Achiral and Chiral Secondary Amines for the Synthesis of Propargylamines and Allenes and for Applications in Electron Transfer Reactions

A Thesis
Submitted for the Degree of
DOCTOR OF PHILOSOPHY

By

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November 2018

Dedicated to
My Family Members

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DECLARATION

I, **SATYANARAYANA IDDUM** hereby declare that this thesis entitled "**Achiral and Chiral Secondary Amines for the Synthesis of Propargylamines and Allenes and for Applications in 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.

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

1 Periasamy. M.;* Reddy. P.O.; **Satyanarayana. I**.; Mohan. L.; Edukondalu. A. *J. Org. Chem*. **2016**, *81*, 987-999.

2 Periasamy. M.;* Mohan. L.; **Satyanarayana. I**.; Reddy. P.O. *J. Org. Chem*. **2018**, *83*, 267-274.

He has also made poster and oral presentations in the following conferences:

1 **Satyanarayana, I**.; Periasamy, M. “New Methods for Synthesis of Allenes Using Secondary Amines”, Poster presentation in the *Chemfest 2016* held at School of Chemistry, University of Hyderabad.

2 **Satyanarayana, I**.; Periasamy, M. “Development of Electron Transfer Reactions After Explorations in Organometallic and Chiral Reagents”, Poster presentation in the “*8th International Collaborative & Cooperative Chemistry Symposium”* held at School of Chemistry, University of Hyderabad.

3 **Satyanarayana, I**.; Periasamy, M. “Synthesis and Applications of Chiral Secondary Amines”, Oral presentation in the *Chemfest 2018* held at School of Chemistry, University of Hyderabad.

4 **Satyanarayana, I**.; Periasamy, M. “Synthesis and Applications of Chiral Secondary Amines”, Poster presentation in the *Chemfest 2018* held at School of Chemistry, University of Hyderabad.

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-821	Organic Reactions and Mechanisms	3	Pass

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Abbreviations

$[\alpha]_D^{25}$	specific rotation at 25 ˚C, $\lambda = 589$ nm.
Ac	acetyl
AC	activated carbon
Al	aluminium
anhyd.	anhydrous
aq.	aqueous
Ar	aryl
BINAP	2,2’-bis(diphenylphosphino)-1,1’-binaphthyl
Bn	benzyl
BQ	1,4-benzoquinone
br	broad (in spectroscopy)
Bu	butyl
Bz	benzoyl
CB	carbon black
conf	configuration
CT	charge transfer
d	doublet (in spectroscopy)
de	diastereomeric excess
DDQ	2,3-dichloro-5,6-dicyano-*p*-benzoquinone
DIPEA	N,N-diisopropylethylamine
DMF	*N*,*N*-dimethylformamide
DMSO	dimethyl sulfoxide
dr	diastereomeric ratio
ee	enantiomeric excess
EI	electron impact (in mass spectrometry)
equiv.	equivalent
Et	ethyl
ET	electron transfer
FF	fill factor
h	hour(s)
HPLC	high performance liquid chromatography

i	iso
IPA	2-propanol
IR	infrared
J	coupling constant (in NMR spectroscopy)
m	multiplet (in spectroscopy)
Me	methyl
min	minute(s)
mp	melting point
MS	mass spectrum
NMR	nuclear magnetic resonance
Nu	nucleophile
ORTEP	Oak Ridge Thermal Ellipsoid Plot
PC	propylene carbonate
PEO	polyethylene oxide
Ph	phenyl
ppm	parts per million
Pr	propyl
q	quartet (in spectroscopy)
ref	reference number
rt	room temperature
s	singlet (in spectroscopy)
sat.	saturated
sec	secondary
SET	single electron transfer
T	temperature
t	tertiary
t	triplet (in spectroscopy)
THF	tetrahydrofuran
TMS	trimethylsilyl
Uv	ultraviolet
y	yield

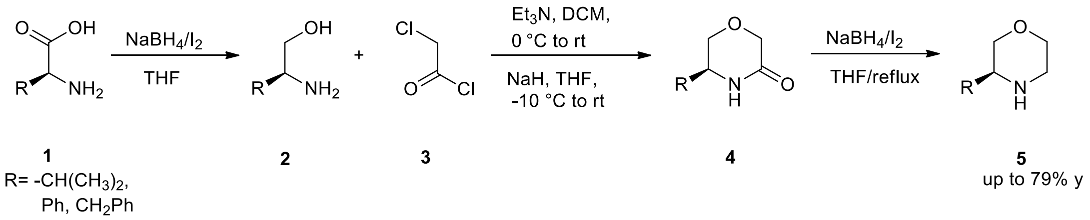
Abstract

This thesis entitled "**Achiral and Chiral Secondary Amines for the Synthesis of Propargylamines and Allenes and for Applications in Electron Transfer Reactions**" comprises of six 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 studies on the synthesis of various secondary chiral amine derivatives using α-amino acids and their applications. In the introductory section, a brief review on the synthesis of chiral secondary amines, tetrasubstituted proprgylamines and corresponding trisubstituted allenes are presented.

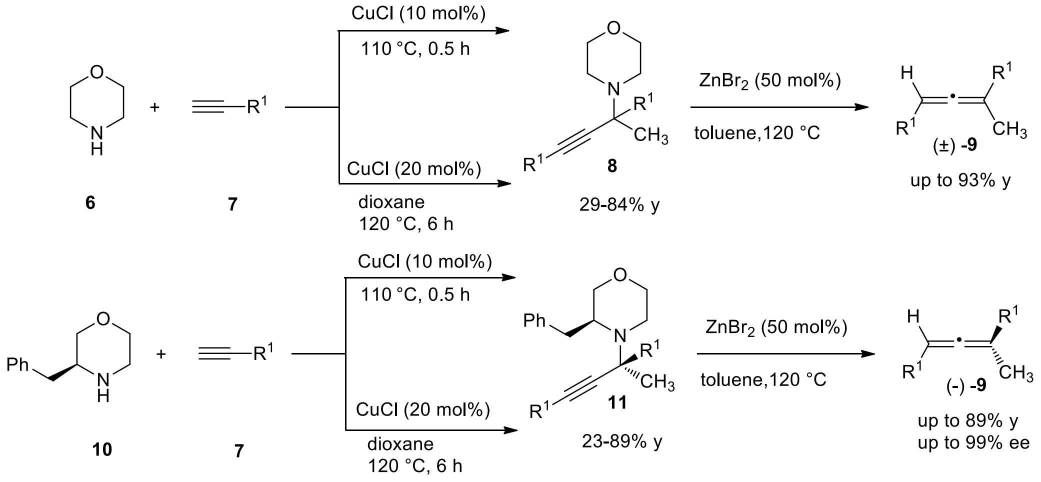
Chiral morpholine derivatives have been prepared from α-amino acids **1** by the reaction of $NaBH_4/I_2$ to obtain the amino alcohols **2**. These compounds were further reacted with chloroacetyl chloride **3** to give the corresponding amides **4** upon reduction using the $NaBH_4/I_2$ reagent system to give the desired products **5** in good yields (Scheme 1).

Scheme 1



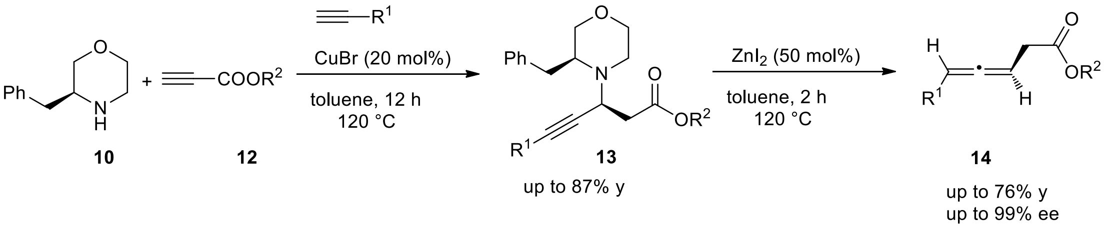
A two step method involving the CuCl promoted synthesis of tetrasubstituted propargylamines **8** and **11** using the morpholine systems **6**, **10** and 1-alkynes **7** and their conversion to allenes **9** are described in Chapter 1 (Scheme 2).

Scheme 2



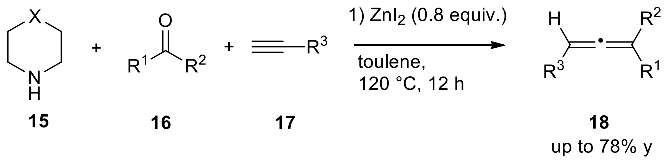
In chapter 2, investigations on the copper catalyzed synthesis of chiral propargylamines and their ZnI$_2$ promoted conversion to the corresponding β-allenoates **14** are described (Scheme 3).

Scheme 3



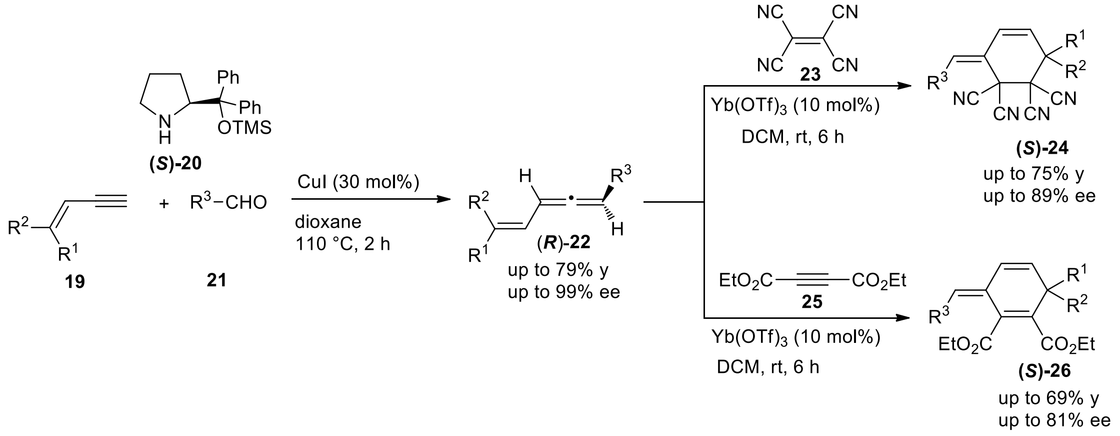
Studies undertaken to examine the scope of the ZnI$_2$ promoted trisubstituted allene synthesis using secondary amines **15**, ketones **16** and terminal alkynes **17** are described in Chapter 3 (Scheme 4).

Scheme 4

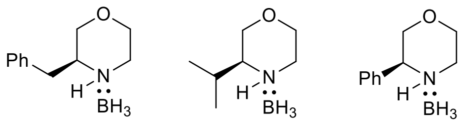


We have also examined the scope of the CuI promoted reaction of the (*S*)-2-(diphenyl((trimethylsilyl)oxy)methyl)pyrrolidine **20**, 1-enynes **19** and aldehydes **21** for the highly enantioselective synthesis of cyclohexenylallenes **22**. Also, ytterbium(III) catalyzed [4 + 2] cycloaddition reactions of chiral cyclohexenylallene **22** with dienophiles **23** and **25** are described in Chapter 4 (Scheme 5).

Scheme 5



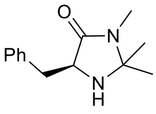
Studies were undertaken on the hydroboration reaction of prochiral olefins using chiral secondary amine-borane complexes **27-29**. The corresponding alcohols were obtained with up to 5% ee (Figure 1). The results are described in Chapter 5.



27 **28** **29**

(Figure 1)

We have also briefly studied the electron transfer reaction of imidazolidinone derivatives **30**-**32** with *p*-chloranil.



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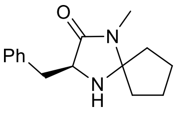

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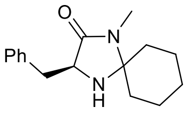

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The nature of the charge transfer and electron transfer complexes formed with *p*-chloranil was investigated by epr spectroscopic methods. Organic electrochemical cells were also constructed using Al foil and graphite sheet electrodes. The results are described in Chapter 6.

Detailed procedures, physical constant and spectral data are provided in the experimental sections under each chapter.

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

1.1 Introduction

Asymmetric synthesis has become an important topic of research in organic chemistry. It is always a challenging task to synthesize enantiomerically pure optically active compounds. It is well-known that Nature induced chiral transformations from one molecule to another molecule are highly stereospecific.[1] Inspired by Nature, synthetic chemists seek to develop new highly selective synthetic methodologies to access natural and unnatural enantiopure biologically active molecules which resulted in the development of new chiral building blocks and chiral catalysts for use in asymmetric organic synthesis. A brief review on this subject using chiral secondary amine derivatives would facilitate the discussion.

1.1.1 Synthesis of chiral morpholine derivatives

Chiral substituted morpholines were prepared previously by the methods outlined in Chart 1.[2]

Chart 1

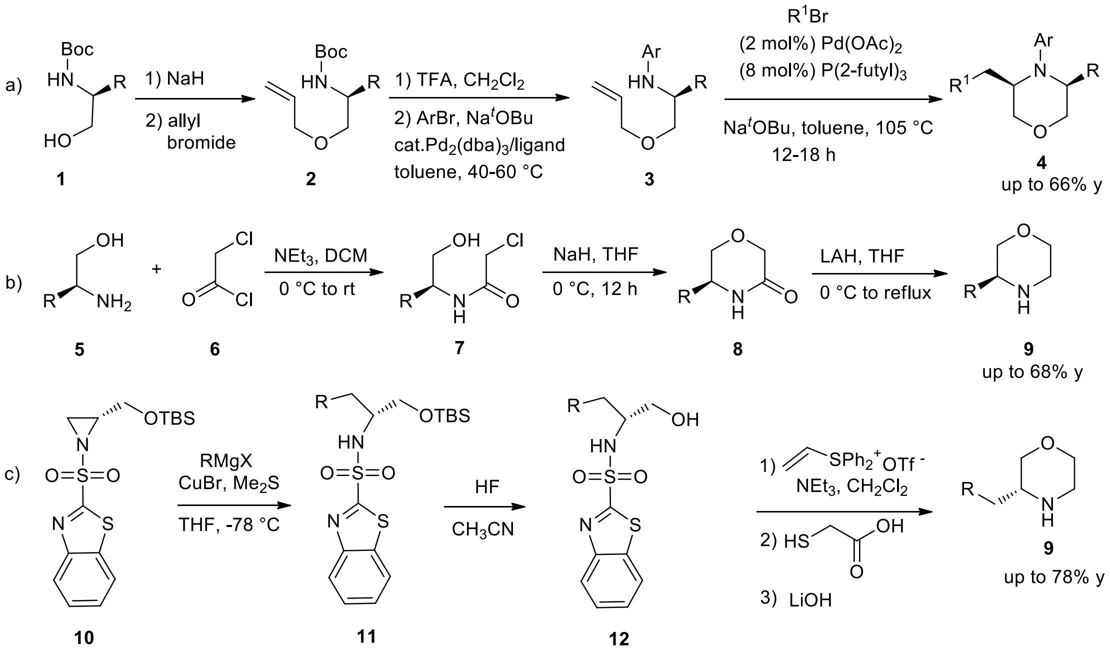
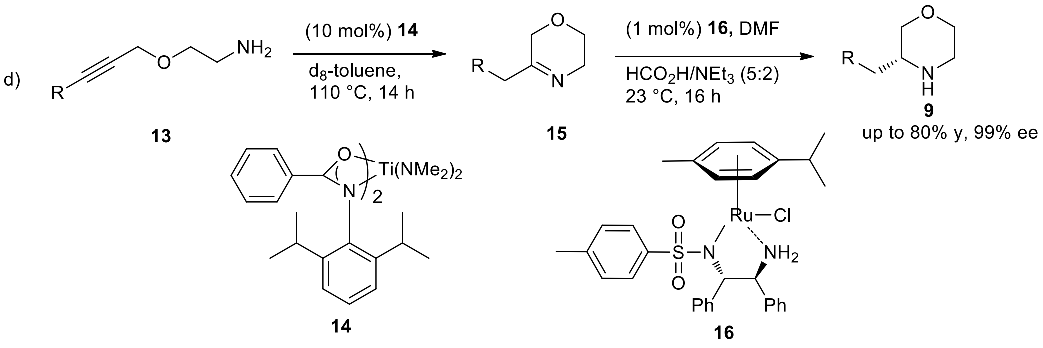


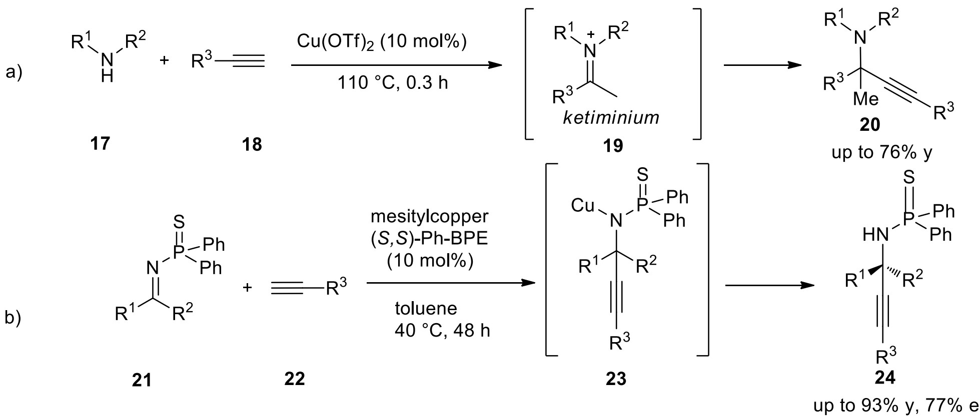
Chart 1 (Continued)



1.1.2 Synthesis of tetrasubstituted propargylamines

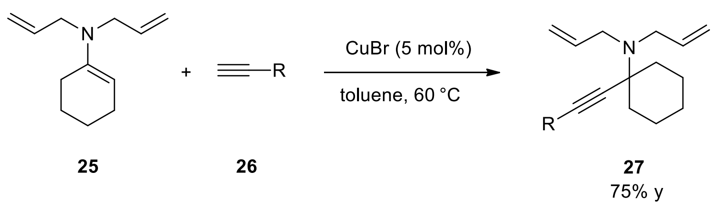
Earlier, the synthesis of tetrasubstituted propargylamines was achieved from secondary amines and 1-alkynes (Scheme 1).[3,4]

Scheme 1



Synthesis of tetrasubstituted propargylamines **27** by the CuBr catalyzed addition of alkynes **26** to ketimine derivative **25** was also reported (Scheme 2).[5]

Scheme 2

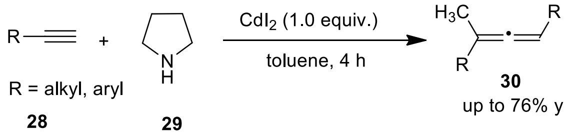


1.1.3 Synthesis of racemic trisubstituted allenes

Allenes are interesting building blocks possessing unique reactivities due to the presence of orthogonal consecutive π-bonds.[6] In recent years, methods were developed for the synthesis of 1,3-disubstituted chiral allenes in this laboratory.[7] It was also of interest to as to to develop a method to access trisubstituted chiral allenes.

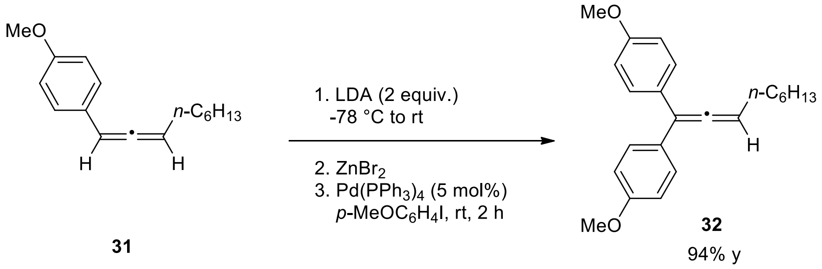
A method for the preparation of trisubstituted allenes **30** by the reaction of pyrrolidine **29** with 1-alkynes **28** in the presence of CdI_2 was reported (Scheme 3).[8]

Scheme 3



A novel methodology for the synthesis of trisubstituted allene **32** was reported by lithiation of 1-aryl-3-alkylpropadiene **31** and subsequent transmetalation using zinc bromide followed by Pd-catalyzed Negishi coupling reaction with halides to obtain the corresponding trisubstituted allene **32** (Scheme 4).[9]

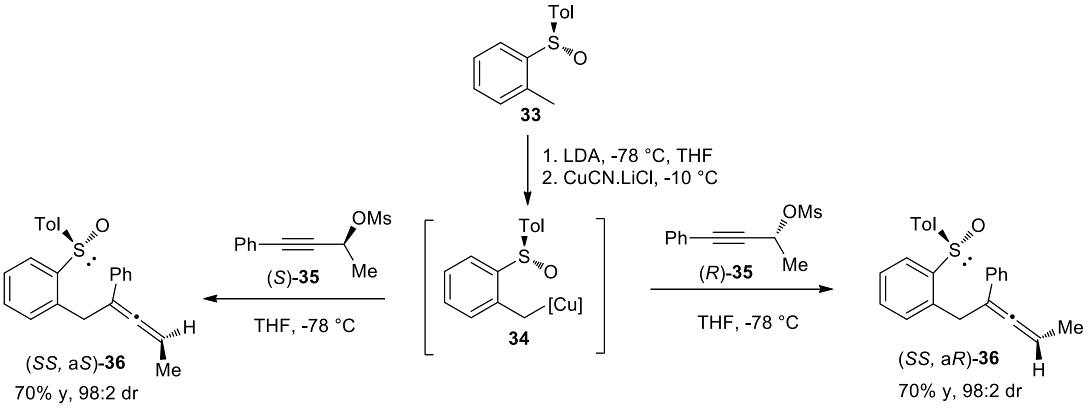
Scheme 4



1.1.3.1 Synthesis of chiral trisubstituted allene

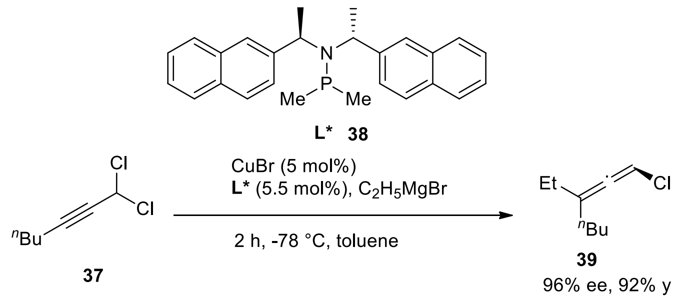
The copper complex **34** prepared using lithium-2-*p*-tolylsulfinylbenzyl carbanion of **33** which upon reaction with the chiral mesylates **35** gave the chiral trisubstituted allene **36** in 70% yield with 98:2 dr (Scheme 5).[10]

Scheme 5



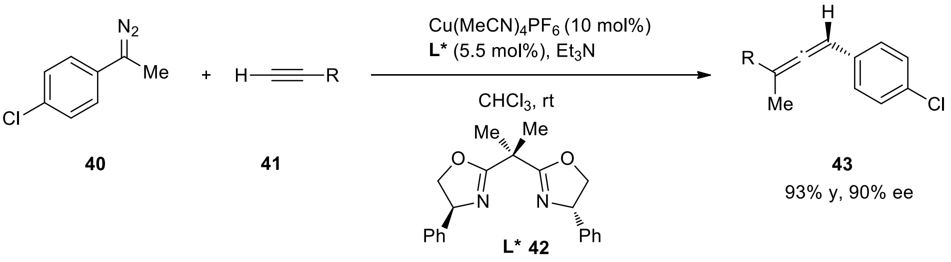
Also, a copper catalyzed enantioselective synthesis of chiral chloro allene **39** was reported by employing catalytic amount of SimplePhos ligand **38** as chiral source in the reaction of the *gem*-dihalide **37** with C_2H_5MgBr (Scheme 6).[11]

Scheme 6



More recently, a highly enantioselective synthesis of trisubstituted chiral allenes **43** by copper catalyzed cross coupling of aryl diazoalkene **40** and terminal alkynes **41** using chiral bisoxazoline ligand **42** was reported (Scheme 7).[12]

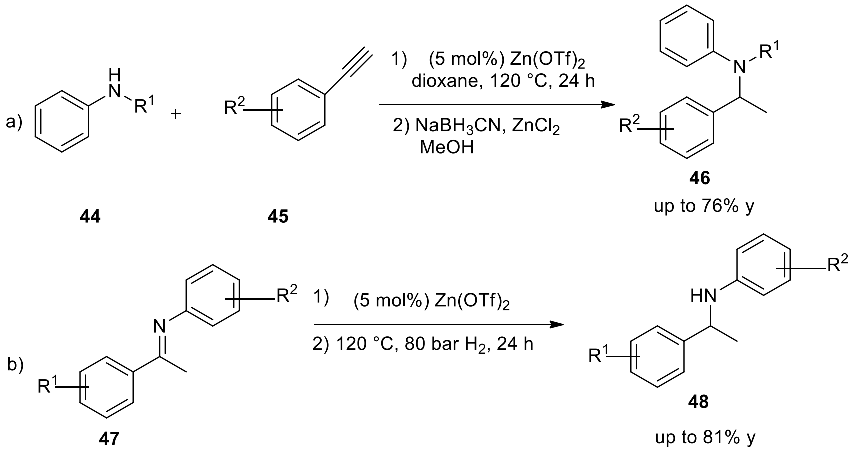
Scheme 7



1.1.4 Reactions of secondary amines with 1-alkynes

In recent years, there have been several reports on the hydroamination of alkynes.[13] For example, it was reported that $Zn(OTf)_2$ promoted hydroamination of 1-alkynes using amines gave the ketimine or ketiminium intermediates which upon reduction afforded trisubstituted amines **46** and **48** (Scheme 8).[14]

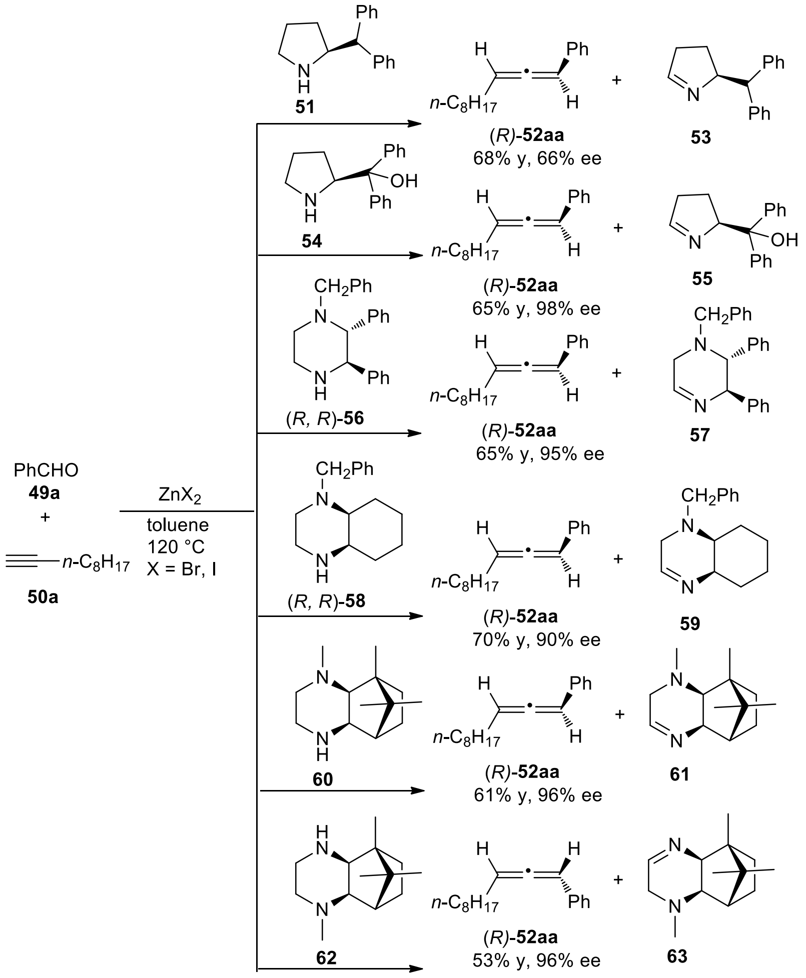
Scheme 8



1.1.5 Chirality transfer from other moieties developed in this laboratory

Previously, the (*S*)-diphenylprolinol **51** was used in this laboratory for the one pot three component (chiral secondary amines **54**, aldehyde **49**, and alkyne **50**) synthesis of chiral allenes in good yields (42-65%) with 78-98% ee.[15a] Also, it was found that the use of (*S*)-diphenylmethanopyrrolidine **51** gave the (*R*)-allene **52aa** only in 68% yield with 66% ee. The readily accessible (*R*, *R*)-2,3-diphenylpiperazine **56** system afforded (*R*)-allene **52aa** in 95% ee and 65% yield using ZnI_2 and the piperazine **58** derived from (1*R*, 2*R*)-cyclohexyldiamine furnished the (*R*)-allene **52aa** in 70% yield with 90% ee. Whereas the chiral camphanyl derivatives **60** and **62** gave the opposite isomers of allenes **52aa** with 61% and 53% yields with up to 96% ee (Chart 2).[15]

Chart 2



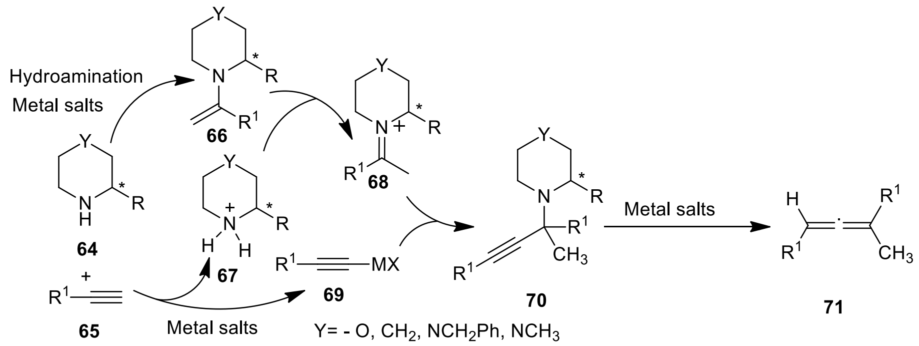
We have undertaken efforts to synthesize tetrasubstituted propargylamines and their conversion to trisubstituted allenes. The results of these studies are described in the next section.

1.2 Results and Discussion

1.2.1 Synthesis of tetrasubstituted propargylamines

We have investigated the preparation of iminium ions and alkynyl metal intermediates *in situ* for the synthesis of tetrasubstituted chiral propargylamines and trisubstituted chiral allenes from 1-alkynes (Scheme 9).

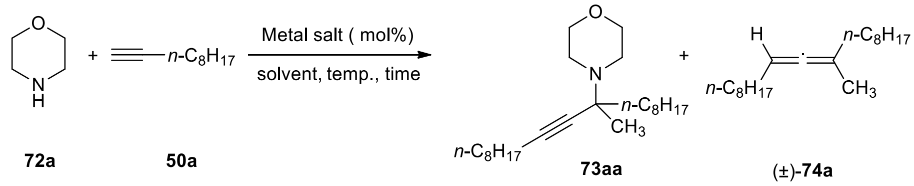
Scheme 9



Initially, we have carried out the reaction using 1-decyne and morpholine with $ZnCl_2$ or $ZnBr_2$ at 120 °C. The propargylamine **73aa** was not formed under these conditions (entries 1 and 2, Table 1) but it was formed in 15% yield after 24 h when ZnI_2 was used (entry 3, Table 1) and obtained 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, the propargylamine **73aa** was formed in 69% yield within 2 h at 120 °C (entry 5, Table 1). Further screening led to the observation that the cheaper CuCl plays the same role affording **73aa** in 83% yield (entry 8, Table 1). The propargylamine **73aa** was also obtained in similar yields using the other copper halides CuBr and CuI under this reaction condition along with some allene byproduct (entries 10, 11, Table 1).

Table 1: Reaction of morpholine **72a** and 1-decyne **50a** with different metal salts to produce tetrasubstituted propargylamine **73aa**.[a,b]



S.No	Solvent	Temp. °C	MX_n	Mol(%)	Time	73aa
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 **72a** (1.0 mmol) and 1-decyne **50a** (2.2 mmol). [b]Yields of propargylamines.

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 **74a** (entry 9, Table 1), whereas lowering the temperature to 100 °C resulted in lower yields of the propargylamine product **73aa** (entry 12, Table 1).

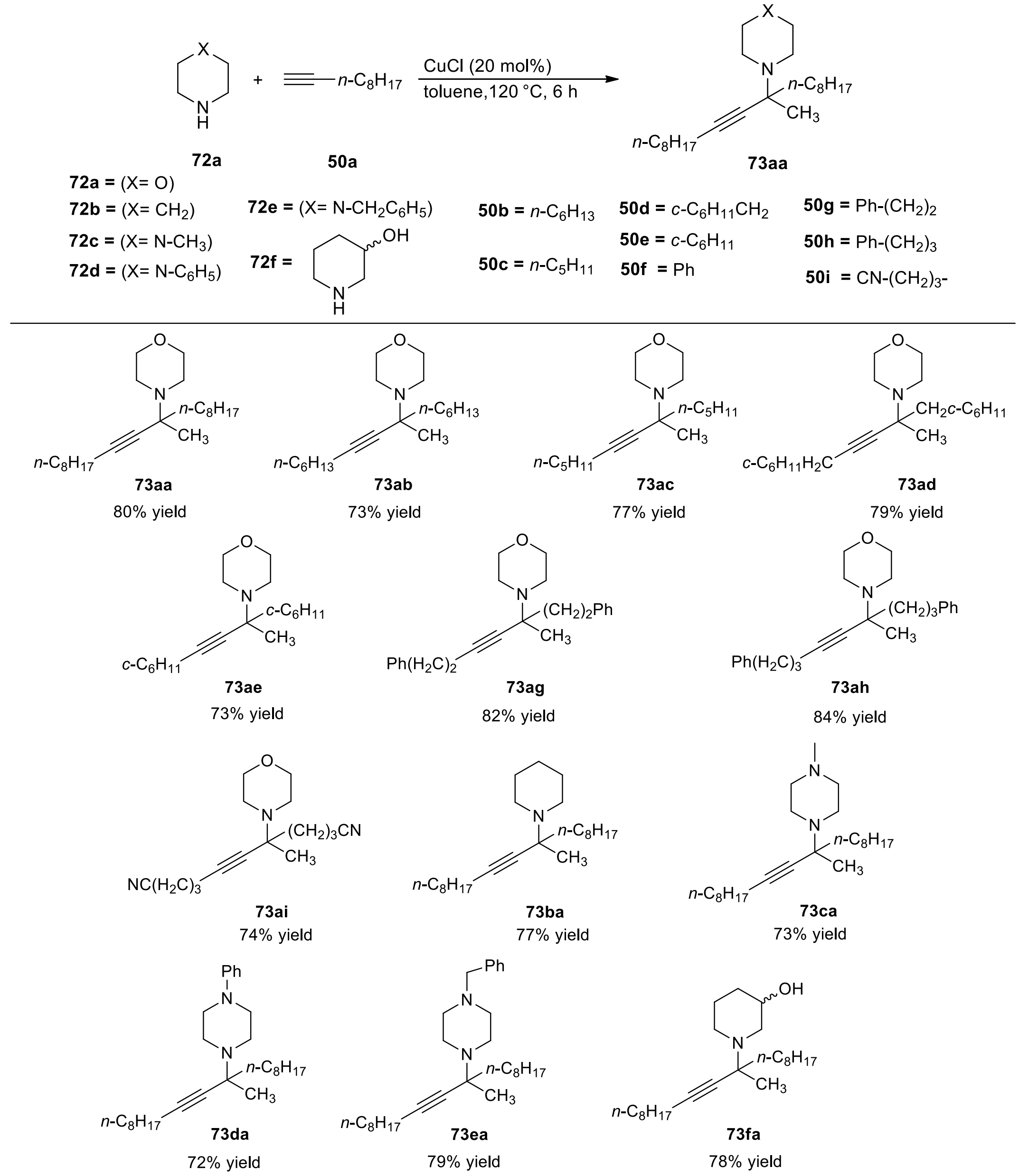
However, experiments carried out at different temperature and time interval conditions to obtain the trisubstituted allene **74a** as major product in a single pot operation were not successful.

The copper(II) salts CuX_2 (Cl or Br) are not effective but the $Cu(OTf)_2$ afforded the product **73aa** in 92% yield within 0.5 h at 100 °C (entries 12 and 13, Table 1). Although, the use of $Cu(OTf)_2$ gave better results, we have explored the scope of the reaction using CuCl in toluene (entries 6 and 8, Table 1) as it is less expensive. The results are summarized in Table 2.

1.2.1.1 Synthesis of tetrasubstituted propargylamines in toluene solvent

The reaction of morpholine and 1-alkynes like 1-octyne **50b** and 1-heptyne **50c** gave the corresponding tetrasubstituted propargylamines **73ab** and **73ac** in 73% and 77% yields (Table 2). Substituted 1-alkynes such as 3-cyclohexyl-1-propyne (**50d**), 2-cyclohexyl-1-acetylene (**50e**) and 4-phenyl-1-butyne (**50g**) furnished the corresponding products in up to 82% yield. The functionalized alkyne like 6-cyano-1-hexyne (**50i**) afforded the corresponding propargylamine **73ai** in 74% yield (Table 2).

Table 2: Synthesis of propargylamines **73** using cyclic amines **72** and 1-alkynes **50**.[a,b]



72a = (X= O)
72b = (X= CH_2)
72c = (X= N-CH_3)
72d = (X= N-C_6H_5)
72e = (X= N-$CH_2C_6H_5$)
72f =
50b = n-C_6H_{13}
50c = n-C_5H_{11}
50d = c-$C_6H_{11}CH_2$
50e = c-C_6H_{11}
50f = Ph
50g = Ph-$(CH_2)_2$
50h = Ph-$(CH_2)_3$
50i = CN-$(CH_2)_3$-

73aa	80% yield
73ab	73% yield
73ac	77% yield
73ad	79% yield
73ae	73% yield
73ag	82% yield
73ah	84% yield
73ai	74% yield
73ba	77% yield
73ca	73% yield
73da	72% yield
73ea	79% yield
73fa	78% yield

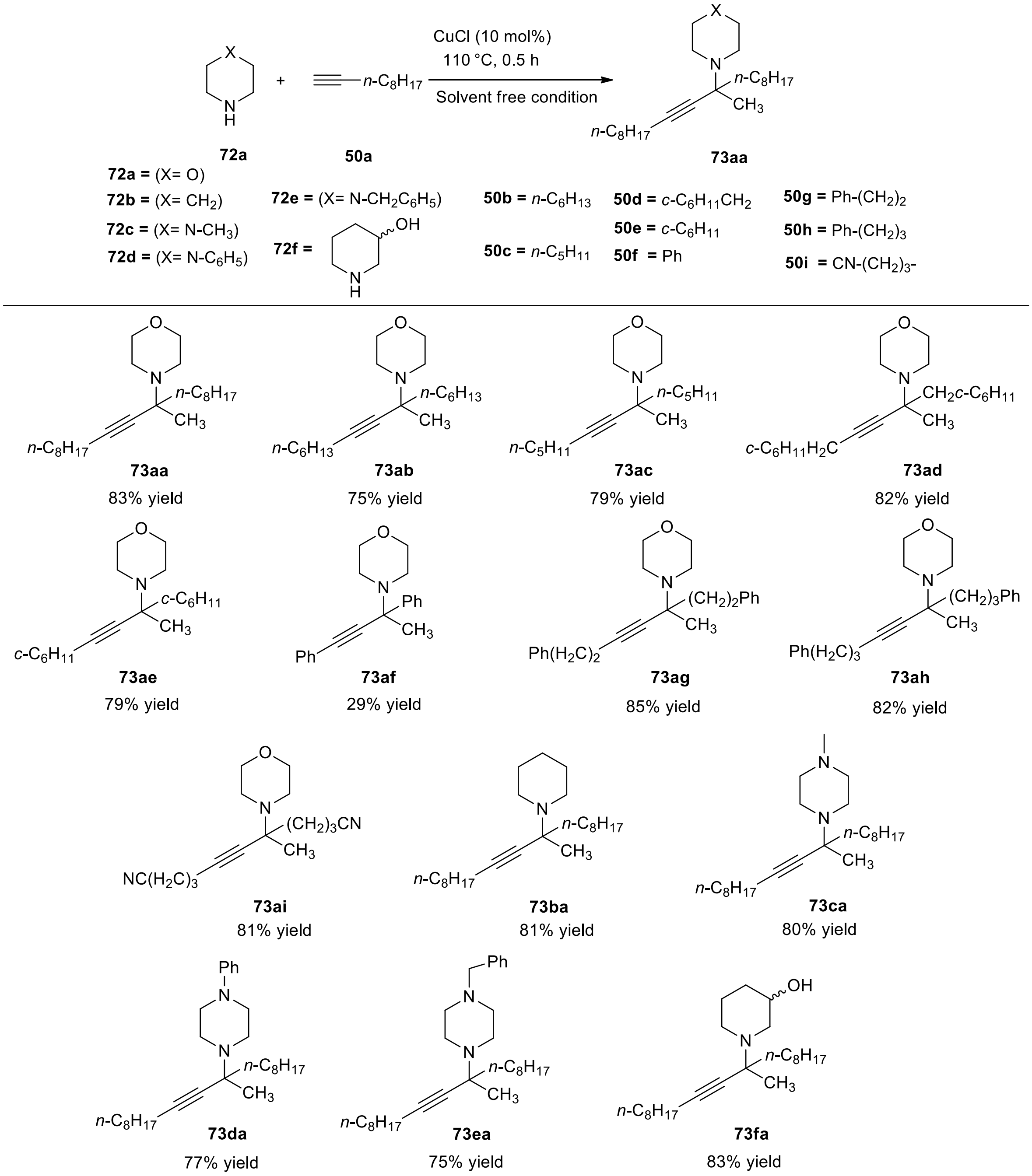
[a]The reactions were carried out by using amines **72** (1.0 mmol) and 1-alkynes **50** (2.2 mmol) in toluene (3 mL) at 120 °C for 6 h. [b]Yields of propargylamines.

1.2.1.2 Synthesis of tetrasubstituted propargylamines under solvent free condition

When the reaction of morpholine and other 1-alkynes like 1-octyne **50b** and 1-heptyne **50c** gave the corresponding tetrasubstituted propargylamines **73ab** and **73ac** in 75% and 79% yields under solvent free condition (Table 3). Reaction using the substituted 1-alkynes 3-cyclohexyl-1-propyne (**50d**), 2-cyclohexyl-1-acetylene (**50e**) and 4-phenyl-1-

butyne (**50g**) furnished the corresponding products with up to 85% yield. The functionalized alkynes, like 6-cyano-1-hexyne (**50i**) afforded the corresponding propargylamine in 81% yield (Table 3). Unexpectedly, the reaction using the aromatic alkyne (**50f)** and morpholine gave the desired product **73af** only in 29% yield (Table 3).

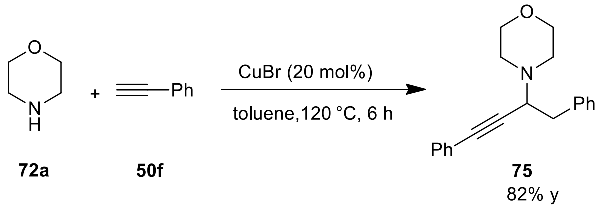
Table 3: Synthesis of propargylamines **73** using cyclic amines **72** and 1-alkynes **50**.[a,b]



[a] The reactions were carried out by using amines **72 (**1.0 mmol) and 1-alkynes **50** (2.2 mmol) at 110 °C for 0.5 h.
[b] Yields of propargylamines.

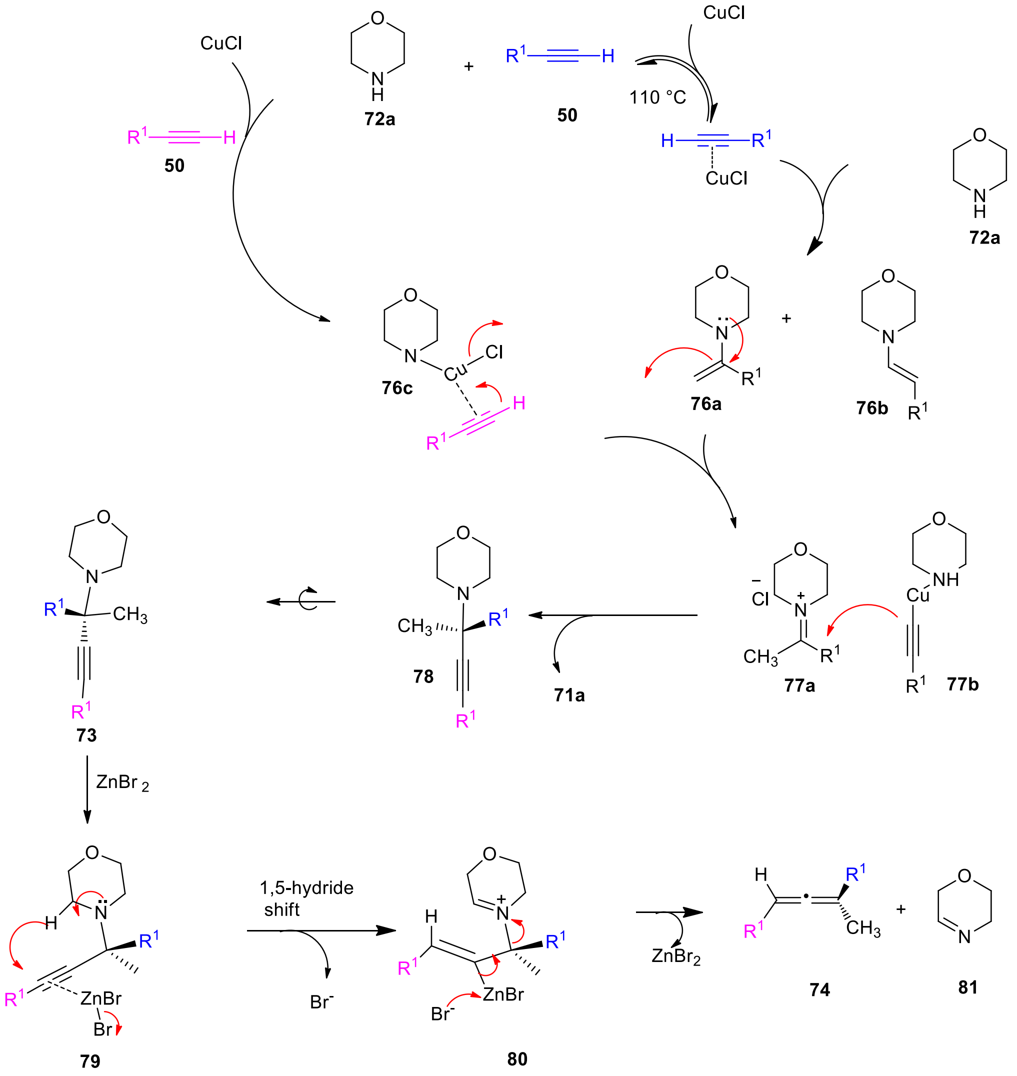
Interestingly, when the reaction of phenylacetylene **50f** and morpholine **72a** was carried out using CuBr, the propargylamine **75** was obtained in 82% yield at 120 °C (Scheme 10).[16]

Scheme 10



1.2.2 Tentative mechanism

Scheme 11

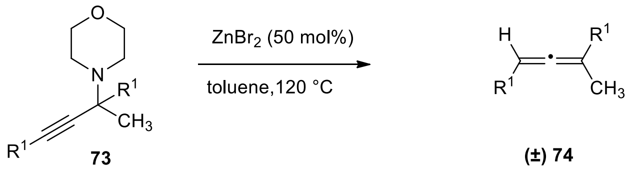


1.2.3 Conversion of propargylamines to allenes

As discussed earlier, the trisubstituted allenes are obtained as side products in 7% to 10% yield in some experiments. We have observed that the propargylamine **73aa** reacted with $ZnBr_2$ (0.5 mmol), at 120 ^{0}C to give the allene **74a** in 87% yield (Table 4).

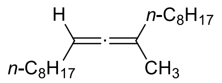
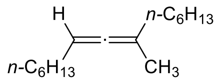
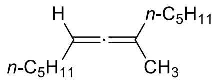
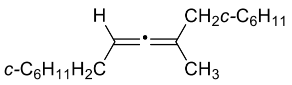
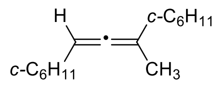
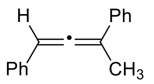
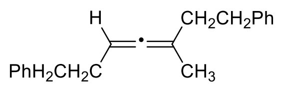
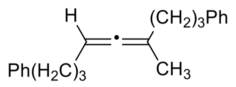
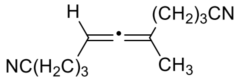
Also, the propargylamines **73ab-ad**, obtained from substituted alkynes react with $ZnBr_2$ to give the corresponding allenes **74b-7d** in up to 83-91% yield (Table 4). Further, the propargylamine **73ai** containing cyano group upon reaction with $ZnBr_2$ (0.5 mmol) gave the allene **74i** in 82% yield (Table 4)

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



R^1

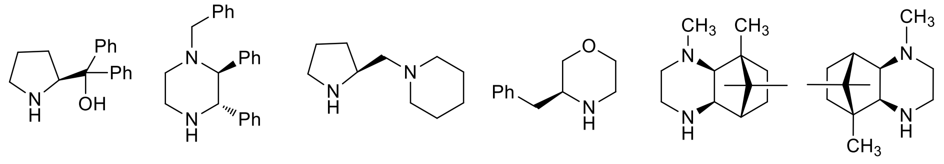
73aa = n-C_8H_{17}
73ab = n-C_6H_{13}
73ac = n-C_5H_{11}
73ad = CH_2c-C_6H_{11}
73ae = c-C_6H_{11}
73af = Ph
73ag = Ph-$(CH_2)_2$
73ah = Ph-$(CH_2)_3$
73ai = CN-$(CH_2)_3$-

 **74a** 4h, 87% y	 **74b** 4h, 90% y	 **74c** 4h, 91% y
 **74d** 6h, 83% y	 **74e** 4h, 81% y	 **74f** 4h, 79% y
 **74g** 6h, 85% y	 **74h** 6h, 93% y	 **74i** 14h, 82% y

The reactions were carried out by taking propargylamines **73** (1 mmol) in toluene (3 mL) with $ZnBr_2$ (0.5 mmol). [b]Isolated yield.

1.2.4 Diastereoselective synthesis of tetrasubstituted propargylamines

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 examined the use of different readily accessible optically active chiral secondary amines in this transformation (Figure 1).[17]

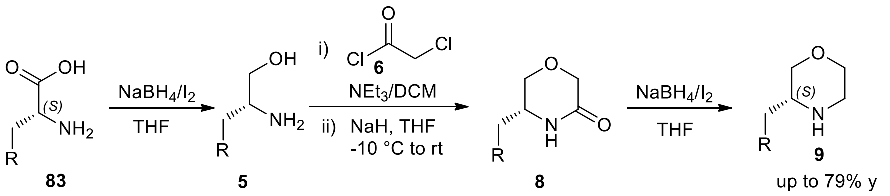


51 **56** **82** **9a** **60** **62**

Figure 1

The chiral amine **51** is commercially available and also readily accessible by the methods developed in this laboratory. Also, chiral amines **82**, **56**, **60** and **62** are readily accessible by the methods developed in this laboratory. We have also developed a simple convenient method for the synthesis of chiral amine **9** (Scheme 12).

Scheme 12



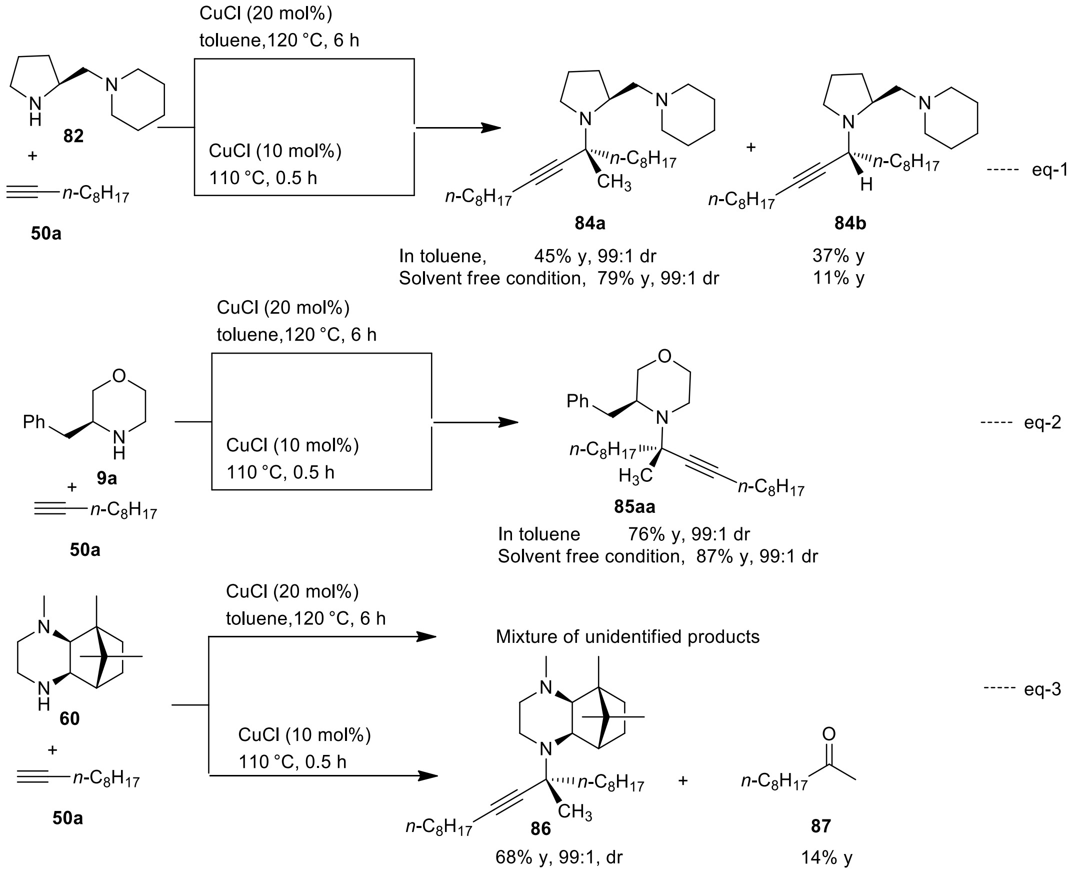
up to 79% y

R= $-CH_2Ph$, Ph, $CH(CH_3)_2$

The chiral amines **51**, **56** and **82** failed to give the corresponding propargylamine under these conditions, presumably, due to sterically crowded nature of these amines. The less hindered chiral amine **82** did give the corresponding tetrasubstituted propargylamine **84a** in 45% yield along with the trisubstituted propargylamine **84b** in 37% yield in the reaction using CuCl in toluene at 120 ºC (Scheme 13). When the reaction was carried out without using toluene, the tetrasubstituted propargylamine **84a** was obtained in 79% yield along with the trisubstituted propargylamine **84b** in 11% yield (Scheme 13**,** eq-1).

The reaction using the chiral morpholine **9a** using toluene gave the tetrasubstituted propargylamine **85aa** in 76% yield with 99:1 dr (Scheme 13, eq-2**)**. Slightly higher yield was realized (87%) in an experiment without using toluene. Whereas, the optically active N-methyl camphanyl piperazine **60** gave unidentified mixture of products in toluene, under solvent free condition the chiral propargylamine **86a** was obtained in 68% yield with 99:1 dr along with the ketone **87** (Scheme 13, eq-3)**.**

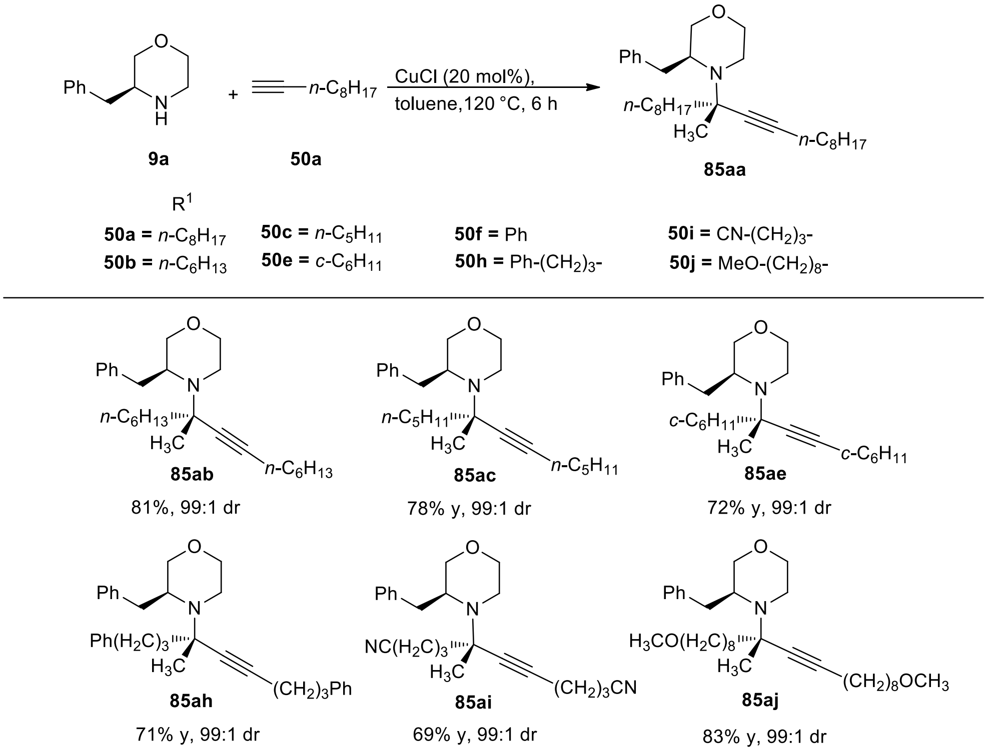
Scheme 13



We have carried out several experiments using the chiral morpholine **9a** with different alkynes and the results are summarized in Table 5. The reactions using 1-alkyne **50b** and **50c** to give the corresponding propargylamines **85ab** and **85ac** in 81% and 78% yield (Table 5).

The reaction is also applicable to substituted aliphatic 1-alkynes as illustrated by the reactions using the alkynes **50e**, **50h**, **50i** and **50j** which gave the corresponding propargylamines **85ae**, **85ah**, **85ai**, **85aj** in 69-83% yields with 99:1 dr.

Table 5: Synthesis of chiral propargylamines **85** using 1-alkynes **50** and the chiral amine **9a** using CuCl.[a,b]



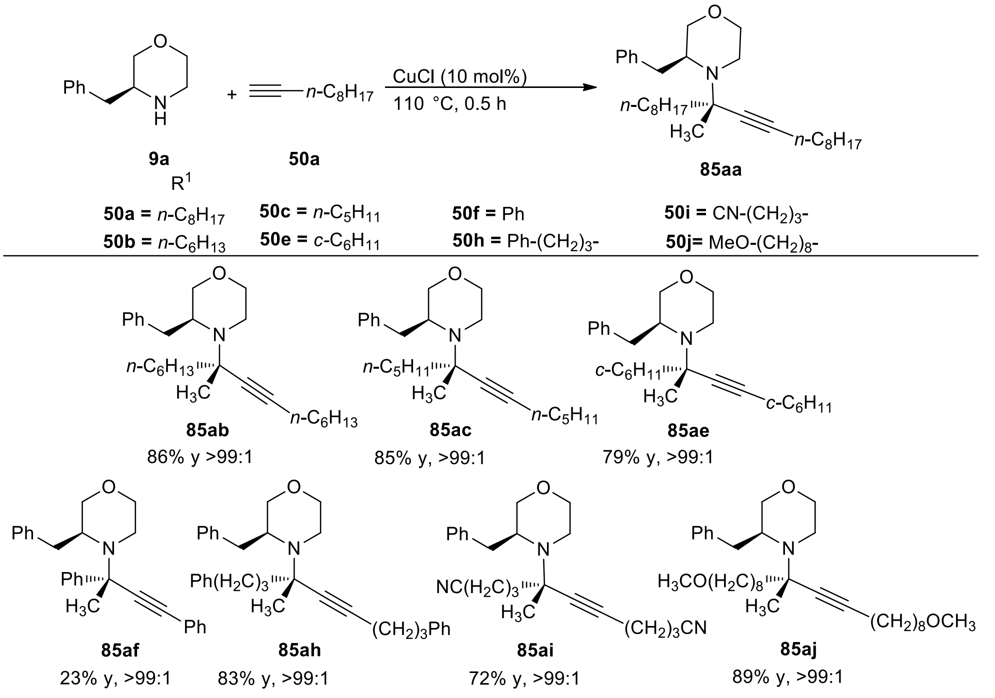
[a]The reactions were carried out by using amine **9a** (1.0 mmol) and 1-alkynes **50** (2.2 mmol) in toluene (3 mL) at 120 ºC for 6 h.[b]Yield of propargylamines.

We have also carried out several experiments using the chiral morpholine **9a** with different alkynes **50** under solvent free condition and the results are summarized in Table 6. The reactions using 1-alkyne **50b** and **50c** to give the corresponding propargylamines **85ab** and **85ac** in 86% and 85% yield (Table 6).

The reaction is also applicable to substituted aliphatic 1-alkynes (**50e, 50h)**, and the corresponding propargylamines **85ae** and **85ah** were obtained in 79-83% yields (Table 6).

Interestingly, when the reaction of phenylacetylene **52f** and chiral morpholine **9a** was carried out the corresponding propargylamine **85af** was obtained in 23% yield (Table 6).

Table 6: Synthesis of chiral propargylamines **85** using 1-alkynes **50** and the chiral amine **9a** using CuCl.[a,b]



[a]The reactions were carried out by using amine **9a** **(**1.0 mmol) and 1-alkynes **50** (2.2 mmol) at 110 °C for 0.5 h. [b]Yield of propargylamines.

The configurations at the newly formed stereogenic centres were assigned as (*S*) on the basis of X-ray single crystal structure analysis of the propargylamine **85af** (Figure 2).

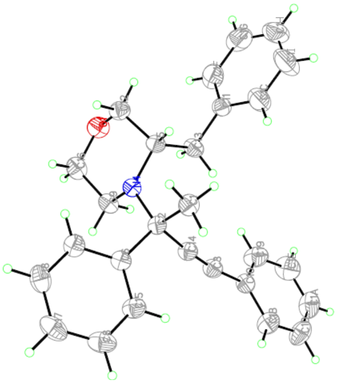


Figure 2. ORTEP representation of propargylamine **85af** and thermal ellipsoids are drawn with 30% probability.

Table 7: Crystal data and structure refinement for compound **85af**.

Identification code	compound 85af
Empirical formula	$C_{27}H_{27}NO$
Formula weight	381.50
Temperature	293(2) K
Wavelength	1.54184 A
Crystal system, space group	Monoclinic, p21
Unit cell dimensions	a = 10.8053(3) A alpha = 90 deg.
	b = 7.24972(20) A beta = 91.614(2) deg.
	c = 14.0896(4) A gamma = 90 deg.
Volume	1103.28(5) A^3
Z, Calculated density	2, 1.148 Mg/m^3
Absorption coefficient	0.530 mm^-1
F(000)	408
Crystal size	0.33 x 0.33 x 0.33 mm
Theta range for data collection	3.14 to 66.59 deg.
Limiting indices	-9<=h<=12, -8<=k<=4, -16<=l<=16
Reflections collected / unique	3653 / 2385 [R(int) = 0.0150]
Completeness to theta = 66.59	97.2 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2385 / 1 / 263
Goodness-of-fit on F^2	1.044
Final R indices [I>2sigma(I)]	R1 = 0.0369, wR2 = 0.0992
R indices (all data)	R1 = 0.0383, wR2 = 0.1007
Absolute structure parameter	0.1(4)
Largest diff. peak and hole	0.122 and -0.211 e.A^-3

1.2.5 Synthesis of chiral trisubstituted allenes from propargylamines

We have observed that the chiral propargylamines **85aa-85aj** react with $ZnBr_2$ at 120 °C to give the corresponding allenes **74a-74j** in 68-89% yield at 120 ºC (Table 8). The propargylamines having functionalized groups also afforded the chiral allenes **74i**, **74j** and in 71% and 68% yields with up to 99% ee (Table 8). It was also found that all propargylamines are converted into the corresponding chiral allenes **74** within 1-3 h under these reaction conditions (Table 8). All the optically active allenes obtained by using chiral amine **9a** are levorotatory.

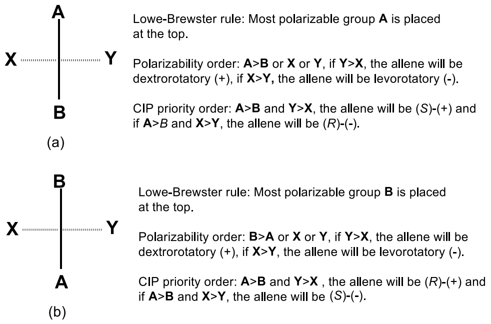
Hence, the absolute configurations of the major enantiomer of the chiral allenes are assigned as *R* based on the Lowe-Brewster rule[18a,b] and Taft[18c] and Runge[18d,e] revised polarizabilty parameters excepted for the substituents in these allenes.[18f] However, since there is some ambiguity in assigning configuration of trisubstituted allenes, it is desirable to discuss this assignment of (*R)* configuration for the trisubstituted allenes reported here.

In recent years, several enantiomerically enriched chiral trisubstituted allenes were reported, but their configurations were assigned based only on reaction mechanisms without even considering the Lowe−Brewster rule. Hence, it is desirable to briefly discuss the assignment of configuration for the enantiomerically enriched trisubstituted allenes considering the Lowe−Brewster rule.

