Development of Direct Organocatalytic Enolate- and Dienamine-mediated Reactions: High-yielding Synthesis of Fully Decorated Triazoles, Benzotriazoles and Chiral Decalines

A
Thesis
Submitted for the Degree of

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By

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With the blessings of

Sri A. L. N. Sastry and Sri G. Seetha Ramaiah....

DEDICATED TO

MY BELOVED PARENTS

DECLARATION

I hereby declare that the entire work embodied in this thesis is the result of investigations carried out by me in the School of Chemistry, University of Hyderabad, Hyderabad, under the guidance of ***Prof. Dhevalapally B. Ramachary*** *and that it has not been submitted elsewhere for any degree or diploma. In keeping with the general practice, due acknowledgements have been made wherever the work described is based on the findings of other investigators.*

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CERTIFICATE

Certified that the work contained in the thesis entitled ***"Development of Direct Organocatalytic Enolate- and Dienamine-mediated Reactions: High-yielding Synthesis of Fully Decorated Triazoles, Benzotriazoles and Chiral Decalines"*** *has been carried out by* ***Mr. Bharanishashank Adluri*** *under my supervision and the same has not been submitted elsewhere for a degree.*

Prof. Dhevalapally B. Ramachary

(*Thesis Supervisor*)

Dean
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CONTENTS

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Bharanishashank Adluri

PREFACE

*The area of organocatalysis is known to mimic the characteristic of enzymes and bio-molecules and now considered as the "third pillar of asymmetric catalysis". In recent years, organocatalytic reactions are becoming powerful tools in the construction of complex molecular skeletons. More importantly, organocatalytic approaches have become alternative to the metal mediated transformations because of their simple structure of the catalyst, simple operation technique, milder conditions, high efficiency and regiospecificity, readily available precursors and potentially greener. The different modes of carbonyl activation in amine catalysis has been developed for the construction of highly functionalized molecules with good selectivity. The present thesis entitled "**Development of Direct Organocatalytic Enolate- and Dienamine-mediated Reactions: High-yielding Synthesis of Fully Decorated Triazoles, Benzotriazoles and Chiral Decalines**" describes the reactions involving enolate- and push-pull dienamine intermediates in the synthesis of highly functionalized molecules of pharmaceutical and biological importance. In all sections, a brief introduction is provided to keep the present work in proper perspective, the compounds are sequentially numbered (bold), and references are marked sequentially as superscript and listed at the end of the thesis. All the figures included in the thesis were obtained by DIRECT PHOTOCOPY OF THE ORIGINAL SPECTRA, and in some of them uninformative areas have been cut to save the space.*

Highly functionalized heterocycles such as 1,4-disubstituted 1,2,3-triazoles have found wide applications in pharmaceuticals, polymer and material chemistry. To construct such functionalized molecules a diversity-oriented green, sustainable and practical synthesis is required. Here we achieved using simple starting materials such as aldehydes, aryl azides and catalytic amount of tertiary amine. The organocatalytic enolate-mediated azide-aldehyde [3+2]-cycloaddition (OrgAAC) reaction proceeds in high rate and regioselctivity and it constitutes an alternative to the previously known CuAAC, RuAAC and IrAAC click reactions.

In continuation to the development of enolate-mediated synthesis of substituted 1,2,3-triazoles, we described the organocatalytic azide-ketone [3+2]-cycloaddition (OrgAKC)

reaction for the synthesis of fully decorated 1,4,5-trisubstituted 1,2,3-triazoles in excellent yields with high regioselectivity. A variety of enolizable arylacetones, deoxybenzoins and aryl azides employed as starting materials under tertiary amine-catalysis. Furthermore, we demonstrated the application of OrgAKC strategy in metal-free synthesis of medicinally important and materially useful triazoles.

In the third chapter we demonstrated the metal-free regioselective synthesis of highly functionalized N-aryl-benzotriazoles from the highly functionalized unmodified cyclic enones, aryl azides through [3+2]-cycloaddition and oxidative aromatization reactions based on push-pull dienamine catalysis. The sequential one-pot reaction proceeds in good yields with high selectivity using pyrrolidine as the catalyst. Herein, we explore the utility of highly functionalized bicyclic N-aryl-1,2,3-triazoles as starting materials for the synthesis of medicinally important N-aryl-benzotriazoles through mild oxidative aromatization. Furthermore, we demonstrated the medicinal applications of benzotriazoles.

In continuation to the development of push-pull dienamine catalysis in organocatalytic cascade reactions, fourth chapter illustrates the amine-catalyzed diastereoselective domino Claisen-Schmidt/Henry reaction that produce highly functionalized chiral decalines from readily available cyclic enones and chiral γ-nitroaldehydes. For the first time chiral γ-nitroaldehydes used as precursors for the synthesis of bicyclic and tricyclic carbon frame works.

LIST OF ABBREVIATIONS

Ac	acetyl
AcOH	acetic acid
Ac_2O	acetic anhydride
Anal.	analysis
aq.	aqueous
Ar	aryl
Bn	benzyl
Bp	boiling point
br	broad
Bu	butyl
*t*Bu or ^{t}Bu	*tertiar*y-butyl
n-BuLi	*n*-butyl lithium
calcd.	calculated
cat.	catalytic
cm	centimeter
CS/H	Claisen-Schmidt/Henry
CS/I	Claisen-Schmidt/isomerisation
CSP	chiral stationary phase
CuAAC	copper catalyzed azide-alkyne cycloaddition
DABCO	1,4-Diazabicyclo[2.2.2]octane
dABq	doublet of AB quartet
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DCE	1,2-dichloroethane
DCM	dichloromethane
dd	doublet of doublet
ddd	doublet of doublet of doublet
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
de	diastereomeric excess
DEPT	distortionless enhancement by polarization transfer
DFT	density functional theory
DIBAL-H	diisobutylaluminium hydride
DMAP	dimethylaminopyridine
DMF	*N,N*-dimethylformamide
DMSO	dimethyl sulfoxide
dr	diastereomeric ratio
dt	doublet of triplet
EDG	electron donating group
ee	enantiomeric excess
eq.	equation
equiv.	equivalent(s)
Et	ethyl
EtOH	ethyl alcohol
Et_2O	diethylether
EWG	electron withdrawing group
Fg	functional group
Fig.	figure
gm	gram (s)

h	hour (s)
Hz	hertz
Hex	hexyl
HIV	human immunodeficiency virus
HOMO	highest occupied molecular orbital
HPLC	high-performance liquid chromatography
^{i}Pr	isopropyl
IR	infrared
$LiAlH_4$	lithium aluminum hydride
lit.	literature
m	multiplet
m-CPBA	*m*-chloro perbenzoic acid
M	molarity
Mp.	melting point
Me	methyl
mg	milligram (s)
mGluR1	metabotropic glutamate receptor 1
mL	milliliter
mmol	millimole
MW	microwave
NMR	nuclear magnetic resonance
NMP	*N*-methylpyrrolidine
OrgAAC	organocatalytic azide-aldehyde cycloaddition
OrgAKC	organocatalytic azide-ketone cycloaddition
OrgRC	organocatalytic reductive coupling
PCC	pyridinium chlorochromate
PET	positron emission tomography
Ph	phenyl
ppm	parts per million
p-TSA	*p*-toluenesulfonic acid
py	pyridine
pr	propyl
q	quartet
RT	room temperature
s	singlet
sec	secondary
t	triplet
TBHP	tertiary-butyl hydroperoxide
*t*BuOK	Potassium tertiarybutoxide
td	triplet of doublet
tert	tertiary
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
Ts	toluenesulphonyl
UV	ultraviolet

Development of Direct Organocatalytic Enolate- and Dienamine-mediated Reactions: High-yielding Synthesis of Fully Decorated Triazoles, Benzotriazoles and Chiral Decalines

1. ABSTRACT

An organocatalytic azide–aldehyde [3+2]-cycloaddition (OrgAAC) reaction of a variety of enolizable aldehydes is reported. The OrgAAC reaction is characterized by a high rate and regioselectivity, mild reaction conditions, easily available substrates with simple operation, and excellent yields with a broad spectrum of substrates. It constitutes an alternative to the previously known CuAAC, RuAAC, and IrAAC click reactions.

An enolate-mediated organocatalytic azide–ketone [3+2]-cycloaddition (OrgAKC) reaction of a variety of enolizable arylacetones and deoxybenzoins with aryl azides was developed for the synthesis of fully decorated 1,4-diaryl-5-methyl(alkyl)-1,2,3-triazoles in excellent yields with high regioselectivity at 25 °C for 0.5-6 h. This reaction has an excellent outcome with reference to reaction rate, yield, regioselectivity, operation simplicity and availability of substrates and catalyst. This reaction has advantages over the previously known metal-mediated reactions.

Herein we report our studies on the sequential one-pot combinations of amine-catalyzed multicomponent reactions (MCRs). We have developed the copper-free synthesis of functionalized bicyclic *N*-aryl-1,2,3-triazole and *N*-arylbenzotriazole products from the simple unmodified starting materials through [3+2]-cycloaddition ([3+2]-CA) and oxidative aromatization reactions in one pot under amine catalysis. The sequential one-pot reaction proceeds in good yields with high selectivity by using pyrrolidine as the catalyst from the simple unmodified substrates of enones, aryl azides and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ). Furthermore, we have demonstrated the medicinal applications of triazoles and benzotriazoles through simple organic reactions.

A practical and novel organocatalytic domino Claisen-Schmidt/Henry (CS/H) process for the synthesis of highly substituted chiral decalines is reported. Herein, we described the (*S*)-1-(pyrrolidin-2-ylmethyl)pyrrolidine catalyzed domino CS/H reaction of cyclic enones with γ-nitroaldehydes at ambient conditions. This novel asymmetric CS/H reaction proceeds in good yields with high enantio- and diastereoselectivity through push–pull dienamine catalysis. Furthermore, we demonstrated the application of chiral products in the synthesis of highly functionalized decalines.

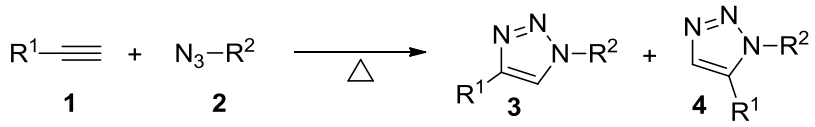
2. *INTRODUCTION*

Over a decade, organocatalysis has been emerged as a powerful tool for the construction of functionalized molecular frameworks in selective manner.[1] A variety of reactions involving intermediates, in situ generated from carbonyl compounds and amines, such as enamine,[1b,c] iminium,[1] dienamine[2] and trienamine[3] were developed in a cascade synthesis. In particular, amine catalysis through enamine activation appeared as a major contributor in the area of organocatalysis and has been applied in several asymmetric transformations/cascade reactions.

Recently organocatalytic azide–carbonyl [3+2]-cycloadditions emerged as a solution to avoid metal residues in the synthesis of substituted 1,2,3-triazoles.[4,5] The intermediate enamine or enolate can be generated in situ from a carbonyl and an amine and it can react as a dipolarophile with an azide to afford the desired five-membered triazole. The organocatalytic methods have certain advantages over the respective metal-mediated transformations as they are potentially greener, highly efficient, regiospecific and considered to be non-toxic towards biological systems. These characteristics able to grab the attention of chemical community to develop new methodologies for the metal-free synthesis of triazoles and also to employ different kinds of dipoles in organocatalytic [3+2]-cycloaddition reactions.

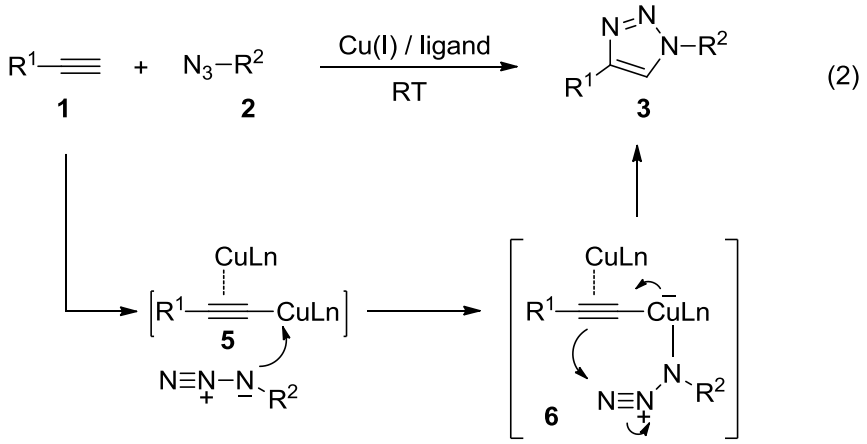
As the research work described in this thesis deals with organocatalytic synthesis of highly substituted 1,2,3-triazoles,[5] a brief overview of the metal-mediated and metal-free synthesis of triazoles are presented below.

The synthesis of 1,2,3-triazoles by thermal 1,3-dipolar cycloadditions between an alkyne **1** and an azide **2** was discovered in 1893 by Arthur Michael[6a] and has been significantly developed by the research group of Huisgen in the 1960s.[6b-e] These cycloadditions are very slow even at higher temperatures and produces mixture of the 1,4 and 1,5 regioisomers **3** and **4** as shown in eq. 1. The relatively poor regioselectivity of the Huisgen 1,3-dipolar cycloaddition has significantly limited the extensive utilization of this strategy.



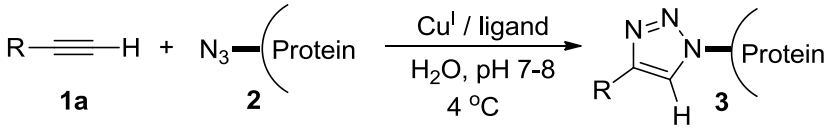
1 **2** **3** **4** (1)

To overcome these limitations, In 2002 Meldal and Sharpless groups reported independently Cu(I)-catalyzed azide-alkyne cycloaddition (CuAAC) reaction which regiospecifically combines terminal alkynes **1** and azides **2** to give exclusively 1,4-disubstituted 1,2,3-triazoles **3** as shown in eq. 2.[7a-b] These seminal reports revealed that the formation of copper acetylide **5** is responsible for the selective addition and also gave a evidence for the stepwise addition of azides for the synthesis of 1,4-disubstituted 1,2,3-triazoles. This CuAAC reaction has become the "cream of the crop" of click chemistry concept due to its wide applicability and efficiency. This discovery has clearly advanced the research on 1,2,3-triazoles and the related chemistry to be one of the "hottest" research fields in the last decade.



1 **2** **3** (2)

In 2003, Finn *et al.* reported the CuAAC strategy in labeling positions on a large protein structure. In this report they conjugated a fluorescein dye molecule **1a** to the different functionalized protein **2** of cowpea mosaic virus *via* the 'click' reaction as shown in eq. 3.[8] Here, the chelating ligand tris(triazolyl)amine plays a crucial role in stabilizing the Cu(I) oxidation state and protecting the protein from Cu(triazole)-induced denaturation. This work paved the way for further developments in the field of *in vitro* and also *in vivo* click chemistry.



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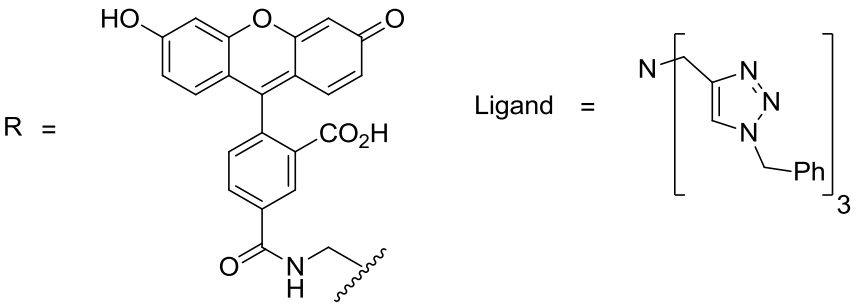
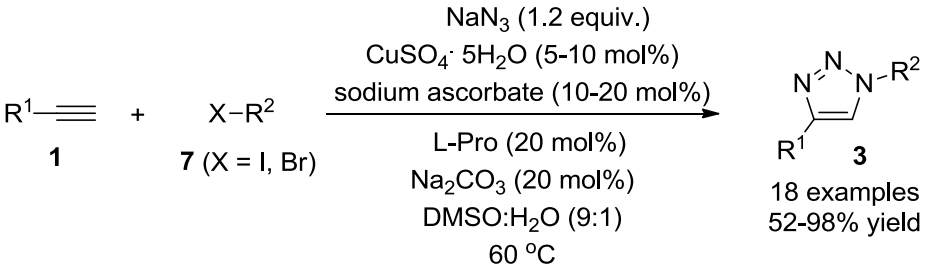


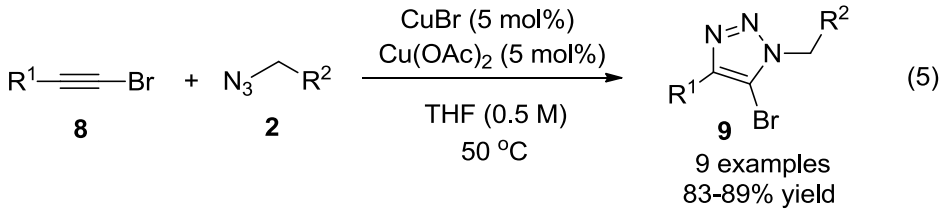
In 2004, Fokin *et al.* reported the Cu(I)-catalyzed one-pot synthesis of 1,4-disubstituted 1,2,3-triazoles in excellent yields from a variety of readily available terminal alkynes **1,** aromatic and aliphatic halides **7** and sodium azide as shown in eq. 4.[9] This procedure eliminates isolation of the organic azides, as they are generated in situ, making this click process even more user-friendly and safe.



(4)

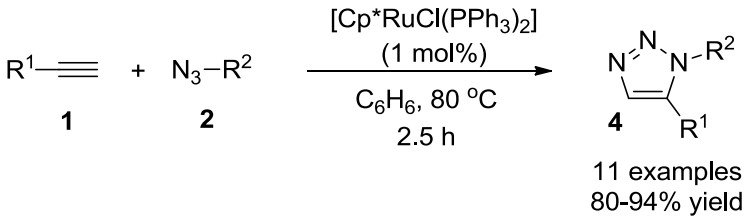
In 2005, Rutjes *et al.* described the synthesis of 1,4,5-trisubstituted 1,2,3-triazoles **9** by Cu-catalyzed coupling between bromo-alkynes **8** and organic azides **2** in high yield and in regioselective manner as shown in eq. 5.[10] This procedure offers facile access to a variety of

halide containing trisubstituted triazoles **9** and can be further functionalized to give fully substituted 1,2,3-triazoles through metal-mediated transformations.



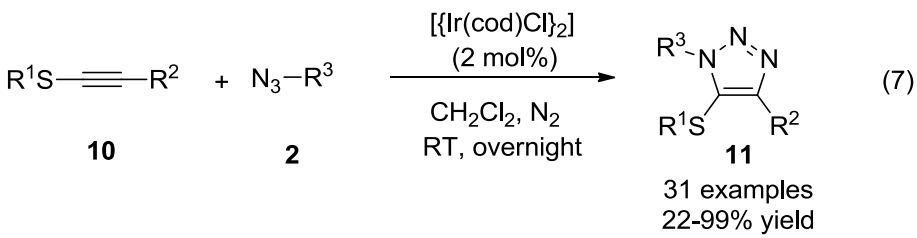
(5)

In 2005, Jia *et al.* demonstrated a convenient Ru-catalyzed process for the regioselective synthesis of 1,5-disubstituted 1,2,3-triazoles **4** from terminal alkynes **1** and organic azides **2** as shown in eq. 6.[11a] 1 mol% of Ru complex pentamethyl analogue Cp*RuCl(PPh$_3$)$_2$ is effective for the formation of only 1,5-regioisomer. Internal alkynes also reported in this catalysis, resulting in fully substituted 1,4,5-trisubstituted 1,2,3-triazoles.



(6)

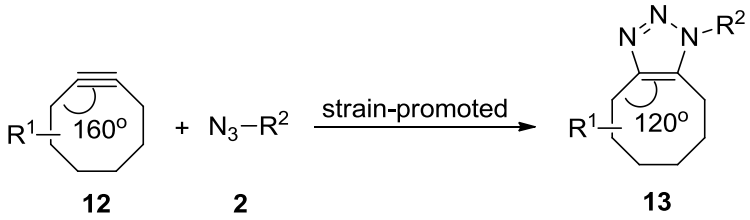
In 2014, Sun *et al.* described an efficient iridium-catalyzed azide–alkyne cycloaddition reaction (IrAAC) of electron-rich internal thioalkynes. The iridium complex [{Ir(cod)Cl}$_2$] able to catalyze the cyclization of internal thioalkynes **10** and azides **2** to furnish a fully substituted triazoles **11** under mild reaction conditions with complete regioselectivity as shown in eq. 7.[11e] This procedure complements the well-known CuAAC and RuAAC click reactions.



(7)

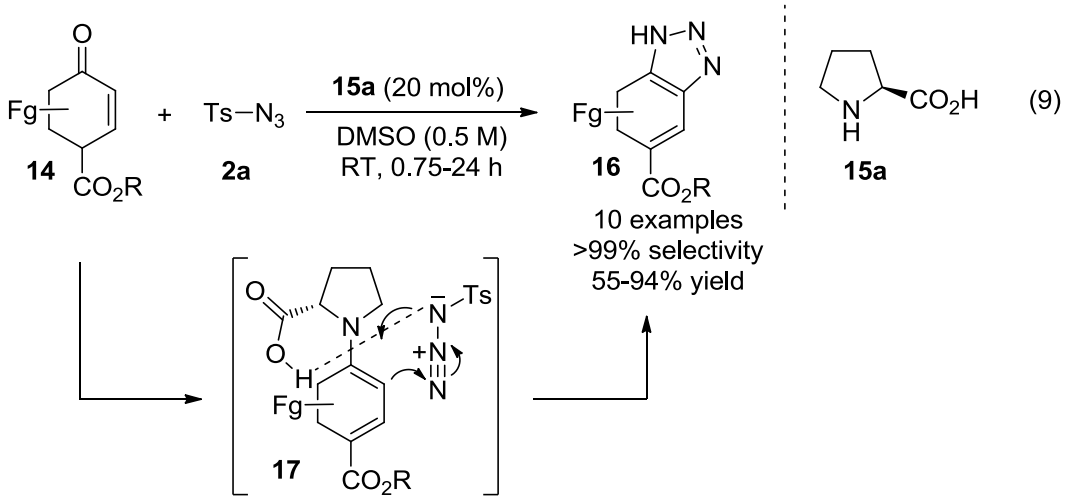
In all the above methods, the presence of Cu(I) or transition metal residues in the synthesis of triazloes limited the application of click chemistry in chemical biology. More importantly, the copper catalysts are potentially toxic for living organisms and may cause copper-induced degradation of viruses or oligonucleotide strands in biological system.

In 2004, Bertozzi *et al.* reported catalyst-free strain-promoted [3+2]- cycloaddition, called as bioorthogonal click reaction, between cyclooctynes and azides that proceeds under physiological conditions. The ring strain energy (~18 kcal/mol) of the cyclooctyne **12** able to accelerate the reaction with azide **2** to form the desired triazole **13** as shown in eq. 8.[12a] This method can be used for selective modification of biomolecules and living cells without apparent physiological harm.

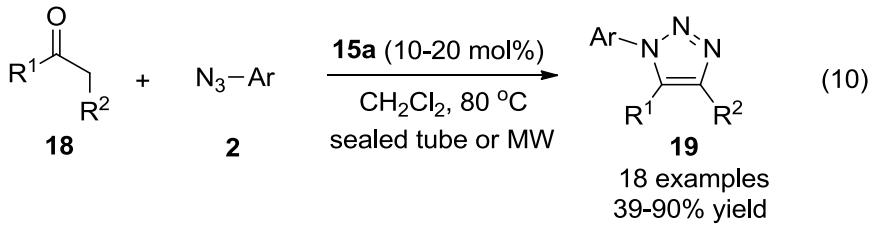


12 **2** **13** (8)

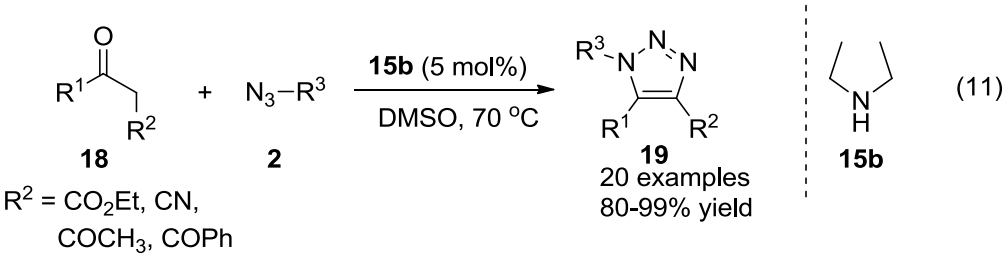
In 2008, our group discovered a copper-free, green technology for the synthesis of highly substituted *N*H-1,2,3-triazoles **16** through domino [3+2]-cycloaddition/hydrolysis ([3+2]-CA/H) reactions at ambient temperature. Reactions between the cyclic enones **14** and tosyl azide **2a** in the presence of proline **15a** afforded the hydrolyzed triazoles **16** in moderate to very good yields through the transition state **17** as shown in eq. 9.[4a] This is the first organocatalytic approach towards the synthesis of *N*H-1,2,3-triazoles based on the push-pull dienamine platform. This study served for launching the studies in organocatalytic click chemistry.



In 2011, Pons *et al.* reported an organocatalytic approach for the synthesis of highly substituted 1,2,3-triazoles **19** starting from unactivated ketones **18** and aryl azides **2** under proline **15a** catalysis as shown in eq. 10.[4b] The reaction rate was dramatically enhanced by microwave activation compared to thermal condition. They stated in their proposed mechanism that the presence of acid-moiety in the catalyst is crucial for the regioselective synthesis of triazoles as mentioned in our previous work.[4a]

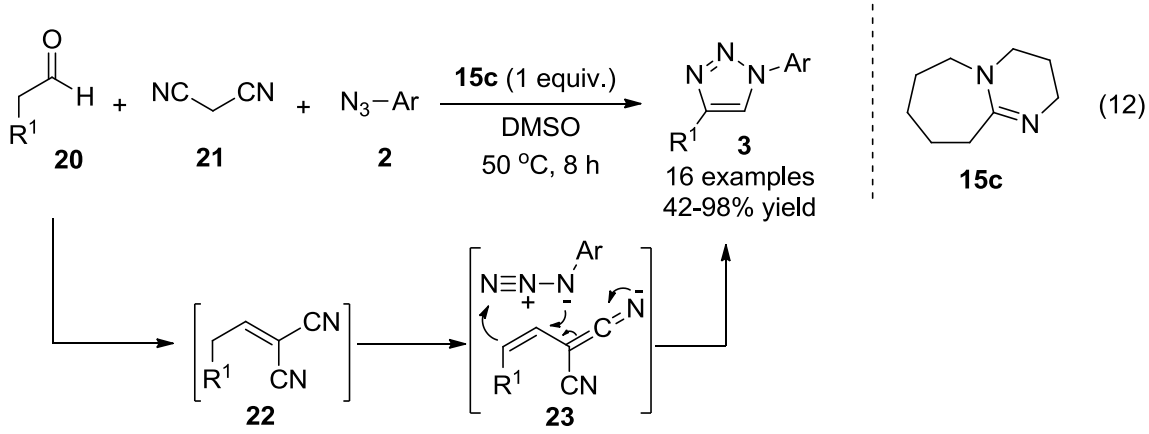


In the same year, Wang *et al.* reported the regioselective organocatalytic enamide–azide cycloaddition reaction in the presence of diethyl amine **15b** as catalyst. A variety of activated aryl ketones, and ketoesters **18** were employed with organic azides **2** to afford the 1,4,5-trisubstituted 1,2,3-triazoles **19** in good to excellent yields as shown in eq. 11.[4c]



(11)

In 2014, Paixao and co-workers described a DBU **15c** mediated one-pot three-component reaction between aldehydes **20**, malononitrile **21** and azides **2** for the synthesis of 1,4-disubstituted 1,2,3-triazoles **3** as shown in eq. 12**.**[13] The in situ generated alkylidene malononitriles **22** acts as reactive intermediates in the inverse-electron-demand 1,3-dipolar cycloaddition reaction. This method has proven to be successful by using preformed alkylidene malononitriles **22** and a range of aryl azides **2** in the presence of stoichiometric amounts of DBU **15c**.



(12)

In continuation to synthesis of highly functionalized 1,2,3-triazoles starting from readily available starting materials, research work has been carried out on the synthesis of highly substituted 1,2,3-triazoles through organocatalytic [3+2]-cycloadditions and functionalized chiral decalines based on push-pull dienamine catalysis, and the results are presented in this thesis.

To begin with, starting from simple starting materials, an enolate-mediated synthesis of substituted 1,2,3-triazoles was developed and the results are presented in the next sections.

3. An Organocatalytic Azide-Aldehyde [3 + 2]-Cycloaddition Reaction: High-yielding Regioselective Synthesis of 1,4-Disubstituted 1,2,3-Triazoles

3.1 Introduction

1,4-**D**isubstituted 1,2,3-triazoles have emerged as an important class of organic compounds, displaying a vast spectrum of properties and are widely used as pharmaceuticals.[14] Many 1,2,3-triazoles have found medicinal applications such as HIV protease inhibitors, anticancer drugs, anti-tuberculosis drugs, antifungal agents, antibacterial drugs, histone deacetylase inhibitors, bioorthogonal probes and also used as corrosion inhibitors, lubricants, dyes, and photo-stabilizers (Figure 1).[14] Thus, the development of more general green methods for the preparation of these compounds is of significant interest.[15]

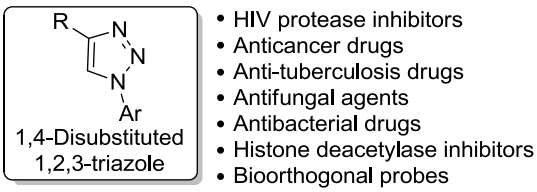
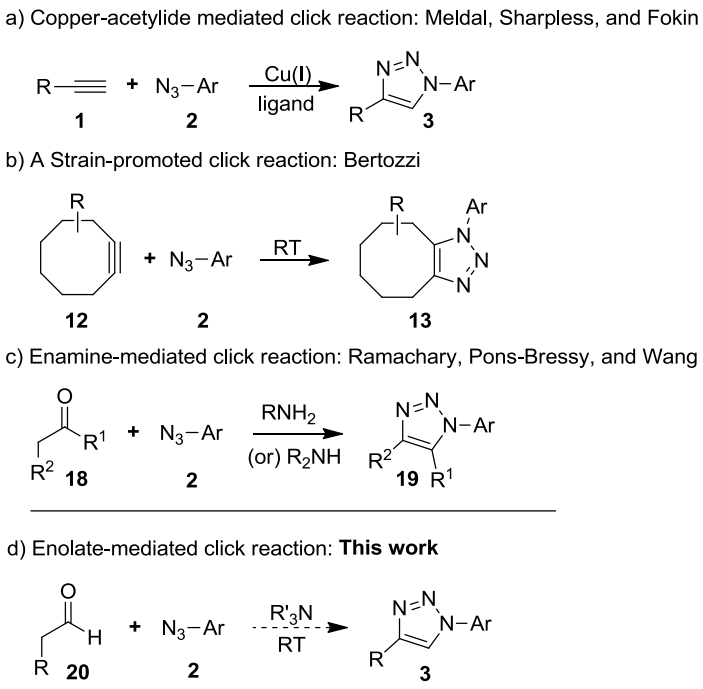


Figure 1: Potential applications based on the 1,2,3-triazoles.

The regioselective formation of 1,4- and 1,5-disubstituted 1,2,3-triazoles can be accomplished by copper-catalyzed azide-alkyne [3+2]-cycloaddition (CuAAC) reactions (Scheme 1a),[7] and ruthenium-catalyzed azide-alkyne [3+2]-cycloaddition (RuAAC) reactions, respectively.[11] Recently, a strain-promoted [3+2]-cycloaddition reaction of substituted cyclooctyne with aryl azides was reported to furnish 1,4,5-trisubstituted 1,2,3-triazoles (Scheme 1b), which have become good bioorthogonal probes.[12] Very recently, an enamine-mediated amino acid- or amine-catalyzed [3+2]-cycloaddition reaction of different

carbonyl compounds (enones, β-keto esters, ketones and enals) with aryl azides was reported to furnish 1,4,5-trisubstituted 1,2,3-triazoles in good yields (Scheme 1c).[4]

Scheme 1. Background and design for the enolate-mediated organocatalytic azide-aldehyde [3+2]-cycloaddition reaction.



In all the above three methods, either they used expensive or not commercially available alkynes, or less reactive carbonyl compounds other than simple aldehydes as the starting materials along with aryl azides. Furthermore, CuAAC only gave 1,4-disubstituted 1,2,3-triazoles, and the remaining two methods gave 1,4,5-trisubstituted 1,2,3-triazoles. Even though the CuAAC reaction has become a paradigm of the "click reaction", its use for labeling of biomolecules in live cells is prohibited because of the cytotoxicity of the copper catalyst.[7d,12a-c] Alkynes used in CuAAC or RuAAC click reactions are more expensive than the corresponding aldehydes. For example the price of phenylacetylene is $76 for 100 mL, whereas that of phenylacetaldehyde is only $33 for 100mL. These obstacles inspired us to develop a novel green protocol for the high-yielding regioselective synthesis of 1,4-disubstituted 1,2,3-triazoles based upon enolate-mediated organocatalytic azide-aldehyde

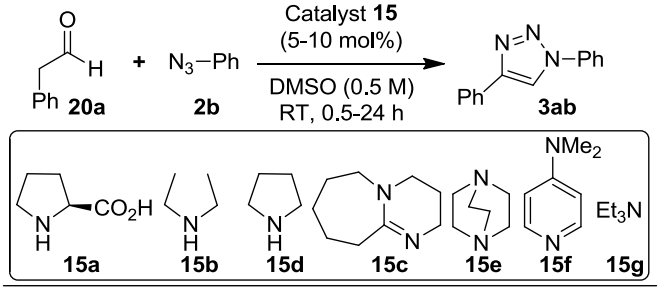
[3+2]-cycloaddition (organo-click) reaction from commercially available enolizable aldehydes, aryl azides, and a catalytic amount of tertiary amine (Scheme 1d). Although in the literature simple enolizable aldehydes and active methylenes were used in reactions with aryl azides to furnish 1,2,3-triazoles through the formation of enolates or enamines with strong bases/amines, further development is required because the known protocols require an excess amount of amine/base and harsh reaction conditions.[16] Herein, we developed the organocatalytic enolate-mediated synthesis of 1,2,3-triazoles from aldehydes and aryl azides.

3.2 Results and Discussion

We initiated our preliminary optimization of the organo-click reaction by screening a number of known simple organocatalysts for the click reaction of phenylacetaldehyde **20a** with 1.0 to 1.5 equiv. of phenyl azide **2b** (Table 1). Interestingly, the reaction of **20a** with 1.5 equiv. of PhN_3 **2b** in DMSO catalyzed by 10 mol% of proline **15a** furnished the product **3ab** as a single regioisomer in moderate (53%) yield (Table 1, entry 1). The same reaction catalyzed by 10 mol% of diethyl amine **15b** or pyrrolidine **15d** did not furnish the 1,2,3-triazole **3ab**, but phenylacetaldehyde **20a** is consumed completely (Table 1, entries 2 and 3). After obtaining discouraging results for the enamine-mediated reaction with catalysts **15a-b**, **15d**, we investigated the reaction through the in situ enolate formation, for which we tested some tertiary amines **15c**, **15e-g** as the catalysts for the organo-click reaction. Intriguingly, the reaction of **20a** with 1.5 equiv of **2b** in DMSO under 10 mol% of DBU **15c**-catalysis at 25 °C for 0.5 h furnished **3ab** in 95% yield (Table 1, entry 4). Deviation from these reaction conditions by switching the solvent to DMF, using 5 mol% of **15c** as the catalyst, or using 1.0 equiv. of PhN_3 **2b** was not so successful in promoting the high-yielding organo-click reaction (Table 1, entries 5, 6, and 7). These results clearly support our hypothesis of the formation of reactive enolates. Relatively less basic tertiary amines like DABCO **15e**, DMAP **15f** and Et_3N **15g** catalysts furnished the 1,2,3-triazole **3ab** with moderate yields compared to DBU **15c** (Table 1, entries 8 to 10), and no reaction was observed without the catalyst in DMSO for 24 h at 25 °C (Table 1, entry 13). The same reaction under 10 mol% of non-amine bases K_2CO_3 **15h** and *t*BuOK **15i**-catalysis also furnished the 1,2,3-triazole **3ab** in moderate

to good yields (Table 1, entries 11-12). The DBU-promoted organo-click reaction is solvent dependent, working well in aprotic polar solvents like DMSO and DMF but only <5% product is observed in other solvents like EtOH and H_2O (results not shown in the Table 1). The optimized conditions for the reaction comprise the catalysis by 10 mol% of **15c** at 25 °C in DMSO to furnish the single 1,2,3-traizole **3ab** in 95% yield from **20a** and **2b** (Table 1, entry 4).

Table 1: Reaction optimization.[a]



Entry	Catalyst **15**	pK_a of **15**[b]	*t* [h]	Yield **3ab** [%][c]
1	**15a** (10 mol%)	10.64	24	53
2[d]	**15b** (10 mol%)	10.84	0.5	–
3[d]	**15d** (10 mol%)	11.31	0.5	–
4	**15c (10 mol%)**	**12**	**0.5**	**95**
5[e]	**15c** (10 mol%)	12	0.5	70
6	**15c** (5 mol%)	12	0.5	70
7[f]	**15c** (10 mol%)	12	0.5	75
8	**15e** (10 mol%)	8.8	24	45
9	**15f** (10 mol%)	9.2	24	40
10	**15g** (10 mol%)	10.75	10	45
11	K_2CO_3 **15h** (10 mol%)	10.33	0.5	65
12	*t*BuOK **15i** (10 mol%)	29.4	0.5	87
13	–	–	24	–

[a] Reactions were carried out in solvent (0.5 M) with 1.5 equiv. of **2b** relative to the **20a** (0.5 mmol) in the presence of 5-10-mol% of catalyst **15**. [b] pK_a values referes to the conjugate acid of **15**. [c] Yield refers to the column-purified product. [d] Phenylacetaldehyde **20a** was consumed totally. [e] DMF was used as solvent. [f] 1.0 equiv. of **2b** was used relative to the **20a** (0.5 mmol).

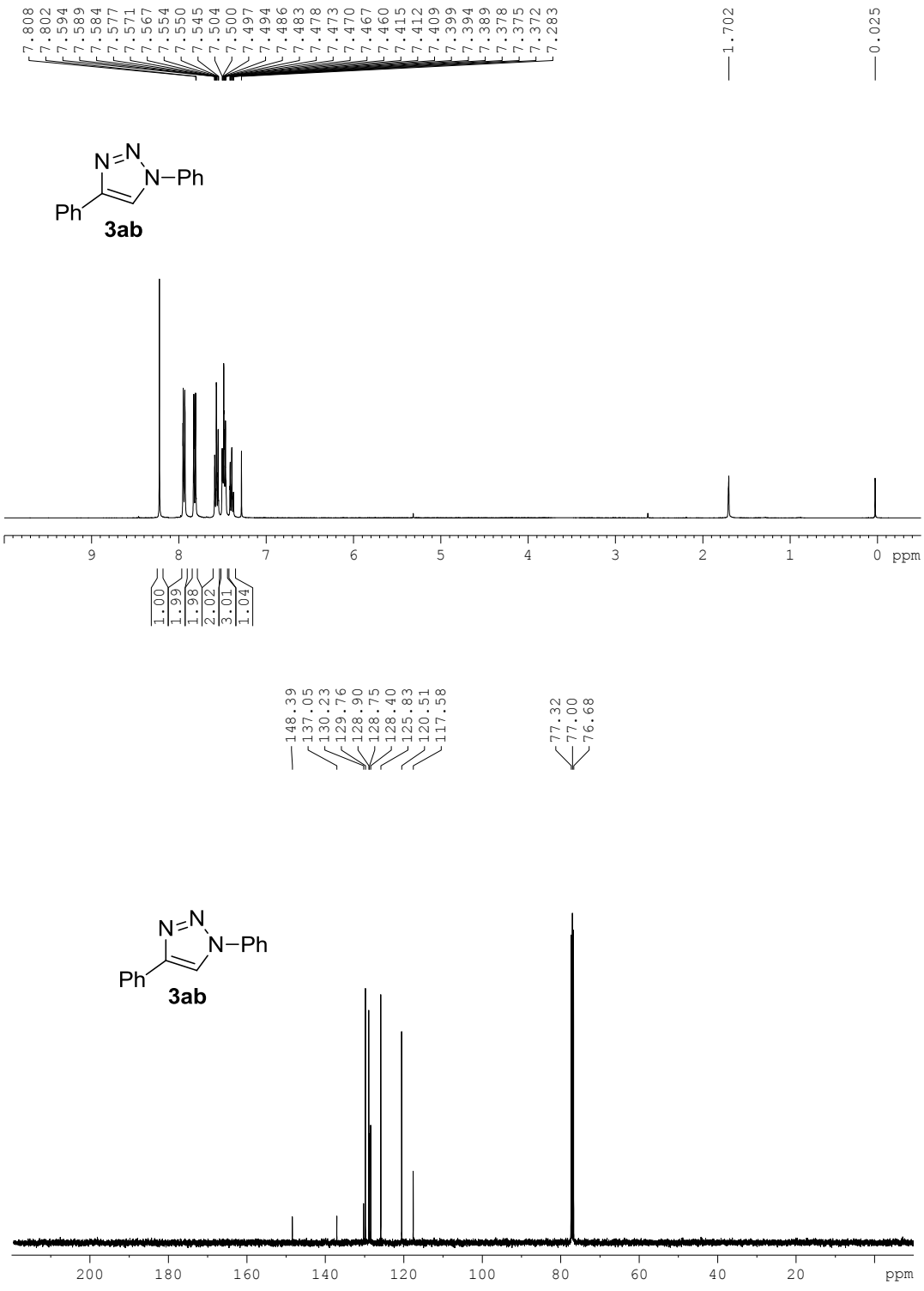


Figure-2: ^{1}H NMR and ^{13}C NMR spectrum of product **3ab**.

With the optimized conditions in hand, the scope and the generality of the DBU-catalyzed organo-click reactions were investigated. A variety of functionalized azides Ar-N_3/ R-N_3 **2a**-**r** were reacted with phenylacetaldehyde **20a** catalyzed by 10 mol% of DBU **15c** at 25 °C in DMSO for 0.5 h (Table 2). Interestingly, aryl azides containing different functional groups like NO_2, CO_2Et, CN, CF_3, CHO, halogen, alkyl and OMe at three different *ortho*-, *meta*- and *para*-positions **2c**-**p** furnished the expected 1,2,3-triazoles **3ac-ap** in excellent to good yields within 0.5 h (Table 2). The yields of products **3ac-ap** were dependent on the substituent at the *para*-position of **2**, increasing with electron-withdrawing groups, and slightly decreasing with alkyl and electron-donating groups. For example, the DBU-catalyzed organo-click reactions of aryl azides 4-$CH_3C_6H_4N_3$ **2n** and 4-$OCH_3C_6H_4N_3$ **2p** with $PhCH_2CHO$ **20a** in DMSO at 25 °C for 0.5 h furnished the expected 1,2,3-triazoles **3an** and **3ap** in 85% and 75% yields, respectively (Table 2, entries 12 and 14). Interestingly, the reaction of **20a** with **2p** under 10 mol% of the more basic **15i**-catalysis furnished **3ap** in slightly improved yield (80%, Table 2, entry 15). On the other hand, the **15c**-catalyzed organo-click reaction of **20a** with alkyl/acyl/tosyl azides **2q-r, 2a** did not furnish the expected products **3**, but the same reactions under the **15i**-catalysis furnished **3aq** in less than 15% and decarboxylated **3ar** in 60% yield, respectively, while **3aa** was not formed at all (Table 2, entries 16-18). The structure and regiochemistry of the organo-click products **3ac-ar** were confirmed by NMR analysis (for example Fig. 4-8) and also finally confirmed by the X-ray structure analysis on **3ac** as shown in Figure 3.[17]

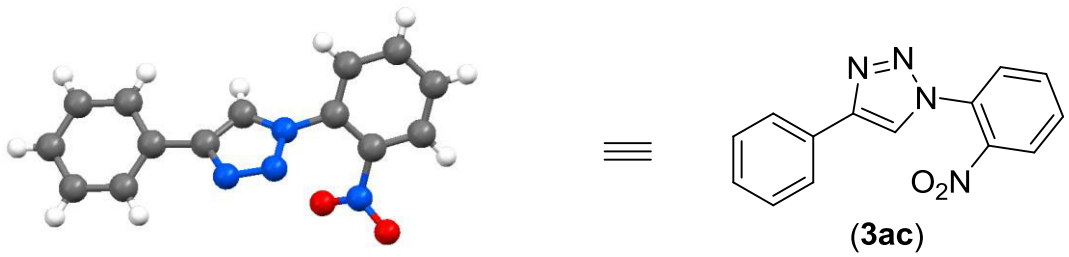
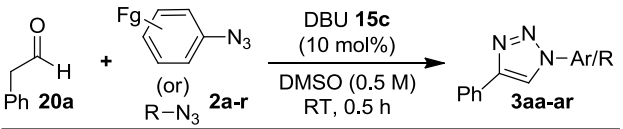


Figure 3: Crystal structure of 1-(2-nitrophenyl)-4-phenyl-1*H*-1,2,3-triazole (**3ac**).

Table 2: Azide scope.[a]



Entry	Ar-N_3 or R-N_3 **2**	Yield **3aa-ar** [%][b]
1	**2c** (Fg = 2-NO_2)	93 (**3ac**)
2	**2d** (Fg = 4-NO_2)	95 (**3ad**)
3	**2e** (Fg = 4-CO_2Et)	93 (**3ae**)
4	**2f** (Fg = 4-CN)	95 (**3af**)
5	**2g** (Fg = 4-CF_3)	95 (**3ag**)
6	**2h** (Fg = 3-CHO)	90 (**3ah**)
7	**2i** (Fg = 4-F)	90 (**3ai**)
8	**2j** (Fg = 4-Cl)	95 (**3aj**)
9	**2k** (Fg = 3-Cl)	93 (**3ak**)
10	**2l** (Fg = 4-Br)	93 (**3al**)
11	**2m** (Fg = 2-Br)	90 (**3am**)
12	**2n** (Fg = 4-Me)	85 (**3an**)
13	**2o** (Ar = 1-Naphthyl)	90 (**3ao**)
14	**2p** (Fg = 4-OMe)	75 (**3ap**)
15[c]	**2p** (Fg = 4-OMe)	80 (**3ap**)
16[c]	**2q** (R = $PhCH_2$)	15 (**3aq**)
17[c,d]	**2r** (R = $EtCO_2$)	60 (**3ar**)
18	**2a** (R = Ts)	– (**3aa**)

[a] Reactions were carried out in DMSO (0.5 M) with 1.5 equiv. of **2a-r** relative to the **20a** (0.5 mmol) in the presence of 10-mol% of **15c**. [b] Yield refers to the column-purified product. [c] *t*BuOK-catalysis at RT for 1-3 h. [d] Decarboxylated 1*H*-1,2,3-triazole **3ar** was obtained.

After clear understanding of the electronic factors of ArN_3/RN_3 **2** in the [3+2]-cycloaddition reaction, we investigated the reaction scope with different 2-arylacetaldehydes **20b-p** in the organo-click reaction with PhN_3 **2b** (Table 3). In this reaction, 2-arylacetaldehydes **20b-p** containing different functional groups, such as NO_2, halogen, alkyl, heteroaryl, and OMe, were used as substrates for the organocatalytic synthesis of the single isomer of 1,2,3-triazoles **3bb-pb** in excellent to good yields within 0.5 h (Table 3).

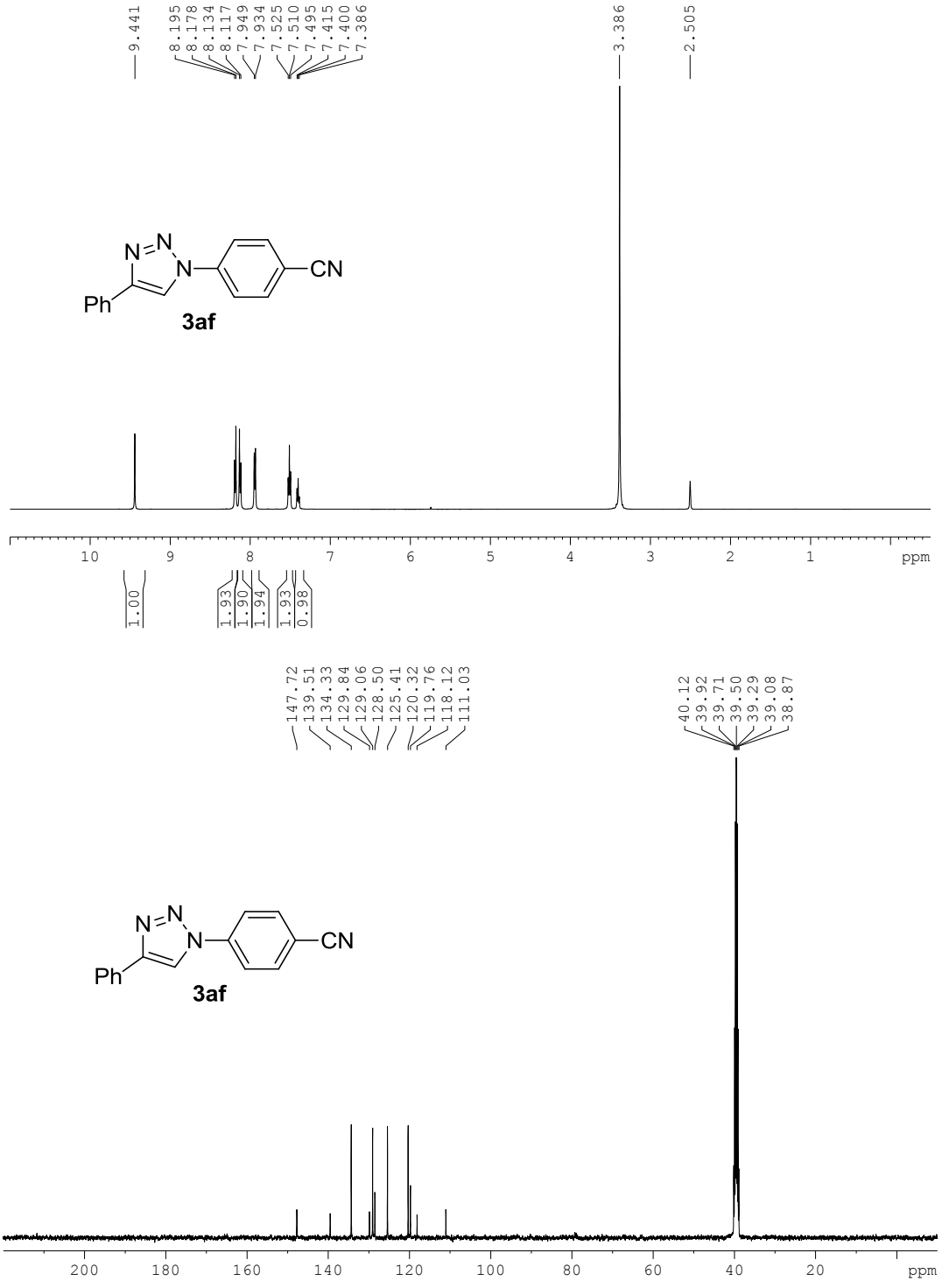


Figure-4: ^{1}H NMR and ^{13}C NMR spectrum of product **3af**.

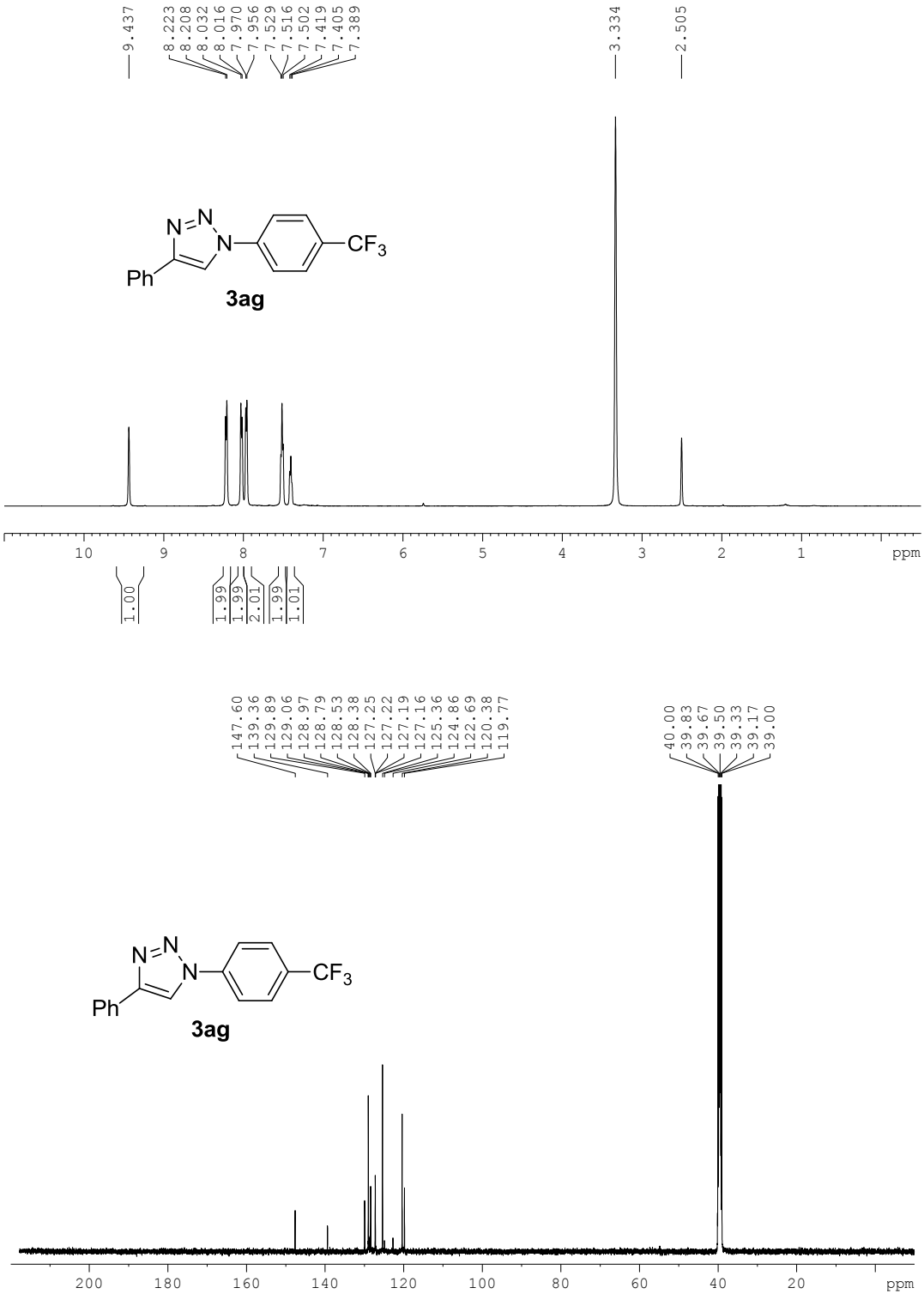


Figure-5: ^{1}H NMR and ^{13}C NMR spectrum of product **3ag**.

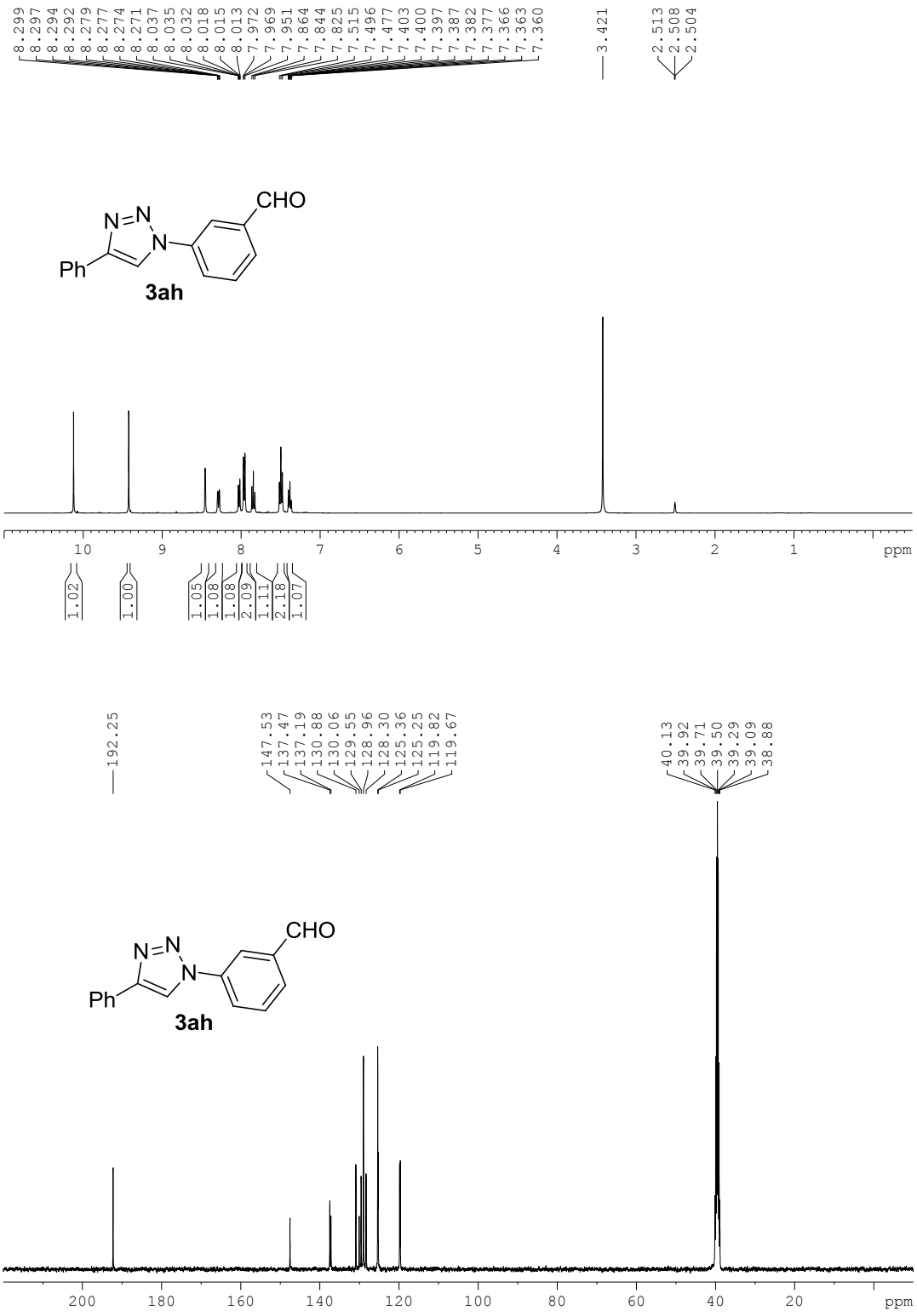


Figure-6: ^{1}H NMR and ^{13}C NMR spectrum of product **3ah**.

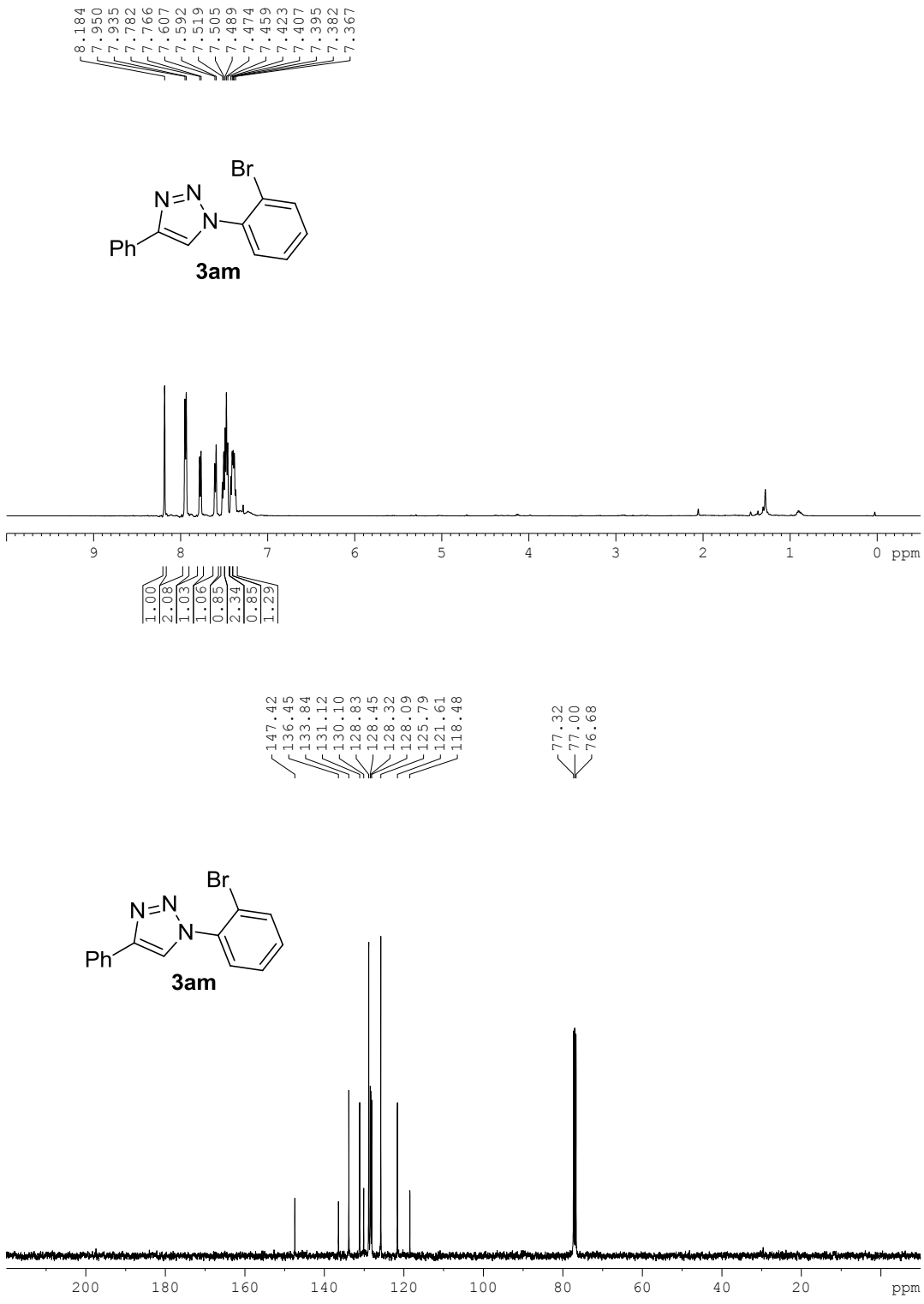


Figure-7: ^{1}H NMR and ^{13}C NMR spectrum of product **3am.**

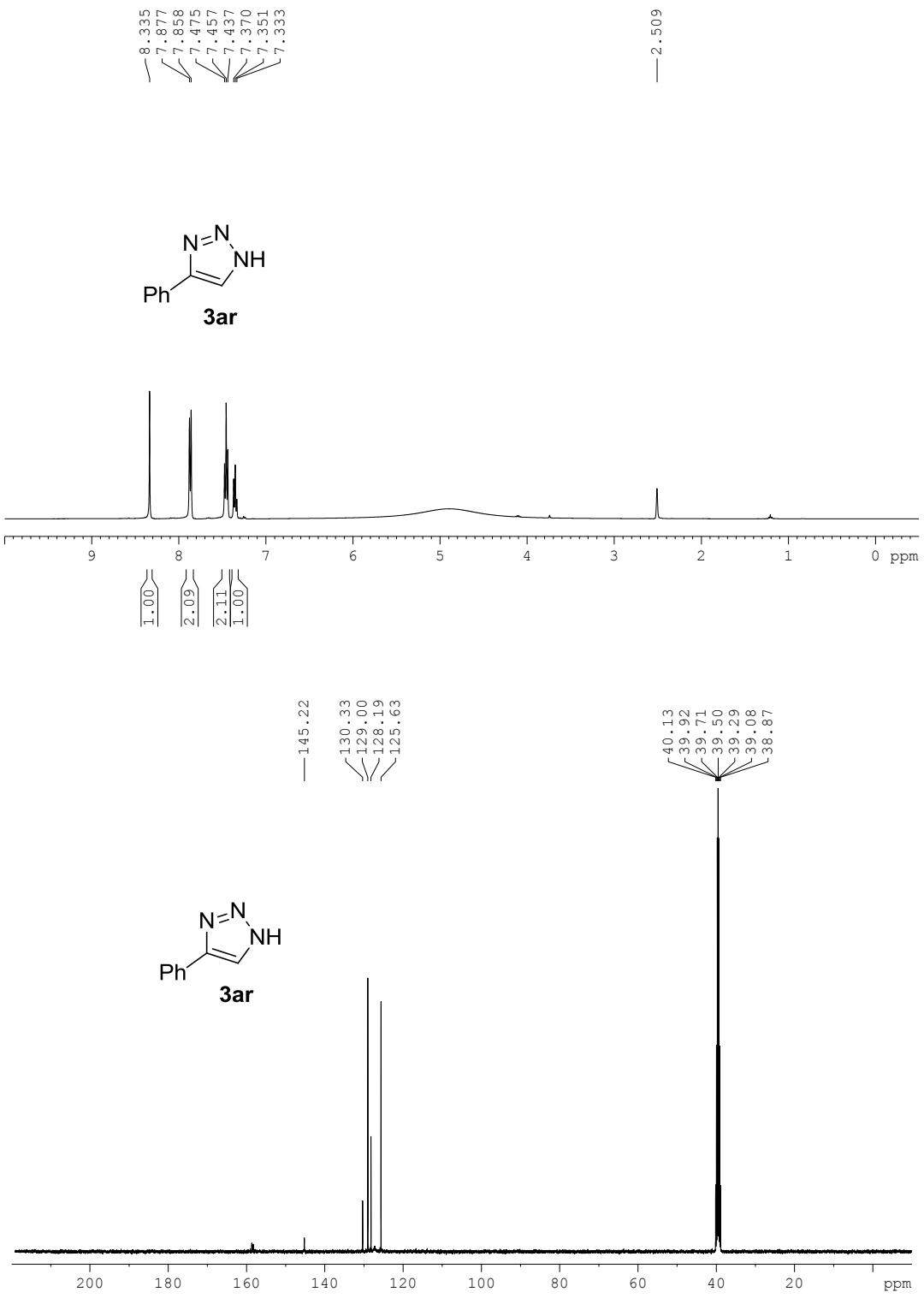
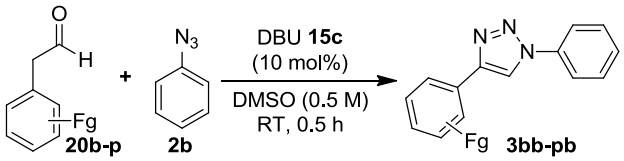


Figure-8: ^{1}H NMR and ^{13}C NMR spectrum of product **3ar.**

Table 3: Aldehyde scope: 2-Arylacetaldehydes.[a]



Entry	Ar-CH_2CHO **20**	Yield **3bb-pb** [%][b]
1	**20b** (Fg = 2-NO_2)	90 (**3bb**)
2	**20c** (Fg = 4-F)	90 (**3cb**)
3	**20d** (Fg = 4-Cl)	90 (**3db**)
4	**20e** (Fg = 2-Cl)	90 (**3eb**)
5	**20f** (Fg = 4-Br)	95 (**3fb**)
6	**20g** (Fg = 2-Br)	92 (**3gb**)
7	**20h** (Fg = 4-Me)	93 (**3hb**)
8	**20i** (Fg = 2-Me)	90 (**3ib**)
9	**20j** (Ar = 2-Naphthyl)	95 (**3jb**)
10	**20k** (Ar = 1*H*-**I**ndol-3-yl)	75 (**3kb**)
11	**20l** (Ar = Thiophen-2-yl)	88 (**3lb**)
12	**20m** (Fg = 4-OMe)	90 (**3mb**)
13	**20n** (Fg = 3-OMe)	80 (**3nb**)
14	**20o** (Fg = 2-OMe)	90 (**3ob**)
15	**20p** [Fg = 3,4-$(OMe)_2$]	75 (**3pb**)

[a] Reactions were carried out in DMSO (0.5 M) with 1.5 equiv. of **2b** relative to the **20b-p** (0.5 mmol) in the presence of 10-mol% of **15c**. [b] Yield refers to the column-purified product.

The results in the Table 3 demonstrate the broad scope of this novel methodology covering a structurally diverse group of 2-arylacetaldehydes **20b-p** and phenyl azide **2b**. Many of the organo-click product **3** yields were obtained very well compared to other routes (Table A1, Annexure-I).

To further understand the importance of the electronic or the acidic nature of α-methylene of aldehydes **20** in the organo-click reaction, we have chosen simple aliphatic aldehydes **20q-x**, which are having less acidic α-methylene compared to 2-arylacetaldehydes **20a-p** (Table 4). Surprisingly, the reaction of 3-phenylpropanaldehyde **20q** with 4-$NO_2C_6H_4N_3$ **2d** under the DBU-catalysis at 25 °C for 0.5 h furnished the expected 1,2,3-triazole **3qd** in 95% yield (Table 4, entry 1).

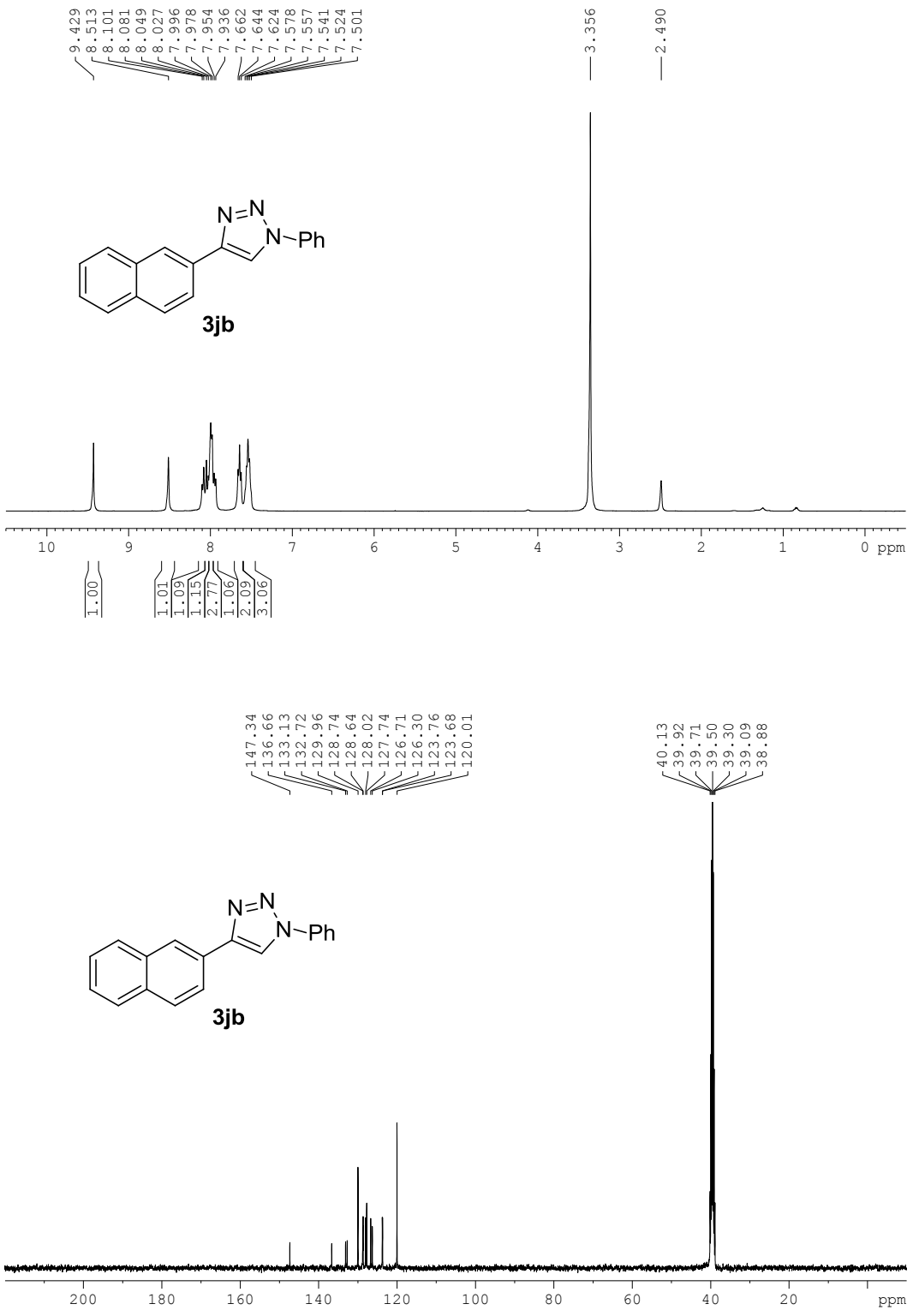


Figure-9: ^{1}H NMR and ^{13}C NMR spectrum of product **3jb.**

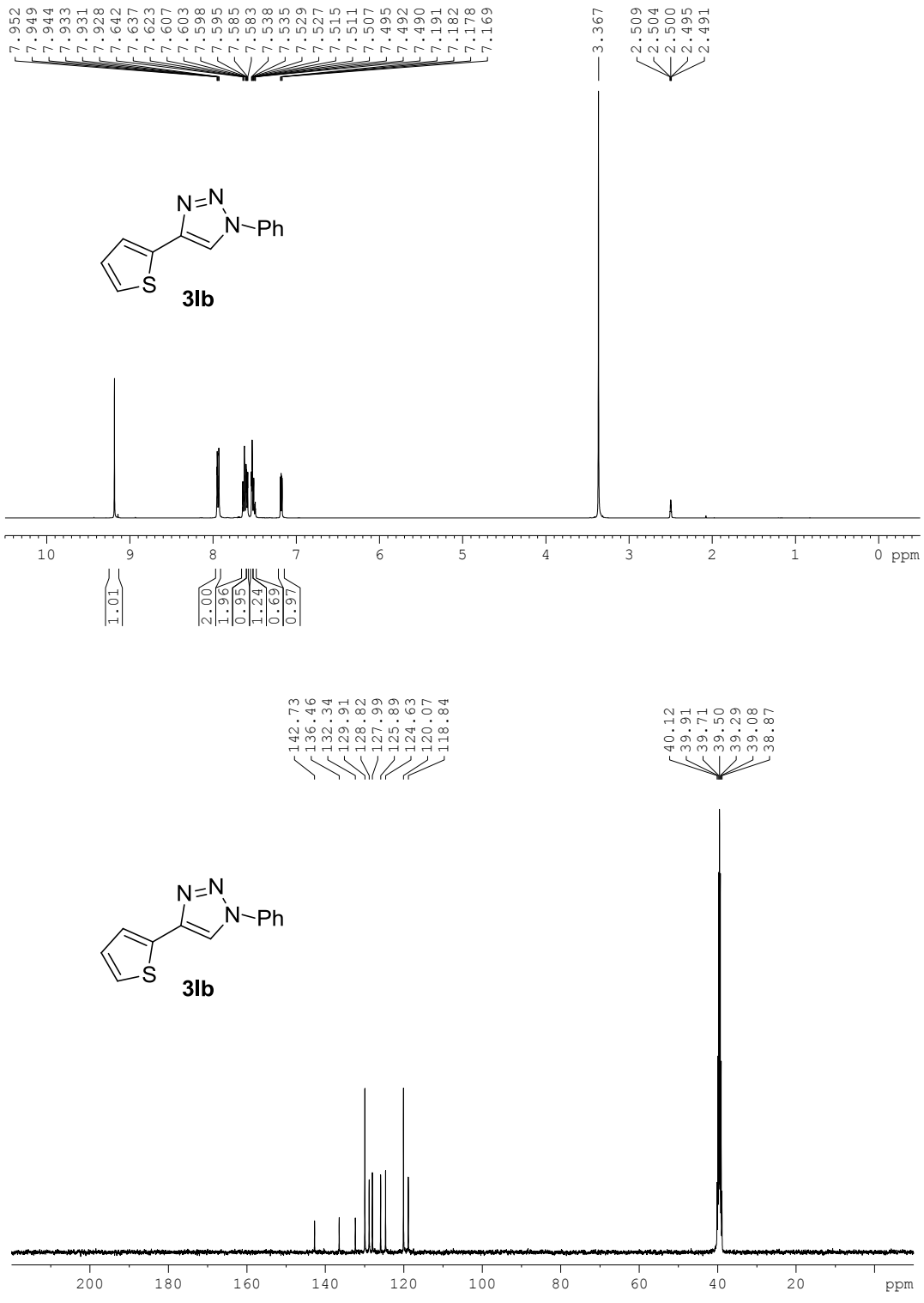


Figure-10: ^{1}H NMR and ^{13}C NMR spectrum of product **3lb.**

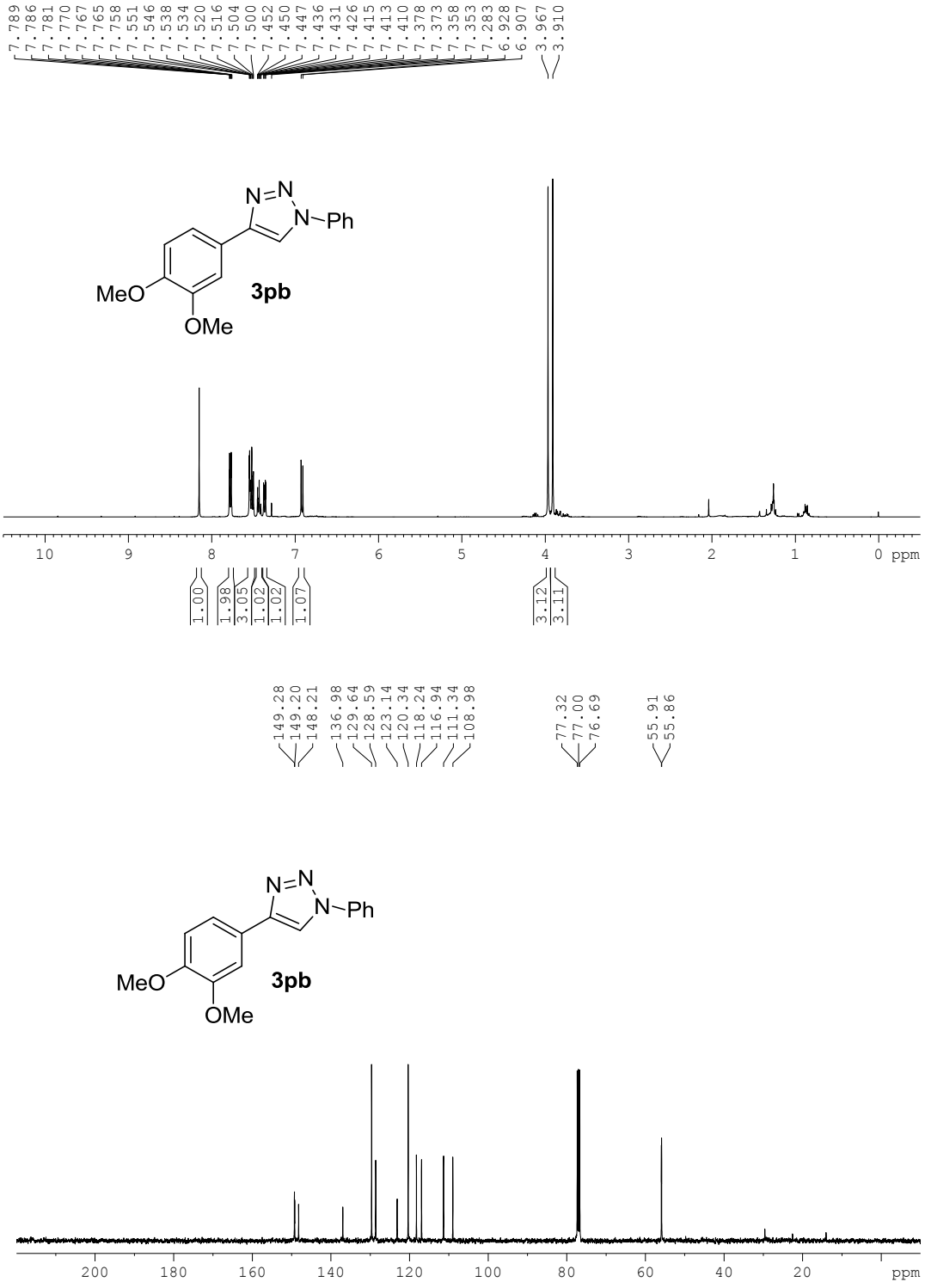
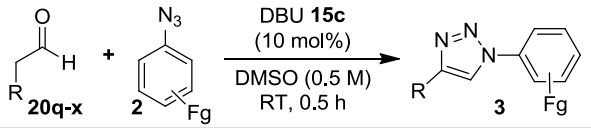


Figure-11: ^{1}H NMR and ^{13}C NMR spectrum of product **3pb.**

Table 4: Aldehyde scope: other aldehydes.[a]



Entry	R-CH_2CHO **20**	Ar-N_3 **2**	Yield **3** [%][b]
1	**20q** (R = $PhCH_2$)	**2d**	95 (**3qd**)
2	**20q** (R = $PhCH_2$)	**2f**	90 (**3qf**)
3	**20r** (R = $MeCH_2$)	**2d**	70 (**3rd**)
4	**20s** (R = $MeCH_2CH_2$)	**2d**	75 (**3sd**)
5	**20t** (R = $MeCH_2CH_2CH_2$)	**2d**	75 (**3td**)
6	**20u** (R = $MeCH_2CH_2CH_2CH_2$)	**2d**	80 (**3ud**)
7	**20v** (R = CH_3)	**2d**	80 (**3vd**)
8	**20w** (R = H)	**2d**	80 (**3wd**)
9	**20x** (R = 1,3-Isoindoledione)	**2d**	– (**3xd**)
10[c]	**20q** (R = $PhCH_2$)	**2b**	60 (**3qb**)
11[d]	**20q** (R = $PhCH_2$)	**2g**	65 (**3qg**)
12[c]	**20q** (R = $PhCH_2$)	**2l**	60 (**3ql**)

[a] Reactions were carried out in DMSO (0.5 M) with 1.5 equiv. of **2** relative to the **20q-x** (0.5 mmol) in the presence of 10-mol% of **15c**. [b] Yield refers to the column-purified product. [c] *t*BuOK-catalysis at RT for 1 h. [d] DBU-catalysis at RT for 0.5 h and 60 °C for 1 h.

