Synthesis of Allenes and Propargylamines and Development of Electron Transfer Reactions

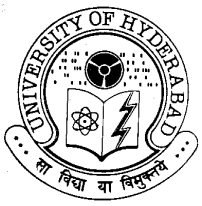
A Thesis

Submitted for the Degree of

DOCTOR OF PHILOSOPHY

By

BANTU UDAYKUMAR



SCHOOL OF CHEMISTRY

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TELANGANA, INDIA

NOVEMBER 2018

Dedicated to

GOD

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DECLARATION

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

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CERTIFICATE

This is to certify that the thesis entitled "Synthesis of Allenes and Propargylamines and Development of Electron Transfer Reactions" submitted by **Mr**. **BANTU UDAYKUMAR** bearing registration number **12CHPH09** in partial fulfillment of the requirements for award of Doctor of Philosophy in the School of Chemistry is a bonafide work carried out by him under my supervision and guidance.

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Parts of this thesis have been published in the following one publication:

1. Periasamy, M.; Reddy, P. O.; Edukondalu, A.; Dalai, M.; Alakonda, L. M.; **Udaykumar, B**. *Eur. J. Org. Chem.* **2014**, 6067.

He has also made presentations in the following conferences:

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

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

	Course	Title	Credits	Pass/Fail
1.	CY-801	Research Proposal	3	Pass
2.	CY-805	Instrumental Methods A	3	Pass
3.	CY-806	Instrumental Methods B	3	Pass
4.	CY-821	Organic Reactions and Mechanism	3	Pass

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Bantu Udaykumar

Contents

Abbreviations

$[\alpha]_D^{25}$	specific rotation at 25 °C, λ = 589 nm
Ac	acetyl
AC	activated charcoal
anhyd.	anhydrous
aq.	aqueous
Ar	aryl
Bn	benzyl
Boc	*tert*-butoxycarbonyl
9-BBN	9-borabicyclononane
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
BINOL	1,1'-bi-2-naphthol
bp	boiling point
bs	broad singlet (spectral)
Bu	butyl
Bz	benzoyl
^{t}Bu	tertiarybutyl
CAN	ceric ammonium nitrate
c-hex	cyclo hexyl
cat.	catalytic
Cbz	benzyloxycarbonyl
cm^{-1}	wavenumber(s)
conf.	configuration
CSA	10-camphorsulfonic acid
CT	charge transfer
DABCO	1,4-diazabicyclo[2.2.2]octane
DCM	dichloromethane
DIPEA	*N*,*N*-diisopropylethylamine

dd	doublet of doublet
de	diastereomeric excess
DEAD	diethyl azodicarboxylate
DEPT	distortionless enhancement by polarization transfer
DIPEA	*N*,*N*-diisopropylethylamine
DMAP	4-(*N*,*N*-dimethylamino)pyridine
DMF	dimethylformamide
DMSO	dimethyl sulfoxide
dr	diastereomeric ratio
ee	enantiomeric excess
EI	electron impact (in mass spectrometry)
epr	electro magnetic resonance
equiv.	equivalent
ESI-MS	electronspray ionization mass spectrometry
Et	ethyl
h	hour(s)
HMPA	hexamethylphosphoramide
HPLC	high-performance liquid chromatography
i	iso
IPA	2-propanol
IR	infrared
O^{i}Pr	isopropyloxy
J	coupling constant (in NMR spectroscopy)
KHMDS	potassium hexamethyldisilazide
LAH	lithium aluminium hydride
LDA	lithium diisopropylamide
LiHMDS	lithium hexamethyldisilazide
liq.	liquid
lit.	literature

LVT	low valent titanium
m	multiplet (spectral)
M	moles/liter
Me	methyl
MHz	megahertz
ms.	minute(s)
mp	melting point
MS	mass spectrum
Ms	methanesulfonyl
M.S.	molecular sieves
MSA	methanesulfonic acid
NMR	nuclear magnetic resonance
Nu	nucleophile
ORTEP	Oak Ridge Thermal Ellipsoid Plot
PC	propylene carbonate
PEO	polyethylene oxide
Ph	phenyl
ppm	parts per million (spectral)
^{i}Pr	isopropyl
psig	pounds per square inch gauge
PTSA	*p*-toluenesulfonic acid
Py	pyridine
q	quartet
rt	room temperature
s	singlet
sec	secondary
SET	single electron transfer
t	tertiary
t	triplet

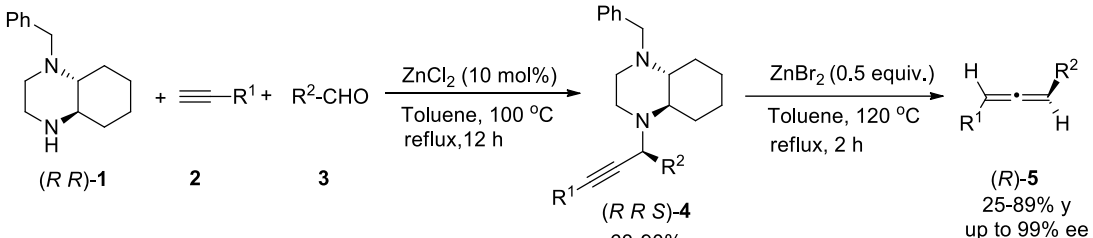
TBAI	tetrabutylammonium iodide
TBSCl	tertiarybutyldimethylsilylchloride
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TMHCDA	*N*,*N*,*N*,*N*-tetramethylcyclohexane-1,2-diamine
TMS	tetramethylsilane
Ts	toluenesulfonyl
Uv	ultraviolet
y	yield

Abstract

This thesis entitled "**Synthesis of Allenes and Propargylamines and Development of Electron Transfer Reactions**". It comprises of Five chapters. Each chapter divided into four sections namely, **Introduction, Results and Discussion, Conclusions** and **Experimental Section**. The work described in this thesis is exploratory in nature.

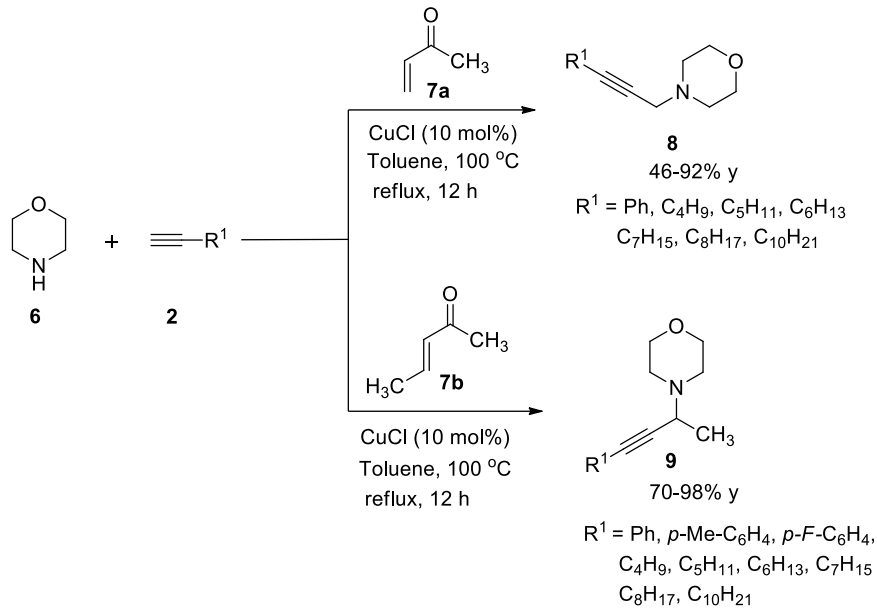
The first chapter describes the zinc chloride catalyzed reactions of chiral (*R,R*)-1-benzylpiperizine **1** with 1-alkynes **2** and aldehydes **3** to give the chiral propargylamines **4** in 63-90% yields with up to 99:1 dr. The chiral propargylamines are converted to chiral allenes **5** using zinc bromide with high enantioselectivities (up to 99% ee) in 25-89% yields. The chiral piperazine recovered in good yield (75%) by the reduction of the imine byproduct *in situ* using $NaBH_4$.

Scheme 1



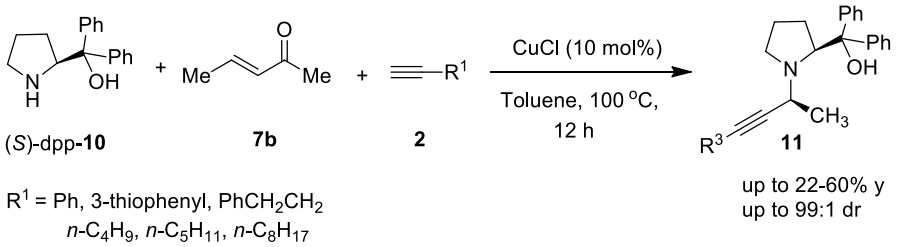
The second chapter deals with the results and discussion on the synthesis of propargylamines **8-9** using methyl vinyl ketone derivatives **7a-7b**, 1-alkynes **2** and secondary amines **6** catalyzed by Cu salts involving Michael addition of amine followed by an unusual C-C bond cleavage reaction and addition of the *in situ* formed metal acetylides to iminium ions (Scheme 2).

Scheme 2



We have also synthesized the chiral propargylamines **11** using chiral (*S*)-diphenylpyrrolidinemethanol **10**, 3-pentene-2-one **7b** and various 1-alkynes **2** in the presence of 10 mol% of CuCl (Scheme 3). The chiral propargylamines **11** are obtained in 22-60% yields with up to 99:1 dr. The aromatic alkynes like phenylacetylene, 3-ethynylthiophene and 4-phenyl-1-butyne gave the corresponding chiral propargylamines in 35-60% yields with up to 99:1 dr. We have also carried out the reaction using aliphatic alkynes such as 1-hexyne, 1-heptyne and 1-decyne under this reaction condition. The corresponding propargylamines were obtained in 22-47% yields with up to 80:20 dr**.**

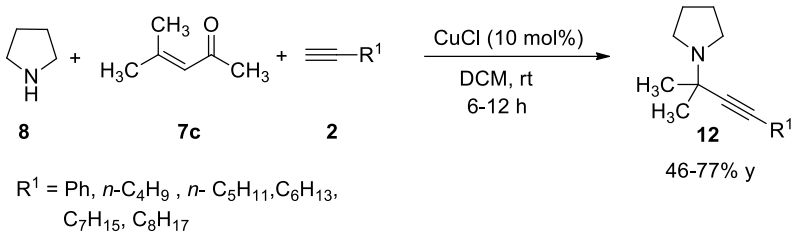
Scheme 3



We have also examined the reaction of pyrrolidine **8** with mesityl oxide **7c** and 1- alkynes in the presence of CuCl (10 mol%) to prepare tetrasubstituted

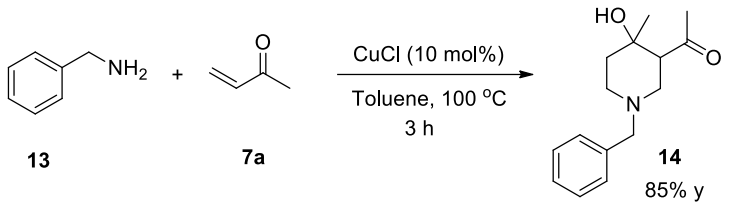
propargylamine deivatives **12** in 46-77% yields (Scheme 4).

Scheme 4



We have observed that the reaction of primary amine like benzylamine **13** with methyl vinyl ketone **7a** in the presence of 10 mol% CuCl gave the 1-(1-benzyl-4-hydroxy-4- methylpiperidin-3-yl) ethanone **14** in 85% yield *via* double Michael addition followed by aldol reaction (Scheme 5).

Scheme 5



In the third chapter, studies undertaken on the electron transfer reactions of primary, secondary and tertiary amine donors with different acceptors such as activated charcoal, viologens and quinones for use in organic transformations are described (Figure 1).

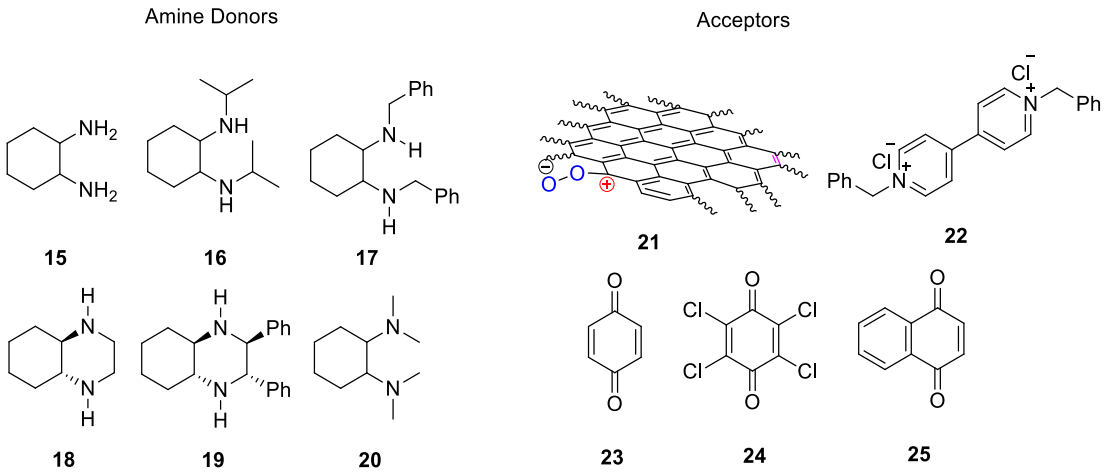
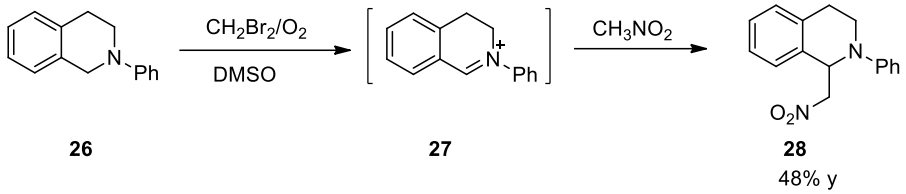


Figure 1. Amine donors and various acceptors

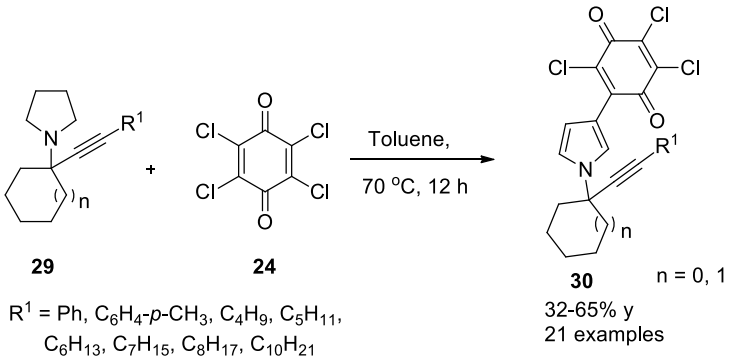
We have synthesized the aza-Henry reaction product **28** in 48% yield, following the method outlined in Scheme 6 using N-phenyltetrahydroisoquinoline, CH_2Br_2 in the presence of oxygen.

Scheme 6



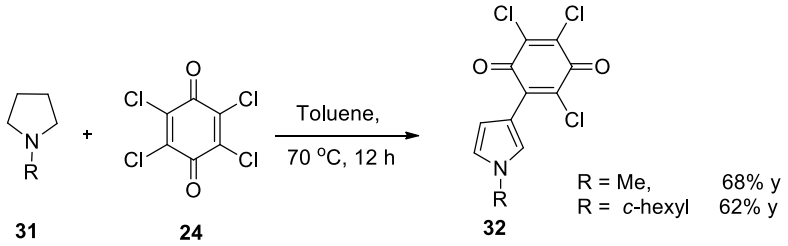
In the fourth chapter, we have described efforts to develop new synthetic methods based on ground state electron transfer reactions between amines and *p*-chloranil. A new method for the synthesis of substituted pyrroles **30** from the reaction of *N*-propargyl pyrrolidines **29** using *p*-chloranil **24** was developed (Scheme 7).

Scheme 7



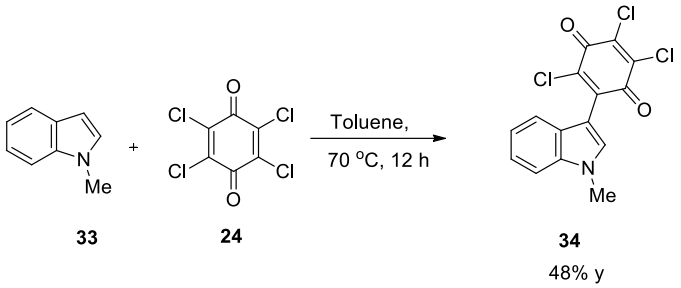
We have also carried out the reaction of *N*-alkyl pyrrolidine derivatives **31** with *p*-chloranil and obtained the corresponding substituted pyrrole derivatives **32** with up to 68% yields (Scheme 8**).**

Scheme 8



We have observed that the reaction of *N*-methyl indole **33** with *p*-chloranil gave the corresponding 3-substituted-*N*-methyl indole product **34** in 48% yield (Scheme 9**)**.

Scheme 9



In the fifth chapter, we have described the construction of organic electrochemical cells based on the electron transfer reactions of N^1,N^1,N^2,N^2-tetramethylcyclohexane-1,2-diamine **20** with *p*-chloranil to generate the electricity. In these cells, the *p*-benzoquinone **23**, dimethyl sulfone **36** and phthalimide derivatives **35** were used as electron transporters (Figure 2).

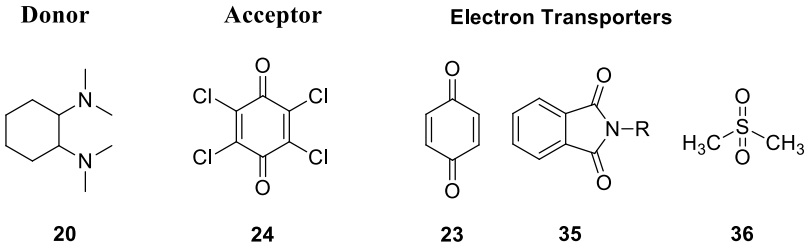
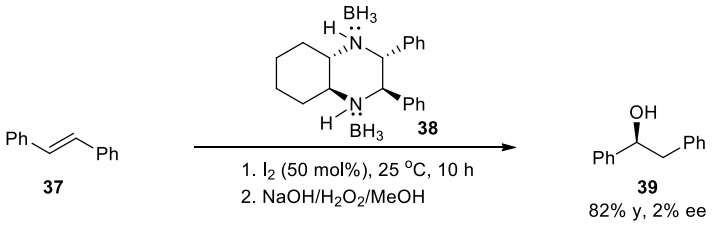


Figure 2

We have also briefly studied the hydroboration reaction of prochiral olefins using chiral 2,3-diphenylpiperazine-borane complexes **38**. The corresponding alcohols were obtained in only up to 2% ee under iodine activation (Scheme 10). The results are discussed considering the mechanistic aspects of the hydroboration reaction in the Annexure III.

Scheme 10



The experimental details, spectral data and references are provided under each chapter.

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

Chapter 1

Synthesis of Chiral Allenes using Chiral Amine, Aldehydes and 1-Alkynes

1.1 Introduction

Chiral amines and their derivates are important building blocks for the synthesis of many pharmaceutical and biologically active molecules.[1] The 1,2-diaminocyclohexane and its derivatives are among the most frequently used chiral ligands for a variety of asymmetric transformations and for the synthesis of a large number of biologically active compounds.[2-4] Several biologically active compounds contain 1,2-diaminocyclohexane moiety such as biotin **(1)**, pencillins **(2)**, oxaliplatin **(3)**, Tamiflu **(4)**, U-50,488 **(5)** as shown in Figure **1**. The 1,2-diamine derivatives are also synthetic precursors for the synthesis of heterocycles and nitrogen containing macrocyles.[5-6] We have investigated the synthesis and applications of enantiomerically pure piperazine derivatives containing chiral (*1R,2R*)-diaminocyclohexane moiety. A brief review on the synthesis of chiral propargylamines and chiral allenes from the chiral piperizine derivatives would facilitate the discussion of the results.