The chiral allenes may be considered to have the structures with substituents A and B at one allene end and groups X and Y at the other allene end, as depicted in Figure 3. In the Lowe model[18a] the group with highest polarity A is placed at the top [Figure 3, structure (a)] and the other group B is also placed above the plane with the X and Y groups placed in the sides below the plane. The Lowe rule predicts the allene to be levorotatory with $(-)[\alpha]_D$ if the polarizability of the group X > Y and the allene to be dextrorotatory with (+)[α]$_D$ if the polarizability is Y > X. For disubstitued chiral allenes, the Cahn−Ingold−Prelog (CIP) priority rules will be in the order A > B (B=H), X > Y (Y=H).

Hence, the disubstitued allene with (*R*) configuration will have (−)[α]$_D$, and the corresponding enantiomer will have (+)[α]$_D$ value with (*S*) configuration. This will also be the case for enantiomerically enriched trisubstituted allenes **74a**−**74k** [A (A=Ph or alkyl) > B (B=CH_3), X (X= Ph or alkyl) > Y (Y=H) reported here, where the expected Lowe−Brewster polarizability order and the CIP priority order are the same as in disubstituted allenes. Hence, the enantiomerically enriched trisubstituted allene derivatives **74a**−**74k** with (−)[α]$_D$ values are assigned to the (*R*) configuration.

Therefore, the (*R*)-(+) configuration reported for the enantiomerically enriched chiral allene with same substituents as in **74f** (Ph, CH_3 and Ph, H) but with [α]$_D$ = +122.4 should be corrected as (*S*)-(+).[18h] Presumably, the (*R*)-(+) configuration was assigned erroneously in the earlier report[18h] by comparison with incorrect drawing of the allene structure (substituents Ph, n-Bu and Ph, H) with [α]$_D$ = +251 for which the original authors did not assign the configuration.[18g]



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 [α]$_D$ values based on Brewster-Lowe-Taft-Runge polarizability parameters and Cahn-Ingold-Prelog (CIP) priority rules.

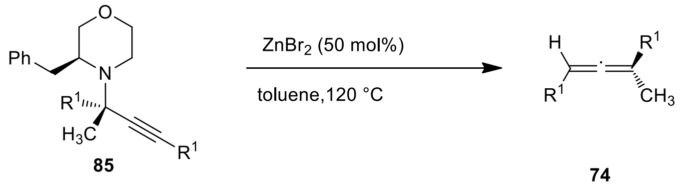
An interesting possibility is that a group may have higher priority as per the CIP rules but may not have the highest polarizability [Figure 3, structure (b)]. In such cases, the allene with (*R*) configuration will give (+)$[\alpha]_D$ and its (*S*) enantiomer will give (−)$[\alpha]_D$ values as per the Lowe−Brewster rule.

There are several reports assigning (*R*)-(+) and (*S*)-(−) configurations for trisubstituted allenes based on reaction mechanisms,[17a−d] but in these reports, the Lowe−Brewster and Taft− Runge polarizability and the CIP priority order for the substituents were not considered while assigning configurations, and the assigned configurations were also not confirmed by X-ray structure analysis or NMR spectral analysis with chiral solvating agents as was done in some other cases.[19e,f]

Such ambiguity is also expected in assigning configurations for tetrasubstituted chiral allenes.[19g] Needless to say, because the Lowe−Brewster rule is based on the sign of optical rotation, this method of assigning configuration may not be reliable if the magnitude of the $[\alpha]_D$ value is small.

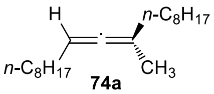
In this regard, it may be of interest to note that an interesting spontaneous resolution of tetrasubstituted allenic phosphinate derivatives was reported recently, and the enantiomers were characterized by X-ray structure analysis but the samples did not have significant $[\alpha]_D$.[19h] Presumably, the differences in polarizability of substituents are small in these cases.

Table 8: $ZnBr_2$ promoted conversion of chiral propargylamines **85** to allenes **74**. [a,b,c]

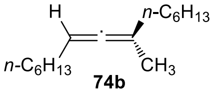


R^1

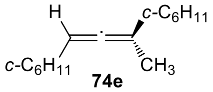
85aa = n-C_8H_{17}
85ab = n-C_6H_{13}
85ae = c-C_6H_{11}
85af = Ph
85ah = Ph-$(CH_2)_3$
85ai = CN-$CH_2)_3$-
85aj = MeO-$(CH_2)_8$-



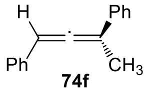
74a
1 h, 86% y, 96% ee



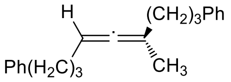
74b
1 h, 89% y, 90% ee



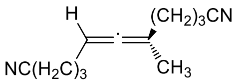
74e
1 h, 87% y, 99% ee



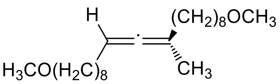
74f
1 h, 71% y, 94% ee



74h
1 h, 84% y, 99% ee



74i
3 h, 71% y, 99% ee



74j
1 h, 68% y, 99% ee

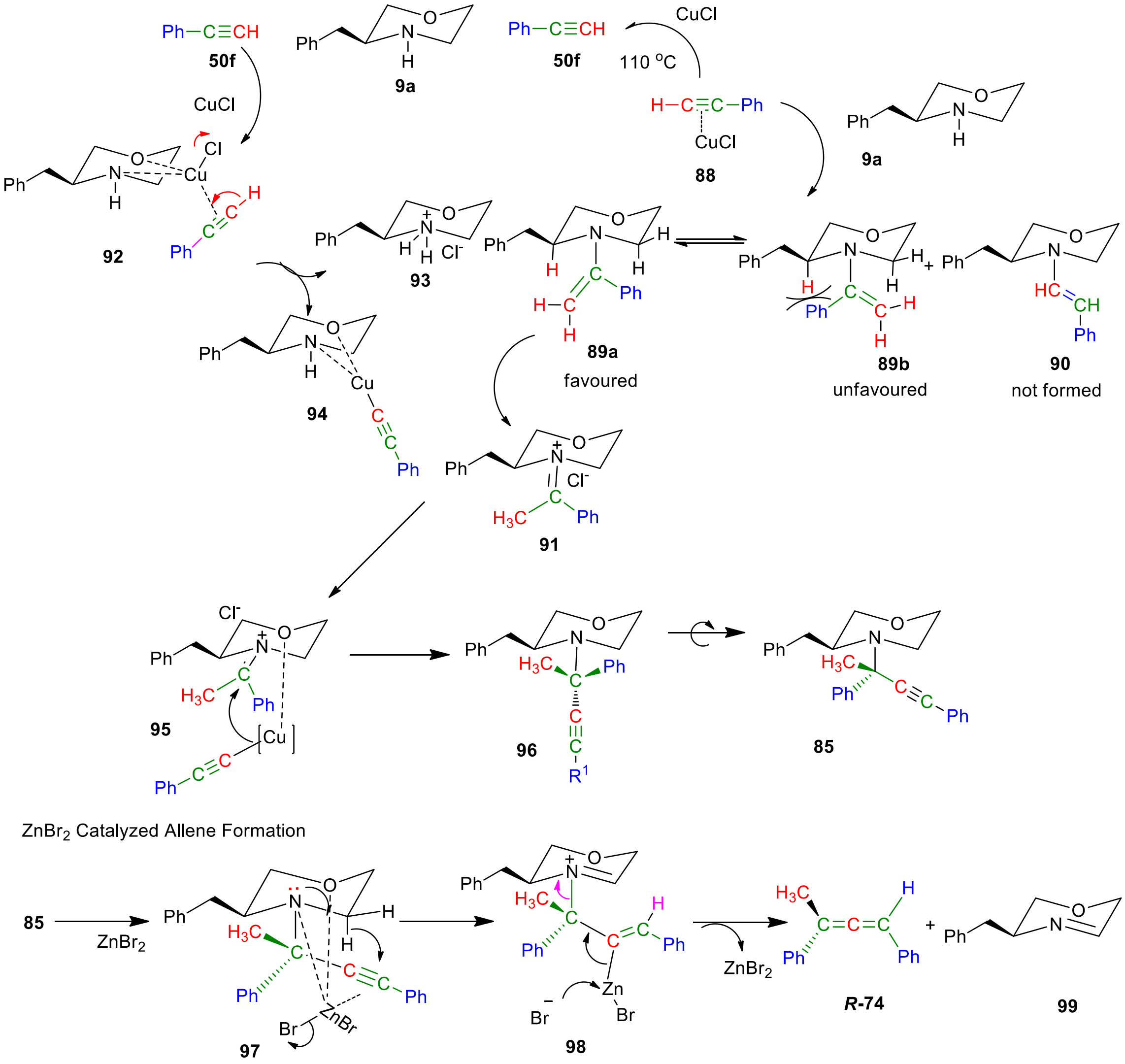
[a] The reactions were carried out by using propargylamines **85** (1 mmol) which obtained from chiral morpholine **9a** in toluene (3 mL) with $ZnBr_2$ (0.5 mmol) at 120 °C. [b] Yield of allenes. [c] The ee was determined by chiral HPLC analysis.

1.2.6 Mechanism for the synthesis of trisubstituted allenes

The CuCl catalyzed formation of propargylamines **85aa-85aj** and their conversion to chiral allenes by the $ZnBr_2$ promoted transformation can be explained by the tentative mechanism outlined in Scheme 14. Initially, the chiral amine **9a** would react with CuCl to form the complex **92**.[20]

The intermediate **89** formed *in situ* by the hydroamination of alkyne by the chiral amine, isomerization to more-substituted ketimine, delivery of the alkynyl group from bottom face of the ketiminium ion species would lead to the new (*S*)-stereogenic center at the propargylamine product **85** that could complex with $ZnBr_2$ to give the intermediate **97**. After an intramolecular hydride shift, the chiral allene (*R*)-**74** would be formed *via* the intermediate **99** (Scheme 14).[17,21]

Scheme 14



We have also found that the imine byproduct **99** could be easily converted *in situ* to the corresponding chiral secondary amine **9a** in 62% yield by simple sodium borohydride reduction in MeOH.

1.3 Conclusions

We have devised a simple, convenient method for the diastereoselective synthesis of tetrasubstituted propargylamine derivatives from the corresponding chiral secondary amine and 1-alkynes using CuCl. Furthermore, these propargylamine derivatives were converted to trisubstituted allenes in high yields with excellent enantioselectivities using $ZnBr_2$. Hence, these chiral propargylamine and allene compounds have considerable potential for further exploitation in asymmetric transformations.

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 ±0.01°) and AUTOPOL-IV (readability ±0.001°) automatic polarimeters. The condition of the polarimeter was checked by measuring the optical rotation of a standard solution of (*S*)-(+)-α,α–diphenylprolinol {$[\alpha]_D^{25} = +67.2$ (*c* 0.52, $CHCl_3$)} supplied by Gerchem Laboratory (Pvt) Ltd., India.

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 chiral morpholines 9

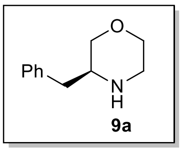
A suspension of **83** (1.0 equiv.) in dry THF (100 mL) was cooled down to 0 ºC and sodium borohydride (2.4 equiv.) was added in one portion. A solution of iodine (2.4 equiv.) in dry THF (30 mL) was added to this suspension over 30 min. Once addition was complete, the bath was removed and the reaction was warmed to reflux for 16 h. After this time, the reaction was cooled to RT and methanol (25 mL) was added very slowly (take care with the hydrogen evolution, violent reaction) until the mixture became a clear solution. After 30 min stirring, the solution was transferred to a one-necked flask, washed with methanol (30 mL) and concentrated. The resulting syrup was dissolved with aqueous 3.5 M KOH (75 mL) and stirred for 30 min at room temperature. The aqueous layer was extracted with dichloromethane (5 x 80 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to yield **5** which was used in the next step without further purification.

Amino alcohol **5** (1 equiv.) was dissolved in DCM and cooled to 0 ºC. Triethylamine (1.1 equiv.) in DCM was added and the solution was stirred for ten minutes. Chloroacetyl chloride **6** (1.1 equiv.) in DCM was slowly added over one hour. The resulted mixture was kept at 0 ºC for thirty minutes, and then allowed slowly warmed to room temperature. When TLC monitoring indicated completion, the reaction was quenched with water (100 mL). The organic phase was separated and the aqueous media was exacted twice with DCM. The combined organic phase was then washed twice with brine and dried with Na_2SO_4. After concentration in vacuum, a slight yellow solid was obtained in nearly quantitative yield and was directly used in the next step without further purification.

Sodium hydride (60% in mineral oil) (1.5 equiv.) was suspended in THF and kept below -10 ºC for ten minutes then crude acetamide was dissolved in THF and the solution was slowly added over one hour. The reaction was stirred for another 30 minutes and slowly warmed to room temperature. After reaction completed, water (5 mL) was carefully added, followed by ethyl acetate (100 mL). The organic phase was separated and the aqueous media was extracted with ethyl acetate three times. The organic phase was combined, dried with Na_2SO_4 and concentrated in vacuum to give amide **8**.

The compound amide **8** (1.0 equiv.) in dry THF was cooled down to 0 ºC and sodium borohydride (2.4 equiv.) was added in one portion. A solution of iodine (2.4 equiv.) in dry THF (3 mL) was added to this suspension over 30 min. Once addition was complete, the bath was removed and the reaction was warmed to reflux for 16 h. After this time, the reaction was cooled to RT and methanol (5 mL) was added very slowly (take care with the hydrogen evolution, violent reaction) until the mixture became a clear solution. After 30 min stirring, the solution was transferred to a one-necked flask, washed with methanol (3 mL) and concentrated. The resulting syrup was dissolved with aqueous 3.5 M KOH (15 mL) and stirred for 30 min at room temperature. The aqueous layer was extracted with dichloromethane (5 x 10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to yield **9** which was purified by column chromatography.

(*S*)-3-Benzylmorpholine (9a):



9a

Yield : 0.139 g, 79%, Yellow liquid.

$[\alpha]_D^{25}$: +28.2 (c = 0.50, CH_3OH).

IR (neat) : 3023, 2953, 2928, 1601, 1495, 1455, 894, 739 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.30-7.16 (m, 5H), 3.81-3.74 (m, 2H), 3.55-3.48 (m, 1H), 3.24-3.22 (m, 1H), 3.04-2.96 (m, 1H), 2.90-2.80 (m, 2H), 2.66-2.34 (m, 1H), 2.49-2.41 (m, 1H), 2.23 (s, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 138.5, 128.8, 128.4, 126.3, 72.1, 69.5, 63.2, 44.1, 38.2.

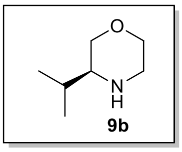
LCMS **:** m/z 177 (M+1).

Analysis **:** for $C_{11}H_{15}NO$

calcd: C 74.54, H 8.53, N 7.90.

found: C 74.48, H 8.49, N 7.81.

(*S*)-3-Isopropylmorpholine (9b):


9b

Yield : 0.082 g, 64%, Yellow liquid.

$[\alpha]_D^{25}$: +11.5 (c = 0.92, CH_3OH).

IR (neat) : 3023, 2953, 2928, 1034, 894, 739 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.72-3.59 (m, 4H), 2.91-2.89 (m, 2H), 2.85-2.83 (m, 1H), 1.42 (m, 2H), 0.93 (d, *J*= 8.0 Hz, 6H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 72.2, 69.5, 67.2, 44.2, 30.5, 19.6.

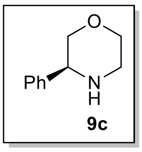
LCMS **:** m/z 129 (M+1).

Analysis **:** for $C_7H_{15}NO$

calcd: C 65.07, H 11.70, N 10.84.

found: C 65.01, H 11.65, N 10.79.

(*S*)-3-Phenylmorpholine (9c):


9c

Yield : 0.117 g, 72%, Yellow liquid.

$[\alpha]_D^{25}$: +32.7 (c = 0.42, CH_3OH).

IR (neat) : 3028, 2958, 1607, 1512, 1491, 1455, 894, 789 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.39-7.23 (m, 5H), 3.92 (d, *J*= 8.0 Hz, 1H), 3.88-3.82 (m, 1H), 3.83 (d, *J*= 8.0 Hz, 1H), 3.66-364 (m, 1H), 3.38 (t, *J*=8.0 Hz, 1H), 3.13-3.09 (m, 1H), 3.00-2.98 (m, 1H), 1.93 (s, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 137.5, 128.8, 123.9, 126.3, 69.5, 65.4, 56.8, 44.1.

LCMS **:** m/z 163 (M+1).

Analysis **:** for $C_{10}H_{13}NO$

calcd: C 73.59, H 8.03, N 8.58.

found: C 73.48, H 7.99, N 8.52.

1.4.3 General procedure for the synthesis of tetrasubstituted propargylamines 73, 85 from 1-alkynes 50 and amines with CuCl in solvent condition.

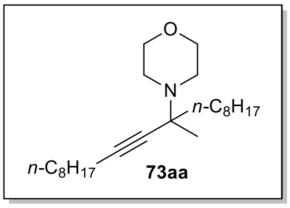
To a stirred suspension of amine (1 mmol), CuCl (0.020 g, 0.2 mmol) and 1-alkyne **50** (2.2 mmol) in toluene (3 mL) at 25 °C under N_2 atmosphere. The contents were stirred at 120 °C for 6 h. The reaction mixture cooled to room temperature. Toluene was removed using reduced pressure. Water (5 mL) and 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 **73** and **85**.

1.4.4 General procedure for the synthesis of tetrasubstituted propargylamines 73, 85 from 1-alkynes 50 and amines with CuCl in solvent free condition:

To a stirred suspension of amines (1 mmol), CuCl (0.010 g, 0.1 mmol) and 1-alkyne **50** (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 **73** and **85**.

4-(9-Methylnonadec-10-yn-9-yl)morpholine (73aa):



73aa

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

IR (neat) : 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.

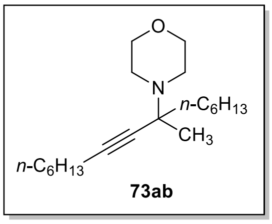
LCMS **:** m/z 364 (M+1).

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 (73ab):



73ab

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

IR (neat) : 2953, 2916, 2845, 2820, 1435, 1118, 945 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.

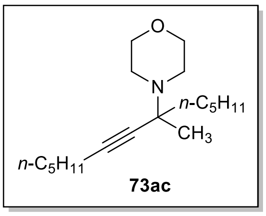
LCMS **:** m/z 307 (M+1).

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 (73ac):



73ac

Yield : Using toluene as solvent: Yield: 0.214 g, 77%; Under the solvent free condition: Yield: 0.220 g, 79%, Yellow oil.

IR (neat) : 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), 1.6-1.28 (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.

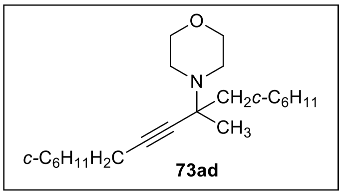
LCMS **:** m/z 280 (M+1).

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 (73ad):



73ad

Yield : Using toluene as solvent: Yield: 0.261 g, 79%; Under the solvent free condition: Yield: 0.271 g, 82%, Yellow oil.

IR (neat) : 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, $CDCl_3$, δ ppm) 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).

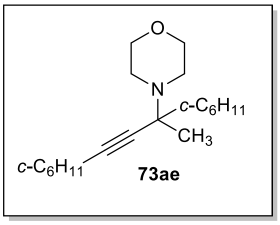
Analysis **:** for $C_{22}H_{37}NO$

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 (73ae):

Yield : Using toluene as solvent: Yield: 0.221 g, 73%; Under the solvent free condition: Yield: 0.239 g, 79%, Yellow oil.



IR (neat) : 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, 2 H), 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).

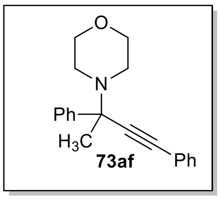
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 84.5, 81.5, 67.4, 57.4, 47.0, 39.3, 31.9, 30.0, 29.6, 29.3, 29.1, 28.8, 24.0, 23.7, 22.7, 18.6, 14.1.

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.



73af

4-(2,4-Diphenylbut-3-yn-2-yl)morpholine (73af):

Yield : Under the solvent free condition: Yield: 0.084 g, 29%, Brown liquid.

IR (neat) : 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, 6.6, 123.1, 88.2, 67.4, 63.4, 48.0, 30.5.

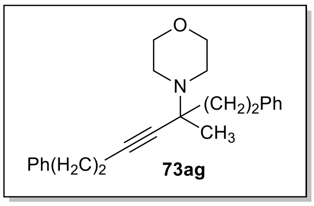
LCMS **:** m/z 292 (M+1).

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-(2,4-Dicyclohexylbut-3-yn-2-yl)morpholine (73ag):



73ag

Yield : Using toluene as solvent: Yield: 0.284 g, 82%,; Under the solvent free condition: Yield: 0.295 g, 85%, Brown liquid.

IR (neat) : 3084, 3057, 3030, 2958, 2931, 2860, 1715, 1649, 1600, 1490, 1452, 1260, 1128, 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).

^{13}C 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.

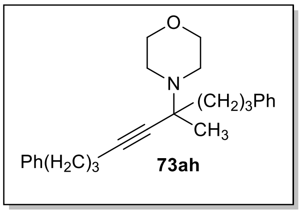
LCMS **:** m/z 349 (M+1).

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 (73ah):



Yield : Using toluene as solvent: Yield: 0.316 g, 84%,; Under the solvent free condition: 0.307 g, 82%, Brown liquid.

IR (neat) : 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).

^{13}C 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.

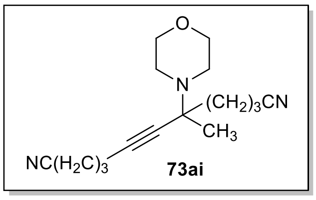
LCMS **:** m/z 376 (M+1).

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.

7-Methyl-7-morpholinoundec-5-ynedinitrile (73ai):



Yield : Using toluene as solvent: Yield: 0.202 g, 74%,; Under the solvent free condition: 0.221 g, 81%, Brown liquid.

IR (neat) : 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), 1.8-1.76 (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.

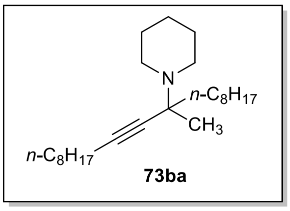
LCMS **:** m/z 274 (M+1).

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.

1-(9-Methylnonadec-10-yn-9-yl)piperidine (73ba):



Yield **:** Using toluene as solvent: Yield: 0.277 g, 77%,; Under the solvent free condition: 0.292 g, 81%, Yellow oil.

IR (neat) : 3040, 2958, 2931, 2860, 1709, 1687, 1605, 1452, 1216, 1172, 1024, 854 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 2.70-2.59 (m, 4H), 2.20 (t, *J*=8.0 Hz, 2H), 1.78-1.58 (m, 6H), 1.49-1.29 (m, 29H), 0.90 (t, *J*=8.0 Hz, 6H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 83.6, 82.7, 57.8, 47.5, 39.7, 31.9, 31.8, 30.1, 29.5, 29.3, 29.2, 29.1, 29.0, 28.8, 26.6, 24.8, 24.2, 24.0, 22.6, 18.6, 14.0.

LCMS **:** m/z 362 (M+1).

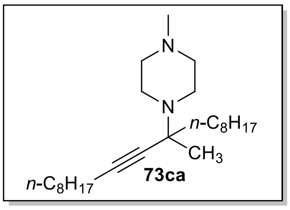
Analysis **:** for $C_{25}H_{47}N$

calcd: C 83.03, H 13.10, N 3.87.

found: C 82.91, H 13.15, N 3.81.

1-Methyl-4-(9-methylnonadec-10-yn-9-yl)piperazine (73ca):

Yield **:** Using toluene as solvent: Yield: 0.274 g, 73%,; Under the solvent free condition: 0.300 g, 80%, Yellow oil.



73ca

IR (neat) : 3063, 2926, 2854, 2800, 2756, 1495, 1245, 1391, 1205, 1128, 1030, 745 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 2.79-2.42 (m, 8H), 2.29 (s, 3H), 2.18 (t, *J*=8.0 Hz, 3H), 1.58-1.39 (m, 9H), 1.35-1.28 (m, 19H), 0.90 (s, 6H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 84.2, 81.9, 57.2, 55.7, 46.3, 45.9, 39.6, 31.9, 31.8, 30.0, 29.5, 29.3, 29.2, 29.1, 29.0, 28.8, 24.1, 23.9, 22.6, 18.6, 14.0.

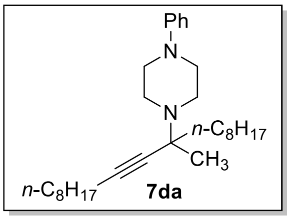
LCMS **:** m/z 377 (M+1).

Analysis **:** for $C_{25}H_{48}N_2$

calcd: C 79.72, H 12.84, N 7.44.

found: C 79.62, H 12.76, N 7.51.

1-(9-Methylnonadec-10-yn-9-yl)-4-phenylpiperazine (73da):



7da

Yield : Using toluene as solvent: Yield: 0.315 g, 72%,; Under the solvent free condition: 0.337 g, 77%, Yellow oil.

IR (neat) : 3062, 3013, 2953, 2925, 2876, 2837, 1665, 1626, 1478, 1391, 1369, 1237, 1117, 1034, 1056 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.31-7.27 (m, 2H), 6.98-6.87 (m, 3H), 3.24 (t, *J*=8.0 Hz, 4H), 2.84-2.79 (m, 4H), 2.22 (t, *J*=8.0 Hz, 4H), 1.67-1.65 (m, 3H), 1.54-1.38 (m, 9H), 1.34-1.29 (m, 15H), 0.93-0.90.

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 151.4, 129.0, 119.4, 115.8, 84.4, 81.8, 57.3, 49.5, 46.5, 43.8, 39.6, 31.9, 31.8, 30.1, 29.6, 29.3, 29.2, 29.1, 28.8, 24.1, 24.0, 23.8, 22.6, 18.6, 14.1.

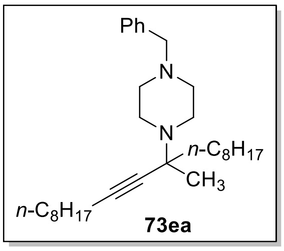
LCMS **:** m/z 439 (M+1).

Analysis **:** for $C_{30}H_{50}N_2$

calcd: C 82.13, H 11.49, N 6.39.

found: C 82.21, H 11.36, N 6.45.

1-Benzyl-4-(9-methylnonadec-10-yn-9-yl)piperazine (73ea):



73ea

Yield : Using toluene as solvent: Yield: 0.357 g, 79%,; Under the solvent free condition: 0.339 g, 75%, Yellow oil.

IR (neat) : 3024, 2953, 2854, 1604, 1583, 1489, 1451, 1325, 1259, 1128, 1051, 728 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.35-7.28 (m, 5H), 3.5 (s, 2H), 2.70-

2.53 (m, 8H), 2.19 (t, *J*=8.0 Hz, 2H), 1.58-1.52 (m, 2H), 1.51-1.49 (m, 3H), 1.43-1.41 (m, 5H), 1.40-1.30 (m, 16H), 1.28 (s, 3H), 0.90 (t, *J*=8.0 Hz, 6H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 138.2, 129.2, 128.1, 126.9, 84.1, 82.2, 63.0, 57.3, 53.6, 46.4, 39.6, 31.9, 31.8, 30.0, 29.5, 29.3, 29.2, 29.1, 28.8, 24.2, 23.9, 22.6. 18.6, 14.0.

LCMS : m/z 451 (M-1).

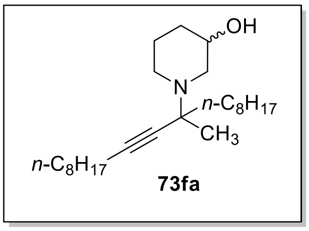
Analysis : for $C_{31}H_{52}N_2$

calcd: C 82.24, H 11.58, N 6.19.

found: C 82.15, H 11.48, N 6.27.

1-(9-Methylnonadec-10-yn-9-yl)piperidin-3-ol (73fa):

Yield : Using toluene as solvent: Yield: 0.294 g, 78%,; Under the solvent free condition: 0.312 g, 83%, Yellow oil.



73fa

IR (neat) : 3342, 2953, 2926, 2854, 1704, 1676, 1621, 1320, 1172, 1128, 1063, cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.81(brs, 1H), 2.73-2.35 (m, 6H), 2.16 (t, *J*=8.0 Hz, 2H), 1.77-1.75 (m, 1H), 1.57-1.55 (m, 5H), 1.49-1.45 (m, 2H) 1.41-1.37 (m, 4H), 1.33-1.23 (m, 20H), 0.87 (t, *J*=8.0 Hz, 6H)

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 83.8, 82.3, 66.5, 57.3, 57.1, 54.0, 53.8, 47.2, 46.8, 39.8, 39.7, 32.0, 31.8, 30.0, 29.0, 28.8, 24.2, 24.0, 23.9, 22.6, 22.0, 18.5, 14.0.

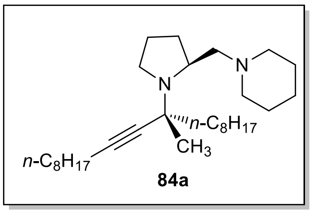
LCMS : m/z 378 (M+1).

Analysis : for $C_{25}H_{47}NO$

calcd: C 79.51, H 12.54, N 3.71.

found: C 79.45, H 12.48, N 3.78.

1-(9-Methylnonadec-10-yn-9-yl)piperidine (84a):



84a

Yield **:** Using toluene as solvent: Yield: 0.199 g, 45%,; Under the solvent free condition: 0.350 g, 79%, Yellow oil.

$[\alpha]_D^{25}$: -32.5 (c=0.50, $CHCl_3$).

IR (neat) : 2931, 2849, 2213, 1704, 1665, 1457, 1369, 1326, 1205, 1150, 1101, 1063, 991, 904, 734 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.30-3.25 (m, 2H), 2.94-2.92 (m, 2H), 2.72-2.54 (m, 6H), 2.29-2.16 (m, 12H), 1.88 (d, *J*=8.0 Hz, 2H), 1.75-1.70 (m, 4H), 1.63-1.54 (m, 8H), 1.49-1.46 (m, 4H), 1.41-1.36 (m, 7H), 1.29 (s, 3H), 0.91-0.86 (m, 6H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 82.7, 82.6, 66.6, 58.8, 56.7, 55.3, 50.0, 41.4, 31.8, 31.3, 29.7, 29.5, 29.1, 28.4, 27.1, 25.8, 24.4, 24.1, 22.6, 18.6.

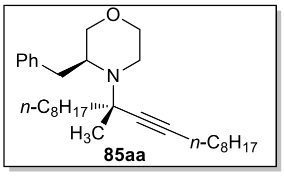
LCMS **:** m/z 445 (M+1).

Analysis **:** for $C_{30}H_{56}NO$

calcd: C 81.01, H 12.68, N 6.30.

found: C 81.12, H 12.61, N 6.21.

(*S*)-3-Benzyl-4-((*S*)-9-methylnonadec-10-yn-9-yl)morpholine (85aa):



85aa

Yield **:** Using toluene as solvent: Yield: 0.344 g, 76%,; Under the solvent free condition: 0.394 g, 87%, Brown liquid.

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

IR (neat) : 3023, 2953, 2928, 2853, 2195, 1601, 1495, 1455, 1366, 1274, 1120, 1079, 949, 894, 739 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.32-7.28 (m, 3H), 7.25-7.21 (m, 2H), 3.93 (d, *J*=8.0 Hz, 2H), 3.63 (t, *J*=8.0 Hz, 2H), 3.40-3.10 (m, 2H), 2.59 (d, *J* =12.0 Hz, 2H), 2.22-2.19 (m, 1H), 1.66-1.53 (m, 6H), 1.50, (s, 3H), 1.4 2-1.30 (m, 10H), 0.95-0.88 (m, 6H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 141.0, 129.4, 128.3, 125.6, 84.9, 83.8, 68.4, 68.0, 57.0, 55.9, 41.0, 40.1, 31.9, 31.8, 30.3, 30.1, 29.6, 29.3, 29.2, 29. 1, 29.0, 28.9, 27.0, 24.2, 22.6, 18.7, 14.1, 14.0.

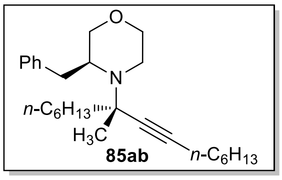
LCMS **:** m/z 454 (M+1).

Analysis **:** for $C_{31}H_{51}NO$

calcd: C 82.06, H 11.33, N 3.09.

found: C 82.16, H 11.26, N 3.15.

(*S*)-3-Benzyl-4-((*S*)-9-methylnonadec-10-yn-9-yl)morpholine (85ab):



Yield **:** Using toluene as solvent: Yield: 0.321 g, 81%,; Under the solvent free condition: 0.341 g, 86%, Brown liquid.

$[\alpha]_D^{25}$ **:** -41.5 (c=0.69, $CHCl_3$)

IR (neat) : 3020, 2953, 2927, 2853, 2033, 1606, 1495, 1364, 1276, 1120, 1077, 955, 843, 739 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.31-7.17 (m, 5H), 3.95-3.37 (m, 2H), 3.23 -3.10 (m, 2H), 2.65-2.42 (m, 3H), 2.22 (t, *J*=8.0 Hz, 2H), 1.52-1.39 (m, 8H), 1.37-1.30 (m, 2H), 0.91-0.86 (m, 6H), 1.48 (s, 3H), 1.31-1.28 (m, 13H), 0.92-0.88 (m, 6H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 140.9, 129.4, 128.4, 125.7, 84.6, 84.1, 68.5, 68.0, 56.8, 55.3, 41.7, 41.4, 31.9, 31.3, 30.0, 29.6, 29.0, 28.6, 24.5, 23.7, 22.7, 22.6, 18.7, 14.1, 14.0.

LCMS : m/z 398 (M-1).

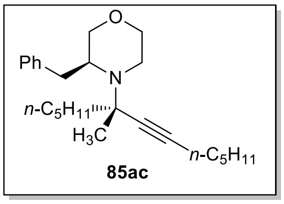
Analysis : for $C_{27}H_{43}NO$

calcd: C 81.55, H 10.90, N 3.52.

found: C 81.46, H 10.82, N 3.48.

(*S*)-3-Benzyl-4-((*S*)-9-methylnonadec-10-yn-9-yl)morpholine (85ac):

Yield : Using toluene as solvent: Yield: 0.287g, 78%,; Under the solvent free condition: 0.313 g, 85%, Brown liquid.



85ac

$[\alpha]_D^{25}$: -39.5 (c=0.36, $CHCl_3$).

IR (neat) : 3023, 2955, 2928, 2854, 2150, 1601, 1455, 1366, 1273, 1120, 1079, 1029, 949, 802, 739 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.33-7.21 (m, 5H), 3.96-3.60 (m, 3H), 3.41 -3.09 (m, 5H), 2.60-2.20 (m, 3H), 1.69-1.55 (m, 4H), 1.50 (s, 1H), 1.46 -1.29 (m, 10H), 0.95-0.88 (m, 6H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 140.9, 129.4, 128.4, 125.7, 84.7, 84.1, 68.5, 68.0, 56.8, 55.3, 41.7, 41.4, 32.1, 31.1, 30.0, 28.7, 24.5, 23.5, 22.7, 22.2, 18.7, 14.1, 14.0.

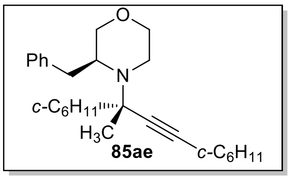
LCMS : m/z 368 (M-1).

Analysis : for $C_{25}H_{39}NO$

calcd: C 81.24, H 10.64, N 3.79.

found: C 81.14, H 10.56, N 3.86.

(*S*)-3-Benzyl-4-((*S*)-2,4-dicyclohexylbut-3-yn-2-yl)morpholine (85ae):



85ae

Yield : Using toluene as solvent: Yield: 0.282 g, 72%,; Under the solvent free condition: 0.310 g, 79%, Brown liquid.

[α]$_D$^{25} : -37.1 (c=0.56, $CHCl_3$).

IR (neat) : 2925, 2864, 1995, 1655, 1495, 1344, 1276, 1120, 1078, 1022, 974, 801, 740 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.30-7.28 (m, 2H), 7.25-7.20 (m, 3H), 3.94 (d, *J*=8.0 Hz, 2H), 3.61 (t, *J*=12.0 Hz, 2H), 3.42-3.13 (m, 2H), 2.6 (d, *J*=8.0 Hz, 2H), 2.37-2.36 (m, 1H), 2.28-2.26 (m, 1H), 2.11-2.10 (m, 4H), 1.81-1.79 (m, 7H), 1.69-1.65 (m, 5H), 1.5 (s, 3H), 1.29-1.26 (m, 5H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 141.2, 129.4, 128.4, 125.6, 89.3, 83.6, 68.6, 68.1, 58.6, 56.8, 45.0, 40.9, 33.1, 33.0, 29.3, 29.1, 27.4, 27.1, 26.3, 25.3, 25.9, 24.8, 19.4.

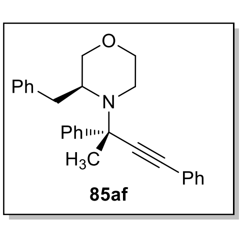
LCMS : m/z 394 (M+1).

Analysis : for $C_{27}H_{39}NO$

calcd: C 82.39, H 9.99, N 3.56.

found: C 82.45, H 9.91, N 3.61.

(*S*)-3-Benzyl-4-((*S*)-2,4-diphenylbut-3-yn-2-yl)morpholine (85af):



85af

Yield : Under the solvent free condition:Yield: 0.087g, 23%, Brown liquid.

[α]$_D$^{25} : -35.8 (c=0.74, $CHCl_3$).

IR (neat) : 3023, 2954, 2850, 2055, 1683, 1597, 1488, 1370, 1277, 1171, 1069, 975, 841, 755 cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.89-7.87 (m, 3H), 7.56-7.54 (m, 2H), 7.39--7.32 (m,10H), 3.82-3.76 (m, 2H), 3.65-3.62 (m, 2H), 3.41-3.35 (m, 2 H), 2.64-2.52 (m, 1H), 2.21 (d, *J*=8.0 Hz, 2H), 1.85 (s, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 146.8, 140.6, 131.5, 129.5, 128.5, 128.3, 128.2, 128.1, 127.1, 126.3, 125.9, 123.2, 91.6, 87.9, 68.7, 67.8, 61.5, 56.8, 42.9, 30.5, 30.3.

LCMS : m/z 380 (M-1).

Analysis : for $C_{27}H_{27}NO$

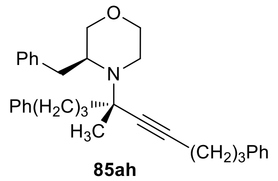
calcd: C 85.00, H 7.13, N 3.67.

found: C 85.12, H 7.18, N 3.75.

(*S*)-3-Benzyl-4-((*S*)-4-methyl-1,9-diphenylnon-5-yn-4-yl)morpholine (85ah):

Yield : Using toluene as solvent: Yield: 0.330 g, 71%,; Under the solvent free condition: 0.385 g, 83%, Brown liquid.

[α]$_D$^{25} : -41.3 (c=0.59, CHCl$_3$).



85ah

IR (neat) : 3024, 2944, 2852, 1954, 1663, 1495, 1370, 1274, 1119, 1080, 950, 834, 741 cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.36-7.30 (m, 7H), 7.28-7.24 (m, 8H), 3.95 (d, *J*=4.0 Hz, 2H), 3.65 (d, *J*=4.0 Hz, 2H), 3.43-3.39 (m, 2H), 2.79-2.75 (m, 2H), 2.71-2.66 (m, 2H), 2.54-2.51 (m, 2H), 2.29-2.25 (m, 3H), 1.90-1.79 (m, 6H), 1.55 (s, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 142.5, 141.7, 140.8, 129.4, 128.5, 128.4, 128.3, 125.8,125.7, 84.6, 84.2, 68.5, 67.9, 56.8, 55.2, 41.4, 41.1, 36.0, 34.9, 30.7, 30.1, 25.6, 24.6, 18.2.

LCMS : m/z 466 (M+1).

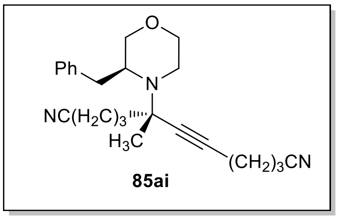
Analysis : for $C_{33}H_{39}NO$

calcd: C 85.11, H 8.44, N 3.01.

found: C 85.03, H 8.49, N 3.18.

(*S*)-7-((*S*)-3-Benzylmorpholino)-7-methylundec-5-ynedinitrile (85ai):

Yield : Using toluene as solvent: Yield: 0.250 g, 69%,; Under the solvent free condition: 0.261 g, 72%, Brown liquid.



85ai

$[\alpha]_D^{25}$: -37.9 (c=0.51, $CHCl_3$).

IR (neat) : 2956, 2854, 2244, 1601, 1454, 1274, 1173, 1081, 1029, 950, 866, 735 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.33-7.29 (m, 2H), 7.28-7.23 (m, 3H), 3.94 (d, *J*=8.0 Hz, 2H), 3.61 (t, *J*=12.0 Hz, 2H), 3.25-3.21 (m, 2H), 2.55-2.5 (m, 7H), 2.19-2.11 (m, 2H), 1.94-1.87 (m, 6H), 1.43 (s, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 140.1, 129.3, 128.5, 126.0, 119.6, 118.9, 85.2, 82.4, 68.4, 67.7, 56.7, 54.8, 41.4, 40.3, 29.9, 24.7, 24.3, 20.0, 17.9, 17.3, 16.3.

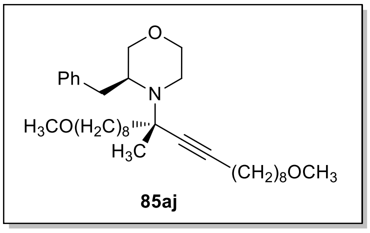
LCMS : m/z 364 (M+1).

Analysis : for $C_{23}H_{29}N_3O$

calcd: C 76.00, H 8.04, N 11.56.

found: C 76.15, H 8.12, N 11.65.

(*S*)-3-Benzyl-4-((*S*)-1,19-dimethoxy-9-methylnonadec-10-yn-9-yl)morpholine (85aj):



85aj

Yield : Using toluene as solvent: Yield: 0.425 g, 83%,; Under the solvent free condition: 0.456 g, 89%, Brown liquid.

$[\alpha]_D^{25}$: -29.3 (c=0.47, $CHCl_3$).

IR (neat) : 2925, 2852, 2201, 1718, 1658, 1455, 1356, 1274, 1173, 1029, 973, 843, 741 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.30-7.17 (m, 5H), 3.92 (d, *J*=4.0 Hz, 2H), 3.59 (t, *J*=8.0 Hz, 2H), 3.38-3.35 (m, 2H), 3.33 (s, 3H), 3.32 (s, 3H), 3.21-3.05 (m, 4H), 2.55 (d, *J*=12.0 Hz, 2H), 2.43-2.39 (m, 1H), 2.18 (t, *J*=8.0 Hz, 2H), 1.58-1.50 (m, 10H), 1.46 (s, 3H), 1.30-1.27 (m, 16H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 140.9, 129.3, 128.3, 125.7, 84.6, 84.1, 72.9, 72.8, 68.5, 68.0, 58.5, 56.8, 55.2, 43.7, 41.7, 41.3, 29.9, 29.8, 29.6, 29.5, 29.4, 29.3, 29.2, 29.0, 28.9, 28.8, 26.1, 26.0, 24.5, 23.8, 18.6.

LCMS : m/z 514 (M+1).

Analysis : for $C_{33}H_{55}NO_3$.

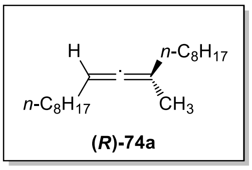
calcd: C 77.14, H 10.79, N 2.73.

found: C 77.26, H 10.72, N 2.71.

1.4.4 General procedure for the preparation of chiral allenes from propargylamines

The chiral propargylamines (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 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 **74**.

(*R*)-9-Methylnonadeca-9,10-diene (74a):



Yield : 0.239 g, 86%, Colorless oil.

[α]D25 : -99.9 (c=0.51, $CHCl_3$).

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).

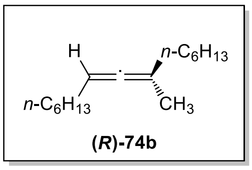
Analysis : for $C_{20}H_{38}$

calcd: C 86.25, H 13.75.

found: C 86.42, H 13.71.

Enanatiomeric purity: 96% 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 (74b):



Yield : 0.197 g, 89%, Colourless oil.

[α]D25 : -98.8 (c=0.42, $CHCl_3$).

IR (neat) : 2958, 2926, 2854, 1961, 1498, 1380, 723 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).

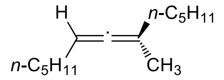
Analysis : for $C_{16}H_{30}$

calcd: C 86.40, H 13.60.

found: C 86.28, H 13.51.

Enanatiomeric purity: 90% 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).

6-Methyltrideca-6,7-diene (74c):



74c

Yield : 0.176 g, 91%, Colourless oil.

IR (neat) : 2962, 2932, 2862, 1963, 1492, 1386, 789 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 4.98-4.92 (m, 1H), 2.10-2.05 (m, 4H), 1.64-1.52 (m, 3H), 1.42- 1.29 (m, 14H), 0.97-0.91 (m, 4H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 201.2, 99.7, 90.0, 34.1, 31.2, 31.9, 29.8, 29.5, 29.3, 29.0, 22.7, 19.4, 14.1.

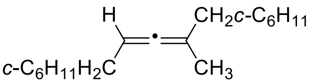
LCMS : *m/z* 194 (M+1).

Analysis : for $C_{14}H_{26}$

calcd: C 86.52, H 13.48.

found: C 86.48, H 13.44.

(2-Methylpenta-2,3-diene-1,5-diyl)dicyclohexane (74d):



74d

Yield : 0.209 g, 83%, Colourless oil.

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.

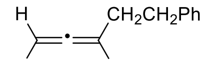
LCMS : *m/z* 247 (M+1).

Analysis : for $C_{18}H_{30}$

calcd: C 87.73, H 12.27.

found: C 87.63, H 12.21.

(3-Methylhepta-3,4-diene-1,7-diyl)dibenzene (74g):



74g

Yield : 0.233 g, 85%, Colourless oil.

IR (neat) : 3084, 3068, 3024, 2854, 1961, 1600, 1495, 1452, 1265, 1035, 745 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.

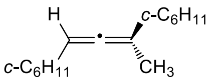
LCMS : *m/z* 263 (M+1).

Analysis : for $C_{20}H_{22}$

calcd: C 91.55, H 8.45.

found: C 91.45, H 8.53.

(*R*)-Buta-1,2-diene-1,3-diyldicyclohexane (74e):



(*R*)-74e

Yield : 0.189 g, 87%, Colourless oil.

$[\alpha]_D^{25}$: -77.9 (c=0.42, $CHCl_3$).

IR (neat) : 2936, 2841, 2239, 1964, 1448, 1416, 1280, 1232, 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).

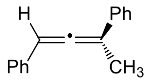
Analysis **:** for $C_{16}H_{26}$

calcd: C 88.00, H 12.0.

found: C 87.91, H 12.06.

Enanatiomeric 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*)-Buta-1,2-diene-1,3-diyldicyclohexane (74f):



(*R*)-74f

Yield : 0.146 g, 71%, Colourless oil.

[α]$_D$^{25} : -962.3 (c=0.47, $CHCl_3$).

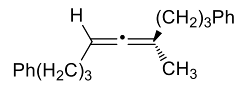
IR (neat) **:** 3060, 3027, 2955, 1936, 1597, 1493, 1452, 758 cm^{-1}.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.59-7.55 (m, 2H), 7.44-7.33 (m, 8H), 6.57 (s, 1H), 2.32 (s, 3H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 206.8, 136.3, 134.5, 128.7, 128.4, 127.0, 126.9, 125.8, 104.5, 96.5, 16.7.

Enanatiomeric purity: 94% ee,The enantioselectivity was determined by HPLC using chiral column, chiralcel OB-H, hexanes:i-PrOH/98:2; flow rate 1.0 mL/min, 220 nm, retention times: 6.15 min. (minor) and 7.05 min. (major).

(*R*)-(4-Methylnona-4,5-diene-1,9-diyl)dibenzene (74h):



(*R*)-74h

Yield : 0.243 g, 84%, Colourless oil.

$[\alpha]_D^{25}$: -85.9 (c=0.46, $CHCl_3$).

IR (neat) : 2958, 2849, 1960, 1447, 1347, 1258, 986, 962, 889, 842 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, 3H), 2.23 (d of t J_1=8.0 Hz, J_2=2.6 Hz, 2H), 2.08-1.99 (m, 4H), 1.80-1.72 (m, 4H), 1.28 (t, *J*=8.0 Hz, 1H).

^{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).

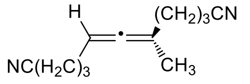
Analysis : for $C_{22}H_{26}$

calcd: C 90.98, H 9.02.

found: C 90.82, H 9.08.

Enanatiomeric 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-dienedinitrile (74i):



(*R*)-74i

Yield : 0.133 g, 71%, Colourless oil.

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

IR (neat) : 3298, 2931, 2854, 2246, 1956, 1446, 1424, 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).

^{13}C 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).

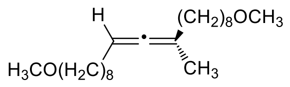
Analysis **:** for $C_{12}H_{16}N_2$

calcd: C 76.55, H 8.57, N 14.88.

found: C 76.63, H 8.51, N 14.72.

Enanatiomeric purity: 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 (74j):



(*R*)-74j

Yield : 0.229 g, 68%, Colourless oil.

$[\alpha]_D^{25}$: -92.3 (c=0.55, $CHCl_3$).

IR (neat) **:** 2920, 2860, 1967, 1714, 1457, 1368, 1261, 1172, 745 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, 3H), 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 12.50.

found: C 78.23, H 12.41.

Enanatiomeric purity: 99% 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).

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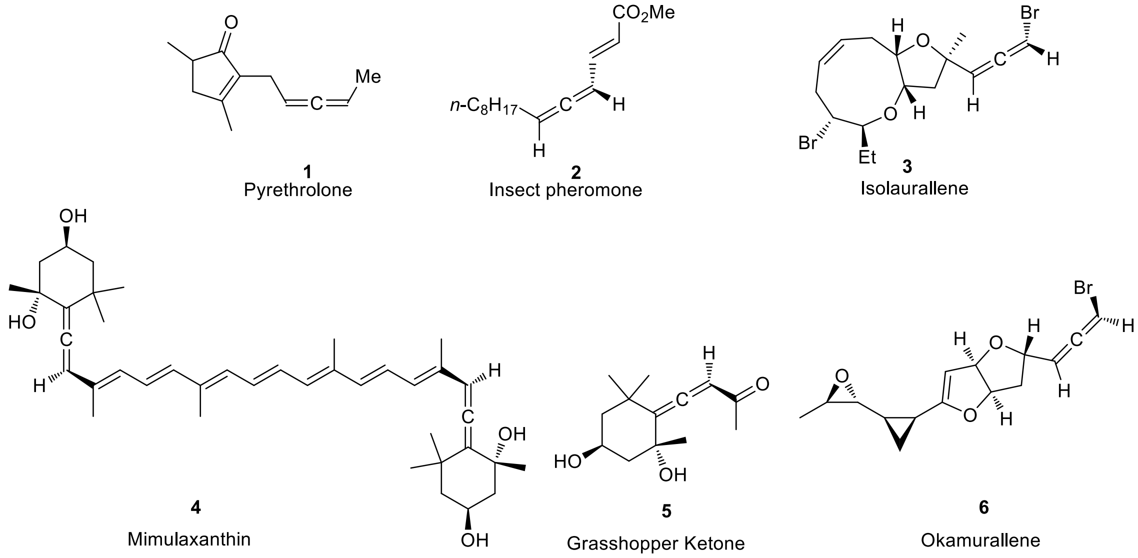
Chapter 2

Diastereoselective Synthesis of Propargylamines *via* Hydroamination of 1-Alkynes and Their Enantioselective Conversion to β-Allenoates

2. 1 Introduction

2.1.1 Chiral allenic natural products

In the last few years, several natural products containing chiral allene moiety were isolated (Figure 1).[1]



1 Pyrethrolone

2 Insect pheromone

3 Isolaurallene

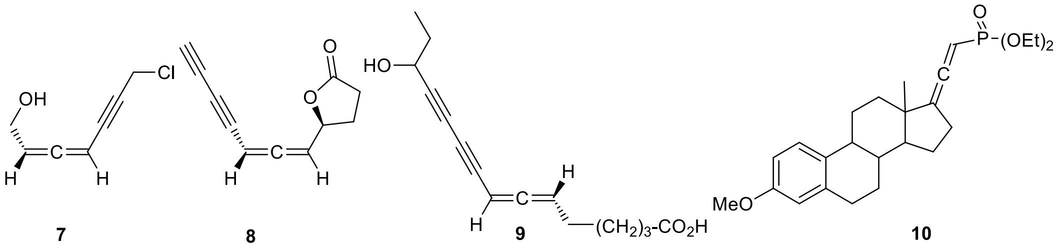
4 Mimulaxanthin

5 Grasshopper Ketone

6 Okamurallene

Figure 1

Allenic derivatives not only occur in nature but also have considerable potential as pharmacologically active molecules. For example, the compounds scorodonin **7**, nemotin **8** and phomallenic acid **9** have inhibiting effects on the growth of bacteria, yeasts and filamentous fungi. Other allenic moieties with such inhibiting effects are sterol biosynthesis inhibitor **10**, gastric acid inhibitor **11**, HIV inhibitor **12**, hepatitis B replication inhibitor **13** and vitamin B_6-dependent decarboxylase inhibitor (suicide substrate) **14** (Figure 2).[2,3]



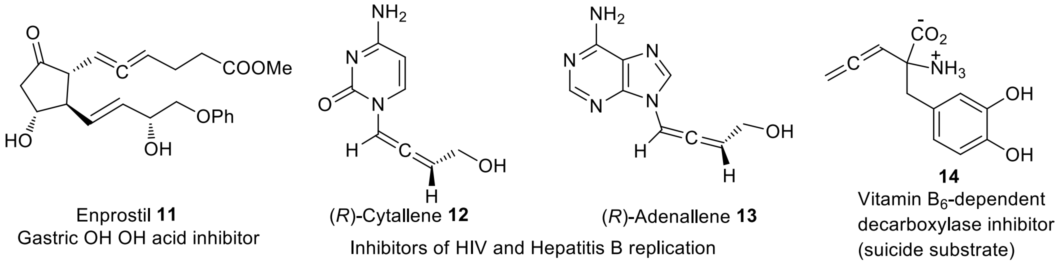
7 Scorodonin

8 Nemotin

9 Phomallenic acid A

10 Sterol biosynthesis inhibitor

Figure 2 (Continued)



Enprostil **11**
Gastric OH OH acid inhibitor

(*R*)-Cytallene **12**

(*R*)-Adenallene **13**

Inhibitors of HIV and Hepatitis B replication

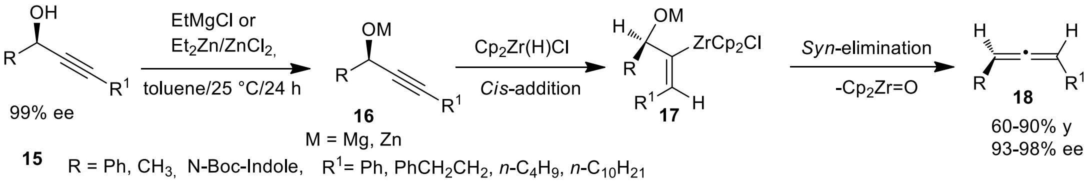
14
Vitamin B_6-dependent decarboxylase inhibitor (suicide substrate)

Figure 2

2.1.2 Methods for the synthesis of axially chiral allenes containing functional groups

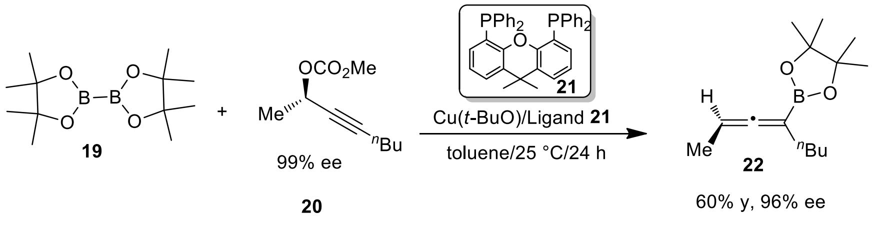
Propargylic derivatives **16** prepared *in situ* by the reaction of organomagnesium or organozinc with propargylic alcohols **15** followed by treatment with $Cp_2Zr(H)Cl$ furnished the allenes **18** in good yields with high optical purities (Scheme 1).[4]

Scheme 1



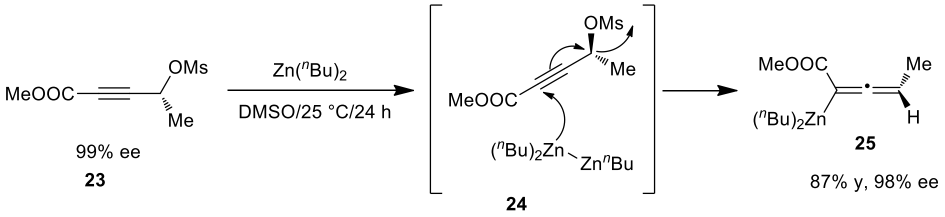
The Cu(*t*-BuO)/triarylphosphine reagent system is useful for the stereoselective substitution of propargylic carbonates **20** with bis(pinacolato)diboron **19** to give the boroallene **22** with 96% ee (Scheme 2).[5]

Scheme 2



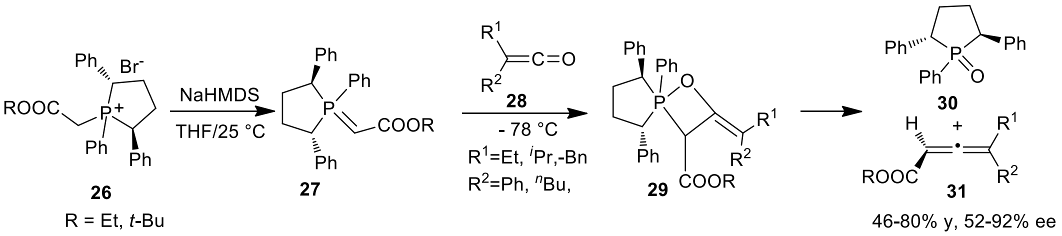
The S_N2' reaction of propragyl mesylates **23** with organozinc reagents gives the chiral allene **25** in 87% yield with up to 98% ee (Scheme 3).[6]

Scheme 3



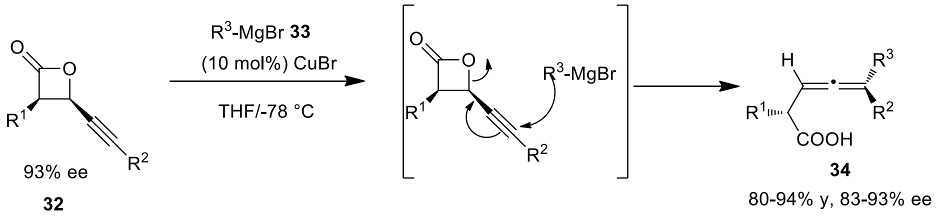
Highly enantioselective synthesis of allenic esters **31** by condensation of pseudo C_2-symmetrical chiral phosphorus ylides **26** with various ketenes **28** using NaHMDS as base at -78 °C was reported.[7] The chiral phosphine oxide **30** was recovered without loss in its optical purity (Scheme 4).

Scheme 4



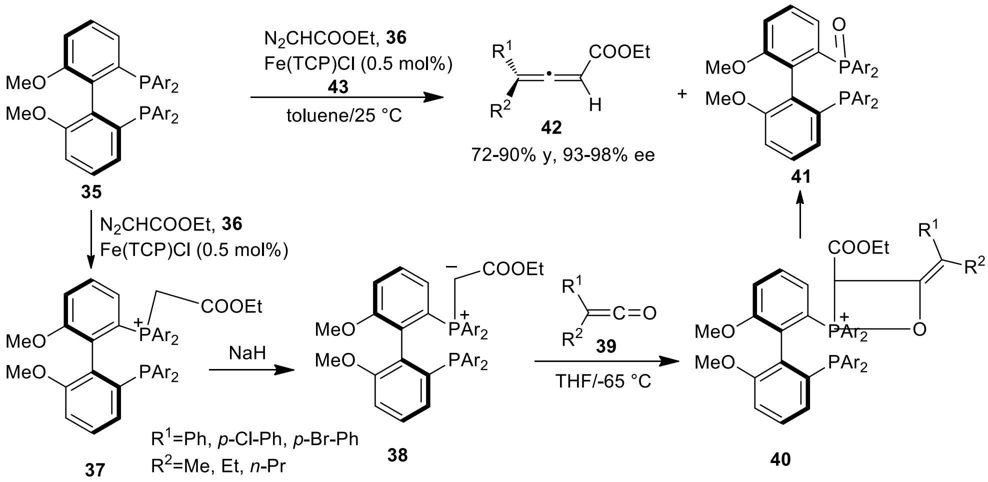
The S_N2' ring opening reaction of β-lactones **32** provides an efficient and operationally simple enantioselective synthesis of *di*- and *tri*-substituted allene derivatives **34** using various Grignard reagents **33** (Scheme 5).[8]

Scheme 5



An efficient method for the synthesis of chiral allenes **42** by olefination of ketenes **39** with ethyl diazoacetate (EDA) **36** in the presence of chiral phosphine **43**-Fe(TCP)-Cl catalyst system was reported (Scheme 6).[9]

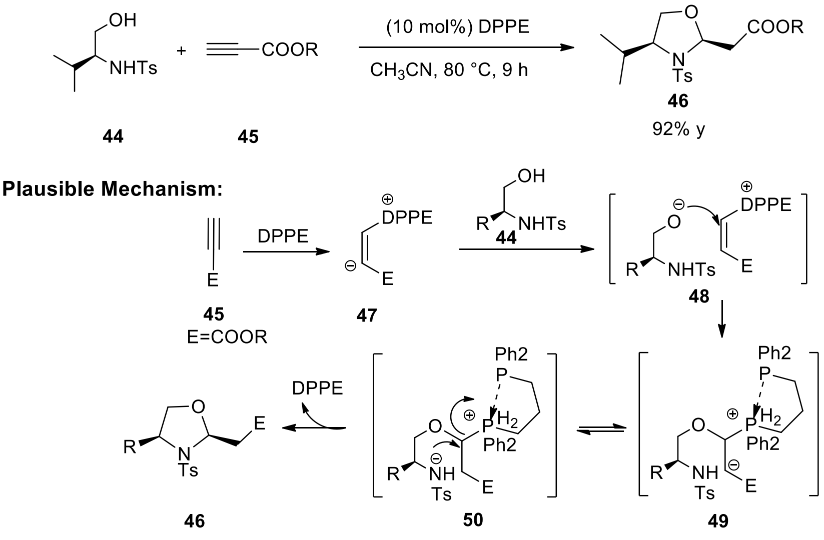
Scheme 6



2.1.3 Synthesis of oxazolidine derivatives

The oxazolidine derivatives have been used as synthetic intermediates, auxiliaries, ligands, and catalysts for asymmetric transformations. Recently, a method has been developed for the construction of oxazolidine derivatives **46** using amino acid derivative **44** and alkyl propiolates **45** *via* double Michael-addition reaction (Scheme 7).[10]

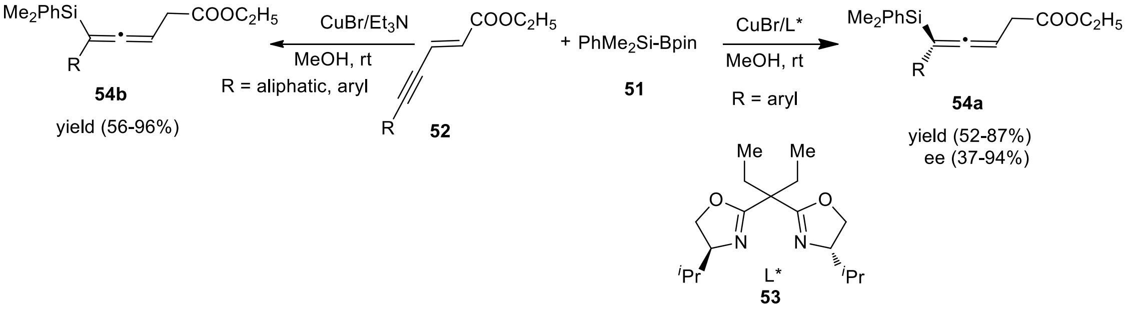
Scheme 7



2.1.4 Synthesis of β-allenoates

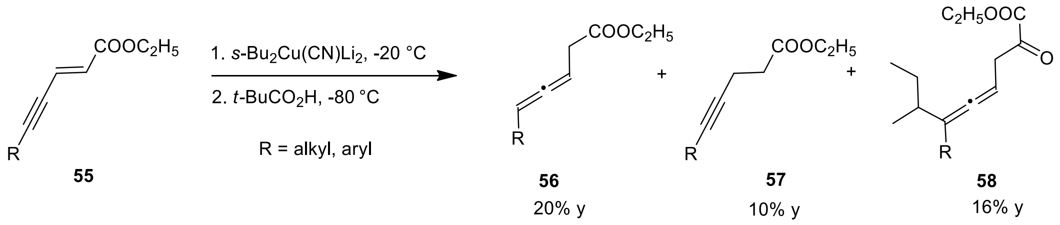
More recently, a copper-catalyzed asymmetric synthesis of highly substituted chiral allene was developed. In this work, the (*Z*)-enynoates **52** react smoothly with the silylboronate **51** to give the corresponding racemic or enantioenriched silyl-substituted allene products **54** in 52% to 96% yields and 37% to 94% ee (Scheme 8).[11]

Scheme 8



Krause *et al.* reported[12] that the reduction of 2-en-4-ynoates **55** with $BuCu(CN)Li_2$ in protic solvent gave the β-allenoate **56** in 20% yield (Scheme 9).