In a similar manner, the reaction of butyraldehyde **20r** with 4-$NO_2C_6H_4N_3$ **2d** under the DBU-catalysis furnished the 1,2,3-triazole **3rd** in 70% yield (Table 4, entry 3).We have also tested six more aliphatic aldehydes **20q-w** as substrates for the organo-click reaction with **2d/2f**, which furnished the expected 1,2,3-triazoles **3** in good to excellent yields (Table 4, entries 2-8). Surprisingly, there is no product formation from the reaction of 2-succinimidoacetaldehyde **20x** with **2d** under the **15c**- or **15i**-catalysis (Table 4, entry 9). The organo-click reaction of 3-phenylpropanaldehyde **20q** with less reactive ArN_3 of **2b**, **2g,** and **2l** under the **15c**- or **15i**-catalysis at 25 °C for 1 h furnished the 1,2,3-triazoles **3qb, 3qg,** and **3ql** in 60-65% yields (Table 4, entries 10-12). The industrial scope of this reaction was investigated by performing the gram-scale synthesis of 1,2,3-triazoles **3ab** and **3ah** from the DBU-promoted reaction of 1.0 gram of **20a** with 1.19 grams of **2b** or 1.47 grams of **2h** in

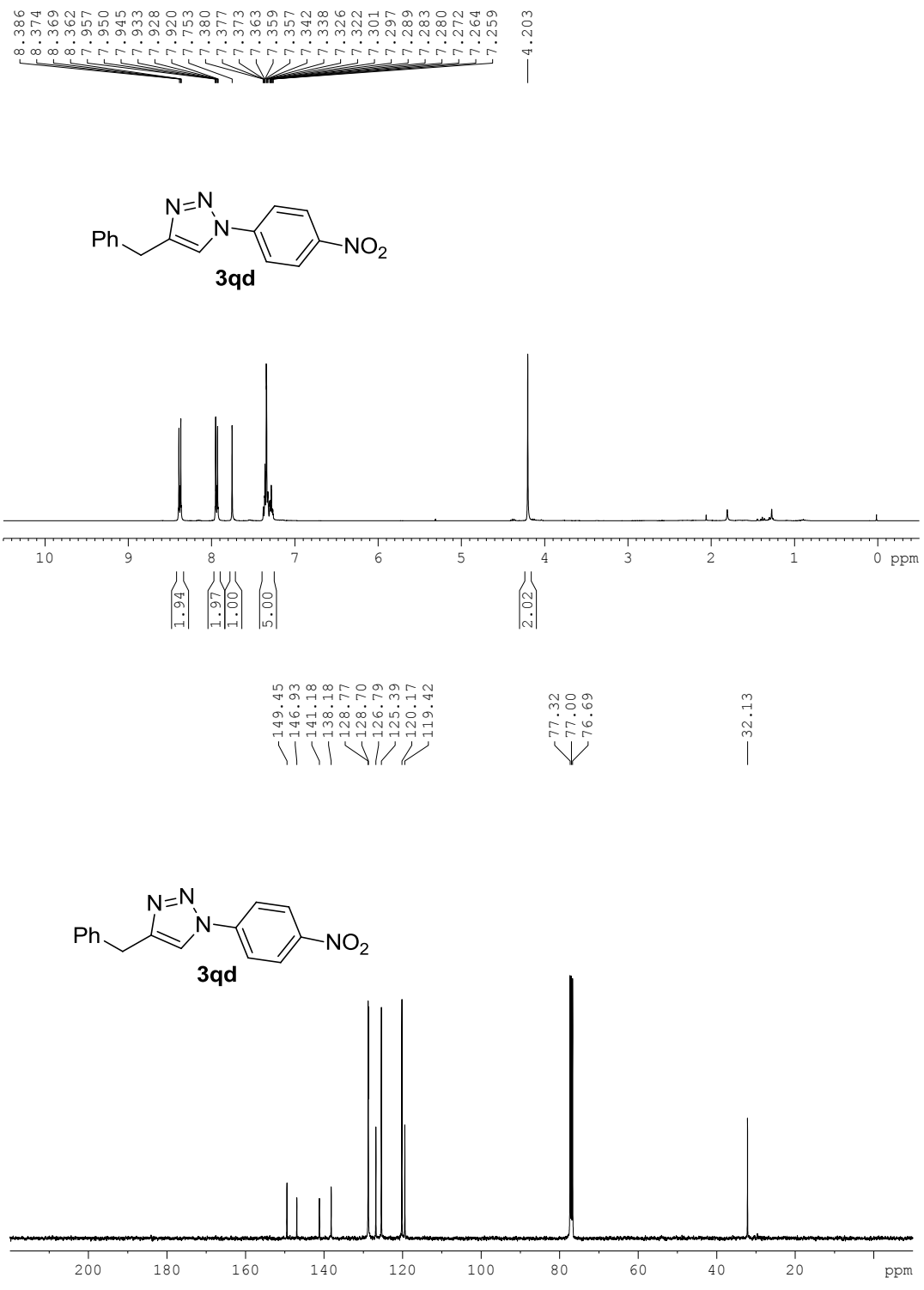


Figure-12: ^{1}H NMR and ^{13}C NMR spectrum of product **3qd.**

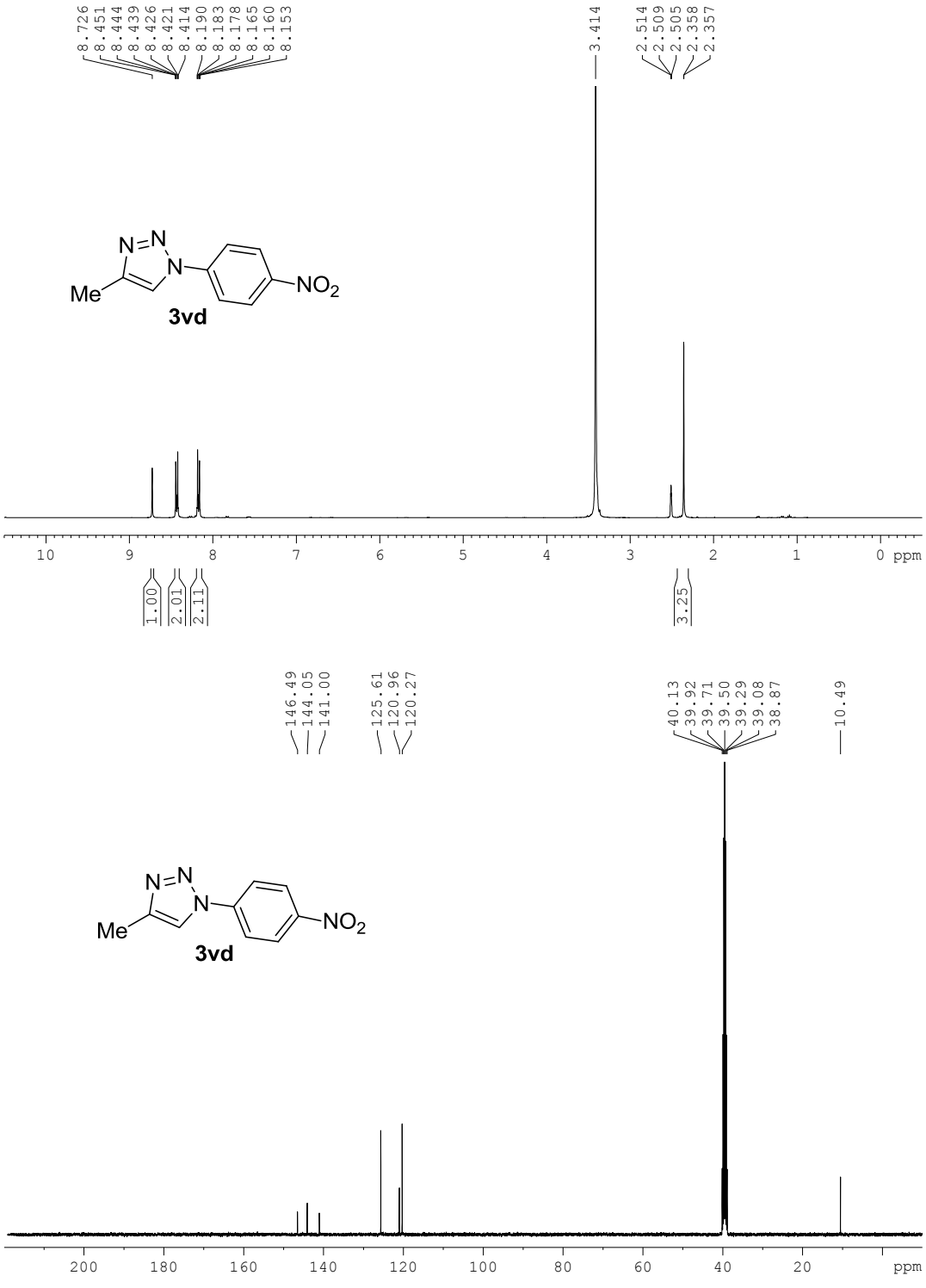


Figure-13: ^{1}H NMR and ^{13}C NMR spectrum of product **3vd.**

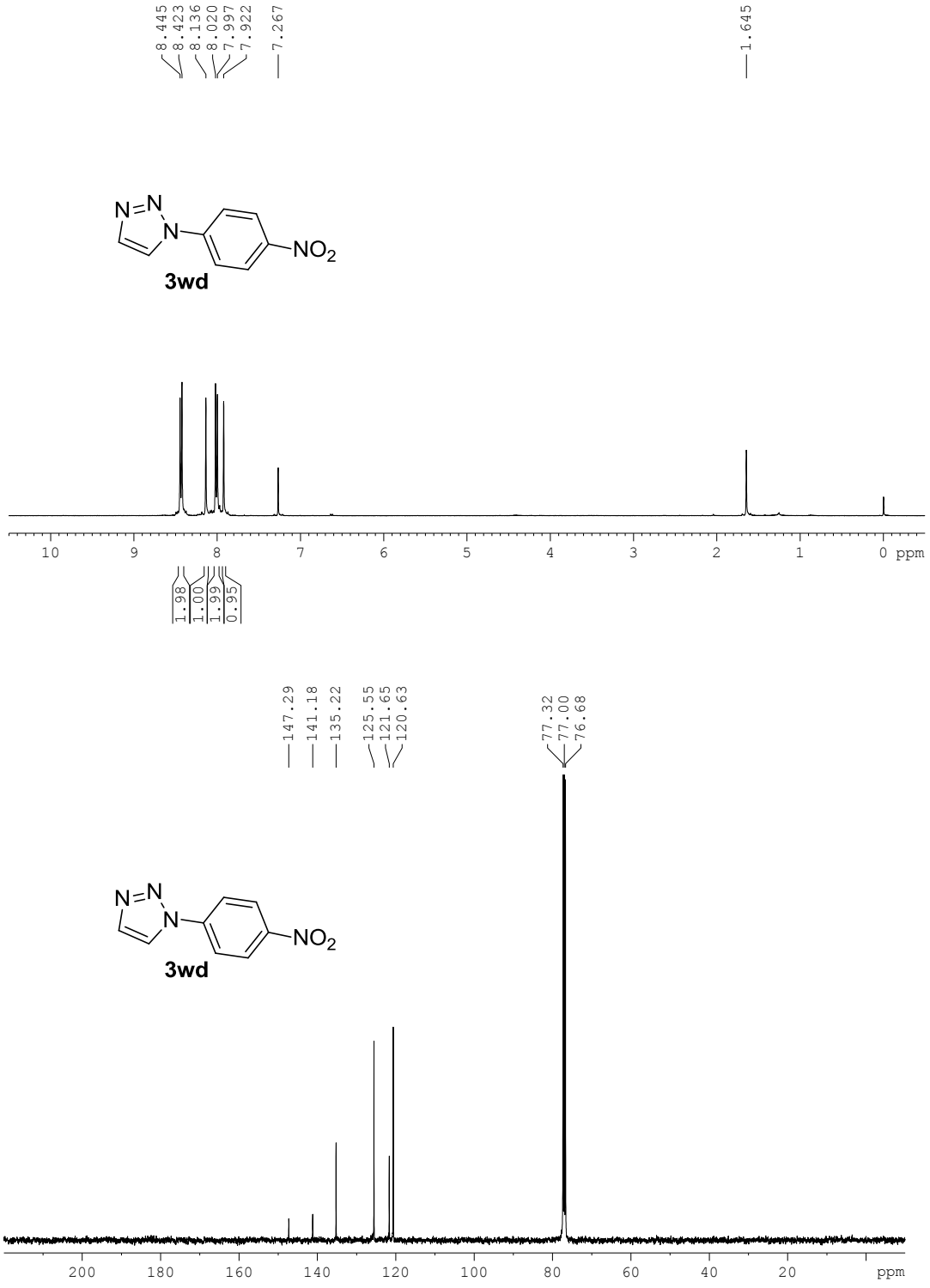
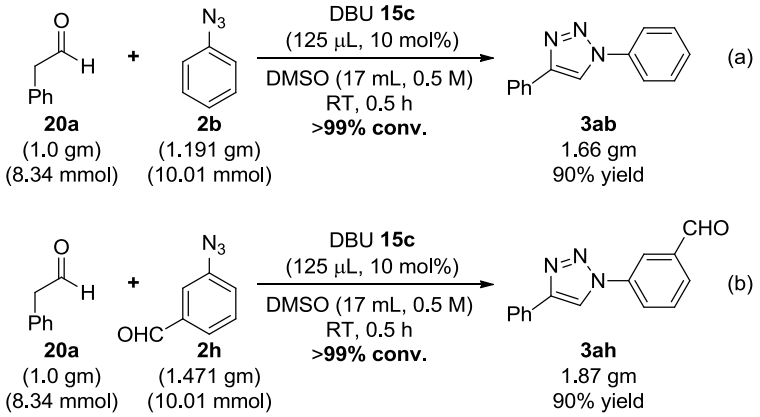


Figure-14: ^{1}H NMR and ^{13}C NMR spectrum of product **3wd.**

17.0 mL of DMSO at 25 °C without compromise in reaction rate, yields and purity (Scheme 2a-b).

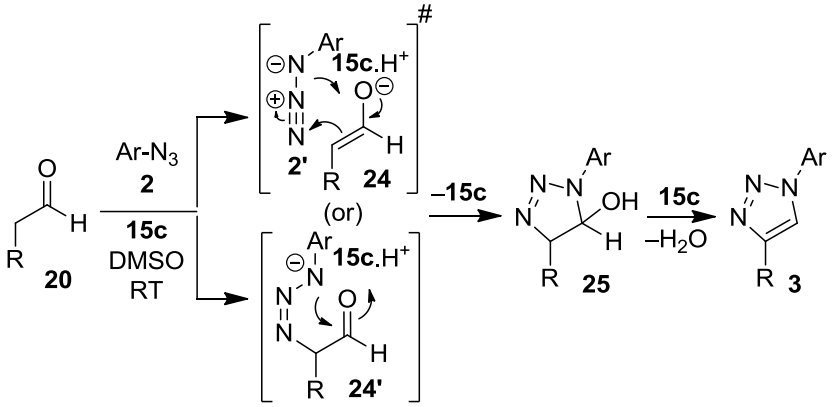
Scheme 2. Gram-scale synthesis of 1,2,3-triazoles **3** through OrgAAC reaction.



3.3 Mechanistic Insights

The possible mechanism for the regioselective synthesis of **3** through the reaction of **20**, **2** and **15c** is illustrated in Scheme 3. Reaction of the catalyst **15c** (pK_a = 12) with aldehyde **20** generates the enolate **24**, which on in situ treatment with probably the major contributing mesomeric structure of Ar-N_3 **2'** furnishes selectively the adduct 1,2,3-triazolines **25** *via* concerted [3+2]-cycloaddition or stepwise amination-cyclization reaction,[16]

Scheme 3. Mechanism of organo-click reaction.



which further transforms into the 1,2,3-triazole **3** through rapid elimination of water induced by the basic nature of **15c**.

3.4 Conclusions

In conclusion, we have developed the metal-free DBU-catalyzed regioselective synthesis of 1,4-disubstituted 1,2,3-triazoles **3** from the simple aldehydes **20** and aryl azides **2** *via* [3+2]-cycloaddition reaction. The organo-click reaction proceeds in very good yields with high rate and selectivity using DBU as the catalyst within 0.5 h at RT.

In continuation to the organocatalytic enolate-mediated azide-aldehyde [3+2]-cycloaddition reaction, organocatalytic azide-ketone [3+2]-cycloaddition (OrgAKC) reaction was developed for the synthesis of fully decorated 1,2,3-triazoles and the results are presented in the next chapter.

ANNEXURE-I

***Table A1*:** Correlation of **Organo-Click** (**OrgAAC**) reaction with **CuAAC** reaction.

Entry	Ref.	Product	CuAAC condition	OrgAAC condition
1	18	**3ab**	25 ^{o}C, 0.33 h, 98%	25 ^{o}C, 0.5 h, 95%
2	19	**3ac**	25 ^{o}C, 8 h, 92%	25 ^{o}C, 0.5 h, 93%
3	20	**3ad**	70 ^{o}C, 4 h, 92%	25 ^{o}C, 0.5 h, 95%
4	21	**3ae**	70 ^{o}C, 4 h, 90%	25 ^{o}C, 0.5 h, 93%
5	22	**3af**	80 ^{o}C, 0.17 h, 92%	25 ^{o}C, 0.5 h, 95%
6	20,23	**3ag**	70 ^{o}C, 3 h, 66%	25 ^{o}C, 0.5 h, 95%
7	24	**3ah**	25 ^{o}C, 1 h, 88%	25 ^{o}C, 0.5 h, 90%
8	23	**3ai**	25 ^{o}C, 12 h, 75%	25 ^{o}C, 0.5 h, 90%
9	25	**3aj**	25 ^{o}C, 5 h, 91%	25 ^{o}C, 0.5 h, 95%
10	18	**3ak**	25 ^{o}C, 0.5 h, 98%	25 ^{o}C, 0.5 h, 93%
11	26	**3al**	25 ^{o}C, 2 h, 71%	25 ^{o}C, 0.5 h, 93%
12	18	**3am**	25 ^{o}C, 5 h, 97%	25 ^{o}C, 0.5 h, 90%
13	25	**3an**	25 ^{o}C, 2 h, 95%	25 ^{o}C, 0.5 h, 85%
14	25	**3ao**	25 ^{o}C, 4 h, 90%	25 ^{o}C, 0.5 h, 90%
15	18	**3ap**	25 ^{o}C, 2 h, 99%	25 ^{o}C, 0.5 h, 75%
16	27	**3cb**	25 ^{o}C, 0.33 h, 95%	25 ^{o}C, 0.5 h, 90%
17	28	**3fb**	25 ^{o}C, 1.5 h, 77%	25 ^{o}C, 0.5 h, 95%
18	29	**3gb**	60 ^{o}C, 24 h, 59%	25 ^{o}C, 0.5 h, 92%
19	30	**3hb**	25 ^{o}C, 0.3 h, 94%	25 ^{o}C, 0.5 h, 93%
20	31	**3lb**	50 ^{o}C, 15 h, 94%	25 ^{o}C, 0.5 h, 88%
21	32	**3mb**	25 ^{o}C, 10 h, 99%	25 ^{o}C, 0.5 h, 90%
22	33	**3rd**	65 ^{o}C, 24 h, 75%	25 ^{o}C, 0.5 h, 70%

4. An Enolate-mediated Organocatalytic Azide-Ketone [3 + 2]-Cycloaddition Reaction: Regioselective High-yielding Synthesis of Fully Decorated 1,2,3-Triazoles

4.1 Introduction

Even though the thermally-induced Huisgen [3+2]-cycloaddition of alkynes with azides has been known for over one century to make 1,2,3-triazoles, these compounds came to the limelight only in the last two decades due to their excellent copper-catalyzed regioselective synthesis developed by the Meldal and Sharpless groups.[7] Recently 1,2,3-triazoles have become important compounds with unique chemical and physical properties and are widely used as pharmaceuticals.[14] Many of the 1,2,3-triazoles have found wide range applications in medicinal, organic, bio-organic, polymer and material chemistry.[14] Design and utilization of 1,2,3-triazoles has mainly depended on their 1,4-disubstitutions or 1,4,5-trisubstitutions and for to this reason, the development of more general catalytic methods for their selective fully decorated synthesis is of significant interest (Fig. 15).[34]

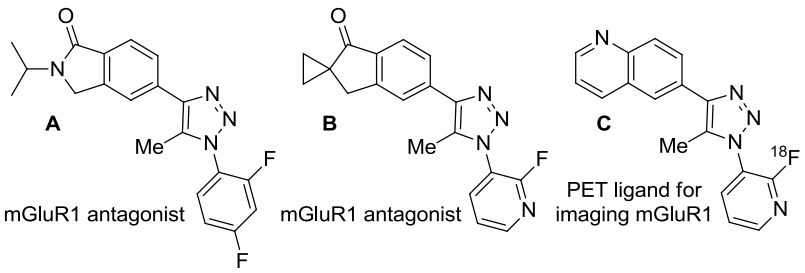
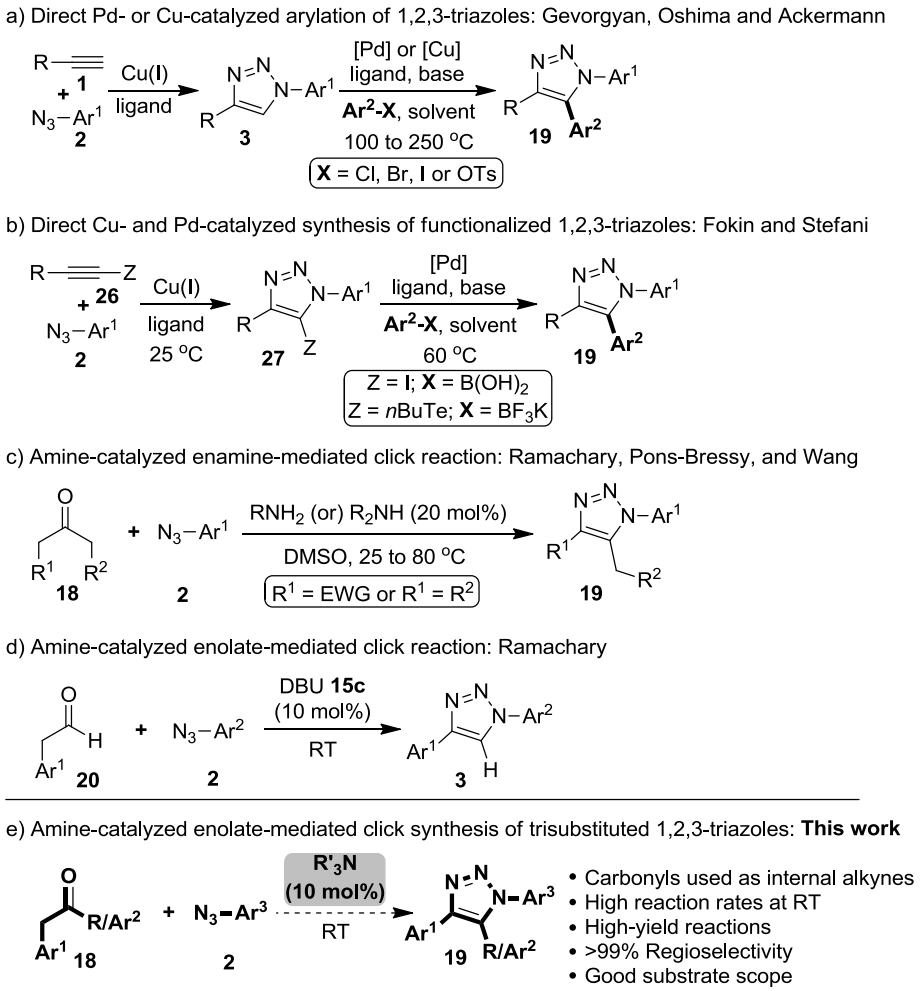


Figure 15: Pharmaceutically active 1,4,5-trisubstituted 1,2,3-triazoles **A-C**.

For example, 1,4-diaryl-5-methyl(alkyl) 1,2,3-triazoles have significant role in pharmaceutical chemistry (Fig. 15) and herein, we have shown interest to develop a single-step general protocol for their high-yielding regioselective synthesis. Very little is known about the regioselective synthesis of 1,4-diaryl-5-methyl(alkyl) 1,2,3-triazoles. When we analyzed the previous approaches, we found that metal-catalyzed or thermally-

induced coupling reactions of internal alkynes with aryl azides lack regioselectivity and also generality.[35] An alternative approach to such 1,4-diaryl-5-methyl(alkyl) 1,2,3-triazoles is the use of in situ generated metalated triazoles, in which metal acetylides (metal = Li, Mg, Zn and Te) were treated with organic azides followed by further in situ reaction with various electrophiles.[36]

Scheme 4. Reaction design for the enolate-mediated OrgAKC reaction.



However, this approach is limited because of the reverse selectivity and high reactivity of the metalated triazoles. Other routes include palladium- or copper-catalyzed arylation of 1,4-disubtituted 1,2,3-triazoles with aryl halides (Scheme 4a),[15g,37] and/or the copper-catalyzed cycloaddition of organic azides with 1-iodoalkynes or 1-*n*butyltelluro alkynes followed by palladium-catalyzed arylation of the corresponding 5-iodo-1,2,3-

triazoles or 5-telluro-1,2,3-triazoles with arylboronic acid or potassium aryltrifluoroborates, respectively (Scheme 4b).[38] Alternative routes include bulky ruthenium-catalyzed azide–internal alkyne cycloaddition reactions,[11] condensation of *N*-tosylhydrazones and anilines under stoichiometric amount of copper salts and excess additives at higher temperatures,[39] and amine/acid-catalyzed three-component condensation of aldehydes, nitroalkanes/malononitrile, and organic azides at higher temperatures for longer reaction times.[13,40] A strain-promoted [3+2]-cycloaddition reaction of aryl azides with functionalized cyclooctyne,[12] and amino acid-catalyzed enamine-mediated azide-carbonyl [3+2]-cycloaddition reaction of active methylenes or symmetrical ketones with aryl azides to furnish the 1,4,5-trisubstituted 1,2,3-triazoles at higher temperatures (Scheme 4c).[4,5a]

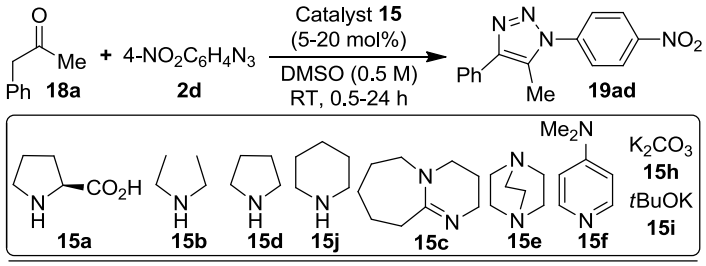
In many of the above methods, either they used costly and less reactive alkynes or non-commercial substrates other than the simple arylacetones as starting materials. Also requirement of toxic transition metal catalysts, heavy ligands and reagents, higher temperatures, longer reaction times and loading stoichiometric amount of catalysts made above reaction conditions inferior. These drawbacks inspired us to develop a general metal-free protocol for the high-yielding regioselective synthesis of 1,4-diaryl-5-methyl(alkyl) 1,2,3-triazoles by using recently discovered enolate-mediated organocatalytic click reaction (Scheme 4d).[5b] Herein, we disclosed general, rapid, and operationally simple either enamine- or enolate-mediated organocatalytic azide-ketone [3+2]-cycloaddition (OrgAKC) reaction for the chemo- and regioselective synthesis of fully decorated 1,2,3-triazoles from the easily available arylacetones/deoxybenzoins, aryl azides and catalytic amount of *sec*-amine or *tert*-amine (Scheme 4e).

4.2 Results and Discussion

We commenced the prior optimization of the OrgAKC reaction by screening simple catalysts for the organo-click reaction of phenylacetone **18a** with 1.5 equiv. of 4-$NO_2C_6H_4N_3$ **2d** (Table 5). Reaction of **18a** with **2d** in DMSO under 20 mol% of proline **15a**-catalysis at RT for 11 h furnished the expected product **19ad** as single regioisomer in only 23% yield (Table 5, entry 1). The same reaction at RT for 2 h under the 20 mol% of diethyl amine **15b**, pyrrolidine **15d** or piperidine **15j**-catalysis furnished the fully substituted 1,2,3-triazole **19ad** in 85, 90 and 90% yields, respectively (Table 5, entries 2-4). But on decreasing the catalyst **15d** loading from 20 mol% to 10 or 5 mol%, the reaction became inferior with respect to rate

and yield (Table 5, entries 5 and 6). After obtaining moderate results with catalysts **15a-b, 15d, 15j** through enamine-formation, we thought of exploring the same reaction through in situ enolate formation, for which we tested some *tert*-amines **15c, 15e-f** and non-amine bases **15h-i** as the catalysts for the OrgAKC reaction (Table 5).[5b] Intriguingly, the reaction of **18a** with **2d** in DMSO under 20 mol% of DBU **15c**-catalysis at 25 °C for 0.5 h furnished **19ad** in 97% yield (Table 5, entry 7). Surprisingly, the same reaction with 10 mol% of **15c**-catalysis also furnished **19ad** in 95% yield within 0.5 h (Table 5, entry 8). But the same OrgAKC reaction under the catalysis of relatively less basic *tert*-amines, DABCO **15e** or DMAP **15f** furnished **19ad** in poor yields (Table 5, entries 9 and 10).

Table 5: Reaction optimization.[a]



Entry	Catalyst **15** [5-20 mol-%]	Time [h]	Yield **19ad** [%][b]
1	**15a** (20 mol%)	11	23
2	**15b** (20 mol%)	2	85
3	**15d** (20 mol%)	2	90
4	**15j** (20 mol%)	2	90
5	**15d** (10 mol%)	8	50
6	**15d** (5 mol%)	9	25
7	**15c** (20 mol%)	0.5	97
8	**15c (10 mol%)**	**0.5**	**95**
9	**15e** (20 mol%)	24	40
10	**15f** (20 mol%)	24	30
11	**15h** (10 mol%)	0.5	60
12	**15i (10 mol%)**	**0.5**	**90**
13	**19ad** (20 mol%)	24	–
14	–	24	–

[a] Reactions were carried out in solvent (0.5 M) with 1.5 equiv. of **2d** relative to the **18a** (0.5 mmol) in the presence of 5-20-mol% of catalyst **15**. [b] Yield refers to the column-purified product.

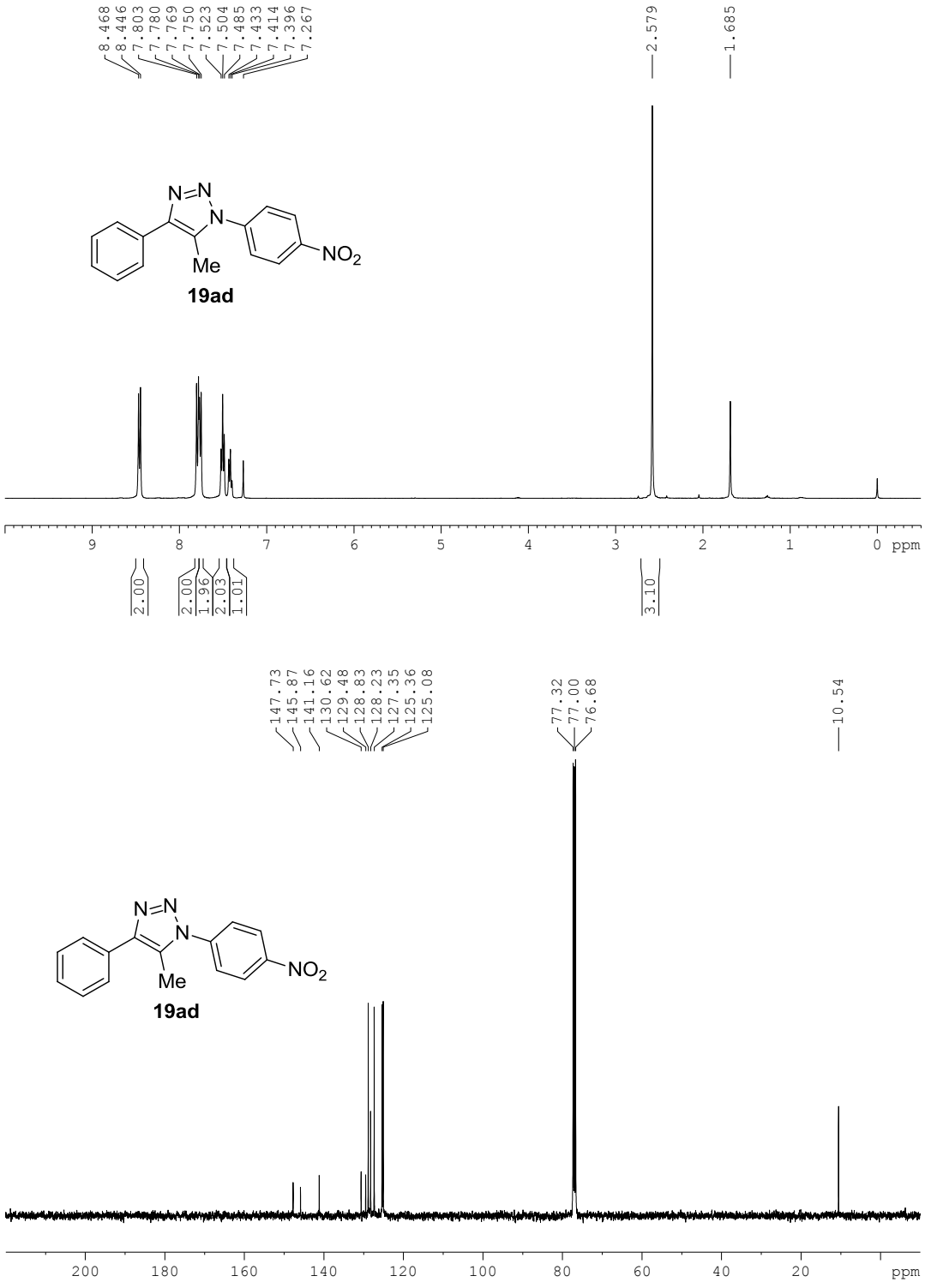


Figure-16: ^{1}H NMR and ^{13}C NMR spectrum of product **19ad**.

Interestingly, the same reaction under 10 mol% of non-amine bases, K_2CO_3 **15h** and *t*BuOK **15i**-catalysis also furnished the 1,2,3-triazole **19ad** in moderate to good yields (Table 5, entries 11-12). There was no reaction observed under the self- or autocatalytic conditions in DMSO for 24 h at 25 °C (Table 5, entry 13 and 14). Finally we envisioned the optimized condition to be 25 °C in DMSO under 10 mol% of **15c**-catalysis to furnish the single isomer of fully decorated 1,2,3-traizole **19ad** in 95% yield from **18a** and **2d** (Table 5, entry 8).

With the best conditions in hand, the generality of the enolate-mediated OrgAKC reaction was investigated. First, various aryl and alkyl azides **2a**-**s** were reacted with phenylacetone **18a** catalyzed by 10 mol% of DBU **15c** at 25 °C in DMSO for 0.5-2 h (Table 6). Fascinatingly, the aryl azides containing different functional groups (H, alkyl, halogen, EWG, and EDG) **2b**-**p** furnished the expected fully substituted 1,2,3-triazoles **19ab-ap** in excellent yields within 0.5-2 h (Table 6). Yields of the 1,2,3-triazoles **19ab-ap** were obtained in a similar manner for different aryl azides **2**, but the reaction rate slightly decreased with *ortho*-substitution and also for EDG substitution. Interestingly, DBU **15c**-catalyzed OrgAKC reaction of **18a** with benzyl/acyl/tosyl/mesyl azides **2q-r, 2a** and **2s** did not furnish the expected products **19**, but the same reaction under *t*BuOK **15i**-catalysis furnished the triazole **19aq** in 90%, decarboxylated triazole **19ar'** along with ester triazole **19ar** in 90% and **19aa/19as** was not formed at all (Table 6, entries 15-18). The structure and the regiochemistry of the OrgAKC products **19ab-ar** were confirmed by NMR analysis (for example Fig. 16-22) and also finally confirmed by the X-ray structure analysis on **19ap** as shown in Figure 17.[41]

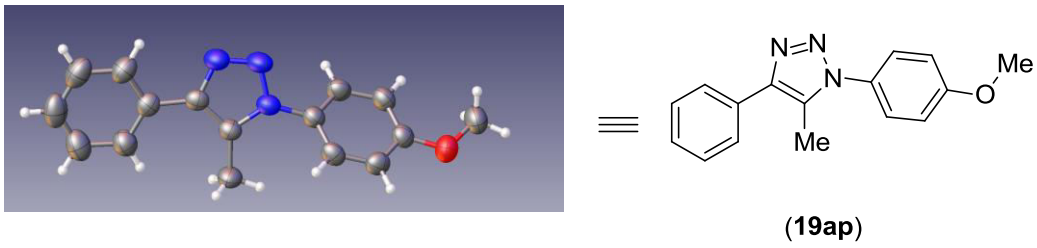
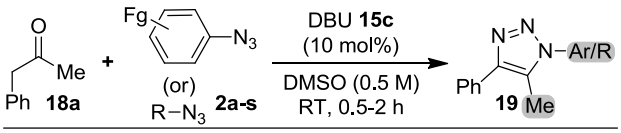


Figure 17: Crystal structure of 1-(4-methoxyphenyl)-5-methyl-4-phenyl-1*H*-1,2,3-triazole (**19ap**).

Table 6: Azide scope with phenylacetone **18a**.[a]



Entry	Ar-N_3 (or) R-N_3 **2**	Yield **19** [%][b]
1	**2b** (Fg = H)	90 (**19ab**)
2	**2c** (Fg = 2-NO_2)	90 (**19ac**)
3	**2e** (Fg = 4-CO_2Et)	95 (**19ae**)
4	**2f** (Fg = 4-CN)	92 (**19af**)
5	**2g** (Fg = 4-CF_3)	92 (**19ag**)
6	**2h** (Fg = 3-CHO)	80 (**19ah**)
7	**2i** (Fg = 4-F)	90 (**19ai**)
8	**2j** (Fg = 4-Cl)	92 (**19aj**)
9	**2k** (Fg = 3-Cl)	93 (**19ak**)
10	**2l** (Fg = 4-Br)	90 (**19al**)
11	**2m** (Fg = 2-Br)	70 (**19am**)
12	**2n** (Fg = 4-Me)	89 (**19an**)
13	**2o** (Ar = 1-Naphthyl)	90 (**19ao**)
14	**2p** (Fg = 4-OMe)	90 (**19ap**)
15[c]	**2q** (R = Bn)	90 (**19aq**)
16[c,d]	**2r** (R = CO_2Et)	90 (**19ar**)
17	**2a** (R = Ts)	– (**19aa**)
18	**2s** (R = Ms)	– (**19as**)

[a] Reactions were carried out in DMSO (0.5 M) with 1.5 equiv. of **2a-s** relative to the **18a** (0.5 mmol) in the presence of 10-mol% of **15c**. [b] Yield refers to the column-purified product. [c] *t*BuOK-catalysis at RT for 1 h. [d] 1.5:1 ratio of decarboxylated triazole **19ar'** and ester triazole **19ar** were obtained, respectively.

After comprehending the OrgAKC reaction by probing the electronic factors of alkyl or aryl azides **2a-s** with **18a**, we further showed interest to investigate the electronic factors of aryl azides **2b-p** with deoxybenzoin **18b** in the OrgAKC reaction (Table 7). Stimulatingly, the reaction of aryl azides **2b-p** containing different functional groups of alkyl, halogen, EWG's, and EDG's with deoxybenzoin **18b** under 10 mol% of **15c**-catalysis furnished the single isomer of 1,4,5-trisubstituted-1,2,3-triazoles **19bb-bp** in excellent yields within 0.5-2 h at 25 °C similar to phenylacetone **18a** (Table 7). The Table 7 results demonstrate the broad

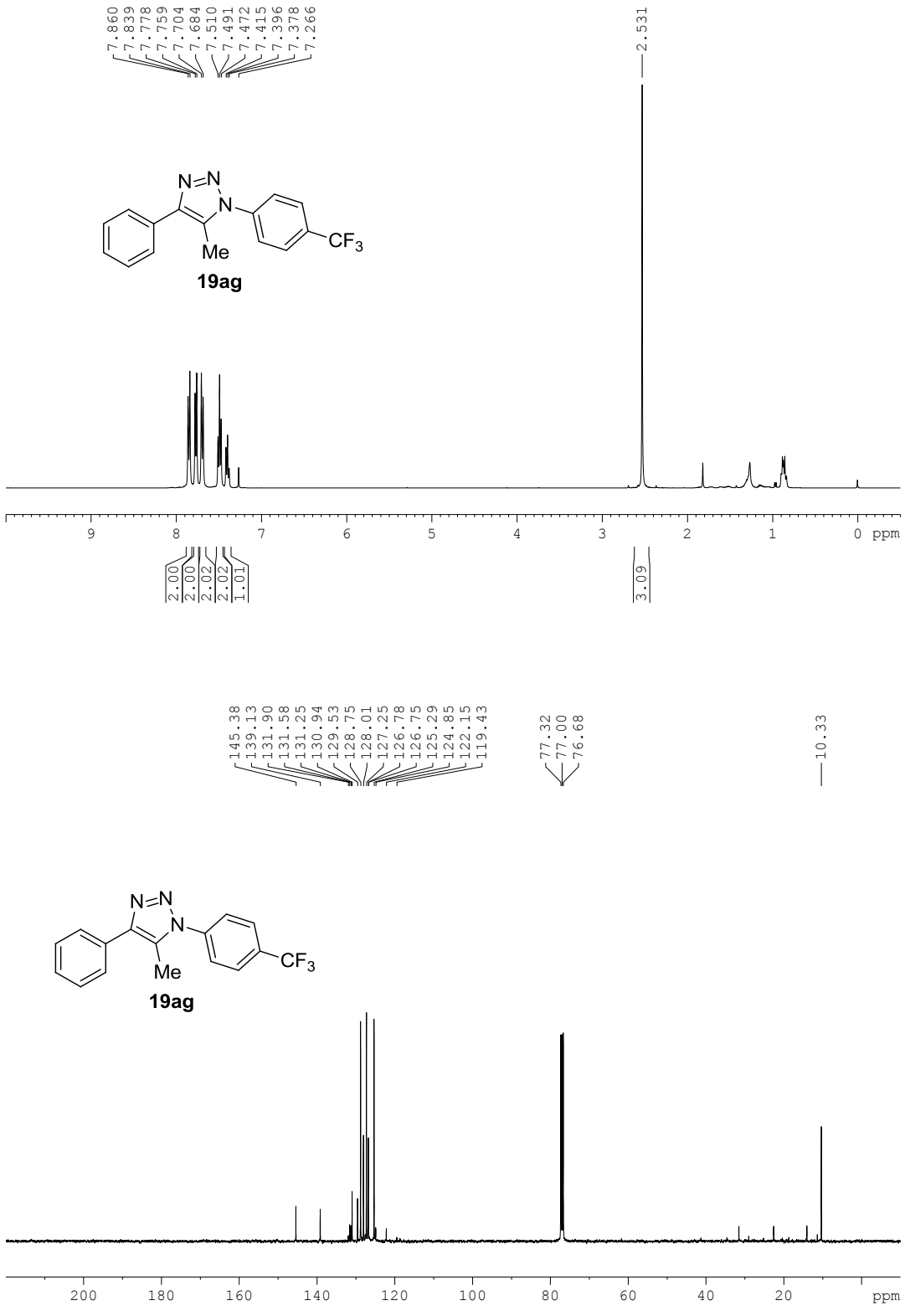


Figure-18: ^{1}H NMR and ^{13}C NMR spectrum of product **19ag**.

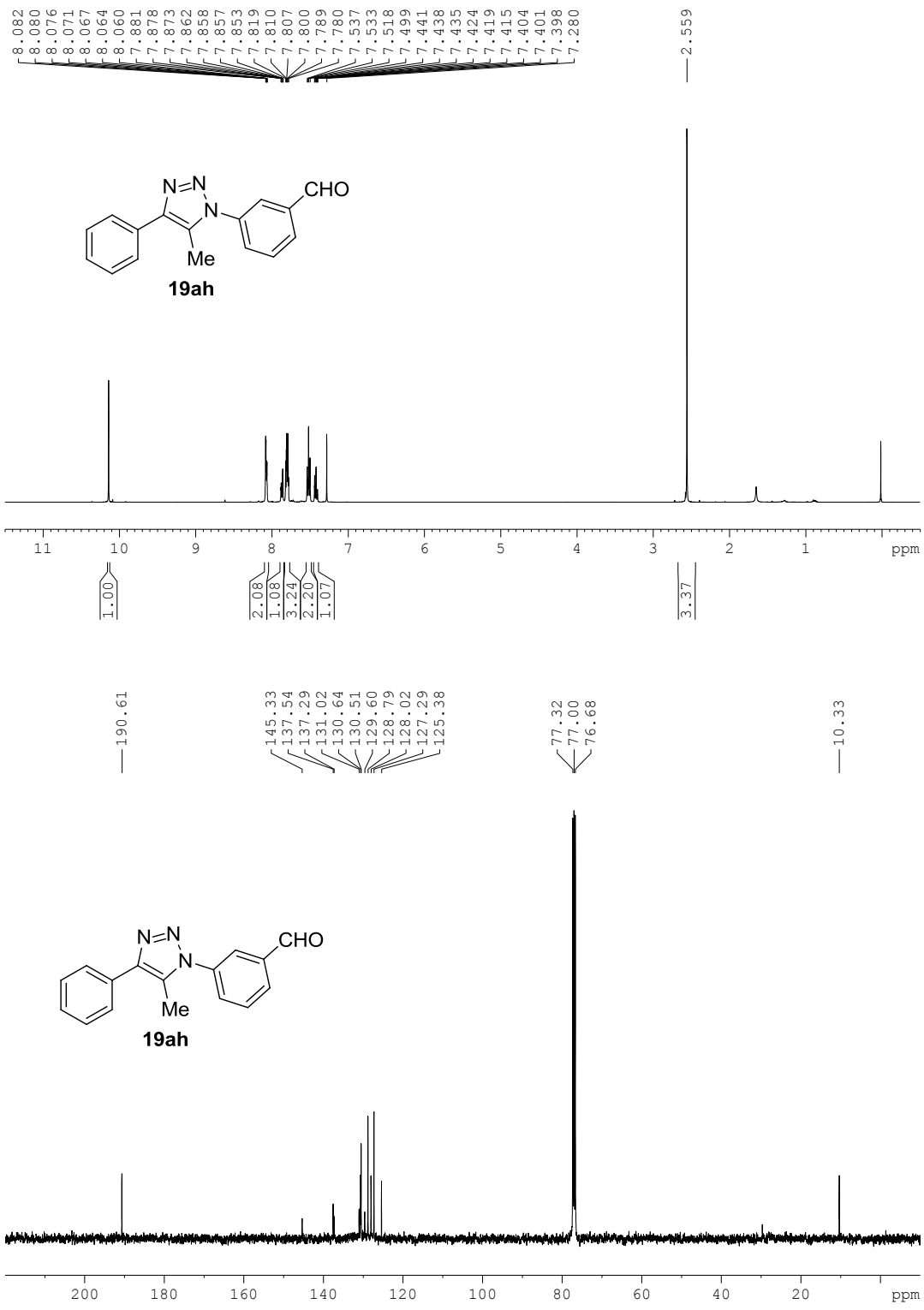


Figure-19: ^{1}H NMR and ^{13}C NMR spectrum of product **19ah**.

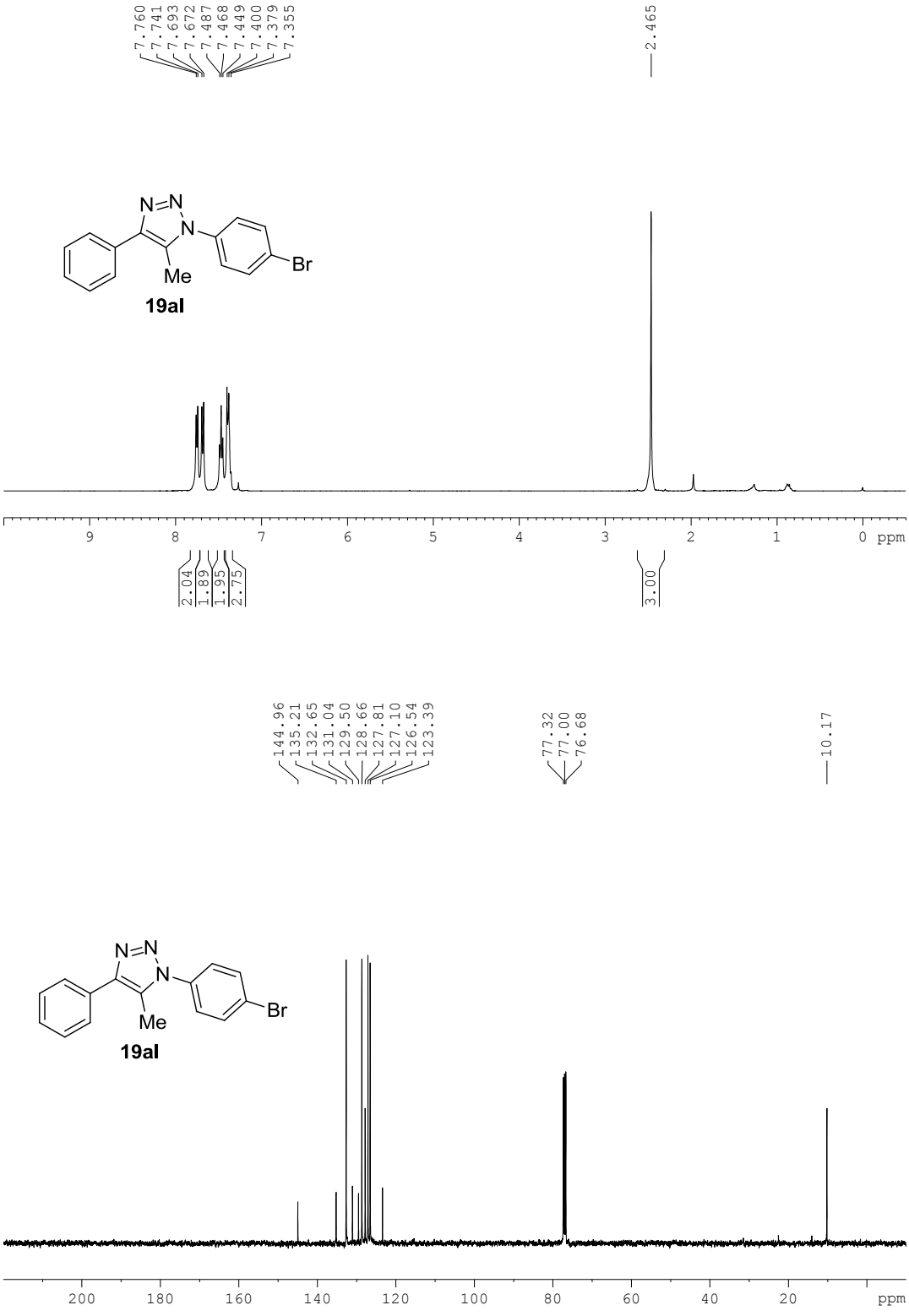


Figure-20: ^{1}H NMR and ^{13}C NMR spectrum of product **19al**.

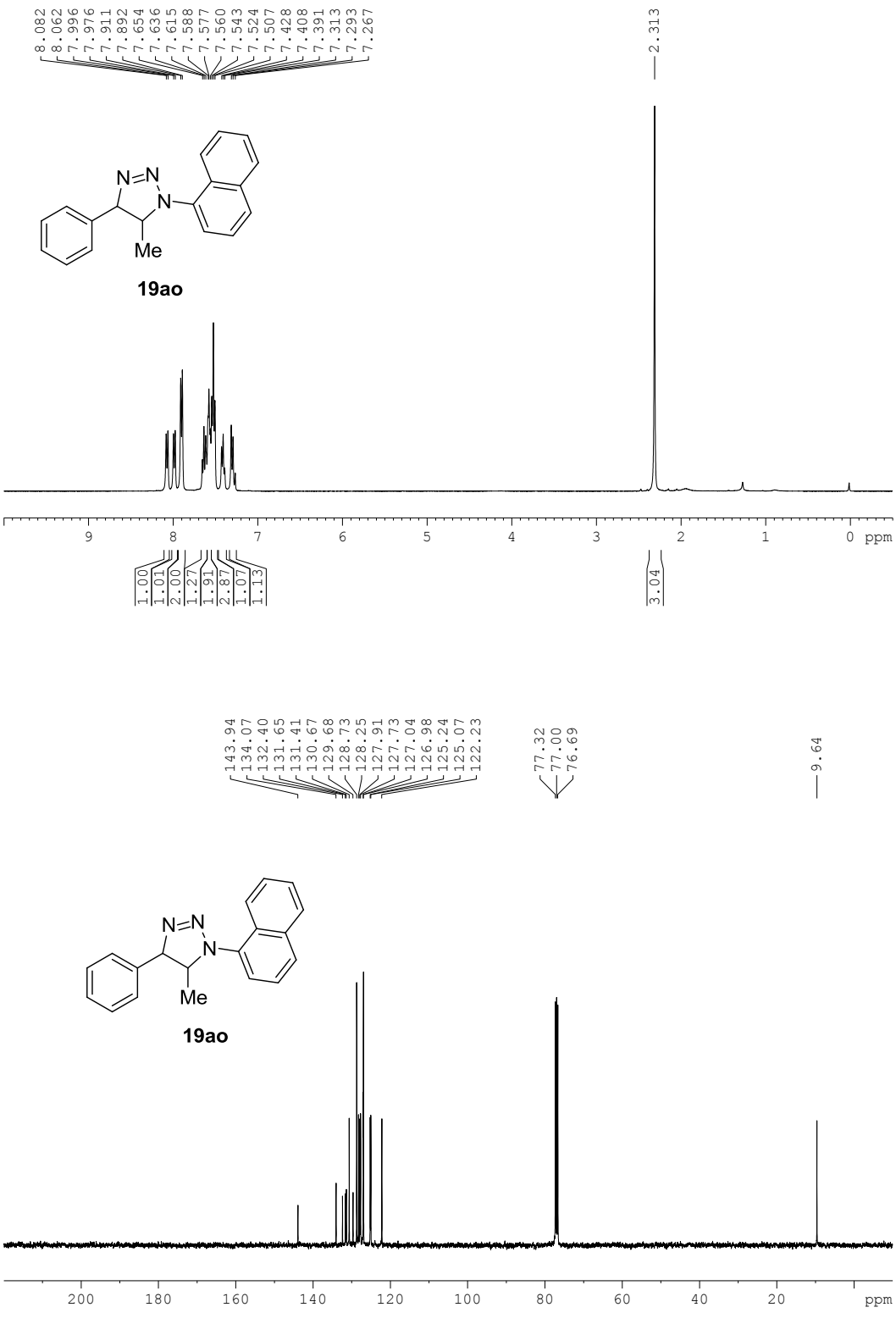


Figure-21: ^{1}H NMR and ^{13}C NMR spectrum of product **19ao**.

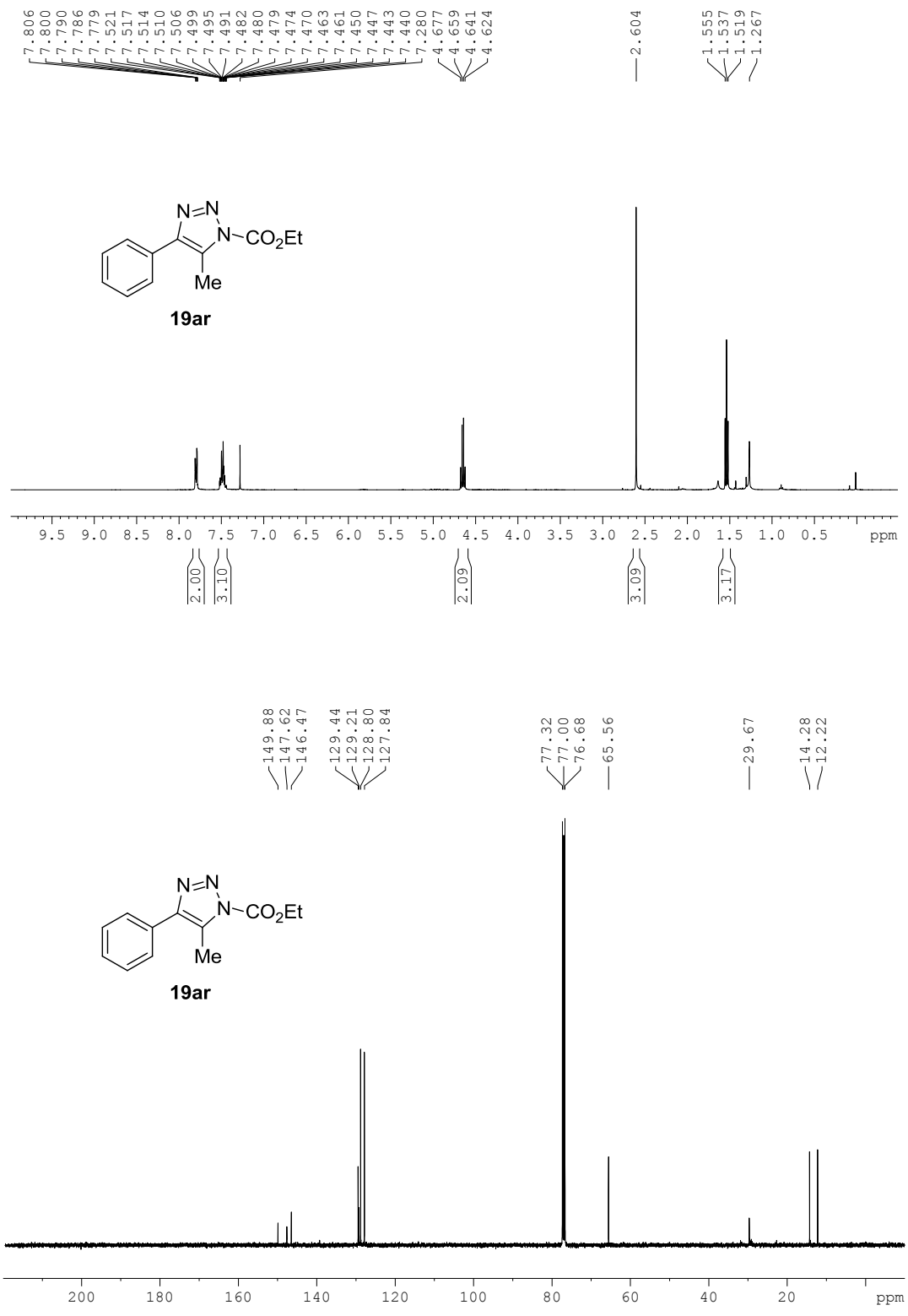
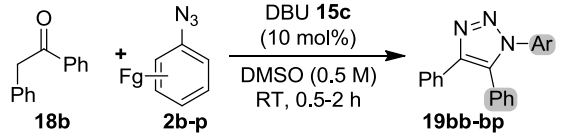


Figure-22: ^{1}H NMR and ^{13}C NMR spectrum of product **19ar**.

scope of this protocol covering a structurally diverse group of aryl azides **2b-p** and simple ketone **18b**.

Table 7: Azide scope with deoxybenzoin **18b**.[a]



Entry	Ar-N_3 **2**	Yield **19** [%][b]
1	**2b** (Fg = H)	90 (**19bb**)
2	**2c** (Fg = 2-NO_2)	95 (**19bc**)
3	**2d** (Fg = 4-NO_2)	96 (**19bd**)
4	**2e** (Fg = 4-CO_2Et)	94 (**19be**)
5	**2f** (Fg = 4-CN)	93 (**19bf**)
6	**2g** (Fg = 4-CF_3)	95 (**19bg**)
7	**2h** (Fg = 3-CHO)	95 (**19bh**)
8	**2i** (Fg = 4-F)	92 (**19bi**)
9	**2j** (Fg = 4-Cl)	95 (**19bj**)
10	**2k** (Fg = 3-Cl)	93 (**19bk**)
11	**2l** (Fg = 4-Br)	95 (**19bl**)
12	**2m** (Fg = 2-Br)	72 (**19bm**)
13	**2n** (Fg = 4-Me)	90 (**19bn**)
14	**2o** (Ar = 1-Naphthyl)	85 (**19bo**)
15	**2p** (Fg = 4-OMe)	90 (**19bp**)

[a] Reactions were carried out in DMSO (0.5 M) with 1.5 equiv. of **2b-p** relative to the **18b** (0.5 mmol) in the presence of 10-mol% of **15c**. [b] Yield refers to the column-purified product.

In order to develop a diverse library of fully decorated triazoles **19** and also to further understand the electronic factors of substituted phenylacetones/deoxybenzoins **18** in the OrgAKC reaction, we have chosen different ketones **18c-r**, which are having less or more acidic α-methylene groups compared to **18a-b** (Table 8). The OrgAKC reaction of 4-nitrophenylacetone **18c** with less reactive $C_6H_5N_3$ **2b** under DBU-catalysis at 25 °C for 0.5 h furnished the expected 1,2,3-triazole **19cb** in 90% yield (Table 8, entry 1). In a similar manner, we have also tested five more examples of halogen-, methoxy-, methyl-, and acetylene-substituted phenylacetones **18d-h** for the OrgAKC reaction with **2b**, which furnished the 1,2,3-triazoles **19db-hb** in excellent yields (Table 8, entries 2-6).

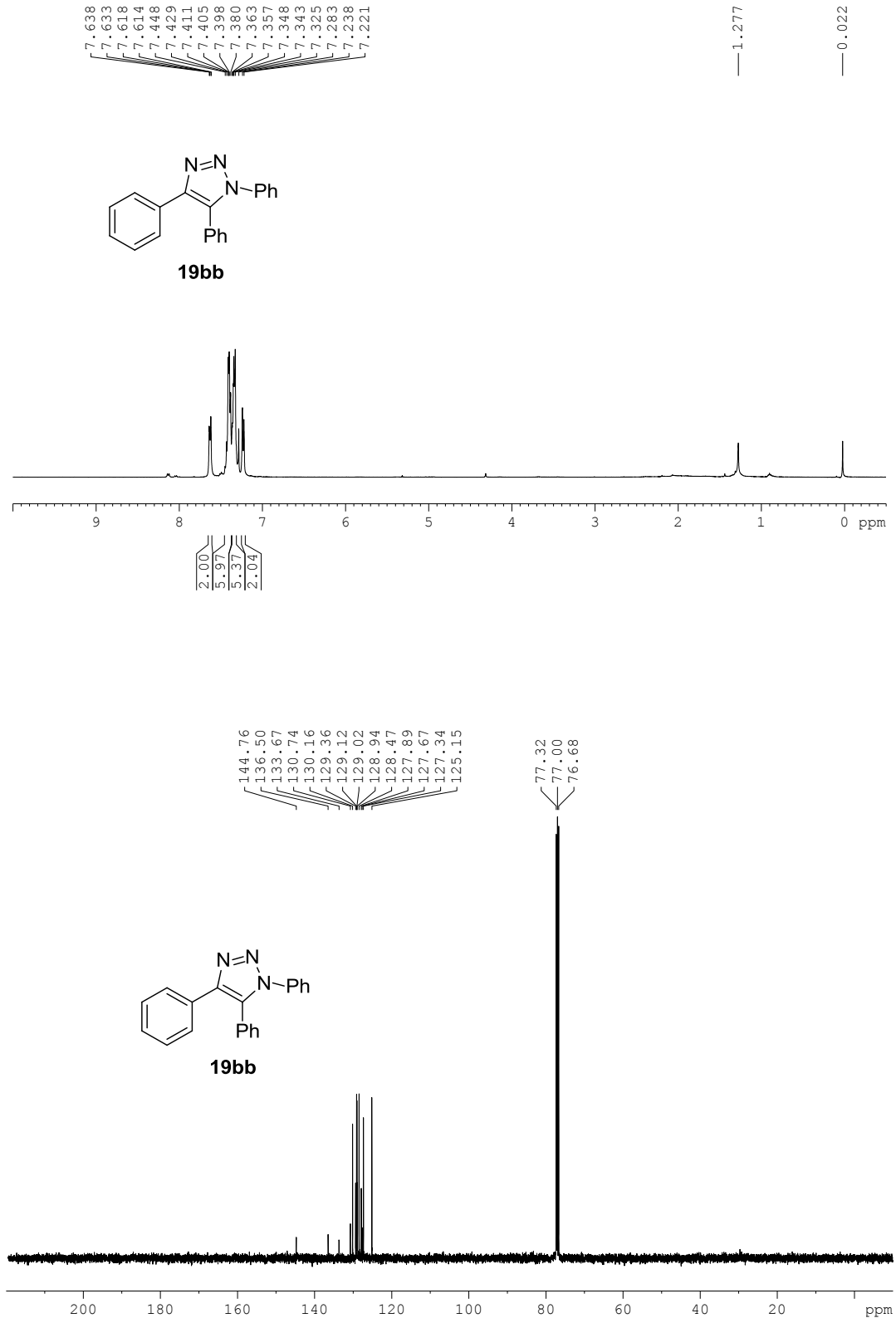


Figure-23: ^{1}H NMR and ^{13}C NMR spectrum of product **19bb**.

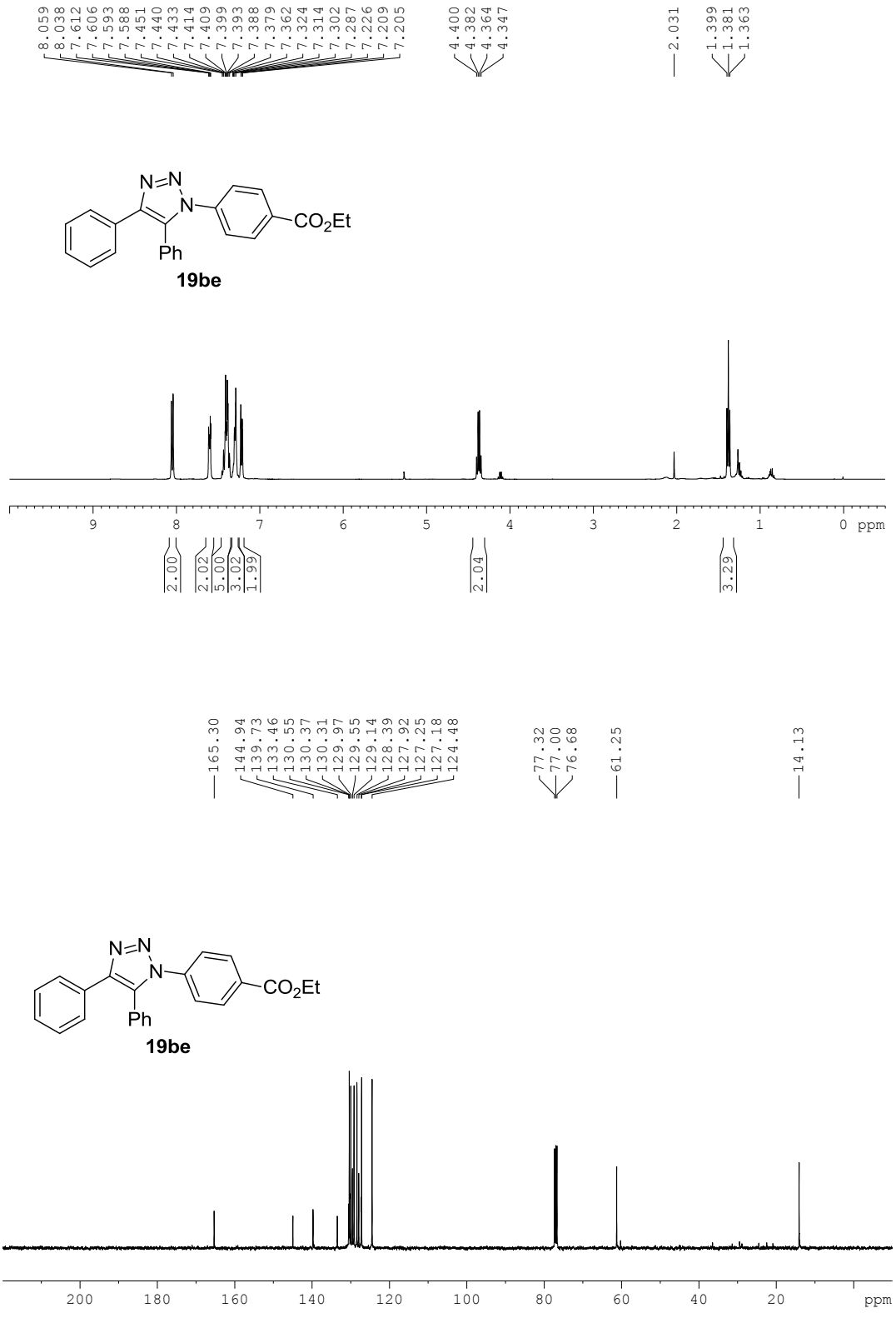


Figure-24: ^{1}H NMR and ^{13}C NMR spectrum of product **19be**.

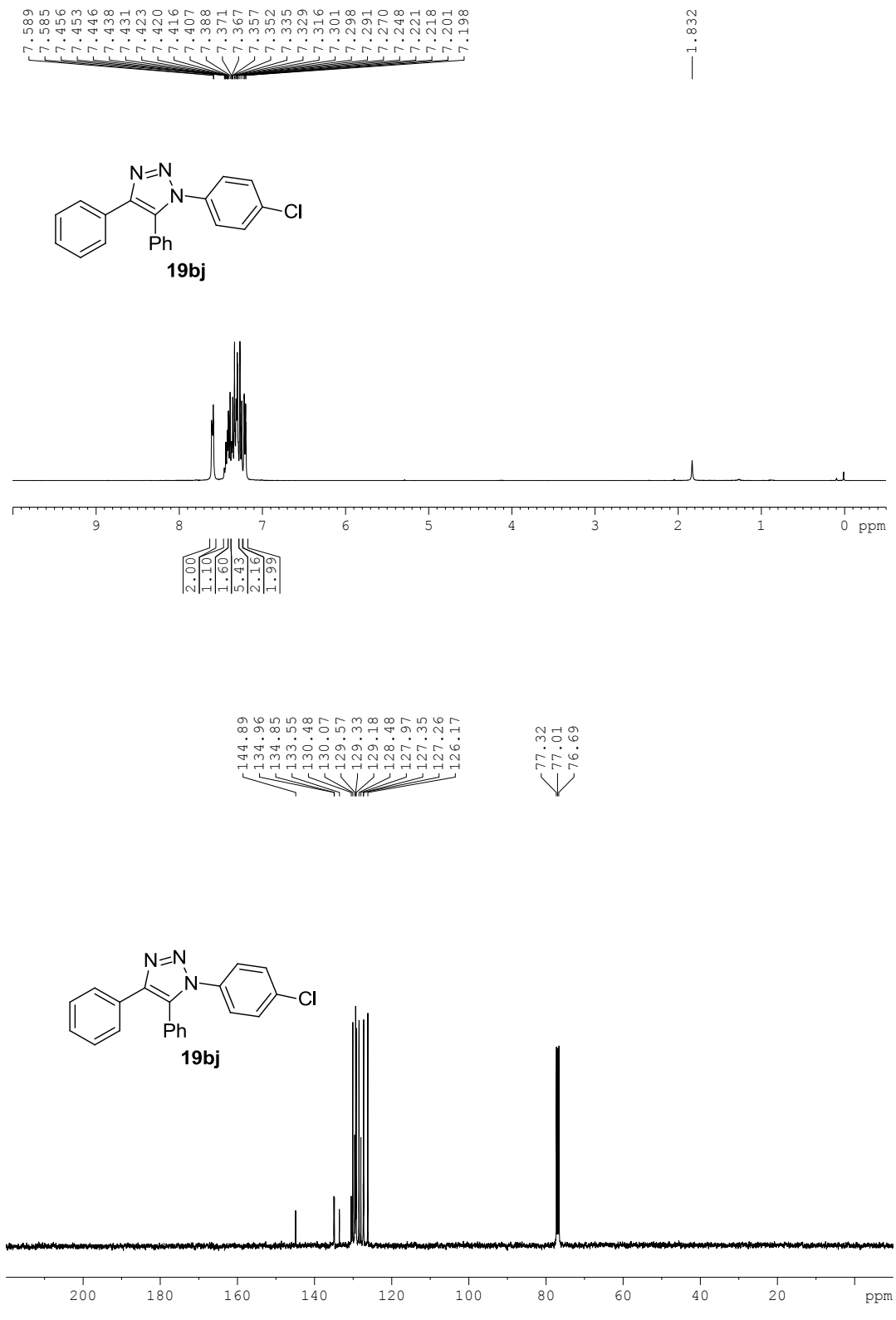
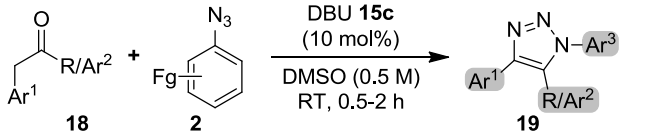


Figure-25: ^{1}H NMR and ^{13}C NMR spectrum of product **19bj**.

The OrgAKC reaction of nitro-, bromo-, chloro-, methyl-, and methoxy-substituted deoxybenzoins **18i-n** with **2d** under **15c**-catalysis at 25 °C for 1.0 h furnished the fully decorated 1,2,3-triazoles **19id-nd** in 88-92% yields without showing much of electronic factors (Table 8, entries 7-12). To understand the in situ enolate formation and their reactivity from cyclic arylacetones with DBU, we have chosen β-tetralone **18o** as the substrate in the OrgAKC reaction.

Table 8: OrgAKC reaction scope with different azides and ketones.[a]



Entry	**18:** Ar^1 and R/Ar^2	Ar^3-N_3 **2**	Yield **19** [%][b]
1	**18c** (Ar^1 = 4-$NO_2C_6H_4$; R = Me)	**2b**	90 (**19cb**)
2	**18d** (Ar^1 = 4-BrC_6H_4; R = Me)	**2b**	93 (**19db**)
3	**18e** (Ar^1 = 4-ClC_6H_4; R = Me)	**2b**	95 (**19eb**)
4	**18f** (Ar^1 = 4-$OMeC_6H_4$; R = Me)	**2b**	74 (**19fb**)
5	**18g** (Ar^1 = 4-MeC_6H_4; R = Me)	**2b**	92 (**19gb**)
6	**18h** (Ar^1 = 4-$HCCC_6H_4$; R = Me)	**2b**	95 (**19hb**)
7	**18i** (Ar^1 = 4-$NO_2C_6H_4$; Ar^2 = Ph)	**2d**	92 (**19id**)
8	**18j** (Ar^1 = 4-BrC_6H_4; Ar^2 = Ph)	**2d**	90 (**19jd**)
9	**18k** (Ar^1 = 4-BrC_6H_4; Ar^2 = 4-MeC_6H_4)	**2d**	90 (**19kd**)
10	**18l** (Ar^1 = Ph; Ar^2 = 4-ClC_6H_4)	**2d**	90 (**19ld**)
11	**18m** (Ar^1 = Ph; Ar^2 = 4-MeC_6H_4)	**2d**	90 (**19md**)
12	**18n** (Ar^1 = Ph; Ar^2 = 4-$OMeC_6H_4$)	**2d**	88 (**19nd**)
13	**18o** (β-Tetralone)	**2b**	85 (**19ob**)
14	**18o** (β-Tetralone)	**2p**	60 (**19op**)
15	**18p** (Ar^1 = 2-Naphthyl; R = Me)	**2b**	92 (**19pb**)
16[c]	**18p** (Ar^1 = 2-Naphthyl; R = Me)	**2t**	90 (**19pt**)
17[c]	**18p** (Ar^1 = 2-Naphthyl; R = Me)	**2u**	92 (**19pu**)
18[c]	**18p** (Ar^1 = 2-Naphthyl; R = Me)	**2v**	93 (**19pv**)
19	**18q** (Ar^1 = $PhCH_2$; R = Me)	**2d**	– (**19qd**)
20	**18r** (Ar^1 = Ph; R = Et)	**2d**	80 (**19rd**)
21	**18r** (Ar^1 = Ph; R = Et)	**2b**	80 (**19rb**)

[a] Reactions were carried out in DMSO (0.5 M) with 1.5 equiv. of **2** relative to the **18** (0.5 mmol) in the presence of 10-mol% of **15c**. [b] Yield refers to the column-purified product. [c] **2t**: 2,3-$F_2C_6H_3N_3$; **2u**: 2,4-$F_2C_6H_3N_3$; **2v**: 3-azido-2-bromopyridine.

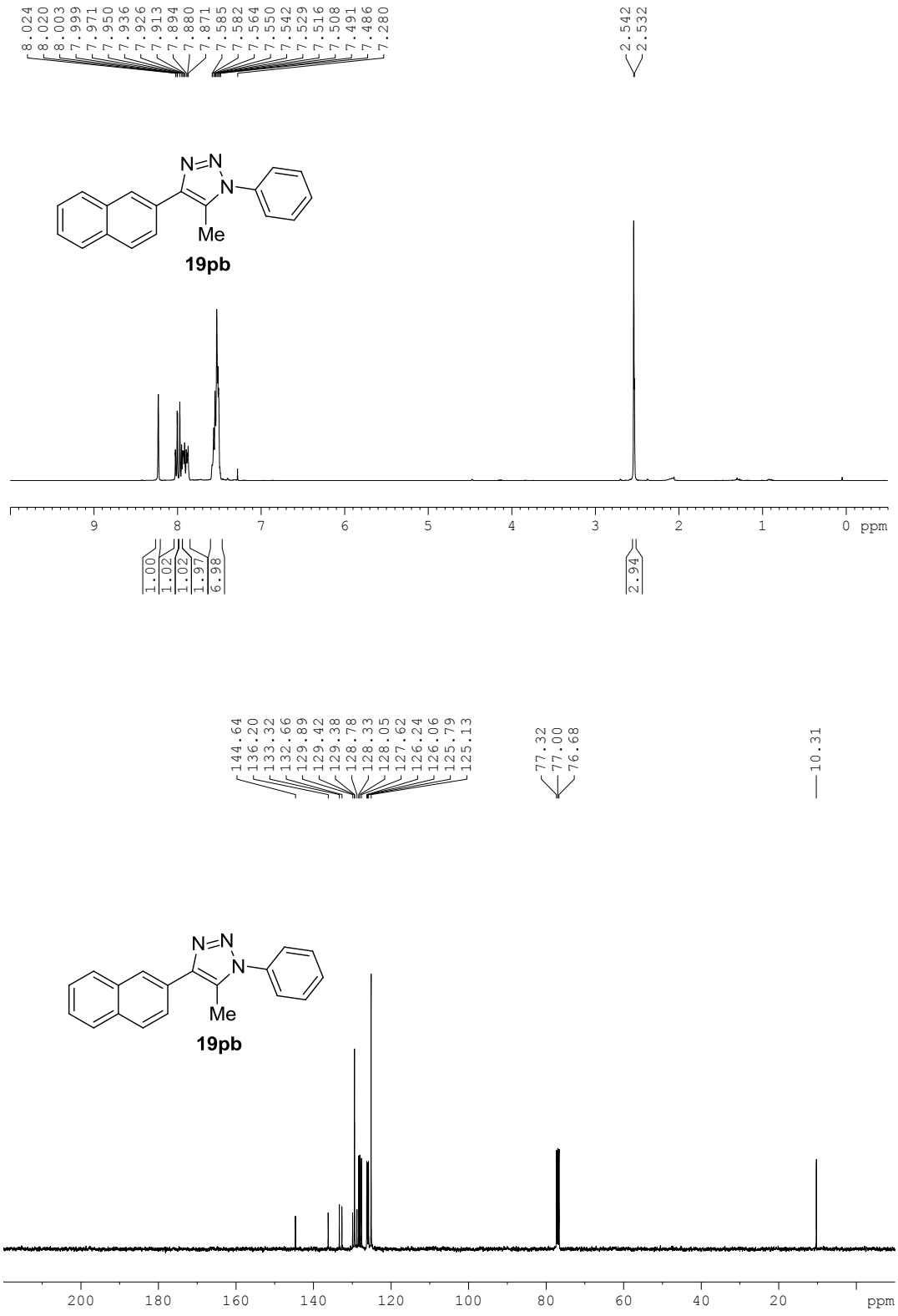


Figure-26: ^{1}H NMR and ^{13}C NMR spectrum of product **19pb**.

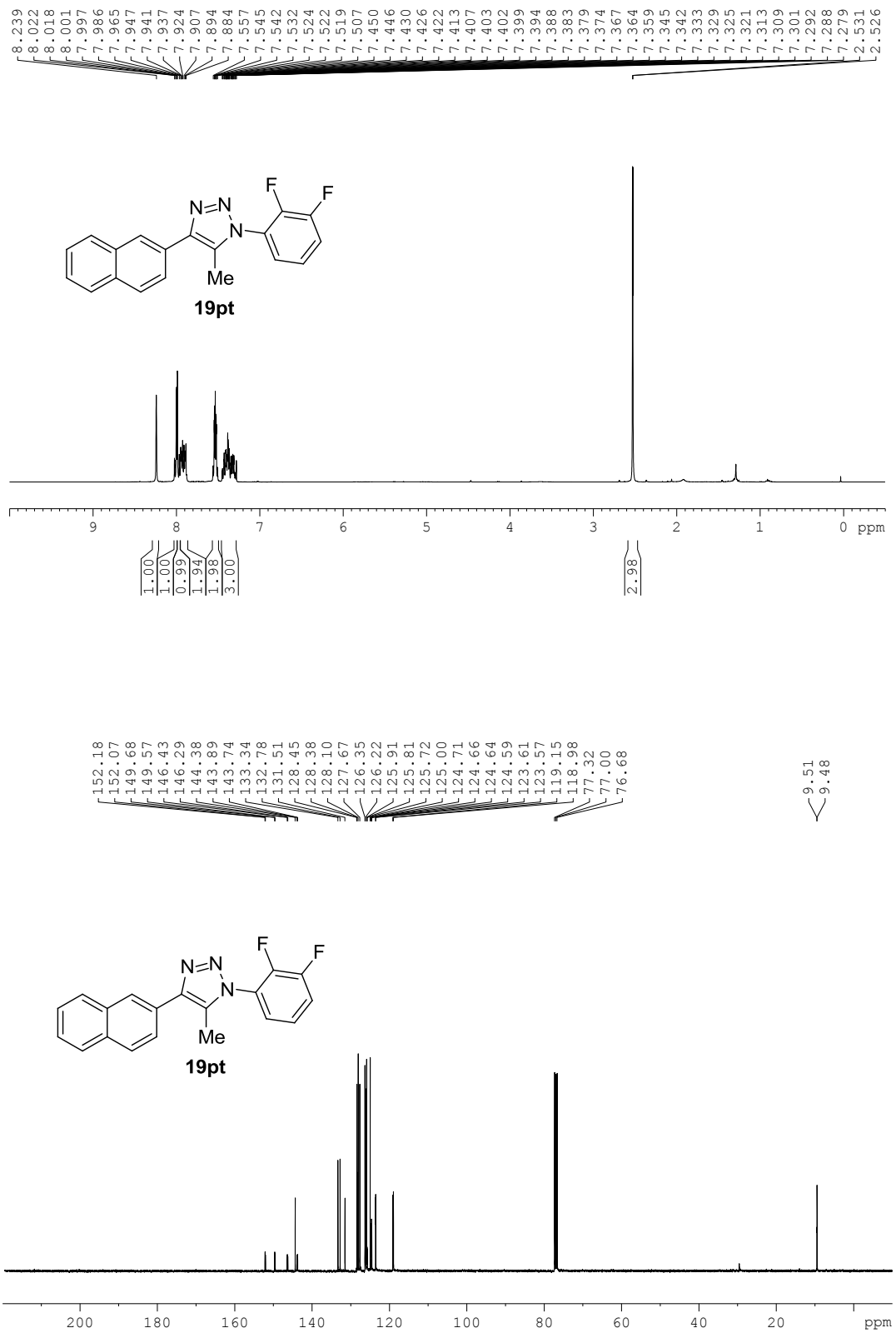


Figure-27: ^{1}H NMR and ^{13}C NMR spectrum of product **19pt**.

