Applications of Amines for the Synthesis of Propargylamines and Allenes and for the Development of Electron Transfer Reactions

A Thesis
Submitted for the Degree of
DOCTOR OF PHILOSOPHY

By

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Dedicated to

My Parents

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Statement

I hereby declare that the matter embodied in this thesis is the result of investigations carried out by me in the School of Chemistry, University of Hyderabad, Hyderabad, under the supervision of **Professor M. Periasamy**.

In keeping with the general practice of reporting scientific observations, due acknowledgement has been made wherever the work described is based on the findings of other investigators.

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DECLARATION

I, **Mohan Lakavathu** hereby declare that this thesis entitled "**Applications of Amines for the Synthesis of Propargylamines and Allenes and for the Development of Electron Transfer Reactions**" submitted by me under the guidance and supervision of **Professor M. Periasamy** is a bonafide research work which is also free from plagiarism. I also declare that it has not been submitted previously in part or in full to this University or any other University or Institution for the award of any degree or diploma. I hereby agree that my thesis can deposit in Turnitin/INFLIBNET.

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CERTIFICATE

This is to certify that the thesis entitled "**Applications of Amines for the Synthesis of Propargylamines and Allenes and for the Development of Electron Transfer Reactions**" submitted by **Mr. Mohan Lakavathu** bearing registration number **12CHPH20** in partial fulfillment of the requirements for award of Doctor of Philosophy in the School of Chemistry is a bonafide work carried out by him under my supervision and guidance.

This thesis is free from plagiarism and has not been submitted previously in part or in full to this or any other University or Institution for the award of any degree or diploma. Further the student has four publications before the submission of his thesis.

Parts of this thesis have been published in the following four publications:

1. Periasamy, M.; Reddy, P. O.; Satyanarayana, I.; Mohan, L.; Edukondalu, A. *J. Org. Chem.* **2016**, *81*, 987.
2. Periasamy, M.; Mohan, L.; Satyanarayana, I.; Reddy, P. O. *J. Org. Chem.* **2018**, *83*, 267.

He has also made presentations in the following conferences:

1. Poster presentation in the *Chemfest 2016* (annual in-house symposium) held at School of Chemistry, University of Hyderabad, INDIA, March-**2016**.
2. Oral presentation in the *Chemfest 2017* (annual in-house symposium) held at School of Chemistry, University of Hyderabad, INDIA, March-**2017**.
3. Poster presentation in the *Chemfest 2018* (annual in-house symposium) held at School of Chemistry, University of Hyderabad, INDIA, March-**2018**.

Further the student has passed the following courses towards fulfillment of coursework requirement for Ph.D.:

	Course	Title	Credits	Pass/Fail
1.	CY-801	Research Proposal	3	Pass
2.	CY-805	Instrumental Methods A	3	Pass
3.	CY-806	Instrumental Methods B	3	Pass
4.	CY-844	Organic Reactions and Mechanisms	3	Pass

Hyderabad
Date:

Prof. M. Periasamy
(Thesis Supervisor)

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Abbreviations

Ac	acetyl
aq.	aqueous
Ar	aryl
Bn	benzyl
Boc	*tert*-butoxycarbonyl
9-BBN	9-borabicyclononane
BINOL	1,1'-bi-2-naphthol
bp	boiling point
brs	broad singlet (spectral)
Bu	butyl
^{s}Bu	*sec*-butyl
cat.	catalytic
Cbz	benzyloxycarbonyl
DABCO	1,4-diazabicyclo[2.2.2]octane
DCM	dichloromethane
dr	diastereomeric ratio
de	diastereomeric excess
DMAP	4-(*N*,*N*-dimethylamino)pyridine
DMF	dimethylformamide
DMSO	dimethyl sulfoxide
Ee	enantiomeric excess
EI	electron impact (in mass spectrometry)
eq.	equation
equiv.	equivalent
Et	ethyl
h	hour(s)
HPLC	high-performance liquid chromatography
IR	infrared

J	coupling constant (in NMR spectroscopy)
O^iPr	isopropyloxy
LAH	lithium aluminium hydride
LDA	lithium diisopropylamide
liq.	liquid
Lit.	literature
m	multiplet (spectral)
Me	methyl
MHz	megahertz
mp	melting point
Ms	methanesulfonyl
n-	primary
Nu	nucleophile
ORTEP	Oak Ridge Thermal Ellipsoid Plot
Ph	phenyl
Py	pyridine
PTSA	*p*-toluenesulfonic acid
q	quartet
rt	room temperature
s	singlet
t-	tertiary
TBAI	tetrabutylammonium iodide
THF	tetrahydrofuran
TMS	tetramethylsilane
Tol	tolyl
Ts	toluenesulfonyl
X	halide
y	yield

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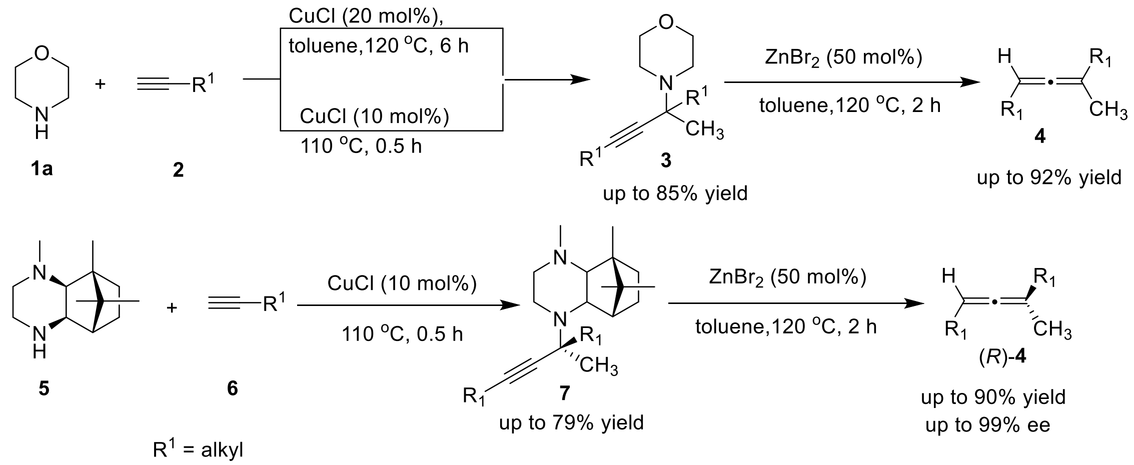
Mohan Lakavathu

Abstract

This thesis entitled "**Applications of Amines for the Synthesis of Propargylamines and Allenes and for the Development of Electron Transfer Reactions**" comprises of five chapters. Each chapter is subdivided into four sections namely **Introduction**, **Results and Discussion**, **Conclusions** and **Experimental Section** along with **References**. The work described in this thesis is exploratory in nature.

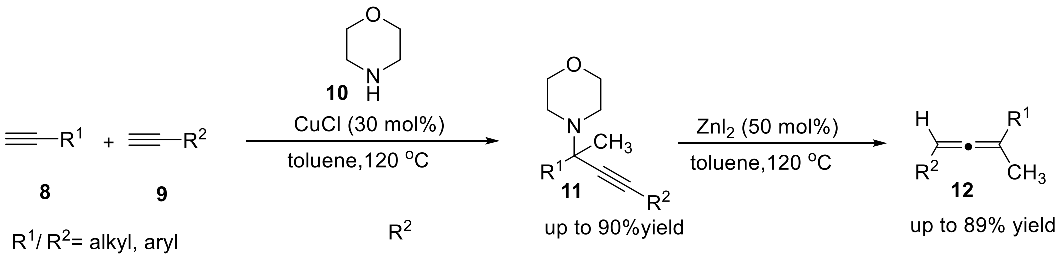
The first chapter describes efforts undertaken on the synthesis of highly enantioselective chiral trisubstituted allene derivatives through tetrasubstituted propargylamines using N-methyl camphanyl piperazine (Scheme 1).

Scheme 1



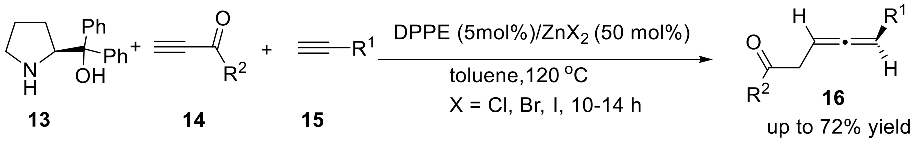
Also, racemic trisubstituted allenes **12** were prepared *via* tetrasubstituted propargylamine **11** using morpholine and two different 1-alkynes (Chapter 1).

Scheme 2



Studies undertaken to examine the scope of the ZnI_2 promoted enantioenriched chiral β-allenoate **16** synthesis using (*S*)-diphenylprolinol **13** are described in Chapter 2 (Scheme 3).

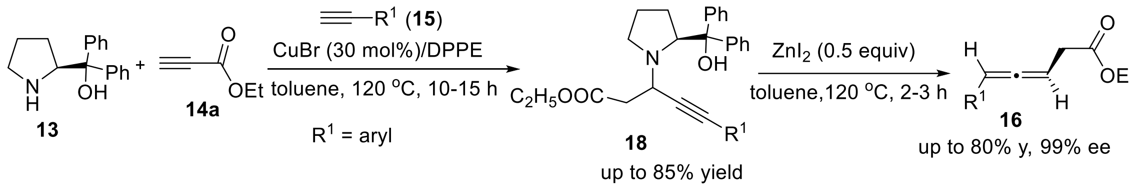
Scheme 3



R^1= aryl
R^2= -OEt, $-O(CH_2)_2Ph$, $-O(CH_2)_3Ph$, $-O(CH_2)_3CH=CH_2$

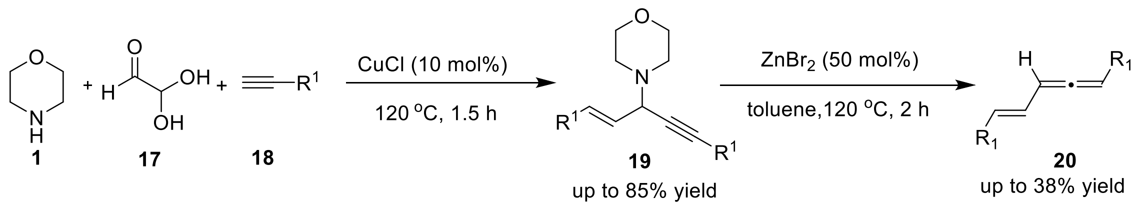
In addition, a method for synthesis of highly enantioenriched chiral β-allenoates **16** *via* chiral propargylamines **18** has been developed by using "chiral amine approach" (Chapter 2).

Scheme 4



In chapter 3, results of a convenient method for the synthesis of vinyl propargylamine **19** derivatives and their conversion to vinyl allenes **20** using morpholine, 1-alkyne and monoglyoxalic acid are described (Scheme 5).

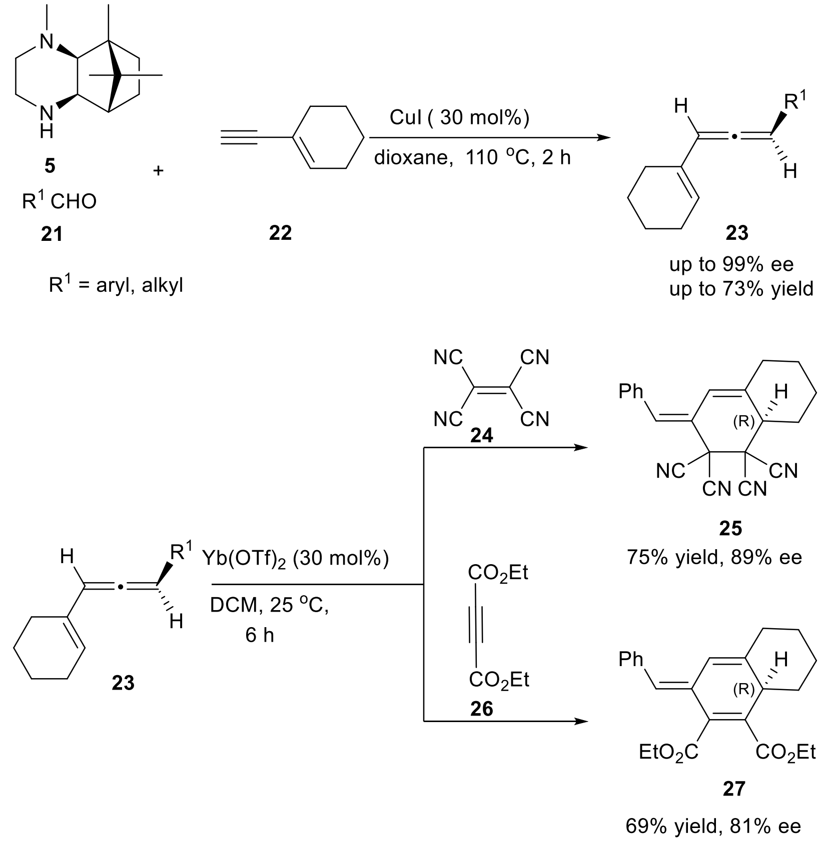
Scheme 5



R^1 = Ph, Ph-pCH$_3$, Ph-pOCH$_3$, Ph-mCH$_3$, Ph-pF, Ph-n-propyl

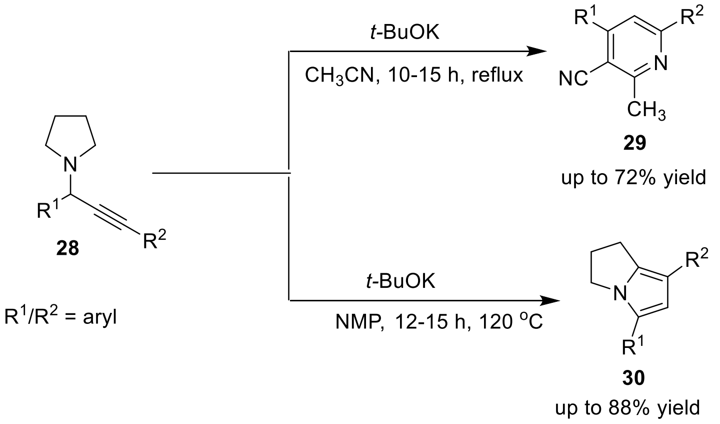
Also, the enantioselective synthesis of chiral vinyl allenes **23** and their applications in [4+2] cycloaddition reactions are described (Scheme 6, Chapter 3).

Scheme 6



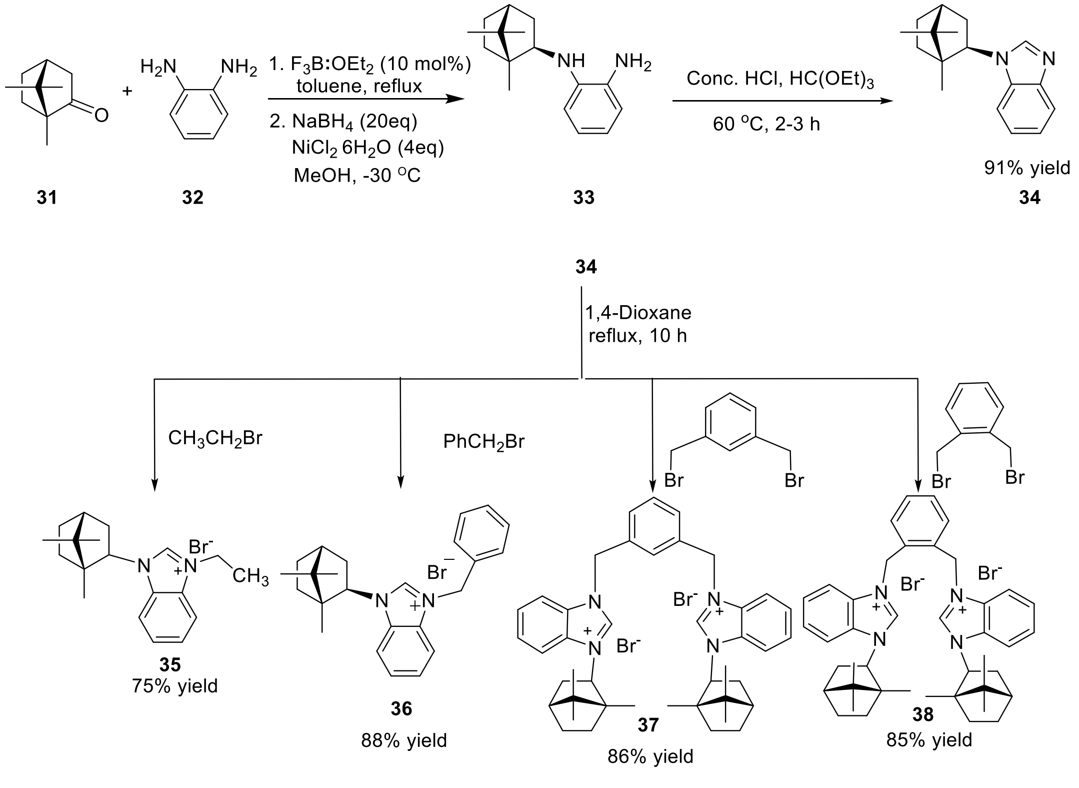
We have also developed methods for the preparation of highly substituted pyridine **29** and pyrrolizine derivatives **30** using trisubstituted propargylamines. These transformations involve electron transfer from *t*-BuOK to the propargylamine derivatives (Scheme 7). The results are described in Chapter 4.

Scheme 7



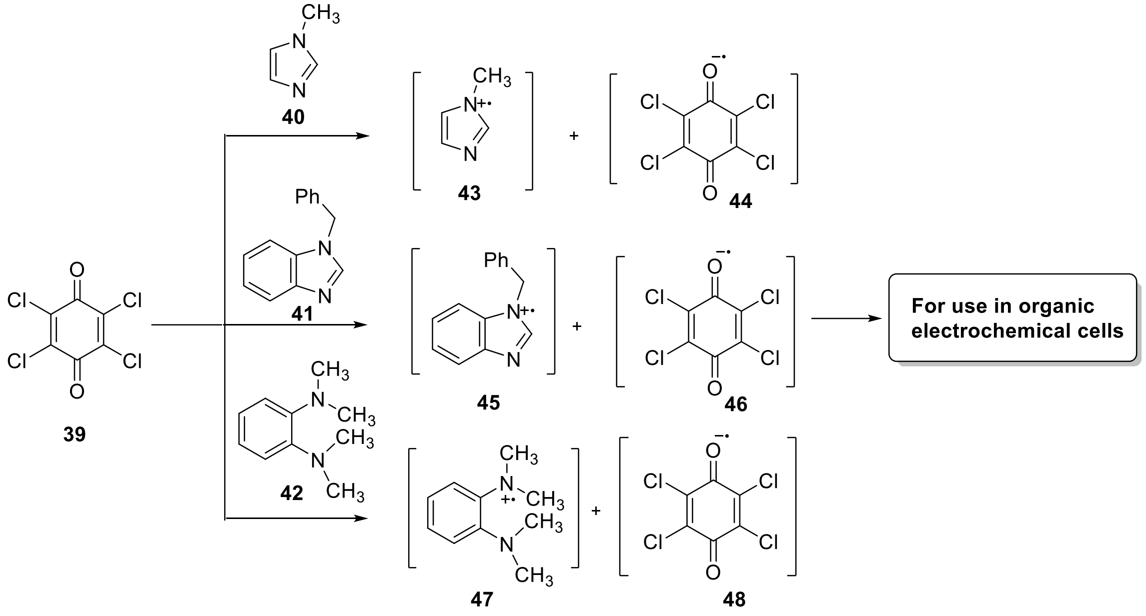
We have envisaged the utility of the camphanyl amine **33** for the synthesis of chiral *N*-camphanyl benzimidazole **34** using triethylorthoformate. The reaction of *N*-camphanyl benzimidazole **34** with alkyl or aryl bromide in 1, 4-dioxane solvent gave the corresponding benzimidazolium salts **35**, **36**, **37**, and **38** with up to 88% yield (Scheme 8). Results of these studies are described in Chapter 5. Preparation of super electron donors (SEDs) with these derivatives (**35**-**38**) were not successful.

Scheme 8



Accordingly, we have turned our attention towards the preparation of tetramethyl-*o*-phenylenediamine and *N*-benzylbenzimidazole which are useful in the construction of electricity harvesting electrochemical cells using *p*-chloranil (Scheme 9). The results are described in chapter 5.

Scheme 9



Representative ^{1}H-NMR, ^{13}C-NMR spectra, and HPLC analysis profiles are presented in Appendix-I and the X-ray crystallographic data are listed in Appendix-II.

Note: Scheme numbers and compound numbers are given in this abstract are different from those given in the chapters.

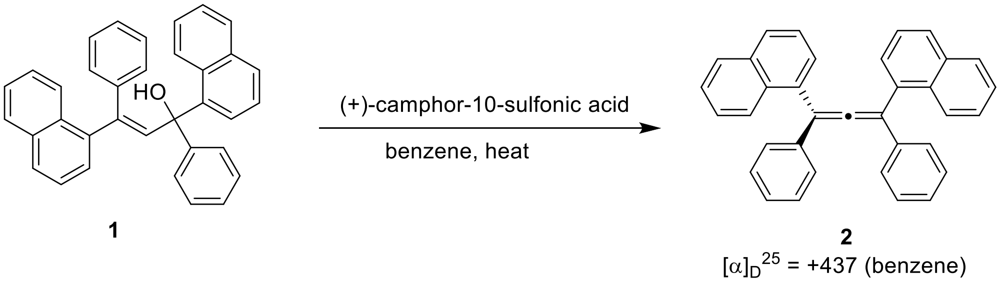
Chapter 1

Diastereoselective Synthesis of Tetrasubstituted Propargylamines and their Conversion to Trisubstituted Allenes

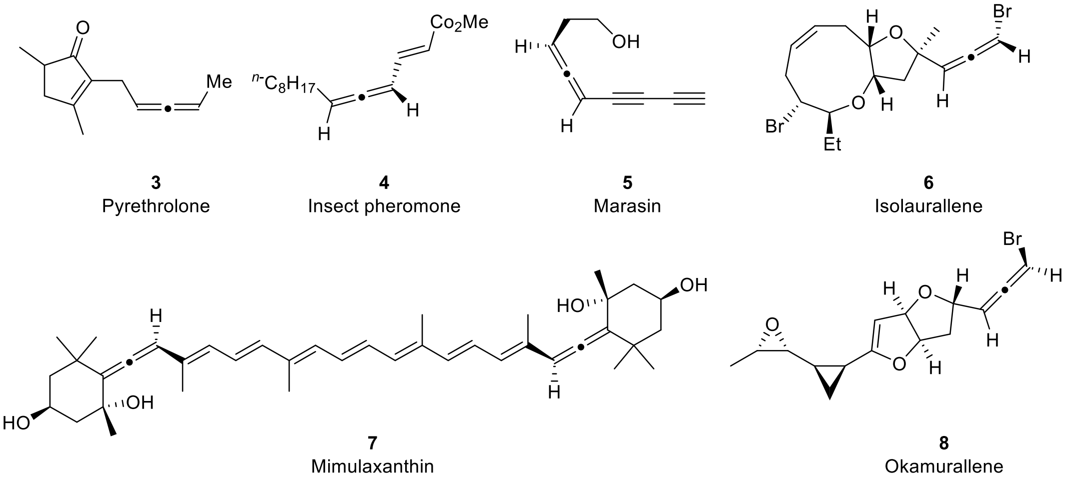
1.1 Introduction

Allenes are interesting building blocks and synthetic targets in organic synthesis. Van't Hoff first predicted the existence of two enantiomeric forms for unsymmetrically substituted allenes in 1875.[1] Although, the first allene was prepared by Burton and Pechmann and the structure of allene was confirmed by Jones in 1887,[2] van't Hoff's prediction of allene chirality was not confirmed until 1935 when Maitland and Mills synthesized the first optically active allene by dehydrating racemic allylic alcohol **1** with (+)-camphor-10-sulfonic acid (Scheme **1**).[3]

Scheme 1



Chiral allenes are highly valuable synthetic precursors in organic chemistry due to the presence of orthogonal π bond and their ability to undergo a variety of transformations.[4] In 1924, the naturally occurring allene pyrethrolone was characterized by Staudinger and Ruzicka.[5] Occurance of allenic structures in a variety of natural products and pharmacologically active compounds have inspired enormous interest on chiral allenes among organic and medicinal chemists. In fact, around 150 natural products comprising cumulenic or allenic structure have been identified and some representative compounds are listed in Figure 1.[6, 7]



3 Pyrethrolone

4 Insect pheromone

5 Marasin

6 Isolaurallene

7 Mimulaxanthin

8 Okamurallene

Figure 1

Since allene moieties are expected to have unique reactivity, several methods were developed for the synthesis of allenic derivatives.[3] Allenes can also be obtained through a variety of synthetic methods *via* preparation of propargylamines.[8] In continuation of our efforts on the synthetic applications of readily accessible chiral amines (Figure 2), we have undertaken studies on the enantioselective synthesis of 1, 3-substituted chiral allenes. Accordingly, a brief discussion on various methods available in the literature for the synthesis of chiral allenes *via* chiral amine approach would facilitate the discussion.

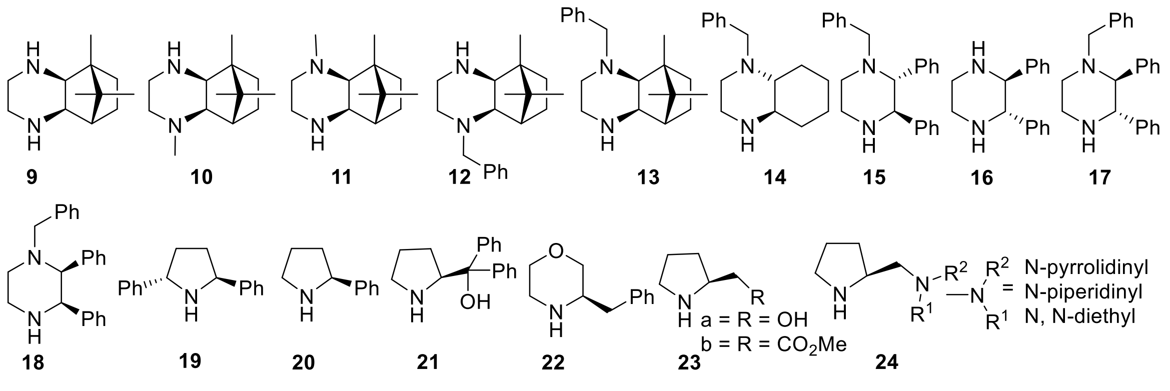
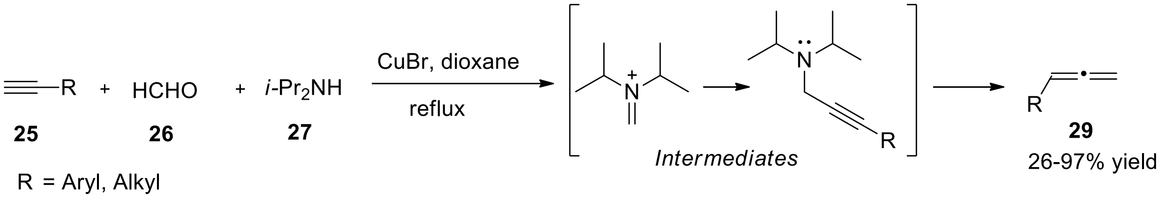


Figure 2. Various chiral secondary amines used in the allene synthesis

1.1.1 By Crabbe homologation reaction of terminal alkynes with formaldehyde and secondary amines

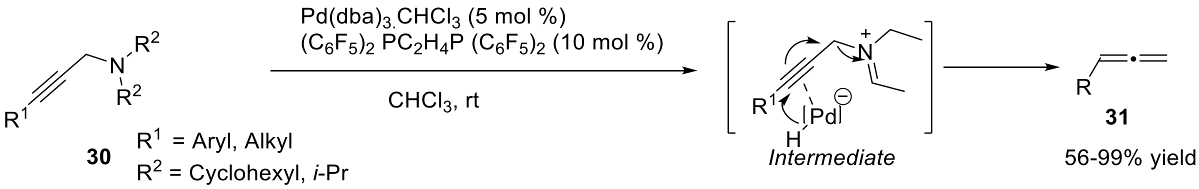
Crabbe homologation reaction produces monosubstituted allenes **29** from readily-available terminal alkyne **25**, formaldehyde **26**, *i*-Pr$_2$NH **27**, and CuBr in dioxane. This reaction involves copper-catalyzed addition of terminal alkyne to the *in situ* formed Schiff base and hydride migration across the triple bond (Scheme 2).[9]

Scheme 2



The Crabbe homologation reaction has inspired several modifications to improve the efficiency and also expand the scope of the reaction. Later, Nakamura *et al.* reported[10] that the palladium-catalyzed allene transformation of propargylic amines **30** in CHCl$_3$ gave the corresponding monosubstituted allenes in 56-99% yields (Scheme 3).

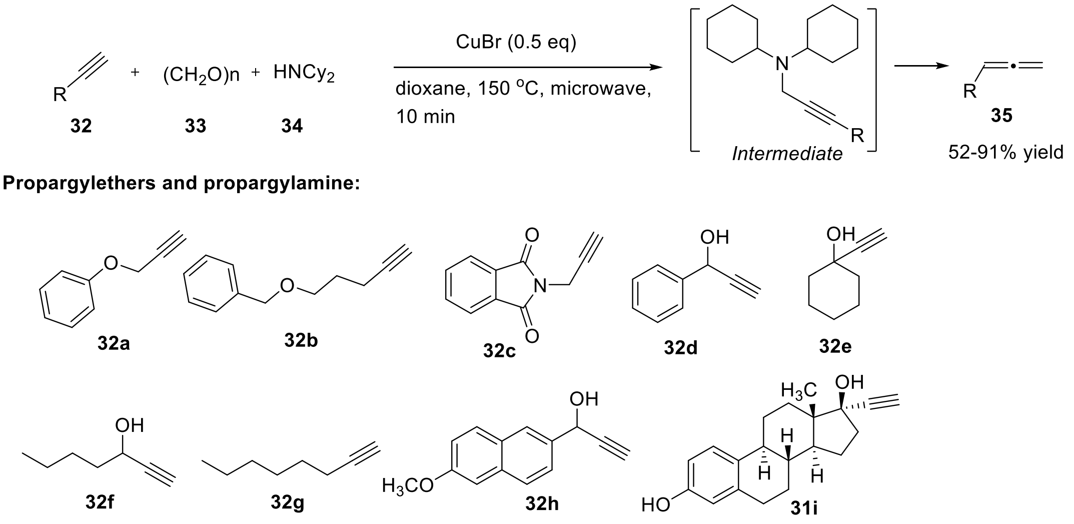
Scheme 3



Also, it was noticed that the reaction under microwave irradiation could accelerate the reaction rate. For example, the reaction of propargyl benzyl ether **32** with formaldehyde and dicyclohexylamine **33** in presence of copper bromide affords good yields in 1-10 min

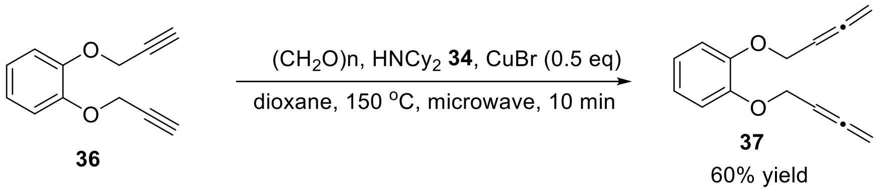
(Scheme 4).[11] Other functional groups such as ether, hydroxyl, and amide were also not affected under the conditions.

Scheme 4



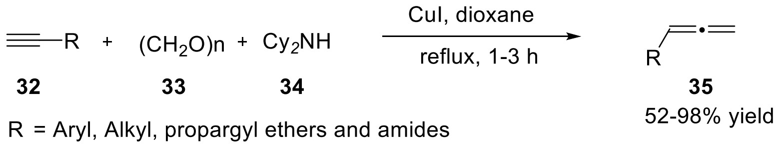
Bisallenes **37** were obtained in 60% yield under the microwave irradiation conditions in dioxane (Scheme 5).[12]

Scheme 5



Later, Ma *et al*. reported[13] that CuI is a better mediator for this transformation leading to much higher yields for the formation of terminal allenes in the presence of different functional groups, such as mesylate, a hydroxyl group, ether, and amide (Scheme 6).

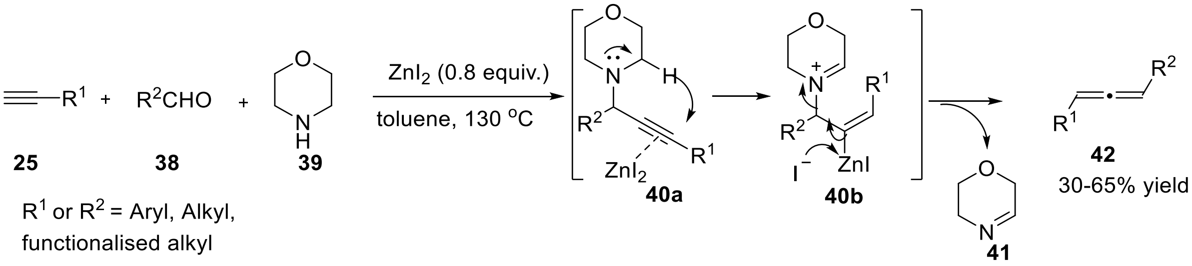
Scheme 6



1.1.2 The reaction of terminal alkynes with aldehydes and secondary amines

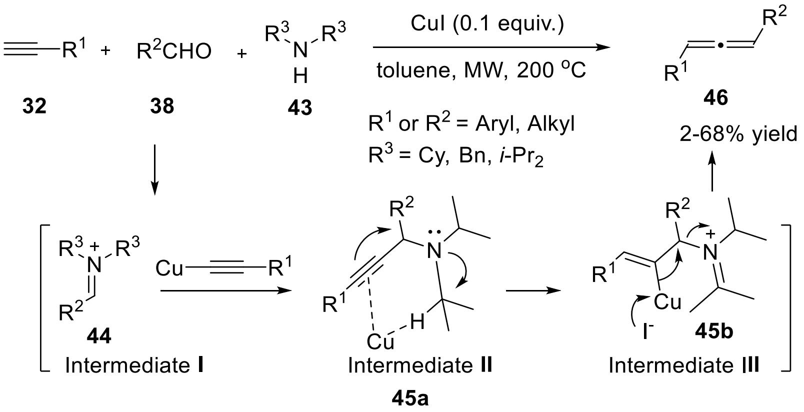
Ma *et al.* also developed a ZnI_2 mediated protocol for the synthesis of 1, 3-disubstituted allenes **42** using 1-alkynes **25**, aldehydes **38** and secondary amine (morpholine) **39** (Scheme 7).[14]

Scheme 7



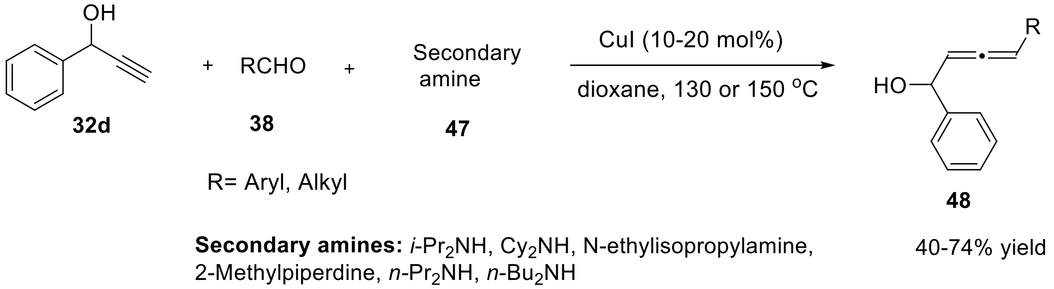
The Crabbe homologation can be rationalized in terms of intermediacy of the propargylamine intermediate, which would be formed by the Mannich-type reaction of copper acetylide with an iminium salt and subsequent hydrogen shift across the triple bond to produce the allene **46** (Scheme 8).[15]

Scheme 8



The use of various secondary amines have also afforded the 1, 3-disubstituted allenes **48** in reactions using propargyl alcohol **32d** and aldehydes **37** in one pot protocol to give the allenes in 40-74% yields (Scheme 9).[16]

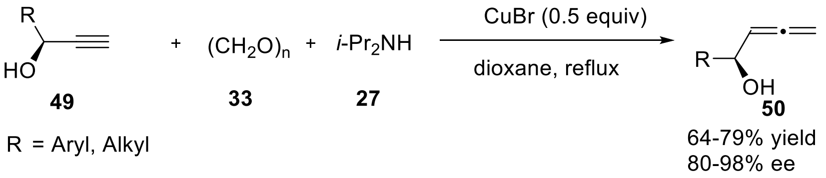
Scheme 9



1.1.3 Synthesis of chiral substituted allenes using terminal alkynes, aldehydes, and secondary amines

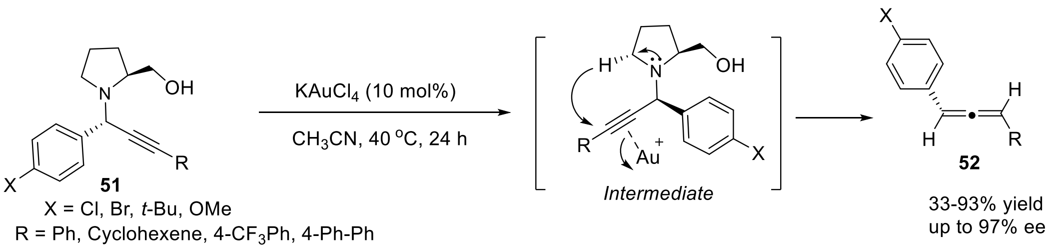
Since optically active propargyl alcohol can be easily prepared using several approaches, the optically active 2, 3-allenols with the chiral center connected to the hydroxyl group could be synthesized under CuBr promoted reaction of terminal propargyl alcohols **49**, paraformaldehyde **33** and secondary amine **27** (Scheme 10).[17]

Scheme 10



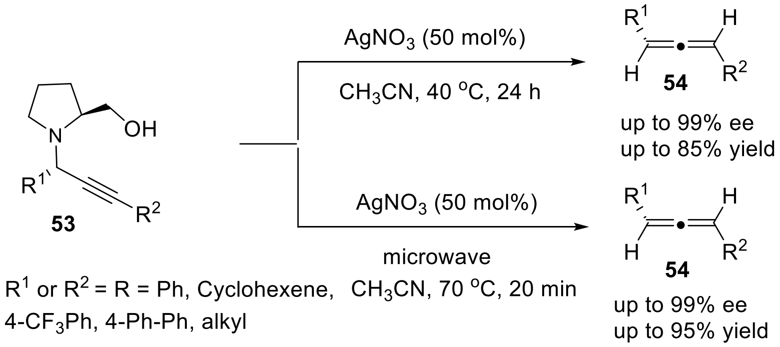
Che *et al.* reported[18] that the gold-catalyzed synthesis of axially chiral 1, 3-disubstituted allene **52** from the propargylamine derivative **51** in up to 97% ee and 33-93% yield (Scheme 11).

Scheme 11



Later, the chiral propargylamines **53** to axially chiral allenes **54** conversions were reported using $AgNO_3$ catalyst in CH_3CN at 40 °C (Scheme 12). Also, the microwave irradiation again allowed the completion of the reaction in a shorter time than that required under conventional thermal conditions (Scheme 12).[19]

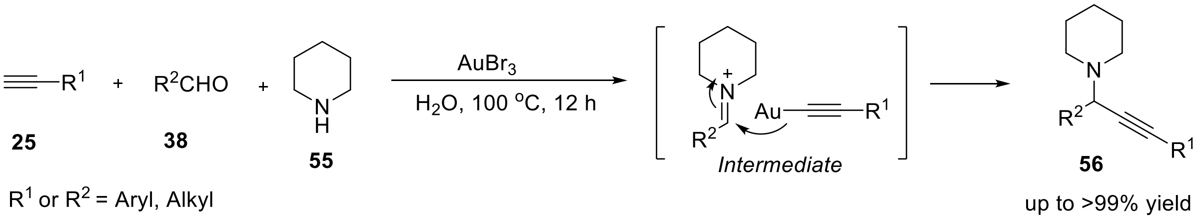
Scheme 12



1.1.4 Synthesis of propargylamines using A^3 coupling

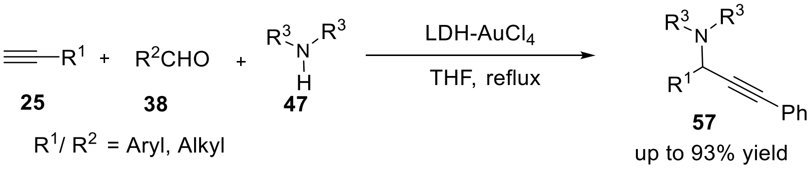
Gold catalyzed preparation of propargylamines using aldehydes, alkynes and amines were reported using water as solvent (Scheme 13).[20]

Scheme 13



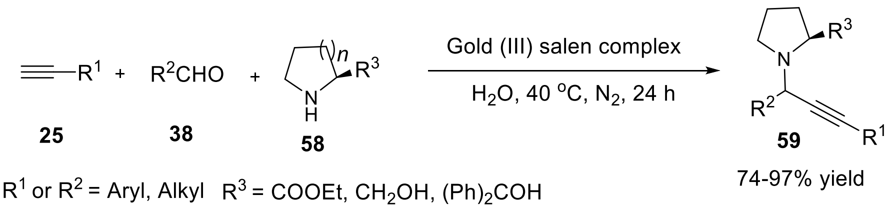
A three-component coupling of aldehydes, alkynes and secondary amines to generate the propargylamines **57** in excellent yields using a gold (LDH-$AuCl_4$) catalyst was reported (Scheme 14).[21]

Scheme 14



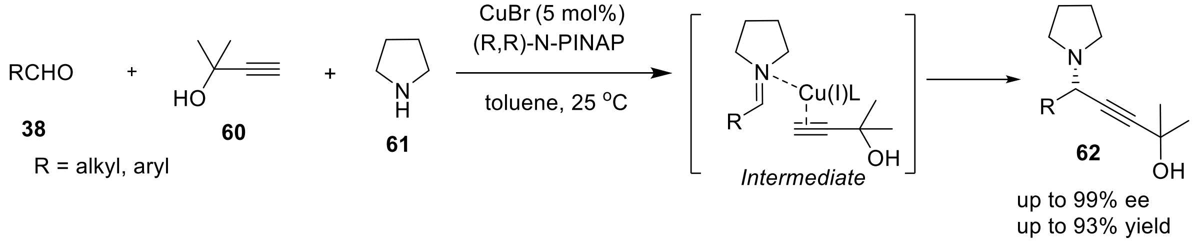
Asymmetric variants of propargylamines **59** synthesis were also reported using gold (III) salen complex (Scheme 15).[22]

Scheme 15



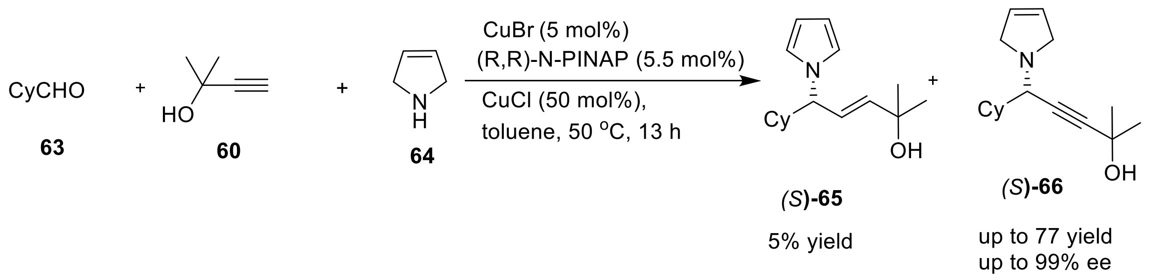
Classical methods using external ligands were also reported for the propargylamine synthesis. For example, Ma *et al.* reported the (R, R)-N-PINAP catalyzed propargylamine synthesis in up to 99% ee (Scheme 16).[23]

Scheme 16



Also, a method for transferring external chirality to the propargylamine **66** with 5% yield under A^3 coupling reaction conditions was reported (Scheme 17).[24]

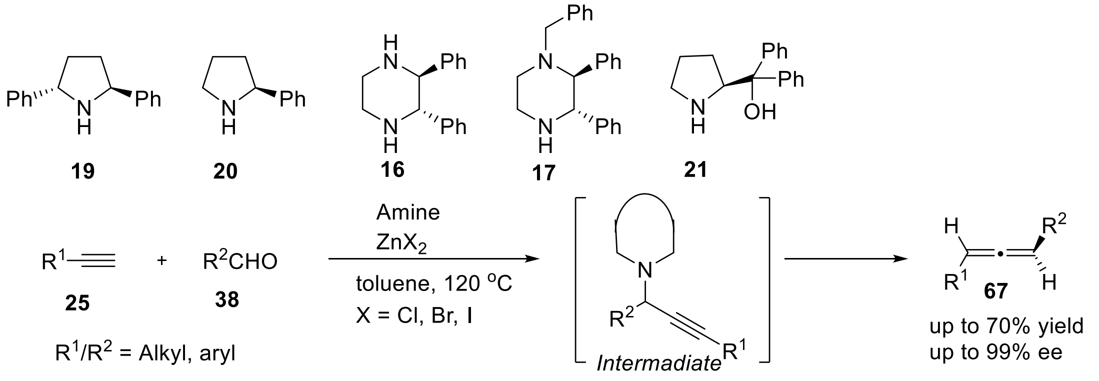
Scheme 17



1.1.5 Enantioselective synthesis of 1, 3-disubstituted allene

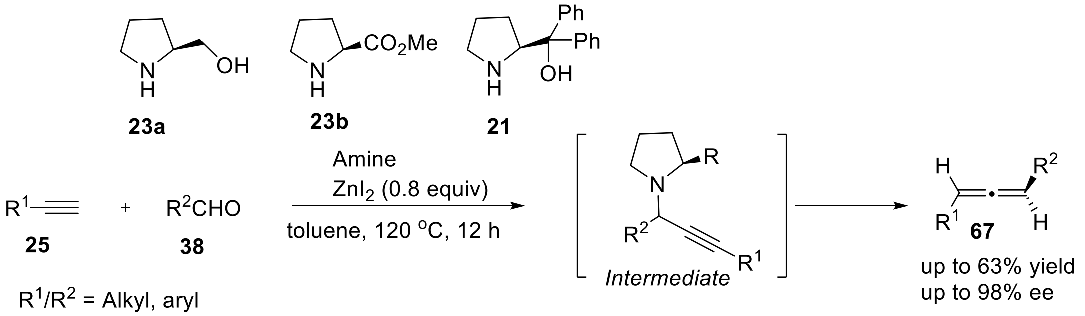
In this laboratory, $ZnBr_2$ promoted method for highly enantioselective synthesis of 1, 3-disubstituted chiral allenes **67** by "Chiral Amine Approach" was developed (Scheme 18).[25]

Scheme 18



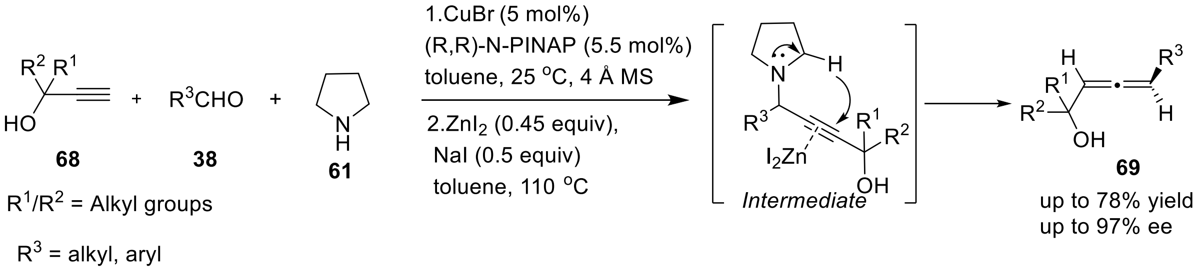
Later, Ma *et al.* reported the ZnI_2 mediated synthesis of chiral allene **67** using chiral secondary amines **21** and **23** (Scheme 19).[26]

Scheme 19



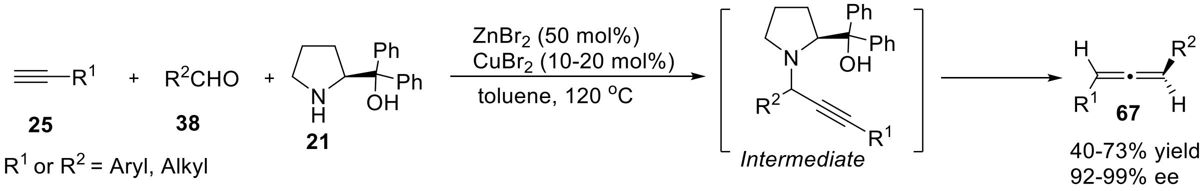
The same group also developed a method to access the 1, 3-disubstituted chiral allene in good yield and enantioselectivity using (R,R)-N-PINAP catalyst (Scheme 20).[27]

Scheme 20



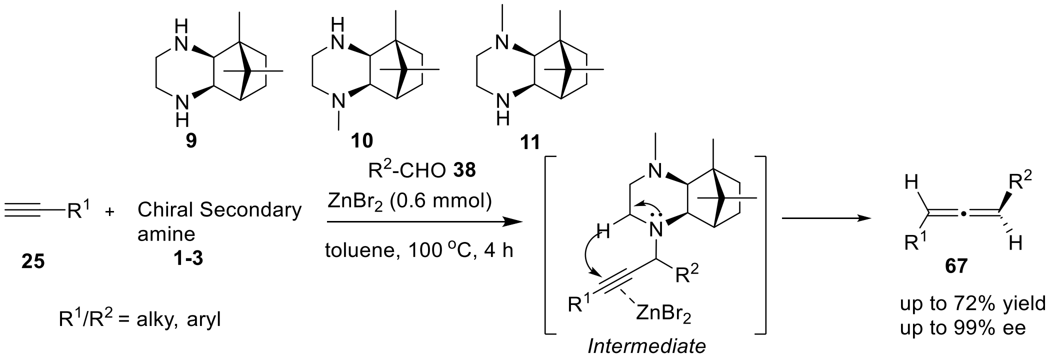
Also, chiral allenes have been accessed *via* chiral amine approach by using bimetallic systems (Scheme 21).[28]

Scheme 21



Syntheses involving preparation of intermediate chiral propargylamines and enantiopure allenes using chiral camphanyl piperazines were reported from this laboratory (Scheme 22).[29]

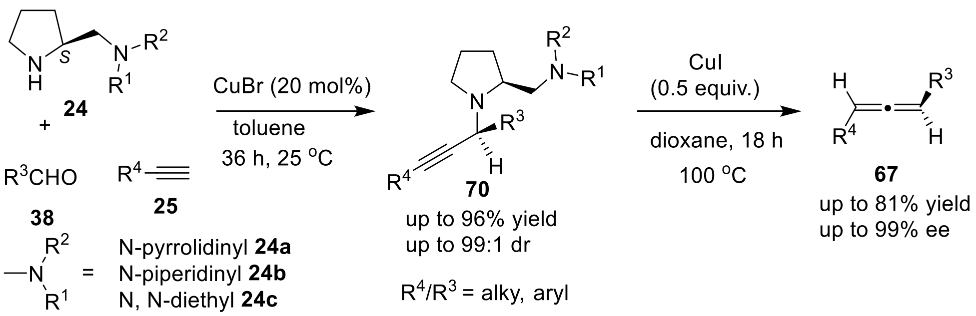
Scheme 22



1.1.6 Enantioselective synthesis of 1, 3-disubstituted allene from chiral propargylamines

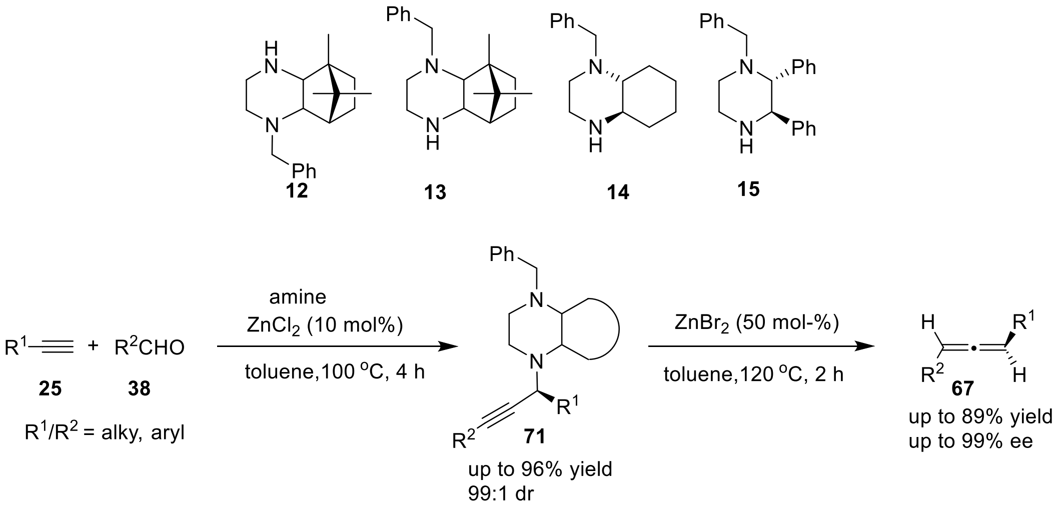
The use of 2-dialkylaminomethylpyrrolidine as a chiral amine to access diastereoselective propargylamine with 99:1dr and their conversion to the highly enantioselective 1, 3-disubstituted allenes was reported from this laboratory (Scheme 23).[30]

Scheme 23



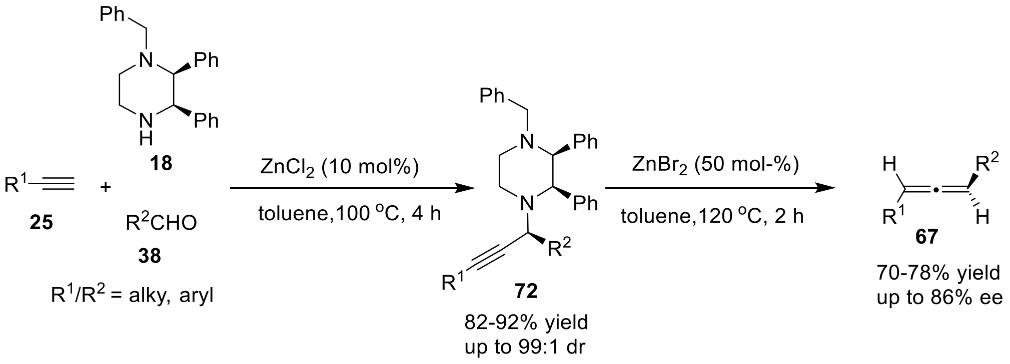
Applications of other piperazine derivatives were also reported from this laboratory (Scheme 24).[31]

Scheme 24



More recently, a method for the resolution of desymmetrized meso piperazine and their application in 1, 3-disubstituted allene was reported (Scheme 25).[32]

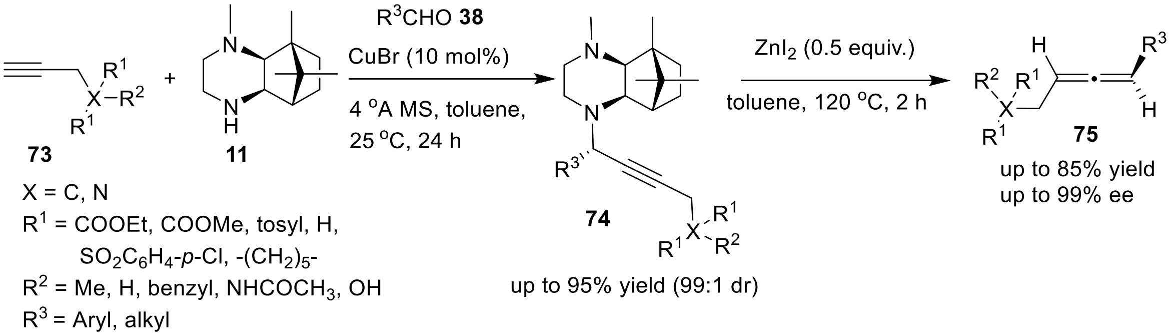
Scheme 25



1.1.7 Allenylation of functionalized terminal alkynes

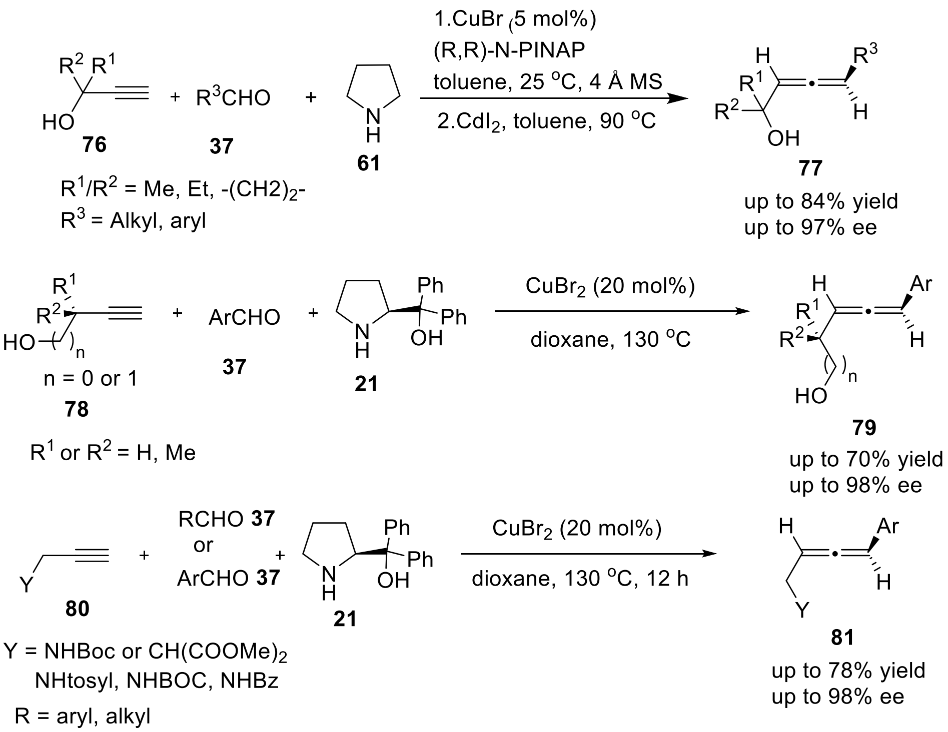
An efficient method for highly enantioselective synthesis of functionalized 1, 3-disubstituted allene **75** *via* chiral propargylamines **74** using the N-methyl camphanyl piperazine **11** was also reported from this laboratory (Scheme 26).[33]

Scheme 26



Ma *et al.* reported methods for the preparation of α-allenols containing different functional groups (Chart 1). [34, 35]

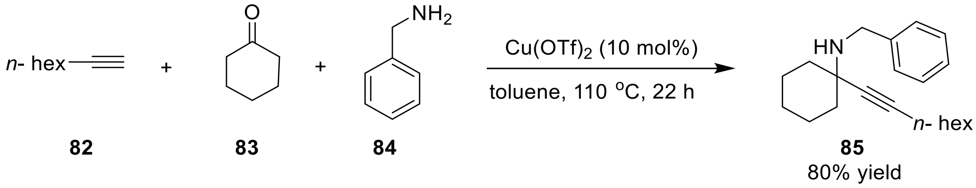
Chart 1



1.1.8 Synthesis of racemic tetrasubstituted propargylamine

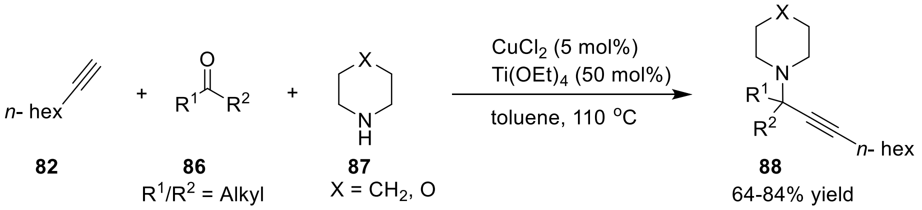
Larsen *et al.* reported[36] that three component alkynylation using a ketone could be catalysed by Cu(OTf)$_2$ to afford the propargylamine **85** in 80% yield (Scheme 27).

Scheme 27



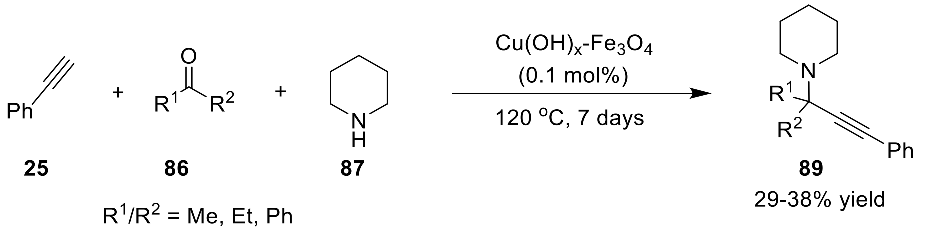
The reaction using $CuCl_2$ and $Ti(OEt)_4$ afforded the propargylamines **88** in 64-84% yield (Scheme 28).[37]

Scheme 28



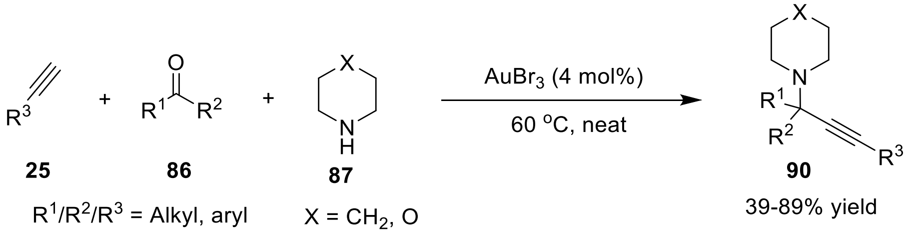
Ramon *et al*. used the $Cu(OH)_x$-Fe_3O_4 for the preparation of tetrasubstituted propargylamine **89** from the amine, ketone and alkyne (Scheme 29).[38]

Scheme 29



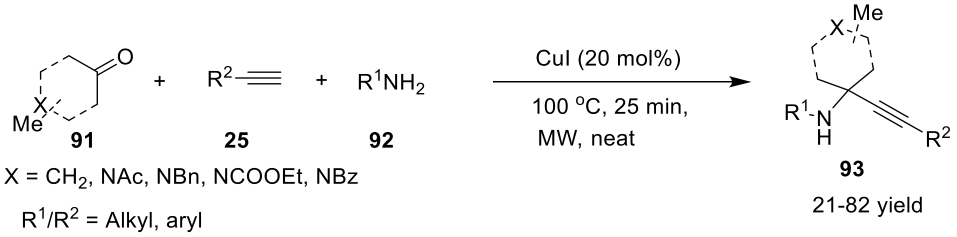
A direct intermolecular gold catalyzed coupling of ketones, secondary amines, and alkynes gave propargylamines **90** (Scheme 30).[39]

Scheme 30



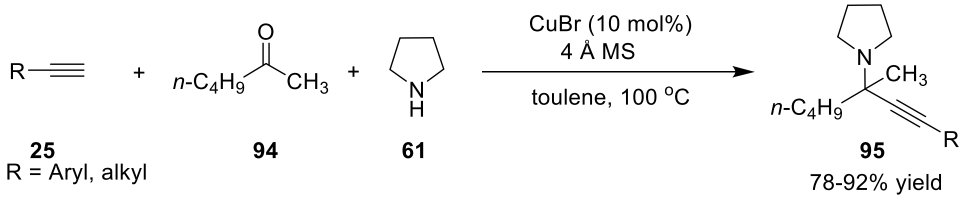
Van der Eycken *et al.* utilized CuI for the synthesis of propargylamines **93** under microwave irradiation (Scheme 31).[40]

Scheme 31



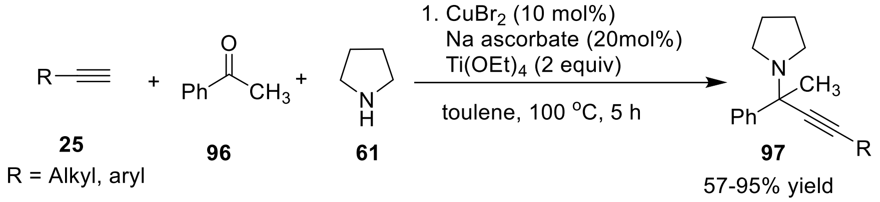
Ma *et al.* reported CuBr and molecular sieves in the synthesis of tetrasubstituted propargylamines **95** (Scheme 32).[41]

Scheme 32



Unactivated aromatic ketone **96**, alkyne **25** and amine **61** were converted to tetrasubstituted propargylamines **97** using CuBr$_2$, Ti(OEt)$_4$ and sodium ascorbate (Scheme 33).[42]

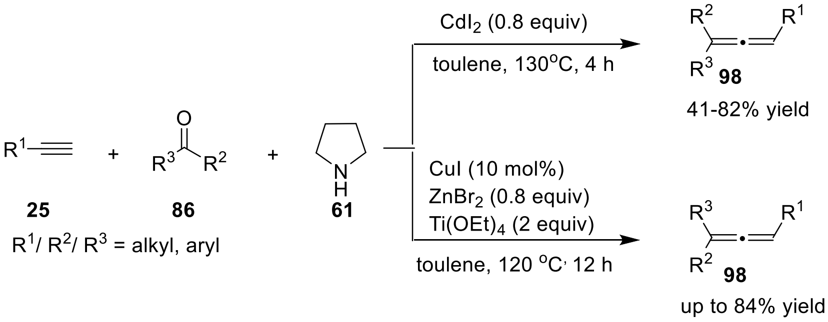
Scheme 33



1.1.9 Synthesis of racemic trisubstituted allenes

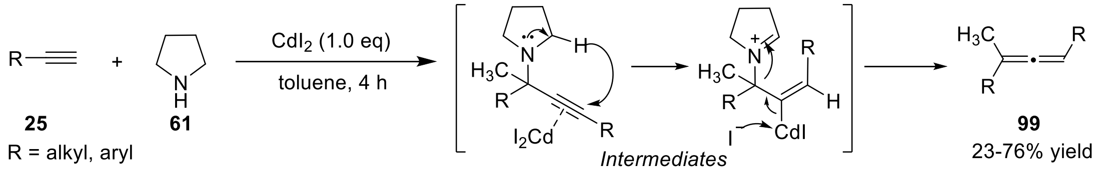
A cadmium iodide mediated one-pot synthesis of trisubstituted allenes using terminal alkynes **25**, ketones **86** and secondary amine **61** was reported (Scheme 34).[43]

Scheme 34



Also, the CdI_2 promoted synthesis of trisubstituted allenes **99** *via* tetrasubstituted propargylamines was reported (Scheme 35).[44]

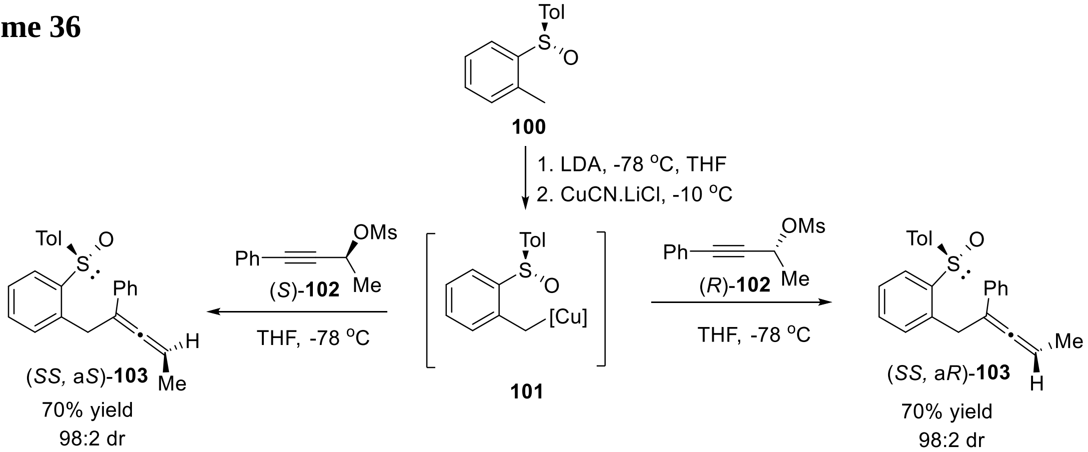
Scheme 35



1.1.10 Synthesis of trisubstituted chiral allene

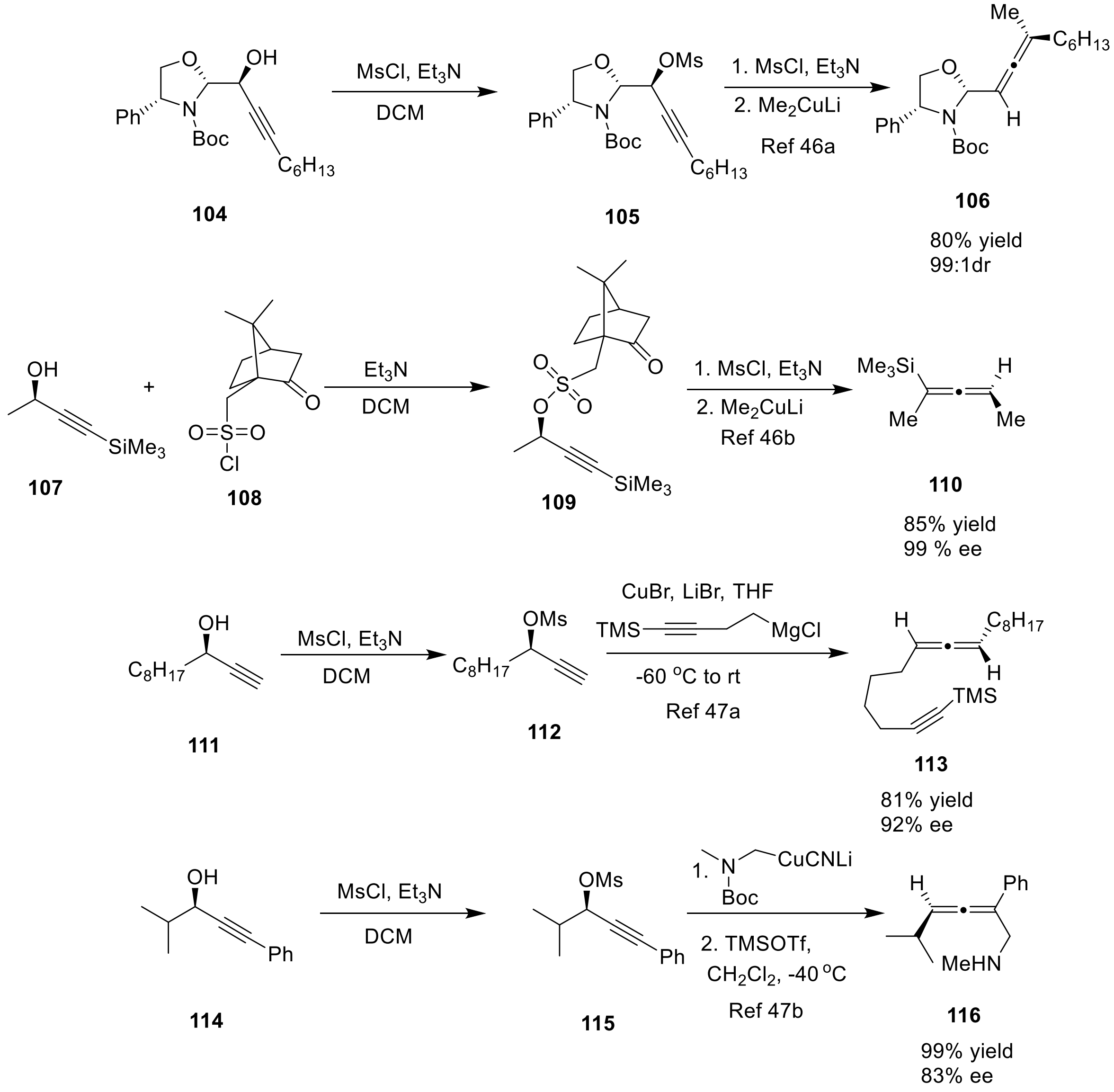
The copper complex **101** converted chiral propargyl derivatives **102** into the chiral trisubstituted allene **103** (Scheme 36).[45]

Scheme 36



Methods reported for the synthesis of disubstituted and trisubstituted chiral allenes by nucleophilic substitution reaction at propargylic position with various leaving groups are summarized in Chart 2.[46, 47]

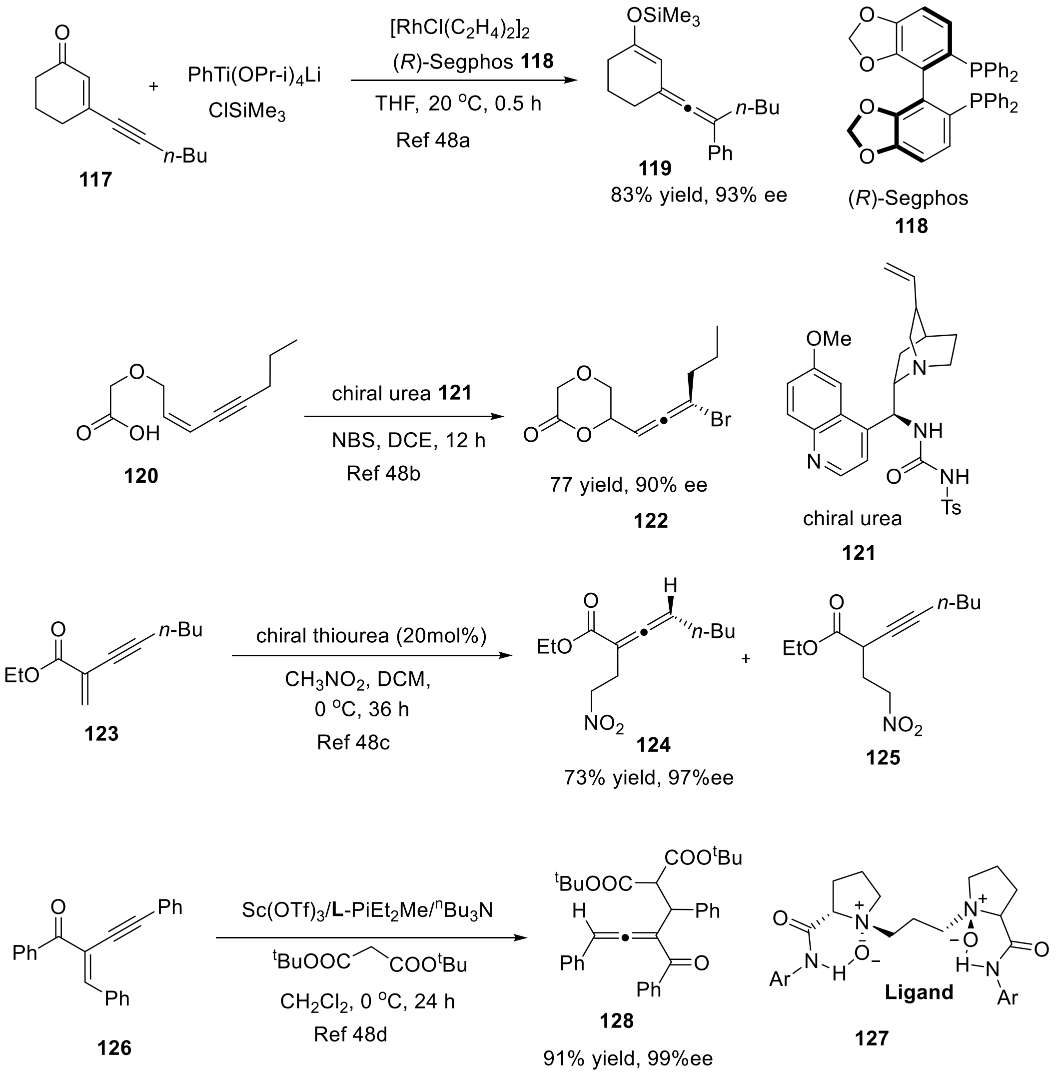
Chart 2



1.1.11. Syntheses of trisubstituted chiral allene derivatives from enynes

Synthesis of trisubstituted chiral allenes were also realized from various enyne derivatives by controlling contiguous axial and carbon center chirality through inter and intramolecular alkene addition as outlined in Chart 3.[48]

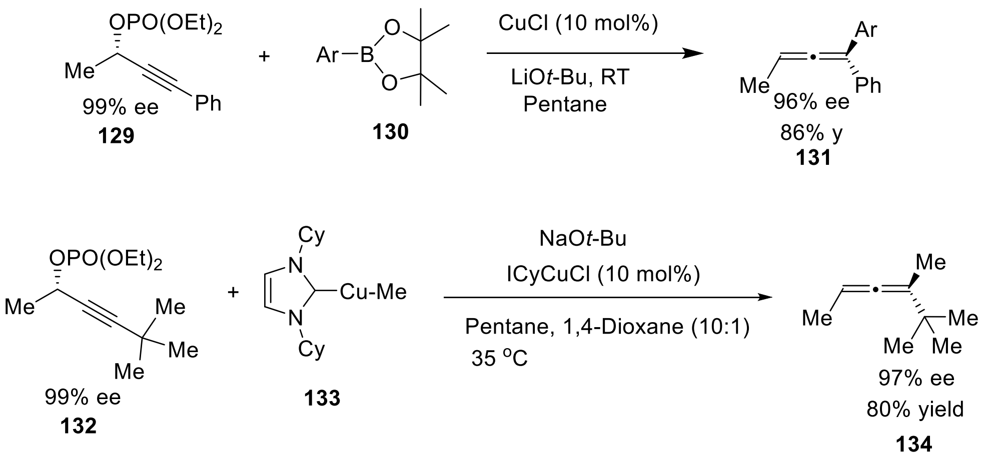
Chart 3



1.1.12 Chirality transfers from propargylic phosphates

An enantioselective synthesis reported for chiral trisubstituted allenes involves the use of propargylic phosphates and aryl boranes as starting material as outlined in Scheme 37.[49]

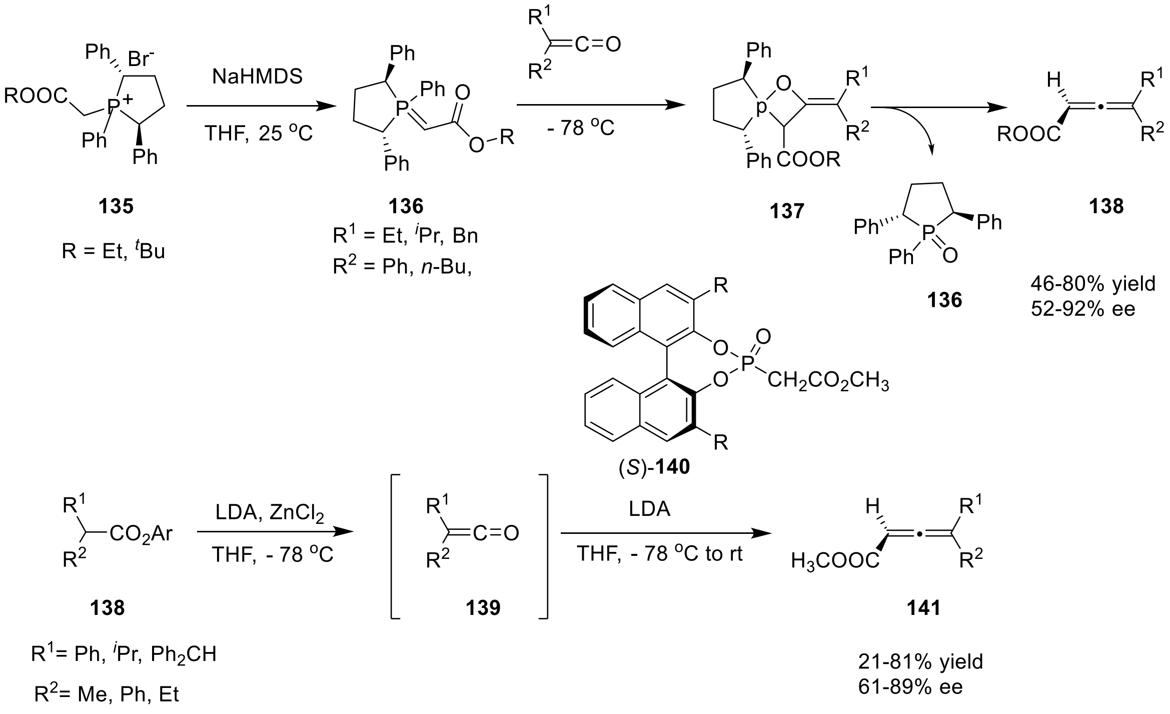
Scheme 37

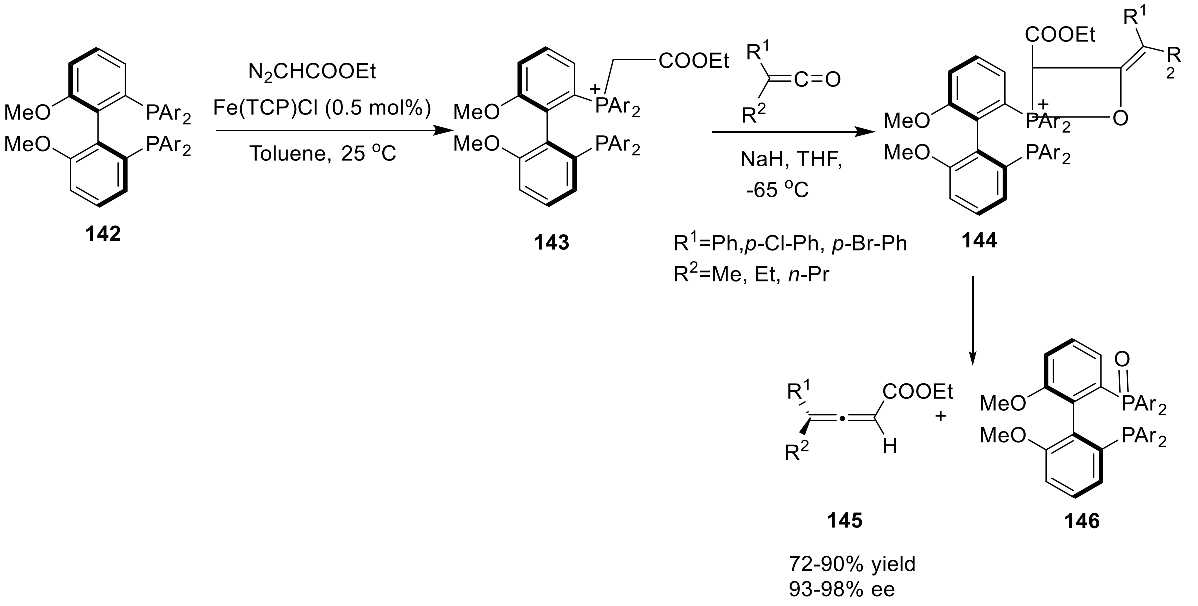


1.1.13 Chirality transfer by Wittig-type reactions

Synthesis of trisubstituted chiral allenes by Wittig-type reactions using ketene with organophosphate reagents were reported (Chart **5**).[50, 51, 52]

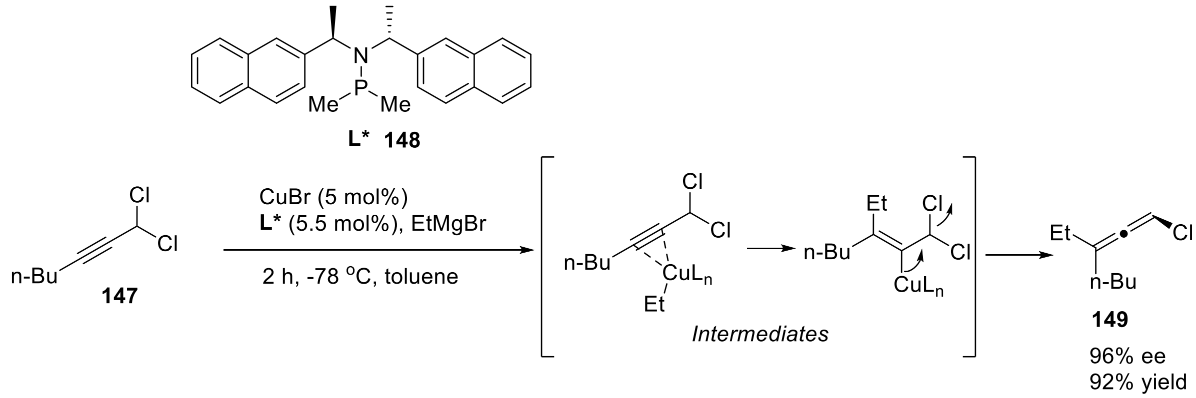
Chart 5





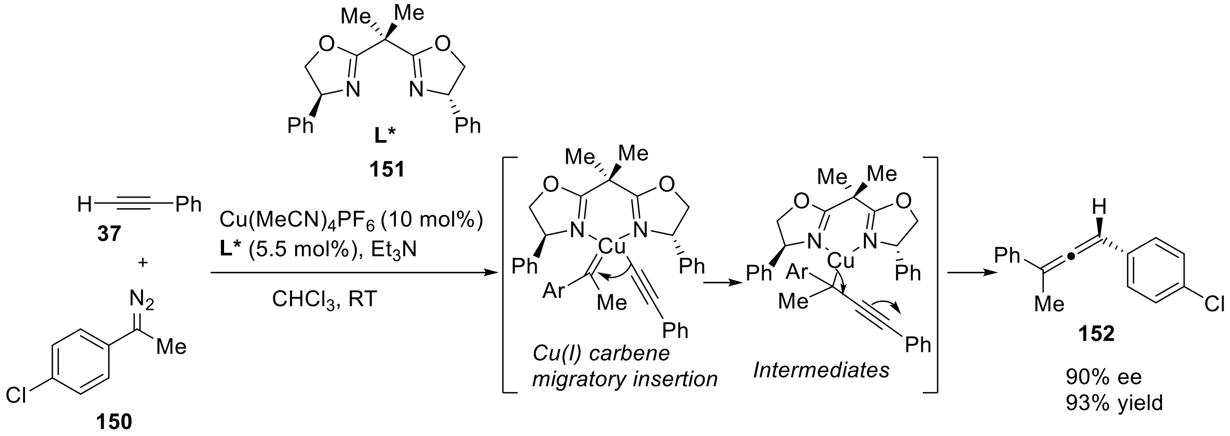
Recently, a copper catalyzed enantioselective synthesis of chiral trisubstituted chloro allenes **149** was reported (Scheme 38).[53]

Scheme 38



Very recently, Wang *et al* reported[54] the synthesis of highly enantioselective trisubstituted chiral allenes were obtained by copper catalyzed cross coupling of aryl diazoalkanes and terminal alkynes in presence of chiral bisoxazoline ligands (Scheme 39).

Scheme 39



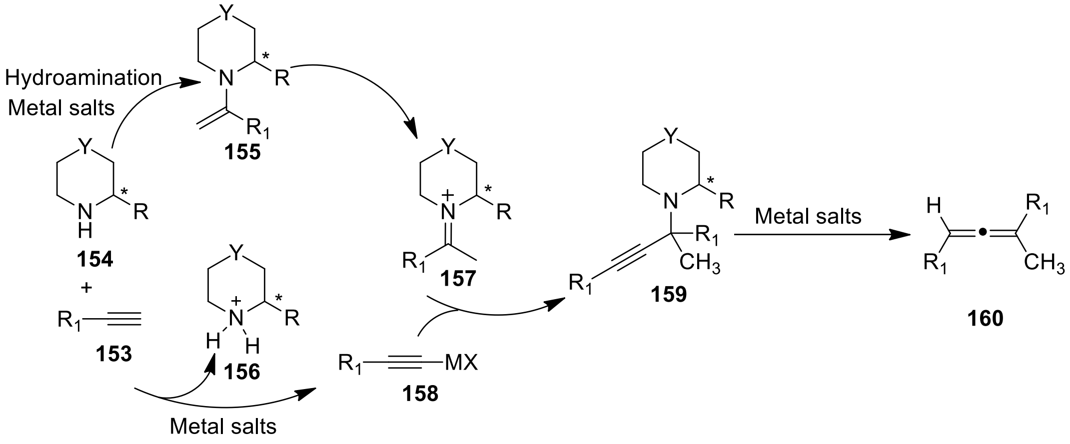
We have undertaken studies to examine the scope of the $ZnBr_2$ promoted enantioselective synthesis of chiral trisubstituted allene using N-methylcamphanyl piperazine. We have also examined the use of two different 1-alkynes and morpholine for this transformation. The results are described in the next section.

1.2 Results and Discussion

1.2.1 Effort towards the synthesis of trisubstituted chiral allenes

We have undertaken systematic studies on the methods of synthesis of propargylamine intermediates by *in situ* preparation of iminium ion, the corresponding enamine and alkynylmetal salts using chiral secondary amines and metal salts like ZnX_2 or CuCl and 1-alkynes (Scheme 40).

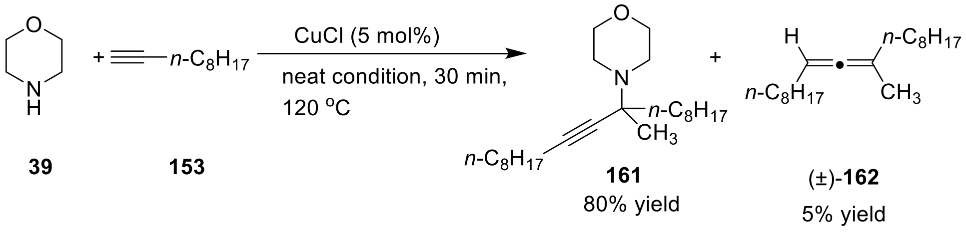
Scheme 40



Y= - O, CH_2, NCH_2Ph, NCH_3,

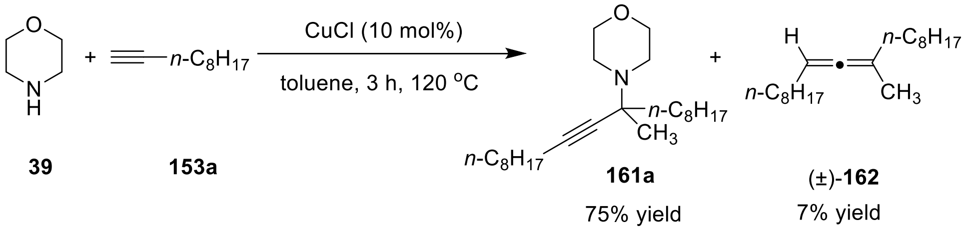
Initially, we have carried out the reaction using racemic morpholine **39**, CuCl and 1-decyne in neat condition for 30 mins at 120 °C and obtained the tetrasubstituted propargylamine **161** in 80% yield (Scheme 41).

Scheme 41



Also, when the reaction was performed in toluene using morpholine **39**, CuCl and 1-decyne, the tetrasubstituted propargylamine **161** in 75% yield (Scheme 42).

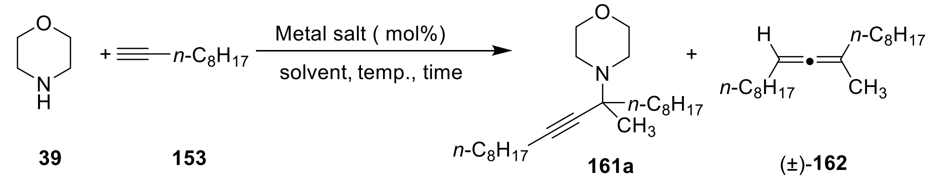
Scheme 42



We have also carried out the experiments using 1-decyne and morpholine with $ZnCl_2$ or $ZnBr_2$ at 120 °C. The propargylamine **161a** was not formed under these conditions (entries 1 and 2, Table 1) but it was formed in 15% yield in 24 h (entry 3, Table 1) when ZnI_2 was used and in 27% yield when $Zn(OTf)_2$ was used (entry 4, Table 1). Interestingly, when the reaction was carried out using $Zn(OTf)_2$ without using toluene 120 °C, the propargylamine **161a** was formed in 69% yield within 2 h (entry 5, Table 1). Further screening led to the observation that the cheaper CuCl plays the same role affording **161a** in 83% yield (entry 8, Table 1).

The propargylamine **161a** was also obtained in good yield using other copper halides like CuBr and CuI under this reaction condition along with some allene byproduct (entries 10 and 11, Table 1). The reaction temperature was also found to be crucial for this transformation. Elevating the temperature above 110 °C led to formation of more amounts of the trisubstituted allene **162a** (entry 9, Table 1), whereas lowering the temperature to 100 °C resulted in lower yields of the propargylamine product **161a** (entry 12, Table 1). However, experiments carried out at different temperatures and time interval conditions to obtain the allene as a major product in single pot operation were not successful.

Table 1. Reaction of morpholine and 1-Decyne with different metal salts to produce tetrasubstituted propargylamine[a,b,c]

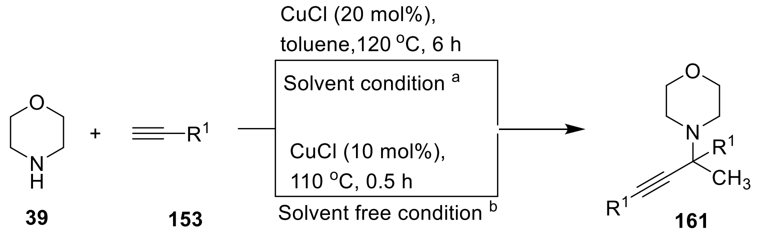


S.No	Solvent	Temp (°C)	MX_n	Mol (%)	Time (h)	161a Yield (%)
1	Toluene	120	$ZnCl_2$	5	24	-
2	Toluene	120	$ZnBr_2$	5	24	-
3	Toluene	120	ZnI_2	5	24	15
4	Toluene	120	$Zn(OTf)_2$	5	24	27
5	-	120	$Zn(OTf)_2$	5	2	69
6	Toluene	120	CuCl	20	6	80
7	-	110	CuCl	5	0.5	68
8	-	110	CuCl	10	0.5	83
9[b]	-	120	CuCl	10	0.5	71
10[b]	-	110	CuBr	10	0.5	79
11[b]	-	110	CuI	10	0.5	77
12	-	100	CuCl	10	0.5	69
13	-	100	$Cu(OTf)_2$	5	0.5	92

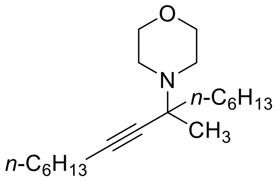
[a] The reactions were carried out by using morpholine **39** (1.0 mmol) and 1-decyne **153a** (2.2 mmol).
[b] The allene **162a** was formed in 7-12 % yields as determined by ^{1}H NMR spectral analysis of the crude reaction mixture.

We have observed that the copper (II) salts CuX_2 (Cl or Br) are not effective but the $Cu(OTf)_2$ afforded the product **161a** in 92% yield within 0.5 h at 100 °C (entry 13, Table 1). Although, the use $Cu(OTf)_2$ gave better results, we have explored the scope of the reaction using CuCl ((entries 6 and 8, Table 1) as it is less expensive.

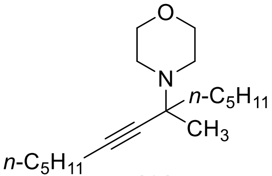
Table 2. Synthesis of propargylamine using cyclic amines and 1-alkyne.[a,b,c]



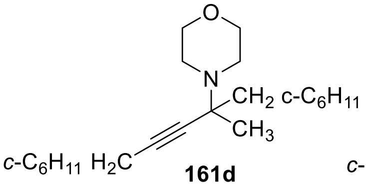
R^1
153a = n-C_8H_{17} **153d** = c-$C_6H_{11}CH_2$ **153g** = Ph-$(CH_2)_2$ **153j** = CN-$(CH_2)_3$-
153b = n-C_6H_{13} **153e** = c-C_6H_{11} **153h** = Ph-$(CH_2)_3$ **153k** = MeO-$(CH_2)_8$-
153c = n-C_5H_{11} **153f** = Ph **153i** = Ph-$(CH_2)_4$ **153l** = TBSO-$(CH_2)_4$-



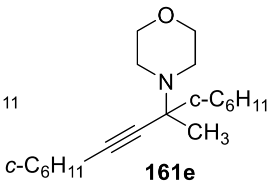
161b
73% yield [a]
75% yield [b]



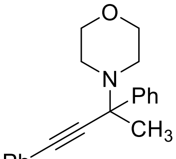
161c
77% yield [a]
79% yield [b]



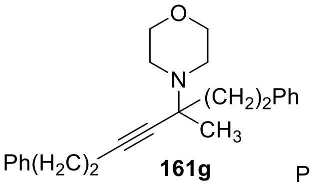
161d
79% yield [a]
82% yield [b]



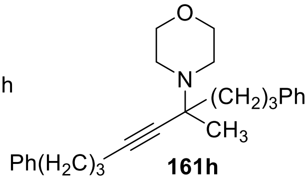
161e
73% yield [a]
79% yield [b]



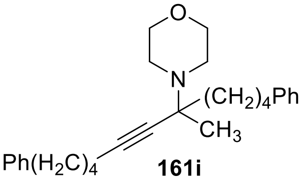
161f
29% yield [b]



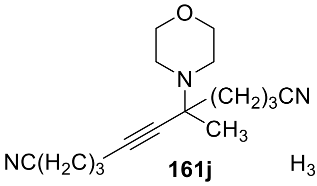
161g
82% yield [a]
85% yield [b]



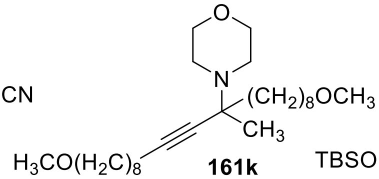
161h
84% yield [a]
82% yield [b]



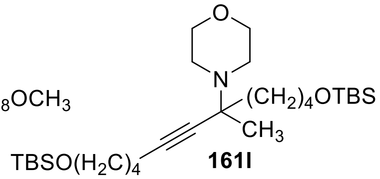
161i
81% yield [a]
83% yield [b]



161j
74% yield [a]
81% yield [b]



161k
69% yield [a]
73% yield [b]



161l
62% yield [a]
69% yield [b]

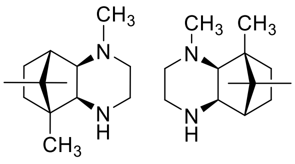
[a] The reactions were carried out by using amine (1.0 mmol) and 1-alkyne (2.2 mmol) in toluene (3mL) at 120 °C for 6 h. [b] The reactions were carried out by using amine (1.0 mmol) and 1-alkyne (2.2 mmol) at 110 °C for 0.5 h. [c] Yields of propargylamines. [d] In this case, the experiment in toluene gave the propargylamine product containing some unidentified impurities.