Scheme 9



We have examined the use of chiral morpholine derivatives for the synthesis of chiral allenoates. The results are described in the next section.

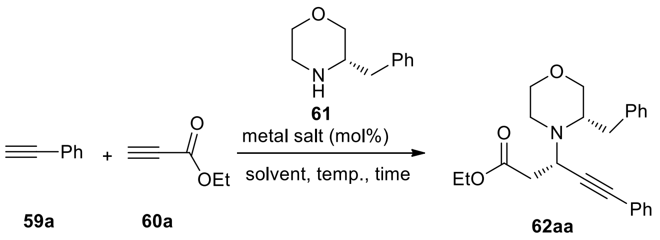
2.2 Results and Discussion

2.2.1 Synthesis of enantioenriched chiral β-allenoates

As outlined in the introduction section chiral allenoates[13,14] are an important class of compounds potentially useful for further synthetic exploitation.[15,16] However, only a few methods have been reported for the synthesis of β-allenoates but with limited scope.[17,18]

Initially, we have carried out the reaction employing ethyl propiolate **60a**, phenylacetylene **59a**, and the chiral secondary cyclic amine **61** and CuCl at 110 °C in toluene solvent. The propargylamine **62aa** was formed in 15% yield (entry 1, Table 1) but it was formed in 56% yield when CuBr was used (entry 2, Table 1).

Table 1: Reaction of different metal salts and solvents with chiral morpholine **61**, ethyl propiolate **60a** and phenylacetylene **59a**.[a,b]



S.No	Solvent	Temp. °C	MX_n	Mol (%)	Time (h)	62aa[b]
1	Toluene	110	CuCl	30	24	15
2	Toluene	110	CuBr	20	12	56
3	Toluene	120	CuBr	20	12	78
4	Toluene	120	CuI	20	12	80
5	Toluene	120	$CuBr_2$	30	18	48
6	Dioxane	120	CuBr	30	24	18

[a] The reaction was performed using amine **61** (1.0 mmol) alkyne **59a** (1.0 mmol) and propiolate **60a** (1.0 mmol). [b]Yields of propargylamines.

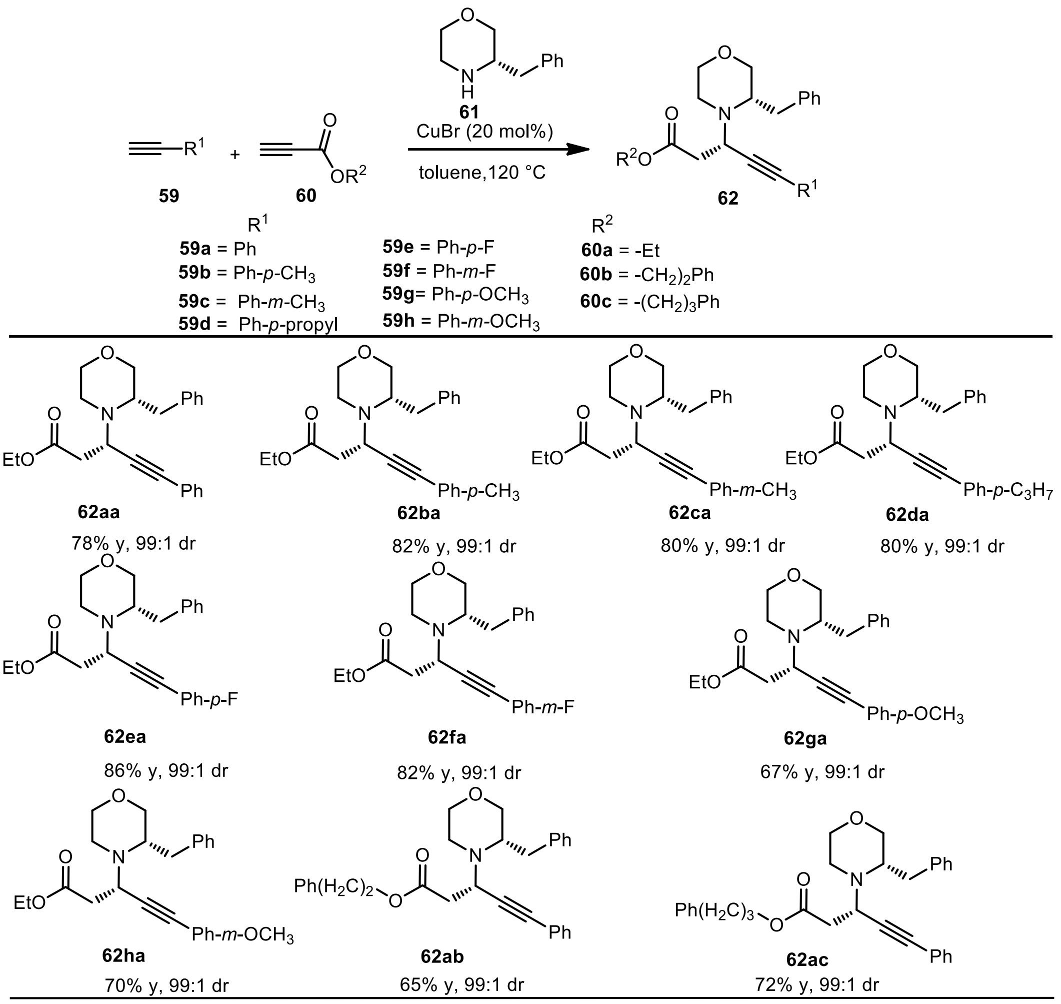
Interestingly, when the reaction was carried out using CuBr, at 120 °C, the propargylamine **62aa** was formed in 78% yield within 12 h (entry 3, Table 1). Reaction using the CuI also gave the propargylamine **62aa** in 80% yield (entry 4, Table 1).

When $CuBr_2$ was used, the propargylamine **62aa** was obtained in 48% yield (entry 5, Table 1). When the reaction was carried out in 1,4-dioxane, the product **62aa** was obtained only in 18% yield (entry 6, Table 1). Whereas the reaction using CuBr gave the product **62aa** in 56% yield, in toluene at 110 °C (entry 2, Table 1), and it was obtained in 78% yield at 120 °C (entry 3, Table 1).

We have examined the substrate scope using various 1-alkynes. When the alkynes **59a**, **59b**, **59c** and **59d** with R^1 groups 4-H-, 4-Me-, 4-C_3H_7-, and 4-C_5H_{11}-substitution in the phenyl ring were reacted with ethyl propiolate **60a,** the trisubstituted propargylamines **62aa-62da** were obtained in 78-82% yields with >99:1 dr (Table 2). Also, alkynes substituted with 4-*tert*-butyl-, 4-OMe- groups in the phenyl ring **59e** and **59f** also gave the corresponding products **62ea** and **62fa** in 86% yield and 82% yield with >99:1 dr, respectively (Table 2).

Further, the alkyne **59g** containing electron withdrawing groups resulted in the formation of the desired product **62ga** in 67% yield (Table 2). We have also examined the use of propiolate esters containing various R^2 groups such as 3-phenylpropyl **60b**, 4-phenylpropyl **60c** and obtained the corresponding propargylamines **62ab**, **62ac** in 65% and 72% yields with 99:1 dr (Table 2).

Table 2: Synthesis of chiral propargylamines **62** using 1-alkynes **59** and the chiral amine **61** using CuBr.[a,b]



62aa 78% y, 99:1 dr

62ba 82% y, 99:1 dr

62ca 80% y, 99:1 dr

62da 80% y, 99:1 dr

62ea 86% y, 99:1 dr

62fa 82% y, 99:1 dr

62ga 67% y, 99:1 dr

62ha 70% y, 99:1 dr

62ab 65% y, 99:1 dr

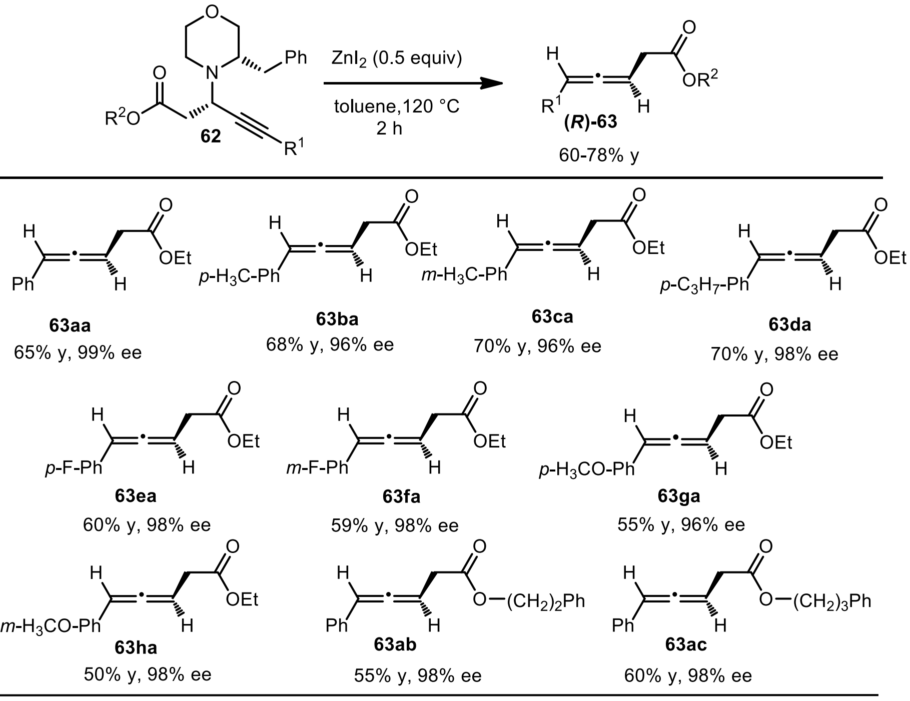
62ac 72% y, 99:1 dr

[a] The reactions were carried out by using amine **61** (1.0 mmol), propiolates **60** (1.0 mmol), and 1-alkynes **59** (1.0 mmol) in toluene (3 mL) at 120 °C. [b] Yields of chiral propargylamines.

2.2.2 Synthesis of β-Allenoates from chiral propargylamine 62

We have observed that the chiral propargylamines **62aa-62ee** react with ZnI_2 at 120 °C to give the corresponding allenes **63aa-63ea** in 60-70% yields (Table 3). The propargylamines having functionalized groups also afforded the chiral allenes **63fa**, **63ga** and in 59% and 55% yields with up to 99% ee (Table 3).

Table 3: Synthesis of β-allenoates from chiral propargylamines **62**.[a,b,c]



[a]The reactions were carried out by using propargylamine **62** (1 mmol) which obtained from chiral amine **61** in toluene (3 mL) with ZnI_2 (0.5 mmol) at 120 °C. [b]Yield of allenes. [c]The ee was determined by chiral HPLC analysis.

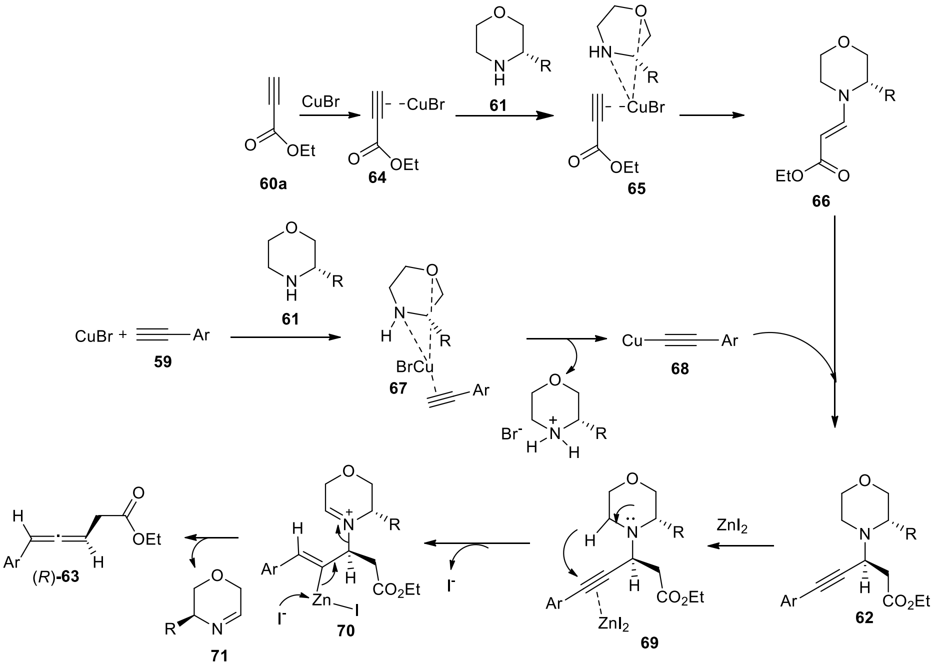
The propargylamines containing various R^2 groups such as 3-phenylpropyl **75b**, 4-phenylpropyl **75c** gave the corresponding β-allenoates **63ab**, **63ac** in 55% and 60% yields with up to 98% ee (Table 3). The absolute configurations of the major enantiomer of the chiral allenes are assigned as *R* based on Lowe-Brewster rule.[19]

2.2.3 Mechanism for the formation of β-allenoates

The CuBr catalyzed formation of propargylamines **62** and their conversion to chiral allenes by the ZnI_2 promoted transformation can be explained by the tentative mechanism outlined in Scheme 10. Initially, the intermediate **66** would be formed by the conjugate addition of chiral amine **61** to the electron-deficient propiolate.

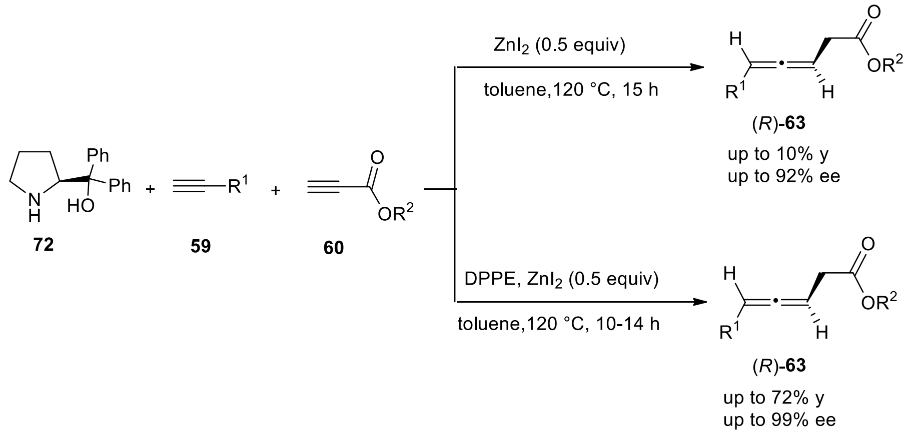
Delivery of the alkynyl group **68** from bottom face of the intermediate **66** would lead to the new trisubstituted propargylamine **62**[20] that could complex with ZnI_2 to give the intermediate **69**, which after an intramolecular hydride shift and *anti* addition of H and ZnI group across the triple bond would give the intermediate **70** that after elimination of ZnI_2 and the imine **71** would afford the chiral allene (*R*)-**63** (Scheme 10).[21,22]

Scheme 10



Recently, we have reported that the (*S*)-diphenypyrrolidinemethanol ((*S*)-DPP) **72** gave the chiral (*R*)-β-allenoates **63** in 72% and 99% ee using ZnX_2, 1-alkynes **59** and propiolates **60** (Scheme 11).[23]

Scheme 11



These new catalytic methodologies are synthetically useful to access the enantioenriched chiral β-allenoates.

2.3 Conclusions

We have developed a simple, practical and inexpensive method for the diastereoselective synthesis of chiral propargylamines **62** in 65% to 86% yield with >99:1 dr using chiral morpholine derivative **61** and propiolates **60** and their enantioselective conversion to chiral β-allenoates **63** up to 70% yield in up to 99% ee.

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.

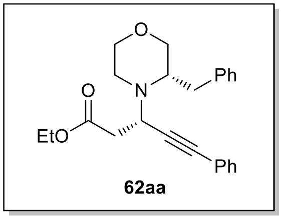
Analytical grade of CuBr, $Cu(OTf)_2$, $AgNO_3$ and ZnI_2 were purchased from Sigma-Aldrich. $ZnBr_2$ was purchased from E-Merck. Toluene supplied by E-Merck, India was freshly distilled over sodium-benzophenone ketyl before use. Analytical thin layer chromatographic tests were carried out on glass plates (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°) and AUTOPOL-IV (readability ±0.001°) 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 the synthesis of propargylamines 62:

To a stirred solution of amine **61** (1 mmol) in toluene (3 mL), CuBr (0.028 g, 0.2 mmol), ethyl propiolate **60a** (0.108 mL, 1.0 mmol), the reaction mixture stirr for 1.5 h and 1-alkynes **59** (1 mmol) at 120 °C under N_2 atmosphere. The contents were stirred for 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_2SO_4) and concentrated. The residue was subjected to column chromatography using hexane and ethyl acetate (90:10) as eluent to isolate the **62**.

(*S*)-Ethyl 3-((*S*)-3-benzylmorpholino)-5-phenylpent-4-ynoate (62aa):



62aa

Yield : 0.294 g, 78%, Orange oil.

$[\alpha]_D^{25}$: -87.3 (c=0.55, $CHCl_3$).

IR (neat) : 3412, 2924, 2931, 2754, 1725, 1469, 1457, 1365, 1248, 1188, 1089, 1023, 744 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.46-7.43 (m, 2H), 7.33-7.29 (m, 5H), 7.25-7.21 (m, 3H), 4.40-4.36 (m, 1H), 4.24-4.19 (m, 2H), 3.90-3.64 (m, 2H), 3.53-3.18 (m, 4H), 3.07-2.91 (m, 2H), 2.85-2.59 (m, 3H), 1.30 (t, *J*=8.0 Hz, 3H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 170.5, 138.4, 131.8, 129.2, 128.3, 126.3, 122.7, 86.7, 84.6, 71.1, 60.7, 59.0, 48.3, 45.9, 38.8, 35.3, 14.4.

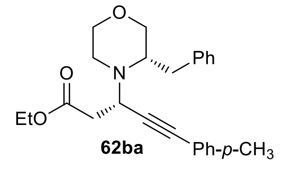
LCMS **:** *m/z* 377 (M-1).

Analysis **:** for $C_{24}H_{27}NO_3$

calcd: C 76.36, N 3.71, H 7.21.

found: C 76.21, N 3.65, H 7.13.

(*S*)-Ethyl 3-((*S*)-3-benzylmorpholino)-5-(*p*-tolyl)pent-4-ynoate (62ba):



62ba

Yield : 0.320 g, 82%, Orange oil.

$[\alpha]_D^{25}$: -93.5 (c=0.55, $CHCl_3$).

IR (neat) **:** 3425, 2924, 2831, 2659, 1725, 1472, 1465, 1368, 1239, 1181, 1091, 1037, 749 cm^{-1}.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.83-7.64 (m, 2H), 7.48-7.12 (m, 7H), 4.39-4.14 (m, 2H), 3.89-3.19 (m, 3H), 3.06-2.81 (m, 2H), 2.54-2.36 (m, 4H), 2.17-1.45 (m, 4H), 1.30 (s, 3H), 0.91 (t, *J*=8.0 Hz, 3H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 170.8, 139.5, 138.4, 132.0, 131.5, 129.4, 129.0, 128.4, 128.2, 126.0, 125.3, 119.7, 86.6, 86.3, 68.8, 67.6, 61.9, 60.6, 52.8, 40.0, 33.2, 32.0, 31.8, 31.6, 29.9, 21.4, 14.3.138.6, 134.8, 129.3, 128.6, 128.4, 128.2, 127.5, 126.2, 120.5, 90.8, 81.1, 70.8, 67.3, 59.2, 56.0, 45.8, 34.8, 29.7, 25.7, 22.4, 21.6.

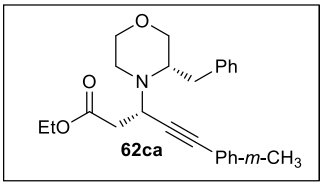
LCMS **:** *m/z* 392 (M+1).

Analysis **:** for $C_{25}H_{29}NO_3$

calcd: C 76.70, N 3.58, H 7.47.

found: C 76.14, N 3.36, H 7.40.

(*S*)-Ethyl 3-((*S*)-3-benzylmorpholino)-5-(*m*-tolyl)pent-4-ynoate (62ca):



62ca

Yield : 0.328 g, 80%, Brown oil.

$[\alpha]_D^{25}$: -107.8 (c= 0.55, CHCl$_3$).

IR (neat) : 3066, 3026, 2925, 1725, 1602, 1492, 1447, 1120, 906.2, 841.4 cm^{-1}.

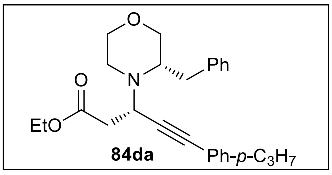
^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.32-7.25 (m, 5H), 7.24-7.13 (m, 4H), 4.40-4.17 (m, 3H), 3.91-3.64 (m, 2H), 3.56-3.16 (m, 4H), 3.11-2.57 (m, 5H), 2.34 (s, 3H), 1.30 (t, *J*= 8.0 Hz, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 170.7, 139.5, 138.0, 132.2, 132.1, 129.5, 128.5, 126.1, 122.5, 86.7, 86.6, 68.8, 62.0, 60.6, 52.7, 43.4, 40.0, 31.8, 21.2, 14.4.

LCMS : *m/z* 391 (M-1).

Analysis : for $C_{26}H_{29}NO_3$
calcd: C 76.70, N 3.58, H 7.47.
found: C 76.45, N 3.26, H 7.12.

(*S*)-Ethyl 3-((*S*)-3-benzylmorpholino)-5-(4-propylphenyl)pent-4-ynoate (62da):



84da

Yield : 0.335 g, 80%, Yellow oil.

$[\alpha]_D^{25}$: -67.8 (c=0.55, CHCl$_3$).

IR (neat) : 3061, 3026, 2935, 1725, 1602, 1492, 1447, 1120, 906.2, 751 cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.44-7.12 (m, 9H), 4.38-3.63 (m, 4H), 3.59-3.16 (m, 3H), 3.12-2.72 (m, 3H), 2.59 (t, *J*=8.0 Hz, 3H), 2.20-2.18 (m, 2H), 1.64 (t, *J*=8.0 Hz, 3H), 1.29 (t, *J*=8.0 Hz, 3H), 0.94 (t, *J*=8.0 Hz, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 170.8, 143.2, 139.5, 132.0, 131.5, 129.4, 128.5, 126.0, 119.9, 68.8, 67.6, 62.0, 60.2, 52.8, 43.4, 37.9, 24.4, 14.4, 13.7.

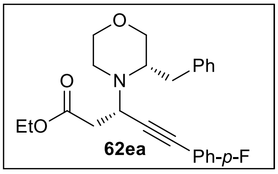
LCMS : *m/z* 419 (M-1).

Analysis : for $C_{27}H_{33}NO_3$

calcd: C 77.29, N 3.34, H 7.93.

found: C 77.12, N 3.12, H 7.48.

(*S*)-Ethyl 3-((*S*)-3-benzylmorpholino)-5-(4-fluorophenyl)pent-4-ynoate (62ea):



62ea

Yield : 0.339 g, 86%, Orange oil.

$[\alpha]_D^{25}$: -87.3 (c=0.55, $CHCl_3$).

IR (neat) : 3056, 3136, 2899, 1725, 1610, 1489, 1454, 1118, 926.2, 702 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.45-7.40 (m, 2H), 7.34-7.28 (m, 2H), 7.25-7.22 (m, 3H), 7.06-6.99 (m, 2H), 4.40-4.20 (m, 3H), 3.91-3.63 (m, 2H), 3.53-3.42 (m, 2H), 3.30-3.17 (m, 2H), 3.07-2.91 (m, 2H), 2.85-2.69 (m, 2H), 2.62-2.59 (m, 1H), 1.31 (t, *J*= 8.0 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 170.7, 163.7, 139.3, 133.5, 133.4, 129.4, 128.5, 126.1, 118.8, 115.7, 115.5, 86.7, 85.5, 68.8, 67.5, 61.9, 60.6, 52.6, 43.5, 39.8, 31.8, 138.6, 134.8, 129.3, 128.6, 128.4, 128.2, 127.5, 126.2, 120.5, 90.8, 81.1, 70.8, 67.3, 59.2, 56.0, 45.8, 34.8, 14.4.

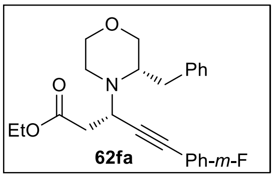
LCMS : *m/z* 395 (M-1).

Analysis : for $C_{24}H_{26}FNO_3$

calcd: C 72.89, N 3.54, H 6.63.

found: C 72.19, N 3.18, H 6.36.

(*S*)-Ethyl 3-((*S*)-3-benzylmorpholino)-5-(3-fluorophenyl)pent-4-ynoate (62fa):



62fa

Yield : 0.323 g, 82%, Brown oil.

$[\alpha]_D^{25}$: -81.3 (c=0.55, $CHCl_3$).

IR (neat) : 3075, 3023, 2875, 1725, 1617, 1485, 1448, 1129, 795, 705 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.48-7.42 (m, 2H), 7.36-7.26 (m, 2H), 7.24-7.22 (m, 3H), 7.02-6.95 (m, 2H), 4.42-4.18 (m, 3H), 3.97-3.68 (m, 2H), 3.54-3.41 (m, 2H), 3.29-3.15 (m, 2H), 3.10-2.95 (m, 2H), 2.89-2.72 (m, 2H), 2.69-2.59 (m, 1H), 1.34 (t, *J*= 8.0 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 170.6, 139.3, 129.9, 129.8, 129.4, 128.5, 127.5, 126.1, 118.5, 118.3, 115.8, 88.1, 85.4, 68.7, 67.5, 61.9, 60.7, 52.6, 43.4, 39.7, 31.7, 14.4.

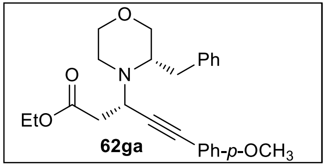
LCMS : *m/z* 395 (M-1).

Analysis : for $C_{24}H_{26}FNO_3$

calcd: C 72.89, N 3.54, H 6.63.

found: C 72.23, N 3.22, H 6.38.

(*S*)-Ethyl 3-((*S*)-3-benzylmorpholino)-5-(4-methoxyphenyl)pent-4-ynoate (62ga):



62ga

Yield : 0.272 g, 67%, Yellow oil.

$[\alpha]_D^{25}$: -78.3 (c=0.55, $CHCl_3$).

IR (neat) : 3065, 3016, 2935, 1725, 1612, 1498, 1457, 1130, 871.4 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.44-7.36 (m, 2H), 7.32-7.2 (m, 5H), 6.91-6.84 (m, 2H), 4.76-4.20 (m, 4H), 3.84 (s, 3H), 3.66-3.55 (m, 2H), 3.27-2.97 (m, 3H), 2.83-2.67 (m, 3H), 2.47-1.94 (m, 2H), 1.33 (t, *J*= 8.0 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 170.5, 159.5, 138.4, 133.2, 129.2, 128.4, 126.2, 114.8, 114.0, 86.5, 83.1, 71.1, 60.6, 59.0, 55.2, 48.4, 45.8, 38.9, 35.2, 14.0.

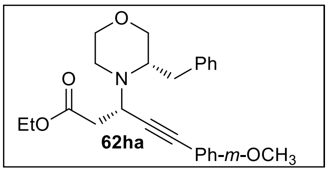
LCMS : *m/z* 407 (M-1).

Analysis : for $C_{25}H_{29}NO_4$

calcd: C 73.68, N 3.44, H 7.17.

found: C 73.45, N 3.25, H 7.09.

(*S*)-Ethyl 3-((*S*)-3-benzylmorpholino)-5-(3-methoxyphenyl)pent-4-ynoate (62ha):



62ha

Yield : 0.284 g, 70%, Orange oil.

[α]D²⁵ : -71.3 (c=0.55, $CHCl_3$).

IR (neat) : 3086, 3126, 2985, 1725, 1599, 1489, 1467, 1112, 916.2, 851.1 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.37-7.15 (m, 6H), 7.08-6.87 (m, 2H), 4.40-3.89 (m, 4H), 3.81 (s, 3H), 3.69-3.19 (m, 4H), 3.07-2.54 (m, 4H), 1.71-1.64 (m, 2H), 1.31 (t, *J*= 8.0 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 170.7, 159.2, 139.4, 129.4, 128.5, 126.0, 124.2, 123.7, 116.5, 114.8, 86.8, 86.5, 68.8, 67.6, 61.9, 55.3, 52.7, 43.5, 39.9, 31.8, 14.4.

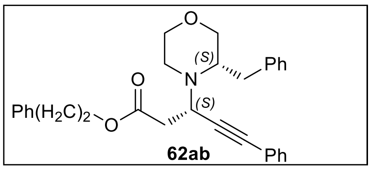
LCMS : *m/z* 407 (M-1).

Analysis : for $C_{25}H_{29}NO_4$

calcd: C 73.68, N 3.44, H 7.17.

found: C 73.21, N 3.36, H 7.09.

(*S*)-Phenethyl 3-((*S*)-3-benzylmorpholino)-5-phenylpent-4-ynoate (62ab):



62ab

Yield : 0.294 g, 65%, Orange oil.

[α]D²⁵ : -102.3 (c=0.55, $CHCl_3$).

IR (neat) : 3056, 3026, 2925, 1732, 1612, 1492, 1437, 1130, 906.2 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.46-7.20 (m, 15H), 4.42-4.13 (m, 3H), 3.87-3.57 (m, 2H), 3.38-3.17 (m, 3H), 3.05-2.78 (m, 6H), 2.59-2.08 (m, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 170.9, 139.5, 137.8, 131.7, 129.5, 128.9, 128.5, 128.3, 126.6, 126.1, 122.7, 87.1, 86.6, 68.8, 67.4, 65.1, 61.8, 52.8, 43.2, 40.0, 35.0, 31.7.

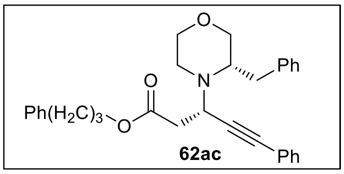
LCMS : *m/z* 453 (M-1).

Analysis : for $C_{30}H_{31}NO_3$

calcd: C 79.44, N 3.09, H 6.89.

found: C 79.12, N 3.01, H 6.38.

(*S*)-3-Phenylpropyl 3-((*S*)-3-benzylmorpholino)-5-phenylpent-4-ynoate (62ac):



62ac

Yield : 0.336 g, 72%, Orange oil.

$[\alpha]_D^{25}$: -107.3 (c=0.55, $CHCl_3$).

IR (neat) : 3063, 3032, 2925, 1735, 1602, 1489, 1447, 1120, 906.2, 843 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.46-7.20 (m, 15H), 4.42-4.18 (m, 3H), 3.90-3.68 (m, 2H), 3.51-3.22 (m, 3H), 3.07-2.64 (m, 6H), 2.07-2.01 (m, 2H), 1.31-0.90 (m, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 170.8, 141.0, 139.4, 131.6, 129.4, 128.5, 128.4, 128.3, 126.0, 122.7, 87.0, 86.6, 68.8, 67.6, 64.0, 61.9, 52.7, 43.7, 39.9, 32.2, 31.9, 30.3.

LCMS : *m/z* 467 (M-1).

Analysis : for $C_{31}H_{33}NO_3$

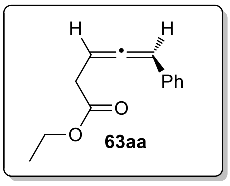
calcd: C 79.63, N 3.00, H 7.11.

found: C 79.38, N 2.98, H 7.04.

2.4.3 General Procedure for Synthesis of Chiral β-Allenoates 63.

To a stirred solution of propargylamine **62** (1 mmol) in toluene (3 mL) and ZnI_2 (0.160 g, 0.5 mmol) and the reaction mixture was stirred at 120 °C 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 **63.**

(***R***)-Ethyl 5-phenylpenta-3,4-dienoate (63aa):



63aa

Yield : 0.131 g, 65%, White liquid.

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

IR (neat) : 3029, 2969, 2903, 1961, 1736, 1659, 1369, 1254, 1177, 1100, 1034, 870, 793 cm^{-1}.

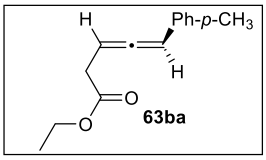
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.84-7.82 (m, 1H), 7.51-7.32 (m, 1H), 7.32-7.27 (m, 3H), 6.25-6.23 (m, 1H), 5.75-5.72 (m, 1H), 4.21 (quin, *J*=4.0 Hz, 2H), 3.19-3.17 (m, 2H), 1.31-1.28 (m, 3H).

^{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) calcd for $C_{13}H_{14}O_2$: 202.0994 $[M+NH_4^+]$; found: 220.1358.

Enanatiomeric purity: 99% ee,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: 17.6min. (major) and 20.4 min. (minor).

(***R***)-Ethyl 5-(***p***-tolyl)penta-3,4-dienoate (63ba):



63ba

Yield : 0.146 g, 68%, Light yellow liquid.

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

IR (neat) : 2985, 2191, 1966, 1736, 1682, 1594, 1512, 1446, 1260, 1178, 1046, 876, 810 cm^{-1}.

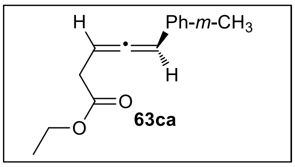
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 8.0-7.98 (m, 1H), 7.67-7.65 (m, 1H), 7.54-7.50 (m, 1H), 7.26-7.10 (m, 1H), 6.20-6.19 (m, 1H), 5.69 (q, *J*=4.0 Hz, 1H), 4.17 (quin, *J*=4.0 Hz, 2H), 3.16-3.13 (m, 2H), 2.35 (s, *J*=4.0 Hz, 3H), 1.32-1.1.26 (m, 3H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 206.0, 171.2, 137.6, 136.9, 132.4, 128.2, 129.3, 126.8, 95.4, 88.1, 60.9, 34.6, 21.2, 14.2.

HRMS : (ESI) calcd for $C_{14}H_{16}O_2$: 216.1150 [*M*+Na$^+$]; found: 239.1048.

Enanatiomeric purity: 96% ee,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 (63ca):



Yield : 0.151 g, 70%, Light yellow liquid.

[α]D^{25} : -232.4 (c=0.5 $CHCl_3$).

IR (neat) **:** 3031, 2934, 1965, 1730, 1675, 1586, 1513, 1435, 1250, 1168, 1033, 856, 715 cm^{-1}.

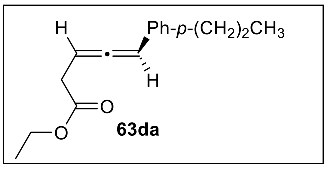
^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.25-7.22 (m, 1H), 7.21-7.18 (m, 2H), 7.14 (d, *J*=4.0 Hz, 1H), 6.22-6.19 (m, 1H), 5.78 (q, *J*=4.0 Hz, 1H), 4.19 (q, *J*=4.0 Hz, 2H), 3.20-3.16 (m, 2H), 2.35 (s, 3H), 1.30 (t, *J*=8.0 Hz, 3H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 206.2, 171.2, 138.2, 133.8, 128.5, 127.9, 127.5, 124.0, 95.6, 88.1, 60.9, 34.6, 21.3, 14.2.

HRMS : (ESI) calcd for $C_{14}H_{16}O_2$: 216.1150 [*M*+Na$^+$]; found 239.1048.

Enanatiomeric purity: 96% ee,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-propylphenyl)penta-3,4-dienoate (63da):



Yield : 0.170, 70%, Yellow liquid.

[α]D^{25} : -209.0 (c=0.1, $CHCl_3$).

IR (neat) **:** 2958, 2920, 1962, 1725, 1654, 1610, 1512, 1254, 898, 734 cm^{-1}.

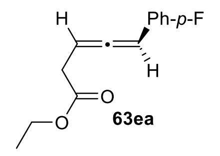
^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.85-7.82 (m, 2H), 7.23-7.15 (m, 2H), 6.23-6.21 (m, 1H), 5.74-5.71 (m, 1H), 4.23-4.18 (m, 2H), 3.18-3.16 (m, 2H), 2.60-2.56 (m, 2H), 1.66-2.61(m, 2H), 1.33-1.28 (m, 3H), 0.95 (t, *J*=4.0 Hz, 3H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 206.1, 171.3, 141.8, 137.6, 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) calcd for $C_{16}H_{20}O_2$: 244.1463 [M+H^+]; found: 245.1542.

Enanatiomeric purity: 98% ee,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-fluorophenyl)penta-3,4-dienoate (63ea):



63ea

Yield : 0.132g, 60%, Yellow liquid.

[α]$_D$^{25} : -189.3 (c=0.5, $CHCl_3$).

IR (neat) **:** 2925, 2854, 1954, 1736, 1661, 1601, 1447, 1319, 1276, 1170, 1036, 789, 702 cm^{-1}.

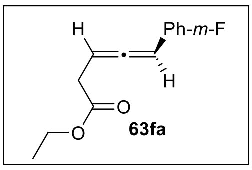
^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.31-7.27 (m, 2H), 7.04-6.99 (m, 2H), 6.23-6.20 (m, 1H), 5.76-5.71 (m, 1H), 4.23-4.218 (m, 2H), 3.19-3.16 (m, 2H), 1.30 (t, *J*=4.0 Hz, 3H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, 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) calcd for $C_{13}H_{13}FO_2$: 220.0900 [M+NH_4^+]; found: 238.1242.

Enanatiomeric purity: 98% ee,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-(3-fluorophenyl)penta-3,4-dienoate (63fa):



63fa

Yield : 0.129g, 59%, Yellow liquid.

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

IR (neat) : 2964, 2853, 1956, 1736, 1662, 1594, 1446, 1260, 1170, 1093, 789, 704 cm^{-1}.

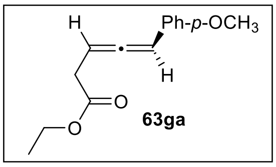
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.83-7.50 (m, 1H), 7.09-7.02 (m, 2H), 7.93-6.89 (m, 1H), 6.22-6.20 (m, 1H), 5.78-5.75 (m, 1H), 4.21-4.20 (m, 2H), 3.18-3.17 (m, 2H), 1.35-1.28 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 206.5, 171.0, 164.3, 163.1, 136.4, 131.2, 122.6, 113.9, 113.4, 94.9, 88.7, 61.0, 34.3, 14.1.

HRMS : (ESI) calcd for $C_{13}H_{13}FO_2$: 220.0900 [M+NH_4^+]; found: 238.1244.

Enanatiomeric purity: 98% ee,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-(4-methoxyphenyl)penta-3,4-dienoate (63ga):



63ga

Yield : 0.127 g, 55%, White liquid.

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

IR (neat) : 2964, 2191, 1956, 1736, 1682, 1594, 1512, 1446, 1260, 1178, 1046, 876, 810 cm^{-1}.

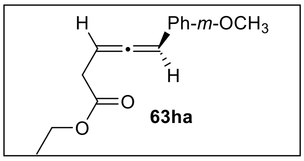
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.25 (d, J=4.0 Hz, 2H), 6.87 (d, J=4.0 Hz, 2H), 6.22-6.18 (m, 1H), 5.70 (q, J=4.0 Hz, 1H), 4.20 (quin, J=4.0 Hz, 2H), 3.82 (s, 3H), 3.16 (d, J=4.0 Hz, 2H), 1.29 (t, J=8.0 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 205.8, 171.3, 158.9, 134.9, 129.9, 128.0, 126.2, 114.1, 95.0, 88.1, 60.9, 55.3, 34.7, 14.2.

HRMS : (ESI) calcd for $C_{14}H_{16}O_3$: 232.1099 [*M*+H$^+$]; found: 233.1178.

Enanatiomeric purity: 96% ee,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 (63ha):



Yield : 0.116g, 50%, White liquid.

[α]D^{25} : -255.7 (c=0.2, $CHCl_3$).

IR (neat) : 3035, 2955, 1961, 1726, 1640, 1612, 1439, 1252, 1188, 850, 824, 712 cm^{-1}.

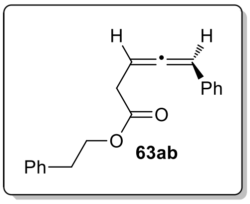
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.36-7.22 (m, 1H), 6.93-6.89 (m, 2H), 6.80-6.78 (m, 1H), 6.23-6.21(m, 1H), 5.74 (q, *J*=4.0Hz, 1H), 4.24-4.21 (m, 2H), 3.85 (s, 3H), 3.20-3.17 (m, 2H), 1.34-1.28 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 206.4, 171.2, 159.8, 135.4, 129.5, 119.5, 112.9, 112.1, 95.6, 88.3, 60.9, 55.2, 34.5, 14.2.

HRMS : (ESI) calcd for $C_{14}H_{16}O_3$: 232.1099 [*M*+H$^+$]; found: 233.1178.

Enanatiomeric purity: 98% ee,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*)-Phenethyl 5-phenylpenta-3,4-dienoate (63ab):



Yield : 0.152 g, 55%, Yellow liquid.

[α]D^{25} : -220.1 (c=0.4, $CHCl_3$).

IR (neat) : 2968, 2910, 1963, 1732, 1650, 1359, 1244, 1167, 1120, 1030, 859, 789 cm^{-1}.

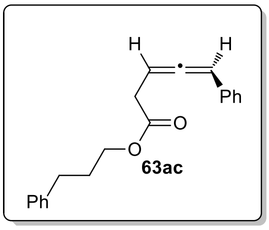
^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.35-7.31 (m, 5H), 7.27-7.24 (m, 5H), 6.25-6.23 (m, 1H), 5.75-5.70 (m, 1H), 4.39-4.35 (m, 2H), 3.21-3.17 (m, 2H), 3.0-2.96 (m, 2H).

^{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) calcd for $C_{19}H_{18}O_2$: 278.1307[M+H$^+$]; found: 279.1389.

Enanatiomeric purity: 98% ee,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 (63ac):



63ac

Yield : 0.175g, 60%, White liquid.

$[\alpha]_D^{25}$: -211.6 (c=0.4 CHCl$_3$).

IR (neat) : 2969, 2910, 1963, 1732, 1649, 1359, 1244, 1167, 1120, 1030, 860, 783 cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.35-7.31 (m, 5H), 7.27-7.24 (m, 5H), 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, 88.1, 65.3, 35.0, 34.4.

HRMS : (ESI) calcd for $C_{20}H_{20}O_2$: 292.1463[M+H$^+$]; found: 293.1545.

Enanatiomeric purity: 98% ee,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: 20.7min. (major) and 30.4 min. (minor).

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Chapter 3

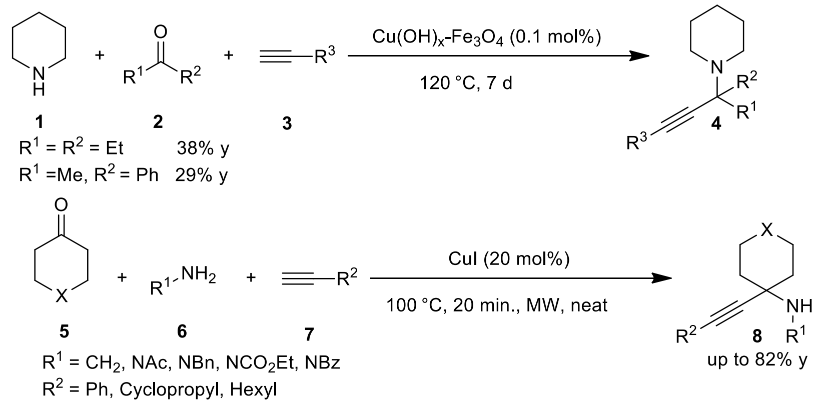
ZnI_2 Catalyzed Synthesis of Trisubstituted Allenes from Ketones and 1-Alkynes

3. 1 Introduction

3.1.1 Synthesis of tetrasubstituted propargylamines using ketones and 1-alkynes

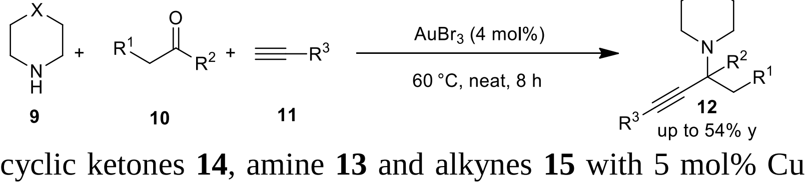
The acyclic or cyclic ketones and amines couple with terminal acetylenes at 120 °C or under microwave conditions in the presence of copper complexes or with copper halides to give the corresponding propargylamines **4**, **8** in 29–82% yields (Scheme 1).[1,2]

Scheme 1



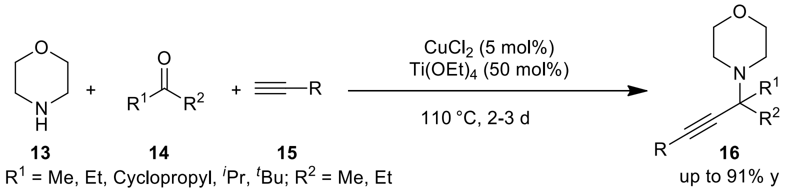
It was also reported that cyclic amines **9** react with 1.5 equivalents each of ketones **10** and 1-alkynes **11** under $AuBr_3$ (4 mol%) catalysis to give the quaternary propargylamines **12** in up to 54% yield (Scheme 2).[3]

Scheme 2



Heating of acyclic ketones **14**, amine **13** and alkynes **15** with 5 mol% $CuCl_2$ and 50 mol% $Ti(OEt)_4$ gave the propargylaminse **16** in up to 91% yield (Scheme 3).[4]

Scheme 3

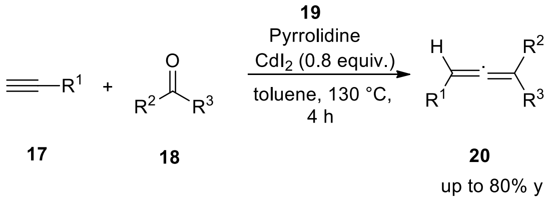


3.1.2 Synthesis of trisubstituted allenes using ketones, 1-alkynes and cyclic secondary amines

Allenes are not only important structural motifs in natural products, drugs, and molecular materials[5] but also useful intermediates in organic synthesis.[6] Therefore, several efforts were directed toward the synthesis of this allenes,[7-11] such as transitionmetal-catalyzed coupling reaction of propargylic derivatives, [3,3]-sigmatropic rearrangement,[7e-9]coupling of terminal alkynes with diazo compounds,[10] and conjugate addition to enynes.[11]

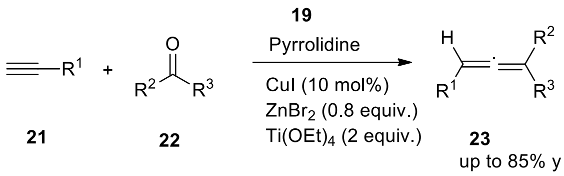
In 2013, the CdI_2-mediated one-pot synthesis of trisubstituted allenes **20** from terminal alkynes **17** and ketones **18** was reported (Scheme 4).[12]

Scheme 4



More recently, synthesis of trisubstituted allenes **23** from readily available terminal alkynes **21** and ketones **22** promoted by $CuI/ZnBr_2/Ti(OEt)_4$ reagent system was reported (Scheme 5).[13]

Scheme 5

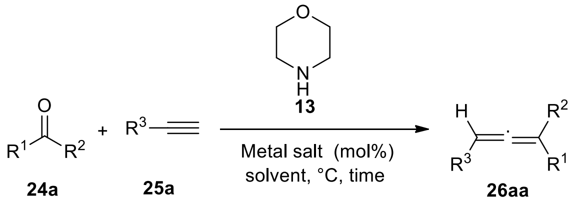


We have developed one-pot synthesis of trisubstituted allenes by the reaction of secondary amines, ketones and 1-alkynes under ZnI_2 catalysis. The results are described in the next section.

3.2 Results and Discussion

We initiated our investigations on the reaction of alkyne **25a,** ketone **24a**, morpholine **13** and ZnI_2 in toluene. After screening different ZnX_2 catalysts, we have observed that Znl_2 (50 mol%) gave the desired allene product **26aa** in 54% yield (entry 3, Table 1). Increasing the loading of Znl_2 to 0.8 mol% improved the yield of **26aa** to 76% (entry 4, Table 1). However, the yield of the product **26aa** dropped when the reaction temperature was decreased from 120 °C to 110 °C (entry 6, Table 1).

Table 1: Reaction of amine **13**, 1-alkyne **25** and ketone **24** with different metal salts to afford allenes **26**.[a,b]

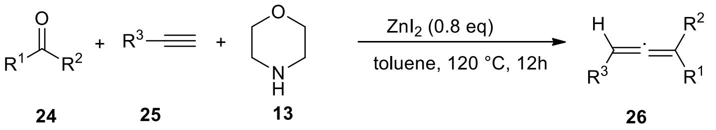


S.No	Solvent	Temp. °C	MX_n	Mol(%)	26aa
1	Toluene	120	$ZnCl_2$	0.5	-
2	Toluene	120	$ZnBr_2$	0.5	34
3	Toluene	120	ZnI_2	0.5	54
4	Toluene	120	ZnI_2	0.8	76
5	Dioxane	120	ZnI_2	0.8	12
6	Toluene	110	ZnI_2	0.8	64
7	Toluene	120	ZnI_2	0.8	68
8	Toluene	120	ZnI_2	0.8	10

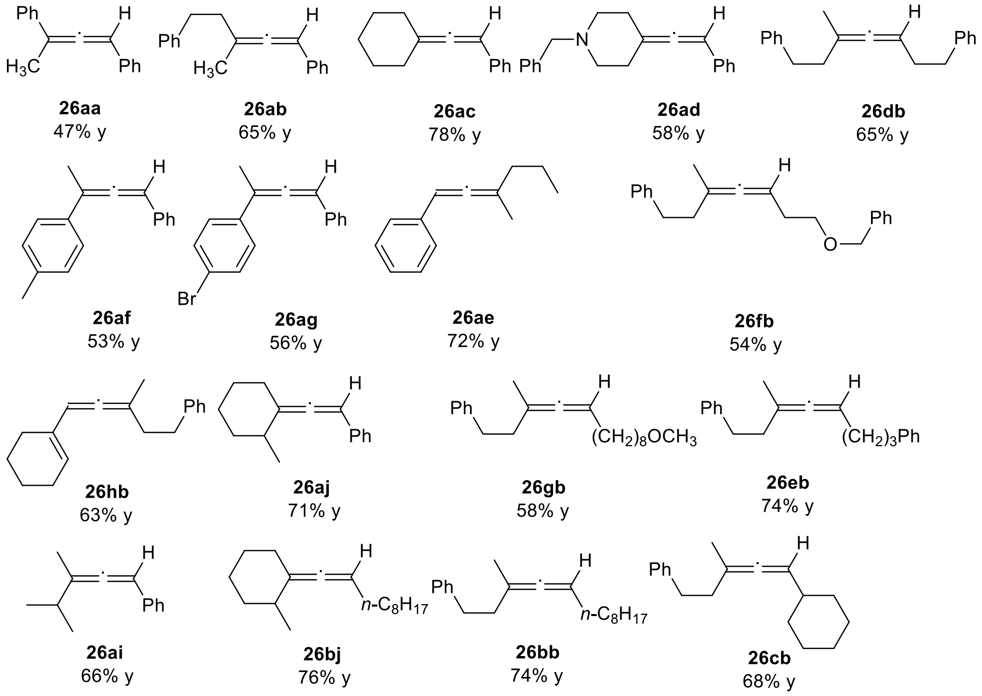
[a]The reactions were carried out by using amine **13 (**1.1 mmol) and ketone **24a** (1.1 mmol) and alkyne **25a** (1.1 mmol). [b]Isolated yield.

With the optimized condition in hand (entry 4, Table 1), we have carried out the reaction using different ketones and alkynes. The results are summarized in Table 2. The acyclic aliphatic ketones 4-phenylbutan-2-one **24b** and pentan-2-one **24c** afforded the product **26ab-26ae** in 65% yield and 72% yield respectively (Table 2).

Table 2: Synthesis of trisubstituted allenes **26** using ketones **24,** 1-alkynes **25** and amine **13**.[a,b]



24a= R^1= Ph, R^2=CH_3
24b= R^1=$Ph(CH_2)_2$, R^2=CH_3
24c= R^1=R^2=C_5H_{10}
24d= R^1=R^2=$C_{10}NH_{15}$
24e= R^1=CH_3, R^2=C_3H_7
24f= R^1= Ph-CH_3, R^2=CH_3
24g= R^1= Ph-Br, R^2=CH_3
24h= R^1=R^2=$C_{10}H_{16}$
24i= R^1= $CH(CH_3)_2$, R^2=CH_3
24j= R^1= R^2=C_7H_{12}
25a= Ph
25b= n-C_8H_{17}
25c= n-C_6H_{11}
25d= $Ph(CH_2)_2$
25e= $Ph(CH_2)_3$
25f= $Ph(CH_2)OCH_2CH_3$
25g= $(CH_2)_8OCH_3$
25h= c-C_6H_9



26aa 47% y
26ab 65% y
26ac 78% y
26ad 58% y
26db 65% y
26af 53% y
26ag 56% y
26ae 72% y
26fb 54% y
26hb 63% y
26aj 71% y
26gb 58% y
26eb 74% y
26ai 66% y
26bj 76% y
26bb 74% y
26cb 68% y

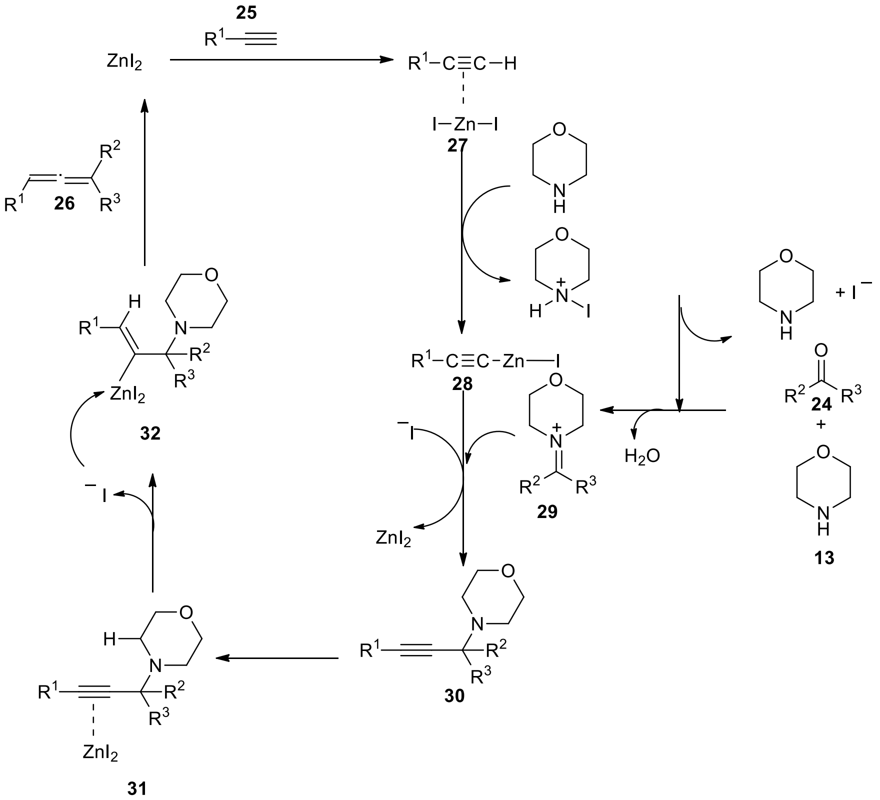
[a] The reactions were carried out by using amine **13** (1.0 mmol), ketones **24** (1.1 mmol), and 1-alkynes **25** (1.1 mmol) in toluene (3 mL) at 120 °C. [b] Yield of allenes.

The aromatic ketones **24a**, **24f** and **24g** gave the products **26aa**, **26af** and **26ag** in 47-56% yield (Table 2). We have also carried out the experiments using various alkynes **25b**, **25c**, **25d**, **25e** and **25h** with the ketone **24b** and the corresponding allene products **26bb-26hb** were obtained in 63-74% yield (Table 2). The alkoxyalkynes **25f** and **25g** reacted under these reaction conditions to give the products **26fb** and **26gb** in 54% and 58% yields, respectively (Table 2).

3.2.1 Plausible mechanism for the formation of allene 26

A plausible mechanism may be considered for this transformation based on previous reports.[14,15] The alkynyl zinc species **28**, generated from terminal alkyne in the presence of amine, would react with the ketiminium intermediate **29** formed *in situ* from ketone and morpholine, to give the corresponding propargylamine **30**. The carbon-carbon triple bond in propargylamine **30** would then coordinate to ZnI_2 forming the complex **31** which after the 1,5-hydride transfer and β-elimination to afford the corresponding trisubstituted allene **26** (Scheme 6).

Scheme 6



After development of convenient methods to access different allene derivatives (chapters 1-3), we have turned our attention toward enantioselective synthesis of cyclohexenylallenes and their applications in [4+2] cycloaddition. The results are described in chapter 4.

3.3 Conclusions

We have devised a ZnI_2 promoted method to access trisubstituted allenes in 47% to 78% yields using morpholine, ketones and terminal alkynes. The method has potential for applications in organic synthesis.

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.

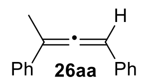
Analytical grade of CuBr, Cu(OTf) and ZnI_2 were purchased from Sigma-Aldrich. $ZnBr_2$, $ZnCl_2$ was purchased from E-Merck. Toluene supplied by E-Merck, India was freshly distilled over sodium-benzophenone ketyl before use. Analytical thin layer chromatographic tests were carried out on glass plates (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 General procedure for synthesis of trisubstituted allene 26.

To a stirred solution of amine **13** (1 mmol) in toluene (3 mL) and ZnI_2 (0.255 g, 0.8 mmol) 1-alkynes **25** (1.1 mmol), ketones **24** (1.1 mmol) and the reaction mixture was stirred at 120 °C for 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_2SO_4), and concentrated. The residue was subjected to column chromatography using hexane and ethyl acetate (95:5) as eluent to isolate the allene **26.**

Buta-1,2-diene-1,3-diyldibenzene (26aa):



26aa

Yield : 0.96 g, 47%, Brown liquid.

IR (neat) : 2925, 2851, 1951, 1620, 1598, 1495, 1444, 1412, 1345, 1307, 1257, 1240, 1198, 1071, 1025 cm^{-1}**.**

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.59-7.55 (m, 2H), 7.44-7.37 (m, 6H), 7.35-7.30 (m, 2H), 6.57 (s, 1H), 2.29 (d, *J*=4.0 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 206.8, 136.3, 134.5, 128.7, 128.5, 127.0, 126.9, 125.8, 104.5, 96.5, 16.7.

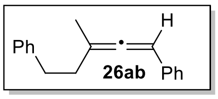
LCMS : m/z 206 (M+1).

Analysis : for $C_{16}H_{14}$

calcd: C 93.16, H 6.84.

found: C 93.07, H 6.71.

(3-Methylpenta-1,2-diene-1,5-diyl)dibenzene (26ab):



Yield : 0.152 g, 65%, Yellow liquid.

IR (neat) : 2935, 2751, 1947, 1628, 1589, 1491, 1434, 1412, 1315, 1327, 1217, 1240, 1191, 1025 cm^{-1}**.**

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.35-7.30 (m, 5H), 7.27-7.22 (m, 5H), 6.14-6.12 (m, 1H), 2.87 (t, *J*=8.0 Hz, 2H), 2.49-2.45 (m, 2H), 1.91 (d, *J*=4.0 Hz, 2H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 202.8, 141.9, 135.8, 128.5, 128.4, 128.3, 126.6, 126.4, 125.8, 103.1, 94.4, 35.8, 33.9, 18.9.

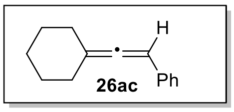
LCMS : m/z 234 (M+1).

Analysis : for $C_{18}H_{18}$

calcd: C 92.26, H 7.74.

found: C 92.05, H 7.28.

(2-Cyclohexylidenevinyl)benzene (26ac):



Yield : 0.143 g, 78%, Orange Oil.

IR (neat) : 2898, 2681, 1959, 1622, 1595, 1491, 1434, 1412, 1315, 1337, 1217, 1239, 1191, 978 cm^{-1}**.**

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.32-7.31 (m, 4H), 7.20-7.18 (m, 1H), 6.03 (s, 1H), 2.33-2.20 (m, 4H), 1.75-1.56 (m, 6H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 199.6, 136.1, 128.5, 126.5, 126.3, 106.5, 92.3, 31.3, 27.7, 26.1.

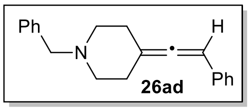
LCMS : m/z 184 (M-1).

Analysis : for $C_{14}H_{16}$

calcd: C 91.25, H 8.75.

found: C 91.08, H 8.56.

1-Benzyl-4-(2-phenylvinylidene)piperidine (26ad):


26ad

Yield : 0.159 g, 58%, Yellow liquid.

IR (neat) : 2916, 2681, 1971, 1625, 1591, 1493, 1434, 1412, 1315, 1337, 1217, 1239, 1191, 978 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.35-7.31 (m, 5H), 7.27-7.24 (m, 5H), 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, 88.1, 65.3, 35.0, 34.4.

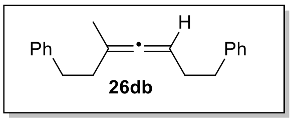
LCMS : m/z 275 (M-1).

Analysis : for $C_{20}H_{21}N$

calcd: C 87.23, H 7.69.

found: C 87.18, H 7.25.

(3-Methylhepta-3,4-diene-1,7-diyl)dibenzene (26db):


26db

Yield : 0.170.3 g, 65%, Brown liquid.

IR (neat) : 2928, 2681, 1968, 1625, 1591, 1493, 1434, 1412, 1315, 1337, 1217, 1239, 1191, 978 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.32-7.28 (m, 4H), 7.21-7.20 (m, 6H), 5.13-5.09 (m, 1H), 2.71-2.66 (m, 4H), 2.30-2.21 (m, 4H), 1.69 (d, *J*=4.0 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 201.4, 142.3, 142.0, 128.5, 128.4, 128.2, 125.7, 99.4, 90.2, 35.6, 35.4, 33.9, 30.9, 19.3.

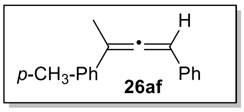
LCMS : m/z 262 (M-1).

Analysis : for $C_{20}H_{22}$

calcd: C 91.55, H 8.45.

found: C 91.44, H 8.32.

1-Methyl-4-(4-phenylbuta-2,3-dien-2-yl)benzene (26af):



26af

Yield : 0.116 g, 53%, Yellow oil.

IR (neat) **:** 3022, 2691, 1965, 1625, 1591, 1453, 1434, 1412, 1315, 1337, 1217, 1239, 1191, 1028 cm^{-1}**.**

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.40-7.34 (m, 6H), 7.28-7.16 (m, 3H), 6.52-6.49 (m, 1H), 2.37 (s, 3H), 2.25 (d, *J*=8.0 Hz, 2H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 206.6, 136.8, 134.7, 133.3, 129.1, 128.6, 126.8, 125.7, 104.4, 96.4, 21.1, 16.8.

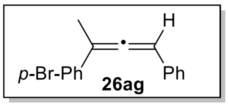
LCMS **:** m/z 220 (M-1).

Analysis **:** for $C_{17}H_{16}$

calcd: C 92.68, H 7.32.

found: C 92.38, H 7.28.

1-Bromo-4-(4-phenylbuta-2,3-dien-2-yl)benzene (26ag):



26ag

Yield : 0.159 g, 56%, Colourless liquid.

IR (neat) **:** 3012, 2679, 1961, 1625, 1591, 1463, 1444, 1412, 1315, 1337, 1217, 1239, 1191, 957 cm^{-1}**.**

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.46-7.44 (m, 2H), 7.34-7.32 (m, 6H), 7.27-7.24 (m, 1H), 6.50-6.48 (m, 1H), 2.22 (d, *J*=4.0 Hz, 3H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 206.8, 135.4, 134.0, 131.5, 128.7, 127.4, 127.2, 126.9, 120.9, 103.8, 96.9, 16.6.

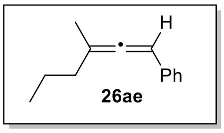
LCMS **:** m/z 284 (M-1).

Analysis **:** for $C_{16}H_{13}Br$

calcd: C 67.39, H 4.59.

found: C 67.24, H 4.29.

(3-Methylhexa-1,2-dien-1-yl)benzene (26ae):



26ae

Yield : 0.123 g, 72%, White liquid.

IR (neat) : 2998, 2679, 1964, 1625, 1591, 1463, 1444, 1412, 1315, 1337, 1217, 1239, 1191, 857 cm^{-1}**.**

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.31-7.27 (m, 4H), 7.20-7.16 (m, 1H), 6.08-6.06 (m, 1H), 2.11-2.06 (m, 2H), 1.83 (d, *J*=4.0 Hz, 3H), 0.96 (d, *J*=8.0 Hz, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 202.7, 136.1, 128.4, 126.5, 126.3, 103.5, 93.7, 36.2, 20.8, 18.7, 13.9.