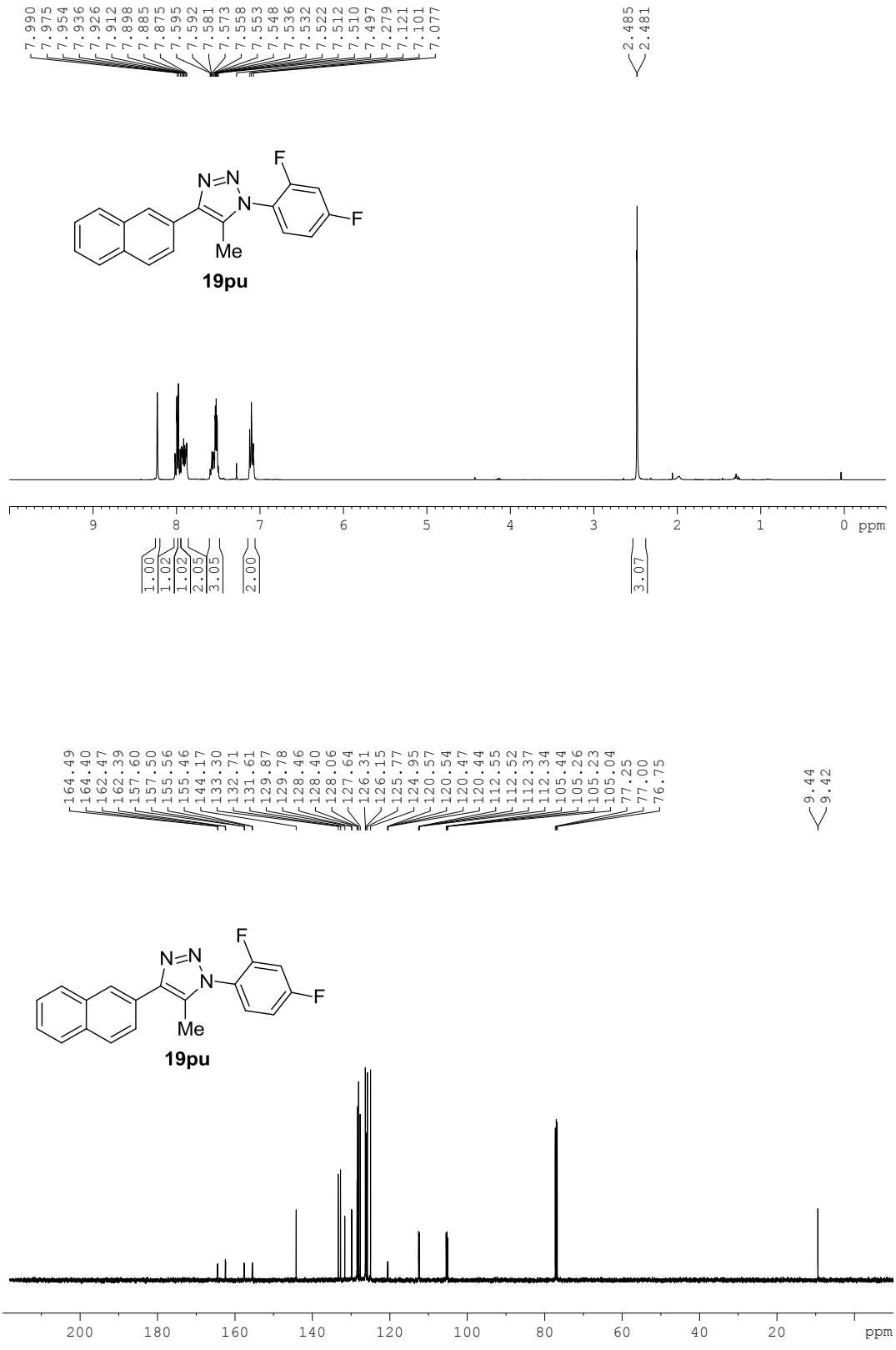


Figure-28: ^{1}H NMR and ^{13}C NMR spectrum of product **19pu**.

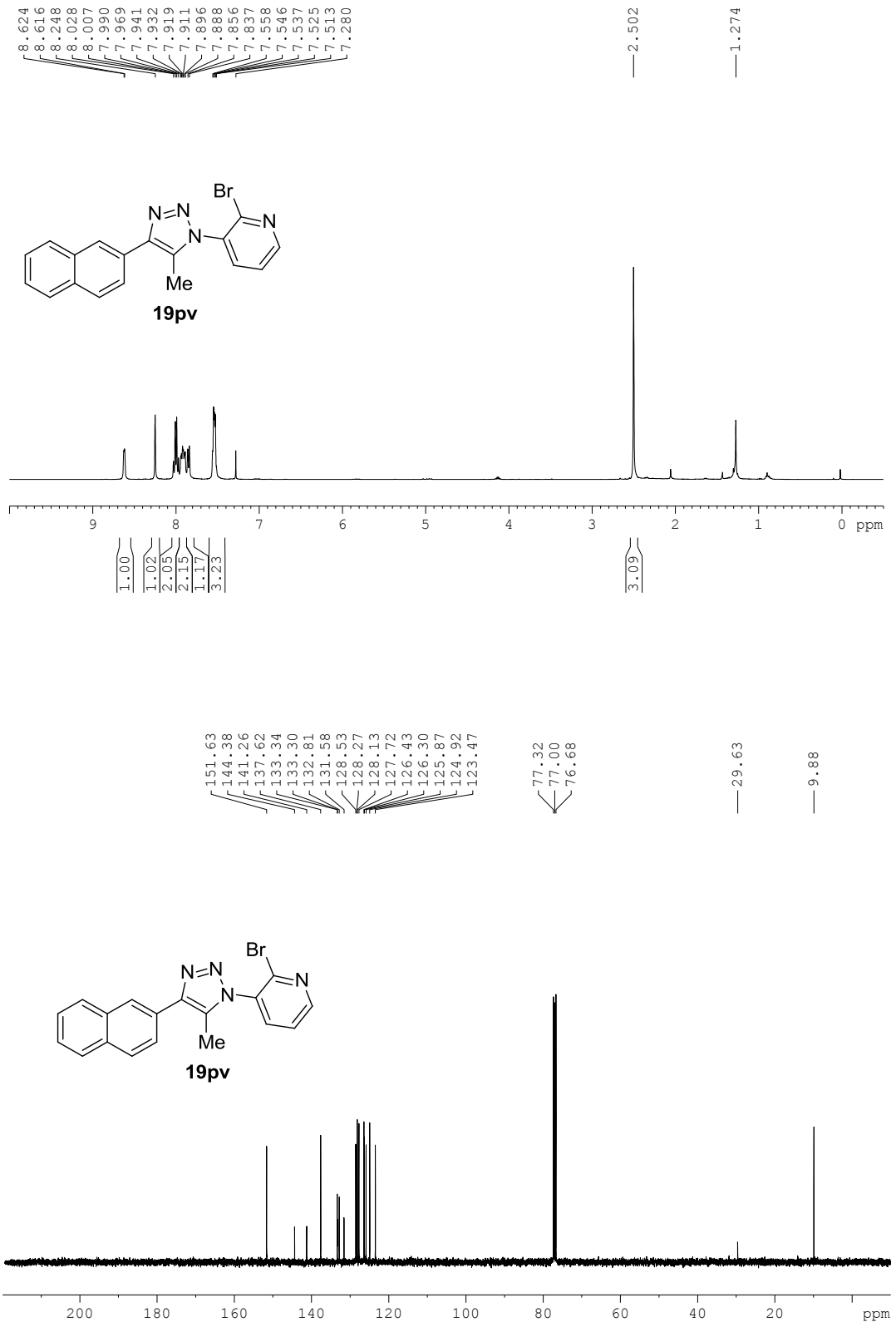


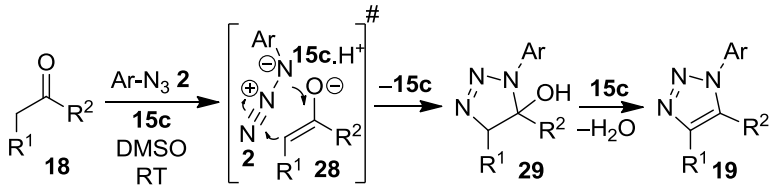
Figure-29: ^{1}H NMR and ^{13}C NMR spectrum of product **19pv**.

The OrgAKC reaction of **18o** with aryl azides **2b** and **2p** under **15c**-catalysis at 25 °C for 0.5 h furnished the single isomer of triazoles **19ob** and **19op** in 85% and 60% yields, respectively (Table 8, entries 13-14). With applications in mind, we have prepared a few more 1,4,5-trisubstituted-1,2,3-triazoles **19pb** and **19pt-pv** from the treatment of 2-naphthylacetone **18p** with aryl azides $C_6H_5N_3$ **2b**, 2,3-$F_2C_6H_3N_3$ **2t**, 2,4-$F_2C_6H_3N_3$ **2u**, and 3-azido-2-bromopyridine **2v** at 25 °C for 0.5 h under **15c**-catalysis (Table 8, entries 15-18). The compounds **19pb** and **19pt-pv** are analogues of PET ligands for imaging mGluR1 **C** as shown in Fig. 15.[14g-i] Surprisingly, there is no triazole formation from the reaction of benzylacetone **18q** with **2d** under **15c**- or **15i**-catalysis (Table 8, entry 19). Interestingly, the OrgAKC reaction of 1-phenylbutan-2-one **18r** with aryl azides **2d** and **2b** under **15c**-catalysis at 25 °C for 0.5 h furnished the single isomer of 1,2,3-triazoles **19rd, 19rb** in 80% yield each (Table 8, entries 20-21). Many of the products **19** yields/selectivity obtained were excellent compared to the previous methods and out of fifty-six compounds synthesized here only seventeen are known (Table A2, Annexure-II).

4.3 Mechanistic Insights

The provisional mechanism for the OrgAKC reaction is illustrated in Scheme 5. Reaction of phenylacetones/deoxybenzoins **18** with catalyst **15c** generates the enolate **28**, which on quick in situ treatment with Ar-N_3 **2** furnishes selectively the adduct 1,2,3-triazolines **29** *via* concerted or stepwise [3+2]-cycloaddition,[5b] which further transforms into the fully decorated triazole **19** through rapid elimination of water at ambient conditions.

Scheme 5. Reaction mechanism of OrgAKC.

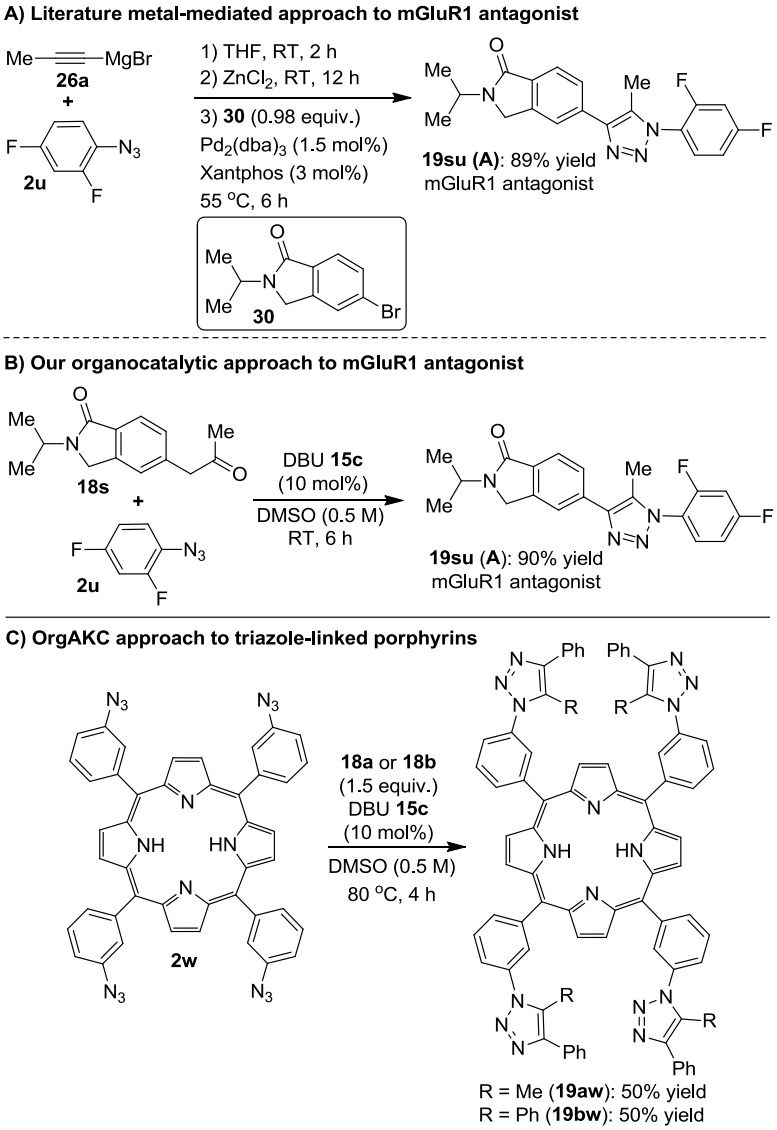


4.4 Application of OrgAKC reaction

The versatility of the OrgAKC reaction was further exemplified by synthesizing medicinally and materially useful compounds **19su**, **19aw** and **19bw** (Scheme 6).[14g-i] As shown in

Scheme 6B, mGluR1 antagonist triazole **19su** (**A**) was synthesized in very good yield with single isomer from the arylacetone **18s** and 2,4-$F_2C_6H_3N_3$ **2u** under the metal-free **15c**-catalysis at ambient conditions. By contrast, the literature synthesis of this antagonist triazole **19su** starting from 1-propynylmagnesiumbromide **26a** and **2u** requires metal (Mg, Zn, Pd)-mediated three reactions (Scheme 6A).[14i]

Scheme 6. Application of OrgAKC reaction.



Further, we synthesized the compounds **19aw/19bw** through the OrgAKC reaction of metal-free fully substituted tetraarylporphyrin azide **2w** with **18a/18b** in DMSO at 80 °C for 4 h.

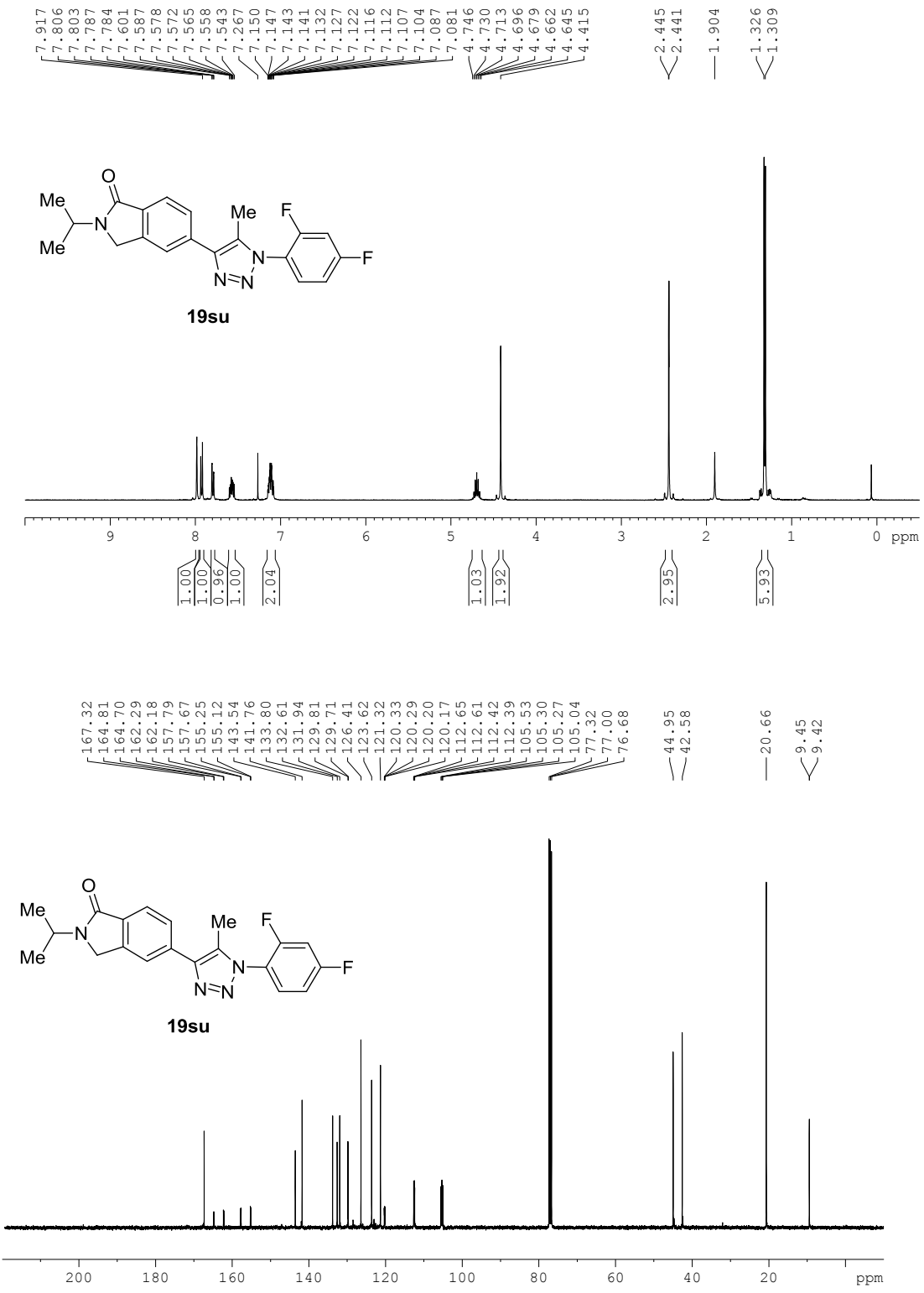


Figure-30: ^{1}H NMR and ^{13}C NMR spectrum of product **19su**.

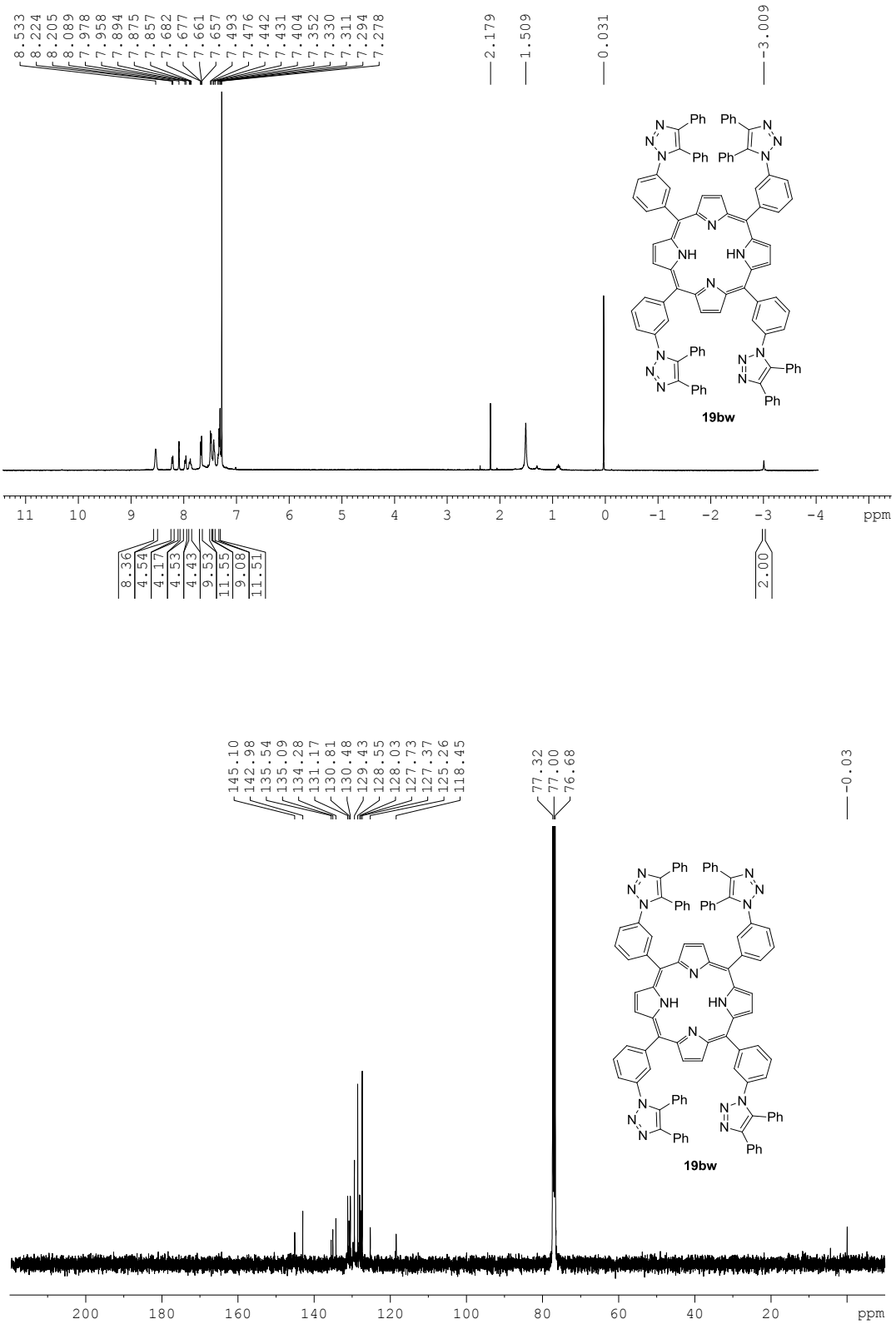


Figure-31: ^{1}H NMR and ^{13}C NMR spectrum of product **19bw**.

Compound **19aw/19bw** was isolated as a single regioisomer in moderate yield (Scheme 6C).[14j] These results clearly demonstrate the exceptional advantages of the OrgAKC protocol, which enables a high-yielding metal-free synthesis of medicinally important triazoles.

4.5 Conclusions

In conclusion, we have developed a versatile enolate-mediated organocatalytic azide-ketone [3+2]-cycloaddition reaction that generates 1,4-diaryl-5-methyl(alkyl) 1,2,3-triazoles decorated with useful functional groups. Our OrgAKC protocol highlights the metal-free conditions with high reaction rate and regioselectivity, and it provides an easy access to a library of functionalized 1,2,3-triazoles that are inaccessible by other methods. This OrgAKC reaction was well tolerated by many functional groups (such as nitro, nitrile, aldehydes, ketones, esters, halides, amides, and alkynes) under these mild reaction conditions. Moreover, many of the reported syntheses have the disadvantage of requiring heavy metals and less available unsymmetric internal alkynes; therefore, this protocol is very convenient. Further work is in progress to utilize the enolate-mediated OrgAKC reactions in medicinal and material chemistry.

In continuation to the organocatalytic enolate-mediated [3+2]-cycloaddition reactions for the synthesis of substituted 1,2,3-triazoles, push-pull dienamine-mediated synthesis of *N*-aryl-benzotriazoles was developed through organocatalytic triazole formation followed by oxidative aromatization and the results are presented in the next chapter.

ANNEXURE-II

***Table A2*:** Correlation of **OrgAKC** reaction with **CuAAC** reaction.

Entry	Ref.	Product	CuAAC condition	OrgAKC condition
1	42	**19ad**	150 ^{o}C, 1 h, 86%	25 ^{o}C, 0.5 h, 95%
2	39	**19ab**	115 ^{o}C, 12 h, 52%	25 ^{o}C, 2.0 h, 90%
3	36d	**19ai**	65 ^{o}C, 12 h, 90%	25 ^{o}C, 1.0 h, 90%
4	43	**19ao**	150 ^{o}C, 1 h, 36%	25 ^{o}C, 1.0 h, 90%
5	34d	**19aq**	80 ^{o}C, 2.5 h, 59% (regio selectivity 1.6:1)	25 ^{o}C, 0.5 h, 95%
6	44	**19ar'**	100 ^{o}C, 4.0 h, 30%	25 ^{o}C, 0.5 h, 90%
7	36e	**19bd**	50 ^{o}C, 20 h, 60%	25 ^{o}C, 1.0 h, 96%
8	45	**19bb**	25 ^{o}C, 5 h, 85%	25 ^{o}C, 1.0 h, 90%
9	37a,46	**19bn**	250 ^{o}C, 0.25 h, 99%	25 ^{o}C, 1.0 h, 90%
10	36e	**19bp**	50 ^{o}C, 20 h, 72%	25 ^{o}C, 2.0 h, 90%
11	39	**19db**	115 ^{o}C, 12 h, 50%	25 ^{o}C, 1.0 h, 93%
12	39	**19eb**	115 ^{o}C, 12 h, 46%	25 ^{o}C, 1.0 h, 95%
13	39	**19fb**	115 ^{o}C, 12 h, 56%	25 ^{o}C, 2.0 h, 74%
14	39	**19gb**	115 ^{o}C, 12 h, 48%	25 ^{o}C, 2.0 h, 92%
15	39	**19ob**	100 ^{o}C, 12 h, 56%	25 ^{o}C, 0.5 h, 85%
16	45	**19rb**	25 ^{o}C, 24 h, 56% (regio selectivity 2:1)	25 ^{o}C, 1.0 h, 80%
17	14i	**19su**	25 ^{o}C, 2 h, 89%	25 ^{o}C, 6.0 h, 88%

5. Organocatalytic Triazole Formation, Followed by Oxidative Aromatization: Regioselective Metal-free Synthesis of Benzotriazoles

5.1 Introduction

N-Aryl-benzotriazoles are an important class of heterocycles that display a large spectrum of structural and biological activities and are widely used in organic, medicinal and material chemistry.[47] For example, benzotriazole **D** is an inhibitor of *c*-Kit protooncogene, compound **E** is potassium channel activator, and compounds **F**, **G** are antiplasmodial and antibacterial agents respectively (Figure 32).[47] Based on their structural and biological importance, the development of new and selective practical methods for their preparation is a challenging task.[48-50]

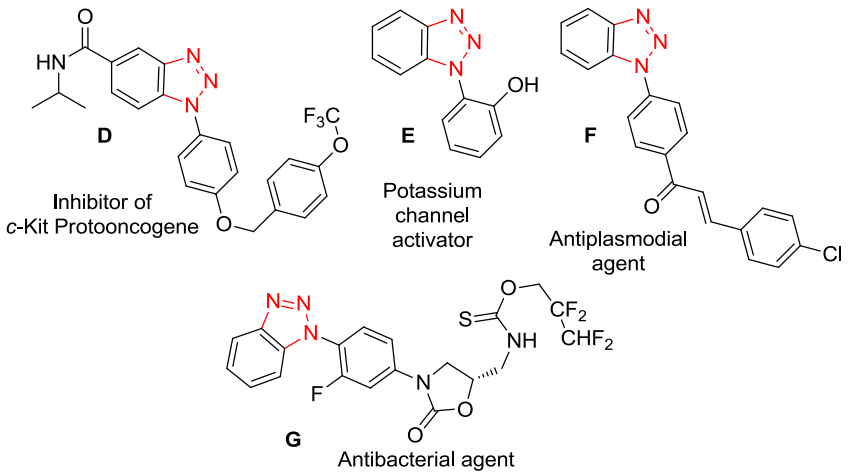
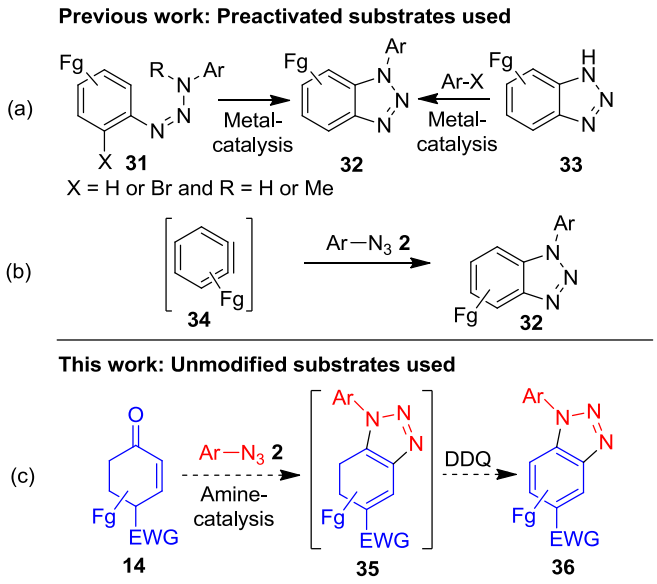


Figure 32: Pharmaceutically active *N*-aryl-benzotriazoles **D-G**.

N-Aryl-benzotriazoles can be prepared by palladium- or copper-catalyzed Buchwald-Hartwig-type reactions of aryltriazenes (Scheme 7a),[48] palladium- or copper-catalyzed arylation of N*H*-benzotriazoles (Scheme 7a),[49] the [3+2]-cycloaddition reaction between aryne and organic azides (Scheme 7b),[50] and the reaction of (*Z*)-1-aryl-3-hexen-1,5-diynes with sodium azide.[51] In all these methods, either they used a limited number of available highly reactive in situ generated arynes or not so readily available aryltriazenes or N*H*-

benzotriazoles as starting materials. Also from these reactions, benzotriazoles were formed as a mixture of *N*-arylated isomers in all the cases except the synthesis involving Buchwald-Hartwig-type reactions.[48] These limitations inspired us to develop a novel protocol for the high-yielding regioselective synthesis of *N*-aryl-benzotriazoles based upon organocatalytic triazole formation followed by oxidative aromatization, from readily available unmodified substrates as shown in Scheme 7c.

Scheme 7. Summary of previous work and the design plan of this work.



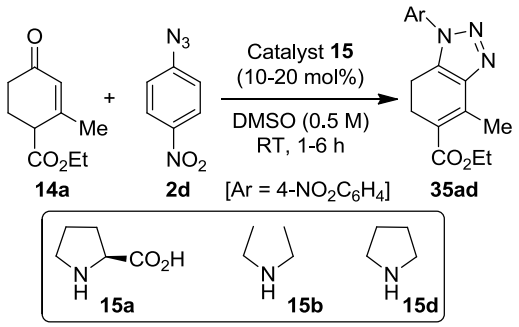
Recently, organocatalytic triazole formation has emerged as a powerful tool in copper free-click chemistry.[4] In 2008, we have discovered a copper-free technology for the synthesis of highly substituted *N*H-1,2,3-triazoles from commercially available unmodified enones and activated organic azides, through domino [3+2]-cycloaddition/hydrolysis ([3+2]-CA/H) reactions under proline-catalysis.[4a] Later in 2011, Pons and co-workers reported the clever synthesis of *N*-aryl-1,2,3-triazoles from unactivated ketones with aryl azides under proline-catalysis.[4b] In the same year, Wang *et al*. reported the cycloaddition of aryl azides with enamides, generated in situ from activated ketones in the presence of catalytic amount of a secondary amine.[4c,d] Recently, Paixao and co-workers reported the cycloaddition of activated azidophenyl arylselenides with β-keto-esters in the presence of catalytic amount of diethylamine.[4e] However, the

strategies of Pons and Wang require high temperatures for the synthesis of less functionalized *N*-aryl-1,2,3-triazoles, and Paixao synthesized simple monocyclic *N*-aryl-1,2,3-triazoles, which may not be suitable starting materials for the synthesis of *N*-aryl-benzotriazoles. By taking the advantage of organocatalytic click reaction, herein, we report the metal-free regioselective synthesis of *N*-aryl-benzotriazoles from the treatment of highly functionalized unmodified cyclic enones with unactivated aryl azides under the amine-catalysis at the 25 °C followed by 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) mediated oxidative aromatization in sequential one-pot manner. Herein, we explore the utility of highly functionalized bicyclic *N*-aryl-1,2,3-triazoles as starting materials for the synthesis of medicinally important *N*-aryl-benzotriazoles through mild oxidative aromatization.

5.2 Results and Discussion

With our previous experience,[4a] we first optimized the high-yielding synthesis of functionalized bicyclic *N*-aryl-1,2,3-triazoles from unmodified substrates at ambient conditions. For this we initiated optimization of the organocatalytic triazole formation by screening a number of known organocatalysts for the reaction of activated cyclic enone **14a** with 0.5 to 1.5 equiv. of *p*-nitrophenyl azide (4-$NO_2C_6H_4N_3$) **2d** (Table 9). Surprisingly, reaction of **14a** with 0.5 equiv. of **2d** in DMSO at 25 °C for 6 h with 20 mol% of proline **15a** furnished *N*-aryl-1,2,3-triazole **35ad** in 83% yield (Table 9, entry 1). The same reaction with 1.5 equiv. of **2d** in DMSO at 25 °C for 6 h furnished **35ad** in 85% yield (Table 9, entry 2). To improve the yield of triazole formation, we performed the reaction under the secondary amine-catalysis as shown in Table 9, entries 3-5. Treatment of **14a** with 1.5 equiv. of **2d** in DMSO at 25 °C for 2 h with 10 mol% of diethyl amine **15b** furnished the *N*-aryl-1,2,3-triazole **35ad** in a reduced (81%) yield (Table 9, entry 3). The same reaction at 70 °C for 1 h furnished the **35ad** in 90% yield (Table 9, entry 4). Reaction of **14a** with 1.5 equiv. of **2d** in DMSO at 25 °C for 1 h with 10 mol% of pyrrolidine **15d** furnished the **35ad** in a very good (95%) yield (Table 9, entry 5). We considered the optimized condition to be 25 °C in DMSO using 10 mol% of pyrrolidine **15d** as catalyst (Table 9, entry 5).

Table 9: Reaction optimization.[a]



Entry	Catalyst **15** [10-20 mol-%]	Time [h]	Product yield [%][b] **35ad**
1[c]	**15a** (20 mol%)	6	83
2	**15a** (20 mol%)	6	85
3	**15b** (10 mol%)	2	81
4[d]	**15b** (10 mol%)	1	90
5	**15d** (10 mol%)	**1**	**95**

[a] Reactions were carried out in solvent (0.5 M) with 1.5 equiv. of **2d** relative to the **14a** (0.5 mmol) in the presence of 10-20-mol% of catalyst **15**. [b] Yield refers to the column-purified product. [c] 0.5 equiv. of **2d** was used relative to the **14a** (0.5 mmol). [d] Reaction performed at 70 °C.

After successful demonstration of room temperature [3+2]-CA reactions of **14a** with **2d** under the amine-catalysis, we investigated the effect of aryl substitution factor on amine-catalyzed [3+2]-CA reaction of **14a** with the other aryl azides **2b-g, 2l, 2n** as shown in Table 10. A series of *ortho*- or *para*-substituted aryl azides **2b-g, 2l, 2n** were reacted with **14a** catalyzed by 10 mol% of pyrrolidine **15d** at 25 °C in DMSO for 1-66 h (Table 10). Both electron deficient (NO_2, CO_2Et, CN, CF_3 and Br) and neutral (CH_3 and H) aryl azides (Ar-N_3) **2** furnished the expected bicyclic *N*-aryl-1,2,3-triazoles **35ab-an** in excellent to good yields (Table 10). Surprisingly, pyrrolidine-catalyzed [3+2]-CA reaction of **14a** with 4-$MeOC_6H_4N_3$ **2p** did not furnished the expected product even at higher temperatures (not shown in Table 10). Structure and regiochemistry of bicyclic *N*-aryl-1,2,3-triazoles **35** were confirmed by NMR analysis (for example Fig. 33-34).

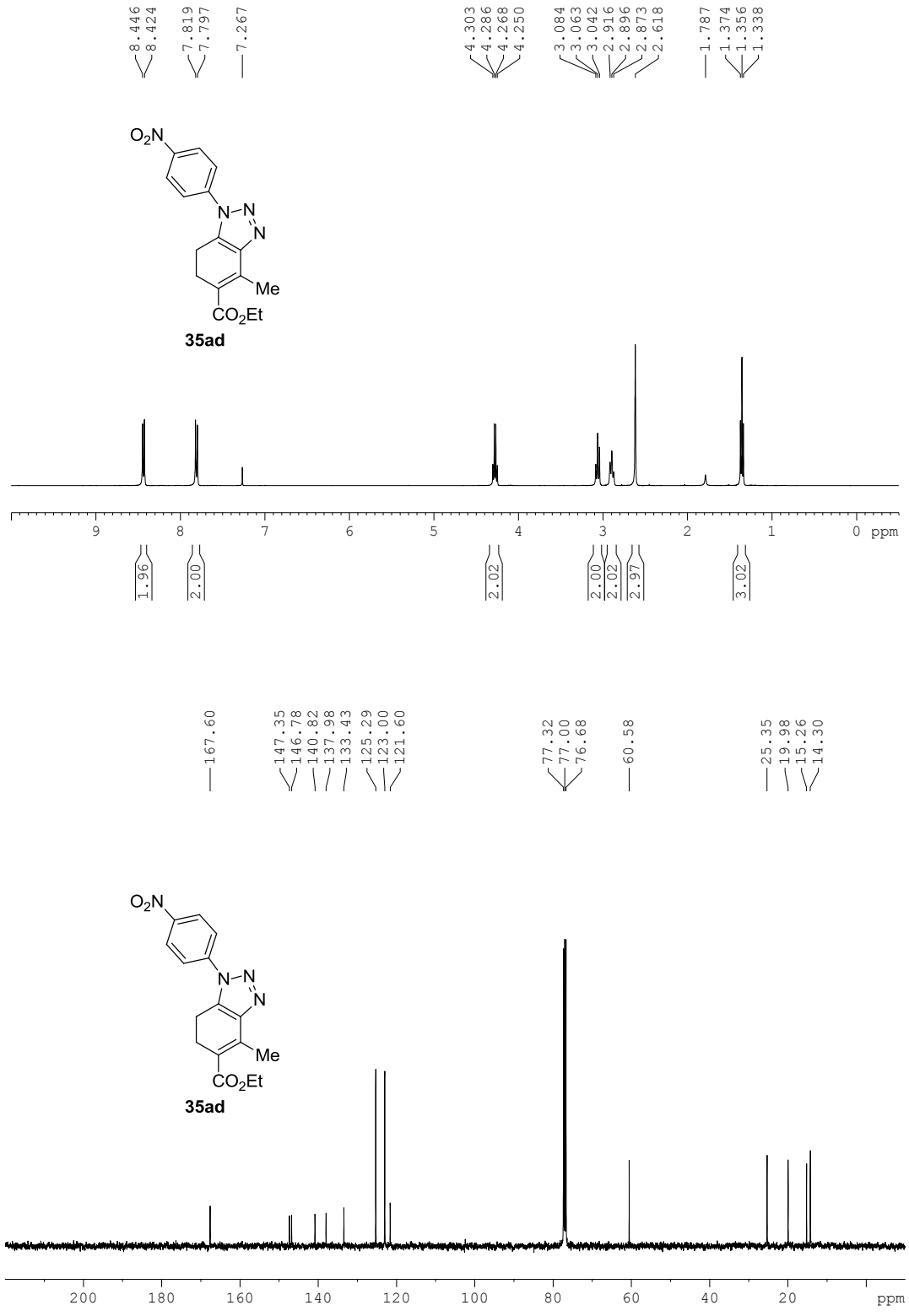
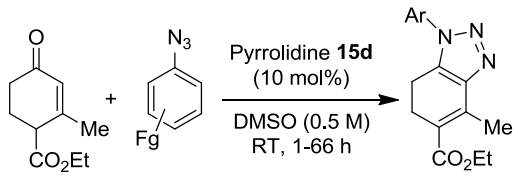


Figure-33: ^{1}H NMR and ^{13}C NMR spectrum of product **35ad**.

Table 10: Substituent effect on the *N*-aryl-1,2,3-triazole formation.[a]



14a **2b-n** **35ab-an**

Entry	Ar-N_3 **2**	Time [h]	Product yield [%][b] **35ab-ah**
1	**2c** (Fg = 2-NO_2)	1	95 (**35ac**)
2	**2e** (Fg = 4-CO_2Et)	1	92 (**35ae**)
3	**2f** (Fg = 4-CN)	0.75	97 (**35af**)
4	**2g** (Fg = 4-CF_3)	1	93 (**35ag**)
5	**2l** (Fg = 4-Br)	24	75 (**35al**)
6[c]	**2n** (Fg = 4-Me)	40	50 (**35an**)
7	**2b** (Fg = 4-H)	66	50 (**35ab**)

[a] Reactions were carried out in DMSO (0.5 M) with 1.5 equiv. of **2b-n** relative to the **14a** (0.5 mmol) in the presence of 10-mol% of **15d**. [b] Yield refers to the column-purified product. [c] Reaction performed at 70 °C.

With the optimized reaction conditions in hand, the substrate scope of the amine-catalyzed [3+2]-CA reactions was investigated before the investigation of oxidative aromatization. A variety of unmodified functionalized cyclic enones **14a**-**r** were reacted with 1.5 equiv. of CF_3 and NO_2 containing aryl azides **2g, 2c-d** catalyzed by 10 mol% of pyrrolidine **15d** at 25 °C in DMSO for 1-17 h (Table 11). Interestingly, both the aliphatic and aromatic functionalized unmodified cyclic enones **14a-r** were furnished the expected bicyclic *N*-aryl-1,2,3-triazoles **35** in excellent to good yields (Table 11). Yields of the organocatalytic [3+2]-CA products **35** were increased by the aryl substitution at the C-6 position of cyclic enones **14**, but yields slightly decreased with aliphatic substitution and these required longer reaction times. For example, pyrrolidine-catalyzed [3+2]-CA reaction of C-6 aliphatic substituted cyclic enones **14d-g** with 4-$CF_3C_6H_4N_3$ **2g** in DMSO at 25 °C for 4-17 h furnished the expected *N*-aryl-1,2,3-triazoles **35dg-gg** in 90%, 60%, 70% and 70% yields, respectively (Table 11, entries 3-6). Fascinatingly, [3+2]-CA reaction of C-6 aryl substituted cyclic enones **14h-o** with 4-$CF_3C_6H_4N_3$ **2g** at 25 °C for 1 h in DMSO under pyrrolidine-catalysis furnished the expected bicyclic *N*-aryl-1,2,3-triazoles **35hg-og** in very good yields

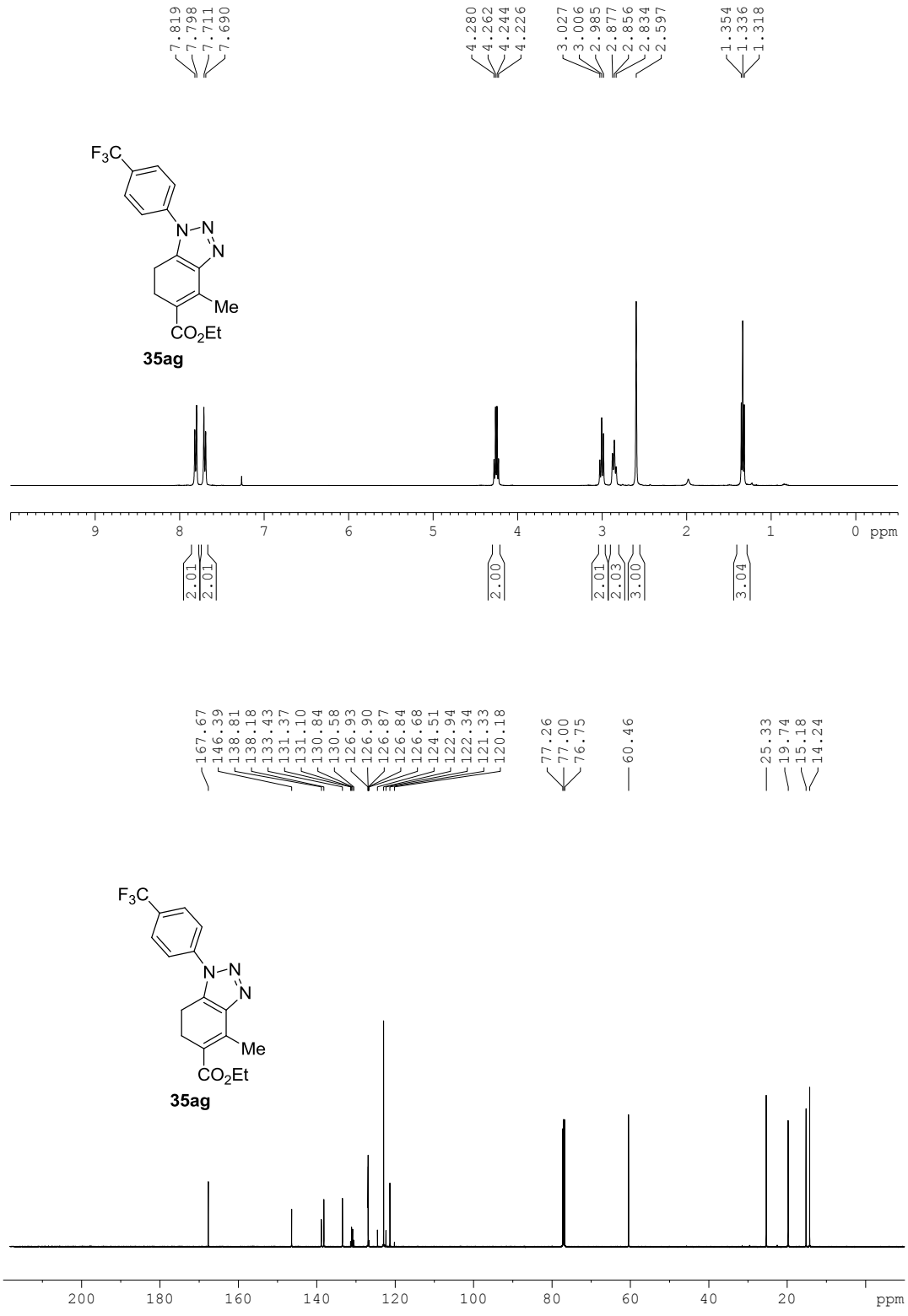
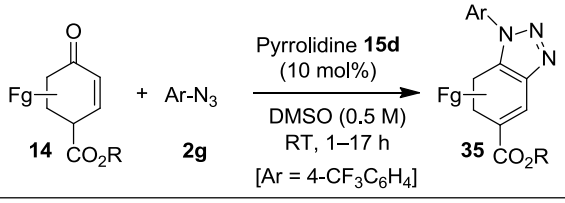
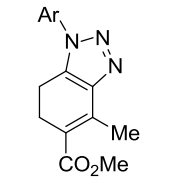


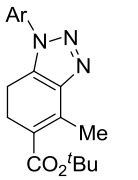
Figure-34: ^{1}H NMR and ^{13}C NMR spectrum of product **35ag**.

Table 11: Diverse libraries of *N*-aryl-1,2,3-triazoles **35**.[a]

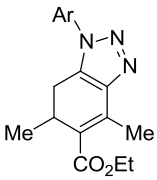




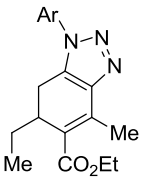
1 h; 86% (**35bg**)



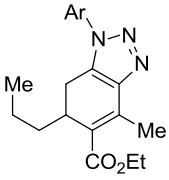
3 h; 80% (**35cg**)



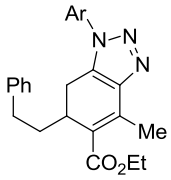
4 h; 90% (**35dg**)



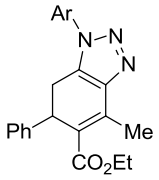
17 h; 60% (**35eg**)



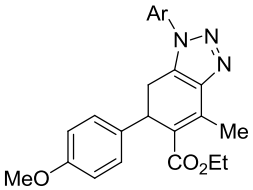
11 h; 70% (**35fg**)



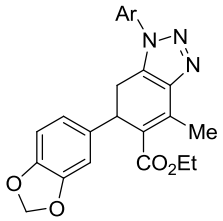
11 h; 70% (**35gg**)



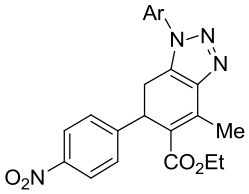
8 h; 75% (**35hg**)



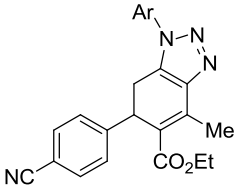
1 h; 65% (**35ig**)[b]



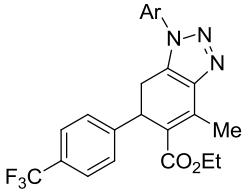
1 h; 80% (**35jg**)



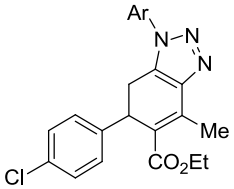
1 h; 90% (**35kg**)



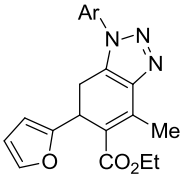
1 h; 85% (**35lg**)



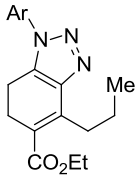
1 h; 85% (**35mg**)



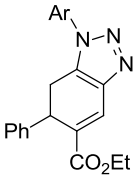
1 h; 70% (**35ng**)



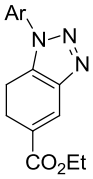
1 h; 75% (**35og**)



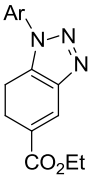
1 h; 95% (**35pg**)



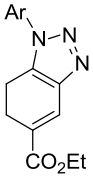
1 h; 80% (**35qg**)



1 h; 80% (**35rg**)



1 h; 80% (**35rd**)[c]



1 h; 80% (**35rc**)[d]

[a] Yield refers to the column-purified product. [b] Reaction performed at 70 °C. [c] Azide used as **2d**. [d] Azide used as **2c**.

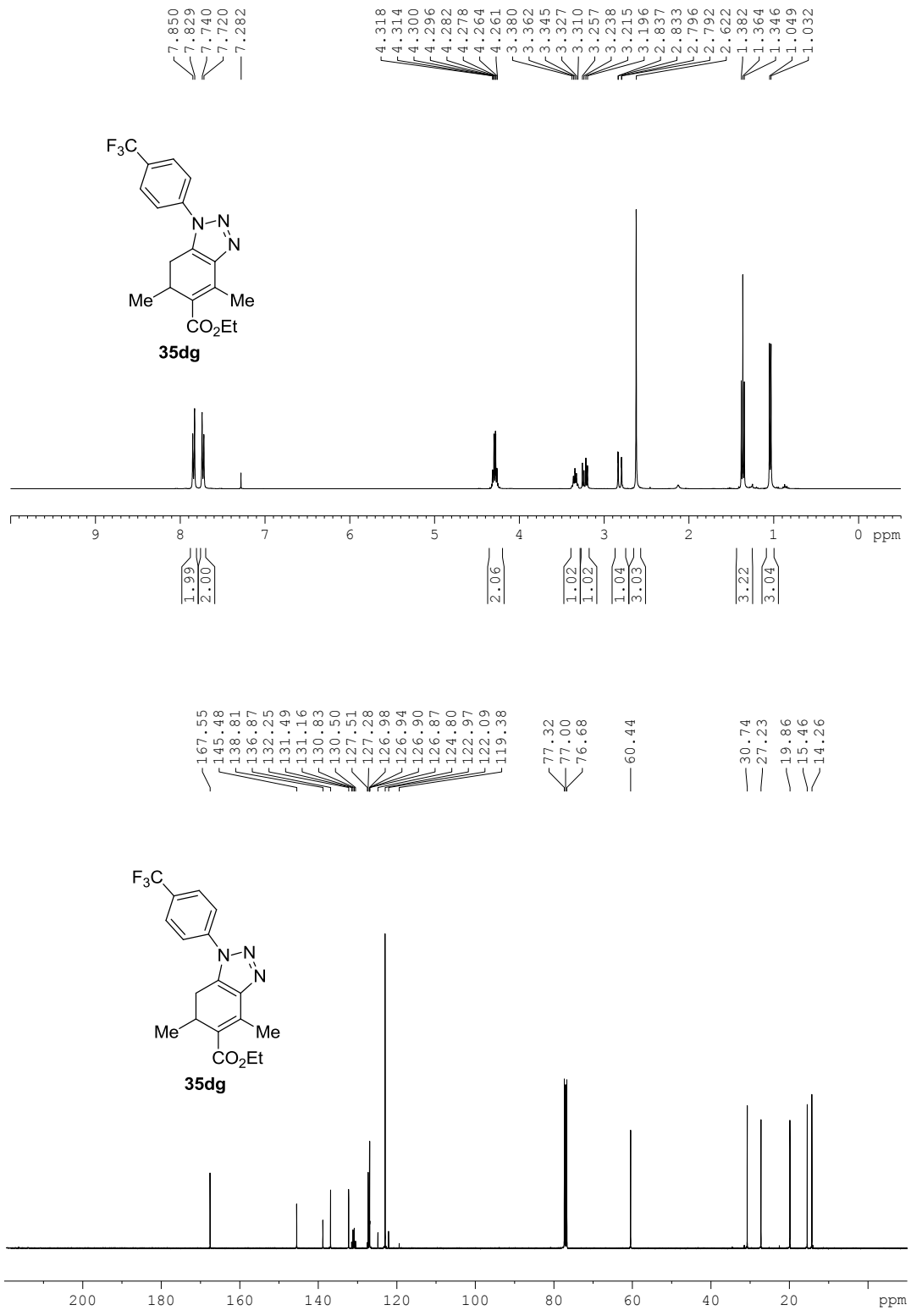


Figure-35: ^{1}H NMR and ^{13}C NMR spectrum of product **35dg**.

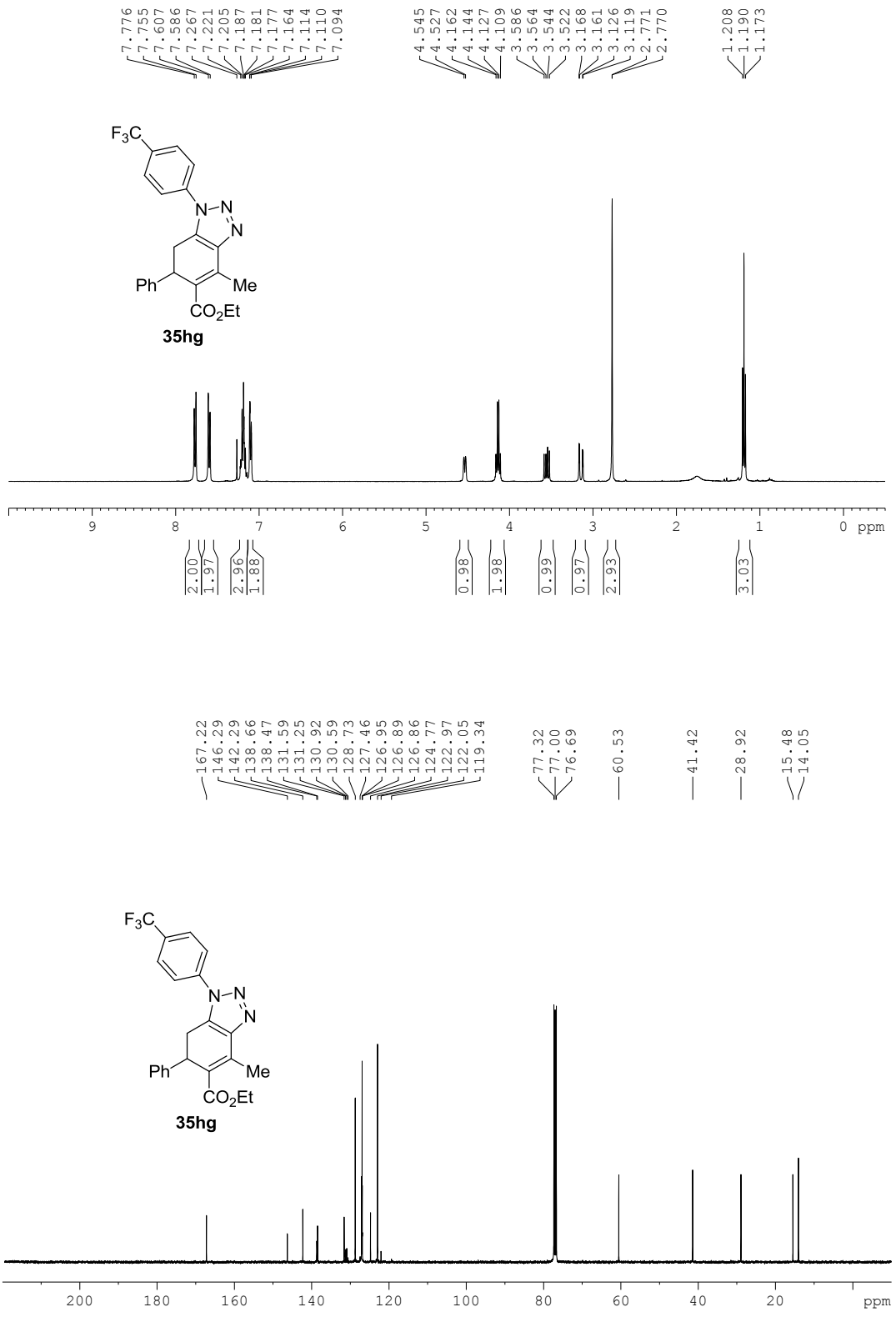


Figure-36: ^{1}H NMR and ^{13}C NMR spectrum of product **35hg**.

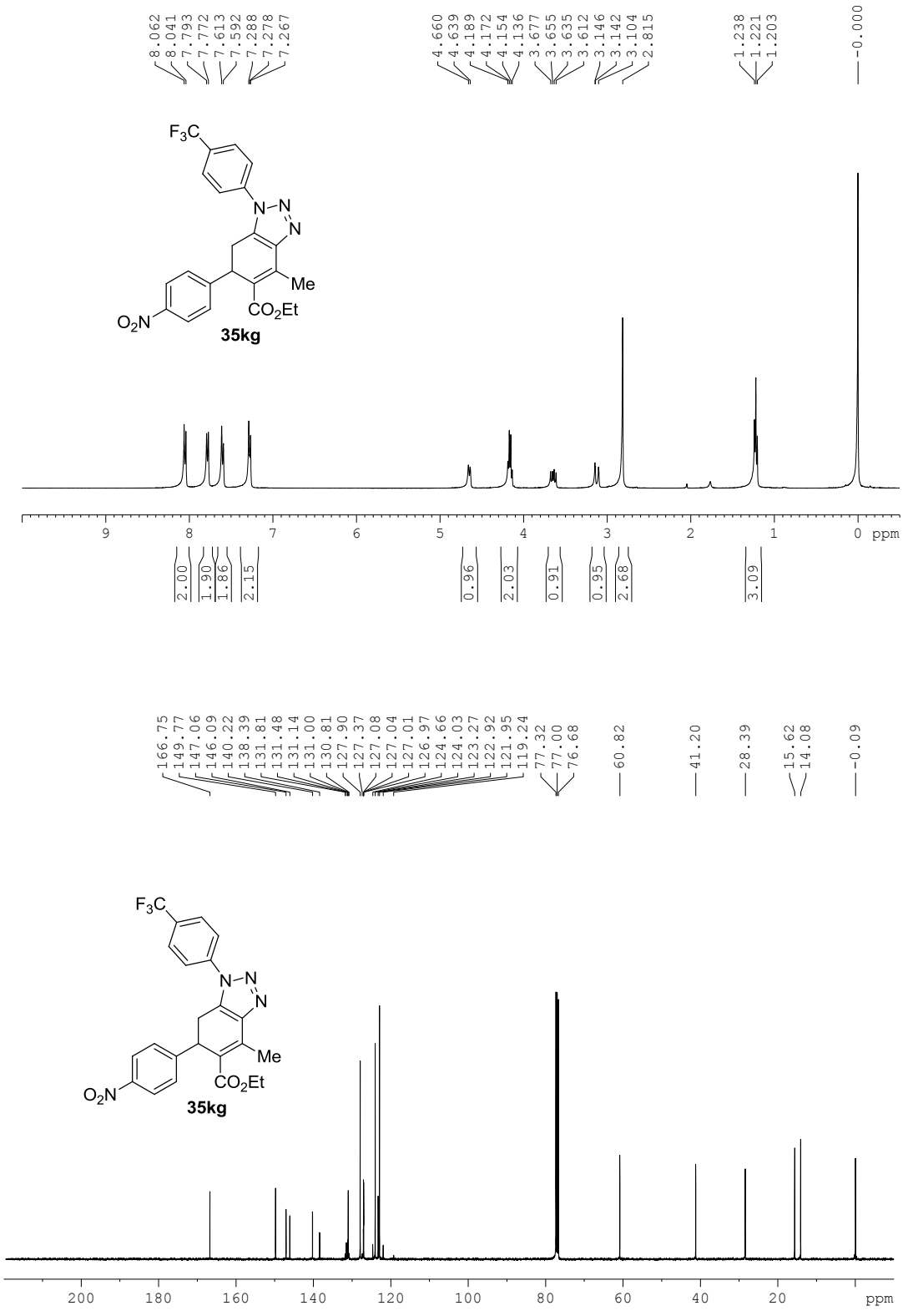


Figure-37: ^{1}H NMR and ^{13}C NMR spectrum of product **35kg**.

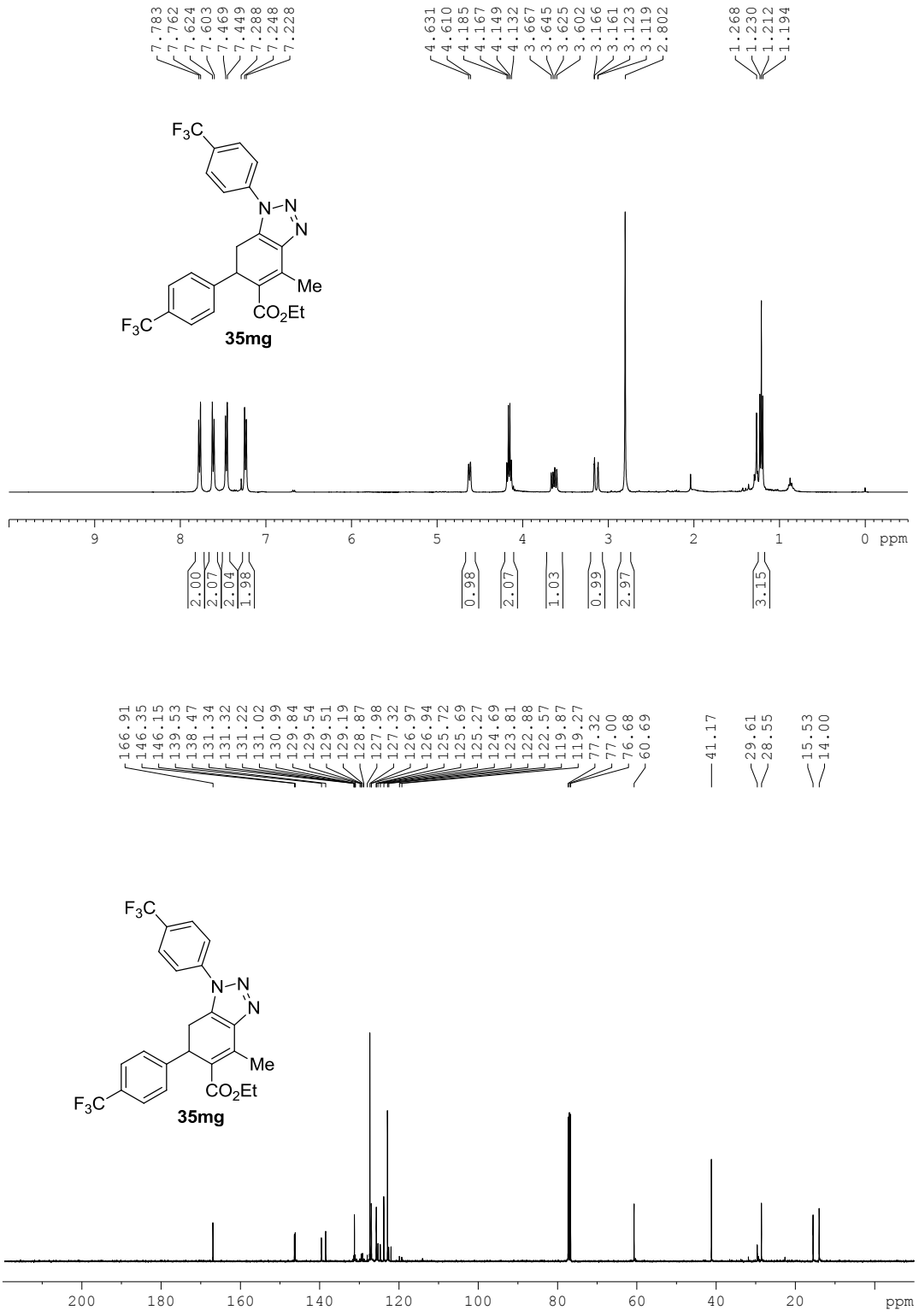


Figure-38: ^{1}H NMR and ^{13}C NMR spectrum of product **35mg**.

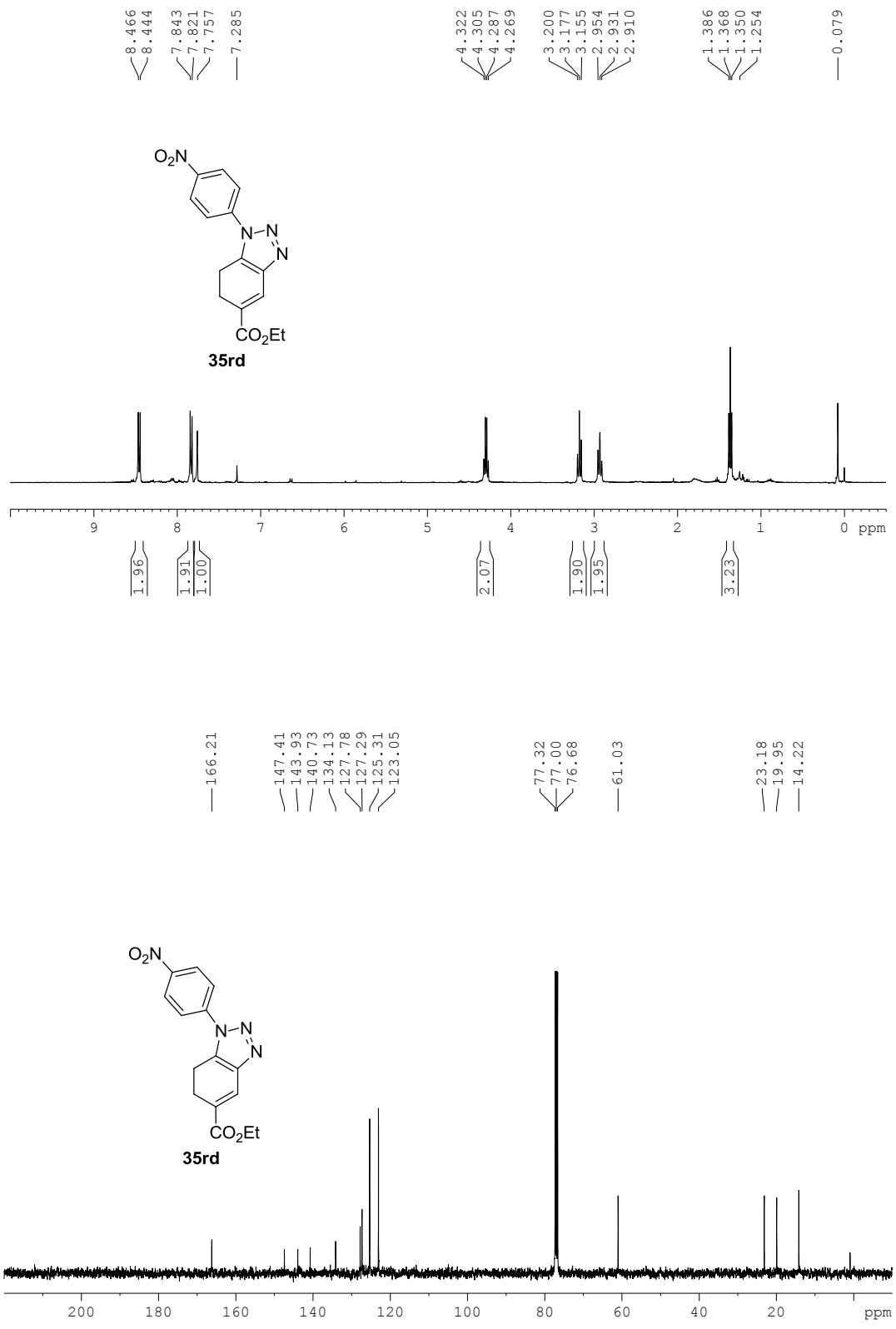


Figure-39: ^{1}H NMR and ^{13}C NMR spectrum of product **35rd**.

with excellent regioselectivity (Table 11, entries 7-14). Surprisingly, C-2 substituted enone **14p** and simple cyclic enones like **14q** and **14r** gave the high-yielding pharmaceutically useful [3+2]-CA products **35pg**, **35qg**, **35rg**, **35rd,** and **35rc** with aryl azides **2c-d, 2g** under the **15d**-catalysis at 25 °C within one hour (Table 11, entries 15-19). Structure and regiochemistry of [3+2]-CA products **35bg-rc** was confirmed by NMR analysis (for example Fig. 35-39) and also finally confirmed by X-ray structure analysis on **35bg** as shown in Figure 40.[52]

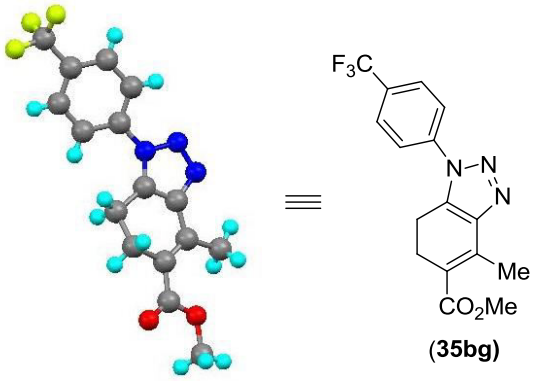
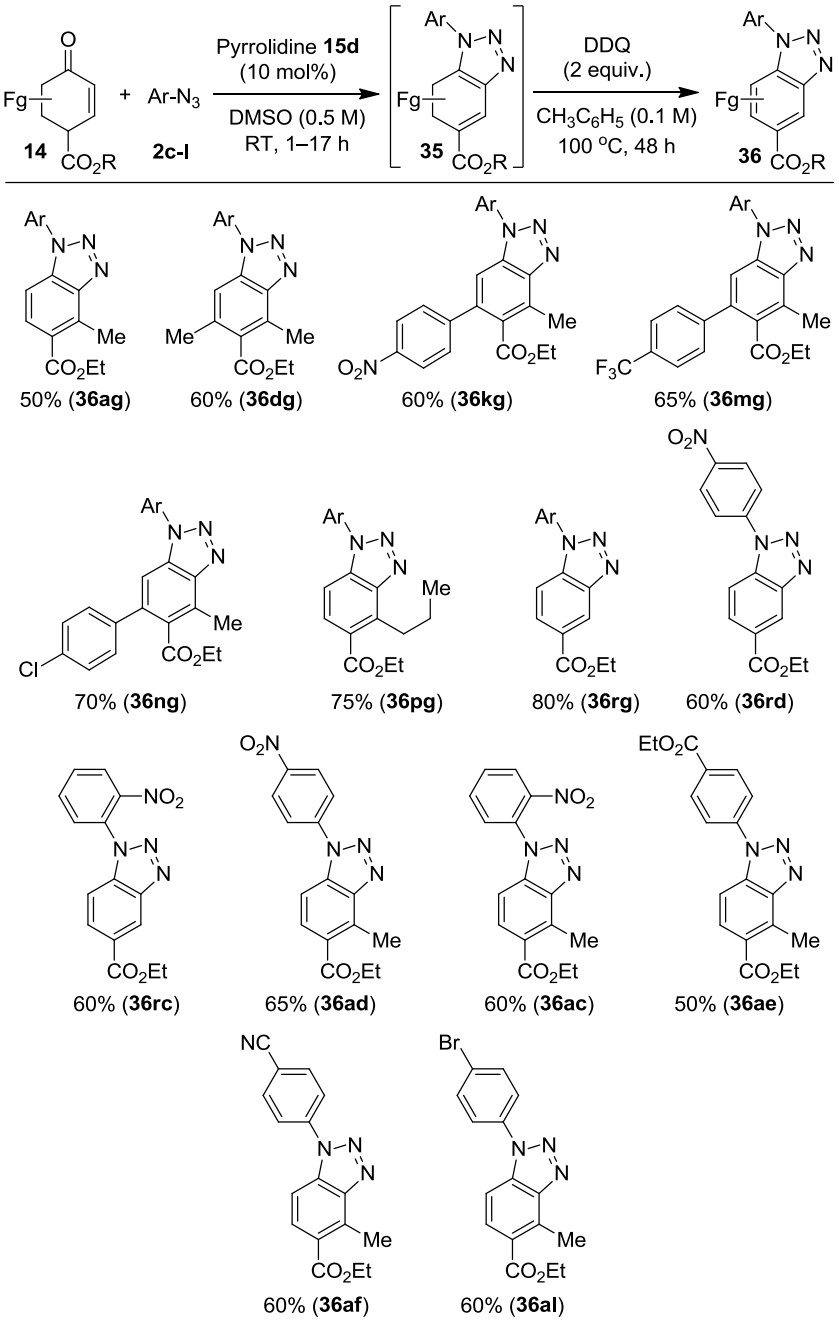


Figure 40: Crystal structure of methyl 4-methyl-1-(4-(trifluoromethyl)phenyl)-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (**35bg**).

After successful synthesis of bicyclic *N*-aryl-1,2,3-triazoles **35**, we then investigated the oxidative aromatization of **35** to *N*-aryl-benzotriazoles **36** in a sequential one-pot manner as shown in Table 12. Surprisingly, treatment of crude product **35ag**, obtained after aqueous workup from [3+2]-CA reaction, with 2 equiv. of DDQ in toluene at 100 °C for 48 h furnished the expected *N*-aryl-benzotriazole **36ag** with 50% overall yield (Table 12). With this result in hand, a variety of bicyclic *N*-aryl-1,2,3-triazoles **35** generated from unmodified functionalized cyclic enones **14a**-**r** and aryl azides **2c-g, 2l** were treated with 2 equiv. of DDQ in toluene at 100 °C for 48 h to furnish the expected *N*-aryl-benzotriazoles **36** in excellent to good overall yields, in a sequential one-pot manner (Table 12). In this reaction, both the electron withdrawing (NO_2, CF_3, CO_2Et, CN and Br) substituted aryl azides **2** and C2/C6-substituted unmodified cyclic enones **14** were used as substrates for the sequential

one-pot synthesis of *N*-aryl-benzotriazoles **36** (Table 12). The results in Table 12 demonstrate the broad scope of this novel methodology covering a structurally diverse group of cyclic enones **14a-r** and aryl azides **2c-g, 2l**.

Table 12: Diverse libraries of *N*-aryl-benzotriazoles **36**. [a,b]



[a] Yield refers to the column-purified product. [b] In entries 1 to 7, Ar is 4-$CF_3C_6H_4$

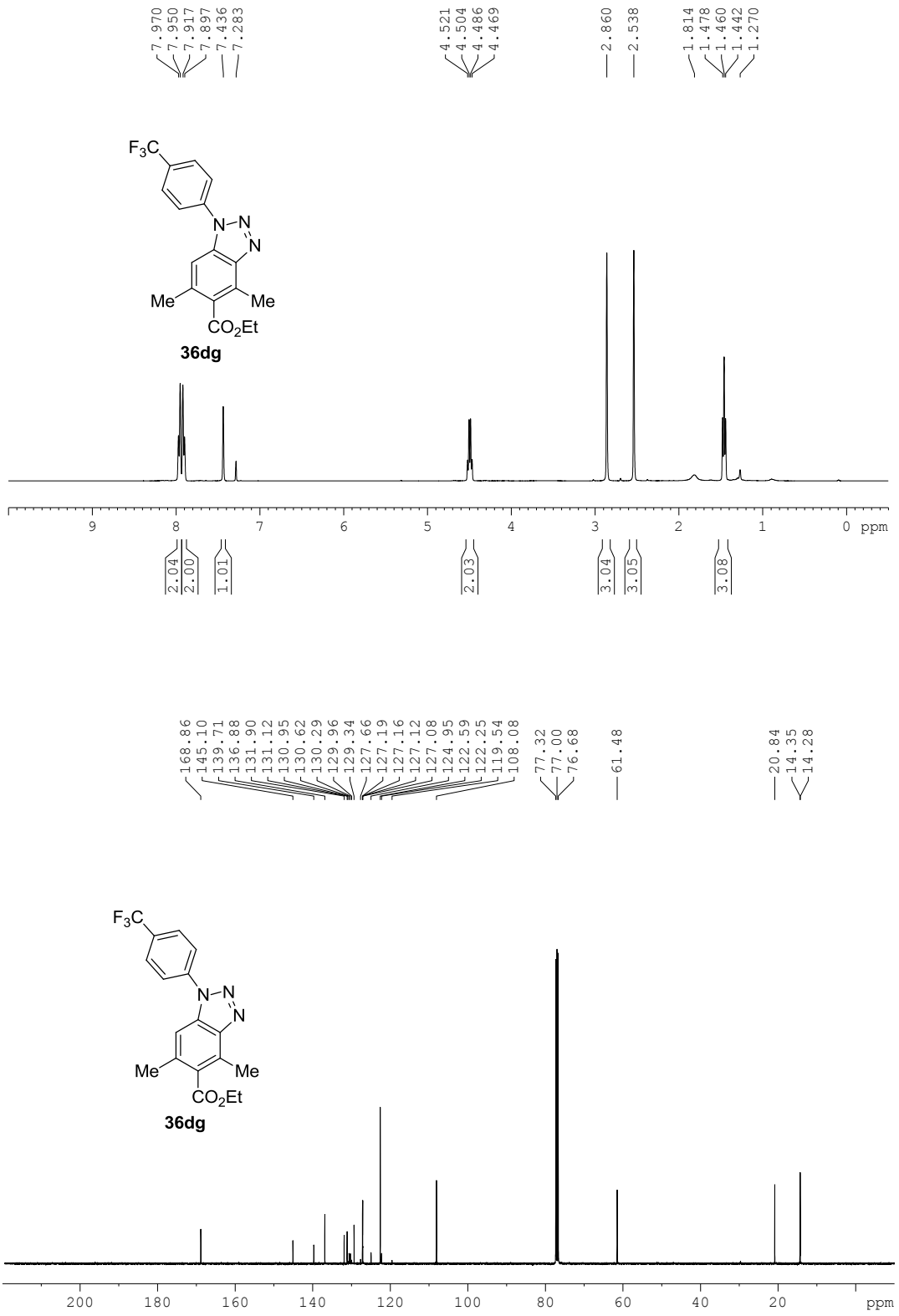


Figure-41: ^{1}H NMR and ^{13}C NMR spectrum of product **36dg**.

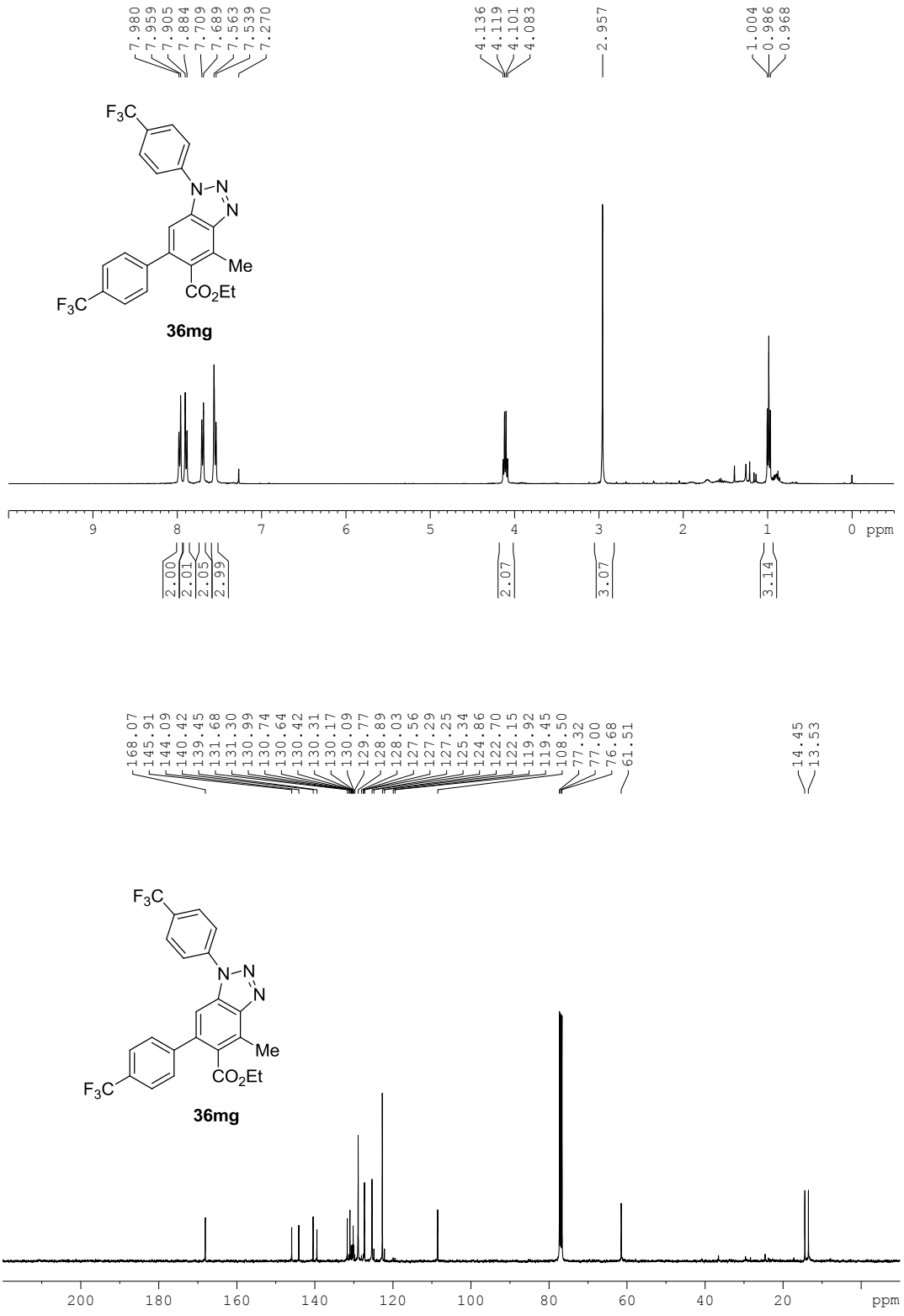


Figure-42: ^{1}H NMR and ^{13}C NMR spectrum of product **36mg**.

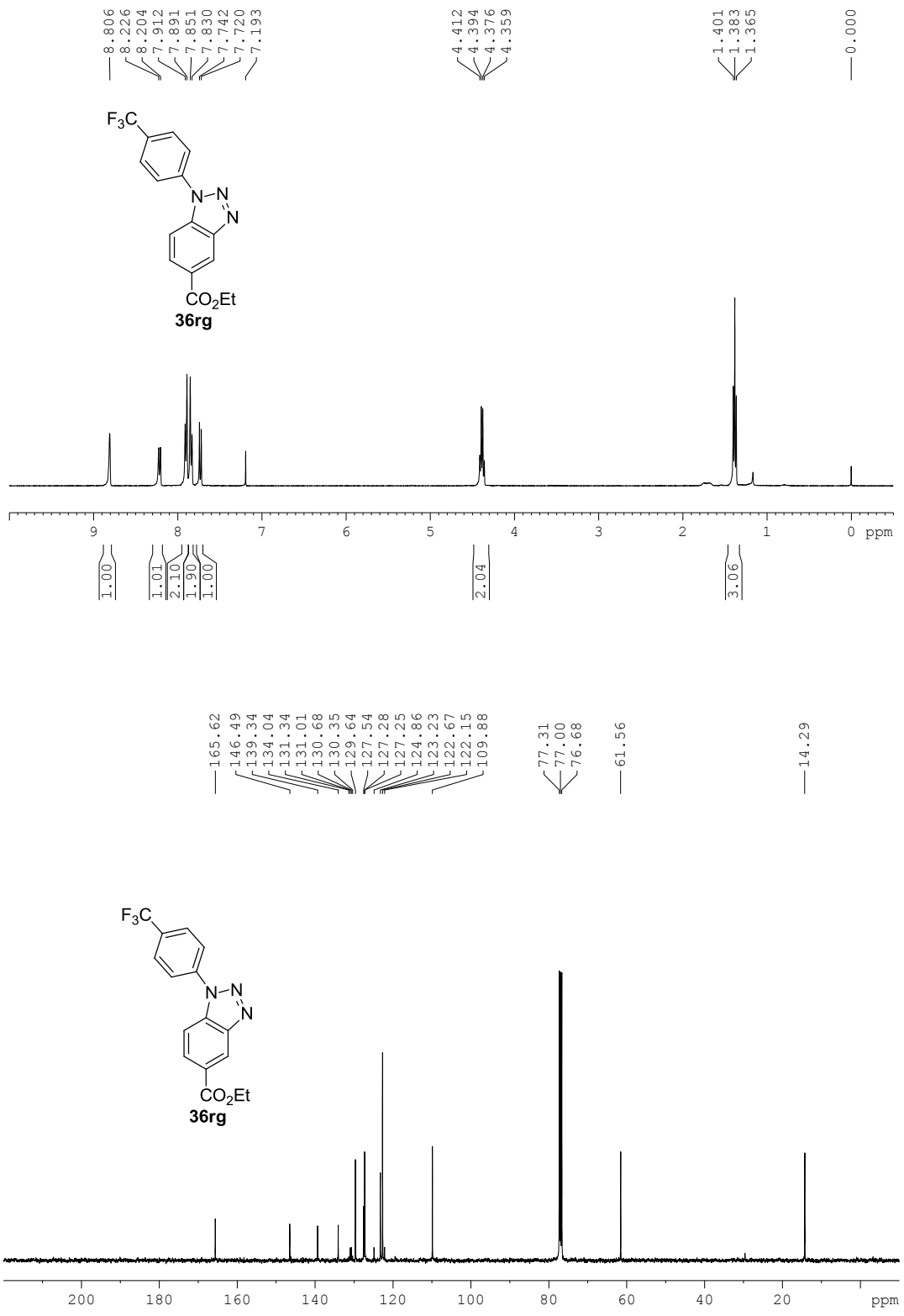


Figure-43: ^{1}H NMR and ^{13}C NMR spectrum of product **36rg**.

