SYNTHESIS OF DRUG-LIKE MOLECULES BASED ON THE PUSH-PULL DIENAMINE PLATFORM

A Thesis
Submitted for the Degree of

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By

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DEDICATED TO

AMMA AND NANNA

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 ***Dr. 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.*

VIDADALA VENKATA NARAYANA

(Candidate)

CERTIFICATE

I hereby certify that the entire work embodied in this thesis has been carried out by ***Mr. Venkata Narayana Vidadala*** *under my guidance in the School of Chemistry, University of Hyderabad, and that no part of it has been submitted elsewhere for any degree or diploma.*

Dr. DHEVALAPALLY B. RAMACHARY
(THESIS SUPERVISOR)

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Venkata Narayana Vidadala

PREFACE

*Nature is the inspiration to develop a new area of catalysis "Organocatalysis" to synthesize stereochemically complex molecules. These molecules, formed through enamine or iminium catalysis by using primary or secondary amines, have been used as key intermediates to synthesize medicinally important heterocycles through appropriate metal catalysis. The present thesis entitled "**Synthesis of Drug-Like Molecules Based on the Push-Pull Dienamine Platform**" describes the applications of push-pull dienamine intermediates in cascade reaction followed by either ring-closing metathesis, base-induced ring-opening, [1,7]-sigmatropic hydrogen shift reactions or ring-closing metathesis, base-induced ring-opening, gold-catalyzed intramolecular hydroamination and cascade intermolecular hydroamination/[4+2]-cycloaddition reactions in a sequential manner for the synthesis of highly functionalized molecules. 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 molecules are widely used as intermediates in the pharmaceuticals and natural product synthesis. To construct such functionalized molecules, a diversity-oriented, general, sustainable and practical process for the sequential cascade synthesis is required. Here we discovered direct sequential one-pot combination of amine- or amino acid-catalyzed cascade Knoevenagel/Michael/aldol condensation/decarboxylation with other reactions like amine- or amino acid-catalyzed cascade Claisen-Schmidt/iso-aromatization (CS/IA), O- and C-allyations, ring closing metathesis (RCM), base-induced ring opening (BIRO), benzylic oxidation (BO) and [1,7]-sigmatropic hydrogen shift ([1,7]-SHS) reactions of alkyl acetoacetates, variety of aldehydes furnished the highly functionalized push-pull phenols and 2-methyl-2H-chromenes with high yields.

Highly functionalized diverse benzo[b]oxepines, (Z)-2-(buta-1,3-dienyl)phenols and 2-methyl-2H-chromenes are having wide applications and considerable importance in

various industries. To construct such complex molecules a diversity-oriented synthesis is required. We reported a novel one-pot and multi-catalysis technology for the synthesis of highly substituted benzo[b]oxepines, (Z)-2-(buta-1,3-dienyl)phenols and 2-methyl-2H-chromenes. Here, we achieved the synthesis of benzo[b]oxepines, (Z)-2-(buta-1,3-dienyl)phenols and 2-methyl-2H-chromenes using simple starting materials such as alkyl acetoacetates, aldehydes and nitrosoarenes in high yields through sequential combination of amine-catalyzed cascade Knoevenagel/Michael/aldol condensation/decarboxylation and cascade enamine amination/isoaromatization, O- and C-allyations, ring closing metathesis, base-induced ring opening and [1,7]-sigmatropic hydrogen shift reactions in a sequential manner.

In continuation for the synthesis of highly functionalized molecules through MCC approach, a sequential combination of multi-catalytic one-pot process for the synthesis of highly functionalized N-substituted benzo[b]azepines, (Z)-2-(buta-1,3-dienyl)phenylamines, 2-methyl-2H-quinolines and phenanthridines starting from simple dienes was demonstrated for the first time via sequential ring-closing metathesis (RCM)/base-induced ring-opening (BIRO) and gold-catalyzed hydroamination followed by [4+2]-cycloaddition reactions.

In a similar manner, a novel and green technology was developed for the three-step synthesis of highly substituted benzoxazocines using amine/potassium carbonate/sodium hydride/ruthenium-catalyses through cascade enamine amination/iso-aromatization/O-allylation (EA/IA/A), N-allylation, and diene or enyne metathesis as key steps starting from commercially available Hagemann's esters. We demonstrated the synthesis of Nefopam analogues for the first time through MCC approach. Also, we developed the application of ruthenium catalysis on olefins containing free amines without in situ formation of salts.

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
Calcd.	calculated
cat.	catalytic
cm	centimeter
DABCO	1,4-diazabicyclo(2.2.2)octane
DBU	1,8-diazabicyclo(5.4.0)undec-7-ene
DCB	1,2-dichlorobenzene
DCE	1,2-dichloroethane
DCM	dichloromethane
dd	doublet of doublet
de	diastereomeric excess
DEPT	distortionless enhancement by polarization transfer
DMAP	dimethylaminopyridine
DMF	*N*,*N*-dimethylformamide
DMSO	dimethyl sulfoxide
DPP	diphenyl prolinol
dr	diastereomeric ratio
dt	doublet of triplet
ee	enantiomeric excess
eq.	equation
equiv.	equivalent(s)
Et	ethyl
EWG	electron withdrawing group
Fig.	figure
gm	gram (s)
h	hour (s)
Hz	hertz
Hex	hexyl
^{i}Pr	isopropyl
IR	infrared
lit.	literature
m	multiplet
m-CPBA	*m*-chloro perbenzoic acid
M	molarity
Mp.	melting point
Me	methyl

mg	milligram (s)
mL	milliliter
mmol	millimole
NMR	nuclear magnetic resonance
NMP	*N*-methylpyrrolidine
Ph	phenyl
Pg	protecting group
ppm	parts per million
p-TSA	*p*-toluenesulfonic acid
py	pyridine
pr	propyl
q	quartet
RT	room temperature
s	singlet
sec	secondary
t	triplet
td	triplet of doublet
tert	tertiary
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
TsCl	toluenesulphonyl chloride

ABOUT THE AUTHOR

The author, **Mr. Venkata Narayana Vidadala** was born on 16th May 1982 at Purushothamapatnam, Guntur Dist, Andhra Pradesh. After his initial schooling in Purushothamapatnam, Guntur (Dist.), he obtained his B.Sc. degree in 2001 from D. R. N. S. C. V. S. College, Chilakaluripet; and he obtained his M. Sc. degree in 2003 from Ideal College, Kakinada. He joined as research scholar in the School of Chemistry, University of Hyderabad for the Ph. D. program from July 2005. In July 2007, he became as SRF and presently he is working as a research associate (RA) in the department.

LIST OF PUBLICATIONS

1. D. B. Ramachary, K. Ramakumar and **V. V. Narayana**, Organocatalytic cascade reactions based on push-pull dienamine platform: synthesis of highly substituted anilines, ***J. Org. Chem.*** **2007**, *72*, 1458–1463.
2. D. B. Ramachary, **V. V. Narayana** and K. Ramakumar, Direct ionic liquid promoted organocatalyzed diazo-transfer reactions: diversity-oriented synthesis of diazo-compounds, ***Tetrahedron Lett.*** **2008**, *49*, 2704–2709.
3. D. B. Ramachary, **V. V. Narayana** and K. Ramakumar, A new one-pot synthetic approach to the highly functionalized (*Z*)-2-(buta-1,3-dienyl)phenols and 2-methyl-2*H*-chromenes: Use of amine, ruthenium and base-catalysis, ***Eur. J. Org. Chem.*** **2008**, 3907–3911.
4. D. B. Ramachary, K. Ramakumar and **V. V. Narayana**, Amino acid-catalyzed cascade [3+2]-cycloaddition/hydrolysis reactions based on the push–pull dienamine platform: Synthesis of highly functionalized *N*H-1,2,3-triazoles, ***Chem. Eur. J.*** **2008**, *14*, 9143–9147.
5. D. B. Ramachary, **V. V. Narayana**, M. S. Prasad and K. Ramakumar, High-yielding synthesis of Nefopam analogues (functionalized benzoxazocines) by

sequential one-pot cascade operations, ***Org. Biomol. Chem.* 2009**, *7*, 3372–3378.

6. D. B. Ramachary, K. Ramakumar, A. B. Shashank and **V. V. Narayana**, Sequential one-pot combination of multi-reactions through multi-catalysis: 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.

7. D. B. Ramachary and **V. V. Narayana**, Sequential combination of ruthenium-, base- and gold-catalysis: A new approach to the synthesis of medicinally important heterocycles (*communicated*).

POSTERS AND PRESENTATIONS

1. Presented a poster entitled "A new one-pot synthetic approach to the highly functionalized (*Z*)-2-(buta-1,3-dienyl)phenols and 2-methyl-2*H*-chromenes: Use of amine, ruthenium and base-catalysis" in 6th in-house symposium **"Chemfest-2009"** held at University of Hyderabad, Hyderabad, India on March 7-9, 2009.
2. Given a flash oral presentation entitled "MCC approach to some important biologically active scaffolds" in 7th in-house symposium "**Chemfest-2010**" held at University of Hyderabad, Hyderabad, India on January 9-10, 2010.

SYNTHESIS OF DRUG-LIKE MOLECULES BASED ON THE PUSH-PULL DIENAMINE PLATFORM

1. *ABSTRACT*

A general, sustainable and practical process for the sequential cascade one-pot synthesis of highly substituted phenols and 2-methyl-2*H*-chromenes was reported through multi-catalysis cascade (MCC) reactions. Direct sequential one-pot combination of amine- or amino acid-catalyzed cascade Knoevenagel/Michael/aldol condensation/decarboxylation with other reactions like amine- or amino acid-catalyzed cascade Claisen-Schmidt/iso-aromatization, ruthenium-base-silica-catalyzed ring closing metathesis/base-induced ring-opening/benzylic oxidation/[1,7]-sigmatropic hydrogen shift, or ruthenium-base-heat-catalyzed ring closing metathesis/base-induced ring-opening/[1,7]-sigmatropic hydrogen shift reactions of alkyl acetoacetates, variety of aldehydes furnished the highly functionalized phenols and 2-methyl-2*H*-chromenes with high yields. The yields and regioselectivities were good to excellent. Evidence for a new reaction pathway involving formation of novel push-pull dienamines under amine- or amino acid-catalysis is presented along with examples demonstrating the amenability of the process to multi-catalysis cascade (MCC) chemistry.

A practical and simple one-pot multi-catalysis process for the synthesis of highly substituted benzo[*b*]oxepines, (*Z*)-2-(buta-1,3-dienyl)phenols and 2-methyl-2*H*-chromenes from simple starting materials was achieved for the first time through ring-

closing metathesis/base-induced ring opening/[1,7]-sigmatropic hydrogen shift reactions. The synthesis of privileged (*Z*)-2-(buta-1,3-dienyl)phenols via base-induced ring opening of highly functionalized benzo[*b*]oxepines is described.

A sequential multi-catalytic one-pot process for the synthesis of highly functionalized *N*-substituted benzo[*b*]azepines, *N*-substituted 2-(buta-1,3-dienyl)phenylamines, *N*-substituted 2-methyl-2*H*-quinolines and *N*-substituted phenanthridines from simple starting materials was achieved for the first time through ring-closing metathesis/base-induced ring opening, intramolecular hydroamination and cascade intermolecular hydroamination/[4+2]-cycloaddition reactions.

An efficient amine/ruthenium-catalyzed three-step process for the synthesis of Nefopam analogues was achieved through a combination of cascade enamine amination/iso-aromatization/allylation and diene or enyne-metathesis as the key steps, starting from functionalized Hagemann's esters. In this thesis, we developed the application of ruthenium catalysis on olefins containing free amines.

2. *INTRODUCTION*

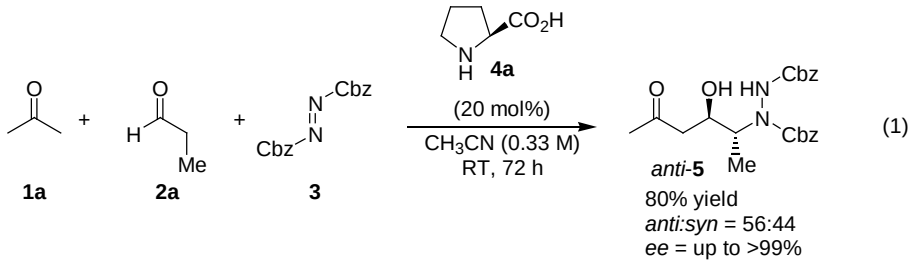
A challenging task in modern synthetic organic chemistry, which deals with the synthesis of natural products, pharmaceuticals, diagnostics, agrochemicals and other important materials, is the improvement of reaction efficiency, avoidance of toxic reagents, reduction of waste, and the responsible utilization of our resources. Towards these goals, one-pot multi-component and multi-catalytic reactions, tandem reactions, organocatalytic cascade or organocatalytic domino reactions were developed. Among them, organocatalytic cascade or domino reactions in which two or more bond-forming transformations take place under the same reaction conditions, address many of these objectives. One of the ultimate goals in organic synthesis is the catalytic asymmetric assembly of simple and readily available precursor molecules into bioactive products, a process that ultimately mimics biological synthesis. Cascade reactions have gained wide acceptance because they increase synthetic efficiency by decreasing the number of

laboratory operations required, the quantities of chemicals and solvents used. Thus, these reactions can facilitate ecologically and economically favorable syntheses.

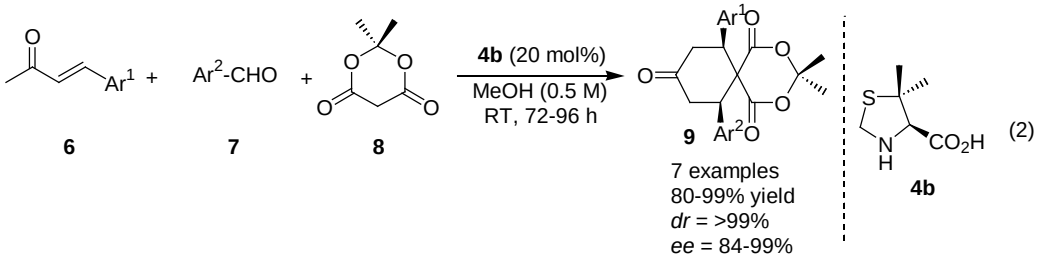
We are in the "golden age of organocatalysis" and organocatalytic reactions in the past few years have emerged as a powerful synthetic tool for the construction of highly functionalized optically active compounds. The use of natural or unnatural amino acids and chiral secondary amines as catalysts for the functionalizations of aldehydes and ketones via iminium and enamine formation gave an important breakthrough in modern asymmetric synthesis. A large variety of functionalizations, such as C-C, C-N, C-O, C-S, and C-X (X = halogen) bond forming reactions has been developed through iminium and enamine catalysis. The combination of two or more organocatalytic reactions with a proper synthetic plan utilizing one or more organocatalysts in one-pot synthesis delivers complex products, which is presently being developed as a new strategy in cascade reactions. The natural amino acid, L-proline has been defined as the universal asymmetric catalyst, because of its high utility in enantioselective aldol, Mannich, amination and α-aminoxylation reactions.

As the research work described in this thesis deals with the synthesis of drug-like molecules based on organocatalytic push-pull dienamines,[1] a brief overview of organocatalytic cascade reactions in one-pot via iminium and enamine intermediates are presented below.

The first organocatalytic cascade reaction was reported by Barbas *et al*. in 2003. In this novel cascade reaction, a simple natural amino acid, L-proline **4a** catalyzed the direct asymmetric assembly of propionaldehyde **2a**, acetone **1a** and azidodicarboxylic acid ester **3** to furnish the β-amino alcohol **5** in good yield with excellent enantio- and diastereoselectivity as shown in eq. 1.[2] This was the first example where both aldehydes and ketones were used as donors in one-pot.

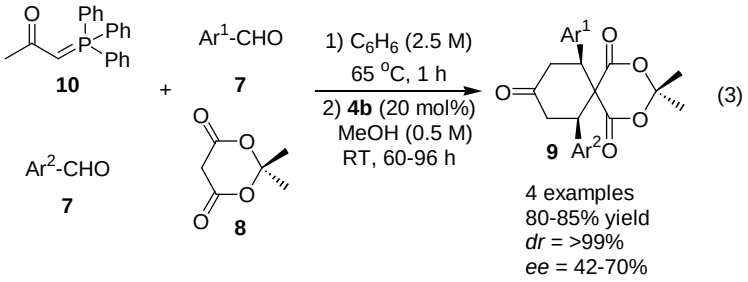


In continuation of the development of organocatalytic cascade reactions, in 2003 the same research group described the synthesis of highly substituted spiro[5,5]undecane-1,5,9-triones **9** with good yields and excellent diastereoselectivities from α,β-unsaturated ketones **6**, aldehydes **7** and 2,2-dimethyl-1,3-dioxane-4,6-dione (Meldrum's acid) **8** via domino Knoevenagel/Diels-Alder reaction as shown in eq. 2.[3]



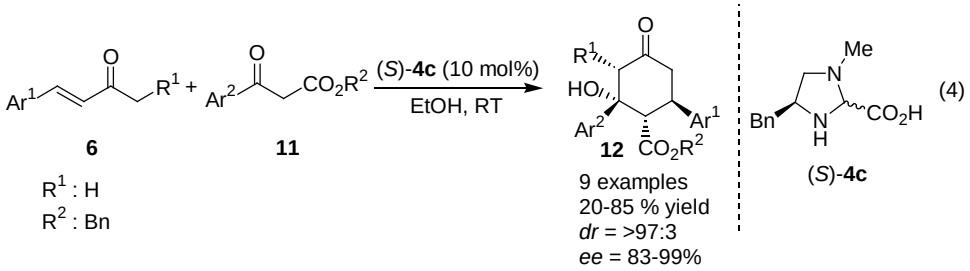
In 2004, Ramachary and Barbas accomplished a four-component Wittig/Knoevenagel/Diels-Alder reactions in one pot, catalyzed by L-DMTC **4b** to provide highly substituted spirocyclic ketones **9** with good yields and excellent

diastereoselectivities from simple starting materials phosphorane **10**, aldehydes **7** and Meldrum's acid **8** as shown in eq. 3.[4] Spirocyclic ketones **9** are excellent starting materials for the synthesis of exotic amino acids which are used to modify the physical properties and biological activities of peptides, peptidomimetics and proteins.



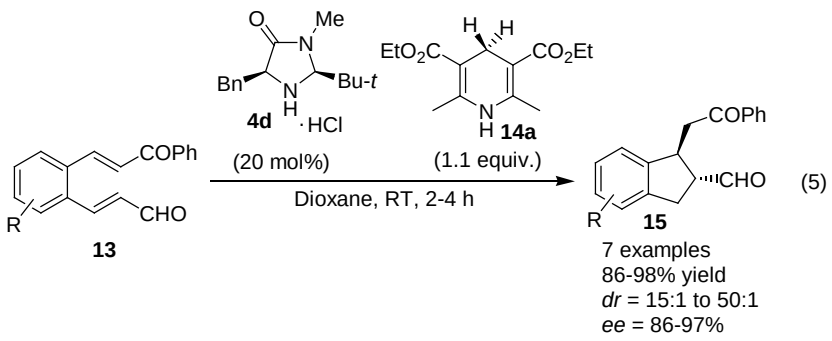
(3)

In the same year, Jørgensen *et al.* reported an impressive organocatalytic asymmetric domino Michael/aldol reaction, catalyzed by a phenylamine-derived imidazolidine **4c** to furnish the cyclohexanones **12** containing four stereogenic centers with high enantio- and diastereoselectivities from acyclic β-ketoesters **11** and α,β-unsaturated ketones **6** as shown in eq. 4.[5]

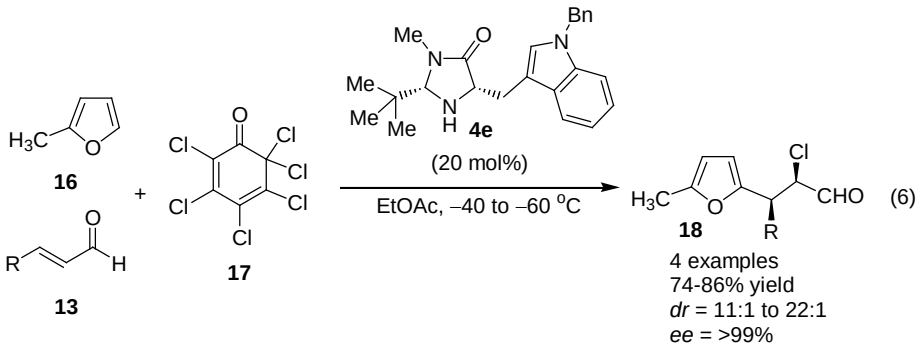


(4)

In 2005, Benjamin List and co-workers described another important class of cascade reactions, which proceeded through organocatalytic reductive Michael cyclizations of enalenones **13** via an iminium conjugate reduction followed by an *in situ* enamine asymmetric Michael cyclization to provide keto aldehydes **15** with good yields and high enantioselectivities as shown in eq. 5.[6]

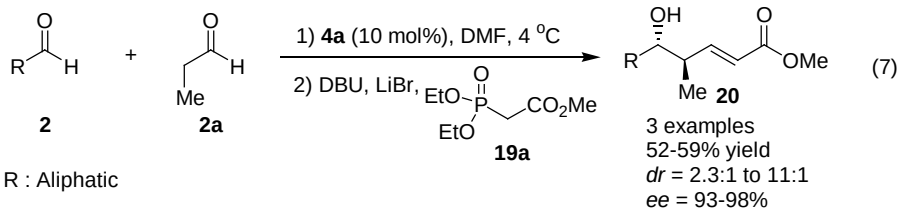


In a subsequent communication, MacMillan and co-workers reported a novel three-component domino Michael/electrophilic addition reaction which led to the invention of enantioselective transformations with two adjacent stereogenic centers. In this report, they described the conjugate addition of heteroatomic nucleophile **16** to the iminium ion of the enal **13**, followed by electrophilic (derived from chlorinating reagent **17)** addition with *in situ* generated enamine to furnish the product **18** with good yields and excellent enantioselectivities as shown in eq. 6.[7]



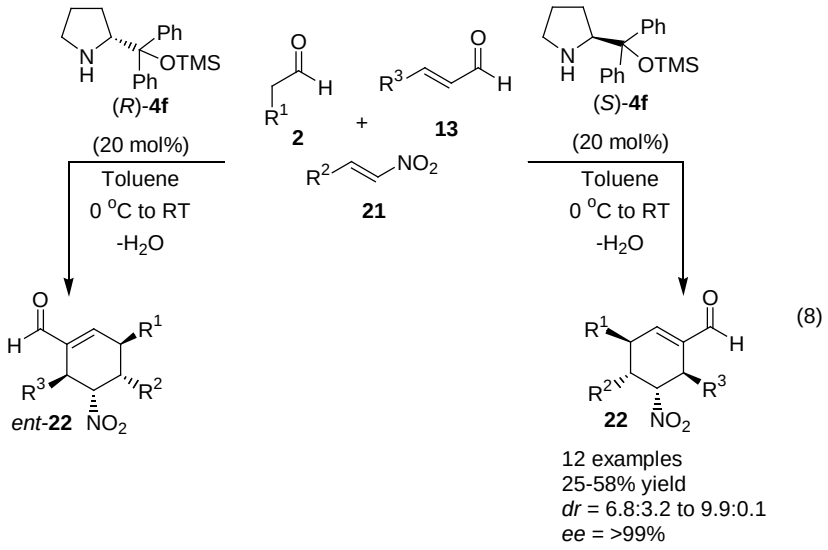
In 2006, Córdova and co-workers used the simple natural amino acid, L-proline **4a** as catalyst to synthesize polyketides **20** with good yields and high enantioselectivities from commercially available aliphatic aldehydes **2**, propionaldehyde **2a** and phosphonate **19a** via a tandem asymmetric cross-aldol/Horner-Wittig-Emmons

(HWE) reaction as shown in eq. 7.[8] Polyketides **20** are excellent starting materials for the synthesis of enantioselective carbohydrate derivatives.



(7)

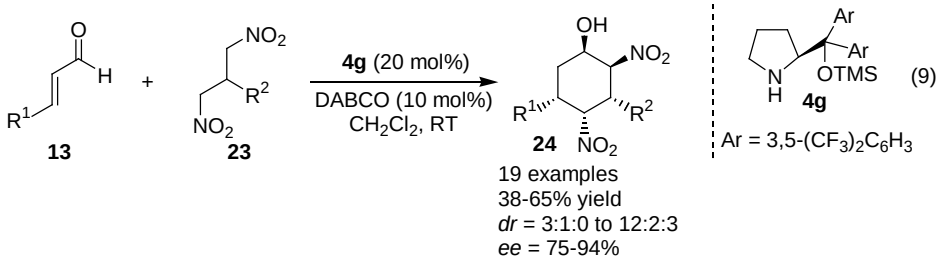
In the same year, Enders *et al*. reported a three-component asymmetric organocatalytic triple cascade Michael/Michael/aldol condensation sequence, catalyzed by **4f** to provide the tetra-substituted cyclohexene carbaldehydes **22** with four stereogenic centers in moderate to good yields and high diastereoselectivities with >99% *ee* from aliphatic aldehydes **2**, α,β-unsaturated aldehydes **13** and nitro olefins **21** as shown in eq. 8.[9]



(8)

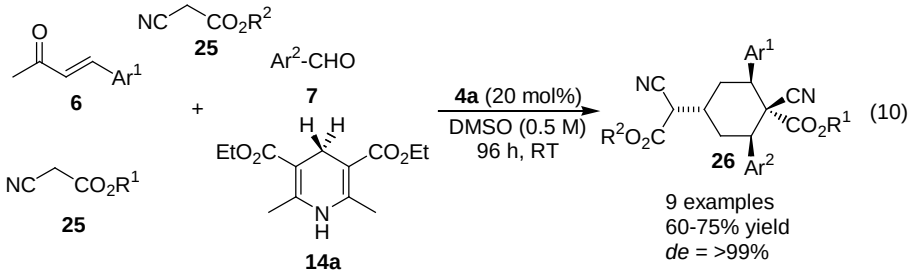
In 2007, Jørgensen *et al.* used (*S*)-diarylprolinol silyl ether **4g** to synthesize cyclohexanols **24** containing five contiguous stereocenters in a highly enantio- and

diastereoselective fashion with moderate to good yields from α,β-unsaturated aldehydes **13** and nitro alkanes **23** via domino nitro-Michael/Henry reaction as shown in eq. 9.[10]



(9)

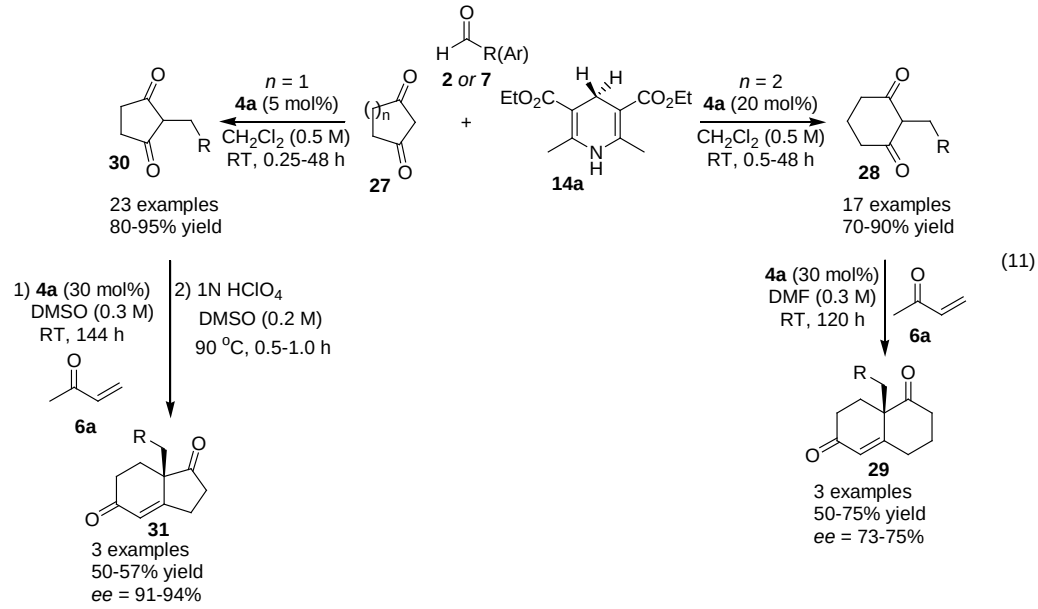
In 2008, Ramachary *et al.* demonstrated a L-proline **4a** catalyzed five-component cascade olefination/Diels-Alder/epimerization/olefination/hydrogenation reactions that provided highly substituted 1-cyano-4-(cyano-alkoxycarbonyl-alkyl)-2,6-diaryl-cyclohexanecarboxylic acid alkyl esters **26** in good yields and excellent diastereoselectivities from α,β-unsaturated ketones **6**, aldehydes **7**, alkyl cyanoesters **25** and Hantzsch ester **14a** as shown in eq. 10.[11]



(10)

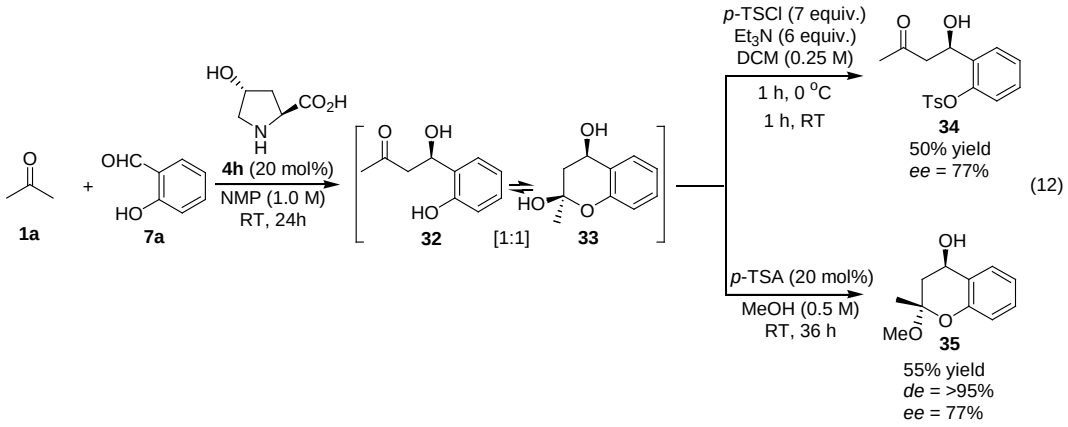
In 2007, Ramachary *et al.* reported a simple natural amino acid L-proline **4a** catalyzed three- and four-component asymmetric cascade Knoevenagel/hydrogenation (K/H) and Knoevenagel/hydrogenation/Robinson annulation (K/H/RA) reactions of cyclic-1,3-diones **27**, aldehydes **2** or **7**, Hantzsch ester **14a** and methyl vinyl ketone **6a** to furnish the substituted 2-alkyl-cyclohexane-1,3-diones **28** and Wieland-Miescher (W-

M) ketone analogues **29** with good yields and high enantioselectivities as shown in eq. 11.[12] In continuation of the development of organocatalytic cascade reactions, in 2008 the same research group demonstrated a one-pot double cascade reaction, catalyzed by L-proline **4a** to provide the substituted 2-alkyl-cyclopentane-1,3-diones **30** and Hajos-Parrish (H-P) ketone analogues **31** with good yields and high enantioselectivities from simple starting materials via olefination/hydrogenation (O/H) and olefination/hydrogenation/Robinson annulations (O/H/RA) sequence as shown in eq. 11.[13]



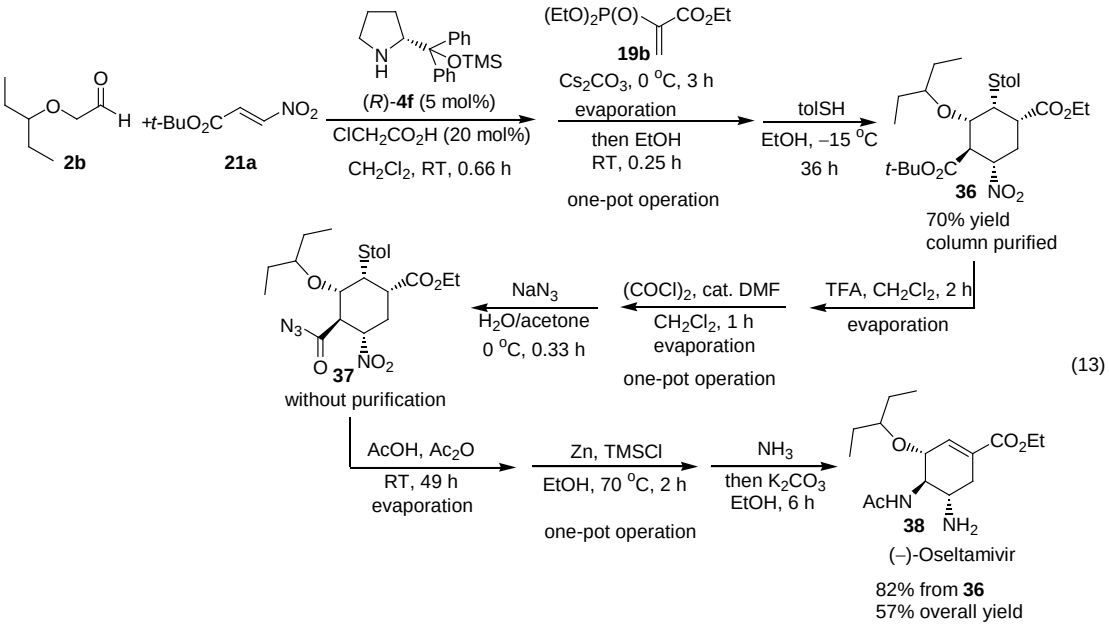
In 2009, Ramachary *et al.* documented an impressive organocatalytic asymmetric Barbas-List aldol (BLA) reaction, catalyzed by *trans*-4-OH-L-proline **4h** to furnish 2-methylchroman-2,4-diol **33** in a highly enantio- and diastereoselective fashion with moderate to good yield from commercially available acetone **1a** and aldehyde **7a**. In this report, they described the existence of fast dynamic equilibrium between 2-methyl-chroman-2,4-diol **33** and 4-hydroxy-4-(2-hydroxy-phenyl)-butan-2-one **32**

under the normal reaction conditions and applied this methodology for the synthesis of functionalized molecules **34** and **35** via acid/base catalysis in a one-pot reaction as shown in eq. 12.[14]



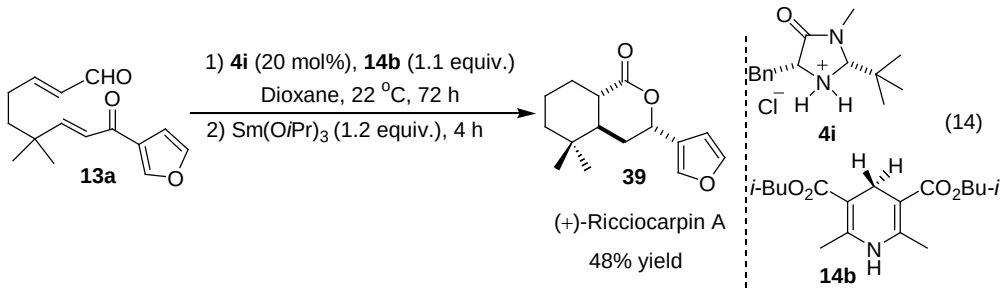
(12)

In the same year, Hayashi *et al*. reported an enantioselective total synthesis of (–)-Oseltamivir **38**, which emphasized the advantages of organocatalysis and one-pot domino reactions. A high-yielding asymmetric total synthesis of (–)-Oseltamivir **38** from simple starting materials alkoxyaldehyde **2b**, nitroalkene **21a** and phosphonate derivative **19b,** required only three separate one-pot operations as shown in eq. 13.[15] Among these three one-pot operations, the first one-pot operation was the most crucial, which involved the diphenylprolinol silyl ether (*R*)-**4f** catalyzed asymmetric Michael reaction, a domino Michael/Horner-Wardsworth-Emmons reaction, followed by thiol-Michael reaction, to furnish the highly functionalized chiral cyclohexane **36** with 70% yield. The remaining two one-pot operations involve the conversion of a *tert*-butoxycarbonyl group into an acetylamino moiety and the reduction of nitro group into an amine moiety.



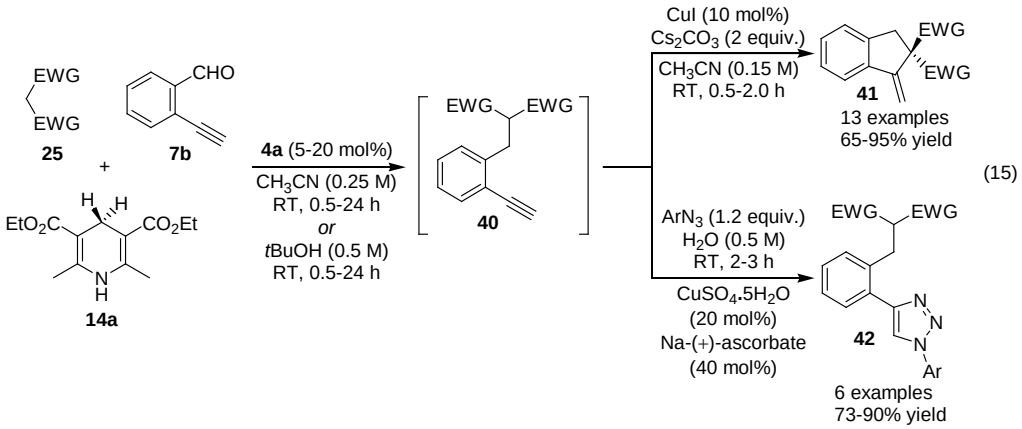
(13)

In 2009, Benjamin List *et al*. reported a highly enantio- and diastereoselective one-pot synthesis of (+)-Ricciocarpin A **39** with 48% yield from the keto aldehyde **13a** and the organic hydride **14b** via organocatalytic reductive Micheal-Tishchenko cascade reaction sequence as shown in eq. 14.[16] They also described the synthesis of four important structural analogues of (+)-Ricciocarpin A. A preliminary biological evaluation of these compounds showed significantly improved molluscicidal activity.



(14)

In 2010, Ramachary *et al.* demonstrated multi-catalytic cascade (MCC) reactions for the synthesis of substituted indenes **41** and 1,2,3-triazoles **42** via sequential combination of organocatalysis and copper catalysis from commercially available 2-ethynylbenzaldehyde **7b**, CH acids **25,** organic hydride **14a** and azides as shown in eq. 15.[17]



(15)

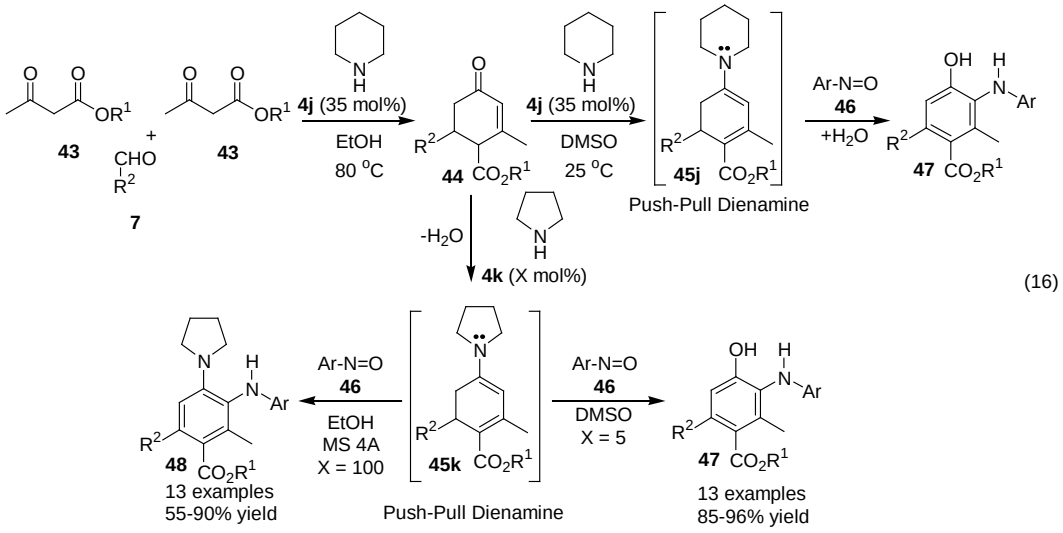
3. BACKGROUND

The field of the organocatalysis is newly emerging green technology in organic synthesis, in which small organic molecules like amines and amino acids catalyze a variety of reactions, as in metal catalysis. Transition metal catalysts are particularly useful in organic synthesis, but may leave toxic traces of heavy metals in the product. Pure organic molecules have been used to catalyze organic reactions since the dawn of synthesis, but they have regretfully been overlooked as transporters of stereochemical information even though this green approach has many important advantages over metal-catalysis. As organocatalysts are robust, inexpensive, readily available, less-toxic, insensitive to moisture and oxygen, they confer a huge direct benefit in the production of active pharmaceutical ingredients (API) and pharmaceutical intermediates when

compared with transition metal catalysts.

Most of the organocatalytic reactions are accomplished by the addition of catalytic amount of chiral amines or amino acids with carbonyl compounds to generate *in situ* enamine or iminium ions, which undergo selective reactions with surrounding electrophiles or nucleophiles. Some of the most powerful organocatalysts in organic synthesis are L-proline and its derivatives, which have been developed and applied successfully for the activation of carbonyl compounds in various ways. Recently, amine- or amino acid-catalysis (organocatalysis) has emerged as a promising sustainable synthetic tool for constructing a combination of C-C, C-N, C-O, C-S, C-P, C-X (X = halogen) and/or C-H bonds in a single operation with high diastereo- and enantioselectivity in a cascade or multi-component process.[18]

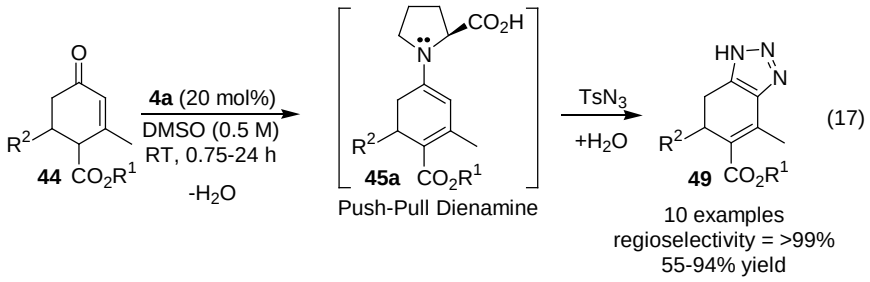
As part of ongoing research in our laboratory to engineer direct combination of organocatalytic multi-component and multi-catalytic reactions,[19] a novel organocatalytic push-pull dienamine and its synthetic applications have been accomplished, which are presented below.



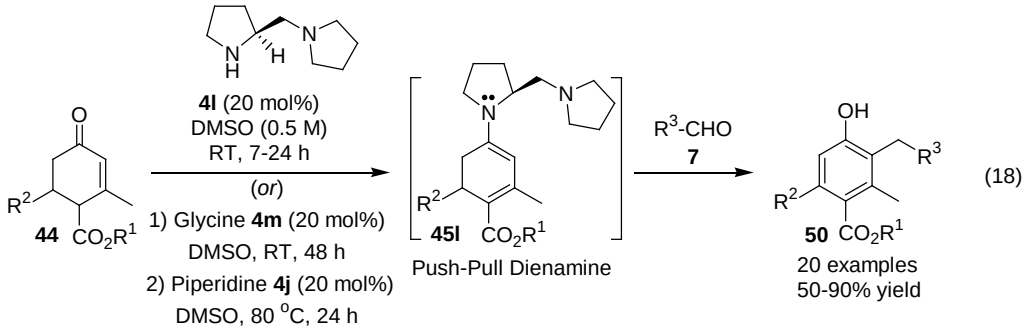
(16)

An amine catalyzed novel one-pot cascade Knoevenagel/Michael/aldol condensation/decarboxylation (K/M/A/DC) and cascade enamine amination/iso-

aromatization (EA/IA) reaction sequence were developed for the synthesis of *o*-hydroxydiarylamines **47** and *o*-pyrrolidin-1-yl-diarylamines **48** from commercially available alkyl acetoacetates **43**, aldehydes **7** and nitrosobenzene **46** as shown in eq. 16.[1d]



In continuation of our discovery of *in situ* generation and application of novel push-pull dienamines in tandem reactions, we developed a novel [3+2]-cycloaddition/hydrolysis reactions of enones **44** and azide, catalyzed by L-proline **4a** to furnish the highly functionalized *N*H-1,2,3-triazoles **49** with good yields and excellent regioselectivity as shown in eq.17.[1e]



We also developed another important application of organocatalytic push-pull dienamines for the synthesis of highly substituted phenols **50** with good yields from Hagemann's esters **44**, aldehydes **7** via Claisen-Schmidt/iso-aromatization (CS/IA) reactions as shown in eq. 18.[1a]

With this background, in continuation of synthesis of highly functionalized molecules from a variety of Hagemann's esters **44**, research work has been carried out on the synthesis of drug-like molecules based on the push-pull dienamine platform,[1] and the results are presented in this thesis.

To begin with, starting from simple starting materials, reactions involving a sequential one-pot combination of cascade Claisen-Schmidt/iso-aromatization/allylation (CS/IA/A), Claisen rearrangement, ring-closing metathesis (RCM), base-induced ring-opening (BIRO) and [1,7]-sigmatropic hydrogen shift (SHS) reactions were developed for the synthesis drug-like molecules,[1a] and the results are presented in the next section.

4. SEQUENTIAL ONE-POT COMBINATION OF MULTI-REACTIONS THROUGH MULTI-CATALYSIS: A GENERAL APPROACH TO RAPID ASSEMBLY OF FUNCTIONALIZED PUSH-PULL OLEFINS AND PHENOLS

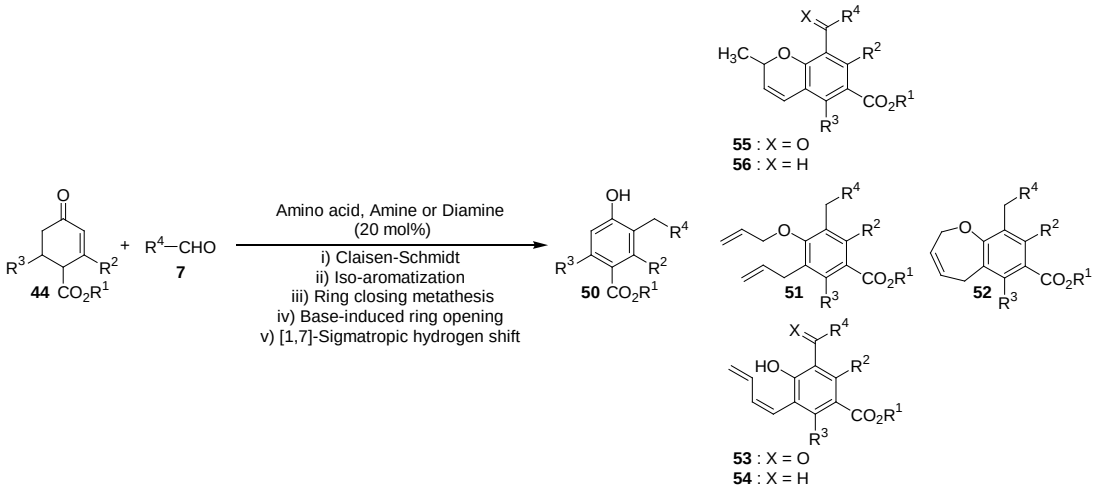
4.1 INTRODUCTION

Critical objectives in modern synthetic organic chemistry include the catalytic asymmetric assembly of simple and readily available precursor molecules into stereochemically and electronically complex compounds under sustainable reaction conditions as mimicking cellular reactions. In this regard, the development of one-pot sequential combination of multi-catalysis and multi-component reaction methodologies can provide expedient access to complex products from simple starting materials.[20] Recently, amine- or amino acid-catalysis (organocatalysis) has emerged as a promising sustainable synthetic tool for the constructing combination of C-C, C-N, C-O, C-S, C-P, C-F and/or C-H bonds in a single operation with high diastereo- and enantioselectivity in a cascade or multi-component process.[18] Generally in organocatalysis, structurally simple and stable chiral organoamines and amino acids facilitate iminium- and enamine-based transformations with carbonyl compounds and are used as catalysts in operationally simple and environmentally friendly cascade reactions.

As a part of our research program to engineer direct combination of organocatalytic multi-component and multi-catalytic reactions,[19] highly substituted phenols **50**, fully functionalized benzenes **51**, highly functionalized benzo[*b*]oxepines **52**, functionalized (*Z*)-2-buta-1,3-dienyl-phenols **53**/**54** and highly substituted 2-methyl-2*H*-chromenes **55**/**56** were synthesized through organocatalytic regioselective direct cascade Claisen-Schmidt/iso-aromatization (CS/IA), *O*- and *C*-allyations, ring closing metathesis (RCM), base-induced ring opening (BIRO), benzylic oxidation (BO) and [1,7]-sigmatropic hydrogen shift ([1,7]-SHS) reactions from commercially available Hagemann's esters **44**, aldehydes **7**, allyl bromide **57a** or propargyl bromide **57b** and

amines or amino acids **4** and the results are discussed in the present section (Scheme 1). Push-pull phenols **50** are attractive intermediates in the synthesis of natural products and in medicinal chemistry,[21] while functionalized 2-methyl-2*H*-chromenes **55**/**56** and analogues thereof have broad utility in pharmaceutical chemistry[22] and in organic synthesis (see Chart 1). Hence, their economical and environmental friendly preparation has continued to attract considerable synthetic interest in developing new methods for their syntheses.[23]

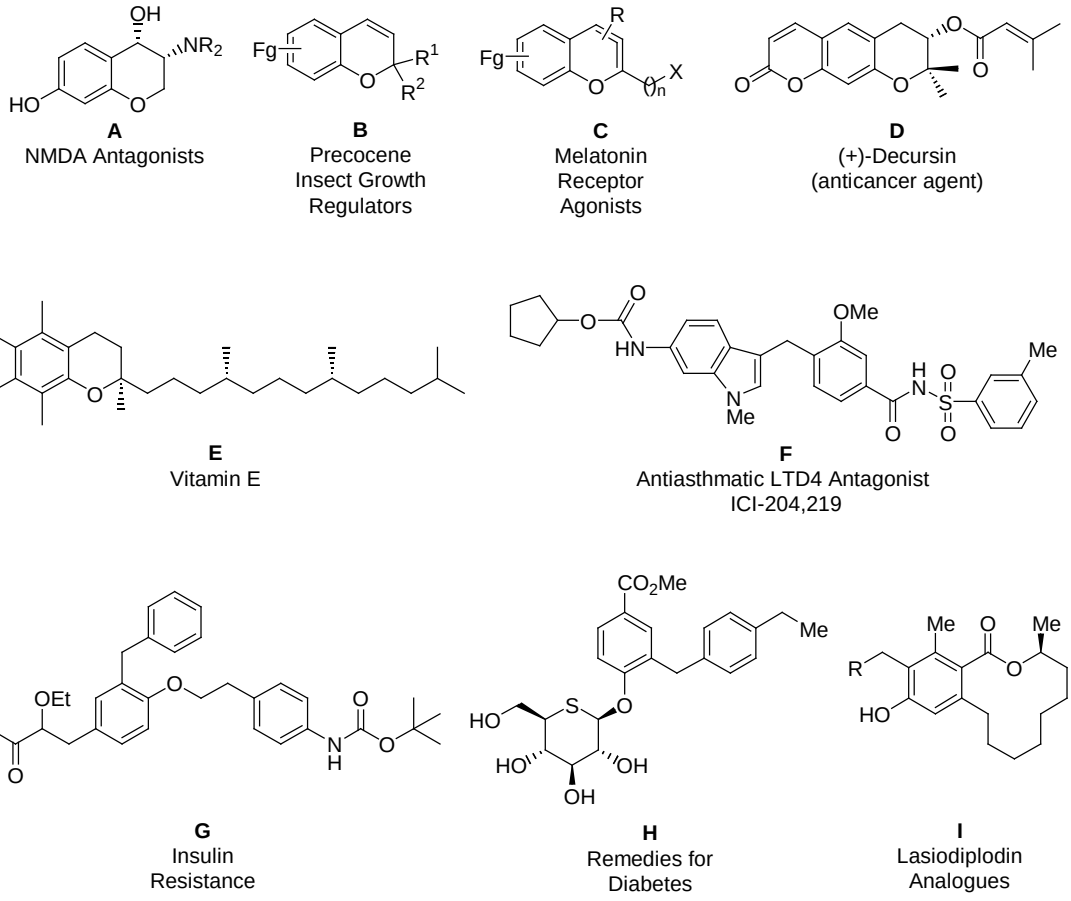
Scheme 1: Sequential One-Pot Cascade Reactions Based on the Push-Pull Dienamine Platform.



As reported, an amine- or amino acid would catalyze the cascade Claisen-Schmidt condensation of variety of aldehydes **7** with *in situ* generated push-pull dienamine (1-amino-1,3-butadiene)[1] intermediate from Hagemann's esters **44** and amine/amino acid **4** to form substituted push-pull olefins (3-arylidene Hagemann's ester) in a highly regioselective manner, which then undergoes iso-aromatization to produce substituted push-pull phenols **50** under base-catalysis based on the electronic nature of aldehydes **7** and amines **4**. Substituted push-pull phenols **50** were transformed into the highly substituted benzo[*b*]oxepines **52**, (*Z*)-2-(buta-1,3-dienyl)phenols **53**/**54**

and 2-methyl-2*H*-chromenes **55**/**56** through RCM, BIRO, BO and [1,7]-SHS reaction sequences respectively.

Chart 1: Some Natural/Non-natural Products and Pharmaceuticals Containing Cascade Compounds Obtained from Push-Pull Dienamine Chemistry.



A NMDA Antagonists

B Precocene Insect Growth Regulators

C Melatonin Receptor Agonists

D (+)-Decursin (anticancer agent)

E Vitamin E

F Antiasthmatic LTD4 Antagonist ICI-204,219

G Insulin Resistance

H Remedies for Diabetes

I Lasiodiplodin Analogues

4.2 RESULTS AND DISCUSSION

4.2.1 Sequential Cascade Synthesis of Substituted 2-Methyl-2H-Chromenes through MCC Reactions Based on CS/IA Platform:

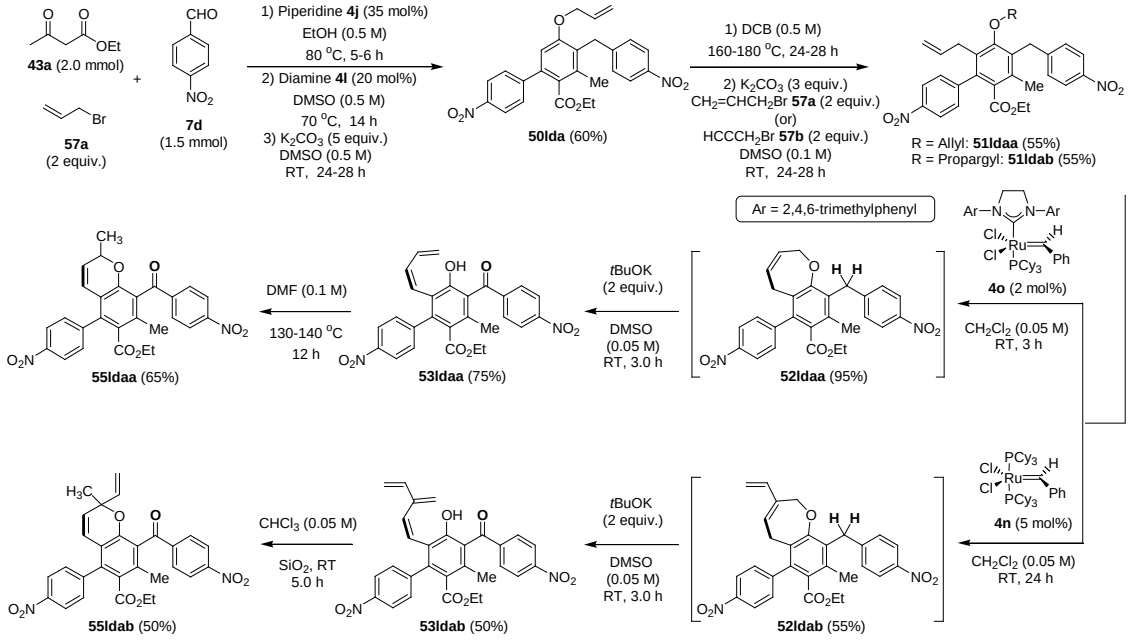
Stereoselective and economical synthesis of highly functionalized 2-methyl-2*H*-chromenes is evergreen task in synthetic organic chemistry.[22] As part of our research program to engineer direct multi-catalysis cascade (MCC) reactions in sequential manner to deliver the highly

functionalized molecules and also based on the demand of pharmaceutical applications, it was extended to two-component cascade Knoevenagel/Michael/aldol condensation/decarboxylation/Claisen-Schmidt/iso-aromatization (K/M/A/DC/CS/IA) and Claisen-Schmidt/iso-aromatization (CS/IA) reactions into novel piperidine-/diamine-/K_2CO_3- or glycine-/piperidine-/K_2CO_3-catalyzed three-component K/M/A/DC/CS/IA/A and CS/IA/A reaction of ethyl acetoacetate **43a**, 4-nitrobenzaldehyde **7d** and allyl bromide **57a** or Hagemann's esters **44a**/**44e**, benzaldehydes **7c**/**7d** and allyl bromide **57a** respectively in one-pot and resulting products **50** were converted into 2-methyl-2*H*-chromenes **55** and **56** with very good yields via four novel synthetic steps [Claisen rearrangement, *O*-allylation or *O*-propargylation, RCM/BIRO/BO or RCM/BIRO and [1,7]-SHS] as shown in Schemes 2/3. MCC products **55** and **56** were constructed in very good yields with high selectivity and this method will be showing much impact on the synthesis of functionalized small molecules with quaternary carbon as shown in Schemes 2 and 3. Highly substituted 2-methyl-2*H*-chromenes **55** and **56** type compounds have gained importance in recent years as they would be good starting materials and intermediates for the synthesis of biologically active compounds, for example NMDA antagonists **A,** precocene insect growth regulators **B**, melatonin receptor agonists **C** and anticancer agents **D**.[22]

Sequential cascade K/M/A/DC/CS/IA reaction of 2.0 equiv. of ethyl acetoacetate **43a** with 1.5 equiv. of 4-nitrobenzaldehyde **7d** under 35 mol% of piperidine-catalysis followed by 20 mol% of diamine-catalysis furnished the compound **50ld** with >99% conversion, which on *in situ* treatment with allyl bromide **57a** at RT for 24-28 h furnished the chemoselectively K/M/A/DC/CS/IA/A product **50lda** with 60% yield as shown in Scheme 2. Claisen rearrangement of **50lda** in DCB at 160-180 °C for 24 h furnished the expected allylated-phenol **50'lda** in good yield, which on *O*-allylation with allyl bromide **57a** and *O*-propargylation with propargyl bromide **57b** under K_2CO_3 in DMSO at RT for 24-28 h furnished the functionalized diene **51ldaa** in 55% yield and enyne **51ldab** in 55% yield respectively. RCM reaction of diene **51ldaa** using 2 mol% of Grubbs' 1st generation catalyst **4n** [Cl_2Ru=$CHPh(PCy_3)_2$] in CH_2Cl_2

at RT for 2-3 h furnished the benzo[*b*]oxepine **52ldaa** in >99% conversion, which on *in situ* treatment with 2.0 equiv. of *t*BuOK in DMSO at RT for 3 h furnished the functionalized (*Z*)-2-(buta-1,3-dienyl)phenol **53ldaa** in only 56% yield through cascade base-induced ring opening (BIRO) and benzylic oxidation (BO)[24] reactions in one-pot with >99% *Z*-selectivity (result not shown in Scheme 2). But the same sequential cascade RCM/BIRO/BO reactions of **51ldaa** under the 2 mol% of Grubbs'

Scheme 2: Rapid Five-step Synthesis of Highly Functionalized 2-Methyl-2*H*-Chromenes via Sequential Combination of Multi-catalysis Cascade Reactions.



2nd generation catalyst **4o** followed by treatment with 2.0 equiv. of *t*BuOK furnished the functionalized (*Z*)-2-(buta-1,3-dienyl)phenol **53ldaa** in improved yield (75%) with >99% *Z*-selectivity as shown in Scheme 2. While testing the *in situ* BIRO reaction induced by 2.0 equiv. of NaH, the reaction yield (66%) was found to be not superior to *t*BuOK as base (result not shown in Scheme 2). Further reaction of **53ldaa** in DMF at 130-140 °C for 12 h furnished the substituted 2-methyl-2*H*-chromene **55ldaa**

Figure-1: ^{1}H NMR and ^{13}C NMR Spectra of product **50lda.**

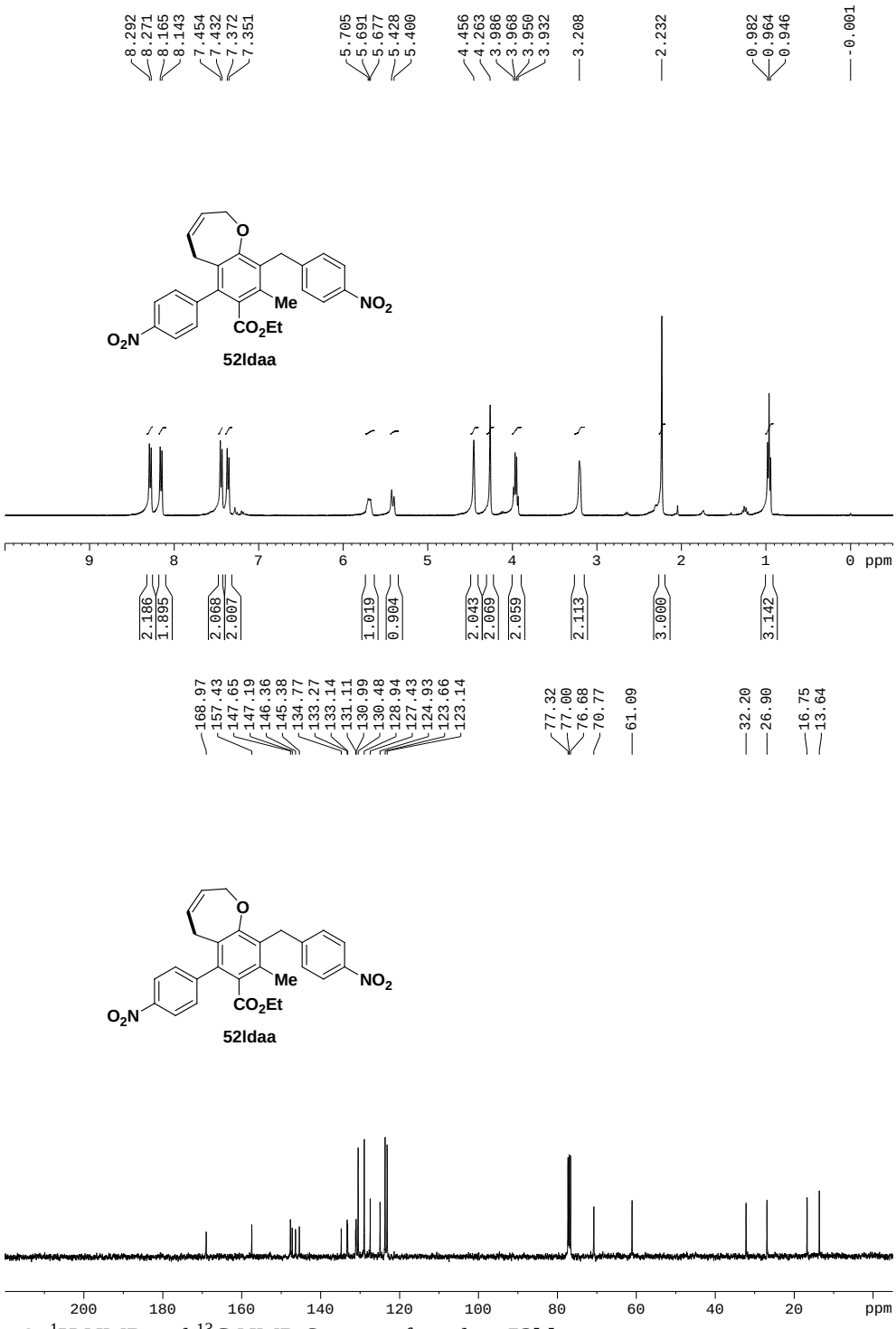


Figure-2: ^{1}H NMR and ^{13}C NMR Spectra of product **52ldaa.**

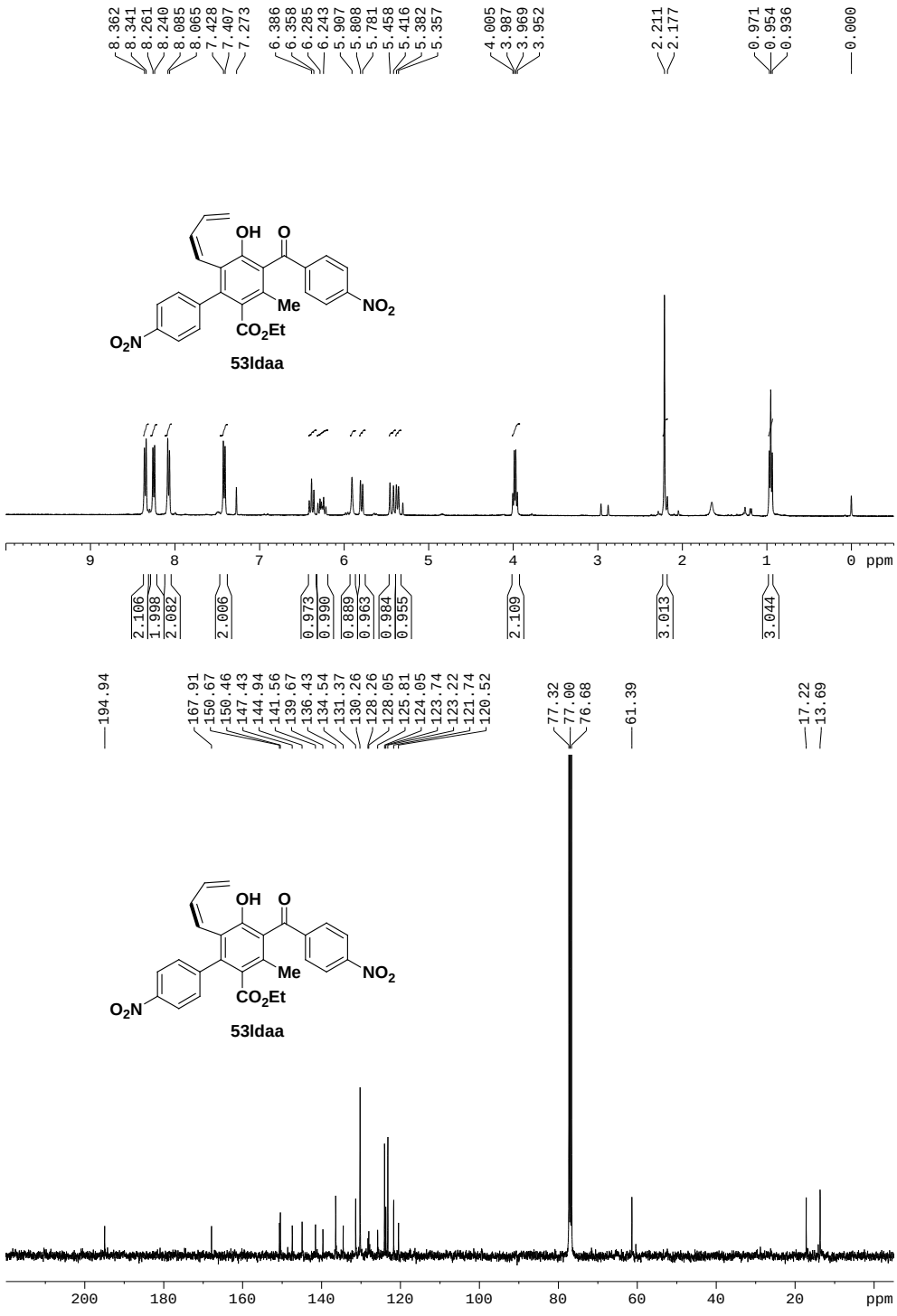


Figure-3: ^{1}H NMR and ^{13}C NMR Spectra of product **53ldaa.**

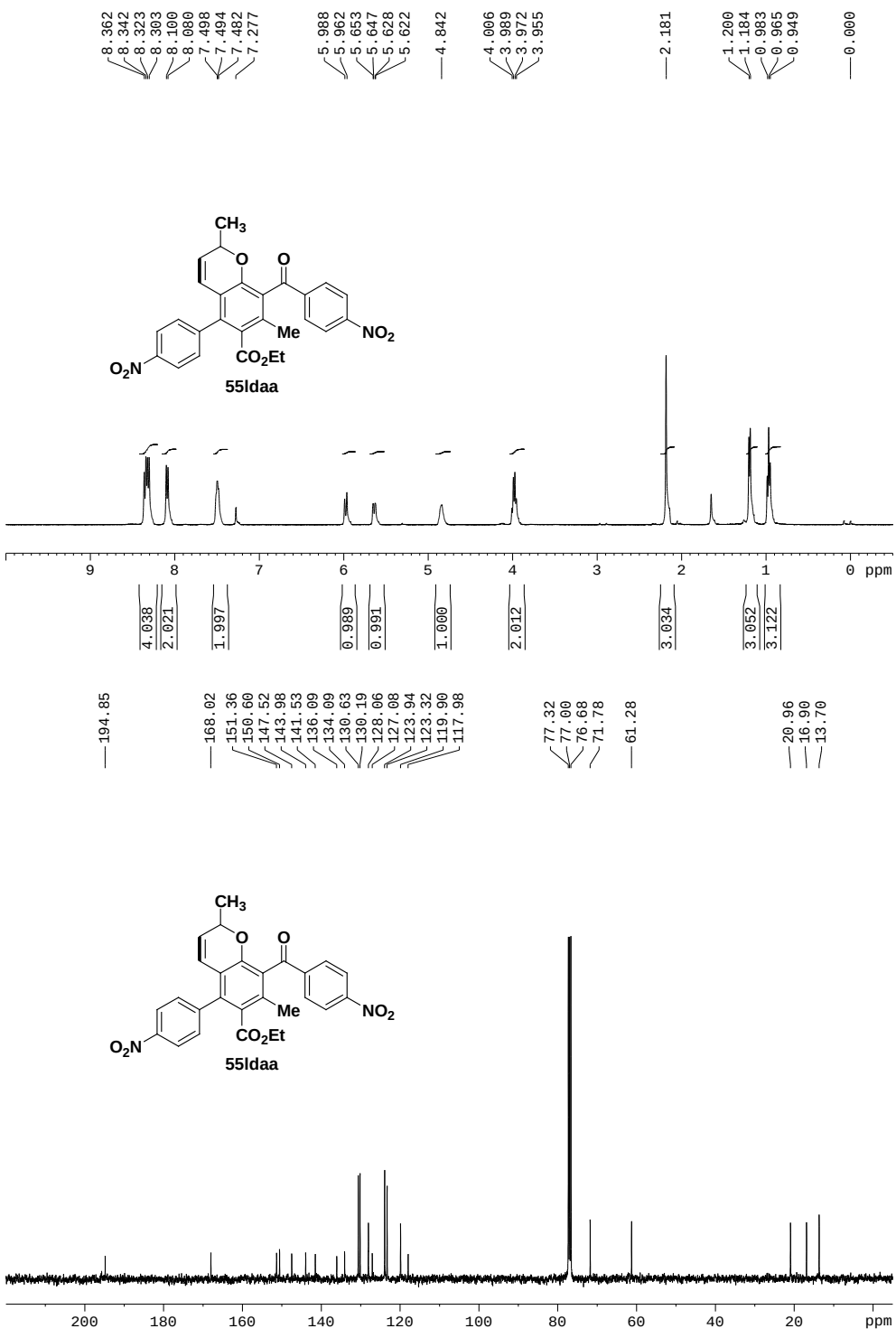
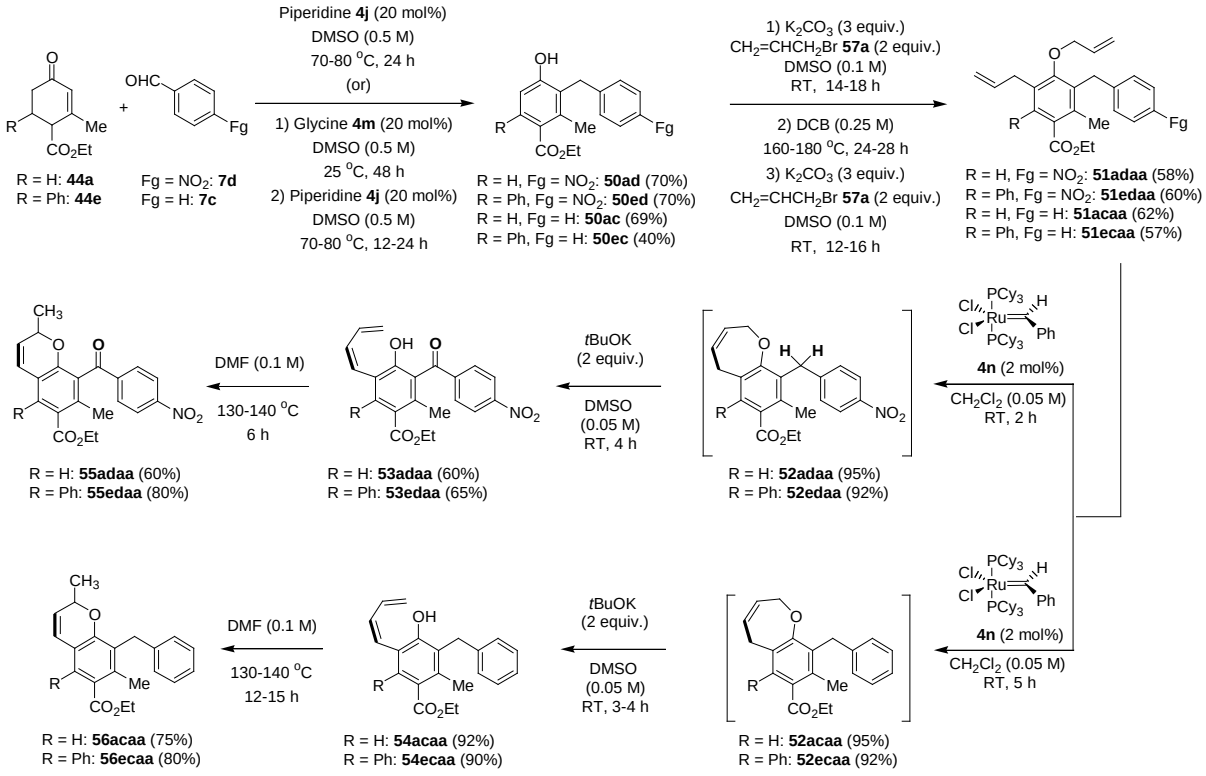


Figure-4: ^{1}H NMR and ^{13}C NMR Spectra of product **55ldaa.**

in 65% yield via [1,7]-SHS reaction as shown in Scheme 2. The optimized condition was found to be addition of 2 equiv. of *t*BuOK to the mixture of *in situ* generated **52ldaa** in DMSO at RT to furnish substituted (*Z*)-2-(buta-1,3-dienyl)phenol **53ldaa** in 75% yield with >99% *Z*-selectivity, which on further heating in DMF at 130-140 °C for 12 h furnished the substituted 2-methyl-2*H*-chromene **55ldaa** in 65% yield (Scheme 2).

Scheme 3: Rapid Six-step Synthesis of Highly Functionalized 2-Methyl-2*H*-Chromenes via Sequential Combination of Multi-catalysis Cascade Reactions.



With the optimized reaction conditions in hand, the scope of the ruthenium- and base-induced RCM/BIRO/BO sequential one-pot reactions was investigated with variety of functionalized enyne **51** and dienes **51** as shown in Schemes 2 and 3. Interestingly, enyne metathesis followed by base-induced ring opening and benzylic oxidation of enyne **51ldab** furnished the expected product (*Z*)-2-(buta-1,3-dienyl)

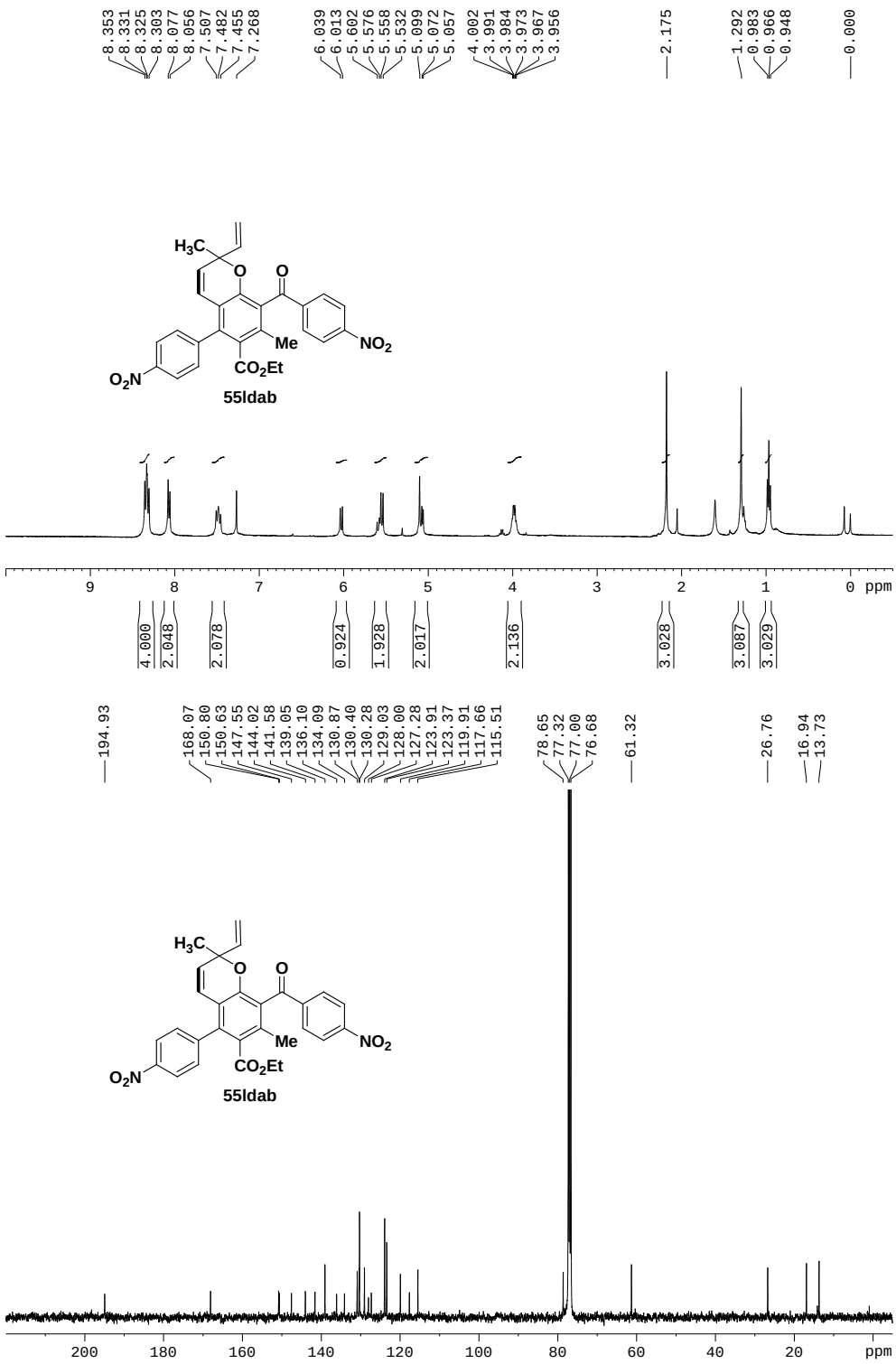


Figure-5: ^{1}H NMR and ^{13}C NMR Spectra of product **55ldab.**

phenol **53ldab** in good yield, which on further treatment with silica gel in $CHCl_3$ at RT for 5 h furnished the 2-methyl-2*H*-chromene **55ldab** in 50% yield with quaternary carbon (Scheme 2).

To demonstrate the further scope of the ruthenium- and base-induced RCM/BIRO/BO sequential one-pot reactions and also to test the role of electronic factors in BO reactions, we synthesized simple dienes **51acaa**, **51adaa**, **51ecaa** and **51edaa** from corresponding Hagemann's esters **44a**/**44e**, benzaldehydes **7c**/**7d** and allyl bromide **57a** through CS/IA/A, Claisen rearrangement/*O*-allylation sequence with good yields as shown in Scheme 3. Sequential one-pot treatment of dienes **51adaa**/**51edaa** containing single *p*-nitro group on phenyl rings with 2 mol% of Grubbs' 1st generation catalyst **4n** followed by treatment with 2.0 equiv. of *t*BuOK furnished the functionalized (*Z*)-2-(buta-1,3-dienyl)phenols **53adaa/53edaa** in 60/65% yield respectively with >99% *Z*-selectivity via RCM/BIRO/BO reactions, which are transformed into substituted 2-methyl-2*H*-chromenes **55adaa/55edaa** in 60/80% yields respectively via [1,7]-SHS reaction induced by heat as shown in Scheme 3. Interestingly, RCM reaction of diene **51acaa** using 2 mol% of Grubbs' 1st generation catalyst **4n** in CH_2Cl_2 at RT for 5 h furnished the benzo[*b*]oxepine **52acaa** in >99% conversion, which on *in situ* treatment with 2.0 equiv. of *t*BuOK in DMSO at RT for 3 h furnished the functionalized (*Z*)-2-(buta-1,3-dienyl)phenol **54acaa** in 92% yield through BIRO reaction in one-pot with >99% *Z*-selectivity without oxidation of benzylic methylene (Scheme 3). In a similar manner, we synthesized one more functionalized (*Z*)-2-(buta-1,3-dienyl)phenol **54ecaa** in 90% yield through sequential RCM/BIRO reactions in one-pot with >99% *Z*-selectivity without oxidation of benzylic methylene (Scheme 3). Two of the RCM/BIRO products, (*Z*)-2-(buta-1,3-dienyl)phenols **54acaa/54ecaa** were converted into the substituted 2-methyl-2*H*-chromenes **56acaa/56ecaa** in 75/80% yields respectively via [1,7]-SHS reaction induced by heat as shown in Scheme 3. As revealed in Schemes 2 and 3, oxidation of benzylic methylenes is completely controlled by electronic factors of substrates under the base-catalysis with air. This present MCC methodology would have much impact for generating diversity-oriented library of small

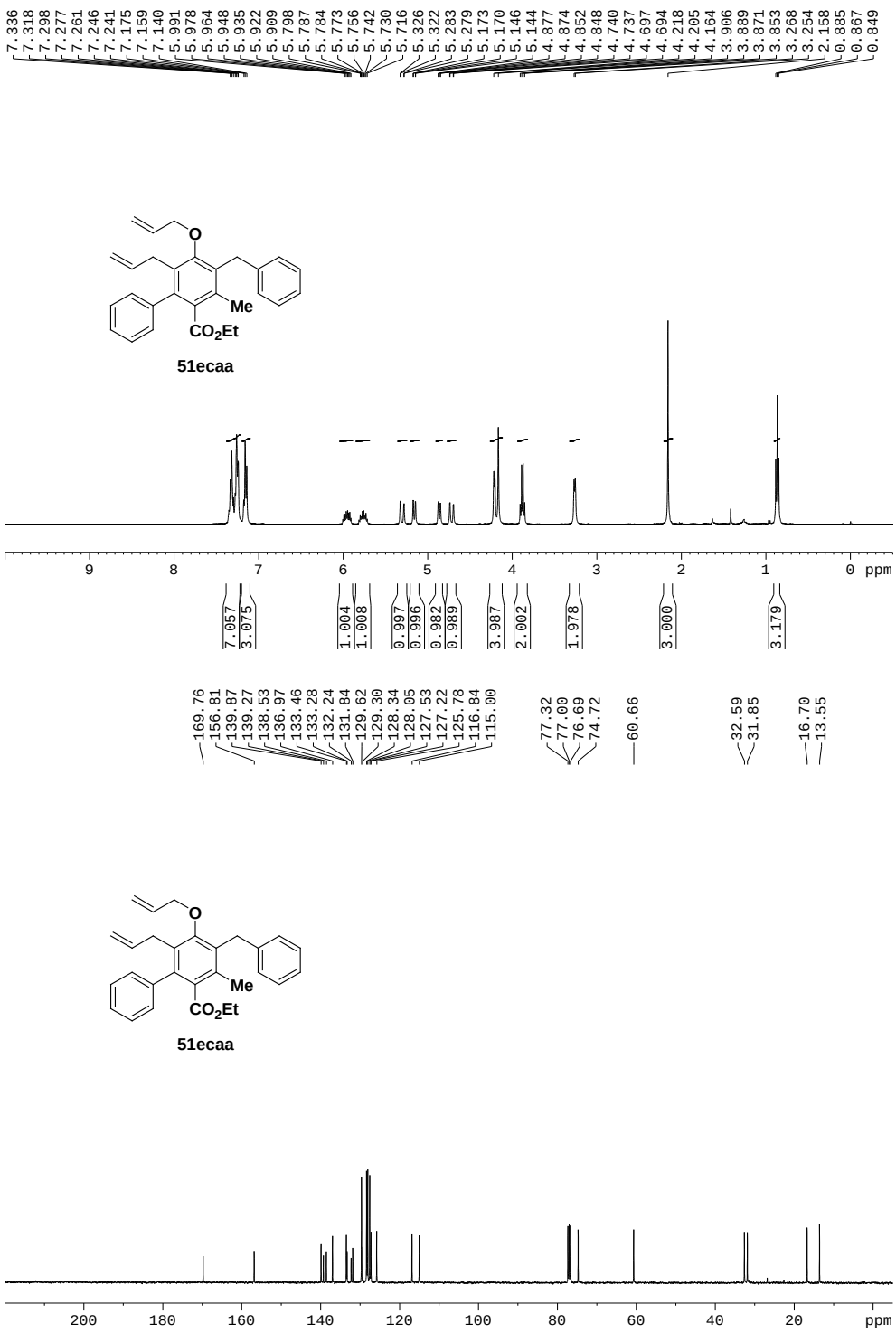


Figure-6: ^{1}H NMR and ^{13}C NMR Spectra of product **51ecaa.**

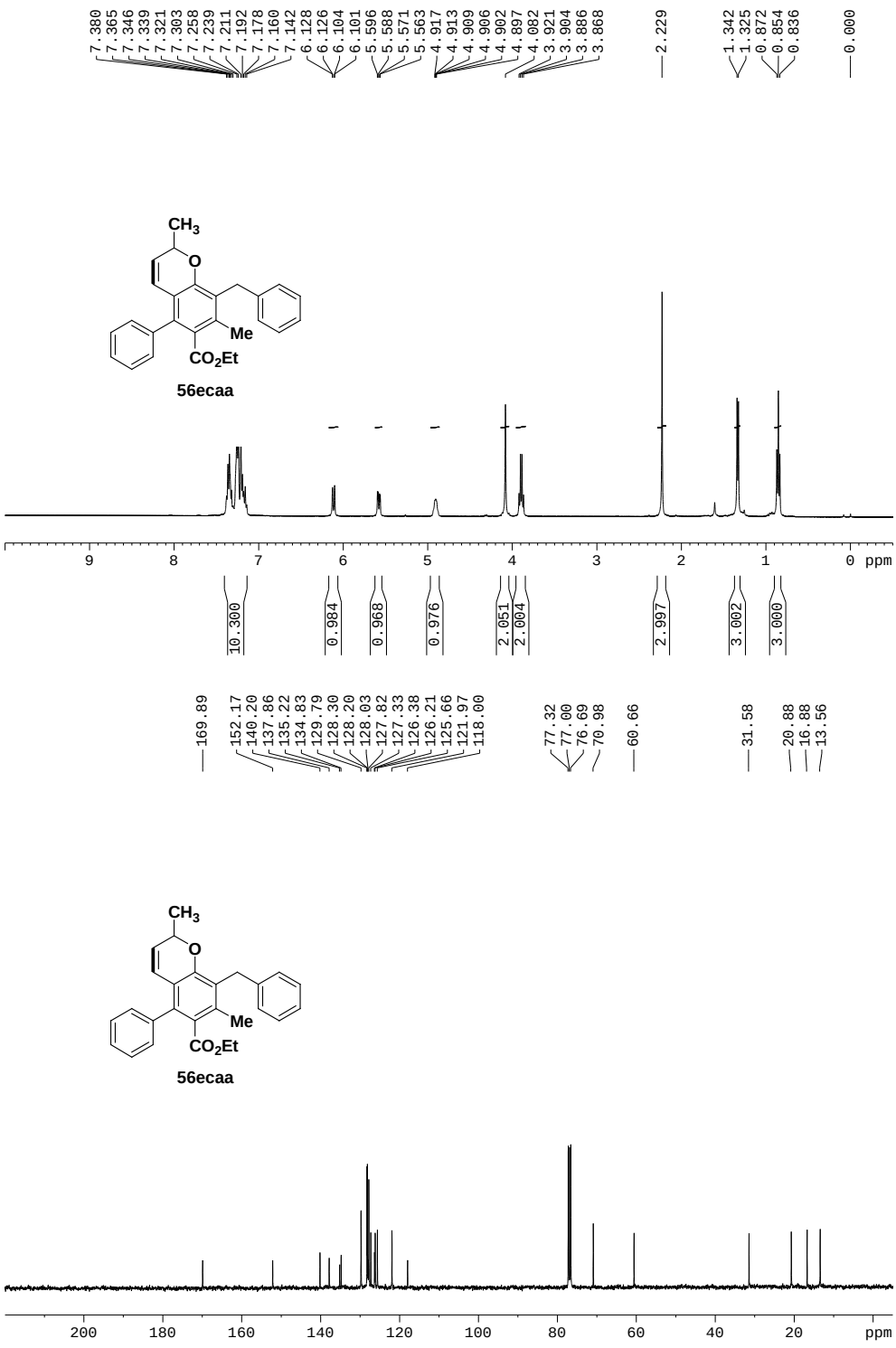
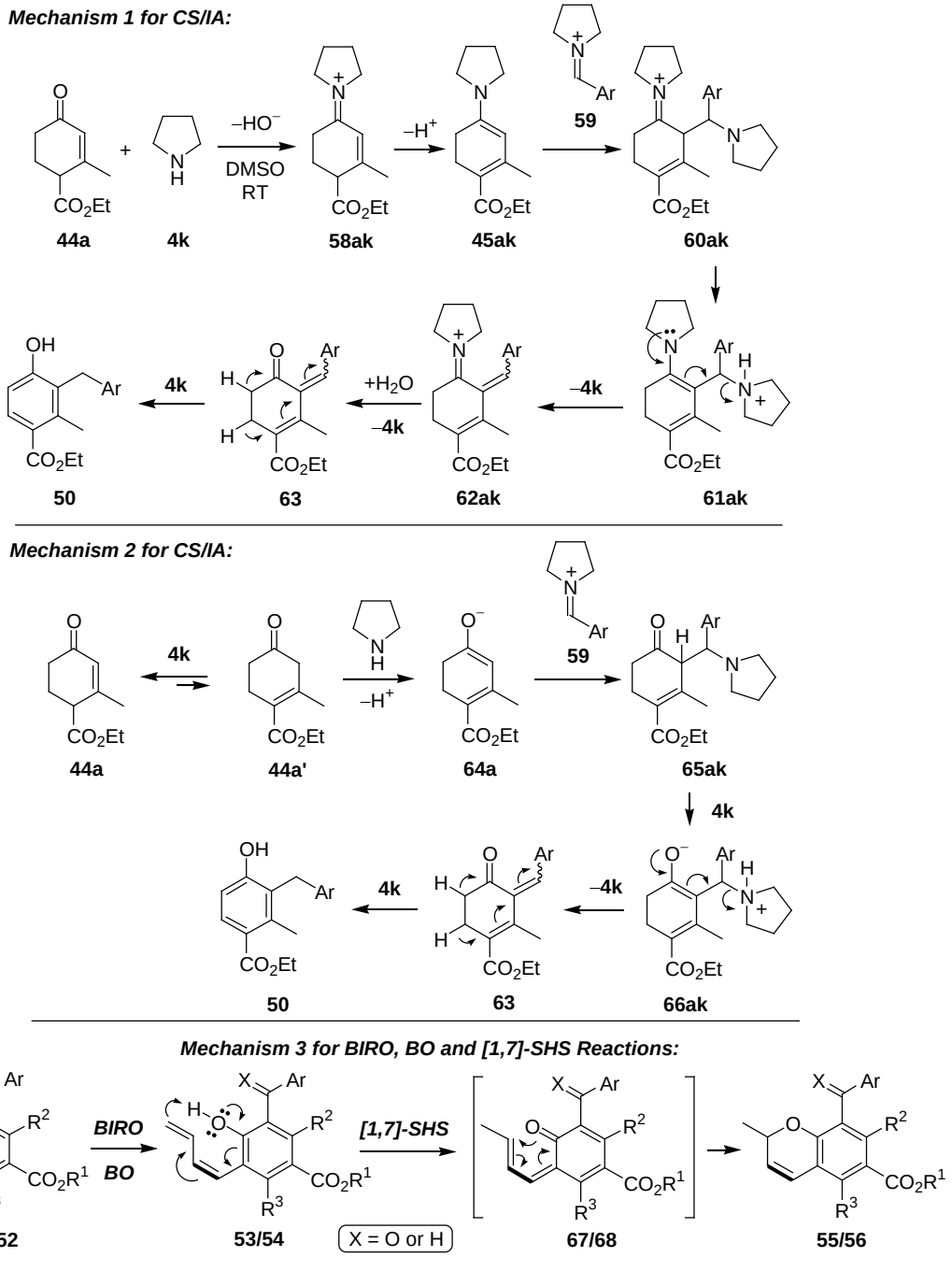


Figure-7: ^{1}H NMR and ^{13}C NMR Spectra of product **56ecaa.**

molecules **55**/**56** which are useful pharmaceutical ingredients.

Scheme 4: Proposed Reaction Mechanisms for Push-Pull Dienamine Chemistry.



***4.2.2 Mechanistic Insights*:** The possible reaction mechanisms for the synthesis of push-pull phenols **50** and 2-methyl-2*H*-chromenes **55/56** via dienamine-catalysis are illustrated in Scheme 4. First, reaction of amino acids (proline **4a** or glycine **4m**) or amines (piperidine **4j**, pyrrolidine **4k**, or (*S*)-diamine **4l**) with the aldehyde **7** generates the imine cation **59**, an excellent electrophile that undergoes Mannich type reactions with the *in situ* generated push-pull dienamine **45ak** or dienolate **64a** of Hagemann's ester **44a** to generate Mannich products **60ak** and **65ak** respectively as shown in mechanism 1 and 2 of Scheme 4 (for the clarity purpose, we represented **4k** as catalyst). Elimination reaction of pyrrolidinium ions from **61** and **66** would furnish selectively *E*/*Z* mixtures of push-pull olefin **63**. Base-induced, electronically- and temperature-controlled iso-aromatization (IA) of the CS product **63** would then give push-pull phenol **50** as shown in mechanism 1 and 2 of Scheme 4.