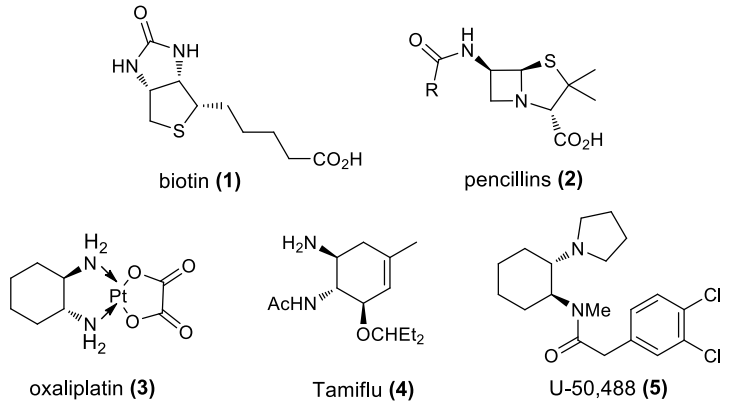
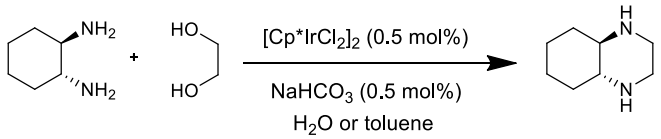


Figure 1

1.1.1 Synthesis of chiral piperizine 8 starting from the (*1R,2R*)-diaminocyclohexane 6.

The chiral decahydroquinoxaline **8** was prepared by the reaction of (1*R*,2*R*)-diaminocyclohexane **6** with1,2-diols **7** under basic conditions in 94% yield as shown in Scheme 1.[7]

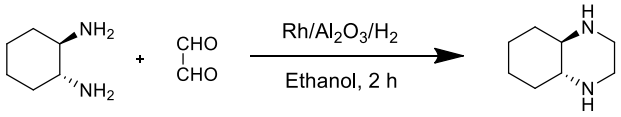
Scheme 1



6 **7** **8**
94-96% y

The reaction between the chiral l,2-diaminocyclohexane **6** and glyoxal **9** with $Rh/Al_2O_3/H_2$, afforded the chiral decahydroquinoxaline **8** in low yields (Scheme 2).[8]

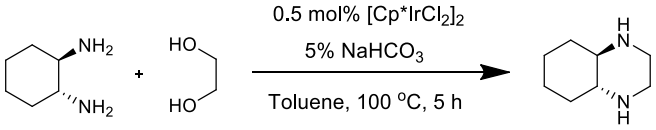
Scheme 2



6 **9** **8**
20 % y

Iridium complex catalyzed synthesis of chiral decahydroquinoxaline **8** was reported (Scheme 3).[9]

Scheme 3

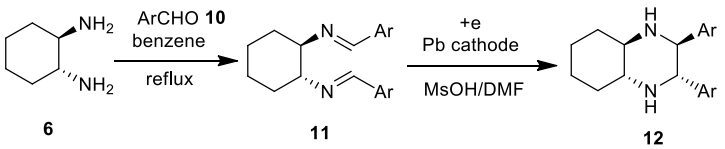


6 **7** **8**
94 % y

1.1.2 Synthesis of chiral 2,3-diphenyldecahydroquinoxaline derivatives using chiral (*1R,2R*)-diaminocyclohexane

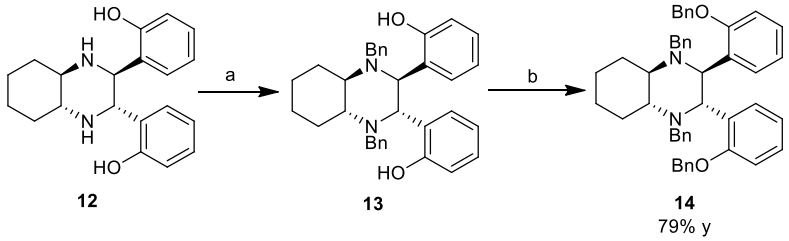
The chiral piperazine analogues (**12** and **14**) were synthesized by electroreductive intramolecular coupling of diimine **11** and used as chiral auxillaries in the enantioselective addition of dialkyllzinc to aldehydes (Scheme 4).[10]

Scheme 4

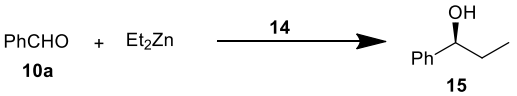


6 **11** **12**
Ar = 2-OH-C_6H_4
78% y

Scheme 4 (continued)

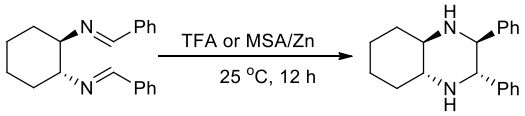


a: i. TMSCl, Et_3N, toluene, reflux ii. BnBr, reflux
b: NaH, BnBr, THF, reflux



The chiral 2,3-diphenyldecahydroquinoxaline **12a** was synthesized from the corresponding diimine **11a** by reductive coupling using zinc and trifluoroacetic acid or methanesulfonic acid (Scheme 5).[11]

Scheme 5



1.1.3 Synthesis of chiral piperazine derivatives

Cyclization of the chiral amino acids followed by reductions afforded the chiral piperazine derivatives as outlined in Chart 1.[12-14]

Chart 1

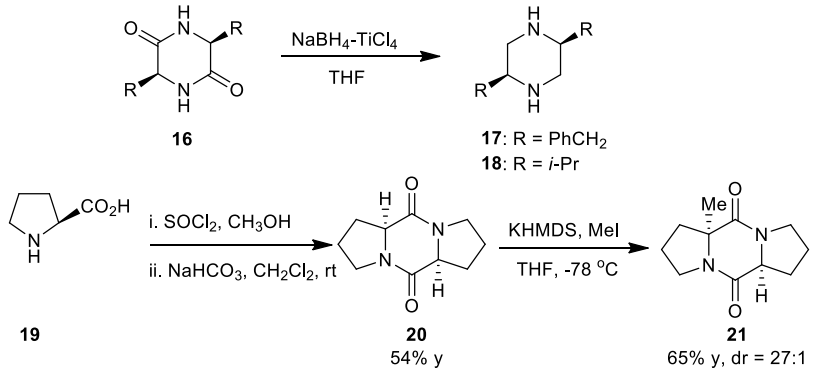
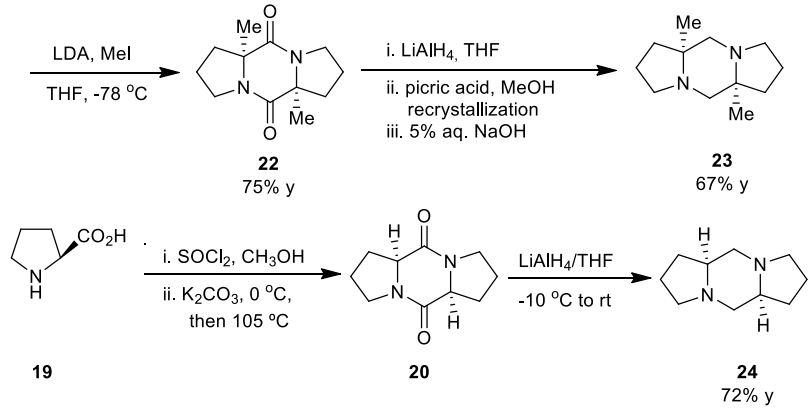
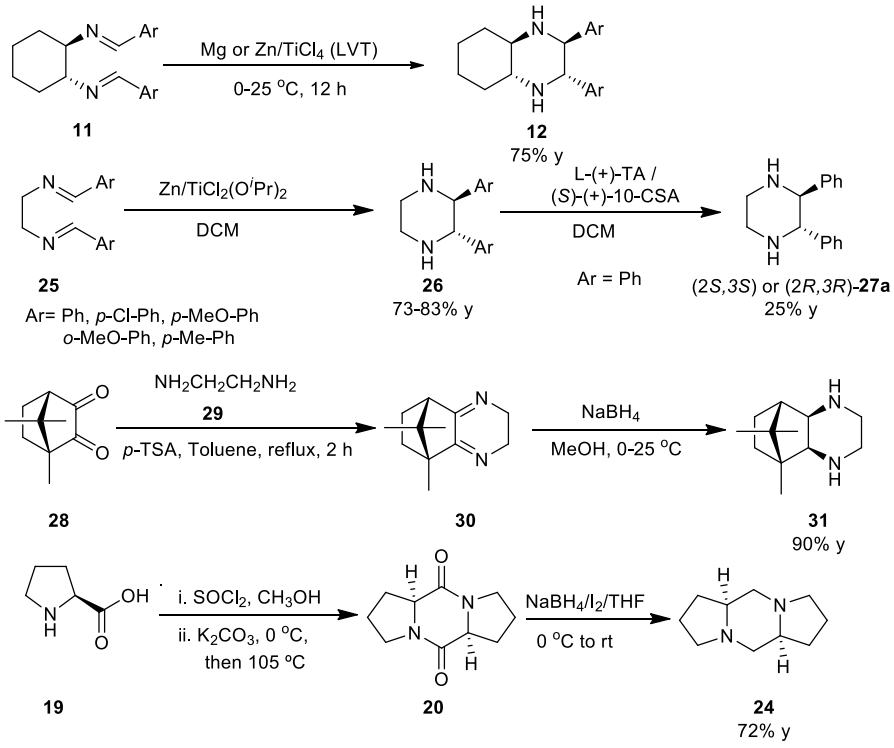


Chart 1 (continued)



Recently, methods have been developed in this laboratory for the synthesis of chiral diamine motif with low valent transition metal agents through intramolecular reductive coupling of diimines (Chart 2).[15-17] Very recently, a method also reported for the synthesis of chiral cyclic diamine **24** starting from L-proline **19** followed by reduction of cyclic diamide **20** with $NaBH_4/I_2$ system.[18]

Chart 2

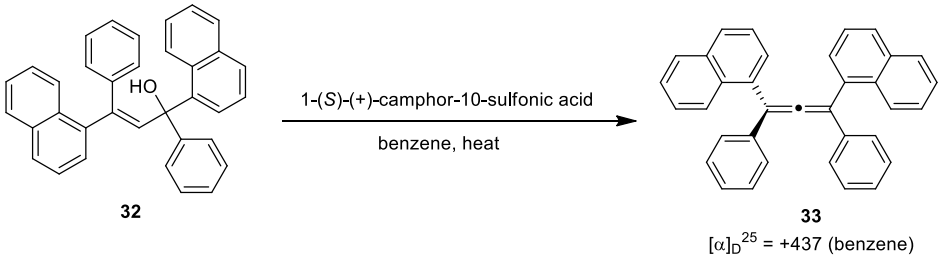


1.1.4 Chiral allenes

We have also decided to perform the reactions of chiral piperizine containing trans-1,2-diaminocyclohexane in diastereoselective synthesis of propargylamines and their conversion to chiral allenes. Accordingly, a brief studies for the synthesis of chiral propargylamines and chiral allenes will be useful for discussion of the results.

Jacobus Henricus van't Hoff envisaged the two enantiomeric forms of substituted allenes.[19] Later, Burton and Pechmann were synthesized the first allene.[20] Initially, chiral allene **33** was prepared by Maitland and Mills from the racemic allylic alcohol **32** using (+)-camphor-10-sulfonic acid (Scheme 6).[21]

Scheme 6



32 **33**

$[\alpha]_D^{25}$ = +437 (benzene)

Chiral allenes are important synthetic molecules in organic chemistry because of orthogonal π bond and capability to experience a diversity of transformations.[22] In 1924, Staudinger and Ruzicka were analyzed the naturally occuring pyrethrolone allene.[23] The optically active allene structures are presented in a diverse natural products and pharmacologically molecules. Hence, these active compounds have motivated immense research activities on allenes by organic and medicinal chemists. More than 150 natural products and pharmaceuticals containing allene moiety have been isolated and some of the natural products which are having allene motif are presented in Figure 2.[24,25]

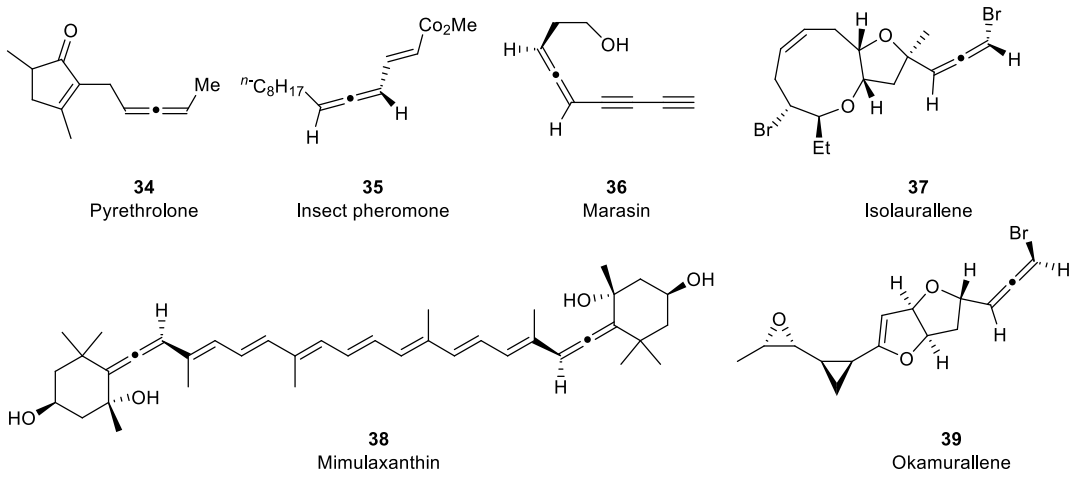


Figure 2

1.1.5 Biologically active chiral allenes

Allenes occur in nature as well as have significant potential for development of biologically active molecules.[26,27] For example, scorodonin **40**, nemotin **41** and phomallenic acid A **42** have inhibiting effects on the growth of bacteria, yeasts and filamentous fungi.[28] Some of the inhibitors containing allene moieties, sterol **43**, enprostil **44**, cytallene **45** and adenallene **46**, vitamin B_6-dependent decarboxylase (suicide substrate) **47** are shown in Figure 3.[29,30]

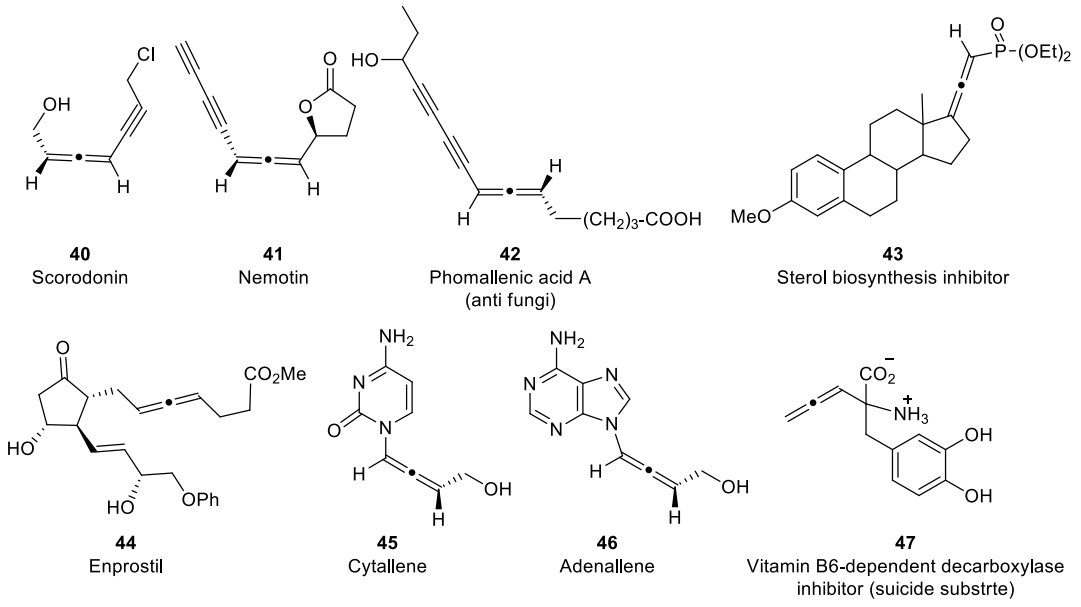
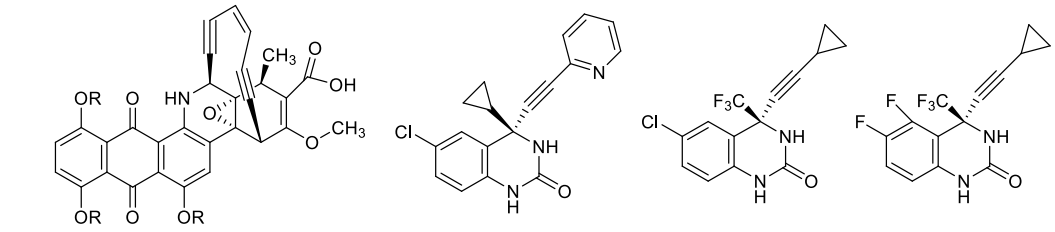


Figure 3

1.1.6 Chirality transfer from propargylic compounds

Chiral propargylamines are valuable precursors for the synthesis of biological active skeletons, natural products and polyfunctional reverse transcriptase inhibition and anti-bacterial activity as outlined in Figure 4.[48,49]



48 R = H Dynemicin A
49 R = $COCH_3$ Triacetyl Dynemicin A

50
HIV reverse transcriptase inhibitor

51
DPC 961

52
NNRTI DPC 963

Figure 4

The chiral propargyl derivatives are also useful for preparation of chiral allenes. A brief review on the synthesis of propargyl derivatives and their conversion to chiral allenes would facilitate the discussion.

Chiral allenes were prepared by the addition of Grignard reagent to the enantiomerically pure propargyl alcohols followed by elimination. Here, the central chirality is transferred to axial chirality of the allene from propargylic position. Methods were also reported for nucleophilic substitution reactions of propargylic alcohols to give chiral allenes using diverse leaving groups (Chart 3).[50,51]

Chart 3

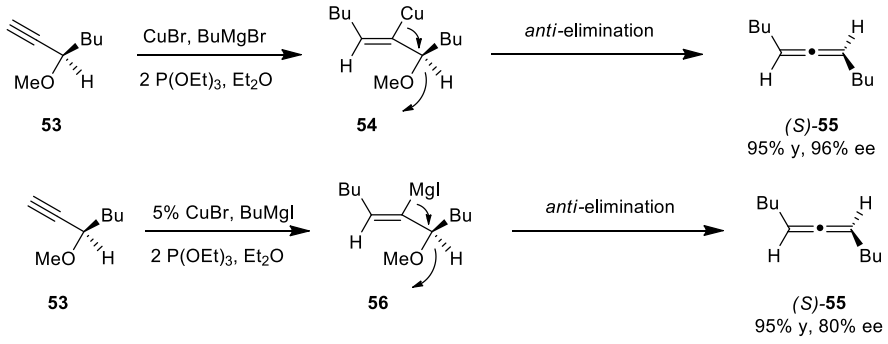
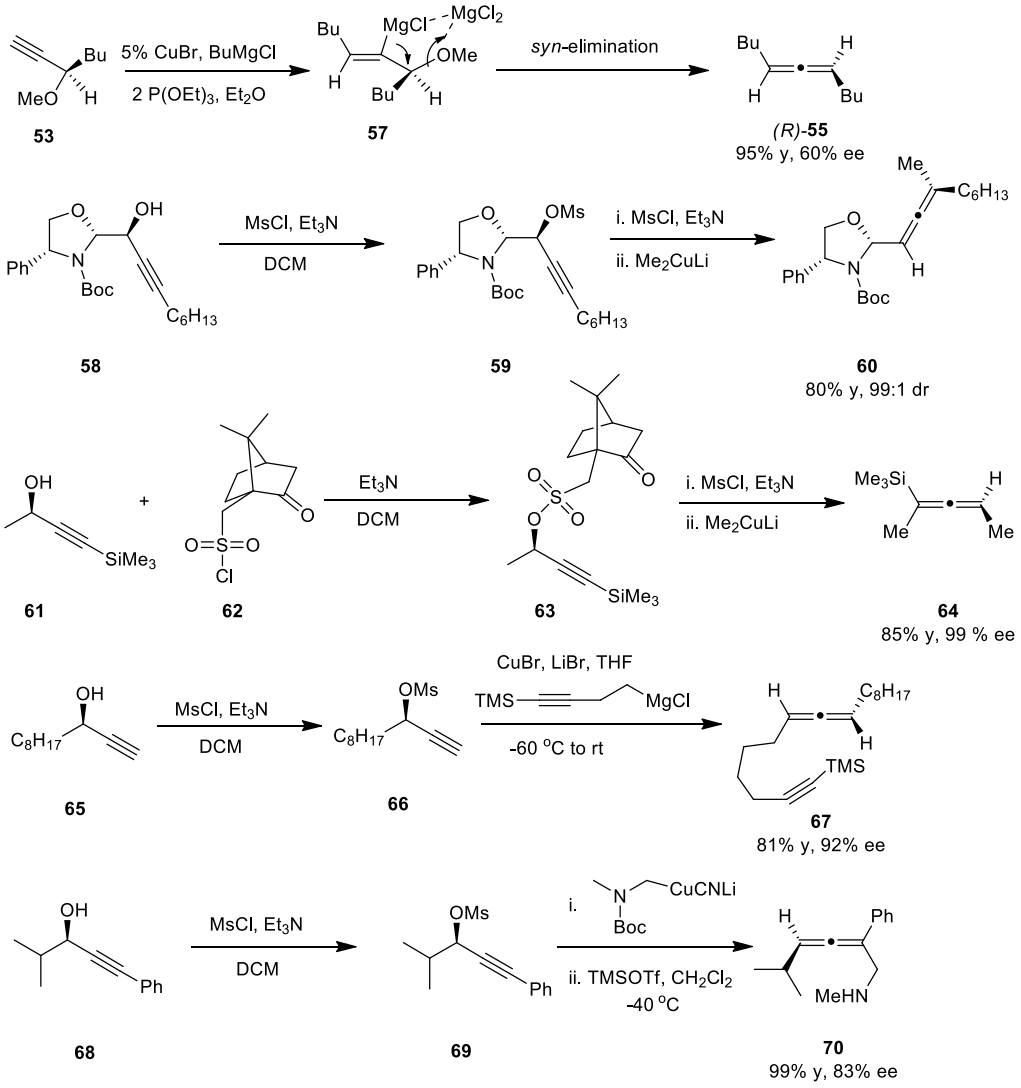
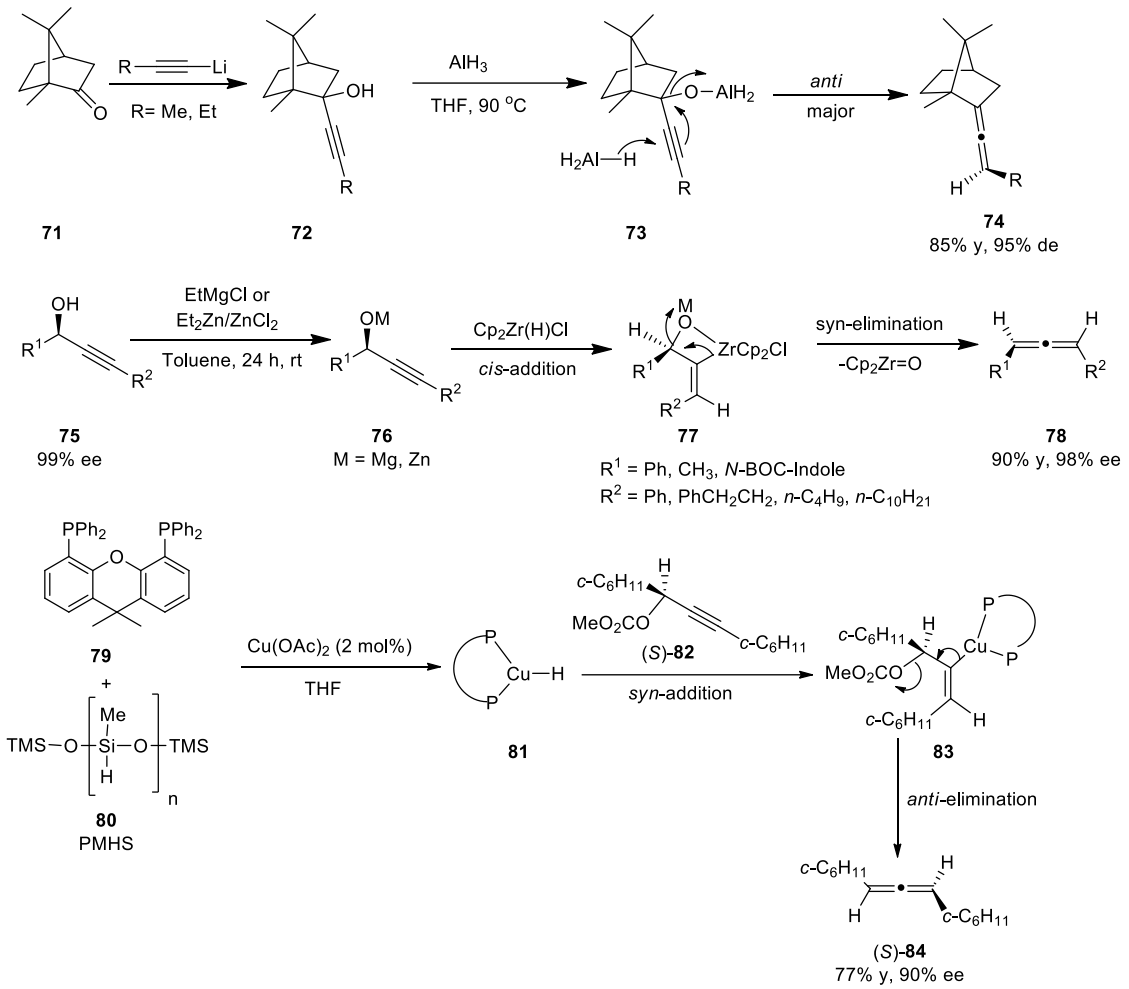