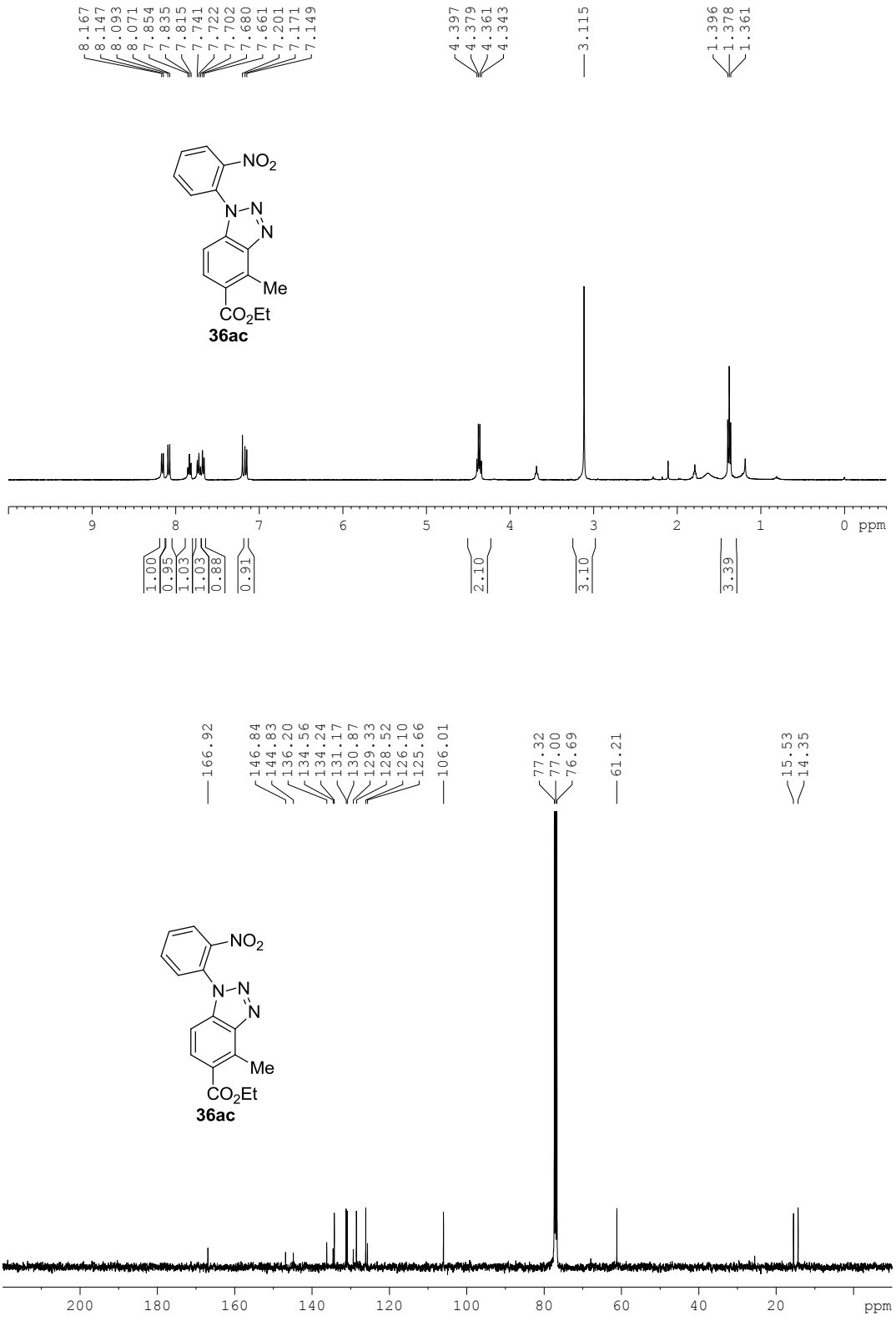


Figure-44: ^{1}H NMR and ^{13}C NMR spectrum of product **36ac**.

Many of the yields obtained were very good compared to other routes. Structure and regiochemistry of products **36** was confirmed by NMR analysis (for example Fig. 41-44) and also finally confirmed by X-ray structure analysis on **36rg** as shown in Figure 45.[52]

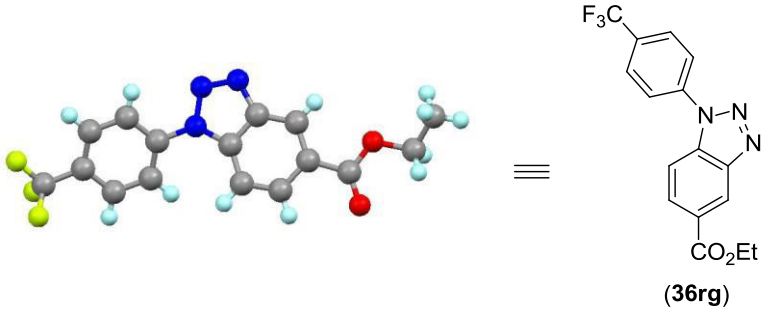
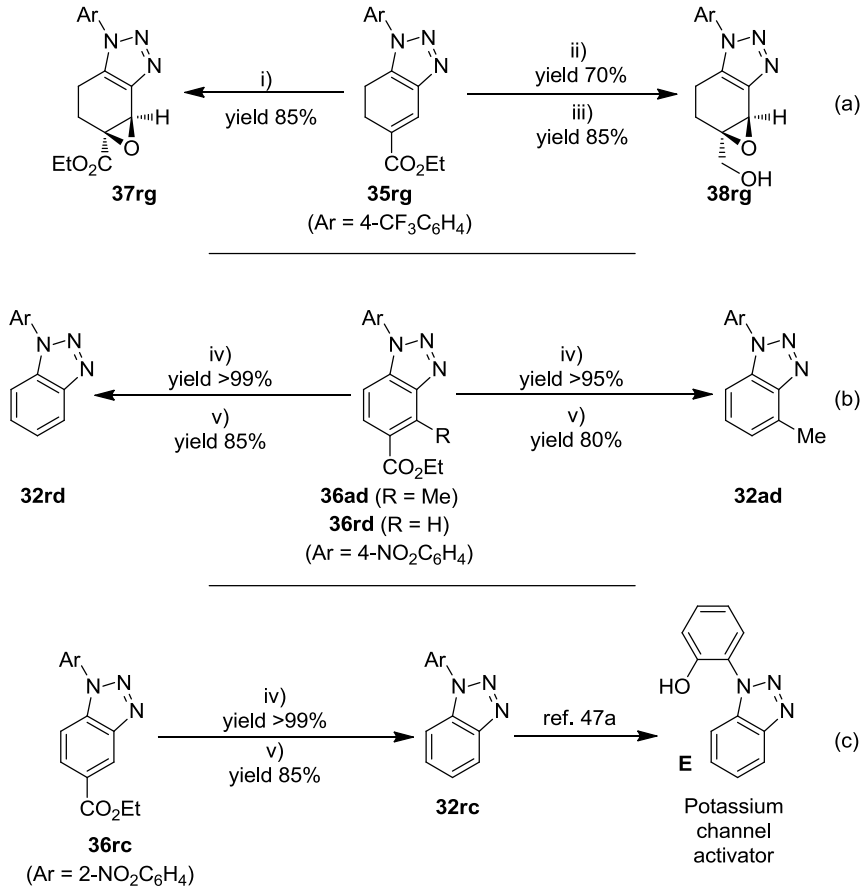


Figure 45: Crystal structure of ethyl 1-(4-(trifluoromethyl)phenyl)-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (**36rg**).

With the medicinal applications in mind, we explored the utilization of heterocycles **35** and **36** bearing aryl CF_3 and NO_2 in the high-yielding synthesis of functionalized *N*-aryl-1,2,3-triazoles and *N*-aryl-benzotriazoles **37, 38, 32** *via* simple reduction, epoxidation, ester hydrolysis, and decarboxylation reactions (Scheme 8a-c). Interestingly, direct oxidation of the *N*-aryl-1,2,3-triazole **35rg** with 1.2 equiv. of *m*CPBA in dry CH_2Cl_2 at 0 °C for 1 h furnished the selective epoxide **37rg** in 85% yield (Scheme 8a). Ester reduction of *N*-aryl-1,2,3-triazole **35rg** with 4 equiv. of $LiAlH_4$ in dry Et_2O at 0-25 °C for 2 h followed by oxidation with 1.2 equiv. of *m*CPBA in dry CH_2Cl_2 at 0 °C for 1 h furnished the functionalized epoxide **38rg** in 85% yield (Scheme 8a). Lithium hydroxide mediated hydrolysis of *N*-aryl-benzotriazoles **36ad** and **36rd** at 25 °C for 4-5 h furnished the acids in very good yields, which on further treatment with copper powder in quinoline at 220 °C for 1 h furnished the decarboxylated *N*-aryl-benzotriazoles **32ad** and **32rd** in good yields (Scheme 8b).

Scheme 8. Synthetic applications of *N*-aryl-1,2,3-triazole **35rg** and *N*-aryl-benzotriazoles **36**.



Reaction conditions: i) *m*CPBA (1.2 equiv), DCM (0.1 M), 0 °C, 1 h, 85%; ii) $LiAlH_4$ (4.0 equiv), Et_2O (0.1 M), 0 °C, 2 h, 70%; iii) *m*CPBA (1.2 equiv), DCM (0.1 M), 0 °C, 1 h, 85%; iv) LiOH (6.0 equiv), MeOH+H_2O+THF (1:1:4; 0.1 M), RT, 4 h; v) Cu powder (40 mol%), quinoline (0.1 M), 220 °C, 1 h.

As we are interested to synthesize the biologically important *N*-aryl-benzotriazoles, herein, we applied the two-step hydrolysis/decarboxylation protocol to generate the key intermediate **32rc** for the synthesis of potassium channel activator **E** (Scheme 8c). Some of the compounds **32ad**, **32rd** and **32rc** obtained from ester hydrolysis and decarboxylation sequence are precursors for the synthesis of drug molecules **D-G** (used as a *c*-Kit protooncogene, potassium channel activator, antiplasmodial and antibacterial agents, respectively), emphasizing the value of this organocatalytic triazole and benzotriazole approach to the pharmaceuticals (Figure 32 and Scheme 8c).[47]

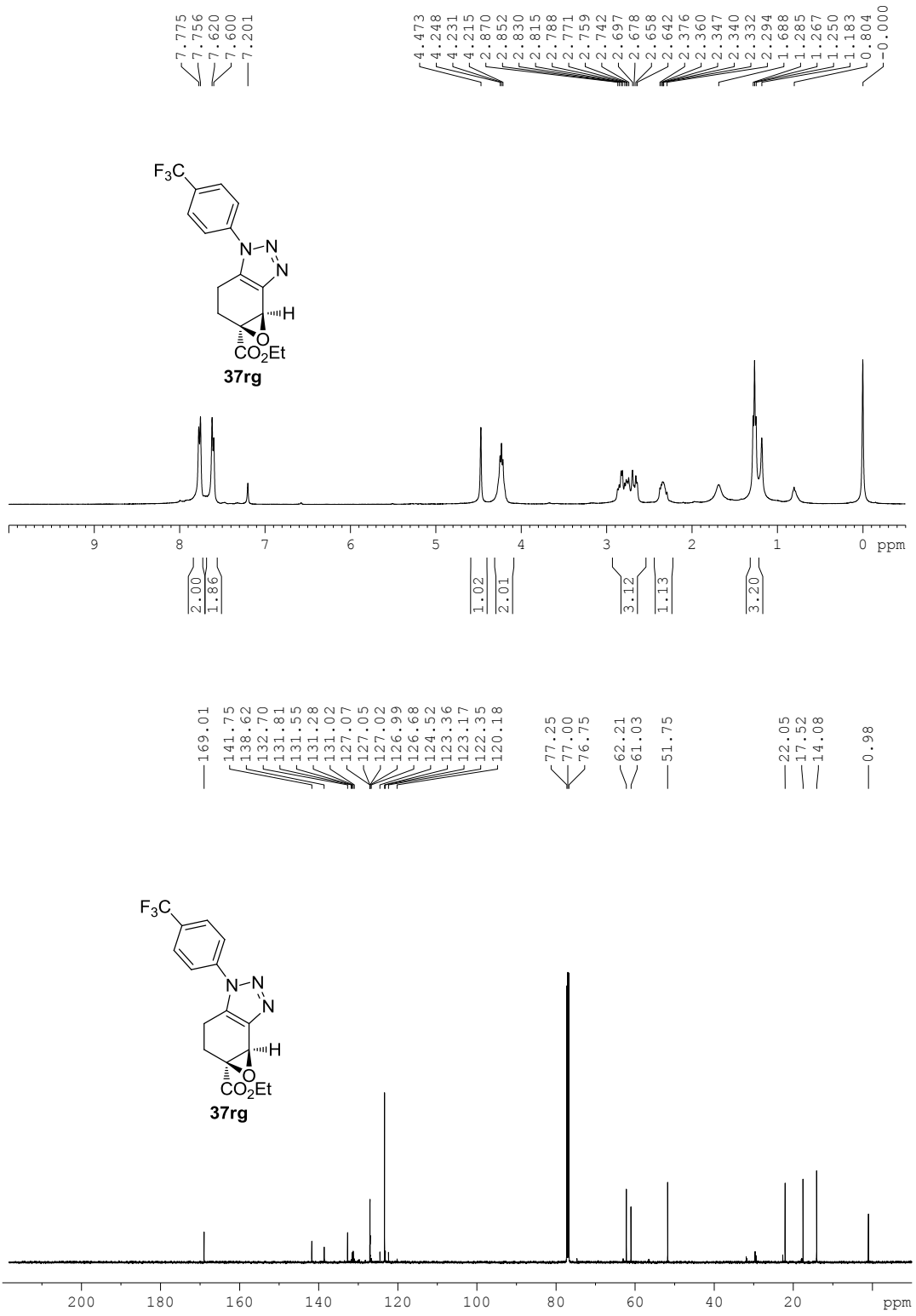


Figure-46: ^{1}H NMR and ^{13}C NMR spectrum of product **37rg**.

Figure-47: ^{1}H NMR and ^{13}C NMR spectrum of product **38rg**.

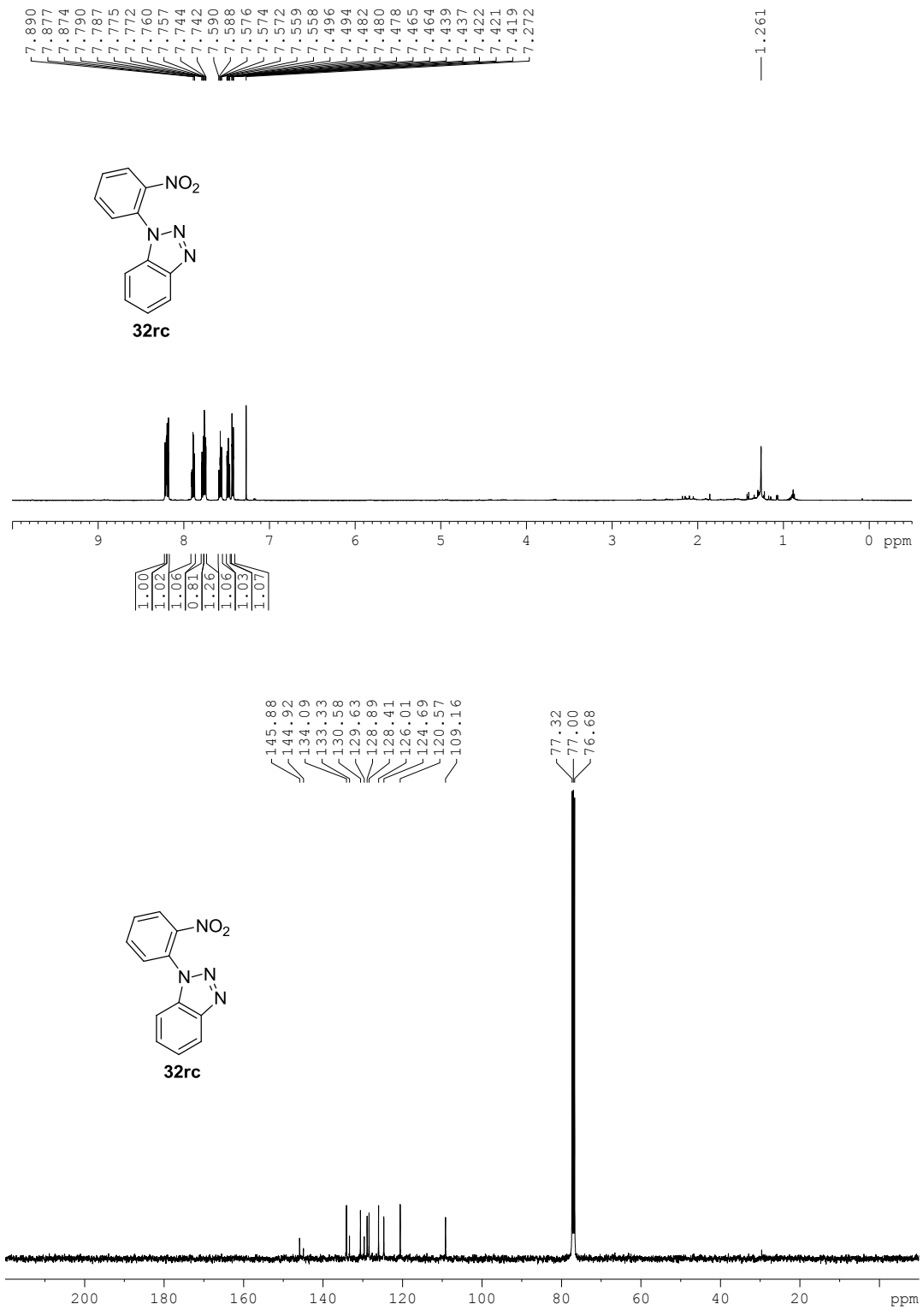
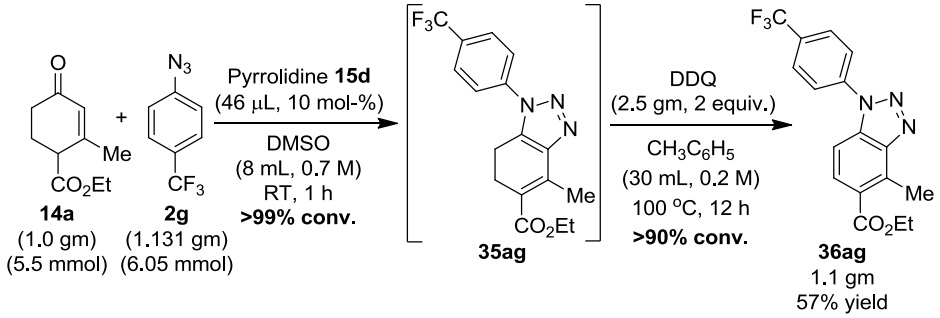


Figure-48: ^{1}H NMR and ^{13}C NMR spectrum of product **32rc**.

Based on their many medicinal applications, herein, we have demonstrated the gram-scale synthesis of *N*-aryl-benzotriazole **36ag** (Scheme 9). By scaling up milligrams to 1.0 gram of enone **14a** with 1.131 grams of aryl azide **2g** in 8.0 mL of DMSO at 25 °C for 1 h under the pyrrolidine-catalysis furnished the crude triazole product **35ag** in >99% conversion with >95% purity, which on further treatment with 2.5 grams of DDQ in 30 mL of toluene at 100 °C for 12 h furnished the **36ag** in >90% conversion with 57% overall yield. The slightly improved yield of benzotriazole **36ag** with shorter reaction time in gram-scale synthesis compared with milligram-scale (Table 12, entry 1), may be due to the slight change in reaction concentration (Scheme 9).[53]

Scheme 9. Gram-scale synthesis of N-aryl-benzotriazole **36ag**.

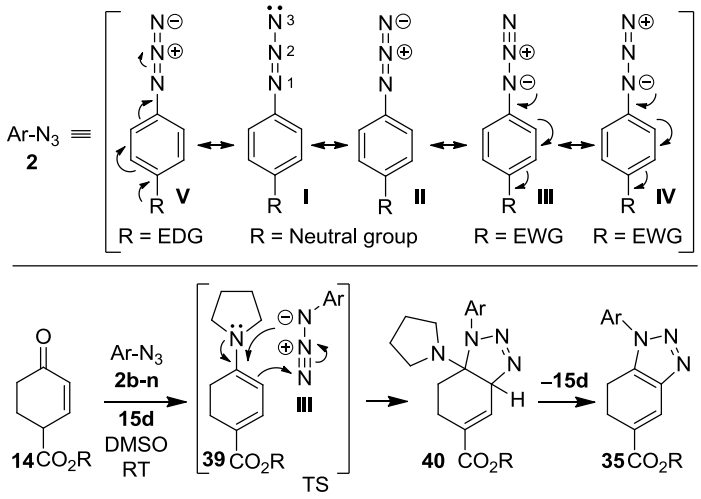


5.3 Mechanistic Insights

The rationale for the observed different reactivity and high selectivity of aryl azides **2b-p** in organoclick reactions could be explained by the mechanism as shown in Scheme 10. Mesomerism or resonance between azido group and the aromatic ring is the most fundamental factor to determine the reactivity of the aryl azides in organic synthesis.[53c] Some of the physicochemical properties of the aryl azides can be explained by a consideration of their mesomeric structures and we have shown the possible dipolar mesomeric structures, when azido group is connected to different aryl groups (**I**-**V**). The excellent reactivity and high regioselectivity of aryl azides **2c-g** with in situ generated nucleophiles of push-pull dienamines **39** is explained on the basis of the probably major contributing mesomeric structures **III** and **IV** (attack on N^3 by **39**) compared to **I**, **II** or **V**. Exploring the organoclick reaction with functionalized aryl azides **2b-p** more clearly demonstrated that the electron withdrawing groups around the aryl azides is the key factor to enhance the reaction rate

(Table 10). Notably, the reaction with *para*-methyl phenyl azide **2n** and phenyl azide **2b** proceeded about 40, 66 times slower than **2d** and there is no reaction with *para*-methoxy phenyl azide **2p** (Table 10), which is indicating that the electronic nature of the substituent is a decisive factor to affect the reaction rate. The possible mechanism for the regioselective synthesis of **35** through reaction of enones **14**, Ar-N_3 **2** and pyrrolidine **15d** is illustrated in Scheme 10. Reaction of **15d** with enone **14** generates the push-pull dienamine **39**,[4a, 54] which on in situ treatment with probably major contributing mesomeric structure **III** of Ar-N_3 **2** furnish the selectively adduct **40** *via* concerted [3+2]-cycloaddition, which further transform into the product **35** through rapid elimination of pyrrolidine **15d**.

Scheme 10. Proposed reaction mechanism.



5.4 Conclusions

In conclusion, we have developed the copper-free synthesis of *N*-aryl-1,2,3-triazole and *N*-aryl-benzotriazole products **35** and **36** from the simple unmodified starting materials *via* [3+2]-CA and oxidative aromatization reactions under the amine-catalysis. The sequential one-pot reaction proceeds in good yields with high selectivity using pyrrolidine as the catalyst. Furthermore, we have demonstrated the medicinal applications of products **35** and **36**. In our laboratory, further work is in progress to develop asymmetric version of [3+2]-CA reactions.

In continuation to the development of push-pull dienamine catalysis in sequential one-pot reactions, asymmetric synthesis of chiral decalines through diastereoselective organocatalytic domino process was reported and the results are presented in the next chapter.

6. Organocatalytic Asymmetric Synthesis of Substituted Chiral Decalines through Diastereoselective Domino Claisen-Schmidt/Henry Reaction

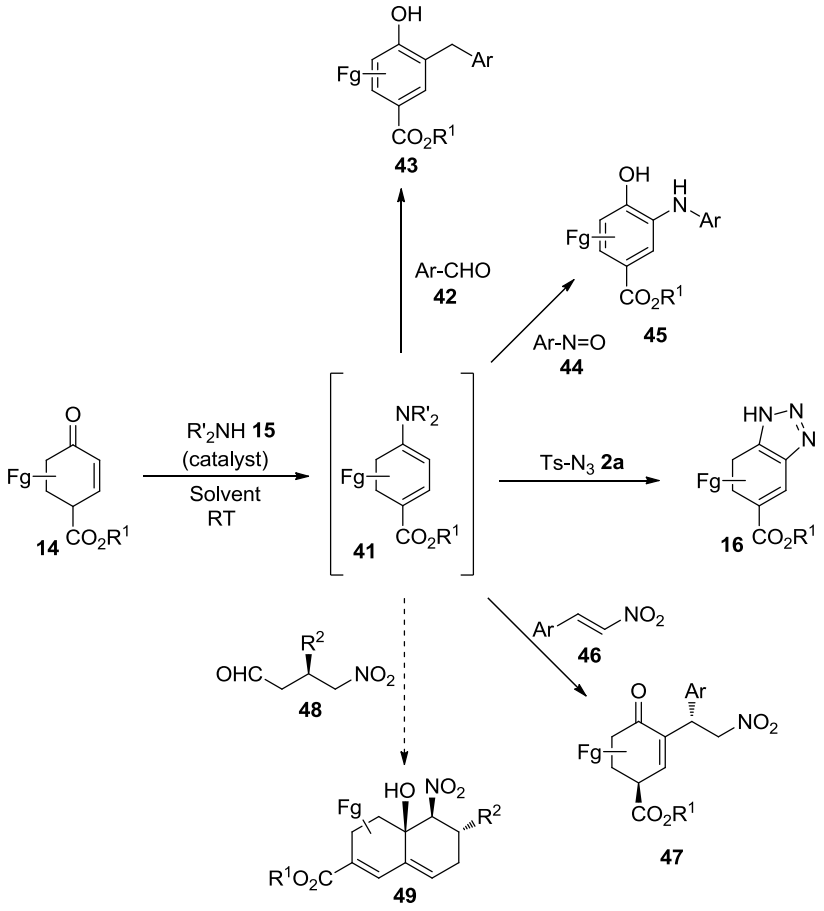
6.1 Introduction

The asymmetric synthesis of functionalized bicyclic carbon frame works is always a challenging task in synthetic chemistry. Chiral bicyclic carbon frame works (decalines) found in a wide variety of polyterpenoid and steroid natural products with interesting biological activity.[55] Recently, organocatalytic cascade/domino processes involving iminium and enamine activation were become very useful for the synthesis of functionalized bicyclic, tricyclic and spirocyclic molecules with high enantio- and diastereoselectivity.[1] The domino reactions of Serebryakov 1-amino-1,3-butadiene,[2,56] Barbas 2-amino-1,3-butadiene,[2,57] Jorgenson/Chen trienamine[3,58] and Ramachary amino-enyne[59] catalysis were well explored for the asymmetric synthesis of functionalized cyclohexanes. Although many organocatalytic domino reactions reported recently, the development of new and more efficient approaches in C-C bond formation with multiple stereogenic centers in a cascade manner is of significant interest.[60]

The Claisen-Schmidt reaction is one of the important C-C bond formation processes in organic chemistry able to provide α, β-unsaturated carbonyl compounds, which are important intermediates for the natural product synthesis.[61] The Henry (nitroaldol) reaction is another powerful C-C bond forming tool for the preparation of valuable synthetic intermediates such as nitro alcohols, which can be further transformed into a number of important nitrogen and oxygen-containing compounds.[62] Recently, domino Michael-Henry processes successfully demonstrated in the synthesis of highly functionalized cyclic frame works with multiple stereogenic centers.[63] However, to the best of our knowledge, there is no report involving a domino Claisen-Schmidt/Henry reaction strategy for the diastereoselective synthesis of bicyclic decalines with three contiguous stereocenters.

Recent discovery of push-pull dienamine[54] catalysis from our group have shown applications for the cascade synthesis of push-pull phenols **43**,[54a,e] o-hydroxydiarylamines **45**,[54b] substituted N*H*-1,2,3 triazoles **16**[4a] and chiral Baylis-Hillman type products **47**[54f] (Scheme 11). In continuation to our research interest in asymmetric organocatalytic reactions,[64] herein we have designed a diastereoselective approach to the functionalized chiral bicyclic decalines **49** from commercially available cyclic enones (Hagemann's esters) **14** and chiral γ-nitroaldehydes **48** through domino Claisen-Schmidt/Henry (CS/H) reaction based on push-pull dienamine catalysis as shown in Scheme 11.

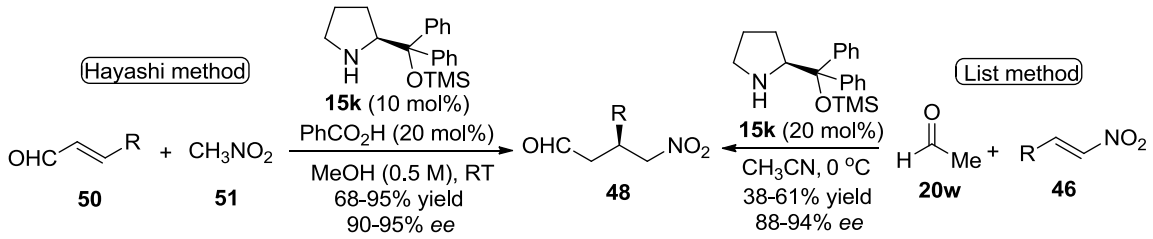
Scheme 11. Reaction design for the domino synthesis of chiral decalines through push-pull dienamine-catalysis.



Herein, we have employed the optically pure γ-nitroaldehydes as starting materials in the organocatalytic cascade reaction.[65] Recent organocatalytic asymmetric Michael approaches in the presence of diphenylprolinol silyl ether catalyst were able to provide γ-

nitroaldehydes in good yields (up to 95%) with high enantioselectivity (up to 95% *ee*) as shown in Scheme 12.[66]

Scheme 12. Synthesis of chiral γ-nitroaldehydes **48** from asymmetric Michael reaction.



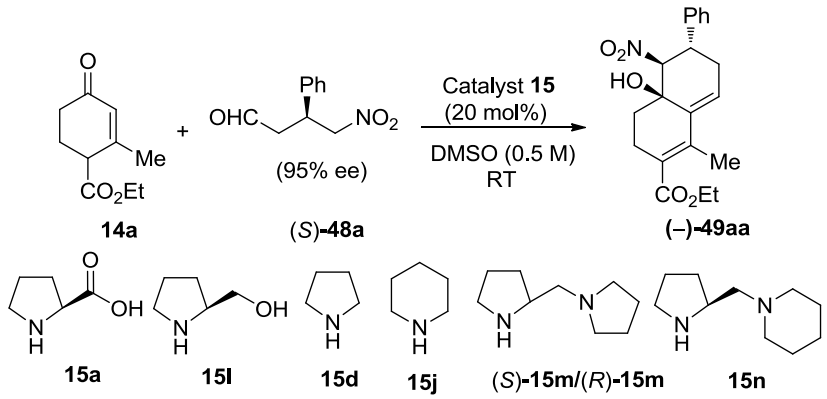
As we were interested to investigate the participation of carbonyl functionality of cyclic enones (Hagemann's esters) in organocatalytic cascade reaction, we decided to explore the functionalized γ-nitroaldehydes as starting materials in an amine-catalyzed CS/H reaction with enones. We envisioned that the reaction of γ-nitroaldehyde with in situ generated push-pull dienamine from cyclic enone under amine-catalysis would lead to Clasien-Schmidt adduct, which would then undergo an intramolecular Henry reaction to provide chiral bicyclic decalines. This unexpected result represents a novel methodology for the preparation of functionalized bicyclic carbon frame work and a new reactivity for amine-catalysts. Herein, we report our findings regarding these new sequential reactions.

6.2 Results and Discussion

For the optimization of designed CS/H reaction, we screened a number of known organocatalysts for the reaction of enone **14a** with 0.5 to 1.5 equiv. of γ-nitroaldehyde **48a** and some important results are shown in Table 13. Reaction of **14a** with 0.5 equiv. of γ-nitroaldehyde **48a** in DMSO catalyzed by 20 mol% of L-proline **15a** didn't furnished the product and the same result was observed with the L-prolinol **15l** also (Table 13, entries 1-2). After obtaining discouraging results with the L-proline **15a** and L-prolinol **15l**, we studied the reaction under slightly more basic secondary amine catalysis (Table 13, entries 3-13). Surprisingly, reaction in the presence of pyrrolidine **15d** (20 mol%) furnished the product (-)-**49aa** in 15% yield (Table 13, entry 3). The same reaction catalyzed by 20 mol% of piperidine **15j** gave the product (-)-**49aa** in 28% yield with 92% *ee* and >99% *de* (Table 13, entry 4). To improve the CS/H cascade reaction, with regard to decreasing the reaction time and

increasing the yields, we tested the cascade reaction of **14a** and **48a** in the presence of more basic chiral diamine catalysts (*S*)-**15m** and (*S*)-**15n** in DMSO at 25 °C (Table 13, entries 5–6). Reaction with 20 mol% of (*S*)-1-(pyrrolidin-2-ylmethyl)pyrrolidine **15m** as catalyst furnishes the product (-)-**49aa** in 64% yield with 94% *ee* (Table 13, entry 5).

Table 13: Reaction optimization.[a-c]



Entry	Catalyst (20 mol%)	Time	Yield (%) of **49aa**	*Ee* (%) of **49aa**
1	**15a**	24 h	-	-
2	**15l**	24 h	-	-
3	**15d**	24 h	15	n.d
4	**15j**	24 h	28	92
5	(*S*)**-15m**	5 h	64	94
6	(*S*)**-15n**	5 h	50	95
7[d]	(*S*)**-15m**	5 h	53	96
8[e]	(*S*)**-15m**	24 h	-	-
9[f]	(*S*)**-15m**	3 h	53	96
10[g]	(*S*)**-15m**	**6 h**	**70**	**>99**
11[g,h]	(*S*)**-15m**	5 h	50	96
12[g]	(*R*)**-15m**	5 h	75	94
13[g,i]	(*S*)**-15m**	4 h	72	–93

[a] Reactions were carried out in solvent (0.5 M) with 2.0 equiv. of **14a** relative to the **48a** in the presence of 20 mol% of catalyst. [b] Yield refers to the column-purified product. [c] *Ee* determined by CSP HPLC analysis.[d] DMF used as solvent. [e] $HClO_4$ (20 mol%) taken as co-catalyst. [f] 1.0 equiv. of **14a** was used. [g] 1.5 equiv. of **48a** was used.[h] Crude compound **48a** was used as such.[i] (*R*)**-48a** was used.

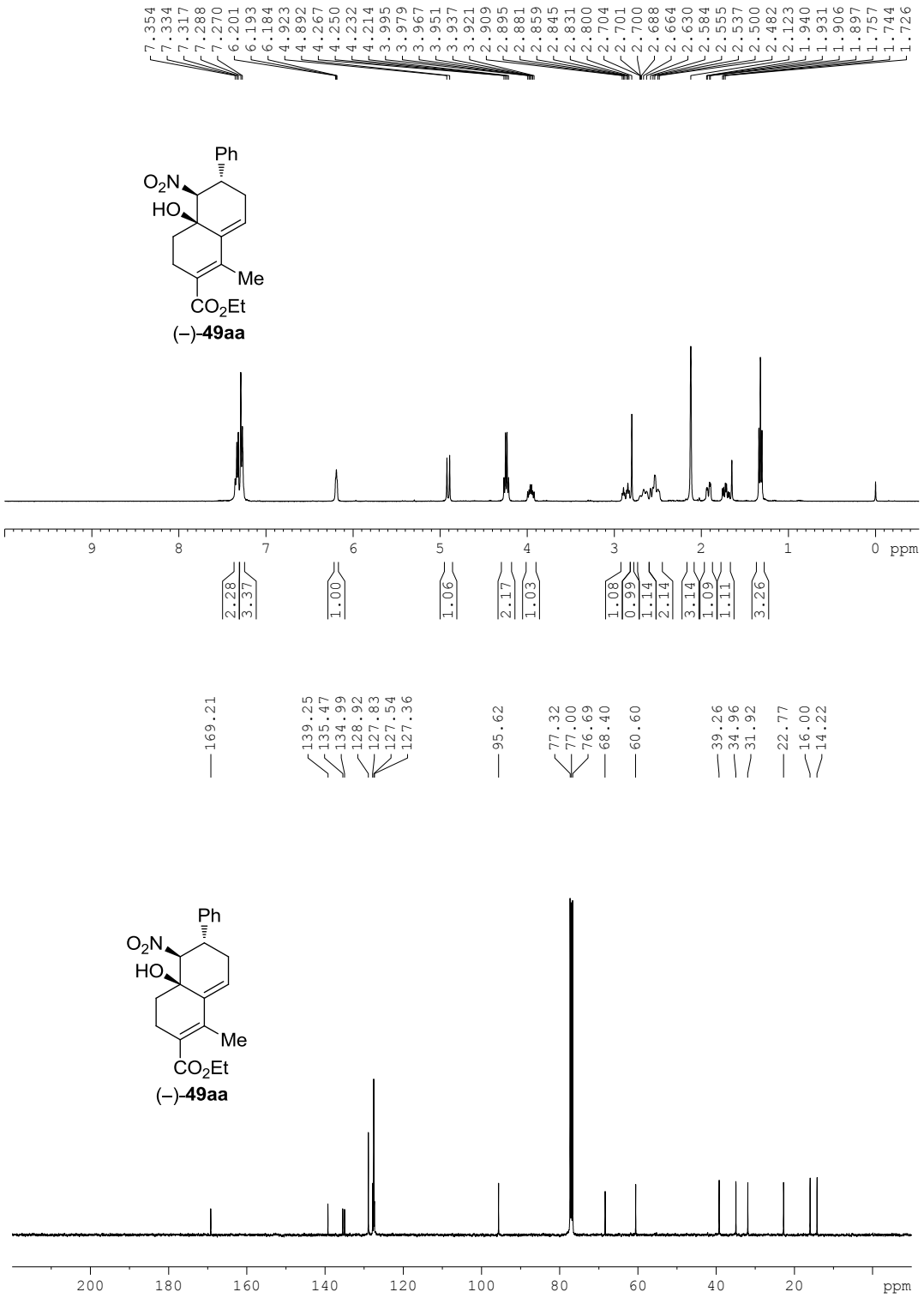
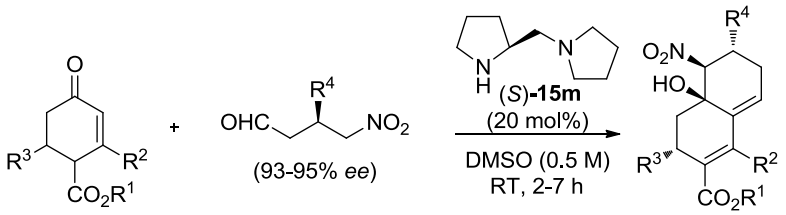


Figure-49: ^{1}H NMR and ^{13}C NMR spectrum of product **49aa**.

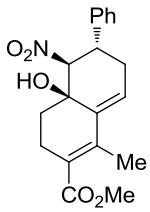
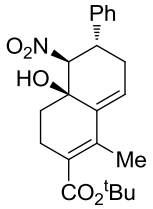
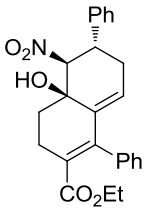
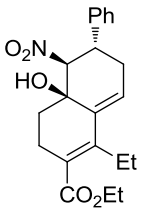
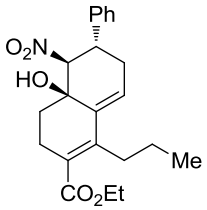
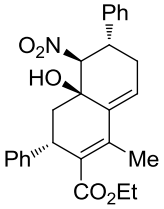
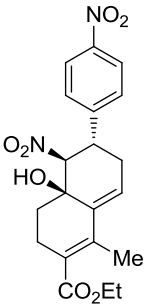
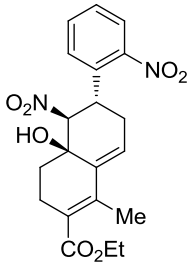
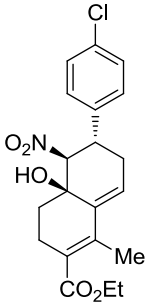
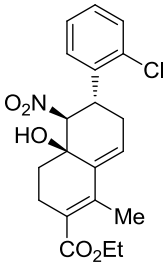
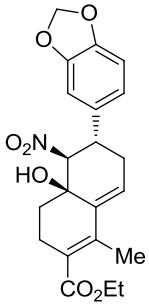
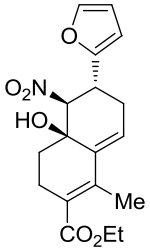
The same reaction catalyzed by diamine (*S*)-**15n** furnishes the product (-)-**49aa** in reduced (50 %) yield with 95% *ee* (Table 13, entry 6). For further improvement in yield and *ee* of product, we performed cascade reaction in DMF and also investigated co-catalyst effect under 20 mol% of (*S*)-**15m** catalysis, respectively (Table 13, entries 7-8). The reaction in DMF (53% yield, 96% *ee*) was not superior compared to DMSO solvent and there is no reaction with 20 mol% of perchloric acid as co-catalyst. Reaction of **14a** with 1.0 equiv. of **48a** in DMSO at 25 °C with 20 mol% of diamine (*S*)-**15m** as catalyst for 3 h furnishes the product (-)-**49aa** in 53% yield with 96% *ee* (Table 13, entry 9). The same reaction with 1.5 equiv of **48a** for 6 h furnished (-)-**49aa** in 70% yield with >99% *ee* (Table 13, entry 10). Surprisingly, treatment of crude aldehyde **48a** (from quick work up of Hayashi method)[66a] also with enone **14a** furnishes the decalin in reduced (50%) yield with 96% *ee* (Table 13, entry 11). For further understanding of the kinetics of the reaction, we carried out the reaction with 20 mol% of opposite enantiomer (*R*)-**15m,** which gave the same cascade product (-)-**49aa** in 75% yield with 94% *ee* (Table 13, entry 12). In another experiment, we performed the reaction with opposite enantiomer of γ-nitroaldehyde (*R*)-**48a** under **(***S***)-15m** catalysis affords the opposite enantiomer of decalin (+)-**49aa** in 72% yield with 93% *ee* (Table 13, entry 13). To our delight, in all the above cases cascade product obtained as single diastereomer (>99% *de*). After the preliminary studies, we considered the optimization conditions to be DMSO at 25 °C using 1.5 equiv. of (*S*)-**48a** and commercially available 20 mol% of (*S*)-**15m** as catalyst (Table 13, entry 10).

With the optimized conditions in hand, the scope and limitations of asymmetric CS/H cascade reaction was investigated between functionalized enones **14b-t** and chiral γ-nitroaldehydes **48a–g** (Table 14). A variety of functionalized cyclic enones **14b-t** with freshly prepared chiral γ-nitroaldehyde **48a** delivered the chiral decalines **49ba-ta** in good to moderate yields with high enantio and diastereoselectivities (Table 14, entries 1-6). Yields of decalines were reduced with increase in bulkiness of C-2 substitution of enone without effecting *ee* and *de* values, for example C-2 substituted enones **14s, 14t, 14p** furnished the expected decalines **49sa, 49ta, 49pa** in 25%, 35% and 40% yields with 94%, 99% and 97% *ee*'s and >99% *de* respectively (Table 14, entries 3-5). Surprisingly, the C2/C6-disubstituted enone **14h** gave the only one cascade CS/H product **49ha** in 21% yield with 93% *ee* and

Table 14: Synthesis of chiral decalines **49**.[a-c]



14 **48** **49**

 **49ba** (75%) *dr* = >99:1 *ee* = 96%	 **49ca** (50%) *dr* = >99:1 *ee* = 94%	 **49sa** (25%)[d] *dr* = >99:1 *ee* = 94%	 **49ta** (35%)[e] *dr* = >99:1 *ee* = 99%
 **49pa** (40%)[e] *dr* = >99:1 *ee* = 97%	 **49ha** (21%) *dr* = >99:1 *ee* = 93%	 **49ab** (65%) *dr* = >99:1 *ee* = 94%	 **49ac** (69%) *dr* = >99:1 *ee* = 96%
 **49ad** (69%) *dr* = >99:1 *ee* = 85%	 **49ae** (68%) *dr* = >99:1 *ee* = 95%	 **49af** (51%) dr = 3:1 ee = 87%, 86%	 **49ag** (40%) *dr* = 8:1 *ee* = 89%, 89%

[a] Reactions were carried out in DMSO (0.5 M) with 1.5 equiv. of **48** relative to the **14** in the presence of 20 mol% of catalyst. [b] Yield refers to the column-purified product. [c] *Ee* and *dr* determined by CSP HPLC analysis. [d] Reaction performed at 50 °C for 70 h. [e] Reaction time 24 h.

>99% *de* (Table 14, entry 6). The cascade CS/H reaction of enone **14a** with γ-nitroaldehydes bearing electron-deficient aryl substituents such as 4-nitrophenyl **48b**, 2-nitro phenyl **48c**, 4-chlorophenyl **48d** and 2-chlorophenyl **48e** gave the expected decalines **49ab-49ae** in good yields with high enantio- and diastereoselctivities (Table 14, entries 7-10), whereas elctron rich aryl substituent such as 3,4-methylenedioxyphenyl **48f** and heteroaryl substituent such as furyl **48g** reduced the diastereoselctivity of decalines **49af-49ag** without effecting *ee*'s (Table 14, entries 11-12). Interestingly, we did not observed the formation of bicyclic cascade product from ethyl keto-ester **14r** [R^2=R^3= H] with **48a** under the optimized conditions, may be because of electronic and steric factors (results not shown in Table 14).The structure and absolute stereochemistry of the chiral CS/H cascade products were confirmed by NMR analysis (for example Fig. 49-54) and also finally confirmed by X-ray structure analysis of **49aa** as shown in Fig. 50.[67]

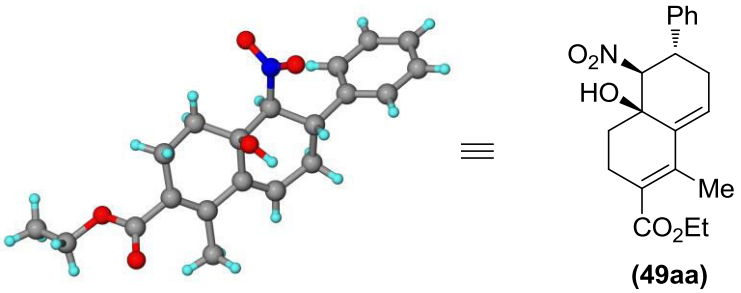


Figure 50: Crystal structure (4a*R*,5*S*,6*S*)-ethyl 4a-hydroxy-1-methyl-5-nitro-6-phenyl-3,4,4a,5,6,7-hexahydronaphthalene-2-carboxylate (**49aa**).

After the investigation of (*S*)-**15m** catalyzed asymmetric CS/H reactions of enones **14** with various β-aryl substituted γ-nitroaldehydes **48**, we further showed interest to screen β-alkyl substituted γ-nitroaldehydes **48h-k** with enone **14a** to investigate the electronic factors of substrates on product formation (Table 15). A series of alkyl substituted γ-nitroaldehydes **48h-k** were reacted with enone **14a** catalyzed by 20 mol % of (*S*)-**15m** at 25 °C for 5-7 h in DMSO (0.5 M). Surprisingly, in all these reactions along with expected bicyclic CS/H products **49ah-ak**, monocyclic CS/I (Claisen-Schmidt/isomerization) chiral (*E*)-1,3-diene products **52ah-ak** were isolated in minor quantities as shown in Table 15. The CS/H products were furnished in good to excellent *ee*'s and *de*'s whereas the CS/I diene products **52** were

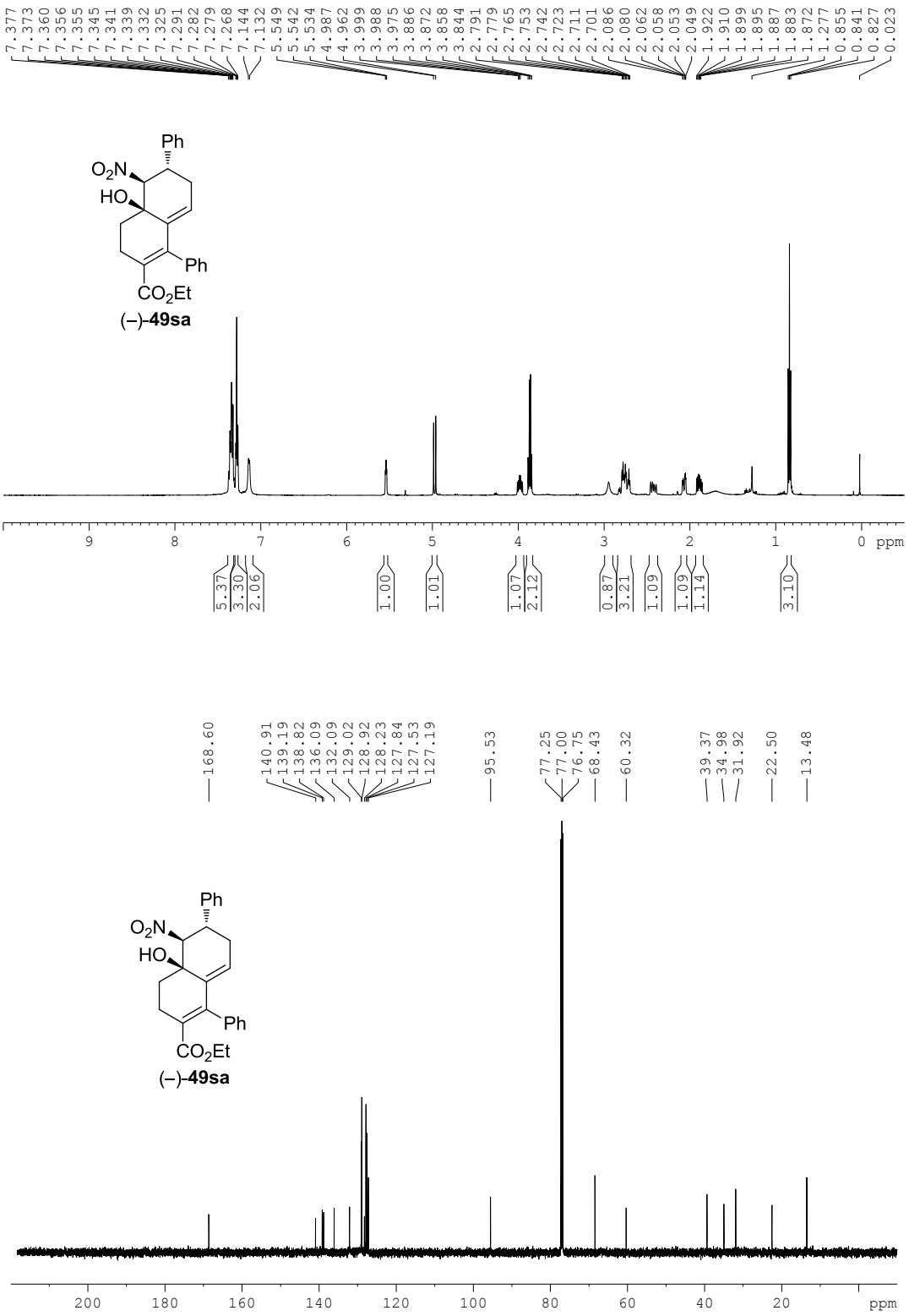


Figure-51: ^{1}H NMR and ^{13}C NMR spectrum of product **49sa**.

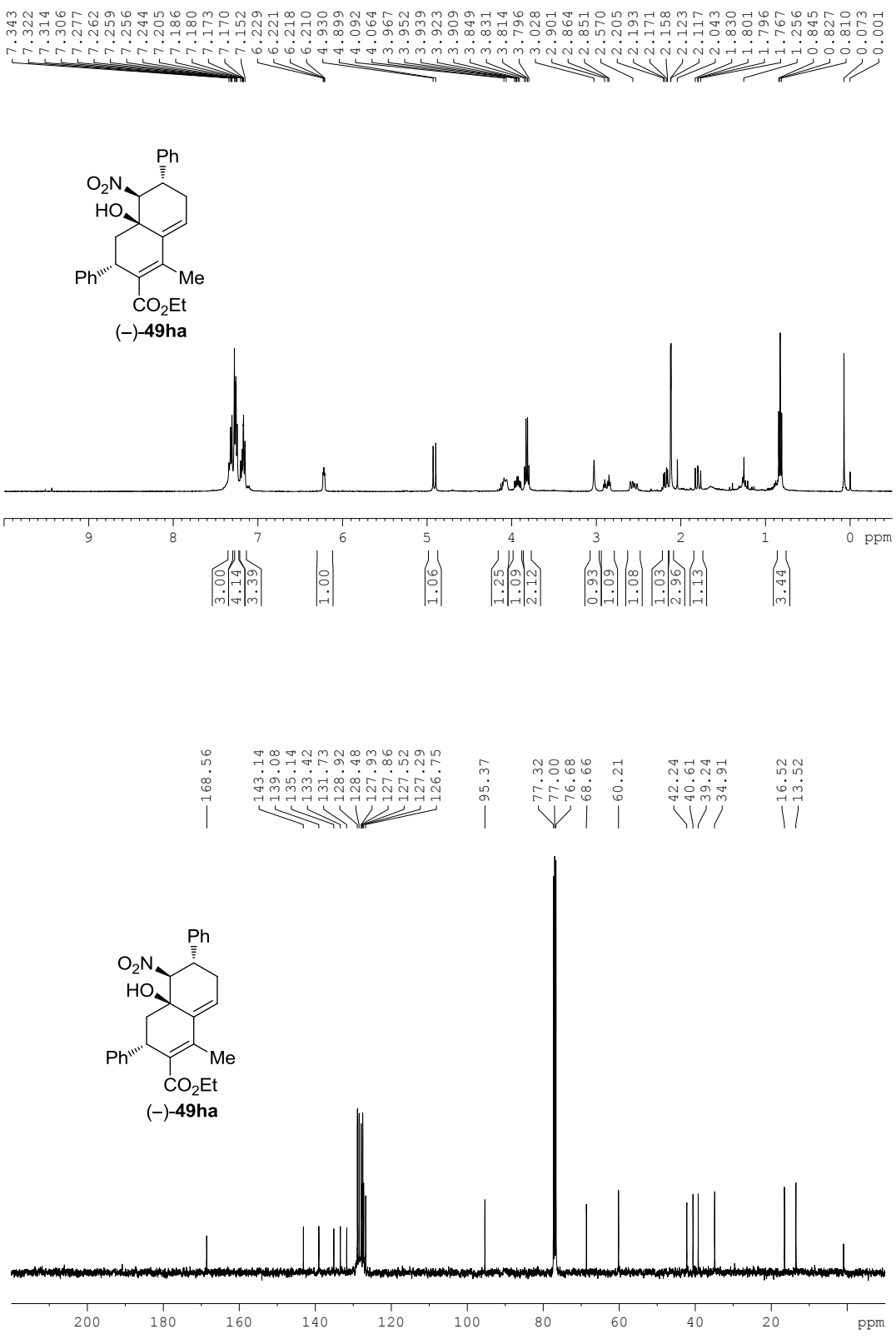


Figure-52: ^{1}H NMR and ^{13}C NMR spectrum of product **49ha**.

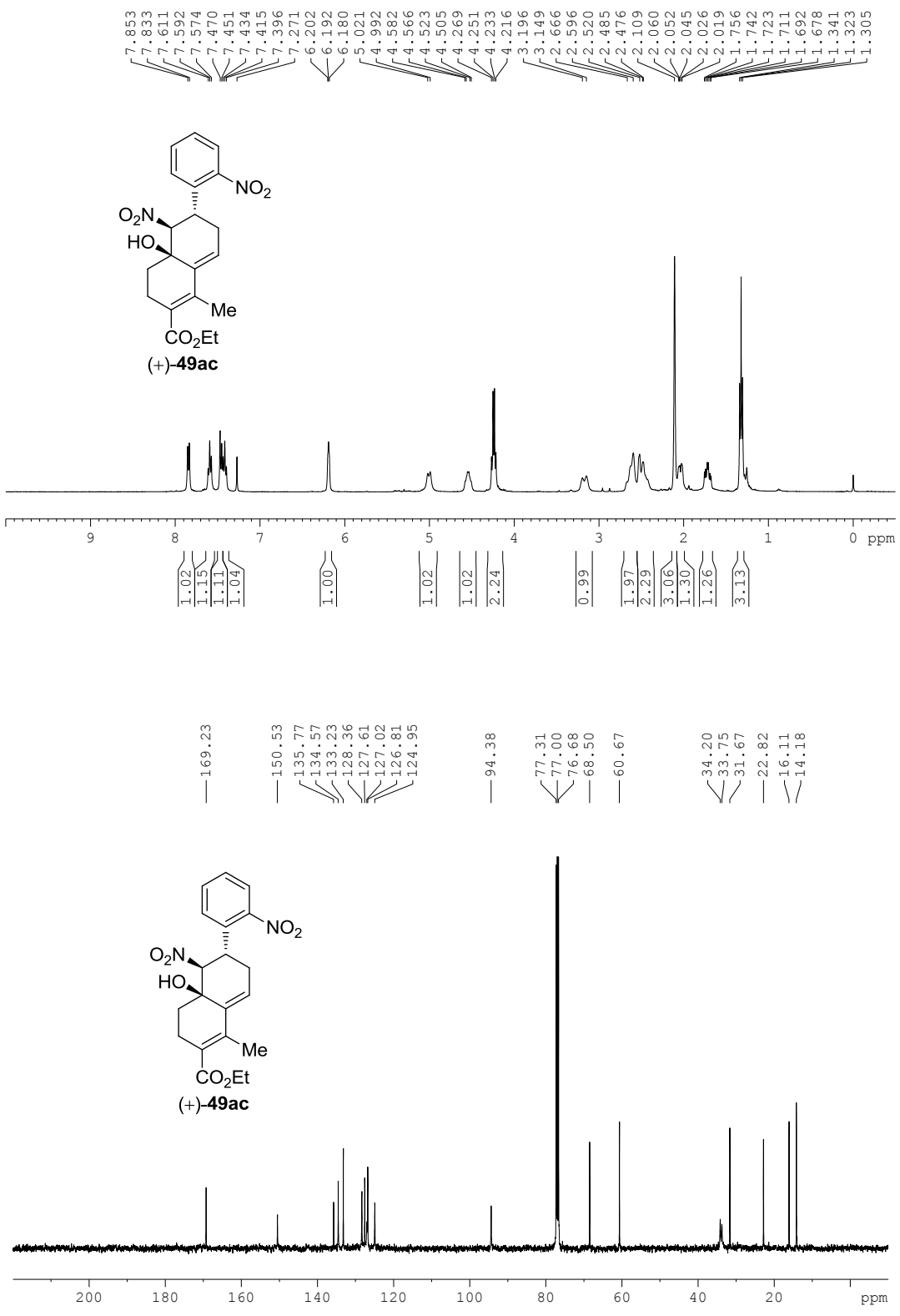


Figure-53: ^{1}H NMR and ^{13}C NMR spectrum of product **49ac**.

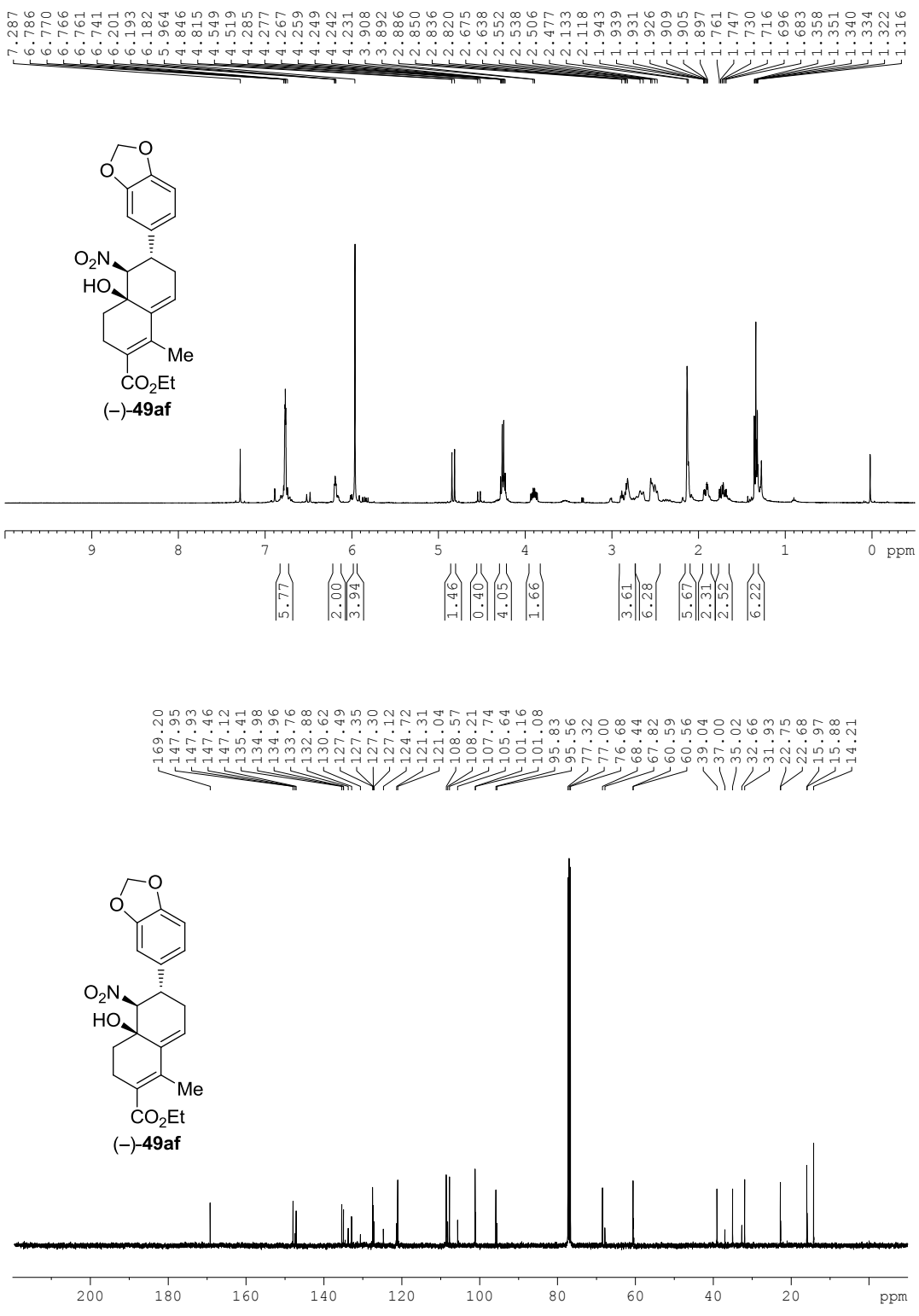
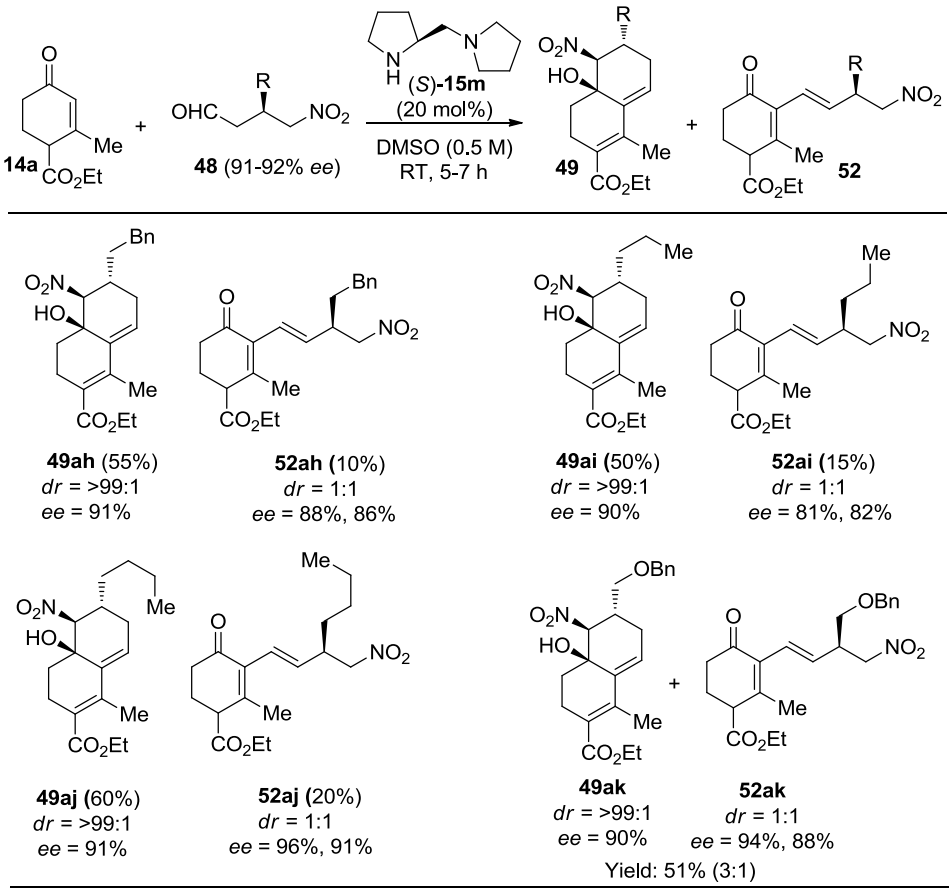


Figure-54: ^{1}H NMR and ^{13}C NMR spectrum of product **49af**.

Table 15: Synthesis of chiral decalines **49** and chiral dienes **52**.[a-c]



[a] Reactions were carried out in DMSO (0.5 M) with 1.5 equiv. of **48** relative to the **14** in the presence of 20 mol% of catalyst. [b] Yield refers to the column-purified product. [c] *Ee* and *dr* determined by CSP HPLC analysis.

furnished in good to excellent *ee*'s with 1:1 diasteromeric ratio. These results suggesting that only *cis*-isomer of CS product converting to decalin, where as the *trans*-isomer is not involving in intramolecular Henry reaction, which is giving the CS/I product. The presence of alkyl chain in **48** is responsible for the formation of major *cis*-isomer and minor *trans*-isomer of CS products, which is not possible with aryl substituted γ-nitroaldehydes due to the less steric hindrance (Table 14).

We further extended the scope of this methodology by employing cyclic chiral γ-nitroaldehyde **48l** for the cascade synthesis of tricyclic products. Interestingly, reaction of cyclic enones **14a/14b** with chiral γ-nitroaldehyde **48l** in DMSO at 25 °C under 30 mol% of

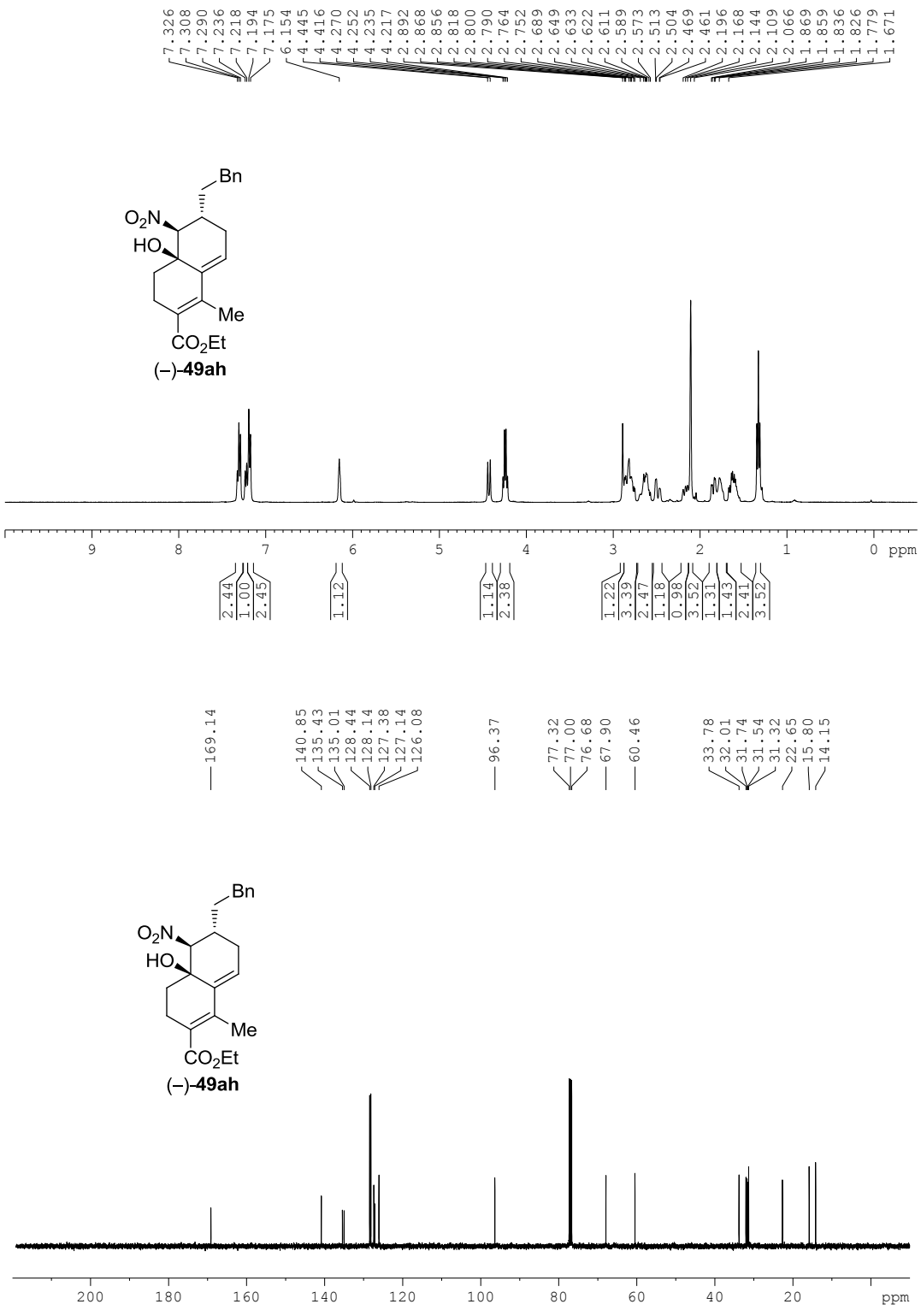


Figure-55: ^{1}H NMR and ^{13}C NMR spectrum of product **49ah**.

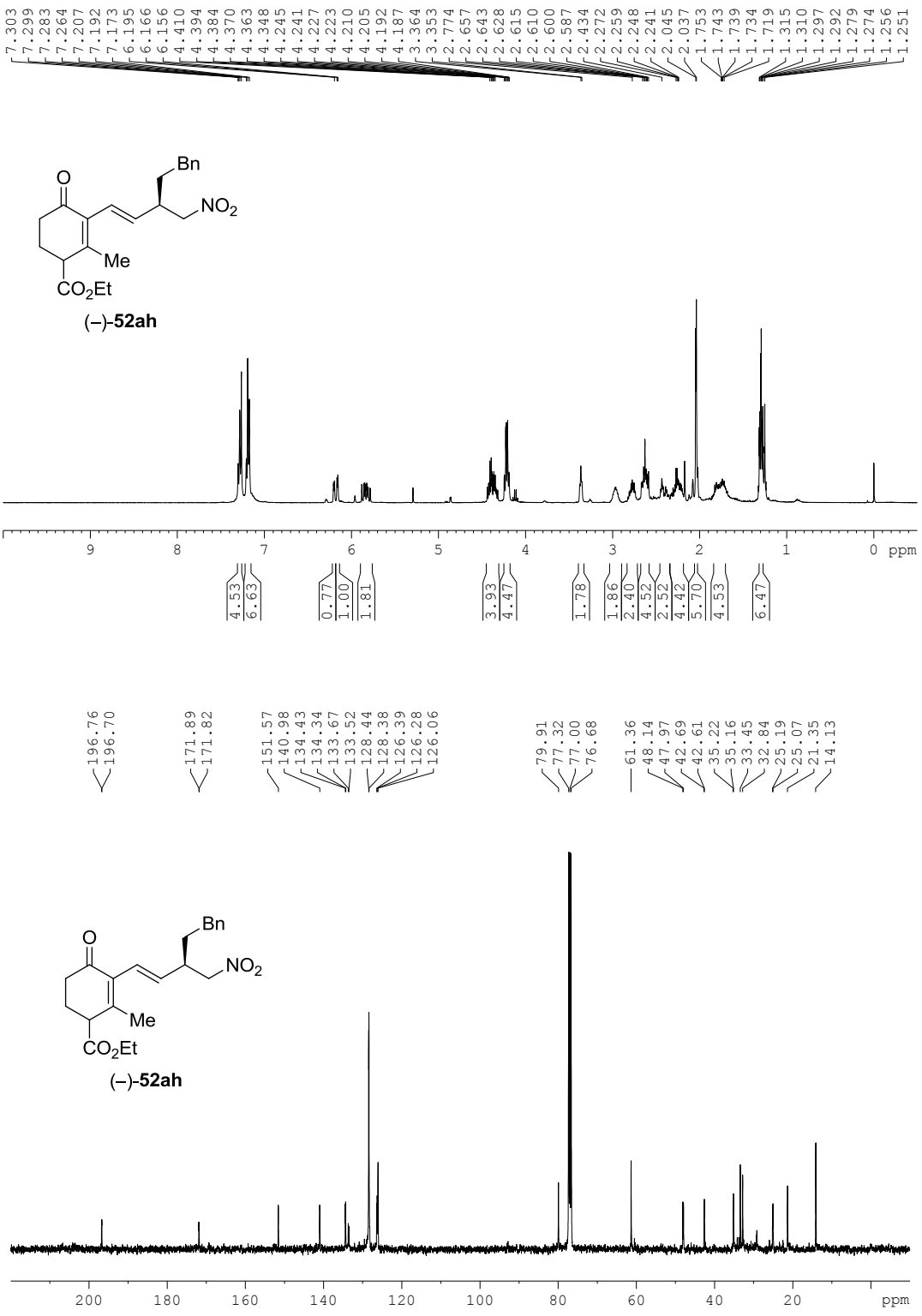
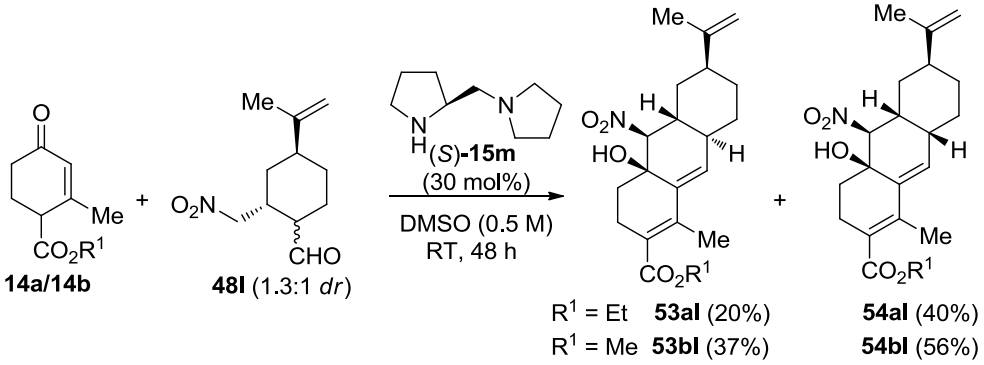


Figure-56: ^{1}H NMR and ^{13}C NMR spectrum of product **52ah**.

Scheme 13. Synthesis of tricyclic esters.



(*S*)-**15m** for 48 h furnished the tricyclic products **53/54** in good yields with 1:1.5-2 *dr* ratio (Scheme 13). In both the cases *cis*-isomer was formed in major compared to *trans*-isomer, which is in agreement with the Table 15 results. These results shows that the diversity of this new methodolgy covering structurally diverse group of cyclic enones **14** and aldehydes **48**. The structure and regiochemistry of products **53/54** was confirmed by NMR analysis (for example Fig. 58) and also finally confirmed by X-ray structure analysis on **54bl** as shown in Fig. 57.[67]

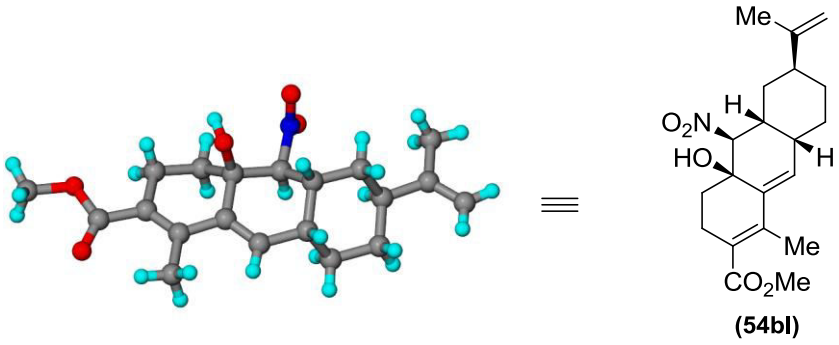


Figure 57: Crystal structure of (4a*R*,6*S*,8a*R*,10*S*,10a*R*)-methyl 4a-hydroxy-1-methyl-10-nitro-6-(prop-1-en-2-yl)-3,4,4a,5,6,7,8,8a,10,10a-decahydroanthracene-2-carboxylate (**54bl**).

With applications in mind, we investigated the utilization of chiral tricyclic ester **54** in the synthesis of highly functionalized tricyclic compound **56** *via* organocatalytic reductive

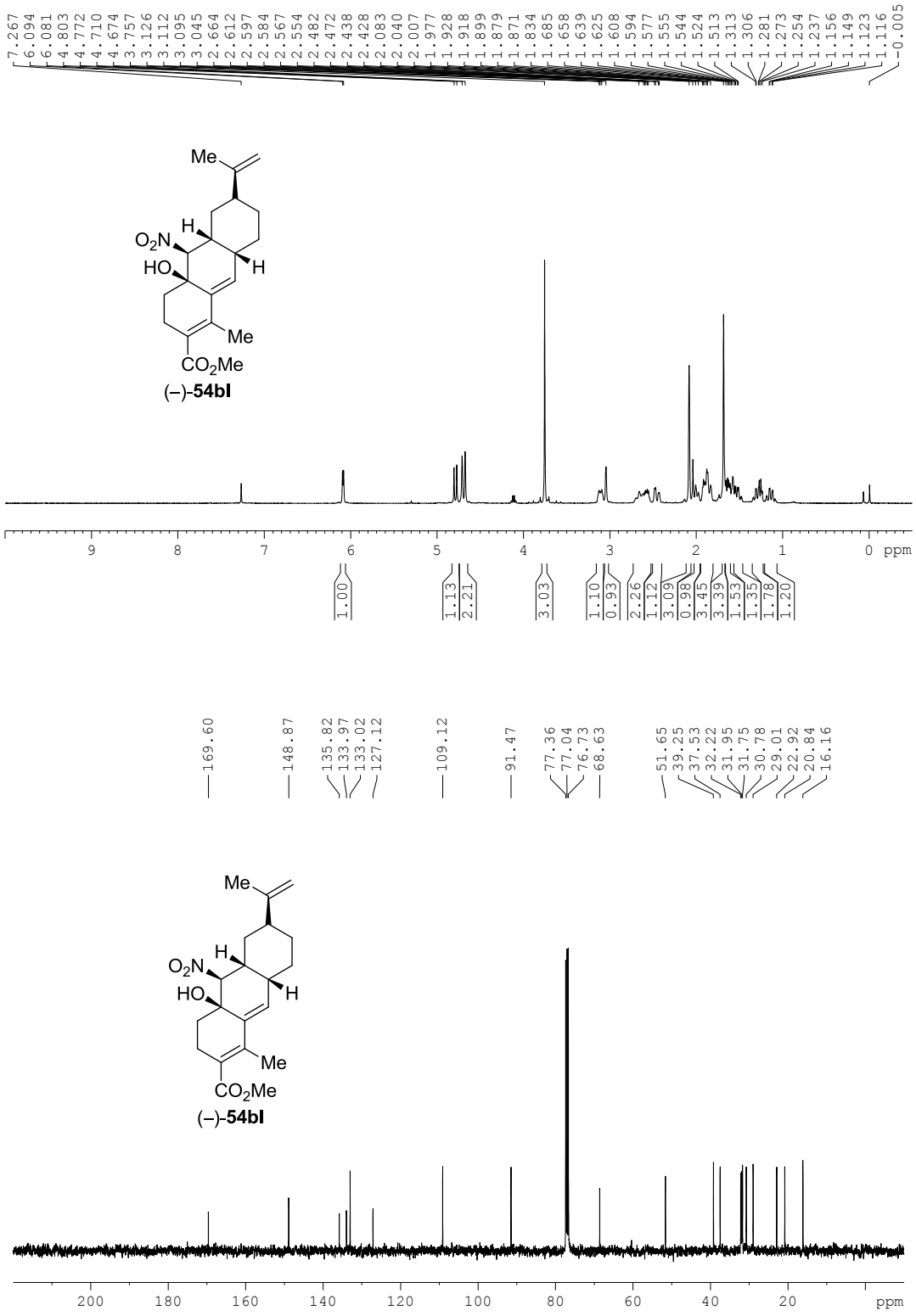
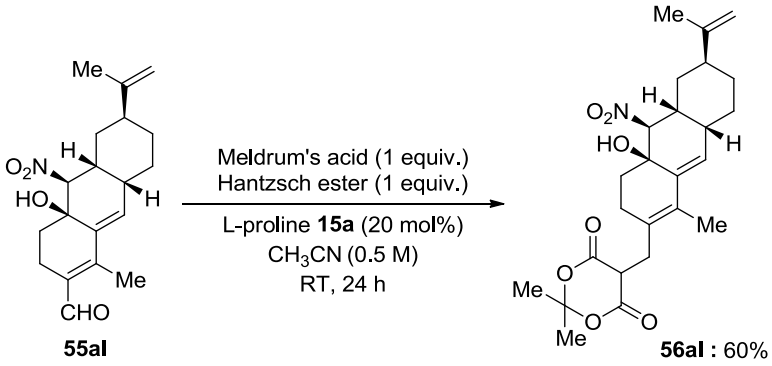


Figure-58: ^{1}H NMR and ^{13}C NMR spectrum of product **54bl**.