The possible reaction mechanism for BIRO/BO/[1,7]-SHS reaction sequence is illustrated in mechanism 3 of Scheme 4. First, reaction of **52** with *t*BuOK generates the carbanion due to the acidic nature of allylic/benzylic hydrogen, which will further rearrange into the ring opened product *cis*-**53** (X = O) and *cis*-**54** (X = H) through concerted pathway. In a similar time, dibenzylic methylene oxidized to ketone with air under base-catalysis in compounds **52** *via* electron transfer reactions may be due to the highly electron withdrawing nature of both aryls connected to methylene. A [1,7]-sigmatropic shift of the phenolic hydrogen in *cis*-**53** (X = O) and *cis*-**54** (X = H) gave to the *ortho*-quinone methides **67** (X = O) and **68** (X = H), which rapidly cyclizes to **55** (X = O) and **56** (X = H) under the standard reaction conditions to regain the thermodynamic stability through oxa-6π electrocyclization or [3,3]-rearrangement.

4.3 CONCLUSION

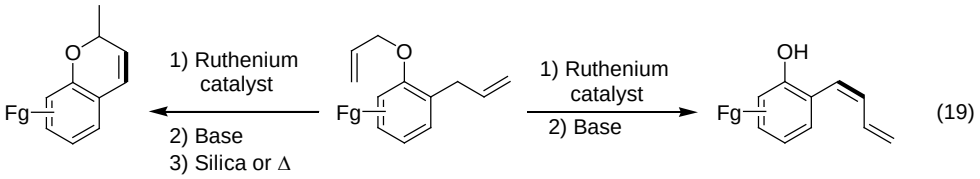
In this chapter, the sequential one-pot combination of amino acid-, amine-, K_2CO_3-, [Ru]-, *t*BuOK- or SiO_2-catalyzed direct cascade CS/IA, K/M/A/DC/CS/IA, RCM/BIRO/BO, RCM/BIRO and [1,7]-SHS reactions from simple substrates was developed. This experimentally simple cascade approach can be used to construct

diversity-oriented library of highly substituted push-pull phenols and 2-methyl-2*H*-chromenes with good yields in a selective fashion. Also the *in situ* generation and application of novel push-pull dienamines in sequential cascade chemistry were demonstrated.

5. A NEW ONE-POT SYNTHETIC APPROACH TO THE HIGHLY FUNCTIONALIZED (*Z*)-2-(BUTA-1,3-DIENYL)PHENOLS AND 2-METHYL-2*H*-CHROMENES: USE OF AMINE, RUTHENIUM AND BASE-CATALYSIS

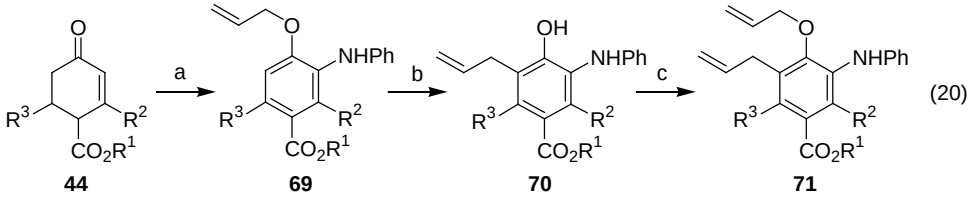
5.1 INTRODUCTION

Functionalized 2-(buta-1,3-dienyl)phenols and 2-methyl-2*H*-chromenes are of considerable importance in a variety of industries. They are, for instance, versatile building blocks for the synthesis of natural products.[25] As such, the development of new and more general catalytic methods for their preparation is of significant interest.[25] Recently Sherburn *et al*.[26a] discovered the phosphane-mediated reaction of 2-hydroxy-benzaldehyde with allyltriphenylphosphonium bromide in the presence of strong base providing a 2-(buta-1,3-dienyl)phenol in moderate yield.



(19)

In this chapter, a novel one-pot and multi-catalysis technology is discussed for the synthesis of highly substituted (*Z*)-2-(buta-1,3-dienyl)phenols and 2-methyl-2*H*-chromenes starting from highly substituted dienes (eq. 19). A ruthenium/base/silica-catalyzed one-pot ring-closing metathesis (RCM)/ring-opening/[1,7]-sigmatropic hydrogen shift reactions are crucial steps in the reaction sequence. Functionalized 2-(buta-1,3-dienyl)phenols are useful materials as additives for rubbers and plastics, antioxidants, antibacterial agents, antibiotics and hair dyeing.[25] The base-induced ring opening of highly substituted 2,5-dihydrobenzo[*b*]oxepines were demonstrated for the first time.



(20)

44a: R^1 = Et, R^2= Me, R^3 = H; **44b**: R^1 = Me, R^2 = Me, R^3 = H; **44c**: R^1 = *t*Bu, R^2 = Me, R^3 = H
44d: R^1 = Et, R^2 = Me, R^3 = Me; **44e**: R^1 = Et, R^2 = Me, R^3 = Ph; **44f**: R^1 = Et, R^2 = H, R^3 = Ph
44g: R^1 = Me, R^2 = H, R^3 = H

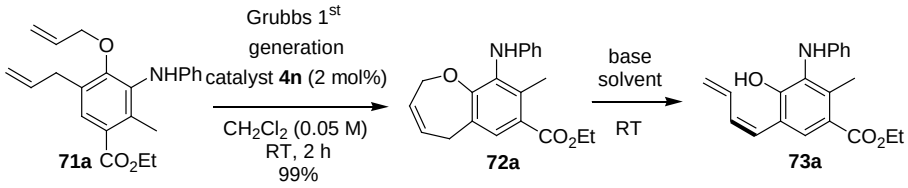
For reagents and conditions, see: (a) Ph-N=O, piperidine (5 mol%), DMF (0.6 M), RT, 1 h; K_2CO_3 (5 equiv.), H_2C=$CHCH_2Br$ (3 equiv.), RT, 24 h, 50-98%; (b) DMF (1.0 M), 190 °C, 18 h, 73-80%; (c) K_2CO_3 (1.5 equiv.), H_2C=$CHCH_2Br$ (1.2 equiv.), EtOH (0.1 M) or DMF (0.5 M), RT, 24 h, 80-95%.

5.2 RESULTS AND DISCUSSION

Based on our recent discovery of piperdine/K_2CO_3-catalyzed cascade enamine amination/iso-aromatization/alkylation (EA/IA/A) reaction of Hagemann's esters **44** with nitrosobenzene **46** and allyl bromide leading to functionalized olefins **69**,[1d] it was thought that these olefins **69** might be suitable starting material for the synthesis of highly functionalized dienes **71** which are precursors for RCM reaction (eq. 20). Studies were directed towards the synthesis of highly substituted benzo[*b*]oxepines **72** starting from Hagemann's ester **44a** and nitrosobenzene **46** by the combination of cascade EA/IA reaction, *O*- and *C*-allylations and diene metathesis as key steps as shown in eq. 20. The piperidine/K_2CO_3-catalyzed cascade EA/IA/A reaction of **44a**, nitrosobenzene **46** and allyl bromide furnished the monoene amine **69a** in 95% yield. Claisen rearrangement of **69a** in DMF at 190 °C for 18 h yielded the expected phenol **70a** in 75% yield, which on *O*-allylation with allyl bromide and K_2CO_3 gave the diene amine **71a** in 80% yield. Six more functionalized dienes **71** were synthesized in very good yields using different Hagemann's esters **44b-g**. Interestingly, Claisen rearrangement of *tert*-butyl 4-allyloxy-2-methyl-3-(phenylamino) benzoate **69c** in DMF at 190 °C for 18

h furnished the decarboxylated phenol **70c**, which on *O*-allylation with allyl bromide and K_2CO_3 furnished the diene amine **71c** in 85% yield (see eq. 20, and also the Annexure-I for more synthetic details). Interestingly, RCM reaction of free diene amine **71a** using Grubbs' 1st generation catalyst **4n** [$Cl_2Ru{=}CHPh(PCy_3)_2$] in CH_2Cl_2 at RT for 2 h furnished the benzo[*b*]oxepine **72a** in 99% yield (Table 1). The technical advantage of this RCM reaction is ruthenium-catalysis applied to the free diene amine **71a** without the need of *in situ* salt formation.[27] May be the secondary amine group ($HNAr_2$) in **71a** does not interact with the ruthenium catalyst, because the nucleophilicity of the amine is decreased as a result of its direct interaction with two electron deficient phenyl groups.

Table 1: Reaction Optimization.



entry	solvent [0.05 M]	base [equiv.]	time [h]	yield **73a** [%][a]
1	NMP	NaH (2.0)	1	96
2	NMP	NaOMe (2.0)	1	96
3	NMP	*t*BuOK (2.0)	0.5	96
4	NMP	*t*BuOK (1.0)	2	90
5	NMP	Bu_3P (0.25)	48	-
6	*t*BuOH	*t*BuOK (2.0)	0.5	76
7	DMF	NaH (2.0)	2	96
8	**DMSO**	**NaH (2.0)**	**1**	**97**
9[b]	**DMSO**	***t*BuOK (2.0)**	**0.5**	**97**
10	THF	NaH (2.0)	17	55

[a] Yield refers to the column purified product. [b] Reaction performed in both two steps and one-pot conditions.

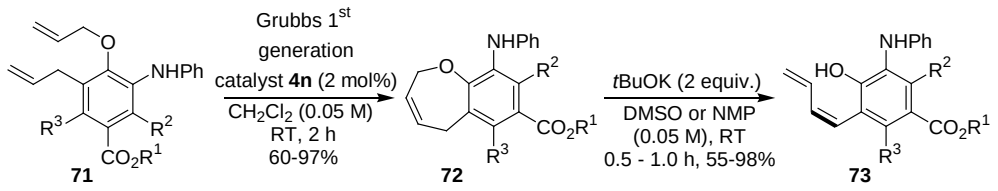
Once the benzo[*b*]oxepine **72a** was formed the base-induced ring opening (BIRO) was initiated as shown in Table 1. Interestingly, as expected treatment of 2

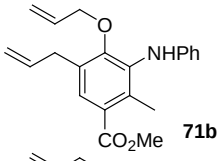
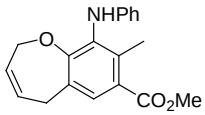
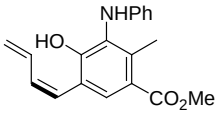
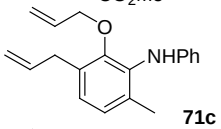
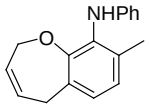
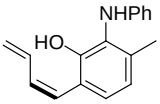
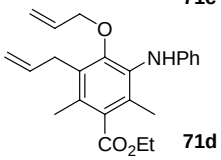
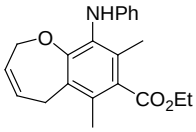
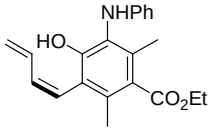
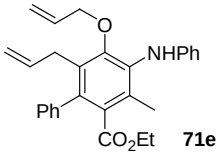
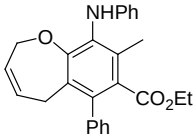
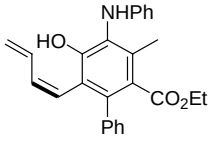
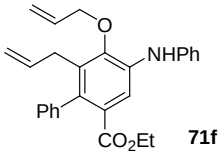
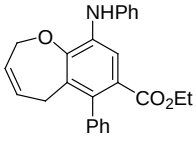
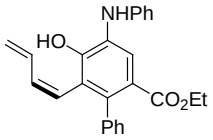
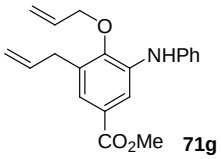
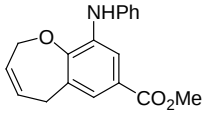
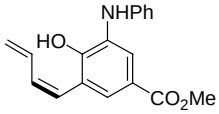
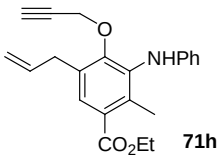
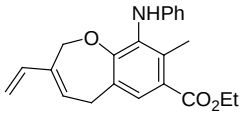
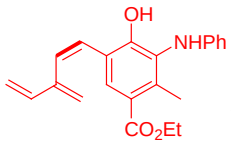
equiv. of NaH with **72a** in *N*-methylpyrrolidin-2-one (NMP) at RT for 1 h furnished the ring-opened product *cis*-**73a** as major single isomeric product with 96% yield and >99% *Z*-selectivity (Table 1, entry 1). The ring-opening reaction of benzo[*b*]oxepine **72a** was further studied by using other bases like NaOMe, *t*BuOK and Bu_3P; among these *t*BuOK gave the best results as shown in Table 1, entries 2–5. The BIRO reaction in protic polar/aprotic polar solvents like *t*BuOH, DMF and DMSO also furnished the product *cis*-**73a** with good yields (entries 6–8). Reaction in THF gave the ring-opened product *cis*-**73a** with poor yield (entry 10). The ruthenium-catalyzed RCM reaction of diene **71a** and *t*BuOK-induced ring opening of the resulting benzo[*b*]oxepine **72a** was conducted according to the one-pot technique and furnished the expected product *cis*-**73a** in 97% yield with >99% *Z*-selectivity (Table 1, entry 9). The optimized condition was confirmed to be addition of 2 equiv. of *t*BuOK to the mixture of *in situ* generated **72a** in DMSO at RT to furnish the substituted (*Z*)-2-(buta-1,3-dienyl)phenol **73a** in 97% yield with >99% *Z*-selectivity (Table 1, entry 9).

With the optimized reaction conditions in hand, the scope of the ruthenium- and base-induced RCM/BIRO one-pot reactions was investigated with variety of functionalized dienes **71** as shown in Table 2. A series of 6-substituted Hagemann's esters **44b**-**g** was converted into diene amines **71b**-**g** in good yields as shown in eq. 20. RCM reaction of free diene amines **71b**-**g** using Grubbs' first-generation catalyst **4n** (2 mol%) in CH_2Cl_2 at RT for 2 h furnished the benzo[*b*]oxepines **72b**-**g** in 95–97% yield, which on treatment with 2 equiv. of *t*BuOK at RT for 0.5 h furnished the expected highly functionalized selective (*Z*)-2-(buta-1,3-dienyl)phenols **73b**-**g** with good yields under both two-step and one-pot conditions (Table 2, entries 1-6). Interestingly, enyne metathesis followed by base-induced ring opening of enyne **71h** furnished the expected product *cis*-**73h** in 55% yield (Table 2, entry 7). To demonstrate the scope of the ruthenium and base-induced RCM/BIRO one-pot reactions, simple dienes **78a-f** were synthesized from corresponding phenols **75a-f** through *O*-allylation/Claisen rearrangement/*O*-allylation sequence (see Annexure-I for details) and transformed them

into the expected single isomeric products *cis*-**80a-f** in very good yields via RCM/BIRO reactions (Table 3, entries 1-6). Structure and regio-chemistry of

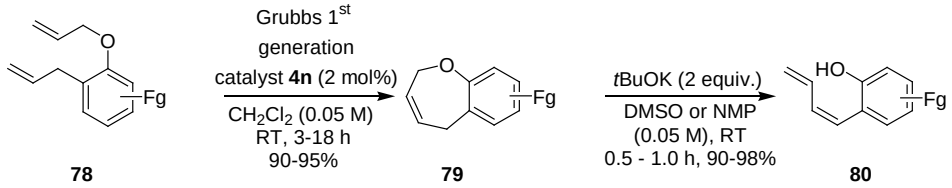
Table 2: Synthesis of the Substituted (*Z*)-2-(Buta-1,3-dienyl)phenols **73**.[a]

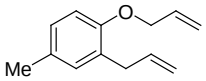
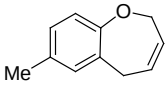
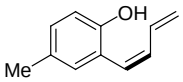
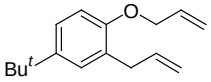
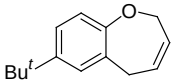
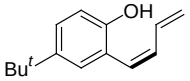
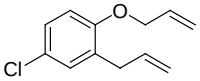
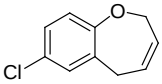
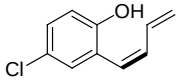
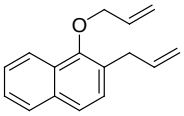
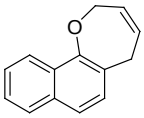
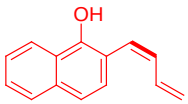
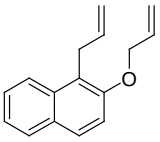
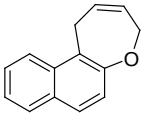
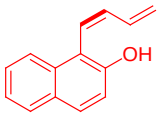
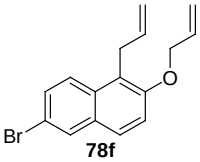
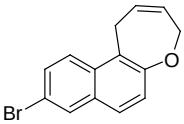
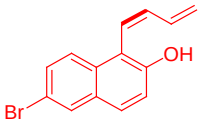


entry	diene **71**	benzo[*b*]oxepine **72**	2-buta-1,3-dienyl-phenols **73**
1	 **71b**	 **72b** (97%)	 **73b** (95%)
2	 **71c**	 **72c** (97%)	 **73c** (75%)
3	 **71d**	 **72d** (97%)	 **73d** (95%)
4	 **71e**	 **72e** (96%)	 **73e** (95%)
5	 **71f**	 **72f** (95%)	 **73f** (95%)
6	 **71g**	 **72g** (97%)	 **73g** (95%)
7	 **71h**	 **72h** (60%)	 **73h** (55%)

[a] Yield refers to the column purified product.

Table 3: Synthesis of the Substituted (*Z*)-2-(Buta-1,3-dienyl)phenols **80**.[a]



entry	diene **78**	benzo[*b*]oxepine **79**	2-buta-1,3-dienyl-phenols **80**
1	 **78a**	 **79a** (90%)	 **80a** (90%)
2	 **78b**	 **79b** (95%)	 **80b** (90%)
3	 **78c**	 **79c** (95%)	 **80c** (90%)
4	 **78d**	 **79d** (95%)	 **80d** (98%)
5	 **78e**	 **79e** (95%)	 **80e** (98%)
6	 **78f**	 **79f** (90%)	 **80f** (98%)

[a] Yield refers to the column purified product.

(*Z*)-2-(buta-1,3-dienyl)phenols **73** was confirmed by X-ray structure analysis on *cis*-**73a** as shown in Scheme 5.[28]

Some of the (*Z*)-2-(buta-1,3-dienyl)phenols **73**/**80** are unstable at RT and slowly rearrange to the 2-methyl-2*H*-chromenes **74**/**81** by [1,7]-sigmatropic hydrogen shift

([1,7]-SHS) followed by rapid cyclization.[29] Compounds *cis*-**73f**, *cis*-**73h** and *cis*-**80d-f** are unstable at RT and are rapidly converted into the functionalized

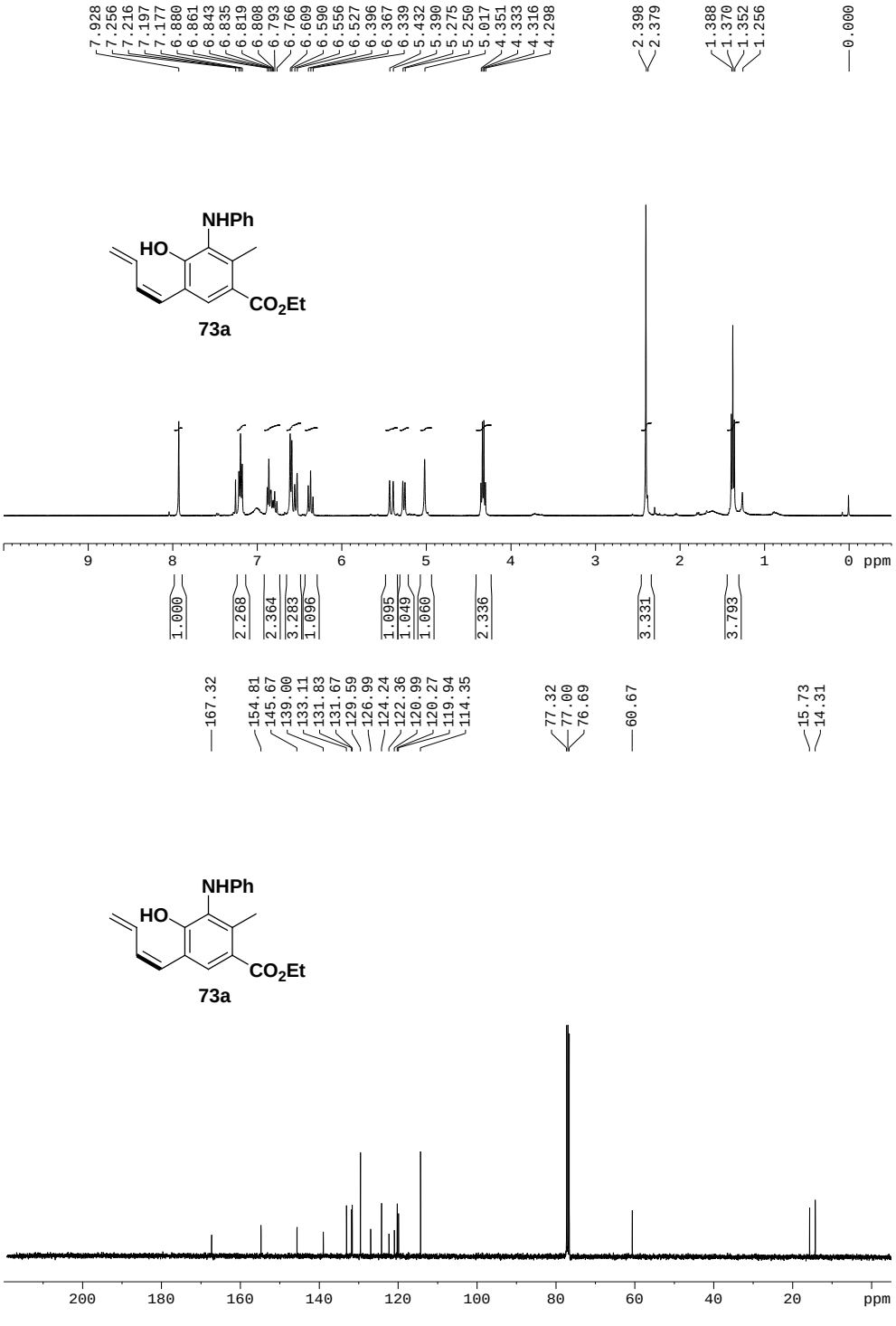


Figure-8: ^{1}H NMR and ^{13}C NMR Spectra of product **73a.**

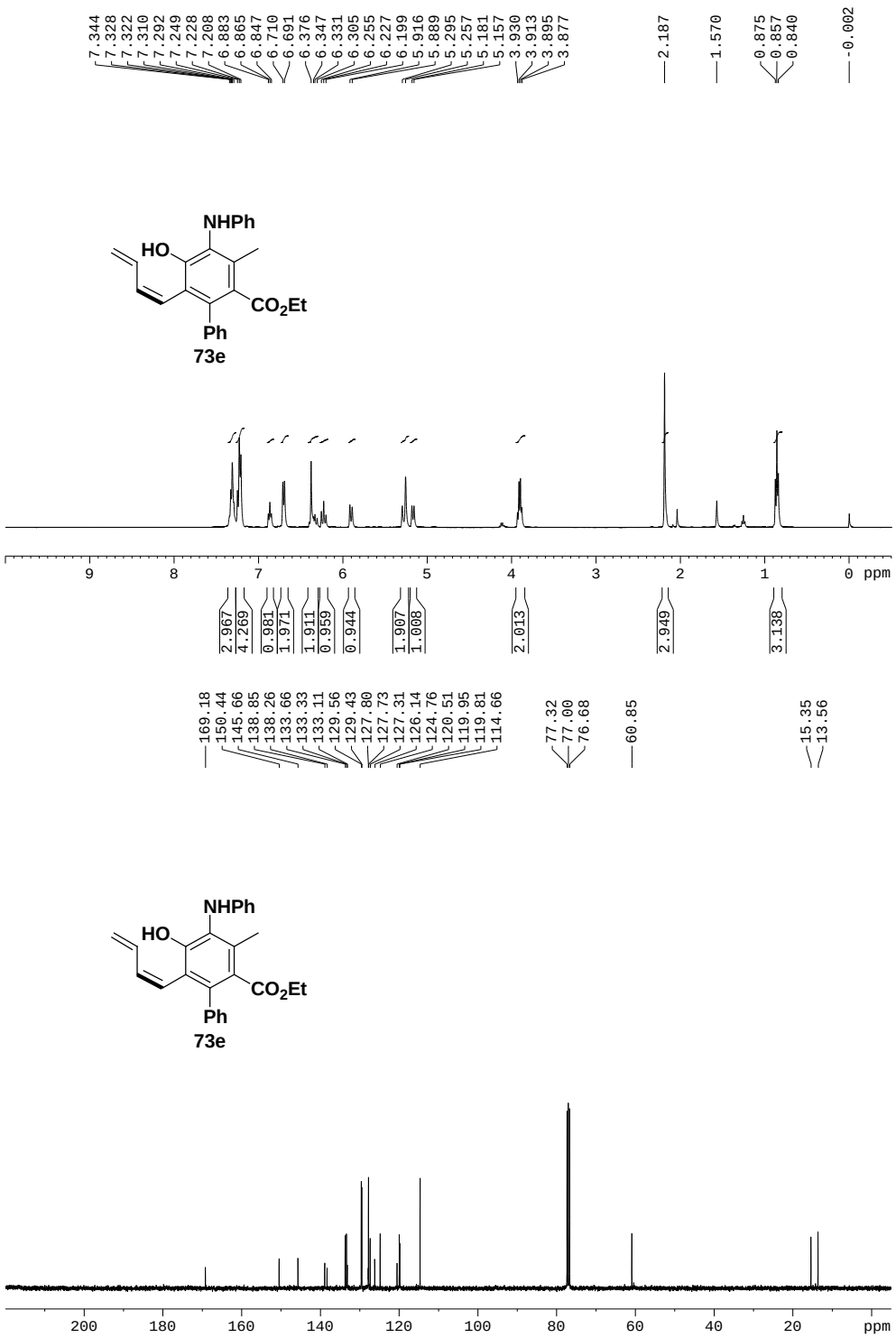
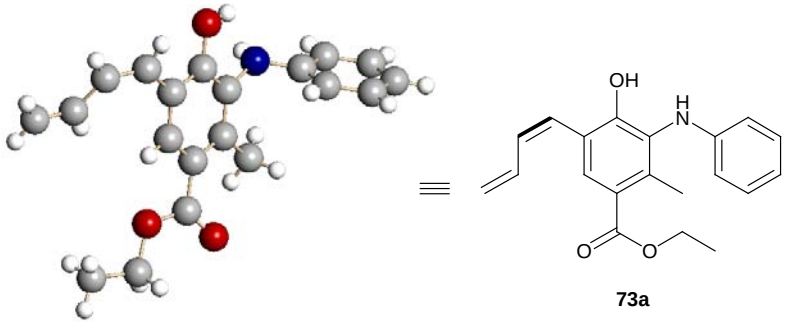


Figure-9: ^{1}H NMR and ^{13}C NMR Spectra of product **73e.**

Scheme 5: Crystal structure of (*Z*)-5-buta-1,3-dienyl-4-hydroxy-2-methyl-3-phenylamino-benzoic acid ethyl ester (**73a**).

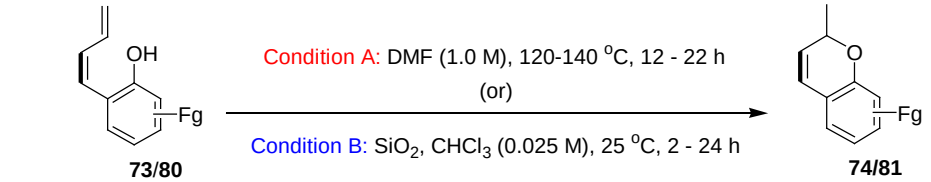


73a

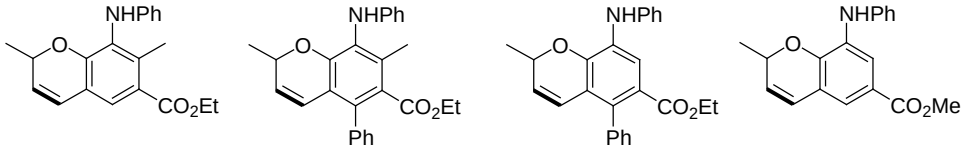
2-methyl-2*H*-chromenes **74f**, **74h** and **81d-f** after aqueous workup. This reaction can be accelerated by heat or addition of silica and $CHCl_3$ to the crude phenols **73**/**80** (see Table 4). With synthetic and pharmaceutical applications in mind,[25] the present methodology was extended to the transformation of other phenols **73**/**80** into functionalized 2-methyl-2*H*-chromenes **74**/**81** by a novel thermal or silica-induced [1,7]-SHS reaction followed by rapid cyclization. Reaction of *cis*-**73a** in DMF at 120-140 °C for 20 h furnished the expected 2-methyl-2*H*-chromene **74a** in 90% yield (Table 4), but the same reaction catalyzed by $SiO_2/CHCl_3$ at RT for 7 days furnished **74a** with only 50% conversion. Functionalized 2-methyl-2*H*-chromenes **74**/**81** were generated in good yields with high selectivity as shown in Table 4. This method will show much impact on synthesis of highly substituted 2-methyl-2*H*-chromenes **74**/**81** for medicinal applications.[25] As shown in Table 4, Condition **A** (thermal activation) is the best method for the conversion of different (*Z*)-2-(buta-1,3-dienyl) phenols **73**/**80** into 2-methyl-2*H*-chromenes **74**/**81**.

In order to check the general applicability of the RCM/BIRO/[1,7]-SHS reaction sequence, the synthesis of C_2-symmetric 2,8-dimethyl-2,8-dihydro-1,7-dioxachrysene **81g**'' was attempted (eq. 21). RCM reaction of 1,5-diallyl-2,6-bis(allyloxy)naphthalene (**78g**) at 50 °C for 6 h in CH_2Cl_2 furnished the C_2-symmetric benzo[*b*]oxepine **79g** in 85% yield, which on treatment with 1.5 equiv. of *t*BuOK followed by treatment with

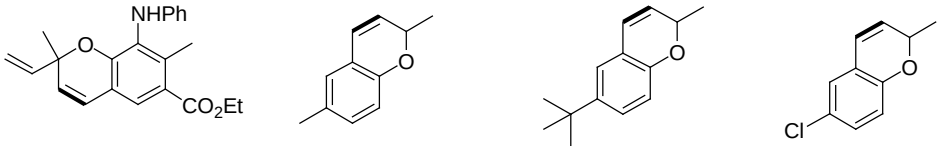
Table 4: Chemically Diverse Libraries of 2-Methyl-2*H*-Chromenes **74**/**81.**[a]



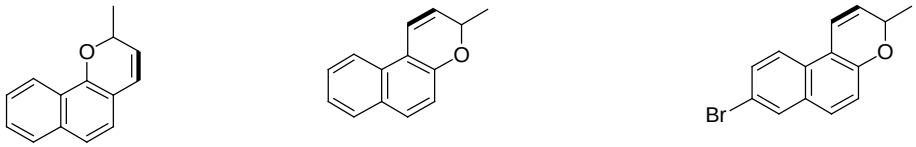
73/80 **74/81**



Condition A **74a** (90%) | Condition A **74e** (95%) | Condition B **74f** (85%) | Condition A **74g** (80%)



Condition B **74h** (55%) | Condition A **81a** (80%) | Condition A **81b** (80%) | Condition A **81c** (80%)



Condition B **81d** (96%) | Condition B **81e** (96%) | Condition B **81f** (98%)

[a] Yield refers to the column purified product.

$SiO_2/CHCl_3$ at RT for 6-8 h furnished the non-symmetric 2-methyl-2*H*-chromene **81g**' in 70% yield (eq. 21). The same RCM reaction when applied to **78g** at 50 °C for 6 h in CH_2Cl_2 followed by reaction with 5 equiv. of *t*BuOK at RT for 3 h and then treatment with $SiO_2/CHCl_3$ at RT for 6-8 h furnished the C_2-symmetric chrysene **81g**'' in 65% yield (eq. 21).

A possible reaction mechanism for the BIRO/[1,7]-SHS reaction sequence is given in Scheme 6. The first step could be the base-catalyzed formation of a carbanion (the allylic/benzylic hydrogen of **72**/**79** is acidic) that will rearrange according to a concerted reaction pathway to give the ring-opened product *cis*-**73**/**80**.

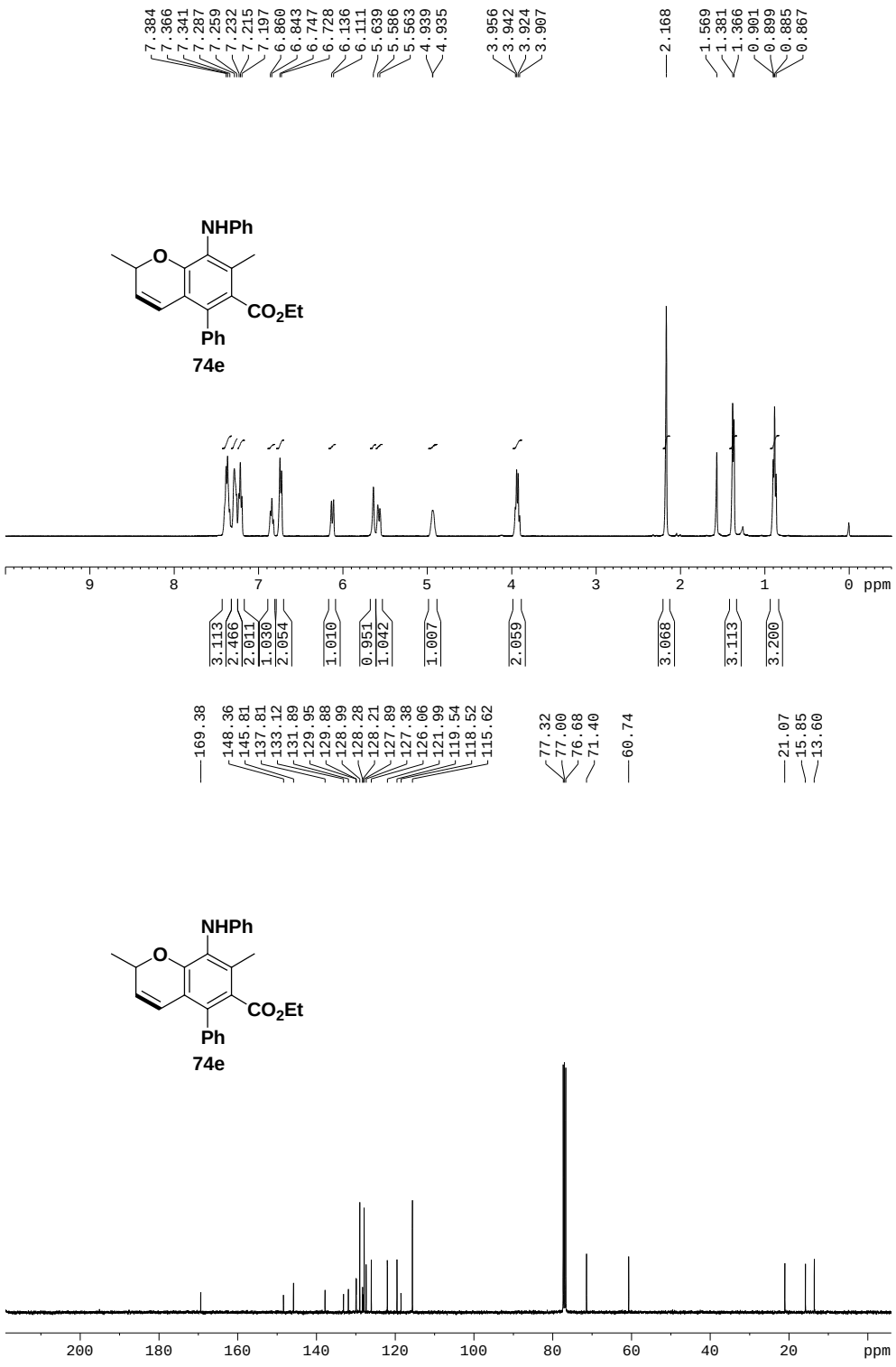


Figure-10: ^{1}H NMR and ^{13}C NMR Spectra of product **74e.**

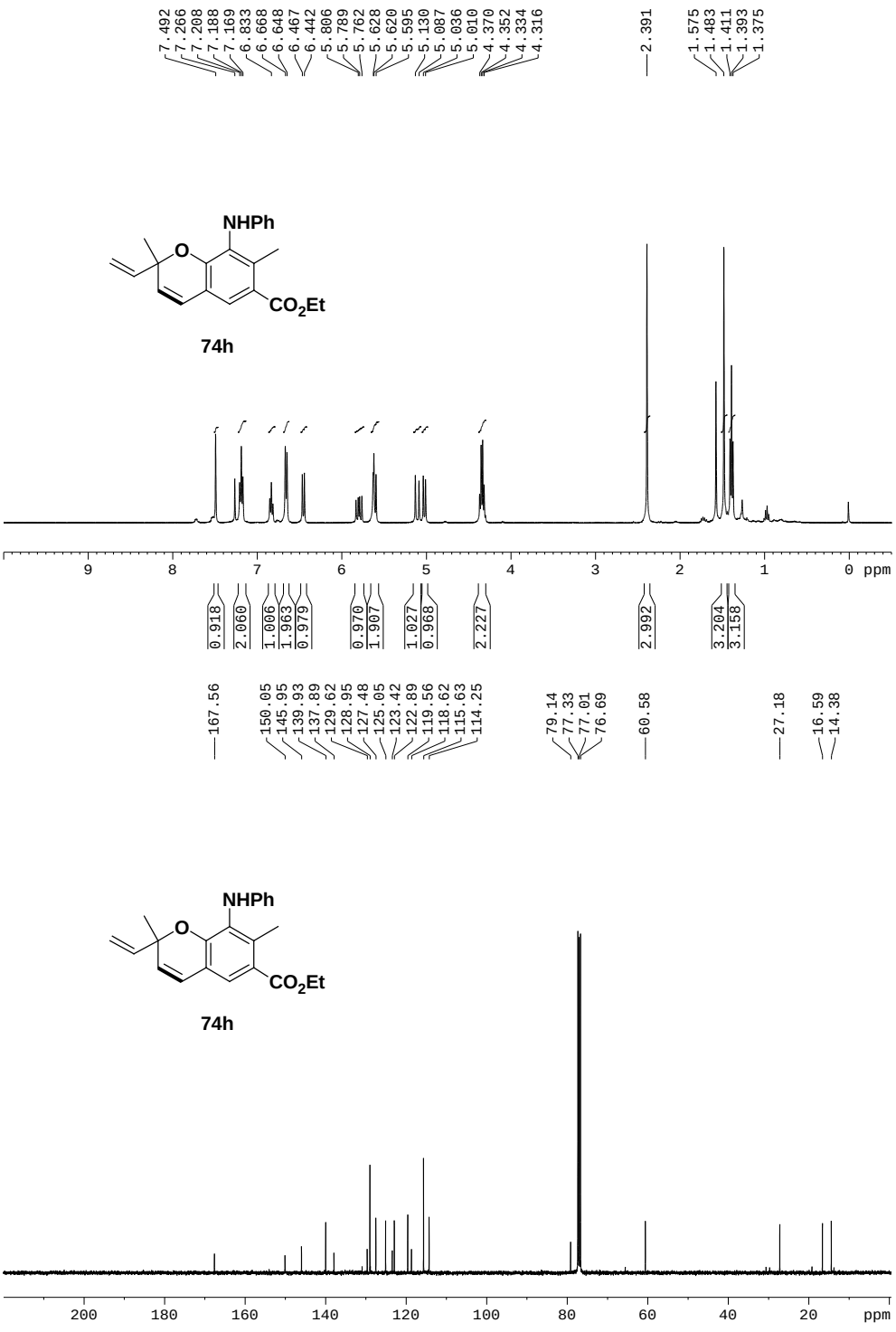


Figure-11: ^{1}H NMR and ^{13}C NMR Spectra of product **74h.**

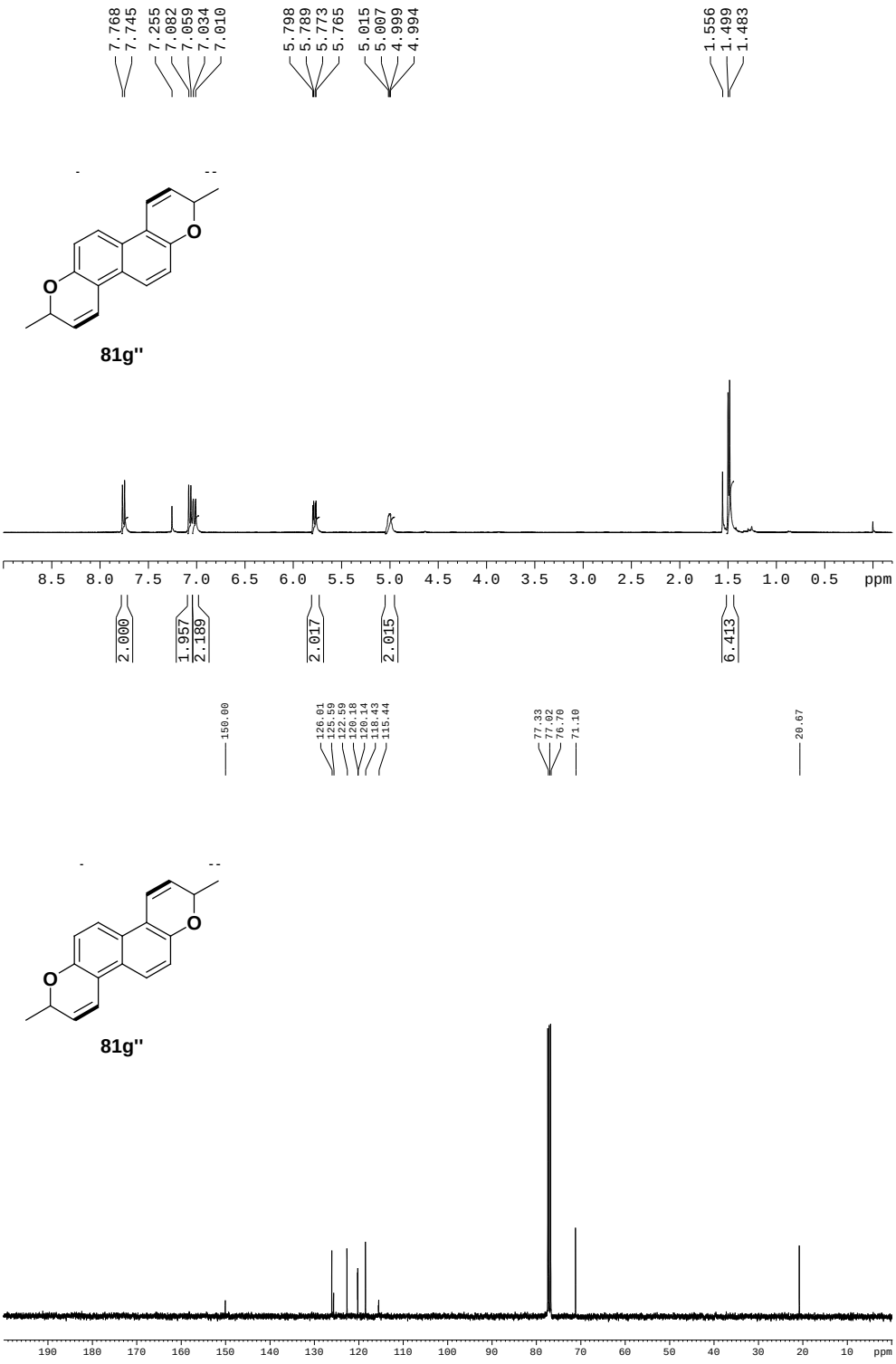
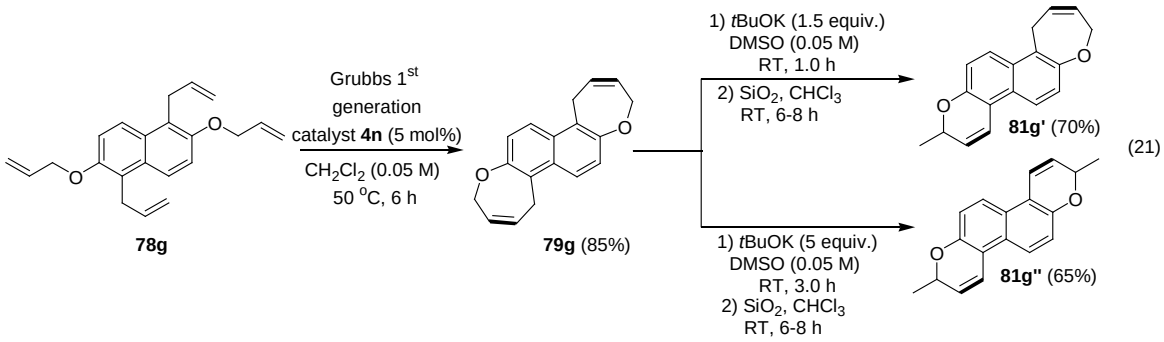


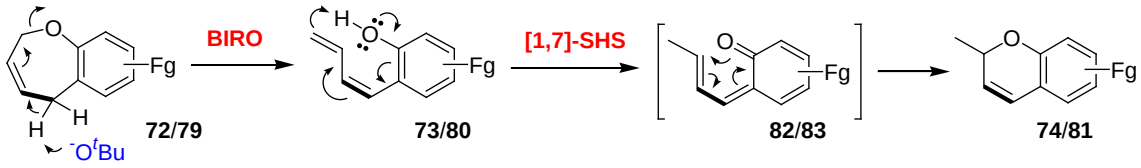
Figure-12: ^{1}H NMR and ^{13}C NMR Spectra of product **81g''.**



(21)

A [1,7]-sigmatropic shift of the phenolic hydrogen in *cis*-**73**/**80** would give rise to the *ortho*-quinone methide **82**/**83**, which rapidly cyclizes to yield **74**/**81** with recovery of the thermodynamic stability through oxa-6π electrocyclization or [3,3]-rearrangement. Interestingly, there was no [1,2]-Wittig-rearrangement products observed under these reaction conditions.[30]

Scheme 6: Proposed Reaction Mechanism.

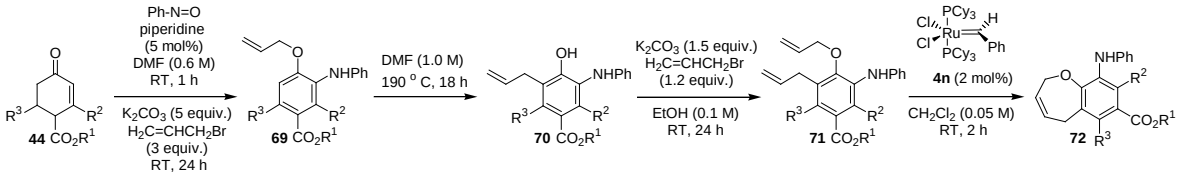


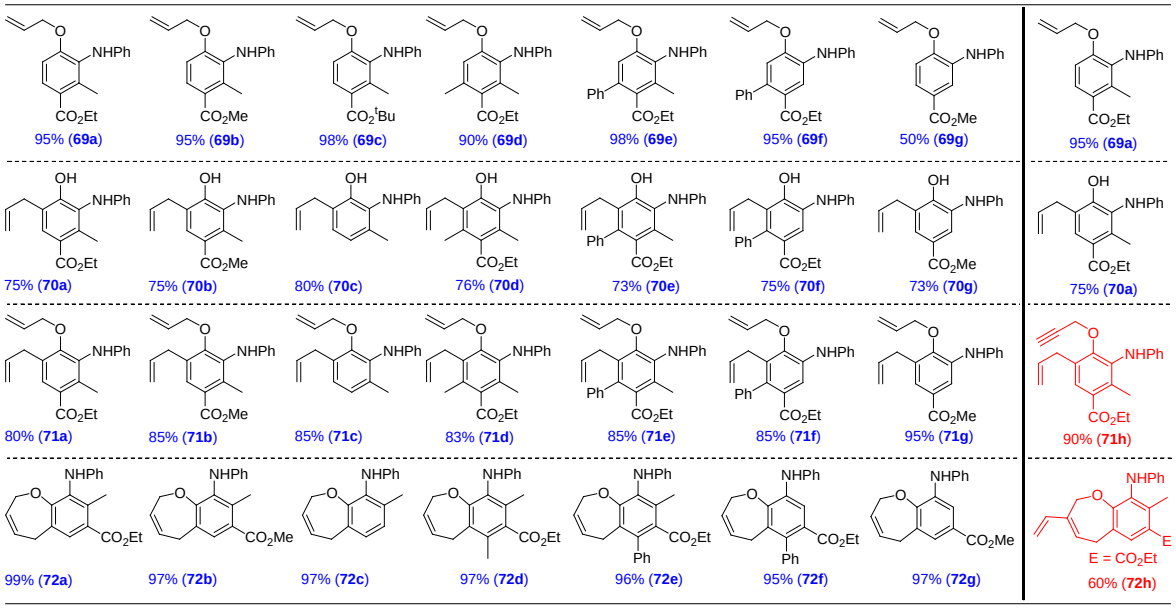
5.3 CONCLUSION

In this chapter, the results on diversity-oriented synthesis of highly functionalized benzo[*b*]oxepines **72**, (*Z*)-2-buta-1,3-dienyl-phenols **73** and 2-methyl-2*H*-chromenes **74** from simple starting materials via EA/IA/A, RCM, BIRO and [1,7]-SHS reactions under amine, ruthenium and base catalysis was disclosed. The RCM/BIRO/[1,7]-SHS reactions were performed in one-pot with good yields and selectivity. In addition, the synthesis of benzo[*b*]oxepines **79**, (*Z*)-2-buta-1,3-dienyl-phenols **80** and 2-methyl-2*H*-chromenes **81** from simple phenols was also demonstrated via *O*-allylation/Claisen rearrangement/*O*-allylation, RCM, BIRO and [1,7]-SHS reaction sequence.

ANNEXURE-I: Diversity-Oriented Synthesis of Highly Substituted 2,5-Dihydro-benzo[*b*]oxepines via Organo-RCM Chemistry.

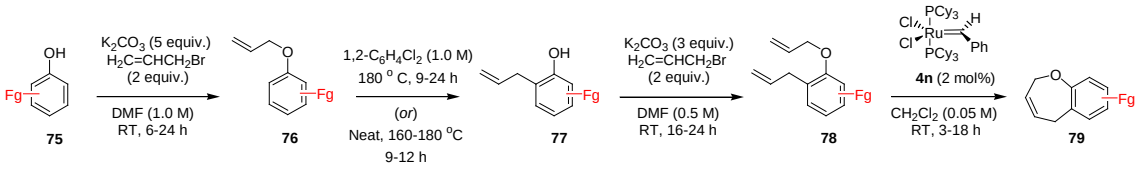
***Table A1*:** Synthesis of Highly Substituted 2,5-Dihydro-benzo[*b*]oxepines **72**.[a]

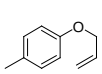
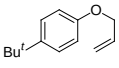
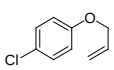
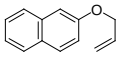
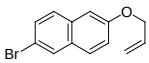
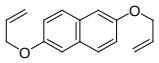
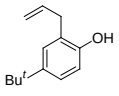
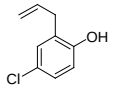
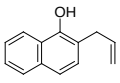
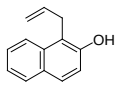
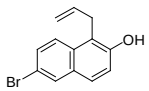
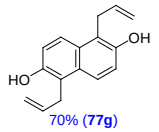
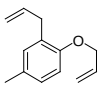
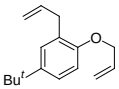
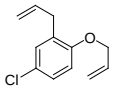
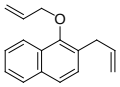
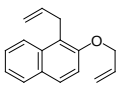
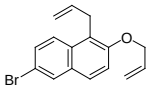
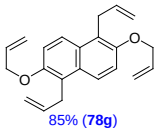
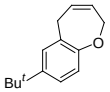
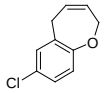
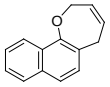
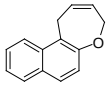
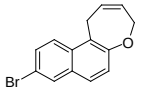
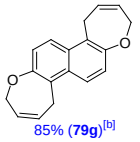




[a] Yield refers to the column purified product.

***Table A2*:** Synthesis of Highly Substituted 2,5-Dihydro-benzo[*b*]oxepines **79**.[a]



						
85% (**76a**)	98% (**76b**)	85% (**76c**)	99% (**76d**)	98% (**76e**)	98% (**76f**)	90% (**76g**)
						
75% (**77a**)	73% (**77b**)	65% (**77c**)	75% (**77d**)	70% (**77e**)	90% (**77f**)	70% (**77g**)
						
75% (**78a**)	85% (**78b**)	75% (**78c**)	95% (**78d**)	90% (**78e**)	90% (**78f**)	85% (**78g**)
						
90% (**79a**)	95% (**79b**)	95% (**79c**)	95% (**79d**)	95% (**79e**)	90% (**79f**)	85% (**79g**)[b]

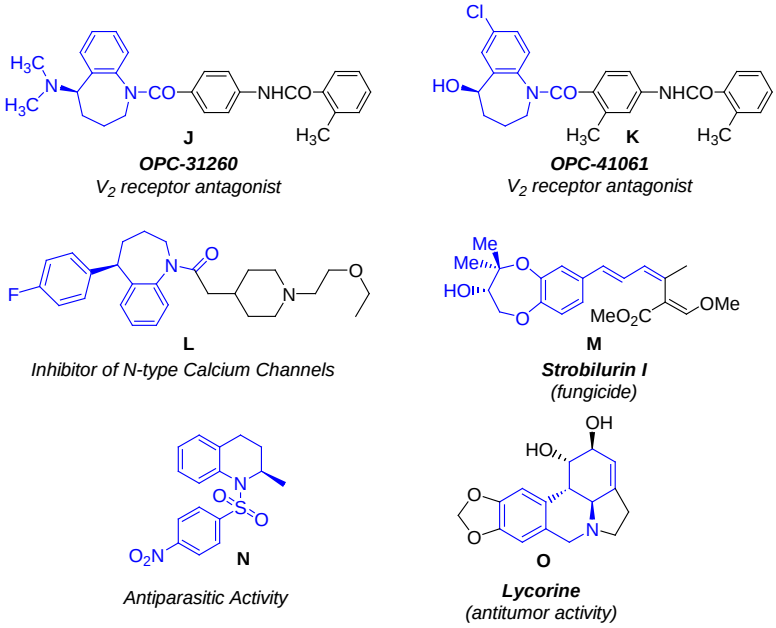
[a] Yield refers to the column purified product. [b] 5 mol% of RCM Catalyst used at 50 °C for 6 h.

6. SEQUENTIAL COMBINATION OF RUTHENIUM-, BASE- AND GOLD-CATALYSIS: A NEW APPROACH TO THE SYNTHESIS OF MEDICINALLY IMPORTANT HETEROCYCLES

6.1 INTRODUCTION

Benzannulated nitrogen heterocycles are well-known biologically active compounds, which are displaying wide range of pharmacological activities.[31] Especially *N*-substituted-2,3-dihydro-1*H*-benzo[*b*]azepines, *N*-substituted-2-(buta-1,3-dienyl)phenylamines, *N*-substituted-1,2,3,4-tetrahydroquinolines and functionalized hexahydrophenanthridines display promising biological activitives.[31] Thus, the diversity-oriented synthesis of these heterocycles represents an important task because

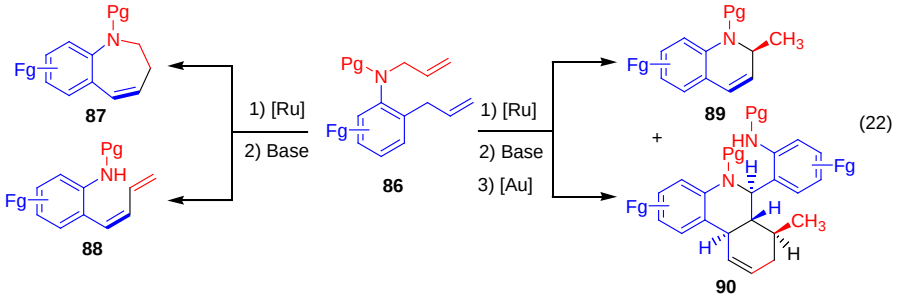
Chart 2: Some Important Biologically Active Molecules.



of the widespread occurrence of such structural scaffolds and their use as building blocks in pharmaceuticals. For example OPC-31260 (**J**), OPC-41061 (**K**), inhibitor of

N-type calcium channels (**L**), Strobilurin I (**M**), antiparasitic activity (**N**) and Lycorine (**O**) are some of the compounds very useful in medicinal chemistry (see Chart 2).[31]

A novel methodology was designed for the synthesis of highly functionalized *N*-substituted-benzo[*b*]azepines, *N*-substituted-2-(buta-1,3-dienyl)phenylamines, *N*-substituted-2-methyl-2*H*-quinolines and *N*-substituted-phenanthridines starting from simple dienes (eq. 22) and the results are discussed in the present section. A ruthenium-catalyzed ring-closing metathesis (RCM), base-induced ring opening (BIRO) and gold-catalyzed hydroamination of olefins followed by [4+2]-cycloaddition reactions are the crucial steps in the designed reaction sequence. Interestingly, to the best of our knowledge there is no report for synthesis of three different heterocycles from one common precursor. Sequential one-pot approach to the synthesis of highly functionalized benzo[*b*]azepines **87**, (*Z*)-2-(buta-1,3-dienyl)phenylamines **88**, 2-methyl-2*H*-quinolines **89** and phenanthridines **90** starting from simple dienes **86** was reported for the first time via sequential RCM/BIRO and gold-catalyzed hydroamination followed by [4+2]-cycloaddition reactions.[19]

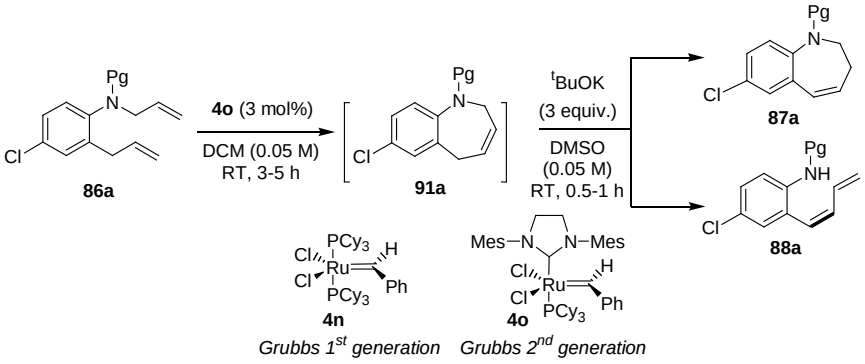


6.2 RESULTS AND DISCUSSION

With the aim of synthesizing highly functionalized molecules through sequential RCM/BIRO and gold-catalyzed hydroamination one-pot reactions, studies were directed towards the synthesis of substituted heterodienes/heteroenynes **86** as precursors through the combination of *N*-allylation, *N*-propargylation, *C*-allylation, and *N*-protection on anilines (see Annexure-II, Scheme A1-A4). First the scope of sequential

RCM/BIRO one-pot reactions was investigated with variety of *N*-substituted heterodienes **86aa-af** by looking at the electronic factors as shown in Table 5. Reaction of ethyl allyl-(2-allyl-4-chlorophenyl)carbamate **86aa** with Grubbs' first-generation catalyst **4n** (3 mol%) in CH_2Cl_2 at RT for 15 h furnished the benzo[*b*]azepine **91aa** in >95% conversion, which on further treatment with 3 equiv. of *t*BuOK in DMSO at 0 ^oC

Table 5: Optimization of RCM/BIRO One-Pot Reactions.



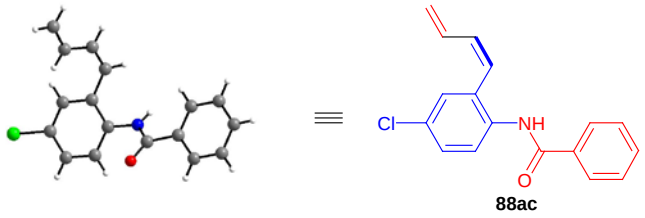
Entry	Pg	Time [h]	Product	Yield [%][a]
1[b]	CO_2Et (**a**)	15 + 0.5	**88aa**	75
2	CO_2Et (**a**)	5 + 0.5	**88aa**	92
3	Ts (**b**)	3 + 0.5	**88ab**	88
4	COPh (**c**)	4 + 0.5	**88ac**	80
5	$COCH_3$ (**d**)	4 + 1.0	**88ad**	71
6	$COCF_3$ (**e**)	3 + 1.0	**88ae**	40
7[c],[d]	H (**f**)	24 + 3.0	**87af**	55

[a] Yield refers to the column purified product. [b] For RCM, catalyst **4n** is used. [c] *p*-TSA (1 equiv.) is used as a co-catalyst for RCM. [d] BIRO reaction performed on isolated RCM product.

to RT for 0.5 h furnished the ethyl (2-buta-1,3-dienyl-4-chlorophenyl)carbamate *cis*-**88aa** with 75% yield and >99% *Z*-selectivity under one-pot conditions (Table 5, entry 1). Interestingly, sequential RCM/BIRO one-pot reaction of **86aa** using Grubbs' second-generation catalyst **4o** (3 mol%) in CH_2Cl_2 at RT for 5 h followed by treatment with 3 equiv. of *t*BuOK in DMSO at 0 ^oC to RT for 0.5 h furnished the carbamate *cis*-**88aa** with 92% yield and >99% *Z*-selectivity (Table 5, entry 2).[32]

After this preliminary information, RCM/BIRO reactions were further investigated on heterodienes containing different *N*-protecting groups to study the electronic factors. Interestingly, sequential RCM/BIRO one-pot reactions on heterodienes containing *N*-Ts **86ab**, *N*-COPh **86ac**, *N*-$COCH_3$ **86ad** and *N*-$COCF_3$ **86ae** furnished the expected products (*Z*)-**88ab-ae** in very good yields as shown in Table 5, entries 3-6. But RCM reaction of heterodiene containing *N*-H **86af** with **4o**/*p*-TSA furnished the 7-chloro-2,5-dihydro-1*H*-benzo[*b*]azepine **91af** in 75% yield, which on further treatment with 3 equiv. of *t*BuOK in DMSO at 0 ^{o}C to RT for 3 h gave only isomerized 7-chloro-2,3-dihydro-1*H*-benzo[*b*]azepine **87af** with 55% yield instead of (*Z*)-**88af** as shown in Table 5, entry 7. Sequential RCM/BIRO one-pot reactions are proved to be extremely facile with heterodienes **86aa-af** containing electron withdrawing groups on nitrogen as shown in Table 5. The optimized condition was found to be reaction of **86aa** using **4o** (3 mol%) in CH_2Cl_2 at RT for 5 h to furnish the

Scheme 7: Crystal structure of (Z) -*N*-(2-buta-1,3-dienyl-4-chloro-phenyl)-benzamide (**88ac**).

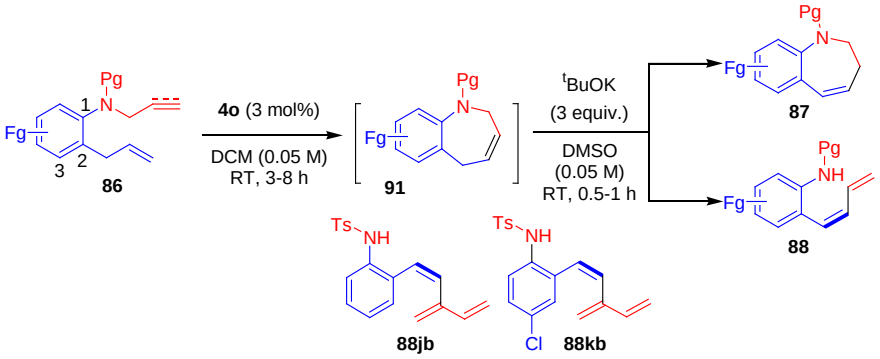


88ac

benzo[*b*]azepine **91aa** in >99% conversion, which on *in situ* treatment with 3 equiv. of *t*BuOK in DMSO at 0 ^{o}C to RT for 0.5 h furnished the one-pot product *cis*-**88aa** with 92% yield and >99% *Z*-selectivity (Table 5, entry 2). Structure and regiochemistry of (*Z*)-2-(buta-1,3-dienyl)phenylamines **88** were confirmed by NMR analysis and also finally confirmed by X-ray structure analysis on *cis*-**88ac** as shown in Scheme 7.[33]

With the optimized reaction conditions in hand, the scope of the ruthenium- and base-induced RCM/BIRO one-pot reactions was investigated with variety of

Table 6: Synthesis of Functionalized *N*-Substituted 2,3-Dihydro-1*H*-benzo[*b*]azepines **87** and (Z)-2-(Buta-1,3-dienyl)phenylamines **88**.



Entry	diene **1** [Fg, Pg]	2-buta-1,3-dienyl-phenylamine **88**	Time [h]	Yield[%][a]
1	Fg = H, Pg = CO_2Et (**86ba**)	**88ba**	3.0 + 1.0	90
2	Fg = 4-F, Pg = CO_2Et (**86ca**)	**88ca**	3.0 + 0.5	85
3	Fg = 4-Br, Pg = CO_2Et (**86da**)	**88da**	3.0 + 1.0	86
4	Fg = 4-CH_3, Pg = CO_2Et (**86ea**)	**88ea**	5.0 + 0.5	89
5	Fg = 4-OCH_3, Pg = CO_2Et (**86fa**)	**88fa**	5.0 + 0.5	82
6	Fg = 4-CO_2Et, Pg = CO_2Et (**86ga**)	**88ga**	4.0 + 1.0	75
7	Fg = 4-NO_2, Pg = $COCF_3$ (**86he**)	**88he**	3.0 + 0.5	55
8[b]	Fg = 5,6-C_4H_4, Pg = Ts (**86ib**)	**88ib**	8.0 + 1.0	85
9[c]	Fg = H, Pg = Ts (**86jb**)	**88jb**	24.0 + 1.0	45
10[c]	Fg = 4-Cl, Pg = Ts (**86kb**)	**88kb**	24.0 + 1.0	40
11[d],[e]	Fg = Pg = H (**86bf**)	**87bf**	24.0 + 1.0	75
12	Fg = H, Pg = Ph (**86bg**)	**87bg**	2 .0 + 1.0	82

[a] Yield refers to the column purified product. [b] **86ib** = *N*-Allyl-*N*-(2-allyl-naphthalen-1-yl)-4-methyl-benzenesulfonamide. [c] RCM reaction performed with Grubbs first-generation (8 mol%) catalyst. [d] *p*-TSA (1 equiv.) is used as a co-catalyst for RCM. [e] BIRO reaction performed on isolated RCM product.

heterodienes and heteroenynes **86** as shown in Table 6. Sequential RCM reaction of the substituted heterodienes **86ba-ib** containing *N*-CO_2Et, *N*-$COCF_3$ or *N*-Ts with Grubbs' second-generation catalyst **4o** (3 mol%) in CH_2Cl_2 at RT for 3-8 h furnished the functionalized benzo[*b*]azepines **91ba-ib** in >99% conversion, which on *in situ* treatment with 3 equiv. of *t*BuOK in DMSO at 0 ^oC to RT for 0.5-1.0 h furnished the functionalized (*Z*)-2-(buta-1,3-dienyl)phenylamines **88ba-ib** in good yields with high *Z*-selectivity as shown in Table 6, entries 1-8. Interestingly, enyne metathesis of the substituted heteroenynes **86jb-kb** [*N*-Ts] with Grubbs' first-generation catalyst **4n** (8 mol%) in CH_2Cl_2 at RT for 24 h furnished the benzo[*b*]azepines **91jb-kb** in >99%

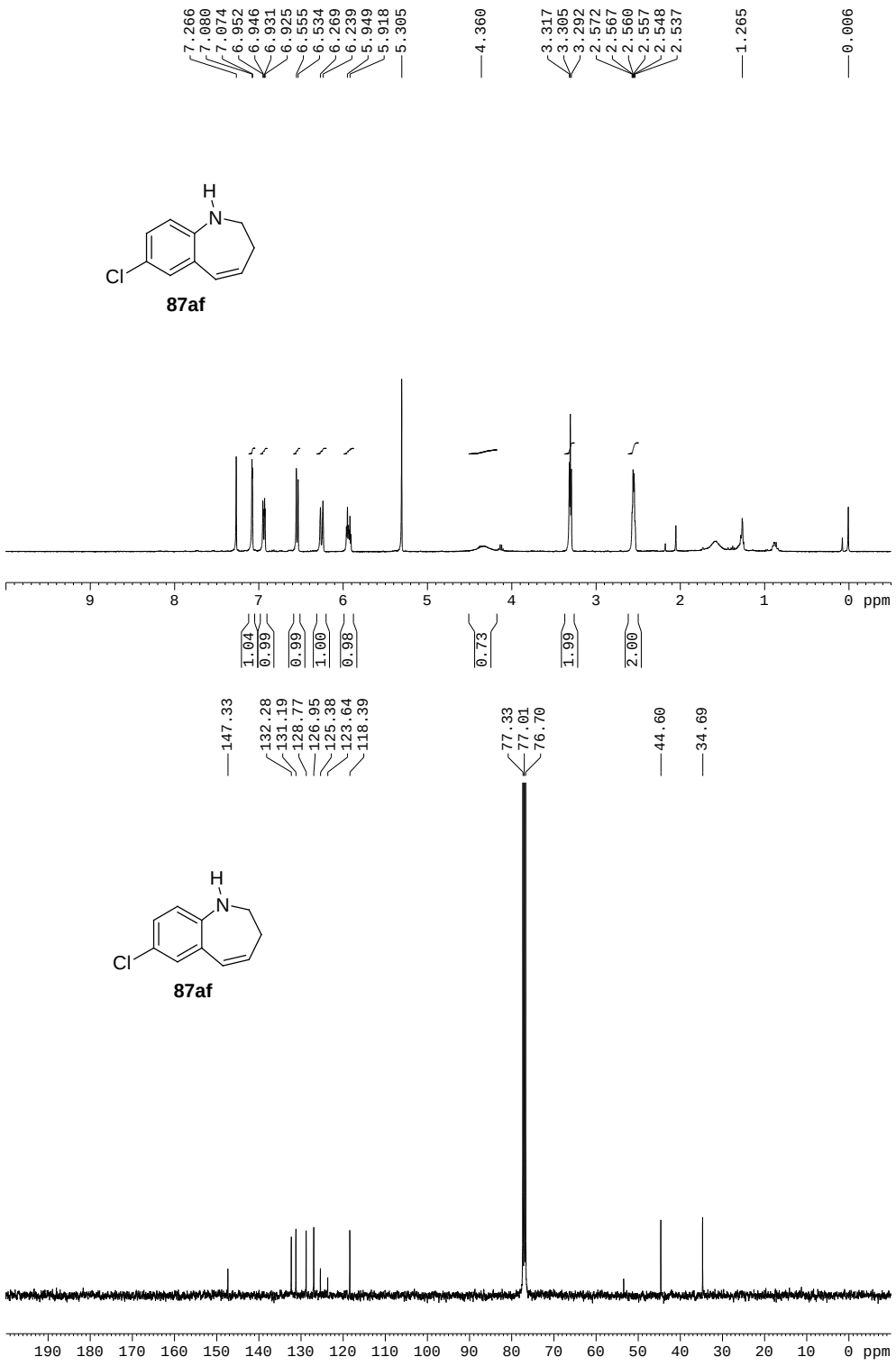


Figure-13: ^{1}H NMR and ^{13}C NMR Spectra of product **87af.**

Figure-14: ^{1}H NMR and ^{13}C NMR Spectra of product **88aa.**

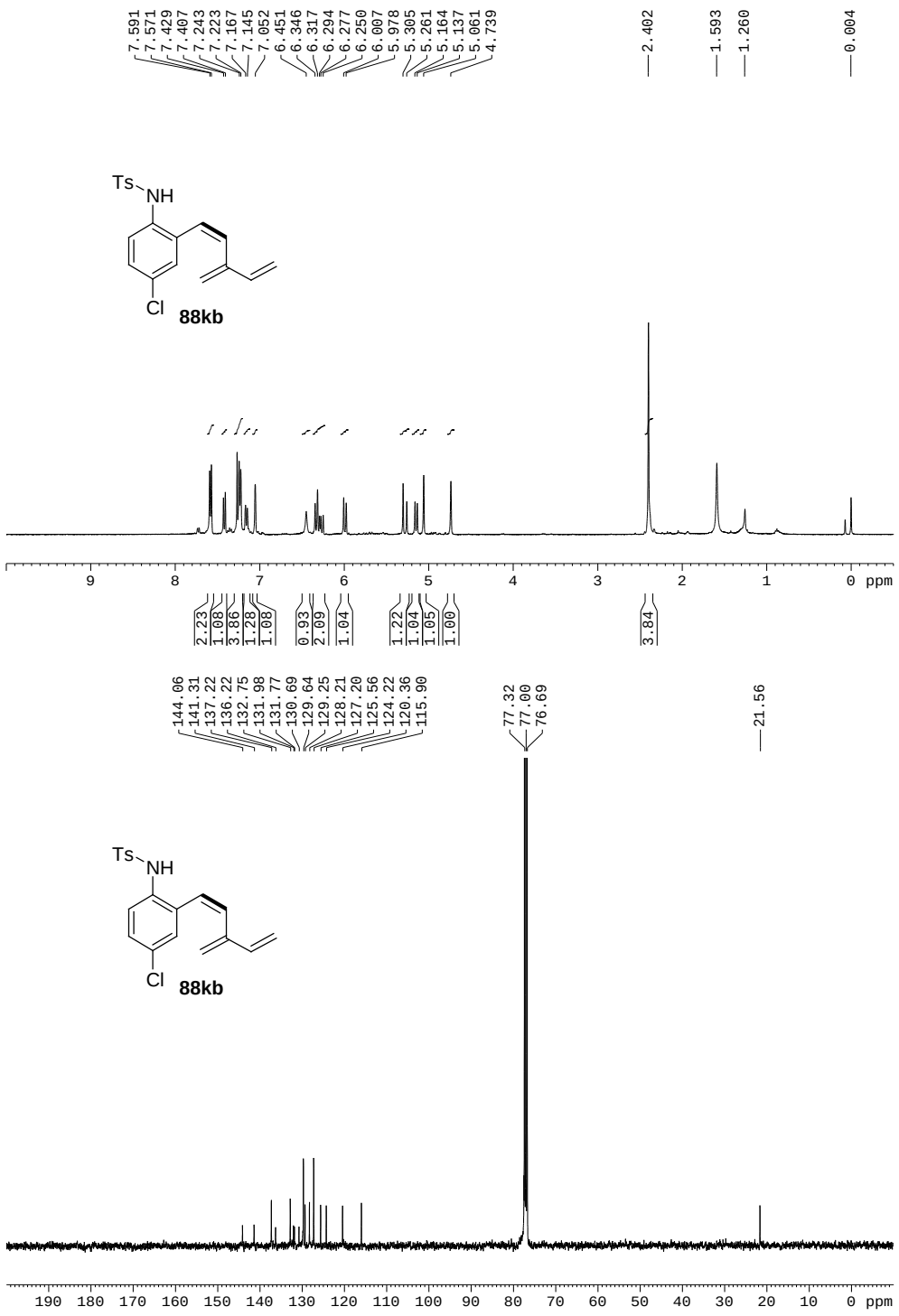
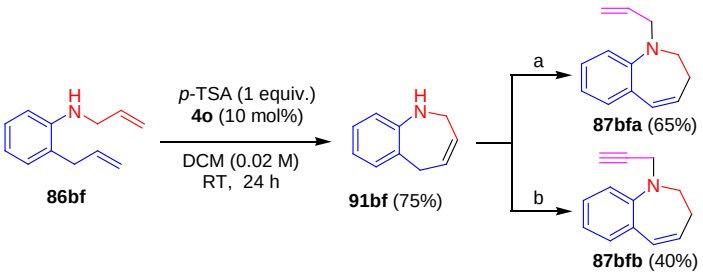


Figure-15: ^{1}H NMR and ^{13}C NMR Spectra of product **88kb.**

conversion, which on *in situ* treatment with base furnished the products *cis*-**88jb-kb** in moderate yields (Table 6, entries 9-10). In order to support the role of electronic factors in BIRO reactions, these reactions were performed on two more benzo[*b*]azepines containing *N*-H/*N*-Ph **86bf-bg** as shown in Table 6, entries 11-12. Interestingly, *in situ* treatment of benzo[*b*]azepines containing *N*-H/*N*-Ph **91bf**/**91bg** with 3 equiv. of *t*BuOK in DMSO at 0 ^{o}C to RT for 1.0 h furnished the only double-bond isomerized products **87bf**/**87bg** in 75/82% yields respectively (Table 6, entries 11-12).



(23)

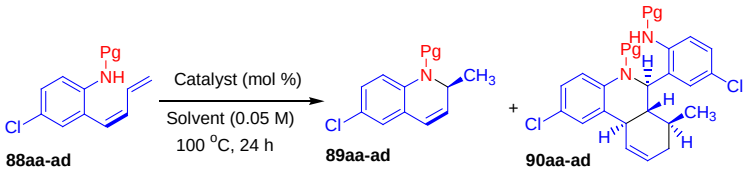
For reagents and conditions, see: (a) *t*BuOK (3 equiv.), DMSO (0.05 M), RT, 1h; H_2C=$CHCH_2Br$ (**57a,** 2 equiv.), RT, 3h, 65%; (b) *t*BuOK (3 equiv.), DMSO (0.05 M), RT, 1h; HC≡CCH_2Br (**57b**, 2 equiv.), RT, 18h, 40%.

The base-induced double bond isomerization with *N*-alkylation reactions in one-pot was utilized to deliver the functionalized 2,3-dihydro-1*H*-benzo[*b*]azepines **87** in good yields (see eq. 23). Reaction of 2,5-dihydro-1*H*-benzo[*b*]azepine **91bf** with 3 equiv. of *t*BuOK at 0 ^{o}C to RT for 1 h, followed by *in situ* treatment with allyl bromide **57a** or propargyl bromide **57b** at RT for 3-18 h furnished the one-pot products *N*-allyl-2,3-dihydro-1*H*-benzo[*b*]azepine **87bfa** in 65% yield and 1-prop-2-ynyl-2,3-dihydro-1*H*-benzo[*b*]azepine **87bfb** in 40% yield respectively and which are good starting materials for the synthesis of drug analogues of **J**-**L**.

After understanding the sequential one-pot combination of RCM, BIRO, isomerisation (I) and alkylation (A) reactions, the intra- and intermolecular hydroamination of (*Z*)-aminodienes **88** were further investigated as shown in Tables 7. The hydroamination of olefins is a prominent and atom-economic reaction for the

synthesis of *N*- heterocycles.[34] Particularly, intra- and intermolecular hydroamination displays an efficient route for accessing multifunctional *N*-heterocycles for natural product synthesis and pharmaceuticals.[34] Since the seminal discovery of metallocene-catalyzed hydroamination by Marks and co-workers,[35] this emerged as a most important reaction to study many aspects. Starting from simple aminoalkenes, the scope of metal-promoted hydroamination reaction was quickly extended to various unsaturated molecules including aminoalkynes, aminoallenes, conjugated (*E*)-aminodienes and aminodialkenes, aminodialkynes, and aminoalkenalkynes.[34] However, the metal-catalyzed intra- or intermolecular hydroamination of conjugated (*Z*)-aminodienes **88**

Table 7: Reaction Optimization.[a]



88aa-ad **89aa-ad** **90aa-ad**

Entry	Catalyst [mol %]	Pg	Solvent	Product **89** Yield [%][b]	Product **90** Yield [%][b]
1[c]	$AuCl_3$ (5)	Ts (**b**)	Toluene	**89ab** (--)	**90ab** (--)
2[c]	AgOTf (5)	Ts (**b**)	Toluene	**89ab** (--)	**90ab** (--)
3[c]	$(PPh_3)AuCl$ (5)	Ts (**b**)	Toluene	**89ab** (--)	**90ab** (--)
4[d]	$AuCl_3$/AgOTf (5)	Ts (**b**)	Toluene	**89ab** (--)	**90ab** (--)
5[c],[e]	$(PPh_3)AuCl$/AgOTf (5)	Ts (**b**)	DCE	**89ab** (--)	**90ab** (--)
6	$(PPh_3)AuCl$/AgOTf (5)	Ts (**b**)	Toluene	**89ab** (50)	**90ab** (--)
7	$(PPh_3)AuCl$/AgOTf (5)	Ts (**b**)	1,4-Dioxane	**89ab** (50)	**90ab** (--)
8	$(PPh_3)AuCl$/AgOTf (5)	CO_2Et (**a**)	Toluene	**89aa** (20)	**90aa** (55)
9	$(PPh_3)AuCl$/AgOTf (5)	$COCH_3$ (**d**)	Toluene	**89ad** (--)	**90ad** (40)
10[c]	*p*-TSA (100)	Ts (**b**)	Toluene	**89ab** (--)	**90ab** (--)
11[d]	$MeSO_3H$ (100)	Ts (**b**)	Toluene	**89ab** (--)	**90ab** (--)
12[c]	$BF_3.Et_2O$ (20)	Ts (**b**)	Toluene	**89ab** (--)	**90ab** (--)

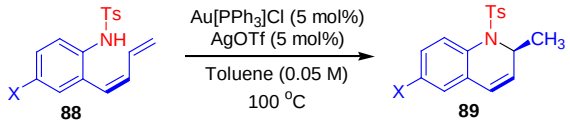
[a] Reactions were performed with **88aa-ad** (0.1 mmol) and catalyst (see column) in dry solvent (2 mL) at 100 °C. [b] Yield refers to the column purified product. [c] Starting material (80-85%) is left-over. [d] Starting material is consumed, complex mixture is isolated. [e] Reaction performed at RT.

was not known and resulting products **89-90** will have a wide range of applications in pharmaceutical chemistry (see Chart 2).[34]

Towards these hydroamination reactions, studies were initiated by taking (*Z*)-aminodiene **88ab** in DMF at 120-140 ^{o}C for 48 h, no reaction took place and only the starting material **88ab** was recovered (result not shown in Table 7). Hydroamination reaction of (*Z*)-aminodiene **88ab** with simple Bronsted acids like *p*-TSA, $MeSO_3H$ and Lewis acid $BF_3{\cdot}Et_2O$ was also not successful (Table 7, entries 10-12). The intra- and intermolecular hydroamination of conjugated (*Z*)-aminodiene **88ab** was also tested with gold chlorides like $AuCl_3$ (5 mol%), $[PPh_3]AuCl$ (5 mol%) and silver salt AgOTf (5 mol%), didn't furnished the expected products (Table 7, entries 1-3). But it was found that 5 mol% of $[PPh_3]AuCl$/AgOTf in refluxing toluene is suitable condition for the designed hydroamination as shown in Table 7.[36] Interestingly, reaction of *N*-Ts-(*Z*)-aminodiene **88ab** with $Au[PPh_3]Cl$/AgOTf (5 mol%) in the toluene at 100 °C for 24 h furnished the selectively **89ab** in 50% yield without **90ab** (Table 7, entry 6). In a similar manner, treatment of *N*-Ts-(*Z*)-aminodienes **88eb-gb** with $Au[PPh_3]Cl$/AgOTf (5 mol%) in toluene at 100 °C for 6-7 h furnished the only intra-molecular hydroamination products **89eb-gb** in moderate yields (Table 8, entries 2-4). However, reaction of *N*-CO_2Et-(*Z*)-aminodiene **88aa** with $Au[PPh_3]Cl$/AgOTf (5 mol%) in toluene at 100 °C for 24 h furnished the unexpected cascade intermolecular hydroamination/[4+2]-cycloaddition product **90aa** in 55% yield with >99% *de* and also **89aa** in 20% yield (Table 7, entry 8). Similar manner, reaction of *N*-$COCH_3$-(*Z*)-aminodiene **88ad** with $Au[PPh_3]Cl$/AgOTf (5 mol%) in toluene at 100 °C for 24 h furnished the only cascade product **90ad** in 40% yield with >99% *de* (Table 7, entry 9). Herein, products **89** were generated through gold-catalyzed intra-molecular hydroamination of **88,** and cascade product **90aa** was formed through gold-catalyzed intermolecular hydroamination of **88aa** followed by unusual gold-catalyzed intra-molecular [4+2]-cycloaddition reactions. Product selectivity of these reactions was mainly controlled by electronic factors as shown with the nature of *N*-protecting groups.

To explore the unusual gold-catalyzed intra-molecular and intermolecular hydroamination followed by selective [4 + 2]-cycloaddition reactions,[37] variety of (*Z*)-ethyl-2-buta-1,3-dienyl-carbamates **88aa-ga** were chosen as substrates (see Table 9). A

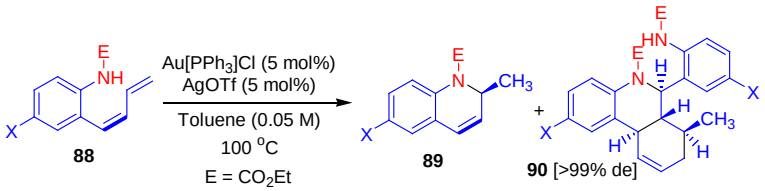
Table 8: Synthesis of Functionalized *N*-Substituted 2-Methyl-1,2-dihydroquinolines **89**.



Entry	X	Product	Time [h]	Yield [%][a]
1	Cl	**89ab**	24	50
2	CH_3	**89eb**	6	30
3	OCH_3	**89fb**	6	25
4	CO_2Et	**89gb**	7	25

[a] Yield refers to the column purified product.

Table 9: Synthesis of Functionalized *N*-Substituted 2-Methyl-2*H*-quinolines **89** and *N*-Substituted Phenanthridines **90**.[a]



Entry	X	Time [h]	Product **89**	Product **90**
1	Cl	24	**89aa** (20%)	**90aa** (55%)
2	H	10	**89ba** (25%)	**90ba** (40%)
3	Br	24	**89da** (24%)	**90da** (47%)
4	CH_3	24	**89ea** (26%)	**90ea** (43%)
5	OCH_3	6	**89fa** (30%)	**90fa** (25%)
6	CO_2Et	8	**89ga** (20%)	**90ga** (60%)
7[b]	Cl	24	-------	**90ad** (40%)

[a] Yield refers to the column purified product. [b] E = $COCH_3$.

series of differently substituted (*Z*)-ethyl-2-buta-1,3-dienylcarbamates **88aa-ga** were transferred into functionalized *N*-substituted 2-methyl-2*H*-quinolines **89aa-ga** in moderate yields and highly functionalized *N*-substituted phenanthridines **90aa-ga** in good yields with >99% *de* via combination of gold-/silver-catalysis as shown in Table 9, entries 1-6. Cascade products **90aa-ga** were furnished with good yields and high diastereoselectivity through gold-catalysis by without showing much of substitution (X) effect on benzene ring of **88aa-ga**. The structure and stereochemistry of *N*-substituted phenanthridines **90** were confirmed by NMR analysis and also finally confirmed by

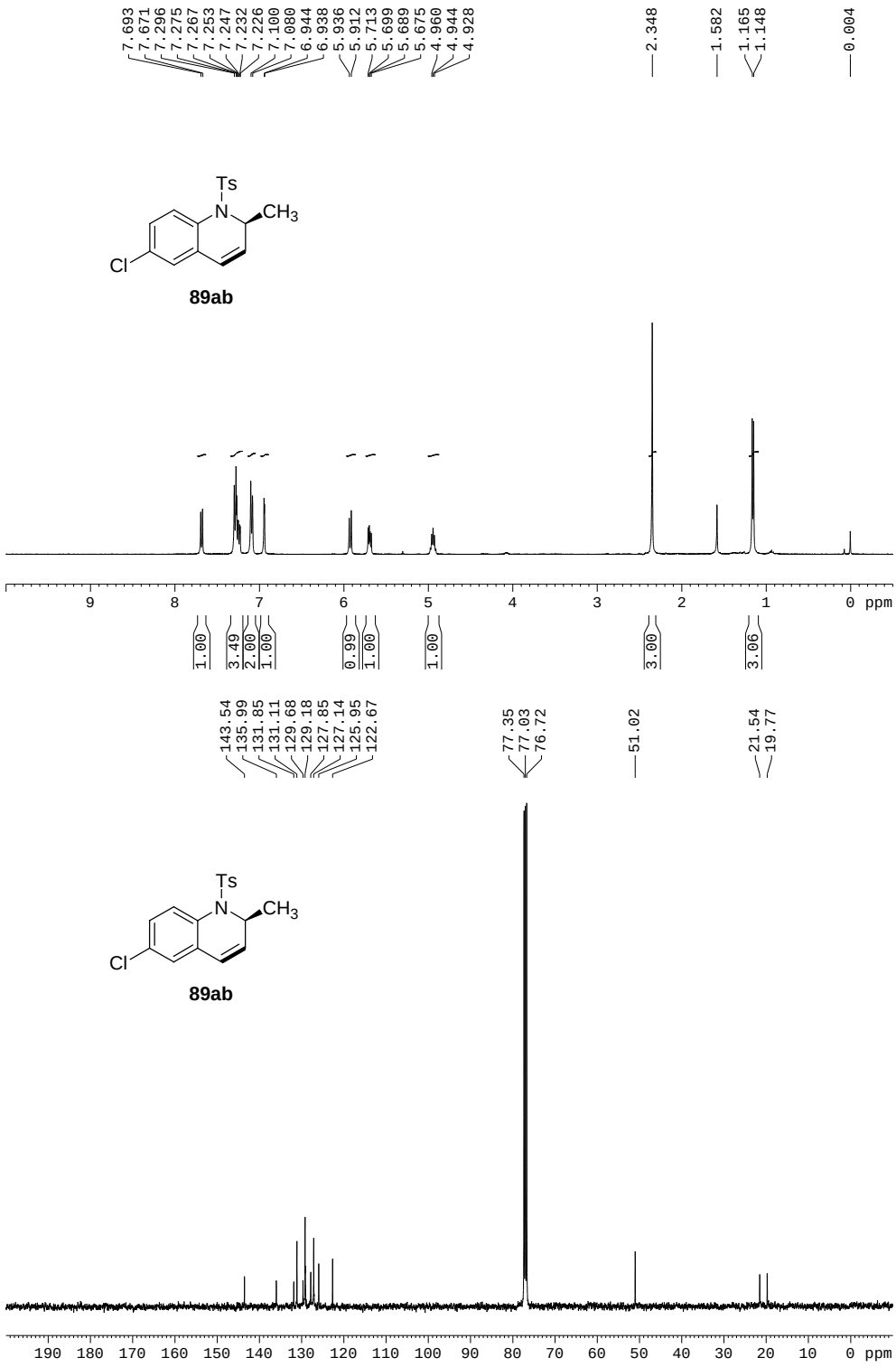


Figure-16: ^{1}H NMR and ^{13}C NMR Spectra of product **89ab.**

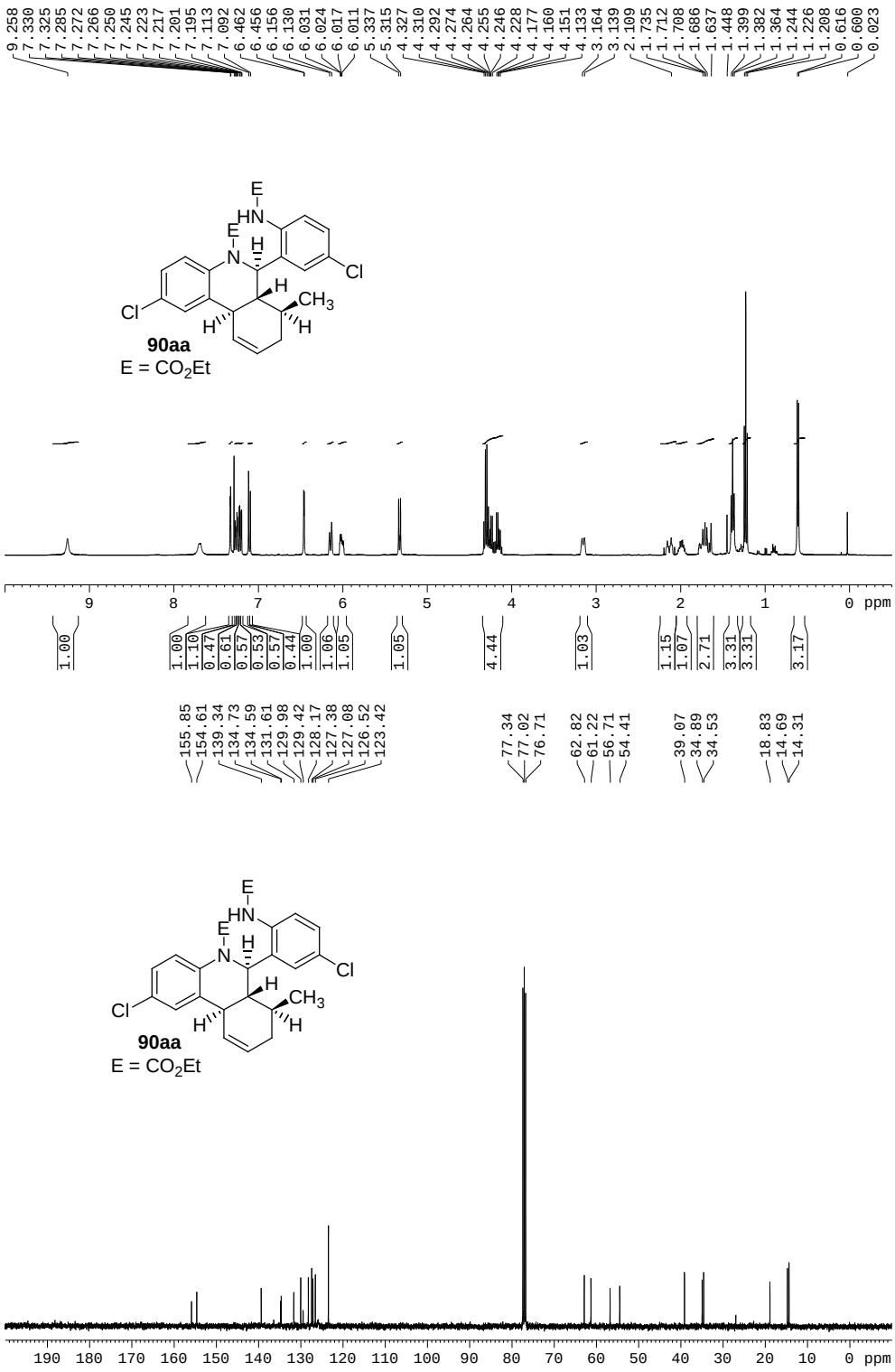
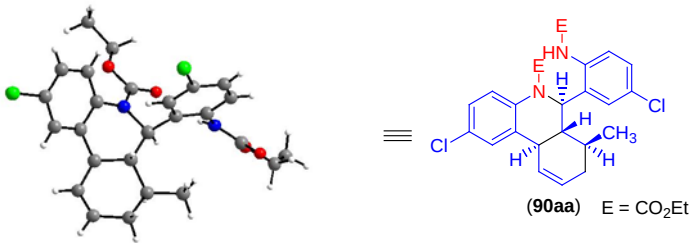


Figure-17: ^{1}H NMR and ^{13}C NMR Spectra of product **90aa.**

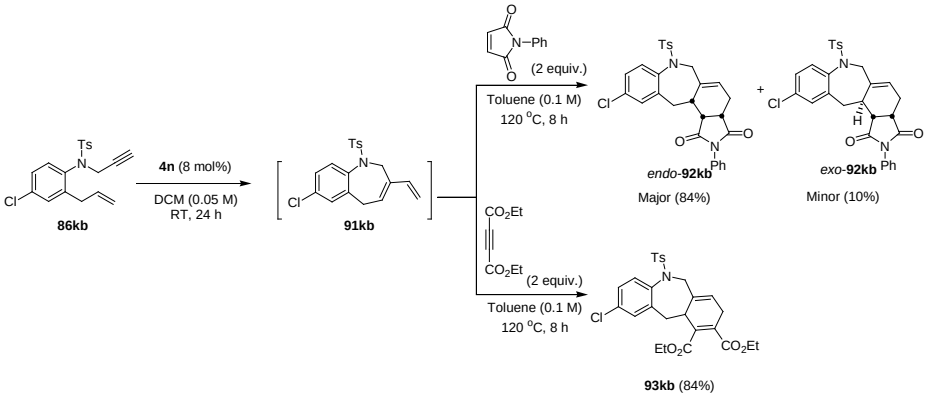
X-ray structure analysis on **90aa** (Scheme 8).[38a]

Scheme 8: Crystal structure of 2-chloro-6-(5-chloro-2-ethoxycarbonylamino-phenyl)-7-methyl-6a,7,8,10a-tetrahydro-6*H*-phenanthridine-5-carboxylic acid ethyl ester (**90aa**).