Chart 3 (continued)



Highly diastereoselective method of synthesis of camphanyl allenes **74** were developed from the corresponding propargyl alcohols **72** by reduction with AlH_3 as shown in Chart 4.[52] The chiral allenes were also prepared with excellent selectivity by syn-elimination of propargylic intermediate **77** and copper(I)-catalyzed anti-S_N2'-type reduction of propargylic esters **82** (Chart 4).[53,54]

Chart 4



1.1.7 Enantioselective sigmatropic rearrangements

A variety of chiral propargyl alcohols undergo Claisen rearrangement to afford the corresponding chiral allenes (Chart 5).[55-58]

Chart 5

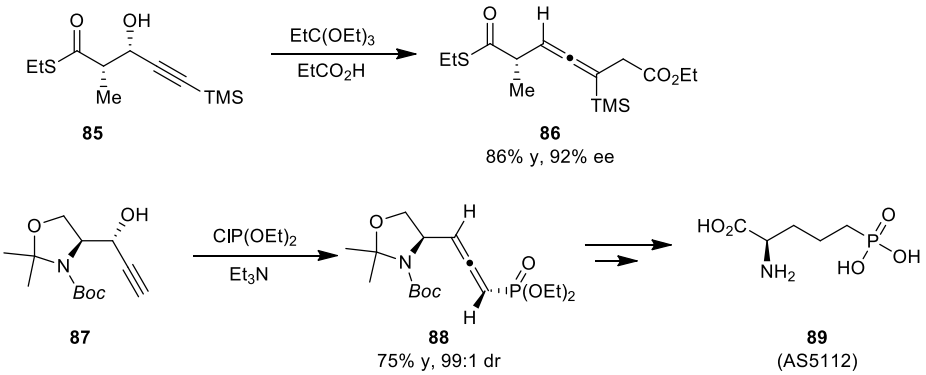
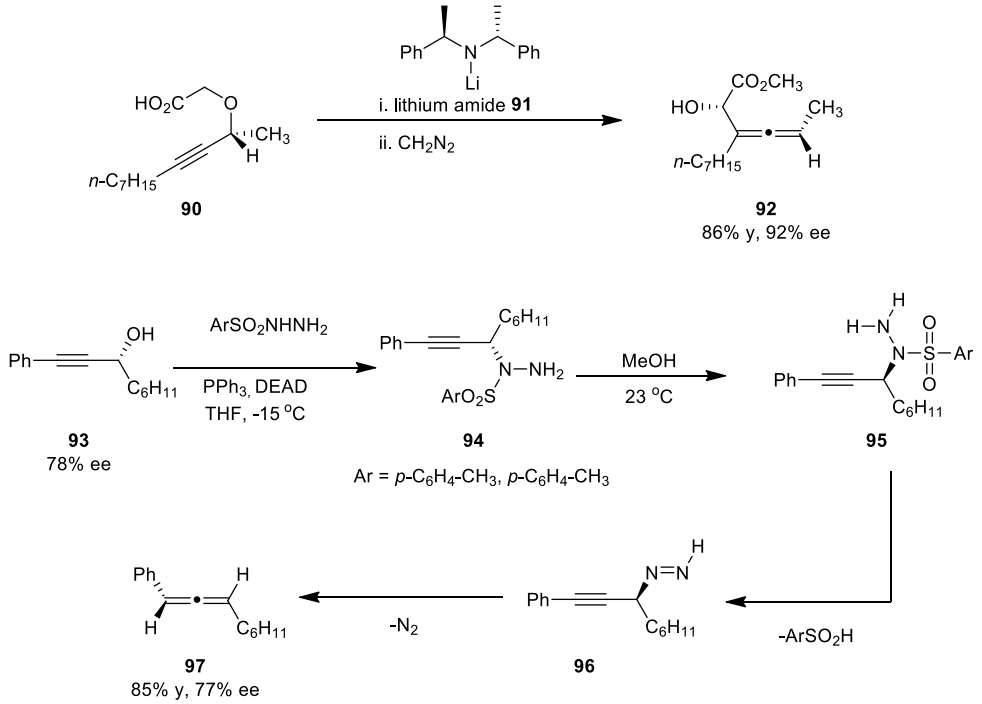


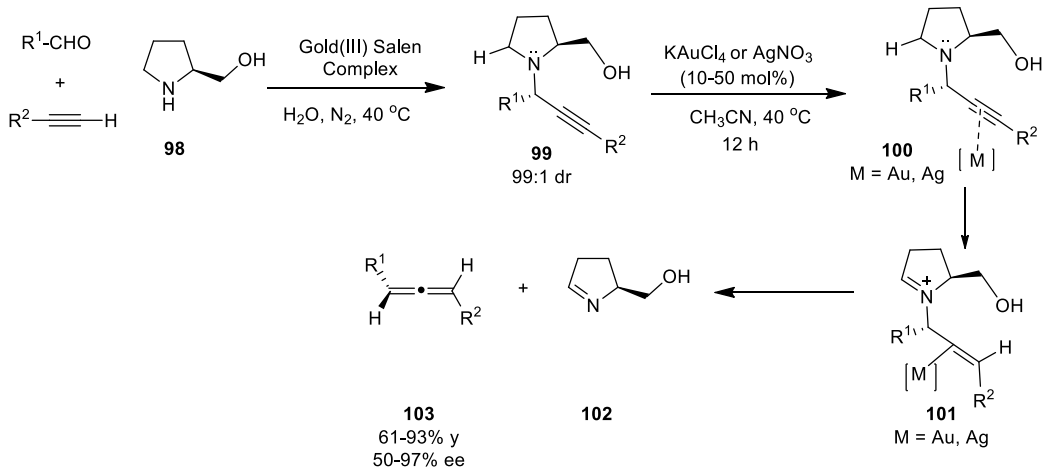
Chart 5 (continued)



1.1.8 Chirality transfer by Crabbe homologative allenylation

The gold catalyzed diastereoselective synthesis of propargylamines was reported using aldehydes, 1-alkynes and chiral amino alcohol **98**. These chiral propagylamines were further converted into chiral allenes **103** using $KAuCl_4$ or $AgNO_3$ catalyst in CH_3CN solvent with up to 97% ee (Scheme 7).[59]

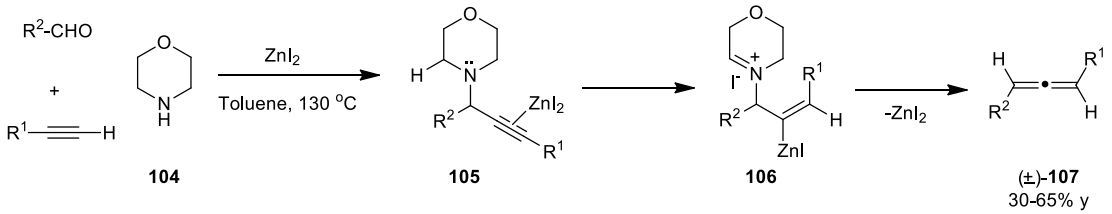
Scheme 7



1.1.9 Synthesis of racemic allenes using 1-alkynes, aldehydes and cyclic amines

Ma et al.[60] reported the racemic allenes **107** by using aldehydes, 1-alkynes, morpholine **104** with ZnI_2 in toluene solvent at 130 ^oC (Scheme 8).

Scheme 8



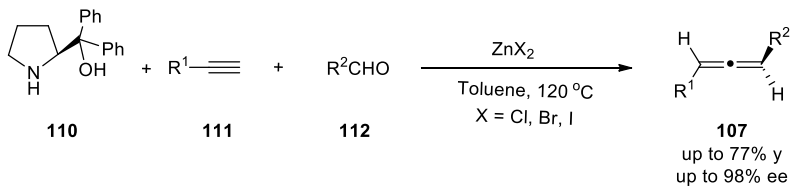
1.1.10 Previous methods on the allene synthesis developed from this laboratory

Previously, racemic chloroallenes **109** were prepared in this laboratory from the corresponding propargylic alcohols **108** using the $TiCl_4/Et_3N$ reagent system (Scheme 9).[61]

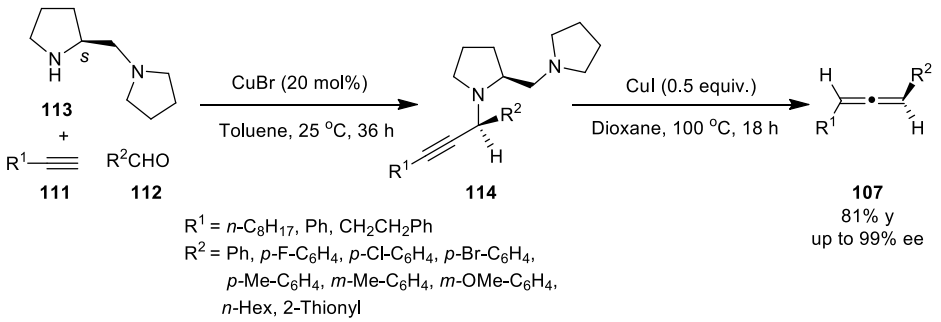
Scheme 9

Recently, a highly enantioselective method for the synthesis of chiral allenes **107** using chiral amines, aldehyde **112** and 1-alkyne **111** with ZnI_2 *via* three component coupling reaction was reported from this laboratory.[62] Very recently, CuX promoted method to give the chiral allenes **107** also reported in a two step process *via* chiral propargylamines **114** using chiral 2-dialkylaminomethyl pyrrolidine **113**, aldehyde **112** and 1-alkyne **111** (Scheme 10).[63]

Scheme 10



Scheme 10 (continued)



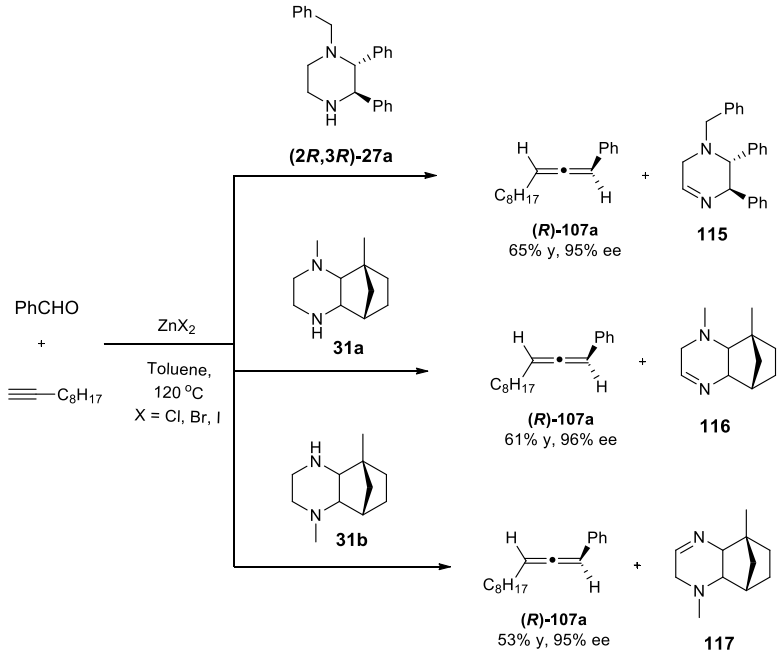
We have studied the applications of chiral 1,2-diamine derivatives to access the chiral propargylamines and chiral allenes. The results are discussed in the next section.

1.2 Results and Discussion

1.2.1 Efforts towards the synthesis of chiral allenes.

In the past decade several methods were reported for the synthesis of chiral allenes by using chiral amines. In recent years, methods have been developed in this laboratory to access several chiral diaminocyclohexane derivatives.[64] Previously, the (*R*,*R*)-*N*-benzyl-2,3-diphenylpiperazine **27a**, *N*-methyl camphanyl piperzine derivatives (**31a** and **31b**) were used as a chiral auxiliary in the enantioselective synthesis of chiral (*R*)-allene **107a** to obtain the product in good yields and selectivities as outlined in Chart 6.[62] We have undertaken efforts to synthesize chiral allenes *via* propargylamines using chiral piperizine containing (1*R*,2*R*)-trans-1,2-diamino-cyclohexane moiety.

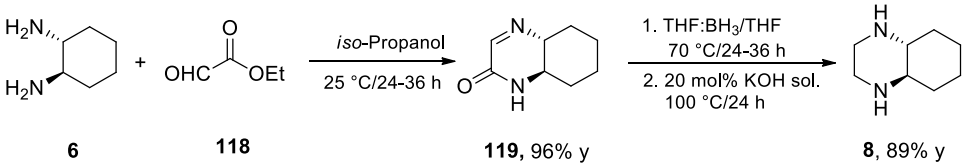
Chart 6



1.2.2 Preparation of *N*-benzyldecahydroquinoxaline and applications for chiral propargylamines and chiral allenes synthesis

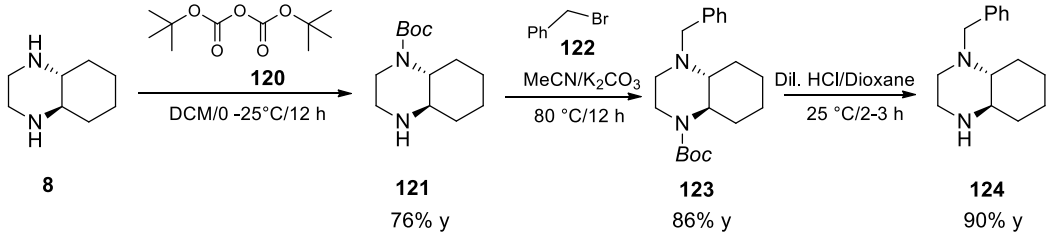
We have prepared the chiral C_2-symmetric decahydroquinoxaline **8** by the reaction of trans-(1*R*,2*R*)-diaminocyclohexane **6** and ethyl glyoxylate **118** followed by reduction of amide **119** with $NaBH_4/I_2$ regent system as outlined in Scheme 11.[65]

Scheme 11



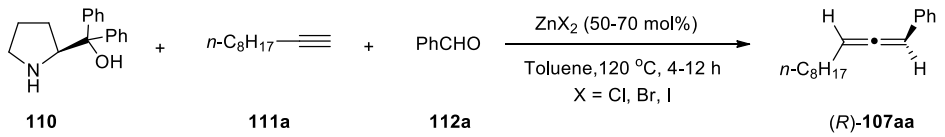
We have then developed a method to access chiral 1-benzyldecahydroquinoxaline **124** from chiral decahydroquinoxaline **8** *via* synthetic sequence using Boc-anhydride **120** to obtain Boc protected chiral decahydroquinoxaline **121**, followed by benzylation and Boc deprotection (Scheme 12).

Scheme 12



Recently, "chiral amine approach" for highly enantioselective synthesis of chiral allenes has been developed in this laboratory using terminal alkynes, aldehydes and chiral amines promoted by zinc halides in a single pot operation.[62] Thus, the zinc halide promoted reaction of chiral secondary amines, 1-decyne **111a** and benzaldehyde **112a** at 120 °C has been developed to access the chiral allenes in very high enantioselectivity (82% to 99% ee) as shown in Scheme 13.[62]

Scheme 13



The easily accessible and commercially available chiral amino alcohol **110** yielded the chiral allene **107aa** in 98% ee and the reaction has been generalized for a variety of aldehydes and alkynes but the results are highly dependent on the sequential addition of the reactants.[62] For instance, inadvertent formation of the oxazolidine intermediate **125** could lower the enantioselectivity of the allene to 86% ee.[62] The imine byproduct **126** could be isolated and recycled back to the chiral diphenyl prolinol **110** in 75% yield by $NaBH_4/CH_3OH$ reduction. However, careful analysis of the imine product mixture indicated the formation of the byproduct **127** (5-10% yields) formed by condensation with the benzaldehyde present in the medium (Figure 5).[71]

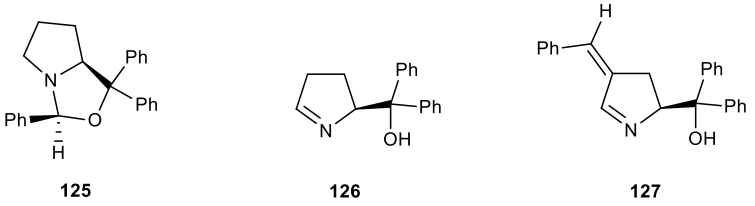


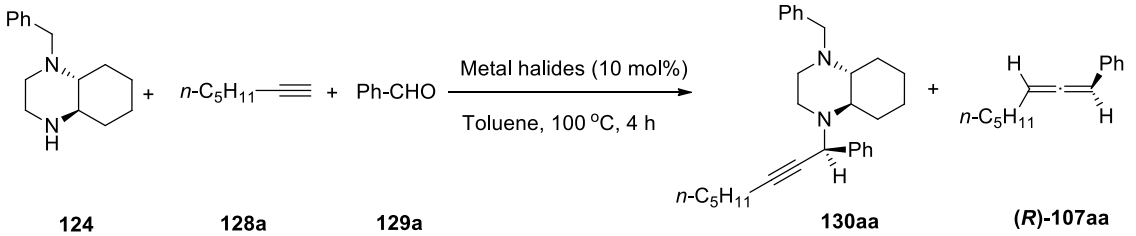
Figure 5

Therefore, we have decided to examine the use of chiral *N*-benzyl-piperazine derivative **124** for applications in this transformation, especially for the two step conversion *via* the corresponding propargylamine as this would avoid the presence of the aldehyde substrates that could react with the corresponding cyclic imine byproduct after the formation of the allene. Previously, a CuBr promoted two step protocol was reported but it takes 36 h at 25 °C for the preparation of chiral propargylamines and another 18 h at 100 °C for the CuI

promoted conversion to chiral allenes.[63]

We have found that the chiral propargylamine **130aa** was obtained in 69% yield with 99:1 dr in the $ZnCl_2$ catalyzed reaction of 1-heptyne **128a**, aldehyde **129a** and the chiral (*R*,*R*)-*N*-benzyl-piperazine **124** at 100 °C. The chiral propargylamine **130aa** was obtained in slightly lower yield using other metal halides like $ZnBr_2$, CuBr and CuI under this reaction condition (Table 1).