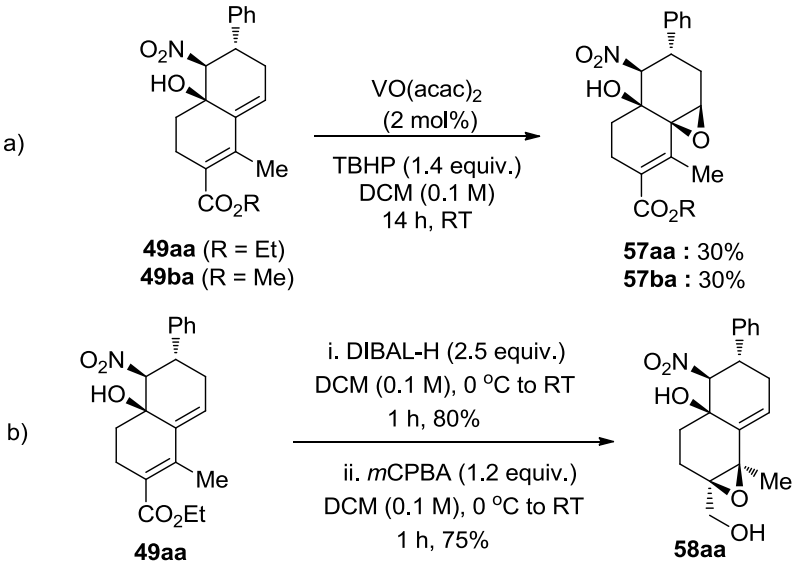
coupling (OrgRC) reaction.[68] The OrgRC reaction of the **55al** (which is obtained after ester reduction followed by oxidation of **54al)** with Meldrum's acid and Hantzsch ester in CH_3CN (0.5 M) at 25 °C for 24 h furnished the chiral OrgRC product **56al** in 60% yield (eq. 13).



(13)

We explored the utilization of chiral decalines **49** in the synthesis of functionalized chiral decalines **57-58** through simple reduction/epoxidation reactions (Scheme 14). Interestingly, direct oxidation of the **49aa** and **49ba** with 2 mol% of $VO(acac)_2$ and TBHP (1.4 equiv.) in CH_2Cl_2 (0.1 M) furnished the selective epoxide **57aa/57ba** in each 30% yields (Scheme 14a). Ester reduction of **49aa** with 2.5 equiv. of DIBAL-H in dry CH_2Cl_2 at 0–25 °C for 1 h followed by oxidation with *m*CPBA (1.2 equiv) in dry CH_2Cl_2 at 0 °C for 1 h furnished the functionalized epoxide **58aa** in 75 % yield with 99% *de* (Scheme 14b).

Scheme 14. Synthetic applications of chiral decalines.



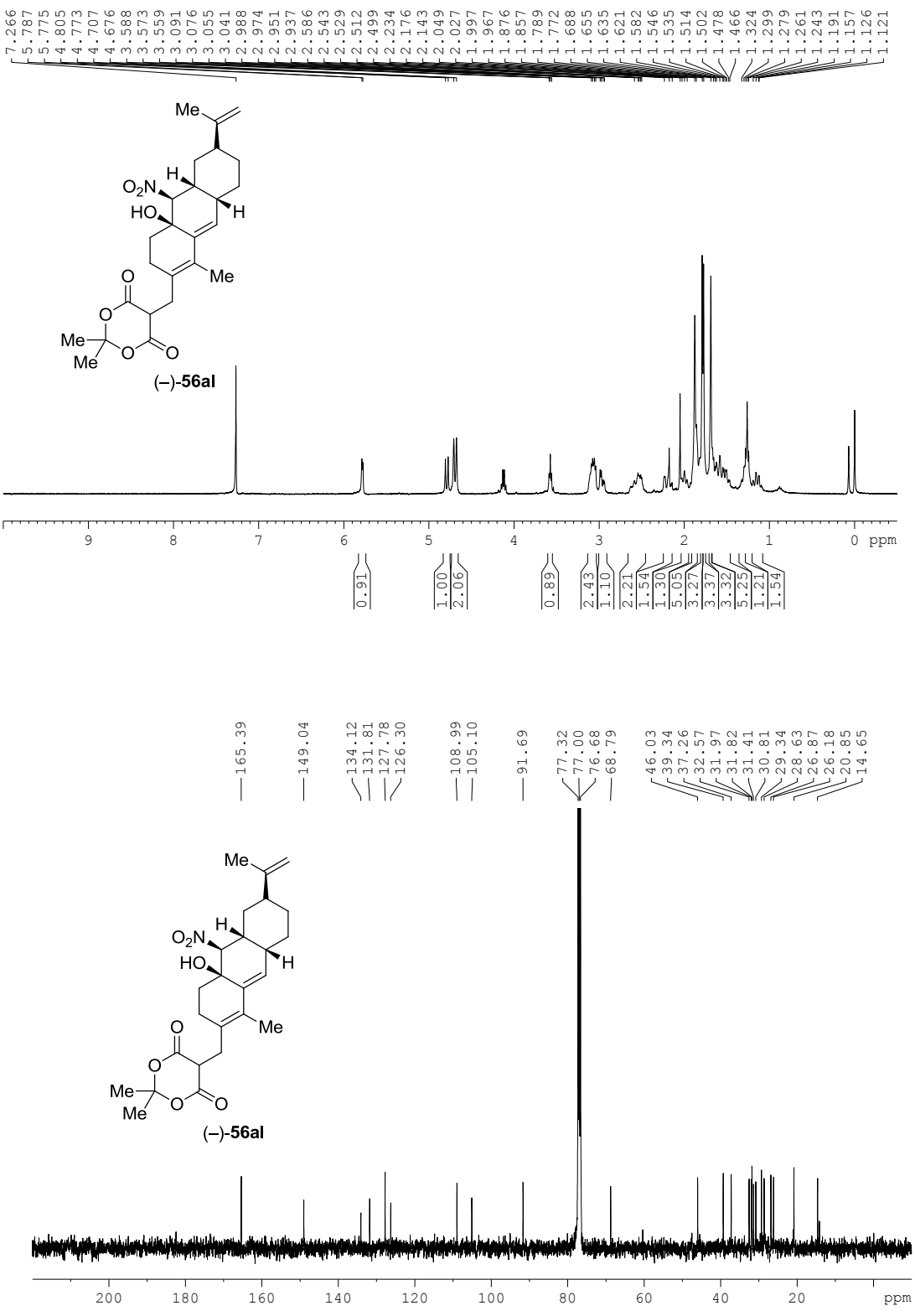


Figure-59: ^{1}H NMR and ^{13}C NMR spectrum of product **56al**.

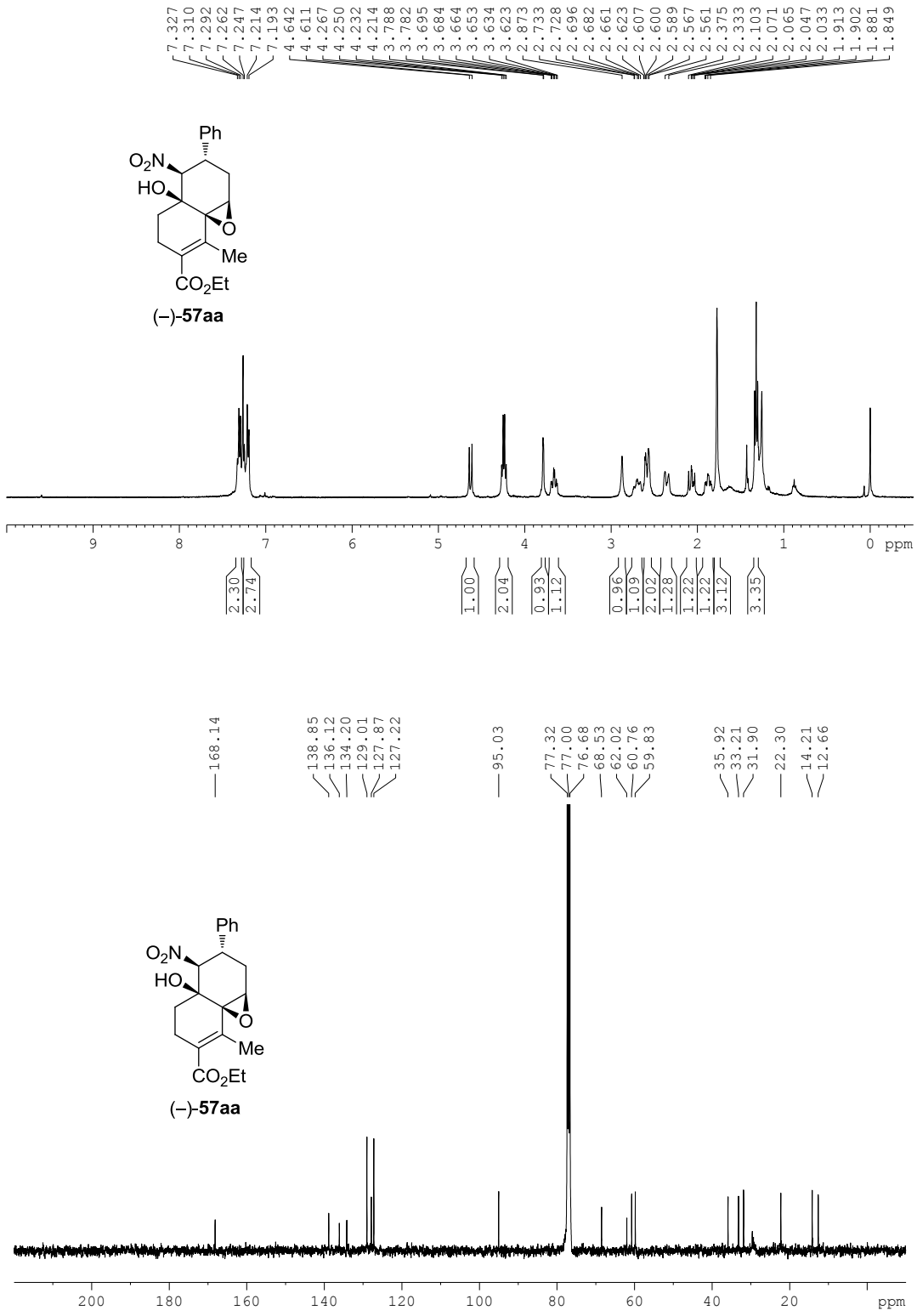


Figure-60: ^{1}H NMR and ^{13}C NMR spectrum of product **57aa**.

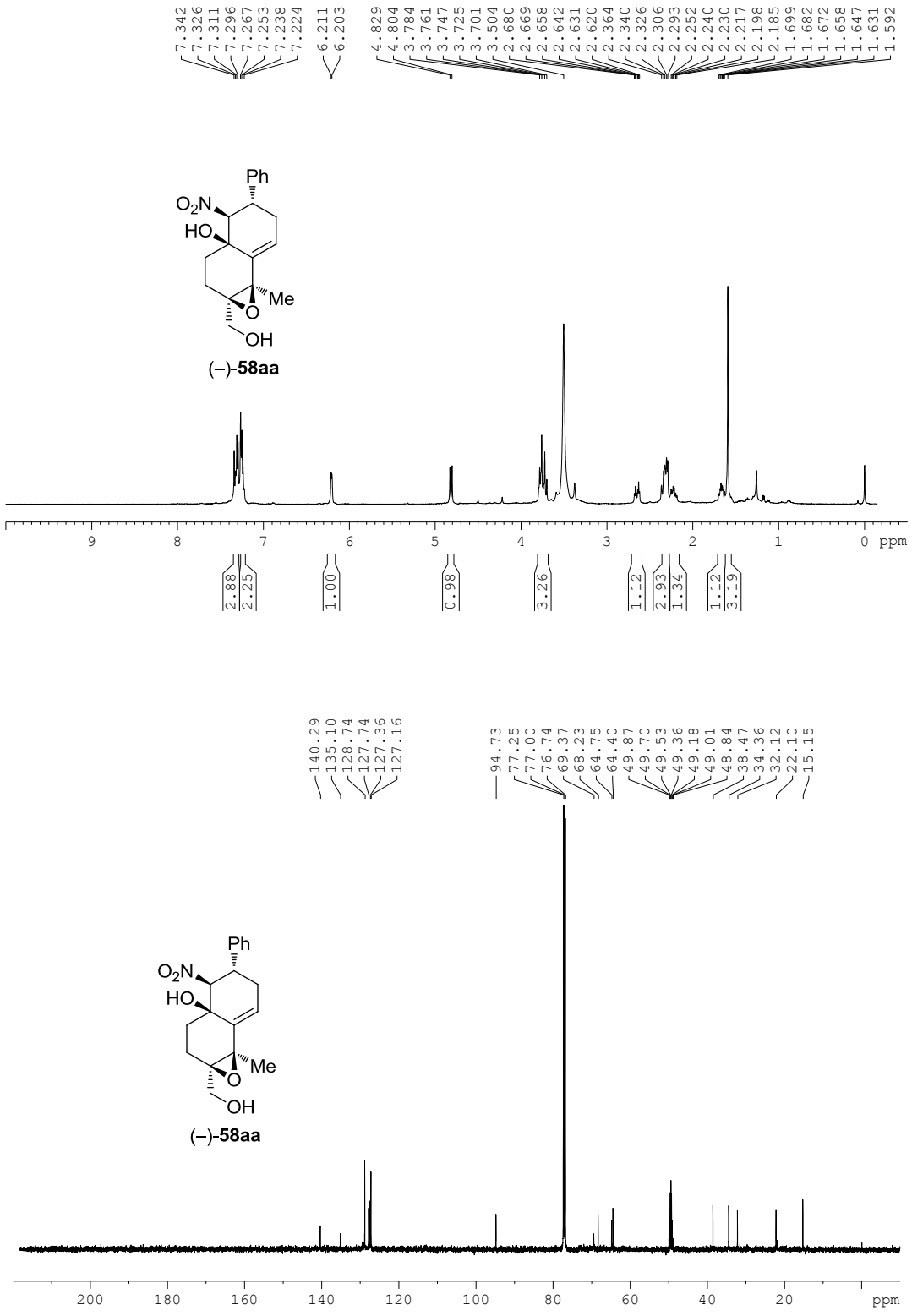


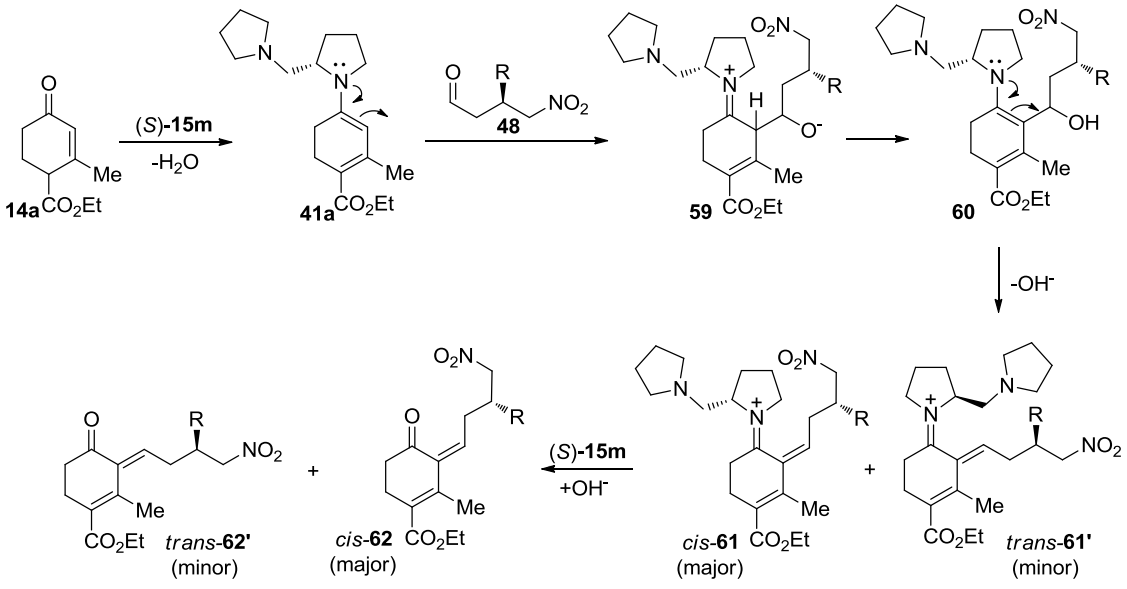
Figure-61: ^{1}H NMR and ^{13}C NMR spectrum of product **58aa**.

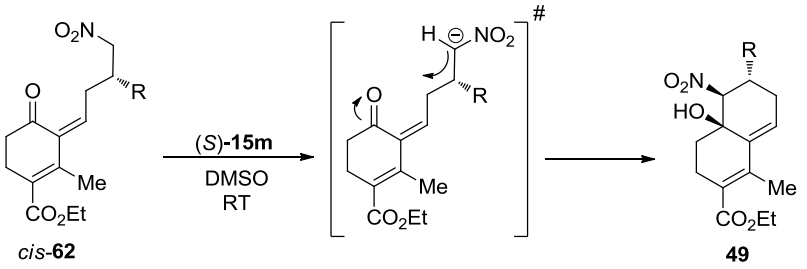
6.3 Mechanistic Insights

The possible mechanism for the synthesis of chiral decalines **49** from **14** and **48** catalyzed by **15m** is illustrated in Scheme 15. First, reaction of (*S*)-**15m** with **14a** generates chiral push–pull dienamine **41a** through iminium formation. The chiral aldehyde **48** reacts with the in situ generated push-pull dienamine to generate **59**, which further transform to *cis*-**61** (major) and *trans*-**61'** (minor) by proton migration followed by elimination of hydroxyl group. In situ hydrolysis of **61** results Claisen-Schmidt adducts *cis*-**62** and *trans*-**62'**, in which *cis*-**62** further transform to chiral decaline **49** *via* intramolecular Henry reaction under the amine catalysis. Based on the outcome of absolute configuration, the *re*-face of the nucleophilic carbon (-NO_2 attached) attacks the *si*-face of the electrophilic carbon (carbonyl) in an intramolecular Henry reaction. In case of β–alkyl sunstituted γ-nitroaldehydes, the formation of chiral (*E*)-1,3-dienes explained by CS/I mechanism. The in situ generated CS product push-pull dienone trans-**62'** under the **15m** catalysis furnished the unexpected (*E*)-1,3-dienes **52** *via* isomerization reaction as shown in Scheme 15.

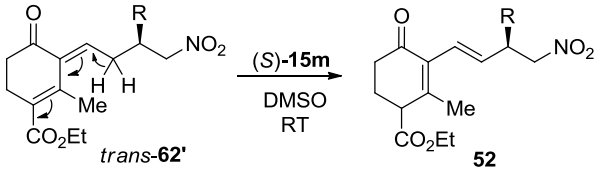
Scheme 15. Proposed reaction mechanism.

Mechanism for CS/H:





Mechanism for CS/I:

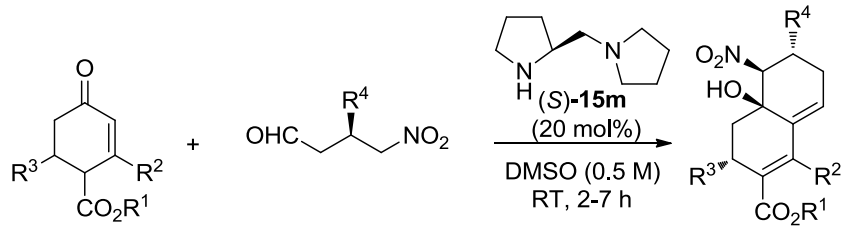


6.4 Conclusions

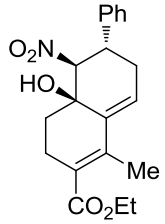
In conclusion, we have developed a domino Claisen-Schmidt/Henry process for the synthesis of highly substituted chiral decalines with three contiguous stereocenters. Herein, we described the (*S*)-1-(pyrrolidin-2-ylmethyl)pyrrolidine **15m** catalyzed domino CS/H reaction from enones **14** with γ-nitroaldehydes **48** at ambient conditions. This novel asymmetric CS/H reaction proceeds in good yields with high enantio- and diastereoselectivity through push–pull dienamine catalysis. Furthermore, we demonstrated the application of chiral products in the synthesis of highly functionalized decalines.

ANNEXURE-III

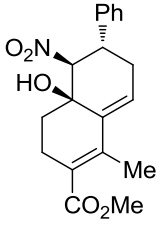
Table A3: Synthesis of achiral decalines **49**.[a-c]



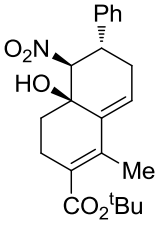
14 (±)-**48** (±)-**49**



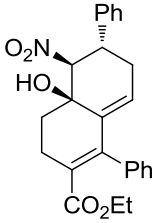
(±)-**49aa** (67%)
dr = >99:1



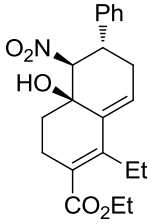
(±)-**49ba** (78%)
dr = >99:1



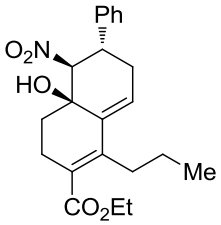
(±)-**49ca** (50%)
dr = >99:1



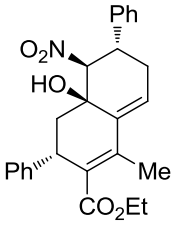
(±)-**49sa** (33%)[d]
dr = >99:1



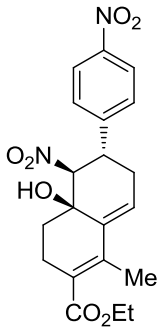
(±)-**49ta** (30%)[e]
dr = >99:1



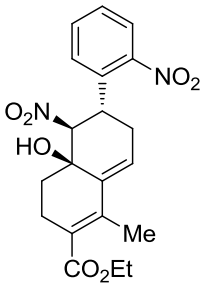
(±)-**49pa** (37%)[e]
dr = >99:1



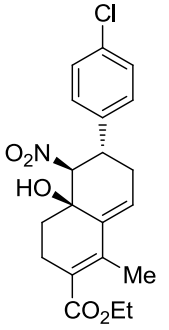
(±)-**49ha** (21%)[e]
dr = >99:1



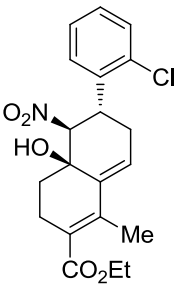
(±)-**49ab** (55%)
dr = >99:1



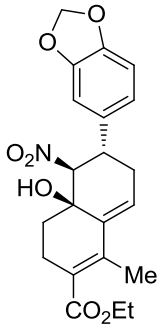
(±)-**49ac** (20%)
dr = >99:1



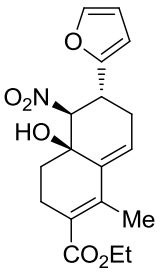
(±)-**49ad** (65%)
dr = >99:1



(±)-**49ae** (65%)
dr = >99:1



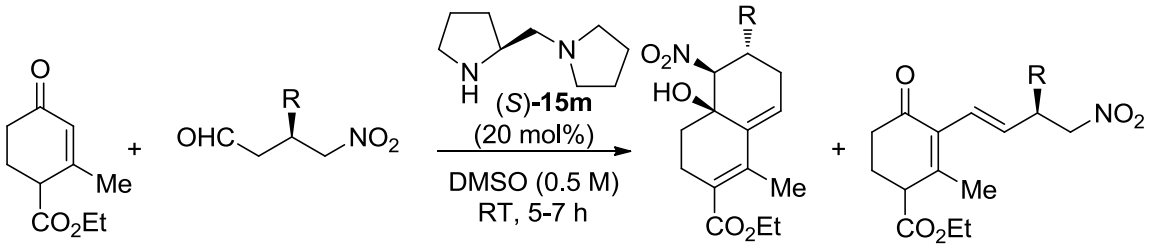
(±)-**49af** (45%)
dr = 3:1



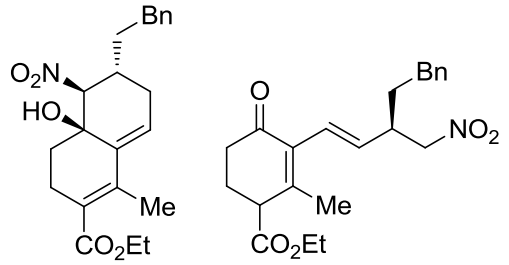
(±)-**49ag** (28%)
dr = 5:1

[a] Reactions were carried out in DMSO (0.5 M) with 1.5 equiv. of **48** relative to the **14** in the presence of 20 mol% of catalyst. [b] Yield refers to the column-purified product. [c] *dr* determined by NMR and CSP HPLC analysis.[d] Reaction performed at 50 °C for 70 h. [e] Reaction time 24 h.

Table A4: Synthesis of achiral decalines **49** and dienes **52**.[a-c]

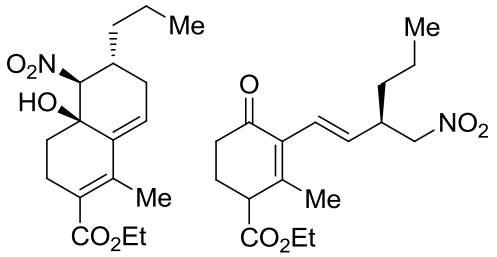


14a (±)-**48** (±)-**49** (±)-**52**



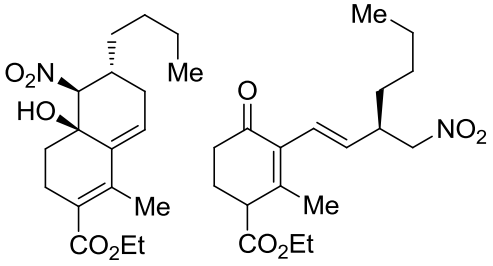
(±)-**49ah** (34%)
dr = >99:1[c]

(±)-**52ah** (39%)
dr = 1:1



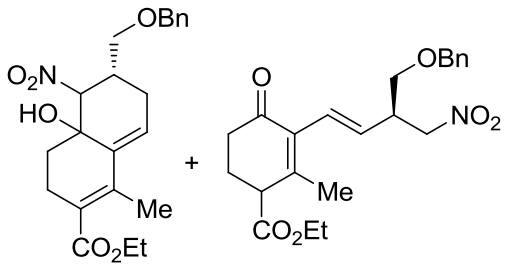
(±)-**49ai** (32%)
dr = >99:1

(±)-**52ai** (35%)
dr = 1:1



(±)-**49aj** (39%)
dr = >99:1

(±)-**52aj** (39%)
dr = 1:1



(±)-**49ak**
dr = >99:1

(±)-**52ak**
dr = 1:1

42% (1.6:1)

[a] Reactions were carried out in DMSO (0.5 M) with 1.5 equiv. of **48** relative to the **14** in the presence of 20 mol% of catalyst. [b] Yield refers to the column-purified product. [c] *dr* determined by NMR and CSP HPLC analysis.

7. *Experimental Section*

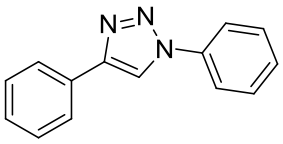
Materials: All solvents and commercially available chemicals were used as received. Functionalized phenyl acetaldehydes **20b-p** were prepared from corresponding acetic acids in good yields according to literature procedures.[69] Functionalized ketones **18a-r** were prepared from corresponding acetic acids in good yields according to literature procedures.[70] Functionalized enones **14a–p** was prepared from alkyl aceto-acetates and aldehydes in high yields according to our recent modified one-step method.[54] Functionalized enone **14q** was prepared from benzylidene acetone in high yield according to literature procedures.[71] Functionalized enone **14r** was prepared from trimethyl-(1-methylene-allyloxy)-silane and ethyl propynoate in high yield according to a literature procedure.[71b] The highly functionalized aryl azides **2a–v** were prepared according to the literature procedures.[72]

General Experimental Procedures:

1a: General procedure for the DBU-catalyzed azide-aldehyde [3+2]-cycloaddition reactions: In an ordinary glass vial equipped with a magnetic stirring bar, to 0.05 mmol of catalyst **15c** in DMSO (1.0 mL), was added 0.75 mmol of aryl azide **2** and 0.5 mmol of aldehyde **20** and the reaction mixture was stirred at 25 °C for 0.5 h. The crude reaction mixture was worked up with aqueous NH_4Cl solution and the aqueous layer was extracted with dichloromethane (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure organo-click products **3** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

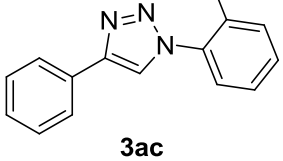
1b: General procedure for the *t*BuOK-catalyzed azide-aldehyde [3+2]-cycloaddition reactions: In an ordinary glass vial equipped with a magnetic stirring bar, to 0.05 mmol of catalyst *t*BuOK **15i** (5.6 mg) in DMSO (1.0 mL), was added 0.75 mmol of aryl azide **2** and 0.5 mmol of aldehyde **20** and the reaction mixture was stirred at 25 °C for 0.5-3 h. The crude reaction mixture was worked up with aqueous NH_4Cl solution and the aqueous layer was extracted with dichloromethane (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure organo-click products **3** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

1,4-Diphenyl-1*H*-1,2,3-triazole (3ab):[18] Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp: 172-174 °C; IR (KBr): ν_{max} 3123, 3096, 3058, 1600, 1512, 1485, 1419, 1233, 1068, 1041, 910, 827, 756 and 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.22 (1H, s), 7.94 (2H, td, *J* = 8.4, 1.2 Hz), 7.82 (2H, br d, *J* = 8.4 Hz), 7.57 (2H, tt, *J* = 7.2, 2.0 Hz), 7.50-7.46 (3H, m), 7.39 (1H, tt, *J* = 7.2, 2.0 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 148.4 (C), 137.1 (C), 130.2 (C), 129.8 (2 x CH), 128.9 (2 x CH), 128.8 (CH), 128.4 (CH), 125.8 (2 x CH), 120.5 (2 x CH), 117.6 (CH); HRMS m/z 222.1031 ($M + H^+$), calcd for $C_{14}H_{11}N_3H$ 222.1031.



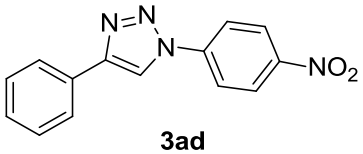
3ab

1-(2-Nitrophenyl)-4-phenyl-1*H*-1,2,3-triazole (3ac):[19] Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a yellow solid. Mp: 142-144 °C; IR (KBr): ν_{max} 3151, 3107, 1600, 1518, 1359, 1227, 1047, 1019, 822, 827, 773 and 745 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.09 (1H, s), 8.05 (1H, d, *J* = 8.0 Hz), 7.88 (2H, d, *J* = 7.2 Hz), 7.78 (1H, t, *J* = 7.6 Hz), 7.68 (1H, t, *J* = 7.6 Hz), 7.64 (1H, d, *J* = 7.6 Hz), 7.45 (2H, t, *J* = 7.2 Hz), 7.37 (1H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 148.2 (C), 144.3 (C), 133.8 (CH), 130.7 (CH), 130.1 (C), 129.7 (C), 128.9 (2 x CH), 128.6 (CH), 127.7 (CH), 125.9 (2 x CH), 125.5 (CH), 121.0 (CH); HRMS m/z 267.0880 ($M + H^+$), calcd for $C_{14}H_{10}N_4O_2H$ 267.0882.



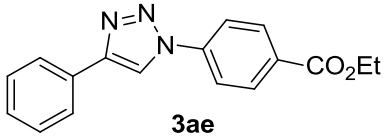
3ac

1-(4-Nitrophenyl)-4-phenyl-1*H*-1,2,3-triazole (3ad):[20] Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a yellow solid. Mp: 238-240 °C; IR (KBr): ν_{max} 3123, 3090, 1600, 1523, 1348, 1222, 1036, 986, 855 and 773 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz) δ 9.47 (1H, s), 8.47 (2H, d, *J* = 7.5 Hz), 8.25 (2H, d, *J* = 7.5 Hz), 7.94 (2H, d, *J* = 7.5 Hz), 7.51 (2H, t, *J* = 7.5 Hz), 7.40 (1H, t, *J* = 7.5 Hz); ^{13}C NMR (DMSO-d_6, DEPT-135) δ 147.9 (C), 146.7 (C), 140.8 (C), 129.8 (C), 129.1 (2 x CH), 128.6 (CH), 125.6 (2 x CH), 125.4 (2 x CH), 120.4 (2 x CH), 119.9 (CH); HRMS m/z 267.0880 ($M + H^+$), calcd for $C_{14}H_{10}N_4O_2H$ 267.0882.



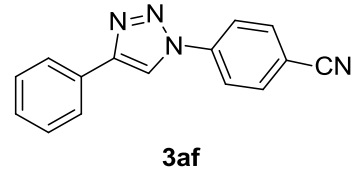
3ad

Ethyl 4-(4-phenyl-1*H*-1,2,3-triazol-1-yl)benzoate (3ae):[21] Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp: 164-168 °C; IR (KBr): ν_{max} 3123, 3096, 3058, 2986, 1704, 1606, 1518, 1458, 1370, 1277, 1184, 1118, 1047, 855 and 773 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.28 (1H, s), 8.21 (2H, d, *J* = 8.4 Hz), 7.90–7.88 (4H, m), 7.46 (2H, t, *J* = 7.2 Hz), 7.37 (1H, t, *J* = 7.2 Hz), 4.42 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 1.43 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.4 (C, O-*C*=O), 148.7 (C), 139.9 (C), 131.3 (2 x CH), 130.5 (C), 129.8 (C), 128.9 (2 x CH), 128.6 (CH), 125.8 (2 x CH), 119.7 (2 x CH), 117.3 (CH), 61.4 (CH_2, OCH_2CH_3), 14.2 (CH_3, OCH_2CH_3); HRMS m/z 294.1242 (M + H^+), calcd for $C_{17}H_{15}N_3O_2H$ 294.1243.



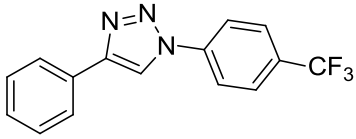
3ae

4-(4-Phenyl-1*H*-1,2,3-triazol-1-yl)benzonitrile (3af):[22] Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp: 216-218 °C; IR (KBr): ν_{max} 3112, 3096, 2236, 1611, 1512, 1485, 1408, 1227, 1025, 992, 844 and 827 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 9.44 (1H, s), 8.19 (2H, d, *J* = 8.5 Hz), 8.13 (2H, d, *J* = 8.5 Hz), 7.94 (2H, d, *J* = 7.5 Hz), 7.51 (2H, t, *J* = 7.5 Hz), 7.40 (1H, t, *J* = 7.5 Hz); ^{13}C NMR (DMSO-d_6, DEPT-135) δ 147.7 (C), 139.5 (C), 134.3 (2 x CH), 129.8 (C), 129.1 (2 x CH), 128.5 (CH), 125.4 (2 x CH), 120.3 (2 x CH), 119.8 (CH), 118.1 (C, CN), 111.0 (C); HRMS m/z 247.0978 (M + H^+), calcd for $C_{15}H_{10}N_4H$ 247.0984.



3af

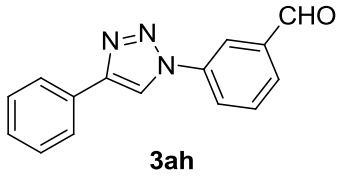
4-Phenyl-1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazole (3ag):[20,23] Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp: 244-246 °C; IR (KBr): ν_{max} 3123, 3096, 3058, 1611, 1529, 1458, 1441, 1408, 1332, 1227, 1173, 1068, 992 and 849 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 9.44 (1H, s), 8.22 (2H, d, *J* = 7.5 Hz), 8.02 (2H, d, *J* = 8.0 Hz), 7.96 (2H, d, *J* = 7.0 Hz), 7.52 (2H, t, *J* = 7.0 Hz), 7.41 (1H, t, *J* = 7.0 Hz); ^{13}C NMR (DMSO-d_6, DEPT-135) δ 147.6 (C), 139.4 (C), 129.9 (C), 129.0 (2 x CH), 128.7 (C, q, *J* = 32.5 Hz), 128.4 (CH), 127.2 (2 x CH, q, *J* = 3.75 Hz), 125.4



3ag

(2 x CH), 123.8 (C, q, *J* = 271.2 Hz), 120.4 (2 x CH), 119.8 (CH); HRMS m/z 290.0904 (M + H^+), calcd for $C_{15}H_{10}F_3N_3H$ 290.0905.

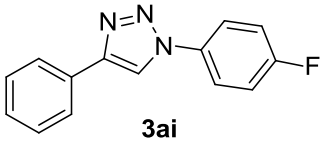
3-(4-Phenyl-1*H*-1,2,3-triazol-1-yl)benzaldehyde (3ah):[24] Prepared following the procedure



3ah

1a and purified by column chromatography using EtOAc/hexane and isolated as a white solid. Mp: 165-167 °C; IR (neat): ν_{max} 2922, 2852, 2114, 1694, 1597, 1491, 1450, 1286, 1075, 1037, 887, 791 and 758 cm^{-1}; ^1H NMR (DMSO-d_6) δ 10.12 (1H, s), 9.42 (1H, s), 8.45 (1H, t, *J* = 1.6 Hz), 8.29 (1H, ddd, *J* = 8.0, 2.4, 1.2 Hz), 8.02 (1H, td, *J* = 7.6, 1.2 Hz), 7.96 (2H, br d, *J* = 7.2 Hz), 7.84 (1H, t, *J* = 8.0 Hz), 7.50 (2H, t, *J* = 7.6 Hz), 7.38 (1H, tt, *J* = 7.6, 1.2 Hz); ^{13}C NMR (DMSO-d_6, DEPT-135) δ 192.2 (CH, *C*HO), 147.5 (C), 137.5 (C), 137.2 (C), 130.9 (CH), 130.1 (C), 129.5 (CH), 129.0 (2 x CH), 128.3 (CH), 125.4 (2 x CH), 125.2 (CH), 119.8 (CH), 119.7 (CH); HRMS m/z 250.0979 (M + H^+), calcd for $C_{15}H_{11}N_3OH$ 250.0980.

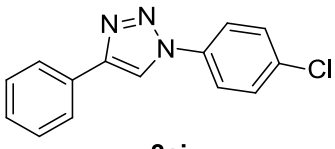
1-(4-Fluorophenyl)-4-phenyl-1*H*-1,2,3-triazole (3ai):[23] Prepared following the procedure



3ai

1a and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp: 152-155 °C; IR (neat): ν_{max} 3052, 3030, 2921, 2855, 1726, 1606, 1512, 1458, 1260, 1074 and 734 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz) δ 9.20 (1H, s), 7.99 (2H, dd, *J* = 7.5, 5.0 Hz), 7.93 (2H, d, *J* = 7.5 Hz), 7.46 (2H, t, *J* = 7.5 Hz), 7.41 (2H, t, *J* = 8.0 Hz), 7.35 (1H, t, *J* = 7.5 Hz); ^{13}C NMR (DMSO-d_6 + $CDCl_3$, DEPT-135) δ 161.5 (C, d, *J* = 243.8 Hz, *C*-F), 147.3 (C), 133.1 (C), 130.1 (C), 128.7 (2 x CH), 127.9 (CH), 125.2 (2 x CH), 122.0 (2 x CH, d, *J* = 8.8 Hz), 119.4 (CH), 116.4 (2 x CH, d, *J* = 22.5 Hz); HRMS m/z 240.0936 (M + H^+), calcd for $C_{14}H_{10}FN_3H$ 240.0937.

1-(4-Chlorophenyl)-4-phenyl-1*H*-1,2,3-triazole (3aj):[25] Prepared following the procedure

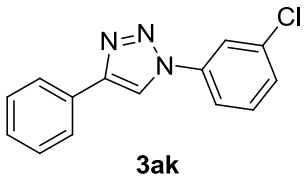


3aj

1a and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp: 196-198 °C; IR (KBr): ν_{max} 3123, 3101, 1594, 1458, 1392, 1222, 1079, 1041, 888, 827 and 773 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz) δ 9.33 (1H, s), 8.00 (2H, d, *J* = 9.0 Hz), 7.94 (2H, d, *J* = 7.5 Hz), 7.72 (2H, d, *J* = 9.0 Hz), 7.51 (2H, t, *J* = 7.5 Hz), 7.39 (1H, t, *J* = 7.5 Hz); ^{13}C NMR (DMSO-d_6, DEPT-135) δ 147.4 (C), 135.4 (C),

133.0 (C), 130.1 (C), 129.9 (2 x CH), 129.0 (2 x CH), 128.3 (CH), 125.3 (2 x CH), 121.7 (2 x CH), 119.7 (CH); HRMS m/z 256.0640 (M + H^+), calcd for $C_{14}H_{10}ClN_3H$ 256.0642.

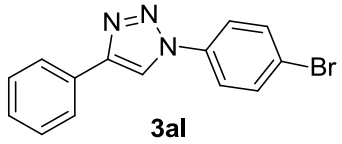
1-(3-Chlorophenyl)-4-phenyl-1*H*-1,2,3-triazole (3ak):[18] Prepared following the procedure



3ak

1a and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp: 167-169 °C; IR (KBr): ν_{max} 3123, 3101, 1594, 1458, 1392, 1222, 1079, 1041, 888, 827 and 773 cm^{-1}; ^1H NMR (DMSO-d_6) δ 9.34 (1H, s), 8.06 (1H, s), 7.95 (1H, d, *J* = 11.6 Hz), 7.92 (2H, d, *J* = 8.0 Hz), 7.64 (1H, t, *J* = 8.0 Hz), 7.56 (1H, d, *J* = 8.0 Hz), 7.49 (2H, t, *J* = 7.2 Hz), 7.37 (1H, t, *J* = 7.2 Hz); ^{13}C NMR (DMSO-d_6, DEPT-135) δ 147.5 (C), 137.7 (C), 134.3 (C), 131.7 (CH), 130.1 (C), 129.1 (2 x CH), 128.6 (CH), 128.4 (CH), 125.4 (2 x CH), 119.8 (2 x CH), 118.6 (CH); HRMS m/z 256.0640 (M + H^+), calcd for $C_{14}H_{10}ClN_3H$ 256.0642.

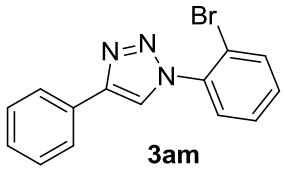
1-(4-Bromophenyl)-4-phenyl-1*H*-1,2,3-triazole (3al):[26] Prepared following the procedure



3al

1a and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp: 238-240 °C; IR (Neat): ν_{max} 3030, 2926, 2855, 1715, 1600, 1496, 1463, 1288, 1079, 740 and 701 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz) δ 9.34 (1H, s), 7.94 (4H, d, *J* = 8.0 Hz), 7.85 (2H, d, *J* = 8.5 Hz), 7.51 (2H, t, *J* = 7.5 Hz), 7.40 (1H, t, *J* = 7.5 Hz); ^{13}C NMR (DMSO-d_6, DEPT-135) δ 147.5 (C), 135.8 (C), 132.9 (2 x CH), 130.1 (C), 129.1 (2 x CH), 128.4 (CH), 125.4 (2 x CH), 121.9 (2 x CH), 121.4 (C), 119.7 (CH); HRMS m/z 300.0136 (M + H^+), calcd for $C_{14}H_{10}BrN_3H$ 300.0136.

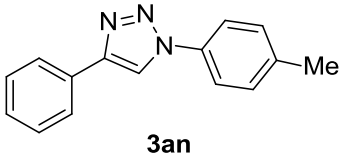
1-(2-Bromophenyl)-4-phenyl-1*H*-1,2,3-triazole (3am):[18] Prepared following the procedure



3am

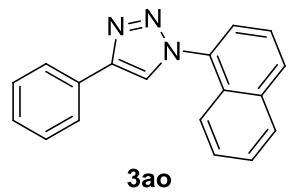
1a and purified by column chromatography using EtOAc/hexane and was isolated as a yellow oily liquid; IR (Neat): ν_{max} 3134, 3052, 2921, 1611, 1589, 1496, 1452, 1266, 1227, 1041, 1019, 762, 734 and 696 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 8.18 (1H, s), 7.94 (2H, d, *J* = 7.5 Hz), 7.77 (1H, d, *J* = 8.0 Hz), 7.60 (1H, d, *J* = 7.5 Hz), 7.51 (1H, t, *J* = 7.5 Hz), 7.47 (2H, t, *J* = 7.5 Hz), 7.41 (1H, t, *J* = 8.0 Hz), 7.38 (1H, t, *J* = 8.0 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 147.4 (C), 136.4 (C), 133.8 (CH), 131.1 (CH), 130.1 (C), 128.8 (2 x CH), 128.4 (CH), 128.3 (CH), 128.1 (CH), 125.8 (2 x CH), 121.6 (CH), 118.5 (C); HRMS m/z 300.0136 (M + H^+), calcd for $C_{14}H_{10}BrN_3H$ 300.0136.

4-Phenyl-1-*p*-tolyl-1*H*-1, 2, 3-triazole (3an):[25] Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. Mp: 162-164 °C; IR (neat): ν_{max} 2924, 2854, 1724, 1601, 1519, 1494, 1453, 1276, 1123, 1074, 1044, 971, 815 and 764 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.16 (1H, s), 7.92 (2H, d, *J* = 7.2 Hz), 7.67 (2H, d, *J* = 8.0 Hz), 7.46 (2H, t, *J* = 7.2 Hz), 7.38 (1H, t, *J* = 7.2 Hz), 7.34 (2H, d, *J* = 8.0 Hz), 2.44 (3H, s, Ar-*C*H_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 148.2 (C), 138.8 (C), 134.8 (C), 130.3 (C), 130.2 (2 x CH), 128.9 (2 x CH), 128.3 (CH), 125.8 (2 x CH), 120.4 (2 x CH), 117.6 (CH), 21.1 (CH_3); HRMS m/z 236.1187 (M + H^+), calcd for $C_{15}H_{13}N_3H$ 236.1188.



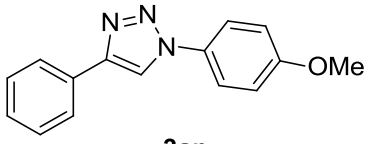
3an

1-(Naphthalen-1-yl)-4-phenyl-1*H*-1,2,3-triazole (3ao):[25] Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a oily liquid; IR (Neat): ν_{max} 3134, 3052, 2915, 1726, 1600, 1512, 1468, 1430, 1266, 1233, 1068, 1019, 806 and 773 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.15 (1H, s), 8.04 (1H, d, *J* = 8.0 Hz), 7.98 (3H, d, *J* = 7.6 Hz), 7.71 (1H, d, *J* = 8.0 Hz), 7.63-7.53 (4H, m), 7.49 (2H, t, *J* = 7.2 Hz), 7.40 (1H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 147.8 (C), 134.2 (C), 133.7 (C), 130.5 (CH), 130.3 (C), 129.0 (2 x CH), 128.6 (C), 128.5 (CH), 128.3 (CH), 128.0 (CH), 127.1 (CH), 125.9 (2 x CH), 125.1 (CH), 123.6 (CH), 122.4 (CH), 122.3 (CH); HRMS m/z 272.1189 (M + H^+), calcd for $C_{18}H_{13}N_3H$ 272.1188.



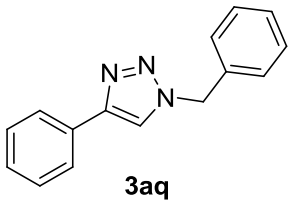
3ao

1-(4-Methoxyphenyl)-4-phenyl-1*H*-1,2,3-triazole (3ap):[18] Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp: 164-166 °C; IR (neat): ν_{max} 2922, 2852, 1722, 1602, 1510, 1494, 1453, 1220, 1182, 1074, 1031 and 832 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.12 (1H, s), 7.90 (2H, d, *J* = 7.6 Hz), 7.68 (2H, d, *J* = 8.8 Hz), 7.45 (2H, t, *J* = 7.2 Hz), 7.36 (1H, t, *J* = 7.2 Hz), 7.02 (2H, d, *J* = 8.8 Hz), 3.86 (3H, s, OC*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 159.8 (C), 148.1 (C), 130.4 (C), 130.3 (C), 128.8 (2 x CH), 128.3 (CH), 125.8 (2 x CH), 122.1 (2 x CH), 117.8 (CH), 114.7 (2 x CH), 55.6 (CH_3, O*C*H_3); HRMS m/z 252.1137 (M + H^+), calcd for $C_{15}H_{13}N_3OH$ 252.1137.



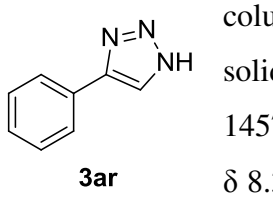
3ap

1-Benzyl-4-phenyl-1*H*-1,2,3-triazole (3aq): Prepared following the procedure **1b** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid.; IR (neat): ν_{max} 3062, 2922, 2852, 1675, 1496, 1454, 1356, 1225, 1075, 1046, 1028 and 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.81 (2H, d, *J* = 8.4 Hz), 7.66 (1H, s), 7.42-7.38 (8H, m), 5.58 (2H, s); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 148.2 (C), 134.7 (C), 130.5 (C), 129.1 (2 x CH), 128.8 (2 x CH), 128.5 (CH), 128.1 (CH), 128.0 (2 x CH), 125.7 (2 x CH), 119.4 (CH), 54.2 (CH_2); HRMS m/z 236.1188 ($M + H^+$), calcd for $C_{15}H_{13}N_3H$ 236.1188.



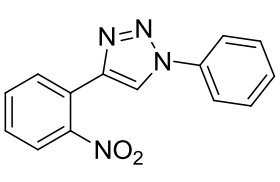
3aq

4-Phenyl-1*H*-1,2,3-triazole (3ar): Prepared following the procedure **1b** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 144-145 °C; IR (neat): ν_{max} 3107, 2925, 2854, 1763, 1707, 1496, 1457, 1365, 1214, 1078 and 968 cm^{-1}; ^1H NMR (DMSO-d_6 + 1 drop TFA) δ 8.33 (1H, s), 7.87 (2H, d, *J* = 7.6 Hz), 7.46 (2H, t, *J* = 7.6 Hz), 7.35 (1H, t, *J* = 7.6 Hz); ^{13}C NMR (DMSO-d_6 + 1 drop TFA, DEPT-135) δ 145.2 (C), 130.3 (C), 129.0 (3 x CH), 128.2 (CH), 125.6 (2 x CH); LRMS m/z 146.00 ($M + H^+$), calcd for $C_8H_7N_3$ 145.0640.



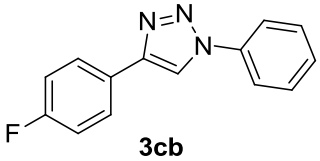
3ar

4-(2-Nitrophenyl)-1-phenyl-1*H*-1,2,3-triazole (3bb): Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and isolated as a red brown liquid; IR (neat): ν_{max} 3064, 1732, 1597, 1525, 1504, 1354, 1265, 1229, 1042, 993 and 853 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.25 (1H, s), 7.97 (1H, d, *J* = 7.6 Hz), 7.78 (1H, d, *J* = 8.0 Hz), 7.72 (2H, d, *J* = 8.0 Hz), 7.61 (1H, t, *J* = 7.6 Hz), 7.47 (3H, m), 7.39 (1H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 148.0 (C), 142.6 (C), 136.4 (C), 132.4 (CH), 130.8 (CH), 129.6 (2 x CH), 129.0 (CH), 128.8 (CH), 124.0 (C), 123.9 (CH), 120.8 (CH), 120.3 (2 x CH); HRMS m/z 267.0882 ($M + H^+$), calcd for $C_{14}H_{10}N_4O_2H$ 267.0884.



3bb

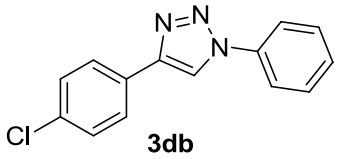
4-(4-Fluorophenyl)-1-phenyl-1*H*-1,2,3-triazole (3cb):[27] Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp: 207-209 °C; IR (neat): ν_{max} 3101, 2918, 2850, 1599, 1556, 1466, 1405, 1230, 1154, 1094,



3cb

1036, 994, 910, 844, 816 and 755 cm^{-1}; ^1H NMR (DMSO-d_6) δ 9.29 (1H, s), 8.00 (2H, dd, *J* = 8.8, 5.6 Hz), 7.95 (2H, d, *J* = 8.0 Hz), 7.65 (2H, t, *J* = 7.2 Hz), 7.53 (1H, t, *J* = 7.2 Hz), 7.35 (2H, t, *J* = 9.2 Hz); ^{13}C NMR (DMSO-d_6, DEPT-135) δ 161.9 (C, d, *J* = 243.0 Hz, *C*-F), 146.4 (C), 136.6 (C), 129.9 (2 x CH), 128.7 (CH), 127.4 (2 x CH, d, *J* = 8.0 Hz), 126.8 (C, d, *J* = 2.0 Hz), 120.0 (2 x CH), 119.5 (CH), 115.9 (2 x CH, d, *J* = 22.0 Hz); HRMS m/z 240.0937 (M + H^+), calcd for $C_{14}H_{10}FN_3H$ 240.0937.

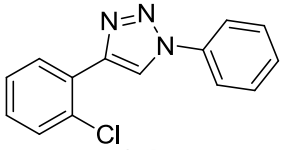
4-(4-Chlorophenyl)-1-phenyl-1*H*-1,2,3-triazole (3db): Prepared following the procedure



3db

1a and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp: 220-222 °C; IR (neat): ν_{max} 3120, 2923, 2852, 1596, 1504, 1466, 1405, 1229, 1098, 1088, 1044, 1014, 819 and 760 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz) δ 9.33 (1H, s), 7.98-7.94 (4H, m), 7.65 (2H, t, *J* = 7.6 Hz), 7.58 (2H, d, *J* = 8.4 Hz), 7.53 (1H, t, *J* = 7.6 Hz); ^{13}C NMR (DMSO-d_6, DEPT-135) δ 146.2 (C), 136.5 (C), 132.7 (C), 129.9 (2 x CH), 129.15 (C), 129.1 (2 x CH), 128.8 (CH), 127.0 (2 x CH), 120.0 (3 x CH); HRMS m/z 256.0643 (M + H^+), calcd for $C_{14}H_{10}ClN_3H$ 256.0642.

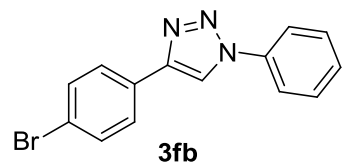
4-(2-Chlorophenyl)-1-phenyl-1*H*-1,2,3-triazole (3eb): Prepared following the procedure **1a**



3eb

and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid; IR (neat): ν_{max} 3063, 1597, 1504, 1471, 1412, 1220, 1040, 994, 755 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.62 (1H, s), 8.33 (1H, d, *J* = 8.0 Hz), 7.81 (2H, d, *J* = 8.0 Hz), 7.55 (2H, t, *J* = 8.0 Hz), 7.47 (1H, d, *J* = 7.2 Hz), 7.45 (1H, t, *J* = 7.2 Hz), 7.40 (1H, t, *J* = 8.0 Hz), 7.30 (1H, t, *J* = 8.0 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 144.5 (C), 136.9 (C), 131.2 (C), 130.2 (CH), 129.9 (CH), 129.7 (2 x CH), 129.2 (CH), 128.85 (C), 128.78 (CH), 127.2 (CH), 121.2 (CH), 120.6 (2 x CH); HRMS m/z 256.0641 (M + H^+), calcd for $C_{14}H_{10}ClN_3H$ 256.0642.

4-(4-Bromophenyl)-1-phenyl-1*H*-1,2,3-triazole (3fb):[28] Prepared following the procedure

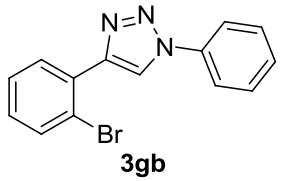


3fb

1a and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp: 227-228 °C; IR (Neat): ν_{max} 3118, 1596, 1546, 1502, 1465, 1402, 1228, 1237, 1072, 1043, 1010, 839, 816 and 760 cm^{-1}; ^1H NMR (DMSO-d_6) δ 9.34 (1H, s), 7.93 (2H, d, *J* = 7.6 Hz), 7.89 (2H, d, *J* = 8.0 Hz), 7.70 (2H, d, *J* =

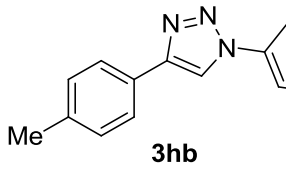
8.0 Hz), 7.63 (2H, t, *J* = 7.2 Hz), 7.51 (1H, t, *J* = 7.2 Hz); ^{13}C NMR (DMSO-d_6, DEPT-135) δ 146.3 (C), 136.6 (C), 132.0 (2 x CH), 130.0 (2 x CH), 129.5 (C), 128.8 (CH), 127.3 (2 x CH), 121.3 (C), 120.0 (3 x CH); HRMS m/z 300.0134 (M + H^+), calcd for $C_{14}H_{10}BrN_3H$ 300.0136.

4-(2-Bromophenyl)-1-phenyl-1*H*-1,2,3-triazole (3gb):[29] Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid; IR (neat): ν_{max} 3119, 3050, 2922, 1594, 1499, 1472, 1411, 1224, 1033, 991, 912, 826, 752 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.66 (1H, s), 8.18 (1H, br d, *J* = 7.6 Hz), 7.80 (2H, d, *J* = 7.6 Hz), 7.67 (1H, d, *J* = 7.6 Hz), 7.54 (2H, t, *J* = 7.6 Hz), 7.45 (1H, t, *J* = 7.6 Hz), 7.43 (1H, t, *J* = 7.6 Hz), 7.22 (1H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 145.8 (C), 136.9 (C), 133.5 (CH), 130.8 (C), 130.6 (CH), 129.7 (2 x CH), 129.5 (CH), 128.8 (CH), 127.7 (CH), 121.2 (C), 121.0 (CH), 120.5 (2 x CH); HRMS m/z 300.0136 (M + H^+), calcd for $C_{14}H_{10}BrN_3H$ 300.0131.



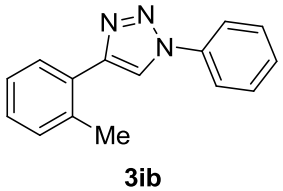
3gb

1-Phenyl-4-(*p*-tolyl)-1*H*-1,2,3-triazole (3hb):[30] Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. Mp: 160-162 °C; IR (neat): ν_{max} 3109, 2913, 1598, 1494, 1410, 1238, 1228, 1042, 993, 906, 812 and 754 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.16 (1H, s), 7.80 (2H, d, *J* = 8.4 Hz), 7.78 (2H, d, *J* = 8.4 Hz), 7.52 (2H, t, *J* = 8.0 Hz), 7.44 (1H, t, *J* = 7.6 Hz), 7.26 (2H, d, *J* = 8.0 Hz), 2.39 (3H, s, Ar-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.4 (C), 138.2 (C), 137.0 (C), 129.6 (2 x CH), 129.5 (2 x CH), 128.6 (CH), 127.3 (C), 125.7 (2 x CH), 120.4 (2 x CH), 117.2 (CH), 21.2 (CH_3); HRMS m/z 236.1186 (M + H^+), calcd for $C_{15}H_{13}N_3H$ 236.1188.



3hb

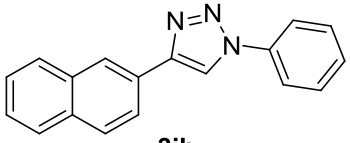
1-Phenyl-4-(*o*-tolyl)-1*H*-1,2,3-triazole (3ib): Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a light yellow solid. Mp: 76-80 °C; IR (neat): ν_{max} 3131, 3051, 2926, 1720, 1597, 1502, 1484, 1463, 1229, 1049, 992, 908, 828 and 755 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.09 (1H, s), 7.85-7.81 (3H, m), 7.56 (2H, t, *J* = 7.6 Hz), 7.47 (1H, t, *J* = 7.6 Hz), 7.32-7.31 (3H, m), 2.55 (3H, s, Ar-CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 147.8 (C), 137.0 (C), 135.7 (C), 130.9 (CH), 129.7 (2



3ib

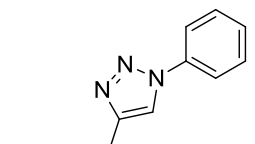
x CH), 129.5 (C), 129.0 (CH), 128.7 (CH), 128.4 (CH), 126.1 (CH), 120.5 (2 x CH), 119.7 (CH), 21.4 (CH_3); HRMS m/z 236.1187 ($M + H^+$), calcd for $C_{15}H_{13}N_3H$ 236.1188.

4-(Naphthalen-2-yl)-1-phenyl-1*H*-1,2,3-triazole (3jb): Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp: 194-196 °C; IR (neat): ν_{max} 3116, 3055, 1595, 1502, 1465, 1379, 1228, 1158, 1039, 906, 862, 822, 764 and 746 cm^{-1}; ^1H NMR (DMSO-d_6) δ 9.43 (1H, s), 8.51 (1H, s), 8.09-7.90 (6H, m), 7.64 (2H, t, *J* = 7.2 Hz), 7.58-7.50 (3H, m); ^{13}C NMR (DMSO-d_6, DEPT-135) δ 147.3 (C), 136.7 (C), 133.1 (C), 132.7 (C), 130.0 (2 x CH), 128.7 (CH), 128.6 (CH), 128.0 (CH), 127.7 (C, CH), 126.7 (CH), 126.3 (CH), 123.8 (CH), 123.7 (CH), 120.0 (3 x CH); HRMS m/z 272.1186 ($M + H^+$), calcd for $C_{18}H_{13}N_3H$ 272.1188.



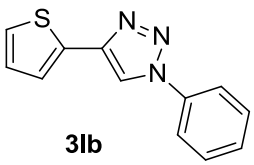
3jb

3-(1-Phenyl-1*H*-1,2,3-triazol-4-yl)-1*H*-indole (3kb): Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a brown solid. Mp: 120-122 °C; IR (neat): ν_{max} 3215, 1627, 1602, 1508, 1459, 1442, 1244, 1230, 1052, 988, 754 and 738 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.93 (1H, br s, N*H*), 8.20 (1H, s), 8.03-8.01 (1H, m), 7.83 (2H, d, *J* = 7.6 Hz), 7.77 (1H, d, *J* = 2.4 Hz), 7.55 (2H, t, *J* = 7.6 Hz), 7.46 (2H, m), 7.29-7.24 (2H, m); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 143.7 (C), 137.2 (C), 136.4 (C), 129.7 (2 x CH), 128.5 (CH), 125.0 (C), 123.0 (CH), 122.6 (CH), 120.50 (CH), 120.46 (2 x CH), 119.7 (CH), 116. 5 (CH), 111.7 (CH), 106.9 (C); HRMS m/z 261.1140 ($M + H^+$), calcd for $C_{16}H_{12}N_4H$ 261.1140.



3kb

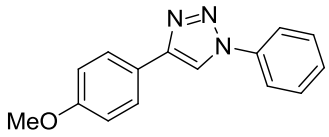
1-Phenyl-4-(thiophen-2-yl)-1*H*-1,2,3-triazole (3lb):[31] Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp: 140-142 °C; IR (neat): ν_{max} 3130, 1594, 1500, 1464, 1373, 1288, 1233, 1036, 989, 929, 845 and 756 cm^{-1}; ^1H NMR (DMSO-d_6) δ 9.18 (1H, s), 7.94 (2H, qd, *J* = 7.2, 1.2 Hz), 7.62 (2H, tt, *J* = 7.2, 2.0 Hz), 7.59 (1H, dd, *J* = 4.8, 1.2 Hz), 7.53 (1H, dd, *J* = 3.6, 1.2 Hz), 7.50 (1H, td, *J* = 7.6, 1.2 Hz), 7.18 (1H, dd, *J* = 5.2, 3.6 Hz); ^{13}C NMR (DMSO-d_6, DEPT-135) δ 142.7 (C), 136.5 (C), 132.3 (C), 129.9 (2 x CH), 128.8 (CH), 128.0 (CH), 125.9 (CH), 124.6



3lb

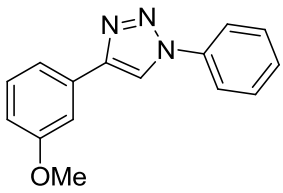
(CH), 120.1 (2 x CH), 118.8 (CH); HRMS m/z 228.0595 (M + H^+), calcd for $C_{12}H_9N_3SH$ 228.0595.

4-(4-Methoxyphenyl)-1-phenyl-1*H*-1,2,3-triazole (3mb):[32] Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp: 118-122 °C; IR (neat): ν_{max} 3106, 3004, 2838, 1616, 1598, 1491, 1463, 1303, 1238, 1229, 1175, 1033, 993, 837, 815 and 763 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.12 (1H, s), 7.84 (2H, d, *J* = 8.4 Hz), 7.79 (2H, d, *J* = 7.6 Hz), 7.54 (2H, t, *J* = 7.6 Hz), 7.45 (1H, t, *J* = 7.2 Hz), 6.99 (2H, d, *J* = 8.4 Hz), 3.86 (3H, s, OC*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 159.8 (C), 148.3 (C), 137.1 (C), 129.7 (2 x CH), 128.7 (CH), 127.2 (2 x CH), 122.9 (C), 120.5 (2 x CH), 116.8 (CH), 114.3 (2 x CH), 55.3 (CH_3, O*C*H_3); HRMS m/z 252.1135 (M + H^+), calcd for $C_{15}H_{13}N_3OH$ 252.1137.



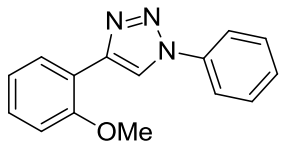
3mb

4-(3-Methoxyphenyl)-1-phenyl-1*H*-1,2,3-triazole (3nb): Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a light yellow liquid; IR (neat): ν_{max} 2920, 2850, 1729, 1579, 1464, 1209, 1041, 967, 884, 824 and 773 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.21 (1H, s), 7.80 (2H, d, *J* = 7.6 Hz), 7.57-7.54 (3H, m), 7.47 (2H, t, *J* = 6.0 Hz), 7.37 (1H, t, *J* = 8.0 Hz), 6.94 (1H, d, *J* = 7.6 Hz), 3.90 (3H, s, OC*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 160.1 (C), 148.2 (C), 137.0 (C), 131.5 (C), 129.9 (CH), 129.7 (2 x CH), 128.7 (CH), 120.5 (2 x CH), 118.2 (CH), 117.8 (CH), 114.4 (CH), 110.9 (CH), 55.3 (CH_3, O*C*H_3); HRMS m/z 252.1139 (M + H^+), calcd for $C_{15}H_{13}N_3OH$ 252.1137.



3nb

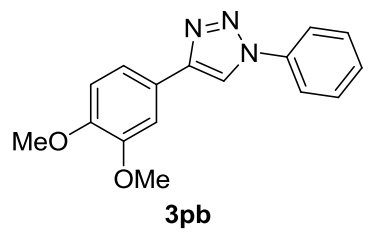
4-(2-Methoxyphenyl)-1-phenyl-1*H*-1,2,3-triazole (3ob): Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a liquid; IR (neat): ν_{max} 3066, 2935, 2837, 1724, 1599, 1489, 1463, 1244, 1122, 1028, 801 and 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.46 (1H, s), 8.44 (1H, dd, *J* = 7.6, 1.6 Hz), 7.81 (2H, d, *J* = 8.0 Hz), 7.52 (2H, t, *J* = 7.6 Hz), 7.42 (1H, t, *J* = 7.6 Hz), 7.34 (1H, dt, *J* = 8.8, 2.0 Hz), 7.11 (1H, t, *J* = 7.6 Hz), 7.00 (1H, d, *J* = 8.4 Hz), 3.96 (3H, s, OC*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 155.7 (C), 143.7 (C), 137.2 (C), 129.6 (2 x CH), 129.1 (CH), 128.4 (CH),



3ob

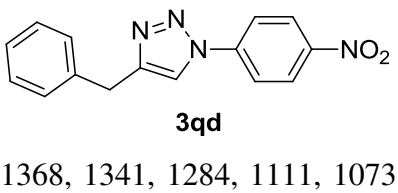
127.7 (CH), 120.96 (CH), 120.89 (CH), 120.4 (2 x CH), 118.9 (C), 110.7 (CH), 55.3 (CH_3, O*C*H_3); HRMS m/z 252.1137 (M + H^+), calcd for $C_{15}H_{13}N_3OH$ 252.1137.

4-(3,4-Dimethoxyphenyl)-1-phenyl-1*H*-1,2,3-triazole (3pb): Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a light yellow solid. Mp: 90-92 °C; IR (neat): ν_{max} 3000, 2921, 2848, 1595, 1498, 1463, 1399, 1360, 1259, 1233, 1140, 1022, 987, 859 and 762 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.15 (1H, s), 7.78 (2H, qd, *J* = 8.8, 1.2 Hz), 7.55 (1H, d, *J* = 6.0 Hz), 7.52 (2H, tt, *J* = 8.0, 1.6 Hz), 7.43 (1H, tt, *J* = 7.6, 1.2 Hz), 7.37 (1H, dd, *J* = 8.0, 2.0 Hz), 6.92 (1H, d, *J* = 8.4 Hz), 3.97 (3H, s, O*C*H_3), 3.91 (3H, s, O*C*H_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 149.3 (C), 149.2 (C), 148.2 (C), 137.0 (C), 129.6 (2 x CH), 128.6 (CH), 123.1 (C), 120.3 (2 x CH), 118.2 (CH), 116.9 (CH), 111.3 (CH), 109.0 (CH), 55.91 (CH_3, O*C*H_3), 55.86 (CH_3, O*C*H_3); HRMS m/z 282.1240 (M + H^+), calcd for $C_{16}H_{15}N_3O_2H$ 282.1243.



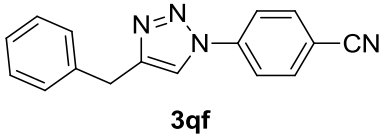
3pb

4-Benzyl-1-(4-nitrophenyl)-1*H*-1,2,3-triazole (3qd): Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a yellow solid. Mp: 165-167 °C; IR (neat): ν_{max} 2925, 2854, 1723, 1597, 1506, 1453, 1368, 1341, 1284, 1111, 1073, 1041, 986, 853 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.38 (2H, td, *J* = 9.2, 2.0 Hz), 7.94 (2H, td, *J* = 9.2, 2.0 Hz), 7.75 (1H, s), 7.38-7.26 (5H, m), 4.20 (2H, s); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 149.4 (C), 146.9 (C), 141.2 (C), 138.2 (C), 128.8 (2 x CH), 128.7 (2 x CH), 126.8 (CH), 125.4 (2 x CH), 120.2 (2 x CH), 119.4 (CH), 32.1 (CH_2); HRMS m/z 281.1037 (M + H^+), calcd for $C_{15}H_{12}N_4O_2H$ 281.1039.



3qd

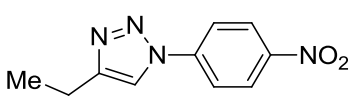
4-(4-Benzyl-1*H*-1,2,3-triazol-1-yl)benzonitrile (3qf): Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp: 122-124 °C; IR (neat): ν_{max} 3147, 2223, 1603, 1514, 1494, 1450, 1405, 1329, 1242, 1176, 1043, 1018, 1009, 984, 838, 828, 738 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.85 (2H, d, *J* = 8.8 Hz), 7.77 (2H, d, *J* = 8.8 Hz), 7.71 (1H, s), 7.34-7.22 (5H, m), 4.16 (2H, s); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 149.2 (C), 139.7 (C), 138.2 (C), 133.7 (2 x CH), 128.7 (2 x



3qf

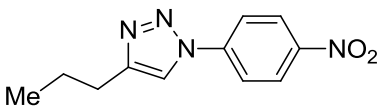
CH), 128.6 (2 x CH), 126.7 (CH), 120.2 (2 x CH), 119.3 (CH), 117.7 (C, CN), 111.9 (C), 32.1 (CH_2); HRMS m/z 261.1135 ($M + H^+$), calcd for $C_{16}H_{12}N_4H$ 261.1140.

4-Ethyl-1-(4-nitrophenyl)-1*H*-1,2,3-triazole (3rd):[36] Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a yellow solid. Mp: 126-128 °C; IR (neat): ν_{max} 3134, 3094, 2961, 2923, 2853, 1673, 1596, 1514, 1504, 1407, 1334, 1226, 1173, 1110, 1042, 993 and 852 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.41 (2H, td, *J* = 9.2, 2.0 Hz), 7.98 (2H, td, *J* = 9.2, 2.0 Hz), 7.87 (1H, br t, *J* = 1.8 Hz), 2.87 (2H, dq, *J* = 7.6, 0.8 Hz), 1.37 (3H, t, *J* = 7.6 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 151.5 (C), 146.9 (C), 141.4 (C), 125.5 (2 x CH), 120.2 (2 x CH), 118.2 (CH), 19.0 (CH_2), 13.4 (CH_3); HRMS m/z 219.0877 ($M + H^+$), calcd for $C_{10}H_{10}N_4O_2H$ 219.0882.



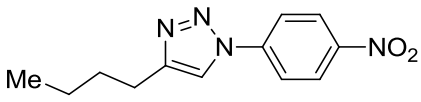
3rd

1-(4-Nitrophenyl)-4-propyl-1*H*-1,2,3-triazole (3sd): Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a light yellow solid. Mp: 102-104 °C; IR (neat): ν_{max} 3137, 2960, 2928, 2873, 1596, 1503, 1405, 1336, 1222, 1173, 1112, 1041, 987, 852, 804, 748 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.40 (2H, d, *J* = 8.8 Hz), 7.98 (2H, d, *J* = 8.8 Hz), 7.87 (1H, br s), 2.80 (2H, t, *J* = 7.6 Hz), 1.78 (2H, sextet, *J* = 7.6 Hz), 1.03 (3H, t, *J* = 7.6 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 149.9 (C), 146.9 (C), 141.3 (C), 125.4 (2 x CH), 120.1 (2 x CH), 118.6 (CH), 27.5 (CH_2), 22.4 (CH_2), 13.7 (CH_3); HRMS m/z 233.1038 ($M + H^+$), calcd for $C_{11}H_{12}N_4O_2H$ 233.1039.



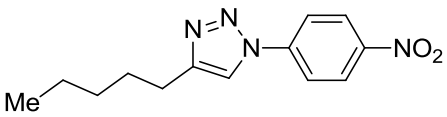
3sd

4-Butyl-1-(4-nitrophenyl)-1*H*-1,2,3-triazole (3td): Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a light yellow solid. Mp: 102-104 °C; IR (neat): ν_{max} 3139, 3096, 2952, 2928, 2854, 1596, 1519, 1504, 1463, 1406, 1338, 1220, 1111, 1042, 986, 853, 830, 748 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.40 (2H, d, *J* = 8.8 Hz), 7.96 (2H, d, *J* = 8.8 Hz), 7.84 (1H, s), 2.82 (2H, t, *J* = 7.6 Hz), 1.73 (2H, quintet, *J* = 7.2 Hz), 1.43 (2H, sextet, *J* = 7.2 Hz), 0.96 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 150.1 (C), 146.9 (C), 141.4 (C), 125.4 (2 x CH), 120.2 (2 x CH), 118.5 (CH), 31.3 (CH_2), 25.2 (CH_2), 22.2 (CH_2), 13.8 (CH_3); HRMS m/z 247.1195 ($M + H^+$), calcd for $C_{12}H_{14}N_4O_2H$ 247.1195.



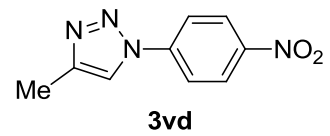
3td

1-(4-Nitrophenyl)-4-pentyl-1*H*-1,2,3-triazole (3ud): Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a light yellow solid. Mp: 86-88 °C; IR (neat): ν_{max} 2957, 2923, 2853, 1595, 1519, 1503, 1337, 1238, 1215, 1111, 1039, 985, 851, 802, 748 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.38 (2H, br d, *J* = 9.2 Hz), 7.98 (2H, td, *J* = 9.2, 2.0 Hz), 7.89 (1H, br s), 2.80 (2H, t, *J* = 7.6 Hz), 1.74 (2H, quintet, *J* = 7.6 Hz), 1.42-1.30 (4H, m), 0.89 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 150.1 (C), 146.8 (C), 141.3 (C), 125.4 (2 x CH), 120.1 (2 x CH), 118.6 (CH), 31.3 (CH_2), 28.8 (CH_2), 25.4 (CH_2), 22.3 (CH_2), 13.9 (CH_3); HRMS m/z 261.1352 ($M + H^+$), calcd for $C_{13}H_{16}N_4O_2H$ 261.1352.



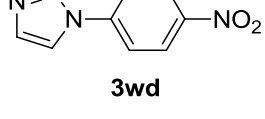
3ud

4-Methyl-1-(4-nitrophenyl)-1*H*-1,2,3-triazole (3vd): Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a yellow solid. Mp 215-218 °C; IR (neat): ν_{max} 2923, 2852, 1595, 1510, 1328, 1236, 1108, 1043, 968 and 850 cm^{-1}; ^1H NMR (DMSO-d_6) δ 8.73 (1H, s), 8.43 (2H, td, *J* = 9.2, 2.8 Hz), 8.17 (2H, td, *J* = 9.2, 2.8 Hz), 2.36 (3H, d, *J* = 0.4 Hz, Ar-CH_3); ^{13}C NMR (DMSO-d_6, DEPT-135) δ 146.5 (C), 144.0 (C), 141.0 (C), 125.6 (2 x CH), 121.0 (CH), 120.3 (2 x CH), 10.5 (CH_3); HRMS m/z 205.0725 ($M + H^+$), calcd for $C_9H_8N_4O_2H$ 205.0726.



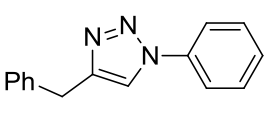
3vd

1-(4-Nitrophenyl)-1*H*-1,2,3-triazole (3wd): Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a yellow solid. Mp 209-211 °C; IR (neat): ν_{max} 3130, 2922, 2852, 1597, 1519, 1510, 1413, 1342, 1236, 1112, 1029, 981 and 855 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.43 (2H, d, *J* = 8.8 Hz), 8.14 (1H, br s), 8.01 (2H, d, *J* = 9.2 Hz), 7.92 (1H, br s); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 147.3 (C), 141.2 (C), 135.2 (CH), 125.6 (2 x CH), 121.6 (CH), 120.6 (2 x CH); HRMS m/z 191.0564 ($M + H^+$), calcd for $C_8H_6N_4O_2H$ 191.0569.



3wd

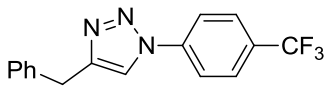
4-Benzyl-1-phenyl-1*H*-1,2,3-triazole (3qb): Prepared following the procedure **1b** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 99-101 °C; IR (neat): ν_{max} 3129, 2922, 2852, 1599, 1496, 1467, 1355, 1049, 991 and 909 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.70 (2H, d, *J* = 7.6 Hz), 7.62 (1H, br s), 7.50 (2H, t, *J* = 7.6 Hz), 7.42 (1H, t, *J* =



3qb

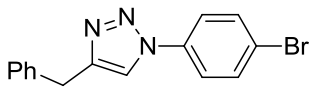
7.6 Hz), 7.36-7.35 (4H, m), 7.31-7.25 (1H, m), 4.20 (2H, s); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 148.4 (C), 138.8 (C), 137.1 (C), 129.6 (2 x CH), 128.8 (2 x CH), 128.7 (2 x CH), 128.5 (CH), 126.6 (CH), 120.4 (2 x CH), 119.6 (CH), 32.3 (CH_2); HRMS m/z 258.1008 (M + Na), calcd for $C_{15}H_{13}N_3Na$ 258.1007.

4-Benzyl-1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazole (3qg): Prepared following the procedure **1a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 101-103 °C; IR (neat): ν_{max} 3125, 3082, 2923, 1618, 1528, 1495, 1446, 1413, 1324, 1232, 1160, 1122, 1112, 1070, 1048, 1022, 988, 844 and 723 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.85 (2H, d, *J* = 8.4 Hz), 7.77 (2H, d, *J* = 8.8 Hz), 7.66 (1H, s), 7.37-7.28 (5H, m), 4.19 (2H, s); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 149.1 (C), 139.5 (C), 138.5 (C), 130.5 (C, q, *J* = 33.0 Hz), 128.8 (4 x CH), 127.0 (2 x CH, q, *J* = 4.0 Hz), 126.8 (CH), 123.6 (C, q, *J* = 270.0 Hz, *C*F_3), 120.2 (2 x CH), 119.4 (CH), 32.3 (CH_2); HRMS m/z 304.1062 (M + H$^+$), calcd for $C_{16}H_{12}F_3N_3H$ 304.1062.



3qg

4-Benzyl-1-(4-bromophenyl)-1*H*-1,2,3-triazole (3ql): Prepared following the procedure **1b** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 122-124 °C; IR (neat): ν_{max} 3124, 2922, 2853, 1497, 1457, 1402, 1230, 1074, 1051, 985 and 823 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.64-7.58 (5H, m), 7.38-7.32 (4H, m), 7.30-7.26 (1H, m), 4.19 (2H, s); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 148.8 (C), 138.6 (C), 136.1 (C), 132.8 (2 x CH), 128.8 (4 x CH), 126.7 (CH), 122.1 (C), 121.7 (2 x CH), 119.4 (CH), 32.2 (CH_2); HRMS m/z 314.0293 (M + H$^+$), calcd for $C_{15}H_{12}BrN_3H$ 314.0293.



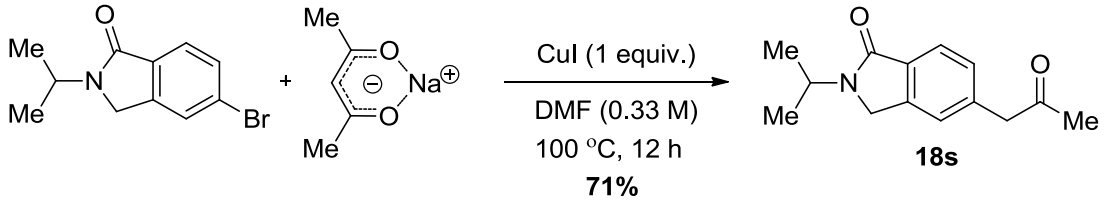
3ql

2a: General procedure for the DBU-catalyzed azide-ketone [3+2]-Cycloaddition reactions: In an ordinary glass vial equipped with a magnetic stirring bar, to 0.05 mmol of catalyst **15c** in DMSO (1.0 mL), was added 0.75 mmol of arylazide **2** and 0.5 mmol of ketone **18** and the reaction mixture was stirred at 25 °C for the time indicated in Tables 5-8. The crude reaction mixture was worked up with aqueous NH_4Cl solution and the aqueous layer was extracted with dichloromethane (2 x 20 mL). The combined organic layers were

dried (Na_2SO_4), filtered and concentrated. Pure domino products **19** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

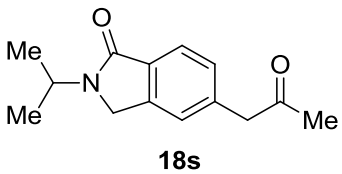
2b: General procedure for the *t*BuOK-catalyzed azide-ketone [3+2]-Cycloaddition reactions: In an ordinary glass vial equipped with a magnetic stirring bar, to 0.05 mmol of *t*BuOK **15i** (5.6 mg) in DMSO (1.0 mL), was added 0.75 mmol of arylazide **2** and 0.5 mmol of ketone **18** and the reaction mixture was stirred at 25 °C for the time indicated in Tables 5-6. The crude reaction mixture was worked up with aqueous NH_4Cl solution and the aqueous layer was extracted with dichloromethane (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure domino products **19** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

***Scheme E1*:** Synthesis of 2-isopropyl-6-(2-oxopropyl)isoindolin-1-one (**18s**)



2c: General Procedure for the Synthesis of Arylacetone 18s: To 6-bromo-2-isopropylisoindolin-1-one (1 equiv.) dissolved in dry DMF (0. 33 M), CuI (1 equiv.) and sodium acetylacetonate (5 equiv.) were added successively under nitrogen atmosphere. The reaction mixture was heated for 12 h at 100 °C and then cooled to room temperature. The crude reaction mixture was worked up with aqueous NH_4Cl solution and the aqueous layer was extracted with dichloromethane (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure product **18s** obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

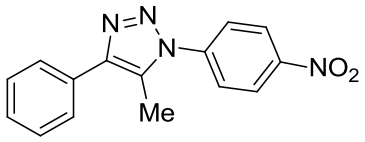
2-Isopropyl-6-(2-oxopropyl)isoindolin-1-one (**18s**): Prepared following the procedure **2c** and purified by column chromatography using EtOAc/hexane and was isolated as a yellow liquid. IR (neat): ν_{max} 2972, 2929, 1711, 1667, 1622, 1576, 1522, 1455, 1409, 1356, 1230, 1159, 1128, 1057, 1020, 841, 768 and 730 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.79 (1H, d, *J* = 7.6 Hz), 7.29–7.25 (2H, m), 4.65 (1H, sep, *J* = 6.8 Hz), 4.32 (2H, s),



18s

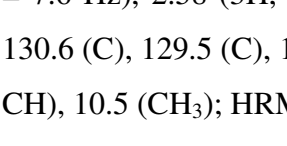
3.80 (2H, s), 2.19 (3H, s), 1.27 (6H, d, J = 6.8 Hz, 2 x CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 205.5 (C), 167.6 (C), 141.9 (C), 137.6 (C), 132.5 (C), 129.5 (CH), 123.92 (CH), 123.87 (CH), 50.9 (CH_2), 45.0 (CH_2), 42.7 (CH), 29.7 (CH_3), 20.9 (2 x CH_3); LCMS m/z 232.15 (M + H^+), calcd for $C_{14}H_{17}NO_2H$ 231.13; HRMS m/z 232.1336 (M + H^+), calcd for $C_{14}H_{17}NO_2H$ 232.1338.

