695 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{28}NaO_3$ $(M+Na)^+$: calcd. 519.1931, found 519.1934.

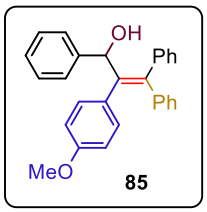
(3-(Benzyloxy)-2-(4-methoxyphenyl)prop-1-ene-1,1,3-triyl)tribenzene (84):



84 (61 mg, 42%) as pale yellow liquid; R_f = 0.51 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.44–7.36 (m, 4H), 7.33–7.24 (m, 10H), 7.21–7.16 (m, 1H), 7.08 (d, J = 7.5 Hz, 2H), 7.05–6.99 (m, 3H), 6.86 (d, J = 8.5 Hz, 2H), 6.56 (d, J = 9.0 Hz, 2H), 5.44 (s, 1H), 4.80 (d, J = 8.0 Hz, 1H), 4.45 (d, J = 7.0 Hz, 1H), 3.59 (s, 3H); ^{13}C NMR (101 MHz, DMSO d_6) δ 158.0, 145.0, 142.8, 142.2, 140.9, 138.8, 138.0, 132.3, 130.5, 130.2, 129.6, 129.0, 128.7, 128.4, 128.1, 127.93, 127.89, 127.6, 127.3, 126.7,

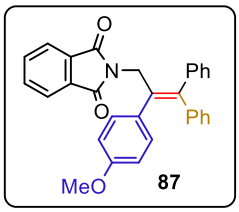
126.6, 113.0, 79.7, 69.8, 55.2; IR (Neat) ν_{max} 1604, 1507, 1491, 1441, 1242, 1027, 747 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{30}NaO_2$ $(M+Na)^+$: calcd. 505.2143, found 505.2151.

2-(4-Methoxyphenyl)-1,3,3-triphenylprop-2-en-1-ol (85):



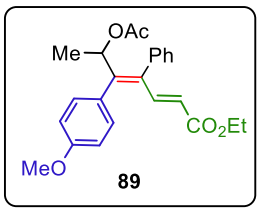
85 (47 mg, 41%) as pale yellow liquid; R_f = 0.51 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.48 (dd, J = 8.5, 1.5 Hz, 2H), 7.43 (t, J = 7.5 Hz, 2H), 7.34–7.28 (m, 1H), 7.23 (d, J = 4.5 Hz, 4H), 7.17–7.12 (m, 1H), 7.05 (t, J = 7.0 Hz, 2H), 7.00–6.92 (m, 3H), 6.77 (d, J = 9.0 Hz, 2H), 6.52 (d, J = 9.0 Hz, 2H), 5.65 (d, J = 3.5 Hz, 1H), 5.56 (d, J = 3.5 Hz, 1H), 3.58 (s, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 157.8, 143.7, 143.0, 142.9, 142.7, 141.6, 132.5, 130.9, 130.2, 129.7, 128.9, 128.1, 128.0, 127.3, 126.7, 126.4, 126.3, 112.6, 72.2, 55.1; IR (Neat) ν_{max} 3413, 2923,. 1604, 1508, 1443, 1244, 699 cm^{-1}; **HRMS (ESI)** for $C_{28}H_{24}O_2Na$ $(M+Na)^+$: calcd. 415.1669, found 415.1670.

2-(2-(4-Methoxyphenyl)-3,3-diphenylallyl)isoindoline-1,3-dione (87):



87 (47 mg, 41%) as pale yellow liquid; R_f = 0.51 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.69–7.64 (m, 2H), 7.62–7.55 (m, 4H), 7.35 (t, J = 8.0 Hz, 2H), 7.26–7.21 (m, 1H), 7.09–6.93 (m, 7H), 6.58 (d, J = 9.0 Hz, 2H), 4.75 (s, 2H), 3.63 (s, 3H); ^{13}C NMR (101 MHz, DMSO d_6) δ 168.0, 158.1, 142.5, 142.4, 141.4, 133.7, 133.6, 131.7, 130.82, 130.76, 130.3, 129.5, 128.4, 127.5, 126.8, 126.0, 122.9, 113.2, 54.9, 42.0; IR (Neat) ν_{max} 1711, 1606, 1509, 1390, 1245, 701 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{24}NO_3$ $(M+Na)^+$: calcd. 446.1751, found 446.1757.

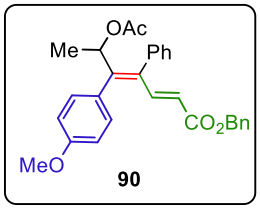
(2E,4Z)-Ethyl 6-acetoxy-5-(4-methoxyphenyl)-4-phenylhepta-2,4-dienoate (89/89′ = 93:7):



89 (97 mg, 82%) as pale yellow liquid; R_f = 0.23 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, DMSO d_6) δ 7.54–7.41 (m, 3H), 7.31–7.16 (m, 5H), 7.07 (d, J = 8.0 Hz, 2H), 5.30 (q, J = 6.8 Hz, 1H), 5.10 (d, J = 15.6 Hz, 1H), 3.97 (q, J = 7.2 Hz, 2H), 3.83 (s, 3H), 1.85 (s, 3H), 1.16 (d, J = 6.8 Hz, 3H), 1.07 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, DMSO d_6) δ 169.8, 166.2, 159.5, 148.1, 145.0, 137.8, 137.1, 131.5, 129.6, 129.1, 128.2, 128.1, 121.9, 114.1, 71.0, 60.4, 55.5, 21.2, 19.3, 14.4; IR (Neat) ν_{max} 1732, 1709, 1508, 1275, 1232, 1168, 1020, 704 cm^{-1}; **HRMS (ESI)** for $C_{24}H_{26}NaO_5$+ $(M+Na)^+$: calcd. 417.1672, found 417.1682.

Representative peaks of the inseparable minor regio-isomer **89′**: ^{1}H NMR (400 MHz, DMSO d_6) δ 6.37 (d, J = 16.4 Hz, 0.08H), 3.78 (s, 0.24H); ^{13}C NMR (101 MHz, DMSO d_6) δ 167.0, 159.8, 151.5, 132.1, 128.8, 55.6, 19.8.

(2E,4Z)-Benzyl 6-acetoxy-5-(4-methoxyphenyl)-4-phenylhepta-2,4-dienoate (90/90′ = 93:7):

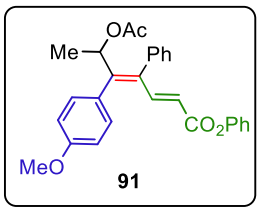


90

90 (104 mg, 76%) as pale yellow liquid; R_f = 0.20 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.49 (t, J = 7.0 Hz, 2H), 7.44–7.39 (m, 1H), 7.31–7.17 (m, 10H), 7.06 (d, J = 8.5 Hz, 2H), 5.29 (q, J = 6.5 Hz, 1H), 5.12 (d, J = 15.5 Hz, 1H), 5.01 (s, 2H), 3.35 (s, 3H), 1.84 (s, 3H), 1.16 (d, J = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, DMSO d_6) δ 169.8, 166.0, 159.5, 148.5, 145.6, 137.8, 137.0, 136.4, 131.5, 129.6, 129.1, 128.8, 128.4, 128.3, 128.1, 121.4, 114.1, 71.0, 65.9, 55.6, 21.2, 19.3; IR (Neat) ν_{max} 1735, 1710, 1606, 1273, 1233, 1158, 1027 cm^{-1}; **HRMS (ESI)** for $C_{29}H_{28}NaO_5$+ $(M+Na)^+$: calcd. 479.1829, found 479.1839.

Representative peaks of the inseparable minor regio-isomer **90′**: ^{1}H NMR (500 MHz, DMSO d_6) δ 6.59 (d, J = 16.5 Hz, 0.08H), 3.77 (s, 0.24H); ^{13}C NMR (101 MHz, DMSO d_6) δ 132.1, 119.4, 19.9.

(2E,4Z)-Phenyl 6-acetoxy-5-(4-methoxyphenyl)-4-phenylhepta-2,4-dienoate (91/91′ = 93:7):

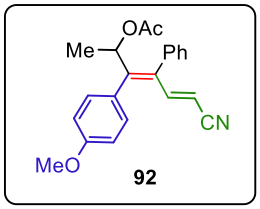


91

91 (62 mg, 47%) as pale yellow liquid; R_f = 0.18 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.36 (d, J = 7.0 Hz, 2H), 7.31–7.22 (m, 2H), 7.21–7.14 (m, 5H), 7.06–7.01 (m, 3H), 6.90–6.83 (m, 4H), 5.17–5.10 (m, 2H), 3.63 (s, 3H), 1.68 (s, 3H), 1.01 (d, J = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, DMSO d_6) δ 169.8, 164.9, 159.6, 150.7, 149.4, 146.8, 137.7, 136.9, 131.5, 129.8, 129.6, 129.2, 128.4, 128.0, 126.3, 122.1, 120.8, 114.2, 71.0, 55.6, 21.2, 19.3; IR (Neat) ν_{max} 1727, 1607, 1507, 1491, 1368, 1272, 1231, 1129, 702 cm^{-1}; **HRMS (ESI)** for $C_{28}H_{26}NaO_5$ $(M+Na)^+$: calcd. 465.1678, found 465.1685.

Representative peaks of the inseparable minor regio-isomer **91′**: ^{1}H NMR (500 MHz, DMSO d_6) δ 6.41 (d, J = 16.0 Hz, 0.08H), 3.58 (s, 0.24H); ^{13}C NMR (126 MHz, DMSO d_6) δ 143.3, 132.2, 128.8, 19.9.

(3Z,5E)-6-Cyano-3-(4-methoxyphenyl)-4-phenylhexa-3,5-dien-2-yl acetate (92/92′ = 93:7):

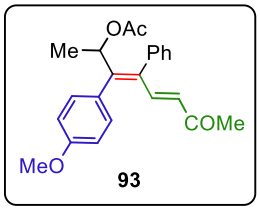


92

92 (53 mg, 51%) as pale yellow liquid; R_f = 0.18 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d$_6$) δ 7.53–7.42 (m, 4H), 7.29–7.25 (m, 3H), 7.19 (d, J = 9.0 Hz, 2H), 7.07 (d, J = 9.0 Hz, 2H), 6.94 (d, J = 16.5 Hz, 1H), 5.25 (q, J = 6.5 Hz, 1H), 4.83 (d, J = 16.5 Hz, 1H), 3.83 (s, 3H), 1.84 (s, 3H), 1.79 (s, 3H), 1.16 (d, J = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, DMSO d$_6$) δ 169.8, 159.6, 150.5, 148.8, 137.5, 135.6, 131.5, 129.7, 129.3, 128.6, 127.6, 118.9, 114.3, 100.2, 70.8, 55.3, 21.2, 19.3; IR (Neat) ν_{max} 2213, 1604, 1507, 1368, 1230, 1176, 1028, 705 cm^{-1}; **HRMS (ESI)** for $C_{22}H_{21}NNaO_3$ $(M+Na)^+$: calcd. 370.1419, found 370.1415.

Representative peaks of the inseparable minor regio-isomer **92′**: ^{1}H NMR (500 MHz, DMSO d$_6$) δ 6.11 (d, J = 17.0 Hz, 0.09H), 3.78 (s, 0.24H); ^{13}C NMR (101 MHz, DMSO d$_6$) δ 157.8, 130.6, 21.0, 19.1.

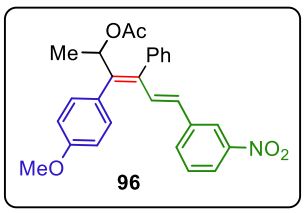
(3Z,5E)-3-(4-Methoxyphenyl)-7-oxo-4-phenylocta-3,5-dien-2-yl acetate (93):



93

93 (mg, 54%) as pale yellow liquid; R_f = 0.17 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d$_6$) δ 7.49–7.36 (m, 3H), 7.21 (d, J = 7.0 Hz, 2H), 7.15 (d, J = 8.5 Hz, 2H), 7.07–6.99 (m, 3H), 5.36 (d, J = 16.0 Hz, 1H), 5.24 (q, J = 6.5 Hz, 1H), 3.78 (s, 3H), 1.89 (s, 3H), 1.79 (s, 3H), 1.12 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d$_6$) δ 198.2, 170.1, 159.4, 148.7, 143.2, 138.1, 137.0, 131.5, 130.3, 129.5, 129.1, 128.3, 128.1, 114.0, 71.1, 55.5, 28.2, 21.1, 19.2; IR (Neat) ν_{max} 1734, 1662, 1586, 1367, 1232, 1175, 1028, 704 cm^{-1}; **HRMS (ESI)** for $C_{23}H_{24}NaO_4$ $(M+Na)^+$: calcd. 387.1572, found 387.1577.

(3Z,5E)-3-(4-Methoxyphenyl)-6-(3-nitrophenyl)-4-phenylhexa-3,5-dien-2-yl acetate (96/96′ = 93:7):



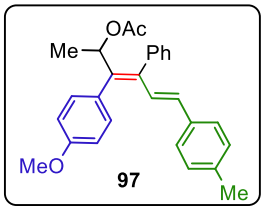
96

96 (109 mg, 82%) as pale yellow liquid; R_f = 0.28 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d$_6$) δ 7.99–7.95 (m, 1H), 7.82–7.78 (m, 1H), 7.54–7.41 (m, 5H), 7.31 (d, J = 8.0 Hz, 2H), 7.23 (d, J = 9.0 Hz, 2H), 7.06 (d, J = 9.0 Hz, 2H), 6.86 (d, J = 16.0 Hz, 1H), 5.95 (d, J = 16.0 Hz, 1H), 5.32 (q, J = 6.5 Hz, 1H), 3.82 (s, 3H), 1.87 (s, 3H), 1.14 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d$_6$) δ 169.7, 159.2, 148.6, 142.6, 139.3, 138.9, 137.9, 132.6, 132.4, 131.8,

130.7, 130.5, 129.8, 129.0, 128.9, 128.0, 122.5, 121.0, 114.1, 71.1, 55.5, 21.3, 19.6; IR (Neat) ν_{max} 1728, 1605, 1526, 1346, 1234, 1029, 828, 699; **HRMS (ESI)** for $C_{27}H_{25}NNaO_5$ $(M+Na)^+$: calcd. 466.1630, found 466.1634.

Representative peaks of the inseparable minor regio-isomer **96′**: ^{1}H NMR (500 MHz, DMSO d_6) δ 6.51 (q, J = 7.0 Hz, 0.08H), 3.75 (s, 0.24H), 1.99 (s, 0.24H); ^{13}C NMR (126 MHz, DMSO d_6) δ 148.7, 145.8, 142.2, 129.4, 20.2.

(3Z,5E)-3-(4-Methoxyphenyl)-4-phenyl-6-(*p*-tolyl)hexa-3,5-dien-2-yl acetate (97/97′ = 91:9):

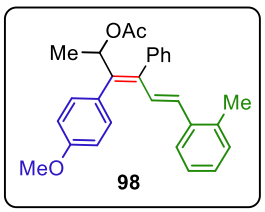


97

97 (89 mg, 72%) as pale yellow liquid; R_f = 0.35 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.48 (t, J = 7.0 Hz, 2H), 7.43–7.38 (m, 1H), 7.28 (d, J = 7.0 Hz, 2H), 7.21 (d, J = 8.5 Hz, 2H), 7.04 (d, J = 8.5 Hz, 2H), 6.97 (d, J = 8.0 Hz, 2H), 6.87 (d, J = 8.5 Hz, 2H), 6.71 (d, J = 16.0 Hz, 1H), 5.80 (d, J = 16.0 Hz, 1H), 5.32 (q, J = 6.5 Hz, 1H), 3.80 (s, 3H), 2.17 (s, 3H), 1.86 (s, 3H), 1.11 (d, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.6, 159.0, 140.1, 139.9, 138.4, 137.6, 134.5, 132.8, 131.9, 129.8, 129.4, 129.3, 129.1, 129.0, 128.9, 127.8, 126.4, 114.0, 71.2, 55.5, 21.3, 21.2, 19.6; ; IR (Neat) ν_{max} 1735, 1599, 1505, 1239, 1030, 700; **HRMS (ESI)** for $C_{28}H_{28}NaO_3$ $(M+Na)^+$: calcd. 435.1931, found 435.1932.

Representative peaks of the inseparable minor regio-isomer **97′**: ^{1}H NMR (500 MHz, DMSO d_6) δ 3.73 (s, 0.31H), 2.24 (s, 0.3H), 1.96 (s, 0.31H). ^{13}C NMR (126 MHz, DMSO d_6) δ 143.2, 137.3, 135.2, 131.0, 126.1, 113.9, 71.4, 20.3.

(3Z,5E)-3-(4-Methoxyphenyl)-4-phenyl-6-(*o*-tolyl)hexa-3,5-dien-2-yl acetate (98/98′ = 91:9):



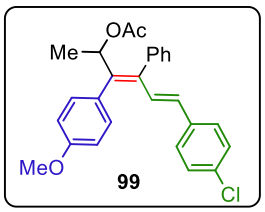
98

98 (72 mg, 58%) as pale yellow liquid; R_f = 0.35 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.50 (t, J = 7.0 Hz, 2H), 7.47–7.35 (m, 3H), 7.32 (d, J = 7.0 Hz, 2H), 7.23 (d, J = 8.5 Hz, 2H), 7.07–7.02 (m, 4H), 5.62 (d, J = 16.0 Hz, 1H), 6.05 (d, J = 16.0 Hz, 1H), 5.35 (q, J = 6.5 Hz, 1H), 3.80 (s, 3H), 1.91 (s, 3H), 1.87 (s, 3H), 1.13 (d, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.7, 159.0, 143.3, 140.4, 140.1, 138.5, 136.1, 135.4, 131.9, 131.3, 130.82, 130.76, 129.8, 129.5, 129.0, 128.8, 128.0, 127.9, 126.7, 125.0, 114.0, 71.2, 55.5, 21.4, 19.7, 19.4; IR (Neat) ν_{max}

1732, 1606, 1508, 1368, 1241, 1177, 1033, 754; **HRMS (ESI)** for $C_{28}H_{28}NaO_3$ $(M+Na)^+$: calcd. 435.1931, found 435.1935.

Representative peaks of the inseparable minor regio-isomer **98′**: ^{1}H NMR (500 MHz, DMSO d_6) δ 3.73 (s, 0.31H), 1.99 (s, 0.3H), 1.98 (s, 0.3H). ^{13}C NMR (126 MHz, DMSO d_6) δ 169.7, 135.3, 129.3, 126.2, 71.4, 20.4, 19.8.

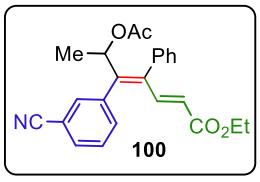
(3Z,5E)-3-(4-Methoxyphenyl)-4-phenyl-6-(*p*-tolyl)hexa-3,5-dien-2-yl acetate (99/99′ = 91:9):



99 (101 mg, 78%) as pale yellow liquid; R_f = 0.35 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.49 (t, J = 7.0 Hz, 2H), 7.45–7.40 (m, 1H), 7.29 (d, J = 7.0 Hz, 2H), 7.24–7.19 (m, 4H), 7.04 (dd, J = 6.5, 2.0 Hz, 2H), 6.99 (d, J = 8.5 Hz, 2H), 6.76 (d, J = 16.00 Hz, 1H), 5.81 (d, J = 16.0 Hz, 1H), 5.32 (q, J = 6.5 Hz, 1H), 3.81 (s, 3H), 1.86 (s, 3H), 1.12 (d, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.6, 159.1, 141.3, 139.6, 138.2, 136.00, 132.5, 131.8, 131.4, 130.8, 129.8, 129.4, 129.2, 129.1, 128.9, 128.1, 114.0, 71.1, 55.5, 21.3, 19.6; IR (Neat) ν_{max} 1733, 1606, 1507, 1284, 1239, 1034, 836, 713; **HRMS (ESI)** for $C_{27}H_{25}NaClO_3$ $(M+Na)^+$: calcd. 455.1384, found 455.1382.

Representative peaks of the inseparable minor regio-isomer **99′**: ^{1}H NMR (500 MHz, DMSO d_6) δ 3.73 (s, 0.3H), 1.97 (s, 0.31H); ^{13}C NMR (126 MHz, DMSO d_6) δ 143.2, 132.5, 126.1, 113.9, 21.3, 20.3.

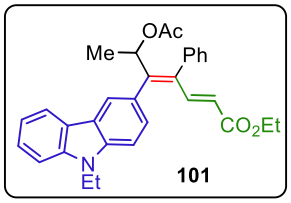
(2E,4Z)-Ethyl 6-acetoxy-5-(3-cyanophenyl)-4-phenylhepta-2,4-dienoate (100/100′ = 89:11):



100 (73 mg, 63%) as pale yellow liquid; R_f = 0.13 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.98 (d, J = 8.0 Hz, 1H), 7.88–7.12 (m, 2H), 7.67–7.60 (m, 1H), 7.56–7.44 (m, 3H), 7.31 (d, J = 8.0 Hz, 2H), 7.01 (d, J = 15.5 Hz, 2H), 5.34 (q, J = 6.5 Hz, 1H), 5.15 (d, J = 15.5 Hz, 1H), 3.98 (q, J = 7.0 Hz, 2H), 1.88 (s, 3H), 1.17 (d, J = 6.5 Hz, 3H), 1.07 (t, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.7, 165.9, 145.6, 143.8, 138.6, 137.5, 136.3, 135.3, 133.7, 132.5, 130.1, 129.5, 129.2, 128.5, 123.2, 119.0, 112.0, 70.3, 60.6, 21.2, 19.2, 14.4; IR (Neat) ν_{max} 1734, 1712, 1620, 1365, 1279, 1168, 1034, 701 cm^{-1}; **HRMS (ESI)** for $C_{24}H_{23}NNaO_4$ $(M+Na)^+$: calcd. 412.1525, found 412.1524.

Representative peaks of the inseparable minor regio-isomer **100′**: ^{1}H NMR (500 MHz, DMSO d_6) δ 6.37 (d, J = 16.0 Hz, 0.12H), 1.98 (s, 0.36H); ^{13}C NMR (126 MHz, DMSO d_6) δ 165.6, 142.2, 140.2, 139.4, 134.8, 133.3, 129.0, 129.0, 121.7, 19.9, 14.5.

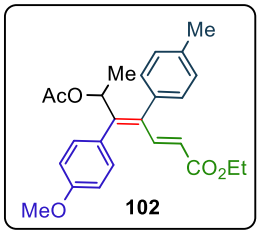
(2E,4Z)-Ethyl 6-acetoxy-5-(9-ethyl-9H-carbazol-3-yl)-4-phenylhepta-2,4-dienoate (101:101′ = 92:8):



101 (64 mg, 44%) as pale yellow liquid; R_f = 0.18 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, DMSO d_6) δ 8.25 (d, J = 7.6 Hz, 1H), 8.06 (br s, 1H), 7.74 (d, J = 8.4 Hz, 1H), 7.67 (d, J = 8.4 Hz, 1H), 7.58–7.43 (m, 4H), 7.38–7.31 (m, 3H), 7.29–7.21 (m, 2H), 5.42 (q, J = 6.8 Hz, 1H), 5.12 (d, J = 15.6 Hz, 1H), 4.51 (q, J = 7.2 Hz, 2H), 3.91 (q, J = 6.8 Hz, 2H), 1.87 (s, 3H), 1.39 (t, J = 7.2 Hz, 3H), 1.24 (d, J = 6.8 Hz, 3H), 1.01 (t, J = 7.2 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.9, 166.2, 149.2, 145.3, 140.4, 139.5, 137.9, 137.3, 129.6, 129.2, 128.3, 128.1, 126.6, 126.4, 122.43, 122.37, 121.9, 121.7, 121.1, 119.5, 109.8, 109.3, 71.2, 60.3, 37.6, 21.3, 19.5, 14.4, 14.3; IR (Neat) ν_{max} 1732, 1707, 1475, 1230, 1171, 700 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{31}NNaO_4$ $(M+Na)^+$: calcd. 504.2151, found 504.2156.

Representative peaks of the inseparable minor regio-isomer **101′**: ^{1}H NMR (500 MHz, DMSO d_6) δ 6.40 (d, J = 16.4 Hz, 0.09H), 2.01 (s, 0.27H).

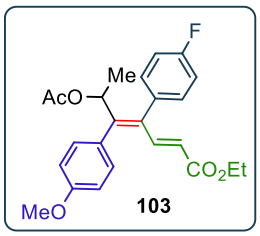
(2E,4Z)-Ethyl 6-acetoxy-5-(4-methoxyphenyl)-4-(*p*-tolyl)hepta-2,4-dienoate (102:102′ = 90:10):



102 (97 mg, 79%) as pale yellow liquid; R_f = 0.26 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.30 (d, J = 7.5 Hz, 2H), 7.22–7.12 (m, 5H), 7.05 (d, J = 9.0 Hz, 2H), 5.32 (q, J = 6.5 Hz, 1H), 5.11 (d, J = 15.5 Hz, 1H), 3.96 (q, J = 7.0 Hz, 2H), 3.82 (s, 3H), 2.37 (s, 3H), 1.85 (s, 3H), 1.15 (d, J = 7.0 Hz, 3H), 1.06 (t, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.8, 166.2, 159.4, 148.0, 145.1, 137.8, 137.5, 134.1, 131.5, 129.7, 129.4, 128.2, 121.9, 114.1, 71.0, 60.4, 55.5, 21.3, 21.2, 19.3, 14.4; IR (Neat) ν_{max} 1734, 1708, 1607, 1510, 1233, 1171, 1030 cm^{-1}; **HRMS (ESI)** for $C_{25}H_{28}NaO_5$ $(M+Na)^+$: calcd. 431.1832, found 431.1836.

Representative peaks of the inseparable minor regio-isomer **102′**: ^{1}H NMR (500 MHz, DMSO d_6) δ 6.35 (d, J = 16.5 Hz, 0.11H), 3.77 (s, 0.34H), 2.32 (s, 0.34H); ^{13}C NMR (126 MHz, DMSO d_6) δ 167.0, 159.8, 142.0, 138.6, 133.3, 132.2, 119.5, 19.8, 14.6.

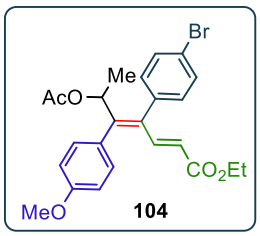
(2E,4Z)-Ethyl 6-acetoxy-4-(4-fluorophenyl)-5-(4-methoxyphenyl)hepta-2,4-dienoate (103:103′ = 93:7):



103 (78 mg, 63%) as pale yellow liquid; R_f = 0.26 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, DMSO d_6) δ 7.35–7.29 (m, 4H), 7.21–7.15 (m, 3H), 7.05 (d, J = 8.5 Hz, 2H), 5.26 (q, J = 7.0 Hz, 1H), 5.08 (d, J = 15.5 Hz, 1H), 3.97 (q, J = 7.0 Hz, 2H), 3.82 (s, 3H), 1.85 (s, 3H), 1.15 (d, J = 7.0 Hz, 3H), 1.06 (t, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.8, 166.2, 162.1 (d, J = 245 Hz, 1C), 159.5, 148.6, 144.9, 136.8, 133.3, 131.7 (d, J = 7.6 Hz, 2C), 131.5, 121.9, 116.1 (d, J = 21.4 Hz, 2C), 114.1, 70.9, 60.4, 55.6, 55.5, 21.2, 19.2, 14.6, 14.4; ^{19}F NMR (471 MHz) δ −114.3; IR (Neat) ν_{max} 1734, 1709, 1604, 1508, 1367, 1233, 1029 cm^{-1}; **HRMS (ESI)** for $C_{24}H_{25}FNaO_5$ $(M+Na)^+$: calcd. 435.1584, found 435.1589.

Representative peaks of the inseparable minor regio-isomer **103′**: ^{1}H NMR (500 MHz, DMSO d_6) δ 6.35 (d, J = 16.0 Hz, 0.08H), 3.77 (s, 0.24H), 1.96 (s, 0.34H); ^{13}C NMR (126 MHz, DMSO d_6) δ 166.9, 55.6, 14.6; ^{19}F NMR (471 MHz) δ −113.8.

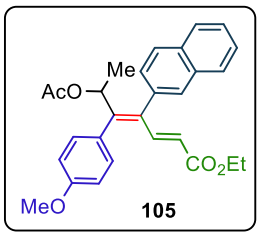
(2E,4Z)-Ethyl 6-acetoxy-4-(4-bromophenyl)-5-(4-methoxyphenyl)hepta-2,4-dienoate (104:104′ =92:8):



104 (103 mg, 73%) as pale yellow liquid; R_f = 0.26 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, DMSO d_6) δ 7.71 (d, J = 8.4 Hz, 2H), 7.27–7.14 (m, 5H), 7.07 (d, J = 9.2 Hz, 2H), 5.25 (q, J = 6.8 Hz, 1H), 5.09 (d, J = 15.6 Hz, 1H), 3.98 (q, J = 7.2 Hz, 2H), 3.84 (s, 3H), 1.87 (s, 3H), 1.16 (d, J = 6.4 Hz, 3H), 1.08 (t, J = 7.2 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.9, 166.1, 159.5, 148.5, 144.6, 136.6, 136.4, 132.1, 131.9, 131.5, 127.9, 121.9, 121.7, 114.2, 70.9, 60.5, 55.6, 21.2, 19.2, 14.4; IR (Neat) ν_{max} 1731, 1710, 1610, 1509, 1244, 1167, 1028, 810 cm^{-1}; **HRMS (ESI)** for $C_{24}H_{25}BrNaO_5$ (M+Na)+: calcd. 495.0783, found 495.0789.

Representative peaks of the inseparable minor regio-isomer **104′**: ^{1}H NMR (400 MHz, DMSO d_6) δ 6.35 (d, J = 16.4 Hz, 0.09H), 3.78 (s, 0.29H), 1.97 (s, 0.34H); ^{13}C NMR (101 MHz, DMSO d_6) δ 19.8, 14.6.

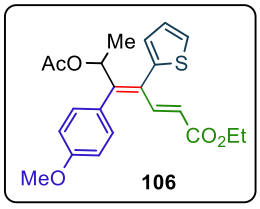
(2E,4Z)-Ethyl 6-acetoxy-5-(4-methoxyphenyl)-4-(naphthalen-2-yl)hepta-2,4-dienoate (105:105′ = 95:5):



105 (88 mg, 70%) as pale yellow liquid; R_f = 0.22 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, DMSO d_6) δ 8.06–7.94 (m, 3H), 7.84 (s, 1H), 7.59–7.54 (m, 2H), 7.40 (br d, J = 8.0 Hz, 1H), 7.32–7.22 (m, 3H), 7.09 (d, J = 9.0 Hz, 2H), 5.34 (q, J = 6.5 Hz, 1H), 5.11 (d, J = 15.5 Hz, 1H), 3.93 (q, J = 7.0 Hz, 2H), 3.83 (s, 3H), 1.84 (s, 3H), 1.17 (d, J = 6.5 Hz, 3H), 1.01 (t, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.8, 166.2, 159.5, 148.5, 144.9, 137.8, 134.7, 133.4, 132.7, 131.5, 128.7, 128.4, 128.20, 128.15, 127.7, 126.94, 126.87, 122.2, 114.2, 71.1, 60.4, 55.6, 21.2, 19.4, 14.3; IR (Neat) ν_{max} 1733, 1707, 1607, 1507, 1366, 1234, 1171, 1029, 746 cm^{-1}; **HRMS (ESI)** for $C_{28}H_{29}O_5$ $(M+H)^+$: calcd. 445.2010, found 445.1997.

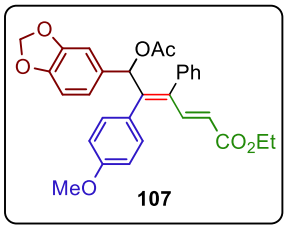
Representative peaks of the inseparable minor regio-isomer **105′**: ^{1}H NMR (500 MHz, DMSO d_6) δ 6.41 (d, J = 16.5 Hz, 0.06H), 3.78 (s, 0.18H), 1.95 (s, 0.19H).

(2E,4Z)-Ethyl 6-acetoxy-5-(4-methoxyphenyl)-4-(thiophen-2-yl)hepta-2,4-dienoate (106):



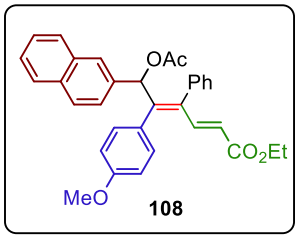
106 (85 mg, 71%) as pale yellow liquid; R_f = 0.16 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.73 (dd, J = 5.5, 1.5 Hz, 1H), 7.22–7.15 (m, 4H), 7.09–7.04 (m, 3H), 5.50 (q, J = 7.0 Hz, 1H), 5.35 (d, J = 15.5 Hz, 1H), 4.00 (q, J = 7.0 Hz, 2H), 3.83 (s, 3H), 1.87 (s, 3H), 1.22 (d, J = 7.0 Hz, 3H), 1.09 (t, J = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.8, 166.2, 159.6, 151.6, 144.8, 136.4, 131.3, 130.5, 128.9, 127.9, 122.1, 114.2, 70.9, 60.5, 55.6, 21.2, 19.5, 14.4; IR (Neat) ν_{max} 1733, 1710, 1617, 1506, 1367, 1231, 1163, 1020, 711 cm^{-1}; **HRMS (ESI)** for $C_{22}H_{24}NaO_5S$ $(M+Na)^+$: calcd. 423.1237, found 423.1240.

(2E,4Z)-Ethyl 6-Acetoxy-6-(benzo[d][1,3]dioxol-5-yl)-5-(4-methoxyphenyl)-4-phenylhexa-2,4-dienoate (107):



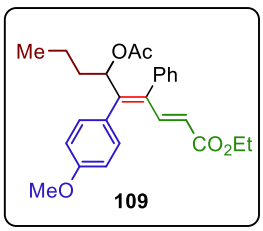
107 (77 mg, 51%) as pale yellow liquid; R_f = 0.13 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.53 (t, J = 8.0 Hz, 2H), 7.49–7.42 (m, 1H), 7.36 (d, J = 6.8 Hz, 2H), 7.26 (d, J = 16.0 Hz, 1H), 7.03–6.94 (m, 4H), 6.80 (d, J = 8.0 Hz, 1H), 6.53–6.48 (m, 1H), 6.45 (d, J = 1.6 Hz, 1H), 6.33 (s, 1H), 5.98 (dd, J = 5.2, 0.8 Hz, 2H), 5.16 (d, J = 15.6 Hz, 1H), 3.99 (q, J = 7.2 Hz, 2H), 3.80 (s, 3H), 2.01 (s, 3H), 1.08 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, DMSO d_6) δ 169.5, 166.2, 159.5, 147.6, 147.1, 145.9, 145.0, 139.4, 137.2, 132.0, 131.9, 129.8, 129.2, 128.5, 128.0, 122.8, 120.1, 113.9, 108.4, 106.9, 101.6, 75.0, 60.5, 55.5, 21.2, 14.4; IR (Neat) ν_{max} 1740, 1708, 1606, 1223, 1172, 1027, 701 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{28}NaO_7$ $(M+Na)^+$: calcd. 523.1733, found 523.1738.

(2E,4Z)-Ethyl 6-acetoxy-5-(4-methoxyphenyl)-6-(naphthalen-2-yl)-4-phenylhexa-2,4-dienoate (108):



108 (62 mg, 41%) as pale yellow liquid; R_f = 0.13 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.87 (dd, J = 6.4, 6.0 Hz, 2H), 7.83 (d, J = 8.4 Hz, 1H), 7.55 (d, J = 7.6 Hz, 3H), 7.52–7.43 (m, 5H), 7.32 (d, J = 15.6 Hz, 1H), 7.21 (dd, J = 8.8, 1.6 Hz, 1H), 7.00 (br d, J = 7.6 Hz, 2H), 6.90 (d, J = 8.8 Hz, 2H), 6.62 (s, 1H), 5.22 (d, J = 15.6 Hz, 1H), 4.00 (q, J = 7.2 Hz, 2H), 3.74 (s, 3H), 2.11 (s, 3H), 1.09 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, DMSO d_6) δ 169.7, 166.2, 159.4, 145.6, 145.1, 139.9, 137.2, 135.5, 133.0, 132.7, 131.9, 129.9, 129.3, 128.5, 128.4, 128.3, 128.1, 127.9, 126.8, 126.7, 125.2, 124.5, 123.0, 113.8, 75.4, 60.5, 55.5, 21.3, 14.4; IR (Neat) ν_{max} 1740, 1707, 1606, 1507, 1366, 1172, 1024, 701 cm^{-1}; **HRMS (ESI)** for $C_{33}H_{30}NaO_5$ $(M+Na)^+$: calcd. 529.1991, found 529.1995.

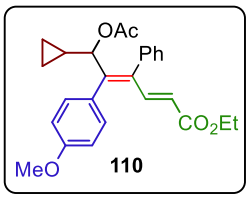
(2E,4Z)-Ethyl 6-acetoxy-5-(4-methoxyphenyl)-4-phenylnona-2,4-dienoate (109):



109 (85 mg, 67%) as pale yellow liquid; R_f = 0.26 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.48 (t, J = 7.5 Hz, 2H), 7.41 (t, J = 7.5 Hz, 1H), 7.29–7.14 (m, 5H), 7.05 (d, J = 8.5 Hz, 3H), 5.23 (q, J = 4.5 Hz, 1H), 5.09 (d, J = 15.5 Hz, 1H), 3.96 (q, J = 7.0 Hz, 2H), 3.82 (s, 3H), 1.86 (s, 3H), 1.59–1.38 (m, 2H), 1.20–0.07 (m, 5H), 0.60 (t, J = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 170.0, 166.2, 159.5, 147.7, 145.0, 138.3, 137.1, 131.4, 129.7, 129.0, 128.4, 128.2, 121.8,

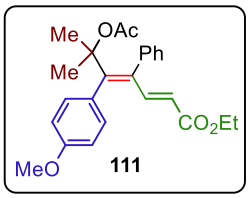
114.1, 74.1, 60.4, 55.6, 35.1, 21.1, 18.6, 14.4, 13.5; IR (Neat) ν_{max} 1745, 1714, 1605, 1515, 1369, 1174, 1043, 700 cm^{-1}; **HRMS (ESI)** for $C_{26}H_{30}NaO_5$: $(M+Na)^+$: calcd. 445.1985, found 445.1992.

(2E,4Z)-Ethyl 6-acetoxy-6-cyclopropyl-5-(4-methoxyphenyl)-4-phenylhexa-2,4-dienoate (110):



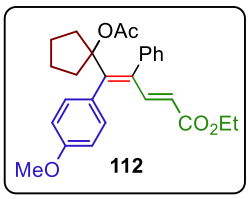
110 (63 mg, 50%) as pale yellow liquid; R_f = 0.26 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO d_6) δ 7.41–7.30 (m, 3H), 7.21–7.13 (m, 5H), 6.99 (d, J = 8.5 Hz, 2H), 5.01 (d, J = 15.5 Hz, 1H), 4.56 (d, J = 9.0 Hz, 1H), 3.89 (q, J = 7.0 Hz, 2H), 3.75 (s, 3H), 1.83 (s, 3H), 0.99 (t, J = 7.0 Hz, 3H), 0.88–0.78 (m, 1H), 0.39–0.27 (m, 2H), 0.05–(-0.19) (m, 2H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.7, 166.2, 159.4, 147.1, 145.2, 138.1, 137.0, 131.5, 129.9, 128.9, 128.3, 122.3, 114.1, 78.2, 60.4, 55.6, 21.3, 14.40, 14.35, 4.8, 3.3; IR (Neat) ν_{max} 2939, 2183, 1598, 1508, 1329, 1292, 1247, 1171, 1027, 813 cm^{-1}; **HRMS (ESI)** for $C_{26}H_{28}NaO_5$ $(M+Na)^+$: calcd. 443.1834, found 443.1839.

(2E,4Z)-Ethyl 6-acetoxy-5-(4-methoxyphenyl)-6-methyl-4-phenylhepta-2,4-dienoate (111):



111 (52 mg, 42%) as pale yellow liquid; R_f = 0.26 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO d_6) δ 7.47 (t, J = 7.5 Hz, 2H), 7.41–7.36 (m, 1H), 7.27 (dt, J = 6.5, 2.0 Hz, 2H), 7.17–7.13 (m, 2H), 7.10–7.03 (m, 3H), 4.75 (d, J = 15.5 Hz, 1H), 3.91 (q, J = 7.0 Hz, 2H), 3.82 (s, 3H), 1.54 (s, 3H), 1.32 (s, 6H), 1.03 (t, J = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.6, 166.3, 159.0, 152.2, 147.9, 138.4, 135.8, 131.6, 130.8, 129.6, 128.7, 127.6, 120.3, 114.1, 81.1, 60.2, 55.5, 29.2, 22.2, 14.4; IR (Neat) ν_{max} 1722, 1700, 1506, 1240, 1176, 1138, 1029, 733 cm^{-1}; **HRMS (ESI)** for $C_{25}H_{28}NaO_5$ $(M+Na)^+$: calcd. 431.1834, found 431.1839.

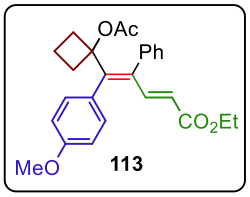
(2E,4Z)-Ethyl 5-(1-acetoxycyclopentyl)-5-(4-methoxyphenyl)-4-phenylpenta-2,4-dienoate (112):



112 (94 mg, 72%) as pale yellow liquid; R_f = 0.26 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO d_6) δ 7.46 (t, J = 7.5 Hz, 2H), 7.40–7.35 (m, 1H), 7.32 (d, J = 9.0 Hz, 2H), 7.15–7.02 (m, 5H), 4.78 (d, J = 15.5 Hz, 1H), 3.92 (q, J = 7.0 Hz, 2H), 3.82 (s, 3H), 2.10–1.92 (m, 2H), 1.69–1.61 (m, 2H), 1.60 (s, 3H), 1.43–1.34 (m, 4H), 1.04 (t, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, DMSO d_6) δ 169.7, 166.3, 159.1, 151.7, 147.7, 138.6, 135.9, 131.7, 130.9, 129.7, 128.5, 127.6, 120.0, 114.1, 90.9,

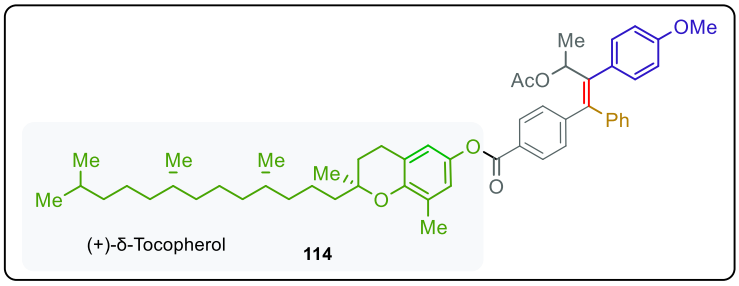
60.2, 55.6, 23.1, 22.2, 14.4; IR (Neat) ν_{max} 1707, 1606, 1507, 1282, 1242, 1169, 1030, 702 cm^{-1}; **HRMS (ESI)** for $C_{27}H_{30}NaO_5$ $(M+Na)^+$: calcd. 457.1991, found 457.1998.

(2E,4Z)-Ethyl 5-(1-acetoxycyclobutyl)-5-(4-methoxyphenyl)-4-phenylpenta-2,4-dienoate (113):



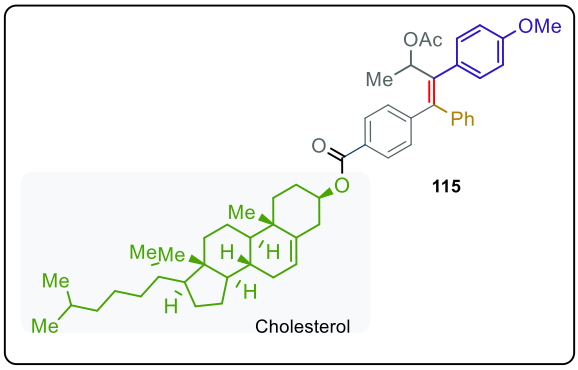
113 (109 mg, 86%) as pale yellow liquid; R_f = 0.26 (10% EtOAc/Hex); ^1H NMR (400 MHz, DMSO d_6) δ 7.47–7.34 (m, 5H), 7.18–7.05 (m, 5H), 4.96 (d, J = 15.2 Hz, 1H), 3.94 (q, J = 6.8 Hz, 2H), 3.84 (s, 3H), 2.38–2.27 (m, 2H), 2.08–1.97 (m, 2H), 1.76–1.62 (m, 4H), 1.39–1.24 (m, 1H), 1.04 (t, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, DMSO d_6) δ 169.5, 166.3, 159.4, 152.2, 147.2, 138.6, 135.8, 131.3, 129.6, 128.5, 127.7, 120.4, 114.1, 83.6, 60.2, 55.5, 35.4, 21.5, 15.3, 14.4; IR (Neat) ν_{max} 1731, 1708, 1607, 1507, 1258, 1168, 1032, 704 cm^{-1}; **HRMS (ESI)** for $C_{26}H_{28}NaO_5$ $(M+Na)^+$: calcd. 443.1834, found 443.1838.

(S)-2,8-Dimethyl-2-((4S,8S)-4,8,12-trimethyltridecyl)chroman-6-yl 4-((Z)-3-acetoxy-2-(4-methoxyphenyl)-1-phenylbut-1-en-1-yl)benzoate (114):



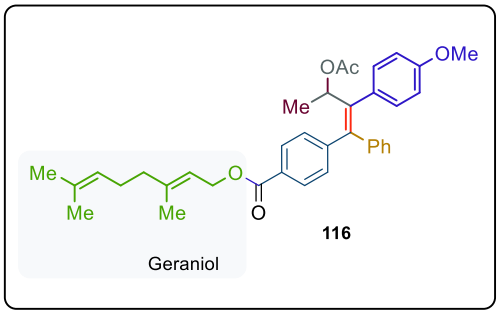
114 (115 mg, 72%, 0.2 mmol scale) as pale yellow liquid; R_f = 0.86 (20% EtOAc/Hex);. ^1H NMR (500 MHz, ACETONE D_6) δ 8.19 (d, J = 8.0 Hz, 2H), 7.57 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 8.5 Hz, 2H), 7.12–6.99 (m, 5H), 6.91–6.78 (m, 4H), 5.71 (q, J = 6.5 Hz, 1H), 3.75 (s, 3H), 2.88–2.78 (m, 4H), 2.18 (s, 3H), 1.92 (s, 3H), 1.91–1.80 (m, 2H), 1.70–1.34 (m, 11H), 1.31–1.01 (m, 13H), 0.95–0.84 (m, 13H); ^{13}C NMR (126 MHz, ACETONE d_6) δ 169.1, 164.8, 158.7, ,149.6, 147.4, 143.2, 141.7, 141.6, 139.7, 132.0, 130.0, 129.8, 129.7, 128.7, 127.6, 126.6, 126.4, 121.4, 121.1, 119.5, 113.0, 76.1, 70.9, 54.5, 39.8, 39.2, 37.32, 37.30, 37.2, 37.1, 32.7, 32.5, 30.9, 27.8, 24.7, 24.3, 23.7, 22.2, 22.13, 22.09, 20.8, 20.2, 19.3, 19.2, 19.0, 15.4; IR (Neat) ν_{max} 1732, 1604, 1509, 1470, 1263, 1241, 1176, 1074, 733 cm^{-1}; **HRMS (ESI)** for $C_{53}H_{68}O_6Na$ $(M+Na)^+$: calcd. 823.4908, found 823.4908.

(3R,8R,9R,10S,13S,14R,17S)-10,13-Dimethyl-17-((S)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 4-((Z)-3-acetoxy-2-(4-methoxyphenyl)-1-phenylbut-1-en-1-yl)benzoate (115):



115 (71 mg, 45%, 0.2 mmol scale) as pale yellow liquid; R_f = 0.86 (20% EtOAc/Hex); ^{1}H NMR (500 MHz, ACETONE d_6) δ 8.07 (d, J = 8.5 Hz, 2H), 7.49 (d, J = 8.5 Hz, 2H), 7.17 (dt, J = 7.0, 2.0 Hz, 2H), 7.09–6.97 (m, 5H), 6.79 (d, J = 8.5 Hz, 2H), 5.68 (q, J = 6.5 Hz, 1H), 5.47 (d, J = 4.5 Hz, 1H), 4.88–4.78 (m, 1H), 3.74 (s, 3H), 2.90 (d, J = 16.5 Hz, 4H), 2.57–6.47 (m, 2H), 2.05–1.95 (m, 3H), 1.90 (s, 3H), 1.70–1.50 (m, 7H), 1.48–1.40 (m, 2H), 1.29 (d, J = 6.5 Hz, 3H), 1.28–1.16 (m, 7H), 1.13 (s, 3H), 1.12–0.92 (m, 3H), 0.99 (d, J = 7.0 Hz, 3H), 0.89 (dd, J = 6.5, 1.5 Hz, 6H), 0.76 (s, 3H); ^{13}C NMR (126 MHz, ACETONE d_6) δ 169.1, 165.1, 158.6, 146.8, 141.7, 141.5, 139.8, 139.5, 132.0, 130.0, 129.9, 129.5, 129.4, 129.3, 127.5, 126.3, 122.5, 113.0, 74.4, 70.9, 56.7, 56.2, 54.5, 50.2, 42.3, 39.8, 39.4, 38.1, 37.0, 36.6, 36.1, 35.8, 31.9, 31.8, 27.8, 27.7, 24.1, 23.7, 22.2, 22.0, 20.9, 20.2, 18.93, 18.86, 18.3, 11.4; IR (Neat) ν_{max} 1736, 1714, 1270, 1239, 1176, 1110, 1032, 760 cm^{-1}; **HRMS (ESI)** for $C_{53}H_{68}O_5Na$ $(M+Na)^+$: calcd. 807.4959, found 807.4959.

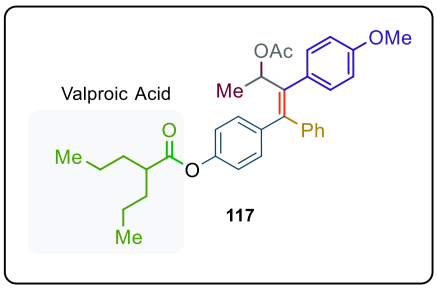
(E)-3,7-Dimethylocta-2,6-dien-1-yl 4-((Z)-3-acetoxy-2-(4-methoxyphenyl)-1-phenylbut-1-en-1-yl)benzoate (116):



116 (60 mg, 54%, 0.2 mmol scale) as pale yellow liquid; R_f = 0.77 (20% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.97 (d, J = 8.5 Hz, 2H), 7.42 (d, J = 8.5 Hz, 2H), 7.11–6.98 (m, 5H), 6.92–6.87 (m, 2H), 6.78 (d, J = 9.0 Hz, 2H), 5.51 (q, J = 6.5 Hz, 1H), 5.46–5.41 (m, 1H), 5.09–5.04 (m, 1H), 4.80 (d, J = 7.0 Hz, 2H), 3.68 (s, 3H), 2.12–2.00 (m, 4H), 1.88 (s, 3H), 1.73 (s, 3H), 1.60 (s, 3H), 1.54 (s, 3H), 1.19 (d, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 169.7, 165.9, 158.4, 146.9, 142.4, 141.6, 141.4, 139.3, 132.1, 131.5, 130.0, 129.8, 129.7, 129.1, 128.1, 126.9, 124.1, 118.9, 113.5, 70.9, 61.8, 55.3, 26.2, 25.9,

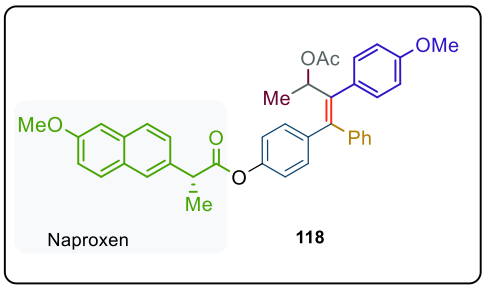
21.3, 19.6, 18.0, 16.7; IR (Neat) ν_{max} 1734, 1714, 1604, 1508, 1441, 1265, 1239, 1095, 1033, 706 cm^{-1}; **HRMS (ESI)** for $C_{36}H_{40}O_5Na$ $(M+Na)^+$: calcd. 575.2768, found 575.2768.

(Z)-4-(3-Acetoxy-2-(4-methoxyphenyl)-1-phenylbut-1-en-1-yl)phenyl 2-propylpentanoate (117):



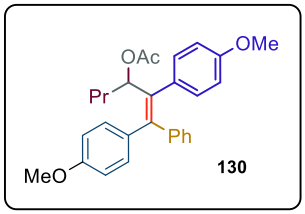
117 (67 mg, 65%, 0.2 mmol scale) as pale yellow liquid; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.97 (dt, J = 8.5, 2.0 Hz, 2H), 7.10 (dt, J = 8.5, 2.0 Hz, 2H), 7.09–7.02 (m, 4H), 7.01–6.96 (m, 1H), 6.93–6.88 (m, 2H), 6.77 (dt, J = 9.0, 2.0 Hz, 2H), 5.58 (q, J = 6.5 Hz, 1H), 3.67 (s, 3H), 2.65–2.56 (m, 1H), 1.89 (s, 3H), 1.70–1.61 (m, 2H), 1.58–1.50 (m, 2H), 1.43–1.34 (m, 4H), 1.21 (d, J = 7.0 Hz, 3H), 0.92 (t, J = 7.5 Hz, 6H); ^{13}C NMR (126 MHz, DMSO d_6) δ 174.7, 169.8, 158.3, 149.8, 142.2, 141.5, 139.4, 139.0, 132.2, 130.5, 130.2, 130.0, 128.0, 126.7, 122.0, 113.5, 71.0, 55.3, 45.0, 34.6, 21.3, 20.6, 19.7, 14.3; IR (Neat) ν_{max} 1735, 1507, 1263, 1241, 1197, 1107, 731, 701 cm^{-1}; **HRMS (ESI)** for $C_{33}H_{38}O_5Na$ $(M+Na)^+$: calcd. 537.2611, found 537.2611.

4-((Z)-3-acetoxy-2-(4-methoxyphenyl)-1-phenylbut-1-en-1-yl)phenyl (2R)-2-(6-methoxynaphthalen-2-yl)propanoate (118):



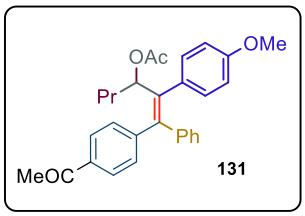
118 (61 mg, 51%, 0.2 mmol scale) as pale yellow liquid; R_f = 0.68 (20% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.89–7.83 (m, 3H), 7.52 (dd, J = 8.5, 1.5 Hz, 1H), 7.32 (d, J = 2.5 Hz, 1H), 7.27 (dt, J = 8.5, 1.5 Hz, 2H), 7.18 (dd, J = 9.0, 2.5 Hz, 1H), 7.09–7.01 (m, 6H), 7.00–6.94 (m, 1H), 6.91–6.85 (m, 2H), 6.76 (d, J = 9.0 Hz, 2H), 5.55 (q, J = 5.0 Hz, 1H), 4.22 (q, J = 7.0 Hz, 1H), 3.87 (s, 3H), 3.67 (s, 3H), 1.87 (s, 3H), 1.60 (d, J = 7.0 Hz, 3H), 1.18 (dd, J = 7.0, 1.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 173.2, 169.7, 158.3, 157.8, 149.9, 142.2, 141.50, 141.48, 139.4, 139.0, 135.7, 134.0, 132.2, 130.4, 130.2, 129.9, 129.7, 129.0, 128.0, 127.7, 126.7, 126.3, 121.8, 119.3, 113.5, 106.3, 71.0, 55.7, 55.3, 45.0, 21.3, 19.7, 18.8; IR (Neat) ν_{max} 1733, 1605, 1507, 1369, 1263, 1240, 1197, 1030, 731, 700cm^{-1}; **HRMS (ESI)** for $C_{39}H_{36}O_6Na$ $(M+Na)^+$: calcd. 623.2404, found 623.2404.

(Z)-1,2-bis(4-methoxyphenyl)-1-phenylhex-1-en-3-yl acetate (130):



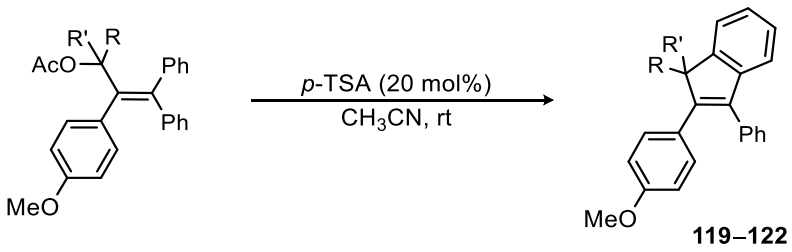
130 (73 mg, 57%) as pale yellow liquid; R_f = 0.77 (20% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d$_6$) δ 7.16 (d, J = 8.5 Hz, 2H), 7.06–7.00 (m, 4H), 6.99–6.92 (m, 3H), 6.89–6.85 (m, 2H), 6.75 (d, J = 8.5 Hz, 2H), 5.59 (t, J = 7.0 Hz, 1H), 3.76 (s, 3H), 3.67 (s, 3H), 1.91 (s, 3H), 1.51 (q, J = 7.5 Hz, 2H), 1.25–1.12 (m, 2H), 0.72 (t, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d$_6$) δ 170.0, 158.6, 158.2, 142.9, 142.8, 137.8, 134.2, 132.1, 130.7, 130.6, 130.0, 127.9, 126.5, 114.0, 113.4, 74.2, 55.5, 55.3, 35.5, 21.3, 18.8, 13.9; IR (Neat) ν_{max} 1733, 1606, 1284, 1240, 1175, 1032, 736 cm^{-1}; **HRMS (ESI)** for $C_{28}H_{30}O_4Na$ $(M+Na)^+$: calcd. 453.2036, found 453.2032.

(Z)-1-(4-acetylphenyl)-2-(4-methoxyphenyl)-1-phenylhex-1-en-3-yl acetate (131):



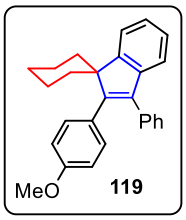
131 (98 mg, 74%) as pale yellow liquid; R_f = 0.64 (20% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d$_6$) δ 7.98 (d, J = 8.5 Hz, 2H), 7.43 (d, J = 8.5 Hz, 2H), 7.09–7.03 (m, 4H), 7.02–6.96 (m, 1H), 6.93–6.88 (m, 2H), 6.77 (d, J = 9.0 Hz, 2H), 5.47 (t, J = 7.0 Hz, 1H), 3.67 (s, 3H), 2.58 (s, 3H), 1.90 (s, 3H), 1.54 (q, J = 7.5 Hz, 2H), 1.25–1.12 (m, 2H), 0.70 (t, J = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d$_6$) δ 198.1, 170.0, 158.4, 146.9, 142.1, 141.9, 138.6, 135.9, 132.0, 130.2, 130.0, 129.8, 128.7, 128.2, 126.9, 113.6, 74.2, 55.3, 27.2, 21.3, 18.8, 13.9; IR (Neat) ν_{max} 1733, 1680, 1601, 1508, 1239, 1176, 1023, 992, 600 cm^{-1}; **HRMS (ESI)** for $C_{29}H_{30}O_4Na$ $(M+Na)^+$: calcd. 465.2036, found 465.2037.

4A.6.3.5. General Procedure for synthesis of indene derivatives 119–122:



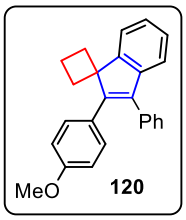
To an independent solution of acetate **19**, **54**, **74**, & **75** (0.2 mmol) in CH_3CN (2.0 mL) was added *p*-TSA (0.04 mmol). The resulting mixture was stirred at rt. The reaction progress was monitored by TLC. Upon completion, the crude mixture was concentrated under reduced pressure. The crude residue was purified using column chromatography on silica gel to afford **119–122**.

2'-(4-methoxyphenyl)-3'-phenylspiro[cyclohexane-1,1'-indene] (119):



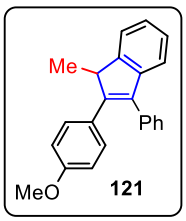
119 (48 mg, 65%) as colorless gummy liquid; R_f = 0.54 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, J = 7.5 Hz, 1H), 7.36–7.14 (m, 8H), 7.01 (d, J = 9.0 Hz, 2H), 6.81 (d, J = 8.5 Hz, 2H), 3.78 (s, 3H), 2.08–1.96 (m, 2H), 1.85 (td, J = 8.5, 1.0 Hz, 3H), 1.73 (dt, J = 13.5, 3.5 Hz, 2H), 1.46 (d, J = 12.5 Hz, 2H), 1.30–1.17 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.4, 154.1, 151.8, 143.8, 138.5, 135.3, 131.7, 129.5, 128.9, 127.9, 126.7, 126.3, 124.8, 124.3, 120.6, 113.3, 55.1, 54.5, 31.5, 25.1, 22.3; IR (Neat) ν_{max} 1610, 1536, 1449, 1239, 1064, 708 cm^{-1}; **HRMS (ESI)** for $C_{27}H_{27}O$ $(M+H)^+$: calcd. 367.2056, found 367.2060.

2'-(4-Methoxyphenyl)-3'-phenylspiro[cyclobutane-1,1'-indene] (120):



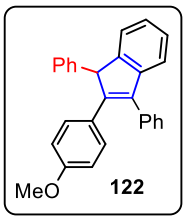
120 (56 mg, 83%) as colorless gummy liquid; R_f = 0.54 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, J = 7.5 Hz, 1H), 7.38–7.21 (m, 10H), 6.90 (d, J = 9.0 Hz, 2H), 3.84 (s, 3H), 2.69–2.51 (m, 4H), 2.28–2.17 (m, 1H), 1.92–1.81 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.6, 152.3, 149.2, 142.8, 137.9, 135.3, 130.9, 129.5, 129.2, 128.0, 126.7, 126.4, , 125.6, 121.3, 120.0, 113.6, 56.5, 55.1, 29.0, 16.7; IR (Neat) ν_{max} 1598, 1555, 1417, 1219, 1068, 709cm^{-1}; **HRMS (ESI)** for $C_{25}H_{23}O$ $(M+H)^+$: calcd. 339.1743, found 339.1747.

2-(4-Methoxyphenyl)-1-methyl-3-phenyl-1H-indene (121):



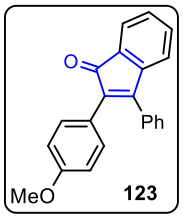
121 (54 mg, 89%) as pale yellow liquid; R_f = 0.58 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.58–7.54 (m, 1H), 7.45–7.39 (m, 2H), 7.38–7.33 (m, 1H), 7.31–7.23 (m, 4H), 7.15–7.10 (m, 3H), 6.83 (dt, J = 9.0, 2.5 Hz, 2H), 4.13 (q, J = 7.5 Hz, 1H), 3.72 (s, 3H), 1.20 (d, J = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 158.7, 148.5, 147.9, 144.9, 136.6, 135.9, 130.8, 129.6, 129.3, 127.78, 128.75, 127.1, 125.4, 123.4, 119.9, 114.2, 55.5, 45.6, 17.3; IR (Neat) ν_{max} 1637, 1589, 1412, 1214, 1068, 699 cm^{-1}; **HRMS (ESI)** for $C_{23}H_{21}O$ $(M+H)^+$: calcd. 313.1587, found 313.1585.

2-(4-Methoxyphenyl)-1,3-diphenyl-1H-indene (122):



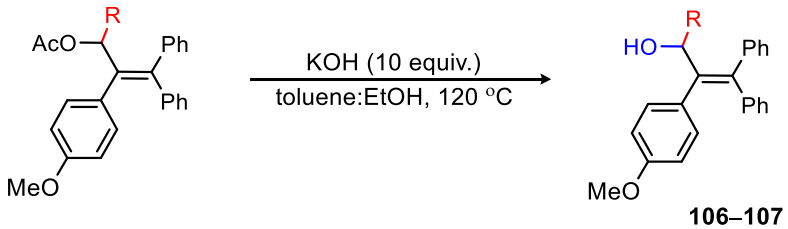
122 (56 mg, 79%) as pale yellow liquid; R_f = 0.54 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.48 (t, J = 7.5 Hz, 2H), 7.40 (t, J = 8.0 Hz, 3H), 7.26–7.16 (m, 6H), 7.15–7.08 (m, 5H), 6.67 (d, J = 8.5 Hz, 2H), 5.38 (s, 1H), 3.62 (s, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 158.6, 148.4, 145.9, 145.2, 140.7, 139.1, 135.8, 130.8, 129.7, 129.4, 129.1, 128.4, 128.0, 127.8, 127.3, 126.9, 125.8, 124.2, 120.1, 113.9, 57.2, 55.3; IR (Neat) ν_{max} 2939, 1509, 1455, 1246, 1176, 1026, 696 cm^{-1}; **HRMS (ESI)** for $C_{28}H_{23}O$ $(M+H)^+$: calcd. 375.1749, found 375.1756.

4A.6.3.6. Synthesis of 2-(4-methoxyphenyl)-3-phenyl-1H-inden-1-one (123):



To a solution of **39** (0.2 mmol, 72 mg) in CH_3CN (2.0 mL) was added *p*-TSA (0.04 mmol, 7.6 mg). The resulting mixture was stirred at rt. The reaction progress was monitored by TLC. Upon completion, the crude mixture was concentrated under reduced pressure. The crude residue was purified using column chromatography on neutral alumina to afford **123** in 58% yield as red gummy liquid; R_f = 0.4 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (br d, J = 7.2 Hz, 1H), 7.48–7.35 (m, 6H), 7.32–7.24 (m, 3H), 7.14 (br d J = 7.2 Hz, 1H), 6.83 (d, J = 9.2 Hz, 2H), 3.82 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.0, 159.2, 153.8, 145.5, 133.4, 133.0, 131.9, 131.2, 130.7, 129.1, 128.8, 128.6, 128.5, 123.1, 122.9, 120.9, 113.6, 55.2 cm^{-1}; IR (Neat) ν_{max} 1706, 1604, 1455, 1291, 1247, 1176, 700 cm^{-1}; **HRMS (ESI)** for $C_{22}H_{17}O_2$ $(M+H)^+$: calcd. 313.1223, found 313.1225.

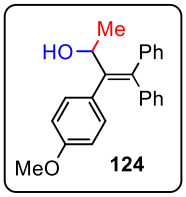
4A.6.3.7. General Procedure for synthesis of allylic alcohol derivatives 106–107:



To a mixture of acetate **54/39** (0.2 mmol) and KOH (2.0 mmol) was added toluene:ethanol (9:1, 2.0 mL). The resulting mixture was stirred at 120 °C overnight. The reaction progress was monitored by TLC. Upon completion, the crude mixture was concentrated under reduced pressure.

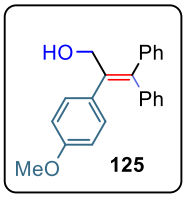
The crude residue was purified using column chromatography on neutral alumina to afford **124**–**125**.

3-(4-Methoxyphenyl)-4,4-diphenylbut-3-en-2-ol (124):



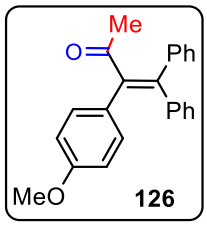
124 (53 mg, 81%) as pale yellow semi-solid; R_f = 0.25 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.38 (t, J = 7.5 Hz, 2H), 7.32–7.24 (m, 3H), 7.18–7.12 (m, 2H), 7.04 (t, J = 7.0 Hz, 2H), 6.96 (t, J = 7.0 Hz, 1H), 6.94–6.88 (m, 2H), 6.72 (dd, J = 8.5, 1.5 Hz, 2H), 4.73–4.67 (m, 1H), 4.64–4.57 (m, 1H), 3.67 (s, 3H), 1.01 (dd, J = 5.5, 3.0 Hz, 3H); ^{13}C NMR (126 MHz, DMSO d_6) δ 157.9, 143.19, 143.15, 142.5, 139.6, 132.6, 131.1, 130.2, 129.7, 128.6, 127.9, 127.2, 126.2, 112.9, 66.5, 55.2, 22.6; IR (Neat) ν_{max} 1435, 1689, 1587, 1389, 1028, 699 cm^{-1}; **HRMS (ESI)** for $C_{23}H_{22}NaO_2$ $(M+Na)^+$: calcd. 353.1512, found 353.1515.

2-(4-Methoxyphenyl)-3,3-diphenylprop-2-en-1-ol (125):



125 (45 mg, 77%) as pale yellow semi-solid; R_f = 0.25 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO d_6) δ 7.36 (t, J = 8.0 Hz, 2H), 7.32–7.24 (m, 3H), 7.12–7.00 (m, 5H), 6.90–6.85 (m, 2H), 6.72 (dd, J = 8.5, 2.0 Hz, 2H), 4.69 (t, J = 5.0 Hz, 1H), 4.21 (d, J = 5.0 Hz, 2H), 3.68 (s, 3H); ^{13}C NMR (101 MHz, DMSO d_6) δ 158.1, 143.3, 142.9, 140.9, 139.7, 133.6, 131.5, 130.7, 129.9, 128.6, 128.1, 127.4, 126.6, 113.5, 63.5, 55.4; IR (Neat) ν_{max} 3412, 1682, 1586, 1415, 1112, 1025, 700 cm^{-1}; **HRMS (ESI)** for $C_{22}H_{20}NaO_2$ $(M+Na)^+$: calcd. 339.1361, found 339.1356.

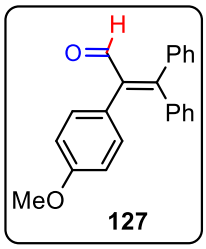
4A.6.3.8. Synthesis of 3-(4-methoxyphenyl)-4,4-diphenylbut-3-en-2-one (126):



To a solution of **124** (0.2 mmol, 66 mg) in CH_2Cl_2 (2.0 mL) was added Dess-Martin Periodinane (DMP; 0.6 mmol, 255 mg). The resulting mixture was stirred at rt. The reaction progress was monitored by TLC. Upon completion of the reaction, the crude mixture was concentrated under the reduced pressure. The crude residue was purified using column chromatography on neutral alumina to afford **126** (51 mg) in 78% yield as a pale yellow liquid; R_f = 0.23 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.29 (m, 3H), 7.25–7.10 (m, 5H), 7.04–6.93 (m, 4H), 6.72 (d, J = 8.8 Hz, 2H), 3.76 (s, 3H), 2.08 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.8, 158.8, 144.0, 142.2, 142.1, 141.1, 131.3, 131.0, 130.8, 129.8, 128.41, 128.36, 127.8, 127.4, 113.8, 55.1, 31.4;

IR (Neat) ν_{max} 1689, 1505, 1352, 1242, 1178, 1026, 691 cm^{-1}; **HRMS (ESI)** for $C_{23}H_{21}O_2$ $(M+H)^+$: calcd. 329.1536, found 329.1539.

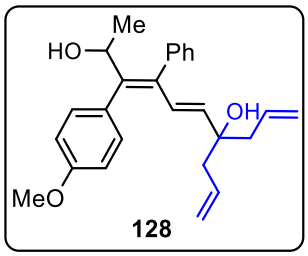
4A.6.3.9. Synthesis of 2-(4-methoxyphenyl)-3,3-diphenylacrylaldehyde (127):



127

To a solution of **125** (0.2 mmol, 63 mg) in CH_2Cl_2 (2.0 mL) was added Dess-Martin Periodinane (DMP; 0.6 mmol, 255 mg). The resulting mixture was stirred at rt. The reaction progress was monitored by TLC. Upon completion of the reaction, the crude mixture was concentrated under reduced pressure. The crude residue was purified using column chromatography on neutral alumina to afford **127** (45 mg) in 72% yield as a pale yellow liquid; R_f = 0.27 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.71 (s, 1H), 7.49–7.38 (m, 3H), 7.31–7.25 (m, 2H), 7.21–7.11 (m, 3H), 7.03–6.97 (m, 4H), 6.79–6.73 (m, 2H), 3.77 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.9, 159.8, 158.9, 141.1, 139.5, 139.3, 132.5, 131.6, 131.0, 129.5, 128.5, 128.24, 128.20, 127.8, 113.6, 55.1; IR (Neat) ν_{max} 1665, 1506, 1440, 1243, 1176, 1026, 756 cm^{-1}; **HRMS (ESI)** for $C_{22}H_{19}O_2$ $(M+H)^+$: calcd. 315.1380, found 315.1381.

4A.6.3.10. Synthesis of (3Z,5E)-7-Allyl-3-(4-methoxyphenyl)-4-phenyldeca-3,5,9-triene-2,7-diol (128):

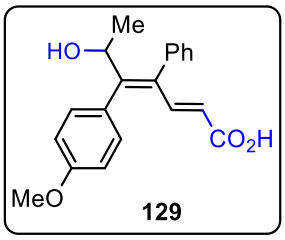


128

To a solution of **89** (0.2 mmol, 79 mg) and CuBr (0.02 mmol, 2.9 mg) in dry THF (2.0 mL) was added allylMgCl (2M in THF, 1.0 mmol). The resulting mixture was stirred at rt. The reaction progress was monitored by TLC. Upon completion of the reaction, the crude mixture was quenched with saturated ammonium chloride solution and extracted with ethyl acetate (2 × 10 mL). The organic layer was concentrated under reduced pressure. The crude residue was purified using column chromatography on neutral alumina to afford **128** (48 mg) in 61% yield as a pale yellow liquid; R_f = 0.13 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (t, J = 7.5 Hz, 2H), 7.35–7.30 (m, 1H), 7.22 (d, J = 8.5 Hz, 2H), 7.17 (d, J = 7.0 Hz, 2H), 6.95 (d, J = 9.0 Hz, 2H), 6.21 (d, J = 16.0 Hz, 1H), 5.64–5.52 (m, 2H), 4.96–4.88 (m, 3H), 4.88–4.80 (m, 2H), 4.46 (d, J = 3.5 Hz, 1H), 4.41 (s, 1H), 4.29–4.22 (m, 1H), 3.79 (s, 3H), 1.98 (d, J = 6.0 Hz, 4H), 0.87 (d, J = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.5, 143.2, 140.3, 139.9, 137.0 134.9, 134.8, 132.3, 130.4, 130.0, 129.3, 128.4, 127.1, 117.7, 117.6, 113.3, 73.6, 66.6,

55.4, 45.4, 22.5; IR (Neat) ν_{max} 1606, 1606, 1507, 1440, 1241, 1175, 913 cm^{-1}; **HRMS (ESI)** for $C_{26}H_{30}NaO_3$ $(M+Na)^+$: calcd. 413.2093, found 413.2090.

4A.6.3.11. Synthesis of (2E,4Z)-6-Hydroxy-5-(4-methoxyphenyl)-4-phenylhepta-2,4-dienoic acid (129):



129

To a solution of **89** (50 mg, 1.0 equiv) in MeOH (2 mL) was added aq. NaOH (2 mL, 10.0%) in a sealed tube. The resulting mixture was stirred at 120 °C for 12 h. The reaction progress was periodically monitored by TLC. Upon completion, MeOH was evaporated under reduced pressure and the reaction mixture was acidified with HCl, extracted with DCM and concentrated under reduced pressure. The product **129** was obtained in 55% yield (36 mg) as a colorless liquid; R_f = 0.32 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.13 (bd s, 1H), 7.48 (t, J = 7.5 Hz, 2H), 7.41 (t, J = 7.5 Hz, 1H), 7.28–7.16 (m, 5H), 7.00 (d, J = 9.0 Hz, 2H), 5.00 (d, J = 15.5 Hz, 1H), 4.76 (br d, J = 3.5 Hz, 1H), 4.33–4.26 (m, 1H), 3.82 (s, 3H), 0.92 (d, J = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 159.1, 152.6, 145.5, 138.0 ,135.8, 132.0, 129.8, 129.1, 129.0, 127.9, 122.1, 113.5, 66.6, 55.5, 22.2; IR (Neat) ν_{max} 2920, 1681, 1604, 1507, 1244, 1175, 698 cm^{-1}; **HRMS (ESI)** for $C_{20}H_{20}NaO_4$ $(M+Na)^+$: calcd. 347.1259, found 347.1255.

4A.7. X-ray crystallography:

X-ray reflections for **74** were collected on Rigaku Oxford diffractometer using Mo-Kα, radiation. OLEX 2 program were used to solve and refine the data. All non-hydrogen atoms were refined anisotropically, and C−H hydrogens were fixed.

Table 4A.4. Crystallographic Data for Compound **74**

Compound	**74**
formula	$C_{29}H_{30}O_3$
Formula weight	426.53
crystal system	triclinic
space group	P -1
T [K]	297 K
a [Å]	9.2741 (7)
b [Å]	9.6365 (5)
c [Å]	15.4637 (7)
α [°]	82.224 (4)

V [Å^3]	1205.61(15)
Z	2
ρ_{calcd} [g cm^{-3}]	1.175
μ [mm^{-1}]	0.075
total reflns	10646
unique reflns	4443
observed	3055
R_1[I>2σ(I)]	0.0876 (3055)
wR2 [all]	0.1125 (4443)
GOF	1.085

β [°]	89.849 (5)	Diffractometer	Rigaku Oxford
γ [°]	61.960 (7)	CCDC Number	CCDC 2096145

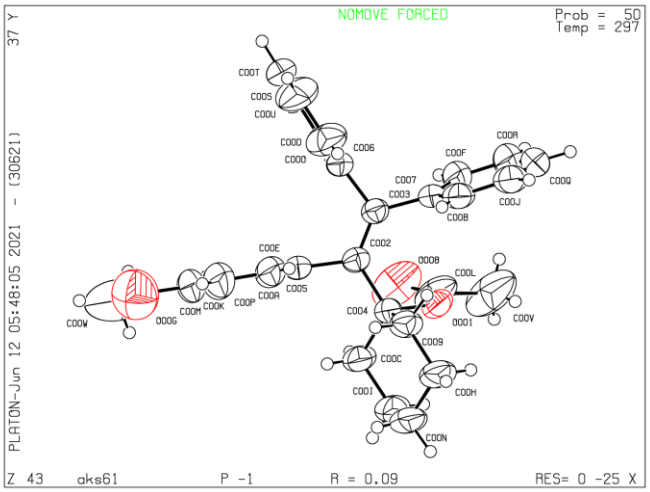


Figure 4A.7. Molecular structure of compound **74**, (Oxygen (red), nitrogen (blue), and sulphur (yellow))

4A.8. References

(1) (a) Kasiotis, K. M.;, Lambrinidis, G.; Fokialakis, N.; Tzanetou, E. N.; Mikros, E.; Haroutounian, S. *Front. Chem.,* 2017, *5*, 10.3389/fchem.2017.00071. (b) Ahmed, N. S.; Elghazawy, N. H.; ElHady, A. K.; Engel M.; Hart-mann, R. W.; Abadi A. H. *Eur. J. Med. Chem.* **2016**, *112*, 171–179. (c) Joly, D.; Tondelier, D.; Deborde, V.; Geffroy, B.; Hissler M.; Réau, R. *New J. Chem.*, **2010**, *34*, 1603–1611. (d) Ran, G.-Y.; Gong, M.; Yue, J.-F.; Yang, X.-X.; Zhou, S.-L.; Du, W.; Chen, Y.-C. *Org. Lett.*, **2017**, *19*, 1874–1877.

(2) (a) Düfert, A.; Werz, D. B. *Chem. Eur.J.*, **2016,** *22*, 16718–16732. (b) Akai, K.; Matsukawa, N.; Takahashi, A.; Fujii, T. *Angew. Chem. Int. Ed.*, **1998,** *37*, 152–155. (c) Liao, L.; Jana, R.; Urkalan, K. B.; Sigman, M. S. *J. Am. Chem. Soc.*, **2011,** *133*, 5784–5787. (d) Wu, X.; Lin, H.-C.; Li, M.-L.; Li, L.-L.; Han, Z.-Y.; Gong, L.-Z. *J. Am. Chem. Soc.*, **2015,** *137*, 13476–13479. (e) Yamamoto, E.; Hilton, M. J.; Orlandi, M.; Saini, V.; Toste, F. D.; Sigman, M. S. *J. Am. Chem. Soc.*, **2016,** *138*, 15877–15880. (f) Tu, H. Y.; Wang, F.; Huo, L.; Li, Y.; Zhu, S.; Zhao,

X.; Li, H.; Qing, F. L.; Chu, L. *J. Am. Chem. Soc.*, **2020,** *142*, 9604–9611. (h) García-Domínguez, A.; Li, Z.; Nevado, C. *J. Am. Chem. Soc.*, **2017,** *139*, 6835–6838.

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(7) (a) Zhou, C.; Emrich, D. E.; Larock, R. C. *Org. Lett.* **2003,** *5*, 1579–1582. (b) Zhou, C.; Larock, R. C. *J. Org. Chem*. **2005**, *70*, 3765–3777.