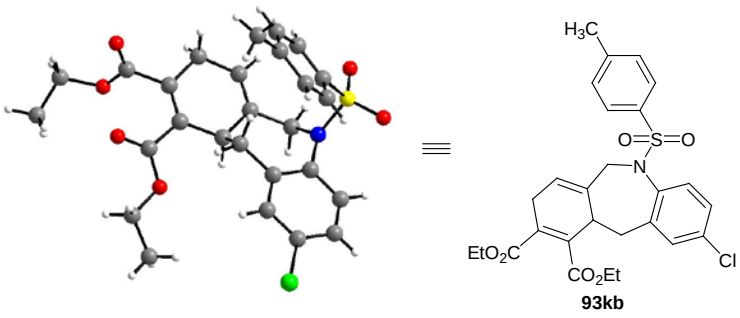
After successful demonstration for the multi-catalytic approach to the synthesis of highly functionalized *N*-substituted benzo[*b*]azepines **87**, *N*-substituted 2-(buta-1,3-dienyl)phenylamines **88**, *N*-substituted 2-methyl-2*H*-quinolines **89** and *N*-substituted phenanthridines **90** starting from simple dienes via sequential RCM/BIRO and gold-catalyzed hydroamination followed by [4+2]-cycloaddition reactions. Further investigation was done for the synthesis of functionalized heterocycles like *endo*-**92kb**, *exo*-**92kb** and **93kb** based on 3-vinyl-2,5-dihydro-1*H*-benzo[*b*]azepine **91kb** through enyne RCM/Diels-Alder (DA) reactions in one-pot. RCM of enyne **86kb** with Grubbs'

Scheme 9: Synthesis of *N*-substituted tri- and tetra-cyclic heterocycles.



first-generation catalyst **4n** (8 mol%) in CH_2Cl_2 at RT for 24 h furnished the expected functionalized 3-vinyl-2,5-dihydro-1*H*-benzo[*b*]azepine **91kb** in good conversion as shown in Scheme 9, which on *in situ* treatment with 1-phenyl-pyrrole-2,5-dione in toluene at 110-120 ^oC for 8 h furnished the highly functionalized tetra-cyclic *endo*-**92kb** with 79% *de* in a stereoselective manner with 84% yield. To show further diversity of enyne **86kb**, highly functionalized tri-cyclic product **93kb** in 84% yield was synthesized via RCM/DA under one-pot conditions. The structure and stereochemistry of functionalized heterocycles *endo*-**92**, *exo*-**92kb** and **93kb** were confirmed by NMR analysis and also finally confirmed by X-ray structure analysis on **93 kb** (Scheme 10).[38b]

Scheme 10: Diethyl 2-chloro-5-(toluene-4-sulfonyl)-6,8,10a,11-tetrahydro-5*H*-dibenzo[*b*,*e*]azepine-9,10-dicarboxylate (**93kb**).



N-substituted 2-(buta-1,3-dienyl)phenylamines **88** are looking good substrates for the synthesis of diepoxides, because diepoxides are very useful intermediates in organic synthesis for the construction of many functionalized molecules. Recently, Williams and co-workers reported novel applications of spirodiepoxides in total synthesis.[39] Towards this goal, epoxidation of **88aa** with 3 equiv. of *m*-CPBA in CH_2Cl_2 at RT for 3 h furnished the mixture of epoxides **94aa** in 20% yield and **95aa** in 40% yield (see Scheme 11). But, unfortunately expected diepoxide was not found as shown in Scheme 11.

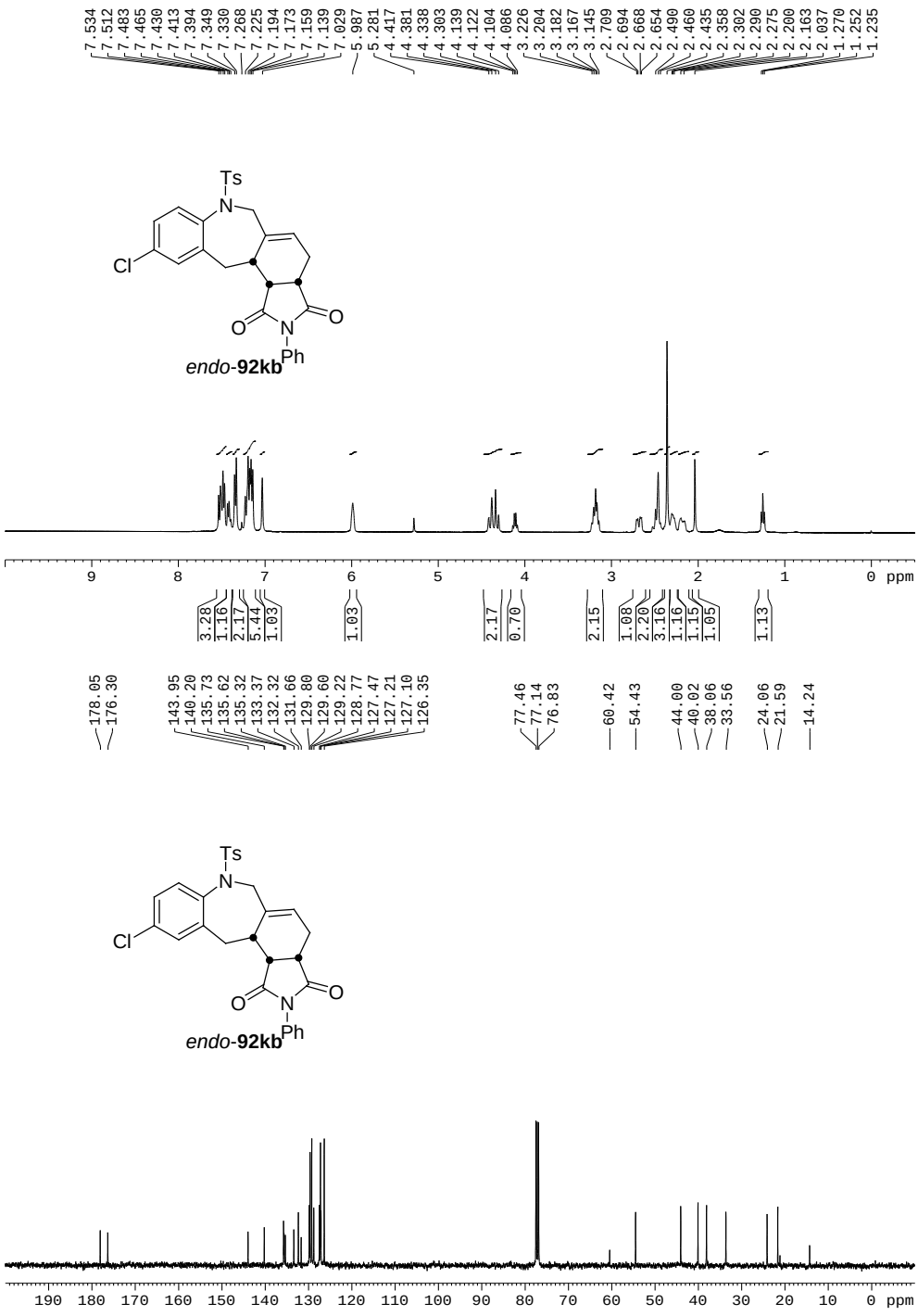


Figure-18: ^{1}H NMR and ^{13}C NMR Spectra of product **92kb.**

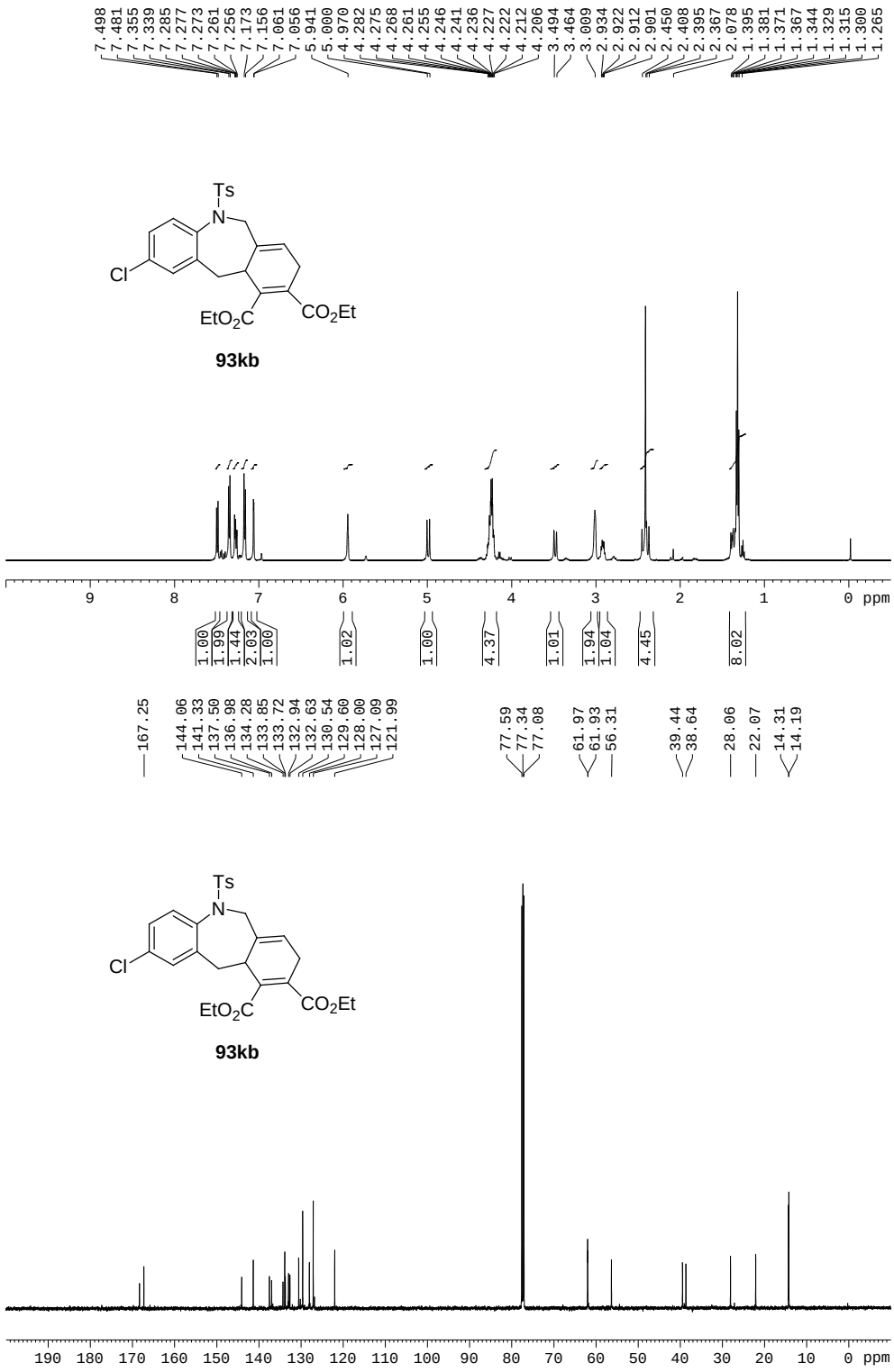


Figure-19: ^{1}H NMR and ^{13}C NMR Spectra of product **93kb.**

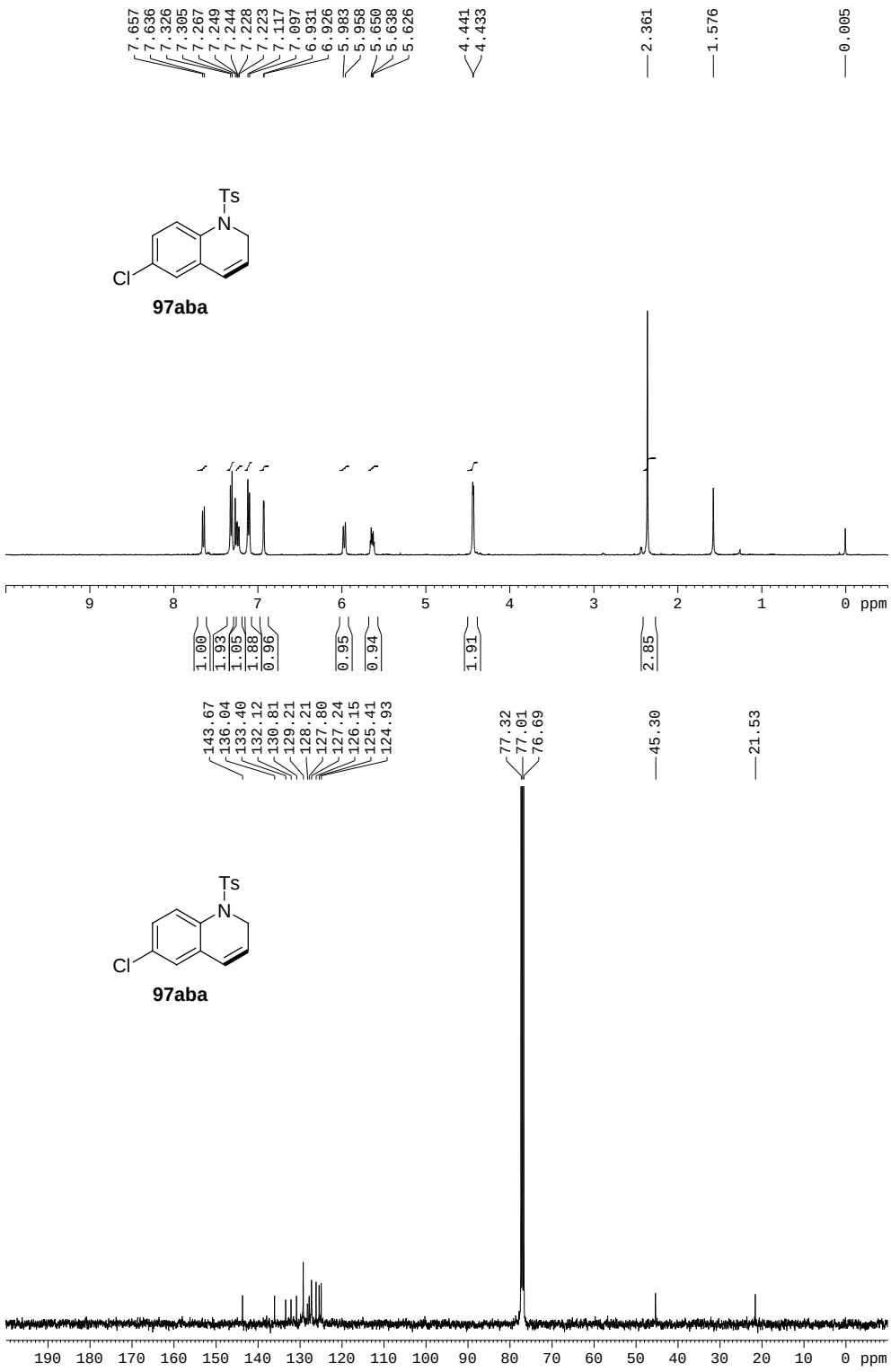
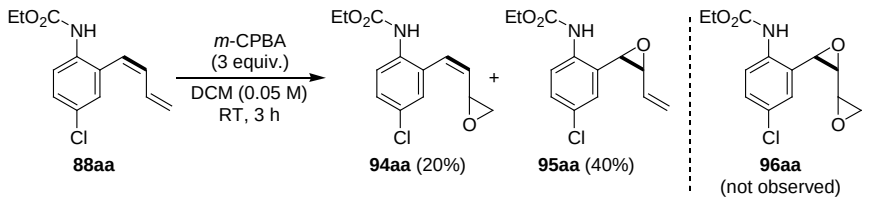


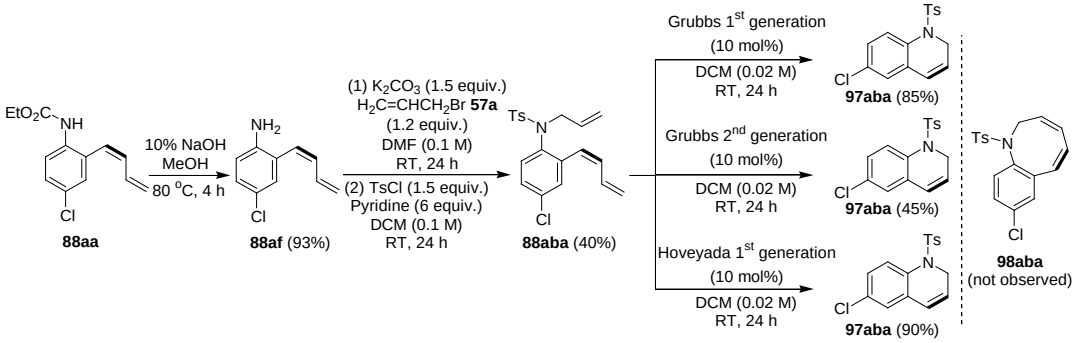
Figure-20: ^{1}H NMR and ^{13}C NMR Spectra of product **97aba.**

Scheme 11: Epoxidation.



N-allyl-*N*-(2-buta-1,3-dienyl-4-chlorophenyl)-4-methylbenzenesufonamide **88aba** with (*Z*)-2-buta-1,3-dienyl system was found to be interested towards RCM reactions. As shown in Scheme 12, decarboxylation of **88aa** with 10% NaOH in MeOH at 80 ^{o}C for 4h furnished the (*Z*)-2-buta-1,3-dienyl-4-chloro-phenylamine **88af** in 93% yield. *N*- Allylation of **88af** with 1.2 equiv. of allyl bromide **57a** and 1.5 equiv. of K_2CO_3 in DMF at RT furnished the amine, which on protection with 6 equiv. of pyridine and 1.5 equiv. of TsCl in CH_2Cl_2 at RT for 24 h furnished the *N*-allyl-*N*-(2-buta-1,3-dienyl-4-chloro-phenyl)-4-methyl-benzenesulfonamide **88aba** in 40% yield. RCM reaction of **88aba** by using Grubbs' second-generation catalyst **4o** (10 mol%) in CH_2Cl_2 at RT for 24 h furnished the *N*-substituted 1,2-dihydro-quinoline **97aba** in 45% yield instead of the expected 8-chloro-1-(toluene-4-sulfonyl)-1,2-dihydro-benzo[*b*]azocine **98aba**. May be due to the (*Z*)-selectivity of

Scheme 12: Synthesis of 6-chloro-2-methyl-1-(toluene-4-sulfonyl)-1,2-dihydro-quinoline **97aba** via RCM.



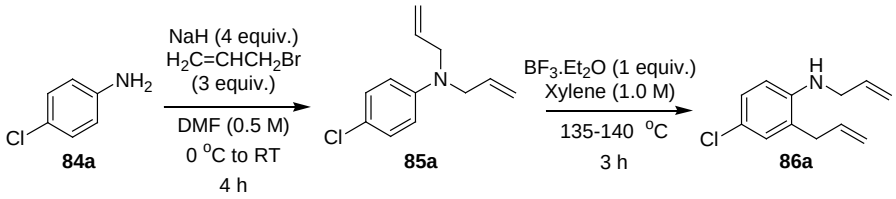
2-buta-1,3-dienyl system in **88aba** does not allow the terminal double-bond interacting with the ruthenium catalyst due to steric considerations. Furthermore RCM reaction of **88aba** with other catalysts such as Grubbs' first-generation catalyst **4n** (10 mol%) and Hoveyada first-generation catalyst **4p** (10 mol%) also didn't produce the product **98aba** rather increased the yield of *N*-substituted 1,2-dihydro-quinoline **97aba** as shown in Scheme 12.

6.3 CONCLUSION

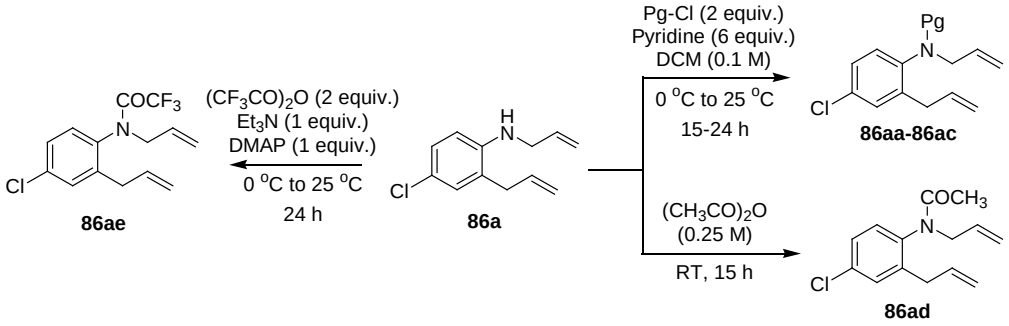
In this chapter, sequential multi-catalytic one-pot approach was demonstrated for the diversity-oriented synthesis of highly functionalized *N*-substituted benzo[*b*]azepines **87/91**, *N*-substituted 2-(buta-1,3-dienyl)phenylamines **88**, *N*-substituted 2-methyl-2*H*-quinolines **89** and *N*-substituted phenanthridines **90** from simple substrates via RCM/BIRO, intramolecular hydroamination and cascade intermolecular hydroamination/[4+2]-cycloaddition reactions. In addition, synthesis of heterocycles **92**, **93**, **94**, **95** and **97** from (Z)-aminodiene **88** were also demonstrated.

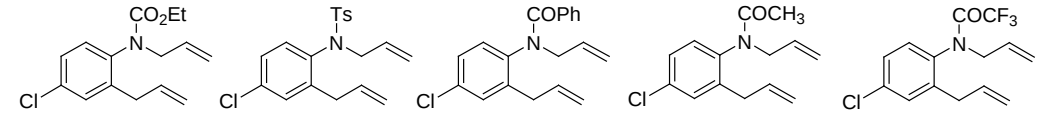
ANNEXURE-II: Synthesis of substituted heterodienes 86/heteroenynes 86jb-86kb.

Scheme A1: Synthesis of allyl-(2-allyl-4-chloro-phenyl)-amine **86a**.

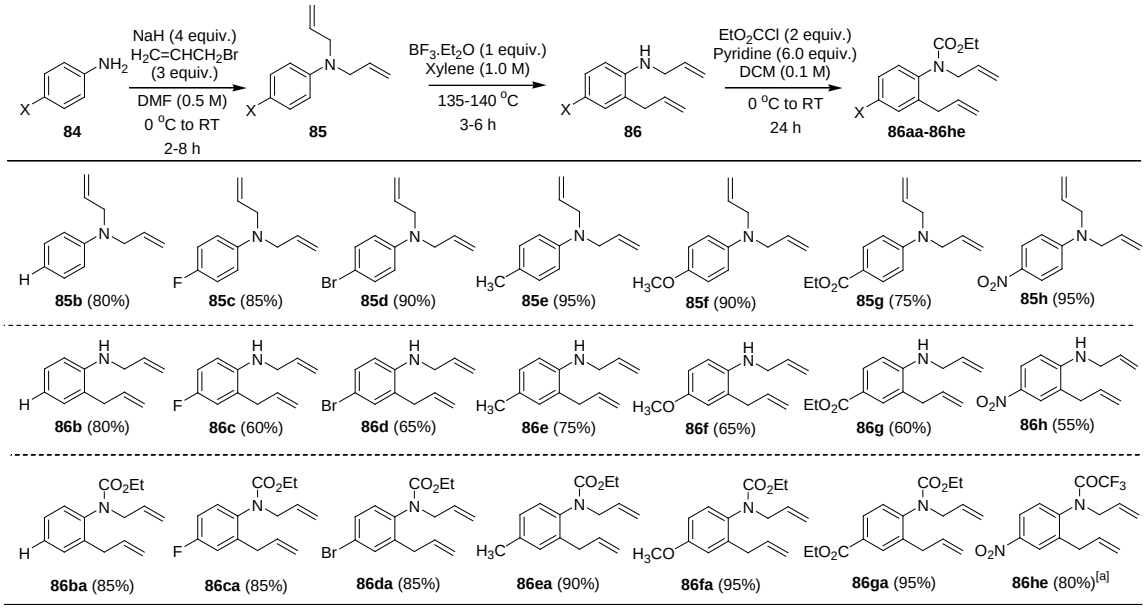


Scheme A2: Protection.



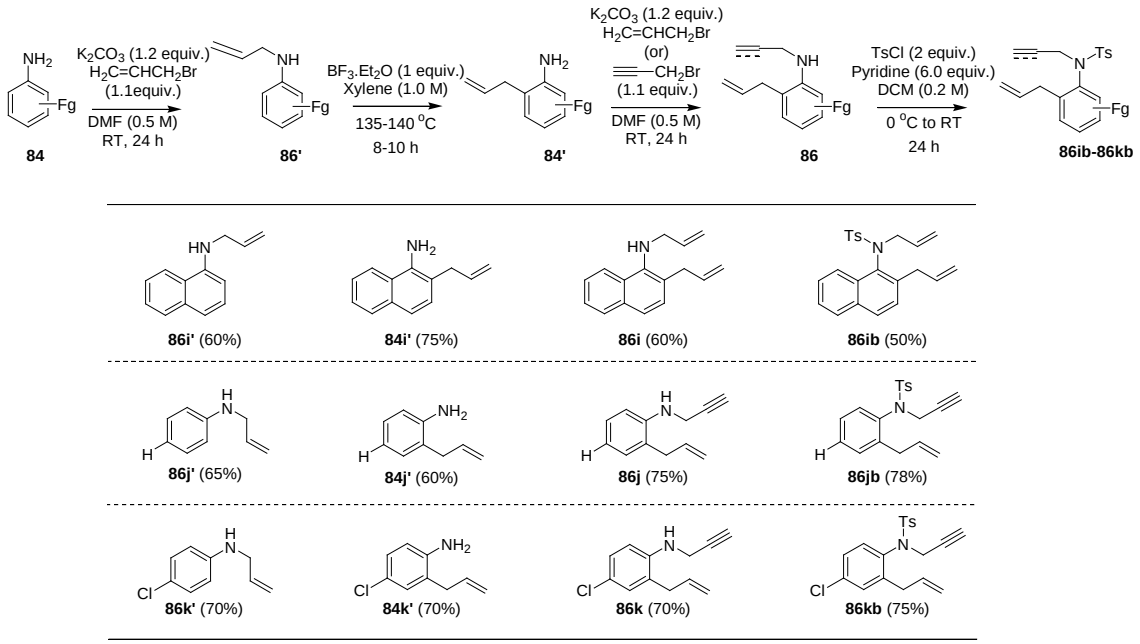


Scheme A3: Synthesis of 4-Substituted Ethyl allyl-(2-allyl-pphenyl)carbamates **86ba-86he**.



[a] Protection done with $(CF_3CO)_2O$

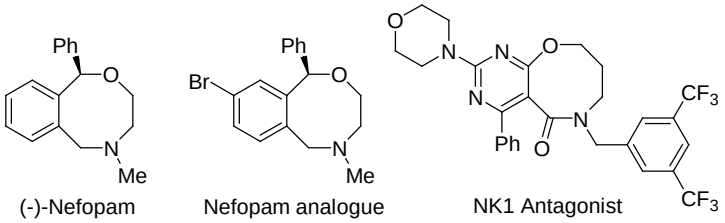
Scheme A4: Synthesis of Highly Substituted Benzenesulfonamides **86ib-86kb**.



7. HIGH-YIELDING SYNTHESIS OF NEFOPAM ANALOGUES (FUNCTIONALIZED BENZOXAZOCINES) BY SEQUENTIAL ONE-POT CASCADE OPERATIONS

7.1 INTRODUCTION

Drug-like highly substituted heterocycles are considerable importance in a variety of industries. As such, the development of new and more general green methods for their preparation is of significant interest.[40] Especially, oxygen- and nitrogen-containing heterocycles have attracted considerable attention as a result of their biological activity and their presence in a variety of natural and unnatural products.[40] Thus, the diversity-oriented synthesis of oxygen- and nitrogen-containing heterocycles represents an important task because of the widespread occurrence of such structural motifs and their use as building blocks in pharmaceuticals. For example functionalized benzoxazocines and pharmaceutically acceptable salts thereof, may be useful as analgesic agents and for the treatment of emesis, depression, posttraumatic stress disorders, attention deficit disorders, obsessive compulsive disorders, sexual dysfunction and centrally acting skeletal muscle relaxants (see eq 24).[40g-o] In this chapter, the organocatalytic approach was reported for the first time to the high yielding synthesis of functionalized benzoxazocines from three-step sequence via "combination of amine-/ruthenium-catalysis".

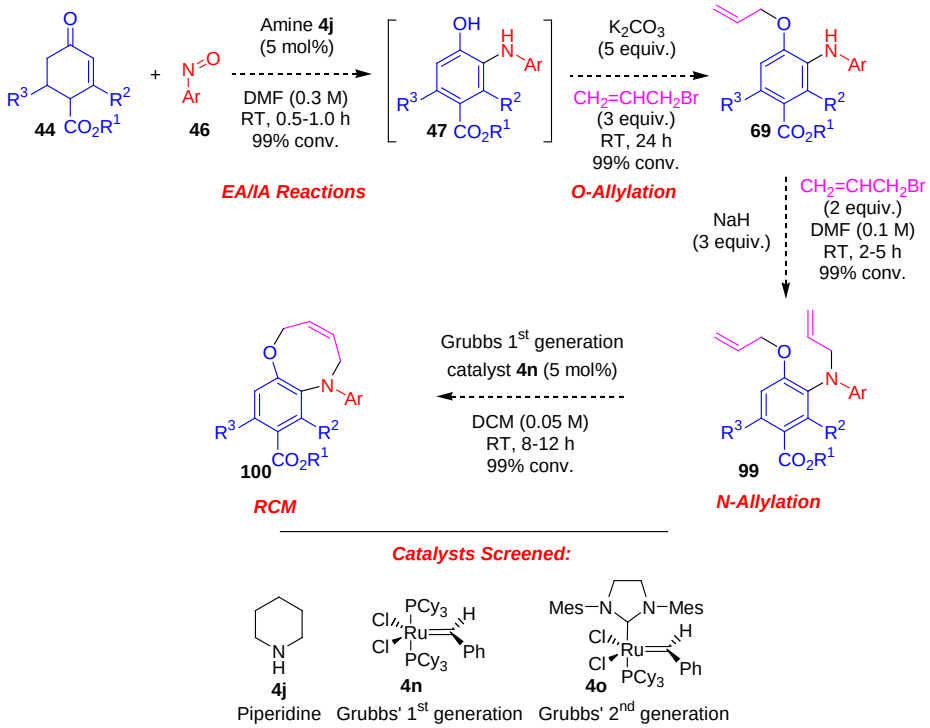


(24)

Recently olefin metathesis of hetero-dienes and enynes catalyzed by Grubbs' catalysts provided a general route to a variety of heterocycles in good yields.[32] The

advent of olefin metathesis technology triggered a burst of activity in the synthesis of a huge variety of differently substituted heterocycles. In a similar manner, reactions performed via combination of multi-component and multi-catalysis approach in one-pot generating desired targets efficiently in a single reaction vessel without the need to purify at each step.[2-18] A particularly attractive green cascade process occurs when two or more sequential reactions are mediated by a catalytic amount of simple amine. The catalytic ability of secondary amine (**4j**) to function as catalyst for cascade enamine amination/iso-aromatization (EA/IA) reactions has led to several examples where combinations of these transformations provide efficient new entries into useful *o*-hydroxydiarylamines **47** products (Scheme 13).[1d]

***Scheme 13*:** Synthesis of Nefopam Analogues via Three-step Sequence.



During our studies on amine-catalyzed cascade EA/IA reactions,[1d] it was noted that functionalized *o*-hydroxydiarylamines **47** can serve as suitable starting materials for the generation of Nefopam analogues via *O*-allylation, *N*-allylation and

ring closing metathesis (RCM) as key processes (Scheme 13). Unfortunately, olefin metathesis, however, is known to be incompatible with free amines due to catalyst inhibition by the basic nitrogen, although the ammonium salts have been shown to undergo metathesis.[41] Furthermore, there have been reports of ring-closing metathesis of secondary and tertiary free amines protonated *in situ* to form six-membered heterocycles, as well as a report of RCM of a tertiary free amine to form a seven-membered ring under acidic conditions, but they required a higher catalyst loading (20 mol%).[27]

A novel and green technology was developed for the three-step synthesis of highly substituted benzoxazocines using amine/potassium carbonate/sodium hydride/ruthenium-catalysis through cascade enamine amination/iso-aromatization/*O*-allylation (EA/IA/A), *N*-allylation and diene or enyne metathesis as key steps starting from commercially available Hagemann's esters **44**, nitrosobenzenes **46**, allyl bromide, secondary amine **4j** and Grubbs' 1st and 2nd generation ruthenium catalysts **4n/4o**, an approach we call "multi-catalysis approach to heterocycles" (Scheme 13). For the first time the RCM reaction of olefins containing free amines without *in situ* salt formation has been presented in this chapter.

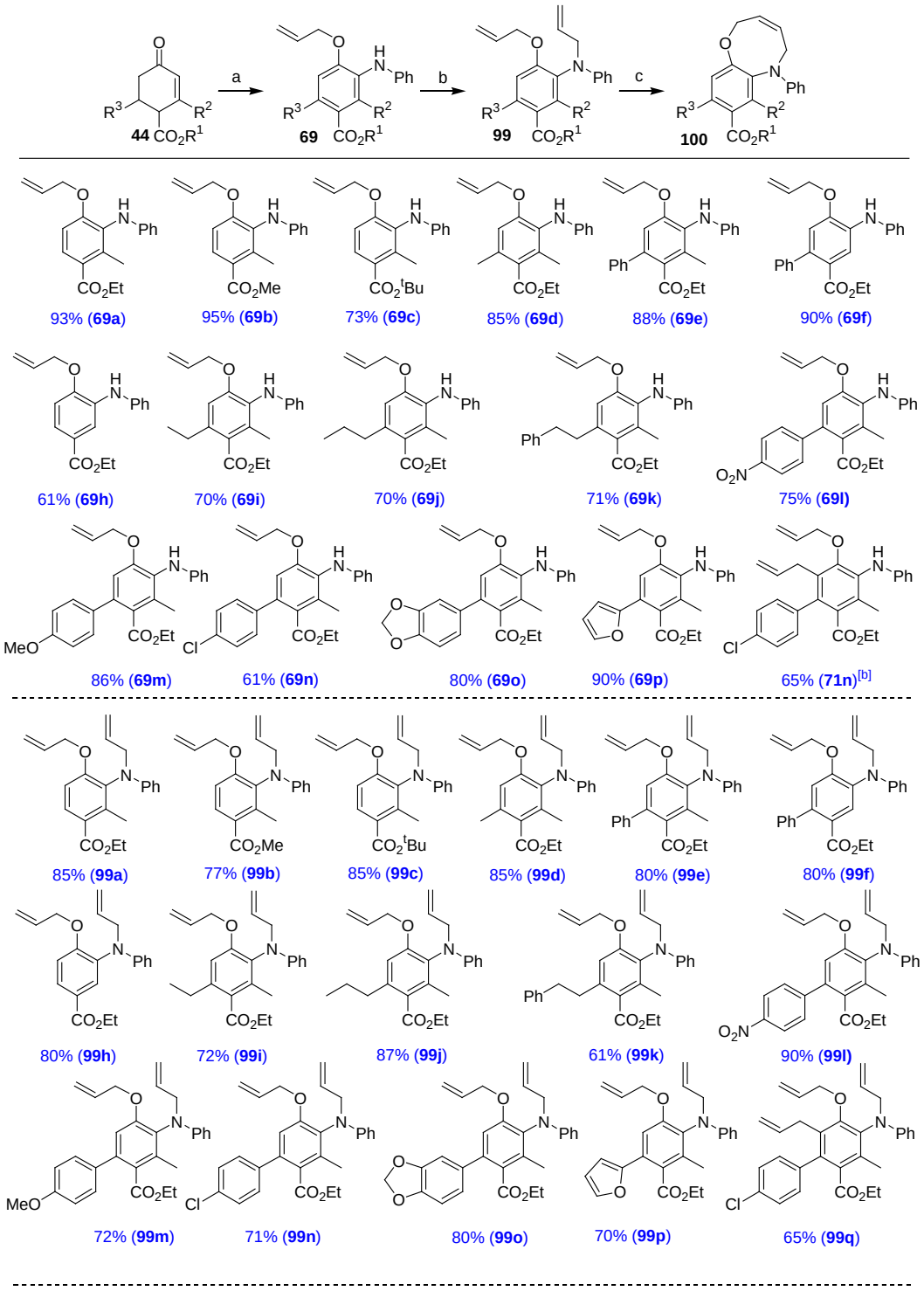
7.2 RESULTS AND DISCUSSION

Studies were intiated on the combination of a cascade EA/IA reaction, *O*- and *N*-allylations and diene metathesis as key steps for the synthesis of highly substituted 5,6-dihydro-*2H*-benzo[*b*][1,4]oxazocine **100a** starting from Hagemann's ester **44a** and nitrosobenzene **46** as shown in Table 10. Piperidine/K_2CO_3-catalyzed cascade EA/IA/A reaction of **44a**, **46** and allyl bromide furnished the monoene amine **69a** in 93% yield. But the same reaction under pyrrolidine/K_2CO_3-catalysis furnished the monoene amine **69a** in 75% yield (result not shown in Table 10). In a similar manner, cascade EA/IA/A reaction of **44a**, **46** and allyl bromide under the combination of other amines like glycine, proline, morpholine or benzylamine with

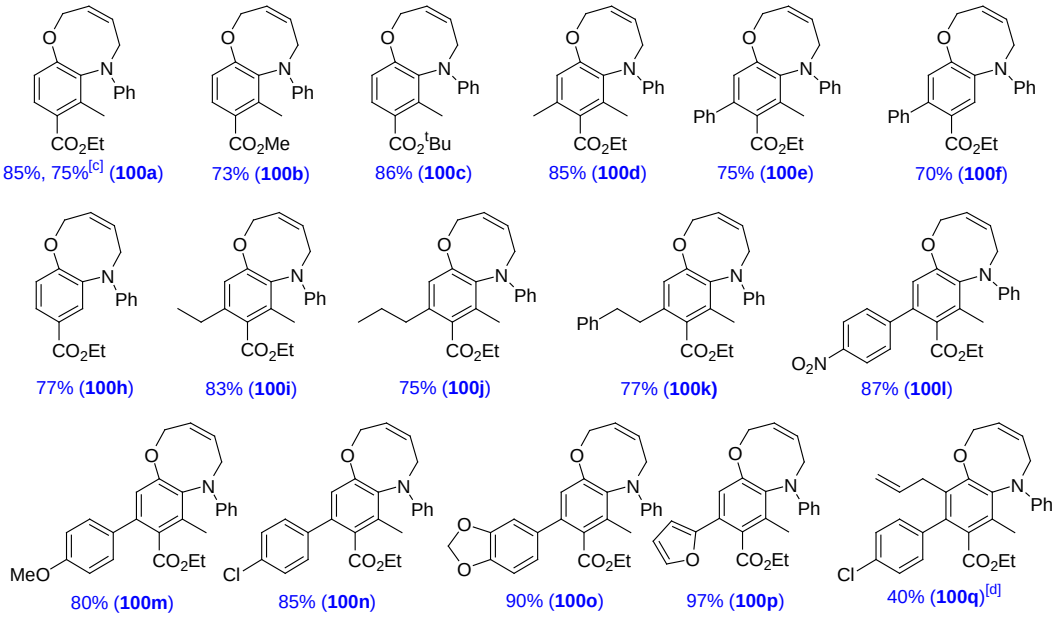
K_2CO_3 is not superior compared to piperidine/K_2CO_3-catalysis (results not shown in Table 10). Further NaH-promoted *N*-allylation of cascade EA/IA/A product **69a** furnished the diene amine **99a** in 85% yield. Interestingly, RCM reaction of free diene amine **99a** using Grubbs' 1st generation catalyst **4n** in CH_2Cl_2 at RT for 8 h furnished the highly functionalized 5,6-dihydro-*2H*-benzo[*b*][1,4]oxazocine **100a** in 85% yield; but the same reaction with Grubbs' 2nd generation catalyst **4o** furnished the **100a** in 75% yield (Table 10). Technical advantage of these reactions is that the ruthenium-catalysis is performed on free diene amines without the need for *in situ* salt formation. With the optimized reaction conditions in hand, the scope of the three-step synthesis of **100** was investigated with various Hagemann's esters **44a-f**, **44h-p** and nitrosobenzene **46**. As summarized in Table 10, series of Hagemann's esters **44a-f** and **44h-p** were transferred into highly substituted 5,6-dihydro-*2H*-benzo[*b*][1,4]oxazocines **100a-f** and **100h-p** in 33 to 67% overall yields via piperidine-/ruthenium-catalysis from three-step sequence. The ruthenium-catalyst **4n** was non-recyclable in these reactions, because reaction mixture was completely homogenous in dichloromethane solution.

Interestingly, monoene amines **69** can be synthesized directly from two equivalents of ethyl acetoacetate and aldehyde under piperidine-catalysis followed by *in situ* reaction with nitrosobenzene **46** and allyl bromide to furnish **69** with moderate to good yields. So, for the synthesis of Hagemann's esters **44a-f** and **44h-p** library, the procedure involves either piperidine-catalyzed condensation of ethyl acetoacetate with different aldehydes in EtOH at 80 °C for 5-8 h or *t*BuOK-catalyzed condensation of ethyl acetoacetate with different aldehydes in *t*BuOH at 80 °C for 24-36 h through cascade Knoevenagel/Michael/aldol condensation/decarboxylation reactions.[31] For example, monoene amine **69n** furnished with moderate yield (61%) from ethyl acetoacetate, 4-chlorobenzaldehyde, nitrosobenzene **46** and allyl bromide under piperidine- and K_2CO_3-catalysis through cascade Knoevenagel/Michael/aldol condensation/decarboxylation and cascade

Table 10: Three-step Synthesis of Nefopam analogues via Combination of Amine-/Potassium carbonate-/Sodium hydride-/Ruthenium-catalysis.[a]



Continuation of Table 10.



[a] Reagents and conditions: (a) Ph-N=O (0.5 equiv.), **4j** (5 mol%), DMF (0.3 M), RT, 1 h; K_2CO_3 (5 equiv.), $H_2C{=}CHCH_2Br$ (3 equiv.), RT, 24 h; (b) NaH (3 equiv.), $H_2C{=}CHCH_2Br$ (2 equiv.), DMF (0.1 M), RT, 2-5 h; (c) CH_2Cl_2 (0.05 M), **4n** (5 mol%), RT, 8-12 h. [b] Yield representing from **69n** via two steps. [c] CH_2Cl_2 (0.05 M), 4o (5 mol%), RT, 4 h. [d] Highly substituted benzo[*b*]oxepine **72q** furnished as byproduct in 60% yield (see Ref. 45).

enamine amination/isoaromatization/*O*-allylation reactions in one-pot (see Table 10). Further, it was interesting to investigate the RCM reaction on triene amine **99q** to test the regioselectivity. Compound **99q** was prepared from a Claisen rearrangement of **69n** in DMF at 180 °C for 18 h followed by *O*- and *N*-allylation with allyl bromide under NaH-catalysis in one-pot to furnish the triene amine **99q** in good yield, which on further RCM reaction under **4n**-catalysis furnished the benzo[*b*]oxepine **72q** with 60% yield[45] and benzoxazocine **100q** with 40% yield as shown in Table 10. Structure and regiochemistry of oxazocines **100a-f** and **100h-p** was confirmed by NMR analysis and also finally confirmed by single crystal X-ray

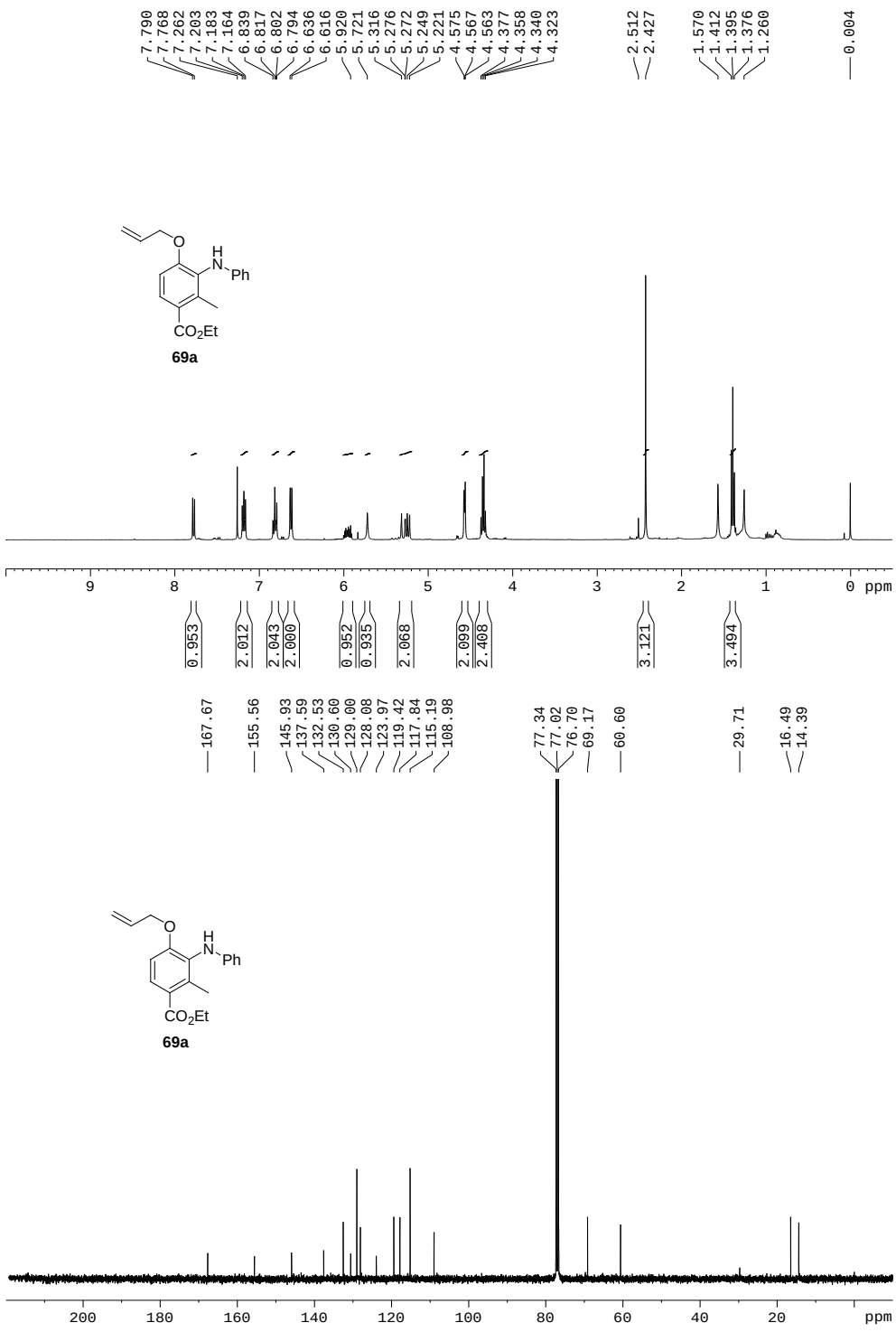


Figure-21: ^{1}H NMR and ^{13}C NMR Spectra of product **69a.**

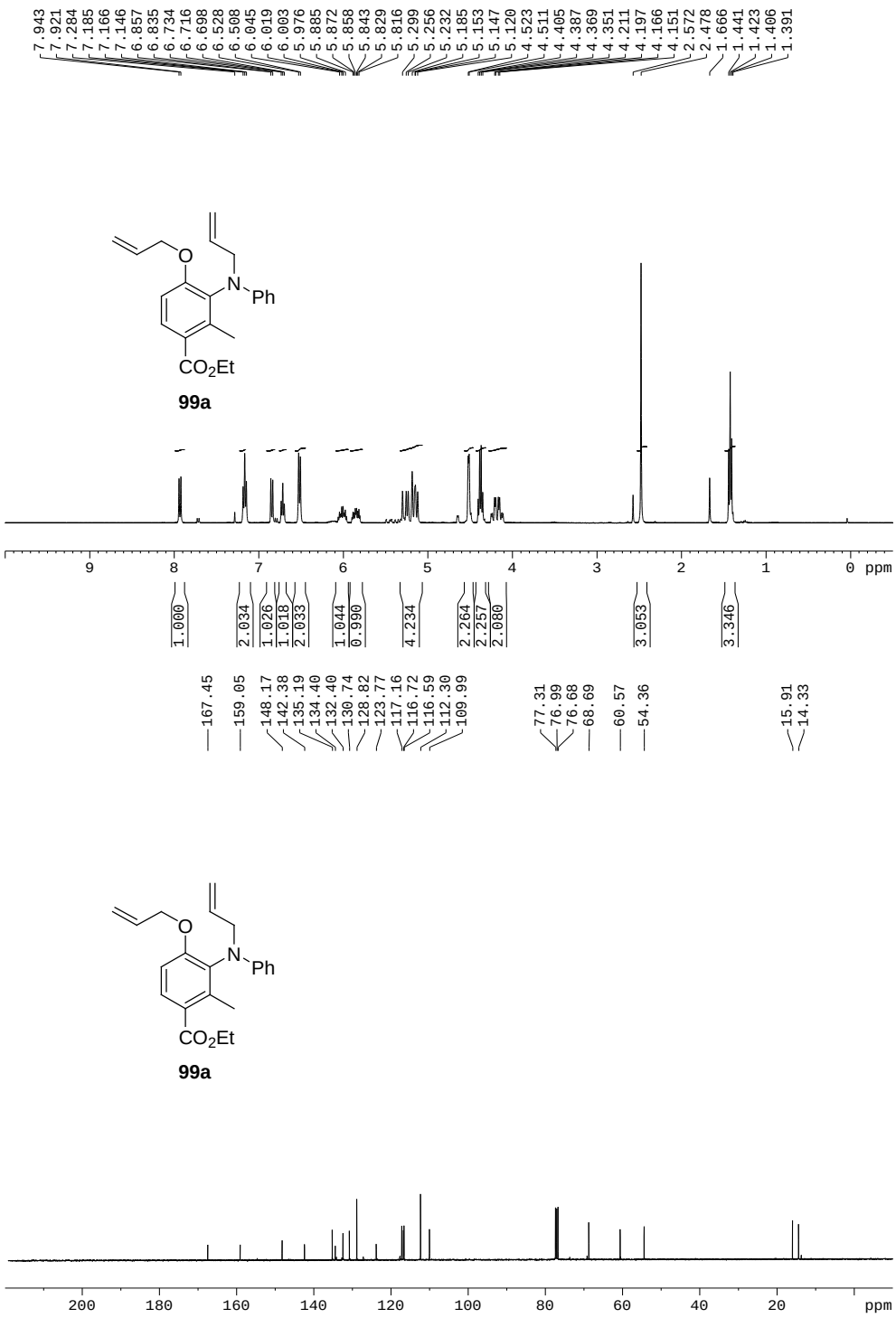


Figure-22: ^{1}H NMR and ^{13}C NMR Spectra of product **99a.**

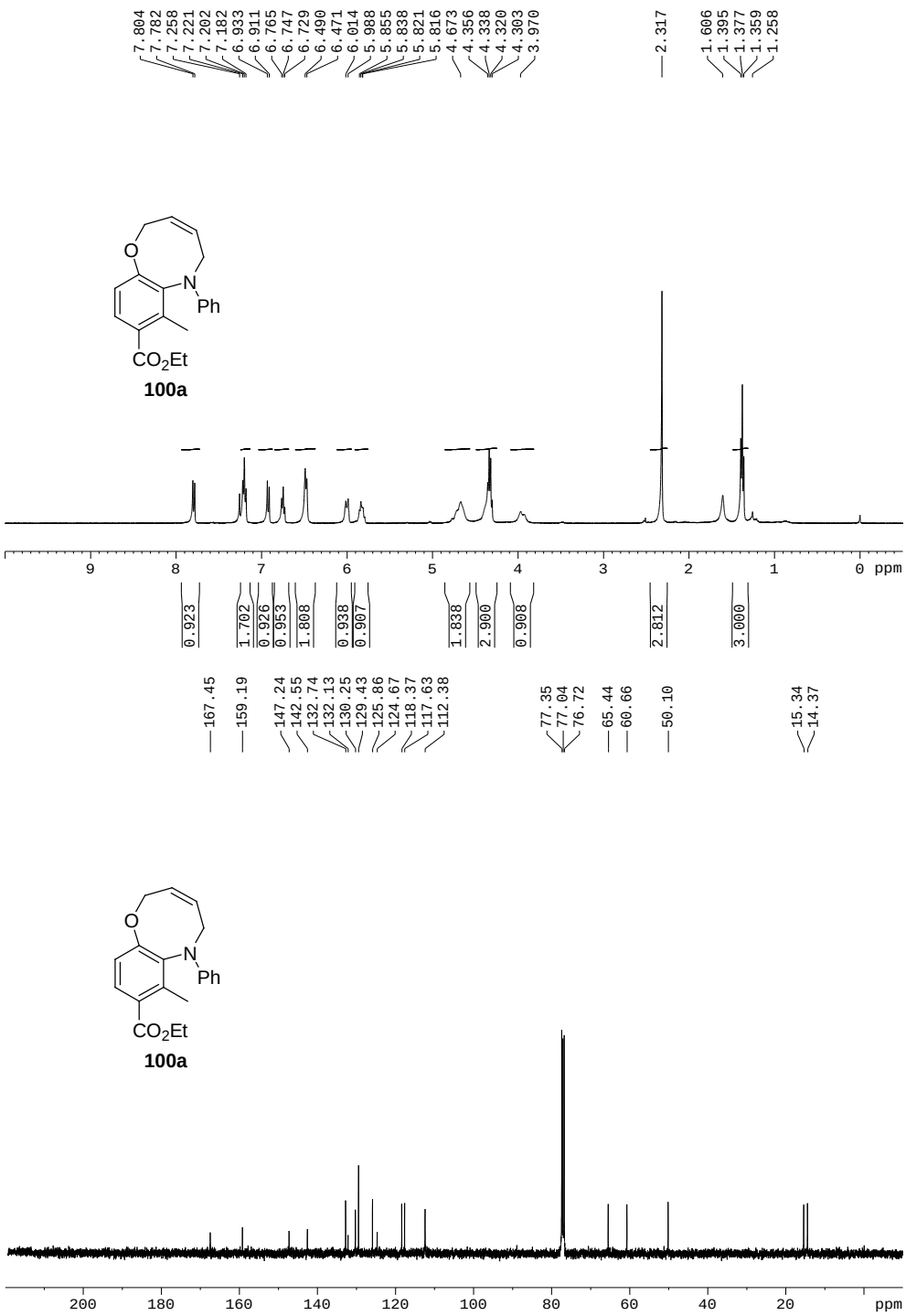


Figure-23: ^{1}H NMR and ^{13}C NMR Spectra of product **100a.**

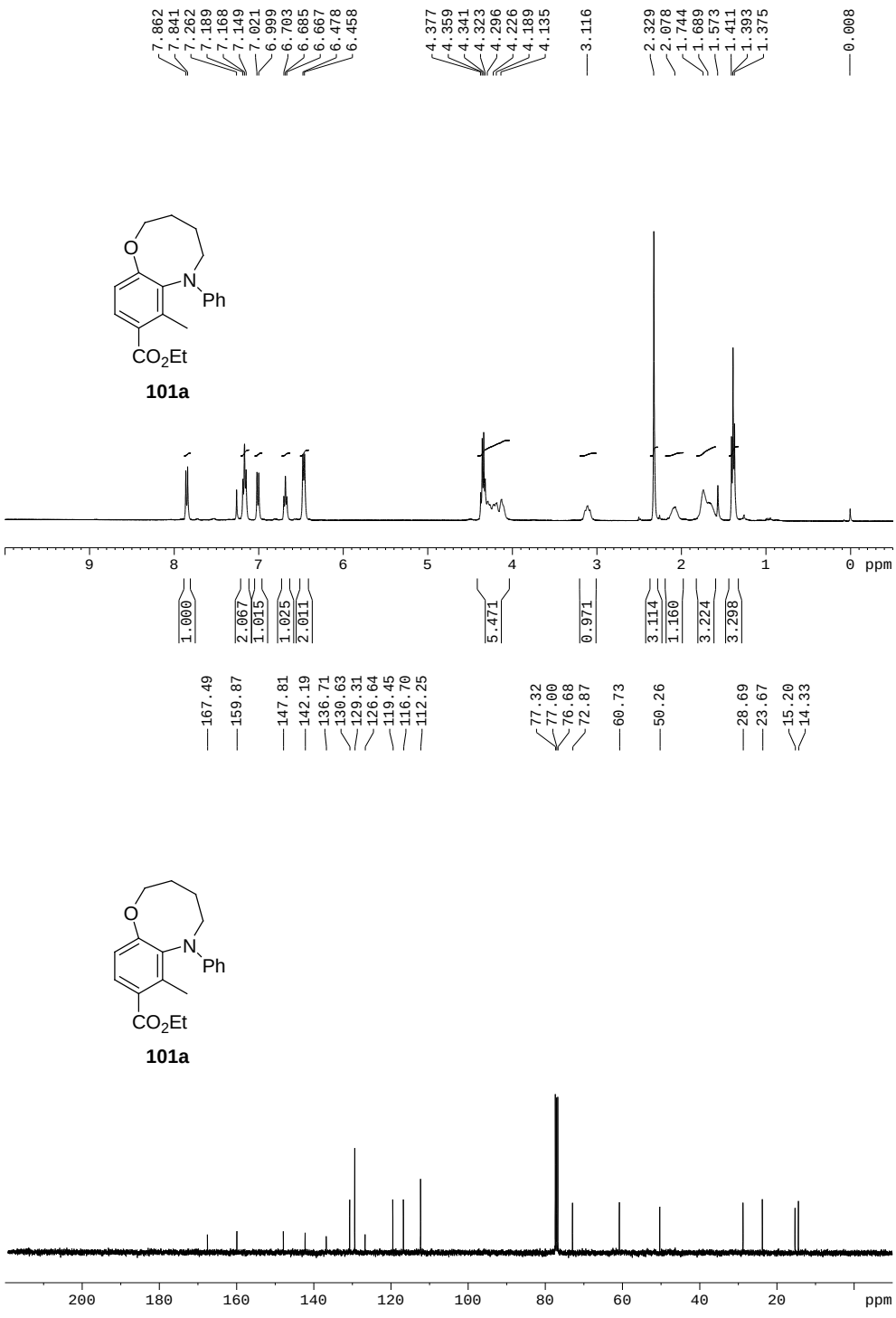
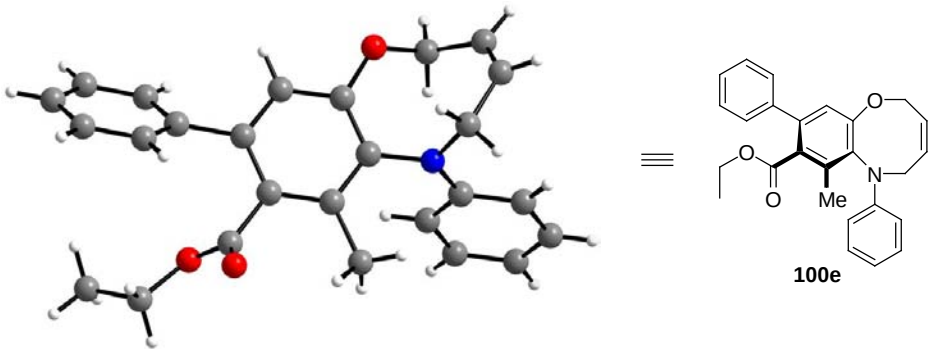


Figure-24: ^{1}H NMR and ^{13}C NMR Spectra of product **101a.**

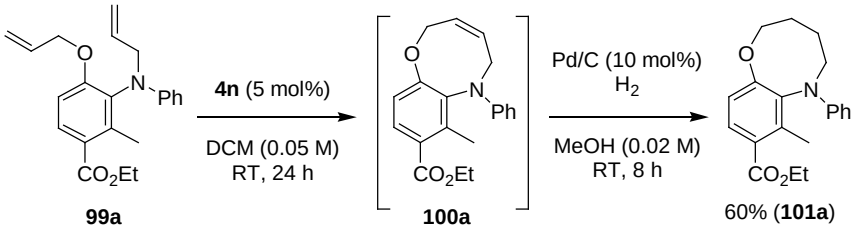
structure analysis on **100e** (Scheme 14).[42] Functionalized oxazocines **100** have shown many pharmaceutical applications like noradrenaline, serotonin reuptake inhibitors for treatment of pain and emesis, neurokinin receptor antagonists, anti-inflammatory activity and anti-depressive activity.[40g-o] This three-step synthetic strategy will have a great impact on the synthesis of diversity-oriented library of substituted oxazocines to find suitable drug molecules.

***Scheme 14*:** Crystal structure of 7-methyl-6,9-diphenyl-5,6-dihydro-2*H*-benzo[*b*][1,4]oxazocine-8-carboxylic acid ethyl ester (**100e**).



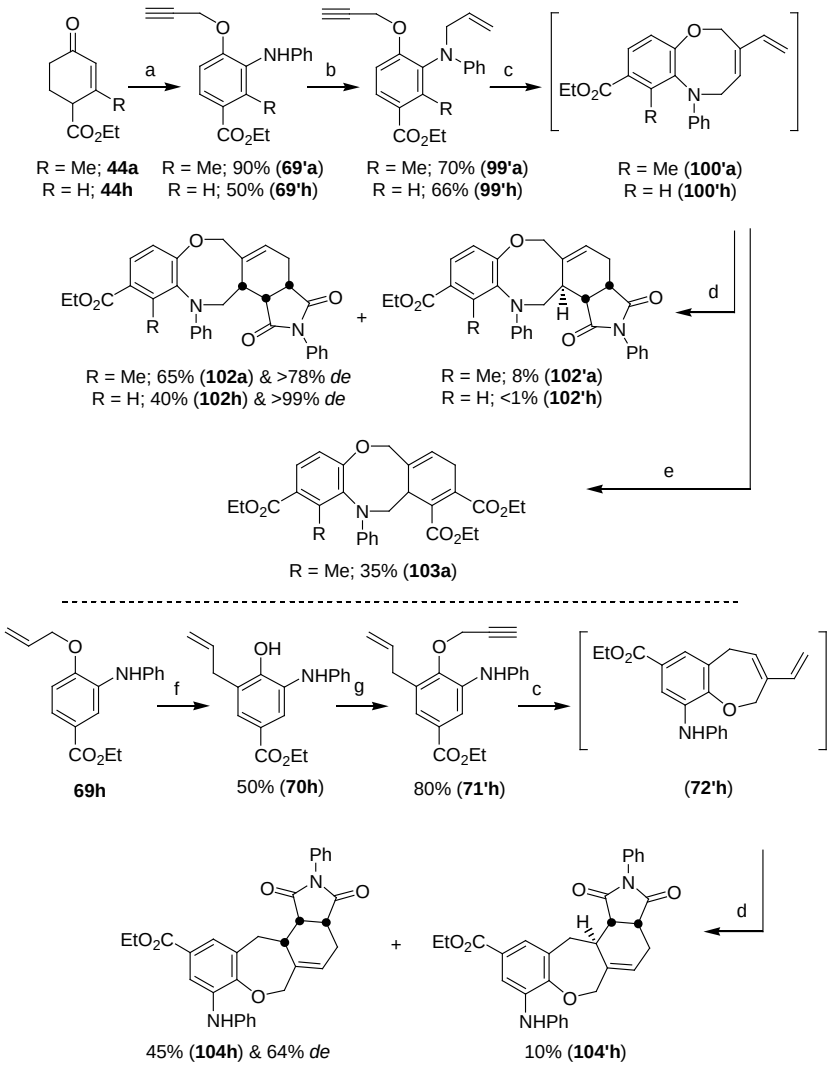
With the success of three-step synthesis of highly functionalized 5,6-dihydro-*2H*-benzo[*b*][1,4]oxazocines **100**, it was extended to the generation of Nefopam analogue of 3,4,5,6-tetrahydro-2*H*-benzo[*b*][1,4]oxazocines **101** through sequential

Scheme 15: Sequential Combination of Ru- and Pd-catalysis in One-Pot for Synthesis of 3,4,5,6-tetrahydro-2*H*-benzo[*b*][1,4]oxazocines **101**.



one-pot combination of [Ru]-mediated ring-closing metathesis and Pd/C-mediated hydrogenation of **99a**. The results in Scheme 15 demonstrate the broad scope of this novel methodology covering a sequential combination of Ru- and Pd-catalysis to take place in one-pot with good yield.[43]

Scheme 16: General Application of Organo-RCM Chemistry in Heterocycles Synthesis.[a]



For reagents and conditions, see: [a] Reagents and conditions: (a) Ph-N=O (0.5 equiv.), **4j** (5 mol%), DMF (0.5 M), RT, 1 h; K_2CO_3 (3 equiv.), $HC{\equiv}CCH_2Br$ (2

equiv.), RT, 24 h; (b) NaH (3 equiv.), H_2C=$CHCH_2Br$ (2 equiv.), DMF (0.5 M), 0 °C → RT, 3-6 h; (c) CH_2Cl_2 (0.05 M), **4n** (5 mol%), RT, 12 h; (d) N-Phenylmaleimide (1.2 equiv.), $C_6H_5CH_3$ (0.16 M), 110-120 °C, 21 h; (e) Diethyl acetylenedicarboxylate (1.2 equiv), $C_6H_5CH_3$ (0.16 M), 120-140 °C, 21 h; (f) DMF (1.0 M), 190 °C, 6-8 h; (g) K_2CO_3 (2 equiv.), HC≡CCH_2Br (1.5 equiv.), DMF (0.5 M), RT, 24 h.

After successful demonstration of high yielding three-step synthesis for the benzo[*b*][1,4]oxazocines **100** and **101**, the three-step synthesis was extended the construction of more functionalized molecules via a combination of cascade enamine amination/iso-aromatization/*O*-propargylation (EA/IA/P), *N*-allylation, cascade RCM/DA reactions (see Scheme 16). Hagemann's ester **44a** was converted into highly functionalized tetra-cyclic *endo*-product **102a** with >78% *de* in a stereoselective manner with 46% overall yield through a sequence of amine/K_2CO_3-catalyzed cascade EA/IA/P, NaH-promoted *N*-allylation, ruthenium-promoted enyne RCM followed by heat-promoted Diels-Alder (DA) reaction with 1-phenyl-pyrrole-2,5-dione in one-pot as shown in Scheme 16. Generality of the amine-/K_2CO_3-/NaH-/Ru-catalyzed stereoselective sequential one-pot cascade EA/IA/P, A and RCM/DA reactions was further confirmed by two more examples using different Hagemann's ester **44h** and dienophile to furnish the expected highly functionalized compound **102h** in 13.2% overall yield with >99% *de* and compound **103a** in 22% overall yield, as shown in Scheme 16. The structure and stereochemistry of oxazocines **102-103** was confirmed by NMR analysis and also finally confirmed by X-ray structure analysis on **102a** (Scheme 17).[44] For the pharmaceutical applications, diversity-oriented library of tetra-cyclic compounds **102** could be generated by using our three-step sequence reactions.

With the success of sequential three-step synthesis of highly functionalized heterocycles **102-103** based on the benzo[*b*][1,4]oxazocines **100** platform, it was further explored into the generation of highly functionalized heterocycles **104h** and **104'h**

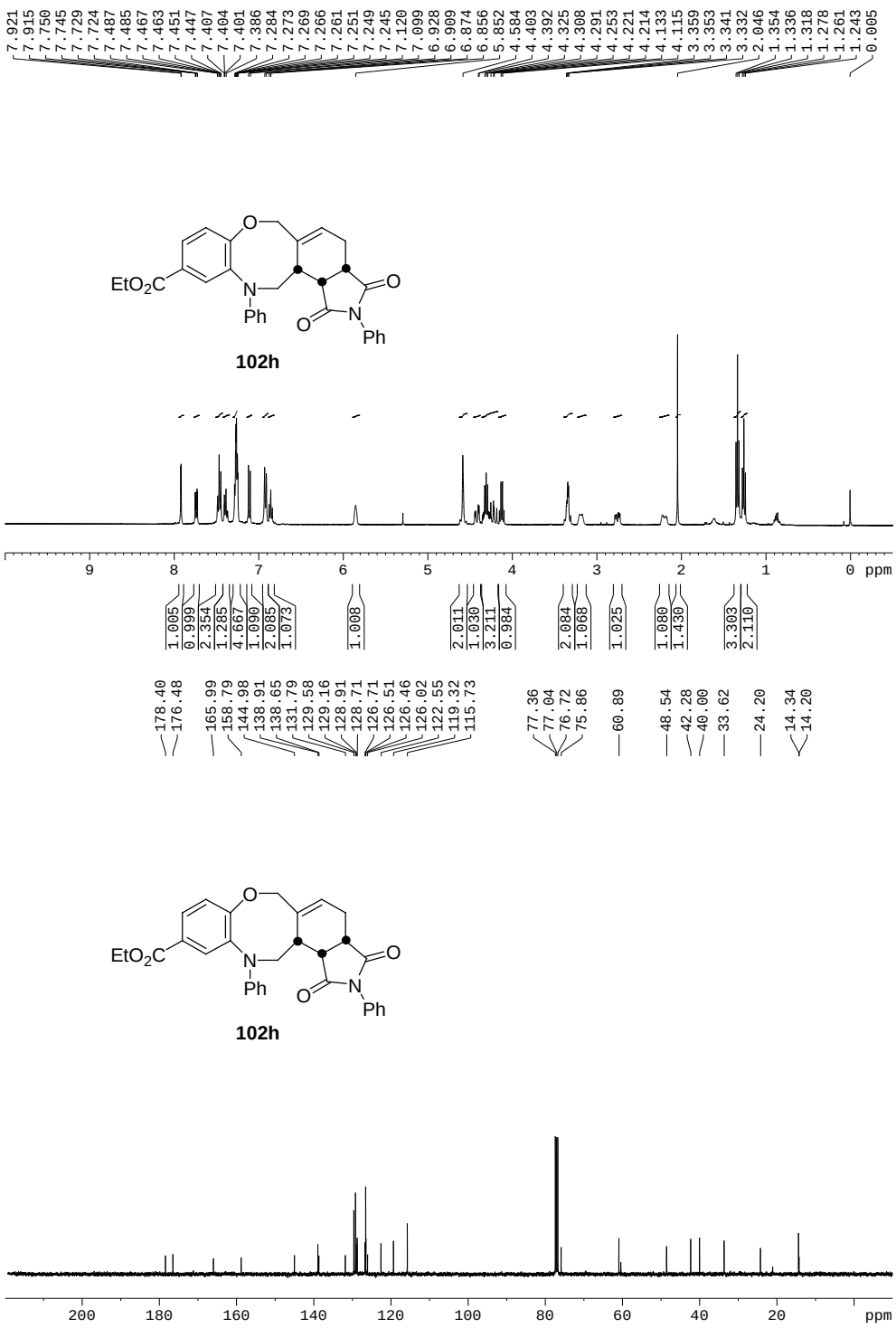


Figure-25: ^{1}H NMR and ^{13}C NMR Spectra of product **102h.**

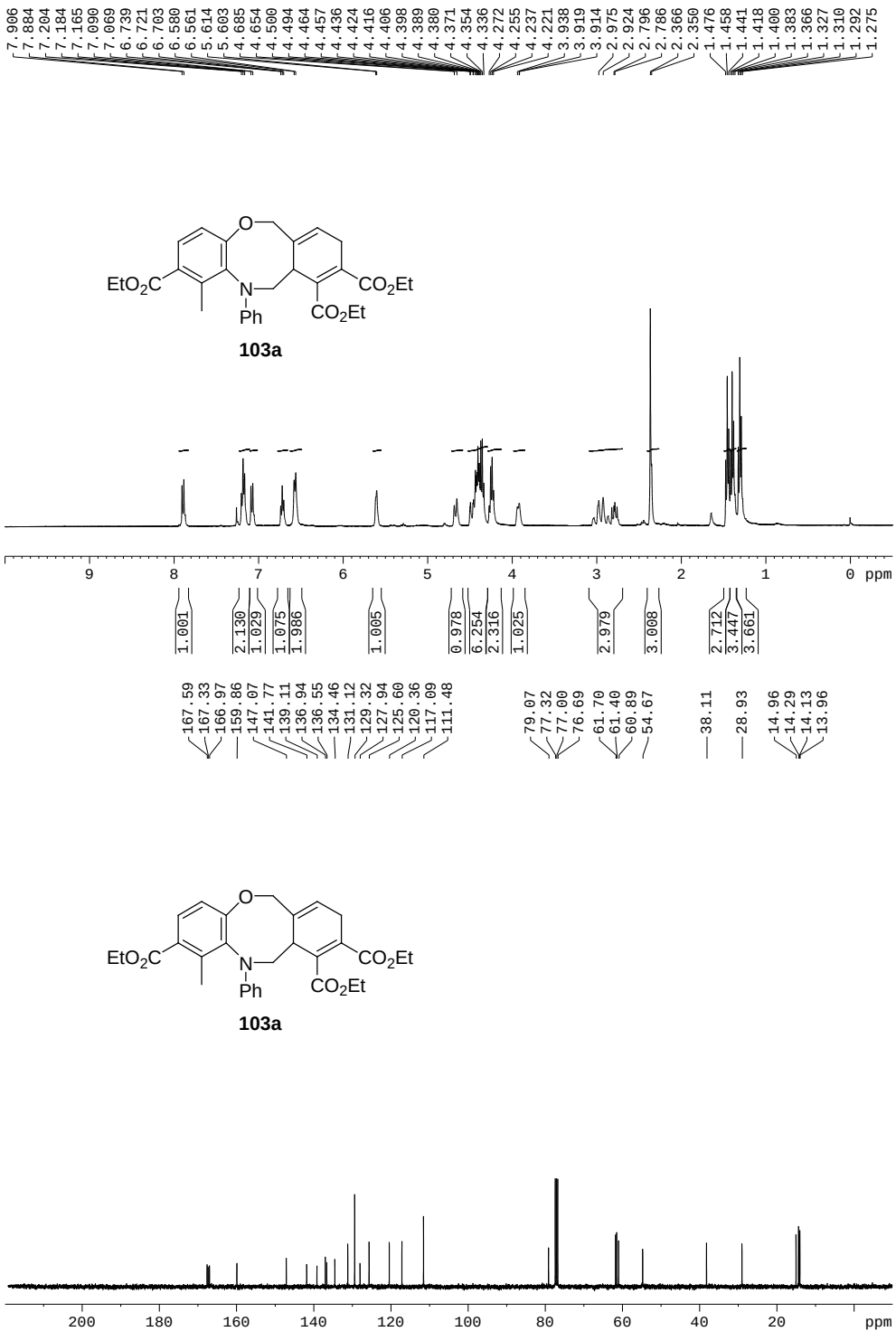
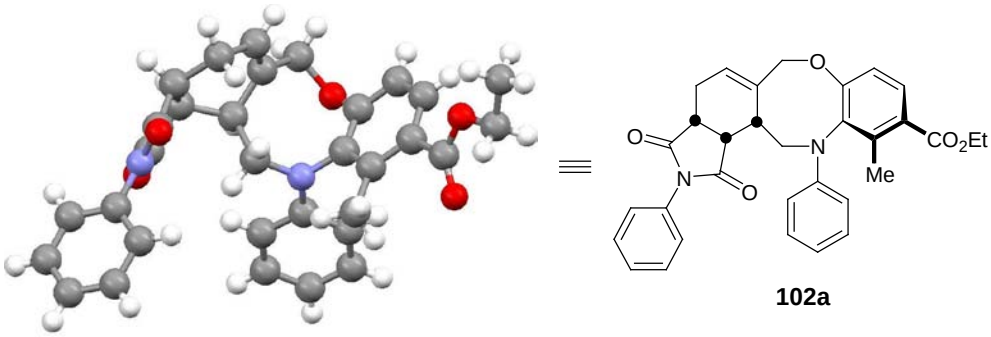


Figure-26: ^{1}H NMR and ^{13}C NMR Spectra of product **103a.**

based on 3-vinyl-2,5-dihydro-benzo[*b*]oxepines **72'h** through a combination of cascade EA/IA/A, Claisen rearrangement, *O*-propargylation, enyne RCM followed by DA reaction. The results in Scheme 16 demonstrate the broad scope of this novel methodology covering a structurally diverse group of Hagemann's esters **44** and nitrosobenzene **46**.

Scheme 17: X-ray crystal structure of **102a**.



102a

Claisen rearrangement of **69h** in DMF at 190 °C for 6-8 h furnished the expected phenol **70h** in 50% yield, which on *O*-propargylation with propargyl bromide and K_2CO_3 furnished the enyne amine **71'h** in 80% yield. Direct treatment of enyne amine **71'h** with Grubbs' 1st generation catalyst **4n** generated the expected highly functionalized 3-vinyl-2,5-dihydro-benzo[*b*]oxepine **72'h** in good conversion as shown in Scheme 16, which on *in situ* treatment with 1-phenyl-pyrrole-2,5-dione in toluene at 110-120 °C for 21 h furnished the highly functionalized tetra-cyclic *endo*-product **104h** with 64% *de* in stereoselective manner with 22% overall yield.

7.3 CONCLUSION

In this chapter, the three-step sequential multi-catalysis chemistry was developed for the synthesis of highly substituted drug-like heterocycles **100**, **101**, **102**, **103**, and **104** from simple starting materials *via* EA/IA/A, EA/IA/P, *C*,*N*,*O*-allylations, Claisen rearrangement, diene RCM, enyne RCM and Diels-Alder reactions. The multi-catalysis

strategy proceeds in good yields with high selectivity using piperidine/K_2CO_3/NaH/ruthenium-complex as the catalysts.

8. EXPERIMENTAL SECTION

1: **General Experimental Procedures for the Synthesis of Hagemann's Esters**: Hagemann's esters **44a-e** and **44i-p** were prepared from alkyl acetoacetates and aldehydes with high yields in one-step according to literature procedures of Sangho Koo method[46a] and Bhaduri method[46b] with minor modifications.[1d] Hagemann's ester **44f** was synthesized from two-steps as described below (see Scheme E1).[47] Hagemann's ester **44g** was prepared from trimethyl-(1-methylene-allyloxy)-silane and propynoic acid methyl ester with high yield in two-steps according to literature procedure (see Scheme E2).[47c]

1A: *t*BuOK-Catalyzed Cascade Knoevenagel/Michael/Aldol condensation/Decarboxylation Reactions: To a stirred solution of β-keto esters **43** (2 equiv.) and aldehydes **2** or **7** (1 equiv.) in *t*BuOH (1 M) was added a catalytic amount of *t*BuOK (0.10 equiv.) at 0 °C. The reaction mixture was stirred at that temperature for 1 h, and 0.25 equiv. of *t*BuOK was added again. The mixture was then heated at 70 ^{o}C for 32-40 h. Upon cooling to RT, the mixture was quenched with 1 M HCl (10 mL) solution, diluted with CH_2Cl_2 (50 mL), washed with 1 M NaOH solution (20 mL) and brine (20 mL). The separated organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. Pure cascade products **44a-e** and **44i-p** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

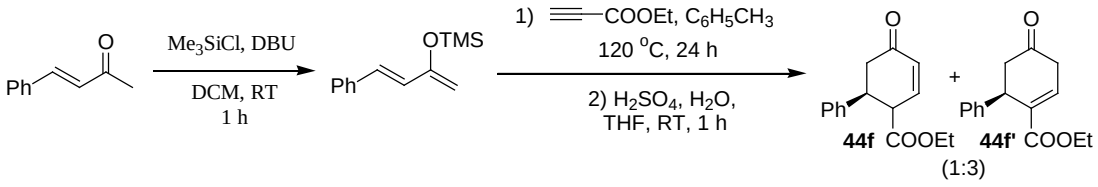
1B: Piperidine-Catalyzed Cascade Knoevenagel/Michael/Aldol condensation/Decarboxylation Reactions: To a stirred solution of β-keto esters **43** (4 mmol) and araomatic aldehydes **7** (2 mmol) in EtOH (4 mL) was added a catalytic amount of piperidine (0.7 mmol, 35 mol%) and the reaction mixture was stirred at 80 °C for 3 h. Upon cooling to RT, the mixture was quenched with aqueous NH_4Cl solution, diluted with diethyl ether (50 mL), washed with brine (10 mL). The separated organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Pure cascade products **44e** and **44l-p** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

1C: Synthesis of Hagemann's Ester 44f: Hagemann's ester **44f** was prepared from benzylidene acetone with high yield in two-steps according to literature procedures.[47]

First Step: A mixture of benzylidene acetone (5.0 mmol), chlorotrimethylsilane (6.0 mmol) and DBU (7.0 mmol) in CH_2Cl_2 (5.0 mL) was stirred at RT for 1 h. Then the mixture was diluted with pentane (10.0 mL) and washed successively with dilute HCl and $NaHCO_3$ solutions and dried over Na_2SO_4; evaporation of the solvent furnished 4-phenyl-2-trimethyl-siloxybuta-1,3-diene (1.03 gm, 95%).

Second Step: A mixture of 4-phenyl-2-trimethyl-siloxybuta-1,3-diene (1.0 gm, 4.58 mmol) and ethyl propiolate (0.45 gm, 4.58 mmol) in anhydrous toluene (9.0 mL) was heated at 120 °C under N_2 in a sealed glass tube for 24 h. The toluene was evaporated by reduced pressure and the residue was dissolved in a mixture of THF (4.0 mL), H_2O (2.6 mL) and H_2SO_4 (0.6 mL); mixture was stirred for 1 h at RT. Reaction mixture was diluted with water (10.0 mL) and the product was isolated by extraction with ether (2 x 10.0 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. Pure Hagemann's ester **44f** was obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate) in a mixture of two isomers **44f**, **44f'** (1:3) with 60% yield and displayed similar spectroscopic properties to the literature data.[47]

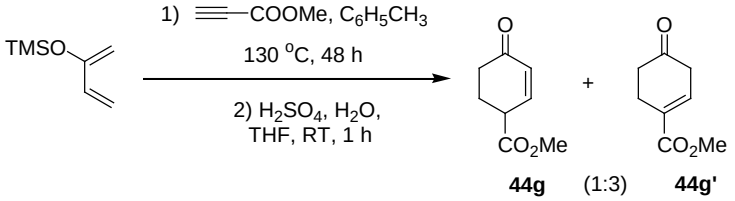
***Scheme E1*:** Synthesis of Hagemann's ester **44f**



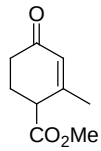
1D: Synthesis of Hagemann's Ester 44g: A mixture of trimethyl-(1-methylene-allyloxy)-silane (0.651 gm, 4.58 mmol) and methyl propiolate (0.385 gm, 4.58 mmol) in anhydrous toluene (9.0 mL) was heated at 130 °C under N_2 in a sealed glass tube for 48 h. The toluene was evaporated by reduced pressure and the residue was dissolved in a

mixture of THF (4.0 mL), H_2O (2.6 mL) and H_2SO_4 (0.6 mL); mixture was stirred for 1 h at RT. Reaction mixture was diluted with water (10.0 mL) and the product was isolated by extraction with ether (2 x 10.0 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. Pure Hagemann's ester **44g** was obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate) in a mixture of two isomers **44g**, **44g'** (1:3) with 56% yield and displayed similar spectroscopic properties to the literature data.[47c]

Scheme E2: Synthesis of Hagemann's Ester **44g**

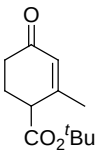


2-Methyl-4-oxo-cyclohex-2-enecarboxylic acid methyl ester (44b): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2955, 1734 (O-C=O), 1670 (C=O), 1251, 1199, 1033, 779 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.96 (1H, s, olefinic-*H*), 3.76 (3H, s, OC*H*$_3$), 3.30 (1H, t, *J* = 4.8 Hz), 2.55 (1H, m), 2.38 (2H, m), 2.23 (1H, m), 2.03 (3H, s, olefinic-C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 198.1 (C, C=O), 171.9 (C, O-C=O), 156.8 (C), 128.4 (CH), 52.4 (CH_3, O*CH*$_3$), 45.8 (CH), 34.2 (CH_2), 26.0 (CH_2), 23.4 (CH_3, olefinic-*CH*$_3$).



44b

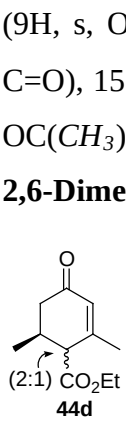
2-Methyl-4-oxo-cyclohex-2-enecarboxylic acid *tert*-butyl ester (44c): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2978, 1718 (O-C=O), 1676 (C=O), 1454, 1369, 1251, 1151, 844 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.94 (1H, s, olefinic-*H*), 3.16 (1H, t, *J* = 5.2 Hz), 2.56 (1H, m), 2.30 (2H, m), 2.17 (1H, m), 2.02 (3H, s, olefinic-C*H*$_3$), 1.43



44c

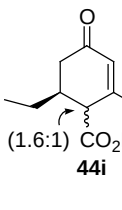
(9H, s, OC(CH_3)$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 198.5 (C, C=O), 170.7 (C, O-C=O), 157.6 (C), 128.1 (CH), 81.9 (C, O*C*(CH_3)$_3$), 47.1 (CH), 34.3 (CH_2), 28.0 (CH_3, OC(CH_3)$_3$), 26.2 (CH_2), 23.5 (CH_3, olefinic-CH_3).

2,6-Dimethyl-4-oxo-cyclohex-2-enecarboxylic acid ethyl ester (44d): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow oil. IR (neat): ν_{max} 2962, 1730 (O-C=O), 1668 (C=O), 1192, 1028, 910, 854, 756 cm^{-1}; ^{1}H NMR ($CDCl_3$, 2.0:1 ratio of diastereomers, major isomer) δ 5.97 (1H, s, olefinic-*H*), 4.24 (2H, q, *J* = 7.2 Hz, OCH_2CH$_3$), 3.03 (1H, d, *J* = 7.2 Hz), 2.59 (2H, m), 2.12 (1H, m), 1.97 (3H, s, olefinic-CH_3), 1.31 (3H, t, *J* = 7.6 Hz, OCH$_2$CH_3), 1.10 (3H, d, *J* = 6.0 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135, 2.0:1 ratio of diastereomers, major isomer) δ 197.9 (C, C=O), 171.8 (C, O-C=O), 155.8 (C), 127.9 (CH), 61.1 (CH_2, O*C*H$_2$CH$_3$), 54.4 (CH), 43.0 (CH_2), 32.7 (CH), 22.6 (CH_3, olefinic-CH_3), 19.7 (CH_3, CH*C*H$_3$), 14.1 (CH_3, OCH$_2$*C*H$_3$).

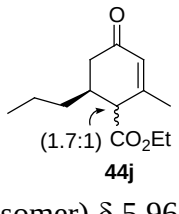


44d

6-Ethyl-2-methyl-4-oxo-cyclohex-2-enecarboxylic acid ethyl ester (44i): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2972, 1734 (O-C=O), 1672 (C=O), 1186, 1030, 758, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 1.6:1 ratio of diastereomers, major isomer) δ 5.95 (1H, s, olefinic-*H*), 4.20 (2H, q, *J* = 7.2 Hz, OCH_2CH$_3$), 3.13 (1H, d, *J* = 6.4 Hz), 2.62 (2H, m), 2.12 (1H, m), 1.97 (3H, s, olefinic-CH_3), 1.48 (2H, m), 1.31 (3H, t, *J* = 7.2 Hz, OCH$_2$CH_3), 0.93 (3H, t, *J* = 7.2 Hz, CH$_2$CH$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135, 1.6:1 ratio of diastereomers, major isomer) δ 198.1 (C, C=O), 171.9 (C, O-C=O), 155.8 (C), 127.9 (CH), 61.2 (CH_2, O*C*H$_2$CH$_3$), 52.3 (CH), 39.9 (CH_2), 39.1 (CH), 26.4 (CH_2), 22.8 (CH_3, olefinic-*C*H$_3$), 14.1 (CH_3, OCH$_2$*C*H$_3$), 10.9 (CH_3, CH$_2$*C*H$_3$).



44i

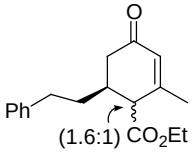


44j

2-Methyl-4-oxo-6-propyl-cyclohex-2-enecarboxylic acid ethyl ester (44j): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2961, 1732 (O-C=O), 1674 (C=O), 1186, 1026 cm^{-1}; ^{1}H NMR ($CDCl_3$, 1.7:1 ratio of diastereomers, major isomer) δ 5.96 (1H, s, olefinic-*H*), 4.22 (2H, q, *J* = 7.2 Hz, OCH_2CH$_3$), 3.10 (1H, d, *J* =

6.8 Hz), 2.61 (2H, m), 2.34 (1H, m), 1.97 (3H, s, olefinic-CH_3), 1.50-1.20 (4H, m), 1.29 (3H, t, J = 7.2 Hz, OCH$_2$CH_3), 0.91 (3H, t, J = 7.2 Hz, CH$_2$CH$_2$CH_3); ^{13}C NMR (CDCl$_3$, DEPT-135, 1.7:1 ratio of diastereomers, major isomer) δ 198.1 (C, C=O), 171.8 (C, O-C=O), 155.8 (C), 128.0 (CH), 61.2 (CH$_2$, OCH$_2$CH$_3$), 52.7 (CH), 40.1 (CH$_2$), 37.2 (CH), 35.7 (CH$_2$), 22.9 (CH$_3$, olefinic-CH$_3$), 19.6 (CH$_2$), 14.1 (CH$_3$, OCH$_2$$CH_3$), 13.8 (CH$_3$, CH$_2CH_2$$CH_3$).

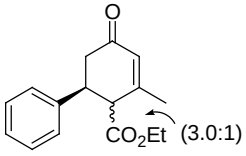
2-Methyl-4-oxo-6-phenethyl-cyclohex-2-enecarboxylic acid ethyl ester (44k):



44k

Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3024, 2932, 2862, 1732 (O-C=O), 1670 (C=O), 1496, 1454, 1259, 1170, 1030, 750, 700 cm^{-1}; ^{1}H NMR (CDCl$_3$, 1.6:1 ratio of diastereomers, major isomer) δ 7.28-7.13 (5H, m, Ph-H), 5.96 (1H, s, olefinic-H), 4.20 (2H, q, J = 7.2 Hz, OCH_2CH$_3$), 3.14 (1H, d, J = 6.4 Hz), 2.69 (2H, m), 2.53 (2H, m), 2.29 (1H, m), 1.95 (3H, s, olefinic-CH_3), 1.72 (2H, m), 1.28 (3H, t, J = 6.8 Hz, OCH$_2$CH_3); ^{13}C NMR (CDCl$_3$, DEPT-135, 1.6:1 ratio of diastereomers, major isomer) δ 197.6 (C, C=O), 171.5 (C, O-C=O), 155.6 (C), 141.1 (C), 128.4 (2 x CH), 128.3 (2 x CH), 128.0 (CH), 125.9 (CH), 61.3 (CH$_2$, OCH$_2$CH$_3$), 52.6 (CH), 40.1 (CH$_2$), 37.0 (CH), 35.4 (CH$_2$), 32.8 (CH$_2$), 23.0 (CH$_3$, olefinic-CH$_3$), 14.2 (CH$_3$, OCH$_2$$CH_3$).

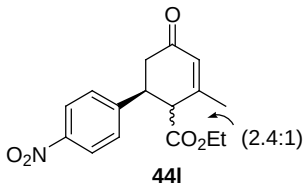
2-Methyl-4-oxo-6-phenyl-cyclohex-2-enecarboxylic acid ethyl ester (44e): Purified



44e

by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3032, 2982, 1732 (O-C=O), 1670 (C=O), 1496, 1454, 1180, 1032, 760, 700 cm^{-1}; ^{1}H NMR (CDCl$_3$, 3.0:1 ratio of diastereomers, major isomer) δ 7.36-7.20 (5H, m, Ph-H), 6.06 (1H, s, olefinic-H), 4.05 (2H, q, J = 7.2 Hz, OCH_2CH$_3$), 3.64 (1H, m), 3.48 (1H, m), 2.68 (2H, m), 2.01 (3H, s, olefinic-CH_3), 1.14 (3H, t, J = 7.2 Hz, OCH$_2$CH_3); ^{13}C NMR (CDCl$_3$, DEPT-135, 3.0:1 ratio of diastereomers, major isomer) δ 197.2 (C, C=O), 171.2 (C, O-C=O), 156.2 (C), 140.9 (C), 128.7 (2 x CH), 128.4 (CH), 127.4 (CH), 127.2 (2 x CH), 61.1 (CH$_2$, OCH$_2$CH$_3$), 54.3 (CH), 44.1 (CH), 42.8 (CH$_2$), 22.4 (CH$_3$, olefinic-CH$_3$), 13.9 (CH$_3$, OCH$_2$$CH_3$).

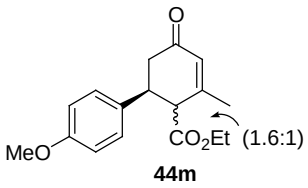
2-Methyl-6-(4-nitro-phenyl)-4-oxo-cyclohex-2-enecarboxylic acid ethyl ester (44l):



44l

Purified by column chromatography using EtOAc/hexane and isolated as a gummy solid. IR (neat): ν_{max} 2982, 1736 (O-C=O), 1668 (C=O), 1601, 1521, 1033, 746, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 2.4:1 ratio of diastereomers, major isomer) δ 8.13 (2H, d, *J* = 7.2 Hz), 7.45 (2H, d, *J* = 7.2 Hz), 6.09 (1H, s, olefinic-*H*), 4.11 (2H, q, *J* = 7.6 Hz, OC*H*$_2$CH$_3$), 3.87 (1H, m), 3.61 (1H, m), 2.70 (2H, m), 2.02 (3H, s, olefinic-C*H*$_3$), 1.11 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135, 2.4:1 ratio of diastereomers, major isomer) δ 195.9 (C, C=O), 170.7 (C, O-C=O), 155.7 (C), 148.3 (C), 147.5 (C), 128.5 (CH), 128.3 (2 x CH), 124.1 (2 x CH), 61.6 (CH_2, O*C*H$_2$CH$_3$), 53.6 (CH), 43.7 (CH), 42.1 (CH_2), 22.4 (CH_3, olefinic-*C*H$_3$), 14.0 (CH_3, OCH$_2$*C*H$_3$).