5-Methyl-1-(4-nitrophenyl)-4-phenyl-1*H*-1,2,3-triazole (19ad):[42] Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a yellow solid. Mp 206-209 °C; IR (KBr): ν_{max} 3090, 1600, 1523, 1496, 1342, 1266, 1008, 970, and 860 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.46 (2H, d, J = 8.8 Hz), 7.79 (2H, d, J = 9.2 Hz), 7.76 (2H, d, J = 7.6 Hz), 7.50 (2H, t, J = 7.6 Hz), 7.41 (1H, t, J = 7.6 Hz), 2.58 (3H, s); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 147.7 (C), 145.9 (C), 141.2 (C), 130.6 (C), 129.5 (C), 128.8 (2 x CH), 128.2 (CH), 127.4 (2 x CH), 125.4 (2 x CH), 125.1 (2 x CH), 10.5 (CH_3); HRMS m/z 281.1038 (M + H^+), calcd for $C_{15}H_{12}N_4O_2H$ 281.1039.



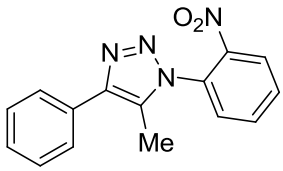
19ad

5-Methyl-1,4-diphenyl-1*H*-1,2,3-triazole (19ab):[39] Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 198-201 °C; IR (neat): ν_{max} 3092, 1597, 1521, 1502, 1441, 1411, 1338, 1267, 1107, 1093, 1007, 974, 862, 855 and 773 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.79 (2H, d, J = 7.6 Hz), 7.60-7.48 (7H, m), 7.39 (1H, t, J = 7.6 Hz), 2.50 (3H, s); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 144.9 (C), 136.4 (C), 131.4 (C), 129.7 (C), 129.6 (2 x CH), 129.5 (CH), 128.8 (2 x CH), 127.8 (CH), 127.2 (2 x CH), 125.3 (2 x CH), 10.3 (CH_3); HRMS m/z 258.1011 (M + Na), calcd for $C_{15}H_{13}N_3Na$ 258.1007.



19ab

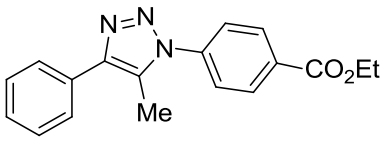
5-Methyl-1-(2-nitrophenyl)-4-phenyl-1*H*-1,2,3-triazole (19ac): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a yellow solid. Mp 142-144 °C; IR (neat): 3063, 2953, 2932, 1721, 1606, 1540, 1501, 1353, 1271, 975, 855 and 778 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.15 (1H, d, J = 8.0 Hz), 7.82 (1H, t, J = 7.6 Hz), 7.78 (2H, d, J = 7.6 Hz), 7.74 (1H, t, J = 8.0 Hz), 7.54 (1H, d, J = 7.6 Hz), 7.48 (2H, t, J = 7.6 Hz), 7.38 (1H, t, J = 7.6 Hz), 2.39 (3H, s);



19ac

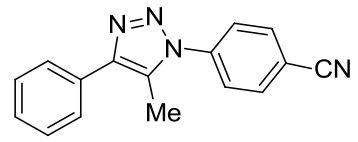
^{13}C NMR ($CDCl_3$, DEPT-135) δ 145.5 (C), 144.3 (C), 134.1 (CH), 131.5 (C), 131.4 (CH), 130.9 (C), 129.7 (CH), 129.4 (C), 128.7 (2 x CH), 127.9 (CH), 127.0 (2 x CH), 125.6 (CH), 9.5 (CH_3); HRMS m/z 281.1036 (M + H^+), calcd for $C_{15}H_{12}N_4O_2H$ 281.1039.

Ethyl 4-(5-methyl-4-phenyl-1*H*-1,2,3-triazol-1-yl)benzoate (19ae): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a light yellow solid. Mp 141-144 °C; IR (KBr): ν_{max} 3058, 2975, 1715, 1611, 1518, 1408, 1375, 1288, 1112, 981, 871 and 773 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.27 (2H, br d, *J* = 8.5 Hz), 7.78 (2H, br d, *J* = 8.5 Hz), 7.65 (2H, br d, *J* = 8.5 Hz), 7.50 (2H, br t, *J* = 7.5 Hz), 7.40 (1H, tt, *J* = 7.5, 1.5 Hz), 4.45 (2H, q, *J* = 7.0 Hz), 2.54 (3H, s), 1.45 (3H, t, *J* = 7.0 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.3 (C), 145.2 (C), 139.6 (C), 131.1 (C), 130.9 (C), 130.8 (2 x CH), 129.5 (C), 128.6 (2 x CH), 127.8 (CH), 127.1 (2 x CH), 124.6 (2 x CH), 61.4 (CH_2, O*C*H_2CH_3), 14.2 (CH_3, OCH_2*C*H_3), 10.3 (CH_3); HRMS m/z 308.1398 (M + H^+), calcd for $C_{18}H_{17}N_3O_2H$ 308.1399.



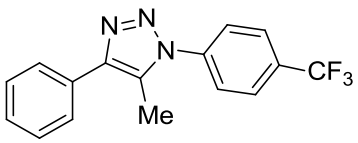
19ae

4-(5-Methyl-4-phenyl-1*H*-1,2,3-triazol-1-yl)benzonitrile (19af): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a light yellow solid. Mp 197-199 °C; IR (KBr): ν_{max} 3063, 2948, 2236, 1721, 1616, 1523, 1447, 1408, 1255, 1096, 844 and 762 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.90 (2H, d, *J* = 8.4 Hz), 7.76 (2H, d, *J* = 7.6 Hz), 7.72 (2H, d, *J* = 8.4 Hz), 7.50 (2H, t, *J* = 7.6 Hz), 7.41 (1H, t, *J* = 7.6 Hz), 2.56 (3H, s); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 145.8 (C), 139.7 (C), 133.6 (2 x CH), 130.7 (C), 129.4 (C), 128.8 (2 x CH), 128.2 (CH), 127.3 (2 x CH), 125.4 (2 x CH), 117.6 (C, *C*≡N), 113.2 (C), 10.5 (CH_3); HRMS m/z 261.1142 (M + H^+), calcd for $C_{16}H_{12}N_4H$ 261.1140.



19af

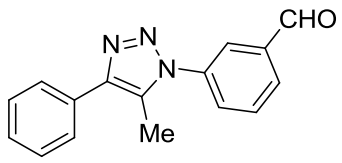
5-Methyl-4-phenyl-1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazole (19ag): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 204-207 °C; IR (KBr): ν_{max} 3079, 2992, 1616, 1523, 1414, 1332, 1266, 1178, 1118, 1074, 975, 855 and 773 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.85 (2H, d, *J* = 8.4 Hz), 7.77 (2H, d, *J* = 7.6 Hz), 7.69 (2H, d, *J* = 8.0 Hz), 7.49 (2H, t, *J* = 7.6 Hz), 7.40 (1H, t, *J* = 7.6 Hz), 2.53 (3H, s); ^{13}C NMR ($CDCl_3$,



19ag

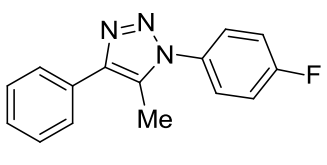
DEPT-135) δ 145.4 (C), 139.1 (C), 131.4 (C, q, *J* = 33.0 Hz), 130.9 (C), 129.5 (C), 128.8 (2 x CH), 128.0 (CH), 127.2 (2 x CH), 126.8 (2 x CH, q, *J* = 3.0 Hz), 125.3 (2 x CH), 123.5 (C, q, *J* = 271.0 Hz, *C*F_3), 10.3 (CH_3); HRMS m/z 304.1061 (M + H^+), calcd for $C_{16}H_{12}F_3N_3H$ 304.1062.

3-(5-Methyl-4-phenyl-1*H*-1,2,3-triazol-1-yl)benzaldehyde (19ah): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and isolated as a White solid. Mp 98-101 °C; IR (KBr): ν_{max} 3085, 2921, 2844, 1704, 1589, 1496, 1441, 1386, 1260, 1162, 1112, 981, 816, 767 and 685 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 10.14 (1H, s), 8.08-8.06 (2H, m), 7.87 (1H, ddd, *J* = 8.0, 2.0, 1.6 Hz), 7.82-7.78 (3H, m), 7.52 (2H, tt, *J* = 7.6, 1.6 Hz), 7.42 (1H, tt, *J* = 7.6, 2.0 Hz), 2.56 (3H, s); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 190.6 (CH, *C*HO), 145.3 (C), 137.5 (C), 137.3 (C), 131.0 (C), 130.6 (CH), 130.5 (2 x CH), 129.6 (C), 128.8 (2 x CH), 128.0 (CH), 127.3 (2 x CH), 125.4 (CH), 10.3 (CH_3); HRMS m/z 264.1136 (M + H^+), calcd for $C_{16}H_{13}N_3OH$ 264.1137.



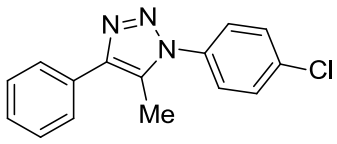
19ah

1-(4-Fluorophenyl)-5-methyl-4-phenyl-1*H*-1,2,3-triazole (19ai):[36d] Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a light yellow solid. Mp 181-184 °C; IR (KBr): ν_{max} 3052, 3008, 2926, 1606, 1512, 1441, 1238, 1162, 1112, 1008, 838 and 773 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.76 (2H, d, *J* = 7.6 Hz), 7.50-7.45 (4H, m), 7.37 (1H, t, *J* = 7.6 Hz), 7.24 (2H, t, *J* = 8.4 Hz), 2.45 (3H, s); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 162.8 (C, d, *J* = 248.0 Hz, *C*-F), 144.7 (C), 132.3 (C), 131.1 (C), 129.7 (C), 128.7 (2 x CH), 127.8 (CH), 127.13 (2 x CH, d, *J* = 10.0 Hz), 127.1 (2 x CH), 116.5 (2 x CH, d, *J* = 23.0 Hz), 10.1 (CH_3); HRMS m/z 276.0913 (M + Na), calcd for $C_{15}H_{12}FN_3Na$ 276.0913.



19ai

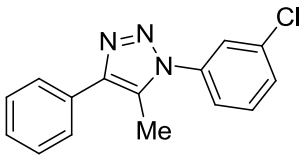
1-(4-Chlorophenyl)-5-methyl-4-phenyl-1*H*-1,2,3-triazole (19aj): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 168-171 °C; IR (KBr): 3096, 2992, 1501, 1403, 1260, 1129, 1096, 1008, 975, 849, 773 and 696 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.75 (2H, d, *J* = 7.2 Hz), 7.52 (2H, d, *J* = 8.4 Hz), 7.48-7.43 (4H, m), 7.36 (1H, t, *J* = 7.2 Hz), 2.46 (3H, s);



19aj

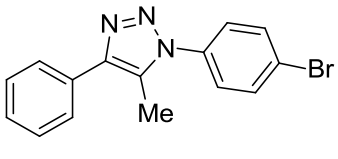
^{13}C NMR ($CDCl_3$, DEPT-135) δ 144.9 (C), 135.4 (C), 134.7 (C), 131.0 (C), 129.64 (2 x CH), 129.55 (C), 128.6 (2 x CH), 127.8 (CH), 127.1 (2 x CH), 126.3 (2 x CH), 10.1 (CH_3); HRMS m/z 270.0799 (M + H^+), calcd for $C_{15}H_{12}ClN_3H$ 270.0798.

1-(3-Chlorophenyl)-5-methyl-4-phenyl-1*H*-1,2,3-triazole (19ak): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 113-116 °C; IR (KBr): 3079, 2981, 1594, 1490, 1441, 1255, 1112, 975, 866, 789, 756 and 685 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.77 (2H, td, *J* = 8.0, 2.0 Hz), 7.58-7.56 (1H, m), 7.52-7.47 (4H, m), 7.45-7.42 (1H, m), 7.39 (1H, tt, *J* = 7.6, 2.0 Hz), 2.50 (3H, s); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 145.0 (C), 137.2 (C), 135.1 (C), 131.0 (C), 130.5 (CH), 129.6 (C, CH), 128.7 (2 x CH), 127.8 (CH), 127.1 (2 x CH), 125.3 (CH), 123.2 (CH), 10.2 (CH_3); HRMS m/z 292.0618 (M + Na), calcd for $C_{15}H_{12}ClN_3Na$ 292.0617.



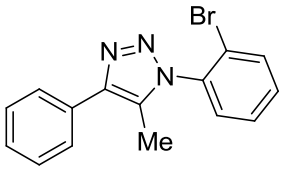
19ak

1-(4-Bromophenyl)-5-methyl-4-phenyl-1*H*-1,2,3-triazole (19al): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 162-165 °C; IR (KBr): ν_{max} 3085, 3052, 2986, 1501, 1452, 1403, 1249, 1123, 1074, 1008, 838, 767 and 696 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.75 (2H, d, *J* = 7.6 Hz), 7.68 (2H, d, *J* = 8.4 Hz), 7.47 (2H, t, *J* = 8.0 Hz), 7.40-7.36 (3H, m), 2.46 (3H, s); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 145.0 (C), 135.2 (C), 132.6 (2 x CH), 131.0 (C), 129.5 (C), 128.7 (2 x CH), 127.8 (CH), 127.1 (2 x CH), 126.5 (2 x CH), 123.4 (C), 10.2 (CH_3); HRMS m/z 336.0113 (M + Na), calcd for $C_{15}H_{12}BrN_3Na$ 336.0112.



19al

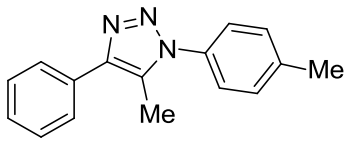
1-(2-Bromophenyl)-5-methyl-4-phenyl-1*H*-1,2,3-triazole (19am): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 109-111 °C; IR (KBr): 3047, 2915, 2849, 1611, 1584, 1501, 1463, 1271, 1101, 1008, 778, 762 and 718 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.85 (2H, dd, *J* = 8.0, 1.0 Hz), 7.81 (1H, dd, *J* = 8.0, 1.5 Hz), 7.55 (1H, dt, *J* = 7.5, 1.5 Hz), 7.53-7.46 (4H, m), 7.40 (1H, tt, *J* = 7.5, 1.5 Hz), 2.39 (3H, s); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 143.9 (C), 135.6 (C), 133.6 (CH), 131.8 (CH), 131.3 (C), 131.1 (C), 129.4



19am

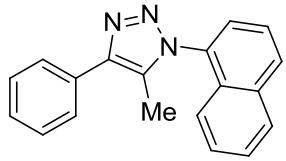
(CH), 128.7 (2 x CH), 128.5 (CH), 127.7 (CH), 127.0 (2 x CH), 121.7 (C), 9.6 (CH_3); HRMS m/z 336.0114 (M + Na), calcd for $C_{15}H_{12}BrN_3Na$ 336.0112.

5-Methyl-4-phenyl-1-(p-tolyl)-1*H*-1,2,3-triazole (19an): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. Mp 164-167 °C; IR (neat): ν_{max} 2926, 1516, 1493, 1368, 1245, 1117, 1103, 1070, 1008, 979, 819 and 772 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.80 (2H, td, *J* = 8.0, 2.0 Hz), 7.49 (2H, t, *J* = 7.6 Hz), 7.40-7.35 (5H, m), 2.47 (3H, s), 2.46 (3H, s); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 144.6 (C), 139.6 (C), 133.8 (C), 131.4 (C), 130.0 (2 x CH), 129.6 (C),128.6 (2 x CH), 127.6 (CH), 127.1 (2 x CH), 125.0 (2 x CH), 21.1 (CH_3), 10.2 (CH_3) ; HRMS m/z 250.1342 (M + H^+), calcd for $C_{16}H_{15}N_3H$ 250.1344.



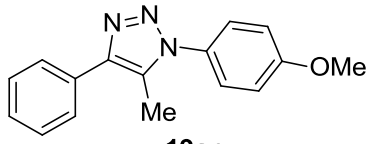
19an

5-Methyl-1-(naphthalen-1-yl)-4-phenyl-1*H*-1,2,3-triazole (19ao):[43] Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a brown solid. Mp 154-157 °C; IR (neat): ν_{max} 3059, 2923, 1598, 1579, 1509, 1491, 1446, 1427, 1396, 1258, 1107, 1013, 960, 803 and 714 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.07 (1H, d, *J* = 8.0 Hz), 7.99 (1H, d, *J* = 8.0 Hz), 7.90 (2H, d, *J* = 7.6 Hz), 7.64 (1H, t, *J* = 7.2 Hz), 7.59-7.50 (5H, m), 7.41 (1H, t, *J* = 6.8 Hz), 7.30 (1H, d, *J* = 8.0 Hz), 2.31 (3H, s); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 143.9 (C), 134.1 (C), 132.4 (C), 131.6 (C), 131.4 (C), 130.7 (CH), 129.7 (C), 128.7 (2 x CH), 128.2 (CH), 127.9 (CH), 127.7 (CH), 127.04 (CH), 126.98 (2 x CH), 125.2 (CH), 125.1 (CH), 122.2 (CH), 9.6 (CH_3); HRMS m/z 286.1347 (M + H^+), calcd for $C_{19}H_{15}N_3H$ 286.1344.



19ao

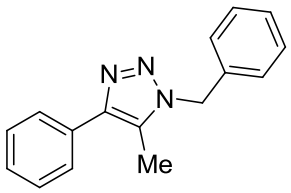
1-(4-Methoxyphenyl)-5-methyl-4-phenyl-1*H*-1,2,3-triazole (19ap): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 147-150 °C; IR (neat): ν_{max} 2963, 1609, 1518, 1443, 1307, 1257, 1171, 1088, 1013, 840 and 795 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.77 (2H, d, *J* = 7.6 Hz), 7.46 (2H, t, *J* = 7.6 Hz), 7.39 (2H, d, *J* = 9.2 Hz), 7.36 (1H, t, *J* = 7.2 Hz), 7.04 (2H, d, *J* = 8.8 Hz), 3.86 (3H, s), 2.43 (3H, s); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 160.2 (C), 144.4 (C), 131.4 (C), 129.8 (C), 129.1 (C), 128.6 (2 x CH), 127.6 (CH), 127.0 (2 x



19ap

CH), 126.6 (2 x CH), 114.5 (2 x CH), 55.5 (CH_3, O*C*H_3), 10.1 (CH_3); HRMS m/z 266.1294 (M + H^+), calcd for $C_{16}H_{15}N_3OH$ 266.1293.

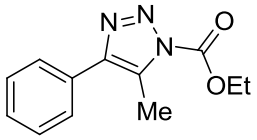
1-Benzyl-5-methyl-4-phenyl-1*H*-1,2,3-triazole (19aq):[34d] Prepared following the procedure



19aq

2b and purified by column chromatography using EtOAc/hexane and was isolated as a yellow liquid; IR (neat): ν_{max} 3033, 2922, 2851, 1673, 1607, 1497, 1455, 1388, 1356, 1243, 1115, 1073, 1014, 978 and 797 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.72 (2H, d, *J* = 8.0 Hz), 7.45 (2H, t, *J* = 7.5 Hz), 7.38-7.31 (4H, m), 7.22 (2H, d, *J* = 7.0 Hz), 5.55 (2H, s), 2.34 (3H, s); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 144.9 (C), 134.8 (C), 131.5 (C), 129.1 (C), 128.9 (2 x CH), 128.6 (2 x CH), 128.2 (CH), 127.5 (CH), 127.1 (2 x CH), 127.0 (2 x CH), 51.9 (CH_2), 9.1 (CH_3); HRMS m/z 250.1346 (M + H^+), calcd for $C_{16}H_{15}N_3H$ 250.1344.

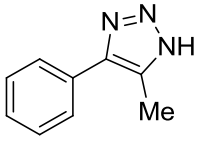
Ethyl 5-methyl-4-phenyl-1*H*-1,2,3-triazole-1-carboxylate (19ar): Prepared following the



19ar

procedure **2b** and purified by column chromatography using EtOAc/hexane and was isolated as a liquid; IR (neat): ν_{max} 2915, 2849, 1775, 1458, 1375, 1293, 1211, 1014, 959, 844 and 778 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.80 (2H, dd, *J* = 8.0, 1.6 Hz), 7.52-7.44 (3H, m), 4.65 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 2.60 (3H, s, ArC*H*$_3$), 1.54 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 149.9 (C), 147.6 (C), 146.5 (C), 129.4 (CH), 129.2 (C), 128.8 (2 x CH), 127.8 (2 x CH), 65.6 (CH_2, O*C*H$_2$CH$_3$), 14.3 (CH_3, OCH$_2$*C*H$_3$) , 12.2 (CH_3); HRMS m/z 254.0906 (M + Na), calcd for $C_{12}H_{13}N_3O_2Na$ 254.0905.

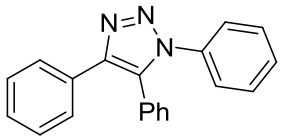
5-Methyl-4-phenyl-1*H*-1,2,3-triazole (19ar'):[44] Prepared following the procedure **2b** and



19ar'

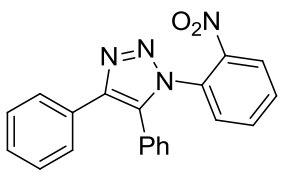
purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 89-92 °C; IR (neat): ν_{max} 3393, 2923, 1618, 1500, 1461, 1448, 1434, 1293, 1202, 1188, 1123, 1051, 1002, 970, 837, 791 and 775 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.72 (2H, dd, *J* = 8.8, 1.6 Hz), 7.47 (2H, tt, *J* = 7.2, 1.2 Hz), 7.39 (1H, tt, *J* = 7.2, 1.2 Hz), 2.55 (3H, s); ^{13}C NMR ($CDCl_3$ + 1 drop TFA, DEPT-135) δ 138.6 (C), 134.5 (C), 131.2 (C), 129.7 (2 x CH), 127.6 (3 x CH), 8.6 (CH_3); HRMS m/z 160.0872 (M + H^+), calcd for $C_9H_9N_3H$ 160.0875.

1,4,5-Triphenyl-1*H*-1,2,3-triazole (19bb):[45] Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 238-241 °C; IR (neat): ν_{max} 3060, 2922, 2852, 1682, 1594, 1496, 1444, 1365, 1264, 1220, 1126, 1072, 995, 916, 773 and 757 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.63 (2H, dd, *J* = 8.0, 2.0 Hz), 7.45-7.38 (6H, m), 7.36-7.32 (5H, m), 7.23 (2H, d, *J* = 6.8 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 144.8 (C), 136.5 (C), 133.7 (C), 130.7 (C),130.2 (2 x CH), 129.4 (CH), 129.1 (2 x CH), 129.0 (2 x CH), 128.9 (CH), 128.5 (2 x CH), 127.9 (CH), 127.7 (C), 127.3 (2 x CH), 125.2 (2 x CH); HRMS m/z 298.1344 ($M + H^+$), calcd for $C_{20}H_{15}N_3H$ 298.1344.



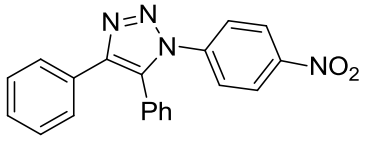
19bb

1-(2-Nitrophenyl)-4,5-diphenyl-1*H*-1,2,3-triazole (19bc): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a yellow solid. Mp 153-156 °C; IR (neat): 3051, 2922, 2850, 1605, 1527, 1443, 1352, 1299, 1262, 1121, 1074, 998, 926, 855, 774 and 747 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.02 (1H, d, *J* = 7.6 Hz), 7.70-7.60 (4H, m), 7.44 (1H, d, *J* = 7.6 Hz), 7.39 (1H, d, *J* = 6.4 Hz), 7.36-7.29 (5H, m), 7.24 (2H, d, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 145.2 (C), 144.3 (C), 134.9 (C), 133.7 (CH), 130.8 (CH), 130.2 (C), 129.8 (2 x CH), 129.69 (C), 129.67 (CH), 129.6 (CH), 129.1 (2 x CH), 128.4 (2 x CH), 128.0 (CH), 127.1 (2 x CH), 126.3 (C), 125.4 (CH); HRMS m/z 343.1198 ($M + H^+$), calcd for $C_{20}H_{14}N_4O_2H$ 343.1195.



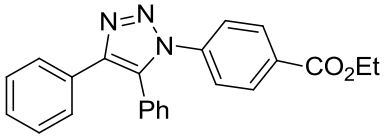
19bc

1-(4-Nitrophenyl)-4,5-diphenyl-1*H*-1,2,3-triazole (19bd):[36e] Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a yellow solid. Mp 250-252 °C; IR (neat): ν_{max} 3058, 2922, 2852, 1595, 1523, 1501, 1449, 1369, 1340, 1276, 1211, 1109, 1052, 1024, 993, 853 and 774 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.26 (2H, td, *J* = 9.2, 2.8 Hz), 7.63-7.59 (2H, m), 7.54 (2H, td, *J* = 9.2, 2.8 Hz), 7.51 (1H, td, *J* = 7.2, 1.2 Hz), 7.46 (2H, tt, *J* = 7.2, 1.2 Hz), 7.36-7.32 (3H, m), 7.28-7.25 (2H, m); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 147.2 (C), 145.5 (C), 141.2 (C), 133.5 (C), 130.1 (CH), 130.0 (2 x CH, C), 129.6 (2 x CH), 128.6 (2 x CH), 128.3 (CH), 127.3 (2 x CH), 127.0 (C), 125.1 (2 x CH), 124.7 (2 x CH); HRMS m/z 343.1194 ($M + H^+$), calcd for $C_{20}H_{14}N_4O_2H$ 343.1195.



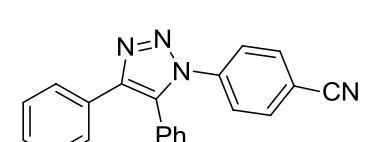
19bd

Ethyl 4-(4,5-diphenyl-1*H*-1,2,3-triazol-1-yl)benzoate (19be): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 155-158 °C; IR (KBr): ν_{max} 3052, 2992, 1710, 1606, 1512, 1441, 1370, 1277, 1167, 1112, 992, 866 and 773 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.05 (2H, d, *J* = 8.4 Hz), 7.60 (2H, dd, *J* = 7.6, 2.4 Hz), 7.45-7.36 (5H, m), 7.32-7.29 (3H, m), 7.22-7.21 (2H, m), 4.37 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 1.38 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.3 (C), 144.9 (C), 139.7 (C), 133.5 (C), 130.6 (C), 130.4 (2 x CH), 130.3 (C), 130.0 (2 x CH), 129.6 (CH), 129.1 (2 x CH), 128.4 (2 x CH), 127.9 (CH), 127.25 (C), 127.18 (2 x CH), 124.5 (2 x CH), 61.2 (CH_2, OCH_2CH_3), 14.1 (CH_3, OCH_2CH_3); HRMS m/z 370.1556 ($M + H^+$), calcd for $C_{23}H_{19}N_3O_2H$ 370.1556.



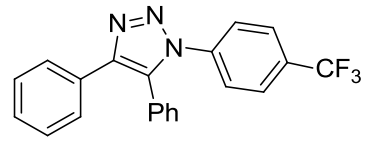
19be

4-(4,5-Diphenyl-1*H*-1,2,3-triazol-1-yl)benzonitrile (19bf): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a light yellow solid. Mp 206-209 °C; IR (KBr): ν_{max} 3063, 2225, 1611, 1512, 1441, 1408, 1364, 1271, 1205, 1003, 844, 773 and 696 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.68 (2H, td, *J* = 8.8, 2.0 Hz), 7.61-7.58 (2H, m), 7.52-7.42 (5H, m), 7.34-7.31 (3H, m), 7.24 (2H, td, *J* = 6.8, 1.6 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 145.3 (C), 139.7 (C), 133.4 (C), 133.1 (2 x CH), 130.1 (C), 130.0 (2 x CH), 129.9 (CH), 129.4 (2 x CH), 128.5 (2 x CH), 128.2 (CH), 127.2 (2 x CH), 127.0 (C), 125.1 (2 x CH), 117.6 (C, *C*N), 112.6 (C); HRMS m/z 323.1295 ($M + H^+$), calcd for $C_{21}H_{14}N_4H$ 323.1297.



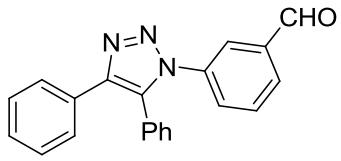
19bf

4,5-Diphenyl-1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazole (19bg): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 149-151 °C; IR (KBr): ν_{max} 3074, 1616, 1523, 1408, 1370, 1326, 1167, 1134, 992 and 844 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.65 (2H, d, *J* = 8.4 Hz), 7.61-7.59 (2H, m), 7.48-7.40 (5H, m), 7.33-7.31 (3H, m), 7.24 (2H, br d, *J* = 7.6 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 145.2 (C), 139.2 (C), 133.5 (C), 130.8 (C, q, *J* = 33.0 Hz), 130.3 (C), 130.1 (2 x CH), 129.8 (CH), 129.3 (2 x CH), 128.5 (2 x CH), 128.1 (CH), 127.3 (2 x CH), 127.2 (C), 126.3 (2 x CH, q, *J* = 3.0 Hz), 125.0 (2 x CH), 123.5 (C, q, *J* = 271.0 Hz, Ar-*C*F_3); HRMS m/z 366.1218 ($M + H^+$), calcd for $C_{21}H_{14}F_3N_3H$ 366.1218.



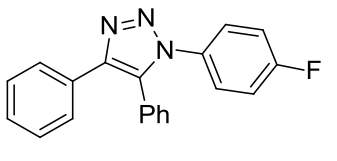
19bg

3-(4,5-Diphenyl-1*H*-1,2,3-triazol-1-yl)benzaldehyde (19bh): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. Mp 158-160 °C; IR (neat): ν_{max} 3074, 2921, 2856, 1699, 1590, 1488, 1451, 1392, 1219, 1206, 1153, 1071, 1013, 801 and 773 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.95 (1H, s), 7.92 (1H, ddd, *J* = 6.4, 2.8, 1.6 Hz), 7.87 (1H, m), 7.63-7.61 (2H, m), 7.58-7.55 (2H, m), 7.48-7.35 (3H, m), 7.35-7.30 (3H, m), 7.24 (2H, td, *J* = 6.8, 1.6 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 190.5 (CH, *C*HO), 145.0 (C), 137.3 (C), 137.1 (C), 133.6 (C), 130.34 (C), 130.26 (CH), 130.1 (2 x CH), 129.9 (CH), 129.7 (CH), 129.5 (CH), 129.2 (2 x CH), 128.5 (2 x CH), 128.0 (CH), 127.2 (2 x CH, C), 125.8 (CH); HRMS m/z 326.1293 ($M + H^+$), calcd for $C_{21}H_{15}N_3OH$ 326.1293.



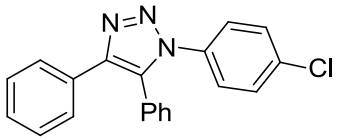
19bh

1-(4-Fluorophenyl)-4,5-diphenyl-1*H*-1,2,3-triazole (19bi): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 236-239 °C; IR (neat): ν_{max} 3058, 1507, 1441, 1375, 1227, 1151, 1129, 997, 844, 773, 729 and 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.61 (2H, dd, *J* = 8.0, 2.4 Hz), 7.45-7.36 (3H, m), 7.32-7.29 (5H, m), 7.21 (2H, dd, *J* = 8.0, 1.2 Hz), 7.07 (2H, t, *J* = 8.4 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 162.5 (C, d, *J* = 248.0 Hz, *C*-F), 144.8 (C), 133.8 (C), 132.6 (C, d, *J* = 4.0 Hz), 130.6 (C), 130.1 (2 x CH), 129.5 (CH), 129.1 (2 x CH), 128.5 (2 x CH), 128.0 (CH), 127.5 (C), 127.3 (2 x CH), 127.0 (2 x CH, d, *J* = 9.0 Hz), 116.2 (2 x CH, d, *J* = 24.0 Hz); HRMS m/z 316.1251 ($M + H^+$), calcd for $C_{20}H_{14}FN_3H$ 316.1250.



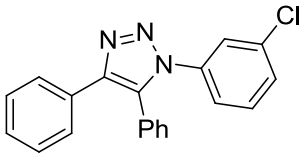
19bi

1-(4-Chlorophenyl)-4,5-diphenyl-1*H*-1,2,3-triazole (19bj): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 192-195 °C; IR (KBr): 3058, 2921, 1496, 1364, 1260, 1085, 997, 838, 778 and 745 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.60 (2H, dd, *J* = 7.6, 2.0 Hz), 7.46-7.38 (3H, m), 7.38-7.30 (5H, m), 7.26 (2H, d, *J* = 8.8 Hz), 7.21 (2H, dd, *J* = 8.0, 1.2 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 144.9 (C), 135.0 (C), 134.8 (C), 133.5 (C), 130.5 (C), 130.1 (2 x CH), 129.6 (CH), 129.3 (2 x CH), 129.2 (2 x CH), 128.5 (2 x CH), 128.0 (CH), 127.4 (C), 127.2 (2 x CH), 126.2 (2 x CH); HRMS m/z 332.0954 ($M + H^+$), calcd for $C_{20}H_{14}ClN_3H$ 332.0955.



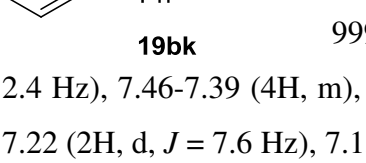
19bj

1-(3-Chlorophenyl)-4,5-diphenyl-1*H*-1,2,3-triazole (19bk): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 148-151 °C; IR (neat): 3079, 2922, 1592, 1484, 1442, 1365, 1257, 1095, 1068, 999, 918 and 792 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.61 (2H, dd, *J* = 8.0, 2.4 Hz), 7.46-7.39 (4H, m), 7.37-7.34 (1H, m), 7.32-7.29 (3H, m), 7.26 (1H, d, *J* = 8.4 Hz), 7.22 (2H, d, *J* = 7.6 Hz), 7.13 (1H, d, *J* = 8.0, 0.8 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 144.8 (C), 137.3 (C), 134.7 (C), 133.5 (C), 130.4 (C), 130.0 (2 x CH, C), 129.6 (CH), 129.2 (2 x CH), 129.0 (CH), 128.4 (2 x CH), 128.0 (CH), 127.20 (2 x CH), 127.15 (CH), 125.2 (CH), 123.0 (CH); HRMS m/z 332.0955 (M + H^+), calcd for $C_{20}H_{14}ClN_3H$ 332.0955.



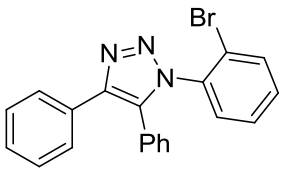
19bk

1-(4-Bromophenyl)-4,5-diphenyl-1*H*-1,2,3-triazole (19bl): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 197-200 °C; IR (neat): ν_{max} 3058, 1602, 1492, 1444, 1397, 1368, 1262, 1180, 1126, 1073, 1058, 995 and 813 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.60 (2H, dd, *J* = 7.6, 2.4 Hz), 7.51 (2H, br d, *J* = 8.8 Hz), 7.46-7.35 (3H, m), 7.34-7.30 (3H, m), 7.22-7.19 (4H, m); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 145.0 (C), 135.5 (C), 133.5 (C), 132.3 (2 x CH), 130.5 (C), 130.1 (2 x CH), 129.6 (CH), 129.2 (2 x CH), 128.5 (2 x CH), 128.0 (CH), 127.4 (C), 127.3 (2 x CH), 126.4 (2 x CH), 122.9 (C); HRMS m/z 376.0450 (M + H^+), calcd for $C_{20}H_{14}BrN_3H$ 376.0449.



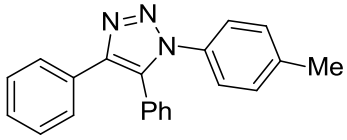
19bl

1-(2-Bromophenyl)-4,5-diphenyl-1*H*-1,2,3-triazole (19bm): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a light yellow solid. Mp 137-140 °C; IR (neat): 3064, 2922, 1578, 1504, 1488, 1444, 1368, 1257, 1126, 1074, 1028, 995, 980 and 734 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.68 (3H, m), 7.41 (2H, br d, *J* = 4.0 Hz), 7.38-7.30 (7H, m), 7.25 (2H, td, *J* = 8.0, 2.0 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 144.0 (C), 135.9 (C), 135.1 (C), 133.6 (CH), 131.5 (CH), 130.6 (C), 129.84 (2 x CH), 129.76 (CH), 129.4 (CH), 128.8 (2 x CH), 128.5 (2 x CH), 128.1 (CH), 128.0 (CH), 127.2 (2 x CH), 127.1 (C), 122.1 (C); HRMS m/z 376.0450 (M + H^+), calcd for $C_{20}H_{14}BrN_3H$ 376.0449.



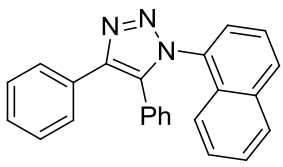
19bm

4,5-Diphenyl-1-(p-tolyl)-1*H*-1,2,3-triazole (19bn):[37a,46] Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. Mp 196-199 °C; IR (neat): ν_{max} 2926, 1515, 1442, 1368, 1261, 1126, 1063, 996, 917, 820 and 731 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.63 (2H, td, *J* = 8.5, 2.0 Hz), 7.42 (1H, tt, *J* = 7.0, 1.5 Hz), 7.37 (2H, tt, *J* = 7.0, 1.5 Hz), 7.34-7.30 (3H, m), 7.22 (2H, td, *J* = 7.0, 1.5 Hz), 7.20-7.15 (4H, m), 2.38 (3H, s, Ar-*C*H_3); ^{13}C NMR (500 MHz, $CDCl_3$) δ 144.6 (C), 139.0 (C), 134.0 (C), 133.6 (C), 130.8 (C), 130.1 (2 x CH), 129.6 (2 x CH), 129.2 (CH), 128.9 (2 x CH), 128.4 (2 x CH), 127.78 (CH), 127.75 (C), 127.3 (2 x CH), 124.9 (2 x CH), 21.1 (CH_3); HRMS m/z 312.1500 (M + H^+), calcd for $C_{21}H_{17}N_3H$ 312.1501.



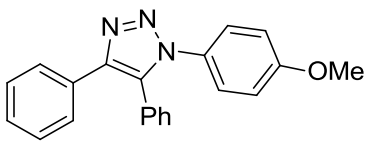
19bn

1-(Naphthalen-1-yl)-4,5-diphenyl-1*H*-1,2,3-triazole (19bo): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a light brown solid. Mp 193-196 °C; IR (neat): ν_{max} 3058, 1599, 1508, 1478, 1445, 1394, 1264, 1207, 1182, 1129, 1073, 1018, 981, 958 and 802 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.96 (1H, br d, *J* = 8.0 Hz), 7.92 (1H, br d, *J* = 7.5 Hz), 7.73 (2H, td, *J* = 6.5, 1.5 Hz), 7.57-7.54 (1H, m), 7.53-7.51 (2H, m), 7.46 (1H, t, *J* = 8.0 Hz), 7.40-7.32 (4H, m), 7.26 (1H, tt, *J* = 7.0, 1.5 Hz), 7.19 (2H, tt, *J* = 7.0, 1.5 Hz), 7.14 (2H, td, *J* = 8.0, 1.5 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 144.1 (C), 135.9 (C), 134.0 (C), 132.7 (C), 130.8 (C), 130.4 (CH), 130.1 (C), 129.6 (2 x CH), 129.2 (CH), 128.7 (2 x CH), 128.5 (2 x CH), 128.1 (CH), 127.9 (CH), 127.7 (CH), 127.4 (C), 127.3 (2 x CH), 126.9 (CH), 125.6 (CH), 124.7 (CH), 122.6 (CH); HRMS m/z 348.1500 (M + H^+), calcd for $C_{24}H_{17}N_3H$ 348.1501.



19bo

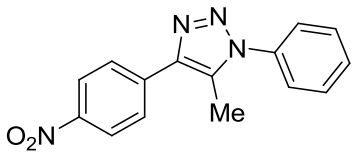
1-(4-Methoxyphenyl)-4,5-diphenyl-1*H*-1,2,3-triazole (19bp):[36e] Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 176-179 °C; IR (neat): ν_{max} 3058, 2992, 2833, 1611, 1518, 1447, 1304, 1255, 1184, 1068, 1041, 992, 827, 773 and 701 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.62 (2H, dd, *J* = 8.0, 1.6 Hz), 7.39-7.28 (6H, m), 7.26-7.21 (4H, m), 6.88 (2H, td, *J* = 8.8, 3.2 Hz), 3.82 (3H, s, O*C*H_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 159.8 (C), 144.5 (C), 133.7 (C), 130.8 (C), 130.1 (2 x CH), 129.5 (C), 129.2 (CH), 128.9 (2 x CH),



19bp

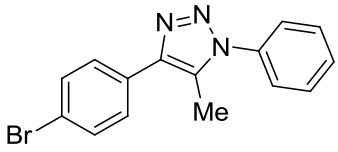
128.4 (2 x CH), 127.8 (CH), 127.7 (C), 127.2 (2 x CH), 126.5 (2 x CH), 114.2 (2 x CH), 55.4 (CH_3, O*C*H_3); HRMS m/z 328.1450 (M + H^+), calcd for $C_{21}H_{17}N_3OH$ 328.1450.

5-Methyl-4-(4-nitrophenyl)-1-phenyl-1*H*-1,2,3-triazole (19cb): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a yellow solid. Mp 222-225 °C; IR (neat): ν_{max} 3112, 1596, 1500, 1488, 1406, 1332, 1269, 1106, 1067, 976, 854, 762 and 713 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 8.36 (2H, d, *J* = 9.0 Hz), 8.02 (2H, d, *J* = 9.0 Hz), 7.64-7.58 (3H, m), 7.53 (2H, dd, *J* = 8.0, 1.5 Hz), 2.58 (3H, s); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 147.0 (C), 142.6 (C), 137.9 (C), 135.8 (C), 131.2 (C), 129.9 (CH), 129.7 (2 x CH), 127.3 (2 x CH), 125.3 (2 x CH), 124.1 (2 x CH), 10.5 (CH_3); HRMS m/z 281.1038 (M + H^+), calcd for $C_{15}H_{12}N_4O_2H$ 281.1039.



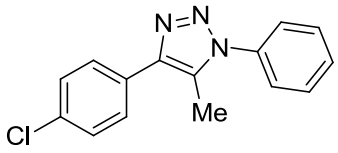
19cb

4-(4-Bromophenyl)-5-methyl-1-phenyl-1*H*-1,2,3-triazole (19db):[39] Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 184-186 °C; IR (neat): ν_{max} 3056, 1598, 1503, 1486, 1396, 1252, 1219, 1100, 1069, 1004, 972, 832 and 824 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.66 (2H, td, *J* = 8.5, 2.0 Hz), 7.61-7.56 (4H, m), 7.53 (1H, tt, *J* = 7.5, 1.5 Hz), 7.49 (2H, td, *J* = 7.0, 1.5 Hz), 2.46 (3H, s); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 143.7 (C), 136.0 (C), 131.8 (2 x CH), 130.3 (C), 129.8 (C), 129.5 (3 x CH), 128.5 (2 x CH), 125.1 (2 x CH), 121.7 (C), 10.2 (CH_3); HRMS m/z 314.0293 (M + H^+), calcd for $C_{15}H_{12}BrN_3H$ 314.0293.



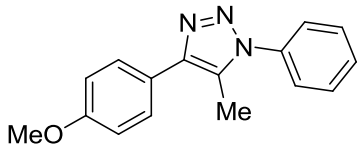
19db

4-(4-Chlorophenyl)-5-methyl-1-phenyl-1*H*-1,2,3-triazole (19eb):[39] Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 175-178 °C; IR (neat): ν_{max} 3059, 2923, 1599, 1489, 1461, 1400, 1363, 1252, 1088, 1070, 1006, 973, 832, 759 and 746 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.72 (2H, br d, *J* = 8.5 Hz), 7.56 (2H, t, *J* = 7.5 Hz), 7.52 (1H, t, *J* = 7.5 Hz), 7.49 (2H, d, *J* = 8.0 Hz), 7.44 (2H, d, *J* = 8.5 Hz), 2.46 (3H, s); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 143.6 (C), 136.1 (C), 133.5 (C), 129.8 (C), 129.7 (C), 129.5 (3 x CH), 128.8 (2 x CH), 128.2 (2 x CH), 125.1 (2 x CH), 10.2 (CH_3); HRMS m/z 270.0798 (M + H^+), calcd for $C_{15}H_{12}ClN_3H$ 270.0798.



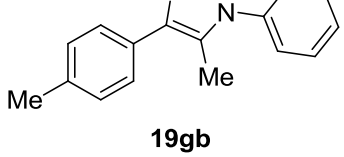
19eb

4-(4-Methoxyphenyl)-5-methyl-1-phenyl-1*H*-1,2,3-triazole (19fb):[39] Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a yellow solid. Mp 117-120 °C; IR (neat): ν_{max} 3000, 2948, 2832, 1614, 1561, 1504, 1465, 1363, 1244, 1176, 1033, 834, and 772 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.71 (2H, td, *J* = 9.0, 2.5 Hz), 7.58-7.55 (2H, m), 7.54-7.50 (3H, m), 7.02 (2H, td, *J* = 9.0, 2.5 Hz), 3.86 (3H, s, Ar-OC*H*$_3$), 2.46 (3H, s, Ar-C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 159.2 (C), 144.7 (C), 136.3 (C), 129.4 (2 x CH), 129.3 (CH), 128.9 (C), 128.4 (2 x CH), 125.1 (2 x CH), 123.9 (C), 114.1 (2 x CH), 55.2 (CH_3, O*C*H$_3$), 10.2 (CH_3); HRMS m/z 266.1292 (M + H^+), calcd for $C_{16}H_{15}N_3OH$ 266.1293.



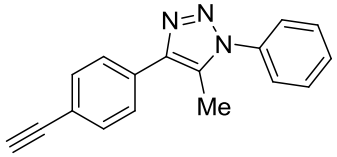
19fb

5-Methyl-1-phenyl-4-(p-tolyl)-1*H*-1,2,3-triazole (19gb):[39] Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 142-144 °C; IR (neat): ν_{max} 2956, 2923, 2853, 1716, 1596, 1508, 1463, 1366, 1246, 1109, 1069, 1008, 976, 905, 820 and 760 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.69 (2H, br d, *J* = 8.0 Hz), 7.56 (2H, t, *J* = 7.5 Hz), 7.52-7.49 (3H, m), 7.30 (2H, d, *J* = 8.0 Hz), 2.46 (3H, s, Ar-C*H*$_3$), 2.41 (3H, s, Ar-C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 144.8 (C), 137.5 (C), 136.3 (C), 129.4 (2 x CH), 129.3 (3 x CH, C), 128.4 (C), 127.0 (2 x CH), 125.1 (2 x CH), 21.2 (CH_3, Ar-*C*H$_3$), 10.2 (CH_3); HRMS m/z 250.1344 (M + H^+), calcd for $C_{16}H_{15}N_3H$ 250.1344.



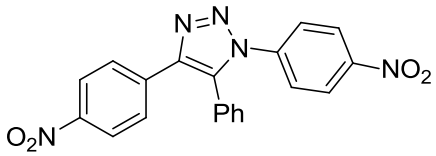
19gb

4-(4-Ethynylphenyl)-5-methyl-1-phenyl-1*H*-1,2,3-triazole (19hb): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. Mp 130-133 °C; IR (neat): ν_{max} 3280, 3056, 2923, 2852, 1598, 1503, 1464, 1405, 1364, 1261, 1105, 1072, 1008, 975, 917, 839, 758 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.78 (2H, br d, *J* = 8.0 Hz), 7.61 (2H, br d, *J* = 8.0 Hz), 7.59-7.53 (3H, m), 7.51 (2H, br d, *J* = 8.0 Hz), 3.16 (1H, s, Ar-C≡C*H*), 2.50 (3H, s); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 144.0 (C), 136.2 (C), 132.5 (2 x CH), 131.9 (C), 130.0 (C), 129.6 (CH), 129.5 (2 x CH), 126.8 (2 x CH), 125.3 (2 x CH), 121.4 (C), 83.4 (C, Ar-*C*≡CH), 77.9 (CH, Ar-C≡*C*H), 10.3 (CH_3); HRMS m/z 260.1187 (M + H^+), calcd for $C_{17}H_{13}N_3H$ 260.1188.



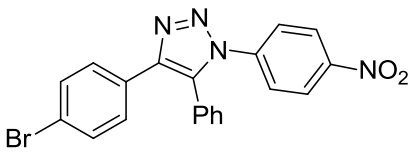
19hb

1,4-bis(4-Nitrophenyl)-5-phenyl-1*H*-1,2,3-triazole (19id): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and isolated as a yellow solid. Mp 251-254 °C; IR (neat): ν_{max} 3117, 3091, 1593, 1519, 1498, 1341, 1281, 1108, 1042, 993, 854, 776 and 750 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 8.28 (2H, td, *J* = 9.0, 2.0 Hz), 8.19 (2H, td, *J* = 9.0, 2.0 Hz), 7.79 (2H, td, *J* = 9.0, 2.0 Hz), 7.59 (1H, tt, *J* = 7.5, 2.0 Hz), 7.55 (2H, td, *J* = 9.5, 2.5 Hz), 7.52 (2H, tt, *J* = 7.5, 1.5 Hz), 7.28 (2H, td, *J* = 7.0, 1.5 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 147.5 (C), 147.3 (C), 143.3 (C), 140.8 (C), 136.5 (C), 135.1 (C), 130.8 (CH), 130.0 (2 x CH), 129.8 (2 x CH), 127.6 (2 x CH), 126.2 (C), 125.2 (2 x CH), 124.8 (2 x CH), 123.9 (2 x CH); HRMS m/z 410.0864 (M + Na), calcd for $C_{20}H_{13}N_5O_4Na$ 410.0865.



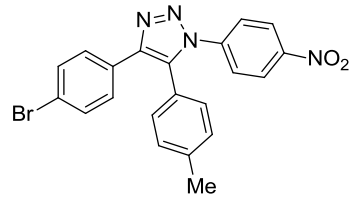
19id

4-(4-Bromophenyl)-1-(4-nitrophenyl)-5-phenyl-1*H*-1,2,3-triazole (19jd): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 217-220 °C; IR (neat): ν_{max} 3085, 1593, 1523, 1497, 1340, 1286, 1263, 1212, 1123, 1111, 1074, 1010, 994, 855, 836 and 745 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.24 (2H, d, *J* = 8.0 Hz), 7.52 (2H, d, *J* = 8.0 Hz), 7.51-7.43 (7H, m), 7.25 (2H, d, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 147.2 (C), 144.4 (C), 141.0 (C), 133.6 (C), 131.7 (2 x CH), 130.2 (CH), 129.9 (2 x CH), 129.7 (2 x CH), 129.0 (C), 128.7 (2 x CH), 126.6 (C), 125.0 (2 x CH), 124.6 (2 x CH), 122.4 (C); HRMS m/z 421.0303 (M + H^+), calcd for $C_{20}H_{13}BrN_4O_2H$ 421.0300.



19jd

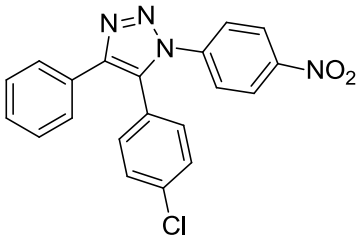
4-(4-Bromophenyl)-1-(4-nitrophenyl)-5-(p-tolyl)-1*H*-1,2,3-triazole (19kd): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a light yellow solid. Mp 250-253 °C; IR (neat): ν_{max} 3125, 3055, 2920, 1593, 1519, 1497, 1481, 1340, 1314, 1293, 1271, 1215, 1073, 1049, 1007, 991, 851, 826 and 744 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.25 (2H, td, *J* = 9.2, 2.0), 7.53 (2H, td, *J* = 8.8, 2.0 Hz), 7.50-7.44 (4H, m), 7.26 (2H, d, *J* = 8.0 Hz), 7.12 (2H, d, *J* = 8.0 Hz), 2.44 (3H, s, Ar-C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 147.3 (C), 144.4 (C), 141.2 (C), 140.6 (C), 133.9 (C),



19kd

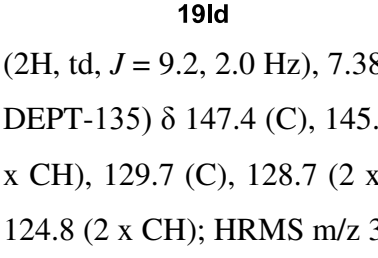
131.8 (2 x CH), 130.5 (2 x CH), 129.8 (2 x CH), 129.2 (C), 128.7 (2 x CH), 125.1 (2 x CH), 124.7 (2 x CH), 123.6 (C), 122.4 (C), 21.5 (CH_3); HRMS m/z 435.0456 ($M + H^+$), calcd for $C_{21}H_{15}BrN_4O_2H$ 435.0457.

5-(4-Chlorophenyl)-1-(4-nitrophenyl)-4-phenyl-1*H*-1,2,3-triazole (19ld): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 206-209 °C; IR (neat): ν_{max} 3083, 3067, 1593, 1524, 1500, 1445, 1344, 1278, 1210, 1126, 1093, 1053, 993, 853 and 827 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.29 (2H, td, *J* = 9.2, 2.0 Hz), 7.59-7.56 (2H, m), 7.53 (2H, td, *J* = 9.2, 2.0 Hz), 7.44 (2H, td, *J* = 9.2, 2.0 Hz), 7.38-7.34 (3H, m), 7.20 (2H, td, *J* = 8.8, 2.0 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 147.4 (C), 145.7 (C), 141.0 (C), 136.4 (C), 132.4 (C), 131.3 (2 x CH), 130.0 (2 x CH), 129.7 (C), 128.7 (2 x CH), 128.5 (CH), 127.3 (2 x CH), 125.4 (C), 125.2 (2 x CH), 124.8 (2 x CH); HRMS m/z 377.0805 ($M + H^+$), calcd for $C_{20}H_{13}ClN_4O_2H$ 377.0805.



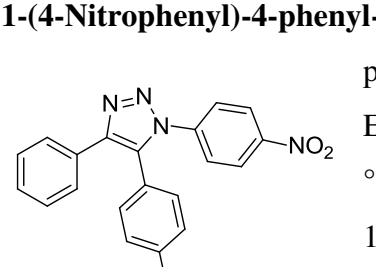
19ld

1-(4-Nitrophenyl)-4-phenyl-5-(p-tolyl)-1*H*-1,2,3-triazole (19md): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a yellow solid. Mp 197-200 °C; IR (neat): ν_{max} 3068, 2920, 2853, 1594, 1522, 1499, 1446, 1368, 1338, 1278, 1213, 1109, 1053, 993, 853, 819 and 780 cm^{-1}; ^1H NMR ($CDCl_3$, DEPT-135) δ 8.24 (2H, d, *J* = 9.2 Hz), 7.62-7.60 (2H, m), 7.53 (2H, d, *J* = 8.8 Hz), 7.35-7.32 (3H, m), 7.24 (2H, d, *J* = 7.6 Hz), 7.12 (2H, d, *J* = 8.0 Hz), 2.43 (3H, s, Ar-C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 147.2 (C), 145.3 (C), 141.3 (C), 140.3 (C), 133.6 (C), 130.3 (2 x CH), 130.2 (C), 129.8 (2 x CH), 128.5 (2 x CH), 128.2 (CH), 127.2 (2 x CH), 125.1 (2 x CH), 124.6 (2 x CH), 123.8 (C), 21.4 (CH_3); HRMS m/z 357.1351 ($M + H^+$), calcd for $C_{21}H_{16}N_4O_2H$ 357.1352.



19md

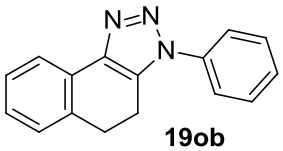
5-(4-Methoxyphenyl)-1-(4-nitrophenyl)-4-phenyl-1*H*-1,2,3-triazole (19nd): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a yellow solid. Mp 213-216 °C; IR (neat): ν_{max} 3078, 2923, 2852,



19nd

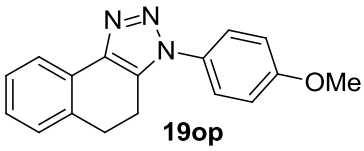
1594, 1523, 1500, 1370, 1341, 1248, 1178, 1110, 1055, 1028, 992, 854, 835 and 775 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.25 (2H, d, *J* = 8.8 Hz), 7.61 (2H, dd, *J* = 7.6, 1.6 Hz), 7.54 (2H, d, *J* = 8.8 Hz), 7.33-7.32 (3H, m), 7.15 (2H, d, *J* = 8.8 Hz), 6.95 (2H, d, *J* = 8.4 Hz), 3.86 (3H, s, Ar-OC*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 160.7 (C), 147.2 (C), 145.2 (C), 141.4 (C), 133.4 (C), 131.3 (2 x CH), 130.2 (C), 128.6 (2 x CH), 128.2 (CH), 127.2 (2 x CH), 125.1 (2 x CH), 124.6 (2 x CH), 118.6 (C), 115.0 (2 x CH), 55.3 (CH_3, O*C*H_3); HRMS m/z 373.1300 (M + H^+), calcd for $C_{21}H_{16}N_4O_3H$ 373.1301.

3-Phenyl-4,5-dihydro-3*H*-naphtho[1,2-d][1,2,3]triazole (19ob):[39] Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a brown solid. Mp 145-150 °C; IR (neat): ν_{max} 3050, 2949, 2889, 1723, 1596, 1511, 1447, 1384, 1285, 1247, 1231, 1215, 1080, 1056, 994, 919, 765 and 724 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 8.04 (1H, d, *J* = 7.5 Hz), 7.62-7.57 (4H, m), 7.53-7.50 (1H, m), 7.37 (1H, dt, *J* = 7.0, 1.5 Hz), 7.29-7.24 (2H, m), 3.15-3.08 (4H, m); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 144.0 (C), 136.4 (C), 133.5 (C), 132.3 (C), 129.6 (2 x CH), 128.9 (CH), 128.5 (C), 128.1 (CH), 127.6 (CH), 127.3 (CH), 123.2 (2 x CH), 122.2 (CH), 28.8 (CH_2), 20.2 (CH_2); HRMS m/z 248.1184 (M + H^+), calcd for $C_{16}H_{13}N_3H$ 248.1188.



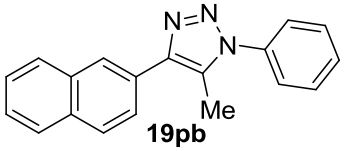
19ob

3-(4-Methoxyphenyl)-4,5-dihydro-3*H*-naphtho[1,2-d][1,2,3]triazole (19op): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a brown liquid. IR (neat): ν_{max} 2922, 2852, 1740, 1600, 1510, 1463, 1378, 1363, 1240, 1178, 1033, 909 and 824 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.02 (1H, dd, *J* = 7.6 Hz), 7.49 (2H, d, *J* = 8.8 Hz), 7.34 (1H, dt, *J* = 6.8, 1.6 Hz), 7.27-7.20 (2H, m), 7.06 (2H, d, *J* = 8.8 Hz), 3.89 (3H, s, Ar-OC*H*$_3$), 3.15-3.00 (4H, m); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 160.0 (C), 143.8 (C), 133.5 (C), 132.4 (C), 129.5 (C), 128.6 (C), 128.1 (CH), 127.5 (CH), 127.3 (CH), 124.8 (2 x CH), 122.2 (CH), 114.7 (2 x CH), 55.6 (CH_3, O*C*H_3), 28.8 (CH_2), 20.0 (CH_2); LCMS m/z 278.15 (M + H^+), calcd for $C_{17}H_{15}N_3O$ 277.12; HRMS m/z 278.1293 (M + H^+), calcd for $C_{17}H_{15}N_3OH$ 278.1293.



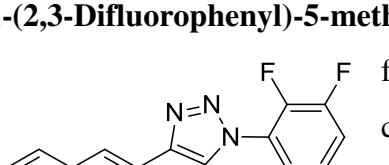
19op

5-Methyl-4-(naphthalen-2-yl)-1-phenyl-1*H*-1,2,3-triazole (19pb): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 158-161 °C; IR (neat): ν_{max} 3044, 2921, 1598, 1504, 1451, 1421, 1368, 1260, 1128, 1099, 1068, 968, 862, 823 and 746 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.23 (1H, s), 8.01 (1H, dd, *J* = 8.4, 1.6 Hz), 7.96 (1H, d, *J* = 8.4 Hz), 7.94-7.87 (2H, m), 7.58-7.49 (7H, m), 2.54 (3H, d, *J* = 4.0 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 144.6 (C), 136.2 (C), 133.3 (C), 132.7 (C), 129.9 (C), 129.42 (2 x CH), 129.38 (CH), 128.8 (C), 128.3 (CH), 128.1 (CH), 127.6 (CH), 126.2 (CH), 126.1 (CH), 125.8 (CH), 125.1 (3 x CH), 10.3 (CH_3); HRMS m/z 286.1344 ($M + H^+$), calcd for $C_{19}H_{15}N_3H$ 286.1344.



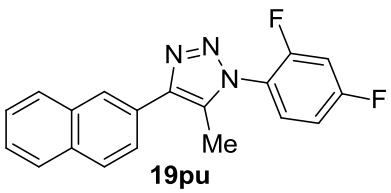
19pb

1-(2,3-Difluorophenyl)-5-methyl-4-(naphthalen-2-yl)-1*H*-1,2,3-triazole (19pt): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a light yellow solid. Mp 130-132 °C; IR (neat): ν_{max} 3052, 1624, 1602, 1513, 1483, 1378, 1267, 1241, 1195, 1131, 1108, 1059, 980, 897, 863, 819, 778 and 747 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.24 (1H, s), 8.01 (1H, dd, *J* = 8.4, 1.6 Hz), 7.98 (1H, d, *J* = 8.4 Hz), 7.95-7.88 (2H, m), 7.56-7.50 (2H, m), 7.45-7.29 (3H, m), 2.53 (3H, d, *J* = 2.0 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 150.9 (C, dd, *J* = 250.0, 11.0 Hz), 145.2 (C, dd, *J* = 254.0, 14.0 Hz), 144.4 (C), 133.3 (C), 132.8 (C), 131.5 (C), 128.45 (CH), 128.38 (C), 128.1 (CH), 127.7 (CH), 126.4 (CH), 126.2 (CH), 125.9 (CH), 125.8 (C, d, *J* = 9.0 Hz), 125.0 (CH), 124.7 (CH, dd, *J* = 7.0, 5.0 Hz), 123.6 (CH, d, *J* = 4.0 Hz), 119.1 (CH, d, *J* = 17.0 Hz), 9.49 (CH_3, d, *J* = 4.0 Hz); HRMS m/z 322.1155 ($M + H^+$), calcd for $C_{19}H_{13}F_2N_3H$ 322.1156.



19pt

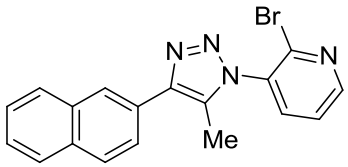
1-(2,4-Difluorophenyl)-5-methyl-4-(naphthalen-2-yl)-1*H*-1,2,3-triazole (19pu): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a light yellow solid. Mp 171-173 °C; IR (neat): ν_{max} 3059, 2922, 2852, 1743, 1614, 1602, 1518, 1435, 1281, 1268, 1143, 1101, 1009, 958, 941, 857, 833, 770 and 755 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.23 (1H, s), 8.01 (1H, dd, *J* = 8.8, 1.6 Hz), 7.96 (1H, d, *J* = 8.4 Hz), 7.94-7.88 (2H, m), 7.60-7.50 (3H, m), 7.10 (2H, br t, *J* = 8.0 Hz), 2.48 (3H, d, *J* = 1.6 Hz); ^{13}C NMR (500 MHz, $CDCl_3$,



19pu

DEPT-135) δ 163.5 (C, dd, *J* = 252.5, 11.2 Hz), 156.6 (C, dd, *J* = 255.0, 12.5 Hz), 144.2 (C), 133.3 (C), 132.7 (C), 131.6 (C), 129.8 (CH, d, *J* = 11.2 Hz), 128.5 (C), 128.4 (CH), 128.1 (CH), 127.6 (CH), 126.3 (CH), 126.2 (CH), 125.8 (CH), 125.0 (CH), 120.5 (C, dd, *J* = 12.5, 3.8 Hz), 112.5 (CH, dd, *J* = 22.5, 3.8 Hz), 105.3 (CH, dd, *J* = 26.2, 22.5 Hz), 9.43 (CH_3, d, *J* = 2.5 Hz); HRMS m/z 322.1156 (M + H^+), calcd for $C_{19}H_{13}F_2N_3H$ 322.1156.

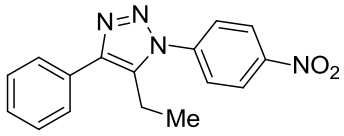
2-Bromo-3-(5-methyl-4-(naphthalen-2-yl)-1*H*-1,2,3-triazol-1-yl)pyridine (19pv):



19pv

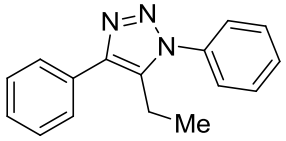
Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a yellow liquid. Mp 126-128 °C; IR (neat): ν_{max} 3052, 2918, 2849, 1604, 1561, 1481, 1406, 1387, 1268, 1220, 1094, 1052, 998, 974, 942, 860, 808 and 771 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.62 (1H, d, *J* = 3.2 Hz), 8.25 (1H, s), 8.02 (1H, d, *J* = 8.4 Hz), 7.98 (1H, d, *J* = 8.4 Hz), 7.92 (2H, dt, *J* = 9.2, 3.2 Hz), 7.85 (1H, d, *J* = 7.6 Hz), 7.56-7.51 (3H, m), 2.50 (3H, s); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 151.6 (CH), 144.4 (C), 141.3 (C), 137.6 (CH), 133.34 (C), 133.30 (C), 132.8 (C), 131.6 (C), 128.5 (CH), 128.3 (C), 128.1 (CH), 127.7 (CH), 126.4 (CH), 126.3 (CH), 125.9 (CH), 124.9 (CH), 123.5 (CH), 9.9 (CH_3); HRMS m/z 365.0401 (M + H^+), calcd for $C_{18}H_{13}BrN_4H$ 365.0402.

5-Ethyl-1-(4-nitrophenyl)-4-phenyl-1*H*-1,2,3-triazole (19rd): Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a yellow solid. Mp 143-145 °C; IR (neat): ν_{max} 3084, 2986, 2941, 1597, 1518, 1501, 1372, 1346, 1263, 1108, 989, 863, 854 and 779 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.45 (2H, d, *J* = 8.0 Hz), 7.76 (2H, d, *J* = 8.8 Hz), 7.74 (2H, d, *J* = 6.8 Hz), 7.49 (2H, t, *J* = 7.6 Hz), 7.41 (1H, t, *J* = 7.2 Hz), 2.99 (2H, q, *J* = 7.6 Hz, Ar-C$H_2$$CH_3$), 1.11 (3H, t, *J* = 7.6 Hz, Ar-CH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 148.0 (C), 145.1 (C), 141.4 (C), 135.4 (C), 130.8 (C), 128.8 (2 x CH), 128.2 (CH), 127.4 (2 x CH), 126.0 (2 x CH), 125.0 (2 x CH), 16.8 (CH_2), 13.2 (CH_3); LCMS m/z 293.20 (M - H^+), calcd for $C_{16}H_{14}N_4O_2$ 294.11; HRMS m/z 295.1195 (M + H^+), calcd for $C_{16}H_{14}N_4O_2H$ 295.1195.



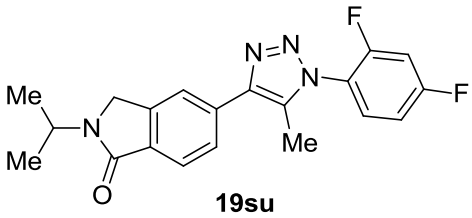
19rd

5-Ethyl-1,4-diphenyl-1*H*-1,2,3-triazole (19rb):[45] Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a white solid. Mp 132-135 °C; IR (neat): ν_{max} 2971, 1594, 1498, 1461, 1369, 1260, 1219, 1118, 1075, 988, 928 and 771 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.78 (2H, d, *J* = 7.6 Hz), 7.60-7.54 (3H, m), 7.51-7.46 (4H, m), 7.39 (1H, t, *J* = 7.6 Hz), 2.91 (2H, q, *J* = 7.6 Hz, Ar-C*H*$_2$CH$_3$), 1.08 (3H, t, *J* = 7.6 Hz, Ar-CH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 144.2 (C), 136.5 (C), 135.6 (C), 131.5 (C), 129.7 (CH), 129.5 (2 x CH), 128.7 (2 x CH), 127.8 (CH), 127.2 (2 x CH), 125.8 (2 x CH), 16.7 (CH_2), 13.2 (CH_3); LCMS m/z 250.00 (M + H), calcd for $C_{16}H_{15}N_3$ 249.13; HRMS m/z 250.1343 (M + H^+), calcd for $C_{16}H_{15}N_3H$ 250.1344.



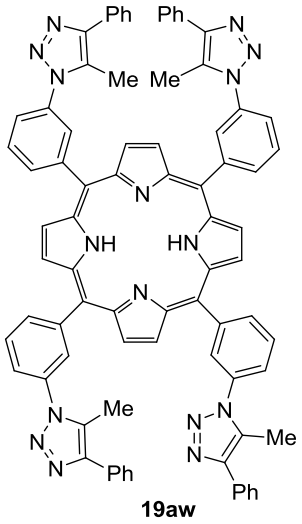
19rb

5-(1-(2,4-Difluorophenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl)-2-isopropylisoindolin-1-one (19su):[14i] Prepared following the procedure **2a** and purified by column chromatography using EtOAc/hexane and was isolated as a light yellow solid. Mp 144-146 °C; IR (neat): ν_{max} 2973, 1671, 1622, 1519, 1456, 1409, 1366, 1278, 1267, 1235, 1220, 1146, 1107, 963, 910, 881, 851 and 726 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.98 (1H, s), 7.93 (1H, d, *J* = 8.0 Hz), 7.80 (1H, dd, *J* = 7.6, 1.2 Hz), 7.60-7.54 (1H, m), 7.15-7.10 (2H, m), 4.70 (1H, sep, *J* = 6.8 Hz), 4.41 (2H, s), 2.44 (3H, d, *J* = 1.6 Hz), 1.32 (6H, d, *J* = 6.8 Hz, 2 x CH_3); ^{13}C NMR (400 MHz, $CDCl_3$) δ 167.3 (C), 163.6 (C, dd, *J* = 252.0, 11.0 Hz), 156.5 (C, dd, *J* = 254.0, 12.0 Hz), 143.5 (C), 141.8 (C), 133.8 (C), 132.6 (C), 131.9 (C), 129.8 (CH, d, *J* = 10.0 Hz), 126.4 (CH), 123.6 (CH), 121.3 (CH), 120.3 (C, dd, *J* = 13.0, 4.0 Hz), 112.5 (CH, dd, *J* = 23.0, 4.0 Hz), 105.4 (CH, dd, *J* = 26.0, 23.0 Hz), 45.0 (CH_2), 42.6 (CH), 20.7 (2 x CH_3), 9.4 (CH_3, d, *J* = 3.0 Hz); LCMS m/z 369.45 (M + H^+), calcd for $C_{20}H_{18}F_2N_4O$ 368.33; HRMS m/z 369.1528 (M + H^+), calcd for $C_{20}H_{18}F_2N_4OH$ 369.1527.



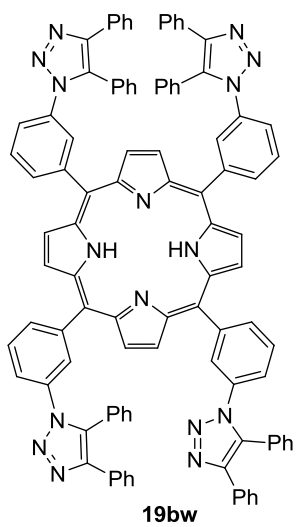
19su

5,10,15,20-tetrakis[3-(5-Methyl-4-phenyl-1*H*-1,2,3-triazol-1-yl)phenyl]porphyrin



19aw

(19aw): Prepared by following the procedure **2a** and purified by column chromatography using EtOAc/hexane and isolated as solid. Mp >300 °C; IR (Neat): ν_{max} 2954, 1602, 1582, 1491, 1440, 1234, 1112, 972, 894 and 747 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, at 50 °C) δ 9.00 (4H, br s), 8.88-8.70 (6H, br m), 8.43 (4H, br t, *J* = 6.4 Hz), 8.31-8.15 (3H, m), 8.04-8.02 (4H, m), 7.95-7.86 (3H, m), 7.80 (6H, br d, *J* = 6.4 Hz), 7.59-7.44 (10H, m), 7.40-7.38 (4H, m), 2.80 (6H, br s), 2.73 (6H, br s), -2.70 (2H, br s); ^{13}C NMR ($CDCl_3$, DEPT-135, at 50 °C) δ 145.3, 143.4, 140.9, 135.4, 135.3, 131.4, 130.9, 129.8, 128.9, 128.8, 128.1, 127.9, 127.5, 127.4, 125.0, 118.8, 10.6; HRMS m/z 1243.5104 (M + H), calcd for $C_{80}H_{58}N_{16}H$ 1243.5109.



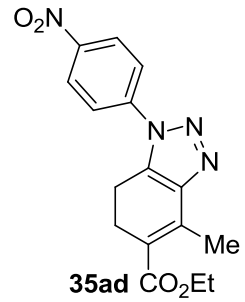
19bw

5,10,15,20-tetrakis[3-(4,5-Diphenyl-1*H*-1,2,3-triazol-1-yl)phenyl]porphyrin (19bw): Prepared by following the procedure **2a** and purified by column chromatography using EtOAc/hexane and isolated as solid. Mp >300 °C; IR (Neat): ν_{max} 2924, 1716, 1683, 1602, 1506, 1366, 1262, 1018, 981 and 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, at 50 °C) δ 8.53 (8H, br s), 8.21 (4H, d, *J* = 7.6 Hz), 8.09 (4H, br s), 7.97 (4H, br d, *J* = 8.0 Hz), 7.87 (4H, br t, *J* = 7.6 Hz), 7.67 (9H, dd, *J* = 8.4, 2.0 Hz), 7.48 (11H, d, *J* = 6.8 Hz), 7.44-7.40 (9H, m), 7.35-7.29 (11H, m), -3.00 (2H, br s); ^{13}C NMR ($CDCl_3$, DEPT-135, at 50 °C) δ 145.1, 143.0, 135.5, 135.1, 134.3, 131.2, 130.8, 130.5, 129.4, 128.5, 128.0, 127.7, 127.4, 125.3, 118.4; HRMS m/z 1491.5738 (M + H), calcd for $C_{100}H_{66}N_{16}H$ 1491.5735.

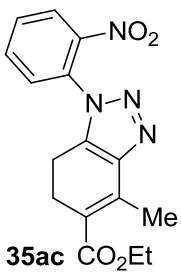
3a: General procedure for the pyrrolidine-catalyzed domino [3+2]-cycloaddition reactions: In an ordinary glass vial equipped with a magnetic stirring bar, to 0.5 mmol of enone **14** and 0.75 mmol of arylazide **2** dissolved in DMSO (1.0 mL) solvent, the catalyst pyrrolidine **15d** (0.05 mmol, 10 mol%) was added and the reaction mixture was stirred at 25 °C for the time indicated in Tables 9-11. The crude reaction mixture was worked up with

aqueous NH_4Cl solution and the aqueous layer was extracted with dichloromethane (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure domino products **35** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

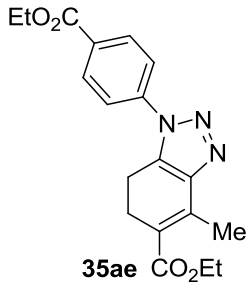
Ethyl 4-methyl-1-(4-nitrophenyl)-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35ad): Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. Mp 140 °C; IR (neat): ν_{max} 2923, 1704, 1592, 1516, 1503, 1282, 1211, 1032, 847, 748 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.44 (2H, d, *J* = 8.8 Hz), 7.81 (2H, d, *J* = 8.8 Hz), 4.28 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 3.06 (2H, t, *J* = 8.4 Hz), 2.90 (2H, t, *J* = 8.0 Hz), 2.62 (3H, s, olefinic-CH_3), 1.36 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.6 (C, O-*C*=O), 147.4 (C), 146.8 (C), 140.8 (C), 138.0 (C), 133.4 (C), 125.3 (2 x CH), 123.0 (2 x CH), 121.6 (C), 60.6 (CH_2, OCH_2CH_3), 25.4 (CH_2), 20.0 (CH_2), 15.3 (CH_3), 14.3 (CH_3, OCH_2CH_3); HRMS m/z 329.1250 ($M + H^+$), calcd for $C_{16}H_{16}N_4O_4H$ 329.1250; Anal. calcd for $C_{16}H_{16}N_4O_4$ (328.11): C, 58.53; H, 4.91; N, 17.06. Found: C, 58.46; H, 4.85, N, 17.15%.



Ethyl 4-methyl-1-(2-nitrophenyl)-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35ac): Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a brown colored liquid. IR (neat): ν_{max} 2981, 1697, 1609, 1534, 1514, 1444, 1350, 1282, 1242, 1200, 1049, 853, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.14 (1H, d, *J* = 8.0 Hz), 7.83 (1H, t, *J* = 8.0 Hz), 7.74 (1H, t, *J* = 8.0 Hz),7.56 (1H, d, *J* = 8.0 Hz), 4.25 (2H, q, *J* = 7.2 Hz), 2.84 (2H, t, *J* = 8.0 Hz), 2.74 (2H, t, *J* = 8.0 Hz), 2.60 (3H, s, olefinic-CH_3), 1.33 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.8 (C, O-C=O), 145.4 (C), 144.8 (C), 138.1 (C), 136.0 (C), 134.1 (CH), 131.2 (CH), 129.0 (C), 128.8 (CH), 125.7 (CH), 121.3 (C), 60.4 (CH_2, OCH_2CH_3), 25.1 (CH_2), 18.6 (CH_2), 15.2 (CH_3), 14.2 (CH_3, OCH_2CH_3); HRMS m/z 329.1250 ($M + H^+$), calcd for $C_{16}H_{16}N_4O_4H$ 329.1250.

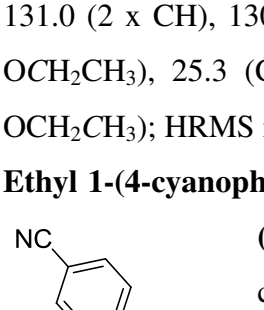


Ethyl 1-(4-(ethoxycarbonyl)phenyl)-4-methyl-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35ae): Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. Mp 144 °C; IR (neat): ν_{max} 3112, 2970, 1715 (O-C=O), 1699 (O-C=O), 1606, 1518, 1468, 1282, 1206, 1112, 1058, 860, 767 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.20 (2H, d, *J* = 8.8 Hz), 7.63 (2H, d, *J* = 8.8 Hz), 4.39 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 4.25 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.00 (2H, t, *J* = 8.0 Hz), 2.85 (2H, t, *J* = 8.0 Hz), 2.60 (3H, s, olefinic-C*H*$_3$), 1.40 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$), 1.33 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.6 (C, O-*C*=O), 165.2 (C, O-*C*=O), 146.2 (C), 139.4 (C), 138.2 (C), 133.4 (C), 131.0 (2 x CH), 130.8 (C), 122.3 (2 x CH), 121.3 (C), 61.4 (CH$_2$, O*C*H$_2$CH$_3$), 60.4 (CH$_2$, O*C*H$_2$CH$_3$), 25.3 (CH$_2$), 19.8 (CH$_2$), 15.2 (CH$_3$), 14.24 (CH$_3$, OCH$_2$*C*H$_3$), 14.19 (CH$_3$, OCH$_2$*C*H$_3$); HRMS m/z 356.1610 (M + H$^+$), calcd for $C_{19}H_{21}N_3O_4H$ 356.1610.



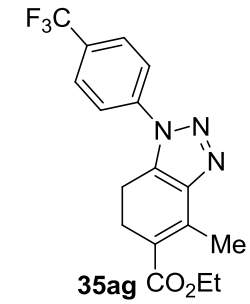
35ae

Ethyl 1-(4-cyanophenyl)-4-methyl-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35af): Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a yellow solid. Mp 139 °C; IR (neat): ν_{max} 2921, 2855, 2236, 1677, 1600, 1501, 1364, 1310, 1200, 1030, 855 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.86 (2H, d, *J* = 8.4 Hz), 7.73 (2H, d, *J* = 8.4 Hz), 4.26 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.02 (2H, t, *J* = 8.8 Hz), 2.87 (2H, t, *J* = 8.8 Hz), 2.60 (3H, s, olefinic-C*H*$_3$), 1.34 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.6 (C, O-C=O), 146.6 (C), 139.4 (C), 138.0 (C), 133.7 (2 x CH), 133.3 (C), 123.0 (2 x CH), 121.5 (C), 117.6 (C), 112.7 (C, *C*N), 60.5 (CH$_2$, O*C*H$_2$CH$_3$), 25.3 (CH$_2$), 19.9 (CH$_2$), 15.2 (CH$_3$), 14.3 (CH$_3$, OCH$_2$*C*H$_3$); HRMS m/z 309.1349 (M + H$^+$), calcd for $C_{17}H_{16}N_4O_2H$ 309.1351.