We have explored the scope of the reaction using CuCl in toluene (Table 1, entry 6) and also without using toluene (Table 1, entry 8). The results are summarized in Table 2.

The reaction using morpholine and other 1-alkynes like 1-octyne **153b** and 1-heptyne **153c** gave the corresponding tetrasubstituted propargylamines **161b** and **161c** in 73-79% yields. Reaction using substituted 1-alkynes such as 3-cyclohexyl-1- propyne (**153d**), 2-cyclohexyl-1-acetylene (**153e**), phenyl acetylene (**153f**), and 4-phenyl-1-butyne (**153g**), pent-4-yn-1-ylbenzene (**153h**), and hex-5-yn-1-ylbenzene (**153i**) furnished the corresponding products with up to 85% yield. The functionalized alkynes, like 6-cyano-1-hexyne (**153j**), 1-methoxy-10-decyne (**153k**) and 1-tert-butyldimethylsilyloxy-5-hexyne (**153l**) afforded the corresponding propargylamines in 74-81% (**161j**), 69-73% (**161k**) and 62-69% (**161l**) yields, respectively.

1.2.2 Synthesis of chiral tetrasubstituted propargylamines using 1-alkynes and chiral camphanyl piperazine derivatives

It was of interest to us to examine whether the hydroamination reaction under these conditions would give the corresponding chiral propargylamines with diastereoselectivity if enantiomerically pure chiral amines are used. Accordingly, we have also examined the use of the readily accessible optically active chiral secondary amines **10** and **11** (Figure 1).[29, 33] The chiral amine **10** failed to give the corresponding propargylamine under these conditions (Scheme 46), presumably due to sterically crowded nature of the amine **10**.

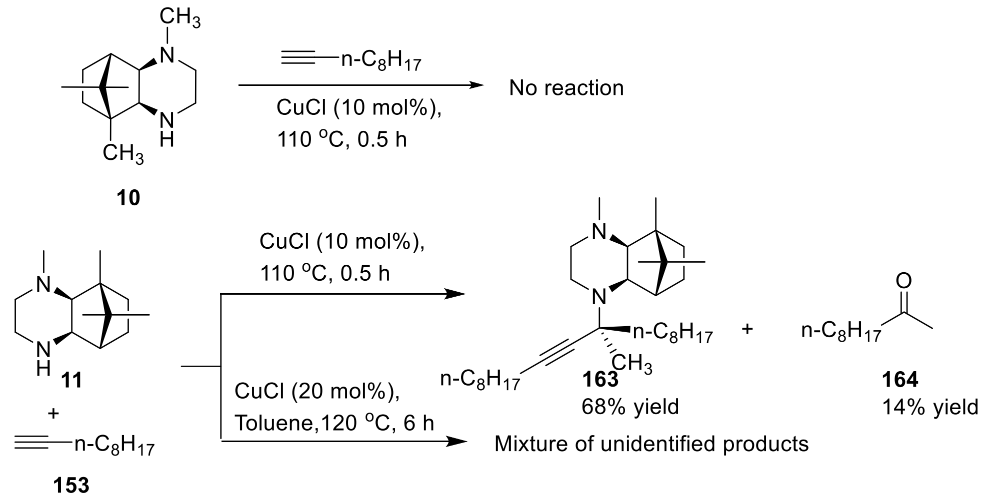


10 **11**

Figure 1. Chiral amines (**10** and **11**) used in CuCl catalyzed chiral propargylamine synthesis.

Whereas, the optically active N-methyl camphanyl piperazine **11** gave unidentified mixture of products in toluene but under solvent free condition the chiral propargylamine **163** was obtained in 68% yield with excellent diastereoselectivity along with the ketone **164** (Scheme 43).

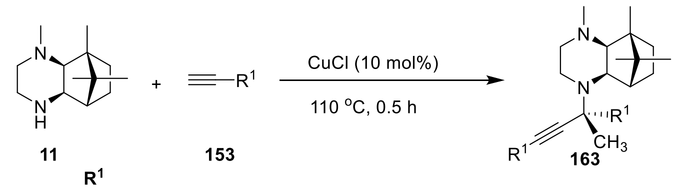
Scheme 43



We have carried out several experiments using the chiral N-methyl camphanyl piperazine **11** with different alkynes and the results are summarized in Table 3. The reaction of 1-decyne **153a**, 1-octyne **153b** and 1-heptyne **153c** with N-methyl camphanylpiperzine **11** led to the corresponding trisubstituted propargylamines **163b-163c** in upto 62-64% yields.

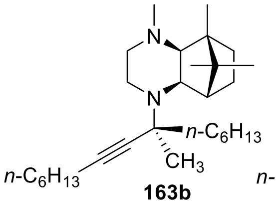
Reaction of N-methyl camphanylpiperzine **11** with substituted alkynes such as 2-cyclopentyl-1-acetylene (**153d**), 3-cyclohexyl-1- propyne (**153e**), ethynylcyclopentane (**153f**), ethynylcyclhexane (**153g**), 4-phenyl-1-butyne (**153h**), pent-4-yn-1-ylbenzene (**153i**), and hex-5-yn-1-ylbenzene (**153j**) proceeded to give the corresponding propargylamine products with up to 79% yield. Also, functionalized alkynes, such as 6-cyano-1-hexyne (**153k**), 1-methoxy-10-decyne (**153l**), and 1-tert-butyldimethylsilyloxy- 5-hexyne (**153m**) gave the corresponding propargylamines in up to 78% yields respectively (Table 3, **163k**, **163l** and **163m**).

Table 3. Synthesis of propargylamine using 1-alkyne, N-methyl camphanyl piperzine 11 and CuCl in the neat condition.

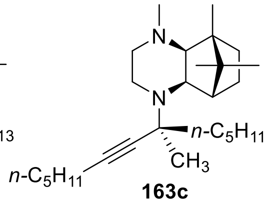


R^1

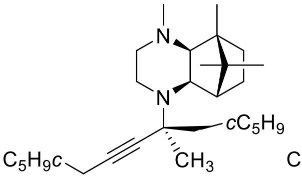
163a = n-C_8H_{17}
163b = n-C_6H_{13}
163c = n-C_5H_{11}
163d = c-$C_5H_9CH_2$
163e = c-$C_6H_{11}CH_2$
163f = c-C_5H_9
163g = c-C_6H_{11}
163h = Ph-$(CH_2)_2$
163i = Ph-$(CH_2)_3$
163j = Ph-$(CH_2)_4$
163k = CN-$(CH_2)_3$-
163l = MeO-$(CH_2)_8$-
163m = TBSO-$(CH_2)_4$-


163b

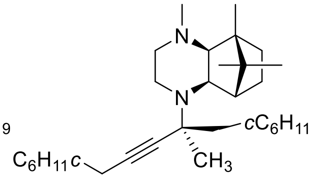
64% yield


163c

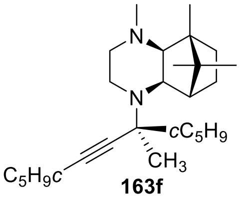
62% yield


163d

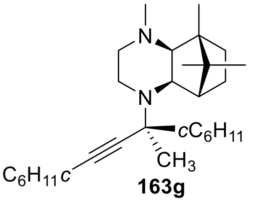
55% yield


163e

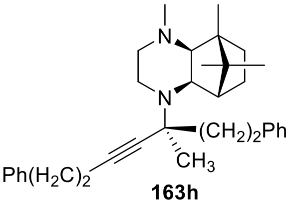
61% yield


163f

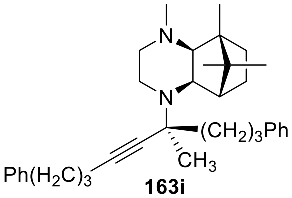
52% yield


163g

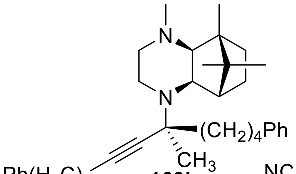
59% yield


163h

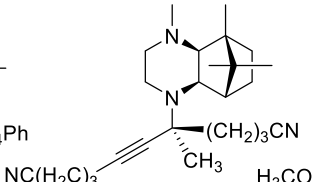
76% yield


163i

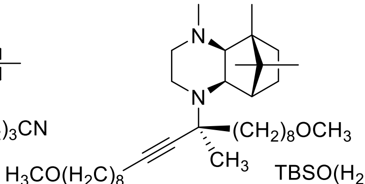
75% yield


163j

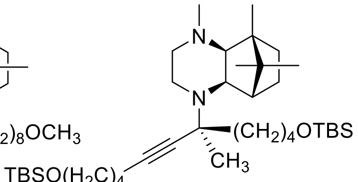
79% yield


163k

60% yield


163l

78% yield

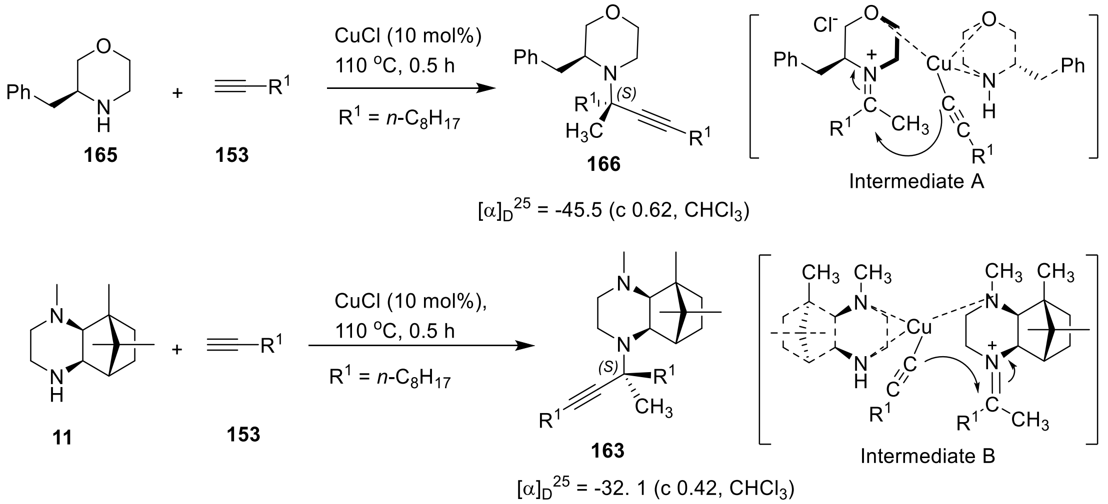

163m

62% yield

^{a}The reactions were carried out by using camphanyl piperzine (1.0 mmol) and 1-alkyne (2.2 mmol). ^{b}Isolated yield. ^{c}The diastereoselectivity was determined by ^{1}H NMR analysis of the crude reaction mixture.

Previously, a method has been developed for synthesis of chiral tetrasubstituted propargylamines *via* formation of intermediate imine using chiral secondary amine **165** and the configurations at the newly formed stereogenic center was assigned as (*S*) by X-ray analysis (Scheme 44).[55] Hence, we have assigned the stereogenic center of N-methylcamphanyl propargylamines as (*S*) configuration in accordance with the formation of intermediate imine as outlined in Scheme 44.[55]

Scheme 44



$[\alpha]_D^{25}$ = -45.5 (c 0.62, $CHCl_3$)

$[\alpha]_D^{25}$ = -32. 1 (c 0.42, $CHCl_3$)

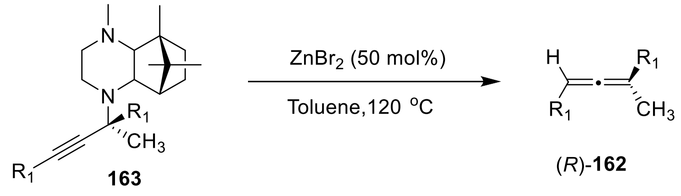
1.2.3 Synthesis of chiral trisubstituted allenes from the tetrasubstituted propargylamines

As discussed earlier, the trisubstituted allenes are obtained as side products in 7% to 12% yield in some experiments (Table 1). The propargylamines are also useful precursors for allenes. For example, the propargylamines can be readily converted to allenes using $ZnBr_2$ in toluene, at 120° C by a procedure developed in this laboratory.[31] We have observed that the propargylamine **163a** reacts with $ZnBr_2$ (0.5 mmol), at 120 ^{0}C to give the allene (*R*)-**162a** in 89% yield (Table 4).

Also, the propargylamines **163b-163j**, obtained from substituted alkynes reacts with $ZnBr_2$ to give the corresponding allenes **162b-162j** in up to 90% yield. The propargylamines substituted with functionalized groups also afforded the desired allene **162k** and **162l** in 88-

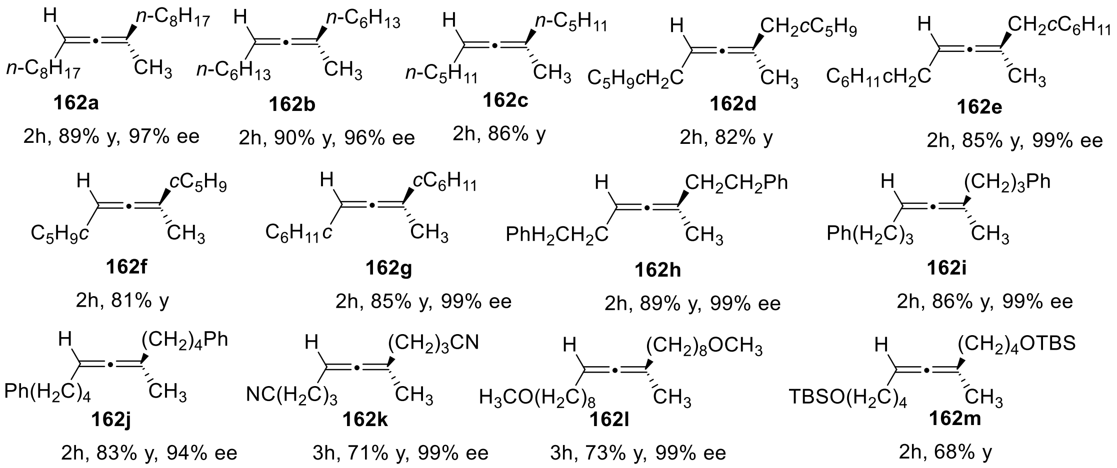
92% yields. In addition, the propargylamine **163m** containing cyano group upon reaction with $ZnBr_2$ (0.5 mmol) gave the allene **162m** in 88% yield (Table 4).

Table 4. $ZnBr_2$ promoted synthesis of chiral allenes from corresponding propargylamines.[a,b]



R^1

163a = n-C_8H_{17}
163b = n-C_6H_{13}
163c = n-C_5H_{11}
163d = c-$C_5H_9CH_2$
163e = c-$C_6H_{11}CH_2$
163f = c-C_5H_9
163g = c-C_6H_{11}
163h = Ph-$(CH_2)_2$
163i = Ph-$(CH_2)_3$
163j = Ph-$(CH_2)_4$
163k = CN-$(CH_2)_3$-
163l = MeO-$(CH_2)_8$-
163m = TBSO-$(CH_2)_4$-

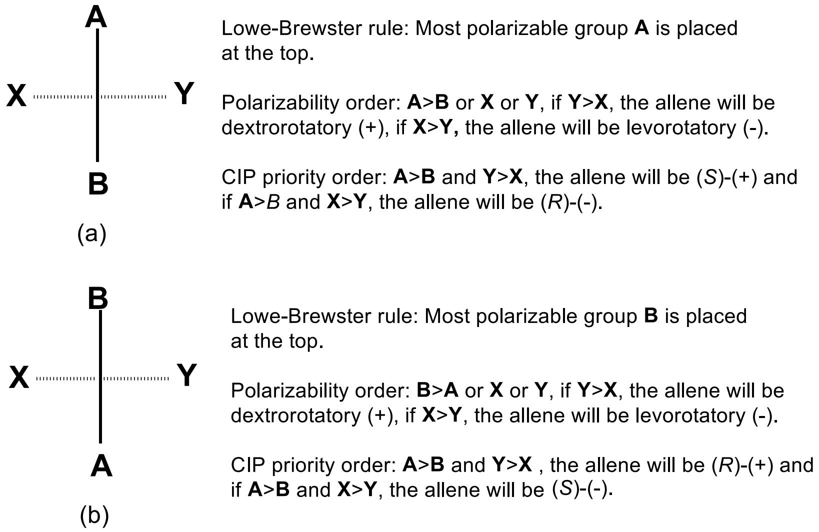


162a 2h, 89% y, 97% ee
162b 2h, 90% y, 96% ee
162c 2h, 86% y
162d 2h, 82% y
162e 2h, 85% y, 99% ee
162f 2h, 81% y
162g 2h, 85% y, 99% ee
162h 2h, 89% y, 99% ee
162i 2h, 86% y, 99% ee
162j 2h, 83% y, 94% ee
162k 3h, 71% y, 99% ee
162l 3h, 73% y, 99% ee
162m 2h, 68% y

[a]The reactions were carried out by taking propargylamine **163** (1 mmol) in toluene (3 mL) with $ZnBr_2$ (0.5 mmol). [b]Isolated yield of allene. [c]ee was determined by chiral HPLC analysis.

All the optically active allenes obtained by using chiral amines **11** are levorotatory based on which the absolute configurations of the major enantiomer of the chiral allenes are assigned as *R* as per the Lowe-Brewster rule[56a,b] and Taft[56c] and Runge[56d,e] revised polarizabilty parameters.[56f] However, since there is some ambiguity in assigning configuration of trisubstituted allenes, it is desirable to discuss this assignment of (*R)* configuration for the trisubstituted allenes reported here.

The chiral allenes may be considered to have the structures with substituents **A**, **B** at one allene end and groups **X**, **Y** at the other allene end as depicted in Figure 3.[56a] As per Lowe model, the group with highest polarity **A** to be placed at the top (Structure (a), Figure 3) and the other group **B** at this allene end also above the plane with the **X**, **Y** groups placed in the sides below the plane. The Lowe rule predicts the $[\alpha]_D$ of the allene will be levorotatory (-) if the polarizability of the group **X**>**Y** and the $[\alpha]_D$ will be dextrorotatory (+) if the polarizability of **Y**>**X**. For disubstitued chiral allenes, the Cahn-Ingold-Prelog (CIP) priority rules will be in the order **A**>**B**(=H), **X**>**Y**(=H), the allene with (*R)* configuration will have (-)$[\alpha]_D$ and the corresponding enantiomer will have (+)$[\alpha]_D$ value with (*S*) configuration. This will be also the case for enantiomerically enriched trisubstituted allenes where the expected Lowe-Brewster polarity order and the CIP priority order are same as in disubstituted allenes. Therefore, the trisubstituted enantiomerically enriched allene samples with (+)$[\alpha]_D$ values could be assigned (*S*) configuration and samples with (-)$[\alpha]_D$ could be assigned (*R*) configuration if the Lowe-Brewster-Taft-Runge[56a-f] polarizability order of the substituents and the corresponding CIP priority order are the same [Figure 3. Structure (a)]. Hence, the trisubstituted allene samples with (-)$[\alpha]_D$ reported here are assigned (*R)*-(-) configuration. However, in an earlier report (*R)*-(+) configuration was assigned for the enantiomerically enriched chiral allene with same substituents as in (Ph/CH_3 and Ph/H) with $[\alpha]_D$ +122.4 which should be corrected as (*S*)-(+).[56h] Presumably, the (*R)*-(+) configuration was assigned erroneously in the earlier report by comparison with incorrect drawings in a reaction scheme for the allene with substituents Ph/*n*-Bu and Ph/H) and $[\alpha]_D$ +251 for which the original authors did not assign the configuration.[56g]



Lowe-Brewster rule: Most polarizable group **A** is placed at the top.

Polarizability order: **A**>**B** or **X** or **Y**, if **Y**>**X**, the allene will be dextrorotatory (+), if **X**>**Y,** the allene will be levorotatory (-).

CIP priority order: **A**>**B** and **Y**>**X**, the allene will be (*S*)-(+) and if **A**>*B* and **X**>**Y**, the allene will be (*R*)-(-).

Lowe-Brewster rule: Most polarizable group **B** is placed at the top.

Polarizability order: **B**>**A** or **X** or **Y**, if **Y**>**X**, the allene will be dextrorotatory (+), if **X**>**Y**, the allene will be levorotatory (-).

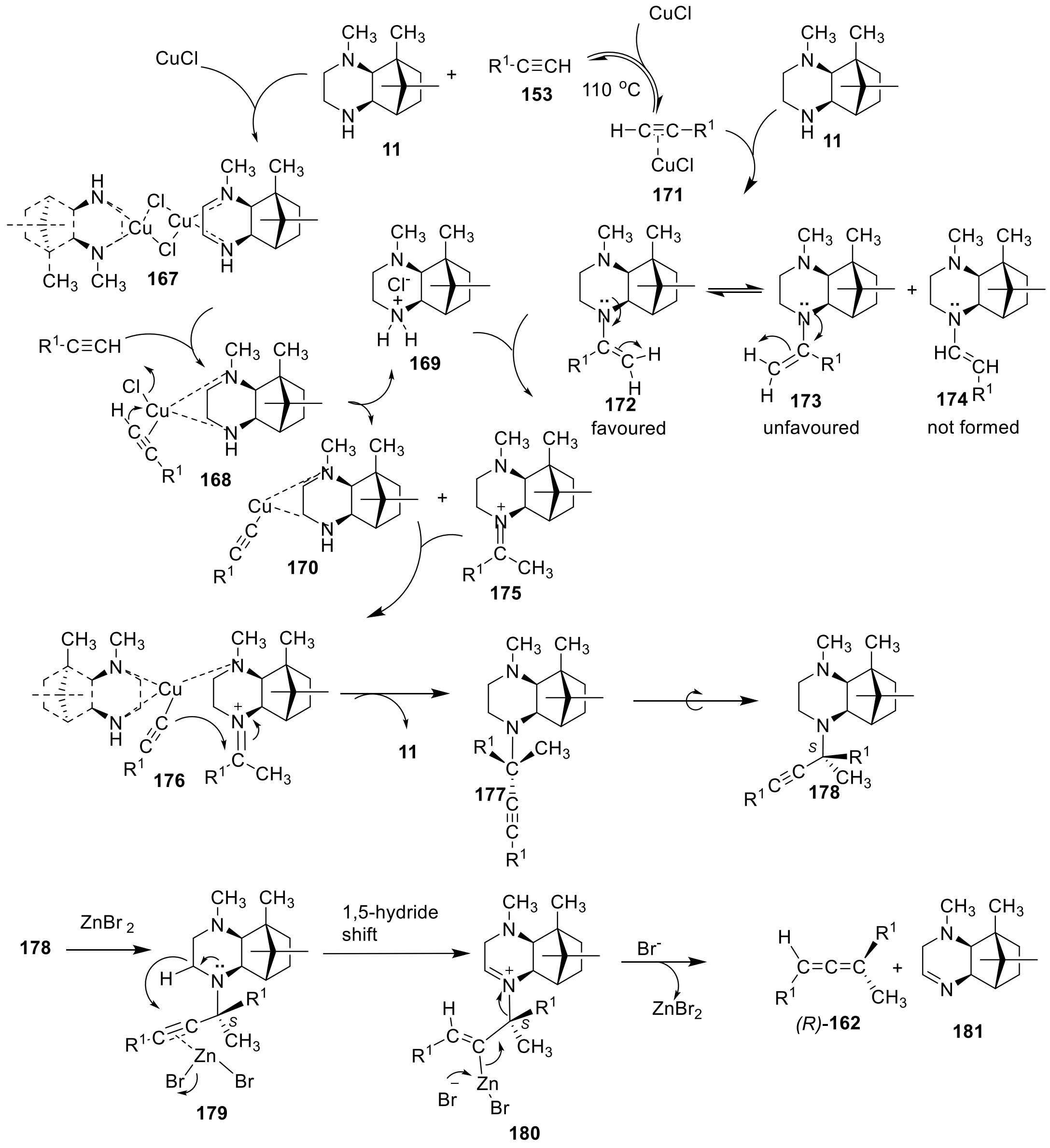
CIP priority order: **A**>**B** and **Y**>**X** , the allene will be (*R*)-(+) and if **A**>**B** and **X**>**Y**, the allene will be (*S*)-(-).

Figure 3. Configuration of allenes and sign of $[\alpha]_D$ values based on Brewster-Lowe-Taft-Runge polarizability parameters and Cahn-Ingold-Prelog (CIP) priority rules

An interesting possibility is that a group may have higher priority as per the CIP rules but may not have highest polarizability [Figure 3, Structure (b)]. In such cases, the allene with (*R)* configuration will give (+)$[\alpha]_D$ and its enantiomer will give (-)$[\alpha]_D$ values as per Lowe-Brewster rule. There are several reports assigning (*R*)-(+) and (*S*)-(-) configurations based on reaction mechanisms but these authors did not consider the expected Lowe-Brewster and Taft-Runge polarizability order along with the CIP priority order for the substituents and also did assign configurations based on techniques like the X-ray structure analysis.[57a-b] Such ambiguity also remains in assigning configurations for tetrasubstituted chiral allenes.[57c] In this regard, it may be of interest to note that recently, an interesting spontaneous resolution of tetrasubstituted allenic phosphinate derivatives was reported and the enantiomers were characterized by X-ray structure analysis but the samples did not have significant $[\alpha]_D$.[57d] It is possible that the difference in polarizability of substituents is small in this case.

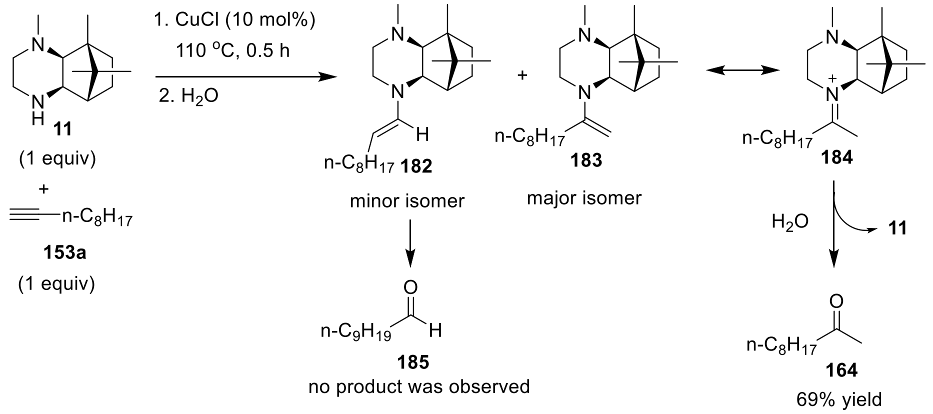
The formation of propargylamines in the reaction of 1-alkynes and chiral N-methyl camphanyl piperazines followed by their conversion to allene can be rationalized by the mechanism outlined in Scheme 45. The reaction would proceed through *in situ* formation of both electrophile (iminium ion) and nucleciophile (alkynyl metal) intermediates using 1-alkynes and amines. Initially chiral piperazine **11** would react with CuCl to form the dimeric copper complex **167**.[58] Then, reaction with 1-alkyne could give the intermediate complex **170** which could react with the intermediate **175** (formed *in situ* by the Markovnikov hydroamination of chiral piperazine and alkyne, which could tautomerize to ketiminium species) to generate the intermediate **176**.[59] Intramolecular attack of alkynyl copper from bottom face of the iminium group would lead to the new (*S*)-stereogenic center at the propargylamine product **178** which could react with $ZnBr_2$ to give the intermediate **179** and undergo a hydride shift to form the chiral allene (*R*)-**162** *via* the intermediate **180** (Scheme 45).[60] We have also found that the imine byproducts **181** could be easily converted *in situ* to the corresponding chiral piperazine **11** in 72% yields by simple sodium borohydride reduction in methanol.

Scheme 45. Mechanism for the formation of chiral propargylamines using chiral amine and their conversion to chiral allenes



We have observed that when the reaction was carried out with a 1:1 mixture of 1-alkynes and amines in the presence of CuCl followed by aqueous workup, the corresponding ketone derivative was formed in 69% yield along with propargylamine in 21% yield with 99:1 dr (Scheme 46).

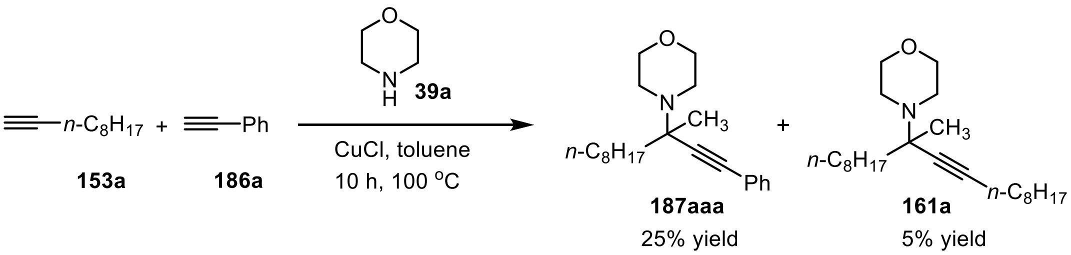
Scheme 46



1.2.4 Synthesis of trisubstituted allenes from tetrasubstituted propargylamine using two different 1-alkynes, and morpholine

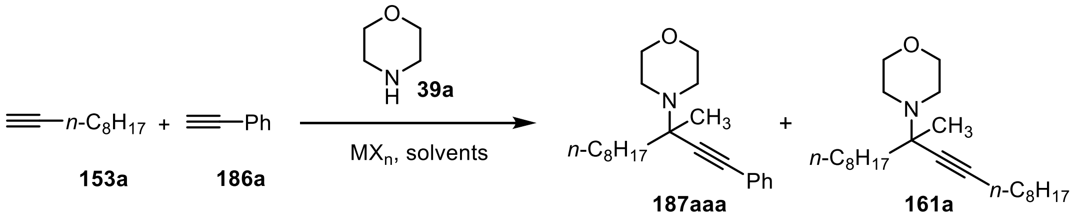
We have also explored the scope of the tetrasubstituted propargylamines synthesis using two different 1-alkynes. Initially, the reaction of phenylacetylene, 1-decyne, morpholine and copper chloride was carried out and the tetrasubstituted propargylamine **187aaa** was isolated in 25% yield along with the propargylamine **161a** in 5% yield (Scheme 47).

Scheme 47



A variety of copper salts and solvents were screened as shown in Table 5, Whereas in dioxane solvent gave the propargylamine **187aaa** in 28% yield besides **161a** (entry 1, Table 5). The propargylamine product **187aaa** was obtained in 65% yield along with **161a** in 7% yield in toluene solvent (entry 2, Table 5).

Table 5. Reaction of morpholine and 1-decyne with different metal salts to produce tetrasubstituted propargylamine[a]

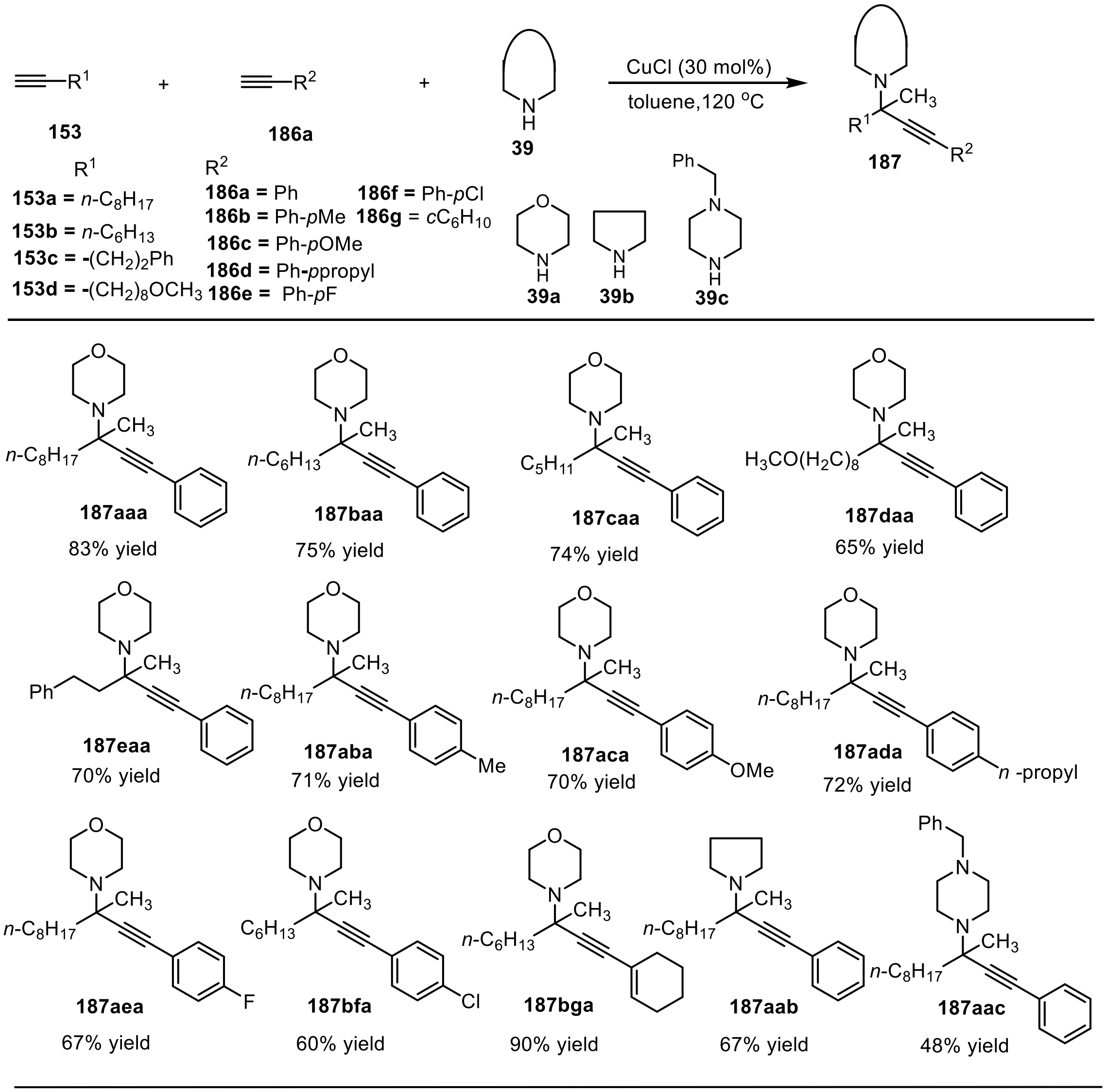


entry	solvent	temp (°C)	MX_n	mol (%)	time (h)	187aaa (%)[b]	161a (%)[c]
1	dioxane	110	CuCl	10	15	28	5
2	toluene	120	CuCl	10	8	65	7
3	toluene	120	CuBr	10	10	27	5
4	toluene	120	CuI	10	10	58	<5
5	dioxane	100	CuI	30	12	62	8
6	toluene	120	CuCl	30	8	83	10
7	toluene	120	ZnI_2	50	15	10	-
8	toluene	120	$ZnBr_2$	50	24	-	-

[a]The reactions were carried out by using morpholine **39a** (1.0 mmol), 1-decyne **153a** (1.0 mmol) and phenylacetylene (1.0 mmol). [b]Yields of propargylamine **187aaa**. [c]The propargylamine **161a** was formed in 5-10% yields as determined by NMR spectral analysis.

When the reaction was run by using copper bromide, and copper iodide the afforded tetrasubstituted propargylamine yields were poor to moderate (entries 3, 4 and 5, Table 5). The propargylamine **187aaa** was formed in 83% yield along with propargylamine **161a** in 10% yield when the CuCl loading increased to 30 mol% under these conditions (entry 6, Table 5). Whereas other salts like ZnI_2 and $ZnBr_2$ did not afford the propargylamine **187aaa** (entries 7 and 8, Table 5).

Table 6. Synthesis of propargylamine using cyclic amines and two different 1-alkynes.[a,b]



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[a]The reactions were carried out by using cyclic amines **39** (1.0 mmol), aliphatic 1-alkynes **153** (1.0 mmol), and aromatic 1-alkynes **186** (1.0 mmol) in toluene at 120 °C for 8-12 h. [b]Yields of tetrasubstituted propargylamine **187**.

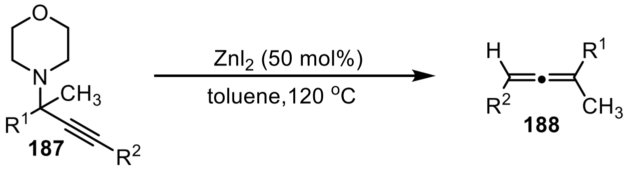
The reactions were tried using different substrates, under optimized conditions (entry 6, Table 5). The reaction using aliphatic 1-alkynes such as **153a**, **153b**, **153c**, **153d**, and **153e** with phenylacetylene also gave the desired products **187aaa**, **187baa**, **187caa**, **187daa**, and

187eaa in 65-83% yield. When the reaction was carried out using 1-decyne as the common reactant with Me, OMe, and *n*-propyl substituted phenylacetylenes (**186b**, **186c**, and **186d**), the tetrasubstituted propargylamines **187aba**, **187aca**, and **187ada** in 70-72% yields. Whereas F, and Cl substitution at the *para* position of phenylacetylene (**186e** and **186f**) furnished the corresponding products **187aea** and **187bfa** with 60-67% yield. Also, the vinyl 1-alkyne **186g** gave the tetrasubstituted propargylamine **187bga** in 90% yield.

We have also screened the different cyclic secondary amines. When the reaction was carried out with phenylacetylene **186a**, 1-decyne **153a**, and pyrrolidine **39b** in toluene condition at 120 °C, the tetrasubstituted propargylamine **187aab** was obtained in 67% yield. However, N-phenyl piperazine could also be furnished the propargylamine **187aac** with 48% yield (Table 6).

The propargylamines are also useful precursors for conversion to allenes. For example, the propargylamines are readily converted to allenes using ZnI_2 in toluene, at 120 °C by a procedure developed in this laboratory (Table 7). We have observed that the propargylamines **187aaa**, **187baa**, **187caa**, **187daa** and **187eaa** react with ZnI_2 (0.5 mmol), at 120 ^{0}C to give the allenes **188aa**, **188ba**, **188ca**, **188da** and **188ea** in 65-89% yields (Table **6**). Also, the propargylamines **187aba**, **187aca**, and **187ada** obtained from substituted alkynes react with ZnI_2 to give the corresponding allenes **188ab**, **188ac**, and **188ad** in up to 75-85% yields (Table 7).

Table 7. Synthesis of trisubstituted allenes from the tetrasubstituted propargylamines 187.[a,b]

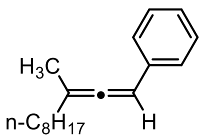


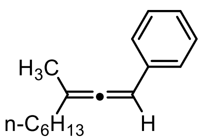
R^1

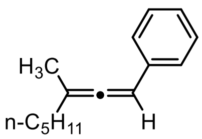
187a = n-C_8H_{17}
187b = n-C_6H_{13}
187c = $-(CH_2)_8OCH_3$
187d = $-(CH_2)_2Ph$

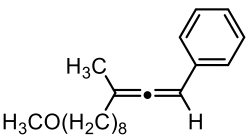
R^2

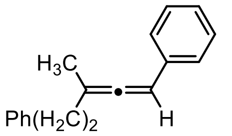
187a = Ph
187b = Ph-*p*Me
187c = Ph-*p*OMe
187d = Ph-*p*propyl
187e = Ph-*p*F
187f = Ph-*p*Cl
187g = *c*C_6H_{10}

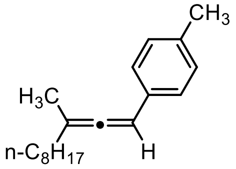

188aa
2 h, 89% y

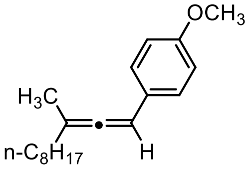

188ba
2 h, 85% y

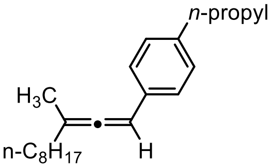

188ca
2 h, 82% y

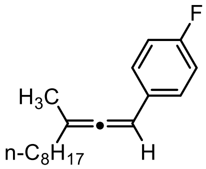

188da
2 h, 65% y

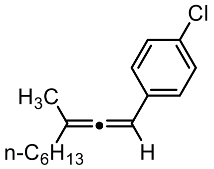

188ea
2h, 72% y

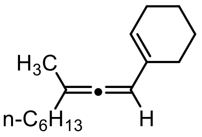

188ab
3h, 79% y


188ac
2h, 85% y


188ad
3h, 75% y


188ae
2h, 80% y


188bf
2h, 70% y

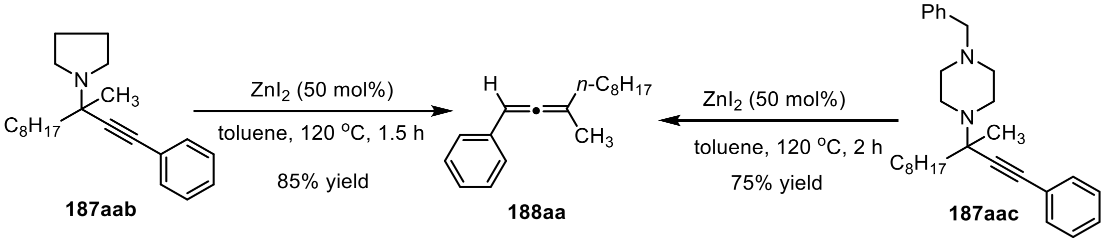

188bg
2 h, 89% y

[a] The reactions were carried out by using propargylamine (1 mmol) which obtained from morpholine **39a** in toluene (3 mL) with ZnI_2 (0.5 mmol) at 120 °C.

Also, the propargylamine **187aea** and **187bfa** containing fluoro and chloro group upon reaction with ZnI_2 (0.5 mmol) gave the allene **188ae** and **188bf** in 70-80% yield (Table **7**). In addition, the propargylamine **187bga** also afforded the desired allene **188bg** in 89% yield. Also, the propargylamines **187aab** and **187aac** obtained from the pyrrolidine **39b** and

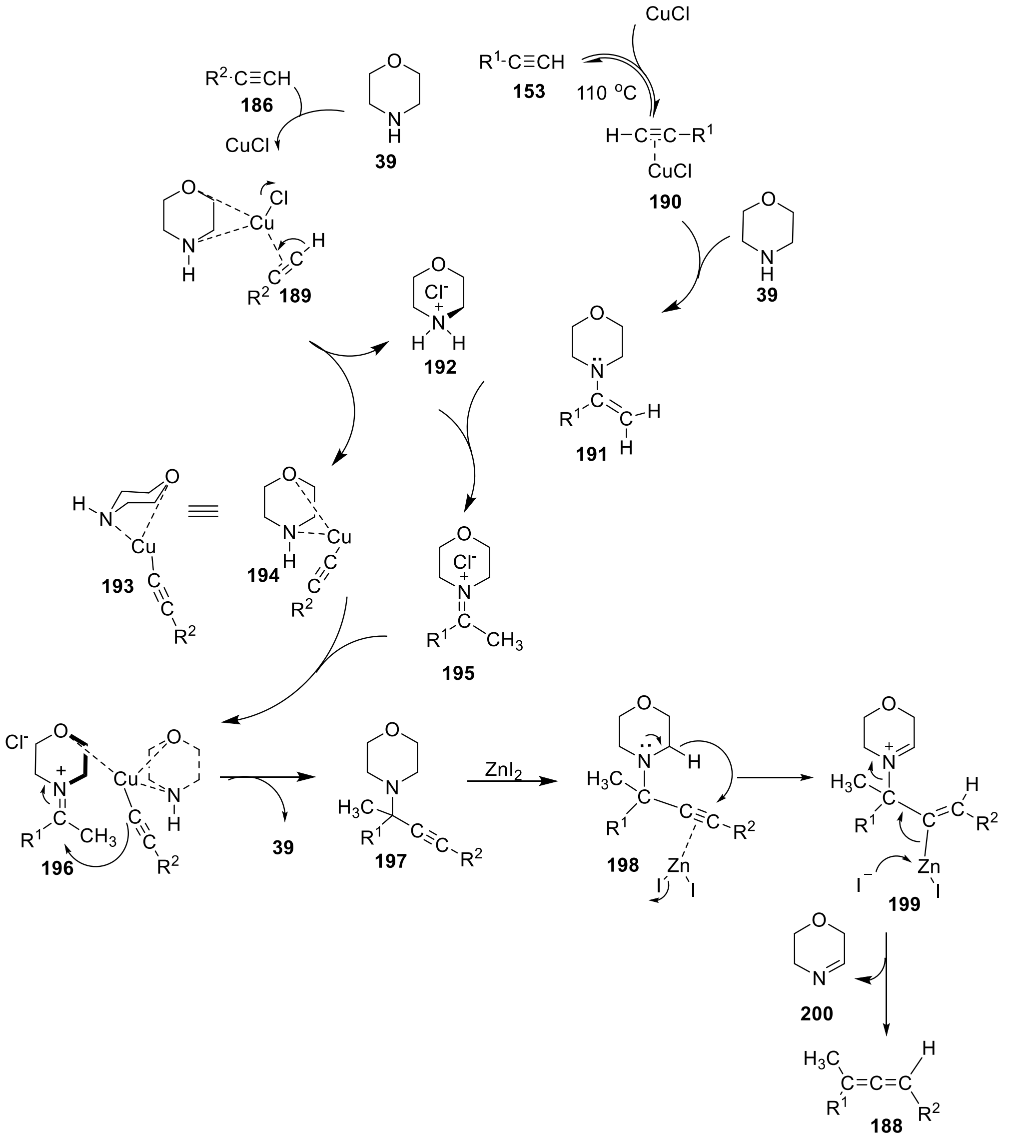
N-benzylpiperazine **39c** with two different 1-alkynes afforded the trisubstituted allene **188aa** in 75-85% yield upon reaction with ZnI_2 in toluene at 120 °C for 1.5-2 h (Scheme 48).

Scheme 48. Synthesis of trisubstituted allene 188aa from the different propargylamines



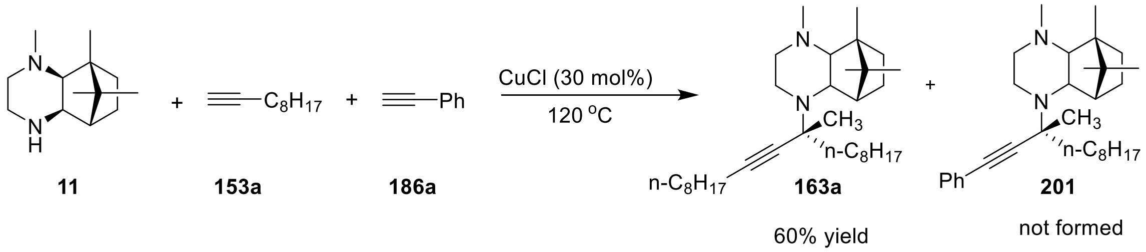
A tentative mechanism may be considered as outlined in the Scheme 49.[55, 58, 59] The reaction would proceed through the formation of both iminium ion and alkynyl metal *in situ* using 1-alkynes and amines. Initially, the amine **39** would react with CuCl to form the monomeric copper complex **189**. Then, its reaction with 1-alkyne would give the complex **194** which could react with the intermediate **195** formed *in situ* by the hydroamination alkyne followed by formation of the more substituted ketenamine and ketiminium ion species to produce the intermediate **197**. Subsequent, complexation with ZnI_2 would lead to the intermediate **198** which after an intramolecular hydride shift and the addition of H and ZnI group across the triple bond would give intermediate **199** that after elimination of ZnI_2 and imine **200** would afford the trisubstituted allene (Scheme 49).

Scheme 49. Plausible mechanism for the formation of trisubstituted allenes



We have also examined the use of readily accessible chiral camphanylpiperzine **11** in this transformation using two different 1-alkynes such as **153a** and **186a** under these conditions (Scheme 50).

Scheme 50. Reaction of chiral amine 11 and two different 1-alkynes



However, only the tetrasubstituted propargylamine **163a** was obtained in 60% yield and the corresponding tetrasubstituted propargylamine **201** was not formed. Clearly, the aliphatic 1-alkynes are more reactive than aromatic 1-alkynes towards cyclic secondary amines for hydroamination and alkynyl metal formation processes (Scheme 50).

We have then undertaken studies on the propargylamine and allene syntheses using propiolate esters and the results are described in the next chapter.

1.3 Conclusions

We have developed a new method for the synthesis of tetrasubstituted propargylamine derivatives *via* the CuCl catalyzed hydroamination of 1-alkynes using the racemic amine derivatives. In addition, a method for the diastereoselective synthesis of chiral propargylamine derivatives was devised using chiral camphanyl amines. Furthermore, we have converted these chiral propargylamine derivatives to trisubstituted chiral allenes in high enantiomeric purities using zinc bromide. Therefore, the methods described herein have considerable potential for further synthetic applications.

We have also developed a method for the synthesis of trisubstituted allenes *via* the formation of tetrasubstituted propargylamines using two different 1-alkynes and morpholine. We have found that the CuCl is uniquely capable of alkenylation of imines, and the three component coupling of amine and two different 1-alkynes gave the corresponding tetrasubstituted propargylamines in moderate to good yields. These methods for isolation of propargylamines and their conversion to trisubstituted allenes should be helpful in designing methods to access such potentially useful multifunctional synthons for further synthetic exploitation.

1.4. Experimental Section

1.4.1 General Information

Melting points reported in this thesis are uncorrected and were determined using a Superfit capillary point apparatus. IR (KBr) spectra were recorded on JASCO FT-IR spectrophotometer Model 5300. The neat IR spectra were recorded on JASCO FT-IR spectrophotometer Model 5300 and SHIMADZU FT-IR spectrophotometer Model 8300 with polystyrene as reference. ^{1}H-NMR (400 MHz), ^{13}C-NMR (100 MHz) spectra were recorded on Bruker-Avance-400 spectrometers, respectively with chloroform-d as solvent and TMS as reference ($\delta = 0$ ppm). The chemical shifts are expressed in δ downfield from the signal of internal TMS. Liquid Chromatography (LC) and mass analysis (LC-MS) were performed on SHIMADZU-LCMS-2010A. The mass spectral analyses were carried out using Chemical Ionization (CI) or Electro Spray Ionization (ESI) techniques. Elemental analyses were carried out using a Perkin-Elmer elemental analyzer model-240C and Thermo Finnegan analyzer series Flash EA 1112. Mass spectral analyses for some of the compounds were carried out on VG 7070H mass spectrometer using EI technique at 70 eV.

Optical rotations were measured on Rudolph Research Analytical AUTOPOL-II (readability $\pm 0.01^{\circ}$) and AUTOPOL-IV (readability $\pm 0.001^{\circ}$) automatic polarimeters. The condition of the polarimeter was checked by measuring the optical rotation of a standard solution of N-methylcampanyl piperazine $\{[\alpha]_D^{25} = +22.7$ (*c* 0.52, $CHCl_3$)$\}$ prepared from our laboratory.

Analytical thin layer chromatographic tests were carried out on glass plates (3 x 10 cm) coated with 250mμ acme's silica gel-G and GF_{254} containing 13% calcium sulfate as binder. The spots were visualized by short exposure to iodine vapor or UV light. Column chromatography was carried out using SRL India silica gel (100-200) and neutral alumina.

All the glassware were pre-dried at 120 °C in an air-oven for 4 h, assembled in hot condition and cooled under a stream of dry nitrogen. Unless otherwise mentioned, all the operations and transfer of reagents were carried out using standard syringe-septum technique recommended for handling air sensitive reagents and organometallic compounds. Reagents prepared *in situ* in solvents were transferred using a double-ended stainless steel (Aldrich) needle under a pressure of nitrogen whenever required.

In all experiments, a round bottom flask of appropriate size with a side arm, a side septum, a magnetic stirring bar, a condenser and a connecting tube attached to a mercury bubbler were used. The outlet of the mercury bubbler was connected to the atmosphere by a long tube. All dry solvents and reagents (liquids) used were distilled from appropriate drying agents. As a routine practice, all organic extracts were washed with saturated sodium chloride solution (brine) and dried over anhydrous $MgSO_4$ or Na_2SO_4 or K_2CO_3 and concentrated on Heidolph-EL-rotary evaporator. All yields reported are of isolated materials judged homogeneous by TLC, IR and NMR spectroscopy.

Dichloromethane and chloroform were distilled over CaH_2 and dried over molecular sieves. Methanol and ethanol supplied by Ranbaxy were distilled over CaO before use. Toluene and THF supplied by E-Merck, India were kept over sodium-benzophenone ketyl and freshly distilled before use. Ethylene diamine, propylene diamine, supplied by Lancaster

Synthesis, Ltd., England were used as purchased. The D-(+)-Camphor was supplied by Aldrich, USA. Iodine was supplied by Spectrochem, India. All aldehydes, supplied by Loba Chemicals (P), Ltd., India were distilled or recrystallized from the appropriate solvents before use. $NaBH_4$ was supplied by E-Merck (India).

The X-ray diffraction measurements for the respective compounds were carried out at 293 K on Bruker-Nonius SMART APEX CCD area detector system. The data were reduced using XTAL 3.4 (or) SAINT program, without applying absorption correction. The refinement for structure was made by full-matrix least squares on F^2 (SHELX 97 or SHELXTL).

1.4.2. General procedure for the synthesis of tetrasubstituted propargylamines 161 from 1-alkyne and amines with CuCl in solvent condition

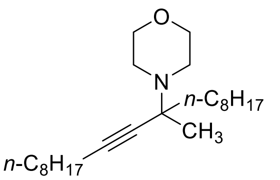
To a stirred suspension of secondary amines (1 mmol), CuCl (0.020 g, 0.2 mmol) and 1-alkyne (2.2 mmol) in toluene (3 mL) at 25 °C under N_2 atmosphere. The contents were stirred at 120 °C for 6 h. The reaction mixture cooled to room temperature. Toluene was removed using reduced pressure. Water (5 mL) and DCM (15 mL) were added. The DCM layer was washed with saturated NaCl solution, dried (Na_2SO_4) and concentrated. The residue was subjected to column chromatography using hexane and ethyl acetate (90:10) as eluent to isolate the propargylamines **161**.

General procedure for the synthesis of tetra substituted propargylamines 161 from 1-alkyne and amine 39 with CuCl in solvent free condition

To a stirred suspension of amines **39** (1 mmol), CuCl (0.010 g, 0.1 mmol) and 1-alkyne **153** (2.2 mmol) in sealed tube at 25 °C under N_2 atmosphere. The contents were stirred at 110 °C for 0.5 h. The reaction mixture cooled to room temperature. Water (5 mL) and DCM (15 mL) were added. The DCM layer was washed with saturated NaCl solution, dried (Na_2SO_4) and concentrated. The residue was subjected to column chromatography using hexane and ethyl acetate (90:10) as eluent to isolate the propargylamines **161**.

4-(9-Methylnonadec-10-yn-9-yl)morpholine (161a)

Yield : Using toluene as solvent; 0.290 g, 80%. Under the solvent free condition 0.301 g, 83%. Colorless oil.



161a

IR (KBr) : 3029, 2947, 2854, 1599, 1495, 1451, 1391, 1352, 1128 cm^{-1}.

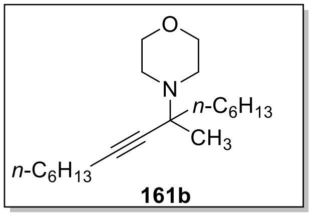
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.70 (t, *J* = 4.0 Hz, 4H), 2.59-2.57 (m, 4H), 2.17 (t, *J* = 8.0 Hz, 2H), 1.48-1.39 (m, 4H), 1.38-1.23 (m, 25H), 0.87 (t, *J* = 8.0 Hz, 6H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 84.5, 81.6, 67.4, 57.5, 47.0, 39.3, 31.8, 30.0, 29.5, 29.3, 29.2, 29.1, 29.0, 28.8, 24.0, 23.7, 22.6, 18.6, 14.0.

LCMS : m/z 364 (M+1); Analysis for $C_{24}H_{45}NO$ calcd: C 79.27, H 12.47, N 3.85 Found: C 79.35, H 12.41, N 3.91.

4-(7-Methylpentadec-8-yn-7-yl)morpholine (161b)

Yield : Using toluene as solvent; 0.224 g, 73%.
Under the solvent free condition;
0.230 g, 75%. Colorless oil.



161b

IR (KBr) : 3029, 2947, 2854, 1599, 1495, 1451, 1391, 1352, 1128 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.02 (t, *J* = 8.0 Hz, 4H), 2.48 (t, *J* = 8.0 Hz, 2H), 2.22-2.15 (m, 4H), 1.66-1.55 (m, 6H), 1.39 (s, 3H), 1.26-1.17 (m, 5H), 1.09-0.98 (m, 3H), 0.90-0.88 (m, 7H), 0.79-0.77(m, 3H).

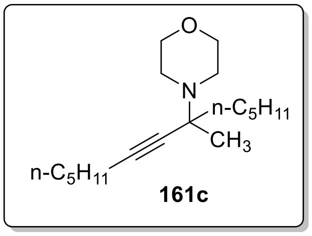
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 84.4, 81.5, 67.4, 57.4, 47.0, 39.3, 31.8, 31.3, 29.0, 28.5, 23.9, 23.7, 22.6, 22.5, 18.5, 14.0.

LCMS : m/z 364 (M+1); Analysis for $C_{20}H_{37}NO$ calcd: C 78.11, H 12.13, N 4.55 Found: C 78.23, H 12.06, N 4.48.

4-(6-Methyltridec-7-yn-6-yl)morpholine (161c)

Yield : Using toluene as solvent; 0.214 g, 77%.
Under the solvent free condition;

0.220 g, 79%. Yellow oil.



161c

IR (KBr) : 2953, 2926, 2854, 1698, 1600, 1501, 1452, 1323, 1156, 838 cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 3.75-3.73 (m, 4H), 2.67-2.58 (m, 4H), 2.20 (t, *J*=8.0 Hz, 2H), 1.61-1.28 (m, 14H), 1.27 (s, 3H), 1.00-0.83 (m, 6H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 84.4, 81.5, 67.4, 57.4, 47.0, 39.3, 32.2, 31.0, 28.8, 23.7, 23.6, 22.5, 22.1, 18.5, 14.0, 13.9.

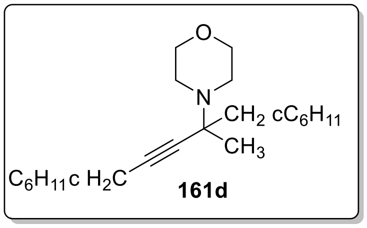
LCMS : m/z 280 (M+1); Analysis for $C_{18}H_{33}NO$ calcd: C 77.36, H 11.90, N 5.01 Found: C 77.23, H 11.82, N 5.12.

4-(1,5-Dicyclohexyl-2-methylpent-3-yn-2-yl)morpholine (161d)

Yield : Using toluene as solvent; 0.261 g, 79%.

Under the solvent free condition;

0.271 g, 82%. Brown liquid.



161d

IR (KBr) : 2949, 2855, 2357, 2341, 1452, 1359, 1326, 1274, 1119, 1071, 1032 cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 3.74(t, *J* = 4.0 Hz, 4H), 2.66-2.61 (m, 4H), 2.22 (d, *J* =4.0 Hz, 2H), 2.06-1.99 (m, 3H), 1.89-1.77 (m, 6H), 1.72-1.68 (m, 3H), 1.66-1.58 (m, 8H), 1.57-1.51 (m, 5H), 1.31 (s, 3H).

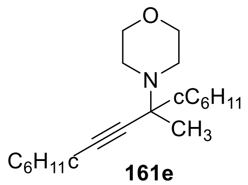
^{13}C NMR : (100 MHz, CDCl$_3$, δppm) 84.0, 81.8, 67.5, 57.6, 47.2, 45.2, 39.3, 36.3, 34.6, 34.4, 32.0, 25.3, 24.9, 24.5.

LCMS : m/z 332 (M+1); Analysis for $C_{22}H_{37}NO$ calcd: C 79.70, H 11.2, N 4.22 Found: C 79.58, H 11.31, N 4.28.

4-(2,4-Dicyclohexylbut-3-yn-2-yl)morpholine (161e)

Yield : Using toluene as solvent; 0.221 g, 73%.

Under the solvent free condition; 0.239 g, 79%. Brown liquid.



161e

IR (KBr) : 2934, 2853, 2354, 2333, 1440, 1268, 1251, 1004, 792 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.72 (t, *J* = 4.0 Hz, 4H), 2.59 (q, *J* = 4.0 Hz, 2H), 2.17 (t, *J* = 8.0 Hz, 4H), 1.57-1.47 (m, 7H), 1.26-1.21 (m, 11H), 0.89-0.86 (m, 5H).

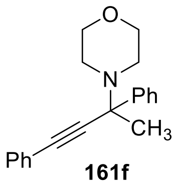
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 84.5, 81.5, 67.4, 57.4, 47.0, 39.3, 31.9, 30.0, 29.6, 29.3, 29.1, 28.8, 24.0, 23.7, 22.7, 18.6, 14.1.

LCMS : m/z 304 (M+1); Analysis for $C_{20}H_{33}NO$ calcd: C 79.15, H 10.96, N 4.62 Found: C 79.23, H 10.85, N 4.56.

4-(2,4-Diphenylbut-3-yn-2-yl)morpholine (161f)

Yield : Using toluene as solvent; 0.084 g, 29%.

Under the solvent free condition; No reaction.



161f

IR (KBr) **:** 3068, 3024, 2954, 2870, 2810, 1498, 1456, 1396, 1254, 1122, 1100, 1073, 1023 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.86-7.82(m, 2H), 7.62-7.59 (m, 2H), 7.42-7.32 (m, 6H), 3.80-3.77 (m, 4H), 2.88-2.75 (m, 2H), 2.64-2.50 (m, 2H), 1.73(s, 3H).

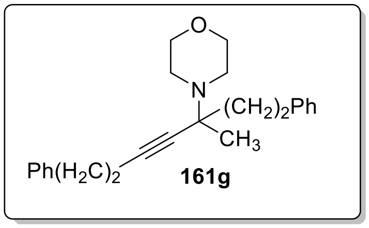
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 144.8, 131.8, 128.3, 128.2, 128.1, 127.2, 126.6, 123.1, 88.2, 67.4, 63.4, 48.0, 30.5.

LCMS : m/z 292 (M+1); Analysis for $C_{20}H_{21}NO$ calcd: C 82.44, H 7.26, N 4.81 Found: C 82.28, H 7.31, N 4.73.

4-(3-Methyl-1,7-diphenylhept-4-yn-3-yl)morpholine (161g)

Yield : Using toluene as solvent ; Yield: 0.284 g, 82%.

Under the solvent free condition: Yield: 0.295 g, 85%; Brown liquid; R_f = 0.6 (silica gel, hexane/EtOAc 90:10).



IR (KBr) : 3084, 3030, 2958, 2860, 1715, 1649, 1490, 1452, 1260, 1013 cm^{-1};

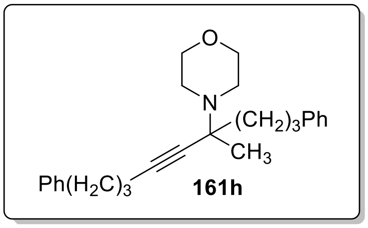
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.33-7.18 (m, 10H), 3.74 (t, *J* = 4.0 Hz, 4H), 2.87 (t, *J* = 8.0 Hz, 2H), 2.73 (t, *J* = 8.0 Hz, 2H), 2.64-2.55 (m, 6H), 1.92-1.88 (m, 2H), 1.35 (s, 3H).

13C NMR : (100 MHz, $CDCl_3$, δ ppm) 142.5, 140.7, 128.5, 128.3, 126.2, 125.7, 84.1, 82.2, 67.4, 57.4, 46.9, 41.1, 35.4, 30.5, 23.4, 20.7;

LCMS : m/z 349 (M+1); Analysis for $C_{24}H_{29}NO$ calcd: C 82.95, H 8.41, N 4.03 Found: C 82.84, H 8.47, N 4.07.

4-(4-Methyl-1,9-diphenylnon-5-yn-4-yl)morpholine (161h)

Yield : Using toluene as solvent: Yield: 0.316 g, 84%, Under the solvent free condition; Yield: 0.307 g, 82%; Brown liquid; R$_f$ = 0.6 (silica gel, hexane/EtOAc 90:10);



161h

IR (KBr) : 2944, 2845, 1733, 1623, 1485, 1435, 1271, 935 cm^{-1}.

^{1}H NMR : 400 MHz, CDCl$_3$, δ ppm) 7.32-7.28 (m, 5H), 7.22-7.19 (m, 5H), 3.73 (t, *J* = 4.0 Hz 4H), 2.66-2.62 (m, 6H), 2.25 (t, *J* = 8.0 Hz, 2H), 1.80-1.73 (m, 3H), 1.64-1.56(m, 5H), 1.27 (s, 3H).

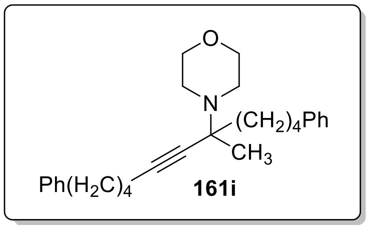
13C NMR : (100 MHz, CDCl$_3$, δ ppm) 142.6, 142.4, 128.3, 128.2, 125.7, 125.6, 84.2, 81.7, 67.4, 57.4, 47.0, 39.1, 35.8, 35.3, 31.8, 30.5, 28.6, 23.8, 23.6, 18.4.

LCMS : m/z 376 (M+1); Analysis for C$_{26}$H$_{33}$NO calcd: C 83.15, H 8.86, N 3.73 Found: C 83.05, H 8.81, N 3.68.

4-(5-Methyl-1,11-diphenylundec-6-yn-5-yl)morpholine (161i)

Yield : Using toluene as solvent; Yield: 0.326 g, 81%.

Under the solvent free condition; Yield: 0.313 g, 83% Brown liquid; R$_f$ = 0.6 (silica gel, hexane/EtOAc 90:10).



161i

IR (KBr) : 3057, 3024, 2926, 2854, 1484, 1441, 1380, 1326, 1254, 1123, 1024, 964 cm^{-1}.

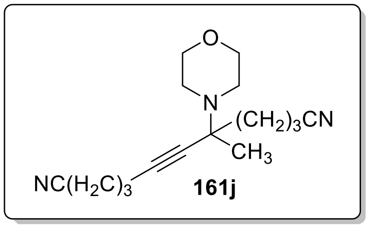
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.32-7.28 (m, 5H), 7.22-7.19 (m, 5H), 3.73 (t, *J* = 4.0 Hz, 4H), 2.67-2.57 (m, 8H), 2.25 (t, *J* = 8.0 Hz, 2H), 1.76 (q, *J* = 8.0 Hz, 4H), 1.66-1.53 (m, 6H), 1.27 (s, 3H);

13C NMR : (100 MHz, $CDCl_3$, δppm) 142.6, 142.4, 128.3, 128.2, 125.7, 125.6, 84.2, 81.7, 67.4, 57.4, 47.0, 39.1, 35.8, 35.3, 31.8, 30.5, 28.6, 23.8, 23.6, 18.4;

LCMS : m/z 402 (M-1); Analysis for $C_{28}H_{37}NO$ calcd: C 83.33, H 9.24, N 3.47 Found: C 83.15, H 9.32, N 3.41.

7-Methyl-7-morpholinoundec-5-ynedinitrile (161j)

Yield : Using toluene as solvent; Yield: 0.202 g, 74% Under the solvent free condition; Yield: 0.221 g, 81% Brown liquid; R_f = 0.5 (silica gel, hexane/EtOAc 70:30).



IR (KBr) : 2942, 2857, 2363, 2242, 1714, 1666, 1454, 1425, 1283, 1115 cm^{-1}.

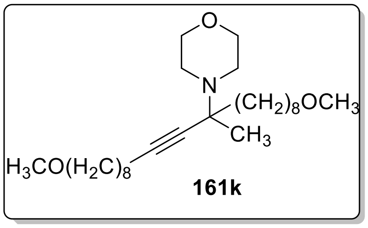
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.73-3.71 (m, 4H), 2.58-2.57 (m, 4H), 2.51-2.47 (m, 2H), 2.43-2.37 (m, 4H), 1.89-1.84 (m, 2H), 1.80-1.76 (m, 4H), 1.29 (s, 3H);

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 119.6, 119.1, 82.8, 82.2, 67.2, 60.3, 56.9, 47.0, 38.0, 24.7, 23.6, 21.0, 20.1, 17.1, 16.2, 14.1.

LCMS : m/z 274 (M+1); Analysis for $C_{16}H_{23}N_3O$ calcd: C 70.30, H 8.48, N 15.37 Found: C 70.21, H 8.41, N 15.26.

4-(1,19-Dimethoxy-9-methylnonadec-10-yn-9-yl)morpholine (161k)

Yield : Using toluene as solvent; Yield: 0.291 g, 69%; Under the solvent free condition; Yield: 0.308 g, 73%, Brown liquid; R$_f$ = 0.6 (silica gel, hexane/EtOAc 85:15).



161k

IR (KBr) : 2926, 2853, 2363, 1708, 1456, 1383, 1273, 1118, 964, 863, 724 cm^{-1}.

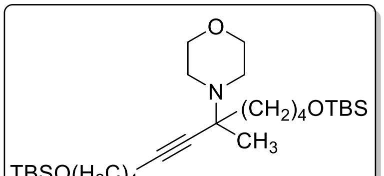
^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 3.71 (t, *J* = 4.0 Hz 4H), 3.35 (t, *J* = 8.0 Hz, 4H), 3.31 (s, 6H), 2.58-2.57 (m, 4H), 2.19 (t, *J* = 8.0 Hz, 2H), 1.59-1.53 (m, 10H), 1.38-1.29 (m, 16H), 1.23 (s, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 84.4, 81.5, 72.9, 67.4, 58.5, 57.4, 47.0, 39.3, 29.9, 29.6, 29.5, 29.4, 29.1, 29.0, 28.7, 26.1, 26.0, 23.9, 23.8, 18.5.

LCMS : m/z 424 (M+1); Analysis for $C_{26}H_{49}NO_3$ calcd: C 73.71, H 11.66, N 3.31 Found: C 73.65, H 11.61, N 3.36.

4-(2,2,3,3,9,17,17,18,18-Nonamethyl-4,16-dioxa-3,17-disilanonadec-10-yn-9-yl)morpholine (161l)

Yield : Using toluene as solvent; Yield: 0.316 g, 62%, Under the solvent free condition Yield: 0.352 g, 69%, Brown liquid; R$_f$ = 0.6 (silica gel, hexane/EtOAc 95:5);



161l

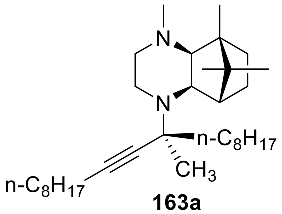
IR(KBr) : 2920, 2854, 2356, 1720, 1643, 1457, 1172 cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 3.69 (t, *J* = 4.0 Hz, 4H), 3.61 (t, *J* = 8.0 Hz, 4H), 2.60-2.56 (m, 4H), 2.19 (t, *J* = 8.0 Hz, 2H), 1.63-1.47 (m, 10H), 1.24 (s, 3H), 0.89 (s, 18H), 0.03 (s, 12H).

^{13}C NMR : (100 MHz, CDCl$_3$, δppm) 84.3, 81.6, 67.4, 63.0, 62.7, 57.3, 47.0, 39.1, 33.1, 32.0, 25.9, 25.6, 23.8, 20.2, 18.4, 18.3, -5.2;

LCMS : m/z 512 (M+1); Analysis for $C_{28}H_{57}NO_3Si_2$ calcd: C 65.69, H 11.22, N 2.74 Found: C 65.58, H 11.06, N 2.81

(4a*S*,5*R*,8*S*,8a*R*)-4,5,9,9-Tetramethyl-1-((*S*)-9-methylnonadec-10-yn-9-yl)decahydro-5,8-methanoquinoxaline (163a)



163a

Yield : Under the solvent free condition; Yield: 0.330 g, 68%, Yellow liquid; R$_f$ = 0.6 (silica gel, hexane/EtOAc 90:10).

[α]$_D^{25}$: -32. 1 (*c* 0.42, CHCl$_3$).

IR (KBr) : 2953, 2925, 2854, 2794, 1462, 1385, 1259, 1150, 1084, 1023, 855, 799, 710 cm^{-1}.

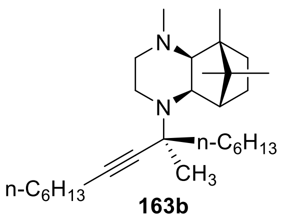
^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 3.09-2.95 (m, 2H), 2.49-2.40 (m, 4H), 2.27-2.21 (m, 4H), 2.14 (s, 3H), 1.64-1.51 (m, 8H), 1.31-1.24 (m, 20H), 1.19 (s, 3H), 0.99 (s, 3H), 0.90-0.87 (m, 10H), 0.79 (s, 3H);

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 85.2, 81.1, 62.1, 60.1, 55.4, 55.1, 49.2, 49.0, 46.3, 44.1, 41.4, 36.9, 31.9, 31.8, 30.0, 29.6, 29.3, 29.1, 28.8, 27.2, 25.7, 23.8, 22.6, 22.0, 20.3, 18.6, 14.4, 14.1;

LCMS : m/z 486 (M+2); Analysis for $C_{33}H_{60}N_2$ calcd: C 81.75, H 12.47, N 5.78 Found: C 81.62, H 12.36, N 5.71.

(4a*S*,5*R*,8*S*,8a*R*)-4,5,9,9-Tetramethyl-1-((*S*)-7-methylpentadec-8-yn-7-yl)decahydro-5,8-methanoquinoxaline (163b)

Yield : Under the solvent free condition: 0.273 g, 64%; Brown liquid; R_f = 0.6 (silica gel, hexane/EtOAc 90:10); yellow liquid;



163b

$[\alpha]_D^{25}$: -48.8 (*c* 0.13, $CHCl_3$);

IR (neat) : 2964, 2926, 2854, 2810, 1457, 1375, 1271, 1128, 958, 931, 860, 830, 750, 706 cm^{-1};

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.08-2.99 (m, 2H), 2.52-2.47 (d, *J* = 4.0Hz, 1H), 2.25-2.16 (m, 7H), 1.73-1.49 (m, 8H), 1.30-1.26 (m, 17H), 1.17 (s, 3H), 1.12-1.07 (m, 1H), 0.99 (s, 3H), 0.90-0.88 (m, 7H), 0.78 (s, 3H);

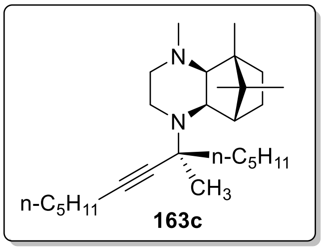
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 85.2, 81.1, 77.3, 62.1, 60.2, 55.4, 55.1, 49.2, 49.0, 46.3, 44.1, 41.4, 36.9, 31.8, 31.4, 29.6, 29.0, 28.5, 27.2, 25.7, 23.7, 22.6, 22.1, 20.3, 18.7, 14.4, 14.1;

LCMS : m/z 428 (M+); Analysis for $C_{29}H_{52}N_2$ calcd: C 81.24, H 12.22, N 6.53 Found: C 81.06, H 12.15, N 6.45.

(4a*S*,5*R*,8*S*,8a*R*)-4,5,9,9-Tetramethyl-1-((*S*)-7-methylpentadec-8-yn-7-yl)decahydro-5,8-methanoquinoxaline (163c)

Yield : Under the solvent free condition: 0.248 g, 62%.

Brown liquid; R_f = 0.6 (silica gel, hexane/EtOAc 90:10); yellow liquid.



163c

[α]$_D^{25}$: -46.2 (*c* 0.10, $CHCl_3$);

IR (neat) : 2960, 2921, 2825, 2810, 2310, 1452, 1373, 1271, 1128, 954, 921, 865, 831, 753, 702 cm^{-1}.

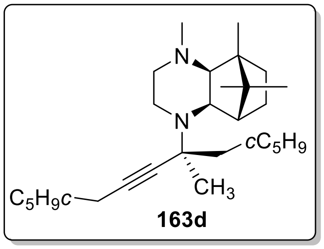
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.07-2.98 (m, 2H), 2.52-2.42 (d, *J* = 4.0Hz, 1H), 2.27-2.13 (m, 7H), 1.75-1.49 (m, 8H), 1.31-1.24 (m, 14H), 1.18 (s, 3H), 0.98 (s, 3H), 0.91-0.87 (m, 7H), 0.78 (s, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 85.5, 81.3, 77.3, 62.4, 60.8, 55.5, 55.2, 49.7, 49.0, 46.3, 44.1, 41.4, 36.6, 31.7, 31.1, 29.6, 29.0, 28.5, 27.2, 25.6, 23.8, 22.6, 22.2, 20.3, 18.9, 14.3, 14.1;

LCMS : m/z 400 (M+); Analysis for $C_{27}H_{48}N_2$ calcd: C 80.93, H 12.08, N 6.99 Found: C 80.93, H 12.08, N 6.99.

(4aS,5R,8S,8aR)-1-((S)-1,5-dicyclopentyl-2-methylpent-3-yn-2-yl)-4,5,9,9-tetramethyldecahydro-5,8-methanoquinoxaline (163d)

Yield : Under the solvent free condition; 0.233 g, 55%; Yellow liquid; R_f = 0.6 (silica gel, hexane/EtOAc 90:10).



163d

$[\alpha]_D^{25}$: -43.1 (*c* 0.40, $CHCl_3$).

IR (neat) : 2914, 2844, 2363, 1669, 1432, 1368, 1277, 1258, 1156, 745 cm^{-1}.

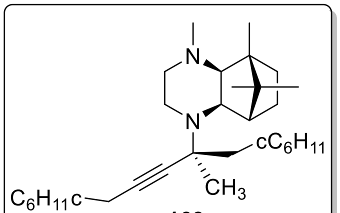
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.45 (t, *J* = 8.0Hz, 1H), 2.90-2.81 (m, 2H), 2.74-2.69 (m, 1H), 2.58-2.53 (m, 1H), 2.26 (s, 3H), 2.12-2.06 (m, 5H), 1.80-1.63 (m, 15H), 1.54-1.41 (m, 5H), 1.24 (s, 3H), 1.18-1.04 (m, 6H), 0.99 (s, 3H), 0.76 (s, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 82.6, 80.1, 78.7, 64.8, 54.3, 53.2, 50.1, 48.3, 47.4, 47.1, 41.8, 37.7, 37.4, 37.2, 34.2, 33.4, 33.2, 32.6, 31.2, 26.7, 26.5, 26.3, 26.2, 25.9, 22.1, 20.9, 14.1.

LCMS : m/z 424 (M+2); Analysis for $C_{29}H_{48}N_2$ calcd: C 82.01, H 11.39, N 6.60 Found: C 82.01, H 11.39, N 6.63.

(4a*S*,5*R*,8*S*,8a*R*)-1-((*S*)-1,5-Dicyclohexyl-2-methylpent-3-yn-2-yl)-4,5,9,9-tetramethyldecahydro-5,8-methanoquinoxaline (163e)

Yield : Under the solvent free condition; Yield: 0.275 g, 61%; Yellow liquid; R_f = 0.6 (silica gel, hexane/EtOAc 90:10).



163e

$[\alpha]_D^{25}$: -42.3 (*c* 0.39, $CHCl_3$).

IR (neat) : 2915, 2864, 2343, 1669, 1432, 1358, 1267, 1258, 1153, 745 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.42 (t, *J* = 8.0 Hz, 1H), 2.89-2.82 (m, 2H), 2.75-2.54 (m, 2H), 2.26 (s, 3H), 2.11-2.08 (m, 5H), 1.81-1.64 (m, 15H), 1.54-1.40 (m, 5H), 1.25 (s, 3H), 1.18-1.04 (m, 10H), 0.99 (s, 3H), 0.77 (s, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 82.9, 80.1, 78.7, 64.8, 54.7, 53.9, 50.0, 48.3, 47.4, 47.1, 41.8, 37.7, 37.4, 37.3, 34.2, 33.4, 33.2, 32.6, 31.2, 26.7, 26.5, 26.3, 26.2, 25.9, 22.1, 20.8, 14.6.

LCMS : m/z 452 (M+2); Analysis for $C_{31}H_{52}N_2$ calcd: C 82.24, H 11.58, N 6.19 Found: C 82.15, H 11.51, N 6.23.

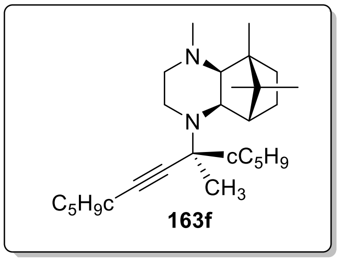
(4a*S*,5*R*,8*S*,8a*R*)-1-((*S*)-2,4-Dicyclohexylbut-3-yn-2-yl)-4,5,9,9-tetramethyldecahydro-5,8-methanoquinoxaline (163f)

Yield : Under the solvent free condition;Yield: 0.205 g, 52%.

Yellow liquid; R_f = 0.6 (silica gel, hexane/EtOAc 90:10).

[α]$_D^{25}$: -39.5 (*c* 0.52, $CHCl_3$).

IR (neat) : 2930, 2823, 1381, 1376, 1341, 1320, 1263, 1117, 1021, 965, 880, 801, 753 cm^{-1}.



163f

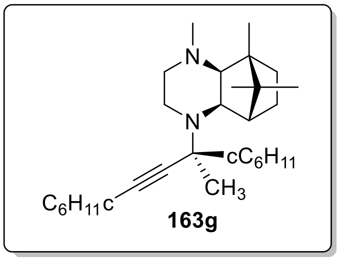
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.04-3.00 (m, 2H), 2.20 (s, 5H), 2.12 (s, 1H), 1.92-1.86 (m, 3H), 1.80-1.64 (m, 2H), 1.59-1.55 (m, 2H), 1.48-1.42 (m, 14H), 1.16 (s, 4H), 1.11 (s, 3H), 1.09 (s, 2H), 0.97 (s, 3H), 0.76 (s, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 85.6, 84.4, 77.4, 63.9, 61.8, 55.5, 55.2, 51.4, 49.2, 49.1, 46.3, 45.8, 43.7, 37.0, 33.2, 32.5, 29.6, 28.9, 28.4, 27.4, 27.1, 26.4, 26.0, 25.5, 24.7, 22.3, 22.0, 20.3, 14.4.

LCMS : m/z 396 (M+1); Analysis for $C_{27}H_{44}N_2$ calcd: C 81.76, H 11.18, N 7.06. Found: C 81.76, H 11.18, N 7.06.

(4a*S*,5*R*,8*S*,8a*R*)-1-((*S*)-2,4-Dicyclohexylbut-3-yn-2-yl)-4,5,9,9-tetramethyldecahydro-5,8-methanoquinoxaline (163g)

Yield : Under the solvent free condition;Yield: 0.250 g, 59%. Yellow liquid; R_f = 0.6 (silica gel, hexane/EtOAc 90:10).



163g

$[\alpha]_D^{25}$: -37.3 (*c* 0.50, $CHCl_3$).

IR (neat) : 2922, 2850, 1447, 1388, 1366, 1341, 1314, 1259, 1117, 1021, 965, 889, 804, 766 cm^{-1}.

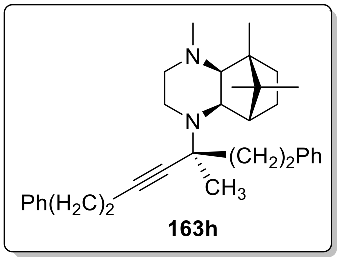
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.02-2.91 (m, 2H), 2.19-2.15 (m, 5H), 2.11 (s, 1H), 1.90-1.76 (m, 3H), 1.73-1.64 (m, 2H), 1.60-1.50 (m, 2H), 1.43-1.20 (m, 16H), 1.13 (s, 4H), 1.11-1.09 (s, 4H), 1.07 (s, 3H), 0.98 (s, 3H), 0.77 (s, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 85.8, 83.5, 77.5, 63.6, 62.0, 56.2, 55.5, 51.4, 49.1, 49.0, 46.8, 45.2, 43.5, 37.1, 33.1, 32.5, 29.6, 28.9, 28.4, 27.4, 27.1, 26.5, 26.8 25.2, 24.7, 22.3, 22.2, 20.5, 14.3.

LCMS : m/z 425 (M+1); Analysis for $C_{29}H_{48}N_2$ calcd: C 82.01, H 11.39, N 6.60. Found: C 82.15, H 11.31, N 6.73.

(4a*S*,5*R*,8*S*,8a*R*)-4,5,9,9-Tetramethyl-1-((*S*)-3-methyl-1,7-diphenylhept-4-yn-3-yl)decahydro-5,8-methanoquinoxaline (163h)

Yield : Under the solvent free condition; Yield: 0.355 g, 76%. Yellow liquid; R_f = 0.6 (silica gel,



163h

hexane/EtOAc 90:10).

$[\alpha]_D^{25}$: -35.1 (*c* 0.39, $CHCl_3$).

IR (neat) : 3024, 2950, 2931, 2849, 1457, 1265, 1213, 1117, 1050, 915, 739, 701 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.36-7.26 (m, 6H), 7.24-7.20 (m, 4H), 3.14-3.10 (m, 3H), 3.04-2.90 (m, 2H), 2.85-2.75 (m, 2H), 2.73-2.60 (m, 2H), 2.55-2.43 (m, 3H), 2.30-2.120 (m, 2H), 2.18-1.80 (m, 4H),1.72-1.60 (m, 2H), 1.38 (s, 3H), 1.23 (s, 3H), 1.18-1.10 (m, 2H), 1.05 (s, 3H), 0.80 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 143.0, 140.8, 128.5, 128.4, 128.3, 126.2, 125.5, 85.5, 80.7, 62.0, 60.1, 55.4, 55.0, 49.3, 49.0, 46.4, 44.1, 43.4, 36.9, 35.4, 30.4, 29.3, 27.1, 25.6, 22.0, 20.7, 20.4, 18.2, 14.4.

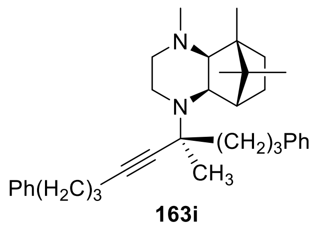
LCMS : m/z 469 (M+1); Analysis for $C_{33}H_{44}N_2$ calcd: C 84.56, H 9.46, N 5.98 Found: C 84.48, H 9.36, N 5.91.

(4a*S*,5*R*,8*S*,8a*R*)-4,5,9,9-Tetramethyl-1-((*S*)-4-methyl-1,9-diphenylnon-5-yn-4-yl)decahydro-5,8-methanoquinoxaline (163i)

Yield : Under the solvent free condition (Table 3): Yield: 0.372 g, 75% Yellow liquid; R_f = 0.6 (silica gel, hexane/EtOAc 90:10).

$[\alpha]_D^{25}$: -41.8 (*c* 0.53, $CHCl_3$).

IR (neat) : 3057, 3018, 2953, 2962, 2832, 1665, 1621, 1473, 1445, 1385,



163i

1232, 1160, 760 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.34-7.27 (m, 5H), 7.24-7.19 (m, 5H), 2.90-2.88 (m, 3H), 2.77 (t, *J* =8.0 Hz, 2H), 2.62 (t, *J* = 8.0 Hz, 2H), 2.29-2.16 (m, 6H), 1.85-1.46 (m, 13H), 1.29 (s, 3H), 1.03 (s, 3H), 0.93 (s, 3H), 0.81 (s, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 142.6, 141.8, 128.5, 128.5, 128.3, 128.2, 125.8, 125.6, 85.5, 80.8, 77.2, 62.1, 60.1, 55.3, 55.1, 49.2, 49.0, 46.3, 44.1, 40.9, 36.9, 36.1, 34.8, 30.7, 27.2, 25.7, 25.5, 22.0, 20.3, 18.1, 14.4;

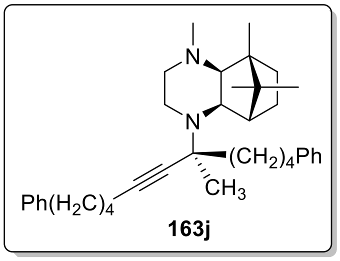
LCMS : m/z 498 (M+2); Analysis for $C_{35}H_{48}N_2$ calcd: C 84.62, H 9.74, N 5.64 Found: C 84.56, H 9.71, N 5.58.

(4a*S*,5*R*,8*S*,8a*R*)-4,5,9,9-Tetramethyl-1-((*S*)-4-methyl-1,10-diphenyldec-5-yn-4-yl)decahydro-5,8-methanoquinoxaline (163j)

Yield : Under the solvent free condition (Table 3): Yield: 0.413 g, 79%; Yellow liquid; R_f = 0.6 (silica gel, hexane/EtOAc 90:10).

[α]$_D$^{25} : -48.2 (*c* 0.50, $CHCl_3$).

IR (neat) : 3050, 3010, 2946, 2834, 2310, 1661, 1620, 1462, 1381, 1232, 1150, 739 cm^{-1}.



163j

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.32-7.21 (m, 10H), 2.92-2.81 (m, 4H), 2.66-2.52 (m, 5H), 2.34-2.26 (m, 8H), 1.79-1.70 (m, 7H), 1.36-1.29 (m, 12H), 1.04 (s, 3H), 0.81 (s, 3H).

13C NMR : (100 MHz, $CDCl_3$, δ ppm) 142.4, 128.4, 128.3, 125.7, 84.8, 78.2, 75.1, 65.3, 54.5, 50.1, 47.7, 47.5, 47.1, 46.5, 43.5, 37.3, 35.4, 30.4, 29.7, 28.6, 26.3, 22.2, 20.5, 18.5, 14.9.

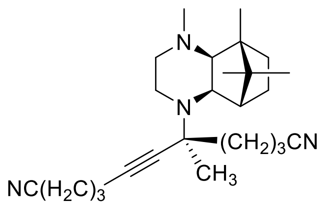
LCMS : m/z 525 (M+1); Analysis for $C_{37}H_{52}N_2$ calcd: C 84.68, H 9.99, N 5.34 Found: C 84.49, H 9.91, N 5.26.

(4a*S*,5*R*,8*S*,8a*R*)-4,5,9,9-Tetramethyl-1-((*S*)-4-methyl-1,10-diphenyldec-5-yn-4-yl)decahydro-5,8-methanoquinoxaline (163k)

Yield : Under the solvent free condition (Table 3): Yield: 0.236 g, 60%. Yellow liquid; R_f = 0.6 (silica gel, hexane/EtOAc 90:10).

$[\alpha]_D^{25}$: -47.6 (*c* 0.56, $CHCl_3$).

IR (neat) : 3056, 3016, 2956, 2849, 2250, 1664, 1625, 1473, 1384, 1236, 1150, 739 cm^{-1}.



163k

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 2.92-2.81 (m, 4H), 2.66-2.52 (m, 5H), 2.34-2.26 (m, 8H), 1.79-1.70 (m, 7H), 1.36-1.29 (m, 8H), 1.04 (s, 3H), 0.81 (s, 3H).

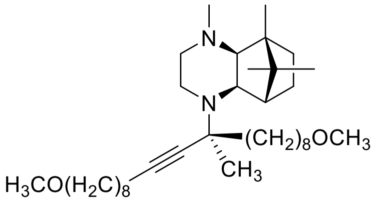
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 119.3, 112.5, 84.5, 79.2, 74.1, 65.6, 54.2, 50.6, 47.8, 47.5, 46.5, 43.5, 37.3, 35.4, 30.4, 29.7, 28.6, 26.3, 22.2, 20.5, 18.4, 14.2.

LCMS : m/z 394 (M+1); Analysis for $C_{25}H_{38}N_4$ calcd: C 76.09, H 9.71, N 14.20. Found: C 76.09, H 9.71, N 14.20.

(4a*S*,5*R*,8*S*,8a*R*)-1-((*S*)-1,19-Dimethoxy-9-methylnonadec-10-yn-9-yl)-4,5,9,9-tetramethyldecahydro-5,8-methanoquinoxaline (163l)

Yield : Under the solvent free condition (Table 3): Yield: 0.424 g, 78%.

Yellow liquid; R_f = 0.6 (silica gel, hexane/EtOAc 90:10).



163l

$[\alpha]_D^{25}$: -48.6 (*c* 0.61, $CHCl_3$).

IR (neat) : 2925, 2951, 2854, 1451, 1391, 1265, 1122, 1030, 910, 854, 730, 701 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.39-3.36 (m, 4H), 3.34 (s, 6H), 3.08-3.00 (m, 3H), 2.23 (s, 4H), 2.20-2.15 (m, 3H), 1.59-1.55 (m, 7H), 1.51-1.46 (m, 4H), 1.34-1.27 (m, 22H), 1.18 (s, 3H), 1.12-1.08 (m, 2H), 0.99 (s, 3H), 0.79 (s, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 85.2, 81.0, 77.1, 72.9, 62.1, 60.1, 58.5, 55.4, 55.1, 49.2, 49.0, 46.3, 44.1, 41.3, 36.9, 29.9, 29.6, 29.5, 29.4, 29.3, 29.1, 29.0, 28.8, 27.2, 26.1, 25.6, 23.7, 22.0, 20.3, 18.6, 14.4.

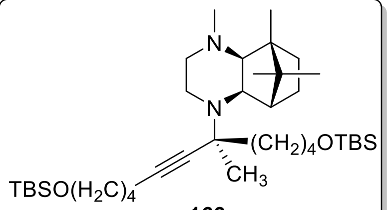
LCMS : m/z 546 (M+2); Analysis for $C_{35}H_{64}N_2O_2$ calcd: C 77.15, H 11.84, N 5.14 Found: C 77.31, H 11.76, N 5.23.

(4a*S*,5*R*,8*S*,8a*R*)-4,5,9,9-Tetramethyl-1-((*S*)-2,2,3,3,9,17,17,18,18-nonamethyl-4,16-dioxa-3,17-disilanonadec-10-yn-9-yl)decahydro-5,8-methanoquinoxaline (163m)

Yield : Under the solvent free condition (Table 3): Yield: 0.391 g, 62%.

Yellow liquid; R_f = 0.6 (silica gel, hexane/EtOAc 85:15).

$[\alpha]_D^{25}$: -31.9 (*c* 0.73, $CHCl_3$).



163m

IR (neat) : 2947, 2931, 2851, 2859, 2788, 1467, 1396, 1254, 1106, 832, 782 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.64-3.61 (m, 4H), 3.08-2.96 (m, 2H), 2.53-2.45 (m, 1H), 2.23-2.14 (m, 6H), 1.73-1.46 (m, 11H), 1.43-1.34 (m, 2H), 1.28 (s, 5H), 1.18 (s, 3H), 1.12-1.07 (m, 2H), 0.99 (s, 3H), 0.90 (s, 18H), 0.78 (s, 3H), 0.06 (s, 12H).

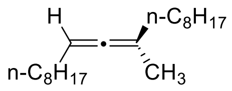
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 85.2, 81.0, 63.3, 62.7, 62.1, 60.1, 55.4, 55.1, 49.2, 49.0, 46.3, 44.0, 41.3, 36.9, 33.2, 32.0, 29.6, 27.2, 25.9, 25.6, 25.5, 22.0, 20.3, 20.2, 18.5, 18.3, 14.4, -5.2.

LCMS : m/z 634 (M+2); Analysis for $C_{37}H_{72}N_2O_2Si_2$ calcd: C 70.09, H 11.46, N 4.42 Found: C 70.27, H 11.37, N 4.36.

General procedure for the preparation of chiral allenes from propargylamines

The chiral propargylamines **163** (1 mmol) were added to a stirred suspension of $ZnBr_2$ (0.113 g, 50 mol%) in dry toluene (3 mL) and the contents were refluxed for 2-3 h at 120 °C under nitrogen atmosphere. Toluene was removed under reduced pressure and the crude product was purified on silica gel (100-200 mesh) column chromatography using hexane/ethyl acetate as eluent to isolate the chiral allenes **162**.

(*R*)-9-Methylnonadeca-9,10-diene (162a)



162a

Yield : 0.239 g, 89%.

[α]$_D$^{25} : -99.9 (*c* 0.51, $CHCl_3$); Colorless liquid.

IR (neat) : 2958, 2926, 2854, 1961, 1468, 1380, 723 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 5.00 (s, 1H), 2.36 (s, 1H), 1.95-1.92 (m, 4H), 1.67-1.66 (t, *J* = 4.0 Hz, 3H), 1.40- 1.36 (m, 21H), 0.90-0.89 (m, 8H).

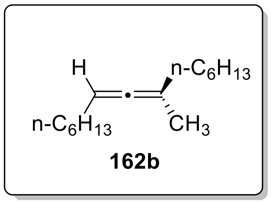
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 201.1, 99.1, 90.0, 34.1, 31.8, 31.7, 29.4, 29.3, 29.0, 28.8, 27.5, 22.7, 19.3, 14.1;

LCMS : m/z 279 (M+1); Analysis for $C_{20}H_{38}$ calcd: C 86.25, H 13.75, Found: C 86.42, H 13.71.

Enantiomeric purity: 97% *ee*, the enantioselectivity was determined by HPLC using chiral column, chiralcel phenomenex cellulose-1, hexanes:i-PrOH/100:0; flow rate 1.5 mL/min, 190 nm, retention times: 2.3 min. (minor) and 3.5 min. (major).

(-)-7-Methylpentadeca-7,8-diene (162b)

Yield : 0.200 g, 90%, Colorless liquid, R_f = 0.8 (silica gel, hexane/EtOAc 100:1).



162b

$[\alpha]_D^{25}$: -121.8 (*c* 0.56, $CHCl_3$).

IR (neat) : 2924, 2915, 2844, 1961, 1493, 1385, 721 cm^{-1}.

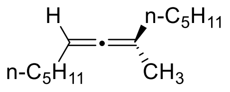
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 5.00-4.97 (m, 1H), 1.99-1.91 (m, 4H), 1.68-1.58 (m, 3H), 1.44- 1.31 (m, 16H), 0.93-0.89 (m, 6H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 201.1, 99.1, 90.0, 34.1, 31.8, 31.7, 29.7, 29.4, 29.3, 29.0, 28.8, 27.5, 22.7, 19.3, 14.1.

LCMS : m/z 223 (M+1); Analysis for $C_{16}H_{30}$ calcd: C 86.40, H 13.60, Found: C 86.28, H 13.51.