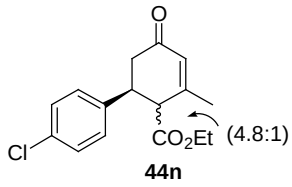
6-(4-Methoxy-phenyl)-2-methyl-4-oxo-cyclohex-2-enecarboxylic acid ethyl ester (44m):



44m

Purified by column chromatography using EtOAc/hexane and isolated as a gummy solid. IR (neat): ν_{max} 2980, 2837, 1734 (O-C=O), 1672 (C=O), 1612, 1514, 1458, 1258, 1033, 769, 734 cm^{-1}; ^1H NMR ($CDCl_3$, 2.8:1 ratio of diastereomers, major isomer) δ 7.14 (2H, d, *J* = 7.2 Hz), 6.85 (2H, d, *J* = 7.2 Hz), 6.05 (1H, s, olefinic-*H*), 4.07 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.79 (CH_3, s, OC*H*$_3$), 3.62 (1H, m), 3.53 (1H, m), 2.67 (2H, m), 1.98 (3H, s, olefinic-C*H*$_3$), 1.11 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135, 2.8:1 ratio of diastereomers, major isomer) δ 197.5 (C, C=O), 171.4 (C, O-C=O), 158.8 (C), 156.3 (C), 133.0 (C), 128.4 (CH), 128.2 (2 x CH), 114.1 (2 x CH), 61.1 (CH_2, O*C*H$_2$CH$_3$), 55.4 (CH_3, O*C*H$_3$), 54.7 (CH), 43.3 (CH), 43.1 (CH_2), 22.3 (CH_3, olefinic-*C*H$_3$), 14.0 (CH_3, OCH$_2$*C*H$_3$).

6-(4-Chloro-phenyl)-2-methyl-4-oxo-cyclohex-2-enecarboxylic acid ethyl ester (44n):

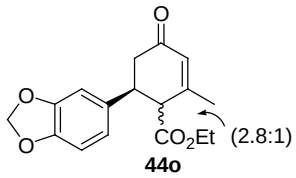


44n

Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 2980, 1734 (O-C=O), 1674 (C=O), 1493, 1014, 736 cm^{-1}; ^1H NMR ($CDCl_3$, 4.8:1 ratio of diastereomers, major isomer) δ 7.29 (2H, d, *J* = 7.2 Hz), 7.17 (2H, d, *J* = 7.2 Hz), 6.06 (1H, s, olefinic-*H*), 4.07 (2H, q, *J* =

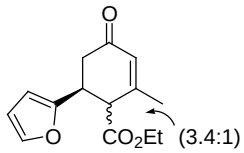
7.2 Hz, OC*H*$_2$CH$_3$), 3.64 (1H, m), 3.53 (1H, m), 2.67 (2H, m), 1.98 (3H, s, olefinic-C*H*$_3$), 1.12 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR (CDCl$_3$, DEPT-135, 4.8:1 ratio of diastereomers, major isomer) δ 196.7 (C, C=O), 171.0 (C, O-C=O), 156.0 (C), 139.3 (C), 133.1 (C), 128.9 (2 x CH), 128.6 (2 x CH), 128.4 (CH), 61.3 (CH$_2$, O*C*H$_2$CH$_3$), 54.1 (CH), 43.3 (CH), 42.6 (CH$_2$), 22.3 (CH$_3$, olefinic-*C*H$_3$), 13.9 (CH$_3$, OCH$_2$*C*H$_3$).

6-Benzo[1,3]dioxol-5-yl-2-methyl-4-oxo-cyclohex-2-enecarboxylic acid ethyl ester (44o): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2986, 2910, 1730 (O-C=O), 1670 (C=O), 1506, 1037, 933 cm^{-1}; ^{1}H NMR (CDCl$_3$, 2.8:1 ratio of diastereomers, major isomer) δ 6.78-6.65 (3H, m, Ph-*H*), 6.04 (1H, s, olefinic-*H*), 5.94 (2H, s, OC*H*$_2$O), 4.10 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.58 (1H, m), 3.43 (1H, m), 2.63 (2H, m), 1.98 (3H, s, olefinic-C*H*$_3$), 1.14 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR (CDCl$_3$, DEPT-135, 2.8:1 ratio of diastereomers, major isomer) δ 197.1 (C, C=O), 171.2 (C, O-C=O), 156.1 (C), 147.8 (C), 146.7 (C), 134.7 (C), 128.4 (CH), 120.5 (CH), 108.3 (CH), 107.4 (CH), 101.1 (CH$_2$, OCH$_2$O), 61.2 (CH$_2$, O*C*H$_2$CH$_3$), 54.6 (CH), 43.8 (CH), 43.1 (CH$_2$), 22.3 (CH$_3$, olefinic-*C*H$_3$), 14.1 (CH$_3$, OCH$_2$*C*H$_3$).



44o

6-Furan-2-yl-2-methyl-4-oxo-cyclohex-2-enecarboxylic acid ethyl ester (44p): Purified by column chromatography using EtOAc/hexane and isolated as a gummy solid. IR (neat): ν_{max} 3119, 2982, 1732 (O-C=O), 1676 (C=O), 1504, 1440, 1186, 1016, 738 cm^{-1}; ^{1}H NMR (CDCl$_3$, 3.4:1 ratio of diastereomers, major isomer) δ 7.29 (1H, br s), 6.26 (1H, m), 6.04 (1H, m), 5.98 (1H, s, olefinic-*H*), 4.20 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.83 (1H, m), 3.63 (1H, m), 2.75 (2H, m), 1.98 (3H, s, olefinic-C*H*$_3$), 1.25 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR (CDCl$_3$, DEPT-135, 3.4:1 ratio of diastereomers, major isomer) δ 196.5 (C, C=O), 170.8 (C, O-C=O), 155.1 (C), 154.2 (C), 141.7 (CH), 128.1 (CH), 110.1 (CH), 106.0 (CH), 61.4 (CH$_2$, O*C*H$_2$CH$_3$), 51.0 (CH), 38.9 (CH$_2$), 37.0 (CH), 23.0 (CH$_3$, olefinic-*C*H$_3$), 14.1 (CH$_3$, OCH$_2$*C*H$_3$).



44p

2: Experimental Procedures for the Synthesis of Highly Functionalized 2-Methyl-2*H*-Chromenes: The synthesis of highly functionalized 2-methyl-2*H*-chromenes **55adaa, 55edaa, 55ldaa, 55ldab, 56acaa** and **56ecaa** from corresponding Hagemann's esters **44a, 44e, 44l** involves the following five or six-step sequence.

2A: **Sequential Combination of Piperidine-Catalyzed Cascade Knoevenagel/Michael/Aldol Condensation/Decarboxylation, (S)-1-(2-Pyrrolidinylmethyl)pyrrolidine-Catalyzed Cascade Claisen-Schmidt/*Iso*-Aromatization and K_2CO_3-Catalyzed Alkylation Reactions in One-Pot:** To a stirred solution of ethyl acetoacetate **43a** (2.0 mmol) and 4-nitrobenzaldehyde **7d** (1.0 mmol) in EtOH (2 mL) was added a catalytic amount of piperidine **4j** (0.35 mmol, 35 mol%) and the reaction mixture was stirred at 80 °C for 5-6 h. Solvent ethanol and piperidine were evaporated under reduced pressure, then solvent DMSO (1.0 mL) was added. To that, catalyst (*S*)-1-(2-pyrrolidinylmethyl)pyrrolidine **4l** (0.1 mmol, 16.3 µL), 4-nitrobenzaldehyde **7d** (0.5 mmol) were added and the reaction mixture was stirred at RT for 14 h. To the crude reaction mixture added 5 equiv. of K_2CO_3 and 2 equiv. of allyl bromide **57a** and stirred at RT for 24-28 h. The crude reaction mixture was worked up with aqueous NH_4Cl solution and the aqueous layer was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure product **50lda** was obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

2B: Sequential Cascade Claisen-Schmidt/*Iso*-Aromatization/Alkylation Reactions in One-Pot: In an ordinary glass vial equipped with a magnetic stirring bar, to 0.5 mmol of the Hagemann's ester **44a**/**44e** were added 1.0 mL of DMSO solvent, and then the catalyst glycine **4m** (0.1 mmol, 7.5 mg) and then 0.5 mmol of benzaldehyde **7c** was added in one-portion and the reaction mixture was stirred at RT for the 48 h. To the reaction mixture, catalyst piperidine **4j** (0.1 mmol) was added and the reaction mixture was stirred at 70 °C for 12-24 hours as indicated in Scheme 3. The *in situ* generated corresponding phenols **50** were allylated by treatment with allyl bromide **57a** (121.0 mg, 1.0 mmol) and K_2CO_3 (207.3 mg, 1.5 mmol) in DMSO (2 mL, 0.1 M) at RT for

14-18 h. The crude reaction mixture was worked up with aqueous NH_4Cl solution and the aqueous layer was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure products were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

The isolated corresponding phenols **50 (**1.0 mmol**)** were allylated by treatment with allyl bromide **57a** (242.0 mg, 2.0 mmol) and K_2CO_3 (691.0 mg, 5.0 mmol) in DMSO (2 mL, 0.5 M) at RT for 24 h. The crude reaction mixture was worked up with aqueous NH_4Cl solution and the aqueous layer was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure products were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

2C: *C*-Allylation through Claisen Rearrangement: *O*-Allylated compounds (1.0 mmol) and solvent DCB (2.0 mL, 0.5 M) were taken in a sealed glass tube and the mixture is heated at 160-180 °C under N_2 for 24 to 28 h. Upon cooling the reaction mixture to RT, the mixture was diluted with CH_2Cl_2 (10 mL), washed with aqueous NH_4Cl solution (2 mL) and brine (2 mL). The separated organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure. Pure *C*-allylated phenols **50'** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

2D: Method A: *O*-Allylation: The corresponding *C*-allylated phenols **50'** (1.0 mmol) were allylated by treatment with allyl bromide **57a** (242.0 mg, 2.0 mmol) and K_2CO_3 (414.6 mg, 3.0 mmol) in DMSO (10 mL, 0.1 M) at RT for 24 h. The crude reaction mixture was worked up with aqueous NH_4Cl solution and the aqueous layer was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure products **51** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

Method B: *O*-Propargylation: The enyne **51** was prepared by treating the corresponding *C*-allylated phenol **50'lda** (1.0 mmol) with propargyl bromide **57b** (238.0 mg, 2.0 mmol) and K_2CO_3 (414.6 mg, 3.0 mmol) in DMSO (10 mL, 0.1 M) at

RT for 24 h. The crude reaction mixture was worked up with aqueous NH_4Cl solution and the aqueous layer was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure product **51ldab** was obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

2E: RCM Reactions:

Method A*:* A 10 mL oven-dried round bottom flask equipped with a stirring bar was charged with diene **51** (0.2 mmol) and Grubbs' first generation catalyst **4n** (3.3 mg, 0.004 mmol, 2 mol%) in dry CH_2Cl_2 (4 mL, 0.05 M) and the reaction mixture was stirred under N_2 at RT for 3 to 5 h. Solvent CH_2Cl_2 was distilled off at ambient pressure and the crude reaction mixture was directly loaded on silica gel column and pure RCM products **52** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

Method B*:* A 10 mL oven-dried round bottom flask equipped with a stirring bar was charged with enyne **51ldab** (0.2 mmol) and Grubbs' first generation catalyst **4n** (8.3 mg, 0.01 mmol, 5 mol%) in dry CH_2Cl_2 (4 mL, 0.05 M) and the reaction mixture was stirred under N_2 at RT for 24 h. Solvent CH_2Cl_2 was distilled off at ambient pressure and the crude reaction mixture was directly loaded on silica gel column and pure RCM product **52ldab** was obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

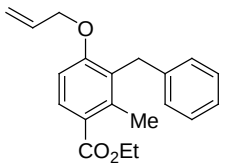
2F: Base-Induced Ring Opening (BIRO) Reactions: A 10 mL oven-dried round bottom flask equipped with a stir bar was charged with **52** (0.2 mmol), dry DMSO (4 mL, 0.05 M), to that *t*BuOK (44.8 mg, 0.4 mmol, 2.0 equiv) was added at 0 °C. The reaction mixture was stirred at RT for 3-4 h. The crude reaction mixture was worked up with water and the aqueous layer was extracted with ether (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure products **53** or **54** [**53ldab** is an unstable product at RT and which was rapidly converted into **55ldab**] were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

2G: [1,7]-Sigmatropic Hydrogen Shift Reactions:

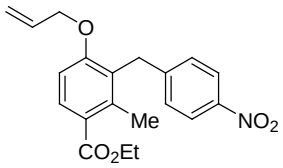
Method A*:* Compounds **53** or **54** (0.1 mmol), DMF (1.0 mL, 0.1 M) were taken in a sealed glass tube and the mixture is heated at 140 °C under N_2 for 12 to 15 h. Upon cooling to RT, the mixture was diluted with CH_2Cl_2 (10 mL), washed with NH_4Cl solution (5 mL) and brine (5 mL). The separated organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. Pure products **55** or **56** respectively were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

Method B*:* To the crude compound **53ldab**, 5 gm of silica (particle size 0.063-0.200 mm), 5 ml of $CHCl_3$ was added and the reaction mixture stirred at RT for 5.0 h. Pure product **55ldab** was obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

4-Allyloxy-3-benzyl-2-methyl-benzoic acid ethyl ester (50aca): Prepared following the procedure **2B** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 2980, 1714 (O-C=O), 1649, 1591, 1454, 1051, 775 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.83 (1H, d, *J* = 8.4 Hz), 7.26 (2H, t, *J* = 5.2 Hz), 7.16 (1H, t, *J* = 6.8 Hz), 7.14 (2H, d, *J* = 7.2 Hz), 6.81 (1H, d, *J* = 8.4 Hz), 6.02-5.94 (1H, m, olefinic-*H*), 5.35 (1H, dd, *J* = 17.2, 1.6 Hz, olefinic-*H*), 5.25 (1H, dd, *J* = 10.4, 1.6 Hz, olefinic-*H*), 4.59 (2H, d, *J* = 4.8 Hz, OC*H*$_2$CH=CH$_2$), 4.35 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 4.20 (2H, s, ArC*H*$_2$Ar), 2.53 (3H, s, Ar-C*H*$_3$), 1.40 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.1 (C, O-C=O), 159.0 (C), 140.4 (C), 140.2 (C), 132.8 (CH), 130.2 (CH), 128.8 (C), 128.1 (2 x CH), 128.0 (2 x CH), 125.6 (CH), 123.9 (C), 117.2 (CH$_2$, CH=*C*H$_2$), 108.6 (CH), 68.8 (CH$_2$, O*C*H$_2$CH=CH$_2$), 60.4 (CH$_2$, O*C*H$_2$CH$_3$), 31.6 (CH$_2$), 16.9 (CH$_3$, Ar-*C*H$_3$), 14.3 (CH$_3$, OCH$_2$*C*H$_3$); LRMS m/z 311.00 (M + H^+), calcd $C_{20}H_{22}O_3$ 310.1569; Anal. calcd for $C_{20}H_{22}O_3$ (310.15): C, 77.39; H, 7.14. Found: C, 77.56; H, 7.08%.



50aca

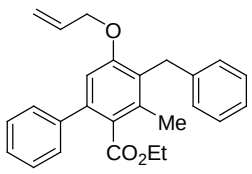


50ada

4-Allyloxy-2-methyl-3-(4-nitrobenzyl)-benzoic acid ethyl ester (50ada): Prepared following the procedure **2B** and purified by column

chromatography using EtOAc/hexane and isolated as a light yellow solid. Mp.: 104 °C.; IR (neat): ν_{max} 3096, 2984, 1701 (O-C=O), 1593, 1516, 1251, 1049, 775, 692 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.07 (2H, d, *J* = 8.8 Hz), 7.84 (1H, d, *J* = 8.8 Hz), 7.24 (2H, d, *J* = 8.8 Hz), 6.80 (1H, d, *J* = 8.8 Hz), 5.99-5.89 (1H, m, olefinic-*H*), 5.29 (1H, dd, *J* = 17.2, 1.2 Hz, olefinic-*H*), 5.22 (1H, dd, *J* = 10.8, 1.2 Hz, olefinic-*H*), 4.57 (2H, d, *J* = 5.2 Hz, $OCH_2CH=CH_2$), 4.32 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 4.23 (2H, s, $ArCH_2Ar$), 2.48 (3H, s, Ar-CH_3), 1.37 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.8 (C, O-C=O), 158.8 (C), 148.4 (C), 146.2 (C), 140.2 (C), 132.5 (CH), 130.9 (CH), 128.7 (2 x CH), 127.1 (C), 124.0 (C), 123.4 (2 x CH), 117.5 (CH_2, $CH=CH_2$), 108.7 (CH), 68.8 (CH_2, $OCH_2CH=CH_2$), 60.5 (CH_2, OCH_2CH_3), 31.7 (CH_2), 16.9 (CH_3, Ar-CH_3), 14.2 (CH_3, OCH_2CH_3); LRMS m/z 354.20 ($M - H^+$), calcd $C_{20}H_{21}NO_5$ 355.1420; Anal. calcd for $C_{20}H_{21}NO_5$ (355.14): C, 67.59; H, 5.96; N, 3.94. Found: C, 67.45; H, 5.88; N, 3.86%.

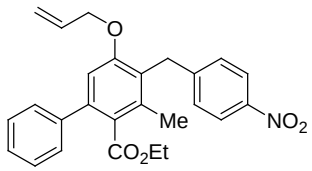
5-Allyloxy-4-benzyl-3-methyl-biphenyl-2-carboxylic acid ethyl ester (50eca):



50eca

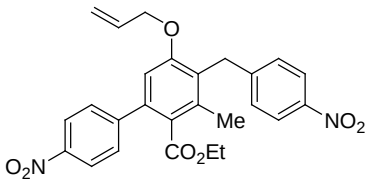
Prepared following the procedure **2B** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3061, 2982, 1722 (O-C=O), 1647, 1494, 1452, 1053, 850, 800 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.41-7.37 (5H, m, Ph-*H*), 7.35-7.19 (5H, m, Ph-*H*), 6.82 (1H, s, Ar-*H*), 6.06-5.97 (1H, m, olefinic-*H*), 5.38 (1H, dd, *J* = 17.2, 1.2 Hz, olefinic-*H*), 5.30 (1H, d, *J* = 11.2 Hz, olefinic-*H*), 4.61 (2H, d, *J* = 4.8 Hz, $OCH_2CH=CH_2$), 4.21 (2H, s, $ArCH_2Ar$), 4.06 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 2.35 (3H, s, Ar-CH_3), 0.97 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 170.2 (C, O-C=O), 156.9 (C), 141.3 (C), 140.1 (C), 139.5 (C), 135.9 (C), 132.9 (CH), 128.3 (4 x CH), 128.2 (2 x CH), 128.1 (2 x CH), 127.4 (C), 127.3 (CH), 127.1 (C), 125.6 (CH), 117.2 (CH_2, $CH=CH_2$), 110.9 (CH), 68.9 (CH_2, $OCH_2CH=CH_2$), 60.8 (CH_2, OCH_2CH_3), 31.7 (CH_2), 16.8 (CH_3, Ar-CH_3), 13.6 (CH_3, OCH_2CH_3); LRMS m/z 387.00 ($M + H^+$), calcd $C_{26}H_{26}O_3$ 386.1882; Anal. calcd for $C_{26}H_{26}O_3$ (386.18): C, 80.80; H, 6.78. Found: C, 80.68; H, 7.89%.

5-Allyloxy-3-methyl-4-(4-nitrobenzyl)-biphenyl-2-carboxylic acid ethyl ester (50eda): Prepared following the procedure **2B** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3051, 1714 (O-C=O), 1595, 1518, 1055, 1014, 858, 736 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.12 (2H, d, *J* = 8.8 Hz), 7.40-7.35 (5H, m, Ph-*H*), 7.33 (2H, d, *J* = 8.8 Hz), 6.80 (1H, s, Ar-*H*), 6.02-5.92 (1H, m, olefinic-*H*), 5.31 (1H, dd, *J* = 16.4, 1.2 Hz, olefinic-*H*), 5.24 (1H, dd, *J* = 10.4, 1.2 Hz, olefinic-*H*), 4.58 (2H, dd, *J* = 3.6, 1.2 Hz, OC*H*$_2$CH=CH_2), 4.24 (2H, s, ArC*H*$_2$Ar), 4.03 (2H, q, *J* = 7.2 Hz, OC*H*$_2$$CH_3$), 2.30 (3H, s, Ar-C*H*$_3$), 0.93 (3H, t, *J* = 7.2 Hz, OCH_2C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.9 (C, O-C=O), 156.6 (C), 148.2 (C), 146.1 (C), 141.0 (C), 140.4 (C), 135.7 (C), 132.7 (CH), 129.1 (2 x CH), 128.2 (2 x CH), 128.1 (2 x CH), 127.4 (CH), 127.3 (C), 125.5 (C), 123.5 (2 x CH), 117.5 (CH_2, CH=*C*H_2), 110.9 (CH), 68.9 (CH_2, O*C*H_2CH=CH_2), 60.8 (CH_2, O*C*$H_2$$CH_3$), 31.8 ($CH_2$), 16.8 ($CH_3$, Ar-*C*$H_3$), 13.6 ($CH_3$, OCH_2*C*H_3); LRMS m/z 430.40 (M - H^+), calcd $C_{26}H_{25}NO_5$ 431.1733; Anal. calcd for $C_{26}H_{25}NO_5$ (431.17): C, 72.37; H, 5.84; N, 3.25. Found: C, 72.51; H, 5.76; N, 3.18%.



50eda

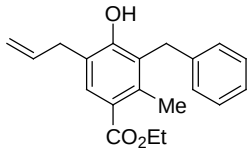
5-Allyloxy-3-methyl-4'-nitro-4-(4-nitrobenzyl)-biphenyl-2-carboxylic acid ethyl ester (50lda): Prepared following the procedure **2A** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 2980, 1722 (O-C=O), 1597, 1520, 1456, 1014, 736 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.22 (2H, d, *J* = 8.4 Hz), 8.08 (2H, d, *J* = 8.4 Hz), 7.54 (2H, d, *J* = 8.8 Hz), 7.31 (2H, d, *J* = 8.4 Hz), 6.79 (1H, s, Ar-*H*), 6.01-5.89 (1H, m, olefinic-*H*), 5.30 (1H, d, *J* = 17.2 Hz, olefinic-*H*), 5.23 (1H, d, *J* = 10.8 Hz, olefinic-*H*), 4.61 (2H, d, *J* = 4.8 Hz, OC*H*$_2$CH=CH_2), 4.25 (2H, s, ArC*H*$_2$Ar), 4.04 (2H, q, *J* = 7.2 Hz, OC*H*$_2$$CH_3$), 2.30 (3H, s, Ar-C*H*$_3$), 0.98 (3H, t, *J* = 7.2 Hz, OCH_2C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.2 (C, O-C=O), 156.8 (C), 147.7 (C), 147.6 (C), 147.0 (C), 146.1 (C), 137.8 (C), 136.3 (C), 132.3 (CH), 129.1 (2 x CH), 128.8 (2 x CH), 126.9 (2 x C), 123.4 (2 x CH), 123.3 (2 x CH), 117.6 (CH_2,



50lda

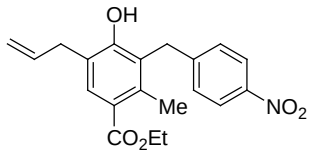
CH=*C*H_2), 110.5 (CH), 69.0 (CH_2, O*C*H_2CH=CH_2), 61.1 (CH_2, O*C*$H_2$$CH_3$), 31.7 ($CH_2$), 16.7 ($CH_3$, Ar-*C*$H_3$), 13.5 ($CH_3$, OCH_2*C*H_3); LRMS m/z 475.00 (M - H^+), calcd $C_{26}H_{24}N_2O_7$ 476.1584; Anal. calcd for $C_{26}H_{24}N_2O_7$ (476.15): C, 65.54; H, 5.08; N, 5.88. Found: C, 65.48; H, 5.12; N, 5.96%.

5-Allyl-3-benzyl-4-hydroxy-2-methyl-benzoic acid ethyl ester (50'aca): Prepared following the procedure **2C** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3481 (O-*H*), 2980, 1705 (O-C=O), 1639, 1602, 1493, 1467, 1047, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.64 (1H, d, *J* = 1.2 Hz), 7.27 (2H, t, *J* = 7.6 Hz), 7.19 (1H, t, *J* = 6.8 Hz), 7.14 (2H, d, *J* = 7.6 Hz), 6.07-6.00 (1H, m, olefinic-*H*), 5.58 (1H, s, O-*H*), 5.23 (2H, m, olefinic-*H*), 4.35 (2H, q, *J* = 7.2 Hz, OC*H*$_2$$CH_3$), 4.15 (2H, s, ArC*H*$_2$Ar), 3.46 (2H, d, *J* = 5.6 Hz, C*H*$_2$CH=CH_2), 2.51 (3H, s, Ar-C*H*$_3$), 1.40 (3H, t, *J* = 7.2 Hz, OCH_2C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.2 (C, O-C=O), 155.7 (C), 139.4 (C), 139.2 (C), 135.8 (CH), 131.0 (CH), 128.4 (2 x CH), 127.9 (2 x CH), 126.8 (C), 125.9 (CH), 123.6 (C), 121.7 (C), 117.3 (CH_2, CH=*C*H_2), 60.5 (CH_2, O*C*$H_2$$CH_3$), 35.5 ($CH_2$), 31.8 ($CH_2$, *C*$H_2$CH=$CH_2$), 16.8 ($CH_3$, Ar-*C*$H_3$), 14.3 ($CH_3$, OCH_2*C*H_3); LRMS m/z 311.00 (M + H^+), calcd $C_{20}H_{22}O_3$ 310.1569; Anal. calcd for $C_{20}H_{22}O_3$ (310.15): C, 77.39; H, 7.14. Found: C, 77.51; H, 7.25%.



50'aca

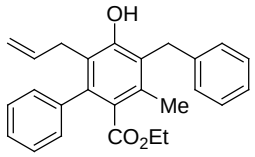
5-Allyl-4-hydroxy-2-methyl-3-(4-nitrobenzyl)-benzoic acid ethyl ester (50'ada): Prepared following the procedure **2C** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. Mp.: 120 °C.; IR (neat): ν_{max} 3427 (O-*H*), 3082, 2982, 1695 (O-C=O), 1637, 1595, 1572, 1512, 1286, 1047, 740, 661 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.05 (2H, d, *J* = 8.4 Hz), 7.63 (1H, s, Ar-*H*), 7.24 (2H, d, *J* = 8.8 Hz), 6.08-6.00 (1H, m, olefinic-*H*), 5.87 (1H, d, *J* = 7.6 Hz, olefinic-*H*), 5.24 (1H, s, O-*H*), 5.21 (1H, d, *J* = 8.0 Hz, olefinic-*H*), 4.31 (2H, q, *J* = 7.2 Hz, OC*H*$_2$$CH_3$), 4.19 (2H, s, ArC*H*$_2$Ar), 3.45 (2H, d, *J* = 6.0 Hz, C*H*$_2$CH=CH_2), 2.43 (3H, s, Ar-C*H*$_3$), 1.36 (3H, t, *J* = 7.2 Hz, OCH_2C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.1



50'ada

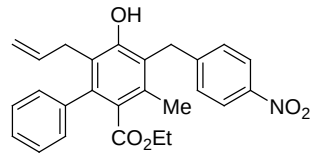
(C, O-C=O), 155.8 (C), 148.2 (C), 146.2 (C), 139.2 (C), 135.6 (CH), 131.7 (CH), 128.8 (2 x CH), 125.9 (C), 123.9 (C), 123.6 (2 x CH), 121.7 (C), 117.8 (CH_2, CH=*C*H_2), 60.8 (CH_2, O*C*H_2CH_3), 35.6 (CH_2, *C*H_2CH=CH_2), 31.9 (CH_2), 16.9 (CH_3, Ar-*C*H_3), 14.3 (CH_3, OCH_2*C*H_3); LRMS m/z 354.20 (M - H^+), calcd $C_{20}H_{21}NO_5$ 355.1420; Anal. calcd for $C_{20}H_{21}NO_5$ (355.14): C, 67.59; H, 5.96; N, 3.94. Found: C, 67.45; H, 5.91; N, 4.02%.

6-Allyl-4-benzyl-5-hydroxy-3-methyl-biphenyl-2-carboxylic acid ethyl ester (50'eca): Prepared following the procedure **2C** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3499 (O-*H*), 2980, 1714 (O-C=O), 1635, 1601, 1566, 1494, 1450, 1047, 727, 702 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.39-7.19 (10H, m, Ph-*H*), 5.95-5.86 (1H, m, olefinic-*H*), 5.36 (1H, br s, O-*H*), 5.16 (1H, dd, *J* = 10.0, 1.2 Hz, olefinic-*H*), 5.10 (1H, dd, *J* = 17.2, 1.6 Hz, olefinic-*H*), 4.15 (2H, s, ArC*H*$_2$Ar), 3.90 (2H, q, *J* = 7.2 Hz, OC*H*$_2$$CH_3$), 3.21 (2H, d, *J* = 5.6 Hz, C*H*$_2$CH=CH_2), 2.28 (3H, s, Ar-C*H*$_3$), 0.89 (3H, t, *J* = 7.2 Hz, OCH_2C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 170.1 (C, O-C=O), 153.7 (C), 139.5 (C), 139.0 (C), 138.7 (C), 135.9 (CH), 133.3 (C), 129.3 (2 x CH), 128.6 (C), 128.4 (2 x CH), 128.1 (2 x CH), 127.8 (2 x CH), 127.3 (CH), 126.0 (CH), 125.6 (C), 120.6 (C), 116.7 (CH_2, CH=*C*H_2), 60.6 (CH_2, O*C*H_2CH_3), 32.3 (CH_2), 32.0 (CH_2, *C*H_2CH=CH_2), 16.7 (CH_3, Ar-*C*H_3), 13.6 (CH_3, OCH_2*C*H_3); LRMS m/z 387.00 (M + H^+), calcd $C_{26}H_{26}O_3$ 386.1882; Anal. calcd for $C_{26}H_{26}O_3$ (386.18): C, 80.80; H, 6.78. Found: C, 80.69; H, 6.71%.



50'eca

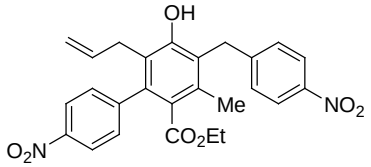
6-Allyl-5-hydroxy-3-methyl-4-(4-nitrobenzyl)-biphenyl-2-carboxylic acid ethyl ester (50'eda): Prepared following the procedure **2C** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3487 (O-*H*), 3059, 1711 (O-C=O), 1637, 1599, 1568, 1047, 733, 704 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.13 (2H, d, *J* = 8.4 Hz), 7.38-7.35 (5H, m, Ph-*H*), 7.23 (2H, d, *J* = 8.8 Hz), 5.91-5.87 (1H, m, olefinic-*H*), 5.49 (1H, s, O-*H*), 5.21 (1H, d, *J* = 10.0



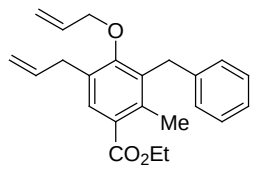
50'eda

Hz, olefinic-*H*), 5.15 (1H, d, *J* = 17.2 Hz, olefinic-*H*), 4.22 (2H, s, ArCH_2Ar), 3.89 (2H, q, *J* = 7.2 Hz, OCH_2CH$_3$), 3.22 (2H, d, *J* = 5.2 Hz, CH_2CH=CH$_2$), 2.23 (3H, s, Ar-CH_3), 0.88 (3H, t, *J* = 7.2 Hz, OCH$_2$CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.9 (C, O-C=O), 153.8 (C), 148.1 (C), 146.3 (C), 139.4 (C), 138.8 (C), 135.7 (CH), 133.3 (C), 129.2 (2 x CH), 129.0 (2 x CH), 128.9 (C), 127.9 (2 x CH), 127.6 (CH), 124.4 (C), 123.6 (2 x CH), 120.5 (C), 117.3 (CH$_2$, CH=*C*H$_2$), 60.8 (CH$_2$, O*C*H$_2$CH$_3$), 32.4 (CH$_2$, *C*H$_2$CH=CH$_2$), 32.1 (CH$_2$), 16.8 (CH$_3$, Ar-*C*H$_3$), 13.6 (CH$_3$, OCH$_2$*C*H$_3$); LRMS m/z 432.30 (M + H$^+$), calcd $C_{26}H_{25}NO_5$ 431.1733; Anal. calcd for $C_{26}H_{25}NO_5$ (431.17): C, 72.37; H, 5.84; N, 3.25. Found: C, 72.21; H, 5.81; N, 3.36%.

6-Allyl-5-hydroxy-3-methyl-4'-nitro-4-(4-nitrobenzyl)-biphenyl-2-carboxylic acid ethyl ester (50'lda): Prepared following the procedure **2C** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3512 (O-*H*), 2935, 1720 (O-C=O), 1637, 1599, 1520, 1444, 1014, 856 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.24 (2H, d, *J* = 8.8 Hz), 8.13 (2H, d, *J* = 8.4 Hz), 7.43 (2H, d, *J* = 8.4 Hz), 7.34 (2H, d, *J* = 8.4 Hz), 5.96-5.80 (1H, m, olefinic-*H*), 5.54 (1H, s, O-*H*), 5.23 (1H, d, *J* = 10.4 Hz, olefinic-*H*), 5.10 (1H, d, *J* = 17.6 Hz, olefinic-*H*), 4.23 (2H, s, ArCH_2Ar), 3.92 (2H, q, *J* = 7.2 Hz, OCH_2CH$_3$), 3.15 (2H, d, *J* = 4.8 Hz, CH_2CH=CH$_2$), 2.24 (3H, s, Ar-CH_3), 0.93 (3H, t, *J* = 7.2 Hz, OCH$_2$CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.2 (C, O-C=O), 153.8 (C), 147.6 (C), 147.3 (C), 146.3 (C), 145.8 (C), 137.0 (C), 134.8 (CH), 134.0 (C), 130.3 (2 x CH), 128.9 (2 x CH), 128.2 (C), 125.5 (C), 123.6 (2 x CH), 123.1 (2 x CH), 120.0 (C), 117.6 (CH$_2$, CH=*C*H$_2$), 61.0 (CH$_2$, O*C*H$_2$CH$_3$), 32.2 (CH$_2$), 32.1 (CH$_2$, *C*H$_2$CH=CH$_2$), 16.8 (CH$_3$, Ar-*C*H$_3$), 13.7 (CH$_3$, OCH$_2$CH$_3$); LRMS m/z 477.00 (M + H$^+$), calcd $C_{26}H_{24}N_2O_7$ 476.1584; Anal. calcd for $C_{26}H_{24}N_2O_7$ (476.15): C, 65.54; H, 5.08; N, 5.88. Found: C, 65.41; H, 5.12; N, 5.81%.



50'lda

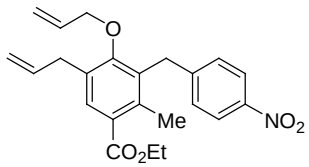


51acaa

5-Allyl-4-allyloxy-3-benzyl-2-methyl-benzoic acid ethyl ester (51acaa): Prepared following the procedure **2D-A** and purified by column chromatography using EtOAc/hexane and isolated as a

light yellow liquid. IR (neat): ν_{max} 2980, 1718 (O-C=O), 1639, 1601, 1494, 1452, 1047, 731 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.63 (1H, s, Ar-*H*), 7.26 (2H, t, *J* = 7.6 Hz), 7.18 (1H, t, *J* = 7.2 Hz), 7.07 (2H, d, *J* = 7.2 Hz), 6.06-5.95 (2H, m, olefinic-*H*), 5.32 (1H, d, *J* = 16.0 Hz, olefinic-*H*), 5.21 (1H, d, *J* = 9.6 Hz, olefinic-*H*), 5.15-5.11 (2H, m, olefinic-*H*), 4.36 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 4.18 (4H, s, OC*H*$_2$CH=CH$_2$, ArC*H*$_2$Ar), 3.48 (2H, d, *J* = 6.0 Hz, C*H*$_2$CH=CH$_2$), 2.39 (3H, s, Ar-C*H*$_3$), 1.39 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.4 (C, O-C=O), 158.5 (C), 140.1 (C), 138.4 (C), 136.8 (CH), 133.5 (C), 133.4 (CH), 130.7 (CH), 130.5 (C), 128.4 (2 x CH), 128.0 (2 x CH), 127.9 (C), 125.8 (CH), 117.3 (CH$_2$, CH=*C*H$_2$), 116.3 (CH$_2$, CH=*C*H$_2$), 74.7 (CH$_2$, O*C*H$_2$CH=CH$_2$), 60.8 (CH$_2$, O*C*H$_2$CH$_3$), 34.0 (CH$_2$), 32.6 (CH$_2$, *C*H$_2$CH=CH$_2$), 17.0 (CH$_3$, Ar-*C*H$_3$), 14.4 (CH$_3$, OCH$_2$CH$_3$); LRMS m/z 351.00 (M + H^+), calcd $C_{23}H_{26}O_3$ 350.1882; Anal. calcd for $C_{23}H_{26}O_3$ (350.18): C, 78.83; H, 7.48. Found: C, 78.71; H, 7.59%.

5-Allyl-4-allyloxy-2-methyl-3-(4-nitrobenzyl)-benzoic acid ethyl ester (51adaa):

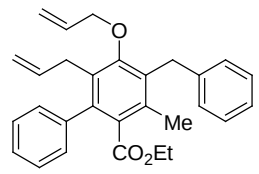


51adaa

Prepared following the procedure **2D-A** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3078, 2980, 2932, 1714 (O-C=O), 1639, 1599, 1568, 1520, 1493, 1109, 1047, 736, 698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.11 (2H, d, *J* = 8.4 Hz), 7.65 (1H, s, Ar-*H*), 7.22 (2H, d, *J* = 8.8 Hz), 6.04-5.95 (2H, m, olefinic-*H*), 5.31 (1H, dd, *J* = 17.2, 1.2 Hz, olefinic-*H*), 5.21 (1H, dd, *J* = 10.4, 1.2 Hz, olefinic-*H*), 5.14-5.08 (2H, m, olefinic-*H*), 4.34 (2H, q, *J* = 7.2 Hz, OC*H*$_2$*C*H$_3$), 4.23 (2H, s, ArC*H*$_2$Ar), 4.21 (2H, d, *J* = 5.2 Hz, OC*H*$_2$*C*H=CH$_2$), 3.45 (2H, d, *J* = 6.4 Hz, C*H*$_2$*C*H=CH$_2$), 2.34 (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 168.1 (C, O-C=O), 158.3 (C), 148.2 (C), 146.3 (C), 138.0 (C), 136.5 (CH), 133.0 (CH), 132.1 (C), 131.4 (CH), 130.8 (C), 128.8 (2 x CH), 128.2 (C), 123.7 (2 x CH), 117.5 (CH$_2$, CH=*C*H$_2$), 116.5 (CH$_2$, CH=*C*H$_2$), 74.7 (CH$_2$, O*C*H$_2$CH=CH$_2$), 61.0 (CH$_2$, O*C*H$_2$CH$_3$), 33.9 (CH$_2$, *C*H$_2$CH=CH$_2$), 32.7 (CH$_2$), 17.0 (CH$_3$, Ar-*C*H$_3$), 14.3 (CH$_3$, OCH$_2$CH$_3$); LRMS

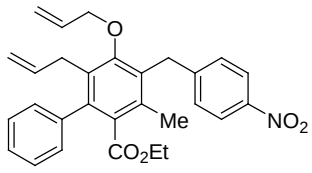
m/z 394.25 (M - H^+), calcd $C_{23}H_{25}NO_5$ 395.1733; Anal. calcd for $C_{23}H_{25}NO_5$ (395.17): C, 69.86; H, 6.37; N, 3.54. Found: C, 69.71; H, 6.31; N, 3.49%.

6-Allyl-5-allyloxy-4-benzyl-3-methyl-biphenyl-2-carboxylic acid ethyl ester (51ecaa): Prepared following the procedure **2D-A** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 2980, 1726 (O-C=O), 1637, 1602, 1562, 1494, 1452, 1186, 702 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40-7.19 (10H, m, Ph-*H*), 6.08-5.98 (1H, m, olefinic-*H*), 5.88-5.78 (1H, m, olefinic-*H*), 5.36 (1H, dd, *J* = 17.2, 1.6 Hz, olefinic-*H*), 5.21 (1H, dd, *J* = 10.4, 1.2 Hz, olefinic-*H*), 4.92 (1H, dd, *J* = 10.0, 1.2 Hz, olefinic-*H*), 4.77 (1H, dd, *J* = 16.8, 1.6 Hz, olefinic-*H*), 4.27 (2H, d, *J* = 5.2 Hz, OC*H*$_2$CH=CH$_2$), 4.22 (2H, s, ArC*H*$_2$Ar), 3.93 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.31 (2H, d, *J* = 5.6 Hz, C*H*$_2$CH=CH$_2$), 2.21 (3H, s, Ar-C*H*$_3$), 0.92 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.7 (C, O-C=O), 156.8 (C), 139.9 (C), 139.3 (C), 138.5 (C), 137.0 (CH), 133.4 (CH), 133.3 (C), 132.2 (C), 131.8 (C), 129.6 (2 x CH), 129.3 (C), 128.3 (2 x CH), 128.0 (2 x CH), 127.5 (2 x CH), 127.2 (CH), 125.8 (CH), 116.8 (CH$_2$, CH=*C*H$_2$), 115.0 (CH$_2$, CH=*C*H$_2$), 74.7 (CH$_2$, O*C*H$_2$CH=CH$_2$), 60.6 (CH$_2$, O*C*H$_2$CH$_3$), 32.6 (CH$_2$), 31.8 (CH$_2$, *C*H$_2$CH=CH$_2$), 16.7 (CH$_3$, Ar-*C*H$_3$), 13.5 (CH$_3$, OCH$_2$CH$_3$); LRMS m/z 427.00 (M + H^+), calcd $C_{29}H_{30}O_3$ 426.2195; Anal. calcd for $C_{29}H_{30}O_3$ (426.21): C, 81.66; H, 7.09. Found: C, 81.45; H, 7.16%.



51ecaa

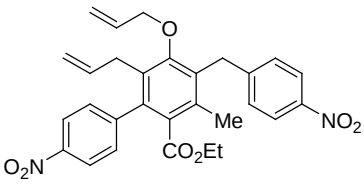
6-Allyl-5-allyloxy-3-methyl-4-(4-nitrobenzyl)-biphenyl-2-carboxylic acid ethyl ester (51edaa): Prepared following the procedure **2D-A** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 2976, 1718 (O-C=O), 1637, 1599, 1520, 1190, 1016, 733 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.15 (2H, d, *J* = 8.8 Hz), 7.36-7.31 (5H, m, Ph-*H*), 7.25 (2H, d, *J* = 7.6 Hz), 6.02-5.92 (1H, m, olefinic-*H*), 5.80-5.70 (1H, m, olefinic-*H*), 5.33 (1H, dd, *J* = 17.2, 0.8 Hz, olefinic-*H*), 5.20 (1H, dd, *J* = 10.4, 1.2 Hz, olefinic-*H*), 4.88 (1H, dd, *J* = 10.0, 1.2 Hz, olefinic-*H*), 4.72 (1H, dd, *J* = 16.8, 1.2 Hz, olefinic-*H*), 4.24 (4H, s,



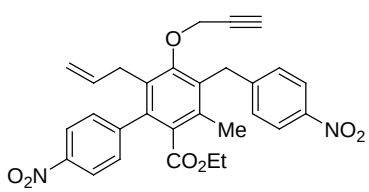
51edaa

OC*H*$_{2C}$H= CH$_2$, ArC*H*$_2$Ar), 3.90 (2H, q, *J* = 7.2 Hz, OC*H*$_2$*C*H$_3$), 3.27 (2H, d, *J* = 5.6 Hz, C*H*$_2$*C*H=CH$_2$), 2.14 (3H, s, Ar-C*H*$_3$), 0.88 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR (CDCl$_3$, DEPT-135) δ 169.6 (C, O-C=O), 156.8 (C), 148.0 (C), 146.4 (C), 140.2 (C), 138.3 (C), 136.8 (CH), 133.3 (CH), 133.0 (C), 132.7 (C), 130.5 (C), 129.8 (C), 129.6 (2 x CH), 128.9 (2 x CH), 127.7 (2 x CH), 127.5 (CH), 123.8 (2 x CH), 117.2 (CH$_2$, CH=*C*H$_2$), 115.3 (CH$_2$, CH=*C*H$_2$), 74.9 (CH$_2$, O*C*H$_2$CH=CH$_2$), 60.9 (CH$_2$, O*C*H$_2$CH$_3$), 32.8 (CH$_2$, *C*H$_2$CH=CH$_2$), 31.9 (CH$_2$), 16.9 (CH$_3$, Ar-*C*H$_3$), 13.6 (CH$_3$, OCH$_2$CH$_3$); LRMS m/z 472.50 (M + H$^+$), calcd $C_{29}H_{29}NO_5$ 471.2046; Anal. calcd for $C_{29}H_{29}NO_5$ (471.20): C, 73.87; H, 6.20; N, 2.97. Found: C, 73.98; H, 6.11; N, 2.85%.

6-Allyl-5-allyloxy-3-methyl-4'-nitro-4-(4-nitrobenzyl)-biphenyl-2-carboxylic acid ethyl ester (51ldaa): Prepared following the procedure **2D-A** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν$_{max}$ 2924, 1726 (O-C=O), 1597, 1520, 1186, 852 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 8.24 (2H, d, *J* = 8.4 Hz), 8.15 (2H, d, *J* = 8.4 Hz), 7.45 (2H, d, *J* = 8.4 Hz), 7.31 (2H, d, *J* = 8.4 Hz), 6.02-5.91 (1H, m, olefinic-*H*), 5.78-5.65 (1H, m, olefinic-*H*), 5.33 (1H, d, *J* = 17.2 Hz, olefinic-*H*), 5.22 (1H, d, *J* = 10.4 Hz, olefinic-*H*), 4.91 (1H, d, *J* = 10.0 Hz, olefinic-*H*), 4.66 (1H, d, *J* = 16.8 Hz, olefinic-*H*), 4.23 (4H, s, OC*H*$_2$CH=CH$_2$, ArC*H*$_2$Ar), 3.92 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.22 (2H, d, *J* = 5.2 Hz, C*H*$_2$CH=CH$_2$), 2.15 (3H, s, Ar-C*H*$_3$), 0.94 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR (CDCl$_3$, DEPT-135) δ 168.9 (C, O-C=O), 156.9 (C), 147.5 (C), 147.2 (C), 146.4 (C), 145.3 (C), 137.8 (C), 136.2 (CH), 133.7 (C), 132.9 (CH), 132.0 (C), 131.7 (C), 130.7 (2 x CH), 129.2 (C), 128.8 (2 x CH), 123.8 (2 x CH), 122.8 (2 x CH), 117.3 (CH$_2$, CH=*C*H$_2$), 115.8 (CH$_2$, CH=*C*H$_2$), 75.0 (CH$_2$, O*C*H$_2$CH=CH$_2$), 61.1 (CH$_2$, O*C*H$_2$CH$_3$), 32.7 (CH$_2$), 31.7 (CH$_2$, *C*H$_2$CH=CH$_2$), 16.9 (CH$_3$, Ar-*C*H$_3$), 13.7 (CH$_3$, OCH$_2$CH$_3$); LRMS m/z 516.00 (M$^+$), calcd $C_{29}H_{28}N_2O_7$ 516.1897; Anal. calcd for $C_{29}H_{28}N_2O_7$ (516.18): C, 67.43; H, 5.46; N, 5.42. Found: C, 67.35; H, 5.36; N, 5.58%.



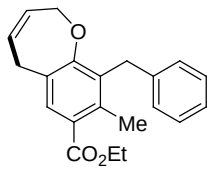
51ldaa



51ldab

6-Allyl-3-methyl-4'-nitro-4-(4-nitrobenzyl)-5-prop-2-ynyloxy-biphenyl-2-carboxylic acid ethyl ester (51ldab): Prepared following the procedure **2D-B** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3292 (C≡C-*H*), 2982, 1724 (O-C=O), 1599, 1521, 1444, 1014, 734 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.23 (2H, d, *J* = 8.4 Hz), 8.14 (2H, d, *J* = 8.0 Hz), 7.44 (2H, d, *J* = 8.4 Hz), 7.32 (2H, d, *J* = 8.0 Hz), 5.73-5.69 (1H, m, olefinic-*H*), 4.93 (1H, d, *J* = 10.0 Hz, olefinic-*H*), 4.69 (1H, d, *J* = 16.8 Hz, olefinic-*H*), 4.45 (2H, s, OCH_2C≡CH), 4.33 (2H, s, ArCH_2Ar), 3.92 (2H, q, *J* = 7.2 Hz, OC$H_2$$CH_3$), 3.26 (2H, s, C$H_2$CH=$CH_2$), 2.53 (1H, s, C≡C *H*), 2.21 (3H, s, Ar-CH_3), 0.94 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.7 (C, O-C=O), 156.1 (C), 147.3 (2 x C), 146.4 (C), 145.1 (C), 137.8 (C), 136.0 (CH), 133.8 (C), 132.5 (C), 132.0 (C), 130.7 (2 x CH), 129.3 (C), 128.8 (2 x CH), 123.7 (2 x CH), 122.8 (2 x CH), 115.9 (CH_2, CH=*C*H_2), 78.1 (C, *C*≡CH), 76.2 (CH, C≡*C*H), 61.9 (CH_2, O*C*H_2C≡CH), 61.1 (CH_2, O*C*$H_2$$CH_3$), 33.0 ($CH_2$), 31.8 ($CH_2$, *C*$H_2$CH=$CH_2$), 16.9 ($CH_3$, Ar-*C*$H_3$), 13.7 ($CH_3$, $OCH_2$$CH_3$); LRMS m/z 515.00 ($M + H^+$), calcd $C_{29}H_{26}N_2O_7$ 514.1740; Anal. calcd for $C_{29}H_{26}N_2O_7$ (514.17): C, 67.70; H, 5.09; N, 5.44. Found: C, 67.85; H, 5.15; N, 5.61%.

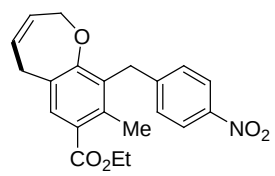
9-Benzyl-8-methyl-2,5-dihydro-benzo[*b*]oxepine-7-carboxylic acid ethyl ester (52acaa): Prepared following the procedure **2E-A** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 2934, 1716 (O-C=O), 1601, 1574, 1493, 1452, 1047, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.54 (1H, s, Ar-*H*), 7.25 (2H, t, *J* = 7.2 Hz), 7.17 (1H, t, *J* = 7.2 Hz), 7.10 (2H, d, *J* = 7.6 Hz), 5.86-5.83 (1H, m, olefinic-*H*), 5.40 (1H, d, *J* = 11.6 Hz, olefinic-*H*), 4.36 (2H, s, OCH_2CH=CH), 4.33 (2H, q, *J* = 7.2 Hz, OC$H_2$$CH_3$), 4.16 (2H, s, ArC$H_2$Ar), 3.50 (2H, br s, C$H_2$CH=CH), 2.44 (3H, s, Ar-CH_3), 1.39 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.2 (C, O-C=O), 159.4 (C), 140.2 (C), 138.4 (C), 133.4 (C), 132.9 (C), 128.9 (CH), 128.3 (2 x CH), 128.0 (2 x CH), 127.0 (C), 126.9 (CH), 125.8 (CH), 125.4 (CH), 70.4 (CH_2, O*C*H_2CH=CH), 60.7 (CH_2, O*C*$H_2$$CH_3$), 32.0 ($CH_2$),



52acaa

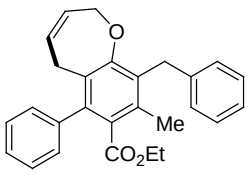
31.5 (CH_2, *C*H_2CH=CH), 16.9 (CH_3, Ar-*C*H_3), 14.3 (CH_3, OCH$_2$*C*H_3); LRMS m/z 323.00 (M + H^+), calcd $C_{21}H_{22}O_3$ 322.1569; Anal. calcd for $C_{21}H_{22}O_3$ (322.15): C, 78.23; H, 6.88. Found: C, 78.35; H, 6.81%.

8-Methyl-9-(4-nitrobenzyl)-2,5-dihydro-benzo[*b*]oxepine-7-carboxylic acid ethyl ester (52adaa): Prepared following the procedure **2E-A** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3080, 2982, 1714 (O-C=O), 1639, 1599, 1568, 1520, 1273, 1109, 1047, 736, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.07 (2H, d, *J* = 8.4 Hz), 7.56 (1H, s, Ar-*H*), 7.24 (2H, d, *J* = 8.8 Hz), 5.84-5.81 (1H, m, olefinic-*H*), 5.40 (1H, dd, *J* = 11.6 Hz, 1.2 Hz, olefinic-*H*), 4.37 (2H, d, *J* = 2.4 Hz, OC*H*$_2$CH=CH), 4.32 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 4.21 (2H, s, ArC*H*$_2$Ar), 3.48 (2H, br s, C*H*$_2$CH=CH), 2.39 (3H, s, Ar-C*H*$_3$), 1.36 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.8 (C, O-C=O), 159.2 (C), 148.2 (C), 146.1 (C), 138.0 (C), 133.2 (C), 131.2 (C), 129.6 (CH), 128.7 (2 x CH), 127.1 (C), 126.6 (CH), 125.5 (CH), 123.4 (2 x CH), 70.2 (CH_2, O*C*H$_2$CH=CH), 60.7 (CH_2, O*C*H$_2$CH$_3$), 32.0 (CH_2), 31.4 (CH_2, *C*H$_2$CH=CH), 16.8 (CH_3, Ar-*C*H$_3$), 14.1 (CH_3, OCH$_2$*C*H$_3$); LRMS m/z 368.10 (M + H^+), calcd $C_{21}H_{21}NO_5$ 367.1420; Anal. calcd for $C_{21}H_{21}NO_5$ (367.14): C, 68.85; H, 5.76; N, 3.81. Found: C, 68.51; H, 5.82; N, 3.75%.



52adaa

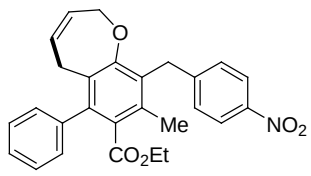
9-Benzyl-8-methyl-6-phenyl-2,5-dihydro-benzo[*b*]oxepine-7-carboxylic acid ethyl ester (52ecaa): Prepared following the procedure **2E-A** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 2976, 1724 (O-C=O), 1601, 1566, 1494, 1452, 1078, 702 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.40-7.17 (10H, m, Ph-*H*), 5.69-5.68 (1H, m, olefinic-*H*), 5.36 (1H, d, *J* = 11.2 Hz, olefinic-*H*), 4.40 (2H, d, *J* = 1.6 Hz, OC*H*$_2$CH=CH), 4.17 (2H, s, ArC*H*$_2$Ar), 3.92 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.27 (2H, d, *J* = 2.8 Hz, C*H*$_2$CH=CH), 2.25 (3H, s, Ar-C*H*$_3$), 0.90 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.9 (C, O-C=O), 157.4 (C), 140.0 (C), 138.6 (C), 136.5 (C), 133.4 (C), 132.7 (C), 131.4



52ecaa

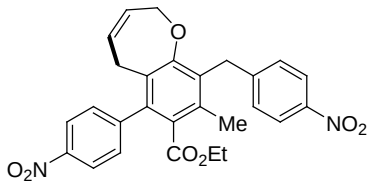
(C), 131.3 (C), 129.5 (2 x CH), 128.3 (2 x CH), 128.2 (2 x CH), 127.8 (2 x CH), 127.3 (CH), 127.2 (CH), 125.8 (CH), 125.6 (CH), 70.7 (CH_2, O*C*H_2CH=CH), 60.7 (CH_2, O*C*H_2CH_3), 32.1 (CH_2), 26.9 (CH_2, *C*H_2CH=CH), 16.7 (CH_3, Ar-*C*H_3), 13.6 (CH_3, OCH_2*C*H_3); LRMS m/z 399.00 ($M + H^+$), calcd $C_{27}H_{26}O_3$ 398.1882; Anal. calcd for $C_{27}H_{26}O_3$ (398.18): C, 81.38; H, 6.58. Found: C, 81.25; H, 6.61%.

8-Methyl-9-(4-nitrobenzyl)-6-phenyl-2,5-dihydro-benzo[*b*]oxepine-7-carboxylic acid ethyl ester (52edaa): Prepared following the procedure **2E-A** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 2976, 1716 (O-C=O), 1637, 1597, 1520, 1184, 1014, 860, 702 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.15 (2H, d, *J* = 7.6 Hz), 7.40-7.34 (5H, m, Ph-*H*), 7.22 (2H, d, *J* = 7.2 Hz), 5.71-5.68 (1H, m, olefinic-*H*), 5.37 (1H, d, *J* = 11.6 Hz, olefinic-*H*), 4.42 (2H, br s, OC*H*$_2$CH=CH), 4.23 (2H, s, ArC*H*$_2$Ar), 3.91 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.25 (2H, br s, C*H*$_2$CH=CH), 2.21 (3H, s, Ar-C*H*$_3$), 0.89 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.6 (C, O-C=O), 157.3 (C), 148.1 (C), 146.4 (C), 138.3 (C), 137.3 (C), 133.6 (C), 132.4 (C), 131.8 (C), 129.7 (C), 129.4 (2 x CH), 129.0 (2 x CH), 127.9 (2 x CH), 127.4 (CH), 127.0 (CH), 125.7 (CH), 123.7 (2 x CH), 70.8 (CH_2, O*C*H_2CH=CH), 60.9 (CH_2, O*C*H_2CH_3), 32.3 (CH_2), 26.9 (CH_2, *C*H_2CH=CH), 16.7 (CH_3, Ar-*C*H_3), 13.6 (CH_3, OCH_2CH_3); LRMS m/z 444.45 ($M + H^+$), calcd $C_{27}H_{25}NO_5$ 443.1733; Anal. calcd for $C_{27}H_{25}NO_5$ (443.17): C, 73.12; H, 5.68; N, 3.16. Found: C, 73.05; H, 5.72; N, 3.25%.



52edaa

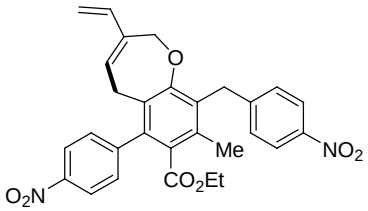
8-Methyl-9-(4-nitrobenzyl)-6-(4-nitrophenyl)-2,5-dihydro-benzo[*b*]oxepine-7-carboxylic acid ethyl ester (52ldaa): Prepared following the procedure **2E-A** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 2918, 1718 (O-C=O), 1643, 1597, 1562, 1520, 1444, 1014, 858 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.26 (2H, d, *J* = 8.4 Hz), 8.14 (2H, d, *J* = 8.4 Hz), 7.43 (2H, d, *J* = 8.8 Hz), 7.34 (2H, d, *J* = 8.4 Hz), 5.68-5.66 (1H, m, olefinic-*H*), 5.40 (1H, d, *J* = 11.2 Hz, olefinic-*H*), 4.44 (2H, s,



52ldaa

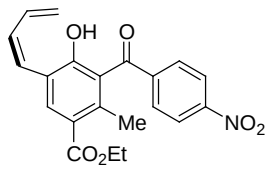
OC*H*$_2$CH=CH), 4.25 (2H, s, ArC*H*$_2$Ar), 3.94 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.19 (2H, br s, C*H*$_2$CH=CH), 2.21 (3H, s, Ar-C*H*$_3$), 0.95 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.1 (C, O-C=O), 157.5 (C), 147.8 (C), 147.3 (C), 146.5 (C), 145.5 (C), 134.9 (C), 133.4 (C), 133.2 (C), 131.2 (C), 131.1 (C), 130.6 (2 x CH), 129.0 (2 x CH), 127.5 (CH), 125.0 (CH), 123.8 (2 x CH), 123.2 (2 x CH), 70.9 (CH_2, O*C*H$_2$CH=CH), 61.2 (CH_2, O*C*H$_2$CH$_3$), 32.3 (CH_2), 27.0 (CH_2, *C*H$_2$CH=CH), 16.8 (CH_3, Ar-*C*H$_3$), 13.7 (CH_3, OCH$_2$*C*H$_3$); LRMS m/z 489.00 (M + H^+), calcd $C_{27}H_{24}N_2O_7$ 488.1584; Anal. calcd for $C_{27}H_{24}N_2O_7$ (488.15): C, 66.39; H, 4.95; N, 5.73. Found: C, 66.25; H, 4.88; N, 5.81%.

8-Methyl-9-(4-nitrobenzyl)-6-(4-nitrophenyl)-3-vinyl-2,5-dihydro-benzo[*b*]oxepine-7-carboxylic acid ethyl ester (52ldab): Prepared following the procedure **2E-B** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 2930, 1724 (O-C=O), 1599, 1520, 1452, 1059, 734, 702 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.28 (2H, d, *J* = 8.4 Hz), 8.17 (2H, d, *J* = 8.0 Hz), 7.43 (2H, d, *J* = 8.4 Hz), 7.36 (2H, d, *J* = 8.4 Hz), 6.17 (1H, dd, *J* = 18.0, 11.2 Hz, olefinic-*H*), 5.76 (1H, br s, olefinic-*H*), 4.90 (1H, d, *J* = 11.2 Hz, olefinic-*H*), 4.77 (1H, d, *J* = 18.0 Hz, olefinic-*H*), 4.66 (2H, s, OC*H*$_2$), 4.23 (2H, s, ArC*H*$_2$Ar), 3.94 (2H, q, *J* = 6.8 Hz, OC*H*$_2$CH$_3$), 3.27 (2H, d, *J* = 4.8 Hz, C*H*$_2$CH=CH), 2.21 (3H, s, Ar-C*H*$_3$), 0.95 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.9 (C, O-C=O), 157.2 (C), 147.5 (C), 147.3 (C), 146.5 (C), 145.2 (C), 136.9 (CH), 135.9 (C), 134.7 (C), 133.4 (C), 132.6 (C), 131.4 (C), 130.8 (C), 130.5 (2 x CH), 129.0 (2 x CH), 127.1 (CH), 123.8 (2 x CH), 123.2 (2 x CH), 111.3 (CH_2, CH=*C*H$_2$), 70.6 (CH_2, O*C*H$_2$CH=CH), 61.2 (CH_2, O*C*H$_2$CH$_3$), 32.2 (CH_2), 26.7 (CH_2, *C*H$_2$CH=CH), 16.8 (CH_3, Ar-*C*H$_3$), 13.7 (CH_3, OCH$_2$*C*H$_3$); LRMS m/z 513.00 (M - H^+), calcd $C_{29}H_{26}N_2O_7$ 514.1740; Anal. calcd for $C_{29}H_{26}N_2O_7$ (514.17): C, 67.70; H, 5.09; N, 5.44. Found: C, 67.85; H, 5.15; N, 5.56%.



52ldab

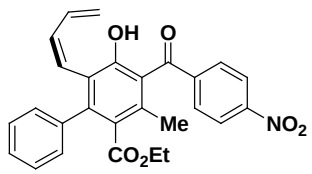
5-Buta-1,3-dienyl-4-hydroxy-2-methyl-3-(4-nitrobenzoyl)-benzoic acid ethyl ester (53adaa): Prepared following the



53adaa

procedure **2F** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3402 (O-*H*), 2928, 1714 (O-C=O), 1684 (C=O), 1601, 1531, 1456, 1230, 1163 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.31 (2H, d, *J* = 8.4 Hz), 7.99 (1H, s, Ar-*H*), 7.98 (2H, d, *J* = 8.4 Hz), 7.08 (1H, s, O-*H*), 6.53-6.39 (3H, m, olefinic-*H*), 5.47 (1H, d, *J* = 15.6 Hz, olefinic-*H*), 5.33 (1H, d, *J* = 9.2 Hz, olefinic-*H*), 4.35 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 2.32 (3H, s, Ar-C*H*$_3$), 1.39 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 197.0 (C=O), 166.6 (C, O-C=O), 154.7 (C), 150.6 (C), 142.6 (C), 139.5 (C), 135.2 (CH), 134.6 (CH), 132.1 (CH), 130.1 (2 x CH), 125.7 (C), 124.1 (2 x CH), 123.3 (C), 122.6 (CH), 122.5 (C), 122.0 (CH_2, CH=*C*H$_2$), 61.0 (CH_2, O*C*H$_2$CH$_3$), 19.9 (CH_3, Ar-*C*H$_3$), 14.3 (CH_3, OCH$_2$*C*H$_3$); LRMS m/z 382.25 (M + H^+), calcd $C_{21}H_{19}NO_6$ 381.1212; Anal. calcd for $C_{21}H_{19}NO_6$ (381.12): C, 66.13; H, 5.02; N, 3.67. Found: C, 66.25; H, 5.10; N, 3.81%; HRMS m/z 404.1110 (M + Na), calcd for $C_{21}H_{19}NO_6Na$ 404.1110.

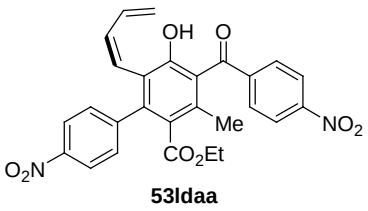
6-Buta-1,3-dienyl-5-hydroxy-3-methyl-4-(4-nitrobenzoyl)-biphenyl-2-carboxylic acid ethyl ester (53edaa): Prepared following the procedure **2F** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3407 (O-*H*), 2976, 1718 (O-C=O), 1682 (C=O), 1531, 1454, 1232, 1008, 848, 704 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.33 (2H, d, *J* = 8.8 Hz), 8.07 (2H, d, *J* = 8.8 Hz), 7.41-7.35 (3H, m, Ph-*H*), 7.22-7.20 (2H, m, Ph-*H*), 6.37-6.27 (2H, m, olefinic-*H*), 5.86 (1H, s, O-*H*), 5.84 (1H, d, *J* = 9.6 Hz, olefinic-*H*), 5.39 (1H, d, *J* = 16.8 Hz, olefinic-*H*), 5.31 (1H, d, *J* = 10.0 Hz, olefinic-*H*), 3.93 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 2.19 (3H, s, Ar-C*H*$_3$), 0.87 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 195.4 (C=O), 168.6 (C, O-C=O), 150.6 (C), 150.2 (C), 142.1 (C), 141.9 (C), 138.0 (C), 135.2 (CH), 133.9 (C), 131.9 (CH), 130.3 (2 x CH), 129.1 (2 x CH), 128.6 (C), 128.0 (2 x CH), 127.9 (CH), 124.8 (C), 124.0 (2 x CH), 123.1 (CH), 122.7 (CH_2, CH=*C*H$_2$), 120.7 (C), 61.1 (CH_2, O*C*H$_2$CH$_3$), 17.1 (CH_3, Ar-*C*H$_3$), 13.5 (CH_3, OCH$_2$*C*H$_3$); LRMS m/z 457.40 (M^+), calcd $C_{27}H_{23}NO_6$ 457.1525; Anal. calcd



53edaa

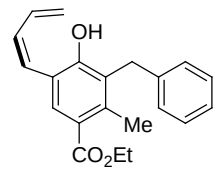
for $C_{27}H_{23}NO_6$ (457.15): C, 70.89; H, 5.07; N, 3.06. Found: C, 70.69; H, 5.12; N, 3.12 %; HRMS m/z 480.1422 (M + Na), calcd for $C_{27}H_{23}NO_6Na$ 480.1423.

6-Buta-1,3-dienyl-5-hydroxy-3-methyl-4'-nitro-4-(4-nitrobenzoyl)-biphenyl-2-carboxylic acid ethyl ester (53ldaa): Prepared following the procedure **2F** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3429 (O-*H*), 2980, 1722 (O-C=O), 1682, 1601, 1525, 1446, 1055, 736 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.34 (2H, d, *J* = 8.4 Hz), 8.24 (2H, d, *J* = 8.0 Hz), 8.07 (2H, d, *J* = 8.4 Hz), 7.41 (2H, d, *J* = 8.4 Hz), 6.38 (1H, t, *J* = 10.8 Hz, olefinic-*H*), 6.31-6.21 (1H, m, olefinic-*H*), 5.90 (1H, s, O-*H*), 5.79 (1H, d, *J* = 10.8 Hz, olefinic-*H*), 5.43 (1H, d, *J* = 16.4 Hz, olefinic-*H*), 5.36 (1H, d, *J* = 10.0 Hz, olefinic-*H*), 3.97 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 2.20 (3H, s, Ar-C*H*$_3$), 0.95 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 195.0 (C, C=O), 167.9 (C, O-C=O), 150.7 (C), 150.5 (C), 147.4 (C), 145.0 (C), 141.6 (C), 139.7 (C), 136.5 (CH), 134.6 (C), 131.4 (CH), 130.3 (4 x CH), 128.1 (C), 125.8 (C), 124.1 (2 x CH), 123.8 (CH_2, CH=*C*H$_2$), 123.2 (2 x CH), 121.8 (CH), 120.5 (C), 61.4 (CH_2, O*C*H$_2$CH$_3$), 17.2 (CH_3, Ar-*C*H$_3$), 13.7 (CH_3, OCH$_2$*C*H$_3$); LRMS m/z 503.00 (M + H^+), calcd $C_{27}H_{22}N_2O_8$ 502.1376; Anal. calcd for $C_{27}H_{22}N_2O_8$ (502.13): C, 64.54; H, 4.41; N, 5.58. Found: C, 64.71; H, 4.47; N, 5.48%; HRMS m/z 525.1147 (M + Na), calcd for $C_{27}H_{22}N_2O_8Na$ 525.1274.



53ldaa

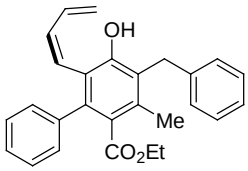
3-Benzyl-5-buta-1,3-dienyl-4-hydroxy-2-methyl-benzoic acid ethyl ester (54acaa): Prepared following the procedure **2F** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3423 (O-*H*), 2930, 1712 (O-C=O), 1562, 1494, 1452, 1047, 781, 698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.67 (1H, s, Ar-*H*), 7.27 (2H, t, *J* = 7.2 Hz), 7.19 (1H, t, *J* = 6.8 Hz), 7.17 (2H, d, *J* = 7.2 Hz), 6.53-6.46 (2H, m, olefinic-*H*), 6.40 (1H, d, *J* = 9.6 Hz, olefinic-*H*), 5.59 (1H, s, O-*H*), 5.45 (1H, d, *J* = 14.8 Hz, olefinic-*H*), 5.31 (1H, d, *J* = 11.6 Hz, olefinic-*H*), 4.34 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 4.18 (2H, s, ArC*H*$_2$Ar), 2.53 (3H, s, Ar-C*H*$_3$), 1.39 (3H, t, *J* = 7.2 Hz,



54acaa

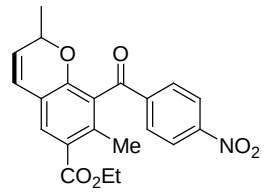
OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.1 (C, O-C=O), 153.7 (C), 140.2 (C), 139.6 (C), 134.6 (CH), 132.4 (CH), 130.5 (CH), 128.3 (2 x CH), 128.0 (2 x CH), 126.5 (C), 125.8 (CH), 123.9 (CH), 123.3 (C), 121.3 (CH_2, CH=CH_2), 120.4 (C), 60.6 (CH_2, OCH_2CH_3), 31.9 (CH_2), 16.9 (CH_3, Ar-CH_3), 14.2 (CH_3, OCH_2CH_3); LRMS m/z 323.00 (M + H^+), calcd $C_{21}H_{22}O_3$ 322.1569; Anal. calcd for $C_{21}H_{22}O_3$ (322.15): C, 78.23; H, 6.88. Found: C, 78.11; H, 6.96%; HRMS m/z 345.1461 (M + Na), calcd for $C_{21}H_{22}O_3Na$ 345.1467.

4-Benzyl-6-buta-1,3-dienyl-5-hydroxy-3-methyl-biphenyl-2-carboxylic acid ethyl ester (54ecaa): Prepared following the procedure **2F** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3522 (O-*H*), 2961, 1722 (O-C=O), 1601, 1556, 1494, 1450, 1047, 760, 702 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.34-7.21 (10H, m, Ph-*H*), 6.39-6.34 (2H, m, olefinic-*H*), 5.94 (1H, d, *J* = 9.2 Hz, olefinic-*H*), 5.61 (1H, s, O-*H*), 5.41 (1H, d, *J* = 14.8 Hz, olefinic-*H*), 5.32 (1H, d, *J* = 8.8 Hz, olefinic-*H*), 4.19 (2H, s, ArCH_2Ar), 3.93 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 2.13 (3H, s, Ar-CH_3), 0.88 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.8 (C, O-C=O), 150.9 (C), 139.9 (C), 138.9 (C), 137.9 (C), 135.0 (C), 134.5 (CH), 132.4 (CH), 129.4 (2 x CH), 128.3 (2 x CH), 128.2 (2 x CH), 127.8 (C), 127.7 (2 x CH), 127.2 (CH), 125.8 (CH), 125.0 (CH), 124.9 (C), 121.7 (CH_2, CH=CH_2), 119.5 (C), 60.7 (CH_2, OCH_2CH_3), 32.2 (CH_2), 16.7 (CH_3, Ar-CH_3), 13.5 (CH_3, $OCH_{2C}H_3$); LRMS m/z 399.00 (M + H^+), calcd $C_{27}H_{26}O_3$ 398.1882; Anal. calcd for $C_{27}H_{26}O_3$ (398.18): C, 81.38; H, 6.58. Found: C, 81.42; H, 6.51%; HRMS m/z 421.1785 (M + Na), calcd for $C_{27}H_{26}O_3Na$ 421.1780.



54ecaa

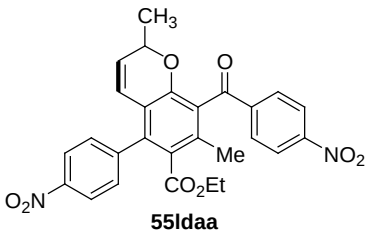
2,7-Dimethyl-8-(4-nitrobenzoyl)-2*H*-chromene-6-carboxylic acid ethyl ester (55adaa): Prepared following the procedure **2G-A** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. Mp.: 148 °C.; IR (neat): ν_{max} 3055, 2926, 1714 (O-C=O), 1698 (C=O), 1570, 1531, 1456, 1259, 1049, 748 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.30 (2H, d, *J* = 8.8 Hz), 8.00 (2H, d, *J*



55adaa

= 8.8 Hz), 7.69 (1H, s, Ar-*H)*, 6.41 (1H, d, *J* = 10.0 Hz, olefinic-*H*), 5.67 (1H, dd, *J* = 10.0, 3.6 Hz, olefinic-*H*), 4.90-4.88 (1H, m, OC*H*), 4.35 (2H, q, *J* = 7.2 Hz, OC$H_2$$CH_3$), 2.36 (3H, s, Ar-C$H_3$), 1.39 (3H, t, *J* = 7.2 Hz, OCH_2CH_3), 1.17 (3H, d, *J* = 6.8 Hz, OCHCH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 195.5 (C=O), 166.7 (C, O-C=O), 153.0 (C), 150.6 (C), 141.7 (C), 139.0 (C), 130.15 (2 x CH), 130.11 (CH), 127.8 (C), 127.2 (CH), 123.9 (2 x CH), 123.6 (C), 122.0 (CH), 119.1 (C), 72.7 (CH, O-*C*H), 60.9 (CH_2, O*C*$H_2$$CH_3$), 21.5 ($CH_3$), 18.0 ($CH_3$, Ar-*C*$H_3$), 14.3 ($CH_3$, $OCH_2$$CH_3$); LRMS m/z 381.60 (M + H^+), calcd $C_{21}H_{19}NO_6$ 381.1212; Anal. calcd for $C_{21}H_{19}NO_6$ (381.12): C, 66.13; H, 5.02; N, 3.67. Found: C, 66.34; H, 5.08; N, 3.58%; HRMS m/z 404.1111 (M + Na), calcd for $C_{21}H_{19}NO_6Na$ 404.1110.

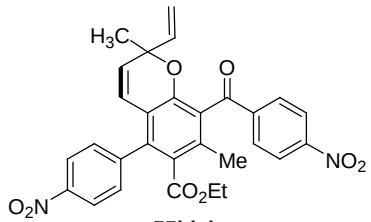
2,7-Dimethyl-8-(4-nitrobenzoyl)-5-phenyl-2*H*-chromene-6-carboxylic acid ethyl ester (55edaa): Prepared following the procedure **2G-A** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3063, 2978, 1724 (O-C=O), 1698 (C=O), 1527, 1234, 1008 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.33 (2H, d, *J* = 8.8 Hz), 8.08 (2H, d, *J* = 8.8 Hz), 7.43-7.38 (3H, m, Ph-*H*), 7.28-7.26 (2H, m, Ph-*H*), 6.11 (1H, dd, *J* = 8.8, 1.2 Hz, olefinic-*H*), 5.57 (1H, dd, *J* = 10.0, 3.2 Hz, olefinic-*H*), 4.80-4.78 (1H, m, OC*H*), 3.93 (2H, q, *J* = 7.2 Hz, OC$H_2$$CH_3$), 2.17 (3H, s, Ar-C$H_3$), 1.15 (3H, d, *J* = 6.8 Hz, OCHCH_3), 0.89 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 195.3 (C=O), 168.7 (C, O-C=O), 151.3 (C), 150.5 (C), 141.9 (C), 138.7 (C), 136.9 (C), 133.5 (C), 130.2 (2 x CH), 129.5 (2 x CH), 128.7 (C), 128.1 (2 x CH), 127.9 (CH), 126.9 (CH), 126.1 (C), 123.9 (2 x CH), 120.9 (CH), 118.3 (C), 71.6 (CH, O*C*H), 61.0 (CH_2, O*C*$H_2$$CH_3$), 21.0 ($CH_3$), 16.8 ($CH_3$, Ar-*C*$H_3$), 13.6 ($CH_3$, $OCH_2$$CH_3$); LRMS m/z 457.40 ($M^+$), calcd $C_{27}H_{23}NO_6$ 457.1526; Anal. calcd for $C_{27}H_{23}NO_6$ (457.15): C, 70.89; H, 5.07; N, 3.06. Found: C, 70.81; H, 5.16; N, 3.16%; HRMS m/z 480.1424 (M + Na), calcd for $C_{27}H_{23}NO_6Na$ 480.1423.



55ldaa

2,7-Dimethyl-8-(4-nitrobenzoyl)-5-(4-nitrophenyl)-2*H*-chromene-6-carboxylic acid ethyl ester (55ldaa): Prepared following the procedure **2G-A** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 2928, 1724 (O-C=O), 1682, 1599, 1523, 1446, 1008, 706 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.34 (2H, d, *J* = 8.0 Hz), 8.30 (2H, d, *J* = 8.0 Hz), 8.08 (2H, d, *J* = 7.6 Hz), 7.48 (2H, d, *J* = 8.0 Hz), 5.96 (1H, d, *J* = 10.0 Hz, olefinic-*H*), 5.63 (1H, dd, *J* = 10.0, 2.4 Hz, olefinic-*H*), 4.83 (1H, br s, OC*H*), 3.97 (2H, q, *J* = 6.8 Hz, OC$H_2$$CH_3$), 2.17 (3H, s, Ar-C$H_3$), 1.18 (3H, d, *J* = 6.4 Hz, OCHCH_3), 0.96 (3H, t, *J* = 6.8 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 194.8 (C, C=O), 168.0 (C, O-C=O), 151.3 (C), 150.6 (C), 147.5 (C), 144.0 (C), 141.5 (C), 136.1 (C), 134.1 (C), 130.6 (2 x CH), 130.2 (2 x CH), 128.0 (CH), 128.0 (C), 127.1 (C), 123.9 (2 x CH), 123.3 (2 x CH), 119.9 (CH), 118.0 (C), 71.8 (CH, O-*C*H), 61.3 (CH_2, O*C*$H_2$$CH_3$), 20.9 ($CH_3$), 16.9 ($CH_3$, Ar-*C*$H_3$), 13.7 ($CH_3$, OCH_2CH_3); LRMS m/z 502.35 (M^+), calcd $C_{27}H_{22}N_2O_8$ 502.1376; Anal. calcd for $C_{27}H_{22}N_2O_8$ (502.13): C, 64.54; H, 4.41; N, 5.58. Found: C, 64.67; H, 4.38; N, 5.65 %; HRMS m/z 525.1273 (M + Na), calcd for $C_{27}H_{22}N_2O_8Na$ 525.1274.

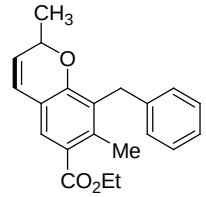
2,7-Dimethyl-8-(4-nitrobenzoyl)-5-(4-nitrophenyl)-2-vinyl-2*H*-chromene-6-carboxylic acid ethyl ester (55ldab): Prepared following the procedure **2G-B** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 3106, 3079, 2982, 1707 (O-C=O), 1684, 1526, 1346, 1233, 1181, 845 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.34 (2H, d, *J* = 8.8 Hz), 8.31 (2H, d, *J* = 8.8 Hz), 8.06 (2H, d, *J* = 8.8 Hz), 7.49 (2H, d, *J* = 8.8 Hz), 6.02 (1H, d, *J* = 10.0 Hz, olefinic-*H*), 5.58 (1H, d, *J* = 10.4 Hz, olefinic-*H*), 5.54 (1H, d, *J* = 10.4 Hz, olefinic-*H*), 5.09-5.05 (2H, m, olefinic-*H*), 3.98 (2H, q, *J* = 7.2 Hz, OC$H_2$$CH_3$), 2.17 (3H, s, Ar-C$H_3$), 1.29 (3H, s, C$H_3$), 0.96 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 194.9 (C, C=O), 168.1 (C, O-C=O), 150.8 (C), 150.7 (C), 147.6 (C), 144.0 (C), 141.6 (C), 139.1 (CH), 136.1 (C), 134.1 (C), 130.9 (CH), 130.4 (CH), 130.3 (2 x CH), 129.1 (CH), 128.0 (C), 127.3 (C), 123.9 (2 x CH), 123.4 (2 x CH), 119.9 (CH), 117.7 (C), 115.5 (CH_2, CH=*C*H_2),



55ldab

78.7 (C), 61.3 (CH_2, O*C*H_2CH_3), 26.8 (CH_3), 16.9 (CH_3, Ar-*C*H_3), 13.8 (CH_3, $OCH_{2C}H_3$); LRMS m/z 529.00 (M + H^+), calcd $C_{29}H_{24}N_2O_8$ 528.1153; Anal. calcd for $C_{29}H_{24}N_2O_8$ (528.11): C, 65.90; H, 4.58; N, 5.30. Found: C, 65.78; H, 4.51; N, 5.45%; HRMS m/z 551.1435 (M + Na), calcd for $C_{29}H_{24}N_2O_8Na$ 551.1430.

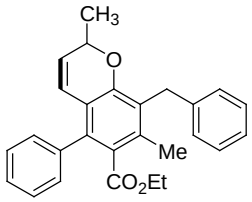
8-Benzyl-2,7-dimethyl-2*H*-chromene-6-carboxylic acid ethyl ester (56acaa):



56acaa

Prepared following the procedure **2G-A** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3026, 2978, 1712 (O-C=O), 1641, 1452, 1385, 1049, 783 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.48 (1H, s, Ar-*H)*, 7.25 (2H, t, *J* = 7.2 Hz), 7.16 (1H, t, *J* = 6.8 Hz), 7.13 (2H, d, *J* = 7.6 Hz), 6.41 (1H, d, *J* = 10.0 Hz, olefinic-*H*), 5.69 (1H, dd, *J* = 10.0, 3.2 Hz, olefinic-*H*), 5.02-4.98 (1H, m, OC*H*), 4.32 (2H, q, *J* = 7.2 Hz, OC$H_2$$CH_3$), 4.09 (2H, s, ArC$H_2$Ar), 2.45 (3H, s, Ar-C$H_3$), 1.38 (3H, t, *J* = 7.2 Hz, OCH_2CH_3), 1.34 (3H, d, *J* = 6.8 Hz, OCHCH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.0 (C, O-C=O), 154.1 (C), 140.7 (C), 140.2 (C), 128.2 (2 x CH), 128.1 (2 x CH), 127.6 (C), 127.1 (CH), 126.4 (CH), 125.6 (CH), 123.5 (C), 123.2 (CH), 118.6 (C), 72.0 (CH, O-*C*H), 60.5 (CH_2, O*C*H_2CH_3), 31.3 (CH_2), 21.4 (CH_3), 17.0 (CH_3, Ar-*C*H_3), 14.3 (CH_3, OCH_2CH_3); LRMS m/z 323.00 (M + H^+), calcd $C_{21}H_{22}O_3$ 322.1569; Anal. calcd for $C_{21}H_{22}O_3$ (322.15): C, 78.23; H, 6.88. Found: C, 78.45; H, 6.75%; HRMS m/z 323.1646 (M + H), calcd for $C_{21}H_{22}O_3H$ 323.1647.

8-Benzyl-2,7-dimethyl-5-phenyl-2*H*-chromene-6-carboxylic acid ethyl ester (56ecaa): Prepared following the procedure **2G-A** and purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 2976, 1722 (O-C=O), 1635, 1494, 1452, 1030, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.39-7.17 (10H, m, Ph-*H*), 6.14 (1H, d, *J* = 10.0 Hz, olefinic-*H*), 5.61 (1H, dd, *J* = 10.0, 3.2 Hz, olefinic-*H*), 4.94-4.92 (1H, m, OC*H*), 4.11 (2H, s, ArCH_2Ar), 3.93 (2H, q, *J* = 7.2 Hz, OC$H_2$$CH_3$), 2.26 (3H, s, Ar-C$H_3$), 1.36 (3H, d, *J* = 6.4 Hz, OCHCH_3), 0.88 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.9 (C, O-C=O),



56ecaa

152.2 (C), 140.2 (C), 137.8 (C), 135.2 (C), 134.8 (C), 129.8 (2 x CH), 128.3 (2 x CH), 128.2 (2 x CH), 128.0 (C), 127.8 (2 x CH), 127.3 (CH), 126.4 (C), 126.2 (CH), 125.6 (CH), 121.9 (CH), 118.0 (C), 70.9 (CH, O-*C*H), 60.6 (CH_2, O*C*H_2CH_3), 31.6 (CH_2), 20.9 (CH_3), 16.9 (CH_3, Ar-*C*H_3), 13.5 (CH_3, OCH_2CH_3); LRMS m/z 399.00 (M + H^+), calcd $C_{27}H_{26}O_3$ 398.1882; Anal. calcd for $C_{27}H_{26}O_3$ (398.18): C, 81.38; H, 6.58. Found: C, 81.45; H, 6.52%; HRMS m/z 421.1783 (M + Na), calcd for $C_{27}H_{26}O_3Na$ 421.1780.

3A: General Experimental Procedures for the Synthesis of Highly Functionalized 2,5-Dihydro-benzo[*b*]oxepines 72a-g: The syntheses of highly functionalized 2,5-dihydro-benzo[*b*]oxepines **72a-g** from corresponding Hagemann's esters **44a-g** involves the following four-step sequence (see Annexure-I, Table A1 and all yields represents column purified products).

Piperidine/K_2CO_3-Catalyzed Three-Component Enamine Amination/Iso-Aromatization/Alkylation (EA/IA/A) Reactions in One-Pot: In an ordinary glass vial equipped with a magnetic stirring bar, to 0.6 mmol of the Hagemann's esters **44** were added 1.0 mL of DMF, and then the catalyst piperidine (0.03 mmol, 2.96 μL) was added and the reaction mixture was stirred at RT for the 0.5 h; then 0.3 mmol of nitrosobenzene **46** was added in one-portion and the reaction mixture was stirred at RT for 1 h. To the reaction mixture, allyl bromide (108.9 mg, 0.9 mmol) and K_2CO_3 (414.6 mg, 3 mmol) was added and stirring continued at RT for 24 h. The crude reaction mixture was worked up with aqueous NH_4Cl solution and the aqueous layer was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure one-pot products **69** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

***C*-Allylation through Claisen Rearrangement:** One-pot EA/IA/A compounds **69** (0.3 mmol) and solvent DMF (0.3 mL, 1 M) were taken in a sealed glass tube and the mixture is heated at 190 °C under N_2 for 16 to 18 h. Upon cooling the reaction mixture to RT, the mixture was diluted with CH_2Cl_2 (10 mL), washed with aqueous NH_4Cl solution (2 mL) and brine (2 mL). The separated organic layer was dried (Na_2SO_4),

filtered, and concentrated under reduced pressure. Pure products **70** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

***O*-Allylation:** The corresponding phenols **70 (**0.3 mmol**)** were allylated by treatment with allyl bromide (43.6 mg, 0.36 mmol) and K_2CO_3 (62.2 mg, 0.45 mmol) in EtOH (3 mL, 0.1 M) at RT for 24 h. The crude reaction mixture was worked up with aqueous NH_4Cl solution and the aqueous layer was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure products **71** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

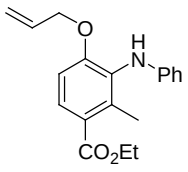
RCM Reaction: A 10 mL oven-dried round bottom flask equipped with a stirring bar was charged with diene amine **71** (0.1 mmol) and Grubbs' first generation catalyst **4n** (1.6 mg, 0.002 mmol, 2 mol %) in a dry CH_2Cl_2 (2 mL, 0.05 M) and the reaction mixture was stirred under N_2 at RT for 2 to 6 h. Solvent CH_2Cl_2 was distilled off at ambient pressure and the crude reaction mixture was directly loaded on silica gel column and pure RCM products **72** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

3B: Experimental Procedure for the Synthesis of Enyne Amine 71h: To a stirred solution of compound **70a** (0.3 mmol) in EtOH (3 mL, 0.1 M) was added K_2CO_3 (62.2 mg, 0.45 mmol, 1.5 equiv). After stirring for 0.16 h, propargyl bromide (42.82 mg, 0.36 mmol, 1.2 equiv) was added to the reaction mixture and the reaction mixture was stirred for 24 h at RT. The crude reaction mixture was worked up with aqueous NH_4Cl solution and the aqueous layer was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure enyne amine product **71h** was obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

3C: Experimental Procedure for the Synthesis of Highly Substituted 3-Vinyl-2,5-dihydro-benzo[*b*]oxepine 72h: A 10 mL oven-dried round bottom flask equipped with a stirring bar was charged with enyne amine **71h** (0.1 mmol), dry CH_2Cl_2 (2 mL, 0.05 M) and Grubbs' first generation catalyst **4n** (1.6 mg, 0.002 mmol, 2 mol %). The

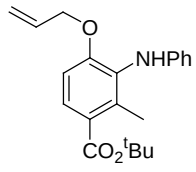
reaction mixture was stirred under N_2 at RT for 12 h. Solvent CH_2Cl_2 was distilled off at ambient pressure and the crude reaction mixture was directly loaded on silica gel column and pure RCM product **72h** was obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

4-Allyloxy-2-methyl-3-phenylamino-benzoic acid ethyl ester (69a): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3387 (N-*H)*, 2928, 1709 (O-C=O), 1601, 1498, 1267, 1055, 748, 694 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.77 (1H, d, *J* = 8.8 Hz), 7.18 (2H, t, *J* = 8.4 Hz), 6.82 (1H, d, *J* = 8.8 Hz), 6.81 (1H, t, *J* = 8.8 Hz), 6.62 (2H, d, *J* = 7.6 Hz), 5.95 (1H, m, olefinic-*H*), 5.72 (1H, s, N-*H*), 5.28 (1H, dd, *J* = 17.6 Hz, 4.0 Hz), 5.23 (1H, dd, *J* = 17.6 Hz, 4.0 Hz), 4.56 (2H, m), 4.36 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 2.42 (3H, s, Ar-C*H*$_3$), 1.39 (3H, t, *J* = 6.8 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.6 (C, O-C=O), 155.5 (C), 145.9 (C), 137.5 (C), 132.5 (CH), 130.6 (C), 129.0 (2 x CH), 128.0 (CH), 123.9 (C), 119.4 (CH), 117.8 (CH_2, CH=*C*H$_2$), 115.2 (2 x CH), 108.9 (CH), 69.1 (CH_2, O*C*H$_2$CH=CH$_2$), 60.6 (CH_2, O*C*H$_2$CH$_3$), 16.5 (CH_3, Ar-*C*H$_3$), 14.4 (CH_3, OCH$_2$C*H*$_3$); LRMS m/z 312.20 (M + H^+), calcd $C_{19}H_{21}NO_3$ 311.1524; HRMS m/z 334.1406 (M + Na^+), calcd $C_{19}H_{21}NO_3Na^+$ 334.1419.



69a

4-Allyloxy-2-methyl-3-phenylamino-benzoic acid methyl ester (69b): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3381 (N-*H)*, 3018, 2949, 1714 (O-C=O), 1604, 1423, 1269, 1055, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.79 (1H, d, *J* = 8.8 Hz), 7.19 (2H, t, *J* = 8.0 Hz), 6.84 (1H, t, *J* = 8.0 Hz), 6.81 (1H, d, *J* = 8.8 Hz), 6.63 (2H, d, *J* = 7.6 Hz), 5.99-5.92 (1H, m, olefinic-*H*), 5.74 (1H, s, N-*H*), 5.30 (1H, dd, *J* = 17.6, 1.6 Hz), 5.24 (1H, dd, *J* = 11.0, 1.6 Hz), 4.57 (2H, d, *J* = 3.6 Hz, OC*H*$_2$CH=CH$_2$), 3.88 (3H, s, OC*H*$_3$), 2.44 (3H, s, Ar-C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.0 (C, O-C=O), 155.6 (C), 145.8 (C), 137.7 (C), 132.4 (CH), 130.5 (C), 128.9 (2 x CH), 128.1 (CH), 123.5 (C), 119.4 (CH), 117.8 (CH_2, CH=*C*H$_2$), 115.1



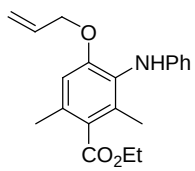
69b

69c

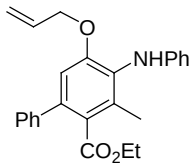
(2 x CH), 108.9 (CH), 69.1 (CH_2, O*C*H_2CH=CH_2), 51.7 (CH_3, O*C*H_3), 16.4 (CH_3, Ar-*C*H_3); GCMS m/z 297.15 (M^+), calcd $C_{18}H_{19}NO_3$ 297.3484.

4-Allyloxy-2-methyl-3-phenylamino-benzoic acid tert-butyl ester (69c): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3391 (N-*H)*, 2976, 2932, 1701 (O-C=O), 1602, 1500, 1367, 1066, 748, 694 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.71 (1H, d, *J* = 8.8 Hz), 7.19 (2H, t, *J* = 7.6 Hz), 6.83 (1H, t, *J* = 7.6 Hz), 6.81 (1H, d, *J* = 8.8 Hz), 6.64 (2H, d, *J* = 8.4 Hz), 5.99-5.92 (1H, m, olefinic-*H*), 5.73 (1H, s, N-*H*), 5.30 (1H, d, *J* = 17.6 Hz), 5.23 (1H, d, *J* = 10.4 Hz), 4.56 (2H, d, *J* = 4.8 Hz, OC*H*$_2$CH=CH_2), 2.42 (3H, s, Ar-C*H*$_3$), 1.61 (9H, s, OC(C*H*$_3$)$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.1 (C, O-C=O), 155.2 (C), 145.9 (C), 136.9 (C), 132.5 (CH), 130.4 (C), 128.9 (2 x CH), 127.8 (CH), 125.7 (C), 119.2 (CH), 117.7 (CH_2, CH=*C*H_2), 115.1 (2 x CH), 108.9 (CH), 80.7 (C, O*C*(C*H*$_3$)$_3$), 69.1 (CH_2, O*C*H_2CH=CH_2), 28.3 (3 x CH_3, OC(*C*H_3)$_3$), 16.4 (CH_3, Ar-*C*H_3); GCMS m/z 339.20 (M^+), calcd $C_{21}H_{25}NO_3$ 339.4281.