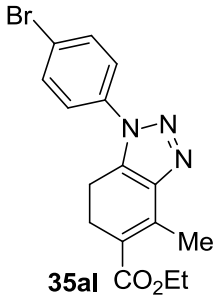
35af

Ethyl 4-methyl-1-(4-(trifluoromethyl)phenyl)-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35ag): Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. Mp 137 °C; IR (neat): ν_{max} 2991, 1686 (O-C=O), 1614, 1522, 1371, 1320, 1299, 1257, 1205, 1166, 1115, 1068, 1030, 841, 778 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.81 (2H,

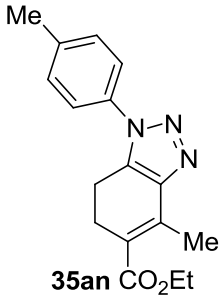


35ag

d, *J* = 8.4 Hz), 7.70 (2H, d, *J* = 8.4 Hz), 4.25 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.01 (2H, t, *J* = 8.4 Hz), 2.86 (2H, t, *J* = 8.4 Hz), 2.60 (3H, s, olefinic-C*H*$_3$), 1.34 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{19}F NMR (376.5 MHz, $CDCl_3$) δ –62.68 (s, 3F); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.7 (C, O-C=O), 146.4 (C), 138.8 (C), 138.2 (C), 133.4 (C), 131.0 (C, q, *J* = 32.5 Hz), 126.9 (2 x CH, q, *J* = 3.75 Hz), 123.4 (C, q, *J* = 271.2 Hz, *C*F$_3$), 122.9 (2 x CH), 121.3 (C), 60.5 (CH$_2$, O*C*H$_2$CH$_3$), 25.3 (CH$_2$), 19.7 (CH$_2$), 15.2 (CH$_3$), 14.2 (CH$_3$, OCH$_2$*C*H$_3$); HRMS m/z 352.1273 (M + H$^+$), calcd for $C_{17}H_{16}F_3N_3O_2H$ 352.1273; Anal. calcd for $C_{17}H_{16}F_3N_3O_2$ (351.11): C, 58.12; H, 4.59; N, 11.96. Found: C, 58.06; H, 4.62, N, 11.89%.

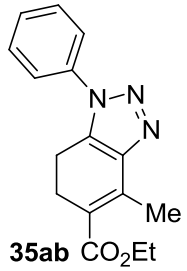


Ethyl 1-(4-bromophenyl)-4-methyl-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35al): Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. Mp 138 °C; IR (neat): ν_{max} 2921, 2855, 1704, 1606, 1507, 1463, 1364, 1266, 1206, 822, 740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.66 (2H, d, *J* = 8.4 Hz), 7.42 (2H, d, *J* = 8.4 Hz), 4.26 (2H, q, *J* = 7.2 Hz), 2.94 (2H, t, *J* = 8.0 Hz), 2.84 (2H, t, *J* = 8.0 Hz), 2.60 (3H, s, olefinic-C*H*$_3$), 1.34 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.7 (C, O-*C*=O), 146.1 (C), 138.4 (C), 135.1 (C), 133.4 (C), 132.8 (2 x CH), 124.3 (2 x CH), 123.0 (C), 121.1 (C), 60.4 (CH$_2$), 25.3 (CH$_2$), 19.6 (CH$_2$), 15.2 (CH$_3$), 14.3 (CH$_3$); HRMS m/z 362.0504 (M + H$^+$), calcd for $C_{16}H_{16}BrN_3O_2H$ 362.0504.



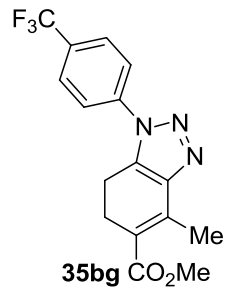
Ethyl 4-methyl-1-(p-tolyl)-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35an): Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a brown colored solid. Mp 99 °C; IR (neat): ν_{max} 2978, 2922, 2852, 1691, 1602, 1518, 1448, 1285, 1204, 1178, 1046, 822, 773 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.42 (2H, d, *J* = 8.4 Hz), 7.34 (2H, d, *J* = 8.4 Hz), 4.27 (2H, q, *J* = 7.2 Hz), 2.94 (2H, t, *J* = 8.0 Hz), 2.84 (2H, t, *J* = 8.0 Hz), 2.64 (3H, s, olefinic-C*H*$_3$), 2.44 (3H, s, Ar-C*H*$_3$), 1.35 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.9 (C, O-*C*=O), 145.7 (C), 139.4 (C), 138.6 (C), 133.6 (2 x C), 130.2 (2 x CH), 122.9 (2 x CH), 121.1 (C), 60.4 (CH$_2$, O*C*H$_2$CH$_3$), 25.4 (CH$_2$), 21.2 (CH$_3$), 19.6 (CH$_2$), 15.4 (CH$_3$), 14.3 (CH$_3$, OCH$_2$*C*H$_3$); HRMS m/z 298.1555 (M + H$^+$), calcd for $C_{17}H_{19}N_3O_2H$ 298.1555.

Ethyl 4-methyl-1-phenyl-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35ab):

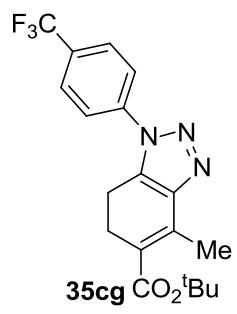


Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a yellow oily liquid. IR (neat): ν_{max} 2923, 1694 (O-C=O), 1599, 1508, 1368, 1284, 1199, 1053, 761 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.56–7.48 (5H, m), 4.28 (2H, q, *J* = 7.2 Hz), 2.97 (2H, t, *J* = 7.6 Hz), 2.86 (2H, t, *J* = 7.6 Hz), 2.64 (3H, s, olefinic-C*H*$_3$), 1.36 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.9 (C, O-*C*=O), 146.0 (C), 138.7 (C), 136.1 (C), 133.5 (C), 129.7 (2 x CH), 129.1 (CH), 123.0 (2 x CH), 121.0 (C), 60.4 (CH_2), 25.4 (CH_2), 19.7 (CH_2), 15.3 (CH_3), 14.3 (CH_3); HRMS m/z 284.1399 (M + H^+), calcd for $C_{16}H_{17}N_3O_2H$ 284.1399; Anal. calcd for $C_{16}H_{17}N_3O_2$ (283.13): C, 67.83; H, 6.05; N, 14.83. Found: C, 67.78; H, 6.12, N, 14.78%.

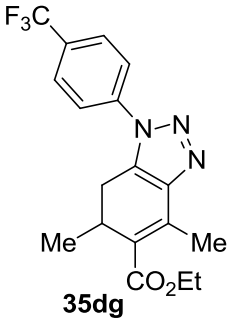
Methyl 4-methyl-1-(4-(trifluoromethyl)phenyl)-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35bg): Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. Mp 142 °C; IR (neat): ν_{max} 2964, 2926, 2849, 1710, 1693, 1622, 1523, 1441, 1321, 1206, 1167, 1112, 844 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.84 (2H, d, *J* = 8.0 Hz), 7.73 (2H, d, *J* = 8.0 Hz), 3.82 (3H, s, CO_2CH_3), 3.04 (2H, t, *J* = 8.4 Hz), 2.89 (2H, t, *J* = 8.4 Hz), 2.63 (3H, s, olefinic-C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.0 (C, O-*C*=O), 146.3 (C), 138.8 (C), 138.7 (C), 133.5 (C), 131.0 (C, q, *J* = 33.0 Hz), 126.9 (2 x CH, q, *J* = 3.0 Hz), 123.4 (C, q, *J* = 271.0 Hz, *C*F_3), 123.0 (2 x CH), 121.0 (C), 51.5 (CH_3), 25.3 (CH_2), 19.8 (CH_2), 15.2 (CH_3); HRMS m/z 360.0938 (M + Na), calcd for $C_{16}H_{14}F_3N_3O_2Na$ 360.0936.



***tert*-Butyl 4-methyl-1-(4-(trifluoromethyl)phenyl)-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35cg):** Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. Mp 148 °C; IR (neat): ν_{max} 2975, 2921, 1699 (O-C=O), 1682, 1616, 1518, 1375, 1326, 1167, 1074, 1030, 838 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.83 (2H, d, *J* = 8.4 Hz), 7.72 (2H, d, *J* = 8.4 Hz), 3.00 (2H, t, *J* = 8.4 Hz), 2.83 (2H, t, *J* = 8.4 Hz), 2.59 (3H, s, olefinic-C*H*$_3$), 1.56 (9H, s, $CO_2C(CH_3)_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.2 (C, O-

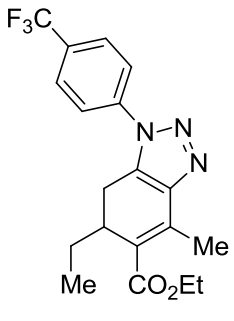


C=O), 146.6 (C), 138.9 (C), 136.5 (C), 133.2 (C), 131.0 (C, q, *J* = 33.0 Hz), 126.9 (2 x CH, q, *J* = 3.0 Hz), 123.5 (C, q, *J* = 271.0 Hz, *C*F_3), 123.1 (C), 123.0 (2 x CH), 81.1 (C), 28.3 (3 x CH_3), 25.6 (CH_2), 19.8 (CH_2), 15.2 (CH_3); HRMS m/z 380.1589 (M + H^+), calcd for $C_{19}H_{20}F_3N_3O_2H$ 380.1586.



35dg

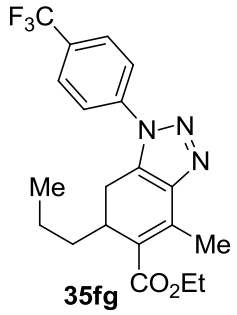
Ethyl 4,6-dimethyl-1-(4-(trifluoromethyl)phenyl)-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35dg): Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a yellow solid. Mp 130 °C; IR (neat): ν_{max} 2966, 2926, 1687 (O-C=O), 1616, 1524, 1373, 1320, 1263, 1170, 1128, 1074, 1036, 837 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.84 (2H, d, *J* = 8.4 Hz), 7.73 (2H, d, *J* = 8.4 Hz), 4.29 (2H, dq, *J* = 7.2, 1.6 Hz, OC*H*$_2$CH$_3$), 3.38–3.31 (1H, m), 3.24 (1H, dd, *J* = 16.8, 7.6 Hz), 2.82 (1H, dd, *J* = 16.4, 1.6 Hz), 2.62 (3H, s, olefinic-C*H*$_3$), 1.36 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$), 1.04 (3H, d, *J* = 6.8 Hz, CHC*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.6 (C, O-C=O), 145.5 (C), 138.8 (C), 136.9 (C), 132.3 (C), 131.0 (C, q, *J* = 33.0 Hz), 127.3 (C), 126.9 (2 x CH, q, *J* = 3.0 Hz), 123.4 (C, q, *J* = 271.0 Hz, *C*F_3), 123.0 (2 x CH), 60.4 (CH_2, O*C*H$_2$CH$_3$), 30.8 (CH), 27.2 (CH_2), 19.9 (CH_3), 15.5 (CH_3), 14.3 (CH_3); HRMS m/z 366.1430 (M + H^+), calcd for $C_{18}H_{18}F_3N_3O_2H$ 366.1429; Anal. calcd for $C_{18}H_{18}F_3N_3O_2$ (365.13): C, 59.17; H, 4.97; N, 11.50. Found: C, 59.25; H, 4.93, N, 11.57%.



35eg

Ethyl 6-ethyl-4-methyl-1-(4-(trifluoromethyl)phenyl)-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35eg): Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. Mp 77 °C; IR (neat): ν_{max} 2964, 2937, 1704, 1622, 1529, 1419, 1332, 1249, 1200, 1167, 1134, 1030, 844 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.86 (2H, d, *J* = 8.8 Hz), 7.74 (2H, d, *J* = 8.8 Hz), 4.36–4.24 (2H, m, OC*H*$_2$CH$_3$), 3.21–3.12 (2H, m), 2.98 (1H, d, *J* = 15.6 Hz), 2.63 (3H, s, olefinic-C*H*$_3$), 1.56-1.46 (1H, m), 1.37 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$), 1.32-1.31 (1H, m), 0.81 (3H, t, *J* = 7.2 Hz, CH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.8 (C, O-*C*=O), 145.9 (C), 138.8 (C), 137.0 (C), 132.5 (C), 131.0 (C, q, *J* = 33.0 Hz), 127.0 (2 x CH, q, *J* = 3.0 Hz), 126.6 (C), 123.5 (C, q, *J* = 271.0 Hz, *C*F_3), 123.0 (2 x

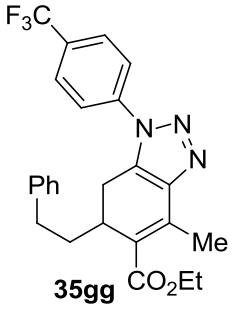
CH), 60.5 (CH_2, O*C*H_2CH_3), 37.1 (CH), 26.2 (CH_2), 23.7 (CH_2), 15.5 (CH_3), 14.2 (CH_3), 11.3 (CH_3); HRMS m/z 380.1586 ($M + H^+$), calcd for $C_{19}H_{20}F_3N_3O_2H$ 380.1586.



35fg

Ethyl 4-methyl-6-propyl-1-(4-(trifluoromethyl)phenyl)-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35fg): Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. Mp 95 °C; IR (neat): ν_{max} 2975, 2932, 1704 (O-C=O), 1611, 1523, 1414, 1326, 1244, 1200, 1178, 1134, 1074, 1036, 844 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.85 (2H, d, *J* = 8.4 Hz), 7.74 (2H, d, *J* = 8.4 Hz), 4.35–4.23 (2H, m, OC*H*$_2$CH$_3$), 3.28 (1H, dd, *J* = 12.8, 6.8 Hz), 3.14 (1H, dd, *J* = 16.8, 7.6 Hz), 2.95 (1H, dd, *J* = 16.8, 1.2 Hz), 2.63 (3H, s, olefinic-C*H*$_3$), 1.37 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$), 1.45–1.14 (4H, m), 0.83 (3H, t, *J* = 7.2 Hz, CH$_2$CH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.8 (C, O-*C*=O), 145.9 (C), 138.9 (C), 137.0 (C), 132.5 (C), 131.0 (C, q, *J* = 33.0 Hz), 127.0 (2 x CH, q, *J* = 3.0 Hz), 126.8 (C), 123.5 (C, q, *J* = 271.0 Hz, *C*F$_3$), 123.0 (2 x CH), 60.5 (CH_2), 35.4 (CH_2), 35.2 (CH), 24.2 (CH_2), 19.8 (CH_2), 15.5 (CH_3), 14.3 (CH_3), 13.8 (CH_3); HRMS m/z 394.1744 ($M + H^+$), calcd for $C_{20}H_{22}F_3N_3O_2H$ 394.1742.

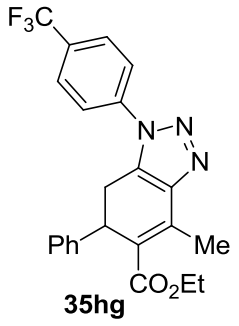
Ethyl 4-methyl-6-phenethyl-1-(4-(trifluoromethyl)phenyl)-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35gg): Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. Mp 88 °C; IR (neat): ν_{max} 2915, 2849, 1715, 1616, 1529, 1326, 1255, 1173, 1112, 1068, 1041, 844 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.82 (2H, d, *J* = 8.4 Hz), 7.65 (2H, d, *J* = 8.4 Hz), 7.17 (2H, t, *J* = 7.6 Hz), 7.09 (1H, d, *J* = 7.2 Hz), 7.04 (2H, d, *J* = 8.0 Hz), 4.27 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.33 (1H, dd, *J* = 13.2, 7.2 Hz), 3.11 (1H, dd, *J* = 16.8, 7.2 Hz), 2.94 (1H, dd, *J* = 16.0, 1.2 Hz), 2.64 (3H, s, olefinic-C*H*$_3$), 2.62–2.50 (2H, m), 1.85–1.77 (1H, m), 1.65–1.56 (1H, m), 1.33 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.6 (C, O-*C*=O), 145.8 (C), 141.3 (C), 138.7 (C), 137.5 (C), 132.4 (C), 130.9 (C, q, *J* = 33.0 Hz), 128.3 (2 x CH), 128.0 (2 x CH), 126.9 (2 x CH, q, *J* = 3.0 Hz), 126.4 (C), 125.9 (CH), 123.4 (C, q, *J* = 271.0 Hz, *C*F$_3$), 122.8 (2 x CH), 60.5 (CH_2, O*C*H_2CH_3), 35.6



35gg

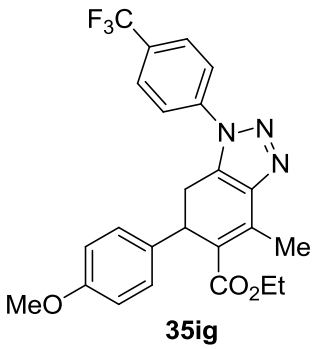
(CH), 34.2 (CH_2), 33.2 (CH_2), 24.1 (CH_2), 15.5 (CH_3), 14.2 (CH_3); HRMS m/z 456.1904 (M + H^+), calcd for $C_{25}H_{24}F_3N_3O_2H$ 456.1899.

Ethyl 4-methyl-6-phenyl-1-(4-(trifluoromethyl)phenyl)-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35hg): Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. Mp 143 °C; IR (neat): ν_{max} 2933, 1690, 1616, 1489, 1371, 1328, 1309, 1257, 1167, 1126, 1070, 845, 791 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.77 (2H, d, *J* = 8.4 Hz), 7.60 (2H, d, *J* = 8.4 Hz), 7.22–7.16 (3H, m), 7.11–7.09 (2H, m), 4.54 (1H, br d, *J* = 7.2 Hz), 4.14 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.56 (1H, dd, *J* = 16.8, 8.8 Hz), 3.15 (1H, dd, *J* = 16.8, 2.8 Hz), 2.77 (3H, d, *J* = 0.4 Hz, olefinic-C*H*$_3$), 1.19 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{19}F NMR (376.5 MHz, $CDCl_3$) δ –62.74 (s, 3F); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.2 (C, O-C=O), 146.3 (C), 142.3 (C), 138.7 (C), 138.5 (C), 131.6 (C), 131.1 (C, q, *J* = 33.0 Hz), 128.7 (2 x CH), 127.1 (CH), 127.0 (2 x CH), 126.9 (2 x CH, q, *J* = 3.0 Hz), 124.8 (C), 123.4 (C, q, *J* = 271.0 Hz, *C*F$_3$), 123.0 (2 x CH), 60.5 (CH_2, O*C*H$_2$CH$_3$), 41.4 (CH), 28.9 (CH_2), 15.5 (CH_3), 14.1 (CH_3, OCH$_2$*C*H$_3$); HRMS m/z 428.1586 (M + H^+), calcd for $C_{23}H_{20}F_3N_3O_2H$ 428.1586; Anal. calcd for $C_{23}H_{20}F_3N_3O_2$ (427.15): C, 64.63; H, 4.72; N, 9.83. Found: C, 64.56; H, 4.68, N, 9.75%.



35hg

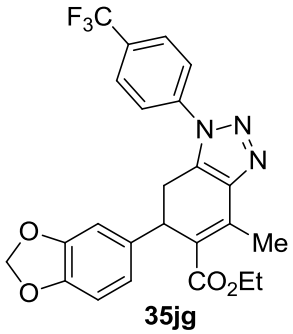
Ethyl 6-(4-methoxyphenyl)-4-methyl-1-(4-(trifluoromethyl)phenyl)-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35ig): Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a yellow solid. Mp 72 °C; IR (neat): ν_{max} 2986, 2921, 1704, 1616, 1512, 1326, 1255, 1206, 1118, 1030, 844 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.77 (2H, d, *J* = 8.4 Hz), 7.60 (2H, d, *J* = 8.4 Hz), 7.01 (2H, d, *J* = 8.8 Hz), 6.72 (2H, d, *J* = 8.4 Hz), 4.49 (1H, br d, *J* = 8.0 Hz), 4.15 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.72 (3H, s, Ar-OC*H*$_3$), 3.53 (1H, dd, *J* = 16.4, 8.4 Hz), 3.11 (1H, dd, *J* = 16.8, 2.4 Hz), 2.76 (3H, s, olefinic-C*H*$_3$), 1.22 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.3 (C, O-*C*=O), 158.6 (C), 146.3 (C), 138.7 (C), 138.0 (C), 134.2 (C), 131.6 (C), 131.0 (C, q, *J* = 33.0 Hz), 128.0 (2 x CH), 126.9 (2 x CH, q, *J* = 3.0 Hz), 125.1 (C),



35ig

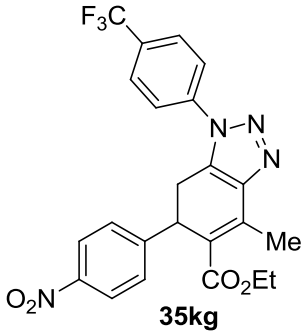
123.4 (C, q, *J* = 271.0 Hz, *C*F_3), 122.9 (2 x CH), 114.0 (2 x CH), 60.5 (CH_2, O*C*H_2CH_3), 55.1 (CH_3, Ar-O*C*H_3), 40.5 (CH), 29.0 (CH_2), 15.4 (CH_3), 14.1 (CH_3, OCH_2*C*H_3); HRMS m/z 458.1693 (M + H^+), calcd for $C_{24}H_{22}F_3N_3O_3H$ 458.1691.

Ethyl 6-(benzo[d][1,3]dioxol-5-yl)-4-methyl-1-(4-(trifluoromethyl)phenyl)-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35jg): Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a yellow solid. Mp 80 °C; IR (neat): ν_{max} 2924, 2849, 1705, 1613, 1485, 1439, 1325, 1246, 1203, 1114, 1040, 936, 844 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.77 (2H, d, *J* = 8.4 Hz), 7.61 (2H, d, *J* = 8.4 Hz), 6.61 (1H, d, *J* = 8.0 Hz), 6.56 (1H, d, *J* = 8.0 Hz), 6.55 (1H, s), 5.85 (2H, d, *J* = 1.2 Hz, OC*H*$_2$O), 4.46 (1H, br d, *J* = 8.4 Hz), 4.16 (2H, q, *J* = 6.8 Hz), 3.54 (1H, dd, *J* = 16.8, 8.8 Hz), 3.10 (1H, dd, *J* = 16.8, 2.0 Hz), 2.74 (3H, s, olefinic-C*H*$_3$), 1.23 (3H, t, *J* = 6.8 Hz, OCH_2C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.2 (C, O-*C*=O), 147.7 (C), 146.5 (C), 146.1 (C), 138.6 (C), 138.3 (C), 136.0 (C), 131.5 (C), 131.0 (C, q, *J* = 33.0 Hz), 126.9 (2 x CH, q, *J* = 3.0 Hz), 124.8 (C), 123.4 (C, q, *J* = 271.0 Hz, *C*F_3), 122.9 (2 x CH), 120.0 (CH), 108.3 (CH), 107.3 (CH), 100.9 (CH_2), 60.6 (CH_2, O*C*H_2CH_3), 40.9 (CH), 29.0 (CH_2), 15.5 (CH_3), 14.1 (CH_3); HRMS m/z 472.1484 (M + H^+), calcd for $C_{24}H_{20}F_3N_3O_4H$ 472.1484.



35jg

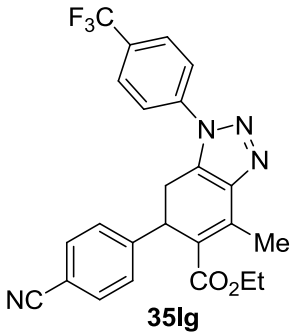
Ethyl 4-methyl-6-(4-nitrophenyl)-1-(4-(trifluoromethyl)phenyl)-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35kg): Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a yellow solid. Mp 150 °C; IR (neat): ν_{max} 1683, 1514, 1347, 1329, 1308, 1212, 1170, 1113, 1072, 1035, 999, 843 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.05 (2H, d, *J* = 8.4 Hz), 7.78 (2H, d, *J* = 8.4 Hz), 7.60 (2H, d, *J* = 8.4 Hz), 7.28 (2H, d, *J* = 8.4 Hz), 4.65 (1H, br d, *J* = 8.4 Hz), 4.16 (2H, q, *J* = 7.2 Hz), 3.66 (1H, dd, *J* = 16.8, 8.8 Hz), 3.12 (1H, dd, *J* = 16.8, 1.6 Hz), 2.82 (3H, s, olefinic-C*H*$_3$), 1.22 (3H, t, *J* = 7.2 Hz, OCH_2C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.8 (C, O-*C*=O), 149.8 (C), 147.1 (C), 146.1 (C), 140.2 (C), 138.4 (C), 131.3 (C, q, *J* = 33.0 Hz), 131.0 (C), 127.9 (2 x CH), 127.0 (2 x CH, q, *J* = 3.0 Hz), 124.0 (2 x CH), 123.31 (C, q, *J* = 271.0



35kg

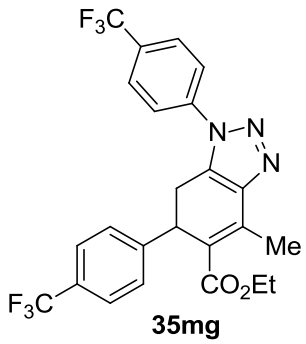
Hz, *C*F_3), 123.27 (C), 122.9 (2 x CH), 60.8 (CH_2, O*C*H_2CH_3), 41.2 (CH), 28.4 (CH_2), 15.6 (CH_3), 14.1 (CH_3); HRMS m/z 473.1437 ($M + H^+$), calcd for $C_{23}H_{19}F_3N_4O_4H$ 473.1436.

Ethyl 6-(4-cyanophenyl)-4-methyl-1-(4-(trifluoromethyl)phenyl)-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35lg): Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. Mp 60 °C; IR (neat): ν_{max} 2918, 2850, 2228, 1699, 1615, 1526, 1322, 1203, 1167, 1113, 1067, 843, 785 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.78 (2H, d, *J* = 8.4 Hz), 7.60 (2H, d, *J* = 8.4 Hz), 7.50 (2H, d, *J* = 8.0 Hz), 7.23 (2H, d, *J* = 8.0 Hz), 4.60 (1H, br d, *J* = 8.8 Hz), 4.16 (2H, q, *J* = 7.2 Hz), 3.64 (1H, dd, *J* = 16.8, 8.8 Hz), 3.11 (1H, dd, *J* = 16.8, 2.0 Hz), 2.79 (3H, s, olefinic-C*H*$_3$), 1.21 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.7 (C, O-*C*=O), 147.7 (C), 146.0 (C), 139.9 (C), 138.4 (C), 132.6 (2 x CH), 131.5 (C, q, *J* = 33.0 Hz), 131.0 (C), 127.8 (2 x CH), 127.0 (2 x CH, q, *J* = 4.0 Hz), 123.3 (C, q, *J* = 271.0 Hz, *C*F_3), 123.28 (C), 122.9 (2 x CH), 118.4 (C), 111.0 (C, *C*N), 60.7 (CH_2, O*C*H_2CH_3), 41.3 (CH), 28.4 (CH_2), 15.5 (CH_3), 14.0 (CH_3); HRMS m/z 453.1538 ($M + H^+$), calcd for $C_{24}H_{19}F_3N_4O_2H$ 453.1538.



35lg

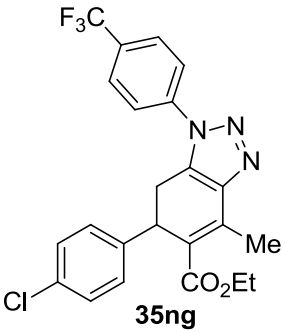
Ethyl 4-methyl-1,6-bis(4-(trifluoromethyl)phenyl)-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35mg): Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a yellow solid. Mp 90 °C; IR (neat): ν_{max} 2921, 1706, 1617, 1418, 1324, 1202, 1162, 1109, 1068, 1017, 841 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.77 (2H, d, *J* = 8.4 Hz), 7.61 (2H, d, *J* = 8.4 Hz), 7.46 (2H, d, *J* = 8.4 Hz), 7.24 (2H, d, *J* = 7.6 Hz), 4.62 (1H, br d, *J* = 8.4 Hz), 4.16 (2H, q, *J* = 7.2 Hz), 3.65 (1H, dd, *J* = 16.8, 8.8 Hz), 3.14 (1H, dd, *J* = 16.8, 2.0 Hz), 2.80 (3H, s, olefinic-C*H*$_3$), 1.21 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.9 (C, O-*C*=O), 146.4 (C), 146.2 (C), 139.5 (C), 138.5 (C), 131.22 (C), 131.16 (C, q, *J* = 33.0 Hz), 129.4 (C, q, *J* = 33.0 Hz), 127.3 (2 x CH), 127.0 (2 x CH, q, *J* = 3.0 Hz), 125.7 (2 x CH, q, *J* = 3.0 Hz), 123.9 (C, q, *J* = 271.0 Hz, *C*F_3), 123.8 (C), 123.3 (C, q, *J* = 271.0 Hz, *C*F_3), 122.9 (2 x CH), 60.7



35mg

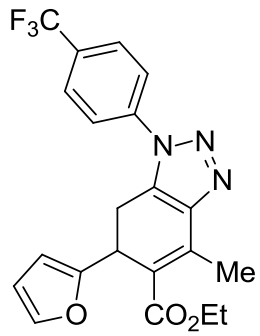
(CH_2, O*C*H_2CH$_3$), 41.2 (CH), 28.6 (CH_2), 15.5 (CH_3), 14.0 (CH_3); HRMS m/z 496.1459 (M + H^+), calcd for $C_{24}H_{19}F_6N_3O_2H$ 496.1459.

Ethyl 6-(4-chlorophenyl)-4-methyl-1-(4-(trifluoromethyl)phenyl)-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35ng): Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. Mp 115 °C; IR (neat): ν_{max} 2976, 2927, 1706, 1612, 1487, 1414, 1320, 1249, 1170, 1133, 1064, 1012, 841, 756 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.78 (2H, d, *J* = 8.4 Hz), 7.60 (2H, d, *J* = 8.4 Hz), 7.16 (2H, d, *J* = 8.4 Hz), 7.03 (2H, d, *J* = 8.4 Hz), 4.52 (1H, br d, *J* = 8.4 Hz), 4.15 (2H, q, *J* = 7.2 Hz), 3.57 (1H, dd, *J* = 16.8, 8.8 Hz), 3.09 (1H, dd, *J* = 16.8, 2.0 Hz), 2.78 (3H, s, olefinic-C*H*$_3$), 1.22 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.0 (C, O-*C*=O), 146.2 (C), 140.7 (C), 139.0 (C), 138.5 (C), 132.8 (C), 131.3 (C), 131.1 (C, q, *J* = 33.0 Hz), 128.8 (2 x CH), 128.3 (2 x CH), 126.9 (2 x CH, q, *J* = 3.0 Hz), 124.2 (C), 123.3 (C, q, *J* = 271.0 Hz, *C*F$_3$), 122.9 (2 x CH), 60.6 (CH_2, O*C*H_2CH$_3$), 40.7 (CH), 28.8 (CH_2), 15.5 (CH_3), 14.1 (CH_3); HRMS m/z 462.1198 (M + H^+), calcd for $C_{23}H_{19}ClF_3N_3O_2H$ 462.1196.



35ng

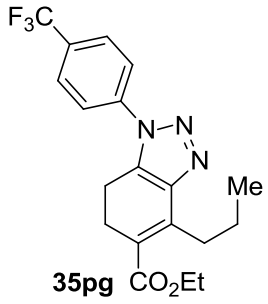
Ethyl 6-(furan-2-yl)-4-methyl-1-(4-(trifluoromethyl)phenyl)-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35og): Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. Mp 120 °C; IR (neat): ν_{max} 2922, 2852, 1702, 1611, 1520, 1425, 1373, 1321, 1286, 1206, 1164, 1118, 1065, 847, 742 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.81 (2H, d, *J* = 8.8 Hz), 7.67 (2H, d, *J* = 8.8 Hz), 7.20 (1H, d, *J* = 1.2 Hz), 6.14 (1H, dd, *J* = 3.2, 2.0 Hz), 5.88 (1H, d, *J* = 3.2 Hz), 4.66 (1H, br d, *J* = 7.2 Hz), 4.25 (2H, dq, *J* = 7.2, 1.2 Hz, OC*H*$_2$CH$_3$), 3.43 (1H, dd, *J* = 16.4, 2.0 Hz), 3.34 (1H, dd, *J* = 16.4, 7.6 Hz), 2.73 (3H, s, olefinic-C*H*$_3$), 1.30 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.9 (C, O-C=O), 154.4 (C), 145.9 (C), 141.7 (CH), 140.0 (C), 138.7 (C), 132.1 (C), 131.1 (C, q, *J* = 33.0 Hz), 127.0 (2 x CH, q, *J* = 3.0 Hz), 123.4 (C, q, *J* = 270.0 Hz, *C*F$_3$), 123.0 (2 x CH), 122.1 (C), 110.2 (CH), 106.2 (CH),



35og

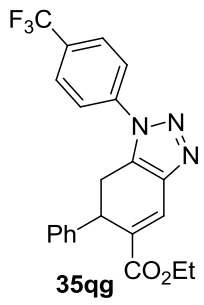
60.7 (CH_2, O*C*H_2CH_3), 35.0 (CH), 25.2 (CH_2), 15.6 (CH_3), 14.2 (CH_3); HRMS m/z 418.1378 ($M + H^+$), calcd for $C_{21}H_{18}F_3N_3O_3H$ 418.1378.

Ethyl 4-propyl-1-(4-(trifluoromethyl)phenyl)-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35pg): Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. Mp 97 °C; IR (neat): ν_{max} 3096, 2965, 2930, 2877, 1691, 1613, 1414, 1372, 1325, 1300, 1201, 1168, 1129, 1069, 856 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.81 (2H, d, *J* = 8.4 Hz), 7.71 (2H, d, *J* = 8.4 Hz), 4.28–4.22 (2H, m, OC*H*$_2$CH$_3$), 3.08–3.04 (2H, m), 3.01 (2H, br t, *J* = 8.4 Hz), 2.85 (2H, br t, *J* = 8.4 Hz), 1.74–1.63 (2H, m), 1.36–1.32 (3H, m), 1.04–0.98 (3H, m); ^{19}F NMR (376.5 MHz, $CDCl_3$) δ –62.68 (s, 3F); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.6 (C, O-*C*=O), 145.7 (C), 142.3 (C), 138.8 (C), 133.6 (C), 130.9 (C, q, *J* = 33.0 Hz), 126.8 (2 x CH, q, *J* = 3.0 Hz), 123.4 (C, q, *J* = 271.0 Hz, *C*F_3), 122.9 (2 x CH), 121.2 (C), 60.4 (CH_2), 30.9 (CH_2), 25.5 (CH_2), 22.8 (CH_2), 19.7 (CH_2), 14.1 (2 x CH_3); HRMS m/z 380.1586 ($M + H^+$), calcd for $C_{19}H_{20}F_3N_3O_2H$ 380.1586; Anal. calcd for $C_{19}H_{20}F_3N_3O_2$ (379.15): C, 60.15; H, 5.31; N, 11.08. Found: C, 60.26; H, 5.28, N, 11.15%.

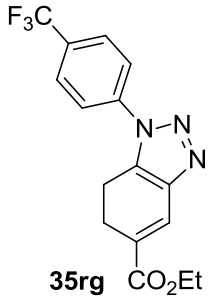


35pg

Ethyl 6-phenyl-1-(4-(trifluoromethyl)phenyl)-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35qg): Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a yellow solid. Mp 194 °C; IR (neat): ν_{max} 2923, 1703, 1614, 1524, 1319, 1220, 1165, 1112, 1065, 843 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.04 (1H, s, olefinic-*H*), 7.78 (2H, d, *J* = 8.4 Hz), 7.63 (2H, d, *J* = 8.4 Hz), 7.23–7.18 (3H, m), 7.16–7.14 (2H, m), 4.55 (1H, br d, *J* = 8.8 Hz), 4.27–4.14 (2H, m, OC*H*$_2$CH$_3$), 3.67 (1H, dd, *J* = 17.2, 9.6 Hz), 3.24 (1H, dd, *J* = 17.2, 1.6 Hz), 1.28 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.7 (C, O-*C*=O), 143.4 (C), 141.4 (C), 138.6 (C), 132.7 (C), 131.1 (C, q, *J* = 33.0 Hz), 130.5 (C), 128.8 (2 x CH), 127.8 (CH), 127.3 (CH), 126.9 (2 x CH, q, *J* = 3.0 Hz), 126.7 (2 x CH), 123.3 (C, q, *J* = 271.0 Hz, *C*F_3), 122.9 (2 x CH), 60.9 (CH_2, O*C*H_2CH_3), 39.3 (CH), 29.0 (CH_2), 14.0 (CH_3); HRMS m/z 414.1429 ($M + H^+$), calcd for $C_{22}H_{18}F_3N_3O_2H$ 414.1429.

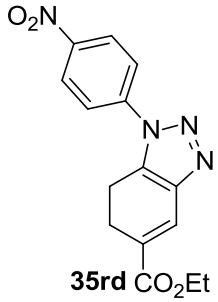


35qg

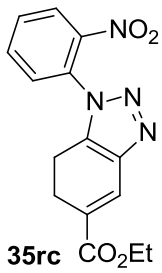


Ethyl 1-(4-(trifluoromethyl)phenyl)-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35rg): Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a yellow solid. Mp 172 °C; IR (neat): ν_{max} 2921, 2849, 1703 (O-C=O), 1611, 1523, 1414, 1381, 1321, 1295, 1233, 1167, 1110, 1067, 841 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.83 (2H, d, *J* = 8.4 Hz), 7.75 (1H, t, *J* = 1.2 Hz, olefinic-*H*), 7.72 (2H, d, *J* = 8.4 Hz), 4.27 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 3.11 (2H, t, *J* = 8.8 Hz), 2.90 (2H, dt, *J* = 8.8, 1.2 Hz), 1.35 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.3 (C, O-*C*=O), 143.6 (C), 138.8 (C), 134.1 (C), 131.2 (C, q, *J* = 33.8 Hz), 127.6 (CH), 127.6 (C), 127.0 (2 x CH, q, *J* = 2.5 Hz), 123.4 (C, q, *J* = 271.2 Hz, CF_3), 123.0 (2 x CH), 60.9 (CH_2, OCH_2CH_3), 23.2 (CH_2), 19.8 (CH_2), 14.2 (CH_3, OCH_2CH_3); HRMS m/z 338.1118 (M + H^+), calcd for $C_{16}H_{14}F_3N_3O_2H$ 338.1116; Anal. calcd for $C_{16}H_{14}F_3N_3O_2$ (337.10): C, 56.97; H, 4.18; N, 12.46. Found: C, 56.85; H, 4.23, N, 12.69%.

Ethyl 1-(4-nitrophenyl)-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35rd):



Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a brown colored solid. Mp 154 °C; IR (neat): ν_{max} 1704, 1633, 1593, 1519, 1500, 1471, 1338, 1289, 1108, 1037, 853, 798 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.46 (2H, d, *J* = 8.8 Hz), 7.83 (2H, d, *J* = 8.8 Hz), 7.76 (1H, s, olefinic-*H*), 4.30 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 3.18 (2H, t, *J* = 8.8 Hz), 2.93 (2H, t, *J* = 8.4 Hz), 1.37 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.2 (C, O-*C*=O), 147.4 (C), 143.9 (C), 140.7 (C), 134.1 (C), 127.8 (C), 127.3 (CH), 125.3 (2 x CH), 123.1 (2 x CH), 61.0 (CH_2, OCH_2CH_3), 23.2 (CH_2), 20.0 (CH_2), 14.2 (CH_3, OCH_2CH_3); HRMS m/z 315.1092 (M + H^+), calcd for $C_{15}H_{14}N_4O_4H$ 315.1093.



Ethyl 1-(2-nitrophenyl)-6,7-dihydro-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (35rc): Prepared following the procedure **3a** and purified by column chromatography using EtOAc/hexane and isolated as a brown colored liquid. IR (neat): ν_{max} 2981, 1692, 1607, 1529, 1340, 1275, 1211, 1066, 1028, 851 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.18 (1H, d, *J* = 8.0 Hz), 7.85 (1H, t, *J* = 8.0

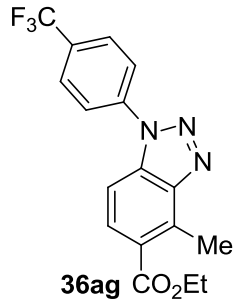
Hz), 7.78 (1H, s, olefinic-*H*), 7.76 (1H, t, *J* = 8.0 Hz), 7.58 (1H, d, *J* = 8.0 Hz), 4.29 (2H, q, *J* = 7.0 Hz, OC*H*$_2$CH$_3$), 2.91–2.82 (4H, m), 1.36 (3H, t, *J* = 7.0 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.4 (C, O-*C*=O), 144.8 (C), 142.6 (C), 136.8 (C), 134.2 (CH), 131.3 (CH), 129.0 (C), 128.8 (CH), 127.6 (CH), 127.4 (C), 125.8 (CH), 60.9 (CH_2, O*C*H$_2$CH$_3$), 22.9 (CH_2), 18.6 (CH_2), 14.2 (CH_3, OCH$_2$*C*H$_3$); HRMS m/z 315.1092 (M + H$^+$), calcd for $C_{15}H_{14}N_4O_4H$ 315.1093.

3b: General procedure for the sequential one-pot synthesis of benzotriazoles:

First step: In an ordinary glass vial equipped with a magnetic stirring bar, to 0.5 mmol of enone **14** and 0.75 mmol of arylazide **2** dissolved in DMSO (1.0 mL) solvent, the catalyst pyrrolidine **15d** (0.05 mmol, 10 mol-%) was added and the reaction mixture was stirred at 25 °C for the time indicated in Table 12. The crude reaction mixture was worked up with aqueous NH_4Cl solution and the aqueous layer was extracted with dichloromethane (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. The crude triazole **35** was preceded for next step without purification.

Second step: In a 10 mL round bottom flask equipped with a magnetic stirring bar, to 0.5 mmol of above triazole **35** was added 5.0 mL dry toluene as a solvent and then DDQ (2 equiv., 1.0 mmol) was added. The reaction mixture was refluxed and monitored through TLC. After the completion of reaction, the crude product was purified by column chromatography on silica gel (hexane/EtOAc) to afford the benzotriazoles **36**.

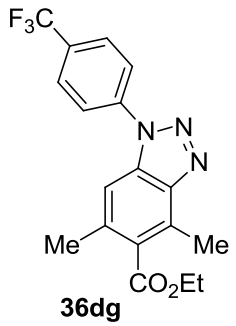
Ethyl 4-methyl-1-(4-(trifluoromethyl)phenyl)-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (36ag): Prepared following the procedure **3b** and purified by column chromatography using



36ag

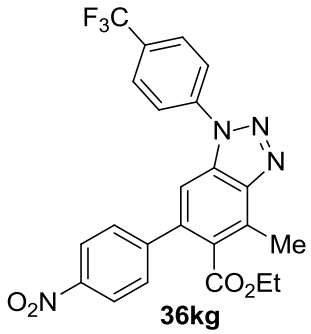
EtOAc/hexane and isolated as a white solid. Mp 130 °C; IR (neat): ν_{max} 2921, 2851, 1716, 1601, 1446, 1320, 1293, 1258, 1216, 1134, 1114, 1048, 842, 752 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.20 (1H, d, *J* = 8.8 Hz), 7.97 (2H, d, *J* = 8.4 Hz), 7.91 (2H, d, *J* = 8.4 Hz), 7.60 (1H, d, *J* = 8.8 Hz), 4.45 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.19 (3H, s, Ar-C*H*$_3$), 1.46 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{19}F NMR (376.5 MHz, $CDCl_3$) δ –62.58 (s, 3F); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.9 (C, O-*C*=O), 147.7 (C), 139.6 (C), 136.2 (C), 133.1 (C), 131.1 (CH), 130.7 (C, q, *J* = 32.5 Hz), 127.2 (2 x CH, q, *J* = 2.5 Hz), 125.8 (C), 123.6 (C, q, *J* = 271.2 Hz, *C*F$_3$), 122.6 (2 x CH), 106.9 (CH), 61.2 (CH_2, O*C*H$_2$CH$_3$), 15.4 (CH_3,

Ar-C*H*$_3$), 14.4 (CH_3, OCH_2CH_3); HRMS m/z 350.1116 (M + H^+), calcd for $C_{17}H_{14}F_3N_3O_2H$ 350.1116; Anal. calcd for $C_{17}H_{14}F_3N_3O_2$ (349.10): C, 58.45; H, 4.04; N, 12.03. Found: C, 58.36; H, 4.09, N, 12.07%.



36dg

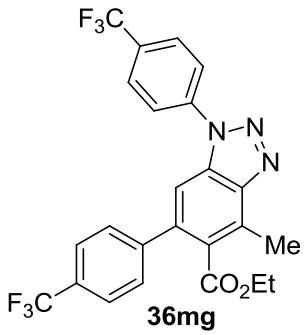
Ethyl 4,6-dimethyl-1-(4-(trifluoromethyl)phenyl)-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (36dg): Prepared following the procedure **3b** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. Mp 112 °C; IR (neat): ν_{max} 2920, 1708, 1321, 1276, 1160, 1115, 1048, 842 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.96 (2H, d, *J* = 8.0 Hz), 7.91 (2H, d, *J* = 8.0 Hz), 7.44 (1H, s), 4.50 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 2.86 (3H, s, Ar-C*H*$_3$), 2.54 (3H, s, Ar-C*H*$_3$), 1.46 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{19}F NMR (376.5 MHz, $CDCl_3$) δ –62.56 (s, 3F); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.9 (C, O-*C*=O), 145.1 (C), 139.7 (C), 136.9 (C), 131.9 (C), 131.1 (C), 130.5 (C, q, *J* = 33.0 Hz), 129.3 (C), 127.1 (2 x CH, q, *J* = 3.0 Hz), 123.6 (C, q, *J* = 271.0 Hz, *C*F$_3$), 122.6 (2 x CH), 108.1 (CH), 61.5 (CH_2, O*C*H$_2$CH$_3$), 20.8 (CH_3), 14.4 (CH_3), 14.3 (CH_3); HRMS m/z 364.1275 (M + H^+), calcd for $C_{18}H_{16}F_3N_3O_2H$ 364.1273.



36kg

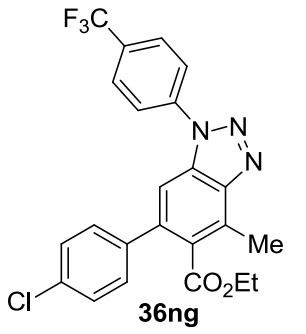
Ethyl 4-methyl-6-(4-nitrophenyl)-1-(4-(trifluoromethyl)phenyl)-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (36kg): Prepared following the procedure **3b** and purified by column chromatography using EtOAc/hexane and isolated as a yellow solid. Mp 196 °C; IR (neat): ν_{max} 2921, 2851, 1713, 1597, 1517, 1468, 1348, 1318, 1276, 1161, 1132, 1114, 1074, 1041, 848, 774 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.23 (2H, d, *J* = 8.8 Hz), 7.89 (2H, d, *J* = 8.4 Hz), 7.84 (2H, d, *J* = 8.4 Hz), 7.52 (2H, d, *J* = 8.8 Hz), 7.48 (1H, s, Ar-*H*), 4.06 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 2.90 (3H, s, Ar-C*H*$_3$), 0.97 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.9 (C, O-*C*=O), 147.5 (C), 147.1 (C), 146.1 (C), 139.5 (C), 139.4 (C), 131.7 (C), 131.4 (C), 131.0 (C, q, *J* = 33.0 Hz), 129.9 (C), 129.5 (2 x CH), 127.4 (2 x CH, q, *J* = 4.0 Hz), 123.6 (2 x CH), 123.5 (C, q, *J* = 271.0 Hz, *C*F$_3$), 122.8 (2 x CH), 108.5 (CH), 61.7 (CH_2, O*C*H$_2$CH$_3$), 14.6 (CH_3), 13.8 (CH_3); HRMS m/z 471.1284 (M + H^+), calcd for $C_{23}H_{17}F_3N_4O_4H$ 471.1280.

Ethyl 4-methyl-1,6-bis(4-(trifluoromethyl)phenyl)-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (36mg): Prepared following the procedure **3b** and purified by column chromatography using EtOAc/hexane and isolated as a yellow liquid.IR (neat): ν_{max} 2929, 1721, 1612, 1322, 1226, 1166, 1108, 1057, 1013, 837 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.97 (2H, d, *J* = 8.4 Hz), 7.89 (2H, d, *J* = 8.4 Hz), 7.70 (2H, d, *J* = 8.0 Hz), 7.56 (1H, s, Ar-*H*), 7.55 (2H, d, *J* = 8.0 Hz), 4.11 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 2.96 (3H, s, Ar-C*H*$_3$), 0.99 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{19}F NMR (376.5 MHz, $CDCl_3$) δ –62.59 (s, 3F), –62.63 (s, 3F); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.1 (C, O-*C*=O), 145.9 (C), 144.1 (C), 140.4 (C), 139.4 (C), 131.7 (C), 131.0 (C), 130.8 (C, q, *J* = 33.0 Hz), 130.24 (C, q, *J* = 33.0 Hz), 130.16 (C), 128.9 (2 x CH), 127.3 (2 x CH, q, *J* = 3.0 Hz), 125.3 (2 x CH, q, *J* = 2.0 Hz), 124.0 (C, q, *J* = 271.0 Hz, *C*F$_3$), 123.5 (C, q, *J* = 271.0 Hz, *C*F$_3$), 122.7 (2 x CH), 108.5 (CH), 61.5 (CH$_2$, O*C*H$_2$CH$_3$), 14.4 (CH$_3$, Ar-C*H*$_3$), 13.5 (CH$_3$, OCH$_2$*C*H$_3$); HRMS m/z 494.1301 (M + H$^+$), calcd for $C_{24}H_{17}F_6N_3O_2H$ 494.1303.



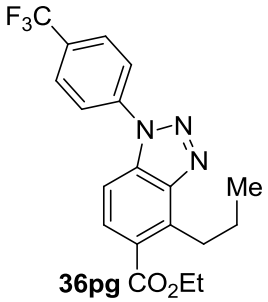
36mg

Ethyl 6-(4-chlorophenyl)-4-methyl-1-(4-(trifluoromethyl)phenyl)-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (36ng): Prepared following the procedure **3b** and purified by column chromatography using EtOAc/hexane and isolated as a yellow solid. Mp 135 °C; IR (neat): ν_{max} 2920, 2851, 1731, 1610, 1457, 1322, 1275, 1198, 1163, 1115, 1047, 828, 776 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.96 (2H, d, *J* = 8.4 Hz), 7.89 (2H, d, *J* = 8.4 Hz), 7.53 (1H, s, Ar-*H*), 7.41 (2H, d, *J* = 8.4 Hz), 7.35 (2H, d, *J* = 8.4 Hz), 4.13 (2H, q, *J* = 7.2 Hz), 2.94 (3H, s), 1.05 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.3 (C, O-*C*=O), 145.8 (C), 140.6 (C), 139.5 (C), 138.8 (C), 134.3 (C), 131.7 (C), 131.0 (C, q, *J* = 32.5 Hz), 130.6 (C), 130.4 (C), 129.8 (2 x CH), 128.6 (2 x CH), 127.2 (2 x CH, q, *J* = 2.5 Hz), 123.5 (C, q, *J* = 271.2 Hz, *C*F$_3$), 122.7 (2 x CH), 108.4 (CH), 61.5 (CH$_2$, O*C*H$_2$CH$_3$), 14.4 (CH$_3$), 13.7 (CH$_3$); HRMS m/z 460.1036 (M + H$^+$), calcd for $C_{23}H_{17}ClF_3N_3O_2H$ 460.1039.



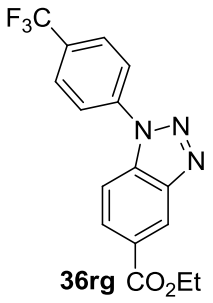
36ng

Ethyl 4-propyl-1-(4-(trifluoromethyl)phenyl)-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (36pg): Prepared following the procedure **3b** and purified by column chromatography using



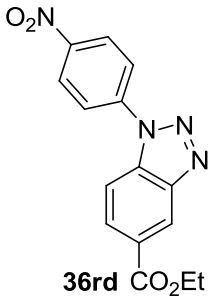
EtOAc/hexane and isolated as a white solid. Mp 97 °C; IR (neat): ν_{max} 2962, 2924, 1697, 1600, 1464, 1322, 1288, 1146, 1114, 1071, 1045, 847 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.15 (1H, d, *J* = 8.8 Hz), 7.97 (2H, d, *J* = 8.4 Hz), 7.90 (2H, d, *J* = 8.4 Hz), 7.59 (1H, d, *J* = 8.8 Hz), 4.44 (2H, q, *J* = 7.2 Hz), 3.64 (2H, t, *J* = 7.6 Hz), 1.91–1.81 (2H, m), 1.45 (3H, t, *J* = 7.2 Hz), 1.10 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.0 (C, O-*C*=O), 147.2 (C), 140.5 (C), 139.5 (C), 133.1 (C), 131.2 (CH), 130.6 (C, q, *J* = 33.0 Hz), 127.2 (2 x CH, q, *J* = 3.0 Hz), 125.5 (C), 123.6 (C, q, *J* = 271.0 Hz, *C*F_3), 122.6 (2 x CH), 107.1 (CH), 61.3 (CH_2, O*C*H_2CH_3), 30.9 (CH_2), 24.8 (CH_2), 14.5 (CH_3), 14.3 (CH_3); HRMS m/z 378.1430 (M + H^+), calcd for $C_{19}H_{18}F_3N_3O_2H$ 378.1429; Anal. calcd for $C_{19}H_{18}F_3N_3O_2$ (377.13): C, 60.47; H, 4.81; N, 11.14. Found: C, 60.36; H, 4.81, N, 11.21%.

Ethyl 1-(4-(trifluoromethyl)phenyl)-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (36rg): Prepared following the procedure **3b** and purified by column chromatography using

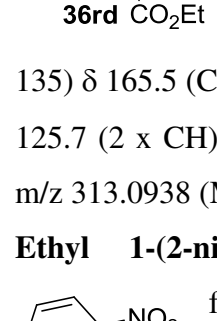


EtOAc/hexane and isolated as a yellow solid. Mp 164 °C; IR (neat): ν_{max} 2915, 2849, 1713, 1611, 1519, 1374, 1295, 1193, 1164, 1113, 1046, 1009, 834, 749 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.81 (1H, s, Ar-*H*), 8.22 (1H, d, *J* = 8.4 Hz), 7.90 (2H, d, *J* = 8.4 Hz), 7.84 (2H, d, *J* = 8.4 Hz), 7.73 (1H, d, *J* = 8.8 Hz), 4.38 (2H, q, *J* = 7.2 Hz, O*C*H_2CH_3), 1.38 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.6 (C, O-*C*=O), 146.5 (C), 139.3 (C), 134.0 (C), 130.8 (C, q, *J* = 33.0 Hz), 129.6 (CH), 127.5 (C), 127.3 (2 x CH, q, *J* = 3.0 Hz), 123.5 (C, q, *J* = 271.0 Hz, *C*F_3), 123.2 (CH), 122.7 (2 x CH), 109.9 (CH), 61.6 (CH_2, O*C*H_2CH_3), 14.3 (CH_3, OCH_2CH_3); HRMS m/z 336.0963 (M + H^+), calcd for $C_{16}H_{12}F_3N_3O_2H$ 336.0960; Anal. calcd for $C_{16}H_{12}F_3N_3O_2$ (335.08): C, 57.32; H, 3.61; N, 12.53. Found: C, 57.28; H, 3.68, N, 12.45%.

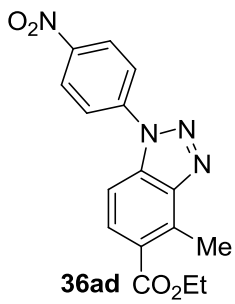
Ethyl 1-(4-nitrophenyl)-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (36rd): Prepared following the procedure **3b** and purified by column chromatography using EtOAc/hexane and isolated as a brown solid. Mp 168 °C; IR (neat): ν_{max} 2922, 1710, 1588, 1526, 1336, 1259, 1190, 1111, 1084, 1049, 1013, 849, 746 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.92 (1H, s), 8.54 (2H, d, *J* = 8.8 Hz), 8.35 (1H, dd, *J* = 8.8, 1.2 Hz), 8.09 (2H, d, *J* = 8.8 Hz), 7.86 (1H, d, *J* = 8.8 Hz), 4.48 (2H, q, *J* = 7.2 Hz), 1.47 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.5 (C, O-*C*=O), 147.2 (C), 146.7 (C), 141.4 (C), 133.8 (C), 130.1 (CH), 127.9 (C), 125.7 (2 x CH), 123.5 (CH), 122.5 (2 x CH), 109.9 (CH), 61.7 (CH_2), 14.3 (CH_3); HRMS m/z 313.0938 ($M + H^+$), calcd for $C_{15}H_{12}N_4O_4H$ 313.0937.



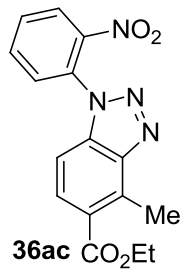
Ethyl 1-(2-nitrophenyl)-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (36rc): Prepared following the procedure **3b** and purified by column chromatography using EtOAc/hexane and isolated as a brown colored liquid. IR (neat): ν_{max} 2922, 2852, 1710, 1608, 1536, 1360, 1278, 1208, 1084, 1053, 781, 748 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.88 (1H, s), 8.24 (1H, d, *J* = 8.0 Hz), 8.22 (1H, d, *J* = 8.0 Hz), 7.92 (1H, t, *J* = 7.5 Hz), 7.80 (1H, t, *J* = 7.5 Hz), 7.75 (1H, d, *J* = 7.5 Hz), 7.45 (1H, d, *J* = 8.5 Hz), 4.46 (2H, q, *J* = 7.0 Hz), 1.45 (3H, t, *J* = 7.0 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.6 (C, O-*C*=O), 145.5 (C), 144.8 (C), 135.5 (C), 134.3 (CH), 131.0 (CH), 129.6 (CH), 129.0 (C), 128.4 (CH), 127.4 (C), 126.1 (CH), 123.0 (CH), 109.1 (CH), 61.4 (CH_2), 14.2 (CH_3); HRMS m/z 335.0757 ($M + Na^+$), calcd for $C_{15}H_{12}N_4O_4Na$ 335.0757.



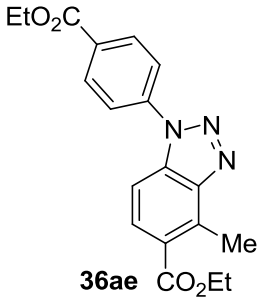
Ethyl 4-methyl-1-(4-nitrophenyl)-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (36ad): Prepared following the procedure **3b** and purified by column chromatography using EtOAc/hexane and isolated as a yellow solid. Mp 162 °C; IR (neat): ν_{max} 2926, 2856, 1720, 1590, 1512, 1343, 1291, 1251, 1212, 1183, 1111, 1042, 991, 857, 830 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.52 (2H, d, *J* = 9.2 Hz), 8.23 (1H, d, *J* = 8.8 Hz), 8.07 (2H, d, *J* = 9.2 Hz), 7.65 (1H, dd, *J* = 8.8, 0.4 Hz), 4.46 (2H, q, *J* = 7.2 Hz), 3.18 (3H, s, Ar-C*H*$_3$), 1.46 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.7 (C, O-*C*=O), 147.8 (C), 147.0 (C), 141.6 (C), 136.4 (C), 132.8 (C), 131.5 (CH), 126.1 (C), 125.6 (2 x CH), 122.4 (2 x CH), 106.9 (CH), 61.3 (CH_2, O*C*H_2CH_3), 15.5 (CH_3), 14.3 (CH_3); HRMS



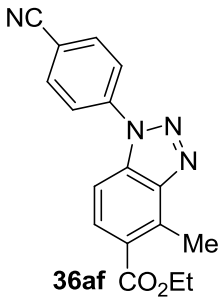
m/z 327.1093 (M + H^+), calcd for $C_{16}H_{14}N_4O_4H$ 327.1093; Anal. calcd for $C_{16}H_{14}N_4O_4$ (326.10): C, 58.89; H, 4.32; N, 17.17. Found: C, 58.76; H, 4.31, N, 17.12%.



Ethyl 4-methyl-1-(2-nitrophenyl)-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (36ac): Prepared following the procedure **3b** and purified by column chromatography using EtOAc/hexane and isolated as a yellow solid. Mp 93 °C; IR (neat): ν_{max} 2987, 2925, 1709, 1600, 1524, 1355, 1307, 1258, 1214, 1186, 1156, 1049, 780, 733 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.16 (1H, d, *J* = 8.4 Hz), 8.08 (1H, d, *J* = 8.8 Hz), 7.84 (1H, t, *J* = 7.6 Hz), 7.72 (1H, t, *J* = 7.6 Hz), 7.67 (1H, d, *J* = 7.6 Hz), 7.16 (1H, d, *J* = 8.8 Hz), 4.37 (2H, q, *J* = 7.2 Hz), 3.12 (3H, s, Ar-C*H*$_3$), 1.38 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.9 (C, O-*C*=O), 146.8 (C), 144.8 (C), 136.2 (C), 134.6 (C), 134.2 (CH), 131.2 (CH), 130.9 (CH), 129.3 (C), 128.5 (CH), 126.1 (CH), 125.7 (C), 106.0 (CH), 61.2 (CH_2, O*C*H$_2$CH$_3$), 15.5 (CH_3, Ar-*C*H$_3$), 14.4 (CH_3, OCH$_2$*C*H$_3$); HRMS m/z 327.1093 (M + H^+), calcd for $C_{16}H_{14}N_4O_4H$ 327.1093.

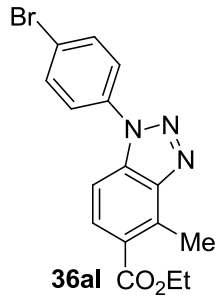


Ethyl 1-(4-(ethoxycarbonyl)phenyl)-4-methyl-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (36ae): Prepared following the procedure **3b** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. Mp 145 °C; IR (neat): ν_{max} 2981, 2926, 1704, 1600, 1512, 1447, 1364, 1271, 1216, 1184, 1101, 1047, 855, 762 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.31 (2H, d, *J* = 8.4 Hz), 8.18 (1H, d, *J* = 8.8 Hz), 7.91 (2H, d, *J* = 8.4 Hz), 7.61 (1H, d, *J* = 8.8 Hz), 4.45 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 4.44 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.18 (3H, s, Ar-C*H*$_3$), 1.46 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$), 1.45 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.9 (C, O-*C*=O), 165.5 (C, O-*C*=O), 147.6 (C), 140.1 (C), 136.1 (C), 133.1 (C), 131.4 (2 x CH), 130.9 (CH), 130.5 (C), 125.6 (C), 122.0 (2 x CH), 107.1 (CH), 61.5 (CH_2, O*C*H$_2$CH$_3$), 61.2 (CH_2, O*C*H$_2$CH$_3$), 15.5 (CH_3, Ar-*C*H$_3$), 14.4 (CH_3, OCH$_2$*C*H$_3$), 14.3 (CH_3, OCH$_2$*C*H$_3$); HRMS m/z 354.1454 (M + H^+), calcd for $C_{19}H_{19}N_3O_4H$ 354.1454.



36af

Ethyl 1-(4-cyanophenyl)-4-methyl-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (36af): Prepared following the procedure **3b** and purified by column chromatography using EtOAc/hexane and isolated as a yellow solid. Mp 205 °C; IR (neat): ν_{max} 2920, 2851, 2227, 1701, 1594, 1463, 1375, 1361, 1282, 1186, 1137, 1041, 968, 832 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.14 (1H, d, *J* = 8.8 Hz), 7.93 (2H, d, *J* = 8.8 Hz), 7.87 (2H, d, *J* = 8.8 Hz), 7.54 (1H, d, *J* = 8.8 Hz), 4.38 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 3.10 (3H, s, Ar-CH_3), 1.39 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.8 (C, O-*C*=O), 147.8 (C), 140.2 (C), 136.4 (C), 134.0 (2 x CH), 132.8 (C), 131.3 (CH), 126.0 (C), 122.6 (2 x CH), 117.8 (C), 112.3 (C, *C*N), 106.8 (CH), 61.3 (CH_2, OCH_2CH_3), 15.5 (CH_3, Ar-CH_3), 14.3 (CH_3, OCH_2CH_3); HRMS m/z 307.1195 ($M + H^+$), calcd for $C_{17}H_{14}N_4O_2H$ 307.1195.

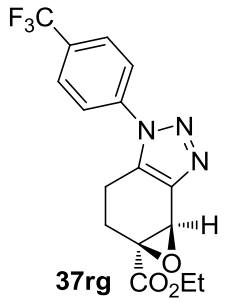


36al

Ethyl 1-(4-bromophenyl)-4-methyl-1*H*-benzo[d][1,2,3]triazole-5-carboxylate (36al): Prepared following the procedure **3b** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. Mp 160 °C; IR (neat): ν_{max} 2917, 1713, 1698, 1498, 1294, 1272, 1212, 1185, 1133, 1049, 1011, 835, 818, 754 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.16 (1H, d, *J* = 8.8 Hz), 7.77 (2H, d, *J* = 8.4 Hz), 7.68 (2H, d, *J* = 8.4 Hz), 7.53 (1H, d, *J* = 8.8 Hz), 4.44 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 3.17 (3H, s, Ar-CH_3), 1.45 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.0 (C, O-*C*=O), 147.5 (C), 136.1 (C), 135.8 (C), 133.2 (C), 133.1 (2 x CH), 130.8 (CH), 125.5 (C), 124.2 (2 x CH), 122.6 (C), 106.9 (CH), 61.2 (CH_2, OCH_2CH_3), 15.4 (CH_3, Ar-CH_3), 14.4 (CH_3, OCH_2CH_3); HRMS m/z 360.0347 ($M + H^+$), calcd for $C_{16}H_{14}BrN_3O_2H$ 360.0347.

3c: General procedure for the direct epoxidation of triazoles: In an oven dried round bottom flask, *m*-CPBA (1.2 equiv., 0.12 mmol) was added to a stirred solution of triazole **35rg** (1.0 equiv., 0.1 mmol) in dry CH_2Cl_2 at 0 °C. After complete consumption of the substrate (as monitored by TLC), the reaction mixture was diluted with CH_2Cl_2, washed with 10% aqueous K_2CO_3 solution, and brine, and dried with Na_2SO_4. Evaporation of solvent under reduced pressure gave crude product, which was further purified by column

chromatography on silica gel eluting with a mixture of hexane and ethyl acetate to yield the **37rg** in 85% yield as white solid.



37rg

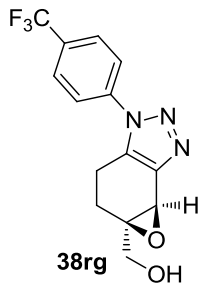
(5aS,6aR)-Ethyl 3-(4-(trifluoromethyl)phenyl)-4,5,5a,6a-tetrahydro-3*H*-oxireno[2',3':3,4]benzo[1,2-d][1,2,3]triazole-5a-carboxylate (37rg): Prepared following the procedure **3c** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. Mp 170 °C; IR (neat): ν_{max} 2962, 2924, 1726, 1616, 1376, 1259, 1092, 1013, 844, 794 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.77 (2H, d, *J* = 8.0 Hz), 7.61 (2H, d, *J* = 8.0 Hz), 4.47 (1H, s), 4.23 (2H, m, OCH_2CH_3), 2.87–2.64 (3H, m), 2.38–2.29 (1H, m), 1.27 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.0 (C, O-*C*=O), 141.8 (C), 138.6 (C), 132.7 (C), 131.4 (C, q, *J* = 32.5 Hz), 127.0 (2 x CH, q, *J* = 3.8 Hz), 123.44 (C, q, *J* = 271.2 Hz, CF_3), 123.36 (2 x CH), 62.2 (CH_2, OCH_2CH_3), 61.0 (C), 51.8 (CH), 22.1 (CH_2), 17.5 (CH_2), 14.1 (CH_3, OCH_2CH_3); HRMS m/z 354.1066 ($M + H^+$), calcd for $C_{16}H_{14}F_3N_3O_3H$ 354.1066; Anal. calcd for $C_{16}H_{14}F_3N_3O_3$ (353.09): C, 54.39; H, 3.99; N, 11.89. Found: C, 54.31; H, 4.03, N, 11.79%.

3d: General procedure for the reduction followed by epoxidation of triazoles:

First step: In an oven dried round bottom flask, $LiAlH_4$ (4 equiv., 3.6 mmol) was added to the solution of triazole (1.0 equiv., 0.9 mmol) **35rg** in dry ether at 0 °C. After stirring the reaction mixture 2 h at the same temperature, EtOAc was added to consume excess $LiAlH_4$, then the reaction quenched with water and extracted with ether. The combined ether extract was washed with brine and dried. Evaporation of the solvent and purification of residue over silica gel column using EtOAc/hexane as eluent furnished the allylic alcohol (70%) as white solid.

Second step: To the above allylic alcohol taken in dry CH_2Cl_2, *m*-CPBA (1.2 equiv.) was added at 0 °C. After complete consumption of the substrate (as monitored by TLC), the reaction mixture was diluted with CH_2Cl_2, washed with 10% aqueous K_2CO_3 solution, and brine, and dried with Na_2SO_4. Evaporation of solvent under reduced pressure gave crude product, which was purified by column chromatography on silica gel eluting with a mixture of hexane and ethyl acetate to yield the **38rg** in 85% yield as white solid.

((5aR,6aR)-3-(4-(Trifluoromethyl)phenyl)-4,5,5a,6a-tetrahydro-3*H*-oxireno[2',3':3,4]benzo[1,2-d][1,2,3]triazol-5a-yl)methanol (38rg):



38rg

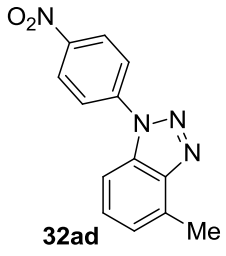
Prepared following the procedure **3d** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. Mp 178 °C; IR (neat): ν_{max} 3330 (OH), 1617, 1524, 1418, 1322, 1168, 1113, 1064, 1007, 844 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.74 (2H, d, *J* = 8.5 Hz), 7.60 (2H, d, *J* = 8.5 Hz), 4.28 (1H, s), 3.92 (1H, br d, *J* = 12.5 Hz), 3.79 (1H, br d, *J* = 12.0 Hz), 2.79–2.74 (2H, m), 2.44–2.40 (1H, m), 2.09 (1H, br s, OH), 1.94–1.87 (1H, m); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 143.0 (C), 138.7 (C), 132.8 (C), 131.2 (C, q, *J* = 32.5 Hz), 126.9 (2 x CH, q, *J* = 3.8 Hz), 123.4 (C, q, *J* = 271.2 Hz, *C*F_3), 123.3 (2 x CH), 65.0 (C), 63.5 (CH_2), 49.8 (CH), 22.6 (CH_2), 17.7 (CH_2); HRMS m/z 312.0965 ($M + H^+$), calcd for $C_{14}H_{12}F_3N_3O_2H$ 312.0960; Anal. calcd for $C_{14}H_{12}F_3N_3O_2$ (311.08): C, 54.02; H, 3.89; N, 13.50. Found: C, 54.12; H, 3.85, N, 13.42%.

3e: General procedure for the hydrolysis followed by decarboxylation of benzotriazoles:

First step: In a 10 mL round bottom flask equipped with a magnetic stirring bar, to 0.3 mmol benzotriazole **36** was added mixture of MeOH (0.5 mL), H_2O (0.5 mL), THF (2 mL) as a solvent and then $LiOH.H_2O$ (1.8 mmol, 6 equiv.) was added and the reaction mixture was stirred for 4-5 h at 25 °C as indicated in Scheme 8b-c. The reaction mixture was neutralized with 2N HCl and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were washed with water and brine and dried. The crude product was preceded for next step without purification.

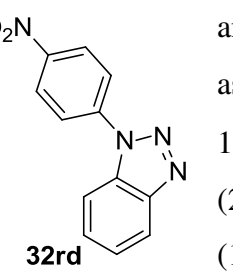
Second step: A mixture of the above acid, copper powder (40 mol-%) and quinoline (0.1 M) were added to a sealed glass tube and the mixture was heated at 220 °C for 1 h. Upon cooling the reaction mixture to room temperature, the mixture was neutralized with 2N HCl and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were washed with water and brine and dried. The residue obtained upon evaporation of the solvent was purified by flash chromatography to yield the benzotrizoles **32**.

4-Methyl-1-(4-nitrophenyl)-1*H*-benzo[d][1,2,3]triazole (32ad): Prepared following the procedure **3e** and purified by column chromatography using EtOAc/hexane and isolated as a yellow solid. Mp 201 °C; IR (neat): ν_{max} 2923, 2852, 1612, 1593, 1522, 1506, 1344, 1323, 1288, 1243, 1163, 1119, 1054, 850, 779 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.49 (2H, d, *J* = 8.8 Hz), 8.07 (2H, d, *J* = 9.2 Hz), 7.64 (1H, d, *J* = 8.4 Hz), 7.53 (1H, t, *J* = 8.4 Hz), 7.27 (1H, d, *J* = 7.6 Hz), 2.88 (3H, s, Ar-C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 146.78 (C), 146.75 (C), 142.2 (C), 132.1 (C), 131.6 (C), 129.2 (CH), 125.5 (2 x CH), 125.1 (CH), 122.2 (2 x CH), 107.4 (CH), 16.8 (CH_3); HRMS m/z 255.0884 (M + H^+), calcd for $C_{13}H_{10}N_4O_2H$ 255.0882; Anal. calcd for $C_{13}H_{10}N_4O_2$ (254.08): C, 61.41; H, 3.96; N, 22.04. Found: C, 61.28; H, 3.91, N, 22.15%.



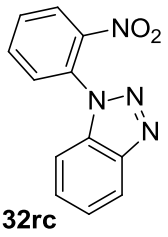
32ad

1-(4-Nitrophenyl)-1*H*-benzo[d][1,2,3]triazole (32rd): Prepared following the procedure **3e** and purified by column chromatography using EtOAc/hexane and isolated as a yellow solid. Mp 181 °C; IR (neat): ν_{max} 2924, 2850, 1590, 1515, 1450, 1322, 1243, 1054, 849, 803, 734 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.52 (2H, d, *J* = 8.8 Hz), 8.22 (1H, d, *J* = 8.4 Hz), 8.09 (2H, d, *J* = 8.4 Hz), 7.85 (1H, d, *J* = 8.4 Hz), 7.67 (1H, t, *J* = 7.2 Hz), 7.52 (1H, t, *J* = 7.6 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 146.94 (C), 146.90 (C), 141.9 (C), 131.7 (C), 129.3 (CH), 125.6 (2 x CH), 125.2 (CH), 122.3 (2 x CH), 121.0 (CH), 110.1 (CH); HRMS m/z 241.0721 (M + H^+), calcd for $C_{12}H_8N_4O_2H$ 241.0725; Anal. calcd for $C_{12}H_8N_4O_2$ (240.06): C, 60.00; H, 3.36; N, 23.32. Found: C, 60.12; H, 3.31, N, 23.42%.



32rd

1-(2-Nitrophenyl)-1*H*-benzo[d][1,2,3]triazole (32rc): Prepared following the procedure **3e** and purified by column chromatography using EtOAc/hexane and isolated as a yellow liquid. IR (neat): ν_{max} 2924, 1607, 1530, 1350, 1283, 1194, 1056, 850, 743 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.21 (1H, dd, *J* = 8.0, 1.5 Hz), 8.19 (1H, td, *J* = 8.5, 1.0 Hz), 7.89 (1H, dt, *J* = 7.5, 1.5 Hz), 7.78 (1H, dd, *J* = 8.0, 1.5 Hz), 7.75 (1H, dd, *J* = 8.0, 1.5 Hz), 7.57 (1H, ddd, *J* = 8.0, 7.0, 1.0 Hz), 7.48 (1H, ddd, *J* = 8.0, 7.0, 1.0 Hz), 7.43 (1H, td, *J* = 8.5, 1.0 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 145.9 (C), 144.9 (C), 134.1 (CH), 133.3 (C), 130.6 (CH), 129.6 (C), 128.9 (CH), 128.4 (CH), 126.0 (CH), 124.7 (CH), 120.6 (CH), 109.2 (CH); HRMS m/z 241.0728



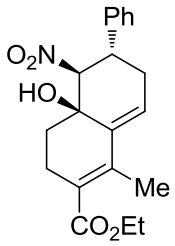
32rc

(M + H^+), calcd for $C_{12}H_8N_4O_2H$ 241.0725; Anal. calcd for $C_{12}H_8N_4O_2$ (240.06): C, 60.00; H, 3.36; N, 23.32. Found: C, 60.07; H, 3.40, N, 23.28%.

4a: **General procedure for the synthesis of γ-nitroaldehydes 48 *via* Hayashi method:** To a MeOH solution (1.2 ml) of (*S*)-DPPOTMS **15k** catalyst (19.5 mg, 0.06 mmol, 10 mol%) and cinnamaldehyde **50** (0.6 mmol) was added $PhCO_2H$ (0.12 mmol, 10 mol%) and nitromethane **51** (1.8 mmol) at room temperature. After stirring the reaction mixture at RT for the time 16-96 h, resulting mixture was quenched with saturated aqueous $NaHCO_3$. The organic materials were extracted with AcOEt and dried over anhydrous Na_2SO_4, then concentrated under reduced pressure. The residue was purified by silica gel column chromatography (AcOEt/hexane) to afford γ-nitroaldehyde **48**.

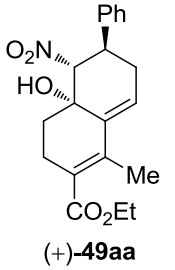
4b: **General procedure for the synthesis of γ-nitroaldehydes 48 *via* Benjamin List method:** 250 mL of a 0.8 M solution of (*S*)-DPPOTMS **15k** catalyst in dry MeCN was added to the corresponding nitroolefin **46** (1 mmol) in a vial under argon at 0°C. Then 1 mL of a 5M solution of acetaldehyde in anhydrous MeCN, prepared at 0°C from freshly distilled acetaldehyde **20w**, was added at 12mL/min (tad= 83.3 min). After stirring for 62-93 h, the reaction mixture was treated with 1N HCl and extracted twice with ethyl acetate. The organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. Purification by flash column chromatography (hexane/ethyl acetate, 3:1) gave the corresponding γ-nitroaldehyde **48.**

4c: **General procedure for the (*S*)-1-(2-pyrrolidinylmethyl)pyrrolidine (15m)-catalyzed cascade Claisen-Schmidt/Henry reactions**: In an ordinary glass vial equipped with a magnetic stirring bar, to 0.5 mmol of the Hagemann's esters **14** was added 1.0 mL of DMSO solvent, and then the catalyst (*S*)-1-(2-pyrrolidinylmethyl)pyrrolidine **15m** (0.1 mmol) was added and then 0.75 mmol of aldehydes **48** was added in one-portion and the reaction mixture was stirred at 25 °C for the time indicated in Tables 13-15. The crude reaction mixture was worked up with aqueous NH_4Cl solution and the aqueous layer was extracted with dichloromethane (2 x 20 mL).The combined organic layers were dried (Na_2SO_4), filtered and concentrated. The pure cascade products **49, 52-54** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).



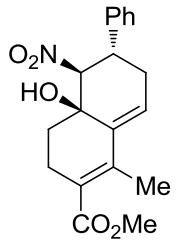
(–)-**49aa**

(4a*R*,5*S*,6*S*)-Ethyl 4a-hydroxy-1-methyl-5-nitro-6-phenyl-3,4,4a,5,6,7-hexahydronaphthalene-2-carboxylate (49aa): Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiral cel OD-H column (hexane/2-propanol = 95:5, flow rate 1.0 mL/min, λ = 254 nm), t_R = 36.25 min (minor), t_R = 42.45 min (major). **$[\alpha]_D^{25}$ = -165.99° (*c* = 0.3 g/100 mL, $CHCl_3$, 99.99% *ee*, 99.99% de);** Mp 207-210 °C; IR (neat): ν_{max} 3518 (O-*H*), 2928, 1705 (O-C=O), 1549, 1497, 1452, 1370, 1246, 1074, 758 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35-7.32 (2H, m), 7.29-7.27 (3H, m), 6.19 (1H, t, *J* = 3.6 Hz), 4.91 (1H, d, *J* = 12.4 Hz), 4.24 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 3.96 (1H, dt, *J* = 12.0, 6.4 Hz), 2.87 (1H, td, *J* = 20.0, 5.6 Hz), 2.80 (1H, s, O-*H*), 2.71-2.63 (1H, m), 2.58-2.48 (2H, m), 2.12 (3H, s, olefinic-CH_3), 1.92 (1H, dd, *J* = 13.6, 3.6 Hz), 1.72 (1H, dt, *J* = 12.4, 5.6 Hz), 1.32 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.2 (C, O-C=O), 139.2 (C), 135.5 (C), 135.0 (C), 128.9 (2 x CH), 127.8 (CH), 127.5 (3 x CH), 127.4 (C), 95.6 (CH), 68.4 (C), 60.6 (CH_2, OCH_2CH_3), 39.3 (CH), 35.0 (CH_2), 31.9 (CH_2), 22.8 (CH_2), 16.0 (CH_3, olefinic-CH_3), 14.2 (CH_3, OCH_2CH_3); LRMS m/z 356.00 (M - H^+), calcd $C_{20}H_{23}NO_5$ 357.1576; Anal. calcd for $C_{20}H_{23}NO_5$ (357.16): C, 67.21; H, 6.49; N, 3.92. Found: C, 67.12; H, 6.41; N, 3.98%; HRMS m/z 375.1920 (M + NH_4^+), calcd for $C_{20}H_{23}NO_5NH_4$ 375.1920.



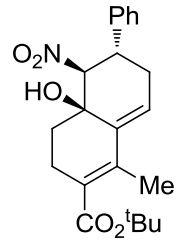
(+)-**49aa**

(4a*S*,5*R*,6*R*)-Ethyl 4a-hydroxy-1-methyl-5-nitro-6-phenyl-3,4,4a,5,6,7-hexahydronaphthalene-2-carboxylate (49aa): Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiral cel OD-H column (hexane/2-propanol = 95:5, flow rate 1.0 mL/min, λ = 254 nm), t_R = 30.70 min (major), t_R = 37.23 min (minor). **$[\alpha]_D^{25}$ = +187.38° (*c* = 0.3 g/100 mL, $CHCl_3$, 93% *ee*, 99.99% de);** IR (neat): ν_{max} 3463 (O-*H*), 2920, 2854, 1709 (O-C=O), 1545, 1451, 1369, 1238, 1073, 761 cm^{-1}**.**



(–)-**49ba**

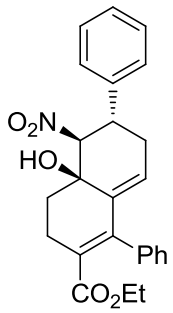
(4a*R*,5*S*,6*S*)-Methyl 4a-hydroxy-1-methyl-5-nitro-6-phenyl-3,4,4a,5,6,7-hexahydronaphthalene-2-carboxylate (49ba): Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiral pak AD-H column (hexane/2-propanol = 80:20, flow rate 1.0 mL/min, λ = 254 nm), t_R = 10.83 min (minor), t_R = 25.02 min (major). **$[\alpha]_D^{25}$ = -160.58° (*c* = 0.186 g/100 mL, $CHCl_3$, 96% *ee*, 99.99% de);** Mp 198-202 °C; IR (KBr): ν_{max} 3428 (O-*H*), 2955, 1701 (O-C=O), 1630, 1547, 1495, 1439, 1233, 1144, 1072, 968 and 822 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35-7.32 (2H, m), 7.29-7.25 (3H, m), 6.21 (1H, t, *J* = 3.6 Hz), 4.91 (1H, d, *J* = 12.4 Hz), 3.96 (1H, dt, *J* = 12.0, 6.4 Hz), 3.78 (3H, s, OCH_3), 2.87 (1H, td, *J* = 20.0, 5.6 Hz), 2.80 (1H, s, O-*H*), 2.70-2.45 (3H, m), 2.13 (3H, s, olefinic-CH_3), 1.93 (1H, ddd, *J* = 13.6, 4.8, 1.6 Hz), 1.72 (1H, dt, *J* = 12.4, 5.2 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.5 (C, O-C=O), 139.2 (C), 135.7 (C), 135.5 (C), 128.9 (2 x CH), 127.85 (CH), 127.82 (CH), 127.5 (2 x CH), 127.0 (C), 95.6 (CH), 68.4 (C), 51.7 (CH_3, OCH_3), 39.3 (CH), 35.0 (CH_2), 31.9 (CH_2), 22.8 (CH_2), 16.1 (CH_3, olefinic-CH_3); HRMS m/z 366.1318 (M + Na), calcd $C_{19}H_{21}NO_5Na$ 366.1317.