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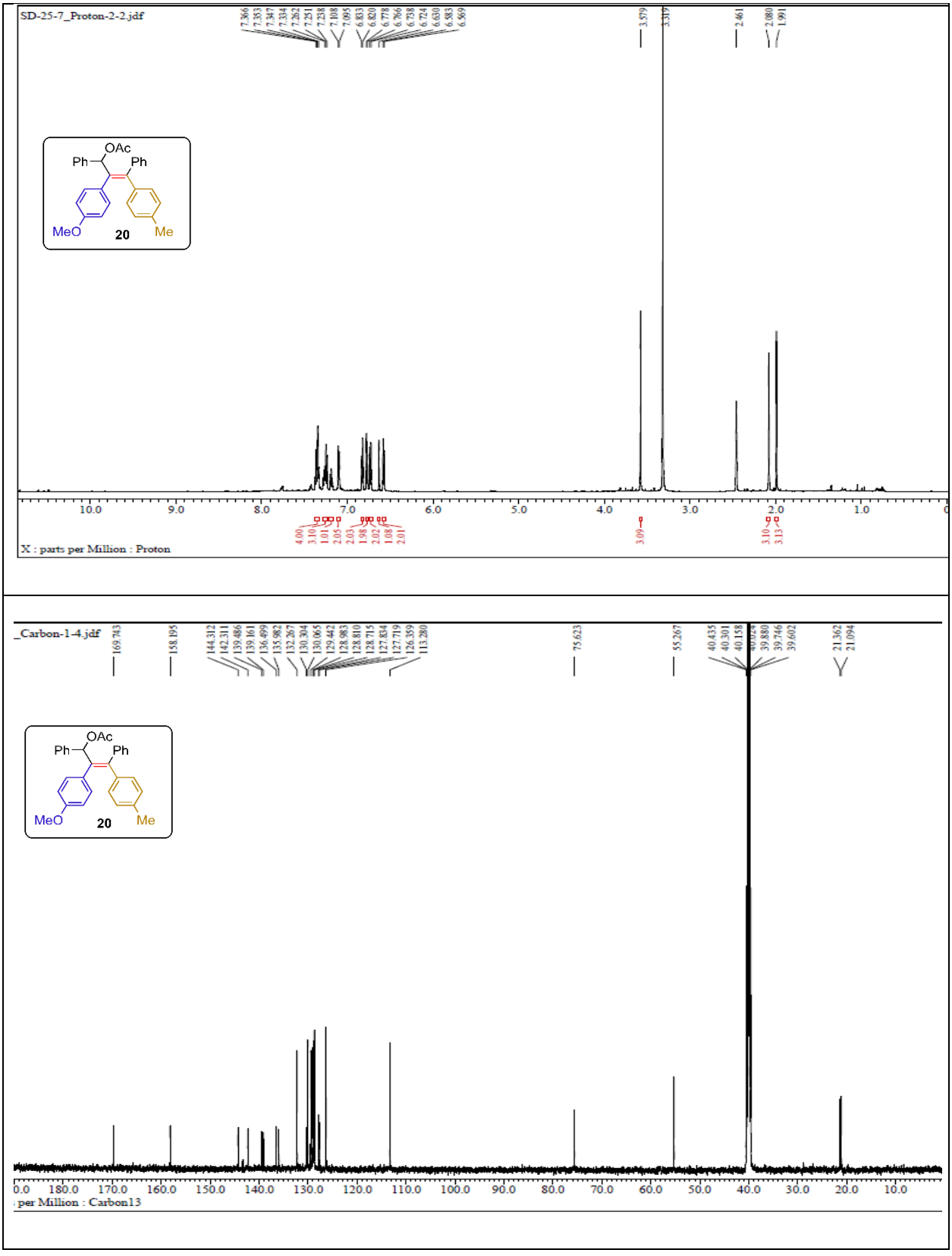
4A.9. Spectra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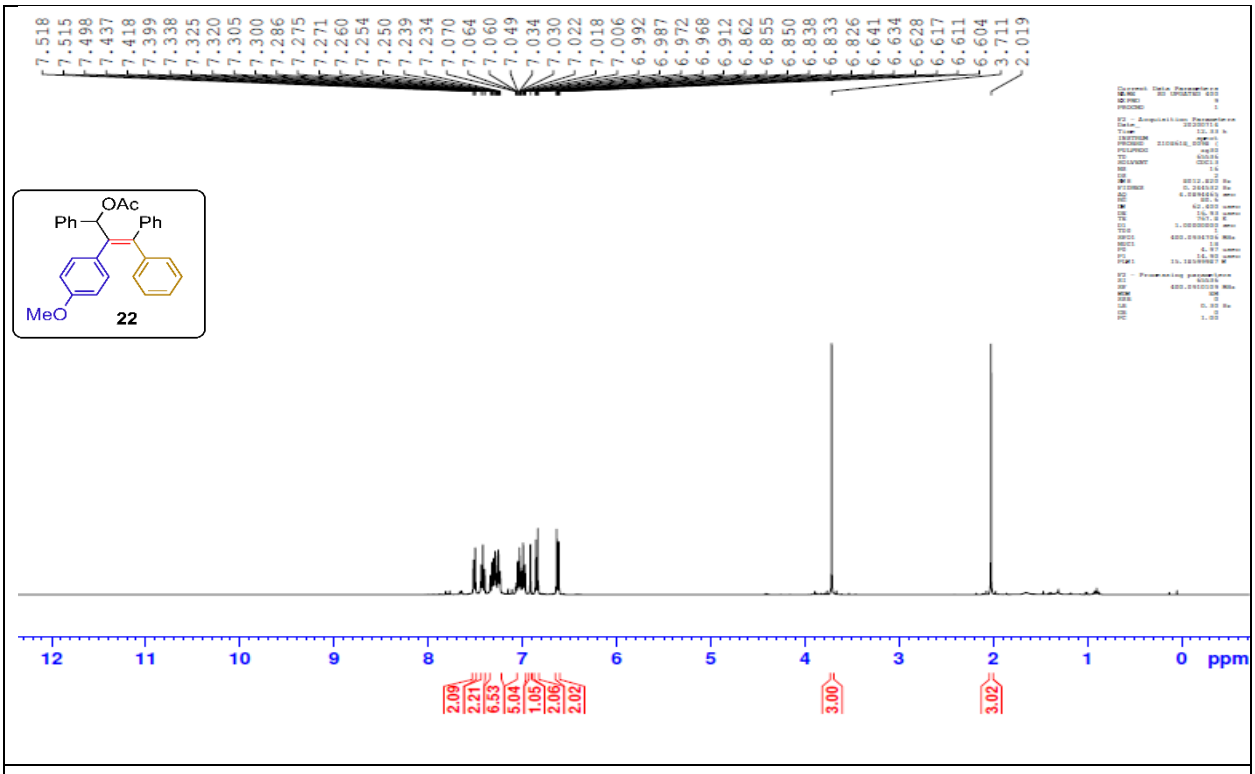
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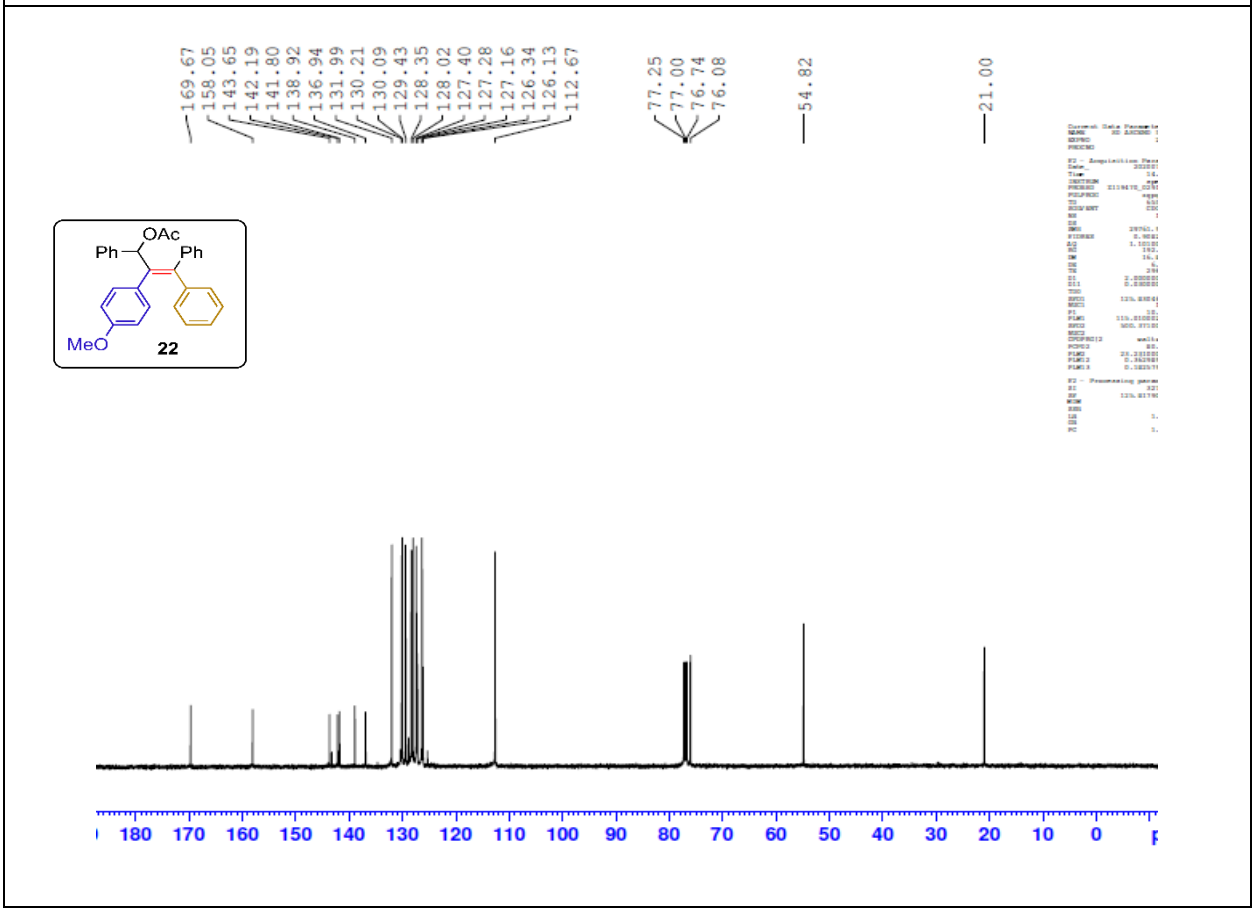
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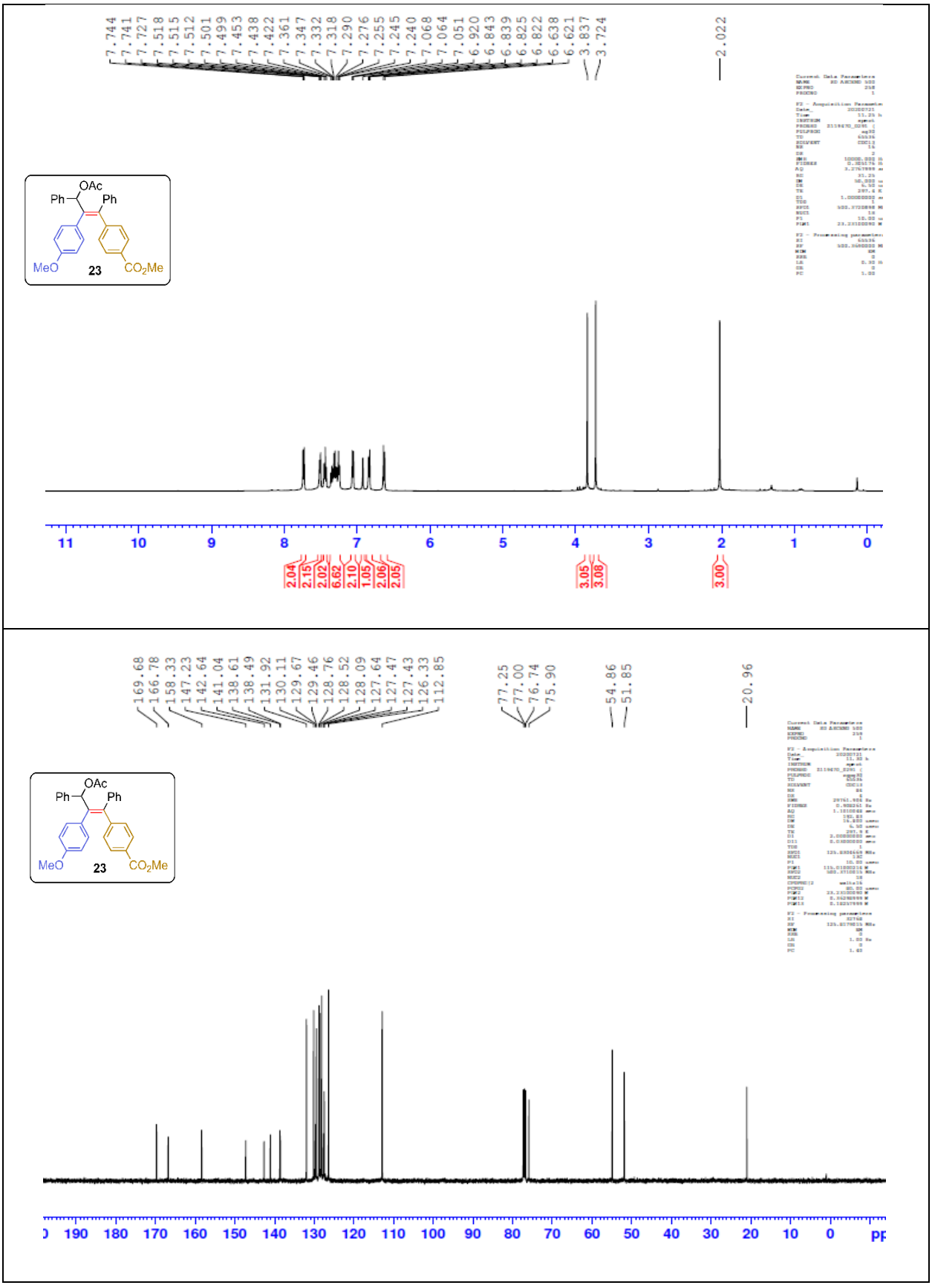
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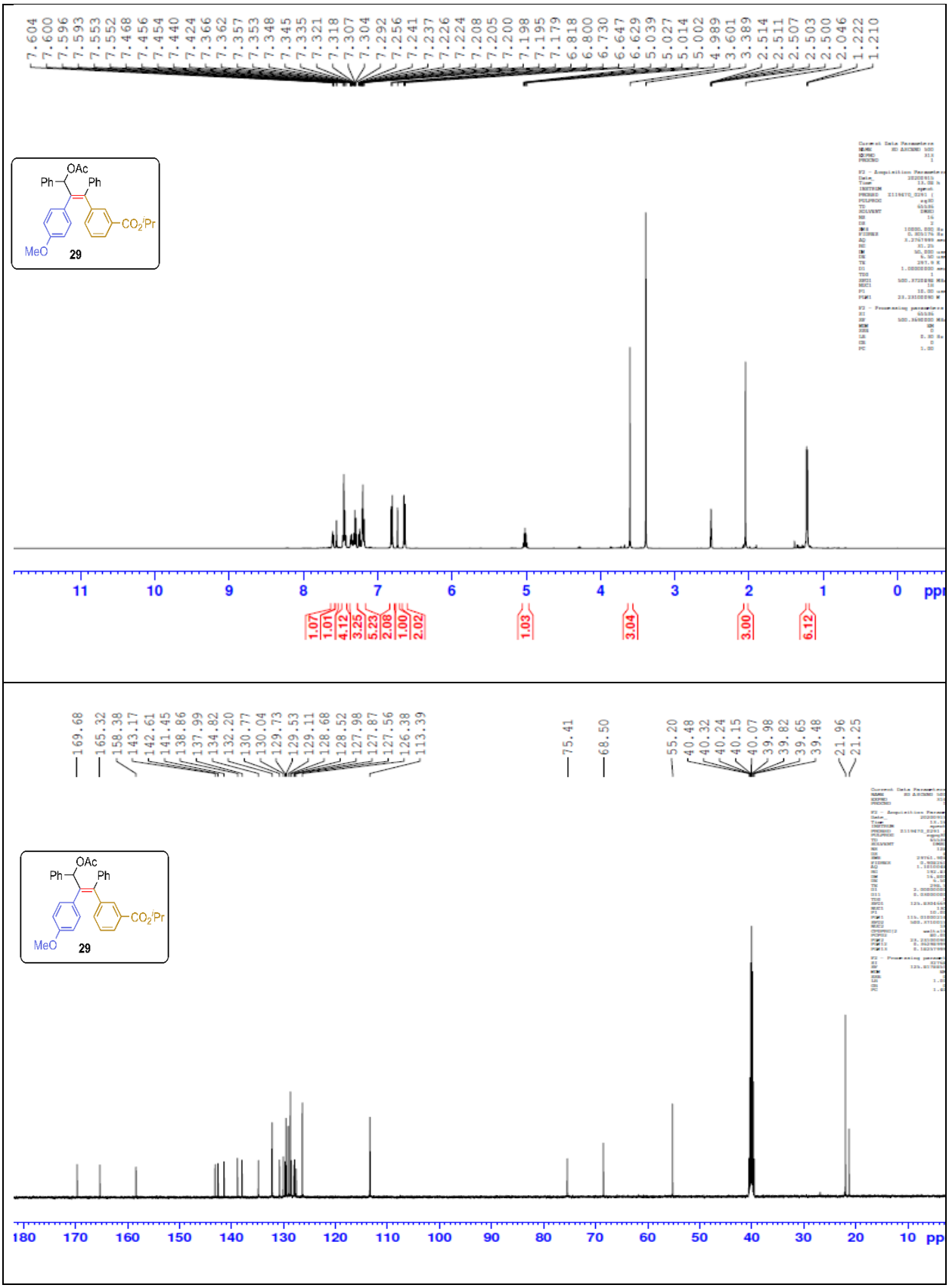
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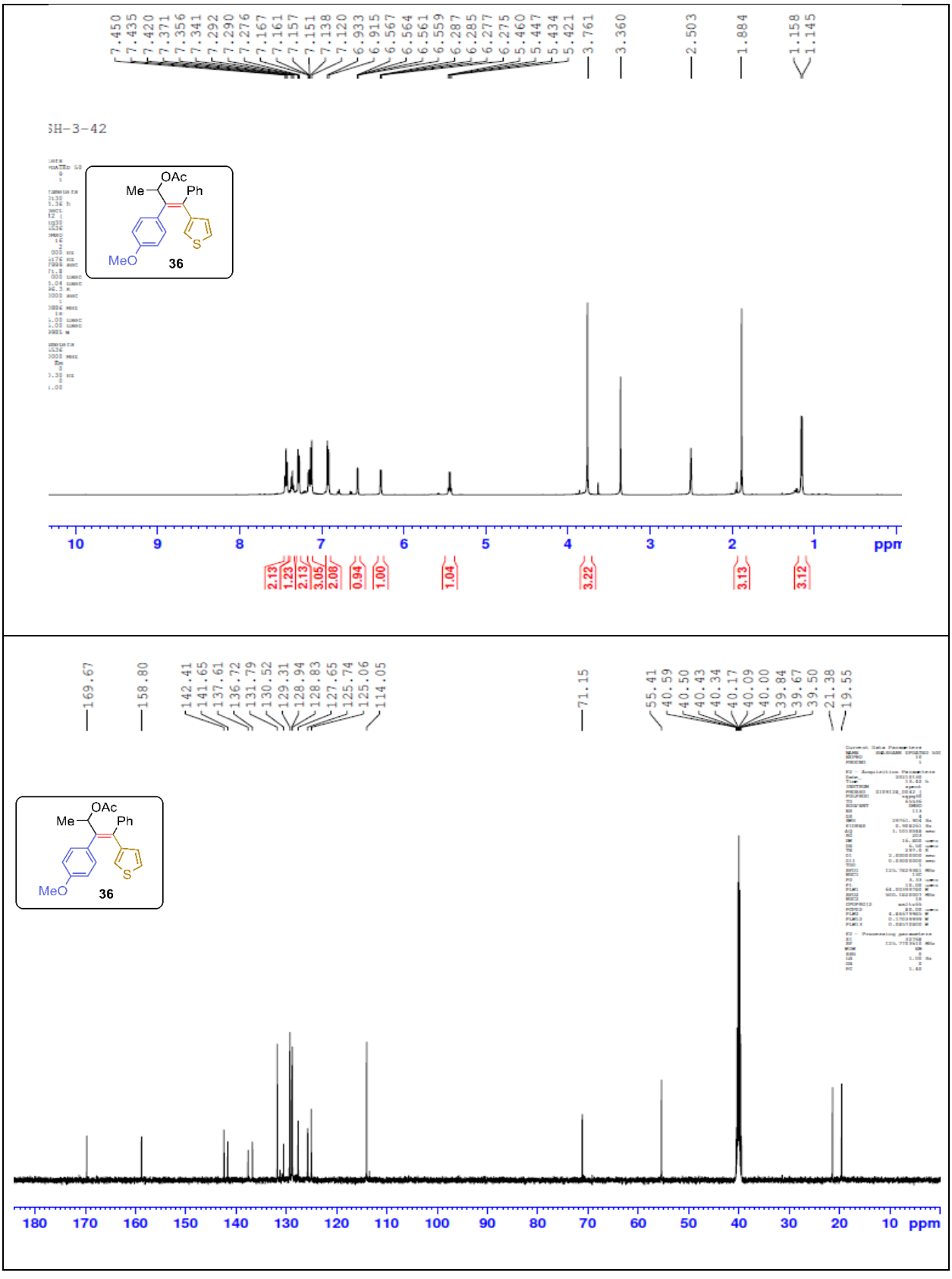
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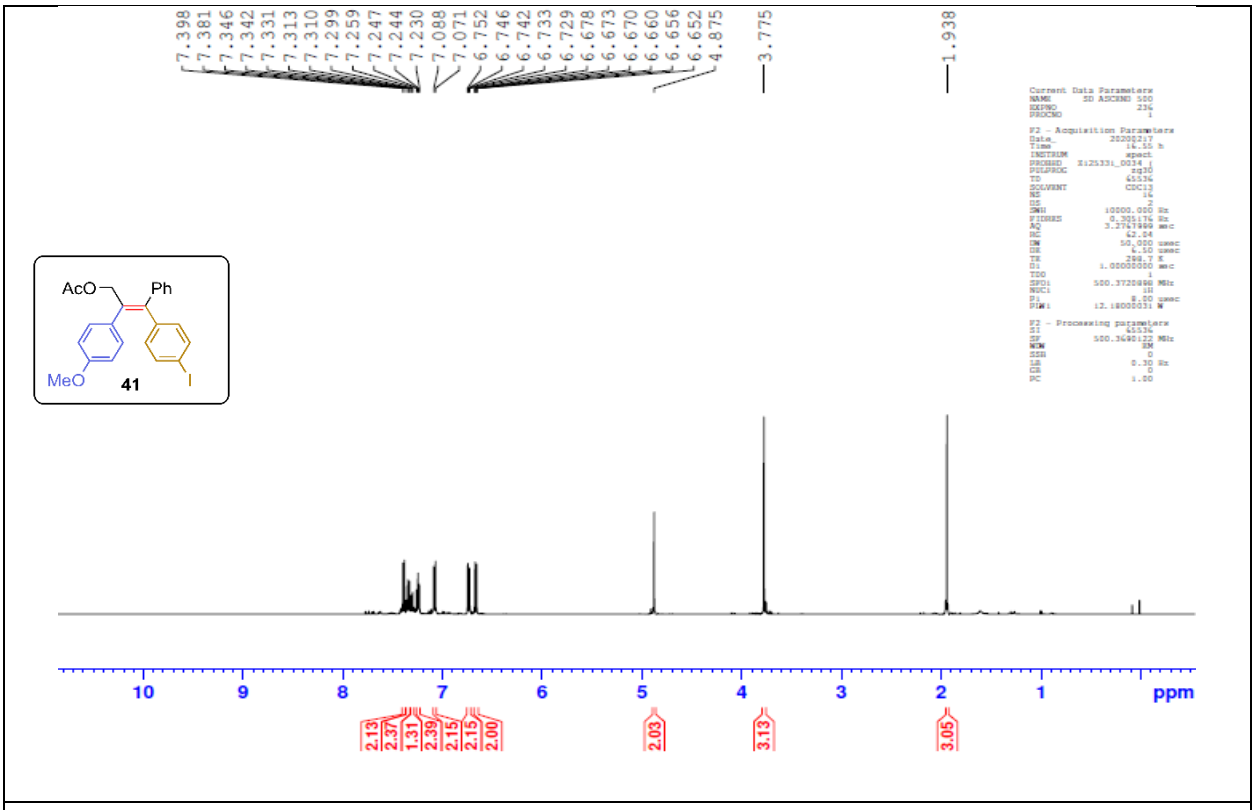
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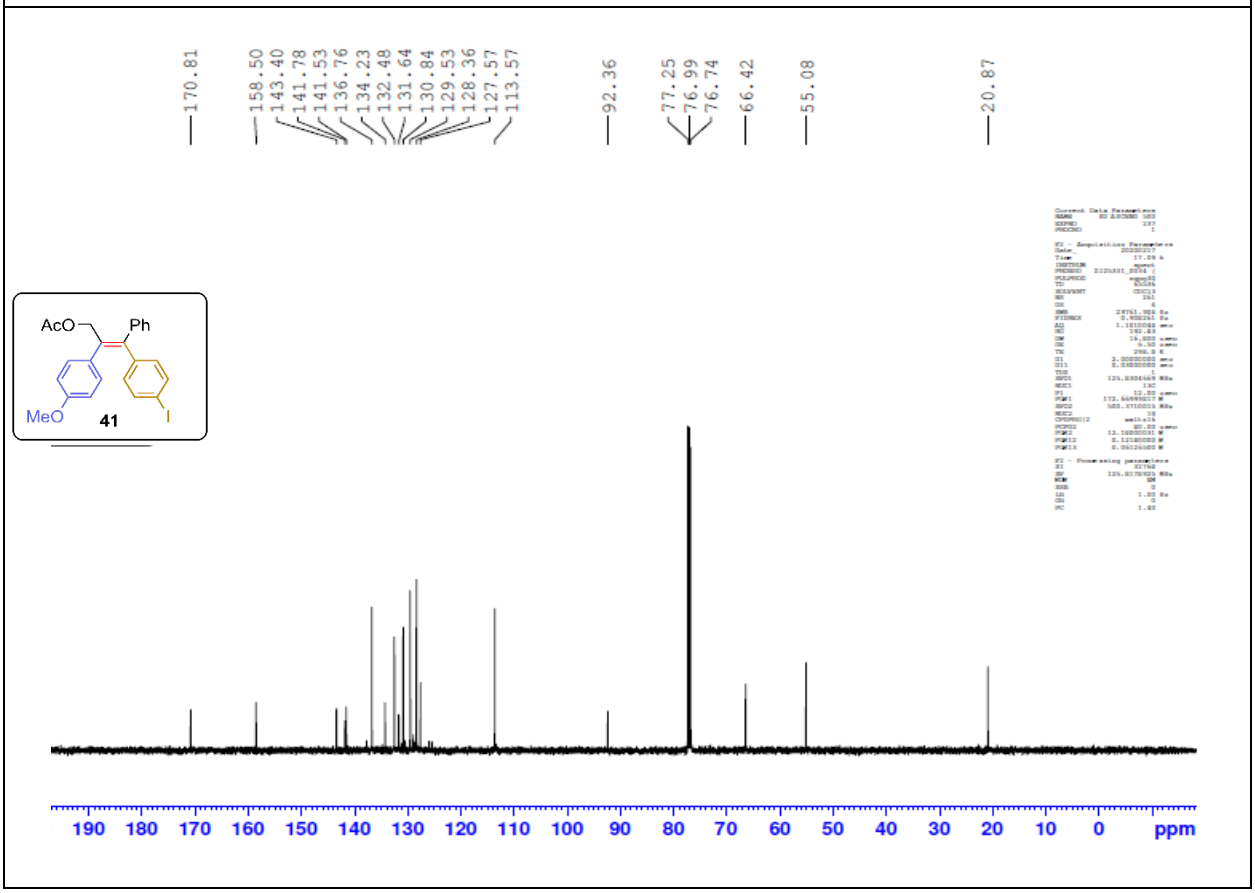
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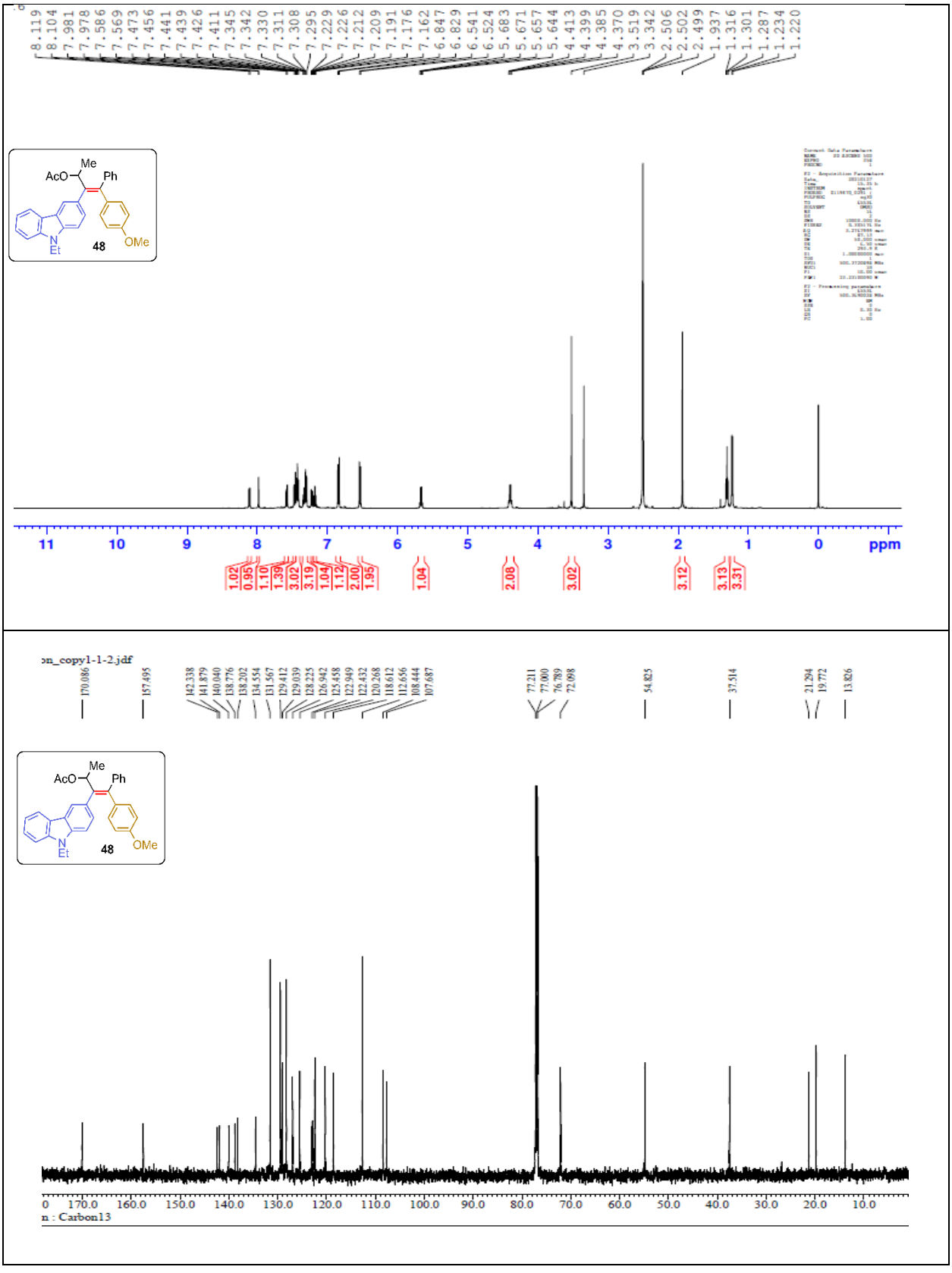
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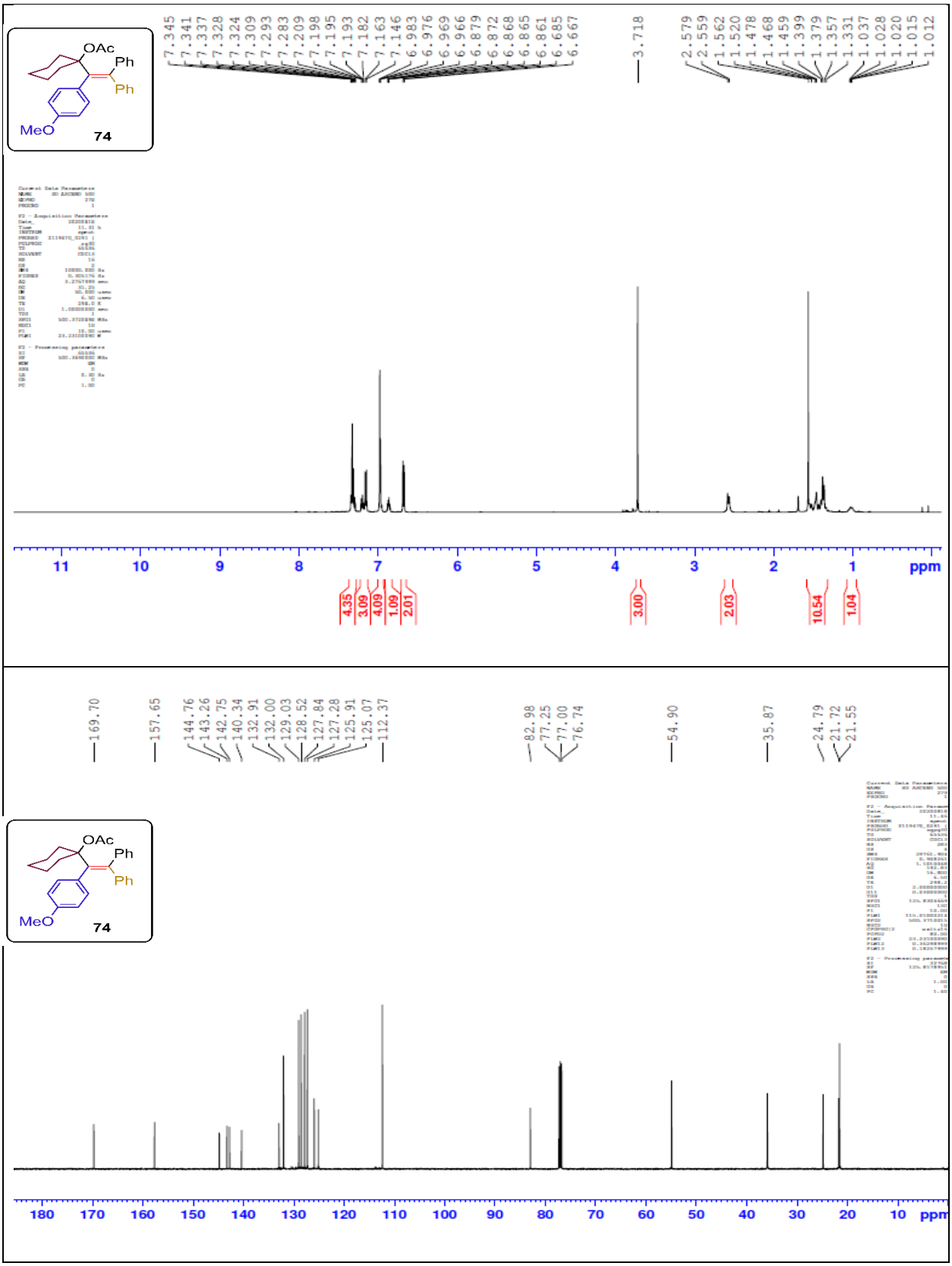
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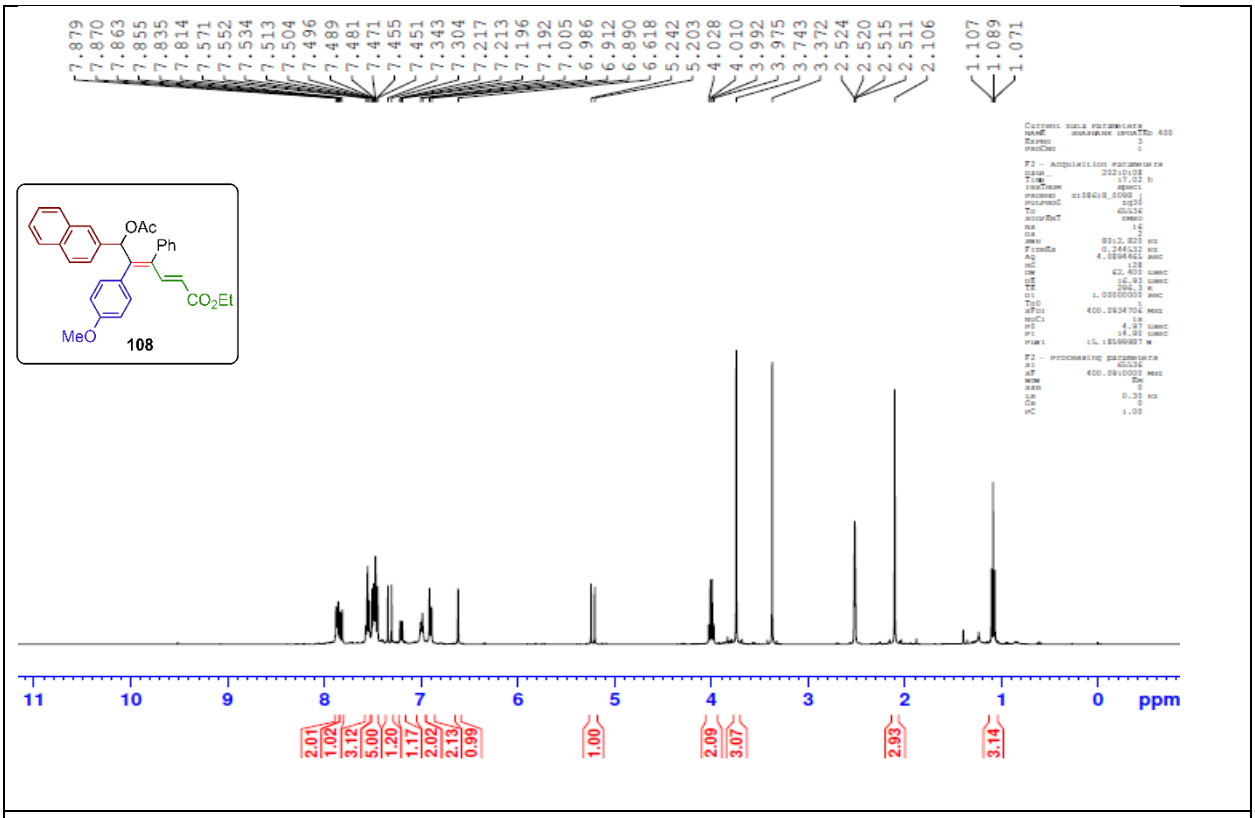
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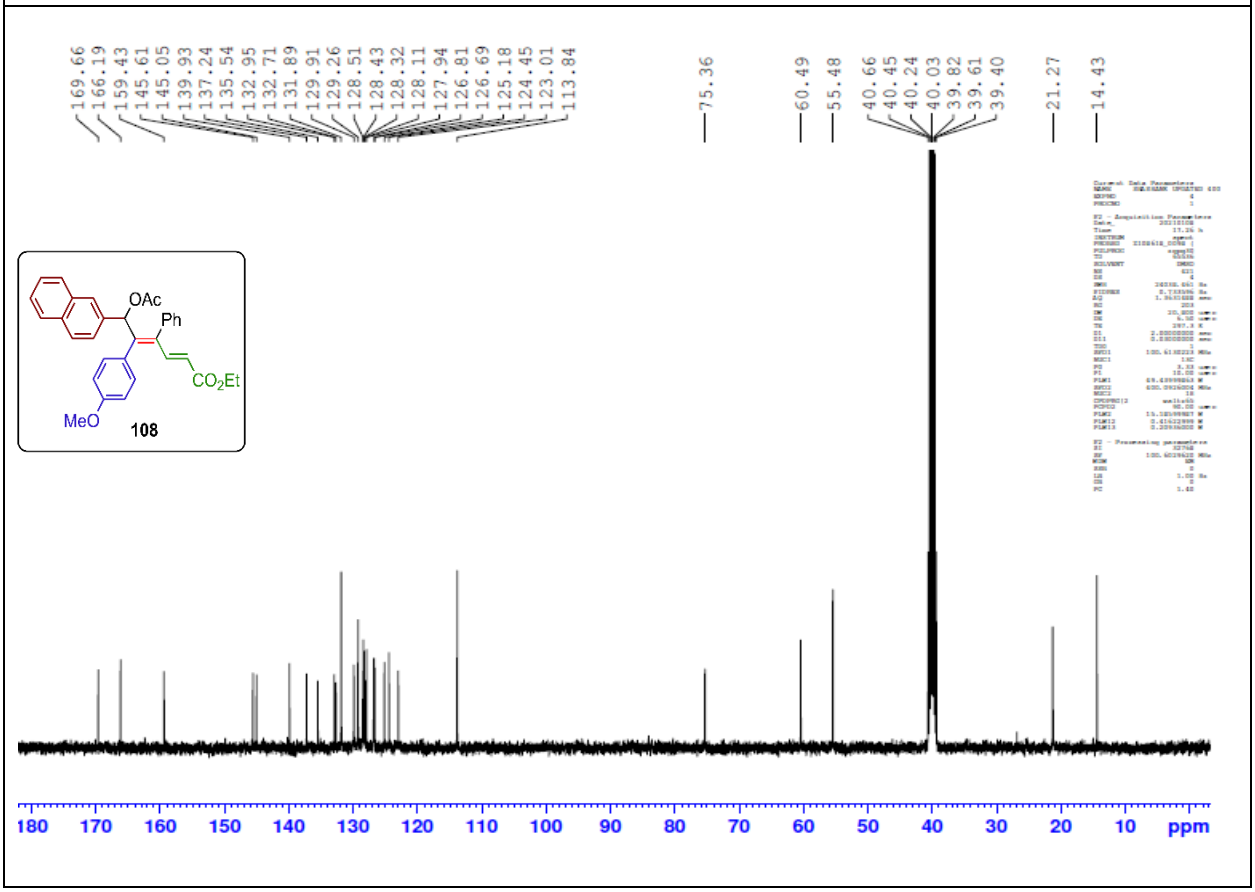
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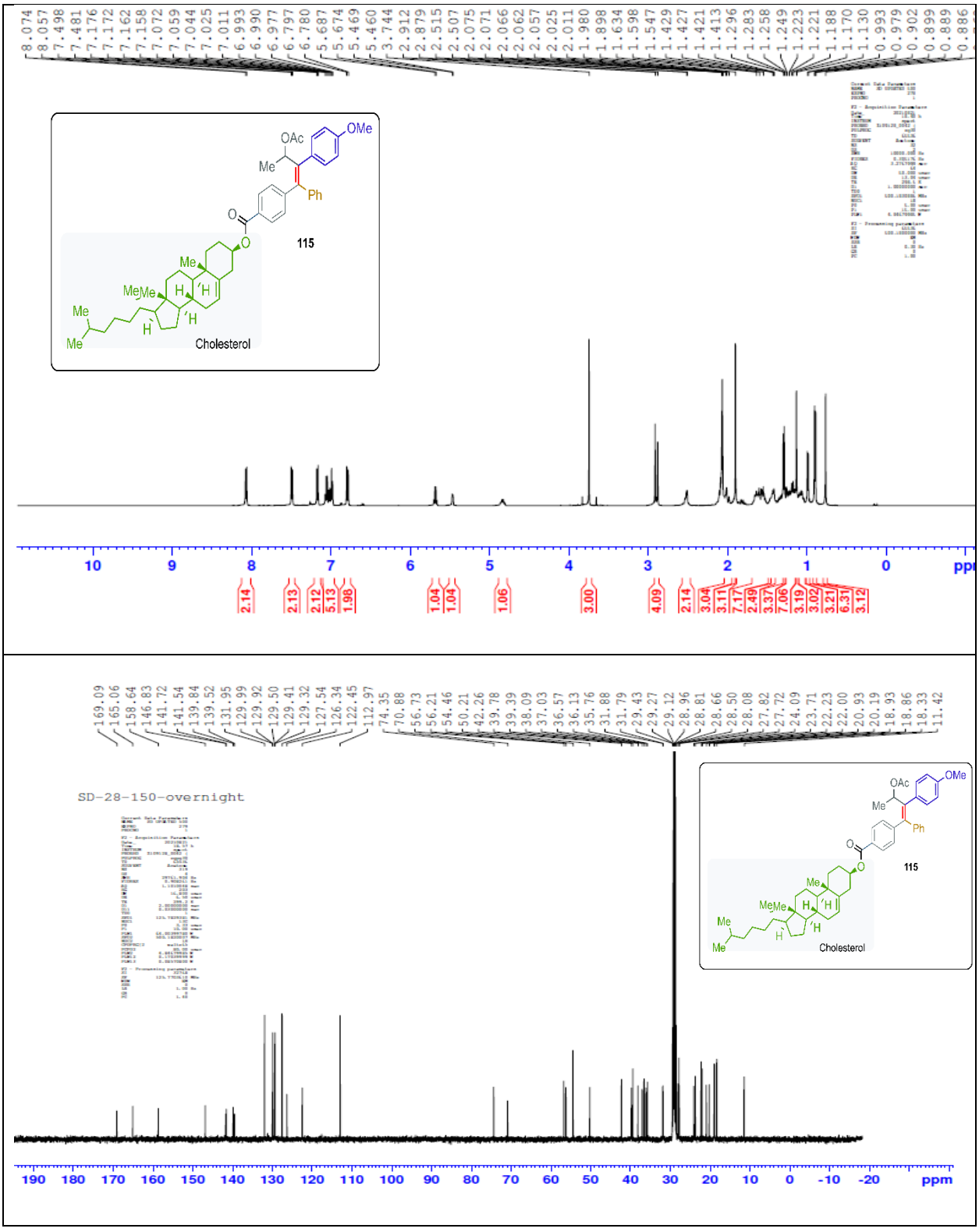
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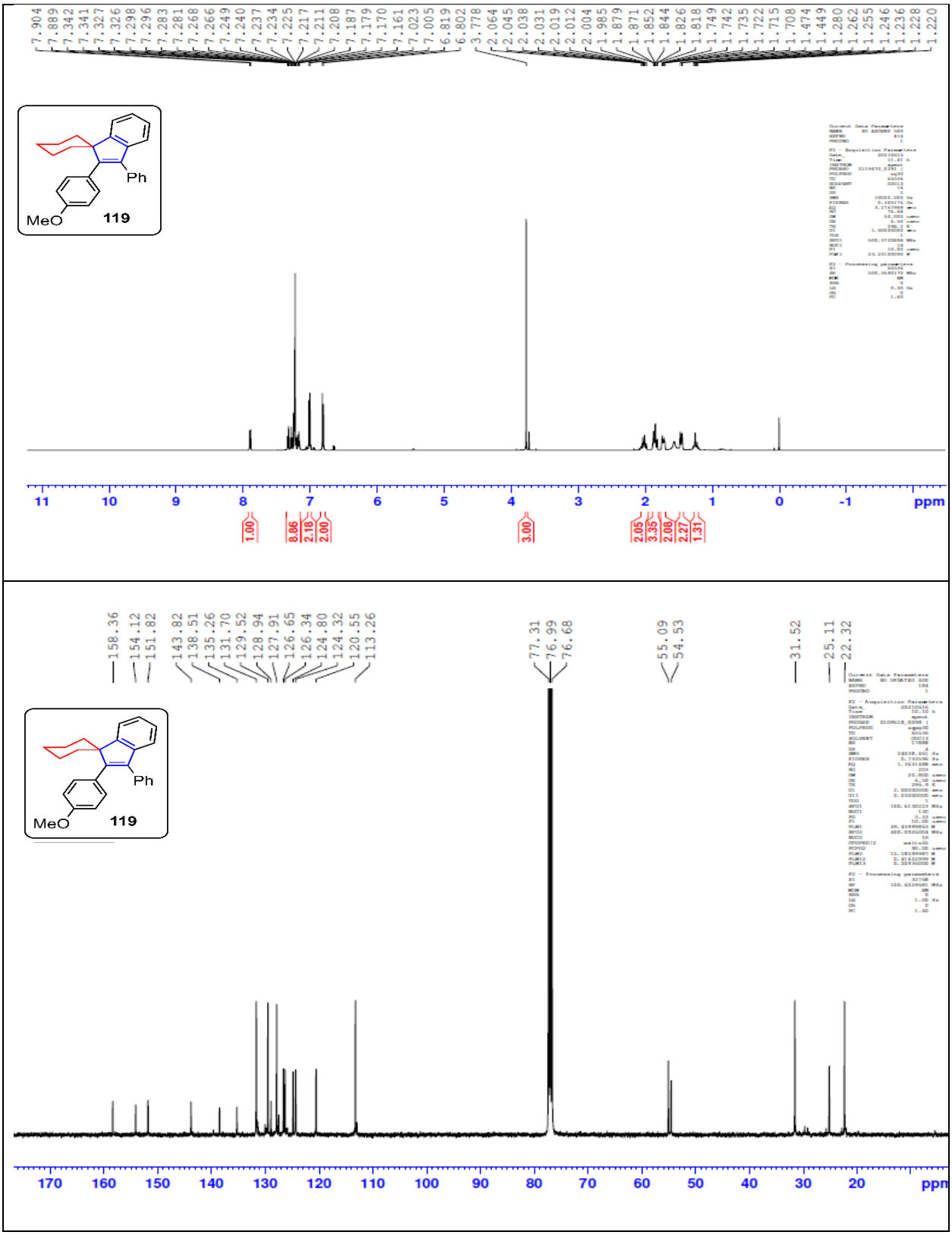
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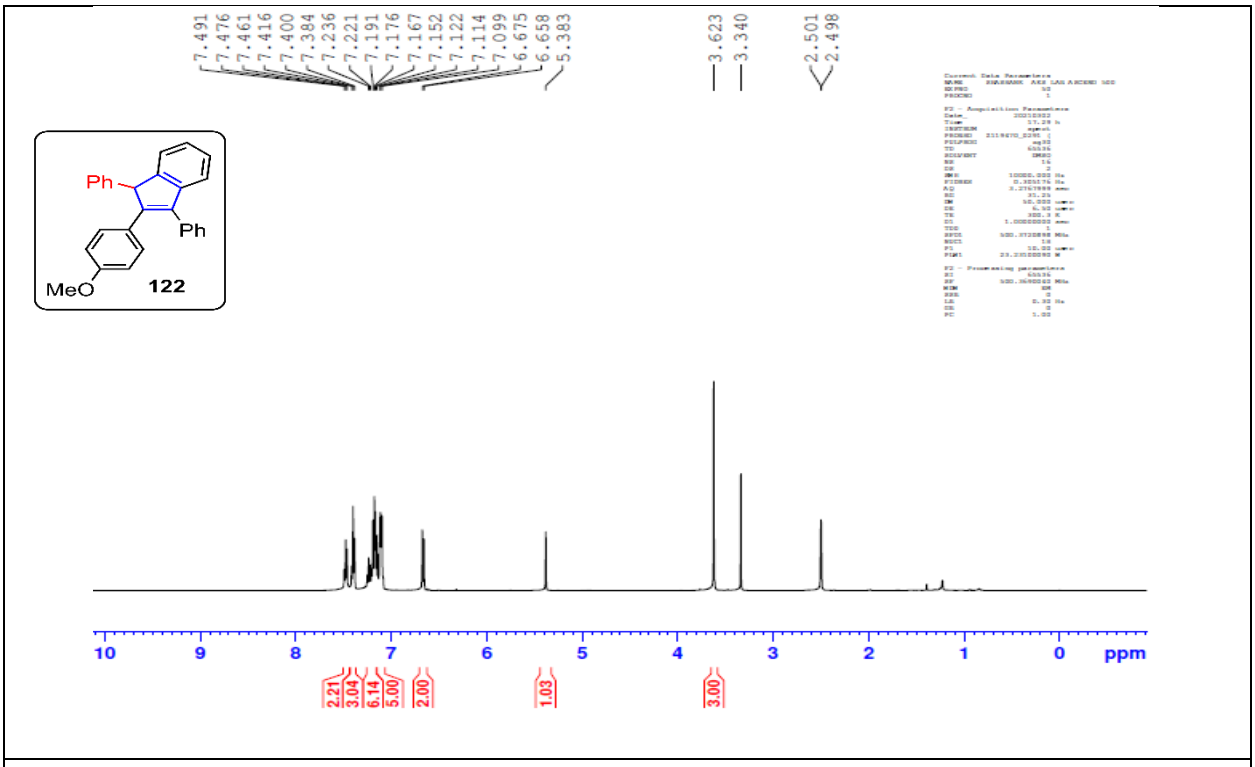
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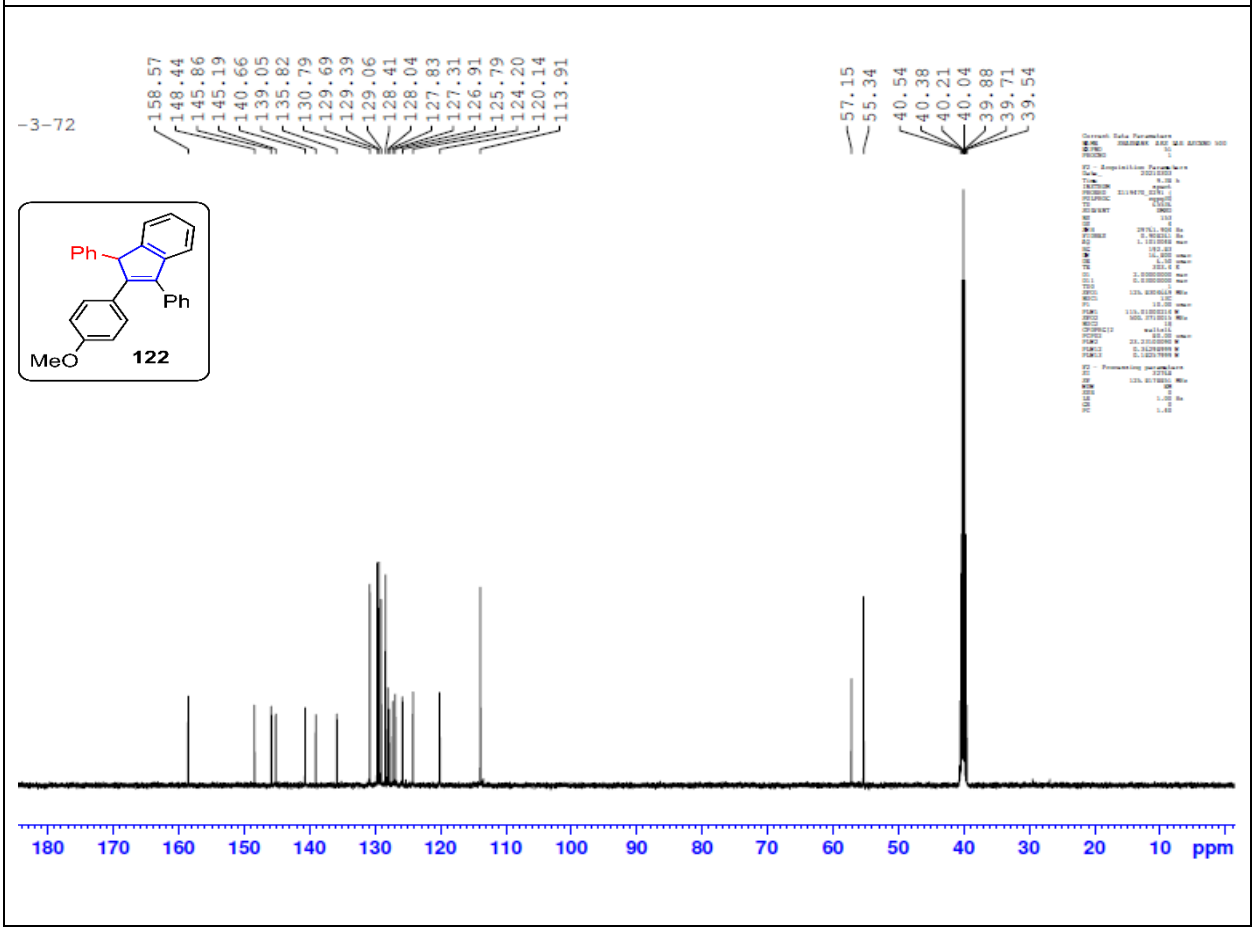
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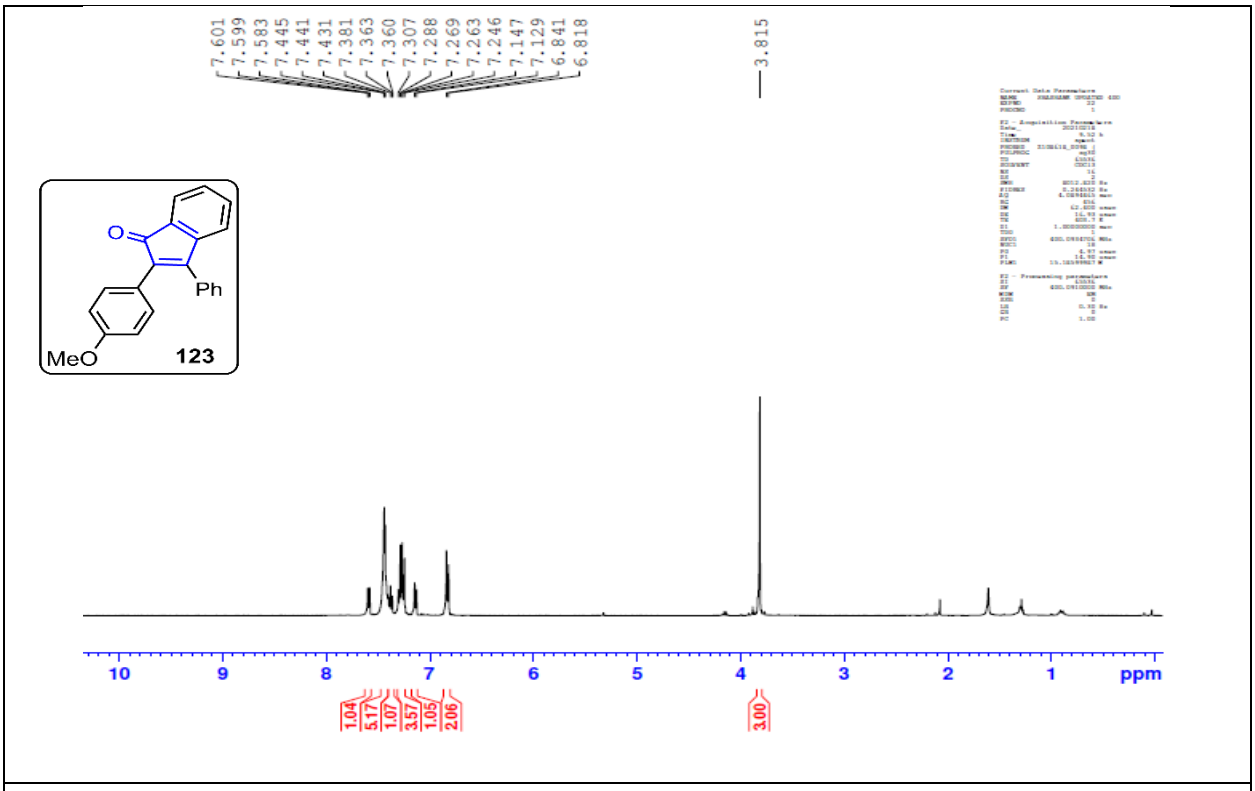
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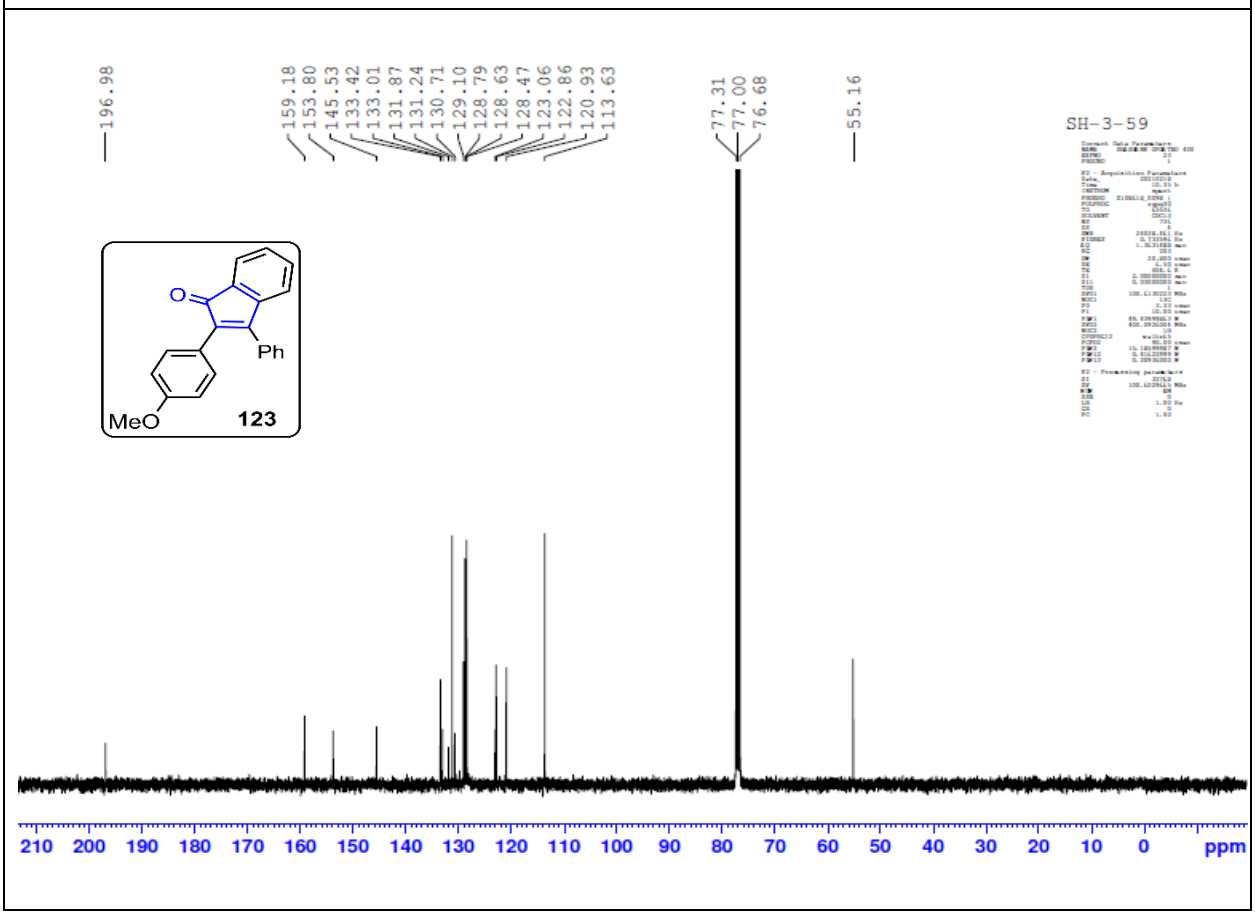
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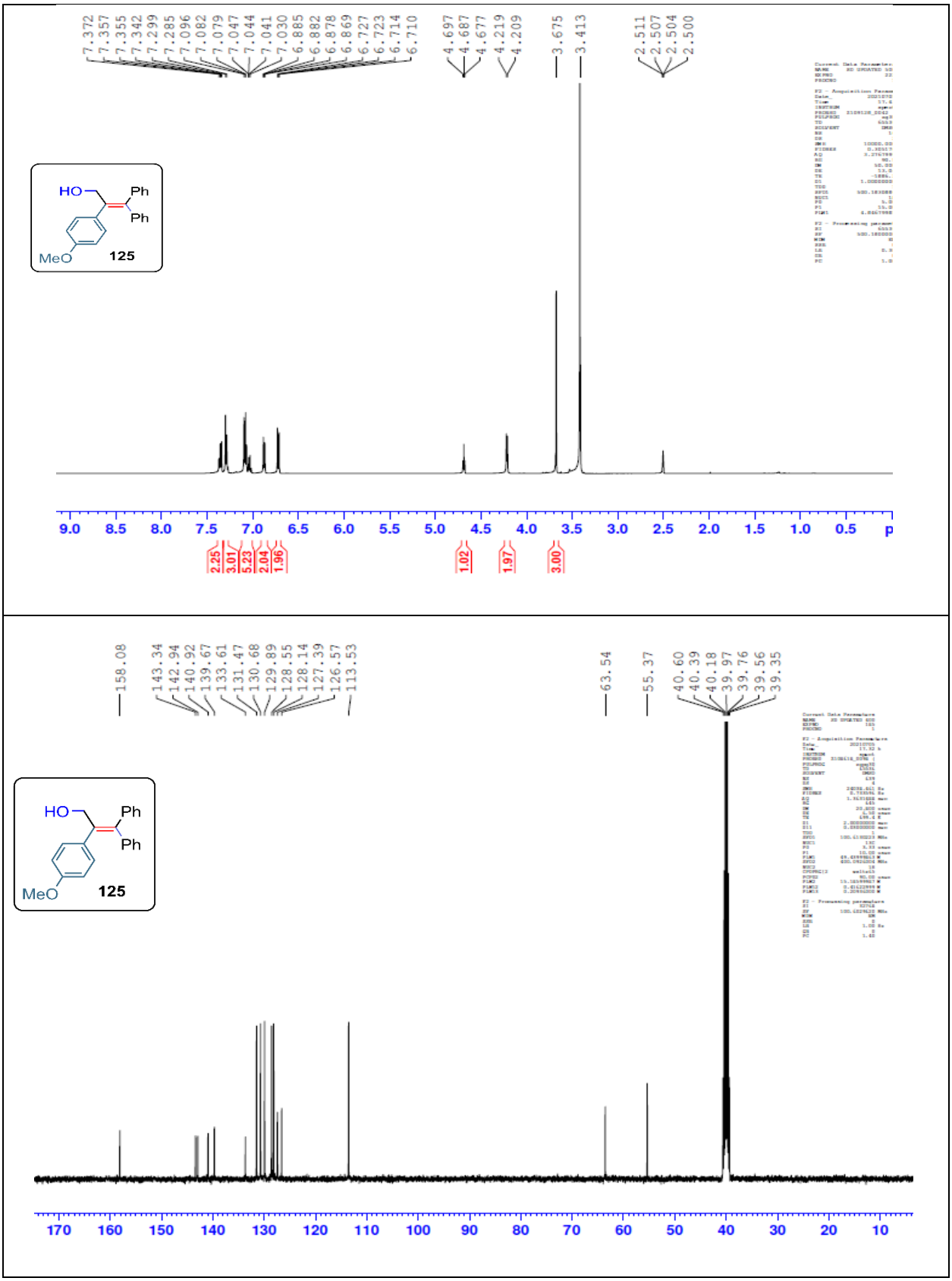
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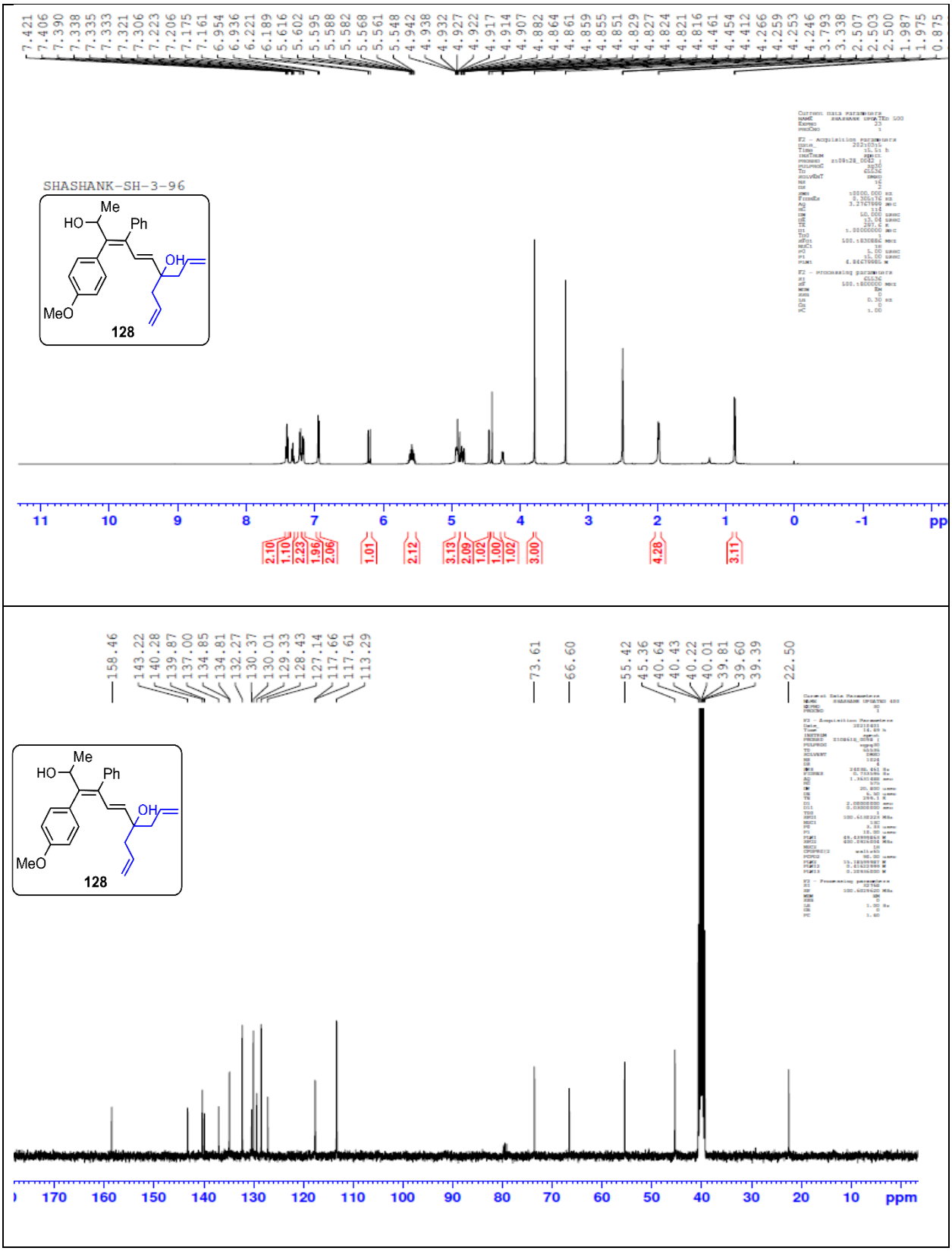
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11 10 9 8 7 6 5 4 3 2 1 0 -1 ppm
2.10 1.10 2.23 1.96 2.06 1.01 2.12 3.13 2.09 1.02 1.00 1.02 3.00 4.28 3.11
158.46 143.22 140.28 139.87 137.00 134.85 134.81 132.27 130.37 130.01 129.33 128.43 127.14 117.66 117.61 113.29 73.61 66.60 55.42 45.36 40.64 40.43 40.22 40.01 39.81 39.60 39.39 22.50
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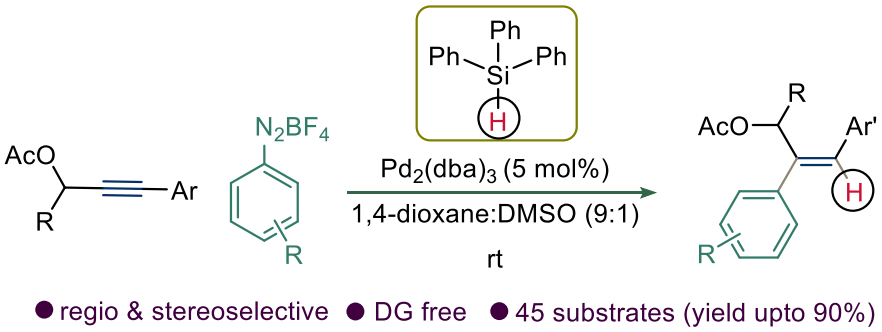
Chapter-4B

Cationic Palladium Catalyzed Regioselective Hydro-Arylation of Unsymmetrical Alkynes

Abstract



An efficient cationic palladium catalyzed regioselective *syn*-1,2-hydroarylation of yne-acetate is scripted. The current transformation uses aryl diazonium salt and triphenyl silane as coupling partners to execute the hydro-arylation of unsymmetrical alkynes without the need of a directing group. The regioselectivity purely depends upon a non-covalent lone pair repulsion between the acetate group and ligated metal species dictating α-addition over β-addition. The scope is broad and its synthetic importance has been demonstrated by direct transformation of yne-acetate containing natural products. Few sets of control experiments and deuterium incorporation study provide solid evidence for the involvement of cationic palladium species. The synthetic application of hydro-arylated product is also demonstrated.

Publication

S. Dutta, M. Sethi,# A. Maity, # A. Sahoo, V. Gandon, A. K. Sahoo. (# equal contribution)

Manuscript Communicated

4B.1. Introduction

Alkyne represents one of the most profound synthons in organic community and provides direct access to tri-substituted alkenes, these are common structural motifs found in natural products, drug molecules, and organic materials (shown in **Figure 4B.1**).[1]

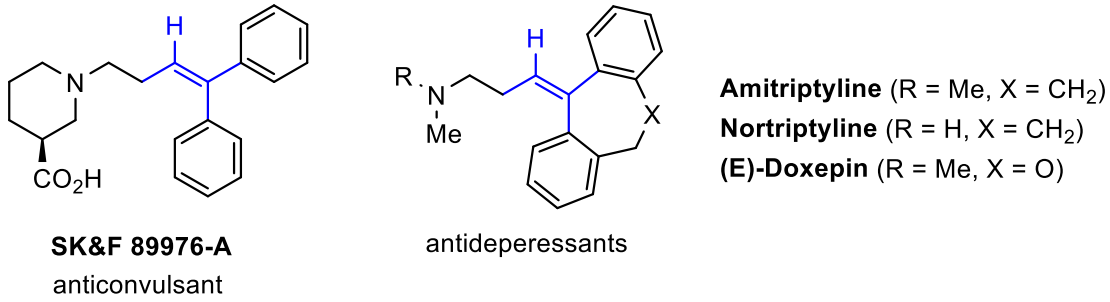


Figure 4B.1. Represetative examples of drugs containing tri-substituted olefins

In this regard, transition metal catalyzed hydro-arylation of alkyne is a persuasive tool for the synthesis of highly substituted alkenes. Till date variuos organometallic reagents have been used to carry out hydro-arylation of alkynes.[2] Although symmetrical alkynes have been well studied for hydro-arylation, the identical studies on unsymmetrical alkynes suffers with regio-selectivity issues. The state of art electron biasness and DG have been incorporated for better regioselectivity. The general strategy for hydroarylation relies on transmetalation of organometallic reagent with metal catalyst, followed by regioselective carbometallation and protodemetalation (**Figure 4B.2**). The approach of aryl group to the alkyne is regulated by electron biasness of alkynes **I**/**II** [having either an electron withdrawing group (EWG) or electron donating group (EDG)] (**Figure 4B.2**). On the other hand, the alkynes **III** with a directing group (DG; pyridine, alcohol, 2-amidopyridyl), could synchronize the approach of aryl group through a metallocycle **IV** (**Figure 4B.2**).[3] Despite these advancements, difunctionalization of alkynes are largely driven by the electron biasness of alkynes, presence of non-removable pyridyl-DG, and use of external ligands; as a result, these reactions possess limited synthetic viability.

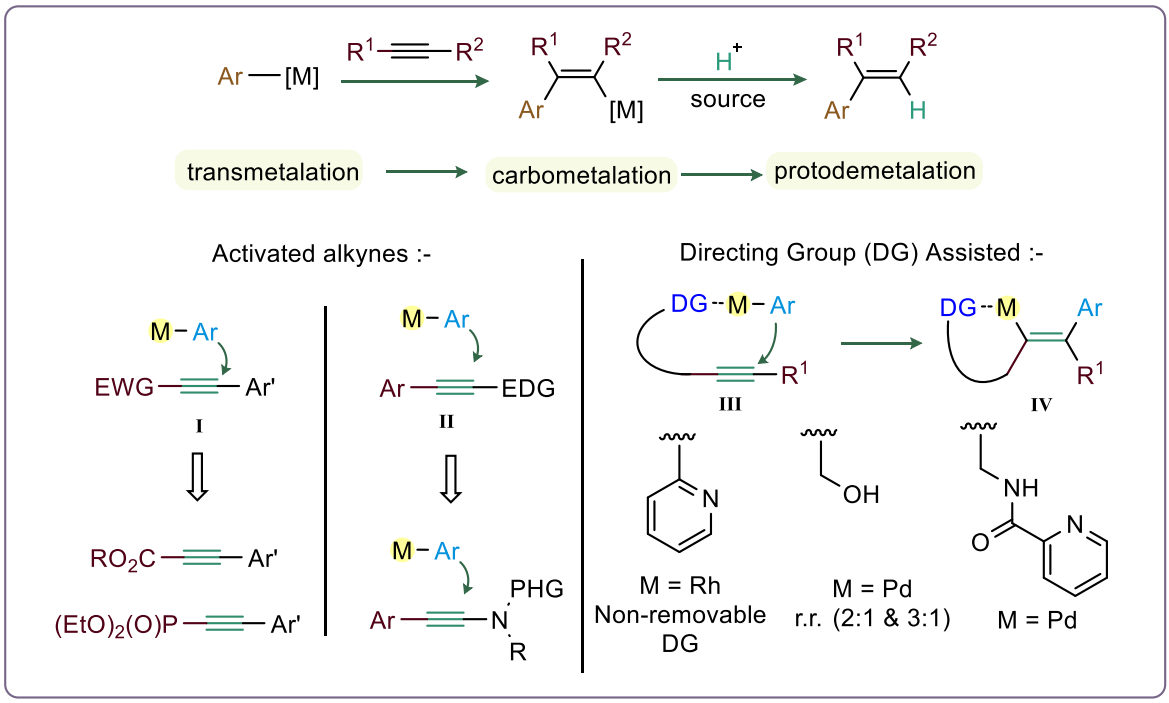


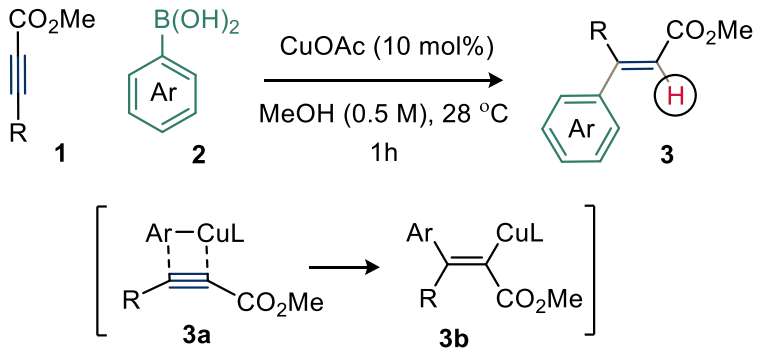
Figure 4B.2. Strategies towards regioselective hydro-arylation of unsymmetrical alkynes

4B.2. Precedents

Some of the representatative examples of regioselective hydro-arylation of unsymmetrical alkynes are discussed.

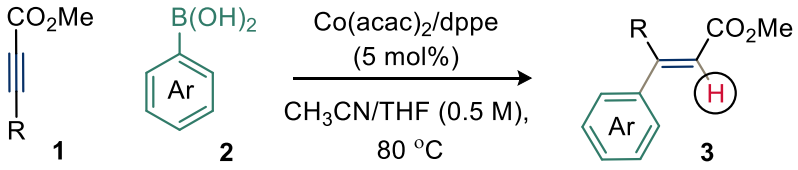
4B.2.1. Transition Metal Catalyzed Hydro-Arylaion of Activated Alkynes

In 2008, Yamamoto and co-workers disclosed a protocol for copper catalyzed hydro-arylation of substituted propiolates **1** to furnish a stereo and regioselective *vinyl acetate* core **3** using aryl-boronic acids **2** (**Scheme 4B.1**).[4] The reaction proceeds with the regioselective attack of aryl-copper species to the *β*-position of propiolate **3a** followed by protodemetalation of **3b** with methanol.



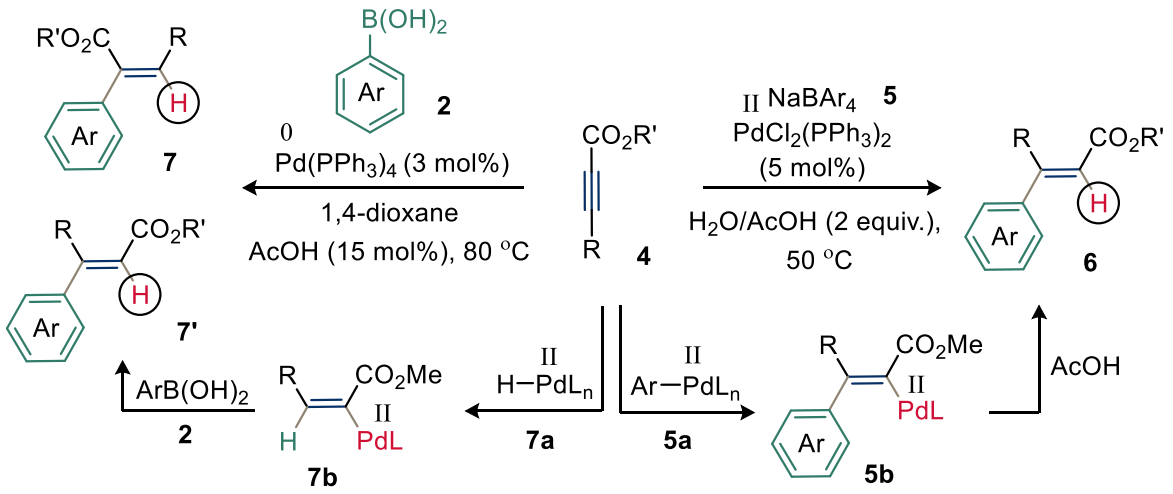
Scheme 4B.1. Cupper catalyzed hydro-arylation of propiolates

Later in same calender year, Cheng group reported a Co-catalyzed regioselective hydro-arylation of internal propiolates **1** to deliver the desired product **3** (**Scheme 4B.2**).[5] Not only, propiolates but also pyridine alkynes were also used for hydro-arylation. The reaction mechanism follows same pathway as discussed previously for the Cu-catalyzed hydro-arylation (**Scheme 4B.1**).