<u>Enantiomeric purity</u>: 96% *ee,* the enantioselectivity was determined by HPLC using chiral column, chiralcel OB-H, hexanes:i-PrOH/90:10; flow rate 0.3 mL/min ,190 nm, retention times:10.3 min. (major) and 13.3 min. (minor).

(R)-6-methyltrideca-6,7-diene (162c)



162c

Yield : 0.164 g, 86%, Colorless liquid, R_f = 0.8 (silica gel, hexane/EtOAc 100:1).

$[\alpha]_D^{25}$: -125.8 (*c* 0.50, $CHCl_3$).

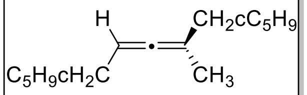
IR (neat) : 2950, 2914, 2854, 1961, 1495, 1380, 722 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 5.01-4.96 (m, 1H), 1.99-1.92 (m, 4H), 1.69-1.57 (m, 3H), 1.45- 1.31 (m, 12H), 0.93-0.90 (m, 6H).

13C NMR : (100 MHz, $CDCl_3$, δ ppm) 201.8, 99.2, 90.1, 34.3, 31.8, 31.7, 29.7, 29.4, 29.0, 28.8, 27.5, 22.8, 19.5, 14.2.

LCMS : m/z 194 (M+1); Analysis for $C_{14}H_{26}$ calcd: C 86.52, H 13.48, Found: C 86.52, H 13.48.

(R)-7-methylpentadeca-7,8-dien-2,4,11,13-tetrayne (162d)



162d

Yield : 0.200 g, 82%, Colorless liquid, R_f = 0.8 (silica gel, hexane/EtOAc 100:1).

$[\alpha]_D^{25}$: -129.2 (*c* 0.26, $CHCl_3$).

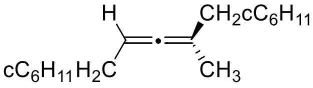
IR (neat) : 2955, 2924, 2854, 1961, 1499, 1385, 723 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 5.04 (s, 1H), 1.90-1.68 (m, 12H), 1.26-1.22 (m, 9H), 1.18-1.01 (m, 4H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 199.8, 105.4, 96.9, 41.6, 37.8, 33.3, 32.1, 32.0, 26.5, 26.2, 26.5, 26.1, 17.5.

LCMS : m/z 218 (M+1); Analysis for $C_{16}H_{26}$ calcd: C 88.0, H 12.0 Found: C 88.0, H 12.0.

(*R*)-(2-Methylpenta-2,3-diene-1,5-diyl)dicyclohexane (162e)



162e

Yield : 0.209 g, 85%, Colorless liquid, R_f = 0.9 (silica gel, hexane/EtOAc 100:0).

$[\alpha]_D^{25}$: -91.1 (*c* 0.39, $CHCl_3$).

IR (neat) : 3059, 3030, 2923, 2853, 1965, 1605, 1495, 1454, 1263, 1074, 1019 cm^{-1}.

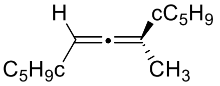
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 4.90 (s, 1H), 1.86-1.80 (m, 3H), 1.71-1.63 (m, 10H), 1.4-1.18 (m, 10H), 0.89 (m, 6H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 202.3, 96.5, 87.6, 42.3, 38.1, 37.5, 35.7, 33.4, 33.3, 33.1, 26.6, 26.3, 19.4.

LCMS : m/z 247 (M+1); Analysis for $C_{18}H_{30}$ calcd: C 87.73, H 12.27 Found: C 87.63, H 12.21.

<u>Enantiomeric purity</u>: 99% *ee*, the enantioselectivity was determined by HPLC using chiral column, chiralcel OJ-H, hexanes:i-PrOH/95:5; flow rate 0.5 mL/min, 190 nm, retention times:6.4 min. (minor) and 8.1 min. (major).

(R)-buta-1,2-diene-1,3-diyldicyclopentane (162f)



162f

Yield : 0.158 g, 81%, Colorless liquid, R_f = 0.8 (silica gel, hexane/EtOAc 100:0).

$[\alpha]_D^{25}$: -72.6 (*c* 0.55, $CHCl_3$).

IR (neat) : 2938, 2845, 2240, 1965, 1447, 1280, 1232, 840 cm^{-1}.

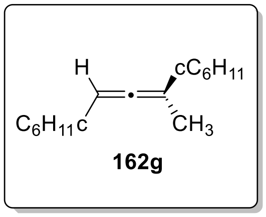
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 5.02 (s, 1H), 1.90-1.67 (m, 10H), 1.26-1.22 (m, 7H), 1.14-1.00 (m, 4H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 199.8, 105.5, 96.9, 41.2, 37.9, 33.3, 32.1, 32.0, 26.5, 26.4, 26.3, 26.1, 17.2.

LCMS : m/z 190 (M+1); Analysis for $C_{14}H_{22}$ calcd: C 88.35, H 11.65 Found: C 88.35, H 11.65.

(*R*)-Buta-1,2-diene-1,3-diyldicyclohexane (162g)

Yield : 0.187 g, 85%, Colorless liquid, R_f = 0.8 (silica gel, hexane/EtOAc 100:0).



162g

[α]$_D^{25}$: -76.8 (*c* 0.59, $CHCl_3$).

IR (neat) : 2936, 2841, 2239, 1964, 1448, 1260, 840 cm^{-1}.

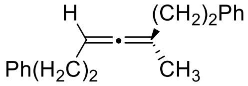
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 5.02 (s, 1H), 1.90-1.67 (m, 12H), 1.26-1.22 (m, 9H), 1.14-1.00 (m, 4H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 199.2, 105.3, 96.9, 41.6, 37.7, 33.3, 32.1, 32.0, 26.5, 26.4, 26.3, 26.1, 17.8.

LCMS : m/z 219 (M+1); Analysis for $C_{16}H_{26}$ calcd: C 88.00, H 12.0 Found: C 87.91, H 12.06.

Enantiomeric purity: 99% *ee*, the enantioselectivity was determined by HPLC using chiral column, chiralcel OJ-H, hexanes:i-PrOH/95:5; flow rate 0.5 mL/min, 190 nm, retention times:6.4 min. (major) and 8.2 min. (minor)

(*R*)-(3-Methylhepta-3,4-diene-1,7-diyl)dibenzene (162h)



162h

Yield : 0.233 g, 89%, Colorless liquid, R_f = 0.6 (silica gel, hexane/EtOAc 97:3).

$[\alpha]_D^{25}$: -109.3 (*c* 0.47, $CHCl_3$).

IR (neat) : 3060, 3027, 2955, 1936, 1597, 1452, 758 cm^{-1}.

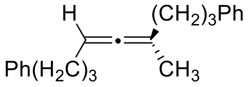
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.31 (t, *J* = 8.0 Hz, 5H), 7.21 (d, *J* = 4.0 Hz, 5H), 5.14-5.10 (m, 1H), 2.69 (t, *J* = 8.0 Hz, 4H), 2.31-2.22 (m, 4H), 1.70 (s, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 201.4, 142.2, 142.0, 128.4, 128.3, 128.1, 125.6, 99.4, 90.2, 35.6, 35.4, 33.8, 30.8, 19.3.

LCMS : m/z 263 (M+1); Analysis for $C_{20}H_{22}$ calcd: C 91.55, H 8.45 Found: C 91.45, H 8.53.

Enantiomeric purity: 99% ee, The enantioselectivity was determined by HPLC using chiral column, chiralcel chiralcel OJ-H, hexanes:i-PrOH/100:0; flow rate 0.5 mL/min, 214 nm, retention times:11.8 min. (major) and 16.1 min. (minor).

(*R*)-(4-Methylnona-4,5-diene-1,9-diyl)dibenzene (162i)



162i

Yield : 0.243 g, 86%, Colorless liquid, R_f = 0.6 (silica gel, hexane/EtOAc 97:3).

$[\alpha]_D^{25}$: -85.9 (*c* 0.47, $CHCl_3$).

IR (neat) : 2958, 2849, 1960, 1450, 1252, 980, 942, 880 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.34-7.29 (m, 5H), 7.24-7.20 (m, 5H), 5.10 (s, 1H), 2.74 (t, *J* = 8.0 Hz, 2H), 2.68-2.64 (m, 2H), 2.23 (dt J_1 = 8.0 Hz, J_2 = 2.6 Hz, 2H), 2.08-1.99 (m, 2H), 1.80-1.72 (m, 4H), 1.28 (t, *J* = 8.0 Hz, 3H).

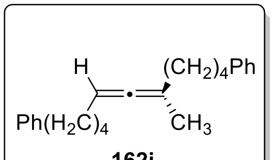
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 201.3, 142.6, 128.4, 128.2, 125.6, 99.1, 90.1, 35.4, 35.3, 33.5, 31.0, 29.3, 28.8, 19.4.

LCMS : m/z 291 (M+1); Analysis for $C_{22}H_{26}$ calcd: C 90.98, H 9.02 Found: C 90.82, H 9.08.

Enantiomeric purity: 99% ee, The enantioselectivity was determined by HPLC using chiral column, chiralcel phenomenex amylose-2 hexanes:i-PrOH/100:0; flow rate 0.5 mL/min, 190 nm, retention times:8.1 min. (major) and 11.7 min. (minor).

(*R*)-(5-Methylundeca-5,6-diene-1,11-diyl)dibenzene (162j)

Yield : 0.263 g, 83%, Colorless liquid, R_f = 0.6 (silica gel, hexane/EtOAc 97:3).



162j

$[\alpha]_D^{25}$: -97.2 (*c* 0.49, $CHCl_3$).

IR (neat) : 2956, 2848, 1962, 1447, 1258, 986, 962, 889 cm^{-1}.

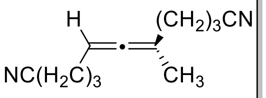
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.30-7.27 (m, 5H), 7.26-7.18 (m, 5H), 5.06-4.96 (m, 1H), 2.65-2.58 (m, 6H), 2.23-2.19 (m, 2H), 1.97 (t, *J* = 8.0 Hz, 4H), 1.66-1.63 (m, 4H), 1.46 (s, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 201.2, 142.8, 128.4, 128.2, 125.6, 99.1, 90.0, 35.8, 33.9, 31.1, 29.2, 29.0, 28.8, 27.2, 19.3.

LCMS : m/z 319 (M+1); Analysis for $C_{24}H_{30}$ calcd: C 90.51, H 9.49 Found: C 90.65, H 9.39.

<u>Enantiomeric purity</u>: 94% ee The enantioselectivity was determined by HPLC using chiral column, chiralcel phenomenex amylose-2, hexanes:i-PrOH/100:0; flow rate 1.0 mL/min, 190 nm, retention times:3.7 min. (major) and 5.2 min. (minor).

(*R*)-5-Methylundeca-5,6-dienedinitrile (162k)



162k

Yield : 0.133 g, 71%, Colorless liquid, $R_f = 0.6$ (silica gel, hexane/EtOAc 97:3).

$[\alpha]_D^{25}$: -56.2 (*c* 0.35, $CHCl_3$).

IR (neat) : 3298, 2931, 2854, 2246, 1956, 1446, 1375, 1238 cm^{-1}.

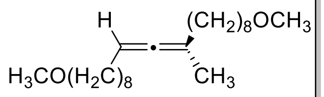
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 5.04 (m, 1H), 2.37 (q, *J* = 8.0 Hz, 4H), 2.14-2.06 (m, 4H), 1.80-1.72 (m, 4H), 1.68 (s, 3H).

13C NMR : (100 MHz, $CDCl_3$, δ ppm) 201.5, 119.5, 98.6, 89.2, 32.5, 27.9, 24.7, 23.2, 19.1, 16.5, 16.4.

LCMS : m/z 188 (M+1); Analysis for $C_{12}H_{16}N_2$ calcd: C 76.55, H 8.57, N 14.88 Found: C 76.63, H 8.51, N 14.72.

<u>Enantiomeric purity</u>: 99% ee, The enantioselectivity was determined by HPLC using chiral column, chiralcel AS-H, hexanes:i-PrOH/100:0; flow rate 0.3 mL/min, 190 nm, retention times: 13.0 min. (minor) and 17.2 min. (major).

(*R*)-1,19-Dimethoxy-9-methylnonadeca-9,10-diene (162l)



162l

Yield : 0.247 g, 73%, Colorless liquid, R_f = 0.6 (silica gel, hexane/EtOAc 97:3).

$[\alpha]_D^{25}$: -92.0 (*c* 0.55, $CHCl_3$).

IR (neat) : 3298, 2931, 2854, 2246, 1956, 1446, 1375, 1238 cm^{-1}.

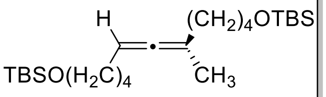
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 4.97 (s, 1H), 3.41-3.32 (m, 10H), 1.95-1.88 (m, 4H), 1.65-1.64 (m, 3H), 1.61-1.52 (m, 4H), 1.42-1.30 (m, 20H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 201.1, 99.1, 90.0, 72.9, 58.5, 34.1, 29.6, 29.5, 29.3, 29.2, 29.0, 27.5, 26.1, 19.3.

LCMS : m/z 339 (M+1); Analysis for $C_{22}H_{42}O_2$ calcd: C 78.05, H 12.5 Found: C 78.23, H 12.41.

<u>Enantiomeric purity</u>: 90% ee; The enantioselectivity was determined by HPLC using chiral column, chiralcel OD-H, hexanes:i-PrOH/100:0; flow rate 1.0 mL/min, 190 nm, retention times: 6.0 min. (major) and 9.2 min. (minor).

(*R*)-2,2,3,3,13,25,25,26,26-Nonamethyl-4,24-dioxa-3,25-disilaheptacosa-13,14-diene (162m)



162m

Yield : 0.289 g, 68%, Colorless liquid, R_f = 0.6 (silica gel, hexane/EtOAc 97:3).

$[\alpha]_D^{25}$: -66.9 (*c* 0.41, $CHCl_3$).

IR (neat) : 2958, 2936, 2806, 1715, 1473, 1260, 1095 cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 5.0 (s, 1H), 3.63-3.59 (m, 4H), 2.21 (s, 3H), 1.98-1.95 (m, 4H), 1.66-1.52 (m, 4H), 1.46-1.26 (m, 4H), 0.89 (s, 18H), 0.05 (s, 12H).

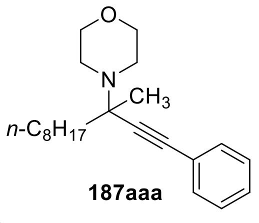
^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 201.2, 99.2, 90.1, 84.5, 68.2, 63.1, 62.5, 33.8, 32.4, 32.3, 31.8, 31.5, 29.1, 25.9, 25.5, 24.9, 23.8,19.2, 18.3, 18.2, -5.2.

LCMS : m/z 427 (M+1); Analysis for $C_{24}H_{50}O_2Si_2$ calcd: C 67.54, H 11.81 Found: C 67.41, H 11.76.

General procedure for synthesis of tetrasubstituted propargylamines

To a stirred solution of amine (1 mmol) in toluene (3 mL), CuCl (30 mol %), 1-alkyne (1.0 mmol), and 1-alkyne (1.0 mmol) at 120 °C under the N$_2$ atmosphere, the reaction mixture was stirred for 8-12 h. The reaction mixture cooled to room temperature. Toluene was removed using reduced pressure. Water (5 mL) and DCM (15 mL) were added. The DCM layer was washed with saturated NaCl solution, dried (Na$_2$SO$_4$) and concentrated. The residue was subjected to column chromatography using hexane and ethyl acetate (95:5) as eluent to isolate the propargylamine **187**.

4-(3-Methyl-1-phenylundec-1-yn-3-yl)morpholine (187aaa)



187aaa

Yield : 0.271 g, 83%; Yellow liquid.

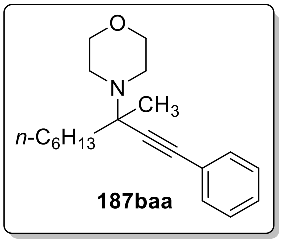
IR (neat) : 2953, 2922, 2851, 2817, 2345, 1598, 1488, 1454, 1369, 1269, 1118, 1070, 1028, 965, 923, 867, 754 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.51-7.38 (m, 5H), 3.86-3.85 (m, 4H), 2.80-2.78 (m, 4H), 1.82-1.77 (m, 2H), 1.56-1.38 (m, 15H), 0.99-0.97 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm) 131.7, 128.2, 127.8, 123.4, 91.4, 84.7, 67.5, 58.0, 47.3, 39.2, 31.9, 30.1, 29.6, 29.4, 23.9, 23.8, 22.7, 14.2.

HRMS : (*m/z*) Calculated for $C_{22}H_{33}NO$:327.2562 Found (M+H): 328.2641.

4-(3-Methyl-1-phenylnon-1-yn-3-yl)morpholine (187baa)



187baa

Yield : 0.224 g, 75%; Yellow liquid.

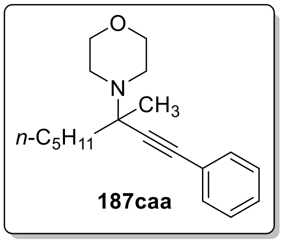
IR (neat) : 2953, 2922, 2851, 2817, 2386, 1509, 1454, 1369, 1269, 1119, 966, 868, 748 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.45-7.43 (m, 2H), 7.32-7.29 (m, 3H), 3.78 (t, *J* = 4.0 Hz, 4H), 2.73-2.70 (m, 4H), 1.75-1.71(m, 2H), 1.52-1.39 (m, 5H), 1.34-1.30 (m, 6H), 0.93-0.90 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm) 131.7, 128.1, 127.8, 123.4, 91.3, 84.6, 67.4, 57.9, 47.2, 39.1, 31.8, 29.7, 23.8, 23.7, 22.6, 14.1.

HRMS : (*m/z*) Calculated for $C_{20}H_{29}NO$: 299.2249 Found (M+H): 300.2331.

4-(3-Methyl-1-phenylnon-1-yn-3-yl)morpholine (187caa)



187caa

Yield : 0.210 g, 74%; Yellow liquid.

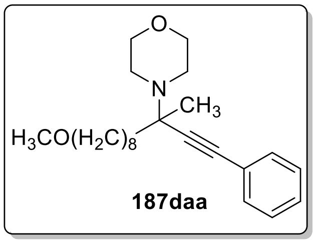
IR (neat) : 2955, 2853, 2818, 2390, 1489, 1455, 1270, 1120, 1070, 970, 870, 756 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.46-7.44 (m, 2H), 7.33-7.29 (m, 3H), 3.79 (t, *J* = 4.0 Hz, 4H), 2.73-2.71 (m, 4H), 1.75-1.71(m, 2H), 1.52-1.50 (m, 2H), 1.48-1.35 (m, 7H), 0.95-0.91 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm): δ =131.7, 128.2, 127.8, 123.3, 91.2, 84.6, 67.4, 57.9, 47.2, 39.2, 32.2, 31.0, 28.8, 23.7, 23.6, 22.6, 22.1, 18.5, 14.1, 14.0.

HRMS : (*m/z*) Calculated for $C_{19}H_{27}NO$: 285.2093 Found (M+H): 286.217.

4-(11-Methoxy-3-methyl-1-phenylundec-1-yn-3-yl)morpholine (187daa)



187daa

Yield : 0.239 g, 65%; Yellow liquid.

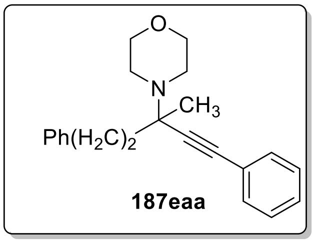
IR (neat) : 2928, 2852, 2821, 1489, 1454, 1271, 1118, 966, 756, 691 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_{3,}$ δ ppm) 7.45-7.42 (m, 2H), 7.31-7.29 (m, 2H), 3.77 (t, *J* = 4.0 Hz, 4H), 3.39-3.34 (m, 5H), 2.72-2.69 (m, 4H), 1.72-1.61 (m, 2H), 1.58-1.39 (m, 5H), 1.34-1.29 (m, 11H).

^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm) 131.7, 128.1, 127.8, 123.3, 91.2, 84.6, 72.9, 67.4, 58.5, 57.9, 47.2, 39.1, 29.9, 29.6, 29.5, 29.4, 26.1, 23.8, 23.7.

HRMS : (*m/z*) Calculated for $C_{23}H_{35}NO_2$: 357.2668 Found (M+H): 357.2747.

4-(3-Methyl-1,5-diphenylpent-1-yn-3-yl)morpholine (187eaa)



187eaa

Yield : 0.223 g, 70%; Light yellow liquid.

IR (neat) : 2956, 2922, 2854, 2818, 2381, 1602, 1509, 1466, 1287, 1246, 1171, 1118, 1031, 962, 835 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.50-7.48 (m, 2H), 7.36-7.32 (m, 4H), 7.27-7.24 (m, 4H), 3.83 (t, *J* = 4.0 Hz, 4H), 2.90-2.85 (m, 2H), 2.81-2.77 (m, 4H), 2.12-2.08(m, 2H), 1.54 (s, 3H).

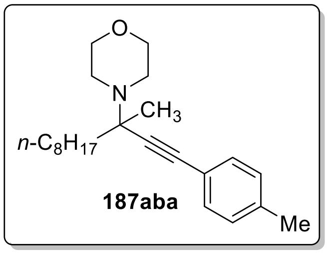
^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm) 142.4, 131.7, 128.4, 128.2, 128.0, 125.8, 123.2, 90.9, 85.1, 67.5, 57.9, 47.3, 41.1, 30.5, 23.6.

HRMS : (*m/z*) Calculated for $C_{22}H_{25}NO$: 319.1936 Found (M+H): 320.2010.

4-(3-Methyl-1-(p-tolyl)undec-1-yn-3-yl)morpholine (187aba)

Yield : 0.242 g, 71%; Yellow liquid.

IR (neat) : 2924, 2852, 2817, 2386, 1606, 1508, 1456, 1288, 1246, 1171, 1119, 1033, 965, 831 cm^{-1}.



187aba

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.34-7.32 (m, 2H), 7.12-7.10 (m, 2H), 3.79-3.77 (m, 4H), 2.73-2.69 (m, 4H), 2.37-2.35 (m, 3H), 1.74-1.70 (m, 2H), 1.51-1.49 (m, 2H), 1.41-1.39 (m, 3H), 1.33-1.30 (m, 10H), 0.92-0.89 (m, 3H).

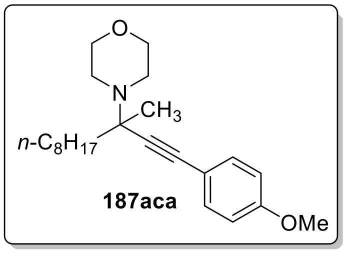
^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm) 137.8, 131.5, 128.9, 120.3, 90.5, 84.7, 67.4, 57.9, 47.2, 39.2, 31.9, 30.0,29.5, 29.3, 23.8, 23.7, 22.6, 21.4, 14.1.

HRMS : (*m/z*) Calculated for $C_{23}H_{35}NO$: 341.2719 Found (M+H): 342.2797.

4-(1-(4-Methoxyphenyl)-3-methylundec-1-yn-3-yl)morpholine (187aca)

Yield : 0.249 g, 70%; Yellow liquid.

IR (neat) : 2953, 2924, 2852, 2818, 2363, 1508, 1456, 1288, 1246, 1171, 965, 924, 831 cm^{-1}.



187aca

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.38-7.36 (m, 2H), 6.85-6.82 (m, 2H), 3.83 (s, 3H), 3.77(t, *J* = 4.0 Hz, 4H), 2.72-2.69 (m, 4H), 1.73-1.69 (m, 2H), 1.49-1.39 (m, 4H), 1.32-1.29 (m, 11H), 0.92-0.88 (m, 3H).

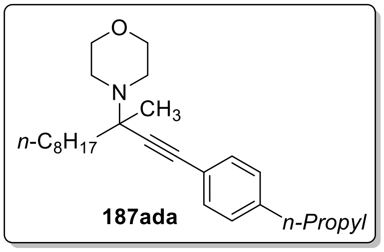
^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm) 159.2, 133.1, 133.0, 115.5, 113.8, 113.4, 89.7, 84.4, 67.4, 57.9, 55.2, 47.2, 39.2, 31.9, 30.0, 29.5, 23.9, 23.7, 22.6, 14.1.

HRMS : (*m/z*) Calculated for $C_{23}H_{35}NO_2$: 357.2668 Found (M+H): 358.2747.

4-(3-Methyl-1-(4-propylphenyl)undec-1-yn-3-yl)morpholine (187ada)

Yield : 0.265 g, 72%; Yellow liquid.

IR (neat) : 2954, 2924, 2852, 2818, 2360, 1508, 1455, 1270, 1120, 1171, 966, 924, 833 cm^{-1}.



187ada

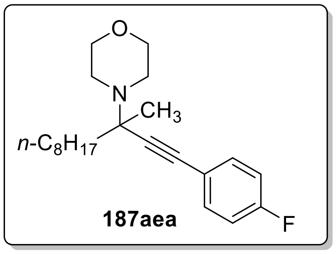
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.36-7.34 (m, 2H), 7.12-7.10 (m, 2H), 3.77 (t, *J* = 4.0 Hz, 4H), 2.72-2.70 (m, 4H), 2.58 (t, *J* = 4.0 Hz, 2H), 1.72-1.61 (m, 4H), 1.50-1.39 (m, 5H), 1.32-1.29 (m, 10H), 0.95-0.89 (m, 6H).

^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm) 142.6, 131.5, 128.3, 120.5, 90.5, 84.7, 67.4, 57.9, 47.2, 39.2, 37.9, 31.8, 30.0, 29.5, 29.3, 24.3, 23.9, 23.7, 22.6, 14.1, 13.6.

HRMS : (*m/z*) Calculated for $C_{25}H_{39}NO$: 369.3032 Found (M+H): 370.3114.

4-(1-(4-Fluorophenyl)-3-methylundec-1-yn-3-yl)morpholine (187aea)

Yield : 0.221 g, 67%; Yellow liquid.



187aea

IR (neat) : 2955, 2924, 2852, 2818, 2332, 1600, 1506, 1456, 1270, 1230, 1220, 1119, 966, 924, 834, 802 cm^{-1}.

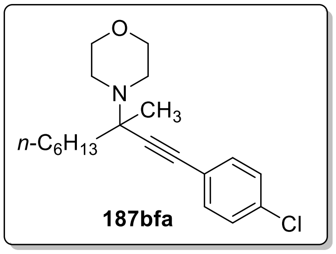
^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.43-7.39 (m, 2H), 7.02-6.98 (m, 2H), 3.77 (t, *J* = 4.0 Hz, 4H), 2.71-2.68 (m, 4H), 1.73-1.69 (m, 2H), 1.49-1.48 (m, 5H), 1.32-1.29 (m, 10H), 0.92-0.89 (m, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$ δ ppm) 163.4, 160.9, 133.5, 133.4, 119.4, 115.5, 115.3, 90.9, 83.6, 67.4, 57.9, 47.2, 39.1, 30.0, 29.5, 29.3, 23.8, 2.307, 22.6, 14.1.

HRMS : (*m/z*) Calculated for $C_{22}H_{32}FNO$: 345.2468 Found (M+H): 346.2549.

4-(1-(4-Chlorophenyl)-3-methylnon-1-yn-3-yl)morpholine (187bfa)

Yield : 0.199 g, 60%; Yellow liquid.



187bfa

IR (neat) : 2956, 2922, 2842, 2819, 2346, 1601, 1502, 1455, 1265, 1231, 1220, 1119, 956, 926, 833, 802 cm^{-1}.

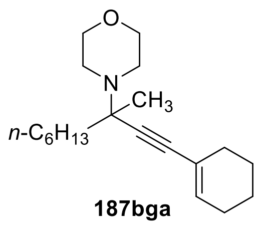
^{1}H NMR : (400 MHz, CDCl$_3$, δppm) 7.39-7.34 (m, 2H), 7.31-29 (m, 2H), 3.77 (t, *J* = 4.0 Hz, 4H), 2.70-2.68 (m, 4H), 1.69-1.66 (m, 4H), 1.33-1.31 (m, 3H), 1.30-1.27 (m, 6H), 0.92-0.89 (m, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$ δ ppm) 133.7, 132.9, 130.6, 128.5, 121.8, 113.6, 92.3, 83.6, 67.4, 57.9, 47.2, 39.1, 31.7, 29.6, 23.7, 22.6, 14.0.

HRMS : (*m/z*) Calculated for C$_{20}$H$_{28}$ClNO: 333.1859 Found (M+H): 334.1938.

4-(1-(Cyclohex-1-en-1-yl)-3-methylnon-1-yn-3-yl)morpholine (187bga)

Yield : 0.272 g, 90%; Yellow liquid.



187bga

IR (neat) : 3020, 2246, 1680, 1606, 1508, 1451, 1262, 1231, 1220, 1119, 952, 926, 835 cm^{-1}.

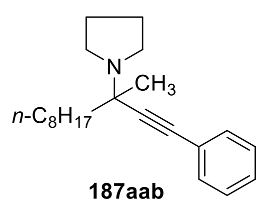
^{1}H NMR : (400 MHz, CDCl$_{3,}$ δ ppm) 6.07-6.06 (m, 1H), 3.75-3.74 (m, 4H), 2.62-2.61 (m, 4H), 2.14-2.08 (m, 4H), 1.64-1.61 (m, 6H), 1.43-1.29 (m, 11H), 0.90-0.87 (m, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$ δ ppm) 133.8, 120.5, 88.2, 86.3, 67.4, 57.7, 47.1, 39.2, 31.7, 31.6, 29.7, 25.5, 23.8, 22.6, 22.3, 21.5, 14.1.

HRMS : (*m/z*) Calculated for C$_{20}$H$_{33}$NO : 303.2562 Found (M+H): 304.2641.

1-(3-Methyl-1-phenylundec-1-yn-3-yl)pyrrolidine (187aab)

Yield : 0.208 g, 67%; Yellow liquid.



187aab

IR (neat) : 2953, 2923, 2853, 1598, 1488, 1463, 1444, 1369, 1190, 1143, 754, 721, 690 cm^{-1}.

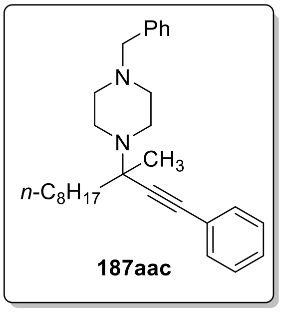
^{1}H NMR : (400 MHz, CDCl$_{3,}$ δ ppm) 7.43-7.41 (m, 2H), 7.30-7.29 (m, 3H), 2.83-2.82 (m, 4H), 1.82-1.77 (m, 7H), 1.69-1.66 (m, 6H), 1.51-1.29 (m, 8H), 0.90-0.88 (m, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$ δ ppm) 131.7, 128.1, 127.7, 123.5, 91.2, 84.5, 58.2, 47.8, 41.3, 31.9, 29.5, 29.3, 25.7, 23.7, 22.6, 18.5, 14.1.

HRMS : (*m/z*) Calculated for $C_{22}H_{33}N$: 311.2613 Found (M+H): 312.2692.

1-Benzyl-4-(3-methyl-1-phenylundec-1-yn-3-yl)piperazine (187aac)

Yield : 0.199 g, 48%; Yellow liquid.



187aac

IR (neat) : 3499, 2956, 2853, 1598, 1505, 1427, 1386, 1334, 1205, 1164, 1092, 994, 870, 808, 730, 674, 550 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.72-7.70 (m, 2H), 7.33-7.24 (m, 8H), 3.53 (s, 2H), 2.50-2.44 (m, 4H), 2.36-2.33 (m, 4H), 1.63-1.56 (m, 3H), 1.33-1.23 (m, 14H), 0.92-0.88 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm) 145.9, 138.1, 129.2, 128.9, 128.1, 127.9, 127.6, 126.9, 126.7, 126.5, 87.9, 78.8, 63.1, 62.5, 53.6, 47.2, 31.8, 31.2, 29.7, 29.2, 29.1, 28.9, 22.6, 18.8, 14.1.

HRMS : (*m/z*) Calculated for $C_{29}H_{40}N_2$:416.3191 Found (M+H): 417.327.

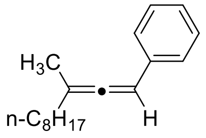
General procedure for the preparation of trisubstituted allenes from propargylamines

The chiral propargylamines **187** (1 mmol) were added to a stirred suspension of ZnI_2 (50 mol%) in dry toluene (3 mL) and the contents were refluxed for 2-3 h at 120 °C under nitrogen atmosphere. Toluene was removed under reduced pressure and the crude product was purified on silica gel (100-200 mesh) column chromatography using hexane/ethyl acetate as eluent to isolate the chiral allenes **188**.

(3-Methylundeca-1,2-dien-1-yl)benzene (188aa)

Yield : 0.215 g, 89%; Yellow liquid.

IR (neat) : 2957, 2925, 1966, 1465, 1376, 1232, 1163, 1115, 1056 cm^{-1}.



188aa

^{1}H NMR : (400 MHz, CDCl$_{3,}$ δ ppm) 7.32-7.29 (m, 4H), 7.21-7.19 (m, 1H), 6.09-6.07 (m, 1H), 2.13-2.09 (m, 2H), 1.84-1.83 (m, 3H), 1.53-1.49 (m, 2H), 1.38-1.28 (m, 10H), 0.90 (t, *J* = 4.0Hz, 3H).

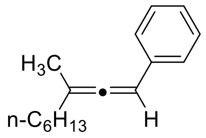
^{13}C NMR : (100 MHz, CDCl$_3$ δ ppm) 202.7, 136.1, 128.4, 126.5, 126.3, 103.7, 93.7, 34.1, 31.8, 29.4, 29.3, 27.57, 22.70, 18.8, 14.1.

HRMS : (*m/z*) Calculated for C$_{18}$H$_{26}$: 242.2035 Found (M+H): 243.2114.

(3-Methylnona-1,2-dien-1-yl)benzene (188ba)

Yield : 0.181 g, 85%; Yellow liquid.

IR (KBr) : 2957, 2924, 2854, 1966, 1465, 1378, 1232, 1153, 1115,1056 cm^{-1}.



188ba

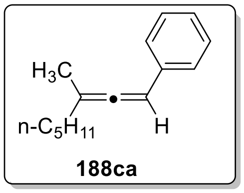
^{1}H NMR : (400 MHz, CDCl$_{3,}$ δ ppm) 7.33-7.30 (m, 1H), 7.29-7.27 (m, 3H), 7.20-7.18 (m, 1H), 6.07-6.06 (m, 1H), 2.10-2.08 (m, 2H), 1.83 (s, 3H), 1.58-1.51 (m, 2H), 1.50-1.48 (m, 2H), 1.37-1.29 (m, 4H), 0.90-0.87 (m, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$ δ ppm) 202.6, 136.1, 131.5, 131.4, 128.4, 128.2, 126.5, 126.3, 103.6, 93.7, 72.9, 58.5, 34.0, 31.4, 29.6, 29.4, 29.3, 29.2, 26.0, 18.8.

HRMS : (*m/z*): Calculated for C$_{16}$H$_{22}$: 214.1722 Found (M+H): 215.1801.

(3-Methylocta-1,2-dien-1-yl)benzene (188ca)

Yield : 0.164 g, 82%; Yellow liquid.



188ca

IR (neat) : 2957, 2854, 1966, 1467, 1375, 1230, 1152, 1105,1054 cm^{-1}.

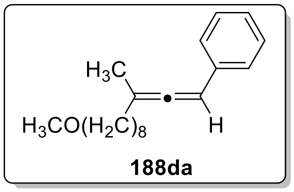
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.32-7.30 (m, 2H), 7.29-7.26 (m, 3H), 6.07-6.04 (m, 1H), 2.10-2.07 (m, 2H), 1.82 (d, *J* = 1.7Hz, 3H), 1.59 (s, 4H), 1.33-1.31 (m, 2H), 1.28-1.27 (m, 2H), 0.89-0.86 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm) 202.6, 136.1, 131.5, 131.4, 128.4, 126.5, 103.7, 93.7, 34.0, 31.5, 29.7, 27.2, 22.4, 18.8, 14.0.

HRMS : (*m/z*) Calculated for $C_{15}H_{22}$: 200.1565 Found (M+H): 201.1644.

(11-Methoxy-3-methylundeca-1,2-dien-1-yl)benzene (188da)

Yield : 0.176 g, 65%; Yellow liquid.



188da

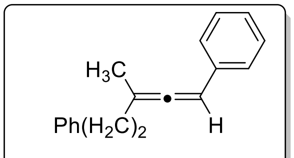
IR (neat) : 2956, 2920, 2860, 1967, 1714, 1457, 1365, 1260, 1170, 745 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.32-7.30 (m, 1H), 7.26-7.25 (m, 2H), 7.20-7.19 (m, 2H), 6.08-6.06 (m, 1H), 3.38-3.31 (m, 5H), 2.10-2.08 (m, 2H), 1.84-1.83 (m, 3H), 1.9-1.59 (m, 2H), 1.59-1.29 (m, 10H).

^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm) 202.6, 136.1, 131.5, 131.4, 128.4, 128.2, 126.5, 126.3, 103.6, 93.7, 72.9, 58.5, 34.0, 31.4, 29.6, 29.4, 29.3, 29.2, 26.0, 18.8.

HRMS : (*m/z*) Calculated for $C_{19}H_{28}O$: 272.2140 Found (M+H): 273.2219.

(3-Methylpenta-1,2-diene-1,5-diyl)dibenzene (188ea)



188ea

Yield : 0.168 g, 72%; Yellow liquid.

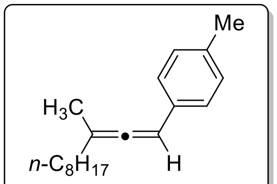
IR (neat) : 2956, 2924, 2854, 1966, 1464, 1378, 1232, 1153, 1117, 1055 cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.27-7.14 (m, 10H), 6.09-6.08 (m, 1H), 2.83-2.78 (m, 2H), 2.43-2.37(m, 2H), 1.87 (s, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$ δ ppm) 202.7, 142.0, 135.7, 128.5, 128.4, 128.2, 126.5, 125.8, 103.0, 94.3, 35.6, 33.8, 18.9.

HRMS : (*m/z*) Calculated for $C_{18}H_{18}$: 234.1409 Found (M+H): 235.1488.

1-Methyl-4-(3-methylundeca-1,2-dien-1-yl)benzene (188ab)



188ab

Yield : 0.202 g, 79%; Yellow liquid.

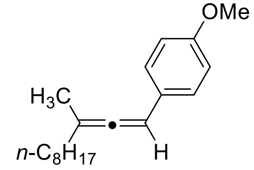
IR (neat) : 2957, 2924, 2854, 1966, 1465, 1378, 1232, 1153, 1115, 1056 cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.20-7.18 (m, 2H), 7.13-7.11 (m, 2H), 6.07-6.04 (m, 1H), 2.37-2.35 (m, 2H), 2.10-2.08 (m, 3H), 1.84-1.82 (m, 2H), 1.56-1.48 (m, 3H), 1.34-1.28 (m, 10H), 0.90(t, *J* = 4.0Hz, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$ δ ppm) 202.3, 136.0, 133.1, 129.1, 126.4, 126.3, 126.2, 103.5, 93.5, 34.1, 31.8, 29.4, 29.3, 27.5, 22.6, 21.1, 18.8, 14.0.

HRMS : (*m/z*) Calculated for $C_{19}H_{28}$: 256.2191 Found (M+H): 257.227.

1-Methoxy-4-(3-methylundeca-1,2-dien-1-yl)benzene (188ac)



188ac

Yield : 0.221 g, 85%; Yellow liquid.

IR (neat) : 2956, 2931, 2872, 2858, 2835, 1951, 1608, 1581, 1510, 1464, 1441, 1395, 1369, 1296, 1249, 1201, 1170, 1106, 1036 cm^{-1}.

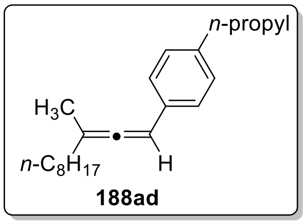
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.23-7.21 (m, 2H), 6.88-6.86 (m, 2H),6.03-6.04 (m, 1H), 3.83 (s, 3H), 2.34-2.32 (m, 4H), 1.95-1.94 (m, 3H), 1.82-1.81 (m, 2H), 1.61-1.58 (m, 2H), 1.36-1.31 (m, 6H), 0.92-0.91 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm) 158.3, 128.5, 127.5, 114.0, 113.9, 103.6, 93.1, 55.2, 37.3, 34.2, 29.0, 28.8, 27.5, 23.1, 22.5, 18.9, 14.0.

HRMS : (*m/z*) Calculated for $C_{18}H_{28}O$: 260.2140 Found (M+H): 261.2219.

1-(3-Methylundeca-1,2-dien-1-yl)-4-propylbenzene (188ad)

Yield : 0.213 g, 75%; Yellow liquid.



188ad

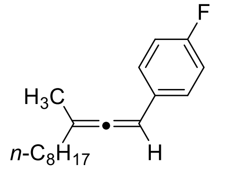
IR (neat) : 2955, 2914, 2824, 1956, 1445, 1464, 1441, 1368, 1205, 1183, 1125, 1036 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.23-7.21 (m, 2H), 7.14-7.12 (m, 2H), 6.07-6.05 (m, 1H), 2.63-2.57 (m, 2H), 2.11-2.07 (m, 2H), 1.83-182 (m, 3H), 1.70-1.61 (m, 2H), 1.54-1.48 (m, 2H), 1.35-1.27 (m, 10H), 0.97 (t, *J* = 4.7Hz, 3H), 0.90 (t, *J* = 4.4 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm) 202.3, 140.9, 133.4, 132.0, 128.6, 128.4, 126.4, 103.5, 93.5, 37.7, 34.1, 29.4, 29.3, 27.5, 24.6, 22.6, 18.9, 14.1, 13.8.

HRMS : (*m/z*) Calculated for $C_{21}H_{32}$: 284.2504 Found (M+H): 285.2583.

1-Fluoro-4-(3-methylundeca-1,2-dien-1-yl)benzene (188ae)



188ae

Yield : 0.208 g, 80%; Yellow liquid.

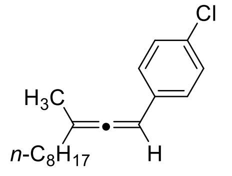
IR (neat) : 3499, 2956, 2853, 1598, 1505, 1427, 1386, 1334, 1236, 1205, 1164, 1092, 808, 730, 674, 550 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_{3,}$ δ ppm) 7.25-7.21 (m, 2H), 7.02-6.96 (m, 2H), 6.04-6.01 (m, 1H), 2.10-2.06 (m, 2H), 1.82-1.81 (m, 3H), 1.82-1.81 (m, 4H), 1.32-1.27 (m, 8H), 0.91-0.86 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm) 202.4, 162.8, 160.3, 132.0, 127.8, 127.7, 115.4, 115.2, 104.0, 92.7, 34.0, 31.6, 29.7, 29.0, 27.4, 22.6, 18.8, 14.0.

HRMS : (*m/z*) Calculated for $C_{18}H_{25}F$: 260.1940 Found (M+H): 261.2019.

1-Chloro-4-(3-methylnona-1,2-dien-1-yl)benzene (188bf)



188bf

Yield : 0.173 g, 70%; Yellow liquid.

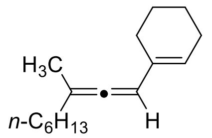
IR (neat) : 2957, 2927, 2871, 2858, 1951, 1488, 1465, 1450, 1440, 1380, 1360, 1221, 1201, 1097, 1072, 1006 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_{3,}$ δ ppm) 7.27-7.25 (m, 2H), 7.20-7.19 (m, 2H), 6.02-6.01 (m, 1H), 2.10-2.06 (m, 2H), 1.82-1.81 (m, 3H), 1.82-1.81 (m, 3H), 1.48-1.45 (m, 3H), 1.35-1.27 (m, 6H), 0.90-0.89 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm) 202.8, 134.7, 133.3, 131.8, 128.6, 128.5, 127.6, 104.2, 92.9, 34.0, 31.6, 29.0, 27.4, 22.6, 18.7, 14.0.

HRMS : (*m/z*) Calculated for $C_{18}H_{25}Cl$: 248.1332 Found (M+H): 249.1411.

1-(3-Methylnona-1,2-dien-1-yl)cyclohex-1-ene (188bg)



188bg

Yield : 0.194 g, 89%; Yellow liquid.

IR (neat) : 2925, 2853, 1965, 1645, 1446, 1378, 1344, 1261, 1239, 1035 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_{3,}$ δ ppm) 5.76-5.75 (m, 1H), 5.65-5.64 (m, 1H), 2.12-1.99 (m, 6H), 1.73-1.62, (m, 3H), 1.65-1.60 (m, 4H), 1.34-1.30 (m, 8H), 0.92-0.0.90 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm) 201.4, 133.5, 124.7, 102.5, 96.8, 34.3, 31.7, 29.1, 27.6, 25.8, 22.7, 22.6, 19.4, 19.3, 14.1.

HRMS : (*m/z*) Calculated for $C_{16}H_{26}$: 218.2035 Found (M+H): 219.2114.

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Chapter 2

Enantioselective Synthesis of Chiral β-Allenoates *via* Phosphine Catalysed Hydroamination of Propiolates and Alkyne Addition Reaction

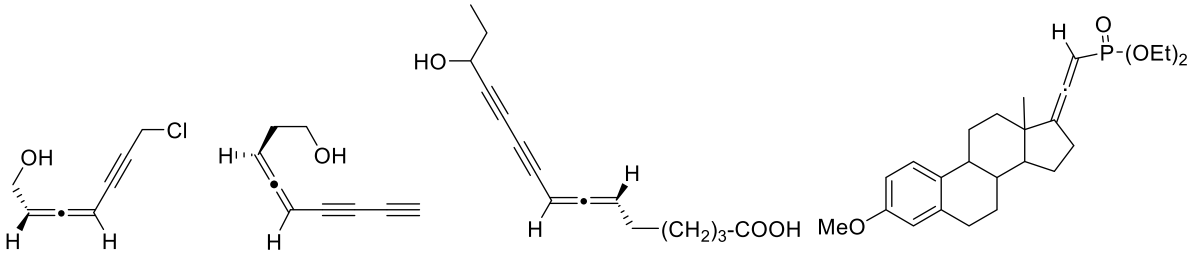
2.1 Introduction

2.1.1 Functionalized chiral allenes

Chiral 1,3-disubstituted allenes containing functional groups have a potential for use in organic synthesis.[1, 2] The allenic natural products exhibit interesting biological activities (Figure 1).[3] For example, the compounds Scorodonin **1**, Marasin **2** and Phomallenic acid **3** have inhibiting effects on the growth of bacteria, yeast and filamentous fungi. Other allenic moieties with inhibiting effects are sterol biosynthesis inhibitor **4**, gastric acid inhibitor **5**, HIV inhibitor **8** and hepatitis B replication inhibitor **7**.[4-6] Therefore, introduction of allene as a functional group into the existing backbone of the pharmacologically active compounds could be expected to result in interesting new biological properties.

All natural and biological active allenes have functional groups, and their synthesis require multistep synthetic operations (Figure 1**)**. It is of our interest to examine the use of methods developed in this laboratory to access functionalized 1,3-disubstituted chiral allenes. A brief review of reports based on the synthesis of functionalized 1,3-disubstituted chiral allenes and their application in organic synthesis would facilitate the discussion.

2.1.2 Naturally occurring and biologically active chiral allenes



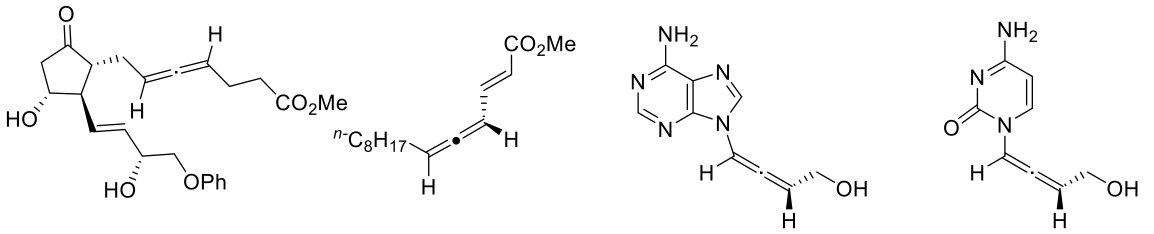
1 Scorodonin (anti bacteria)

2 Marasin (anti bacteria)

3 Phomallenic acid A (anti fungi)

4 Sterol biosynthesis inhibitor

Figure 1 (continued)



5 Enprostil (gastric acid inhibitor)

6 Tetradeca 2, 4, 5-trienoate (insect pheromone)

7 Adenallene (Hepatitis B replication inhibitor)

8 Cytallene (HIV inhibitor)

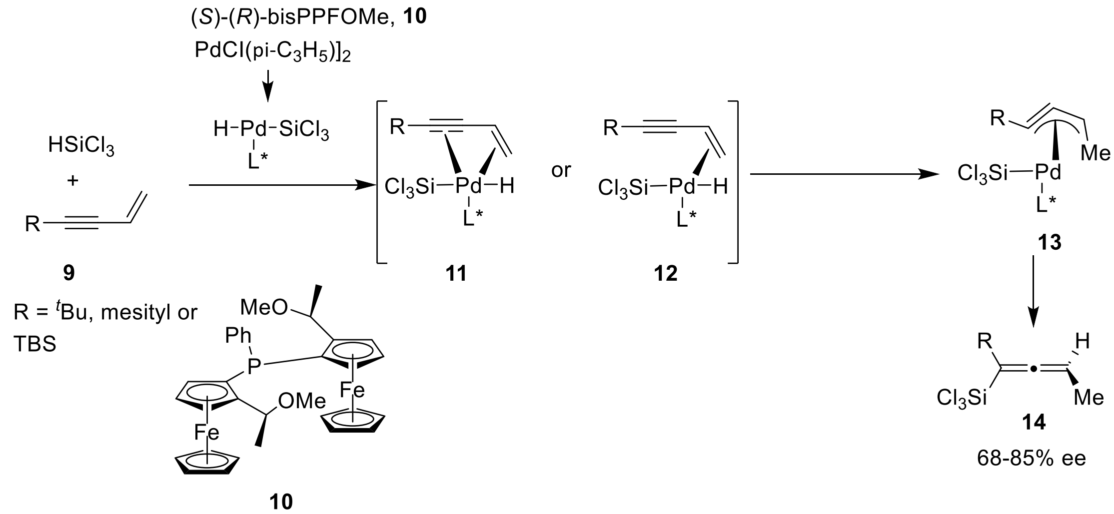
Figure 1. Biologically active chiral allenes

Total synthesis of several functionalized chiral allenes were reported.[7-11]

2.1.3 Synthesis of highly functionalized chiral allenes using a chiral catalyst

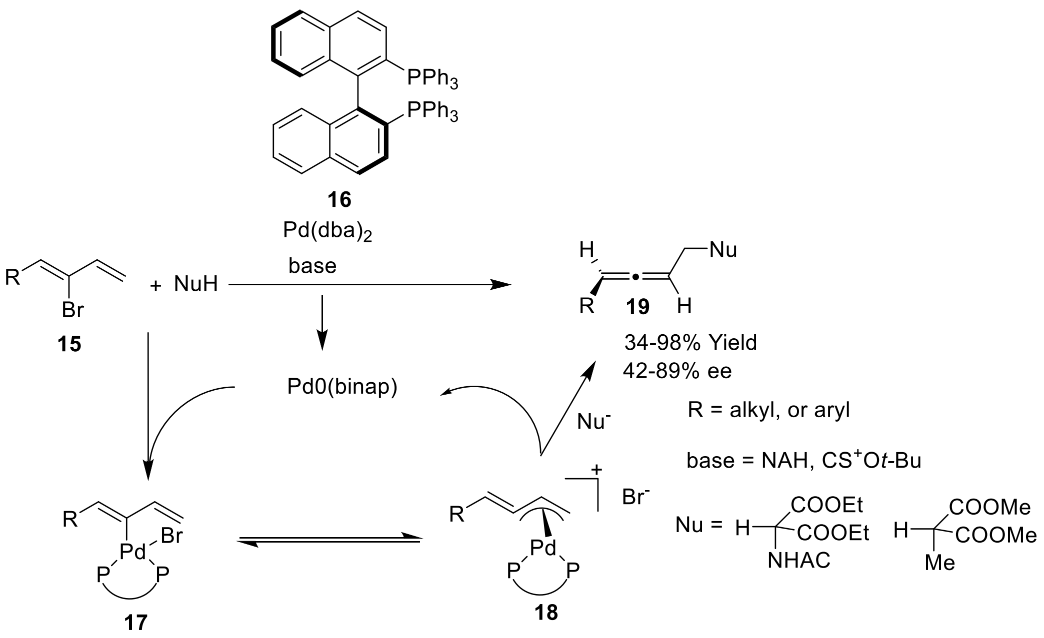
An interesting method for the synthesis of chiral allenylsilanes *via* palladium catalyzed asymmetric hydrosilylation of 1,3-enynes was reported (Scheme 1).[12]

Scheme 1



Another approach involves a palladium catalyzed formal S$_N$2 reaction of achiral conjugated dienes as outlined in Scheme 2.[13]

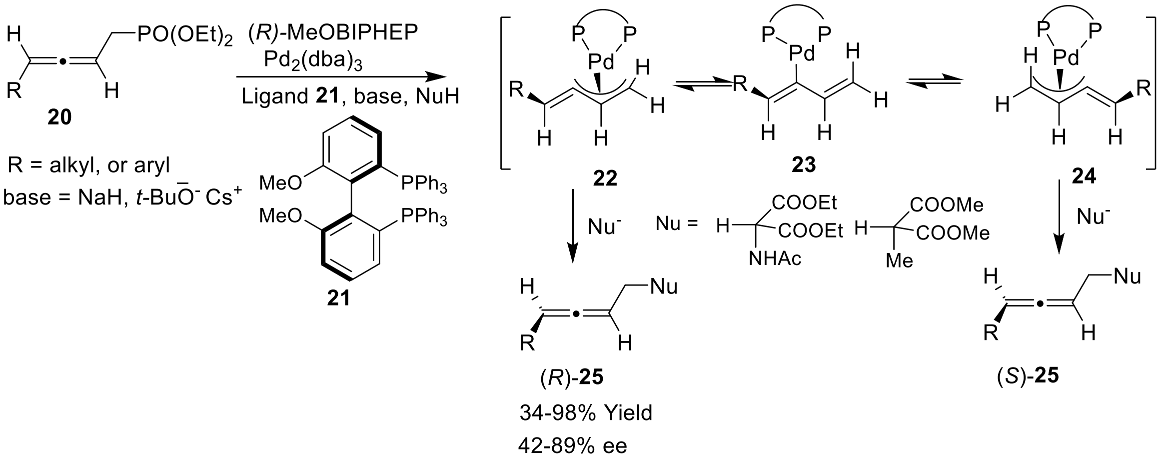
Scheme 2



2.1.4 Palladium catalysed kinetic resolution of racemic allenes

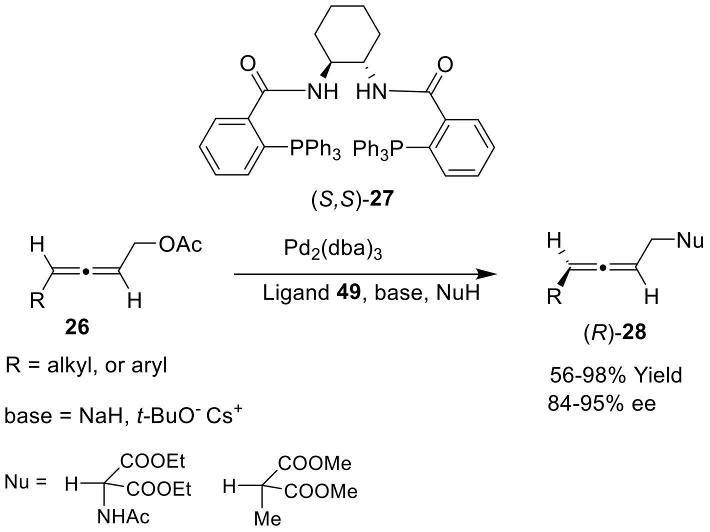
The reaction of racemic dienyl phosphates **20** with soft nucleophiles in the presence of $Pd_2(dba)_3$ (1 mol%), chiral ligand **21** (4 mol%) and base gave the allenic product (*R*)-**25** in 34-98% yield with up to 89% ee. It was proposed that nucleophilic attack occurs preferentially on intermediate **22** from the opposite face on the palladium complex gave the optically active allenes (*R*)-**25** (Scheme 3).[14]

Scheme 3



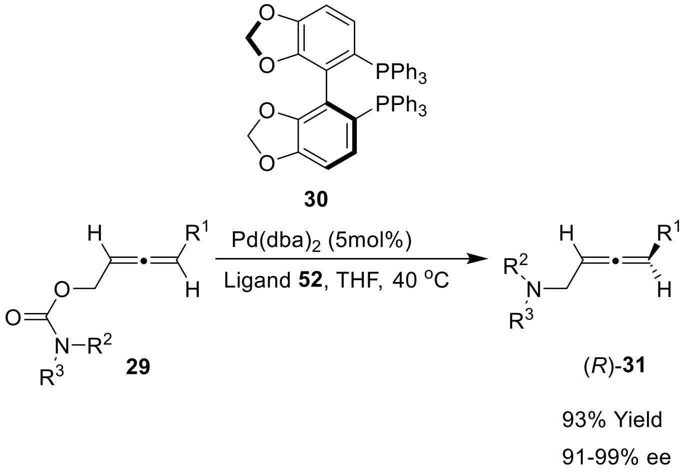
Reaction of racemic allenic acetates **26** with Pd(0) (2.5 mol%) and chiral ligand (*S,S*)-**27** (7.5 mol%) in the presence of a soft nucleophile and base gave the allenes **28** in high yields with good enantioselectivity (Scheme 4).[15]

Scheme 4



Enantioselective decarboxylative amination is another approach for the synthesis of functionalized chiral allenyl amines **31** with up to 93% yield with 99% ee (Scheme 5).[16]

Scheme 5

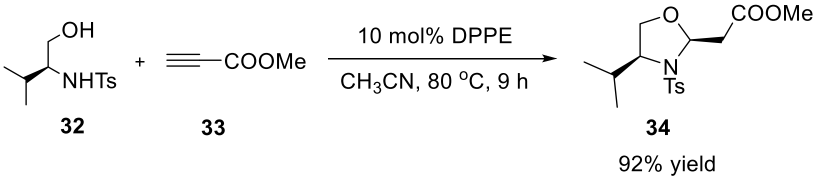


These approaches give the chiral allenes in reasonable yields and enantioselectivities but they still require synthesis of the racemic allene and hence require extra steps.

2.1.5 Synthesis of oxazolidine derivatives

The oxazolidine derivatives have been used as synthetic intermediates, auxiliaries, ligands, and catalysts in asymmetric transformations.[17] Recently, a method was developed for the construction of oxazolidine derivative using an amino acid derivative and methyl propiolate *via* double Michael-addition reaction (Scheme 6).[18]

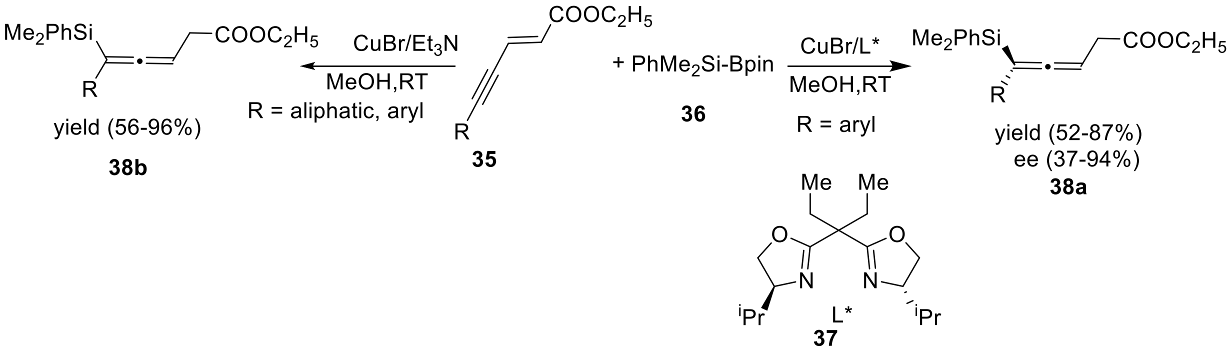
Scheme 6



2.1.6 Synthesis of β-allenoates

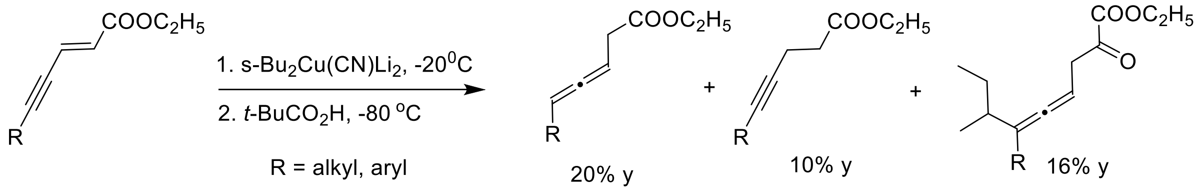
Very recently, a copper-catalyzed asymmetric synthesis of highly substituted chiral β-allenoates was reported. In this method, the (Z)-enynoates react smoothly with the silylboronate and the corresponding racemic and enantioenriched silyl-substituted allene products were obtained in 52-87% yields with 37-94% ee (Scheme 7).[19]

Scheme 7



Krause *et al.* reported the reduction of 2-en-4-ynoates with s-BuCu(CN)Li_2 in a protic solvent to obtain the β-allenoate in 20% yield (Scheme 8).[20]

Scheme 8



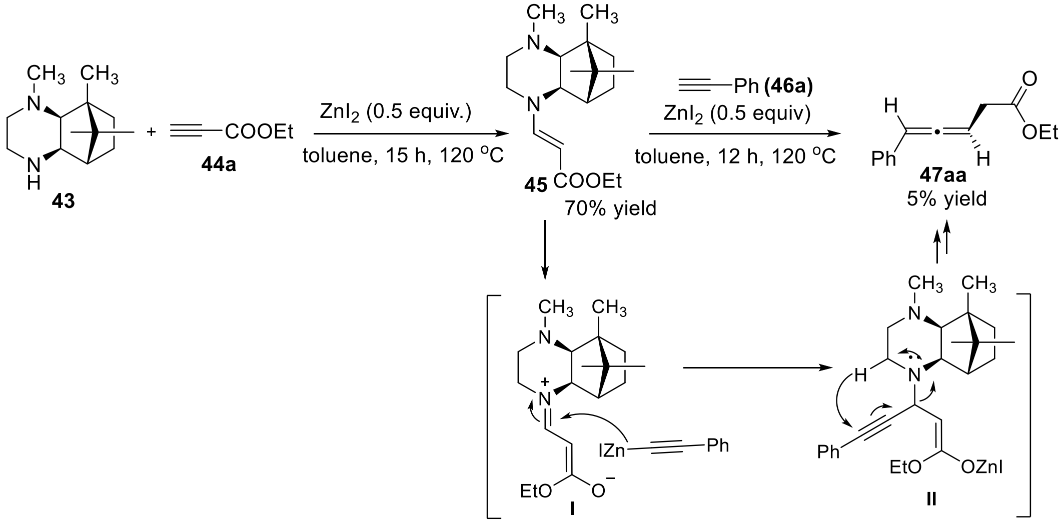
39 **40** **41** **42**

Reports on the synthesis of functionalized chiral allenes are still limited and the reported methods involve multistep operations using expensive reagents. Therefore, it is highly desirable to develop an efficient and a simple method for synthesis of functionalized chiral allenoates. We have undertaken efforts towards the highly enantioselective synthesis of β-allenoates through the chiral propargylamine intermediates by using (*S*)-DPP. The results are described in the next section.

2.2.1 Enantioselective synthesis of chiral allenes from 1-alkyne, ethylpropiolate and (*S*)-diphenylprolinol

As discussed in Chapter 1**,** chiral trisubstituted allenes are accessible by CuCl promoted hydroamination reaction of 1-alkynes using chiral secondary amine derivatives. It was of interest to us to examine whether hydroamination propiolates under these conditions would give the corresponding chiral allenoates with enantioselectivity. Accordingly, we have carried out the reaction of ethyl propiolate **44a** with chiral amine **43**. However, the reaction did not afford the functionalised trisubstituted allene but gave the enamine derivative **45** in 70% yield (Scheme 9).[21]

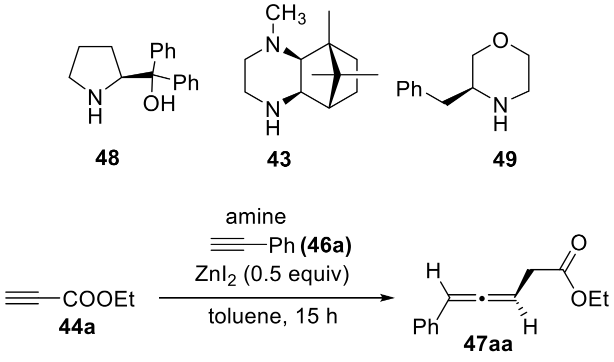
Scheme 9. Synthesis of enamine derivative and their conversion to beta-allenoate



The enamine derivative **45** could be transformed into the corresponding (*R*)-β-allenoate **47aa** but only in 5% yield using phenylacetylene and ZnI_2 at 120 °C (Scheme 9). The enamine intermediate **I** reacts with the alkenyl zinc complex produced *in situ* to give the intermediate **II** which affords the allenoate in low yield besides a complex mixture of unidentified products.

We have then examined the use of different readily accessible optically active chiral secondary amines, **43**, **48** and **49** in a single pot reaction under these conditions (Scheme 10). We have found that when the reaction was carried out using chiral amine **48**, the corresponding allene (*R*)-**47aa** was obtained in 10% yield and 92% ee. Whereas the reaction using chiral secondary amine **43** gave the product (*R*)-**47aa** in 5% yield with 90% ee, the chiral secondary amine **49** afforded the product (*R*)-**47aa** in 10% yield with 92% ee besides a complex mixture of unidentified products. Presumably, intermediates similar to the compound **45** which are expected to be formed are unstable under the present reaction conditions.

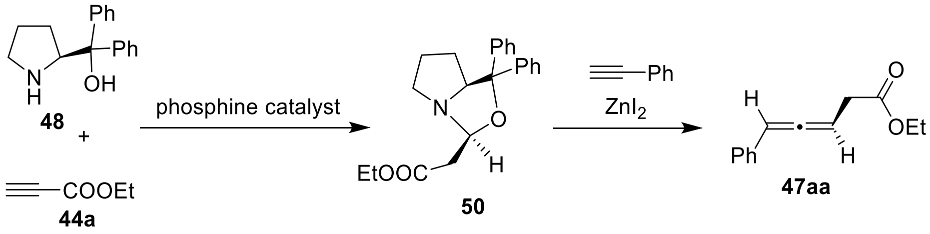
Scheme 10. Reaction of different optically active chiral amines



amine **48,** 10% y, 92% ee
amine **43,** 5% y, 90% ee
amine **49,** 10% y, 92% ee

Recently, reports appeared on asymmetric synthesis of oxazolidine derivatives by a bi-phosphine catalyzed synthetic protocol.[17] Also, a two-step synthesis involving preparation of oxazolidine derivative using benzaldehyde and their conversion to allene was also reported.[21a] Accordingly, we envisioned that preparation of oxazolidine *in situ* by phosphine catalysis followed by preparation of alkynyl zinc compounds *in situ* using 1-alkynes would afford the corresponding β-allenoates (Scheme 11).

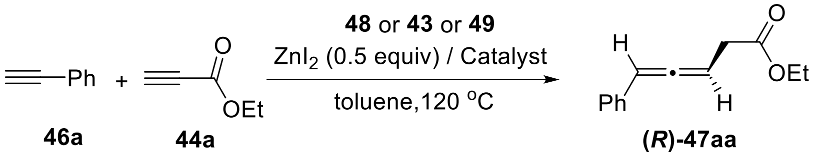
Scheme 11. Reaction of oxazolidine intermediate with 1-alkyne and ZnI_2



In the initial experiments, we examined the efficacy of phosphine catalysts to initiate the hydroamination of the propiolate ester followed by ZnI_2 promoted β-allenoate formation. We chose the ethyl propiolate **44a**, phenylacetylene **46a**, and chiral secondary cyclic amines **48**, **43**, and **49** for the optimization of reaction conditions. The results are presented in Table 1. The allenoate (*R*)-**47aa** was obtained in 20% yield with 92% ee when PPh_3 was used as a catalyst (Table 1, entry 1). However, replacement of chiral amine **48** with other chiral secondary amines such as **43** and **49** resulted in the very low conversion of the substrates (Table 1, entry 2 and 3). Also, the allenoate product (*R*)-**47aa** was obtained only in 20% yield using 10 mol% of catalyst (Table 1, entry 4). The lower yield could be attributed to the absence of hydroxyl group in chiral amine **43** and **49** (Table 1).

Further improvement of the yield of the allenoate product was achieved by screening various phosphine catalysts with chiral amine **48**. It was formed that when PCy_3 used, the corresponding β-allenoate obtained in 10%yield and 90% ee (entry 5, Table 1). When DPPE used, the allenoate was obtained in 62% yield and 99% ee (entry 6, Table 1). The phosphines DPPP, DPPB, and DPPPent also gave the allenoate (*R*)-**47aa** in good yields and enantioselectivity (entry 7, 8, and 9, Table 1). We have explored further scope of the reaction using DPPE as the catalyst.

Table 1. Reaction of different phosphene catalysts with chiral amines, ethyl propiolate and phenylacetylene.

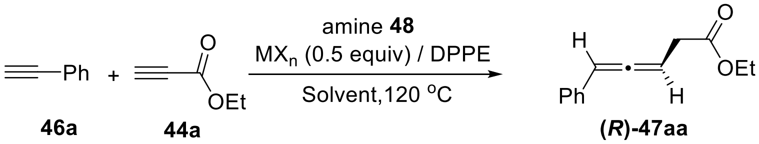


entry	catalyst[a]	amine	mol%	47aa (%)[b]	ee[c](%)
1	PPh_3	**48**	5	20	92
2	PPh_3	**43**	5	5	90
3	PPh_3	**49**	5	10	92
4	PPh_3	**48**	10	20	92
5[b]	PCy_3	**48**	10	10	90
6[b]	DPPE[d]	**48**	5	62	99
7[b]	DPPP[d]	**48**	5	65	92
8	DPPB[d]	**48**	5	60	93
9	DPPPent[d]	**48**	5	65	85

[a] All reactions were performed using amines **48**, **43**, **49** (1 mmol), 1.0 mmol of **46a**, 1.0 mmol of ethyl propiolate **44a**, and 5 mol % of the catalyst at 120 °C for 12 h. [b] These reactions were run for 10-12 h. [c] The ee was determined by chiral HPLC analysis. [d] DPPE, DPPP, DPPB, and DPPPent are acronyms for diphenylphosphinoethane, -propane, -butane, and -pentane, respectively.

We have also carried out the reaction of $ZnCl_2$, $ZnBr_2$ and ZnI_2 promoted chiral β-allenoate synthesis using DPPE as the catalyst. The $ZnCl_2$ and $ZnBr_2$ gave the chiral β-allenoate in 5% and 20% yields (entry 1, and 2, Table 2). However, the use of ZnI_2 promoted reaction gave the chiral β-allenoate in 62% yield with an excellent enantioselectivity (99% ee) (entry 3, Table 2).

Table 2. Reaction of Different Metal salts and Solvents with Chiral Amine 48, DPPE, Ethyl propiolate and phenylacetylene.[a]



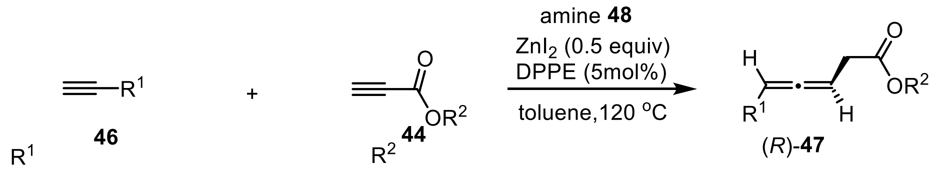
S.No	Solvent	Temp (°C)	MX$_n$	Time (h)[b]	47aa Yield(%)[c]	ee(%)[d]
1	Toluene	120	$ZnCl_2$	15	20	90
2	Toluene	110	$ZnBr_2$	12	50	99
3	Toluene	120	ZnI_2	10	62	99
4	Toluene	140	ZnI_2	10	68	85
5	Toluene	110	ZnI_2	10	55	99
6	Dioxane	100	ZnI_2	15	20	92

[a] The reaction was performed using amine **48**, 1 mmol of **44a**, 1.0 mmol of **46a**, and 5 mol % of the DPPE. [b] These reactions were run for 10-15 h. [c]Yields of β-allenoate . [d]The ee was determined by chiral HPLC analysis.

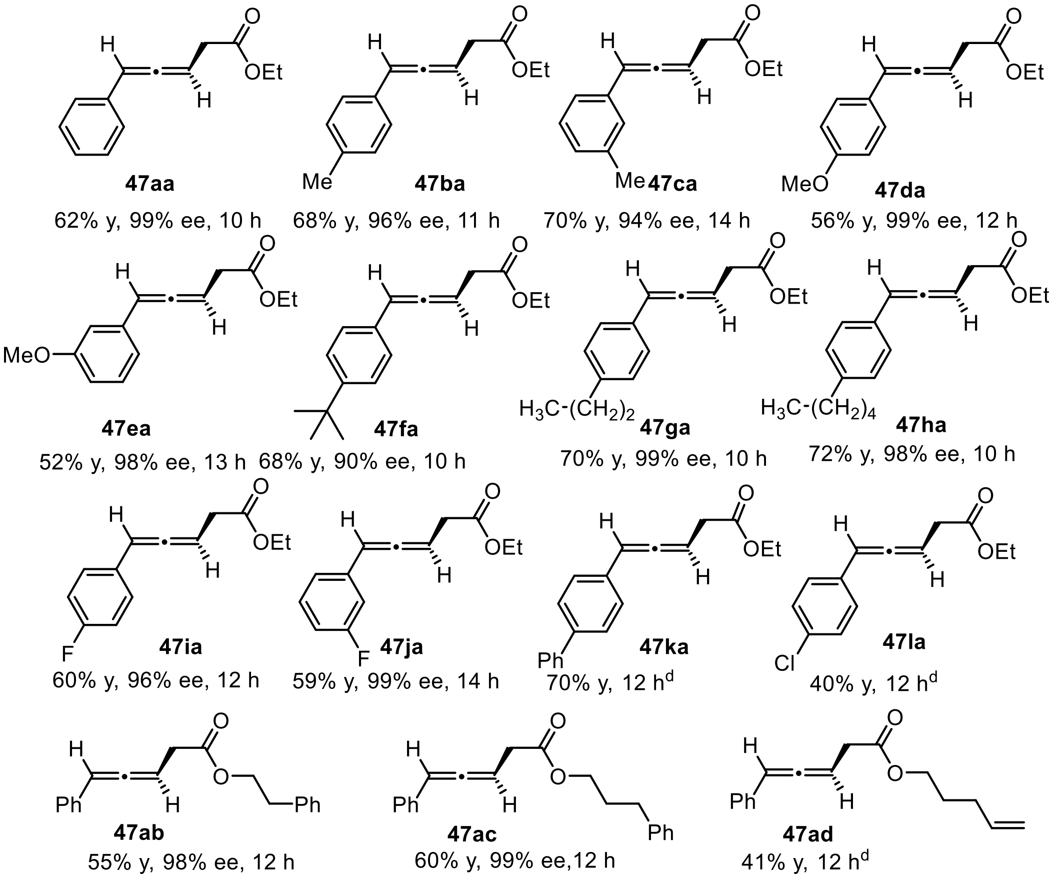
The reaction temperature was also found to be crucial for this transformation. An elevating the temperature above 120 °C led to the formation of chiral β-allenoate **47aa** in 68% yield (entry 4, Table 2), whereas lowering the temperature to 110 °C resulted in 55% yield of chiral β-allenoate **47aa** (entry 5, Table 2). In dioxane solvent, this transformation gave the chiral β-allenoate **47aa** in 20% yield (entry 6, Table 2). Thus, ZnI_2 gave the better optimum result under this condition (entry 3, Table 2).

Under the optimum conditions (entry 3, Table 2), we have examined the substrate scope using various 1-alkynes. When the alkynes with **46b**, **46c**, **46d**, and **46e** R^1 groups 4-Me-, 3-Me-, 4-OMe-, and 3-OMe-substitution in the phenyl ring react with ethyl propiolate **44a** to give the (*R*)-β-allenoates **47ba-47ae** in good yields with very good enantioselectivities (Table 3).

Table 3. Synthesis of β-Allenoates[a, b, c]



46a = Ph
46b = Ph-*p*CH_3
46c = Ph-*m*CH_3
46d = Ph-*p*OCH_3
46e = Ph-*m*OCH_3
46f = Ph-*p*-*tert*.butyl
46g = Ph-*p*-propyl
46h = Ph-*p*-*n*pentyl
46i = Ph-*p*F
46j = Ph-*m*F
46k = Ph-*p*Ph
46l = Ph-*p*Cl
44a = -Et
44b = $-(CH_2)_2Ph$
44c = $-(CH_2)_3Ph$
44d = $-(CH_2)_3CH=CH_2$



47aa 62% y, 99% ee, 10 h
47ba 68% y, 96% ee, 11 h
47ca 70% y, 94% ee, 14 h
47da 56% y, 99% ee, 12 h
47ea 52% y, 98% ee, 13 h
47fa 68% y, 90% ee, 10 h
47ga 70% y, 99% ee, 10 h
47ha 72% y, 98% ee, 10 h
47ia 60% y, 96% ee, 12 h
47ja 59% y, 99% ee, 14 h
47ka 70% y, 12 h[d]
47la 40% y, 12 h[d]
47ab 55% y, 98% ee, 12 h
47ac 60% y, 99% ee,12 h
47ad 41% y, 12 h[d]

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[a] The reactions were carried out by using amine **48** (1.0 mmol), propiolates **44** (1.0 mmol), DPPE (5 mol%) and 1-alkynes **46** (1.0 mmol) in toluene (3 mL) at 120 °C for 10-14h. [b] Yields of β-allenoate. [c] The ee was determined by chiral HPLC analysis. [d] The ee could not be determined by chiral HPLC as the AD-H, AS-H, OB-H, OD-H and OJ-H columns available with us failed to separate the enantiomers of **47ka, 47la,** and **47ad**.

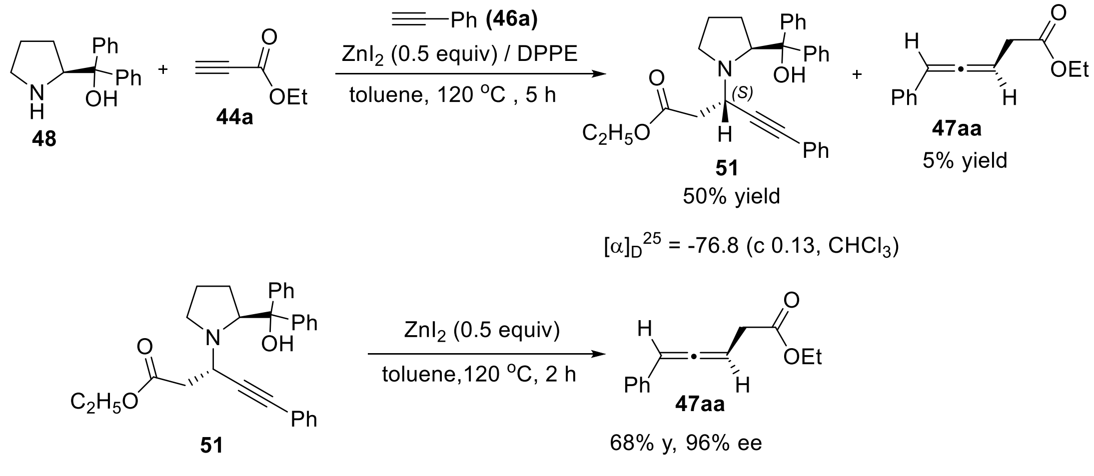
In addition, alkynes substituted with 4-*tert*-butyl-, 4-propyl and 4-pentyl groups in the phenyl ring **46f**, **46g**, and **46h** also gave the allenoates with excellent enantioselectivity

(Table 3, **47fa-47ha**). Also, alkynes **46i**, **46j**, and **46l** with electron withdrawing 4-F-, 3-F-, and 4-Cl, resulted in the formation of the allenoates in 40-60% yields with 96-99% ee (Table 3, **47ia**, **47ja,** and **47la**). Similarly, the alkyne **46k** with 4-Ph substitution gave the corresponding (*R*)-β-allenoate in 70% yield (Table 3, **47ka**). We have also examined the use of propiolate esters containing different R^2 groups such as 3-phenylpropyl **44b**, 4-phenylpropyl **44c,** and pent-4-en-1-yl **44d** and obtained the corresponding β-allenoates **47ab-47ad** in 41-60% yield with 98-99% ee (Table 3). All the optically active β-allenoates obtained by using chiral amine **48** are levorotatory from which the absolute configurations of the major enantiomer of the chiral allenes are assigned as *R* according to the Lowe-Brewster rule[23] and comparison with previous reports.[21]

2.2.2 Isolation of propargylamine derivative 51

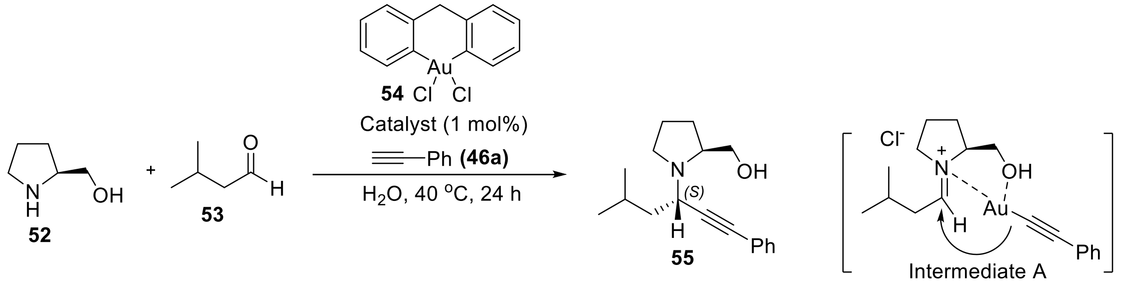
We have also carried out an experiment to isolate the propargylamine intermediate **51** that is expected to form in this transformation by stopping the reaction after 5 h (Scheme **12**). In this case, the propargylamine **51** was obtained in 50% yield besides the allenoate **47aa** (5% yield). Also, the propargylamine intermediate **51** is readily converted to the chiral β-allenoate **47aa** upon reaction with ZnI_2 (Scheme 12).

Scheme 12



Previously, methods have been developed for the preparation of chiral propargylamines *via* imine intermediates formed *in situ* using (*S*)-prolinol or (*S*)-DPP which generates the new stereogenic center with (*S*) configuration which was also confirmed by X-ray crystal structure analysis (Scheme 13).[22a] In case of functionalized propargylamine **51**, the newly formed stereogenic center configuration was assigned in accordance with mechanism outlined in Scheme **13** and also by comparison with reports. [21, 22]

Scheme 13



2.2.3 Isolation of intermediate enamine derivative and β-allenoate

We have examined the intermediates involved in this transformation by recording the NMR spectrum of the reaction mixture after removing toluene solvent which indicated the presence of the oxazolidine **50** and enamine derivative **56** intermediates (Scheme 14). However, upon silica gel column chromatography, the reaction mixture gave only the enamine derivative **56**. The structure of the enamine product **56** was confirmed by single crystal X-ray analysis (Figure 2). Presumably, the oxazolidine derivative present in the mixture is also converted to the enamine derivative **56** in the presence of silica gel.[24] We have observed that the enamine derivative **56**, upon reaction with 1-alkyne, afforded the β-allenoate **47aa** in only 10% yield with 92% ee (Scheme 14).

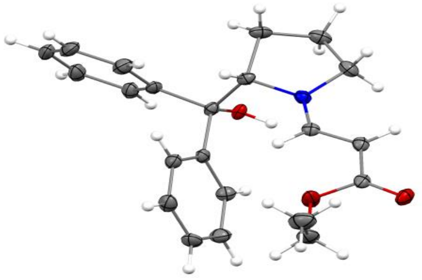
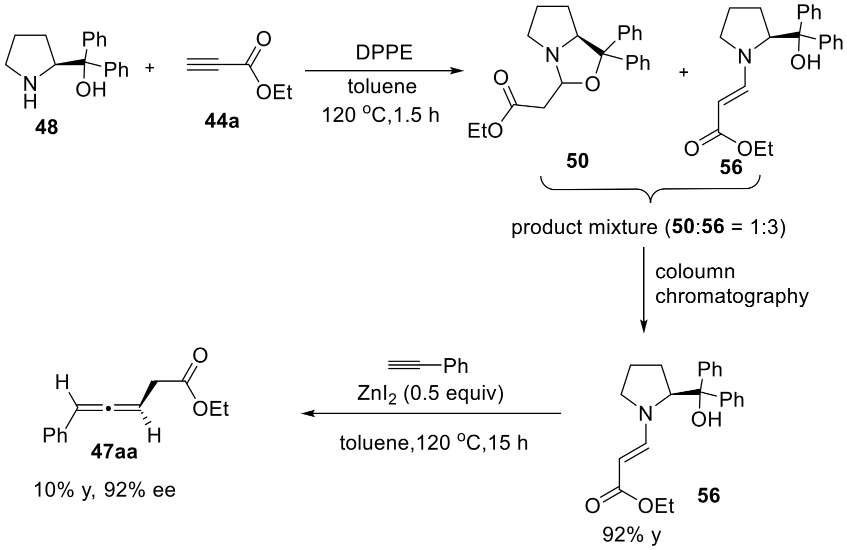


Figure 2. ORTEP representation of compound **56** and thermal ellipsoids are drawn with 50% probability.

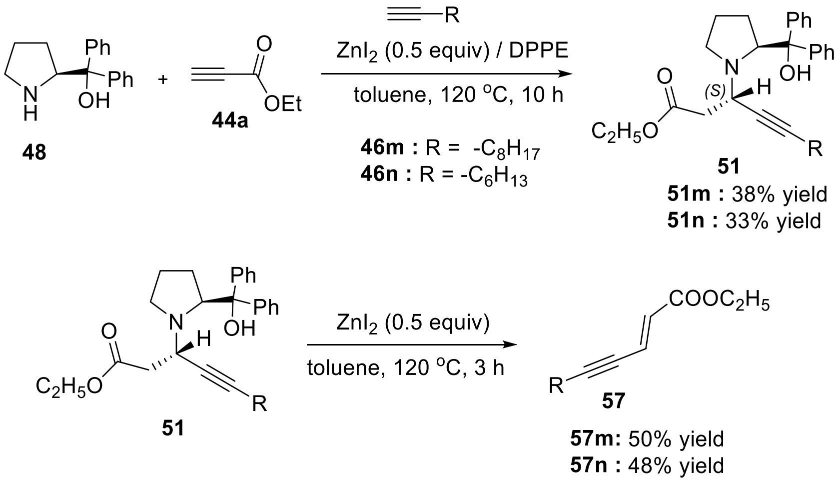
Scheme 14



2.2.4 Isolation of propargylamine derivative 51m and 51n

We have also attempted the reaction of 1-alkynes **51m** and **51n** with alkyl substitution with ethyl propiolate **44a**, DPPE, and chiral amine **48** in toluene. It was found that the reaction did not give the desired β-allenoate but gave the corresponding propargylamine derivatives **57** in 33-38% yield along with some unidentified products (Scheme 15).

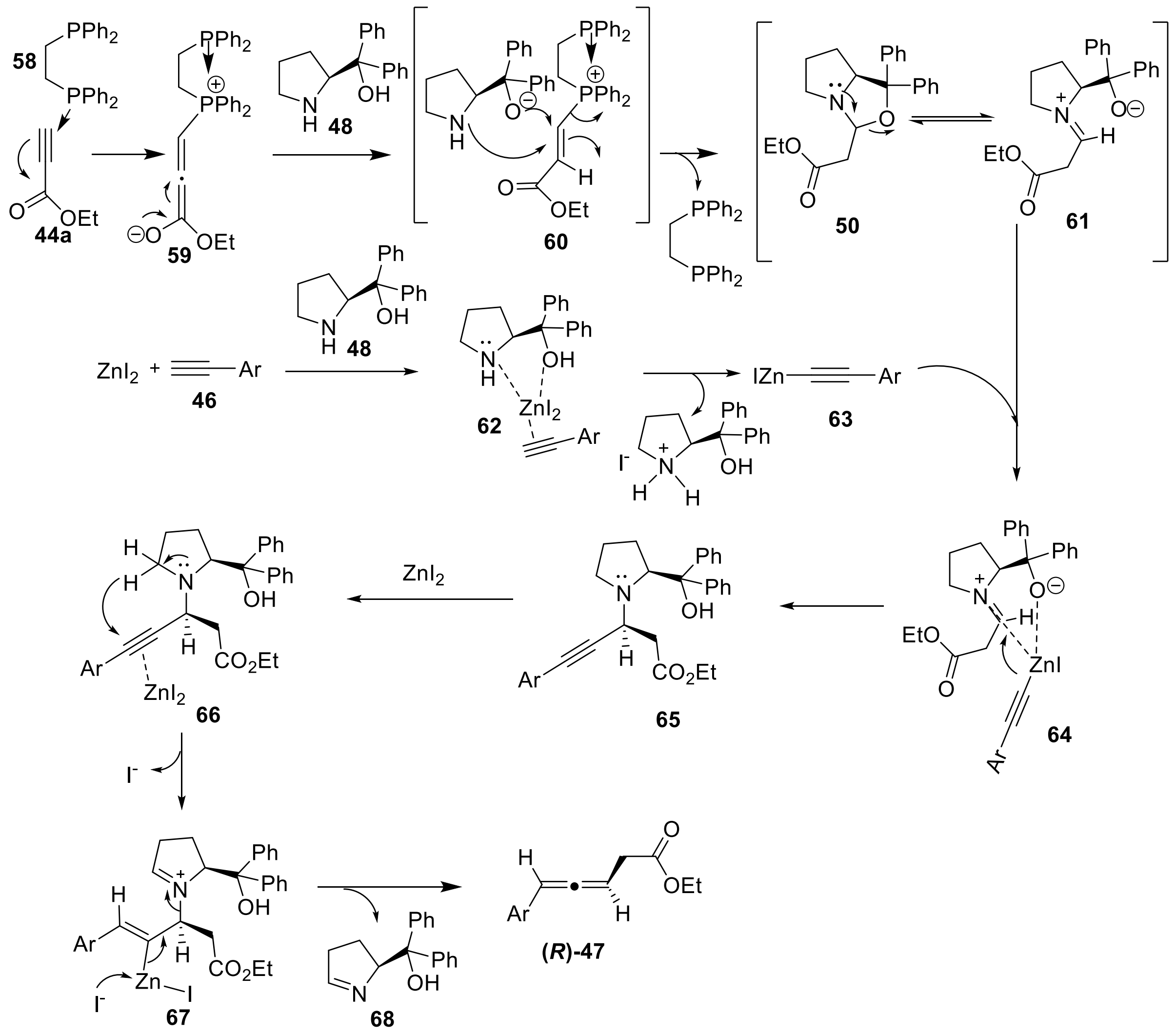
Scheme 15



In this case, the oxazolidine **50** expected to be formed *in situ* reacts with aliphatic 1-alkynes in the presence of ZnI_2 to afford the propargylamines in low yield due to lesser reactivity of aliphatic 1-alkyne towards oxazolidine derivative **50** compared to aromatic 1-alkynes. Also, the propargylamine derivatives (**51m** and **51n**) upon reaction with ZnI_2 did not give the desired β-allenoate **47**. In this case, however, only the enynoate **57** was obtained in 48-50% yield (Scheme 15).[24]

A tentative reaction mechanism depicted in Scheme 16 may be considered for the formation of allenoates.[17, 21, 26] Initially, the intermediate **59** would be formed by the conjugate addition of bi-phosphine to the electron-deficient propiolate. The chiral amine **48** would be deprotonated by the intermediate **59**. Subsequent conjugate addition would generate the intermediate **60** which could undergo intramolecular Michael addition and elimination of the bi-phosphine to generate the cyclized oxazolidine product **50** and the iminium species **61**. Reaction of the alkynyl zinc formed *in situ* with the intermediate **61** would result in the formation of the propargylamine **65.** Subsequently, complexation with ZnI_2 would give the intermediate **66** which after an intramolecular hydride shift and addition of the H and ZnI group across the triple bond would give the intermediate **67**. After elimination of ZnI_2 and the imine **68**, the chiral (*R*)-β-allenoate **47** would be formed.

Scheme 16. Plausible Mechanism for Chiral β-Allenoates



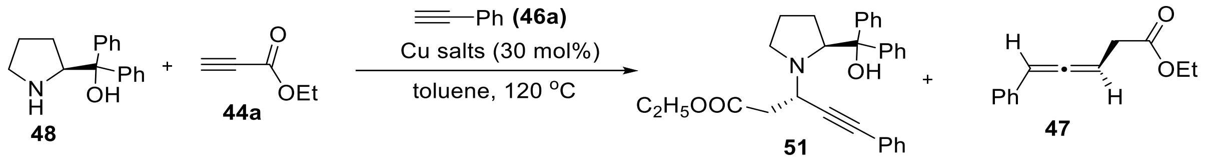
The spectral data of the imine byproduct **68** showed 1:1 correspondence with the reported data.[21a] The product could be easily reduced and isolated for reuse by adding sodium borohydride in methanol at -20 °C before workup and bringing the contents to 25 °C and stirring for 2 h following a reported procedure.[21]

2.2.5 Synthesis of β-allenoates from propargylamine derivatives

2.2.5.1 Synthesis of propargylamine derivatives

As described in previous sections, synthesis of β-allenoates was achieved using a phosphine catalyst. We have observed that when the reaction carried out using (*S*)-DPP with ethyl propiolate and phenylacetylene in presence of some copper salts, the propargylamine derivatives were obtained in 67-80% yields as summarized in Table 4.

Table 4. Reaction of (*S*)-DPP, ethylpropiolate and 1-alkyne Cu (I) salts[a]



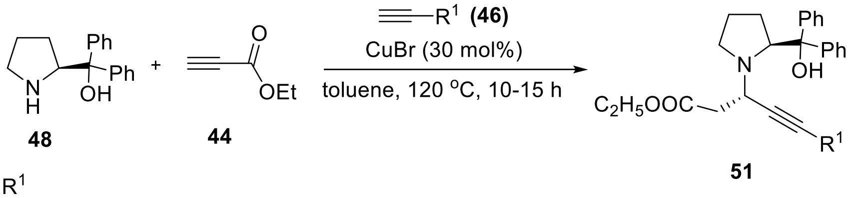
Entry	Solvent	Temp (°C)	MX_n	Time (h)	Compound 51Yield (%)[b]	Compound 47 Yield (%)[c]	ee (%)[d]
1	Toluene	120	CuI	12	68	8	95
2	Toluene	120	CuBr	12	80	12	96
3	Toluene	120	CuCl	12	67	5	97
4	Dioxane	100	CuI	15	70	10	96
5	Dioxane	100	CuBr	15	69	10	96

[a]The reaction was performed using amine **48**, 1 mmol of **46a**, 1.0 mmol of **44a**, and 5 mol % of the DPPE and the reactions were stirred for 12-15 h. [b]Yields of propargylamines. [c]Yields of β-allenoate. [d]The ee was determined by chiral HPLC analysis.

Initially, we have carried out the experiments using ethyl propiolate, phenylacetylene, and (*S*)-DPP for the reaction with copper salts at 120 °C. The propargylamine **51** was formed along with β-allenoate **47aa** in 8% yield when CuI used under these conditions (entry 1, Table 4). When CuBr was used the propargylamine **51** formed in 80% yield (entry 2, Table 4) along with β-allenoate in 12% yield. The use of CuCl gave the propargylamine **51** in 67% yield (entry 3, Table 4) along with β-allenoate (5% yield). Similar results were also realized in dioxane solvents (entries 4, and 5, Table 4).

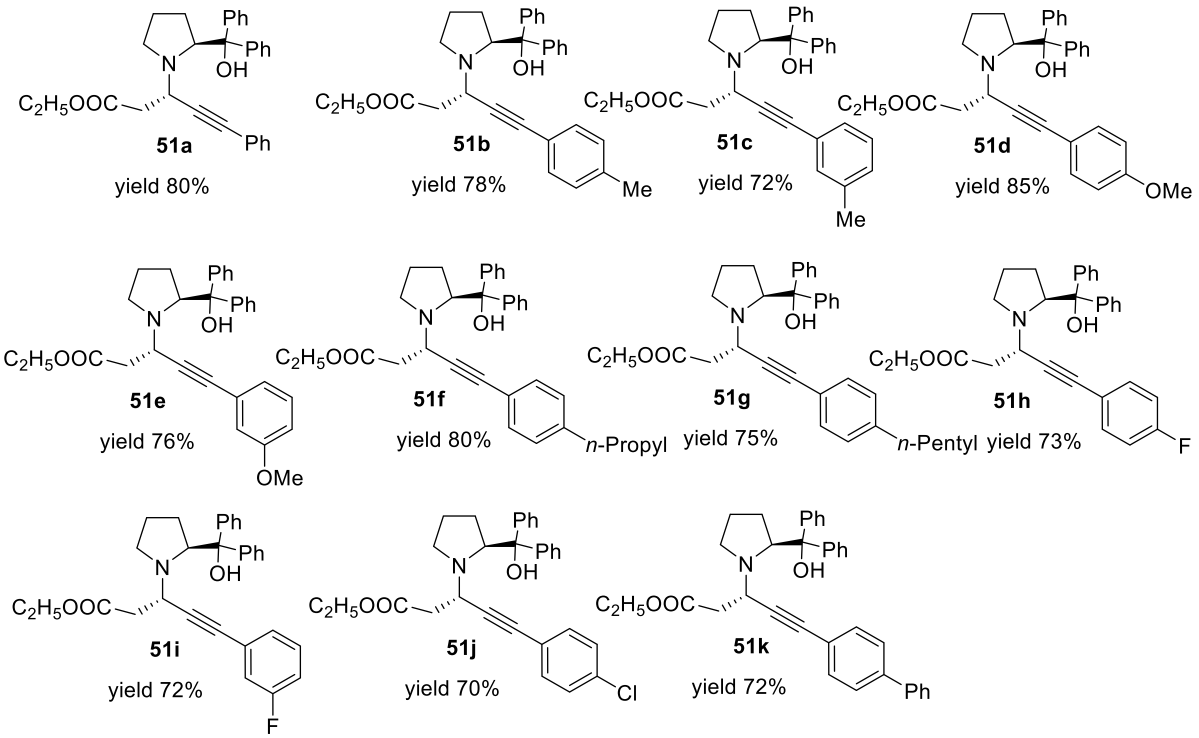
It is evident from the Table 4 that the CuBr (30 mol %) (Table 4, entry 2) gave optimum results. Therefore, we have carried out the reactions with different alkynes using CuBr (30 mol %) to obtain the corresponding chiral propargylamines in 70-85% yields (Table 5).