(–)-**49ca**

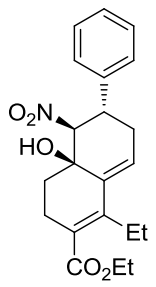
(4a*R*,5*S*,6*S*)-*tert*-Butyl 4a-hydroxy-1-methyl-5-nitro-6-phenyl-3,4,4a,5,6,7-hexahydronaphthalene-2-carboxylate (49ca): Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiral pak AD-H column (hexane/2-propanol = 80:20, flow rate 1.0 mL/min, λ = 254 nm), t_R = 6.02 min (major), t_R = 8.28 min (minor). **$[\alpha]_D^{25}$ = -183.58° (*c* = 0.314 g/100 mL, $CHCl_3$, 94% *ee*, 99.99% de);** Mp 187-190 °C; IR (KBr): ν_{max} 3463 (O-*H*), 2921, 1677 (O-C=O), 1545, 1452, 1359, 1288, 1162, 1079, 833, 756 and 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38-7.34 (2H, m), 7.31-7.29 (3H, m), 6.16 (1H, t, *J* = 3.6 Hz), 4.92 (1H, d, *J* = 12.4 Hz), 3.98 (1H, dt, *J* = 12.4, 6.4 Hz), 2.88 (1H, td, *J* = 20.0, 5.6 Hz), 2.78 (1H, s, O-*H*), 2.69-2.44 (3H, m), 2.10 (3H, s, olefinic-CH_3), 1.93 (1H, ddd, *J* = 13.6, 4.8, 1.6 Hz), 1.74 (1H, dt, *J* = 12.8, 5.6 Hz), 1.54 (9H, s, OC(CH_3)$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.9 (C, O-*C*=O), 139.3 (C), 135.5 (C), 132.8 (C), 129.1 (C), 128.9 (2 x CH), 127.8 (CH), 127.6 (2 x CH),

126.7 (CH), 95.7 (CH), 81.1 (C, O*C*$(CH_3)_3$), 68.5 (C), 39.3 (CH), 35.0 (CH_2), 32.0 (CH_2), 28.2 (3 x CH_3, OC(CH_3)$_3$), 22.9 (CH_2), 15.9 (CH_3, olefinic-CH_3); HRMS m/z 408.1787 (M + Na), calcd $C_{22}H_{27}NO_5Na$ 408.1787.



(–)-**49sa**

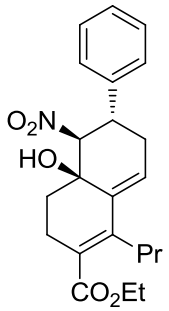
(4a*R*,5*S*,6*S*)-Ethyl 4a-hydroxy-5-nitro-1,6-diphenyl-3,4,4a,5,6,7-hexahydronaphthalene-2-carboxylate (49sa): Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a yellow solid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiral cel OD-H column (hexane/2-propanol = 90:10, flow rate 1.0 mL/min, λ = 254 nm), t_R = 15.85 min (major), t_R = 18.58 min (minor). **$[\alpha]_D^{25}$ = -222.74° (*c* = 0.086 g/100 mL, $CHCl_3$, 94% *ee*, 99.99% de);** Mp 228-230 °C; IR (neat): ν_{max} 3518 (O-*H*), 2924, 1732, 1688, 1549, 1454, 1373, 1262, 1074, 1024, 802 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$) δ 7.38-7.32 (5H, m), 7.29-7.28 (3H, m), 7.14 (2H, d, *J* = 6.0 Hz), 5.54 (1H, t, *J* = 4.0 Hz), 4.97 (1H, d, *J* = 12.5 Hz), 3.98 (1H, dt, *J* = 11.5, 6.0 Hz), 3.86 (2H, q, *J* = 7.0 Hz, OC$H_2$$CH_3$), 2.95 (1H, s, O-*H*), 2.83-2.70 (3H, m), 2.44 (1H, dd, *J* = 20.5, 11.0 Hz), 2.08 (1H, ddd, *J* = 13.5, 4.5, 2.0 Hz), 1.92-1.86 (1H, m), 0.84 (3H, t, *J* = 7.0 Hz, $OCH_2C$$H_3$); ^{13}C NMR (500 MHz, $CDCl_3$, DEPT-135) δ 168.6 (C, O-C=O), 140.9 (C), 139.2 (C), 138.8 (C), 136.1 (C), 132.1 (CH), 129.0 (2 x CH), 128.9 (2 x CH), 128.2 (C), 127.8 (3 x CH), 127.5 (2 x CH), 127.2 (CH), 95.5 (CH), 68.4 (C), 60.3 (CH_2, OCH_2CH_3), 39.4 (CH), 35.0 (CH_2), 31.9 (CH_2), 22.5 (CH_2), 13.5 (CH_3, $OCH_2$$CH_3$); LRMS m/z 420.30 (M + H^+), calcd $C_{25}H_{25}NO_5$ 419.1733; Anal. calcd for $C_{25}H_{25}NO_5$ (419.17): C, 71.58; H, 6.01; N, 3.34. Found: C, 71.45; H, 6.15; N, 3.26%; HRMS m/z 437.2077 (M + NH_4^+), calcd for $C_{25}H_{25}NO_5NH_4$ 437.2076.



(–)-**49ta**

(4a*R*,5*S*,6*S*)-Ethyl 1-ethyl-4a-hydroxy-5-nitro-6-phenyl-3,4,4a,5,6,7-hexahydronaphthalene-2-carboxylate (49ta): Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiral cel OD-H column (hexane/2-propanol = 90:10, flow rate 1.0 mL/min, λ = 254 nm), t_R = 13.81

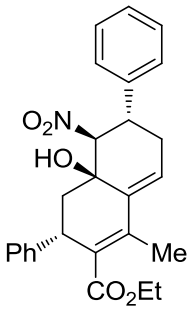
min (minor), t_R = 15.77 min (major). **$[\alpha]_D^{25}$ = -149.11° (*c* = 0.41 g/100 mL, $CHCl_3$, 99% *ee*, 99.99% de);** Mp 167-170 °C; IR (neat): ν_{max} 3449 (O-*H*), 2924, 1875, 1696, 1547, 1493, 1470, 1452, 1370, 1269, 1119 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.35-7.32 (2H, m), 7.29-7.26 (3H, m), 6.21 (1H, t, *J* = 3.5 Hz), 4.91 (1H, d, *J* = 12.5 Hz), 4.24 (2H, q, *J* = 7.0 Hz, OCH_2CH_3), 3.96 (1H, dt, *J* = 11.5, 6.5 Hz), 2.87 (1H, td, *J* = 20.0, 5.5 Hz), 2.75 (1H, s, O-*H*), 2.67-2.58 (2H, m), 2.57-2.49 (3H, m), 1.91 (1H, ddd, *J* = 13.5, 5.0, 1.5 Hz), 1.73-1.67 (1H, m), 1.32 (3H, t, *J* = 7.0 Hz, OCH_2CH_3), 1.13 (3H, t, *J* = 7.0 Hz, CH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.9 (C, O-*C*=O), 140.9 (C), 139.3 (C), 133.7 (C), 128.9 (2 x CH), 127.8 (CH), 127.6 (2 x CH), 127.1 (CH), 126.6 (C), 95.7 (CH), 68.4 (C), 60.5 (CH_2, OCH_2CH_3), 39.2 (CH), 35.0 (CH_2), 31.8 (CH_2), 22.8 (CH_2), 22.7 (CH_2), 14.4 (CH_3, olefinic-CH_3), 14.2 (CH_3); LRMS m/z 372.25 ($M + H^+$), calcd $C_{21}H_{25}NO_5$ 371.1733; Anal. calcd for $C_{21}H_{25}NO_5$ (371.17): C, 67.91; H, 6.78; N, 3.77. Found: C, 67.85; H, 6.81; N, 3.72%; HRMS m/z 394.1631 (M + Na), calcd $C_{21}H_{25}NO_5Na$ 394.1630.



(–)-**49pa**

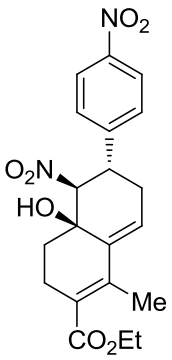
(4a*R*,5*S*,6*S*)-Ethyl 4a-hydroxy-5-nitro-6-phenyl-1-propyl-3,4,4a,5,6,7-hexahydronaphthalene-2-carboxylate (49pa): Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiral cel OD-H column (hexane/2-propanol = 90:10, flow rate 0.5 mL/min, λ = 254 nm), t_R = 23.03 min (minor), t_R = 25.25 min (major). **$[\alpha]_D^{25}$ = -160.11° (*c* = 0.49 g/100 mL, $CHCl_3$, 97% *ee*, 99.99% de);** Mp 143-146 °C; IR (neat): ν_{max} 3453 (O-*H*), 3032, 2967, 1958, 1877, 1682, 1549, 1368, 1263, 1146, 1016, 964 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38-7.34 (2H, m), 7.31-7.29 (3H, m), 6.20 (1H, t, *J* = 4.0 Hz), 4.93 (1H, d, *J* = 12.4 Hz), 4.26 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 3.98 (1H, dt, *J* = 12.0, 6.4 Hz), 2.89 (1H, td, *J* = 20.0, 5.6 Hz), 2.78 (1H, brs, -O-*H*), 2.71-2.45 (5H, m), 1.94 (1H, ddd, *J* = 13.6, 4.8, 1.6 Hz), 1.72 (1H, dt, *J* = 12.4, 5.6 Hz), 1.62-1.47 (2H, m), 1.35 (3H, t, *J* = 7.2 Hz, OCH_2CH_3), 0.98 (3H, t, *J* = 7.2 Hz, $CH_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.0 (C, O-C=O), 139.5 (C), 139.3 (C), 134.0 (C), 128.9 (2 x CH), 127.8 (CH), 127.5 (2 x CH), 127.1 (CH), 127.0 (C), 95.7 (CH), 68.4 (C), 60.5 (CH_2, OCH_2CH_3), 39.2 (CH), 35.0 (CH_2), 31.8 (CH_2), 31.5 (CH_2), 23.2 (CH_2),

22.8 (CH_2), 14.3 (CH_3), 14.2 (CH_3); LRMS m/z 386.25 (M + H^+), calcd $C_{22}H_{27}NO_5$ 385.1889; Anal. calcd for $C_{22}H_{27}NO_5$ (385.19): C, 68.55; H, 7.06; N, 3.63. Found: C, 68.59; H, 7.12; N, 3.69%; HRMS m/z 403.2233 (M + NH_4^+), calcd for $C_{22}H_{27}NO_5NH_4$ 403.2233.



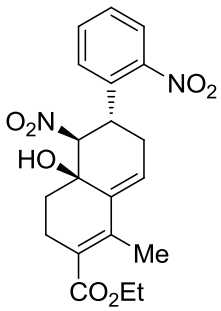
(–)-**49ha**

(3*S*,4a*R*,5*S*,6*S*)-Ethyl 4a-hydroxy-1-methyl-5-nitro-3,6-diphenyl-3,4,4a,5,6,7-hexahydronaphthalene-2-carboxylate (49ha): Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a yellow solid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiral cel OD-H column (hexane/2-propanol = 85:15, flow rate 1.0 mL/min, λ = 254 nm), t_R = 9.02 min (minor), t_R = 10.78 min (major). **$[\alpha]_D^{25}$ = -35.100° (*c* = 0.2 g/100 mL, $CHCl_3$, 93% *ee*, 99.99% de);** Mp 208-211 °C; IR (neat): ν_{max} 3524 (O-*H*), 2920, 2307, 1952, 1881, 1715 (O-C=O), 1551, 1495, 1454, 1368, 1262 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.34-7.30 (3H, m), 7.26-7.24 (4H, m), 7.20-7.15 (3H, m), 6.22 (1H, dd, *J* = 4.8, 3.2 Hz), 4.91 (1H, d, *J* = 12.4 Hz), 4.13-4.06 (1H, m), 3.93 (1H, dt, *J* = 11.6, 6.4 Hz), 3.82 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.03 (1H, s, O-*H*), 2.88 (1H, td, *J* = 20.0, 5.6 Hz), 2.57 (1H, dd, *J* = 20.0, 11.2 Hz), 2.18 (1H, dd, *J* = 14.0, 5.2 Hz), 2.12 (3H, d, *J* = 2.0 Hz), 1.81 (1H, dd, *J* = 13.6, 12.0 Hz), 0.83 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.6 (C, O-C=O), 143.1 (C), 139.1 (C), 135.1 (C), 133.4 (C), 131.7 (C), 128.9 (2 x CH), 128.5 (2 x CH), 127.93 (2 x CH), 127.86 (CH), 127.5 (2 x CH), 127.3 (CH), 126.8 (CH), 95.4 (CH), 68.7 (C), 60.2 (CH_2, O*C*H$_2$CH$_3$), 42.2 (CH_2), 40.6 (CH), 39.2 (CH), 34.9 (CH_2), 16.5 (CH_3, olefinic-*C*H$_3$), 13.5 (CH_3, OCH$_2$*C*H$_3$); LRMS m/z 432.00 (M - H^+), calcd $C_{26}H_{27}NO_5$ 433.1889; Anal. calcd for $C_{26}H_{27}NO_5$ (433.19): C, 72.04; H, 6.28; N, 3.23. Found: C, 72.18; H, 6.31; N, 3.16%; HRMS m/z 451.2233 (M + NH_4^+), calcd for $C_{26}H_{27}NO_5NH_4$ 451.2233.



(–)-**49ab**

(4a*R*,5*S*,6*S*)-Ethyl 4a-hydroxy-1-methyl-5-nitro-6-(4-nitrophenyl)-3,4,4a,5,6,7-hexahydronaphthalene-2-carboxylate (49ab): Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a yellow solid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiral cel OD-H column (hexane/2-propanol = 90:10, flow rate 1.0 mL/min, λ = 254 nm), t_R = 44.13 min (minor), t_R = 53.55 min (major). **$[\alpha]_D^{25}$ = -133.50° (*c* = 0.7 g/100 mL, $CHCl_3$, 94% *ee*, 99.99% de);** Mp 195-200 °C; IR (neat): ν_{max} 3503 (O-*H*), 2928, 1684, 1522, 1456, 1348, 1242, 1105, 856, 756 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.20 (2H, d, *J* = 8.4 Hz), 7.49 (2H, d, *J* = 8.4 Hz), 6.19 (1H, t, *J* = 3.6 Hz), 4.95 (1H, d, *J* = 12.4 Hz), 4.26 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 4.13 (1H, dt, *J* = 11.6, 6.4 Hz), 2.89 (1H, dt, *J* = 20.0, 5.6 Hz), 2.82 (1H, s, O-*H*), 2.70-2.49 (3H, m), 2.12 (3H, s, olefinic-CH_3), 2.00 (1H, dd, *J* = 13.6, 4.8 Hz), 1.75 (1H, dt, *J* = 12.4, 5.6 Hz), 1.33 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.1 (C, O-C=O), 147.4 (C), 147.1 (C), 135.8 (C), 134.5 (C), 128.5 (2 x CH), 127.7 (C), 126.4 (CH), 124.1 (2 x CH), 94.9 (CH), 68.4 (C), 60.7 (CH_2, OCH_2CH_3), 39.1 (CH), 34.4 (CH_2), 31.7 (CH_2), 22.7 (CH_2), 16.0 (CH_3, olefinic-CH_3), 14.2 (CH_3, OCH_2CH_3); LRMS m/z 401.00 ($M - H^+$), calcd $C_{20}H_{22}N_2O_7$ 402.1427; Anal. calcd for $C_{20}H_{22}N_2O_7$ (402.14): C, 59.70; H, 5.51; N, 6.96. Found: C, 59.81; H, 5.48; N, 6.85%; HRMS m/z 425.1325 (M + Na), calcd $C_{20}H_{22}N_2O_7Na$ 425.1325.

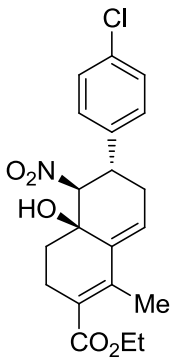


(+)-**49ac**

(4a*R*,5*S*,6*S*)-Ethyl 4a-hydroxy-1-methyl-5-nitro-6-(2-nitrophenyl)-3,4,4a,5,6,7-hexahydronaphthalene-2-carboxylate (49ac): Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a yellow solid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiral cel OD-H column (hexane/2-propanol = 95:5, flow rate 1.0 mL/min, λ = 254 nm), t_R = 47.94 min (major), t_R = 54.17 min (minor). **$[\alpha]_D^{25}$ = +4.888° (*c* = 0.8 g/100 mL, $CHCl_3$, 96% *ee*, 99.99% de);** Mp 189-192 °C; IR (neat): ν_{max} 3445 (O-*H*), 2965, 2926, 1726, 1682, 1551, 1528, 1447, 1356, 1260, 1092, 926 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.84 (1H, d, *J* = 8.0 Hz), 7.59 (1H, t, *J* = 7.2 Hz),

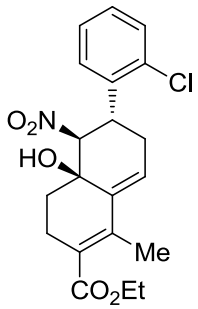
7.46 (1H, d, *J* = 7.6 Hz), 7.42 (1H, t, *J* = 7.6 Hz), 6.19 (1H, t, *J* = 3.6 Hz), 5.01 (1H, d, *J* = 11.6 Hz), 4.58-4.51 (1H, m), 4.24 (2H, q, *J* = 7.2 Hz, OCH_2CH$_3$), 3.17 (1H, d, *J* = 18.8 Hz), 2.67-2.60 (2H, m), 2.50 (2H, dd, *J* = 18.4, 4.4 Hz), 2.11 (3H, s, olefinic-CH_3), 2.06-2.02 (1H, m), 1.72 (1H, dt, *J* = 12.4, 5.6 Hz), 1.32 (3H, t, *J* = 7.2 Hz, OCH$_2$CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.2 (C, O-*C*=O), 150.5 (C), 135.8 (C), 134.6 (C), 133.2 (2 x CH), 128.4 (CH), 127.6 (C), 127.0 (C), 126.8 (CH), 125.0 (CH), 94.4 (CH), 68.5 (C), 60.7 (CH_2, O*C*H$_2$CH$_3$), 34.2 (CH_2), 33.8 (CH), 31.7 (CH_2), 22.8 (CH_2), 16.1 (CH_3, olefinic-*C*H$_3$), 14.2 (CH_3, OCH$_2$*C*H$_3$); LRMS m/z 401.30 (M - H^+), calcd $C_{20}H_{22}N_2O_7$ 402.1427; Anal. calcd for $C_{20}H_{22}N_2O_7$ (402.14): C, 59.70; H, 5.51; N, 6.96. Found: C, 59.85; H, 5.48; N, 6.88%; HRMS m/z 420.1771 (M + NH_4^+), calcd for $C_{20}H_{22}N_2O_7NH_4$ 420.1771.

(4a*R*,5*S*,6*S*)-Ethyl 6-(4-chlorophenyl)-4a-hydroxy-1-methyl-5-nitro-3,4,4a,5,6,7-hexahydronaphthalene-2-carboxylate (49ad): Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a yellow solid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiral cel OD-H column (hexane/2-propanol = 90:10, flow rate 0.5 mL/min, λ = 254 nm), t_R = 33.62 min (minor), t_R = 37.29 min (major). **$[\alpha]_D^{25}$ = -141.37° (*c* = 0.637 g/100 mL, $CHCl_3$, 85% *ee*, 99.99% de);** Mp 189-191 °C; IR (neat): ν_{max} 3468 (O-*H*), 2932, 1694, 1543, 1495, 1447, 1368, 1260, 1088, 1046 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.30 (2H, d, *J* = 8.4 Hz), 7.22 (2H, d, *J* = 8.4 Hz), 6.17 (1H, t, *J* = 3.6 Hz), 4.86 (1H, d, *J* = 12.4 Hz), 4.24 (2H, q, *J* = 7.2 Hz, OCH_2CH$_3$), 3.95 (1H, dt, *J* = 11.6, 6.4 Hz), 2.84 (2H, td, *J* = 20.0, 5.2 Hz), 2.81 (1H, brs, O-*H*), 2.69-2.61 (1H, m), 2.52-2.45 (2H, m), 2.11 (3H, s, olefinic-CH_3), 1.92 (1H, dd, *J* = 13.6, 3.6 Hz), 1.71 (1H, dt, *J* = 12.4, 5.2 Hz), 1.32 (3H, t, *J* = 7.2 Hz, OCH$_2$CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.2 (C, O-C=O), 137.9 (C), 135.6 (C), 134.9 (C), 133.7 (C), 129.2 (2 x CH), 129.0 (2 x CH), 127.5 (C), 127.2 (CH), 95.5 (CH), 68.4 (C), 60.7 (CH_2, O*C*H$_2$CH$_3$), 38.7 (CH), 34.8 (CH_2), 31.9 (CH_2), 22.8 (CH_2), 16.0 (CH_3, olefinic-*C*H$_3$), 14.3 (CH_3, OCH$_2$*C*H$_3$); LRMS m/z 390.00 (M - H^+), calcd $C_{20}H_{22}ClNO_5$ 391.1187; Anal. calcd for $C_{20}H_{22}ClNO_5$ (391.12): C, 61.30; H, 5.66; N, 3.57.



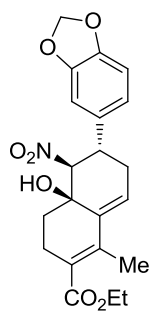
(–)-**49ad**

Found: C, 61.45; H, 5.59; N, 3.51%; HRMS m/z 409.1496 (M + NH_4^+), calcd for $C_{20}H_{22}ClNO_5NH_4$ 409.1530.



(–)-**49ae**

(4a*R*,5*S*,6*S*)-Ethyl 6-(2-chlorophenyl)-4a-hydroxy-1-methyl-5-nitro-3,4,4a,5,6,7-hexahydronaphthalene-2-carboxylate (49ae): Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiral cel OD-H column (hexane/2-propanol = 90:10, flow rate 0.5 mL/min, λ = 254 nm), t_R = 32.95 min (major), t_R = 37.36 min (minor). **$[\alpha]_D^{25}$ = -129.03°** (***c* = 0.7 g/100 mL, $CHCl_3$, 95% *ee*, 99.99% de);** Mp 155-158 °C; IR (neat): ν_{max} 3493 (O-*H*), 2971, 2938, 1732, 1680, 1591, 1551, 1443, 1372, 1233, 1036, 922 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40 (1H, d, *J* = 8.0 Hz), 7.30-7.18 (3H, m), 6.17 (1H, brs), 5.00 (1H, d, *J* = 12.4 Hz), 4.66 (1H, dt, *J* = 11.6, 6.0 Hz), 4.25 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 2.95 (1H, td, *J* = 20.0, 5.6 Hz), 2.77 (1H, brs, O-*H*), 2.71-2.64 (1H, m), 2.53 (1H, dd, *J* = 18.0, 5.2 Hz), 2.31 (1H, dd, *J* = 19.2, 10.8 Hz), 2.13 (3H, s, olefinic-CH_3), 2.02 (1H, dd, *J* = 13.2, 4.0 Hz), 1.79-1.71 (1H, m), 1.33 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.2 (C, O-C=O), 137.4 (C), 135.7 (C), 134.8 (C), 134.4 (C), 130.2 (CH), 128.6 (CH), 127.5 (C, CH), 127.1 (CH), 126.2 (CH), 94.3 (CH), 68.5 (C), 60.6 (CH_2, OCH_2CH_3), 34.7 (CH), 33.8 (CH_2), 31.9 (CH_2), 22.8 (CH_2), 16.0 (CH_3, olefinic-CH_3), 14.2 (CH_3, OCH_2CH_3); LRMS m/z 390.00 (M - H^+), calcd $C_{20}H_{22}ClNO_5$ 391.1187; Anal. calcd for $C_{20}H_{22}ClNO_5$ (391.12): C, 61.30; H, 5.66; N, 3.57. Found: C, 61.45; H, 5.71; N, 3.51%; HRMS m/z 409.1539 (M + NH_4^+), calcd for $C_{20}H_{22}ClNO_5NH_4$ 409.1530.

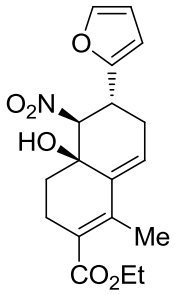


(–)-**49af**

(4a*R*,5*S*,6*S*)-Ethyl 6-(benzo[d][1,3]dioxol-5-yl)-4a-hydroxy-1-methyl-5-nitro-3,4,4a,5,6,7-hexahydronaphthalene-2-carboxylate (49af): Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a yellow solid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Lux 5u Cellulose-2 column (hexane/2-propanol = 70:30, flow rate 1.0 mL/min, λ = 254 nm), t_{R1} = 14.69 min (major), t_{R1} = 22.95 min (minor), t_{R2} = 25.79 min (major), t_{R2} =

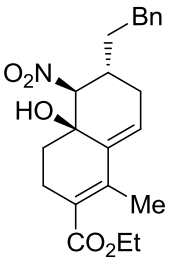
28.78 min (minor). **$[\alpha]_D^{25}$ = -148.85° (*c* = 0.514 g/100 mL, $CHCl_3$, 87% *ee*, 86% *ee*, 50.7% de);** Mp 178-182 °C; IR (neat): ν_{max} 3491 (O-*H*), 2920, 1686, 1553, 1489, 1445, 1370, 1234, 1038, 930 cm^{-1}; ^1H NMR ($CDCl_3$, **3:1 mixture of diastereomers**) δ 6.84-6.71 (6H, m), 6.19 (1H, t, *J* = 4.4 Hz), 6.16 (1H, t, *J* = 4.0 Hz), 5.96 (4H, s, OCH_2O), 4.83 (1H, d, *J* = 12.4 Hz), 4.53 (1H, d, *J* = 12.0 Hz), 4.26 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 4.25 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 3.90 (2H, dt, *J* = 12.4, 6.4 Hz), 2.86 (1H, td, *J* = 20.0, 6.0 Hz), 2.82 (2H, brs, O-*H*), 2.82-2.73 (1H, m), 2.71-2.48 (6H, m), 2.13 (3H, s, olefinic-CH_3), 2.12 (3H, s, olefinic-CH_3), 1.93 (1H, ddd, *J* = 13.6, 4.8, 1.6 Hz), 1.92-1.87 (1H, m), 1.76-1.64 (2H, m), 1.34 (3H, t, *J* = 7.2 Hz, OCH_2CH_3), 1.33 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.2 (2 x C, O-C=O), 148.0 (C), 147.9 (C), 147.5 (C), 147.1 (C), 135.4 (2 x C), 135.0 (2 x C), 132.9 (C), 130.6 (C), 127.5 (CH), 127.4 (C), 127.3 (C), 127.1 (CH), 121.3 (CH), 121.0 (CH), 108.6 (CH), 108.2 (CH), 107.7 (CH), 105.6 (CH), 101.2 (CH_2, OCH_2O), 101.1 (CH_2, OCH_2O), 95.8 (CH), 95.6 (CH), 68.4 (C), 67.8 (C), 60.59 (CH_2, OCH_2CH_3), 60.56 (CH_2, OCH_2CH_3), 39.0 (CH), 37.0 (CH), 35.0 (CH_2), 32.7 (CH_2), 31.9 (2 x CH_2), 22.8 (CH_2), 22.7 (CH_2), 16.0 (CH_3, olefinic-CH_3), 15.9 (CH_3, olefinic-CH_3),14.2 (2 x CH_3, OCH_2CH_3); LRMS m/z 400.25 (M - H^+), calcd $C_{21}H_{23}NO_7$ 401.1475; Anal. calcd for $C_{21}H_{23}NO_7$ (401.15): C, 62.83; H, 5.78; N, 3.49. Found: C, 62.75; H, 5.71; N, 3.41%; HRMS m/z 409.1819 (M + NH_4^+), calcd for $C_{21}H_{23}NO_7NH_4$ 409.1818.

(4a*R*,5*S*,6*R*)-Ethyl 6-(furan-2-yl)-4a-hydroxy-1-methyl-5-nitro-3,4,4a,5,6,7-hexahydronaphthalene-2-carboxylate (49ag): Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a yellow solid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Lux 5u Cellulose-1 column (hexane/2-propanol = 90:10, flow rate 1.0 mL/min, λ = 254 nm), t_{R1} = 12.63 min (major), t_{R1} = 13.72 min (minor), t_{R2} = 17.24 min (minor), t_{R2} = 22.15 min (major). **$[\alpha]_D^{25}$ = -207.68° (*c* = 0.3 g/100 mL, $CHCl_3$, 89% *ee*, 89%*ee*, 76.87%de);** Mp 130-132 °C; IR (neat): ν_{max} 3389 (O-*H*), 2930, 1724, 1707, 1551, 1445, 1368, 1248, 1144, 1074, 1015, 951 cm^{-1}; ^1H NMR ($CDCl_3$, **7.65:1 mixture of diastereomers**) δ 7.35 (1H, brs), 6.30 (1H, dd, *J* = 3.2, 2.0 Hz), 6.20 (1H, d, *J* = 3.2 Hz),



(–)-49ag

6.18 (1H, t, *J* = 4.0 Hz), 4.84 (1H, d, *J* = 12.4 Hz), 4.23 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 4.12 (1H, dt, *J* = 12.0, 8.0 Hz), 2.87 (1H, s, O-*H*), 2.83-2.61 (3H, m), 2.50 (1H, dd, *J* = 18.0, 4.8 Hz), 2.11 (3H, s, olefinic-C*H*$_3$), 1.92-1.87 (1H, m), 1.69 (1H, dt, *J* = 12.8, 5.6 Hz), 1.32 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR (CDCl$_3$, DEPT-135) δ 169.2 (C, O-C=O), 152.0 (C), 142.5 (CH), 135.2 (C), 134.9 (C), 127.4 (C), 127.1 (CH), 110.4 (CH), 107.7 (CH), 94.2 (CH), 68.2 (C), 60.6 (CH$_2$, O*C*H$_2$CH$_3$), 33.0 (CH), 31.7 (CH$_2$), 31.3 (CH$_2$), 22.7 (CH$_2$), 15.9 (CH$_3$, olefinic-*C*H$_3$), 14.2 (CH$_3$, OCH$_2$*C*H$_3$); LRMS m/z 346.00 (M - H$^+$), calcd $C_{18}H_{21}NO_6$ 347.1369; Anal. calcd for $C_{18}H_{21}NO_6$ (347.14): C, 62.24; H, 6.09; N, 4.03. Found: C, 62.16; H, 6.02; N, 4.12%; HRMS m/z 370.1267 (M + Na), calcd $C_{18}H_{21}NO_6Na$ 370.1267.



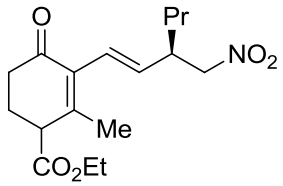
(–)-**49ah**

(4a*R*,5*S*,6*R*)-Ethyl 4a-hydroxy-1-methyl-5-nitro-6-phenethyl-3,4,4a,5,6,7-hexahydronaphthalene-2-carboxylate (49ah): Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiral cel OJ-H column (hexane/2-propanol = 80:20, flow rate 1.0 mL/min, λ = 254 nm), t_R = 15.98 min (minor), t_R = 26.42 min (major). **$[\alpha]_D^{25}$ = –74.997° (*c* = 0.21 g/100 mL, CHCl$_3$, 91% *ee*, 99.99% de);** Mp 128-131 °C; IR (neat): ν_{max} 3497 (O-*H*), 2926, 1682, 1630, 1607, 1547, 1495, 1445, 1370, 1277, 1140, 1053 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.31 (2H, t, *J* = 7.2 Hz), 7.23 (1H, d, *J* = 7.2 Hz), 7.18 (2H, d, *J* = 7.6 Hz), 6.15 (1H, brs), 4.43 (1H, d, *J* = 11.6 Hz), 4.24 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 2.89 (1H, s, O-*H*), 2.87-2.75 (3H, m), 2.69-2.57 (2H, m), 2.49 (1H, dd, *J* = 17.6, 3.6 Hz), 2.17 (1H, dd, *J* = 20.8, 11.2 Hz), 2.11 (3H, s, olefinic-C*H*$_3$), 1.85 (1H, dd, *J* = 13.2, 4.0 Hz), 1.78-1.73 (1H, m), 1.67-1.55 (2H, m), 1.33 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR (CDCl$_3$, DEPT-135) δ 169.1 (C, O-*C*=O), 140.8 (C), 135.4 (C), 135.0 (C), 128.4 (2 x CH), 128.1 (2 x CH), 127.4 (CH), 127.1 (C), 126.1 (CH), 96.4 (CH), 67.9 (C), 60.5 (CH$_2$, O*C*H$_2$CH$_3$), 33.8 (CH$_2$), 32.0 (CH$_2$), 31.7 (CH$_2$), 31.5 (CH$_2$), 31.3 (CH), 22.6 (CH$_2$), 15.8 (CH$_3$, olefinic-*C*H$_3$), 14.2 (CH$_3$, OCH$_2$*C*H$_3$); LRMS m/z 384.35 (M - H$^+$), calcd $C_{22}H_{27}NO_5$ 385.1889; Anal. calcd for $C_{22}H_{27}NO_5$ (385.19): C, 68.55; H, 7.06; N, 3.63. Found: C, 68.43; H, 7.11; N, 3.58%; HRMS m/z 403.2260 (M + NH$_4^+$), calcd for $C_{22}H_{27}NO_5NH_4$ 403.2233.

Ethyl 2-methyl-3-((*R*,*E*)-3-(nitromethyl)-5-phenylpent-1-en-1-yl)-4-oxocyclohex-2-enecarboxylate (52ah): Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a yellow liquid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiral cel OD-H column (hexane/2-propanol = 80:20, flow rate 1.0 mL/min, λ = 254 nm), t_{R1} = 17.35 min (major), t_{R1} = 19.02 min (minor), t_{R2} = 22.92 min (minor), t_{R2} = 25.32 min (major). **$[\alpha]_D^{25}$ = –19.566° (*c* = 0.2 g/100 mL, $CHCl_3$, 88% *ee*, 86% *ee*);** IR (neat): ν_{max} 2930, 1728, 1672, 1553, 1495, 1454, 1379, 1267, 1159, 1030 cm^{-1}; ^1H NMR ($CDCl_3$, **1:1 mixture of diastereomers**) δ 7.30-7.26 (4H, m), 7.21-7.17 (6H, m), 6.20 (1H, d, *J* = 4.4 Hz), 6.16 (1H, d, *J* = 4.0 Hz), 5.86 (1H, dd, *J* = 13.6, 9.2 Hz), 5.82 (1H, dd, *J* = 13.6, 8.8 Hz), 4.44-4.32 (4H, m), 4.22 (2H, q, *J* = 7.2 Hz, OC$H_2$$CH_3$), 4.21 (2H, q, *J* = 7.2 Hz, OC$H_2$$CH_3$), 3.36 (2H, t, *J* = 4.8 Hz), 3.02-2.92 (2H, m), 2.82-2.73 (2H, m), 2.67-2.59 (4H, m), 2.44-2.38 (2H, m), 2.33-2.19 (4H, m), 2.045 (3H, s, olefinic-CH_3), 2.037 (3H, s, olefinic-CH_3), 1.82-1.70 (4H, m), 1.30 (3H, t, *J* = 7.2 Hz), 1.29 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 196.8 (C, C=O), 196.7 (C, C=O), 171.9 (C, O-C=O), 171.8 (C, O-C=O), 151.6 (2 x C), 141.0 (2 x C), 134.4 (CH), 134.3 (CH), 133.7 (C), 133.5 (C), 128.44 (4 x CH), 128.38 (4 x CH), 126.4 (CH), 126.3 (CH), 126.1 (2 x CH), 79.9 (2 x CH_2), 61.4 (2 x CH_2, O*C*$H_2$$CH_3$), 48.1 (CH), 48.0 (CH), 42.7 (CH), 42.6 (CH), 35.22 (CH_2), 35.16 (CH_2), 33.4 (2 x CH_2), 32.8 (2 x CH_2), 25.2 (CH_2), 25.1 (CH_2), 21.4 (2 x CH_3, olefinic-*C*H_3), 14.1 (2 x CH_3, OCH_2*C*H_3); LRMS m/z 386.40 (M + H^+), calcd $C_{22}H_{27}NO_5$ 385.1889; Anal. calcd for $C_{22}H_{27}NO_5$ (385.19): C, 68.55; H, 7.06; N, 3.63. Found: C, 68.49; H, 7.12; N, 3.58%; HRMS m/z 386.1967 (M + H^+), calcd for $C_{22}H_{27}NO_5H$ 386.1967.

(4a*R*,5*S*,6*R*)-Ethyl 4a-hydroxy-1-methyl-5-nitro-6-propyl-3,4,4a,5,6,7-hexahydronaphthalene-2-carboxylate (49ai): Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiral cel OJ-H column (hexane/2-propanol = 75:25, flow rate 0.5 mL/min, λ = 254 nm), t_R = 11.97 min (minor), t_R = 14.93 min (major). **$[\alpha]_D^{25}$ = -185.78° (*c* = 0.412 g/100 mL, $CHCl_3$,**

90% *ee*, 99.99% de); Mp 128-130 °C; IR (neat): ν_{max} 3501 (O-*H*), 2961, 2926, 1719, 1690, 1549, 1456, 1370, 1279, 1234, 1154, 1067, 957 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.13 (1H, t, *J* = 3.6 Hz), 4.36 (1H, d, *J* = 11.6 Hz), 4.22 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 2.87 (1H, s, O-*H*), 2.78-2.71 (2H, m), 2.68-2.60 (1H, m), 2.46 (1H, dd, *J* = 17.6, 4.0 Hz), 2.08 (3H, s, olefinic-CH_3), 2.05-2.00 (1H, m), 1.82 (1H, ddd, *J* = 13.2, 4.8, 1.6 Hz), 1.61 (1H, dt, *J* = 12.4, 5.2 Hz), 1.50-1.41 (1H, m), 1.37-1.24 (3H, m), 1.31 (3H, t, *J* = 7.2 Hz, OCH_2CH_3), 0.92 (3H, t, *J* = 6.8 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.2 (C, O-*C*=O), 135.4 (C), 135.1 (C), 127.7 (CH), 127.1 (C), 96.6 (CH), 67.9 (C), 60.5 (CH_2, OCH_2CH_3), 34.2 (CH_2), 31.8 (CH_2), 31.6 (CH_2), 31.4 (CH), 22.7 (CH_2), 18.9 (CH_2), 15.8 (CH_3, olefinic-CH_3), 14.2 (CH_3, OCH_2CH_3), 13.9 (CH_3, $CH_2CH_2CH_3$); LRMS m/z 324.50 ($M + H^+$), calcd $C_{17}H_{25}NO_5$ 323.1733; Anal. calcd for $C_{17}H_{25}NO_5$ (323.17): C, 63.14; H, 7.79; N, 4.33. Found: C, 63.28; H, 7.71; N, 4.26%; HRMS m/z 341.2055 ($M + NH_4^+$), calcd for $C_{17}H_{25}NO_5NH_4$ 341.2076.

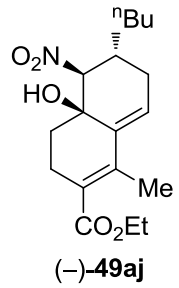


(+)-**52ai**

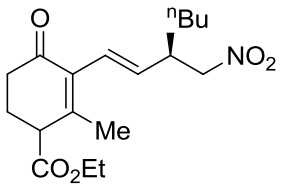
Ethyl 2-methyl-3-((*R*,*E*)-3-(nitromethyl)hex-1-en-1-yl)-4-oxocyclohex-2-enecarboxylate (52ai): Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a yellow liquid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiral cel OD-H column (hexane/2-propanol = 97:3, flow rate 0.5 mL/min, λ = 212 nm), t_{R1} = 40.67 min (major), t_{R1} = 43.79 min (minor), t_{R2} = 52.27 min (minor), t_{R2} = 83.12 min (major). **$[\alpha]_D^{25}$ = +4.691° (*c* = 0.385 g/100 mL, $CHCl_3$, 81% *ee*, 82% *ee*);** IR (neat): ν_{max} 2932, 1732, 1667, 1551, 1447, 1377, 1157, 1030 cm^{-1}; ^1H NMR ($CDCl_3$, **1:1 mixture of diastereomers**) δ 6.17 (1H, d, *J* = 4.0 Hz), 6.13 (1H, d, *J* = 4.0 Hz), 5.79 (1H, dd, *J* = 14.8, 8.8 Hz), 5.77 (1H, dd, *J* = 15.6, 9.2 Hz), 4.42 (2H, dd, *J* = 11.6, 6.0 Hz), 4.37-4.30 (2H, m), 4.214 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 4.208 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 3.35 (2H, brs), 2.99-2.93 (2H, m), 2.64 (1H, dd, *J* = 11.2, 5.6 Hz), 2.59 (1H, dd, *J* = 11.2, 5.2 Hz), 2.43-2.36 (2H, m), 2.30-2.16 (4H, m), 2.033 (3H, s, olefinic-CH_3), 2.026 (3H, s, olefinic-CH_3), 1.47-1.40 (6H, m), 1.33-1.26 (2H, m), 1.30 (3H, t, *J* = 7.2 Hz, OCH_2CH_3), 1.29 (3H, t, *J* = 7.2 Hz, OCH_2CH_3), 0.93 (6H, t, *J* = 6.4 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 196.82 (C, C=O), 196.77 (C, C=O), 172.0 (C, O-C=O), 171.9 (C, O-C=O), 151.4 (2 x C), 135.0 (CH), 134.9

(CH), 133.8 (C), 133.6 (C), 125.6 (CH), 125.5 (CH), 80.10 (CH_2), 80.07 (CH_2), 61.4 (2 x CH_2, O*C*H_2CH$_3$), 48.2 (CH), 48.0 (CH), 43.1 (CH), 43.0 (CH), 35.3 (CH_2), 35.2 (CH_2), 34.0 (2 x CH_2), 25.2 (CH_2), 25.1 (CH_2), 21.43 (CH_3, olefinic-*C*H$_3$), 21.39 (CH_3, olefinic-*C*H$_3$), 20.0 (2 x CH_2), 14.2 (2 x CH_3, OCH$_2$*C*H$_3$), 13.8 (2 x CH_3); LRMS m/z 324.30 (M + H^+), calcd $C_{17}H_{25}NO_5$ 323.1733; Anal. calcd for $C_{17}H_{25}NO_5$ (323.17): C, 63.14; H, 7.79; N, 4.33. Found: C, 63.25; H, 7.71; N, 4.48%; HRMS m/z 324.1849 (M + H^+), calcd for $C_{17}H_{25}NO_5H$ 324.1811.

(4a*R*,5*S*,6*R*)-Ethyl 6-butyl-4a-hydroxy-1-methyl-5-nitro-3,4,4a,5,6,7-hexahydronaphthalene-2-carboxylate (49aj): Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiral cel OJ-H column (hexane/2-propanol = 80:20, flow rate 1.0 mL/min, λ = 254 nm), t_R = 5.65 min (minor), t_R = 7.49 min (major). **$[\alpha]_D^{25}$ = -142.27° (*c* = 0.387 g/100 mL, $CHCl_3$, 91% *ee,* 99.99% de);** Mp 84-86 °C; IR (neat): ν_{max} 3526 (O-*H*), 2930, 1707, 1632, 1549, 1447, 1370, 1267, 1229, 1119, 1047 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.13 (1H, brs), 4.36 (1H, d, *J* = 11.6 Hz), 4.22 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 2.88 (1H, s, O-*H*), 2.77-2.72 (2H, m), 2.63-2.60 (1H, m), 2.46 (1H, dd, *J* = 18.0, 4.4 Hz), 2.08 (3H, s, olefinic-C*H*$_3$), 1.81 (1H, dd, *J* = 13.2, 4.0 Hz), 1.60 (1H, dt, *J* = 12.8, 5.6 Hz), 1.39-1.26 (7H, m), 1.30 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$), 0.89 (3H, t, *J* = 6.0 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.2 (C, O-C=O), 135.4 (C), 135.2 (C), 127.8 (CH), 127.1 (C), 96.6 (CH), 67.9 (C), 60.5 (CH_2, O*C*H$_2$CH$_3$), 31.8 (CH_2), 31.64 (CH_2), 31.58 (CH_2), 31.5 (CH), 27.8 (CH_2), 22.7 (CH_2), 22.5 (CH_2), 15.8 (CH_3, olefinic-*C*H$_3$), 14.2 (CH_3, OCH$_2$*C*H$_3$), 13.8 (CH_3, CH$_2$CH$_2$*C*H$_3$); LRMS m/z 338.20 (M + H^+), calcd $C_{18}H_{27}NO_5$ 337.1889; Anal. calcd for $C_{18}H_{27}NO_5$ (337.19): C, 64.07; H, 8.07; N, 4.15. Found: C, 64.15; H, 7.98; N, 4.21%; HRMS m/z 360.1787 (M + Na), calcd for $C_{18}H_{27}NO_5Na$ 360.1787.

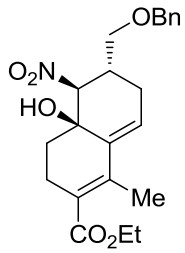


(–)-**49aj**



(+)-**52aj**

Ethyl 2-methyl-3-((*R*,*E*)-3-(nitromethyl)hept-1-en-1-yl)-4-oxocyclohex-2-enecarboxylate (52aj): Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a yellow liquid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiral cel OD-H column (hexane/2-propanol = 95:5, flow rate 0.5 mL/min, λ = 254 nm), t_{R1} = 28.65 min (major), t_{R1} = 30.56 min (minor), t_{R2} = 35.12 min (minor), t_{R2} = 59.44 min (major). **$[\alpha]_D^{25}$ = +8.382° (*c* = 0.371 g/100 mL, $CHCl_3$, 96% *ee*, 91% *ee*);** IR (neat): ν_{max} 2957, 1727, 1670, 1550, 1376, 1240, 1157, 1044, 619 cm^{-1}; ^1H NMR ($CDCl_3$, **1:1 mixture of diastereomers**) δ 6.17 (1H, d, *J* = 4.0 Hz), 6.13 (1H, d, *J* = 4.0 Hz), 5.82 (1H, dd, *J* = 15.2, 9.2 Hz), 5.78 (1H, dd, *J* = 15.6, 9.2 Hz), 4.43 (2H, dd, *J* = 11.6, 6.4 Hz), 4.37-4.30 (2H, m), 4.214 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 4.212 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 3.35 (2H, t, *J* = 5.6 Hz), 3.00-2.89 (2H, m), 2.64 (1H, dd, *J* = 10.8, 5.2 Hz), 2.60 (1H, dd, *J* = 11.2, 5.6 Hz), 2.42-2.38 (2H, m), 2.30-2.20 (4H, m), 2.04 (3H, s, olefinic-CH_3), 2.03 (3H, s, olefinic-CH_3), 1.45-1.33 (9H, m), 1.31-1.28 (9H, m), 0.90 (6H, t, *J* = 7.2 Hz, 2 x OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 196.81 (C, C=O), 196.76 (C, C=O), 172.0 (C, O-C=O), 171.9 (C, O-C=O), 151.4 (2 x C), 135.04 (CH), 134.96 (CH), 133.8 (C), 133.6 (C), 125.6 (CH), 125.5 (CH), 80.11 (CH_2), 80.08 (CH_2), 61.4 (2 x CH_2, OCH_2CH_3), 48.2 (CH), 48.1 (CH), 43.3 (CH), 43.2 (CH), 35.3 (CH_2), 35.2 (CH_2), 31.6 (2 x CH_2), 28.9 (2 x CH_2), 25.2 (CH_2), 25.1 (CH_2), 22.4 (2 x CH_2), 21.44 (CH_3, olefinic-CH_3), 21.40 (CH_3, olefinic-CH_3), 14.2 (2 x CH_3, OCH_2CH_3), 13.9 (2 x CH_3, OCH_2CH_3); LRMS m/z 338.35 ($M + H^+$), calcd $C_{18}H_{27}NO_5$ 337.1889; Anal. calcd for $C_{18}H_{27}NO_5$ (337.19): C, 64.07; H, 8.07; N, 4.15. Found: C, 63.89; H, 8.12; N, 4.25%; HRMS m/z 338.1967 ($M + H^+$), calcd for $C_{18}H_{27}NO_5H$ 338.1967.

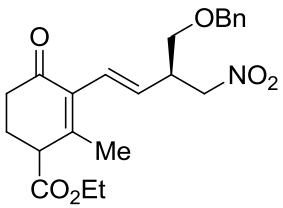


(–)-**49ak**

(4a*R*,5*S*,6*R*)-Ethyl 6-((benzyloxy)methyl)-4a-hydroxy-1-methyl-5-nitro-3,4,4a,5,6,7-hexahydronaphthalene-2-carboxylate (49ak): Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a yellow gummy liquid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel

Chiralpak IC-3 column (hexane/ethanol = 85:15, flow rate 1.0 mL/min, λ = 254 nm), t_R = 7.14 min (major), t_R = 7.78 min (minor). **$[\alpha]_D^{25}$ = –83.601° (*c* = 0.337 g/100 mL, $CHCl_3$, 90% *ee*, 99.99% de);** IR (neat): ν_{max} 3503 (O-*H*), 2926, 2863, 1726, 1682, 1553, 1454, 1372, 1248, 1107 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.37-7.34 (5H, m), 6.14 (1H, t, *J* = 4.0 Hz), 4.70 (1H, d, *J* = 12.0 Hz), 4.52 (2H, s), 4.22 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 2.78 (1H, s, O-*H*), 2.66-2.56 (3H, m), 2.53-2.34 (3H, m), 2.30-2.18 (1H, m), 2.08 (3H, s, olefinic-CH_3), 1.88 (1H, dd, *J* = 13.6, 3.6 Hz), 1.66 (1H, dt, *J* = 12.4, 5.6 Hz), 1.31 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.2 (C, O-*C*=O), 137.7 (C), 135.2 (C), 135.1 (C), 128.5 (CH), 128.42 (2 x CH), 128.37 (2 x CH), 128.0 (CH), 127.0 (C), 92.7 (CH), 73.5 (CH_2), 69.6 (CH_2), 68.0 (C), 60.5 (CH_2, OCH_2CH_3), 32.9 (CH), 31.6 (CH_2), 28.8 (CH_2), 22.7 (CH_2), 15.9 (CH_3, olefinic-CH_3), 14.2 (CH_3, OCH_2CH_3); HRMS m/z 424.1736 ($M + H^+$), calcd for $C_{22}H_{27}NO_6Na$ 424.1747.

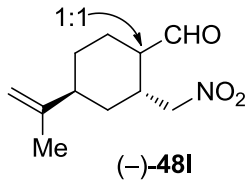
Ethyl 3-((*R,E*)-4-(benzyloxy)-3-(nitromethyl)but-1-en-1-yl)-2-methyl-4-oxocyclohex-2-enecarboxylate (52ak): Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a yellow liquid. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using Daicel Chiralpak IC-3 column (hexane/ethanol = 85:15, flow rate 1.0 mL/min, λ = 254 nm), t_{R1} = 12.95 min (minor), t_{R1} = 17.21 min (minor), t_{R2} = 19.59 min (major), t_{R2} =37.42 min (major). **$[\alpha]_D^{25}$ = –83.601° (*c* = 0.337 g/100 mL, $CHCl_3$, 94% *ee*, 88% *ee*);** ^1H NMR ($CDCl_3$, **1:1 mixture of diastereomers**) δ 7.32-7.29 (10H, m), 6.25 (2H, d, *J* = 16.4 Hz), 5.94 (1H, dd, *J* = 16.0, 8.4 Hz), 5.90 (1H, dd, *J* = 16.0, 8.4 Hz), 4.69 (2H, d, *J* = 12.0 Hz), 4.50-4.42 (4H, m), 4.22 (4H, q, *J* = 7.2 Hz, OCH_2CH_3), 3.64 (2H, dd, *J* = 9.6, 4.4 Hz), 3.52-3.44 (6H, m), 3.38-3.29 (2H, m), 3.05-2.95 (2H, m), 2.66-2.36 (6H, m), 2.02 (6H, s, olefinic-CH_3), 1.31 (6H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 196.81 (C, *C*=O), 196.77 (C, *C*=O), 171.82 (C, O-*C*=O), 171.76 (C, O-*C*=O), 152.0 (2 x C), 137.6 (2 x C), 133.6 (C), 133.4 (C), 131.6 (CH), 131.5 (CH), 127.80 (CH), 127.76 (CH), 127.7 (4 x CH), 127.6 (4 x CH), 126.6 (CH), 126.5 (CH), 77.32 (CH_2), 77.27 (CH_2), 73.3 (2 x CH_2), 70.2 (2 x CH_2), 61.4 (2 x CH_2, OCH_2CH_3), 48.2 (CH), 48.0 (CH), 43.2 (CH), 43.1 (CH),



(–)-**52ak**

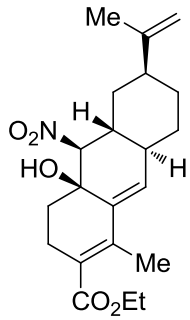
35.13 (CH_2), 35.07 (CH_2), 25.1 (CH_2), 25.0 (CH_2), 21.44 (CH_3, olefinic-*C*H_3), 21.40 (CH_3, olefinic-*C*H_3), 14.1 (2 x CH_3, OCH_2*C*H_3).

(2*R*,4*S*)-2-(nitromethyl)-4-(prop-1-en-2-yl)cyclohexanecarbaldehyde (48l): Prepared following the procedure **4a** and purified by column chromatography using EtOAc/hexane and isolated as a yellow liquid. **$[\alpha]_D^{25}$ = -13.557° (*c* = 0.185 g/100 mL, $CHCl_3$);** Mp °C; IR (neat): ν_{max} 2938, 1724, 1551, 1447, 1381, 894, 656, 642 cm^{-1}; ^1H NMR ($CDCl_3$, **1:1 mixture of diastereomers**) δ 9.70 (1H, s), 9.65 (1H, s), 4.78 (1H, s), 4.77 (1H, s), 4.73 (1H, s), 4.68 (1H, s), 4.59 (1H, dd, *J* = 12.4, 7.6 Hz), 4.53-4.47 (3H, m), 3.19-3.10 (2H, m), 2.61 (1H, td, *J* = 11.6, 4.0 Hz), 2.38 (1H, q, *J* = 4.4 Hz), 2.21-2.04 (4H, m), 1.94-1.91 (1H, m), 1.85-1.75 (3H, m), 1.72 (3H, s), 1.67 (3H, s), 1.58-1.49 (3H, m), 1.46-1.35 (3H, m); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 202.5 (CH, H-*C*=O), 202.3 (CH, H-*C*=O), 147.7 (C), 147.4 (C), 110.0 (CH_2), 109.7 (CH_2), 77.9 (CH_2), 74.8 (CH_2), 51.1 (CH), 48.5 (CH), 38.4 (CH), 38.3 (CH), 32.2 (CH), 32.1 (CH_2), 31.4 (CH), 30.1 (CH_2), 29.6 (CH_2), 27.5 (CH_2), 21.2 (CH_2), 21.0 (CH_2), 20.89 (CH_3), 20.86 (CH_3); LRMS m/z 212.05 ($M + H^+$), calcd $C_{11}H_{17}NO_3$ 211.1208; Anal. calcd for $C_{11}H_{17}NO_3$ (211.12): C, 62.54; H, 8.11; N, 6.63. Found: C, 62.39; H, 8.21; N, 6.73%.



(–)-**48l**

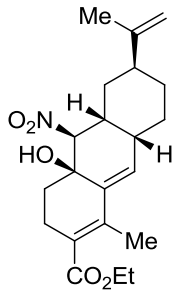
(4a*R*,6*S*,8a*S*,10*S*,10a*R*)-Ethyl 4a-hydroxy-1-methyl-10-nitro-6-(prop-1-en-2-yl)-3,4,4a,5,6,7,8,8a,10,10a-decahydroanthracene-2-carboxylate (53al): Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a yellow liquid. **$[\alpha]_D^{25}$ = -44.109° (*c* = 0.2 g/100 mL, $CHCl_3$, 99.99% *ee*);** IR (neat): ν_{max} 3415 (O-*H*), 1708 (O-C=O), 1547, 1368, 1281, 1230, 1044, 642 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.87 (1H, s), 4.97 (1H, s), 4.87 (1H, s), 4.37 (1H, d, *J* = 12.0 Hz), 4.22 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 2.67-2.61 (1H, m), 2.49-2.41 (3H, m), 2.19 (1H, d, *J* = 13.2 Hz), 2.06 (3H, s, olefinic-CH_3), 2.03-1.92 (3H, m), 1.74 (3H, s), 1.70-1.57 (4H, m), 1.46-1.36 (2H, m), 1.30 (3H, t, *J* = 7.2 Hz , OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.3 (C, O-*C*=O), 145.4 (C), 135.5 (C), 135.0 (C), 132.1 (CH), 127.4 (C), 111.8 (CH_2), 96.1 (CH), 68.3 (C), 60.5 (CH_2, O*C*H_2CH_3), 43.4 (CH), 38.3 (CH), 33.5



(–)-**53al**

(CH), 31.8 (CH_2), 30.1 (CH_2), 28.2 (CH_2), 27.9 (CH_2), 23.1 (CH_2), 22.5 (CH_3), 16.2 (CH_3, olefinic-*C*H_3), 14.2 (CH_3, OCH_2*C*H_3); LRMS m/z 374.30 (M - H^+), calcd $C_{21}H_{29}NO_5$ 375.2046; Anal. calcd for $C_{21}H_{29}NO_5$ (375.20): C, 67.18; H, 7.79; N, 3.73. Found: C, 67.25; H, 7.71; N, 3.88%; HRMS m/z 398.1945 (M + Na), calcd for $C_{21}H_{29}NO_5Na$ 398.1943.

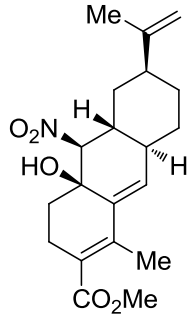
(4a*R*,6*S*,8a*R*,10*S*,10a*R*)-Ethyl 4a-hydroxy-1-methyl-10-nitro-6-(prop-1-en-2-yl)-3,4,4a,5,6,7,8,8a,10,10a-decahydroanthracene-2-carboxylate (54al):



(–)-**54al**

Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a yellow solid. **$[\alpha]_D^{25}$ = -169.82° (*c* = 0.17 g/100 mL, $CHCl_3$, 99.99% *ee*);** Mp 108-110 °C; IR (neat): ν_{max} 3503 (O-*H*), 2928, 2863, 1699 (O-C=O), 1645, 1549, 1454, 1373, 1229, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.08 (1H, d, *J* = 4.8 Hz), 4.79 (1H, d, *J* = 12.4 Hz), 4.70 (2H, d, *J* = 14.0 Hz), 4.22 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 3.14-3.11 (1H, m), 3.03 (1H, s, O-*H*), 2.71-2.56 (2H, m), 2.46 (1H, dd, *J* = 18.0, 4.8 Hz), 2.08 (3H, s, olefinic-CH_3), 2.02-1.98 (1H, m), 1.93-1.84 (3H, m), 1.69 (3H, s), 1.67-1.64 (1H, m), 1.58-1.48 (3H, m) 1.31 (3H, t, *J* = 7.2 Hz , OCH_2CH_3), 1.14 (1H, dq, *J* = 13.6, 3.2 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.3 (C, O-C=O), 148.9 (C), 135.1 (C), 133.9 (C), 132.7 (CH), 127.5 (C), 109.1 (CH_2), 91.5 (CH), 68.6 (C), 60.5 (CH_2, OCH_2CH_3), 39.2 (CH), 37.5 (CH), 32.2 (CH_2), 32.0 (CH), 31.7 (CH_2), 30.8 (CH_2), 29.0 (CH_2), 22.9 (CH_2), 20.8 (CH_3), 16.1 (CH_3, olefinic-*C*H_3), 14.2 (CH_3, OCH_2*C*H_3); LRMS m/z 374.30 (M - H^+), calcd $C_{21}H_{29}NO_5$ 375.2046; Anal. calcd for $C_{21}H_{29}NO_5$ (375.20): C, 67.18; H, 7.79; N, 3.73. Found: C, 67.25; H, 7.71; N, 3.65%; HRMS m/z 398.1942 (M + Na), calcd for $C_{21}H_{29}NO_5Na$ 398.1943.

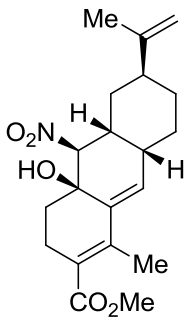
(4a*R*,6*S*,8a*S*,10*S*,10a*R*)-Methyl 4a-hydroxy-1-methyl-10-nitro-6-(prop-1-en-2-yl)-3,4,4a,5,6,7,8,8a,10,10a-decahydroanthracene-2-carboxylate (53bl):



(–)-**53bl**

Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a yellow liquid. **$[\alpha]_D^{25}$ = -75.155° (*c* = 0.2 g/100 mL, $CHCl_3$, 99.99% *ee*);** IR (neat): ν_{max} 3468 (O-*H*), 2928, 2859, 1713 (O-C=O), 1642, 1547, 1445, 1372, 1231, 1128, 1044 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.89 (1H, s), 4.97 (1H, s), 4.87 (1H,

s), 4.37 (1H, d, *J* = 11.6 Hz), 3.76 (3H, s, OC*H*$_3$), 2.64 (1H, s, O-*H*), 2.49-2.41 (3H, m), 2.21-2.17 (1H, m), 2.07 (3H, s, olefinic-C*H*$_3$), 2.03-1.92 (3H, m), 1.77-1.70 (3H, m), 1.74 (3H, s), 1.58-1.46 (2H, m), 1.39 (1H, dt, *J* = 12.8, 5.2 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.6 (C, O-C=O), 145.4 (C), 135.8 (C), 135.5 (C), 132.4 (CH), 127.0 (C), 111.8 (CH_2), 96.1 (CH), 68.3 (C), 51.6 (CH_3, O*C*H$_3$), 43.4 (CH), 38.3 (CH), 33.5 (CH), 31.8 (CH_2), 30.1 (CH_2), 28.2 (CH_2), 27.9 (CH_2), 23.1 (CH_2), 22.6 (CH_3), 16.3 (CH_3, olefinic-*C*H$_3$); LRMS m/z 360.30 (M - H$^+$), calcd $C_{20}H_{27}NO_5$ 361.1889; Anal. calcd for $C_{20}H_{27}NO_5$ (361.19): C, 66.46; H, 7.53; N, 3.88. Found: C, 66.59; H, 7.48; N, 3.76%; HRMS m/z 384.1787 (M + Na), calcd for $C_{20}H_{27}NO_5Na$ 384.1787.

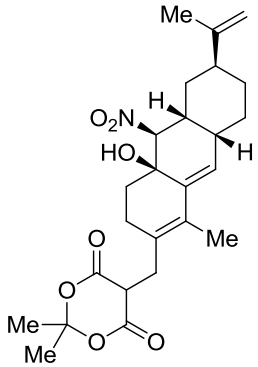


(–)-**54bl**

(4a*R*,6*S*,8a*R*,10*S*,10a*R*)-Methyl 4a-hydroxy-1-methyl-10-nitro-6-(prop-1-en-2-yl)-3,4,4a,5,6,7,8,8a,10,10a-decahydroanthracene-2-carboxylate (54bl): Prepared following the procedure **4c** and purified by column chromatography using EtOAc/hexane and isolated as a yellow solid. **[α]$_D^{25}$ = -207.49° (*c* = 0.3 g/100 mL, $CHCl_3$, 99.99% *ee*);** Mp 102-105 °C; IR (neat): ν_{max} 3482 (O-*H*), 3079, 2928, 2861, 1713, 1698, 1553, 1435, 1372, 1254, 891 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.09 (1H, d, *J* = 4.8 Hz), 4.79 (1H, d, *J* = 12.8 Hz), 4.69 (2H, d, *J* = 14.0 Hz), 3.76 (3H, s, OC*H*$_3$), 3.13-3.10 (1H, m), 3.04 (1H, s, O-*H*), 2.66-2.55 (2H, m), 2.46 (1H, dd, *J* = 18.0, 4.0 Hz), 2.08 (3H, s, olefinic-C*H*$_3$), 2.01-1.98 (1H, m), 1.93-1.83 (3H, m), 1.68 (3H, s), 1.66-1.59 (1H, m), 1.52 (1H, dt, *J* = 12.8, 4.8 Hz), 1.34-1.24 (2H, m), 1.14 (1H, dq, *J* = 12.8, 2.8 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.6 (C, O-C=O), 148.9 (C), 135.8 (C), 134.0 (C), 133.0 (CH), 127.1 (C), 109.1 (CH_2), 91.5 (CH), 68.6 (C), 51.6 (CH_3, O*C*H$_3$), 39.2 (CH), 37.5 (CH), 32.2 (CH_2), 32.0 (CH), 31.8 (CH_2), 30.8 (CH_2), 29.0 (CH_2), 22.9 (CH_2), 20.8 (CH_3), 16.2 (CH_3, olefinic-*C*H$_3$); LRMS m/z 362.20 (M + H$^+$), calcd $C_{20}H_{27}NO_5$ 361.1889; Anal. calcd for $C_{20}H_{27}NO_5$ (361.19): C, 66.46; H, 7.53; N, 3.88. Found: C, 66.34; H, 7.58; N, 3.82%; HRMS m/z 384.1787 (M + Na), calcd for $C_{20}H_{27}NO_5Na$ 384.1787.

4d: General procedure for the L-proline catalyzed cascade OrgRC reaction: In an ordinary glass vial equipped with a magnetic stirring bar, to 0.1 mmol of the aldehyde **55al** (which is obtained after ester reduction followed by oxidation of **54al**), 0.1 mmol of

Meldrum's acid and 0.1 mmol of Hantzsch ester was added 0.2 mL of acetonitrile, and then the catalyst L-proline **15a** (0.02 mmol, 20 mol%) was added and the reaction mixture was stirred at 25 °C for the time 24 h. The crude reaction mixture was directly loaded onto a silica gel column with or without aqueous work-up, and pure cascade product **56al** was obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate) in 60% yield as yellow liquid.



(–)-**56al**

5-(((4a*R*,6*S*,8a*R*,10*S*,10a*R*)-4a-Hydroxy-1-methyl-10-nitro-6-(prop-1-en-2-yl)-3,4,4a,5,6,7,8,8a,10,10a-decahydroanthracen-2-yl)methyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (56al): Prepared following the procedure **4d** and purified by column chromatography using EtOAc/hexane and isolated as a yellow liquid. **$[\alpha]_D^{25}$ = -84.147° (*c* = 0.1 g/100 mL, $CHCl_3$, 99.99% *ee*);** IR (neat): ν_{max} 3426 (O-*H*), 2928, 2859, 1728, 1622, 1549, 1452, 1381, 1265, 741 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.78 (1H, d, *J* = 5.2 Hz), 4.79 (1H, d, *J* = 12.8 Hz), 4.69 (2H, d, *J* = 12.8 Hz), 3.57 (1H, t, *J* = 6.0 Hz), 3.09-3.04 (2H, m), 2.96 (1H, dd, *J* = 14.4, 5.6 Hz), 2.63-2.47 (2H, m), 2.23-2.14 (1H, m), 2.00-1.97 (1H, m), 1.88 (3H, s), 1.88-1.86 (2H, m), 1.79 (3H, s), 1.77 (3H, s), 1.69 (3H, s), 1.66-1.47 (5H, m), 1.32-1.30 (1H, m), 1.19-1.10 (1H, m); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.4 (2 x C, O-C=O), 149.0 (C), 134.1 (C), 131.8 (C), 127.8 (CH), 126.3 (C), 109.0 (CH_2), 105.1 (C), 91.7 (CH), 68.8 (C), 46.0 (CH), 39.3 (CH), 37.3 (CH), 32.6 (CH_2), 32.0 (CH), 31.8 (CH_2), 31.4 (CH_2), 30.8 (CH_2), 29.3 (CH_2), 28.6 (CH_3), 26.9 (CH_3), 26.2 (CH_2), 20.8 (CH_3), 14.7 (CH_3, olefinic-*C*H_3); LRMS m/z 458.00 ($M - H^+$), calcd $C_{25}H_{33}NO_7$ 459.2257; Anal. calcd for $C_{25}H_{33}NO_7$ (459.23): C, 65.34; H, 7.24; N, 3.05. Found: C, 65.48; H, 7.19; N, 3.12%.

4e: General procedure for the catalytic oxidation with *tert*-butyl hydroperoxide: To a stirred solution of a decalin **49aa/49ba** (0.23 mmol) and vanadyl acetylacetonate (2 mol%) in dichloromethane (2.5 ml) was added 70% aqueous *tert*-butyl hydroperoxide (0.32 mmol) and the mixture was stirred at RT for 14 h. The mixture was then filtered through a pad of aluminium oxide to remove inorganic materials, the filtrate was worked up and the crude

products were purified by column chromatography (silica gel, mixture of hexane/ethyl acetate) to afford the pure cascade products **57aa/57ba**.

(1a*R*,3*S*,4*S*,4a*S*,8a*R*)-Ethyl 4a-hydroxy-8-methyl-4-nitro-3-phenyl-2,3,4,4a,5,6-hexahydro-1aH-naphtho[1,8a-b]oxirene-7-carboxylate (57aa): Prepared following the procedure **4e** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. **$[\alpha]_D^{25}$ = -43.355° (*c* = 0.157 g/100 mL, $CHCl_3$, 99.99% *ee*, 99.99% *de*);** Mp 140-144 °C; IR (Neat): ν_{max} 2924, 1713, 1552, 1457, 1369, 1331, 1261, 1230, 1071, 1045, 1010, 968, 903 and 761 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.31 (2H, t, *J* = 7.2 Hz), 7.25-7.19 (3H, m), 4.63 (1H, d, *J* = 12.4 Hz), 4.24 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.78 (1H, d, *J* = 2.4 Hz), 3.66 (1H, dt, *J* = 12.4, 4.4 Hz), 2.87 (1H, s, -O*H*), 2.73-2.66 (1H, m), 2.62-2.56 (2H, m), 2.38-2.33 (1H, m), 2.10-2.03 (1H, m), 1.88 (1H, dt, *J* = 12.4, 4.4 Hz), 1.78 (3H, s), 1.32 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.1 (C, O-*C*=O), 138.8 (C), 136.1 (C), 134.2 (C), 129.0 (2 x CH), 127.9 (CH), 127.2 (2 x CH), 95.0 (CH), 68.5 (C), 62.0 (C), 60.8 (CH_2, O*C*H$_2$CH$_3$), 59.8 (CH), 35.9 (CH), 33.2 (CH_2), 31.9 (CH_2), 22.3 (CH_2), 14.2 (CH_3, olefinic-*C*H$_3$), 12.6 (CH_3, OCH$_2$*C*H$_3$); HRMS m/z 396.1423 (M + Na), calcd $C_{20}H_{23}NO_6Na$ 396.1423.

(–)-**57aa**

(1a*R*,3*S*,4*S*,4a*S*,8a*R*)-Methyl 4a-hydroxy-8-methyl-4-nitro-3-phenyl-2,3,4,4a,5,6-hexahydro-1aH-naphtho[1,8a-b]oxirene-7-carboxylate (57ba): Prepared following the procedure **4e** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. **$[\alpha]_D^{25}$ = -35.26° (*c* = 0.2 g/100 mL, $CHCl_3$, 99.99% *ee*, 99.99% *de*);** Mp 138-140 °C; IR (KBr): ν_{max} 3449, 2926, 2853, 1724, 1545, 1458, 1283, 1076, 758 and 700 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.34-7.32 (2H, m), 7.26 (1H, td, *J* = 7.0, 2.5 Hz), 7.23-7.22 (2H, m), 4.65 (1H, d, *J* = 12.5 Hz), 3.80 (3H, s, OC*H*$_3$), 3.68 (1H, dt, *J* = 12.5, 4.5 Hz), 2.88 (1H, d, *J* = 2.5 Hz), 2.75-2.68 (1H, m), 2.63-2.58 (2H, m), 2.40-2.36 (1H, m), 2.11 (1H, dd, *J* = 15.0, 13.0 Hz), 1.92-1.86 (1H, m), 1.80 (3H, q, *J* = 1.0 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.4 (C, O-*C*=O), 138.8 (C), 137.0 (C), 133.8 (C), 129.0 (2 x CH), 127.9

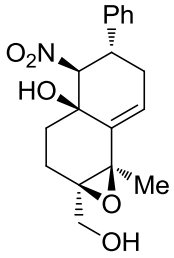
(–)-**57ba**

(CH), 127.2 (2 x CH), 95.0 (CH), 68.5 (C), 62.0 (C), 59.9 (CH), 51.8 (CH_3, OCH_3), 35.9 (CH), 33.2 (CH_2), 31.9 (CH_2), 22.3 (CH_2), 12.7 (CH_3).

4f: General procedure for the epoxidation of decalin 49aa:

First step: In an oven dried round bottom flask, DIBAL-H (2.5 equiv., 1 M) was added to the solution of **49aa** (1.0 equiv.) in dry DCM at 0 °C. After stirring the reaction mixture 1 h at the room temperature, methanol was added slowly with cooling, followed by 2.0 M hydrochloric acid solution. The resulting solid aluminum salts were filtered, the organic layer was separated, and aqueous layer was extracted twice with 20-mL portions of ether. The combined organic layers were dried (Na_2SO_4) and concentrated. Purification of residue over silica gel column using EtOAc/hexane as eluent furnished the allylic alcohol (80%) as white solid.

Second step: To the above allylic alcohol taken in dry CH_2Cl_2, *m*CPBA (1.2 equiv.) was added at 0 °C. After complete consumption of the substrate (as monitored by TLC), the reaction mixture was diluted with CH_2Cl_2, washed with 10% aqueous K_2CO_3 solution, and brine, and dried with Na_2SO_4.Evaporation of solvent under reduced pressure gave crude product, which was purified by column chromatography on silica gel eluting with a mixture of hexane and ethyl acetate to yield the **58aa** in 85% yield as white solid.



(–)-**58aa**

(1a*R*,3a*R*,4*S*,5*S*,7b*R*)-1a-(hydroxymethyl)-7b-methyl-4-nitro-5-phenyl-1a,2,3,3a,4,5,6,7b-octahydronaphtho[1,2-b]oxiren-3a-ol (58aa): Prepared following the procedure **4f** and purified by column chromatography using EtOAc/hexane and isolated as a white solid. **$[\alpha]_D^{25}$ = -28.0° (*c* = 1.0 g/100 mL, EtOH, 99.99% *ee*, 99.99% de);** Mp 185-188 °C; IR (KBr): ν_{max} 3455, 2924, 2853, 1726, 1636, 1553, 1435, 1287, 1173, 1040, 804, 774 and 702 cm^{-1}; ^1H NMR ($CDCl_3$+MeOD, 500 MHz) δ 7.34-7.30 (3H, m), 7.25-7.22 (2H, m), 6.21 (1H, d, *J* = 4.0 Hz), 4.82 (1H, d, *J* = 12.5 Hz), 3.78-3.70 (3H, m), 2.65 (1H, td, *J* = 19.0, 5.5 Hz), 2.36-2.29 (3H, m), 2.25-2.18 (1H, m), 1.70-1.65 (1H, m), 1.59 (3H, s); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 140.3 (C), 135.1 (C), 128.7 (2 x CH), 127.7 (CH), 127.4 (CH), 127.2 (2 x CH), 94.7 (CH), 69.4 (C), 68.2 (C), 64.7 (C), 64.4 (CH_2), 38.5 (CH), 34.4 (CH_2), 32.1 (CH_2), 22.1 (CH_2), 15.2 (CH_3); HRMS m/z 354.1318 (M + Na), calcd $C_{18}H_{21}NO_5Na$ 354.1317.

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53. Azides are energy–rich molecules with many applications. Caution, however, should be exercised when using azides. Both organic and inorganic azides can be heat and shock sensitive and can explosively decompose with little input of external energy. In general, olefinic, aromatic, or carbonyl azides are much less stable than aliphatic azides. For these reasons, azides should not be distilled or treated in a careless fashion. However, when common sense is employed, they can be prepared, stored, and used without risk in the standard organic chemistry laboratory. We have never experienced a safety problem with these organic azides, even at the gram–scale synthesis. For more information, see: a) M. Peer, *Spec. Chem.* **1998**, *18*, 256–263; b) H. C. Kolb, M. G. Finn, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2001**, *40*, 2004–2021; c) S. Bräse, C. Gil, K. Knepper, V. Zimmermann, *Angew. Chem. Int. Ed.* **2005**, *44*, 5188–5240.
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LIST OF PUBLICATIONS

1. D. B. Ramachary, K. Ramakumar, **A. B. Shashank** and V. V. Narayana, "Sequential One-pot Combination of Multi-reactions through Multicatalysis: A General Approach to Rapid Assembly of Functionalized Push-Pull Olefins, Phenols and 2-Methyl-2*H*-chromenes", ***J. Comb. Chem.* 2010**, *12*, 855-876.

2. D. B. Ramachary and **A. B. Shashank,** "Organocatalytic Triazole Formation, Followed by Oxidative Aromatization: Regioselective Metal-free Synthesis of Benzotriazoles", ***Chem. Eur. J.* 2013**, *19*, 13175-13181.

3. D. B. Ramachary, **A. B. Shashank** and S. Karthik, "An Organocatalytic Azide–Aldehyde [3+2]-Cycloaddition: High-yielding Regioselective Synthesis of 1,4-Disubstituted 1,2,3-Triazoles", ***Angew. Chem. Int. Ed.* 2014**, *53*, 10420-10424.

4. **A. B. Shashank**, S. Karthik, R. Madhavachary and D. B. Ramachary, "An Enolate-mediated Organocatalytic Azide–Ketone [3+2]-Cycloaddition Reaction: Regioselective High-yielding Synthesis of Fully Decorated 1,2,3-Triazoles", ***Chem. Eur. J.* 2014,** *20*, 16877-16881.

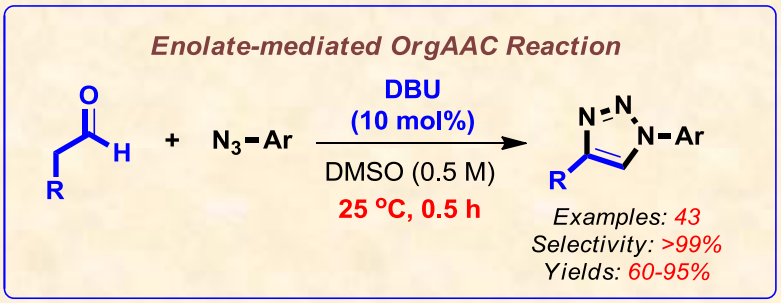
5. **A. B. Shashank** and D. B. Ramachary, "Organocatalytic Asymmetric Synthesis of Substituted Chiral Decalines through Diastereoselective Domino Claisen-Schmidt/Henry Reaction", (*to be communicated*).

POSTER AND ORAL PRESENTATIONS

1. Presented a poster entitled "**Organocatalytic Triazole Formation, Followed by Oxidative Aromatization: Regioselective Metal-free Synthesis of Benzotriazoles**" in "***National symposium on Frontiers in Organic Chemistry*** (***NSFOC***)" held at University of Hyderabad, Hyderabad, India on Oct. 11-12th, 2013.

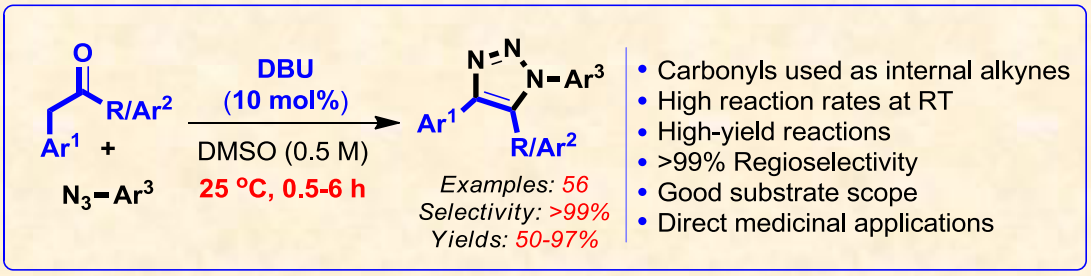
2. Given a flash oral presentation entitled "**Organocatalytic Triazole Formation, Followed by Oxidative Aromatization: Regioselective Metal-free Synthesis of Benzotriazoles**" in 11th in-house symposium "***Chemfest-2014***" held at University of Hyderabad, Hyderabad, India on Feb 21-22nd, 2014.

1. **An Organocatalytic Azide-Aldehyde [3+2]-Cycloaddition Reaction: High-yielding Regioselective Synthesis of 1,4-Disubstituted 1,2,3-Triazoles.**



Angew. Chem. Int. Ed. **2014**, *53,* 10420-10424.

2. **An Enolate-mediated Organocatalytic Azide-Ketone [3+2]-Cycloaddition Reaction: Regioselective High-yielding Synthesis of Fully Decorated 1,2,3-Triazoles.**



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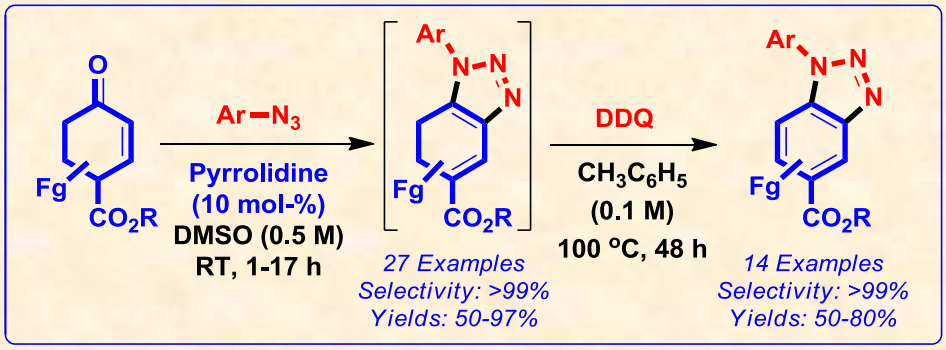
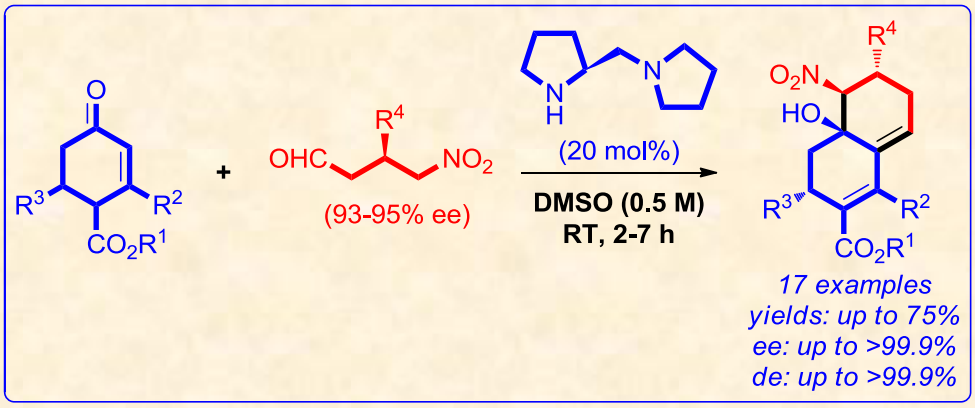
3. **Organocatalytic Triazole Formation Followed by Oxidative Aromatization: Regioselective Metal-free Synthesis of Benzotriazoles.**



Chem. Eur. J. **2013**, *19*, 13175-13181.

4. **Organocatalytic Asymmetric Synthesis of Substituted Chiral Decalines through Diastereoselective Claisen-Schmidt/Henry Reaction.**



to be communicated..