4-Allyloxy-2,6-dimethyl-3-phenylamino-benzoic acid ethyl ester (69d): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. Mp 42 °C; IR (neat): ν_{max} 3391 (N-*H)*, 2928, 1720 (O-C=O), 1602, 1498, 1265, 1053, 748, 694 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.16 (2H, t, *J* = 7.6 Hz), 6.79 (1H, d, *J* = 7.6 Hz), 6.62 (1H, s), 6.60 (2H, d, *J* = 7.6 Hz), 5.92 (1H, m, OCH_2C*H*=CH_2), 5.56 (1H, s, N-*H*), 5.25 (1H, br d, *J* = 17.6 Hz, olefinic-*H*), 5.19 (1H, br d, *J* = 17.6 Hz, olefinic-*H*) 4.49 (2H, m), 4.38 (2H, q, *J* = 7.2 Hz, OC*H*$_2$$CH_3$), 2.33 (3H, s, Ar-C*H*$_3$), 2.15 (3H, s, Ar-C*H*$_3$), 1.38 (3H, t, *J* =7.2 Hz, OCH_2C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.8 (C, O-C=O), 153.4 (C), 146.2 (C), 132.8 (CH), 132.2 (C), 128.9 (2 x CH), 128.8 (C), 127.9 (C), 127.7 (C), 119.0 (CH), 117.4 (CH_2, CH=*C*H_2), 114.9 (2 x CH), 111.9 (CH), 69.2 (CH_2, O*C*H_2CH=CH_2), 60.9 (CH_2, O*C*$H_2$$CH_3$), 20.0 ($CH_3$, Ar-*C*$H_3$), 15.6 ($CH_3$, Ar-*C*$H_3$), 14.3 ($CH_3$, OCH_2*C*H_3); LRMS m/z 326.25 (M + H^+), calcd $C_{20}H_{23}NO_3$ 325.1680; HRMS m/z 326.1769 (M + H^+), calcd $C_{20}H_{23}NO_3H^+$ 326.1756.



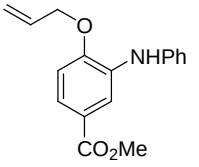
69d



69e

5-Allyloxy-3-methyl-4-phenylamino-biphenyl-2-carboxylic acid ethyl ester (69e): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 3391 (N-*H)*, 2980, 1722 (O-C=O), 1602, 1496, 1255, 1055, 748, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.36-7.33 (5H, m, Ph-*H*), 7.20 (2H, t, *J* = 8.4 Hz), 6.83 (1H, t, *J* = 7.2 Hz), 6.79 (1H, s), 6.70 (2H, d, *J* = 7.6 Hz), 5.97-5.90 (1H, m, olefinic-*H*), 5.74 (1H, s, N-*H*), 5.27 (1H, dd, *J* = 17.2, 1.2 Hz), 5.21 (1H, dd, *J* = 17.2, 1.2 Hz), 4.54 (2H, d, *J* = 5.2 Hz, O*CH*$_2$CH=CH_2), 4.03 (2H, q, *J* = 7.2 Hz, O*CH*$_2$$CH_3$), 2.21 (3H, s, Ar-*CH*$_3$), 0.94 (3H, t, *J* = 7.2 Hz, OCH_2*CH*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.6 (C, O-C=O), 153.0 (C), 145.7 (C), 141.2 (C), 137.1 (C), 132.7 (C), 132.6 (CH), 129.3 (C), 129.0 (2 x CH), 128.3 (2 x CH), 128.2 (2 x CH), 127.4 (C), 127.3 (CH), 119.5 (CH), 117.7 (CH_2, CH=*CH*$_2$), 115.4 (2 x CH), 111.5 (CH), 69.3 (CH_2, O*CH*$_2$CH=CH_2), 60.9 (CH_2, O*CH*$_2$$CH_3$), 15.8 ($CH_3$, Ar-*CH*$_3$), 13.6 ($CH_3$, OCH_2*CH*$_3$); GCMS m/z 386.95 (M^+), calcd $C_{25}H_{25}NO_3$ 387.4709.

5-Allyloxy-4-phenylamino-biphenyl-2-carboxylic acid ethyl ester (69f): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3416 (N-*H)*, 3055, 2982, 1714 (O-C=O), 1649, 1595, 1521, 1232, 1022, 748, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.68 (1H, s), 7.33-7.24 (7H, m, Ph-*H*), 7.20 (2H, t, *J* = 7.2 Hz), 6.99 (1H, t, *J* = 7.2 Hz), 6.81 (1H, s), 6.22 (1H, s, N-*H*), 6.11-6.03 (1H, m, olefinic-*H*), 5.41 (1H, dd, *J* = 17.2, 1.6 Hz), 5.32 (1H, dd, *J* = 11.6, 1.6 Hz), 4.66 (2H, d, *J* = 5.2 Hz, O*CH*$_2$CH=CH_2), 4.02 (2H, q, *J* = 7.2 Hz, O*CH*$_2$$CH_3$), 0.94 (3H, t, *J* = 7.2 Hz, OCH_2*CH*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.4 (C, O-C=O), 148.6 (C), 142.0 (C), 141.8 (C), 134.9 (C), 132.5 (CH), 132.3 (C), 129.4 (2 x CH), 128.5 (2 x CH), 127.8 (2 x CH), 126.7 (CH), 123.3 (C), 121.8 (CH), 119.2 (2 x CH), 118.4 (CH_2, CH=*CH*$_2$), 115.3 (CH), 113.7 (CH), 69.5 (CH_2, O*CH*$_2$CH=CH_2), 60.6 (CH_2, O*CH*$_2$$CH_3$), 13.6 ($CH_3$, OCH_2*CH*$_3$); GCMS m/z 373.15 (M^+), calcd $C_{24}H_{23}NO_3$ 373.1678**.**



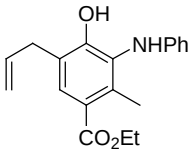
69f

4-Allyloxy-3-phenylamino-benzoic acid methyl ester (69g): Purified by column

69g

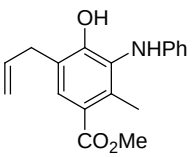
chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3414 (N-*H*), 2948, 1710 (O-C=O), 1592, 1526, 1494, 1443, 1247, 1129, 743, 697 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.96 (1H, d, *J* = 2.0 Hz), 7.56 (1H, dd, *J* = 8.4 Hz, 2.0 Hz), 7.32 (2H, t, *J* = 7.6 Hz), 7.19 (2H, d, *J* = 7.6 Hz), 7.00 (1H, t, *J* = 7.2 Hz), 6.88 (1H, d, *J* = 8.4 Hz), 6.20 (1H, s, N-*H*), 6.10-6.08 (1H, m, olefinic-*H*), 5.43 (1H, dd, *J* = 17.2 Hz, 1.2 Hz), 5.34 (1H, dd, *J* = 10.4, 1.2 Hz), 4.67 (2H, d, *J* = 5.2 Hz, $OCH_2CH=CH_2$), 3.85 (3H, s, OCH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.1 (C, O-C=O), 150.5 (C), 141.9 (C), 133.2 (C), 132.5 (CH), 129.4 (2 x CH), 122.9 (C), 121.9 (CH), 121.8 (CH), 119.2 (2 x CH), 118.4 (CH_2, $CH=CH_2$), 114.8 (CH), 110.8 (CH), 69.4 (CH_2, $OCH_2CH=CH_2$), 51.8 (CH_3, OCH_3); LCMS m/z 284.00 ($M+H^+$), calcd $C_{17}H_{17}NO_3$ 283.1208.

5-Allyl-4-hydroxy-2-methyl-3-phenylamino-benzoic acid ethyl ester (70a): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3366 (O-H & N-*H)*, 3047, 2980, 1699 (O-C=O), 1602, 1498, 1469, 1049, 750, 692 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.75 (1H, s), 7.19 (2H, t, *J* = 8.4 Hz), 6.95 (1H, s, O-*H*), 6.85 (1H, t, *J* = 7.2 Hz), 6.58 (2H, d, *J* = 8.8 Hz), 6.07-6.01 (1H, m, olefinic-*H*), 5.15-5.09 (2H, m, $CH=CH_2$), 5.01 (1H, s, N-*H*), 4.33 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 3.45 (2H, d, *J* = 6.4 Hz, $CH_2CH=CH_2$), 2.38 (3H, s, Ar-CH_3), 1.37 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.5 (C, O-C=O), 155.4 (C), 145.8 (C), 137.9 (C), 136.0 (CH), 131.5 (CH), 129.5 (2 x CH), 126.6 (C), 123.1 (C), 122.4 (C), 120.1 (CH), 115.9 (CH_2, $CH=CH_2$), 114.2 (2 x CH), 60.5 (CH_2, OCH_2CH_3), 34.0 (CH_2, $CH_2CH=CH_2$), 15.5 (CH_3, Ar-CH_3), 14.3 (CH_3, OCH_2CH_3); GCMS m/z 311.20 (M^+), calcd $C_{19}H_{21}NO_3$ 311.1524.



70a

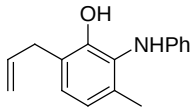
5-Allyl-4-hydroxy-2-methyl-3-phenylamino-benzoic acid methyl ester (70b): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 3364 (O-H & N-*H)*, 2928, 1714 (O-C=O), 1604, 1053, 752 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.79 (1H, s),



70b

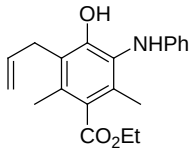
7.21 (2H, t, *J* = 7.2 Hz), 7.03 (1H, s, O-*H*), 6.88 (1H, t, *J* = 7.2 Hz), 6.59 (2H, d, *J* = 7.6 Hz), 6.11-6.04 (1H, m, olefinic-*H*), 5.17-5.13 (2H, m, CH=C*H*$_2$), 5.07 (1H, s, N-*H*), 3.87 (3H, s, OC*H*$_3$), 3.48 (2H, d, *J* = 6.4 Hz, C*H*$_2$CH=CH$_2$), 2.40 (3H, s, Ar-C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.8 (C, O-C=O), 155.5 (C), 145.8 (C), 138.2 (C), 135.9 (CH), 131.5 (CH), 129.5 (2 x CH), 126.6 (C), 123.1 (C), 121.8 (C), 120.0 (CH), 115.9 (CH$_2$, CH=*CH*$_2$), 114.1 (2 x CH), 51.6 (CH$_3$, O*CH*$_3$), 33.9 (CH$_2$, *CH*$_2$CH=CH$_2$), 15.5 (CH$_3$, Ar-*CH*$_3$); GCMS m/z 297.20 (M^+), calcd $C_{18}H_{19}NO_3$ 297.3484.

6-Allyl-3-methyl-2-phenylamino-phenol (70c): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3433 (O-H & N-*H)*, 3045, 2976, 1639, 1601, 1494, 1456, 1053, 790, 750, 692 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.17 (2H, t, *J* = 8.0 Hz), 6.99 (1H, d, *J* = 7.6 Hz), 6.82 (1H, t, *J* = 7.6 Hz), 6.72 (1H, d, *J* = 8.0 Hz), 6.58 (2H, d, *J* = 7.6 Hz), 6.44 (1H, s, O-H), 6.07-6.00 (1H, m, olefinic-*H*), 5.11-5.05 (2H, m, CH=C*H*$_2$), 4.86 (1H, s, N-*H*), 3.42 (2H, d, *J* = 6.4 Hz, C*H*$_2$CH=CH$_2$), 2.09 (3H, s, Ar-C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 152.1 (C), 146.3 (C), 136.8 (CH), 134.8 (C), 129.5 (2 x CH), 128.4 (CH), 125.9 (C), 123.6 (C), 121.5 (CH), 119.7 (CH), 115.5 (CH$_2$, CH=*CH*$_2$), 114.3 (2 x CH), 34.2 (CH$_2$, *CH*$_2$CH=CH$_2$), 17.7 (CH$_3$, Ar-*CH*$_3$); GCMS m/z 239.10 (M^+), calcd $C_{16}H_{17}NO$ 239.3123.



70c

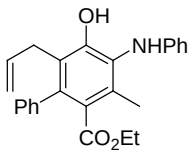
3-Allyl-4-hydroxy-2,6-dimethyl-5-phenylamino-benzoic acid ethyl ester (70d): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 3385 (O-H & N-*H)*, 2982, 1712 (O-C=O), 1602, 1498, 1201, 1041, 750, 696 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.20 (2H, t, *J* = 8.4 Hz), 6.86 (1H, t, *J* = 7.2 Hz), 6.68 (1H, s, O-*H*), 6.61 (2H, d, *J* = 8.0 Hz), 6.00-5.93 (1H, m, olefinic-*H*), 5.06-5.00 (2H, m, CH=C*H*$_2$), 5.00 (1H, s, N-*H*), 4.41 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.50 (2H, d, *J* = 5.6 Hz, C*H*$_2$CH=CH$_2$), 2.29 (3H, s, Ar-C*H*$_3$), 2.06 (3H, s, Ar-C*H*$_3$), 1.40 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 170.5 (C, O-C=O), 153.1 (C), 146.1 (C), 135.5 (CH), 133.6 (C), 131.7 (C), 129.5 (2 x CH), 127.7 (C), 123.8 (C), 122.2 (C), 119.8 (CH), 114.9 (CH$_2$, CH=*CH*$_2$), 114.2 (2 x CH), 61.1 (CH$_2$, O*CH*$_2$CH$_3$), 30.8



70d

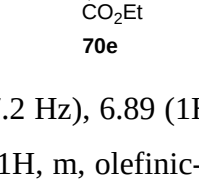
(CH_2, *CH_2*CH=CH_2), 16.4 (CH_3, Ar-*CH_3*), 14.9 (CH_3, Ar-*CH_3*), 14.3 (CH_3, OCH_2C*H_3*); GCMS m/z 325.20 (M^+), calcd $C_{20}H_{23}NO_3$ 325.1678**.**

6-Allyl-5-hydroxy-3-methyl-4-phenylamino-biphenyl-2-carboxylic acid ethyl ester (70e): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 3416 (O-H & N-*H)*, 3055, 2982, 1709 (O-C=O), 1601, 1498, 1469, 1265, 1033, 738, 702 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.41-7.28 (5H, m, Ph-*H*), 7.25 (2H, t, *J* = 7.2 Hz), 6.89 (1H, t, *J* = 7.2 Hz), 6.74 (1H, s, O-H), 6.69 (2H, d, *J* = 7.6 Hz), 5.93-5.86 (1H, m, olefinic-*H*), 5.07 (1H, s, N-*H*), 4.96 (1H, dd, *J* = 10.0, 1.6 Hz), 4.84 (1H, dd, *J* = 16.8, 1.6 Hz), 3.91 (2H, q, *J* = 7.2 Hz, OC*H_2*CH_3), 3.25 (2H, d, *J* = 6.0 Hz, C*H_2*$CH=CH_2$), 2.16 (3H, s, Ar-C*H_3*), 0.89 (3H, t, *J* = 7.2 Hz, OCH_2C*H_3*); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.4 (C, O-C=O), 153.2 (C), 145.7 (C), 139.7 (C), 138.7 (C), 136.3 (CH), 132.0 (C), 129.5 (2 x CH), 129.4 (2 x CH), 127.6 (C), 127.6 (2 x CH), 127.3 (CH), 125.2 (C), 122.1 (C), 120.0 (CH), 114.8 (CH_2, CH=*CH_2*), 114.3 (2 x CH), 60.7 (CH_2, O*CH_2*CH_3), 31.7 (CH_2, *CH_2*CH=CH_2), 15.0 (CH_3, Ar-*CH_3*), 13.5 (CH_3, OCH_2*CH_3*); GCMS m/z 387.05 (M^+), calcd $C_{25}H_{25}NO_3$ 387.4709.

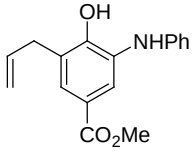


70e

6-Allyl-5-hydroxy-4-phenylamino-biphenyl-2-carboxylic acid ethyl ester (70f): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3369 (O-H & N-*H)*, 3057, 2978, 1699 (O-C=O), 1635, 1599, 1498, 1211, 1033, 750, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ 7.58 (1H, s, Ar-*H*), 7.33-7.31 (4H, m, O-*H* & Ph-*H*), 7.19 (2H, t, *J* = 8.0 Hz), 7.10 (2H, d, *J* = 7.6 Hz), 6.94 (2H, d, *J* = 8.0 Hz), 6.78 (1H, t, *J* = 7.2 Hz), 5.80-5.72 (1H, m, olefinic-*H*), 4.85 (1H, d, *J* = 10.4 Hz), 4.67 (1H, d, *J* = 17.6 Hz), 3.79 (2H, q, *J* = 7.2 Hz, OC*H_2*CH_3), 3.14 (2H, d, *J* = 5.6 Hz, C*H_2*$CH=CH_2$), 0.78 (3H, t, *J* = 7.2 Hz, OCH_2C*H_3*); ^{13}C NMR ($CDCl_3$ + DMSO-d_6, DEPT-135) δ 167.6 (C, O-C=O), 150.9 (C), 145.2 (C), 140.7 (C), 137.8 (C), 136.8 (CH), 130.2 (C), 129.4 (2 x CH), 129.4 (2 x CH), 127.7 (2 x CH), 126.8 (CH), 126.7 (C), 123.0 (C), 120.8 (CH), 119.5 (CH), 116.5 (2 x CH), 114.9 (CH_2, CH=*CH_2*), 60.1 (CH_2,



70f

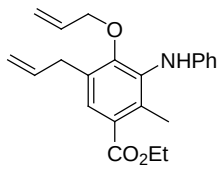


70g

O*CH*$_2$CH$_3$), 31.9 (CH$_2$, *CH*$_2$CH=CH$_2$), 13.8 (CH$_3$, OCH$_2$*CH*$_3$); GCMS m/z 373.20 (M$^+$), calcd $C_{24}H_{23}NO_3$ 373.4444.

3-Allyl-4-hydroxy-5-phenylamino-benzoic acid methyl ester (70g): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3351 (O-*H* and N-*H)*, 1696 (O-C=O), 1598, 1495, 1436, 1214, 1003, 746, 694 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.71 (1H, s, Ar-*H*), 7.61 (1H, s, Ar-*H*), 7.15 (2H, t, *J* = 8.0 Hz), 6.83 (1H, t, *J* = 7.2 Hz), 6.70 (2H, d, *J* = 8.0 Hz), 6.39 (1H, s, O-*H*), 5.97-5.92 (1H, m, olefinic-*H*), 5.21 (1H, s, N-*H*), 5.09 (1H, d, *J* = 16.8 Hz), 5.08 (1H, d, *J* = 9.6 Hz), 3.76 (3H, s, OC*H*$_3$), 3.40 (2H, d, *J* = 6.4 Hz, ArC*H*$_2$CH=CH$_2$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.8 (C, O-C=O), 153.3 (C), 144.9 (C), 135.7 (CH), 129.4 (2 x CH), 129.2 (C), 128.3 (CH), 125.9 (C), 124.0 (CH), 122.3 (C), 120.8 (CH), 116.6 (CH$_2$, CH=*CH*$_2$), 116.2 (2 x CH), 51.9 (CH$_3$, OC*H*$_3$), 34.6 (CH$_2$, *CH*$_2$CH=CH$_2$); LCMS m/z 284.00 (M+H$^+$), calcd $C_{17}H_{17}NO_3$ 283.1208**.**

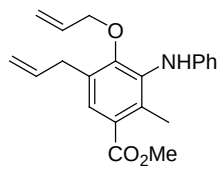
5-Allyl-4-allyloxy-2-methyl-3-phenylamino-benzoic acid ethyl ester (71a): Purified



71a

by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3381 (N-*H)*, 2978, 1714 (O-C=O), 1602, 1500, 1051, 748, 694 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.53 (1H, s, Ar-*H*), 7.19 (2H, t, *J* = 8.0 Hz), 6.82 (1H, t, *J* = 7.2 Hz), 6.62 (2H, d, *J* = 8.4 Hz), 6.01-5.86 (2H, m, olefinic-*H*), 5.72 (1H, s, N-H), 5.22-5.07 (4H, m, olefinic-*H*), 4.36 (2H, q, *J* = 6.8 Hz, OC*H*$_2$CH$_3$), 4.18 (2H, d, *J* = 5.6 Hz, OC*H*$_2$CH=CH$_2$), 3.44 (2H, d, *J* = 6.4 Hz, ArC*H*$_2$CH=CH$_2$), 2.35 (3H, s, Ar-C*H*$_3$), 1.39 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.8 (C, O-C=O), 154.7 (C), 145.5 (C), 136.6 (CH), 135.3 (C), 134.8 (C), 133.3 (CH), 130.9 (C), 129.1 (2 x CH), 128.2 (CH), 127.6 (C), 119.5 (CH), 117.8 (CH$_2$, CH=*CH*$_2$), 116.1 (CH$_2$, CH=*CH*$_2$), 114.8 (2 x CH), 74.5 (CH$_2$, O*CH*$_2$CH=CH$_2$), 60.8 (CH$_2$, O*CH*$_2$CH$_3$), 34.1 (CH$_2$, Ar*CH*$_2$CH=CH$_2$), 16.2 (CH$_3$, Ar-*CH*$_3$), 14.3 (CH$_3$, OCH$_2$*CH*$_3$); GCMS m/z 351.10 (M$^+$), calcd $C_{22}H_{25}NO_3$ 351.4388.

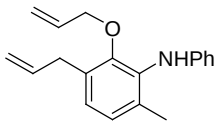
5-Allyl-4-allyloxy-2-methyl-3-phenylamino-benzoic acid methyl ester (71b):



71b

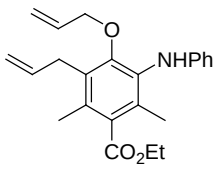
Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3381 (N-*H)*, 3080, 2932, 1716 (O-C=O), 1639, 1602, 1504, 1087, 750, 694 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.63 (1H, s, Ar-*H*), 7.22 (2H, t, *J* = 8.0 Hz), 6.85 (1H, t, *J* = 7.2 Hz), 6.65 (2H, d, *J* = 8.0 Hz), 6.04-5.89 (2H, m, olefinic-*H*), 5.76 (1H, s, N-*H*), 5.25 (4H, m, olefinic-*H*), 4.21 (2H, d, *J* = 5.6 Hz, OC*H*$_2$CH=CH_2), 3.91 (CH_3, s, OC*H*$_3$), 3.46 (2H, d, *J* = 6.4 Hz, ArC*H*$_2$CH=CH_2), 2.38 (3H, s, Ar-C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.2 (C, O-C=O), 154.8 (C), 145.5 (C), 136.7 (CH), 135.6 (C), 134.9 (C), 133.3 (CH), 131.0 (C), 129.2 (2 x CH), 128.4 (CH), 127.1 (C), 119.5 (CH), 117.9 (CH_2, CH=*CH*$_2$), 116.3 (CH_2, CH=*CH*$_2$), 114.9 (2 x CH), 74.5 (CH_2, O*CH*$_2$CH=CH_2), 51.9 (CH_3, O*CH*$_3$), 34.1 (CH_2, Ar*CH*$_2$CH=CH_2), 16.3 (CH_3, Ar-*CH*$_3$); LRMS m/z 337.20 (M^+), calcd $C_{21}H_{23}NO_3$ 337.4123.

(3-Allyl-2-allyloxy-6-methyl-phenyl)-phenyl-amine (71c): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3383 (N-*H)*, 3016, 2924, 1639, 1602, 1494, 1176, 1060, 748, 694 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.17 (2H, t, *J* = 7.6 Hz), 6.95 (1H, d, *J* = 8.0 Hz), 6.92 (1H, d, *J* = 8.0 Hz), 6.79 (1H, t, *J* = 7.6 Hz), 6.22 (2H, d, *J* = 7.6 Hz), 6.01-5.86 (2H, m, olefinic-*H*), 5.66 (1H, s, N-*H*), 5.21-5.04 (4H, m, olefinic-*H*), 4.16 (2H, d, *J* = 5.6 Hz, OC*H*$_2$CH=CH_2), 3.41 (2H, d, *J* = 6.4 Hz, ArC*H*$_2$CH=CH_2), 2.13 (3H, s, Ar-C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 151.7 (C), 145.8 (C), 137.4 (CH), 133.9 (C), 133.8 (CH), 133.4 (C), 131.3 (C), 129.1 (2 x CH), 126.3 (CH), 125.8 (CH), 119.2 (CH), 117.4 (CH_2, CH=*CH*$_2$), 115.6 (CH_2, CH=*CH*$_2$), 114.8 (2 x CH), 74.5 (CH_2, O*CH*$_2$CH=CH_2), 34.1 (CH_2, Ar*CH*$_2$CH=CH_2), 18.3 (CH_3, Ar-*CH*$_3$); GCMS m/z 279.20 (M^+), calcd $C_{19}H_{21}NO$ 279.3762.



71c

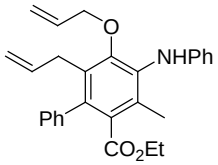
3-Allyl-4-allyloxy-2,6-dimethyl-5-phenylamino-benzoic acid ethyl ester (71d): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 3356 (N-*H)*, 2980, 2924, 1712 (O-C=O), 1604, 1510, 1097, 754, 696 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.21 (2H, t, *J* = 8.0 Hz), 6.83 (1H, t, *J* = 7.6 Hz), 6.65 (2H, d, *J* = 7.6 Hz), 5.93 (2H, m, olefinic-*H*), 5.65 (1H, s, N-H), 5.23-4.94 (4H, m,



71d

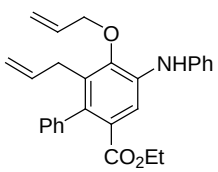
olefinic-*H*), 4.44 (2H, q, *J* = 7.6 Hz, OC*H*$_2$CH$_3$), 4.16 (2H, d, *J* = 5.6 Hz, OC*H*$_2$CH=CH$_2$), 3.50 (2H, d, *J* = 5.6 Hz, ArC*H*$_2$CH=CH$_2$), 2.26 (3H, s, Ar-C*H*$_3$), 2.13 (3H, s, Ar-C*H*$_3$), 1.43 (3H, t, *J* = 6.8 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 170.4 (C, O-C=O), 152.9 (C), 145.8 (C), 136.1 (CH), 133.5 (CH), 132.4 (C), 131.8 (C), 130.7 (C), 130.2 (C), 130.0 (C), 129.1 (2 x CH), 119.2 (CH), 117.5 (CH_2, CH=*CH*$_2$), 115.3 (CH_2, CH=*CH*$_2$), 114.7 (2 x CH), 74.8 (CH_2, O*CH*$_2$CH=CH_2), 61.1 (CH_2, O*CH*$_2$CH$_3$), 31.1 (CH_2, Ar*CH*$_2$CH=CH_2), 16.2 (CH_3, Ar-*CH*$_3$), 15.4 (CH_3, Ar-*CH*$_3$), 14.3 (CH_3, OCH$_2$*CH*$_3$); GCMS m/z 365.00 (M^+), calcd $C_{23}H_{27}NO_3$ 365.4654.

6-Allyl-5-allyloxy-3-methyl-4-phenylamino-biphenyl-2-carboxylic acid ethyl ester (71e): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 3379 (N-H), 3057, 2980, 1718 (O-C=O), 1637, 1602, 1498, 1199, 1093, 748, 702 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.38-7.28 (5H, m, Ph-*H*), 7.25 (2H, t, *J* = 7.6 Hz), 6.87 (1H, t, *J* = 7.6 Hz), 6.73 (2H, d, *J* = 8.0 Hz), 5.93 (1H, m, olefinic-*H*), 5.77 (1H, m, olefinic-*H*), 5.74 (1H, s, N-*H*), 5.23 (1H, dd, *J* = 16.8, 1.2 Hz), 5.17 (1H, dd, *J* = 10.4, 1.2 Hz), 4.92 (1H, dd, *J* = 10.0, 1.6 Hz), 4.77 (1H, dd, *J* = 16.8, 1.6 Hz), 4.24 (2H, d, *J* = 5.6 Hz, OC*H*$_2$CH=CH_2), 3.94 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.26 (2H, d, *J* = 6.0 Hz, ArC*H*$_2$CH=CH_2), 2.19 (3H, s, Ar-C*H*$_3$), 0.92 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.3 (C, O-C=O), 152.9 (C), 145.4 (C), 138.5 (C), 137.0 (CH), 136.7 (C), 133.5 (CH), 133.3 (C), 132.3 (C), 130.1 (C), 130.0 (C), 129.8 (2 x CH), 129.1 (2 x CH), 127.6 (2 x CH), 127.3 (CH), 119.5 (CH), 117.4 (CH_2, CH=*CH*$_2$), 115.1 (CH_2, CH=*CH*$_2$), 115.0 (2 x CH), 74.4 (CH_2, O*CH*$_2$CH=CH_2), 60.8 (CH_2, O*CH*$_2$CH$_3$), 31.9 (CH_2, Ar*CH*$_2$CH=CH_2), 15.6 (CH_3, Ar-*CH*$_3$), 13.6 (CH_3, OCH$_2$*CH*$_3$); GCMS m/z 428.8 (M+1), calcd $C_{28}H_{29}NO_3$ 427.5348.



71e

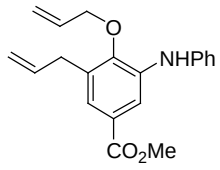
6-Allyl-5-allyloxy-4-phenylamino-biphenyl-2-carboxylic acid ethyl ester (71f): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 3400 (N-*H*), 3065, 2959, 1716 (O-C=O), 1593, 1508, 1458, 1265, 1026, 746, 700 cm^{-1};



71f

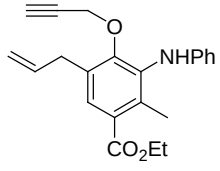
^{1}H NMR ($CDCl_3$) δ 7.68 (1H, s), 7.34-7.30 (5H, m, Ph-*H*), 7.19-7.14 (4H, m, Ph-*H*), 6.99 (1H, t, *J* = 7.2 Hz), 6.10 (1H, s, N-H), 6.13-6.03 (1H, m, olefinic-*H*), 5.79-5.71 (1H, m, olefinic-*H*), 5.44 (1H, br d, *J* = 17.2 Hz), 5.28 (1H, br d, *J* = 10.4 Hz), 4.90 (1H, br d, *J* = 10.0 Hz), 4.76 (1H, br d, *J* = 17.2 Hz), 4.44 (2H, d, *J* = 4.8 Hz, OC*H*$_2$CH=CH_2), 3.90 (2H, q, *J* = 7.2 Hz, OC*H*$_2$$CH_3$), 3.25 (2H, d, *J* = 5.2 Hz, ArC*H*$_2$CH=CH_2), 0.85 (3H, t, *J* = 7.2 Hz, OCH_2C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.5 (C, O-C=O), 148.6 (C), 141.9 (C), 139.8 (C), 136.9 (CH), 136.1 (C), 134.9 (C), 133.6 (CH), 132.8 (C), 129.6 (2 x CH), 129.5 (2 x CH), 128.7 (C), 127.5 (2 x CH), 126.8 (CH), 121.8 (CH), 118.8 (2 x CH), 117.7 (CH_2, CH=*CH*$_2$), 115.3 (CH_2, CH=*CH*$_2$), 114.9 (CH), 73.5 (CH_2, O*CH*$_2$CH=CH_2), 60.6 (CH_2, O*CH*$_2$$CH_3$), 32.0 ($CH_2$, Ar*CH*$_2$CH=$CH_2$), 13.5 ($CH_3$, OCH_2*CH*$_3$); GCMS m/z 413.1 (M^+), calcd $C_{27}H_{27}NO_3$ 413.1991.

3-Allyl-4-allyloxy-5-phenylamino-benzoic acid methyl ester (71g): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3404 (N-*H*), 2949, 1718 (O-C=O), 1589, 1497, 1437, 1255, 1099, 769, 743 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.77 (1H, s, Ar-*H*), 7.36 (1H, s, Ar-*H*), 7.23 (2H, t, *J* = 7.6 Hz), 7.04 (2H, d, *J* = 8.0 Hz), 6.91 (1H, t, *J* = 7.6 Hz), 6.03 (1H, s, N-*H*), 5.96 (2H, m, olefinic-*H*), 5.33 (1H, d, *J* = 17.2 Hz), 5.19 (1H, d, *J* = 10.4 Hz), 5.03 (2H, d, *J* = 12.8 Hz), 4.32 (2H, d, *J* = 5.6 Hz, OC*H*$_2$CH=CH_2), 3.76 (CH_3, s, OC*H*$_3$), 3.37 (2H, d, *J* = 6.4 Hz, ArC*H*$_2$CH=CH_2); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.9 (C, O-C=O), 149.6 (C), 141.9 (C), 137.1 (C), 136.4 (CH), 133.5 (C), 133.3 (CH), 129.4 (2 x CH), 126.2 (C), 123.1 (CH), 121.7 (CH), 118.7 (2 x CH), 118.0 (CH_2, CH=*CH*$_2$), 116.3 (CH_2, CH=*CH*$_2$), 114.9 (CH), 73.6 (CH_2, O*CH*$_2$CH=CH_2), 51.9 (CH_3, O*CH*$_3$), 34.0 (CH_2, Ar*CH*$_2$CH=CH_2); LRMS m/z 324.00 ($M+H^+$), calcd $C_{20}H_{21}NO_3$ 323.1521.



71g

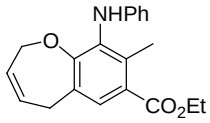
5-Allyl-2-methyl-3-phenylamino-4-prop-2-ynyloxy-benzoic acid ethyl ester (71h): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3387 (*N-H)*, 3304



71h

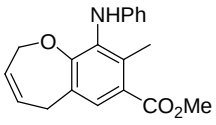
(≡C*H*)**,** 3080, 2930, 1711 (O-C=O), 1639, 1602, 1194, 1053, 748, 694 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.59 (1H, s, Ar-*H*), 7.22 (2H, t, *J* = 8.0 Hz), 6.85 (1H, t, *J* = 7.2 Hz), 6.65 (2H, d, *J* = 7.6 Hz), 6.05-5.98 (1H, m, olefinic-*H*), 5.75 (1H, s, *N*-*H*), 5.15 (1H, s, olefinic-*H*), 5.11 (1H, s, olefinic-*H*), 4.42 (2H, d, *J* = 2.0 Hz, OCH_2), 4.38 (2H, q, *J* = 7.2 Hz, OC$H_2$$CH_3$), 3.51 (2H, d, *J* = 6.4 Hz, CH_2CH=CH_2), 2.44 (1H, s, C≡C *H*), 2.36 (3H, s, Ar-CH_3), 1.41 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.8 (C, O-C=O), 154.0 (C), 145.3 (C), 136.6 (CH), 135.5 (C), 134.6 (C), 131.4 (C), 129.2 (2 x CH), 128.3 (CH), 128.2 (C), 119.6 (CH), 116.3 (CH_2, CH=CH_2), 114.9 (2 x CH), 78.7 (C), 75.8 (CH), 60.9 (CH_2, OCH_2), 60.9 (CH_2, O$CH_2$$CH_3$), 34.2 ($CH_2$, CH_2CH=CH_2), 16.2 (CH_3, Ar-CH_3), 14.3 (CH_3, OCH_2CH_3); GCMS m/z 349.20 (M^+), calcd $C_{22}H_{23}NO_3$ 349.4230.

8-Methyl-9-phenylamino-2,5-dihydro-benzo[*b*]oxepine-7-carboxylic acid ethyl ester (72a): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3379 (N-*H*), 2976, 2934, 1716 (O-C=O), 1602, 1496, 1448, 1049, 750, 694 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.50 (1H, s, Ar-*H*), 7.19 (2H, t, *J* = 8.0 Hz), 6.84 (1H, t, *J* = 8.0 Hz), 6.65 (2H, d, *J* = 7.6 Hz), 5.87 (1H, s, N-H), 5.85-5.82 (1H, m, olefinic-*H*), 5.43-5.39 (1H, m, olefinic-*H*), 4.41-4.39 (2H, m, OCH_2), 4.36 (2H, q, *J* = 6.8 Hz, OC$H_2$$CH_3$), 3.50 (2H, m, C$H_2$CH=CH), 2.36 (3H, s, Ar-CH_3), 1.38 (3H, t, *J* = 6.8 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.7 (C, O-C=O), 155.4 (C), 146.1 (C), 135.6 (C), 134.8 (C), 133.3 (C), 129.1 (2 x CH), 126.9 (C), 126.8 (CH), 126.7 (CH), 125.9 (CH), 119.8 (CH), 115.6 (2 x CH), 70.7 (CH_2, OCH_2CH=CH), 60.8 (CH_2, O$CH_2$$CH_3$), 31.4 ($CH_2$, CH_2CH=CH), 16.3 (CH_3, Ar-CH_3), 14.3 (CH_3, OCH_2CH_3); GCMS m/z 323.00 (M^+), calcd $C_{20}H_{21}NO_3$ 323.1521; Anal. calcd for $C_{20}H_{21}NO_3$ (323.15): C, 74.28; H, 6.55; N, 4.33. Found: C, 74.304; H, 6.513; N, 4.564%.



72a

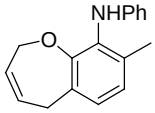
8-Methyl-9-phenylamino-2,5-dihydro-benzo[*b*]oxepine-7-carboxylic acid methyl ester (72b): Purified by column chromatography using



72b

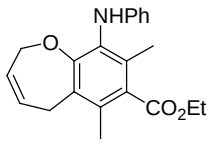
EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3377 (N-*H)*, 3042, 2945, 1716 (O-C=O), 1602, 1496, 1072, 748, 694 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.51 (1H, s, Ar-*H*), 7.19 (2H, t, *J* = 7.6 Hz), 6.84 (1H, t, *J* = 7.2 Hz), 6.65 (2H, d, *J* = 7.6 Hz), 5.87 (1H, s, N-H), 5.85-5.83 (1H, m, olefinic-*H*), 5.42 (1H, dd, *J* = 11.2, 1.2 Hz, olefinic-*H*), 4.41 (2H, br s, OC*H*$_2$), 3.88 (3H, s, OC*H*$_3$), 3.49 (2H, br s, C*H*$_2$CH=CH), 2.36 (3H, s, Ar-C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.1 (C, O-C=O), 155.5 (C), 146.1 (C), 135.7 (C), 134.8 (C), 133.3 (C), 129.1 (2 x CH), 126.9 (CH), 126.8 (CH), 126.5 (C), 125.9 (CH), 119.8 (CH), 115.6 (2 x CH), 70.6 (CH_2, *OCH*$_2$CH=CH), 51.8 (CH_3, O*CH*$_3$), 31.4 (CH_2, *CH*$_2$CH=CH), 16.3 (CH_3, Ar-*CH*$_3$); GCMS m/z 309.20 (M^+), calcd $C_{19}H_{19}NO_3$ 309.3591; Anal. calcd for $C_{19}H_{19}NO_3$ (309.35): C, 73.77; H, 6.19; N, 4.53. Found: C, 73.758; H, 6.162; N, 4.493%.

(8-Methyl-2,5-dihydro-benzo[*b*]oxepin-9-yl)-phenyl-amine (72c): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3381 (N-*H)*, 3024, 2924, 1601, 1494, 796, 750, 694 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.19 (2H, t, *J* = 7.6 Hz), 6.89 (1H, d, *J* = 8.4 Hz), 6.82 (1H, t, *J* = 7.2 Hz), 6.80 (1H, d, *J* = 8.4 Hz), 6.66 (2H, d, *J* = 7.6 Hz), 5.85 (1H, s, N-*H*), 5.83 (1H, br s, olefinic-*H*), 5.38 (1H, br d, *J* = 12.0 Hz, olefinic-*H*), 4.37 (2H, m, OC*H*$_2$), 3.46 (2H, m, C*H*$_2$CH=CH), 2.13 (3H, s, Ar-C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 152.5 (C), 146.3 (C), 134.4 (C), 133.7 (C), 133.3 (C), 129.0 (2 x CH), 127.1 (CH), 126.0 (CH), 125.9 (CH), 124.1 (CH), 119.5 (CH), 115.7 (2 x CH), 70.8 (CH_2, O*CH*$_2$CH=CH), 31.5 (CH_2, *CH*$_2$CH=CH), 18.3 (CH_3, Ar-*CH*$_3$); GCMS m/z 251.10 (M^+), calcd $C_{17}H_{17}NO$ 251.3230; Anal. calcd for $C_{17}H_{17}NO$ (251.32): C, 81.24; H, 6.82; N, 5.57. Found: C, 81.208; H, 6.824; N, 5.519%.



72c

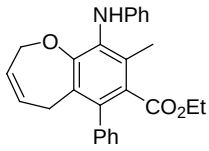
6,8-Dimethyl-9-phenylamino-2,5-dihydro-benzo[*b*]oxepine-7-carboxylic acid ethyl ester (72d): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3379 (N-*H)*, 3026, 2980, 1722 (O-C=O), 1602, 1496, 1195, 1043, 750, 696 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.18 (2H, t, *J* = 8.4 Hz), 6.82 (1H, t, *J* = 8.4 Hz), 6.70 (2H, d, *J* = 7.6 Hz), 5.84-5.81 (1H, m, olefinic-*H*), 5.74 (1H, s, N-H), 5.33 (1H, dd,



72d

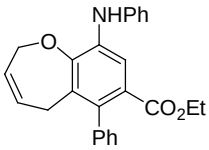
J = 11.6, 1.2 Hz, olefinic-*H*), 4.41 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 4.34 (2H, br s, OC*H*$_2$), 3.48 (2H, br s, C*H*$_2$CH=CH), 2.25 (3H, s, Ar-C*H*$_3$), 2.10 (3H, s, Ar-C*H*$_3$), 1.40 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR (CDCl$_3$, DEPT-135) δ 170.3 (C, O-C=O), 153.3 (C), 146.3 (C), 134.7 (C), 132.2 (C), 131.9 (C), 129.6 (C), 129.1 (2 x CH), 127.3 (CH), 127.2 (C), 125.2 (CH), 119.5 (CH), 115.3 (2 x CH), 71.0 (CH$_2$, O*CH*$_2$CH=CH), 61.1 (CH$_2$, O*CH*$_2$CH$_3$), 25.8 (CH$_2$, *CH*$_2$CH=CH), 16.6 (CH$_3$, Ar-*CH*$_3$), 15.3 (CH$_3$, Ar-*CH*$_3$), 14.3 (CH$_3$, OCH$_2$*CH*$_3$); GCMS m/z 336.95 (M$^+$), calcd $C_{21}H_{23}NO_3$ 337.4123; Anal. calcd for $C_{21}H_{23}NO_3$ (337.41): C, 74.75; H, 6.87; N, 4.15. Found: C, 74.713; H, 6.894; N, 4.154%.

8-Methyl-6-phenyl-9-phenylamino-2,5-dihydro-benzo[*b*]oxepine-7-carboxylic acid ethyl ester (72e): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν$_{max}$ 3377 (N-*H)*, 3022, 2978, 1722 (O-C=O), 1601, 1496, 1448, 1199, 1047, 752, 702 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.42-7.36 (3H, m, Ph-*H*), 7.28-7.23 (4H, m, Ph-*H*), 6.89 (1H, t, *J* = 7.2 Hz), 6.78 (2H, d, *J* = 7.6 Hz), 5.90 (1H, s, *N-H*), 5.71-5.68 (1H, m, olefinic-*H*), 5.35 (1H, br d, *J* = 11.6 Hz, olefinic-*H*), 4.45 (2H, m, OC*H*$_2$), 3.95 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.28 (2H, m, C*H*$_2$CH=CH), 2.17 (3H, s, Ar-C*H*$_3$), 0.92 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR (CDCl$_3$, DEPT-135) δ 169.4 (C, O-C=O), 153.0 (C), 145.9 (C), 138.5 (C), 134.0 (C), 133.9 (C), 133.4 (C), 131.9 (C), 129.7 (2 x CH), 129.5 (C), 129.1 (2 x CH), 127.9 (2 x CH), 127.3 (CH), 127.1 (CH), 125.8 (CH), 119.8 (CH), 115.8 (2 x CH), 71.1 (CH$_2$, O*CH*$_2$CH=CH), 60.8 (CH$_2$, O*CH*$_2$CH$_3$), 26.9 (CH$_2$, *CH*$_2$CH=CH), 15.5 (CH$_3$, Ar-*CH*$_3$), 13.6 (CH$_3$, OCH$_2$*CH*$_3$); GCMS m/z 398.90 (M$^+$), calcd $C_{26}H_{25}NO_3$ 399.4816; Anal. calcd for $C_{26}H_{25}NO_3$ (399.48): C, 78.17; H, 6.31; N, 3.51. Found: C, 78.449; H, 6.351; N, 3.436%.



72e

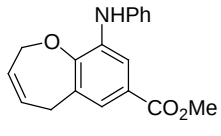
6-Phenyl-9-phenylamino-2,5-dihydro-benzo[*b*]oxepine-7-carboxylic acid ethyl ester (72f): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν$_{max}$ 3400 (*N-H)*, 3022, 2959, 1716 (O-C=O), 1595, 1514, 1466, 1184, 1066, 746, 659 cm^{-1}; ^{1}H NMR



72f

($CDCl_3$) δ 7.68 (1H, s, Ar-*H*), 7.41-7.34 (5H, m, Ph-*H*), 7.26 (2H, t, *J* = 8.0 Hz), 7.18 (2H, d, *J* = 6.8 Hz), 7.05 (1H, t, *J* = 6.8 Hz), 6.38 (1H, s, N-H), 5.78-5.72 (1H, m, olefinic-*H*), 5.48 (1H, br d, *J* = 11.2 Hz), 4.68 (2H, br s, OCH_2), 3.94 (2H, q, *J* = 7.2 Hz, OC$H_2$$CH_3$), 3.28 (2H, br s, C$H_2$CH=CH), 0.88 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.6 (C, O-C=O), 148.1 (C), 141.7 (C), 139.8 (C), 136.4 (C), 135.6 (C), 131.6 (C), 129.53 (2 x CH), 129.50 (2 x CH), 128.4 (C), 127.8 (2 x CH), 127.1 (CH), 126.7 (CH), 125.9 (CH), 122.2 (CH), 119.6 (2 x CH), 113.3 (CH), 70.2 (CH_2, OCH_2CH=CH), 60.6 (CH_2, O$CH_2$$CH_3$), 27.0 ($CH_2$, CH_2CH=CH), 13.5 (CH_3, OCH_2CH_3); GCMS m/z 385.20 (M^+), calcd $C_{25}H_{23}NO_3$ 385.4551; Anal. calcd for $C_{25}H_{23}NO_3$ (385.45): C, 77.90; H, 6.01; N, 3.63. Found: C, 77.963; H, 6.017; N, 3.690%.

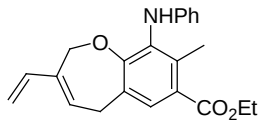
9-Phenylamino-2,5-dihydro-benzo[*b*]oxepine-7-carboxylic acid methyl ester (72g):



72g

Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3402 (N-*H*), 3023, 2948, 1711 (O-C=O), 1591, 1519, 1495, 1439, 1229, 1071, 736, 695 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.87 (1H, d, *J* = 1.6 Hz, Ar-*H*), 7.33 (2H, t, *J* = 8.0 Hz), 7.31 (1H, s, Ar-*H*), 7.19 (2H, d, *J* = 7.6 Hz), 7.02 (1H, t, *J* = 7.6 Hz), 6.33 (1H, s, N-*H*), 5.91-5.88 (1H, m, olefinic-*H*), 5.52 (1H, dd, *J* = 11.6 Hz, 1.2 Hz, olefinic-*H*), 4.63 (2H, d, *J* = 2.0 Hz, OCH_2), 3.85 (3H, s, OCH_3), 3.52 (2H, d, *J* = 2.8 Hz, CH_2CH=CH); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.9 (C, O-C=O), 149.8 (C), 141.7 (C), 136.5 (C), 135.8 (C), 129.4 (2 x CH), 126.7 (CH), 125.9 (CH), 125.7 (C), 122.1 (CH), 121.1 (CH), 119.4 (2 x CH), 113.9 (CH), 69.9 (CH_2, OCH_2CH=CH), 51.9 (CH_3, OCH_3), 31.6 (CH_2, CH_2CH=CH); LCMS m/z 296.00 ($M+H^+$), calcd $C_{18}H_{17}NO_3$ 295.1208; Anal. calcd for $C_{18}H_{17}NO_3$ (295.12): C, 73.20; H, 5.80; N, 4.74. Found: C, 73.226; H, 5.775; N, 5.006%.

8-Methyl-9-phenylamino-3-vinyl-2,5-dihydro-benzo[*b*]oxepine-7-carboxylic acid ethyl ester (72h): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3381 (*N*-



72h

H), 2926, 1716 (O-C=O), 1649, 1602, 1496, 1246, 1053, 750, 694 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.50 (1H, s, Ar-*H*), 7.23 (2H, t, *J* = 8.0 Hz), 6.88 (1H, t, *J* = 7.6 Hz), 6.70 (2H, d, *J* = 8.0 Hz), 6.20 (1H, dd, *J* = 18.0, 11.2 Hz, olefinic-*H*), 5.97 (1H, t, *J* = 5.6 Hz, olefinic-*H*), 5.91 (1H, s, *N*-*H*), 4.89 (1H, br d, *J* = 11.2 Hz), 4.79 (1H, br d, *J* = 18.0 Hz), 4.64 (2H, br s, OC*H*$_2$), 4.37 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.59 (2H, d, *J* = 5.6 Hz), 2.36 (3H, s, Ar-C*H*$_3$), 1.40 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.7 (C, O-C=O), 155.0 (C), 145.8 (C), 137.3 (CH), 135.7 (C), 135.4 (C), 134.4 (C), 132.1 (C), 129.1 (2 x CH), 128.2 (CH), 127.1 (C), 126.4 (CH), 119.9 (CH), 115.7 (2 x CH), 111.2 (CH_2, CH=*CH*$_2$), 70.1 (CH_2, O*CH*$_2$), 60.8 (CH_2, O*CH*$_2$CH$_3$), 31.1 (CH_2), 16.4 (CH_3, Ar-*C*H$_3$), 14.3 (CH_3, OCH$_2$C*H*$_3$); GCMS m/z 349.20 (M^+), calcd $C_{22}H_{23}NO_3$ 349.4230; Anal. calcd for $C_{22}H_{23}NO_3$ (349.42): C, 75.62; H, 6.63; N, 4.01. Found: C, 75.617; H, 6.613; N, 4.139%.

3D: General Experimental Procedures for the Synthesis of Highly Functionalized 2,5-Dihydro-benzo[*b*]oxepines 79a-g: The syntheses of highly functionalized 2,5-dihydro-benzo[*b*]oxepines **79a-g** from corresponding phenols **75a-g** involves the following four-step sequence (see Annexure-I, Table A2 and all yields represents column purified products).

***O*-Allylation:** The starting materials phenols **75 (**5 mmol**)** were allylated by treatment with allyl bromide (1.20 g, 10 mmol) and K_2CO_3 (3.45 g, 25 mmol) in DMF (5 mL, 1.0 M) at RT for 6-24 h. The crude reaction mixture was worked up with aqueous NH_4Cl solution and the aqueous layer was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure products **76** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

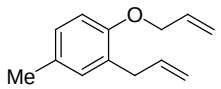
***C*-Allylation through Claisen Rearrangement:** Compounds **76** (2.0 mmol) and solvent 1,2-dichlorobenzene (2.0 mL, 1.0 M) were taken in a sealed glass tube and the mixture was heated at 180 °C under N_2 for 9 to 24 h. Upon cooling the reaction mixture to RT, the mixture was diluted with CH_2Cl_2 (20 mL), washed with aqueous NH_4Cl solution (5 mL) and brine (5 mL). The separated organic layer was dried (Na_2SO_4),

filtered and concentrated under reduced pressure. Pure products **77** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

***O*-Allylation:** The corresponding phenols **77 (**2.0 mmol**)** were allylated by treatment with allyl bromide (483.9 mg, 4.0 mmol) and K_2CO_3 (829.2 mg, 6 mmol) in DMF (4 mL, 0.5 M) at RT for 16-24 h. The crude reaction mixture was worked up with aqueous NH_4Cl solution and the aqueous layer was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure products **78** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

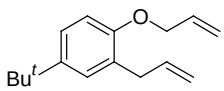
RCM Reaction: A 10 mL oven-dried round bottom flask equipped with a stirring bar was charged with diene amine **78** (0.1 mmol) and Grubbs' first generation catalyst **4n** (1.6 mg, 0.002 mmol, 2 mol %) in a dry CH_2Cl_2 (2 mL, 0.05 M) and the reaction mixture was stirred under N_2 at RT for 3 to 18 h. Solvent CH_2Cl_2 was distilled off at ambient pressure and the crude reaction mixture was directly loaded on silica gel column and pure RCM products **79** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

2-Allyl-1-allyloxy-4-methyl-benzene (78a): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2913, 1549, 1501, 1457, 1225, 1027, 803 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.95 (1H, s, Ar-*H*), 6.94 (1H, d, *J* = 6.8 Hz), 6.72 (1H, d, *J* = 6.8 Hz), 6.07-5.96 (2H, m, olefinic-H), 5.40 (1H, dd, *J* = 17.2 Hz, 1.6 Hz), 5.24 (1H, dd, *J* = 10.4 Hz, 1.6 Hz), 5.08-5.01 (2H, m, olefinic-H), 4.49 (2H, d, *J* = 4.8 Hz, OC*H*$_2$CH=CH$_2$), 3.38 (2H, d, *J* = 6.4 Hz, C*H*$_2$CH=CH$_2$), 2.25 (3H, s, Ar-*CH*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 154.1 (C), 137.1 (CH), 133.7 (CH), 130.6 (CH), 129.9 (C), 128.7 (C), 127.4 (CH), 116.7 (CH_2, CH=*CH*$_2$), 115.2 (CH_2, CH=*CH*$_2$), 111.8 (CH), 68.9 (CH_2, O*CH*$_2$CH=CH$_2$), 34.4 (CH_2, *CH*$_2$CH=CH$_2$), 20.5 (CH_3, Ar-*CH*$_3$).



78a

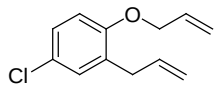
2-Allyl-1-allyloxy-4-tert-butyl-benzene (78b): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2959,



78b

1501, 1460, 1245, 1025, 915 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.17 (1H, s, Ar-*H*), 7.16 (1H, d, *J* = 6.0 Hz), 6.76 (1H, d, *J* = 9.2 Hz), 6.06-5.98 (2H, m, olefinic-H), 5.41 (1H, dd, *J* = 17.2 Hz, 1.6 Hz), 5.24 (1H, dd, *J* = 10.8 Hz, 1.6 Hz), 5.09-5.01 (2H, m, olefinic-H), 4.51 (2H, d, *J* = 4.8 Hz, OC*H*$_2$CH=CH$_2$), 3.42 (2H, d, *J* = 6.4 Hz, C*H*$_2$CH=CH$_2$), 1.98 (9H, s, C(*C*H$_3$)$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 154.1 (C), 143.3 (C), 137.2 (CH), 133.8 (CH), 128.2 (C), 127.0 (CH), 123.7 (CH), 116.7 (CH$_2$, CH=*CH*$_2$), 115.2 (CH$_2$, CH=*CH*$_2$), 111.2 (CH), 68.8 (CH$_2$, O*CH*$_2$CH=CH$_2$), 34.7 (CH$_2$, *CH*$_2$CH=CH$_2$), 34.1 (C, *C*(CH$_3$)$_3$), 31.5 [3 x CH$_3$, C(*C*H$_3$)$_3$].

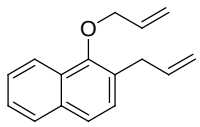
2-Allyl-1-allyloxy-4-chloro-benzene (78c): Purified by column chromatography using



78c

EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 1485, 1456, 1427, 1242, 1021, 919, 803, 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.11 (1H, s, Ar-*H*), 7.10 (1H, d, *J* = 5.6 Hz), 6.74 (1H, d, *J* = 9.2 Hz), 6.07-5.92 (2H, m, olefinic-H), 5.40 (1H, br d, *J* = 17.2 Hz), 5.27 (1H, br d, *J* = 10.4 Hz), 5.09-5.05 (2H, m, olefinic-H), 4.51 (2H, d, *J* = 4.4 Hz, OC*H*$_2$CH=CH$_2$), 3.37 (2H, d, *J* = 6.4 Hz, C*H*$_2$CH=CH$_2$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 154.8 (C), 136.0 (CH), 133.1 (CH), 130.9 (C), 129.7 (CH), 126.8 (CH), 125.5 (C), 117.2 (CH$_2$, CH=*CH*$_2$), 116.2 (CH$_2$, CH=*CH*$_2$), 112.8 (CH), 69.1 (CH$_2$, O*CH*$_2$CH=CH$_2$), 34.1 (CH$_2$, *CH*$_2$CH=CH$_2$).

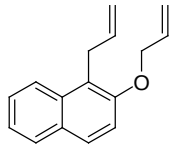
2-Allyl-1-allyloxy-naphthalene (78d): Purified by column chromatography using



78d

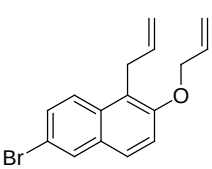
EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3072, 1624, 1593, 1511, 1432, 1243, 1114, 1070, 913, 804, 744 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.93 (1H, br s), 7.76 (1H, br s), 7.70 (1H, br s), 7.46 (1H, br s), 7.33 (1H, br s), 7.23 (1H, br s), 6.07-6.05 (2H, m, olefinic-*H*), 5.43 (1H, br d, *J* = 17.2 Hz, olefinic-*H*), 5.26 (1H, d, *J* = 8.4 Hz, olefinic-*H*), 5.01-4.98 (2H, m, olefinic-*H*), 4.65 (2H, br s, OC*H*$_2$CH=CH$_2$), 3.88 (2H, br s, C*H*$_2$CH=CH$_2$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 153.5 (C), 136.7 (CH), 133.8 (CH), 133.2 (C), 129.4 (C), 128.4 (CH), 127.9 (CH), 126.2 (CH), 123.6 (CH), 123.4 (CH), 121.7 (C), 117.0 (CH$_2$, CH=*CH*$_2$), 115.1 (CH), 114.9 (CH$_2$, CH=*CH*$_2$), 70.3 (CH$_2$, O*CH*$_2$CH=CH$_2$), 29.3 (CH$_2$, *CH*$_2$CH=CH$_2$).

1-Allyl-2-allyloxy-naphthalene (78e): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3072, 2931, 1640, 1596, 1180, 1077, 756 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.09 (1H, d, *J* = 8.4 Hz), 7.79 (1H, d, *J* = 7.6 Hz), 7.56 (1H, d, *J* = 8.8 Hz), 7.48-7.40 (2H, m), 7.31 (1H, d, *J* = 8.4 Hz), 6.22-6.15 (1H, m, olefinic-*H*), 6.05-5.98 (1H, m, olefinic-*H*), 5.50 (1H, dd, *J* = 18.0 Hz, 1.6 Hz), 5.31 (1H, dd, *J* = 10.4 Hz, 1.2 Hz), 5.11-5.06 (2H, m, olefinic-*H*), 4.50 (2H, d, *J* = 5.2 Hz, $OCH_2CH=CH_2$), 3.59 (2H, d, *J* = 6.4 Hz, $CH_2CH=CH_2$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 152.3 (C), 137.3 (CH), 134.0 (CH), 133.9 (C), 129.7 (C), 128.4 (C), 128.3 (CH), 127.9 (CH), 125.9 (CH), 125.6 (CH), 124.1 (CH), 122.2 (CH), 117.3 (CH_2, $CH=CH_2$), 115.9 (CH_2, $CH=CH_2$), 75.3 (CH_2, $OCH_2CH=CH_2$), 34.1 (CH_2, $CH_2CH=CH_2$).



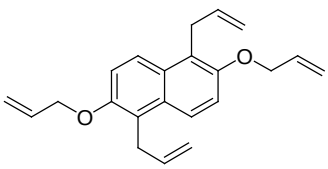
78e

1-Allyl-2-allyloxy-6-bromo-naphthalene (78f): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3076, 2975, 1617, 1586, 1497, 1221, 1069, 813, 737, 666 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.92 (1H, d, *J* = 2.0 Hz), 7.80 (1H, d, *J* = 8.8 Hz), 7.62 (1H, d, *J* = 9.2 Hz), 7.51 (1H, dd, J = 9.2 Hz, 2.0 Hz), 7.25 (1H, d, *J* = 9.2 Hz), 6.12-5.98 (2H, m, olefinic-*H*), 5.43 (1H, br dd, *J* = 17.2 Hz, 2.8 Hz), 5.28 (1H, br dd, *J* = 10.8 Hz, 1.6 Hz), 5.01-4.93 (2H, m, olefinic-H), 4.66 (2H, br d, *J* = 5.2 Hz, $OCH_2CH=CH_2$), 3.85 (2H, br d, *J* = 6.0 Hz, $CH_2CH=CH_2$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 153.7 (C), 136.4 (CH), 133.5 (CH), 131.7 (C), 130.5 (C), 130.2 (CH), 129.5 (CH), 127.0 (CH), 125.5 (CH), 121.9 (C), 117.2 (CH_2, $CH=CH_2$), 117.1 (C), 115.9 (CH), 115.2 (CH_2, $CH=CH_2$), 70.2 (CH_2, $OCH_2CH=CH_2$), 29.2 (CH_2, $CH_2CH=CH_2$).



78f

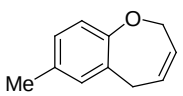
1,5-Diallyl-2,6-bis-allyloxy-naphthalene (78g): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 2851, 1641, 1594, 1511, 1452, 1120, 1037, 915, 804 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.84 (2H, d, *J* = 9.2 Hz), 7.25 (2H, d, *J* = 9.2 Hz), 6.13-5.99 (4H, m, olefinic-H), 5.43 (2H, dd, *J* = 17.2 Hz, 1.6 Hz), 5.26 (2H, dd, *J* = 10.4 Hz, 1.2 Hz), 5.02-4.98 (4H, m, olefinic-H),



78g

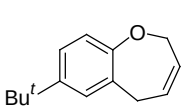
4.64 (4H, d, *J* = 3.6 Hz, OC*H*$_2$CH=CH$_2$), 3.87 (4H, d, *J* = 6.0 Hz, C*H*$_2$CH=CH$_2$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 151.9 (2 x C), 136.9 (2 x CH), 133.9 (2 x CH), 129.2 (2 x C), 123.5 (2 x CH), 122.2 (2 x C), 116.9 (2 x CH$_2$, 2 x CH=*CH*$_2$), 115.9 (2 x CH), 114.9 (2 x CH$_2$, 2 x CH=*CH*$_2$), 70.5 (2 x CH$_2$, 2 x O*CH*$_2$CH=CH$_2$), 29.5 (2 x CH$_2$, 2 x *CH*$_2$CH=CH$_2$); LCMS m/z 321.00 (M+H$^+$), calcd $C_{22}H_{24}O_2$ 320.18; Anal. calcd for $C_{22}H_{24}O_2$ (320.18): C, 82.46; H, 7.55. Found: C, 82.428; H, 7.518.

7-Methyl-2,5-dihydro-benzo[*b*]oxepine (79a):[49] Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3020, 2923, 1663, 1572, 1500, 1386, 1061, 824, 664 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.95-6.88 (3H, m, *Ph-H*), 5.83-5.79 (1H, m, olefinic-*H*), 5.45-5.42 (1H, m, olefinic-*H*), 4.55-4.53 (2H, m, OC*H*$_2$), 3.43-3.42 (2H, m, C*H*$_2$CH=CH), 2.27 (3H, s, Ar-C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 156.5 (C), 135.8 (C), 133.4 (C), 129.4 (CH), 128.2 (CH), 127.4 (CH), 125.7 (CH), 121.1 (CH), 71.3 (CH$_2$, O*CH*$_2$CH=CH), 31.7 (CH$_2$, *CH*$_2$CH=CH), 20.7 (CH$_3$, Ar-*C*H$_3$); LCMS m/z 161 (M+H$^+$), calcd $C_{11}H_{12}O$ 160.0888.



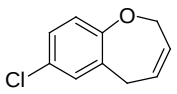
79a

7-tert-Butyl-2,5-dihydro-benzo[*b*]oxepine (79b): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2959, 1559, 1501, 1462, 1233, 1061, 833, 635 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.19 (1H, dd, *J* = 8.4 Hz, 2.4 Hz), 7.09 (1H, d, *J* = 2.0 Hz), 6.97 (1H, d, *J* = 8.4 Hz), 5.86-5.83 (1H, m, olefinic-*H*), 5.45 (1H, dd, *J* = 10 Hz, 2.0 Hz, olefinic-*H*), 4.56 (2H, m, OC*H*$_2$), 3.47 (2H, d, *J* = 2.8 Hz, C*H*$_2$CH=CH), 1.29 (9H, s, C(*C*H$_3$)$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 156.4 (C), 146.7 (C), 135.2 (C), 127.4 (CH), 125.9 (CH), 125.8 (CH), 124.5 (CH), 120.7 (CH), 71.1 (CH$_2$, O*CH*$_2$CH=CH), 34.2 (C), 32.2 (CH$_2$, *CH*$_2$CH=CH), 31.5 (CH$_3$, C(*C*H$_3$)$_3$); LCMS m/z 203.00 (M+H$^+$), calcd $C_{14}H_{18}O$ 202.1358; Anal. calcd for $C_{14}H_{18}O$ (202.13): C, 83.12; H, 8.97. Found: C, 83.245; H, 8.980 %.



79b

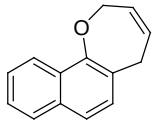
7-Chloro-2,5-dihydro-benzo[*b*]oxepine (79c):[49] Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 1663,



79c

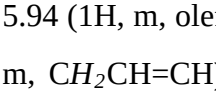
1483, 1308, 1237, 1172, 1057, 876, 824 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.13 (1H, dd, *J* = 8.4 Hz, 2.4 Hz), 7.07 (1H, d, *J* = 2.4 Hz), 6.97 (1H, d, *J* = 8.4 Hz), 5.80-5.78 (1H, m, olefinic-*H*), 5.48-5.43 (1H, m, olefinic-*H*), 4.56-4.54 (2H, m, O*CH*$_2$), 3.43-3.42 (2H, m, *CH*$_2$CH=CH); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 157.3 (C), 137.8 (C), 128.8 (C), 128.6 (CH), 127.6 (CH), 127.4 (CH), 125.1 (CH), 122.8 (CH), 71.2 (CH_2, O*CH*$_2$CH=CH), 31.4 (CH_2, *CH*$_2$CH=CH); LCMS m/z 181 ($M+H^+$), calcd $C_{10}H_9ClO$ 180.0342.

7,10-Dihydro-11-oxa-cyclohepta[*a*]naphthalene (79d):[48a] Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 2928, 1593, 1465, 1224, 1025, 742, 653 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.02 (1H, d, *J* = 8.8 Hz), 7.82 (1H, d, *J* = 8.0 Hz), 7.71 (1H, d, *J* = 8.4 Hz), 7.49 (1H, t, *J* = 6.8 Hz), 7.39 (1H, t, *J* = 8.0 Hz), 7.28 (1H, d, *J* = 8.8 Hz), 5.98-5.94 (1H, m, olefinic-*H*), 5.54-5.50 (1H, m, olefinic-*H*), 4.65 (2H, m, O*CH*$_2$), 3.92 (2H, m, *CH*$_2$CH=CH); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 156.1 (C), 131.6 (C), 131.1 (C), 130.5 (C), 128.6 (CH), 128.1 (CH), 127.9 (CH), 126.1 (CH), 125.8 (CH), 124.3 (CH), 122.9 (CH), 121.8 (CH), 70.7 (CH_2, O*CH*$_2$CH=CH), 24.6 (CH_2, *CH*$_2$CH=CH); LCMS m/z 197 ($M+H^+$), calcd $C_{14}H_{12}O$ 196.0888.



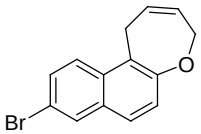
79d

1,4-Dihydro-naphtho[2,1-*b*]oxepine (79e):[48] Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 2928, 1593, 1465, 1224, 1025, 742, 653 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.18 (1H, d, *J* = 8.4 Hz), 7.81 (1H, d, *J* = 8.0 Hz), 7.52 (1H, d, *J* = 8.4 Hz), 7.48-7.43 (2H, m), 7.22 (1H, d, *J* = 8.4 Hz), 5.93-5.90 (1H, m, olefinic-*H*), 5.55 (1H, d, *J* = 11.2 Hz, olefinic-*H*), 4.70 (2H, d, *J* = 4.8 Hz, O*CH*$_2$), 3.64 (2H, d, *J* = 4.4 Hz, *CH*$_2$CH=CH); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 153.5 (C), 133.8 (C), 131.1 (C), 127.9 (C), 127.6 (CH), 127.5 (CH), 127.4 (CH), 125.9 (CH), 125.6 (CH), 125.5 (CH), 123.3 (CH), 121.4 (CH), 70.0 (CH_2, O*CH*$_2$CH=CH), 32.1 (CH_2, *CH*$_2$CH=CH); LCMS m/z 197.00 ($M+H^+$), calcd $C_{14}H_{12}O$ 196.0888.

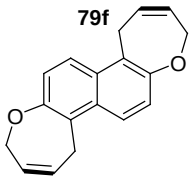


79e

9-Bromo-1,4-dihydro-naphtho[2,1-*b*]oxepine (79f):[48b] Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR



79f



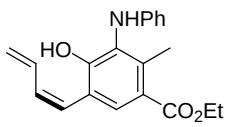
79g

(neat): ν_{max} 2933, 1587, 1497, 1222, 1062, 880, 824 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.96 (1H, d, *J* = 2.0 Hz), 7.88 (1H, d, *J* = 9.2 Hz), 7.61 (1H, d, *J* = 8.8 Hz), 7.54 (1H, dd, *J* = 9.2 Hz, 2.0 Hz), 7.29 (1H, d, *J* = 8.8 Hz), 5.99-5.93 (1H, m, olefinic-*H*), 5.55-5.51 (1H, m, olefinic-*H*), 4.66-4.64 (2H, m, OCH_2), 3.89-3.87 (2H, m, CH_2CH=CH); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 156.3 (C), 132.2 (C), 130.9 (C), 130.5 (CH), 130.2 (C), 129.3 (CH), 128.0 (CH), 127.2 (CH), 125.6 (CH), 124.9 (CH), 123.0 (CH), 118.3 (C), 70.6 (CH_2, OCH_2CH=CH), 24.7 (CH_2, CH_2CH=CH); LCMS m/z 275 ($M+H^+$), calcd $C_{14}H_{11}BrO$ 273.9993.

***C*$_2$-Symmetric 1,4-Dihydro-naphtho[2,1-*b*]oxepine (79g):** Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3029, 2928, 1596, 1514, 1427, 1240, 1061, 726, 636 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.89 (2H, d, *J* = 9.2 Hz), 7.26 (2H, d, *J* = 8.8 Hz), 5.94-5.92 (2H, m, olefinic-H), 5.47 (2H, d, *J* = 10.8 Hz), 4.60 (4H, br s, OCH_2), 3.88 (4H, br s, CH_2CH=CH); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 155.0 (2 x C), 131.3 (2 x C), 129.2 (2 x C), 127.9 (2 x CH), 125.8 (2 x CH), 122.9 (2 x CH), 121.9 (2 x CH), 70.8 (2 x CH_2, 2 x OCH_2CH=CH), 24.9 (2 x CH_2, 2 x CH_2CH=CH); LCMS m/z 265 ($M+H^+$), calcd $C_{18}H_{16}O_2$ 264.1150; Anal. calcd for $C_{18}H_{16}O_2$ (264.11): C, 81.79; H, 6.10. Found: C, 81.742; H, 6.121%.

3E: General Experimental Procedure for the Base-Induced Ring Opening (BIRO) Reactions: A 10 mL oven-dried round bottom flask equipped with a stir bar was charged with **72**/**79** (0.1 mmol), dry DMSO (2 mL, 0.05 M), to that *t*BuOK (22.4 mg, 0.2 mmol, 2 equiv.) was added at 0 °C. The reaction mixture was stirred at RT for 1 h. The crude reaction mixture was worked up with water and the aqueous layer was extracted with ether (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure products **73**/**80** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

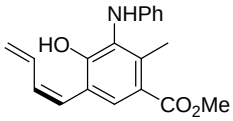
5-Buta-1,3-dienyl-4-hydroxy-2-methyl-3-phenylamino-benzoic acid ethyl ester (73a): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3383 (O-H*)*, 3345 (N-H),



73a

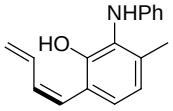
1691 (O-C=O), 1652, 1605, 1500, 1468, 1234, 1056, 750, 708 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.93 (1H, s, Ar-*H*), 7.20 (2H, t, *J* = 8.0 Hz), 6.86 (1H, t, *J* = 8.0 Hz), 6.83-6.77 (1H, m, olefinic-*H*), 6.60 (2H, d, *J* = 8.0 Hz), 6.55 (1H, d, *J* = 12 Hz, olefinic-*H*), 6.37 (1H, t, *J* = 12 Hz, olefinic-*H*), 5.41 (1H, br d, *J* = 16 Hz, olefinic-*H*), 5.26 (1H, br d, *J* = 12 Hz, olefinic-*H*), 5.02 (1H, s, *N*-*H*), 4.31 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 2.40 (3H, s, Ar-CH_3), 1.37 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.3 (C, O-C=O), 154.8 (C), 145.7 (C), 139.0 (C), 133.1 (CH), 131.8 (CH), 131.7 (CH), 129.6 (2 x CH), 127.0 (C), 124.2 (CH), 122.3 (C), 121.0 (C), 120.3 (CH), 119.9 (CH_2, CH=CH_2), 114.2 (2 x CH), 60.7 (CH_2, OCH_2CH_3), 15.7 (CH_3, Ar-CH_3), 14.3 (CH_3, OCH_2CH_3); LCMS m/z 324.00 ($M+H^+$), calcd $C_{20}H_{21}NO_3$ 323.1521; Anal. calcd for $C_{20}H_{21}NO_3$ (323.15): C, 74.28; H, 6.55; N, 4.33. Found: C, 74.194; H, 6.560; N, 4.300%.

5-Buta-1,3-dienyl-4-hydroxy-2-methyl-3-phenylamino-benzoic acid methyl ester (73b): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3379 (O-H & *N*-*H*), 2926, 1720 (O-C=O), 1600, 1495, 1454, 1239, 1196, 1045, 749, 655 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.93 (1H, s, Ar-*H*), 7.19 (2H, t, *J* = 7.6 Hz), 7.01 (1H, s, *O*-*H*), 6.86 (1H, t, *J* = 7.2 Hz), 6.83-6.76 (1H, m, olefinic-*H*), 6.59 (2H, d, *J* = 7.6 Hz), 6.53 (1H, d, *J* = 11.6 Hz, olefinic-*H*), 6.36 (1H, t, *J* = 11.2 Hz, olefinic-*H*), 5.41 (1H, br d, *J* = 16 Hz, olefinic-*H*), 5.27 (1H, br d, *J* = 10 Hz, olefinic-*H*), 5.01 (1H, s, *N*-*H*), 3.86 (3H, s, OCH_3), 2.40 (3H, s, Ar-CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.7 (C, O-C=O), 154.9 (C), 145.6 (C), 139.2 (C), 133.1 (CH), 131.9 (CH), 131.7 (CH), 129.6 (2 x CH), 127.0 (C), 124.2 (CH), 121.9 (C), 121.0 (C), 120.3 (CH), 120.0 (CH_2, CH=CH_2), 114.3 (2 x CH), 51.8 (CH_3, OCH_3), 15.7 (CH_3, Ar-CH_3); LCMS m/z 308.00 ($M-H^+$), calcd $C_{19}H_{19}NO_3$ 309.3591; Anal. calcd for $C_{19}H_{19}NO_3$ (309.35): C, 73.77; H, 6.19; N, 4.53. Found: C, 73.758; H, 6.197; N, 4.778%.



73b

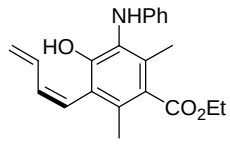
6-Buta-1,3-dienyl-3-methyl-2-phenylamino-phenol (73c): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat):



73c

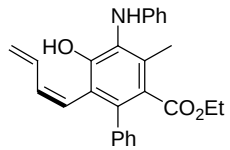
ν_{max} 3386 (O-H & *N-H)*, 3042, 2973, 1601, 1493, 1448, 1230, 1111, 1030, 749, 635 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.20-7.16 (3H, m, Ph-*H*), 6.86-6.81 (2H, m, Ph-*H*), 6.76 (1H, d, *J* = 7.6 Hz), 6.62-6.57 (3H, m), 6.52 (1H, s, *O-H*), 6.31 (1H, t, *J* = 11.2 Hz, olefinic-*H*), 5.37 (1H, br d, *J* = 16.8 Hz, olefinic-*H*), 5.21 (1H, br d, *J* = 10 Hz, olefinic-*H*), 4.89 (1H, s, N-H), 2.12 (3H, s, Ar-C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 151.7 (C), 146.0 (C), 136.2 (C), 133.6 (CH), 130.7 (CH), 129.5 (2 x CH), 128.7 (CH), 126.2 (C), 125.3 (CH), 121.6 (C), 121.3 (CH), 119.8 (CH), 119.1 (CH_2, CH=*CH*$_2$), 114.3 (2 x CH), 17.8 (CH_3, Ar-*CH*$_3$); LCMS m/z 252 ($M+H^+$), calcd $C_{17}H_{17}NO$ 251.3230; Anal. calcd for $C_{17}H_{17}NO$ (251.32): C, 81.24; H, 6.82; N, 5.57. Found: C, 81.302; H, 6.822; N, 5.336%.

3-Buta-1,3-dienyl-4-hydroxy-2,6-dimethyl-5-phenylamino-benzoic acid ethyl ester (73d): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3391 (*O-H*), 3316 (*N-H)*, 2981, 1711 (O-C=O), 1601, 1497, 1451, 1203, 1038, 743, 634 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.18 (2H, t, *J* = 8.0 Hz), 6.83 (1H, t, *J* = 7.2 Hz), 6.61 (2H, d, *J* = 8.0 Hz), 6.45 (1H, t, *J* = 11.2 Hz, olefinic-*H*), 6.34 (1H, s, *O-H*), 6.29-6.21 (2H, m, olefinic-*H*), 5.34 (1H, br d, *J* = 16.8 Hz, olefinic-*H*), 5.17 (1H, br d, *J* = 10 Hz, olefinic-*H*), 5.06 (1H, s, *N-H*), 4.37 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 2.19 (3H, s, Ar-C*H*$_3$), 2.10 (3H, s, Ar-C*H*$_3$), 1.37 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.9 (C, O-C=O), 151.1 (C), 145.9 (C), 133.8 (CH), 133.6 (CH), 132.8 (C), 132.7 (C), 129.4 (2 x CH), 127.8 (C), 124.4 (CH), 124.2 (C), 121.2 (C), 119.8 (CH), 119.6 (CH_2, CH=*CH*$_2$), 114.4 (2 x CH), 61.1 (CH_2, O*CH*$_2$CH$_3$), 17.3 (CH_3, Ar-*CH*$_3$), 15.2 (CH_3, Ar-*CH*$_3$), 14.2 (CH_3, OCH$_2$*CH*$_3$); LCMS m/z 338.00 ($M+H^+$), calcd $C_{21}H_{23}NO_3$ 337.4123; Anal. calcd for $C_{21}H_{23}NO_3$ (337.41): C, 74.75; H, 6.87; N, 4.15. Found: C, 74.802; H, 6.872; N, 4.285%.



73d

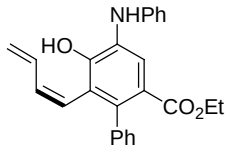
6-Buta-1,3-dienyl-5-hydroxy-3-methyl-4-phenylamino-biphenyl-2-carboxylic acid ethyl ester (73e): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max}



73e

3315 (O-H & N-H), 1710 (O-C=O), 1602, 1497, 1449, 1207, 1082 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.32-7.20 (7H, m, Ph-*H*), 6.87 (1H, t, *J* = 7.2 Hz), 6.70 (2H, d, *J* = 7.6 Hz), 6.37 (1H, s, O-H), 6.33 (1H, m, olefinic-*H*), 6.23 (1H, t, *J* = 10.8 Hz, olefinic-*H*), 5.90 (1H, d, *J* = 10.8 Hz, olefinic-*H*), 5.28 (1H, br d, *J* = 15.2 Hz, olefinic-*H*), 5.27 (1H, s, *N*-*H*), 5.17 (1H, br d, *J* = 10 Hz, olefinic-*H*), 3.90 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 2.19 (3H, s, Ar-CH_3), 0.86 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.2 (C, O-C=O), 150.4 (C), 145.7 (C), 138.8 (C), 138.3 (C), 133.7 (CH), 133.3 (CH), 133.1 (C), 129.5 (2 x CH), 129.4 (2 x CH), 127.8 (C), 127.7 (2 x CH), 127.3 (CH), 126.1 (C), 124.8 (CH), 120.5 (C), 119.9 (CH), 119.8 (CH_2, CH=CH_2), 114.7 (2 x CH), 60.8 (CH_2, OCH_2CH_3), 15.3 (CH_3, Ar-CH_3), 13.5 (CH_3, OCH_2CH_3); LCMS m/z 400.00 ($M+H^+$), calcd $C_{26}H_{25}NO_3$ 399.4816; Anal. calcd for $C_{26}H_{25}NO_3$ (399.48): C, 78.17; H, 6.31; N, 3.51. Found: C, 78.152; H, 6.321; N, 3.509%.

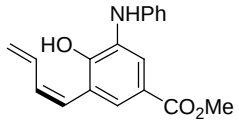
6-Buta-1,3-dienyl-5-hydroxy-4-phenylamino-biphenyl-2-carboxylic acid ethyl ester



73f

(73f): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 3414 (O-H & N-H), 2980, 1709 (O-C=O), 1592, 1502, 1464, 1269, 1094, 737, 699 cm^{-1}; ^1H NMR (Acetone-d_6) δ 7.68 (1H, s, O-*H*), 7.67 (1H, s, Ar-*H*), 7.23-7.18 (5H, m, Ph-*H*), 7.07 (2H, d, *J* = 7.6 Hz), 7.03 (2H, d, *J* = 8.0 Hz), 6.82 (1H, t, *J* = 7.6 Hz), 6.80 (1H, s, *N*-*H*), 6.26 (1H, m, olefinic-*H*), 6.10 (1H, t, *J* = 11.2 Hz, olefinic-*H*), 5.84 (1H, d, *J* = 10.8 Hz, olefinic-*H*), 5.16 (1H, br d, *J* = 16.4 Hz, olefinic-*H*), 5.07 (1H, br d, *J* = 10 Hz, olefinic-*H*), 3.77 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 0.74 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR (Acetone-d_6, DEPT-135) δ 168.4 (C, O-C=O), 147.9 (C), 144.9 (C), 141.5 (C), 136.7 (C), 134.7 (2 x CH), 130.3 (2 x CH), 130.1 (2 x CH), 128.3 (2 x CH), 127.3 (CH), 126.1 (CH), 124.7 (C), 124.6 (C), 121.4 (CH), 119.8 (CH_2, CH=CH_2), 119.6 (C), 119.3 (CH), 118.5 (CH), 118.4 (CH), 60.8 (CH_2, OCH_2CH_3), 13.9 (CH_3, OCH_2CH_3); LCMS m/z 386.00 ($M+H^+$), calcd $C_{25}H_{23}NO_3$ 385.4551; Anal. calcd for $C_{25}H_{23}NO_3$ (385.45): C, 77.90; H, 6.01; N, 3.63. Found: C, 77.790; H, 6.105; N, 3.477%.

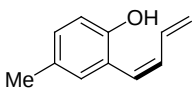
3-Buta-1,3-dienyl-4-hydroxy-5-phenylamino-benzoic acid methyl ester (73g):



73g

Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3374 (O-H & *N-H)*, 2950, 1710 (O-C=O), 1589, 1495, 1436, 1202, 1082, 887 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.86 (1H, s, Ar-*H*), 7.70 (1H, s, Ar-*H*), 7.28 (2H, t, *J* = 7.6 Hz), 7.27 (1H, d, *J* = 6.4 Hz), 6.95 (1H, t, J = 7.2 Hz), 6.92 (2H, d, *J* = 7.6 Hz), 6.66-6.62 (1H, m, olefinic-*H*), 6.48 (1H, t, *J* = 8.4 Hz), 6.47 (1H, s, *O-H*), 5.55 (1H, s, *N-H*), 5.45 (1H, br d, *J* = 16.4 Hz, olefinic-*H*), 5.31 (1H, br d, *J* = 10 Hz, olefinic-*H*), 3.86 (3H, s, O*CH*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.7 (C, O-C=O), 150.2 (C), 143.9 (C), 133.6 (CH), 132.6 (CH), 130.1 (C), 129.5 (2 x CH), 126.7 (CH), 123.9 (CH), 123.5 (C), 122.3 (C), 121.7 (CH), 121.2 (CH), 121.1 (CH_2, CH=*CH*$_2$), 117.1 (2 x CH), 51.9 (CH_3, OC*H*$_3$); LCMS m/z 296.00 ($M+H^+$), calcd $C_{18}H_{17}NO_3$ 295.1208; Anal. calcd for $C_{18}H_{17}NO_3$ (295.12): C, 73.20; H, 5.80; N, 4.74. Found: C, 73.231; H, 5.819; N, 5.089%.

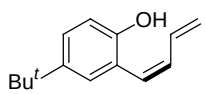
2-Buta-1,3-dienyl-4-methyl-phenol (80a): Purified by column chromatography using



80a

EtOAc/hexane and isolated as a yellow liquid. IR (neat): ν_{max} 3423 (O-H), 3022, 2919, 1609, 1495, 1458, 1219, 1004, 807 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.98 (1H, d, *J* = 8.0 Hz), 6.97 (1H, s), 6.78 (1H, d, *J* = 8.0 Hz), 6.58-6.53 (1H, m, olefinic-*H*), 6.40-6.39 (2H, m, olefinic-*H*), 5.40 (1H, dd, *J* = 16.8 Hz, 1.2 Hz, olefinic-*H*), 5.24 (1H, br d, *J* = 10.8 Hz, olefinic-*H*), 4.88 (1H, s, O-H), 2.27 (3H, s, Ar-C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 150.5 (C), 133.2 (CH), 132.9 (CH), 130.3 (CH), 129.5 (CH), 129.4 (C), 125.0 (CH), 123.1 (C), 120.4 (CH_2, CH=*CH*$_2$), 115.3 (CH), 20.4 (CH_3, Ar-*C*H$_3$); LCMS m/z 161 ($M+H^+$), calcd $C_{11}H_{12}O$ 160.0888; Anal. calcd for $C_{11}H_{12}O$ (160.08): C, 82.46; H, 7.55. Found: C, 82.567; H, 7.599 %.

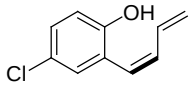
2-Buta-1,3-dienyl-4-tert-butyl-phenol (80b): Purified by column chromatography



80b

using EtOAc/hexane and isolated as a yellow liquid. IR (neat): ν_{max} 3426 (*O-H*), 2960, 1498, 1269, 1204, 1123, 1089, 821, 673 cm^{-1}; ^1H

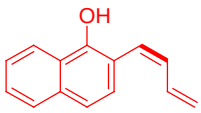
NMR ($CDCl_3$) δ 7.21-7.16 (2H, m), 6.81 (1H, d, *J* = 8.4 Hz), 6.62-6.51 (1H, m, olefinic-*H*), 6.47-6.36 (2H, m, olefinic-*H*), 5.39 (1H, br d, *J* = 16.8 Hz, olefinic-*H*), 5.24 (1H, br d, *J* = 10.0 Hz, olefinic-*H*), 4.94 (1H, s, O-H), 1.29 (9H, s, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 150.4 (C), 143.0 (C), 133.03 (CH), 133.00 (CH), 126.9 (CH), 125.9 (CH), 125.5 (CH), 122.7 (C), 120.4 (CH_2, CH=CH_2), 115.0 (CH), 34.0 (C), 31.5 (CH_3, C(CH_3)$_3$); LCMS m/z 203.00 ($M+H^+$), calcd $C_{14}H_{18}O$ 202.1358; Anal. calcd for $C_{14}H_{18}O$ (202.13): C, 83.12; H, 8.97. Found: C, 83.255; H, 9.027 %.



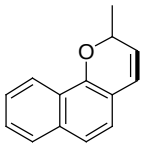
80c

2-Buta-1,3-dienyl-4-chloro-phenol (80c): Purified by column chromatography using EtOAc/hexane and isolated as a yellow liquid. IR (neat): ν_{max} 3412 (*O-H*), 1481, 1435, 1200, 1109, 911, 798, 652 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.14-7.12 (2H, m, Ph-*H*), 6.82 (1H, d, *J* = 9.2 Hz), 6.51-6.45 (1H, m), 6.43 (1H, d, *J* = 12.8 Hz, olefinic-*H*), 6.32 (1H, d, *J* = 10.0 Hz, olefinic-*H*), 5.44 (1H, br d, *J* = 17.6 Hz, olefinic-*H*), 5.31 (1H, dd, *J* = 9.6 Hz, 2.0 Hz, olefinic-*H*), 5.01 (1H, s, O-H); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 151.4 (C), 134.5 (CH), 132.4 (CH), 129.5 (CH), 128.8 (CH), 125.2 (C), 124.9 (C), 123.4 (CH), 121.7 (CH_2, CH=CH_2), 116.8 (CH); LCMS m/z 181 ($M+H^+$), calcd $C_{10}H_9ClO$ 180.0342; Anal. calcd for $C_{10}H_9ClO$ (180.03): C, 66.49; H, 5.02. Found: C, 66.452; H, 5.084%.

2-Buta-1,3-dienyl-naphthalen-1-ol (80d) and 2-Methyl-2*H*-benzo[*h*]chromene (81d): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3057, 1632, 1588, 1513, 1463, 1231, 1105, 1030, 814, 701, 659 cm^{-1}; ^{1}H NMR (Acetone-d_6, 1:1 mixture of **80d** and **81d**) δ 8.00 (1H, s, O-*H*), 7.88 (1H, d, *J* = 8.4 Hz), 7.67-7.56 (5H, m, Ph-*H*), 7.34 (1H, t, *J* = 7.2 Hz), 7.28 (1H, t, *J* = 7.2 Hz), 7.18 (1H, t, *J* = 8.0 Hz), 7.15 (1H, d, *J* = 7.2 Hz), 7.09 (1H, d, *J* = 8.8 Hz), 7.03 (1H, d, *J* = 9.6 Hz), 6.91 (1H, d, *J* = 8.8 Hz), 6.54-6.41 (2H, m), 6.05-5.98 (1H, m, olefinic-*H*), 5.73 (1H, dd, *J* = 10 Hz, 3.2 Hz, olefinic-*H*), 5.19 (1H, br d, *J* = 16.8 Hz, olefinic-*H*), 4.93 (1H, br d, *J* = 9.2 Hz, olefinic-*H*), 4.92 (1H, m, O*CH*), 1.31 (3H, d, *J* = 6.4 Hz); ^{13}C NMR (Acetone-d_6, DEPT-135, 1:1 mixture of **80d** and **81d**) δ 152.7 (C), 152.6 (C), 135.5 (CH), 134.7 (CH), 134.0 (C), 130.9 (C), 130.3 (C),



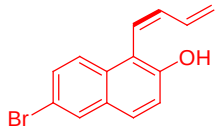
80d



81d

130.2 (CH), 129.9 (CH), 129.6 (C), 129.4 (CH), 129.1 (CH), 127.6 (CH), 127.1 (CH), 126.8 (CH), 125.5 (CH), 125.2 (CH), 124.4 (CH), 123.8 (CH), 122.3 (CH), 120.5 (CH), 118.9 (CH_2, $CH{=}CH_2$), 118.9 (CH), 118.8 (CH), 117.1 (C), 115.4 (C), 72.1 (CH, O*CH*), 21.1 (CH_3); LCMS m/z 197 ($M+H^+$), calcd $C_{14}H_{12}O$ 196.0888.

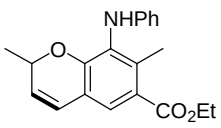
6-Bromo-1-buta-1,3-dienyl-naphthalen-2-ol (80f): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 2922, 1624, 1584, 1501, 1208, 1104, 1032, 770, 659 cm^{-1}; ^1H NMR (Acetone-d_6) δ 8.29 (1H, s, Ar-*H*), 7.88 (1H, d, *J* = 2.0 Hz), 7.62 (1H, d, *J* = 9.2 Hz), 7.55 (1H, d, *J* = 8.8 Hz), 7.38 (1H, dd, *J* = 8.8 Hz, 2.0 Hz), 7.15 (1H, d, *J* = 8.8 Hz), 6.46-6.42 (2H, m, olefinic-*H*), 6.03-5.94 (1H, m, O*H*), 5.21 (1H, dd, *J* = 17.2 Hz, 2.0 Hz, olefinic-*H*), 4.96 (1H, dd, *J* = 10.4 Hz, 2.0 Hz, olefinic-*H*); ^{13}C NMR (Acetone-d_6, DEPT-135) δ 153.3 (C), 135.2 (CH), 135.0 (CH), 132.5 (C), 131.2 (C), 130.8 (CH), 130.7 (C), 130.0 (CH), 129.1 (CH), 127.5 (CH), 124.8 (CH), 120.2 (CH), 119.4 (CH_2, $CH{=}CH_2$), 116.9 (C); LCMS m/z 275 ($M+H^+$), calcd $C_{14}H_{11}BrO$ 273.9993; Anal. calcd for $C_{14}H_{11}BrO$ (273.99): C, 61.11; H, 4.03. Found: C, 61.114; H, 4.059%.



80f

3F: General Experimental Procedure for the Synthesis of Highly Functionalized 2-Methyl-2*H*-chromenes: Method 1: Compounds **73/80** (0.1 mmol), DMF (0.1 mL, 1 M) were taken in a sealed glass tube and the mixture was heated at 140 °C under N_2 for 12 to 14 h. Upon cooling to room temperature, the mixture was diluted with CH_2Cl_2 (10 mL), washed with NH_4Cl solution (5 mL) and brine (5 mL). The separated organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. Pure products **74/81** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate). **Method 2:** To the crude compounds **73/80**, 5 gm of silica (particle size 0.063-0.200 mm), 5 ml of $CHCl_3$ was added and the reaction mixture stirred at RT for 6 to 8 h. Pure products **74/81** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

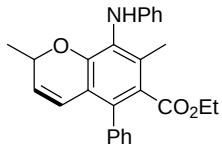
2,7-Dimethyl-8-phenylamino-2*H*-chromene-6-carboxylic acid ethyl ester (74a):



74a

Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3384 (N-*H*), 2976, 1711 (O-C=O), 1602, 1497, 1455, 1246, 1125, 1051, 749, 694 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.47 (1H, s, Ar-*H*), 7.19 (2H, t, *J* = 7.6 Hz), 6.83 (1H, t, *J* = 7.6 Hz), 6.65 (2H, d, *J* = 7.6 Hz), 6.40 (1H, dd, *J* = 10 Hz, 1.6 Hz, olefinic-*H*), 5.67 (1H, dd, *J* = 10 Hz, 3.2 Hz, olefinic-*H*), 5.58 (1H, s, *N*-*H*), 5.04-5.01 (1H, m, OC*H*), 4.35 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 2.39 (3H, s, Ar-C*H*$_3$), 1.41 (3H, d, *J* = 7.2 Hz), 1.37 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.5 (C, O-C=O), 150.6 (C), 145.9 (C), 137.9 (C), 129.4 (C), 128.9 (2 x CH), 126.3 (CH), 125.1 (CH), 123.4 (C), 123.0 (CH), 119.4 (CH), 118.9 (C), 115.3 (2 x CH), 72.5 (CH, O-*CH*), 60.6 (CH$_2$, O*CH*$_2$CH$_3$), 21.6 (CH$_3$), 16.5 (CH$_3$, Ar-*CH*$_3$), 14.4 (CH$_3$, OCH$_2$*CH*$_3$); LCMS m/z 324.00 ($M+H^+$), calcd $C_{20}H_{21}NO_3$ 323.1521; Anal. calcd for $C_{20}H_{21}NO_3$ (323.15): C, 74.28; H, 6.55; N, 4.33. Found: C, 74.214; H, 6.526; N, 4.298%.