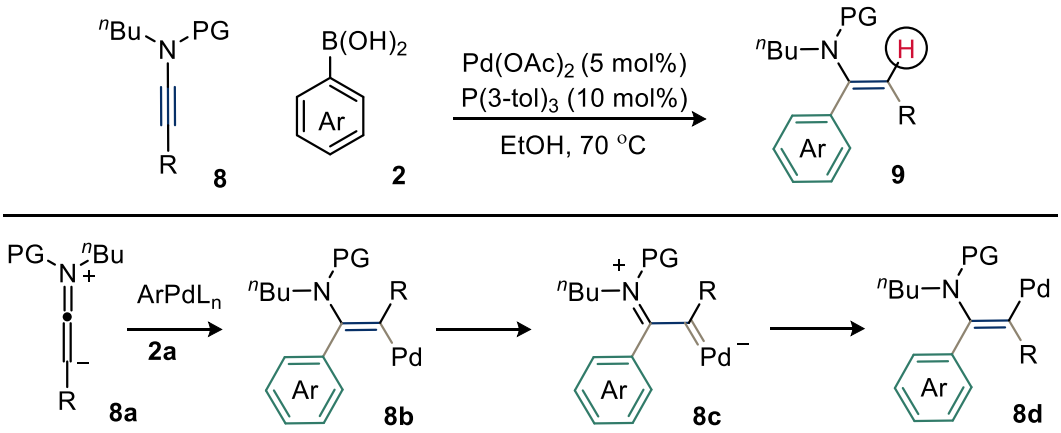
Scheme 4B.2. Cobalt catalyzed hydro-arylation of propiolates

Two interesting demonstrations of hydro-arylation of propiolates were showcased in 2003 and 2008 by Oh and Hua research group, respectively. Acetic acid has been used as hydrogen source for hydro-paladation or for protodemetalation (**Scheme 4B.3**).[6] When $NaBPh_4$ **5** was used as the aryl source, transmetalation of **5** with Pd-cat gives **5a** which upon carbopalladation generates int-**5b**. Finally, protodemetalation of **5b** yields the final product **6**. Unlike the former mechanism, in presence of aryl-boronic acid and catalytic amount of acetic acid, Pd(0) catalyst opts to undergo oxidation addition with acetic acid to give int-**7a**, which undergoes hydro-paladation with propiolate to give int-**7b**. Next, transmetalation of **7b** with $ArB(OH)_2$ and reductive elimination affords the final product.



Scheme 4B.3. Palladium catalyzed hydro-arylation of propiolates

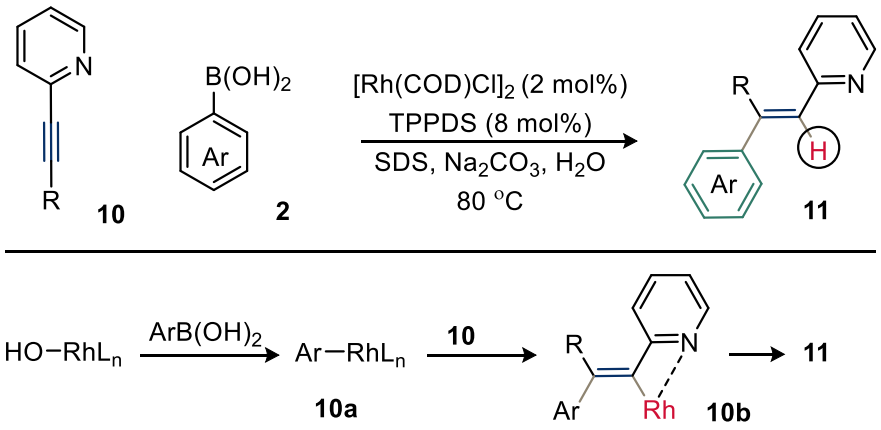
In 2014, Zhu et. al. disclosed a palladium catalyzed *trans*-addition of arylboronic acid to electron rich ynamide **8** (**Scheme 4B.4**).[7] The transformation initiates with the transmetallation of Pd(II) catalyst and aryl boronic acid **2** to form aryl palladium species **2a**. Next, *syn*-addition to keteniminium species **8a** gives vinyl palladium species **8b** which eventually isomerises to **8d** via **8c**. Finally, protonation gives the desired product **9**.



Scheme 4B.4. Pd-catalyzed catalyzed *trans*-hydro-arylation of ynamide

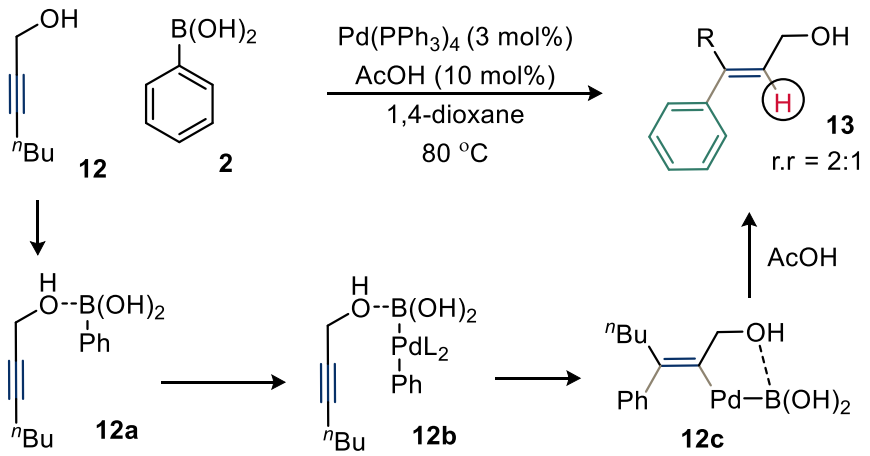
4B.2.2. Directing Group (DG) Assisted Hydro-Arylaion of Unsymmetrical Alkynes

Lauten and co-worker reported a pyridine directed rhodium catalyzed regioselective hydro-arylation of alkyne **10** to yield vinyl pyridine **11** (**Scheme 4B.5**).[7] This is the first example of DG assisted hydro-arylation of alkyne. The reaction initiates with transmetalation of arylboronic acid to Rh-I catalyst to give Ar-Rh species **10a** which undergoes regioselctive addition of aryl group to form metallocycle **10b**. Protodemetalation terminates the catalytic cycle yielding vinyl pyridines **11**.



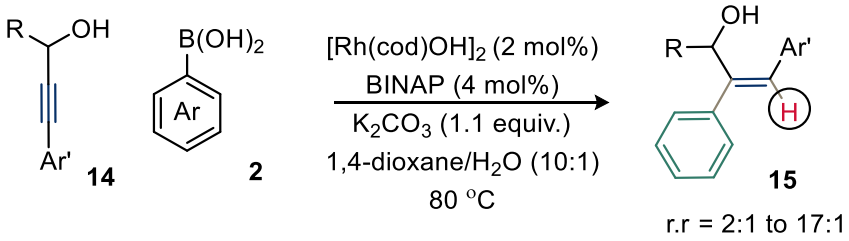
Scheme 4B.5. Pyridine directed Rh-catalyzed hydro-arylation of alkyne

Oh and co-workers reported a protocol for palladium catalyzed hydro-arylation of propargyl alcohol **12** with aryl boronic acid **2** and catalytic amount of acetic acid to yield substituted allyl alcohol **13** in moderate regioselectivity (**Scheme 4B.6**).[3b] The initial step involves co-ordination of aryl boronic acid **2** to the OH group followed by oxidative addition of Pd(0) between Ar-B bond. Next carbopalladation and protodemetalation gives the final product **13**.



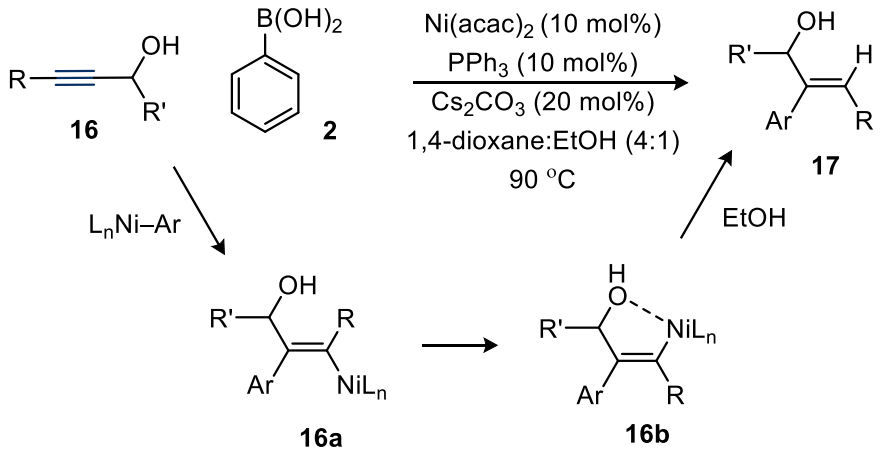
Scheme 4B.6. Palladium catalyzed hydro-aryation of propargyl alcohols

In 2011, Lauten group disclosed Rh-catalyzed hydro-arylaion of propargyl alcohol **14** in opposite regioselectivity (**Scheme 4B.7**).[8] However, in most cases the regioselectivity ratio is good to moderate. The incoming aryl group goes to the alkyne carbon having small group. At the end, water terminates the catalytic cycle via protodemtalation to provide **15**.



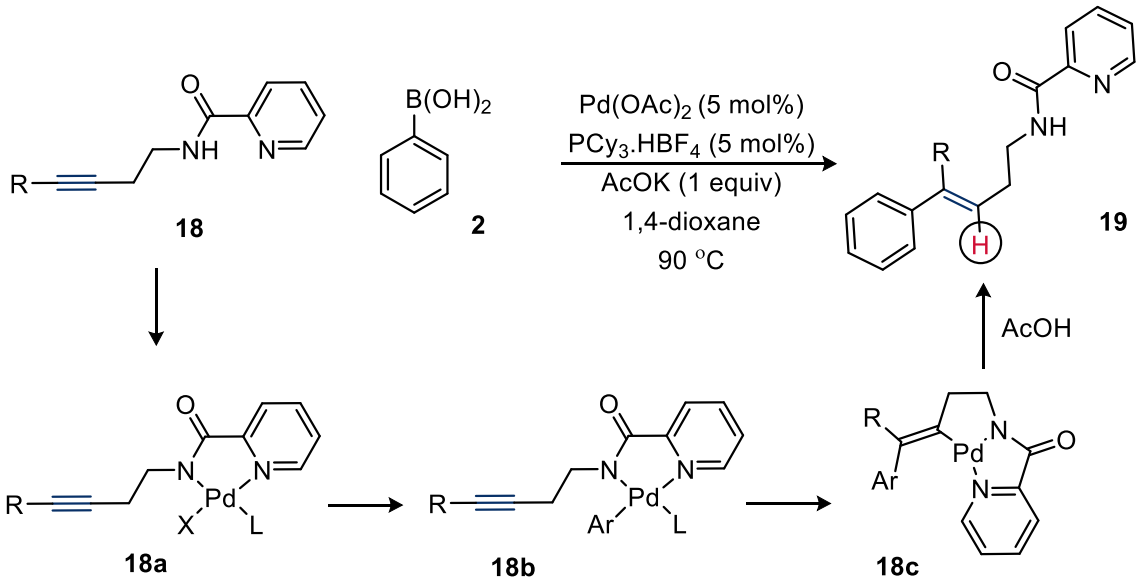
Scheme 4B.7. Palladium catalyzed hydro-aryation of propargyl alcohols

In 2017, Reddy and co-workers reported *trans*-addition of aryl boronic acid **2** to propagyl alcohols **16** under Ni-catalysis yet with moderate regioselectivity (**Scheme 4B.8**).[9] As usual, carbonickelation with **16** at first provides int-**16a**. Isomerization of int-**16a** to int-**16b** facilitates the co-ordination of Ni-complex with the alcohol moiety. Finally, protodemtalation of **16b** with ethanol yield the product **17**.



Scheme 4B.8. Ni-catalyzed trans-hydroarylation of propargyl alcohols

In 2016, Engle and co-workers showcased an interesting strategy for regioselective hydro-arylation of unsymmetrical alkynes **18** to accesss substituted homoproallyl amino derivatives **19** (**Scheme 4B.9**).[10] 2-amido pyridyl group has been used as DG under palladium catalysis. At first ligated Pd (II) complex co-ordinate to amido pyridyl group by ligand exchange, followed by transmetalation of int-**18a** with aryl boronic acid **2** gives int-**18b**. Next, aryl-paladation provides metallocycle int-**18c** which upon protodemtalation yields the final product **19**.



Scheme 4B.9. 2-Amido pyridyl directed palladium catalyzed hydro-arylation of unsymmetrical alkynes

4B.3. Motivation and Scheme Design

Despite the numerous developments made on hydro-arylation of unsymmetrical alkynes, the issue of regioselectivity and use of strong DG and external ligands significantly poses undisputed concerns. Hence, the development of DG-free regioselective hydro-arylation of unsymmetrical unbaised alkynes without any external ligands always attracts attention. We therefore embarked envisaging the cationic Pd-catalyzed regioselective hydro-arylation of propargyl acetates. Thus, the mechanistic cycle reshuffle from [transmetalation→carbometalation→protodemetalation] to [oxidative addition→carbometalation→hydride ligand substitution→reductive elemination] would enable making the hydro-arylation of unsymmetrical alkyne regioselective. Thus, cationic palladium catalyzed hydroarylation of propargyl acetate is planned (**Figure 4B.3**).[11]

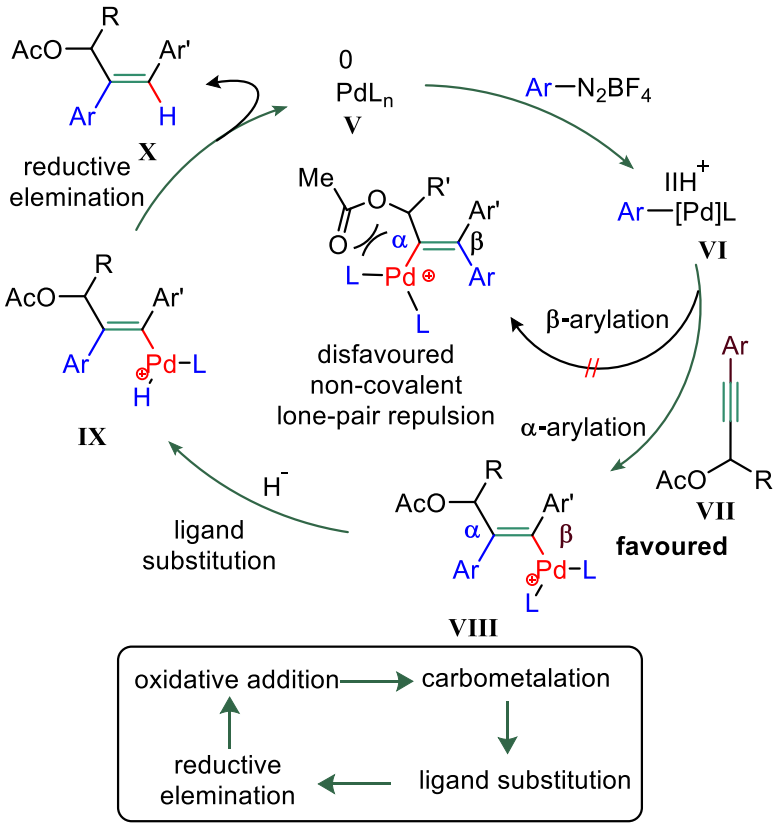


Figure 4B.3. Reaction design of regioselective hydroarylation of alkyne

The reaction possibly begins with the formation of Ar-Pd cationic species **VI** by oxidative addition of the aryl diazonium salt with Pd(0)-catalyst **V**. The aryl group insertion at the α-position of propargyl acetate **VII** then forms int-**VIII**; due to non-covalent lone pairs repulsion between the acetate group and ligated Pd species β-arylation is ruled out int-**VIII'**.[12] Finally, ligand substitution at the Pd center of int-**VIII** by hydride followed by reductive elimination produced the desired regioselective hydro-arylation product **X** (**Figure 4B.3**).

In general, propargyl acetate tends to undergo oxidative addition and isomerization to form allenyl metal complex **XII** (**Figure 4B.4**). By contrast, the use of cationic palladium species overcomes the formation of allenyl moiety in the presence of low-valent metal species.

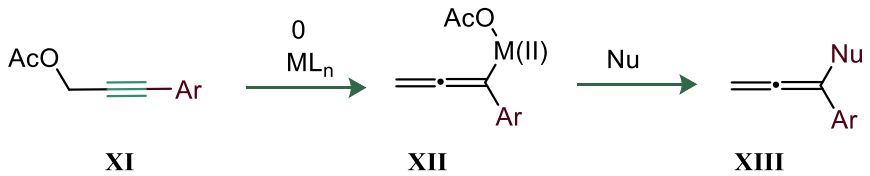


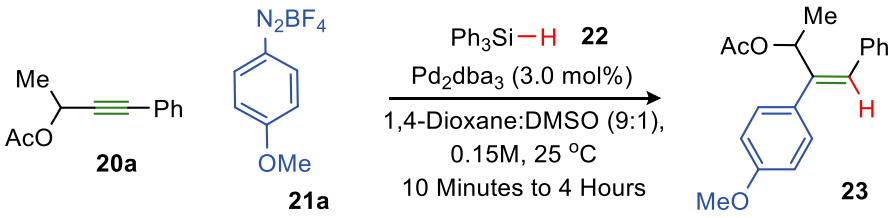
Figure 4B.4. Challenges of propargyl acetate in presence of low valent transition metal

4B.4. Result and Discussion

4B.4.1. Reaction Optimization

To investigate the hydro-arylation of structurally simple propargyl acetate, a three-component reaction of 4-phenylbut-3-yn-2-yl acetate (**20a**), *p*–methoxyphenyl diazonium tetrafluoroborate (**21a**), and triphenylsilane (**22**) in presence of $Pd_2(dba)_3$ catalyst was performed (**Table 4B.1**). To our delight, extensive screening of catalyst and solvents led us to optimized condition [**20a** (1.0 equiv), **21a** (3.0 equiv), **22** (1.2 equiv), and $Pd_2(dba)_3$ (3.0 mol%) in 1,4-dioxane/DMSO (9:1) at 25 °C, 4 h] and the desired hydro-arylation product **23** was isolated in 94% yield (entry 1, **Table 4B.1**).

Table 4B.1 Optimization of reaction conditions[a,b]



entry	conditions	**4b23** (%)
1	None	94%
2	6 mol% $Pd(dba)_2$	73%
3	$Pd_2(dba)_3 \cdot CHCl_3$	82%
4	1,4-dioxane	77%
5	DMSO	61%
6	DMF	65%
7	1,2–DME	62%
8	toluene	<5%
9	0 °C	71%
10	40 °C	75%
11	Et_3SiH as hydride source	82%
12	$PhSiH_3$ as hydride source	trace

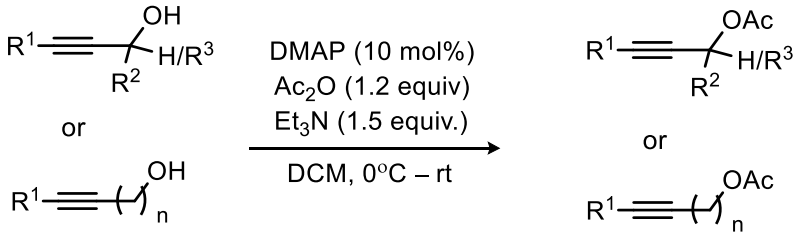
[a]Reactions were carried out using **20a** (0.1 mmol), **21a** (0.3 mmol), silane **22** (0.12 mmol) in solvent (0.15M); [b]Isolated yield.

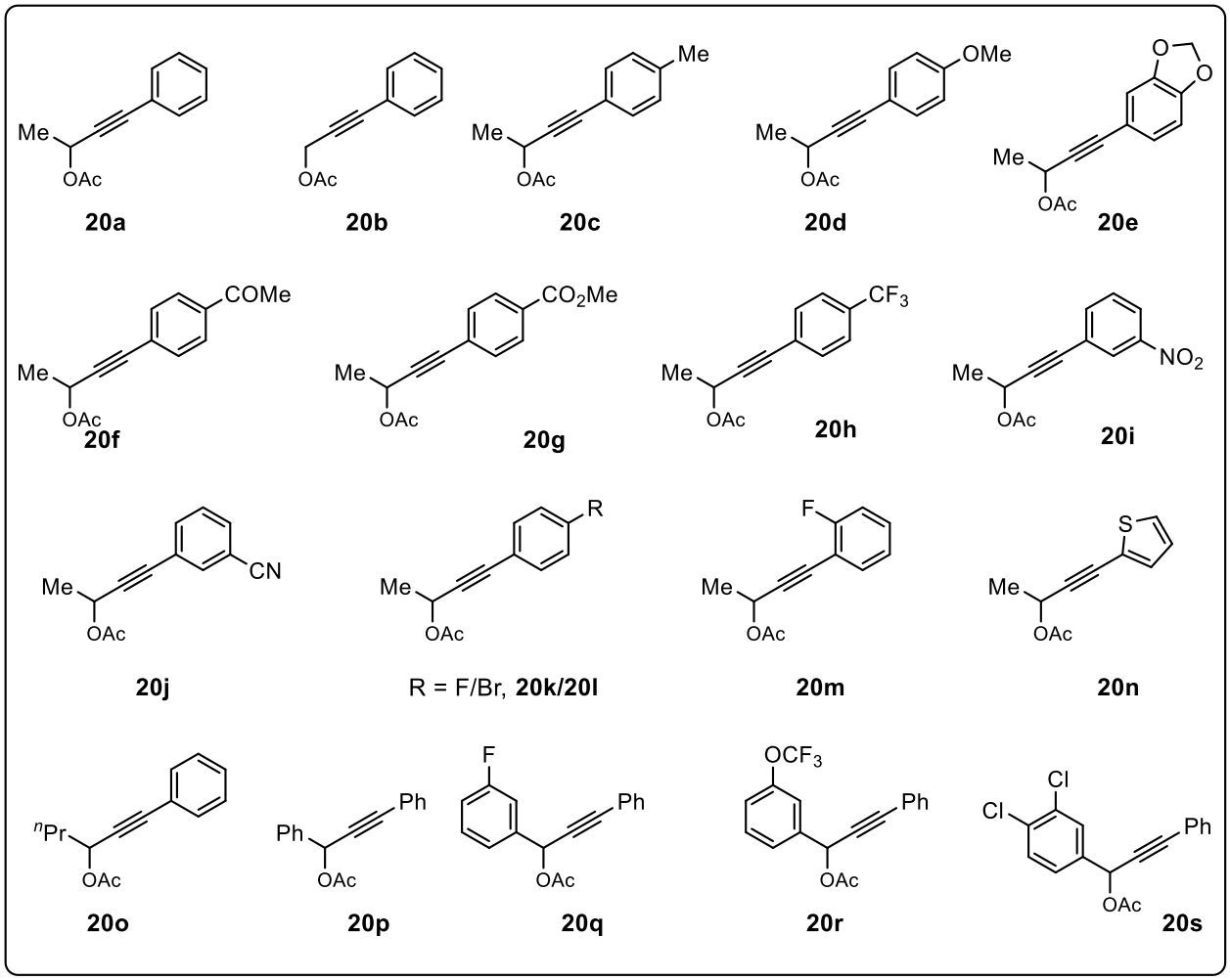
Lesser yields were observed when other Pd(0) catalysts for example [$Pd(dba_2)$ & $Pd_2(dba)_3.CHCl_3$] were tested (entry 2–3, **Table 4B.1**). Solvents like 1,4-dioxane, DMSO, DMF, 1,2-DME, and toluene were less efficient as compared to the mixture of 1,4-dioxane:DMSO (entry 4–8, **Table 4B.1**). The reaction at different temperature affected product yield (entry 9 and 10, **Table 4B.1**). Other than triphenyl silane, triethyl silane provided the desired prouct in 82% yield (entry 11, **Table 4B.1**), whereas phenyl silane ($PhSiH_3$) failed to give the final product (entry 12, **Table 4B.1)**.

4B.4.2. Synthesis of yne acetates

Following the known Cu-catalyzed C-N coupling procdure, yne-acetaes **19a-1av** were synthesized from corresponding alcohols (Table 4B.2).

Table 4B.2. Propargyl acetate chart





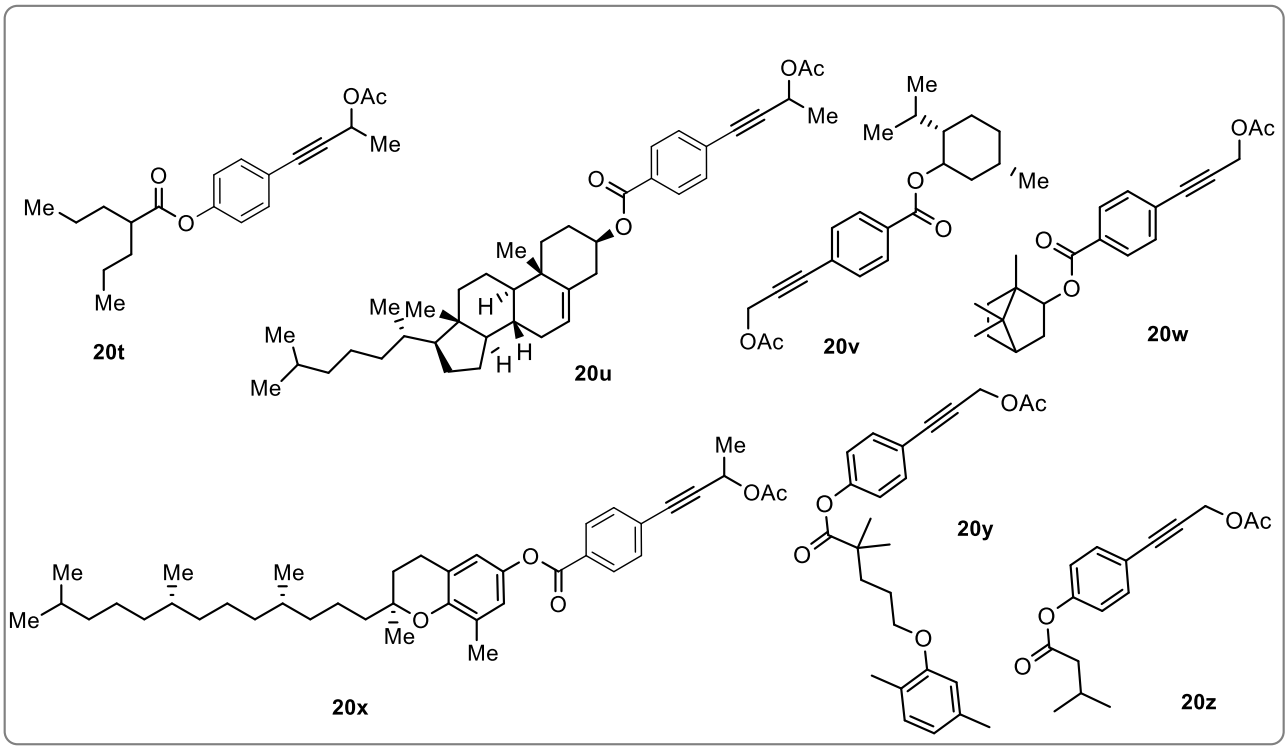
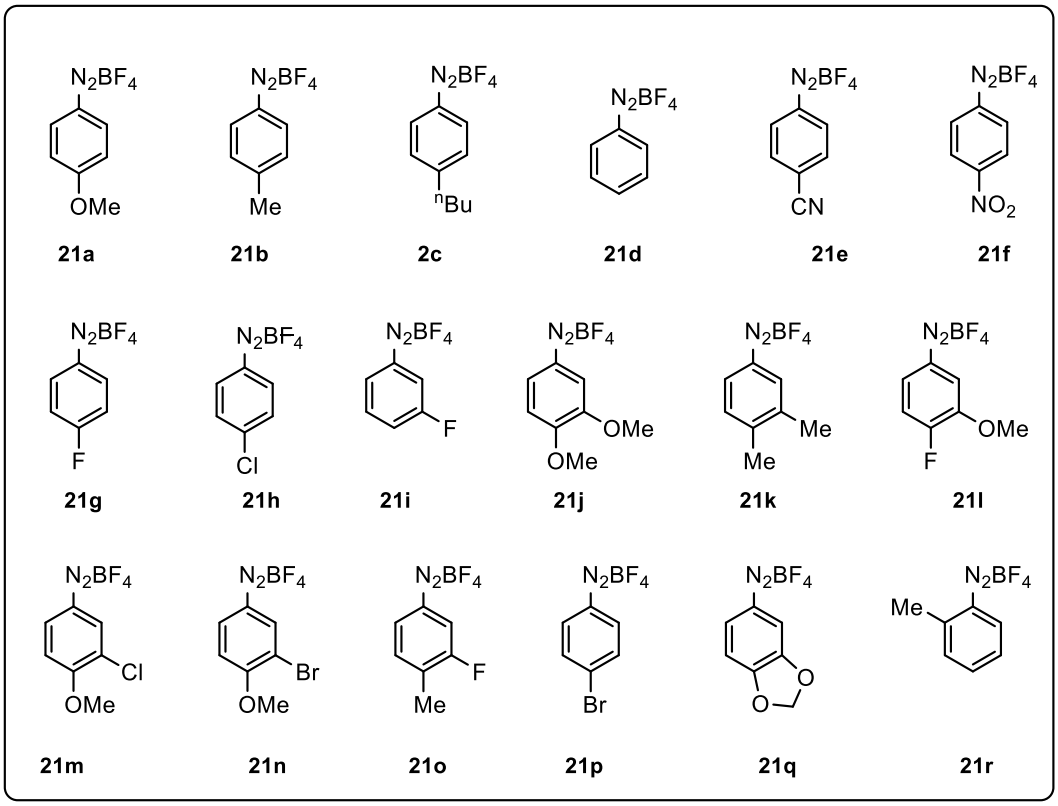
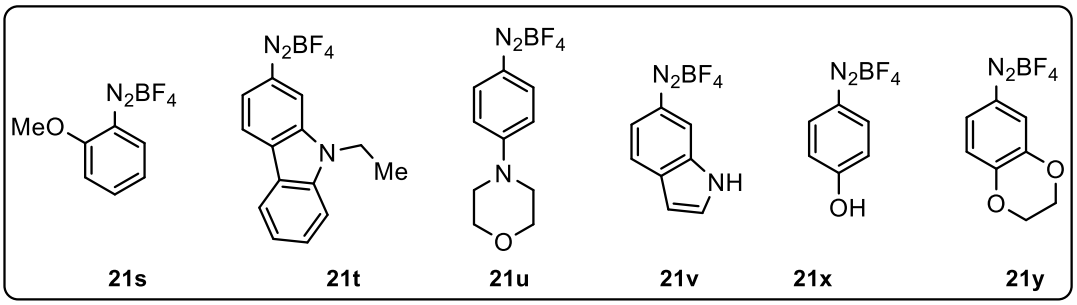


Table 4B.3. Aryl Diazonium Salt chart



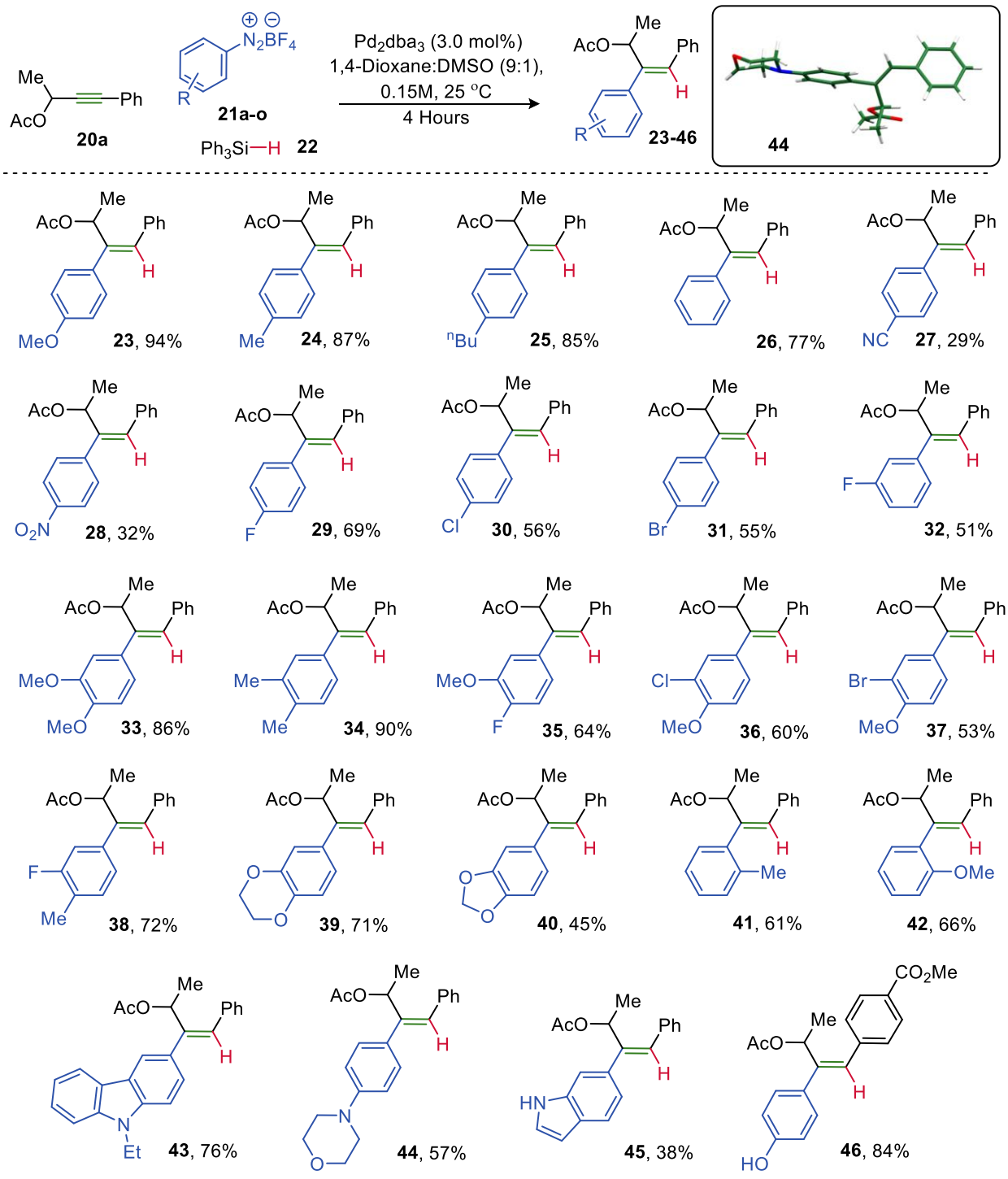


4B.4.3. Substrate Scope-I

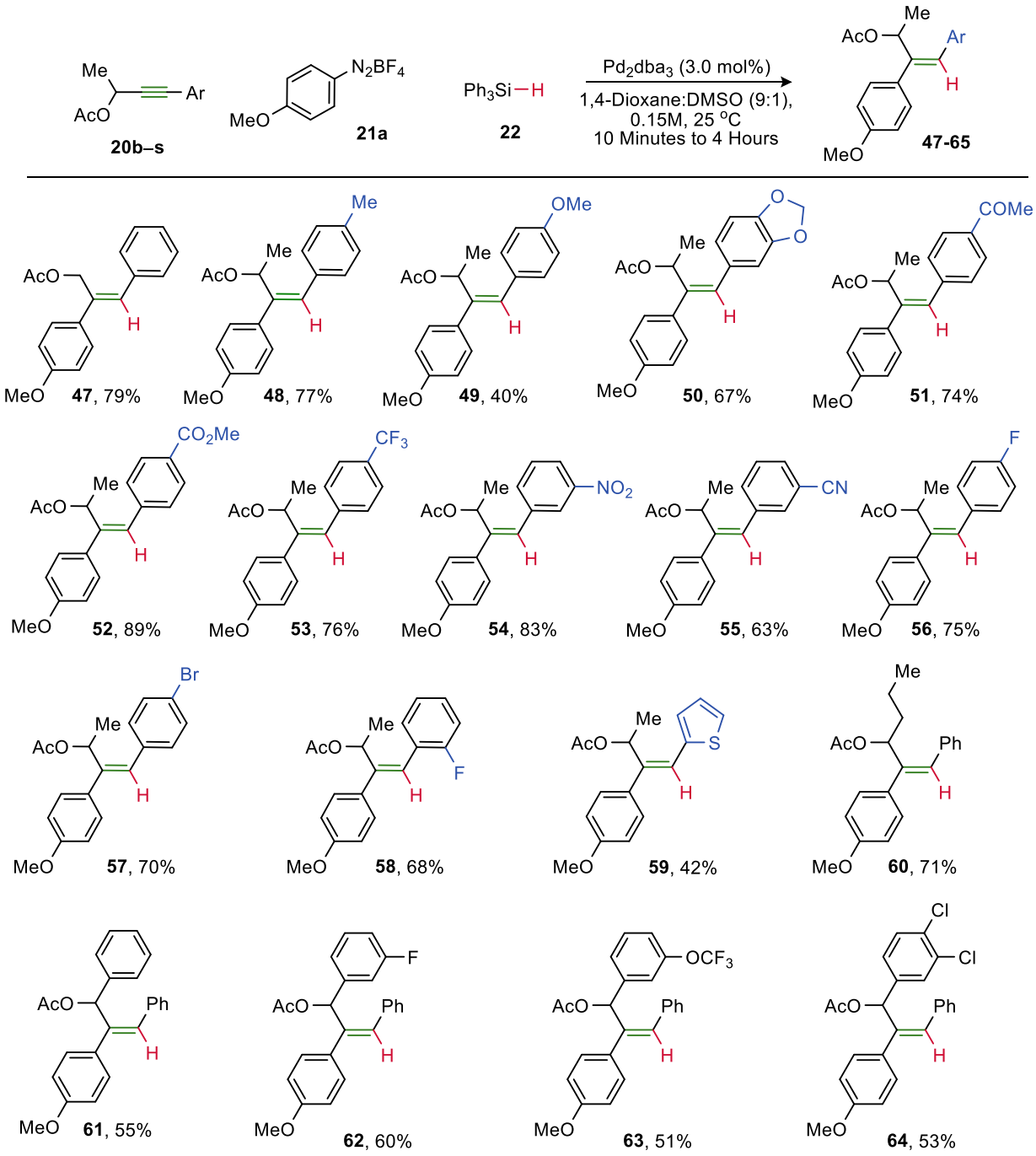
With the optimized conditions outlined in entry 1, **Table 4B.1**, the scope of aryl diazonium tetrafluoroborate salts were probed by independently exposing **20a** and **22** (**Scheme 4B.10**). Aryl diazonium salts having electron donating [OMe, Me, ^{n}Bu] groups at the *para*-position reacted efficiently affording **23**–**25** in excellent yields. Neutral phenyl diazonium salt did not affect the reaction yield. Pleasingly, highly reactive and unstable under Pd(0), the electron withdrawing *p*-CN and *p*-NO_2 benzene diazonium salts provided the products **27** and **28** albeit in low yields. The aryl diazonium salt having transformable halogens at both *para* and *meta* positions were well tolerated yielding **29-32**. The sterically crowded and electronically biased *meta-para* disubstituted aryl-diazonium salts were efficient in producing hydroarylation products **33-40** with good to excellent yields. The reaction outcome was unaffected by *ortho* substituted aryl diazonium salts constructing **41**–**42** in 61–66% yield. Moderate to good yields of **43**–**45** was observed upon independent reaction of heterocycle, for example: carbazole, morpholine, and indole containing aryl diazonium salts with propargyl acetate **20a**. It is worth noting that even free -OH group was well tolerated providing **46** in excellent yield.

4B.4.4. Substrate Scope-II

The scope of propargyl acetates (**20b**–**s**) for the reaction with **21a** was next explored (**Scheme 4B.11**). The propargyl acetates [**20b**–**20c**; having electron neutral, electron-rich (*p*-Me, *p*-OMe, and *m,p*-methylenedioxy) and electron deficient (*p*-COMe, *p*-COOMe, *p*-CF_3, *m*-NO_2, and *m*-CN) substituted arene in alkyne-terminus] effectively reacted with **21a** to provide **47**–**55** in excellent yields. Once again, reaction probed to be efficient in



Scheme 4B.10. Scope of aryl-diazonium tetrafluoroborate salts[a] Reactions were carried out using **20a/g** (0.3 mmol), **21** (0.9 mmol), silane **22** (0.36 mmol) in 1,4-dioxane:DMSO (9:1; 0.15M).



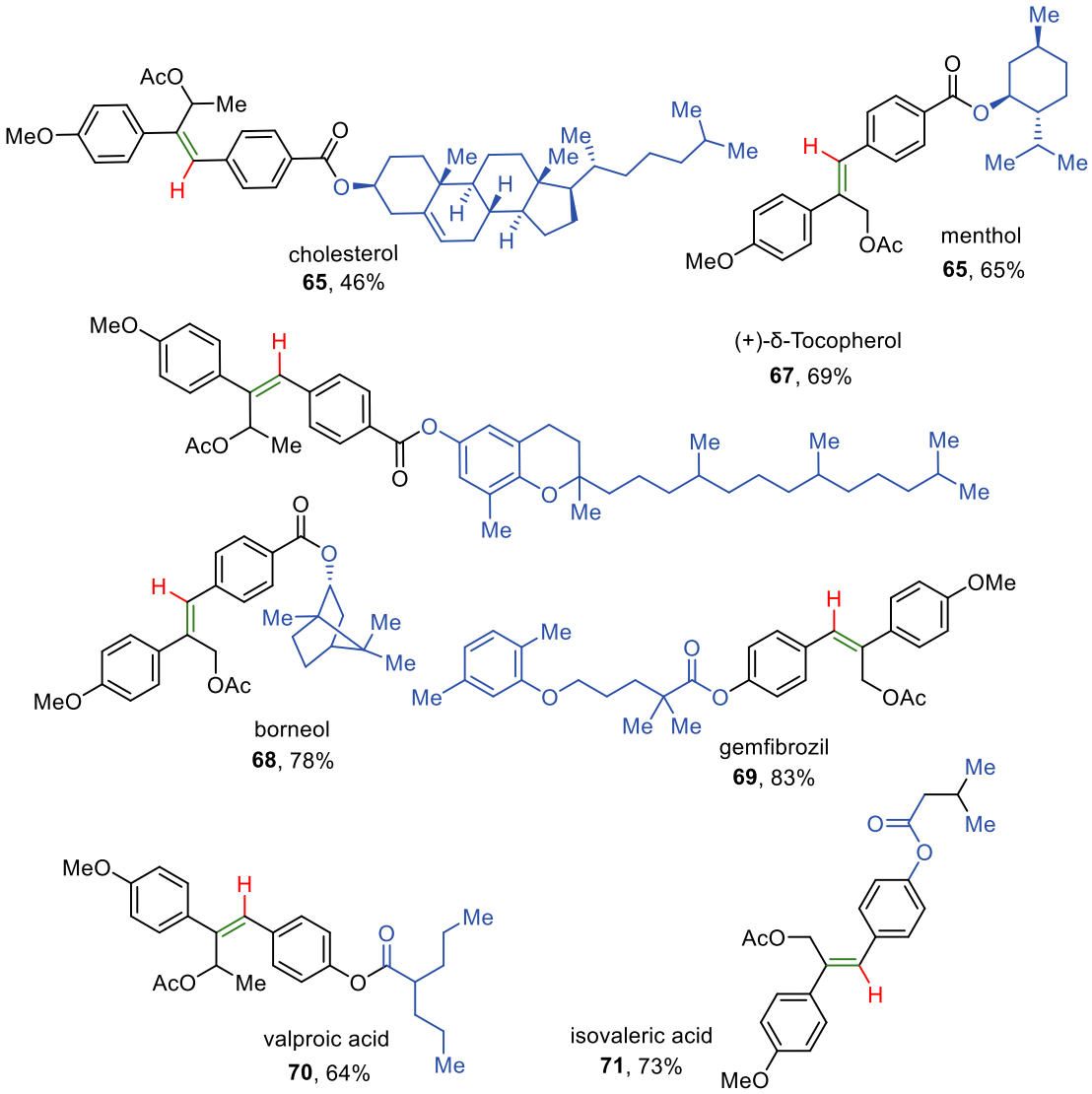
Scheme 4B.11: Scope of propargyl acetates[a] [a]Reactions were carried out using **20** (0.3 mmol), **21a** (0.9 mmol), silane **4b22** (0.36 mmol) in 1,4-dioxane:DMSO (9:1; 0.15M).

tolerating the transformable halogen groups and provided the final products **56**–**57**. Yield as well as regioselectivity was not affected by the *ortho*-fluoro-aryl substituted propargyl acetate affording **58**. Delightfully, thiophene substituted propargyl acetate also

participated and delivered the desired product **59** in moderate yield. Irrespective of *n*-propyl and various aryl-moieties at the propargyl position of PAs, the hydro-arylation was equally effective in making **60**–**64**.

4B.4.5. Substrate Scope-III

In the sustainable development of complex molecules with enhanced pharmacokinetic properties, late-stage difunctionalization of unsymmetrical alkynes with biologically



Scheme 4B.12: Late-stage hydro-arylation of BRMs [a]Reactions were carried out using **20t-z** (0.3 mmol), **21a** (0.9 mmol), silane **22** (0.36 mmol) in 1,4-dioxane:DMSO (9:1; 0.15M).

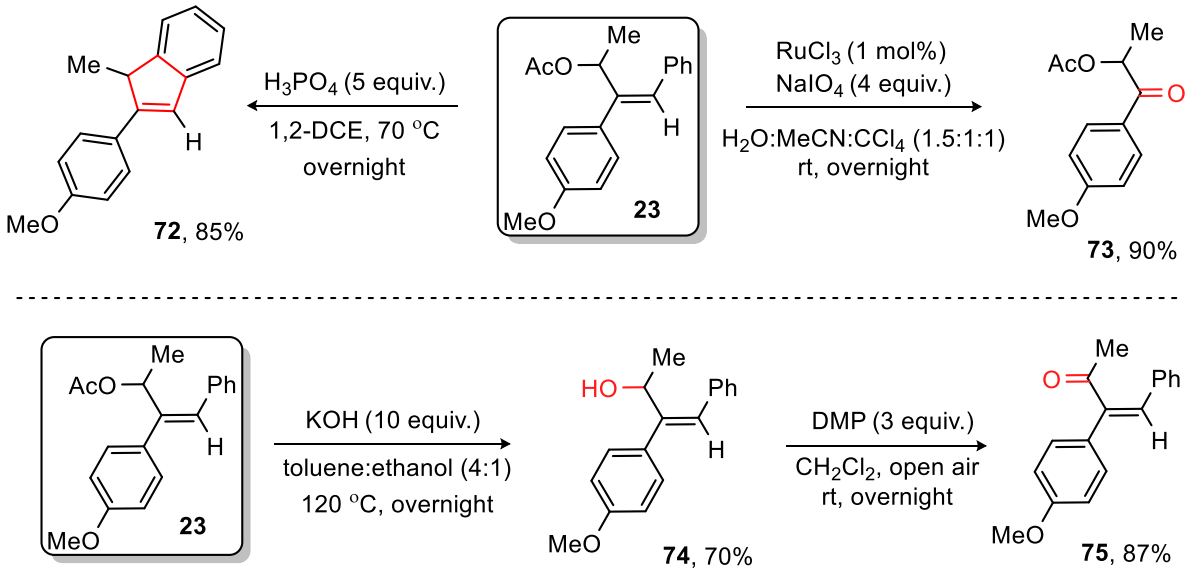
relevant motifs (BRMs) is invaluable. BRMs with polar groups and unsaturated moieties can typically cause problems for cross-coupling reactions, as their TM binding capability may lead to substrate decomposition. Thus, the cationic Pd-catalyzed hydro-arylation of pharmacophore-coupled alkynes **20t–z** was investigated (**Scheme 4B.12**). Once again, the title reaction proved reliable: tri-substituted allyl acetates encapsulated steroid [cholesterol (**65**)], terpenoid [menthol (**66**)], fatty alcohol [vitamin-E-tocopherol (**67**)], and borneol (**68**) were produced in 46–78% yields from the hydro-arylation of respective BRMs-coupled propargyl acetates with **21a** and **22**. The efficacy of the regioselective hydro-arylation using marketed drug molecules containing unsymmetrical alkynes was next probed. Thus, reaction of the [(abnormal blood lipid level preventer gemifrozil), and (anti-epileptic drug, bipolar disorder, and migraine preventer valproic acid)] coupled propargyl acetate with **21a** and **22** provided highly substituted allyl acetate **69** and **70** in good yield. Likewise, isobutyric acid containing allyl acetate **71** was made in 73% yield.

4B.4.6. Synthetic application

Bronsted acid mediated fridel-craft cyclization of tri-substituted allyl acetate **23** gives the highly substituted indene **72** (**Scheme 4B.13**). Ru-catalyzed oxidative cleavage of the substituted olefin **23** provides α-acetyl ketone **73**. KOH mediated acetate deprotection followed by DMP assited oxidation provided vinyl ketone **75**.

4B.5. Conclusion

In summary, a regioselective hydro-arylation of unsymmtrical alkynes (yne-acetates) has been developed. The reaction is general having a broad substrate scope with excellent functional group tolerance. Synthetic potential of unusual tri-substituted allyl acetate has also been demonstrated.



Scheme 4B.13: Synthetic versatility

4B.6. Experimental Section

4B.6.1. General Information

All the reactions were performed in oven-dried sealed tubes. Commercial grade solvents were distilled prior to use. Column chromatography was performed using either 100-200 Mesh or 230-400 Mesh silica gel or neutral alumina. Thin layer chromatography (TLC) was performed on silica gel GF254 plates and alumina plates.

Proton, carbon, and fluorine nuclear magnetic resonance spectra (^{1}H NMR, ^{13}C NMR, and ^{19}F NMR) were recorded based on the resonating frequencies as follows:(^{1}H NMR, 400 MHz; ^{13}C NMR, 101 MHz; ^{19}F NMR, 376 MHz), (^{1}H NMR, 500 MHz; ^{13}C NMR, 126 MHz; ^{19}F NMR, 470 MHz) and (^{1}H NMR, 600 MHz; ^{13}C NMR, 151 MHz) having the solvent resonance as internal standard (^{1}H NMR, $CDCl_3$ at 7.26 ppm; ^{13}C NMR, $CDCl_3$ at 77.0 ppm). Few cases tetramethylsilane (TMS) at 0.00 ppm was used as reference standard. Data for ^{1}H NMR are reported as follows: chemical shift (ppm), multiplicity (s = singlet; br s = broad singlet; d = doublet; br d = broad doublet, t = triplet; br t = broad triplet; q = quartet; m = multiplet; tt = triplet of triplet; dt = doublet of triplet), coupling constant, *J*, in (Hz), and integration. Data for ^{13}C NMR, ^{19}F NMR were reported in terms of chemical shift (ppm). IR spectra were reported in cm^{-1}. High resolution mass spectra were obtained in ESI mode. Melting points were determined by electro-thermal heating and are uncorrected. X-ray data was collected at 293 K using graphite monochromated Mo-Kα radiation (0.71073 Å).

4B.6.2. Materials

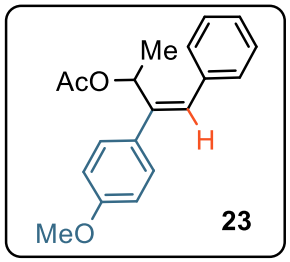
Unless otherwise noted, all the reagents and intermediates were obtained commercially and used without purification. Toluene and 1,4-dioxane were distilled over CaH_2. $Pd_2(dba)_3$ and aryl boronic acids were purchased from commercially available source, and used as received. Analytical and spectral data of all the known compounds are exactly matching with the reported values.

4B.6.3. General procedure and spectral/analytical data

4B.6.3.1. General Procedure for hydro-arylation.

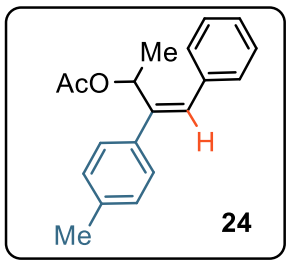
To a mixture of **20** (0.3 mmol), aryl(hetero) diazonium-tetrafluoroborate **21** (0.9 mmol), triphenyl silane **22** (0.45 mmol), and $Pd_2(dba)_3$ (0.009 mmol) was added 1,4-dioxane:DMSO (9:1, 2.0 mL). The reaction mixture was stirred at 25 °C for 10 min to 4 h. The reaction progress was periodically monitored by TLC. The reaction mixture was diluted with EtOAc (20 mL) and washed with water (3 × 10 mL) and brine. The organic layer was dried over Na_2SO_4. The solvent was evaporated and purified by column chromatography over neutral alumina eluting with EtOAc/hexane to afford desired product.

(*Z*)-3-(4-Methoxyphenyl)-4-phenylbut-3-en-2-yl acetate (23):



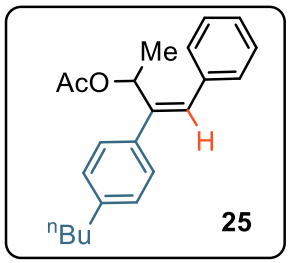
23 (52 mg, 87%) was obtained as red liquid; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO D_6) δ 7.46 (dt, J = 9.5, 2.6 Hz, 2H), 7.40 (t, J = 7.5 Hz, 2H), 7.34–7.28 (m, 3H), 6.96 (dt, J = 9.2, 2.5 Hz, 2H), 6.69 (s, 1H), 5.99 (q, J = 6.7 Hz 1H), 3.78 (s, 3H), 1.93 (s, 3H), 1.31 (d, J = 7.0 Hz, 3H) ; ^{13}C NMR (126 MHz, DMSO D_6) δ 169.8, 159.1, 140.9, 136.9, 132.4, 131.0, 129.9, 129.2, 128.8, 127.6, 114.0, 69.0, 55.5, 21.4, 20.1; IR (Neat) ν_{max} 2924, 1733, 1604, 1508, 1369, 1234, 1030, 822 cm^{-1}; **HRMS (ESI)** for $C_{19}H_{20}NaO_3^+$ $(M+Na)^+$: calcd. 319.1305 found 319.1308.

(*Z*)-4-Phenyl-3-(*p*-tolyl)but-3-en-2-yl acetate (24):



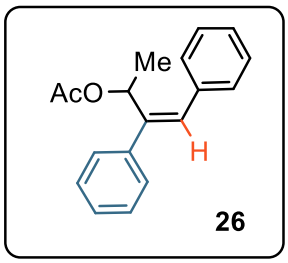
24 (49 mg, 87%) as red liquid; R_f = 0.6 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO D_6) δ 7.44–7.37(m, 4H), 7.34–7.29 (m, 3H), 7.21 (d, J = 8.0 Hz, 2H), 6.70 (s, 1H), 5.98 (q, J = 6.5 Hz, 1H), 2.33 (s, 3H), 1.92 (s, 3H), 1.31 (d, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, DMSO D_6) δ 169.8, 141.3, 137.3, 137.1, 136.8, 131.4, 129.22, 129.19, 128.8, 128.6, 127.7, 68.9, 21.4, 21.2, 20.0; IR (Neat) ν_{max} 2923, 1734, 1510, 1369, 1233, 1038, 811 cm^{-1}; **HRMS (ESI)** for $C_{19}H_{20}NaO_2^+$ $(M+Na)^+$: calcd. 303.1356 found 303.1356.

(*Z*)-3-(4-Butylphenyl)-4-phenylbut-3-en-2-yl acetate (25):



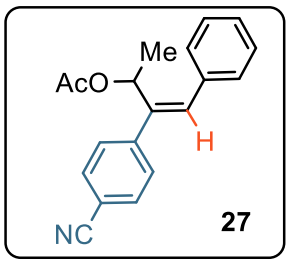
25 (55 mg, 85%) as yellow liquid; R_f = 0.6 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO-D$_6$) δ 7.45–7.57 (m, 4H), 7.34–7.26 (m, 3H), 7.21 (d, *J* = 8.0 Hz, 2H), 6.71 (s, 1H), 5.98 (q, *J* = 6.7 Hz, 1H), 2.60 (t, *J* = 7.8 Hz, 2H), 1.92 (s, 3H), 1.62-1.52 (m, 2H), 1.37-1.28 (m, 5H), 0.91 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO-D$_6$) δ 169.8, 142.0, 141.3, 137.6, 136.8, 131.5, 129.2, 128.8, 128.6, 128.5, 127.7, 68.9, 35.0, 33.5, 22.3, 21.4, 20.0, 14.3; IR (Neat) ν_{max} 2927, 1736, 1619, 1369, 1236, 839 cm^{-1}; **HRMS (ESI)** for $C_{22}H_{26}NaO_2^+$ (M+Na)$^+$: calcd. 345.1825 found 345.1828.

(*Z*)-3,4-Diphenylbut-3-en-2-yl acetate (26):



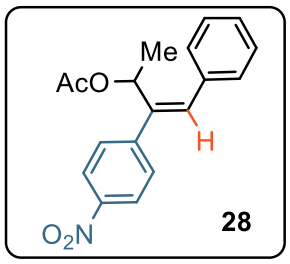
26 (41 mg, 77%) as red liquid; R_f = 0.7 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO D$_6$) δ 7.54–7.48 (m, 2H), 7.44–7.38 (m, 4H), 7.37–7.29 (m, 4H), 6.73 (s, 1H), 6.00 (q, *J* = 6.5 Hz, 1H), 1.93 (s, 3H), 1.31 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, DMSO D$_6$) δ 169.8, 141.5, 140.3, 136.7, 132.0, 129.2, 128.81, 128.76, 128.6, 127.9, 127.8, 68.8, 21.3, 20.0; IR (Neat) ν_{max} 2924, 1736, 1445, 1370, 1237, 1041, 936 cm^{-1}; **HRMS (ESI)** for $C_{18}H_{18}NaO_2^+$ (M+Na)$^+$: calcd. 289.1199 found 289.1199.

(*Z*)-3-(4-Cyanophenyl)-4-phenylbut-3-en-2-yl acetate (27):



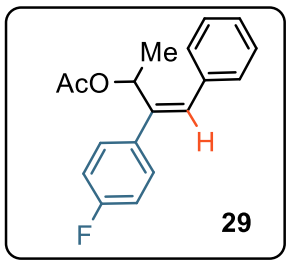
27 (17 mg, 29%) as colorless liquid; R_f = 0.4 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO D$_6$) δ 7.88 (d, *J* = 8.5 Hz, 2H), 7.73 (d, *J* = 8.5 Hz, 2H), 7.43 (t, *J* = 7.5 Hz, 2H), 7.39-7.32- (m, 3H), 6.88 (s, 1H), 6.01 (q, *J* = 6.7 Hz, 1H), 1.95 (s, 3H), 1.33 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, DMSO D$_6$) δ 169.7, 145.1, 140.0, 136.1, 133.9, 132.6, 129.7, 129.3, 128.9, 128.2, 119.3, 110.6, 68.5, 21.3, 20.0; IR (Neat) ν_{max} 2927, 2227, 1735, 1602, 1370, 1232, 1039, 845cm^{-1}; **HRMS (ESI)** for $C_{19}H_{17}NNaO_2^+$ (M+Na)$^+$: calcd. 314.1151 found 314.1155.

(*Z*)-3-(4-Nitrophenyl)-4-phenylbut-3-en-2-yl acetate (28):



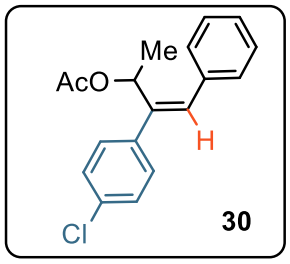
28 (20 mg, 32%) as red liquid; R_f = 0.4 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO-D$_6$) δ 8.27 (dt, J = 9.3, 2.3 Hz, 2H), 7.82 (dt, J = 9.3, 2.3 Hz, 2H), 7.49-7.41 (m, 2H), 7.40-7.33 (m, 3H), 6.93 (s, 1H), 6.03 (q, J = 6.7 Hz, 1H), 1.96 (s, 3H), 1.36 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO-D$_6$) δ 169.8, 147.1, 139.7, 136.1, 134.3, 130.1, 129.3, 129.0, 128.3, 123.8, 68.4, 21.4, 20.0; IR (Neat) ν_{max} 2929, 1735, 1594, 1515, 1341, 1231, 1039, 853 cm^{-1}; **HRMS (ESI)** for $C_{18}H_{17}NNaO_4^+$ $(M+Na)^+$: calcd. 334.1050 found 334.1054.

(*Z*)-3-(4-Fluorophenyl)-4-phenylbut-3-en-2-yl acetate (29):



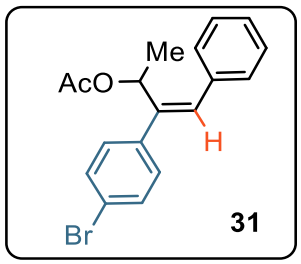
29 (39 mg, 69%) as red liquid; R_f = 0.7 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO D$_6$) δ 7.58–7.51(m, 2H), 7.41 (t, J = 7.5 Hz, 2H), 7.35–7.28 (m, 3H), 7.23 (tt, J = 8.8, 2.3 Hz, 2H), 6.73 (s, 1H), 5.96 (q, J = 6.7 Hz, 1H), 1.94 (s, 3H), 1.30 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO D$_6$) δ 169.8, 162.1 (d, J = 244.4 Hz, 1C), 140.4, 136.5, 132.2, 130.8 (d, J = 8.8 Hz, 1C), 129.0 (d, J = 50.4 Hz, 2C), 127.9, 115.4 (d, J = 21.4 Hz, 2C), 68.7, 21.3, 19.9; ^{19}F NMR (471 MHz) δ −115.1; IR (Neat) ν_{max} 2925, 1735, 1599, 1506, 1222, 1039, 837 cm^{-1}; **HRMS (ESI)** for $C_{18}H_{17}FNaO_2^+$ $(M+Na)^+$: calcd. 307.1105 found 307.1101.

(*Z*)-3-(4-Chlorophenyl)-4-phenylbut-3-en-2-yl acetate (30):



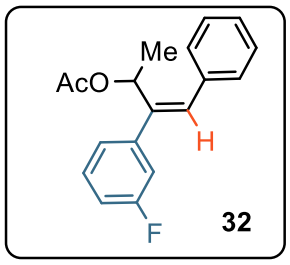
30 (33 mg, 55%) as light yellow liquid; R_f = 0.7 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO-D$_6$) δ 7.54 (dt, J = 8.8, 2.3 Hz, 2H), 7.47 (dt, J = 8.8, 2.3 Hz, 2H), 7.42 (t, J = 7.5 Hz, 2H), 7.36–7.30 (m, 3H), 6.77 (s, 1H), 5.98 (q, J = 6.7 Hz, 1H), 1.94 (s, 3H), 1.31 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO-D$_6$) δ 169.8, 140.2, 139.0, 136.4, 132.7, 132.5, 130.6, 129.2, 128.9, 128.6, 127.9, 68.6, 21.4, 20.0; IR (Neat) ν_{max} 2923, 1736, 1600, 1507, 1225, 1040, 838 cm^{-1}; **HRMS (ESI)** for $C_{18}H_{17}ClNaO_2^+$ $(M+Na)^+$: calcd. 323.0806, found 323.0809.

(*Z*)-3-(4-Bromophenyl)-4-phenylbut-3-en-2-yl acetate (31):



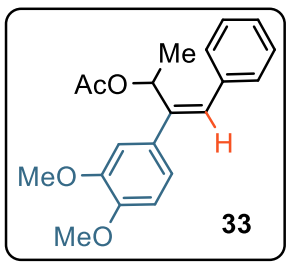
31 (39 mg, 56%) as red liquid; R_f = 0.7 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO-D$_6$) δ 7.60 (dt, J = 8.8, 2.3 Hz, 2H), 7.47 (dt, J = 8.8, 2.3 Hz, 2H), 7.42 (t, J = 7.5 Hz, 2H), 7.36-7.30 (m, 3H), 6.77 (s, 1H), 5.98 (q, J = 6.7 Hz, 1H), 1.94 (s, 3H), 1.31 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO-D$_6$) δ 169.7, 140.3, 139.4, 136.4, 132.5, 131.5, 130.9, 129.2, 128.8, 127.9, 121.3, 68.6, 21.3, 20.0; IR (Neat) ν_{max} 2979, 1734, 1486, 1368, 1230, 1008, 934, 814 cm^{-1}; **HRMS (ESI)** for $C_{18}H_{17}BrNaO_2^+$ $(M+Na)^+$: calcd. 367.0304 found 367.0304.

(*Z*)-3-(3-Fluorophenyl)-4-phenylbut-3-en-2-yl acetate (32):



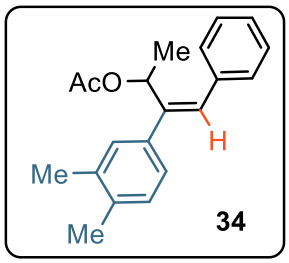
32 (29 mg, 51%) as red liquid; R_f = 0.7 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO-D$_6$) δ 7.49-7.44 (m, 1H), 7.42 (t, J = 7.5 Hz, 2H), 7.58 (dt, J = 8.0, 1.3 Hz, 1H), 7.35-7.29 (m, 4H), 7.23-7.15 (m, 1H), 6.83 (s, 1H), 5.99 (q, J = 6.7 Hz, 1H), 1.96 (s, 3H), 1.32 (d, J = 6.5 Hz, 3H) ; ^{13}C NMR (126 MHz, DMSO-D$_6$) δ 169.8, 162.3 (d, J = 244.4 Hz, 1C), 142.6 (d, J = 7.6 Hz, 1C), 140.1, 136.4, 132.9, 130.6 (d, J = 7.6 Hz, 1C), 129.3, 128.8, 128.0, 125.0 (d, J = 2.5 Hz, 1C), 115.5 (d, J = 21.4 Hz, 1C), 114.7 (d, J = 21.4 Hz, 1C), 68.6, 21.3, 19.9; ^{19}F NMR (471 MHz) δ –113.2; IR (Neat) ν_{max} 2923, 1735, 1600, 1507, 1370, 1224, 1158, 838 cm^{-1}; **HRMS (ESI)** for $C_{18}H_{17}FNaO_2^+$ $(M+Na)^+$: calcd. 307.1105 found 307.1105.

(*Z*)-3-(3,4-Dimethoxyphenyl)-4-phenylbut-3-en-2-yl acetate (33):



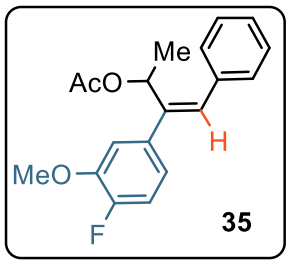
33 (56 mg, 86%) as colorless liquid; R_f = 0.2 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO-D$_6$) δ 7.40 (t, J = 7.8 Hz, 2H), 7.35-7.25 (m, 3H), 7.10 (d, J = 1.5 Hz, 1H), 7.07 (dd, J = 8.5, 2.0 Hz, 1H), 6.97 (d, J = 8.5 Hz, 1H), 6.74 (s, 1H), 6.00 (q, J = 6.5 Hz 1H), 3.80 (s, 3H), 3.78 (s, 3H), 1.95 (s, 3H), 1.32 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO-D$_6$) δ 169.8, 148.9, 148.6, 141.0, 136.9, 132.8, 131.1, 129.2, 128.8, 127.6, 121.2, 112.6, 111.9, 69.0, 55.94, 55.92, 21.4, 20.1; IR (Neat) ν_{max} 2932, 1732, 1511, 1368, 1234, 1025, 855 cm^{-1}; **HRMS (ESI)** for $C_{20}H_{22}NaO_4^+$ $(M+Na)^+$: calcd. 349.1410 found 349.1410.

(*Z*)-3-(3,4-Dimethylphenyl)-4-phenylbut-3-en-2-yl acetate (34):



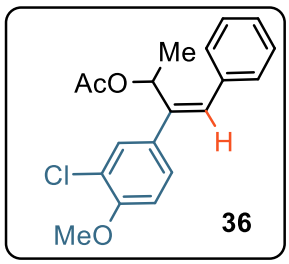
34 (53 mg, 90%) yellow liquid; R_f = 0.6 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO-D$_6$) δ 7.43-7.36 (m, 2H), 7.34-7.28 (m, 3H), 7.26 (s, 1H), 7.18 (dd, J = 8.0, 1.5 Hz, 1H), 7.15 (d, J = 8.0 Hz, 1H), 6.68 (s, 1H), 5.96 (q, J = 6.5 Hz 1H), 2.26 (s, 3H), 2.24 (s, 3H), 1.92 (s, 3H), 1.30 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO-D$_6$) δ 169.8, 141.5, 137.8, 136.8, 136.3, 135.9, 131.3, 129.9, 129.6, 128.8, 127.6, 126.1, 69.0, 21.4, 20.1, 20.0, 19.5; IR (Neat) ν_{max} 2920, 1733, 1445, 1371, 1233, 1039, 826 cm^{-1}; **HRMS (ESI)** for $C_{20}H_{22}NaO_2^+$ (M+Na)$^+$: calcd. 317.1512 found 317.1512.

(Z)-3-(3-Fluoro-4-methoxyphenyl)-4-phenylbut-3-en-2-yl acetate (35):



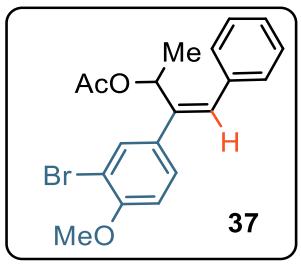
35 (40 mg, 64%) as yellow liquid; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO-D$_6$) δ 7.44-7.35 (m, 3H), 7.34-7.27 (m, 4H), 7.19 (t, J = 8.8 Hz, 1H), 6.77 (s, 1H), 5.98 (q, J = 6.7 Hz, 1H), 3.87 (s, 3H), 1.95 (s, 3H), 1.32 (d, J = 6.5 Hz, 3H) ; ^{13}C NMR (126 MHz, DMSO-D$_6$) δ 169.7, 151.3 (d, J = 243.2 Hz, 1C), 147.0 (d, J = 11.3 Hz, 1C), 139.8, 136.6, 132.9 (d, J = 5.0 Hz, 1C), 131.9, 129.2, 128.8, 127.8, 125.1 (d, J = 2.5 Hz, 1C), 116.1 (d, J = 17.6 Hz, 1C), 114.0, 69.0, 56.4, 21.3, 20.0; ^{19}F NMR (471 MHz) δ −135.5; IR (Neat) ν_{max} 2922, 1734, 1513, 1445, 1233, 1025, 875 cm^{-1}; **HRMS (ESI)** for $C_{19}H_{19}FNaO_3^+$ (M+Na)$^+$: calcd. 337.1210 found 337.1211.

(Z)-3-(3-Chloro-4-methoxyphenyl)-4-phenylbut-3-en-2-yl acetate (36):



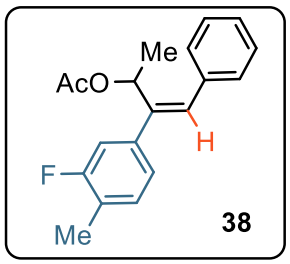
36 (40 mg, 60%) as yellow liquid; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO-D$_6$) δ 7.56 (d, J = 7.0 Hz, 1H), 7.48 (dd, J = 8.5, 2.5 Hz, 1H), 7.46-7.37 (m, 2H), 7.35-7.29 (m, 3H), 7.18 (d, J = 9.0 Hz, 1H), 6.75 (s, 1H), 5.97 (q, J = 6.5 Hz, 1H), 3.89 (s, 3H), 1.95 (s, 3H), 1.31 (d, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, DMSO-D$_6$) δ 169.7, 154.4, 139.6, 136.6, 133.4, 132.0, 130.0, 129.2, 128.8, 127.8, 121.1, 112.9, 68.8, 56.6, 21.3, 20.0; IR (Neat) ν_{max} 2927, 1733, 1500, 1369, 1233, 1037, 1067, 809 cm^{-1}; **HRMS (ESI)** for $C_{19}H_{19}ClNaO_3^+$ (M+Na)$^+$: calcd. 353.0915 found 353.0913.

(Z)-3-(3-Bromo-4-methoxyphenyl)-4-phenylbut-3-en-2-yl acetate (37):



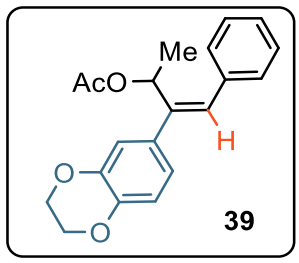
37 (40 mg, 53%) as red liquid; R_f = 0.4 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO-D$_6$) δ 7.59 (d, J = 8.5 Hz, 1H), 7.42 (t, J = 7.5 Hz, 2H), 7.38-7.30 (m, 3H), 7.19 (d, J = 2.0 Hz, 1H), 7.05 (dd, J = 8.0, 2.0 Hz, 1H), 6.83 (s, 1H), 6.00 (q, J = 6.5 Hz, 1H), 3.91 (s, 3H), 1.96 (s, 3H), 1.33 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO-D$_6$) δ 169.8, 155.5, 141.3, 140.4, 132.9, 132.6, 129.3, 128.9, 128.0, 122.4, 113.1, 110.4, 68.7, 56.6, 21.4, 20.0; IR (Neat) ν_{max} 2932, 1731, 1586, 1447, 1236, 1042, 855 cm^{-1}; **HRMS (ESI)** for $C_{19}H_{19}BrNaO_3^+$ (M+Na)$^+$: calcd. 397.0410 found 397.0412.

(Z)-3-(3-Fluoro-4-methylphenyl)-4-phenylbut-3-en-2-yl acetate (38):



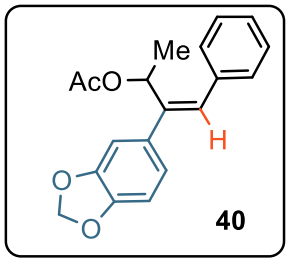
38 (43 mg, 72%) as red liquid; R_f = 0.6 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO-D$_6$) δ 7.42 (t, J = 7.5 Hz, 2H), 7.35-7.30 (m, 4H), 7.29-7.24 (m, 2H), 6.79 (s, 1H), 5.97 (q, J = 6.7 Hz, 1H), 2.26 (s, 3H), 1.95 (s, 3H), 1.31 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO-D$_6$) δ 169.8, 160.7 (d, J = 243.2 Hz, 1C), 140.0, 139.8 (d, J = 8.2 Hz, 1C), 136.5, 132.4, 131.8 (d, J = 5.0 Hz, 1C), 129.2, 128.8, 127.9, 124.6 (d, J = 2.5 Hz, 1C), 123.8 (d, J = 17.6 Hz, 1C), 115.1 (d, J = 22.7 Hz, 1C), 68.7, 21.4, 20.0, 14.4; ^{19}F NMR (471 MHz) δ −117.7; IR (Neat) ν_{max} 2926, 1736, 1505, 1369, 1232, 1040, 870 cm^{-1}; **HRMS (ESI)** for $C_{19}H_{19}FNaO_2^+$ (M+Na)$^+$: calcd. 321.1261 found 321.1265.

(Z)-3-(2,3-Dihydrobenzo[b][1,4]dioxin-6-yl)-4-phenylbut-3-en-2-yl acetate (39):



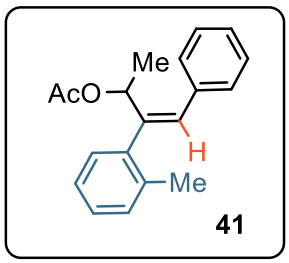
39 (46 mg, 71%) as light yellow liquid; R_f = 0.3 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO-D$_6$) δ 7.39 (t, J = 7.8 Hz, 2H), 7.33-7.27 (m, 3H), 7.02 (d, J = 2.0 Hz, 1H), 6.99 (dd, J = 8.5, 2.5 Hz, 1H), 6.87 (d, J = 8.0 Hz, 1H), 6.70 (s, 1H), 5.96 (q, J = 6.5 Hz, 1H), 4.26 (s, 4H), 1.94 (s, 3H), 1.30 (d, J = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, DMSO-D$_6$) δ 169.8, 143.5, 143.3, 140.6, 136.8, 133.4, 131.4, 129.3, 128.8, 127.7, 121.8, 117.4, 117.2, 68.9, 64.62, 64.56, 21.4, 20.0; IR (Neat) ν_{max} 2930, 1731, 1577, 1502, 1282, 1236, 1066, 808 cm^{-1}; **HRMS (ESI)** for $C_{20}H_{20}NaO_4^+$ (M+Na)$^+$: calcd. 347.1254 found 347.1256.

(Z)-3-(Benzo[d][1,3]dioxol-5-yl)-4-phenylbut-3-en-2-yl acetate (40):



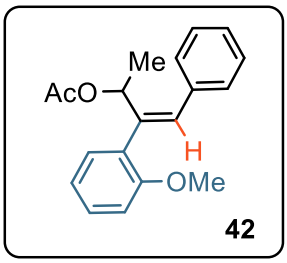
40 (28 mg, 45%) as yellow liquid; R_f = 0.4 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO-D$_6$) δ 7.40 (t, J = 7.5 Hz, 2H), 7.34-7.26 (m, 3H), 7.07 (d, J = 1.5 Hz, 1H), 7.00 (dd, J = 8.0, 1.5 Hz, 1H), 6.94 (d, J = 8.0 Hz, 1H), 6.71 (s, 1H), 6.05 (s, 2H), 5.95 (q, J = 6.5 Hz, 1H), 1.94 (s, 3H), 1.30 (d, J = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, DMSO-D$_6$) δ 169.8, 147.5, 147.2, 140.9, 136.7, 134.2, 131.7, 129.3, 128.8, 127.7, 122.4, 109.2, 108.5, 101.5, 68.9, 21.4, 20.0; IR (Neat) ν_{max} 2920, 1733, 1485, 1369, 1220, 1034, 934, 807 cm^{-1}; **HRMS (ESI)** for $C_{19}H_{18}NaO_4^+$ (M+Na)$^+$: calcd. 333.1097 found 333.1098.

(Z)-4-Phenyl-3-(*o*-tolyl)but-3-en-2-yl acetate (41):



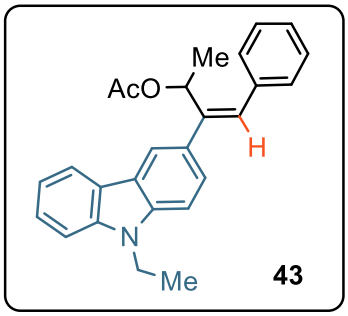
41 (34 mg, 61%) as yellow liquid; R_f = 0.7 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO-D$_6$) δ 7.42 (t, J = 7.5 Hz, 2H), 7.36-7.31 (m, 3H), 7.29 (d, J = 7.5 Hz, 2H), 7.26-7.19 (m, 3H), 6.45 (s, 1H), 5.98 (q, J = 6.7 Hz, 1H), 2.31 (s, 3H), 3.78 (s, 3H), 1.88 (s, 3H), 1.28 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO-D$_6$) δ 169.8, 140.1, 139.7, 136.7, 136.4, 132.6, 130.6, 130.1, 129.1, 128.8, 127.8, 127.7, 125.4, 69.0, 21.4, 20.3, 19.7; IR (Neat) ν_{max} 2927, 1734, 1445, 1369, 1233, 1035, 802 cm^{-1}; **HRMS (ESI)** for $C_{19}H_{20}NaO_2^+$ (M+Na)$^+$: calcd. 303.1356 found 303.1355.

(Z)-3-(2-Methoxyphenyl)-4-phenylbut-3-en-2-yl acetate (42):



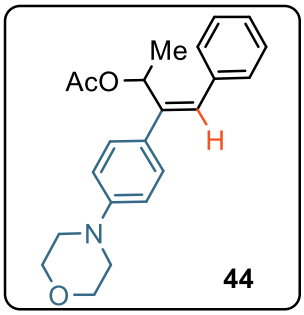
42 (39 mg, 66%) as yellow liquid; R_f = 0.4 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO-D$_6$) δ 7.41 (t, J = 7.5 Hz, 2H), 7.38-7.28 (m, 4H), 7.13 (dd, J = 7.5, 1.5 Hz, 1H), 7.04 (d, J = 7.5 Hz, 1H), 6.96 (td, J = 7.5, 1.0 Hz, 1H), 6.40 (s, 1H), 5.99 (q, J = 6.5 Hz, 1H), 3.76 (s, 3H), 1.83 (s, 3H), 1.28 (d, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, DMSO-D$_6$) δ 169.8, 157.6, 139.3, 136.6, 131.9, 131.6, 129.3, 128.8, 127.7, 120.3, 111.6, 68.6, 55.9, 21.3, 19.7; IR (Neat) ν_{max} 2933, 1734, 1489, 1368, 1241, 1025, 852 cm^{-1}; **HRMS (ESI)** for $C_{19}H_{20}NaO_3^+$ (M+Na)$^+$: calcd. 319.1305 found 319.1307.

(Z)-3-(9-Ethyl-9H-carbazol-3-yl)-4-phenylbut-3-en-2-yl acetate (43):



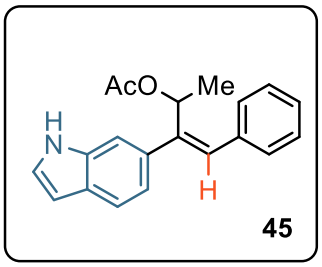
43 (58 mg, 76%) as fluorescent yellow liquid; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO-D$_6$) δ 8.30 (d, J = 1.0 Hz 1H), 8.22 (d, J = 7.5 Hz 1H), 7.65 (dd, J = 8.5, 2.0 Hz 1H), 7.60 (d, J = 8.0 Hz 2H), 7.50-7.45 (m, 1H), 7.43 (t, J = 7.5 Hz, 2H), 7.38 (d, J = 7.0 Hz, 2H), 7.35-7.29 (m, 1H), 7.22 (t, J = 7.5 Hz, 1H),), 6.82 (s, 1H), 6.11 (q, J = 6.5 Hz, 1H), 4.44 (q, J = 7.0 Hz, 2H), 1.97 (s, 3H), 1.39 (d, J = 7.0 Hz, 3H), 1.33 (t, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, DMSO-D$_6$) δ 169.8, 142.2, 140.4, 139.4, 137.1, 131.3, 131.1, 129.3, 128.8, 127.6, 126.7, 126.3, 122.7, 122.5, 120.9, 120.6, 119.3, 109.6, 109.0, 69.3, 37.5, 21.4, 20.3, 14.2; IR (Neat) ν_{max} 2924, 1731, 1596, 1472, 1331, 1230, 1037, 936, 805 cm^{-1}; **HRMS (ESI)** for $C_{26}H_{26}NO_2^+$ $(M+H)^+$: calcd. 384.1958 found 384.1956.