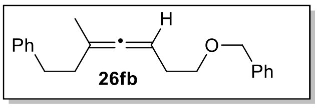
LCMS : m/z 172 (M-1).

Analysis : for $C_{13}H_{16}$

calcd: C 90.64, H 9.36.

found: C 90.48, H 9.21.

(7-(Benzyloxy)-3-methylhepta-3,4-dien-1-yl)benzene (26fb):



26fb

Yield : 0.157 g, 54%, Brown oil.

IR (neat) : 2969, 2910, 1963, 1732, 1649, 1359, 1244, 1167, 1120, 1030, 860, 783 cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.35-7.31 (m, 5H), 7.27-7.24 (m, 5H), 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, 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.

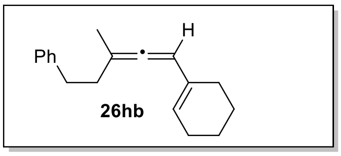
LCMS **:** m/z 292 (M-1).

Analysis **:** for $C_{21}H_{24}O$

calcd: C 86.26, H 8.27.

found: C 86.05, H 8.13.

(5-(Cyclohex-1-en-1-yl)-3-methylpenta-3,4-dien-1-yl)benzene (26hb):



26hb

Yield : 0.149 g, 63%, White liquid.

IR (neat) **:** 3022, 2679, 1959, 1625, 1591, 1463, 1434, 1412, 1315, 1337, 1218 1239, 1191, 951 cm^{-1}**.**

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.29-7.27 (m, 2H), 7.22-7.21 (m, 3H), 5.79-5.77 (m, 1H), 5.65-5.63 (m, 1H), 2.75 (d, *J*=8.0 Hz, 2H), 2.34-2.29 (m, 2H), 2.17-2.11 (m, 2H), 1.78 (d, *J*=8.0 Hz, 2H), 1.62-1.59 (m, 6H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 20.1.5, 142.0, 133.3, 128.4, 125.7, 125.0, 101.9, 97.6, 36.0, 34.0, 25.8, 25.7, 22.6, 22.5, 19.4.

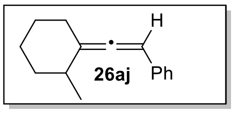
LCMS **:** m/z 238 (M+1).

Analysis **:** for $C_{18}H_{22}$

calcd: C 90.70, H 9.30.

found: C 89.99, H 9.18.

(2-(2-Methylcyclohexylidene)vinyl)benzene (26aj):



26aj

Yield : 0.140 g, 71%, Brown oil.

IR (neat) **:** 2969, 2910, 1963, 1732, 1649, 1359, 1244, 1167, 1120, 1030, 860, 789 cm^{-1}.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.31-7.29 (m, 4H), 7.20-7.17 (m, 1H), 6.05-6.03 (m, 1H), 2.41-2.33 (m, 2H), 2.15-2.09 (m, 2H), 1.90-1.84 (m, 2H), 1.83-1.75 (m, 2H), 1.72-1.67 (m, 1H), 1.55-1.47 (m, 2H), 1.16-1.08 (m, 1H), 1.01 (d, *J*=6.0 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 200.0, 136.2, 128.4, 128.1, 126.5, 126.4, 126.2, 105.6, 92.3, 39.1, 34.3, 32.9, 30.7, 26.1, 22.0.

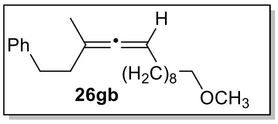
LCMS : m/z 198 (M-1).

Analysis : for $C_{15}H_{18}$

calcd: C 90.85, H 9.15.

found: C 90.56, H 9.08.

(14-Methoxy-3-methyltetradeca-3,4-dien-1-yl)benzene (26gb):



26gb

Yield : 0.182 g, 58%, White liquid.

IR (neat) : 3012, 2679, 1961, 1625, 1591, 1463, 1444, 1412, 1315, 1337, 1219, 1239, 1191, 957 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.31-7.19 (m, 5H), 5.06-5.03 (m, 1H), 3.40-3.36 (m, 2H), 3.35 (s, 3H), 2.74 (t, *J*=8.0 Hz, 2H), 2.28-2.25 (m, 3H), 1.96-1.92 (m, 3H), 1.73 (t, *J*=8.0 Hz, 2H), 1.34-1.33 (m, 10H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 201.2, 128.3, 128.2, 125.6, 98.7, 90.9, 72.9, 58.5, 35.8, 34.0, 29.6, 29.5, 29.4, 29.2, 29.0, 26.1, 19.5.

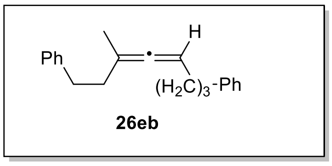
LCMS : m/z 314 (M-1).

Analysis : for $C_{22}H_{34}O$

calcd: C 84.02, H 10.90.

found: C 83.98, H 10.86.

(3-Methylocta-3,4-diene-1,8-diyl)dibenzene (26eb):



26eb

Yield : 0.204 g, 74%, White liquid.

IR (neat) : 2965, 2910, 1963, 1732, 1649, 1389, 1244, 1167, 1120, 1030, 860, 991 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.32-7.28 (m, 4H), 7.21-7.20 (m, 6H), 5.13-5.09 (m, 1H), 2.71-2.66 (m, 4H), 2.30-2.21 (m, 4H), 1.69 (d, *J*= 8.0 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 201.4, 142.3, 142.0, 128.5. 128.4, 128.2, 125.7, 99.4, 90.2, 35.6, 35.4, 33.9, 30.9.

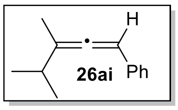
LCMS : m/z 276 (M-1).

Analysis : for $C_{21}H_{24}$

calcd: C 91.25, H 8.75.

found: C 91.08, H 8.12.

(3,4-Dimethylpenta-1,2-dien-1-yl)benzene (26ai):



26ai

Yield : 0.113 g, 66%, White liquid.

IR (neat) : 3012, 2679, 1961, 1625, 1591, 1463, 1444, 1412, 1315, 1337, 1215, 1239, 1191, 957 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.35-7.31 (m, 5H), 7.27-7.24 (m, 5H), 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, 88.1, 65.3, 35.0, 34.4.

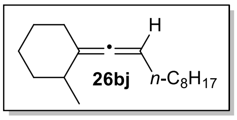
LCMS : m/z 172 (M-1).

Analysis : for $C_{13}H_{16}$

calcd: C 90.64, H 9.36.

found: C 90.38, H 9.15.

1-(-Dec-1-en-1-ylidene)-2-methylcyclohexane (26bj):



26bj

Yield : 0.177 g, 76%, Brown oil.

IR (neat) : 2976, 2910, 1953, 1732, 1649, 1359, 1244, 1167, 1120, 1030, 860, 946 cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.35-7.31 (m, 5H), 7.27-7.24 (m, 5H), 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, 88.1, 65.3, 35.0, 34.4.

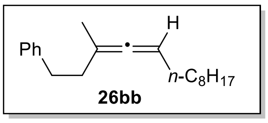
LCMS : m/z 234 (M-1).

Analysis : for C$_{17}$H$_{30}$

calcd: C 87.10, H 12.90.

found: C 86.98, H 12.76.

(3-Methyltrideca-3,4-dien-1-yl)benzene (26bb):



26bb

Yield : 0.199 g, 74%, Orange oil.

IR (neat) : 2946, 2905, 1938, 1649, 1477, 1425, 1359, 1244, 1167, 1120, 1030, 860 cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.32-7.28 (m, 2H), 7.23-7.20 (m, 3H), 5.08-5.03 (m, 1H), 2.75 (d, *J*=8.0 Hz, 2H), 2.29-2.24 (m, 2H), 1.96-1.91 (m, 2H), 1.74 (d, *J*=8.0 Hz, 2H), 1.33-1.30 (m, 12H), 0.91 (t, *J*=8.0 Hz, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 201.2, 142.4, 128.3, 128.2, 125.6, 98.7, 90.9, 35.8, 34.1, 31.9, 29.5, 29.3, 29.1, 22.7, 19.5, 14.1.

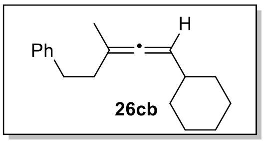
LCMS : m/z 270 (M-1).

Analysis **:** for $C_{20}H_{30}$

calcd: C 88.82, H 11.18.

found: C 88.61, H 11.04.

(5-Cyclohexyl-3-methylpenta-3,4-dien-1-yl)benzene (26cb):



Yield : 0.163 g, 68%, White liquid.

IR (neat) **:** 3029, 2679, 1967, 1625, 1591, 1453, 1444, 1412, 1315, 1337, 1212, 1239, 1161, 757 cm^{-1}**.**

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.31-7.28 (m, 3H), 7.23-7.21 (m, 2H), 5.06-5.03 (m, 1H), 2.75 (d, *J*=8.0 Hz, 2H), 2.28-2.24 (m, 2H), 1.74 (d, *J*=8.0 Hz, 2H), 1.32-1.03 (m, 11H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 200.0, 142.7, 128.4, 128.2, 125.6, 99.6, 97.1, 37.4, 35.8, 34.1, 33.2, 26.2, 26.1, 19.6.

LCMS **:** m/z 240 (M-1).

Analysis **:** for $C_{18}H_{24}$.

calcd: C 89.94, H 10.06.

found: C 89.78, H 9.98.

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Chapter 4

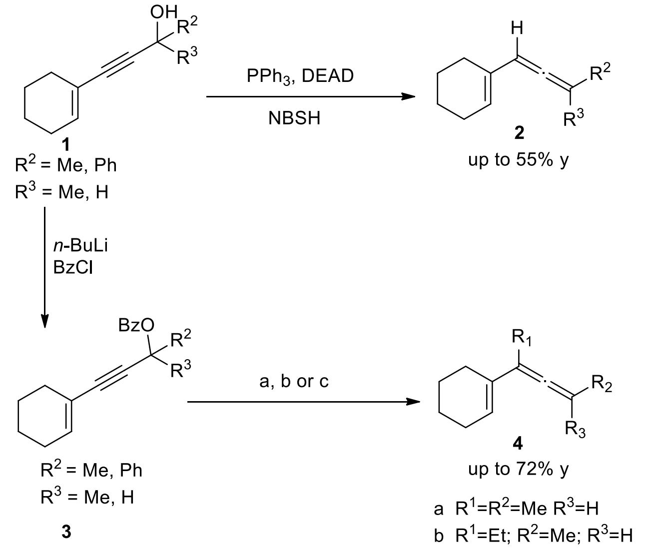
Copper(I)-Catalyzed Enantioselective Synthesis of Chiral Cyclohexenylallenes and Their Application in Yb(III) Catalyzed [4+2] Cycloaddition Reactions

4.1 Introduction

4.1.1 Synthesis of vinylallenes

Previously, the cyclohexenylallenes **2** and **4** were prepared in racemic forms using the corresponding propargyl alcohols **1** (Scheme 1).[1]

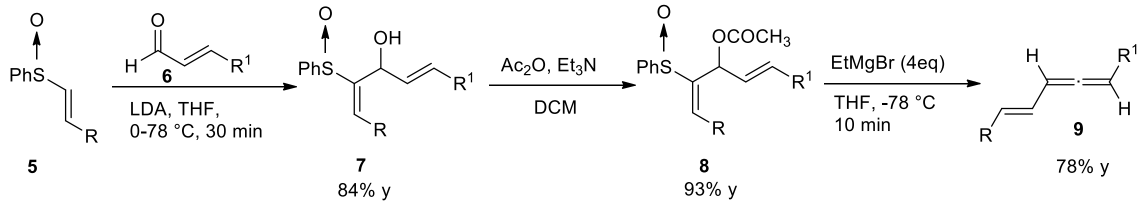
Scheme 1



(a) MeMgBr, CuI, LiBr, 0 °C; (b) EtMgBr, CuBr.Me_2S, -60 °C; (c) *t*-BuLi, CuCN, -78 °C

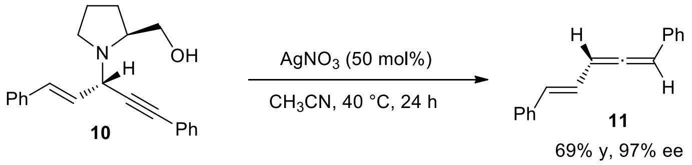
The lithium α-sulfinyl carbanion **5** smoothly reacted with *trans*-aldehyde **6** to give the alcohol product **7** which after acetylation and reaction with EtMgBr gave the corresponding vinylallene **9** (Scheme 2).[2]

Scheme 2



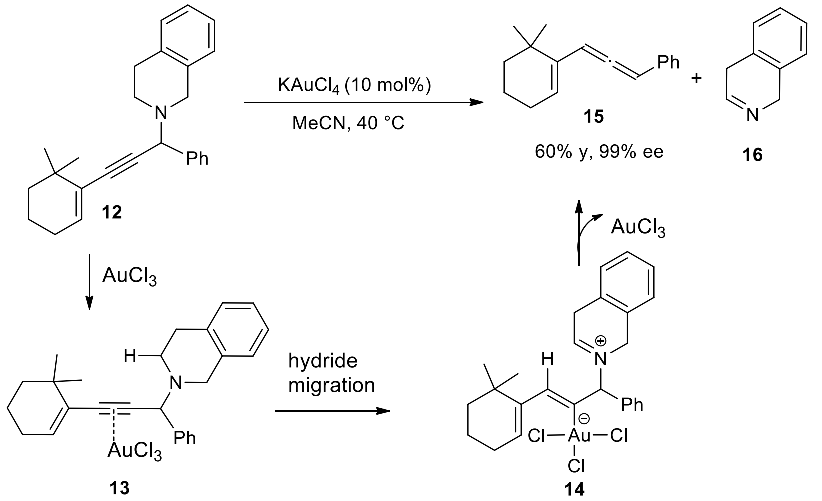
Chiral vinylallene **11** was synthesized from chiral propargylamine **10** under $AgNO_3$ catalysis in 69% yield and 97% ee (Scheme 3).[3]

Scheme 3



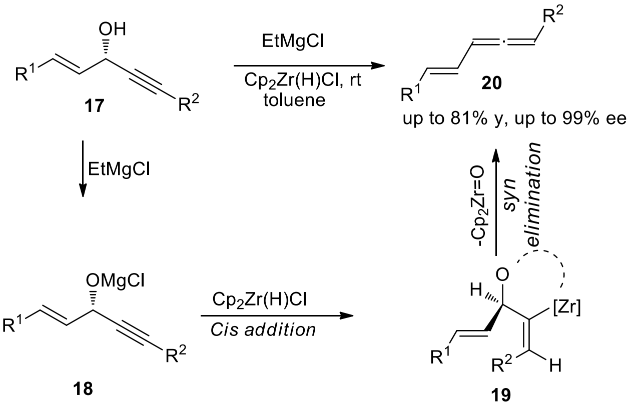
Recently, cyclohexene-functionalized propargylamine **12** was converted to the vinylallene derivative **15** upon reaction with $KAuCl_4$ (Scheme 4).[4]

Scheme 4



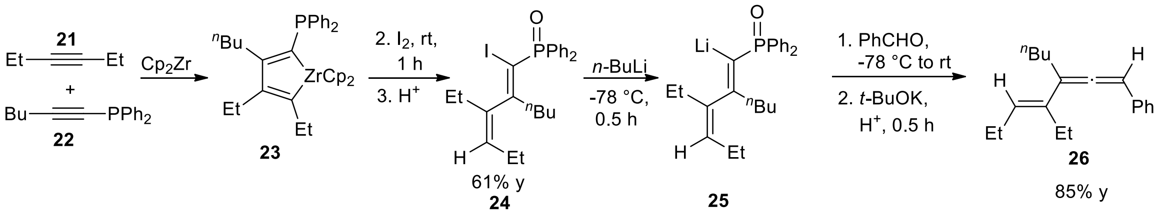
Deprotonation of the propargylic alcohols **17** with EtMgCl followed by hydrozirconation of alkynes with the Schwartz reagent ($Cp_2Zr(H)Cl$) gave the vinylallenes **20** (Scheme 5).[5]

Scheme 5



Vinylallenes **26** were also prepared from two different alkynes and an aldehyde by the Wittig-Horner reaction. For example, 1-lithio-1,3-dienyl phosphine oxides **25** generated *in situ* by lithiation of 1-iodo-1,3-dienyl phosphine oxides **24** were converted to the allene **26** (Scheme 6).[6]

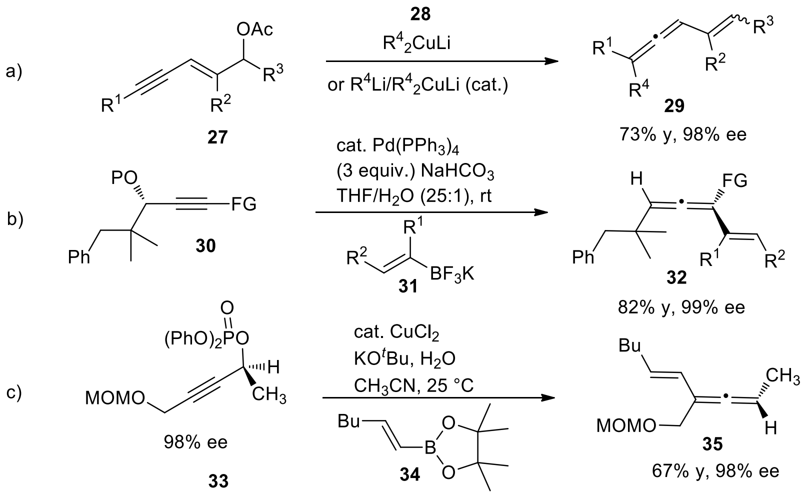
Scheme 6



4.1.2 Other reports on the synthesis of vinylallenes

There are several other methods reported for the synthesis of racemic and chiral vinylallenes (Chart 1). For example, copper promoted enantioselective synthesis of vinylallenes **29** by 1,5-substitution of enyne acetates was reported.[7] Recently, Pd(0) catalyzed cross-coupling reaction of propargylic carbonates and phosphates with alkenyl trifluoroborates to enantioriched ene-allenes **32** were reported.[8] More recently, a Cu catalyzed γ-selective coupling between propargylic phosohates and aryl- or alkenylboronates afforded aryl- or alkenyl-conjugated chiral allenes **35** were reported (Chart 1).[9]

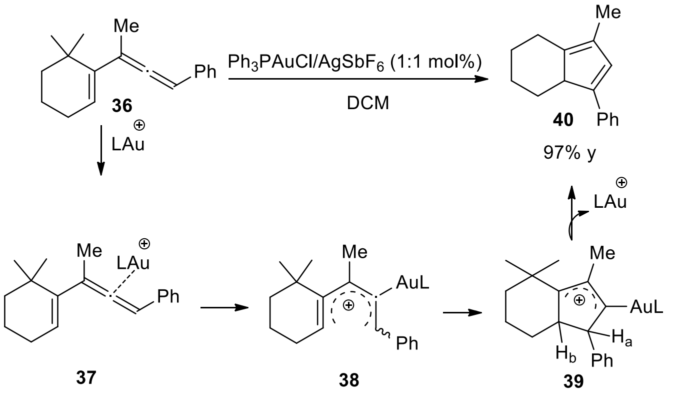
Chart 1



4.1.3 Vinylallenes used in cycloaddition reactions

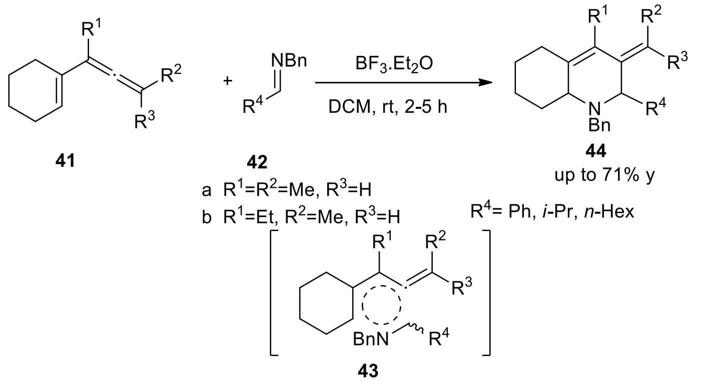
A gold (I) catalysed cycloisomerization of vinylallene **36** for the synthesis of cyclopentadiene **40** was also reported (Scheme 7).[10]

Scheme 7



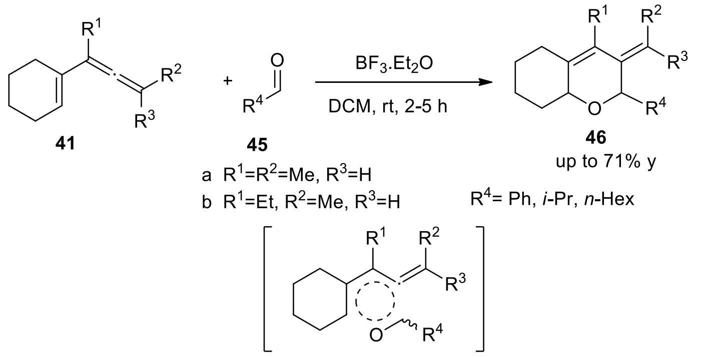
An interesting method for the synthesis of octahydroquinoline derivatives **44** *via* $BF_3.Et_2O$ catalyzed cyclization of vinylallenes **41** was reported (Scheme 8).[11]

Scheme 8



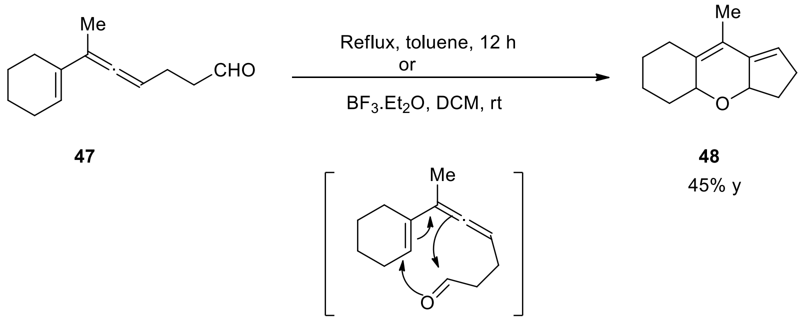
Another approach involves an acid catalyzed reaction of vinylallene derivatives **41** with aldehydes **45** to afford the cyclized products **46** (Scheme 9).[12]

Scheme 9



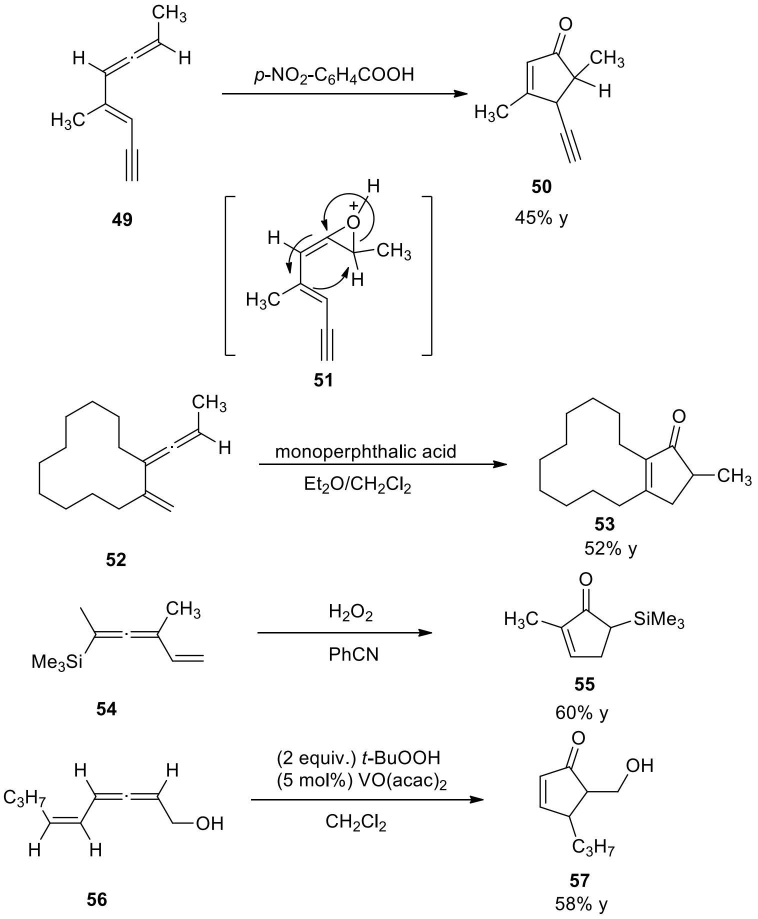
Diels -Alder reaction is another approach for the synthesis of cyclized product **48** with 45% yield using the vinylallene **47** (Scheme 10).[13]

Scheme 10



There were several reports on the utility of vinylallenes as precursors for the formation of oxypentadienyl cations, which undergo Nazarov-type cyclizations to give substituted cyclopentenones (Chart 2).[14,15,16,17]

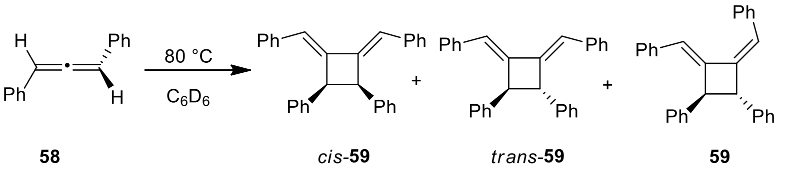
Chart 2



4.1.4 Cycloaddition reactions of chiral allenes

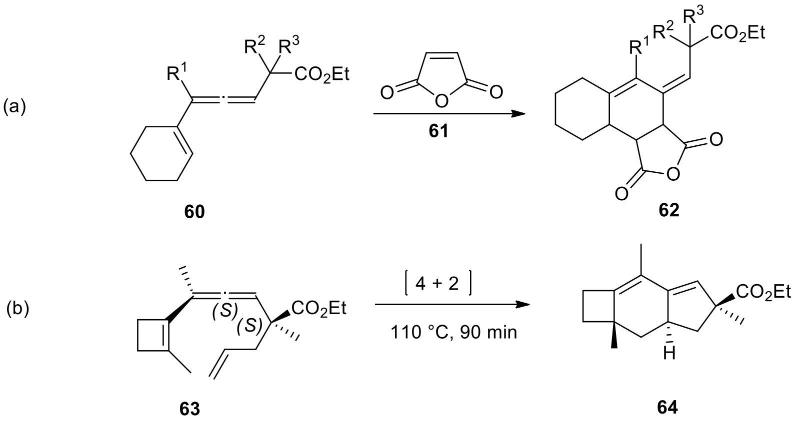
It was observed in this laboratory that the chiral allenes containing aryl substituents readily undergo cyclodimerization under ambient conditions. Previously, it was reported that the 1,3-diphenyl allene **58** gave dimerization at 80 °C in benzene-d_6 (Scheme 11).[18]

Scheme 11



Vinylallenes were also used as dienes in both inter and intramolecular Diels-Alder reactions (Scheme 12).[19]

Scheme 12



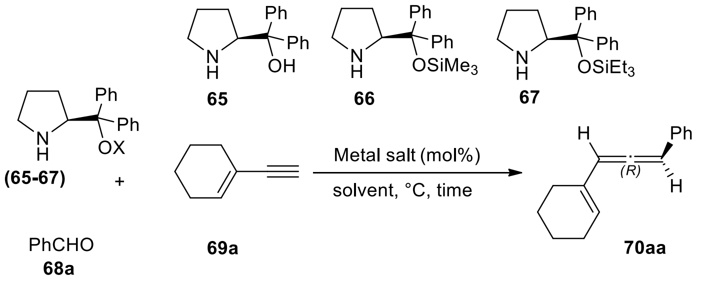
We have undertaken studies to prepare chiral cyclohexenylallenes for use in [4 + 2] cycloaddition reactions. The results are described in the next section.

4.2 Results and Discussion

4.2.1 Synthesis of cyclohexenylallenes using chiral amines, aldehydes and 1-alkynes

Initially, we have carried out experiments using the readily accessible chiral amine (*S*)-DPP **65** and its silyl derivatives **66** and **67** along with 1-ethynylcyclohex-1-ene **69a**, benzaldehyde **68a** and (*S*)-DPP **65** for the preparation of cyclohexenylallene **70aa** (Scheme 13). The results are summarized in Table 1.

Scheme 13

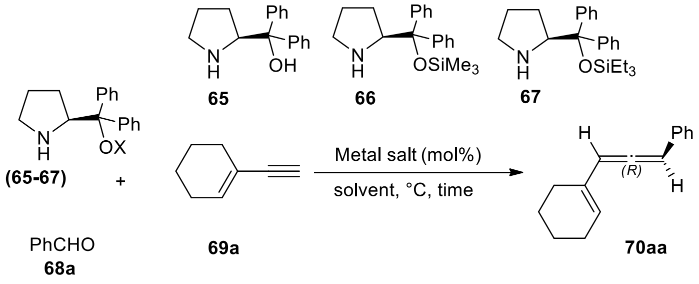


Whereas, the product cyclohexenylallene (*R*)-**70aa** was obtained in low yield (10-18%) using CuBr, CuI (entries 2 and 3, Table 1) with 99% enantioselectivity, there was no reaction using CuCl (entry 1, Table 1). When the experiment was performed using the amine **66** and 30 mol% of CuCl, CuBr and CuI at 110 °C, within 2 h, the allene (*R*)-**70aa** was obtained in 47-79% yield (entries 11, 8 and 9, Table 1).

Further, increase in the catalyst loading from 30 mol% to 50 mol%, led to slight improvement in the yield of the product (*R*)-**70aa** (entries 6 and 9, Table 1). Lowering the temperature to 100 °C, resulted in 61% yield of the product (*R*)-**70aa** (entry 12, Table 1). The reaction using $CuBr_2$ (entry 7, Table 1) gave the cyclohexenylallene (*R*)-**70aa** only in 59% yield with 95% ee. Also, the reaction of the amine **67** with CuI (0.3 mmol) at 110 °C gave the chiral allene (*R*)-**70aa** in 68% yield and 96% ee (entry 10, Table 1).

Under the optimum conditions (entry 9, Table 1), this transformation was carried out using various aldehydes, 1-enynes and chiral amine **66** and the results are summarized in Table 2.

Table 1: Reaction of chiral amines (**65-67**), 1-ethynylcyclohex-1-ene **69a** and benzaldehyde **68a** with different metal salts to afford chiral allenes.[a,b,c]



Entry	Copper Salt	X	Temp (°C)	Mol (%)	70aa (%)[b]	ee (%)[c]
1	CuCl	H	120	50	-	-
2	CuBr	H	120	50	10	99
3	CuI	H	120	50	18	99
4	CuCl	TMS	110	50	51	99
5	CuBr	TMS	110	50	64	99
6	CuI	TMS	110	50	81	99
7	$CuBr_2$	TMS	120	30	59	95
8	CuBr	TMS	110	30	62	97
9	CuI	TMS	110	30	79	99
10	CuI	TME	120	30	68	96
11	CuCl	TMS	110	30	47	99
12	CuI	TMS	100	30	61	99

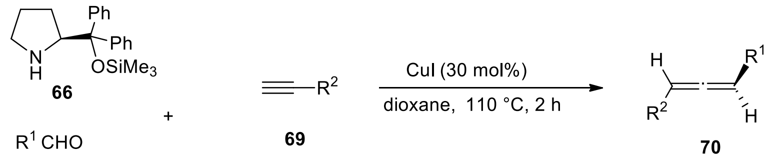
[a]The reactions were carried out by using amines **65-67** **(**1.0 mmol) and 1-enynes **69** (1.1 mmol) and aldehydes **68** (1.1 mmol) in dioxane. [b]Yield of allenes. [c]The ee was determined by chiral HPLC as the OD-H, OJ-H,OB-H and AS-H columns.

The reaction using benzaldehyde **68b**, **68c**, and **68d,** with the *p*-Me-, *p*-OMe-, and *m*-OMe groups in the phenyl ring and 1-ethynylcyclohex-1-ene **69a** gave the (*R*)-vinylallenes **70ba-70da** in 62-66% yield with 97-99% ee (Table 2). Also, the aldehydes 3-phenylpropanal **68e**, 3-(benzyloxy)propanal **68f** and 1-ethynylcyclohex-1-ene **69a** gave the (*R*)-allene **70ea** in 63% yield with 98% ee and (*R*)-allene **70fa** in 61% yield (Table 2).

Further, the aldehydes **68g**, **68h**, and **68i** containing electron withdrawing *p*-Cl, *p*-Br, *p*-NO_2 groups and 1-ethynylcyclohex-1-ene **69a** resulted in the formation of the (*R*)-cyclohexenylallenes **70ga-70ia** in 64% to 70% yield with up to 99% ee (Table 2). We have also examined the reaction of but-1-en-3-yn-1-ylbenzene **69b**, 9-ethynyl-3,3-dimethyl-2,4-dioxaspiro[5.5]undec-8-ene **69c** and benzaldehyde **68a** to obtain the corresponding (*R*)-cyclohexenylallene **70ab** and **70ac** in 69% to 72% yield in 99% ee (Table 2). In addition, cyclohexanecarbaldehyde **68j** and but-1-en-3-yn-1-ylbenzene **69b** gave the corresponding (*R*)-cyclohexenylallene **70jb** in 65% yield with 99% ee (Table 2).

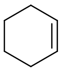
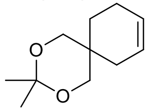
Moreover, the reaction using 3-phenylpropanal **68k** with (*E*)-but-1-en-3-yn-1-ylbenzene **69b** and (*E*)-pent-3-en-1-yne proceeded with 67% yields with 99% ee (Table 2). Furthermore, the reaction using isophthalaldehyde **68l** gave the product **70la** in 68% yield with 99% ee (Table 2).

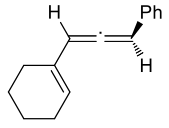
Table 2: Synthesis of vinylallenes **70** using aldehydes **68**, 1-enynes **69** and chiral amine **66**.[a,b,c,d]



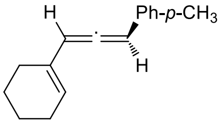
68a = R^1 = Ph
68b = R^1= Ph-*p*-CH_3
68c = R^1= Ph-*p*-OCH_3
68d = R^1= Ph-*m*-OCH_3
68e = R^1= Ph-CH_2-CH_2
68f = R^1= Ph-CH_2O-CH_2-CH_2

68g = R^1= Ph-*p*-Cl
68h = R^1= Ph-*p*-Br
68i = R^1= Ph-*p*-NO_2
68j = R^1= $C_7H_{12}O$
68k = R^1= $C_9H_{10}O$
68l = R^1= Ph-*m*-CHO

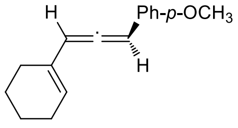
69a = R^2=

69b = R^2= Ph-CH=CH
69c = R^2=




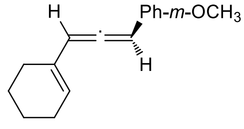
70aa
79% yield, 99% ee



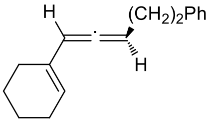
70ba
66% yield, 99% ee



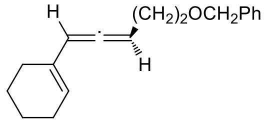
70ca
63% yield, 97% ee



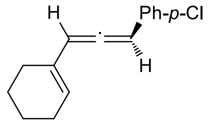
70da
62% yield, 99% ee



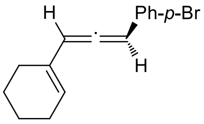
70ea
63% yield, 98% ee



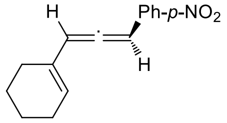
70fa
61% yield[d]



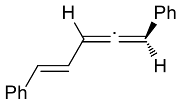
70ga
67% yield, 99% ee



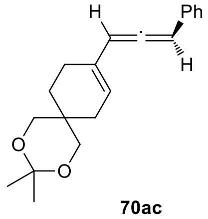
70ha
70% yield, 99% ee



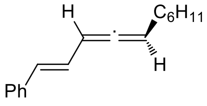
70ia
64% yield, 99% ee



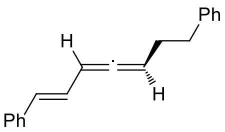
70ab
69% yield, 99% ee



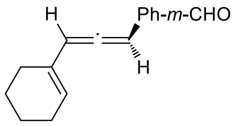
70ac
72% yield, 99% ee



70jb
65% yield, 99% ee



70kb
67% yield, 99% ee



70la
68% yield, 99% ee

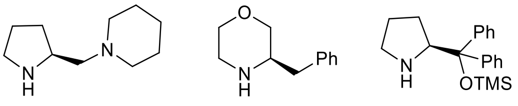
---

[a]The reactions were carried out by using amine **66** (1.0 mmol), aldehydes **68** (1.1 mmol), and 1-enynes **69** (1.1 mmol) in dioxane (3 mL) at 110 °C. [b]Yield of vinylallenes. [c] The ee was determined by chiral HPLC as the OD-H, OJ-H, OB-H and AS-H columns. [d]Could not be resolved by HPLC.

All the optically active allenes obtained by using chiral amine **66** are levorotatory from which the absolute configurations of the major enantiomer of the chiral allenes are assigned as *R* according to Lowe-Brewster rule[20] and comparison with reported data.[21]

4.2.2 Synthesis of cyclohexenylallenes using cyclic secondary amines

We have also carried out experiments using other readily accessible optically active chiral secondary amines **71**, **72** and **66** (Figure 1).

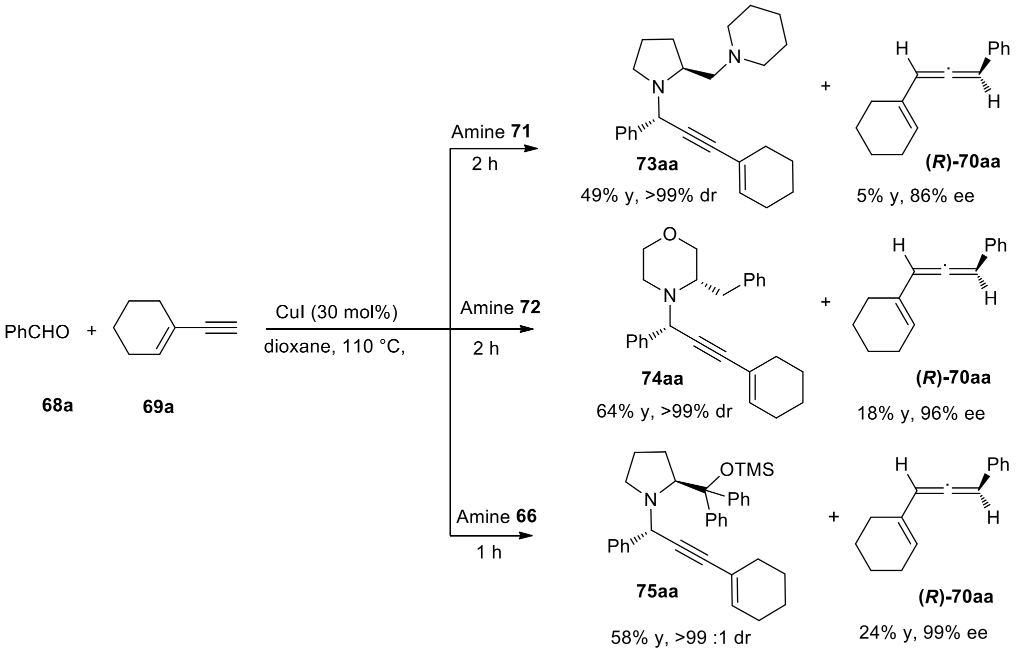


71 **72** **66**

Figure 1*:* Chiral amines (**71**, **72** & **66**) used in CuI catalyzed synthesis of vinylallenes

We have observed that the reaction using chiral amine **71** gave the trisubstituted propargylamine **73aa** in 49% yield and the corresponding allene (*R*)-**70aa** was formed in 5% yield and 86% ee. Whereas, the reaction using the chiral secondary amine **72** afforded the propargylamine **74aa** in 64% yield and the product (*R*)-**70aa** was formed in 18% yield and 96% ee (Scheme 14).

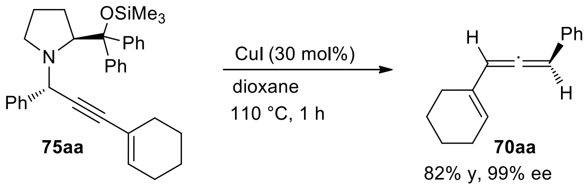
Scheme 14



We have also carried out experiments to isolate the propargylamine intermediate that is expected to form in this transformation by stopping the reaction after 1h (Scheme 2). In this case, the propargylamine **75aa** was obtained in 58% yield along with the corresponding allene (*R*)**-70aa** in 24% yield.

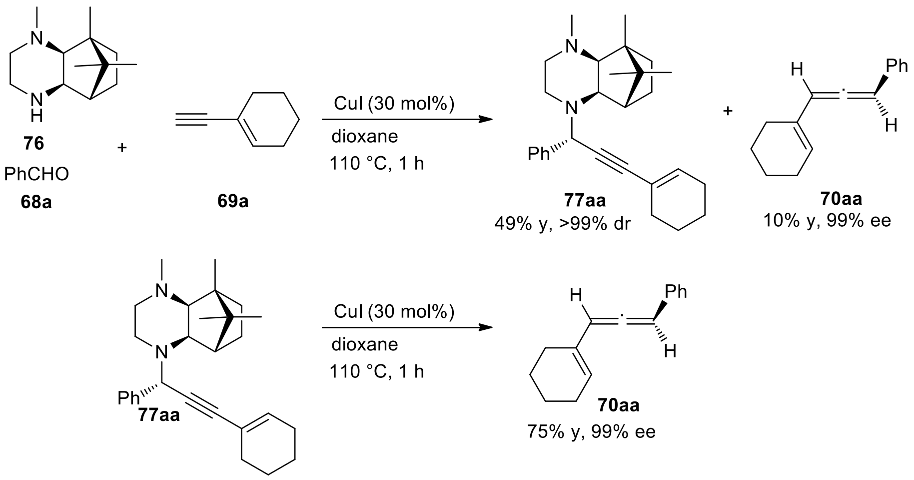
Also, the propargylamine intermediate **75aa** was readily converted to the chiral cyclohexenylallene **70aa** in 82% yield and 99% ee upon reaction with CuI (Scheme 15).

Scheme 15



It was observed in this laboratory that the chiral camphanyl secondary amine **76** also give similar results (Scheme 16).

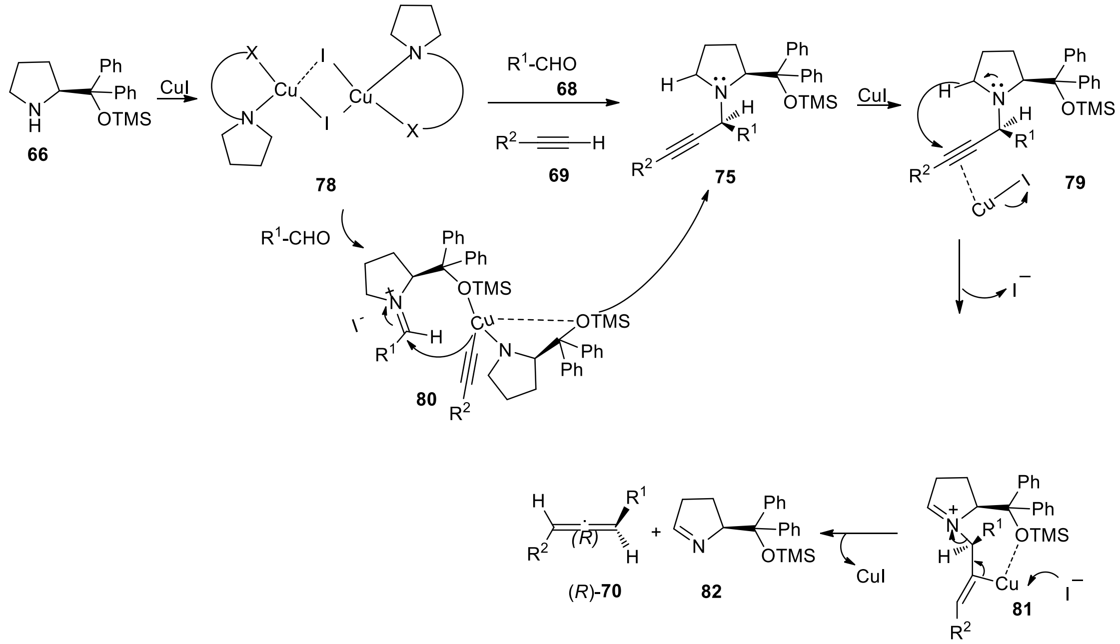
Scheme 16



4.2.3 Plausible mechanism for the formation of cyclohexenylallene

The mechanism outlined in Scheme 17 can be considered for the formation of cyclohexenylallenes.[22] Initially, the chiral amine **66** would react with CuI to generate the dimeric chiral copper complex **78.**[23] Subsequent addition of aldehyde and 1-alkyne would give the intermediate complex **80**, which could give the propargylamine **75.**[24] Further reaction with CuI would afford the intermediate **79**, that after a 1,5- hydride shift could give the alkenyl copper species **81**. Antiperiplanar elimination of the CuI and the imine would then give the chiral allene (*R*)-**70** along with the imine **82** as a byproduct. The imine intermediate could be readily converted to the starting chiral amine **66** by simple addition of sodium borohydride reduction in MeOH as a solvent at -10 °C to the reaction mixture and stirring at room temperature for 3 h before workup.

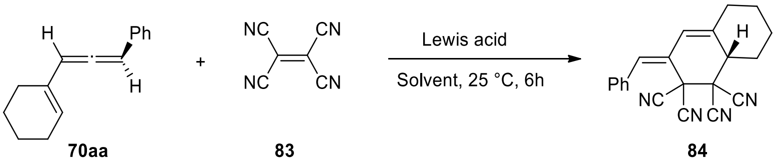
Scheme 17



4.2.4 Diels-Alder reaction of cyclohexenylallene 70aa:

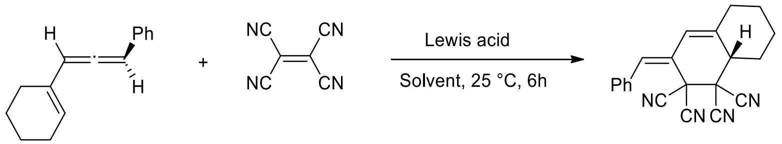
We have then carried out experiments an Lewis acid catalyzed [4 + 2] cycloaddition reaction of the chiral cyclohexeneylallene **70aa** with electron deficient dienophile tetracyanoethylene **83** in different solvents at room temperature (Scheme 18).

Scheme 18



The results are summarized in Table 3.

Table 3: Intermolecural Diels-Alder reaction of cyclohexenylallene 70aa and TCE 83.[a,b]



70aa **83** **84**

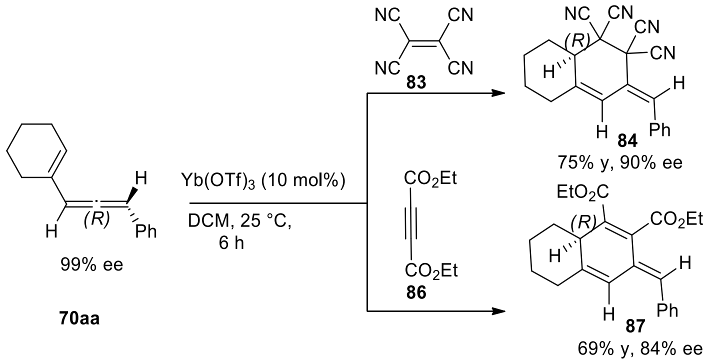
entry	Solvent	Lewis acid	Mol (%)	Yield (84aa) (%)
1	Toluene	BF_3OEt_2	100	-
2	THF	TfOH	100	-
3	Diethyl ether	$Cu(OTf)_2$	30	15
4	DCM	AgOTf	10	45
5	DCM	$Zn(OTf)_2$	10	10
6	DCM	$Yb(OTf)_3$	10	75
7	DCM	$In(OTf)_3$	10	52

[a]The reactions were carried out by using allene **70aa (**1.0 mmol) and dienophile **83** (1.2 mmol) at 25 °C for 6 h. [b]The yield of cyclic product **84** .

When the reaction was performed using 30 mol% $Cu(OTf)_2$ [4 + 2] cycloaddition product **84** was obtained in 15% yield (entry 3, Table 3). We have also examined other Lewis acids such as AgOTf, $Zn(OTf)_2$, $Yb(OTf)_3$ and $In(OTf)_3$ (entries 4, 5, 6 and 7, Table 3). Among these Lewis acids, $Yb(OTf)_3$ showed the best catalytic activity, and the expected product **84** was obtained in 75% yield (entry 6, Table 3).

We have then carried out an experiment using the chiral allene **70aa,** TCE **83** and $Yb(OTf)_3$ in DCM solvent to obtain the product **84** in 75% yield with 90% ee (Scheme 19). We have observed that reaction of cyclohexenylallene (*R*)-**70aa** wth diethyl acetylenedicarboxalate **86** proceeded smoothly to give the product **87** in 69% yield and 84% ee (Scheme 19).

Scheme 19. The Reaction of cyclohexenylallene **70aa** with dienophiles



A mechanism outlined in Scheme 20 may be considered to rationalize the ytterbium catalyzed [4+2] cycloaddition of cyclohexenylallene **70aa** with tetracyanoethylene to give the corresponding cycloadduct **84**.[25] Initially, the Yb(OTf)3 would interact with tetracyanoethylene **83** which could then react with the allene (*R*)-**70aa** through the transition state **85** or **85A.**

The steric interactions between the dienophile and the phenyl substituent in allene would make the transition state **85A** not favourable and hence the reaction would go through the lower energy transition state **85** to give the cycloadduct **84**, with (*R*) configuration at the newly formed stereogenic centre. The configuration (*R*) at the newly formed stereogenic centre was also confirmed by X-ray single crystal structure analysis of the cycloadduct **84** (Figure 2).

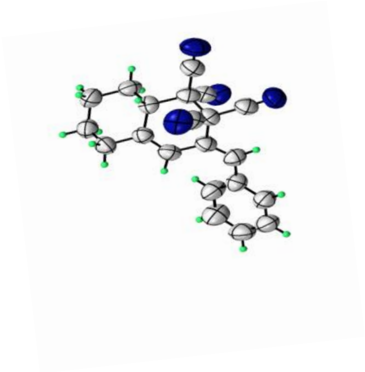
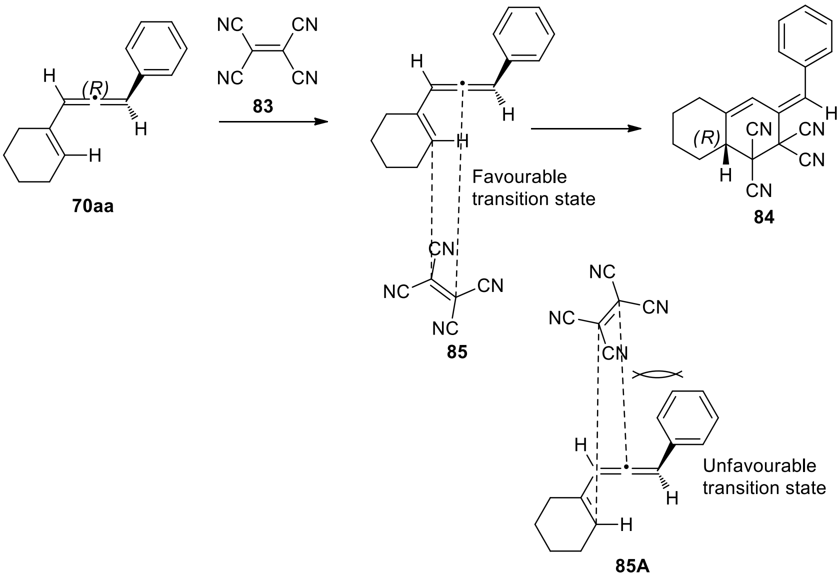


Figure 2. ORTEP representation of the compound **84** and thermal ellipsoids are drawn with 30% probability.

Table 5: Crystal data and structure refinement for **84.**

Identification code	84
Empirical formula	$C_{21}H_{16}N_4$
Formula weight	27.03
Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1$
a/Å	8.0933(4)
b/Å	12.5626(6)
c/Å	18.0001(7)
α/°	90.00
β/°	98.218(4)
γ/°	90.00
Volume/Å^3	1811.34(14)
Z	51
ρ_{calc}mg/mm^3	1.264
m/mm^{-1}	0.742
F(000)	714.0
Crystal size/mm^3	? × ? × ?
2Θ range for data collection	8.62 to 143.74°
Index ranges	$-9 \leq h \leq 8$, $-15 \leq k \leq 13$, $-21 \leq l \leq 21$
Reflections collected	7127
Independent reflections	5198[R(int) = 0.0327]
Data/restraints/parameters	5198/1/451
Goodness-of-fit on F^2	0.914
Final R indexes [I>=2σ (I)]	R_1 = 0.0684, wR_2 = 0.1541
Final R indexes [all data]	R_1 = 0.1306, wR_2 = 0.2162
Largest diff. peak/hole / e Å^{-3}	0.13/-0.24
Flack parameter	0.9(12)

Scheme 20: Plausible mechanistic pathway



The mechanism of cycloaddition reaction of cyclohexenylallene **70aa** and diethyl acetylenedicaboxalate **86** is expected to be similar and hence, the configuration (*R*) can be also assigned for the newly formed stereogenic centre in the product **87**.

We have also carried out studies on hydroboration of olefins using the borane complex of the chiral morpholine derivative **72.** These results are described in the next chapter.

4.3 Conclusions

We have developed a convenient method for the synthesis of chiral cyclohexenyl allenes by CuI catalyzed reactions of 1-alkynes, aldehydes and chiral secondary amines. The allenes were obtained in 61% to 79% yields and 97% to 99% ee. In addition, we have devised a method for the ytterbium catalyzed preparation of Diels-Alder adducts using enantiomerically enriched cyclohexenylallene with tetracyanoethylene and acetylene dicarboxylic ester. The methods described here have considerable potential for further synthetic applications.

4.4. Experimental Section

4.4.1 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 ±0.01^{o}) and AUTOPOL-IV (readability ±0.001^{o}) automatic polarimeters. The condition of the polarimeter was checked by measuring the optical rotation of a standard solution of (*S*)-(+)-α,α–diphenylprolinol {$[\alpha]_D^{25} = +67.2$ (*c* 0.52, $CHCl_3$)} supplied by Gerchem Laboratory (Pvt) Ltd., India.

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.

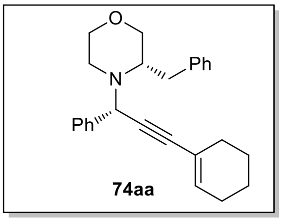
Dichloromethane and chloroform were distilled over CaH_2 and dried over molecular sieves. Methanol and ethanol supplied by Ranbaxy were distilled over CaO before use. Toluene and THF supplied by E-Merck, India were kept over sodium-benzophenone ketyl and freshly distilled before use. Ethylene diamine,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

4.4.2 General procedure for the synthesis of Propargylamines from 1-enyne, aldehyde and amines with CuI/dioxane condition.

To a stirred suspension of amines (1 mmol), CuI (0.057 g, 0.3 mmol), aldehydes **68** (1.1 mmol) and 1-alkynes **69** (1.1 mmol) 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 corresponding products.

(3)-3-Benzyl-4-(3-(cyclohex-1-en-1-yl)-1-phenylprop-2-yn-1-yl)morpholine (74aa):



74aa

Yield : 0.237 g, 64%, Orange oil.

$[\alpha]_D^{25}$: -97.3 (c= 0.55, $CHCl_3$).

IR (neat) : 3066, 3026, 2925, 1602, 1492, 1447, 1120, 906.2, 841.4 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.68-7.66 (d, *J*= 8.0 Hz, 2H), 7.43-7.39 (t, *J*= 8.0 Hz, 2H), 7.37-7.26 (m, 6H), 6.29-6.28 (m, 1H), 5.39 (s, 1H), 3.73-3.64 (m, 2H), 3.56-3.50 (m, 1H), 3.43-3.31 (m, 2H), 3.21-3.16 (m, 1H), 2.63-2.53 (m, 2H), 2.32-2.20 (m, 5H), 1.79-1.68 (m, 4H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 138.6, 134.8, 129.3, 128.6, 128.4, 128.2, 127.5, 126.2, 120.5, 90.8, 81.1, 70.8, 67.3, 59.2, 56.0, 45.8, 34.8, 29.7, 25.7, 22.4, 21.6.

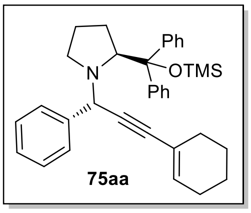
LCMS : *m/z* 370 (M-1).

Analysis : for $C_{26}H_{29}NO$

calcd: C 84.06, N 3.77, H 7.87

found: C 84.11, N 3.72, H 7.91.

(2)-1-(3-(Cyclohex-1-en-1-yl)-1-phenylprop-2-yn-1-yl)-2-(diphenyl((trimethylsilyl)oxy)methyl)pyrrolidine (75aa):



75aa

Yield : 0.301 g, 58%, Brown oil.

$[\alpha]_D^{25}$: -113.3 (c=0.55, $CHCl_3$).

IR (neat) : 3086, 3058, 3027, 1492, 1447, 1092, 879 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.62-7.60 (d, *J*= 8.0 Hz 4H), 7.40-7.27 (m, 11H), 6.21 (m, 1H), 5.27 (m, 1H), 4.31-4.29 (m, 1H), 2.56-2.54 (m, 1H), 2.28-2.12 (m, 6H), 1.97-1.66 (m, 5H), 1.32-1.30 (m, 2H), 0.149 (s, 9H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 144.3, 143.8, 140.5, 133.9, 129.8, 129.7, 128.1, 127.7, 127.0, 126.7, 120.8, 88.7, 84.8, 84.6, 69.2. 59.4, 48.8, 29.8, 29.5, 25.6, 23.6, 22.4, 21.6, 1.99.

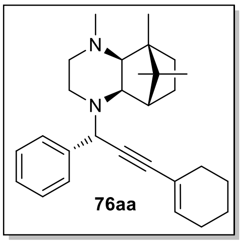
LCMS : m/z 519 (M+1).

Analysis : for $C_{35}H_{41}NOSi$

calcd: C 80.87, N 2.69, H 7.95.

found: C 80.71, N 2.62, H 7.91.

(4,5,8,8)-1-(3-(Cyclohex-1-en-1-yl)-1-phenylprop-2-yn-1-yl)-4,5,9,9-tetramethyldecahydro-5,8-methanoquinoxaline(76aa):



76aa

Yield : 0.196 g, 49%, Brown oil.

$[\alpha]_D^{25}$: -89.3 (c=0.55, $CHCl_3$).

IR (neat) : 3026, 2930, 1675, 1448, 1260, 1061, 908 cm^{-1}.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.64-7.62 (d, *J*= 8.0 Hz, 2H), 7.34-7.25 (m, 3H), 6.21-6.20 (m, 1H), 5.13 (m, 1H), 3.05-3.03 (d, *J*= 8.0 Hz, 1H), 2.74-2.69 (m, 1H), 2.54-2.47 (m, 1H), 2.40-2.35 (m, 1H), 2.29 (s, 3H), 2.26-2.11 (m, 5H), 1.95-1.94 (m, 1H), 1.74-1.63 (m, 7H), 1.50 (s, 3H), 1.28-1.18 (m, 2H), 1.05 (s, 3H), 0.87 (s, 3H).

^{13}C NMR **:** 139.3, 134.3, 128.2, 127.9, 127.0, 120.6, 89.7, 82.7, 78.1, 65.5, 58.0, 54.4, 50.3, 48.1, 47.4, 42.7, 37.2, 29.8, 26.2, 25.6, 22.3, 22.1, 21.5, 21.1, 14.6.

LCMS **:** m/z 403 (M+1).

Analysis **:** for $C_{28}H_{38}N_2$.

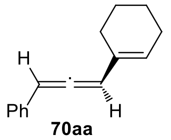
calcd: C 83.53, N 6.96, H 9.51.

found: C 83.45, N 6.91, H 9.56.

4.4.3 General procedure for the synthesis of vinylallenes 70 from 1-enyne 69, aldehyde 68 and amine 66 with CuI/dioxane condition.

To a stirred suspension of amine **66** (1 mmol), CuI (0.057 g, 0.3 mmol), aldehyde **68** (1.1 mmol) and 1-alkyne **69** (1.1 mmol) 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 allenes **70**.

***(R)*-(3-(Cyclohex-1-en-1-yl)propa-1,2-dien-1-yl)benzene (70aa):**



70aa

Yield : 0.154 g, 79%, Colourless oil.

$[\alpha]_D^{25}$: -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), 6.4 (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).

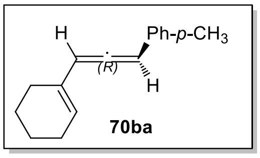
Analysis : for $C_{15}H_{16}$

calcd: C 91.78, H 8.22

found: C 91.63, H 8.28.

Enanatiomeric purity: 99% ee,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: 12.7 min. (major) and 15.2 min. (minor).

(*R*)-1-(3-(Cyclohex-1-en-1-yl)propa-1,2-dien-1-yl)-4-methylbenzene (70ba):



70ba

Yield : 0.144 g, 66%, Colourless oil.

$[\alpha]_D^{25}$: -186.3 (c=0.62, $CHCl_3$).

IR (neat) : 3049, 2925, 2848, 1947, 1618, 1510, 1086, 875 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.23 (d, *J*= 8.0 Hz, 2H), 7.14 (d, *J*= 8.0 Hz, 2H), 6.39 (s, 1H), 6.25 (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).

^{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).

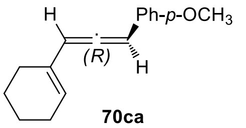
Analysis : for $C_{16}H_{18}$

calcd: C 91.37, H 8.63

found: C 91.25, H 8.56.

Enanatiomeric purity: 99% ee,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: 7.45 min. (major) and 8.59 min. (minor).

(*R*)-1-(3-(Cyclohex-1-en-1-yl)propa-1,2-dien-1-yl)-4-methoxybenzene (70ca):



70ca

Yield : 0.142 g, 63%, Colourless oil.

$[\alpha]_D^{25}$: -149.8 (c=0.50, $CHCl_3$).

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).

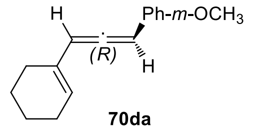
Analysis : for $C_{16}H_{18}O$

calcd: C 84.91, H 8.02

found: C 84.81, H 8.07.

Enanatiomeric purity: 97% ee,The enantioselectivity was determined by HPLC using chiral column, chiralcel OJ-H, hexanes:i-PrOH/95:5; flow rate 0.5 mL/min, 254 nm, retention times: 11.9 min. (major) and 13.8 min. (minor).

(*R*)-1-(3-(Cyclohex-1-en-1-yl)propa-1,2-dien-1-yl)-3-methoxybenzene (70da):



70da

Yield : 0.140 g, 62%, Colourless oil.

$[\alpha]_D^{25}$: -145.6 (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) 7.28-7.21 (m, 1H), 6.93-6.87 (m, 2H), 6.79-6.76 (m, 1H), 6.38 (d, *J*= 8.0 Hz, 1H), 6.27 (d, *J*= 8.0 Hz, 1H), 5.79-5.78 (m, 1H), 3.82 (s, 3H), 2.17-2.05 (m, 4H), 1.67-1.62 (m, 4H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 206.5, 159.9, 136.2, 131.7, 129.5, 127.1, 119.4, 112.5, 112.0, 101.6, 97.5, 55.2, 25.9, 25.8, 22.4, 22.3.

LCMS : *m/z* 227 (M+1).

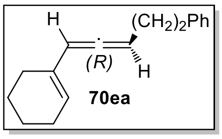
Analysis : for $C_{16}H_{18}O$

calcd: C 84.91, H 8.02

found: C 84.81, H 8.07.

Enanatiomeric 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, 254 nm, retention times: 12.7 min. (major) and 20.2 min. (minor).

(*R*)-(5-(Cyclohex-1-en-1-yl)penta-3,4-dien-1-yl)benzene (70ea):



70ea

Yield : 0.147 g, 63%, Colourless oil.

[α]$_D$^{25} : -144.3 (c=0.45, $CHCl_3$).

IR (neat) : 3059, 3028, 2920, 1613, 1494, 1453, 1076, 808 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.30-7.28 (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).

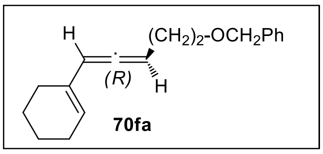
Analysis : for $C_{17}H_{20}$

calcd: C 91.01, H 8.99

found: C 91.15, H 8.91.

Enanatiomeric purity: 98% ee,The enantioselectivity was determined by HPLC using chiral column, chiralcel OB-H, hexanes:i-PrOH/100:0; flow rate 0.5 mL/min, 254 nm, retention times: 13.2 min. (minor) and 16.3 min. (major).

(*R*)-(((5-(Cyclohex-1-en-1-yl)penta-3,4-dien-1-yl)oxy)methyl)benzene (70fa):



Yield : 0.162 g, 61%, Colourless oil.

$[\alpha]_D^{25}$: -109.2 (c=0.38, $CHCl_3$).