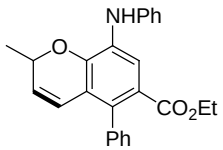
2,7-Dimethyl-5-phenyl-8-phenylamino-2*H*-chromene-6-carboxylic acid ethyl ester



74e

(74e): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3384 (N-*H*), 2977, 1719 (O-C=O), 1600, 1497, 1450, 1248, 1127, 1054, 745, 699 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38-7.26 (5H, m, Ph-*H*), 7.21 (2H, t, *J* = 7.6 Hz), 6.84 (1H, t, *J* = 7.2 Hz), 6.74 (2H, d, *J* = 7.2 Hz), 6.12 (1H, d, *J* = 10 Hz, olefinic-*H*), 5.64 (1H, s, *N*-*H*), 5.57 (1H, d, *J* = 9.2 Hz, olefinic-*H*), 4.93 (1H, m, OC*H*), 3.93 (2H, q, *J* = 6.8 Hz, OC*H*$_2$CH$_3$), 2.17 (3H, s, Ar-C*H*$_3$), 1.37 (3H, d, *J* = 6.4 Hz), 0.88 (3H, t, *J* = 6.8 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.4 (C, O-C=O), 148.4 (C), 145.8 (C), 137.8 (C), 133.1 (C), 131.9 (C), 129.9 (CH), 129.8 (CH), 128.9 (2 x CH), 128.3 (C), 128.2 (C), 127.9 (2 x CH), 127.4 (CH), 126.1 (CH), 122.0 (CH), 119.5 (CH), 118.5 (C), 115.6 (2 x CH), 71.4 (CH, O-*CH*), 60.7 (CH$_2$, O*CH*$_2$CH$_3$), 21.1 (CH$_3$), 15.8 (CH$_3$, Ar-*CH*$_3$), 13.6 (CH$_3$, OCH$_2$*CH*$_3$); LCMS m/z 400.00 ($M+H^+$), calcd $C_{26}H_{25}NO_3$ 399.4816; Anal. calcd for $C_{26}H_{25}NO_3$ (399.48): C, 78.17; H, 6.31; N, 3.51. Found: C, 78.369; H, 6.326; N, 3.727%.

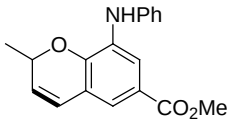
2-Methyl-5-phenyl-8-phenylamino-2*H*-chromene-6-carboxylic acid ethyl ester



74f

(74f): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3410 (N-*H*), 2978, 1708 (O-C=O), 1591, 1503, 1463, 1232, 1133, 1026, 699 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.74 (1H, s, Ar-*H*), 7.38-7.29 (5H, m, Ph-*H*), 7.19 (4H, t, *J* = 7.6 Hz), 6.98 (1H, t, *J* = 7.2 Hz), 6.11 (1H, s, *N*-*H*), 6.10 (1H, dd, *J* = 10.4 Hz, 2.0 Hz, olefinic-*H*), 5.60 (1H, dd, *J* = 10.4 Hz, 3.2 Hz, olefinic-*H*), 5.07-5.05 (1H, m, OC*H*), 3.94 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 1.51 (3H, d, *J* = 6.8 Hz), 0.87 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.2 (C, O-C=O), 144.1 (C), 142.0 (C), 139.0 (C), 131.5 (C), 131.1 (C), 129.8 (2 x CH), 129.4 (2 x CH), 127.6 (2 x CH), 126.8 (CH), 126.2 (CH), 123.9 (C), 122.4 (CH), 121.7 (CH), 120.4 (C), 118.9 (2 x CH), 115.7 (CH), 71.6 (CH, O-*CH*), 60.4 (CH_2, OCH_2CH_3), 21.3 (CH_3), 13.5 (CH_3, OCH_2CH_3); LCMS m/z 386.00 ($M+H^+$), calcd $C_{25}H_{23}NO_3$ 385.4551; Anal. calcd for $C_{25}H_{23}NO_3$ (385.45): C, 77.90; H, 6.01; N, 3.63. Found: C, 77.823; H, 6.061; N, 3.662%.

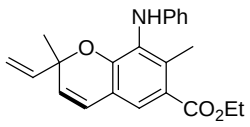
2-Methyl-8-phenylamino-2*H*-chromene-6-carboxylic acid methyl ester (74g):



74g

Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3346 (N-*H*), 2920, 1710 (O-C=O), 1586, 1496, 1435, 1200, 1083, 770, 695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.84 (1H, d, *J* = 2.0 Hz, Ar-*H*), 7.31 (2H, t, *J* = 8.0 Hz), 7.28 (1H, d, *J* = 2.0 Hz, Ar-*H*), 7.16 (2H, d, *J* = 7.6 Hz), 6.98 (1H, t, *J* = 7.6 Hz), 6.42 (1H, dd, *J* = 10 Hz, 1.6 Hz, olefinic-*H*), 6.04 (1H, s, *N*-*H*), 5.72 (1H, dd, *J* = 10 Hz, 2.8 Hz, olefinic-*H*), 5.16-5.13 (1H, m, OC*H*), 3.84 (3H, s, OCH_3), 1.51 (3H, d, *J* = 6.4 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.0 (C, O-C=O), 145.3 (C), 142.1 (C), 131.8 (C), 129.4 (2 x CH), 126.7 (CH), 123.5 (CH), 122.6 (C), 121.7 (CH), 120.8 (C), 119.6 (CH), 118.9 (2 x CH), 115.8 (CH), 72.6 (CH, O-*CH*), 51.9 (CH_3, OCH_3), 21.7 (CH_3); LCMS m/z 296.00 ($M+H^+$), calcd $C_{18}H_{17}NO_3$ 295.1208; Anal. calcd for $C_{18}H_{17}NO_3$ (295.12): C, 73.20; H, 5.80; N, 4.74. Found: C, 73.236; H, 5.834; N, 4.808%.

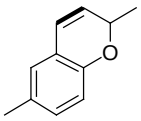
2,7-Dimethyl-8-phenylamino-2-vinyl-2*H*-chromene-6-carboxylic acid ethyl ester (74h): Purified by column chromatography using EtOAc/hexane



74h

and isolated as a solid. IR (neat): ν_{max} 3388 (*N-H)*, 2961, 1713 (O-C=O), 1602, 1497, 1453, 1214, 1116, 1051, 744 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.49 (1H, s, Ar-*H*), 7.18 (2H, t, *J* = 8.0 Hz), 6.83 (1H, t, *J* = 7.6 Hz), 6.65 (2H, d, *J* = 8.0 Hz), 6.45 (1H, d, *J* = 9.6 Hz, olefinic-*H*), 5.81 (1H, dd, *J* = 17.6 Hz, 10.8 Hz, olefinic-*H*), 5.62 (1H, s, *N*-*H*), 5.61 (1H, d, *J* = 12.8 Hz), 5.11 (1H, br d, *J* = 17.6 Hz), 5.02 (1H, br d, *J* = 10.8 Hz), 4.34 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 2.39 (3H, s, Ar-CH_3), 1.48 (3H, s, CH_3), 1.39 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.6 (C, O-C=O), 150.0 (C), 145.9 (C), 139.9 (CH), 137.9 (C), 129.6 (C), 128.9 (2 x CH), 127.5 (CH), 125.0 (CH), 123.4 (C), 122.9 (CH), 119.6 (CH), 118.6 (C), 115.6 (2 x CH), 114.2 (CH_2, CH=CH_2), 79.1 (C), 60.6 (CH_2, OCH_2CH_3), 27.1 (CH_3), 16.6 (CH_3, Ar-CH_3), 14.4 (CH_3, OCH_2CH_3); LCMS m/z 350.00 ($M+H^+$), calcd $C_{22}H_{23}NO_3$ 349.4230; Anal. calcd for $C_{22}H_{23}NO_3$ (349.42): C, 75.62; H, 6.63; N, 4.01. Found: C, 75.572; H, 6.614; N, 4.014%.

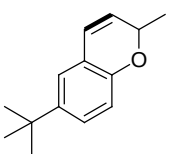
2,6-Dimethyl-2*H*-chromene (81a): Purified by column chromatography using



81a

EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2974, 1492, 1220, 1150, 1029, 814, 767, 710 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.89 (1H, d, *J* = 8.0 Hz), 6.77 (1H, s, Ar-H), 6.67 (1H, d, *J* = 8.4 Hz), 6.33 (1H, d, *J* = 10.0 Hz, olefinic-*H*), 5.64 (1H, dd, *J* = 10 Hz, 2.8 Hz, olefinic-*H*), 4.95-4.93 (1H, m, OC*H*), 2.24 (3H, s, Ar-CH_3), 1.42 (3H, d, *J* = 6.4 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 151.2 (C), 130.2 (C), 129.5 (CH), 127.0 (CH), 126.9 (CH), 123.9 (CH), 121.7 (C), 115.7 (CH), 71.3 (CH, O*CH*), 21.2 (CH_3, Ar-CH_3), 20.5 (CH_3); LCMS m/z 161 ($M+H^+$), calcd $C_{11}H_{12}O$ 160.0888; Anal. calcd for $C_{11}H_{12}O$ (160.08): C, 82.46; H, 7.55. Found: C, 82.464; H, 7.558 %.

6-tert-Butyl-2-methyl-2*H*-chromene (81b): Purified by column chromatography using

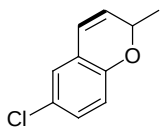


81b

EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2960, 1496, 1366, 1200, 1129, 827, 736 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.12 (1H, dd, *J* = 8.4 Hz, 2.4 Hz), 6.96 (1H, d, *J* = 2.4 Hz), 6.71 (1H, d, *J* = 8.4 Hz), 6.37 (1H, d, *J* = 9.6 Hz, olefinic-*H*), 5.63 (1H, dd, *J* = 9.6 Hz, 2.8 Hz, olefinic-*H*), 4.98-4.95 (1H, m, OC*H*), 1.42 (3H, d, *J* = 6.4 Hz), 1.28 (9H, s, $C(CH_3)_3$);

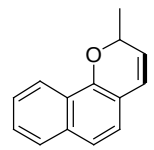
^{13}C NMR ($CDCl_3$, DEPT-135) δ 151.2 (C), 143.7 (C), 126.7 (CH), 125.9 (CH), 124.2 (CH), 123.5 (CH), 121.1 (C), 115.3 (CH), 71.3 (CH, O*CH*), 34.0 (C), 31.4 (CH_3, C(*CH*$_3$)$_3$), 21.3 (CH_3); LCMS m/z 203 ($M+H^+$), calcd $C_{14}H_{18}O$ 202.1358; Anal. calcd for $C_{14}H_{18}O$ (202.13): C, 83.12; H, 8.97. Found: C, 83.189; H, 8.995%.

6-Chloro-2-methyl-2*H*-chromene (81c): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2976, 1479, 1444, 1260, 1207, 1081, 816, 703, 639 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.03 (1H, dd, *J* = 8.4 Hz, 2.4 Hz), 6.92 (1H, d, *J* = 2.4 Hz), 6.69 (1H, d, *J* = 8.8 Hz), 6.29 (1H, d, *J* = 9.6 Hz, olefinic-*H*), 5.69 (1H, dd, *J* = 10 Hz, 3.2 Hz, olefinic-*H*), 4.99-4.95 (1H, m, OC*H*), 1.42 (3H, d, *J* = 6.8 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 151.9 (C), 128.6 (CH), 128.1 (CH), 125.9 (CH), 125.6 (C), 123.1 (C), 122.8 (CH), 117.2 (CH), 71.6 (CH, O*CH*), 21.2 (CH_3); LCMS m/z 181 ($M+H^+$), calcd $C_{10}H_9ClO$ 180.0342; Anal. calcd for $C_{10}H_9ClO$ (180.03): C, 66.49; H, 5.02. Found: C, 66.602; H, 5.013 %.



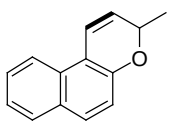
81c

2-Methyl-2*H*-benzo[*h*]chromene (81d): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2972, 2925, 1632, 1587, 1513, 1462, 1231, 1106, 1031, 735 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.92 (1H, d, *J* = 8.4 Hz), 7.13 (1H, d, *J* = 8.4 Hz), 7.64 (1H, d, *J* = 8.8 Hz), 7.46 (1H, t, *J* = 8.0 Hz), 7.32 (1H, t, *J* = 7.2 Hz), 7.08-7.05 (2H, m), 5.77 (1H, dd, *J* = 9.6 Hz, 3.2 Hz, olefinic-*H*), 5.07-5.02 (1H, m, OC*H*), 1.50 (3H, d, *J* = 6.8 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 151.6 (C), 129.9 (C), 129.3 (CH), 129.2 (C), 128.5 (CH), 126.5 (CH), 125.4 (CH), 123.5 (CH), 121.3 (CH), 120.0 (CH), 118.0 (CH), 114.7 (C), 71.3 (CH, O*CH*), 20.8 (CH_3); LCMS m/z 197 ($M+H^+$), calcd $C_{14}H_{12}O$ 196.0888; Anal. calcd for $C_{14}H_{12}O$ (196.08): C, 85.68; H, 6.16. Found: C, 85.778; H, 6.128 %.



81d

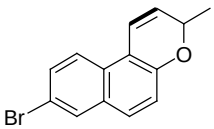
3-Methyl-3*H*-benzo[*f*]chromene (81e): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3050, 2972, 1616, 1566, 1509, 1226, 1029, 754, 663 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.16



81e

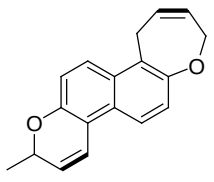
(1H, d, *J* = 8.4 Hz), 7.71 (1H, d, *J* = 7.2 Hz), 7.44-7.40 (2H, m), 7.34 (1H, d, *J* = 8.4 Hz), 7.12 (1H, d, *J* = 8.4 Hz), 6.49 (1H, dd, *J* = 9.6 Hz, 1.6 Hz, olefinic-*H*), 5.69 (1H, dd, *J* = 9.6 Hz, 3.2 Hz, olefinic-*H*), 5.19-5.17 (1H, m, OC*H*), 1.53 (3H, d, *J* = 6.4 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 148.7 (C), 134.4 (C), 127.6 (CH), 126.1 (CH), 125.4 (CH), 125.3 (CH), 124.7 (C), 124.5 (CH), 124.2 (CH), 121.9 (CH), 120.1 (CH), 116.1 (C), 71.9 (CH, O*CH*), 21.1 (CH_3); LCMS m/z 197 ($M+H^+$), calcd $C_{14}H_{12}O$ 196.0888; Anal. calcd for $C_{14}H_{12}O$ (196.08): C, 85.68; H, 6.16. Found: C, 85.643; H, 6.163 %.

8-Bromo-3-methyl-3*H*-benzo[*f*]chromene (81f): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 2971, 1623, 1585, 1502, 1234, 1070, 808, 772 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.86 (1H, d, *J* = 2.0 Hz), 7.76 (1H, d, *J* = 9.2 Hz), 7.53 (1H, d, *J* = 8.8 Hz), 7.51 (1H, dd, *J* = 8.8 Hz, 2.0 Hz), 7.06 (1H, d, *J* = 8.8 Hz), 6.99 (1H, d, *J* = 10.0 Hz, olefinic-*H*), 5.78 (1H, dd, *J* = 9.6 Hz, 3.2 Hz, olefinic-*H*), 5.07-5.04 (1H, m, OC*H*), 1.49 (3H, d, *J* = 6.4 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 151.8 (C), 130.4 (C), 130.3 (CH), 129.7 (CH), 128.4 (C), 128.3 (CH), 125.9 (CH), 123.1 (CH), 119.5 (CH), 119.1 (CH), 117.1 (C), 114.8 (C), 71.4 (CH, O*CH*), 20.8 (CH_3); LCMS m/z 275 ($M+H^+$), calcd $C_{14}H_{11}BrO$ 273.9993; Anal. calcd for $C_{14}H_{11}BrO$ (273.99): C, 61.11; H, 4.03. Found: C, 61.206; H, 4.019%.



81f

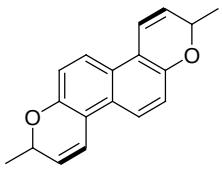
2-Methyl-8,11-dihydro-2*H*-1,7-dioxa-cyclohepta[*a*]phenanthrene (81g'): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 2974, 1586, 1515, 1385, 1235, 1165, 1064, 819, 731, 637 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.86 (1H, d, *J* = 9.2 Hz), 7.81 (1H, d, *J* = 8.8 Hz), 7.28 (1H, d, *J* = 9.2 Hz), 7.09 (1H, d, *J* = 9.6 Hz), 7.06 (1H, d, *J* = 12 Hz, olefinic-*H*), 5.97-5.94 (1H, m, olefinic-*H*), 5.79 (1H, dd, *J* = 9.6 Hz, 3.2 Hz, olefinic-*H*), 5.50 (1H, d, *J* = 11.2 Hz, olefinic-*H*), 5.02-5.00 (1H, m, OC*H*), 4.63 (2H, m, OCH_2), 3.87 (2H, m, CH_2CH=CH), 1.48 (3H, d, *J* = 6.4 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 154.5 (C), 150.6 (C), 131.5 (C), 128.1 (CH), 127.6 (C), 127.3 (C), 125.8 (CH), 125.7 (CH), 124.4 (CH), 122.3 (CH), 121.2 (CH), 120.3 (CH), 118.2 (CH), 115.3 (C), 71.2 (CH, O*CH*), 70.8 (CH_2, OCH_2CH=CH), 24.7



81g'

(CH_2, *CH_2*CH=CH), 20.7 (CH_3); LCMS m/z 265 ($M+H^+$), calcd $C_{18}H_{16}O_2$ 264.1150; Anal. calcd for $C_{18}H_{16}O_2$ (264.11): C, 81.79; H, 6.10. Found: C, 81.716; H, 6.107 %.

2,8-Dimethyl-2,8-dihydro-1,7-dioxa-chrysene (81g"): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 2972, 1628, 1516, 1450, 1379, 1226, 1057, 818, 738 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.76 (2H, d, *J* = 8.8 Hz), 7.07 (2H, d, *J* = 8.8 Hz), 7.02 (2H, d, *J* = 10 Hz, olefinic-*H*), 5.78 (2H, dd, *J* = 10 Hz, 3.2 Hz, olefinic-*H*), 5.01-4.99 (2H, m, OC*H*), 1.49 (6H, d, *J* = 6.4 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 150.0 (2 x C), 126.0 (2 x CH), 125.6 (2 x C), 122.6 (2 x CH), 120.18 (CH), 120.14 (CH), 118.4 (2 x CH), 115.4 (2 x C), 71.1 (2 x CH, O*CH*), 20.7 (2 x CH_3); LCMS m/z 265 ($M+H^+$), calcd $C_{18}H_{16}O_2$ 264.1150; Anal. calcd for $C_{18}H_{16}O_2$ (264.11): C, 81.79; H, 6.10. Found: C, 81.813; H, 6.064 %.



81g"

4. Experimental Procedures for the Synthesis of Highly Functionalized *N*-substituted 2-(buta-1,3-dienyl)phenylamines: The synthesis of functionalized *N*-substituted 2-(buta-1,3-dienyl)phenylamines **88** from corresponding anilines involves the following four or five-step sequence.

4A: *N*-Alkylations*:*

Method A: *N*-Diallylations: The starting material anilines **84** (1 mmol) were diallylated by treatment with allyl bromide (3 mmol) and sodium hydride (4 mmol) in dry DMF (2 mL, 0.5 M) at 0 ^oC, and the reaction mixture was stirred at RT for 2-8 h. The crude reaction mixture was worked up with aqueous NH_4Cl solution and the aqueous layer was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure *N*-diallylated products **85** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

Method B*: N*-Monoallylations: The starting material anilines **84** (1 mmol) were monoallylated by treatment with allyl bromide (1.1 mmol) and K_2CO_3 (1.2 mmol) in dry DMF (2 mL, 0.5 M), and the reaction mixture was stirred at RT for 24 h. The crude reaction mixture was worked up with aqueous NH_4Cl solution and the aqueous layer was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried

(Na_2SO_4), filtered and concentrated. Pure *N*-monoallylated products **86'** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

Method C*: N*-Propargylation: The enynes **86j & 86k** were prepared by treating the corresponding *C*-allylated anilines **84'** (1.0 mmol) with propargyl bromide (130.8 mg, 1.1 mmol) and K_2CO_3 (165.8 mg, 1.2 mmol) in DMF (2 mL, 0.5 M), and the reaction mixture was stirred at RT for 24 h. The crude reaction mixture was worked up with aqueous NH_4Cl solution and the aqueous layer was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure products **86j & 86k** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

4B: *C*-Allylation through Claisen Rearrangement*:* The corresponding *N*-allylated products **85** (1 mmol), $BF_3{\cdot}Et_2O$ (1 mmol) and freshly distilled xylene (1 mL, 1.0 M) were taken in a sealed glass tube and the mixture was heated at 135-140 °C under N_2 for 2 to 8 h. Upon cooling the reaction mixture to room temperature, the mixture was diluted with CH_2Cl_2 (10 mL), washed with aqueous NH_4Cl solution (2 mL) and brine (2 mL). The separated organic layer was dried (Na_2SO_4), filtered and concentrated under reduced pressure. Pure products **86** were obtained by column chromatography (basic alumina, mixture of hexane/ethyl acetate).

4C: *N*-Protection*:*

Method A*: Synthesis of 86aa-ga, 86ab, 86eb-kb and 86ac:* The corresponding amines **86a-k** (1 mmol) were protected by treatment with pyridine (6 mmol) and Pg-Cl [Here, Pg = CO_2Et (**a**), Ts (**b**), COPh (**c**), 2 mmol] in dry CH_2Cl_2 (10 mL, 0.1 M), and the reaction mixture was stirred at RT for 24 h. The reaction mixture was quenched with water and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with dilute HCl (2 mL) and brine, dried over (Na_2SO_4), filtered and concentrated. Pure products were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

Method B*: Synthesis of 86ad:* Acetic anhydride (1 mL) was added to the diallyl derivative **86a** (51.75 mg, 0.25 mmol) and the reaction mixture was stirred at RT for 15

h. The reaction mixture was quenched with water and extracted with CH_2Cl_2. The separated organic layer was dried (Na_2SO_4), filtered and concentrated under reduced pressure. Pure product **86ad** was obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

Method C: Synthesis of 86ae*:* Trifluoroacetic anhydride (420 mg, 2 mmol) was added to a solution of **86a** (207 mg, 1 mmol), Et_3N (101.2 mg, 1 mmol) and DMAP (122.2 mg, 1 mmol) in dry CH_2Cl_2 (5 mL), and the reaction mixture was stirred at RT for 24 h. The reaction mixture was quenched with water and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with dilute HCl (2 mL) and brine, dried over (Na_2SO_4), filtered and concentrated. Pure product **86ae** was obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

4D: RCM/BIRO Reactions in One-Pot*:*

Method A*:* A 10 mL oven-dried round bottom flask equipped with a stirring bar was charged with diene **86aa-ib** (0.5 mmol) and Grubbs' second generation catalyst **4o** (12.73 mg, 0.015 mmol, 3 mol%) in dry CH_2Cl_2 (10 mL, 0.05 M), and the reaction mixture was stirred under N_2 at room temperature for 2 to 5 h. Solvent CH_2Cl_2 was distilled off at ambient pressure and the crude reaction mixture was dissolved in dry DMSO (10 mL, 0.05 M), to that *t*BuOK (168.3 mg, 1.5 mmol, 3 equiv.) was added at 0 °C. The reaction mixture was stirred at RT for 1 h. The crude reaction mixture was worked up with water and the aqueous layer was extracted with ether (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure products **88aa-ib** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

Method B*:* A 10 mL oven-dried round bottom flask equipped with a stirring bar was charged with enyne **86jb-kb** (0.5 mmol) and Grubbs' first generation catalyst **4n** (32.9 mg, 0.04 mmol, 8 mol%) in dry CH_2Cl_2 (25 mL, 0.02 M), and the reaction mixture was stirred under N_2 at room temperature for 24 h. Solvent CH_2Cl_2 was distilled off at ambient pressure and the crude reaction mixture was dissolved in dry DMSO (10 mL, 0.05 M), to that *t*BuOK (168.3 mg, 1.5 mmol, 3 equiv.) was added at 0 °C. The reaction

mixture was stirred at RT for 1 h. The crude reaction mixture was worked up with water and the aqueous layer was extracted with ether (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure products **88jb-kb** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

4E: Synthesis of 91af & 91bf*:* A 10 mL oven-dried round bottom flask equipped with a stirring bar was charged with diene **86af-bf** (0.25 mmol), *p*-TSA (0.25 mmol, 47.5 mg) and Grubbs' second generation catalyst **4o** (21.22 mg, 0.025 mmol, 10 mol%) in dry CH_2Cl_2 (25 mL, 0.01 M), and the reaction mixture was stirred under N_2 at room temperature for 24 h. The crude reaction mixture was worked up with aqueous $NaHCO_3$ solution and the aqueous layer was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure products **91af-bf** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

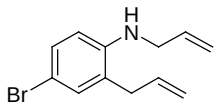
4F: Base–Induced Double-bond Isomerization Reactions*:*

Method A*:* Synthesis of 87af-bf & 87bg*:* A 10 mL oven-dried round bottom flask equipped with a stir bar was charged with **91af-bf & 91bg** (0.2 mmol), dry DMSO (4 mL, 0.05M), to that *t*BuOK (67.3 mg, 0.6 mmol, 3.0 equiv.) was added at 0 °C. The reaction mixture was stirred at RT for 1 h. The crude reaction mixture was worked up with water and the aqueous layer was extracted with ether (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure products **87af-bf & 87bg** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

Method B*:* Synthesis of 87bfa*:* A 10 mL oven-dried round bottom flask equipped with a stir bar was charged with **91bf** (0.2 mmol), dry DMSO (4 mL, 0.05M), to that *t*BuOK (67.3 mg, 0.6 mmol, 3.0 equiv.) was added at 0 °C. After 1h, allyl bromide **57a** (48.4 mg, 0.4 mmol, 2 equiv.) was added to the reaction mixture. The reaction mixture was stirred at RT for another 3 h. The crude reaction mixture was worked up with water and the aqueous layer was extracted with ether (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure product **87bfa** was obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

Method C*:* Synthesis of 87bfb*:* A 10 mL oven-dried round bottom flask equipped with a stir bar was charged with **87bf** (0.2 mmol), dry DMSO (4 mL, 0.05M), to that *t*BuOK (67.3 mg, 0.6 mmol, 3.0 equiv.) was added at 0 °C. After 1h, propargyl bromide **57b** (47.5mg, 0.4 mmol, 2 equiv.) was added to the reaction mixture. The reaction mixture was stirred at RT for another 18 h. The crude reaction mixture was worked up with water and the aqueous layer was extracted with ether (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure product **87bfb** was obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

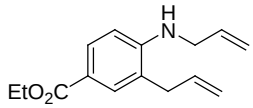
Allyl-(2-allyl-4-bromo-phenyl)-amine (86d): Prepared following the procedure **4B**



86d

and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3412 (N-*H*), 1575, 1502, 1260, 918, 665 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.21 (1H, dd, *J* = 8.4, 2.0 Hz), 7.14 (1H, d, *J* = 2.4 Hz), 6.47 (1H, d, *J* = 8.4 Hz), 5.96-5.84 (2H, m, olefinic-*H*), 5.23 (1H, dd, *J* = 16.8, 1.6 Hz, olefinic-*H*), 5.17-5.07 (3H, m, olefinic-*H*), 3.82 (1H, s, N-*H*), 3.74 (2H, d, *J* = 5.2 Hz, NCH_2), 3.24 (2H, d, *J* = 6.4 Hz, ArCH_2); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 145.0 (C), 135.0 (CH), 134.8 (CH), 132.2 (CH), 130.1 (CH), 125.6 (C), 116.9 (CH_2), 116.2 (CH_2), 112.2 (CH), 108.9 (C), 46.2 (CH_2), 36.0 (CH_2); LRMS m/z 251.90 ($M + H^+$), calcd $C_{12}H_{14}BrN$ 251.0310.

Ethyl 3-allyl-4-allylamino-benzoate (86g): Prepared following the procedure **4B** and

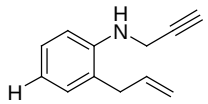


86g

purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3421 (N-*H*), 1708 (O-C=O), 1606, 1277, 1023, 737 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.86 (1H, dd, *J* = 8.8, 2.0 Hz), 7.75 (1H, d, *J* = 2.4 Hz), 6.58 (1H, d, *J* = 8.8 Hz), 5.97-5.88 (2H, m, olefinic-*H*), 5.25 (1H, dd, *J* = 17.2, 1.6 Hz, olefinic-*H*), 5.19-5.09 (3H, m, olefinic-*H*), 4.32 (3H, q, *J* = 7.2 Hz, N-*H*, OC$H_2$$CH_3$), 3.84 (2H, t, *J* = 5.2 Hz, NCH_2), 3.33 (2H, d, *J* = 6.0 Hz, ArCH_2), 1.36 (3H, t, *J* = 7.2 Hz, $OCH_2C$$H_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.0 (C, O-C=O), 149.9 (C), 135.3 (CH), 134.3 (CH), 131.5 (CH), 130.1 (CH), 122.3 (C), 118.5 (C), 116.8 (CH_2), 116.5 (CH_2), 109.4 (CH), 60.2 (CH_2, OCH_2CH_3),

45.8 (CH_2), 36.4 (CH_2), 14.5 (CH_3, OCH_2CH_3); LRMS m/z 246.15 ($M + H^+$), calcd. $C_{15}H_{19}NO_2$ 245.1416.

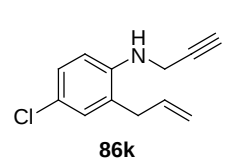
(2-Allyl-phenyl)-prop-2-ynyl-amine (86j): Prepared following the procedure **4A** & **4B**



86j

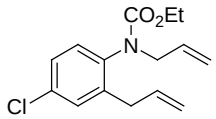
and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3424 (N-*H*), 3299 (C≡C-*H*), 1603, 1509, 1454, 1256, 1026, 749 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.21 (1H, t, *J* = 7.6 Hz), 7.09 (1H, d, *J* = 7.2 Hz), 6.79 (1H, d, *J* = 7.2 Hz), 6.75 (1H, d, *J* = 8.0 Hz), 6.00-5.93 (1H, m, olefinic-*H*), 5.15 (1H, d, *J* = 10.0 Hz, olefinic-*H*), 5.12 (1H, d, *J* = 17.2 Hz, olefinic-*H*), 3.96 (3H, s, NC*H*$_2$C≡C-H, N-*H*), 3.32 (2H, d, *J* = 6.0 Hz), 2.27 (1H, s, NCH_2C≡C-*H*); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 145.1 (C), 135.8 (CH), 130.0 (CH), 127.6 (CH), 124.4 (C), 118.5 (CH), 116.4 (CH_2), 111.2 (CH), 81.0 (C, NCH_2C≡C-H), 71.2 (CH, NCH_2C≡*C*-H), 36.3 (CH_2, N*C*H_2C≡C-H), 33.5 (CH_2); LRMS m/z 172.10 ($M + H^+$), calcd $C_{12}H_{13}N$ 171.1048.

(2-Allyl-4-chloro-phenyl)-prop-2-ynyl-amine (86k): Prepared following the procedure **4A** & **4B** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3295 (C≡C-*H*), 1606, 1503, 1436, 1260, 1000, 666 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.19 (1H, d, *J* = 8.0 Hz), 7.09 (1H, s, Ar-*H*), 6.69 (1H, d, *J* = 7.6 Hz), 5.99-5.90 (1H, m, olefinic-*H*), 5.21 (1H, d, *J* = 10.0 Hz, olefinic-*H*), 5.14 (1H, d, *J* = 17.2 Hz, olefinic-*H*), 3.96 (3H, s, NC*H*$_2$C≡C-H, N-*H*), 3.29 (2H, d, *J* = 4.8 Hz), 2.26 (1H, s, NCH_2C≡C-*H*); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 143.6 (C), 134.9 (CH), 129.7 (CH), 127.3 (CH), 126.2 (C), 123.1 (C), 117.1 (CH_2), 112.4 (CH), 80.6 (C, NCH_2C≡C-H), 71.5 (CH, NCH_2C≡*C*-H), 35.9 (CH_2, N*C*H_2C≡C-H), 33.6 (CH_2); LRMS m/z 206.05 ($M + H^+$), calcd $C_{12}H_{12}ClN$ 205.0658.



86k

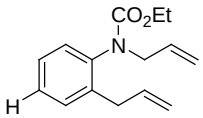
Ethyl allyl-(2-allyl-4-chloro-phenyl)-carbamate (86aa): Prepared following the procedure **4C** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 1708 (N-C=O), 1644, 1485, 1408, 1297, 1027, 771, 648 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.24 (1H, d, *J* = 2.0 Hz), 7.17 (1H, dd, *J* = 8.4, 2.0 Hz), 7.01 (1H, d, *J* = 8.4



86aa

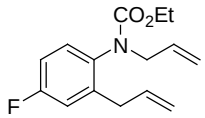
Hz), 5.94-5.84 (2H, m, olefinic-*H*), 5.14-5.05 (4H, m, olefinic-*H*), 4.37-4.29 (1H, m, NCH_2), 4.20-4.05 (2H, m, OCH_2CH$_3$), 3.86 (1H, dd, *J* = 13.2, 5.6 Hz, NCH_2), 3.25 (2H, d, *J* = 5.6 Hz, ArCH_2), 1.31-1.12 (3H, m, OCH$_2$CH_3); ^{13}C NMR (CDCl$_3$, DEPT-135) δ 155.3 (C, N-C=O), 139.8 (C), 138.4 (C), 135.4 (CH), 133.2 (CH), 132.9 (C), 130.0 (CH), 129.9 (CH), 127.0 (CH), 118.4 (CH$_2$), 117.1 (CH$_2$), 61.6 (CH$_2$, O*C*H$_2$CH$_3$), 53.2 (CH$_2$), 35.1 (CH$_2$), 14.5 (CH$_3$, OCH$_2$*C*H$_3$); LRMS m/z 280.00 (M + H$^+$), calcd $C_{15}H_{18}ClNO_2$ 279.1026.

Ethyl allyl-(2-allyl-phenyl)-carbamate (86ba): Prepared following the procedure **4C** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2979, 1705 (N-C=O), 1491, 1403, 1149, 736 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.29-7.17 (3H, m, Ph-*H*), 7.10 (1H, d, *J* = 7.2 Hz), 5.99-5.89 (2H, m, olefinic-*H*), 5.17-5.09 (4H, m, olefinic-*H*), 4.42 (1H, dd, *J* = 18.0, 4.8 Hz, NCH_2), 4.23-4.07 (2H, m, OCH_2CH$_3$), 3.90 (1H, dd, *J* = 14.0, 6.0 Hz, NCH_2), 3.32 (2H, d, *J* = 5.6 Hz, ArCH_2), 1.14 (3H, t, *J* = 7.2 Hz, OCH$_2$CH_3); ^{13}C NMR (CDCl$_3$, DEPT-135) δ 155.5 (C, N-C=O), 137.7 (2 x C), 136.3 (CH), 133.3 (CH), 129.9 (CH), 128.7 (CH), 127.6 (CH), 126.8 (CH), 118.0 (CH$_2$), 116.3 (CH$_2$), 61.5 (CH$_2$, O*C*H$_2$CH$_3$), 53.3 (CH$_2$), 35.2 (CH$_2$), 14.6 (CH$_3$, OCH$_2$*C*H$_3$); LRMS m/z 246.20 (M + H$^+$), calcd $C_{15}H_{19}NO_2$ 245.1416.



86ba

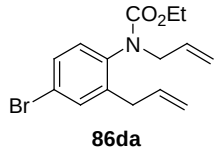
Ethyl allyl-(2-allyl-4-fluoro-phenyl)-carbamate (86ca): Prepared following the procedure **4C** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 1708 (N-C=O), 1645, 1591, 1499, 1221, 1026, 738 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.06 (1H, t, *J* = 7.6 Hz), 6.98 (1H, dd, *J* = 9.6, 3.2 Hz), 6.91 (1H, dt, *J* = 8.0, 2.8 Hz), 5.97-5.83 (2H, m, olefinic-*H*), 5.15-5.07 (4H, m, olefinic-*H*), 4.40 (1H, dd, *J* = 14.4, 5.2 Hz, NCH_2), 4.22-4.06 (2H, m, OCH_2CH$_3$), 3.88 (1H, dd, *J* = 14.4, 6.8 Hz, NCH_2), 3.28 (2H, d, *J* = 6.0 Hz, ArCH_2), 1.14 (3H, t, *J* = 6.8 Hz, OCH$_2$CH_3); ^{13}C NMR (CDCl$_3$, DEPT-135) δ 161.6 (C, d, *J* = 245.0 Hz), 155.6 (C, N-C=O), 140.7 (C), 135.8 (C), 135.5 (CH), 133.1 (CH), 130.3 (CH, d, *J* = 8.7 Hz), 118.3 (CH$_2$), 117.1 (CH$_2$), 116.5 (CH, d, *J* = 22.4 Hz), 113.7 (CH, d, *J* = 22.0 Hz), 61.7 (CH$_2$, O*C*H$_2$CH$_3$), 53.4 (CH$_2$),



86ca

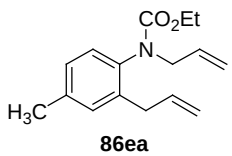
35.3 (CH_2), 14.6 (CH_3, OCH_2CH_3); LRMS m/z 264.15 ($M + H^+$), calcd $C_{15}H_{18}FNO_2$ 263.1322.

Ethyl allyl-(2-allyl-4-bromo-phenyl)-carbamate (86da): Prepared following the procedure **4C** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2981, 1708 (N-C=O), 1644, 1484, 1406, 1147, 659 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40 (1H, d, *J* = 2.0 Hz), 7.32 (1H, dd, *J* = 8.4, 2.0 Hz), 6.95 (1H, d, *J* = 6.8 Hz), 5.93-5.83 (2H, m, olefinic-*H*), 5.13-5.05 (4H, m, olefinic-*H*), 4.38-4.36 (1H, m, NCH_2), 4.19-4.05 (2H, m, OCH_2CH_3), 3.86-3.82 (1H, m, NCH_2), 3.26 (2H, d, *J* = 4.8 Hz, $ArCH_2$), 1.12 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 155.3 (C, N-C=O), 140.2 (C), 138.9 (C), 135.3 (CH), 132.9 (2 x CH), 130.3 (CH), 130.0 (CH), 121.3 (C), 118.4 (CH_2), 117.2 (CH_2), 61.7 (CH_2, OCH_2CH_3), 53.2 (CH_2), 35.0 (CH_2), 14.5 (CH_3, OCH_2CH_3); LRMS m/z 324.00 ($M + H^+$), calcd $C_{15}H_{18}BrNO_2$ 323.0521.



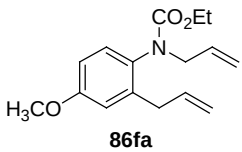
86da

Ethyl allyl-(2-allyl-4-methyl-phenyl)-carbamate (86ea): Prepared following the procedure **4C** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2980, 1704 (N-C=O), 1502, 1404, 917 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.07 (1H, s, Ar-*H*), 7.00 (2H, t, *J* = 7.2 Hz), 5.95-5.87 (2H, m, olefinic-*H*), 5.10 (2H, d, *J* = 17.6 Hz, olefinic-*H*), 5.08 (2H, d, *J* = 10.4 Hz, olefinic-*H*), 4.38 (1H, dd, *J* = 13.6, 4.4 Hz, NCH_2), 4.22-4.05 (2H, m, OCH_2CH_3), 3.86 (1H, dd, *J* = 14.4, 6.0 Hz, NCH_2), 3.26 (2H, d, *J* = 5.6 Hz, $ArCH_2$), 2.33 (3H, s, Ar-CH_3), 1.13 (3H, s, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 155.8 (C, N-C=O), 137.3 (3 x C), 136.5 (CH), 133.5 (CH), 130.6 (CH), 128.5 (CH), 127.6 (CH), 117.9 (CH_2), 116.2 (CH_2), 61.5 (CH_2, OCH_2CH_3), 53.5 (CH_2), 35.0 (CH_2), 21.1 (CH_3, Ar-CH_3), 14.7 (CH_3, OCH_2CH_3); LRMS m/z 260.20 ($M + H^+$), calcd $C_{16}H_{21}NO_2$ 259.1572.



86ea

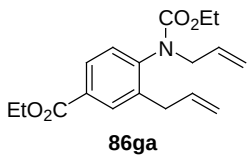
Ethyl allyl-(2-allyl-4-methoxy-phenyl)-carbamate (86fa): Prepared following the procedure **4C** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 1703 (N-



86fa

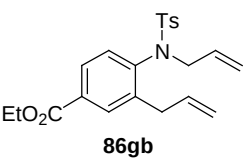
C=O), 1645, 1502, 1228, 1040, 773 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.00 (1H, d, *J* = 8.4 Hz), 6.78 (1H, d, *J* = 2.8 Hz), 6.73 (1H, dd, *J* = 8.4, 3.2 Hz), 5.94-5.86 (2H, m, olefinic-*H*), 5.11-5.06 (4H, m, olefinic-*H*), 4.37 (1H, dd, *J* = 14.4, 4.8 Hz, NCH_2), 4.11-4.04 (2H, m, OC$H_2$$CH_3$), 3.85 (1H, dd, *J* = 14.4, 6.4 Hz, NCH_2), 3.78 (3H, s, OCH_3), 3.26 (2H, d, *J* = 5.6 Hz, ArCH_2), 1.14 (3H, t, *J* = 6.8 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 158.5 (C), 155.9 (C, N-C=O), 139.0 (C), 136.1 (CH), 133.4 (CH), 132.9 (C), 129.6 (CH), 117.9 (CH_2), 116.4 (CH_2), 115.0 (CH), 111.9 (CH), 61.4 (CH_2, OCH_2CH_3), 55.2 (CH_3, OCH_3), 53.5 (CH_2), 35.4 (CH_2), 14.6 (CH_3, OCH_2CH_3); LRMS m/z 276.00 (M + H^+), calcd $C_{16}H_{21}NO_3$ 275.1521.

Ethyl 3-allyl-4-(allyl-ethoxycarbonyl-amino)-benzoate (86ga): Prepared following the procedure **4C** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2981, 1709 (N-C=O), 1607, 1403, 1252, 1023, 772 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.94 (1H, d, *J* = 1.6 Hz), 7.88 (1H, dd, *J* = 8.4, 2.0 Hz), 7.15 (1H, d, *J* = 6.8 Hz), 5.94-5.84 (2H, m, olefinic-*H*), 5.12-5.04 (4H, m, olefinic-*H*), 4.36 (3H, q, *J* = 7.2 Hz, OC$H_2$$CH_3$, NC$H_2$), 4.09-4.06 (2H, m, OC$H_2$$CH_3$), 3.90 (1H, dd, *J* = 13.6, 5.6 Hz, NCH_2), 3.32 (2H, d, *J* = 5.6 Hz, ArCH_2), 1.38 (3H, t, *J* = 7.2 Hz, OCH_2CH_3), 1.10 (3H, s, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.1 (C, O-C=O), 155.2 (C, N-C=O), 138.3 (C), 135.7 (CH), 133.0 (CH), 131.5 (CH), 129.7 (2 x C), 128.8 (CH), 128.2 (CH), 118.5 (CH_2), 117.0 (CH_2), 61.8 (CH_2, OCH_2CH_3), 61.1 (CH_2, OCH_2CH_3), 53.2 (CH_2), 35.3 (CH_2), 14.6 (CH_3, OCH_2CH_3), 14.3 (CH_3, OCH_2CH_3); LRMS m/z 318.20 (M + H^+), calcd $C_{18}H_{23}NO_4$ 317.1627.

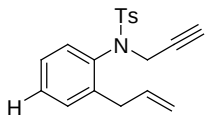


86ga

Ethyl 3-allyl-4-[allyl-(toluene-4-sulfonyl)-amino]-benzoate (86gb): Prepared following the procedure **4C** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 1711 (N-C=O), 1603, 1448, 1253, 1162, 1021, 716 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.97 (1H, s, Ar-*H*), 7.73 (1H, dd, *J* = 8.0, 2.0 Hz), 7.54 (2H, d, *J* = 8.0 Hz), 7.29 (2H, d, *J* = 8.0 Hz), 6.63 (1H, d, *J* = 8.0 Hz), 5.98-5.88 (1H, m, olefinic-*H*), 5.74-5.64 (1H, m, olefinic-*H*), 5.14 (2H, d, *J* = 12.4 Hz, olefinic-*H*), 4.98



86gb

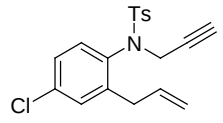


86jb

(1H, d, *J* = 10.0 Hz, olefinic-*H*), 4.93 (1H, d, *J* = 17.6 Hz, olefinic-*H*), 4.35 (3H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$, NC*H*$_2$), 3.84 (1H, br s, NC*H*$_2$), 3.59 (2H, d, *J* = 18.0 Hz, ArC*H*$_2$), 2.43 (3H, s, Ar-C*H*$_3$), 1.36 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.9 (C, O-C=O), 143.9 (C), 142.2 (C), 141.6 (C), 136.2 (CH), 135.4 (C), 132.1 (CH), 131.7 (CH), 130.3 (C), 129.6 (2 x CH), 128.3 (CH), 128.0 (2 x CH), 127.6 (CH), 119.8 (CH_2), 117.2 (CH_2), 61.2 (CH_2, O*C*H$_2$CH$_3$), 54.8 (CH_2), 35.3 (CH_2), 21.6 (CH_3, Ar-*C*H$_3$), 14.3 (CH_3, OCH$_2$*C*H$_3$); LRMS m/z 400.20 (M + H$^+$), calcd $C_{22}H_{25}NO_4S$ 399.1504.

***N*-(2-Allyl-phenyl)-4-methyl-*N*-prop-2-ynyl-benzenesulfonamide (86jb):** Prepared following the procedure **4C** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν$_{max}$ 3298 (C≡C-*H*), 1488, 1349, 1161, 1093, 864, 738 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.64 (2H, d, *J* = 8.0 Hz), 7.34-7.26 (4H, m, Ph-*H*), 7.09 (1H, dt, *J* = 8.4, 2.0 Hz), 6.82 (1H, d, *J* = 7.6 Hz), 5.99-5.92 (1H, m, olefinic-*H*), 5.14-5.09 (2H, m, olefinic-*H*), 4.54 (1H, d, *J* = 17.2 Hz, NC*H*$_2$), 4.22 (1H, d, *J* = 17.2 Hz, NC*H*$_2$), 3.68-3.66 (1H, m, ArC*H*$_2$), 3.52-3.51 (1H, m, ArC*H*$_2$), 2.45 (3H, s, Ar-C*H*$_3$), 2.14 (1H, t, *J* = 2.4 Hz, NCH$_2$C≡C-*H*); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 143.7 (C), 141.5 (C), 137.3 (C), 136.9 (CH), 136.0 (C), 130.5 (CH), 129.3 (2 x CH), 129.0 (CH), 128.9 (CH), 128.2 (2 x CH), 126.5 (CH), 116.4 (CH_2), 77.7 (C, NCH$_2$*C*≡C-H), 73.7 (CH, NCH$_2$C≡*C*-H), 41.5 (CH_2), 35.4 (CH_2), 21.5 (CH_3, Ar-*C*H$_3$); LRMS m/z 326.20 (M + H$^+$), calcd $C_{19}H_{19}NO_2S$ 325.1136.

***N*-(2-Allyl-4-chloro-phenyl)-4-methyl-*N*-prop-2-ynyl-benzenesulfonamide (86kb):**

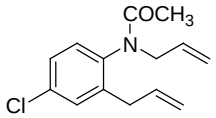


86kb

Prepared following the procedure **4C** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν$_{max}$ 3298 (C≡C-*H*), 1481, 1352, 1162, 1092, 737, 667 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.61 (2H, d, *J* = 8.0 Hz), 7.31 (1H, s, Ar-*H*), 7.29 (2H, d, *J* = 8.0 Hz), 7.06 (1H, dd, *J* = 8.4, 2.0 Hz), 6.73 (1H, d, *J* = 8.8 Hz), 5.95-5.85 (1H, m, olefinic-*H*), 5.15-5.12 (2H, m, olefinic-*H*), 4.49 (1H, d, *J* = 17.6 Hz, NC*H*$_2$), 4.21 (1H, d, *J* = 17.6 Hz, NC*H*$_2$), 3.66-3.61 (1H, m, ArC*H*$_2$), 3.49-3.45 (1H, m, ArC*H*$_2$), 2.44 (3H, s, Ar-C*H*$_3$), 2.16 (1H, s, NCH$_2$C≡C-*H*); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 144.1 (C), 143.7

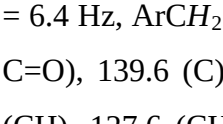
(C), 136.0 (CH), 135.9 (C), 135.6 (C), 134.9 (C), 130.6 (CH), 130.2 (CH), 129.6 (2 x CH), 128.2 (2 x CH), 126.9 (CH), 117.4 (CH_2), 77.5 (C, $NCH_2C{\equiv}C$-H), 74.2 (CH, $NCH_2C{\equiv}C$-H), 41.5 (CH_2), 35.3 (CH_2), 21.6 (CH_3, Ar-CH_3); LRMS m/z 360.00 ($M + H^+$), calcd $C_{19}H_{18}ClNO_2S$ 359.0747.

***N*-Allyl-*N*-(2-allyl-4-chloro-phenyl)-acetamide (86ad):** Prepared following the procedure **4C** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 1659 (N-C=O), 1483, 1385, 1097, 654 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.32 (1H, s, Ar-*H*), 7.23 (1H, dd, *J* = 8.4, 2.4 Hz), 7.01 (1H, d, *J* = 8.4 Hz), 5.89-5.82 (2H, m, olefinic-*H*), 5.18-5.10 (3H, m, olefinic-*H*), 5.04 (1H, d, *J* = 16.8 Hz, olefinic-*H*), 4.68 (1H, dd, *J* = 14.4, 5.6 Hz, NCH_2), 3.69 (1H, dd, *J* = 14.0, 7.2 Hz, NCH_2), 3.29 (2H, d, *J* = 6.4 Hz, ArCH_2), 1.76 (3H, s, COCH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 170.2 (C, N-C=O), 139.6 (C), 139.5 (C), 134.8 (CH), 134.2 (C), 132.5 (CH), 130.8 (CH), 130.7 (CH), 127.6 (CH), 118.7 (CH_2), 117.8 (CH_2), 51.6 (CH_2), 34.9 (CH_2), 22.4 (CH_3); LRMS m/z 248.10 ($M - H^+$), calcd $C_{14}H_{16}ClNO$ 249.0920.



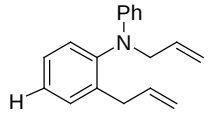
86ad

***N*-Allyl-*N*-(2-allyl-4-chloro-phenyl)-2,2,2-trifluoro-acetamide (86ae):** Prepared following the procedure **4C** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 1702 (N-C=O), 1487, 1415, 1211, 925, 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.33 (1H, s, Ar-*H*), 7.22 (1H, dd, *J* = 8.4, 2.0 Hz), 7.03 (1H, d, *J* = 8.4 Hz), 5.90-5.79 (2H, m, olefinic-*H*), 5.24-5.10 (4H, m, olefinic-*H*), 4.76 (1H, dd, *J* = 14.4, 6.0 Hz, NCH_2), 3.66 (1H, dd, *J* = 16.8, 8.0 Hz, NCH_2), 3.29 (2H, t, *J* = 6.0 Hz, ArCH_2); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 156.8 (C, q, *J* = 36.0 Hz, N*C*OCF_3), 139.9 (C), 135.5 (C), 135.4 (C), 134.6 (CH), 131.2 (CH), 130.5 (CH), 130.1 (CH), 127.1 (CH), 120.8 (CH_2), 118.2 (CH_2), 116.1 (C, q, *J* = 287.0 Hz, NCO*C*F_3), 54.1 (CH_2), 34.5 (CH_2); LRMS m/z 304.00 ($M + H^+$), calcd $C_{14}H_{13}ClF_3NO$ 303.0638.



86ae

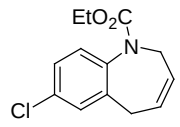
Allyl-(2-allyl-phenyl)-phenyl-amine (86bg): Prepared following the procedure **4A** & **4B** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3062, 1594, 1495, 1454, 1225,



86bg

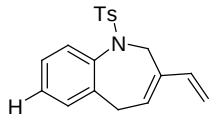
747, 694 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.36 (1H, d, *J* = 3.6 Hz), 7.28 (2H, t, *J* = 3.6 Hz), 7.21-7.18 (1H, m), 7.17 (2H, t, *J* = 8.0 Hz), 6.72 (1H, t, *J* = 7.6 Hz), 6.55 (2H, d, *J* = 8.4 Hz), 6.04-5.85 (2H, m, olefinic-*H*), 5.29 (1H, dd, *J* = 17.2, 1.2 Hz, olefinic-*H*), 5.21 (1H, dd, *J* = 10.0, 1.2 Hz, olefinic-*H*), 5.06 (1H, dd, *J* = 8.4, 1.6 Hz, olefinic-*H*), 5.03 (1H, dd, *J* = 15.2, 1.2 Hz, olefinic-*H*), 4.22 (2H, d, *J* = 5.2 Hz, NCH_2), 3.30 (2H, d, *J* = 6.8 Hz, ArCH_2); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 148.5 (C), 145.3 (C), 139.0 (C), 136.9 (CH), 134.4 (CH), 130.6 (CH), 129.7 (CH), 128.9 (2 x CH), 127.9 (CH), 126.8 (CH), 116.9 (CH), 116.5 (CH_2), 116.1 (CH_2), 113.4 (2 x CH), 54.9 (CH_2), 35.4 (CH_2); LRMS m/z 250.50 ($M + H^+$), calcd $C_{18}H_{19}N$ 249.1517.

Ethyl 7-chloro-2,5-dihydro-benzo[*b*]azepine-1-carboxylate (91aa): Prepared following the procedure **4D** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 2981, 1708 (N-C=O), 1489, 1409, 1264, 1092, 736 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.20 (1H, d, *J* = 8.0 Hz), 7.16 (1H, d, *J* = 2.0 Hz), 7.09 (1H, d, *J* = 8.0 Hz), 5.78-5.68 (1H, m, olefinic-*H*), 5.48 (1H, d, *J* = 11.6 Hz, olefinic-*H*), 4.22 (2H, br s, NCH_2), 4.12 (2H, q, *J* = 6.4 Hz, OC$H_2$$CH_3$) 3.35 (2H, br s, ArC$H_2$), 1.25 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 155.4 (C, N-C=O), 141.1 (C), 139.7 (C), 132.9 (C), 129.4 (CH), 128.6 (CH), 127.3 (CH), 127.0 (CH), 124.0 (CH), 61.9 (CH_2, O$CH_2$$CH_3$), 47.3 ($CH_2$), 31.7 ($CH_2$), 14.6 ($CH_3$, OCH_2CH_3); LRMS m/z 252.00 ($M + H^+$), calcd $C_{13}H_{14}ClNO_2$ 251.0713.



91aa

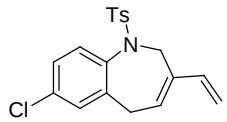
1-(Toluene-4-sulfonyl)-3-vinyl-2,5-dihydro-1*H*-benzo[*b*]azepine (91jb): Prepared following the procedure **4D** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2926, 1599, 1493, 1186, 1042, 811, 726 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.65 (2H, d, *J* = 7.6 Hz), 7.32-7.22 (5H, m, Ph-*H*), 7.08 (1H, d, *J* = 3.6 Hz), 6.24 (1H, dd, *J* = 17.6, 11.2 Hz, olefinic-*H*), 5.73 (1H, br s, olefinic-*H*), 5.05 (1H, d, *J* = 17.6 Hz, olefinic-*H*), 4.96 (1H, d, *J* = 11.2 Hz, olefinic-*H*), 4.53 (2H, s, NCH_2), 3.05 (2H, d, *J* = 3.2 Hz, ArCH_2), 2.42 (3H, s, Ar-CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 143.3 (C), 140.6 (C), 138.8 (C), 138.6 (C), 138.5 (CH), 134.6 (C), 129.7 (CH), 129.6 (2 x CH),



91jb

129.0 (CH), 128.6 (CH), 127.7 (CH), 127.6 (CH), 127.1 (2 x CH), 111.1 (CH_2), 48.6 (CH_2), 32.1 (CH_2), 21.6 (CH_3, Ar-*C*H_3); LRMS m/z 326.30 (M + H^+), calcd $C_{19}H_{19}NO_2S$ 325.1136.

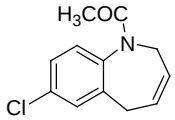
7-Chloro-1-(toluene-4-sulfonyl)-3-vinyl-2,5-dihydro-1*H*-benzo[*b*]azepine (91kb):



91kb

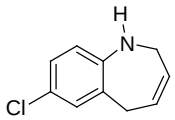
Prepared following the procedure **4D** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 1482, 1350, 1163, 1090, 1058, 738 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.63 (2H, d, *J* = 7.6 Hz), 7.26 (3H, d, *J* = 7.2 Hz), 7.20 (1H, d, *J* = 8.4 Hz), 7.07 (1H, s, Ar-*H*), 6.23 (1H, dd, *J* = 17.6, 10.8 Hz, olefinic-*H*), 5.86 (1H, t, *J* = 5.6 Hz, olefinic-*H*), 5.06 (1H, d, *J* = 18.0 Hz, olefinic-*H*), 4.98 (1H, d, *J* = 11.2 Hz, olefinic-*H*), 4.51 (2H, s, NCH_2), 2.97 (2H, d, *J* = 5.2 Hz, ArCH_2), 2.43 (3H, s, Ar-CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 143.5 (C), 142.2 (C), 138.3 (C), 138.2 (CH), 137.3 (C), 134.7 (C), 134.1 (C), 131.1 (CH), 129.6 (2 x CH), 129.0 (CH), 127.6 (CH), 127.0 (2 x CH), 126.7 (CH), 115.2 (CH_2), 48.4 (CH_2), 31.7 (CH_2), 21.5 (CH_3, Ar-*C*H_3); LRMS m/z 360.20 (M + H^+), calcd $C_{19}H_{18}ClNO_2S$ 359.0747.

1-(7-Chloro-2,5-dihydro-benzo[*b*]azepin-1-yl)-ethanone (91ad): Prepared following the procedure **4D** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 2925, 1668 (N-C=O), 1489, 1433, 1266, 1086, 739 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.23 (1H, dd, *J* = 8.0, 2.0 Hz), 7.20 (1H, s, Ar-*H*), 7.10 (1H, d, *J* = 8.0 Hz), 5.69 (1H, dd, *J* = 10.8, 2.0 Hz, olefinic-*H*), 5.45 (1H, dd, *J* = 11.2, 1.2 Hz, olefinic-*H*), 5.30 (1H, d, *J* = 18.0 Hz, NCH_2), 3.69 (1H, d, *J* = 16.8 Hz, NCH_2), 3.33 (1H, d, *J* = 18.0 Hz, ArCH_2), 2.93 (1H, dd, *J* = 16.8, 8.4 Hz, ArCH_2), 1.81 (3H, s, COCH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.6 (C, N-C=O), 141.4 (C), 140.7 (C), 133.7 (C), 129.0 (CH), 128.9 (CH), 127.8 (CH), 126.9 (CH), 123.5 (CH), 44.7 (CH_2), 31.4 (CH_2), 21.9 (CH_3); LRMS m/z 222.10 (M + H^+), calcd $C_{12}H_{12}ClNO$ 221.0607.



91ad

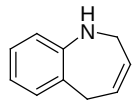
7-Chloro-2,5-dihydro-1*H*-benzo[*b*]azepine (91af): Prepared following the procedure **4E** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3440 (N-*H*), 3060, 1502, 1411, 1261,



91af

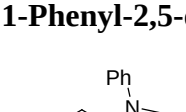
1143, 804 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.04 (2H, s, Ar-*H*), 6.73 (1H, d, *J* = 8.4 Hz), 5.83-5.80 (1H, m, olefinic-*H*), 5.54 (1H, d, *J* = 10.8 Hz, olefinic-*H*), 3.76 (2H, br s, NCH_2), 3.44 (2H, br s, ArCH_2); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 147.4 (C), 136.3 (C), 129.0 (CH), 127.2 (CH), 126.9 (CH), 126.6 (C), 125.4 (CH), 121.8 (CH), 48.1 (CH_2), 32.8 (CH_2); LRMS m/z 180.10 ($M + H^+$), calcd $C_{10}H_{10}ClN$ 179.0502.

2,5-Dihydro-1*H*-benzo[*b*]azepine (91bf): Prepared following the procedure **4E** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3382 (N-*H*), 3016, 1572, 1487, 1329, 1165, 1098, 750 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.15-7.09 (2H, m), 6.93 (1H, dt, *J* = 7.6, 1.2 Hz), 6.85 (1H, d, *J* = 8.0 Hz), 5.88-5.85 (1H, m, olefinic-*H*), 5.59-5.55 (1H, m, olefinic-*H*), 3.81-3.79 (2H, m, NCH_2), 3.53 (2H, d, *J* = 4.8 Hz, ArCH_2), 3.19 (1H, s, N*H*); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 148.8 (C), 134.6 (C), 129.2 (CH), 127.2 (CH), 127.1 (CH), 125.8 (CH), 121.9 (CH), 120.6 (CH), 48.3 (CH_2), 33.1 (CH_2); LRMS m/z 146.00 ($M + H^+$), calcd $C_{10}H_{11}N$ 145.0891.



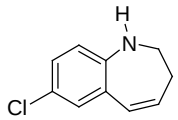
91bf

1-Phenyl-2,5-dihydro-1*H*-benzo[*b*]azepine (91bg): Prepared following the procedure **4D** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3055, 2947, 1660, 1591, 1494, 1039, 692 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.30-7.19 (6H, m, Ph-*H*), 6.80 (1H, t, *J* = 7.2 Hz), 6.72 (2H, d, *J* = 8.4 Hz), 5.82-5.77 (1H, m, olefinic-*H*), 5.66-5.63 (1H, m, olefinic-*H*), 4.25 (2H, t, *J* = 2.4 Hz, NCH_2), 3.23 (2H, d, *J* = 2.8 Hz, ArCH_2); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 148.8 (C), 146.8 (C), 141.2 (C), 129.5 (CH), 129.3 (CH), 129.0 (2 x CH), 127.9 (CH), 126.9 (CH), 126.8 (CH), 125.8 (CH), 117.9 (CH), 113.8 (2 x CH), 48.7 (CH_2), 32.6 (CH_2); LRMS m/z 221.80 ($M + H^+$), calcd $C_{16}H_{15}N$ 221.1204.



91bg

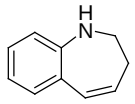
7-Chloro-2,3-dihydro-1*H*-benzo[*b*]azepine (87af): Prepared following the procedure **4F** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3391 (N-*H*), 2916, 1593, 1566, 1491, 1251, 1089, 767 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.08 (1H, d, *J* = 2.4 Hz), 6.94 (1H, dd, *J* = 8.4, 2.4 Hz), 6.54 (1H, d, *J* = 8.4 Hz), 6.25 (1H, d, *J* = 12.0 Hz,



87af

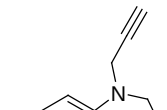
olefinic-*H*), 5.96-5.49 (1H, m, olefinic-*H*), 4.32 (1H, s, N-*H*), 3.30 (2H, t, *J* = 4.8 Hz), 2.57-2.53 (2H, m); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 147.3 (C), 132.3 (CH), 131.2 (CH), 128.8 (CH), 126.9 (CH), 125.4 (C), 123.6 (C), 118.4 (CH), 44.6 (CH_2), 34.7 (CH_2); LRMS m/z 179.95 ($M + H^+$), calcd $C_{10}H_{10}ClN$ 179.0502.

2,3-Dihydro-1*H*-benzo[*b*]azepine (87bf): Prepared following the procedure **4F** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3405 (N-*H*), 1600, 1487, 1421, 1165, 1279, 750, 649 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.11 (1H, d, *J* = 8.0 Hz), 6.99 (1H, t, *J* = 7.2 Hz), 6.76 (1H, t, *J* = 7.2 Hz), 6.61 (1H, d, *J* = 7.6 Hz), 6.34 (1H, d, *J* = 12.0 Hz, olefinic-*H*), 5.87 (1H, td, *J* = 12.0, 4.8 Hz olefinic-*H*), 3.32 (2H, t, *J* = 4.8 Hz, NC*H*$_2$), 2.56-2.52 (2H, m); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 148.7 (C), 133.2 (CH), 129.9 (CH), 129.8 (CH), 127.3 (CH), 123.9 (C), 119.1 (CH), 117.2 (CH), 44.6 (CH_2), 34.8 (CH_2); LRMS m/z 146.00 ($M + H^+$), calcd $C_{10}H_{11}N$ 145.0891.



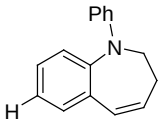
87bf

1-Prop-2-ynyl-2,3-dihydro-1*H*-benzo[*b*]azepine (87bfb): Prepared following the procedure **4F** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3293 (C≡C-*H*), 2921, 1594, 1495, 1448, 1215, 752, 670 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.17 (1H, d, *J* = 7.2 Hz), 7.15 (1H, t, *J* = 8.0 Hz), 7.01 (1H, d, *J* = 8.0 Hz), 6.86 (1H, t, *J* = 7.2 Hz), 6.40 (1H, d, *J* = 12.0 Hz, olefinic-*H*), 5.96 (1H, td, *J* = 12.0, 4.4 Hz, olefinic-*H*), 4.01 (2H, d, *J* = 2.0 Hz, NC*H*$_2$C≡C-H), 3.29 (2H, t, *J* = 5.2 Hz), 2.57-2.56 (2H, m), 2.27 (1H, t, *J* = 2.0 Hz, $NCH_2C\equiv C$-*H*); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 149.4 (C), 133.4 (CH), 130.2 (CH), 130.0 (CH), 127.4 (CH), 126.9 (C), 120.0 (CH), 115.3 (CH), 80.2 (C, $NCH_2C\equiv C$-H), 71.9 (CH, $NCH_2C\equiv C$-H), 50.6 (CH_2, NC*H*$_2$C≡C-H), 42.4 (CH_2), 33.6 (CH_2); LRMS m/z 184.00 ($M + H^+$), calcd $C_{13}H_{13}N$ 183.1048.



87bfb

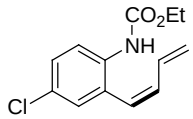
1-Phenyl-2,3-dihydro-1*H*-benzo[*b*]azepine (87bg): Prepared following the procedure **4F** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3063, 1591, 1494, 1463, 1246, 745, 693 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.35 (1H, d, *J* = 7.6 Hz), 7.28-7.11 (5H, m, Ph-*H*), 6.88 (2H, d, *J* = 8.0 Hz), 6.81 (1H, t, *J* = 7.2 Hz), 6.45 (1H, d, *J* = 12.0 Hz,



87bg

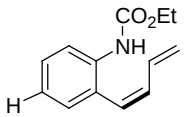
olefinic-*H*), 5.92 (1H, td, *J* = 12.0, 4.0 Hz, olefinic-*H*), 3.80 (2H, t, *J* = 5.6 Hz, NC*H*$_2$CH$_2$), 2.61-2.60 (2H, m, NCH$_2$C*H*$_2$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 146.9 (C), 145.6 (C), 133.0 (CH), 132.3 (C), 130.7 (CH), 129.2 (2 x CH), 128.5 (CH), 126.9 (CH), 126.6 (CH), 124.1 (CH), 118.6 (CH), 115.7 (2 x CH), 46.7 (CH$_2$, N*C*H$_2$CH$_2$), 30.5 (CH$_2$, NCH$_2$*C*H$_2$); LRMS m/z 222.20 (M + H$^+$), calcd $C_{16}H_{15}N$ 221.1204.

Ethyl (2-buta-1,3-dienyl-4-chloro-phenyl)-carbamate (88aa): Prepared following the procedure **4D** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3277 (N-*H*), 1689 (N-C=O), 1529, 1249, 1065, 659 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.96 (1H, d, *J* = 7.2 Hz), 7.24 (1H, dd, *J* = 8.8, 2.4 Hz), 7.14 (1H, d, *J* = 2.0 Hz), 6.54 (1H, s, N-*H*), 6.48-6.38 (2H, m, olefinic-*H*), 6.26 (1H, d, *J* = 9.2 Hz, olefinic-*H*), 5.46-5.38 (1H, m, olefinic-*H*), 5.27 (1H, d, *J* = 8.4 Hz, olefinic-*H*), 4.20 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 1.29 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 153.4 (C, N-C=O), 135.0 (CH), 134.2 (2 x C), 132.2 (CH), 129.4 (CH), 128.2 (CH), 128.0 (C), 124.1 (CH), 121.7 (CH$_2$), 120.9 (CH), 61.4 (CH$_2$, O*C*H$_2$CH$_3$), 14.5 (CH$_3$, OCH$_2$*C*H$_3$); LRMS m/z 252.00 (M + H$^+$), calcd $C_{13}H_{14}ClNO_2$ 251.0713; Anal. calcd for $C_{13}H_{14}ClNO_2$ (251.07): C, 62.03; H, 5.61; N, 5.56. Found: C, 62.12; H, 5.55; N, 5.61%.



88aa

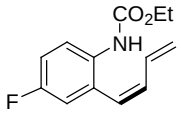
Ethyl (2-buta-1,3-dienyl-phenyl)-carbamate (88ba): Prepared following the procedure **4D** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3332 (N-*H*), 1728 (N-C=O), 1584, 1528, 1452, 1223, 1062, 737 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.01 (1H, d, *J* = 7.2 Hz), 7.29 (1H, t, *J* = 7.2 Hz), 7.18 (1H, d, *J* = 8.8 Hz), 7.05 (1H, d, *J* = 7.6 Hz), 6.57 (1H, s, N-*H*), 6.54-6.35 (3H, m, olefinic-*H*), 5.41 (1H, dd, *J* = 16.4, 1.6 Hz, olefinic-*H*), 5.23 (1H, dd, *J* = 8.8, 1.6 Hz, olefinic-*H*), 4.22 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 1.31 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 153.5 (C, N-C=O), 135.5 (2 x C), 134.1 (CH), 132.7 (2 x CH), 129.8 (CH), 128.3 (CH), 125.6 (CH), 122.9 (CH), 120.6 (CH$_2$), 61.2 (CH$_2$, O*C*H$_2$CH$_3$), 14.5 (CH$_3$,



88ba

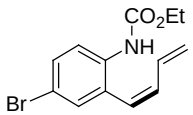
OCH_2CH_3); LRMS m/z 218.00 ($M + H^+$), calcd $C_{13}H_{15}NO_2$ 217.1103; Anal. calcd for $C_{13}H_{15}NO_2$ (217.11): C, 71.87; H, 6.96; N, 6.45. Found: C, 71.93; H, 6.90; N, 6.55%.

Ethyl (2-buta-1,3-dienyl-4-fluoro-phenyl)-carbamate (88ca): Prepared following the procedure **4D** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3291 (N-*H*), 1690 (N-C=O), 1534, 1246, 1065, 738 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.92 (1H, s, N-*H*), 6.99 (1H, dt, *J* = 8.4, 5.6 Hz), 6.93 (1H, dd, *J* = 8.8, 3.2 Hz), 6.52-6.41 (3H, m, olefinic-*H*), 6.31 (1H, d, *J* = 9.6 Hz, olefinic-*H*), 5.44 (1H, dd, *J* = 14.8, 1.2 Hz, olefinic-*H*), 5.29 (1H, td, *J* = 9.6, 1.6 Hz, olefinic-*H*), 4.21 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 1.30 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 158.5 (C, d, *J* = 241.7 Hz), 153.8 (C, N-C=O), 134.6 (CH), 132.3 (CH), 131.6 (C), 128.9 (C), 124.5 (CH), 122.0 (CH), 121.5 (CH_2), 116.3 (CH, d, *J* = 22.7 Hz), 114.9 (CH, d, *J* = 22.1 Hz), 61.3 (CH_2, OCH_2CH_3), 14.5 (CH_3, OCH_2CH_3); LRMS m/z 234.10 ($M - H^+$), calcd $C_{13}H_{14}FNO_2$ 235.1009; Anal. calcd for $C_{13}H_{14}FNO_2$ (235.10): C, 66.37; H, 6.00; N, 5.95. Found: C, 66.31; H, 5.95; N, 6.11%.



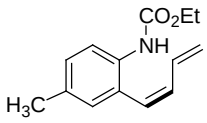
88ca

Ethyl (4-bromo-2-buta-1,3-dienyl-phenyl)-carbamate (88da): Prepared following the procedure **4D** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3288 (N-*H*), 1691 (N-C=O), 1564, 1530, 1246, 1080, 738 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.93 (1H, d, *J* = 8.0 Hz), 7.39 (1H, dd, *J* = 8.8, 2.0 Hz), 7.29 (1H, d, *J* = 2.0 Hz), 6.53 (1H, s, N-*H*), 6.49-6.38 (2H, m, olefinic-*H*), 6.26 (1H, d, *J* = 9.2 Hz, olefinic-*H*), 5.44 (1H, d, *J* = 14.8 Hz, olefinic-*H*), 5.29 (1H, d, *J* = 9.6 Hz, olefinic-*H*), 4.21 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 1.29 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 153.3 (C, N-C=O), 135.1 (CH), 134.7 (2 x C), 132.2 (2 x CH), 131.1 (CH), 123.9 (CH), 121.7 (CH_2), 121.1 (CH), 115.5 (C), 61.4 (CH_2, OCH_2CH_3), 14.5 (CH_3, OCH_2CH_3); LRMS m/z 296.00 ($M + H^+$), calcd $C_{13}H_{14}BrNO_2$ 295.0208; Anal. calcd for $C_{13}H_{14}BrNO_2$ (295.02): C, 52.72; H, 4.76; N, 4.73. Found: C, 52.65; H, 4.71; N, 4.85%.



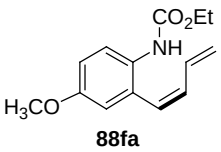
88da

Ethyl (2-buta-1,3-dienyl-4-methyl-phenyl)-carbamate (88ea): Prepared following the procedure **4D** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3433 (N-*H*), 2925, 1732 (N-C=O), 1522, 1206, 1060, 738 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.87 (1H, s, N-*H*), 7.12 (1H, d, *J* = 8.4 Hz), 7.02 (1H, s, Ar-*H*), 6.55-6.35 (4H, m, olefinic-*H*), 5.42 (1H, dd, *J* = 18.0, 1.2 Hz, olefinic-*H*), 5.25 (1H, dd, *J* = 9.6, 1.2 Hz, olefinic-*H*), 4.23 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 2.33 (3H, s, Ar-CH_3), 1.32 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 153.7 (C, N-C=O), 133.8 (2 x C), 133.0 (CH), 132.9 (CH), 132.6 (C), 130.2 (CH), 129.0 (CH), 125.9 (CH), 120.4 (CH_2), 120.1 (CH), 61.1 (CH_2, OCH_2CH_3), 20.7 (CH_3, Ar-CH_3), 14.6 (CH_3, OCH_2CH_3); LRMS m/z 232.05 ($M + H^+$), calcd $C_{14}H_{17}NO_2$ 231.1259; Anal. calcd for $C_{14}H_{17}NO_2$ (231.12): C, 72.70; H, 7.41; N, 6.06. Found: C, 72.65; H, 7.36; N, 6.15%.



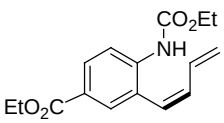
88ea

Ethyl (2-buta-1,3-dienyl-4-methoxy-phenyl)-carbamate (88fa): Prepared following the procedure **4D** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3285 (N-*H*), 2984, 1691 (N-C=O), 1533, 1246, 1069, 654 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.78 (1H, s, N-*H*), 6.85 (1H, dd, *J* = 8.8, 2.8 Hz), 6.75 (1H, d, *J* = 3.2 Hz), 6.54-6.32 (4H, m, olefinic-*H*), 5.40 (1H, dd, *J* = 15.2, 1.2 Hz, olefinic-*H*), 5.23 (1H, d, *J* = 10.0 Hz, olefinic-*H*), 4.19 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 3.79 (3H, s, OCH_3), 1.29 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 155.5 (C), 154.0 (C, N-C=O), 133.8 (CH), 132.7 (CH), 128.7 (2 x C), 125.7 (CH), 120.7 (CH_2), 115.1 (2 x CH), 113.5 (CH), 61.1 (CH_2, OCH_2CH_3), 55.5 (CH_3, OCH_3), 14.5 (CH_3, OCH_2CH_3); LRMS m/z 248.15 ($M + H^+$), calcd $C_{14}H_{17}NO_3$ 247.1208; Anal. calcd for $C_{14}H_{17}NO_3$ (247.12): C, 68.00; H, 6.93; N, 5.66. Found: C, 68.12; H, 6.85; N, 5.72%.



88fa

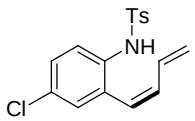
Ethyl 3-buta-1,3-dienyl-4-ethoxycarbonylamino-benzoate (88ga): Prepared following the procedure **4D** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 2985, 1741 (O-C=O), 1720 (N-C=O), 1522, 1214, 1058, 770 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.19 (1H, d, *J* = 8.8 Hz), 7.97 (1H, dd, *J* = 8.8, 2.0



88ga

Hz), 7.85 (1H, d, *J* = 2.0 Hz), 6.78 (1H, s, N-*H*), 6.53-6.31 (3H, m, olefinic-*H*), 5.44 (1H, dd, *J* = 16.0, 1.6 Hz, olefinic-*H*), 5.27 (1H, dd, *J* = 10.8, 1.2 Hz, olefinic-*H*), 4.36 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 4.23 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 1.38 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$), 1.31 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR (CDCl$_3$, DEPT-135) δ 166.2 (C, O-C=O), 153.1 (C, N-C=O), 139.7 (C), 135.3 (CH), 132.2 (CH), 131.2 (CH), 130.0 (CH), 125.4 (C), 124.5 (C), 124.4 (CH), 121.6 (CH$_2$), 118.0 (CH), 61.5 (CH$_2$, O*C*H$_2$CH$_3$), 60.8 (CH$_2$, O*C*H$_2$CH$_3$), 14.5 (CH$_3$, OCH$_2$*C*H$_3$), 14.3 (CH$_3$, OCH$_2$*C*H$_3$); LRMS m/z 289.95 (M + H$^+$), calcd C$_{16}$H$_{19}$NO$_4$ 289.1314; Anal. calcd for C$_{16}$H$_{19}$NO$_4$ (289.13): C, 66.42; H, 6.62; N, 4.84. Found: C, 66.34; H, 6.58; N, 4.95%.

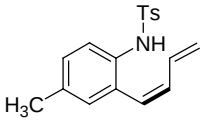
***N*-(2-Buta-1,3-dienyl-4-chloro-phenyl)-4-methyl-benzenesulfonamide (88ab):**



88ab

Prepared following the procedure **4D** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν$_{max}$ 3280 (N-*H*), 1597, 1481, 1392, 1161, 1091, 736, 661 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.59 (2H, d, *J* = 8.0 Hz), 7.50 (1H, d, *J* = 8.8 Hz), 7.21 (3H, d, *J* = 8.4 Hz), 7.05 (1H, d, *J* = 2.0 Hz), 6.51 (1H, s, N-*H*), 6.30 (1H, t, *J* = 11.2 Hz, olefinic-*H*), 6.21-6.12 (1H, m, olefinic-*H*), 5.84 (1H, d, *J* = 10.8 Hz, olefinic-*H*), 5.38 (1H, d, *J* = 16.4 Hz, olefinic-*H*), 5.22 (1H, d, *J* = 9.6 Hz, olefinic-*H*), 2.37 (3H, s, Ar-C*H*$_3$); ^{13}C NMR (CDCl$_3$, DEPT-135) δ 144.1 (C), 136.1 (C), 135.4 (CH), 132.8 (C), 131.7 (CH), 131.0 (C), 130.4 (C), 129.8 (CH), 129.7 (2 x CH), 128.4 (CH), 127.1 (2 x CH), 123.5 (CH), 123.4 (CH), 122.1 (CH$_2$), 21.5 (CH$_3$, Ar-*C*H$_3$); LRMS m/z 334.00 (M + H$^+$), calcd C$_{17}$H$_{16}$ClNO$_2$S 333.0590; Anal. calcd for C$_{17}$H$_{16}$ClNO$_2$S (333.05): C, 61.16; H, 4.83; N, 4.20. Found: C, 61.25; H, 4.80; N, 4.26%.

***N*-(2-Buta-1,3-dienyl-4-methyl-phenyl)-4-methyl-benzenesulfonamide (88eb):**

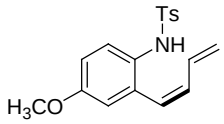


88eb

Prepared following the procedure **4D** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν$_{max}$ 3252 (N-*H*), 1484, 1398, 1167, 1045, 701 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.59 (2H, d, *J* = 7.6 Hz), 7.42 (1H, d, *J* = 8.0 Hz), 7.18 (2H, d, *J* = 8.0 Hz), 7.05 (1H, d, *J* = 7. 6 Hz), 6.89 (1H, s, Ar-*H*), 6.51 (1H, s, N-*H*), 6.25-6.22 (2H, m, olefinic-*H*), 5.91 (1H, d, *J* = 8.8 Hz, olefinic-*H*), 5.33 (1H, d, *J* = 14.4 Hz, olefinic-*H*),

5.16 (1H, d, *J* = 8.4 Hz, olefinic-*H*), 2.36 (3H, s, Ar-CH_3), 2.27 (3H, s, Ar-CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 143.7 (C), 136.5 (C), 135.0 (C), 134.2 (CH), 132.4 (CH), 131.5 (C), 130.6 (CH), 129.9 (C), 129.6 (2 x CH), 129.1 (CH), 127.2 (2 x CH), 125.3 (CH), 123.0 (CH), 120.8 (CH_2), 21.5 (CH_3, Ar-*C*H_3), 20.8 (CH_3, Ar-*C*H_3); LRMS m/z 314.15 (M + H^+), calcd $C_{18}H_{19}NO_2S$ 313.1136; Anal. calcd for $C_{18}H_{19}NO_2S$ (313.13): C, 68.98; H, 6.11; N, 4.47. Found: C, 69.85; H, 6.22; N, 4.43%.

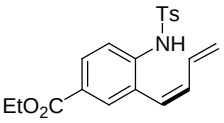
***N*-(2-Buta-1,3-dienyl-4-methoxy-phenyl)-4-methyl-benzenesulfonamide (88fb):**



88fb

Prepared following the procedure **4D** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3256 (N-*H*), 1599, 1492, 1158, 1033, 702 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.51 (2H, d, *J* = 8.4 Hz), 7.35 (1H, d, *J* = 8.8 Hz), 7.10 (2H, d, *J* = 8.0 Hz), 6.83 (1H, d, *J* = 2.0 Hz), 6.74 (1H, dd, *J* = 8.8, 2.4 Hz), 6.60 (1H, d, *J* = 2.4 Hz), 6.29-6.19 (1H, m, olefinic-*H*), 6.09 (1H, t, *J* = 11.2 Hz, olefinic-*H*), 5.93 (1H, d, *J* = 11.2 Hz, olefinic-*H*), 5.23 (1H, d, *J* = 16.8 Hz, olefinic-*H*), 5.08 (1H, d, *J* = 10.0 Hz, olefinic-*H*), 3.69 (3H, s, OCH_3), 2.28 (3H, s, Ar-CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 157.1 (C), 143.3 (C), 136.0 (C), 133.3 (CH), 133.0 (C), 132.1 (CH), 129.3 (2 x CH), 126.9 (2 x CH), 126.6 (CH), 126.5 (C), 125.2 (CH), 120.2 (CH_2), 115.3 (CH), 113.1 (CH), 55.1 (CH_3, O*C*H_3), 21.2 (CH_3, Ar-*C*H_3); LRMS m/z 330.00 (M + H^+), calcd $C_{18}H_{19}NO_3S$ 329.1086; Anal. calcd for $C_{18}H_{19}NO_3S$ (329.10): C, 65.63; H, 5.81; N, 4.25. Found: C, 65.77; H, 5.73; N, 4.18%.

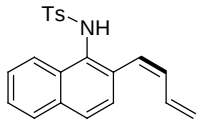
Ethyl 3-buta-1,3-dienyl-4-(toluene-4-sulfonylamino)-benzoate (88gb): Prepared following the procedure **4D** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3261 (N-*H*), 1718 (O-C=O), 1598, 1265, 1165, 1020, 737 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.89 (1H, dd, *J* = 8.8, 2.0 Hz), 7.74 (1H, d, *J* = 1.6 Hz), 7.67 (2H, d, *J* = 8.4 Hz), 7.61 (1H, d, *J* = 8.4 Hz), 7.20 (2H, d, *J* = 8.4 Hz), 6.99 (1H, s, N-*H*), 6.38 (1H, t, *J* = 11.2 Hz, olefinic-*H*), 6.18-6.08 (1H, m, olefinic-*H*), 6.06 (1H, d, *J* = 11.2 Hz, olefinic-*H*), 5.38 (1H, d, *J* = 16.8 Hz, olefinic-*H*), 5.19 (1H, d, *J* = 10.0 Hz, olefinic-*H*), 4.32 (2H, q, *J* = 7.2 Hz, OCH_2CH$_3$), 2.35 (3H, s, Ar-CH_3), 1.34 (3H, t, *J* =



88gb

7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.8 (C, O-C=O), 144.2 (C), 138.3 (C), 135.9 (C), 135.6 (CH), 131.8 (CH), 131.5 (CH), 129.7 (3 x CH), 127.5 (C), 127.1 (2 x CH), 126.1 (C), 123.6 (CH), 121.9 (CH_2), 119.2 (CH), 60.9 (CH_2, OCH_2CH_3), 21.4 (CH_3, Ar-CH_3), 14.2 (CH_3, OCH_2CH_3); LRMS m/z 370.15 (M + H^+), calcd $C_{20}H_{21}NO_4S$ 371.1191; Anal. calcd for $C_{20}H_{21}NO_4S$ (371.11): C, 64.67; H, 5.70; N, 3.77. Found: C, 64.58; H, 5.75; N, 3.71%.

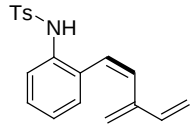
***N*-(2-Buta-1,3-dienyl-naphthalen-1-yl)-4-methyl-benzenesulfonamide (88ib):**



88ib

Prepared following the procedure **4D** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3276 (N-*H*), 1625, 1598, 1497, 1158, 1085, 810 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.29 (1H, br s, Ar-*H*), 7.80-7.79 (1H, m), 7.74 (1H, d, *J* = 8.4 Hz), 7.52-7.46 (4H, m, Ph-*H*), 7.31 (1H, d, *J* = 8.4 Hz), 7.15 (2H, d, *J* = 7.6 Hz), 6.73 (1H, s, N-*H*), 6.40-6.36 (1H, m, olefinic-*H*), 6.02-6.00 (2H, m, olefinic-*H*), 5.32 (1H, d, *J* = 16.8 Hz, olefinic-*H*), 5.19 (1H, d, *J* = 9.6 Hz, olefinic-*H*), 2.37 (3H, s, Ar-CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 143.8 (C), 136.6 (C), 133.8 (C), 133.5 (C), 132.7 (CH), 132.5 (CH), 132.2 (C), 129.6 (2 x CH), 129.1 (C), 127.9 (CH), 127.6 (3 x CH), 127.5 (CH), 126.8 (CH), 126.6 (CH), 126.5 (CH), 125.0 (CH), 120.7 (CH_2), 21.5 (CH_3, Ar-CH_3); LRMS m/z 350.25 (M + H^+), calcd $C_{21}H_{19}NO_2S$ 349.1136; Anal. calcd for $C_{21}H_{19}NO_2S$ (349.11): C, 72.18; H, 5.48; N, 4.01. Found: C, 72.26; H, 5.39; N, 4.12%.

4-Methyl-*N*-[2-(3-methylene-penta-1,4-dienyl)-phenyl]-benzenesulfonamide (88jb):

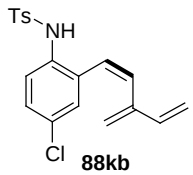


88jb

Prepared following the procedure **4D** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3263 (N-*H*), 1490, 1332, 1161, 1091, 820, 736 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.61 (2H, d, *J* = 7.6 Hz), 7.46 (1H, d, *J* = 8.4 Hz), 7.22-7.18 (3H, m, Ph-*H*), 7.08 (1H, d, *J* = 7.2 Hz), 7.03 (1H, d, *J* = 7.2 Hz), 6.59 (1H, s, N-*H*), 6.31-6.24 (2H, m, olefinic-*H*), 6.13 (1H, d, *J* = 12.0 Hz, olefinic-*H*), 5.29 (1H, d, *J* = 17.6 Hz, olefinic-*H*), 5.12 (1H, d, *J* = 10.8 Hz, olefinic-*H*), 5.01 (1H, s, olefinic-*H*), 4.72 (1H, s, olefinic-*H*), 2.38 (3H, s, Ar-CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 143.8 (C), 141.7 (C), 137.5 (CH), 136.6 (C), 133.4 (C), 131.6 (CH), 130.1 (C), 129.6 (CH),

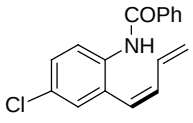
129.5 (2 x CH), 128.2 (CH), 127.2 (2 x CH), 126.9 (CH), 125.2 (CH), 122.7 (CH), 119.9 (CH_2), 115.6 (CH_2), 21.5 (CH_3, Ar-*C*H_3); LRMS m/z 326.20 (M + H^+), calcd $C_{19}H_{19}NO_2S$ 325.1136; Anal. calcd for $C_{19}H_{19}NO_2S$ (325.11): C, 70.12; H, 5.88; N, 4.30. Found: C, 70.21; H, 5.81; N, 4.23%.

***N*-[4-Chloro-2-(3-methylene-penta-1,4-dienyl)-phenyl]-4-methyl-benzenesulfonamide (88kb):** Prepared following the procedure **4D** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3263 (N-*H*), 1597, 1481, 1161, 1089, 736 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.58 (2H, d, *J* = 8.0 Hz), 7.42 (1H, d, *J* = 8.8 Hz), 7.23 (2H, d, *J* = 8.0 Hz), 7.16 (1H, d, *J* = 8.8 Hz), 7.05 (1H, s, Ar-*H*), 6.45 (1H, s, N-*H*), 6.33 (1H, d, *J* = 11.6 Hz, olefinic-*H*), 6.29 (1H, dd, *J* = 16.0, 10.8 Hz, olefinic-*H*), 5.99 (1H, d, *J* = 12.0 Hz, olefinic-*H*), 5.28 (1H, d, *J* = 17.6 Hz, olefinic-*H*), 5.15 (1H, d, *J* = 10.4 Hz, olefinic-*H*), 5.06 (1H, s, olefinic-*H*), 4.74 (1H, s, olefinic-*H*), 2.40 (3H, s, Ar-C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 144.0 (C), 141.3 (C), 137.2 (CH), 136.2 (C), 132.7 (CH), 132.0 (C), 131.8 (C), 130.7 (C), 129.6 (2 x CH), 129.2 (CH), 128.2 (CH), 127.2 (2 x CH), 125.6 (CH), 124.2 (CH), 120.4 (CH_2), 115.9 (CH_2), 21.6 (CH_3, Ar-*C*H_3); LRMS m/z 359.60 (M + H^+), calcd $C_{19}H_{18}ClNO_2S$ 359.0747; Anal. calcd for $C_{19}H_{18}ClNO_2S$ (359.07): C, 63.41; H, 5.04; N, 3.89. Found: C, 63.52; H, 5.11; N, 3.81%.



88kb

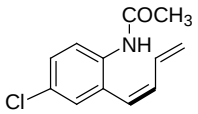
***N*-(2-Buta-1,3-dienyl-4-chloro-phenyl)-benzamide (88ac):** Prepared following the procedure **4D** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3276 (N-*H*), 1641 (N-C=O), 1514, 1394, 1309, 914, 660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.36 (1H, d, *J* = 8.8 Hz), 7.92 (1H, s, N-*H*), 7.81 (1H, d, *J* = 7.2 Hz), 7.80 (1H, d, *J* = 7.6 Hz), 7.57-7.52 (1H, m), 7.47 (2H, dt, *J* = 8.0, 1.6 Hz), 7.32 (1H, dd, *J* = 8.8, 2.4 Hz), 7.21 (1H, d, *J* = 2.4 Hz), 6.54 (1H, t, *J* = 10.8 Hz, olefinic-*H*), 6.50-6.40 (1H, m, olefinic-*H*), 6.37 (1H, d, *J* = 11.2 Hz, olefinic-*H*), 5.47 (1H, dd, *J* = 15.2, 2.0 Hz, olefinic-*H*), 5.31 (1H, dd, *J* = 11.2, 1.6 Hz, olefinic-*H*); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.2 (C, N-C=O), 135.2 (CH), 134.7 (C), 134.0 (C), 132.2 (CH), 132.0 (CH), 129.3



88ac

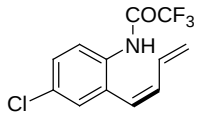
(CH), 129.1 (C), 128.9 (C), 128.8 (2 x CH), 128.3 (CH), 126.9 (2 x CH), 124.3 (CH), 122.4 (CH), 122.3 (CH_2); LRMS m/z 284.00 ($M + H^+$), calcd $C_{17}H_{14}ClNO$ 283.0764; Anal. calcd for $C_{17}H_{14}ClNO$ (283.07): C, 71.96; H, 4.97; N, 4.94. Found: C, 71.85; H, 4.92; N, 5.05%.

***N*-(2-Buta-1,3-dienyl-4-chloro-phenyl)-acetamide (88ad):** Prepared following the procedure **4D** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3257 (N-*H*), 1659 (N-C=O), 1521, 1434, 1255, 1112, 730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.12 (1H, d, *J* = 8.8 Hz), 7.25 (1H, dd, *J* = 7.6, 2.0 Hz), 7.16 (1H, s, Ar-*H*), 7.10 (1H, s, N-*H*), 6.49-6.38 (2H, m, olefinic-*H*), 6.28 (1H, d, *J* = 10.4 Hz, olefinic-*H*), 5.45 (1H, dd, *J* = 14.8, 2.0 Hz, olefinic-*H*), 5.30 (1H, d, *J* = 8.4 Hz, olefinic-*H*), 2.13 (3H, s, COC*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.1 (C, N-C=O), 134.9 (CH), 133.8 (C), 132.2 (CH), 129.3 (CH), 129.0 (C), 128.6 (C), 128.2 (CH), 124.3 (CH), 122.7 (CH), 121.9 (CH_2), 24.7 (CH_3); LRMS m/z 222.00 ($M + H^+$), calcd $C_{12}H_{12}ClNO$ 221.0607; Anal. calcd for $C_{12}H_{12}ClNO$ (221.06): C, 65.02; H, 5.46; N, 6.32. Found: C, 65.12; H, 5.41; N, 6.38%.