(Z)-3-(4-Morpholinophenyl)-4-phenylbut-3-en-2-yl acetate (44):



44 (40 mg, 57%) as white solid. mp = 206-208°C; R_f = 0.2 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO-D$_6$) δ 7.49-7.36 (m, 4H), 7.35-7.25 (m, 3H), 6.96 (d, J = 8.5 Hz, 2H), 6.69 (s, 1H), 5.99 (q, J = 6.3 Hz 1H), 3.75 (bt, J = 4.5 Hz, 4H), 3.14 (bt, J = 4.0 Hz ,4H), 1.93 (s, 3H), 1.32 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO-D$_6$) δ 169.8, 150.7, 141.0, 137.1, 130.6, 130.2, 129.3, 129.2, 128.8, 127.5, 69.1, 66.5, 48.6, 21.4, 20.1; IR (Neat) ν_{max} 2921, 2850, 1728, 1604, 1512, 1449, 1372, 1232, 1118, 1032, 925, 811 cm^{-1}; **HRMS (ESI)** for $C_{22}H_{26}NO_3^+$ $(M+Na)^+$: calcd. 352.1907 found 352.1906.

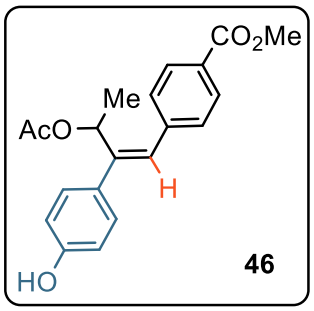
(*Z*)-3-(1H-indol-6-yl)-4-phenylbut-3-en-2-yl acetate (45):



45 (23 mg, 38%) as colorless liquid; R_f = 0.1 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO-D$_6$) δ 11.13 (s, 1H), 7.55 (d, J = 8.0 Hz, 2H), 7.41 (t, J = 7.5 Hz, 2H), 7.38 (t, J = 7.3 Hz, 1H), 7.36-7.28 (m, 3H), 7.18 (d, J = 8.5 Hz, 1H), 6.74 (s, 1H), 6.44 (bs, 1H), 6.03 (q, J = 6.5 Hz, 1H), 1.94 (s, 3H), 1.35 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz,

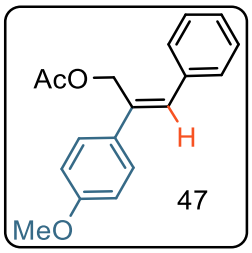
DMSO-D_6) δ 169.8, 142.6, 137.2, 136.3, 133.2, 131.0, 129.3, 128.7, 127.5, 127.4, 126.4, 120.2, 120.0, 111.6, 69.4, 21.4, 20.2; IR (Neat) ν_{max} 3414, 2926, 1715, 1452, 1370, 1243, 1036, 809 cm^{-1}; **HRMS (ESI)** for $C_{20}H_{19}NNaO_2^+$ $(M+Na)^+$: calcd. 328.1308 found 328.1306.

(Z)-Methyl-4-(3-acetoxy-2-(4-hydroxyphenyl)but-1-en-1-yl)benzoate (46):



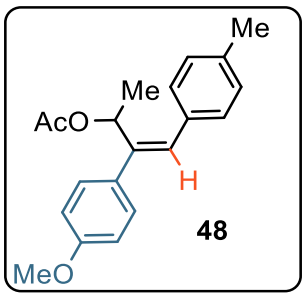
46 (57 mg, 84%) as white solid. mp=185-187°C; R_f = 0.2 (20% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO-D_6) δ 9.57 (s, 1H), 7.97 (d, J = 8.5 Hz, 2H), 7.44 (d, J = 8.0 2H), 7.36 (d, J = 8.5 Hz, 2H), 6.81 (d, J = 9.0 Hz, 2H), 6.70 (s, 1H), 5.92 (q, J = 6.7 Hz, 1H), 3.86 (s, 3H), 1.89 (s, 3H), 1.33 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO-D_6) δ 169.7, 166.5, 157.6, 143.1, 142.1, 135.0, 130.4, 129.8, 129.6, 129.5, 129.1, 128.5, 115.5, 69.0, 52.6, 21.3, 20.1; IR (Neat) ν_{max} 3370, 2982, 1715, 1605, 1512, 1434, 1235, 1104, 1036, 834 cm^{-1}; **HRMS (ESI)** for $C_{20}H_{20}NaO_5^+$ $(M+Na)^+$: calcd. 363.1203 found 363.1201.

(Z)-2-(4-Methoxyphenyl)-3-phenylallyl acetate (47):



47 (45 mg, 79%) as colourless liquid; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO D_6) δ 7.52 (dt, J = 8.5, 3.5 Hz, 2H), 7.45–7.39 (m, 2H), 7.37 (d, J = 7.0 Hz, 2H), 7.34–7.30 (m, 1H), 7.12 (s, 1H), 6.97 (dt, J = 9.0, 3.0 Hz, 2H), 5.05 (s, 2H), 3.78 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (126 MHz, DMSO D_6) δ 170.8, 159.5, 137.0, 135.1, 132.5, 131.6, 129.2, 128.9, 127.88, 127.86, 114.4, 61.8, 55.6, 21.1; IR (Neat) ν_{max} 2923, 1735, 1606, 1512, 1462, 1244, 1181, 1027, 954, 826 cm^{-1}; **HRMS (ESI)** for $C_{18}H_{18}NaO_3^+$ $(M+Na)^+$: calcd. 305.1148, found 305.1149.

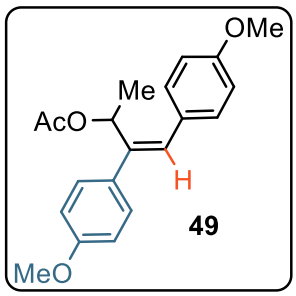
(Z)-3-(4-Methoxyphenyl)-4-(p-tolyl)but-3-en-2-yl acetate (48):



48 (48 mg, 77%) as red gummy liquid; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO D_6) δ 7.44 (d, J = 8.5 Hz, 2H), 7.24–7.16 (m, 4H), 6.95 (d, J = 8.5 Hz, 2H), 6.64 (s, 1H), 5.99 (q, J = 6.5 Hz, 1H), 3.78 (s, 3H), 2.32 (s, 3H), 1.94 (s, 3H), 1.29 (d, J = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, DMSO D_6) δ 169.8, 159.1, 140.4, 137.0, 134.0, 132.6, 131.1, 129.9, 129.4, 129.2, 114.0, 69.0, 55.5, 21.4, 21.3, 20.1;

IR (Neat) ν_{max} 2929, 1733, 1605, 1510, 1285, 1235, 1178, 1032, 932, 829 cm^{-1}; **HRMS (ESI)** for $C_{20}H_{22}NaO_3^+$ $(M+Na)^+$: calcd. 333.1461, found 333.1461.

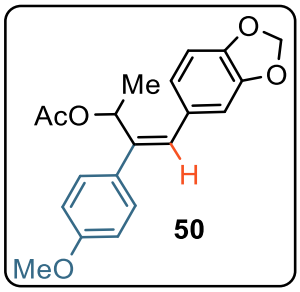
(Z)-3,4-Bis(4-methoxyphenyl)but-3-en-2-yl acetate (49):



49

49 (26 mg, 40%) as red gummy liquid; R_f = 0.3 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO D_6) δ 7.43 (dt, J = 8.5, 3.0 Hz, 2H), 7.25 (d, J = 8.5 Hz, 2H), 6.99–6.93 (m, 4H), 6.62 (s, 1H), 6.01 (q, J = 6.5 Hz, 1H), 3.78 (s, 6H), 1.95 (s, 3H), 1.31 (d, J = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, DMSO D_6) δ 169.9, 159.0, 158.9, 139.5, 132.7, 130.8, 130.6, 129.9, 129.2, 114.3, 114.0, 69.0, 55.6, 55.5, 21.5, 20.0; IR (Neat) ν_{max} 2929, 2836, 1733, 1606, 1509, 1285, 1236, 1175, 1030, 828 cm^{-1}; **HRMS (ESI)** for $C_{20}H_{22}NaO_4$ $(M+Na)^+$: calcd. 349.1410, found 349.1417.

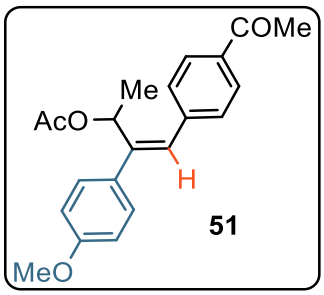
(Z)-4-(Benzo[d][1,3]dioxol-5-yl)-3-(4-methoxyphenyl)but-3-en-2-yl acetate (50):



50

50 (37.9 mg, 67%) as yellow liquid; R_f = 0.3 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO D_6) δ 7.42 (dt, J = 9.0, 3.0 Hz, 2H), 6.98–6.91 (m, 3H), 6.89 (d, J = 1.5 Hz, 1H), 6.82–6.77 (m, 1H), 6.59 (s, 1H), 6.07–6.03 (m, 2H), 6.00 (q, J = 6.5 Hz, 1H), 3.78 (s, 3H), 1.96 (s, 3H), 1.29 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO D_6) δ 169.8, 159.1, 147.7, 146.9, 140.0, 132.5, 130.8, 130.7, 129.9, 123.1, 114.0, 109.4, 108.7, 101.6, 68.9, 55.5, 21.4, 20.0; IR (Neat) ν_{max} 2920, 1733, 1651, 1620, 1485, 1433, 1369, 1220, 1076, 1034, 934 cm^{-1}; **HRMS (ESI)** for $C_{20}H_{20}NaO_5^+$ $(M+Na)^+$: calcd. 363.1203, found 363.1200.

(Z)-4-(4-Acetylphenyl)-3-(4-methoxyphenyl)but-3-en-2-yl acetate (51):

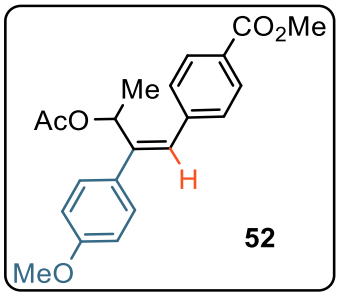


51

51 (62.4 mg, 74%) as yellow liquid; R_f = 0.3 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO D_6) δ 7.98 (d, J = 8.0 Hz, 2H), 7.52–7.40 (m, 4H), 6.97 (dt, J = 7.0, 2.5 Hz, 2H), 6.75 (s, 1H), 5.95 (q, J = 6.5 Hz, 1H), 3.78 (s, 3H), 2.59 (s, 3H), 1.92 (s, 3H), 1.33 (d, J = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, DMSO D_6) δ 197.9, 169.8, 159.4, 142.6, 141.8, 135.8, 132.0, 129.9, 129.6, 128.7, 114.1, 68.9, 55.6, 27.2, 21.3,

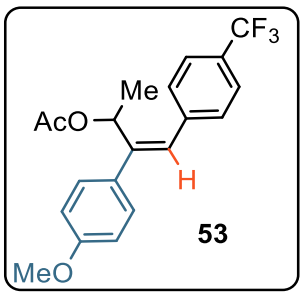
20.1; IR (Neat) ν_{max} 2930, 2040, 1733, 1679, 1600, 1506, 1360, 1234, 1179, 1031, 956 cm^{-1}; **HRMS (ESI)** for $C_{21}H_{22}NaO_4^+$ $(M+Na)^+$: calcd. 361.1410, found 361.1409.

Methyl (Z)-4-(3-acetoxy-2-(4-methoxyphenyl)but-1-en-1-yl)benzoate (52):



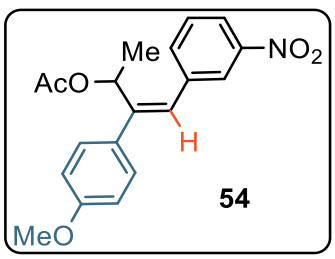
52 (61.5 mg, 89%) as red liquid; R_f = 0.3 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO D_6) δ 7.97 (d, J = 8.5 Hz, 2H), 7.49–7.42 (m, 4H), 6.97 (dt, J = 9.0 Hz, 3.0 Hz, 2H), 6.73 (s, 1H), 5.93 (q, J = 6.5 Hz, 1H), 3.86 (s, 3H), 3.78 (s, 3H), 1.90 (s, 3H), 1.33 (d, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, DMSO D_6) δ 169.8, 166.5, 159.4, 142.7, 142.0, 132.1, 129.9, 129.8, 129.61, 129.58, 128.6, 114.1, 68.9, 55.6, 52.6, 21.3, 20.1; IR (Neat) ν_{max} 2950, 2838, 1717, 1603, 1510, 1435, 1276, 1234, 1032, 829 cm^{-1}; **HRMS (ESI)** for $C_{21}H_{22}NaO_5^+$ $(M+Na)^+$: calcd. 377.1359, found 377.1356.

(*Z*)-3-(4-Methoxyphenyl)-4-(4-(trifluoromethyl)phenyl)but-3-en-2-yl acetate (53):



53 (52.7 mg, 76%) as yellow liquid; R_f = 0.5 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO D_6) δ 7.75 (d, J = 8.5 Hz, 2H), 7.54 (d, J = 8.5 Hz, 2H), 7.48 (dt, J = 9.0, 3.0 Hz, 2H), 6.98 (dt, J = 9.0, 3.0 Hz, 2H), 6.76 (s, 1H), 5.91 (q, J = 6.5 Hz, 1H), 3.79 (s, 3H), 1.90 (s, 3H), 1.33 (d, J = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, DMSO D_6) δ 169.8, 159.4, 142.8, 141.3, 131.9, 130.0, 129.9, 129.3, 127.9 (q, J = 31 Hz, 1C), 125.58, 125.55, 124.8 (q, J = 274 Hz, 1C), 114.1, 68.9, 55.6, 21.2, 20.0; ^{19}F NMR (471 MHz) δ –61.0; IR (Neat) ν_{max} 2935, 1736, 1606, 1509, 1370, 1321, 1287, 1235, 1162, 1065, 829 cm^{-1}; **HRMS (ESI)** for $C_{20}H_{19}F_3NaO_3^+$ $(M+Na)^+$: calcd. 387.1179, found 387.1182.

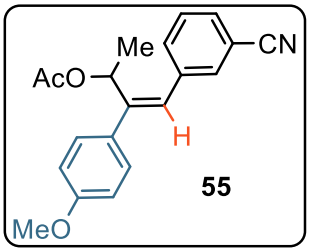
(Z)-3-(4-Methoxyphenyl)-4-(3-nitrophenyl)but-3-en-2-yl acetate (54):



54 (54.5 mg, 83%) as yellow liquid; R_f = 0.4 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO D_6) δ 8.21–8.15 (m, 2H), 7.79 (d, J = 7.5 Hz, 1H), 7.71 (t, J = 8.0 Hz, 1H), 7.49 (dt, J = 8.5, 3.0 Hz, 2H), 6.99 (dt, J = 8.5, 3.0 Hz, 2H), 6.80 (s, 1H), 5.87 (q, J = 6.5 Hz, 1H), 3.80 (s, 3H), 1.93 (s, 3H), 1.34 (d, J = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, DMSO D_6) δ 169.8, 159.5, 148.2, 143.1, 138.7, 135.8, 131.8, 130.3, 129.9, 128.6, 123.8, 122.4, 114.1, 69.0, 55.6, 21.2, 20.0; IR (Neat) ν_{max} 2932, 1733, 1605, 1573, 1525, 1509, 1369, 1346,

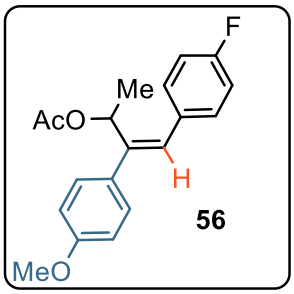
1285, 1232, 1179, 1032, 832 cm^{-1}; **HRMS (ESI)** for $C_{19}H_{19}NaO_5^+$ $(M+Na)^+$: calcd. 364.1155, found 364.1157.

(Z)-4-(3-Cyanophenyl)-3-(4-methoxyphenyl)but-3-en-2-yl acetate (55):



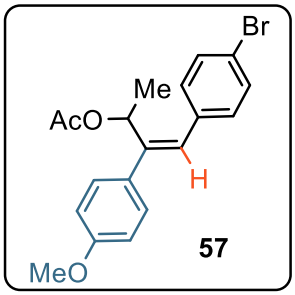
55 (40.5 mg, 63%) as pale yellow liquid; R_f = 0.4 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO D_6) δ 7.79-7.75 (m, 2H), 7.68–7.59 (m, 2H), 7.49–7.44 (m, 2H), 7.00–6.96 (m, 2H), 6.70 (s, 1H), 5.87 (q, J = 6.5 Hz, 1H), 3.79 (s, 3H), 1.91 (s, 3H), 1.32 (d, J = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, DMSO D_6) δ 169.8, 159.4, 142.8, 138.3, 134.0, 132.8, 131.9, 131.2, 130.0, 129.9, 128.7, 119.2, 114.1, 111.9, 68.9, 55.6, 21.3, 20.0; IR (Neat) ν_{max} 3427, 1733, 1679, 1601, 1510, 1368, 1239, 1026, 825 cm^{-1}; **HRMS (ESI)** for $C_{20}H_{19}NaO_3^+$ $(M+Na)^+$: calcd. 344.1257, found 344.1260.

(Z)-4-(4-Fluorophenyl)-3-(4-methoxyphenyl)but-3-en-2-yl acetate (56):



56 (47.2 mg, 75%) as colourless liquid; R_f = 0.5 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO D_6) δ 7.44 (d, J = 9.0 Hz, 2H), 7.38–7.32 (m, 2H), 7.23 (t, J = 9.0 Hz, 2H), 6.96 (d, J = 8.5 Hz, 2H), 6.66 (s, 1H), 5.94 (q, J = 7 Hz, 1H), 3.78 (s, 3H), 1.92 (s, 3H), 1.31 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO D_6) δ 169.8, 161.7 (d, J = 246 Hz, 1C), 159.2, 141.1, 133.3 (d, J = 2.5 Hz, 1C), 132.3, 131.3 (d, J = 8.8 Hz, 2C), 129.9, 129.8, 115.6 (d, J = 21 Hz, 2C), 114.0, 68.9, 55.5, 21.3, 20.0; ^{19}F NMR (471 MHz) δ −114.9; IR (Neat) ν_{max} 2926, 2852, 1734, 1604, 1509, 1370, 1285, 1233, 1179, 1034, 831 cm^{-1}; **HRMS (ESI)** for $C_{19}H_{19}FNaO_3^+$ $(M+Na)^+$: calcd. 337.1210, found 337.1211.

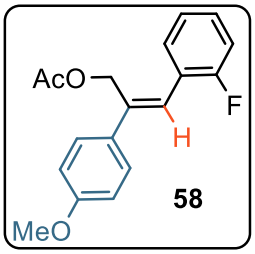
(Z)-4-(4-Bromophenyl)-3-(4-methoxyphenyl)but-3-en-2-yl acetate (57):



57 (52.6 mg, 70%) as pale yellow liquid; R_f = 0.5 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO D_6) δ 7.58 (d, J = 8.5 Hz, 2H), 7.45 (d, J = 9.0 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H), 6.96 (d, J = 8.5 Hz, 2H), 6.63 (s, 1H), 5.92 (q, J = 6.5Hz, 1H), 3.78 (s, 3H), 1.92 (s, 3H), 1.31 (d, J = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, DMSO D_6) δ 169.8, 159.3, 141.7, 136.2, 132.2, 131.7, 131.4, 129.9, 129.7, 120.9, 114.1, 68.9, 55.6, 21.3, 20.0;

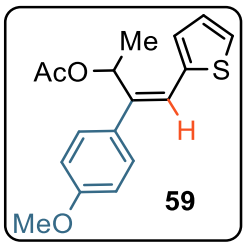
IR (Neat) ν_{max} 2918, 2850, 1725, 1603, 1509, 1485, 1287, 1238, 1072, 1028, 837 cm^{-1}; **HRMS (ESI)** for $C_{19}H_{19}BrNaO_3^+$ $(M+Na)^+$: calcd. 397.0410, found 397.0407.

(Z)-3-(2-Fluorophenyl)-2-(4-methoxyphenyl)allyl acetate (58):



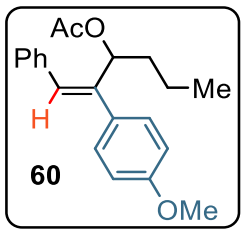
58 (51.1mg, 68%) as yellow gummy liquid; R_f = 0.5 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO D_6) δ 7.53 (dt, J = 9.0, 3.0 Hz, 2H), 7.38 (t, J = 7.5 Hz, 2H), 7.29–7.22 (m, 2H), 7.00–6.95 (m, 3H), 5.00 (s, 2H), 3.78 (s, 3H), 1.93 (s, 3H); ^{13}C NMR (126 MHz, DMSO D_6) δ 170.7, 160.2 (d, J = 246 Hz, 1C), 159.7, 137.6, 131.7, 131.0 (d, J = 2.5 Hz, 1C), 130.2 (d, J = 8.8 Hz, 1C), 128.1, 124.9 (d, J = 3.8 Hz, 1C), 124.6 (d, J = 14.0 Hz, 1C), 123.5 (d, J = 2.5 Hz, 1C), 116.0 (d, J = 21.0 Hz, 1C), 114.4, 61.7, 55.6, 21.0; ^{19}F NMR (471 MHz) δ −114.6; IR (Neat) ν_{max} 2935, 1733, 1512, 1484, 1223, 1180, 1097, 1025, 956 cm^{-1}; **HRMS (ESI)** for $C_{18}H_{17}FNaO_3^+$ $(M+Na)^+$: calcd. 323.1054, found 323.1053.

(Z)-3-(4-Methoxyphenyl)-4-(thiophen-2-yl)but-3-en-2-yl acetate (59):



59 (33.6 mg, 42%) as yellow liquid; R_f = 0.5 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO D_6) δ 7.63 (dd, J = 5.5, 4.5 Hz, 1H), 7.40 (dt, J = 9.0, 3.0 Hz, 2H), 7.20 (d, J = 3.0 Hz, 1H), 7.12 (dd, J = 5.0, 3.5 Hz, 1H), 6.94 (dt, J = 8.5, 3.5 Hz, 2H), 6.77 (s, 1H), 6.23 (q, J = 6.5 Hz, 1H), 3.78 (s, 3H), 1.93 (s, 3H), 1.44 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO D_6) δ 169.9, 159.1, 139.3, 138.7, 132.2, 130.0, 129.7, 127.9, 127.8, 122.9, 114.0, 69.2, 55.6, 21.3, 19.8; IR (Neat) ν_{max} 2918, 1733, 1604, 1508, 1455, 1369, 1383, 1286, 1237, 1177, 1030 cm^{-1}; **HRMS (ESI)** for $C_{17}H_{18}NaO_3S^+$ $(M+Na)^+$: calcd. 325.0869, found 325.0867.

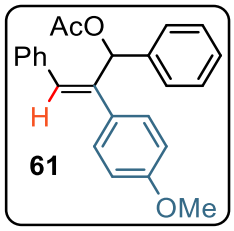
(Z)-2-(4-Methoxyphenyl)-1-phenylhex-1-en-3-yl acetate (60):



60 (46 mg, 71%) as yellow gummy liquid ; R_f = 0.6 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO-D_6) δ 7.47–7.43 (m, 2H), 7.41–7.37 (m, 2H), 7.34–7.27 (S, 3H), 6.98–6.93 (m, 2H), 6.72 (S, 1H), 5.92 (q, J = 1.5 Hz, 1H), 3.77 (S, 1H), 1.94 (S, 3H), 1.72–1.64 (m, 1H), 1.56–1.48 (m, 1H), 1.20–1.10 (m, 2H), 0.70 (t, J = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO-D_6) δ 169.4, 158.6, 139.6, 136.5, 132.2, 131.5, 129.4, 128.7, 128.2, 127.0, 113.5, 71.8, 55.0, 20.8,

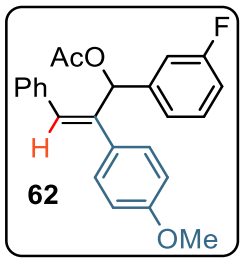
18.3, 13.4; IR (Neat) ν_{max}2957, 1734, 1509, 1286, 1232, 1028, 823, 697 cm^{-1}; **HRMS (ESI)** for $C_{21}H_{24}O_3S$ $(M+Na)^+$: calcd.347.1618, found 347.1619.

(Z)-2-(4-Methoxyphenyl)-1,3-diphenylallyl acetate (61):



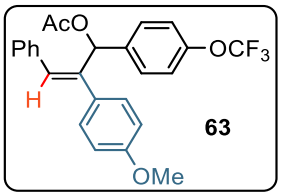
61 (35 mg, 49%) as red gummy liquid. R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO-D_6) δ 7.42–7.30 (m, 9H), 7.28–7.24 (m, 3H), 7.10 (S, 2H), 6.84 (S, 1H), 6.82 (S, 1H), 3.71 (S, 3H), 2.02 (S, 3H); ^{13}C NMR (126 MHz, DMSO-D_6) δ 169.4, 158.6, 138.5, 137.6, 136.4, 131.6, 131.2, 129.1, 128.54, 128.48, 128.4, 127.5, 127.3, 125.8, 113.4, 72.6, 55.0, 20.7;IR (Neat) ν_{max}2929, 1737, 1509, 1283, 1224, 1178, 1023, 748, 696 cm^{-1}; **HRMS (ESI)** for $C_{24}H_{22}O_3$ $(M+Na)^+$: calcd.381.1461, found 381.1460.

(Z)-1-(3-Fluorophenyl)-2-(4-methoxyphenyl)-3-phenylallyl acetate (62):



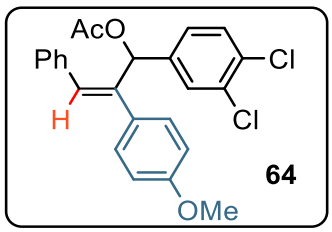
62 (45 mg, 60%) as yellow gummy liquid. R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO-D_6) δ 7.42–7.36 (m, 5H), 7.36–7.30 (m, 3H), 7.12–7.08 (m, 3H), 7.06-7.01 (m, 2H), 6.85 (S, 1H), 6.84 (S, 1H), 3.72 (S, 3H), 2.01 (S, 3H); ^{13}C NMR (101 MHz, DMSO-D_6) δ 169.5, 162,2 (d, J 158.6, 138.5, 137.6, 136.4, 131.6, 131.2, 129.1, 128.54, 128.48, 128.4, 127.5, 127.3, 125.8, 113.4, 72.6, 55.0, 20.7; ^{19}F NMR (376 MHz) δ –112.6; IR (Neat) ν_{max}2930, 2361, 1740, 1606, 1509, 1283, 1179, 1026, 825, 757, 722 cm^{-1}; **HRMS (ESI)** for $C_{24}H_{21}FO_3$ $(M+Na)^+$: calcd.399.1367, found 399.1368.

(Z)-2-(4-Methoxyphenyl)-3-phenyl-1-(4-(trifluoromethoxy)phenyl)allyl acetate (63):



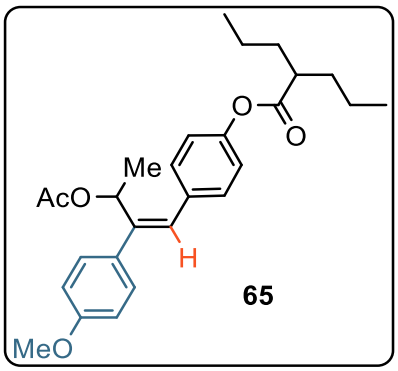
63 (45 mg, 51%) as yellow gummy liquid. R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO-D_6) δ 7.39 (d, J = 5.0 Hz, 4H), 7.38–7.34 (m, 3H), 7.34–7.29 (m, 4H), 7.11 (S, 1H), 7.07 (S, 1H), 6.85 (S, 1H), 6.84 (S, 1H), 3.71 (S, 3H), 2.04 (S, 3H); ^{13}C NMR (126 MHz, DMSO-D_6) δ 169.4, 158.7, 147.6, 137.8, 137.3, 136.3 132.1, 130.9, 129.1, 128.5, 128.4, 127.9, 127.4, 121.2, 120.0 (q, J = 257.0 Hz, 1C), 113.5, 72.0, 55.0, 20.6 ; ^{19}F NMR (376 MHz) δ –56.8; IR (Neat) ν_{max}2934, 1741, 1508, 1508, 1217, 1158, 1018, 823 cm^{-1}; **HRMS (ESI)** for $C_{25}H_{21}F_3O_4$ $(M+Na)^+$: calcd.465.1284, found 465.1284.

(Z)-1-(3,4-Dichlorophenyl)-2-(4-methoxyphenyl)-3-phenylallyl acetate (64):



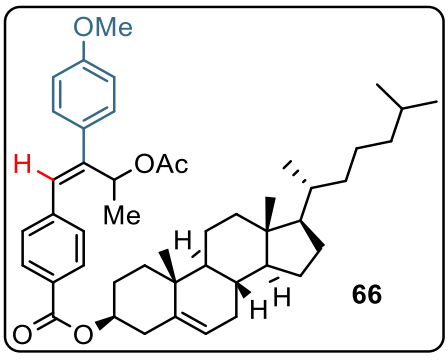
64 (45 mg, 53%) as yellow gummy liquid. R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO-D_6) δ 7.59 (d, J = 8.5 Hz, 1H), 7.44–7.42 (m, 1H), 7.41–7.37 (m, 4H), 7.35 (S, 1H), 7.33–7.29 (m, 2H), 7.26–7.22 (m, 1H), 7.13 (S, 1H), 7.00 (S, 1H), 6.87 (S, 1H), 6.85 (S, 1H), 3.72 (S, 3H), 2.05 (S, 3H); ^{13}C NMR (101 MHz, DMSO-D_6) δ169.4, 158.8, 139.7, 136.7, 136.2, 132.5, 131.4, 130.8, 130.6, 130.3, 129.1, 128.6, 127.8, 127.6, 126.4, 113.6, 71.5, 55.0, 20.7; IR (Neat) ν_{max}2931, 2360, 1598, 1740, 1509, 1221, 1179, 1025, 823, 729 cm^{-1}; **HRMS (ESI)** for $C_{24}H_{20}Cl_2O_3$ $(M+Na)^+$: calcd.449.0682, found 449.0681.

(Z)-4-(3-Acetoxy-2-(4-methoxyphenyl)but-1-en-1-yl)phenyl 2-propylpentanoate (65):



65 (44.3 mg, 64%) as yellow liquid; R_f = 0.3 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO D_6) δ7.46 (dt, J = 8.5, 3 Hz, 2H), 7.36 (d, J = 8.5 Hz, 2H), 7.11 (dt, J = 8.5, 2.5 Hz, 2H), 6.96 (dt, J = 8.5, 3.0 Hz, 2H), 6.68 (s, 1H), 5.95 (q, J = 6.5 Hz, 1H), 3.78 (s, 3H), 2.65–2.58 (m, 1H), 1.93 (s, 3H), 1.71–1.62 (m, 2H), 1.59–1.50 (m, 2H), 1.44–1.35 (m, 4H), 1.32 (d, J = 6.5 Hz, 3H), 0.94 (t, J = 7.5 Hz, 6H); ^{13}C NMR (101 MHz, DMSO D_6) δ174.8, 169.8, 159.2, 149.8, 141.2, 134.6, 132.4, 130.5, 130.0, 129.9, 122.1, 114.0, 69.0, 55.5, 45.0, 34.6, 21.4, 20.6, 20.1, 14.4; IR (Neat) ν_{max} 2957, 1736, 1605, 1509, 1370, 1285, 1236, 1197, 1105, 1034, 880 cm^{-1}; **HRMS (ESI)** for $C_{27}H_{34}NaO_5^+$ $(M+Na)^+$: calcd. 461.2298, found 461.2298.

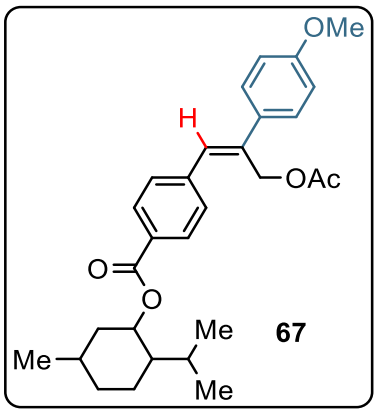
(3S,8S,9S,10R,13R,14S,17R)-10,13-Dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 4-((Z)-3-acetoxy-2-(4-methoxyphenyl)but-1-en-1-yl)benzoate (66):



66 (27.3 mg, 46%) as Pale yellow liquid ; R_f = 0.3 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ8.07 (d, J = 8.5 Hz, 2H), 7.47 (dt, J = 9.0, 3.0 Hz, 2H), 7.38 (d, J = 8.0 Hz, 2H), 6.94 (dt, J = 9.0, 2.5 Hz, 2H), 6.73 (s, 1H), 6.70 (s,

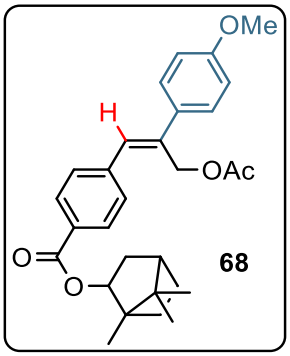
1H), 6.10 (q, *J* = 7.0 Hz, 1H), 5.45 (d, *J* = 4.0 Hz, 1H), 4.93–4.84 (m, 1H), 3.87 (s, 3H), 2.49 (d, *J* = 8.0 Hz, 2H), 2.07–1.94 (m, 10H), 1.63–1.48 (m, 9H),1.38 (d, *J* = 6.5 Hz, 4H), 1.28 (s, 4H), 1.10 (s, 4H), 0.95 (d, *J* = 6.5 Hz, 3H), 0.89 (dd, *J* = 6.5, 2.5 Hz, 9H), 0.72 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.0, 165.8, 159.2, 142.7, 141.5, 139.7, 132.4, 130.1, 129.60, 129.57, 128.8, 122.8, 116.2, 113.5, 74.6, 69.5, 56.7, 56.2, 55.3, 50.1, 42.4, 39.8, 39.5, 38.3, 37.1, 36.7, 36.2, 35.8, 32.0, 31.9, 28.3, 28.0, 24.3, 23.9, 22.8, 22.6, 21.2, 21.1, 19.8, 19.4, 18.7; IR (Neat) ν_{max} 2922, 2851, 1740, 1714, 1606, 1511, 1463, 1369, 1272, 1244, 1178, 1035 cm^{-1}; **HRMS (ESI)** for $C_{47}H_{64}NaO_5^+$ $(M+Na)^+$: calcd. 731.4646, found 731.4647.

2-Isopropyl-5-methylcyclohexyl(Z)-4-(3-acetoxy-2-(4-methoxyphenyl)prop-1-en-1-yl)benzoate (67):



67 (44.5 mg, 65%) as Pale yellow liquid; R_f = 0.3 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO D_6) δ 7.98 (d, *J* = 8.5 Hz, 2H), 7.54 (d, *J* = 9.0 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.17 (s, 1H), 6.97 (d, *J* = 9.0 Hz, 2H), 5.03 (s, 2H), 4.90–4.80 (m, 1H), 3.78 (s, 3H), 1.99 (s, 3H), 1.92–1.85 (m, 1H), 1.70–1.63 (m, 2H), 1.57–1.47 (m, 2H), 1.14–1.04 (m, 2H), 0.88 (t, *J* = 6.5 Hz, 8H), 0.74 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, DMSO D_6) δ 170.7, 165.4, 159.7, 141.8, 137.0, 132.1, 130.4, 129.7, 129.5, 129.1, 128.0, 114.4, 74.6, 61.5, 55.6, 47.1, 34.2, 31.3, 26.7, 23.7, 22.3, 21.1, 20.9, 16.9; IR (Neat) ν_{max} 2953, 1738, 1708, 1603, 1513, 1271, 1246, 1178, 1102, 1019, 981 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{36}NaO_5^+$ $(M+Na)^+$: calcd. 487.2455, found 487.2453.

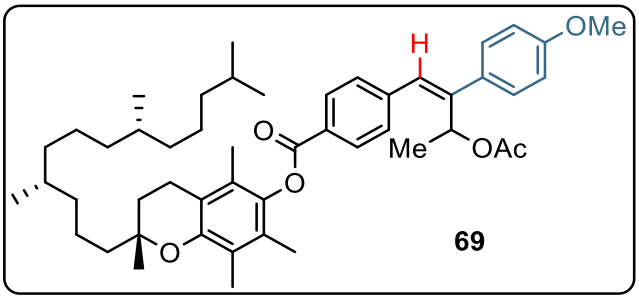
1,7,7-Trimethylbicyclo[2.2.1]heptan-2-yl (Z)-4-(3-acetoxy-2-(4-methoxyphenyl)prop-1-en-1-yl)benzoate (68):



68 (71.8 mg, 78%) as Pale yellow liquid; R_f = 0.3 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO D_6) δ 8.00 (d, *J* = 8.0 Hz, 2H), 7.57–7.48 (m, 4H), 7.16 (s, 1H), 6.97 (d, *J* = 8.5 Hz, 2H), 5.04 (s, 3H), 3.78 (s, 3H), 2.43–2.34 (m, 1H), 2.12–2.04 (m, 1H), 1.99 (s, 3H), 1.79–1.67 (m, 2H), 1.41–1.33 (m, 1H), 1.32–1.24 (m, 1H), 1.07 (dd, *J* = 14.0, 3.5 Hz, 1H), 0.92 (s, 3H), 0.86 (d, *J* = 5.0 Hz, 6H); ^{13}C NMR (101 MHz, DMSO

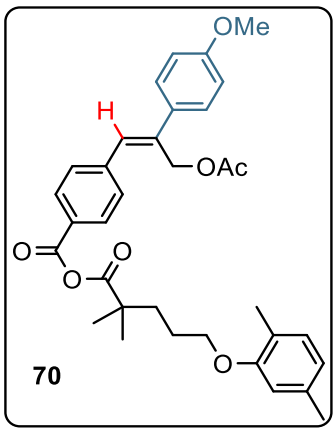
D_6) δ 170.8, 166.0, 159.7, 141.8, 137.0, 132.1, 130.5, 129.7, 129.6, 129.2, 128.0, 114.4, 80.2, 61.5, 55.6, 49.2, 48.0, 44.8, 36.9, 28.1, 27.5, 21.1, 20.0, 19.1, 13.9; IR (Neat) ν_{max} 3384, 2924, 1737, 1710, 1653, 1604, 1512,1456, 1366, 1274, 1179, 1023, 992 cm^{-1}; **HRMS (ESI)** for $C_{29}H_{34}NaO_5^+$ $(M+Na)^+$: calcd. 485.2298, found 485.2299.

(R)-2,5,7,8-Tetramethyl-2-((4R,8R)-4,8,12-trimethyltridecyl)chroman-6-yl 4-((Z)-3-acetoxy-2-(4-methoxyphenyl)prop-1-en-1-yl)benzoate (69):



69 (55.12 mg, 69%) as pale yellow liquid; R_f = 0.2 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20–8.15 (m, 2H), 7.45 (dt, J = 9.0, 3.0 Hz, 2H), 7.42 (d, J = 8.0 Hz, 2H), 6.92 (dt, J = 9.0, 3.0 Hz, 2H), 6.81 (s, 1H), 6.75 (s, 1H), 6.70 (s, 1H), 6.05 (q, J = 6.5 Hz, 1H), 3.85 (s, 3H), 2.79–2.72 (m, 2H), 2.18 (s, 3H), 1.96 (s, 3H), 1.87–1.71 (m, 4H), 1.64–1.44 (m, 5H), 1.40 (d, J = 6.5 Hz, 4H), 1.31–1.23 (m, 11H), 1.17–1.03(m, 7H), 0.8–0.3 (m, 14H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.0, 165.7, 159.3, 149.9, 143.0, 142.7, 142.2, 132.3, 130.1, 129.9, 129.6, 129.0, 128.4, 127.4, 121.3, 121.1, 119.2, 113.6, 76.2, 69.5, 55.3, 40.2, 39.4, 37.5, 37.3, 32.8, 32.7, 31.1, 28.0, 24.8, 24.5, 24.3, 22.8, 22.7, 22.5, 21.2, 21.0, 19.9, 19.8, 19.7, 16.2; IR (Neat) ν_{max} 2924, 2865, 1734, 1605, 1510, 1468, 1374, 1222, 1176, 1138, 1073, 1033, 892 cm^{-1} ; **HRMS (ESI)** for $C_{49}H_{68}O_6^+$ $(M+H)^+$: calcd. 531.2741, found 531.2741.

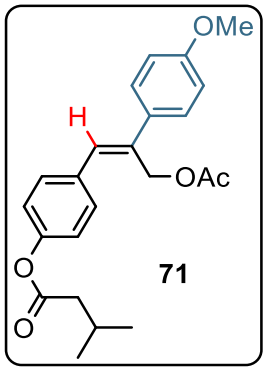
(Z)-(Z)-4-(3-Acetoxy-2-(4-methoxyphenyl)prop-1-en-1-yl)benzoic 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoic anhydride (70):



70 (73.8 mg, 83%) as colorless liquid; R_f = 0.2 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO D_6) δ 7.52 (d, J = 8.5 Hz, 2H), 7.39 (d, J = 8.5 Hz, 2H), 7.12–7.05 (m, 3H), 7.00–6.94 (m, 3H), 6.74 (s, 1H), 6.63 (d, J = 7.5 Hz, 1H), 5.03 (s, 2H), 4.00 (t, J = 6.0 Hz, 2H), 3.79 (s, 3H), 2.25 (s, 3H), 2.09 (s, 3H), 1.99 (s, 3H), 1.90–1.70 (m, 4H), 1.31 (s, 6H); ^{13}C NMR (101 MHz, DMSO D_6) δ 176.2, 170.8, 159.5, 156.9, 150.3, 136.6, 135.2, 134.6, 132.4, 130.8, 130.6, 130.4, 127.9, 123.0, 122.2, 121.0, 114.4, 112.5, 67.7, 61.8, 55.6, 42.4, 37.1, 25.2,

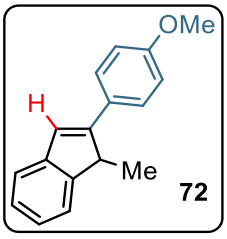
21.5, 21.2, 16.1; IR (Neat) ν_{max} 2923, 1737, 1606, 1509, 1462, 1244, 1201, 1164, 1107, 1027, 828 cm^{-1}; **HRMS (ESI)** for $C_{34}H_{39}O_7^+$ $(M+H)^+$: calcd. 531.2741, found 531.2741.

(Z)-4-(3-Acetoxy-2-(4-methoxyphenyl)prop-1-en-1-yl)phenyl 3-methylbutanoate (71):



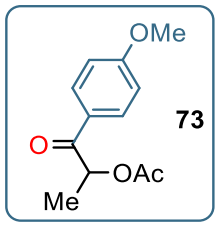
71 (64.2 mg, 73%) as colorless liquid; R_f = 0.3 (10% EtOAc/Hex); ^1H NMR (500 MHz, DMSO D_6) δ 7.51 (dt, J = 9.0, 3.0 Hz, 2H), 7.40 (d, J = 8.5 Hz, 2H), 7.18–7.14 (m, 2H), 7.10 (s, 1H), 6.96 (dt, J = 8.5, 3.0 Hz, 2H), 5.03 (s, 2H), 3.78 (s, 3H), 2.47 (d, J = 7.0 Hz, 2H), 2.17–2.07 (m, 1H), 1.98 (s, 3H), 1.00 (d, J = 6.5 Hz, 6H); ^{13}C NMR (101 MHz, DMSO D_6) δ 171.5, 170.9, 159.5, 150.1, 135.2, 134.6, 132.4, 130.8, 130.4, 127.9, 122.4, 114.4, 61.7, 55.6, 42.9, 25.8, 22.6, 21.2; IR (Neat) ν_{max} 3408, 2958, 1755, 1730, 1606, 1361, 1239, 1199, 1100, 1022, 999, 888 cm^{-1} ; **HRMS (ESI)** for $C_{23}H_{27}O_5^+$ $(M+H)^+$: calcd. 383.1853, found 383.1853.

4B.6.3.2. Synthesis of 2-(4-Methoxyphenyl)-1-methyl-1H-indene (72):



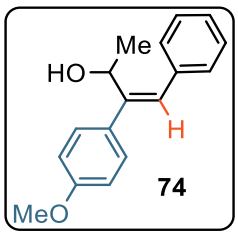
To an independent solution of acetate **23** (0.2 mmol) in 1,2-DCE (2.0 mL) was added H_3PO_4 (1 mmol). The resulting mixture was stirred at 75 °C. The reaction progress was monitored by TLC. Upon completion, the crude mixture was concentrated under reduced pressure. The crude residue was purified using column chromatography on silica gel to afford **72** (20.4 mg, 85%) as colorless liquid; R_f = 0.8 (10% EtOAc/Hex); ^1H NMR (500 MHz, $CDCl_3$) δ 7.52 (dt, J = 8.5, 3.0 Hz, 2H), 7.50–7.45 (m, 1H), 7.42–7.38 (m, 1H), 7.33–7.29 (m, 1H), 7.25–7.20 (m, 1H), 7.01 (s, 1H), 7.00–6.96 (m, 2H), 3.92 (q, J = 7.5 Hz, 1H), 3.88 (s, 3H), 1.38 (d, J = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 152.2, 149.3, 143.8, 129.4, 128.1, 126.7, 124.5, 124.2, 122.8, 120.7, 114.2, 55.4, 44.2, 17.5; IR (Neat) ν_{max} 2957, 2920, 2851, 1603, 1508, 1461, 1303, 1247, 1178, 1034, 828 cm^{-1}; **HRMS (ESI)** for $C_{17}H_{17}O^+$ $(M+Na)^+$: calcd.237.1274, found 237.1270.

4B.6.3.3. Synthesis of 1-(4-Methoxyphenyl)-1-oxopropan-2-yl acetate (73):



To an independent solution of acetate **23** (0.2 mmol) in CCl_4:CH_3CN:H_2O (1:1:1.5) (2.0 mL) was added $NaIO_4$ and $RuCl_3$ (4 equiv. and 1 mol%). The resulting mixture was stirred at rt. The reaction progress was monitored by TLC. Upon completion, the crude mixture was concentrated under reduced pressure. The crude residue was purified using column chromatography on silica gel to afford **73** (20 mg, 90%) as colorless liquid; R_f = 0.3 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (dt, J = 9.0, 3.0 Hz, 2H), 6.97 (dt, J = 9.0, 3.0 Hz, 2H), 5.96 (q, J = 7.0 Hz, 1H), 3.89 (s, 3H), 2.16 (s, 3H), 1.54 (d, J = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.3, 170.5, 163.9, 130.8, 127.2, 114.0, 71.2, 55.5, 20.8, 17.4; IR (Neat) ν_{max} 2935, 1737, 1685, 1598, 1574, 1510, 1421, 1371, 1230, 1174, 1028, 841 cm^{-1}; **HRMS (ESI)** for $C_{12}H_{14}NaO_4^+$ $(M+Na)^+$: calcd.245.0784, found 245.0788.

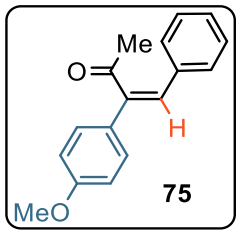
4B.6.3.4. Synthesis of (Z)-3-(4-Methoxyphenyl)-4-phenylbut-3-en-2-ol (74):



To a mixture of acetate **23** (0.2 mmol) and KOH (2.0 mmol) was added toluene:ethanol (9:1, 2.0 mL). The resulting mixture was stirred at 120 ^{o}C overnight. The reaction progress was monitored by TLC. Upon completion, the crude mixture was concentrated under reduced pressure. The crude residue was purified using column chromatography on neutral alumina to afford **74** (122.68 mg, 93%) as yellow gummy liquid; R_f = 0.2 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO D_6) δ 7.59 (dt, J = 9.0, 3.0 Hz, 2H), 7.43–7.36 (m, 4H), 7.30–7.25 (m, 1H), 6.92 (dt, J = 9.0, 3.0 Hz, 2H), 6.58 (s, 1H), 5.10 (d, J = 3.5 Hz, 1H), 5.00–4.90 (m, 1H), 3.77 (s, 3H), 1.13 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, DMSO D_6) δ 158.8, 145.4, 137.5, 133.6, 130.0, 129.4, 128.8, 128.6, 127.2, 113.6, 64.5, 55.5, 22.9; IR (Neat) ν_{max} 2929, 1605, 1507, 1442, 1283, 1241, 1177, 1105, 1029, 919 cm^{-1}; **HRMS (ESI)** for $C_{17}H_{18}NaO_2^+$ $(M+Na)^+$: calcd.277.1199, found 277.1199.

4B.6.3.5. Synthesis of (Z)-3-(4-Methoxyphenyl)-4-phenylbut-3-en-2-one (75):

To a solution of **74** (0.2 mmol, 66 mg) in CH_2Cl_2 (2.0 mL) was added Dess-Martin Periodinane (DMP; 0.6 mmol, 255 mg). The resulting mixture was stirred at rt. The reaction progress was monitored by TLC. Upon completion of the reaction, the crude mixture was concentrated under



the reduced pressure. The crude residue was purified using column chromatography on neutral alumina to afford **75** (23 mg, 80%) as colorless liquid; R_f = 0.3 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40–7.30 (m, 7H), 6.96–6.90 (m, 3H), 3.85 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 207.8, 159.8, 143.4, 135.9, 129.5, 128.7, 128.5, 128.1, 127.9, 127.6, 114.3, 55.4, 31.6; IR (Neat) ν_{max} 2932, 1954, 1695, 1572, 1509, 1417, 1282, 1246, 1205, 1181, 1030 cm^{-1}; **HRMS (ESI)** for $C_{17}H_{16}NaO_2^+$ $(M+Na)^+$: calcd.275.1043, found 275.1043.

4B.7. X-ray crystallography:

X-ray reflections for **44** were collected on Rigaku Oxford diffractometer using Mo-Kα, radiation. OLEX 2 program were used to solve and refine the data. All non-hydrogen atoms were refined anisotropically, and C−H hydrogens were fixed.

Table 4B.4. Crystallographic Data for Compound **44**

Compound	**44**	V [Å^3]	950.66 (15)
formula	$C_{22}H_{23}NO_3$	Z	2
Formula weight	349.41	ρ_{calcd} [g cm^{-3}]	1.221
crystal system	triclinic	μ [mm^{-1}]	0.081
space group	P -1	total reflns	36799
T [K]	297 K	unique reflns	4396
a [Å]	9.7695 (9)	observed	2694
b [Å]	10.1839 (8)	R_1[I>2σ(I)]	0.0797 (2694)
c [Å]	11.1377 (10)	wR2 [all]	0.1086 (4396)
α [°]	66.757 (3)	GOF	1.013
β [°]	79.058 (4)	Diffractometer	Rigaku Oxford
γ [°]	69.275 (3)	CCDC Number	CCDC 2170362

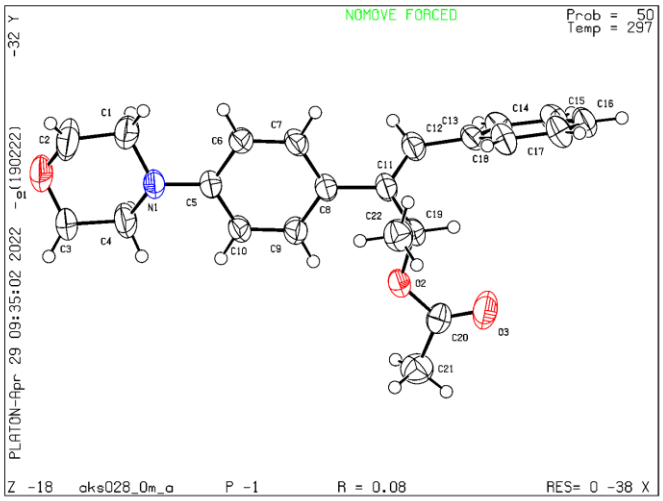


Figure 4B.5. Molecular structure of compound **44**, (Oxygen (red), nitrogen (blue), and sulphur (yellow))

4B.8. References

(1) (a) Negishi, E. Handbook of Organopalladium Chemistry for Organic Synthesis; *Wiley-Interscience: New York*, **2002**. (b) Fallis, A. G.; Forgione, P. Tetrahedron 2001, 57, 5899. (c) Fagnou, K.; Lautens, M. *Chem. Rev*. **2003**, *103*, 169.

(2) For organosilane reagents, see: (a) Fujii, T.; Koike, T.; Mori, A.; Osakada, K. *Synlett* **2002**, 295. (b) Lin, B.; Liu, M.; Ye, Z.; Zhang, Q.; Cheng, J. *Tetrahedron Lett.* **2009**, *50*, 1714. For organostannane reagents, see: (c) Oda, H.; Morishita, M.; Fugami, K.; Sano, H.; Kosugi, M. *Chem. Lett.* **1996**, 811. (d) Fugami, K.; Hagiwara, S.; Oda, H.; Kosugi, M. *Synlett.* **1998**, 477. For organomagnesium reagents, see: (e) Yamagami, T.; Shintani, R.; Shirakawa, E.; Hayashi, T. *Org. Lett*. **2007**, *9*, 1045. For organozinc reagents, see: (f) Murakami, K.; Yorimitsu, H.; Oshima, K. *Org. Lett*. **2009**, *11*, 2373. For organolithium reagents, see: (g) Hojo, M.; Murakami, Y.; Aihara, H.; Sakuragi, R.; Baba, Y.; Hosomi, A. *Angew. Chem. Int. Ed.* **2001**, *40*, 621. For organocopper reagents, see: (h) Chechik-Lankin, H.; Livshin, S.; Marek, I. *Synlett.* **2005**, 2098.

(3) (a) Lautens, M.; Yoshida, M. *J. Org. Chem.* **2003**, *68*, 762. (b) Kim, N.; Kim, K. S.; Gupta, A. K.; Oh, C. H. *Chem. Commun*. **2004**, 618. (c) Liu, Z.; Derosa, J.; Engle, K. M. *J. Am. Chem. Soc*. **2016**, *138*, 13076− 13081.

(4) Yamamoto, Y.; Kirai, N.; Harada, Y. *Chem. Commun*. **2008**, 2010.

(5) Lin, P.-S.; Jeganmohan, M.; Cheng, C.-H. *Chem. Eur. J.* **2008**, *14*, 11296-11299.

(6) (a) Zeng, H.; Hua, R. *J. Org. Chem*. **2008**, *73*, 558−562. (b) Oh, C. H.; Jung, H. H.; Kim, K. S.; Kim, N. *Angew. Chem., Int. Ed*. **2003**, *42*, 805−808.

(7) Yang, Y.; Wang, L.; Zhang, J.; Jin, Y.; Zhu, G. *Chem. Commun*. **2014**, *50*, 2347

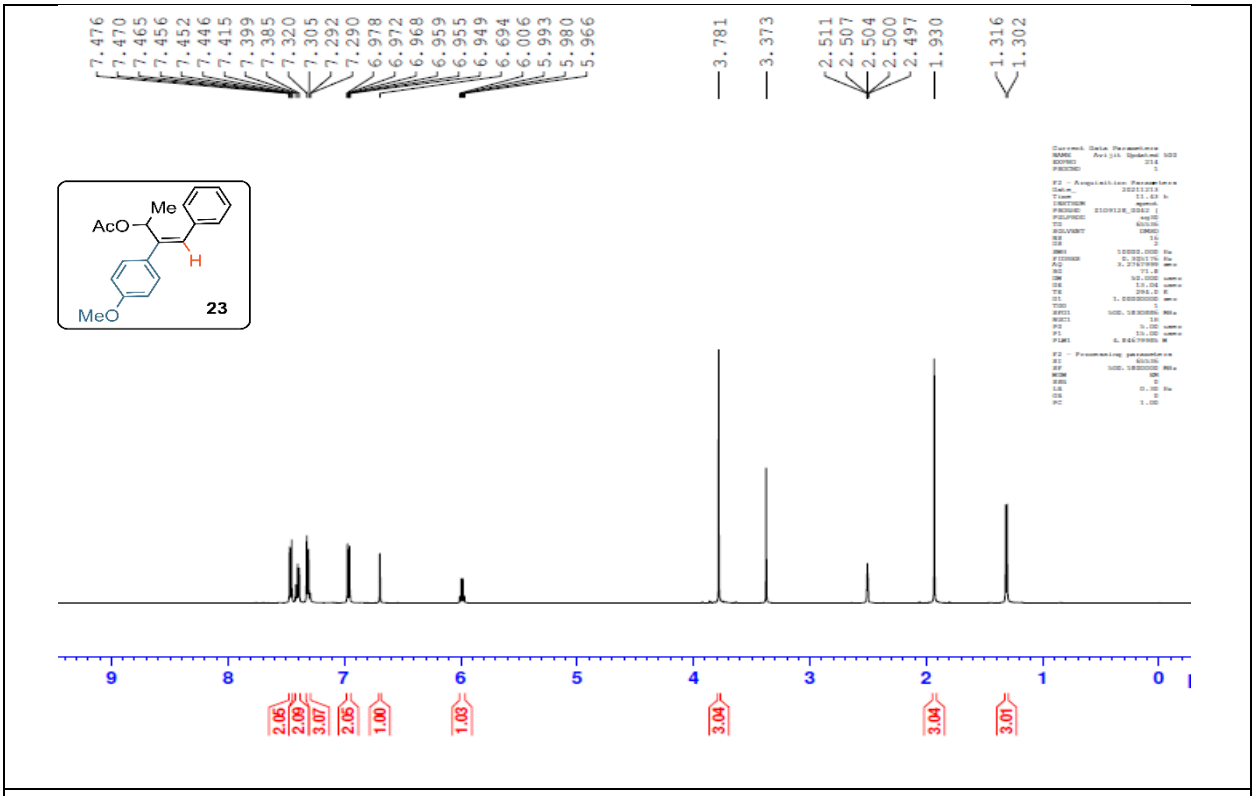
(8) Panteleev, J.; Huang, R. Y.; Lui, E. K. J.; Lautens, M. *Org. Lett.* **2011**, *13*, 5314−5317.

(9) Babu, M. H.; Kumar, G. R.; Kant, R.; Reddy, M. S. *Chem. Commun*. **2017**, *53*, 3894.

(10) Liu, Z.; Derosa, J.; Engle, K. M. *J. Am. Chem. Soc*. **2016**, *138*, 13076.

(11) Dutta, S.; Shandilya, S.; Yang, S.; Gogoi, M. P.; Gandon, V.; Sahoo, A. K. *Nat. Commun*. **2022**, *13*, 1360