Table 5. Reaction of ethyl propiolate, 1-alkyne and (*S*)-DPP[a,b]



R^1

46a = Ph
46b = Ph-*p*CH_3
46c = Ph-*m*CH_3
46d = Ph-*p*OCH_3
46e = Ph-*m*OCH_3
46f = Ph-*p*-propyl
46g = Ph-*p*-*n*pentyl
46h = Ph-*p*F
46i = Ph-*m*F
46j = Ph-*p*Cl
46k = Ph-*p*Ph



51a yield 80%
51b yield 78%
51c yield 72%
51d yield 85%
51e yield 76%
51f yield 80%
51g yield 75%
51h yield 73%
51i yield 72%
51j yield 70%
51k yield 72%

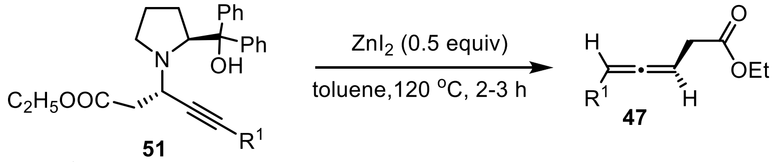
[a] The reactions were carried out by using amine (1.0 mmol), ethyl propiolate (1.0 mmol) and 1-alkyne (1.0 mmol) in toluene (3mL) at 120 °C for 10-15 h. [b] Yields of propargylamines.

The substituted 1-alkynes having electron donating group **46a**, **46b**, **46c**, **46d** and **46e** reacted with ethyl propiolate to give the propargylamines **51a**, **51b**, **51c**, **51d** and **51e** in 72-85% yields. Similarly, the reaction using the 1-alkynes **46f** and **46g** furnished the corresponding propargylamine **51f** and **51g** in up to 75-80% yields. The alkynes substituted with electron withdrawing group at *para* and *meta* postions **46h**, **46i** and **46j** afforded the corresponding propargylamines **51h**, **51i** and **51j** in 70-73% yields, respectively. Also, the Phenyl group substitution on *para* postion of 1-alkyne **46k** gave the corresponding propargylamine **51k** in 72% yield (Table 5).

The chiral propargylamines **51a-51k** react with ZnI_2 at 120 °C to give the corresponding allenes **47a-47k** in 61-80% yield at 120 ºC (Table 6). The propargylamines having electron donating groups afforded the chiral allenes **47a**, **47b**, **47c**, **47d**, **47e**, **47f** and **47g** and in 67-80% yields with up to 99% ee. The electron withdrawing group containing propargylamines afforded the allenoates **47h**, **47i**, and **47j** in 61-65% yields with 99% ee. Also, the propargylamine **51k** afforded the allenoate **47k** in 75% yield.

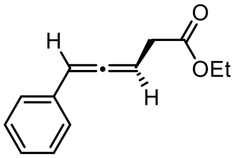
All the optically active allenes obtained by using chiral amines **48** are levorotatory from which the absolute configurations of the major enantiomer of the chiral allenes are assigned as *R* by the Lowe-Brewster rule[22] and also by comparison with the $[\alpha]_D^{25}$ values reported for similar trisubstituted allene derivatives.[21]

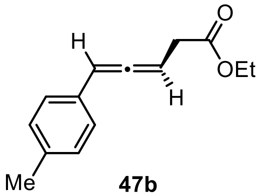
Table 6. Synthesis of β-allenoates from propargylamine derivatives[a]

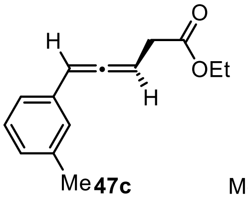


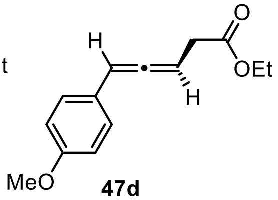
R^1

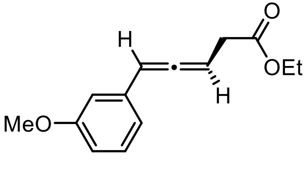
51a = Ph
51b = Ph-pCH$_3$
51c = Ph-mCH$_3$
51d = Ph-pOCH$_3$
51e = Ph-mOCH$_3$
51f = Ph-p-propyl
51g = Ph-p-$n$pentyl
51h = Ph-pF
51i = Ph-mF
51j = Ph-pCl
51k = Ph-pPh

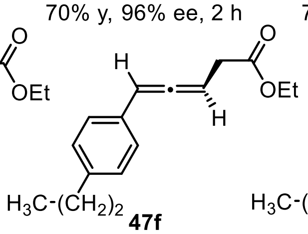

47a
68% y, 99% ee, 2 h

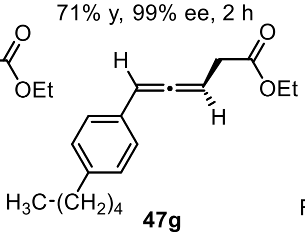

47b
70% y, 96% ee, 2 h

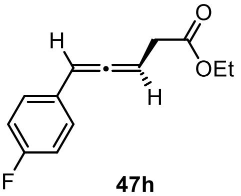

47c
71% y, 99% ee, 2 h

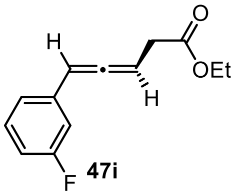

47d
69% y, 99% ee, 3 h

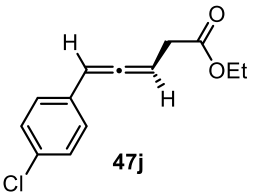

47e
67% y, 98% ee, 3 h

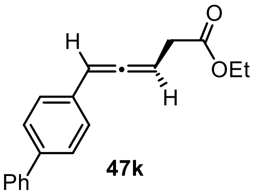

47f
80% y, 99% ee, 2 h


47g
78% y, 98% ee, 2h


47h
65% y, 3 h[c]


47i
61% y, 99% ee, 2.5 h

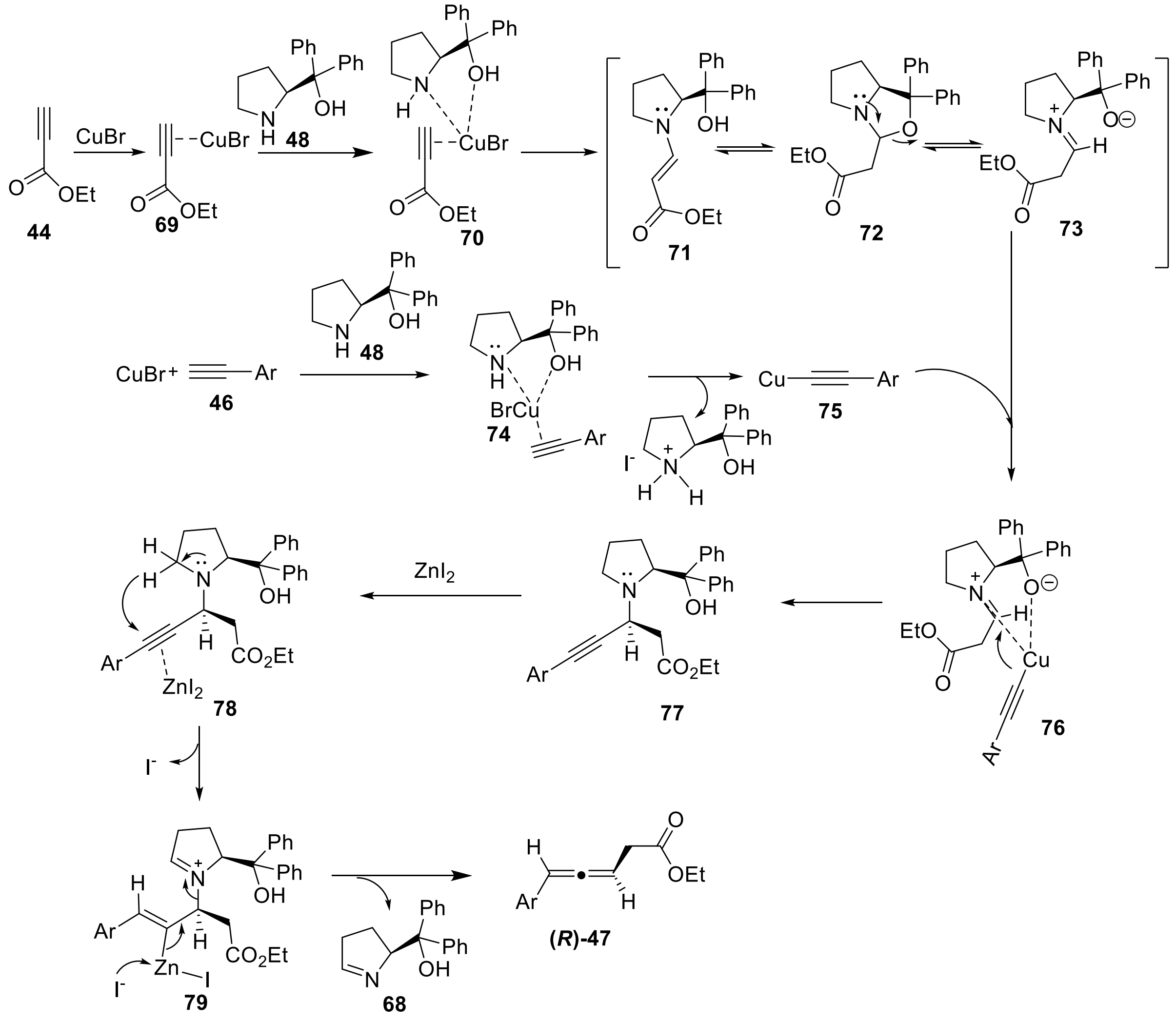

47j
62% y, 2 h[c]


47k
75% y, 2 h[c]

[a]The reactions were carried out by using propargylamine (0.5 mmol) and ZnI$_2$ (0.5 eq) in toluene (3mL) at 120 °C for 2-3 h. [b]Yields of β-allenoates. [c]The ee could not be determined by chiral HPLC as the AD-H, AS-H, OB-H, OD-H and OJ-H columns available with us failed to separate the enantiomers of **47h, 47j,** and **47k**. [d]The ee was determined by chiral HPLC analysis.

The formation of chiral propargylamines and their conversion to chiral allenoates can be rationalized by the mechanism outlined in Scheme 17. The initially formed alkenyl copper intermediate **69** would lead to the **70** and the imine **73** *in situ*.[27] The alkenyl intermediate **98** would react with the imine **73** derived from ethyl propiolate and (*S*)-DPP to give selectively the corresponding propargylamine **77** which upon reaction with ZnI_2 could give the intermediate **78**. Subsequent, intermolecular hydride shift and addition of H and ZnI group across the triple bond would give intermediate **79** that after elimination of ZnI_2 and the imine **68** would afford the chiral (*R*)-β-allenoate **47**.

Scheme 17. Plausible mechanism for chiral β-allenoates



The methods described here to access to chiral β-allenoates have potential to stimulate further research efforts on the development of synthetic methods based on the functional groups present in this synthon.

Next, we have undertaken studies on the enantioselective synthesis of chiral vinyl allene for application in [4+2] cycloaddition. The results are described in the next chapter.

2.3 Conclusions

We have developed a convenient method for the highly enantioselective synthesis of chiral β-allenoates from 1-alkynes, propiolates and chiral secondary amines *via* the corresponding transient oxazolidine intermediates and propargylamine derivatives. Methods for isolation of oxazolidine, enamine and propargylamine intermediates and subsequent zinc iodide promoted conversion to chiral β-allenoate should be helpful in designing methods to access these potentially useful multifunctional synthons for further synthetic exploitation.

We have also developed a simple, practical and inexpensive method for the Cu (I) promoted diastereoselective synthesis of chiral propargylamines using (*S*)-DPP and their enantioselective conversion to chiral β-allenoates upon reaction using ZnI_2.

2.4 Experimental Section

2.4.1 General information

Melting points were determined using a Superfit capillary point apparatus. IR (KBr) spectra were recorded on JASCO FT-IR spectrophotometer Model 5300. The neat IR spectra were recorded on JASCO FT-IR spectrophotometer Model 5300. ^{1}H-NMR (400 MHz), ^{13}C-NMR (100 MHz) spectra were recorded on Bruker-AC-200 and Bruker-Avance-400 spectrometers, respectively with chloroform-d as solvent and TMS as reference ($\delta = 0$ ppm). The chemical shifts are expressed in δ downfield from the signal of internal TMS. Liquid Chromatography (LC) and mass analysis (LC-MS) were performed on SHIMADZU-LCMS-2010A and BRUKER MARXIS High Resolution Mass Spectrometry (HRMS). The mass spectral analyses were carried out using Chemical Ionization (CI) or Electro Spray Ionization (ESI) techniques. Elemental analyses were carried out using a Perkin-Elmer elemental analyzer model-240C and Thermo Finnigan analyzer series Flash EA 1112. Mass spectral analyses for some of the compounds were carried out on VG 7070H mass spectrometer using EI technique at 70 eV.

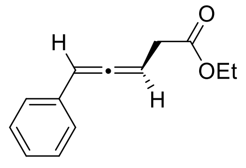
Analytical grade of CuBr, $Cu(OTf)_2$, $AgNO_3$ and ZnI_2 were purchased from Sigma-Aldrich. $ZnBr_2$ was purchased from E-Merck. Toluene supplied by E-Merck, India was freshly distilled over sodium-benzophenone ketyl before use. Analytical thin layer chromatographic tests were carried out on glass plates (3 x 10 cm) coated with 250mμ E-Merck and acme's silica gel-G and GF_{254} containing 13% calcium sulfate as binder. The spots were visualized by short exposure to iodine vapor or UV light. Column chromatography was carried out using E-Merck and acme's silica gel (100-200 or 230-400 mesh) and neutral alumina.

Optical rotations were measured on Rudolph Research Analytical AUTOPOL-II (readability ±0.01^o) and AUTOPOL-IV (readability ±0.001^o) automatic polarimeters. HPLC analyses were performed on an SCL-10ATVP SHIMADZU instrument. The ee values were determined using various chiral columns e.g., CHIRALCEL OD-H column (4.6 x 250 mm) with eluents: hexane, 2-propanol, ethanol and heptane at a rate 0.5-1 mL/min, with the monitoring wave length 254 nm.

2.4.2. General procedure for synthesis of chiral β-allenoates

To a stirred solution of amine **48** (1 mmol) in toluene (3 mL), DPPE (0.020 g, 0.005 mmol), propiolates **44** (0.108 mL, 1.0 mmol), the reaction mixture stirr for 1.5 h and add the ZnI_2 (0.160 g, 0.5 mmol), 1-alkyne **46** (1 mmol) at 120 °C under N_2 atmosphere. The contents were stirred for 10 h. The reaction mixture cooled to room temperature. Toluene was removed using reduced pressure. Water (5 mL) and DCM (15 mL) were added. The DCM layer was washed with saturated NaCl solution, dried (Na_2SO_4) and concentrated. The residue was subjected to column chromatography using hexane and ethyl acetate (95:5) as eluent to isolate the allenoates **47**.

5-Phenyl-penta-3,4-dienoic acid ethyl ester (47aa)



47aa

Yield : 0.135 g, 62%, 99% ee; white liquid.

$[\alpha]_D^{25}$: -198.9 (*c* 0.11g, $CHCl_3$)

IR (neat) : 3419, 2361, 1731 cm^{-1}.

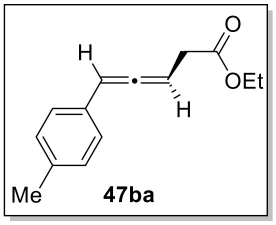
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.43-7.32 (m, 4H), 7.23-7.22 (m, 1H), 6.25-6.23 (m, 1H), 5.75-5.72 (m, 1H), 4.21 (quin, *J* = 4.0 Hz, 2H), 3.19-3.17 (m, 2H), 1.31-1.28 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 206.3, 171.2, 133.9, 132.3, 128.6, 127.1, 95.6, 88.2, 60.9, 34.5, 14.2.

HRMS : (ESI-TOF) m/z : $[M+H]^+$ calcd for $C_{13}H_{14}O_2\ NH_4$: 220.1338, Found: 220.1338.

<u>Enantiomeric purity</u>: The enantioselectivity was determined by HPLC using chiral column, chiralcel OB-H, hexanes:i-PrOH/98:2; flow rate 0.5 mL/min, 254 nm, retention times: 17.6 min. (major) and 20.4 min. (minor).

5-p-Tolyl-penta-3,4-dienoic acid ethyl ester (47ba)


47ba

Yield : 0.146 g, 68%, 96% ee; light yellow liquid.

$[\alpha]_D^{25}$: -241 (*c* 0.5, $CHCl_3$)

IR (neat) : 1966, 1736 cm^{-1}.

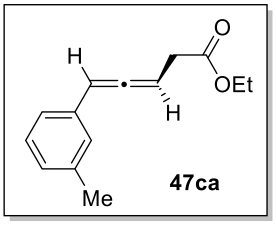
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.22-7.20 (m, 1H), 7.18-7.14 (m, 2H), 7.05-7.03 (m, 1H), 6.20-6.19 (m, 1H), 5.69 (q, *J* = 4.0 Hz, 1H), 4.17 (quin, *J* = 4.0 Hz, 2H), 3.16-3.13 (m, 2H), 2.35 (s, *J* = 4.0 Hz, 3H), 1.32-1.1.26 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 206.1, 171.3, 136.9, 132.4, 128.2, 129.3, 126.8, 95.4, 88.1, 60.9, 34.6, 21.2, 14.2.

HRMS : (ESI-TOF) m/z : [M+H]$^+$ calcd for $C_{14}H_{16}O_2Na$: 239.1047, Found: 239.1048.

<u>**Enantiomeric purity**</u>**:** The enantioselectivity was determined by HPLC using chiral column, chiralcel OB-H, hexanes:i-PrOH/98:2; flow rate 0.5 mL/min, 254 nm, retention times: 16.5 min. (minor) and 21.6 min. (major).

(R)-Ethyl-5-(m-tolyl)penta-3,4-dienoate (47ca)


47ca

Yield : 0.151 g, 70%, 94% ee; yellow liquid.

$[\alpha]_D^{25}$: -232.4 (*c* 0.5 $CHCl_3$)

IR (neat) : 1966, 1736 cm^{-1}.

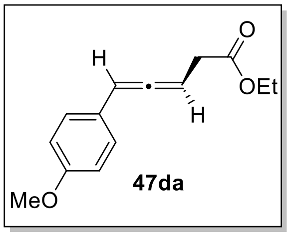
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.22-7.20 (m, 1H), 7.18-7.14 (m, 2H), 7.05-7.03 (m, 1H), 6.20-6.19 (m, 1H), 5.69 (q, *J* = 4.0 Hz, 1H), 4.17 (quin, *J* = 4.0 Hz, 2H), 3.16-3.13 (m, 2H), 2.35 (s, *J* = 4.0 Hz, 3H), 1.32-1.1.26 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 206.1, 171.3, 136.9, 132.4, 128.2, 129.3, 126.8, 95.4, 88.1, 60.9, 34.6, 21.2, 14.2.

HRMS : (ESI-TOF) m/z : $[M+H]^+$ calcd for $C_{14}H_{16}O_2Na$: 239.1047, Found: 239.1048.

<u>Enantiomeric purity</u>: The enantioselectivity was determined by HPLC using chiral column, chiralcel AS-H, hexanes:i-PrOH/100:0; flow rate 1 mL/min, 254 nm, retention times: 13.6 min. (major) and 16.1 min. (minor).

(R)-Ethyl 5-(4-methoxyphenyl)penta-3,4-dienoate (47da)



Yield : 0.129 g, 56%, 99% ee; white liquid.

$[\alpha]_D^{25}$: -260.3 (*c* 0.4, $CHCl_3$)

IR (neat) : 1956, 1725 cm^{-1}.

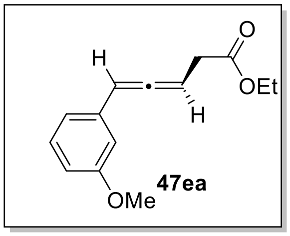
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.27-7.24 (d, *J* = 4.0 Hz, 2H), 6.88-6.85 (d, *J* = 4.0 Hz, 2H), 6.20-6.18 (m, 1H), 5.70 (q, *J* = 4.0 Hz, 1H), 4.20 (quin, *J* = 4.0 Hz, 2H), 3.82 (s, 3H), 3.16 (d, *J* = 4.0 Hz, 2H), 1.29 (t, *J* = 8.0 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 205.7, 171.3, 158.8, 128.0, 126.1, 114.1, 95.0, 88.1, 60.9, 55.3, 34.7, 14.2.

HRMS : (ESI-TOF) m/z : $[M+H]^+$ calcd for $C_{14}H_{17}O_3$: 233.1178; Found: 233.1178.

<u>Enantiomeric purity</u>: The enantioselectivity was determined by HPLC using chiral column, chiralcel OD-H, hexanes:i-PrOH/95:5; flow rate 0.5 mL/min, 254 nm, retention times: 16.1 min. (major) and 19.0 min. (minor).

(R)-Ethyl 5-(3-methoxyphenyl)penta-3,4-dienoate(47ea)



Yield : 0.120g, 52%, 98% ee; white liquid.

$[\alpha]_D^{25}$: -255.7 (*c* 0.2, $CHCl_3$)

IR (neat) : 1961, 1726 cm^{-1}.

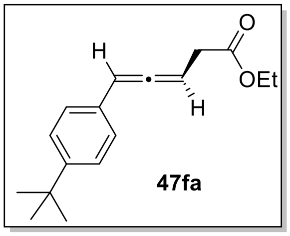
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.27-7.24 (d, *J* = 4.0 Hz, 2H), 6.88-6.85 (d, *J* = 4.0 Hz, 2H), 6.20-6.18 (m, 1H), 5.70 (q, *J* = 4.0 Hz, 1H), 4.20 (quin, *J* = 4.0 Hz, 2H), 3.82 (s, 3H), 3.16 (d, *J* = 4.0 Hz, 2H), 1.29 (t, *J* = 8.0 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 205.7, 171.3, 158.8, 128.0, 126.1, 114.1, 95.0, 88.1, 60.9, 55.3, 34.7, 14.2.

HRMS : (ESI-TOF) m/z : $[M+H]^+$ calcd for $C_{14}H_{17}O_3$: 233.1178; Found: 233.1178.

<u>Enantiomeric purity</u>: The enantioselectivity was determined by HPLC using chiral column, chiralcel AS-H, hexanes:i-PrOH/95:5; flow rate 0.5 mL/min, 254 nm, retention times: 13.4 min. (major) and 14.8 min. (minor).

(R)- Ethyl 5-(4-(tert-butyl)phenyl)penta-3,4-dienoate (47fa)



Yield : 0.175, 68%, 90% ee; yellow liquid.

$[\alpha]_D^{25}$: -219.3 (*c* 0.40, $CHCl_3$)

IR (neat) : 1965, 1725 cm^{-1}.

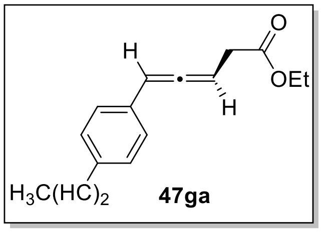
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.36-7.33 (m, 2H), 7.27-7.25 (m, 2H), 6.23-6.21 (m, 1H), 5.71-5.70 (m, 1H), 4.22-4.18 (m, 2H), 3.17-3.15 (m, 2H), 1.62-1.58 (m, 3H), 1.32-1.28 (m, 9H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 206.2, 171.2, 150.2, 134.8, 130.9, 126.6, 125.9, 125.5, 95.2, 88.0, 60.8, 34.6, 34.5, 31.2, 14.2.

HRMS : (ESI-TOF) m/z : M+H]$^+$ calcd for $C_{17}H_{23}O_2$: 259.1699; Found: 259.1698.

<u>Enantiomeric purity</u>: The enantioselectivity was determined by HPLC using chiral column, chiralcel OD-H, hexanes:i-PrOH/98:2; flow rate 0.5 mL/min, 254 nm, retention times: 16.8 min (minor) and 18.8 min (major).

(R)-Ethyl 5-(4-propylphenyl)penta-3,4-dienoate (47ga)



47ga

Yield : 0.170, 70%, 99% ee; yellow liquid.

[α]$_D^{25}$: -209.0 (*c* 0.1, $CHCl_3$)

IR (neat) : 1962, 1725 cm^{-1}.

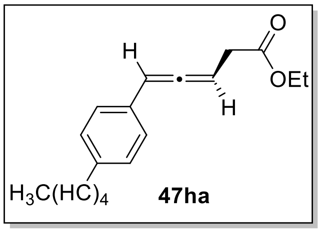
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.27-7.22 (m, 2H), 7.15-7.13 (m, 2H), 6.23-6.21 (m, 1H), 5.74-5.71 (m, 1H), 4.23-4.18 (m, 2H), 3.18-3.16 (m, 2H), 2.60-2.56 (m, 2H), 1.66-2.61 (m, 2H), 1.33-1.28 (m, 3H), 0.95 (t, *J* = 4.0 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 206.1, 171.3, 141.8, 132.4, 128.7, 128.3, 126.8, 95.4, 88.1, 60.9, 37.7, 34.6, 24.5, 14.2, 13.8.

HRMS : (ESI-TOF) m/z : [M+H]$^+$ calcd for $C_{16}H_{21}O_2$: 245.1542; Found: 245.1542.

<u>Enantiomeric purity</u>: The enantioselectivity was determined by HPLC using chiral column, chiralcel OJ-H, hexanes:i-PrOH/98:2; flow rate 0.5 mL/min, 254 nm, retention times: 18.8 min. (major) and 16.8 min. (minor).

(R)-Ethyl-5-(4-pentylphenyl)penta-3,4-dienoate (47ha)



47ha

Yield : 0.195 g, 72%, 98% ee; yellow liquid.

[α]D^{25} : -211.7 (*c* 0.2, $CHCl_3$)

IR (neat) : 1952, 1726 cm^{-1}.

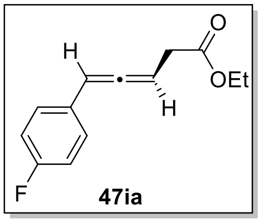
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.24 (d, *J* = 4.0 Hz, 2H), 7.14 (d, *J* = 4.0 Hz, 2H), 6.23-6.18 (m, 1H), 5.71 (q, *J* = 4.0 Hz, 1H), 4.20 (q, *J* = 4.0 Hz, 2H), 3.18-3.15 (m, 2H), 2.60 (t, *J* = 8.0 Hz, 2H), 1.58 (s, 3H), 1.33-1.27 (m, 6H), 0.91 (t, *J* = 4.0 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 206.1, 171.2, 142.0, 131.1, 129.9, 128.7, 126.8, 95.4, 88.0, 60.8, 35.6, 34.6, 31.4, 31.1, 14.1, 13.9.

HRMS : (ESI-TOF) m/z : $[M+NH_4]^+$ calcd for $C_{18}H_{24}O_2NH_4$: 290.2120; Found: 290.2119.

<u>Enantiomeric purity</u>: The enantioselectivity was determined by HPLC using chiral column, chiralcel OD-H, hexanes:i-PrOH/99:1; flow rate 0.5 mL/min, 254 nm, retention times: 11.0 min. (major) and 13.9 min. (minor).

(R)-Ethyl 5-(4-fluorophenyl)penta-3,4-dienoate (47ia)



47ia

Yield : 0.132g, 60%, 96% ee; light yellow liquid.

[α]D^{25} : -185.4 (*c* 0.5, $CHCl_3$)

IR (neat) : 1954, 1736 cm^{-1}.

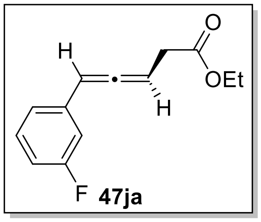
^{1}H NMR : (400 MHz, $CDCl_3$, δppm) 7.31-7.27 (m, 2H), 7.04-6.99 (m, 2H), 6.22-6.19 (m, 1H), 5.76-5.71 (m, 1H), 4.23-4.21 (m, 2H), 3.19-3.16 (m, 2H), 1.30 (t, *J* = 4.0 Hz, 3H).

^{13}C NMR : (100 MHz, $\mathrm{CDCl_3}$, δ ppm) 206.1, 171.1, 163.2, 160.8, 132.4, 130.0, 129.8, 128.3, 115.6, 115.4, 94.6, 88.5, 60.9, 34.5, 14.2.

HRMS : (ESI-TOF) m/z : $[\mathrm{M+NH_4}]^+$ calcd for $\mathrm{C_{13}H_{13}FO_2\ NH_4}$: 238; Found: 238.1242.

Enantiomeric purity: The enantioselectivity was determined by HPLC using chiral column, chiralcel OD-H, hexanes:i-PrOH/100:0; flow rate 0.5 mL/min, 254 nm, retention times: 16.7 min. (major) and 19.6 min. (minor).

(R)-Ethyl 5-(3-fluorophenyl)penta-3,4-dienoate (47ja)



47ja

Yield : 0.129g, 59%, 99% ee; light yellow liquid.

$[\alpha]_D^{25}$: -193.9 (*c* 0.5, $\mathrm{CHCl_3}$)

IR (neat) : 1956, 1736 cm^{-1}.

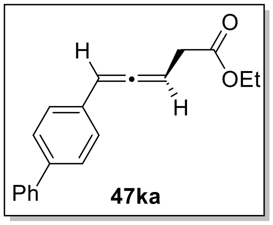
^{1}H NMR : (400 MHz, $\mathrm{CDCl_3}$, δ ppm) 7.30-7.29 (m, 2H), 7.03-7.01 (m, 2H), 6.22-6.20 (m, 1H), 5.76-5.71 (m, 1H), 4.23-4.17 (m, 2H), 3.18-3.17 (m, 2H), 1.35-1.28 (m, 3H).

^{13}C NMR : (100 MHz, $\mathrm{CDCl_3}$, δ ppm) 206.5, 171.0, 164.3, 163.1 ($J_{\mathrm{C\text{-}F}}$ = 240 Hz), 136.4 ($J_{\mathrm{C\text{-}F}}$ = 1 Hz), 131.2 ($J_{\mathrm{C\text{-}F}}$ = 240 Hz), 122.6, 113.9 ($J_{\mathrm{C\text{-}F}}$ = 30 Hz), 113.4 ($J_{\mathrm{C\text{-}F}}$ = 20 Hz), 94.9, 88.7, 61.0, 34.3, 14.1.

HRMS : (ESI-TOF) m/z : $[\mathrm{M+NH_4}]^+$ calcd for $\mathrm{C_{13}H_{13}FO_2\ NH_4}$: 238.1244; Found: 238.1244.

Enantiomeric purity: The enantioselectivity was determined by HPLC using chiral column, chiralcel OB-H, hexanes:i-PrOH/98:2; flow rate 1.0mL/min, 254 nm, retention times: 23.6 min. (major) and 18.8 min. (minor).

(R)-Ethyl 5-([1,1'-biphenyl]-4-yl)penta-3,4-dienoate (47ka)



47ka

Yield : 0.194, 70%; white liquid.

$[\alpha]_D^{25}$: -270.3 (*c* 1.0, $CHCl_3$)

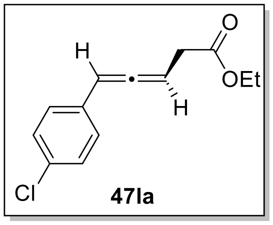
IR (neat) : 1955, 1721 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.62-7.57 (m, 4H), 7.48-7.37 (m, 5H), 6.30-6.29 (m, 1H), 5.78 (q, *J* = 4.0 Hz, 1H), 4.25-4.20 (m, 2H), 3.22-3.19 (m, 2H), 1.31 (t, *J* = 4.0 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 206.5, 171.2, 140.7, 140.0, 133.0, 128.8, 128.7, 127.3, 127.2, 126.9, 95.3, 88.3, 60.9, 34.5, 14.2.

HRMS : (ESI-TOF) m/z : $[M+NH_4]^+$ calcd for $C_{19}H_{18}O_2NH_4$:296.1651; Found: 296.1651.

(R)-Ethyl 5-(4-chlorophenyl)penta-3,4-dienoate (47la)



47la

Yield : 0.094, 40%; colorless liquid.

$[\alpha]_D^{25}$: -213.0 (*c* 0.75, $CHCl_3$)

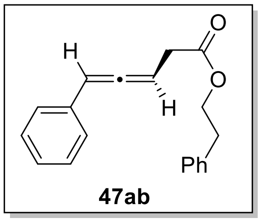
IR (neat) : 1955, 1725 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.33-7.30 (m, 2H), 7.29-7.25 (m, 2H), 6.20-6.19 (m, 1H), 5.75-5.73 (m, 1H), 4.21-4.19 (m, 2H), 3.18-3.16 (m, 2H), 1.31-1.28 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 206.4, 171.0, 132.7, 132.5, 130.0, 128.7, 128.2, 94.7, 88.6, 60.9, 34.4, 14.2.

HRMS : (ESI-TOF) m/z : $[M+NH_4]^+$ calcd for $C_{13}H_{13}ClO_2NH_4$: 254.0948; Found: 254.0948.

(R)-Phenethyl 5-phenylpenta-3,4-dienoate (47ab)



47ab

Yield : 0.152 g, 55%, 98% ee; white liquid.

$[\alpha]_D^{25}$: -220.1 (*c* 0.4, $CHCl_3$)

IR (neat) : 1963, 1732 cm^{-1}.

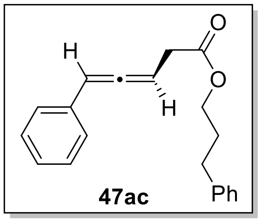
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.35-7.31 (m, 6H), 7.27-7.24 (m, 4H), 6.25-6.23 (m, 1H), 5.75-5.70 (m, 1H), 4.39-4.35 (m, 2H), 3.21-3.17 (m, 2H), 3.0-2.96 (m, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 206.3, 171.1, 137.6, 133.9, 129.0, 128.9, 128.6, 128.5, 127.1, 126.9, 126.6, 95.6, 88.1, 65.3, 35.0, 34.4.

HRMS : (ESI-TOF) m/z : $[M+H]^+$ calcd for $C_{19}H_{19}O_2$: 279.1386; Found: 279.1389.

<u>Enantiomeric purity</u>: The enantioselectivity was determined by HPLC using chiral column, chiralcel OJ-H, hexanes:i-PrOH/95:5; flow rate 1mL/min, 254 nm, retention times: 36.4 min. (major) and 33.8 min. (minor).

(R)-3-Phenylpropyl 5-phenylpenta-3,4-dienoate (47ac)



47ac

Yield : 0.175 g, 60%, 99% ee; white liquid.

$[\alpha]_D^{25}$: -211.6 (*c* 0.4 $CHCl_3$)

IR (neat) : 1963, 1732 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.35-7.31 (m, 6H), 7.27-7.24 (m, 4H), 6.25-6.23 (m, 1H), 5.75-5.70 (m, 1H), 4.39-4.35 (m, 2H), 3.21-3.17 (m, 2H), 3.0-2.96 (m, 2H), 2.03-1.99 (m, 2H).

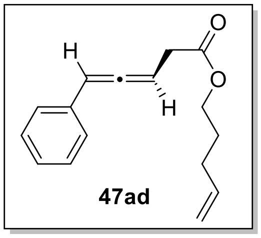
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 206.3, 171.1, 137.6, 133.9, 129.0, 128.9, 128.6, 128.5, 127.1, 126.9, 126.6, 95.6, 88.2, 64.3,34.7, 32.1, 30.1.

HRMS : (ESI-TOF) m/z : $[M+H]^+$ calcd for $C_{20}H_{21}O_2$: 293.1542;

Found: 293.1542.

Enantiomeric purity: The enantioselectivity was determined by HPLC using chiral column, chiralcel OJ-H, hexanes:i-PrOH/90:10; flow rate 1mL/min, 254 nm, retention times: 20.7 min. (major) and 30.4 min. (minor).

(R)-Pent-4-en-1-yl 5-phenylpenta-3,4-dienoate (47ad)



47ad

Yield : 0.098 g, 41%; white liquid.

$[\alpha]_D^{25}$: -210.3 (*c* 0.2, $CHCl_3$)

IR (neat) : 1960, 1730, 1649 cm^{-1}.

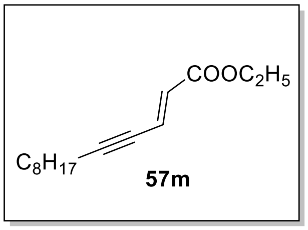
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.33-7.22 (m, 5H), 6.24-6.23 (m, 1H), 5.84-5.72 (m, 2H), 5.07-5.02 (m, 2H), 4.16-4.14 (m, 2H), 3.20-3.17 (m, 2H), 2.16-2.14 (m, 2H), 1.78-1.75 (m, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 206.3, 171.2, 137.3, 133.9, 132.4, 130.0, 128.6, 126.9, 115.3, 95.6, 88.2, 64.4, 34.5, 30.0, 27.7.

HRMS : (ESI-TOF) m/z : $[M+H]^+$ calcd for $C_{16}H_{19}O_2$: 243.1386;

Found: 243.1386.

Ethyl tridec-2-en-4-ynoate (57m)



57m

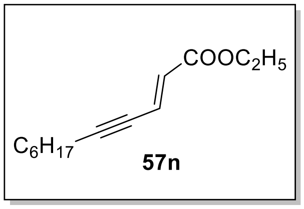
Yield : 0.118g, 50%, white liquid.

IR (neat) : 2215, 1716, 1620 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 6.77 (dt, *J*= 15.5 Hz, 2.3 Hz, 1H), 6.15 (d, *J*=15.8 Hz, 1H), 4.21 (q, *J*=7.1 Hz, 2H), 2.37 (td, *J*=7.1, 2.2 Hz, 2H), 1.56 (quin, *J* = 5.5 Hz, 2H), 1.42–1.37 (m, 2H), 1.32–1.26 (m, 11H), 0.90 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δppm) 166.1, 129.2, 126.1, 100.8, 77.9, 60.5, 31.8, 29.1, 29.0, 28.8, 28.3, 22.6, 19.7, 14.2, 14.0.

Ethyl undec-2-en-4-ynoate (57n)



57n

Yield : 0.079g, 48%; white liquid.

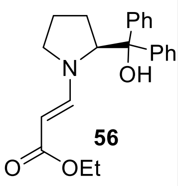
IR (neat) : 2205, 1718, 1623 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm)) 6.76 (d, *J* = 16 Hz, 1H), 6.14 (d, *J* = 16.0 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 2.39-2.35 (m, 2H), 1.60-1.50 (m, 2H), 1.44-1.26 (m, 13H), 0.89 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 166.1, 129.2, 126.1, 100.8, 77.9, 60.5, 31.2, 28.5, 28.2, 22.5, 19.7, 14.2, 14.0.

2.4.3. General procedure for chiral enamine intermediate

To a stirred solution of amine **48** (1 mmol) in toluene (3 mL), DPPE (0.020 g, 0.005 mmol), ethylpropiolate **44a** (0.108 mL, 1.0 mmol), the reaction mixture stirr for 2 h at 120 °C under N_2 atmosphere. The reaction mixture cooled to room temperature. Toluene was removed using reduced pressure. Water (5 mL) and DCM (15 mL) were added. The DCM layer was washed with saturated NaCl solution, dried (Na_2SO_4) and concentrated. The residue was subjected to column chromatography using hexane and ethyl acetate (80:20) as eluent to isolate the **56**.



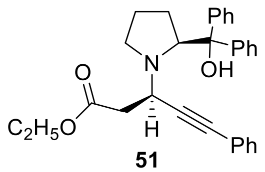
56

(S)-Ethyl 3-(2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)acrylate (56)

Yield	**:**	0.322 g, 92%; white solid.
$[\alpha]_D^{25}$	**:**	-90.2 (*c* 0.1, $CHCl_3$)
IR (neat)	**:**	3416, 1671, 1616, 1063 cm^{-1}.
^{1}H NMR	**:**	(400 MHz, $CDCl_3$, δ ppm) 7.47-7.40 (m, 1H), 7.38-7.34 (m, 5H), 7.33-7.25 (m, 5H), 4.63-4.61 (m, 1H), 4.47-4. 44 (d, *J* = 8.0 Hz, 1H), 3.90-3.87 (m, 2H), 3.03 (t, *J* = 8.0 Hz, 2H), 2.15-1.98 (m, 3H), 1.32-1.29 (m, 2H), 1.14 (t, *J* = 8.0 Hz, 3H).
^{13}C NMR	**:**	(100 MHz, $CDCl_3$, δ ppm) 169.3, 150.7, 144.7, 144.2, 128.3, 128.1, 127.5, 127.3, 127.0, 126.8, 86.5, 80.4, 69.2, 58.7, 49.0, 28.5, 23.0, 14.5.
HRMS	**:**	(ESI-TOF) m/z : $[M+H]^+$ calcd for $C_{22}H_{26}NO_3$: 352.1913; Found: 352.1915.

2.4.4. General procedure for preparation of the chiral propargylamines

To a stirred solution of amine **48** (1 mmol) in toluene (3 mL), DPPE (0.020 g, 0.005 mmol), ethyl propiolate **44a** (0.108 mL, 1.0 mmol), the reaction mixture stirr for 1.5 h and add the ZnI_2 (0.160 g, 0.5 mmol), 1-alkyne **46** (1 mmol) at 120 °C under N_2 atmosphere. The contents were stirred for 5 h. The reaction mixture cooled to room temperature. Toluene was removed using reduced pressure. Water (5 mL) and DCM (15 mL) were added. The DCM layer was washed with saturated NaCl solution, dried (Na_2SO_4) and concentrated. The residue was subjected to column chromatography using hexane and ethyl acetate (94:6) as eluent to isolate the **51**.



51

Ethyl 3-((S)-2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)-5-phenylpent-4-ynoate (51a)

Yield : 0.226 g, 50%; light yellow liquid.

$[\alpha]_D^{25}$: -76.8 (*c* 0.13, CHCl$_3$)

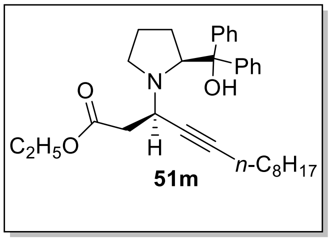
IR (neat) : 3418, 2356, 1730 cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.81-7.82 (m, 2H), 7.62-7.53 (m, 5H), 7.43-7.38 (m, 5H), 7.34-7.29 (m, 2H), 7.24-7.16 (m, 1H), 4.35-4.15 (m, 4H), 3.78-3.68 (m, 1H), 3.14-3.0 (m, 2H), 2.68-2.53 (m, 2H), 1.89-1.77 (m, 4H), 1.36-1.26 (m, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 170.2, 147.6, 146.6, 132.4, 131.8, 130.1, 128.4, 128.3, 128.2, 128.1, 127.9, 126.6, 126.2, 125.5, 125.4, 122.9, 86.2, 85.7, 77.3, 67.9, 60.7, 60.6, 50.6, 48.6, 40.3, 29.5, 23.7, 14.3.

HRMS : (ESI-TOF) m/z : $[M+H]^+$ calcd for $C_{30}H_{32}NO_3$: 454.2383; Found: 454.2389.

Ethyl 3-(2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)tridec-4-ynoate (51m)



51m

Yield : 0.185 g, 38%; light yellow liquid.

$[\alpha]_D^{25}$: -165.3 (*c* 0.25, CHCl$_3$)

IR (neat) : 3419, 2361, 1731cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_3$, δppm) 7.74-7.72 (m, 2H), 7.62-7.53 (m, 2H), 7.34-7.25 (m, 3H), 7.22-15 (m, 3H), 4.21-4.17 (m, 1H), 4.08-4.07 (m, 2H), 3.39-3.32 (m, 1H), 3.08-2.91 (m, 1H), 2.45-2.41 (m, 2H), 2.27-2.24 (m, 2H), 1.68-1.60 (m, 1H), 1.58-1.53 (m, 8H), 1.49-1.24 (m, 12H), 0.94 (t, *J* = 8.0 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δppm) 170.4, 147.6, 146.8, 128.3, 128.0, 127.9, 126.5, 126.0, 125.8, 125.4, 85.8, 76.4, 67.6, 60.5, 50.2, 48.3, 40.6, 31.9, 29.4, 29.3, 29.1, 29.0, 28.8, 23.7, 22.7, 18.6, 14.2, 14.1.

HRMS : (ESI-TOF) m/z : $[M+H]^+$ calcd for $C_{32}H_{44}NO_3$: 490.3321

Found: 490.3329.

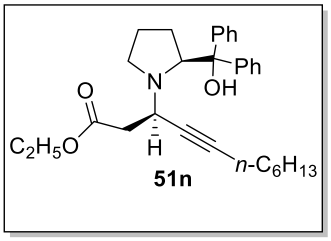
Ethyl 3-(2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)undec-4-ynoate (51n)

Yield : 0.283 g, 33%; light yellow liquid.

$[\alpha]_D^{25}$: -160.8 (*c* 0.20, $CHCl_3$)

IR (neat) : 3419, 2361, 1731 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.74-7.72 (m, 2H), 7.55-7.53 (m, 2H), 7.34-7.29 (m, 3H), 7.27-7.25 (m, 1H), 7.23-7.13 (m, 2H), 4.61 (s, 1H), 4.22-4.17 (m, 2H), 4.10-4.02 (m, 1H), 3.41-3.36 (m, 1H), 3.02-2.86 (m, 2H), 2.48-2.36 (m, 2H), 2.27-2.23 (m, 2H), 1.80-1.62 (m, 4H), 1.60-1.48 (m, 4H). 1.41-1.34 (m, 4H), 1.27-1.23 (m, 3H), 0.96 (t, *J* = 8.0 Hz, 3H).



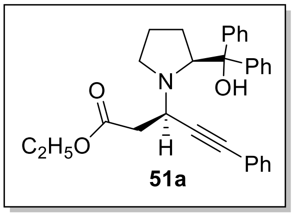
51n

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 170.4, 147.6, 146.8, 128.0, 127.8, 126.4, 125.5, 125.4, 85.7, 77.3, 76.7, 76.4, 67.6, 60.5, 50.2, 48.3, 40.6, 31.4, 29.4, 29.4, 29.1, 28.9, 28.5, 23.7, 22.6, 18.6, 14.2, 14.1.

HRMS : (ESI-TOF) m/z : $[M+H]^+$ calcd for $C_{30}H_{40}NO_3$: 462.3009;

Found: 462.3008.

2.4.4. General procedure for chiral propargylamines



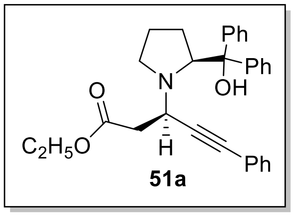
51a

To a stirred solution of amine **48** (1 mmol) in toluene (3 mL), ethyl propiolate **44a** (0.108 mL, 1.0 mmol), the reaction mixture stirr for 1.5 h and add the CuBr (30 mol %), 1-alkyne **46** (1 mmol) at 120 °C under N_2 atmosphere. The contents were stirred for 10 h. The reaction mixture cooled to room temperature. Toluene was removed using reduced pressure. Water (5 mL) and DCM (15 mL) were added. The DCM layer was washed with saturated NaCl solution, dried (Na_2SO_4) and concentrated. The residue was subjected to column chromatography using hexane and ethyl acetate (94:6) as eluent to isolate the **51**.

Ethyl 3-((S)-2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)-5-phenylpent-4-ynoate (51a)

Yield : 0.362 g, 80%; light yellow liquid.

$[\alpha]_D^{25}$: -78.8 (*c* 0.15, $CHCl_3$)



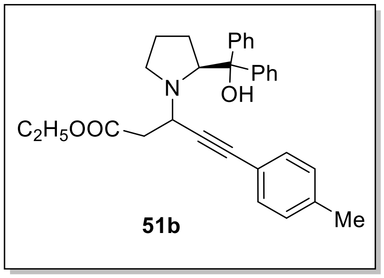
51a

Ethyl 3-((S)-2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)-5-(p-tolyl)pent-4-ynoate (51b)

Yield : 0.364 g, 78%; yellow liquid.

$[\alpha]_D^{25}$: -76.2 (*c* 0.13, $CHCl_3$)

IR (neat) : 3416, 2358, 1730 cm^{-1}.



51b

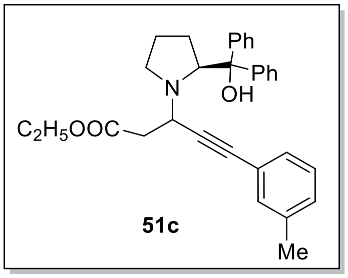
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.83-7.81 (m, 2H), 7.64-7.54 (m, 4H), 7.45-7.39 (m, 5H), 7.34-7.29 (m, 2H), 7.24-7.16 (m, 1H), 4.35-4.15 (m, 4H), 3.78-3.68 (m, 3H), 3.14-3.0 (m, 2H), 2.68-2.34 (m, 3H), 1.89-1.77 (m, 4H), 1.36-1.26 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 170.0, 147.2, 146.1, 132.2, 131.7, 130.1, 128.4, 128.3, 128.2, 128.1, 127.9, 126.6, 126.2, 125.5, 125.4, 122.9, 86.5, 85.4, 77.3, 67.7, 60.7, 60.3, 50.6, 48.6, 40.3, 29.5, 23.7, 21.2 14.1.

HRMS : (ESI-TOF) m/z : $[M+H]^+$ calcd for $C_{31}H_{34}NO_3$: 468.2539; Found: 468.2539.

Ethyl 3-((S)-2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)-5-(m-tolyl)pent-4-ynoate (51c)

Yield : 0.336 g, 72%; yellow liquid.



51c

$[\alpha]_D^{25}$: -70.8 (*c* 0.12, $CHCl_3$)

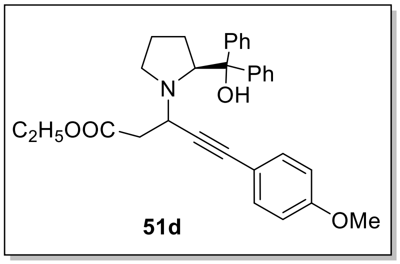
IR (neat) : 3410, 2357, 1733 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.86-7.82 (m, 2H), 7.63-7.53 (m, 4H), 7.43-7.38 (m, 5H), 7.33-7.29 (m, 2H), 7.24-7.15 (m, 1H), 4.35-4.15 (m, 4H), 3.79-3.65 (m, 3H), 3.13-3.05 (m, 2H), 2.69-2.59 (m, 2H), 1.89-1.71 (m, 4H), 1.36-1.25 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 170.2, 147.9, 146.5, 132.9, 131.8, 130.1, 128.4, 128.3, 128.2, 128.0, 127.7, 126.5, 126.1, 125.3, 125.2, 122.2, 86.2, 85.7, 77.3, 67.8, 60.6, 60.6, 50.6, 48.6, 40.3, 29.5, 23.7, 21.5 14.3.

HRMS : (ESI-TOF) m/z : $[M+H]^+$ calcd for $C_{31}H_{34}NO_3$: 468.2539; Found: 468.2539.

Ethyl-3-((S)-2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)-5-(4-methoxyphenyl)pent-4-ynoate (51d)



51d

Yield : 0.410 g, 85%; yellow liquid.

[α]D

[α]$_D^{25}$: -79.8 (*c* 0.50, $CHCl_3$)

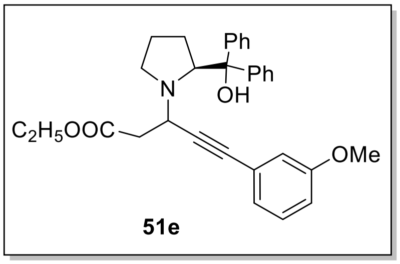
IR (neat) : 3420, 2355, 1733 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.81-7.82 (m, 2H), 7.61-7.53 (m, 4H), 7.42-7.35 (m, 5H), 7.35-7.29 (m, 2H), 7.25-7.17 (m, 1H), 4.33-4.15 (m, 4H), 3.81 (s, 3H), 3.78-3.68 (m, 1H), 3.14-3.02 (m, 2H), 2.65-2.51 (m, 2H), 1.90-1.78 (m, 4H), 1.36-1.27 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 170.5, 148.6, 147.6, 133.4, 131.2, 130.5, 128.5, 128.3, 128.2, 128.1, 127.9, 126.6, 126.2, 125.5, 125.4, 122.8, 86.3, 85.9, 77.2, 67.9, 60.7, 60.6, 55.3, 50.6, 48.6, 40.3, 29.5, 23.7, 14.2.

HRMS : (ESI-TOF) m/z : $[M+H]^+$ calcd for $C_{31}H_{34}NO_4$: 484.2489; Found: 484.2489.

Ethyl-3-((S)-2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)-5-(4-methoxyphenyl)pent-4-ynoate (51e)



51e

Yield : 0.367 g, 76%; yellow liquid.

[α]$_D^{25}$: -72.3 (*c* 0.50, $CHCl_3$)

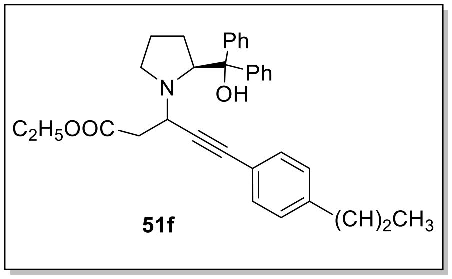
IR (neat) : 3418, 2356, 1730 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.85-7.81 (m, 2H), 7.65-7.53 (m, 4H), 7.42-7.38 (m, 5H), 7.35-7.29 (m, 2H), 7.24-7.16 (m, 1H), 4.34-4.15 (m, 4H), 3.83 (s, 3H), 3.78-3.67 (m, 1H), 3.14-3.12 (m, 2H), 2.67-2.52 (m, 2H), 1.88-1.75 (m, 4H), 1.36-1.25 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 170.1, 147.1, 146.3, 132.2, 131.8, 130.1, 128.4, 128.3, 128.2, 128.1, 127.9, 126.6, 126.2, 125.5, 125.4, 122.5, 86.5, 85.4, 77.4, 67.8, 60.6, 60.6, 55.2, 50.6, 48.2, 40.1, 29.5, 23.7, 14.3.

HRMS : (ESI-TOF) m/z : $[M+H]^+$ calcd for $C_{32}H_{34}NO_4$: 484.2489; Found: 484.2489.

Ethyl-3-((S)-2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)-5-(4-(prop-1-en-1-yl) phenyl)pent-4-ynoate (51f)



51f

Yield : 0.394g, 80%; yellow liquid.

$[\alpha]_D^{25}$: -60.5 (*c* 0.50, $CHCl_3$)

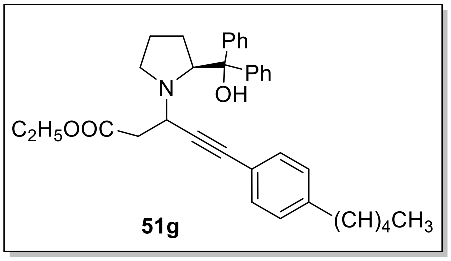
IR (neat) : 3417, 2355, 1730 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.88-7.82 (m, 2H), 7.62-7.53 (m, 5H), 7.43-7.38 (m, 4H), 7.35-7.29 (m, 2H), 7.23-7.16 (m, 1H), 4.34-4.16 (m, 4H), 3.72-3.62 (m, 1H), 3.10-3.01 (m, 2H), 2.68-2.53 (m, 2H), 1.89-1.77 (m, 6H), 1.36-1.26 (m, 3H), 0.95 (t, *J* = 4.0 Hz, 3H). .

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 170.2, 147.5, 146.4, 132.4, 131.5, 130.1, 128.4, 128.3, 128.2, 128.1, 127.9, 126.6, 126.2, 125.5, 125.4, 122.9, 86.2, 85.7, 77.3, 67.9, 60.7, 60.6, 50.6, 48.6, 40.3, 34.1, 29.5, 24.3, 23.7, 14.3, 13.6.

HRMS : (ESI-TOF) m/z : $[M+H]^+$ calcd for $C_{33}H_{36}NO_3$: 494.2696; Found: 494.2696.

Ethyl-3-((S)-2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)-5-(4-((1E,3E)-penta-1,3-dien-1-yl)phenyl)pent-4-ynoate (51g)



51g

Yield : 0.389 g, 75%; yellow liquid.

$[\alpha]_D^{25}$: -72.4 (*c* 0.50, $CHCl_3$)

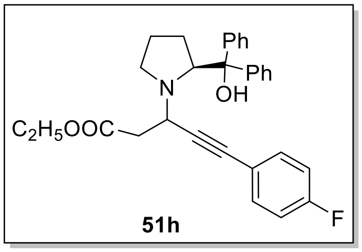
IR (neat) : 3426, 2326, 1735 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.80-7.79 (m, 2H), 7.62-7.52 (m, 4H), 7.41-7.36 (m, 5H), 7.37-7.29 (m, 2H), 7.22-7.12 (m, 1H), 4.28-4.12 (m, 4H), 3.68-3.61 (m, 1H), 3.17-3.06 (m, 2H), 2.68-2.40 (m, 4H), 1.89-1.70 (m, 6H), 1.36-1.19 (m, 6H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 170.5, 147.2, 146.6, 132.4, 131.8, 130.1, 128.4, 128.3, 128.2, 128.1, 127.9, 126.6, 126.2, 125.5, 125.4, 122.9, 86.3, 85.2, 77.3, 67.9, 60.7, 60.6, 50.6, 48.6, 40.3, 29.5, 34.5, 31.3, 31.2, 23.7, 14.3, 13.9.

HRMS : (ESI-TOF) m/z : $[M+H]^+$ calcd for $C_{35}H_{38}NO_3$: 520.2852; Found: 520.2852.

Ethyl-5-(4-fluorophenyl)-3-((S)-2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)pent-4-ynoate (51h)



51h

Yield : 0.343 g, 73%; yellow liquid.

$[\alpha]_D^{25}$: -80.6 (*c* 0.51, $CHCl_3$)

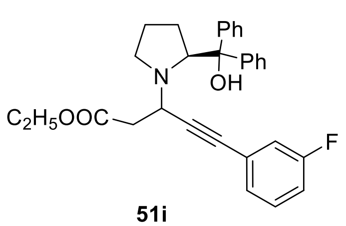
IR (neat) : 3396, 2310, 1738 cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.81-7.83 (m, 2H), 7.62-7.37 (m, 9H), 7.34-7.29 (m, 2H), 7.24-7.16 (m, 1H), 4.32-4.13 (m, 4H), 3.78-3.68 (m, 1H), 3.12-3.01 (m, 2H), 2.62-2.51 (m, 2H), 1.85-1.72 (m, 4H), 1.33-1.21 (m, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 170.2, 163.2, 160.5, 147.6, 146.6, 132.4, 131.8, 130.1, 128.4, 128.3, 128.2, 128.1, 127.9, 126.6, 126.2, 125.5, 125.4, 122.9, 115.4, 115.2, 86.8, 85.9, 77.3, 67.5, 60.7, 60.6, 50.6, 48.6, 40.2, 29.5, 23.7, 14.1.

HRMS : (ESI-TOF) m/z : [M+H]$^+$ calcd for $C_{30}H_{31}FNO_3$: 472.2289; Found: 472.2289.

Ethyl-5-(3-fluorophenyl)-3-((S)-2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)pent-4-ynoate (51i)



51i

Yield : 0.339 g, 72%; yellow liquid.

[α]$_D$^{25} : -78.2 (*c* 0.56, CHCl$_3$).

IR (neat) : 3418, 2355, 1732 cm^{-1}.

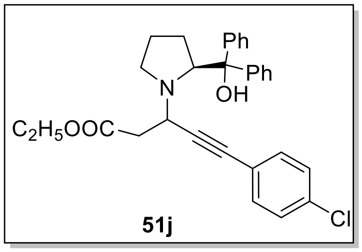
^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.82-7.80 (m, 2H), 7.63-7.52 (m, 4H), 7.43-7.37 (m, 5H), 7.35-7.30 (m, 2H), 7.25-7.17 (m, 1H), 4.35-4.15 (m, 4H), 3.78-3.64 (m, 1H), 3.10-3.02 (m, 2H), 2.68-2.51 (m, 2H), 1.90-1.72 (m, 4H), 1.33-1.25 (m, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 170.1, 163.4, 161.5, 147.2, 146.3, 132.4, 131.8, 130.1, 128.4, 128.3, 128.2, 128.1, 127.9, 126.6, 126.2, 125.5, 125.4, 122.9, 115.2, 115.3, 113.5, 86.2, 85.7, 77.3, 67.9, 60.7, 60.6, 50.6, 48.6, 40.3, 29.5, 23.7, 14.3.

HRMS : (ESI-TOF) m/z : $[M+H]^+$ calcd for $C_{30}H_{31}FNO_3$: 472.2289;

Found: 472.2289.

Ethyl-5-(4-chlorophenyl)-3-((S)-2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)pent-4-ynoate (51j)


51j

Yield : 0.340 g, 70%; yellow liquid.

$[\alpha]_D^{25}$: -75.5 (*c* 0.55, $CHCl_3$).

IR (neat) : 3420, 2343, 1731 cm^{-1}.

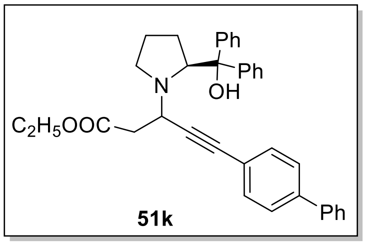
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.85-7.51 (m, 7H), 7.42-7.36 (m, 4H), 7.33-7.29 (m, 2H), 7.23-7.10 (m, 1H), 4.30-4.18 (m, 4H), 3.68-3.61 (m, 1H), 3.10-3.03 (m, 2H), 2.60-2.51 (m, 2H), 1.85-1.73 (m, 4H), 1.34-1.21 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 170.2, 132.4, 131.8, 130.1, 128.4, 128.3, 128.2, 128.1, 127.9, 126.6, 126.2, 125.5, 125.4, 122.9, 86.2, 85.7, 77.3, 67.9, 60.7, 60.6, 50.6, 48.6, 40.3, 29.5, 23.7, 14.3.

HRMS : (ESI-TOF) m/z : $[M+H]^+$ calcd for $C_{30}H_{31}ClNO_3$: 488.1993;

Found: 488.1993.

Ethyl-5-([1,1'-biphenyl]-4-yl)-3-((S)-2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)pent-4-ynoate (51k)


51k

Yield : 0.380 g, 72%; yellow liquid.

$[\alpha]_D^{25}$: -90.5 (*c* 0.50, $CHCl_3$)

IR (neat) : 3386, 2342, 1729 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.86-7.70 (m, 4H), 7.65-7.52 (m, 5H), 7.48-7.39 (m, 5H), 7.36-7.14 (m, 5H), 4.34-4.16 (m, 4H), 3.72-3.67 (m, 1H), 3.10-2.98 (m, 2H), 2.63-2.51 (m, 2H), 1.82-1.71 (m, 4H), 1.34-1.21 (m, 3H).

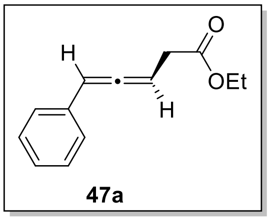
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 170.2, 142.6, 141.6, 132.6, 130.1, 128.5, 128.8, 128.3, 128.1, 127.9, 126.6, 126.2, 125.7, 125.4, 122.2, 86.3, 85.7, 77.3, 67.9, 60.7, 60.6, 50.6, 48.6, 40.3, 29.5, 23.7, 14.1.

HRMS : (ESI-TOF) m/z : $[M+H]^+$ calcd for $C_{36}H_{36}NO_3$: 530.2696; Found: 530.2696.

2.4.5. General procedure for the preparation of β-allenoates from propargylamines

The chiral propargylamines **51**(1 mmol) were added to a stirred suspension of ZnI_2 (50 mol%) in dry toluene (3 mL) and the contents were refluxed for 1-3 h at 120 °C under nitrogen atmosphere. Toluene was removed under reduced pressure and the crude product was purified on silica gel (100-200 mesh) column chromatography using hexane/ethyl acetate as eluent to isolate the chiral allenes **47**.[28]

5-Phenyl-penta-3,4-dienoic acid ethyl ester (47a)



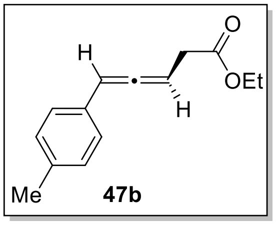
47a

Yield : 0.135 g, 68%, 99% ee; white liquid.

$[\alpha]_D^{25}$: -198.9 (*c* 0.11g, $CHCl_3$)

<u>Enantiomeric purity</u>: The enantioselectivity was determined by HPLC using chiral column, chiralcel OB-H, hexanes:i-PrOH/98:2; flow rate 0.5 mL/min, 254 nm, retention times: 17.6 min. (major) and 20.4 min. (minor).

5-*p*-Tolyl-penta-3,4-dienoic acid ethyl ester (47b)



47b

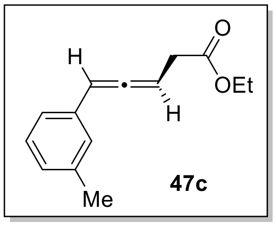
Yield : 0.167 g, 70%, 96% ee; light yellow liquid.

$[\alpha]_D^{25}$: -241 (*c* 0.5, $CHCl_3$)

<u>Enantiomeric purity</u>: The enantioselectivity was determined by

HPLC using chiral column, chiralcel OB-H, hexanes:i-PrOH/98:2; flow rate 0.5 mL/min, 254 nm, retention times: 16.5 min. (minor) and 21.6 min. (major).

(R)-Ethyl-5-(m-tolyl)penta-3,4-dienoate (47c)



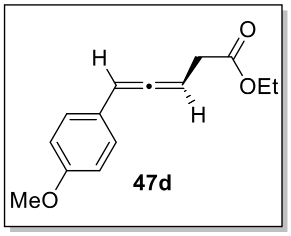
47c

Yield : 0.168 g, 71%, 99% ee; yellow liquid.

$[\alpha]_D^{25}$: -244.3 (*c* 0.5 $CHCl_3$)

<u>Enantiomeric purity</u>: The enantioselectivity was determined by HPLC using chiral column, chiralcel AS-H, hexanes:i-PrOH/100:0; flow rate 1 mL/min, 254 nm, retention times: 13.6 min. (major) and 16.1 min. (minor).

(R)-Ethyl 5-(4-methoxyphenyl)penta-3,4-dienoate (47d)



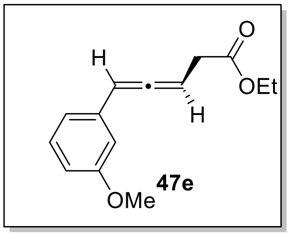
47d

Yield : 0.160 g, 69%, 99% ee; white liquid.

$[\alpha]_D^{25}$: -260.2 (*c* 0.4, $CHCl_3$)

<u>Enantiomeric purity</u>: The enantioselectivity was determined by HPLC using chiral column, chiralcel OD-H, hexanes:i-PrOH/95:5; flow rate 0.5 mL/min, 254 nm, retention times: 16.1 min. (major) and 19.0 min. (minor).

(R)-Ethyl 5-(3-methoxyphenyl)penta-3,4-dienoate (47e)



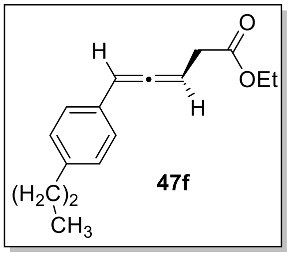
47e

Yield : 0.155 g, 67%, 98% ee; white liquid.

$[\alpha]_D^{25}$: -255.8 (*c* 0.2, $CHCl_3$)

<u>Enantiomeric purity</u>: The enantioselectivity was determined by HPLC using chiral column, chiralcel AS-H, hexanes:i-PrOH/95:5; flow rate 0.5 mL/min, 254 nm, retention times: 13.4 min. (major) and 14.8 min. (minor).

(R)- Ethyl 5-(4-propylphenyl)penta-3,4-dienoate (47f)



47f

Yield : 0.195 g, 80%, 99% ee; yellow liquid.

$[\alpha]_D^{25}$: -209.3 (*c* 0.40, $CHCl_3$)

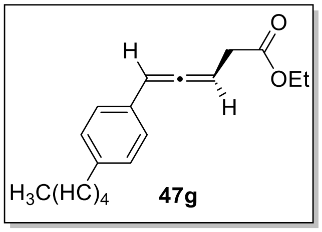
<u>Enantiomeric purity</u>: The enantioselectivity was determined by HPLC using chiral column, chiralcel OJ-H, hexanes:i-PrOH/98:2; flow rate 0.5 mL/min, 254 nm, retention times: 18.8 min. (major) and 16.8 min. (minor).

(R)-Ethyl-5-(4-pentylphenyl)penta-3,4-dienoate (47g)

Yield : 0.225 g, 78%, 98% ee; yellow liquid.

$[\alpha]_D^{25}$: -211.2 (*c* 0.2, $CHCl_3$)

<u>Enantiomeric purity</u>: The enantioselectivity was determined by HPLC using chiral column, chiralcel OD-H, hexanes:i-PrOH/99:1; flow rate 0.5 mL/min, 254 nm, retention times: 11.0 min. (major) and 13.9 min. (minor).



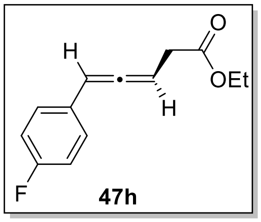
47g

(R)-Ethyl 5-(4-fluorophenyl)penta-3,4-dienoate (47h)

Yield : 0.154 g, 65%; light yellow liquid.

$[\alpha]_D^{25}$: -183.4 (*c* 0.5, $CHCl_3$)

<u>Enantiomeric purity</u>: The enantioselectivity was determined by HPLC using chiral column, chiralcel OD-H, hexanes:i-PrOH/100:0; flow rate 0.5 mL/min, 254 nm, retention times: 16.7 min. (major) and 19.6 min. (minor).



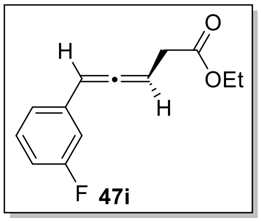
47h

(R)-Ethyl 5-(3-fluorophenyl)penta-3,4-dienoate (47i)

Yield : 0.144 g, 61%, 99% ee; light yellow liquid.

$[\alpha]_D^{25}$: -193.5 (*c* 0.5, $CHCl_3$)

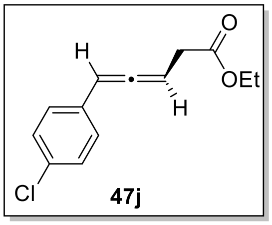
<u>Enantiomeric purity</u>: The enantioselectivity was determined by HPLC using chiral column, chiralcel OB-H, hexanes:i-



47i

PrOH/98:2; flow rate 1.0mL/min, 254 nm, retention times: 23.6 min. (major) and 18.8 min. (minor).

(R)-Ethyl 5-(4-chlorophenyl)penta-3,4-dienoate (47j)

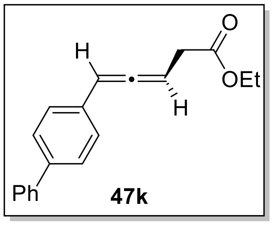


47j

Yield **:** 0.156 g, 62%; colorless liquid.

$[\alpha]_D^{25}$ **:** -212.5 (*c* 0.75, $CHCl_3$)

(R)-Ethyl 5-([1,1'-biphenyl]-4-yl)penta-3,4-dienoate (47k)



47k

Yield **:** 0.221, 75%; white liquid.

$[\alpha]_D^{25}$ **:** -270.3 (*c* 1.0, $CHCl_3$)

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Chapter 3

Highly Enantioselective Synthesis of Chiral Vinyl allenes for Application in [4 + 2] Cycloaddition

3. 1 Introduction

3.1.1 Vinyl allenes

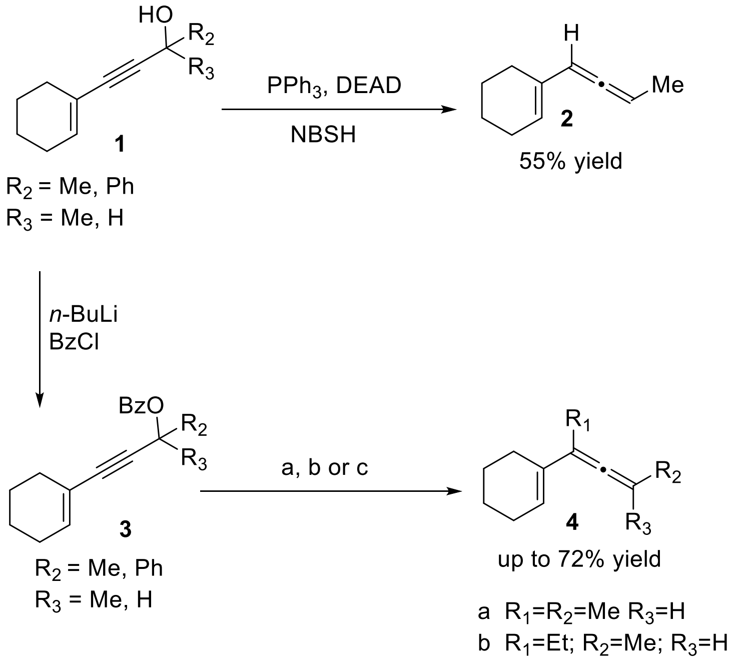
Vinyl allenes are class of compounds with potential for applications in various cycloaddition, cyclization, and isomerisation reactions.[1] Among the different reactions of allenes, methods involving cycloaddition reactions are particularly interesting since these allenes are versatile synthons with the potential to provide excellent axis to center chirality transfer in organic synthesis.[2] The [4+2] cycloaddition reactions using allenes could be also beneficial in the synthesis of several naturally occurring compounds.[3] If the allene bears another conjugated double bond, it can be used as diene in Diels-Alder type reaction with dienophiles to create six-membered carbocycles bearing *exo*-methylene groups.

As described in Chapter 1 and 2, several methods for highly enantiselective synthesis of disubstituted chiral allenes using chiral secondary amines, 1-alkynes and aldehydes were reported.[4] Very recently, a method was reported for the prepatation of chiral disubstituted allenes via coupling of diazo compounds and propargylamine.[4f] Over the years, a few methods were also reported for the synthesis of vinyl allenes but with limited in scope.[5,6] It was of inerest to us to develop a method for the preparation of enantiomerically enriched cyclohexenylallenes for application in [4+2] cycloadditions. Thus, a brief review on the preparartion of vinyl allenes and their applications in cycloaddition reactions would facilitate the discussion.

3.1.2 Synthesis of vinyl allenes

The vinyl allene **2** was prepared in a 55% yield using PPh_3, DEAD and *o*-nitrobenzenesulfonylhydrazine (NBSH) starting from propargyl alcohol **1**. Also, the products **4** were obtained in 60-72% yields by S_N2 displacement reactions of benzoates **3** obtained from the corresponding propargyl alcohols **1** (Scheme 1).[7]

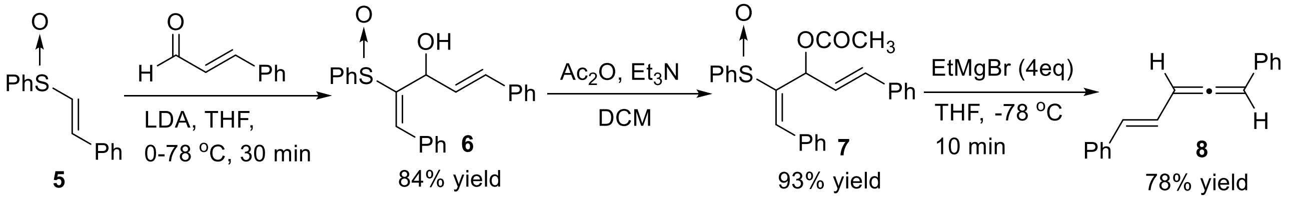
Scheme 1



(a) MeMgBr, CuI, LiBr, 0 °C; (b) EtMgBr, $CuBr.Me_2S$, -60 °C; (c) *t*-BuLi, CuCN, -78 °C

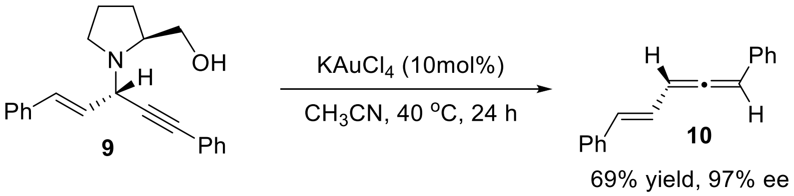
Later, Satoh *et. al.* reported[8] that the lithium α-sulfinyl carbanion smoothly reacted with *trans*-cinnamaldehyde to give the alcohol product **6**. Subsequent, acetylation of the hydroxyl group of compound **6** followed by the reaction with EtMgBr gave the vinyl allene **8** as shown in Scheme 2.

Scheme 2



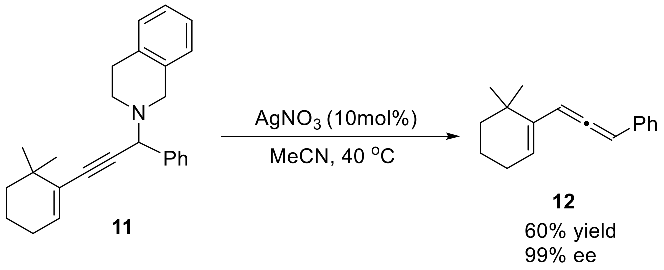
Recently, axially chiral allenes **10** were synthesized from chiral propargylamines **9** catalyzed by KAuCl4 in 93% yield and 99% ee (Scheme 3).[9]

Scheme 3



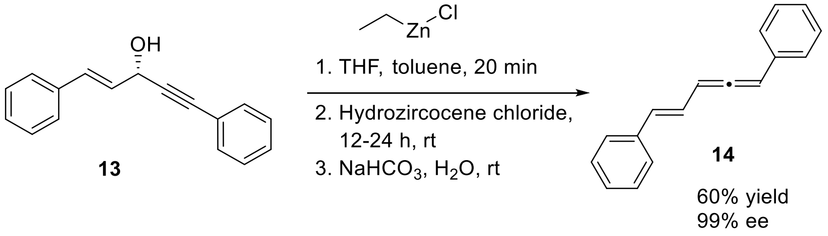
A facile method to access the chiral vinyl allenes from cyclohexene-functionalized propargylamine **11** by AgNO3 catalysis was also reported (Scheme 4).[10]

Scheme 4



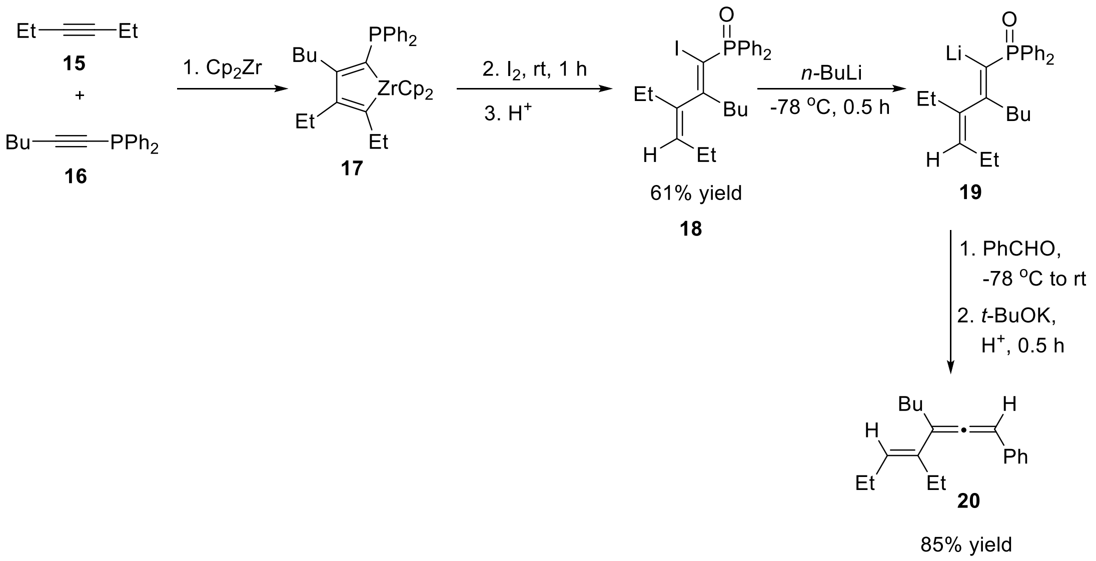
It was reported that deprotonation of the propargylic alcohol with EtZnCl followed by hydrozirconation of alkynes with the Schwartz reagent (Cp2Zr(H)Cl) lead to the formation of the corresponding vinyl allene **14** (Scheme 5).[11]

Scheme 5



Vinyl allene **20** was also prepared from two different alkynes and an aldehyde by the Wittig-Horner reaction. Thus, the 1-Lithio-1,3-dienyl phosphine oxides **19** generated *in situ* by lithiation of 1-iodo-1,3-dienyl phosphine oxides **18**, obtained by iodination of (*R*)-phosphinozirconacyclopentadienes **17** gave the corresponding vinyl allene **20** in 80% yield (Scheme 6).[12]

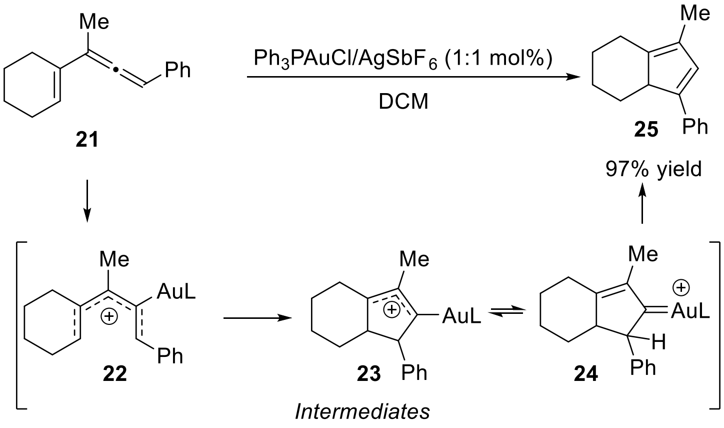
Scheme 6



3.1.2 Vinyl allenes in cycloaddition reactions

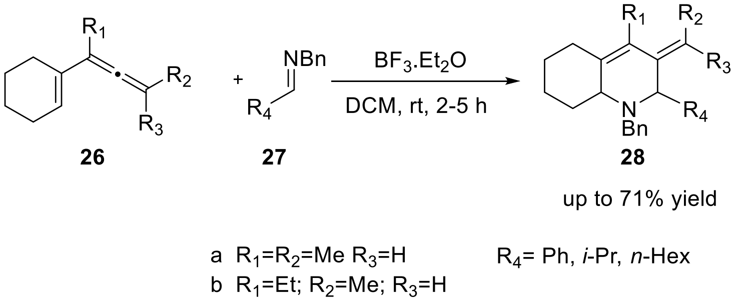
Toste *et al.* reported[13] a gold (I) catalysed cycloisomerization of vinyl allenes for the synthesis of cyclopentadienes *via* a concerted rearrangement involving direct addition of the olefin (Scheme 7).

Scheme 7



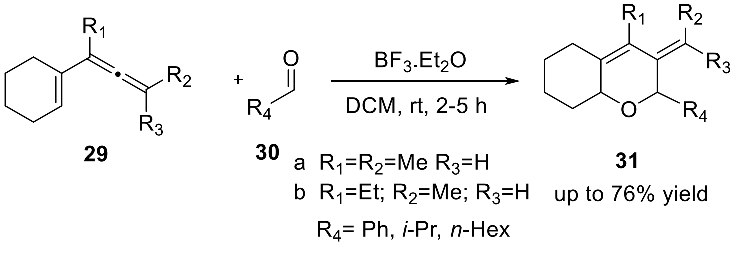
An interesting method for synthesis of octahydroquinoline derivatives *via* $BF_3.Et_2O$ catalyzed cyclization of vinyl allenes was reported (Scheme 8).[14]

Scheme 8



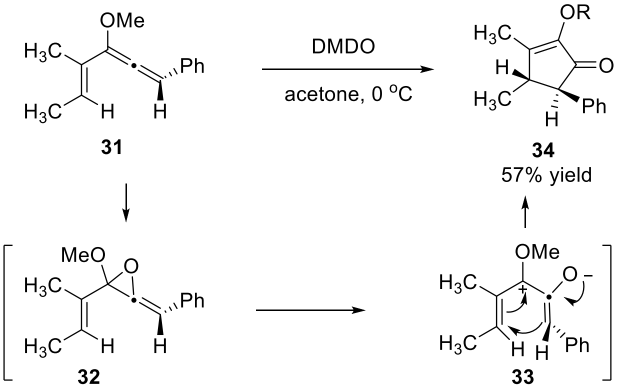
Another approach involves an acid catalyzed reaction of vinyl allene derivatives with aldehydes to afford the cyclized products (Scheme 9).[15]

Scheme 9



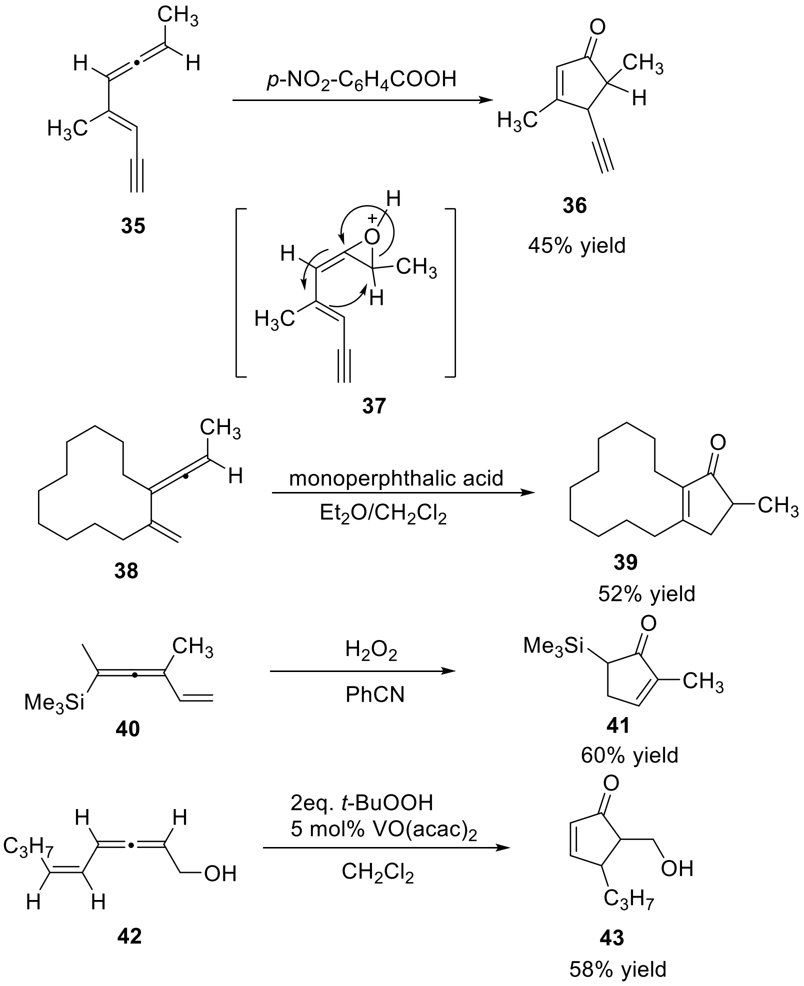
A mild method for the C_4-C_5 disubstituted cyclopentenones **34** was reported, involving formation of a pentadienyl cation *via* diastereoselective oxidation of a vinyl alkoxyallene (Scheme 10).[16]

Scheme 10



Applications of vinyl allenes as precursors for the synthesis of substituted cyclopentenones *via* Nazarov-type cyclizations were reported (Chart 1).[17]

Chart 1



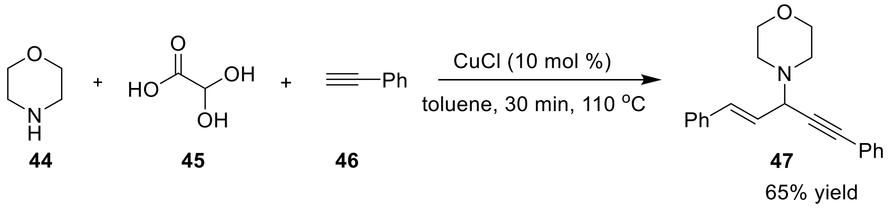
Reports on the synthesis of functionalized chiral vinyl allenes are still limited and the reported methods involve multistep operations using expensive reagents. Therefore, we have undertaken efforts towards the synthesis of highly enantioselective synthesis of vinyl allenes through the chiral propargylamine intermediates by using N-methyl camphanyl piperazine. The results are described in the next section.

3.2 Results and Discussion

3.2.1 Synthesis of aromatic vinylallenes using morpholine, 1-alkyne and monoglyoxalic acid derivative

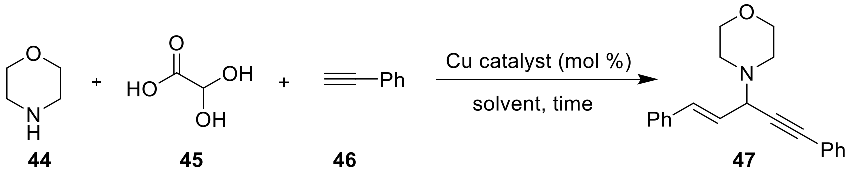
Allenes are important class of compounds possessing orthogonal consecutive π-bonds.[17, 18] It was of our interest to us to develop a method for the synthesis of vinyl allenes. We have observed that the reaction of secondary amine, monoglyoxalic acid and 1-alkyne with CuCl (10 mol%) gave the propargylamine **47** in 65% yield (Scheme 11).

Scheme 11



Reactions employing glyoxylic acid **45**, morpholine **44**, and phenylacetylene **46** as substrates in combination with 20% CuI gave the vinyl propargylamines in 40-70% yield (Table 5, entries 1-4). Among the solvents tested, toluene was found to be the most effective for this decarboxylative coupling reaction (Table 1, entry 5). A slightly lower yield of propargylamine **47** was obtained when acetonitrile was used as a solvent. Further experiments led to the discovery that CuBr and CuCl were superior catalysts compared to CuI (Table 1, entries 6-10). Also, use of 15% CuBr resulted in the formation of propargylamine in 78% yield in 1 h (Table 1, entry 11). Increasing time to 2 h and using 30 mol% of CuBr resulted in propargylamine 85% yield (Table 1, entry 12).

Table 1. **Reaction of amine, 1-alkyne and monogylyoxalic acid with different metal salts**[a,b]

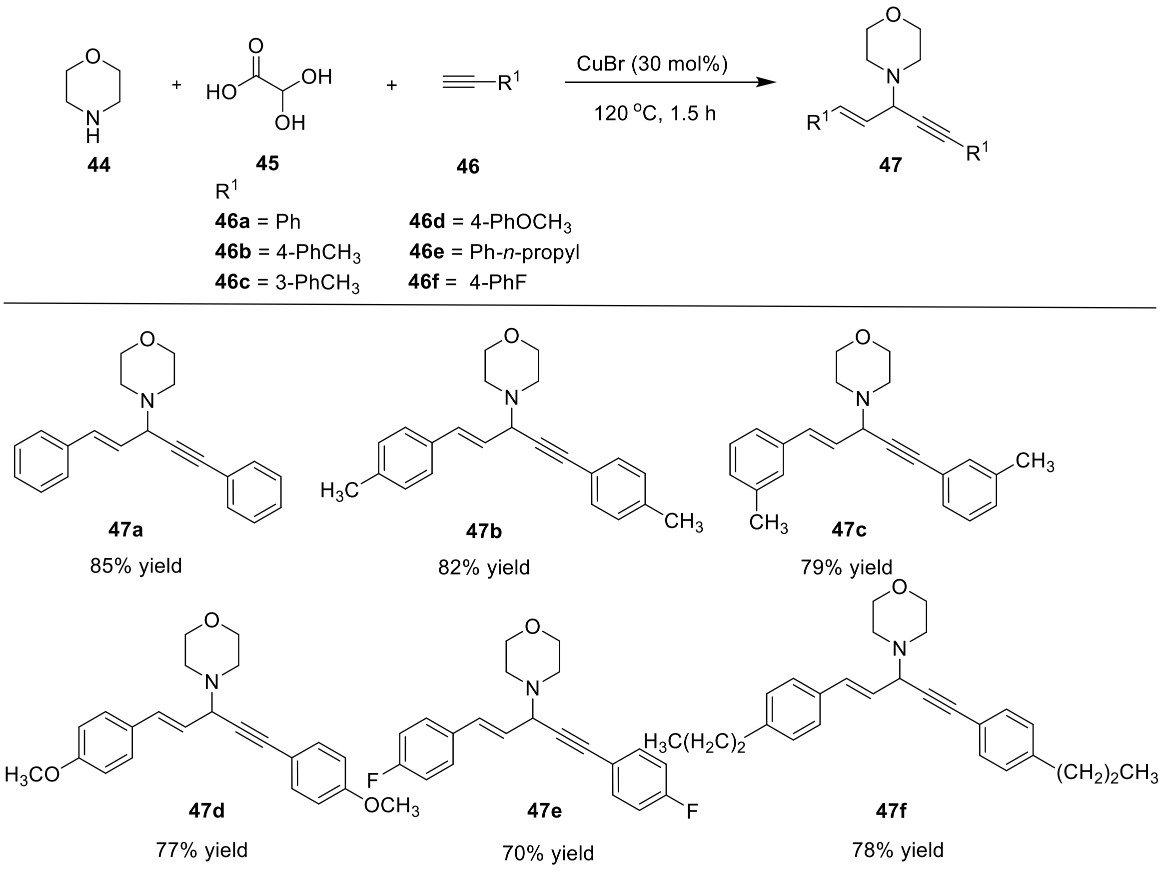


entry	Cu catalyst (mol %)	solvent	time (h)	yield (%)
1	CuI (20)	THF	0.5	40
2	CuI (20)	MeCN	0.5	70
3	CuI (20)	DCE	0.5	65
4	CuI (20)	toluene	0.5	70
5	CuCl (20)	toluene	0.5	72
6	$Cu(OAc)_2$ (20)	toluene	1.0	40
7	Cu_2O (20)	toluene	0.5	20
8	$Cu(OTf)_2$ (20)	toluene	0.5	60
9	CuCl (15)	toluene	0.5	65
10	CuBr (15)	toluene	0.5	75
11	CuBr (15)	toluene	1.0	78
12	CuBr (30)	toluene	2.0	85

[a]The reactions were carried out by using amine (1.0 mmol), mono glyoxalic acid (1.0 mmol), and 1-alkyne (2.0 mmol) in toluene (3 mL) at 110 °C. [b]Yield of vinyl propargylamines.

Under the optimum conditions (Table 1, entry 13), we have examined the substrate scope using various 1-alkynes **46**. The results are summarized in Table 2. The alkynes with **46b**, **46c**, and **46d** R^1 groups 4-Me-, 3-Me-, and 4-OMe groups react with monoglyoxalic acid and morpholine **44** to give the vinyl propargylamine **47b-47d** in 77-82% yields (Table 2). Also, 1-alkyne **46e** with electron withdrawing 4-F resulted in the formation of the vinyl propargylamine **47e** in 70% yield (Table 2). Similarly, the 1-alkyne **46f** gave the propargylamine **47f** in 78% yield (Table 2).

Table 2. Synthesis of vinyl propargylamine derivatives



44 + **45** + **46** → **47**

R^1

46a = Ph

46b = 4-$PhCH_3$

46c = 3-$PhCH_3$

46d = 4-$PhOCH_3$

46e = Ph-*n*-propyl

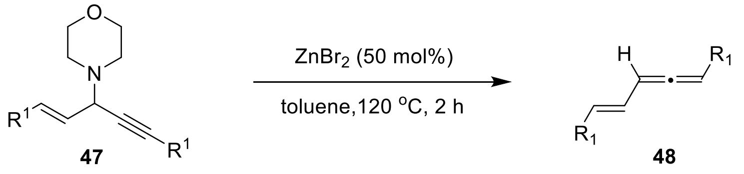
46f = 4-PhF

47a 85% yield	**47b** 82% yield	**47c** 79% yield
47d 77% yield	**47e** 70% yield	**47f** 78% yield

[a]The reactions were carried out by using amine **44** (1.0 mmol), monoglyoxalic acid **45** (1.0 mmol), and 1-alkyne **46** (2.0 mmol) in toluene (3 mL) at 110 °C. [b]Yield of propargylamines **47**.

Then, we have turned our attention towards conversion of the vinyl propargylamines obtained in this way to aromatic vinyl allenes using $ZnBr_2$. We have observed that the reaction of propargylamine derivatives **47a-47e** with $ZnBr_2$ at 120 °C gives the vinyl allenes **48a-48e** in up to 38% yield. The propargylamine **47f** also gave the corresponding vinyl allene **48f** in 22% yield (Table 3).