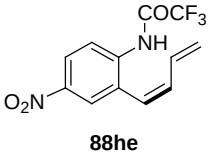
88ad

***N*-(2-Buta-1,3-dienyl-4-chloro-phenyl)-2,2,2-trifluoro-acetamide (88ae):** Prepared following the procedure **4D** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3296 (N-*H*), 2924, 1726 (N-C=O), 1641, 1597, 1093, 715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.15 (1H, d, *J* = 8.8 Hz), 7.94 (1H, s, N-*H*), 7.33 (1H, d, *J* = 8.4 Hz), 7.24 (1H, s, Ar-*H*), 6.56 (1H, t, *J* = 11.2 Hz, olefinic-*H*), 6.34-6.25 (2H, m, olefinic-*H*), 5.52 (1H, d, *J* = 16.8 Hz, olefinic-*H*), 5.37 (1H, d, *J* = 10.0 Hz, olefinic-*H*); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 154.6 (C, q, *J* = 36.9 Hz, N-C=O), 136.1 (CH), 131.5 (CH), 131.2 (C), 131.1 (C), 129.7 (C), 129.6 (CH), 128.6 (CH), 123.2 (CH_2), 122.8 (CH), 122.5 (CH), 115.6 (C, q, *J* = 287.0 Hz, NCO*C*F_3); LRMS m/z 274.10 ($M - H^+$), calcd $C_{12}H_9ClF_3NO$ 275.0325; Anal. calcd for $C_{12}H_9ClF_3NO$ (275.03): C, 52.29; H, 3.29; N, 5.08. Found: C, 52.12; H, 3.32; N, 5.13%.



88ae

***N*-(2-Buta-1,3-dienyl-4-nitro-phenyl)-2,2,2-trifluoro-acetamide (88he):** Prepared following the procedure **4D** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3363 (N-*H*), 1728 (N-C=O), 1580, 1549, 1266, 1150, 740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.50 (1H, d, *J* = 8.8 Hz), 8.24 (1H, dd, *J* = 8.8, 2.4 Hz), 8.23 (1H, s, N-*H*), 8.14 (1H, d, *J* = 2.4 Hz), 6.68 (1H, t, *J* = 11.2 Hz, olefinic-*H*), 6.36 (1H, d, *J* = 11.2 Hz, olefinic-*H*), 6.29-6.19 (1H, m, olefinic-*H*), 5.59 (1H, d, *J* = 16.8 Hz, olefinic-*H*), 5.43 (1H, d, *J* = 10.0 Hz, olefinic-*H*); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 154.8 (C, q, *J* = 38.0 Hz), 144.6 (C), 138.0 (C), 137.4 (CH), 130.9 (CH), 128.5 (C), 125.2 (CH), 124.5 (CH_2), 124.1 (CH), 121.6 (CH), 120.9 (CH), 115.3 (C, q, *J* = 287.0 Hz, NCO*C*F_3); LRMS m/z 285.00 (M - H^+), calcd $C_{12}H_9F_3N_2O_3$ 286.0565; Anal. calcd for $C_{12}H_9F_3N_2O_3$ (286.05): C, 50.36; H, 3.17; N, 9.79. Found: C, 50.25; H, 3.21; N, 9.65%.



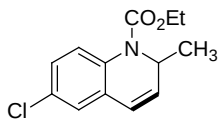
88he

4G: Gold-Catalyzed Cascade Hydroamination and Diels-Alder Reactions*:*

Synthesis of 89ab & 89eb-gb*:* Compounds **88ab** & **88eb-gb** (0.1 mmol) were added to mixture of Au[PPh_3]Cl (2.42 mg, 0.005 mmol, 5 mol%) and AgOTf (1.28 mg, 0.005 mmol, 5 mol%) in dry toluene (2 mL, 0.05M), taken in a sealed glass tube and the mixture is heated at 100 °C under N_2 for 6 to 24 h. The crude reaction mixture was purified by column chromatography (silica gel, mixture of hexane/ethyl acetate). Pure products **89ab** & **89eb-gb** were obtained in moderate yields.

Synthesis of 89aa-ga, 90aa-ga & 90ad*:* Compounds **88aa-ga** & **88ad** (0.1 mmol) were added to mixture of Au[PPh_3]Cl (2.42 mg, 0.005 mmol, 5 mol%) and AgOTf (1.28 mg, 0.005 mmol, 5 mol%) in dry toluene (2 mL, 0.05M), taken in a sealed glass tube and the mixture is heated at 100 °C under N_2 for 6 to 24 h. Purification of crude reaction mixtures by column chromatography (silica gel, mixture of hexane/ethyl acetate). gave products **89aa-ga, 90aa-ga** & **90ad** in moderate to good yields.

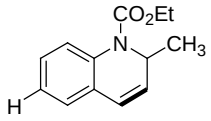
Ethyl 6-chloro-2-methyl-2*H*-quinoline-1-carboxylate (89aa): Prepared following the procedure **4G** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 1719 (N-



89aa

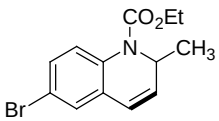
C=O), 1671, 1498, 1216, 1043, 732 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.57-7.55 (1H, m), 7.18 (1H, dd, *J* = 8.8, 2.8 Hz), 7.07 (1H, d, *J* = 2.4 Hz), 6.38 (1H, d, *J* = 9.6 Hz, olefinic-*H*), 6.08 (1H, dd, *J* = 9.6, 6.0 Hz, olefinic-*H*), 5.13 (1H, quintet, *J* = 6.4 Hz, NC*H*), 4.33-4.24 (2H, m, OC$H_2$$CH_3$), 1.34 (3H, t, *J* = 7.2 Hz, OCH_2CH_3), 1.12 (3H, d, *J* = 6.8 Hz, $CHCH_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 154.0 (C, N-C=O), 132.8 (C), 132.0 (CH), 129.0 (C), 128.4 (C), 127.2 (CH), 125.8 (CH), 125.7 (CH), 123.3 (CH), 62.2 (CH_2, OCH_2CH_3), 48.9 (CH), 18.5 (CH_3), 14.5 (CH_3, OCH_2CH_3); LRMS m/z 252.25 (M + H^+), calcd $C_{13}H_{14}ClNO_2$ 251.0713; Anal. calcd for $C_{13}H_{14}ClNO_2$ (251.07): C, 62.03; H, 5.61; N, 5.56. Found: C, 62.13; H, 5.58; N, 5.65%; HRMS m/z 274.0611 (M + Na), calcd for $C_{13}H_{14}ClNO_2Na$ 274.0611.

Ethyl 2-methyl-2*H*-quinoline-1-carboxylate (89ba): Prepared following the procedure **4G** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2925, 1706 (N-C=O), 1490, 1456, 1277, 1051, 758 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.59 (1H, br s, Ar-*H*), 7.21 (1H, dt, *J* = 8.4, 2.4 Hz), 7.06 (2H, d, *J* = 6.4 Hz), 6.42 (1H, d, *J* = 9.6 Hz, olefinic-*H*), 6.02 (1H, dd, *J* = 9.6, 6.0 Hz, olefinic-*H*), 5.12 (1H, quintet, *J* = 6.4 Hz, NC*H*), 4.32-4.20 (2H, m, OC$H_2$$CH_3$), 1.33 (3H, t, *J* = 7.2 Hz, OCH_2CH_3), 1.11 (3H, d, *J* = 6.8 Hz, $CHCH_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 154.2 (C, N-C=O), 134.2 (C), 130.7 (CH), 127.3 (CH), 126.9 (C), 126.2 (CH), 124.4 (CH), 124.2 (CH), 124.0 (CH), 62.0 (CH_2, OCH_2CH_3), 48.9 (CH), 18.5 (CH_3), 14.5 (CH_3, OCH_2CH_3); LRMS m/z 218.10 (M + H^+), calcd $C_{13}H_{15}NO_2$ 217.1103; Anal. calcd for $C_{13}H_{15}NO_2$ (217.11): C, 71.87; H, 6.96; N, 6.45. Found: C, 71.81; H, 6.88; N, 6.52%; HRMS m/z 240.1002 (M + Na), calcd for $C_{13}H_{15}NO_2Na$ 240.1001.



89ba

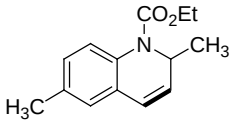
Ethyl 6-bromo-2-methyl-2*H*-quinoline-1-carboxylate (89da): Prepared following the procedure **4G** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2973, 1704 (N-C=O), 1482, 1299, 1042, 737 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.51 (1H, br s, Ar-*H*), 7.32 (1H, dd, *J* = 8.8, 2.4 Hz), 7.22 (1H, d, *J* = 2.4 Hz), 6.37 (1H, d, *J* = 9.6 Hz, olefinic-*H*), 6.07 (1H, dd, *J* = 9.6, 6.0 Hz, olefinic-*H*), 5.12 (1H, quintet, *J* =



89da

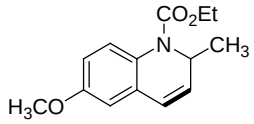
6.4 Hz, NC*H*), 4.30-4.25 (2H, m, OCH_2CH$_3$), 1.34 (3H, t, *J* = 7.2 Hz, OCH$_2$CH_3), 1.12 (3H, d, *J* = 6.8 Hz, CHCH_3); ^{13}C NMR (CDCl$_3$, DEPT-135) δ 154.0 (C, N-C=O), 133.2 (C), 131.9 (CH), 130.1 (CH), 128.8 (C), 128.6 (CH), 126.1 (CH), 123.2 (CH), 116.7 (C), 62.2 (CH$_2$, O*C*H$_2$CH$_3$), 49.0 (CH), 18.6 (CH$_3$), 14.4 (CH$_3$, OCH$_2$*C*H$_3$); LRMS m/z 296.25 (M + H$^+$), calcd $C_{13}H_{14}BrNO_2$ 295.0208; Anal. calcd for $C_{13}H_{14}BrNO_2$ (295.02): C, 52.72; H, 4.76; N, 4.73. Found: C, 52.85; H, 4.79; N, 4.68%; HRMS m/z 318.0158 (M + Na), calcd for $C_{13}H_{14}BrNO_2Na$ 318.0106.

Ethyl 2,6-dimethyl-2*H*-quinoline-1-carboxylate (89ea): Prepared following the procedure **4G** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2925, 1707 (N-C=O), 1496, 1444, 1041, 738 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.49 (1H, s, Ar-*H*), 7.03 (1H, d, *J* = 8.4 Hz), 6.90 (1H, s, Ar-*H*), 6.40 (1H, d, *J* = 9.6 Hz, olefinic-*H*), 6.01 (1H, dd, *J* = 9.6, 6.0 Hz, olefinic-*H*), 5.11 (1H, quintet, *J* = 6.4 Hz, NC*H*), 4.32-4.23 (2H, m, OCH_2CH$_3$), 2.32 (3H, s, Ar-CH_3), 1.33 (3H, t, *J* = 7.2 Hz, OCH$_2$CH_3), 1.12 (3H, d, *J* = 6.8 Hz, CHCH_3); ^{13}C NMR (CDCl$_3$, DEPT-135) δ 154.3 (C, N-C=O), 133.5 (C), 131.8 (C), 130.6 (CH), 128.1 (CH), 126.7 (C), 126.7(CH), 124.3 (CH), 124.2 (CH), 61.9 (CH$_2$, O*C*H$_2$CH$_3$), 48.9 (CH), 20.7 (CH$_3$, Ar-*C*H$_3$), 18.4 (CH$_3$), 14.5 (CH$_3$, OCH$_2$*C*H$_3$); LRMS m/z 232.00 (M + H$^+$), calcd $C_{14}H_{17}NO_2$ 231.1259; Anal. calcd for $C_{14}H_{17}NO_2$ (231.12): C, 72.70; H, 7.41; N, 6.06. Found: C, 72.85; H, 7.37; N, 6.12%; HRMS m/z 254.1156 (M + Na), calcd for $C_{14}H_{17}NO_2Na$ 254.1157.



89ea

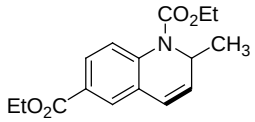
Ethyl 6-methoxy-2-methyl-2*H*-quinoline-1-carboxylate (89fa): Prepared following the procedure **4G** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2923, 1699 (N-C=O), 1497, 1463, 1266, 1031, 811 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.51 (1H, br s, Ar-*H*), 6.79 (1H, dd, *J* = 8.8, 2.8 Hz), 6.63 (1H, d, *J* = 3.2 Hz), 6.40 (1H, d, *J* = 9.6 Hz, olefinic-*H*), 6.05 (1H, dd, *J* = 9.2, 6.0 Hz, olefinic-*H*), 5.15-5.09 (1H, m, NC*H*), 4.31-4.20 (2H, m, OCH_2CH$_3$), 3.82 (3H, s, OCH_3), 1.33 (3H, t, *J* = 7.2 Hz, OCH$_2$CH_3), 1.11 (3H, d, *J* = 6.8 Hz, CHCH_3); ^{13}C NMR (CDCl$_3$, DEPT-135) δ 156.0



89fa

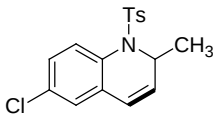
(C), 154.3 (C, N-C=O), 131.6 (CH), 128.0 (C), 127.4 (C), 125.6 (CH), 124.2 (CH), 112.9 (CH), 110.9 (CH), 61.8 (CH_2, O*C*H_2CH_3), 55.4 (CH_3, O*C*H_3), 48.7 (CH), 18.4 (CH_3), 14.7 (CH_3, OCH_2*C*H_3); LRMS m/z 248.35 (M + H^+), calcd $C_{14}H_{17}NO_3$ 247.1208; Anal. calcd for $C_{14}H_{17}NO_3$ (247.12): C, 68.00; H, 6.93; N, 5.66. Found: C, 68.12; H, 6.89; N, 5.54%; HRMS m/z 270.1103 (M + Na), calcd for $C_{14}H_{17}NO_3Na$ 270.1106.

Ethyl 2-methyl-2*H*-quinoline-1,6-dicarboxylate (89ga): Prepared following the procedure **4G** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2980, 1711 (N-C=O), 1607, 1489, 1442, 1278, 1028, 737 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.88 (1H, dd, *J* = 8.4, 1.6 Hz), 7.76 (1H, d, *J* = 1.6 Hz), 7.70 (1H, d, *J* = 8.8 Hz), 6.47 (1H, d, *J* = 9.6 Hz, olefinic-*H*), 6.05 (1H, dd, *J* = 9.6, 6.0 Hz, olefinic-*H*), 5.12 (1H, quintet, *J* = 6.4 Hz, NC*H*), 4.37 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 4.32-4.24 (2H, m, OCH_2CH_3), 1.39 (3H, t, *J* = 7.2 Hz, OCH_2CH_3), 1.34 (3H, t, *J* = 7.2 Hz, OCH_2CH_3), 1.12 (3H, d, *J* = 6.8 Hz, $CHCH_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.2 (C, O-C=O), 153.9 (C, N-C=O), 138.6 (C), 131.0 (CH), 128.8 (CH), 127.7 (CH), 126.5 (C), 125.7 (C), 123.8 (2 x CH), 62.3 (CH_2, O*C*H_2CH_3), 60.9 (CH_2, O*C*H_2CH_3), 49.3 (CH), 18.9 (CH_3), 14.4 (CH_3, OCH_2*C*H_3), 14.4 (CH_3, OCH_2*C*H_3); LRMS m/z 289.95 (M + H^+), calcd $C_{16}H_{19}NO_4$ 289.1314; Anal. calcd for $C_{16}H_{19}NO_4$ (289.13): C, 66.42; H, 6.62; N, 4.84. Found: C, 66.57; H, 6.68; N, 4.79%; HRMS m/z 312.1213 (M + Na), calcd for $C_{16}H_{19}NO_4Na$ 312.1212.



89ga

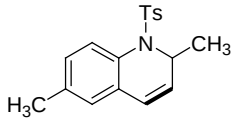
6-Chloro-2-methyl-1-(toluene-4-sulfonyl)-1,2-dihydro-quinoline (89ab): Prepared following the procedure **4G** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 1473, 1345, 1091, 1037, 737, 661 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.68 (1H, d, *J* = 8.8 Hz), 7.28 (2H, d, *J* = 8.4 Hz), 7.24 (1H, dd, *J* = 8.4, 2.4 Hz), 7.09 (2H, d, *J* = 8.0 Hz), 6.94 (1H, d, *J* = 2.4 Hz), 5.92 (1H, d, *J* = 9.6 Hz, olefinic-*H*), 5.70 (1H, dd, *J* = 9.6, 5.6 Hz, olefinic-*H*), 4.94 (1H, quintet, *J* = 6.4 Hz, NC*H*), 2.35 (3H, s, Ar-CH_3), 1.16 (3H, d, *J* = 6.8 Hz, $CHCH_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 143.5 (C), 136.0 (C),



89ab

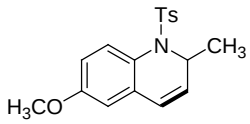
131.8 (C), 131.1 (C & CH), 129.7 (C), 129.2 (2 x CH), 129.1 (CH), 127.8 (CH), 127.1 (2 x CH), 125.9 (CH), 122.7 (CH), 51.0 (CH), 21.5 (CH_3, Ar-*C*H_3), 19.8 (CH_3); LRMS m/z 334.00 (M + H^+), calcd $C_{17}H_{16}ClNO_2S$ 333.0590; Anal. calcd for $C_{17}H_{16}ClNO_2S$ (333.05): C, 61.16; H, 4.83; N, 4.20. Found: C, 61.22; H, 4.78; N, 4.32%; HRMS m/z 356.0485 (M + Na), calcd for $C_{17}H_{16}NO_2SNa$ 356.0488.

2,6-Dimethyl-1-(toluene-4-sulfonyl)-1,2-dihydro-quinoline (89eb): Prepared following the procedure **4G** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 1496, 1348, 1162, 1062, 736 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.61 (1H, d, *J* = 8.0 Hz), 7.27 (2H, d, *J* = 8.0 Hz), 7.08 (1H, d, *J* = 8.4 Hz), 7.06 (2H, d, *J* = 8.4 Hz), 6.75 (1H, s, Ar-*H*), 5.93 (1H, d, *J* = 9.6 Hz, olefinic-*H*), 5.61 (1H, dd, *J* = 9.6, 5.6 Hz, olefinic-*H*), 4.91 (1H, quintet, *J* = 6.4 Hz, NC*H*), 2.34 (3H, s, Ar-CH_3), 2.32 (3H, s, Ar-CH_3), 1.15 (3H, d, *J* = 7.2 Hz, CHCH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 143.1 (C), 136.2 (2 x C), 129.9 (C), 129.5 (CH), 128.9 (2 x CH), 128.7 (CH), 128.1 (C), 127.7 (CH), 127.2 (2 x CH), 126.7 (CH), 123.6 (CH), 50.9 (CH), 21.5 (CH_3, Ar-*C*H_3), 21.0 (CH_3, Ar-*C*H_3), 19.7 (CH_3); LRMS m/z 314.20 (M + H^+), calcd $C_{18}H_{19}NO_2S$ 313.1136; Anal. calcd for $C_{18}H_{19}NO_2S$ (313.11): C, 68.98; H, 6.11; N, 4.47. Found: C, 68.81; H, 6.15; N, 4.53%; HRMS m/z 336.1035 (M + Na), calcd for $C_{18}H_{19}NO_2SNa$ 336.1034.



89eb

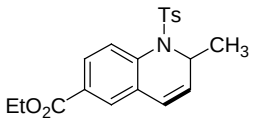
6-Methoxy-2-methyl-1-(toluene-4-sulfonyl)-1,2-dihydro-quinoline (89fb): Prepared following the procedure **4G** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 1602, 1490, 1266, 1155, 1042, 737 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.64 (1H, d, *J* = 9.2 Hz), 7.25 (2H, d, *J* = 8.4 Hz), 7.06 (2H, d, *J* = 8.0 Hz), 6.84 (1H, dd, *J* = 8.8, 2.8 Hz), 6.47 (1H, s, Ar-*H*), 5.90 (1H, d, *J* = 9.6 Hz, olefinic-*H*), 5.62 (1H, dd, *J* = 9.6, 5.6 Hz, olefinic-*H*), 4.89 (1H, quintet, *J* = 6.4 Hz, NC*H*), 3.81 (3H, s, OCH_3), 2.34 (3H, s, Ar-CH_3), 1.15 (3H, d, *J* = 6.8 Hz, CHCH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 158.0 (C), 143.1 (C), 136.1 (C), 130.3 (CH), 129.5 (C), 129.3 (CH), 128.9 (2 x CH), 127.3 (2 x CH), 125.3 (C), 123.5 (CH), 113.0 (CH), 111.3 (CH),



89fb

55.4 (CH_3, O*C*H_3), 50.9 (CH), 21.5 (CH_3, Ar-*C*H_3), 19.5 (CH_3); LRMS m/z 330.15 (M + H^+), calcd $C_{18}H_{19}NO_3S$ 329.1086; Anal. calcd for $C_{18}H_{19}NO_3S$ (329.10): C, 65.63; H, 5.81; N, 4.25. Found: C, 65.48; H, 5.86; N, 4.33%; HRMS m/z 352.0986 (M + Na), calcd for $C_{18}H_{19}NO_3SNa$ 352.0984.

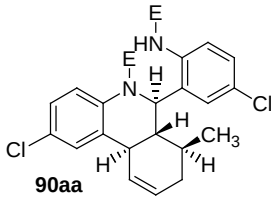
Ethyl 2-methyl-1-(toluene-4-sulfonyl)-1,2-dihydro-quinoline-6-carboxylate (89gb):



89gb

Prepared following the procedure **4G** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 1718 (O-C=O), 1602, 1431, 1267, 1039, 738 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.94 (1H, dd, *J* = 8.8, 1.6 Hz), 7.83 (1H, d, *J* = 8.8 Hz), 7.65 (1H, d, *J* = 1.6 Hz), 7.31 (2H, d, *J* = 8.4 Hz), 7.08 (2H, d, *J* = 8.0 Hz), 6.09 (1H, d, *J* = 9.6 Hz, olefinic-*H*), 5.74 (1H, dd, *J* = 9.6, 5.6 Hz, olefinic-*H*), 5.00 (1H, quintet, *J* = 6.4 Hz, NC*H*), 4.38 (2H, q, *J* = 7.2 Hz, OC$H_2$$CH_3$), 2.34 (3H, s, Ar-C$H_3$), 1.40 (3H, t, *J* = 7.2 Hz, OCH_2CH_3), 1.18 (3H, d, *J* = 6.8 Hz, CHCH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.1 (C, O-C=O), 143.6 (C), 136.9 (C), 136.2 (C), 130.3 (CH), 129.2 (2 x CH), 129.1 (CH), 128.1 (C), 127.9 (C), 127.7 (CH), 127.0 (2 x CH), 126.9 (CH), 123.3 (CH), 61.1 (CH_2, O*C*$H_2$$CH_3$), 51.3 (CH), 21.5 ($CH_3$, Ar-*C*$H_3$), 20.2 ($CH_3$), 14.3 ($CH_3$, OCH_2*C*H_3); LRMS m/z 370.15 (M - H^+), calcd $C_{20}H_{21}NO_4S$ 371.1191; Anal. calcd for $C_{20}H_{21}NO_4S$ (371.11): C, 64.67; H, 5.70; N, 3.77. Found: C, 64.51; H, 5.78; N, 3.81%; HRMS m/z 394.1090 (M + Na), calcd for $C_{20}H_{21}NO_4SNa$ 394.1089.

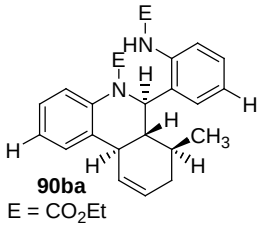
Ethyl 2-chloro-6-(5-chloro-2-ethoxycarbonylamino-phenyl)-7-methyl-6a,7,8,10a-tetrahydro-6*H*-phenanthridine-5-carboxylate (90aa):



90aa
E = CO_2Et

Prepared following the procedure **4G** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 1726 (N-C=O), 1682 (N-C=O), 1481, 1401, 1221, 1053, 739 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.26 (1H, s, N-*H*), 7.69 (1H, br d, *J* = 5.2 Hz), 7.33 (1H, d, *J* = 2.0 Hz), 7.26 (1H, dd, *J* = 8.8, 2.4 Hz), 7.21 (1H, dd, *J* = 8.8, 2.4 Hz), 7.10 (1H, d, *J* = 8.4 Hz), 6.46 (1H, d, *J* = 2.4 Hz), 6.14 (1H, br d, *J* = 10.4 Hz, olefinic-*H*), 6.03-5.99 (1H, m, olefinic-*H*), 5.32 (1H, d, *J* = 10.4 Hz, NC*H*), 4.30 (2H, q, *J* = 7.2 Hz, OC$H_2$$CH_3$), 4.26-4.13 (2H, m, OC$H_2$$CH_3$), 3.15 (1H, d, *J* =

10.0 Hz), 2.15-2.09 (1H, m), 2.05-1.95 (1H, m), 1.77-1.65 (2H, m), 1.38 (3H, t, *J* = 7.2 Hz, OCH_2CH_3), 1.23 (3H, t, *J* = 7.2 Hz, OCH_2CH_3), 0.61 (3H, d, *J* = 6.4 Hz, $CHCH_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 155.8 (C, N-C=O), 154.6 (C, N-C=O), 139.4 (2 x C), 136.3 (CH), 134.7 (C), 134.6 (C), 131.6 (C), 130.0 (CH), 129.4 (C), 128.2 (CH), 127.4 (CH), 127.1 (CH), 126.5 (CH), 123.4 (2 x CH), 62.8 (CH_2, OCH_2CH_3), 61.2 (CH_2, OCH_2CH_3), 56.7 (CH), 54.4 (CH), 39.1 (CH), 34.9 (CH_2), 34.5 (CH), 18.8 (CH_3), 14.7 (CH_3, OCH_2CH_3), 14.3 (CH_3, OCH_2CH_3); LRMS m/z 503.30 ($M + H^+$), calcd $C_{26}H_{28}Cl_2N_2O_4$ 502.1426; Anal. calcd for $C_{26}H_{28}Cl_2N_2O_4$ (502.14): C, 62.03; H, 5.61; N, 5.56. Found: C, 62.18; H, 5.67; N, 5.46%; HRMS m/z 525.1323 (M + Na), calcd for $C_{26}H_{28}Cl_2N_2O_4Na$ 525.1324.

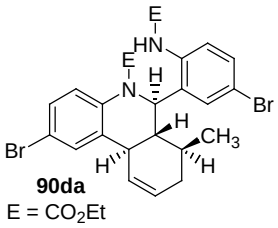


90ba
E = CO_2Et

Ethyl 6-(2-ethoxycarbonylamino-phenyl)-7-methyl-6a,7,8,10a-tetrahydro-6*H*-phenanthridine-5-carboxylate (90ba): Prepared following the procedure **4G** and purified by column chromatography using EtOAc/hexane and isolated as a solid. column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 1719 (N-C=O), 1675 (N-C=O), 1587, 1523, 1224, 1061, 739 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.37 (1H, s, N-*H*), 7.73 (1H, s, Ar-*H*), 7.33 (1H, d, *J* = 6.8 Hz), 7.28-7.19 (3H, m, Ph-*H*), 7.12 (1H, d, *J* = 7.2 Hz), 6.87 (1H, t, *J* = 7.6 Hz), 6.44 (1H, d, *J* = 8.0 Hz), 6.21 (1H, d, *J* = 10.4 Hz, olefinic-*H*), 5.98-5.93 (1H, m, olefinic-*H*), 5.38 (1H, d, *J* = 8.8 Hz, NC*H*), 4.29 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 4.24-4.12 (2H, m, OCH_2CH_3), 3.17 (1H, d, *J* = 10.8 Hz), 2.10-2.08 (1H, m), 1.98-1.94 (1H, m), 1.76-1.71 (2H, m), 1.37 (3H, t, *J* = 6.8 Hz, OCH_2CH_3), 1.20 (3H, t, *J* = 7.2 Hz, OCH_2CH_3), 0.59 (3H, d, *J* = 6.4 Hz, $CHCH_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 156.1 (C, N-C=O), 154.8 (C, N-C=O), 137.8 (2 x C), 136.6 (C), 135.8 (C), 134.9 (CH), 129.3 (CH), 127.8 (CH), 127.5 (CH), 126.3 (CH), 126.2 (CH), 125.7 (CH), 124.4 (CH), 124.2 (CH), 122.7 (CH), 62.5 (CH_2, OCH_2CH_3), 61.0 (CH_2, OCH_2CH_3), 56.8 (CH), 54.7 (CH), 39.1 (CH), 35.1 (CH_2), 34.6 (CH), 18.8 (CH_3), 14.7 (CH_3, OCH_2CH_3), 14.3 (CH_3, OCH_2CH_3); LRMS m/z 435.00 ($M + H^+$), calcd $C_{26}H_{30}N_2O_4$ 434.2206; Anal. calcd for $C_{26}H_{30}N_2O_4$

(434.20): C, 71.87; H, 6.96; N, 6.45. Found: C, 71.82; H, 6.91; N, 6.42%; HRMS m/z 457.2103 (M + Na), calcd for $C_{26}H_{30}N_2O_4Na$ 457.2104.

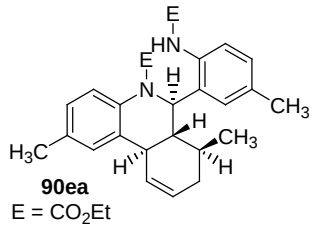
Ethyl 2-bromo-6-(5-bromo-2-ethoxycarbonylamino-phenyl)-7-methyl-6a,7,8,10a-tetrahydro-6*H*-phenanthridine-5-carboxylate (90da):



90da
E = CO_2Et

Prepared following the procedure **4G** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3336 (N-*H*), 2939, 1720 (N-C=O), 1681 (N-C=O), 1483, 1462, 1214, 1053, 734 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.24 (1H, s, N-*H*), 7.62 (1H, br s, Ar-*H*), 7.47 (1H, d, *J* = 2.0 Hz), 7.42 (1H, dd, *J* = 8.4, 2.0 Hz), 7.36 (1H, dd, *J* = 8.8, 2.0 Hz), 7.05 (1H, d, *J* = 8.4 Hz), 6.60 (1H, d, *J* = 2.0 Hz), 6.14 (1H, d, *J* = 10.0 Hz, olefinic-*H*), 6.03-6.00 (1H, m, olefinic-*H*), 5.31 (1H, d, *J* = 9.2 Hz, NC*H*), 4.30 (2H, q, *J* = 7.2 Hz, OC$H_2$$CH_3$), 4.26-4.13 (2H, m, OC$H_2$$CH_3$), 3.15 (1H, d, *J* = 10.4 Hz), 2.15-2.10 (1H, m), 1.99-1.95 (1H, m), 1.78-1.65 (2H, m), 1.38 (3H, t, *J* = 7.2 Hz, OCH_2CH_3), 1.22 (3H, t, *J* = 7.2 Hz, OCH_2CH_3), 0.61 (3H, d, *J* = 6.4 Hz, $CHCH_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 155.8 (C, N-C=O), 154.6 (C, N-C=O), 139.7 (2 x C), 136.7 (CH), 135.2 (C), 135.1 (C), 131.1 (CH), 130.0 (2 x CH), 129.5 (CH), 127.7 (CH), 126.4 (CH), 123.4 (CH), 119.6 (C), 117.2 (C), 62.9 (CH_2, OCH_2CH_3), 61.3 (CH_2, OCH_2CH_3), 56.6 (CH), 54.4 (CH), 39.0 (CH), 34.9 (CH_2), 34.5 (CH), 18.8 (CH_3), 14.7 (CH_3, OCH_2CH_3), 14.3 (CH_3, OCH_2CH_3); LRMS m/z 591.25 (M + H^+), calcd $C_{26}H_{28}Br_2N_2O_4$ 590.0416; Anal. calcd for $C_{26}H_{28}Br_2N_2O_4$ (590.04): C, 52.72; H, 4.76; N, 4.73. Found: C, 52.88; H, 4.81; N, 4.65%; HRMS m/z 613.0293 (M + Na), calcd for $C_{26}H_{28}Br_2N_2O_4Na$ 613.0314.

Ethyl 6-(2-ethoxycarbonylamino-5-methyl-phenyl)-2,7-dimethyl-6a,7,8,10a-tetrahydro-6*H*-phenanthridine-5-carboxylate (90ea):

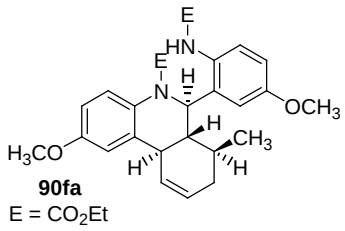


90ea
E = CO_2Et

Prepared following the procedure **4G** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 2925, 1720 (N-C=O), 1680 (N-C=O), 1507, 1465, 1208, 1052, 820 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.26 (1H, s, N-*H*), 7.57 (1H, br s, Ar-*H*), 7.15 (1H, s, Ar-*H*), 7.07-7.01 (3H, m, Ph-*H*), 6.27 (1H, s,

Ar-*H*), 6.23 (1H, d, *J* = 10.4 Hz, olefinic-*H*), 6.00-5.96 (1H, m, olefinic-*H*), 5.35 (1H, d, *J* = 8.4 Hz, NC*H*), 4.29 (2H, q, *J* = 7.2 Hz, OCH_2CH$_3$), 4.24-4.12 (2H, m, OCH_2CH$_3$), 3.16 (1H, d, *J* = 10.8 Hz), 2.43 (3H, s, Ar-CH_3), 2.17-2.10 (1H, m), 2.10 (3H, s, Ar-CH_3), 2.01-1.93 (1H, m), 1.75-1.69 (2H, m), 1.38 (3H, t, *J* = 6.8 Hz, OCH$_2$CH_3), 1.21 (3H, t, *J* = 7.2 Hz, OCH$_2$CH_3), 0.61 (3H, d, *J* = 6.4 Hz, CHCH_3); ^{13}C NMR (CDCl$_3$, DEPT-135) δ 156.1 (C, N-C=O), 154.9 (C, N-C=O), 137.4 (2 x C), 135.3 (C), 135.1 (CH), 134.0 (C), 133.6 (C), 133.2 (C), 129.2 (CH), 128.5 (CH), 127.8 (CH), 126.7 (CH), 126.0 (CH), 124.6 (CH), 123.4 (CH), 62.3 (CH$_2$, O*C*H$_2$CH$_3$), 60.9 (CH$_2$, OCH$_2$CH$_3$), 56.8 (CH), 54.5 (CH), 39.1 (CH), 35.1 (CH$_2$), 34.6 (CH), 21.4 (CH$_3$, Ar-*C*H$_3$), 21.0 (CH$_3$, Ar-*C*H$_3$), 18.9 (CH$_3$), 14.8 (CH$_3$, OCH$_2$*C*H$_3$), 14.4 (CH$_3$, OCH$_2$*C*H$_3$); LRMS m/z 463.20 (M + H$^+$), calcd $C_{28}H_{34}N_2O_4$ 462.2519; Anal. calcd for $C_{28}H_{34}N_2O_4$ (462.25): C, 72.70; H, 7.41; N, 6.06. Found: C, 72.58; H, 7.41; N, 6.15%; HRMS m/z 485.2419 (M + Na), calcd for $C_{28}H_{34}N_2O_4$Na 485.2416.

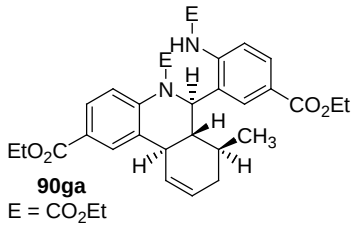
Ethyl 6-(2-ethoxycarbonylamino-5-methoxy-phenyl)-2-methoxy-7-methyl-6a,7,8,10a-tetrahydro-6*H*-phenanthridine-5-carboxylate (90fa): Prepared following the procedure **4G** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 1723 (N-C=O), 1674 (N-C=O), 1498, 1406, 1216, 1042, 733 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 9.11 (1H, s, N-*H*), 7.59 (1H, br s, Ar-*H*), 7.06 (1H, d, *J* = 8.8 Hz), 6.87 (1H, d, *J* = 2.8 Hz), 6.79 (2H, dt, *J* = 8.0, 2.8 Hz), 6.16 (1H, d, *J* = 10.4 Hz, olefinic-*H*), 6.02 (1H, d, *J* = 2.8 Hz), 5.99-5.96 (1H, m, olefinic-*H*), 5.36 (1H, d, *J* = 8.8 Hz, NC*H*), 4.29 (2H, q, *J* = 7.2 Hz, OCH_2CH$_3$), 4.23-4.10 (2H, m, OCH_2CH$_3$), 3.87 (3H, s, OCH_3), 3.58 (3H, s, OCH_3), 3.16 (1H, d, *J* = 10.8 Hz), 2.14-2.09 (1H, m), 2.00-1.95 (1H, m), 1.75-1.67 (2H, m), 1.37 (3H, t, *J* = 6.8 Hz, OCH$_2$CH_3), 1.21 (3H, t, *J* = 7.2 Hz, OCH$_2$CH_3), 0.63 (3H, d, *J* = 6.4 Hz, CHCH_3); ^{13}C NMR (CDCl$_3$, DEPT-135) δ 157.6 (2 x C), 156.1 (C, N-C=O), 155.1 (C, N-C=O), 139.1 (2 x C), 136.6 (CH), 129.5 (CH), 129.4 (C), 128.8 (C), 127.1 (CH), 124.2 (CH), 113.0 (CH), 112.8 (CH), 111.3 (CH), 108.6 (CH), 62.3 (CH$_2$, O*C*H$_2$CH$_3$), 60.9 (CH$_2$, O*C*H$_2$CH$_3$), 56.8 (CH), 55.5 (CH$_3$,



90fa
E = CO_2Et

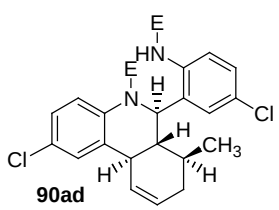
O*C*H$_3$), 55.2 (CH$_3$, O*C*H$_3$), 54.4 (CH), 39.3 (CH), 35.0 (CH$_2$), 34.5 (CH), 18.8 (CH$_3$), 14.8 (CH$_3$, OCH$_2$*C*H$_3$), 14.4 (CH$_3$, OCH$_2$*C*H$_3$); LRMS m/z 494.60 (M + H$^+$), calcd $C_{28}H_{34}N_2O_6$ 494.2417; Anal. calcd for $C_{28}H_{34}N_2O_6$ (494.24): C, 68.00; H, 6.93; N, 5.66. Found: C, 68.12; H, 6.85; N, 5.71%; HRMS m/z 517.2318 (M + Na), calcd for $C_{28}H_{34}N_2O_6Na$ 517.2314.

Ethyl 6-(5-ethoxycarbonyl-2-ethoxycarbonylamino-phenyl)-7-methyl-6a,7,8,10a-tetrahydro-6*H*-phenanthridine-2,5-dicarboxylate (90ga): Prepared following the procedure **4G** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 2924, 1715 (N-C=O), 1679 (N-C=O), 1610, 1587, 1222, 1055, 740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 9.45 (1H, s, N-*H*), 8.03 (1H, s, Ar-*H*), 7.96 (1H, d, *J* = 8.0 Hz), 7.87 (2H, s, Ar-*H*), 7.20 (1H, d, *J* = 8.0 Hz), 7.11 (1H, s, Ar-*H*), 6.28 (1H, d, *J* = 10.0 Hz, olefinic-*H*), 6.03-5.94 (1H, m, olefinic-*H*), 5.35 (1H, d, *J* = 8.4 Hz, NC*H*), 4.41 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 4.31 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 4.26-4.13 (4H, m, 2 x OC*H*$_2$CH$_3$), 3.20 (1H, d, *J* = 10.4 Hz), 2.14-2.09 (1H, m), 2.01-1.99 (1H, m), 1.79-1.71 (2H, m), 1.42 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$), 1.38 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$), 1.28-1.08 (6H, t, *J* = 7.2 Hz, 2 x OCH$_2$C*H*$_3$), 0.58 (3H, d, *J* = 6.4 Hz, CHC*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.3 (C, O-C=O), 165.8 (C, O-C=O), 155.9 (C, N-C=O), 154.4 (C, N-C=O), 140.6 (C), 140.2 (C), 137.4 (2 x C), 134.1 (C), 129.8 (CH), 129.2 (2 x CH), 127.9 (CH), 127.7 (CH), 126.0 (C), 125.9 (CH), 124.4 (CH), 123.7 (CH), 62.9 (CH$_2$, O*C*H$_2$CH$_3$), 61.4 (CH$_2$, O*C*H$_2$CH$_3$), 61.0 (CH$_2$, O*C*H$_2$CH$_3$), 60.7 (CH$_2$, O*C*H$_2$CH$_3$), 56.9 (CH), 54.7 (CH), 39.0 (CH), 34.9 (CH$_2$), 34.6 (CH), 18.8 (CH$_3$), 14.7 (CH$_3$, OCH$_2$*C*H$_3$), 14.4 (CH$_3$, OCH$_2$*C*H$_3$), 14.3 (CH$_3$, OCH$_2$*C*H$_3$), 14.1 (CH$_3$, OCH$_2$*C*H$_3$); LRMS m/z 578.20 (M $^+$), calcd $C_{32}H_{38}N_2O_8$ 578.2628; Anal. calcd for $C_{32}H_{38}N_2O_8$ (578.26): C, 66.42; H, 6.62; N, 4.84. Found: C, 66.57; H, 6.68; N, 4.75%; HRMS m/z 601.2524 (M + Na), calcd for $C_{32}H_{38}N_2O_8Na$ 601.2526.



90ga
E = CO_2Et

***N*-[2-(5-Acetyl-2-chloro-7-methyl-5,6,6a,7,8,10a-hexahydro-phenanthridin-6-yl)-4-chloro-phenyl]-acetamide (90ad):** Prepared following the

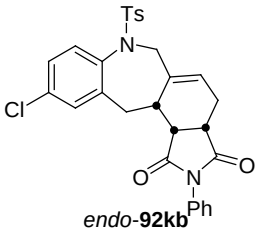


90ad
E = $COCH_3$

procedure **4G** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 2917, 1692 (N-C=O), 1637, 1603, 1482, 1298, 1038, 737 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 10.38 (1H, s, N-*H*), 7.82 (1H, d, *J* = 8.8 Hz), 7.39 (1H, d, *J* = 1.6 Hz), 7.31 (1H, dd, *J* = 8.8, 2.4 Hz), 7.20 (1H, dd, *J* = 8.8, 2.4 Hz), 6.92 (1H, d, *J* = 8.0 Hz), 6.34 (1H, d, *J* = 2.0 Hz), 6.13 (1H, d, *J* = 8.8 Hz, olefinic-*H*), 6.03-5.99 (1H, m, olefinic-*H*), 5.57 (1H, d, *J* = 8.4 Hz, NC*H*), 3.09 (1H, d, *J* = 10.8 Hz), 2.32 (3H, s, COCH_3), 2.16-2.08 (1H, m), 2.08 (3H, s, COCH_3), 1.97-1.94 (1H, m), 1.76-1.65 (2H, m), 0.59 (3H, d, *J* = 6.4 Hz, CHCH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 171.0 (C, N-C=O), 168.9 (C, N-C=O), 140.8 (C), 135.5 (C), 135.0 (C), 134.6 (C), 133.4 (C), 130.5 (CH), 129.6 (C), 128.3 (CH), 127.3 (CH), 127.1 (CH), 127.0 (CH), 126.4 (CH), 124.2 (CH), 122.9 (CH), 55.7 (CH), 53.8 (CH), 39.2 (CH), 34.8 (CH_2), 34.6 (CH), 24.3 (CH_3, CO*C*H_3), 22.4 (CH_3, CO*C*H_3), 19.0 (CH_3); LRMS m/z 443.35 ($M + H^+$), calcd $C_{24}H_{24}Cl_2N_2O_2$ 442.1215; Anal. calcd for $C_{24}H_{24}Cl_2N_2O_2$ (442.12): C, 65.02; H, 5.46; N, 6.32. Found: C, 65.12; H, 5.51; N, 6.23%; HRMS m/z 465.1112 (M + Na), calcd for $C_{24}H_{24}Cl_2N_2O_2Na$ 465.1113.

4H: Experimental Procedure for the Synthesis of Functionalized Heterocycles 92kb and 93kb via RCM/Diels-Alder Reactions: A 10 mL oven-dried round bottom flask equipped with a stir bar was charged with enyne amine **86kb** (0.1 mmol), CH_2Cl_2 (2 mL, 0.05 M) and first generation Grubb's catalyst **4n** (6.58 mg, 0.008 mmol, 8 mol%). The reaction mixture was stirred under N_2 at room temperature for 18 to 24 h. Solvent CH_2Cl_2 was distilled off at ambient pressure and to the crude reaction mixture, *N*-phenylmaleimide (34.64 mg, 0.20 mmol, 2.0 equiv.) or diethyl acetylenedicarboxylate (0.20 mmol, 2.0 equiv) and anhydrous toluene (2.0 ml) were added and heated at 110-120 °C under N_2 in a sealed glass tube for 21 h. The toluene was removed and the residue was purified by column chromatography (silica gel, mixture of hexane/ethyl acetate) to gave **92kb** and **93kb** respectively (see Scheme 9).

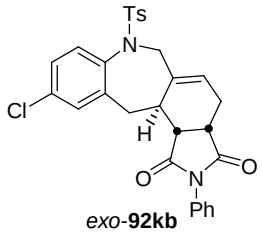
***endo*-10-Chloro-7-(4-methylphenylsulfonyl)-2-phenyl-1,2,3,3a,4,6,7,12,12a,12b-decahydrobenzo[6,7]azepino[4,3-*e*]isoindole-1,3-dione (*endo*-92kb):** Prepared following the procedure **4H** and purified by column



endo-**92kb**

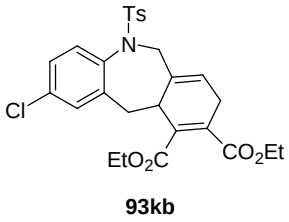
chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 1711 (O=C-N), 1484, 1382, 1060, 737 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.52 (2H, d, *J* = 8.4 Hz), 7.48 (1H, t, *J* = 7.6 Hz), 7.42 (1H, d, *J* = 6.8 Hz), 7.34 (2H, d, *J* = 7.6 Hz), 7.22-7.14 (5H, m, Ph-*H*), 7.03 (1H, s, Ar-*H*), 5.99 (1H, s, olefinic-*H*), 4.40 (1H, d, *J* = 14.0 Hz), 4.32 (1H, d, *J* = 14.4 Hz), 3.18 (2H, quintet, *J* = 8.8 Hz), 2.69 (1H, dd, *J* = 16.4, 5.6 Hz), 2.52-2.43 (2H, m), 2.36 (3H, s, Ar-CH_3), 2.30-2.27 (1H, m), 2.18 (1H, br d, *J* = 14.4 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 178.0 (C, O=C-N), 176.3 (C, O=C-N), 143.9 (C), 140.2 (C), 135.7 (C), 135.6 (C), 135.3 (C), 133.4 (C), 132.3 (CH), 131.7 (C), 129.8 (CH), 129.6 (2 x CH), 129.2 (2 x CH), 128.8 (CH), 127.5 (CH), 127.2 (2 x CH), 127.1 (CH), 126.3 (2 x CH), 54.4 (CH_2), 44.0 (CH), 40.0 (CH), 38.0 (CH), 33.5 (CH_2), 24.1 (CH_2), 21.6 (CH_3, Ar-*C*H_3); LRMS m/z 533.00 (M + H^+), calcd $C_{29}H_{25}ClN_2O_4S$ 532.124; Anal. calcd for $C_{29}H_{25}ClN_2O_4$ S (532.1224): C, 65.34; H, 4.73; N, 5.26. Found: C, 65.47; H, 4.68; N, 5.19%.

***exo*-10-Chloro-7-(4-methylphenylsulfonyl)-2-phenyl-1,2,3,3a,4,6,7,12,12a,12b-decahydrobenzo[6,7]azepino[4,3-*e*]isoindole-1,3-dione (*exo*-92kb):** Prepared following the procedure **4H** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 1712 (O=C-N), 1483, 1381, 1091, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.51 (1H, d, *J* = 8.4 Hz), 7.48-7.36 (5H, m, Ph-*H*), 7.27-7.22 (5H, m, Ph-*H*), 7.16 (1H, d, *J* = 2.0 Hz), 5.98 (1H, s, olefinic-*H*), 4.46 (1H, d, *J* = 13.6 Hz), 4.10 (1H, d, *J* = 13.2 Hz), 2.99 (1H, dd, *J* = 14.8, 8.8 Hz), 2.61 (1H, t, *J* = 8.8 Hz), 2.54-2.41 (2H, m), 2.39 (3H, s, Ar-CH_3), 2.39-2.35 (2H, m), 2.31 (1H, dd, *J* = 13.6, 3.2 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 177.74 (C, O=C-N), 177.68 (C, O=C-N), 143.9 (C), 137.6 (C), 136.4 (C), 135.8 (C), 133.1 (C), 132.4 (CH), 132.3 (C), 131.6 (C), 130.5 (CH), 129.6 (2 x CH), 129.2 (2 x CH), 128.6 (2 x CH), 127.9 (CH), 127.2 (2 x CH), 126.2 (2 x CH), 55.4 (CH_2), 42.5 (CH), 37.3 (CH), 35.8 (CH), 35.2 (CH_2), 22.3 (CH_2), 21.6 (CH_3, Ar-*C*H_3); LRMS m/z 533.00 (M + H^+), calcd $C_{29}H_{25}ClN_2O_4S$ 532.124; Anal. calcd for $C_{29}H_{25}ClN_2O_4$ S (532.1224): C, 65.34; H, 4.73; N, 5.26. Found: C, 65.45; H, 4.70; N, 5.20%.



exo-**92kb**

Diethyl 2-chloro-5-(toluene-4-sulfonyl)-6,8,10a,11-tetrahydro-5*H*-dibenzo[*b*,*e*]azepine-9,10-dicarboxylate (93kb): Prepared following the procedure **4H** and purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 1723 (O=C-O), 1483, 1350, 1161, 1051, 735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.41 (3H, br s, Ar-*H*), 7.22 (1H, d, *J* = 8.4 Hz), 7.42 (2H, br s, Ar-*H*), 7.05 (1H, br s, Ar-*H*), 5.89 (1H, s, olefinic-*H*), 5.00-4.96 (1H, m), 4.28-4.20 (1H, m), 4.23 (4H, q, *J* = 6.8 Hz, 2 x OC*H*$_2$CH$_3$), 3.48 (1H, br s), 2.99 (3H, br s), 2.39 (3H, s, Ar-C*H*$_3$), 1.31 (6H, t, *J* = 7.2 Hz, 2 x OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.7 (C, O=C-O), 167.0 (C, O=C-O), 143.7 (2 x C), 141.4 (C), 137.9 (C), 137.5 (C), 133.7 (2 x C), 132.9 (C), 132.3 (CH), 130.2 (CH), 129.4 (CH), 127.7 (2 x CH), 127.1 (2 x CH), 121.8 (CH), 61.4 (CH$_2$, 2 x O*C*H$_2$CH$_3$), 56.2 (CH$_2$), 39.5 (CH$_2$), 38.9 (CH), 28.0 (CH$_2$), 21.6 (CH$_3$, Ar-*C*H$_3$), 14.0 (CH$_3$, OCH$_2$*C*H$_3$), 13.9 (CH$_3$, OCH$_2$*C*H$_3$); ^1H NMR (500 MHz, $CDCl_3$, recorded at –40 ^oC) δ 7.49 (1H, d, *J* = 8.5 Hz), 7.35 (2H, d, *J* = 8.0 Hz), 7.27 (1H, dd, *J* = 8.0, 2.0 Hz), 7.16 (2H, d, *J* = 8.5 Hz), 7.06 (1H, d, *J* = 2.5 Hz), 5.94 (1H, s, olefinic-*H*), 4.99 (1H, d, *J* = 15.0 Hz), 4.28-4.20 (4H, m, 2 x OC*H*$_2$CH$_3$), 3.48 (1H, d, *J* = 15.0 Hz), 3.00 (2H, br s), 2.92 (1H, quintet, *J* = 6.0 Hz), 2.41 (3H, s, Ar-C*H*$_3$), 2.39 (1H, t, *J* = 12.5 Hz), 1.39-1.34 (1H, m), 1.31 (6H, t, *J* = 7.5 Hz, 2 x OCH$_2$C*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$, DEPT-135, recorded at –40 ^oC) δ 167.4 (C, O=C-O), 167.3 (C, O=C-O), 144.0 (C), 141.3 (C), 137.5 (C), 137.0 (C), 134.3 (C), 133.8 (C), 133.7 (C), 132.9 (CH), 132.6 (C), 130.5 (CH), 129.6 (2 x CH), 128.0 (CH), 127.1 (2 x CH), 122.0 (CH), 61.9 (CH$_2$, 2 x O*C*H$_2$CH$_3$), 56.3 (CH$_2$), 39.4 (CH$_2$), 38.6 (CH), 28.0 (CH$_2$), 22.1 (CH$_3$, Ar-*C*H$_3$), 14.3 (CH$_3$, OCH$_2$*C*H$_3$), 14.2 (CH$_3$, OCH$_2$*C*H$_3$); LRMS m/z 530.50 (M + H^+), calcd $C_{27}H_{28}ClNO_6S$ 529.1326; Anal. calcd for $C_{27}H_{28}ClNO_6S$ (529.13): C, 61.18; H, 5.32; N, 2.64. Found: C, 61.09; H, 5.38; N, 2.71%.

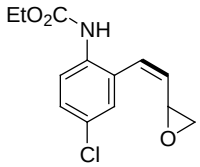


93kb

4I: Experimental Procedure for the Synthesis of Epoxides 94 and 95: A 25 mL oven-dried round bottom flask equipped with a stir bar was charged with **88aa** (0.5 mmol), CH_2Cl_2 (10 mL, 0.05 M) and *m*-CPBA (3 equiv.). The reaction mixture was

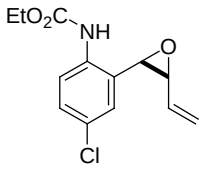
stirred at room temperature for 2 to 3 h. The crude reaction mixture was washed with a $NaHSO_3$ solution (40%) and then with saturated aqueous $NaHCO_3$. The organic layer was dried (Na_2SO_4), filtered and concentrated under reduced pressure. Pure products **94aa** and **95aa** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

Ethyl [4-chloro-2-(2-oxiranylvinyl)phenyl]carbamate (94aa): Prepared following the procedure **4I** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3277 (N-*H*), 1730 (N-C=O), 1514, 1216, 1056, 736 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.99 (1H, d, *J* = 6.4 Hz), 7.29 (1H, dd, *J* = 8.8, 2.0 Hz), 7.21 (1H, d, *J* = 2.4 Hz), 6.61 (1H, d, *J* = 11.2 Hz, olefinic-*H*), 6.56 (1H, s, N-*H*), 5.54 (1H, t, *J* = 11.2 Hz, olefinic-*H*), 4.23 (2H, q, *J* = 7.2 Hz, OC$H_2$$CH_3$), 3.46-3.42 (1H, m), 3.03 (1H, t, *J* = 4.8 Hz), 2.78 (1H, dd, *J* = 5.2, 2.8 Hz), 1.32 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 153.4 (C, N-C=O), 134.5 (CH), 134.2 (2 x C), 129.2 (CH), 129.1 (CH), 128.8 (CH), 128.2 (C), 121.3 (CH), 61.6 (CH_2, OCH_2CH_3), 48.6 (CH_2), 48.4 (CH) 14.5 (CH_3, OCH_2CH_3); LRMS m/z 268.15 (M + H^+), calcd $C_{13}H_{14}ClNO_3$ 267.0662; Anal. calcd for $C_{13}H_{14}ClNO_3$ (267.06): C, 58.32; H, 5.27; N, 5.23. Found: C, 58.21; H, 5.32; N, 5.45%.



94aa

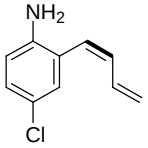
Ethyl [4-chloro-2-(3-vinyloxiranyl)phenyl]carbamate (95aa): Prepared following the procedure **4I** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3277 (N-*H*), 1729 (N-C=O), 1519, 1222, 1059, 736 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.92 (1H, s, Ar-*H*), 7.44 (1H, s, N-*H*), 7.26 (1H, dd, *J* = 8.0, 2.0 Hz), 7.20 (1H, s, Ar-*H*), 5.59 (1H, d, *J* = 17.2 Hz, olefinic-*H*), 5.35 (1H, d, *J* = 9.6 Hz, olefinic-*H*), 5.28 (1H, dd, *J* = 16.8, 8.4 Hz, olefinic-*H*), 4.25-4.17 (1H, m, OC*H*), 4.21 (2H, q, *J* = 7.2 Hz, OC$H_2$$CH_3$), 3.76 (1H, dd, *J* = 8.0, 4.0 Hz), 1.31 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 153.6 (C, N-C=O), 135.5 (2 x C), 131.4 (CH), 128.6 (CH), 128.4 (C), 127.4 (CH), 122.9 (CH_2), 122.1 (CH), 61.4 (CH_2, OCH_2CH_3), 58.8 (CH), 56.7 (CH), 14.5 (CH_3, OCH_2CH_3); LRMS m/z 268.15 (M +



95aa

H^+), calcd $C_{13}H_{14}ClNO_3$ 267.0662; Anal. calcd for $C_{13}H_{14}ClNO_3$ (267.06): C, 58.32; H, 5.27; N, 5.23. Found: C, 58.21; H, 5.22; N, 5.36%.

Procedure 4J-1: Decarboxylation: A magnetically stirred solution of the ester **88aa** (0.1 mmol) in methanol (3 mL) and 10% aq. NaOH (3 mL) was refluxed in an oil-bath for 5 h. Upon cooling the reaction mixture to room temperature, the mixture was diluted with dichloromethane (10 mL), washed with aqueous HCl solution (2 mL) and brine (2 mL). The separated organic layer was dried (Na_2SO_4), filtered and concentrated under reduced pressure. Pure product **88af** was obtained by column chromatography (basic alumina, mixture of hexane/ethyl acetate).

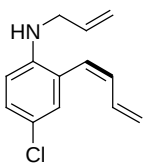


88af

2-Buta-1,3-dienyl-4-chloro-phenylamine (88af): Prepared following the procedure **4J-1** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3376 (N-*H*), 1617, 1484, 1143, 1046, 804 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.08 (1H, s, Ar-*H*), 7.05 (1H, dd, *J* = 8.4, 2.0 Hz), 6.63 (1H, d, *J* = 8.4 Hz), 6.61-6.55 (1H, m, olefinic-*H*), 6.37 (1H, t, *J* = 10.8 Hz, olefinic-*H*), 6.26 (1H, d, *J* = 11.2 Hz, olefinic-*H*), 5.40 (1H, dd, *J* = 16.8, 0.8 Hz, olefinic-*H*), 5.25 (1H, d, *J* = 10.0 Hz, olefinic-*H*), 3.69 (2H, s, N*H*$_2$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 142.6 (C), 133.1 (CH), 133.0 (CH), 129.6 (CH), 128.2 (CH), 125.4 (CH), 124.1 (C), 122.7 (C), 120.3 (CH_2), 116.4 (CH); LRMS m/z 180.00 (M + H^+), calcd $C_{10}H_{10}ClN$ 179.0502.

Procedure 4J-2: *N*-Monoallylation: The starting material aniline **88af** (1 mmol) was monoallylated by treatment with allyl bromide (1.1 mmol) and K_2CO_3 (1.2 mmol) in dry DMF (2 mL, 0.5 M) at RT for 24 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 *N*-monoallylated product **88afa** was obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

Allyl-(2-buta-1,3-dienyl-4-chloro-phenyl)-amine (88afa): Prepared following the procedure **4J-2** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3393 (N-*H*), 1515,

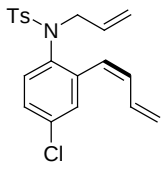


88afa

1444, 1219, 1059, 736 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.12 (1H, d, *J* = 8.8 Hz), 7.08 (1H, s, Ar-*H*), 6.65-6.58 (1H, m, olefinic-*H*), 6.54 (1H, d, *J* = 8.4 Hz), 6.38 (1H, t, *J* = 11.2 Hz, olefinic-*H*), 6.24 (1H, d, *J* = 10.8 Hz, olefinic-*H*), 5.97-5.88 (1H, m, olefinic-*H*), 5.39 (1H, d, *J* = 16.8 Hz, olefinic-*H*), 5.28-5.22 (2H, m, olefinic-*H*), 5.18 (1H, d, *J* = 10.4 Hz, olefinic-*H*), 3.85 (1H, s, N*H*), 3.78 (2H, d, *J* = 4.8 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 144.0 (C), 134.8 (CH), 133.5 (CH), 133.1 (CH), 129.5 (CH), 128.2 (CH), 125.3 (CH), 124.0 (C), 121.3 (C), 120.2 (CH_2), 116.4 (CH_2), 111.5 (CH), 46.4 (CH_2); LRMS m/z 220.00 ($M + H^+$), calcd $C_{13}H_{14}ClN$ 219.0815.

Procedure 4J-3: *N*-Protection: The corresponding amines **88afa** (1 mmol) was protected by treatment with pyridine (6 mmol) and TsCl (2 mmol) in dry CH_2Cl_2 (10 mL, 0.1 M), the reaction mixture was stirred at RT for 24 h. The reaction mixture was quenched with water and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with dilute HCl (2 mL) and brine, dried over (Na_2SO_4), filtered and concentrated. Pure product **88aba** was obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

***N*-Allyl-*N*-(2-buta-1,3-dienyl-4-chloro-phenyl)-4-methyl-benzenesulfonamide**

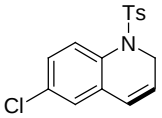


88aba

(88aba): Prepared following the procedure **4J-3** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 1482, 1350, 1163, 848, 738 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.60 (2H, d, *J* = 8.0 Hz), 7.33 (1H, d, *J* = 2.0 Hz), 7.29 (2H, d, *J* = 8.0 Hz), 7.14 (1H, dd, *J* = 8.4, 2.4 Hz), 6.74 (1H, d, *J* = 8.4 Hz), 6.62-6.51 (1H, m, olefinic-*H*), 6.41 (1H, d, *J* = 11.6 Hz), 6.27 (1H, t, *J* = 11.2 Hz, olefinic-*H*), 5.71-5.61 (1H, m, olefinic-*H*), 5.39 (1H, d, *J* = 16.8 Hz, olefinic-*H*), 5.25 (1H, d, *J* = 10.0 Hz, olefinic-*H*), 4.98 (1H, d, *J* = 10.0 Hz, olefinic-*H*), 4.92 (1H, d, *J* = 16.8 Hz, olefinic-*H*), 4.07 (2H, br s, NC*H*$_2$), 2.44 (3H, s, Ar-CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 143.7 (C), 140.2 (C), 136.3 (C), 135.9 (C), 133.8 (C), 132.8 (CH), 132.4 (CH), 132.3 (2 x CH), 130.8 (2 x CH), 129.6 (CH), 127.8 (CH), 127.7 (2 x CH), 126.5 (CH), 121.0 (CH_2), 119.5 (CH_2), 54.4 (CH_2), 21.6 (CH_3, Ar-*C*H_3); LRMS m/z 372.25 ($M - H^+$), calcd $C_{20}H_{20}ClNO_2S$ 373.0903.

Procedure 4J-4: RCM Reaction: A 10 mL oven-dried round bottom flask equipped with a stir bar was charged with diene amine **88aba** (0.1 mmol), CH_2Cl_2 (5 mL, 0.02 M) and Grubbs' catalyst (10 mol%) as shown in Scheme 12. The reaction mixture was stirred under N_2 at room temperature for 24 h. Solvent CH_2Cl_2 was distilled off at ambient pressure and the RCM products **97aba** was purified by column chromatography (silica gel, mixture of hexane/ethyl acetate).

6-Chloro-1-(toluene-4-sulfonyl)-1,2-dihydro-quinoline (97aba): Prepared following the procedure **4J-4** and purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 1595, 1480, 1164, 1037, 813, 736 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.65 (1H, d, *J* = 8.4 Hz), 7.31 (2H, d, *J* = 8.4 Hz), 7.24 (1H, dd, *J* = 8.4, 2.0 Hz), 7.11 (2H, d, *J* = 8.0 Hz), 6.93 (1H, d, *J* = 2.0 Hz), 5.97 (1H, d, *J* = 10.0 Hz), 6.50-6.26 (1H, m, olefinic-*H*), 4.44 (2H, d, *J* = 3.2 Hz), 2.36 (3H, s, Ar-CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 143.7 (C), 136.0 (C), 133.4 (C), 132.1 (C), 130.8 (CH), 129.2 (2 x CH), 128.2 (CH), 127.8 (CH), 127.2 (2 x CH), 126.1 (CH), 125.4 (CH), 124.9 (CH), 45.3 (CH_2), 21.5 (CH_3, Ar-*C*H_3); LRMS m/z 319.15 ($M + H^+$), calcd $C_{16}H_{14}ClNO_2S$ 318.0434.



97aba

5A.General Experimental Procedures for the Synthesis of Highly Functionalized 5,6-Dihyro-2*H*-benzo[*b*][1,4]oxazocines: The syntheses of highly functionalized 5,6-dihyro-2*H*-benzo[*b*][1,4]oxazocines from corresponding Hagemann's esters involves the following three-steps.

Piperidine/K_2CO_3-Catalyzed Three-Component Enamine Amination/Iso-Aromatization/*O*-Allylation Reactions in One-Pot: In an ordinary glass vial equipped with a magnetic stirring bar, to 1.0 mmol of the Hagemann's esters **44** were added 2.0 mL of solvent, and then the catalyst piperidine **4j** (0.05 mmol, 4.95 μL) and the reaction mixture was stirred at RT for the 0.5 h; then 0.5 mmol of nitrosobenzene **46** was added in one-portion and the reaction mixture was stirred at RT for 1 h. To the reaction mixture, allyl bromide **57a** (181.5 mg, 1.5 mmol) and K_2CO_3 (345.5 mg, 2.5 mmol) was added and stirring continued at RT for 24 h. The crude reaction mixture was worked up with aqueous NH_4Cl solution and the aqueous layer was extracted with

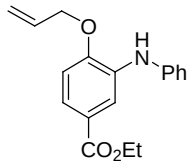
CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure one-pot products **69** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

***N*-Allylation**: At 0 °C, to a suspension of sodium hydride (14.4 mg, 0.6 mmol, 3.0 equiv.), in DMF (2 mL, 0.1 M) were added monoene amine **69** (0.2 mmol). After stirring for 0.16 h, allyl bromide **57a** (48.39 mg, 0.4 mmol, 2.0 equiv.) was added to the reaction mixture at 0 °C, and then the reaction mixture was stirred for 3 to 5 h from 0 °C to RT. The reaction mixture poured into saturated NH_4Cl solution and extracted with CH_2Cl_2 (2 x 15 mL). The combined CH_2Cl_2 extracts were washed with brine, dried over Na_2SO_4, and evaporated to dryness. Purification of residue by column chromatography (silica gel, mixture of hexane/ethyl acetate) gave **99**.

RCM Reaction: A 10 mL oven-dried round bottom flask equipped with a stir bar was charged with diene amine **99** (0.1 mmol), CH_2Cl_2 (2 mL, 0.05 M) and first generation Grubbs' catalyst **4n** (4.11 mg, 0.005 mmol, 5 mol%). The reaction mixture was stirred under N_2 at room temperature for 8 to 12 h. Solvent CH_2Cl_2 was distilled off at ambient pressure and the RCM products **100** were purified by column chromatography (silica gel, mixture of hexane/ethyl acetate).

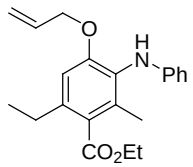
5B.Experimental Procedure for the Cascade Synthesis of Functionalized Heterocycles 102, 103 and 104 via RCM/Diels-Alder Reactions: A 10 mL oven-dried round bottom flask equipped with a stir bar was charged with enyne amine **99'a**, **99'h** or **71'h** (0.1 mmol), CH_2Cl_2 (2 mL, 0.05 M) and first generation Grubbs' catalyst **4n** (4.11 mg, 0.005 mmol, 5 mol%). The reaction mixture was stirred under N_2 at room temperature for 8 to 12 h. Solvent CH_2Cl_2 was distilled off at ambient pressure and to the crude reaction mixture, *N*-phenylmaleimide (207.8 mg, 0.12 mmol, 1.2 equiv.) or diethyl acetylenedicarboxylate (0.12 mmol, 1.2 equiv.) and anhydrous toluene (0.6 ml) were added and heated at 110-120 °C under N_2 in a sealed glass tube for 21 h. The toluene was removed and the residue was purified by column chromatography (silica gel, mixture of hexane/ethyl acetate) to gave **102, 103** and **104** respectively (see Scheme 16).

4-Allyloxy-3-phenylamino-benzoic acid ethyl ester (69h): Purified by column chromatography using EtOAc/hexane and isolated as light yellow liquid. IR (neat): ν_{max} 3387 (N-*H)*, 1701 (O-C=O), 1673, 1592, 1247, 1020, 761, 664 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.97 (1H, d, *J* = 2.0 Hz), 7.56 (1H, dd, *J* = 8.4 Hz, 2.0 Hz), 7.32 (2H, t, *J* = 7.2 Hz), 7.19 (2H, d, *J* = 7.6 Hz), 6.99 (1H, t, *J* = 7.2 Hz), 6.88 (1H, d, *J* = 8.4 Hz), 6.20 (1H, s, N-*H*), 6.12-6.04 (1H, m, olefinic-*H*), 5.43 (1H, dd, *J* = 17.2 Hz, 1.2 Hz, olefinic-*H*), 5.34 (1H, dd, *J* = 10.8 Hz, 1.2 Hz, olefinic-*H*), 4.67 (2H, d, *J* = 4.8 Hz, OC*H*$_2$CH=CH$_2$), 4.32 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 1.36 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.6 (C, O-C=O), 150.5 (C), 142.0 (C), 133.1 (C), 132.5 (CH), 129.4 (2 x CH), 123.3 (C), 121.9 (CH), 121.8 (CH), 119.0 (2 x CH), 118.4 (CH$_2$, CH=*CH*$_2$), 115.0 (CH), 110.8 (CH), 69.5 (CH$_2$, O*CH*$_2$CH=CH$_2$), 60.6 (CH$_2$, O*CH*$_2$CH$_3$), 14.4 (CH$_3$, OCH$_2$C*H*$_3$); LRMS m/z 298.05 ($M+H^+$), calcd for $C_{18}H_{19}NO_3$ 297.1365.



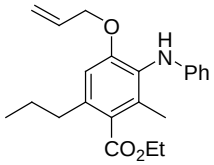
69h

4-Allyloxy-6-ethyl-2-methyl-3-phenylamino-benzoic acid ethyl ester (**69i**): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 3372 (N-*H)*, 2971, 1719 (O-C=O), 1600, 1497, 1281, 1176, 1054, 748 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.16 (2H, t, *J* = 7.6 Hz), 6.78 (1H, t, *J* = 7.2 Hz), 6.65 (1H, s, Ar-*H*), 6.62 (2H, d, *J* = 8.4 Hz), 5.95-5.88 (1H, m, olefinic-*H*), 5.63 (1H, s, N-*H*), 5.26 (1H, dd, *J* = 17.2 Hz, 1.6 Hz, olefinic-*H*), 5.19 (1H, dd, *J* = 10.4 Hz, 1.2 Hz, olefinic-*H*), 4.51 (2H, d, *J* = 5.2 Hz, OC*H*$_2$CH=CH$_2$), 4.38 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 2.62 (2H, q, *J* = 7.2 Hz, ArC*H*$_2$CH$_3$), 2.13 (3H, s, Ar-C*H*$_3$), 1.38 (3H, t, *J* = 7.2 Hz, ArCH$_2$C*H*$_3$), 1.23 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 170.0 (C, O-C=O), 153.6 (C), 146.2 (C), 138.3 (C), 132.9 (CH), 132.5 (C), 129.0 (2 x CH), 127.8 (C), 127.6 (C), 119.1 (CH), 117.5 (CH$_2$, CH=*CH*$_2$), 115.0 (2 x CH), 110.5 (CH), 69.2 (CH$_2$, O*CH*$_2$CH=CH$_2$), 61.0 (CH$_2$, O*CH*$_2$CH$_3$), 27.0 (CH$_2$, Ar*C*H$_2$CH$_3$), 15.7 (CH$_3$, Ar-*CH*$_3$), 15.6 (CH$_3$, ArCH$_2$*C*H$_3$), 14.3 (CH$_3$, OCH$_2$*CH*$_3$); LRMS m/z 339.45 (M^+), calcd $C_{21}H_{25}NO_3$ 339.1834.



69i

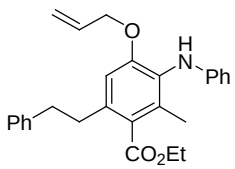
4-Allyloxy-2-methyl-3-phenylamino-6-propyl-benzoic acid ethyl ester (69j):



69j

Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 3373 (N-*H)*, 2966, 1721 (O-C=O), 1600, 1496, 1464, 1266, 1096, 949, 748 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.18 (2H, t, *J* = 7.6 Hz), 6.80 (1H, t, *J* = 7.2 Hz), 6.64 (1H, s, Ar-*H*), 6.63 (2H, d, *J* = 9.2 Hz), 5.97-5.90 (1H, m, olefinic-*H*), 5.59 (1H, s, N-*H*), 5.27 (1H, d, *J* = 17.6 Hz, olefinic-*H*), 5.21 (1H, d, *J* = 10.8 Hz, olefinic-*H*), 4.51 (2H, d, *J* = 5.2 Hz, O*C*H_2CH=CH_2), 4.40 (2H, q, *J* = 6.8 Hz, O*C*$H_2$$CH_3$), 2.58 (2H, t, *J* = 7.2 Hz, Ar*C*$H_2$$CH_2$$CH_3$), 2.15 (3H, s, Ar-C$H_3$), 1.68-1.63 (2H, m, Ar$CH_2$*C*$H_2$$CH_3$), 1.40 (3H, t, *J* = 7.2 Hz, OCH_2*C*H_3), 0.98 (3H, t, *J* = 7.2 Hz, Ar$CH_2$$CH_2$*C*$H_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.9 (C, O-C=O), 153.4 (C), 146.1 (C), 136.8 (C), 132.8 (CH), 132.4 (C), 128.9 (2 x CH), 128.6 (C), 127.8 (C), 119.0 (CH), 117.4 (CH_2, CH=*C*H_2), 114.9 (2 x CH), 111.1 (CH), 69.2 (CH_2, O*C*H_2CH=CH_2), 60.9 (CH_2, O*C*$H_2$$CH_3$), 36.0 ($CH_2$, Ar*C*$H_2$$CH_2$$CH_3$), 24.6 ($CH_2$, Ar$CH_2$*C*$H_2$$CH_3$), 15.7 ($CH_3$, Ar-*C*$H_3$), 14.2 ($CH_3$, O$CH_2$*C*$H_3$), 14.0 ($CH_3$, Ar$CH_2$$CH_2$*C*$H_3$); LRMS m/z 354.00 ($M+H^+$), calcd $C_{22}H_{27}NO_3$ 353.1991.

4-Allyloxy-2-methyl-6-phenethyl-3-phenylamino-benzoic acid ethyl ester (69k):

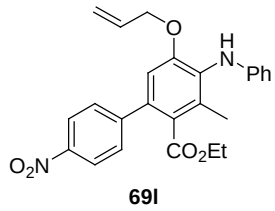


69k

Purified by column chromatography using EtOAc/hexane and isolated as light yellow oil. IR (neat): ν_{max} 3360 (N-*H)*, 2933, 1708 (O-C=O), 1597, 1493, 1263, 1053, 747, 698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.29 (2H, t, *J* = 7.2 Hz), 7.22-7.16 (5H, m, Ph-*H*), 6.81 (1H, t, *J* = 7.2 Hz), 6.63 (2H, d, *J* = 7.6 Hz), 6.51 (1H, s, Ar-*H*), 5.90-5.85 (1H, m, olefinic-*H*), 5.59 (1H, s, N-*H*), 5.24 (1H, d, *J* = 17.2 Hz, olefinic-*H*), 5.19 (1H, d, *J* = 10.8 Hz, olefinic-*H*), 4.40 (2H, d, *J* = 7.2 Hz, O*C*H_2CH=CH_2), 4.40 (2H, q, *J* = 7.2 Hz, O*C*$H_2$$CH_3$), 2.94-2.88 (4H, m), 2.16 (3H, s, Ar-CH_3), 1.40 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.3 (C, O-C=O), 153.3 (C), 146.1 (C), 141.6 (C), 135.8 (C), 132.8 (CH), 132.6 (C), 128.9 (2 x CH), 128.5 (2 x CH), 128.4 (2 x CH), 128.3 (C), 128.1 (C), 126.0 (CH), 119.2 (CH), 117.5 (CH_2, CH=*C*H_2), 115.1 (2 x CH), 111.4 (CH), 69.2 (CH_2, O*C*H_2CH=CH_2), 61.0 (CH_2, O*C*$H_2$$CH_3$), 37.8 ($CH_2$),

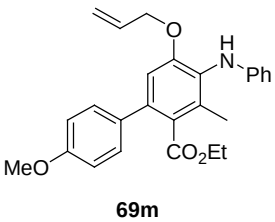
36.2 (CH_2), 15.7 (CH_3, Ar-*CH_3*), 14.3 (CH_3, OCH_2*CH_3*); LRMS m/z 416.45 ($M+H^+$), calcd for $C_{27}H_{29}NO_3$ 415.2147.

5-Allyloxy-3-methyl-4'-nitro-4-phenylamino-biphenyl-2-carboxylic acid ethyl ester (69l): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 3387 (N-*H*), 2976, 1727 (O-C=O), 1598, 1515, 1473, 1258, 1056, 743, 702 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.26 (2H, d, *J* = 8.8 Hz), 7.57 (2H, d, *J* = 8.8 Hz), 7.23 (2H, t, *J* = 7.6 Hz), 6.88 (1H, t, *J* = 7.2 Hz), 6.79 (1H, s, Ar-*H*), 6.73 (2H, d, *J* = 8.4 Hz), 6.02-5.92 (1H, m, olefinic-*H*), 5.88 (1H, s, N-*H*), 5.31 (1H, d, *J* = 17.6 Hz, olefinic-*H*), 5.26 (1H, d, *J* = 10.8 Hz, olefinic-*H*), 4.59 (2H, d, *J* = 5.2 Hz, OC*H*$_2$CH=CH_2), 4.09 (2H, q, *J* = 7.2 Hz, OC*H*$_2$$CH_3$), 2.22 (3H, s, Ar-C*H*$_3$), 1.03 (3H, t, *J* = 7.2 Hz, OCH_2C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.1 (C, O-C=O), 153.0 (C), 148.0 (C), 147.0 (C), 145.2 (C), 134.4 (C), 132.8 (C), 132.4 (CH), 130.8 (C), 129.2 (2 x CH), 129.1 (2 x CH), 127.4 (C), 123.5 (2 x CH), 120.0 (CH), 118.0 (CH_2, CH=*CH_2*), 115.8 (2 x CH), 111.2 (CH), 69.5 (CH_2, OC*H*$_2$CH=CH_2), 61.2 (CH_2, OC*H*$_2$$CH_3$), 16.2 ($CH_3$, Ar-*$CH_3$*), 13.8 ($CH_3$, OCH_2C*H*$_3$); LCMS m/z 433.35 ($M+H^+$), calcd for $C_{25}H_{24}N_2O_5$ 432.1685.



69l

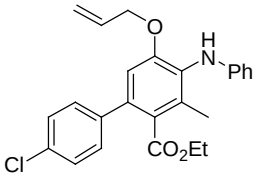
5-Allyloxy-4'-methoxy-3-methyl-4-phenylamino-biphenyl-2-carboxylic acid ethyl ester (69m): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 3054, 1724 (O-C=O), 1608, 1580, 1498, 1263, 1057, 737, 704 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (2H, d, *J* = 8.8 Hz), 7.22 (2H, t, *J* = 7.6 Hz), 6.95 (2H, d, *J* = 8.4 Hz), 6.84 (1H, t, *J* = 7.2 Hz), 6.78 (1H, s, Ar-*H*), 6.71 (2H, d, *J* = 8.4 Hz), 5.98-5.91 (1H, m, olefinic-*H*), 5.74 (1H, s, N-*H*), 5.29 (1H, dd, *J* = 17.2 Hz, 1.6 Hz, olefinic-*H*), 5.23 (1H, dd, *J* = 10.8 Hz, 1.6 Hz, olefinic-*H*), 4.55 (2H, d, *J* = 4.8 Hz, OC*H*$_2$CH=CH_2), 4.12 (2H, q, *J* = 7.2 Hz, OC*H*$_2$$CH_3$), 3.85 ($CH_3$, s, OC*H*$_3$), 2.05 (3H, s, Ar-C*H*$_3$), 1.04 (3H, t, *J* = 7.2 Hz, OCH_2C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.8 (C, O-C=O), 159.0 (C), 153.0 (C), 145.8 (C), 136.7 (C), 133.5 (C), 132.7 (CH), 132.6 (C), 129.4 (2 x CH), 128.9 (C), 128.9 (2 x CH), 127.4 (C), 119.4



69m

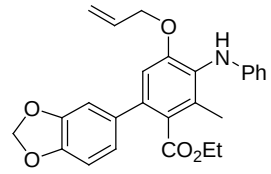
(CH), 117.6 (CH_2, CH=*CH_2*), 115.3 (2 x CH), 113.6 (2 x CH), 111.5 (CH), 69.2 (CH_2, O*CH_2*CH=CH_2), 60.8 (CH_2, O*CH_2*CH_3), 55.3 (CH_3, O*CH_3*), 15.7 (CH_3, Ar-*CH_3*), 13.8 (CH_3, OCH_2CH_3); LCMS m/z 417.80 ($M+H^+$), calcd for $C_{26}H_{27}NO_4$ 417.1940.

5-Allyloxy-4'-chloro-3-methyl-4-phenylamino-biphenyl-2-carboxylic acid ethyl ester (69n): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 3352 (N-*H)*, 2985, 1705 (O-C=O), 1601, 1494, 1277, 1059, 745 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38 (2H, d, *J* = 8.4 Hz), 7.34 (2H, d, *J* = 8.4 Hz), 7.22 (2H, t, *J* = 7.6 Hz), 6.86 (1H, t, *J* = 7.2 Hz), 6.76 (1H, s, Ar-*H*), 6.72 (2H, d, *J* = 8.4 Hz), 5.99-5.92 (1H, m, olefinic-*H*), 5.78 (1H, s, N-*H*), 5.29 (1H, d, *J* = 17.6 Hz, olefinic-*H*), 5.24 (1H, d, *J* = 10.4 Hz, olefinic-*H*), 4.56 (2H, d, *J* = 5.2 Hz, OC*H_2*CH=CH_2), 4.09 (2H, q, *J* = 7.2 Hz, OC*H_2*CH_3), 2.22 (3H, s, Ar-C*H_3*), 1.03 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.4 (C, O-C=O), 153.0 (C), 145.5 (C), 139.6 (C), 135.6 (C), 133.4 (C), 132.7 (C), 132.6 (CH), 129.7 (C), 129.6 (2 x CH), 129.0 (2 x CH), 128.4 (2 x CH), 127.4 (C), 119.6 (CH), 117.8 (CH_2, CH=*CH_2*), 115.5 (2 x CH), 111.3 (CH), 69.3 (CH_2, O*CH_2*CH=CH_2), 61.0 (CH_2, O*CH_2*CH_3), 15.9 (CH_3, Ar-*CH_3*), 13.7 (CH_3, OCH_2CH_3); LCMS m/z 420.90 (M^+), calcd for $C_{25}H_{24}ClNO_3$ 421.1445.



69n

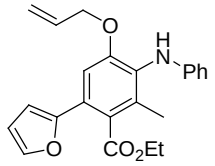
4-Allyloxy-6-benzo[1,3]dioxol-5-yl-2-methyl-3-phenylamino-benzoic acid ethyl ester (69o): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3316 (N-*H*), 2982, 1713 (O-C=O), 1599, 1494, 1236, 1039, 754, 661 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.21 (2H, t, *J* = 7.6 Hz), 6.90 (1H, d, *J* = 1.2 Hz), 6.86 (3H, m), 6.75 (1H, s), 6.70 (2H, d, *J* = 7.6 Hz), 5.99 (2H, s, OC*H_2*O), 5.98-5.91 (1H, m, olefinic-*H*), 5.74 (1H, s, N-*H*), 5.28 (1H, dd, *J* = 16.8 Hz, 1.2 Hz, olefinic-*H*), 5.22 (1H, dd, *J* = 10.4 Hz, 1.2 Hz, olefinic-*H*), 4.55 (2H, d, *J* = 5.2 Hz, OC*H_2*CH=CH_2), 4.13 (2H, q, *J* = 7.2 Hz, OC*H_2*CH_3), 2.19 (3H, s, Ar-C*H_3*), 1.09 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.7 (C, O-C=O), 152.9 (C), 147.5 (C) 146.9 (C), 145.7 (C), 136.5 (C), 135.0 (C), 132.6 (CH), 132.5 (C), 129.2



69o

(C), 129.0 (2 x CH), 127.5 (C), 121.8 (CH), 119.5 (CH), 117.7 (CH_2, CH=*CH_2*), 115.4 (2 x CH), 111.4 (CH), 108.9 (CH), 108.1 (CH), 101.2 (CH_2, O*CH_2*O), 69.3 (CH_2, O*CH_2*CH=CH_2), 60.9 (CH_2, O*CH_2*CH_3), 15.8 (CH_3, Ar-*CH_3*), 13.9 (CH_3, OCH_2*CH_3*); LCMS m/z 430.50 ($M\text{-}H^+$), calcd for $C_{26}H_{25}NO_5$ 431.1733.

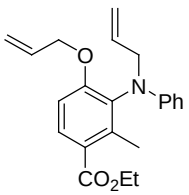
4-Allyloxy-6-furan-2-yl-2-methyl-3-phenylamino-benzoic acid ethyl ester (69p):



69p

Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 3387 (N-*H)*, 3054, 1723 (O-C=O), 1599, 1497, 1265, 1057, 737, 703 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.47 (1H, d, *J* = 1.6 Hz), 7.21 (2H, t, *J* = 7.6 Hz), 7.08 (1H, s, Ar-*H*), 6.85 (1H, t, *J* = 7.2 Hz), 6.69 (2H, d, *J* = 8.4 Hz), 6.52 (1H, d, *J* = 3.2 Hz), 6.47 (1H, dd, *J* = 3.2 Hz, 2.0 Hz), 6.02-5.92 (1H, m, olefinic-*H*), 5.79 (1H, s, N-*H*), 5.31 (1H, d, *J* = 17.6 Hz, olefinic-*H*), 5.24 (1H, d, *J* = 10.4 Hz, olefinic-*H*), 4.59 (2H, d, *J* = 4.8 Hz, OC*H_2*CH=CH_2), 4.35 (2H, q, *J* = 7.2 Hz, OC*H_2*CH_3), 2.16 (3H, s, Ar-C*H_3*), 1.30 (3H, t, *J* = 7.2 Hz, OCH_2C*H_3*); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.8 (C, O-C=O), 152.8 (C), 152.2 (C), 145.4 (C), 142.2 (CH), 132.6 (CH), 132.0 (C), 129.9 (C), 129.0 (2 x CH), 125.5 (C), 124.6 (C), 119.7 (CH), 117.8 (CH_2, CH=*CH_2*), 115.7 (2 x CH), 111.6 (CH), 108.3 (CH), 107.0 (CH), 69.4 (CH_2, O*CH_2*CH=CH_2), 61.3 (CH_2, O*CH_2*CH_3), 15.6 (CH_3, Ar-*CH_3*), 14.1 (CH_3, OCH_2C*H_3*); LCMS m/z 378.10 ($M+H^+$), calcd for $C_{23}H_{23}NO_4$ 377.1627.

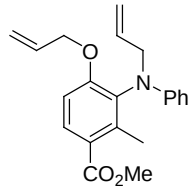
4-Allyloxy-3-(allyl-phenyl-amino)-2-methyl-benzoic acid ethyl ester (99a): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3084, 2980, 1714 (O-C=O), 1599, 1500, 1161, 1068, 748, 692 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.93 (1H, d, *J* = 8.8 Hz), 7.17 (2H, t, *J* = 7.6 Hz), 6.85 (1H, d, *J* = 8.8 Hz), 6.72 (1H, t, *J* = 7.2 Hz), 6.52 (2H, d, *J* = 8.0 Hz), 6.04-5.97 (1H, m, olefinic-*H*), 5.88-5.81 (1H, m, olefinic-*H*), 5.30-5.12 (4H, m, olefinic-*H*), 4.52 (2H, d, *J* = 4.8 Hz, OC*H_2*CH=CH_2), 4.38 (2H, q, *J* = 7.2 Hz, OC*H_2*CH_3), 4.18 (2H, dABq, *J* = 18.0, 5.6 Hz, NC*H_2*CH=CH_2), 2.45 (3H, s, Ar-C*H_3*), 1.42 (3H, t, *J* = 7.2 Hz, OCH_2C*H_3*); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.4 (C, O-C=O), 159.0 (C), 148.2 (C), 142.4 (C), 135.2



99a

(CH), 134.4 (C), 132.4 (CH), 130.7 (CH), 128.8 (2 x CH), 123.8 (C), 117.7 (CH_2, CH=*CH_2*), 116.8 (CH), 116.6 (CH_2, CH=*CH_2*), 112.4 (2 x CH), 110.0 (CH), 68.7 (CH_2, O*CH_2*CH=CH_2), 60.5 (CH_2, O*CH_2*CH_3), 54.4 (CH_2, N*CH_2*CH=CH_2), 15.9 (CH_3, Ar-*CH_3*), 14.3 (CH_3, OCH_2*CH_3*); GCMS m/z 351.25 (M^+), calcd for $C_{22}H_{25}NO_3$ 351.4388.

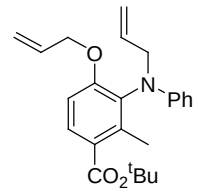
4-Allyloxy-3-(allyl-phenyl-amino)-2-methyl-benzoic acid methyl ester (99b):



99b

Purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 1718 (O-C=O), 1597, 1499, 1267, 1064, 749 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.87 (1H, d, *J* = 8.4 Hz), 7.13 (2H, t, *J* = 8.0 Hz), 6.81 (1H, d, *J* = 8.8 Hz), 6.68 (1H, t, *J* = 7.6 Hz), 6.48 (2H, d, *J* = 8.0 Hz), 6.00-5.94 (1H, m, olefinic-*H*), 5.86-5.78 (1H, m, olefinic-*H*), 5.26-5.08 (4H, m, olefinic-*H*), 4.49 (2H, d, *J* = 4.4 Hz, O*CH_2*CH=CH_2), 4.12 (2H, dABq, *J* = 17.2, 5.6 Hz, N*CH_2*CH=CH_2), 3.88 (CH_3, s, O*CH_3*), 2.44 (3H, s, Ar-C*H_3*); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.8 (C, O-C=O), 159.2 (C), 148.2 (C), 142.6 (C), 135.2 (CH), 134.4 (C), 132.4 (CH), 130.9 (CH), 128.8 (2 x CH), 123.4 (C), 117.7 (CH_2, CH=*CH_2*), 116.8 (CH), 116.6 (CH_2, CH=*CH_2*), 112.3 (2 x CH), 110.0 (CH), 68.7 (CH_2, O*CH_2*CH=CH_2), 54.4 (CH_2, N*CH_2*CH=CH_2), 51.7 (CH_3, O*CH_3*), 15.9 (CH_3, Ar-*CH_3*); LCMS m/z 337.35 (M^+), calcd for $C_{21}H_{23}NO_3$ 337.1678.

4-Allyloxy-3-(allyl-phenyl-amino)-2-methyl-benzoic acid *tert*-butyl ester (99c):

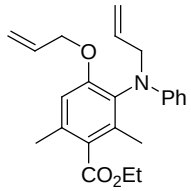


99c

Purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 2977, 1709 (O-C=O), 1595, 1500, 1248, 1066, 747 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.81 (1H, d, *J* = 8.4 Hz), 7.13 (2H, t, *J* = 7.6 Hz), 6.80 (1H, d, *J* = 8.8 Hz), 6.68 (1H, t, *J* = 7.2 Hz), 6.49 (2H, d, *J* = 8.4 Hz), 6.04-5.94 (1H, m, olefinic-*H*), 5.85-5.78 (1H, m, olefinic-*H*), 5.27-5.09 (4H, m, olefinic-*H*), 4.48 (2H, d, *J* = 4.8 Hz, O*CH_2*CH=CH_2), 4.15 (2H, dABq, *J* = 17.2, 5.6 Hz, N*CH_2*CH=CH_2), 2.41 (3H, s, Ar-C*H_3*), 1.60 (9H, s, $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.0 (C, O-C=O), 158.7 (C), 148.2 (C), 141.7 (C), 135.3 (CH), 134.4 (C), 132.5 (CH), 130.5 (CH), 128.8 (2 x CH), 125.6 (C), 117.1 (CH_2, CH=*CH_2*), 116.7 (CH), 116.5 (CH_2, CH=*CH_2*), 112.3 (2 x CH), 109.9

(CH), 80.8 (C, *C*(CH_3)$_3$), 68.7 (CH_2, O*C*H_2CH=CH_2), 54.5 (CH_2, N*C*H_2CH=CH_2), 28.3 (3 x CH_3, C(*C*H_3)$_3$), 16.0 (CH_3, Ar-*C*H_3); LCMS m/z 379.60 ($M+H^+$), calcd $C_{24}H_{29}NO_3$ 379.2147.

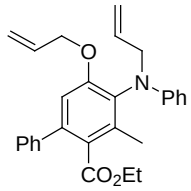
4-Allyloxy-3-(allyl-phenyl-amino)-2,6-dimethyl-benzoic acid ethyl ester (99d):



99d

Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 2976, 1722 (O-C=O), 1601, 1500, 1271, 1186, 748 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.15 (2H, t, *J* = 7.2 Hz), 6.69 (1H, t, *J* = 7.2 Hz), 6.66 (1H, s, Ar-*H*), 6.53 (2H, d, *J* = 8.4 Hz), 6.03-5.96 (1H, m, olefinic-*H*), 5.87-5.80 (1H, m, olefinic-*H*), 5.30-5.12 (4H, m, olefinic-*H*), 4.45 (2H, d, *J* = 4.4 Hz, OC*H*$_2$CH=CH_2), 4.41 (2H, q, *J* = 7.2 Hz, OC*H*$_2$$CH_3$), 4.20 (2H, dABq, *J* = 16.0, 5.2 Hz, NC*H*$_2$CH=CH_2), 2.37 (3H, s, Ar-C*H*$_3$), 2.17 (3H, s, Ar-C*H*$_3$), 1.41 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.8 (C, O-C=O), 156.5 (C), 148.3 (C), 136.8 (C), 135.5 (CH), 134.8 (C), 132.8 (CH), 131.8 (C), 128.8 (2 x CH), 127.8 (C), 116.9 (CH_2, CH=*CH*$_2$), 116.6 (CH), 116.4 (CH_2, CH=*CH*$_2$), 112.9 (CH), 112.4 (2 x CH), 68.8 (CH_2, O*C*H_2CH=CH_2), 60.9 (CH_2, O*C*$H_2$$CH_3$), 54.6 ($CH_2$, N*C*$H_2$CH=$CH_2$), 20.2 ($CH_3$, Ar-*C*$H_3$), 15.5 ($CH_3$, Ar-*C*$H_3$), 14.3 ($CH_3$, OCH$_2$*C*$H_3$); GCMS m/z 365.15 ($M^+$), calcd $C_{23}H_{27}NO_3$ 365.4654.