4B.9. Spectra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7.452
7.446
7.415
7.399
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7.320
7.305
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7.290
6.978
6.972
6.968
6.959
6.955
6.949
6.694
6.006
5.993
5.980
5.966
3.781
3.373
2.511
2.507
2.504
2.500
2.497
1.930
1.316
1.302
AcO
Me
H
MeO
23
9
8
7
6
5
4
3
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2.08
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2.06
1.00
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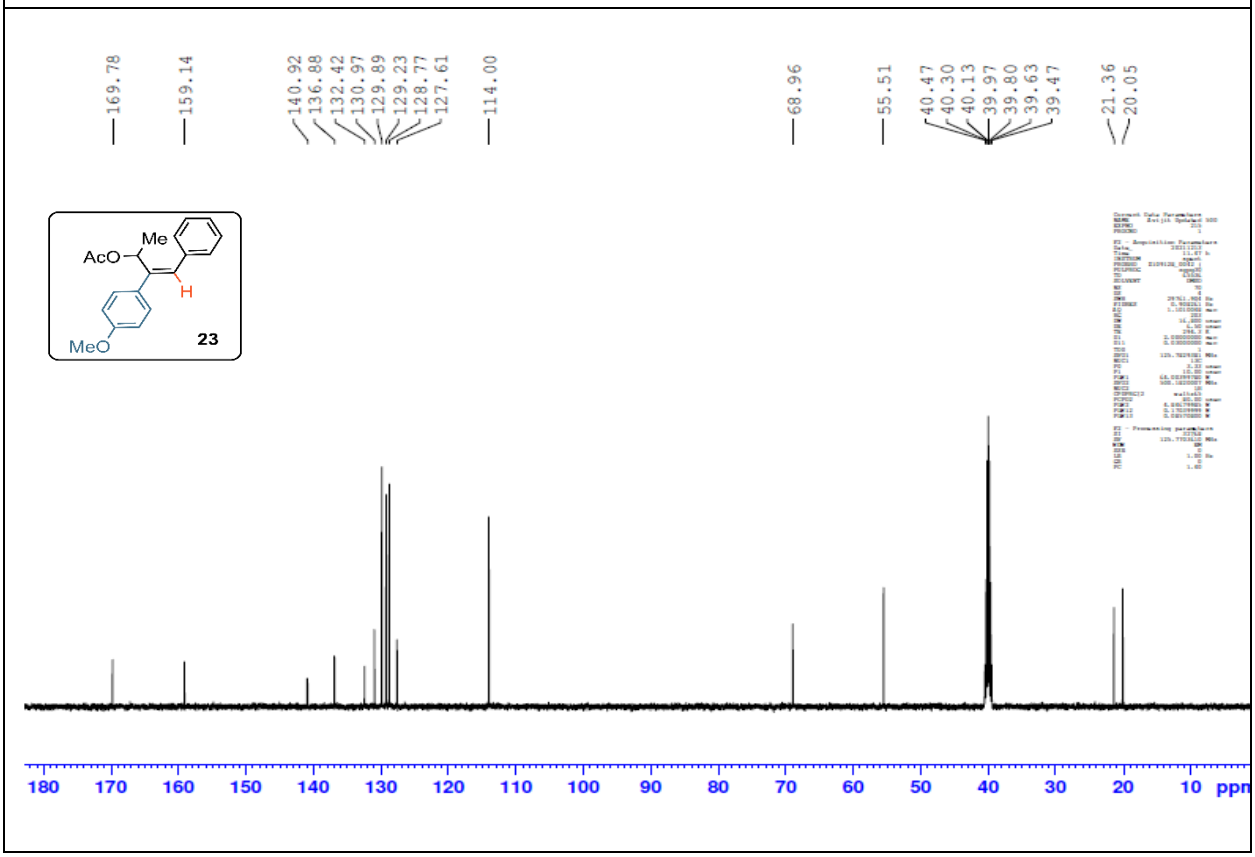
3.04
3.01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136.88
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129.89
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127.61
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40.47
40.30
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39.97
39.80
39.63
39.47
21.36
20.05
AcO
Me
H
MeO
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130
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110
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70
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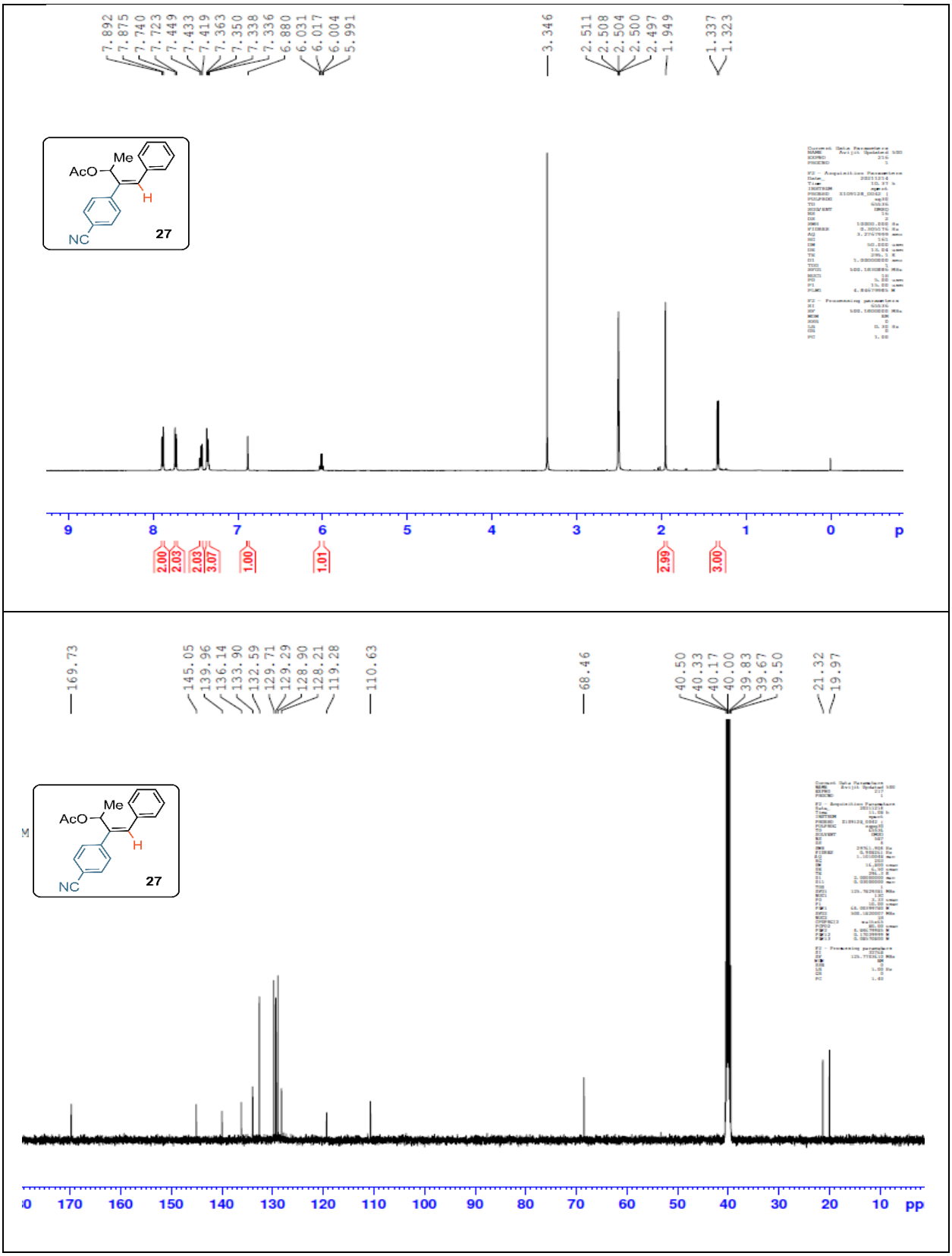
10
ppm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6.004
5.991
3.346
2.511
2.508
2.504
2.500
2.497
1.949
1.337
1.323
Me
AcO
H
NC
27
9
8
7
6
5
4
3
2
1
0
p
2.00
2.03
2.03
3.07
1.00
1.01
2.99
3.00
169.73
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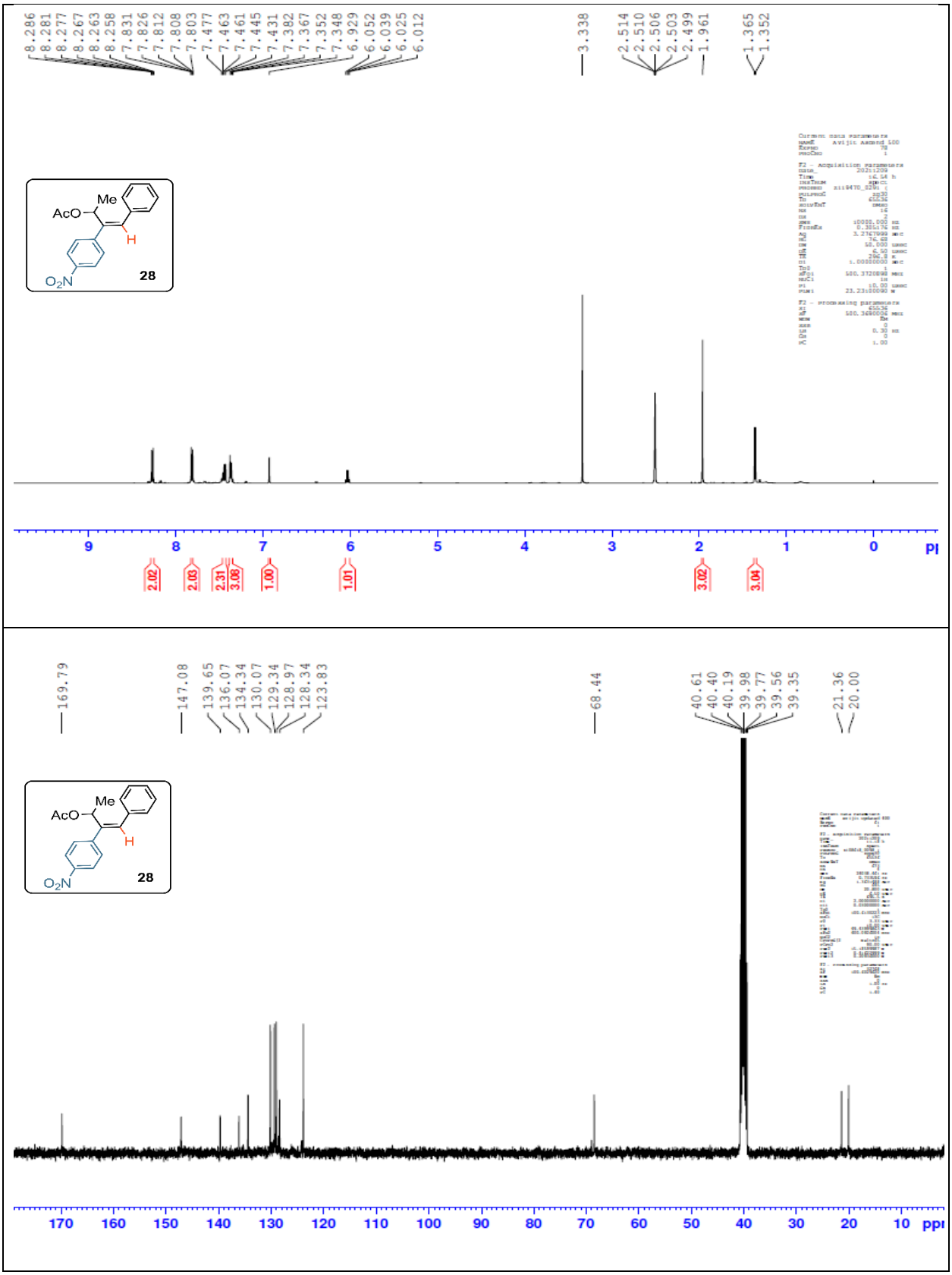
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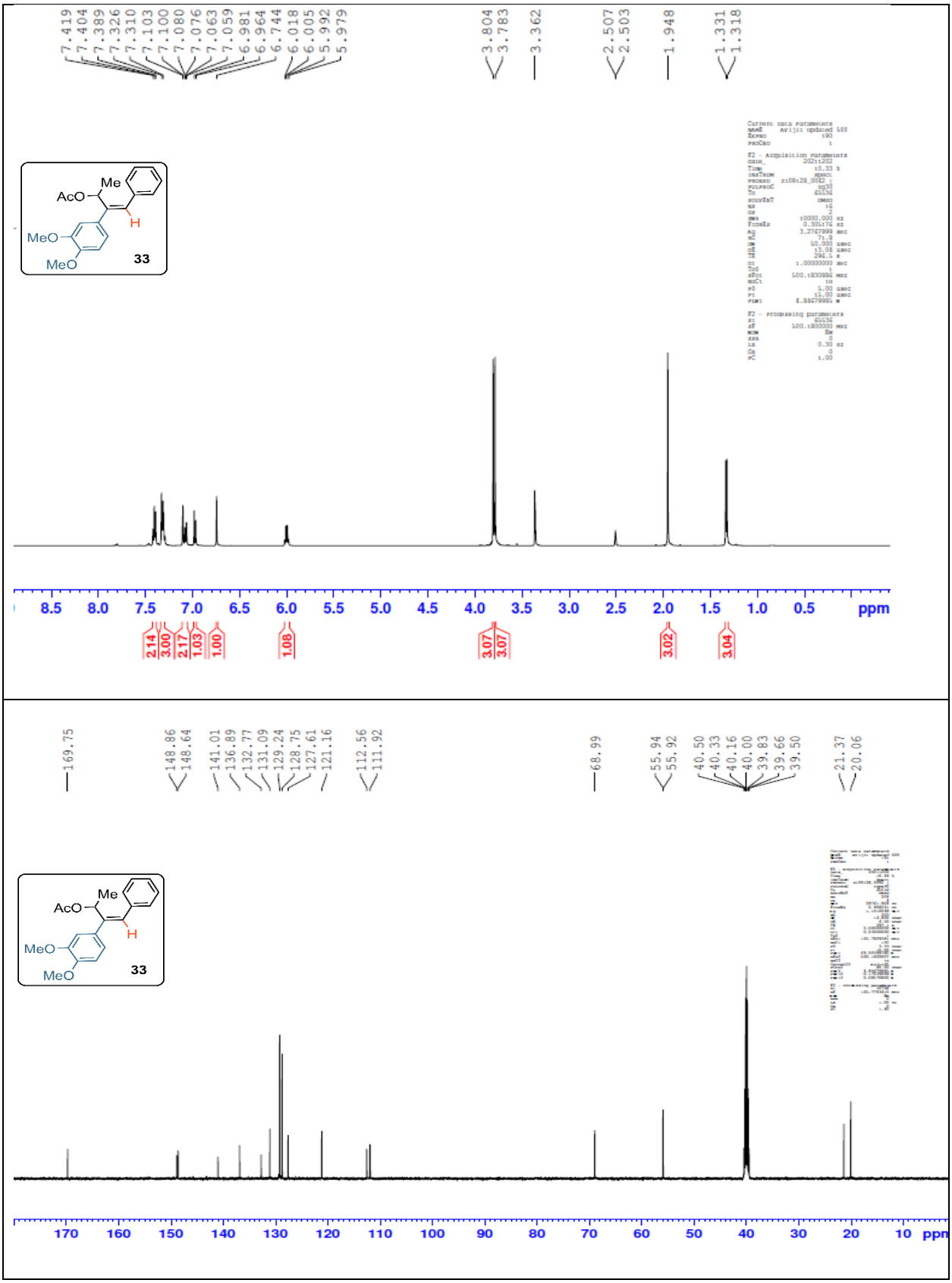
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MeO
MeO
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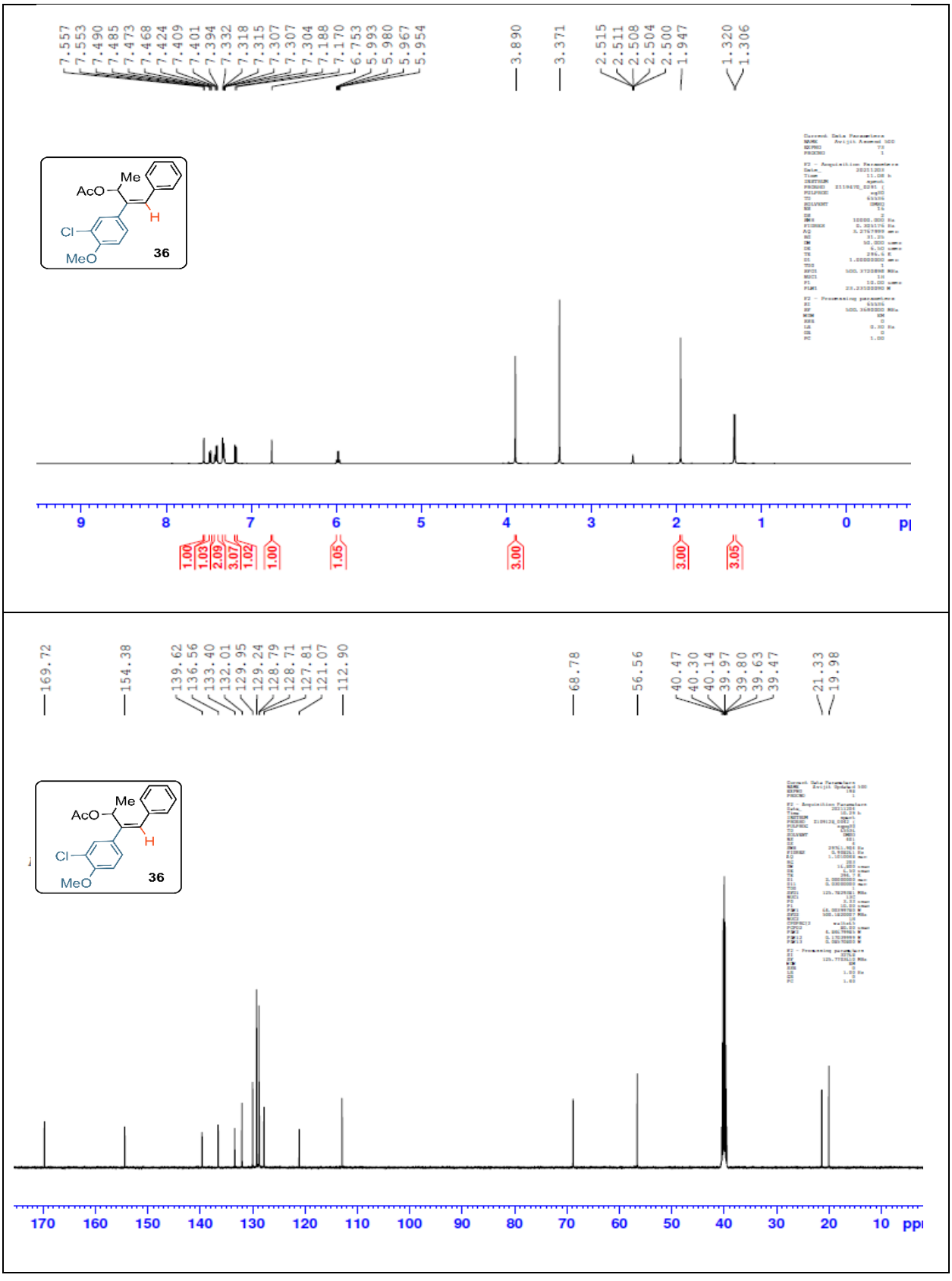
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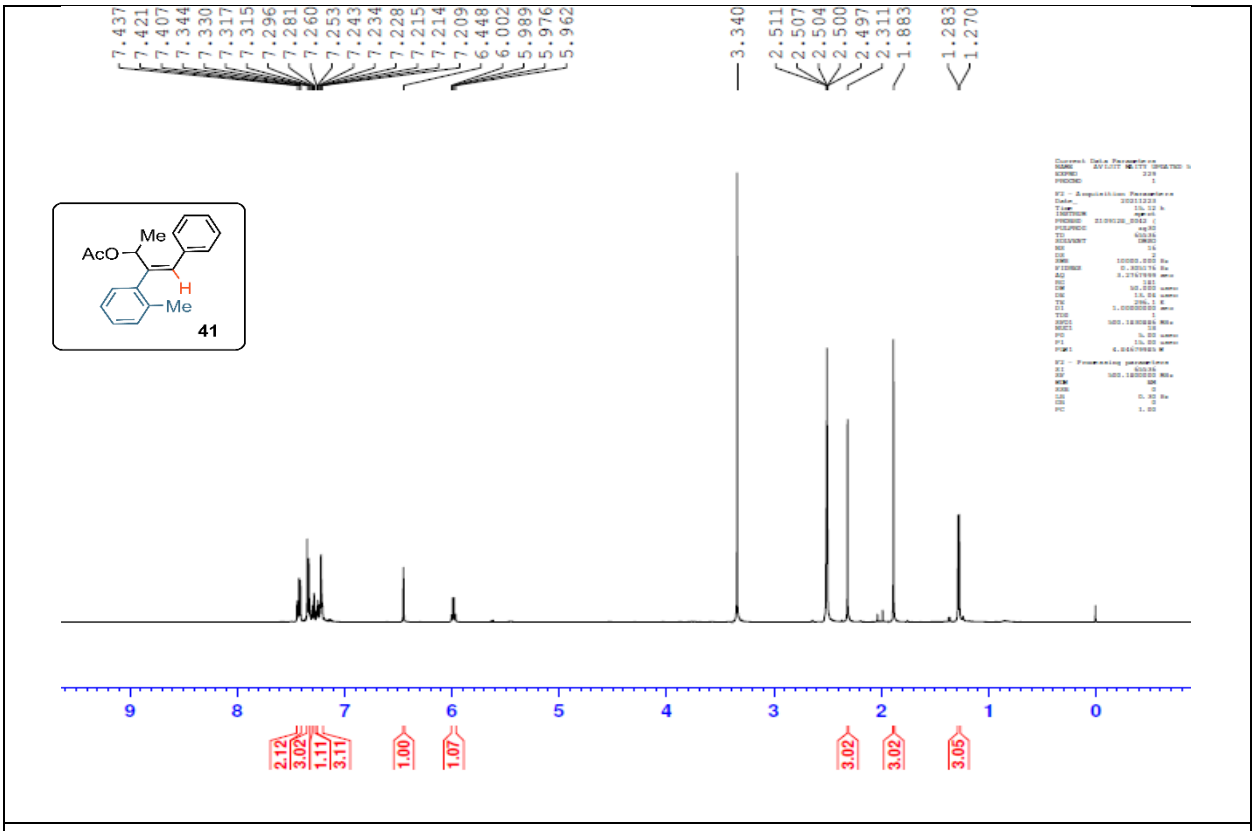
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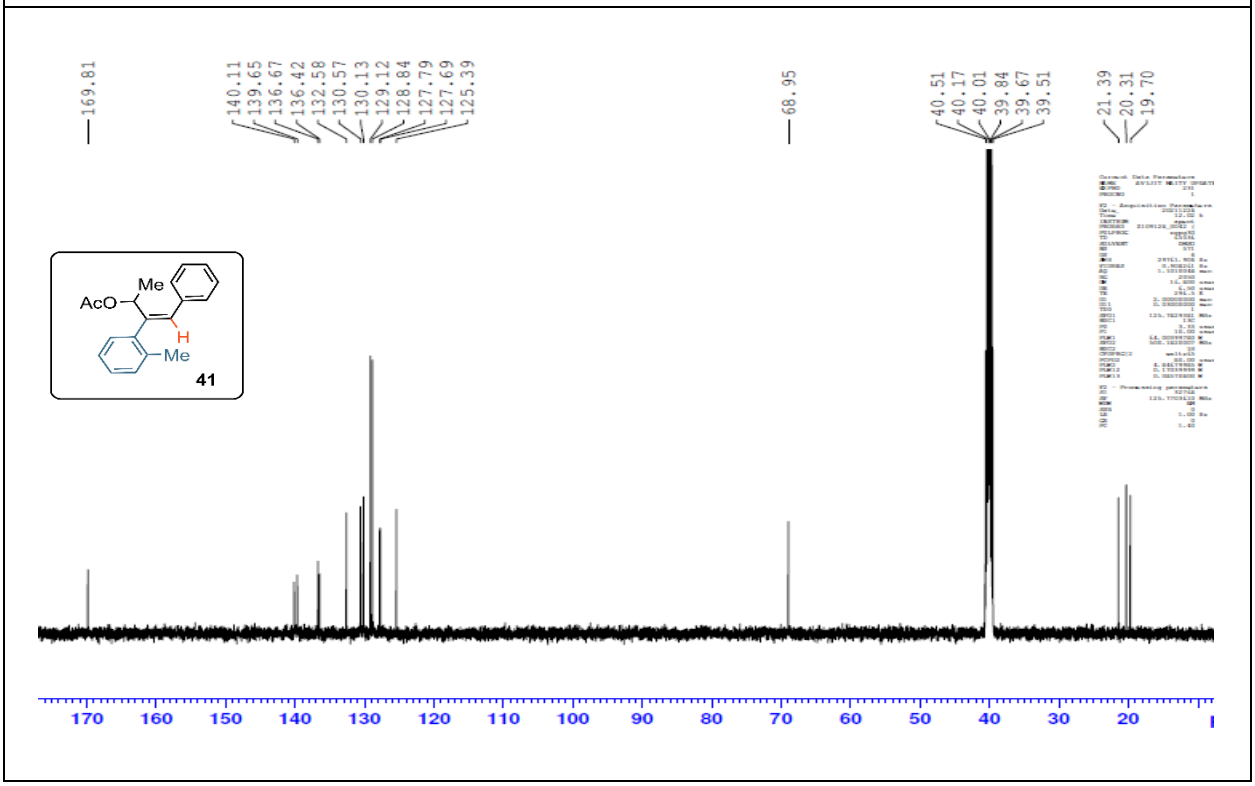
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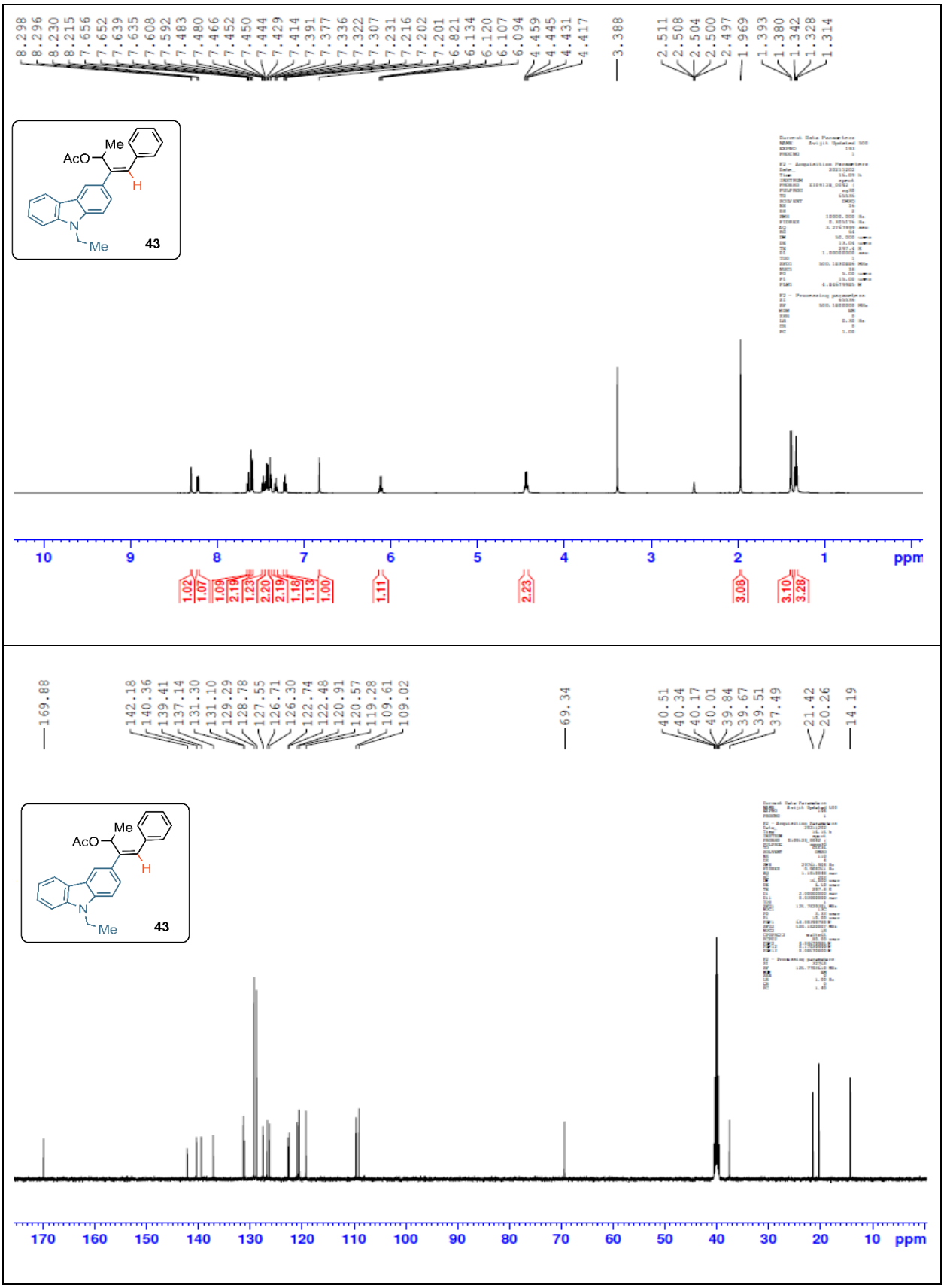
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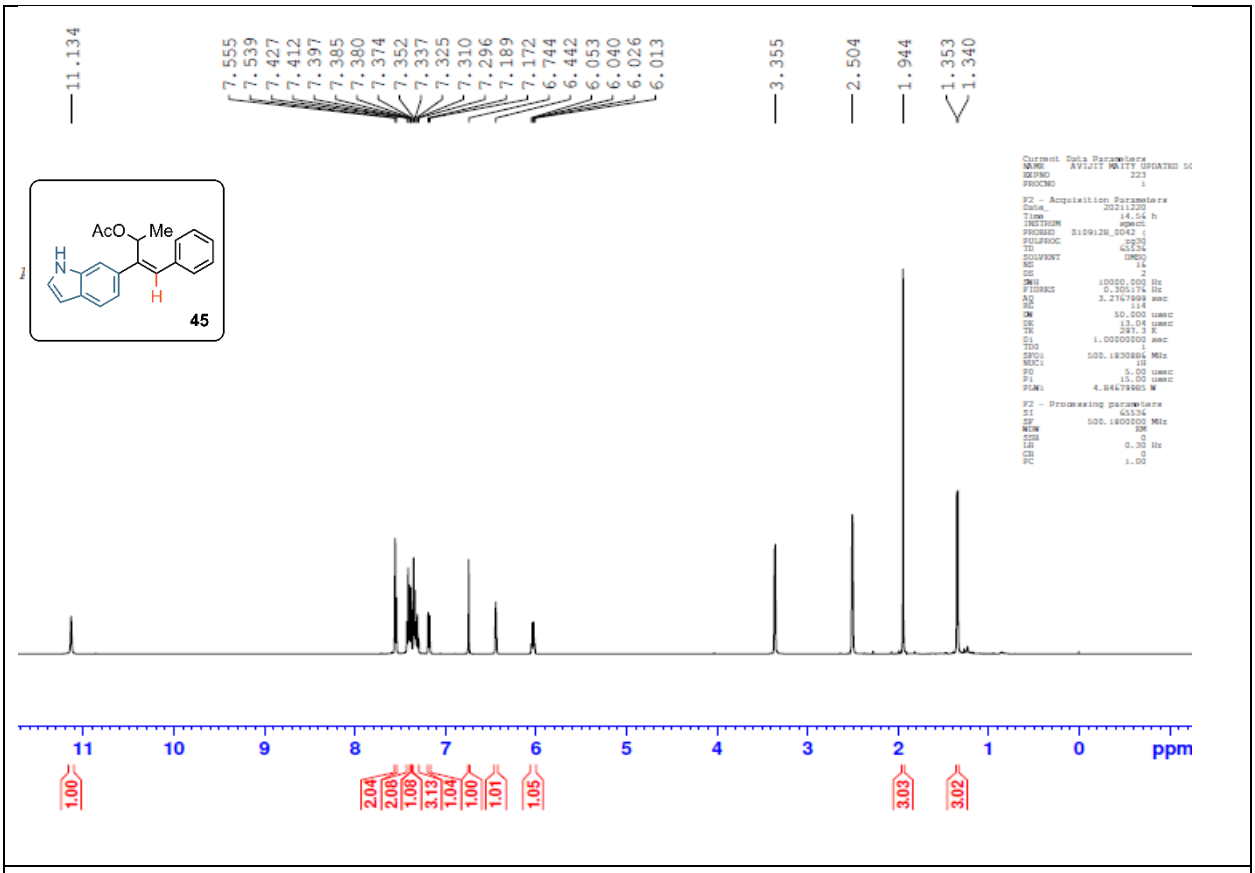
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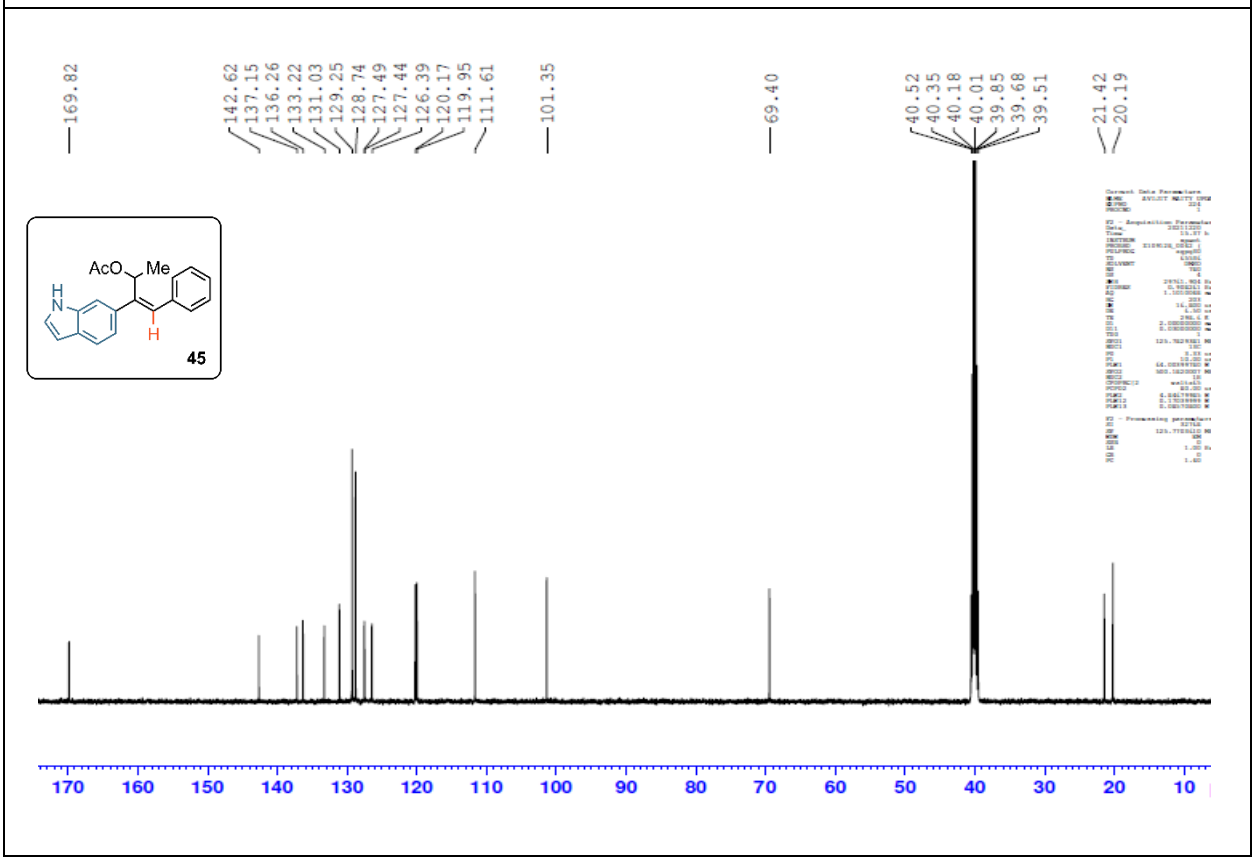
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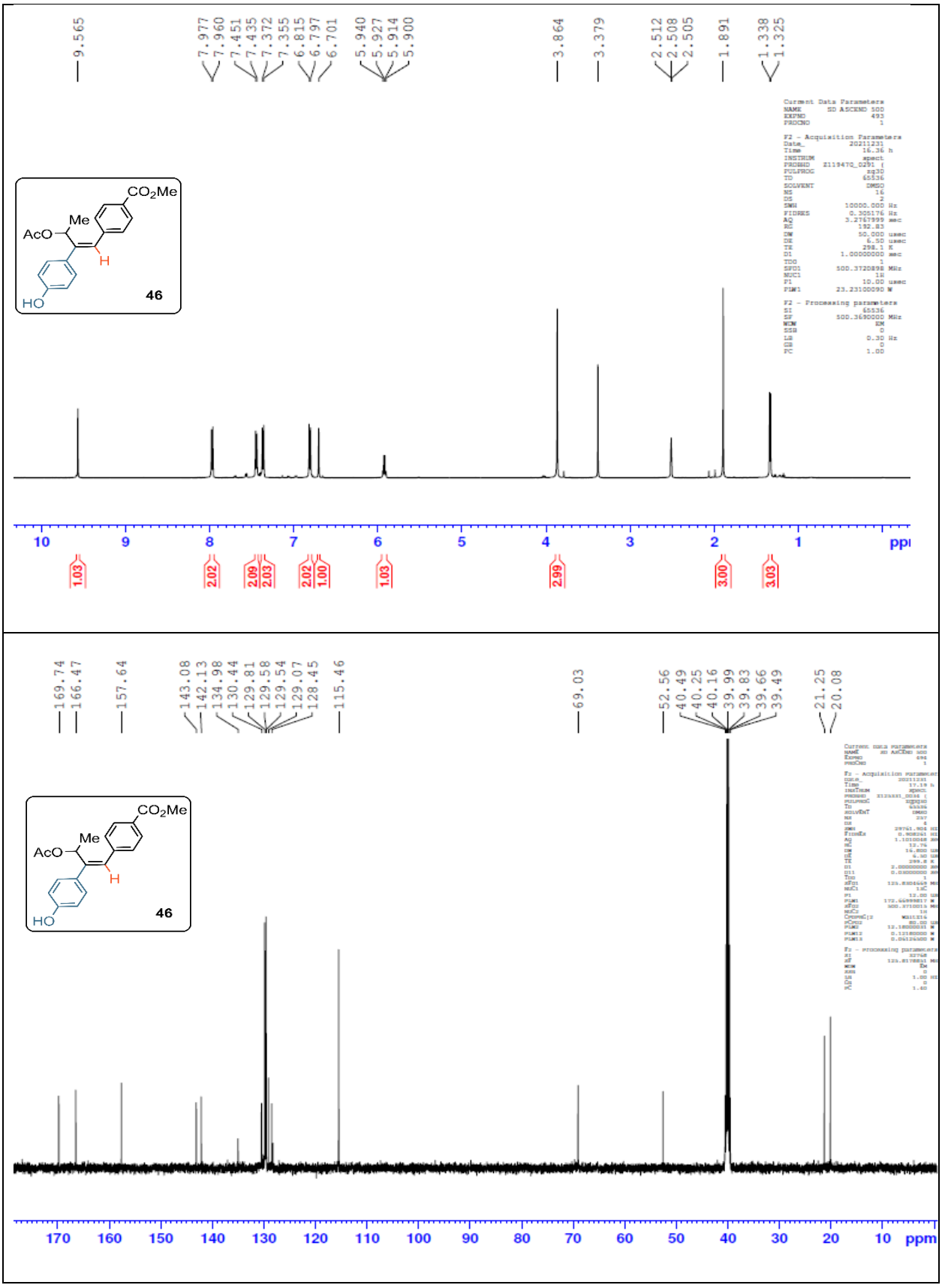
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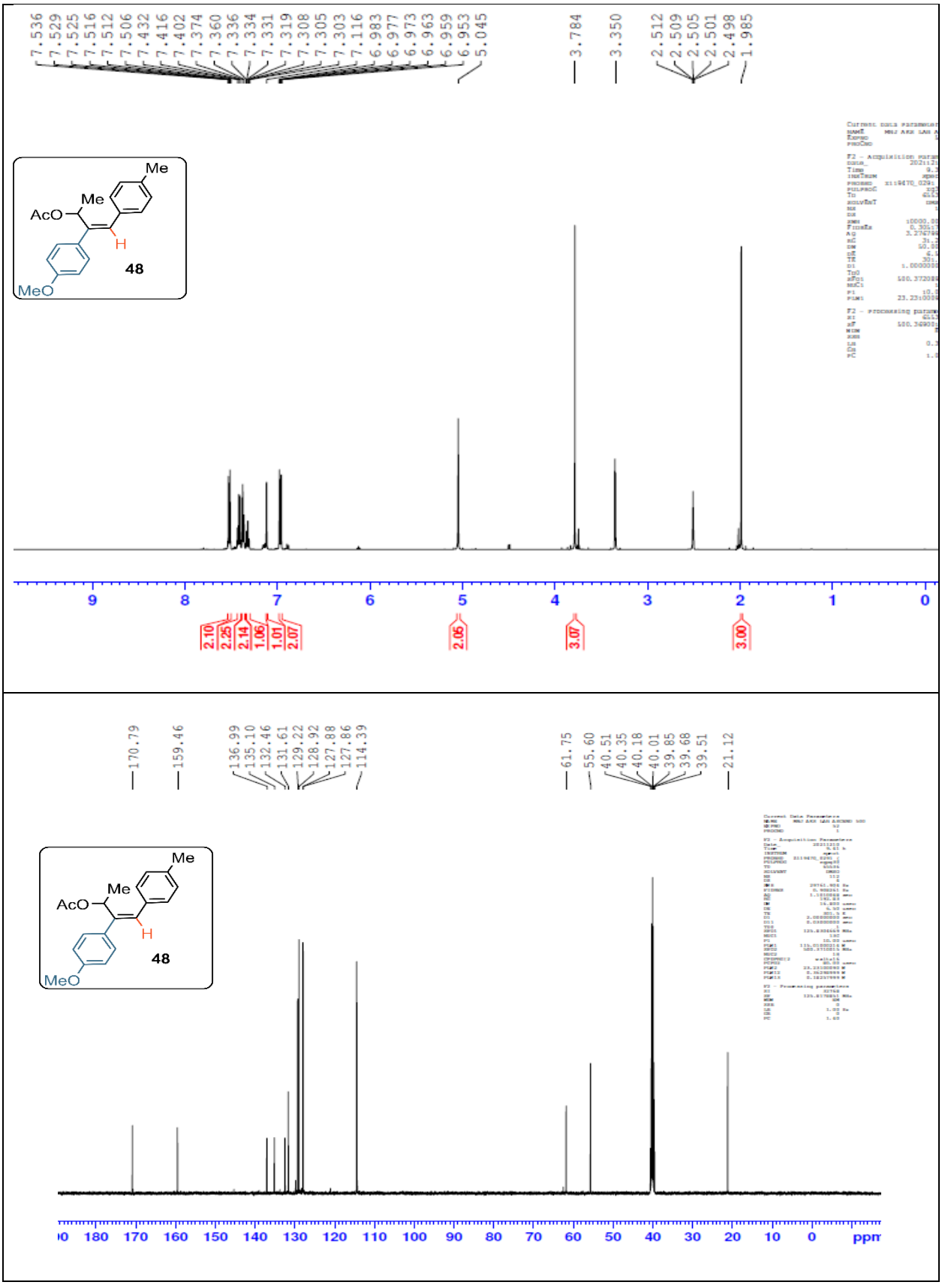
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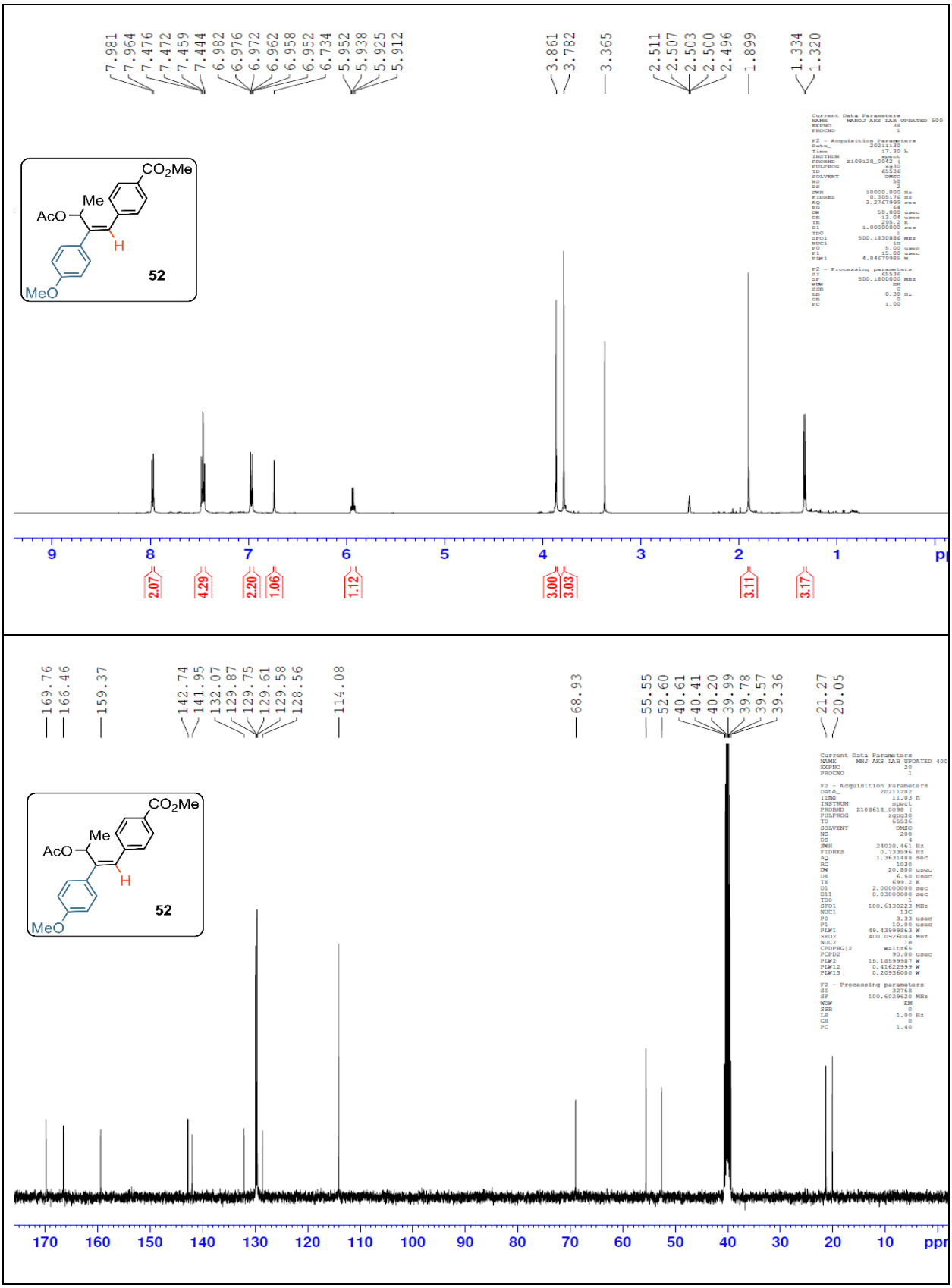
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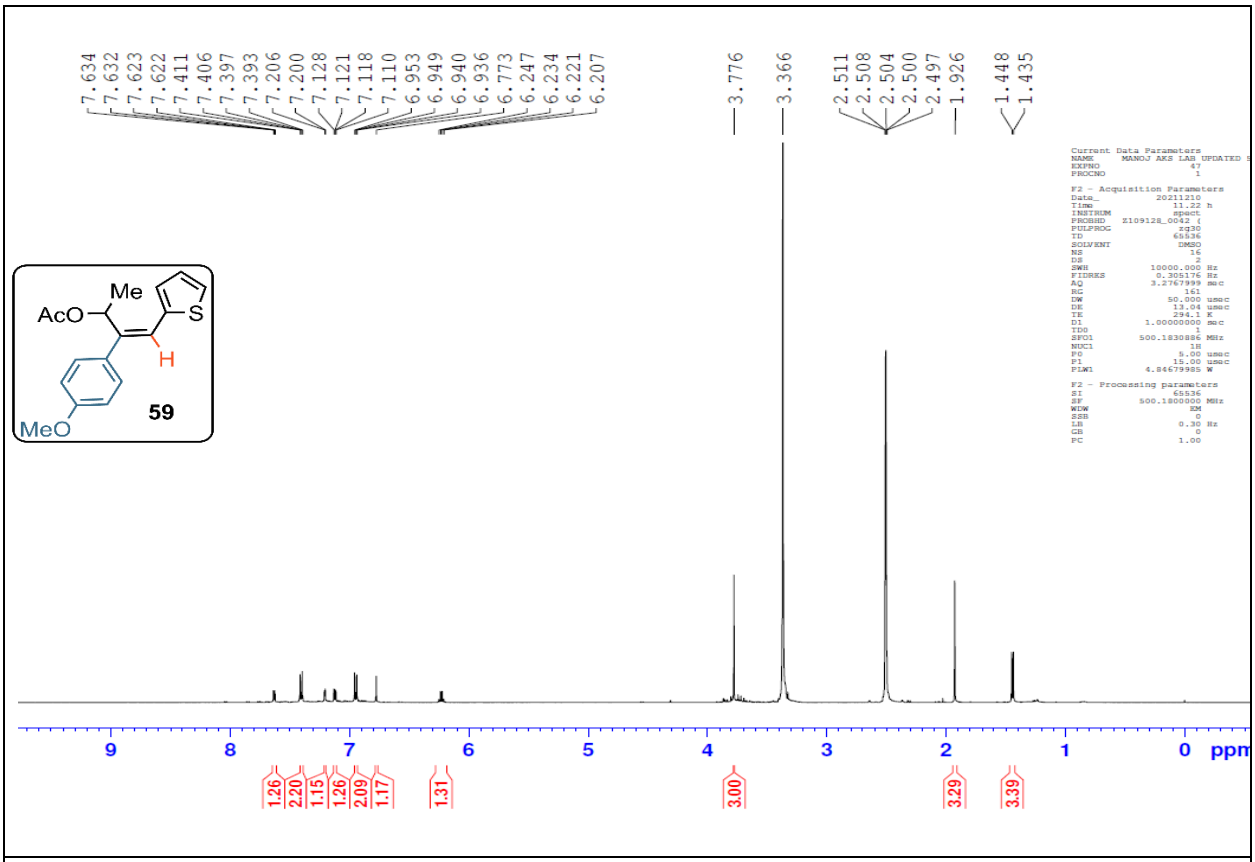
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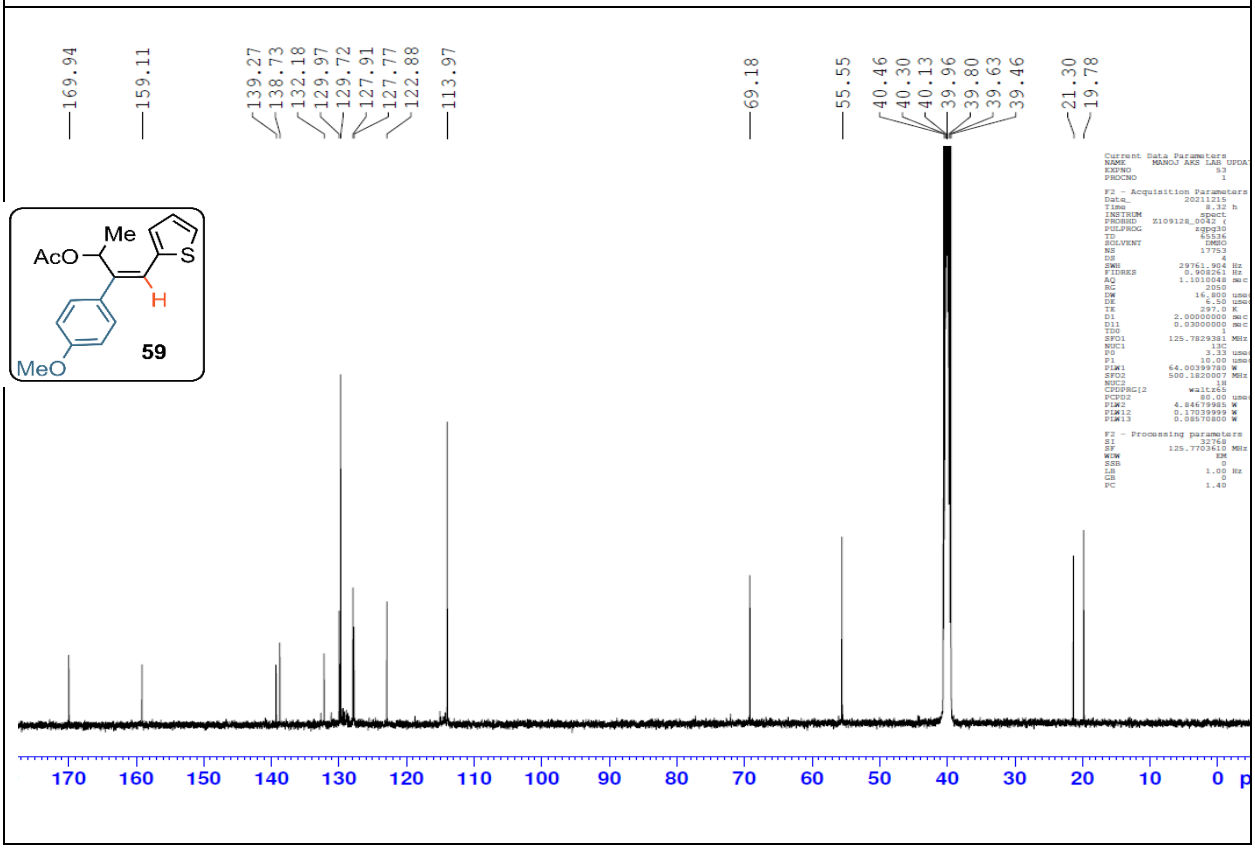
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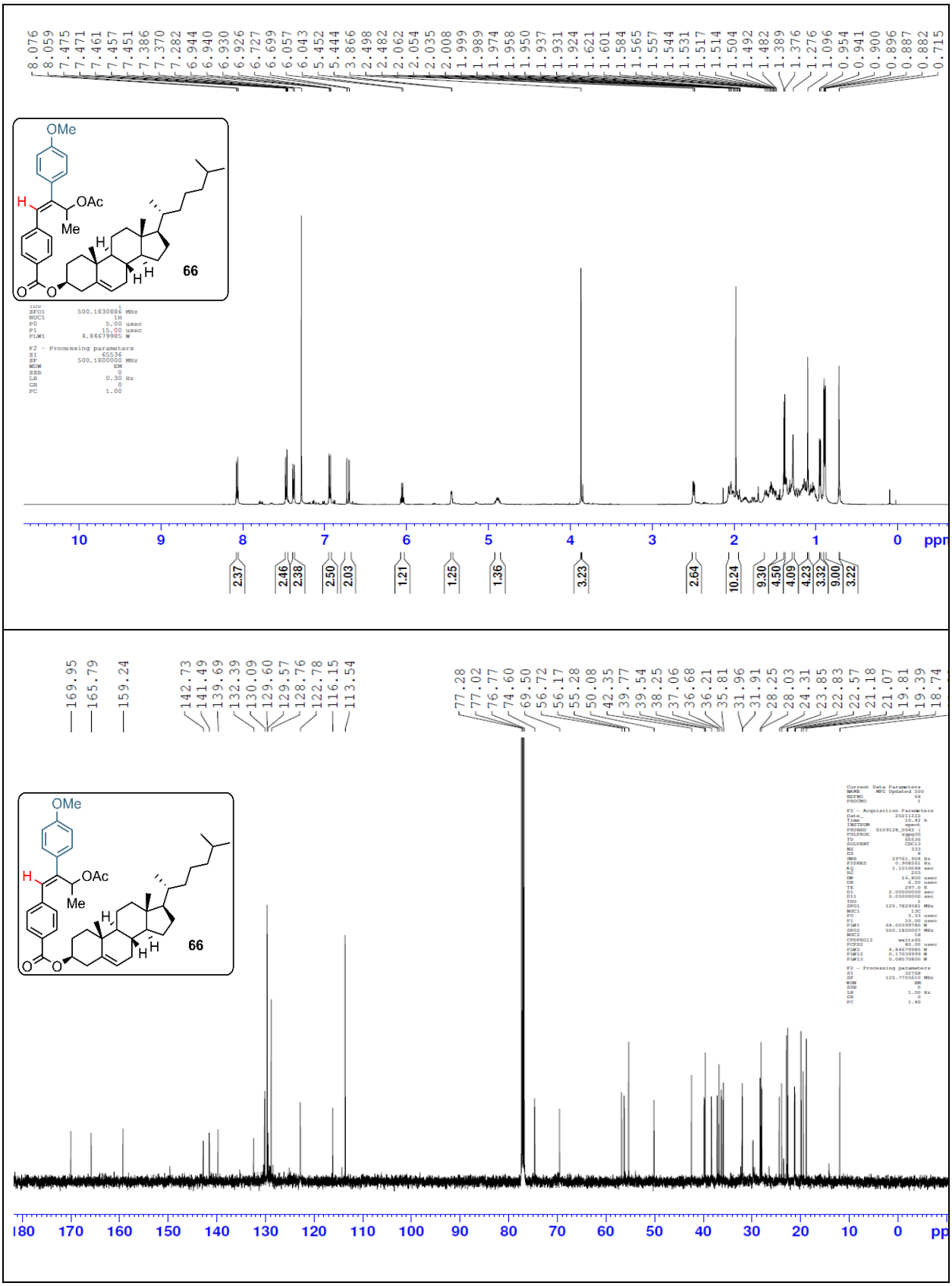
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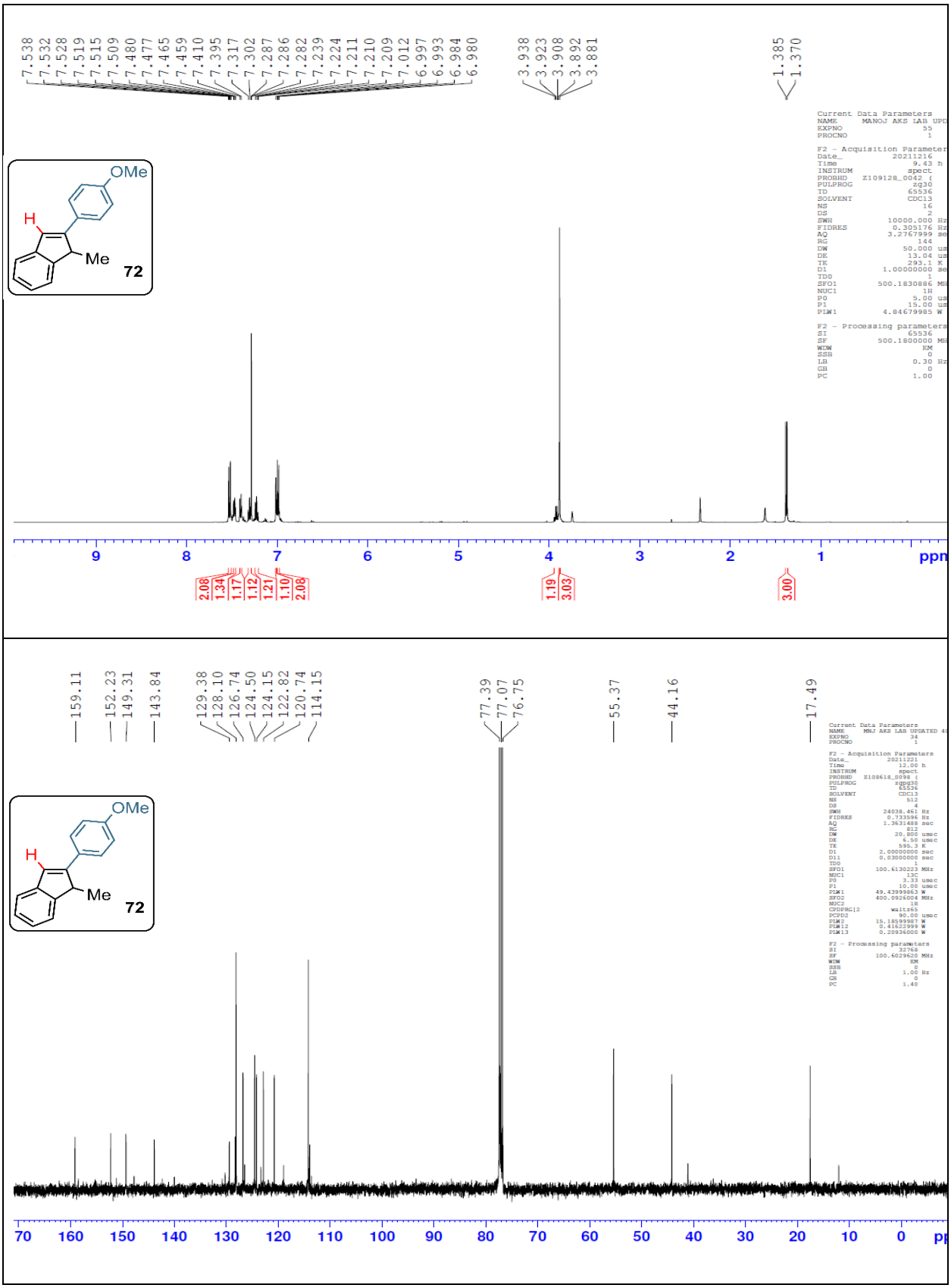
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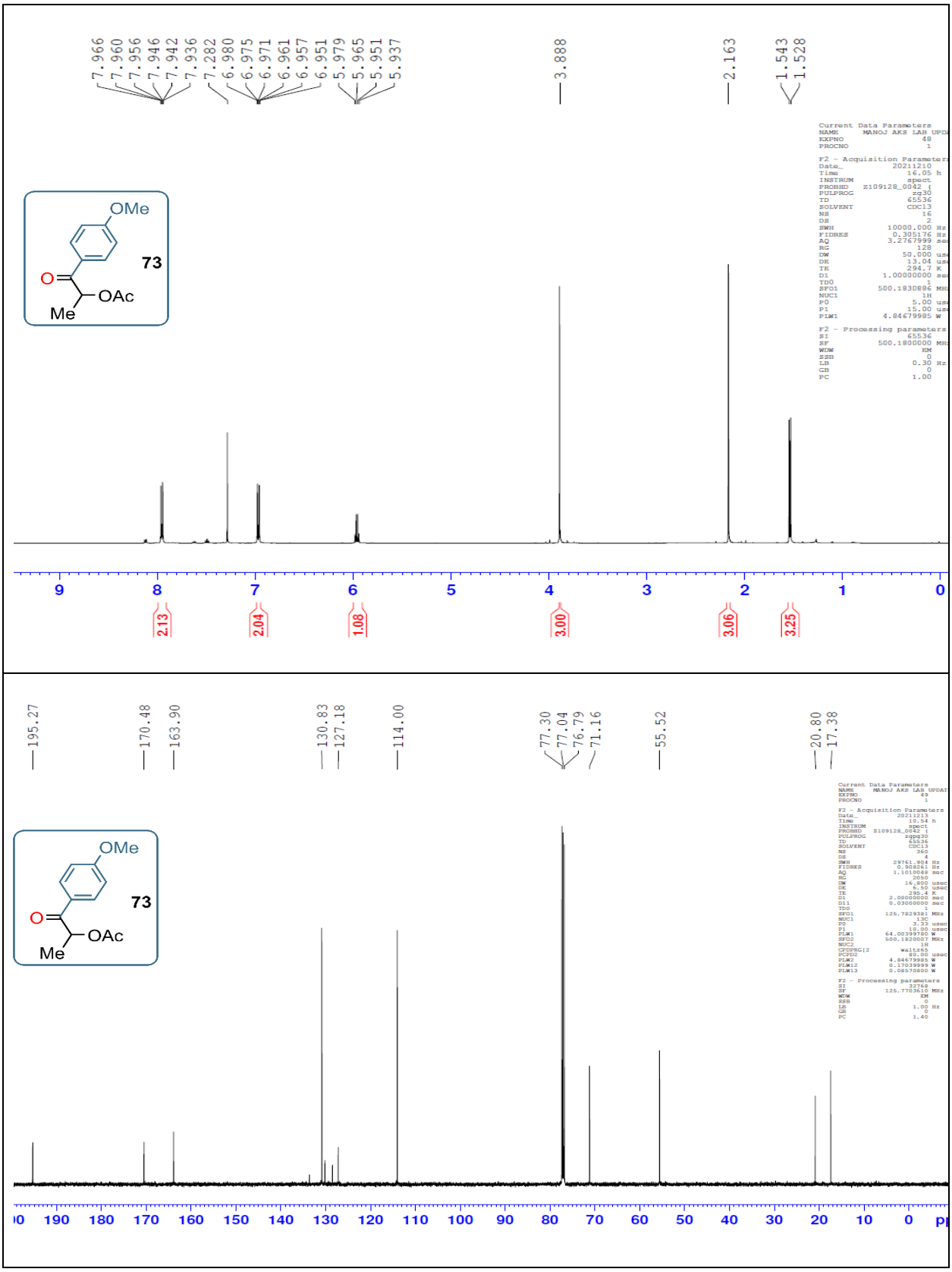
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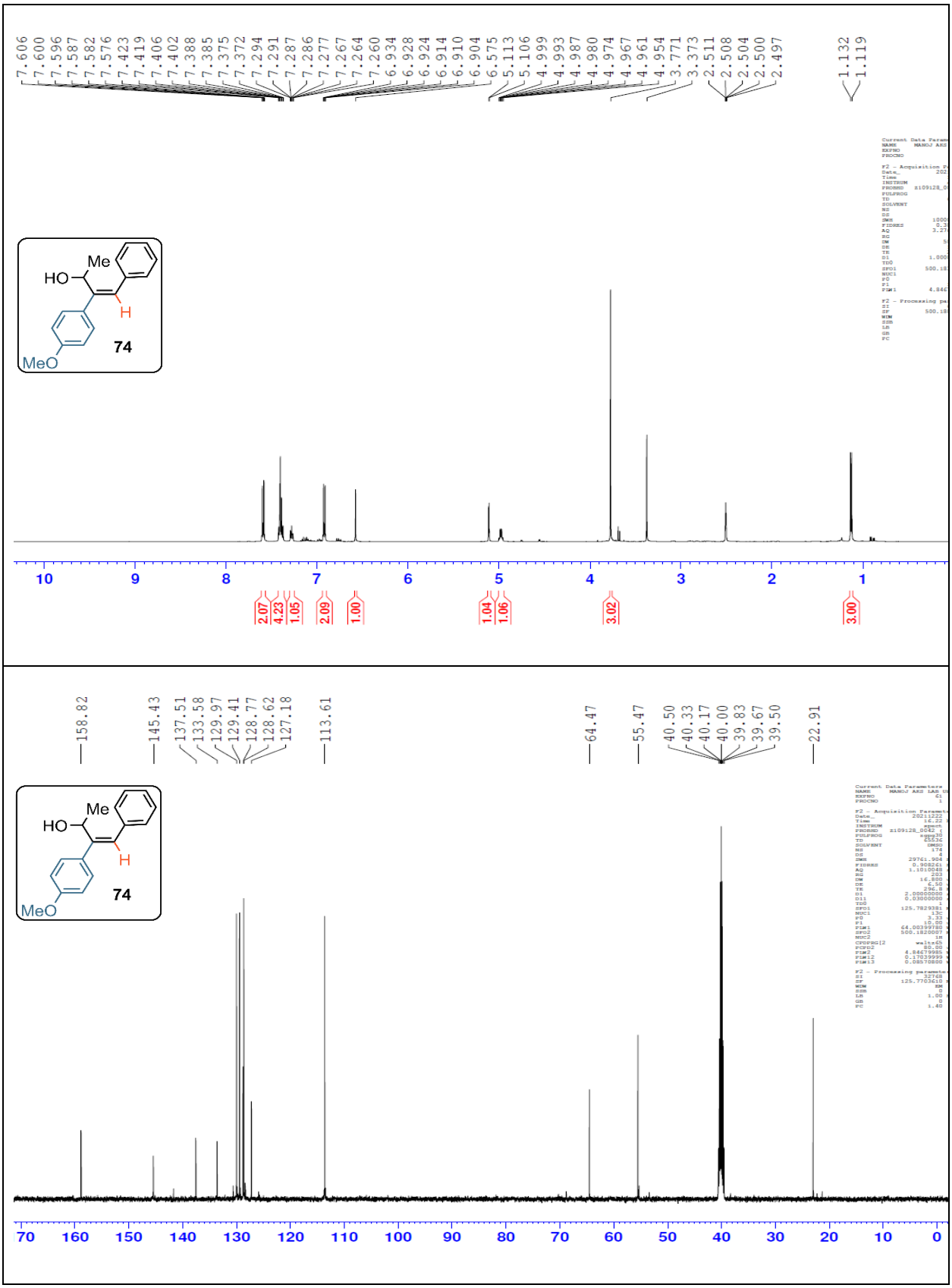
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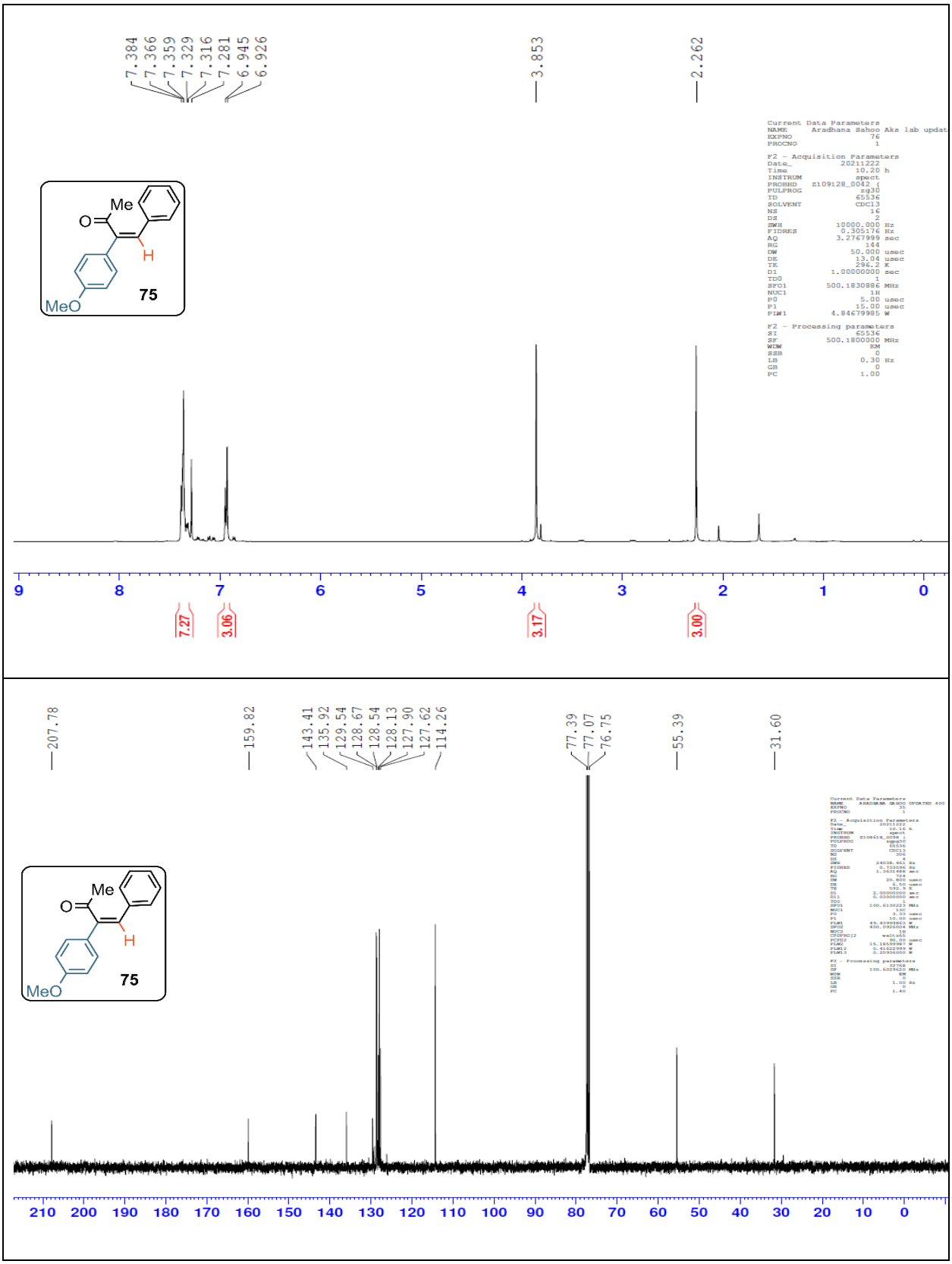
7.384
7.366
7.359
7.329
7.316
7.281
6.945
6.926
3.853
2.262
Me
O
H
MeO
75
9
8
7
6
5
4
3
2
1
0
7.27
3.06
3.17
3.00
207.78
159.82
143.41
135.92
129.54
128.67
128.54
128.13
127.90
127.62
114.26
77.39
77.07
76.75
55.39
31.60
Me
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MeO
75
210
200
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150
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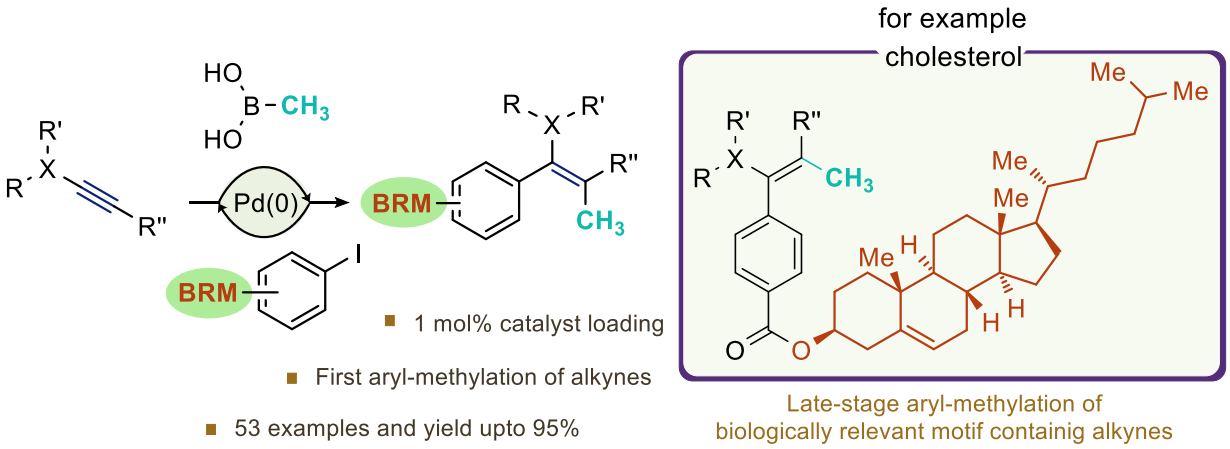
Chapter-5

Palladium Catalyzed *Syn*-1,2-Aryl-Methylation of Internal Alkynes

Abstract



A Pd-catalyzed s*yn*-1,2-arylmethylayion of internal alkynes (ynamides/ yne-acetates/ propargyl phthalimide) is described. The reaction uses readily available and bench stable iodo-arenes and methyl boronic acid as coupling partners to provide access to methyl containing tetra-substituted olefins. The reaction is regio as well stereoselective. Notably, the reaction involves a vinylic [Pd]-Me complex, participation of such intermediate in the three-component alkyne difunctionalization is reported first time. The scope is broad (53 examples), showing excellent functional-group tolerance. The synthetic manifestations of the products are also demonstrated.

Publication

S. Dutta, A. K. Sahoo. *Manuscript Communicated*

5.1. Introduction

Being the smallest nonpolar substituent in organic chemistry, the "methyl group" is most commonly structural motifs found in many drug candidates (~80% of top-selling small-molecule pharmaceuticals in 2018 contains methyl moiety).[1] The "methyl group" in the molecule modulates solubility, hydrophilicity, and conformation of the biologically important compounds, which is commonly known as "magic methyl effect".[2] In addition, trideuteriomethyl (CD_3) group has also been used in many drug candidates.[3] That being the case, developement of synthetic method that instals a methyl group in the organic compounds has gained a remarkable amount of attention. Thus, numerous breakthrough in catalytic two-component C-Me bond formation via cross-coupling reactions and C–H functionalization have been developed; CH_3-I, CH_3-OTs, $PO(OCH_3)_3$, $CH(OCH_3)_3$, trimethylboroxine, and $CH_3B(OH)_2$ have been used as methylating reagents (**Figure 5.1**).[3f-l] Despite the progresses made in the methylation process, multi-component reactions forming C–Me bond have received less attention. Thus, stitching an alkyne, a carbon-based reaction partner, and a methyl group for the construction of C–C and C–Me bond in a single operation would make a methyl containing tetra-substituted olefins. Interestingly, alkynes are prone to undergo hydro-methylation reaction when exposed to air-sensitive methylating reagents, like $AlMe_3$ and MeMgX (**Figure 5.1**). While $AlMe_3$ has been used for the allyl-methylation of symmetrical alkyne (**Figure 5.1**, left side, bottom).

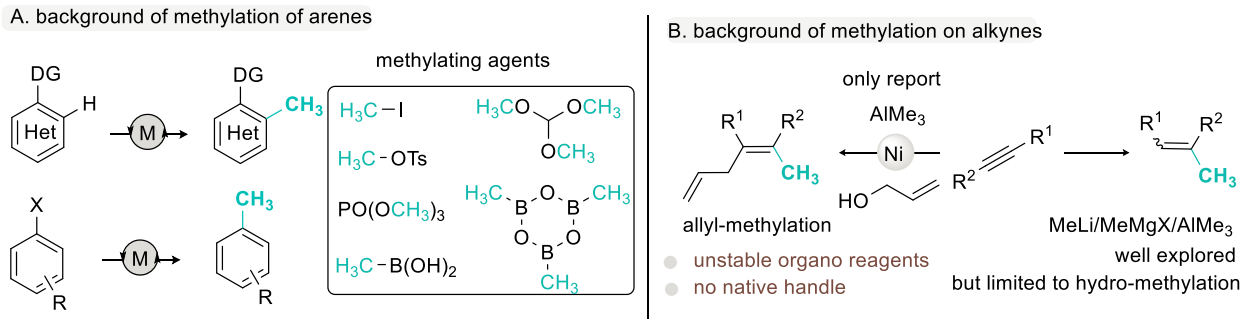
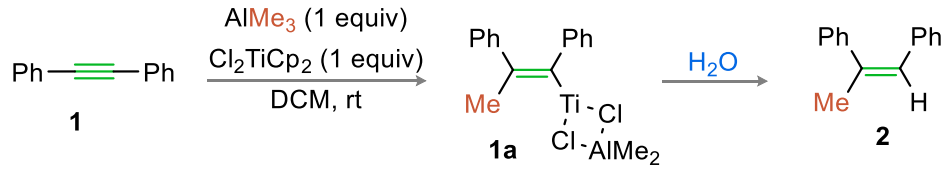


Figure 5.1. Methylation strategies

5.2. Precedents

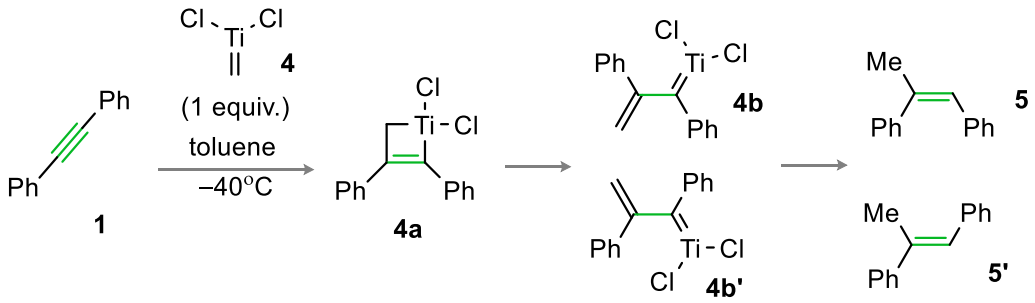
5.2.1 Hydro-methylation of alkynes

In 1996, the Negishi group reported hydro-methylation of diphenylacetylene. $AlMe_3$ Cl_2TiCp_2 in DCM was used as methylating agent as well promoter **(Scheme 5.1)**.[4] Water has been used quenching the vinylic Ti-species **1a**.



Scheme 5.1. Titanocene mediated hydro-methylation of diphenylacetylene

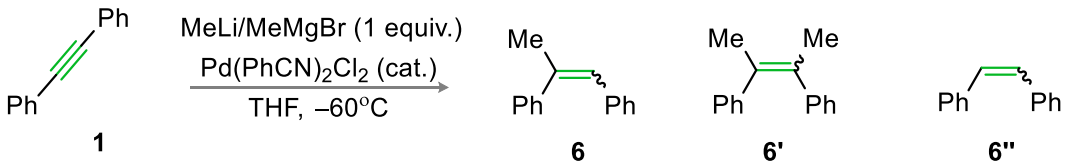
Eisch and co-worker in 2005 reported hydro-methylation of dipheylacetylene using vinylidene Ti-complex **4** (**Scheme 5.2**).[5] Reaction begins with 2+2 cycloadition of **4** and **1** to give **4a** followed by formation of **4b** via electrocyclic ring opening. Meanwhile, **4b** isomerizes to **4b'** which upon hydrolysis gives cis/trans mixture of hydro-methylated product **5/5'**.



Scheme 5.2. Vinyledene Ti-complex promoted hydro-methylation of alkyne

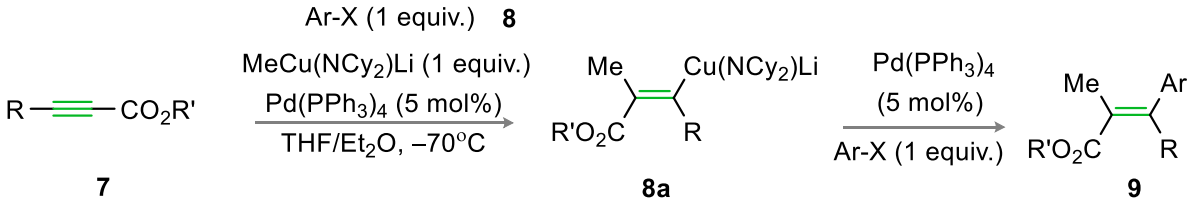
Michman et.al. in 1976 disclosed a Pd-catalyzed methylation of alkyne. The reaction of $Pd(PhCN)_2Cl_2$ with MeLi or MeMgBr generates a methylpalladium complex, which reacts with diphenylethyne to give a mixture of *cis*- and *trans*–2,3-diphenylbut-2-enes **6'** as major products (**Scheme 5.3**).[6] Meanwhile, a mixture of

cis-/*trans*-1,2-diphenylprop-1-ene **6** and *cis*-/*trans*-1,2- diphenylethene **6''** has been formed as by-product.



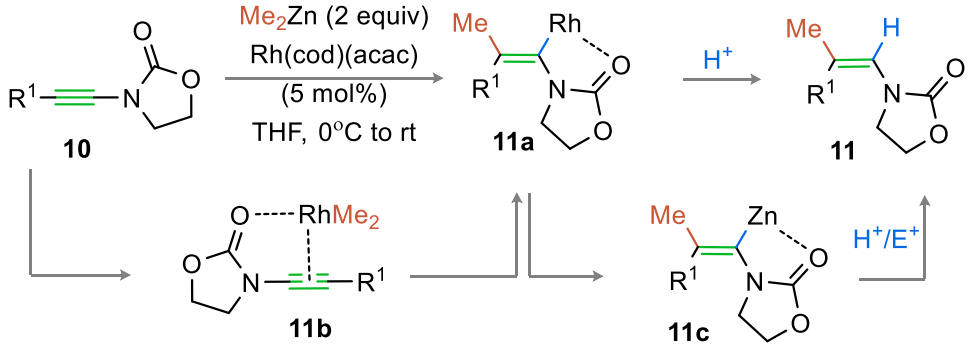
Scheme 5.3. Palladium catalyzed methylation of alkynes

In 1987, a remarkable protocol of methyl-arylation of proipiolates are showcased by Saegusa and coworkers (**Scheme 5.4**).[7] MeCu(NCy2)Li was used as methyl regant which undergoes methyl-cupration of propiolate 7 (b-methylation) to give vinyl-Cu complex **8a**. Next, **8a** undergoes Pd-catalyzed arylation of arylation using aryl halides **8** yielding the final methylated product **9**.



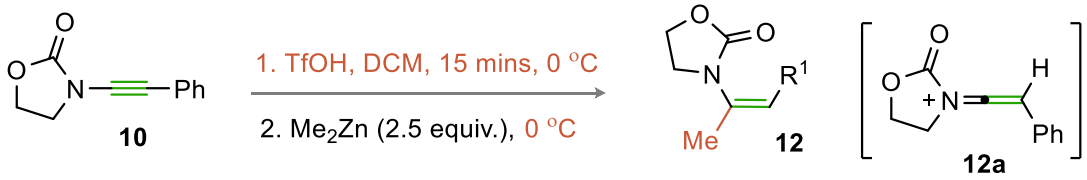
Scheme 5.4. Alkyl-zincation of ynamides

In 2009, the Lam group elegantly adopted a chelation strategy for hydro-methylation of oxazolidinone ynamide (**Scheme 5.5**).[8] The reaction of ynamide **10** in presence of dimethyl zinc, Rh(cod)(acac), and proton source furnishes N-enabled methylated tetrasubstituted olefin **11**. The transformation initiates a carbamate assisted alkyne activation by a Rh-catalyst to form **11b**. Next, methyl-zincation of **11b** happens by a regioselective methylation at the β-position of ynamide to form **11a**; this process involves a β-methyl-α-Rh intermediate **11a**. Further, trap of alkenyl-zinc species with proton/electrophiles furnishes **11** (**Scheme 5.5**).



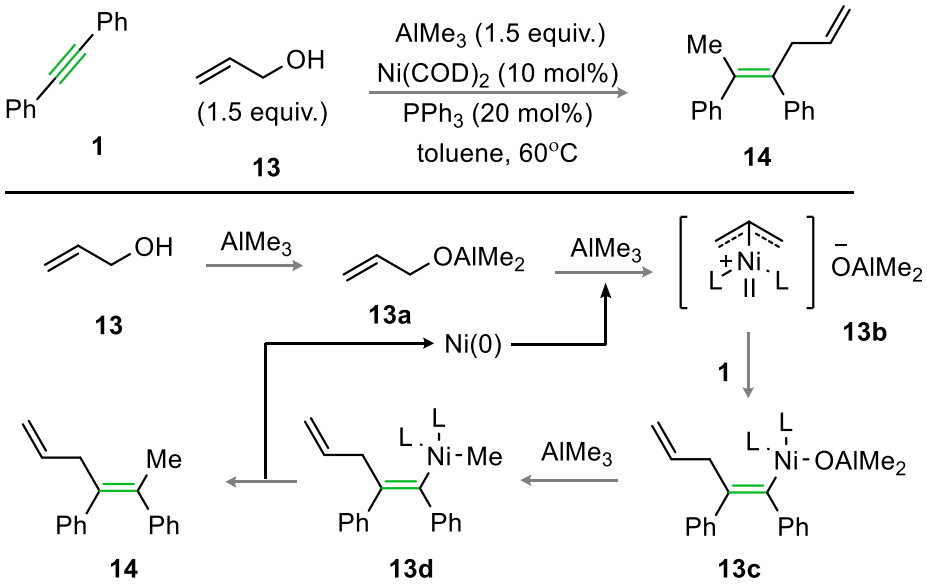
Scheme 5.5. Chelation assisted hydro-methylation of ynamide

An interesting breakthrough of Bronsted acid promoted hydro-methylation of oxazolidinone ynamide **10** by Moulide and coworker in 2017 (**Scheme 5.6**).[9] Preactivation of ynamide in presence of TfOH leads to keteniminium species and dimethylzinc was used for methylation at the α-position of keteniminium species **12a**.



Scheme 5.6. Hydro-methylation of ynamide using preactivation

Very recently, Li and co-workers have developed a Ni(0) catalyzed allyl-methylation of alkynes (**Scheme 5.7**).[10] The alkoxyaluminium species, allyloxydimethylaluminium **13a** is at first formed, which would react with Ni^0 to give π-allynickel intermediate **13b.** Next, carbonickelation of the internal alkyne with **13b** forms vinyl nickel species **13c**. $AlMe_3$ and newly generated **13a**, could participate to produce intermediate **13d**. Finally, reductive elimination releases allylmethylation product with regeneration of Ni^0.



Scheme 5.7. Nickel catalyzed allyl-methylation of alkyne

5.3. Motivation and Scheme Design

In light of our recent demonstration of regioselective dicarbofunctionalization of ynamide and unsymmetrical alkynes, we envisaged that 1,2-arylmethylation of unsymmetrical alkynes could be achieved under Pd-catalysis using aryl-iodides and methyl boronic acid as couplin g partners (**Figure 5.2**). We model the reaction as site-selective coordination of aryl-Pd(II) species, generated in-situ by the oxidative insertion of an aryl iodide to Pd(0), to the alkyne (**A**) which could result the intermediate **B** (our prior studies established this).[11] Next, transmetalation of int-B with methyl boronic acid would lead to int-**C**, which would rapidly reductively eliminate to yield the arylmethylated product **D**. In addition, the reaction has the following challenges: protodemetalation of **B** leading to **E**, formation of methane **F** from Int-**C,** and the classical homo/cross couplings[11] of the respective reactive intermediates (**Figure 5.2**).

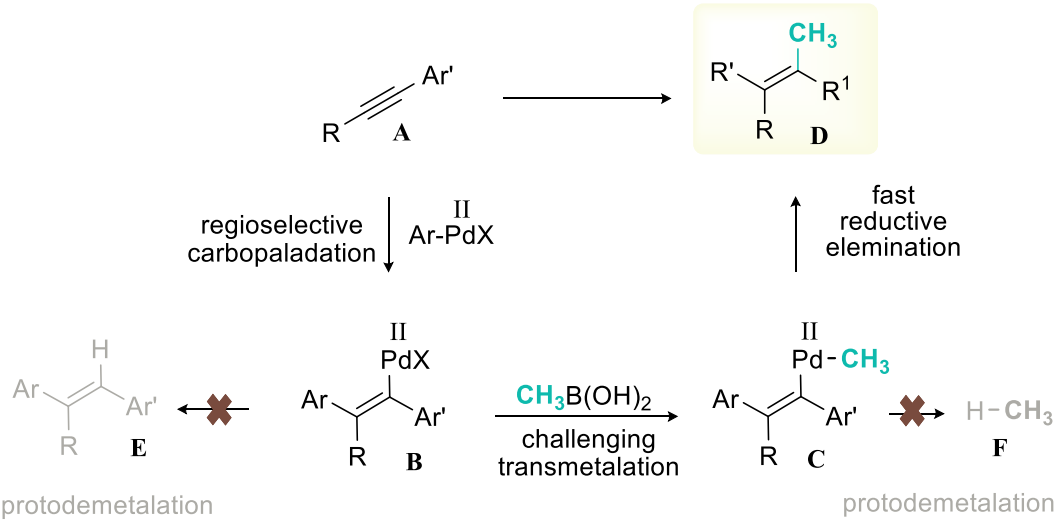


Figure 5.2. Working hypothesis and challenges

To the best of our knowledge, incorporation of both aryl and methyl group across unsymmetrical alkynes remains unknown. We herein report aryl-methylation of alkyne (ynamide and yne-acetates) using aryl iodide and methyl boronic acid under Pd-catalysis with high regioselectivity (**Figure 5.3**).

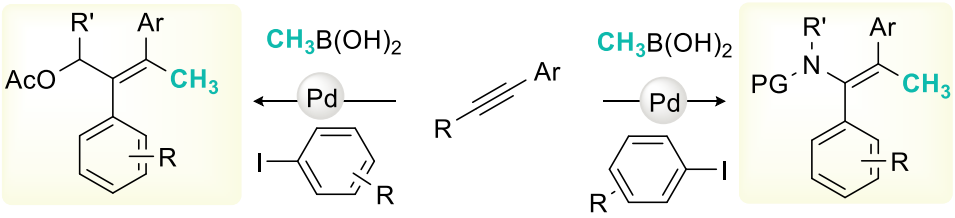
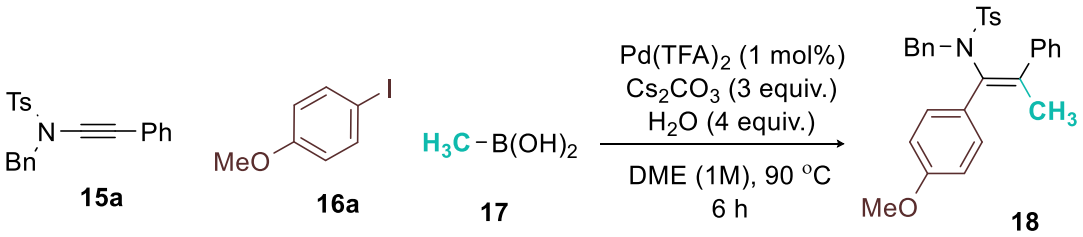


Figure 5.3. Pd-catalyzed aryl-methylation of internal alkynes

5.4. Result and Discussion

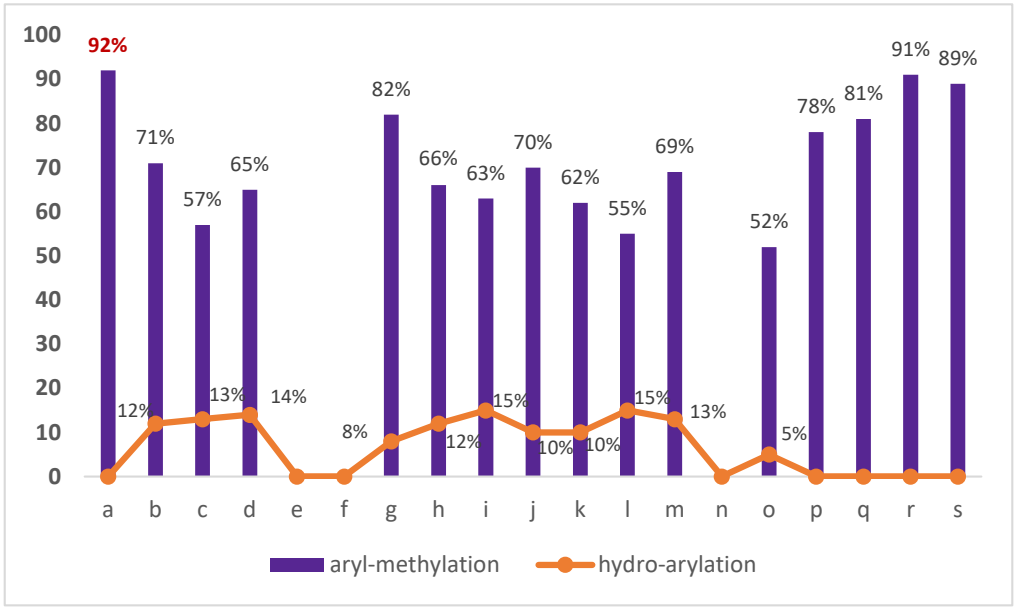
5.4.1. Reaction Optimization

To accomplish aryl methylation of unsymmetrical alkyne, a reaction of N-benzyl-4-methyl-N-(phenylathynyl)benzenesulfonamide (**15a**), 4-iodoanisole (**16a**), and methyl boronic acid (**17**) is planned (**Scheme 5.8**). Extensive studies of various bases, catalysts and solvents



deviation from standard conditions

a) none
b) K_2CO_3 as base
c) K_3PO_4 as base
d) CsF as base
e) LiO^tBu as base
f) Li_2CO_3 as abse
g) $Pd(OAc)_2$ as catalyst
h) $PdCl_2$(dppf).DCM as catalyst
i) $Pd(acac)_2$ as catalyst
j) $PdCl_2$ as catalyst
k) toluene as solvent
l) THF as solvent
m) 1,4-dioxane as solvent
n) DMSO as solvent
o) 120 °C
p) 70 °C
q) without water
r) 2 mol% catalyst
s) 5 mol% catalyst



Scheme 5.8. Optimization Graph [Reaction condition: ynamide **15a** (0.15 mmol), aryl iodide **16a** (0.3 mmol), methyl-boronic acid **17** (0.45 mmol) for overnight; isolated yield].

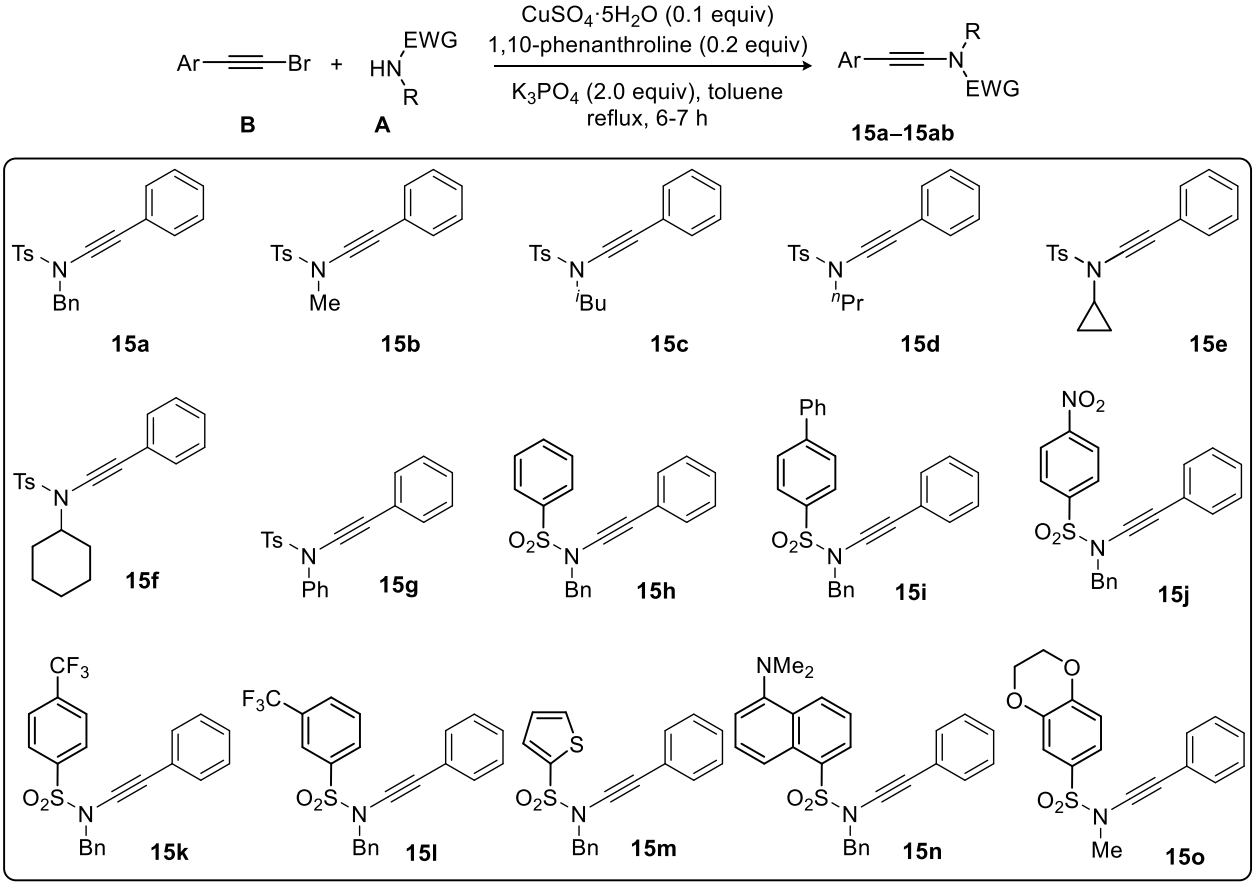
led us to the optimized condition; **15a** (1.0 equiv), **16a** (2.0 equiv), **17** (3.0 equiv), $Pd(TFA)_2$ (1.0 mol%), Cs_2CO_3 (3.0 equiv.), H_2O (4.0 equiv), 1,2–DME (1M). Aryl-methylated product **18** was isolated in 92 % yield (**Scheme 5.8**, entry a). Moderate yields are obtained when bases like K_2CO_3, K_3PO_4, CsF are used (**Scheme 5.8**, entries b–d). On contrary,

LiOtBu and Li_2CO_3 failed to give **18** (**Scheme 5.8**, entries e–f). Comparable results were observed in case of other Pd-catalysts, for example; $Pd(OAc)_2$, $PdCl_2(dppf).DCM$, $Pd(acac)_2$, $PdCl_2$ (**Scheme 5.8**, entries g–j). Solvents like toluene, THF, and 1,4-dioxane were moderate delivering **18** in 55-69% yield (**Scheme 5.8**, entries k–m). No product formation was observed when DMSO solvent was used (**Scheme 5.8**, entry n). Unsatisfactory results were observed upon temperature regulation (**Scheme 5.8**, entries o–p). 81% yield of **18** was observed in the absence of water (**Scheme 5.8**, entry q). Increasing the catalyst loading to 2.0 and 5.0 mol% did not significantly improve the reaction yield.

5.4.2. Synthesis of ynamides

Following the known Cu-catalyzed C-N coupling procdure, ynamides **1e-1aq** were synthesized from corresponding sulfonamides (A) and bromoalkynes (B) (Table 5.1).