IR (neat) : 2936, 2853, 1963, 1546, 1448, 1355, 1262, 1071, 968 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.36-7.27 (m, 5H), 5.84-5.82 (m, 1H), 5.66-5.65 (m, 1H), 5.41-5.40 (m, 1H), 4.54-4.52 (m, 2H), 3.55-3.49 (m, 2H), 2.18-2.02 (m, 6H), 1.81-1.66 (m, 4H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 204.2, 138.6, 132.3, 128.7, 128.3, 127.6, 127.5, 125.5, 98.2, 93.5, 72.9, 69.7, 29.1, 25.8, 25.7, 22.5, 22.5.

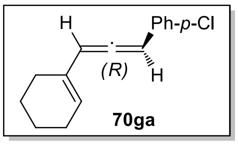
LCMS : *m/z* 255 (M+1).

Analysis : for $C_{18}H_{22}O$

calcd: C 84.99, H 8.72

found: C 84.91, H 8.65.

(*R*)-1-Chloro-4-(3-(cyclohex-1-en-1-yl)propa-1,2-dien-1-yl)benzene (70ga):



Yield : 0.154 g, 67%, Colourless oil.

$[\alpha]_D^{25}$: -144.7 (c=0.50, $CHCl_3$).

IR (neat) : 2936, 2853, 1955, 1613, 1587, 1448, 1086 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.

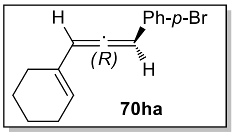
LCMS **:** *m/z* 231 (M+1).

Analysis **:** for $C_{15}H_{15}Cl$

calcd: C 78.08, H 6.55.
found: C 78.21, H 6.48.

Enanatiomeric purity: 99% ee,The enantioselectivity was determined by HPLC using chiral column, chiralcel OJ-H, hexanes:i-PrOH/100:0; flow rate 0.5 mL/min, 254 nm, retention times: 18.8 min. (major).

(*R*)-1-Chloro-4-(3-(cyclohex-1-en-1-yl)propa-1,2-dien-1-yl)benzene (70ha):



70ha

Yield : 0.191g, 70%, Colourless oil.

[α]$_D^{25}$: -132.3 (c=0.55, $CHCl_3$).

IR (neat) **:** 2930, 2853, 1892, 1696, 1582, 1443, 1345, 1169, 916 cm^{-1}.

^{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), 1.65-1.60 (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).

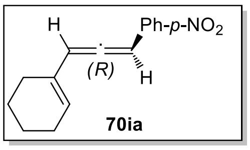
Analysis **:** for $C_{15}H_{15}Br$

calcd: C 65.47, H 5.49

found: C 65.58, H 5.41.

Enanatiomeric purity: 99% ee,The enantioselectivity was determined by HPLC using chiral column, chiralcel OJ-H, hexanes:i-PrOH/100:0; flow rate 1.0 mL/min, 254 nm, retention times: 10.9 min. (major).

(*R*)-1-(3-(Cyclohex-1-en-1-yl)propa-1,2-dien-1-yl)-4-nitrobenzene (70ia):



70ia

Yield : 0.159 g, 64%, Colourless oil.

[α]D^{25} : -128.9 (c=0.45, $CHCl_3$).

IR (neat) : 2956, 2920, 2848, 1901, 1598, 1448, 1340, 1024, 859 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 8.17 (d, *J*= 8.0 Hz, 2H), 7.44 (d, *J*= 8.0 Hz, 2H), 6.48 (d, *J*= 8.0 Hz, 1H), 6.38 (d, *J*= 8.0 Hz, 1H), 5.85-5.81 (m, 1H), 2.19-2.00 (m, 4H), 1.68-1.63 (m, 4H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 208.8, 146.5, 142.1, 130.6, 128.7, 127.0, 124.0, 102.4, 96.6, 25.9, 25.8, 22.3, 22.2.

LCMS : *m/z* 242 (M+1).

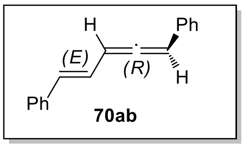
Analysis : for $C_{15}H_{15}NO_2$

calcd: C 74.67, H 6.27, N 5.81

found: C 74.52, H 6.21, N 5.89.

Enanatiomeric purity: 99% ee,The enantioselectivity was determined by HPLC using chiral column, chiralcel OJ-H, hexanes:i-PrOH/90:10; flow rate 0.5 mL/min, 254 nm, retention times: 13.1 min (major).

(*E*)-Penta-1,2,4-triene-1,5-diyldibenzene (70ab):



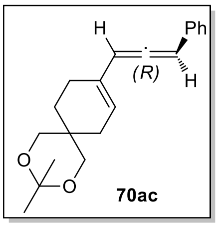
70ab

Yield : 0.150 g, 69%, Colourless oil.

[α]D^{25} : -576.8 (c=0.55, $CHCl_3$).

Enanatiomeric purity: 99% ee,The enantioselectivity was determined by HPLC using chiral column, chiralcel AS-H, hexanes:i-PrOH/99:1; flow rate 0.5 mL/min, 254 nm, retention times: 5.75 min. (major) and 8.1min. (minor).

(*R*)-3,3-Dimethyl-9-(3-phenylpropa-1,2-dien-1-yl)-2,4-dioxaspiro[5.5]undec-8-ene (70ac):



70ac

Yield : 0.219 g, 72%, Colourless oil.

[α]D^{25} : -132.6 (c=0.55, CHCl$_3$).

IR (neat) **:** 3059, 2951, 2868, 1937, 1624, 1469, 1391, 1107, 906 cm^{-1}.

^{1}H NMR **:** (400 MHz, CDCl$_3$, δ ppm) 7.34-7.21 (m, 5H), 6.43 (d, *J*= 8.0 Hz, 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), 2.25-1.99 (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).

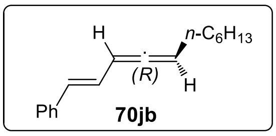
Analysis **:** for $C_{20}H_{24}O_2$

calcd: C 81.04, H 8.16

found: C 80.91, H 8.23.

Enanatiomeric 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, 254 nm, retention times: 13.6 min. (minor) and 16.7 min. (major).

(*R*,*E*)-Undeca-1,3,4-trien-1-ylbenzene (70jb):



70jb

Yield : 0.187 g, 65%, Colourless oil.

[α]D^{25} : -139.8 (c=0.54, CHCl$_3$).

IR (neat) **:** 3065, 2951, 2853, 1955, 1696, 1598, 1448, 1267, 1076 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.44-7.42 (m, 2H), 7.38-7.33 (m, 2H), 7.27-7.25 (m, 1H), 6.69-6.63 (m, 1H), 6.54 (d, *J*= 8.0 Hz, 1H), 6.06-6.01 (m, 1H), 5.47-5.45 (m, 1H), 2.16-2.10 (m, 2H), 1.53-1.49 (m, 2H), 1.43-1.36 (m, 6H), 0.97-.94 (m, 3H).

^{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, 22.7, 14.1.

LCMS : *m/z* 227 (M+1).

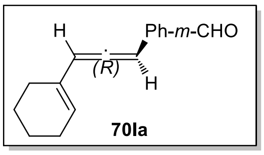
Analysis : for $C_{17}H_{22}$

calcd: C 90.20, H 9.80

found: C 90.12, H 9.85.

Enanatiomeric purity: 99% ee,The enantioselectivity was determined by HPLC using chiral column, chiralcel OJ-H, hexanes:i-PrOH/100:0; flow rate 0.5 mL/min, 254 nm, retention times: 18.0 min. (major).

3-(3-(Cyclohex-1-en-1-yl)propa-1,2-dien-1-yl)benzaldehyde (70la):



70la

Yield : 0.152 g, 68%, Brown oil.

[α]$_D^{25}$: -133.8 (c=0.54, $CHCl_3$).

IR (neat) : 1938, 1667, 1598, 1448, 1267, 1076 cm^{-1}

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 10.03 (s, 1H), 7.81 (m, 1H), 7.73-7.72 (m, 1H), 7.59-7.57 (m, 1H), 7.50-7.47 (m, 1H), 6.48-6.47 (m, 1H), 6.34-6.33 (m, 1H), 5.83-5.82 (m, 1H), 2.19-2.00 (m, 4H), 1.68-1.63 (m, 4H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 206.9, 192.3, 136.8, 136.1, 132.4, 131.2, 129.2, 128.1, 127.9, 127.7, 102.2, 96.8, 25.9, 25.8, 22.4, 22.9.

LCMS : *m/z* 227 (M+1).

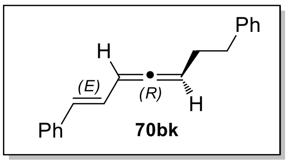
Analysis **:** for $C_{17}H_{22}$

calcd: C 90.20, H 9.80

found: C 90.12, H 9.85.

Enanatiomeric purity: 99% ee,The enantioselectivity was determined by HPLC using chiral column, chiralcel OD-H, hexanes:i-PrOH/100:0; flow rate 1.0 mL/min, 254 nm, retention times: 8.12 min. (major).

(*E*)-Hepta-1,3,4-triene-1,7-diyldibenzene (70kb):



70bk

Yield : 0.164 g, 67%, Colourless Oil.

$[\alpha]_D^{25}$: -225.8 (c=0.55, $CHCl_3$).

IR (neat) **:** 3068, 2851, 2753, 1965, 1686, 1591, 1439, 1167, 1066 cm^{-1}

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.35-7.21 (m, 10H), 6.18-6.16 (m, 1H), 5.66-5.61 (m, 1H), 2.88-2.83 (m, 2H), 2.56-2.49 (m, 2H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 205.3, 141.5, 134.8, 128.5, 128.3, 126.6, 125.9, 95.0, 94.3, 35.4, 30.5.

LCMS **:** *m/z* 227 (M+1).

Analysis **:** for $C_{17}H_{22}$

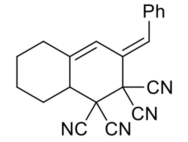
calcd: C 90.20, H 9.80

found: C 90.12, H 9.85.

Enanatiomeric purity: 99% ee,The enantioselectivity was determined by HPLC using chiral column, chiralcel OJ-H, hexanes:i-PrOH/100:0; flow rate 1.0 mL/min, 254 nm, retention times: 8.12 min. (major) and 8.90 (minor).

4.4.4 (*E*)-3-Benzylidene-6,7,8,8a-tetrahydronaphthalene-1,1,2,2(3H,5H)-tetracarbonitrile (84):

To a stirred solution of vinylallene **70aa** (196 mg, 1.0 mmol) in DCM (3 mL) at 25 °C was slowly added tetracyanaoethylene (140 mg, 1.1mmol). The reaction mixture was allowed to warm to rt and was stirred for 6 h. Then it was diluted with ethyl acetate (5 mL), poured water, and extracted with ethyl acetate (4 × 15 mL). After drying (Na_2SO_4), concentration, and column chromatography (90:10 hexane/EtOAc), a compound **84** was obtained (0.243 mg, 75%) as an orange oil.



84

Yield : 0.243 g, 75%, Colourless oil.

$[\alpha]_D^{25}$: -86.7 (c=0.50, $CHCl_3$).

IR (neat) : 3059, 2936, 2858, 2235, 1649, 1567, 1443, 1262, 1107, 906 cm^{-1}.

^{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), 2.29-1.76 (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 $C_{21}H_{16}N_4$

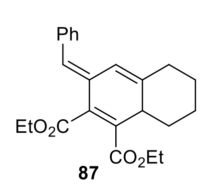
calcd: C 77.76, H 4.97, N 17.27

found: C 77.85, H 4.91, N 17.12.

Enanatiomeric purity: 90% ee,The enantioselectivity was determined by HPLC using chiral column, chiralcel OJ-H, hexanes:i-PrOH/90:10; flow rate 0.5 mL/min, 254 nm, retention times: 26.8 min. (minor) and 34.7 min. (major).

(*E*)-Diethyl 3-benzylidene-3,5,6,7,8,8a-hexahydronaphthalene-1,2-dicarboxylate (87):

To a stirred solution of vinylallene **70aa** (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 with ethyl acetate (5 mL), poured water, and extracted with ethyl acetate (4 × 15 mL). After drying (Na_2SO_4), concentration, and column chromatography (85:15 hexane/EtOAc), a compound **87** was obtained (252 mg, 69%) as an yellow oil.



87

Yield : 0.252 g, 69%, Colourless oil.

$[\alpha]_D^{25}$: -56.3 (c=0.55, $CHCl_3$).

IR (neat) : 3054, 2930, 1763, 1722, 1665, 1448, 1365, 1185, 1024 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, 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.

Enanatiomeric purity: 84% ee,The enantioselectivity was determined by HPLC using chiral column, chiralcel AS-H, hexanes:i-PrOH/90:10; flow rate 0.5 mL/min, 254 nm, retention times: 9.5min. (major) and 10.7 min. (minor).

4.5 References

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Chapter 5

Hydroboration of Prochiral Olefins using Chiral Morpholine-Borane Complex

5.1 Introduction

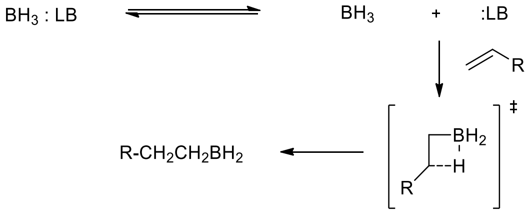
5.1.1 Asymmetric hydroboration using chiral amine-borane complexes

Since Brown and Subba Rao discovery that ether complexes of borane hydroborate olefins, diverse hydroborating agents like BH_3:SMe_2, BH_3:$N(C_2H_5)_2Ph$ and 9-BBN became commercially available.[1] The amine-borane complexes are relatively stable and therefore are ‘easy to handle’ carriers of borane. Due to strong complexation, most of the amine-boranes hydroborate olefins only at elevated temperatures. For example, the pyridine-borane hydroborates alkenes in diglyme at 100 °C.[2] However, the N, N-diethyl aniline-borane hydroborates olefins at ambient conditions due to decrease in strength of the N-B bond by steric or electronic effects.[3]

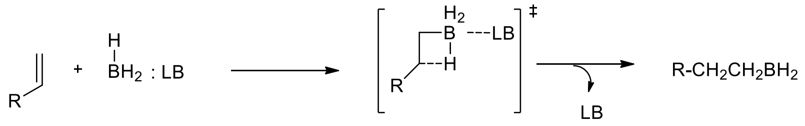
Three types of mechanism were proposed for the hydroboration of olefins (Scheme 1).[4]

Scheme 1

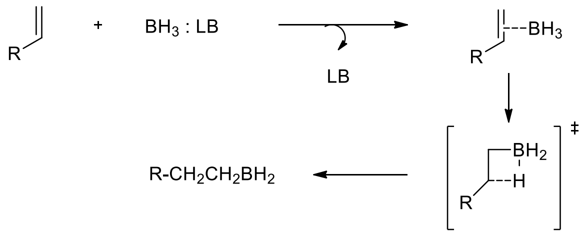
S_N1 type mechanism



S_N2 type mechanism

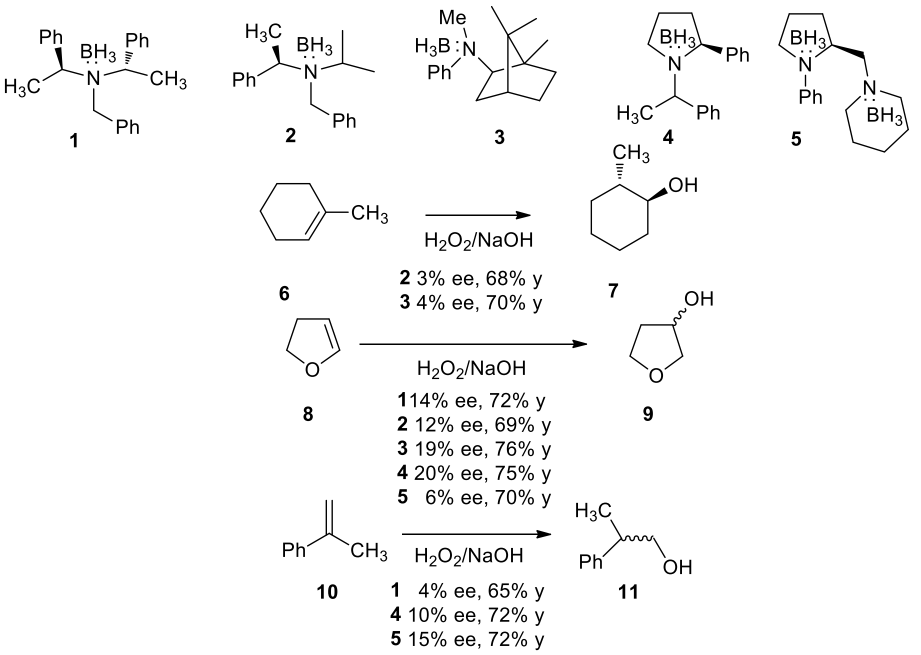


S_N2-type mechanism with π-complex intermediate



Whereas the reaction with electron rich olefins may take the S_N2 mechanistic pathway, the reaction involving sterically crowded borane complex or olefin may go through S_N2 reaction with a π-complex intermediate or the S_N1 reaction in which the borane complex dissociates into free BH_3 species before hydroboration. Previous efforts from this laboratory indicated that the S_N2 type mechanism cannot be ruled out as hydroboration of prochiral olefins by various borane chiral amine complexes gave the corresponding alcohols with 3-20% ee after H_2O_2/NaOH oxidation (Chart 1).[5]

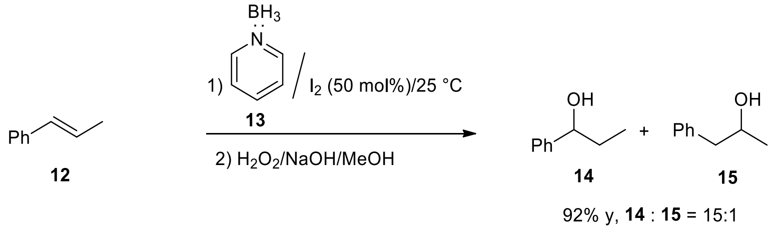
Chart 1



5.1.2 Iodine activation of chiral amine borane complexes

The hydroboration by iodine activation of strong amine-BH_3 complexes offers new opportunities for the asymmetric hydroboration as the BH_2I moiety is expected to be bonded with amines during the course of reaction with iodide behaving like a leaving group.[6] Vedejs *et al.*[6] reported that the hydroboration reaction of β-methylstyrene **12** by the pyridine borane complex **13** is activated by iodine at 25 °C (Scheme 2).

Scheme 2



Chiral primary amine borane complexes such as α-methylbenzylamine **16** and (*R*)-BINAM **17** were found to give the product **11** in 13% and 11% ee respectively, under iodine activation (Chart 2).[7] However, the hydroboration of α-methylstyrene **10** using the secondary amine **18** and tertiary amine **19** borane complexes was reported to give only racemic alcohols under iodine activation. Also, the hydroboration reaction of α-methylstyrene with the Tröger base borane **20** also resulted only in the formation of racemic alcohols (Chart 2).[7]

Chart 2

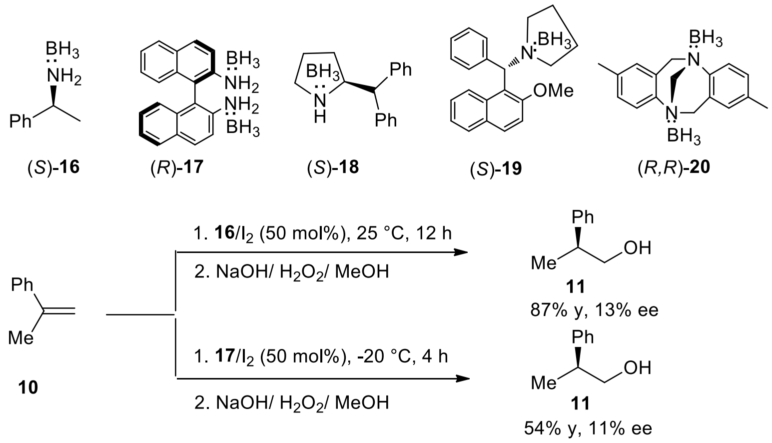
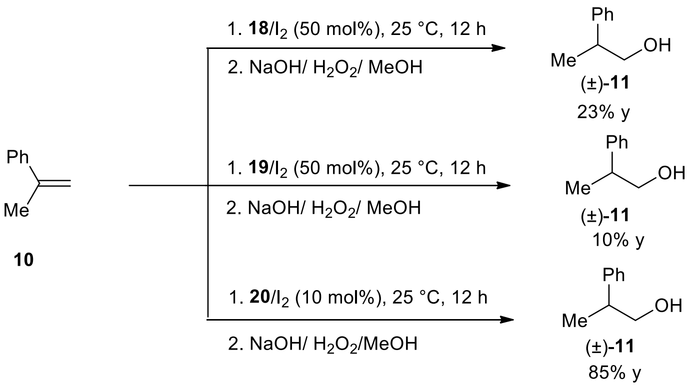
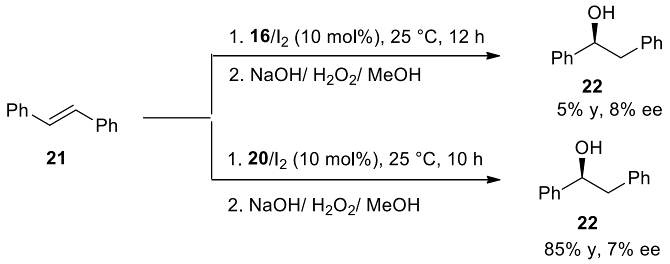


Chart 2 (Continued)

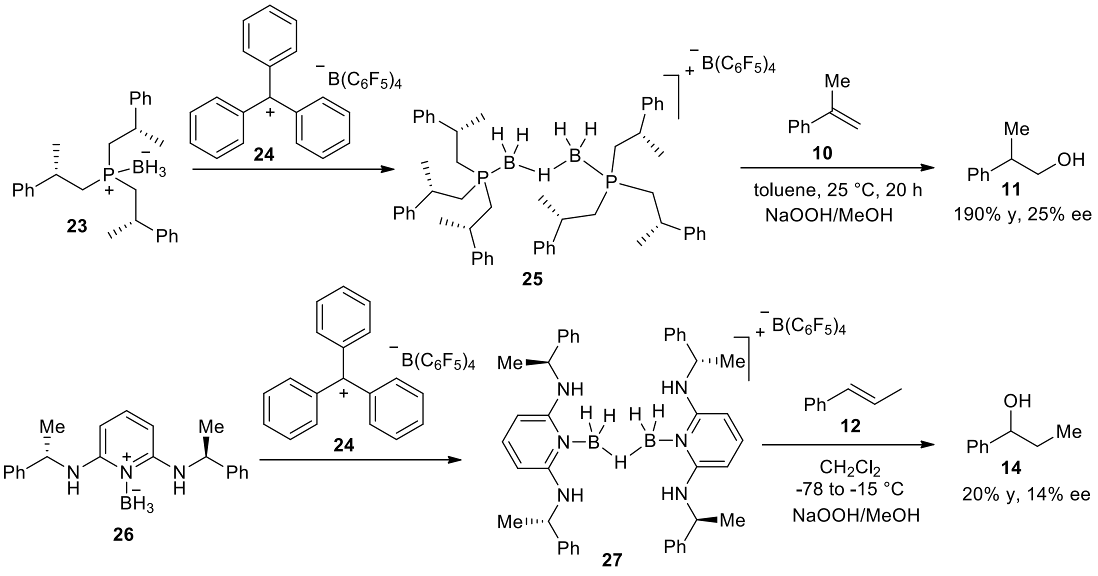




The hydroboration reaction of *trans*-stilbene **21** using α-methylbenzylamine-borane **16** and Tröger base-borane **20** with catalytic amount of iodine was reported to give the alcohol **22** in 5% yield and 8% ee and 85% yield and 7% ee, respectively (Chart 2).[7]

Very recently, Vedejs *et al.*[8] reported that the asymmetric hydroboration of α-methylstyrene **10** using C_3-symmetric chiral phosphine-borane complex **23** under trityl cation activation gave the corresponding alcohol in 190% yield and 25% ee. In another transformation using a chiral amine-borane chiral system **26**, the alcohol product **14** was obtained in 14% ee (Scheme 3). Clearly, in these cases, the Lewis base moiety is present in the hydroboration transition state (Scheme 3, S_N2 Type Mechanism) to more extent.

Scheme 3



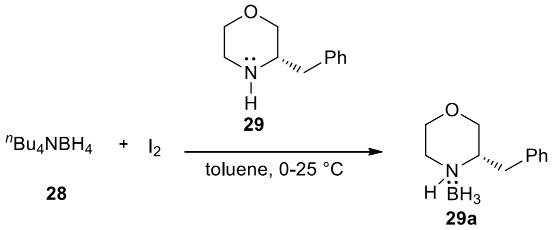
Since chiral secondary amines can be easily accessed *via* methods reported in previous sections, it was of our interest to examine the hydroboration of prochiral olefins using chiral amine-morpholine complexes.

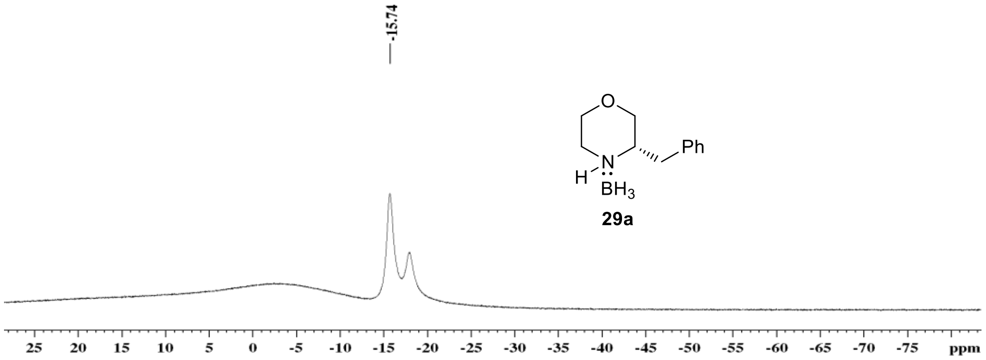
5.2 Results and Discussion

5.2.1 Hydroboration of prochiral olefins using secondary chiral morpholine-borane complex

We have prepared the borane complex by the reaction B_2H_6 generated in the reaction of $^{n}Bu_4NBH_4$ **28** with I_2 in toluene (Scheme 4).[7, 9]

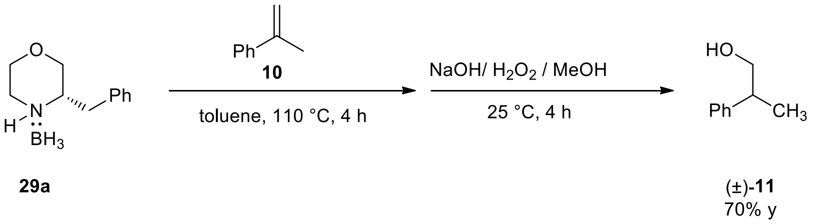
Scheme 4





We have carried out the hydroboration of α-methylstyrene **10** using this borane complex **29a** at 25 °C. However, this borane complex was found to be stable and there was no reaction with olefin under these conditions. The hydroboration did take place at 110 °C. However, after oxidation with NaOH/H_2O_2, only the racemic alcohol product **11** was isolated in 70% yield (Scheme 5).

Scheme 5

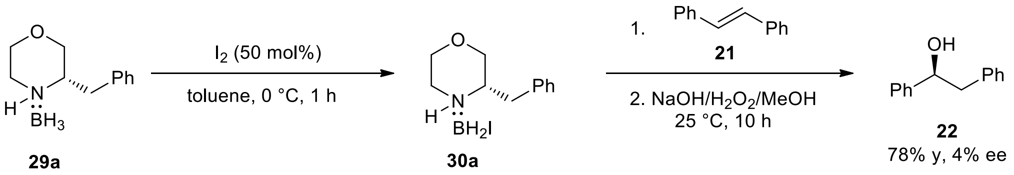


Accordingly, we have decided to examine this reaction under iodine activation.

5.2.2 Hydroboration of prochiral olefins using chiral morpholine-borane complex under iodine activation

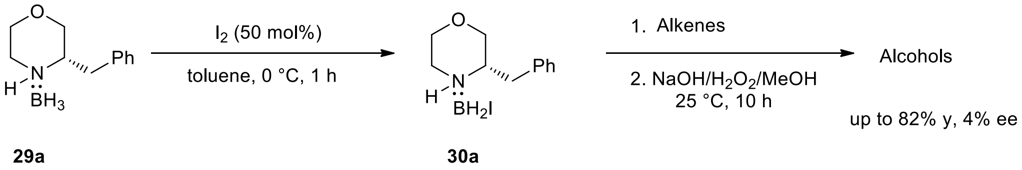
Since the amine moiety is anchored on the boron centre in iodine activated borane complexes with iodide behaving like leaving group, it was of our interest to prepare the chiral amine-BH_2I complexes to examine the enantioselectivity in the hydroboration of prochiral olefins (Scheme 6).[6] The borane complex **29a** was prepared by the reaction B_2H_6 produced *in situ* with chiral amine (Scheme 4). It was used for the hydroboration of *trans*-stilbene **21** under iodine activation. After the H_2O_2/NaOH oxidation, the corresponding alcohol **22** was obtained only in 4% ee (entry 1, Table 1).

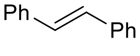
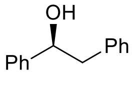
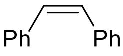
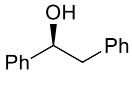
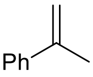
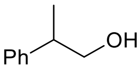
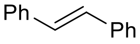
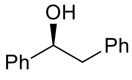
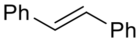
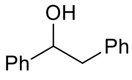
Scheme 6



We have also carried out the hydroboration reaction of *trans*-stilbene under iodine activation in the presence of N,N-diethylaniline as additive to examine whether this could lead to better selectivities through formation of complex like $R_3N^*BH_2{:}N(C_6H_5)Et_2I^-$complex. Unfortunately, the corresponding alcohol product obtained was found to be racemic after H_2O_2/NaOH oxidation (entry 5, Table 1). This could be explained if the hindered chiral morpholine-BH_2I **30a** complex reacts with the external Lewis base before the hydroboration reaction resulting in hydroboration by the achiral $Et_2(C_6H_5)N{:}BH_2I$ species.

Table 1. Hydroboration of prochiral olefins using chiral morpholine.[a,b,c]



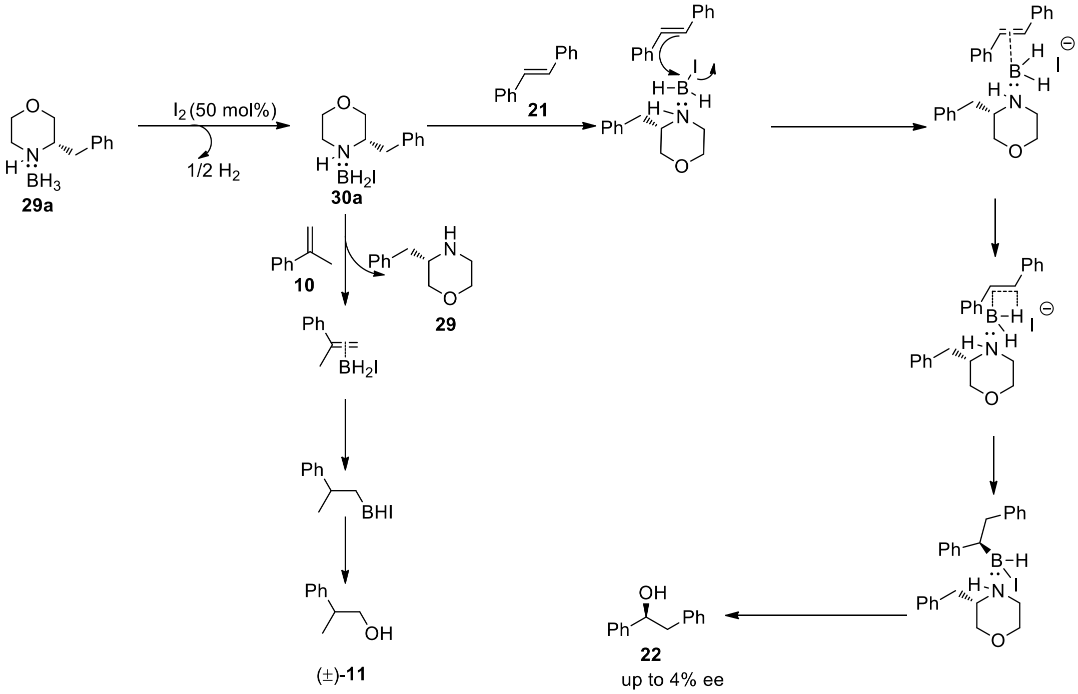
Entry	Substrate	Borane complex	Product	Yield[b]	% ee[c]
1	 **21**	**29a**	 **22**	78	4
2	 **31**	**29a**	 **22**	72	2
3	 **10**	**29a**	 **11**	82	0
4[d]	 **21**	**29a**	 **22**	76	3
5[e]	 **21**	**29a**	 **22**	74	0

[a] All the reactions were carried out in 1 mmol scale at 25 °C for 10 h. [b] Products were isolated after oxidation $NaOH/H_2O_2$. [c] HPLC analyses were carried out on chiral column OB-H; *n*-Hexane:*i*-PrOH-97:3, 0.3 mL/min. and OD-H using *n*-Hexane:*i*-PrOH-90:10, 0.5 mL/min. [d] In this case, addition of I_2 (20 mol%) in dry toluene (5 mL). [e] In this case, after the addition of I_2 (50 mol%) in dry toluene (5 mL) to chiral morpholine-borane complex **29a**, to the reaction mixture was added N,N-diethylaniline (weaker than chiral morpholine) (1 mmol) and allowed to stir for 30 min. Then *trans*-stilbene (1 mmol) was added and stirred for 10 h.

We have also examined the hydroboration-oxidation reaction of *cis*-stilbene **31** with the borane complex **29a** under iodine activation. The corresponding alcohol was isolated only in 2% ee after H_2O_2/NaOH oxidation (entry 2, Table 1). In the case of hydroboration of α-methylstyrene, only racemic alcohol was obtained (entry 3, Table 1).

5.2.3 Plausible mechanism for the hydroboration of olefins

Scheme 7



The results obtained in the hydroboration by borane complexes of chiral morpholine derivatives can be rationalized by considering the mechanism as outlined in Scheme 7. The reaction of iodine with chiral morpholine-BH_3 complexes would give the chiral morpholine-BH_2I complex **30a** and hydrogen. In the reaction of olefin with chiral amine-BH_2I, if the iodide leaves, the chiral morpholine would be attached to the boron in the transition state leading to optically active products. However, if chiral morpholine acts as a leaving group, the hydroboration reaction would lead to racemic mixtures. It appears that this seems to be the case. Since the enantioselectivity realized was poor, we did not pursue further studies under this topic.

We have also synthesized chiral imidazolidinone derivatives for applications in electron transfer reactions. The results are discussed in the next chapter.

5.3 Conclusions

Efforts were undertaken towards the hydroboration of prochiral olefins using chiral morpholine-borane complex. It was found that under iodine activation the borane complexes of chiral morpholine hydroborate olefins give alcohols in only up to 4% ee indicating that the hindered chiral amine derivative may not be present in the transition state of the reaction.

5.4. Experimental Section

5.4.1 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 ±0.01^{o}) and AUTOPOL-IV (readability ±0.001^{o}) automatic polarimeters. The condition of the polarimeter was checked by measuring the optical rotation of a standard solution of (*S*)-(+)-α,α–diphenylprolinol {$[\alpha]_D^{25} = +67.2$ (*c* 0.52, $CHCl_3$)} supplied by Gerchem Laboratory (Pvt) Ltd., India.

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.

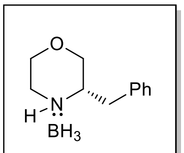
Dichloromethane and chloroform were distilled over CaH_2 and dried over molecular sieves. Methanol and ethanol supplied by Ranbaxy were distilled over CaO before use. Toluene and THF supplied by E-Merck, India were kept over sodium-benzophenone ketyl and freshly distilled before use. Ethylene diamine,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

5.4.2 Preparation chiral morpholine-borane complexes

To a two neck reaction flask containing $^{n}Bu_4NBH_4$ in toluene (5 mL) was added a solution of I_2 in toluene (15 mL) dropwise through addition funnel. The diborane gas generated in this way was bubbled through a side arm using bubbler into another reaction flask containing chiral morpholine (5 mmol) in dry toluene (40 mL) at 0 °C. When the bubbling of the gas had ceased, the bubbler was removed and replaced by a glass stopper under nitrogen atmosphere. The concentration of this stock solution is approximately 0.12 M.

^{11}B NMR (128.3 MHz, toluene, δ ppm) -15.7

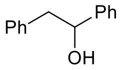
{δ = 0, BF_3:Et_2O (external reference)}


29a

5.4.3 General procedure for the hydroboration of olefins using chiral morpholine-borane complex

The reaction flask cooled under N_2, containing the corresponding borane complex (1 mmol, 8 mL in toluene), was added olefin (1 mmol) at 25 °C. This content was allowed to stir for 10 h at 110 ˚C. The mixture was brought to 25 °C after the required time. The reaction mixture was quenched with methanol (2 mL) and then oxidation was carried out for 4 h by adding 3N NaOH (4 mL) and H_2O_2 (30%, 4 mL). The organic layer was separated and the aqueous layer was extracted using ethyl acetate (2 x 10 mL). The combined organic layer was successively washed with water, brine and dried over Na_2SO_4. The solvent was evaporated and the crude product was purified by chromatography on silica gel column using hexane/ethyl acetate (90:10) as eluent to isolate the product **22**.

1,2-Diphenylethanol (22):


22

Yield : 70%

mp : 66-68 ˚C

IR (KBr) : 3315, 3024, 2920, 2854, 1030, 701 cm^{-1}.

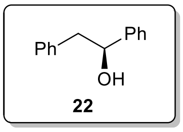
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm): 7.32-7.22 (m, 10 H), 4.94-4.90 (m, 1H), 3.00-3.09 (m, 2H), 2.14 (s, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm): 143.8, 138.1, 129.5, 128.5, 128.4, 127.6, 126.6, 125.9, 75.3, 46.1.

5.4.4 General procedure for the hydroboration of olefins using chiral morpholine-borane complexes activated by iodine

The reaction flask cooled under N_2, containing the corresponding borane complex (1 mmol, 8 mL in toluene), was added iodine (0.1 to 0.5 mmol, 0.025 to 0.125 g) in toluene (5 mL) at 0 ˚C. Then, olefin (1 mmol) was added at 0 ˚C. The resulting content was allowed to stir for 10 h at 25 °C. The reaction mixture was quenched with methanol (2 mL) and then oxidation was carried out for 4 h by adding 3N NaOH (4 mL) and H_2O_2 (30%, 4 mL). The organic layer was separated and the aqueous layer was extracted using ethyl acetate (2 x 10 mL). The combined organic layer was successively washed with water, brine and dried over Na_2SO_4. The solvent was evaporated and the crude product was purified by chromatography on silica gel column using hexane/ethyl acetate (90:10) as eluent to isolate the product.

1,2-Diphenylethanol (22):



22

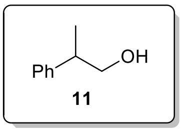
Yield : 72-78%

IR (KBr) : 3315, 3024, 2920, 2854, 1030, 701 cm^{-1}

$[\alpha]_D^{25}$: +3.5 (c, 0.5, EtOH), {lit.[201] for 100% ee, $[\alpha]_D^{25}$ = +52.8 (c, 1.40, EtOH} (4% ee, confirmed by HPLC using chiral column, chiralcel OD-H, hexane/*i*-propanol= 90:10, flow rate: 0.3 mL/min., 254 nm, retention times: 26.66 min.(*R*) and 30.27 min. (*S*)).

The spectral data of the corresponding products were showed 1:1 correspondence with the data obtained in the earlier experiments.

2-Phenylpropanol (11):



11

Yield : 82%

IR (neat) : 3336, 3030, 2958, 1600, 1495, 1035, 756 cm^{-1}.

^{1}H NMR : (400 MHz, CDCl$_3$): δ 7.38-7.26 (m, 5H), 3.72 (d, *J* = 8.0 Hz, 2H), 2.97 (d, *J* = 8.0 Hz, 1H), 1.48 (s, 1H), 1.31 (d, *J* = 8.0 Hz, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$): δ 143.7, 128.7, 127.5, 126.7, 68.7, 42.5, 17.6.

The spectral data of the corresponding products were showed 1:1 correspondence with the data obtained in the earlier experiments.

5.5 References

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Chapter 6

Electron Transfer Reaction of Amines with *p*-Chloranil

6.1 Introduction

6.1.1 Organic Electricity Harvesting Cells

6.1.1.1 Organic solar cells

In a solar cell, light is converted to electrical power, a technology with high potential to significantly contribute to energy supply in the future.[1] When light is absorbed in the active material of the solar cell, excitons [electrons and holes (+ve charges)] are produced. If the exciton binding energy can be overcome in an electric field, the holes (+ve charges) move to the cathode and the electrons move to the anode to generate electric current.

In a solid-state organic solar cell, semiconducting materials sandwiched between the electrodes are organic small molecules, oligomers, or polymers and the processes involved are (i) optical absorption and exciton formation, (ii) exciton migration to the donor-acceptor interface, (iii) exciton dissociation into charge carriers, resulting in the generation of holes (+ve charges) in the donor and electrons in the acceptor, (iv) charge carriers, mobility, and (v) charge collection at the electrodes (Figure 1).

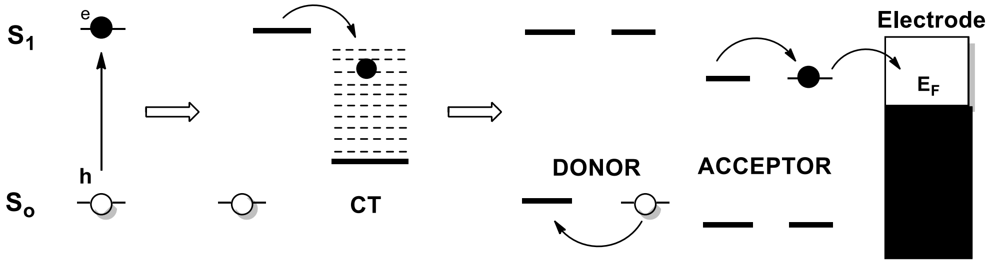
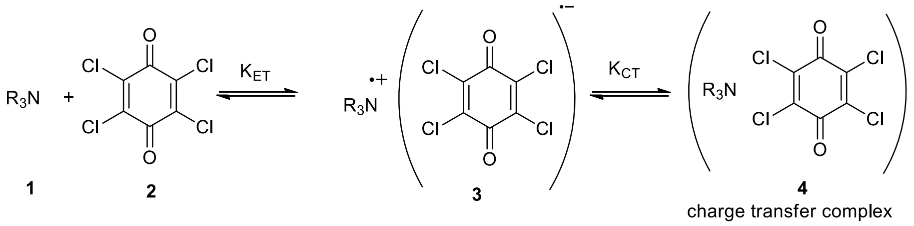


Figure 1

6.1.2 Ground state electricity harvesting cell

The electron transfer also readily takes place in the ground state of donor amines and acceptor quinones in a cross exchange process, resulting in the corresponding radical cation and anion pair followed by formation of the charge transfer complex (Scheme 1).[2]

Scheme 1



These reversible reactions take place at ambient temperature conditions in the ground state of the donor and acceptor. Accordingly, the energy barrier or activation energy for the formation of the ions is overcome by the surrounding heat (Figure 2).

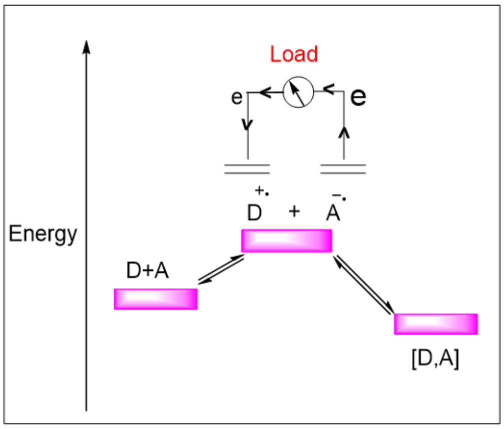


Figure 2. Ground state electron transfer between organic electron donor (D) and acceptor (A)-Construction of an electricity harvesting cell.

Therefore, it was envisaged in this laboratory that an electrochemical cell that could transport the charge carriers (i.e. electron in $Q^{-\cdot}$and the hole in $R_3N^{+\cdot}$) generated in such reactions to produce electricity can be constructed (Figure 1). Accordingly, electrochemical cells were constructed for generating electricity by utilizing donor-acceptor organic molecules. The following donors and acceptors were used in the construction of the ground state electricity harvesting cell (Figure 3).

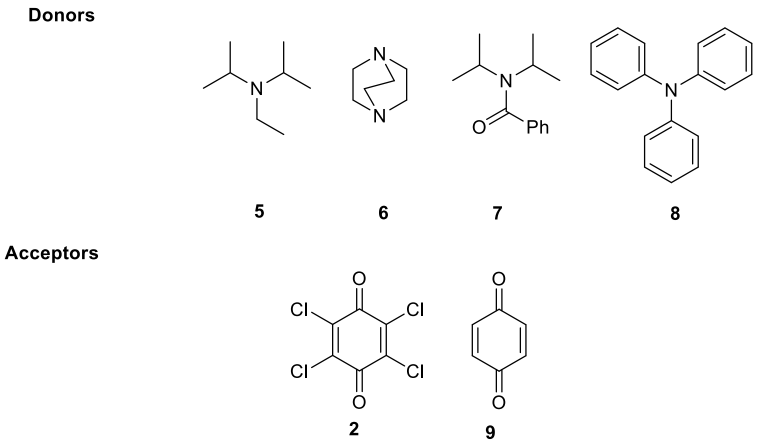


Figure 3: Eelectron donors and acceptors for use in electrochemical cell studies.

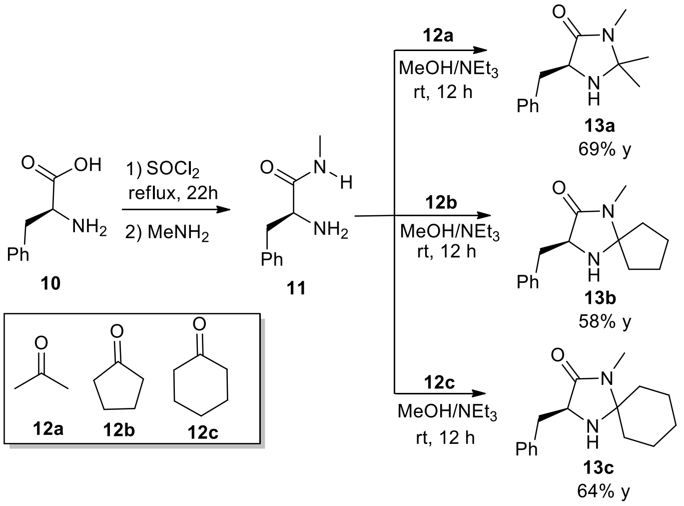
We have decided to examine the construction of such cells using imidazolidinone derivatives prepared from L-phenyl alanine. The results are discussed in the next section.

6.2 Results and Discussion

6.2.1 Synthesis of imidazolidinone derivatives starting from L-phenyl alanine

The imidazolidinone derivatives **13a-c** have been prepared following a simple protocol starting from L-phenyl alanine as outlined in Scheme 2.[3]

Scheme 2



6.2.2 Synthetic applications of chiral imidazolidinone derivatives

In recent years, secondary amine-mediated organocatalysis enabled methods for catalytic generation of radical cation of enamine nucleophiles were reported (Chart 1).[4,5,6]

Chart 1

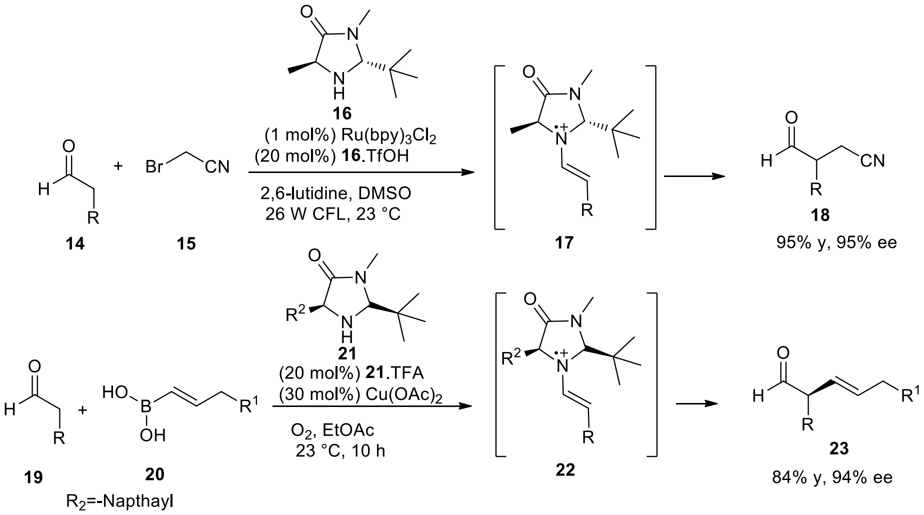
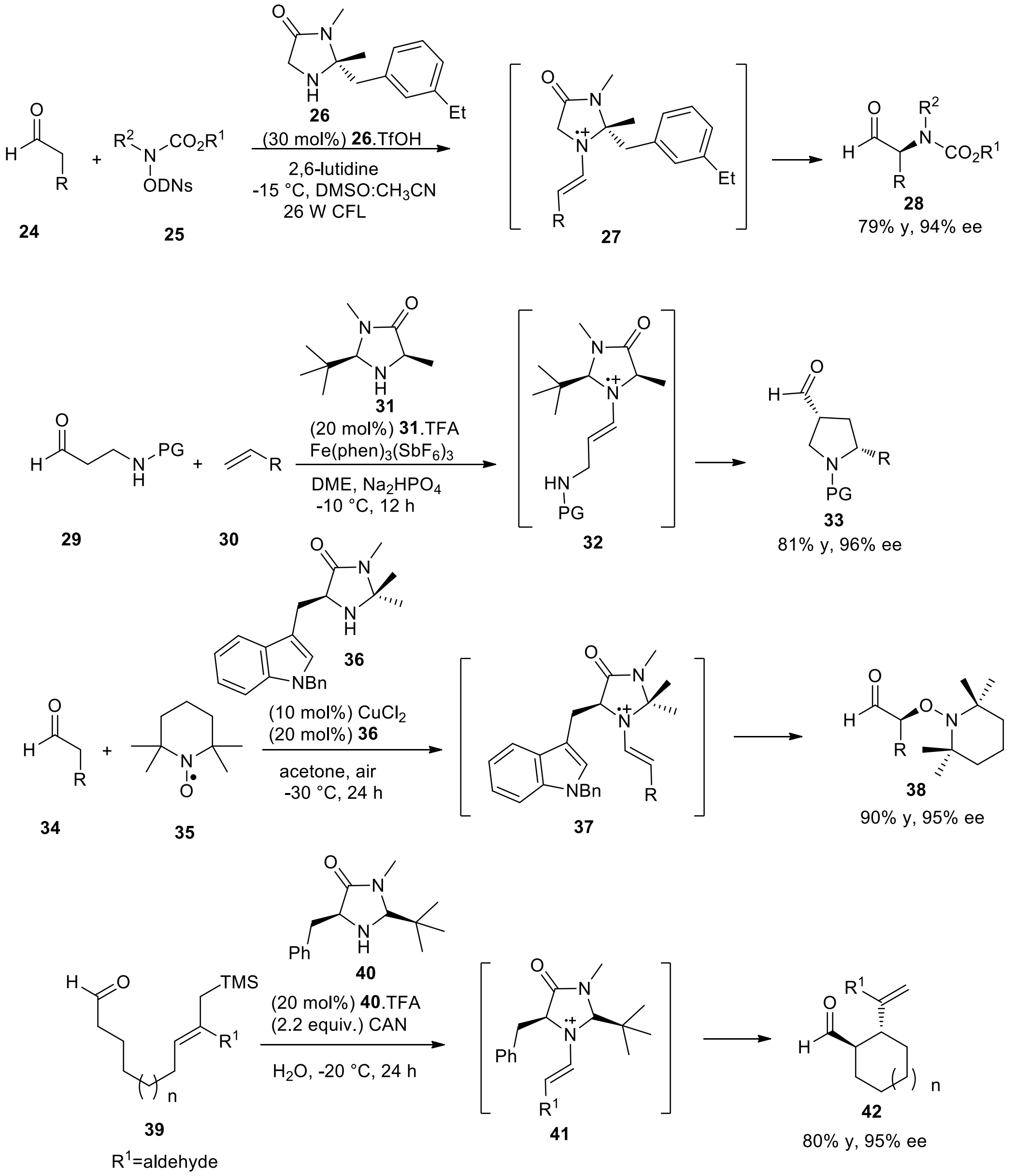
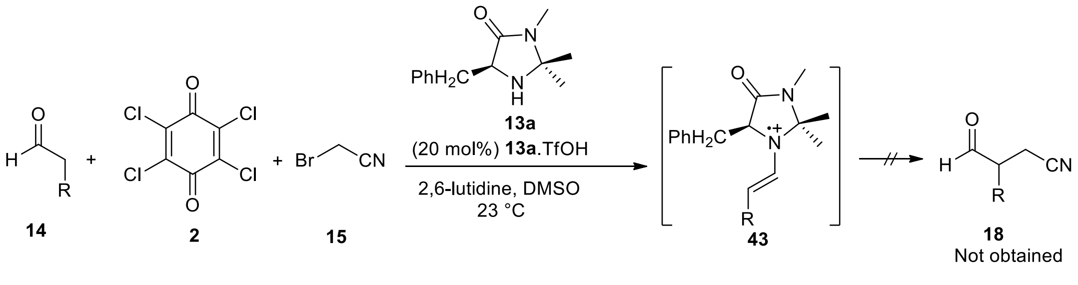


Chart 1 (continued)



We have carried out experiments using chiral amine **13a**, aldehyde **14**, α-bromonitrile **15** and chloranil **2** in DMSO solvent, but only a mixture of unidentified products were formed (Scheme 3).

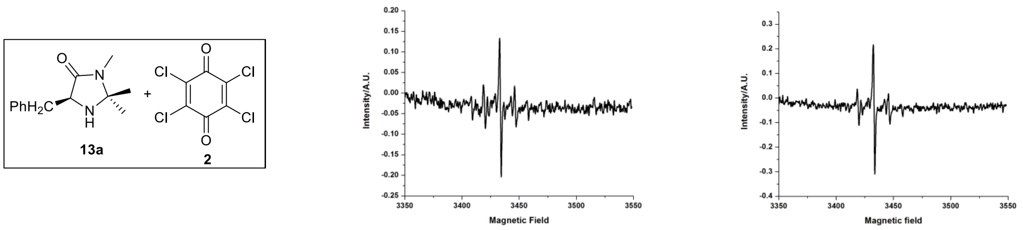
Scheme 3



Therefore, we have decided to investigate the intermediates formed in the reaction of the amine **13a** with *p*-chloranil.

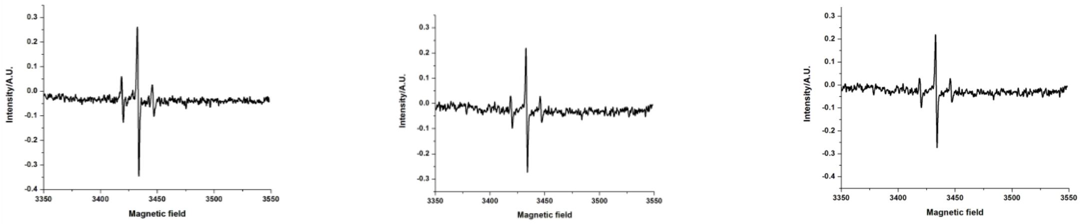
6.2.3 Reaction of secondary amines with *p*-chloranil 2 in DCM

We have observed that the (*S*)-5-benzyl-2,2,3-trimethylimidazolidin-4-one **13a** reacts with *p*-chloranil **2** in DCM solvent to give paramagnetic species by electron transfer from (*S*)-5-benzyl-2,2,3-trimethylimidazolidin-4-one (Figure 4).



(a) at 5 min

(b) at 1 h



(c) at 6 h

(d) at 12 h

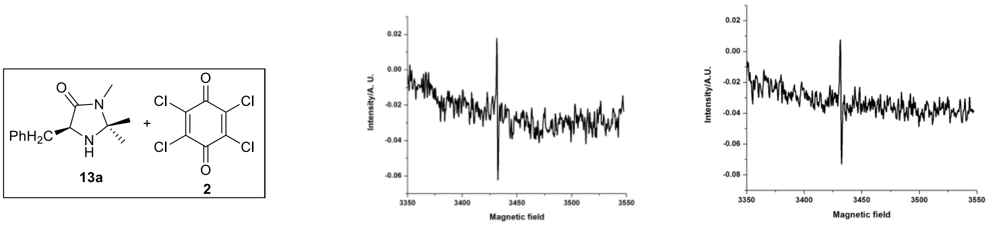
(e) at 24 h

Figure 4. EPR spectra of *p*-chloranil **2** (0.05 mmol) and the amine **13a** (0.05 mmol) in DCM (0.5 mL) solvent.

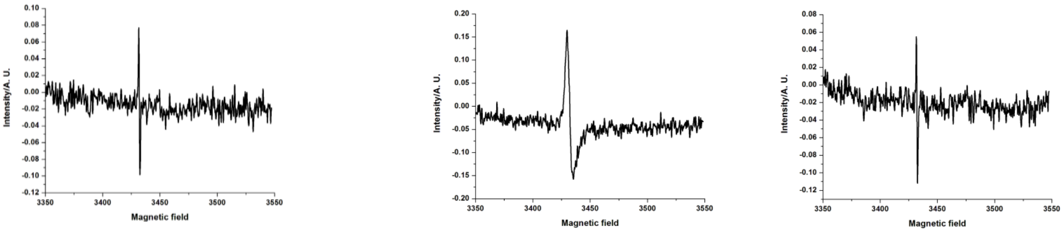
We have observed a triplet signal in the epr spectrum corresponding to amine radical cation with central peak overlapping with the epr signal of the *p*-chloranil radical anion.

6.2.4 Reaction of secondary amines with *p*-chloranil 2 in PC

Similarly, the reaction of (*S*)-5-benzyl-2,2,3-trimethylimidazolidin-4-one **13a** with *p*-chloranil **2** in PC solvent also gives paramagnetic intermediates as confirmed by epr spectroscopy (Figure 5).



(a) at 5 min (b) at 1 h

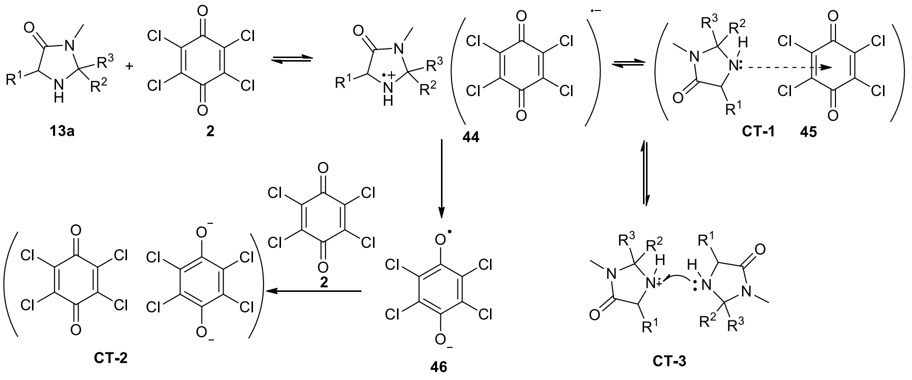


(c) at 6 h (d) at 12 h (e) at 24 h

Figure 5. EPR spectra of *p*-chloranil **2** (0.05 mmol) and secondary amine (0.05 mmol) in PC (0.5 mL) solvent.

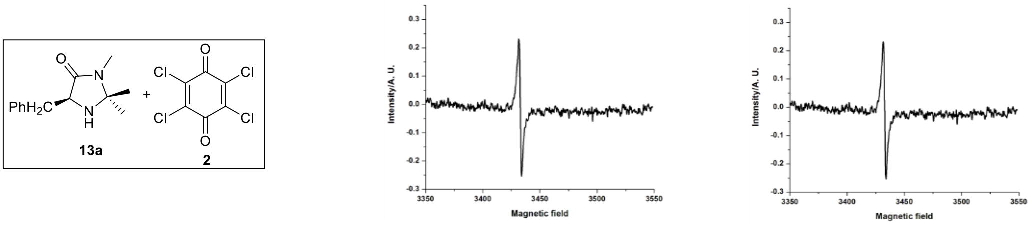
In PC solvent, the epr signal obtained is mainly due to the presence of quinone radical anion **46** as the amine radical cation formed would undergo fast exchange of electron with the neutral amine and hence may not exhibit epr signal (Scheme 4). Also, formation of the corresponding charge transfer complexes CT-1, CT-2 may also lead to weaker epr signals for the quinone radical anion.

Scheme 4

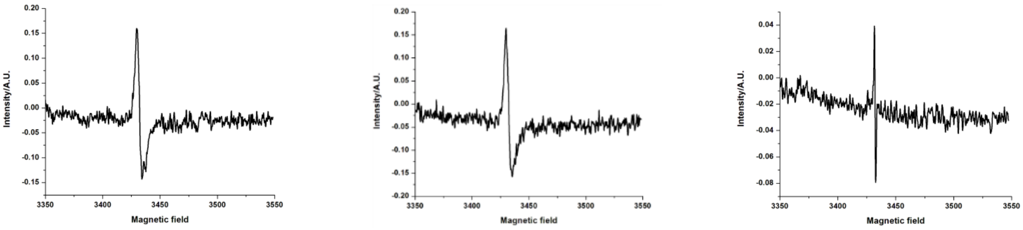


6.2.5 Reaction of secondary amines with *p*-chloranil 2 under neat condition

We have also reacted the (*S*)-5-benzyl-2,2,3-trimethylimidazolidin-4-one **13a** with *p*-chloranil **2** under the neat condition (without solvent). The paramagnetic species formed were detected by epr spectroscopy (Figure 6).



(a) at 5 min (b) at 1 h



(c) at 6 h (d) at 12 h (e) at 24 h

Figure 6. EPR spectra of *p*-chloranil **2** (0.05 mmol) and secondary amine (0.05 mmol) in neat condition.

In this case also, a single signal was observed in the epr spectrum and the strength decreased in with time. The results are in accordance with slow formation of radical ions followed by formation of the corresponding charge transfer complexes (Scheme 4).

6.2.6 Construction of donor and acceptor electrochemical cell: Previous work from this laboratory

Previously, the TiO_2 was used as solid support for construction of the cell device as it is widely used in the construction of solar cell and other electronic devices. The polar propylene carbonate (PC) was selected as it is widely used in rechargeable batteries. After extensive studies, it was found that the cells can be easily constructed by making donor and acceptor pastes using TiO_2, polyethylene oxide (PEO) and PC and coating on Al foil (0.2mm x 5cm x 5cm) and graphite sheet (0.4mm x 5cm x 5cm) electrodes (SI). Initially, a simple two layer cell was constructed using Al (5 cm x 5 cm) and SS (SS 304, 5 cm x 5 cm) foils. The mixture TiO_2 (rutile), *p*-chloranil, PC, EC and polyethylene oxide (PEO) was coated on Al foil and the mixture of TiO_2 (rutile), amines, PC, EC and PEO was coated on SS foil (SI). The foils were then sandwiched to construct the electrochemical cell. The charge transport in this two layer electrochemical cell is expected to have contributions from both ionic conductivity and also through exchange reactions involving $D/D^{\cdot+}$ and $A^{\cdot-}/A$ species. The cell constructed this way did produce power (Pmax/FF = 1.415/0.235) but there was only very little power after 24 h.[7]

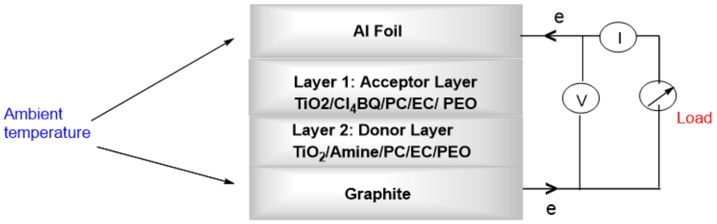
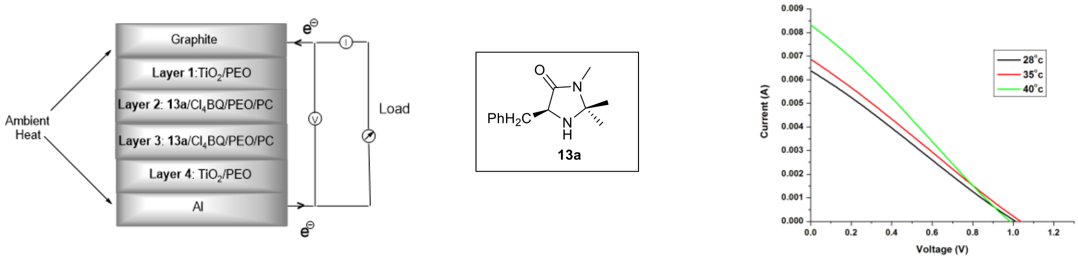


Figure 7. Cell Configuration

6.2.7 Four layers cell configuration

It was of interest to us to construct the electrochemical cell using 5-benzyl-2,2,3-trimethylimidazolidin-4-one donor. Accordingly, we have constructed the cell with four layers configuration by coating TiO_2/PEO pastes on two electrodes followed by coating of Amine/Cl_4BQ/PEO/PC on TiO_2/PEO/Al as well as on TiO_2/PEO/Gr. The results are summarized in Figure 8.