Table 1. Synthesis of chiral propargylamine **130aa** using 1-heptyne **128a**, benzaldehyde **129a** and the chiral piperazine **124** using metal salts[a]



124 **128a** **129a** **130aa** **(*R*)-107aa**

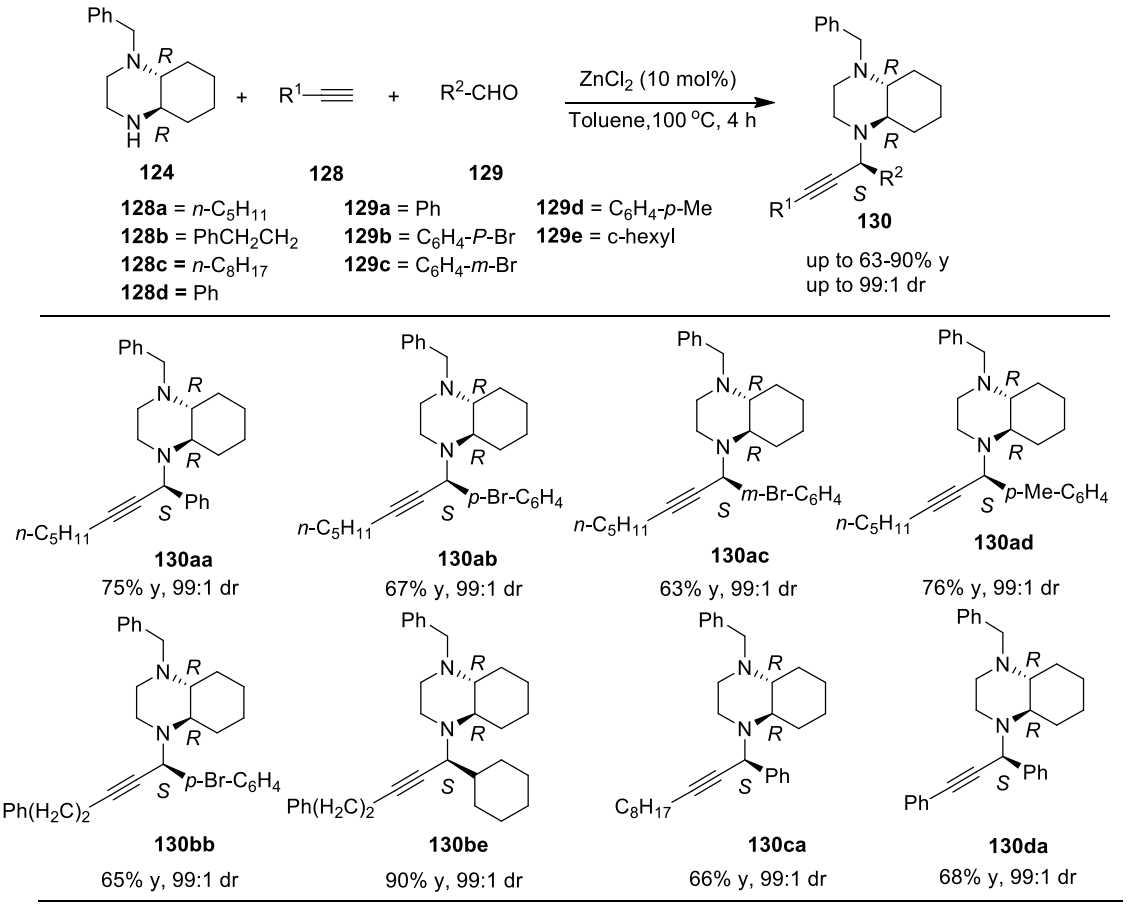
Entry	Metal halides	mol%	Time (h)	**130aa**[b]	dr[c]	**107aa**[b]	% ee[d]
1	$ZnCl_2$	10	4	69	99:1	-	-
2	$ZnBr_2$	10	4	65	99:1	10	94
3	CuBr	10	4	58	98:2	8	94
4[e]	CuBr	10	24	60	99:1	-	-
5	CuI	10	4	62	97:3	15	94

[a]The reactions were carried out using amines (1.0 mmol), 1-alkyne (1.1 mmol) and aldehyde (1.0 mmol) in toluene (3 mL) at 100 °C for 4 h. [b]Isolated yield of the products **130aa** and **107aa**. [c]dr ratio based on ^{1}H NMR of crude products of the mixture. [d]The % ee of allene **107aa** was determined by HPLC analysis on chiralcel OD-H column. [e]The reactions were carried out at 25 °C for 24 h.

When the reaction was carried out using chiral (*R*,*R*)-*N*-benzyl-piperazine **124** with 1-heptyne **128a,** benzaldehyde **129a** and $ZnBr_2$, the corresponding chiral propargylamine **130aa** was obtained in 65% yield with 99:1 dr at 100 °C about 4 h. In this case we have also observed the chiral allene **130aa** in 10% yield with up to 94% ee. The reaction also gave the chiral propargylamines with 10 mol% CuBr and CuI with up to 62% yield with 98:2 dr along with the chiral allene (15% y) **130aa** with 94% ee (Table 1). These results (Table 1) clearly indicate that 10 mol% of $ZnCl_2$ exhibits a higher catalytic activity in the synthesis of chiral propargylamine without formation of chiral allene. Next, we have investigated the synthesis of various chiral propargylamine derivatives from the corresponding (*R*,*R*)-*N*-benzyl-decahydroquinoxaline **124** using different alkynes **128** and aldehydes **129**. The results are summarized in Table 2.

The reaction using amine **124**, benzaldehyde **129a** and 1-heptyne gave the desired product **130aa** in 75% yield with 99:1 dr. The arylaldehydes containing electron-donating group such as para methyl **130g** undergo this reaction to give the corresponding propargylamine in 76% yield with 99:1 dr. Electron-deficient aryl aldehydes **129b**–**129c** transformed smoothly into the desired propargylamine derivatives **130ab**, **130ac**, and **130bb** in 63–67% yields with up to 99:1 *dr*. The propargylamine **130be** was obtained in 90% yield with 99:1 dr. Propargylamines **130ca**–**da** were obtained in 66–68% yields with up to 99:1 dr by using the chiral piperazine derivative **124** (Table 2).

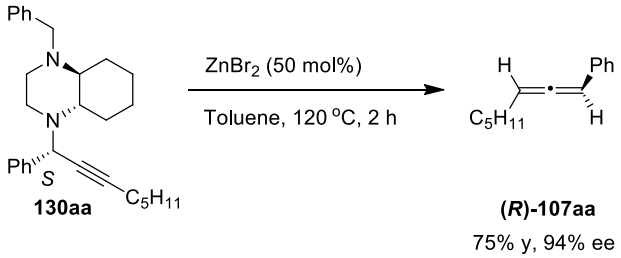
Table 2. $ZnCl_2$ promoted synthesis of chiral propargylamines **130** using 1-alkynes **128**, aldehydes **129** and chiral piperazine **124**[a,b,c]



[a]The reactions were carried out by taking amine (1.0 mmol), 1-alkyne (1.1 mmol) and aldehyde (1.0 mmol) in toluene (3 mL) at 100 °C for 4 h. [b]dr ratio based on crude ^{1}H NMR. [c]Isolated yield of the product **130**.

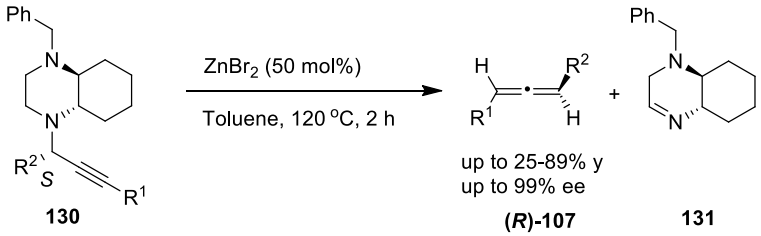
We then turned our attention toward the conversion of chiral propargylamines into the corresponding chiral allenes. We have observed that the reaction of chiral propargylamine **130aa** with $ZnBr_2$ (0.5 mmol) at 120 °C gave the chiral allene **107aa** in up to 75% yield with 94%*ee*. The same procedure was followed for the conversion of other diastereomerically pure propargylamines into the corresponding chiral allenes. The results are summarized in Table 3.

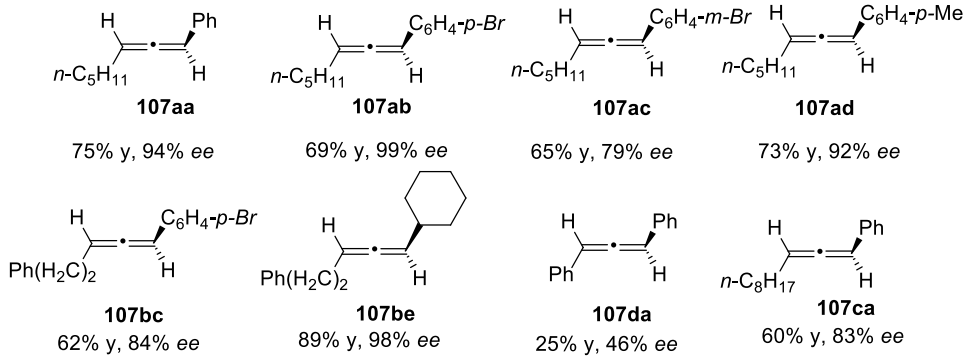
Scheme 14 Conversion of chiral propargylamine to chiral allene



The chiral propargylamine **130ad** substituted with *para* methyl group afforded the corresponding chiral allene **107ad** in 73% yield with up to 92% ee. We have also carried out the reaction using the *para*-bromo and *meta*-bromo containing propargylamines **130ab-130ac** with $ZnBr_2$ (0.5 mmol) at 120 °C. In this experiment, the chiral allenes **107ab-107ac** were

Table 3. $ZnBr_2$ promoted synthesis of chiral allenes **107** from chiral propargylamines **130**[a,b,c]





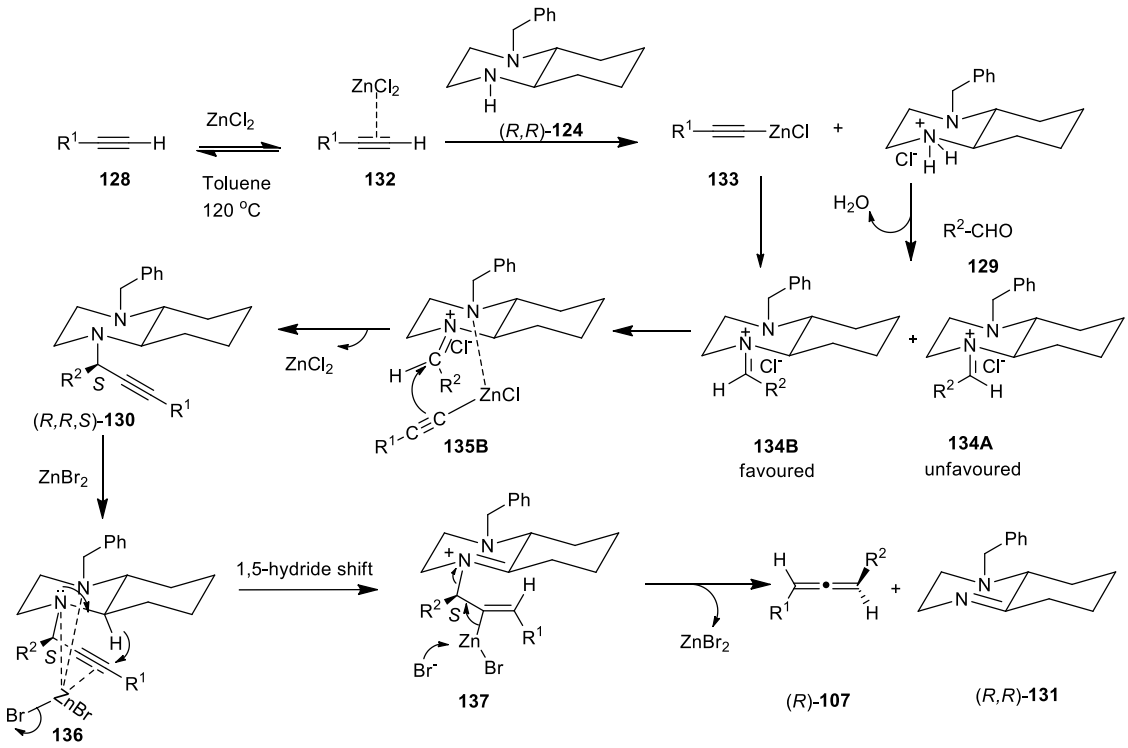
[a]The reactions were carried out using propargylamine **130** (1 mmol) in toluene (3 mL) with $ZnBr_2$ (0.5 mmol). [b]Isolated yield of the product **107**. [c]The % ee of allene **107** was determined by HPLC analysis on chiralcel OD-H, OJ-H column.

obtained in 65-69% yield with up to 99% ee (Table 14). The propargylamines **130bb** and **130be** gave corresponding chiral allenes **107bc** and **107be** in 62% and 89% yields with 84% and 98% ee (Table 3).

Plausible mechanistic pathway for the formation of allene

The formation of chiral propargylamines and their conversion to chiral allenes can be rationalized by the mechanism outlined in Scheme 15. The initially formed alkynyl zinc intermediate[72] **133** would react with the favoured conformer **134B** of the iminium ion derived from aldehyde **129** and chiral piperazine **124** to give selectively the corresponding propargylamine **130**. The corresponding zinc bromide complex of **136** would then undergo intramolecular hydride shift from the piperazine skeleton to the acetylenic moiety leading to

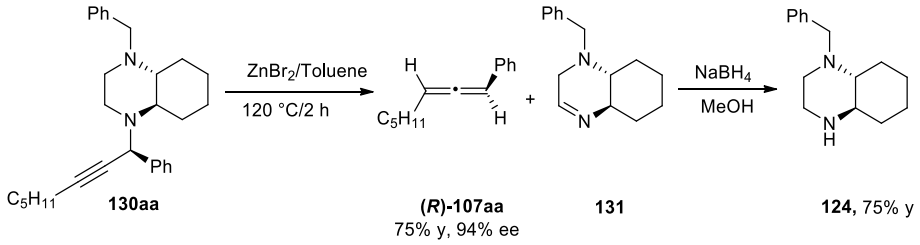
Scheme 15



the formation of alkenyl zinc intermediate **137**. Subsequently, cleavage of C-N bond in the intermediate **137** releases the chiral allenes **107** and the imine **131** byproduct.[62,73] It should be noted that all the present experiments require shorter reaction times (1-2 hours) for the formation of chiral allenes compared to other procedures (18-24 hours).[59,63]

All the optically active allenes obtained by using chiral piperazine derivatives are levorotatory from which the absolute configurations of the major enantiomer assigned as *R* (Table 14) by the Lowe-Brewster rule and also by comparison with reported $[\alpha]_D^{25}$ values.[74] We have also found that the imine byproducts **131** could be easily converted *in situ* to the corresponding chiral piperazine **124** in 75% yield by simple sodium borohydride reduction (Scheme 16).

Scheme 16



Next, we have undertaken systematic efforts on the synthesis of various substituted propargylamines *via* Michael addition to α,β-unsaturated ketones. The results are described in the next chapter.

1.3 Conclusions

We have synthesized the chiral *N*-benzylpiperizine *via* ^{t}BOC protection followed by benzylation and ^{t}BOC deprotection starting from chiral (1*R*,2*R*)-diaminocyclohexane and ethyl glyoxylate. We have also developed a simple and inexpensive method for the diastereoselective synthesis of propargylamines using chiral *N*-benzylpiperizine and their enantioselective conversion to chiral allenes by reaction with $ZnBr_2$.

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) and IR (neat) spectra were recorded on JASCO FT-IR spectrophotometer model-5300. ^{1}H (400 MHz), ^{13}C (100 MHz) NMR spectra were recorded on Bruker-Avance-400 spectrometers chloroform-d as solvent. Chemical shifts were determined with tetramethylsilane (TMS) as internal reference (δ = 0 ppm). Coupling constants *J* are in Hz. High-resolution mass spectra (HRMS) were recorded on micromass ESI-TOF. HPLC analyses were performed on a SCL-10ATVP SHIMADZU instrument. Elemental analyses were carried out using a Perkin-Elmer elemental analyzer model-240C and Thermo Finnigan analyzer series Flash EA 1112. Optical rotations were measured on Rudolph Research Analytical 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-methylbenzylamine $[\alpha]_D^{25} = -29.6$ (c 0.74, EtOH) supplied by Aldrich.

All the glasswares were pre-dried at 100-120 °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 reagent were carried out using standard syringe-septum technique recommended for handling air sensitive reagents and organometallic compounds.

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 was used. The outlet of the mercury bubbler was connected to the atmosphere by a

long tube. All dry solvents and reagents used were distilled from appropriate drying agents. As a routine practice, all organic extracts were washed with saturated NaCl solution (brine) and dried over Na_2SO_4 or K_2CO_3 and concentrated on Heidolph-EL-rotary evaporator. All the yields reported are of isolated materials characterized by IR and NMR.

Toluene and THF supplied by E-Merck, India were kept over sodium-benzophenone ketyl and freshly distilled before use. All aldehydes, supplied by Loba Chemicals (P), Ltd., India were distilled or recrystallized from the appropriate solvents before use. L-(+)-tartaric acid and $NaBH_4$ were purchased from E-Merck (India was supplied by E-Merck (India) was used as received. Iodine was supplied by Spectrochem, India.

Analytical grade of CuCl, CuBr, CuI, $ZnCl_2$ and ZnI_2 were purchased from Sigma-Aldrich. $ZnBr_2$ was purchased from E-Merck. Analytical thin layer chromatographic tests were carried out on glass plates (3 x 10 cm) coated with 250 mμ E-Merck and acme's silica gel-G and GF-254 containing 13% calcium sulfate as a 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.

1.4.2 Resolution of 1,2-diaminocyclohexane 6

A reported procedure was followed.[75] In a 250 ml beaker, L(+)-tartaric acid (37.5 g, 250 mmol) and water (100 mL) were taken. The mixture was stirred at room temperature until complete dissolution occurred. At this point, a mixture of cis/trans-1,2-diaminocyclohexane (60 ml, 500 mmol) was added at a rate such that the reaction temperature was below 70 ^oC. To the resulting solution, glacial acetic acid (25 mL) was added at a rate such that the reaction temperature was below 90 ^oC. The precipitate was formed immediately upon the addition of

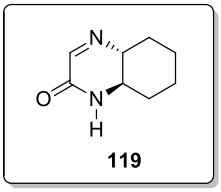
glacial acetic acid and the slurry was vigorously stirred. It was cooled to 25 ^{o}C over a period of 2 h. The mixture was cooled to 5 ^{o}C for 2 h and the precipitate was collected by suction filtration. The wet cake was washed with cooled water (25 mL) followed by cold methanol until the cake turned to white solid. The product (*R*,*R*)-trans-1,2-diammoniumcyclohexane mono-(+)-tartrate salt was dried in air.

Yield: 111 g (85%)

The (*R*,*R*)-trans-1,2-diammoniumcyclohexane mono-(+)-tartrate salt (42 g, 159 mmol) was taken in a separating funnel. Approximately, 30 g of KOH dissolved in water (20 mL) was added. The (*R*,*R*)-trans-1,2-diaminocyclohexane **6** was distilled under the reduced pressure.

1.4.3 (4a*R*,8a*R*)-4a,5,6,7,8,8a-Hexahydro-1H-quinoxalin-2-one 119

To a solution of *trans*-1,2-diaminocyclohexae **6** (2.28 g, 20 mmol) in isopropanol (20 ml), a solution of ethyl glyoxylate polymer form (45-50% in toluene, 4 ml, 20 mmol) in isopropanol (20 ml) was added drop wise over 30 min at 25 ^{o}C. The mixture was stirred for 12 h. The solvent was evaporated and the residue was purified on silicagel (100-200 mesh) using ethylacetate as eluent to afford **119**.



119

Yield **:** 2.920 g, 96%; colorless solid.

$[\alpha]_D^{25}$ **:** -207.90 (*c* 0.76, $CHCl_3$).

IR (KBr) **:** 3172, 3068, 2936, 2860, 1687, 1616, 1452, 1413, 1364, 1123, 1030, 947, 794, 739, 487 cm^{-1}.

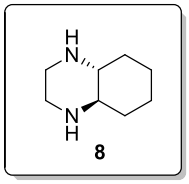
^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.71 (s, 1H), 6.95 (s, 1H), 3.19-3.05 (m,

2H), 2.37 (d, *J* = 7.2 Hz, 1H), 1.96-1.88 (m, 2H), 1.80 (d, *J* = 12.8 Hz, 1H), 1.45-1.30 (m, 4H).

^{13}C NMR : (100 MHz, $CDCl_3$, δppm); 157.9, 156.3, 63.0, 54.1, 31.4, 31.0, 25.2, 23.6.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_8H_{12}N_2O$: 153.1028; found: 153.1029.

1.4.4 (4a*R*,8a*R*)-decahydroquinoxaline 8



8

To a suspension of $NaBH_4$ (3.8 g, 100 mmol) in THF (100 ml) was added a solution of I_2 (12.64 g, 50 mmol) in THF (80 ml) at 0 ^oC under N_2 atmosphere over 30 min. The imide **119** (3.04 g, 20 mmol) was added to the generated diborane and refluxed for 24 h. The reaction was brought to the room temperature and quenched with methanol and the solvents were evaporated. The residue obtained after evaporations was refluxed with 10 N KOH for 12 h and the resultant polymer was extracted with DCM (2 X 60 ml). The combined organic extract was evoparated to obtain the decahydroquinoxaline **8**. The crude amine was chromatographed on a basic Al_2O_3–column using ethylacetate as eluent to isolate the decahydroquinoxaline **8.**

Yield : 1.25 g, 89%; colorless solid.

$[\alpha]_D^{25}$: +12.33 (*c* 0.52, $CHCl_3$).

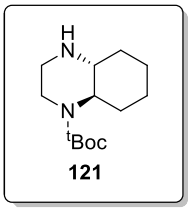
IR (KBr) : 3210, 2931, 2849, 2789, 1490, 1446, 1342, 1134, 1057, 991, 931, 876, 821, 602 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 2.96-2.88 (m, 2H), 2.87-2.80 (m, 2H), 2.22-2.19 (m, 2H), 1.68-1.60 (m, 6H), 1.32-1.26 (m, 2H), 1.21-1.15 (m,2H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δppm); 61.5, 47.3, 32.2, 25.0.

HRMS **:** (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_8H_{16}N_2$: 141.1391; found: 141.1392.

1.4.5 (4a*R*,8a*R*)-tert-butyl octahydroquinoxaline-1(2H)-carboxylate 121



121

To the decahydroquinoxaline **8** (2.80 g, 20.0 mmol) solution in DCM (20 ml), di-t-butyldicarbonate (4.4 mL, 20 mmol) was added at 0 ^oC slowly through a syringe under N_2 atmosphere. The reaction mixture was brought to room temperature slowly and further stirred for 12 h. After the completion of the reaction monitored by TLC, the solvent was evaporated under reduced pressure. Purification of the residue by column chromatography on silica gel (100-200 mesh) using hexane/EtoAc (50:50) to afford Octahydro-quinoxaline-1-carboxylic acid ester tert-butyl ester **121**.

Yield **:** 1.820 g, 76%; colorless liquid.

$[\alpha]_D^{25}$ **:** (*c* 0.52, $CHCl_3$).