Table 5.1. Ynamide chart



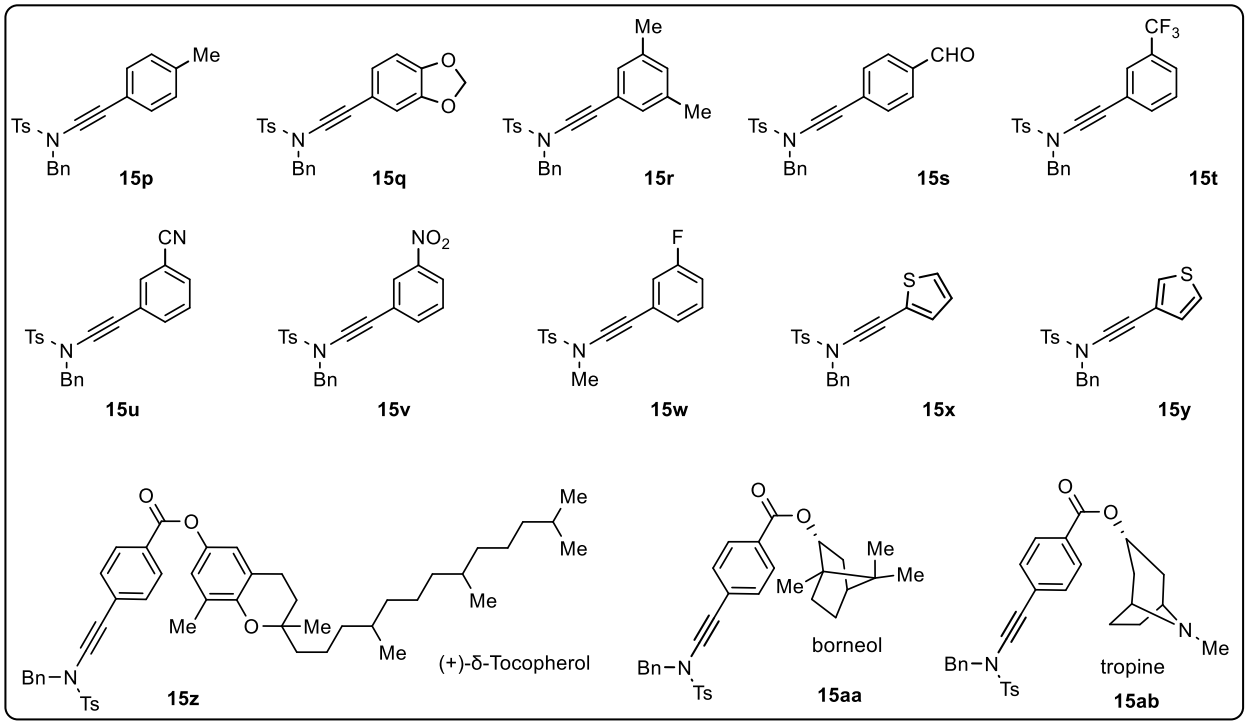
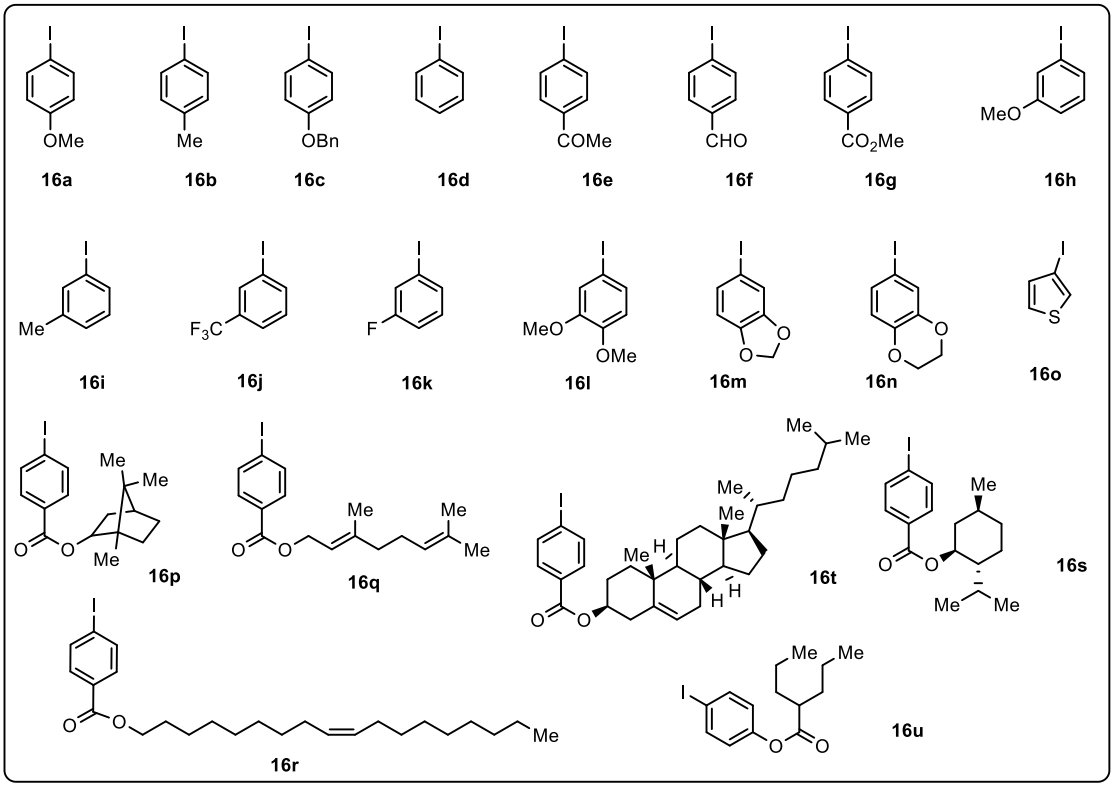
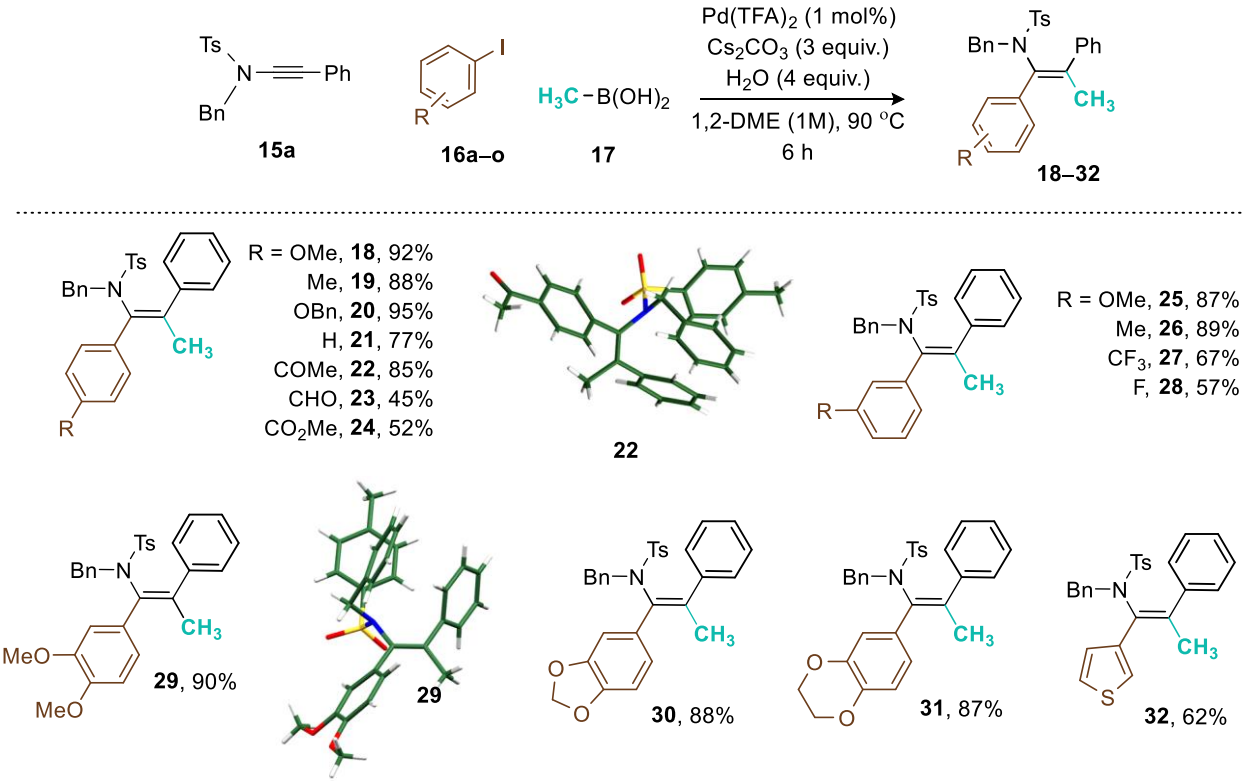


Table 5.2. Aryl diazonium salt chart



5.4.3. Substrate Scope-I

Under the optimized set of conditions (**Scheme 5.8**, entry a), the substrate scope of the reaction was evaluated. At first, variety of iodo arenes **16a-o** were exposed to ynamide **15a** and methyl boronic acid **17** (**Scheme 5.9**). The iodoarenes **16a-c** having electron donating groups like OMe, Me and OBn at the *para*-position reacted well to provide **18-20** in excellent yields. Good yield of **21** was observed when iodobenzene was used. Iodoarenes having transformable electron withdrawing groups [*p*-COMe, *p*-CO2Me and *p*-CHO] successfully participated the reaction providing the final aryl-methylated products **22-24** in 45-85% yield. Gratifingly, *m*-substituted iodo arenes **15h-l** upon exposing to **15a** and **17** independently provided **25**–**29** in good to excellent yields. Aryl-methylated



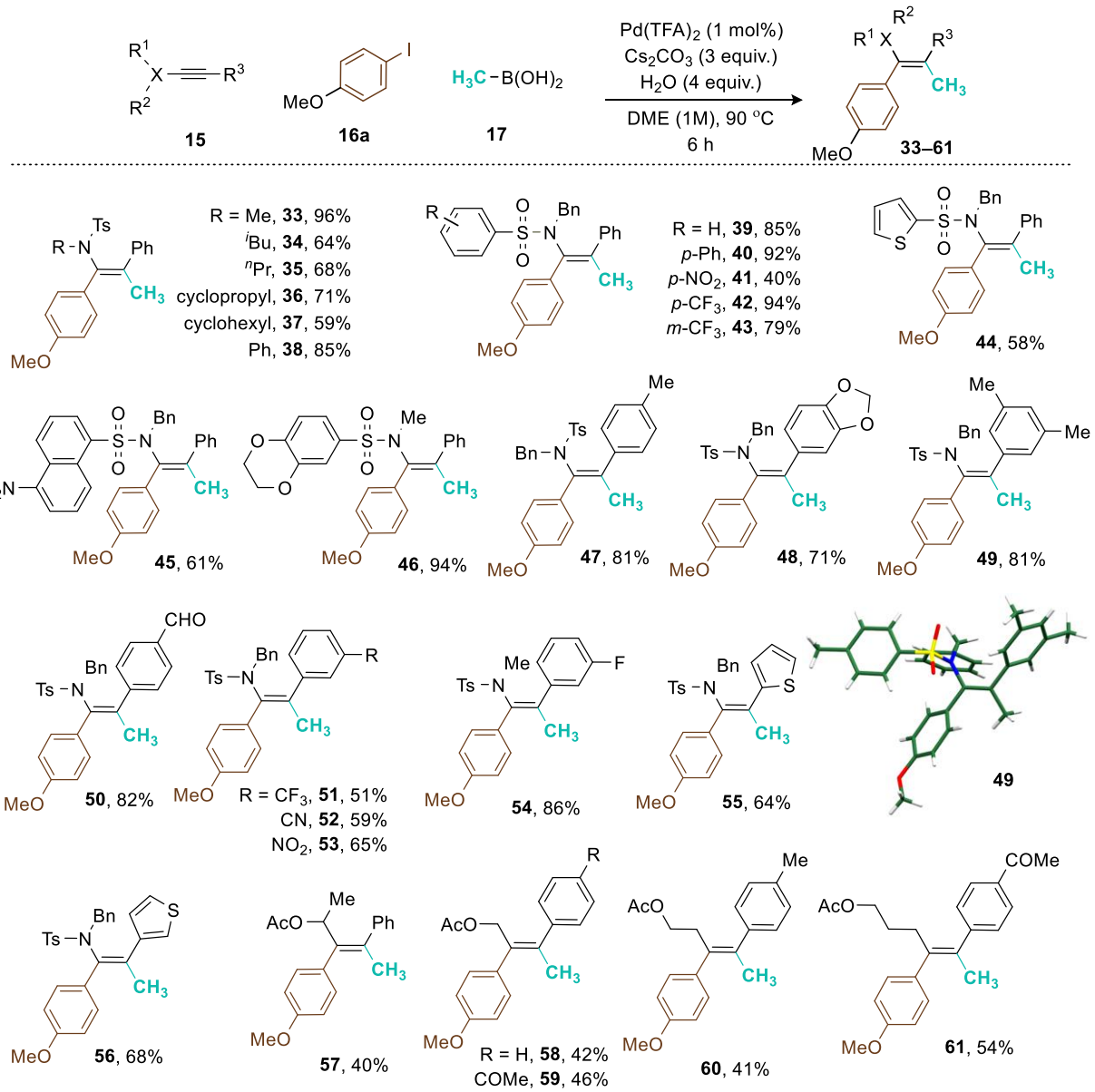
Scheme 5.9. Scope of Aryl iodides. Reactions were carried out using **15a** (0.3 mmol), **16** (0.6 mmol), **17** (0.9 mmol) in 1,2-DME (1M).

products **30**–**32** were synthesized in 62-88% yield when electronically rich heterocyclic iodo compounds for example 5-iodobenzo[*d*][1,3]dioxole, 6-iodo-2,3-dihydrobenzo[*b*][1,4]dioxine, and 3-iodothiophene are used. The structures of **22** and **29** are confirmed by single crystal XRD.[R]

5.4.4. Substrate Scope-II

Following successful arylmethylation of ynamides with various iodoarenes, the scope of the ynamide reacting with **156** and **17** under optimized reaction conditions was investigated (**Scheme 5.10**). Other than Ts*N*-(Bn) protected ynamide **15a**, Ts*N*-(Me/ ^{i}Bu/ ^{n}Pr/ cyclopropyl/ cyclohexyl/ phenyl) protected ynamides **15b-15j** furnished the desired aryl-methylation products **33-38** in good to excellent yields (59-96%). Likewise, various sulfonyl protecting groups other than Ts at *N*-atom of ynamide for example, Bn*N*-($SO_2C_6H_5$/ $SO_2C_6H_5$-*p*-Ph/ $SO_2C_6H_5$-*p*-NO_2/ $SO_2C_6H_5$-*p*-CF_3/ $SO_2C_6H_5$-*m*-CF_3/ $SO_2C_6H_5$- *2-thienyl*) were well tolerated in the catalytic conditions of aryl-methylation reaction and gave the respective difunctionalized products **39-44** in 40-92% yield. The desired products **45** and **46** were isolated in 61 and 94 % yield form electron rich sulfonyl protected ynamides **15n** and **15o**. Reaction outcomes were not much affected by the electron distribution on the aryl group at ynamide terminus. Ynamides with electron rich [*p*-Me (**15p**), *m,p*-methylenedioxy (**15q**), *m,p*-diMe (**15r**)] and electron deficient (*p*-CHO (**15s**), *m*-CF_3/ CN/ NO_2/ F (**15t-15w**)) substitution at the arene ring independently reacted with **16a** and **17** to give **47**–**54** in 51-86% yield. The structure **49** was confirmed by X-ray crystallographic analysis.[R] To our delight, 2/3-thienyl ynamides also participated in the reaction furnishing **55** and **56** in 64 and 68 % yield, respectively.

The scope of this arylmethylation was further extended to yne-acetates (**15z-15ad**). Upon extensive screening, 1,4-dioxane was found optimum solvent for yne-acetates. Propargyl acetates **15z**, **15aa**, and **15ab** independently reacted with **16a** and **17** giving **57**, **58**, and **59** in moderate yields and 95:5 regioselectivity. In addition, isomerization of propargyl

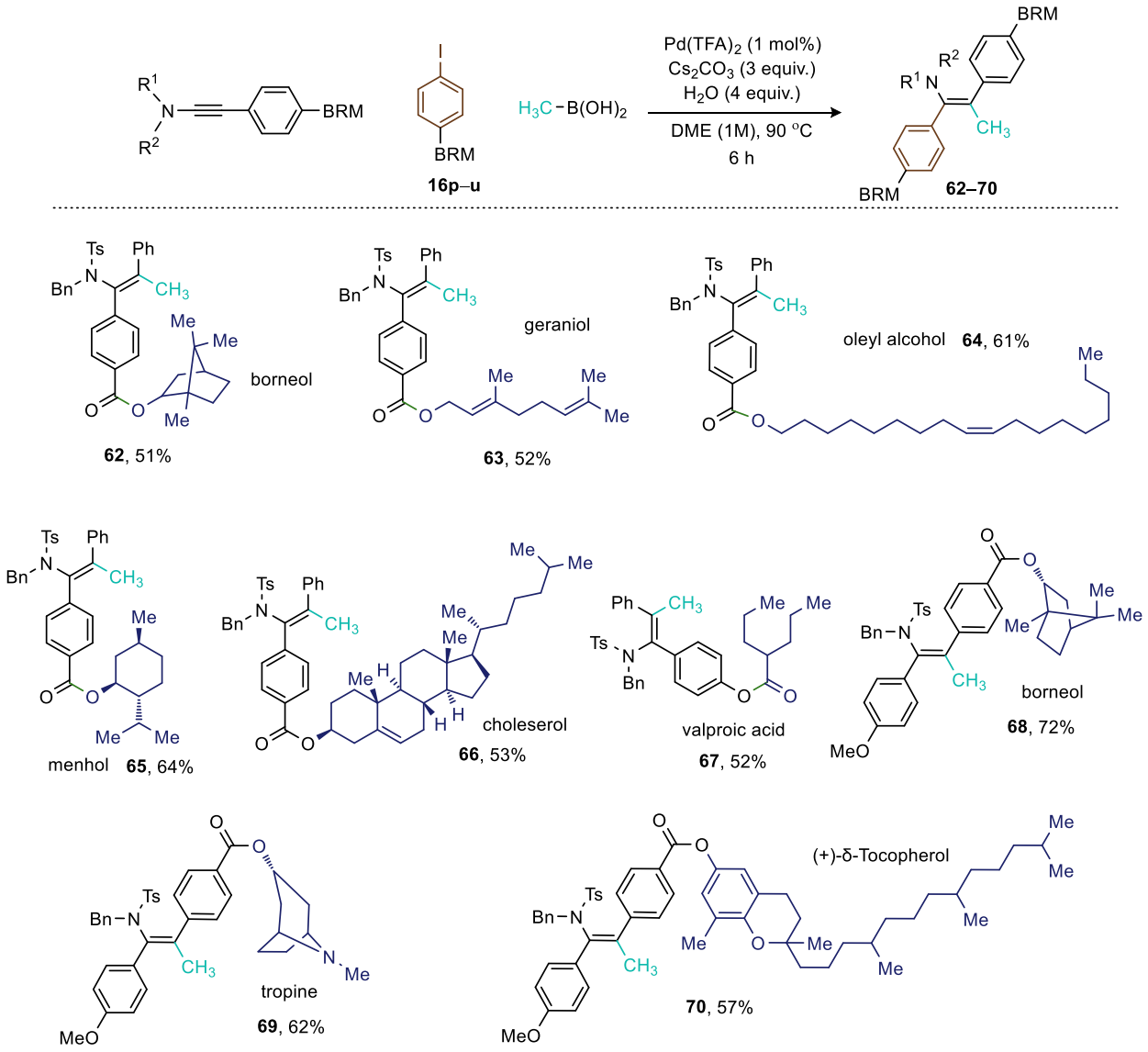


Scheme 5.10. Scope of alkynes. Reactions were carried out using **15** (0.3 mmol), **16a** (0.6 mmol), **17** (0.9 mmol) in solvent (1M).

acetates to α-ylidene-β-diketones explains the mass balance of the moderate methylation product outcome. Increment in chain length between acetate and alkyne did not affect the reaction outcome furnishing **60** and **61** in moderate to good yields and 90:10 regioselectivity.

5.4.5. Substrate Scope-III

The late-stage methylation of unsymmetrical alkynes with biologically relevant motifs can modulate their solubility, hydrophilicity, and conformation (magic methyl effect). The TM binding ability of BRMs with polar groups and unsaturated moieties can affect the efficiency of methylation reaction. We were therefore intrigued by the viability of the Pd-catalyzed arylmethylation of pharmacophore-coupled alkynes **15z/15aa/15ab** in

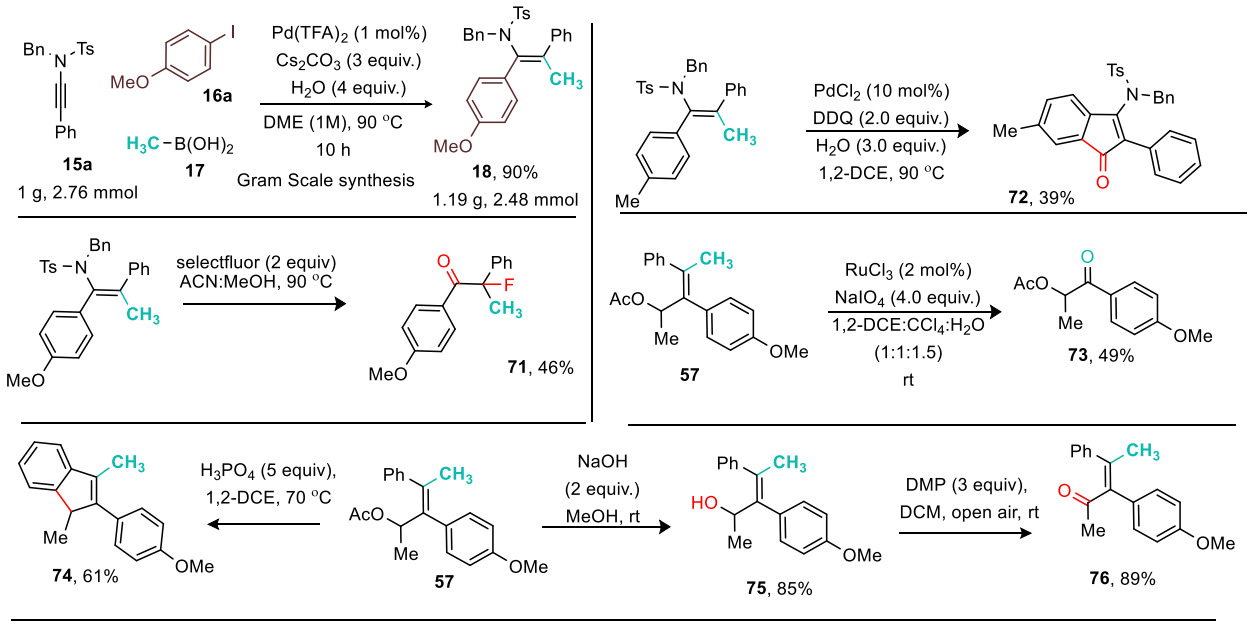


Scheme 5.11. Scope of biologically relevant motifs (BRM) coupled iodo-erenes and ynamides. Reactions were carried out using **15** (0.3 mmol), **16a** (0.6 mmol), **17** (0.9 mmol) in DME (1M).

presence of pharmacophore-coupled iodo coupling partners **16p-16u** (**Scheme 5.11**). Again, the title reaction proved dependable: iodo arenes encapsulated borneol [bornane monoterpenoid (**16p**)], terpenoid [geraniol (**16q**)], fatty alcohol nonionic surfactant, emulsifier, emollient and thickener in skin creams, lotions [oleyl alcohol (**16r**)], menthol [**16s**], steroid [cholesterol (**16t**)], and marketed anti-epileptic drug, bipolar disorder, and migraine preventer [valproic acid (**16u**)] independently reacted with **15a** and **3** furnishing biologically important methylated enamides **62-67** in moderate to good yields. We further probed the efficacy of this catalytic condition by synthesizing methylated enamide containing terpenoids [borneol (**68**) and tropine (**69**)] and fatty alcohol [vitamin-E-tocopherol (**70**)] in good yields by direct methylation of respective ynamides **15z-15ab**.

5.4.6. Gram-scale synthesis and synthetic application

The reaction scalability was verified through the gram scale synthesis of **18** (1.2 g, 90%) from **15a** (1.0 g, 2.67 mmol), **16a** (2.0 equiv.), and **17** (3.0 equiv.) in $Pd(TFA)_2$ (1.0 mol%; **Scheme 5.12**). We next surveyed the synthetic flexibility of the newly constructed methylated enamide **18** and methylated allyl acetate **57**. The selectfluor-assisted oxyfluorination of **18/19** provided **71/72** in 40/46% yield, respectively. The Pd-catalyzed DDQ promoted methyl oxidation followed by intramolecular arene cyclization of **18/19/47** led to unusual β-amino indenone derivatives **73**–**75** in moderate yields. The H_3PO_4 driven intramolecular Friedel-Crafts arene cyclization of **57** led to unusual indene derivative **76** (61%). Fully substituted methylated allyl alcohol [**57**→**77** (85%)] was accessed from the NaOH mediated hydrolysis of the acetate motif. Dess-Martin periodinane (DMP)-mediated oxidation of **77** delivered methyl-vinyl ketone **78** (89%). Ru-catalyzed oxidative cleavage of **57/19** provided α-acetylketone **79** and fully substituted amide **80**, respectively in moderate yields.



Scheme 5.12: Synthetic versatility.

5.5. Conclusion

In summary, palladium catalyzed arylmethylation of internal alkynes is unrevealed for the very first time. The use of readily available and bench stable iodo-arenes, and methyl boronic acid as coupling partners makes the process viable. Notably, this work witnesses an unusual vinylic [Pd]-Me complex as a catalytic intermediate in the three-component alkyne difunctionalition reactions. The scope is broad (53 examples), showing excellent regio and stereoselectivity and also functional-group tolerance. This process is thus practical and even successful on a gram scale. Synthetic application of methylated enamides and allyl acetates provided access to useful organic cyclic compounds. This finding paves the way for a diverse range of unknown methylated difunctionalization of alkynes, and the results will be reported in due course.

5.6. Experimental Section

5.6.1. General Information

All the reactions were performed in oven-dried sealed tubes. Commercial grade solvents were distilled prior to use. Column chromatography was performed using either 100–200 Mesh Mesh silica gel or neutral alumina. Thin layer chromatography (TLC) was performed on silica gel GF254 plates and alumina plates.

Proton, carbon, and fluorine nuclear magnetic resonance spectra (^{1}H NMR, ^{13}C NMR, and ^{19}F NMR) were recorded based on the resonating frequencies as follows: (^{1}H NMR, 400 MHz; ^{13}C NMR, 101 MHz; ^{19}F NMR, 376 MHz) and (^{1}H NMR, 500 MHz; ^{13}C NMR, 126 MHz; ^{19}F NMR, 470 MHz) having the solvent resonance as internal standard (^{1}H NMR, $CDCl_3$ at 7.26 ppm; ^{13}C NMR, $CDCl_3$ at 77.0 ppm). In few cases, tetramethylsilane (TMS) was used as reference standard (at 0.00 ppm). Data for ^{1}H NMR are reported as follows: chemical shift (ppm), multiplicity (s = singlet; br s= broad singlet; d = doublet; br d = broad doublet, t = triplet; br t = broad triplet; q = quartet; m = multiplet), coupling constants, *J*, in (Hz), and integration. Data for ^{13}C NMR, ^{19}F NMR are reported in terms of chemical shift (ppm). IR spectra are reported in cm^{-1}. High resolution mass spectra were obtained in ESI mode. Melting points were determined by electro-thermal heating and are uncorrected. X-ray data was collected at 293 K using graphite monochromated Mo-Kα radiation (0.71073 Å).

5.6.2. Materials

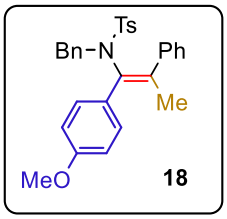
Unless otherwise noted, all the reagents and intermediates were obtained commercially and used without purification. Toluene, DME, and 1,4-dioxane were distilled over CaH_2 and THF, and DMSO were used as received. $Pd(TFA)_2$ was purchased from commercially available source, and used as received. Commercially available iodoarenes and other reagents were purchased and directly used without purification. Following a known procedure, ynamides (**15a-ab**) were prepared.[1] Analytical and spectral data of all the known compounds are exactly matching with the reported values.

5.6.3. General procedure and spectral/analytical data

5.6.3.1. General Procedure for aryl-methylation.

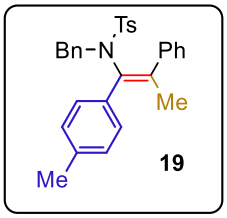
To a mixture of **15** (0.3 mmol), aryl(hetero) iodide **16** (0.6 mmol), methyl boronic acid **17** (0.9 mmol), $Pd(TFA)_2$ (0.003 mmol), and Cs_2CO_3 (0.9 mmol) was added DME (0.3 mL) and H_2O (1.2 mmol). The reaction mixture was stirred at 90 °C for 6 h. The reaction progress was periodically monitored by TLC. The reaction mixture was diluted with CH_2Cl_2 (10 mL), filtered through small pad of celite and washed with CH_2Cl_2 (5x2 mL). The solvent was evaporated and purified by column chromatography over silica gel eluting with EtOAc/hexane to afford **18**–**70**.

(Z)-N-Benzyl-N-(1-(4-methoxyphenyl)-2-phenylprop-1-en-1-yl)-4-methylbenzenesulfonamide (18):



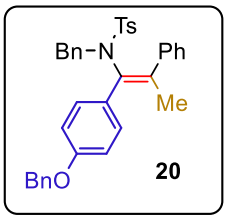
18 (112 mg, 92%) as pale yellow solid; M.P = 169–171; R_f = 0.43 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33–7.24 (m, 4H), 7.22–7.16 (m, 4H), 7.03–6.98 (m, 4H), 6.87 (d, J = 9.0 Hz, 2H), 6.84 (d, J = 8.5 Hz, 2H), 6.61 (d, J = 7.0 Hz, 2H), 3.97 (s, 2H), 3.85 (s, 3H), 2.36 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.1, 142.9, 142.3, 138.9, 137.3, 135.7, 132.0, 131.2, 130.0, 129.3, 129.1, 128.9, 128.4, 128.2, 128.1, 127.9, 126.8, 113.4, 55.3, 51.2, 23.6, 21.4; IR (Neat) ν_{max} 1604, 1508, 1440, 1244, 1153, 1023, 836 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{30}NO_3S$ $(M+H)^+$: calcd. 484.1941, found 484.1944.

(*Z*)-N-Benzyl-4-methyl-N-(2-phenyl-1-(p-tolyl)prop-1-en-1-yl)benzenesulfonamide (19):



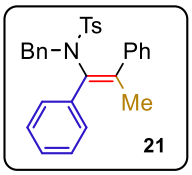
19 (123 mg, 88%) as colorless solid; M.P = 168–170; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.27 (m, 4H), 7.22–7.14 (m, 6H), 7.12–6.97 (m, 4H), 6.83 (d, J = 10.5 Hz, 2H), 6.60 (d, J = 9.0 Hz, 2H), 3.97 (s, 2H), 2.40 (s, 3H), 2.36 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.9, 142.3, 139.4, 137.5, 137.3, 135.3, 135.7, 133.9, 131.5, 130.6, 130.0, 128.9, 128.8, 128.4, 128.2, 128.1, 127.9, 126.8, 51.2, 23.6, 21.4, 21.2; IR (Neat) ν_{max} 1598, 1493, 1324, 1209, 1183, 1026, 830 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{30}NO_2S$ $(M+H)^+$: calcd. 468.1992, found 468.1991.

(*Z*)-N-Benzyl-N-(1-(4-(benzyloxy)phenyl)-2-phenylprop-1-en-1-yl)-4-methylbenzenesulfonamide (20):



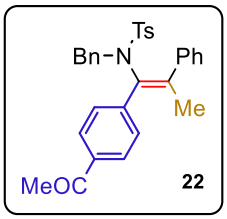
20 (159 mg, 95%) as pale yellow solid; M.P = 154–156; R_f = 0.45 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, J = 7.5 Hz, 2H), 7.44 (t, J = 7.5 Hz, 2H), 7.38 (t, J = 7.0 Hz, 1H), 7.36–7.27 (m, 4H), 7.25–7.18 (m, 4H), 7.05 (br d, J = 7.5 Hz, 2H), 7.01 (d, J = 8.0 Hz, 2H), 6.97 (d, J = 8.5 Hz, 2H), 6.86 (d, J = 8.0 Hz, 2H), 6.63 (d, J = 7.0 Hz, 2H), 5.13 (s, 2H), 3.99 (br d, J = 4.0 Hz, 2H), 2.37 (s, 3H), 2.01 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.3, 142.9, 142.3, 138.9, 137.3, 136.9, 135.7, 132.0, 131.2, 130.0, 129.4, 128.9, 128.6, 128.3, 128.05, 127.97, 127.4, 126.7, 114.3, 70.0, 51.2, 23.6, 21.4; IR (Neat) ν_{max} 1599, 1504, 1332, 1252, 1216, 1154, 1090, 1007, 835 cm^{-1}; **HRMS (ESI)** for $C_{36}H_{34}NO_3S$ $(M+H)^+$: calcd. 560.2254, found 560.2255.

(*Z*)-N-Benzyl-N-(1,2-diphenylprop-1-en-1-yl)-4-methylbenzenesulfonamide (21):



21 (105 mg, 77%) as colorless solid; M.P = 158–160; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39–7.26 (m, 4H), 7.21 (t, J = 7.5 Hz, 2H), 7.09–7.05 (m, 2H), 7.02 (d, J = 8.0 Hz, 2H), 6.85 (d, J = 8.0 Hz, 2H), 6.63 (d, J = 7.5 Hz, 2H), 3.99 (s, 2H), 2.38 (s, 3H), 2.01 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.9, 142.1, 139.6, 137.3, 136.9, 135.7, 131.6, 130.7, 130.0, 128.9, 128.6, 128.3, 128.2, 128.1, 127.9, 127.7, 126.9, 51.3, 23.5, 21.4; IR (Neat) ν_{max} 1590, 1493, 1354, 1232, 1183, 1022, 838 cm^{-1}; **HRMS (ESI)** for $C_{29}H_{28}NO_2S$ $(M+H)^+$: calcd. 454.1835, found 454.1838.

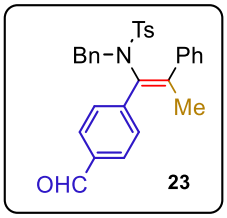
(Z)-N-(1-(4-acetylphenyl)-2-phenylprop-1-en-1-yl)-N-benzyl-4-methylbenzenesulfonamide (22):



22 (126 mg, 85%) as pale yellow solid; M.P = 189–191; R_f = 0.3 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, J = 9.0 Hz, 2H), 7.37–7.31 (m, 3H), 7.30–7.26 (m, 4H), 7.19 (t, J = 8.0 Hz, 2H), 7.12–7.07 (m, 2H), 7.00 (d, J = 8.0 Hz, 2H), 6.86 (d, J = 8.5 Hz, 2H), 6.61 (d, J = 7.0 Hz, 2H), 3.96 (br s, 1H), 3.93 (br s, 1H), 2.63 (s, 3H), 2.36 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.7, 143.3, 142.1, 141.6, 140.7, 137.1, 136.1, 135.5, 130.9, 130.8, 129.9, 129.0, 128.34, 128.33, 128.2, 128.1, 128.0, 127.3, 51.3, 26.7, 23.5, 21.4; IR (Neat)

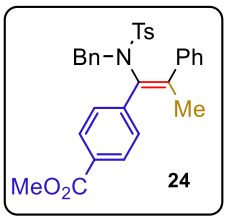
ν_{max} 1678, 1599, 1328, 1262, 1152, 1012, 816 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{30}NO_3S$ $(M+H)^+$: calcd. 496.1941, found 496.1942.

(Z)-N-benzyl-N-(1-(4-formylphenyl)-2-phenylprop-1-en-1-yl)-4-methylbenzenesulfonamide (23):



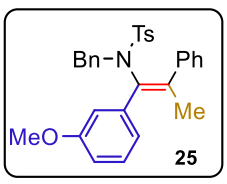
23 (65 mg, 45%) as pale yellow gummy liquid; R_f = 0.3 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.0 (s, 1H), 7.82 (d, J = 8.0 Hz, 2H), 7.38–7.27 (m, 6H), 7.21 (t, J = 7.5 Hz, 2H), 7.15–7.10 (m, 2H), 7.01 (d, J = 7.5 Hz, 2H), 6.86 (d, J = 8.0 Hz, 2H), 6.62 (d, J = 7.0 Hz, 2H), 3.95 (d, J = 29.0 Hz, 2H), 2.36 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.8, 143.6, 143.3, 141.4, 140.9, 137.1, 135.5, 135.4, 131.3, 130.7, 130.3, 129.9, 129.40, 129.37, 128.2, 128.0, 127.9, 127.5, 51.4, 23.5, 21.4; IR (Neat) ν_{max} 1690, 1543, 1321, 1265, 1076, 843 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{28}NO_3S$ $(M+H)^+$: calcd. 482.1784, found 482.1782.

methyl (Z)-4-(1-((N-benzyl-4-methylphenyl)sulfonamido)-2-phenylprop-1-en-1-yl)benzoate (24):



24 (8032 mg, 52%) as pale yellow gummy liquid; R_f = 0.35 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J = 8.0 Hz, 2H), 7.38–7.33 (m, 3H), 7.31–7.27 (m, 2H), 7.21 (t, J = 8.0 Hz, 2H), 7.16–7.10 (m, 2H), 7.03 (d, J = 8.0 Hz, 2H), 6.87 (d, J = 8.5 Hz, 2H), 6.62 (d, J = 7.5 Hz, 2H), 3.97 (s, 3H), 3.94 (bs, 3H), 2.38 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.8, 143.2, 141.9, 141.6, 140.6, 137.1, 135.5, 130.9, 130.7, 129.9, 129.31, 129.25, 129.0, 128.33, 128.30, 128.2, 128.1, 128.0, 127.3, 52.1, 51.4, 23.4, 21.4; IR (Neat) ν_{max} 1718, 1274, 1153, 1108, 1014, 750 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{30}NO_4S$ $(M+H)^+$: calcd. 512.1890, found 512.1890.

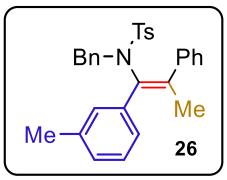
(Z)-N-benzyl-N-(1-(3-methoxyphenyl)-2-phenylprop-1-en-1-yl)-4-methylbenzenesulfonamide (25):



25 (126 mg, 87%) as pale yellow gummy liquid; R_f = 0.45 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.19 (m, 7H), 7.17–7.11 (m, 2H), 7.08–6.96 (m, 3H), 6.88 (d, J = 8.4 Hz, 2H), 6.71 (d, J = 7.6 Hz, 2H), 6.62 (bs, 1H), 4.06 (bs, 1H), 3.98 (bs, 1H), 3.62 (s, 3H), 2.39 (s, 3H), 2.06 (s, 3H); ^{13}C

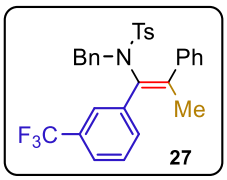
NMR (101 MHz, $CDCl_3$) δ 159.4, 143.0, 142.1, 139.1, 138.1, 137.4, 135.8, 131.5, 130.1, 128.92, 128.88, 128.3, 128.2, 128.1, 128.0, 127.9, 127.0, 123.7, 114.6, 114.5, 55.1, 51.3, 23.5, 21.4; IR (Neat) ν_{max} 1604, 1543, 1441, 1246, 1153, 1023, 821 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{29}NO_4SNa$ $(M+Na)^+$: calcd. 506.1760, found 506.1763.

(Z)-N-benzyl-4-methyl-N-(2-phenyl-1-(m-tolyl)prop-1-en-1-yl)benzenesulfonamide (26):



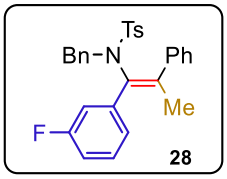
26 (125 mg, 89%) as pale yellow gummy liquid; R_f = 0.5 (10% EtOAc/Hex); ^1H NMR (500 MHz, $CDCl_3$) δ 7.34–7.29 (m, 3H), 7.27–7.22 (m, 1H), 7.21 (d, J = 7.5 Hz, 1H), 7.17 (t, J = 7.5 Hz, 2H), 7.13–7.07 (m, 4H), 6.98 (d, J = 8.0 Hz, 2H), 6.86–6.80 (m, 3H), 6.64 (d, J = 7.0 Hz, 2H), 3.99 (bs, 1H), 3.95 (bs, 1H), 2.34 (s, 3H), 2.24 (s, 3H), 1.98 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.8, 142.1, 139.0, 137.5, 137.4, 136.7, 135.8, 131.8, 131.0, 130.0, 128.84, 128.35, 128.3, 128.2, 128.1, 128.1, 128.0, 127.9, 127.8, 126.9, 51.4, 23.4, 21.4, 21.3; IR (Neat) ν_{max} 1598, 1491, 1151, 1044, 753 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{29}NO_2SNa$ $(M+Na)^+$: calcd. 490.1811, found 490.1817.

(Z)-N-benzyl-4-methyl-N-(2-phenyl-1-(3-(trifluoromethyl)phenyl)prop-1-en-1-yl)benzenesulfonamide (27):



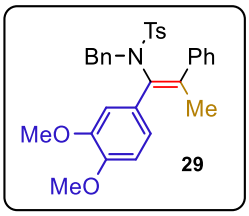
27 (105 mg, 67%) as pale yellow gummy liquid; R_f = 0.5 (10% EtOAc/Hex); ^1H NMR (500 MHz, $CDCl_3$) δ 7.57–7.36 (m, 8H), 7.30–7.25 (m, 1H), 7.20 (t, J = 7.0 Hz, 2H), 7.00 (d, J = 8.0 Hz, 2H), 6.89 (d, J = 8.0 Hz, 2H), 6.74 (brs, 1H), 6.70 (d, J = 7.5 Hz, 2H), 4.12 (bs, 1H), 3.80 (bs, 1H), 2.35 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.2, 141.2, 139.4, 138.1, 137.5, 135.7, 134.6, 130.8, 130.3 (q, J = 31.5 Hz, 1C), 129.8, 129.0, 128.54, 128.46, 128.4, 128.2, 128.1, 127.7, 127.5, 126.9 (q, J = 3.8 Hz, 1C), 123.9 (q, J = 273 Hz, 1C), 124.3 (q, J = 3.8 Hz, 1C), 51.5, 22.9, 21.4; ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.6; IR (Neat) ν_{max} 1618, 1545, 1423, 1241, 1136, 1020, 842 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{27}F_3NO_2S$ $(M+H)^+$: calcd. 522.1709, found 522.1709.

(Z)-N-benzyl-N-(1-(3-fluorophenyl)-2-phenylprop-1-en-1-yl)-4-methylbenzenesulfonamide (28):



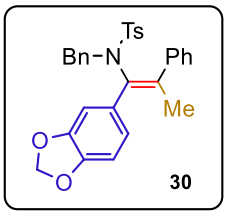
28 (81 mg, 57%) as pale yellow liquid; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28–7.17 (m, 5H), 7.11 (t, J = 7.5 Hz, 2H), 7.05–6.97 (m, 3H), 6.95–6.90 (m, 3H), 6.80 (d, J = 8.0 Hz, 2H), 6.68 (br d, J = 10.0 Hz, 1H), 6.55 (d, J = 8.0 Hz, 2H), 3.91 (bs, 1H), 3.85 (bs, 1H), 2.29 (s, 3H), 1.91 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5 (q, J = 246 Hz, 1C), 143.2, 141.6, 140.2, 139.3 (d, J = 7.1 Hz, 1C), 137.1, 135.5, 130.5, 129.9, 129.5 (d, J = 8.1 Hz, 1C), 129.0, 128.3, 128.2, 128.1, 127.9, 127.2, 126.6 (d, J = 2.0 Hz, 1C), 117.4 (d, J = 21.2 Hz, 1C), 114.7 (d, J = 21.2 Hz, 1C), 51.3, 23.4, 21.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.2; IR (Neat) ν_{max} 1580, 1330, 1263, 1185, 1153, 1089, 880 cm^{-1}; **HRMS (ESI)** for $C_{29}H_{27}FNO_2S$ $(M+H)^+$: calcd. 472.1741, found 472.1742.

(Z)-N-benzyl-N-(1-(3,4-dimethoxyphenyl)-2-phenylprop-1-en-1-yl)-4-methylbenzenesulfonamide (29):



29 (139 mg, 90%) as pale yellow solid; M.P = 188–190 °C; R_f = 0.34 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37–7.30 (m, 3H), 7.26–7.22 (m, 1H), 7.22–7.16 (m, 4H), 7.01 (d, J = 8.0 Hz, 2H), 6.93 (dd, J = 8.0, 2.0 Hz, 1H), 6.86 (t, J = 8.0 Hz, 3H), 6.70 (d, J = 7.0 Hz, 2H), 6.41 (bs, 1H), 4.10 (d, J = 15.5 Hz, 1H), 3.92 (s, 3H), 3.87 (d, J = 14.5 Hz, 1H), 3.53 (s, 3H), 2.35 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.38, 148.35, 142.9, 142.1, 137.5, 136.0, 131.6, 130.1, 129.3, 128.8, 128.3, 128.2, 127.92, 127.89, 127.0, 124.2, 112.8, 110.2, 55.8, 55.6, 51.2, 23.4, 21.4; IR (Neat) ν_{max} 1516, 1440, 1324, 1259, 1209, 1154, 751 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{32}NO_4S$ $(M+H)^+$: calcd. 514.2047, found 514.2050.

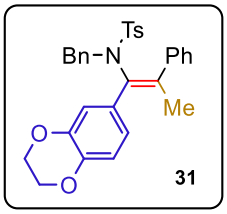
(Z)-N-(1-(benzo[d][1,3]dioxol-5-yl)-2-phenylprop-1-en-1-yl)-N-benzyl-4-methylbenzenesulfonamide (30):



30 (131 mg, 88%) as pale yellow solid; M.P = 194–196 °C; R_f = 0.32 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.26 (m, 4H), 7.20 (t, J = 7.5 Hz, 2H), 7.03 (d, J = 7.5 Hz, 4H), 6.89 (d, J = 8.5 Hz, 2H), 6.80 (s, 3H), 6.65 (t, J = 7.0 Hz, 2H), 5.98 (s, 2H), 4.02 (bs, 1H), 3.97 (bs, 1H), 2.37 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.3, 147.0, 143.0, 142.1, 139.2, 1372, 135.6, 131.1,

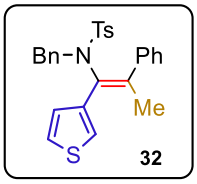
130.6, 129.9, 128.9, 128.24, 128.17, 128.0, 127.9, 126.8, 124.8, 110.8, 107.8, 101.0, 51.2, 23.6, 21.4; IR (Neat) ν_{max} 1485, 1435, 1321, 1240, 1153, 1036, 752 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{28}NO_4S$ $(M+H)^+$: calcd. 498.1734, found 498.1734.

(Z)-N-benzyl-N-(1-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-2-phenylprop-1-en-1-yl)-4-methylbenzenesulfonamide (31):



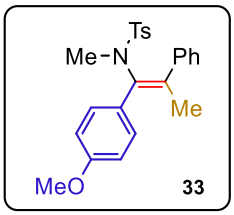
31 (133 mg, 87%) as pale yellow solid; M.P = 168–170 °C; R_f = 0.3 (10% EtOAc/Hex); ^1H NMR (500 MHz, $CDCl_3$) δ 7.34–7.26 (m, 4H), 7.21 (t, J = 7.0 Hz, 2H), 7.04 (d, J = 8.0 Hz, 2H), 6.99 (d, J = 7.0 Hz, 2H), 6.92–6.80 (m, 5H), 6.65 (d, J = 7.5 Hz, 2H), 4.30 (d, J = 7.0 Hz, 4H), 4.02 (s, 2H), 2.39 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.2, 143.0, 142.9, 142.2 139.2, 137.3, 135.7, 131.0, 130.03, 129.96, 128.9, 128.3, 128.14, 128.09, 127.90, 127.85, 126.7, 124.1, 119.6, 116.7, 64.4, 64.2, 51.3, 23.6, 21.4; IR (Neat) ν_{max} 1577, 1498, 1336, 1303, 1181, 1066, 881, 776 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{30}NO_4S$ $(M+H)^+$: calcd. 512.1890, found 512.1889.

(Z)-N-benzyl-N-(1-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-2-phenylprop-1-en-1-yl)-4-methylbenzenesulfonamide (32):



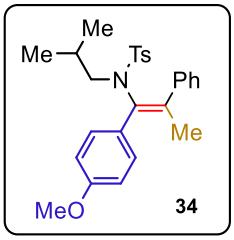
32 (85 mg, 62%) as pale yellow solid; M.P = 173–175 °C; R_f = 0.5 (10% EtOAc/Hex); ^1H NMR (500 MHz, $CDCl_3$) δ 7.35–7.26 (m, 5H), 7.21 (t, J = 7.5 Hz, 2H), 7.09–7.04 (m, 5H), 6.96 (dd, J = 5.0, 1.0 Hz, 1H), 6.92 (d, J = 8.5 Hz, 2H), 6.65 (d, J = 7.5 Hz, 2H), 4.04 (br s, 1H), 3.93 (br s, 1H), 2.40 (s, 3H), 2.06 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.0, 141.8, 140.4, 137.9, 137.3, 135.6, 130.0, 129.8, 129.0, 128.21, 128.15, 128.1, 128.0, 126.9, 126.4, 126.1, 124.7, 51.3, 23.3, 21.4; IR (Neat) ν_{max} 1735, 1597, 1447, 1238, 720 cm^{-1}; **HRMS (ESI)** for $C_{27}H_{26}NO_2S_2$ $(M+H)^+$: calcd. 460.1399, found 460.1396.

(Z)-N-(1-(4-methoxyphenyl)-2-phenylprop-1-en-1-yl)-N,4-dimethylbenzenesulfonamide (33):



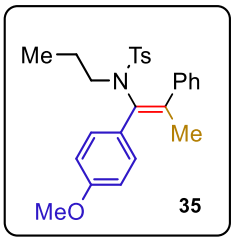
33 (117 mg, 96%) as pale yellow solid; M.P = 148–150 °C; R_f = 0.45 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, J = 7.0 Hz, 2H), 7.39 (t, J = 7.5 Hz, 2H), 7.34–7.28 (m, 1H), 7.22 (d, J = 9.0 Hz, 2H), 6.99–6.91 (m, 4H), 6.80 (dt, J = 7.0, 2.5 Hz, 1H), 3.83 (s, 1H), 2.67 (s, 1H), 2.32 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 142.3, 142.0, 137.2, 136.8, 134.7, 131.1, 129.5, 128.8, 128.3, 128.0, 127.2, 127.0, 113.4, 55.2, 37.3, 22.1, 21.3; IR (Neat) ν_{max} 1603, 1507, 1337, 1244, 1147, 1114, 1028, 836 cm^{-1}; **HRMS (ESI)** for $C_{24}H_{25}NO_3SNa$ $(M+Na)^+$: calcd. 430.1447, found 430.1454.

(Z)-N-isobutyl-N-(1-(4-methoxyphenyl)-2-phenylprop-1-en-1-yl)-4-methylbenzenesulfonamide (34):



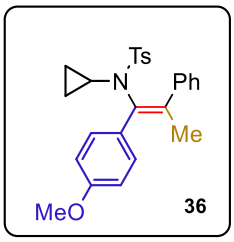
34 (86 mg, 64%) as pale yellow gummy liquid; R_f = 0.45 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47–7.44 (m, 2H), 7.43–7.33 (m, 5H), 6.97 (d, J = 8.0 Hz, 2H), 6.91 (d, J = 9.0 Hz, 2H), 6.88 (d, J = 8.0 Hz, 2H), 3.85 (s, 3H), 2.73–2.65 (m, 1H), 2.50–2.40 (m, 1H), 2.31 (s, 3H), 1.99 (s, 3H), 1.78–1.69 (m, 1H), 0.58 (d, J = 6.5 Hz, 3H), 0.32 (d, J = 6.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.1, 142.7, 142.6, 139.2, 136.9, 131.8, 131.7, 129.4, 128.7, 128.5, 128.2, 128.0, 126.8, 113.5, 55.7, 55.3, 26.4, 23.9, 21.3, 20.7, 20.3; IR (Neat) ν_{max} 1606, 1510, 1319, 1241, 1151, 999, 842, 758 cm^{-1}; **HRMS (ESI)** for $C_{27}H_{32}NO_3S$ $(M+H)^+$: calcd. 450.2097, found 450.2096.

(Z)-N-(1-(4-methoxyphenyl)-2-phenylprop-1-en-1-yl)-4-methyl-N-propylbenzenesulfonamide (35):



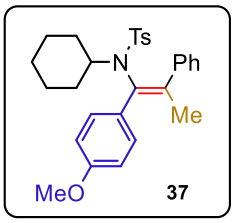
35 (89 mg, 68%) as pale yellow gummy liquid; R_f = 0.45 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54–7.32 (m, 7H), 6.99 (d, J = 8.0 Hz, 2H), 6.95–6.86 (m, 4H), 3.87 (s, 3H), 2.90 (br s, 1H), 2.70 (br s, 1H), 2.34 (s, 3H), 2.06 (s, 3H), 1.46–1.35 (m, 2H), 0.60 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 142.6, 142.4, 138.0, 137.4, 131.9, 131.6, 129.4, 128.8, 128.30, 128.25, 127.5, 126.9, 113.4, 55.3, 50.1, 23.3, 21.5, 21.4, 11.2; IR (Neat) ν_{max} 1599, 1508, 1331, 1245, 1151, 1033, 981 cm^{-1}; **HRMS (ESI)** for $C_{26}H_{30}NO_3S$ $(M+H)^+$: calcd. 436.1941, found 436.1941.

(Z)-N-cyclopropyl-N-(1-(4-methoxyphenyl)-2-phenylprop-1-en-1-yl)-4-methylbenzenesulfonamide (36):



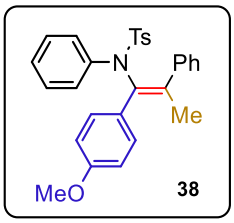
36 (92 mg, 71%) as pale yellow liquid; R_f = 0.43 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26–7.19 (m, 4H), 7.16–7.11 (m, 1H), 7.09 (d, J = 9.0 Hz, 2H), 6.81 (d, J = 8.0 Hz, 2H), 6.75 (d, J = 8.5 Hz, 2H), 6.71 (d, J = 9.0 Hz, 2H), 3.69 (s, 3H), 2.16 (s, 1H), 1.99–1.91 (m, 1H), 1.88 (s, 3H), 0.38–0.30 (m, 2H), 0.24–0.16 (m, 1H), 0.07–-0.05 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.0, 142.7, 142.6, 137.2, 136.2, 134.0, 131.4, 130.1, 128.5, 128.4, 128.2, 128.0, 126.7, 113.4, 55.3, 30.5, 22.7, 21.4, 8.3, 7.9; IR (Neat) ν_{max} 1597, 1507, 1336, 1241, 1155, 1025, 813, 761 cm^{-1}; **HRMS (ESI)** for $C_{26}H_{27}NO_3SNa$ $(M+Na)^+$: calcd. 456.1604, found 456.1606.

(Z)-N-cyclohexyl-N-(1-(4-methoxyphenyl)-2-phenylprop-1-en-1-yl)-4-methylbenzenesulfonamide (37):



37 (80 mg, 59%) as pale yellow gummy liquid; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (d, J = 7.0 Hz, 2H), 7.39 (d, J = 8.5 Hz, 2H), 7.36 (t, J = 7.0 Hz, 2H), 7.32–7.27 (m, 4H), 6.93 (d, J = 8.0 Hz, 2H), 6.89 (d, J = 8.0 Hz, 2H), 6.85 (d, J = 9.0 Hz, 2H), 3.84 (s, 3H), 3.10–3.01 (m, 1H), 2.30 (s, 3H), 2.00 (s, 3H), 1.64–1.47 (m, 4H), 1.07–0.79 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.9, 142.9, 142.08, 142.06, 138.4, 131.8, 131.7, 131.6, 128.8, 128.7, 128.1, 127.4, 126.9, 113.3, 61.9, 55.2, 32.5, 32.2, 26.54, 26.46, 25.3, 24.3, 21.3; IR (Neat) ν_{max} 1606, 1510, 1329, 1246, 1149, 1031, 837 cm^{-1}; **HRMS (ESI)** for $C_{29}H_{33}NO_3SNa$ $(M+Na)^+$: calcd. 476.2254, found 476.2256.

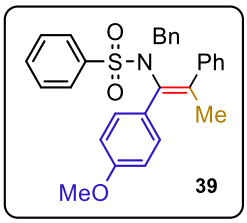
(Z)-N-(1-(4-methoxyphenyl)-2-phenylprop-1-en-1-yl)-4-methyl-N-phenylbenzenesulfonamide (38):



38 (120 mg, 85%) as pale yellow solid; M.P = 140–142 °C; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (d, J = 9.0 Hz, 2H), 7.31–7.27 (m, 4H), 7.27–7.24 (m, 1H), 7.05–7.00 (m, 3H), 6.97–6.93 (m, 2H), 6.90 (d, J = 8.0 Hz, 2H), 6.85 (d, J = 8.0 Hz, 2H), 6.82 (d, J = 8.5 Hz, 2H), 3.86 (s, 3H), 2.28 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.0, 142.5, 142.0, 141.2, 138.5, 137.4, 135.2, 131.8, 129.6, 128.5, 128.1, 128.0, 127.3, 126.8,

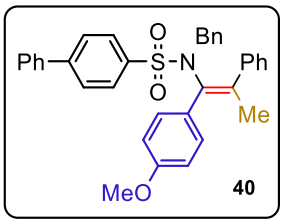
126.4, 125.4, 113.2, 55.2, 22.9, 21.3; IR (Neat) ν_{max} 1598, 1509, 1441, 1245, 1158, 1091, 1029, 757 cm^{-1}; **HRMS (ESI)** for $C_{29}H_{28}NO_3S$ $(M+H)^+$: calcd. 470.1784, found 470.1782.

(Z)-N-benzyl-N-(1-(4-methoxyphenyl)-2-phenylprop-1-en-1-yl)benzenesulfonamide (39):



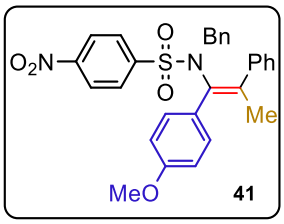
39 (120 mg, 85%) as pale yellow solid; M.P = 140-142 °C; R_f = 0.45 (10% EtOAc/Hex); ^1H NMR (500 MHz, $CDCl_3$) δ 7.43 (t, J = 7.5 Hz, 1H), 7.33–7.28 (m, 3H), 7.25–7.13 (m, 7H), 7.08–7.02 (m, 2H), 6.97 (d, J = 7.5 Hz, 2H), 6.86 (d, J = 8.5 Hz, 2H), 6.61 (d, J = 7.0 Hz, 2H), 3.99 (br s, 2H), 3.85 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 142.2, 140.2, 138.8, 135.6, 132.2, 132.0, 131.2, 129.9, 129.1, 128.3, 128.22, 128.19, 128.0, 127.9, 126.9, 113.4, 55.2, 51.3, 23.5; IR (Neat) ν_{max} 1605, 1508, 1331, 1249, 1331, 1249, 1159, 1020, 839 cm^{-1}; **HRMS (ESI)** for $C_{29}H_{28}NO_3S$ $(M+H)^+$: calcd. 470.1784, found 470.1784.

(Z)-N-benzyl-N-(1-(4-methoxyphenyl)-2-phenylprop-1-en-1-yl)-[1,1'-biphenyl]-4-sulfonamide (40):



40 (150 mg, 92%) as pale yellow solid; M.P = 180–182 °C; R_f = 0.5 (10% EtOAc/Hex); ^1H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, J = 7.0 Hz, 2H), 7.51 (t, J = 7.5 Hz, 2H), 7.44 (d, J = 8.5 Hz, 3H), 7.38–7.33 (m, 3H), 7.32–7.27 (m, 1H), 7.24–7.19 (m, 4H), 7.14–7.09 (m, 2H), 7.04 (d, J = 8.5 Hz, 2H), 6.89 (d, J = 9.0 Hz, 2H), 6.72 (d, J = 7.5 Hz, 2H), 4.07 (br d, J = 9.0 Hz, 2H), 3.87 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.1, 145.0, 142.2, 139.5, 139.0, 138.7, 135.7, 132.0, 131.5, 130.0, 129.2, 129.0, 128.5, 128.33, 128.26, 128.2, 127.9, 127.2, 126.89, 126.86, 113.4, 55.3, 51.6, 23.5; IR (Neat) ν_{max} 1507, 1334, 1245, 11536, 1026, 840 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{31}NO_3SNa$ $(M+Na)^+$: calcd. 568.1917, found 568.1916.

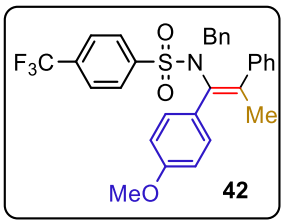
(Z)-N-benzyl-N-(1-(4-methoxyphenyl)-2-phenylprop-1-en-1-yl)-4-nitrobenzenesulfonamide (41):



41 (62 mg, 40%) as pale yellow solid; M.P = 190–192; R_f = 0.4 (10% EtOAc/Hex); ^1H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, J = 9.0 Hz, 2H), 7.38–7.33 (m, 3H), 7.30–7.17 (m, 5H), 7.08–6.98 (m, 4H), 6.84–6.77 (m, 4H), 4.12 (br s, 1H), 4.00 (br s, 1H), 3.81 (s, 3H), 2.01 (s, 3H); ^{13}C NMR

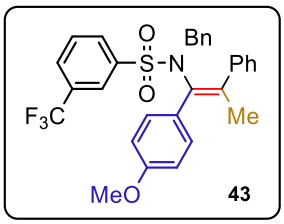
(126 MHz, $CDCl_3$) δ 159.4, 149.3, 146.5, 141.7, 138.3, 135.2, 131.9, 131.8, 130.0, 128.9, 128.8, 128.6, 128.4, 128.3, 128.1, 127.4, 123.2, 113.5, 55.3, 52.8, 23.3; IR (Neat) ν_{max} 1507, 1334, 1245, 11536, 1026, 840 cm^{-1}; **HRMS (ESI)** for $C_{29}H_{26}N_2O_5SNa$ $(M+Na)^+$: calcd. 537.1455, found 537.1450.

(*Z*)-N-Benzyl-N-(1-(4-methoxyphenyl)-2-phenylprop-1-en-1-yl)-4-(trifluoromethyl)benzenesulfonamide (42):



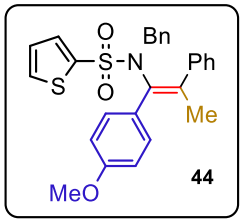
42 (112 mg, 94%) as pale yellow gummy liquid; R_f = 0.5 (10% EtOAc/Hex); ^1H NMR (400 MHz, $CDCl_3$) δ 7.48–7.35 (m, 5H), 7.34–7.19 (m, 5H), 7.10 (d, J = 8.4 Hz, 2H), 7.05 (d, J = 8.0 Hz, 2H), 6.83 (d, J = 8.8 Hz, 2H), 6.77 (d, J = 8.0 Hz, 2H), 4.13 (br s, 1H), 4.03 (br s, 1H), 3.85 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 144.1, 141.9, 138.4, 135.4, 133.5 (q, J = 32 Hz, 1C), 131.9, 130.3 (q, J = 279 Hz, 1C), 129.9, 128.5, 128.4, 128.2, 127.2, 125.2 (q, J = 3.0 Hz, 2C), 113.4, 55.2, 52.3, 23.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.1; IR (Neat) ν_{max} 1605, 1508, 1321, 1275, 1122, 839 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{26}F_3NO_3SNa$ $(M+Na)^+$: calcd. 560.1478, found 560.1476.

(*Z*)-N-Benzyl-N-(1-(4-methoxyphenyl)-2-phenylprop-1-en-1-yl)-3-(trifluoromethyl)benzenesulfonamide (43):



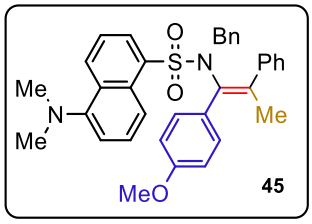
43 (127 mg, 79%) as pale yellow liquid; R_f = 0.5 (10% EtOAc/Hex); ^1H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 7.5 Hz, 1H), 7.41–7.30 (m, 6H), 7.30–7.23 (m, 2H), 7.19 (t, J = 7.5 Hz, 2H), 7.10 (br d, J = 8.0 Hz, 1H), 6.92 (d, J = 8.5 Hz, 2H), 6.81 (d, J = 7.0 Hz, 2H), 6.73 (d, J = 9.0 Hz, 2H), 4.16 (br s, 1H), 3.94 (br s, 1H), 3.80 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 142.1, 141.6, 136.6 (q, J = 266 Hz, 1C), 132.1, 131.8, 130.81 (q, J = 42 Hz, 1C), 129.9, 128.9, 128.5, 128.4, 128.2, 128.0, 127.5, 124.6 (q, J = 3.8 Hz, 1C), 113.4, 55.1, 52.6, 23.1; ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.6; IR (Neat) ν_{max} 1605, 1508, 1321, 1275, 1122, 839 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{26}F_3NO_3SNa$ $(M+Na)^+$: calcd. 560.1478, found 560.1479.

(*Z*)-N-Benzyl-N-(1-(4-methoxyphenyl)-2-phenylprop-1-en-1-yl)thiophene-2-sulfonamide (44):



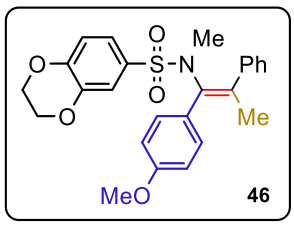
44 (83 mg, 58%) as pale yellow solid; M.P = 151–153 °C; R_f = 0.45 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (dd, J = 4.8, 0.8 Hz, 1H), 7.37–7.30 (m, 4H), 7.26 (t, J = 7.6 Hz, 3H), 7.18–7.07 (m, 4H), 6.90–7.83 (m, 3H), 6.80 (d, J = 7.2 Hz, 2H), 6.64–6.58 (m, 1H), 4.12 (d, J = 10.8 Hz, 2H), 3.86 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 142.0, 141.7, 139.0, 135.6, 132.7, 131.9, 131.8, 131.6, 130.1, 129.0, 128.26, 128.25, 128.2, 128.0, 127.0, 126.8, 113.4, 55.2, 51.9, 23.3; IR (Neat) ν_{max} 1604, 1508, 1338, 1258, 1148, 1021, 834 cm^{-1}; **HRMS (ESI)** for $C_{27}H_{26}NO_3S_2$ $(M+H)^+$: calcd. 476.1349, found 476.1347.

(*Z*)-N-Benzyl-5-(dimethylamino)-N-(1-(4-methoxyphenyl)-2-phenylprop-1-en-1-yl)naphthalene-1-sulfonamide (45):



45 (103 mg, 61%) as pale yellow solid; R_f = 0.38 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.44 (d, J = 9.0 Hz, 1H), 7.37 (d, J = 8.5 Hz, 1H), 7.38 (dd, J = 7.5, 7.5 Hz, 1H), 7.27–7.20 (m, 4H), 7.18–7.09 (m, 6H), 7.07–7.01 (m, 3H), 6.75 (d, J = 9.0 Hz, 4H), 4.16 (br s, 2H), 3.81 (s, 3H), 2.85 (s, 3H), 1.97 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 151.4, 142.1, 138.7, 136.4, 135.9, 132.0, 131.9, 130.3, 130.1, 129.6, 129.4, 129.0, 128.2, 128.1, 127.88, 127.87, 127.1, 123.0, 119.8, 114.8, 113.3, 55.2, 51.5, 45.4, 23.9; IR (Neat) ν_{max} 2359, 1605, 1571, 1508, 1320, 1244, 11139, 835 cm^{-1}; **HRMS (ESI)** for $C_{35}H_{35}N_2O_3S$ $(M+H)^+$: calcd. 563.2363, found 563.2363.

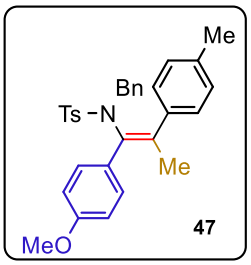
(*Z*)-N-(1-(4-Methoxyphenyl)-2-phenylprop-1-en-1-yl)-N-methyl-2,3-dihydrobenzo[b][1,4]dioxine-6-sulfonamide (46):



46 (112 mg, 72%) as pale yellow solid; R_f = 0.3 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (dd, J = 8.5, 1.5 Hz, 2H), 7.41 (t, J = 7.5 Hz, 2H), 7.35–7.29 (m, 1H), 7.20 (d, J = 8.5 Hz, 2H), 6.80 (d, J = 8.5 Hz, 2H), 6.68–6.61 (m, 2H), 6.56 (d, J = 2.0 Hz, 1H), 4.28–4.24 (m, 2H), 4.23–4.19 (m, 2H), 3.86 (s, 3H), 2.73 (s, 3H), 2.04 (s, 3H); ^{13}C NMR

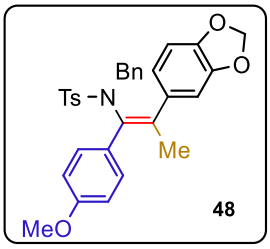
(126 MHz, $CDCl_3$) δ 159.1, 146.6, 142.7, 141.8, 136.9, 134.8, 132.6, 131.0, 129.5, 128.3, 127.9, 127.1, 120.6, 117.0, 116.8, 113.3, 64.4, 64.0, 55.2, 37.7, 21.9; IR (Neat) ν_{max} 1606, 1509, 1488, 1332, 1248, 1140 1032, cm^{-1}; **HRMS (ESI)** for $C_{25}H_{26}NO_5S$ $(M+H)^+$: calcd. 452.1526, found 452.1528.

(Z)-N-Benzyl-N-(1-(4-methoxyphenyl)-2-(p-tolyl)prop-1-en-1-yl)-4-methylbenzenesulfonamide (47):



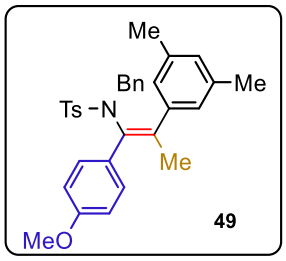
47 (120 mg, 81%) as pale yellow gummy liquid; R_f = 0.45 (10% EtOAc/Hex); ^1H NMR (500 MHz, $CDCl_3$) δ 7.28 (t, J = 7.0 Hz, 1H), 7.21 (t, J = 7.0 Hz, 2H), 7.19–7.10 (m, 4H), 7.02 (d, J = 7.5 Hz, 4H), 6.91 (d, J = 8.0 Hz, 2H), 6.86 (d, J = 8.5 Hz, 2H), 6.68 (d, J = 7.0 Hz, 2H), 4.04 (br s, 1H), 3.99 (br s, 1H), 3.86 (s, 3H), 2.44 (s, 3H), 2.39 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.0, 142.7, 139.2, 138.3, 137.6, 136.5, 135.9, 131.9, 131.2, 130.0, 129.4, 128.82, 128.76, 128.14, 128.11, 128.0, 127.8, 113.3, 55.2, 51.3, 23.4, 21.4, 21.2; IR (Neat) ν_{max} 1601, 1509, 1327, 1250, 1154, 1029, 838 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{32}NO_3S$ $(M+H)^+$: calcd. 498.2097, found 498.2098.

(*Z*)-N-(2-(Benzo[*d*][1,3]dioxol-5-yl)-1-(4-methoxyphenyl)prop-1-en-1-yl)-N-benzyl-4-methylbenzenesulfonamide (48):



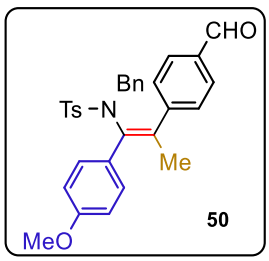
48 (112 mg, 71%) as pale yellow solid; M.P = 205–207 °C; R_f = 0.35 (10% EtOAc/Hex); ^1H NMR (500 MHz, $CDCl_3$) δ 7.27–7.23 (m, 1H), 7.18 (t, J = 8.0 Hz, 2H), 7.05 (t, J = 9.0 Hz, 4H), 6.98 (d, J = 8.5 Hz, 2H), 6.81 (d, J = 9.0 Hz, 2H), 6.76 (d, J = 8.0 Hz, 1H), 6.60 (dd, J = 8.0, 1.5 Hz, 1H), 6.54 (d, J = 1.5 Hz, 1H), 5.97 (s, 2H), 4.04 (br s, 2H), 3.83 (s, 3H), 2.37 (s, 3H), 1.93 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.0, 147.3, 146.6, 142.9, 137.9, 137.7, 135.9, 135.8, 131.9, 131.6, 129.9, 129.5, 128.9, 128.2, 127.9, 121.7, 113.4, 109.0, 108.1, 100.9, 55.3, 51.5, 23.5, 21.5; IR (Neat) ν_{max} 1606, 1509, 1487, 1326, 1275, 1033, 842 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{30}NO_5S$ $(M+H)^+$: calcd. 528.1839, found 528.1836.

(*Z*)-N-Benzyl-N-(2-(3,5-dimethylphenyl)-1-(4-methoxyphenyl)prop-1-en-1-yl)-4-methylbenzenesulfonamide (49):



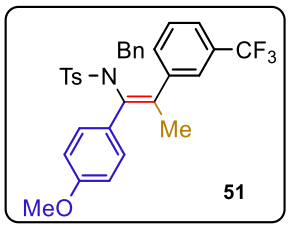
49 (112 mg, 81%) as pale yellow solid; M.P = 206–208 °C; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26–7.15 (m, 5H), 7.05 (d, J = 8.0 Hz, 2H), 6.94 (br s, 1H), 6.89 (d, J = 8.5 Hz, 2H), 6.87 (d, J = 8.5 Hz, 2H), 6.65 (br s, 2H), 6.61 (d, J = 7.0 Hz, 2H), 3.98 (br s, 2H), 3.86 (s, 3H), 2.38 (s, 3H), 2.25 (s, 3H), 1.98 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.02, 142.8, 142.2, 139.2, 137.6, 137.5, 135.9, 132.0, 130.9, 129.9, 129.4, 128.8, 128.4, 128.2, 128.1, 127.7, 126.0, 113.4, 55.3, 51.1, 23.6,21.4, 21.3; IR (Neat) ν_{max} 2359, 1598, 1510, 1332, 1245, 1152, 1089, 1050, 1026, 840, 813 cm^{-1}; **HRMS (ESI)** for $C_{32}H_{34}NO_3S$ $(M+H)^+$: calcd. 512.2254, found 512.2254.

(Z)-N-benzyl-N-(2-(4-formylphenyl)-1-(4-methoxyphenyl)prop-1-en-1-yl)-4-methylbenzenesulfonamide (50):



50 (126 mg, 82%) as pale yellow gummy liquid; R_f = 0.35 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.05 (s, 2H), 7.75 (d, J = 8.0 Hz, 2H), 7.33–7.27 (m, 4H), 7.20 (t, J = 7.5 Hz, 2H), 7.06 (d, J = 8.0 Hz, 2H), 6.98 (d, J = 8.0 Hz, 2H), 6.91 (d, J = 8.5 Hz, 2H), 6.85 (d, J = 8.5 Hz, 2H), 6.59 (d, J = 7.5 Hz, 1H), 4.04 (br s, 1H), 3.97 (br s, 1H), 3.87 (s, 3H), 2.35 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.0, 159.4, 142.2, 148.4, 138.3, 136.8, 135.3, 134.8, 132.4, 132.0, 129.9, 129.5, 129.3, 129.0, 128.3, 128.1, 128.0, 113.7, 55.3, 51.4, 23.3, 21.4; IR (Neat) ν_{max} 1694, 1598, 1508, 1326, 1249, 1154, 1027, 831 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{30}NO_4S$ $(M+H)^+$: calcd. 512.1890, found 512.1891.

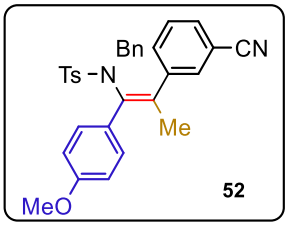
(*Z*)-N-Benzyl-N-(1-(4-methoxyphenyl)-2-(3-(trifluoromethyl)phenyl)prop-1-en-1-yl)-4-methylbenzenesulfonamide (51):



51 (84 mg, 51%) as pale yellow liquid; R_f = 0.44 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, J = 7.5 Hz, 1H), 7.32 (t, J = 8.0 Hz, 1H), 7.22 (t, J = 9.0 Hz, 3H), 7.17 (t, J = 7.5 Hz, 1H), 7.13–7.06 (m, 3H), 6.93 (d, J = 8.0 Hz, 2H), 6.85 (d, J = 9.0 Hz, 2H), 6.77 (d, J = 8.5 Hz, 2H), 6.52 (d, J = 7.5 Hz, 2H), 3.97 (br s, 1H), 3.86 (br s, 1H), 3.78 (s, 3H), 2.27 (s, 3H), 1.89 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 143.31, 143.27, 138.1, 136.6, 135.0, 132.5, 131.1, 132.0, 130.2 (q, J = 32 Hz, 1C), 129.8, 129.0, 128.6, 128.3, 128.0, 127.9,

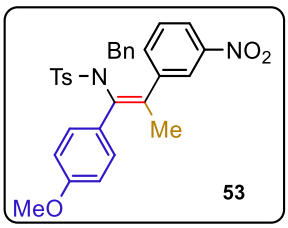
124.9, 124.1 (q, J = 273 Hz, 1C), 123.4, 113.6, 55.3, 51.3, 23.7, 21.4; ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.1; IR (Neat) ν_{max} 1604, 1509, 1438, 1331, 1296, 1256, 1159, 1120, 810 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{29}F_3NO_3S$ $(M+H)^+$: calcd. 552.1815, found 552.1817.

(*Z*)-N-Benzyl-N-(2-(3-cyanophenyl)-1-(4-methoxyphenyl)prop-1-en-1-yl)-4-methylbenzenesulfonamide (52):



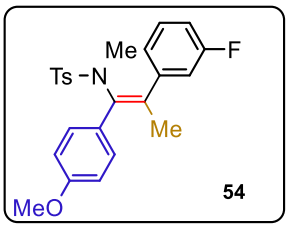
52 (84 mg, 59%) as pale yellow liquid; R_f = 0.35 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (dt, J = 7.5, 1.5 Hz, 1H), 7.45 (dt, J = 8.0, 1.5 Hz, 1H), 7.42–7.35 (m, 3H), 7.34–7.30 (m, 3H), 7.25 (t, J = 7.5 Hz, 2H), 7.06 (d, J = 8.0 Hz, 2H), 6.95 (d, J = 9.0 Hz, 2H), 6.86 (d, J = 8.5 Hz, 2H), 6.59–6.53 (m, 3H), 4.13 (br s, 1H), 3.87 (s, 3H), 3.82 (br s, 1H), 2.39 (s, 3H), 1.94 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159,5, 143.74, 143.65, 138.0, 136.5, 134.8, 133.6, 132.3, 132.0, 131.7, 130.0, 129.7, 129.2, 128.9, 128.6, 128.4, 128.0, 127.9, 118.6, 113.8, 112.0, 55.3, 51.2, 23.5, 21.5; IR (Neat) ν_{max} 1604, 1508, 1329, 1274, 1253, 1158, 1125, 809 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{29}N_2O_3S$ $(M+H)^+$: calcd. 509.1893, found 509.1906.

(Z)-N-benzyl-N-(1-(4-methoxyphenyl)-2-(3-nitrophenyl)prop-1-en-1-yl)-4-methylbenzenesulfonamide (53):



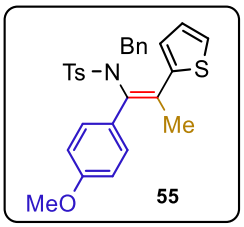
53 (84 mg, 65%) as pale yellow solid; R_f = 0.38 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (dt, J = 7.5, 1.5 Hz, 1H), 7.45 (dt, J = 8.0, 1.5 Hz, 1H), 7.42–7.35 (m, 3H), 7.34–7.30 (m, 3H), 7.25 (t, J = 7.5 Hz, 2H), 7.06 (d, J = 8.0 Hz, 2H), 6.95 (d, J = 9.0 Hz, 2H), 6.86 (d, J = 8.5 Hz, 2H), 6.59–6.53 (m, 3H), 4.13 (br s, 1H), 3.87 (s, 3H), 3.82 (br s, 1H), 2.39 (s, 3H), 1.94 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159,5, 143.74, 143.65, 138.0, 136.5, 134.8, 133.6, 132.3, 132.0, 131.7, 130.0, 129.7, 129.2, 128.9, 128.6, 128.4, 128.0, 127.9, 118.6, 113.8, 112.0, 55.3, 51.2, 23.5, 21.5; IR (Neat) ν_{max} 1604, 1508, 1329, 1274, 1253, 1158, 1125, 809 cm^{-1}; **HRMS (ESI)** for $C_{31}H_{29}N_2O_3S$ $(M+H)^+$: calcd. 509.1893, found 509.1906.

(*Z*)-N-(2-(3-Fluorophenyl)-1-(4-methoxyphenyl)prop-1-en-1-yl)-N,4-dimethylbenzenesulfonamide (54):



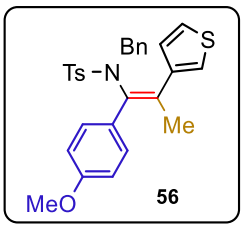
54 (110 mg, 86%) as pale yellow gummy liquid; R_f = 0.4 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40–7.34 (m, 3H), 7.32–7.28 (m, 1H), 7.22 (d, J = 9.0 Hz, 2H), 7.13 (dt, J = 9.5, 2.0 Hz, 1H), 7.04–6.97 (m, 5H), 6.82 (d, J = 8.5 Hz, 2H), 3.85 (s, 3H), 2.73 (s, 3H), 2.35 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.7 (d, J = 246 Hz, 1C), 159.2, 144.2 (d, J = 7.8 Hz, 1C), 142.5, 136.8, 135.9, 135.5, 131.1, 129.0 (d, J = 7.8 Hz, 1C), 129.2, 128.8, 127.2, 123.9 (d, J = 2.5 Hz, 1C), 114.9 (d, J = 21.4 Hz, 1C), 113.9 (d, J = 20.2 Hz, 1C), 113.5, 55.3, 37.4, 22.0, 21.4; ^{19}F NMR (471 MHz, $CDCl_3$) δ -113.3; IR (Neat) ν_{max} 16004, 1577, 1509, 1335, 1244, 1154, 1087, 1030, 977, 841 cm^{-1}; **HRMS (ESI)** for $C_{24}H_{24}FNO_3SNa$ $(M+Na)^+$: calcd. 448.1353, found 448.1352.

(*Z*)-N-Benzyl-N-(1-(4-methoxyphenyl)-2-(thiophen-2-yl)prop-1-en-1-yl)-4-methylbenzenesulfonamide (55):



55 (110 mg, 86%) as pale yellow gummy liquid; R_f = 0.45 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (dd, J = 5.0, 1.0 Hz, 1H), 7.32 (dd, J = 3.5, 1.0 Hz, 1H), 7.25–7.16 (m, 3H), 7.09–7.05 (m, 3H), 7.12 (d, J = 8.5 Hz, 2H), 6.89 (d, J = 7.0 Hz, 2H), 6.70 (d, J = 8.5 Hz, 2H), 6.64 (d, J = 9.0 Hz, 2H), 4.45 (br d, J = 13.5 Hz, 1H), 4.21 (br d, J = 13.0 Hz, 1H), 3.78 (s, 3H), 2.35 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.1, 142.8, 142.6, 138.1, 136.1, 132.7, 131.8, 130.1, 129.7, 129.3, 128.8, 128.2, 127.9, 127.5, 127.1, 127.0, 125.5, 113.1, 55.2, 51.9, 23.4, 21.4; IR (Neat) ν_{max} 1606, 1507, 1332, 1244, 1149, 1089, 1031, 842, 817 cm^{-1}; **HRMS (ESI)** for $C_{28}H_{28}NO_3S_2$ $(M+H)^+$: calcd. 490.1505, found 490.1504.

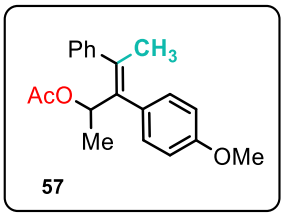
(*Z*)-N-Benzyl-N-(1-(4-methoxyphenyl)-2-(thiophen-3-yl)prop-1-en-1-yl)-4-methylbenzenesulfonamide (56):



56 (110 mg, 86%) as pale yellow gummy liquid; R_f = 0.45 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (dd, J = 5.0, 2.0 Hz, 1H), 7.25–7.22 (m, 1H), 7.21–7.16 (m, 3H), 7.07 (dd, J = 3.0, 1.5 Hz, 1H), 7.06–7.00 (m, 4H), 6.92 (d, J = 8.5 Hz, 2H), 6.77 (d, J = 7.0 Hz, 2H), 6.74

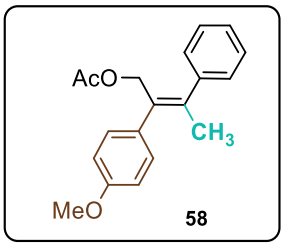
(d, J = 9.0 Hz, 2H), 4.22 (br d, J = 13.0 Hz, 1H), 4.05 (br d, J = 13.5 Hz, 1H), 3.81 (s, 3H), 2.36 (s, 3H), 1.96 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.0, 142.7, 141.8, 137.8, 136.0, 132.5, 132.0, 131.8, 129.9, 129.5, 128.9, 128.22, 128.20, 127.9, 127.7, 124.9, 122.8, 113.2, 55.2, 51.6, 22.7, 21.4; IR (Neat) ν_{max} 1606, 1508, 1457, 1327, 1244, 1149, 1109, 1030, 758 cm^{-1}; **HRMS (ESI)** for $C_{28}H_{28}NO_3S_2$ $(M+H)^+$: calcd. 490.1505, found 490.1505.