5-Allyloxy-4-(allyl-phenyl-amino)-3-methyl-biphenyl-2-carboxylic acid ethyl ester (99e):

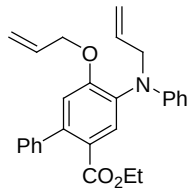


99e

Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 3061, 2924, 1724 (O-C=O), 1599, 1500, 1093, 748, 702 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.43-7.28 (5H, m, Ph-*H*), 7.19 (2H, t, *J* = 7.6 Hz), 6.83 (1H, s, Ar-*H*), 6.74 (1H, t, *J* = 7.2 Hz), 6.60 (2H, d, *J* = 7.6 Hz), 6.08-6.00 (1H, m, olefinic-*H*), 5.88-5.81 (1H, m, olefinic-*H*), 5.38-5.14 (4H, m, olefinic-*H*), 4.50 (2H, br s, OC*H*$_2$CH=CH_2), 4.26 (2H, dABq, *J* = 16.0, 5.2 Hz, NC*H*$_2$CH=CH_2), 4.08 (2H, q, *J* = 7.2 Hz, OC*H*$_2$$CH_3$), 2.27 (3H, s, Ar-C*H*$_3$), 0.97 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.5 (C, O-C=O), 156.4 (C), 148.1 (C), 141.0 (C), 139.9 (C), 137.5 (C), 135.4 (CH), 133.3 (C), 132.6 (CH), 128.9 (2 x CH), 128.24 (2 x CH), 128.2 (2 x CH), 127.4 (CH), 127.2 (C), 117.1 (CH_2, CH=*CH*$_2$), 116.8 (CH), 116.5

(CH_2, CH=*CH_2*), 112.5 (CH), 112.4 (2 x CH), 68.9 (CH_2, O*CH_2*CH=CH_2), 60.9 (CH_2, O*CH_2*CH_3), 54.6 (CH_2, N*CH_2*CH=CH_2), 15.5 (CH_3, Ar-*CH_3*), 13.6 (CH_3, OCH_2*CH_3*); GCMS m/z 427.20 (M^+), calcd $C_{28}H_{29}NO_3$ 427.5348.

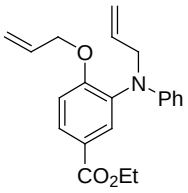
5-Allyloxy-4-(allyl-phenyl-amino)-biphenyl-2-carboxylic acid ethyl ester (99f):



99f

Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 3061, 3026, 2982, 1714 (O-C=O), 1645, 1599, 1554, 1107, 1022, 746, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.85 (1H, s, Ar-*H*), 7.46-7.36 (5H, m, Ph-*H*), 7.19 (2H, t, *J* = 7.2 Hz), 6.91 (1H, s, Ar-*H*), 6.77 (1H, t, *J* = 7.2 Hz), 6.73 (2H, d, *J* = 8.4 Hz), 6.04-5.97 (1H, m, olefinic-*H*), 5.89-5.81 (1H, m, olefinic-*H*), 5.39 (1H, br d, *J* = 17.2 Hz, olefinic-*H*), 5.20 (1H, br d, *J* = 10.4 Hz, olefinic-*H*), 5.17-5.15 (2H, m), 4.56 (2H, br d, *J* = 4.8 Hz, O*CH_2*CH=CH_2), 4.35 (2H, br d, *J* = 4.8 Hz, N*CH_2*CH=CH_2), 4.09 (2H, q, *J* = 7.2 Hz, O*CH_2*CH_3), 1.02 (3H, t, *J* = 7.2 Hz, OCH_2*CH_3*); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.6 (C, O-C=O), 156.8 (C), 148.3 (C), 142.2 (C), 141.6 (C), 134.8 (CH), 134.5 (C), 132.3 (CH), 131.9 (CH), 128.7 (2 x CH), 128.4 (2 x CH), 127.9 (2 x CH), 127.2 (CH), 123.7 (C), 117.8 (CH), 117.4 (CH_2, CH=*CH_2*), 116.3 (CH_2, CH=*CH_2*), 116.0 (CH), 114.3 (2 x CH), 69.0 (CH_2, O*CH_2*CH=CH_2), 60.7 (CH_2, O*CH_2*CH_3), 54.5 (CH_2, N*CH_2*CH=CH_2), 13.7 (CH_3, OCH_2*CH_3*); GCMS m/z 413.10 (M^+), calcd $C_{27}H_{27}NO_3$ 413.5082.

4-Allyloxy-3-(allyl-phenyl-amino)-benzoic acid ethyl ester (99h): Purified by column

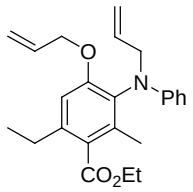


99h

chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 2980, 1711 (O-C=O), 1599, 1539, 1499, 1237, 1021, 747, 693 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.97-7.93 (2H, m), 7.15 (2H, t, *J* = 7.6 Hz), 6.99 (1H, d, *J* = 8.8 Hz), 6.74 (1H, t, *J* = 7.2 Hz), 6.64 (2H, d, *J* = 8.0 Hz), 6.04-5.98 (1H, m, olefinic-*H*), 5.90-5.80 (1H, m, olefinic-*H*), 5.35-5.14 (4H, m, olefinic-*H*), 4.56 (2H, br d, *J* = 4.8 Hz, O*CH_2*CH=CH_2), 4.35 (2H, q, *J* = 7.2 Hz, O*CH_2*CH_3), 4.31 (2H, br d, *J* = 12 Hz, N*CH_2*CH=CH_2), 1.38 (3H, t, *J* = 7.2 Hz, OCH_2*CH_3*); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.1 (C, O-C=O), 158.8 (C), 148.4 (C), 135.3 (C), 134.74 (CH), 132.3 (CH), 131.7 (CH), 128.9 (CH),

128.7 (2 x CH), 123.8 (C), 117.6 (CH), 117.4 (CH_2, CH=CH_2), 116.3 (CH_2, CH=CH_2), 113.9 (2 x CH), 113.6 (CH), 68.9 (CH_2, OCH_2CH=CH_2), 60.8 (CH_2, O$CH_2$$CH_3$), 54.4 ($CH_2$, N$CH_2$CH=$CH_2$), 14.4 ($CH_3$, OCH$_2$$CH_3$); LCMS m/z 338.00 ($M+H^+$), calcd $C_{21}H_{23}NO_3$ 337.1678.

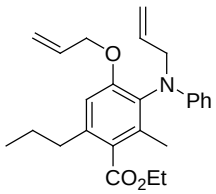
4-Allyloxy-3-(allyl-phenyl-amino)-6-ethyl-2-methyl-benzoic acid ethyl ester (99i):



99i

Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 2975, 1720 (O-C=O), 1598, 1500, 1424, 1240, 1040, 743, 693 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.13 (2H, t, *J* = 8.0 Hz), 6.68 (1H, t, *J* = 8.0 Hz), 6.67 (1H, s, Ar-*H*), 6.51 (2H, d, *J* = 8.4 Hz), 6.02-5.95 (1H, m, olefinic-*H*), 5.85-5.78 (1H, m, olefinic-*H*), 5.28-5.11 (4H, m, olefinic-*H*), 4.45 (2H, d, *J* = 4.0 Hz, OCH_2CH=CH_2), 4.39 (2H, q, *J* = 7.2 Hz, O$CH_2$$CH_3$), 4.18 (2H, dABq, *J* = 16.4, 5.2 Hz, NCH_2CH=CH_2), 2.65 (2H, q, *J* = 7.6 Hz, Ar$CH_2$$CH_3$), 2.14 (3H, s, Ar-C$H_3$), 1.39 (3H, t, *J* = 7.2 Hz, OCH$_2$CH_3), 1.26 (3H, t, *J* = 7.2 Hz, ArCH$_2$CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.9 (C, O-C=O), 156.6 (C), 148.3 (C), 140.8 (C), 136.5 (C), 135.5 (CH), 132.8 (CH), 131.9 (C), 128.8 (2 x CH), 127.4 (C), 116.9 (CH_2, CH=CH_2), 116.6 (CH), 116.3 (CH_2, CH=CH_2), 112.4 (2 x CH), 111.4 (CH), 68.8 (CH_2, OCH_2CH=CH_2), 61.0 (CH_2, O$CH_2$$CH_3$), 54.6 ($CH_2$, N$CH_2$CH=$CH_2$), 27.1 ($CH_2$, Ar$CH_2$$CH_3$), 15.6 ($CH_3$, Ar-$CH_3$), 15.4 ($CH_3$, ArCH$_2$$CH_3$), 14.2 ($CH_3$, OCH$_2$$CH_3$); LCMS m/z 379.60 ($M+H^+$), calcd $C_{24}H_{29}NO_3$ 379.2147.

4-Allyloxy-3-(allyl-phenyl-amino)-2-methyl-6-propyl-benzoic acid ethyl ester (99j):

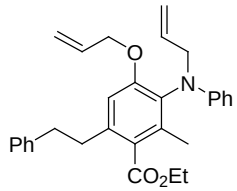


99j

Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 2964, 1722 (O-C=O), 1597, 1500, 1460, 1272, 1045, 747, 691 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.13 (2H, t, *J* = 7.2 Hz), 6.67 (1H, t, *J* = 7.6 Hz), 6.65 (1H, s, Ar-*H*), 6.50 (2H, d, *J* = 8.4 Hz), 6.01-5.95 (1H, m, olefinic-*H*), 5.85-5.78 (1H, m, olefinic-*H*), 5.29-5.10 (4H, m, olefinic-*H*), 4.44 (2H, d, *J* = 2.4 Hz, OCH_2CH=CH_2), 4.39 (2H, q, *J* = 7.2 Hz, O$CH_2$$CH_3$), 4.14 (2H, dABq, *J* = 16.4, 5.2 Hz, NCH_2CH=CH_2), 2.59 (2H, dt, *J* = 7.6, 3.2 Hz, Ar$CH_2$$CH_2$$CH_3$), 2.13 (3H, s, Ar-C$H_3$), 1.66 (2H, sextet, *J* =

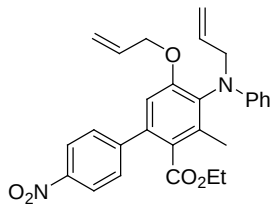
7.6 Hz, $ArCH_2CH_2CH_3$), 1.39 (3H, t, *J* = 7.2 Hz, OCH_2CH_3), 0.98 (3H, t, *J* = 7.2 Hz, $ArCH_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.9 (C, O-C=O), 156.4 (C), 148.3 (C), 139.4 (C), 136.5 (C), 135.6 (CH), 132.8 (CH), 131.9 (C), 128.8 (2 x CH), 127.7 (C), 116.9 (CH_2, CH=CH_2), 116.6 (CH), 116.3 (CH_2, CH=CH_2), 112.4 (2 x CH), 112.0 (CH), 68.8 (CH_2, $OCH_2CH=CH_2$), 60.9 (CH_2, OCH_2CH_3), 54.6 (CH_2, $NCH_2CH=CH_2$), 36.2 (CH_2, $ArCH_2CH_2CH_3$), 24.5 (CH_2, $ArCH_2CH_2CH_3$), 15.4 (CH_3, Ar-CH_3), 14.3 (CH_3, OCH_2CH_3), 14.1 (CH_3, $ArCH_2CH_2CH_3$); LCMS m/z 393.85 ($M+H^+$), calcd $C_{25}H_{31}NO_3$ 393.2304.

4-Allyloxy-3-(allyl-phenyl-amino)-2-methyl-6-phenethyl-benzoic acid ethyl ester (99k): Purified by column chromatography using EtOAc/hexane and isolated as a yellow oil. IR (neat): ν_{max} 2979, 1722 (O-C=O), 1597, 1497, 1454, 1268, 1047, 748, 696 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.30 (2H, t, *J* = 7.2 Hz), 7.22 (1H, t, *J* = 8.0 Hz), 7.19 (2H, d, *J* = 8.4 Hz), 7.14 (2H, t, *J* = 7.2 Hz), 6.86 (1H, t, *J* = 7.2 Hz), 6.52 (1H, s, Ar-*H*), 6.51 (2H, d, *J* = 8.4 Hz), 5.99-5.94 (1H, m, olefinic-*H*), 5.78-5.74 (1H, m, olefinic-*H*), 5.26 (1H, dd, *J* = 17.2, 1.2 Hz, olefinic-*H*), 5.16-5.08 (3H, m, olefinic-*H*), 4.40 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 4.34 (2H, dd, *J* = 3.2, 1.0 Hz, $OCH_2CH=CH_2$), 4.14 (2H, dABq, *J* = 18.0, 5.6 Hz, $NCH_2CH=CH_2$), 2.93-2.90 (4H, m, $PhCH_2CH_2Ar$), 2.16 (3H, s, Ar-CH_3), 1.39 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.8 (C, O-C=O), 156.5 (C), 148.3 (C), 141.5 (C), 138.4 (C), 136.8 (C), 135.5 (CH), 132.8 (CH), 132.2 (C), 128.8 (2 x CH), 128.5 (2 x CH), 128.4 (2 x CH), 127.7 (C), 126.0 (CH), 116.9 (CH_2, CH=CH_2), 116.7 (CH), 116.4 (CH_2, CH=CH_2), 112.46 (2 x CH), 112.4 (CH), 68.8 (CH_2, $OCH_2CH=CH_2$), 61.1 (CH_2, OCH_2CH_3), 54.5 (CH_2, $NCH_2CH=CH_2$), 37.7 (CH_2, $PhCH_2CH_2Ar$), 36.3 (CH_2, $PhCH_2CH_2Ar$), 15.5 (CH_3, Ar-CH_3), 14.3 (CH_3, OCH_2CH_3); LCMS m/z 454.00 ($M-H^+$), calcd $C_{30}H_{33}NO_3$ 455.2460.



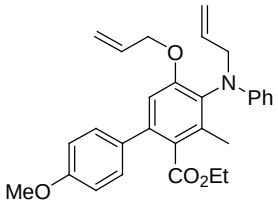
99k

5-Allyloxy-4-(allyl-phenyl-amino)-3-methyl-4'-nitro-biphenyl-2-carboxylic acid ethyl ester (99l): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 1722 (O-C=O), 1597, 1519, 1500, 1243, 1068 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.28 (2H, d, *J* = 8.4 Hz), 7.58 (2H, d, *J* = 8.8 Hz), 7.18 (2H, t, *J* = 7.6 Hz), 6.77 (1H, s, Ar-*H*), 6.73 (1H, t, *J* = 7.2 Hz), 6.57 (2H, d, *J* = 8.4 Hz), 6.04-5.98 (1H, m, olefinic-*H*), 5.86-5.79 (1H, m, olefinic-*H*), 5.30 (1H, dd, *J* = 17.2, 1.6 Hz, olefinic-*H*), 5.19 (1H, dd, *J* = 15.2, 1.2 Hz, olefinic-*H*), 5.16 (2H, dd, *J* = 10.4, 1.2 Hz, olefinic-*H*), 4.50 (2H, d, *J* = 4.8 Hz, OCH_2CH=CH_2), 4.20 (2H, dABq, *J* = 17.2, 5.6 Hz, NCH_2CH=CH_2), 4.08 (2H, q, *J* = 7.2 Hz, OC$H_2$$CH_3$), 2.25 (3H, s, Ar-C$H_3$), 1.02 (3H, t, *J* = 6.4 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.9 (C, O-C=O), 156.8 (C), 147.9 (C), 147.8 (C), 147.3 (C), 138.3 (C), 137.5 (C), 135.2 (CH), 134.5 (C), 132.3 (CH), 129.2 (2 x CH), 129.0 (2 x CH), 127.1 (C), 123.5 (2 x CH), 117.5 (CH_2, CH=CH_2), 117.2 (CH), 116.8 (CH_2, CH=CH_2), 112.7 (2 x CH), 112.3 (CH), 69.0 (CH_2, OCH_2CH=CH_2), 61.2 (CH_2, OC$H_2$$CH_3$), 54.5 ($CH_2$, NC$H_2$CH=$CH_2$), 15.6 ($CH_3$, Ar-C$H_3$), 13.8 ($CH_3$, OCH_2CH_3); LCMS m/z 471.00 ($M-H^+$), calcd $C_{28}H_{28}N_2O_5$ 472.1998.



99l

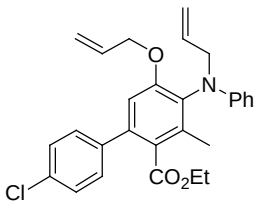
5-Allyloxy-4-(allyl-phenyl-amino)-4'-methoxy-3-methyl-biphenyl-2-carboxylic acid ethyl ester (99m): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2979, 1721 (O-C=O), 1600, 1500, 1246, 1037, 745 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.34 (2H, d, *J* = 8.4 Hz), 7.16 (2H, t, *J* = 7.6 Hz), 6.94 (2H, d, *J* = 8.4 Hz), 6.77 (1H, s, Ar-*H*), 6.70 (1H, t, *J* = 7.2 Hz), 6.57 (2H, d, *J* = 8.0 Hz), 6.02-6.00 (1H, m, olefinic-*H*), 5.82-5.80 (1H, m, olefinic-*H*), 5.29 (1H, d, *J* = 17.2 Hz, olefinic-*H*), 5.19-5.11 (3H, m, olefinic-*H*), 4.47 (2H, d, *J* = 4.8 Hz, OCH_2CH=CH_2), 4.18 (2H, dABq, *J* = 18.0, 5.2 Hz, NCH_2CH=CH_2), 4.08 (2H, q, *J* = 7.2 Hz, OC$H_2$$CH_3$), 3.84 ($CH_3$, s, OC$H_3$), 2.21 (3H, s, Ar-C$H_3$), 1.03 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.7 (C, O-C=O), 159.2 (C), 156.4 (C), 148.2 (C), 139.4 (C), 137.2 (C), 135.4 (CH), 133.4 (C), 133.0 (C), 132.6



99m

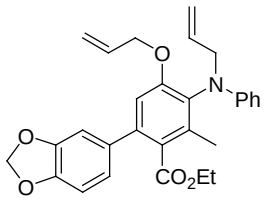
(CH), 129.3 (2 x CH), 128.8 (2 x CH), 127.3 (C), 117.1 (CH_2, CH=*CH_2*), 116.8 (CH), 116.5 (CH_2, CH=*CH_2*), 113.7 (2 x CH), 112.6 (CH), 112.5 (2 x CH), 68.8 (CH_2, O*CH_2*CH=CH_2), 60.9 (CH_2, O*CH_2*CH_3), 55.3 (CH_3, OCH_3), 54.6 (CH_2, N*CH_2*CH=CH_2), 15.4 (CH_3, Ar-*CH_3*), 13.8 (CH_3, OCH_2*CH_3*); LCMS m/z 457.0 (M^+), calcd $C_{29}H_{31}NO_4$ 457.2253.

5-Allyloxy-4-(allyl-phenyl-amino)-4'-chloro-3-methyl-biphenyl-2-carboxylic acid ethyl ester (99n): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 2980, 1722 (O-C=O), 1598, 1498, 1249, 1070, 741 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.39 (2H, d, *J* = 8.4 Hz), 7.35 (2H, d, *J* = 8.4 Hz), 7.17 (2H, t, *J* = 8.0 Hz), 6.75 (1H, s, Ar-*H*), 6.72 (1H, t, *J* = 7.6 Hz), 6.57 (2H, d, *J* = 8.4 Hz), 6.05-5.98 (1H, m, olefinic-*H*), 5.85-5.78 (1H, m, olefinic-*H*), 5.30 (1H, d, *J* = 17.2 Hz, olefinic-*H*), 5.18 (1H, d, *J* = 17.2 Hz, olefinic-*H*), 5.14 (2H, br d, *J* = 10.4 Hz, olefinic-*H*), 4.48 (2H, d, *J* = 4.4 Hz, OC*H_2*CH=CH_2), 4.22 (2H, dABq, *J* = 16.4, 5.6 Hz, NC*H_2*CH=CH_2), 4.08 (2H, q, *J* = 7.2 Hz, OC*H_2*CH_3), 2.24 (3H, s, Ar-C*H_3*), 1.03 (3H, t, *J* = 7.2 Hz, OCH_2C*H_3*); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.3 (C, O-C=O), 156.5 (C), 148.0 (C), 139.4 (C), 138.5 (C), 137.7 (C), 135.3 (CH), 133.64 (C), 133.61 (C), 132.5 (CH), 129.6 (2 x CH), 128.9 (2 x CH), 128.4 (2 x CH), 127.2 (C), 117.2 (CH_2, CH=*CH_2*), 116.9 (CH), 116.6 (CH_2, CH=*CH_2*), 112.4 (2 x CH), 112.4 (CH), 68.9 (CH_2, O*CH_2*CH=CH_2), 61.0 (CH_2, O*CH_2*CH_3), 54.5 (CH_2, N*CH_2*CH=CH_2), 15.4 (CH_3, Ar-*CH_3*), 13.7 (CH_3, OCH_2*CH_3*); LCMS m/z 461.10 (M^+), calcd $C_{28}H_{28}ClNO_3$ 461.1758.



99n

4-Allyloxy-3-(allyl-phenyl-amino)-6-benzo[1,3]dioxol-5-yl-2-methyl-benzoic acid ethyl ester (99o): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2981, 1721 (O-C=O), 1597, 1498, 1477, 1239, 1040, 744 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.15 (2H, t, *J* = 7.6 Hz), 6.90-6.82 (3H, m), 6.75 (1H, s, Ar-*H*), 6.69 (1H, t, *J* = 7.2 Hz), 6.55 (2H, d, *J* = 8.0 Hz), 6.04-5.97 (1H, m, olefinic-*H*), 5.99 (2H, s, OC*H_2*O), 5.84-5.77 (1H, m, olefinic-



99o

H), 5.30 (1H, dd, *J* = 17.2, 1.6 Hz, olefinic-*H*), 5.17 (1H, dd, *J* = 17.2, 1.2 Hz, olefinic-*H*), 5.12-5.11 (2H, m, olefinic-*H*), 4.46 (2H, d, *J* = 4.4 Hz, OCH_2CH=CH_2), 4.19 (2H, dABq, *J* = 17.2, 5.6 Hz, NCH_2CH=CH_2), 4.12 (2H, q, *J* = 7.2 Hz, OC$H_2$$CH_3$), 2.21 (3H, s, Ar-C$H_3$), 1.09 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.6 (C, O-C=O), 156.4 (C), 148.2 (C), 147.6 (C), 147.2 (C), 139.3 (C), 137.3 (C), 135.4 (CH), 134.9 (C), 133.2 (C), 132.6 (CH), 128.9 (2 x CH), 127.4 (C), 121.8 (CH), 117.2 (CH_2, CH=CH_2), 116.9 (CH), 116.5 (CH_2, CH=CH_2), 112.6 (2 x CH), 112.59 (CH), 108.9 (CH), 108.2 (CH), 101.2 (CH_2, OCH_2O), 68.9 (CH_2, OCH_2CH=CH_2), 61.0 (CH_2, O$CH_2$$CH_3$), 54.6 ($CH_2$, N$CH_2$CH=$CH_2$), 15.5 ($CH_3$, Ar-$CH_3$), 13.9 ($CH_3$, $OCH_2$$CH_3$); LCMS m/z 472.50 ($M+H^+$), calcd $C_{29}H_{29}NO_5$ 471.2046.

4-Allyloxy-3-(allyl-phenyl-amino)-6-furan-2-yl-2-methyl-benzoic acid ethyl ester (99p): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 2982, 1725 (O-C=O), 1597, 1498, 1468, 1267, 1069, 746 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.47 (1H, s, Ar-*H*), 7.14 (2H, t, *J* = 8.0 Hz), 7.07 (1H, s, Ar-*H*), 6.69 (1H, t, *J* = 7.6 Hz), 6.55-6.52 (3H, m), 6.47-6.46 (1H, m), 6.03-5.97 (1H, m, olefinic-*H*), 5.87-5.76 (1H, m, olefinic-*H*), 5.26 (1H, dd, *J* = 17.2, 1.2 Hz, olefinic-*H*), 5.19 (1H, d, *J* = 17.2 Hz, olefinic-*H*), 5.14 (1H, dd, *J* = 10.0, 1.2 Hz, olefinic-*H*), 5.12 (1H, dd, *J* = 10.0, 1.2 Hz, olefinic-*H*), 4.50 (2H, d, *J* = 3.2 Hz, OCH_2CH=CH_2), 4.34 (2H, q, *J* = 7.2 Hz, OC$H_2$$CH_3$), 4.16 (2H, dABq, *J* = 18.0, 5.6 Hz, NCH_2CH=CH_2), 2.17 (3H, s, Ar-CH_3), 1.29 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.7 (C, O-C=O), 156.5 (C), 151.2 (C) 148.0 (C), 142.5 (CH), 137.3 (C), 135.2 (CH), 133.6 (C), 132.5 (CH), 128.9 (2 x CH), 127.4 (C), 125.4 (C), 117.2 (CH_2, CH=CH_2), 116.9 (CH), 116.6 (CH_2, CH=CH_2), 112.6 (2 x CH), 111.7 (CH), 109.3 (CH), 107.7 (CH), 68.9 (CH_2, OCH_2CH=CH_2), 61.4 (CH_2, O$CH_2$$CH_3$), 54.4 ($CH_2$, N$CH_2$CH=$CH_2$), 15.2 ($CH_3$, Ar-$CH_3$), 14.1 ($CH_3$, $OCH_2$$CH_3$); LCMS m/z 418.00 ($M+H^+$), calcd $C_{26}H_{27}NO_4$ 417.1940.

99p

6-Allyl-5-allyloxy-4-(allyl-phenyl-amino)-4'-chloro-3-methyl-biphenyl-2-carboxylic

99q

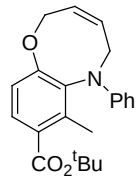
100a

acid ethyl ester (99q): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 2979, 1726 (O-C=O), 1598, 1497, 1442, 1206, 1122, 1090, 919 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.35-7.33 (2H, m), 7.24-7.19 (4H, m), 6.74 (1H, t, *J* = 7.2 Hz), 6.62 (2H, d, *J* = 8.0 Hz), 6.03-5.96 (1H, m, olefinic-*H*), 5.91-5.83 (1H, m, olefinic-*H*), 5.80-5.74 (1H, m, olefinic-*H*), 5.28 (1H, d, *J* = 17.2 Hz, olefinic-*H*), 5.20-5.10 (3H, m, olefinic-*H*), 4.90 (1H, dd, *J* = 8.4, 1.6 Hz, olefinic-*H*), 4.70 (1H, dd, *J* = 8.8, 1.6 Hz, olefinic-*H*), 4.32-4.19 (3H, m, OC*H*$_2$CH=CH$_2$, NC*H*$_2$CH=CH$_2$), 4.08-4.03 (1H, m, NC*H*$_2$CH=CH$_2$), 3.93 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.20 (2H, d, *J* = 5.6 Hz, ArC*H*$_2$CH=CH$_2$), 2.03 (3H, s, Ar-C*H*$_3$), 0.96 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.0 (C, O-C=O), 155.9 (C), 147.6 (C), 137.7 (C), 137.6 (C), 136.9 (C), 136.8 (CH), 134.9 (CH), 134.2 (C), 133.7 (CH), 133.5 (C), 132.2 (C), 131.2 (C), 131.1 (CH), 130.9 (CH), 129.3 (3 x CH), 127.9 (CH), 127.8 (CH), 117.2 (CH), 117.2 (CH_2, CH=*CH*$_2$), 117.1 (CH_2, CH=*CH*$_2$), 115.2 (CH_2, CH=*CH*$_2$), 112.6 (CH), 74.1 (CH_2, O*CH*$_2$CH=*CH*$_2$), 60.9 (CH_2, O*CH*$_2$CH$_3$), 54.5 (CH_2, N*CH*$_2$CH=*CH*$_2$), 32.0 (CH_2, Ar*CH*$_2$CH=CH$_2$), 15.7 (CH_3, Ar-*CH*$_3$), 13.7 (CH_3, OCH$_2$C*H*$_3$); LCMS m/z 501.20 (M^+), calcd $C_{31}H_{32}ClNO_3$ 501.2071.

7-Methyl-6-phenyl-5,6-dihydro-2*H*-benzo[*b*][1,4]oxazocine-8-carboxylic acid ethyl ester (100a): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3030, 2978, 1712 (O-C=O), 1597, 1500, 1105, 1022, 746, 692 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.79 (1H, d, *J* = 8.8 Hz), 7.20 (2H, t, *J* = 7.6 Hz), 6.92 (1H, d, *J* = 8.8 Hz), 6.75 (1H, t, *J* = 7.2 Hz), 6.48 (2H, d, *J* = 8.4 Hz), 6.00 (1H, br d, *J* = 10.4 Hz, olefinic-*H*), 5.85-5.81 (1H, m, olefinic-*H*), 4.67 (2H, m, OC*H*$_2$CH=CH), 4.31 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 4.30 (1H, m, NC*H*$_2$), 3.97 (1H, m, NC*H*$_2$), 2.32 (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 167.4 (C, O-C=O), 159.2 (C), 147.2 (C), 142.5 (C), 132.7 (CH), 132.1 (C), 130.2 (CH), 129.4 (CH), 129.4 (2 x CH), 125.8 (CH), 124.6 (C), 118.4 (CH), 117.6 (CH), 112.4 (CH), 65.4 (CH_2, O*CH*$_2$), 60.6 (CH_2, O*CH*$_2$CH$_3$), 50.1 (CH_2, N*CH*$_2$), 15.3 (CH_3, Ar-*CH*$_3$), 14.4 (CH_3, OCH$_2$*CH*$_3$); GCMS m/z 323.20 (M^+), calcd

$C_{20}H_{21}NO_3$ 323.3857; Anal. calcd for $C_{20}H_{21}NO_3$ (323.38): C, 74.28; H, 6.55; N, 4.33. Found: C, 74.314; H, 6.549; N, 4.348%.

7-Methyl-6-phenyl-5,6-dihydro-2*H*-benzo[*b*][1,4]oxazocine-8-carboxylic acid methyl ester (100b): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 2949, 1719 (O-C=O), 1595, 1500, 1436, 1236, 1022, 741 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.79 (1H, d, *J* = 8.8 Hz), 7.20 (2H, t, *J* = 7.6 Hz), 6.92 (1H, d, *J* = 8.8 Hz), 6.75 (1H, t, *J* = 7.2 Hz), 6.48 (2H, d, *J* = 8.0 Hz), 6.00 (1H, br d, *J* = 10.8 Hz, olefinic-*H*), 5.84-5.81 (1H, m, olefinic-*H*), 4.67 (2H, m, OCH_2CH=CH), 4.37 (1H, m, NCH_2), 3.97 (1H, m, NCH_2), 3.86 (3H, s, OCH_3), 2.32 (3H, s, Ar-CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.8 (C, O-C=O), 159.3 (C), 147.2 (C), 142.7 (C), 132.7 (CH), 132.1 (C), 130.2 (CH), 129.4 (CH), 129.4 (2 x CH), 125.8 (CH), 124.2 (C), 118.4 (CH), 117.6 (CH), 112.4 (CH), 65.4 (CH_2, OCH_2), 51.8 (CH_3, OCH_3), 50.1 (CH_2, NCH_2), 15.3 (CH_3, Ar-CH_3); LCMS m/z 309.85 ($M+H^+$), calcd $C_{19}H_{19}NO_3$ 309.1365; Anal. calcd for $C_{19}H_{19}NO_3$ (309.13): C, 73.77; H, 6.19; N, 4.53. Found: C, 73.65; H, 6.22; N, 4.62%.

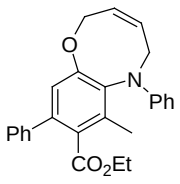


100c

7-Methyl-6-phenyl-5,6-dihydro-2*H*-benzo[*b*][1,4]oxazocine-8-carboxylic acid *tert*-butyl ester (100c): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 2975, 1709 (O-C=O), 1595, 1499, 1240, 1061, 744, 688 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.71 (1H, d, *J* = 8.8 Hz), 7.20 (2H, t, *J* = 7.6 Hz), 6.91 (1H, d, *J* = 8.8 Hz), 6.75 (1H, t, *J* = 7.2 Hz), 6.49 (2H, d, *J* = 8.0 Hz), 6.00-5.97 (1H, m, olefinic-*H*), 5.85-5.78 (1H, m, olefinic-*H*), 4.66 (2H, m, OCH_2CH=CH), 4.36 (1H, m, NCH_2), 3.98 (1H, m, NCH_2), 2.29 (3H, s, Ar-CH_3), 1.58 (9H, s, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.9 (C, O-C=O), 158.7 (C), 147.3 (C), 141.7 (C), 132.7 (CH), 132.0 (C), 130.1 (CH), 129.38 (CH), 129.4 (2 x CH), 126.5 (C), 125.9 (CH), 118.2 (CH), 117.5 (CH), 112.4 (CH), 80.9 (C), 65.4 (CH_2, OCH_2), 50.0 (CH_2, NCH_2), 28.3 (3 x CH_3, C(CH_3)$_3$), 15.3 (CH_3, Ar-CH_3); LCMS m/z 351.95 ($M+H^+$), calcd $C_{22}H_{25}NO_3$ 351.1834; Anal.

calcd for $C_{22}H_{25}NO_3$ (351.18): C, 75.19; H, 7.17; N, 3.99. Found: C, 75.25; H, 7.20; N, 4.05%.

7,9-Dimethyl-6-phenyl-5,6-dihydro-2*H*-benzo[*b*][1,4]oxazocine-8-carboxylic acid ethyl ester (100d): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 2926, 1724 (O-C=O), 1599, 1500, 1180, 1103, 748, 692 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.22 (2H, t, *J* = 8.0 Hz), 6.78 (1H, s, Ar-*H*), 6.75 (1H, t, *J* = 7.2 Hz), 6.53 (2H, d, *J* = 8.0 Hz), 6.00 (1H, br d, *J* = 10.8 Hz, olefinic-*H*), 5.84-5.81 (1H, m, olefinic-*H*), 4.58 (2H, m, OCH_2CH=CH), 4.40 (2H, q, *J* = 7.2 Hz, OC$H_2$$CH_3$), 4.40-4.35 (1H, m, NC$H_2$), 3.98 (1H, m, NC$H_2$), 2.31 (3H, s, Ar-C$H_3$), 2.04 (3H, s, Ar-C$H_3$), 1.40 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.7 (C, O-C=O), 156.4 (C), 147.2 (C), 136.5 (C), 134.7 (C), 132.5 (CH), 129.4 (C), 129.3 (CH), 129.3 (2 x CH), 128.9 (C), 126.1 (CH), 120.3 (CH), 117.4 (CH), 112.4 (CH), 65.3 (CH_2, OCH_2), 60.9 (CH_2, O$CH_2$$CH_3$), 49.8 ($CH_2$, N$CH_2$), 19.5 ($CH_3$, Ar-$CH_3$), 14.9 ($CH_3$, Ar-$CH_3$), 14.3 ($CH_3$, OCH_2CH_3); GCMS m/z 337.20 (M^+), calcd $C_{21}H_{23}NO_3$ 337.4123; Anal. calcd for $C_{21}H_{23}NO_3$ (337.41): C, 74.75; H, 6.87; N, 4.15. Found: C, 74.727; H, 6.852; N, 4.273%.



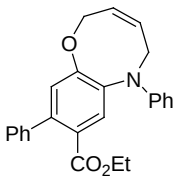
100d

7-Methyl-6,9-diphenyl-5,6-dihydro-2*H*-benzo[*b*][1,4]oxazocine-8-carboxylic acid ethyl ester (100e): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 3034, 2976, 1722 (O-C=O), 1599, 1500, 1197, 1062, 748, 702 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38-7.32 (5H, m, Ph-*H*), 7.23 (2H, t, *J* = 7.6 Hz), 6.95 (1H, s, Ar-*H*), 6.77 (1H, t, *J* = 7.2 Hz), 6.58 (2H, d, *J* = 8.0 Hz), 6.04-6.00 (1H, m, olefinic-*H*), 5.84-5.81 (1H, m, olefinic-*H*), 4.49 (2H, m, OCH_2), 4.02 (2H, q, *J* = 7.2 Hz, OC$H_2$$CH_3$), 4.02 (1H, m, NC$H_2$), 3.65 (1H, m, NC$H_2$), 2.11 (3H, s, Ar-C$H_3$), 0.93 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.5 (C, O-C=O), 156.6 (C), 147.0 (C), 140.5 (C), 139.7 (C), 137.2 (C), 132.3 (CH), 131.1 (C), 129.4 (2 x CH), 128.2 (C), 128.2 (2 x CH), 128.16 (2 x CH), 128.1 (CH), 127.4 (CH), 126.3 (CH), 120.1 (CH), 117.7 (CH), 112.7 (CH), 65.8 (CH_2, OCH_2), 60.9 (CH_2, O$CH_2$$CH_3$), 49.7

100e

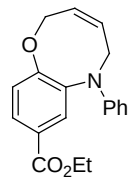
(CH_2, N*CH*$_2$), 15.1 (CH_3, Ar-*CH*$_3$), 13.6 (CH_3, OCH$_2$*CH*$_3$); GCMS m/z 399.20 (M^+), calcd $C_{26}H_{25}NO_3$ 399.4816; Anal. calcd for $C_{26}H_{25}NO_3$ (399.48): C, 78.17; H, 6.31; N, 3.51. Found: C, 78.31; H, 6.302; N, 3.56%.

6,9-Diphenyl-5,6-dihydro-2*H*-benzo[*b*][1,4]oxazocine-8-carboxylic acid ethyl ester (100f): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 3030, 2959, 2926, 1714 (O-C=O), 1597, 1545, 1500, 1105, 746, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.77 (1H, s, Ar-*H*), 7.43-7.34 (5H, m, Ph-*H*), 7.27 (2H, t, *J* = 7.2 Hz), 7.07 (1H, s, Ar-*H*), 6.84 (1H, t, *J* = 7.2 Hz), 6.79 (2H, d, *J* = 8.0 Hz), 6.07-6.04 (1H, m, olefinic-*H*), 5.89-5.84 (1H, m, olefinic-*H*), 4.62 (2H, d, *J* = 6.4 Hz, OC*H*$_2$), 4.42 (2H, d, *J* = 2.0 Hz, NC*H*$_2$), 4.07 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 1.01 (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), 157.7 (C), 147.4 (C), 141.9 (C), 141.0 (C), 133.1 (CH), 133.0 (C), 132.1 (CH), 129.3 (2 x CH), 128.3 (2 x CH), 127.9 (2 x CH), 127.2 (CH), 126.6 (CH), 125.1 (C), 123.9 (CH), 118.4 (CH), 113.9 (2 x CH), 66.9 (CH_2, O*CH*$_2$), 60.7 (CH_2, O*CH*$_2$CH$_3$), 50.1 (CH_2, N*CH*$_2$), 13.7 (CH_3, OCH$_2$*CH*$_3$); GCMS m/z 385.05 (M^+), calcd $C_{25}H_{23}NO_3$ 385.4551; Anal. calcd for $C_{25}H_{23}NO_3$ (385.45): C, 77.90; H, 6.01; N, 3.63. Found: C, 77.937; H, 6.059; N, 3.709%.



100f

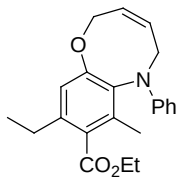
6-Phenyl-5,6-dihydro-2*H*-benzo[*b*][1,4]oxazocine-8-carboxylic acid ethyl ester (100h): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 2982, 1711 (O-C=O), 1598, 1540, 1243, 1024, 745, 691 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.91 (1H, d, *J* = 2.4 Hz), 7.85 (1H, dd, *J* = 8.8, 2.4 Hz), 7.22 (2H, t, *J* = 7.6 Hz), 7.10 (1H, d, *J* = 8.8 Hz), 6.79 (1H, t, *J* = 7.2 Hz), 6.69 (2H, d, *J* = 8.8 Hz), 6.04-6.00 (1H, m, olefinic-*H*), 5.86-5.80 (1H, m, olefinic-*H*), 4.58 (2H, d, *J* = 6.4 Hz, OC*H*$_2$CH=CH), 4.37 (2H, d, *J* = 1.6 Hz, NC*H*$_2$), 4.35 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 1.35 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.9 (C, O-C=O), 159.8 (C), 147.4 (C), 133.8 (C), 133.0 (CH), 132.3 (CH), 129.3 (2 x CH), 128.6 (CH), 126.3 (CH), 124.9 (C), 121.5 (CH), 118.1 (CH), 113.5 (2 x CH), 66.6 (CH_2, O*CH*$_2$), 60.8 (CH_2,



100h

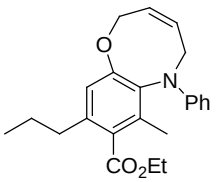
O*CH*$_2$CH$_3$), 50.1 (CH$_2$, N*CH*$_2$), 14.3 (CH$_3$, OCH$_2$*CH*$_3$); LCMS m/z 309.85 (M+H$^+$), calcd $C_{19}H_{19}NO_3$ 309.1365; Anal. calcd for $C_{19}H_{19}NO_3$ (309.13): C, 73.77; H, 6.19; N, 4.53. Found: C, 73.81; H, 6.22; N, 4.62%.

9-Ethyl-7-methyl-6-phenyl-5,6-dihydro-2*H*-benzo[*b*][1,4]oxazocine-8-carboxylic acid ethyl ester (100i): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 2975, 1716 (O-C=O), 1598, 1563, 1501, 1249, 1057, 746 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.20 (2H, t, *J* = 7.2 Hz), 6.80 (1H, s, Ar-*H*), 6.74 (1H, t, *J* = 7.2 Hz), 6.52 (2H, d, *J* = 8.4 Hz), 6.00-5.96 (1H, m, olefinic-*H*), 5.83-5.79 (1H, m, olefinic-*H*), 4.68 (2H, m, OC*H*$_2$CH=CH), 4.38 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 4.38-4.35 (1H, m, NC*H*$_2$), 3.98 (1H, m, NC*H*$_2$), 2.62 (2H, q, *J* = 7.6 Hz, ArC*H*$_2$CH$_3$), 2.02 (3H, s, Ar-C*H*$_3$), 1.38 (3H, t, *J* = 7.2 Hz, ArCH$_2$C*H*$_3$), 1.24 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.8 (C, O-C=O), 156.6 (C), 147.2 (C), 140.7 (C), 136.2 (C), 132.4 (CH), 129.4 (C), 129.33 (CH), 129.3 (2 x CH), 128.5 (C), 126.1 (CH), 118.6 (CH), 117.4 (CH), 112.5 (CH), 65.4 (CH$_2$, O*CH*$_2$), 61.0 (CH$_2$, O*CH*$_2$CH$_3$), 49.8 (CH$_2$, N*CH*$_2$), 26.4 (CH$_2$, Ar*CH*$_2$CH$_3$), 15.2 (CH$_3$, Ar-*CH*$_3$), 14.9 (CH$_3$, ArCH$_2$*C*H$_3$), 14.2 (CH$_3$, OCH$_2$*CH*$_3$); LCMS m/z 351.95 (M+H$^+$), calcd $C_{22}H_{25}NO_3$ 351.1834; Anal. calcd for $C_{22}H_{25}NO_3$ (351.18): C, 75.19; H, 7.17; N, 3.99. Found: C, 75.25; H, 7.22; N, 4.12%.



100i

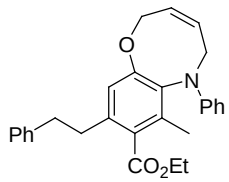
7-Methyl-6-phenyl-9-propyl-5,6-dihydro-2*H*-benzo[*b*][1,4]oxazocine-8-carboxylic acid ethyl ester (100j): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 2961, 1721 (O-C=O), 1598, 1564, 1500, 1182, 1103, 747 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.19 (2H, t, *J* = 8.0 Hz), 6.77 (1H, s, Ar-*H*), 6.73 (1H, t, *J* = 7.2 Hz), 6.50 (2H, d, *J* = 8.0 Hz), 5.97 (1H, br d, *J* = 10.8 Hz, olefinic-*H*), 5.83-5.77 (1H, m, olefinic-*H*), 4.54 (2H, m, OC*H*$_2$CH=CH), 4.37 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 4.37-4.35 (1H, m, NC*H*$_2$), 3.98 (1H, m, NC*H*$_2$), 2.53 (2H, t, *J* = 7.6 Hz, ArC*H*$_2$CH$_2$CH$_3$), 2.01 (3H, s, Ar-C*H*$_3$), 1.63 (2H, sextet, *J* = 7.6 Hz, ArCH$_2$C*H*$_2$CH$_3$), 1.37 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$), 0.96 (3H, t, *J* = 7.2 Hz,



100j

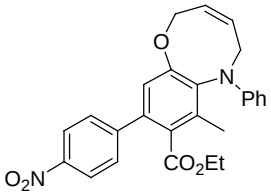
$ArCH_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.8 (C, O-C=O), 156.4 (C), 147.2 (C), 139.2 (C), 136.2 (C), 132.4 (CH), 129.5 (C), 129.33 (CH), 129.3 (2 x CH), 128.8 (C), 126.2 (CH), 119.4 (CH), 117.4 (CH), 112.5 (CH), 65.4 (CH_2, OCH_2), 61.0 (CH_2, OCH_2CH_3), 49.8 (CH_2, NCH_2), 35.5 (CH_2, $ArCH_2CH_2CH_3$), 24.1 (CH_2, $ArCH_2CH_2CH_3$), 14.9 (CH_3, Ar-CH_3), 14.2 (CH_3, OCH_2CH_3), 14.1 (CH_3, $ArCH_2CH_2CH_3$); LCMS m/z 365.50 (M^+), calcd $C_{23}H_{27}NO_3$ 365.1991; Anal. calcd for $C_{23}H_{27}NO_3$ (365.19): C, 75.59; H, 7.45; N, 3.83. Found: C, 75.62; H, 7.49; N, 3.88%.

7-Methyl-9-phenethyl-6-phenyl-5,6-dihydro-2*H*-benzo[*b*][1,4]oxazocine-8-carboxylic acid ethyl ester (100k): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3028, 1722 (O-C=O), 1598, 1562, 1498, 1248, 1054, 748, 696 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.31 (2H, t, *J* = 8.0 Hz), 7.23-7.19 (5H, m, Ph-*H*), 6.82 (1H, s, Ar-*H*), 6.75 (1H, t, *J* = 7.2 Hz), 6.53 (2H, d, *J* = 8.0 Hz), 5.99 (1H, br d, *J* = 10.8 Hz, olefinic-*H*), 5.83-5.80 (1H, m, olefinic-*H*), 4.74 (2H, m, OCH_2CH=CH), 4.39 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 4.40-4.35 (1H, m, NCH_2), 3.98 (1H, m, NCH_2), 2.94-2.84 (4H, m, $PhCH_2CH_2Ar$), 2.04 (3H, s, Ar-CH_3), 1.38 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.8 (C, O-C=O), 156.6 (C), 147.2 (C), 141.7 (C), 138.5 (C), 136.5 (C), 132.4 (CH), 129.8 (C), 129.37 (CH), 129.4 (2 x CH), 128.7 (C), 128.4 (2 x CH), 128.3 (2 x CH), 126.2 (CH), 126.0 (CH), 119.5 (CH), 117.5 (CH), 112.5 (CH), 65.5 (CH_2, OCH_2), 61.2 (CH_2, OCH_2CH_3), 49.7 (CH_2, NCH_2), 37.6 (CH_2), 35.8 (CH_2), 15.0 (CH_3, Ar-CH_3), 14.3 (CH_3, OCH_2CH_3); LCMS m/z 428.00 ($M+H^+$), calcd $C_{28}H_{29}NO_3$ 427.2147; Anal. calcd for $C_{28}H_{29}NO_3$ (427.21): C, 78.66; H, 6.84; N, 3.28. Found: C, 78.71; H, 6.88; N, 3.32%.



100k

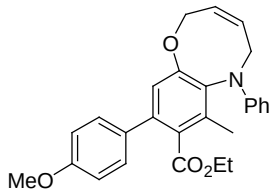
7-Methyl-9-(4-nitro-phenyl)-6-phenyl-5,6-dihydro-2*H*-benzo[*b*][1,4]oxazocine-8-carboxylic acid ethyl ester (100l): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 2978, 1721 (O-C=O), 1597, 1552,



100l

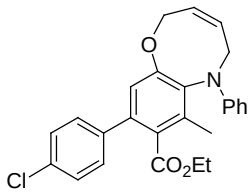
1498, 1265, 1061, 733, 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.26 (2H, d, *J* = 8.8 Hz), 7.55 (2H, d, *J* = 8.8 Hz), 7.25 (2H, t, *J* = 8.4 Hz), 6.94 (1H, s, Ar-*H*), 6.79 (1H, t, *J* = 7.2 Hz), 6.58 (2H, d, *J* = 8.0 Hz), 6.05-6.02 (1H, m, olefinic-*H*), 5.86-5.83 (1H, m, olefinic-*H*), 4.51 (3H, m, OCH_2, NCH_2), 4.06 (2H, q, *J* = 7.2 Hz, OC$H_2$$CH_3$), 4.10-4.02 (1H, m, NC$H_2$), 2.13 (3H, s, Ar-C$H_3$), 1.00 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.8 (C, O-C=O), 157.0 (C), 147.3 (C), 147.2 (C), 146.7 (C), 138.1 (C), 137.3 (C), 132.4 (C), 132.4 (CH), 129.5 (2 x CH), 129.13 (CH), 129.1 (2 x CH), 127.9 (C), 126.2 (CH), 123.5 (2 x CH), 120.1 (CH), 118.0 (CH), 112.7 (CH), 66.0 (CH_2, OCH_2), 61.2 (CH_2, OC$H_2$$CH_3$), 49.7 ($CH_2$, NC$H_2$), 15.2 ($CH_3$, Ar-C$H_3$), 13.7 ($CH_3$, OCH_2CH_3); LCMS m/z 443.00 ($M-H^+$), calcd $C_{26}H_{24}N_2O_5$ 444.1685; Anal. calcd for $C_{26}H_{24}N_2O_5$ (444.16): C, 70.26; H, 5.44; N, 6.30. Found: C, 70.15; H, 5.47; N, 6.41%.

9-(4-Methoxy-phenyl)-7-methyl-6-phenyl-5,6-dihydro-2*H*-benzo[*b*][1,4]oxazocine-8-carboxylic acid ethyl ester (100m): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow oil. IR (neat): ν_{max} 3058, 1722 (O-C=O), 1601, 1551, 1499, 1465, 1247, 1029, 737, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.31 (2H, d, *J* = 8.4 Hz), 7.23 (2H, t, *J* = 8.4 Hz), 6.93 (2H, d, *J* = 8.4 Hz), 6.92 (1H, s, Ar-*H*), 6.76 (1H, t, *J* = 7.2 Hz), 6.58 (2H, d, *J* = 8.0 Hz), 6.03-6.00 (1H, m, olefinic-*H*), 5.87-5.79 (1H, m, olefinic-*H*), 4.54-4.47 (3H, m, OCH_2, NCH_2), 4.07 (2H, q, *J* = 7.2 Hz, OC$H_2$$CH_3$), 4.10-4.05 (1H, m, NC$H_2$), 3.84 (3H, s, OC$H_3$), 2.10 (3H, s, Ar-C$H_3$), 1.01 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.7 (C, O-C=O), 159.1 (C), 156.5 (C), 147.0 (C), 139.2 (C), 136.9 (C), 132.9 (C), 132.3 (CH), 130.8 (C), 129.4 (2 x CH), 129.3 (CH), 129.29 (2 x CH), 128.3 (C), 126.3 (CH), 120.0 (CH), 117.6 (CH), 113.7 (2 x CH), 112.6 (CH), 65.7 (CH_2, OCH_2), 60.9 (CH_2, OC$H_2$$CH_3$), 55.3 ($CH_3$, OC$H_3$), 49.7 ($CH_2$, NC$H_2$), 15.0 ($CH_3$, Ar-C$H_3$), 13.8 ($CH_3$, OCH_2CH_3); LCMS m/z 430.00 ($M+H^+$), calcd $C_{27}H_{27}NO_4$ 429.1940; Anal. calcd for $C_{27}H_{27}NO_4$ (429.19): C, 75.50; H, 6.34; N, 3.26. Found: C, 75.58; H, 6.32; N, 3.32%.



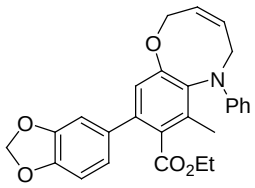
100m

9-(4-Chloro-phenyl)-7-methyl-6-phenyl-5,6-dihydro-2*H*-benzo[*b*][1,4]oxazocine-8-carboxylic acid ethyl ester (100n): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 2980, 1724 (O-C=O), 1596, 1550, 1494, 1269, 1063, 744 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.36-7.29 (4H, m, Ph-*H*), 7.25-7.20 (2H, m), 6.91 (1H, s, Ar-*H*), 6.78 (1H, t, *J* = 7.2 Hz), 6.57 (2H, d, *J* = 8.0 Hz), 6.04-6.00 (1H, m, olefinic-*H*), 5.85-5.82 (1H, m, olefinic-*H*), 4.49 (3H, m, OCH_2, NCH_2), 4.06 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 4.08-4.05 (1H, m, NCH_2), 2.10 (3H, s, Ar-CH_3), 1.01 (3H, t, *J* = 7.2 Hz, OCH$_2$CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.3 (C, O-C=O), 156.7 (C), 146.9 (C), 138.9 (C), 138.3 (C), 137.5 (C), 133.6 (C), 132.4 (CH), 131.4 (C), 129.5 (2 x CH), 129.4 (CH), 129.4 (2 x CH), 128.2 (2 x CH), 128.1 (C), 126.2 (CH), 120.1 (CH), 117.8 (CH), 112.7 (CH), 65.8 (CH_2, OCH_2), 61.1 (CH_2, OCH_2CH_3), 49.7 (CH_2, NCH_2), 15.1 (CH_3, Ar-CH_3), 13.7 (CH_3, OCH$_2$$CH_3$); LCMS m/z 434.25 ($M+H^+$), calcd $C_{26}H_{24}ClNO_3$ 433.1445; Anal. calcd for $C_{26}H_{24}ClNO_3$ (433.14): C, 71.97; H, 5.57; N, 3.23. Found: C, 72.11; H, 5.53; N, 3.28%.



100n

9-Benzo[1,3]dioxol-5-yl-7-methyl-6-phenyl-5,6-dihydro-2*H*-benzo[*b*][1,4]oxazocine-8-carboxylic acid ethyl ester (100o): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 2908, 1714 (O-C=O), 1596, 1550, 1500, 1471, 1239, 1030, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.23 (2H, t, *J* = 7.6 Hz), 6.91 (1H, s, Ar-*H*), 6.89 (1H, d, *J* = 1.6 Hz), 6.88-6.81 (2H, m), 6.77 (1H, t, *J* = 7.2 Hz), 6.57 (2H, d, *J* = 8.0 Hz), 6.04-5.98 (1H, m, olefinic-*H*), 5.98 (2H, s, OCH_2O), 5.84-5.81 (1H, m, olefinic-*H*), 4.68-4.49 (3H, m, OCH_2, NCH_2), 4.11 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 4.10-4.05 (1H, m, NCH_2), 2.09 (3H, s, Ar-CH_3), 1.08 (3H, t, *J* = 7.2 Hz, OCH$_2$CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.6 (C, O-C=O), 156.6 (C), 147.5 (C), 147.1 (C), 147.0 (C), 139.3 (C), 137.0 (C), 134.4 (C), 132.3 (CH), 131.0 (C), 129.4 (2 x CH), 129.4 (CH), 128.3 (C), 126.3 (CH), 121.8 (CH), 120.1 (CH), 117.7 (CH), 112.7 (CH), 108.9 (CH),



100o

108.1 (CH), 101.1 (CH_2, O*C*H_2O), 65.8 (CH_2, O*C**H**$_2$*), 61.0 (CH_2, O*C**H**$_2$*CH_3), 49.7 (CH_2, N*C**H**$_2$*), 15.1 (CH_3, Ar-*C**H**$_3$*), 13.9 (CH_3, OCH$_2$*C**H**$_3$*); LCMS m/z 442.70 (M-H^+), calcd $C_{27}H_{25}NO_5$ 443.1733; Anal. calcd for $C_{27}H_{25}NO_5$ (443.17): C, 73.12; H, 5.68; N, 3.16. Found: C, 73.22; H, 5.63; N, 3.12%.

9-Furan-2-yl-7-methyl-6-phenyl-5,6-dihydro-2*H*-benzo[*b*][1,4]oxazocine-8-arboxylic acid ethyl ester (100p): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2920, 1726 (O-C=O), 1599, 1498, 1270, 1063, 745, 694 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.45 (1H, s), 7.21 (2H, t, *J* = 8.4 Hz), 7.21 (1H, s), 6.76 (1H, t, *J* = 7.6 Hz), 6.55 (2H, d, *J* = 8.4 Hz), 6.55 (1H, s, Ar-*H*), 6.46-6.44 (1H, m), 6.02-5.99 (1H, m, olefinic-*H*), 5.84-5.80 (1H, m, olefinic-*H*), 4.48 (3H, m, OC*H*$_2$, NC*H*$_2$), 4.33 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 4.33-4.30 (1H, m, NC*H*$_2$), 2.05 (3H, s, Ar-C*H*$_3$), 1.28 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.7 (C, O-C=O), 156.7 (C), 151.8 (C), 146.8 (C), 142.5 (CH), 136.9 (C), 132.2 (CH), 131.8 (C), 129.4 (2 x CH), 129.38 (CH), 127.3 (C), 126.4 (CH), 126.0 (C), 117.8 (CH), 117.1 (CH), 112.8 (CH), 111.6 (CH), 107.6 (CH), 66.1 (CH_2, O*C**H**$_2$*), 61.4 (CH_2, O*C**H**$_2$*CH_3), 49.5 (CH_2, N*C**H**$_2$*), 14.8 (CH_3, Ar-*C**H**$_3$*), 14.1 (CH_3, OCH$_2$*C**H**$_3$*); LCMS m/z 389.16 (M^+), calcd $C_{24}H_{23}NO_4$ 389.1627; Anal. calcd for $C_{24}H_{23}NO_4$ (389.16): C, 74.02; H, 5.95; N, 3.60. Found: C, 74.15; H, 5.98; N, 3.68%.

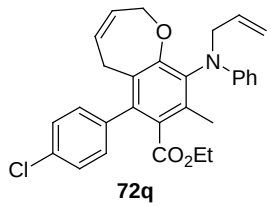
100p

10-Allyl-9-(4-chloro-phenyl)-7-methyl-6-phenyl-5,6-dihydro-2*H*-benzo[*b*][1,4]oxazocine-8-carboxylic acid ethyl ester (100q): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 2974, 1720 (O-C=O), 1598, 1497, 1271, 1087, 738 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.34 (2H, d, *J* = 7.6 Hz), 7.28-7.18 (4H, m), 6.77 (1H, t, *J* = 7.2 Hz), 6.59 (2H, d, *J* = 7.2 Hz), 6.06-6.02 (1H, m, olefinic-*H*), 5.83-5.77 (2H, m, olefinic-*H*), 4.90 (1H, dd, *J* = 10.4, 1.2 Hz, olefinic-*H*), 4.73 (1H, dd, *J* = 17.2, 1.2 Hz, olefinic-*H*), 4.66 (1H, br s, NC*H*$_2$), 4.45-4.44 (2H, m, OC*H*$_2$), 4.06-4.02 (1H, m, NC*H*$_2$), 3.93 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.15 (2H, m, ArC*H*$_2$CH=CH$_2$), 2.02 (3H, s, Ar-C*H*$_3$),

100q

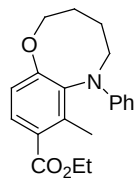
0.94 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.2 (C, O-C=O), 155.5 (C), 146.7 (C), 137.3 (C), 137.0 (C), 136.9 (CH), 133.4 (C), 133.2 (C), 132.6 (C), 131.9 (CH), 130.9 (2 x CH), 129.6 (C), 129.2 (3 x CH), 128.3 (C), 127.9 (2 x CH), 126.9 (CH), 117.7 (CH), 114.7 (CH_2), 113.0 (CH), 66.9 (CH_2, OCH_2), 60.9 (CH_2, OCH_2CH_3), 48.9 (CH_2, NCH_2), 32.3 (CH_2), 15.1 (CH_3, Ar-CH_3), 13.7 (CH_3, OCH_2CH_3); LCMS m/z 473.17 (M^+), calcd $C_{29}H_{28}ClNO_3$ 473.1758; Anal. calcd for $C_{29}H_{28}ClNO_3$ (473.17): C, 73.48; H, 5.95; N, 2.96. Found: C, 73.43; H, 5.98; N, 2.92%.

9-(Allyl-phenyl-amino)-6-(4-chloro-phenyl)-8-methyl-2,5-dihydro-benzo[*b*]oxepine-7-carboxylic acid ethyl ester (72q): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. IR (neat): ν_{max} 1723 (O-C=O), 1599, 1497, 1247, 1087, 733 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40 (2H, t, *J* = 8.0 Hz), 7.28-7.18 (4H, m), 6.75 (1H, t, *J* = 7.6 Hz), 6.62 (2H, d, *J* = 8.0 Hz), 6.09-6.00 (1H, m, olefinic-*H*), 5.69-5.63 (1H, m, olefinic-*H*), 5.37-5.29 (2H, m, olefinic-*H*), 5.23-5.19 (1H, m), 4.49-4.43 (1H, m), 4.33 (1H, dd, *J* = 16.4, 5.6 Hz), 4.20-4.06 (2H, m), 4.00 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 3.54 (1H, br d, *J* = 16.0 Hz), 2.90 (1H, dd, *J* = 15.6, 8.0 Hz), 2.18 (3H, s, Ar-CH_3), 1.03 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 169.1 (C, O-C=O), 157.2 (C), 148.3 (C), 138.7 (C), 136.9 (C), 135.6 (C), 135.5 (C), 135.35 (CH), 135.3 (C), 134.1 (C), 133.6 (C), 130.9 (2 x CH), 129.0 (CH), 129.0 (2 x CH), 128.2 (CH), 127.7 (CH), 125.0 (CH), 117.2 (CH), 116.7 (CH_2), 112.9 (2 x CH), 70.7 (CH_2, OCH_2), 61.0 (CH_2, OCH_2CH_3), 55.0 (CH_2, NCH_2), 27.1 (CH_2), 15.3 (CH_3, Ar-CH_3), 13.7 (CH_3, OCH_2CH_3); LCMS m/z 473.10 (M^+), calcd $C_{29}H_{28}ClNO_3$ 473.1758; Anal. calcd for $C_{29}H_{28}ClNO_3$ (473.17): C, 73.48; H, 5.95; N, 2.96. Found: C, 73.55; H, 5.91; N, 3.05%.



72q

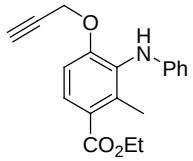
7-Methyl-6-phenyl-3,4,5,6-tetrahydro-2*H*-benzo[*b*][1,4]oxazocine-8-carboxylic acid ethyl ester (101a): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 2933,



101a

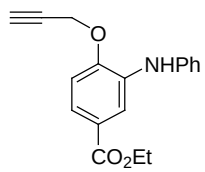
1712 (O-C=O), 1595, 1499, 1278, 1050, 747 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.85 (1H, d, *J* = 8.4 Hz), 7.17 (2H, t, *J* = 8.4 Hz), 7.01 (1H, d, *J* = 8.8 Hz), 6.68 (1H, t, *J* = 7.2 Hz), 6.47 (2H, d, *J* = 8.0 Hz), 4.35 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 4.29-4.13 (3H, m), 3.11 (1H, m), 2.33 (3H, s, Ar-CH_3), 2.08 (1H, m), 1.74-1.60 (3H, m), 1.39 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.5 (C, O-C=O), 159.9 (C), 147.8 (C), 142.2 (C), 136.7 (C), 130.6 (CH), 129.31 (CH), 129.3 (2 x CH), 126.6 (C), 119.4 (CH), 116.7 (CH), 112.2 (CH), 72.9 (CH_2, OCH_2), 60.7 (CH_2, OCH_2CH_3), 50.2 (CH_2, NCH_2), 28.7 (CH_2), 23.7 (CH_2), 15.2 (CH_3, Ar-CH_3), 14.3 (CH_3, OCH_2CH_3); LCMS m/z 325.55 (M^+), calcd $C_{20}H_{23}NO_3$ 325.1678; Anal. calcd for $C_{20}H_{23}NO_3$ (325.16): C, 73.82; H, 7.12; N, 4.30. Found: C, 73.78; H, 7.16; N, 4.36%.

2-methyl-3-phenylamino-4-prop-2-ynyloxy-benzoic acid ethyl ester (69'a): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow solid. Mp 60 °C; IR (neat): ν_{max} 3381 (N-*H*), 3292 (C≡C-*H*), 1714 (O-C=O), 1601, 1504, 1265, 1070, 777, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.80 (1H, d, *J* = 8.8 Hz), 7.18 (2H, t, *J* = 8.0 Hz), 6.96 (1H, d, *J* = 8.4 Hz), 6.83 (1H, t, *J* = 7.2 Hz), 6.62 (2H, d, *J* = 7.6 Hz), 5.70 (1H, s, N-*H*), 4.72 (2H, d, *J* = 2.4 Hz), 4.36 (2H, q, *J* = 6.8 Hz, OCH_2CH_3), 2.46 (1H, t, *J* = 2.4 Hz, $OCH_2C{\equiv}CH$), 2.42 (3H, s, Ar-CH_3), 1.39 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.5 (C, O-C=O), 154.5 (C), 145.6 (C), 137.7 (C), 130.7 (C), 129.0 (2 x CH), 127.8 (CH), 124.8 (C), 119.4 (CH), 115.1 (2 x CH), 109.4 (CH), 77.8 (C, *C*≡CH), 76.2 (CH, C≡*C*H), 60.6 (CH_2, OCH_2CH_3), 56.3 (CH_2, $OCH_2C{\equiv}CH$), 16.4 (CH_3, Ar-*C*H_3), 14.3 (CH_3, OCH_2CH_3); LRMS m/z 310.10 ($M + H^+$), calcd $C_{19}H_{19}NO_3$ 309.1365; HRMS m/z 332.1268 ($M + Na^+$), calcd $C_{19}H_{19}NO_3Na^+$ 332.1263.



69'a

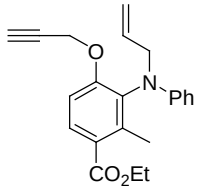
3-Phenylamino-4-prop-2-ynyloxy-benzoic acid ethyl ester (69'h): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3297 (N-*H*), 3294 (C≡C-H), 1709 (O-C=O), 1594, 1572, 1495, 1245, 1022, 753, 694 cm^{-1}; ^1H NMR



69'h

($CDCl_3$) δ 8.00 (1H, d, *J* = 2.0 Hz), 7.59 (1H, dd, *J* = 8.8, 2.4 Hz), 7.30 (2H, t, *J* = 7.6 Hz), 7.18 (2H, d, *J* = 8.8 Hz), 7.02-6.98 (2H, m), 6.19 (1H, s, N-*H*), 4.81 (2H, d, *J* = 2.4 Hz, OC*H*$_2$C≡CH), 4.33 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 2.59 (1H, t, *J* = 2.4 Hz, OCH$_2$C≡C*H*), 1.36 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.5 (C, O-C=O), 149.5 (C), 141.8 (C), 133.4 (C), 129.5 (2 x CH), 124.1 (C), 121.9 (CH), 121.7 (CH), 119.1 (2 x CH), 115.3 (CH), 111.3 (CH), 77.8 (C, *C*≡CH), 76.4 (CH, C≡*CH*), 60.8 (CH_2, O*CH*$_2$CH$_3$), 56.4 (CH_2, O*CH*$_2$C≡CH), 14.4 (CH_3, OCH$_2$*CH*$_3$); LRMS m/z 296.00 (M^+), calcd $C_{18}H_{17}NO_3$ 296.1208.

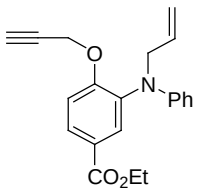
3-(Allyl-phenyl-amino)-2-methyl-4-prop-2-ynyloxy-benzoic acid ethyl ester (99'a):



99'a

Purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3290 (C≡C-H), 2980, 1712 (O-C=O), 1599, 1500, 1168, 1068, 746, 690 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.93 (1H, d, *J* = 8.4 Hz), 7.15 (2H, t, *J* = 7.2 Hz), 6.99 (1H, d, *J* = 8.8 Hz), 6.70 (1H, t, *J* = 7.2 Hz), 6.48 (2H, d, *J* = 8.4 Hz), 6.02-5.95 (1H, m, olefinic-*H*), 5.27 (1H, dd, *J* = 17.2, 1.6 Hz, olefinic-*H*), 5.12 (1H, dd, *J* = 10.4, 1.6 Hz, olefinic-*H*), 4.72 (2H, dABq, *J* = 16.4, 2.8 Hz, OC*H*$_2$C≡CH), 4.35 (2H, q, *J* = 6.8 Hz, OC*H*$_2$CH$_3$), 4.18 (2H, dABq, *J* = 16.0, 5.6 Hz, NC*H*$_2$CH=CH$_2$), 2.46 (1H, t, *J* = 2.4 Hz, OCH$_2$C≡C*H*), 2.42 (3H, s, Ar-C*H*$_3$), 1.39 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.4 (C, O-C=O), 158.0 (C), 147.9 (C), 142.5 (C), 135.0 (CH), 134.5 (C), 130.6 (CH), 128.9 (2 x CH), 124.6 (C), 116.9 (CH), 116.8 (CH_2), 112.3 (2 x CH), 110.4 (CH), 77.9 (C, *C*≡CH), 75.9 (CH, C≡*CH*), 60.7 (CH_2, O*CH*$_2$CH$_3$), 55.8 (CH_2, O*CH*$_2$C≡CH), 54.5 (CH_2, NC*H*$_2$CH=CH$_2$), 15.9 (CH_3, Ar-*CH*$_3$), 14.4 (CH_3, OCH$_2$*CH*$_3$); GCMS m/z 349.25 (M^+), calcd $C_{22}H_{23}NO_3$ 349.1678.

3-(Allyl-phenyl-amino)-4-prop-2-ynyloxy-benzoic acid ethyl ester (**99'h**): Purified

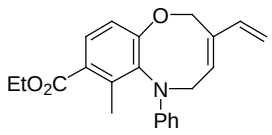


99'h

by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3289 (C≡C-H), 1712 (O-C=O), 1590, 1517, 1438, 1180, 1030, 743, 696 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.98-7.94 (2H, m), 7.17-7.12 (3H, m), 6.74 (1H, t, *J* = 8.0 Hz), 6.62 (2H, d, *J* = 8.4

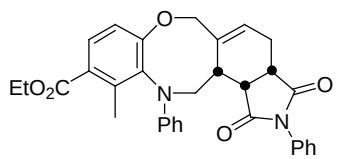
Hz), 6.05-5.98 (1H, m, olefinic-*H*), 5.35-5.25 (1H, m, olefinic-*H*), 5.16 (1H, dd, *J* = 10.4, 1.6 Hz, olefinic-*H*), 4.70 (2H, d, *J* = 2.4 Hz, OCH_2C≡CH), 4.34 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 4.24 (2H, d, *J* = 5.2 Hz, NCH_2CH=CH_2), 2.47 (1H, t, *J* = 2.0 Hz, OCH_2C≡C*H*), 1.36 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.9 (C, O-C=O), 157.7 (C), 148.1 (C), 135.6 (C), 134.5 (CH), 131.9 (CH), 128.8 (3 x CH), 124.6 (C), 117.6 (CH), 116.4 (CH_2), 113.9 (2 x CH), 113.7 (CH), 77.7 (C), 76.06 (CH), 60.8 (CH_2, O$CH_2$$CH_3$), 56.1 ($CH_2$, O$CH_2$C≡CH), 54.3 ($CH_2$, N$CH_2$), 14.3 ($CH_3$, OCH_2CH_3); LCMS m/z 336.35 ($M+H^+$), calcd $C_{21}H_{21}NO_3$ 335.1521.

7-Methyl-6-phenyl-3-vinyl-5,6-dihydro-2*H*-benzo[*b*][1,4]oxazocine-8-carboxylic acid ethyl ester (100'a): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 2980, 2932, 1714 (O-C=O), 1597, 1500, 1103, 1049, 748, 690 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.79 (1H, d, *J* = 8.8 Hz), 7.20 (2H, t, *J* = 7.2 Hz), 6.93 (1H, d, *J* = 8.8 Hz), 6.76 (1H, t, *J* = 7.2 Hz), 6.50 (2H, d, *J* = 8.0 Hz), 6.32 (1H, dd, *J* = 17.6, 11.2 Hz, olefinic-*H*), 5.95 (1H, t, *J* = 4.0 Hz, olefinic-*H*), 5.28 (1H, br d, *J* = 17.6 Hz, olefinic-*H*), 5.02 (1H, br d, *J* = 10.8 Hz, olefinic-*H*), 4.78-4.77 (3H, m), 4.33 (2H, q, *J* = 7.2 Hz, O$CH_2$$CH_3$), 4.10 (1H, m), 2.29 (3H, s, Ar-CH_3), 1.38 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.4 (C, O-C=O), 159.1 (C), 147.0 (C), 142.2 (C), 137.6 (CH), 135.9 (C), 132.6 (C), 131.9 (CH), 130.3 (CH), 129.41 (CH), 129.4 (2 x CH), 125.1 (C), 118.4 (CH), 117.7 (CH), 112.5 (CH), 112.3 (CH_2), 64.7 (CH_2, OCH_2), 60.6 (CH_2, O$CH_2$$CH_3$), 48.9 ($CH_2$, N$CH_2$), 15.3 ($CH_3$, Ar-$CH_3$), 14.3 ($CH_3$, OCH_2CH_3); GCMS m/z 349.20 (M^+), calcd $C_{22}H_{23}NO_3$ 349.1678; Anal. calcd for $C_{22}H_{23}NO_3$ (349.16): C, 75.62; H, 6.63; N, 4.01. Found: C, 75.773; H, 6.629; N, 4.024%.



100'a

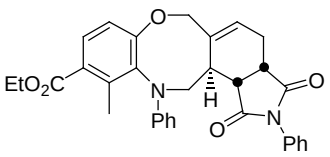
***endo*-Ethyl-11-methyl-1,3-dioxo-2,12-diphenyl-1,2,3,3a,4,6,12,13,13a,13b-decahydrobenzo[2,3][1,4]oxazocino[6,7-*e*]isoindole-10-carboxylate (102a):** Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max}



102a

3061, 2924, 1776 (C=O), 1705 (O-C=O), 1601, 1496, 1105, 1037, 748, 694 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.84 (1H, d, *J* = 8.4 Hz), 7.49 (2H, t, *J* = 7.6 Hz, *P*h-*H*), 7.41 (1H, t, *J* = 7.6 Hz, *P*h-*H*), 7.32 (2H, d, *J* = 7.6 Hz), 7.19 (2H, t, *J* = 8.0 Hz), 7.05 (1H, d, *J* = 8.4 Hz), 6.73 (1H, t, *J* = 7.2 Hz), 6.54 (2H, d, *J* = 7.6 Hz), 5.73 (1H, t, *J* = 5.2 Hz, olefinic-*H*), 4.64 (1H, d, *J* = 12.4 Hz), 4.35 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 4.35-4.27 (2H, m), 3.65-3.61 (1H, m), 3.38-3.32 (3H, m), 2.56-2.50 (1H, m), 2.39-2.35 (1H, m), 2.29 (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 178.3 (C=O), 176.9 (C=O), 167.3 (C, O-C=O), 159.8 (C), 146.4 (C), 141.0 (C), 139.2 (C), 139.1 (C), 131.6 (C), 130.5 (CH), 129.5 (2 x CH), 129.2 (2 x CH), 128.8 (CH), 127.9 (C), 127.8 (CH), 126.3 (3 x CH), 120.4 (CH), 117.5 (CH), 112.3 (CH), 78.5 (CH$_2$, O*CH*$_2$), 60.9 (CH$_2$, O*CH*$_2$CH$_3$), 48.7 (CH$_2$, N*CH*$_2$), 42.7 (CH), 38.9 (CH), 34.5 (CH), 23.1 (CH$_2$), 15.6 (CH$_3$, Ar-*CH*$_3$), 14.3 (CH$_3$, OCH$_2$*CH*$_3$); GCMS m/z 522.10 (M^+), calcd $C_{32}H_{30}N_2O_5$ 522.2155.

***exo*-Ethyl-11-methyl-1,3-dioxo-2,12-diphenyl-1,2,3,3a,4,6,12,13,13a,13b-decahydrobenzo[2,3][1,4]oxazocino[6,7-e]isoindole-10-carboxylate (102'a):** Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3061, 2924, 1705 (O-C=O), 1601, 1496, 1105, 1037, 748, 694 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.88 (1H, d, *J* = 8.4 Hz), 7.45 (2H, t, *J* = 7.2 Hz), 7.40-7.36 (1H,m), 7.22 (2H, d, *J* = 8.0 Hz), 7.21 (2H, t, *J* = 8.0 Hz), 7.05 (1H, d, *J* = 8.4 Hz), 6.74 (1H, t, *J* = 7.6 Hz), 6.50 (2H, d, *J* = 8.0 Hz), 5.62 (1H, dd, *J* = 6.8, 2.0 Hz, olefinic-*H*), 4.58 (1H, d, *J* = 12.0 Hz), 4.37 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 4.28-4.22 (2H, m), 3.74 (1H, d, *J* = 11.2 Hz), 3.29-3.18 (3H, m), 2.66-2.59 (1H, m), 2.52-2.47 (1H, m), 2.40 (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 178.5 (C=O), 177.5 (C=O), 167.3 (C, O-C=O), 159.7 (C), 146.7 (C), 141.4 (C), 139.6 (C), 138.6 (C), 131.8 (C), 131.0 (CH), 129.5 (2 x CH), 129.1 (2 x CH), 128.7 (CH), 128.1 (C), 127.5 (CH), 126.2 (3 x CH), 120.7 (CH), 117.5 (CH), 111.9 (CH), 79.6 (CH$_2$, O*CH*$_2$), 60.9 (CH$_2$, O*CH*$_2$CH$_3$), 53.1 (CH$_2$, N*CH*$_2$), 43.8 (CH), 38.1 (CH),



102'a

35.7 (CH), 23.8 (CH_2), 15.2 (CH_3, Ar-*CH_3*), 14.3 (CH_3, OCH_2*CH_3*); GCMS m/z 522.10 (M^+), calcd $C_{32}H_{30}N_2O_5$ 522.2155.

***endo*-Ethyl-1,3-dioxo-2,12-diphenyl-1,2,3,3a,4,6,12,13,13a,13b-decahydrobenzo[2,3][1,4]oxazocino[6,7-*e*]isoindole-10-carboxylate (102h):** Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 1709 (O-C=O), 1597, 1498, 1265, 1107, 736, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.92 (1H, d, *J* = 2.0 Hz), 7.74 (1H, dd, *J* = 8.4, 2.4 Hz), 7.46 (2H, t, *J* = 7.6 Hz), 7.38 (1H, t, *J* = 7.6 Hz), 7.28-7.24 (4H, m), 7.11 (1H, d, *J* = 8.4 Hz), 6.92 (2H, d, *J* = 8.0 Hz), 6.85 (1H, t, *J* = 7.2 Hz), 5.85 (1H, m, olefinic-*H*), 4.58 (2H, m, OC*H_2*), 4.41 (1H, dd, *J* = 15.6, 4.4 Hz), 4.35-4.21 (3H, m, OC*H_2*CH_3, NC*H_2*), 3.35-3.30 (2H, m), 3.20-3.17 (1H, m), 2.78-2.72 (1H, m), 2.22-2.18 (1H, m), 1.35 (3H, t, *J* = 7.2 Hz, OCH_2C*H_3*); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 178.4 (C=O), 176.5 (C=O), 166.0 (C, O-C=O), 158.8 (C), 144.99 (C), 138.92 (C), 138.6 (C), 131.8 (C), 129.6 (2 x CH), 129.3 (2 x CH), 128.9 (CH), 128.7 (CH), 126.7 (CH), 126.5 (3 x CH), 126.4 (CH), 126.0 (C), 122.5 (CH), 119.3 (CH), 115.7 (CH), 75.8 (CH_2, O*CH_2*), 60.9 (CH_2, O*CH_2*CH_3), 48.5 (CH_2, N*CH_2*), 42.3 (CH), 40.0 (CH), 33.6 (CH), 24.2 (CH_2), 14.3 (CH_3, OCH_2*CH_3*); LCMS m/z 507.00 ($M-H^+$), calcd $C_{31}H_{28}N_2O_5$ 508.1998; Anal. calcd for $C_{31}H_{28}N_2O_5$ (508.19): C, 73.21; H, 5.55; N, 5.51. Found: C, 73.28; H, 5.57; N, 5.56%.

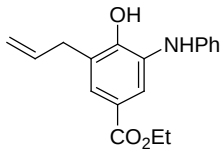
102h

Triethyl-1-methyl-12-phenyl-8,10a,11,12-tetrahydro-6*H*-dibenzo[*b*,*f*][1,4]oxazocine-2,9,10-tricarboxylate (103a): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 2985, 1721 (O-C=O), 1597, 1502, 1480, 1263, 1071, 737, 701 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.89 (1H, d, *J* = 8.4 Hz), 7.18 (2H, t, *J* = 8.0 Hz), 7.08 (1H, d, *J* = 8.4 Hz), 6.72 (1H, t, *J* = 7.2 Hz), 6.57 (2H, d, *J* = 7.6 Hz), 5.61-5.60 (1H, m, olefinic-*H*), 4.67 (1H, br d, *J* = 12.0 Hz), 4.50-4.33 (6H, m), 4.24 (2H, q, *J* = 7.2 Hz, OC*H_2*CH_3), 3.93-3.91 (1H, m), 2.97-2.75 (3H, m), 2.36 (3H, s, Ar-C*H_3*), 1.45 (3H, t, *J* = 7.2 Hz, OCH_2C*H_3*), 1.40 (3H, t, *J* = 7.2 Hz,

103a

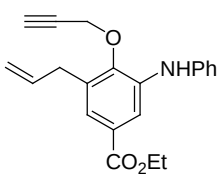
OCH_2CH_3), 1.31 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.6 (C, O-C=O), 167.3 (C, O-C=O), 167.0 (C, O-C=O), 159.8 (C), 147.1 (C), 141.2 (C), 139.1 (C), 136.9 (C), 136.5 (C), 134.4 (C), 131.1 (CH), 129.3 (2 x CH), 127.9 (C), 125.6 (CH), 120.3 (CH), 117.1 (CH), 111.5 (2 x CH), 79.1 (CH_2, OCH_2), 61.7 (CH_2, OCH_2CH_3), 61.4 (CH_2, OCH_2CH_3), 60.9 (CH_2, OCH_2CH_3), 54.7 (CH_2, NCH_2), 38.1 (CH), 28.9 (CH_2), 14.9 (CH_3, Ar-CH_3), 14.3 (CH_3, OCH_2CH_3), 14.1 (CH_3, OCH_2CH_3), 13.9 (CH_3, OCH_2CH_3); LCMS m/z 520.00 ($M+H^+$), calcd $C_{30}H_{33}NO_7$ 519.2257; Anal. calcd for $C_{30}H_{33}NO_7$ (519.22): C, 69.35; H, 6.40; N, 2.70. Found: C, 69.28; H, 6.45; N, 2.78%.

3-Allyl-4-hydroxy-5-phenylamino-benzoic acid ethyl ester (70h): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3371 (O-H & N-*H)*, 1685 (O-C=O), 1677, 1598, 1517, 1219, 1026, 745, 697 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.80 (1H, d, *J* = 1.6 Hz), 7.70 (1H, s, Ar-*H*), 7.23 (2H, t, *J* = 8.0 Hz), 6.91 (1H, t, *J* = 7.2 Hz), 6.78 (2H, d, *J* = 8.0 Hz), 6.43 (1H, s, O-*H*), 6.08-6.03 (1H, m, olefinic-*H*), 5.31 (1H, s, N-*H*), 5.19-5.15 (2H, m, olefinic-*H*), 4.31 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 3.48 (2H, d, *J* = 6.0 Hz, $CH_2CH{=}CH_2$), 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), 153.4 (C), 145.1 (C), 135.8 (CH), 129.5 (2 x CH), 129.0 (C), 128.5 (CH), 125.9 (C), 124.3 (CH), 122.8 (C), 120.8 (CH), 116.6 (CH_2, CH=CH_2), 116.1 (2 x CH), 60.7 (CH_2, OCH_2CH_3), 34.6 (CH_2, $CH_2CH{=}CH_2$), 14.3 (CH_3, OCH_2CH_3); LCMS m/z 298.05 ($M+H^+$), calcd $C_{18}H_{19}NO_3$ 297.1365.



70h

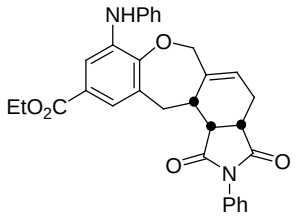
3-Allyl-5-phenylamino-4-prop-2-ynyloxy-benzoic acid ethyl ester (71'h): Purified by column chromatography using EtOAc/hexane and isolated as a light yellow liquid. IR (neat): ν_{max} 3389 (C≡C-H & N-*H)*, 1712 (O-C=O), 1590, 1517, 1256, 1030, 743, 696 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.87 (1H, d, *J* = 2.4 Hz), 7.45 (1H, d, *J* = 2.0 Hz), 7.32 (2H, t, *J* = 8.4 Hz), 7.13 (2H, dd, *J* = 7.6 Hz, 2.0 Hz), 7.00 (1H, t, *J* = 7.2 Hz), 6.19 (1H, s, N-*H*), 6.04-5.99 (1H, m, olefinic-*H*), 5.14-5.10 (2H, m, olefinic-*H*), 4.60 (2H, d, *J* = 2.4 Hz,



71'h

OC*H*$_2$C≡CH), 4.33 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.50 (2H, d, *J* = 2.4 Hz, ArC*H*$_2$CH=CH$_2$), 2.54 (1H, t, *J* = 2.4 Hz, OCH$_2$C≡C*H*), 1.35 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR (CDCl$_3$, DEPT-135) δ 166.4 (C, O-C=O), 149.1 (C), 142.0 (C), 137.2 (C), 136.4 (CH), 133.8 (C), 129.5 (2 x CH), 127.2 (C), 123.2 (CH), 121.8 (CH), 118.7 (2 x CH), 116.5 (CH$_2$, CH=*CH*$_2$), 115.5 (CH), 78.7 (C, *C*≡CH), 76.1 (CH, C≡*CH*), 60.9 (CH$_2$, O*CH*$_2$C≡CH), 60.5 (CH$_2$, O*CH*$_2$CH$_3$), 34.3 (CH$_2$, Ar*CH*$_2$CH=CH$_2$), 14.3 (CH$_3$, OCH$_2$C*H*$_3$); LCMS m/z 336.55 (M+H$^+$), calcd $C_{21}H_{21}NO_3$ 335.1521.

***endo*-Ethyl-8-anilino-1,3-dioxo-2-phenyl-2,3,3a,4,6,12,12a,12b-octahydro-1*H*-benzo[6,7]oxepino[4,3-*e*]isoindole-10-carboxylate (104h):** Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 1709 (O-C=O), 1586 1496, 1470, 1035, 736, 696 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.82 (1H, d, *J* = 1.2 Hz), 7.46 (2H, t, *J* = 7.6 Hz), 7.39 (1H, t, *J* = 7.6 Hz), 7.36 (1H, d, *J* = 1.2 Hz), 7.29 (2H, t, *J* = 8.4 Hz), 7.20 (2H, d, *J* = 8.0 Hz), 7.15 (2H, d, *J* = 8.0 Hz), 6.98 (1H, t, *J* = 7.6 Hz), 6.17-6.16 (2H, m, ArPhN*H* and olefinic-*H*), 5.25 (1H, d, *J* = 12.4 Hz), 4.54 (1H, d, *J* = 12.4 Hz), 4.31 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 4.25 (1H, d, *J* = 14.8 Hz), 3.43-3.35 (2H, m), 3.02-2.88 (3H, m), 2.35-2.31 (1H, m), 1.35 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR (CDCl$_3$, DEPT-135) δ 178.3 (C=O), 176.5 (C=O), 166.5 (C, O-C=O), 148.1 (C), 142.0 (C), 139.8 (C), 133.9 (C), 131.7 (C), 129.4 (2 x CH), 129.1 (2 x CH), 128.7 (CH), 127.3 (CH), 126.3 (2 x CH), 124.7 (C), 124.6 (CH), 122.9 (C), 121.7 (CH), 119.1 (2 x CH), 113.8 (CH), 70.4 (CH$_2$, O*CH*$_2$), 60.6 (CH$_2$, O*CH*$_2$CH$_3$), 44.5 (CH), 40.2 (CH), 38.9 (CH), 33.9 (CH$_2$), 24.9 (CH$_2$), 14.4 (CH$_3$, OCH$_2$*CH*$_3$); LCMS m/z 509.05 (M+H$^+$), calcd $C_{31}H_{28}N_2O_5$ 508.1998; Anal. calcd for $C_{31}H_{28}N_2O_5$ (508.19): C, 73.21; H, 5.55; N, 5.51. Found: C, 73.35; H, 5.52; N, 5.58%.



104h

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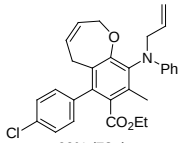
44. X-ray Crystal data of **102q**: $C_{32}H_{30}N_2O_5$, MW = 522.58, Monoclinic, space group $P2_1/n$, with a = 12.9791(7) Å, b = 15.0018(8) Å, c = 13.9935(8) Å, α = 90, β = 91.827(1), γ = 90°. CCDC-637092 contains the supplementary crystallographic data for this crystal structure.
45. Structure of functionalized benzo[*b*]oxepine **72q**.



60% (**72q**)

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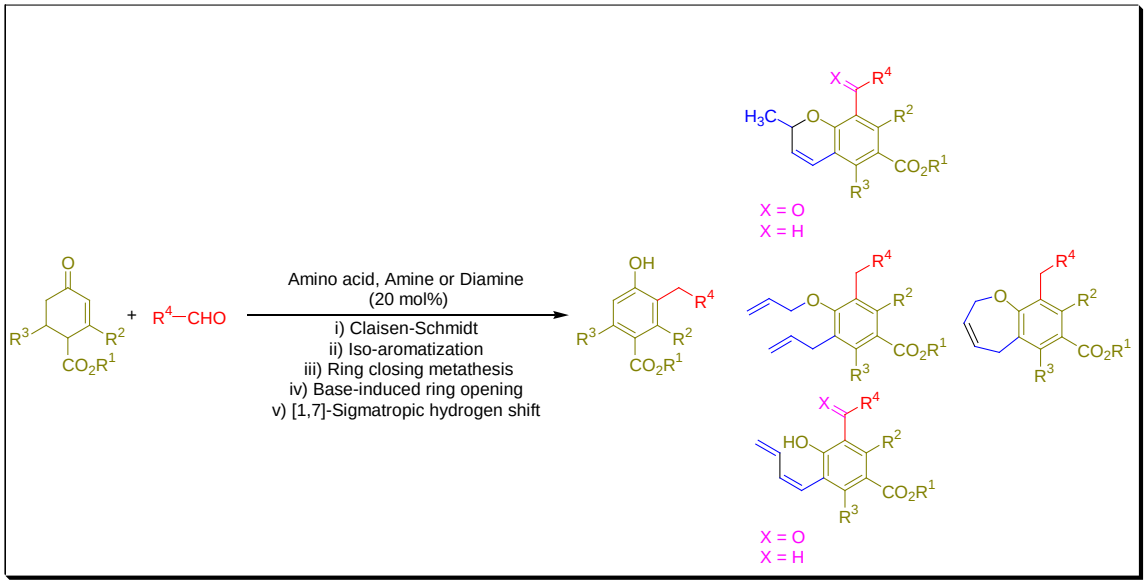
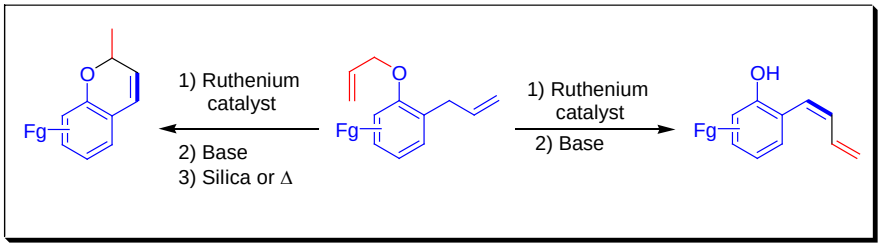
1. SEQUENTIAL ONE-POT COMBINATION OF MULTIREACTIONS THROUGH MULTICATALYSIS: A GENERAL APPROACH TO RAPID ASSEMBLY OF FUNCTIONALIZED PUSH-PULL PHENOLS, AND 2-METHYL-2*H*-CHROMENES.



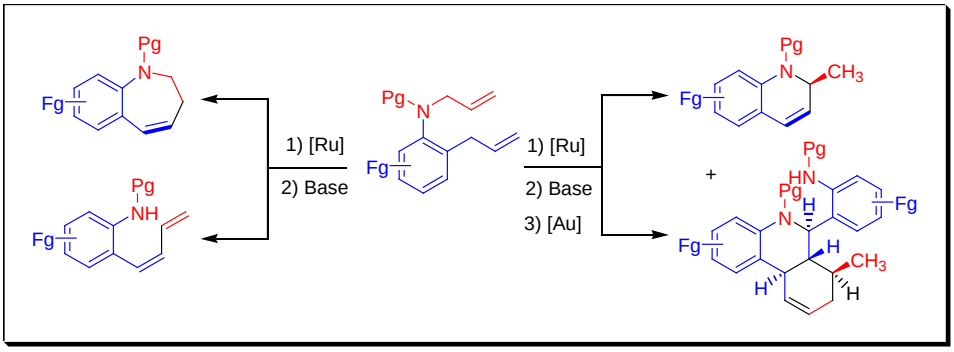
J. Comb. Chem. **2010**, *12*, 855–876.

2. A NEW ONE-POT SYNTHETIC APPROACH TO THE HIGHLY FUNCTIONALIZED (*Z*)-2-(BUTA-1,3-DIENYL)PHENOLS AND 2-METHYL-2*H*-CHROMENES: USE OF AMINE, RUTHENIUM AND BASE-CATALYSIS.



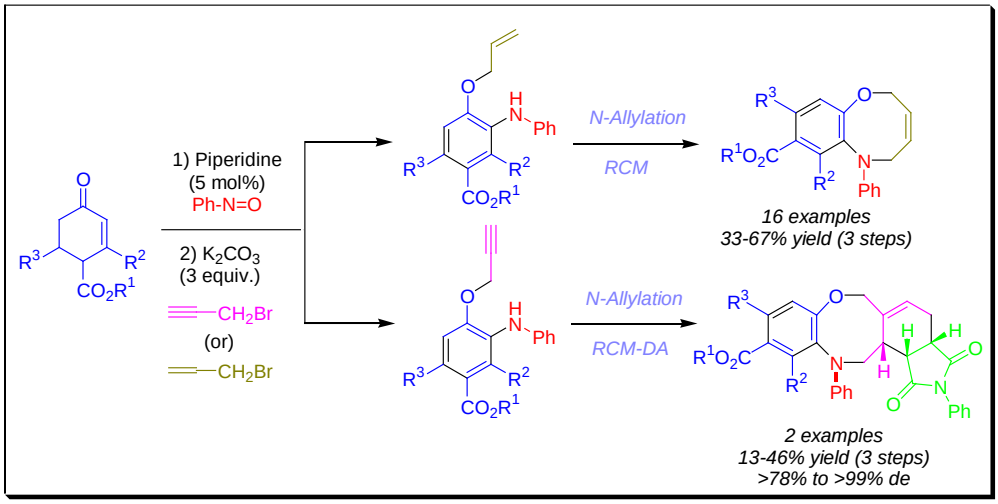
Eur. J. Org. Chem. **2008**, 3907–3911.

3. SEQUENTIAL COMBINATION OF RUTHENIUM-, BASE- AND GOLD-CATALYSIS: A NEW APPROACH TO THE SYNTHESIS OF MEDICINALLY IMPORTANT HETEROCYCLES.



Communicated

4. HIGH-YIELDING SYNTHESIS OF NEFOPAM ANALOGUES (FUNCTIONALIZED BENZOXAZOCINES) BY SEQUENTIAL ONE-POT CASCADE OPERATIONS.



Org. Biomol. Chem. **2009**, *7*, 3372–3378.