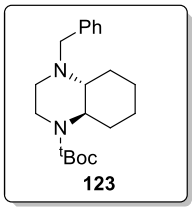
IR (neat) **:** 3320, 2969, 2931, 2854, 1693, 1457, 1413, 1369, 1249, 1150, 1095, 1013, 767 cm^{-1}.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 3.51-3.47 (m, 2H), 3.08-2.99 (m, 2H), 2.98-2.93 (m, 1H), 2.60 (dt, *J* = 10.8 Hz, 3.6Hz, 1H), 2.21 (d, *J* = 12.8 Hz, 1H), 1.80 (d, *J* = 12.8 Hz, 1H), 1.70 (t, *J* = 18.4 Hz, 2H), 1.59-1.46 (m, 2H), 1.43 (s, 9H), 1.33-1.08 (m, 3H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δppm); 155.5, 79.4, 63.7, 56.2, 44.8, 41.2, 33.2, 30.3, 28.5, 25.3, 25.1.

HRMS **:** (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{13}H_{24}N_2O_2$: 241.1916; found: 241.1917.

1.4.6 (4a*R*,8a*R*)-tert-butyl 4-benzyloctahydroquinoxaline-1(2H)-carboxylate 123



123

To a solution of (4aR,8aR)-*t*-Butyl octahydroquinoxaline-1-(2H)-carboxylate **121** (3.0 g, 12.50 mmol) in acetonitrile (50 mL) was added benzyl bromide **122** (1.66 mL,14 mmol), K_2CO_3 (2.58 g, 26 mmol), KI (0.996 g) and the mixture was stirred under reflux condition for 12 h. it was cooled to room temperature and filtered off to remove K_2CO_3 and the solvent was evaporated under reduced pressure. The residue was extracted with with DCM (2 X 40 ml) and water (20 ml). The combined organic extract was washed with brine (20 ml) and dried over anhydrous Na_2SO_4. The solvent was evaporated and purification of the residue by column chromatography on silica gel (100-200 mesh) using hexane/EtoAc (50:50) afforded (*R,R*)-*t*-butyl-4-benzyl-2,3-diphenyl-1-piperizinecarboxylate **123,** as colorless liquid. We have proceeded to next step without further purification of this product.

Yield **:** 0.280 g, 86%; colorless liquid.

$[\alpha]_D^{25}$ **:** -71.07 (*c* 0.45, $CHCl_3$).

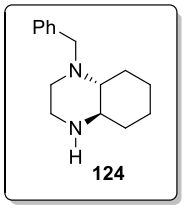
IR (neat) **:** 3084, 3068, 3030, 2975, 2931, 2854, 2794, 1693, 1446, 1402, 1353, 1282, 1249, 1161, 1013, 849, 734, 695 cm^{-1}.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.28 (d, *J* = 4.4 Hz, 4H), 7.23-7.21 (m, 1H), 3.99 (d, *J* = 13.2 Hz, 1H), 3.63-3.57 (m, 1H), 2.82-2.76 (m, 1H), 2.45-2.40 (m, 1H), 2.34-2.28 (m, 1H), 2.21 (s, 2H), 1.76 (d, *J* = 8.8 Hz, 3H), 1.45 (s, 9H), 1.32-1.27 (m, 3H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δppm) 155.2, 139.4, 128.7, 128.1, 126.7, 79.2, 62.2, 61.9, 56.7, 51.8, 42.9, 30.7, 30.5, 28.5, 25.6, 25.2.

HRMS **:** (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{20}H_{30}N_2O_2$: 353.2205; found: 353.2206.

1.4.7 (4a*R*,8a*R*)-1-benzyldecahydroquinoxaline 124



124

To a solution of (*R*, *R*)-*t*-butyl-4-benzyl-2,3-diphenyl-1-piperizinecarboxylate **123** (0.90 g) in 1,4-dioxane (10 ml), 6M HCl (5 ml) was added slowly through a syringe for 15 min. under N_2 atmosphere. The resulting mixture was stirred for 12 h at room temperature. The solvent was evaporated and the residue was neutralized with 6N NaOH solution and the organic layer was extracted with DCM. The combined organic extract was washed with brine (10 ml) and dried over anhydrous Na_2SO_4. The solvent was evaporated and the residue was column chromatographed on basic alumina (100-200 mesh) using hexane/EtoAc(50:50) as eluent to obtain the 1-benzyl-decahydroquinoxaline **124**.

Yield **:** 1.160 g, 90%; colorless solid.

mp **:** 95-96 ºC

$[\alpha]_D^{25}$ **:** -109.81 (*c* 0.52, $CHCl_3$);

IR (KBr) **:** 3254, 3046, 3030, 2980, 2904, 2854, 2794, 1605, 1512, 1446, 1347, 1309, 1254, 1150, 1128, 1084, 1073, 1052, 1002, 827, 756 cm^{-1}.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.30 (d, *J* = 4.4 Hz, 4H), 7.26 (s, 1H), 4.11 (d, *J* = 13.2 Hz, 1H), 3.14 (d, *J* = 13.2 Hz, 1H), 2.94-2.84 (m, 2H), 2.71 (d, *J* = 11.6 Hz, 1H), 2.48-2.42 (m, 1H), 2.25 (d, *J* = 13.2 Hz, 1H), 2.12

(dt, *J* = 11.2 Hz, 4Hz, 1H), 1.87-1.78 (m, 2H), 1.71 (d, *J* = 7.2 Hz, 2H), 1.38-1.13 (m, 5H).

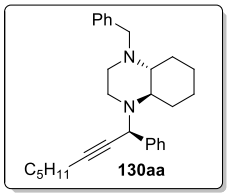
^{13}C NMR : (100 MHz, $CDCl_3$, δppm) 139.0, 129.1, 128.1, 126.7, 67.0, 60.4, 57.3, 53.7, 46.0, 32.8, 29.0, 25.2, 24.9.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{15}H_{22}N_2$: 231.1861; found: 231.1861.

1.4.8 General procedure for the preparation of chiral propargylamines 130 using chiral 1-Benzyl decahydroquinoxaline 124.

A flame dried 25 ml reaction flask was charged with $ZnCl_2$ (0.014g, 10 mol%), 1-benzyl decahydroquinoxaline derivative **124** (0.230 g, 1 mmol), 1-alkyne **128** (1.2 mmol) and aryl benzaldehyde **129** (1.2 mmol) and dissolved in 5 ml of dry.toluene and these contents were heated to 100 ^oC for 12 h. The reaction mixture was brought to room temperature after the required time. After evaporation of the toluene solvent, the residue was column chromatograhed on silica gel (100-200 mesh) using hexane/EtoAc (98:2) as a eluent to obtain the chiral propargylamines.

(4a*R*,8a*R*)-1-benzyl-4-((*S*)-1-phenyloct-2-yn-1-yl)decahydroquinoxaline



Yield : 0.287 g, 69%; yellow liquid.

$[\alpha]_D^{25}$: -81.11 (*c* 0.42, $CHCl_3$).

IR (neat) : 3090, 3063, 3035, 2926, 2860, 2810, 1605, 1495, 1446, 1309, 1150, 1096, 827, 739, 701 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.62 (d, *J* = 7.2 Hz, 2H), 7.35-7.24 (m, 8H),

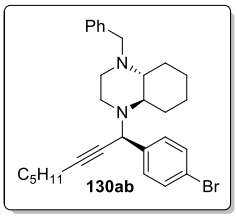
5.18 (s, 1H), 4.12 (d, *J* = 13.6 Hz, 1H), 2.63 (d, *J* = 11.2 Hz, 1H), 2.51-2.44 (m, 2H), 2.40-2.34 (m, 2H), 2.22-2.10 (m, 3H), 1.86 (s, 2H), 1.69-1.62 (m, 2H), 1.56-1.51 (m, 2H), 1.14-1.37 (m, 4H), 1.33-123 (m, 2H), 1.0 (t, *J* = 14.4 Hz, 3H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δppm) 139.8, 139.0, 129.2, 128.6, 128.1, 127.9, 127.0, 126.7, 88.7, 74.2, 66.0, 63.5, 57.5, 54.3, 52.6, 45.5, 31.2, 29.6, 28.9, 25.3, 25.0, 22.3, 18.8, 14.1.

HRMS **:** (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{29}H_{38}N_2$: 415.3113; found: 415.3114.

(4a*R*,8a*R*)-1-benzyl-4-((*S*)-1-(4-bromophenyl)oct-2-yn-1-yl)decahydroquinoxaline

Yield **:** 0.332 g, 67%; yellow liquid.



130ab

$[\alpha]_D^{25}$ **:** -78.66 (*c* 0.45, $CHCl_3$);

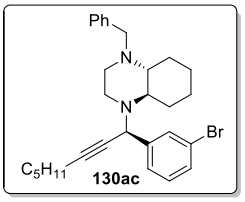
IR (neat) **:** 2930, 2847, 1610, 1490, 1458, 1098 cm^{-1}.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.42 (q, *J* = 25.2 Hz, 4H), 7.28-7.26 (m, 5H), 7.23-7.20 (m, 1H) 5.05 (s, 1H), 4.07 (d, *J* = 13.6 Hz, 1H), 3.22 (d, *J* = 13.6 Hz, 1H), 2.58 (d, *J* = 11.2 Hz, 1H), 2.44-2.36 (m, 2H), 2.33-2.25 (m, 4H), 2.10-2.04 (m, 3H), 1.82 (s, 2H), 1.62-1.56 (m, 2H), 1.50-1.42 (m, 2H), 1.40-1.29 (m, 4H), 1.27-1.15 (m, 1H), 0.94 (t, *J* = 14.4 Hz, 3H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δppm) 139.1, 138.9, 131.0, 130.3, 129.2, 128.1, 126.7, 120.9, 89.2, 73.7, 66.0, 63.4, 57.4, 53.8, 52.6, 45.5, 31.2, 29.6, 28.8, 28.6, 25.2, 25.0, 22.3, 18.8, 14.1.

HRMS **:** (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{29}H_{37}BrN_2$: 493.2218; found: 493.2218.

(4a*R*,8a*R*)-1-benzyl-4-((*S*)-1-(3-bromophenyl)oct-2-yn-1-yl)decahydroquinoxaline



Yield **:** 0.310 g, 63%; yellow liquid.

$[\alpha]_D^{25}$ **:** -72.06 (*c* 0.45, $CHCl_3$).

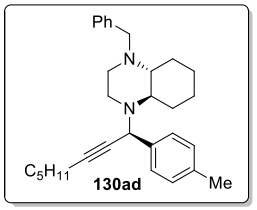
IR (neat) **:** 2928, 2845, 1608, 1494, 1460, 1100 cm^{-1}.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.73 (s, br, 1H), 7.52-7.50 (s, br, 1H), 4.11-4.07 (m, 1H), 3.23-3.20 (m, 1H), 2.61-2.58 (m, 1H), 2.44-2.38 (m, 1H), 2.35-2.32 (m, 2H), 2.29-2.24 (m, 2H), 2.12-2.07 (m, 2H), 1.82 (s, br, 2H), 1.64-1.57 (m, 2H), 1.51-1.43 (m, 2H), 1.39-1.36 (m, 2H), 1.32-1.28 (m, 2H), 1.19-1.13 (m, 1H), 0.99-0.93 (m, 2H), 0.91-0.85 (m, 4H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δppm) 142.5, 138.9, 131.5, 130.1, 129.4, 129.1, 128.0, 127.1, 126.6, 122.1, 89.3, 73.5, 66.0, 63.3, 57.4, 53.8, 52.5, 45.6, 31.4, 29.5, 28.7, 28.5, 25.2, 24.9, 22.2, 18.8, 14.1.

HRMS **:** (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{29}H_{37}BrN_2$: 493.2218; found: 493.2218.

(4a*R*,8a*R*)-1-benzyl-4-((*S*)-1-(p-tolyl)oct-2-yn-1-yl) decahydroquinoxaline



Yield **:** 0.338 g, 76%; yellow liquid.

$[\alpha]_D^{25}$ **:** -79.89 (*c* 0.51, $CHCl_3$).

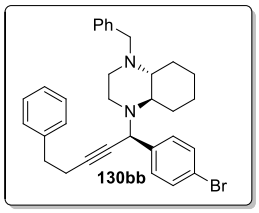
IR (Neat) **:** 3063, 3024, 2936, 2860, 2800, 1605, 1512, 1452, 1364, 1309, 1260, 1167, 1090, 1019, 832, 734, 690 cm^{-1}.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.46 (d, *J* = 7.6 Hz, 2H), 7.29 (d, *J* = 4.0 Hz, 4H), 7.24-7.21 (m, 1H), 7.12 (d, *J* = 7.6 Hz, 2H), 5.11 (s, 1H), 4.09 (d, *J* = 13.6 Hz, 1H), 3.24 (d, *J* = 13.6 Hz, 1H), 2.60 (d, *J* = 11.2 Hz, 1H), 2.47-2.39 (m, 2H), 2.34 (s, 3H), 2.18 (d, *J* = 11.2 Hz, 1H), 2.15-2.07 (m, 2H), 1.84 (s, 2H), 1.66-1.59 (m, 2H), 1.56-1.44 (m, 3H), 1.43-1.37 (m, 3H), 1.34-1.30 (m, 2H), 1.27-1.17 (m, 2H), 0.96 (t, *J* = 14.4 Hz, 3H), 0.92-0.88 (m, 2H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δppm) 138.9, 136.8, 136.5, 129.2, 128.5, 128.0, 126.6, 88.4, 74.3, 65.9, 63.4, 57.4, 53.9, 52.6, 45.3, 31.1, 29.6, 28.9, 28.5, 25.2, 25.0, 22.2, 21.0, 18.8, 14.1.

HRMS **:** (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{30}H_{40}N_2$: 429.3269; found 429.3268.

(4a*R*,8a*R*)-1-benzyl-4-((*S*)-1-(4-bromophenyl)-5-phenylpent-2-yn-1-yl)decahydro quinoxaline.



Yield **:** 0.332 g, 63%; yellow liquid.

$[\alpha]_D^{25}$ **:** -75.44 (*c* 0.45, $CHCl_3$).

IR (neat) **:** 3082, 3054, 3028, 2924, 2856, 2803, 1602 cm^{-1}.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.37-7.35 (m, 2H), 7.32 (s, br, 1H), 7.30-7.28 (m, 5H), 7.27-7.26 (m, 1H), 5.0 (s, br, 1H), 4.08 (d. *J* = 13.44 Hz, 1H), 3.20 (d, *J* = 13.40 Hz, 1H), 2.91 (t, *J* = 7.24 Hz, 2H), 2.68-2.64 (m, 2H), 2.59-2.56 (m, 1H), 2.39-2.29 (m, 3H), 2.23-2.18 (m, 1H),

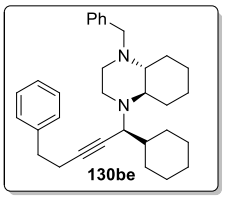
2.07-2.04 (m, 2H), 1.82-1.80 (m, 2H), 1.71 (s, br, 1H), 1.40-1.24 (m, 3H), 1.19-1.11 (m, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δppm) 140.6, 138.8, 138.7, 130.8, 130.2, 129.2, 128.6, 128.4, 128.1, 126.7, 126.2, 120.8, 88.1, 74.5, 66.0, 63.2, 57.4, 53.6, 52.5, 45.4, 35.2, 29.4, 28.5, 28.5, 25.1, 24.9, 20.8.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{29}H_{37}BrN_2$: 527.2062; found: 527.2065.

(4a*R*,8a*R*)-1-benzyl-4-((*S*)-1-cyclohexyl-5-phenylpent-2-yn-1-yl) decahydroquinoxaline

Yield : 0.403 g, 90%; yellow liquid.



130be

$[\alpha]_D^{25}$: -57.72 (*c* 0.57, $CHCl_3$).

IR (neat) : 3084, 3057, 3030, 2920, 2854, 2805, 1605, 1495, 1452, 1315, 1161, 1090, 1030, 821, 739, 695 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.32-7.31 (d, *J* = 4.0 Hz, 4H), 7.29-7.18 (m, 6H), 4.10 (d, *J* = 13.2 Hz, 1H), 3.29 (d, *J* = 10.0 Hz, 1H), 3.19 (d, *J* = 13.6 Hz, 1H), 2.82 (t, *J* = 14.8 Hz, 2H), 2.71 (d, *J* = 10.8 Hz, 1H), 2.51 (t, *J* = 14.4 Hz, 2H), 2.46-2.36 (m, 2H), 2.28-2.17 (m, 3H), 2.07-1.87 (m, 4H), 1.71-1.63, (m, 4H), 1.28-1.12 (m, 5H), 0.89-0.85 (m, 6H).

^{13}C NMR : (100 MHz, $CDCl_3$, δppm).140.9, 139.1, 129.3, 128.5, 128.3, 128.1, 126.7, 126.1, 84.9, 77.2, 66.1, 62.9, 57.6, 55.3, 52.8, 45.1, 39.2, 35.7, 31.6, 30.1, 29.5, 28.3, 26.8, 26.2, 25.9, 25.2, 24.9, 20.9.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{32}H_{42}N_2$: 455.3426; found: 455.3428.

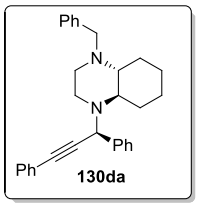
(4a*R*,8a*R*)-1-benzyl-4-((*S*)-1,3-diphenylprop-2-yn-1-yl)decahydroquinoxaline

Yield **:** 0.303 g, 72%; colorless solid.

$[\alpha]_D^{25}$ **:** -78.06 (*c* 0.45, $CHCl_3$).

IR (neat) **:** 2963, 2843, 1623, 1508, 1436, 1059, 742 cm^{-1}.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.67-7.63 (m, 2H), 7.57-7.56 (m, 2H), 7.37-7.34 (m, 6H), 7.31-7.28 (m, 5H), 5.40 (s, br, 1H), 4.11 (d, *J* = 12.0 Hz, 1H), 3.35 (d, *J* = 12.0 Hz, 1H), 2.64 (d, *J* = 12.0 Hz, 1H), 2.28-2.53 (m, 2H), 2.43-2.29 (m, 4H), 2.17-2.09 (m, 3H), 1.90-1.84 (m, 2H) 1.51-1.40 (m, 2H), 1.37-1.25 (m, 3H).



^{13}C NMR **:** (100 MHz, $CDCl_3$, δppm) : 139.2, 138.8, 131.9, 129.3, 128.6, 128.3, 128.1, 127.8, 127.3, 126.7, 123.4, 88.6, 88.3, 66.1, 63.6, 57.5, 54.6, 52.9, 52.6, 45.7, 29.6, 28.7, 25.3, 25.0.

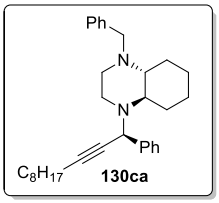
HRMS **:** (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{30}H_{32}N_2$: 421.2643; found 421.2644.

(4a*R*,8a*R*)-1-benzyl-4-((S)-1-phenylundec-2-yn-1-yl)decahydroquinoxaline

Yield **:** 0.330 g, 73%; yellow liquid.

$[\alpha]_D^{25}$ **:** -76.54 (*c* 0.45, $CHCl_3$).

IR (neat) **:** 3061, 3054, 3024, 2928, 2856, 2804, 1602, 1493, 1448, 1312, 1148, 1092, 824, 733, 702.cm^{-1}.



^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.59-7.57 (m, 2H), 7.32-7.28 (m, 6H), 7.25-7.21(m, 2H), 5.14 (s, br, 1H), 4.09 (d, *J* = 16.0 Hz, 1H), 3.24 (d, *J* = 12.

0 Hz , 1H), 2.61-2.58 (m, 1H), 2.48-2.42 (m, 2H), 2.36-2.31 (m, 4H), 2.18-2.06 (m, 3H), 1.86-1.81 (m, 2H), 1.64-1.57 (m, 2H), 1.53-1.47 (m, 3H), 1.39-1.19 (m, 14H), 0.92-0.89 (m, 4H).

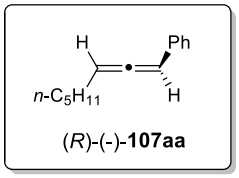
^{13}C NMR : (100 MHz, $CDCl_3$, δppm) 139.8, 138.8, 129.3, 128.6, 128.0, 127.8, 126.9, 126.7, 88.7, 74.2, 65.9, 63.4, 57.4, 54.3, 55.6, 31.9, 29.6, 29.3, 29.2, 28.9, 28.6, 25.3, 25.0, 22.7, 18.8, 14.1.

HRMS : (ESI-TOF) $[M+H]^+$ calculated for $C_{32}H_{44}N_2$: 457.3582; found 457.3581.

1.4.9 General procedure for the synthesis of (*R*)-(-)-chiral allenes 107 from the chiral propargylamine derivatives 130

To a reaction flask cooled under N_2, was added $ZnBr_2$ (0.113 g, 0.5 mmol) and chiral propargylamines **130** (1 mmol) in dry toluene (3 mL) and the contents were refluxed for 2 h at 120 °C under nitrogen atmosphere. The reaction mixture was brought to room temperature after the required time. Toluene was removed under reduced pressure and the residue was subjected to chromatography on silica gel (100-200 mesh) using hexane as eluent to isolate the chiral allenes **(***R*)-(-)-**107**.

(*R*)-Octa-1,2-dien-1-ylbenzene



(*R*)-(-)-**107aa**

Yield : 0.139 g, 75%; colorless oil.

$[\alpha]_D^{25}$: -194.7 (*c* 0.22, $CHCl_3$).

IR (neat) : 3066, 2954, 2930, 2854, 1946, 1597, 1462, 775 cm^{-1}.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.30-7.29 (m, 4H), 7.21-7.15 (m, 1H), 6.13-6.10 (m, 1H), 5.59-5.54 (m, 1H), 2.16-2.09 (m, 2H), 1.51-1.45 (m, 2H), 1.37-1.27 (m, 4H), 0.89 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 205.2, 135.2, 128.5, 126.8, 126.6, 95.1, 94.5, 31.4, 28.9, 28.7, 22.4, 14.0.

LCMS **:** *m/z* 185 (M-1).

Analysis **:** for $C_{14}H_{18}$

calcd: C, 90.26%; H, 9.74%.

found: C, 90.50%; H, 9.79%.

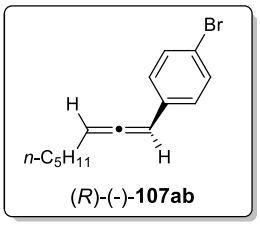
Enantiomeric purity : 94% ee (97.3:2.6 er) from HPLC.