Table 3. Synthesis of aromatic vinyl allenes

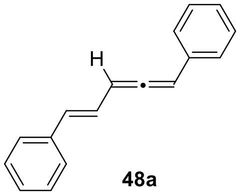


R^1

47a = Ph **47d** = 4-PhOCH_3

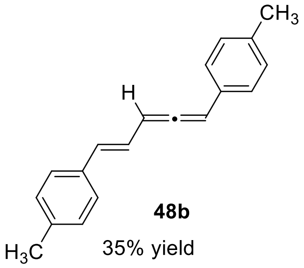
47b = 4-PhCH_3 **47e** = Ph-*n*-propyl

47c = 3-PhCH_3 **47f** = 4-PhF



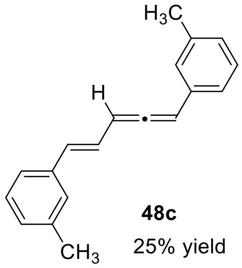
48a

38% yield



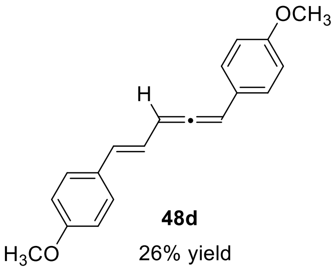
48b

35% yield



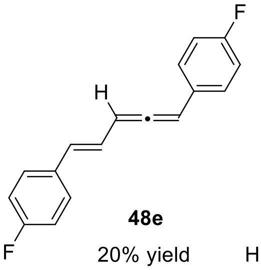
48c

25% yield



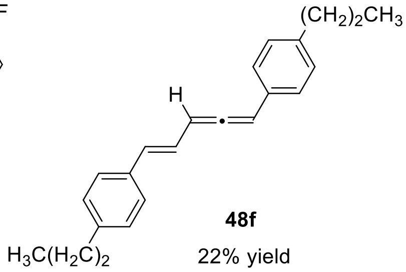
48d

26% yield



48e

20% yield



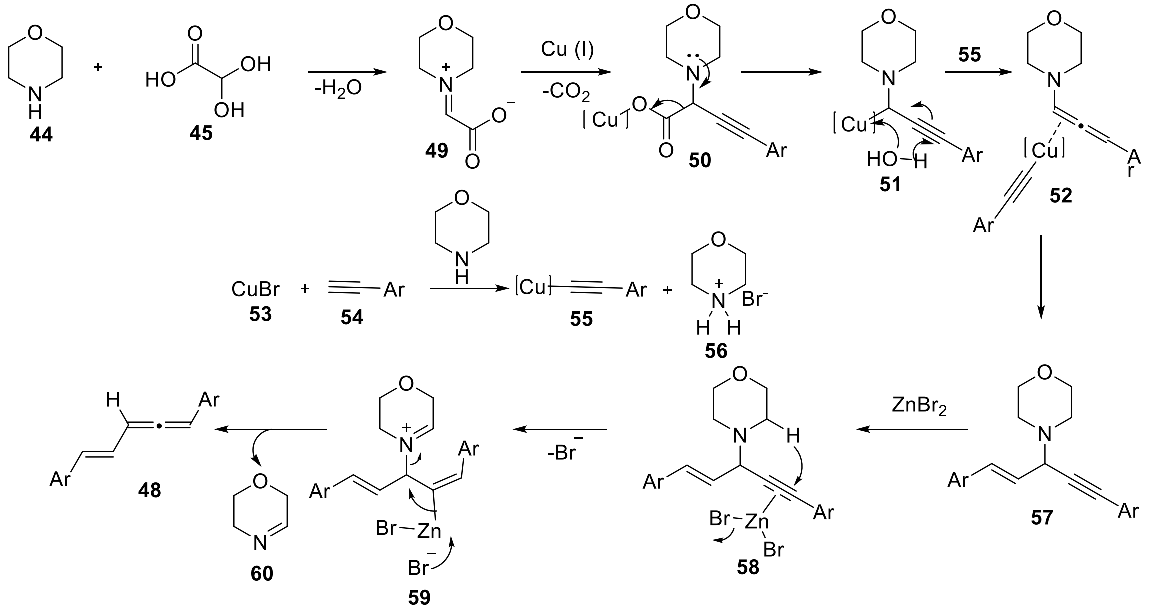
48f

22% yield

[a]The reactions were carried out by using amine (1.0 mmol), aldehyde (1.1 mmol), and 1-enyne (1.1 mmol) in toluene (3 mL) at 120 °C. [b]Yield of vinyl allenes.

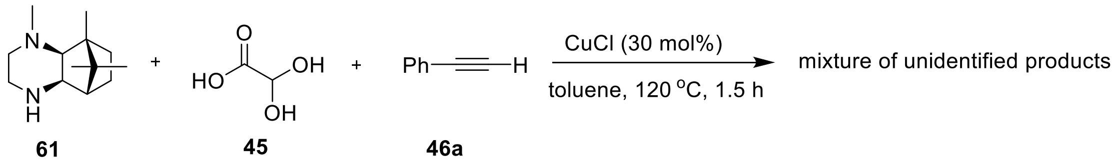
A plausible mechanism for this A^3-coupling/decarboxylative coupling is presented based on earlier reports (Scheme 12).[19] The iminium salt **49** formed *in situ* from glyoxylic acid **45** and amine **44** is expected to undergo a Cu(I)-catalyzed A^3-coupling of copper acetylide resulting in the formation of the intermediate **50**. Then, the Cu(I)-catalyzed decarboxylation of **50** would lead to the propargylamine species **51** to intermediate **52**. The intermediate **52** would react with zinc bromide to give the complex **58**, which would then undergo an intramolecular hydride shift to give the intermediate **59**. Subsequent, elimination of zinc bromide and the imine *via anti*-periplanar cleavage of C-N bond would lead to the vinyl allenes **48** and the corresponding imine **60**.[17]

Scheme 12. Plausible mechanism



We have also examined the reaction with chiral secondary amines **61**, monoglyoxalic acid and phenyl acetylene with CuCl (30 mol%) (Scheme 13). Unfortunately, The propargylamine product could not be obtained but only a mixture of unidentified products were isolated.

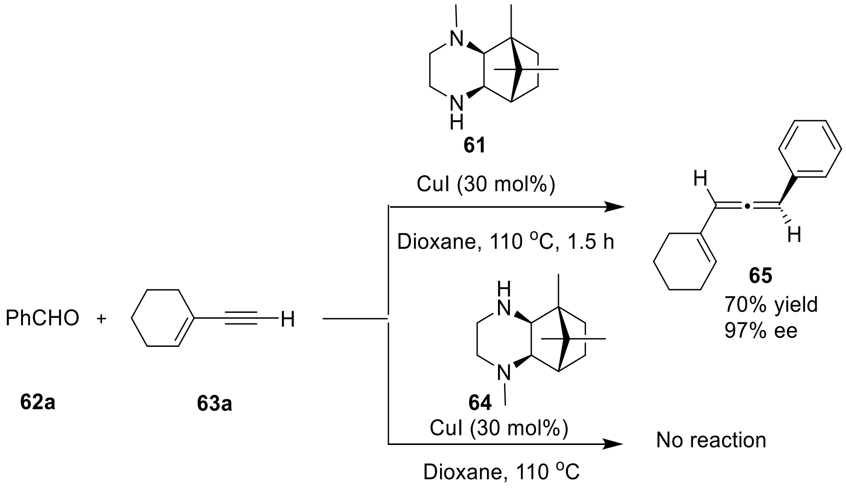
Scheme 13



3.2.2 Efforts toward the synthesis of highly enantioselctive chiral vinyl allenes

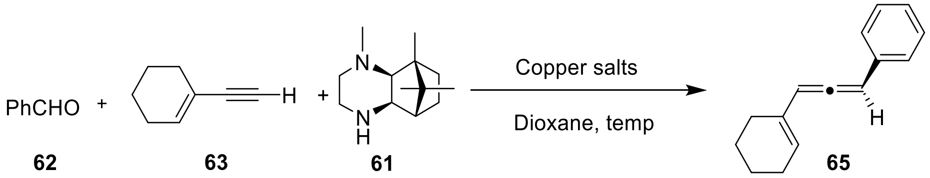
We have observed that the cyclohexenyl alkyne **63a**, benzaldehyde **62a** and N-methyl camphanyl piperazine **61** react with CuI (30 mol%), the product **65** in 70% yield and 99% ee (Scheme 14**)**.[20] However, the chiral secondary amine **64** did not give the allene product **65** under these conditions (Scheme 14), due to the steric crowding of the chiral amine **64**.

Scheme 14



We have also examined the reactivity of CuCl, CuBr, $CuBr_2$ and CuI in this reaction. We have observed that 1-ethynylcyclohex-1-ene **63a**, benzaldehyde **62a** and N-methyl camphanyl piperazine **61** at 120 °C in the presence of CuCl, gave the desired product **65aa** in 50% yield (entry 1, Table 4). Whereas, the product **65aa** was obtained in 60-74% yield using CuBr, CuI (entries 2, and 3, Table 4) with 96-97% ee within 1.5 h at 120 °C. However, when the reaction was performed with copper (II) halide such as $CuBr_2$ (entry 4, Table 4), the allene product **65aa** only in 59% yield. When we used other copper halides CuBr and CuI, the desired product **65aa** were obtained in 55% and 68% yield (entries 5 and 6, Table 4) with up to 97% ee. The yield was further improved to 73% by increasing the reaction time to 2 h (entry 7, Table 4). Whereas, the reaction of the corresponding amine **61** with CuCl (30 mol%) at 110 ^{0}C gave the chiral allene **65aa** in 47% yield and 96% ee (entry 8, Table 4). The use of CuI (30 mol%), gave the allene **65aa** in 58% yield and 96% ee (entry 9, Table 4).

Table 4. **Reaction of chiral amine, 1-alkyne and benzaldehyde with different metal salts to afford chiral allenes**[a, b, c]



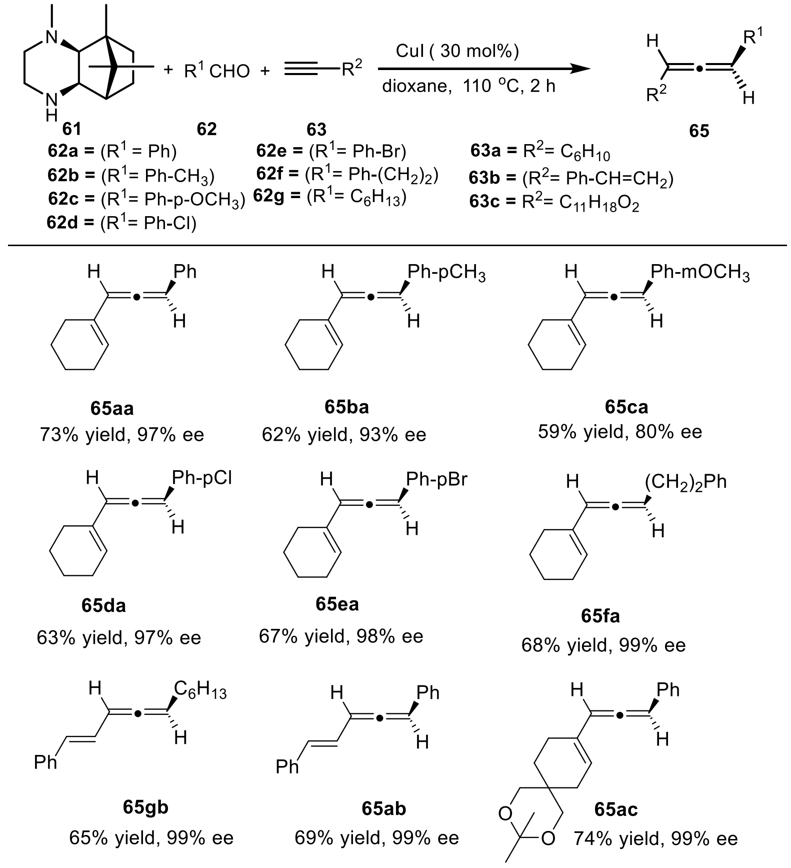
entry	Cu catalyst	temp	mol (%)	time (h)	65aa (% yield)	ee (%)[c]
1	CuCl	120	50	1.5	50	96
2	CuBr	120	50	1.5	60	97
3	CuI	120	50	1.5	74	96
4	$CuBr_2$	110	30	2	59	96
5	CuBr	110	30	2	55	97
6	CuI	110	30	1.5	68	97
7	CuI	110	30	2	73	97
8	CuCl	110	30	2	47	96
9	CuI	100	30	2	58	96

[a] The reactions were carried out by using amine **(**1.0 mmol) and 1-enyne (1.1 mmol) and aldehyde (1.1 mmol). [b] Isolated yield. [c] The % ee was determined by chiral HPLC analysis.

Since the chiral amine **61** is easily prepared from commercially available camphor,[5c] we have examined the scope of this transformation using various aldehydes, 1-enynes and chiral amine **61**. The chiral amine **61** reacts with the alkyne **63a** and aldehydes **62b**, **62c** R^1 groups 4-Me, 4-OMe phenyl ring react to give the (*R*)-allene **65ba**-**65ca** in 59-62 yields with 80-93% ee (Table 5). Also, the aldehydes **62d**, and **62e** with electron withdrawing 4-Cl, and 4-Br resulted in the formation of the allenes in 63-67% yields in up to 98% ee (Table 5, **65da**, and **65ea**). In addition, the aldehyde **62f** gave the allene **65fa** in 68% yield and 99% ee. We have also examined the applications of the alkynes **63b** and **63c** and obtained the corresponding allene (**65ab** and **65ac**) in 69-74% yield with 99% ee. Further, the vinyl 1-alkyne **63b** and aldehyde **62g** gave the corresponding allene **65gb** in 65% yield with 99% ee.

All the optically active allenes, obtained by using chiral amine **61** are levorotatory from which the absolute configurations of the major enantiomer of the chiral allenes are assigned as *R* by the Lowe-Brewster rule and also by comparison with the $[\alpha]_D^{25}$ values reported for similar allene derivatives.[21]

Table 5. Synthesis of vinyl allenes using aldehyde, 1-alkyne and amine.[a,b,c]

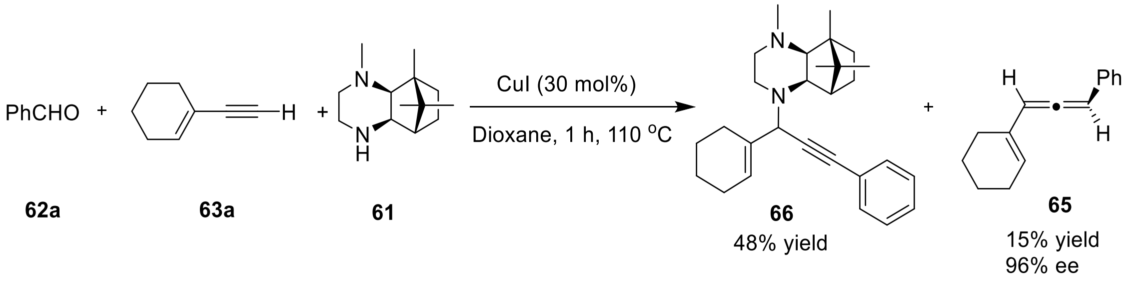


[a]The reactions were carried out by using amine (1.0 mmol), aldehyde (1.1 mmol), and 1-enyne (1.1 mmol) in dioxane (3 mL) at 110 °C. [b]Yield of vinylallenes. [c]The ee was determined by chiral HPLC analysis.

3.2.3 Isolation of propargylamine intermediate and their conversion to cyclohexenylallene

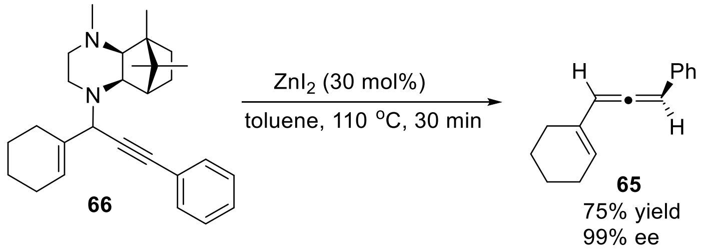
We have observed that the reaction of benzaldehyde **62a**, 1-alkyne **63a**, and camphanyl piperazine derivative **61** resulted in the formation intermediate propargylamine **66** in 48% yield along with chiral cyclohexenyl allene **65** in 15% yield (Scheme 15).

Scheme 15



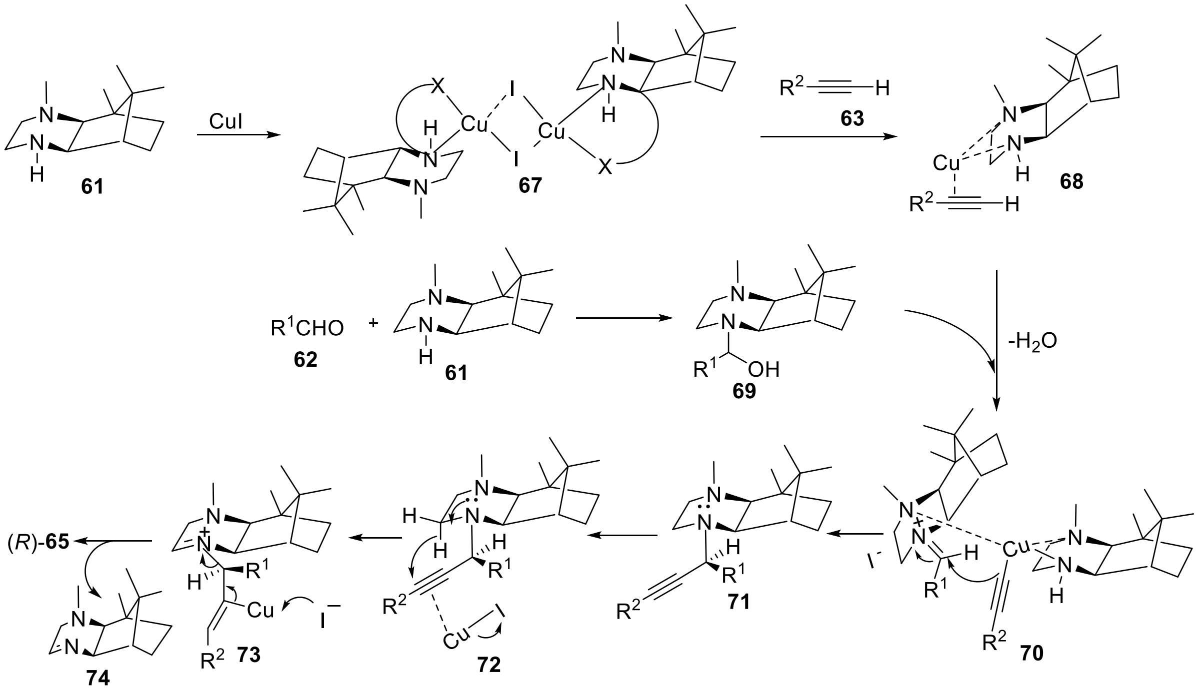
We have also observed that the reaction of propargylamine **66** with ZnI_2 at 110 °C for 30 min gave the chiral cyclohexenyl allene **65** in 75% yields with 99% ee (Scheme 16).

Scheme 16



The mechanism outlined in Scheme 17 can be considered for the formation of allenes, in accordance with previous reports.[22] Initially, the chiral amine **61** would react with CuI to generate the dimeric chiral copper complex **67**.[5, 23] Subsequently, the reaction with 1-alkyne gives intermediate complex **68**, which after then reacts with the intermediate imine obtained from the aminal **69**, formed *in situ* with the reaction of chiral caamphanyl piperazine and aldehyde to produce the complex **70** to the intermediate **71**. The intermediate **71** could complex with CuI to afford intermediate **72**, which after undergo 1,5- hydride shift to give the alkenyl copper species **73**. Antiperiplanar elimination of the CuI and the imine would then give the chiral allene (*R*)-**65** along with the imine **74** as a byproduct. The imine intermediate could be readily converted to the starting chiral amine **61** in 62% yields by simple sodium borohydride reduction in MeOH as a solvent at -10 °C and the resulting reaction mixture stirred at room temperature for 3h.

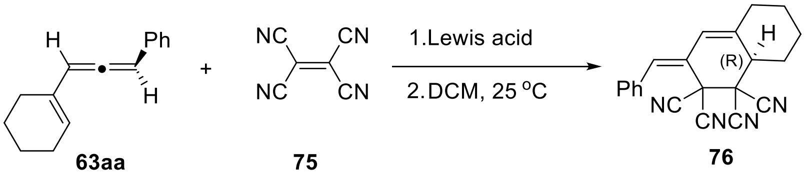
Scheme 17. **A tentative mechanism for copper (I) catalyzed allene formation**



3.2.4 The [4+2] cyclo-addition reaction of vinylallene and dienophile

We have developed a Lewis acid catalyzed [4 + 2] cycloaddition reaction of allene **63aa** with the electron deficient tetracyanoethylene (TCE) in different solvents at room temperature. The results are summarized in Table 6.

Table 6: Intermolecular Diels-Alder reaction using allene 65aa and TCE 75 [a,b]



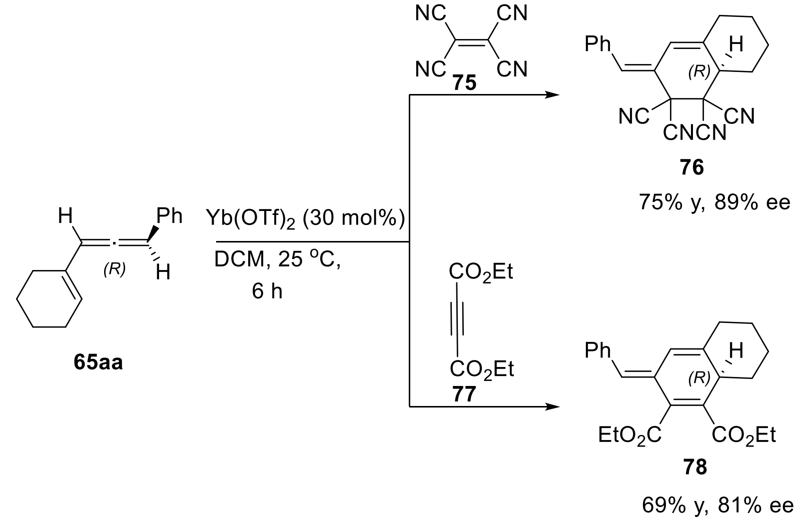
entry	solvent	temp	acid	mol (%)	time (h)	76 yield (%)[b]
1	Toluene	25	BF_3OEt_2	100	24	mixture of products
2	THF	25	TfOH	100	24	mixture of products
3	Diethyl ether	25	CuOTf	30	12	15%
4	DCM	25	AgOTf	10	12	45%
5	DCM	25	$Zn(OTf)_2$	10	12	10%
6	DCM	25	$Yb(OTf)_2$	10	6	73%
7	DCM	25	$In(OTf)_2$	10	6	52%

[a]The reactions were carried out by using allene (0.5 mmol) and a dienophile (0.7 mmol) at 25 °C. [b]Isolated yields.

We have initiated our studies using chiral allene **65aa** as diene in the presence of BF_3OEt_2 and triflic acid. In these cases, only complex mixtures of unidentifiable products were obtained after 24 h (entry 1 and 2, Table 6). When the reaction was performed using 30 mol% CuOTf, the product **76** was obtained in 15% yield after 12 h at 25 °C (entry 3, Table 6). We have also examined the other Lewis acids AgOTf , $Zn(OTf)_2$, $Yb(OTf)_2$ and $In(OTf)_2$ (entries 4, 5, 6 and 7, Table 6). Among these Lewis acids, $Yb(OTf)_3$ showed greater catalytic activity and gave the product **76** in 73% isolated yield (entry 6, Table 6).

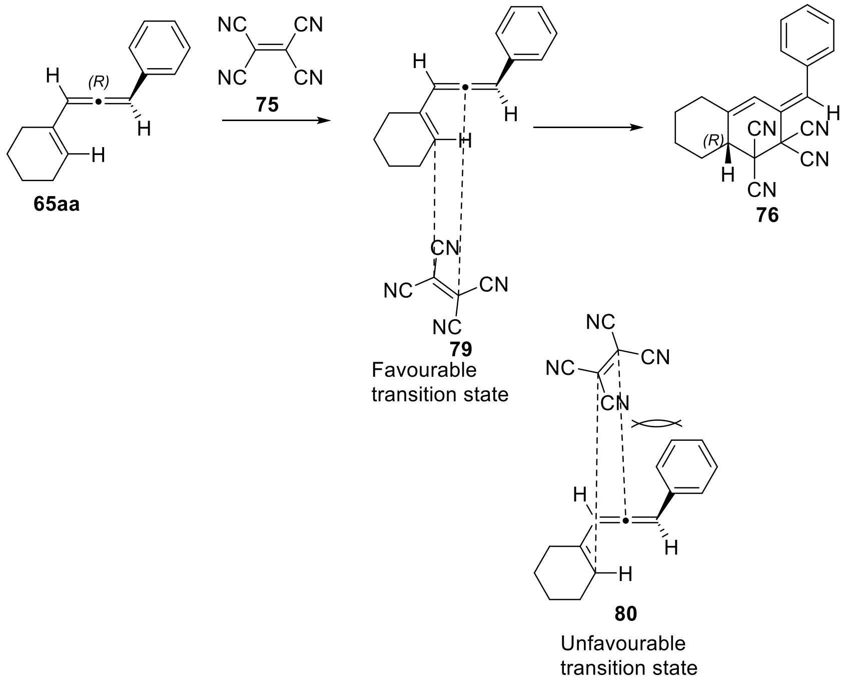
Under this optimized condition, we have carried out an experiment using the chiral allene **65aa** with TCE (tetracyanoethylene) **75** to obtain the product **76** in 75% with 89% ee (Scheme 18). Also, the use of internal alkyne **77** gave [4 + 2] Diels-Alder reaction product **78** in 69% yield with 81% ee (Scheme 18).

Scheme 18



A mechanism outlined in Scheme 19 can be considered to rationalize the ytterbium catalyzed [4+2] cycloaddition of cyclohexenylallene **65aa** with tetracyanoethylene to give the corresponding cycloadduct **76**.[11] Initially, the Yb(OTf)$_3$ would interact with tetracyanoethylene which would then react with the allene (*R*)-**65aa** in a Diels-Alder type reaction, through the transition state **79** or **80.** The steric interactions between the dienophile and the phenyl substituent in allene would make the transition state **80** not favourable and hence the reaction would go through the lower energy transition state **79** to give the cycloadduct **76,** with (*R*) configuration at the newly formed stereogenic centre**.** As the mechanism of cycloaddition reaction of cyclohexenylallene **65aa** and diethyl acetylenedicaboxalate is expected to be the same, the configuration (*R*) can be also assigned for the newly formed stereogenic centre in the product **78**.

Scheme 19. **Plausible mechanistic pathway**



The results obtained on the enentioselective synthesis of chiral cyclohexenylallene **65aa** and its application in cycloaddition reactions would stimulate further exploitation of these chiral allenes in organic synthesis.

Next, we have undertaken studies toward conversion of propargylamine to other useful organic compounds. The results are discussed in the next chapter.

3.3 Conclusions

We have developed a method for synthesis of vinyl allenes *via* trisubstituted vinyl propargylamines using morpholine, monoglyoxalic acid, and 1-alkynes. Also, a convenient method for the synthesis of chiral vinylallenes *via* CuI catalyzed reactions of 1-alkynes, aldehydes and chiral N-methyl camphanyl piperazine was developed. In addition, we have devised a method for cycloaddition using enantiomerically enriched cyclohexenyl allene. These methods described herein have considerable potential for further synthetic applications.

3.4 Experimental Section

3.4.1 General information

Melting points were determined using a Superfit capillary point apparatus. IR (KBr) spectra were recorded on JASCO FT-IR spectrophotometer Model 5300. The neat IR spectra were recorded on JASCO FT-IR spectrophotometer Model 5300. ^{1}H-NMR (400 MHz), ^{13}C-NMR (100 MHz) spectra were recorded on Bruker-AC-200 and Bruker-Avance-400 spectrometers, respectively with chloroform-d as solvent and TMS as reference ($\delta = 0$ ppm). The chemical shifts are expressed in δ downfield from the signal of internal TMS. Liquid Chromatography (LC) and mass analysis (LC-MS) were performed on SHIMADZU-LCMS-2010A and BRUKER MARXIS High Resolution Mass Spectrometry (HRMS). The mass spectral analyses were carried out using Chemical Ionization (CI) or Electro Spray Ionization (ESI) techniques. Elemental analyses were carried out using a Perkin-Elmer elemental analyzer model-240C and Thermo Finnigan analyzer series Flash EA 1112. Mass spectral analyses for some of the compounds were carried out on VG 7070H mass spectrometer using EI technique at 70 eV.

Analytical grade of CuBr, Cu(OTf) and ZnI_2 were purchased from Sigma-Aldrich. $ZnBr_2$, $ZnCl_2$ was purchased from E-Merck. Toluene supplied by E-Merck, India was freshly distilled over sodium-benzophenone ketyl before use. Analytical thin layer chromatographic tests were carried out on glass plates (3 x 10 cm) coated with 250mμ E-Merck and acme's silica gel-G and GF_{254} containing 13% calcium sulfate as binder. The spots were visualized by short exposure to iodine vapour or UV light. Column chromatography was carried out using E-Merck and acme's silica gel (100-200 or 230-400 mesh) and neutral alumina.

Optical rotations were measured on Rudolph Research Analytical AUTOPOL-II (readability ±0.01°) and AUTOPOL-IV (readability ±0.001°) automatic polarimeters. HPLC analyses were performed on an SCL-10ATVP SHIMADZU instrument.

3.4.2 Genaral procedure for vinyl propargylamine (47)

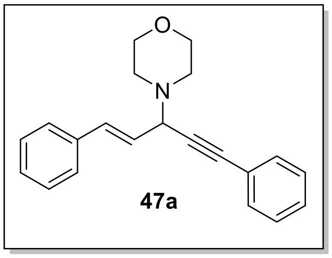
To a stirred suspension of amine (1 mmol), CuI (0.057 g, 0.3 mmol), monoglyoxalic acid **63** (1.1mmol) and1-alkyne (2.0 mmol) in toluene (3 mL) under N_2 atmosphere. The contents were stirred at 110 °C for 2 h. The reaction mixture cooled to room temperature. Touene was removed using reduced pressure. The residue was subjected to column chromatography using hexane and ethyl acetate (90:10) as eluent to isolate the propargylamine **47**.

(E)-4-(1,5-Diphenylpent-1-en-4-yn-3-yl)morpholine (47a)

Yield : 0.257 g, 85% yellow liquid.

IR (neat) : 2936, 2236, 2132, 1760, 1721, 1660, 1455, 1363, 1181, 1022 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.50-7.42 (m, 5H), 7.39-7.30 (m, 5H), 6.96-6.92 (m, 1H), 6.35-6.31 (m, 1H), 4.42 (s, 1H), 3.82-3.81 (m, 4H), 2.84-2.70 (m, 4H).



47a

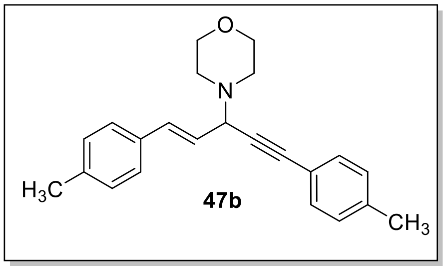
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 139.2, 136.3, 133.0, 132.2, 129.1, 128.5, 128.5, 128.2, 127.4, 126.5, 123.8, 122.4, 89.7, 82.7, 67.5, 59.5, 50.3.

LCMS : m/z 303 (M+1); Analysis for $C_{21}H_{21}NO$ calcd: C 83.13, N 6.98, H 4.62; Found: C 83.13, N 6.98, H 4.62.

(E)-4-(1,5-Di-p-tolylpent-1-en-4-yn-3-yl)morpholine (47b)

Yield : 0.271g, 82% light yellow liquid.

IR (neat) : 3027, 2825, 2215, 2130, 1761, 1715, 1655, 1459, 1368, 1179, 1025, 989 cm^{-1}.



47b

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.39-7.26 (m, 4H), 7.20-7.18 (m, 2H), 7.12-7.11 (m, 2H), 6.94-6.90 (d, *J* = 8.0 Hz, 1H), 6.39-6.29 (d, *J* = 8.0 Hz, 1H), 4.42 (s, 1H), 3.82-3.81 (m, 4H), 2.82-2.73 (m, 4H), 2.39 (m, 6H).

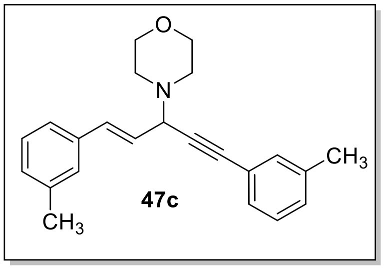
^{13}C NMR : (100 MHz, $CDCl_3$, δppm) 138.1, 138.0, 136.4, 133.2, 132.4, 129.2, 128.6, 128.5, 128.2, 127.4, 126.5, 123.8, 122.7, 88.7, 83.9, 67.1, 59.9, 50.0, 21.2.

LCMS : m/z 331 (M+1); Analysis for $C_{23}H_{25}NO$ calcd: C 83.34, N 7.60, H 4.23; Found: C 83.34, N 7.60, H 4.23.

(E)-4-(1,5-Di-m-tolylpent-1-en-4-yn-3-yl)morpholine (47c)

Yield : 0.261 g, 79% yellow liquid.

IR (neat) : 3052, 3029, 2836, 2236, 2134, 1763, 1722, 1662, 1450, 1365, 1185, 1021 cm^{-1}.



47c

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.39-7.36 (m, 1H), 7.35-7.31 (m, 1H), 7.29-7.27 (m, 2H), 7.26-7.20 (m, 2H), 7.12-7.10 (m, 2H), 6.93-6.90 (d, *J* =

8.0 Hz, 1H), 6.37-6.28 (d, *J* = 8.0 Hz, 1H), 4.42 (s, 1H), 3.82-3.81 (m, 4H), 2.83-2.70 (m, 4H), 2.37 (m, 6H).

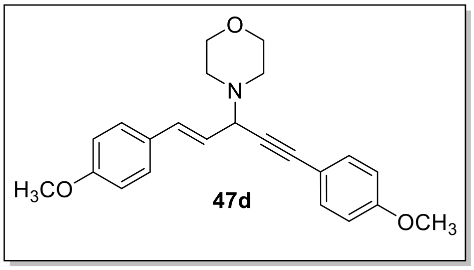
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 138.9, 138.2, 136.5, 133.1, 132.3, 129.2, 128.6, 128.5, 128.2, 127.4, 126.5, 123.5, 122.3, 88.3, 83.5, 67.2, 59.7, 49.8, 21.2.

LCMS : m/z 331 (M+1); Analysis for $C_{23}H_{25}NO$ calcd: C 83.34, N 7.60, H 4.23; Found: C 83.34, N 7.61, H 4.22.

(E)-4-(1,5-Bis(4-methoxyphenyl)pent-1-en-4-yn-3-yl)morpholine (47d)

Yield : 0.279 g, 77% yellow liquid.

IR (neat) : 3052, 3025, 2837, 2226, 2124, 1753, 1712, 1665, 1456, 1355, 1175, 1025 cm^{-1}.



47d

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.41-7.38 (m, 2H), 7.37-7.34 (m, 2H), 7.29-7.26 (m, 2H), 7.24-7.20 (m, 2H), 6.96-6.92 (m, 1H), 6.36-6.29 (d, *J* = 8.0 Hz, 1H), 4.40 (s, 1H), 3.82-3.80 (m, 4H), 3.18 (s, 6H), 2.84-2.72 (m, 4H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 141.3, 140.5, 138.9, 138.5, 138.2, 136.5, 133.1, 132.3, 129.2, 128.6, 128.5, 128.2, 127.4, 126.5, 123.5, 122.3, 88.3, 83.5, 67.2, 59.7, 49.8, 55.6.

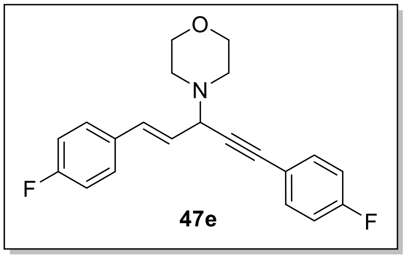
LCMS : m/z 363 (M+1); Analysis for $C_{23}H_{25}NO_3$ calcd: C 76.01, N 3.85, H 4.62; Found: C 76.01, N 3.85, H 4.62.

(E)-4-(1,5-Bis(4-fluorophenyl)pent-1-en-4-yn-3-yl)morpholine (47e)

Yield : 0.237 g, 70% yellow liquid.

IR (neat) : 3021, 3011, 2830, 2216, 2118, 1753, 1712, 1659, 1458, 1362, 1185, 1021, 846, 665 cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.40-7.38 (m, 2H), 7.36-7.32 (m, 2H), 7.29-7.25 (m, 2H), 7.24-7.219 (m, 2H), 6.95-6.92 (m, 1H), 6.36-6.29 (d, *J* = 8.0 Hz, 1H), 4.42 (s, 1H), 3.82-3.81 (m, 4H), 2.86-2.74 (m, 4H).



47e

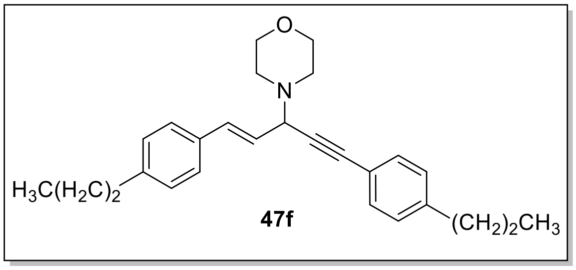
^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 161.5, 161.2, 159.2, 139.0, 134.7, 128.3, 127.9, 122.6, 115.6, 115.2, 114.2, 88.7, 82.6, 67.2, 59.6, 49.9,

LCMS : m/z 339 (M+1); Analysis for C$_{21}$H$_{19}$FN$_2$O calcd: C 74.32, N 4.13, H 5.64; Found: C 74.32, N 4.13, H 5.64.

(E)-4-(1,5-Bis(4-propylphenyl)pent-1-en-4-yn-3-yl)morpholine (47f)

Yield : 0.301g, 78% yellow liquid.

IR (neat) : 3042, 3028, 2820, 2243, 2121, 1753, 1712, 1642, 1440, 1315, 1155, 1025, 985 842, 663 cm^{-1}.



47f

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.47-7.30 (m, 4H), 7.29-7.27 (m, 4H), 6.95-6.92 (m, 1H), 6.31-6.26 (m, 1H), 4.42 (s, 1H), 3.82-3.78 (m, 4H), 2.64-

2.61 (m, 4H), 1.68-1.66 (m, 4H), 1.30-1.25 (m, 4H), 0.99-0.96 (m, 6H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 143.2, 142.6, 138.2, 134.5, 128.1, 127.3, 127.1, 122.6, 88.7, 83.5, 67.0, 59.9, 49.8, 37.9, 37.7, 24.5, 24.4, 13.8, 13.7.

LCMS : m/z 387 (M+1); Analysis for $C_{27}H_{33}NO$ calcd: C 83.68, N 3.61, H 8.58; Found: C 83.68, N 3.61, H 8.58.

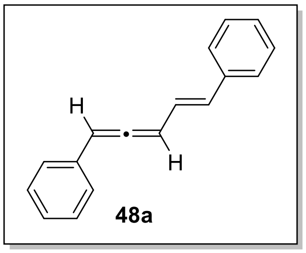
3.4.3 Genaral procedure for vinyl allene (48)

The propargylamines **47** (1 mmol) were added to a stirred suspension of ZnI_2 (50 mol%) in dry toluene (3 mL) and the contents were refluxed for 1-2 h at 120 °C under nitrogen atmosphere. Toluene was removed under reduced pressure and the crude product was purified on silica gel (100-200 mesh) column chromatography using hexane/ethyl acetate as eluent to isolate the chiral allenes **48**.

(E)-Penta-1,2,4-triene-1,5-diyldibenzene (48a)

Yield : 0.085 g, 38%, yellow liquid.

IR (neat) : 3081, 2926, 1928, 1597, 1494 cm^{-1}.



48a

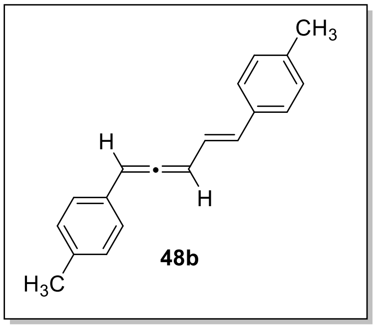
^{1}H NMR : (400 MHz, $CDCl_3$, δppm) 7.32-7.25 (m, 5H), 7.24-7.18 (m, 5H), 6.68-6.63 (m, 1H), 6.61-6.10 (m, 1H), 6.44-6.42 (m, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 209.2, 137.4, 129.7, 128.6, 127.2, 126.1, 125.6, 122.2, 95.7, 92.7.

HRMS : (ESI-TOF) m/z : $[M+H]^+$ calcd for $C_{17}H_{15}$: 219.1175

Found: 219.1175.

(E)-4,4'-(Penta-1,2,4-triene-1,5-diyl)bis(methylbenzene) (48b)



48b

Yield : 0.086 g, 35%, yellow liquid.

IR (neat) : 3085, 2936, 1925, 1591, 1494, 729 cm^{-1}.

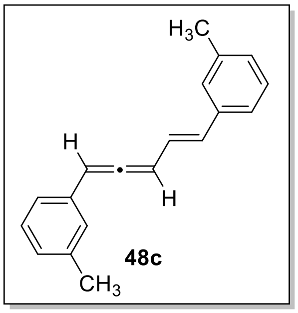
^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.34-7.20 (m, 8H), 6.68-6.60 (m, 1H), 6.65-6.53 (m, 1H), 6.44-6.41 (m, 2H), 2.35 (s, 6H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 208.9, 137.2, 129.3, 128.6, 128.1, 127.2, 126.1, 125.6, 98.5, 96.1, 21.9.

HRMS : (ESI-TOF) m/z : [M+H]$^+$ calcd for C$_{19}$H$_{19}$: 247.1488

Found: 247.1488.

(E)-3,3'-(Penta-1,2,4-triene-1,5-diyl)bis(methylbenzene) (48c)



48c

Yield : 0.061 g, 25%, yellow liquid.

IR (neat) : 3080, 2936, 1925, 1591, 1454, 728 cm^{-1}.

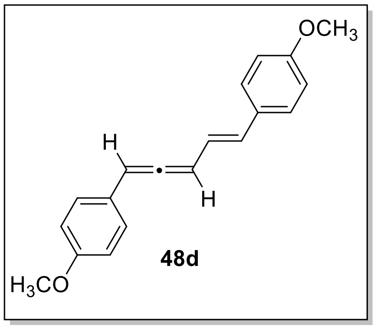
^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.32-7.28 (m, 4H), 7.23-7.20 (m, 4H), 6.68-6.60 (m, 1H), 6.55-6.41 (m, 3H), 2.32 (s, 6H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 208.3, 137.9, 132.3, 128.9, 128.6, 128.1, 127.4, 122.3, 98.1, 96.3, 21.8.

HRMS : (ESI-TOF) m/z : [M+H]$^+$ calcd for C$_{19}$H$_{19}$: 247.1488,

Found: 247.1488.

((E)-4,4'-(Penta-1,2,4-triene-1,5-diyl)bis(methoxybenzene) (48d)



48d

Yield : 0.072 g, 26%, yellow liquid.

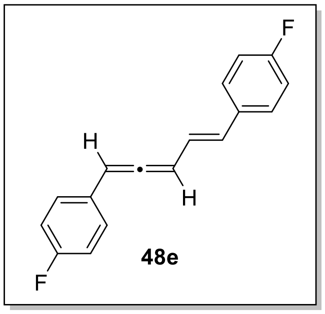
IR (neat) : 3081, 2937, 1925, 1494, 1125, 1024, 729 cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.35-7.29 (m, 4H), 7.27-7.19 (m, 4H), 6.62-6.59 (m, 1H), 6.55-6.50 (m, 1H), 6.45-6.42 (m, 2H), 3.80 (s, 6H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 207.3, 137.6, 133.9, 132.3, 127.1, 125.3, 122.4, 95.6, 88.2, 55.6.

HRMS : (ESI-TOF) m/z : [M+H]$^+$ calcd for $C_{19}H_{19}O_2$: 279.1386, Found: 279.1386.

(E)-4,4'-(Penta-1,2,4-triene-1,5-diyl)bis(fluorobenzene) (48e)



48e

Yield : 0.051 g, 20%, yellow liquid.

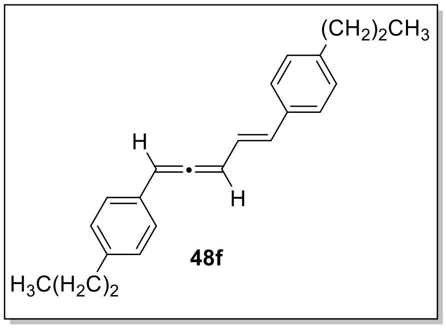
IR (neat) : 3052, 2959, 1929, 1695, 1634 cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.40-7.20 (m, 8H), 6.65-6.62 (m, 1H), 6.55-6.45 (m, 2H), 6.44-6.41 (m, 1H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 209.3, 162.5, 161.3, 137.9, 132.3, 128.6, 127.1, 125.6, 122.5, 115.3, 115.2, 114.9, 98.4, 96.6.

HRMS : ((ESI-TOF) m/z : [M+H]$^+$ calcd for $C_{17}H_{13}F_2$: 255.0986, Found: 255.0986.

(E)-4,4'-(Penta-1,2,4-triene-1,5-diyl)bis(propylbenzene) (48f)



48f

Yield : 0.066 g, 22%, yellow liquid.

IR (neat) : 3015, 2985, 2366, 1928, 1632, 850, 725 cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.39-7.20 (m, 8H), 6.65-6.63 (m, 1H), 6.55-6.40 (m, 3H), 2.58-2.54 (m, 4H), 1.31-1.28 (m, 4H), 0.91-0.89 (m, 6H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 208.3, 139.8, 133.9, 132.3, 128.6, 127.1, 122.3, 98.6, 96.2, 37.7, 29.5, 24.5, 13.8, 13.7.

HRMS : (ESI-TOF) m/z : [M+H]$^+$ calcd for $C_{23}H_{27}$: 303.2114, Found: 303.2114.

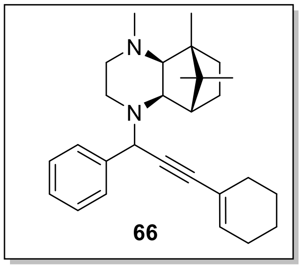
3.4.4. Reaction of 1-alkyne, aldehyde and amine 61 with CuI: Synthesis of chiral vinyl allene

To a stirred suspension of amine **61** (1 mmol), CuI (0.057 g, 0.3 mmol), aldehyde **62** (1.1mmol) and1-alkyne **63** (1.1mmol) in dioxane (3 mL) at 25 °C under N$_2$ atmosphere. The contents were stirred at 110 °C for 2 h. The reaction mixture cooled to room temperature. Dioxane was removed using reduced pressure. The residue was subjected to column chromatography using hexane and ethyl acetate (99:01) as eluent to isolate the allnes **65**.

3.4.2 Genaral procedure for (4*S*,5*R*,8*S*,8*R*)-1-(3-(cyclohex-1-en-1-yl)-1-phenylprop-2-yn-1-yl)-4,5,9,9 tetramethyldecahydro-5,8-methanoquinoxaline (66)

To a stirred suspension of amine **61** (1 mmol), CuI (0.057 g, 0.3 mmol), aldehyde **62**(1.1mmol) and1-alkyne **63** (1.1mmol) in dioxane (3 mL) at 25 °C under N$_2$ atmosphere.

The contents were stirred at 110 °C for 1 h. The reaction mixture cooled to room temperature. Dioxane was removed using reduced pressure. The residue was subjected to column chromatography using hexane and ethyl acetate (90:10) as eluent to isolate the propargylamine **66**.



66

Yield : 0.243 g, 48% yellow liquid.

$[\alpha]_D^{25}$: $[\alpha]_D^{25}$ -89.3 (*c* 0.50, $CHCl_3$).

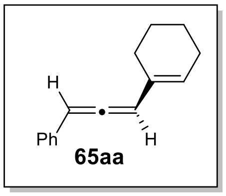
IR (neat) : 3052, 2931, 2236, 2134, 1763, 1722, 1662, 1450, 1365, 1185, 1021 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.39-7.34 (m, 4H), 7.29-7.27 (m, 1H), 6.58 (s, 1H), 6.40 (s, 1H), 4.40 (q, *J* = 8.0 Hz, 2H), 3.38 (t, *J* = 8.0 Hz, 3H), 2.37-2.10 (m, 4H), 1.94-1.60 (m, 16H), 1.40 (t, *J* = 8.0 Hz, 3H), 1.34 (t, *J* = 8.0 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 139.2, 134.3, 128.3, 127.9, 120.6, 89.7, 82.7, 78.1, 65.5, 58.0, 50.3, 48.1, 47.4, 47.3, 42.7, 37.2, 29.8, 26.2, 25.6, 22.3, 22.1, 21.5, 21.2, 14.6.

LCMS : m/z 403 (M+1); Analysis for $C_{28}H_{38}N_2$ calcd: C 83.53, N 6.96, H 9.51 Found: C 83.45, N 6.91, H 9.56.

(*R*)-(3-(Cyclohex-1-en-1-yl)propa-1,2-dien-1-yl)benzene (65aa)



65aa

Yield : 0.151 g, 73%, 97%ee, yellow liquid.

$[\alpha]_D^{25}$: $[\alpha]_D^{25}$ -159.8 (*c* 0.50, $CHCl_3$).

IR (neat) : 3054, 2925, 2853, 1932, 1619, 1593, 1489, 1262, 1066, 983 cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.35-7.24 (m, 5H), 6.40 (d, *J* = 8.0 Hz, 1H), 6.32 (d, *J* = 8.0 Hz, 1H), 5.82 (m, 1H), 2.19-2.09 (m, 4H); 1.68-1.57 (m, 4H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 206.5, 134.7, 131.8, 128.6, 127.1, 126.9, 126.7, 101.6, 97.5, 25.9, 25.8, 22.5, 22.4.

LCMS : m/z 197 (M+1); Analysis for $C_{15}H_{16}$ calcd: C 91.78, H 8.22 Found: C 91.63, H 8.28.

<u>Enantiomeric purity</u>: The enantioselectivity was determined by HPLC using chiral column, chiralcel AS-H, hexanes:i-PrOH/95:5; flow rate 0.5 mL/min, 254 nm, retention times: 13.4 min. (major) and 14.8 min. (minor).

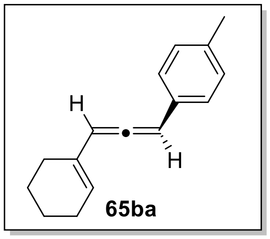
(*R*)-1-(3-(Cyclohex-1-en-1-yl) propa-1,2-dien-1-yl)-4-methylbenzene (65ba)

Yield : 0.130 g, 62%, 93% ee, yellow liquid.

$[\alpha]_D^{25}$: $[\alpha]_D^{25}$-186.3 (*c* 0.62, CHCl$_3$).

IR (neat) : 3049, 2925, 2848, 1947, 1618, 1510, 1086, 875 cm^{-1}.

^{1}H NMR : **(**400 MHz, CDCl$_3$, δppm) 7.22 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 6.39 (s, 1H), 6.24 (d, *J* = 8.0 Hz, 1H), 5.83-5.78 (m, 1H), 2.35 (s, 3H), 2.16-2.01 (m, 4H), 1.73-1.64 (m, 4H).



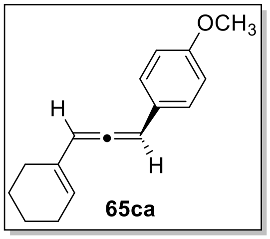
65ba

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 206.1, 136.6, 132.0, 131.7, 129.3, 126.8, 126.6, 101.4, 97.3, 25.9, 25.7, 22.4, 22.4, 21.5.

LCMS : m/z 211 (M+1); Analysis for $C_{16}H_{18}$ calcd: C 91.37, H 8.63 Found: C 91.25, H 8.56.

Enantiomeric purity: The enantioselectivity was determined by HPLC using chiral column, chiralcel AS-H, hexanes:i-PrOH/95:5; flow rate 0.5 mL/min, 254 nm, retention times: 13.4 min. (major) and 14.8 min. (minor).

(*R*)-1-(3-(Cyclohex-1-en-1-yl)propa-1,2-dien-1-yl)-4-methoxybenzene (65ca)



65ca

Yield : 0.142 g, 59%, 80% *ee*, yellow liquid.

$[\alpha]_D^{25}$: $[\alpha]_D^{25}$ -141.5 (*c* 0.55, $CHCl_3$).

IR (neat) : 2920, 2848, 1948, 1598, 1458, 1381, 1169, 895 cm^{-1}.

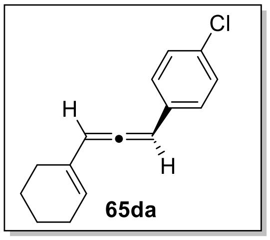
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.27-7.23 (m, 2H), 6.87-6.85 (m, 2H), 6.38-6.36 (m, 1H), 6.23 (d, *J* = 8.0 Hz, 1H), 5.78-5.77 (m, 1H), 3.18 (s, 3H), 2.15-2.03 (m, 4H), 1.66-1.61 (m, 4H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 205.7, 158.7, 132.1, 127.7, 127.0, 126.8, 114.1, 101.5, 96.9, 55.3, 25.9, 25.7, 22.4, 22.4.

LCMS : m/z 227 (M+1); Analysis for $C_{16}H_{18}O$ calcd: C 84.91, H 8.02 Found: C 84.81, H 8.07.

Enantiomeric purity: The enantioselectivity was determined by HPLC using chiral column, chiralcel AS-H, hexanes:i-PrOH/95:5; flow rate 0.5 mL/min, 254 nm, retention times: 13.4 min. (major) and 14.8 min. (minor).

(*R*)-1-Chloro-4-(3-(cyclohex-1-en-1-yl)propa-1,2-dien-1-yl)benzene (65da)



65da

Yield : 0.150 g, 63%, 97% *ee*, yellow liquid.

$[\alpha]_D^{25}$: $[\alpha]_D^{25}$ -144.5 (*c* 0.50, $CHCl_3$).

IR (neat) : 2925, 2842, 1948, 1593, 1454, 1382, 1168, 893 cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.29-7.22 (m, 4H), 6.37 (d, *J* = 8.0 Hz, 1H), 6.28 (d, *J* = 8.0 Hz, 1H), 5.80 (m, 1H), 2.18-201 (m, 4H), 1.67-1.61 (m, 4H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 206.5, 133.3, 132.4, 131.5, 128.7, 127.8, 127.6, 101.9, 96.6, 25.9, 25.7, 22.4, 22.3.

LCMS : m/z 231 (M+1); Analysis for $C_{15}H_{15}Cl$ calcd: C 78.08, H 6.55 Found: C 78.21, H 6.48.

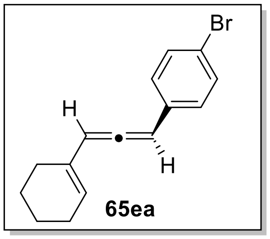
<u>Enantiomeric purity</u>: The enantioselectivity was determined by HPLC using chiral column, chiralcel AS-H, hexanes:i-PrOH/95:5; flow rate 0.5 mL/min, 254 nm, retention times: 13.4 min. (major) and 14.8 min. (minor).

(*R*)-1-Bromo-4-(3-(cyclohex-1-en-1-yl)propa-1,2-dien-1-yl)benzene (65ea)

Yield : 0.154 g, 67%, 98% *ee*, yellow liquid.

$[\alpha]_D^{25}$: $[\alpha]_D^{25}$ -132.2 (*c* 0.55, CHCl$_3$).

IR (neat) : 2923, 2840, 1949, 1593, 1454, 1382, 1165, 891 cm^{-1}.



65ea

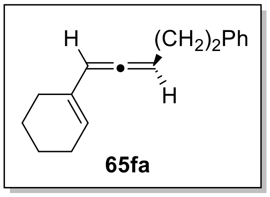
^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.43 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 6.35 (d, *J* = 8.0 Hz, 1H), 6.27 (d, *J* = 8.0 Hz, 1H), 5.80-5.76 (m, 1H), 2.16-1.98 (m, 4H), 1.65-1.59 (m, 4H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 206.6, 133.8, 131.6, 131.4, 128.2, 127.6, 120.5, 102.0, 96.7, 25.9, 25.8, 22.4, 22.3.

LCMS : m/z 275 (M+1); Analysis for $C_{15}H_{15}Br$ calcd: C 65.47, H 5.49 Found: C 65.58, H 5.41.

Enantiomeric purity: The enantioselectivity was determined by HPLC using chiral column, chiralcel AS-H, hexanes:i-PrOH/95:5; flow rate 0.5 mL/min, 254 nm, retention times: 13.4 min. (major) and 14.8 min. (minor).

(*R*)-(5-(Cyclohex-1-en-1-yl)penta-3,4-dien-1-yl)benzene (65fa)

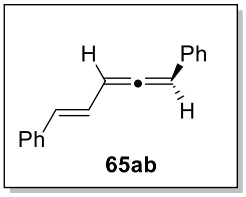


65fa

Yield	:	0.149 g, 68%, 99% *ee*, yellow liquid.
$[\alpha]_D^{25}$	:	$[\alpha]_D^{25}$ -144.3 (*c* 0.55, $CHCl_3$).
IR (neat)	:	3059, 2928, 2847, 1952, 1598, 1457, 1385, 1169, 895 cm^{-1}.
^{1}H NMR	:	(400 MHz, $CDCl_3$, δ ppm) 7.30-7.27 (m, 2H), 7.22-7.20 (m, 3H), 5.85-5.82 (m, 1H), 5.65-5.64 (m, 1H), 5.42-5.41 (m, 1H), 2.77-2.73 (m, 2H), 2.41-2.33 (m, 2H), 2.15-1.94 (m, 4H), 1.64-1.58 (m, 4H).
^{13}C NMR	:	(100 MHz, $CDCl_3$, δ ppm) 204.3, 141.8, 132.3, 128.5, 128.3, 125.8, 125.6, 98.2, 93.4, 35.4, 30.9, 25.8, 25.5, 22.5, 22.4.
LCMS	:	m/z 225 (M+1); Analysis for $C_{17}H_{20}$calcd: C 91.01, H 8.99 Found: C 91.15, H 8.91.

Enantiomeric purity: The enantioselectivity was determined by HPLC using chiral column, chiralcel AS-H, hexanes:i-PrOH/95:5; flow rate 0.5 mL/min, 254 nm, retention times: 13.4 min. (major) and 14.8 min. (minor).

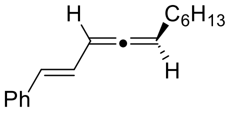
(*E*)-Penta-1,2,4-triene-1,5-diyldibenzene (65ab)



65ab

Yield	:	0.151 g, 69%, 99% *ee*, yellow liquid.
$[\alpha]_D^{25}$	:	$[\alpha]_D^{25}$ -142.3 (*c* 0.54, $CHCl_3$).

(*R,E*)-Undeca-1,3,4-trien-1-ylbenzene (65gb)



65gb

Yield : 0.187 g, 65%, 99% *ee*, yellow liquid.

[α]$_D$^{25} : [α]$_D$^{25} -139.1 (*c* 0.52, $CHCl_3$).

IR (neat) : 3059, 2928, 2847, 1952, 1620, 1598, 1451, 1386, 1170, 893 cm^{-1}.

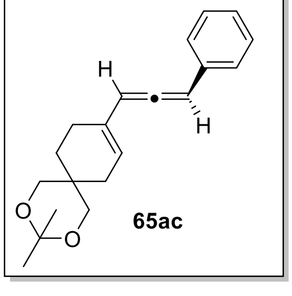
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.48-7.42 (m, 2H), 7.38-7.33 (m, 2H), 7.27-7.25 (m, 1H), 6.70-6.63 (m, 1H), 6.54 (d, *J* = 8.0 Hz, 1H), 6.06-6.01 (m, 1H), 5.49-5.44 (m, 1H), 2.16-2.09 (m, 2H), 1.53-1.48 (m, 2H), 1.44-1.34 (m, 9H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 208.2, 137.4, 129.7, 128.6, 127.2, 126.1, 125.6, 94.7, 92.7, 31.7, 29.0, 28.8, 25.6, 22.7, 14.1.

LCMS : m/z 227 (M+1); Analysis for $C_{17}H_{22}$calcd: C 90.20, H 9.80Found: C 90.12, H 9.85.

<u>Enantiomeric purity</u>: The enantioselectivity was determined by HPLC using chiral column, chiralcel AS-H, hexanes:i-PrOH/95:5; flow rate 0.5 mL/min, 254 nm, retention times: 13.4 min. (major) and 14.8 min. (minor).

(*R*)-3,3-Dimethyl-9-(3-phenylpropa-1,2-dien-1-yl)-2,4-dioxaspiro[5.5]undec-8-ene (65ac)



65ac

Yield : 0.219 g, 74%, 99% *ee*, yellow liquid.

[α]$_D$^{25} : [α]$_D$^{25} -132.1 (*c* 0.55, $CHCl_3$).

IR (neat) : 3059, 2951, 2868, 1937, 1624, 1469, 1391, 1107, 906cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.34-7.21 (m, 5H), 6.43 (d, *J*= 8.0Hz, 1H), 6.30 (d, *J* = 8.0 Hz, 1H), 5.64 (m, 1H), 3.63-3.59 (m, 2H), 3.51-3.48 (m, 2H), 2.52-2.48 (m, 2H), 2.25-1.90 (m, 4H), 1.07 (s, 3H), 0.92 (s, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 206.8, 134.4, 131.5, 128.6, 127.0, 126.8, 122.8, 100.5, 97.6, 97.2, 70.3, 35.7, 30.2, 26.8, 23.9, 22.8, 22.4.

LCMS : m/z 297 (M+1); Analysis for $C_{20}H_{24}O_2$calcd: C 81.04, H 8.16 Found: C 80.91, H 8.23.

<u>Enantiomeric purity</u>: The enantioselectivity was determined by HPLC using chiral column, chiralcel AS-H, hexanes:i-PrOH/95:5; flow rate 0.5 mL/min, 254 nm, retention times: 13.4 min. (major) and 14.8 min. (minor).

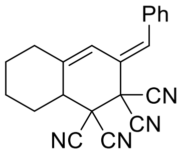
3.4.5 General procedure for (*E*)-3-benzylidene-6,7,8,8a-tetrahydronaphthalene-1,1,2,2(3H,5H)-tetracarbonitrile (76)

To a stirred solution of vinyl allene **65aa** (196 mg, 1.0 mmol) in DCM (3 mL) at 25 °C was slowly added tetracyanao ethylene (140 mg, 1.1mmol). The reaction mixture was allowed to warm to rt and was stirred for 6 h. Then it was diluted ethylacetate (5mL), poured water, and extracted with ethylacetate (4 × 15 mL). After drying (Na_2SO_4), concentration, and column chromatography (90:10 hexane/EtOAc), a compound **76** was obtained (0.243 mg, 75%) as orange oil.

Yield : 0.243 g, 75%, 89% *ee*.

$[\alpha]_D^{25}$: $[\alpha]_D^{25}$ -86.7 (*c* 0.50, $CHCl_3$).

IR (neat) : 3059, 2936, 2858, 2235, 1649, 1567, 1443, 1262, 1107, 906 cm^{-1}.



76

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.48-7.44 (m, 2H), 7.40-7.38 (m, 2H), 7.25 (m, 1H), 6.45 (s, 1H), 3.17 (t, *J* = 8.0 Hz, 1H), 2.56-2.45 (m, 2H), 2.28-1.79 (m, 3H), 1.74-1.32 (m, 4H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 139.9, 135.1, 133.3, 129.6; 129.0, 128.8, 121.0, 116.8, 111.1, 110.2, 109.7, 109.0, 46.9, 45.5, 43.8, 34.3, 29.7, 29.7, 25.5, 24.6.

LCMS : m/z 325 (M+1); Analysis for $C_{21}H_{16}N_4$calcd: C 77.76, H 4.97, N 17.27 Found: C 77.85, H 4.91, N 17.12.

Enantiomeric purity: The enantioselectivity was determined by HPLC using chiral column, chiralcel AS-H, hexanes:i-PrOH/95:5; flow rate 0.5 mL/min, 254 nm, retention times: 13.4 min. (major) and 14.8 min. (minor).

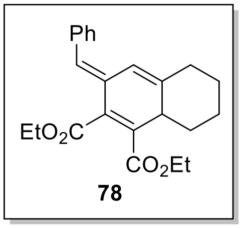
3.4.6 General procedure for (*E*)-diethyl 3-benzylidene-3,5,6,7,8,8a-hexahydronaphthalene-1,2-dicarboxylate (78)

To a stirred solution of vinyl allene **65aa** (196 mg, 1.0 mmol) in DCM (3 mL) at 25 °C was slowly added DEAD (0.175 mL, 1.1mmol). The reaction mixture was allowed to warm to rt and was stirred for 6 h. Then it was diluted ethylacetate(5mL), poured water, and extracted with ethylacetate (4 × 15 mL). After drying (Na_2SO_4), concentration, and column chromatography (85:15 hexane/EtOAc), a compound **78** was obtained (252 mg, 69%) as yellow oil.

Yield : 0.243 g, 69%, 81% *ee*.

[α]$_D^{25}$: [α]$_D^{25}$ -86.7 (*c* 0.50, $CHCl_3$).

IR (neat) : 3054, 2930, 1763, 1722, 1665, 1448, 1365, 1185, 1024 cm^{-1}.



78

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.39-7.34 (m, 4H), 7.29-7.27 (m, 1H), 6.58 (s, 1H), 6.40 (s, 1H), 4.40 (q, J = 8.0 Hz, 2H), 3.38 (t, J = 8.0 Hz, 3H), 2.37-2.10 (m, 4H), 1.94-1.60 (m, 4H), 1.40 (t, J = 8.0 Hz, 3H), 1.34 (t, J = 8.0 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 168.6, 166.1, 145.3, 140.1, 136.7, 130.9, 129.8, 129.2, 128.2, 127.7, 127.2, 115.1, 61.4, 61.0, 41.5, 35.7, 35.2, 28.9, 26.4, 14.1, 14.0.

LCMS : m/z 367 (M+1); Analysis for $C_{23}H_{26}O_4$calcd: C 75.38, H 7.15, Found: C 75.41, H 7.23.

Enantiomeric purity: The enantioselectivity was determined by HPLC using chiral column, chiralcel AS-H, hexanes:i-PrOH/95:5; flow rate 0.5 mL/min, 254 nm, retention times: 13.4 min. (major) and 14.8 min. (minor).

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Chapter 4

Nuleophilic Addition to Propargylamines to Access Highly Substituted Pyridines and Pyrrolizines

4.1 Introduction

Nucleophilic addition to acetylenes or internal alkynes has been well studied in organic synthesis. In recent years, nucleophiles such as hydroxyl, nitriles, amines and amides were effectively used in reactions with π-allyl intermediate prepared from alkynes by different metal complexes like palladium, mercury, rhodium, ruthenium and other metals with varying levels of reactivity (Figure 1).[1, 2]

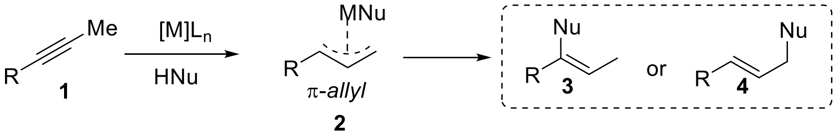


Figure 1. General metal catalysed addition to C-C triple bond

Alkynes also readily undergo electron transfer reaction. For example, internal alkynes can be reduced to *trans*-alkenes using Na in NH_3. This reaction proceeds *via* single electron transfer from Na with protonation by the NH_3 resulting in the formation of *trans*-olefins.[3]

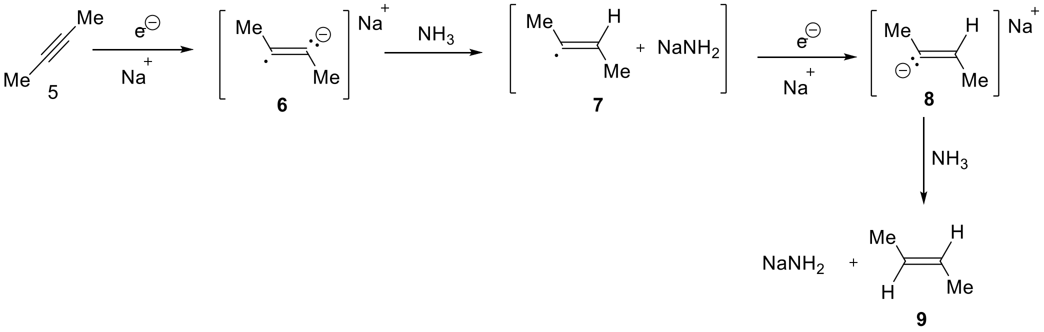


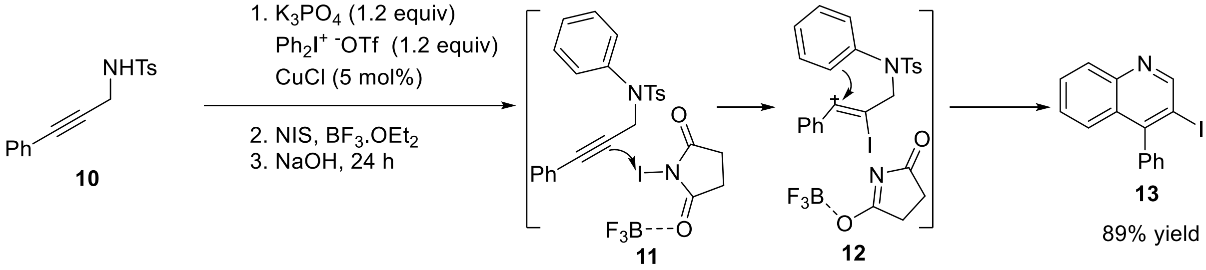
Figure 2. Catalytic hydrogenation of alkynes

Heterocyclic compounds have unequivocal importance in organic synthesis as these moieties are widely present in natural products, pharmaceuticals, and functional materials.[4,5] Hence, development of efficient methods for the synthesis of these compounds is of great value. In recent years, methods for the preparation of heterocyclic compounds using internal or terminal alkynes have been reported.[6] Therefore, it was of interest to us to develop methods for the prepartion of heterocyclic compounds using propargylamine derivatives. Hence, a brief review on the preparartion of substituted pyridines would facilitate the discussion.

4.1.1 Reaction using internal or terminal alkynes

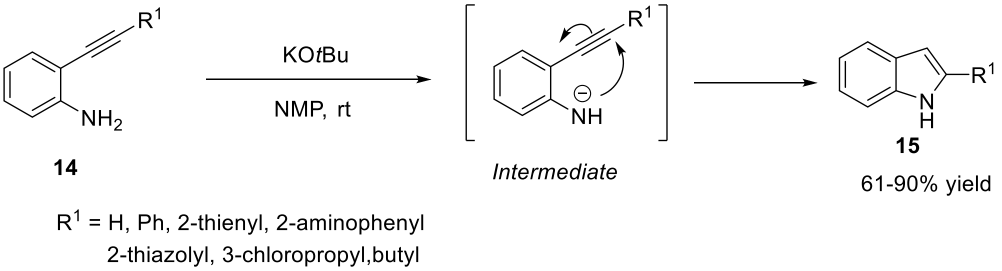
Togo *et. al*. reported that the 4-aryl- iodoquinolines were smoothly obtained in one pot by the reaction of N-tosyl 3- aryl-2-propynylamines with diaryliodonium triflate in the presence of K_3PO_4 and CuCl, followed by the reaction with NIS and $BF_3{\cdot}OEt_2$ (Scheme 1).[7]

Scheme 1



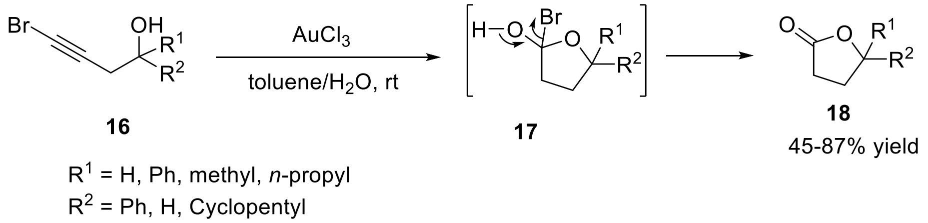
Knochel *et al.* reported[8] that hetero atom addition to internal alkyne leads to the formation of indoline derivative **15** *via* an intramolecular cyclization of **14** (Scheme 2).

Scheme 2



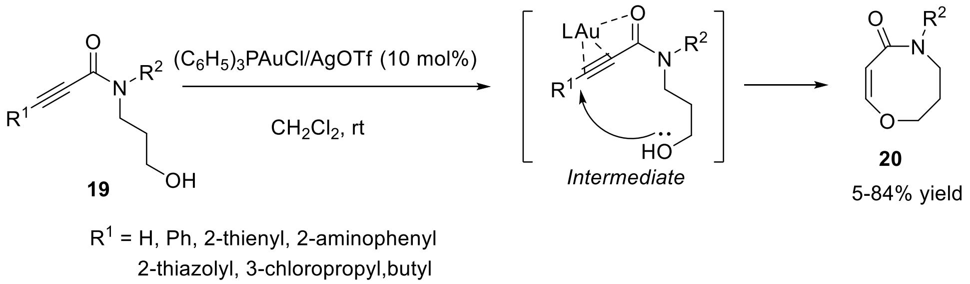
Reddy and coworkers reported[9] that 4-bromo-3-yn-ols **16** are easily converted to the corresponding butyrolactone products **18** upon reaction with $AuCl_3$ (Scheme 3).

Scheme 3



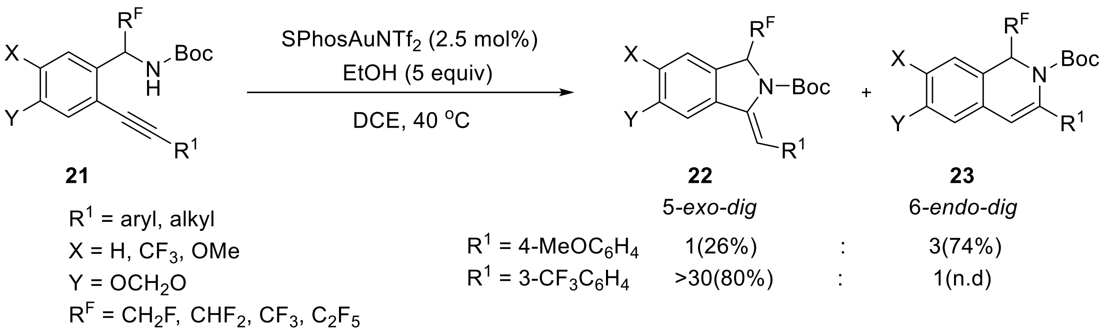
The gold (I)-catalyzed hydroalkoxylation of alkynamides **19** to oxazocenones **20** *via* 8-endo-dig cyclization was recently reported (Scheme 4).[10]

Scheme 4



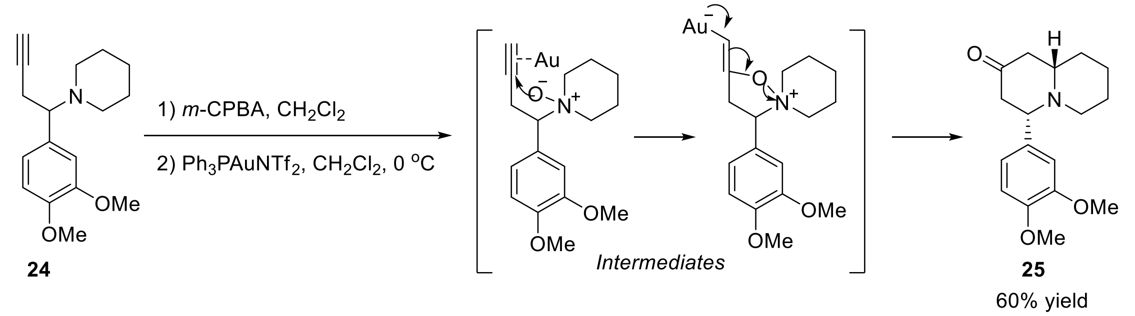
Gold catalyzed 6-endo-dig and 5-exo-dig cyclizations of amides were reported (Scheme 5).[11]

Scheme 5



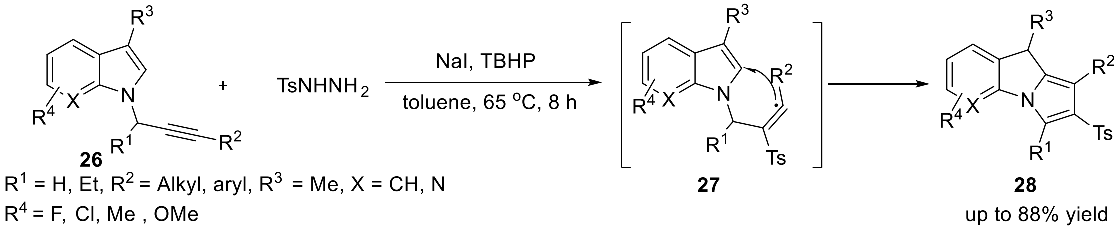
Intramolecular cyclization of **24** through the N-oxide formed *in situ* to the 4-piperidone **25** was reported (Scheme 6).[12]

Scheme 6



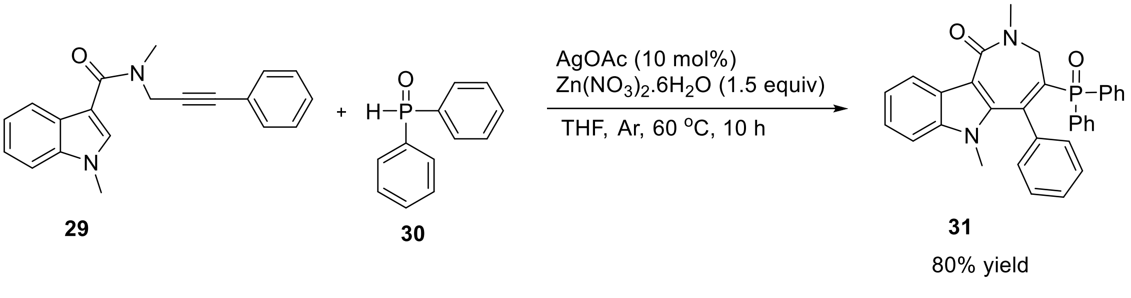
A new approach for the construction of various 2-sulfonated *9H*-pyrrolo[1,2-a]indoles **28** *via* sulfonylation-cyclization-isomerization of various *N*-propargyl substituted indoles **26** was reported (Scheme 7).[13]

Scheme 7



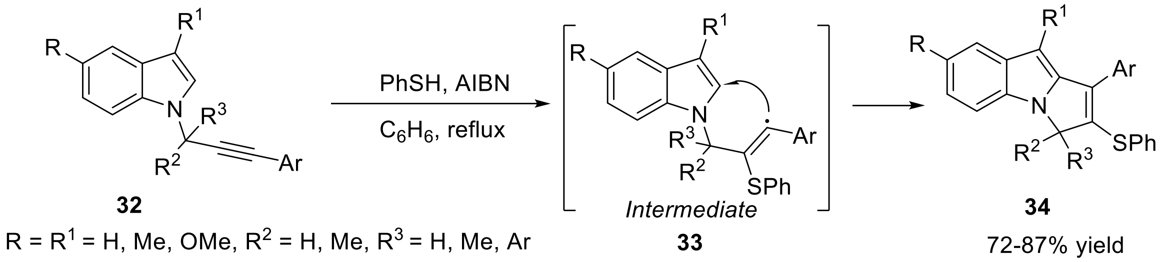
A silver-catalyzed oxidative cyclization of propargylamide substituted indoles to construct the seven membered phosphorated indoloazepinone derivatives was reported (Scheme 8).[14, 15, 16]

Scheme 8



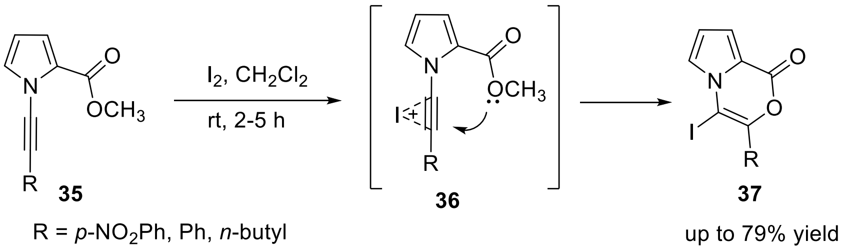
An efficient protocol for the synthesis of pyrrolo[1,2-a] indole derivatives **34** containing sulfide functionality by cascade radical cyclization on propargylindole **32** was reported (Scheme 9).[17]

Scheme 9



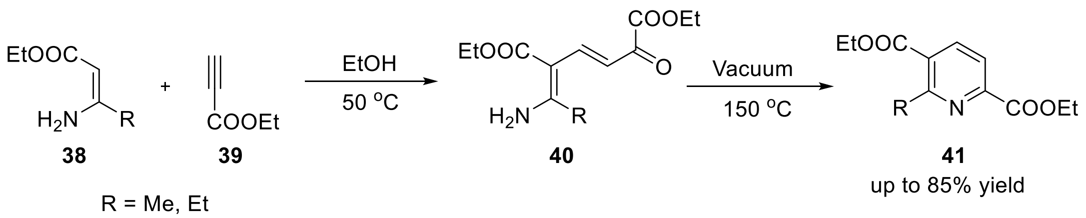
Intramolecular cyclization of N-alkyne-substituted methyl 1*H*-pyrrole-2-carboxylate derivatives **35** to the corresponding pyrrolooxazinone derivatives **37** in 76–79% yield using iodine in dichloromethane was reported (Scheme 10).[18]

Scheme 10

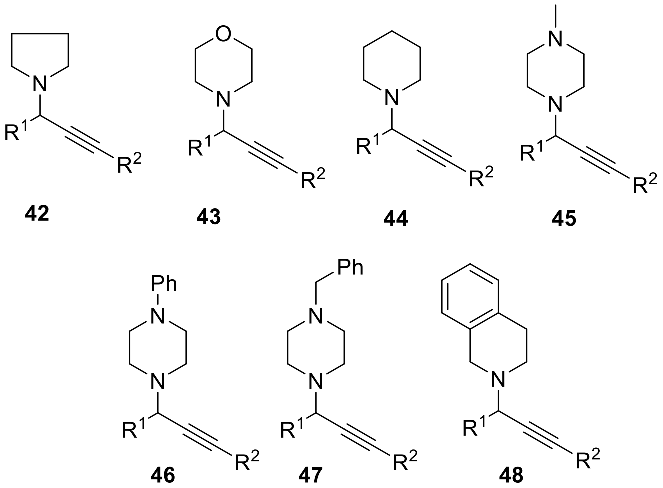


Synthesis of substituted pyridine derivative using amino alkenyl ester **38** and propiolate **39** was reported (Scheme 11).[19]

Scheme 11



It is of interest to us to examine the utility of the readily accessible propargylamine derivatives **42-48** prepared in this laboratory.[19]



42 **43** **44** **45**

46 **47** **48**

Figure 3. Various propargylamines derivatives

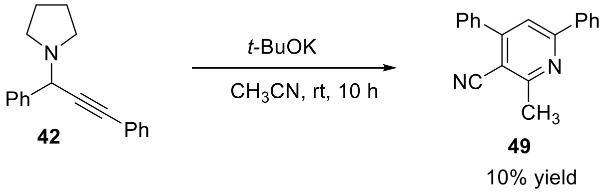
Results of studies on the reaction of *t*-BuOK with these propargylamines are described in the next section.

4.2 Results and Discussion

4.2.1 Reaction of highly substituted pyridine derivatives

Initially, we have carried out the reaction of the propargylamine derivative **42** (0.5 mmol) in acetonitrile (3 ml) solvent and *t*-BuOK (2 equiv) and isolated the pyridine derivative **49** in 10% yield (Scheme 12).

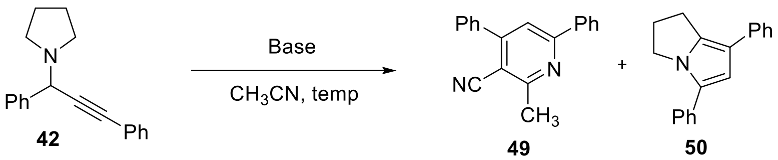
Scheme 12



The yield was poor but this finding is an interesting observation. Therefore, we have undertaken detailed studies. The results are summarized in Table 1.

We have observed that the substituted pyridine derivative **49** was obtained only in 15% yield when the reaction was carried out for 24 h (Table 1, entry 1). It was obtained in 50% yield at 80 ^{o}C for 15 h (Table 1, entry 2). Elevating the temperature to 90 ^{o}C further increased the yield to 65% but traces of pyrrolizine product **50** (2% yield) was also isolated (Table 1, entry 3). Increasing the time to 10-12 h at 90 ^{o}C resulted in slight increase in the yield of the pyridine product **49** (68%) besides the pyrrolizine product **50** (5%) (Table 1, entry 4). The pyridine derivative **49** was obtained in 60-65% yield besides the pyrrolizine product **50** in 5-7% yield when the reaction temperature was increased to 100 ^{o}C (Table 1, entries 5, 6). Also, the use of other bases like NaH, NaOH, and KOH gave the pyridine derivative **49** only in 5-15% yield (Table 1, entries 7-9). The weaker base K_2CO_3 and organic bases DBU and Et_3N did not give the pyridine derivative (Table 1, entries 10-12).

Table 1. Optimization of the reaction[a,b,c]

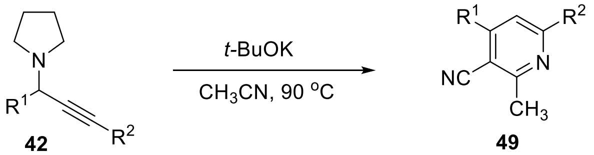


entry	base	temp (°C)	time (h)	yield of 49 (%)	yield of 50 (%)
1	*t*-BuOK	30	24	15	-
2	*t*-BuOK	80	15	50	-
3	*t*-BuOK	90	10	65	2
4	*t*-BuOK	90	12	68	5
5	*t*-BuOK	100	10	60	5
6	*t*-BuOK	100	15	65	7
7	NaH	100	24	10	-
8	NaOH	100	24	15	-
9	KOH	100	24	5	-
10	K_2CO_3	100	24	-	-
11	Et_3N	100	24	-	-
12	DBU	100	24	-	-

[a]The reactions were carried out by using propargylamine **42a** (0.3 mmol) and base (2.0 equiv). [b]The yields of pyridine derivative **49a**. [c]The yields of pyrrolizine derivative **50a**.

We have then performed the reaction using various propargylamine derivatives under these optimum conditions (Table 1, entry 4). The results are summarized in Table 2. The propargylamines **42b** and **42c** containing the electron donating group 4-Me-, and 4-OMe in the phenyl rings react with *t*-BuOK to give the pyridine derivative **49b** and **49c** in 71-72% yields (Table 2). The propargylamines **42d**, **42e**, and **42f** containing electron withdrawing groups 4-F-, 4-Cl-, and 4-Br- gave the corresponding pyridine derivative in 65-70% yields (**49d**, **49e**, and **49f**, Table 2). Also, the propargylamines **42g** and **42h** containing the furan and thiophene moieties afforded the substituted pyridine derivatives in 55% and 58% yields respectively (Table 2).

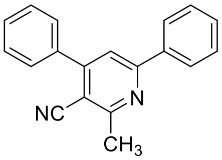
Table 2. The reaction of propargylamine derivatives with *t*-BuOK

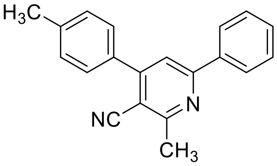


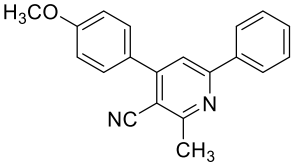
42 **49**

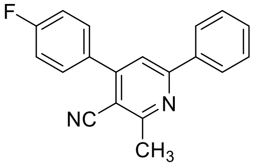
R^1
42a = Ph
42b = Ph-*p*CH_3
42c = Ph-*p*OCH_3
42d = Ph-*p*F
42e = Ph-*p*Cl
42f = Ph-*p*Br
42g = C_4H_3O
42h = C_4H_3S

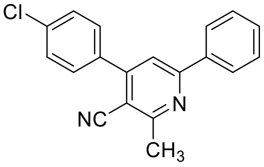
R^2
42i = Ph-*p*CH_3
42j = Ph-*n*-propyl
42k = Ph-*p*OCH_3
42l = Ph-*p*F

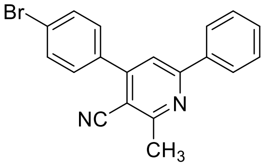

68% yield
49a

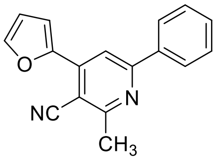

71% yield
49b

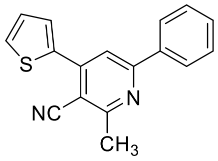

72% yield
49c

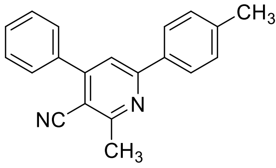

70% yield
49d

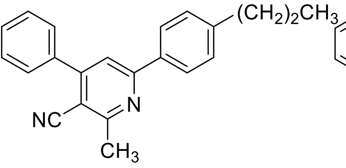

67% yield
49e

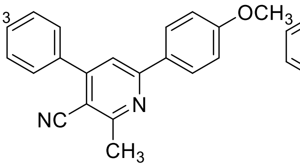

65% yield
49f

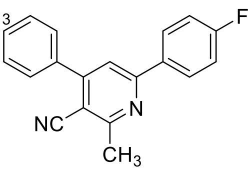

55% yield
49g


58% yield
49h


70% yield
49i


67% yield
49j


62% yield
49k

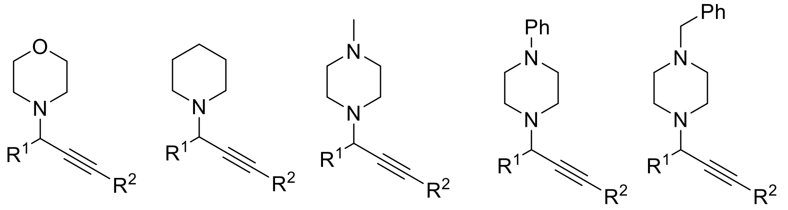

60% yield
49l

[a]The reactions were carried out by using propargylamine **42** (0.5 mmol) and base (2 equiv.) in acetonitrile (2 mL) at 120 °C for 10-15 h. [b]Yields of substituted pyridine derivatives **49**.

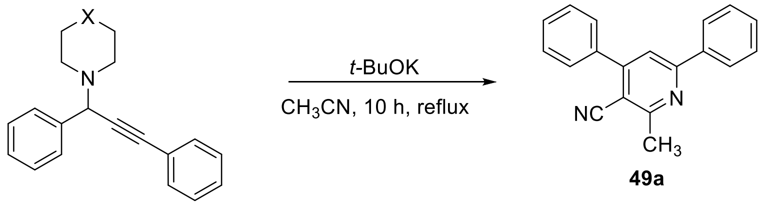
Similarly, the other propargylamines **42i**, **42j**, **42k** and **42l** react with *t*-BuOK to give the pyridine derivatives **49i**, **49j**, **49k** and **49l** in 60-70 yields (Table 2).

We have also carried out the reaction of *t*-BuOK with propargylamines containing morpholine, piperdine, N-methyl piperazine, N-phenyl piperazine and N-benzyl piperazine moieties. The corresponding terasubstituted pyridine **49** only in 15-35% yield in these cases (Scheme 13a).

Scheme 13a. The reaction of various propargylamine derivatives



43 **44** **45** **46** **47**



43-47

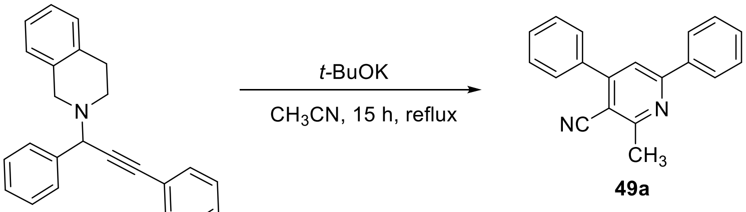
49a

up to 35% yield

Propargylamines	Yield of 49a
43	15%
44	35%
45	26%
46	29%
47	25%

Also, the propargylamine **48** also gave the tetrasubstituted pyridine **49** in 15% yield with some other unidentified products under these conditions (Scheme 13b).

Scheme 13b



48

49a

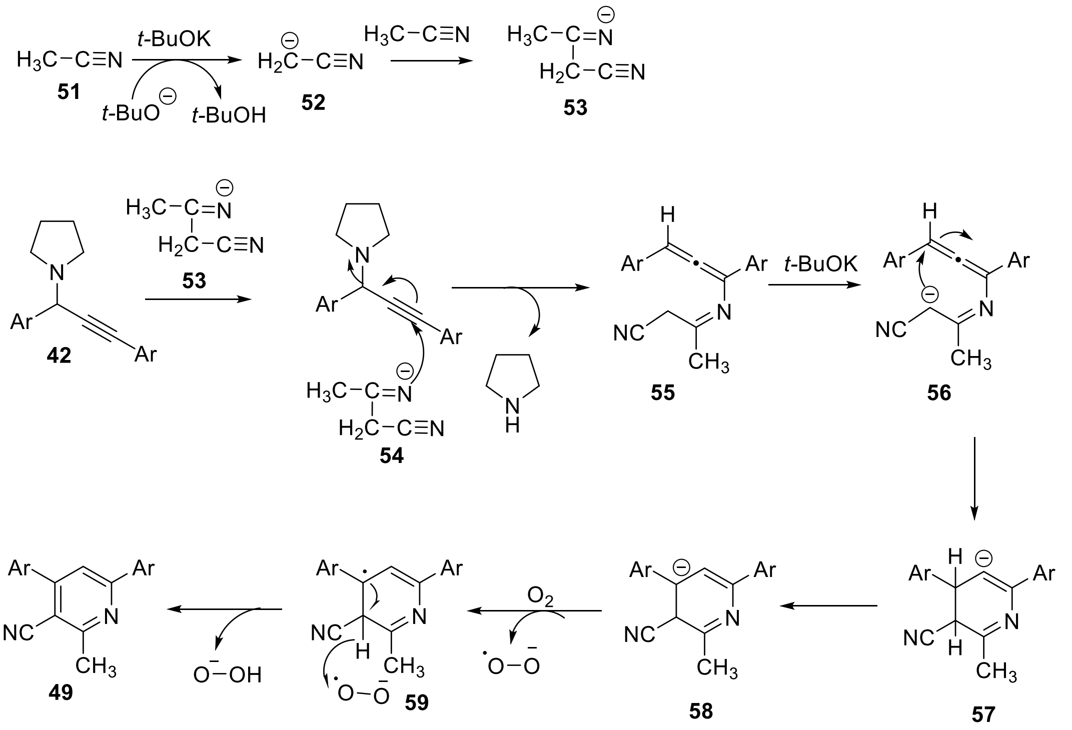
15% yield

The structure of the pyridine derivative **49a** was confirmed by the X-ray analysis as shown in Figure 4.

Figure 4. ORTEP representation of compound **49a** and thermal ellipsoids are drawn with 50% probability.

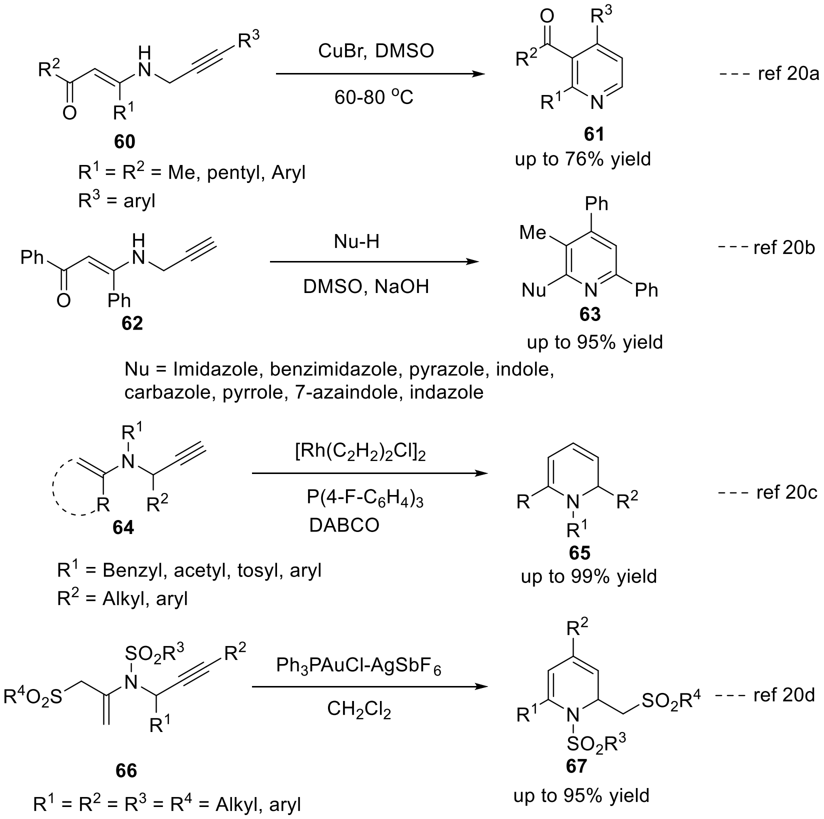
The formation of highly substituted pyridine derivatives from the propargylamine derivatives can be rationalized by tentative mechanism outlined in Scheme 14.[8, 13] Initially, the base could abstract the proton from the acetonitrile which could react with another equivalent of acetonitrile to give the intermediate **53**. Subsequent reaction of the intermediate **53** with propargylamine and elimination of pyrrolidine would lead to the intermediate **55** that could undergo intramolecular cyclization followed by the sequence of reactions with air could result in the formation of the highly substituted pyridine derivatives **49**.