(Z)-3-(4-Methoxyphenyl)-4-phenylpent-3-en-2-yl acetate (57):



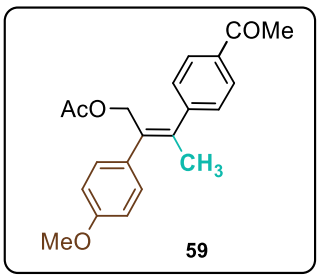
57 (37 mg, 40%) as colorless liquid; R_f = 0.3 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO D_6) δ 7.40 (t, J = 7.5 Hz, 2H), 7.33–7.29 (m, 1H), 7.26 (d, J = 8.0 Hz, 2H), 7.13 (d, J = 8.5 Hz, 2H), 6.99 (d, J = 9.0 Hz, 2H), 5.42 (q, J = 6.5 Hz, 1H), 3.79 (s, 3H), 1.88 (s, 3H), 1.69 (s, 3H), 1.07 (d, J = 6.5 Hz, 2H); ^{13}C NMR (101 MHz, DMSO D_6) δ 169.6, 158.6, 142.9, 137.7, 136.1, 131.4, 130.4, 128.8, 128.1, 127.4, 114.0, 70.7, 55.5, 23.4, 21.5, 19.8; IR (Neat) ν_{max} 1730, 1655, 1507, 1374, 1248, 1025, 991, 760 cm^{-1}; **HRMS (ESI)** for $C_{20}H_{22}O_3Na$ $(M+Na)^+$: calcd. 333.1461, found 333.1461.

(Z)-2-(4-Methoxyphenyl)-3-phenylbut-2-en-1-yl acetate (58):



58 (38 mg, 42%) as colorless liquid; R_f = 0.3 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO D_6) δ 7.40 (t, J = 7.0 Hz, 2H), 7.35–7.29 (m, 3H), 7.25 (d, J = 8.0 Hz, 2H), 6.97 (d, J = 9.0 Hz, 2H), 4.58 (s, 2H), 3.78 (s, 3H), 1.90 (s, 3H), 1.85 (s, 3H); ^{13}C NMR (101 MHz, DMSO D_6) δ 170.4, 158.6, 142.8, 139.6, 132.3, 131.9, 130.4, 128.8, 128.2, 127.6, 114.1, 65.9, 55.5, 23.1, 21.0; IR (Neat) ν_{max} 1730, 1657, 1509, 1374, 1244, 1023, 1001, 760 cm^{-1}; **HRMS (ESI)** for $C_{19}H_{20}O_3Na$ $(M+Na)^+$: calcd.319.1305, found 319.1298.

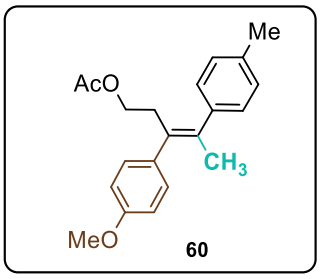
(Z)-3-(4-acetylphenyl)-2-(4-methoxyphenyl)but-2-en-1-yl acetate (59):



59 (47 mg, 46%) as colorless liquid; R_f = 0.3 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO D_6) δ 7.99 (d, J = 8.0 Hz, 2H), 7.46 (d, J = 8.5 Hz, 2H), 7.27 (d, J = 9.0 Hz, 2H), 6.98 (d, J = 8.5 Hz, 2H), 4.57 (s, 2H), 3.78 (s, 3H), 2.60 (s, 3H), 1.92 (s, 3H), 1.85 (s, 3H); ^{13}C NMR (126 MHz, DMSO D_6) δ 197.9, 170.4, 158.7, 147.7, 138.7, 136.1, 132.8, 132.0, 130.4, 128.8, 128.6, 114.1, 65.7, 55.5, 27.2, 22.7, 21.0;

IR (Neat) ν_{max} 1734, 1681, 1602, 1510, 1244, 761 cm^{-1}; **HRMS (ESI)** for $C_{21}H_{22}O_4Na^+$ $(M+Na)^+$: calcd. 361.1410, found 361.1414.

(E)-3-(4-Methoxyphenyl)-4-(p-tolyl)pent-3-en-1-yl acetate (60):

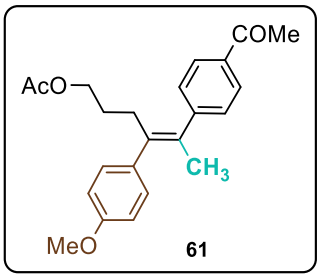


60

60 (40 mg, 41%) as pale yellow gummy liquid; R_f = 0.41 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO D_6) δ 7.22–7.13 (m, 6H), 6.99–6.93 (m, 2H), 3.77 (s, 3H), 3.78–3.70 (m, 2H), 2.52–2.43 (m, 2H), 2.32 (s, 3H), 1.89 (s, 3H), 1.79 (s, 3H); ^{13}C NMR (126 MHz, DMSO D_6) δ 170.5, 158.4, 141.0, 136.0, 135.6, 133.7, 132.8, 130.2, 129.4, 128.1, 114.2, 62.6, 55.5, 34.2, 23.2, 21.2, 21.0; IR (Neat) ν_{max} 1736, 1658, 1510, 1241, 1023, 998, 760 cm^{-1}; **HRMS (ESI)** for $C_{21}H_{24}O_3$ $(M+Na)^+$: calcd.347.1618, found 347.1619.

Minor isomer; ^{1}H NMR (500 MHz, DMSO D_6) δ 6.87–6.83 (m, 0.38H), 2.26 (s, 0.57H), 1.97 (s, 0.54H), 1.65 (s, 0.55H); ^{13}C NMR (126 MHz, DMSO D_6) δ 130.7, 129.2, 113.9, 62.5, 34.7;

(*E*)-5-(4-Acetylphenyl)-4-(4-methoxyphenyl)hex-4-en-1-yl acetate (61):

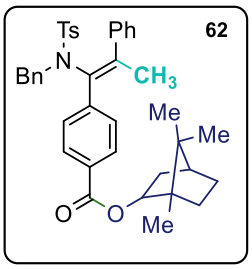


61

61 (59 mg, 54%) as pale yellow liquid; R_f = 0.23 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO D_6) δ 7.98 (d, J = 8.5 Hz, 2H), 7.38 (d, J = 8.5 Hz, 2H), 7.20 (d, J = 8.5 Hz, 2H), 6.97 (d, J = 9.0 Hz, 2H), 3.78 (s, 3H), 3.79–3.71 (m, 2H), 2.59 (s, 3H), 2.22 (t, J = 7.5 Hz, 2H), 1.81 (s, 3H), 180 (s, 3H), 1.45–1.35 (m, 2H); ^{13}C NMR (126 MHz, DMSO D_6) δ 197.8, 170.6, 158.4, 149.4, 137.2, 135.5, 133.6, 133.0, 130.1, 128.8, 128.7, 114.2, 63.5, 55.4, 31.2, 27.5, 27.1, 22.7, 20.9; IR (Neat) ν_{max} 1734, 1680, 1601, 1509, 1361, 1241, 1031, 836 cm^{-1}; **HRMS (ESI)** for $C_{23}H_{26}O_4Na^+$ $(M+Na)^+$: calcd.389.1723, found 389.1726.

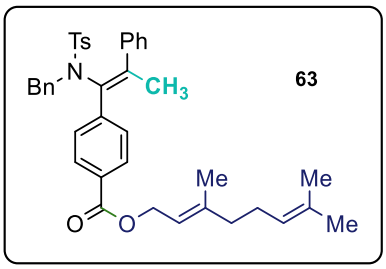
Minor isomer; ^{1}H NMR (500 MHz, DMSO D_6) δ 7.90 (d, J = 8.5 Hz, 0.28H), 6.87 (d, J = 8.5 Hz, 0.25H), 2.54 (s, 0.45H); ^{13}C NMR (126 MHz, DMSO D_6) δ 134.4, 130.9, 129.8, 128.6, 63.7, 31.6, 27.2;

(1R,4S)-1,7,7-Trimethylbicyclo[2.2.1]heptan-2-yl 4-((Z)-1-((N-benzyl-4-methylphenyl)sulfonamido)-2-phenylprop-1-en-1-yl)benzoate (62):



62 (97 mg, 51%) as pale yellow gummy liquid; R_f = 0.45 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, J = 8.5 Hz, 2H), 7.36–7.27 (m, 6H), 7.21 (t, J = 8.0 Hz, 2H), 7.08 (br d, J = 6.5 Hz, 2H), 7.01 (d, J = 8.0 Hz, 2H), 6.85 (d, J = 8.5 Hz, 2H), 6.74 (d, J = 9.0 Hz, 2H), 5.16 (dt, J = 7.0, 2.0 Hz, 1H), 3.96 (d, J = 6.0 Hz, 2H), 2.56–2.48 (m, 1H), 2.36 (s, 3H), 2.22–2.14 (m, 1H), 2.00 (s, 3H), 1.89–1.80 (m, 1H), 1.77 (t, J = 4.5 Hz, 1H), 1.49–1.41 (m, 1H), 1.40–1.31 (m, 1H), 1.16 (dd, J = 9.0, 3.0 Hz, 1H), 1.00 (s, 3H), 0.96 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 143.2, 141.6, 140.5, 137.0, 135.4, 130.8, 130.7, 129.9, 129.3, 129.0, 128.3, 128.2, 128.1, 128.0, 127.2, 80.6, 51.3, 49.1, 47.9, 45.0, 36.9, 28.1, 27.4, 23.5, 21.4, 19.7, 18.9, 13.6; IR (Neat) ν_{max} 1606, 1508, 1457, 1327, 1244, 1149, 1109, 1030, 758 cm^{-1}; **HRMS (ESI)** for $C_{40}H_{44}NO_4S$ $(M+H)^+$: calcd. 634.2986, found 634.2985.

(E)-3,7-dimethylocta-2,6-dien-1-yl 4-((Z)-1-((N-benzyl-4-methylphenyl)sulfonamido)-2-phenylprop-1-en-1-yl)benzoate (63):

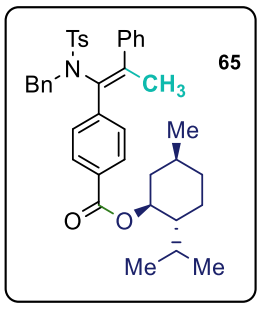


63 (97 mg, 52%) as pale yellow gummy liquid; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, J = 8.5 Hz, 2H), 7.37–7.32 (m, 3H), 7.25 (t, J = 7.5 Hz, 3H), 7.19 (t, J = 7.5 Hz, 2H), 7.14–6.99 (m, 2H), 7.00 (d, J = 8.0 Hz, 2H), 6.86 (d, J = 8.5 Hz, 2H), 6.61 (d, J = 8.5 Hz, 2H), 5.50 (td, J = 7.0, 1.0 Hz, 1H), 5.12 (td, J = 6.5, 1.0 Hz, 1H), 4.88 (d, J = 7.0 Hz, 2H), 3.95 (br d, J = 12.0 Hz, 2H), 2.36 (s, 3H), 2.18–2.08 (m, 4H), 1.98 (s, 3H), 1.80 (s, 3H), 1.69 (s, 3H), 1.62 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.3, 143.2, 142.4, 11.7, 141.6, 140.4, 137.1, 135.5, 131.8, 130.9, 130.6, 129.9, 129.6, 129.3, 129.0, 128.29, 128.26, 128.2, 128.0, 127.9, 127.2, 123.7, 118.3, 61.9, 51.3, 39.5, 26.3, 25.6, 23.4, 21.4, 17.7, 16.5; IR (Neat) ν_{max} 1606, 1508, 1457, 1327, 1244, 1149, 1109, 1030, 758 cm^{-1}; **HRMS (ESI)** for $C_{40}H_{44}NO_4S$ $(M+H)^+$: calcd. 634.2986, found 634.2982.

(*Z*)-Octadec-9-en-1-yl-4-((Z)-1-((N-benzyl-4-methylphenyl)sulfonamido)-2-phenylprop-1-en-1-yl)benzoate (64):

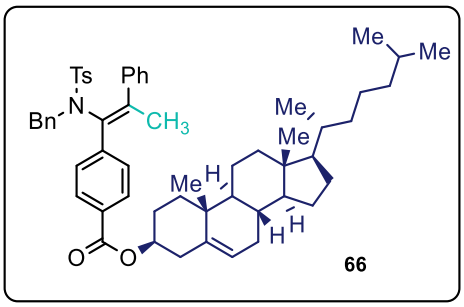
64 (137 mg, 61%) as pale yellow gummy liquid; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, J = 8.5 Hz, 2H), 7.37–7.26 (m, 6H), 7.19 (t, J = 7.5 Hz, 2H), 7.13–6.97 (m, 2H), 7.01 (d, J = 8.0 Hz, 2H), 6.85 (d, J = 8.0 Hz, 2H), 6.61 (d, J = 8.0 Hz, 2H), 5.36 (t, J = 4.5 Hz, 2H), 4.35 (t, J = 6.5 Hz, 2H), 3.95 (br d, J = 7.5 Hz, 2H), 2.36 (s, 3H), 2.07–2.00 (m, 4H), 1.99 (s, 3H), 1.83–1.76 (m, 2H), 1.51–1.44 (m, 2H), 1.42–1.27 (m, 20H), 0.88 (t, J = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4, 143.2, 141.7, 141.6, 140.5, 137.0, 135.5, 130.8, 130.7, 129.9, 129.7, 129.6, 129.3, 129.0, 128.3, 128.2, 128.1, 127.9, 127.2, 65.2, 51.2, 32.5, 31.8, 29.7, 29.5, 29.4, 29.3, 29.2, 28.7, 27.2, 26.0, 23.4, 22.6, 21.4, 14.1; IR (Neat) ν_{max} 2923, 1715, 1334, 1270, 1155, 1102, 698 cm^{-1}; **HRMS (ESI)** for $C_{48}H_{61}NO_4SNa$ $(M+Na)^+$: calcd. 770.4214, found 770.4219.

(1S,2R,5S)-2-Isopropyl-5-methylcyclohexyl 4-((Z)-1-((N-benzyl-4-methylphenyl)sulfonamido)-2-phenylprop-1-en-1-yl)benzoate (65):



65 (121 mg, 64%) as pale yellow gummy liquid; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, J = 8.5 Hz, 2H), 7.37–7.32 (m, 3H), 7.25 (t, J = 7.5 Hz, 3H), 7.19 (t, J = 7.5 Hz, 2H), 7.14–6.99 (m, 2H), 7.00 (d, J = 8.0 Hz, 2H), 6.86 (d, J = 8.5 Hz, 2H), 6.61 (d, J = 8.5 Hz, 2H), 5.50 (td, J = 7.0, 1.0 Hz, 1H), 5.12 (td, J = 6.5, 1.0 Hz, 1H), 4.88 (d, J = 7.0 Hz, 2H), 3.95 (br d, J = 12.0 Hz, 2H), 2.36 (s, 3H), 2.18–2.08 (m, 4H), 1.98 (s, 3H), 1.80 (s, 3H), 1.69 (s, 3H), 1.62 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.3, 143.2, 142.4, 11.7, 141.6, 140.4, 137.1, 135.5, 131.8, 130.9, 130.6, 129.9, 129.6, 129.3, 129.0, 128.29, 128.26, 128.2, 128.0, 127.9, 127.2, 123.7, 118.3, 61.9, 51.3, 39.5, 26.3, 25.6, 23.4, 21.4, 17.7, 16.5; IR (Neat) ν_{max} 1606, 1508, 1457, 1327, 1244, 1149, 1109, 1030, 758 cm^{-1}; **HRMS (ESI)** for $C_{40}H_{44}NO_4S$ $(M+H)^+$: calcd. 634.2986, found 634.2982.

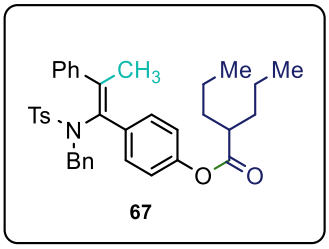
(3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 4-((Z)-1-((N-benzyl-4-methylphenyl)sulfonamido)-2-phenylprop-1-en-1-yl)benzoate (66):



66

66 (134 mg, 53%) as pale yellow gummy liquid; R_f = 0.45 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J = 8.5 Hz, 2H), 7.37–7.30 (m, 4H), 7.26–7.23 (m, 2H), 7.19 (t, J = 8.0 Hz, 2H), 7.13–7.08 (m, 2H), 6.85 (d, J = 8.0 Hz, 2H), 6.61 (d, J = 8.0 Hz, 2H), 5.45 (d, J = 4.0 Hz, 1H), 4.95–4.85 (m, 1H), 3.96 (bs, 1H), 3.93 (bs, 1H), 2.50 (d, J = 7.5 Hz, 2H), 2.36 (s, 3H), 2.08–2.01 (m, 3H), 1.99 (s, 3H), 1.97–1.91 (m, 1H), 1.90–1.76 (m, 2H), 1.43–1.30 (m, 7H), 1.25–1.12 (m, 5H), 1.09 (s, 3H), 1.08–0.98 (m, 4H), 0.94 (d, J = 6.5 Hz, 2H), 0.88 (dd, J = 6.5, 2.0 Hz, 6H), 0.7 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.7, 143.2, 141.6, 140.5, 139.6, 137.0, 135.5, 130.8, 130.6, 129.9, 129.7, 129.3, 129.0, 28.3, 128.2, 128.1, 127.9, 127.3, 122.8, 74.6, 56.7, 56.1, 51.3, 50.0, 42.3, 39.7, 39.5, 38.2, 37.0, 36.6, 36.3, 35.8, 31.9, 31.8, 28.2, 28.0, 27.9, 24.3, 23.8, 23.5, 22.8, 22.5, 21.4, 21.0, 19.4, 18.7, 11.8; IR (Neat) ν_{max} 1708, 1457, 1332, 1272, 1155, 1116, 812, 754 cm^{-1}; **HRMS (ESI)** for $C_{57}H_{72}NO_4S$ $(M+H)^+$: calcd. 866.5177, found 866.5177.

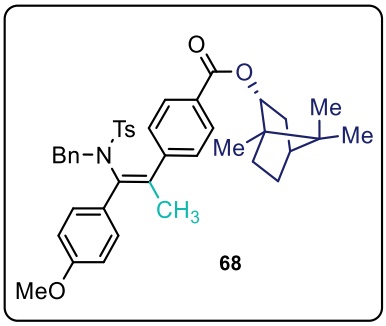
(*Z*)-4-(1-((N-benzyl-4-methylphenyl)sulfonamido)-2-phenylprop-1-en-1-yl)phenyl 2-propylpentanoate (67):



67

67 (108 mg, 52%) as pale yellow gummy liquid; R_f = 0.45 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.31 (m, 3H), 7.27–7.23 (m, 1H), 7.20–7.10 (m, 6H), 7.03 (d, J = 8.0 Hz, 2H), 7.00 (d, J = 9.0 Hz, 2H), 6.86 (d, J = 8.5 Hz, 2H), 6.64 (d, J = 7.0 Hz, 2H), 4.03 (bs, 1H), 3.90 (bs, 1H), 2.69–2.60 (m, 1H), 2.36 (s, 3H), 1.99 (s, 3H), 1.83–1.74 (m, 2H), 1.63–1.54 (m, 2H), 1.52–1.42 (m, 4H), 1.00 (d, J = 7.0 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.8, 150.2, 143.0, 141.8, 139.3, 138.2, 137.2, 135.7, 134.5, 131.7, 129.9, 129.0, 128.3, 128.2, 128.0, 127.9, 127.1, 121.2, 51.3, 45.4, 34.7, 23.3, 21.4, 20.7, 14.0; IR (Neat) ν_{max} 1748, 1502, 1454, 1332, 1198, 1152, 1089, 724 cm^{-1}; **HRMS (ESI)** for $C_{37}H_{41}NO_4SNa$ $(M+H)^+$: calcd. 618.2649, found 618.2649.

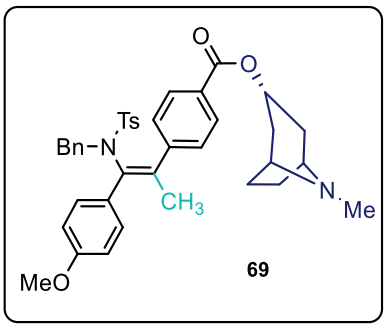
(2R,4R)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl 4-((Z)-1-((N-benzyl-4-methylphenyl)sulfonamido)-1-(4-methoxyphenyl)prop-1-en-2-yl)benzoate (68):



68

68 (95 mg, 72%, 0.2 mmol) as pale yellow gummy liquid; R_f = 0.38 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, J = 8.5 Hz, 2H), 7.30–7.17 (m, 6H), 7.02 (d, J = 8.0 Hz, 2H), 6.98 (d, J = 8.0 Hz, 2H), 6.89 (d, J = 8.5 Hz, 6.84 (d, J = 8.0 Hz, 2H), 6.60 (d, J = 7.5 Hz, 2H), 5.19 (br d, J = 9.5 Hz, 1H), 4.02 (bs, 1H), 3.98 (bs, 1H), 3.86 (s, 3H), 2.58–2.49 (m, 1H), 2.34 (s, 3H), 2.22–2.13 (m, 1H), 1.99 (s, 3H), 1.87–1.74 (m, 2H), 1.50–1.31 (m, 2H), 1.17 (dd, J = 6.5, 3.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.8, 159.3, 147.1, 143.2, 138.3, 135.4, 132.1, 132.0, 129.9, 129.3, 129.3, 128.9, 128.6, 128.5, 128.3, 128.04, 127.98, 113.5, 80.4, 55.3, 51.4, 49.1, 47.9, 45.0, 37.0, 28.1, 27.4, 23.3, 21.4, 19.7, 18.9, 13.6; IR (Neat) ν_{max} 1710, 1601, 1274, 1251, 1177, 1031, 750 cm^{-1}; **HRMS (ESI)** for $C_{41}H_{46}NO_5S$ $(M+H)^+$: calcd. 664.3091, found 664.3092.

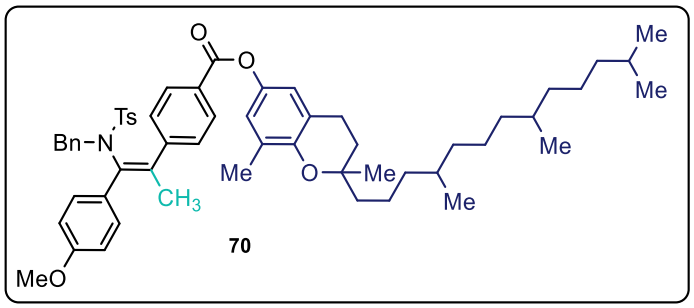
(1R,3r,5S)-8-Methyl-8-azabicyclo[3.2.1]octan-3-yl-4-((Z)-1-((N-benzyl-4-methylphenyl)sulfonamido)-1-(4-methoxyphenyl)prop-1-en-2-yl)benzoate (69):



69

69 (81 mg, 62%, 0.2 mmol) as pale yellow gummy liquid; R_f = 0.39 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, J = 8.5 Hz, 2H), 7.29–7.27 (m, 1H), 7.19 (d, J = 7.5 Hz, 2H), 7.16 (d, J = 7.0 Hz, 2H), 7.05 (d, J = 8.0 Hz, 7.00 (d, J = 8.0 Hz, 2H), 6.86 (d, J = 8.5 Hz, 2H), 6.59 (d, J = 7.5 Hz, 2H), 3.96 (s, 2H), 3.84 (s, 3H), 2.35 (s, 3H), 2.10–2.04 (m, 2H), 1.97 (s, 3H), 1.83–1.72 (m, 3H), 1.50–1.40 (m, 2H), 1.34–1.22 (m, 5H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4, 159.3, 145.5, 143.2, 138.0, 137.1, 135.4, 133.5, 132.1, 132.0, 129.9, 129.0, 128.7, 128.6, 128.3, 128.1, 127.9, 126.7, 113.5, 55.3, 51.4, 48.7, 33.3, 25.6, 24.9, 23.3, 21.4; IR (Neat) ν_{max} 1700, 1621, 1502, 1478, 1312, 1212, 1200, 1106, 1049, 759 cm^{-1}; **HRMS (ESI)** for $C_{39}H_{43}N_2O_5S$ $(M+H)^+$: calcd. 651.2887, found 651.2887.

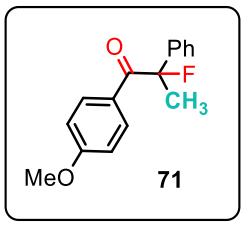
2,8-Dimethyl-2-(4,8,12-trimethyltridecyl)chroman-6-yl-(Z)-4-(1-((N-benzyl-4-methylphenyl)sulfonamido)-1-(4-methoxyphenyl)prop-1-en-2-yl)benzoate (70):



70

70 (104 mg, 57%, 0.2 mmol) as pale yellow gummy liquid; R_f = 0.42 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, J = 8.5 Hz, 2H), 7.30–7.15 (m, 6H), 7.04 (d, J = 8.5 Hz, 2H), 7.00 (d, J = 8.0 Hz, 2H), 6.87 (t, J = 8.5 Hz, 4H), 6.84–6.75 (m, 2H), 6.61 (t, J = 7.0 Hz, 2H), 4.02 (bs, 1H), 3.97 (bs, 1H), 3.84 (s, 3H), 2.80–2.73 (m, 2H), 2.35 (s, 3H), 2.18 (s, 3H), 2.17–2.08 (m, 1H), 1.98 (s, 3H), 1.86–1.75 (m, 3H), 1.43–1.30 (m, 4H), 1.25–1.20 (m, 3H), 1.26–1.01 (m, 8H), 0.89–0.80 (m, 15H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.8, 159.3, 149.8, 147.8, 143.2, 142.7, 138.2, 137.0, 135.4, 132.3, 132.0, 130.0, 129.9, 129.0, 128.7, 128.6, 128.3, 128.2, 128.1, 128.0, 127.4, 121.2, 119.1, 113.6, 76.2, 55.3, 51.4, 40.1, 39.3, 37.4, 37.3, 32.8, 32.7, 31.0, 27.9, 24.8, 24.4, 24.2, 23.3, 22.7, 22.6, 21.5, 21.0; IR (Neat) ν_{max} 1650, 1603, 1293, 1178, 1028, 751, 727, 698 cm^{-1}; **HRMS (ESI)** for $C_{58}H_{74}NO_6S$ $(M+H)^+$: calcd. 912.5231, found 912.5233.

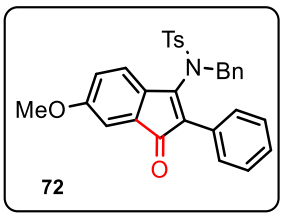
5.6.3.2. Synthesis of 2-fluoro-1-(4-methoxyphenyl)-2-phenylpropan-1-one (71):



71

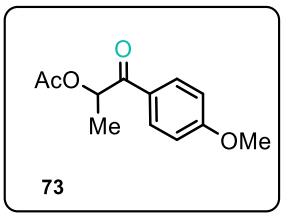
To a solution of **18** (0.2 mmol) in MeOH:CH_3CN (1:9, 2.0 mL) was added selectfluor (0.24 mmol). The resulting mixture was stirred at 80 °C overnight. The reaction progress was monitored by TLC. Upon completion, the crude mixture was concentrated under the reduced pressure. The crude residue was purified using column chromatography on silica gel to afford **71** (24 mg, 46%) as pale yellow gummy liquid; R_f = 0.42 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (dd, J = 9.0, 3.5 Hz, 2H), 7.47 (d, J = 9.0 Hz, 2H), 7.37 (t, J = 7.5 Hz, 2H), 7.34–7.28 (m, 1H), 6.83 (d, J = 9.5 Hz, 2H), 3.81 (s, 3H), 1.91 (d, J = 8.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.9 (d, J = 27 Hz, 1C), 163.4, 140.8 (d, J = 21 Hz, 1C), 132.80, 132.75, 128.7, 128.1, 127.0 (d, J = 3.8 Hz, 1C), 123.8, 123.7, 113.5, 101.3 (d, J = 185 Hz, 1C), 55.4, 26.9 (d, J = 27 Hz, 1C); ^{19}F NMR (471 MHz, $CDCl_3$) δ –149.7; IR (Neat) ν_{max} 1675, 1597, 1571, 1254, 1147, 697 cm^{-1}; **HRMS (ESI)** for $C_{16}H_{15}FO_2Na$ $(M+Na)^+$: calcd. 281.0948, found 281.0948.

5.6.3.3. Synthesis of N-Benzyl-N-(6-methoxy-1-oxo-2-phenyl-1H-inden-3-yl)-4-methylbenzenesulfonamide (72):



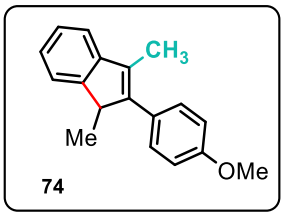
To a solution of **18** (0.2 mmol) in 1,2-DCE:H_2O (9:1, 2.0 mL) was added $PdCl_2$ (10 mol%), DDQ (3.0 equiv.) (0.24 mmol). The resulting mixture was stirred at 80 ^oC overnight. The reaction progress was monitored by TLC. Upon completion, the crude mixture was concentrated under the reduced pressure. The crude residue was purified using column chromatography on silica gel to afford **72** (39 mg, 39%) as pale yellow gummy liquid; R_f = 0.32 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, J = 8.5 Hz, 2H), 7.40 (d, J = 8.0 Hz, 2H), 7.26–7.23 (m, 2H), 7.18–7.09 (m, 5H), 7.02–6.95 (m, 3H), 6.80 (dd, J = 8.0, 2.5 Hz, 1H), 6.67 (d, J = 7.0 Hz, 2H), 4.39 (bs, 2H), 3.81 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.5, 160.9, 153.7, 144.6, 135.9, 135.2, 134.8, 132.1, 130.1, 129.7, 129.2, 128.4, 128.3, 128.1, 127.9, 123.9, 116.8, 109.5, 55.8, 52.3, 21.6; IR (Neat) ν_{max} 1710, 1480, 1354, 1395, 1259, 1024, 762 cm^{-1}; **HRMS (ESI)** for $C_{30}H_{26}NO_4S$ $(M+H)^+$: calcd. 496.1577, found 496.1575.

5.6.3.4. Synthesis of 1-(4-Methoxyphenyl)-1-oxopropan-2-yl acetate (73):



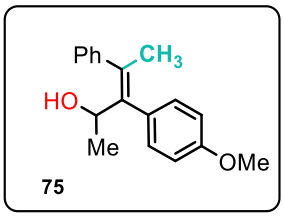
To an independent solution of acetate **57** (0.2 mmol) in CCl_4:CH_3CN:H_2O (1:1:1.5) (2.0 mL) was added $NaIO_4$ and $RuCl_3$ (4 equiv. and 1 mol%). The resulting mixture was stirred at rt. The reaction progress was monitored by TLC. Upon completion, the crude mixture was concentrated under reduced pressure. The crude residue was purified using column chromatography on silica gel to afford **73** (20 mg, 90%) as colorless liquid; R_f = 0.3 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (dt, J = 9.0, 3.0 Hz, 2H), 6.97 (dt, J = 9.0, 3.0 Hz, 2H), 5.96 (q, J = 7.0 Hz, 1H), 3.89 (s, 3H), 2.16 (s, 3H), 1.54 (d, J = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.3, 170.5, 163.9, 130.8, 127.2, 114.0, 71.2, 55.5, 20.8, 17.4; IR (Neat) ν_{max} 2935, 1737, 1685, 1598, 1574, 1510, 1421, 1371, 1230, 1174, 1028, 841 cm^{-1}; **HRMS (ESI)** for $C_{12}H_{14}NaO_4^+$ $(M+Na)^+$: calcd.245.0784, found 245.0788.

5.6.3.5. Synthesis of 2-(4-Methoxyphenyl)-1,3-dimethyl-1H-indene (74):



To an independent solution of acetate **57** (0.2 mmol) in 1,2-DCE (2.0 mL) was added H_3PO_4 (1 mmol). The resulting mixture was stirred at 75 °C. The reaction progress was monitored by TLC. Upon completion, the crude mixture was concentrated under reduced pressure. The crude residue was purified using column chromatography on silica gel to afford **74** (31 mg, 61%) as colorless gummy liquid; R_f = 0.5 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (br d, J = 7.0 Hz, 2H), 7.37–7.30 (m, 4H), 7.26–7.22 (m, 1H), 6.99 (d, J = 8.5 Hz, 2H), 3.89 (s, 3H), 3.85 (q, J = 5.5 Hz, 1H), 2.25 (s, 3H), 1.21 (d, J = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.4, 148.2, 146.4, 146.0, 132.1, 130.1, 129.0, 126.6, 124.6, 122.4, 118.9, 113.8, 55.3, 45.6, 16.5, 11.6; IR (Neat) ν_{max} 1655, 1507, 1374, 1248, 1025, 991, 760 cm^{-1}; **HRMS (ESI)** for $C_{18}H_{18}ONa$ $(M+Na)^+$: calcd. 273.1250, found 273.1247.

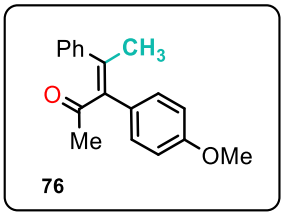
5.6.3.6. Synthesis of (*Z*)-3-(4-Methoxyphenyl)-4-phenylpent-3-en-2-ol (75):



To a mixture of acetate **57** (0.2 mmol) and KOH (2.0 mmol) was added toluene:ethanol (9:1, 2.0 mL). The resulting mixture was stirred at 120 °C overnight. The reaction progress was monitored by TLC. Upon completion, the crude mixture was concentrated under reduced pressure. The crude residue was purified using column chromatography on neutral alumina to afford **75** (46 mg, 85%) as colorless liquid; R_f = 0.2 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, DMSO D_6) δ 7.38 (t, J = 7.5 Hz, 2H), 7.33–7.26 (m, 3H), 7.18 (d, J = 8.5 Hz, 2H), 6.94 (d, J = 8.5 Hz, 2H), 4.42–4.37 (m, 2H), 3.77 (s, 3H), 1.68 (s, 3H), 0.88 (d, J = 6.0 Hz, 3H); ^{13}C NMR (126 MHz, DMSO D_6) δ 158.2, 143.6, 141.0, 134.0, 131.7, 131.3, 128.6, 128.4, 127.0, 66.0, 55.4, 23.2, 22.6; IR (Neat) ν_{max} 3397, 1365, 1220, 1134, 1045, 758 cm^{-1}; **HRMS (ESI)** for $C_{18}H_{21}O_2^+$ $(M+H)^+$: calcd. 269.1536, found 269.1536.

5.6.3.7. Synthesis of (*Z*)-3-(4-Methoxyphenyl)-4-phenylpent-3-en-2-one (76):

To a solution of **75** (0.2 mmol, 66 mg) in CH_2Cl_2 (2.0 mL) was added Dess-Martin Periodinane (DMP; 0.6 mmol, 255 mg). The resulting mixture was stirred at rt. The reaction progress was monitored by TLC. Upon completion of the reaction, the crude mixture was concentrated under the reduced pressure. The crude residue was purified using column chromatography on neutral



alumina to afford **76** (47 mg, 89%) as colorless liquid; R_f = 0.24 (10% EtOAc/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38–7.31 (m, 3H), 7.31–7.28 (m, 2H), 7.22 (dt, *J* = 6.5, 2.0 Hz, 2H), 6.93 (dt, *J* = 7.0, 2.0 Hz, 2H), 3.84 (s, 3H), 2.05 (s, 3H), 1.87 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.6, 159.0, 142.6, 141.5, 140.7, 130.4, 130.1, 128.5, 127.9, 127.7, 113.9, 55.3, 31.0, 22.4; IR (Neat) ν_{max} 1710, 1680, 1607, 1509, 1331, 127, 1033, 831 cm^{-1}; **HRMS (ESI)** for $C_{18}H_{19}O_2$ $(M+H)^+$: calcd.267.1380, found 267.1380.

5.7. X-ray crystallography:

5.7.1. X-ray reflections for **22** were collected on Rigaku Oxford CCD diffractometer using Mo-Kα, radiation. Data reduction was performed using CrysAlisPro (version 1.171.33.55). Apex 2 and SHELXL 97 program were used to solve and refine the data. All non-hydrogen atoms were refined anisotropically, and C−H hydrogens were fixed.

Table 5.3. Crystallographic Data for Compound **22**

Compound	**22**		
formula	$C_{31}H_{29}NO_3S$	*V* [Å^3]	653.00 (8)
Formula weight	495.61	*Z*	1
crystal system	Triclinic	ρ_{calcd} [g cm^{-3}]	1.260
space group	P 1	μ [mm^{-1}]	0.157
T [K]	298 K	total reflns	30858
a [Å]	8.7290 (3)	unique reflns	5939
b [Å]	9.5351 (6)	observed	3362
c [Å]	9.6043 (7)	R_1[I>2σ(I)]	0.0555 (3362)
α [°]	82.797 (3)	wR2 [all]	0.1281 (5939)
β [°]	66.640 (3)	GOF	0.991
γ [°]	63.095 (3)	Diffractometer	Rigaku Oxford
		CCDC Number	CCDC 2170318

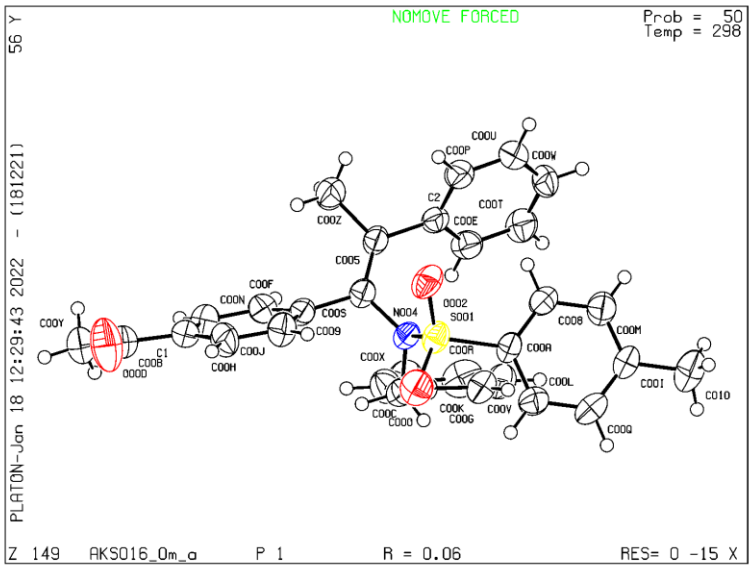


Figure 5.4. Molecular structure of compound **22**, (Oxygen (red), nitrogen (blue), and sulphur (yellow))

5.7.2. X-ray reflections for **29** were collected on Bruker D8 Quest CCD diffractometer using Mo-Kα, radiation. Data reduction was performed using CrysAlisPro (version 1.171.33.55). Apex 2 and SHELXL 97 program were used to solve and refine the data. All non-hydrogen atoms were refined anisotropically, and C−H hydrogens were fixed.

Table 5.4. Crystallographic Data for Compound **29**

Compound	**29**		
formula	$C_{31}H_{31}NO_4S$	V [Å^3]	5385.3 (4)
Formula weight	513.63	Z	8
crystal system	Monoclinic	ρ_{calcd} [g cm^{-3}]	1.267
space group	C 2/c	μ [mm^{-1}]	0.157
T [K]	295 K	total reflns	92155
a [Å]	14.9057 (6)	unique reflns	6193
b [Å]	12.2229 (5)	observed	4614
c [Å]	29.6074 (14)	R_1[I>2σ(I)]	0.0466 (4614)
α [°]	90	wR2 [all]	0.0659 (6193)
β [°]	93.291 (2)	GOF	2.019
γ [°]	90	Diffractometer	Bruker APEX-II CCD
		CCDC Number	CCDC 2170317

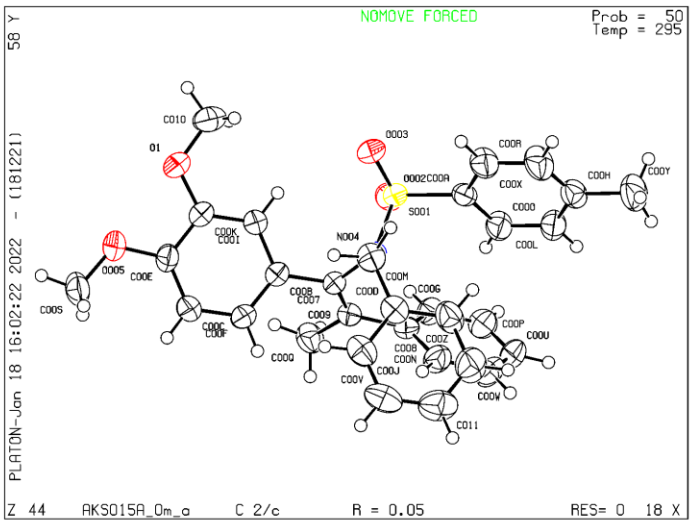


Figure 5.5. Molecular structure of compound **29**, (Oxygen (red), nitrogen (blue), and sulphur (yellow))

5.7.3. X-ray reflections for **49** were collected on Rigaku Oxford CCD diffractometer using Mo-Kα, radiation. Data reduction was performed using CrysAlisPro (version 1.171.33.55). Apex 2 and SHELXL 97 program were used to solve and refine the data. All non-hydrogen atoms were refined anisotropically, and C−H hydrogens were fixed.

Table 5.5. Crystallographic Data for Compound **49**

Compound	**49**		
formula	$C_{32}H_{33}NO_3S$	V [Å^3]	2867.33 (12)
Formula weight	511.65	Z	4
crystal system	Monoclinic	ρ_{calcd} [g cm^{-3}]	1.185
space group	P 21/c	μ [mm^{-1}]	0.145
T [K]	293 K	total reflns	34993
a [Å]	11.4779 (3)	unique reflns	6002
b [Å]	15.1981 (3)	observed	3616
c [Å]	16.6944 (4)	R_1[I>2σ(I)]	0.0522 (3616)
α [°]	90	wR2 [all]	0.0921 (6002)
β [°]	100.072(2)	GOF	1.033
γ [°]	90	Diffractometer	Rigaku Oxford
		CCDC Number	CCDC 2170317

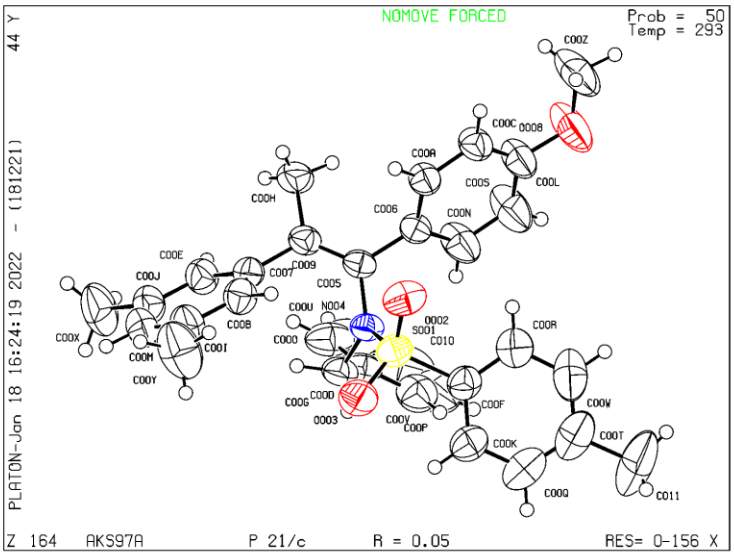


Figure 5.6. Molecular structure of compound **49**, (Oxygen (red), nitrogen (blue), and sulphur (yellow))

5.8. References

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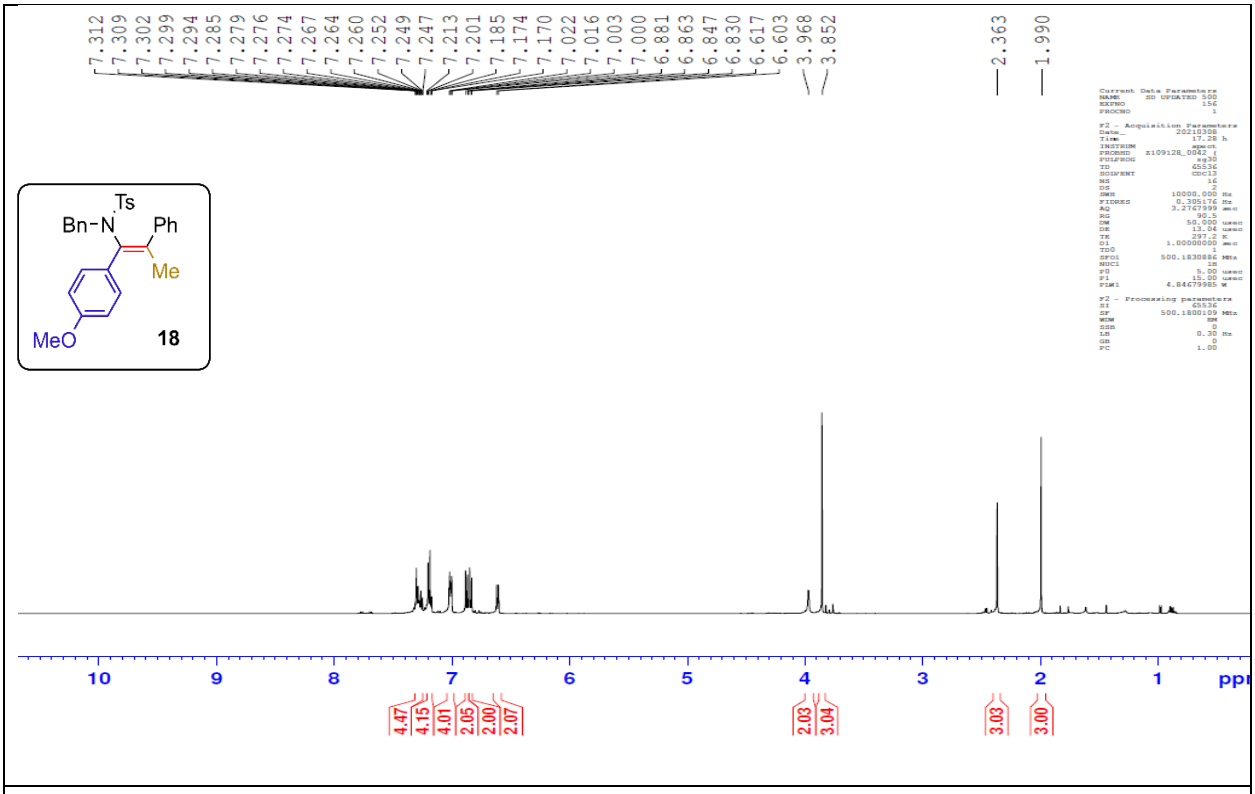
5.8. Spectra