Figure 8: Four layers cell Configuration


(a) (b)

	1 h after packing	48h after packing
Donor	**Pmax/mW/FF(40 °C)**	**Pmax/mW/FF(40 °C)**
Amine **13a**	2.161/0.263	0.017/0.249

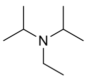
Figure 8. (a) Schematic diagrams of multi-layers cell using donor along with *p*-chloranil and PEO in PC layer. (b) Representative IV curve for the cell.

The power output (Pmax) was very little after 48 h (Figure 8).

6.2.8 Electrochemical cells with multilayers configurations

Earlier, it was reported that radical ion intermediates were formed when *p*-chloranil was absorbed on the TiO_2 surface.[8] Also, radical anions formed from lower electron affinity acceptors like benzoquinone (EA 1.91 eV) are solvated to more extent compared to *p*-chloranil (2.78 eV). The electrochemical cells constructed in this way using various amine donors using BQ layer gave the higher power output (Figure 9).[7]

Figure 9: Multilayers cell experiments using BQ: Previous results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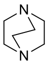
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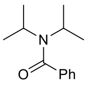
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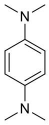
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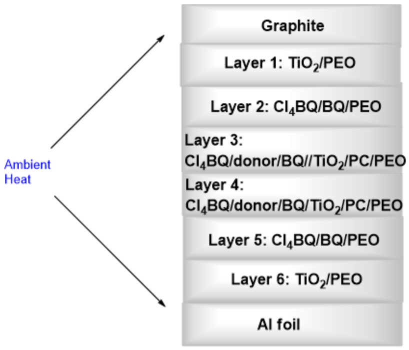


1 h after packing

Donor	**Pmax/mW/F (40 °C)**
TMPDA	3.099/0.261
DABCO	6.155/0.206
DIPEA	8.147/0.347
DiPrBA	4.193/0.295

48 h after packing

Donor	**Pmax/mW/F (40 °C)**
TMPDA	1.822/0.250
DABCO	1.206/0.249
DIPEA	2.057/0.334
DiPrBA	2.969/0.273

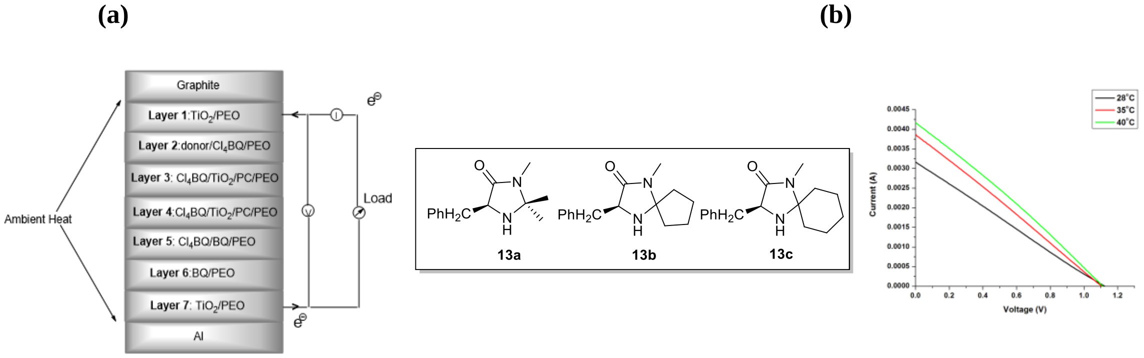
Figure 9. (a) Cell configuration and power (Pmax) output.

Therefore, we have undertaken studies on construction of organic electrochemical cells using the amine derivatives **13a**, **13b** and **13c** in different configurations using BQ and Me_2SO_2 as electron transporters.

6.2.9 Seven layers cell configuration

We have constructed the cell in the two different layer configuration using BQ in PC solvent (Figure 10 & 11). The cell configuration as in Figure 9a gave better results with the electron transporter BQ using the donors **13a**, **13b** and **13c** compared to Figure 11a. Among the three donors investigated, the sterically hindered amine donor **13c** gave better results [amine **13c,** (Pmax=3.512mW, Figure 10) and Pmax=2.949mW, Figure 11)].

Figure 10: Seven layers configuration with amines 13 and Cl_4BQ in layer 2

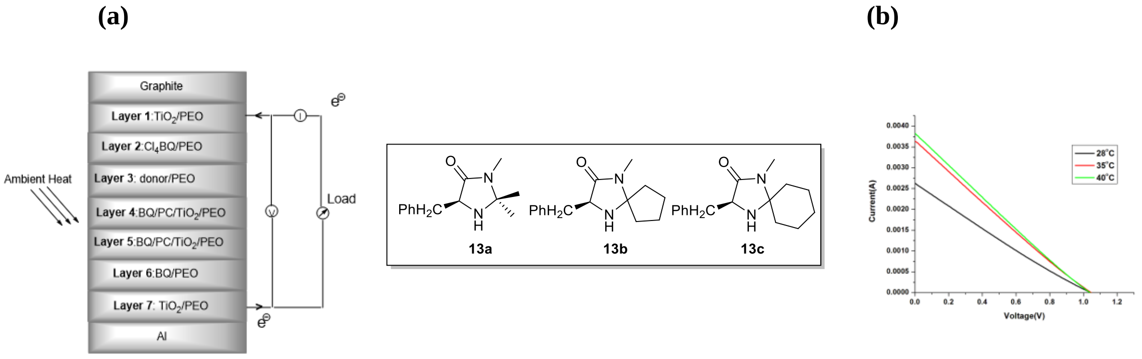


1 h after packing		**48 h after packing**
Donor	**Pmax/mW/FF(40 °C)**	**Pmax/mW/FF(40 °C)**
Amine **13a**	2.982/0.258	1.260/0.272
Amine **13b**	3.185/0.270	0.952/0.247
Amine **13c**	3.512/0.255	2.081/0.288

Figure 10. (a) Schematic diagram of multi-layers cell using *p*-chloranil, amine with TiO_2, PEO and BQ. (b) Representative IV curve for the cell using amine donor **13c**.

However, the power output decreased with time.

Figure 11: Seven layers configuration using Cl_4BQ and amines 13 and in layer 2 & 3



1 h after packing		48 h after packing
Donor	**Pmax/mW/FF/(40 °C)**	**Pmax/mW/FF/(40 °C)**
Amine **13a**	2.941/0.257	0.951/0.240
Amine **13b**	2.185/0.248	1.271/0.250
Amine **13c**	2.949/0.247	0.249/0.234

(c)

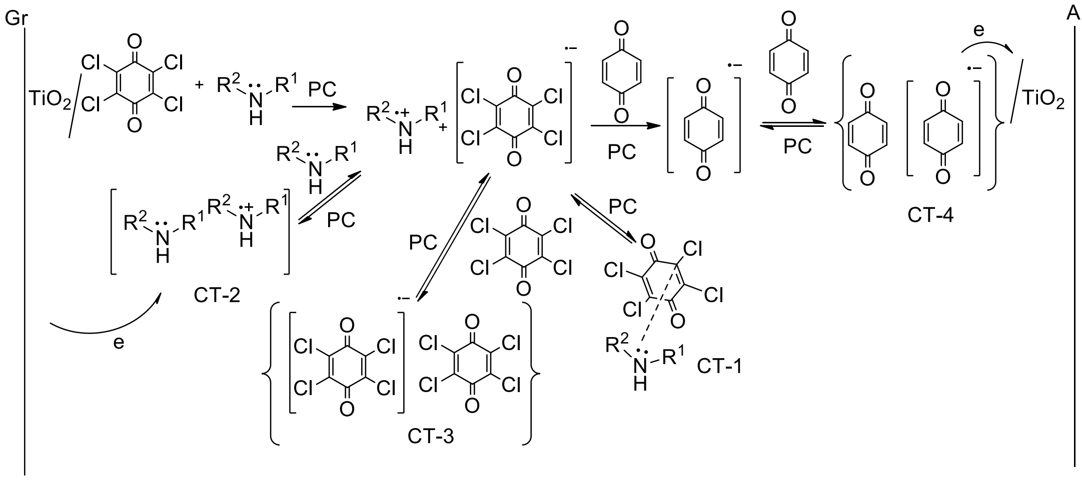


Figure 11. (a) Multilayers cell using BQ along with PEO and TiO_2 in PC layer (b) Representative IV curve for the amine **13c**. (c)Tentative mechanism for electron transport to the electrodes via D/D.+ and A-/A exchanges.

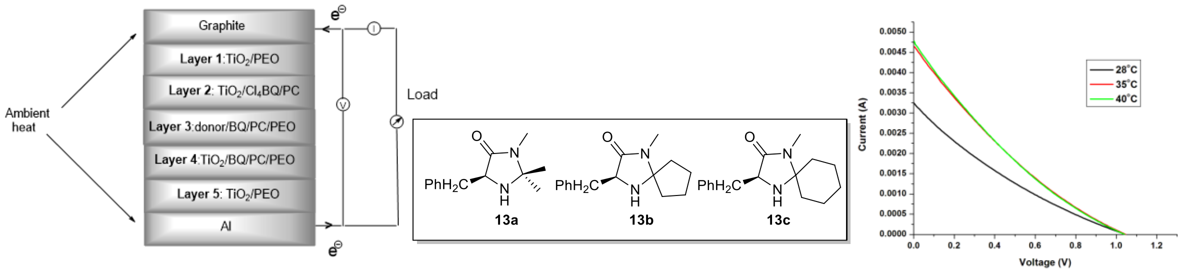
In this case also, power output decreased with time.

6.2.10 Five layers cell configuration

We have then carried out experiments by constructing five layers cell in two different configurations. When BQ was used as electron transporter, the Pmax values increased with time for amines **13a** and **13b** (Figure 12).

Figure 12: Five layer cell using BQ as electron transporter

(a) **(b)**



1 h after packing		**48 h after packing**
Donor	**Pmax/mW/FF/(40 ^{o}C)**	**Pmax/mW/FF/(40 ^{o}C)**
Amine **13a**	2.527/0.288	0.928/0.187
Amine **13b**	2.371/0.302	1.650/0.202
Amine **13c**	2.565/0.268	1.363/0.187

(c)

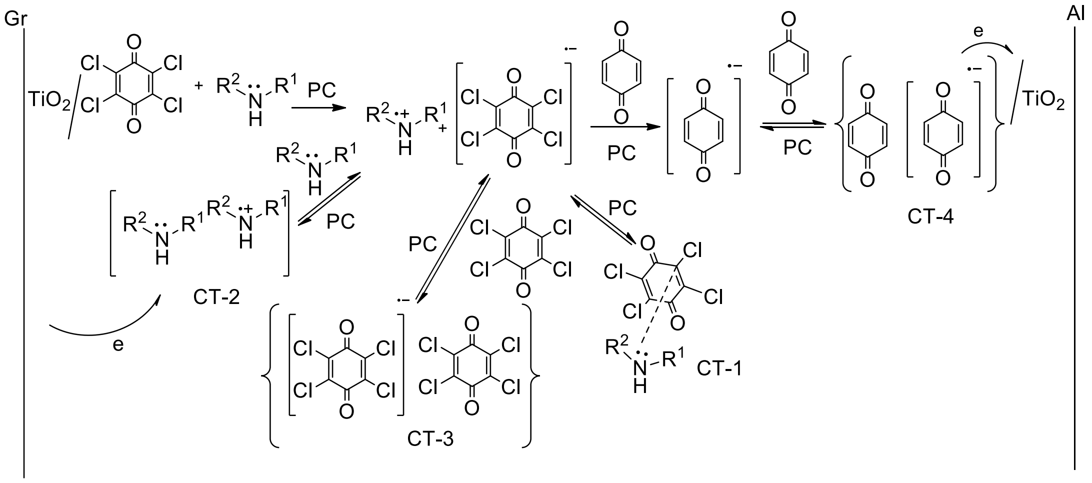
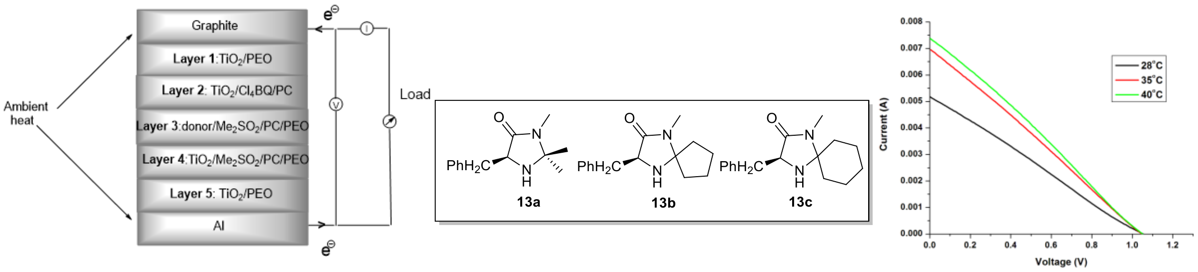


Figure 12. (a) Schematic diagrams of multi-layers cell using *p*-chloranil, amine with TiO_2, PEO, PC and BQ. (b) Representative curve for the amine **13c**. (c) Tentative mechanism for electron transport to the electrodes via D/D.+ and A-/A exchanges.

When Me_2SO_2 was used as electron acceptor, higher power output (Pmax) was obtained after 1 h packing but the Pmax decreased after 48 h. Comparison of the results indicate that the cell with BQ as electron transporter gives higher power for longer time.

Figure 13: Five layer cell with Me_2SO_2 as electron transporter

(a) **(b)**



1 h after packing		**48 h after packing**
Donor	**Pmax/mW/FF(40 ºC)**	**Pmax/mW/FF(40 ºC)**
Amine **13a**	1.770/0.240	2.077/0.268
Amine **13b**	1.772/0.242	2.079/0.270
Amine **13c**	4.201/0.268	2.430/0.268

(c)

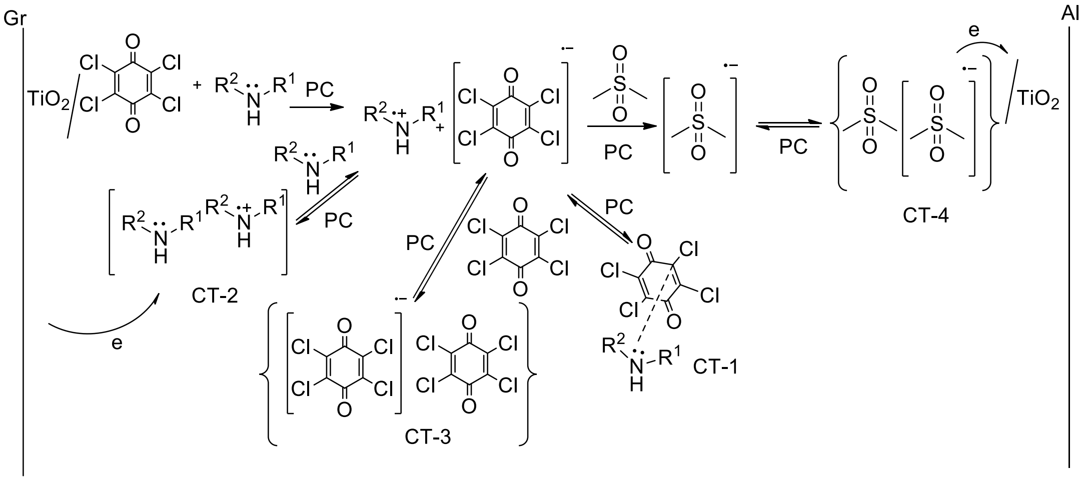


Figure 13. (a) Schematic diagrams of multi-layers cell using *p*-chloranil and amine with TiO_2, PEO, PC and Me_2SO_2. (b) Representative curve for the amine **13c** (c) Tentative mechanism for electron transport to the electrodes via D/D.+ and A-/A exchanges.

The results 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. Also, the dissociation of the formed charge transfer complexes into radical ion pairs is also expected to be more effective at higher temperature.

6.3 Conclusions

We have developed a simple device for constructing the electrochemical cell based on ground state electron transfer reaction of (*S*)-5-benzyl-2,2,3-trimethylimidazolidin-4-one donor and *p*-chloranil acceptor in various configurations. The power produced was somewhat low compared to that produced using simple tertiary amine like diisopropylethylamine. Presumably, the concentration of the amine radical cation produced using amines **13a**, **13b** and **13c** are relatively low compared to the concentration of radical ions produced using diisopropylethylamine and hence the current and power (Pmax) produced by the cell using the amines are also low. The results described here will be useful in understanding the factors involved in the functioning of such electrochemical cells.

6.4. Experimental Section

6.4.1 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 ±0.01°) and AUTOPOL-IV (readability ±0.001°) automatic polarimeters. The condition of the polarimeter was checked by measuring the optical rotation of a standard solution of (*S*)-(+)-α,α–diphenylprolinol $\{[\alpha]_D^{25} = +67.2$ (*c* 0.52, $CHCl_3$)$\}$ supplied by Gerchem Laboratory (Pvt) Ltd., India.

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.

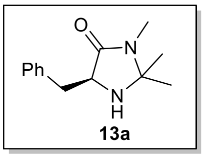
p-Chloranil, N, N-diisopropylethylamine (DIPEA), 1,4-diazabicyclo[2.2.2]octane (DABCO), *P*-benzoquinone (BQ),and TiO_2 were purchased from Avra chemicals (India). Triphenylamine (TPA), *N,N'*-tetramethyl-1,4-phenylenediamine (TMPD), propylene carbonate (PC), ethylene carbonate (EC) and polyethylene oxide (PEO) were purchased from Sigma Aldrich. Netural alumina (Al_2O_3) was purchased from SRL chemicals, India. Zinc oxide (ZnO) was purchased from E-Merck, India. The metal oxides were heated at 150 °C in a vacuum oven for 2 h before use. PC and EC were always kept under molecular sieves. *N*, *N*-diisopropylbenzamide was prepared from the literature procedure. Graphite sheet (0.4mm thickness, 5cm x 5cm, Resistivity, $\rho = 2x10^{-4}\Omega$.m) was purchased from Falcon Graphite Industries, Hyderabad, India. Aluminium Foil (0.2mm thickness, 5cm x 5cm, Resistivity, $\rho = 2x10^{-5}\Omega$.m) and Stainless steel (0.4mm thickness, 5cm x 5cm, Resistivity, $\rho = 5x10^{-4}\Omega$.m) were purchased from Aluminium Enterprises and Rasik Metals, Hyderabad, India. EPR spectra was recorded on a Bruker-ER073 instrument equipped with an EMX micro X source for X band measurement using Xenon 1.1b.60 software provided by the manufacturer. Electrical measurements were carried out by ZAHNER instrument using CIMPS software. The current-voltage curve was drawn using Origin software.

6.4.2 General procedure for the synthesis of imidazolidinone derivatives from L-phenyl alanine (13):

To a suspension of L-phenylalanine **10** (1.0 equiv.) in MeOH (10 equiv.) was added thionyl chloride (1.2 equiv.) over 15 min at 0 °C, the resulting solution was warmed to RT before being heated at reflux for 22 h. The solution was cooled to RT and evaporated *in vacuo* to give the L-phenylalanine methyl ester hydrochloride as a white solid. To the ester was added $MeNH_2$ (8N in EtOH, 4.0 equiv.) at RT and the solution stirred for 23 h. The reaction was concentrated *in vacuo* and a saturated aqueous solution of $NaHCO_3$ (45 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (3 x 55 mL). The combined organic layers were dried over $MgSO_4$, filtrated and concentrated *in vacuo* to give the amide **11.**

To a solution of amide **11** (1 equiv.) in MeOH (12.0 mL) was added ketone **12** (5.0 equiv.) and NEt_3 (0.8 equiv.) at RT under an atmosphere of argon. The solution was heated at reflux overnight then cooled to RT and concentrated*in vacuo* to give **13**.

(*S*)-5-Benzyl-2,2,3-trimethylimidazolidin-4-one (13a):



13a

Yield : 0.150 g, 69%, Brown liquid.

$[\alpha]_D^{25}$: –32.2 (c=0.94, CH_3OH).

IR (neat) : 3315, 2925, 1683, 1602, 1496, 1424, 1089, 922 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.34–7.17 (m, 5H), 3.81 (dd, *J* = 6.8 Hz, 4.5 Hz, 1H), 3.12-3.08 (m, 1H), 3.01-2.99 (m, 1H), 2.78 (s, 3H), 1.71 (b, 1H), 1.23 (s, 3H), 1.16 (s, 3H,).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 172.9, 137.5, 129.1, 128.2, 127.1, 75.4, 59. 5, 37.4, 27.3, 25.5, 25.3.

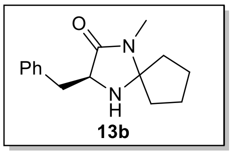
LCMS : m/z 218 (M+1).

Analysis : for $C_{13}H_{18}N_2O$

calcd: C 71.53, H 8.31, N 12.83.

found: C 71.45, H 8.15, N 12.78.

(*S*)-3-Benzyl-1-methyl-1,4-diazaspiro[4.4]nonan-2-one (13b):



13b

Yield : 0.141 g, 58%, Brown liquid.

[α]$_D$^{25} : –54.2 (c=1.05, CH_3Cl).

IR (neat) : 3308, 2952, 1679, 1602, 1494, 1414, 1096, 1030, cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.33–7.26 (m, 2H), 7.24–7.15 (m, 3H), 3.79 -3.69 (m, 1H), 3.14-3.06 (m, 1H), 3.01-2.65 (m, 1H), 2.75 (s, 3H), 1.68–1.41 (m, 8H), 0.96 (d, *J* = 12.4 Hz, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 174.2, 137.4, 129.9, 128.4, 126.6, 85.7, 59. 4, 36.9, 36.9, 34.5, 25.5, 23.8.

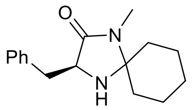
LCMS : m/z 244 (M+1).

Analysis : for $C_{15}H_{20}N_2O$

calcd: C 73.74, H 8.25, N 11.47.

found: C 73.69, H 8.21, N 11.39.

(*S*)-3-Benzyl-1-methyl-1,4-diazaspiro[4.5]decan-2-one (13c):



13c

Yield : 0.165 g, 64%, Yellow liquid.

$[\alpha]_D^{25}$: –56.8 (c=1.05, CH$_3$Cl).

IR (neat) : 3319, 2928, 1686, 1612, 1484, 1418, 1098, 1028, cm^{-1}**.**

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.34–7.29 (m, 2H), 7.24–7.09 (m, 3H), 3.78 -3.72 (m, 1H), 3.11-3.06 (m, 1H), 2.97-2.89 (m, 1H), 2.72 (s, 3H), 1.74–1.38 (m, 9H,), 1.13-0.96 (m, 1H), 0.93 (d, *J* = 12.3, 1H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 173.6, 137.8, 129.9, 128.7, 126.8, 77.6, 59.4, 38.1, 36.6, 33.8, 25.5, 25.1, 22.9, 22.2.

LCMS : m/z 258 (M+1).

Analysis : for C$_{16}$H$_{22}$N$_2$O

calcd: C 74.38, H 8.58, N 10.84.

found: C 74.32, H 8.52, N 10.79.

6.4.3 Preparation of Electrochemical Cells

Simple solution processing and casting techniques were followed for the construction of the cell device.

Table 1: Cell configuration 8a

The PEO was dissolved in dichloromethane and mixed with TiO$_2$ powder. DCM was removed to obtain a paste for coating on Al and Graphite foils. After 1 h, (*S*)-5-benzyl-2,2,3-trimethylimidazolidin-4-one **13a** /Cl$_4$BQ/PC/PEO mixed in DCM for drop coated on Graphite foils and dried also coated layer on Al and dried in air at room temperature for overnight. The cell was prepared by sandwiching the coated Al/Gr layers. The rim of the cell was sealed all around using a commercial adhesive paste and covered with cellophane tape.

Table 1. Cell Experiments – Four layers configuration

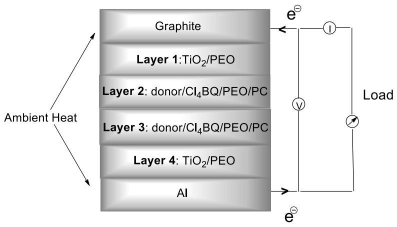
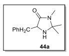
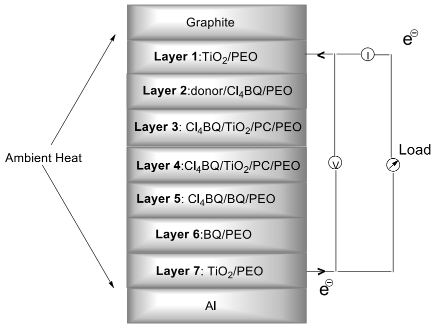
Cell Configuration 8a 									
1 	Gr----------------- Layer 1: TiO_2 (0.75 g) + PEO (0.05 g) Layer 2: amine **13a** (0.1 g) + Cl_4BQ (0.1 g) + PC (0.5 g) + PEO (0.05 g) Layer 3: amine **13a** (0.1) + Cl_4BQ (0.1 g) + PC (0.5 g) + PEO (0.05 g) Layer 4: TiO_2 (0.75 g) + PEO (0.05 g) Al-----------------	1 h	28 ºC	1.012	6.360	0.494	3.324	1.641	0.255
			35 ºC	1.038	6.839	0.505	3.607	1.821	0.256
			40 ºC	0.986	8.330	0.485	4.455	2.161	0.263
		48 h	40 ºC	0.125	0.359	0.059	0.190	0.017	0.249

Table 2: Cell configuration 10a

The PEO was dissolved in dichloromethane and mixed with TiO_2 powder. DCM was removed to obtain a paste for coating on Al or Graphite foils. After 1 h, Amine donor **13**/Cl_4BQ/ PEO in DCM was drop coated on TiO_2/PEO/Gr and dried. The Cl_4BQ/BQ/PEO and BQ/PEO layers were coated on TiO_2/PEO/Al. The Cl_4BQ/TiO_2/PC/PEO 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 was sealed all around using a commercial adhesive paste and covered with cellophane tape.

Table 2. Cell Experiments – Seven layer configuration with amine **13** and Cl_4BQ

Cell Confguration 10a



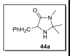
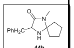
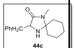
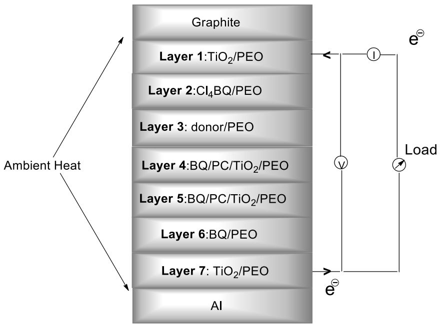
1  44a	Gr----------------- Layer 1: TiO_2 (0.5 g) + PEO (0.05 g) Layer 2: amine **13a** (0.218 g) + Cl_4BQ (0.25 g) + PEO (0.05 g) Layer 3: Cl_4BQ (0.025 g) + TiO_2 (0.25 g) +PC (0.5 g) + PEO (0.05 g) Layer 4: Cl_4BQ (0.025 g) + TiO_2 (0.25 g) +PC (0.5 g) + PEO (0.05 g) Layer 5: Cl_4BQ (0.1 g) +BQ (0.1 g) + PEO (0.05 g) Layer 6: BQ (0.2 g) + PEO (0.05 g) Layer 7: TiO_2 (0.5 g) + PEO (0.05 g) Al------------------	1 h	28 ºC	1.128	8.031	0.523	3.977	2.080	0.230
			35 ºC	1.134	9.758	0.550	4.963	2.729	0.247
			40 ºC	1.137	10.18	0.561	5.318	2.982	0.258
		48 h	28 ºC	1.124	3.156	0.541	1.630	0.880	0.249
			35 ºC	1.106	3.860	0.549	2.013	1.105	0.259
			40 ºC	1.113	4.161	0.580	2.174	1.260	0.272
2  44b	Gr----------------- Layer 1: TiO_2 (0.5 g) + PEO (0.05 g) Layer 2: amine **13b** (0.244 g) + Cl_4BQ (0.25 g) + PEO (0.05 g) Layer 3: Cl_4BQ (0.025 g) + TiO_2 (0.25 g) +PC (0.5 g) + PEO (0.05 g) Layer 4: Cl_4BQ (0.025 g) + TiO_2 (0.25 g) +PC (0.5 g) + PEO (0.05 g) Layer 5: Cl_4BQ (0.1 g) +BQ (0.1 g) + PEO (0.05 g) Layer 6: BQ (0.2 g) + PEO (0.05 g) Layer 7: TiO_2 (0.5 g) + PEO (0.05 g) Al------------------	1 h	28 ºC	1.127	8.866	0.535	4.544	2.429	0.243
			35 ºC	1.134	8.811	0.555	4.570	2.535	0.254
			40 ºC	1.143	10.34	0.581	5.487	3.185	0.270
		48 h	28 ºC	1.070	2.643	0.514	1.346	0.691	0.245
			35 ºC	1.071	3.140	0.520	1.640	0.853	0.254
			40 ºC	1.076	3.582	0.527	1.807	0.952	0.247
3  44c	Gr----------------- Layer 1: TiO_2 (0.5 g) + PEO (0.05 g) Layer 2: amine **13c** (0.258 g) + Cl_4BQ (0.25 g) + PEO (0.05 g) Layer 3: Cl_4BQ (0.025 g) + TiO_2 (0.25 g) +PC (0.5 g) + PEO (0.05 g) Layer 4: Cl_4BQ (0.025 g) + TiO_2 (0.25 g) +PC (0.5 g) + PEO (0.05 g) Layer 5: Cl_4BQ (0.1 g) +BQ (0.1 g) + PEO (0.05 g) Layer 6: BQ (0.2 g) + PEO (0.05 g) Layer 7: TiO_2 (0.5 g) + PEO (0.05 g) Al------------------	1 h	28 ºC	1.140	9.598	0.528	4.701	2.480	0.227
			35 ºC	1.144	10.51	0.544	5.831	2.847	0.237
			40 ºC	1.152	11.98	0.558	6.297	3.512	0.255
		48 h	28 ºC	1.128	4.415	0.539	2.189	1.179	0.237
			35 ºC	1.141	5.645	0.566	2.851	1.613	0.250
			40 ºC	1.122	6.512	0.591	3.520	2.081	0.288

Table 3: Cell configuration 11a

The PEO was dissolved in dichloromethane and mixed with TiO_2 powder. DCM was removed to obtain a paste for coating on Al or Graphite foils. After 1 h, BQ/PEO in DCM was drop coated on TiO_2/PEO/Al and dried. The Cl_4BQ/PEO and Amine donor **13**/PEO layers were coated on TiO_2/PEO/Gr and dried over 1 h. The BQ/TiO_2/PC/PEO 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 was sealed all around using a commercial adhesive paste and covered with cellophane tape.

Table 3. Cell Experiments – Seven layers with Cl_4BQ and amine in layer 2 and 3

Cell Confguration 11a



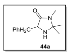
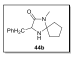
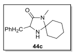
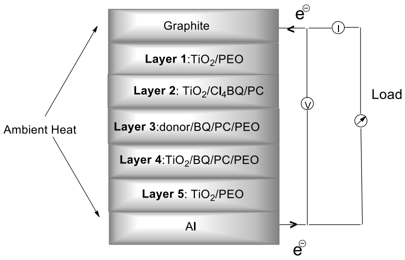
1 	Gr----------- Layer 1: TiO_2 (0.5 g) + PEO (0.05 g) Layer 2: Cl_4BQ (0.25 g) + PEO (0.05 g) Layer 3: amine **13a** (0.218 g) + PEO (0.05 g) Layer 4: BQ (0.11 g) + PC (0.5 g) + TiO_2 (0.25 g + PEO (0.05 g) Layer 5: BQ (0.11 g) + PC (0.5 g) + TiO_2 (0.25 g + PEO (0.05 g) Layer 6: BQ (0.22 g) + PEO (0.05 g) Layer 7: TiO_2 (0.5 g) + PEO (0.05 g) Al----------	1 h	28 °C	1.140	9.004	0.528	4.568	2.411	0.235
			35 °C	1.135	10.22	0.526	5.083	2.672	0.231
			40 °C	1.143	10.03	0.568	5.180	2.941	0.257
		48 h	28 °C	1.044	2.626	0.497	1.280	0.636	0.232
			35 °C	1.045	3.637	0.505	1.790	0.903	0.238
			40 °C	1.039	3.821	0.489	1.946	0.951	0.240
2 	Gr----------- Layer 1: TiO_2 (0.5 g) + PEO (0.05 g) Layer 2: Cl_4BQ (0.25 g) + PEO (0.05 g) Layer 3: amine **13b** (0.244 g) + PEO (0.05 g) Layer 4: BQ (0.11 g) + PC (0.5 g) + TiO_2 (0.25 g + PEO (0.05 g) Layer 5: BQ (0.11 g) + PC (0.5 g) + TiO_2 (0.25 g + PEO (0.05 g) Layer 6: BQ (0.22 g) + PEO (0.05 g) Layer 7: TiO_2 (0.5 g) + PEO (0.05 g) Al----------	1 h	28 °C	1.133	6.888	0.537	3.352	1.801	0.231
			35 °C	1.144	7.121	0.540	3.612	1.950	0.239
			40 °C	1.150	7.666	0.567	3.850	2.185	0.248
		48 h	28 °C	1.102	3.446	0.529	1.690	0.893	0.255
			35 °C	1.114	4.264	0.545	2.159	1.177	0.248
			40 °C	1.112	4.573	0.544	2.335	1.271	0.250
3 	Gr----------- Layer 1: TiO_2 (0.5 g) + PEO (0.05 g) Layer 2: Cl_4BQ (0.25 g) + PEO (0.05 g) Layer 3: amine **13c** (0.258 g) + PEO (0.05 g) Layer 4: BQ (0.11 g) + PC (0.5 g) + TiO_2 (0.25 g + PEO (0.05 g) Layer 5: BQ (0.11 g) + PC (0.5 g) + TiO_2 (0.25 g + PEO (0.05 g) Layer 6: BQ (0.22 g) + PEO (0.05 g) Layer 7: TiO_2 (0.5 g) + PEO (0.05 g) Al----------	1 h	28 °C	1.119	9.520	0.539	4.713	2.595	0.241
			35 °C	1.121	9.584	0.531	4.878	2.588	0.241
			40 °C	1.118	10.68	0.522	5.347	2.949	0.247
		48 h	28 °C	0.851	0.941	0.402	0.438	0.176	0.220
			35 °C	0.855	1.164	0.425	0.542	0.230	0.212
			40 °C	0.855	1.247	0.408	0.612	0.249	0.234

Table 4: Cell configuration 12a with five layers

The PEO was dissolved in dichloromethane and mixed with TiO_2 powder. DCM was removed to obtain a paste for coating on Al or Graphite foils. After 1 h, TiO_2/BQ/PC/PEO in DCM was drop coated on TiO_2/PEO/Al and dried. The Cl_4BQ/PC/TiO_2/PEO layer was coated on TiO_2/PEO/Gr and dried over 1 h. The amine donor **13**/BQ/PC/PEO slurry was prepared and casted above the heat coated layer on Al side before packing. The cell was prepared by sandwiching the coated Al/Gr layers. The rim of the cell was sealed all around using a commercial adhesive paste and covered with cellophane tape.

Table 4. Cell Experiments – Five layers cell using BQ as electron transporter

Cell Confguration 12a



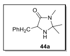
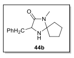
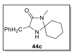
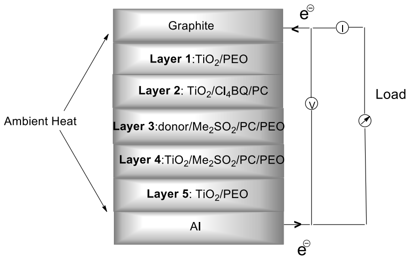
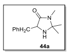
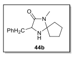
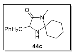
1  44a	Gr------- Layer 1: TiO$_2$ (0.5 g) + PEO (0.05 g) Layer 2: TiO$_2$ (0.5 g) + Cl$_4$BQ (0.25 g) + PC (0.5 g) + PEO (0.05 g) Layer 3: McMillan Me$_2$ (0.218 g) + BQ (0.11 g) + PC (0.5 g) + PEO (0.1 g) Layer 4: TiO$_2$ (0.5 g) + BQ (0.44 g) + PC (0.5 g) + PEO (0.05 g) Layer 5: TiO$_2$ (0.5 g) + PEO (0.05 g) Al----------	1 h	28 °C	1.079	6.780	0.561	3.699	2.076	0.284
			35 °C	1.099	7.930	0.591	4.181	2.469	0.283
			40 °C	1.096	8.081	0.568	4.448	2.527	0.288
		48 h	28 °C	1.046	3.240	0.448	1.426	0.638	0.188
			35 °C	1.047	4.630	0.444	2.090	0.927	0.191
			40 °C	1.042	4.770	0.438	2.120	0.928	0.187
2  44b	Gr------- Layer 1: TiO$_2$ (0.5 g) + PEO (0.05 g) Layer 2: TiO$_2$ (0.5 g) + Cl$_4$BQ (0.25 g) + PC (0.5 g) + PEO (0.05 g) Layer 3: amine **13b** (0.244 g) + BQ (0.11 g) + PC (0.5 g) + PEO (0.1 g) Layer 4: TiO$_2$ (0.5 g) + BQ (0.44 g) + PC (0.5 g) + PEO (0.05 g) Layer 5: TiO$_2$ (0.5 g) + PEO (0.05 g) Al----------	1 h	28 °C	1.074	5.465	0.598	3.030	1.813	0.309
			35 °C	1.102	7.071	0.604	3.834	2.317	0.297
			40 °C	1.096	7.171	0.610	3.886	2.371	0.302
		48 h	28 °C	1.108	4.926	0.463	2.339	1.083	0.199
			35 °C	1.108	6.806	0.469	3.287	1.541	0.204
			40 °C	1.103	7.390	0.467	3.537	1.650	0.202
3  44c	Gr------- Layer 1: TiO$_2$ (0.5 g) + PEO (0.05 g) Layer 2: TiO$_2$ (0.5 g) + Cl$_4$BQ (0.25 g) + PC (0.5 g) + PEO (0.05 g) Layer 3: amine **13c** (0.258 g) + BQ (0.11 g) + PC (0.5 g) + PEO (0.1 g) Layer 4: TiO$_2$ (0.5 g) + BQ (0.44 g) + PC (0.5 g) + PEO (0.05 g) Layer 5: TiO$_2$ (0.5 g) + PEO (0.05 g) Al----------	1 h	28 °C	1.119	7.996	0.578	4.161	2.404	0.269
			35 °C	1.113	8.624	0.583	4.358	2.538	0.268
			40 °C	1.096	8.715	0.528	4.438	2.565	0.268
		48 h	28 °C	1.075	2.069	0.489	0.972	0.475	0.214
			35 °C	1.074	3.444	0.463	1.583	0.737	0.198
			40 °C	1.071	6.823	0.432	3.154	1.363	0.187

Table 5: Cell configuration 13a with five layers

The PEO was dissolved in dichloromethane and mixed with TiO$_2$ powder. DCM was removed to obtain a paste for coating on Al or Graphite foils. After 1 h, TiO$_2$/Me$_2$SO$_2$/PC/PEO in DCM was drop coated on TiO$_2$/PEO/Al and dried. The

$Cl_4BQ/PC/TiO_2/PEO$ layer was coated on $TiO_2/PEO/Gr$ and dried over 1 h. The amine donor **13**/$Me_2SO_2/PC/PEO$ slurry was prepared and casted above the heat coated layer on Al side before packing. The cell was prepared by sandwiching the coated Al/Gr layers. The rim of the cell was sealed all around using a commercial adhesive paste and covered with cellophane tape.

Table 5. Cell Experiments – Five layers cell using Me_2SO_2 as electron transporter

Cell Confguration 13a 									
1 	Gr----------- Layer 1: TiO_2 (0.5 g) + PEO (0.05 g) Layer 2: TiO_2 (0.5 g) + Cl_4BQ (0.25 g) + PC (0.5 g) + PEO (0.05 g) Layer 3: amine **13a** (0.218 g) + Me_2SO_2 (0.094 g) + PC (0.5 g) + PEO (0.1 g) Layer 4: TiO_2 (0.5 g) + Me_2SO_2 (0.188 g) + PC (0.5 g) + PEO (0.05 g) Layer 5: TiO_2 (0.5 g) + PEO (0.05 g) Al----------	1 h	28 °C	1.023	12.19	0.487	6.412	3.119	0.250
			35 °C	1.030	14.35	0.506	7.685	3.887	0.262
			40 °C	1.132	6.520	0.559	3.168	1.770	0.240
		48 h	28 °C	1.055	5.175	0.519	2.689	1.395	0.255
			35 °C	1.046	6.944	0.525	3.636	1.909	0.263
			40 °C	1.051	7.373	0.591	4.002	2.077	0.268
2 	Gr----------- Layer 1: TiO_2 (0.5 g) + PEO (0.05 g) Layer 2: TiO_2 (0.5 g) + Cl_4BQ (0.25 g) + PC (0.5 g) + PEO (0.05 g) Layer 3: amine **13b** (0.244 g) + Me_2SO_2 (0.094 g) + PC (0.5 g) + PEO (0.1 g) Layer 4: TiO_2 (0.5 g) + Me_2SO_2 (0.188 g) + PC (0.5 g) + PEO (0.05 g) Layer 5: TiO_2 (0.5 g) + PEO (0.05 g) Al----------	1 h	28 °C	1.023	12.19	0.487	6.412	3.119	0.250
			35 °C	1.030	14.35	0.506	7.685	3.887	0.262
			40 °C	1.132	6.520	0.559	3.168	1.772	0.242
		48 h	28 °C	1.055	5.175	0.519	2.689	1.395	0.255
			35 °C	1.046	6.944	0.525	3.636	1.909	0.263
			40 °C	1.051	7.373	0.591	4.002	2.079	0.270
3 	Gr------- Layer 1: TiO_2 (0.5 g) + PEO (0.05 g) Layer 2: TiO_2 (0.5 g) + Cl_4BQ (0.25 g) + PC (0.5 g) + PEO (0.05 g) Layer 3: amine **13c** (0.258 g) + Me_2SO_2 (0.094 g) + PC (0.5 g) + PEO (0.1 g) Layer 4: TiO_2 (0.5 g) + Me_2SO_2 (0.188 g) + PC (0.5 g) + PEO (0.05 g) Layer 5: TiO_2 (0.5 g) + PEO (0.05 g) Al----------	1 h	28 °C	1.016	11.44	0.483	5.869	2.834	0.244
			35 °C	1.032	14.52	0.491	7.777	3.816	0.255
			40 °C	1.034	15.18	0.525	8.001	4.201	0.268
		48 h	28 °C	1.044	6.745	0.530	3.362	1.782	0.253
			35 °C	1.047	8.579	0.520	4.598	2.391	0.266
			40 °C	1.037	8.734	0.530	4.583	2.430	0.268

6.5 References

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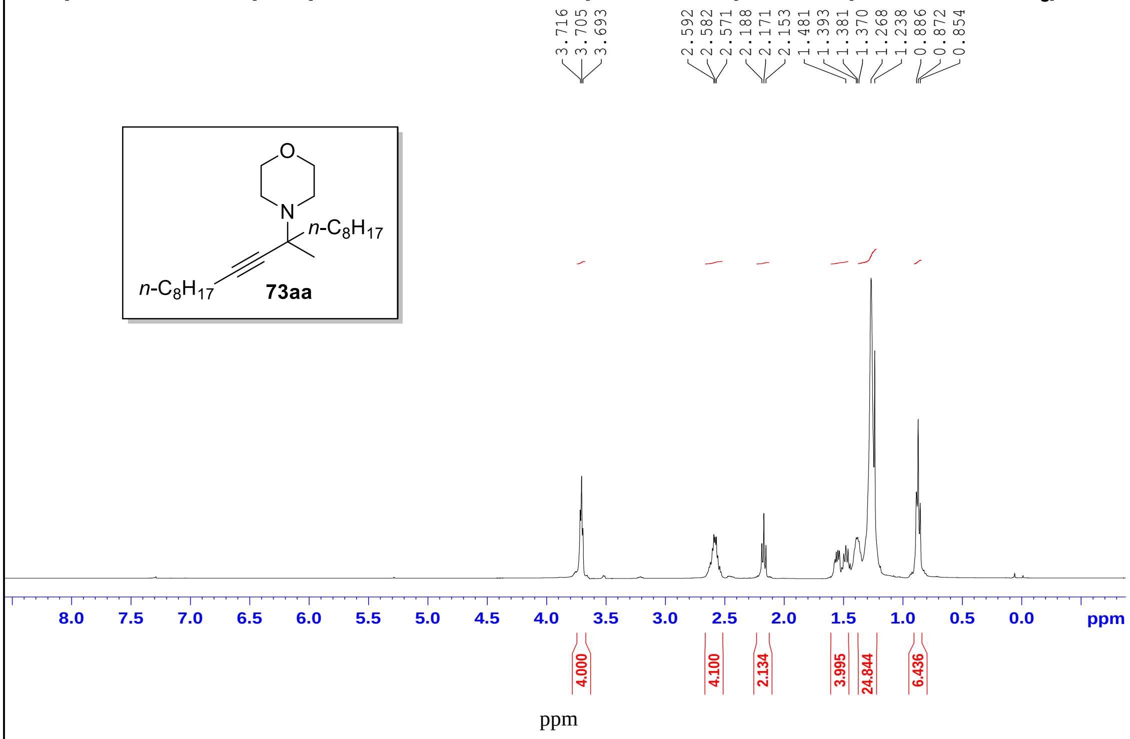
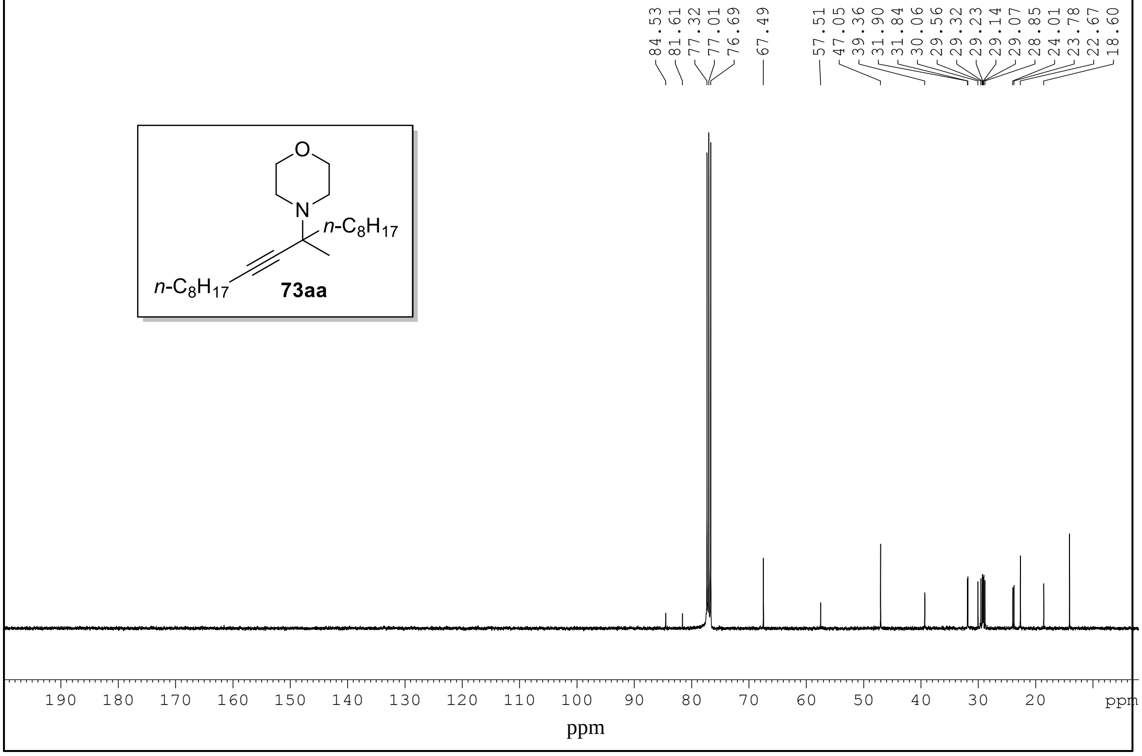
Appendix I

Representative Spectra

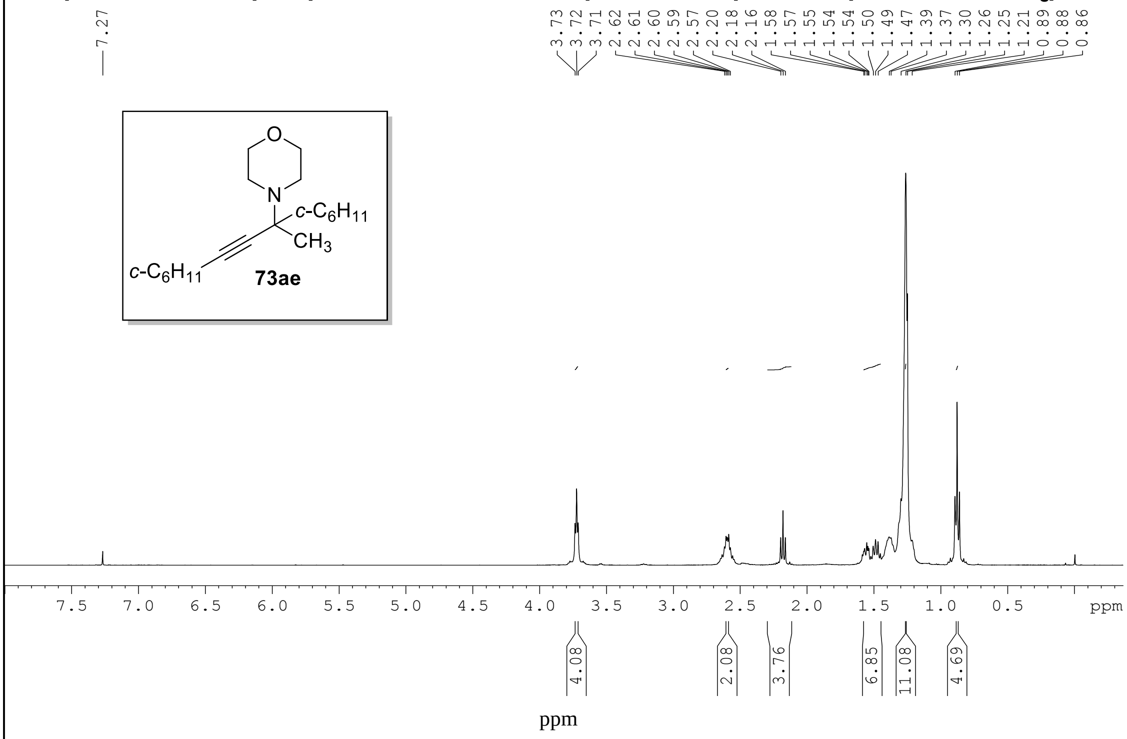
Spectrum No. 1 (Chapter 1 , Section 1.2.1.1), ^{1}H NMR Spectrum (400 MHz, CDCl$_3$)



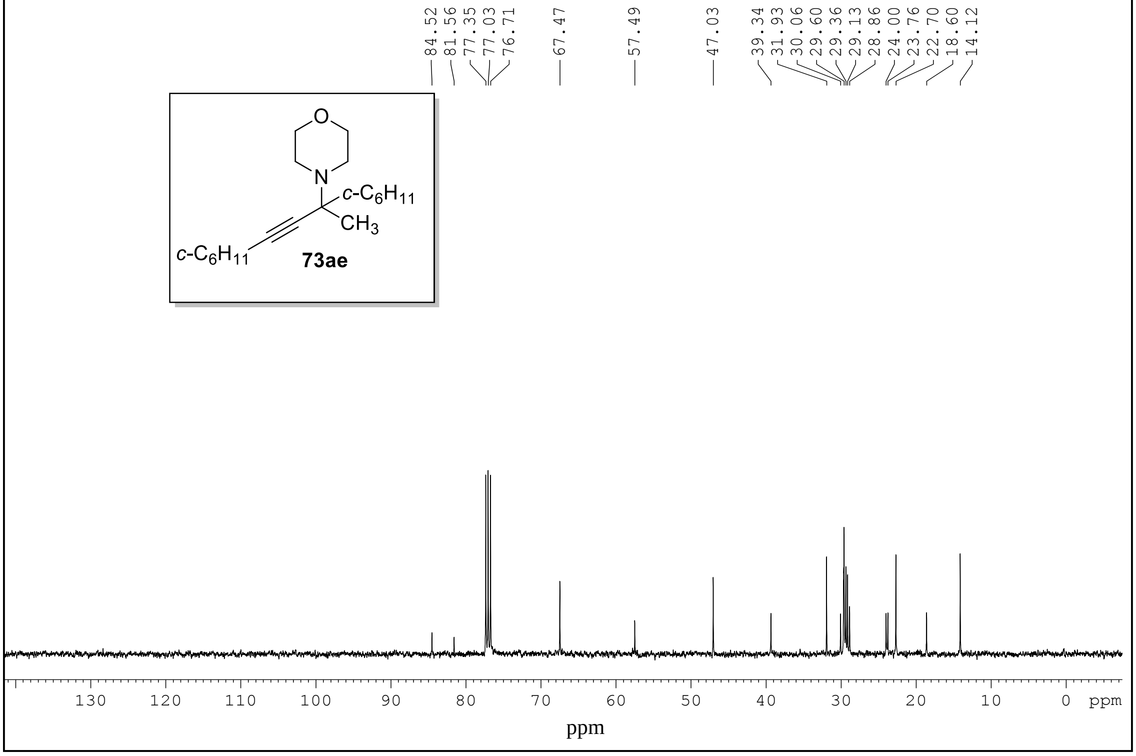
Spectrum No. 2 (Chapter 1, Section 1.2.1.1), ^{13}C NMR Spectrum (100 MHz, CDCl$_3$)



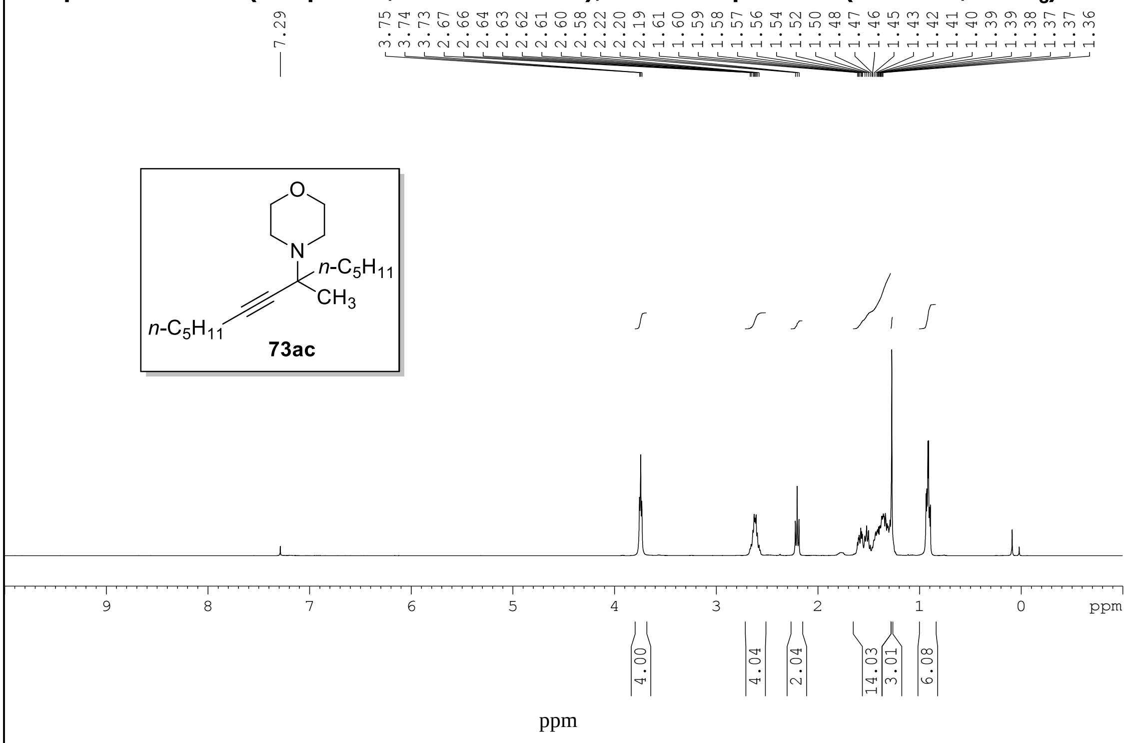
Spectrum No. 3 (Chapter 1 , Section 1.2.1.1), ^{1}H NMR Spectrum (400 MHz, CDCl$_3$)



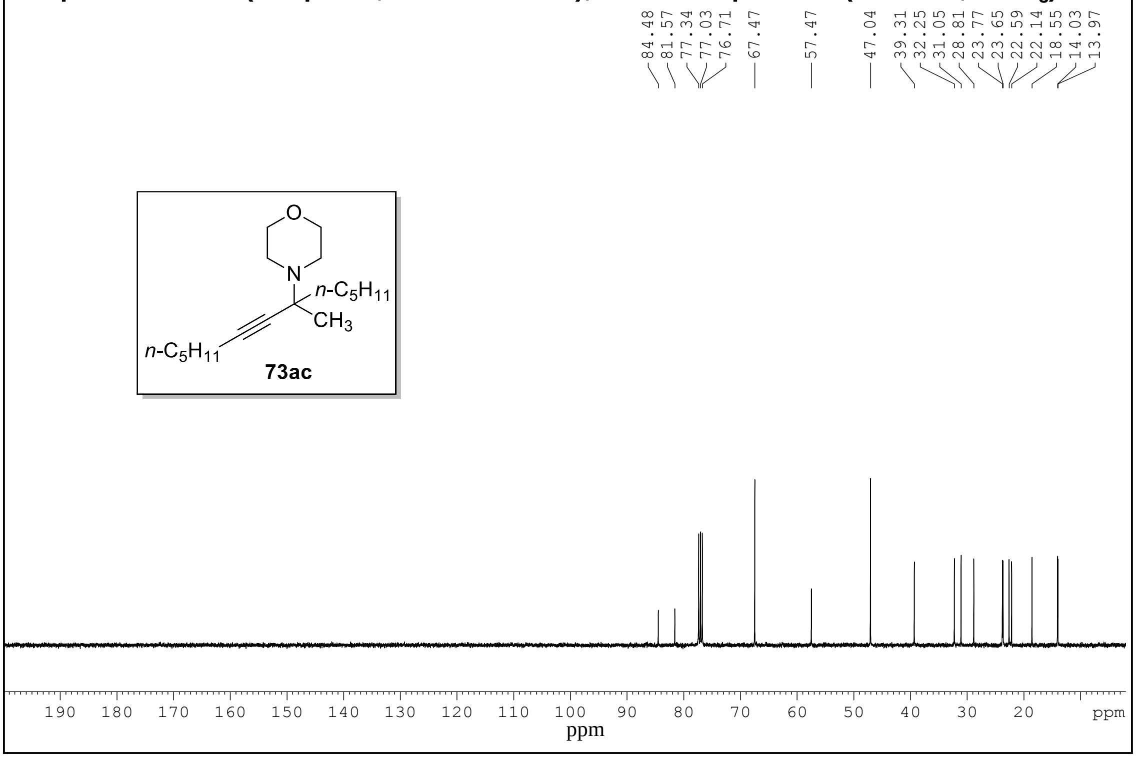
Spectrum No. 4 (Chapter 1, Section 1.2.1.1), ^{13}C NMR Spectrum (100 MHz, CDCl$_3$)



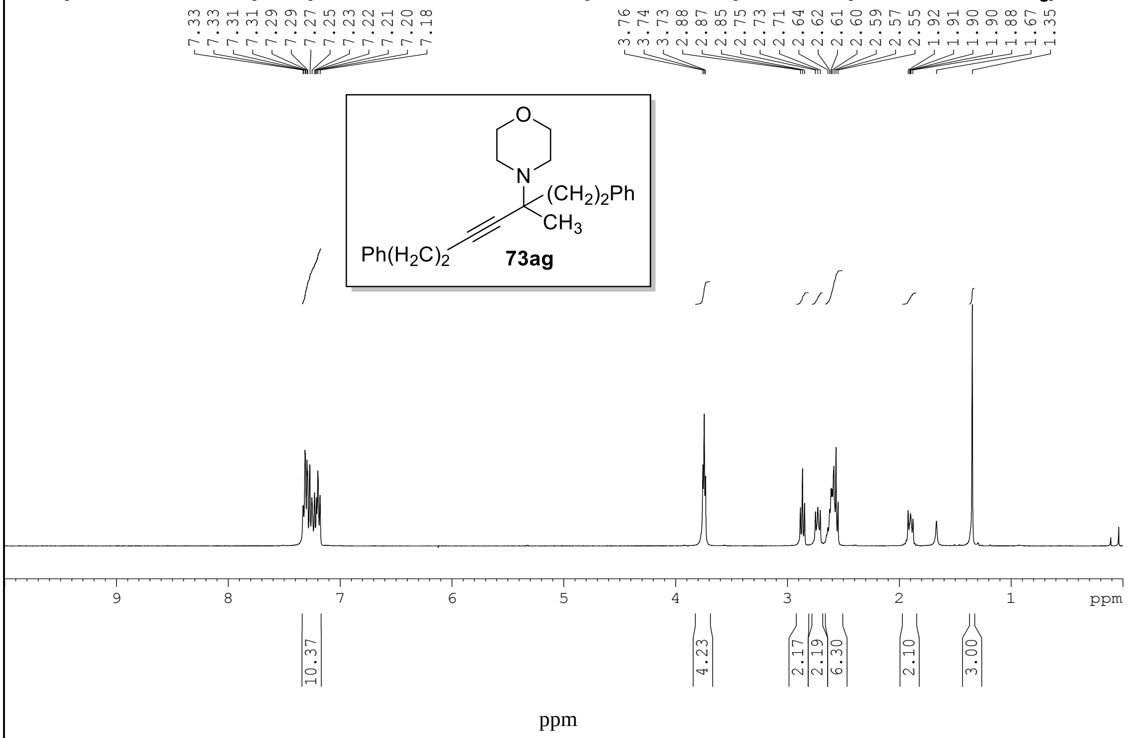
Spectrum No. 5 (Chapter 1 , Section 1.2.1.1), ^{1}H NMR Spectrum (400 MHz, CDCl$_3$)



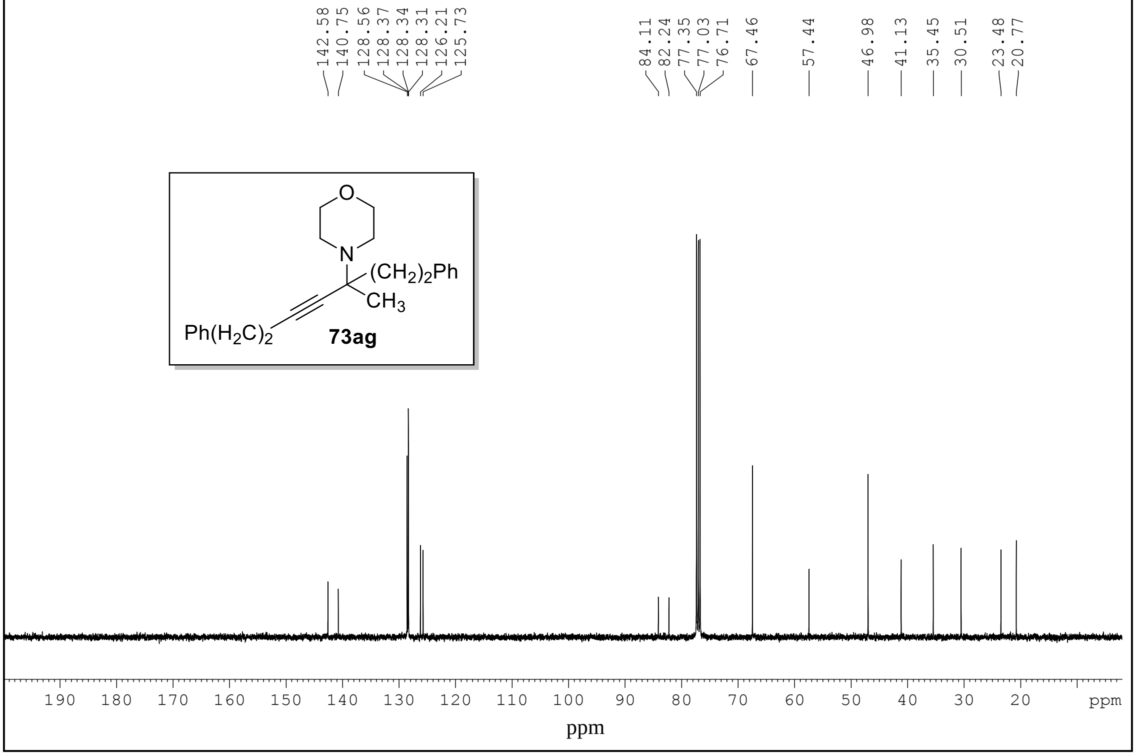
Spectrum No. 6 (Chapter 1, Section 1.2.1.1), ^{13}C NMR Spectrum (100 MHz, CDCl$_3$)