Scheme 14. Proposed reaction mechanism for the tetrasubstituted pyridines



Previously, several methods were reported for the preparation of pyridine derivatives using compounds containing alkynyl moieties (Chart 1).[21]

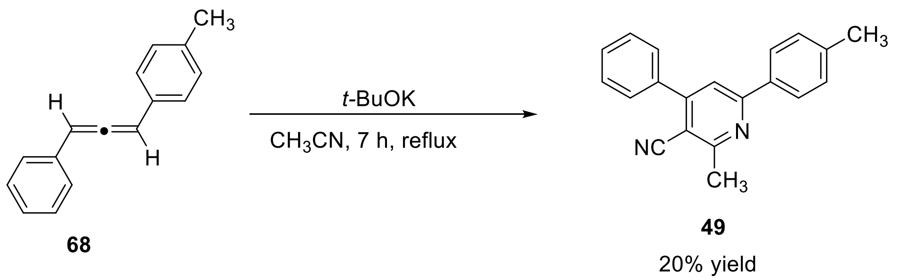
Chart 1



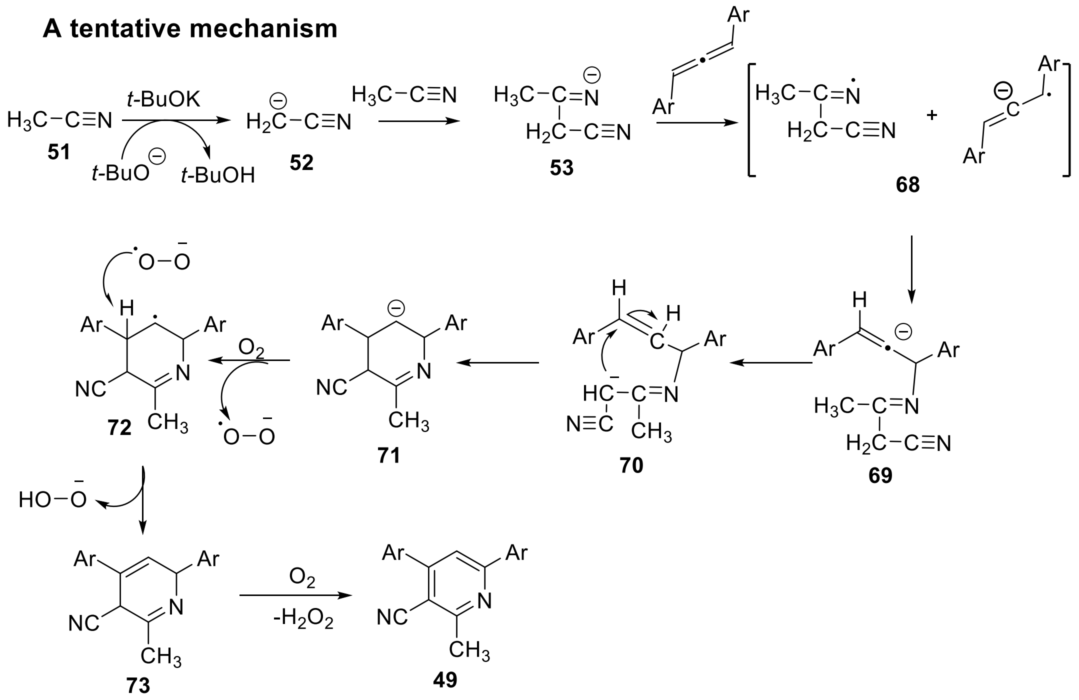
The methods described here by using the readily accessible propargylamines is a simple alternative to this pool of reported methods.

Interestingly, the reaction of 1,3-substituted allene **68** gave the highly substituted pyridine derivative **49** in 20% yield along with some unidentified products (Scheme 15). A similar mechanism may be considered involving addition of radical species produced *in situ* using acetonitrile.

Scheme 15. The reaction of allene and acetonitrile



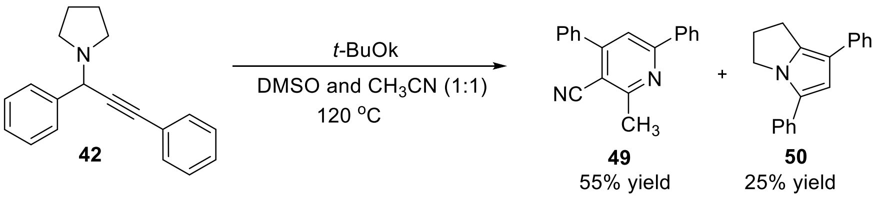
A tentative mechanism



4.2.2 Efforts toward the synthesis of pyrrolizine derivatives

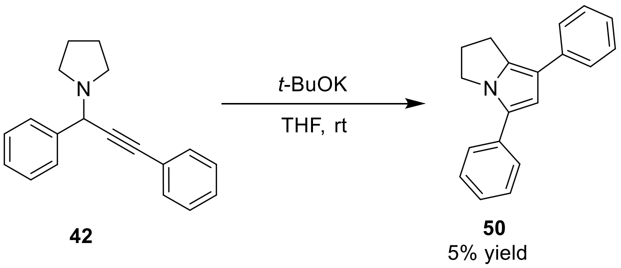
We have also examined the reaction of *t*-BuOK with propargylamine **42** in the 1:1 mixture of DMSO and acetonitrile (3 ml) at 120 °C (Scheme 16). Interestingly, in this reaction the tetrasubstituted pyridine **49** was obtained in 55% yield along with the pyrrolizine derivative **50** (Scheme 16).

Scheme 16. The reaction of propargylamine with DMSO and acetonitrile



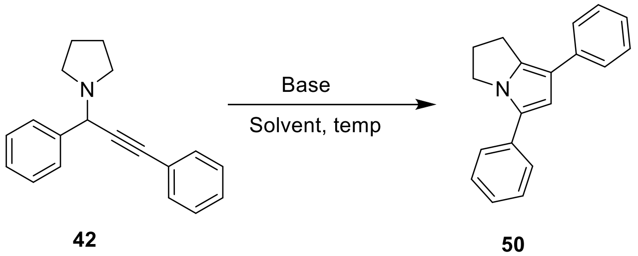
Hence, it was of interest to us to examine this reaction in different solvents. We have observed that the propargylamine derivative **42** and *t*-BuOk in THF solvent gave the pyrrolizine derivative **50** in 5% yield (Scheme 17).

Scheme 17. The reaction of propargylamine with *t*-BuOK



We have also carried out the reaction of propargylamine with other bases and solvents. The results are summarized in Table 3. Whereas the reaction of the propargylamine derivative **42** with *t*-BuOK in THF solvent at reflux condition gave the pyrrolizine derivative **50** in 12% yields (entry 1, Table 3). We have then carried out the reaction of propargylamine derivative **42** and ^{t}BuOK at various temperatures and different solvents to obtain the pyrrolizine derivative **50** in 5-15% yield (entry 2, 3, 4, 5, and 6, Table 3). After further investigation, it was found that in PhCN solvent the product **50** was obtained only in 10 % yield (entry 7, Table 3) but in propionitrile solvent, it was obtained in 67% yield (entry 8, Table 3). Further increasing the reaction temperature to 100 °C, gave the product **50** in 75% yield (entry 9, Table 3).

Table 3. Optimization of the reaction[a, b]



42 **50**

entry	base	solvents	temp (ºC)	time (h)	50 yield (%)
1	^{t}BuOK	THF	60	15	12
2	^{t}BuOK	toluene	120	15	15
3	^{t}BuOK	DCE	85	12	10
4	^{t}BuOK	DMSO	190	12	5
5	^{t}BuOK	DMF	155	12	>5
6	^{t}BuOK	acetone	60	12	-
7	^{t}BuOK	PhCN	100	15	10
8	^{t}BuOK	C_2H_5CN	90	12	67
9	^{t}BuOK	C_2H_5CN	100	12	75
10	NaH	C_2H_5CN	100	12	30
11	^{t}BuOLi	C_2H_5CN	100	12	50
12	K_2CO_3	C_2H_5CN	100	15	-
13	DBU	C_2H_5CN	100	24	-
14	Et_3N	C_2H_5CN	100	24	-
15	^{t}BuOK	NMP	30	5	46
16	^{t}BuOK	NMP	80	7	70
17	^{t}BuOK	NMP	100	5	72
18	^{t}BuOK	NMP	120	12	80
19	^{t}BuOK	NMP	150	12	85

[a]The reactions were carried out by propargylamine (0.5 mmol) and base (2 equiv.) in solvent (3mL) at 100 ºC. [b]Yields of pyrrolizine derivative **50**.

Also, other bases like NaH, ^{t}BuOLi, K_2CO_3, DBU and Et_3N in propionitrile solvent gave the corresponding product **50** in up to 50% yield (entries 10, 11, 12, 13 and 14, Table 3). We have also observed the product **50** in 46% yield in 5 h at room temperature when

NMP solvent was used and increasing the reaction time (5-12 h) at higher temperature gave the product **50** from 46% to 85% (entries 15, 16, and 17, 18 and 19, Table 3).

We have examined the substrate scope of this transformation using various trisubstituted propargylamine derivatives under optimum conditions (entry 19, Table 3). Propargylamines containing 4-Me-, and 3-OMe-substituted phenyl rings **42b**, and **42c** react with *t*-BuOK to give the corresponding pyrrolizine product **50b** and **50c** in 85% and 86% yields respectively (Table 4). Also, propargylamines containing with electron withdrawing substituents 4-F- and 4-Br- **42d** and **42e** resulted in the formation of pyrrolizine product **50d** and **50e** in 74% and 76% yields respectively. In addition, propargylamines **42f**, **42g** and **42h** containing furan, thiophene and anthracene moieties gave the corresponding pyrrolizine product **50f**, **50g** and **50h** in 70-78% yields (Table 4). Further, the propargylamines containing CH_3, *n*-propyl, OCH_3, and F groups on phenyl ring **42i**, **42j**, **42k**, and **42l** also gave the corresponding pyrrolizine products **50i**, **50j**, **50k**, and **50l** in 69-88% yields.

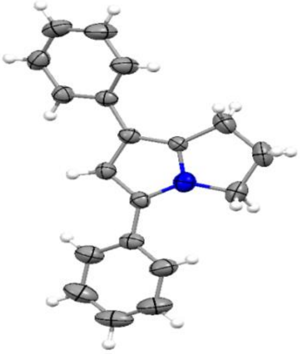
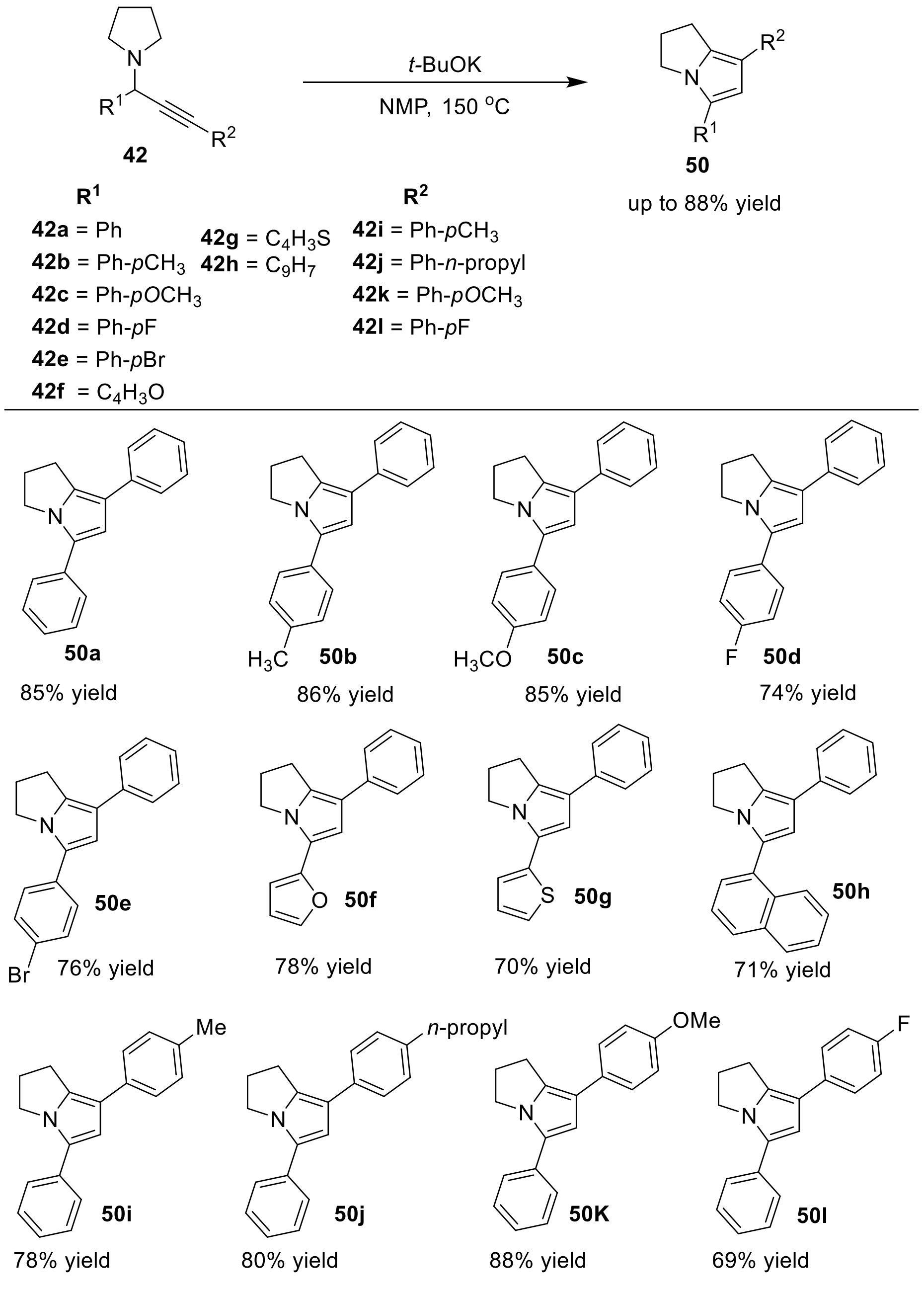


Figure 4. ORTEP representation of compound **50a** and thermal ellipsoids are drawn with 50% probability.

Table 4. The reaction of propargylamine derivatives with base[a,b]



[a]The reactions were carried out by propargylamine (1.0 equiv) and base (2.0 equiv) in NMP (3mL) at 150 °C for 12-15 h. [b]Yields of pyrrolizine derivatives.

We have also performed the epr experiments to understand the intermediates involved in this transformation (Figure 5). A weak epr signal (*g* value 2.0056) was observed when the trisubstituted propargylamine **42** and *t*-BuOK were mixed (Figure 5). The epr signal (*g* value

2.0061) was strong when NMP solvent was added to mixture. This indicates that the reaction undergoes *via* radiacal mechanism to give pyrrolizine product **50** in NMP solvent. The epr signal was not observed in propionitrile solvent.

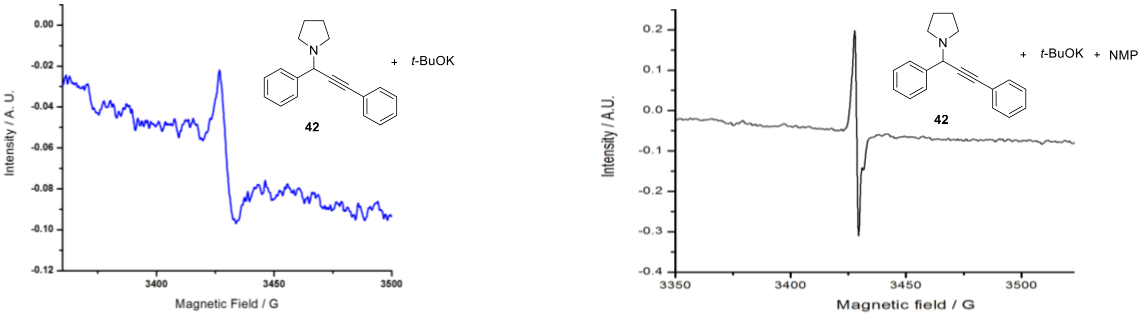
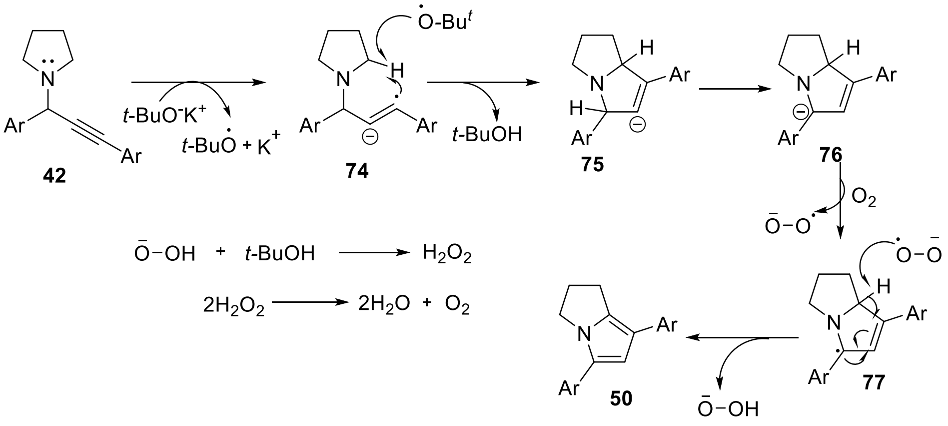


Figure 5. The paramagnetic intermediates in the reaction of propargylamine **50** with *t*-BuOK.

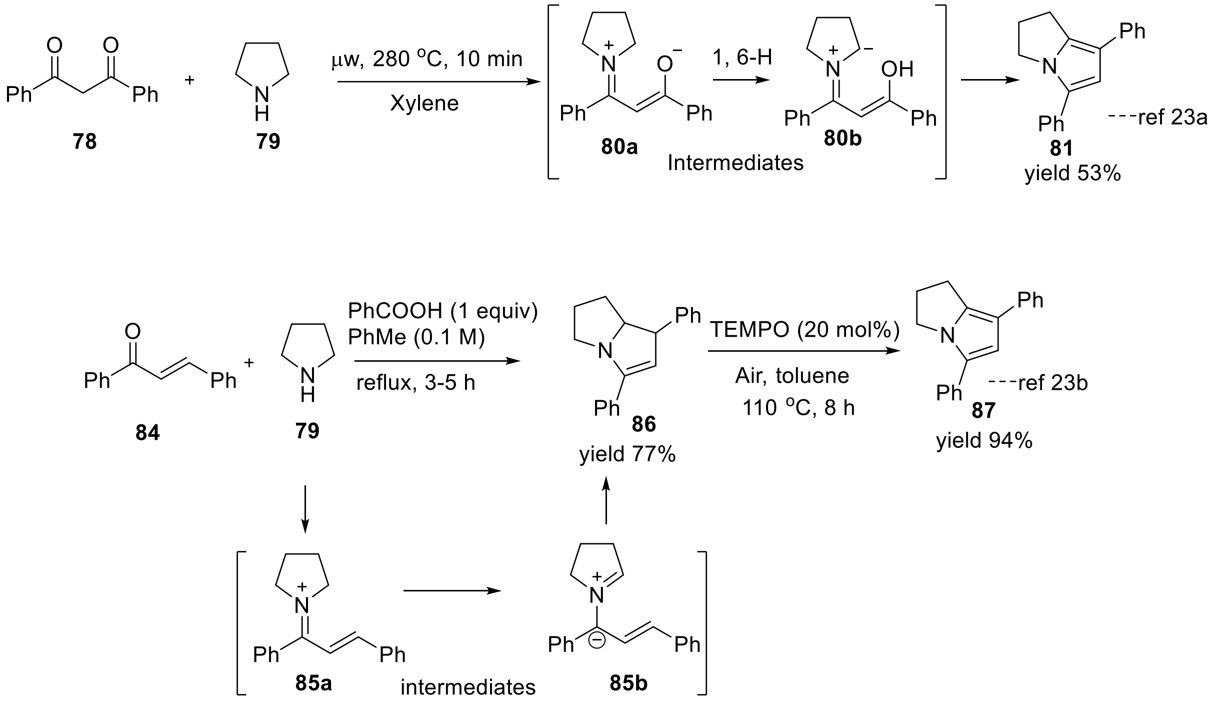
Propargylamine derivatives were used in radical reactions in recent years.[3, 14-18, 22] A tentative mechanism outlined in Scheme 18 for the reaction of propargylamine **42** with *t*-BuOK. Initially, the *t*-BuOK could react with the propargylamine **42** to give the radical anion intermediate **74** which could undergo abstraction of H atom from the pyrrolidine ring followed by cyclization to give the intermediate **75**. Subsequent, proton shift and aromatization involving atmospheric oxygen could result in the pyrrolizine derivative **50**.

Scheme 18. Proposed reaction mechanism



There were very few reports on the synthesis of pyrrolizine derivatives (Scheme 19).[23]

Scheme 19



These methods involve multistep operation using expensive reagents. Therefore, the method described here for the conversion of propargylamines to pyrrolizines has significant potential in organic synthesis.

We have also undertaken studies on the electron transfer reactions of amine donors for synthetic applications. The results are described in the next chapter.

4.3 Conclusions

In conclusion, we have developed an unprecedented base promoted synthesis of highly substituted pyridine derivatives using propargylamine derivatives in good yields. In addition, we have also developed a method for the intramolecular annulations of propargylamine to access the pyrrolizine derivatives through the formation of C-C bond *via* C-H functionalizations involving the radical intermediates. These methods should be helpful in designing methods to access potentially useful fused ring synthons for further synthetic exploitation.

4.4 Experimental Section

4.4.1 General information

Melting points were determined using a Superfit capillary point apparatus. IR (KBr) spectra were recorded on JASCO FT-IR spectrophotometer Model 5300. The neat IR spectra were recorded on JASCO FT-IR spectrophotometer Model 5300. ^{1}H-NMR (400 MHz), ^{13}C-NMR (100 MHz) spectra were recorded on Bruker-AC-200 and Bruker-Avance-400 spectrometers, respectively with chloroform-d as solvent and TMS as reference ($\delta = 0$ ppm). The chemical shifts are expressed in δ downfield from the signal of internal TMS. Liquid Chromatography (LC) and mass analysis (LC-MS) were performed on SHIMADZU-LCMS-2010A and BRUKER MARXIS High Resolution Mass Spectrometry (HRMS). The mass spectral analyses were carried out using Chemical Ionization (CI) or Electro Spray Ionization (ESI) techniques. Elemental analyses were carried out using a Perkin-Elmer elemental analyzer model-240C and Thermo Finnigan analyzer series Flash EA 1112. Mass spectral analyses for some of the compounds were carried out on VG 7070H mass spectrometer using EI technique at 70 eV.

Analytical grade of CuBr, Cu(OTf) and ZnI_2 were purchased from Sigma-Aldrich. $ZnBr_2$, $ZnCl_2$ was purchased from E-Merck. Toluene supplied by E-Merck, India was freshly distilled over sodium-benzophenone ketyl before use. Analytical thin layer chromatographic tests were carried out on glass plates (3 x 10 cm) coated with 250mμ E-Merck and acme's silica gel-G and GF_{254} containing 13% calcium sulfate as binder. The spots were visualized by short exposure to iodine vapour or UV light. Column chromatography was carried out using E-Merck and acme's silica gel (100-200 or 230-400 mesh) and neutral alumina.

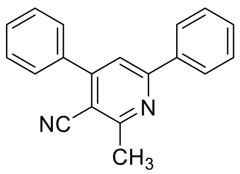
Optical rotations were measured on Rudolph Research Analytical AUTOPOL-II (readability ±0.01^{o}) and AUTOPOL-IV (readability ±0.001^{o}) automatic polarimeters. HPLC analyses were performed on an SCL-10ATVP SHIMADZU instrument.

4.4.2. General procedure for synthesis of pyridine derivatives

To a stirred solution of propargylamine **42** (0.5 mmol) in acetonitrile solvent (3 mL), and *t*-BuOK (2 equiv.) at 100 °C under the N_2 atmosphere, the reaction mixture was stirred for 12-15 h. The reaction mixture cooled to room temperature. Acetonitrile was removed using reduced pressure. Water (5 mL) and DCM (15 mL) were added. The DCM layer was washed with saturated NaCl solution, dried (Na_2SO_4) and concentrated. The residue was subjected to column chromatography using hexane and ethyl acetate (95:5) as eluent to isolate the pyridine **49**.

2-Methyl-4,6-diphenylnicotinonitrile (49a)

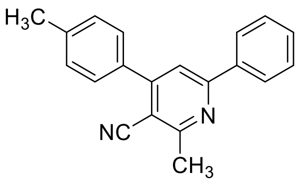
Yield	**:**	White solid; 0.091 g, 68% yield.
mp	**:**	118-119 °C
IR (neat)	**:**	2215, 1589, 1543, 1383, 819 cm^{-1}.
^{1}H NMR	**:**	(400 MHz, $CDCl_3$, δ ppm) 8.07-8.05 (m, 2H), 7.64-7.59 (m, 1H), 7.56-7.49 (m, 5H), 7.38-7.36 (m, 2H), 6.98-6.96 (m, 1H), 2.93 (s, 3H).
^{13}C NMR	**:**	(100 MHz, $CDCl_3$ δ ppm) 162.5, 159.0, 153.6, 140.9, 136.6, 134.9, 129.8, 129.7, 129.0, 128.2, 127.2, 117.5, 117.4, 24.3.
HRMS	:	(*m/z*): $[M+H]^+$ Calculated for $C_{19}H_{15}N_2$: 271.1236 Found: 271.1236.



49a

2-Methyl-6-phenyl-4-(p-tolyl)nicotinonitrile (49b)

Yield	**:**	White solid; 0.101 g, 71% yield.
mp	**:**	138-139 °C
IR (neat)	**:**	2217, 1585, 1523, 1380, 810 cm^{-1}.



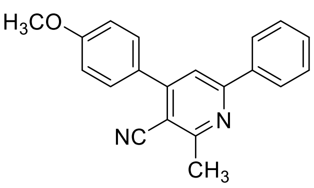
49b

^{1}H NMR : ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 8.10-8.09 (m, 2H), 7.65 (s, 1H), 7.58-7.52 (m, 5H), 7.39-7.37 (m, 2H), 2.94 (s, 3H), 2.47 (s, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 162.7, 159.1, 153.7, 140.7, 136.6, 134.9, 129.8, 129.7, 129.0, 128.4, 127.3, 117.5, 117.4, 24.6, 21.4.

HRMS : m/z : $[M+H]^+$ calcd for $C_{20}H_{17}N_2$: 285.1391 Found: 285.1390.

4-(4-Methoxyphenyl)-2-methyl-6-phenylnicotinonitrile (49c)



49c

Yield : White solid; 0.108 g, 72% yield.

mp : 157-158 °C

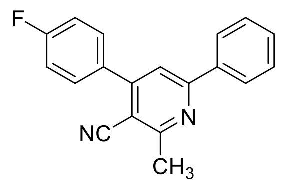
IR (neat) : 2216, 1587, 1539, 1236, 1033, 822 cm^{-1}.

^{1}H NMR : ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 8.09-8.02 (m, 2H), 7.65-7.62 (m, 3H), 7.56-7.54 (m, 3H), 7.04.7.02 (m, 2H), 3.90 (s, 3H), 2.91 (s, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 162.6, 161.5, 158.7, 153.6, 136.7, 130.2, 129.8, 128.9, 128.4, 117.5, 116.9, 114.3, 104.9, 55.4, 24.4.

HRMS : m/z : $[M+H]^+$ calcd for $C_{20}H_{17}N_2O$: 301.1341 Found: 301.1342.

4-(4-Fluorophenyl)-2-methyl-6-phenylnicotinonitrile (49d)



49d

Yield : White solid; 0.100 g, 70% yield.

mp : 172-173 °C

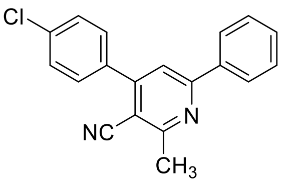
IR (neat) : 2216, 1587, 1539, 1236, 1033, 822 cm^{-1}.

^{1}H NMR : ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 8.13-8.09 (m, 2H), 7.66-7.64 (m, 3H), 7.57-7.55 (m, 3H), 7.23-7.18 (m, 2H), 2.93 (s, 3H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 165.5, 163.0, 162.8, 158.0, 154.0, 136.5, 133.9, 129.9, 129.5, 129.4, 128.4, 117.5, 116.0, 115.8, 105.8, 24.3.

HRMS : m/z : $[M+H]^+$ calcd for $C_{19}H_{14}FN_2$: 289.1141 Found: 289.1141.

4-(4-Chlorophenyl)-2-methyl-6-phenylnicotinonitrile (49e)



49e

Yield **:** White solid; 0.101 g, 67% yield.

mp **:** 177-178 ^{o}C

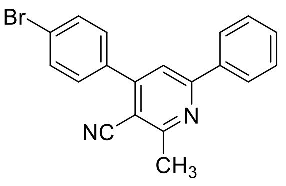
IR (neat) **:** 2215, 1583, 1538, 1095, 832 cm^{-1}.

^{1}H NMR **:** ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 8.11-8.09 (m, 2H), 7.70-7.65 (m, 1H), 7.59-7.55 (m, 2H), 7.54-7.50 (m, 5H), 2.95 (s, 3H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 162.8, 159.2, 153.8, 137.8, 136.5, 130.3, 129.9, 128.9, 128.4, 127.4, 117.9, 117.3, 105.8, 24.4.

HRMS : m/z : $[M+H]^+$ calcd for $C_{19}H_{14}FN_2$: 305.0845 Found: 305.0845.

4-(4-Bromophenyl)-2-methyl-6-phenylnicotinonitrile (49f)



49f

Yield **:** White solid; 0.118 g, 65% yield.

mp **:** 185-186 ^{o}C

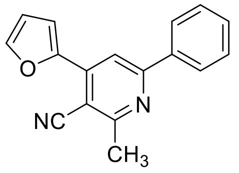
IR (neat) **:** 2214, 1583, 1538, 1248, 1037, 829 cm^{-1}.

^{1}H NMR **:** ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 8.12-8.07 (m, 2H), 7.71-7.67 (m, 1H), 7.56-7.53 (m, 2H), 7.53-7.49 (m, 5H), 2.94 (s, 3H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 162.5, 159.1, 153.3, 137.2, 136.9, 131.3, 129.8, 128.2, 128.1, 127.8, 117.5, 117.1, 105.2, 24.3.

HRMS : m/z : $[M+H]^+$ calcd for $C_{19}H_{14}BrN_2$: 349.0340 Found: 349.0340.

4-(Furan-2-yl)-2-methyl-6-phenylnicotinonitrile (49g)


49g

Yield : White solid; 0.071 g, 55% yield.

mp : 120-121 ^{o}C

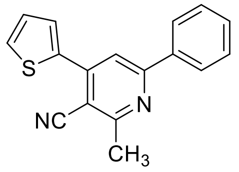
IR (neat) : 2221, 1650, 1578, 1532, 1235, 1120, 1032, 825 cm^{-1}.

^{1}H NMR : ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 7.66-7.62 (m, 3H), 7.59-7.55 (m, 3H), 7.32-7.20 (m, 2H), 6.62-6.61 (m, 1H), 2.89 (s, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 163.0, 153.8, 150.5, 146.3, 144.8, 136.3, 129.9, 128.9, 128.4, 117.2, 115.7, 112.6, 105.9, 99.9, 24.3.

HRMS : m/z : $[M+H]^+$ calcd for $C_{17}H_{13}N_2O$: 261.1028 Found: 261.1027.

2-Methyl-6-phenyl-4-(thiophen-2-yl)nicotinonitrile (49h)


49h

Yield : White solid; 0.080 g, 58% yield.

mp : 133-134 ^{o}C

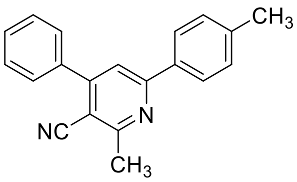
IR (neat) : 2215, 1653, 1575, 1530, 1242, 1135, 1041, 850 cm^{-1}.

^{1}H NMR : ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 8.11-8.09 (m, 2H), 7.65 (s, 1H), 7.58-7.51 (m, 5H), 7.39-7.37 (m, 2H), 2.94 (s, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 163.0, 154.1, 153.7, 143.4, 136.4, 133.5, 131.8, 130.0, 129.9, 129.0, 128.4, 128.3, 126.9, 117.2, 116.0, 105.2, 24.2.

HRMS : m/z : $[M+H]^+$ calcd for $C_{17}H_{13}N_2S$: 277.0799 Found: 277.0795.

2-Methyl-4-phenyl-6-(p-tolyl)nicotinonitrile (49i)



49i

Yield : White solid; 0.099 g, 70% yield.

mp : 138-139 ^{o}C

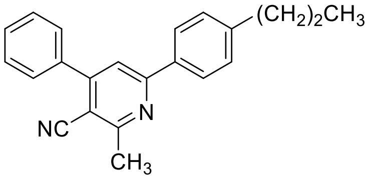
IR (neat) : 2215, 1589, 1543, 1383, 819 cm^{-1}.

^{1}H NMR : ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 8.10-8.06 (m, 2H), 7.64 (s, 1H), 7.58-7.52 (m, 5H), 7.39-7.37 (m, 2H), 2.93 (s, 3H), 2.47 (s, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 162.7, 159.1, 153.9, 140.1, 137.9, 130.2, 129.7, 128.9, 128.3, 127.4, 117.8, 105.7, 24.4, 21.3.

HRMS : m/z : $[M+H]^+$ calcd for $C_{20}H_{17}N_2$: 285.1391 Found: 285.1391.

2-Methyl-4-phenyl-6-(4-propylphenyl)nicotinonitrile (49j)



49j

Yield : White solid; 0.104 g, 67% yield.

mp : 138-139 ^{o}C

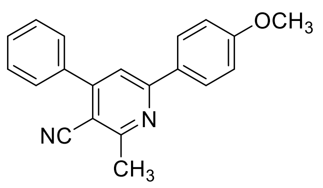
IR (neat) : 2215, 1553, 1523, 1340, 820 cm^{-1}.

^{1}H NMR : ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 8.13-8.11 (m, 2H), 7.71 (s, 1H), 7.62-7.52 (m, 5H), 7.40-7.38 (m, 2H), 2.95 (s, 3H), 2.72 (t, *J* = 4.0 Hz, 2H), 1.78-1.73 (m, 2H), 1.06-1.02 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 162.7, 159.1, 153.8, 144.9, 137.9, 133.9, 130.2, 129.1, 128.9, 128.8, 128.7, 128.3, 127.9, 127.4, 117.8, 117.4, 105.7, 37.8, 24.4, 13.9, 13.7.

HRMS : m/z : $[M+H]^+$ calcd for $C_{22}H_{21}N_2$: 313.1704 Found: 313.1704.

6-(4-Methoxyphenyl)-2-methyl-4-phenylnicotinonitrile (49k)



49k

Yield : White solid; 0.093 g, 62% yield.

mp : 150-151 °C

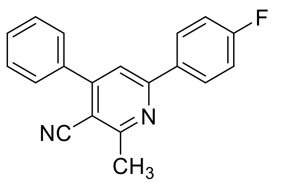
IR (neat) : 2218, 1565, 1525, 1423, 1020, 810 cm^{-1}.

^{1}H NMR : ^{1}H NMR (400 MHz, CDCl$_3$, δ ppm) 8.09-8.07 (m, 2H), 7.65-7.55 (m, 6H), 7.04-7.02 (m, 2H), 3.89 (s, 3H), 2.91 (s, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 162.6, 161.5, 158.7, 153.6, 136.7, 130.2, 129.8, 128.9, 128.4, 117.5, 116.9, 114.3, 104.9, 55.4, 24.4.

HRMS : m/z : [M+H]$^+$ calcd for $C_{20}H_{17}N_2O$: 301.1341 Found: 301.1342.

6-(4-Fluorophenyl)-2-methyl-4-phenylnicotinonitrile (49l)



49l

Yield : White solid; 0.086 g, 60% yield.

mp : 145-146 °C

IR (neat) : 2216, 1586, 1535, 1236, 822 cm^{-1}.

^{1}H NMR : ^{1}H NMR (400 MHz, CDCl$_3$, δ ppm) 8.13-8.10 (m, 2H), 7.65-7.63 (m, 3H), 7.57-7.53 (m, 3H), 7.23-7.18 (m, 2H), 2.93 (s, 3H).

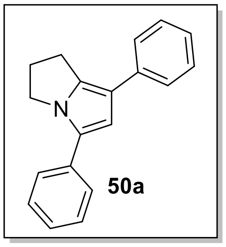
^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 165.5, 163.0 162.8, 158.0, 153.9, 136.5, 133.9, 129.9, 129.4, 129.0, 128.4, 117.5, 116.0, 115.8, 105.8, 24.3.

HRMS : m/z : [M+H]$^+$ calcd for $C_{19}H_{14}FN_2$: 289.1141 Found: 289.1141.

4.4.3. General procedure for synthesis of pyrrolizine derivatives

To a stirred solution of propargylamine **42** (1 mmol) in NMP solvent (3 mL), and *t*-BuOK (2 equiv.) at 120 °C under the N_2 atmosphere, the reaction mixture was stirred for 12-15 h. The reaction mixture cooled to room temperature. Water (5 mL) and DCM (15 mL) were added. The DCM layer was washed with saturated NaCl solution, dried (Na_2SO_4) and concentrated. The residue was subjected to column chromatography using hexane and ethyl acetate (95:5) as eluent to isolate the pyrrolizine **50**.

5, 7-Diphenyl-2,3-dihydro-1H-pyrrolizine (50a)



50a

Yield : White solid; 0.220 g, 85% yield.

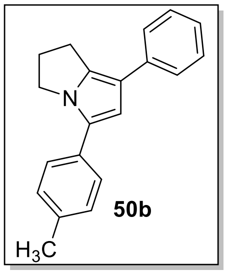
IR (neat) : 3096, 3051, 3024, 2986, 2954, 2899, 1948, 1871, 1740, 1601, 1531, 1493, 1383, 1367, 1295, 1092, 773 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$ δ ppm) 7.60-7.57 (m, 4H), 7.46-7.44 (m, 4H), 7.42-7.40 (m, 1H), 7.31-7.21 (m, 1H), 6.79 (s, 1H), 4.21-4.18 (t, *J* = 8.0 Hz, 2H), 3.19-3.15 (t, *J* = 8.0 Hz, 2H), 2.64-2.60 (m, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm) 136.3, 136.0, 133.4, 129.3, 128.7, 128.6, 128.5, 125.9, 125.8, 125.2, 124.7, 116.1, 108.6, 46.6, 27.9, 25.3.

HRMS : *m/z*: [M+H] Calculated for $C_{19}H_{18}N$: 260.1440; Found: 260.1440.

7-Phenyl-5-(p-tolyl)-2,3-dihydro-1H-pyrrolizine (50b)



50b

Yield : White solid, 0.234 g, 86% yield.

IR (neat) : 2959, 2910, 2885, 2704, 1630, 1492, 1739, 1445, 1357, 1253, 1025, 851, 741, 773, 695 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.58-7.56 (m, 2H), 7.47-7.45 (m, 2H), 7.42.7.39 (m, 2H), 7.25-7.24 (m, 2H), 7.21-7.18 (m, 1H), 6.73 (s, 1H), 4.19-4.16 (t, *J* = 8.0 Hz, 2H), 3.18-3.15 (t, *J* = 8.0 Hz, 2H), 2.63-2.60 (m, 2H), 2.43 (s, 3H).

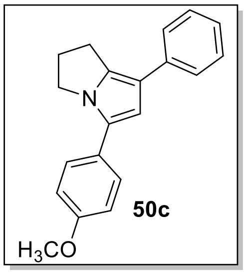
^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm) 136.4, 135.6, 130.6, 129.4, 128.6, 125.8, 125.1, 124.6, 116.0, 108.2, 46.5, 27.9, 25.3, 21.1.

HRMS : (*m/z*): (M+H) Calculated for $C_{20}H_{20}N$: 274.1596, Found: 274.1596.

5-(4-Methoxyphenyl)-7-phenyl-2,3-dihydro-1H-pyrrolizine (50c)

Yield : White solid; 85% yield.

IR (neat) : 2965, 2830, 2752, 2714, 1660, 1609, 1509, 1493, 1445, 1357, 1245, 1173, 1105, 1030, 890, 763 cm^{-1}.



50c

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.56-7.55 (m, 2H), 7.48-7.46 (m, 4H), 7.41-7.37 (m, 1H), 7.320.7.16 (m, 2H), 6.96 (s, 1H), 4.16-4.12 (t, *J* = 6.0 Hz, 2H), 3.87 (s, 3H), 3.17-3.14 (t, *J* = 5.0 Hz, 2H), 2.63-2.59 (m, 2H).

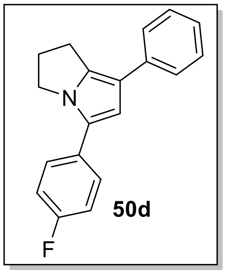
^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm) 136.4, 135.1, 129.2, 128.5, 127.2, 126.2, 125.1, 124.6, 115.8, 114.1, 107.6, 55.3, 46.4, 27.9, 25.4.

HRMS : (*m/z*): (M+H) Calculated for $C_{20}H_{20}NO$: 290.1546 Found: 290.1546.

5-(4-Fluorophenyl)-7-phenyl-2,3-dihydro-1H-pyrrolizine (50d)

Yield : White solid; 0.204 g, 74% yield.

IR (neat) : 3058, 2960, 2872, 2793, 1950, 1890, 1739, 1660, 1601, 1493, 1450, 1338, 1287, 1155,



50d

1025, 832, 665 cm^{-1}.

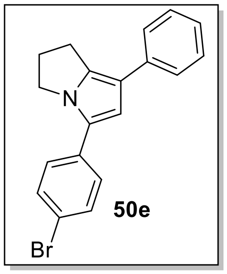
^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.53-7.51 (m, 2H), 7.49-7.47 (m, 2H), 7.39-7.37 (m, 2H), 7.15-7.12 (m, 1H), 7.09-7.07 (m, 2H), 6.68 (s, 1H), 4.16-4.13 (t, *J* = 6.0 Hz, 2H), 3.17-3.14 (t, *J* = 6.0 Hz, 2H), 2.64-2.63 (m, 2H).

^{13}C NMR : (100 MHz, CDCl$_3$ δ ppm) 161.8, 159.4, 135.5, 133.2, 132.4, 129.3, 128.7, 126.5, 126.4, 126.0, 125.8, 115.4, 115.2, 108.4, 46.6, 27.9, 25.2.

HRMS : (*m/z*): (M+H) Calculated for $C_{19}H_{17}FN$: 278.1346 Found: 278.1346.

5-(4-Bromophenyl)-7-phenyl-2,3-dihydro-1H-pyrrolizine (50e)

Yield : White solid; 0.256 g, 76% yield.



50e

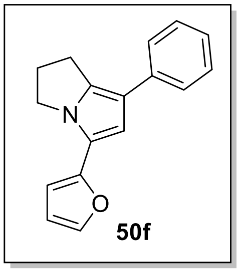
IR (neat) : 3058, 2951, 2870, 2791, 2760, 2704, 1954, 1891, 1739, 1670, 1601, 1505, 1443, 1348, 1223, 1094, 980, 919, 830, 763, 692 cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.68-7.67 (m, 1H), 7.55-7.52 (m, 2H), 7.46-7.35 (m, 4H), 7.27-7.19 (m, 2H), 6.76-6.75 (m, 1H), 4.21-4.17 (m, 2H), 3.18-3.14 (m, 2H), 2.65-2.62 (m, 2H).

^{13}C NMR : (100 MHz, CDCl$_3$ δppm) 136.7, 130.2, 128.6, 128.3, 125.7, 125.1, 124.9, 124.0, 109.4, 46.7, 27.8, 25.3.

HRMS : (*m/z*): (M+H) Calculated for $C_{19}H_{17}BrN$: 338.0548 Found: 338.0548.

5-(Furan-2-yl)-7-phenyl-2,3-dihydro-1H-pyrrolizine (50f)



50f

Yield : White solid; 0.194 g, 78% yield.

IR (neat) : 2951, 2874, 2793, 2762, 2704, 1739, 1660, 1601, 1531, 1493, 1450, 1338, 1367, 996, 773 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.53-7.50 (m, 2H), 7.40-7.34 (m, 3H), 7.18-7.14 (m, 1H), 6.78 (s, 1H), 6.46-6.45 (m, 1H), 6.34-6.33 (m, 1H), 4.22-4.18 (t, *J* = 8.0 Hz, 2H), 3.15-3.11 (t, *J* = 8.0 Hz, 2H), 2.65-2.62 (m, 2H).

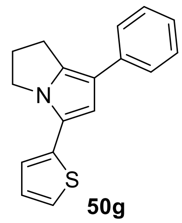
^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm) 148.3, 140.3, 136.1, 135.2, 128.5, 125.1, 124.7, 120.5, 115.9, 111.2, 107.5, 102.5, 46.5, 27.5, 25.2.

HRMS : (*m/z*): (M+H) Calculated for $C_{17}H_{16}NO$: 250.1233 Found: 250.1233.

7-Phenyl-5-(thiophen-2-yl)-2,3-dihydro-1H-pyrrolizine (50g)

Yield : White solid; 0.185 g, 70% yield.

IR (neat) : 3052, 2950, 2864, 2783, 2752, 2701, 1722, 1665, 1606, 1523, 1495, 1455, 1328, 1310, 1120, 920, 765 cm^{-1}.



50g

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.52-7.50 (m, 2H), 7.38-7.35 (m, 2H), 7.19-7.17 (m, 2H), 7.08-7.05 (m, 2H), 6.74 (s, 1H), 4.20-4.17 (t, *J* = 8.0 Hz, 2H), 3.16-3.13 (t, *J* = 8.0 Hz, 2H), 2.65-2.62 (m, 2H).

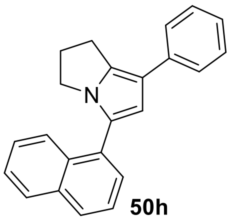
^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm) 136.0, 135.9, 135.4, 128.5, 127.5, 125.1, 124.7, 123.1, 122.5, 121.5, 116.1, 108.9, 46.3, 27.5, 25.4.

HRMS : (*m/z*): (M+H) Calculated for $C_{17}H_{16}NS$: 266.1004 Found: 266.1004.

5-(Naphthalen-1-yl)-7-phenyl-2,3-dihydro-1H-pyrrolizine (50h)

Yield : White solid; 0.219 g, 71% yield.

IR (neat) : 3052, 2951, 2872, 2793, 1739, 1669, 1596, 1531, 1492, 1450, 1359, 1367, 1263, 1251, 1091, 739 cm^{-1}.



50h

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 8.23-8.21 (m, 1H), 7.96-7.88 (m, 2H), 7.65-7.58 (m, 6H), 7.45-7.41 (m, 2H), 7.23-7.21 (m, 1H), 6.78 (s, 1H), 3.90-3.88 (t, *J* = 4.0 Hz, 2H), 3.27-3.24 (t, *J* = 4.0 Hz, 2H), 2.62-2.59 (m, 2H).

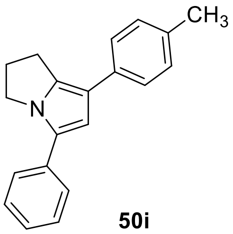
^{13}C NMR : (100 MHz, CDCl$_3$ δ ppm) 136.5, 134.9, 133.9, 132.1, 131.2, 128.6, 127.2, 126.2, 125.9, 125.3, 125.1, 124.6, 115.7, 111.3, 46.6, 27.7, 25.8.

HRMS : (*m/z*): (M+H) Calculated for $C_{23}H_{20}N$: 310.1596 Found: 310.1596.

5-Phenyl-7-(p-tolyl)-2,3-dihydro-1H-pyrrolizine (50i)

Yield : White solid; 0.212 g, 78% yield.

IR (neat) : 2958, 2911, 2884, 2702, 1630, 1492, 1739, 1443, 1358, 1253, 1025, 851, 741, 773, 695 cm^{-1}.



50i

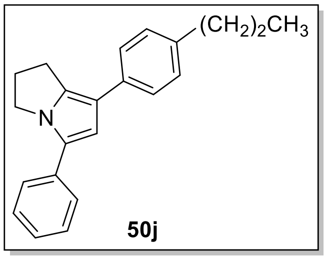
^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.57-7.55 (m, 2H), 7.47-7.42 (m, 4H), 7.27-7.21 (m, 3H), 6.74 (s, 1H), 4.22-4.18 (t, *J* = 4.0 Hz, 2H), 3.17-3.14 (t, *J* = 4.0 Hz, 2H), 2.66-2.59 (m, 2H), 2.40 (s, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$ δ ppm) 135.6, 134.2, 133.4, 129.3, 129.1, 128.6, 125.8, 125.7, 125.1, 116.1, 108.6, 46.6, 27.9, 25.2, 21.1.

HRMS : (*m/z*): (M+H) Calculated for $C_{20}H_{20}N$: 274.1596 Found: 274.1596.

5-Phenyl-7-(4-propylphenyl)-2,3-dihydro-1H-pyrrolizine (50j)

Yield : White solid; 0.240 g, 80% yield.



50j

IR (neat) : 2968, 2921, 2874, 2790, 2702, 1631, 1495, 1749, 1423, 1338, 1253, 1025, 891, 721, 763, 655 cm^{-1}.

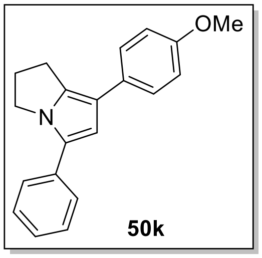
^{1}H NMR : (400 MHz, CDCl$_{3,}$ δ ppm) 7.57-7.53 (m, 2H), 7.47-7.41 (m, 4H), 7.21-7.19 (m, 3H), 6.73 (s, 1H), 4.21-4.17 (t, *J* = 4.0 Hz, 2H), 3.15-3.13 (t, *J* = 4.0 Hz, 2H), 2.64-2.60 (m, 4H), 1.72-1.67 (m, 2H) 1.02-0.98 (t, *J* = 6.0 Hz, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$ δ ppm) 139.0, 135.6, 133.7, 133.4, 129.1, 128.9, 128.6, 125.7, 125.0, 116.1, 108.6, 46.6, 37.7, 27.9, 25.2, 24.6, 13.9.

HRMS : (*m/z*): (M+H) Calculated for $C_{22}H_{24}N$: 302.1909 Found: 302.1909.

7-(4-Methoxyphenyl)-5-phenyl-2,3-dihydro-1H-pyrrolizine (50k)

Yield : White solid; 0.254 g, 88% yield.



50k

IR (neat) : 2962, 2830, 2753, 2714, 1660, 1619, 1508, 1494, 1445, 1359, 1245, 1173, 1105, 1030, 893, 761, 665 cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_{3,}$ δppm) 7.57-7.41 (m, 6H), 7.27-7.26 (m, 1H), 6.98-6.96 (m, 2H), 6.71 (s, 1H), 4.22-4.20 (t, *J* = 4.0 Hz, 2H), 3.88-3.84 (m, 3H), 3.16-3.14 (m, 2H), 2.66-2.63 (m, 2H).

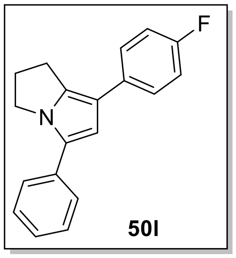
^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm) 157.1, 135.1, 133.4, 129.1, 128.6, 128.0, 126.3, 125.8, 114.0, 113.9, 108.4, 55.3, 46.6, 28.0, 25.1.

HRMS : (*m/z*): (M+H) Calculated for $C_{20}H_{20}NO$: 290.1546 Found: 290.1546.

7-(4-Fluorophenyl)-5-phenyl-2,3-dihydro-1H-pyrrolizine (50l)

Yield : White solid; 0.191 g, 69% yield.

IR (neat) : 3052, 2959, 2870, 2783, 1952, 1894, 1737, 1669, 1603, 1493, 1451, 1338, 1287, 1156, 1020, 822, 663 cm^{-1}.



50l

^{1}H NMR : (400 MHz, $CDCl_{3,}$ δ ppm) 7.54-7.39 (m, 6H), 7.30-7.26 (m, 1H), 7.09-7.05 (m, 1H), 6.68 (s, 1H), 4.21-4.18 (t, *J* = 6.0 Hz, 2H), 3.15-3.11(t, *J* = 6.0 Hz, 2H), 2.65-2.61 (m, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm) 161.6, 159.6, 135.4, 133.2, 132.5, 132.4, 129.4, 128.6, 128.0, 126.5, 126.4, 126.0, 125.7, 115.4, 115.2, 115.2, 108.5, 46.6, 27.9, 25.2.

HRMS : (*m/z*): (M+H) Calculated for $C_{19}H_{17}FN$: 278.1346 Found: 278.1346.

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Chapter 5

Development of Electron Transfer Reactions using Amine Donors

5.1 Introduction

Electron transfer reactions are important both in chemistry and biology. Surface electron transfer between metals and oxygen is responsible for corrosion in electrochemical systems.[1] In organic chemistry, several popular reactions were shown to proceed by single electron transfer (SET) mechanism with appropriate substrates.[2] Photo excitation of donors facilitate electron transfer processes.[3]

Reaction of donors using low ionization potentials and acceptors with high electron affinities takes place by electron transfer mechanism.[3b-d] Single electron transfer (SET) reactions are generally considered as radical generating ground state reactions as illustrated in the case of $S_{RN}1$ mechanism (Substitution, Radical, Nucleophilic, Unimolecular) (Fig 1).[4,5]

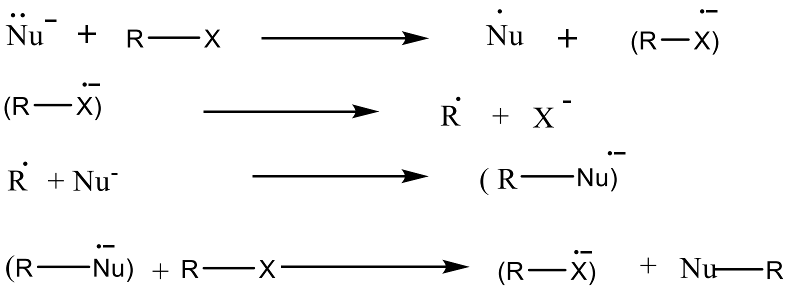


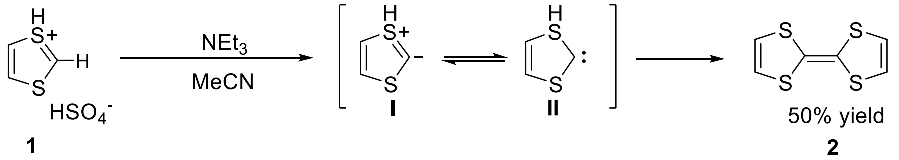
Figure 1. $S_{RN}1$ mechanism

Super electron donors (SED)

Organic electron donors (OEDs) are neutral, ground state organic molecules that reduce substrates by single electron transfer. Reactions with OEDs involve the intermediacy of radicals, which are subsequently converted into organic products. The sufficiently low oxidation potential of some donors even allow them to promote single-electron reduction of aryl halides, and hence such donors are regarded as "super electron donors" (SEDs). A brief review on the preparation and reaction of super electron donors would facilitate the discussion.

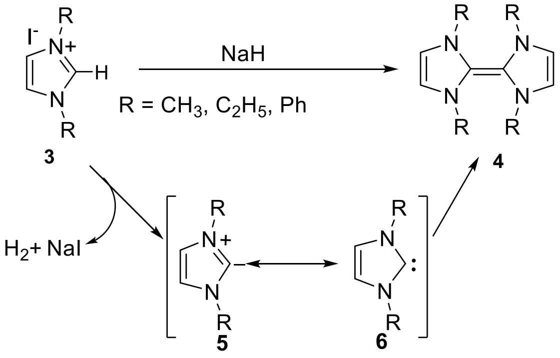
Since early 1970s, TTF (tetrathiafulvalene) derivative **2** was recognized as strong organic π-electron donor of great significance. The TTF can be prepared in 50% yield from 1, 3 dithiolium hydrogen **1** sulphate using triethylamine in acetonitrile (Scheme 1).[6]

Scheme 1



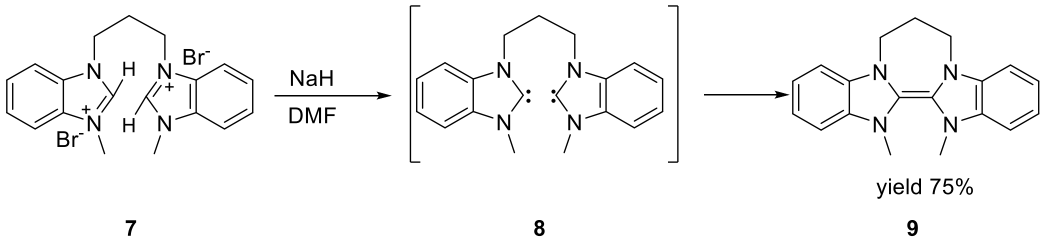
The reaction between an imidazolium salt **3** and NaH leads to C–C bond formation and deprotonation to afford intensely colored super electron donor **4** (Scheme **2**).[7]

Scheme 2



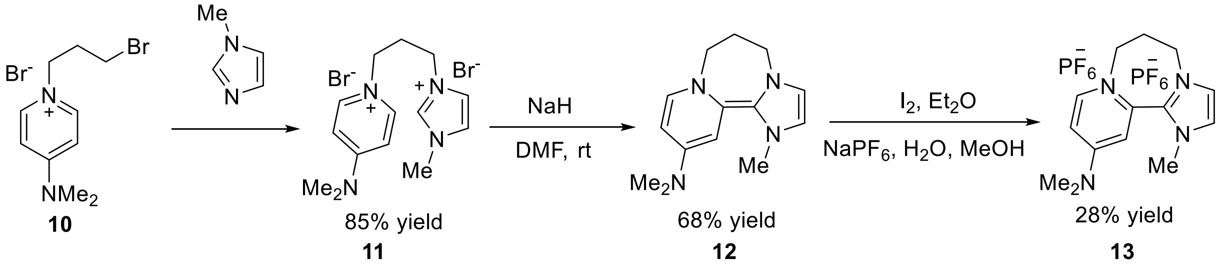
In a similar way, the super electron donor **9** was obtained from dibenzimidazolium salt **7** and NaH in DMF solvent (Scheme 3).[8]

Scheme 3



Similarly, the salt **11**, the SED derivative **12** and the salt **13** were prepared (Scheme 4).[9]

Scheme 4



Over the years, several SEDs and related compounds were reported (Figure 2).[10] [11]

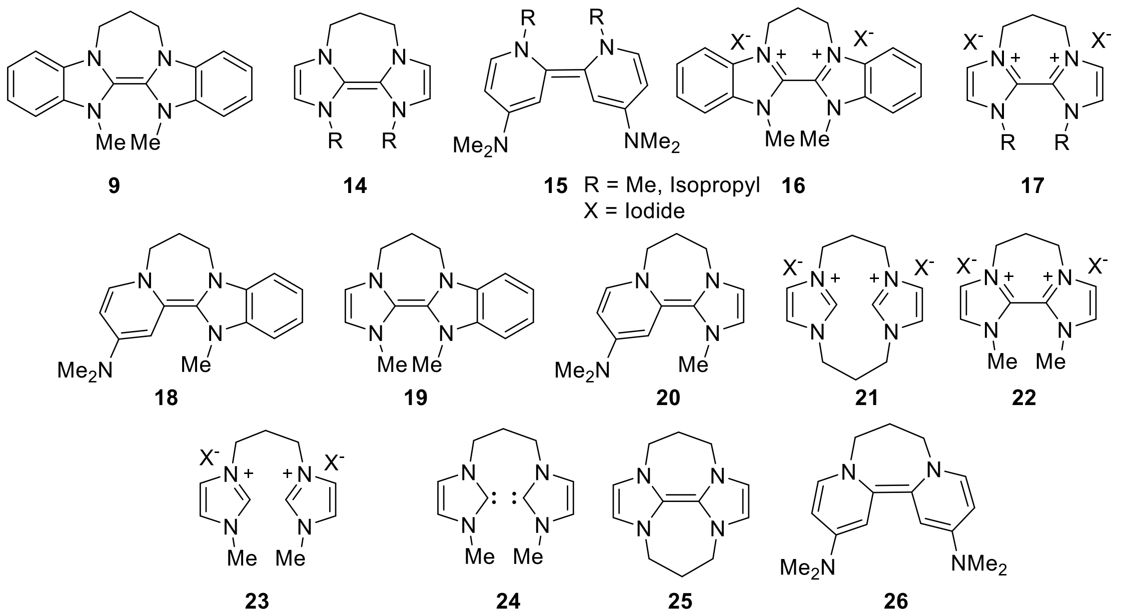
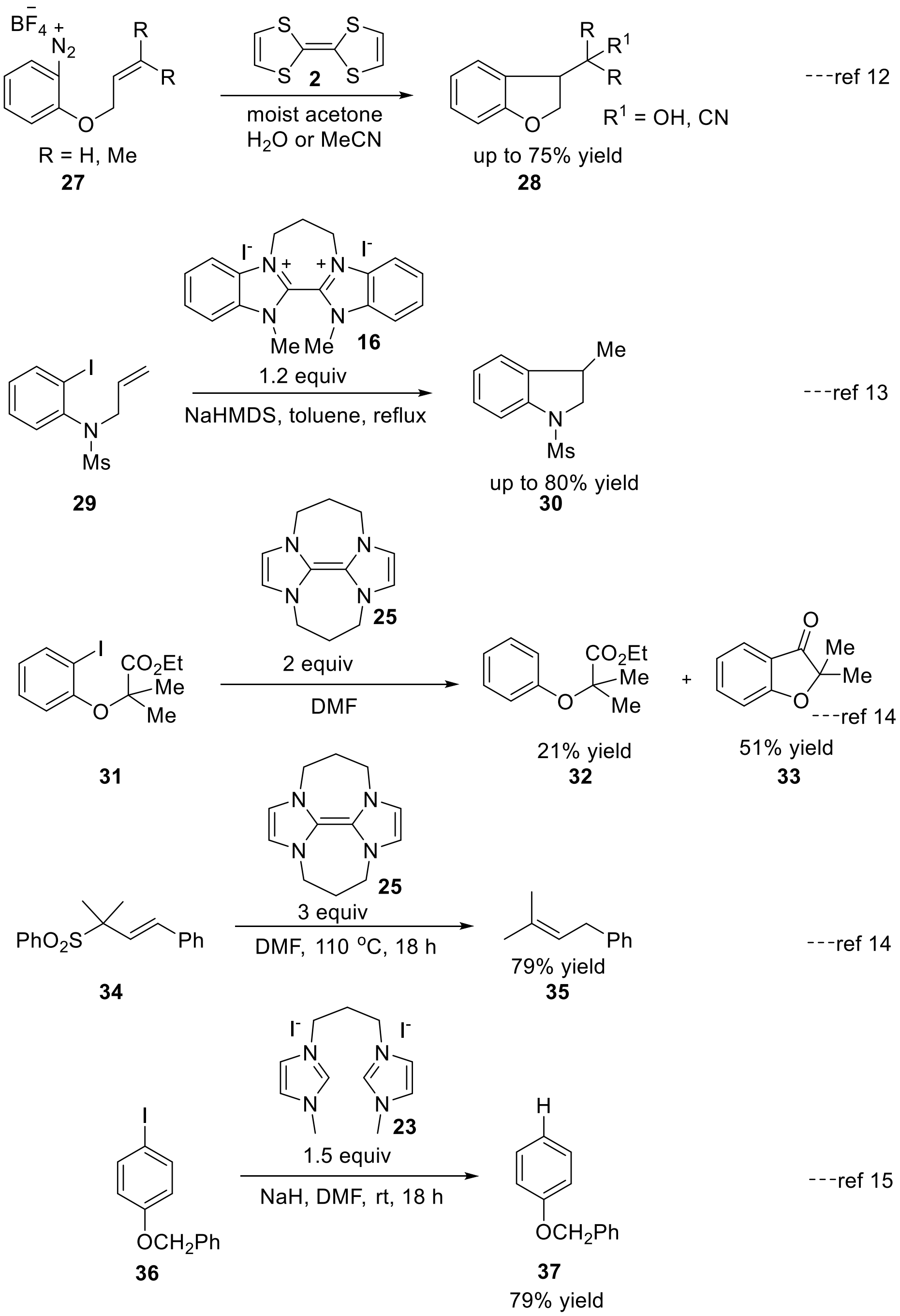


Figure 2. Super-electron-donors and related compounds

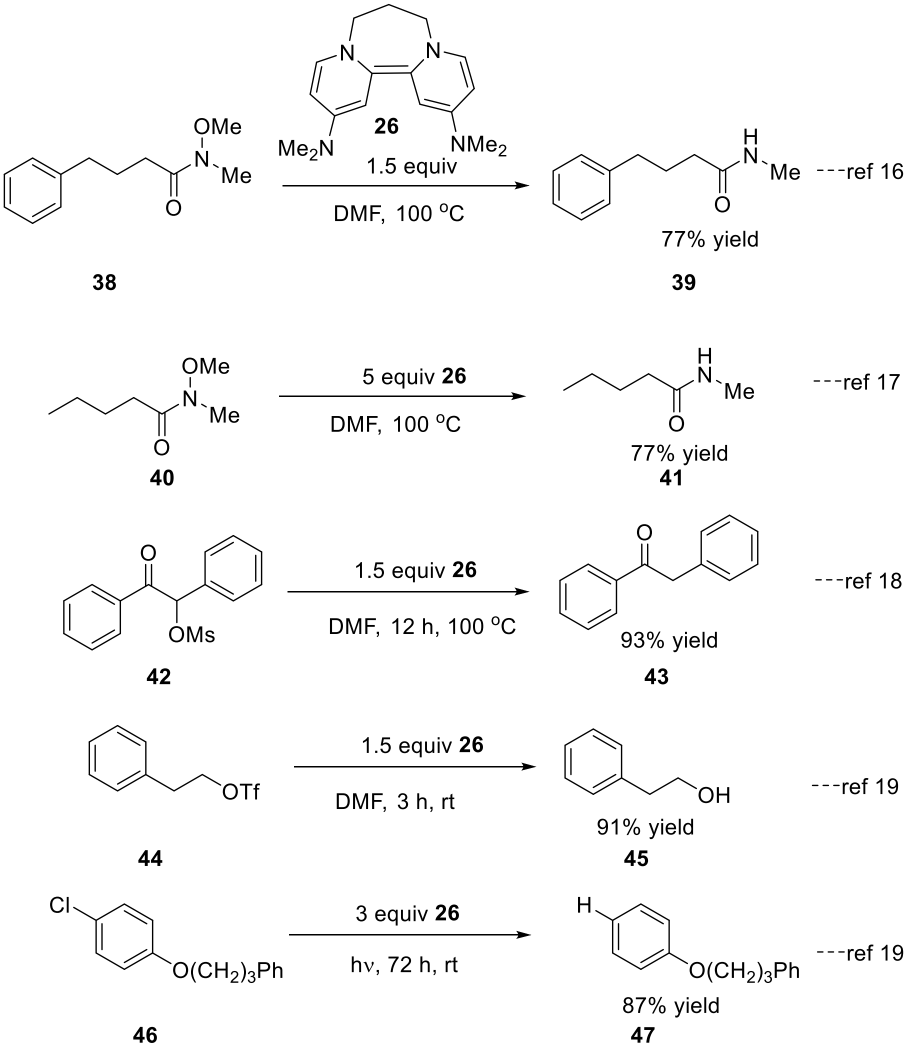
A few representative applications of super electron donors (SEDs) are outlined in Chart 1.[12-15]

Chart 1



The super electron donor **26** was also reported as reagents in various reactions as shown in Chart 2.[16-19]

Chart 2



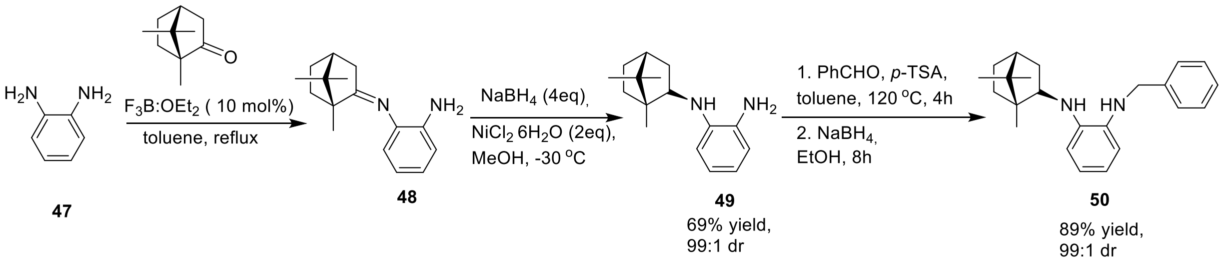
We have prepared chiral camphanyl salts and attempted their conversion to super electron donors. The results of these studies and also results on the construction of organic electrochemical cells using some tertiary amines and *p*-chloranil are described in the next chapter.

5.2 Results and Discussion

5.2.1 Synthesis of chiral *N, N*-dicamphanyl-*o*-phenylene diamine derivatives

Previously, synthesis of the diamine **50** was carried out by the condensation of D-(+)-camphor and *o*-phenyldiamine **47** to the *N*-camphanyl phenylenediamine **49** and reduction of imine **48** in the presence of $NiCl_2.6H_2O$ (2 equiv.) and $NaBH_4$ (4 equiv.) in MeOH and further condensation with benzaldehyde and reduction using $NaBH_4$ (Scheme 5).[20]

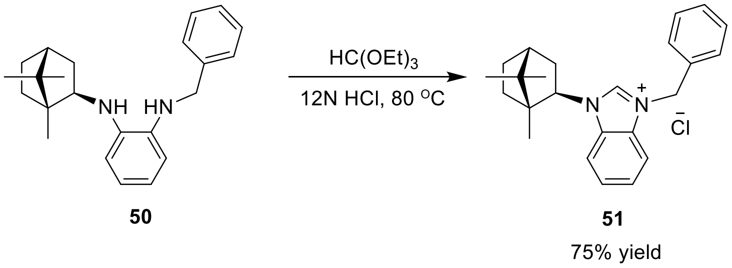
Scheme 5



5.2.2 Synthesis of chiral benzimidazolium salts

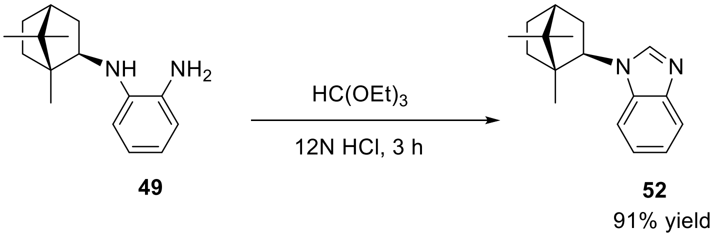
We have observed that the reaction of chiral diamine **50** with triethyl orthoformate in the presence of 12N HCl gave the corresponding benzimidazolium salt **51** in 75% yield (Scheme 6).[21]

Scheme 6



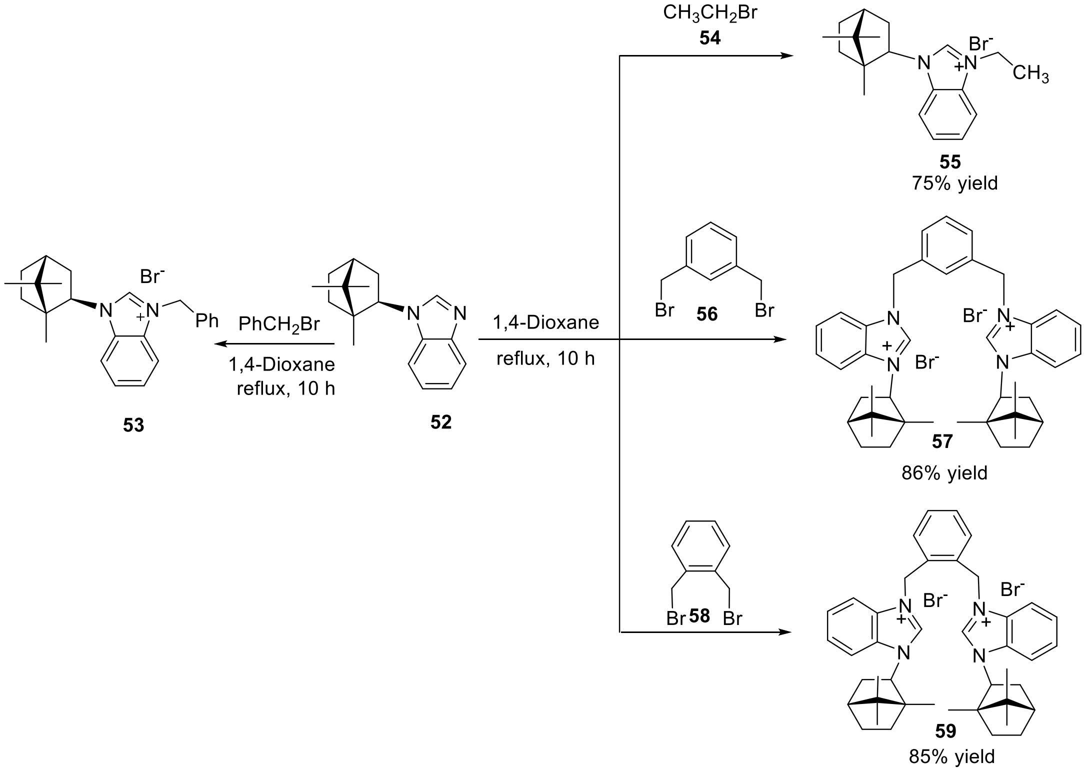
Also, the camphanyl amine **49** was readily converted to chiral *N*-camphanyl benzimidazole **52** in presence of triethoxyorthoformate and conc.HCl (Scheme 7).

Scheme 7



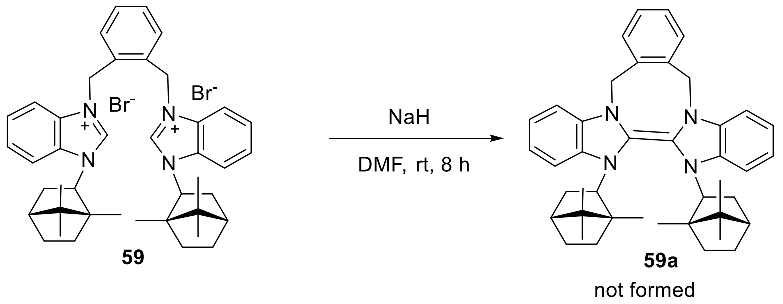
Subsequently, the *N*-camphanyl benzimidazole **52** was readily converted to *N*-heterocyclic carbene precursors **53**, **55**, **57** and **59** using benzyl halide, alkyl halide or benzyl dihalide (**56** and **58**) in the presence of 1,4-dioxane solvent at reflux conditions (Scheme 8).

Scheme 8



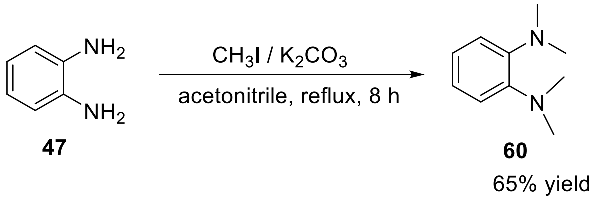
However, these NHC precursors could not be converted to the corresponding super electron donor (Scheme 9).

Scheme 9

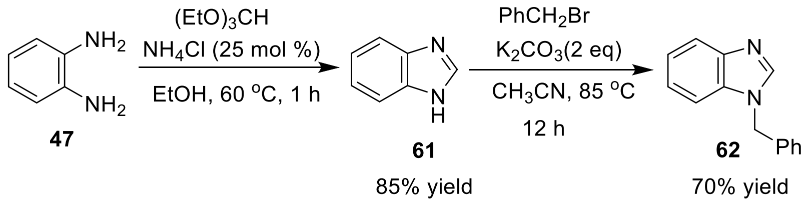


Hence, we turned our efforts towards preparation of simple donors like tetramethyl-*o*-phenyldiamine **60** and *N*-benzylbenzimidazoles **62** from *o*-phenyldiamine (Scheme 10 and 11) for studies on the electron transfer reactions with *p*-chloranil acceptor.

Scheme 10. Reaction of diamine and iodomethane



Scheme 11. Synthesis of *N*-benzylbenzimidazole

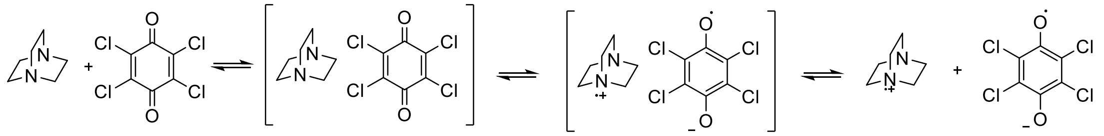


5.2.3 Paramagnetic intermediates in the reaction of amine donors with *p*-chloranil

Reaction of several organic donors and acceptors lead to the formation of charge transfer complexes and the cation radical and anion radical pair, especially in polar solvents. In 2008 Kochi *et. al.*[22] proposed a model based on the van der Waals radii and distance dependence on the reaction of electron acceptors and donors.[23] As per this proposals, molecular interactions in outer-sphere complexes are seen as between acceptor and donor separated beyond their van der Waals radii. Whereas inner-sphere complexes acceptor/donor are closely packed with enhanced interactions because the distance between acceptor and donor is likely to be less than their van der Waals radii.[24] As a result, sterically hindered acceptor/donor complexes are expected to form outer-sphere complexes, while less sterically hindered donor and acceptor complexes would prefer to form inner-sphere complexes.[25]

Formation of stable radical ions of 1,4-diazabicyclo[2.2.2] octane (DABCO) **63** was reported in 1965.[26, 27] In 1977, it was reported[28] that the reaction of DABCO with chloranil **64** gave paramagnetic intermediates (Scheme 12). The strength of the esr signals were found to be higher in a more polar THF solvent compared to that in benzene.[28]

Scheme 12

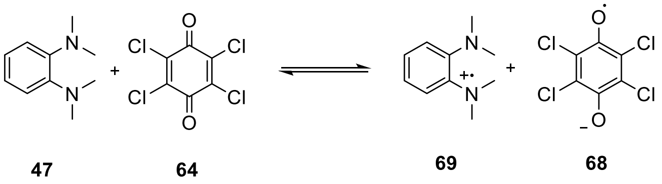


63 **64** **65** **66** **67** **68**

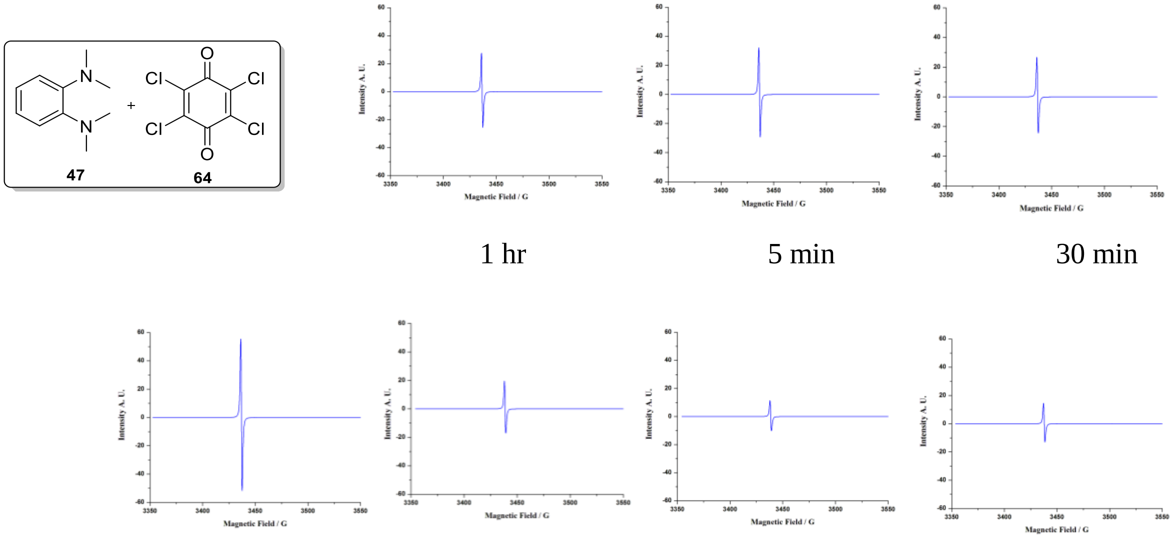
5.2.4 Electron transfer reaction of N^1,N^1,N^2,N^2-tetramethylbenzene-1,2-diamine with quinones

We have observed that upon mixing tetramethyl-*o*-phenyldiamine **47** with the electron acceptor *p*-chloranil **64** in solvents such as dichloromethane (DCM) and propylene carbonate (PC), paramagnetic intermediates were detected (g value 2.00534) (Scheme 13). We made attempts to crystallize the product using solvents such as CH_2Cl_2, PC, dimethylformamide (DMF) and N-methyl-2-pyrrolidone (NMP) but these attempts were not successful.

Scheme 13



We have found that paramagnetic species prepared in this way are stable up to 24 h (Figure 3).

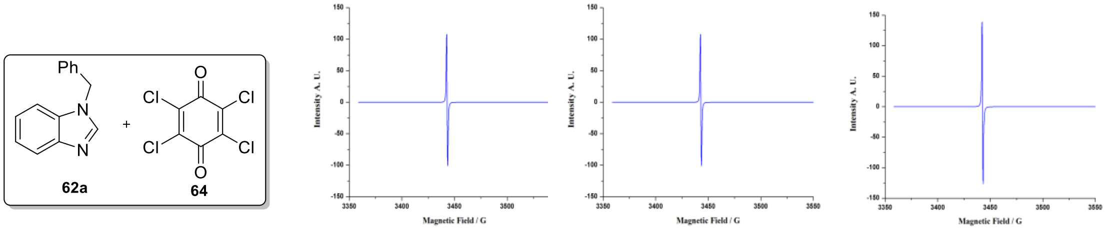


1 hr 5 min 30 min

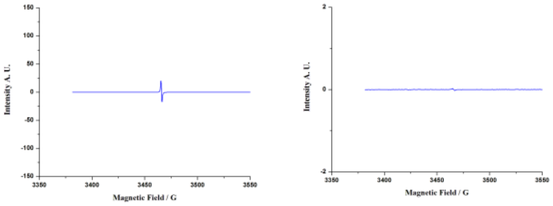
2 hr 6 hr 12 hr 24 hr

Figure 3. EPR spectra for the reaction of tetramethyl-*o*-phenyldiamine (0.05 mmol) in PC solvent with *p*-chloranil (0.05 mmol).

The strength of the signal increased up to 1 h and then decreased indicating the formation of the corresponding charge transfer complex and no organic product could be isolated.

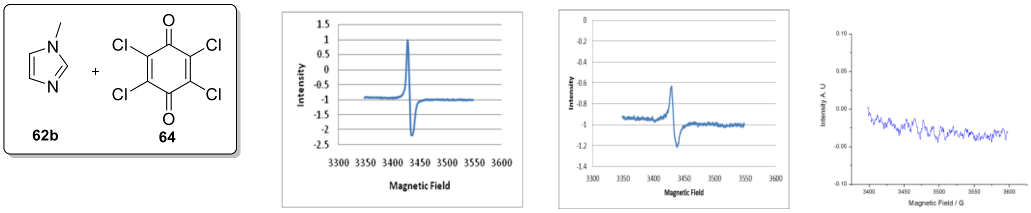


5 min 30 min 1 hr



2 hr 6 hr

Figure 4. EPR spectra for the reaction of N-benzylbenzimidazole (0.05 mmol) in PC solvent with *p*-chloranil (0.05 mmol).

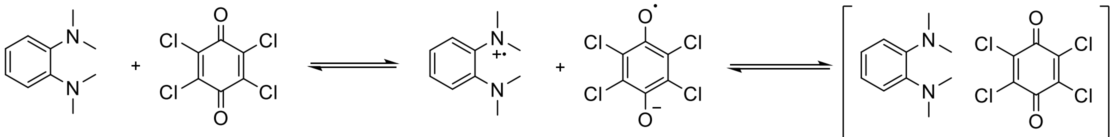


5 min 30 min 1 hr

Figure 5. EPR spectra for the reaction of N-methylimidazole (0.05mmol) in PC solvent with *p*-chloranil (0.05mmol).

A single line epr spectrum was obtained in PC solvent. The signal strength increased with time up to 2 h and then decreased but the signal was seen even after 24 h (Figure 3). A similar initial increase in signal strength was noticed in the case of *N*-benzylbenzimidazole but the strength deceased with time and disappeared in 6 h (Figure 4). The results are in accordance with slow formation of radical ions in a cross exchange process followed by the diamine and *p*-chloranil complex in equilibrium with the radical ions (Scheme 14).

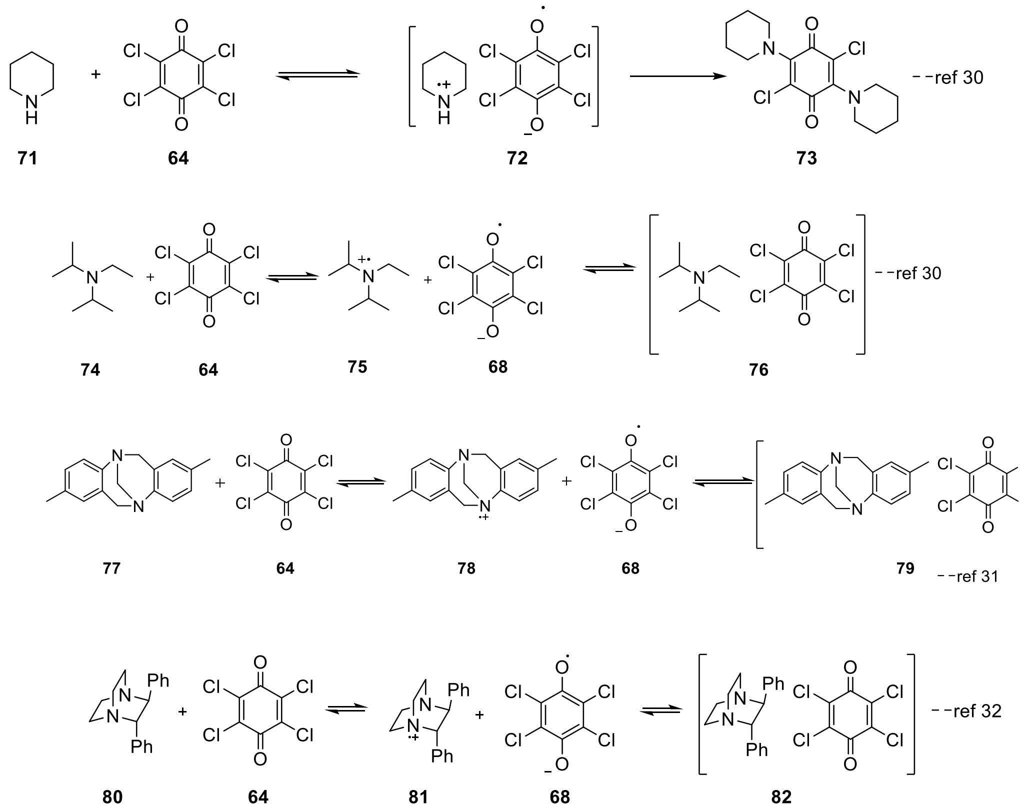
Scheme 14.



In the reaction using *N*-methylimidazole, a broad epr signal was observed but it disappeared in 1 h (Figure 5). It was reported that broadening of epr signal of naphthalenide ion was observed by adding excess naphthalene.[29] Such line broadening esr spectra was also reported in the case of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone radical anion with DDQ with rapid exchange rate constant 2.5 x 10^9 M^{-1} S^{-1} and activation energy of 1.6 kcal mol^{-1} at 23 °C.[22] Accordingly, the line broadening observed may be due to exchange interaction with neutral *p*-chloranil.

Earlier, the reaction of chloranil **64** with various secondary and tertiary amines were reported in this laboratory. In the case of secondary amine **71**, the strength of the signal diminishes with time and vanished within 24 h with the formation of aminoquinone product **73** (Chart 3).[30, 31, 32]

Chart 3



In the case of the tertiary amines **74**, **77** and **80** also the strength of epr signal decreased with time but stable organic products were not formed. Presumably, formation of outer-sphere (or inner- sphere in the case of sterically less hindered amines) charge transfer complexes leads to decrease in signal strength in the epr spectra.

5.2.5 Electricity Harvesting Cells: Organic Solar Cells

In 1839, Alexandre-Edmond Becquerel observed the photovoltaic effect in an electrolyte solution.[33] The era of solid-state solar cells began at Bell Labs in 1954.[34] Over the years, many solar cell technologies were developed. A brief review of organic solar cells (donor–acceptor solar cells) would facilitate the discussion on the present efforts on ground state organic electricity harvesting cells.

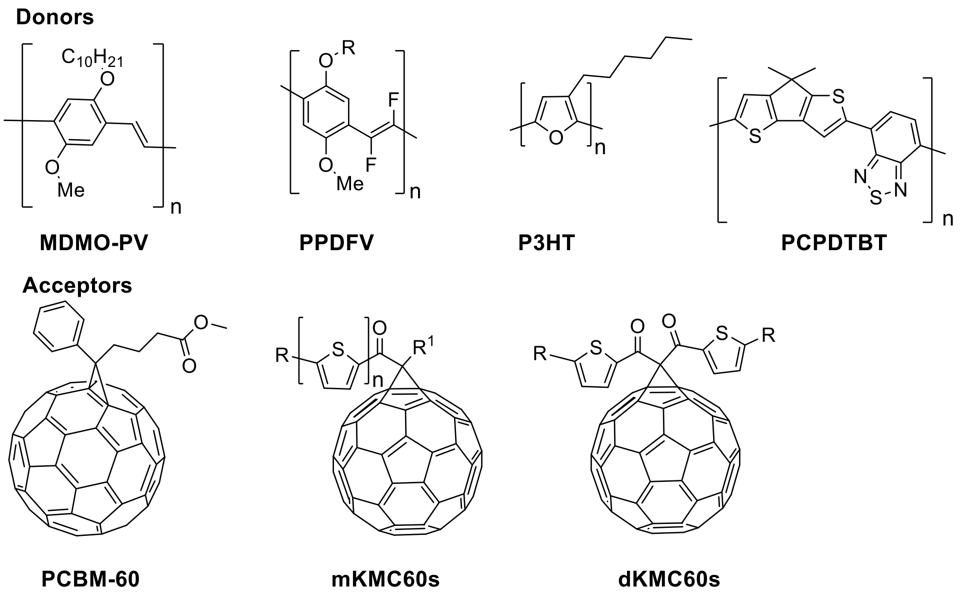


Figure 6. Chemical Structure of Organic solar cell Donor and Acceptor Materials

In recent years, the solar cells using various oraganic donors and acceptors were reported (Figure 6).[35] Efficient photoinduced electron transfer (ET) can occur between the electron acceptor (A) and donor (D) interface. As outlined in Figure 7, the electron would be excited in donor molecule in presence of light. The excited electron could be transferred to the LUMO of the acceptor and then transported to the anode and the holes (+ charges) could be transported to the cathode leading to production of electricity.[36]

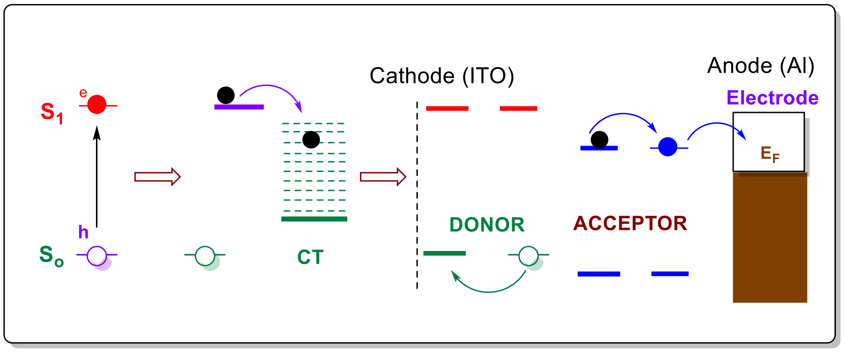


Figure 7. Organic solar cell-Excitation of electron and transport

5.2.6 Construction of Organic Electricity Harvesting Cell

We have already discussed that the reaction of amine with chloranil in polar solvent like PC (propylene carbonate) gives paramagnetic species at room temperature. We have decided to construct an ambient heat harvesting electrochemical cell using the amine donor **47**, **62a** and **62b** and *p*-chloranil **64** acceptor (Figure 8).

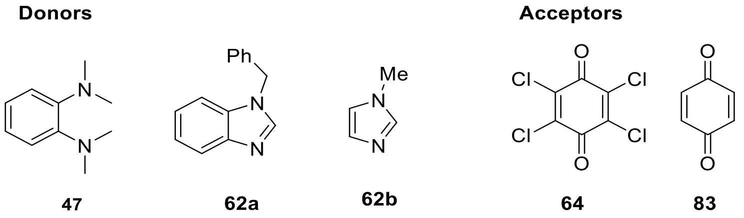


Figure 8. Donors and Acceptors

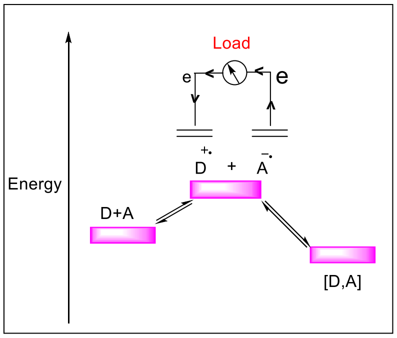


Figure 9. Ground state electron transfer between organic electron donor (D) and acceptor (A) - Construction of an electricity harvesting cell

5.2.6.1 Previous reports on construction of energy harvesting electrochemical cell

In this laboratory, previously, an electrochemical cell was constructed in two layer and multilayer cell configuration using donors and acceptors pastes prepared using TiO_2, polyethylene oxide (PEO) and propylene carbonate (PC) and coating on commercially available Al (0.2mm x 5cm x 5cm) and SS (SS 304, 0.05mm x 5cm x 5cm) foils or graphite sheet (0.4mm x 5cm x 5cm). The foils were then sandwiched to construct the electrochemical cell. The charge transport in this two layer electrochemical cell would be similar to the bilayer in organic solar cell[37] but the electron transport would have contributions from both ionic conduction and also through exchange reactions involving $D/D^{\cdot +}$ and $A^{\cdot -}/A$ processes. The cell constructed this way did produce power (Pmax/FF = 1.415/0.235) but there was no power after 24 h.[38]

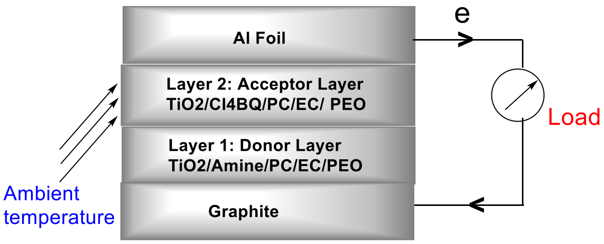
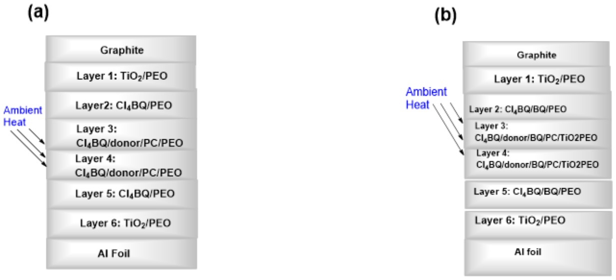


Figure 10. Cell configuaration

5.2.6.2 Electrochemical cells with various configurations

Earliar, it was reported that radical ion intermediates were formed when *p*-chloranil was adsorbed on the TiO_2 surface.[39] Also, radical anions formed from lower electron affinity acceptors like benzoquinone (EA 1.91eV) are solvated to more extent compared to *p*-chloranil (EA 2.78eV). Previously, the electrochemical cells were constructed using TMPDA donor and with BQ layer and without BQ layer gave the less power outputs (Pmax) after 48 h (Figure 11).[38]



1 h after packing:

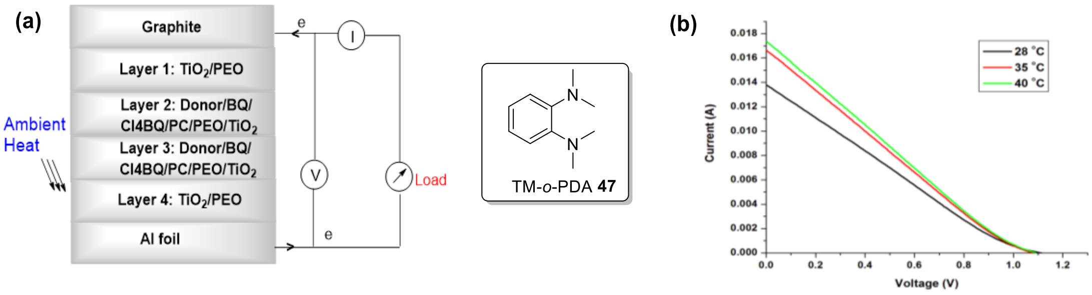
Donor	**Pmax/mW/FF (40 °C)**	**Donor**	**Pmax/mW/F (40 °C)**
TMPDA	1.469/0.221	TMPDA	1.614/0.282
TPA	1.333/0.255	TPA	0.939/0.219
DABCO	5.492/0.313	DABCO	4.806/0.432
DIPEA	5.695 /0.296	DIPEA	11.74/0.296
DiPrBA	2.198/0.260	DiPrBA	1.871/0.232

48 h after packing:

Donor	**Pmax/mW/FF (40 °C)**	**Donor**	**Pmax mW/FF(40 °C)**
TMPDA	0.790/0.309	TMPDA	1.299/0.263
TPA	0.428/0.285	TPA	0.728/0.219
DABCO	2.320/0.267	DABCO	3.776/0.434
DIPEA	2.228 /0.347	DIPEA	8.338/0.394
DiPrBA	1.047/0.261 (35 °C)	DiPrBA	1.411/0.243

Figure 11. Schematic diagram of multi-layer with Cl_4BQ/donor/PC/PEO configuration without BQ and with BQ.

It was of interest to us to construct the electrochemical cell using TM-*o*-PDA donor with BQ layer. Accordingly, we have constructed the cells with four layer configuration by coating TiO_2/PEO pastes on two electrodes followed by coating of Amine/BQ/Cl_4BQ/PC/PEO on TiO_2/PEO/Al. Then, the Amine/BQ/Cl_4BQ/PC/PEO coated above the TiO_2/PEO/Gr. The results are summarized in the Figure 11 (Table ES1, entry 1). The I-V data recorded after 1 h and after 48 h packing, the Pmax/FF of TM-*o*-PDA decreased after 48 h. A possibility is that the formation of amine-*p*-chloranil complex (CT1) to more extent with time, may lead to decrease in power output, especially if this complex precipitates out of the PC solution.