7.312
7.309
7.302
7.299
7.294
7.285
7.279
7.276
7.274
7.267
7.264
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7.249
7.247
7.213
7.201
7.185
7.174
7.170
7.022
7.016
7.003
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6.863
6.847
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6.603
3.968
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Me
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18
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8
7
6
5
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3
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4.47
4.15
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2.00
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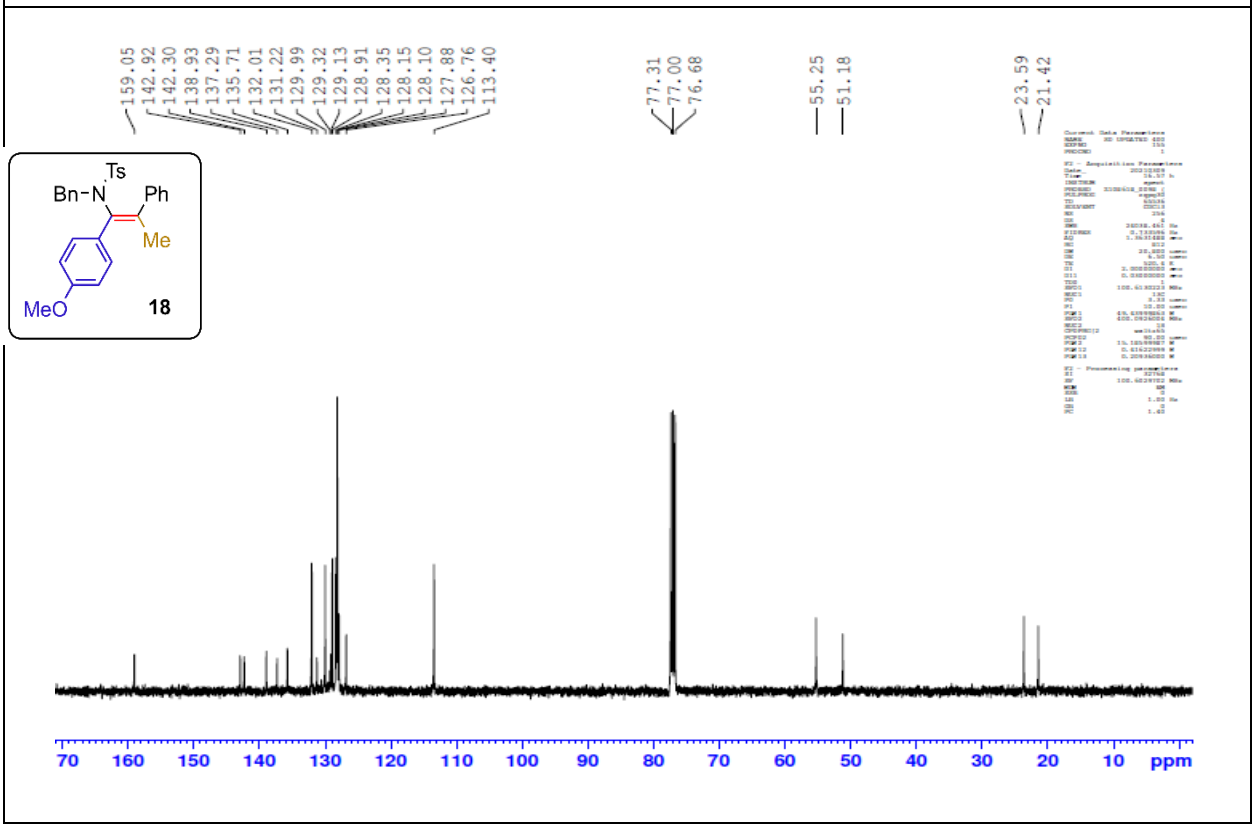
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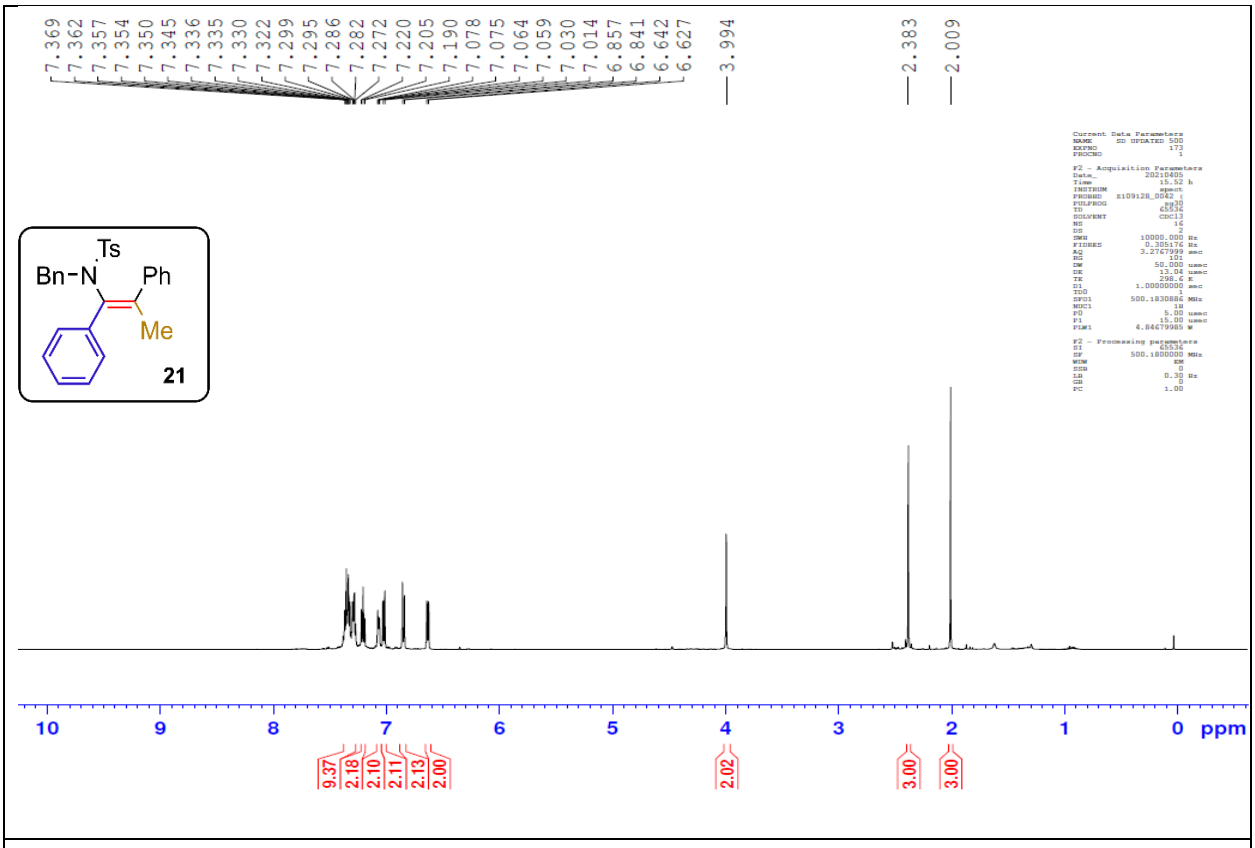
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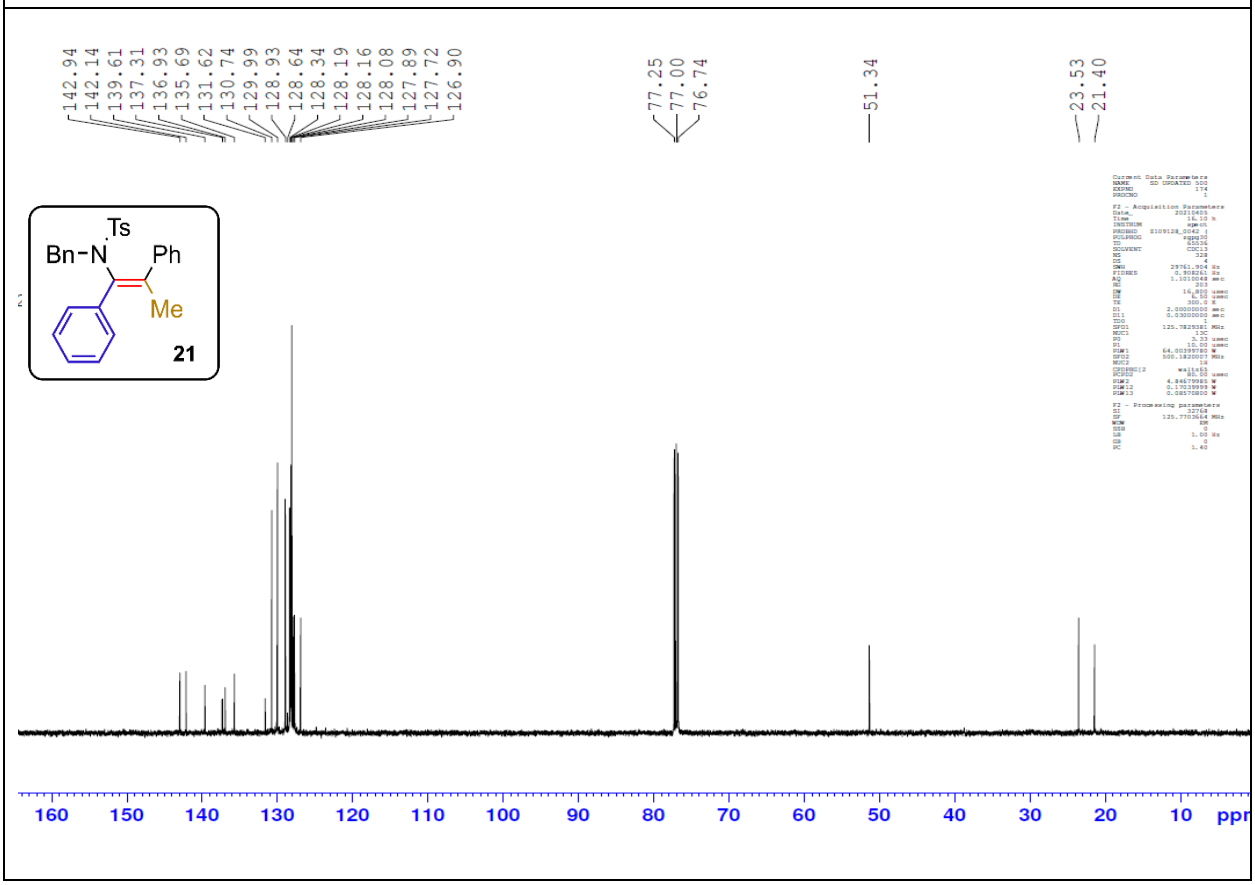
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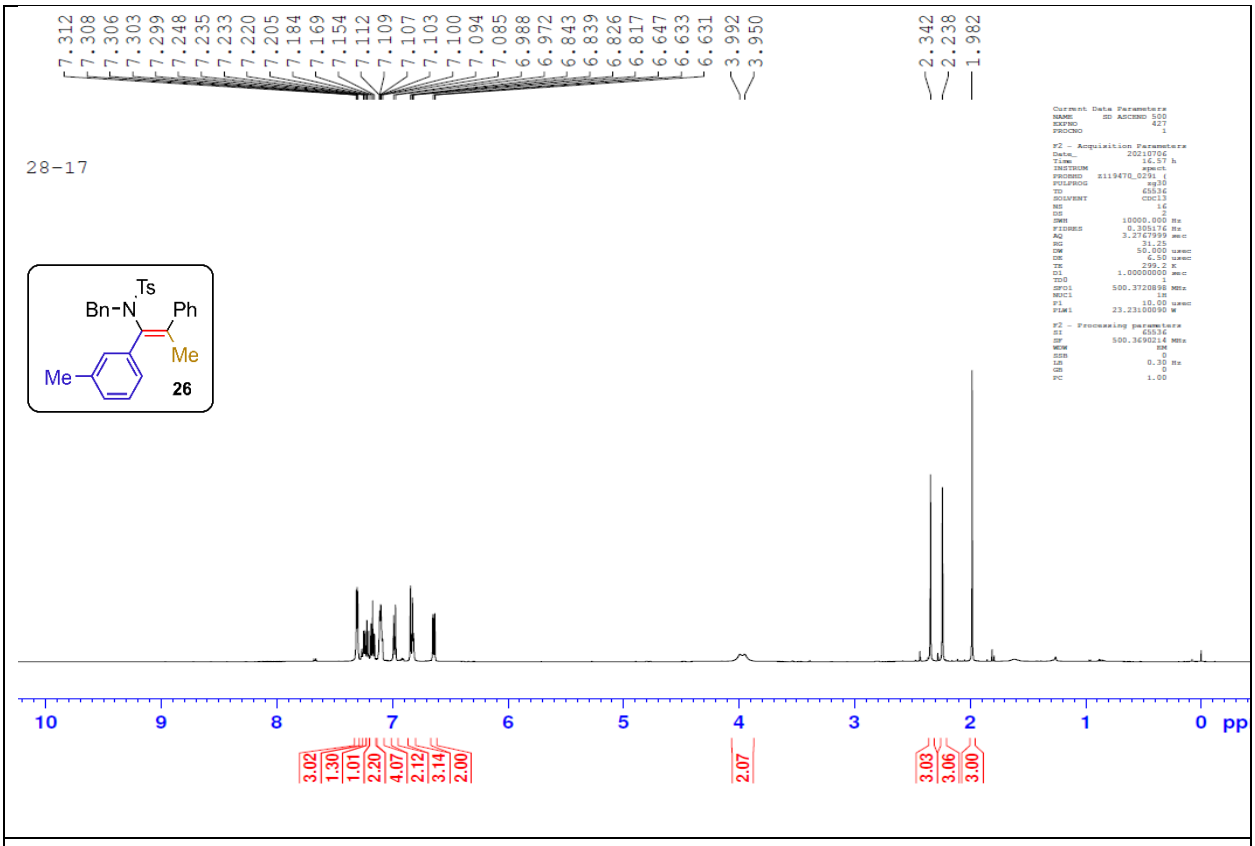
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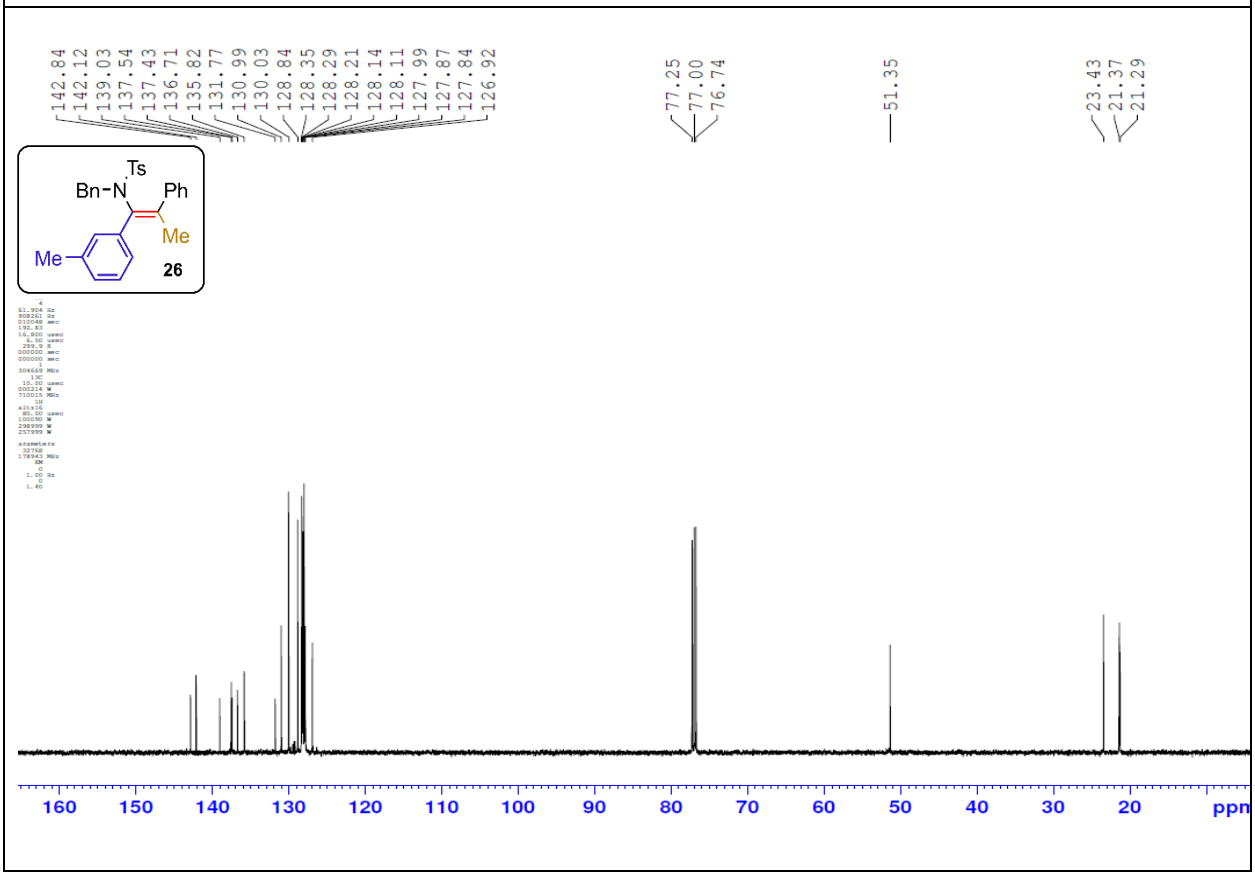
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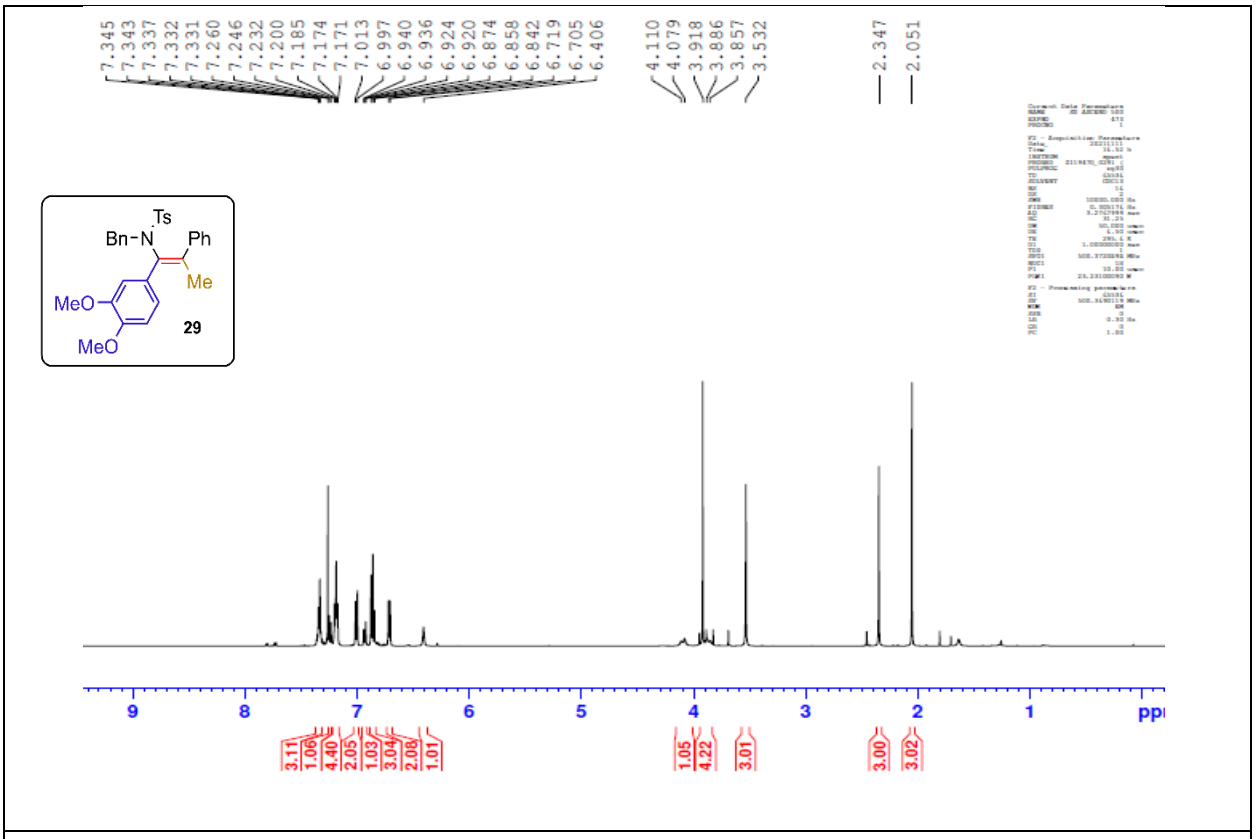
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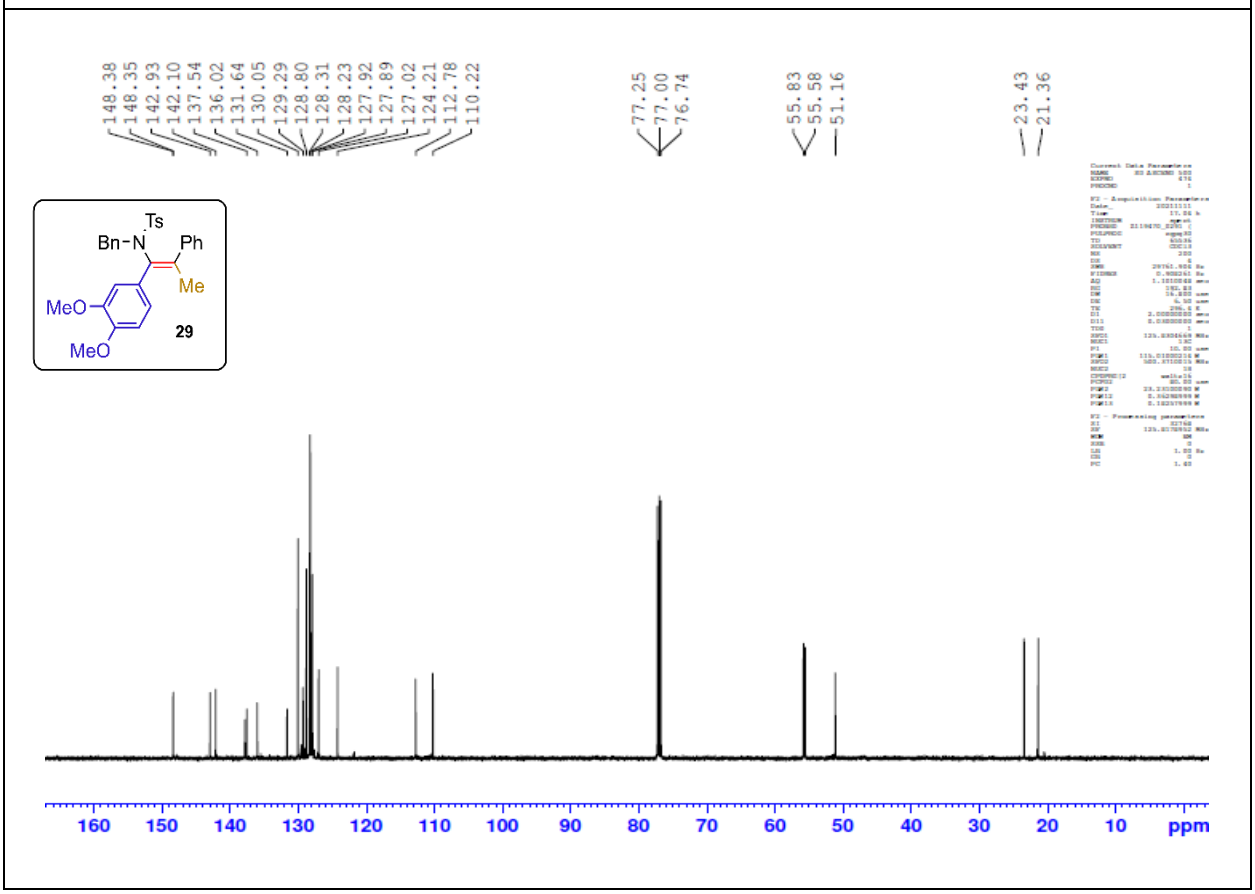
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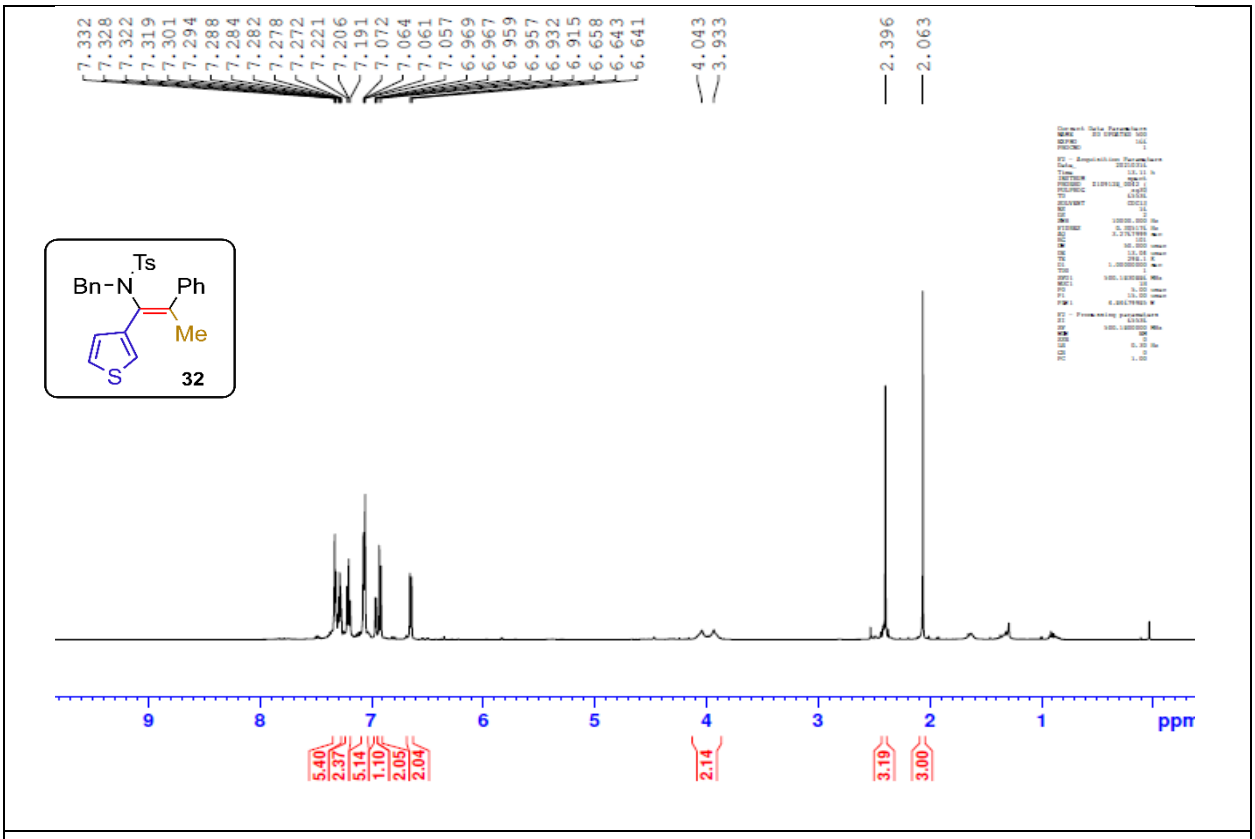
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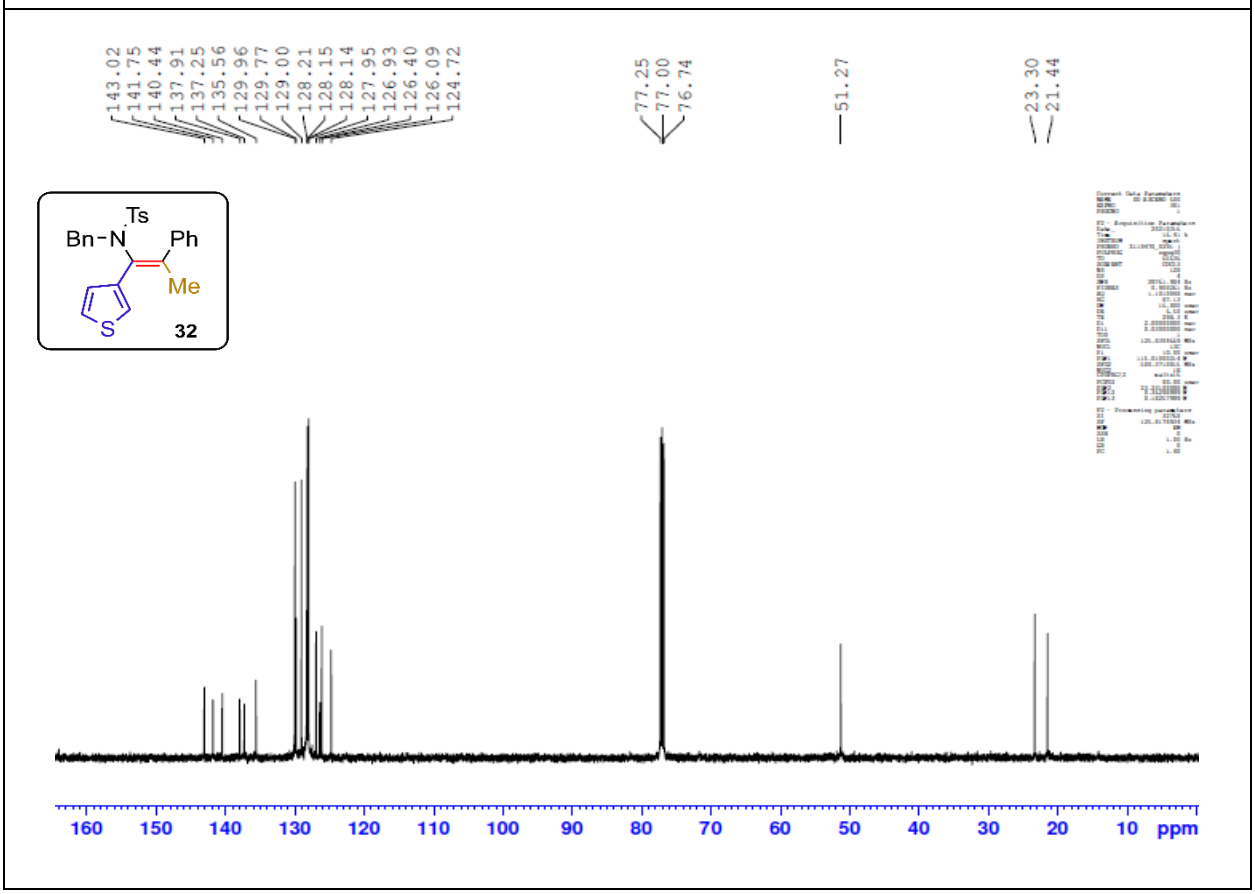
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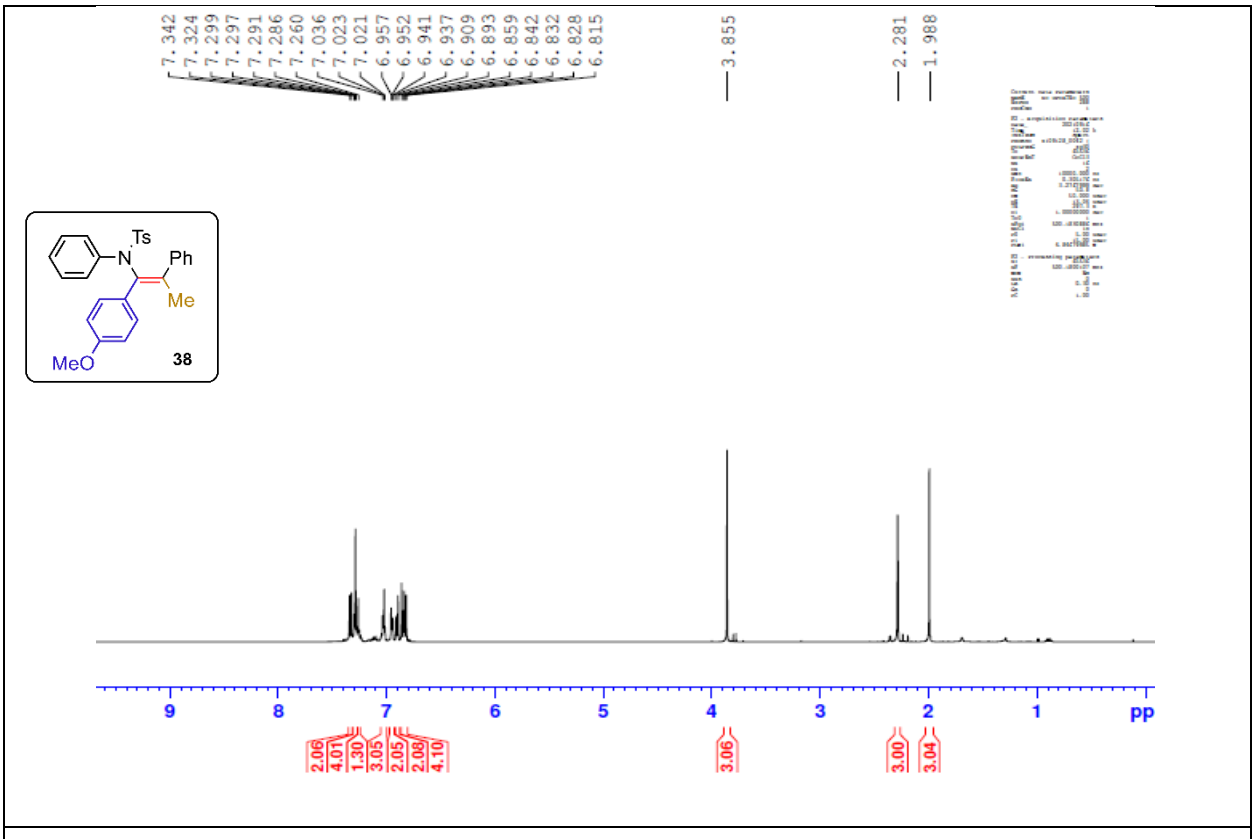
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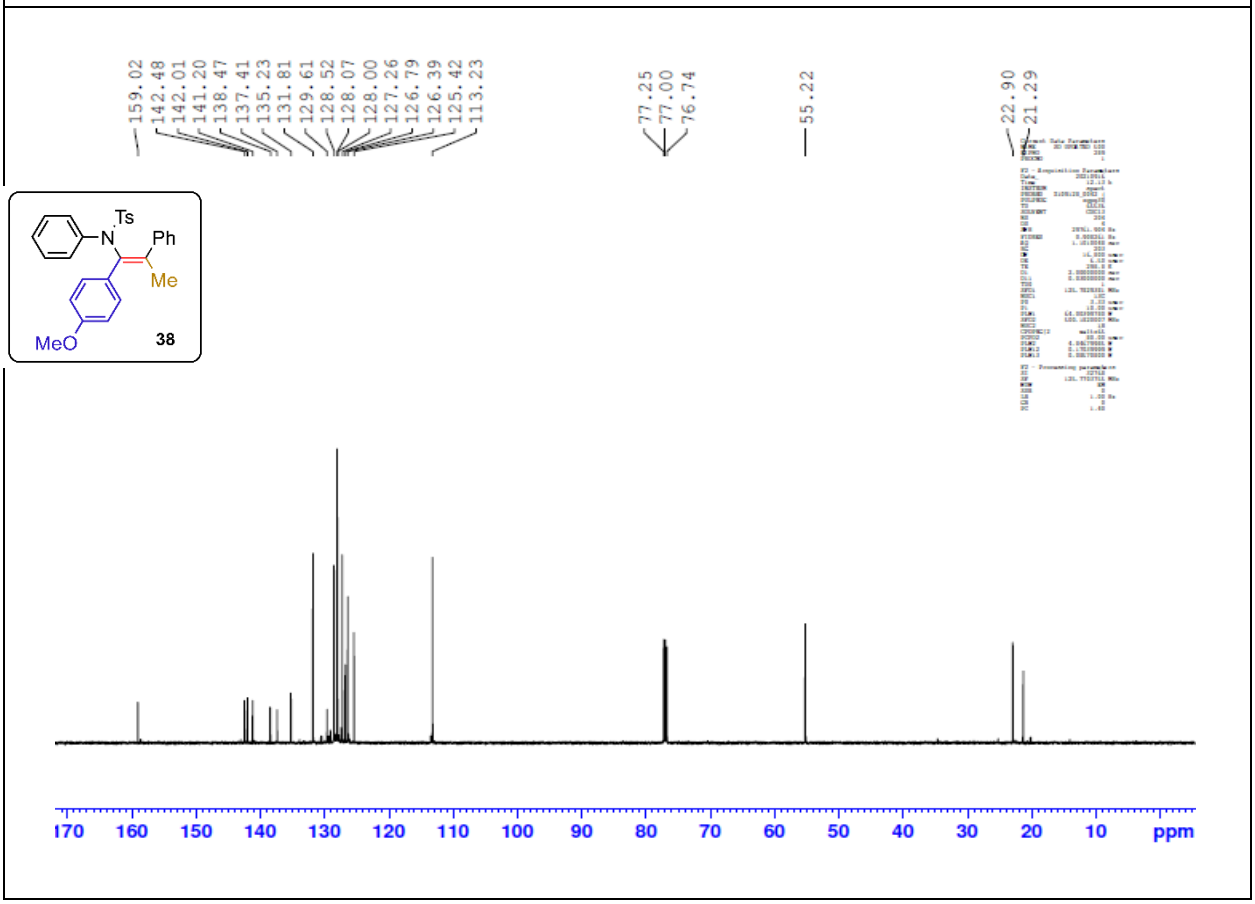
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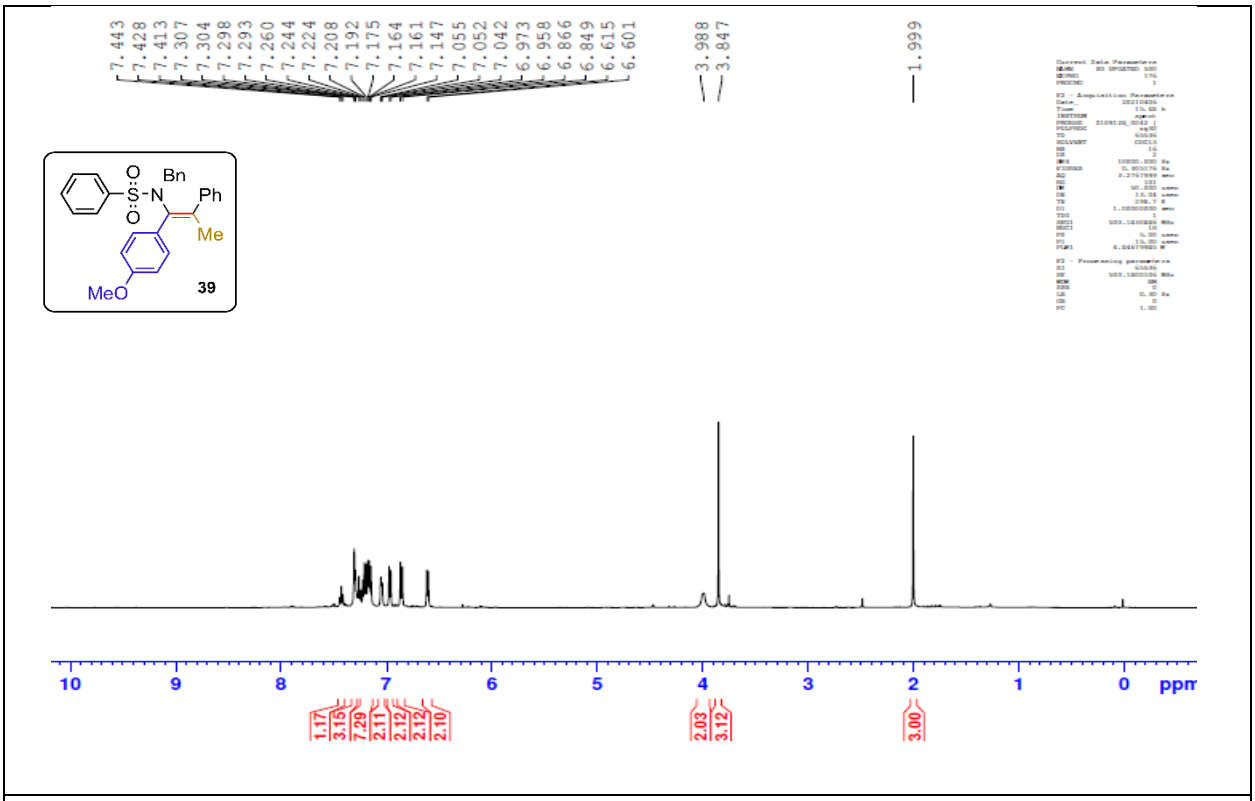
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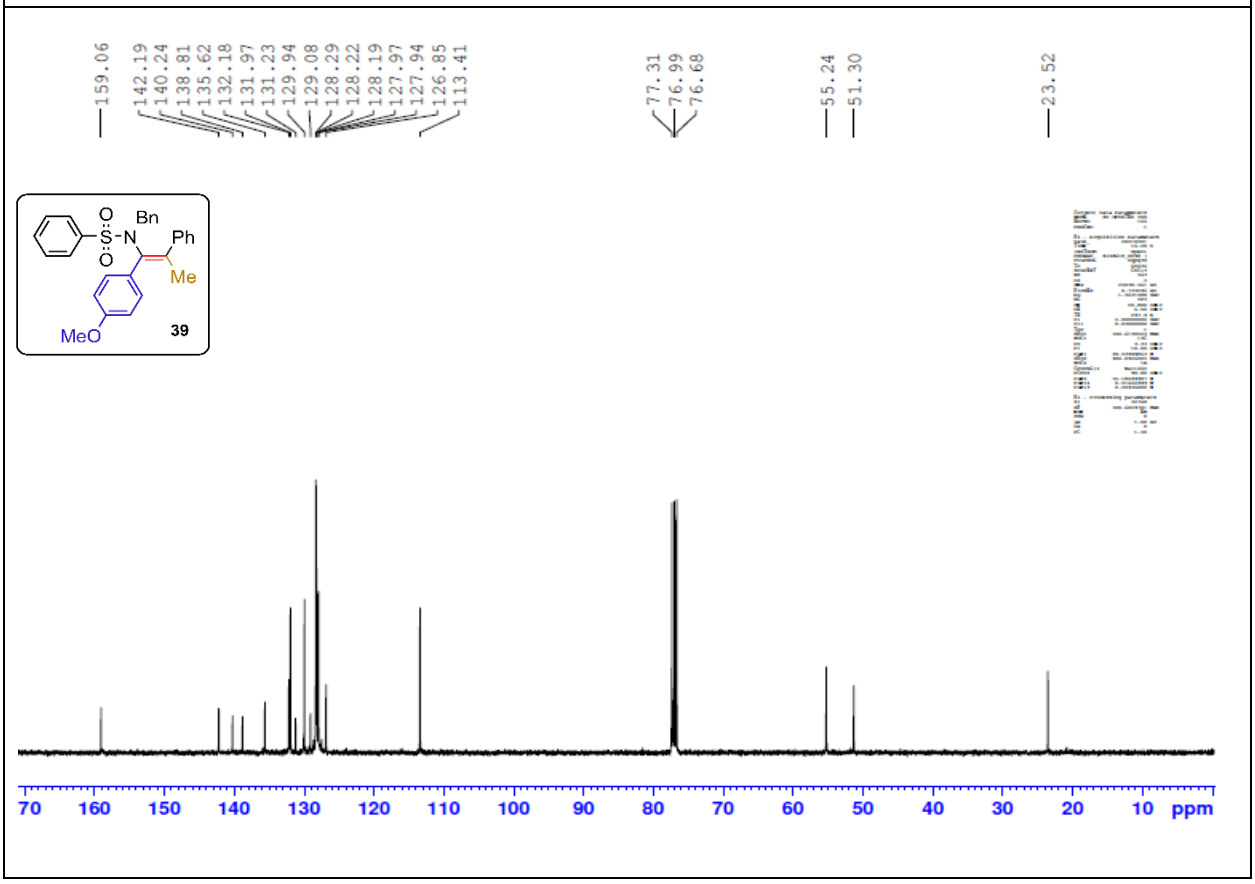
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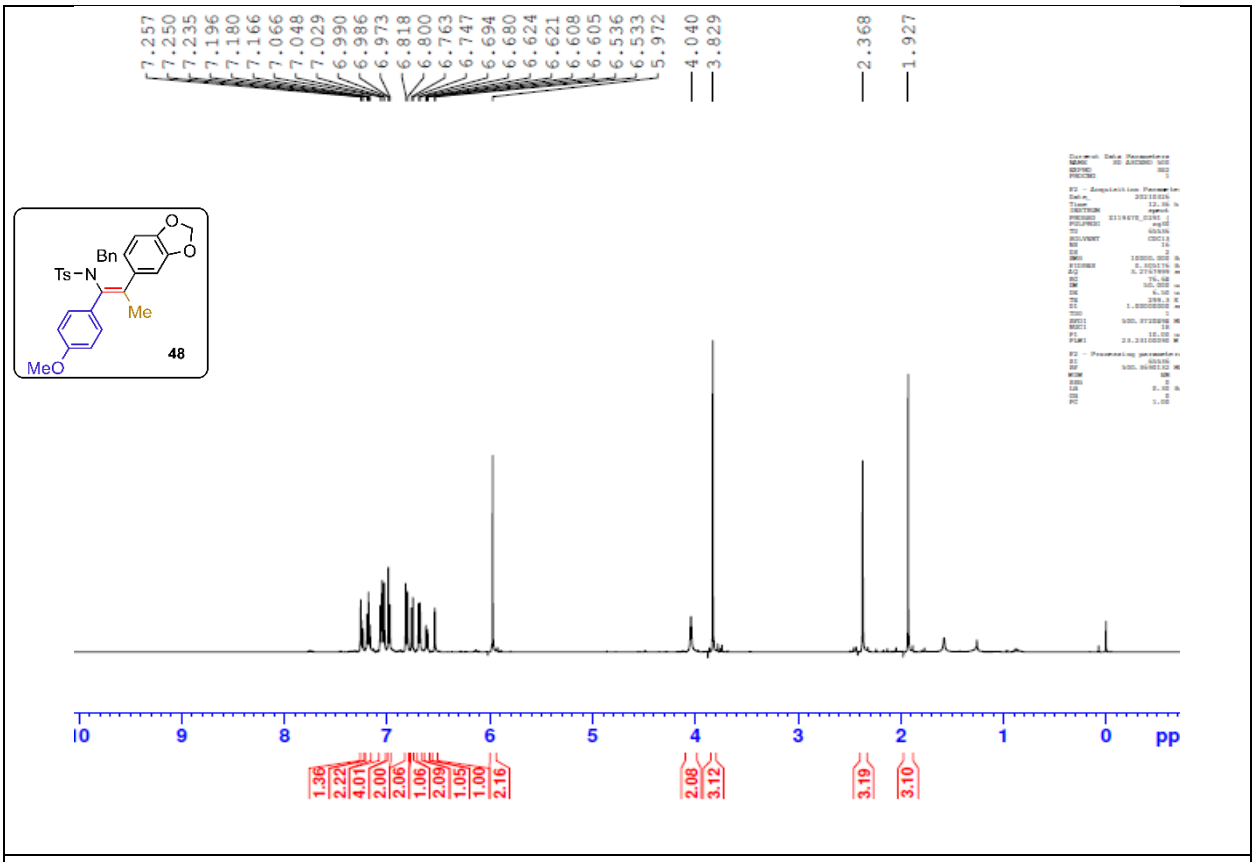
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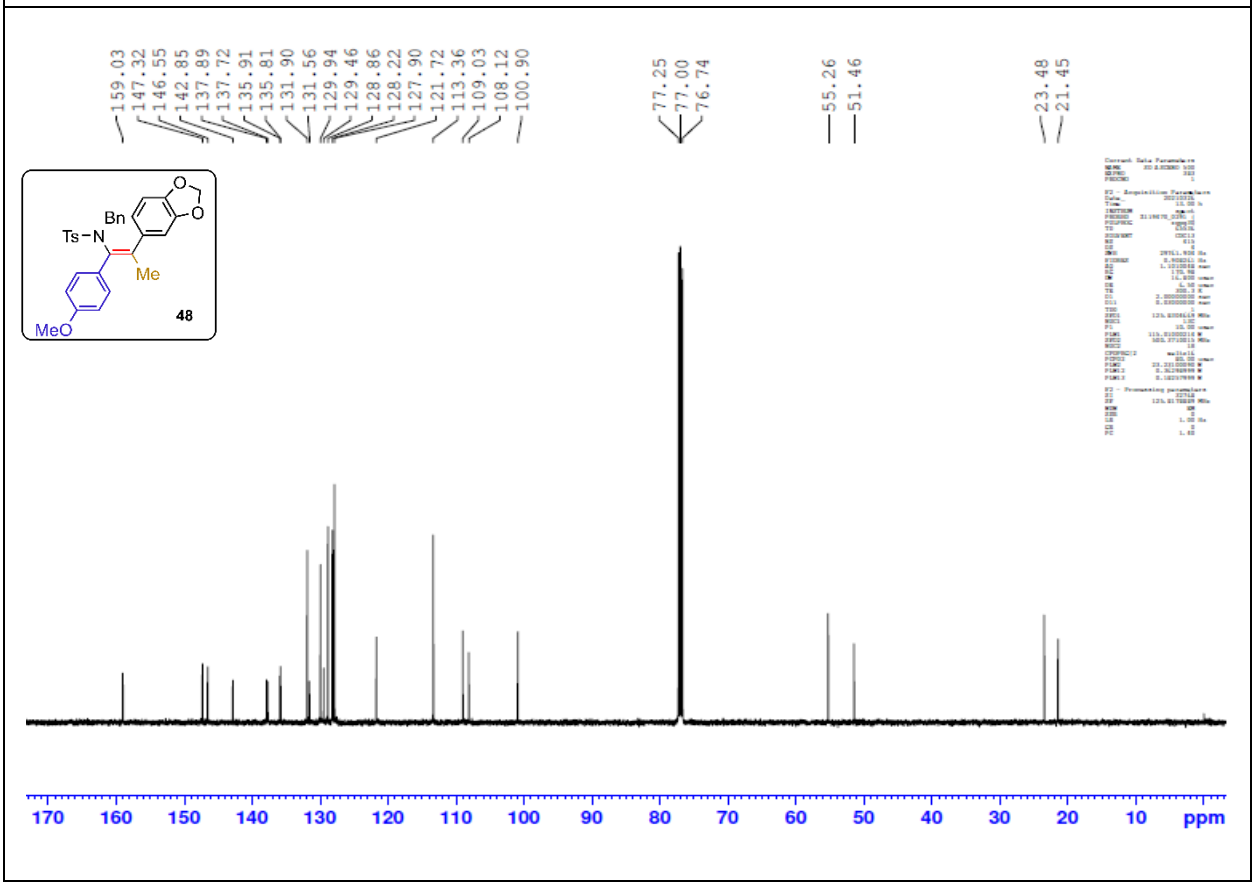
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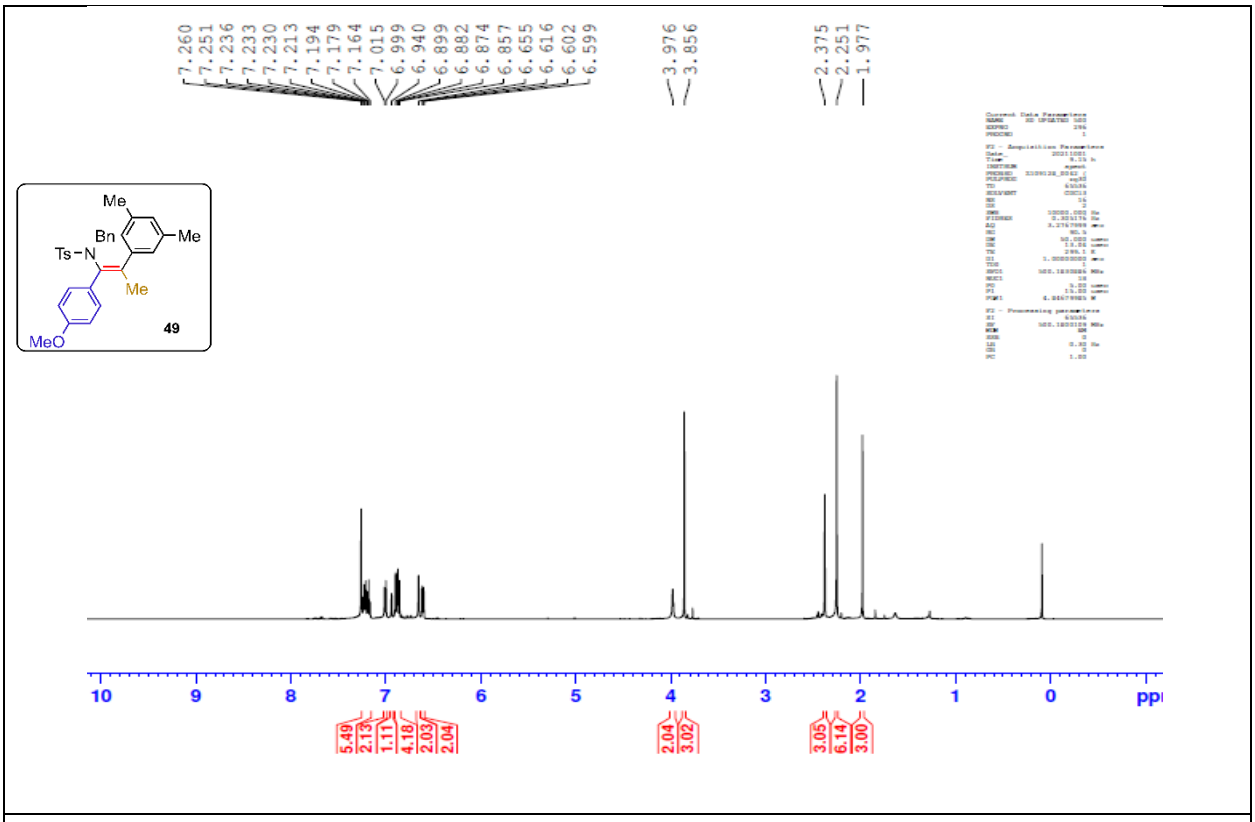
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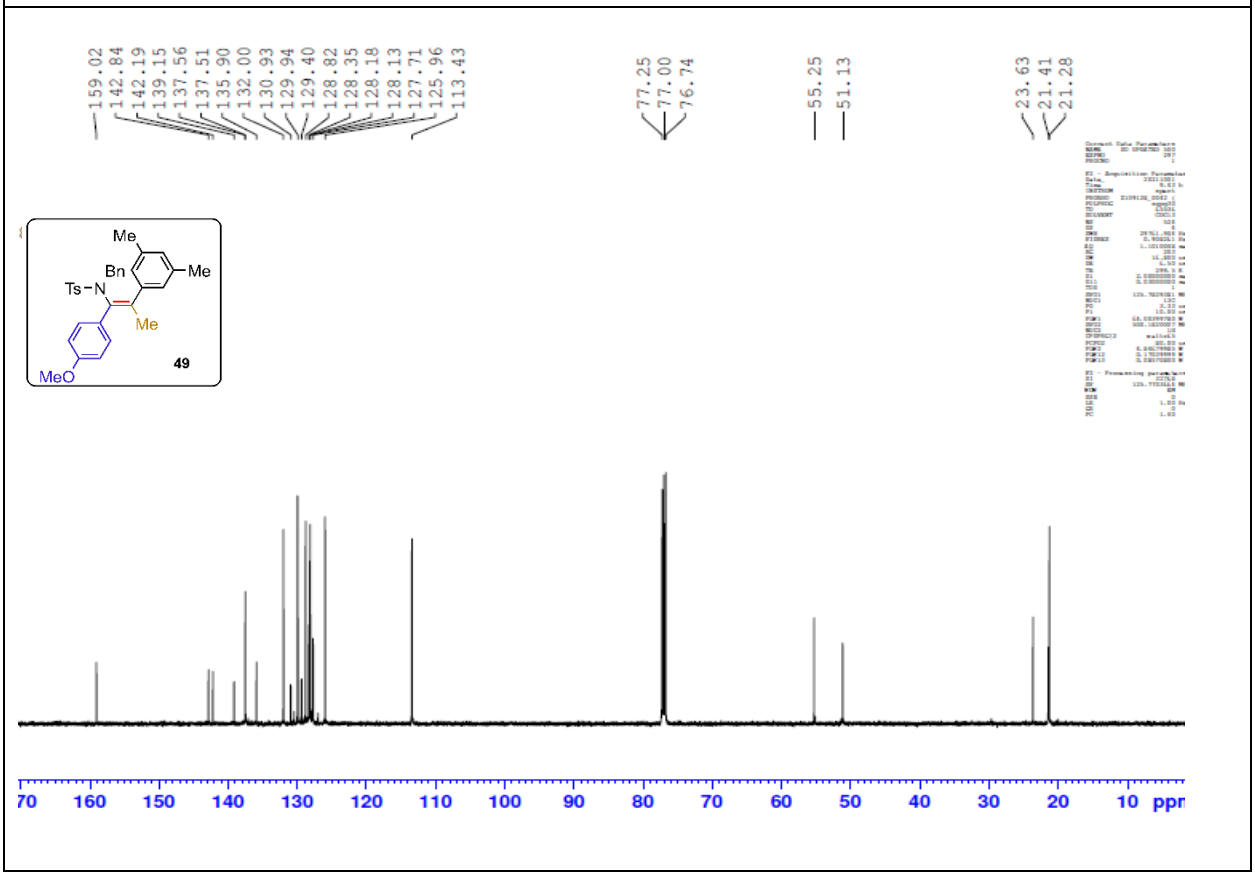
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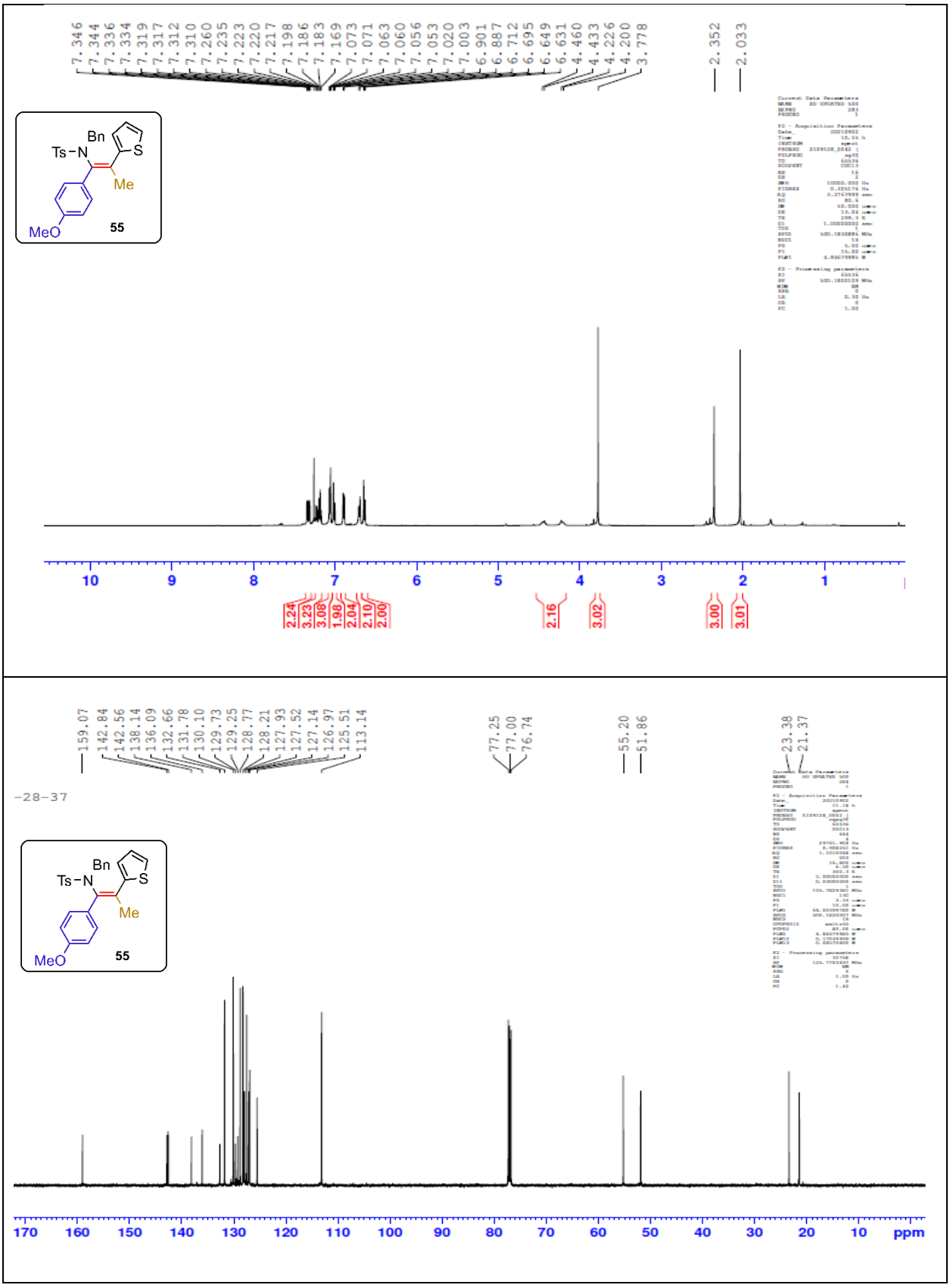
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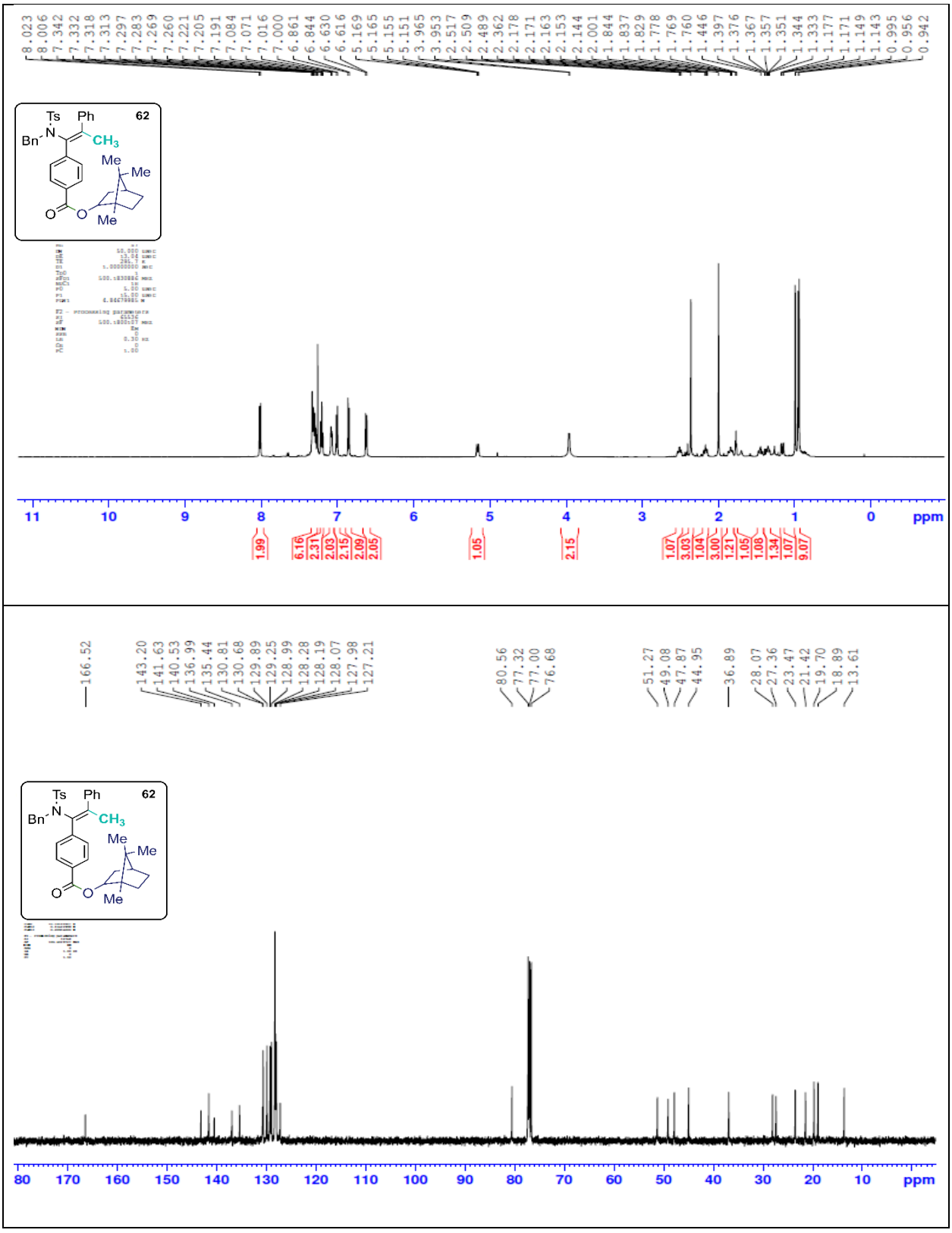
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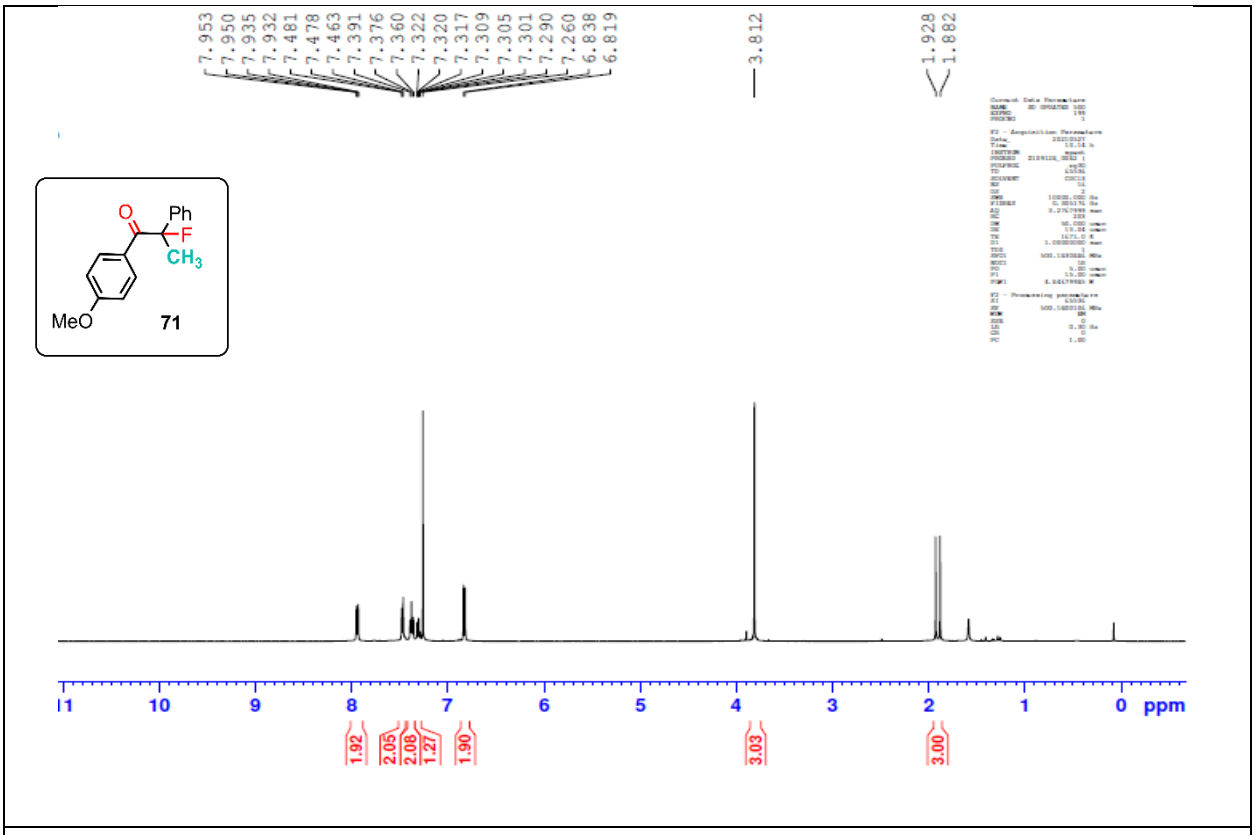
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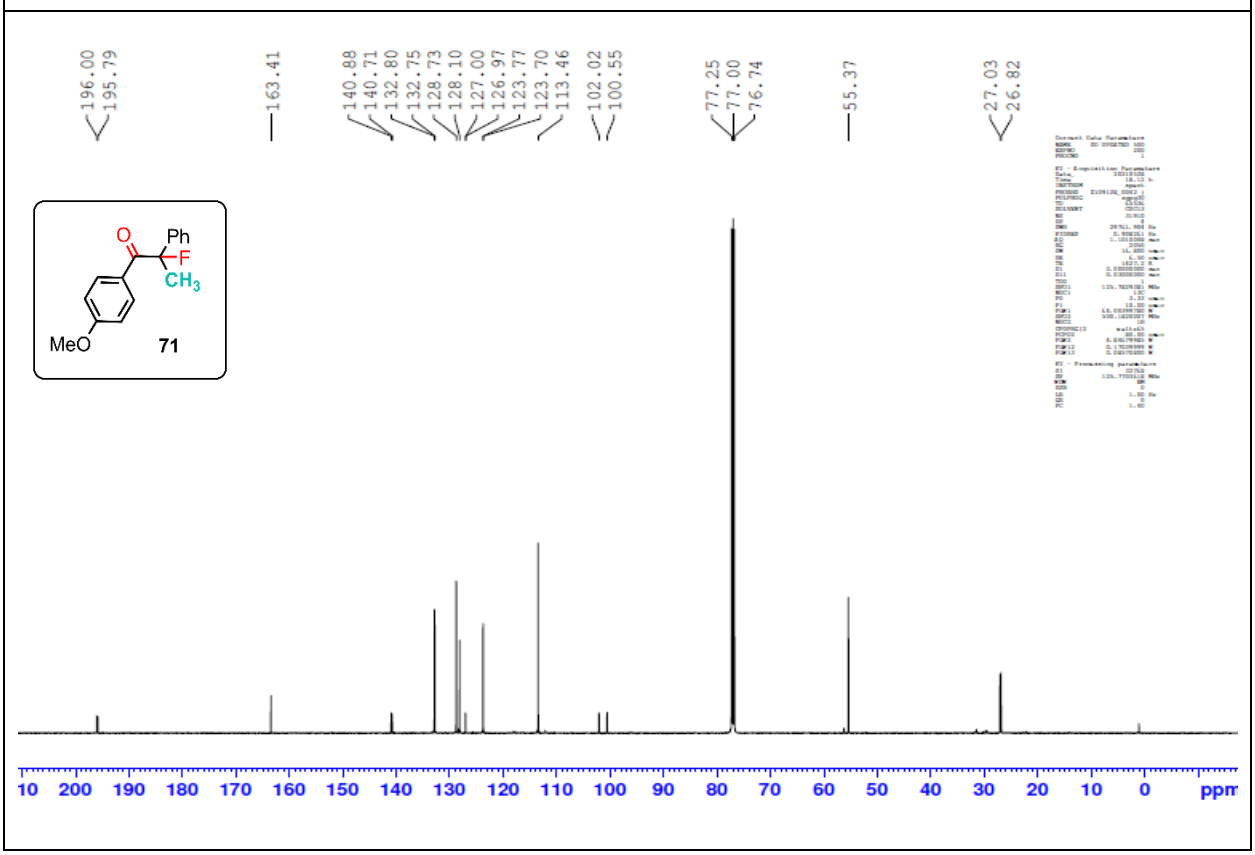
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102.02
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77.25
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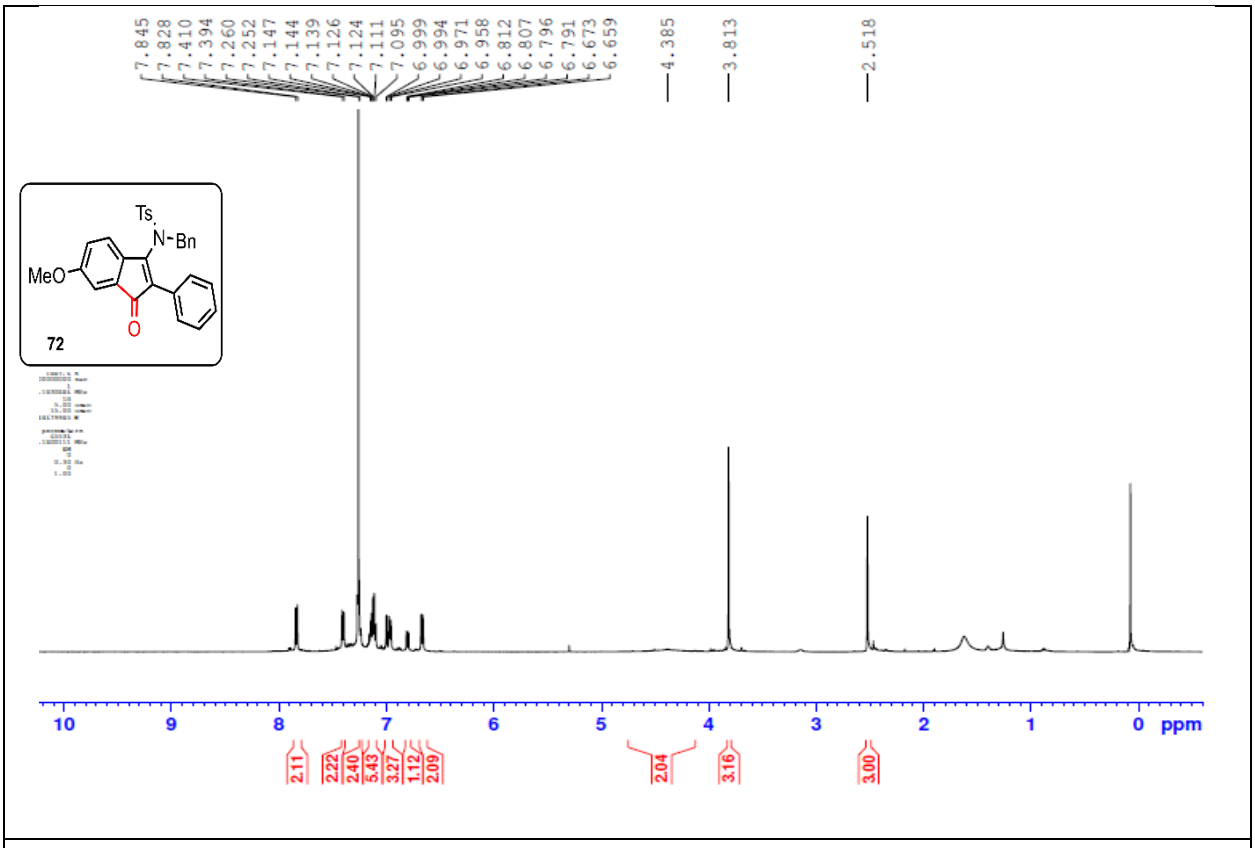
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6.994
6.971
6.958
6.812
6.807
6.796
6.791
6.673
6.659
4.385
3.813
2.518
Ts
N-Bn
MeO
O
72
10 9 8 7 6 5 4 3 2 1 0 ppm
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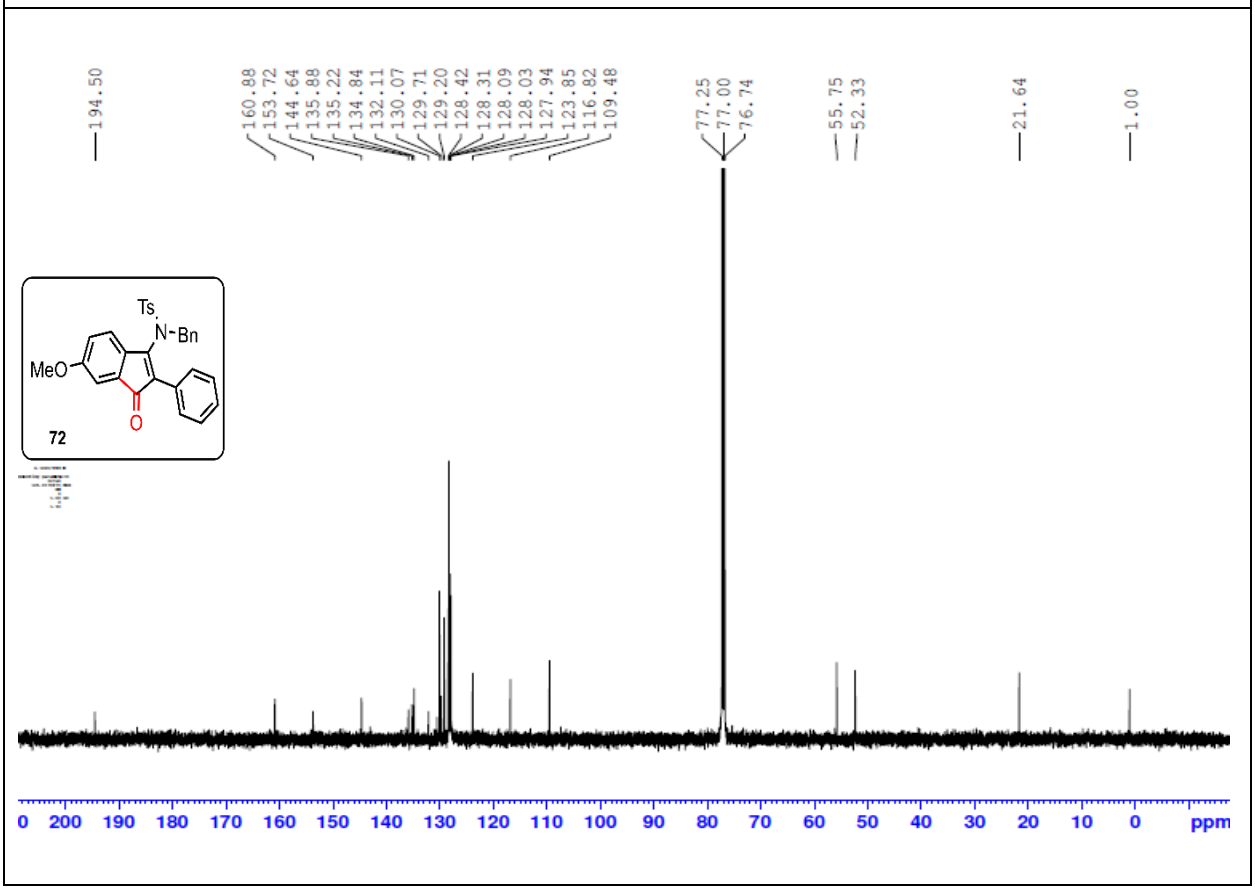
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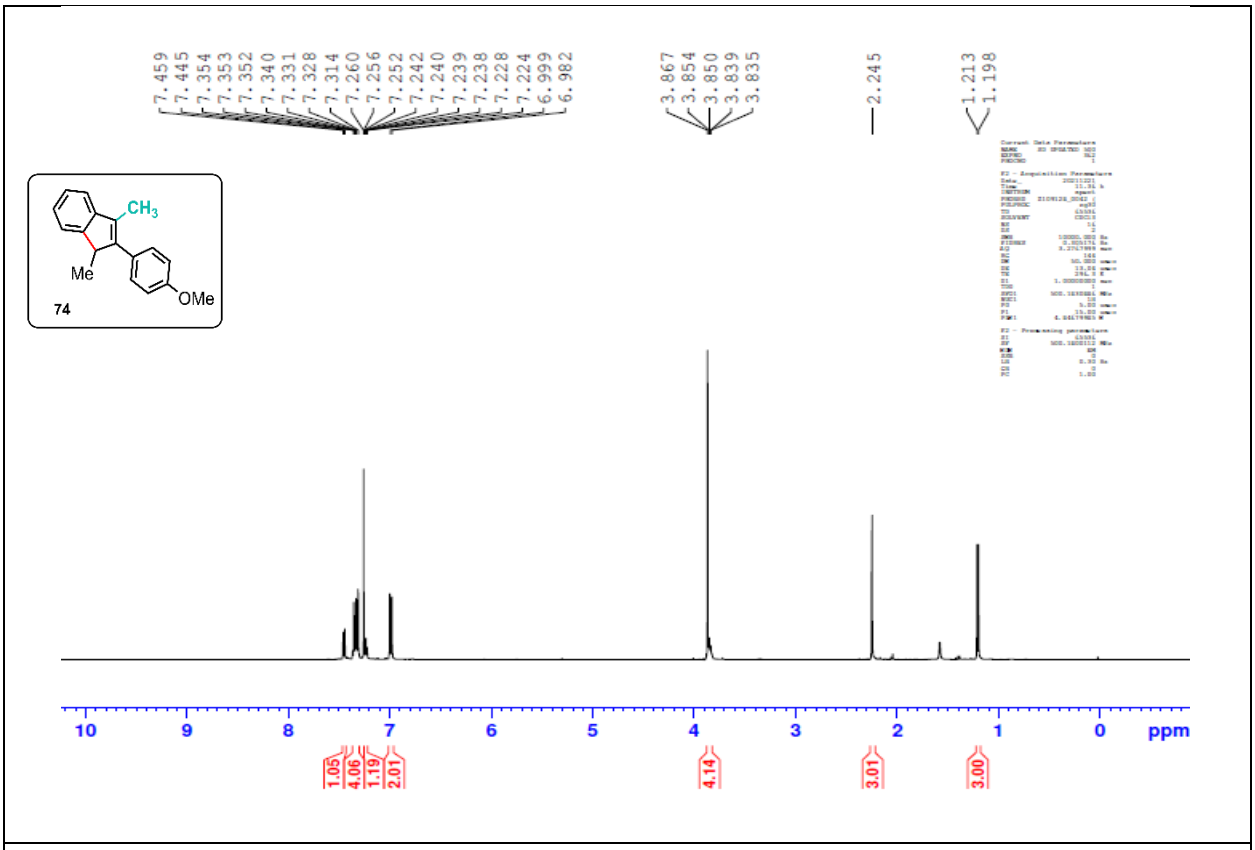
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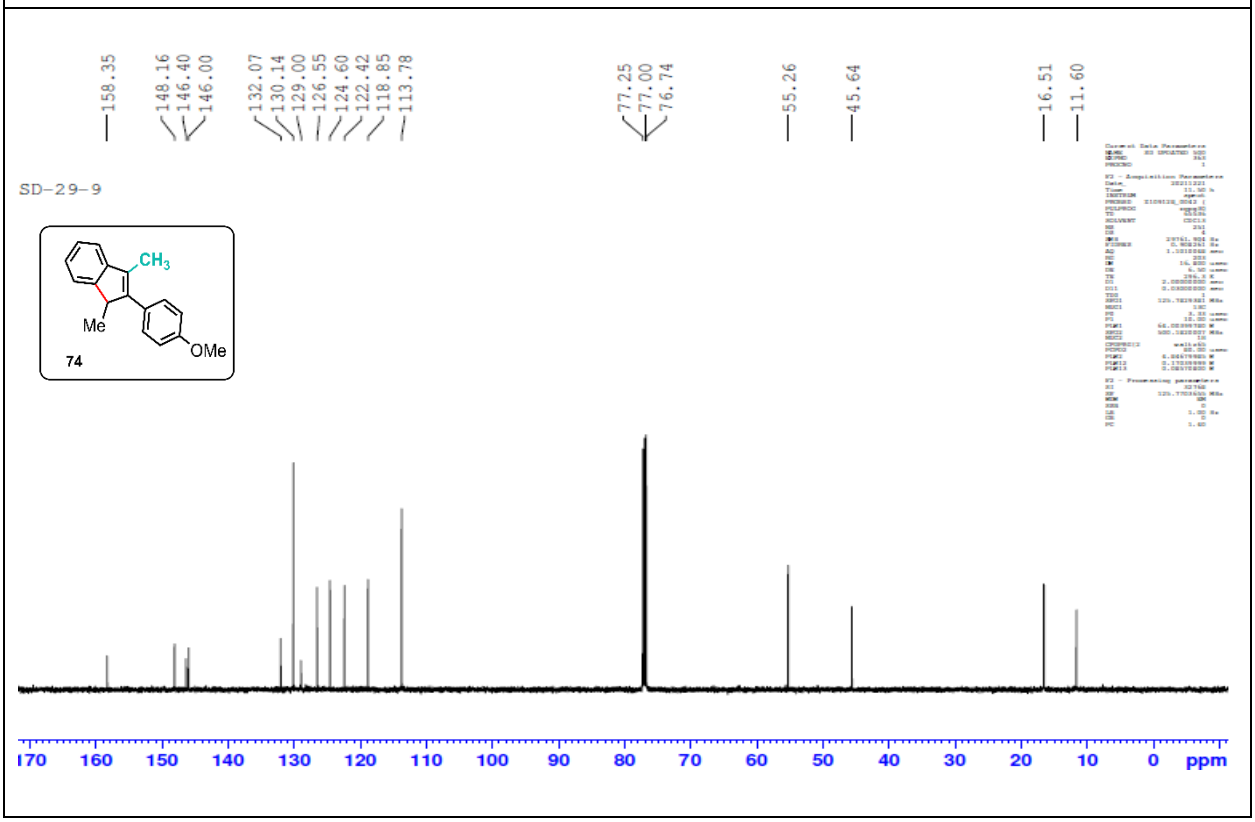
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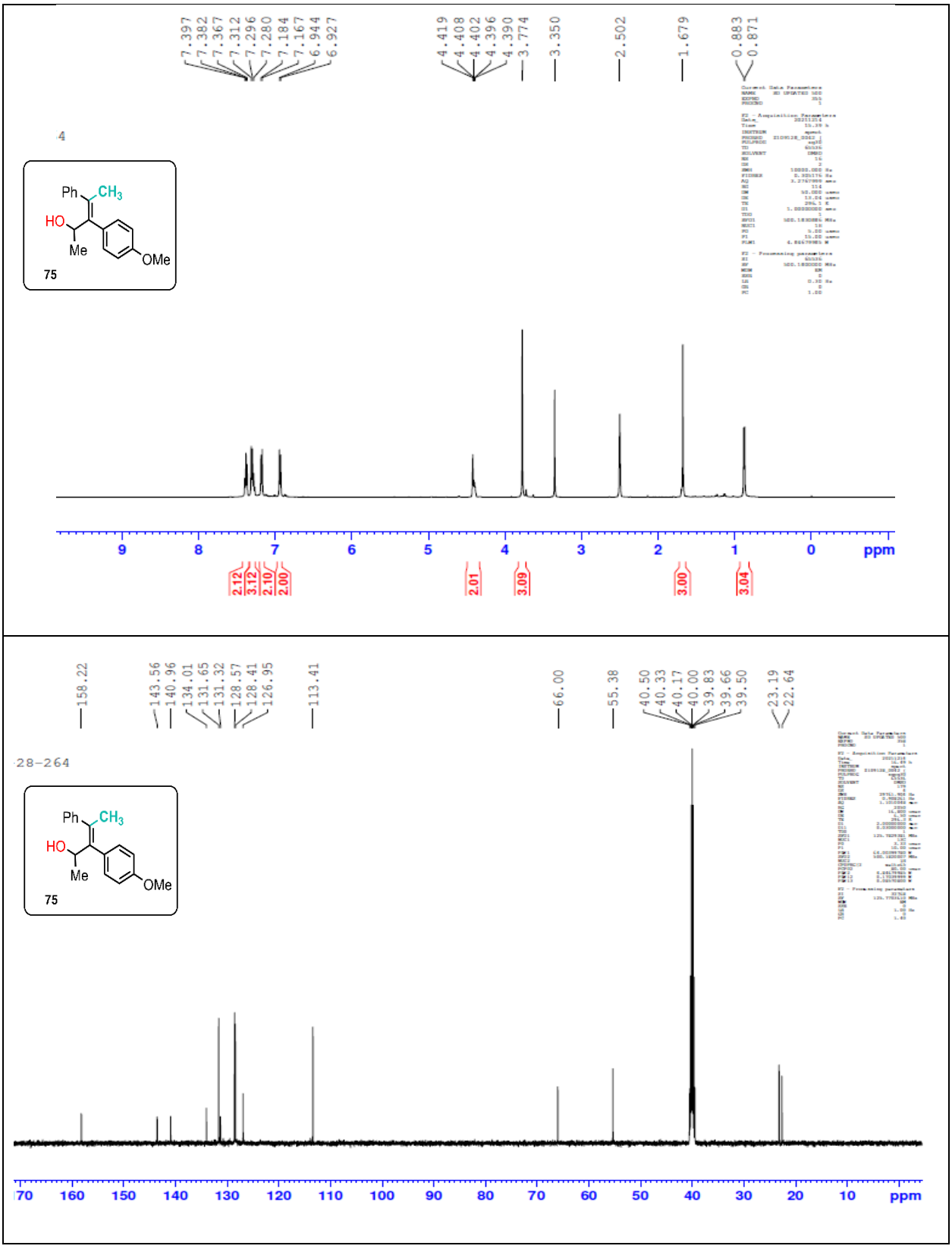
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OMe
75
170
160
150
140
130
120
110
100
90
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30
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List of Publications

14. Cationic Palladium Catalyzed Regioselective Hydro-Arylation of Unsymmetrical Alkynes. *(communicated)*

S. Dutta, M. Sethi,¥ A. Maity,¥ A. Sahoo, V. Gandon, A. K. Sahoo*. (¥equal contribution).

13. Palladium Catalyzed Syn-1,2-ArylMethylation of Internal Alkynes. *(communicated)*

S. Dutta, A. K. Sahoo*.

12. Palladium-Catalyzed Regioselective Arylalkenylation of Ynamides.

R. Vanjari,¥ **S. Dutta**,¥ S. Yang, V. Gandon, A. K. Sahoo*. (¥equal contribution). *Org. Lett.* **2022**, *24*, 1524.

11. Cationic-Palladium Catalyzed Regio- and Stereoselective *syn*-1,2-Dicarbofunctionalization of Unsymmetrical Internal Alkynes.

S. Dutta, S. Shandilya, S. Yang, M. P. Gogoi, V. Gandon, A. K. Sahoo*. *Nature Communications.* **2022**, *13*, 1360.

10. Keteniminium Induced Dienone-Phenol Rearrangement and Intramolecular 6-endo-dig Cyclization Cascade of Yne-Dienone.

R. K. Mallick, **S. Dutta**, M. P. Gogoi, A. K. Sahoo*. *Hevetica Chemica Acta.* **2022**, *105*, e202100198.

9. Gold-Catalyzed Transformation of Ynamides.

S. Shandilya,¥ M. P. Gogoi,¥ **S. Dutta**,¥ A. K. Sahoo*. (¥equal contribution). *Chem. Rec.* **2021**, *21*, 4123.

8. Yb(III)-catalysed syn-thioallylation of ynamides.

M. P. Gogoi, R. Vanjari, B. Prabagar, S. Yang, **S. Dutta**, R. K. Mallick, V. Gandon, A. K. Sahoo*. *Chem. Commun.*, **2021**, *57*, 7521.

7. Keteniminium Driven Umpolung Difunctionalization of Ynamides.

S. Dutta, S. Yang, R. Vanjari, R. K. Mallick, V. Gandon, A. K. Sahoo*. *Angew. Chem., Int. Ed.* **2020**, *59,* 10785.

6. An Unconventional Sulfur-to-Selenium-to-Carbon Radical Transfer: Chemo-and Regioselective Cyclization of Yne-Ynamides.

S. Dutta, B. Prabagar, R. Vanjari, V. Gandon*, A. K. Sahoo*. *Green Chem.,* **2020**, *22,* 1113.

5. Ring Expansion and 1,2-Migration Cascade of Benzisoxazoles with Ynamides: Experimental and Theoretical Studies.

R. Vanjari, **S. Dutta**, B. Prabagar, V. Gandon, A. K. Sahoo* *Chem. Asian J.* **2019,** *14,* 4282.

4. Thioarylative Radical Cyclization of Yne-Dienone.

R. K. Mallick, **S. Dutta**, R. Vanjari, A. Voituriez, A. K. Sahoo* *J. Org. Chem.* **2019,** *84,* 10509.

3. Gold Catalyzed Regioselective Tetradehydro Diels-Alder Reaction of Yne-Ynamides: Access to 2,3-Dihydrobenzo[f]indoles.

B. Prabagar, **S. Dutta**, V. Gandon*, A. K. Sahoo*. *Asian J. Org. Chem.* **2019,** *8*, 1128.

2. Alkyne Versus Ynamide Reactivity: Regioselective Radical Cyclization of Yne-Ynamides.

S. Dutta, R. K. Mallick, R. Prasad, V. Gandon*, A. K. Sahoo*. *Angew. Chem. Int. Ed.* ***2019****, 131,* 2311.

1. Gold-Catalyzed *syn*-1,2-Difunctionalization of Ynamides via Nitrile Activation.

R. Vanjari, **S. Dutta**, M. P. Gogoi, V. Gandon*, A. K. Sahoo*. *Org. Lett.* **2018**, *20*, 8077.

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Palladium-Catalyzed Regioselective Arylalkenylation of Ynamides

Rajeshwer Vanjari,[‖] Shubham Dutta,[‖] Shengwen Yang, Vincent Gandon,* and Akhila K. Sahoo*

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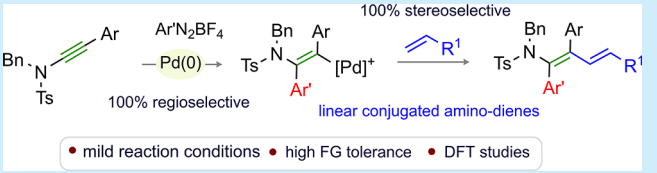
ABSTRACT: A cationic palladium-catalyzed arylalkenylation of ynamides is presented. The putative keteniminium arylpalladium intermediate likely dictates the regioselective carbopalladation of the ynamide to form a vinylpalladium species. The capture of this complex by the olefin yields linear conjugated *β*-alkenyl amino-dienes (especially with *trans* selectivity). The transformation features a broad scope with labile functional group tolerance and makes 42 unusual molecular scaffolds with structural diversity. DFT studies provide valuable insights into the reaction mechanism.



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π-Conjugated olefins are versatile synthons in organic chemistry and may also be found in active pharmaceutical ingredients, agrochemicals, and electron-transport materials.[1] While the synthesis of dienes through three-component arylative dicarbofunctionalization of alkynes is a proven strategy,[2] direct access to aminodienes[3] is not a thoroughly explored domain.[4−6] By analogy, the use of N-substituted alkynes (i.e., ynamides)[7] comes to mind. To date, however, direct olefination of these inherently polarizable compounds has been less explored than that of simple alkynes.[7,8] The known reactions allowing direct alkenylation of ynamides primarily deliver *α*-alkenylated enamides.[9] For instance, Pd(0)-catalyzed Heck coupling of ynamides with activated *α,β*-unsaturated amides produces hydroalkenylation products by the introduction of an alkenyl group at the *α*-position (next to the nitrogen) of the ynamide (Figure 1a).[4] Likewise, Pd(II)-catalyzed cross-coupling of ynamides with alkenylboronic acids provides *α*-alkenylated enamides (Figure 1a).[5] An elegant demonstration of chelation-assisted Rh-catalyzed *syn*-1,2-difunctionalization of oxazolidinone-derived ynamides with dialkylzinc and iodoalkenyl reagents leads to *β*-alkyl-*α*-alkenyl species (Figure 1b).[6] *To date, no strategy enables the formation of α-aryl-β-alkenyl enamides by the direct introduction of two distinct C(sp²) functionalities on ynamides.* In contrast with the known *α*-alkenylation of ynamides that explicitly makes branched aminodienes, devising a regioselective *β*-alkenylation of ynamides is certainly a worthwhile endeavor. This process could lead to linear *π*-conjugated aminodienes (Figure 1c). Our interest in the development of keteniminium-driven dicarbofunctionalization[10a] inspired us to develop an arylalkenylation of electron-rich ynamides (Figure 1c). The transformation relies on *β*-nucleophilic attack of ynamide **I** to a cationic Pd(II) species, generated in situ by the oxidative addition of an aryl diazonium salt[10b] with Pd(0), to form keteniminium species **II**. Next, *syn*-1,3-aryl migration from the Pd center to the *α*-carbon of **II** forms cationic vinylpalladium species **III**. Finally, olefin insertion into the Pd−C bond of **III**

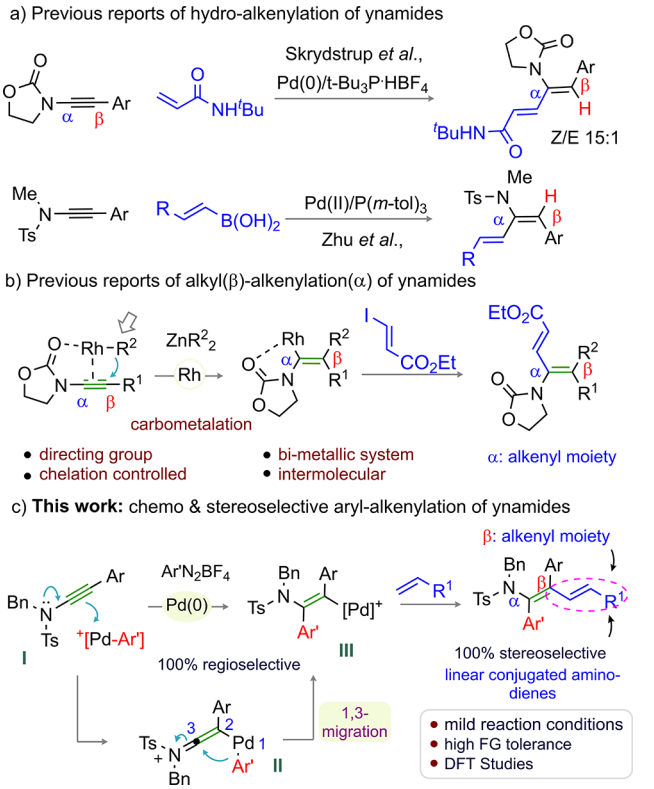

Figure 1. (Aryl)alkenylation of ynamides: (a, b) background and (c) this work.

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Cationic-palladium catalyzed regio- and stereoselective *syn*-1,2-dicarbofunctionalization of unsymmetrical internal alkynes

Shubham Dutta[1], Shashank Shandilya[1], Shengwen Yang[2], Manash Protim Gogoi[1], Vincent Gandon[2,3]✉ & Akhila K. Sahoo[1]✉

π-Extended tetrasubstituted olefins are widely found motifs in natural products, leading drugs, and agrochemicals. Thus, development of modular strategies for the synthesis of complex all-carbon-substituted olefins always draws attention. The difunctionalization of unsymmetrical alkynes is an attractive approach but it has remained faced with regioselectivity issues. Here we report the discovery of a regio- and stereoselective *syn*-1,2-dicarbofunctionalization of unsymmetrical internal alkynes. A cationic Pd-catalyzed three-component coupling of aryl diazonium salts, aryl boronic acids (or olefins) and yne-acetates enables access to all-carbon substituted unsymmetrical olefins. The transformation features broad scope with labile functional group tolerance, building broad chemical space of structural diversity (94 molecules). The value of this synthetic method is demonstrated by the direct transformation of natural products and drug candidates containing yne-acetates, to enable highly substituted structurally complex allyl acetate analogues of biologically important compounds. Synthetic versatility of the carboxylate bearing highly substituted olefins is also presented. The reaction outcome is attributed to the in situ formation of stabilized cationic aryl-Pd species, which regulates regioselective aryl-palladation of unsymmetrical yne-acetates. Control experiments reveal the synergy between the carboxylate protecting group and the cationic Pd-intermediate in the regioselectivity and reaction productivity; density functional theory (DFT) studies rationalize the selectivity of the reaction.

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Synthetic Methods

Keteniminium-Driven Umpolung Difunctionalization of Ynamides

Shubham Dutta, Shengwen Yang[+], Rajeshwer Vanjari[+], Rajendra K. Mallick, Vincent Gandon, and Akhila K. Sahoo**

Abstract: *A three-component Pd-catalyzed coupling of ynamides, aryl diazonium salts, and aryl boronic acids for the synthesis of novel triaryl-substituted enamides is described. This transformation represents the first example of an umpolung regioselective unsymmetrical syn-1,2-diarylation/aryl-olefination of ynamides. The aryl moieties of the diazonium salt (electrophile) and boronic acid (nucleophile) are explicitly incorporated in the electrophilic α- and nucleophilic β-position, respectively, of the ynamide, resulting in a single isomer of the N-bearing tetrasubstituted olefin. The scope is broad (68 examples), showing excellent functional-group tolerance. DFT calculations substantiate the rationale of the mechanistic cycle and the regioselectivity. The chemoselectivity and synthetic potential of the enamide products were also studied.*

Ynamide, a versatile N-containing alkyne synthon, has had a profound impact in uncovering novel synthetic methods. It has also been used for the synthesis of complex molecular frameworks.[1] In this regard, functionalization of the electron-rich polarizable N-bearing alkyne (i.e. ynamide; **I**) by trapping of a nucleophile and an electrophile at the α- and β-positions, respectively, of the keteniminium species **II** provides the substituted olefins **III** (Figure 1a, path-I).[2] However, on a conceptual note, umpolung difunctionalization of ynamides with electrophiles and nucleophiles at the α- and β-positions, respectively, is significantly challenging although exceedingly valuable (Figure 1a, path-II). Such umpolung difunctionalization of ynamides is confined to: i) a strain-controlled intramolecular trapping of a nucleophile (Figure 1b, path-I),[3] or ii) a chelation-driven carbometalation and functionalization sequence that primarily requires a bimetallic system (Figure 1b, path-II).[4] In these approaches, the attack of the nucleophile is pivotal in making such strategies synthetically viable. In contrast, the development of a nondirected multicomponent umpolung difunctionalization of ynamides initiated by the attack of the electrophile is undoubtedly a worthwhile endeavor.

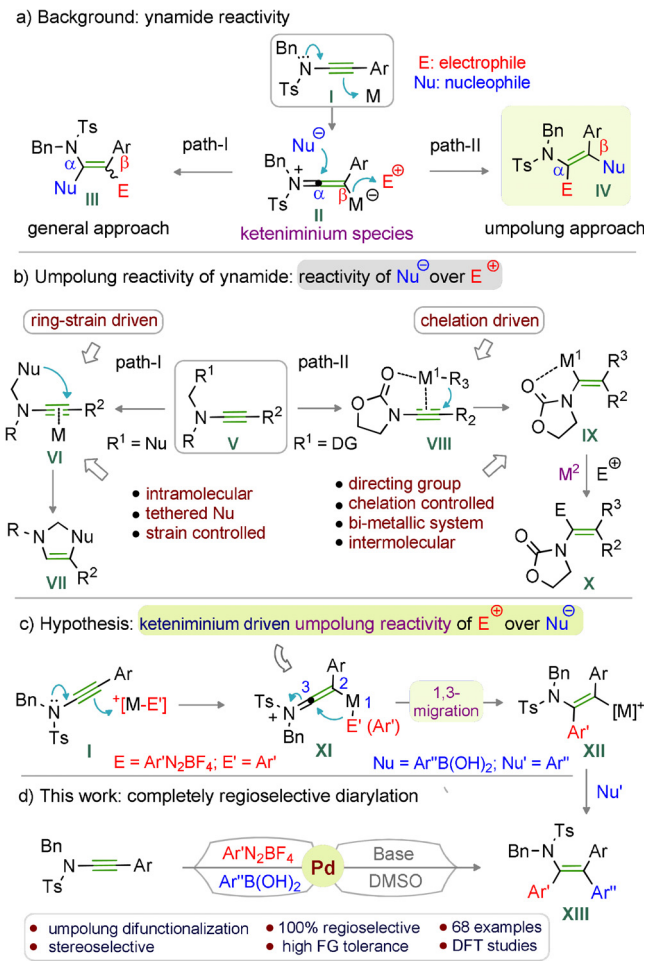

Figure 1. a) Background. b) Umpolung reactivity of ynamides. c) Hypothesis. d) This work: regioselective diarylation of ynamides.

Thus, electrophilic activation of **I** with an aryl metal complex (generated in situ from an electrophile $Ar^1N_2BF_4$ [E][5] with a low-valent transition-metal species [that is, Pd^0]) into the keteniminium species **XI**, regioselective 1,3-aryl (E′) migration to the α-position of **XI** to give the vinylic metal-complex **XII**, and then trapping of the nucleophile $Ar^2B(OH)_2$ with **XII** for the synthesis of the tetrasubstituted N-bearing olefin **XIII** is precisely envisaged (Figure 1c). Inspired by the challenges and shortcomings related to regioselectivity and harsh reaction conditions in the unsymmetrical difunctionalization of unsaturated systems for the

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[+] These authors contributed equally to this work.
Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under: https://doi.org/10.1002/anie.201915522.

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An unconventional sulfur-to-selenium-to-carbon radical transfer: chemo-and regioselective cyclization of yne-ynamides†

Shubham Dutta,[a] B. Prabagar,‡[a] Rajeshwer Vanjari, ‡[a] Vincent Gandon *[b,c] and Akhila K. Sahoo *[a]

An uncommon sulfur → selenium → carbon radical transfer process is employed to develop an unprecedented selenyl radical-mediated regioselective cyclization of yne-tethered-ynamides. Density functional theory studies and HRMS experiments are used to establish a reactivity scale between thiyl and selenyl radicals. The unique features of this transformation include, (1) the chemo-selective reactivity of RSe˙ over RS˙, (2) regioselective RSe˙ attack on alkyne over ynamide, (3) 5-*exo*-dig cyclization of yne-ynamide to unusual 4-selenyl-pyrroles, and (4) the green synthetic method. The reaction of methyldiselenide with yne-ynamides to methyl-selenopyrroles is also described.

Selenium is a micronutrient essentially found in natural products, amino acids, and proteins.[1] Se-Bearing heteroaryls are invaluable building blocks exhibiting distinct chemical, physical, and biological properties of pharmaceutical relevance.[2] Therefore, green synthetic methods that allow the rapid introduction of Se into heteroaromatic scaffolds are highly desirable. In this regard, binary chalcogens of type $(RS)_2$ and $(RSe)_2$ exhibit diverse synthetic applications, primarily including the homo-difunctionalization of unactivated olefins and alkynes.[3] Another notable application is the hetero-difunctionalization of olefins and alkynes involving the dominance of two reactive radical species, PhSe˙ and PhS˙, through the sequential radical transfer: Se˙ → S˙ → C˙, *via* the attack of PhS˙ to olefin or alkyne (Fig. 1a).[4] These reactions are dependent on the preferential reactivity of PhS˙, with the rate constant for the addition to the unsaturated system being 10–50 fold higher than that of PhSe˙.[5] Surprisingly, a reverse S˙ → Se˙ cross-radical transfer to promote the addition of PhSe˙ radicals to unsaturated bonds remains unexplored (Fig. 1).

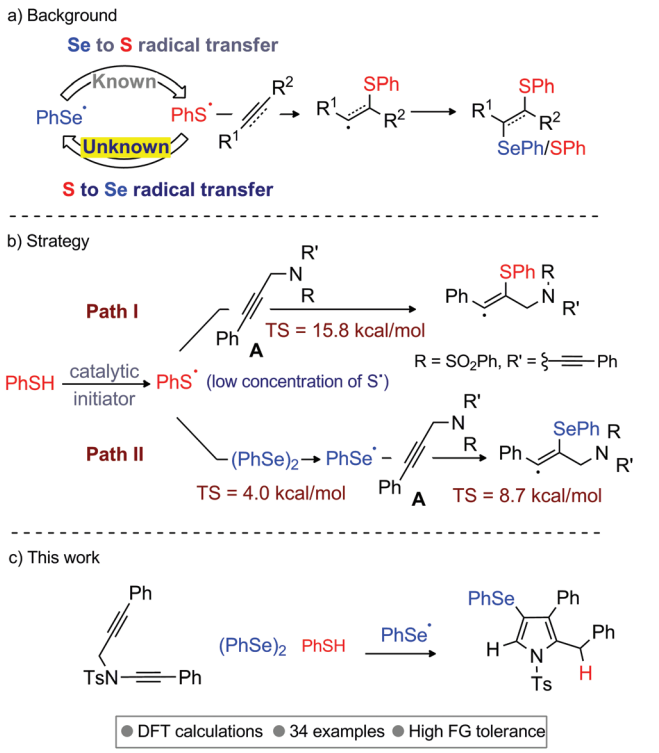

Fig. 1 (a) Background: Se to S radical transfer; (b) strategy: S to Se radical transfer; (c) this work: chemo and regioselective selenyl radical attack to alkyne. FG = functional group.

To address this challenge, the density functional theory (DFT) studies (detailed in Fig. 2) were sought; the reaction between PhS˙ and alkyne (**A**) requires 15.8 kcal mol^{-1} (Path I, Fig. 1b), whereas the PhS˙ with $(PhSe)_2$ needs 4.0 kcal mol^{-1} (Path II, Fig. 1b). These valuable pieces of information can

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[c]*Vincent Gandon, Laboratoire de Chimie Moléculaire (LCM), CNRS UMR 9168, Ecole Polytechnique, Institut Polytechnique de Paris, route de Saclay, 91128 Palaiseau cedex, France*

†Electronic supplementary information (ESI) available. CCDC 1945002. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c9gc03745d

‡These authors contributed equally.

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Radical Cyclization

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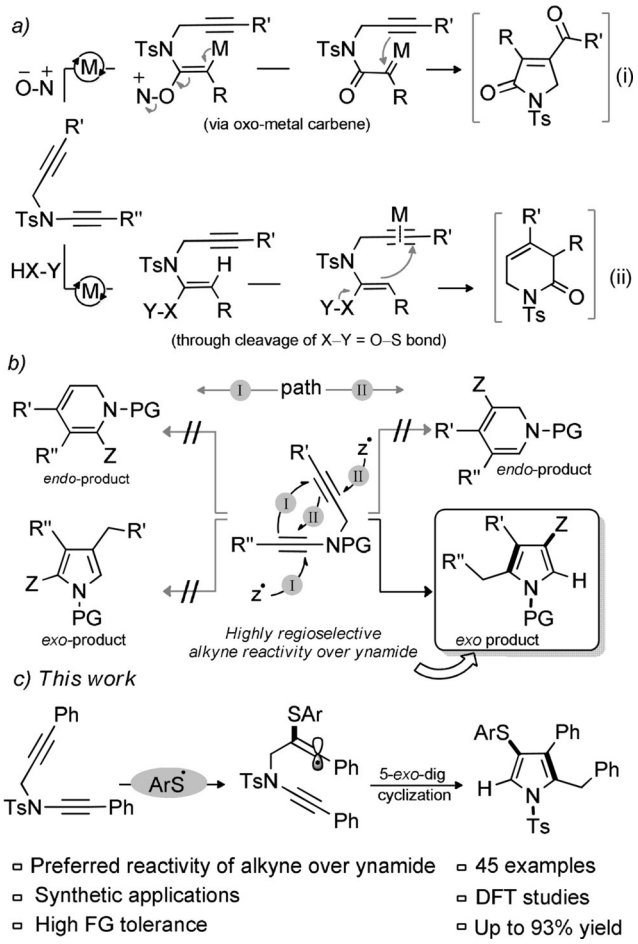
Alkyne Versus Ynamide Reactivity: Regioselective Radical Cyclization of Yne-Ynamides

Shubham Dutta, Rajendra K. Mallick, Rangu Prasad, Vincent Gandon, and Akhila K. Sahoo**

Abstract: *Ynamides are typically more reactive than simple alkynes and olefins. However, a serendipitous observation revealed a rare case where the reactivity of simple alkynes exceeds that of ynamides. This led to the development of a unique sulfur-radical-triggered cyclization of yne-tethered ynamides, which involves attack of the alkyne by a thiyl radical followed by cyclization with the ynamide. A wide range of novel 4-thioaryl pyrroles that could tolerate common functional moieties and N-protecting groups were expediently constructed by this strategy. The current method contrasts with the typical cyclization of yne-ynamides, which involves the attack of the alkyne moiety by the ynamide core. Control experiments and DFT calculations supported the participation of the sulfur radical in the reaction and the regioselective cyclization. The synthetic potential of the substituted pyrroles is also discussed.*

Ynamides, a distinct class of N-substituted alkynes, have been used for various cyclization/cycloisomerization processes towards the construction of structurally diverse complex N-heterocyclic building blocks.[1] In this context, transition-metal-catalyzed N-oxide and Brønsted/Lewis acid triggered cyclizations of yne-tethered ynamides have shown great potential. Importantly, all these transformations involve nucleophilic attack by the ynamide motif (via an oxo-metal carbene[2]/ketene N,O-acetal) on the alkyne scaffold (Scheme 1a).[3,4] In contrast, synthetic techniques that are based on reversing the usual reactivity of ynamides over alkynes have been only rarely reported.[5] A worthwhile endeavor would thus be to unravel a radical-mediated cyclization[6] of yne-tethered ynamides, with the prediction of a preferred radical attack on the alkyne rather than the inherently polarized ynamide (path II over path I; Scheme 1b), which, to the best of our knowledge, is unprecedented. Thus, radical-triggered 6-*endo*-/5-*exo*-cyclization of the alkyne to the ynamide would result in the formation of 6- or 5-membered N-heterocycles, respectively (path II, Scheme 1b). To overcome this challenge, we have developed a highly regioselective thiyl-radical attack on an alkyne motif, followed by regioselective 5-*exo*-dig intramolecular attack on the ynamide moiety of yne-tethered ynamides. This reaction yields novel highly substituted 4-thioaryl-pyrroles (Scheme 1c). The reaction has a broad scope and enables the synthesis of unnatural pyrrole derivatives (Scheme 1c).



Scheme 1. a) Known cyclization methods for ynamides, b) Radical-triggered cyclization and hypothesis, c) Current work. Ts = SO_2*p*-tolyl.

We started by examining the reaction of yne-tethered ynamide **1a** with 3-methylbenzenethiol (**2a**) and a radical initiator. The results are detailed in Table 1. When the reaction was performed in the presence of AIBN (1.5 equiv)

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Conference Attended

1. **Alkyne versus Ynamide Reactivity: Regioselective Radical Cyclization of Yne-ynamides**

   Shubham Dutta and Akhila K. Sahoo*

   Poster Presentation at "Chem Fest-2019" held at School of Chemistry, University of Hyderabad, Hyderabad, India *(Selected for best poster presentation).*

2. **Alkyne versus Ynamide Reactivity & Unconventional S→Se radical transfer**

   Shubham Dutta and Akhila K. Sahoo*

   Oral Presentation at "J-NOST 2019" held at Delhi University (DU), New Delhi, India on **October, 2019**. *(Selected for best poster presentation).*

3. **Keteniminium Driven Umpolung Difunctionalization of Ynamides**

   Shubham Dutta and Akhila K. Sahoo*

   Poster Presentation at "Chem Fest-2020" held at School of Chemistry, University of Hyderabad, Hyderabad, India.

4. **Umpolung Difunctionalization of Ynamides & Alkyne vs Ynamide in Radical Cyclization**

   Shubham Dutta and Akhila K. Sahoo*

   Oral Presentation at "Chem Fest-2021" held at School of Chemistry, University of Hyderabad, Hyderabad, India. *(Selected for best oral presentation).*

5. **Cationic-Palladium Catalyzed Regio- and Stereoselective Dicarbofunctionalization of Ynamides & Unsymmetrical Alkynes**

   Shubham Dutta and Akhila K. Sahoo*

   Oral Presentation at "JNOST-2022" held at School of Chemistry, University of Hyderabad, Hyderabad, India. *(Selected for best oral presentation).*

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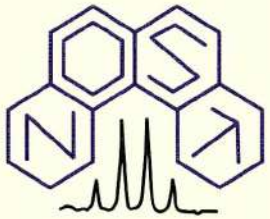

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by Shubham Dutta

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Biographical Sketch

Shubham Dutta was born in Bahalda (village), Mayurbhanj (dist), Odisha, India on 12th July, 1994. He did primary schooling in Bahalda High School (10th standard), Bahalda. He finished Intermediate education at Rairangpur College, Rairangpur. Then he received B. Sc degree from M.P.C Autonomous College, Baripada, Odisha in 2014 where he gained some interest in chemistry. He obtained Master's degree in Chemical Science (Organic chemistry) in 2016 from Utkal University, Bhubaneswar. In June-2016 he cleared CSIR-JRF (82 rank). In July-2016, he started the research work at the School of Chemistry, University of Hyderabad under the guidance of Prof. Akhila Kumar Sahoo. His research interest deals with the development of "Regioselective Difunctionalization Reactions of Unsymmetrical Alkynes".