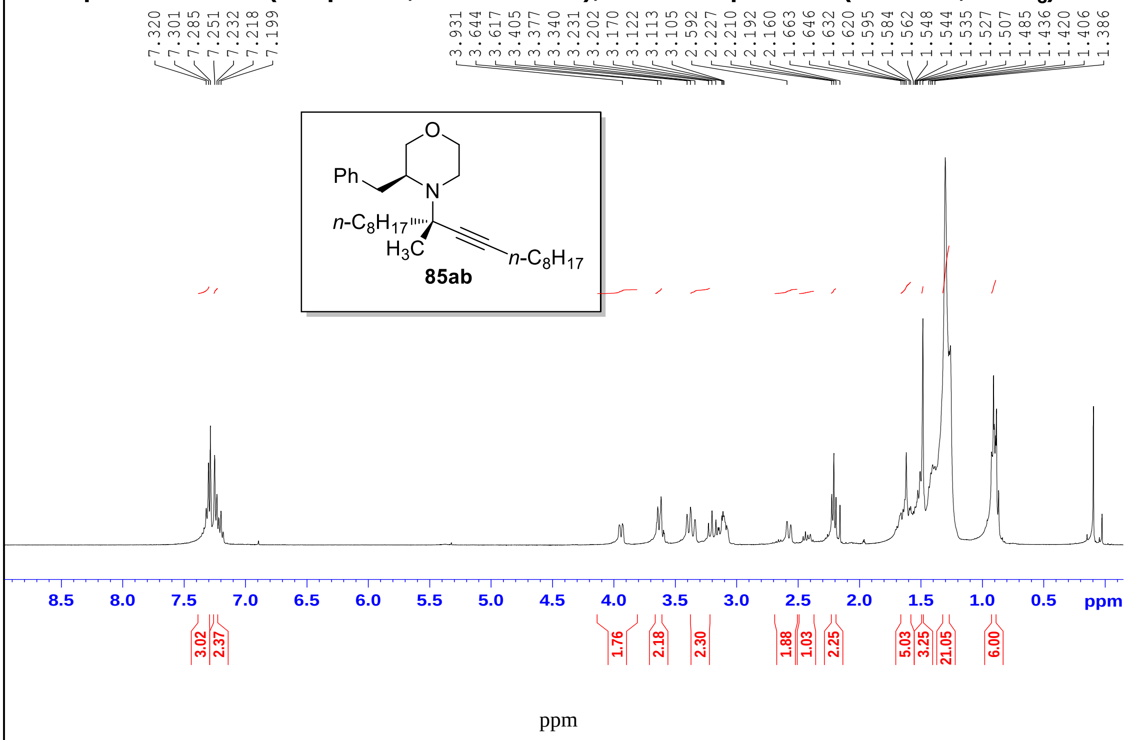
Spectrum No. 7 (Chapter 1 , Section 1.2.1.1), ^{1}H NMR Spectrum (400 MHz, CDCl$_3$)



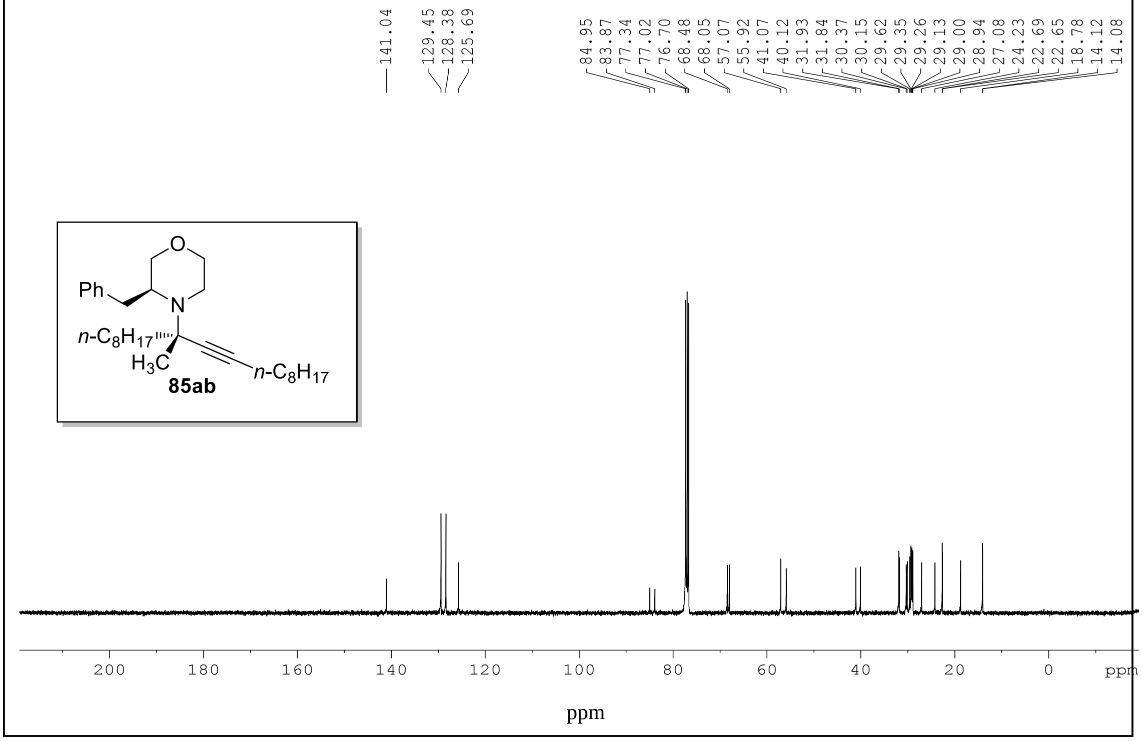
Spectrum No. 8 (Chapter 1, Section 1.2.1.1), ^{13}C NMR Spectrum (100 MHz, CDCl$_3$)



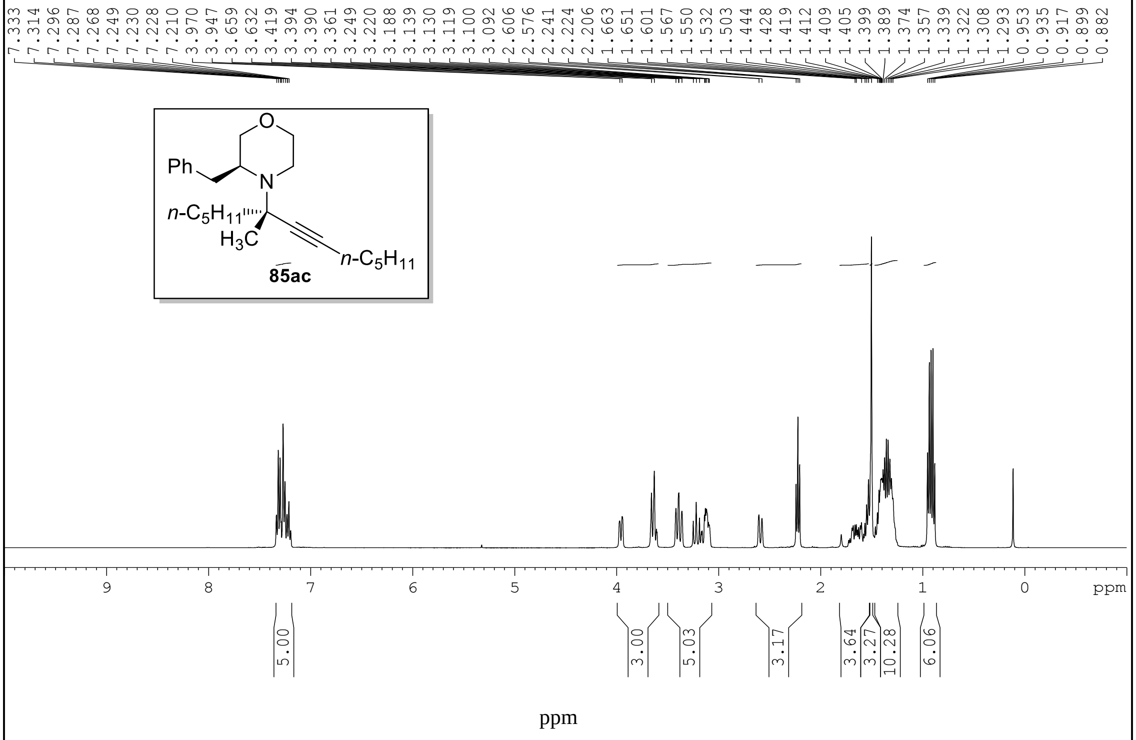
Spectrum No. 9 (Chapter 1 , Section 1.2.4), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



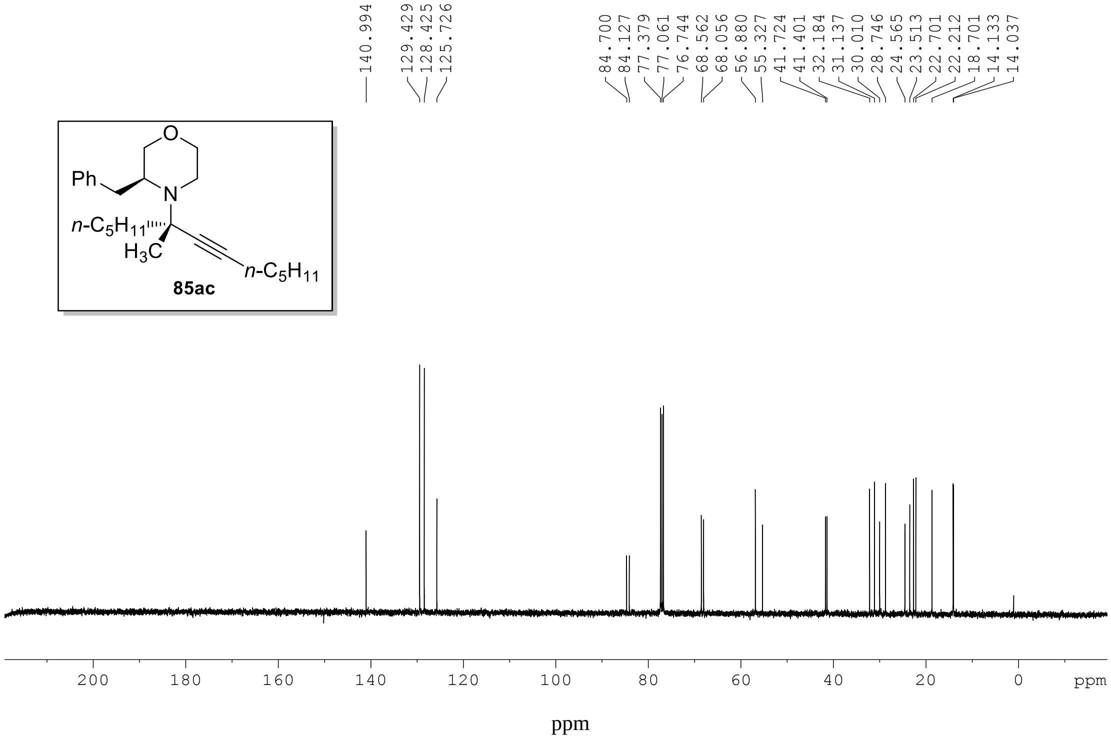
Spectrum No. 10 (Chapter 1, Section 1.2.4), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



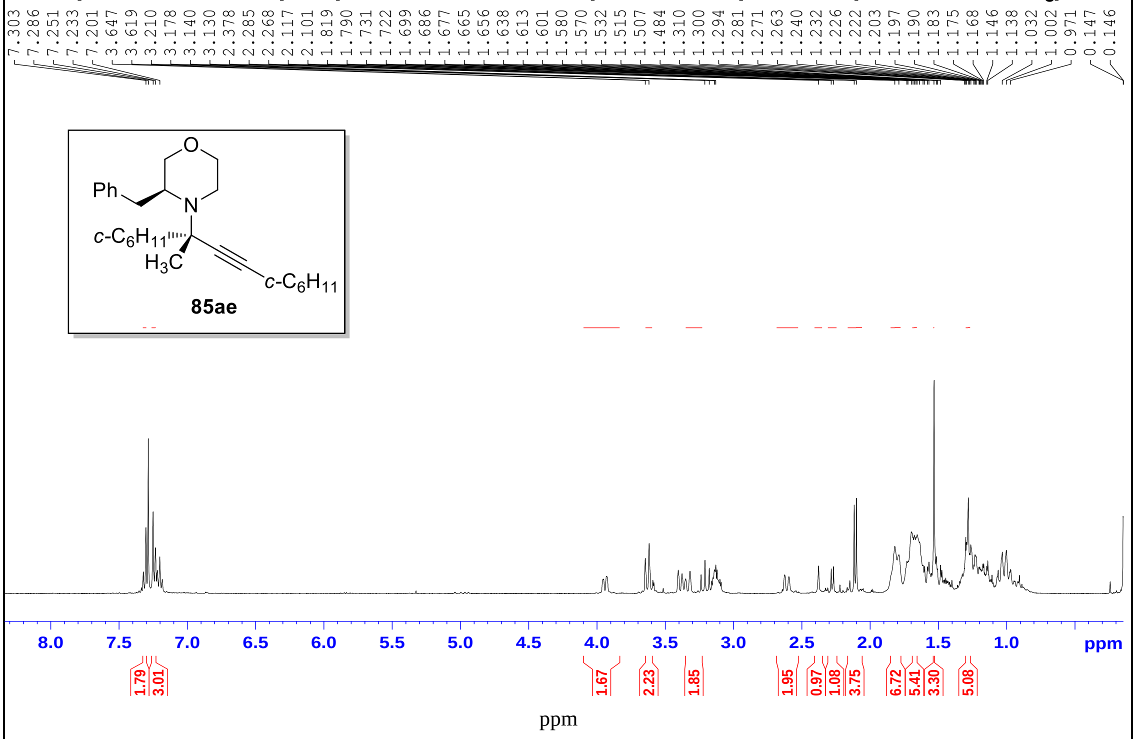
Spectrum No. 11 (Chapter 1 , Section 1.2.4), ^{1}H NMR Spectrum (400 MHz, CDCl$_3$)



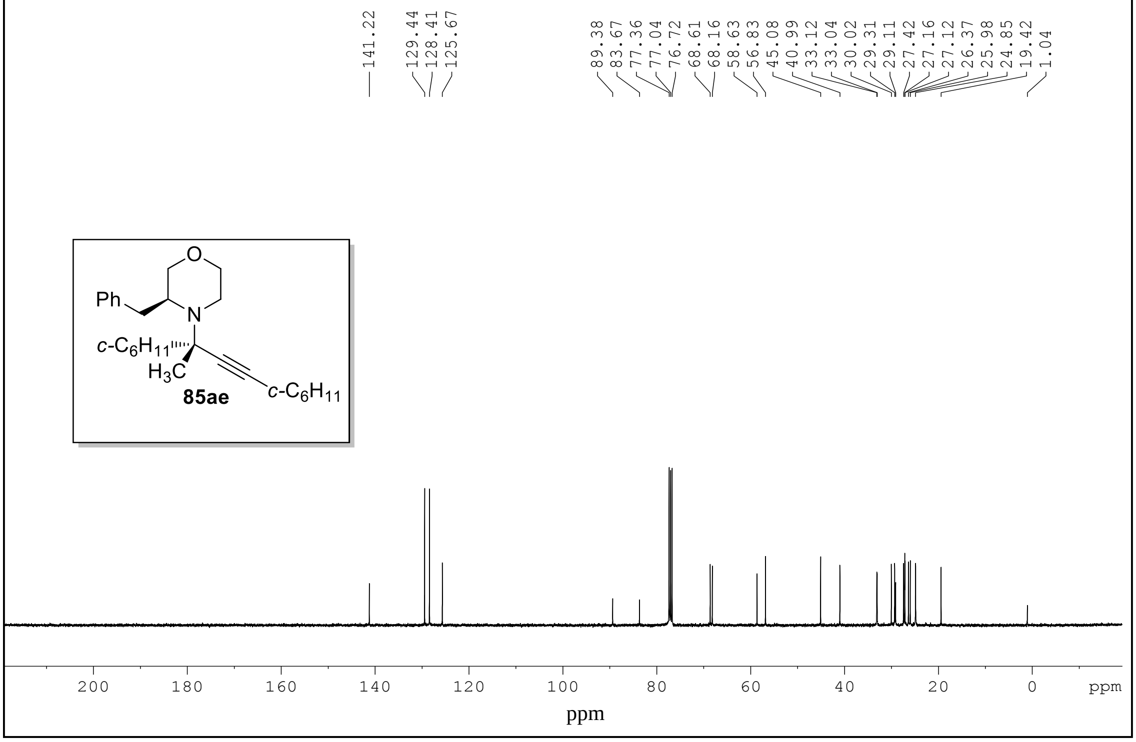
Spectrum No. 12 (Chapter 1, Section 1.2.4), ^{13}C NMR Spectrum (100 MHz, CDCl$_3$)



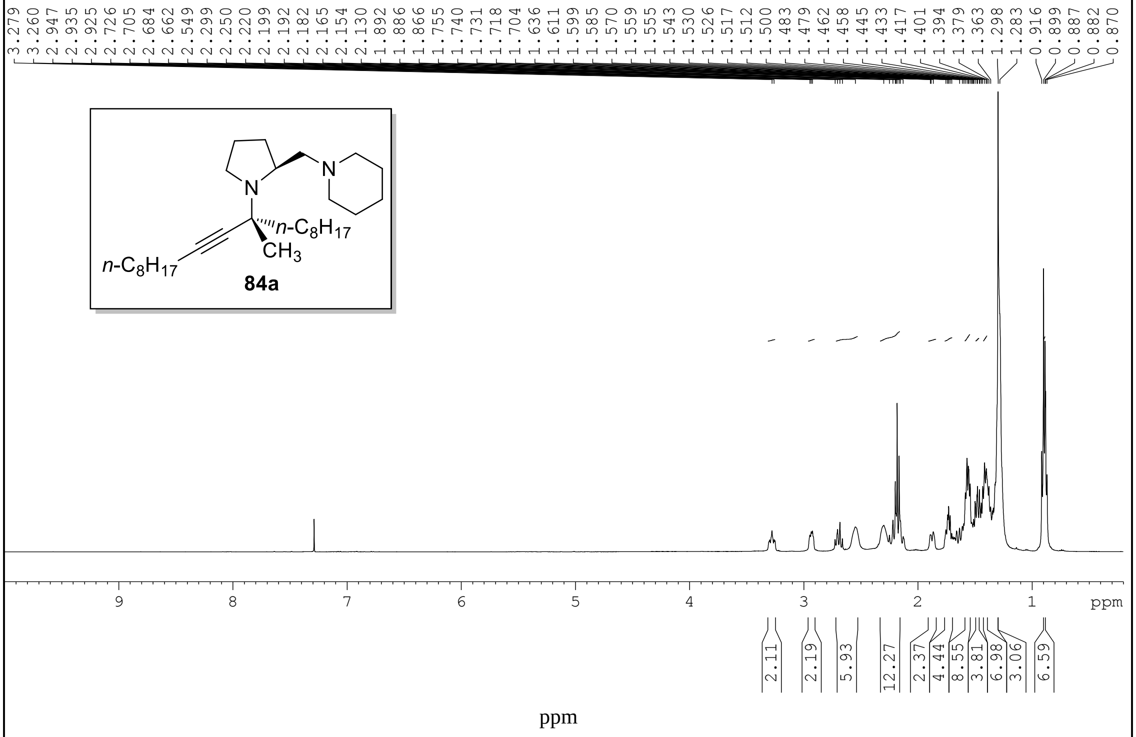
Spectrum No. 13 (Chapter 1 , Section 1.2.4), ^{1}H NMR Spectrum (400 MHz, CDCl$_3$)



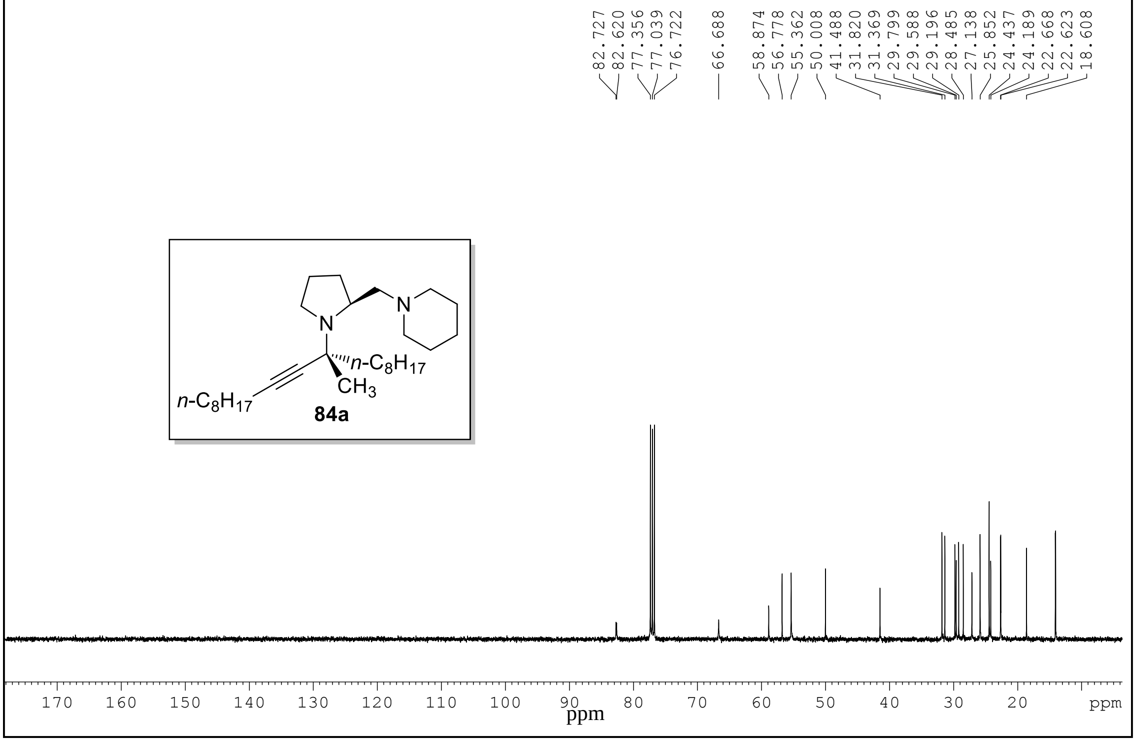
Spectrum No. 14 (Chapter 1, Section 1.2.4), ^{13}C NMR Spectrum (100 MHz, CDCl$_3$)



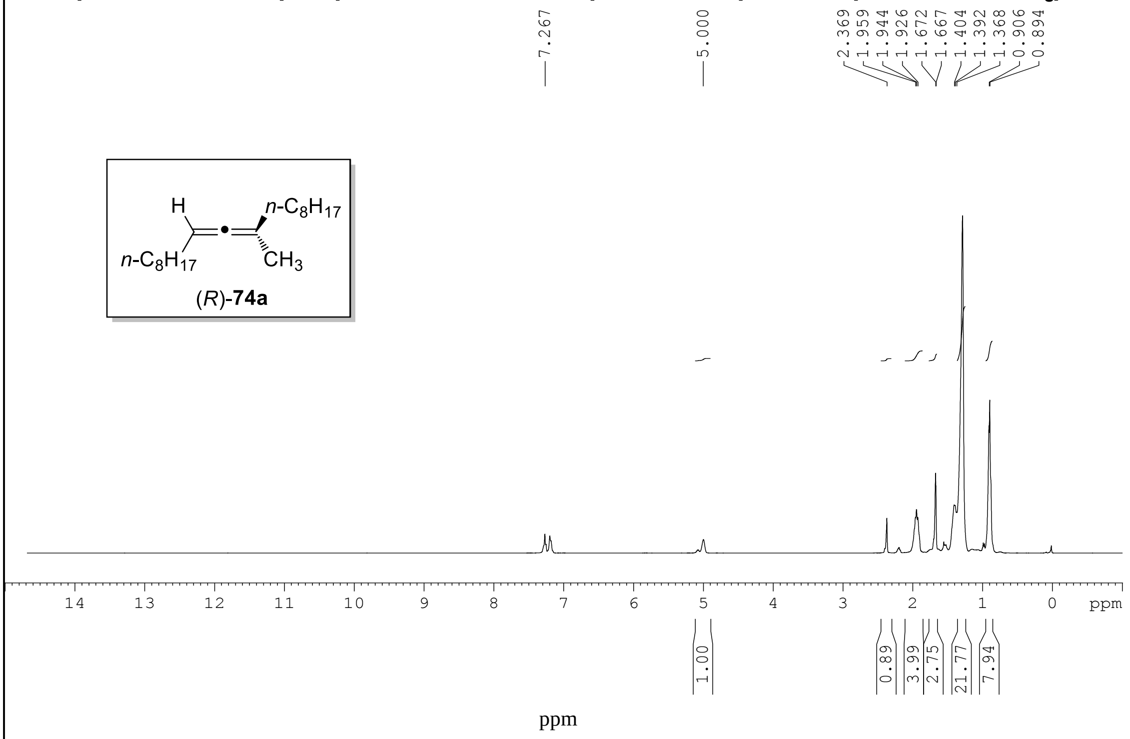
Spectrum No. 15 (Chapter 1 , Section 1.2.4), ^{1}H NMR Spectrum (400 MHz, CDCl$_3$)



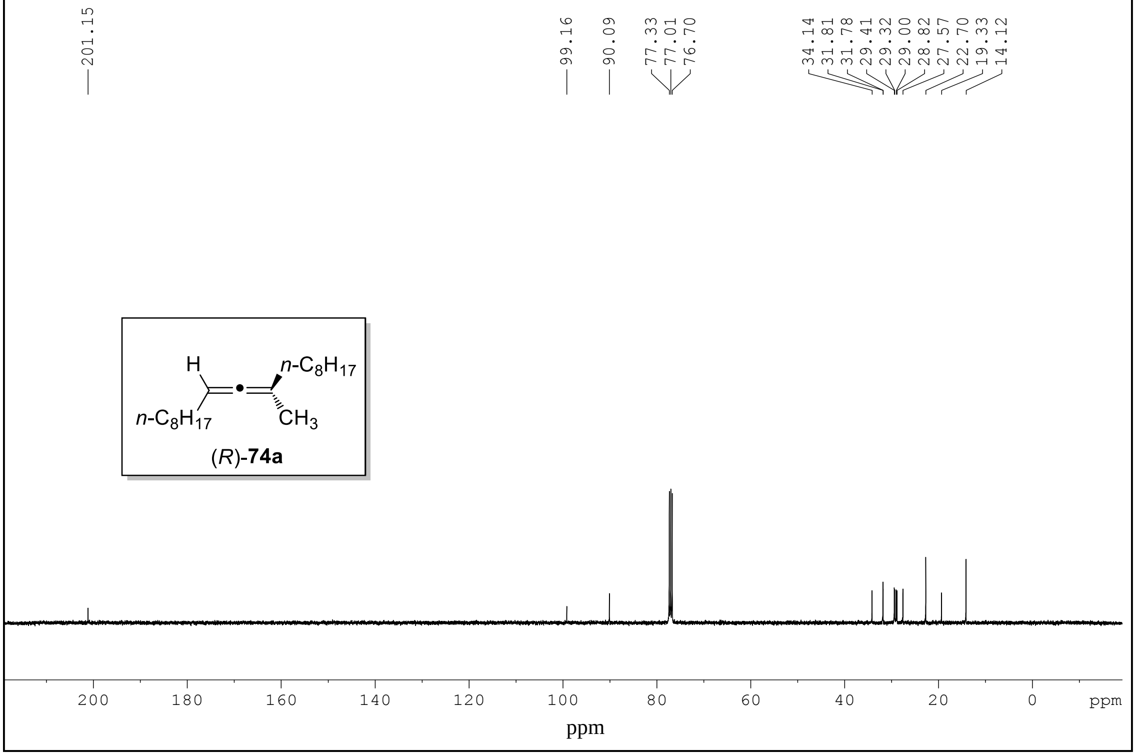
Spectrum No. 16 (Chapter 1, Section 1.2.4), ^{13}C NMR Spectrum (100 MHz, CDCl$_3$)



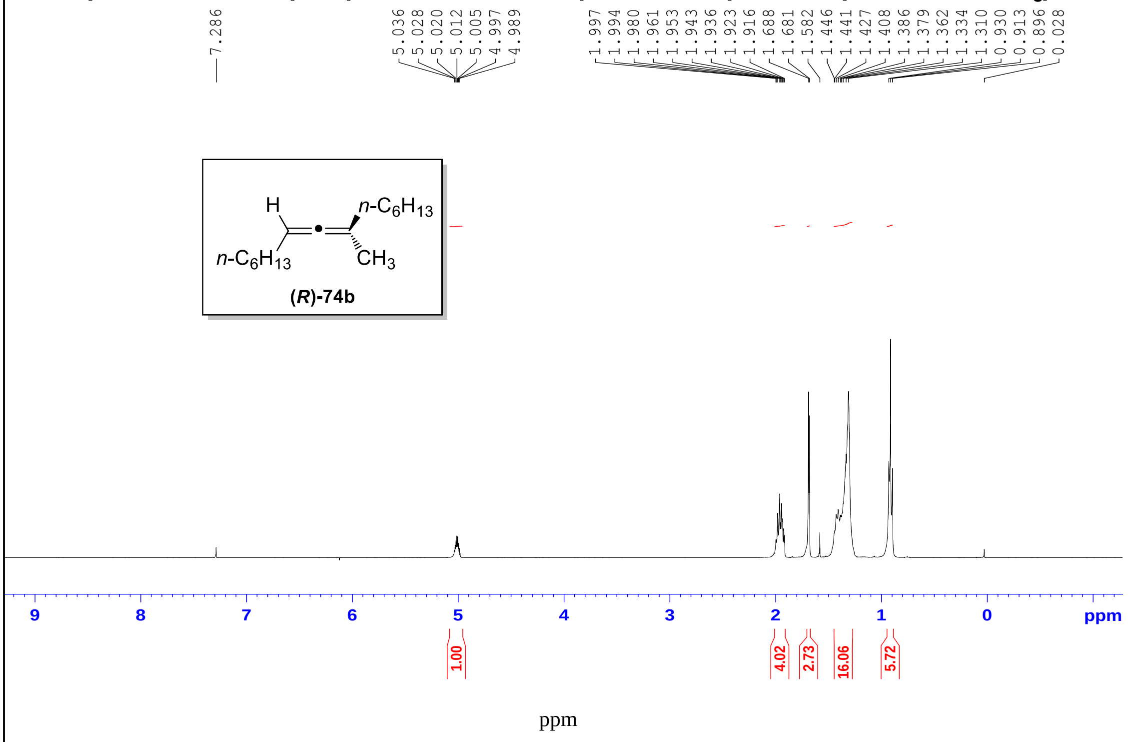
Spectrum No. 17 (Chapter 1 , Section 1.2.5), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



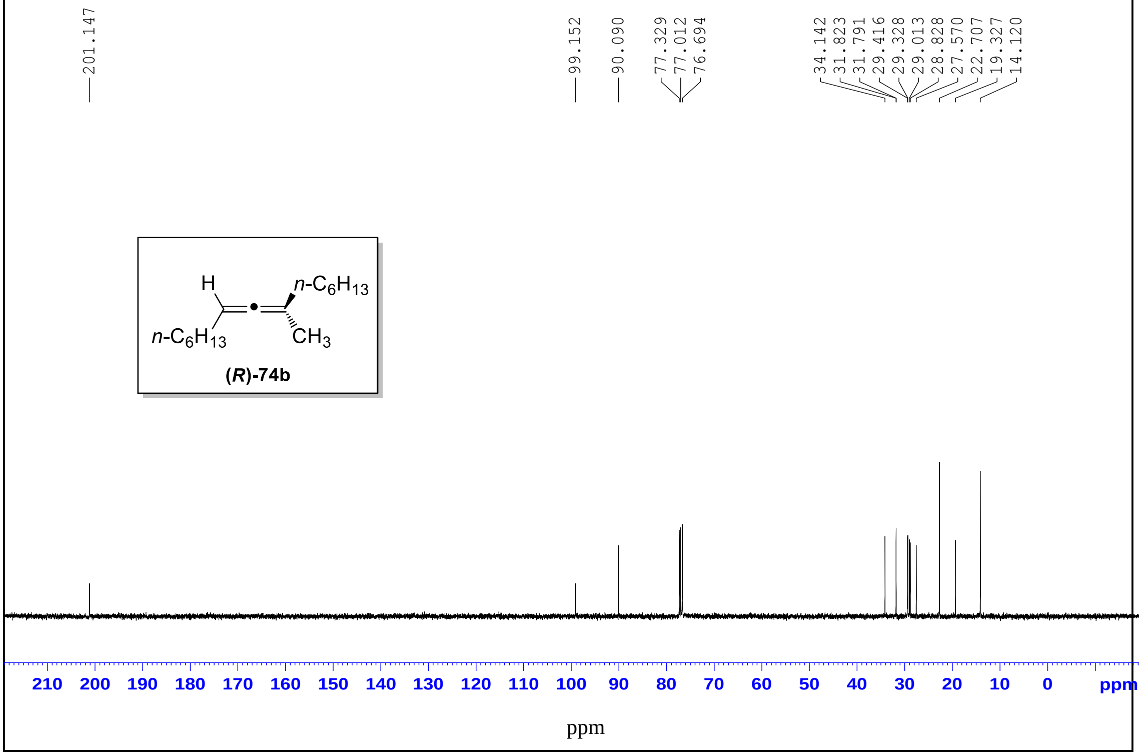
Spectrum No. 18 (Chapter 1, Section 1.2.5), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



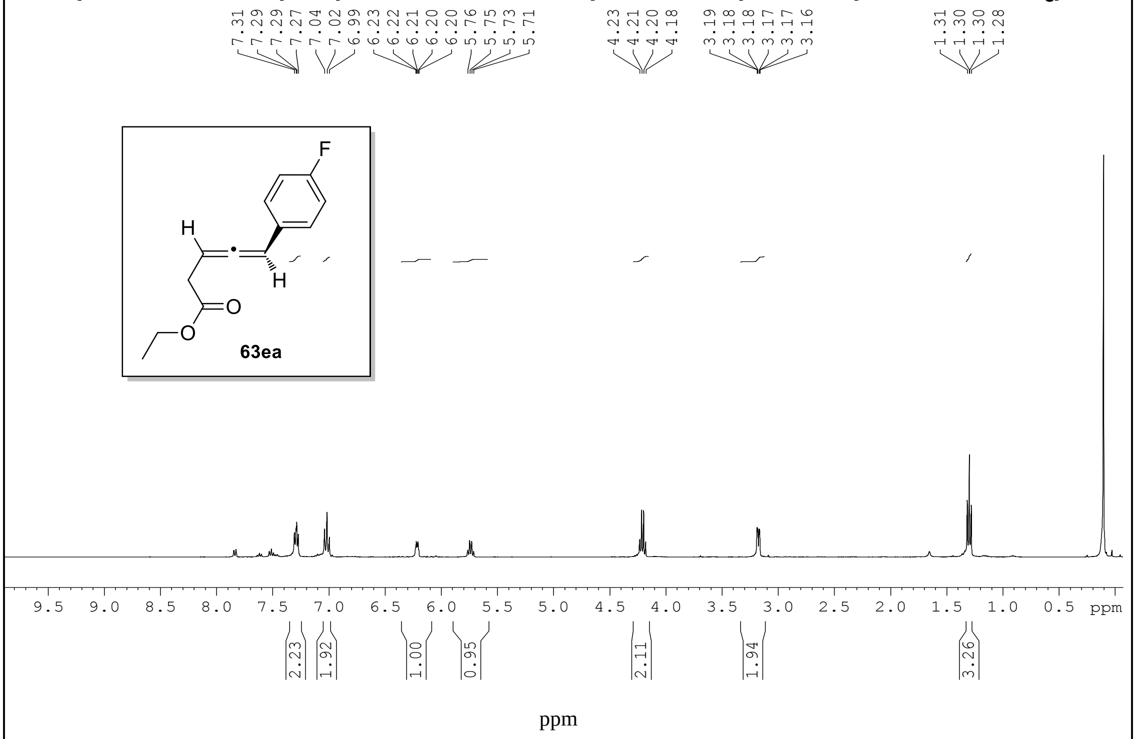
Spectrum No. 19 (Chapter , Section 1.2.5), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



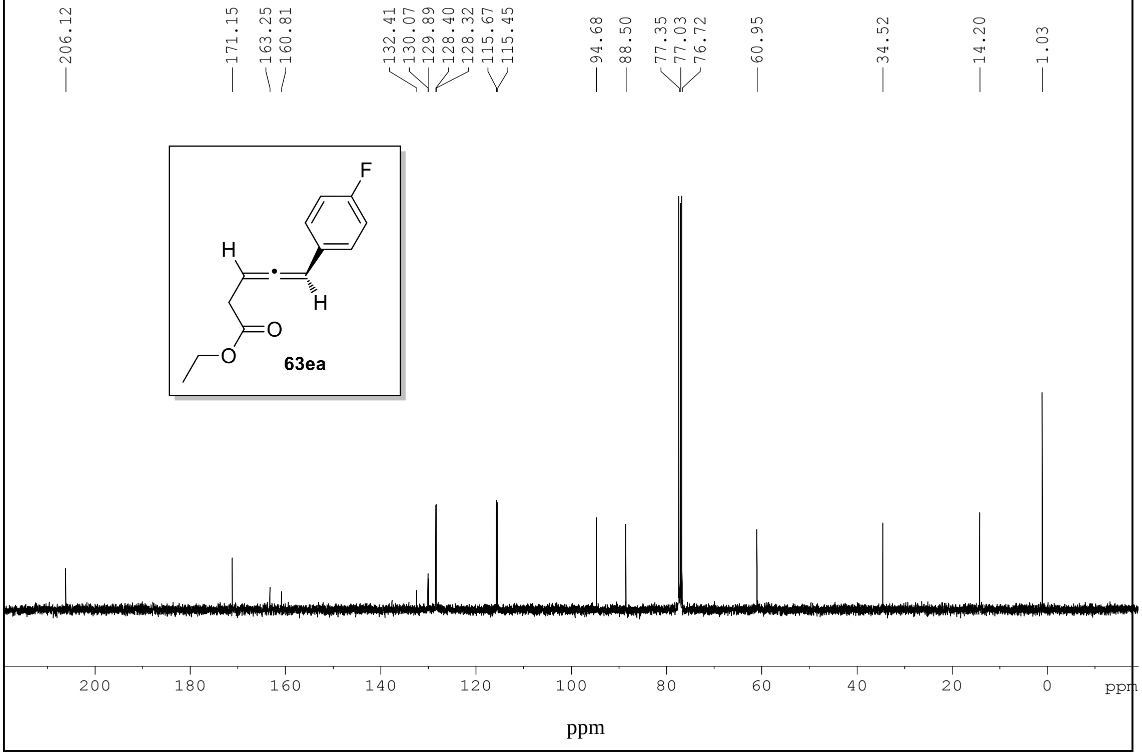
Spectrum No. 20 (Chapter 1, Section 1.2.5), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



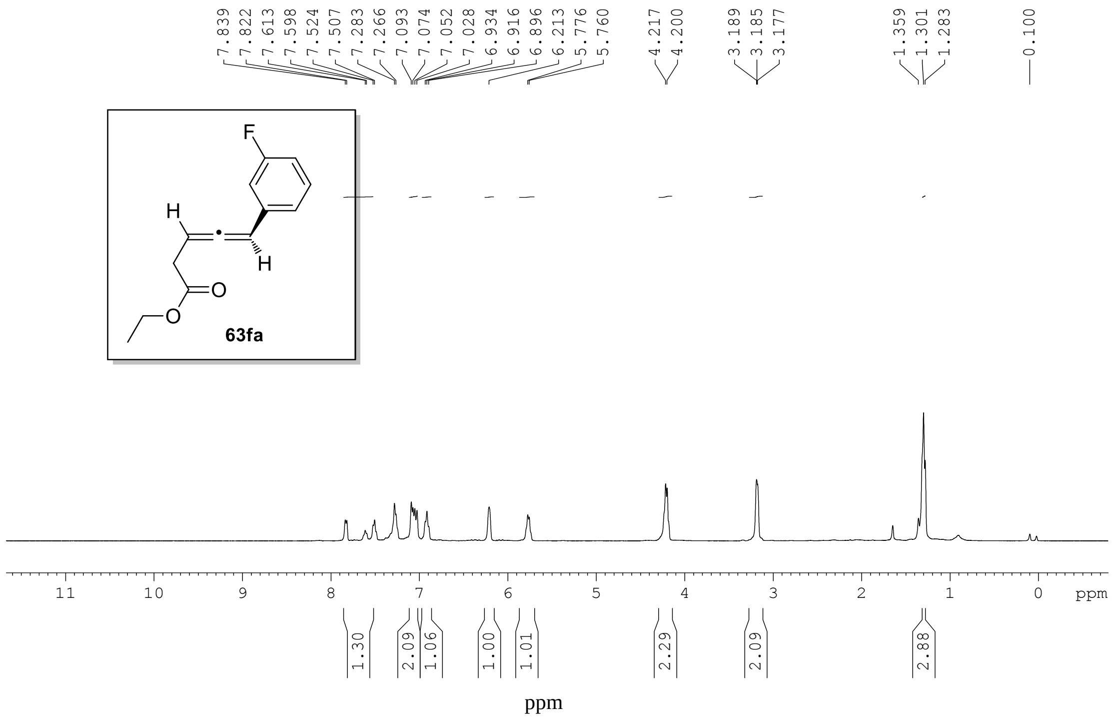
Spectrum No. 21 (Chapter 2 , Section 2.2.2), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



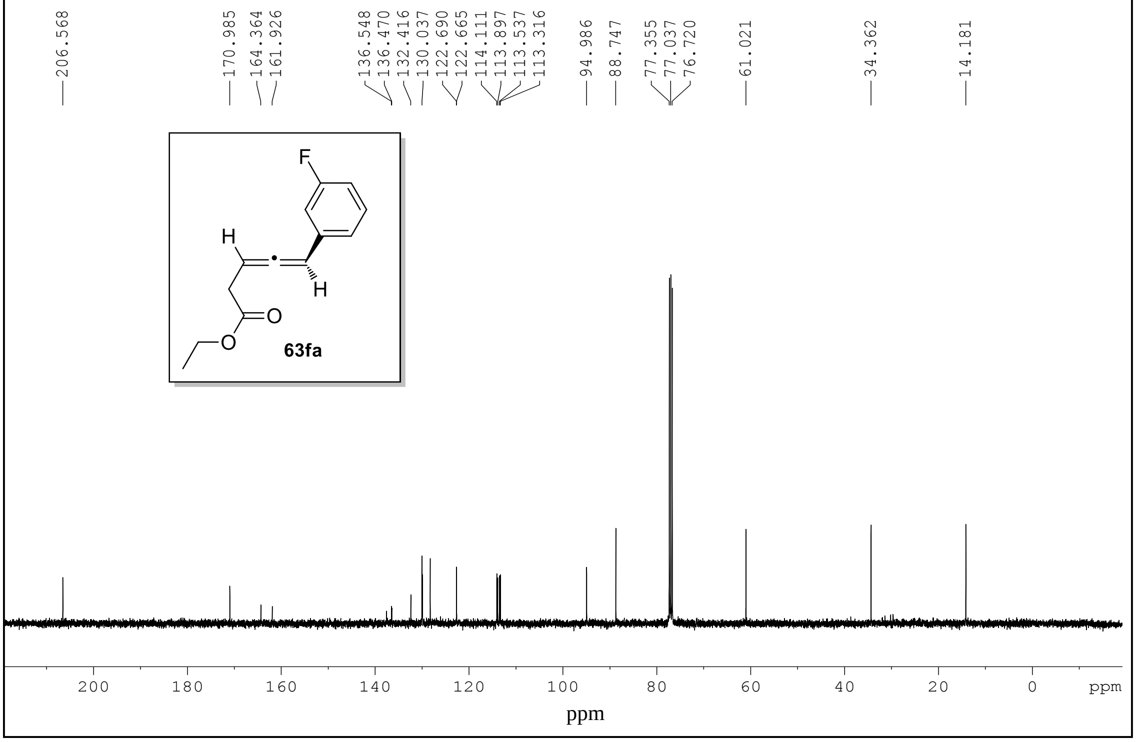
Spectrum No. 22 (Chapter 2, Section 2.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



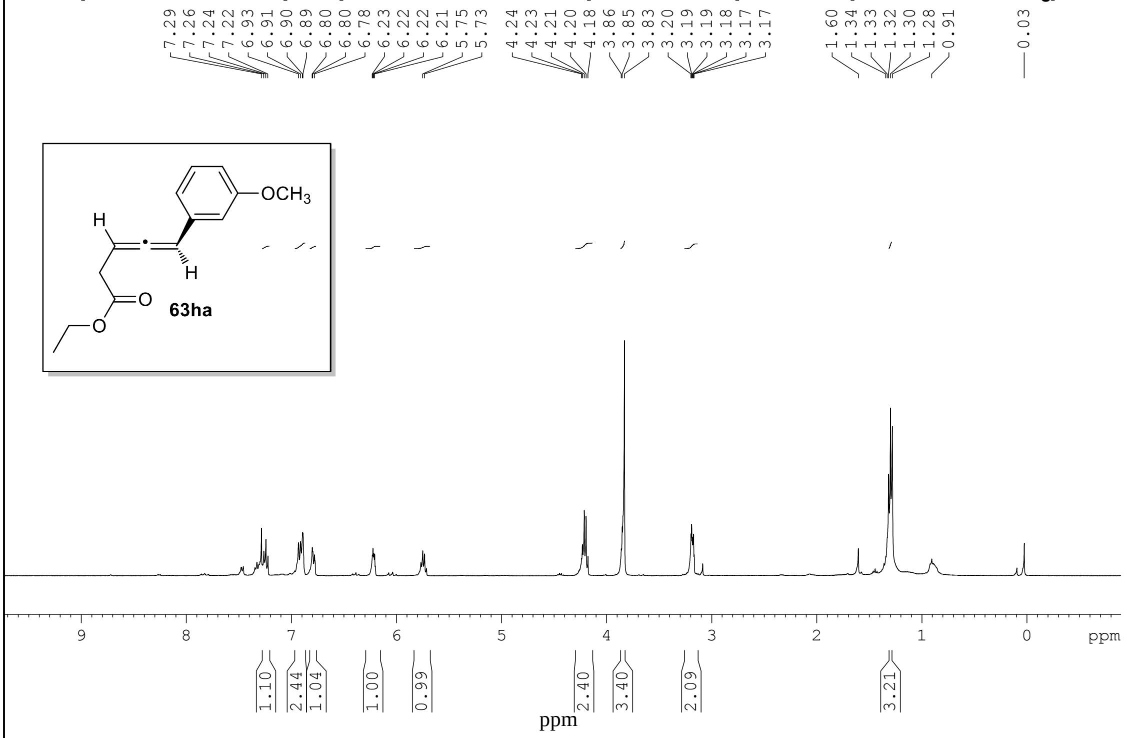
Spectrum No. 23 (Chapter 2 , Section 2.2.2), ^{1}H NMR Spectrum (400 MHz, CDCl$_3$)



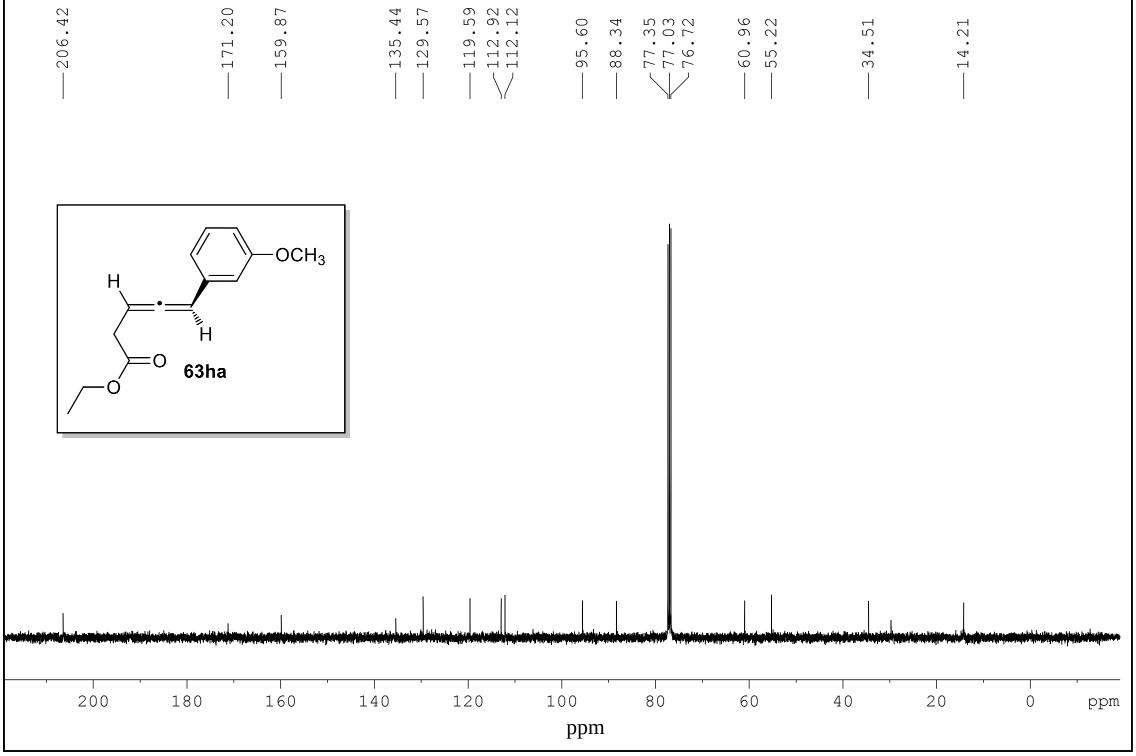
Spectrum No. 24 (Chapter 2, Section 2.2.2), ^{13}C NMR Spectrum (100 MHz, CDCl$_3$)



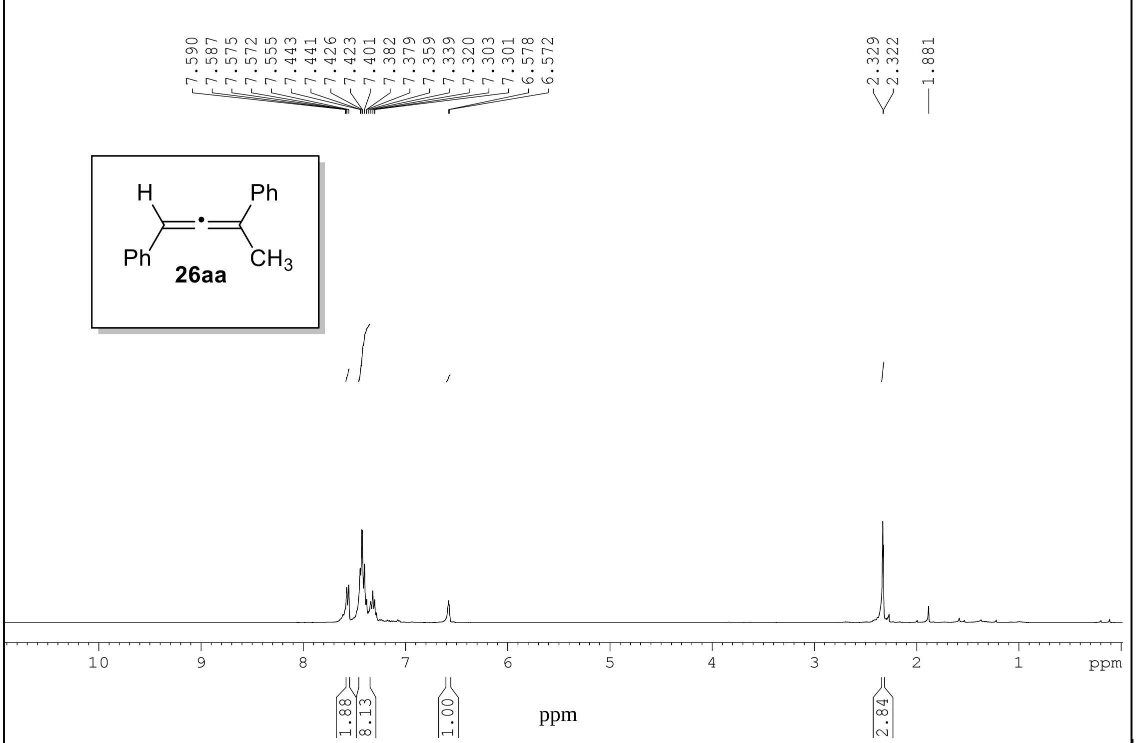
Spectrum No. 25 (Chapter 2, Section 2.2.2), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



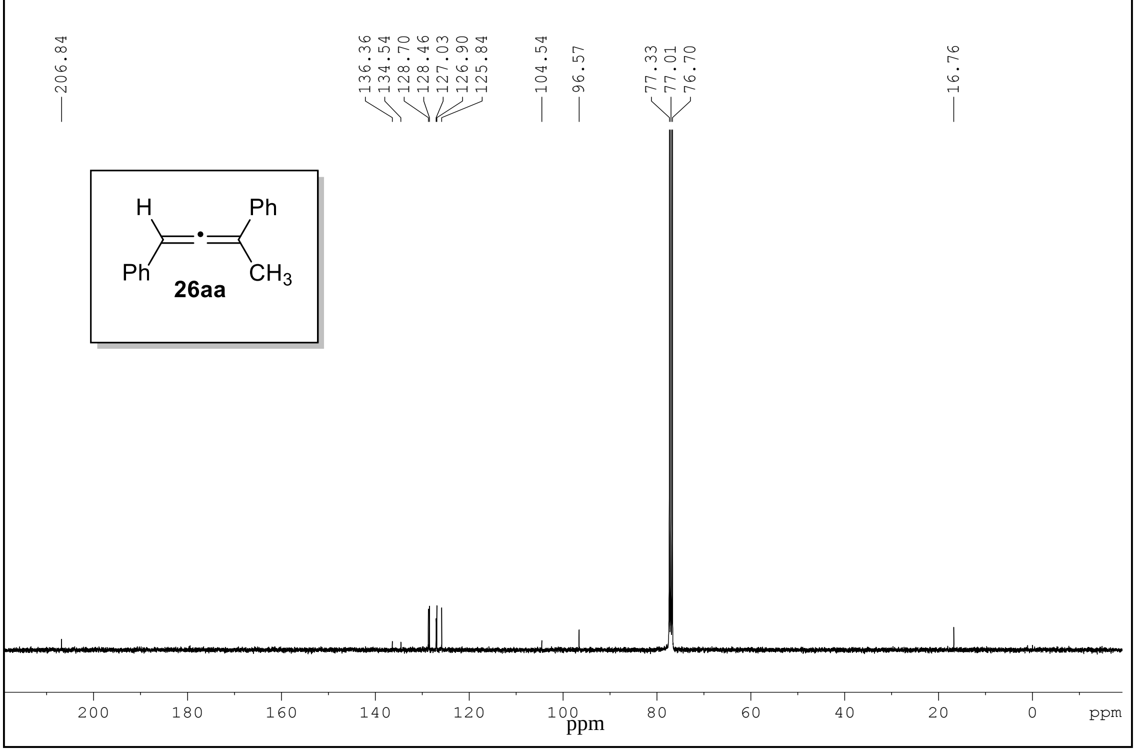
Spectrum No. 26 (Chapter 2, Section 2.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



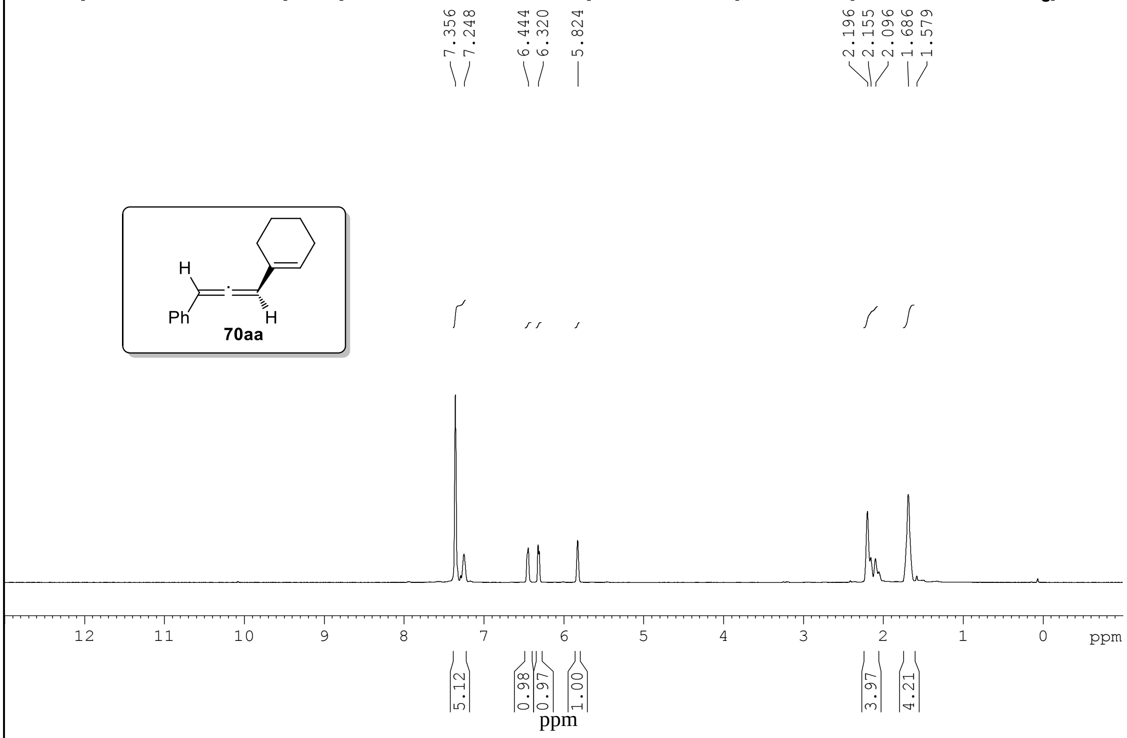
Spectrum No. 27 (Chapter 3, Section 3.2), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



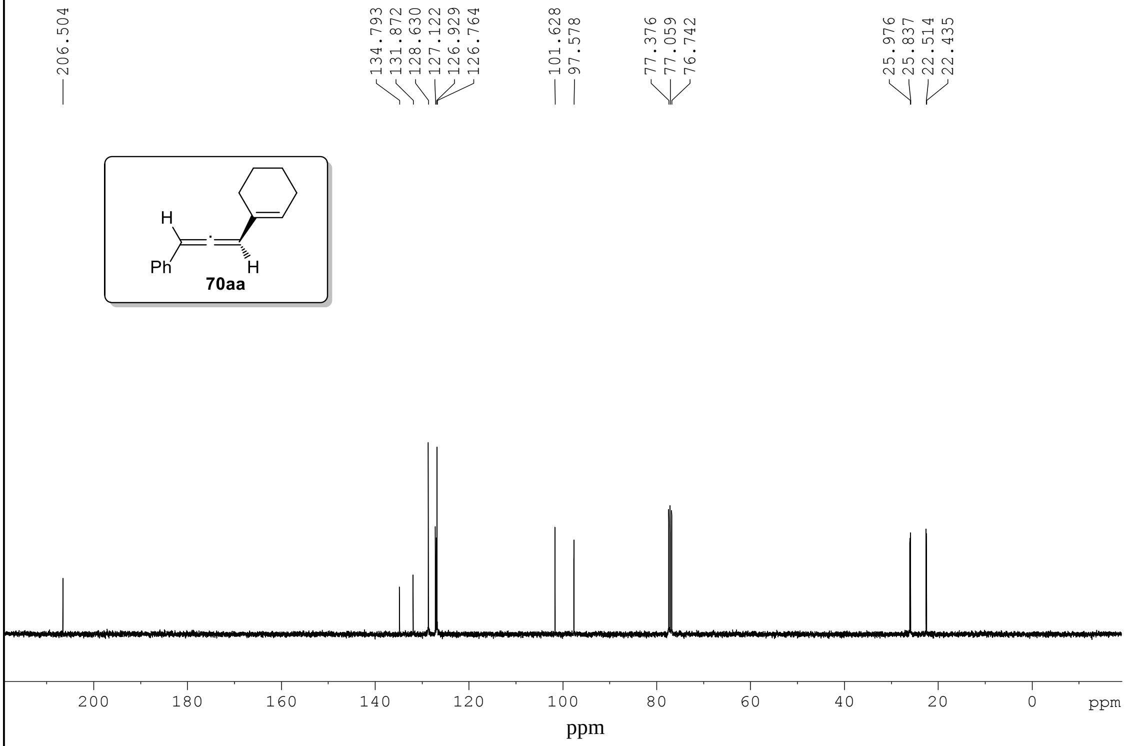
Spectrum No. 28 (Chapter 3, Section 3.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



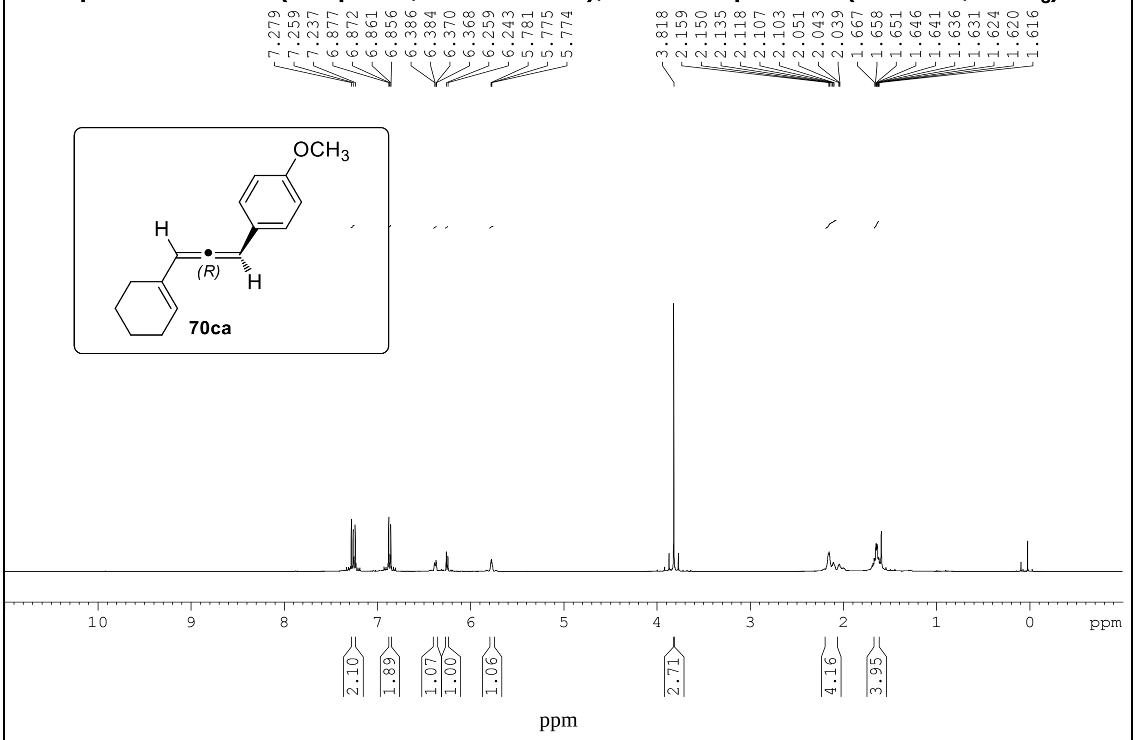
Spectrum No. 29 (Chapter 4, Section 4.2.1), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



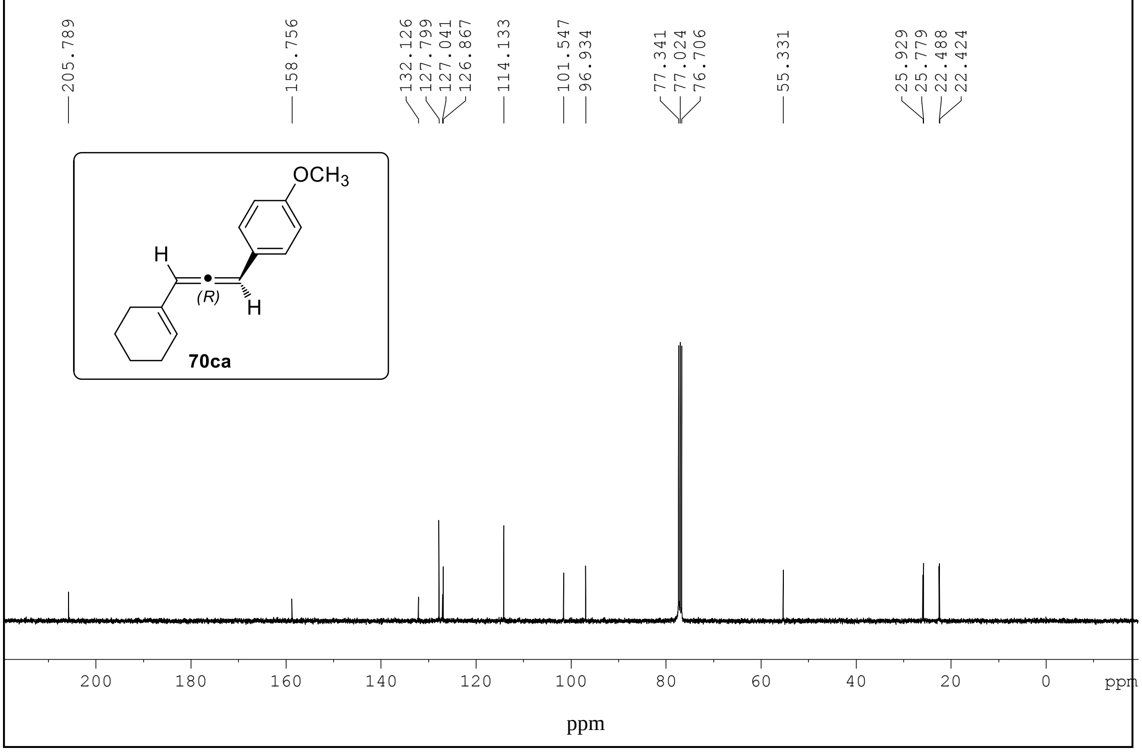
Spectrum No. 30 (Chapter 4, Section 4.2.1), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