1 h after packing

Donor	**Pmax(mW)/FF(40 ºC)**
TM-*o*-PDA	8.931/0.230

48 h after packing

Donor	**Pmax(mW)/FF(40 ºC)**
TM-*o*-PDA	4.361/0.230

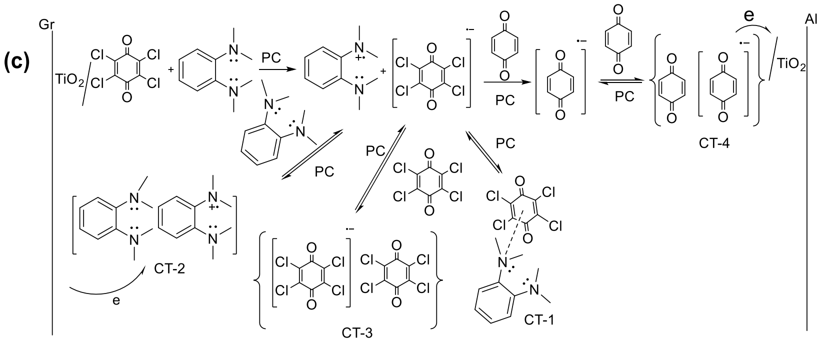
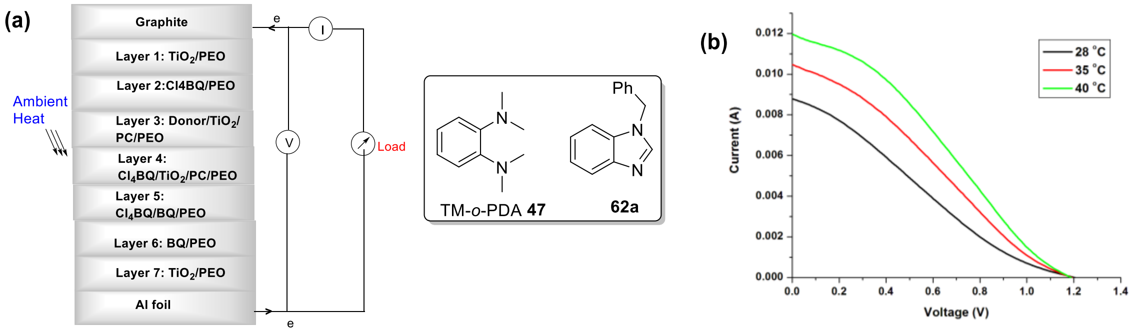


Figure 11. (a) Schematic diagram of multi-layer with TiO_2/Amine/TiO_2/PC/TiO_2 configuration. (b) Representative I-V curve for the cell (Table ES 1, entry 1). (c) Tentative mechanism for electron transport to the electrodes *via* D/$D^{\cdot+}$ and $A^{\cdot-}$/A exchange reactions.

We have also observed improvement in results when amine donor coated in two different layers in different configurations (Figure 13 and 14). The I-V data recorded at 40 °C with Pmax and FF values are also listed (Figure 13 and 14). The Pmax values were less after 48 h when amine donor was also present in layer 3 (Figure 13). When the amine donor was used in layer 2, a slight increase in power outputs (Pmax) were observed at 48 h after packing compared to that observed after 1 h (Figure 14). The lower power output (Pmax) may be due to reduction in the concentrations of radical cations and anions with time.



1 h after packing

Donor	**Pmax(mW)/FF(40 ^{o}C)**
TM-*o*-PDA	3.635/0.221
N-benzylbenzimidazole	5.759/0.283

48 h after packing

Donor	**Pmax(mW)/FF(40 ^{o}C)**
TM-*o*-PDA	2.783/0.210
N-benzylbenzimidazole	4.334/0.305

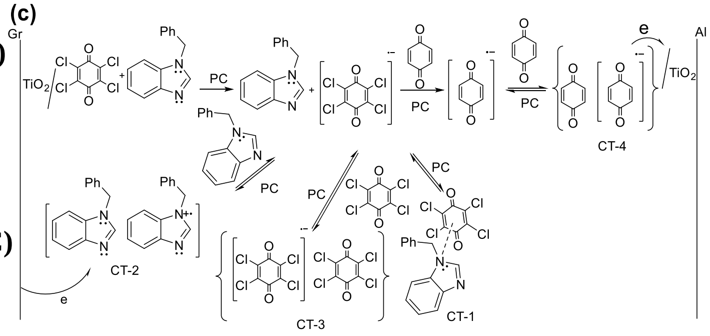
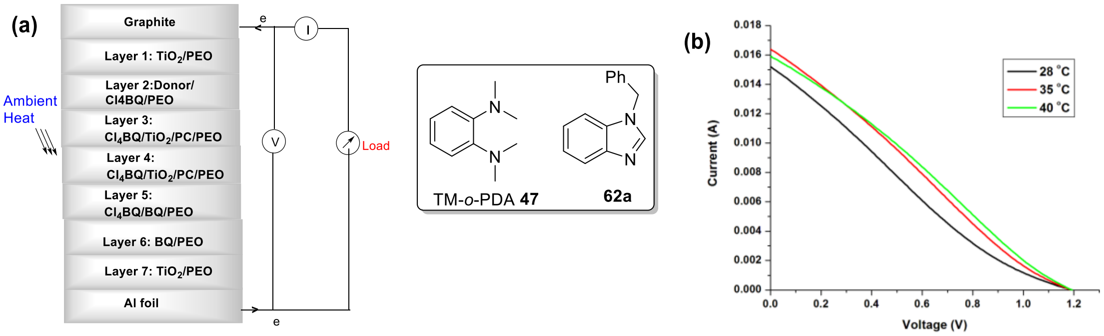


Figure 13. (a) Schematic diagram of six layer with TiO$_2$/Amine/TiO$_2$/PC/TiO$_2$ configuration. (b) Representative IV for the cell (Table ES1, entry 2-3). (c) Possible mechanism for electron transport.



1 h after packing

Donor	**Pmax(mW)/FF(40 ^{o}C)**
TM-*o*-PDA	2.773/0.213
N-benzylbenzimidazole	5.048/0.216

48 h after packing

Donor	**Pmax(mW)/FF(40 ^{o}C)**
TM-*o*-PDA	3.477/0.216
N-benzylbenzimidazole	5.380/0.267

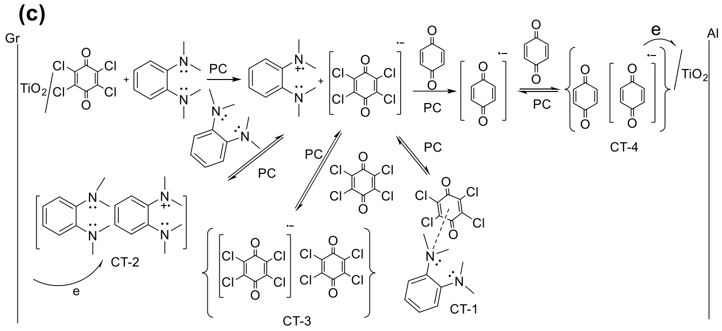
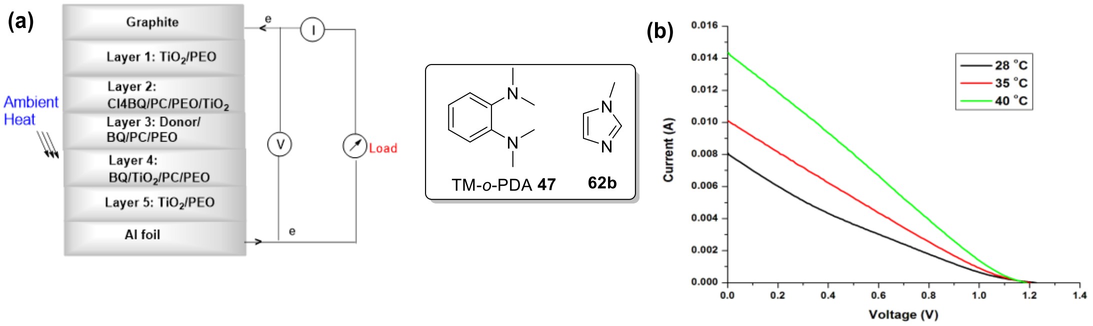


Figure 14. (a) Schematic diagram of six layer with TiO$_2$/Amine/TiO$_2$/PC/TiO$_2$ configuration. (b) Representative I-V for the cell (Table ES1, entry 4-5). (c) Possible mechanism for electron transport.

We have also carried out experiments by constructing cell in two different five layer configurations (Figure 15 and 16). Some improvements were observed in the power outputs but still the Pmax values decreased with time when the electron transporter BQ was used (e.g. Figure 15; Pmax values for Me*N*-imidazole, 9.906 mW at 1 h and 4.036 mW at 48 h). However, when the TM-*o*-PDA was used in five layer configurations (Figure 15), Pmax values could not be improved compared to that observed in the previous configurations (Figure 11).



1 h after packing

Donor	**Pmax(mW)/FF(40 ºC)**
TM-*o*-PDA	3.601/0.260
MeN-imidazole	9.906/0.243

48 h after packing

Donor	**Pmax(mW)/FF(40 ºC)**
TM-*o*-PDA	2.262/0.219
MeN-imidazole	4.036/0.237

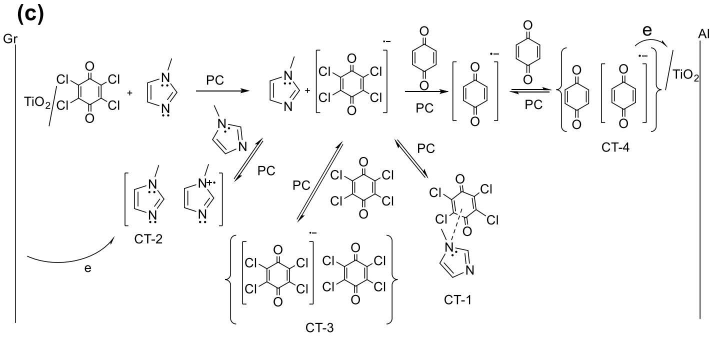
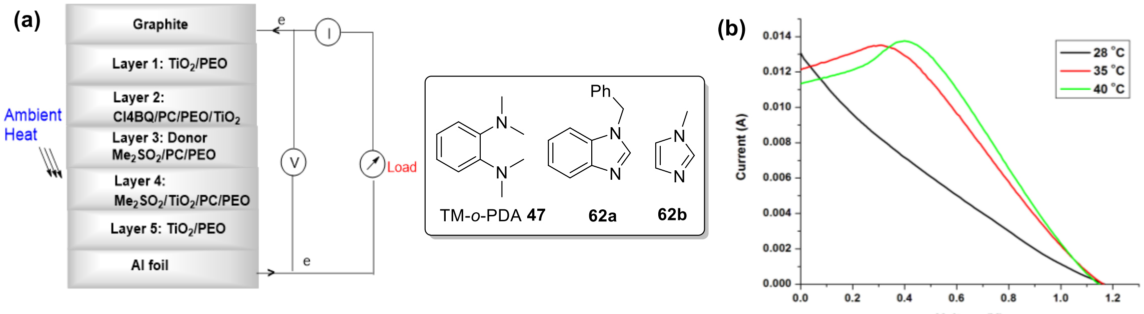


Figure 15. (a) Schematic diagram of multi-layer with TiO_2/Amine/TiO_2/PC/TiO_2 configuration. (b) Representative I-V curve for the cell (Table ES1, entry 6-7). (c) Possible mechanism for electron transport.

However, the replacement of BQ with other acceptor such as Me_2SO_2 (Figure 16), gave higher power outputs (Pmax) after 1 h packing but the Pmax decreased after 48 h (Figure 16; Pmax values for *N*-benzyl benzimidazole, 8.952 mW at 1 h and 6.644 mW at 48 h). Also, the I-V curve was good at 35 ºC and 40 ºC. Presumably, the more soluble Me_2SO_2

(EA -0.39eV) accepts electrons from *p*-chloranil anion radical effectively for transporting to the Al electrode improving the power output to some extent.[40]



1 h after packing

Donor	**Pmax(mW)/FF(40 ºC)**
TM-*o*-PDA	6.040/0.318
N-benzylbenzimidazole	8.952/0.377
MeN-imidazole	14.270/0.322

48 h after packing

Donor	**Pmax(mW)/FF(40 ºC)**
TM-*o*-PDA	1.588/0.265
N-benzylbenzimidazole	6.644/0.510
MeN-imidazole	3.945/0.402

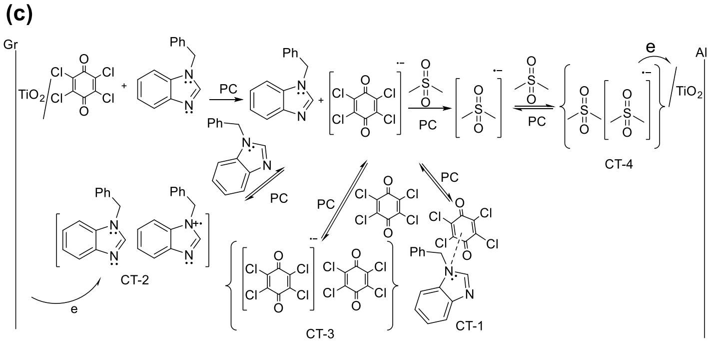


Figure 16. (a) Schematic diagram of multi-layer with TiO_2/Amine/TiO_2/PC/TiO_2 configuration. (b) Representative I-V curve for the cell (Table ES1, entry 8-10). (c) Possible mechanism for electron transport.

The results (Table ES1) indicate that increase in the temperature of the cell (28 ºC to 40 ºC) increases the power output due to increase in the rate of electron transfer between the donor and acceptor and also dissociation of formed charge transfer complexes in to radical ion pairs. Also, the increase in temperature would help in crossing the activation energy barrier of ions to the electrodes and hence would improve the conductance. Therefore, the formation of charge transfer complexes could be prevented and the concentration of ions increased if suitable donor-acceptor used, which would lead to give more fruitful results.

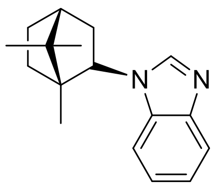
5.3 Conclusions

Convenient methods were developed for accessing several super electron donors to good yields using D-(+)–camphor. Also, tetramethyl-*o*-phenyldiamine and *N*-benzyl benzimidazoles were prepared and their use in epr studies. These amine derivatives with acceptors have considerable potential for use in the construction of organic electrochemical cells.

5.4 Experimental Section

5.4.1 1-((1R,2S,4R)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)-1H-benzo[d]imidazole (36)

In a 50 mL round bottomed flask, N1-((1R,2R,4R)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)benzene-1,2-diamine (0.245g, 1.0 mmol) was dissolved in $CH(OEt)_3$ (10 ml), and Conc. HCl(10 mol%) added. The resulting solution was stirred at room temperature for 30 min under nitrogen and then heated to 80°C until condensation was observed on the neck of the flask. At this point the rubber septum was removed and the solution was allowed to stir open to the air for 4h. After cooling to room temperature, apply high vacuum for 1h, completely remove ethanol. The suspension obtained was diluted with dry diethyl ether (100ml) and allowed to crystallization. The obtained off white solid **52** was washed with diethyl ether and the residual solvents removed under high vacuum.



52

Yield : 0.218 g, 86%,

$[\alpha]_D^{25}$: –32.1 (*c* 0.56, $CHCl_3$).

IR (KBr) : 3472, 3353, 3260, 3019, 2958, 2876, 1638, 1550, 1457, 1320, 1243, 1084, 1052, 1024, 805, 761 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 10.1 (s, 1H), 7.81-7.58 (m, 2H), 7.14-20 (m, 2H), 4.48- 4.27 (m, 2H), 2.91-2.67 (m, 2H), 2.34 (s, 2H), 2.11-2.81 (m, 2H), 1.52-1.19 (m, 3H), 1.01-0.71 (m, 6H).

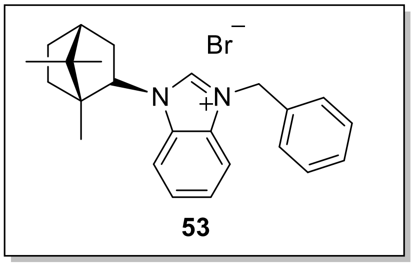
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 143.7, 142.7, 139.0, 132.0, 128.4, 127.1, 126.7, 126.0, 114.1, 113.1, 66.6, 50.9, 48.0, 44.6, 37.2, 36.0, 33.9, 26.6, 21.2, 21.1, 19.8, 12.6.

HRMS : (ESI) $C_{17}H_{22}N_2$: 254.1783 [*M*+H$^+$]; Found: 255.1862.

5.4.2. Preparation of NHC precursors

In a 25 mL round bottomed flask, N-camphanyl benzimidazole (0.334 g, 1.0 mmol) and bromide compounds (1.5 mmol) in 1, 4 –dioxane (5 mL) solvent. The reaction mixture was stirred for overnight at reflux. Upon cooling to room temperature, Et_2O (100 mL) was added, and the resulting precipitate was collected by filtration, and washed with Et_2O (10 mL) and apply high vacuum to give NHC precursors as white solid.

1-Benzyl-3-(1,7,7-trimethyl-bicyclo[2.2.1]hept-2-yl)-3H-benzoimidazol-1-ium



53

Yield : 0.394 g, 91%.

$[\alpha]_D^{25}$: -21.6 (*c* 0.22, $CHCl_3$).

IR (KBr) : 3150, 3084, 2964, 2876, 1720, 1561, 1479, 1446, 1265, 1210, 1084, 1057, 800, 756 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 9.61 (s, 1H), 7.73-7.71 (d, *J* = 8.0 Hz, 1H), 7.66-7.64 (d, *J* = 8.0 Hz, 1H), 7.60-7.50 (d, *J* = 8.0 Hz, 1H), 7.38-7.37 (d, *J* = 4.0 Hz, 2H), 7.30-7.26 (m, 4H), 5.76-5.64 (q, *J* = 24.0 Hz, 2H), 4.62-4.58 (t, *J* = 16.0 Hz, 1H), 2.68- 2.23 (m, 2H), 2.06-1.92 (t, *J* =24.0 Hz, 1H), 1.54-1.37 (m, 2H), 1.22-1.17 (m, 2H), 1.03 (s, 3H), 0.89 (s, 3H), 0.74 (s, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 140.2, 133.2, 133.0, 131.0, 129.3, 129.0, 128.2, 127.5, 114.4, 113.9, 66.6, 65.8, 56.2, 51.6, 51.3, 50.9, 48.0, 44.7, 37.2, 36.1, 26.5, 21.0, 19.7, 15.2, 12.6.

HRMS : (ESI) C$_{24}$H$_{29}$BF$_4$N$_2$: 432.2360, [M+H$^+$]; Found: 433.2436.

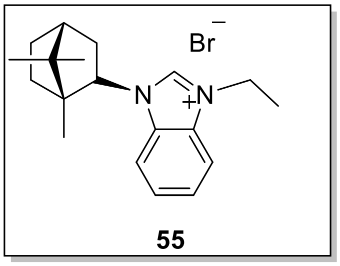
3-Ethyl-1-((1R,2S,4R)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)-1H-benzo[d]imidazol-3-ium (55)

Yield : 0.271 g, 75%.

$[\alpha]_D^{25}$: -169.4 (*c* 0.20, CHCl$_3$).

IR (KBr) : 3159, 3074, 2963, 2886, 1715, 1551, 1481, 1436, 1263, 1228, 1065, 1042, 809, 751 cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 11.53 (s, 1H), 7.39-7.28 (m, 4H), 4.96-4.93 (m, 2H), 4.55-4.52 (m, 1H), 3.09-3.07 (m, 1H), 2.21-2.18 (m, 3H), 1.91-1.81 (m, 6H), 1.78-1.18 (m, 3H), 0.97-0.89 (m, 6H).



55

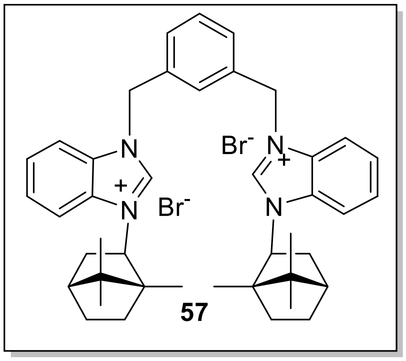
^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 142.1, 133.0, 130.9, 127.2, 126.8, 114.5, 113.1, 66.8, 56.2, 51.0, 48.2, 44.6, 43.0, 37.2, 36.6, 26.7, 21.2, 20.3, 15.5, 14.3, 12.8.

HRMS : (ESI) C$_{19}$H$_{27}$BrN$_2$: 362.1358, [M+H$^+$]; Found: 363.1437.

1-((1S,4S)-1,7,7-Trimethylbicyclo[2.2.1]heptan-2-yl)-3-(3-((3-((1R,4R)-1,7,7 trimethylbicyclo[2.2.1]heptan-2-yl)-1H-3l4-benzo[d]imidazol-1-yl)methyl)benzyl)-1H-3l4-benzo[d]imidazole (57)

Yield : 0.662 g, 86%.

$[\alpha]_D^{25}$: -231.3 (*c* 0.32, CHCl$_3$).



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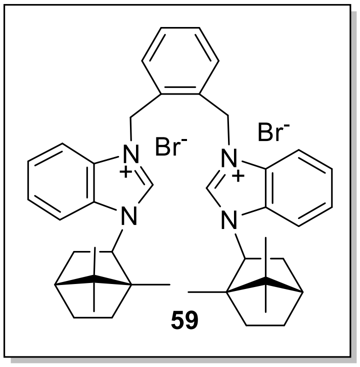
IR (KBr) : 3155, 3081, 2962, 2879, 1725, 1560, 1469, 1466, 1264, 1213, 1081, 1055, 810, 752 cm$^{-1.}$

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 10.59-10.55 (s, 2H), 7.80-7.64 (m, 10H), 7.29-7.15 (m, 2H), 4.52 (s, 2H), 4.34-4.32 (m, 4H), 2.90-2.89 (s, 2H), 2.34-2.24 (m, 4H), 2.17-2.08 (m, 6H), 1.93-1.80 (m, 3H), 1.47-1.36 (t, *J* = 24.0 Hz, 3H), 1.22-1.17 (m, 2H), 1.03-0.98 (m, 6H), 0.89-0.74 (m, 6H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 143.1, 139.1, 132.9, 132.1, 128.5, 127.1, 126.6, 126.0, 114.0, 113.0, 66.7, 56.9, 51.0, 48.0, 44.6, 37.3, 36.0, 34.0, 26.7, 21.3, 21.1, 19.9, 12.6.

HRMS : (ESI) $C_{42}H_{52}Br_2N_4$: 770.2570, [M+H$^+$]; Found: 771.2649.

1,2-Bis((1-((1S,4S)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)-1H-3l4-benzo[d]imidazol-3-yl)methyl)benzene (59)



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Yield : 0.654 g, 85%.

$[\alpha]_D^{25}$: -458.7 (*c* 0.36, $CHCl_3$).

IR (KBr) : 3149, 3064, 2954, 2856, 2871, 1710, 1556, 1479, 1446, 1265, 1210, 1082, 1051, 809, 756 cm$^{-1.}$

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 11.3 (s, 2H), 7.93-7.91 (m, 2H), 7.73-7.54 (m, 4H), 7.22-7.20 (d, *J* = 8.0 Hz, 2H), 7.10-7.06 (d, *J* = 4.0 Hz, 2H), 6.72-6.47 (m, 2H), 4.69 (s, 4H), 3.70-3.69 (m, 6H), 2.84-2.80 (m, 2H), 2.33-2.30 (m, 2H), 2.11-2.06 (m, 2H), 1.78-1.52 (m, 8H), 1.14-1.12 (m, 4H), 1.12-1.11 (m, 3H), 0.98-0.89 (m, 6H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 141.9, 134.3, 133.0, 132.7, 130.9, 129.9, 129.8, 129.1, 127.6, 127.3, 126.7, 114.7, 114.5, 114.3, 113.4, 67.0, 66.8, 64.5, 51.8, 56.8, 51.0, 50.3, 48.3, 44.6, 37.2, 36.7, 34.8, 32.7, 28.3, 27.1, 26.7, 21.2, 20.3, 19.9, 18.5, 15.2, 12.9.

HRMS : (ESI) $C_{42}H_{52}Br_2N_4$: 770.2570, [M+H^+]; Found: 771.2649.

5.4.3 Procedure for I-V measurement for electrochemical cell

The voltage and current of the fabricated cell was initially measured using an multimeter. The I-V characteristics were measured by ZAHNER instrument using CIMPS software. The I-V characteristics of the cell were done under dark condition without illumination of light. The cell was recorded at scan rate of 1mV/S to get maximum power (Pmax) and fill factor (FF). The cell potentiostat should be open circuit voltage (Voc) before the measurement.

5.4.4 Preparation of Electrochemical Cells

Simple solution processing and casting techniques were followed for the construction of the cell device.

Table ES1. Configuration 1

The PEO (0.05 g) was dissolved in dichloromethane and mixed with TiO_2 (0.5 g) powder. DCM was removed to obtain a paste. The amine donor (1 mmol), *p*-chloranil (0.125 g), BQ (0.22 g), TiO_2 (0.25 g), PC (0.5 g) and PEO (0.05 g) were added to the above made paste as well as amine donor (1 mmol), *p*-chloranil (0.125 g), BQ (0.22 g), TiO_2 (0.25 g), PC (0.5 g) and PEO (0.05 g) and slurry was prepared and casted above the coated layer on Al and Graphite and dried in air at room temperature overnight. The cell was prepared by sandwiching the coated Al/Gr layers. The rim of the cell prepared in this way was sealed all around using TiO_2/PEO paste, then with commercial adhesive Bondfix and covered with cellophone tape.

Table ES1. Configuration 2

The PEO (0.05 g) was dissolved in dichloromethane and mixed with TiO_2 (0.5 g) powder. DCM was removed to obtain a paste. The *p*-chloranil (0.025 g) and PEO (0.05 g) were added to the above made paste as well as amine donor (1 mmol), PEO (0.05 g) and BQ (0.11 g), PC (0.25 g), PEO (0.05 g) and TiO_2 (0.025 g) slurry was prepared and casted on Al layer. The layer was dried in air at room temperature overnight. Similarly, PEO (0.05 g), TiO_2 (0.5 g) and BQ (0.2 g), PC (0.5 g) were mixed and cast above Graphite layer. The layer was dried in air at room temperature overnight. The cell was prepared by sandwiching the coated Al/Gr layers. The rim of the cell prepared in this way was sealed all around using TiO2/PEO paste, then with commercial adhesive Bondfix and covered with cellophone tape.

Table ES1. Configuration 3

The PEO (0.05 g) was dissolved in dichloromethane and mixed with TiO_2 (0.5 g) powder. DCM was removed to obtain a paste. The amine donor (1 mmol), *p*-chloranil (0.025 g) and PEO (0.05 g) were added to the above made paste as well as TiO_2 (0.025 g), *p*-chloranil (0.025 g), PC (0.25 g) and PEO (0.05 g) and it was caste over the Al (0.2 mm thickness, 5x5 cm^2). The layer was dried in air at room temperature overnight. Similarly, PEO (0.05 g), TiO_2 (0.5 g) and BQ (0.2 g), Cl_4BQ (0.1 g), PC (0.5 g) were mixed and cast above Graphite (0.4 mm thickness, 5x5 cm^2). The layer was dried in air at room temperature overnight. The cell was prepared by sandwiching the coated Al/Gr layers. The rim of the cell prepared in this way was sealed all around using TiO2/PEO paste, then with commercial adhesive Bondfix and covered with cellophone tape.

Table ES1. Configuration 4

The PEO (0.05 g) was dissolved in dichloromethane and mixed with TiO_2 (0.5 g) powder. DCM was removed to obtain a paste. The *p*-chloranil (0.025 g), TiO_2 (0.5 g), PC (0.5 g) and PEO (0.05 g) were added to the above made paste as well as amine donor (1 mmol), BQ (0.11 g), PEO (0.05 g) and PC (0.25 g), PEO (0.05 g) heat coat on Al side before packing and slurry was prepared and casted on Al layer. The layer was dried in air at room temperature overnight. Similarly, TiO_2 (0.5 g), BQ (0.44 g), PEO (0.05 g) and PC (0.5 g) were mixed and cast above TiO_2 (0.5 g)/PEO (0.05 g)/Graphite layer. The layer was dried in air at room temperature overnight. The cell was prepared by sandwiching the coated Al/Gr layers. The rim of the cell prepared in this way was sealed all around using TiO_2/PEO paste, then with commercial adhesive Bondfix and covered with cellophone tape.

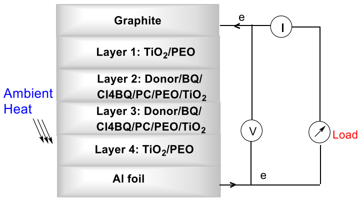
Table ES1. Configuration 5

The PEO (0.05 g) was dissolved in dichloromethane and mixed with TiO_2 (0.5 g) powder. DCM was removed to obtain a paste. The *p*-chloranil (0.025 g), TiO_2 (0.5 g), PC (0.5 g) and PEO (0.05 g) were added to the above made paste as well as amine donor (1 mmol), Me_2SO_2 (0.098 g), PEO (0.05 g) and PC (0.25 g), PEO (0.05 g) heat coat on Al side before packing and slurry was prepared and casted on Al layer. The layer was dried in air at room temperature overnight. Similarly, TiO_2 (0.5 g), Me_2SO_2 (0.188 g), PEO (0.05 g) and PC (0.5 g) were mixed and cast above TiO_2 (0.5 g)/PEO (0.05 g)/Graphite layer. The layer was dried in air at room temperature overnight. The cell was prepared by sandwiching the coated

Al/Gr layers. The rim of the cell prepared in this way was sealed all around using TiO$_2$/PEO paste, then with commercial adhesive Bondfix and covered with cellophone tape.

Table 1. Cell experiments

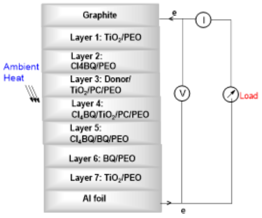
Cell Configuration 1



(Entries 1)

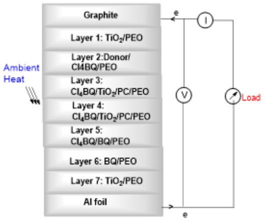
1	Gr----------------- Layer1: TiO$_2$(0.5g) + PEO(0.05g) Layer2: TM-O-PDA (0.164g)+ + Cl$_4$BQ(0.125g) + BQ(0.22g)+ PC (0.5g) + PEO(0.05g) +TiO2 (0.25g) Layer3: TM-O-PDA (0.164g)+ + Cl$_4$BQ(0.0.125g) + BQ(0.22g)+ PC (0.5g) + PEO(0.05g) +TiO2 (0.25g) Layer4: TiO$_2$(0.5g) + PEO(0.05g) Al------------------	1h after packing	28 ºC	1.144	24.07	0.495	12.270	6.075	0.221
			35 ºC	1.133	32.360	0.534	16.260	8.677	0.237
			40 ºC	1.142	34.03	0.517	17.280	8.931	0.230
		48h after packing	28 ºC	1.142	34.03	0.517	17.280	8.931	0.230
			35 ºC	1.114	13.770	0.501	6.981	3.494	0.228
			40 ºC	1.091	17.360	0.497	8.784	4.361	0.230

Cell Configuration 2



(Entries 2-3)

Cell Configuration 3

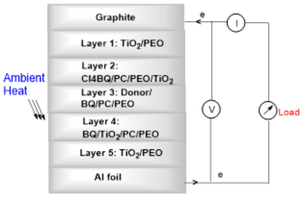


(Entries 4-5)

2	Gr-------------- Layer1: TiO$_2$(0.5g) + PEO (0.05g) Layer2: Cl4BQ(0.25g) + PEO (0.05g) Layer3: TM-*o*-PDA(0.164g) + PEO(0.05g) Layer4: BQ(0.11g)+PC(0.5g) + PEO(0.05g)+ TiO2 (0.25g) Layer5: BQ(0.11g)+PC(0.5g) + PEO(0.05g)+ TiO2 (0.25g) Layer6: BQ(0.2g)+PEO(0.05g) Layer7: TiO$_2$(0.5g) + PEO (0.05g) Al------------	1h after packing	28 ºC	1.187	8.817	0.522	1.203	2.195	0.210
			35 ºC	1.187	9.668	0.492	4.770	2.347	0.204
			40 ºC	1.188	13.860	0.529	6.872	3.635	0.221
		48h after packing	28 ºC	1.186	7.129	0.468	3.311	1.551	0.183
			35 ºC	1.182	10.550	0.494	5.036	2.487	0.199
			40 ºC	1.17	11.340	0.5	5.561	2.783	0.210
3	Gr-------------- Layer1: TiO$_2$(0.5g) + PEO (0.05g) Layer2: Cl4BQ(0.0.25g) + PEO (0.05g) Layer3: N-benzylbenzimidazole(0.208g) + EO(0.05g) Layer4: BQ(0.11g)+PC(0.5g) + PEO(0.05g)+ TiO2 (0.25g) Layer5: BQ(0.11g)+PC(0.5g) + PEO(0.05g)+ TiO2 (0.25g) Layer6: BQ(0.2g)+PEO(0.05g) Layer7: TiO$_2$(0.5g) + PEO (0.05g) Al------------	1h after packing	28 ºC	1.191	12.150	0.495	7.562	3.745	0.259
			35 ºC	1.189	14.910	0.560	9.111	5.10	0.288
			40 ºC	1.191	17.07	0.551	10.460	5.759	0.283
		48h after packing	28 ºC	1.205	8.776	0.483	5.075	2.452	0.232
			35 ºC	1.193	10.460	0.548	6.258	3.431	0.278
			40 ºC	1.189	11.970	0.566	7.663	4.334	0.305

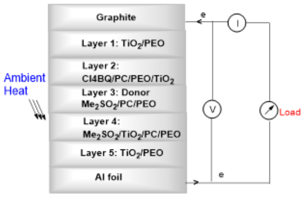
4	Gr-------------- Layer1: TiO_2(0.5g) + PEO (0.05g) Layer2: TM-*o*-PDA(0.164g) + Cl4BQ(0.0.25g) + PEO (0.05g) Layer3: Cl_4BQ(0.025g) + TiO_2 (0.25g) + PC(0.5g) + PEO(0.05g) Layer4: Cl_4BQ(0.025g)+ TiO2 (0.25g) +PC(0.5g) + PEO(0.05g Layer5: Cl4BQ(0.1g)+ BQ(0.1g) + PEO(0.05g) Layer6: BQ(0.2g)+PEO(0.05g) Layer7: TiO_2(0.5g) + PEO (0.05g) Al------------	1h after packing	28 °C	1.195	5.132	0.477	2.206	1.051	0.171
			35 °C	1.196	9.019	0.476	4.332	2.060	0.191
			40 °C	1.193	10.930	0.507	5.467	2.773	0.213
		48h after packing	28 °C	1.191	8.858	0.441	4.171	1.839	0.173
			35 °C	1.186	12.430	0.451	6.270	2.862	0.174
			40 °C	1.176	13.690	0.504	6.903	3.477	0.216
5	Gr-------------- Layer1: TiO_2(0.5g) + PEO (0.05g) Layer2: N-benzylbenzimidazole(0.208g) + Cl4BQ(0.0.25g) + PEO (0.05g) Layer3: Cl_4BQ(0.025g) + TiO_2 (0.25g) + PC(0.5g) + PEO(0.05g) Layer4: Cl_4BQ(0.025g)+ TiO2 (0.25g) +PC(0.5g) + PEO(0.05g Layer5: Cl4BQ(0.1g)+ BQ(0.1g) + PEO(0.05g) Layer6: BQ(0.2g)+PEO(0.05g) Layer7: TiO_2(0.5g) + PEO (0.05g) Al------------	1h after packing	28 °C	1.195	15.19	0.470	8.256	3.876	0.214
			35 °C	1.190	16.390	0.537	8.959	4.806	0.246
			40 °C	1.193	15.910	0.579	8.715	5.048	0.266
		48h after packing	28 °C	1.228	11.570	0.489	5.994	2.931	0.206
			35 °C	1.205	14.80	0.544	8.058	4.385	0.246
			40 °C	1.193	16.870	0.577	9.325	5.380	0.267

Cell Configuration 4



(Entries 6-7)

Cell Configuration 5



(Entries 8-10)

6	Gr----------------- Layer1: TiO_2(0.5g) + PEO(0.05g) Layer2: TiO2 (0.5g) + Cl_4BQ(0.25g) +PC (0.5g) + PEO(0.05g) Layer3: TM-O-PDA (0.164g) +BQ(0.11g)+PC (0.5g) + PEO (0.1g) heat coat on Al side before packing Layer4: TiO_2(0.5g) + BQ(0.44g) + PC (0.5g) + PEO(0.05g) Layer5: TiO_2(0.5g) + PEO(0.05g) Al------------------	1h after packing	28 °C	1.108	10770	0.581	5.428	3.154	0.264
			35 °C	1.121	11.290	0.577	5.725	3.302	0.261
			40 °C	1.132	12.260	0.569	6.332	3.601	0.260
		48h after packing	28 °C	1.190	7.17	0.476	3.583	1.704	0.200
			35 °C	1.178	8.238	0.524	4.064	2.130	0.220
			40 °C	1.160	8.915	0.518	4.367	2.262	0.219
7	Gr----------------- Layer1: TiO_2(0.5g) + PEO(0.05g) Layer2: TiO2 (0.5g) + Cl_4BQ(0.25g) +PC (0.5g) + PEO(0.05g) Layer3: MeN-benzimidazole (0.082g) +BQ(0.11g)+PC (0.5g) + PEO (0.1g) heat coat on Al side before packing Layer4: TiO_2(0.5g) + BQ(0.44g) + PC (0.5g) + PEO(0.05g) Layer5: TiO_2(0.5g) + PEO(0.05g) Al------------------	1h after packing	28 °C	1.145	23.190	0.516	10.600	5.478	0.206
			35 °C	1.155	31.700	0.533	15.710	8.315	0.229
			40 °C	1.161	35.150	0.522	17.960	9.906	0.243
		48h after packing	28 °C	1.227	8.072	0.547	3.351	1.834	0.185
			35 °C	1.204	10.090	0.520	5.121	2.661	0.219
			40 °C	1.188	14.354	0.551	1.329	4.036	0.237
8	Gr----------------- Layer1: TiO_2(0.5g) + PEO(0.05g) Layer2: TiO2 (0.5g) + Cl_4BQ(0.25g) +PC (0.5g) + PEO(0.05g) Layer3: TM-*o*-PDA (0.164g) +Me_2SO_2 (0.094)+PC	1h after packing	28 °C	1.074	17.05	0.546	9.241	5.046	0.275
			35 °C	1.088	16.460	0.559	9.059	5.067	0.283
			40 °C	1.065	17.82	0.561	10.780	6.040	0.318

	(0.5g) + PEO (0.1g) heat coat on Al side before packing Layer4: TiO_2(0.5g) +Me_2SO_2 (0.188g) + PC (0.5g) + PEO(0.05g) Layer5: TiO_2(0.5g) + PEO(0.05g) Al------------------	48h after packing	28 ºC	1.001	4.228	0.492	2.221	1.093	0.258
			35 ºC	0.971	5.381	0.476	2.876	1.372	0.262
			40 ºC	0.987	6.079	0.502	3.161	1.588	0.265
9	Gr----------------- Layer1: TiO_2(0.5g) + PEO(0.05g) Layer2: TiO2 (0.5g) + Cl_4BQ(0.25g) +PC (0.5g) + PEO(0.05g) Layer3: N-benzylbenzimidazole(0.208g) +Me_2SO_2 (0.094)+PC (0.5g) + PEO (0.1g) heat coat on Al side before packing Layer4: TiO_2(0.5g) +Me_2SO_2 (0.188g) + PC (0.5g) + PEO(0.05g) Layer5: TiO_2(0.5g) + PEO(0.05g) Al------------------	1h after packing	28 ºC	1.146	18.840	0.600	13.500	8.101	0.375
			35 ºC	1.157	20.610	0.605	14.600	8.825	0.370
			40 ºC	1.143	20.800	0.611	14.650	8.952	0.377
		48h after packing	28 ºC	1.169	13.04	0.532	5.739	3.052	0.200
			35 ºC	1.165	12.140	0.550	10.620	5.841	0.413
			40 ºC	1.148	11.344	0.588	11.340	6.644	0.510
10	Gr----------------- Layer1: TiO_2(0.5g) + PEO(0.05g) Layer2: TiO2 (0.5g) + Cl_4BQ(0.25g) +PC (0.5g) + PEO(0.05g) Layer3: MeN-imidazole (0.082g) +Me_2SO_2 (0.094)+PC (0.5g) + PEO (0.1g) heat coat on Al side before packing Layer4: TiO_2(0.5g) +Me_2SO_2 (0.188g) + PC (0.5g) + PEO(0.05g) Layer5: TiO_2(0.5g) + PEO(0.05g) Al------------------	1h after packing	28 ºC	1.147	32.850	0.598	20.030	11.970	0.318
			35 ºC	1.150	40.370	0.641	20.480	13.140	0.283
			40 ºC	1.144	38.780	0.617	23.140	14.270	0.322
		48h after packing	28 ºC	1.156	13.04	0.515	6.461	3.712	0.328
			35 ºC	1.142	8.538	0.647	6.047	3.920	0.402
			40 ºC	1.123	8.747	0.633	6.238	3.945	0.402

5.5 References

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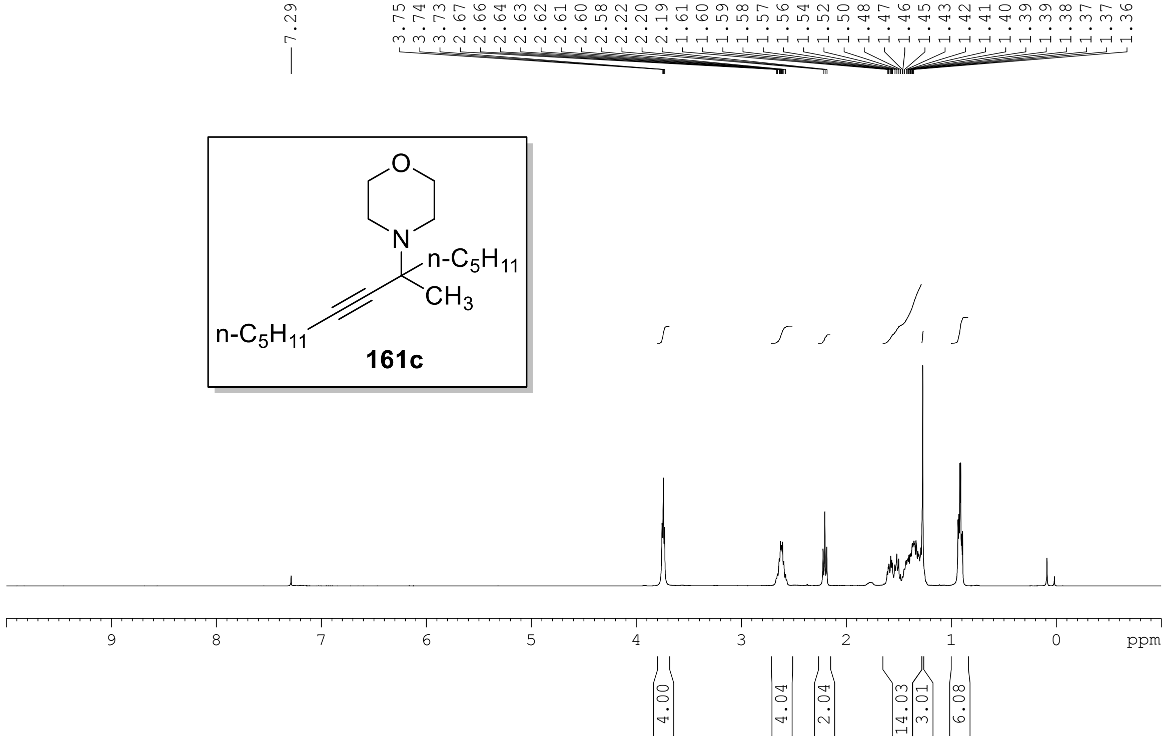
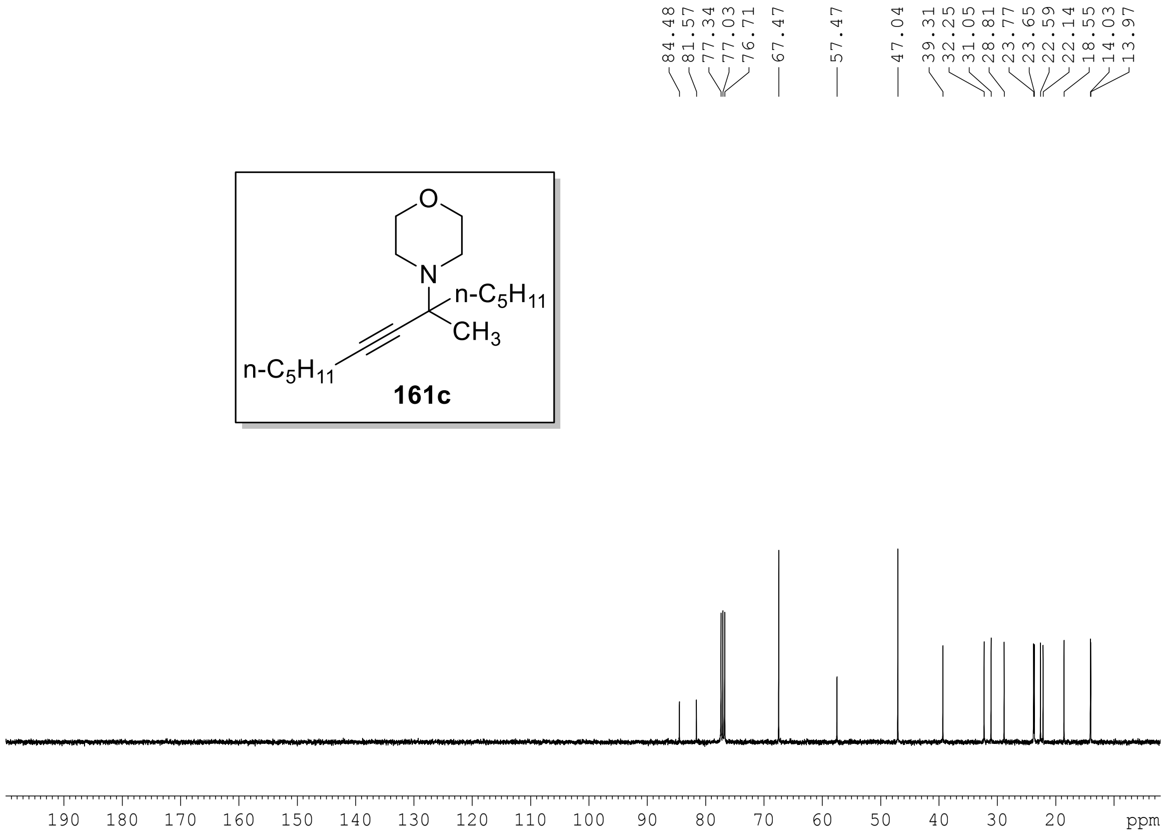
Appendix I

Representative Spectra

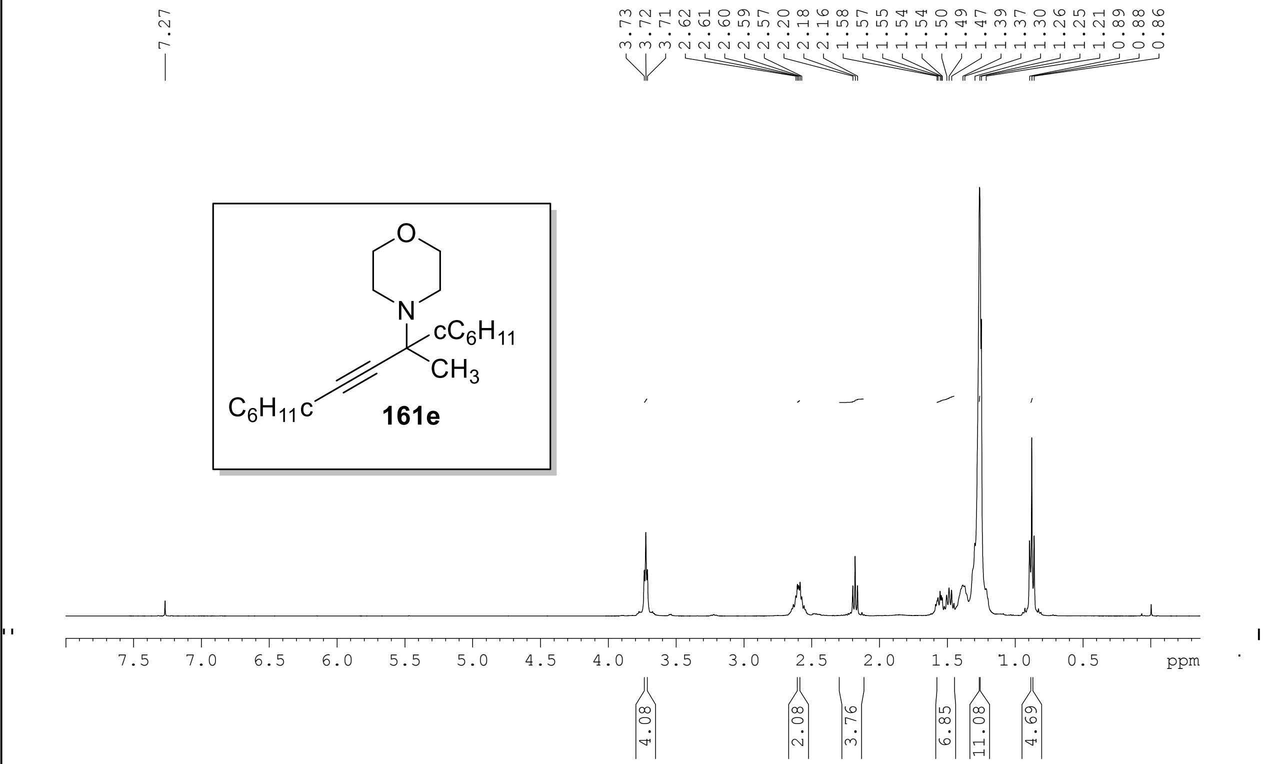
Spectrum No. 1 (Chapter 1, Section 1.2.1) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



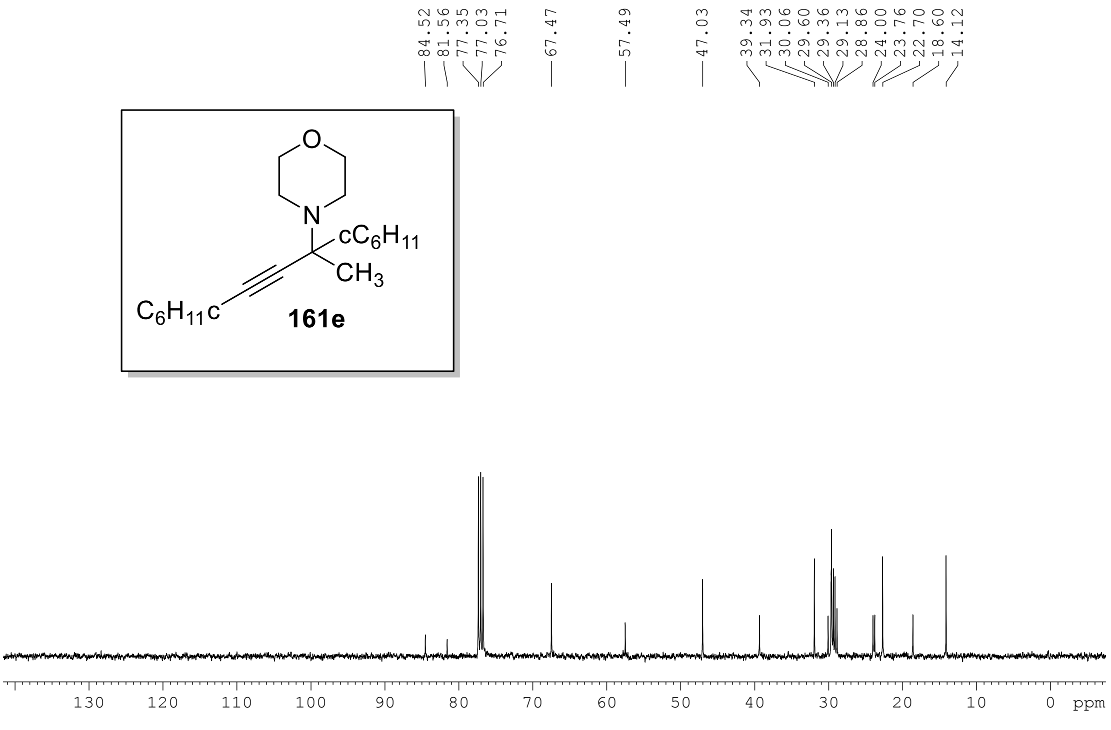
Spectrum No. 2 (Chapter 1, Section 1.2.1) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



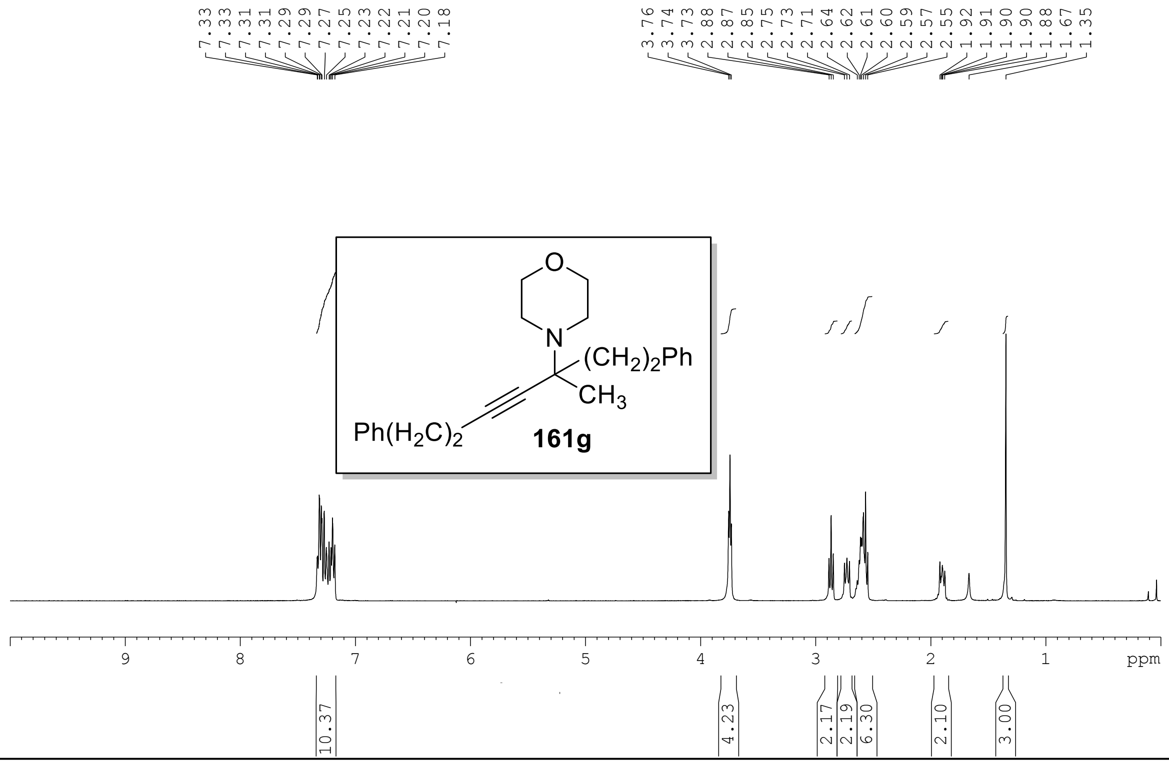
Spectrum No. 3 (Chapter 1, Section 1.2.1) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



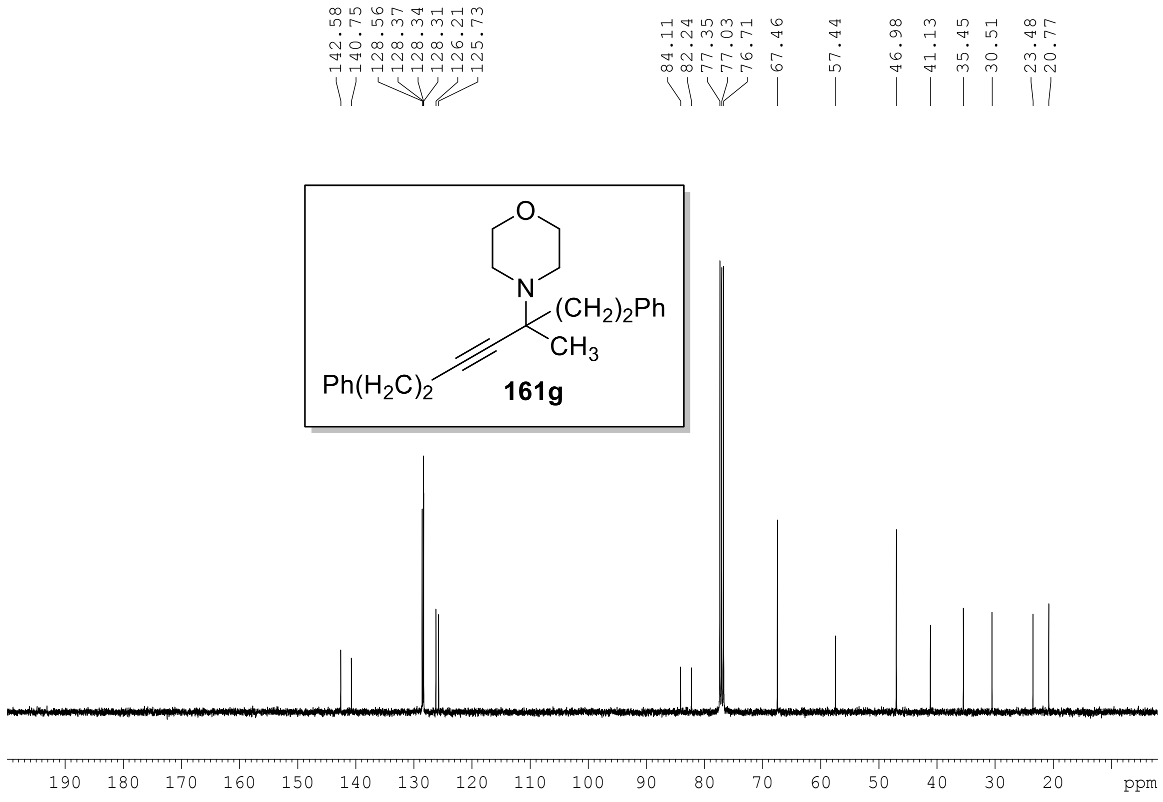
Spectrum No. 4 (Chapter 1, Section 1.2.1) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



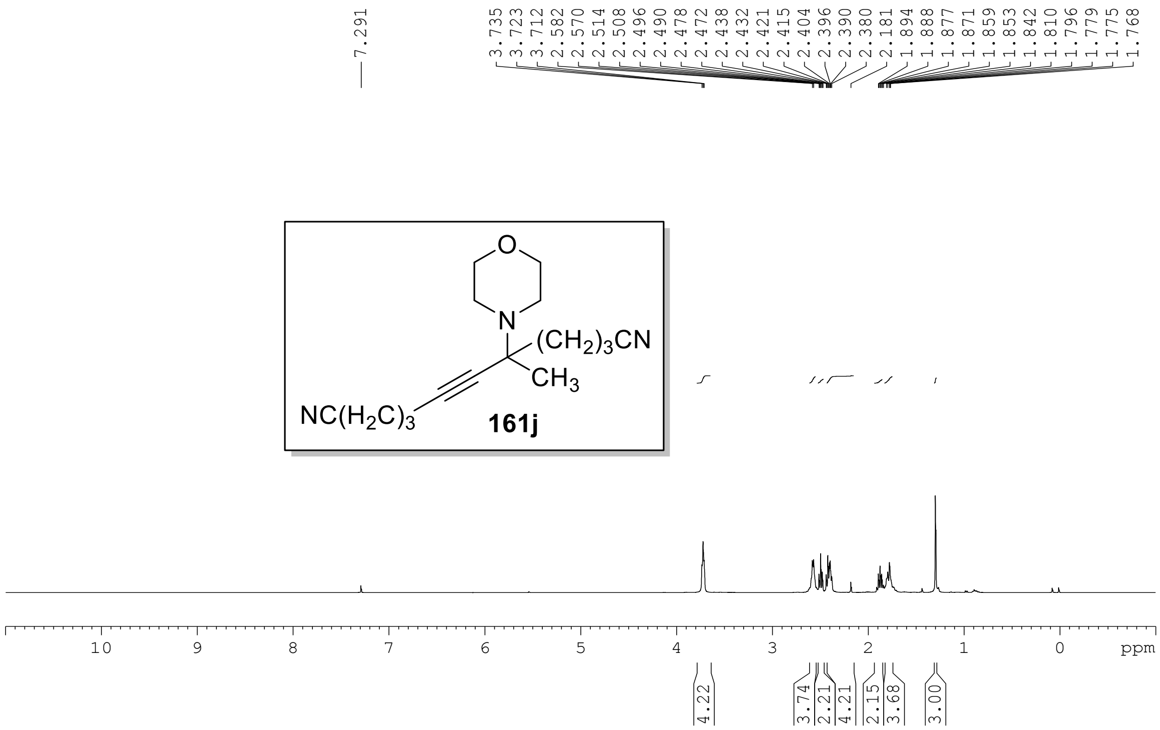
Spectrum No. 5 (Chapter 1, Section 1.2.1) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



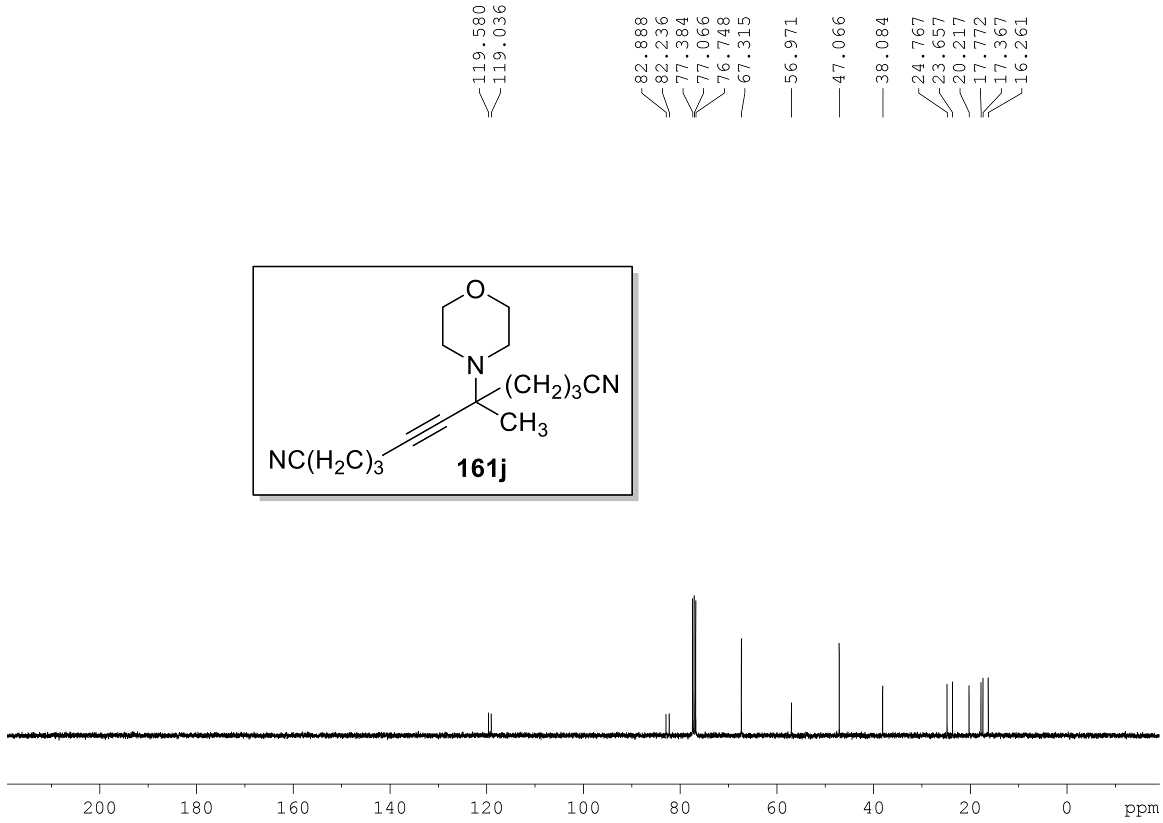
Spectrum No. 6 (Chapter 1, Section 1.2.1) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



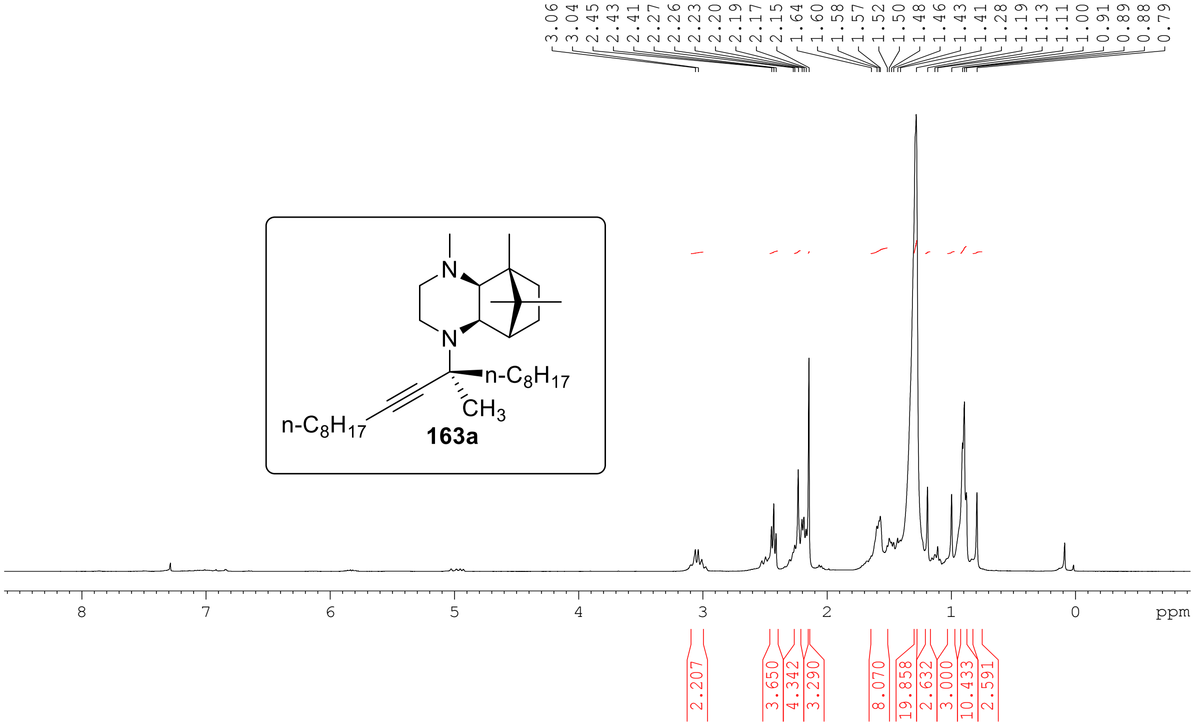
Spectrum No. 7 (Chapter 1, Section 1.2.1) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



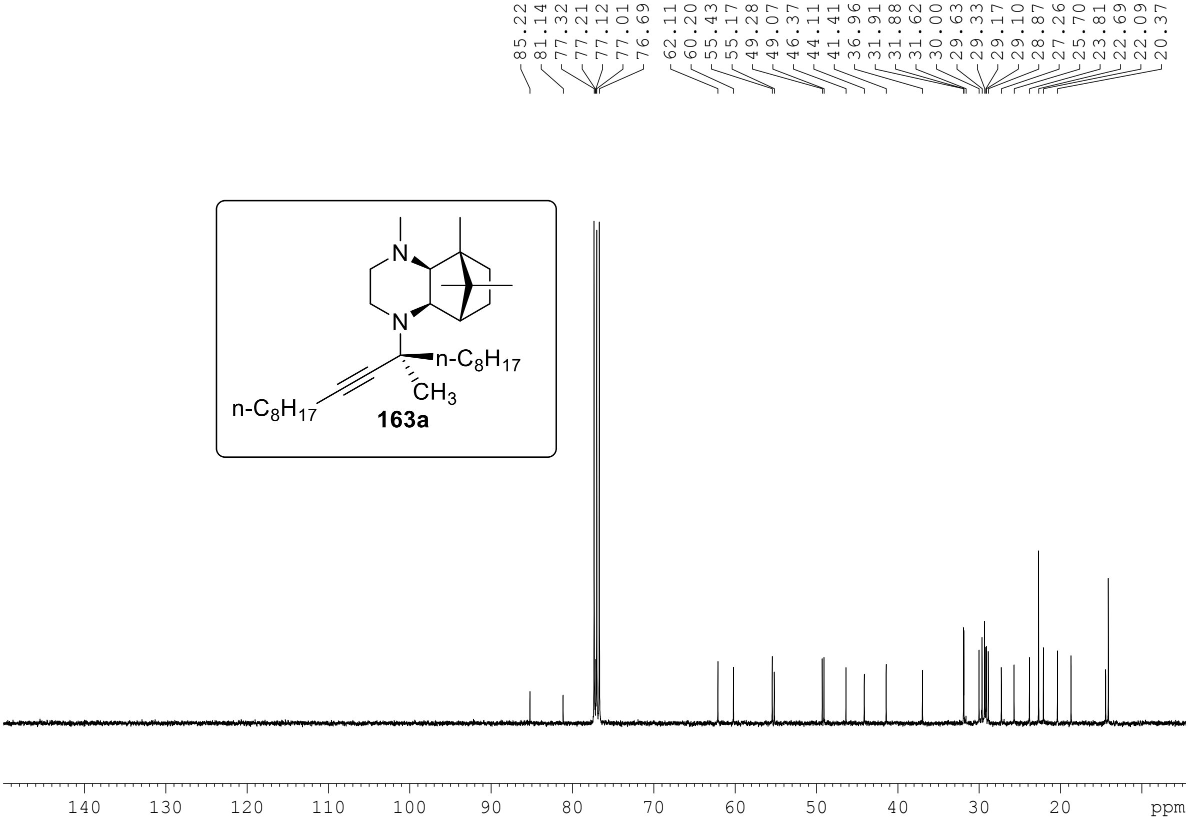
Spectrum No. 8 (Chapter 1, Section 1.2.1) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



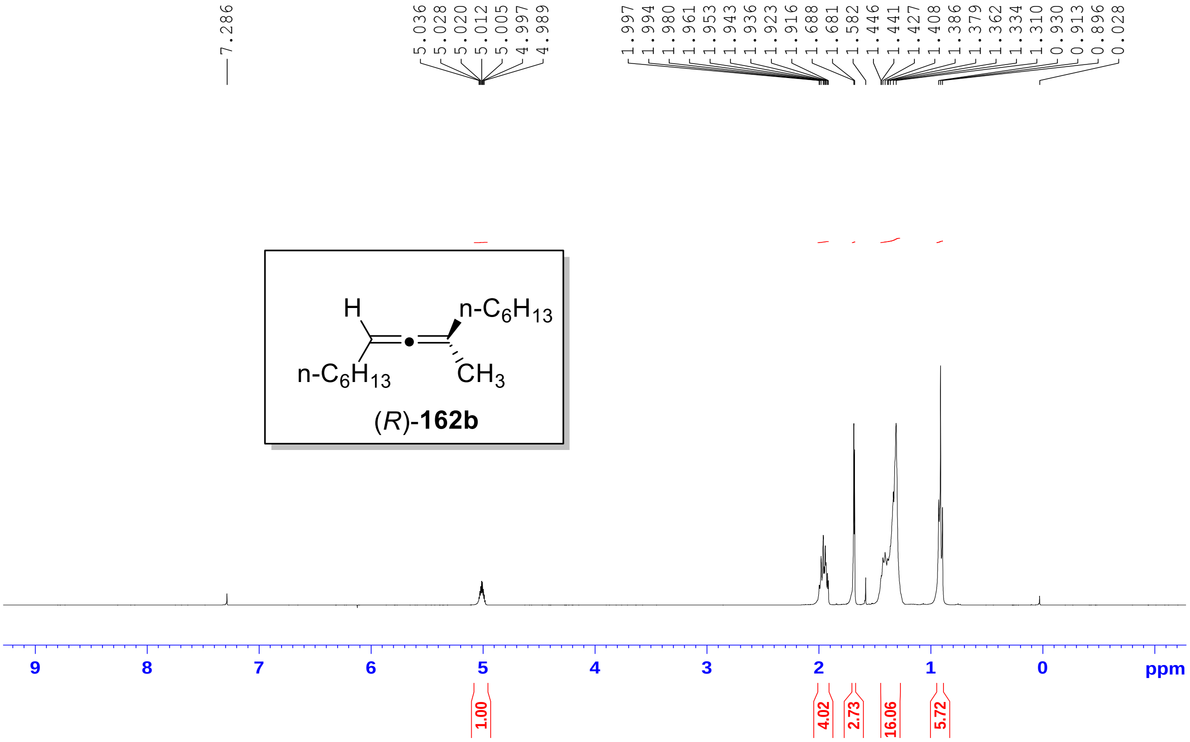
Spectrum No. 9 (Chapter 1, Section 1.2.3) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



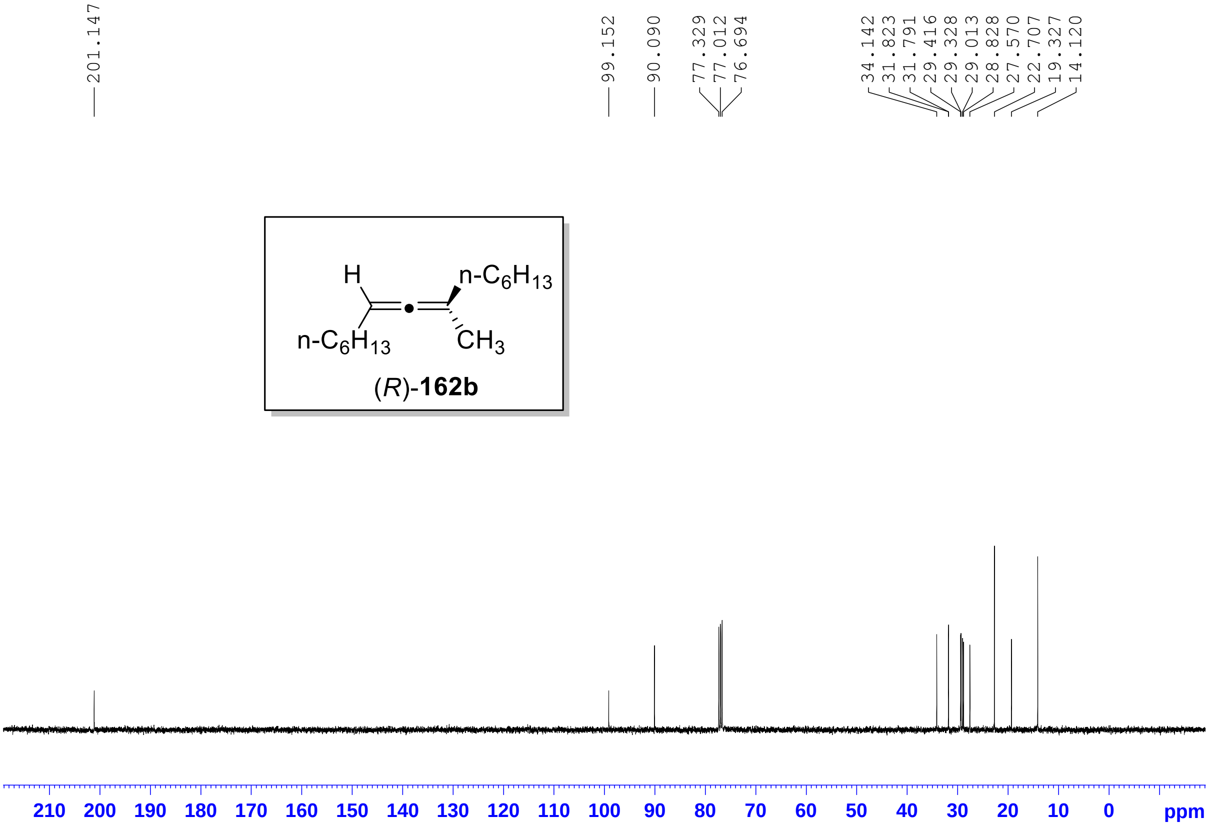
Spectrum No. 10 (Chapter 1, Section 1.2.3) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



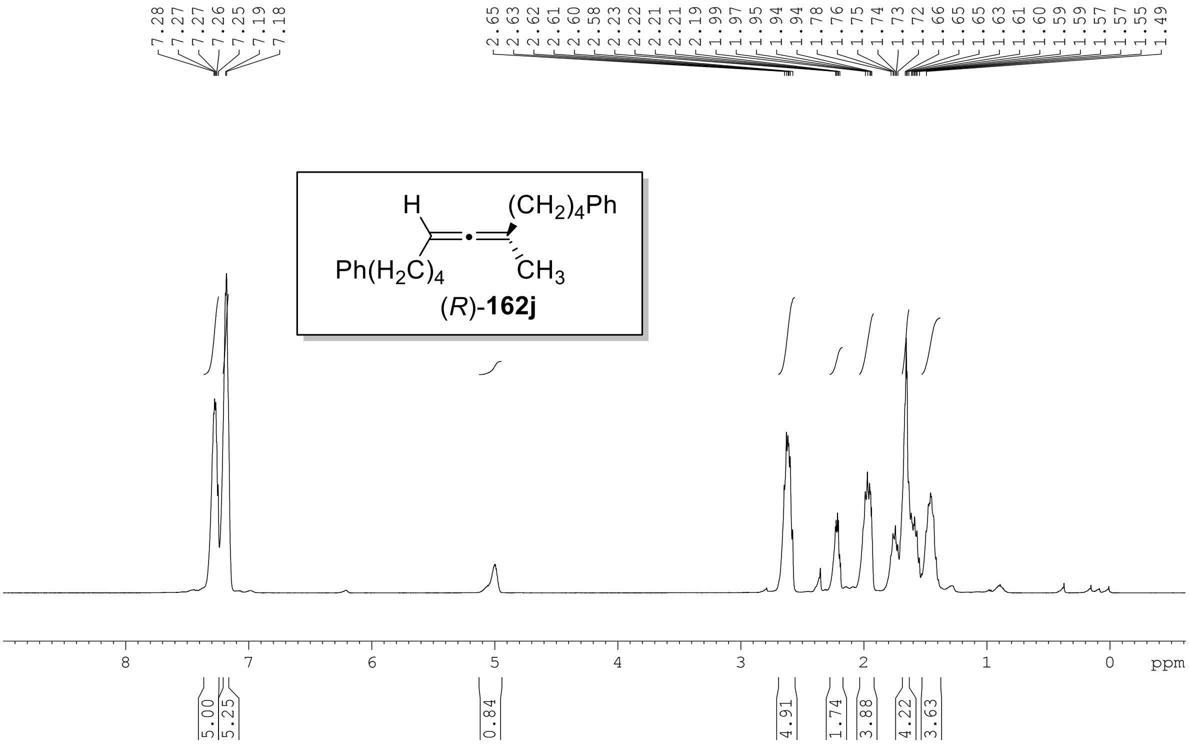
Spectrum No. 11 (Chapter 1, Section 1.2.4) ^{1}H NMR Spectrum (400 MHz, CDCl$_3$)



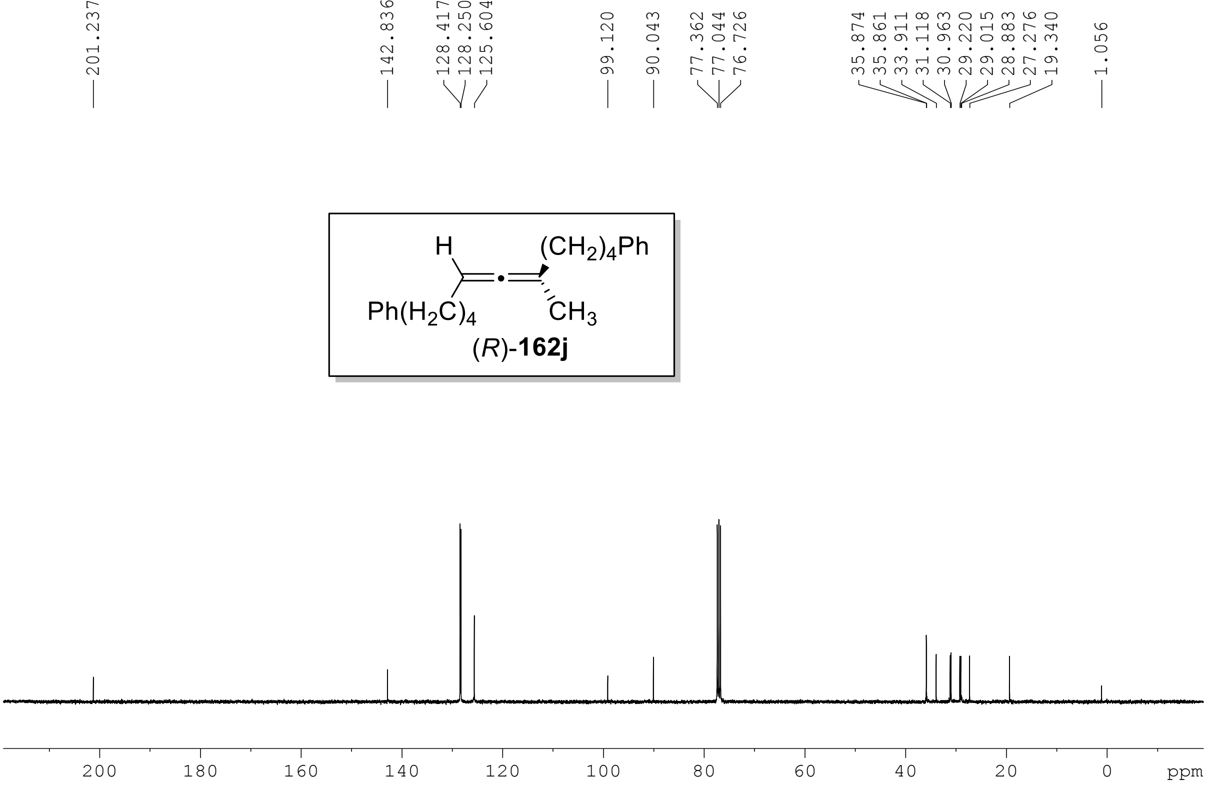
Spectrum No. 12 (Chapter 1, Section 1.2.4) ^{13}C NMR Spectrum (100 MHz, CDCl$_3$)



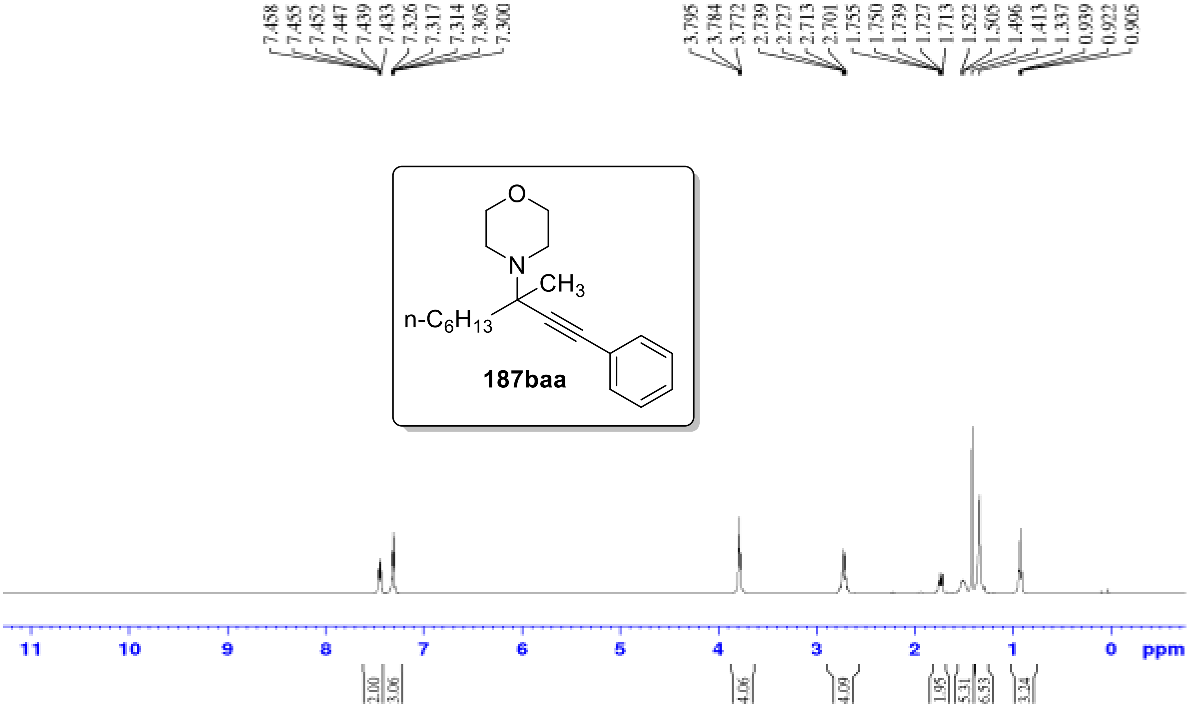
Spectrum No. 13 (Chapter 1, Table 4) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



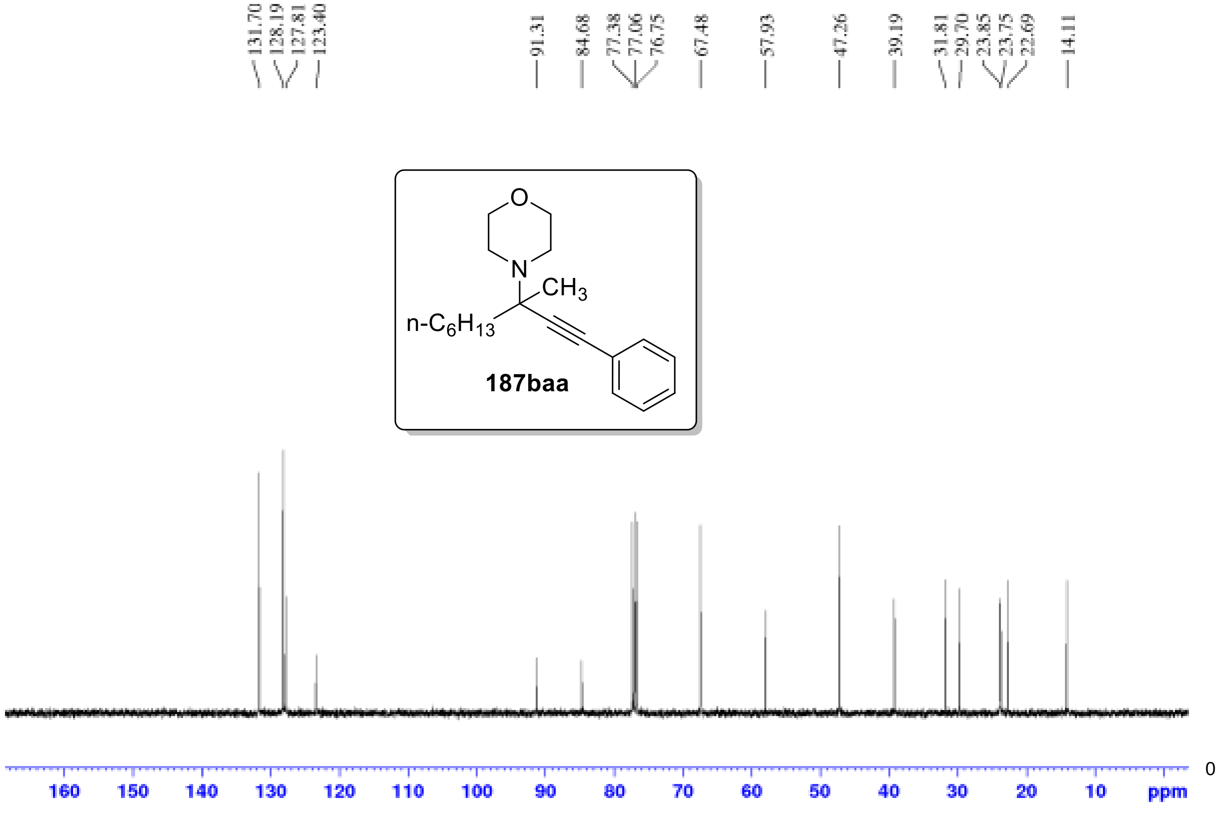
Spectrum No. 14 (Chapter 2, Table 4) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



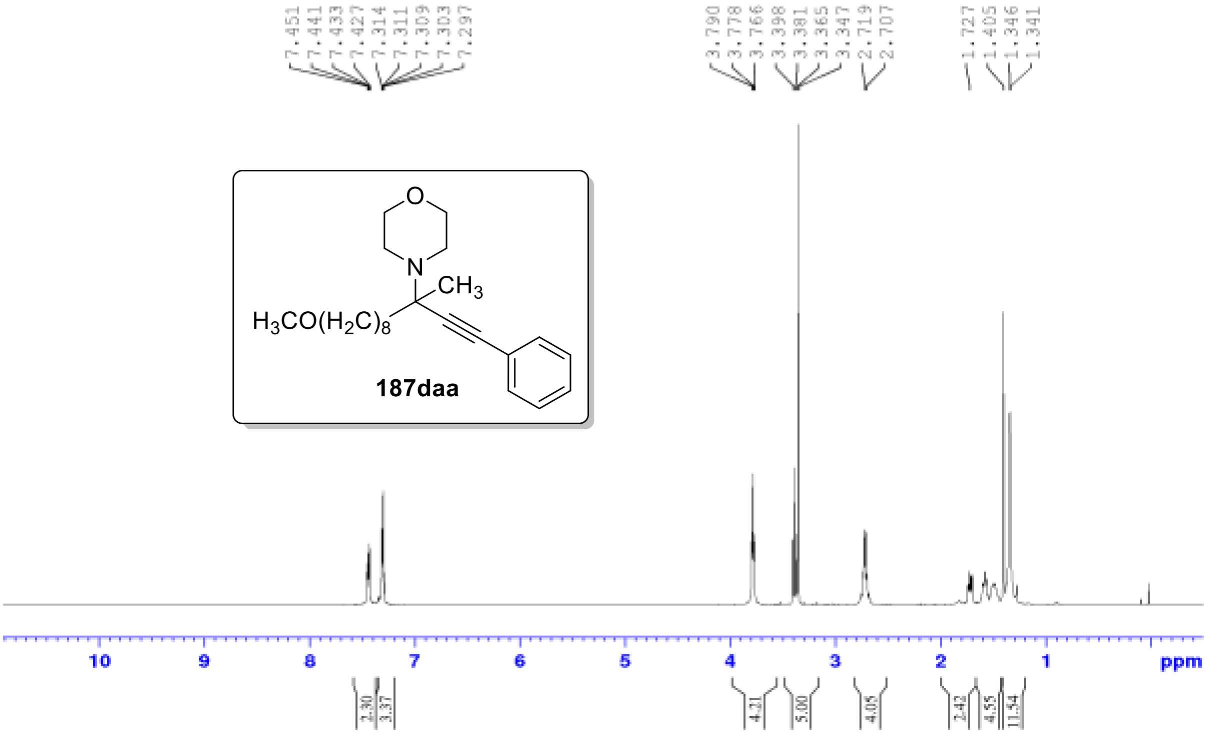
Spectrum No. 15 (Chapter 1, Table 6) ^{1}H NMR Spectrum (400 MHz, CDCl$_3$)



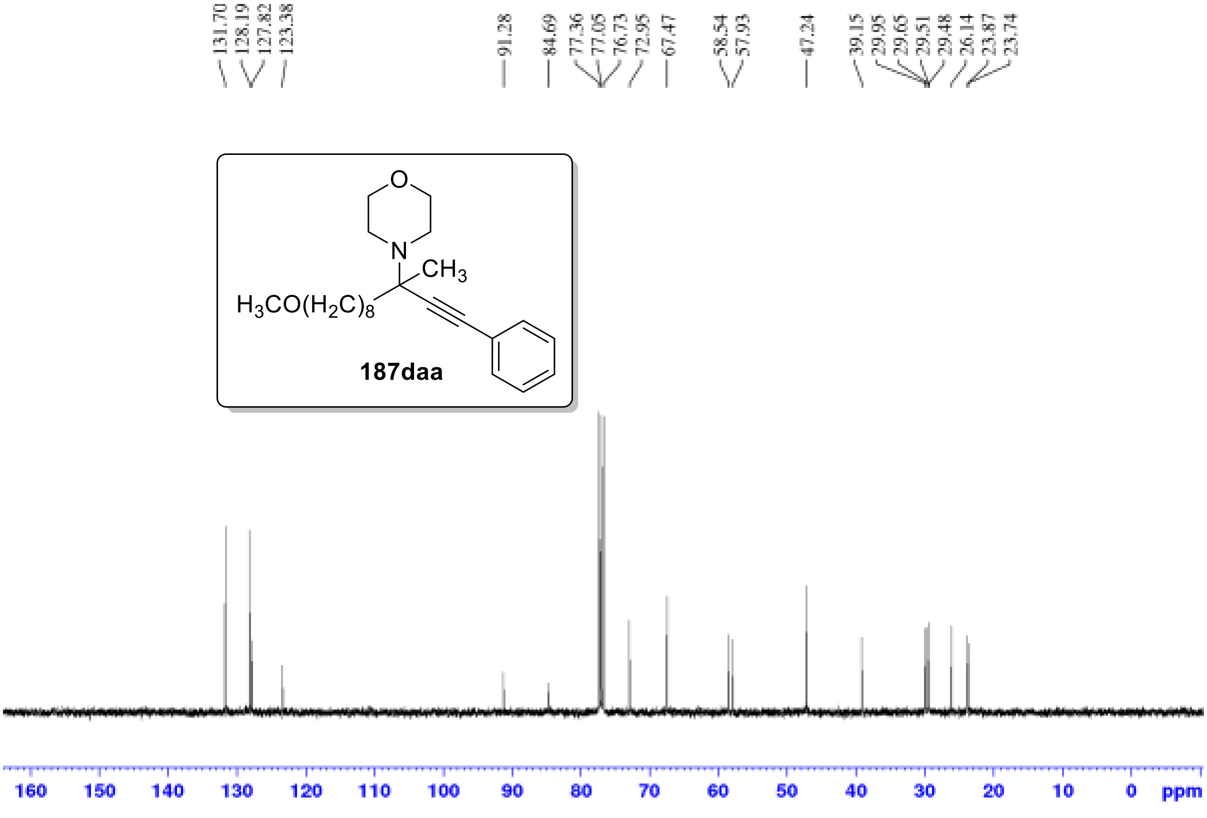
Spectrum No. 16 (Chapter 1, Table 6) ^{13}C NMR Spectrum (100 MHz, CDCl$_3$)



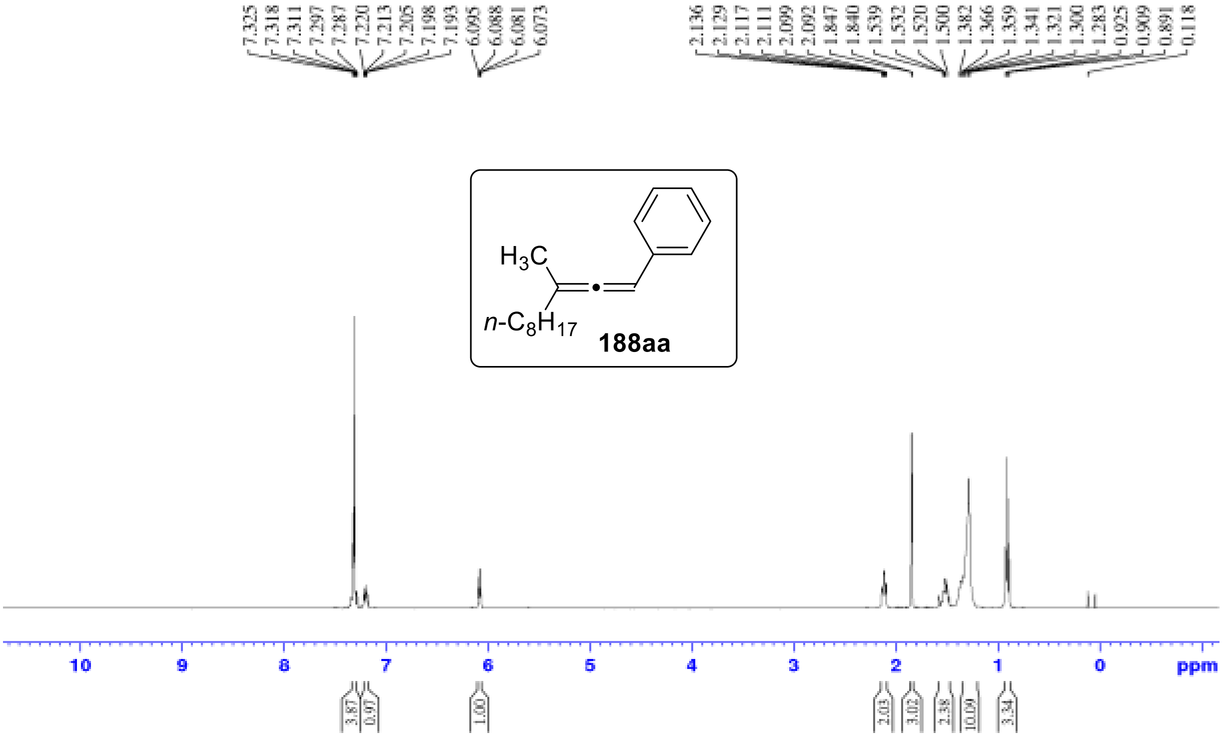
Spectrum No. 17 (Chapter 1, Table 6) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