HPLC using chiral column, chiralcel OD-H, solvent system, hexanes:*i*-PrOH/100:0; flow rate 0.5 mL/min., 254 nm, retention times: 12.7 min.(*R*) and 14.7 min.(*S*).

(*R*)-1-Bromo-4-(1,2-octadienyl)-benzene

Yield **:** 0.183 g, 69%; colorless oil.

$[\alpha]_D^{25}$ **:** -223.5 (*c* 0.20, $CHCl_3$).



(*R*)-(-)-**107ab**

IR (neat) **:** 2924, 1948, 1487, 1589, 1385, 1010 cm^{-1}.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.43 (s, 1H), 7.42-7.28 (m, 1H), 7.20-7.12 (m, 2H), 6.06-6.03 (m, 1H), 5.62-5.57 (m, 1H), 2.16-2.10 (m, 2H), 1.50-1.44 (m, 2H), 1.38-1.29 (m, 4H), 0.89 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 205.4, 137.6, 130.0, 129.5, 129.3, 125.1, 122.7, 95.7, 93.5, 31.4, 28.7, 28.6, 22.4, 14.1.

LCMS **:** *m/z* 266 (M+1).

Analysis **:** for $C_{14}H_{17}Br$

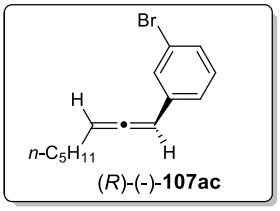
calcd: C, 63.41%; H, 6.46%: Br, 30.13%.

found: C, 63.31%; H, 6.53%; Br, 30.16%.

Enantiomeric purity : >99% ee from HPLC.

HPLC using chiral column, chiralcel OD-H, solvent system, hexanes:*i*-PrOH/100:0; flow rate 0.3 mL/min., 254 nm, retention times: 17.0 min.(*R* isomer)

(*R*)-1-Bromo-3-octa-1,2-dienyl-benzene



(*R*)-(-)-**107ac**

Yield **:** 0.075 g, 57%; colorless oil.

$[\alpha]_D^{25}$ **:** -110.5 (*c* 0.28, $CHCl_3$).

IR (neat) **:** 2959, 2858, 1950, 1589, 1068, 883, 785 cm^{-1}.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.41-7.39 (m, 2H), 7.15-7.13 (m, 2H), 6.07-6.04 (m, 1H), 5.58-5.54 (m, 1H), 2.14-2.09 (m, 2H), 1.50-1.44 (m, 2H), 1.35-1.30 (m, 4H), 0.89 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 205.3, 134.3, 131.6, 128.5, 128.1, 120.1, 95.6, 93.8, 31.4, 28.8, 28.6, 22.4, 14.0.

LCMS **:** *m/z* 266 (M+1).

Analysis **:** for $C_{14}H_{17}Br$

calcd: C, 63.41%; H, 6.46%: Br, 30.13%.

found: C, 63.31%; H, 6.53%; Br, 30.16%.

Enantiomeric purity : 79 % ee (89.7:10.2 er) from HPLC.

HPLC using chiral column, chiralcel OD-H, solvent system, hexanes:*i*-PrOH/100:0; flow rate 0.5 mL/min., 254 nm, retention times: 12.3 min.(*R* isomer) and 13.9 min (*S* isomer).

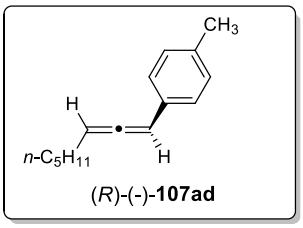
(*R*)-1-Methyl-4-(1,2-octadienyl)-benzene

Yield **:** 0.146 g, 73%; colorless oil.

$[\alpha]_D^{25}$ **:** -237.2 (*c* 0.31, $CHCl_3$).

IR (neat) **:** 3022, 2926, 1487, 1498, 1512, 1464, 819 cm^{-1}.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.17 (d, *J* = 10.0 Hz, 2H), 7.08 (d, *J* = 10.1 Hz, 2H), 6.10-6.07 (m, 1H), 5.55-5.48 (m, 1H), 2.31 (s, 3H), 2.13-2.08 (m, 2H), 1.50-1.44 (m, 2H), 1.37-1.30 (m, 4H), 0.89 (t, *J* = 6.8 Hz, 3H).



(*R*)-(-)-**107ad**

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 204.8, 136.3, 132.1, 129.2, 126.4, 95.0, 94.3, 31.4, 28.9, 28.8, 22.4, 22.1, 14.1.

LCMS **:** *m/z* 201 (M+1).

Analysis **:** for $C_{15}H_{20}$

calcd: C, 89.94%; H, 10.06%.

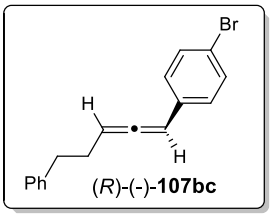
found: C, 89.87%; H, 9.98%.

Enantiomeric purity: 93% ee (96.3:3.6 er) from HPLC.

HPLC using chiral column, chiralcel OD-H, solvent system, hexanes:*i*-PrOH/100:0; flow rate 0.5 mL/min., 254 nm, retention times: 14.3 min.(*R* isomer) and 16.0 min. (*S*-isomer).

(*R*)-1-bromo-4-(5-phenylpenta-1,2-dien-1-yl)benzene

Yield **:** 0.090 g, 61%; colorless oil.



$[\alpha]_D^{25}$ **:** -175.54 (*c* 0.60, $CHCl_3$).

IR (neat) **:** 2928, 2856, 1951, 1616, 1325, 844 cm^{-1}.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.36 (d, *J* = 8.36 Hz, 2H), 7.29-7.20 (m, 5H), 6.97 (d, *J* = 8.4 Hz, 2H), 6.07-6.04 (m, 1H), 5.58 (q, *J* = 6.68, 1H), 2.84-2.76 (m, 2H), 2.52-2.42 (m, 2H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 205.4, 141.4, 133.9, 131.6, 128.6, 128.4, 128.2, 126.0, 120.2, 94.8, 94.1, 35.3, 30.4.

LCMS **:** *m/z* 300 (M+2).

Analysis **:** for $C_{17}H_{15}Br$

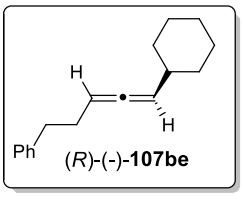
calcd: C, 68.24%; H, 5.05%.

found: C, 68.36%; H, 5.12%.

Enantiomeric purity : 84% ee (8.2:91.7 er) from HPLC.

HPLC using chiral column, chiralcel OD-H, solvent system, hexanes:*i*-PrOH/100:0; flow rate 0.5 mL/min., 254 nm, retention times: 14.3 min.(*R* isomer) and 16.0 min. (*S*-isomer).

(*R*)-1-(4-Bromophenyl),5-phenylpenta-1,2-diene



Yield **:** 0.201 g, 90%; colorless oil.

$[\alpha]_D^{25}$ **:** -79.2 (*c* 0.60, $CHCl_3$).

IR (neat) **:** 2928, 2856, 1951, 1616, 1325, 844 cm^{-1}.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.33-7.29 (m, 2H), 7.26-7.19 (m, 3H), 5.22-5.17 (m, 1H), 5.14-5.10 (m, 1H), 2.78-2.73 (m, 2H), 2.37-2.31 (m, 2H), 1.95-1.93 (m, 1H), 1.74-1.72 (m, 4H), 1.34-1.20 (m, 3H), 1.14-1.02 (m, 2H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 202.8, 142.0, 128.5, 128.2, 125.8, 97.6, 91.1, 37.2, 35.5, 33.1, 26.2, 26.0.

LCMS **:** *m/z* 226 (M^+).

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

calcd: C, 90.20%; H, 9.80%.

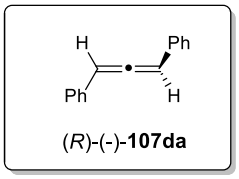
found: C, 90.35%; H, 9.71%.

Enantiomeric purity : 98% ee (1.0:98.9 er) from HPLC.

HPLC using chiral column, chiralcel OJ-H, solvent system, hexanes:*i*-PrOH/100:0; flow rate 0.3 mL/min., 215 nm, retention times: 18.6 min.(*S* isomer) and 19.4 min. (*R*-isomer).

(*R*)-1,3-diphenylpropa-1,2-diene

Yield **:** 0.048 g, 25%; colorless solid.



(*R*)-(-)-**107da**

mp **:** 48-50 ^oC 46% ee.

$[\alpha]_D^{25}$ **:** -425.2 (*c* 0.32, $CHCl_3$).

IR (neat) **:** 3061, 3028, 1936, 1597, 1493, 1450, 758 cm^{-1}.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.36-7.30 (m, 8H), 7.25-7.21 (m, 2H), 6.60-(s, 2H).

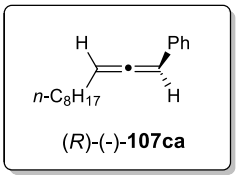
^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 207.8, 133.6, 128.5, 128.7, 127.3, 127.0, 98.4, 31.8, 29.4, 29.3, 29.1, 28.7, 22.6, 14.1.

LCMS **:** *m/z* 193(M+1).

Enantiomeric purity: 84% ee (1.0:98.9 er) from HPLC.

HPLC using chiral column, chiralcel OD-H, solvent system, hexanes:*i*-PrOH/99:1; flow rate 0.5 mL/min., 254 nm, retention times: 11.3 min. (*R* isomer) and 26.9 min. (*S*-isomer).

(*R*)-Undeca-1,2-dien-1-ylbenzene



(*R*)-(-)-**107ca**

Yield **:** 0.170 g, 70%; colorless oil.

$[\alpha]_D^{25}$ **:** -223.2 (*c* 0.60, $CHCl_3$).

IR (neat) **:** 2924, 2853, 1948, 1600, 1465, 772 cm^{-1}.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.34-7.28 (m, 4H), 7.24-7.20 (m, 1H), 6.19-6.14 (m, 1H), 5.64-5.58 (m, 1H), 2.19-2.15 (m, 2H), 1.56-1.51 (m, 2H), 1.41-1.32 (m, 12H), 0.95-0.91 (m, 3H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 205.1, 135.1, 128.5, 126.4, 95.5, 94.5, 31.8, 29.4, 29.3, 29.1, 28.7, 22.6, 14.1.

LCMS **:** *m/z* 229 (M+1).

Enantiomeric purity : 90% ee (1.0:98.9 er) from HPLC.

HPLC using chiral column, chiralcel OD-H, solvent system, hexanes:*i*-PrOH/100:0; flow rate 1.5 mL/min., 254 nm, retention times: 4.4 min. (*S* isomer) and 4.8 min. (*R*-isomer).

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Chapter 2

Synthesis of Propargylamines using

Amines, α,β-Unsaturated Ketones and 1-Alkynes

2.1 Introduction

Propargylamines are versatile building blocks useful in the synthesis of natural products and bioactive compounds.[1] Propargylamines can also be used as synthetic intermediates to access therapeutic agents,[2] muscarinic antagonists[3] and polyfunctional amino derivatives.[4-5] Propargylamine containing compounds such as resagiline, PF960IN (Figure 1) are known as highly potent, selective, irreversible MAO-B inhibitors.[6] In addition, propargylamines are widely used as synthons for the synthesis of β-lactams,[7-8] pyrroles,[9] pyrrolidines,[10] pyrrolophanes,[11] 3-aminobenzofurans,[12] aminoindolizines,[13] 2-aminoimidazoles,[14] oxazolidinones,[15] and quinolines [16] (Figure 1).

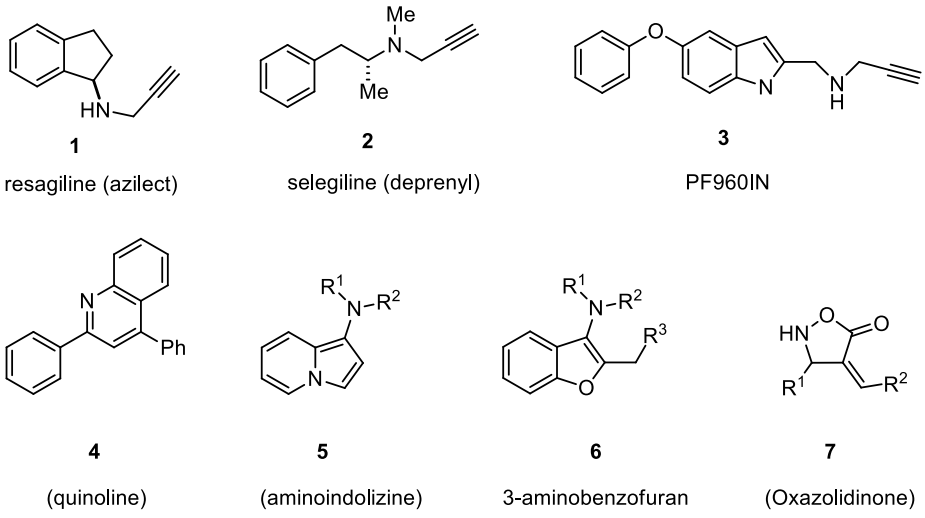


Figure 1. Propargylamine moiety containing drugs and various *N*-heterocycles

2.1.1 Methods for the synthesis of propargylamines

In recent years, synthesis of propargylamine derivatives attracted considerable interest due to the presence of propargylamine moieties in several bioactive compounds, conformationally restricted peptides, isosteres, natural products, oxotremorine analogues

etc.[9,17] A brief overview on the synthesis of propargylamines will be useful for the discussion.

2.1.2 Synthesis of disubstitutedpropargylamines

Reactions of various amines with formaldehyde (or) DCM and 1-alkynes for the synthesis of disubstituted propargylamines with various metal salts were developed (Chart 1).[18-26]

Chart1

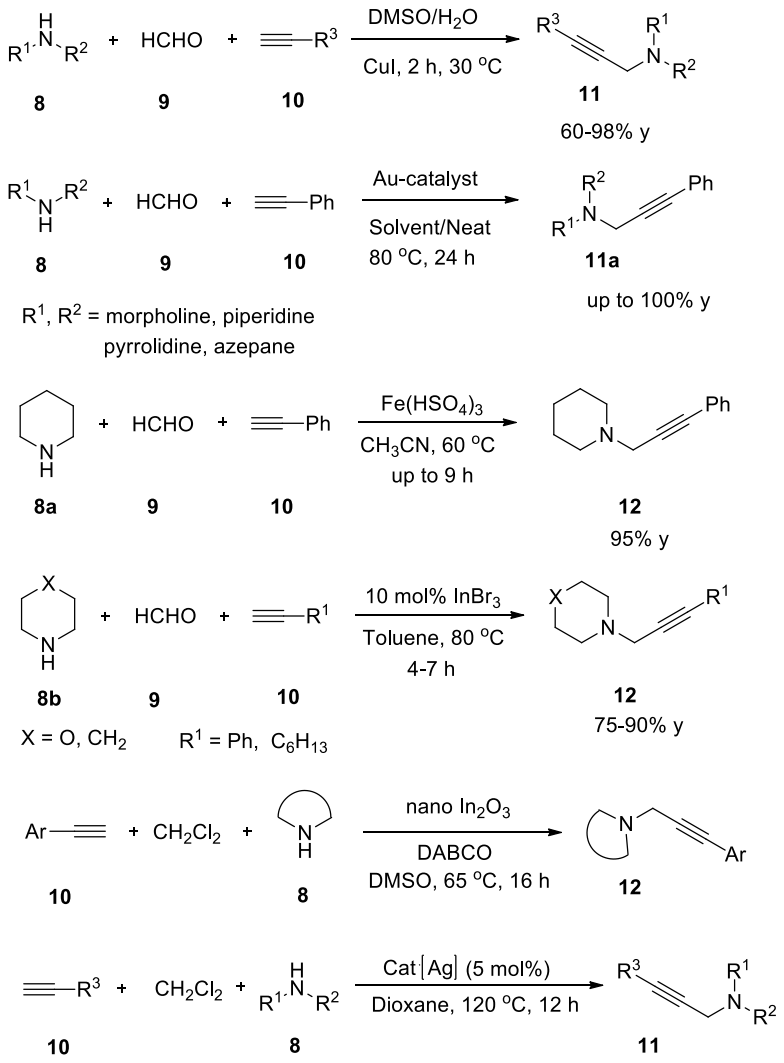
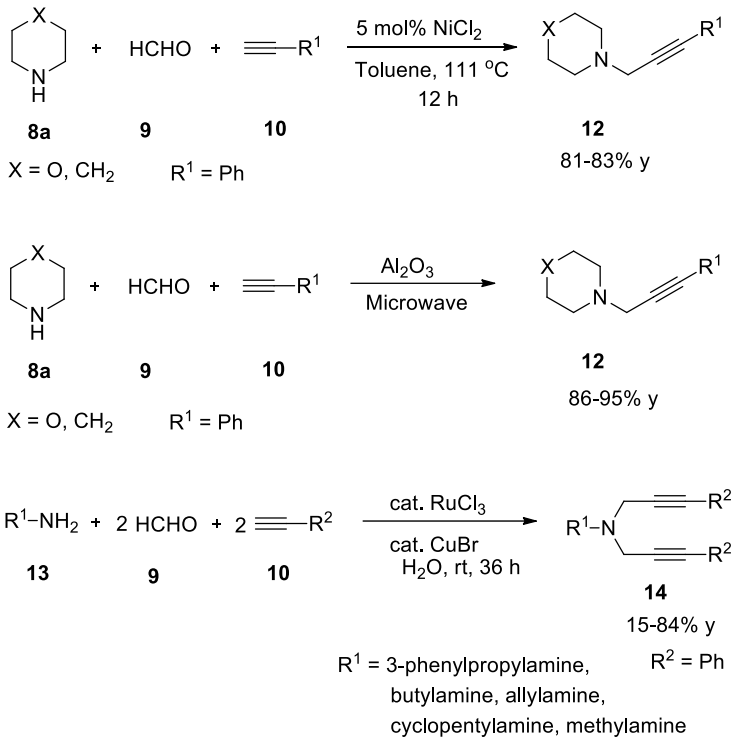


Chart 1 (continued)



Methods were developed for the synthesis of disubstitutedpropargylamines via alkynylation of unactivated aliphatic tertiary methylamines with terminal alkynes under different conditions to access the propargylamines (Chart 2).[27-31]

Chart 2

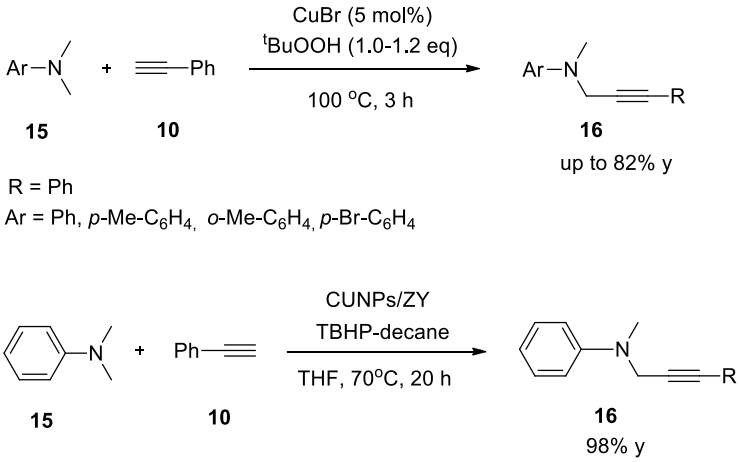
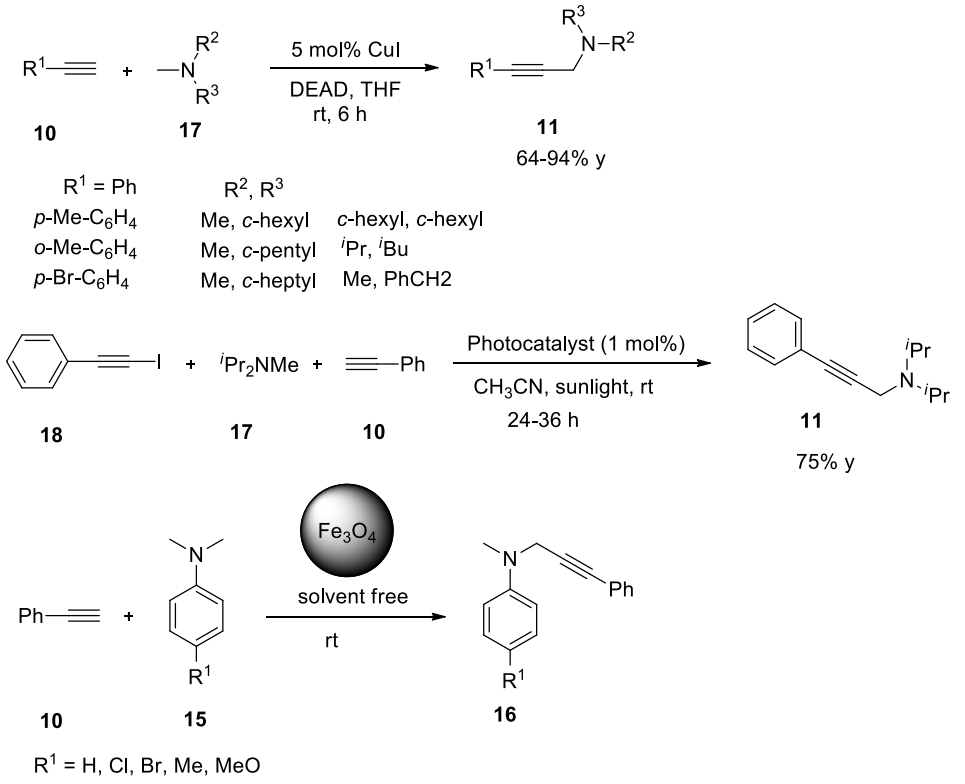
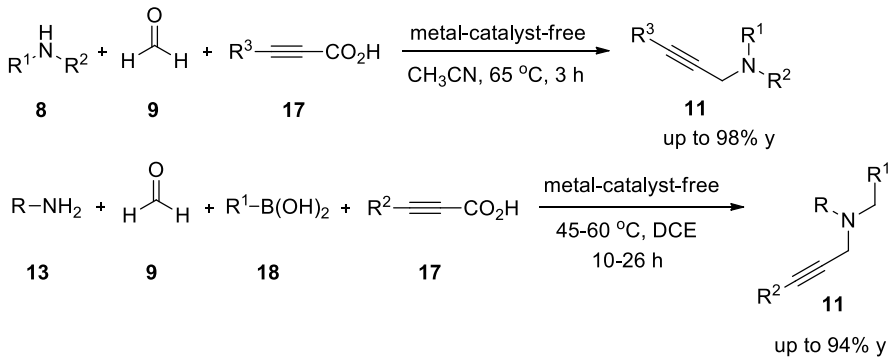