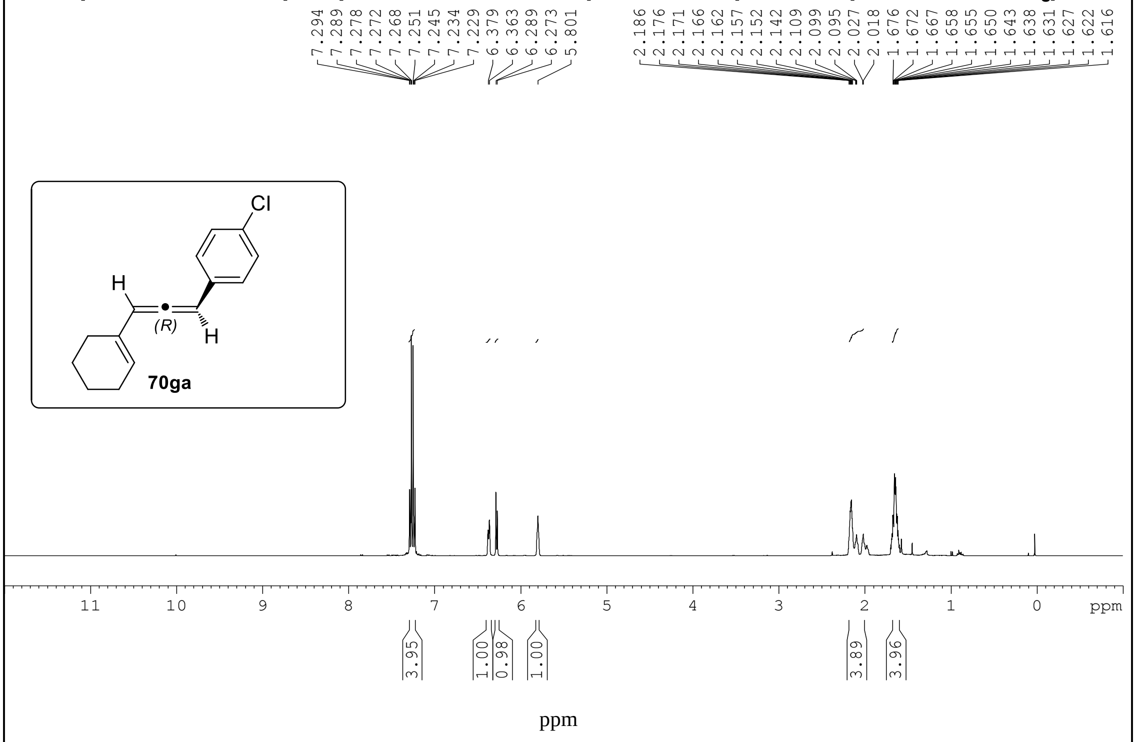
Spectrum No. 31 (Chapter 4, Section 4.2.1), ^{1}H NMR Spectrum (400 MHz, CDCl$_3$)



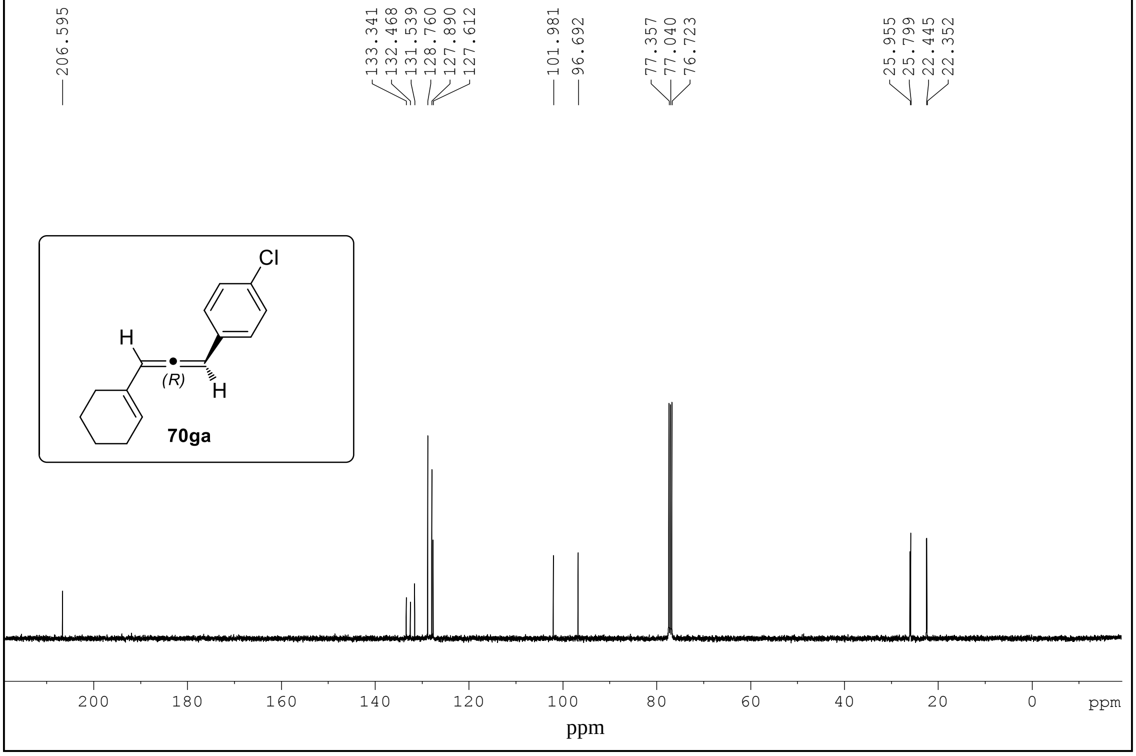
Spectrum No. 32 (Chapter 4, Section 4.2.1), ^{13}C NMR Spectrum (100 MHz, CDCl$_3$)



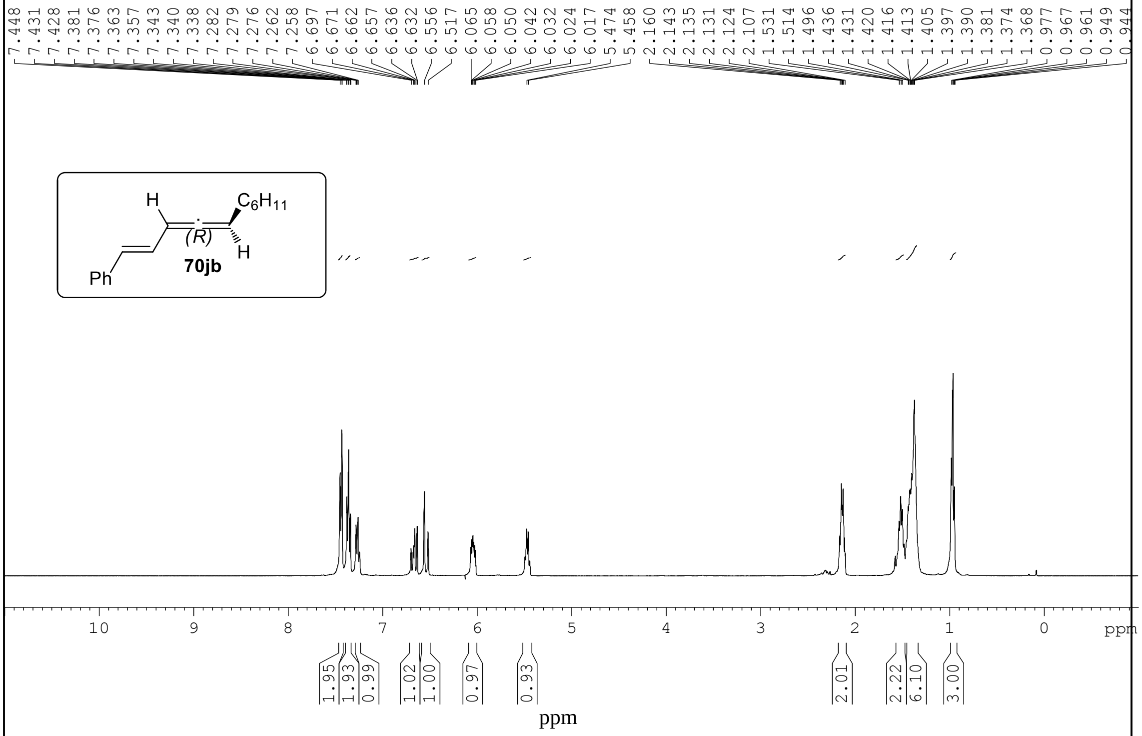
Spectrum No. 33 (Chapter 4, Section 4.2.1), ^{1}H NMR Spectrum (400 MHz, CDCl$_3$)



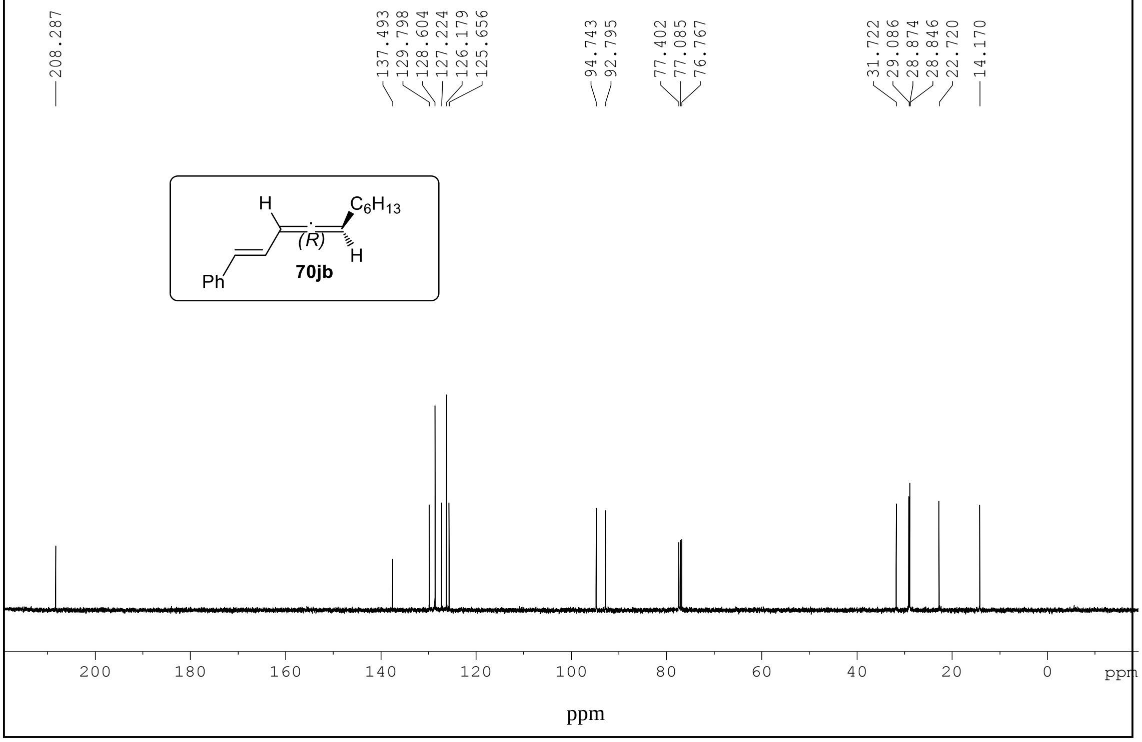
Spectrum No. 34 (Chapter 4, Section 4.2.1), ^{13}C NMR Spectrum (100 MHz, CDCl$_3$)



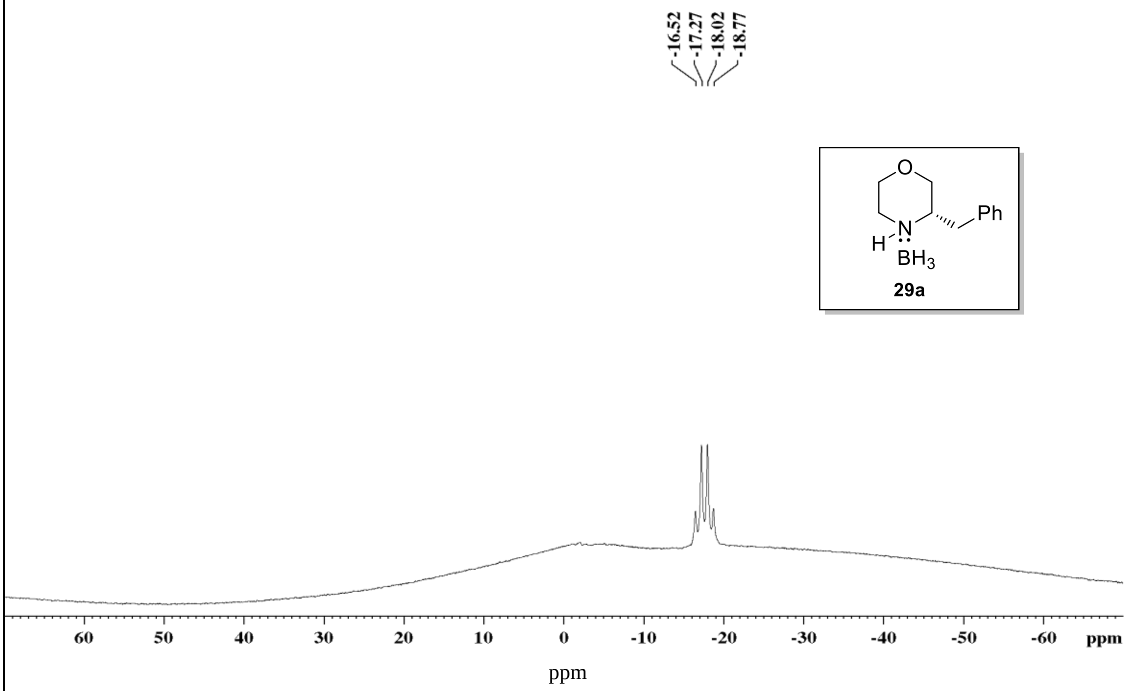
Spectrum No. 35 (Chapter 4, Section 4.2.1), ^{1}H NMR Spectrum (400 MHz, CDCl$_3$)



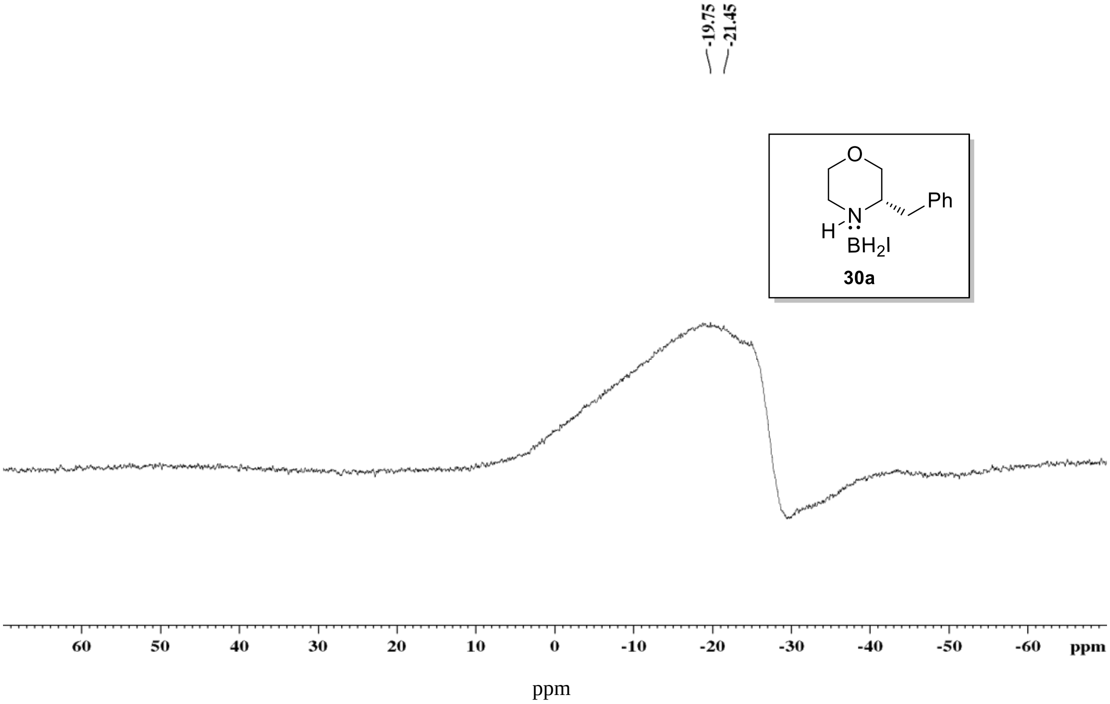
Spectrum No. 36 (Chapter 4, Section 4.2.1), ^{13}C NMR Spectrum (100 MHz, CDCl$_3$)



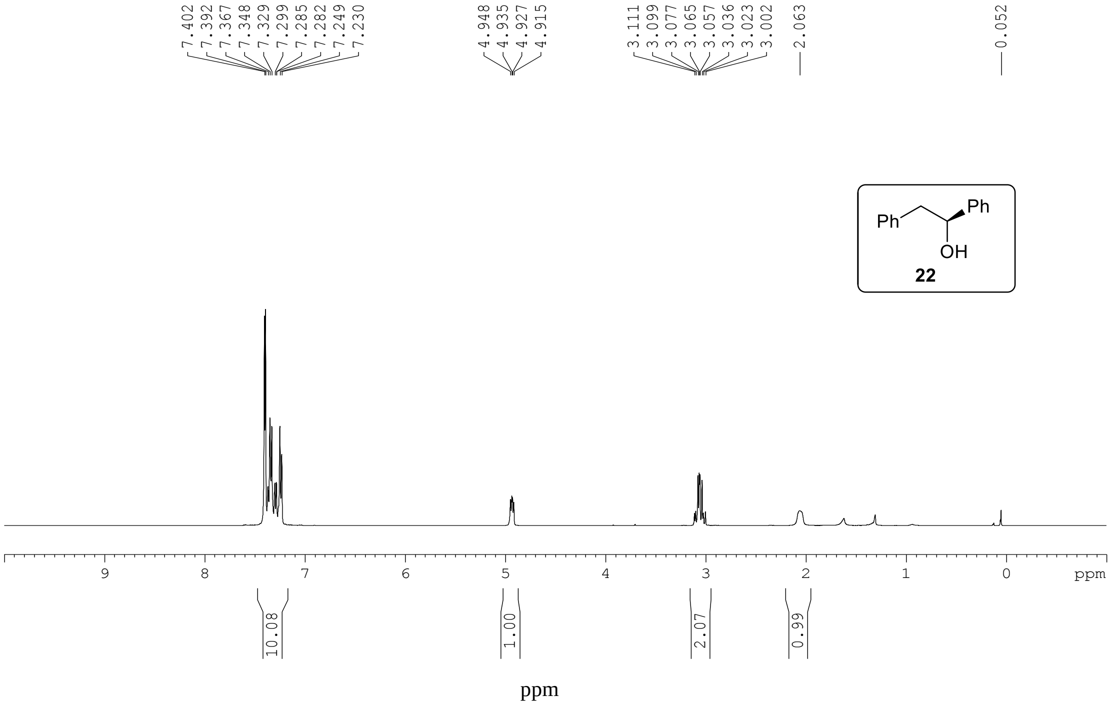
Spectrum No. 37 (Chapter 5, Section 5.2.1), ^{11}B NMR Spectrum (128.3 MHz, Toluene)



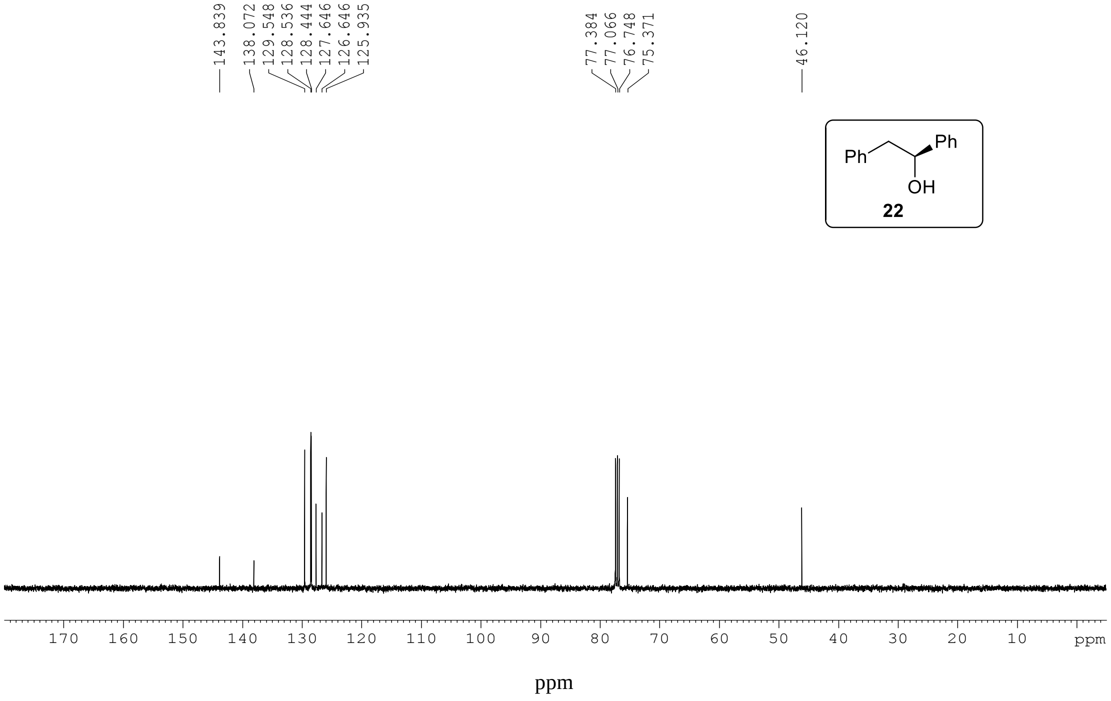
Spectrum No. 38 (Chapter 5, Section 5.2.1), ^{11}B NMR Spectrum (128.3 MHz, Toluene)



Spectrum No. 39 (chapter 5, Section 5.2.2), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)

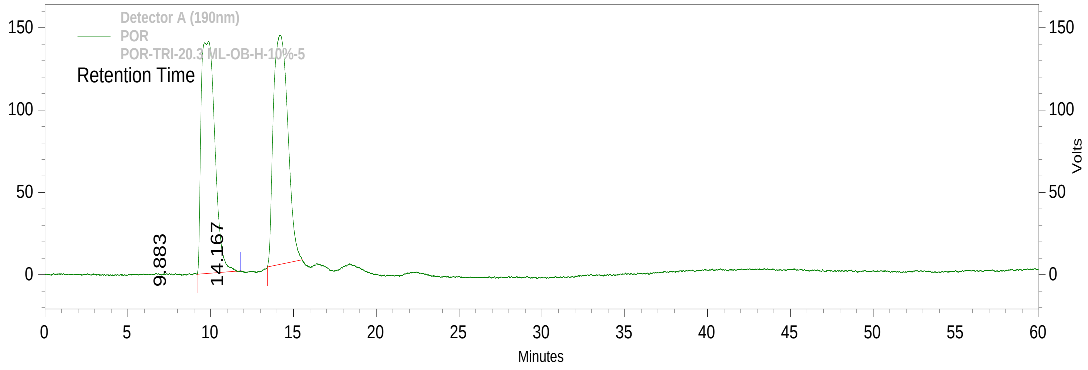


Spectrum No. 40 (Chapter 5, Section 5.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



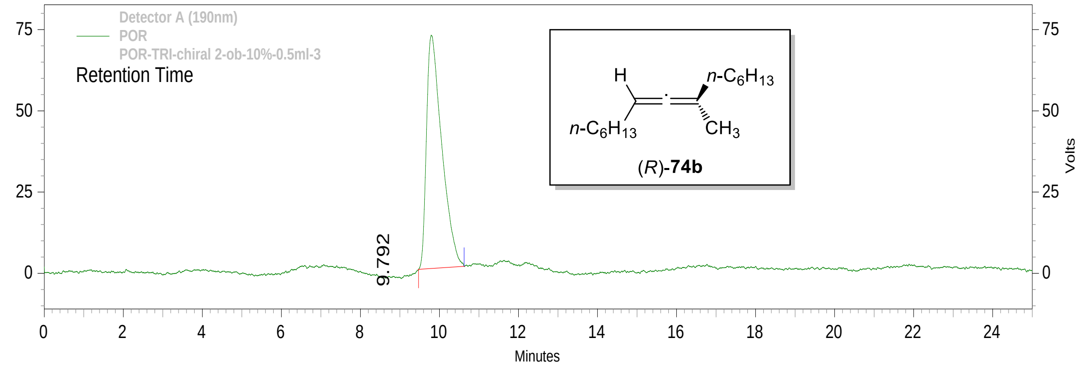
HPLC Profile of 74b: Chiralcel OB-H, hexanes:i-PrOH /90.10; flow rate 0.3 mL/min.

Racemic 74b:



Detector A (190nm)					
Pk #	**Retention Time**	**Area**	**Area %**	**Height**	**Height %**
1	9.883	8119387	48.946	140947	50.310
2	14.167	8469120	51.054	139210	49.690
Totals		16588507	100.000	280157	100.000

***(R)*-74b: (Chapter 1, Table 8)**

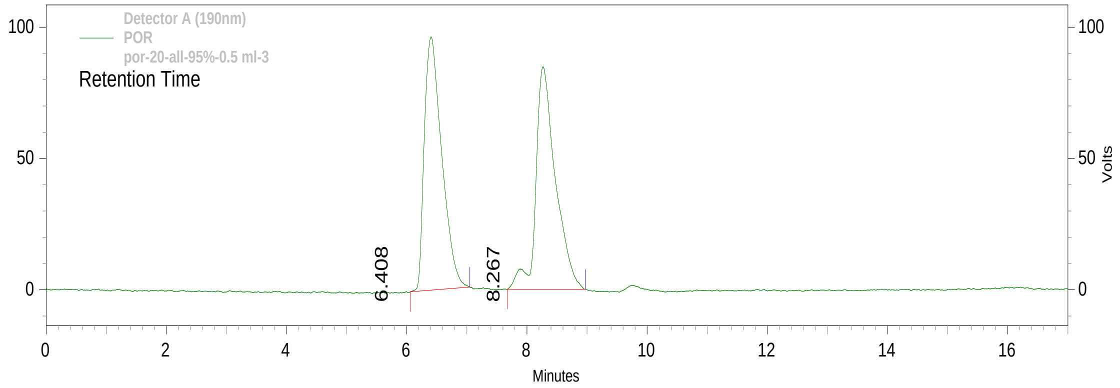


Detector A (190nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	9.792	1928812	100.000	71798	100.000
Totals		1928812	100.000	71798	100.000

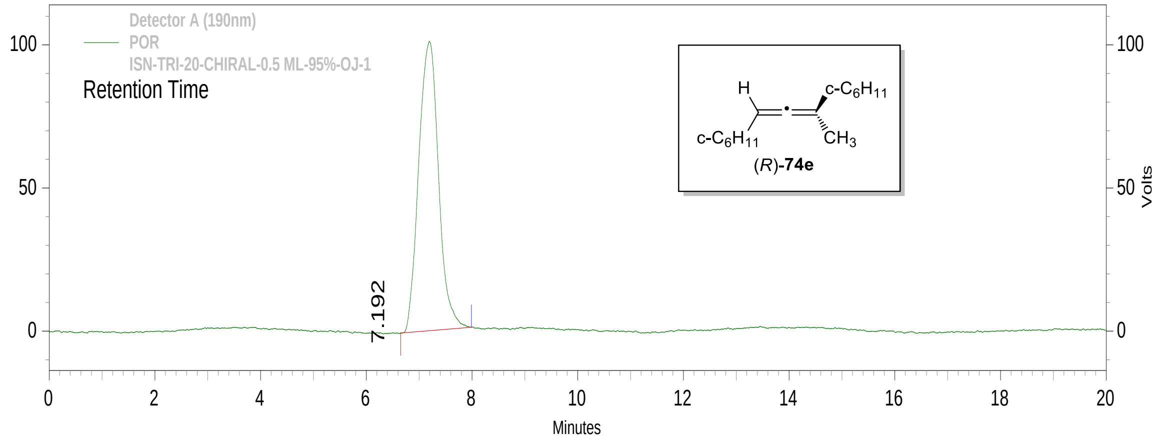
HPLC Profile of 74e: chiralcel OJ-H, hexanes:i-PrOH /95.5; flow rate 0.5 mL/min

Racemic 74e:



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

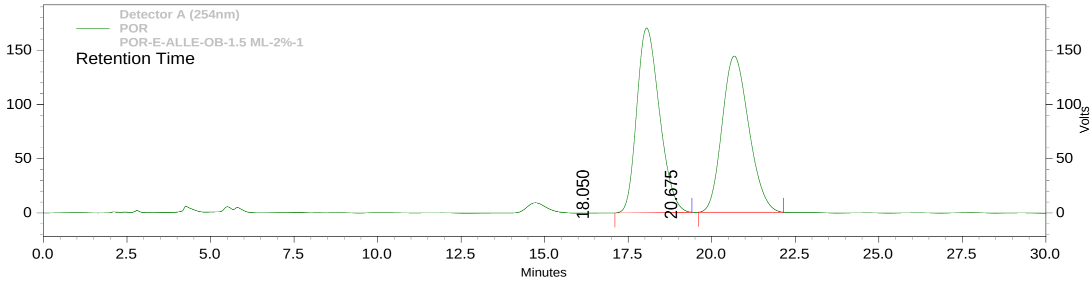
***(R)*-74e: (Chapter 1, Table 8)**



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 63aa: chiralcel OB-H, hexanes:i-PrOH/98:2; flow rate 0.5 mL/min.

Racemic-63aa:

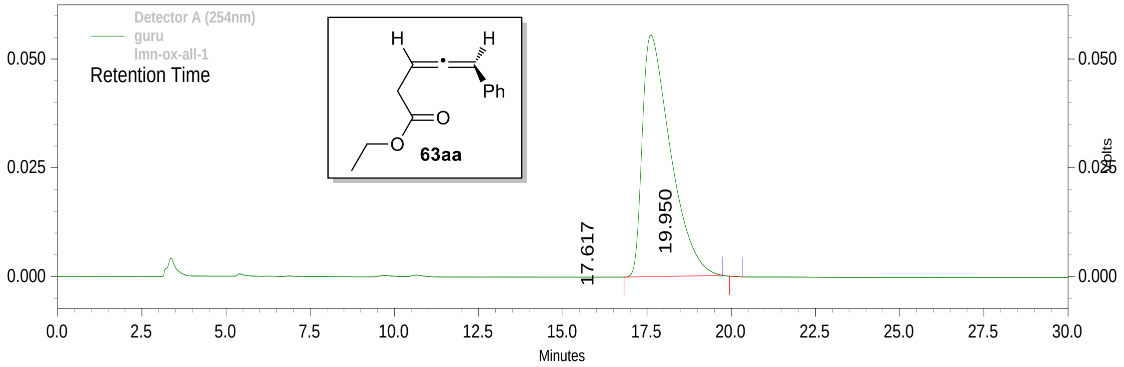


Detector A (254nm)

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)-63aa: (Chapter 2, Table 3)

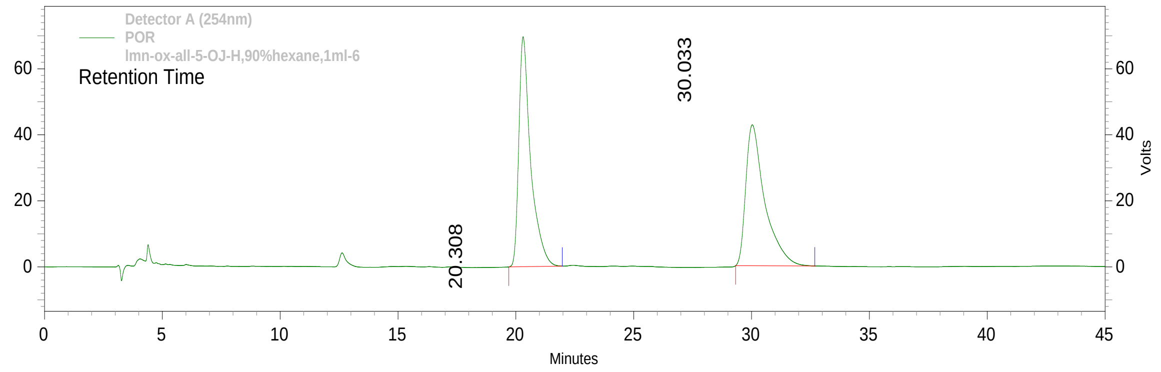


Detector A (254nm)

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 63ac: Chiralcel OJ-H, hexanes:i-PrOH/90:10; flow rate 1.0 mL/min
Racemic-63ac.

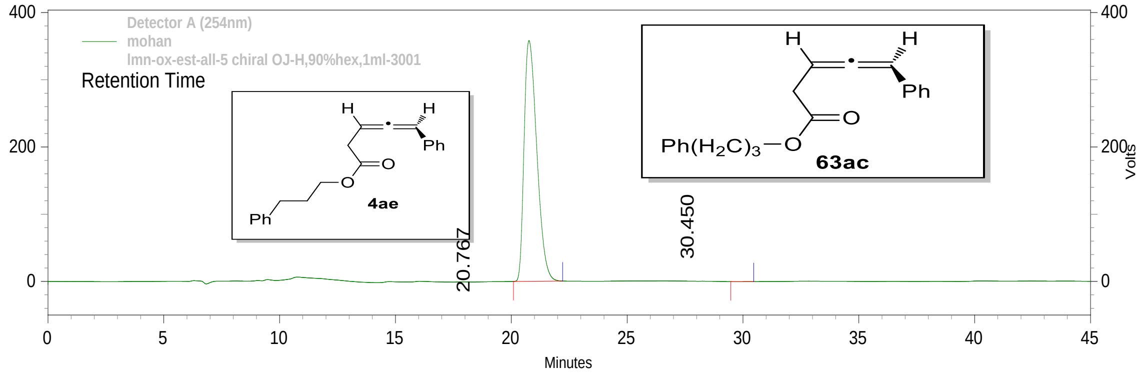


Detector A (254nm)

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)*-63ac: (Chapter 2, Table 3)**



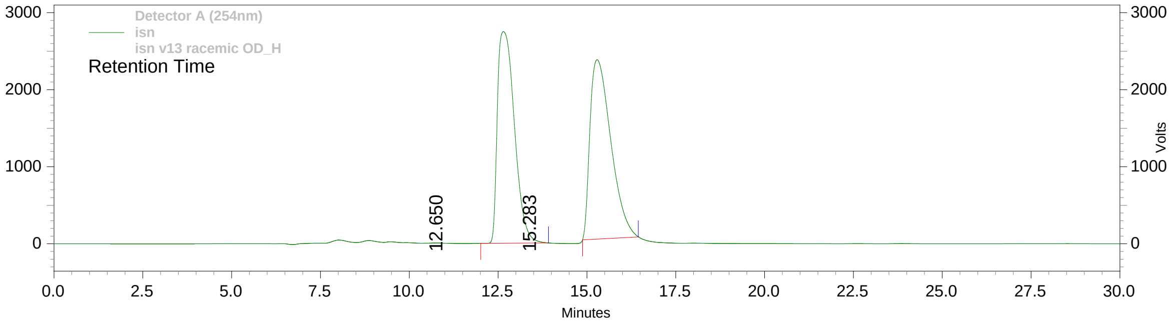
Detector A (254nm)

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 70aa: Chiralcel OD-H, hexanes:i-PrOH/100:0; flow rate 0.5 mL/min.

Racemic 70aa:

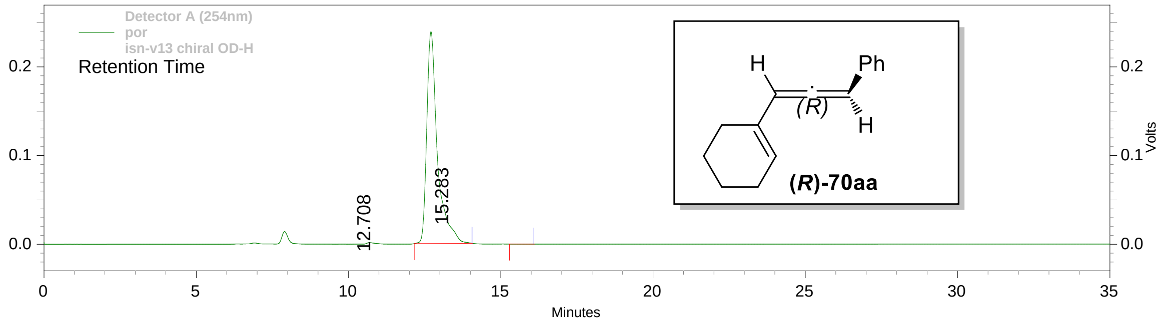


Detector A (254nm)

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)*-70aa: (Chapter 4, Table 2)**

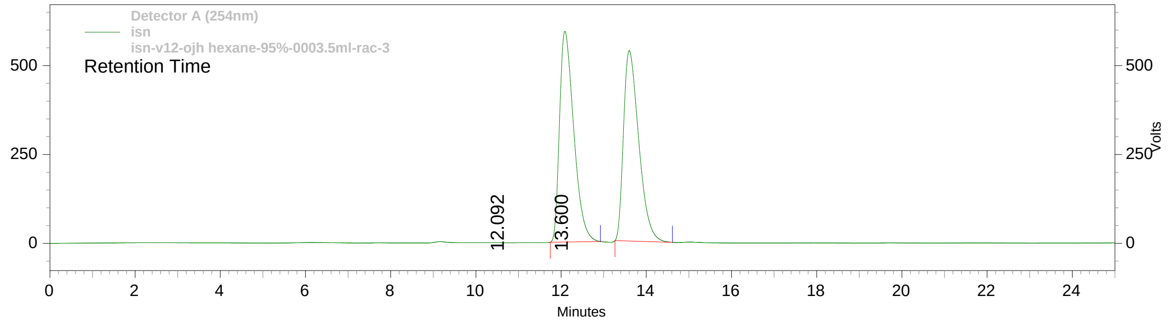


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	12.708	5846732	99.991	238892	100.000
2	15.283	498	0.009	0	0.000

Totals		5847230	100.000	238892	100.000

HPLC Profile of 70ca: Chiralcel OJ-H, hexanes:i-PrOH/95:5; flow rate 0.5 mL/min.
Racemic 70ca:

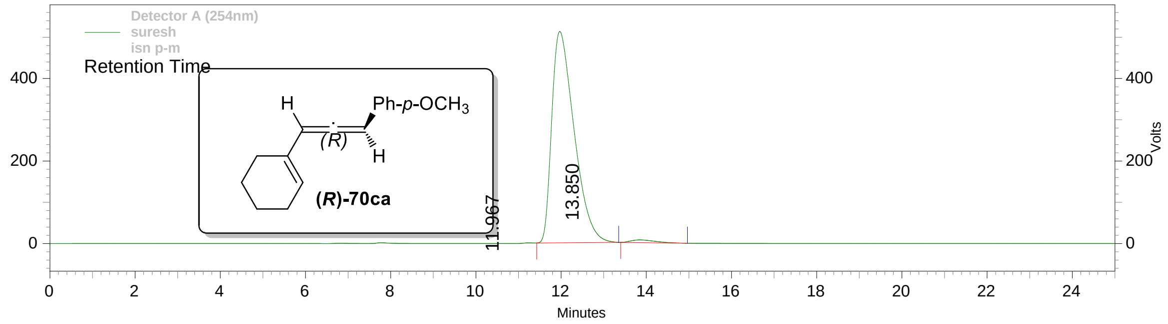


Detector A (254nm)

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)*-70ca: (Chapter 4, Table 2)**



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	11.967	18692849	98.662	512386	98.750
2	13.850	253415	1.338	6484	1.250

Totals		18946264	100.000	518870	100.000

Appendix II

X-Ray Crystallographic Data

Table 1. Atomic coordinates (x 10^4) and equivalent isotropicdisplacement parameters (A^2 x 10^3)

for compound **85af**.U(eq) is defined as one third of the trace of the orthogonalizedUij tensor.

	X	y	z	U(eq)
O(1)	9997(2)	7861(2)	6025(1)	59(1)
C(2)	8617(2)	3098(3)	7434(1)	39(1)
C(3)	6628(2)	4377(3)	8318(1)	48(1)
N(4)	9235(1)	4557(2)	6899(1)	39(1)
C(5)	8703(2)	5106(3)	5966(1)	41(1)
C(6)	9556(2)	2210(3)	8143(1)	41(1)
C(7)	10815(2)	2246(3)	7984(2)	50(1)
C(9)	9577(2)	6176(3)	7467(1)	47(1)
C(10)	5453(2)	5061(3)	8635(1)	48(1)
C(11)	6814(2)	6335(4)	5037(1)	51(1)
C(12)	9679(2)	6269(3)	5489(1)	50(1)
C(13)	7447(2)	6126(4)	5994(1)	51(1)
C(14)	7529(2)	3801(3)	7961(1)	45(1)
C(15)	9152(2)	1248(4)	8922(1)	55(1)
C(16)	10486(2)	7339(4)	6937(2)	58(1)
C(17)	11216(3)	455(4)	9391(2)	68(1)
C(18)	11634(2)	1381(4)	8610(2)	61(1)
C(8)	9964(3)	363(4)	9535(2)	68(1)
C(19)	4930(2)	6594(5)	8204(2)	71(1)
C(1A)	3098(2)	6232(5)	9083(2)	76(1)
C(1B)	4780(2)	4137(4)	9307(2)	63(1)
C(1C)	6062(3)	4961(5)	4681(2)	78(1)
C(1D)	3613(2)	4742(5)	9526(2)	74(1)
C(1E)	3754(3)	7156(5)	8426(2)	82(1)
C(1F)	6933(3)	7894(5)	4494(2)	81(1)
C(1G)	6324(3)	8007(8)	3601(3)	108(2)
C(1H)	5580(3)	6629(9)	3283(2)	112(2)
C(1I)	5449(3)	5141(8)	3814(2)	110(2)
C(1)	8147(2)	1546(3)	6774(1)	48(1)

Table 2.Bond lengths [A] and angles [deg] for compound **85af**.

O(1)-C(12)	1.416(3)
O(1)-C(16)	1.427(3)
C(2)-N(4)	1.470(3)
C(2)-C(14)	1.497(2)
C(2)-C(1)	1.537(3)
C(2)-C(6)00000000000	1.544(3)
C(3)-C(14)	1.185(3)
C(3)-C(10)	1.445(3)
N(4)-C(9)	1.462(3)
N(4)-C(5)	1.476(2)
C(5)-C(12)	1.521(3)
C(5)-C(13)	1.547(3)
C(6)-C(15)	1.381(3)
C(6)-C(7)	1.386(3)
C(7)-C(18)	1.381(3)
C(9)-C(16)	1.509(3)
C(10)-C(19)	1.380(4)
C(10)-C(1B)	1.383(3)
C(11)-C(1C)	1.371(4)
C(11)-C(1F)	1.373(4)
C(11)-C(13)	1.502(2)
C(15)-C(8)	1.373(3)
C(17)-C(8)	1.376(4)
C(17)-C(18)	1.376(4)
C(19)-C(1E)	1.379(4)
C(1A)-C(1E)	1.358(4)
C(1A)-C(1D)	1.359(5)
C(1B)-C(1D)	1.379(3)
C(1C)-C(1I)	1.379(4)
C(1F)-C(1G)	1.406(5)
C(1G)-C(1H)	1.351(7)
C(1H)-C(1I)	1.323(7)
C(12)-O(1)-C(16)	109.98(17)
N(4)-C(2)-C(14)	112.56(17)
N(4)-C(2)-C(1)	111.35(15)
C(14)-C(2)-C(1)	107.41(16)
N(4)-C(2)-C(6)	109.32(15)
C(14)-C(2)-C(6)	109.39(14)
C(1)-C(2)-C(6)	106.63(17)
C(14)-C(3)-C(10)	172.7(2)
C(9)-N(4)-C(2)	114.12(14)
C(9)-N(4)-C(5)	110.93(16)

C(2)-N(4)-C(5)	118.63(14)
N(4)-C(5)-C(12)	106.60(15)
N(4)-C(5)-C(13)	115.22(14)
C(12)-C(5)-C(13)	111.45(19)
C(15)-C(6)-C(7)	118.11(19)
C(15)-C(6)-C(2)	120.52(17)
C(7)-C(6)-C(2)	121.22(17)
C(18)-C(7)-C(6)	120.2(2)
N(4)-C(9)-C(16)	109.57(16)
C(19)-C(10)-C(1B)	118.3(2)
C(19)-C(10)-C(3)	119.5(2)
C(1B)-C(10)-C(3)	121.9(2)
C(1C)-C(11)-C(1F)	117.3(2)
C(1C)-C(11)-C(13)	120.3(2)
C(1F)-C(11)-C(13)	122.4(3)
O(1)-C(12)-C(5)	112.18(16)
C(11)-C(13)-C(5)	113.77(16)
C(3)-C(14)-C(2)	175.4(2)
C(8)-C(15)-C(6)	121.7(2)
O(1)-C(16)-C(9)	111.40(17)
C(8)-C(17)-C(18)	119.2(2)
C(17)-C(18)-C(7)	120.9(2)
C(15)-C(8)-C(17)	119.8(2)
C(1E)-C(19)-C(10)	120.5(3)
C(1E)-C(1A)-C(1D)	119.4(2)
C(1D)-C(1B)-C(10)	120.1(3)
C(11)-C(1C)-C(1I)	121.4(4)
C(1A)-C(1D)-C(1B)	121.0(3)
C(1A)-C(1E)-C(19)	120.7(3)
C(11)-C(1F)-C(1G)	119.8(4)
C(1H)-C(1G)-C(1F)	120.9(4)
C(1I)-C(1H)-C(1G)	119.1(3)
C(1H)-C(1I)-C(1C)	121.5(4)

Symmetry transformations used to generate equivalent atoms:

Table 3.Anisotropic displacement parameters (A^2 x 10^3) for compound **85af**.

The anisotropic displacement factor exponent takes the form:-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]
]

	U11	U22	U33	U23	U13	U12

O(1)	72(1)	41(1)	63(1)	9(1)	0(1)	-5(1)
C(2)	41(1)	37(1)	40(1)	-3(1)	4(1)	4(1)
C(3)	49(1)	54(1)	43(1)	-3(1)	3(1)	9(1)
N(4)	42(1)	34(1)	39(1)	-2(1)	0(1)	2(1)
C(5)	48(1)	38(1)	37(1)	-4(1)	1(1)	5(1)
C(6)	48(1)	33(1)	43(1)	-3(1)	1(1)	6(1)
C(7)	51(1)	42(1)	58(1)	2(1)	2(1)	5(1)
C(9)	58(1)	37(1)	46(1)	-5(1)	-7(1)	3(1)
C(10)	45(1)	54(1)	45(1)	-9(1)	4(1)	9(1)
C(11)	45(1)	64(1)	45(1)	5(1)	1(1)	8(1)
C(12)	56(1)	47(1)	48(1)	6(1)	6(1)	7(1)
C(13)	51(1)	60(1)	42(1)	-4(1)	-2(1)	13(1)
C(14)	47(1)	45(1)	42(1)	1(1)	3(1)	7(1)
C(15)	61(1)	54(1)	51(1)	7(1)	8(1)	8(1)
C(16)	66(1)	42(1)	67(1)	1(1)	-11(1)	-7(1)
C(17)	84(2)	55(2)	62(1)	1(1)	-19(1)	23(1)
C(18)	51(1)	52(1)	80(1)	-5(1)	-11(1)	10(1)
C(8)	88(2)	62(2)	52(1)	12(1)	3(1)	17(2)
C(19)	73(1)	75(2)	66(1)	9(1)	19(1)	24(2)
C(1A)	51(1)	84(2)	95(2)	-23(2)	14(1)	15(2)
C(1B)	61(1)	59(2)	68(1)	-2(1)	16(1)	9(1)
C(1C)	83(2)	85(2)	66(1)	3(2)	-16(1)	-12(2)
C(1D)	61(1)	75(2)	87(2)	-11(2)	30(1)	-2(2)
C(1E)	78(2)	84(2)	86(2)	0(2)	6(1)	39(2)
C(1F)	61(1)	84(2)	96(2)	38(2)	-6(1)	4(2)
C(1G)	74(2)	158(4)	94(2)	74(3)	6(2)	24(2)
C(1H)	79(2)	200(6)	55(1)	20(3)	-10(1)	28(3)
C(1I)	103(2)	149(4)	77(2)	-18(3)	-33(2)	-5(3)
C(1)	52(1)	41(1)	52(1)	-4(1)	2(1)	-3(1)

Table 4. Hydrogen bonds for compound **85af** [A and deg.].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)

Table 5: Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for **84**. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	***x***	***y***	***z***	**U(eq)**
C1	8845(7)	2(5)	1593(3)	70.8(14)
C2	9391(9)	554(6)	-54(3)	81.4(17)
C3	6718(7)	930(5)	390(3)	73.4(15)
C4	8541(6)	1047(5)	1607(3)	74.8(16)
C5	8483(7)	-668(5)	902(3)	74.2(15)
C7	7698(7)	1643(5)	978(3)	73.7(16)

C10	7623(7)	2705(5)	905(3)	78.0(16)
C11	7944(7)	17(5)	200(3)	77.2(16)
C15	9527(8)	-605(6)	2286(3)	93.0(19)
C16	7124(8)	-660(5)	-421(3)	88.1(18)
C17	8491(7)	3495(5)	1432(3)	78.3(16)
C19	7707(8)	4464(5)	1510(3)	85.5(18)
C23	5314(8)	426(6)	691(3)	91(2)
N25	10527(8)	967(5)	-214(3)	102.4(17)
C27	10919(9)	-1357(6)	2176(4)	102(2)
C28	10044(8)	3327(5)	1825(4)	97(2)
C35	6012(8)	1507(5)	-298(3)	93(2)
C36	9929(8)	-1396(5)	789(3)	88.3(18)
N37	6466(8)	-1205(6)	-869(3)	127(2)
C38	8418(10)	5206(6)	2010(4)	102(2)
N40	4243(7)	9(6)	922(3)	121(2)
N44	5457(8)	1951(6)	-826(3)	134(3)
C45	10415(9)	-2067(6)	1497(4)	105(2)
C48	10755(11)	4089(8)	2328(5)	128(3)
C49	9894(12)	5028(7)	2419(4)	114(3)
C6	6166(6)	1609(5)	3986(3)	70.0(14)
C8	6875(6)	2225(5)	4701(3)	75.0(15)
C9	7358(6)	3834(5)	3967(3)	71.8(15)
C12	5926(7)	2309(5)	3301(3)	71.1(15)
C13	5074(7)	1777(5)	2604(3)	84.5(18)
N14	4558(8)	3375(5)	5183(3)	107.4(18)
C18	9048(7)	3556(5)	5226(3)	84.6(18)
C20	4586(7)	1004(5)	4091(3)	80.8(16)
C21	5563(8)	2853(5)	4988(3)	79.1(16)
C22	8237(6)	3045(5)	4521(3)	72.7(15)
C24	7476(7)	4891(5)	4096(3)	76.6(15)
C26	6628(7)	5748(5)	3651(3)	77.5(15)
N29	9669(8)	3918(5)	5768(3)	118(2)
C30	7610(8)	1470(6)	5287(3)	90.5(19)
C31	5105(8)	5654(6)	3205(4)	96.6(19)
C32	3485(7)	1204(5)	2736(3)	83.8(17)
C33	9527(8)	2464(6)	4192(3)	85.6(18)
C34	7398(8)	6744(5)	3672(3)	86.9(17)
C39	6434(6)	3321(5)	3318(3)	74.7(16)
C41	3854(8)	422(5)	3376(3)	93.7(19)
C42	6695(9)	7567(5)	3258(4)	95(2)
N43	8243(7)	884(6)	5715(3)	125(2)
C46	4424(9)	6484(6)	2777(4)	107(2)
C47	5224(10)	7438(6)	2783(4)	102(2)
N50	10499(7)	1974(6)	3933(4)	123(2)

Table 6: Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for **84**. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+...+2hka\times b\times U_{12}]$

Atom	**U_{11}**	**U_{22}**	**U_{33}**	**U_{23}**	**U_{13}**	**U_{12}**
C1	67(3)	81(4)	63(3)	1(3)	3(2)	0(3)
C2	84(4)	84(5)	74(3)	-8(4)	6(3)	11(4)
C3	73(3)	79(4)	65(3)	-8(3)	0(3)	4(3)
C4	69(3)	88(4)	66(3)	-7(3)	6(3)	-4(3)
C5	82(3)	75(4)	65(3)	5(3)	9(3)	-10(3)
C7	68(3)	81(4)	70(3)	-14(3)	4(3)	1(3)
C10	76(4)	87(5)	71(3)	-3(3)	10(3)	10(3)
C11	79(4)	81(4)	69(3)	-15(3)	4(3)	-10(3)
C15	106(5)	92(5)	80(4)	13(4)	9(3)	0(4)
C16	90(4)	92(5)	80(4)	-18(4)	3(3)	7(4)
C17	75(4)	85(4)	74(4)	8(3)	9(3)	5(4)
C19	92(4)	87(5)	77(4)	1(3)	11(3)	6(4)
C23	67(4)	107(6)	95(4)	-20(4)	2(3)	1(4)
N25	105(4)	99(4)	108(4)	4(3)	29(3)	7(4)
C27	116(5)	90(5)	94(4)	7(4)	-5(4)	14(5)
C28	85(4)	83(5)	119(5)	-13(4)	-3(4)	-9(4)
C35	96(4)	104(5)	73(4)	-15(4)	-5(3)	15(4)
C36	100(4)	75(4)	88(4)	-11(4)	5(3)	9(4)
N37	115(4)	143(6)	113(4)	-53(4)	-16(3)	-2(4)
C38	125(6)	82(5)	104(5)	-17(4)	33(5)	-16(5)
N40	87(4)	140(6)	133(5)	-16(5)	12(4)	-12(4)
N44	176(6)	127(5)	85(4)	0(4)	-33(4)	23(5)
C45	120(5)	79(4)	111(5)	3(4)	0(4)	3(4)
C48	119(6)	124(7)	130(6)	6(6)	-24(5)	-33(6)
C49	147(7)	99(6)	97(5)	-23(5)	21(5)	-48(6)
C6	66(3)	74(4)	71(3)	-6(3)	9(2)	3(3)
C8	70(3)	81(4)	72(3)	9(3)	4(3)	10(3)
C9	67(3)	83(4)	63(3)	3(3)	2(2)	0(3)
C12	70(3)	80(4)	65(3)	1(3)	15(2)	-4(3)
C13	95(4)	93(5)	65(3)	-6(3)	9(3)	-1(4)
N14	104(4)	102(4)	122(5)	-2(4)	39(3)	11(4)
C18	88(4)	88(4)	72(4)	12(4)	-6(3)	8(4)
C20	79(3)	77(4)	86(4)	17(3)	9(3)	-8(3)
C21	81(4)	87(4)	70(3)	8(3)	13(3)	4(4)
C22	67(3)	87(4)	64(3)	-3(3)	7(3)	1(3)
C24	68(3)	76(4)	86(4)	3(3)	11(3)	-5(3)
C26	70(3)	78(4)	83(4)	-3(3)	9(3)	-5(3)
N29	142(5)	108(5)	90(4)	-4(4)	-28(4)	10(4)
C30	89(4)	104(5)	75(4)	5(4)	1(3)	1(4)
C31	86(4)	76(4)	124(5)	8(4)	0(4)	-2(4)

C32	83(4)	85(4)	82(4)	-10(3)	9(3)	-12(4)
C33	72(4)	97(5)	86(4)	-1(4)	6(3)	-8(4)
C34	93(4)	79(4)	90(4)	-4(4)	15(3)	-7(4)
C39	71(3)	88(4)	66(3)	12(3)	12(3)	-1(3)
C41	97(4)	81(4)	100(4)	-2(4)	5(4)	-14(4)
C42	117(6)	73(4)	95(5)	4(4)	21(4)	0(4)
N43	128(5)	137(6)	102(4)	40(4)	-10(4)	9(5)
C46	88(4)	101(6)	128(6)	6(5)	1(4)	13(5)
C47	130(6)	84(5)	91(5)	20(4)	20(4)	17(5)
N50	90(4)	132(5)	152(5)	-17(5)	31(4)	16(4)

Table 7: Bond Lengths for **84**.

Atom	**Atom**	**Length/Å**	**Atom**	**Atom**	**Length/Å**
C1	C4	1.337(8)	C6	C8	1.541(7)
C1	C5	1.496(7)	C6	C12	1.504(7)
C1	C15	1.498(7)	C6	C20	1.522(7)
C2	C11	1.479(9)	C8	C21	1.475(8)
C2	N25	1.129(7)	C8	C22	1.576(7)
C3	C7	1.521(7)	C8	C30	1.479(8)
C3	C11	1.586(8)	C9	C22	1.510(7)
C3	C23	1.471(9)	C9	C24	1.349(8)
C3	C35	1.477(8)	C9	C39	1.446(7)
C4	C7	1.445(8)	C12	C13	1.500(7)
C5	C11	1.539(7)	C12	C39	1.335(8)
C5	C36	1.522(8)	C13	C32	1.522(8)
C7	C10	1.341(8)	N14	C21	1.138(7)
C10	C17	1.480(8)	C18	C22	1.489(8)
C11	C16	1.482(8)	C18	N29	1.128(7)
C15	C27	1.505(9)	C20	C41	1.524(7)
C16	N37	1.132(7)	C22	C33	1.465(8)
C17	C19	1.389(8)	C24	C26	1.455(8)
C17	C28	1.368(8)	C26	C31	1.377(7)
C19	C38	1.364(8)	C26	C34	1.396(8)
C23	N40	1.140(8)	C30	N43	1.133(7)
C27	C45	1.521(8)	C31	C46	1.365(9)
C28	C48	1.385(10)	C32	C41	1.511(7)
C35	N44	1.137(7)	C33	N50	1.149(7)
C36	C45	1.531(7)	C34	C42	1.350(8)
C38	C49	1.329(10)	C42	C47	1.372(9)
C48	C49	1.392(11)	C46	C47	1.361(10)

Table 8: Bond Angles for **84**.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C4	C1	C5	123.5(5)	C12	C6	C8	112.4(5)
C4	C1	C15	122.1(6)	C12	C6	C20	112.4(4)
C5	C1	C15	114.3(5)	C20	C6	C8	111.5(4)
N25	C2	C11	176.9(6)	C6	C8	C22	110.1(4)
C7	C3	C11	107.2(4)	C21	C8	C6	111.2(4)
C23	C3	C7	110.5(5)	C21	C8	C22	106.4(5)
C23	C3	C11	107.9(5)	C21	C8	C30	109.2(5)
C23	C3	C35	107.1(5)	C30	C8	C6	109.8(5)
C35	C3	C7	113.3(5)	C30	C8	C22	110.2(4)
C35	C3	C11	110.7(4)	C24	C9	C22	121.2(5)
C1	C4	C7	124.2(6)	C24	C9	C39	126.4(5)
C1	C5	C11	111.6(5)	C39	C9	C22	112.4(5)
C1	C5	C36	112.7(4)	C13	C12	C6	114.5(5)
C36	C5	C11	111.1(4)	C39	C12	C6	122.4(5)
C4	C7	C3	112.4(5)	C39	C12	C13	123.1(5)
C10	C7	C3	120.4(5)	C12	C13	C32	112.2(5)
C10	C7	C4	127.0(5)	N29	C18	C22	178.2(7)
C7	C10	C17	126.4(5)	C6	C20	C41	111.5(5)
C2	C11	C3	106.5(5)	N14	C21	C8	176.6(6)
C2	C11	C5	111.3(5)	C9	C22	C8	106.7(4)
C2	C11	C16	108.6(5)	C18	C22	C8	110.0(4)
C5	C11	C3	109.9(4)	C18	C22	C9	112.8(5)
C16	C11	C3	110.6(4)	C33	C22	C8	108.5(5)
C16	C11	C5	110.0(5)	C33	C22	C9	110.9(4)
C1	C15	C27	113.8(5)	C33	C22	C18	107.8(4)
N37	C16	C11	176.7(8)	C9	C24	C26	128.2(5)
C19	C17	C10	118.1(5)	C31	C26	C24	124.7(6)
C28	C17	C10	123.0(6)	C31	C26	C34	116.9(6)
C28	C17	C19	118.8(6)	C34	C26	C24	118.4(5)
C38	C19	C17	120.6(6)	N43	C30	C8	176.3(7)
N40	C23	C3	178.2(8)	C46	C31	C26	121.2(7)
C15	C27	C45	110.8(5)	C41	C32	C13	110.3(5)
C17	C28	C48	119.8(7)	N50	C33	C22	177.3(7)
N44	C35	C3	179.5(7)	C42	C34	C26	121.3(6)
C5	C36	C45	109.4(5)	C12	C39	C9	124.3(5)
C49	C38	C19	120.8(7)	C32	C41	C20	110.0(5)
C27	C45	C36	110.7(5)	C34	C42	C47	120.8(7)
C28	C48	C49	119.6(7)	C47	C46	C31	121.0(7)
C38	C49	C48	120.2(7)	C46	C47	C42	118.6(7)

Table 9: Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters

(Å^2×10^3) for **84**.

Atom	***x***	***y***	***z***	**U(eq)**
H4	8895	1414	2050	90
H5	7535	-1126	968	89
H10	6960	2970	481	94
H15A	8628	-1009	2455	112
H15B	9934	-103	2679	112
H19	6688	4609	1219	103
H27A	11193	-1795	2620	122
H27B	11906	-952	2105	122
H28	10620	2703	1754	117
H36A	10877	-974	690	106
H36B	9604	-1858	362	106
H38	7864	5843	2065	122
H45A	9478	-2509	1583	126
H45B	11337	-2532	1427	126
H48	11802	3974	2603	154
H49	10353	5533	2766	137
H6	7003	1074	3903	84
H13A	5833	1269	2428	101
H13B	4800	2309	2215	101
H20A	3766	1500	4232	97
H20B	4842	493	4495	97
H24	8190	5097	4523	92
H31	4529	5012	3194	116
H32A	2668	1719	2853	101
H32B	3019	828	2283	101
H34	8415	6843	3976	104
H39	6177	3722	2882	90
H41A	4639	-110	3252	112
H41B	2834	61	3455	112
H42	7215	8229	3296	113
H46	3398	6397	2477	129
H47	4783	7990	2473	122

List of publications

1 Diastereoselective synthesis of tetrasubstituted propargylamines *via* hydroamination and metalation of 1-alkynes and their enantioselective conversion to trisubstituted chiral allenes; Periasamy. M.;* Reddy. P.O.; **Satyanarayana. I**.; Mohan. L.; Edukondalu. A. *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. (*Submitted to J. Org. Chem).*

4 Chiral secondary amine approach to chiral allene *via* propargylamines, Periasamy. M.;* Mohan. L.; **Satyanarayana. I**.; Reddy. P.O. *JOC Perspective* (*submitted).*

5 Copper (I) promoted synthesis of tetrasubstituted propargylamines and their conversion to the trisubstituted allenes *via* hydroamination reaction, Periasamy. M.;* Mohan. L.; **Satyanarayana. I.** (*To be communicated)*

6 Copper (I) promoted diastereoselective synthesis of propargylamines *via* hydroamination and metallation of 1-alkynes and their highly enantioselective conversion to β-allenoates, Periasamy. M.;* **Satyanarayana. I**.; Mohan. L. (*To be communicated)*

7 Zn (II) salt promoted synthesis of trisubstituted allenes using amine, ketones, and 1-alkynes, Periasamy. M.;* **Satyanarayana. I**.; Mohan. L. (*To be communicated)*

Achiral and Chiral Secondary Amines for the Synthesis of Propargylamines and Allenes and for Applications in Electron Transfer Reactions

by Satyanarayana Iddum

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Achiral and Chiral Secondary Amines for the Synthesis of Propargylamines and Allenes and for Applications in Electron Transfer Reactions

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1	Mariappan Periasamy, Polimera Obula Reddy, Iddum Satyanarayana, Lakavathu Mohan, Athukuri Edukondalu. "Diastereoselective Synthesis of Tetrasubstituted Propargylamines via Hydroamination and Metalation of 1-Alkynes and Their Enantioselective Conversion to Trisubstituted Chiral Allenes", The Journal of Organic Chemistry, 2016 Publication	19%
2	Mariappan Periasamy, Lakavathu Mohan, Iddum Satyanarayana, Polimera Obula Reddy. " Enantioselective Synthesis of β-Allenoates via Phosphine-Catalyzed and ZnI -Promoted Preparation of Oxazolidines and Propargylamines Using Chiral Amines, 1-Alkynes, and Propiolates ", The Journal of Organic Chemistry, 2017 Publication	3%
3	Ramani Gurubrahamam, Mariappan	

	Periasamy. "Copper(I) Halide Promoted Diastereoselective Synthesis of Chiral Propargylamines and Chiral Allenes using 2-Dialkylaminomethylpyrrolidine, Aldehydes, and 1-Alkynes", The Journal of Organic Chemistry, 2013 Publication	1%
4	Qi Liu, Xinjun Tang, Yujuan Cai, Shengming Ma. "Catalytic One-Pot Synthesis of Trisubstituted Allenes from Terminal Alkynes and Ketones", Organic Letters, 2017 Publication	1%
5	Periasamy, Mariappan, Polimera Obula Reddy, Athukuri Edukondalu, Manasi Dalai, Laxman M. Alakonda, and Bantu Udaykumar. "Zinc Salt Promoted Diastereoselective Synthesis of Chiral Propargylamines Using Chiral Piperazines and Their Enantioselective Conversion into Chiral Allenes : Synthesis of Chiral Propargylamines, Piperazines, and Allenes", European Journal of Organic Chemistry, 2014. Publication	1%
6	ubm.opus.hbz-nrw.de Internet Source	1%
7	Mariappan Periasamy, Polimera Obula Reddy, Nalluri Sanjeevakumar. "Convenient methods	1%