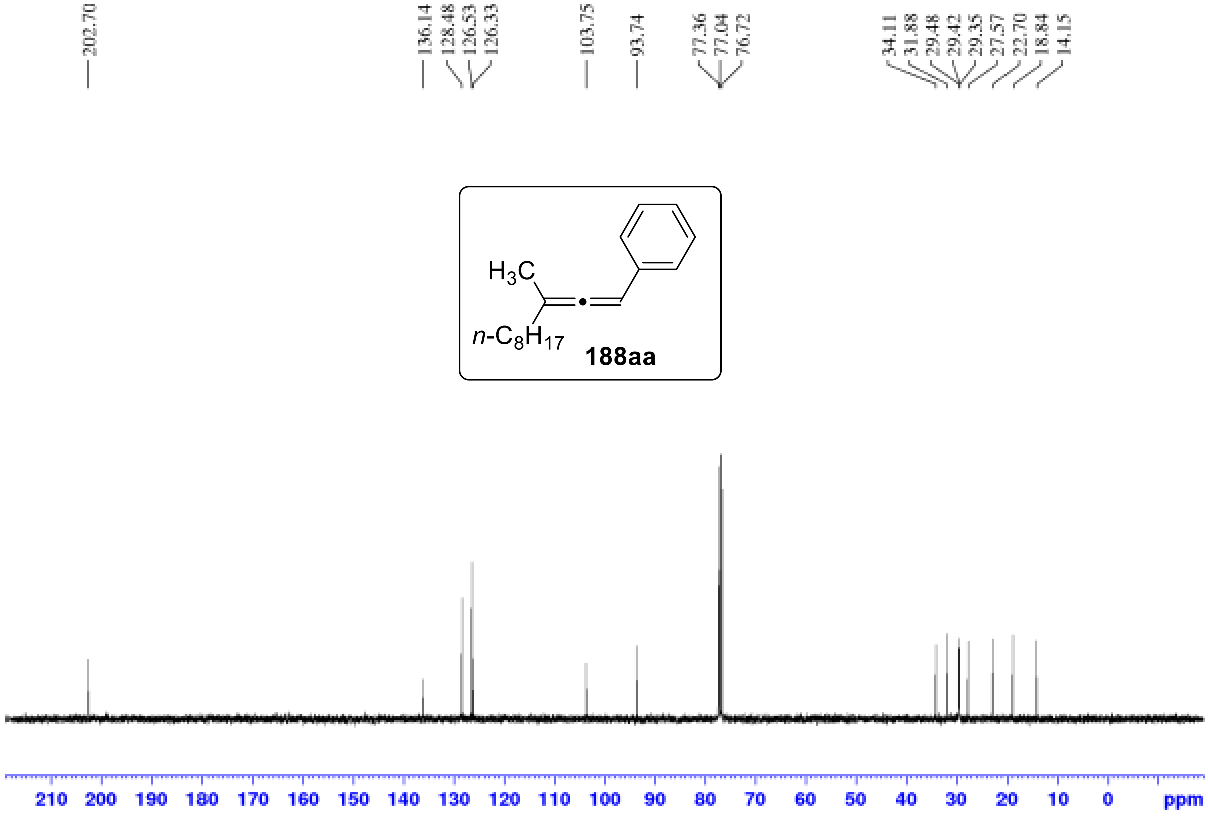
Spectrum No. 18 (Chapter 1, Table 6) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



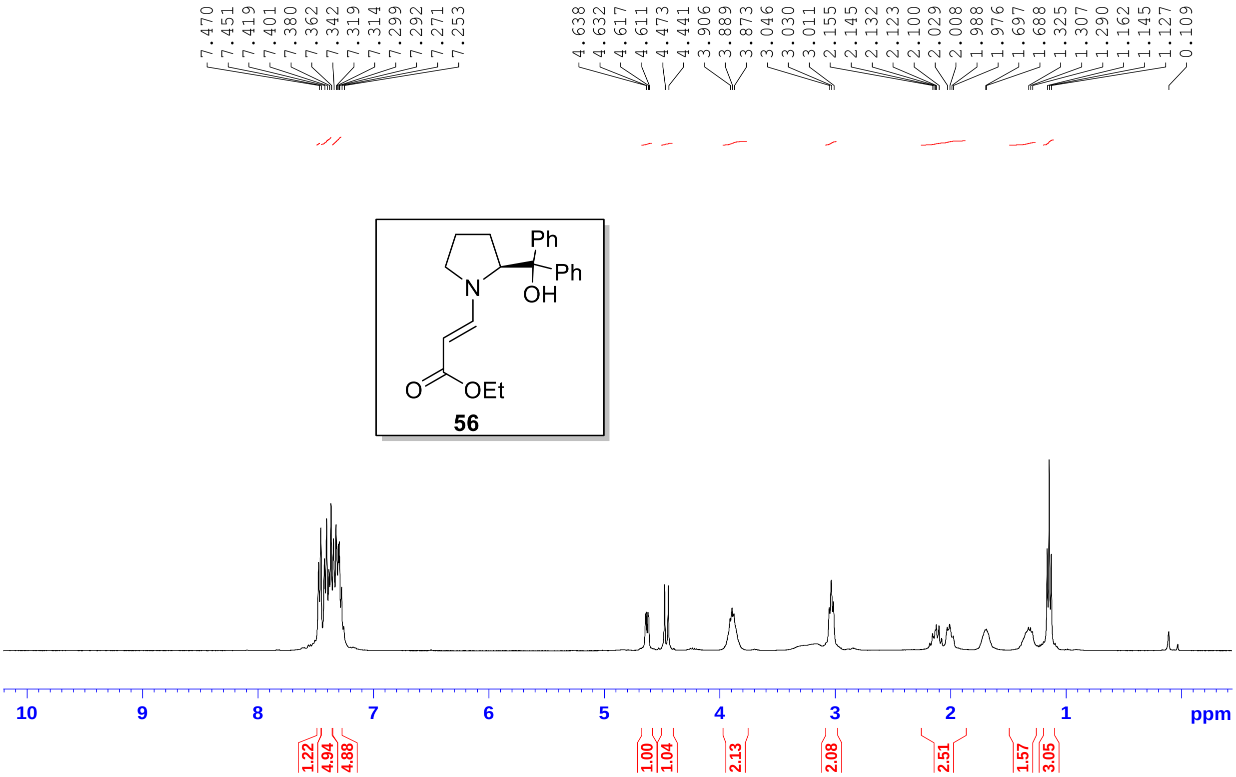
Spectrum No. 19 (Chapter 1, Table 7) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



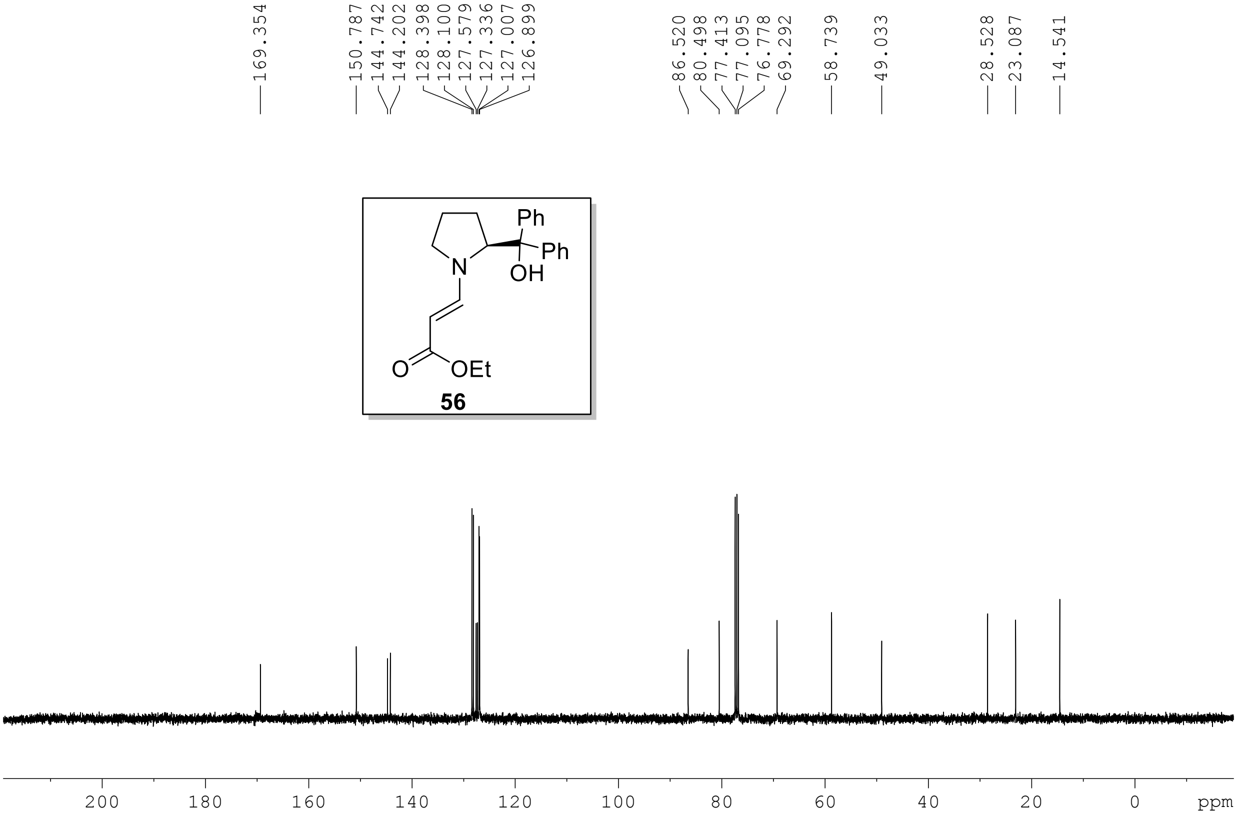
Spectrum No. 20 (Chapter 1, Table 7) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



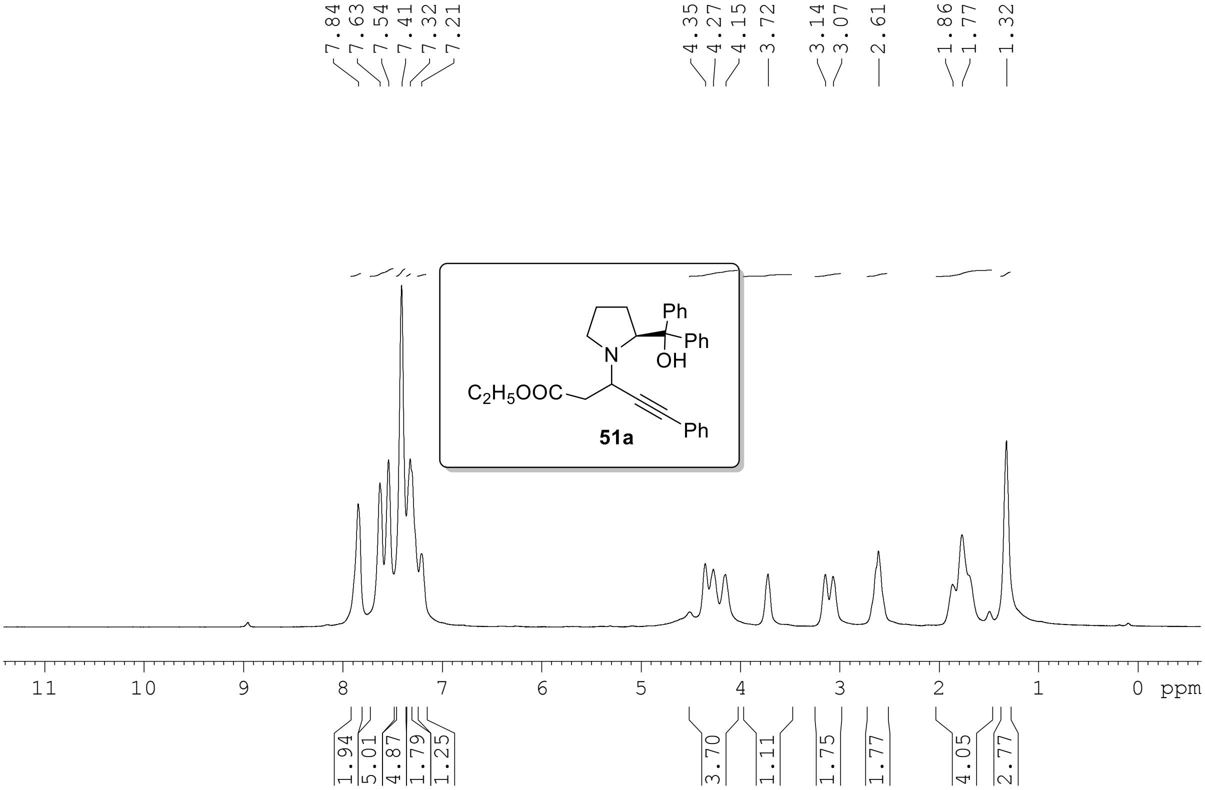
Spectrum No. 21 (Chapter 2, Section 2.2.6) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



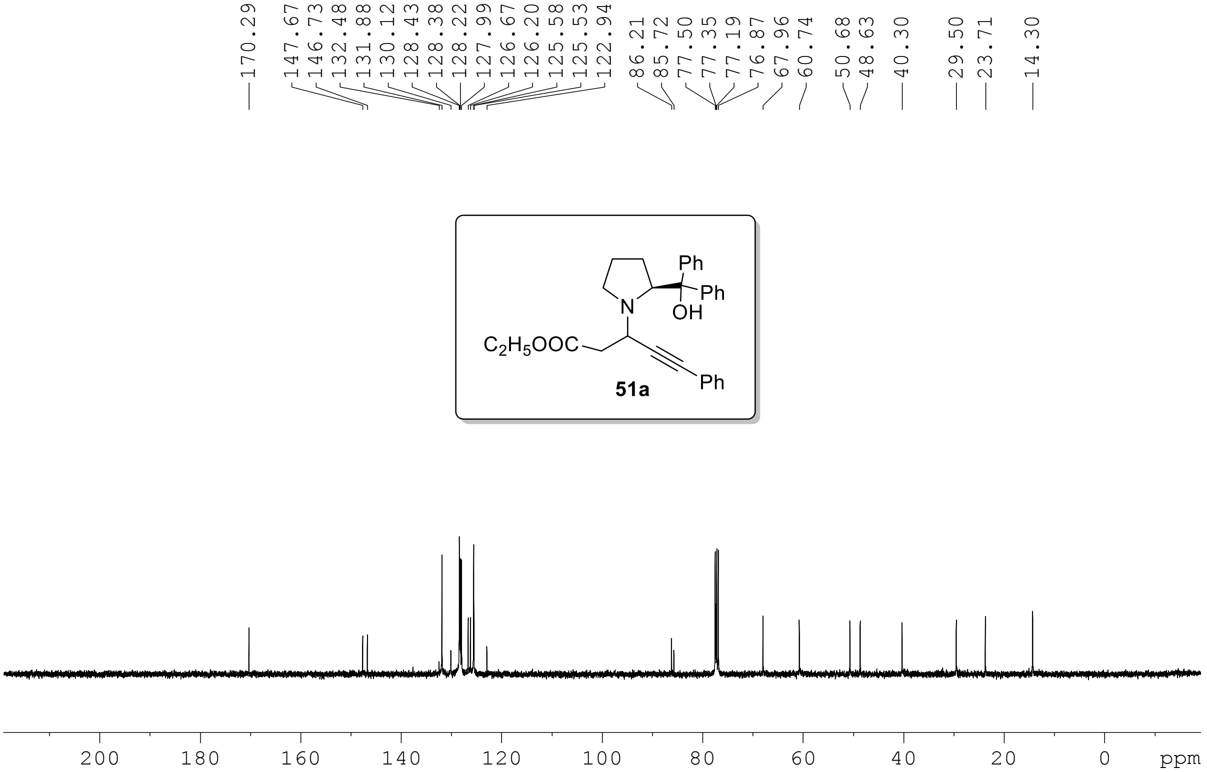
Spectrum No. 22 (Chapter 2, Section 2.2.6) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



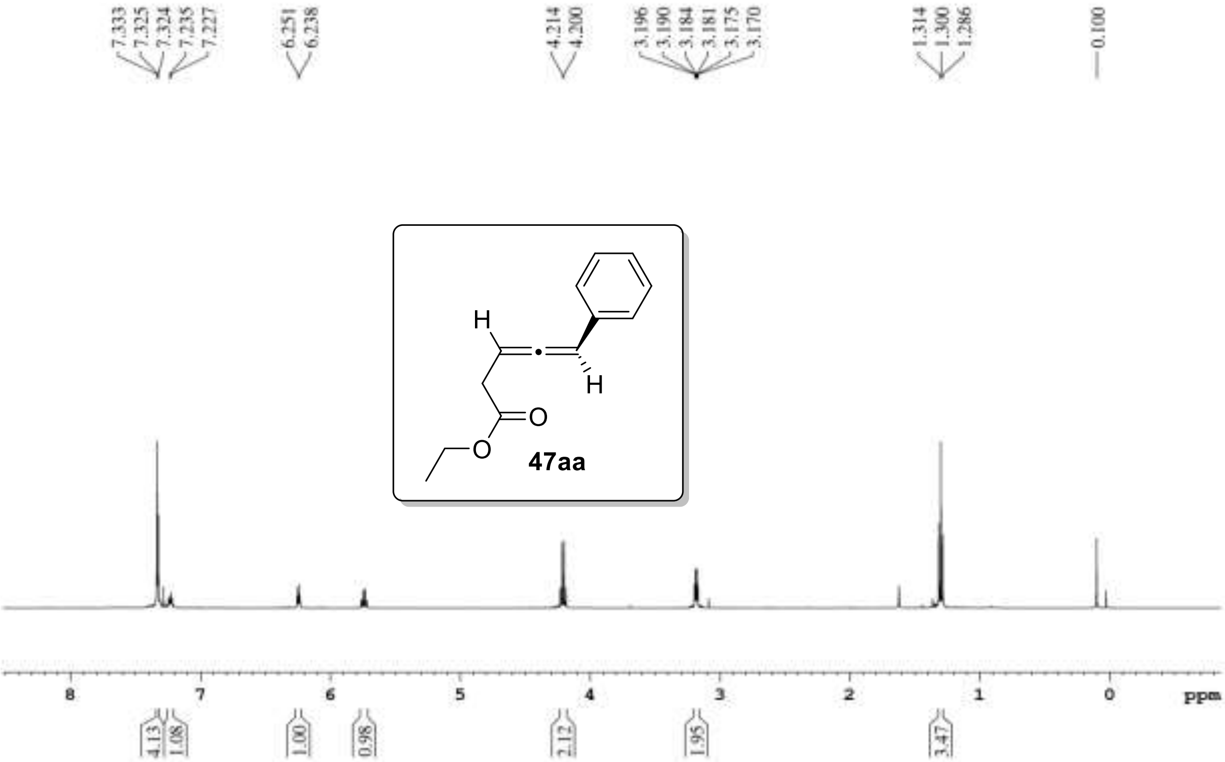
Spectrum No. 23 (Chapter 2, Section 2.2.5) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



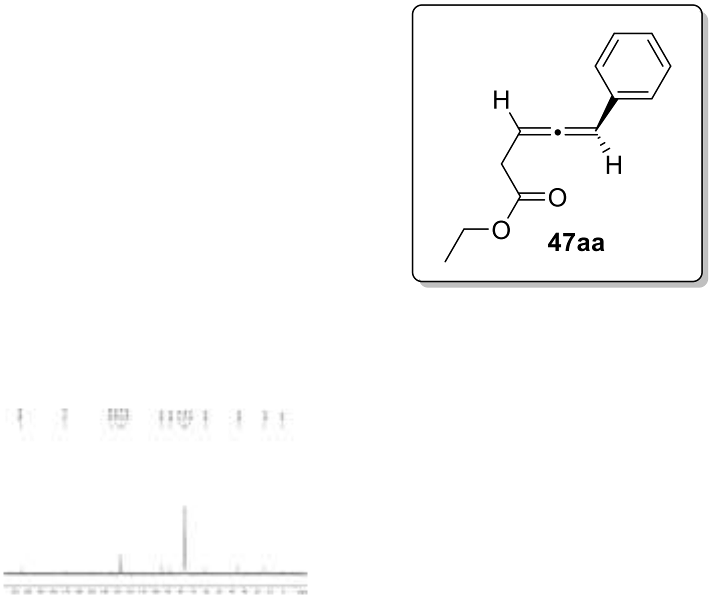
Spectrum No. 24 (Chapter 2, Section 2.2.5) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



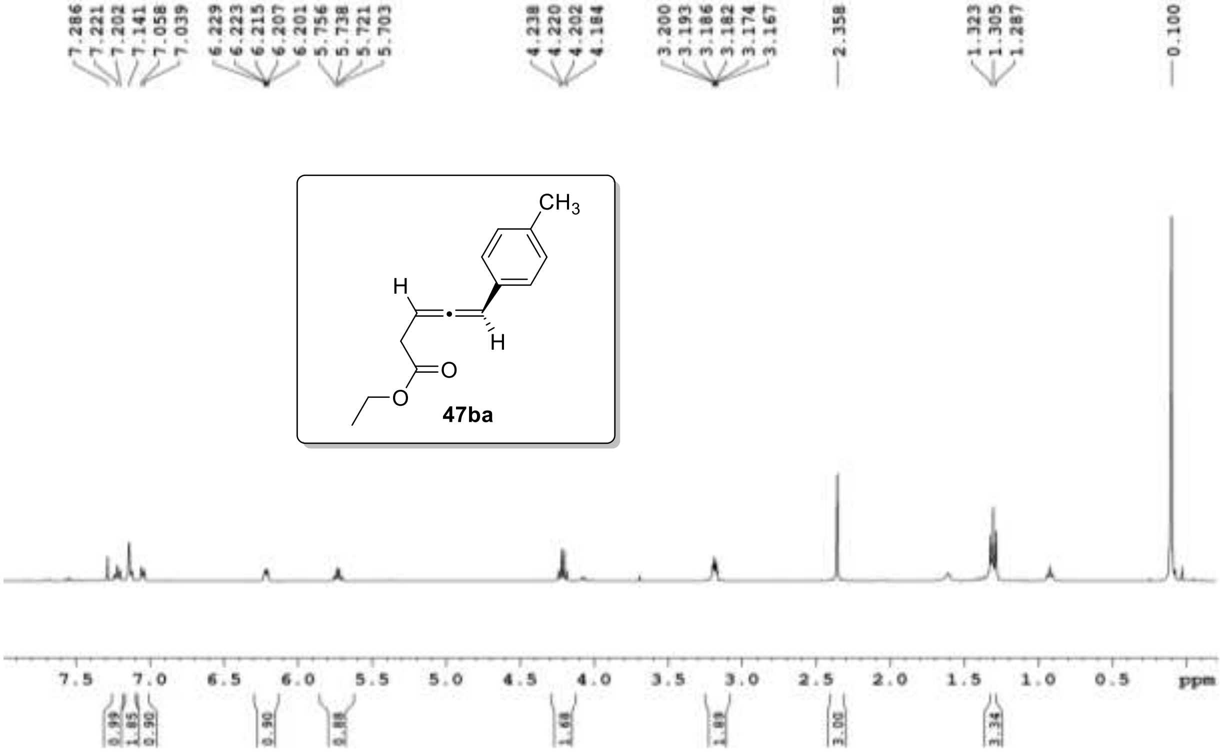
Spectrum No. 25 (Chapter 2, Table 3) ^{1}H NMR Spectrum (400 MHz, CDCl$_3$)



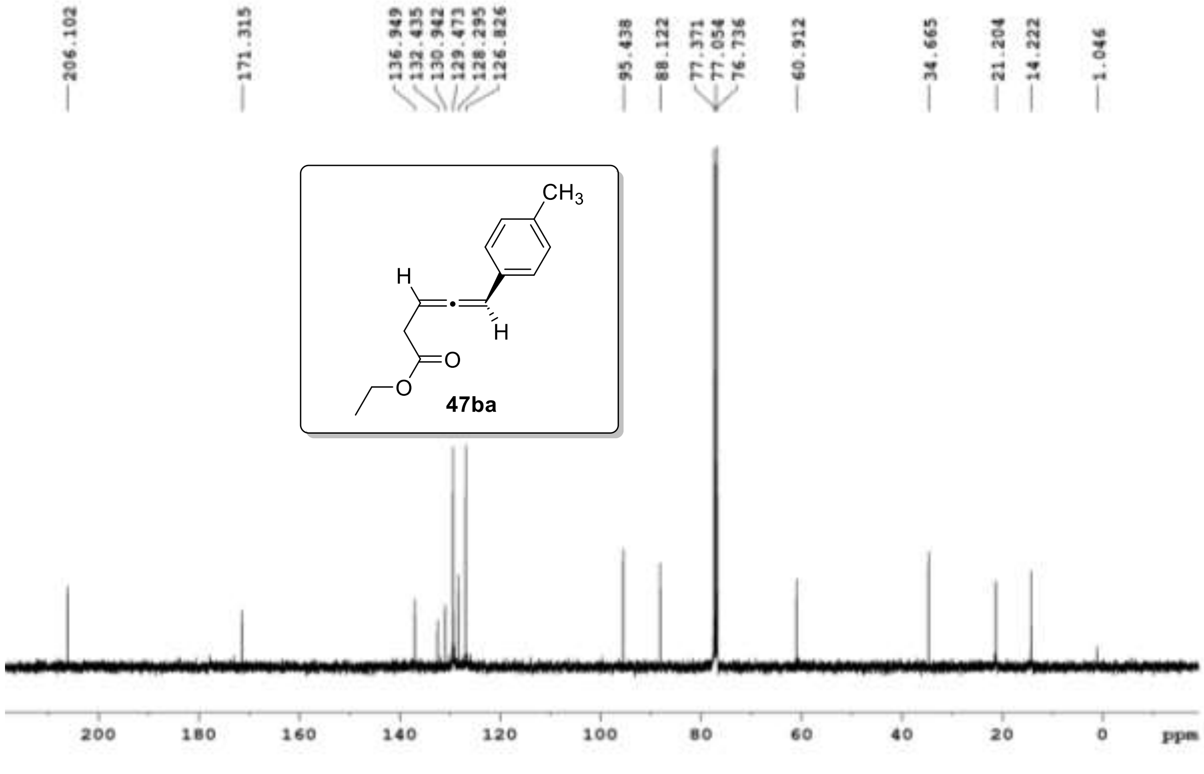
Spectrum No. 26 (Chapter 2, Table 3) ^{13}C NMR Spectrum (100 MHz, CDCl$_3$)



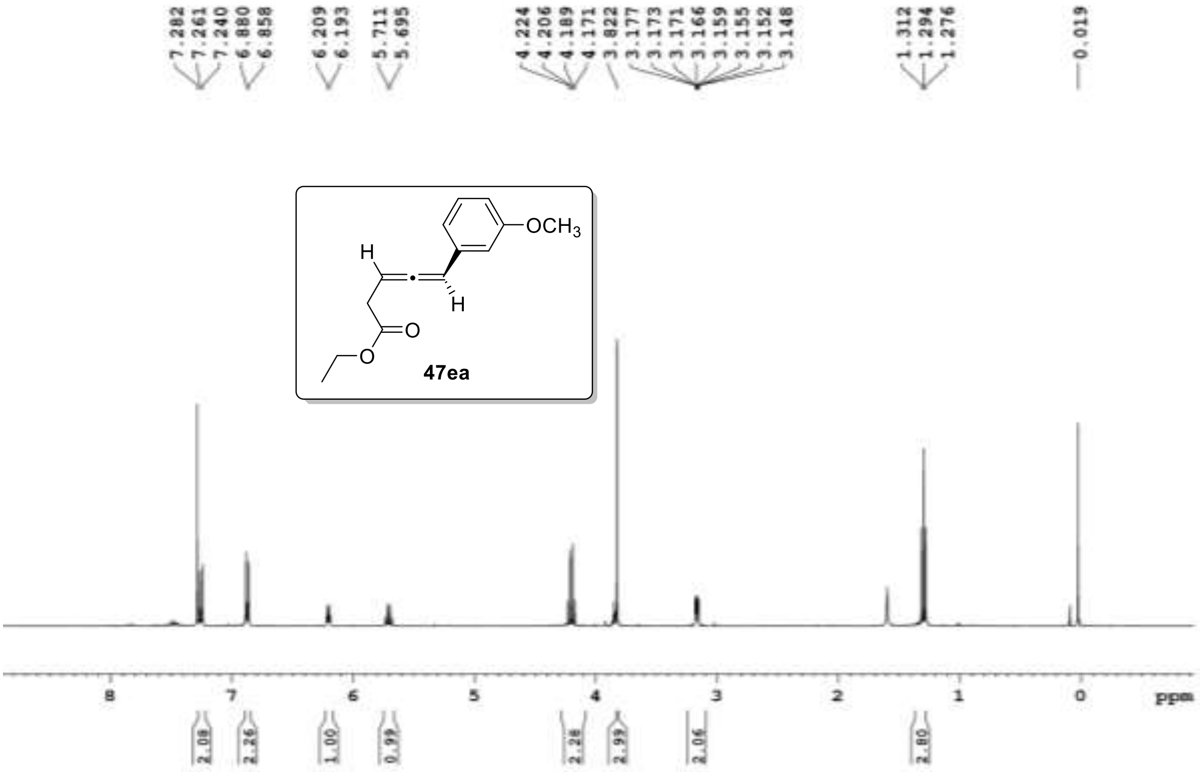
Spectrum No. 27 (Chapter 2, Table 3) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



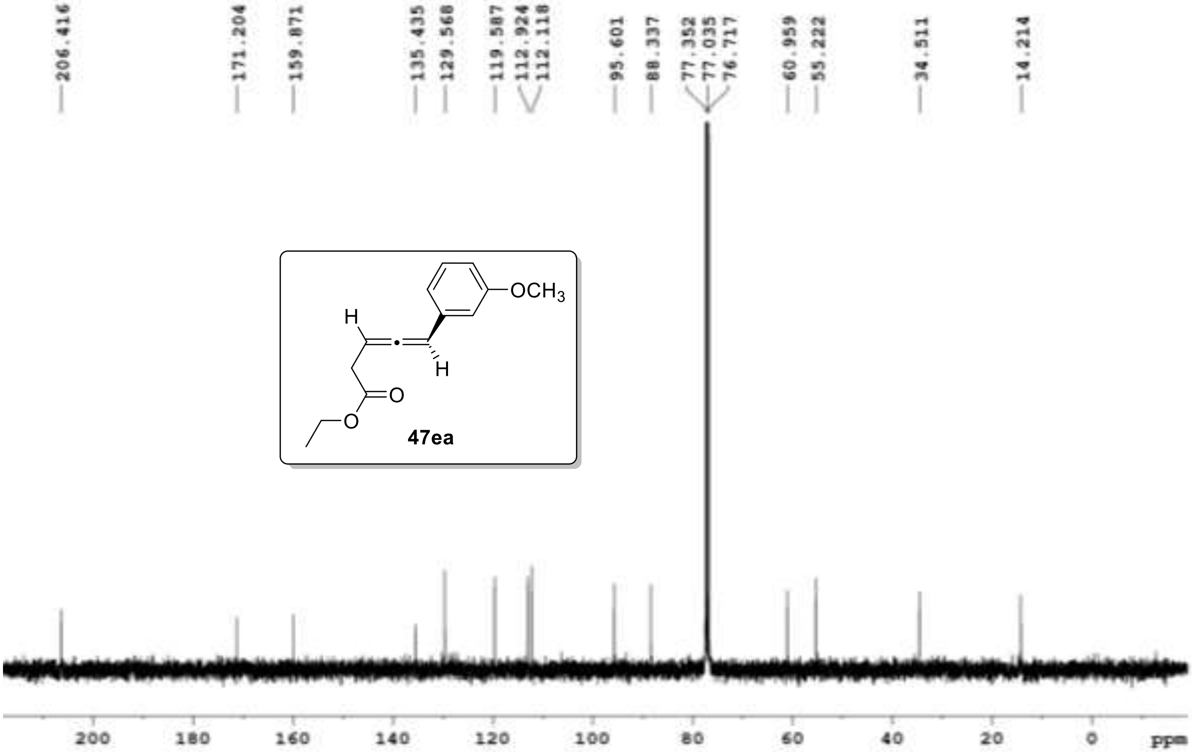
Spectrum No. 28 (Chapter 2, Table 3) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



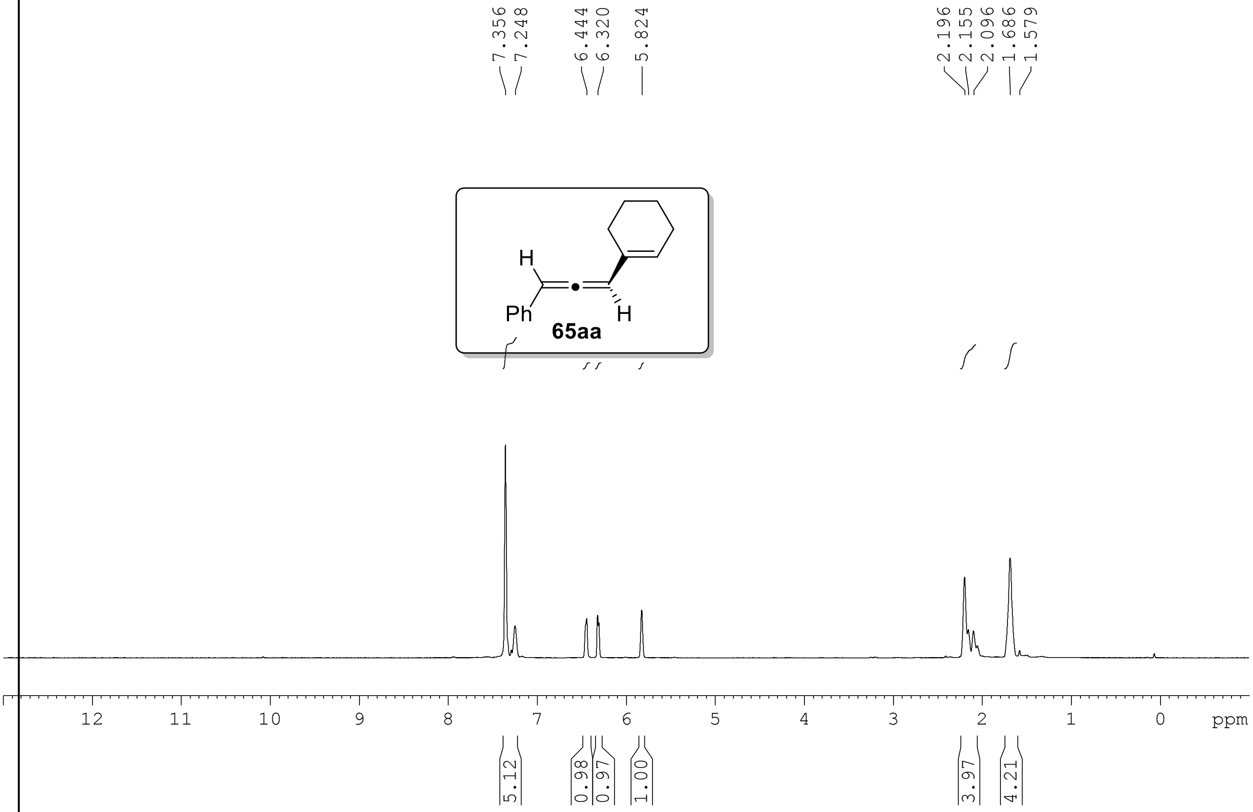
Spectrum No. 29 (Chapter 2, Table 3) ^{1}H NMR Spectrum (400 MHz, CDCl$_3$)



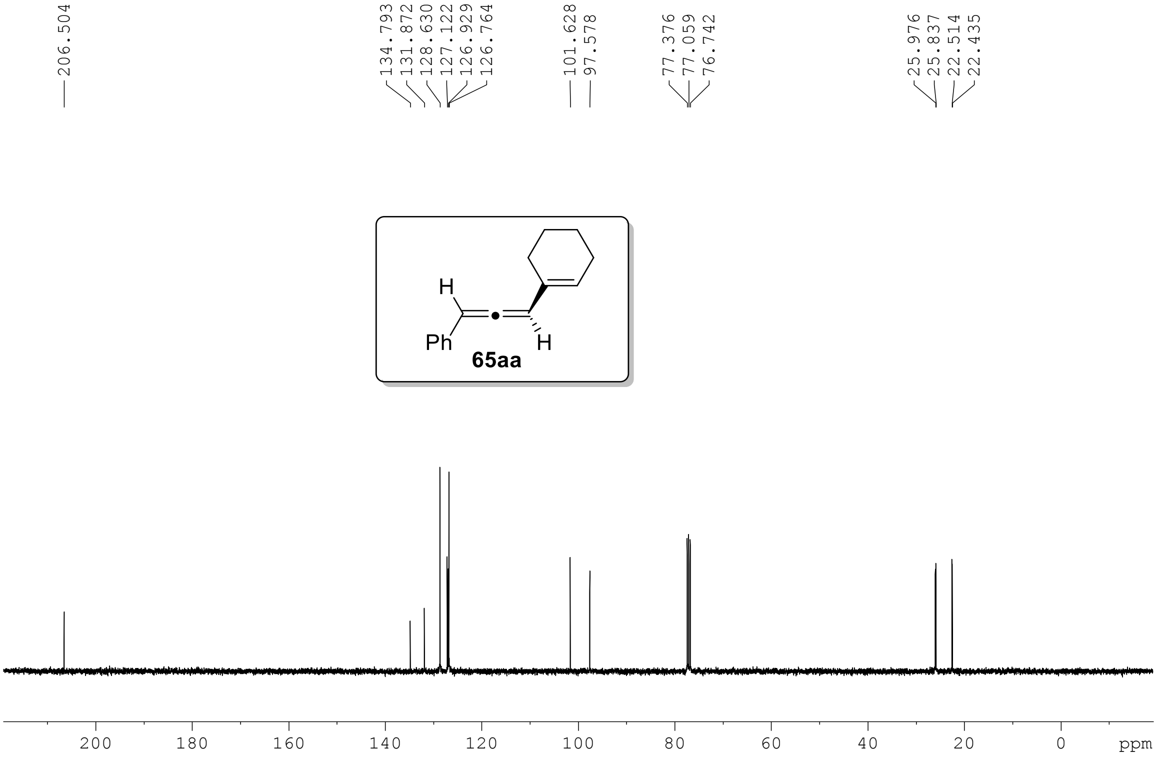
Spectrum No. 30 (Chapter 2, Table 3) ^{13}C NMR Spectrum (100 MHz, CDCl$_3$)



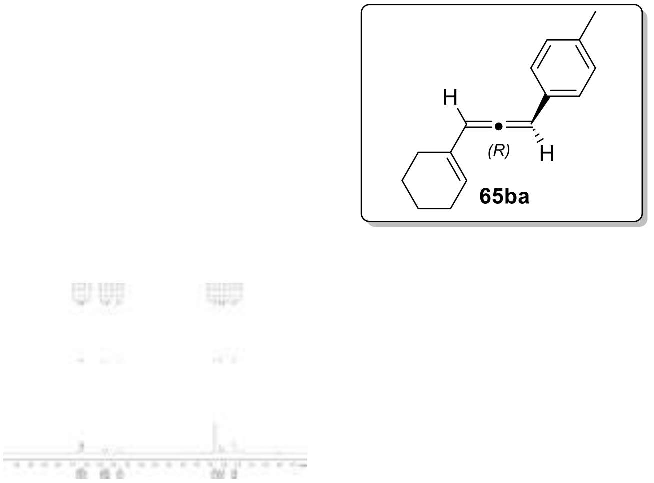
Spectrum No. 31 (Chapter 3, Table 5) ^{1}H NMR Spectrum (400 MHz, CDCl$_3$)



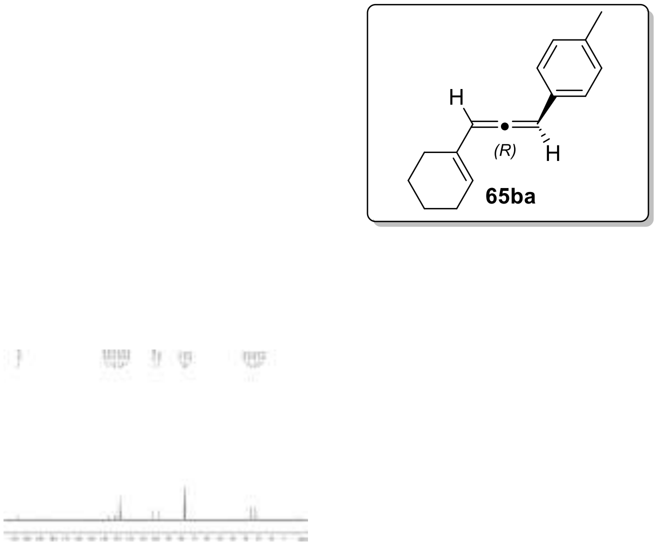
Spectrum No. 32 (Chapter 3, Table 5) ^{13}C NMR Spectrum (100 MHz, CDCl$_3$)



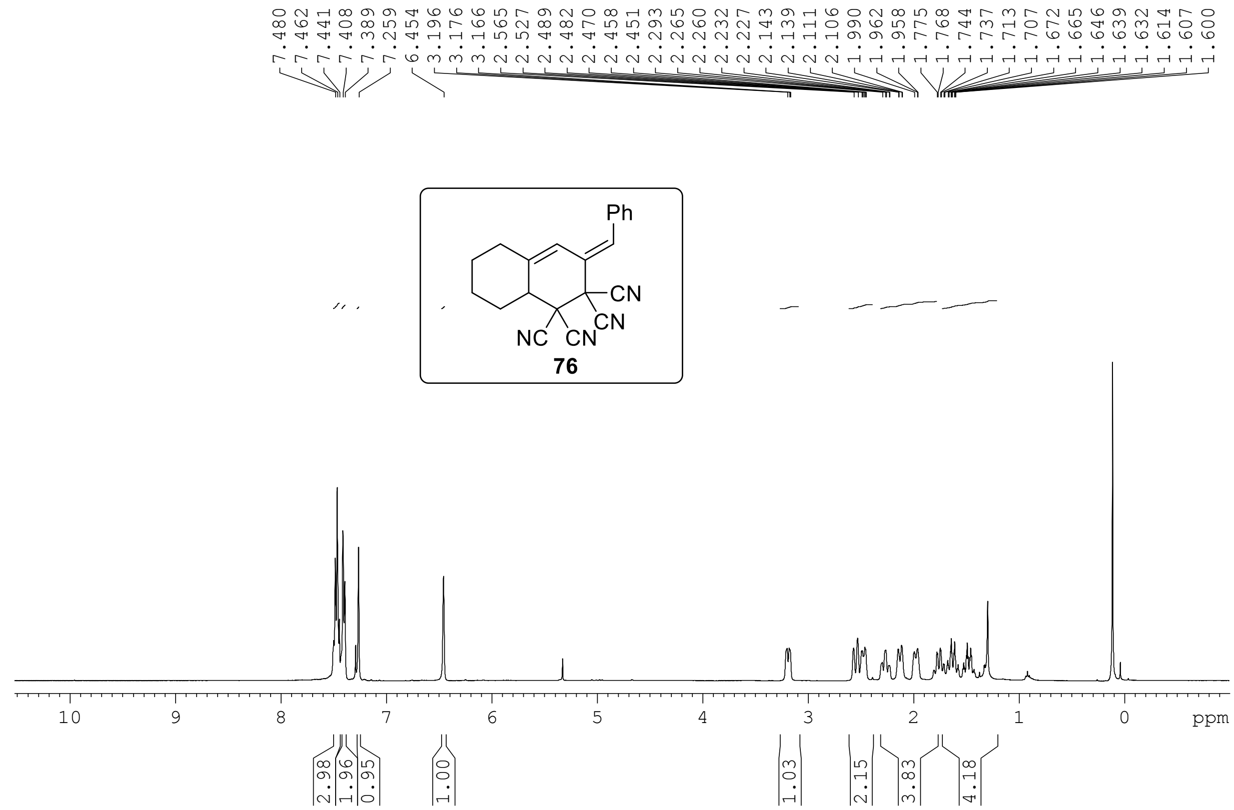
Spectrum No. 33 (Chapter 3, Table 5) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



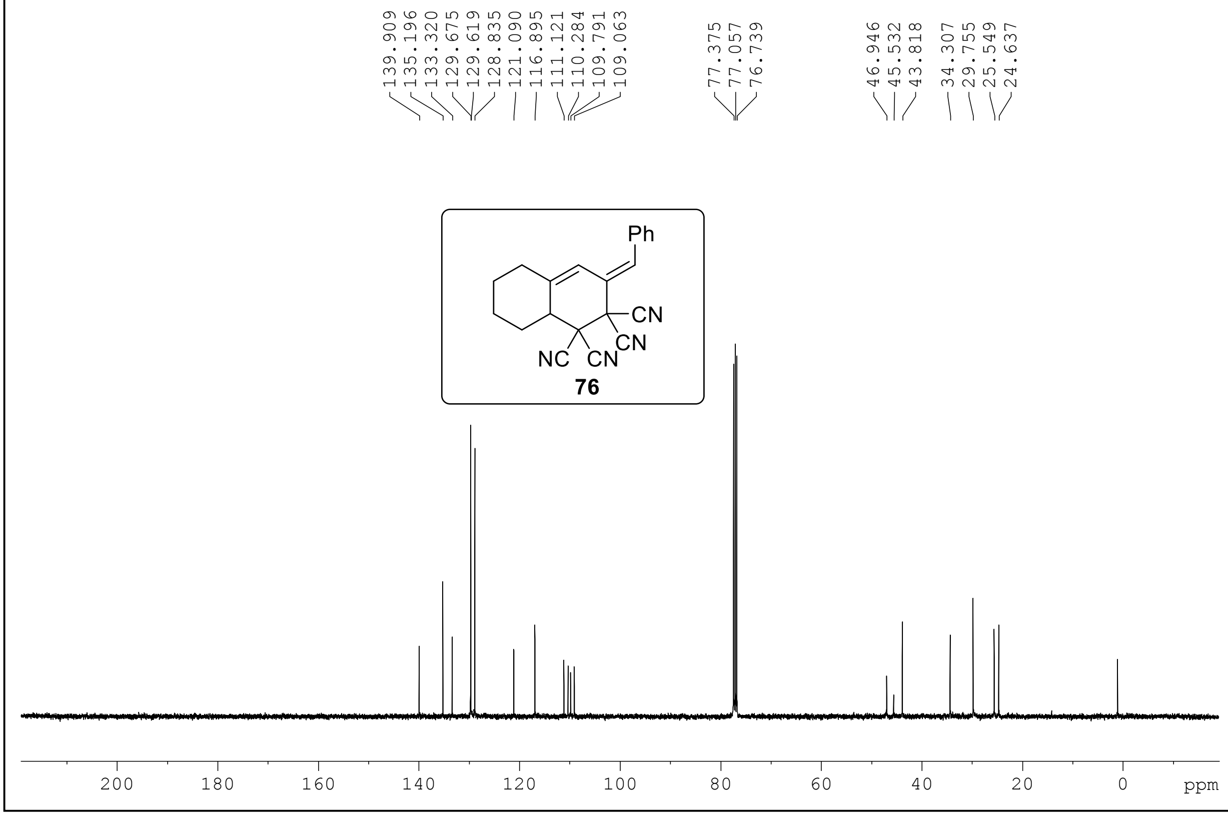
Spectrum No. 34 (Chapter 3, Table 5) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



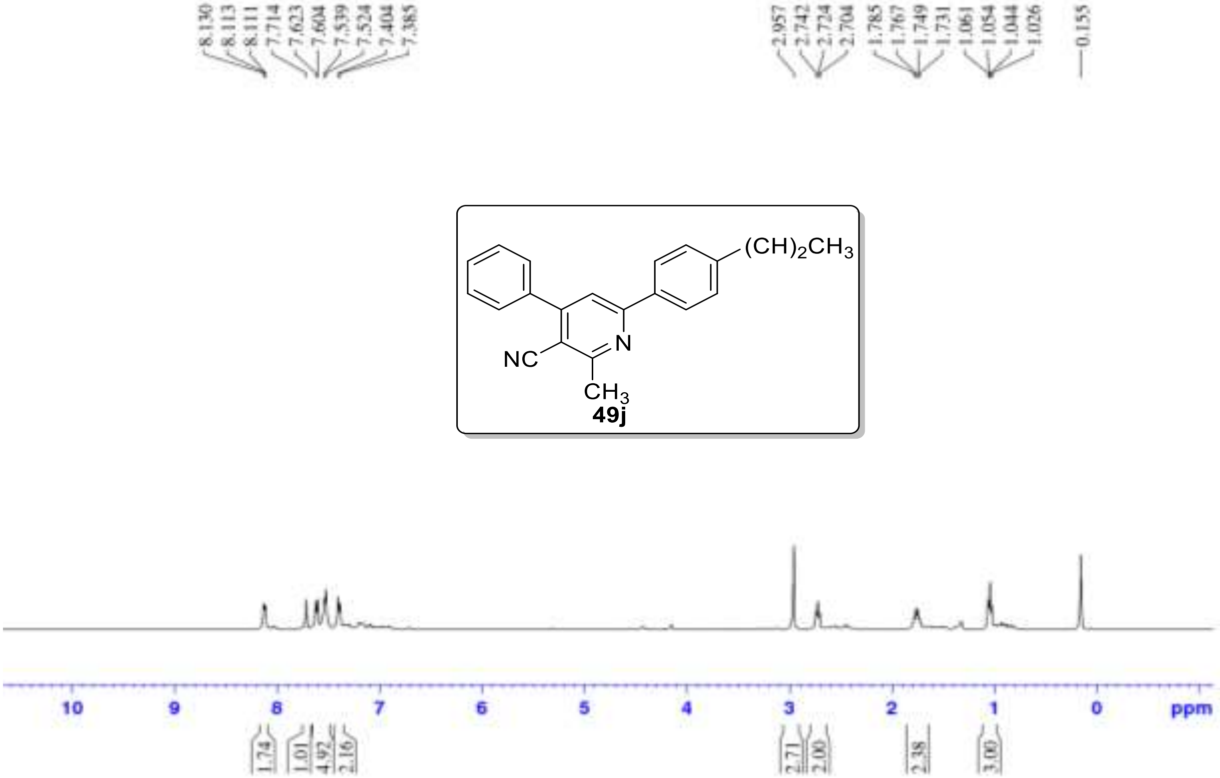
Spectrum No. 35 (Chapter 3, Section 3.2.4) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



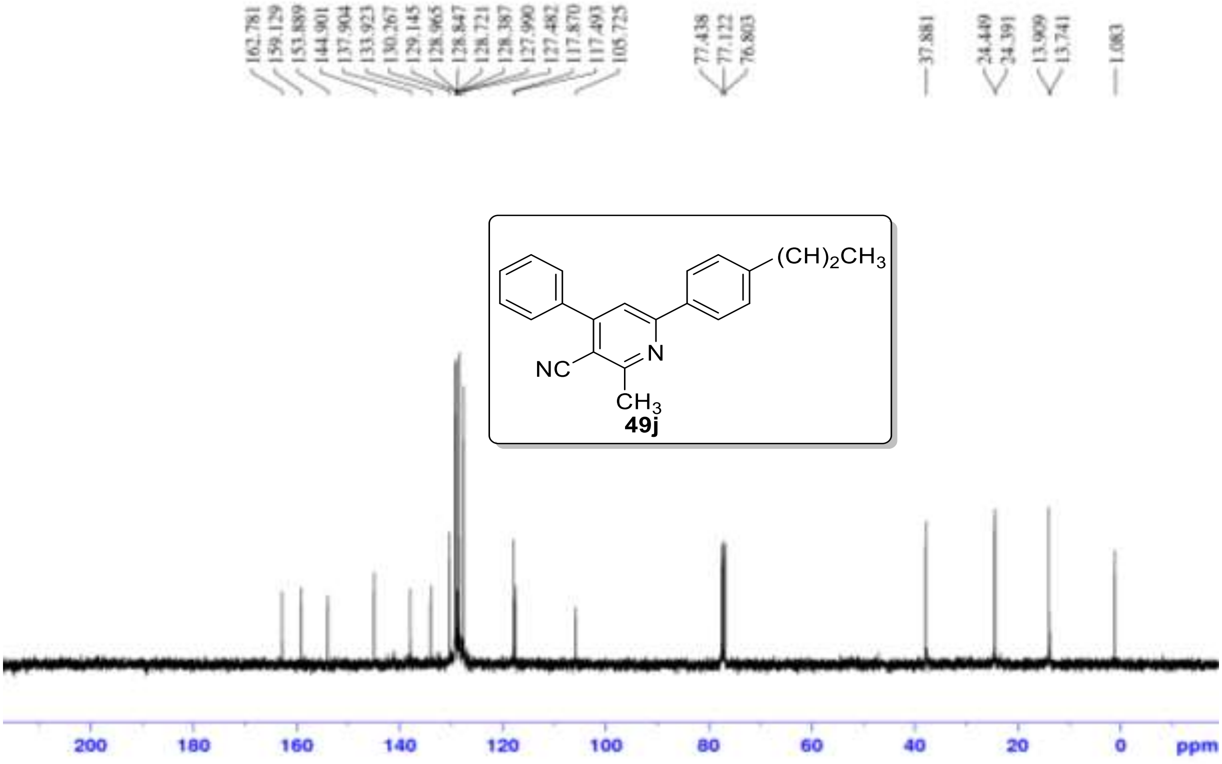
Spectrum No. 36 (Chapter 3, Section 3.2.4) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



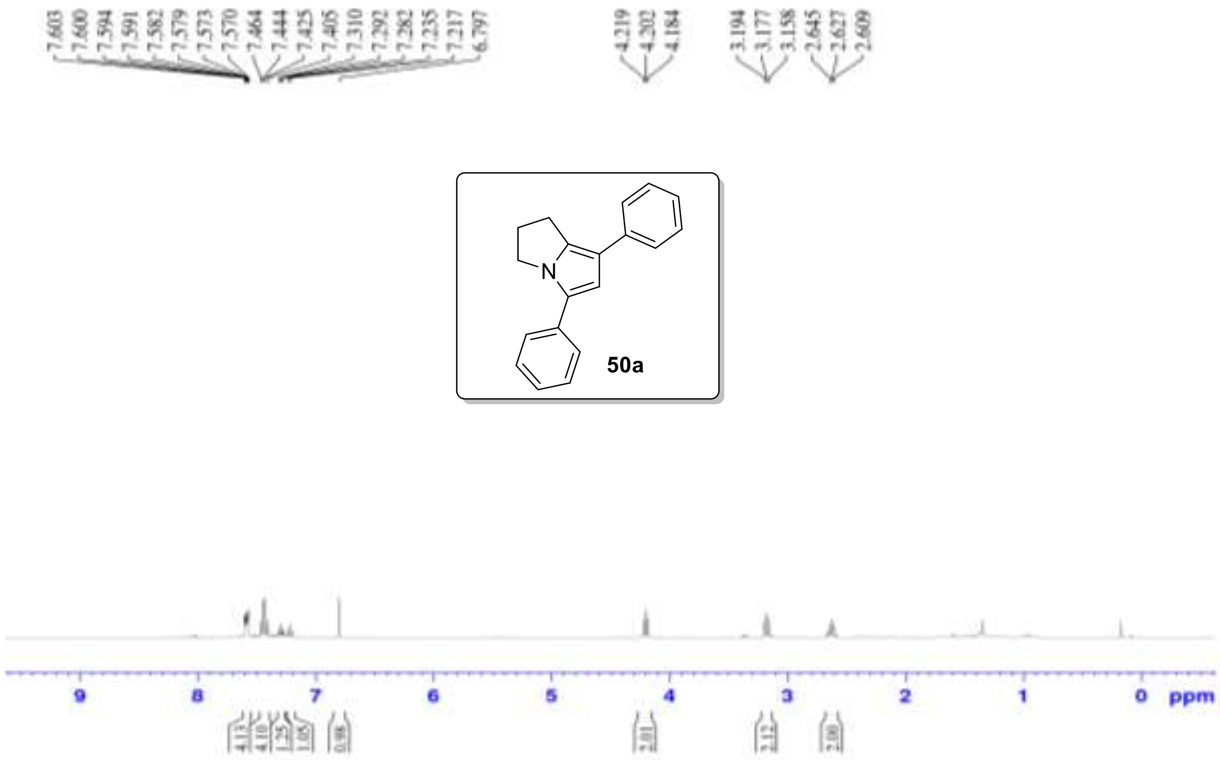
Spectrum No. 37 (Chapter 4, Table 2) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



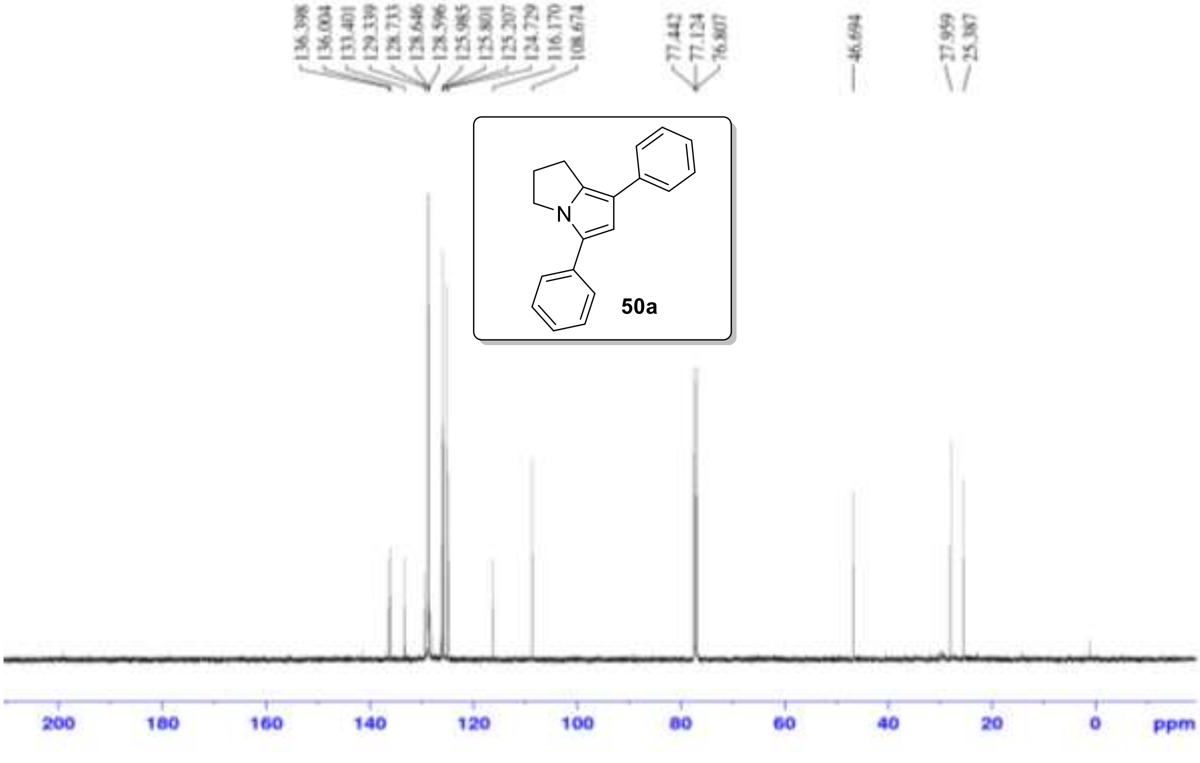
Spectrum No. 38 (Chapter 4, Table 2) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



Spectrum No. 39 (Chapter 4, Table 4) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)

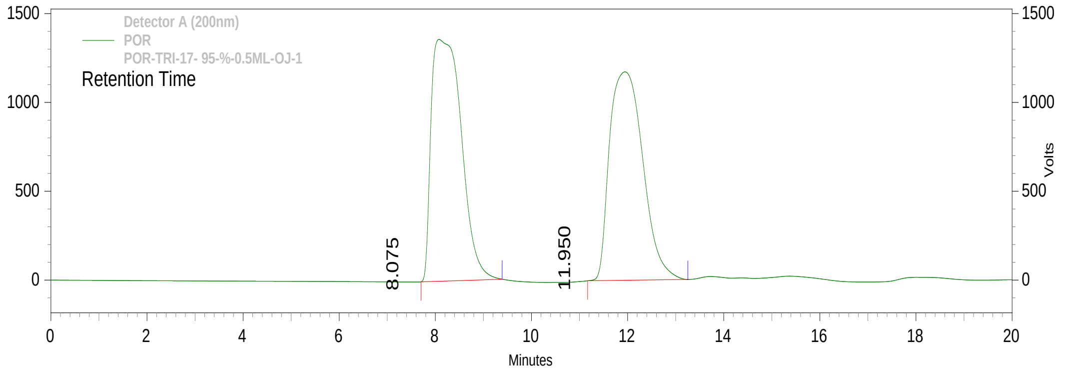


Spectrum No. 40 (Chapter 2, Table 4) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



HPLC profile of 162e: chiralcel OJ-H, hexanes:i-PrOH /95.5; flow rate 0.5 mL/min

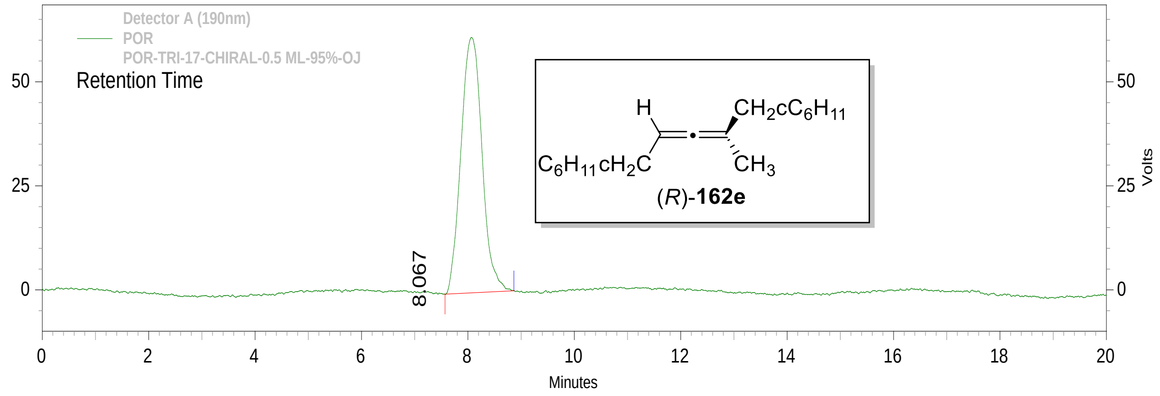
Racemic 162e:



Detector A (200nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	8.075	59434483	51.185	1361391	53.709
2	11.950	56681458	48.815	1173354	46.291
Totals		116115941	100.000	2534745	100.000

***(R)*-162e: (Chapter 1, Table 4)**

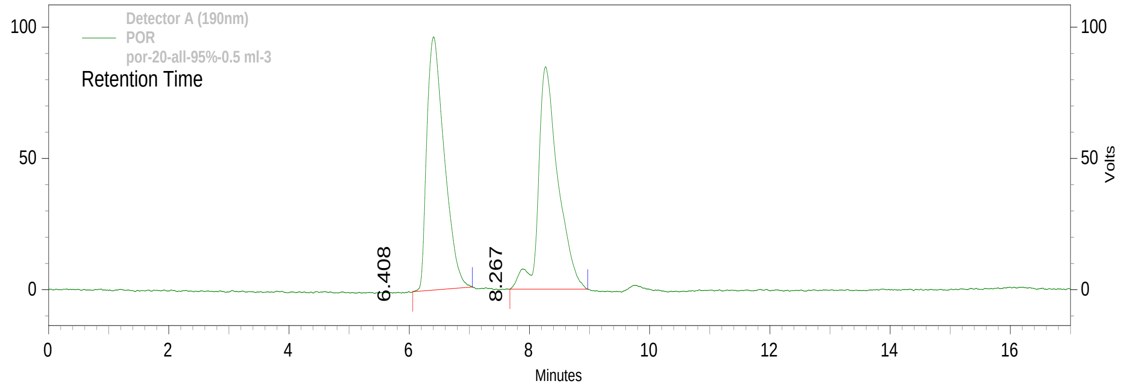


Detector A (190nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	8.067	1691474	100.000	61349	100.000
Totals		1691474	100.000	61349	100.000

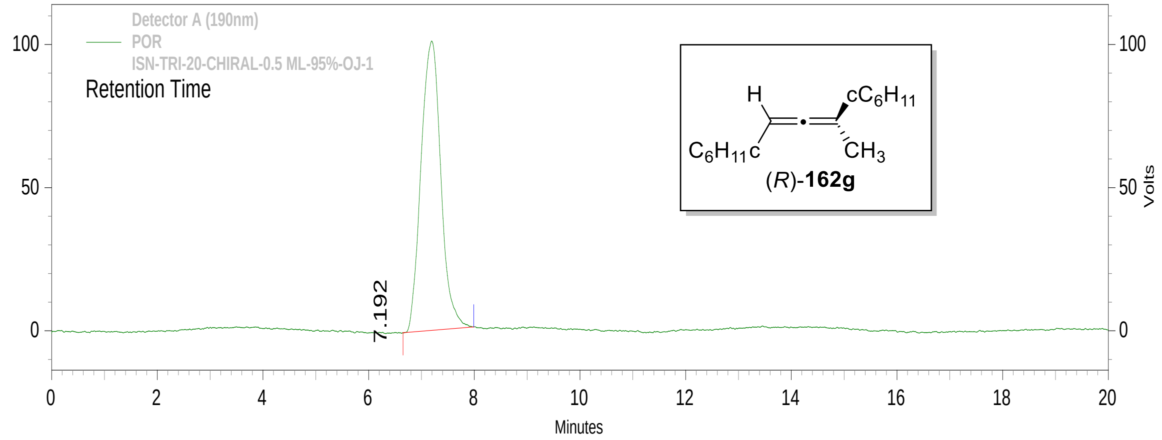
HPLC profile of 162g: chiralcel OJ-H, hexanes:i-PrOH /95.5; flow rate 0.5 mL/min

Racemic 162g:



Detector A (190nm)					
Pk #	**Retention Time**	**Area**	**Area %**	**Height**	**Height %**
1	6.408	1950310	50.272	96422	53.244
2	8.267	1929175	49.728	84674	46.756
Totals		3879485	100.000	181096	100.000

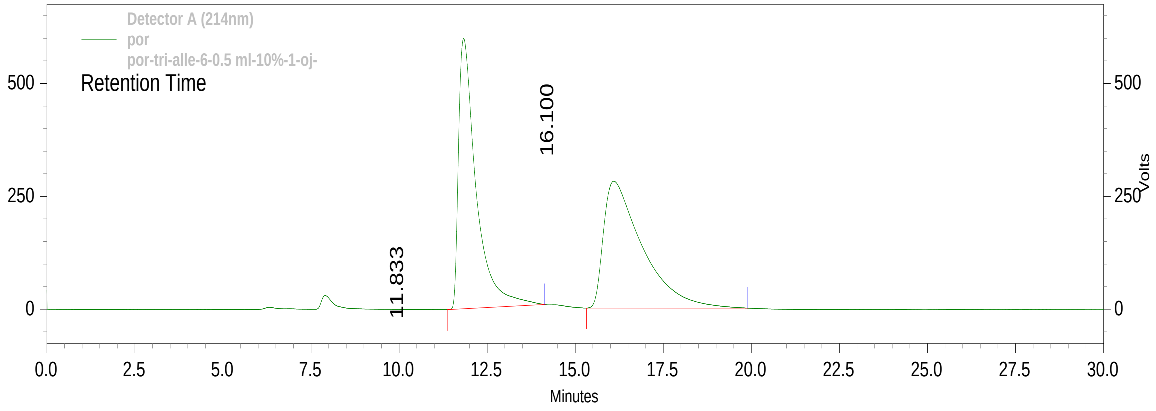
***(R)*-162g: (Chapter 1, Table 4)**



Detector A (190nm)					
Pk #	**Retention Time**	**Area**	**Area %**	**Height**	**Height %**
1	7.192	2638670	100.000	101075	100.000
Totals		2638670	100.000	101075	100.000

HPLC profile of 162h: chiralcel OJ-H, hexanes:i-PrOH /90.10; flow rate 0.5 mL/min

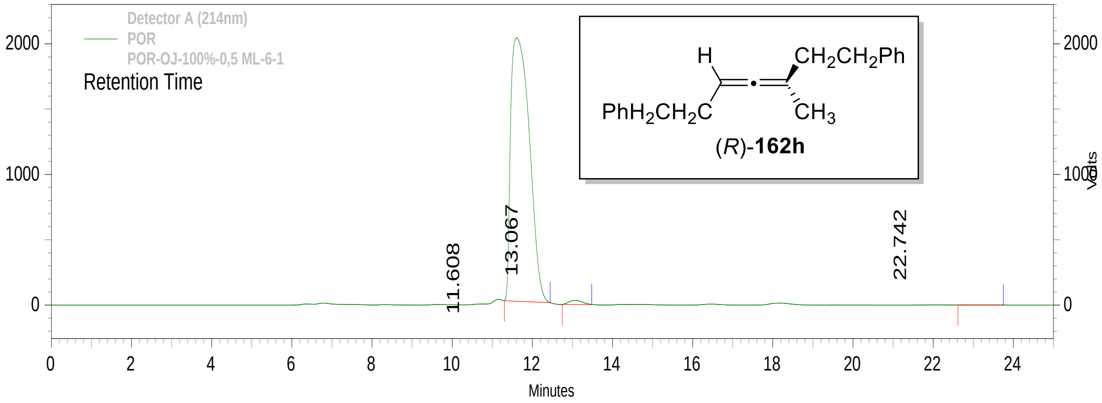
Racemic 162h:



Detector A (214nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	11.833	20817811	49.086	598357	68.041
2	16.100	21593346	50.914	281049	31.959
Totals		42411157	100.000	879406	100.000

***(R)*-162h: (Chapter 1, Table 4)**

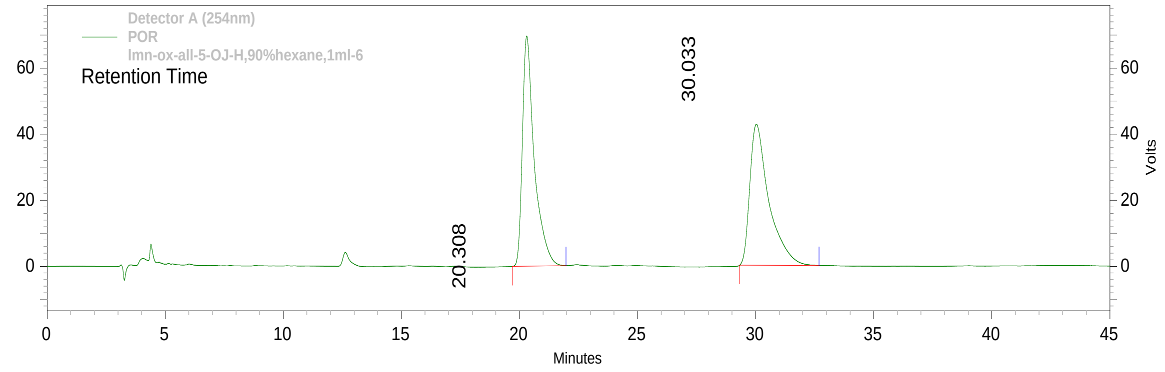


Detector A (214nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	11.608	65557901	98.896	2016312	98.455
2	13.067	721714	1.089	31468	1.537
3	22.742	10455	0.016	182	0.009
Totals		66290070	100.000	2047962	100.000

HPLC profile of 47ac: chiralcel OJ-H, hexanes:i-PrOH/90:10; flow rate 1.0 mL/min

Racemic 47ac:

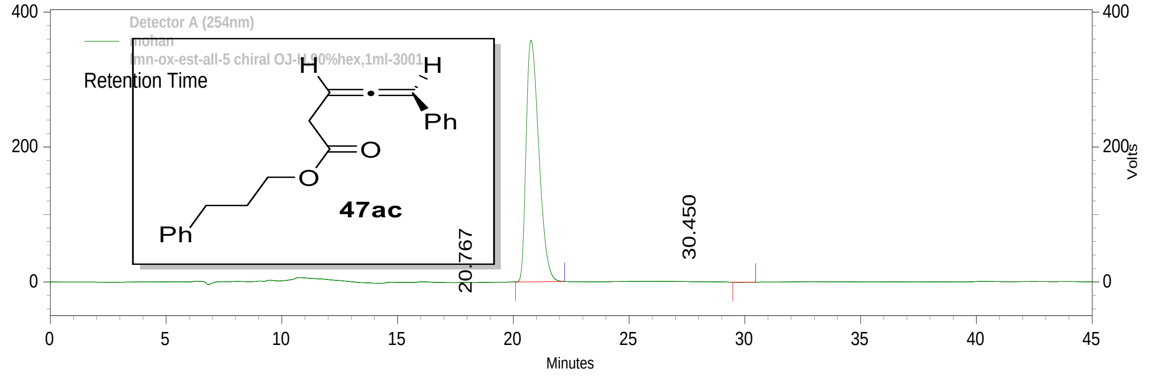


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	20.308	2440312	50.539	69643	61.993
2	30.033	2388237	49.461	42697	38.007

Totals		4828549	100.000	112340	100.000

(R)- 47ac: (Chapter 2, Table 3)



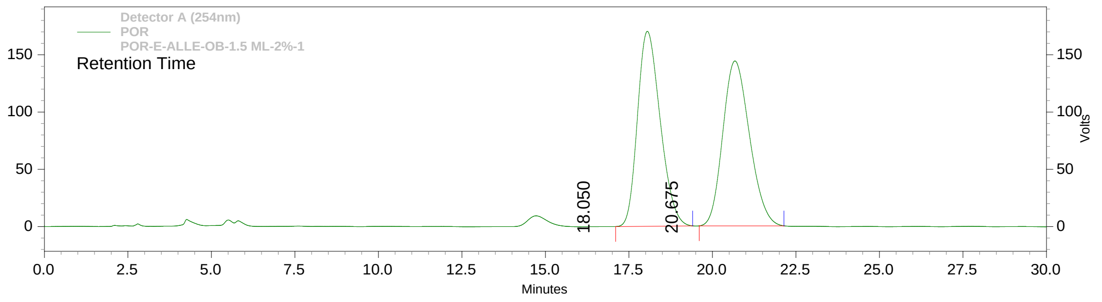
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	20.767	13686911	99.983	358192	100.000
2	30.450	2325	0.017	1	0.000

Totals		13689236	100.000	358193	100.000

HPLC profile of 47aa: chiralcel OB-H, hexanes:i-PrOH/98:2; flow rate 0.5 mL/min.

Racemic 47aa:

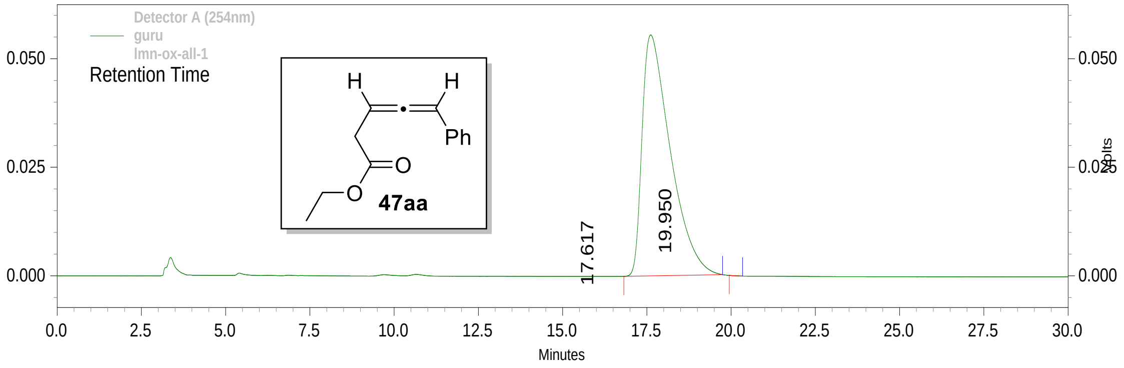


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	18.050	8057864	50.129	170257	54.180
2	20.675	8016420	49.871	143988	45.820

Totals		16074284	100.000	314245	100.000

(*R*)- 47aa: (Chapter 2, Table 3)



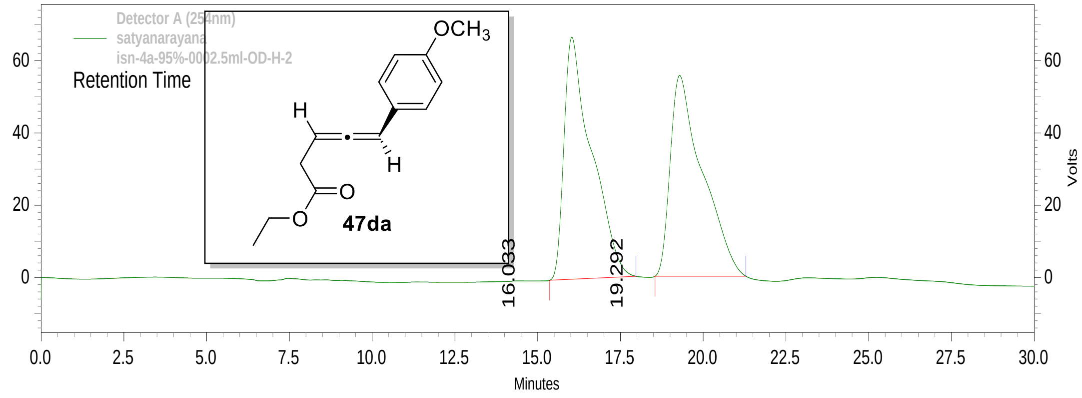
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	17.617	3237300	99.988	55487	100.000
2	19.950	393	0.012	0	0.000

Totals		3237693	100.000	55487	100.000

HPLC profile of 47da: chiralcel OD-H, hexanes:i-PrOH/95:5; flow rate 0.5mL/min.

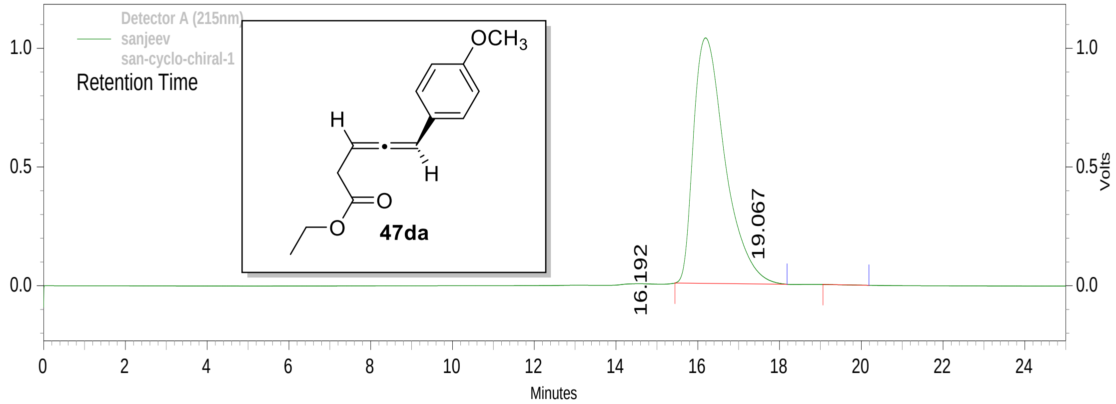
Racemic 47da:



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	16.033	3880222	50.864	67035	54.669
2	19.292	3748469	49.136	55585	45.331
Totals		7628691	100.000	122620	100.000

(*R*)-47da: (Chapter 2, Table 3)

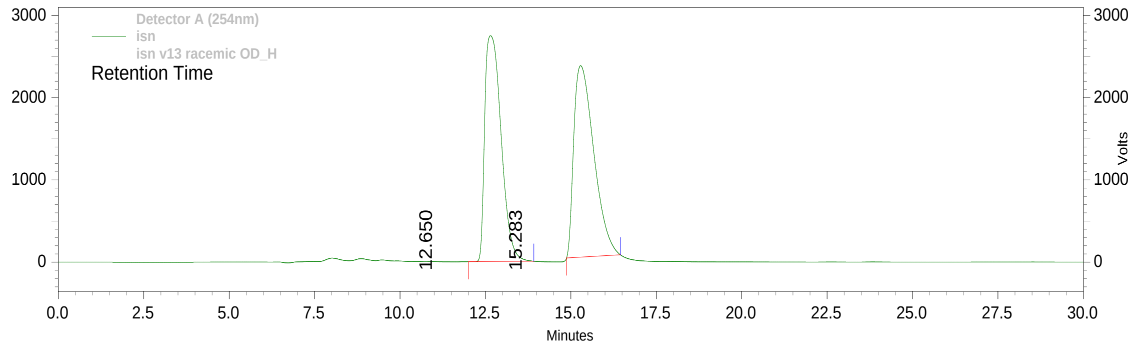


Detector A (215nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	16.192	55545420	99.991	1033574	100.000
2	19.067	5140	0.009	0	0.000
Totals		55550560	100.000	1033574	100.000

HPLC profile of 65aa: Chiralcel OD-H, hexanes:i-PrOH/100:0; flow rate 0.5 mL/min.

Racemic 65aa:

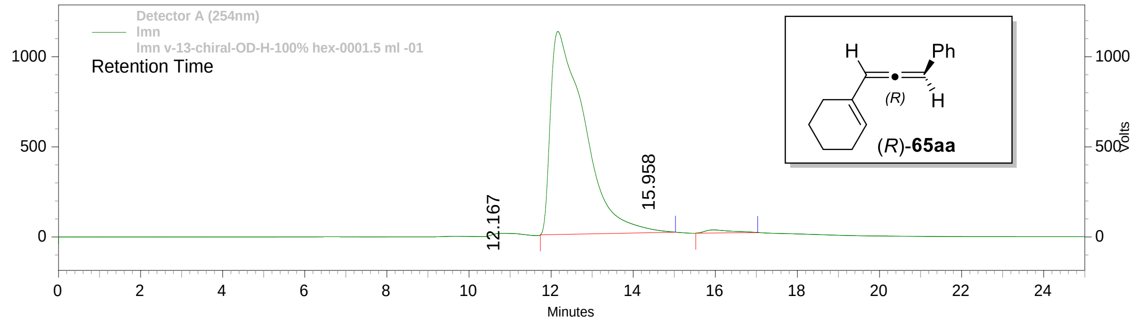


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	12.650	91586858	49.073	2746735	54.118
2	15.283	95047927	50.927	2328730	45.882

Totals		186634785	100.000	5075465	100.000

(R)-65aa: (Chapter 3, Table 5)



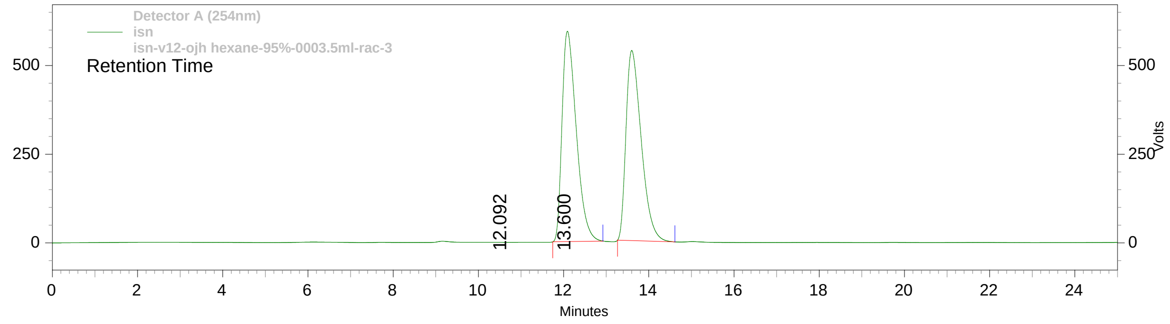
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	12.167	65005050	98.810	1126448	98.492
2	15.958	782624	1.190	17245	1.508

Totals		65787674	100.000	1143693	100.000

HPLC profile of 65ba: Chiralcel OJ-H, hexanes:i-PrOH/95:5; flow rate 0.5 mL/min, 254 nm

Racemic 65ca:

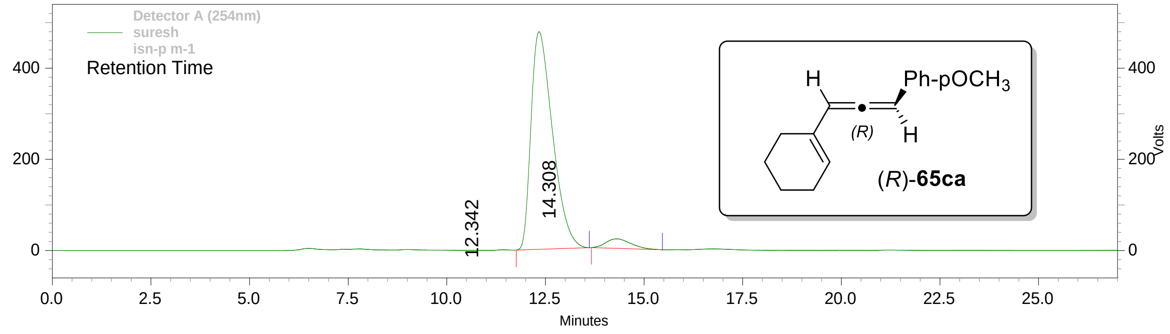


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	12.092	13737256	50.748	592828	52.509
2	13.600	13332354	49.252	536171	47.491

Totals					
		27069610	100.000	1128999	100.000

(R)-65ca: (Chapter 3, Table 5)



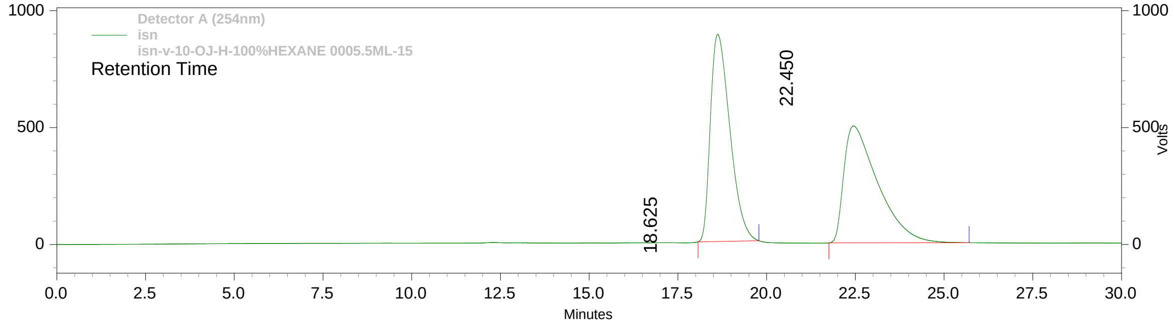
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	12.342	18119389	95.181	477165	95.849
2	14.308	917400	4.819	20666	4.151

Totals					
		19036789	100.000	497831	100.000

HPLC profile of 65da: Chiralcel OJ-H, hexanes:i-PrOH/100:0; flow rate 0.5 mL/min

Racemic 65da:

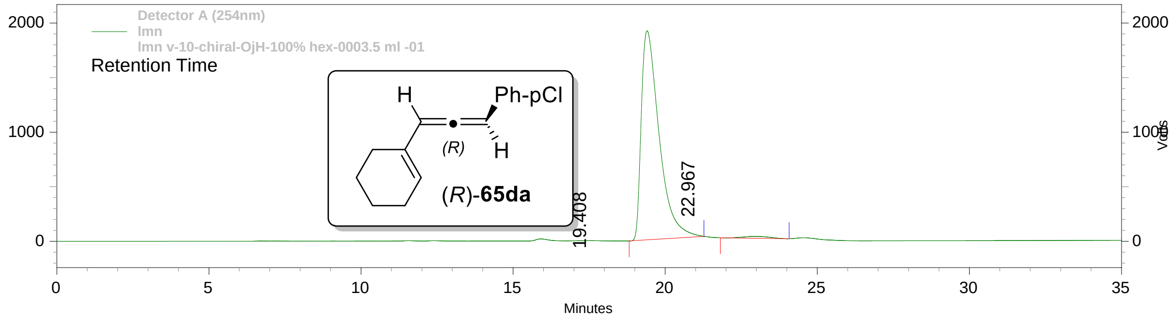


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	18.625	33910003	50.419	885975	63.925
2	22.450	33345977	49.581	499977	36.075

Totals		67255980	100.000	1385952	100.000

(R)-65da: (Chapter 3, Table 5)



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	19.408	78103589	98.680	1915502	99.089
2	22.967	1044660	1.320	17618	0.911

Totals		79148249	100.000	1933120	100.000

Appendix II

X-Ray Crystallographic Data

Table A1. **Crystal data and structure refinement for compound 56**

Identification code	Compound **56**	
Empirical formula	$C_{22} H_{25} N O_3$	
Formula weight	351.43	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 11.1961(6) Å	α= 90°.
	b = 6.5619(3) Å	β= 100.474(2)°.
	c = 12.9957(8) Å	γ= 90°.
Volume	938.86(9) $Å^3$	
Z	2	
Density (calculated)	1.243 Mg/m^3	
Absorption coefficient	0.082 mm^{-1}	
F(000)	376	
Crystal size	0.24 x 0.20 x 0.18 mm^3	
Theta range for data collection	2.65 to 27.44°.	
Index ranges	-14<=h<=14, -8<=k<=8, -16<=l<=15	
Reflections collected	10684	
Independent reflections	3996 [R(int) = 0.0327]	
Completeness to theta = 27.44°	96.9 %	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3996 / 1 / 235	
Goodness-of-fit on F^2	1.108	
Final R indices [I>2sigma(I)]	R1 = 0.0378, wR2 = 0.0804	
R indices (all data)	R1 = 0.0469, wR2 = 0.0837	
Absolute structure parameter	-0.1(9)	
Largest diff. peak and hole	0.201 and -0.188 e.$Å^{-3}$	

Table A2. **Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3)**

for mp30vr_a. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	2513(1)	6234(2)	2247(1)	16(1)
C(2)	3182(1)	7933(2)	2642(1)	20(1)
C(3)	4191(2)	8540(3)	2233(1)	26(1)
C(4)	4539(2)	7473(3)	1425(1)	26(1)
C(5)	3869(2)	5802(3)	1010(1)	26(1)
C(005)	1437(1)	5470(2)	2737(1)	16(1)
C(6)	2864(2)	5187(3)	1417(1)	21(1)
C(7)	287(1)	5416(3)	1891(1)	18(1)
C(8)	35(2)	3803(3)	1188(1)	25(1)
C(9)	-986(2)	3830(3)	399(1)	30(1)
C(10)	-1779(2)	5457(3)	307(1)	31(1)
C(11)	-1545(2)	7061(3)	999(1)	29(1)
C(12)	-517(1)	7050(3)	1790(1)	23(1)
C(13)	1698(1)	3310(2)	3217(1)	17(1)
C(14)	704(2)	2531(3)	3798(1)	23(1)
C(15)	1165(2)	3034(3)	4952(1)	25(1)
C(16)	2528(2)	2747(3)	5079(1)	21(1)
C(17)	3918(1)	3154(2)	3831(1)	16(1)
C(18)	4966(1)	2796(2)	4512(1)	18(1)
C(19)	6112(1)	2859(2)	4162(1)	18(1)
C(20)	7111(2)	3471(3)	2716(2)	31(1)
C(21)	7435(2)	1442(4)	2325(2)	39(1)
N(1)	2796(1)	3254(2)	4047(1)	17(1)
O(1)	1195(1)	6837(2)	3517(1)	16(1)
O(2)	7112(1)	2538(2)	4705(1)	24(1)
O(3)	6008(1)	3357(2)	3141(1)	29(1)

Table A3. Crystal data and structure refinement for compounds **49a**.

Identification code	Compound **49a**	
Empirical formula	C1.85 H1.66 N0.10	
Formula weight	25.30	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C 2/c	
Unit cell dimensions	a = 30.105(4) Å	α= 90°.
	b = 5.7409(6) Å	β= 132.84°.
	c = 22.136(3) Å	γ = 90°.
Volume	2805.1(6) $Å^3$	
Z	82	
Density (calculated)	1.228 Mg/m^3	
Absorption coefficient	0.071 mm^{-1}	
F(000)	1104	
Crystal size	0.14 x 0.12 x 0.10 mm^3	
Theta range for data collection	2.510 to 25.072°.	
Index ranges	-35<=h<=35, -6<=k<=6, -25<=l<=26	
Reflections collected	10295	
Independent reflections	2457 [R(int) = 0.0909]	
Completeness to theta = 25.072°	98.4 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2457 / 15 / 181	
Goodness-of-fit on F^2	1.059	
Final R indices [I>2sigma(I)]	R1 = 0.0752, wR2 = 0.1758	
R indices (all data)	R1 = 0.1006, wR2 = 0.1908	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.275 and -0.376 e.$Å^{-3}$	

Table A4. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3)
for mp62_a. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(001)	3662(1)	2898(3)	5531(1)	36(1)
N(002)	3425(1)	1802(4)	5801(1)	56(1)
C(1)	4043(1)	4660(4)	6069(1)	44(1)
C(004)	4397(1)	6229(4)	6011(1)	46(1)
C(005)	3648(1)	2827(4)	6529(1)	44(1)
C(006)	4032(1)	4606(4)	6689(1)	47(1)
C(007)	3494(1)	2195(4)	7011(1)	49(1)
C(008)	4615(1)	8311(4)	6453(1)	51(1)
C(009)	4978(1)	9780(5)	6455(2)	60(1)
C(00A)	3012(1)	-112(5)	5243(2)	59(1)
C(00B)	3635(1)	3716(5)	7609(2)	66(1)
C(00C)	4557(1)	5733(5)	5566(2)	67(1)
C(00D)	5126(1)	9251(5)	6012(2)	69(1)
C(00E)	3442(1)	1891(5)	4757(2)	65(1)
C(00F)	3212(1)	133(5)	6905(2)	70(1)
C(00G)	3003(1)	17(5)	4547(2)	74(1)
C(00H)	4907(2)	7236(5)	5559(2)	80(1)
C(00I)	3488(2)	3187(7)	8062(2)	85(1)
C(00J)	3197(2)	1136(7)	7929(2)	86(1)
C(00K)	3066(2)	-384(7)	7360(2)	86(1)

Table A5. Crystal data and structure refinement for compound **50a**.

Identification code	Compound **50a**	
Empirical formula	C19 H14 N2	
Formula weight	270.32	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C 2	
Unit cell dimensions	a = 22.984(2) Å	α= 90°.
	b = 3.9981(3) Å	β= 107.974(9)°.
	c = 16.2669(16) Å	γ = 90°.
Volume	1421.9(2) Å^3	
Z	4	
Density (calculated)	1.263 Mg/m^3	
Absorption coefficient	0.075 mm^{-1}	
F(000)	568	
Crystal size	0.12 x 0.10 x 0.08 mm^3	
Theta range for data collection	2.592 to 27.545°.	
Index ranges	-29<=h<=29, -5<=k<=5, -21<=l<=21	
Reflections collected	23083	
Independent reflections	3271 [R(int) = 0.2249]	
Completeness to theta = 25.242°	99.8 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3271 / 1 / 191	
Goodness-of-fit on F^2	1.024	
Final R indices [I>2sigma(I)]	R1 = 0.0869, wR2 = 0.1288	
R indices (all data)	R1 = 0.2050, wR2 = 0.1523	
Absolute structure parameter	0.2(3)	
Extinction coefficient	n/a	

Largest diff. peak and hole 0.179 and -0.211 e.Å^{-3}

Table A6. Atomic coordinates (x 10^{4}) and equivalent isotropic displacement parameters (Å^{2}x 10^{3}) for mp61_a. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
N(1)	5004(2)	4757(10)	1432(2)	37(1)
C(1)	4116(2)	2832(12)	1775(3)	31(1)
C(7)	4746(2)	4185(11)	2058(3)	31(1)
C(14)	5992(2)	6678(13)	4093(3)	34(1)
C(11)	5561(2)	6085(14)	1648(3)	40(1)
C(9)	5648(2)	6144(13)	3167(3)	32(1)
C(6)	3726(2)	3181(14)	2269(3)	41(1)
C(10)	5894(2)	6858(13)	2498(3)	33(1)
C(13)	6471(2)	8575(15)	2658(3)	41(1)
N(2)	6920(2)	9981(14)	2761(3)	62(2)
C(8)	5061(2)	4810(13)	2923(3)	35(1)
C(15)	6591(2)	5596(14)	4432(3)	37(1)
C(16)	6906(2)	5987(14)	5294(3)	43(1)
C(19)	5719(2)	8167(13)	4648(3)	39(1)
C(2)	3891(2)	1206(14)	988(3)	43(1)
C(18)	6035(2)	8567(15)	5507(3)	48(2)
C(17)	6633(2)	7491(14)	5835(3)	45(2)
C(4)	2923(2)	430(15)	1194(4)	55(2)
C(3)	3301(3)	37(16)	702(3)	54(2)
C(5)	3130(2)	2040(15)	1986(4)	52(2)
C(12)	5820(2)	6799(17)	924(3)	62(2)

LIST OF PUBLICATIONS

1. Periasamy. M.;* Reddy. P.O.; Satyanarayana. I.; **Mohan. L**.; Edukondalu. A. Diastereoselective synthesis of tetrasubstituted propargylamines via hydroamination and metalation of 1-alkynes and their enantioselective conversion to trisubstituted chiral allenes; *J. Org. Chem*. **2016**, *81*, 987-999.
2. Highly enantioselective synthesis chiral β-allenoates *via* phosphine catalysed hydroamination of propiolates and alkyne addition reaction; Periasamy. M.;* **Mohan. L**.; Satyanarayana. I.; Reddy. P.O. *J. Org. Chem*. **2018**, *83*, 267-274.
3. Highly enantioselective synthesis of chiral vinylallenes for use in [4 + 2] cycloaddition; Periasamy. M.; Satyanarayana. I.; **Mohan. L**.; Reddy. P.O. (*To be communicated)*.
4. Copper (I) promoted tetrasubstituted propargylamines and their conversion into the trisubstituted allenes via hydroamination reaction, Periasamy. M.;* **Mohan. L**.; Satyanarayana. I. (*To be communicated)*.
5. A Base Promoted Metal-Free Intra-molecular Annulations of Propargylamine Derivatives *via* C-H Functionalization to Access the Pyrrolizine Derivatives; **Mohan. L**.; Periasamy. M.* (*To be communicated)*.
6. Nucleophilic addition to propargylamines to access highly substituted pyridines *via* radical mechanism; **Mohan. L**.; Periasamy. M.* (*To be communicated)*.
7. Copper (I) promoted diastereoselective synthesis of propargylamines *via* hydroamination and metallation of 1-alkynes and their highly enantioselective conversion to β-allenoates Periasamy. M.;* **Mohan. L**.; Satyanarayana. I. (*To be communicated)*.
8. Zn (II) salt promoted synthesis of trisubstituted allenes using amine, ketone, and 1-alkyne Periasamy. M.;* Satyanarayana. I.**; Mohan. L**.; (*To be communicated)*.
9. "Chiral secondary amine approach" to chiral allenes *via* propargylamines; **Mohan. L**.; Periasamy. M.* (Review: *To be communicated)*.