Chart 2(continued)



Very recently, metal-free decarboxylative three-component coupling reaction was reported (Chart 3).[32] More recently, Sun and co-workers described a method using primary amines **13**, formaldehyde, propiolic acid **17** and a boronic acid **18** to synthesize the propargylamines in up to 94% yield (Chart 3).[33]

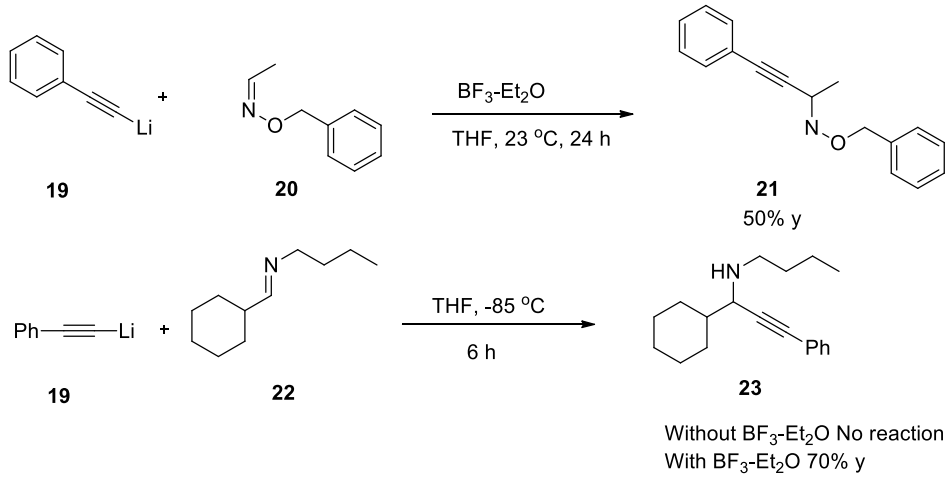
Chart 3



2.1.3 Synthesis of trisubstitutedpropargylamines

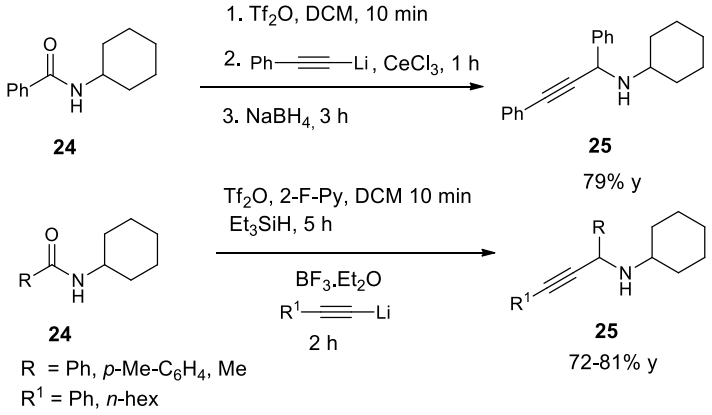
Addition of lithium acetylide **19** to oximes **20** (or) imines **22** to access propargylamines were reported (Chart 4).[34,35]

Chart 4



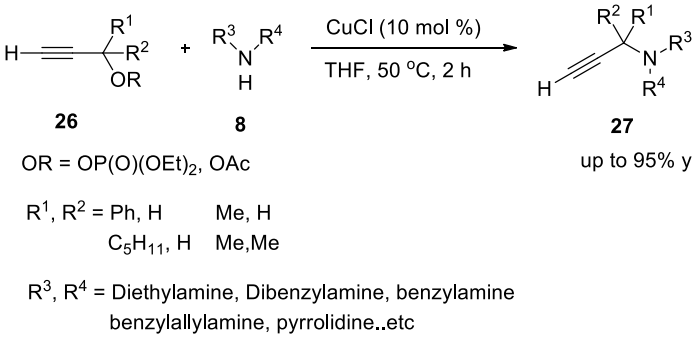
An interesting approach to propargylamines was reported via $CeCl_3$-mediated one-pot conversion of secondary amides **24** into propargylamines **25** in 79% yield. Later, a cerium-free modified approach also reported to afford the propargylamines **25** in 72-81% yields (Chart 5).[36]

Chart 5



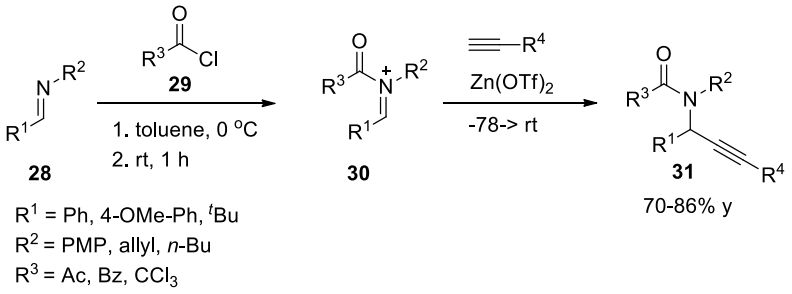
Copper(1)-catalyzed aminations of propargyl phosphates and acetates **36** gave the corresponding propargylamines **37** up to 95% yield (Scheme 1).[37]

Scheme 1



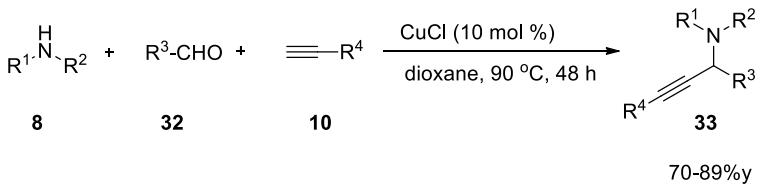
The acyl-iminium compound **30** synthesized by the reaction of *N*-Aryl and *N*-alkylimines **28** with an acyl chloride **29** underwent addition with metal-acetylide to give the propargylamides **31** in 70-86% yields (Scheme 2).[38]

Scheme 2



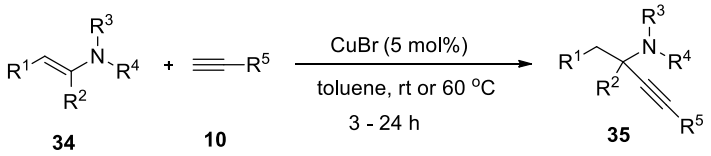
Dyatkin et al. reported[39] that the polymer supported aryl acetylene reacted with aryl aldehyde and secondary amine in dioxane solvent in the presence of CuCl catalyst to produce the resin-bound propargylamines **33** (Scheme 3).[39]

Scheme 3



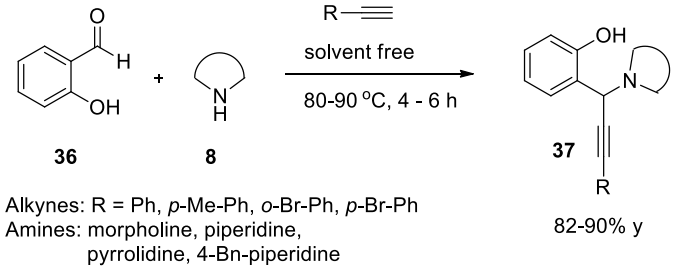
The copper(I)-catalyzed addition of alkynes to enamines produced the propargyl amines **35** (Scheme 4).[40]

Scheme 4



Very recently, Basu and co-workers reported a metal-free A^3 coupling of salicylaldehyde with amines and alkynes to prepare 1-arylpropargylamines **37** (Scheme 5).[41]

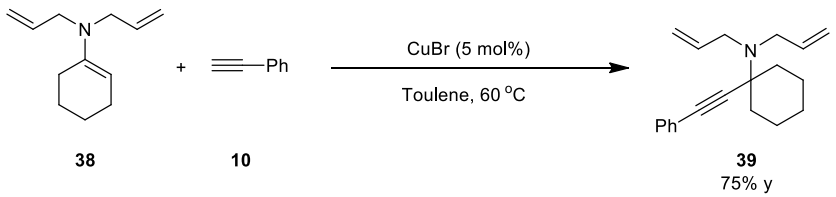
Scheme 5



2.1.4 Synthesis of tetrasubstitutedpropargylamines

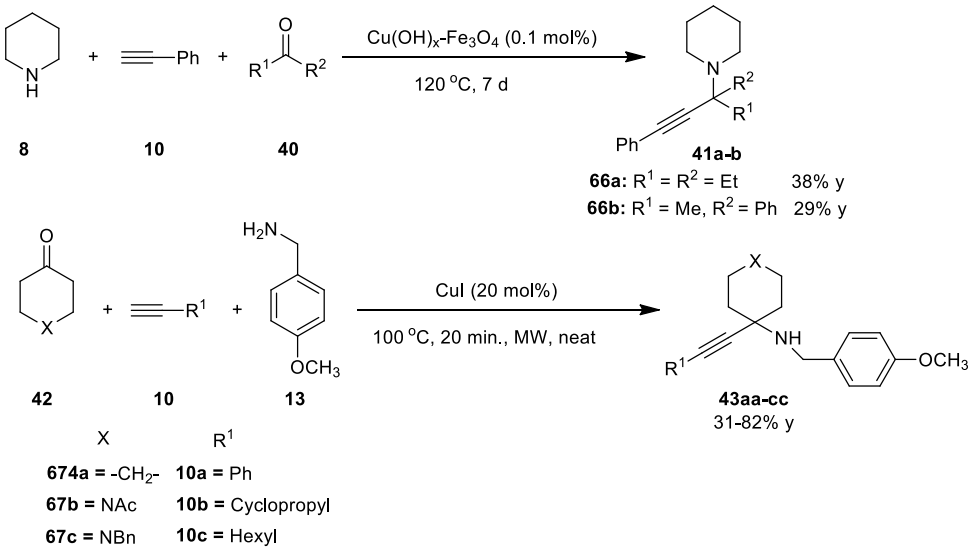
Addition of alkynes **10** to ketenamine derivative **38** in the presence of copper catalyst gave the tetrasubstituted propargylamine **39** in 75% yield. (Scheme 6).[42]

Scheme 6



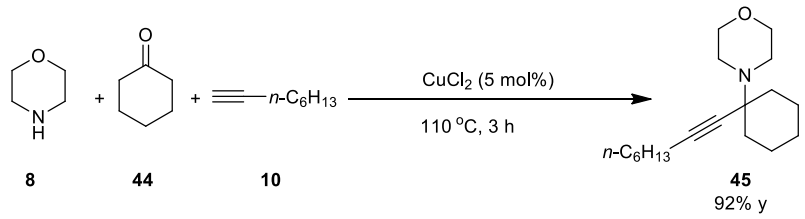
Acyclic and cyclic ketones (**40, 42)** react with amines **8, 13** and 1-alkynes in the presence of copper salts gave the propargylamines **41**, **43** in low to good yields (Chart 6).[43,44]

Chart 6



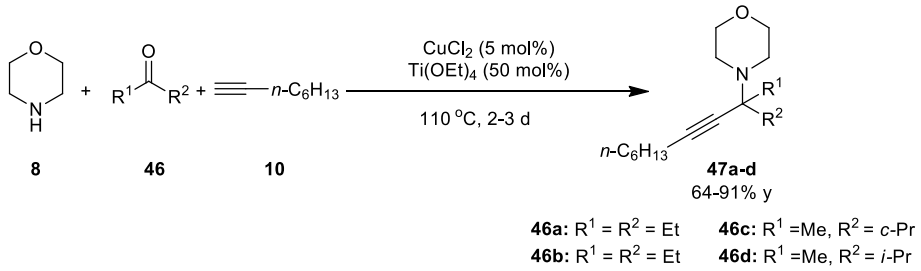
A method involving coupling reaction using morpholine, cyclohexanone and 1-octyne in the presence of 5 mol% $CuCl_2$ was reported (Scheme 7).[45]

Scheme 7



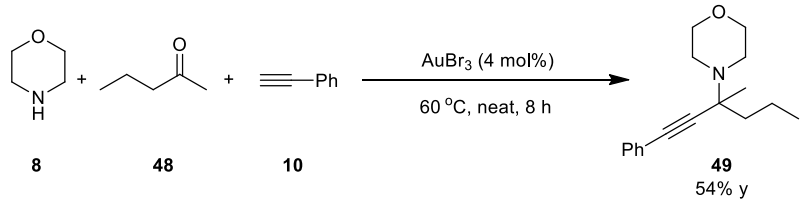
The reaction of morpholine with acyclic ketones and 1-alkynes using 5 mol% $CuCl_2$ and 50 mol% $Ti(OEt)_4$ afforded the tetrasubstituted propargylamine **47** in 91% yield at 110 °C (Scheme 8).[46]

Scheme 8



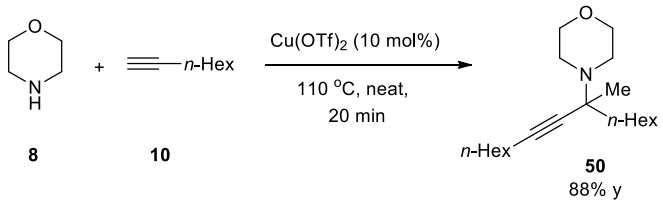
A gold catalyzed method was reported to produce the quarternary propargylamine **49** by using morpholine, 2-pentanone **48** and phenylacetylene at 60 °C (Scheme 9).[47]

Scheme 9



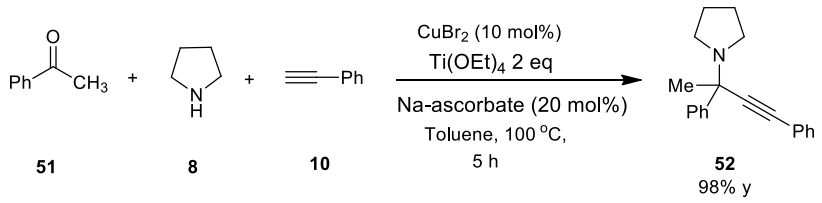
Recently, the Markovnikov hydroamination–alkynylation reaction was developed using morpholine and 1-octyne to access the tetrasubstituted propargylamines **50** in 50% yield (Scheme 10).[48]

Scheme 10



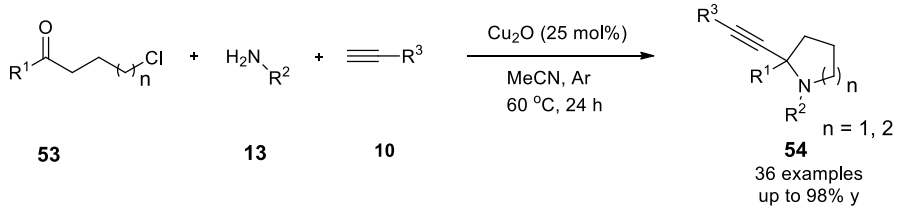
Ma et al. reported[49] a method for the synthesis of propargylamine **52** with $CuBr_2$/sodium ascorbate reagent system using aromatic ketone, pyrrolidine, and alkyne (Scheme 11).

Scheme 11



Very recently, alkynylpyrrolidines or piperidines **54** were prepared by using ketones, amine and 1-alkynes using a copper(I)-catalyst (Scheme 12).[50]

Scheme 12



We have undertaken research efforts on the synthesis of propargylamine deivatives by Michael reaction of α,β-unsaturated ketones. The results are discussed in the next section.

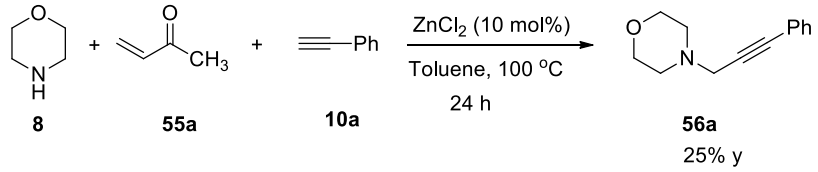
2.2 Results and Discussion

2.2.1 Synthesis of propargylamines using α,β-unsaturated ketones

As outlined in the introductory section, propargylamine derivatives are versatile building blocks useful for the synthesis of natural products and bioactive compounds. Recently, convenient methods have been developed to access chiral propargylamines and chiral allenes via CuX and ZnX_2 promoted transformations from this laboratory.[51] In continuation of these studies, we have developed a new protocol for the synthesis of propargylamines via Michael addition[52] using readily available methyl vinyl ketone derivatives, secondary amines and 1-alkynes.

We have examined the reaction using different metal salts like $ZnCl_2$, $ZnBr_2$, ZnI_2 and CuCl, CuBr, CuI at room temperature in different sovents. Initially, we have carried out the reaction using $ZnCl_2$ and CuCl at room temperature in DCM, CH_3CN, toluene, dioxane solvents with respectively, but the expected propargylamine **56a** was not formed (entries 1-5, Table 1). However, when the reaction was carried using $ZnCl_2$ in toluene (4 mL), the corresponding propargylamine **56a** was isolated in 25% yield at 100 ^oC (Scheme 13).

Scheme 13



Whereas with $ZnBr_2$, the propargylamine product was obtained in 33% yield in 24 h, the reaction also gave the propargylamine in 60% yield using ZnI_2 (entries 1-3, Table 1). The copper(I) chloride gave the corresponding propargylamine **56a** product in 92% yield at 100 ^oC

(entry 4, Table 1). The propargylamine **56a** was also obtained in similar yields using other copper halides like CuBr and CuI under this reaction condition (entries 5 and 6, Table 1).

Table 1. Reaction of morpholine with methyl vinyl ketone and phenyl acetylene promoted by metal salts[a,b]

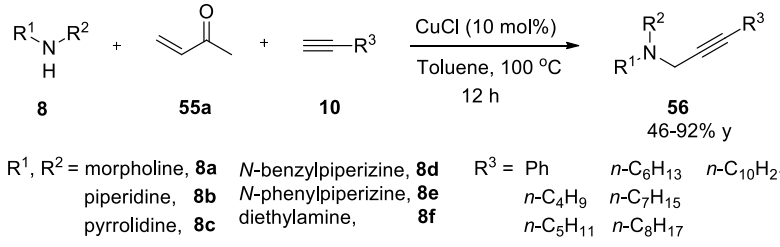
entry	solvent	temp (^oC)	MX_n	mol (%)	time (h)	yield (%)[b]
1	DCM	25	$ZnCl_2$	10	24	NR
2	CH_3CN	25	$ZnCl_2$	10	24	NR
3	Toluene	25	$ZnCl_2$	10	24	NR
4	Dioxane	25	$ZnCl_2$	10	24	NR
5	DCM	25	CuCl	10	24	NR
6	Toluene	100	$ZnCl_2$	10	24	25
7	Toluene	100	$ZnBr_2$	10	24	33
8	Toluene	100	ZnI_2	10	12	60
9	Toluene	100	CuCl	10	12	92
10	Toluene	100	CuBr	10	12	90
11	Toluene	100	CuI	10	12	87

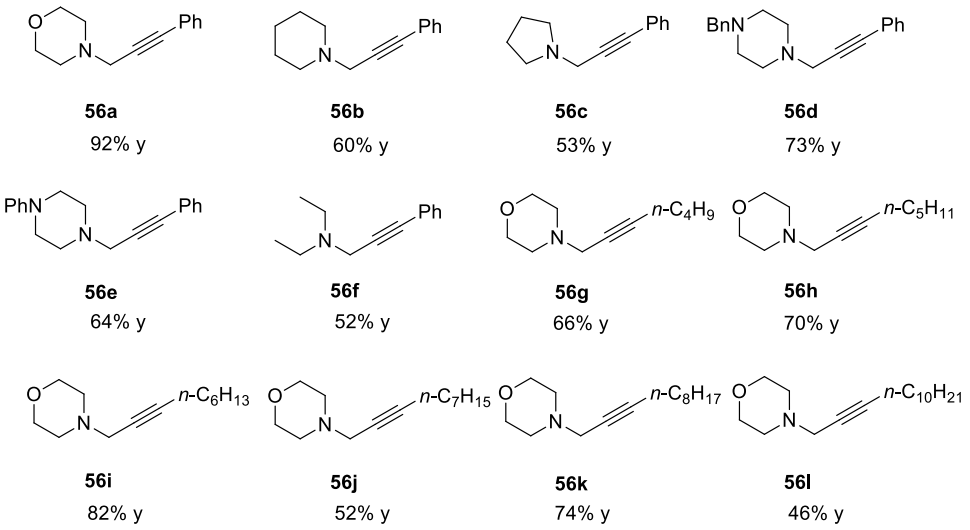
[a]The reactions were carried out by taking morpholine **8 (**2.0 mmol), phenyl acetylene **10a** (2.2 mmol) and methyl vinyl ketone **55a** (2.0 mmol) in toluene (4 mL) at 100 °C for 12 h.
[b]Isolated yield.

Under the optimized conditions (entry 9, Table 1), a broad range of secondary amines were employed for this transformation. For example, the cyclic amines such as morpholine (**8a**) piperidine (**8b**) pyrrolidine (**8c**) *N*-benzylpiperizine (**8d**) and *N*-phenylpiperizine (**8e**) readily participate under these reaction conditions to deliver the corresponding propargylamines **56a-56e** in moderate to good yields (53-92%). The acyclic amine like

diethylamine (**8f**) also gave the desired propargylamine **56f** in 52% yield. The reaction of morpholine with aliphatic 1-alkynes, also afforded the propargylamines **56g-56l** in moderate to good yields (Table 2).

Table 2. CuCl-promoted synthesis of propargylamines **56** using secondary amines **8**, methyl vinyl ketone **55a** and 1-alkynes[a,b]





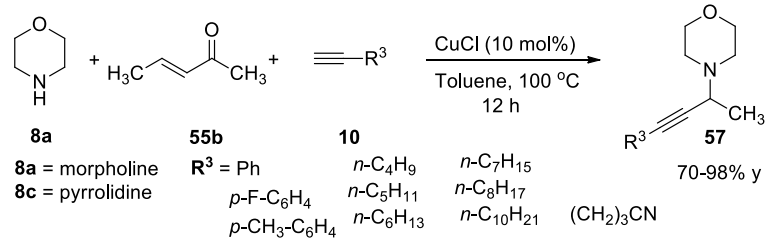
[a]The reactions were carried out by taking amine **8** (2.0 mmol), 1-alkyne **10** (2.2 mmol) and methyl vinyl ketone **55a** (2.0 mmol) in toluene (4 mL) and heating at 100 °[b]Isolated yield.

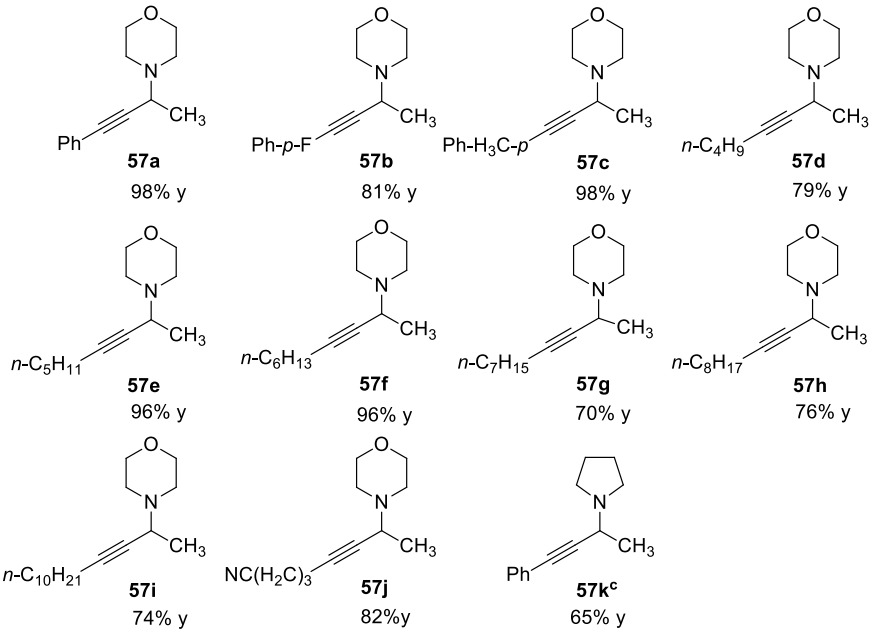
It is of interest to note that the use of paraformaldehyde, 1-alkyne and amine at 80 °C in dioxane solvent gave only the corresponding allenes.[53]

After successful preparation of propargylamine derivatives **56**, 3-pentene-2-one **55b** was employed to examine the scope of this method for the synthesis of propargylamine derivatives **57**. The results are summarised in Table 3. The aromatic alkyne like phenyl

acetylene gave the desired propargylamine in 98% yield (**57a**, Table 3). The substituted phenylacetylenes like *p*-fluorophenylacetylene and *p*-tolylacetylene reacted readily with

Table 3. CuCl-promoted synthesis of propargylamines **57** using morpholine **8a**, 3-penten-2-one **55b** and 1-alkynes[a-c]





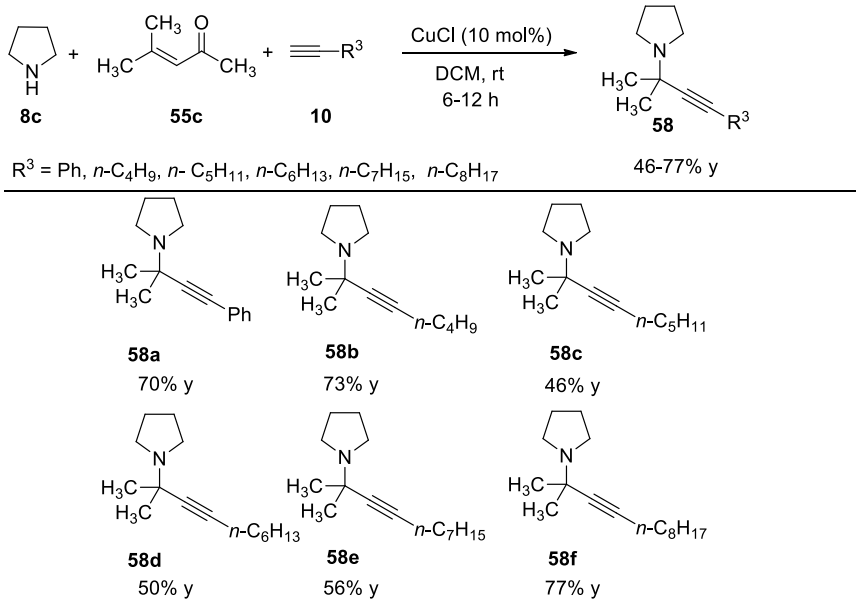
[a]The reactions were carried out by taking amine **8** (2.0 mmol), 1-alkyne **10** (2.2 mmol) and 3-penten-2-one **55b** (2.0 mmol) in toluene (4 mL) at 100 ˚C for 12 h. [b]Isolated yield. [c]DCM solvent at 25 °C for 12 h.

morpholine and 3-pentene-2-one to give the corresponding propargylamines in 81-98% yields (**57b**-**57c**, Table 3). The reaction was also extended to aliphatic alkynes to access the corresponding propargylamines in 70−96% yields (**57d**-**57i**, Table 3). The functionalized alkyne such as 5-cyano-1-pentyne also afforded the corresponding propargylamine in 82%

yield (**57j**, Table 3). Interestingly, the reaction of pyrrolidine with 3-pentene-2-one, phenyl acetylene in dichloromethane solvent gave the propargylamine in 65% yield at room temperature (**57k**, Table 3).

Finally, we have examined the reaction of pyrrolidine **8c** with mesityl oxide **55c** and 1-alkynes in the presence of CuCl (10 mol%) to prepare the propargylamine deivatives **58** with two methyl groups. We have observed that these propargylamine deivatives **58** are obtained in 46-77% yields at room temperature. The results are summarised in Table 4.

Table 4. CuCl-promoted synthesis of propargylamines **58** using pyrrolidine **8c**, mesityloxide **55c** and 1-alkynes[a,b]



[a]The reactions were carried out by taking amine **8** (2.0 mmol), 1-alkyne **10** (2.2 mmol) and mesityloxide **55c** (2.0 mmol) in DCM (4 mL) at 25 ˚C about 6-12 h.

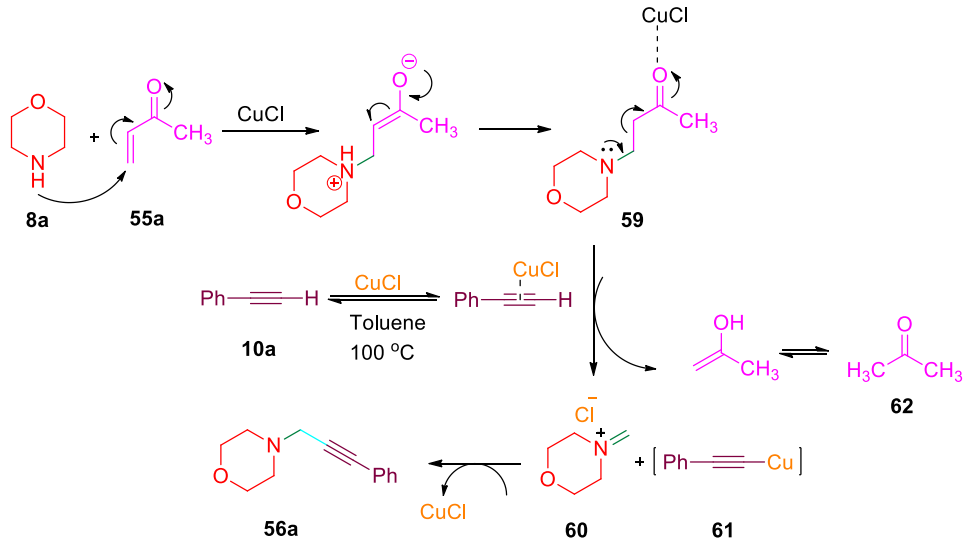
[b]Isolated yield.

The CuCl-catalyzed formation of propargylamines **56a** can be rationalized by the tentative mechanism and intermediates as outlined in Scheme 14. Morpholine would first

react with methyl vinyl ketone **55a** in a Michael fashion. The corresponding Michael adduct **59** would then undergo C-C bond cleavage to give the corresponding iminium intermediate **60**. Subsequent addition of copper acetylides to iminium ion affords the propargylamine **56a** and regenerates the copper catalyst.

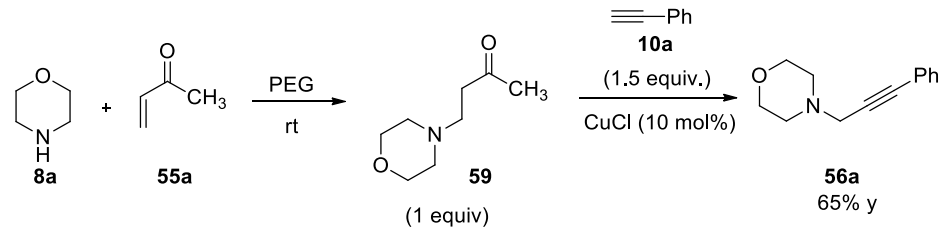
A tentative mechanism outlined in Scheme 14 may be considered for the formation of the propargylamine derivative **56a** (Scheme 14).

Scheme 14 Tentative mechanism



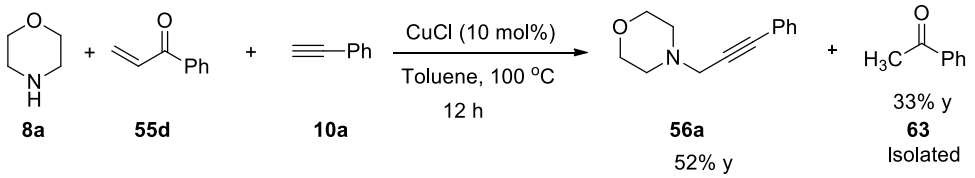
We have also performed the reaction of morpholine **8a** with methyl vinyl ketone **55a** in PEG solvent at room temperature.[52b] The resulting Michael addition product **59** was isolated and freshly reacted with phenyl acetylene **10a** and CuCl (10 mol%) at 100 °C to obtain the propargylamine **56a** in 65% yield (Scheme 15).

Scheme 15 Reaction of Michael adduct intermediate **59** with phenylacetylene **10a** and CuCl



Also, we have observed that the reaction of morpholine **8a** with 1-phenylprop-2-en-1-one **55d** and phenylacetylene **10a** in toluene solvent at 100 ^{o}C gave the propargylamine **56a** in 52% yield along with the acetophenone **63** (33% y) side product as shown in Scheme 16. Clearly, the transformations goes through the C-C bond cleavage of the Michael adduct **59** as outlined in Scheme 14.

Scheme 16 Synthesis of propargylamine **56a** using morpholine **8a**, 1-phenylprop-2-en-1-one **55d** and phenyl acetylene **10a** with CuCl



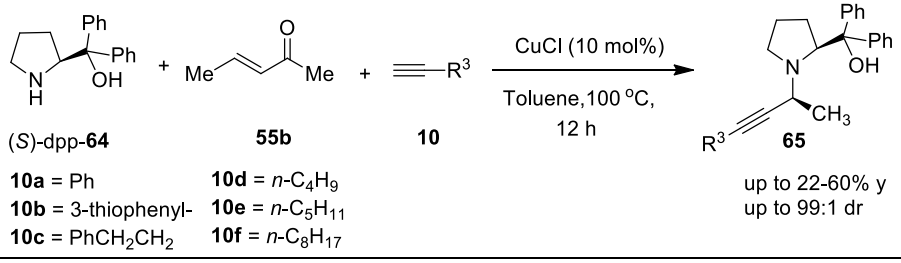
2.2.2 Efforts towards the synthesis of chiral propargylamines 65

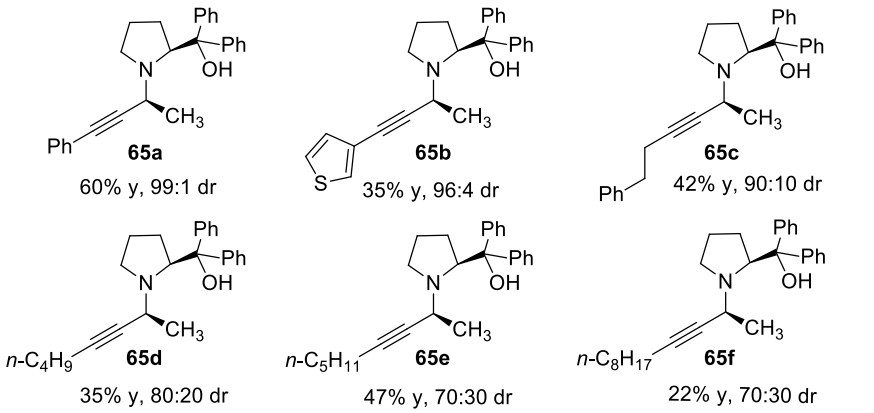
As outlined in the introduction section, classical methods of synthesizing chiral propargylamines involves the asymmetric alkynylation of imines or enamines. Recently, convenient methods to access chiral propargylamines and chiral allenes with CuX, ZnX_2 promoted transformations have been developed from this laboratory.[54] Thus, we became interested in developing the synthesis of chiral propagylamines using this methodology.

The CuBr catalyzed three-component coupling reactions of amines, *n*-alkyl aldehydes and 1-alkynes were also reported for the synthesis of chiral propargylamines using pinap and

quinap ligands.[55] It was of interest to us to examine whether such transformation under the present conditions would give the corresponding chiral propargylamines with diastereoselectivity, if enantiomerically pure chiral amine is used. Accordingly, we have examined the use of the readily accessible optically active chiral (*S*)-diphenylpyrrolidinemethanol (**64**, (*S*)-dpp) with 3-pentene-2-one **55b** and various 1-alkynes in the presence of CuCl (10 mol%). The chiral propargylamines **65** are obtained in 22-60% yields with up to 99:1 dr. The results are summarized in Table 5. The aromatic alkynes like phenylacetylene, 3-ethynylthiophene and 4-phenyl-1-butyne gave the corresponding chiral propargylamines in 35-60% yields with up to 99:1 dr (**65a-65c**, Table 5).

Table 5. Diastereoselective synthesis of propargylamines **65** using chiral (*S*)- dpp **64**, 3-penten-2-one **55b** and 1-alkynes with copper(I)chloride[a-c]





[a]The reactions were carried out by taking chiral amine **64** (1.0 mmol), 1-alkyne **3** (1.2 mmol) and 3-penten-2-one **55b** (1.0 mmol) in toluene (3 mL) at 100 ˚C for 12 h. [b]dr ratio based on crude ^{1}H NMR. [c]Isolated yield.

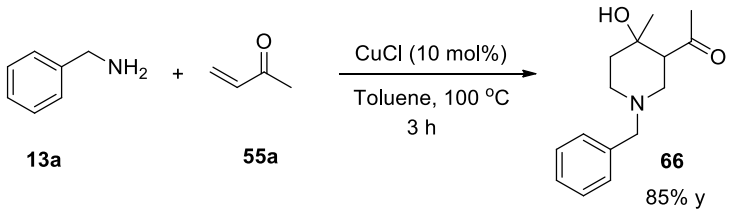
We have also carried out the reaction using aliphatic alkynes such as 1-hexyne, 1-heptyne and 1-decyne under this reaction condition but the corresponding propargylamines **65** were obtained in only 22-47% yields with lower dr (**65d-65f**, Table 5). The new chiral centre at the propargylic position is assigned *S* configuration based on comparision of $[\alpha]_D^{25}$ value with previous reports.[51a,55]

We have observed that small amount of benzophenone (18% y) was formed as byproduct in these reactions. It is of interest to note that previously benzophenone was reported as byproduct in the preparation of phenyl-substituted oxazaborolidines from the corresponding (*S*)-diphenylprolinol **64** and trimethoxyborane.[56]

2.2.3 Efforts towards the reactions of primary amines with methyl vinyl ketone

We have also examined the reaction of primary amines like benzylamine **13a** with methyl vinyl ketone **55a** and phenylacetylene in the presence of CuCl in toluene solvent at 100 ^oC. Interestingly, benzylamine was reacted with methyl vinyl ketone to give the substituted-*N*-benzylpiperidine **66** in 3 hours at 100 ^oC instead of propargylamine derivative (Scheme 17).

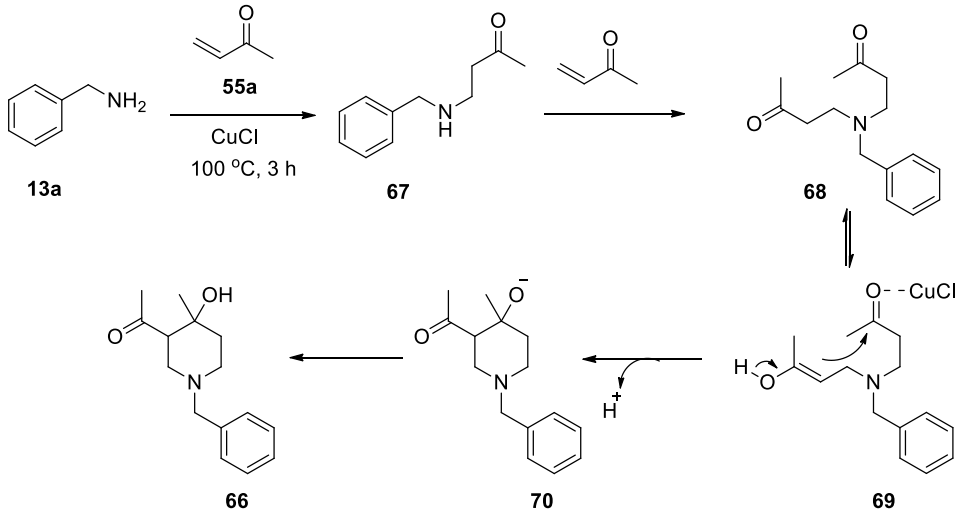
Scheme 17 Synthesis of 1-(1-benzyl-4-hydroxy-4-methylpiperidin-3-yl) ethanone **66** using benzylamine **13a** methyl vinyl ketone **55a** with CuCl



A tentative mechanism can be considered for the formation of substituted-*N*-benzylpiperidine as outlined in Scheme 18. Initially, the benzylamine **13a** would react with

methyl vinyl ketone **55a** in Michael addition fashion to give the Michael adduct **67**. Subsequently, the resulting Michael adduct **67** would again undergo double Michael addition with methyl vinyl ketone to form the product **68**. The enol intermediate **69** would then undergo cyclization to give the substituted-*N*-benzylpiperidine product **66**.

Scheme 18 Plausible mechanism for the formation of substituted-*N*-benzylpiperidine **66**



Next, we have undertaken efforts on the development of electron transfer reactions using diamines and propargylamines. The results are described in chapter 3, 4 and 5.

2.3 Conclusions

In summary, we have developed a CuCl-promoted, convenient method for the synthesis of propargylamines using amines, α,β-unsaturated ketones and 1-alkynes *via* Michael addition followed by C-C bond cleavage and addition of metal acetylides to iminium ion intermediates. This method involving use of inexpensive cheaper CuCl as catalyst is applicable to both aromatic, aliphatic alkynes and also for various secondary amines to produce di, tri, tetrasubstituted propargylamines in a single-pot synthesis. Also, this method has been employed for the synthesis of chiral propargylamines with up to 99:1 dr. Propargylamines are an important class of intermediates and attractive starting materials in the synthesis of nitrogen heterocycles, natural products and biologically active compounds.[57] Hence, the method to access propargylamines described here has good synthetic potential.

2.4 Experimental Section

2.4.1 General information

IR (neat) spectra were recorded on JASCO FT-IR spectrophotometer model-5300. ^{1}H (400 MHz), ^{13}C (100 MHz) NMR spectra were recorded on Bruker-Avance-400 spectrometers chloroform-d as solvent. Chemical shifts were determined with tetramethylsilane (TMS) as internal reference (δ = 0 ppm). Coupling constants *J* are in Hz. Optical rotations were measured on Rudolph Research Analytical 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-methylbenzylamine $[\alpha]_D^{25}$ = –29.6 (c 0.74, EtOH) supplied by Aldrich.

All the glasswares were pre-dried at 100-120 °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 reagent were carried out using standard syringe-septum technique recommended for handling air sensitive reagents and organometallic compounds.

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

Toluene supplied by E-Merck, India was kept over sodium-benzophenone ketyl and freshly distilled before use. Analytical grade of CuCl, CuBr, CuI, $ZnCl_2$ and ZnI_2 were purchased from Sigma-Aldrich. $ZnBr_2$ was purchased from E-Merck. Analytical thin layer chromatographic tests were carried out on glass plates (3 x 10 cm) coated with 250 mμ E-Merck and acme's silica gel-G and GF-254 containing 13% calcium sulfate as a 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.

2.4.1 General procedure for the synthesis of propargylamines

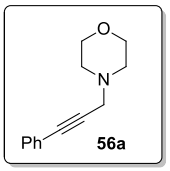
To a stirred suspension of amine **8** (2 mmol), CuCl (0.020 g, 0.2 mmol) and 1-alkyne **10** (2.2 mmol) in toluene (3 mL), α,β-unsaturated ketone **55a-55c** (2.2 mmol) was added at 25 ^oC. The contents were stirred at 100 ^oC for 12 h. Toluene was removed, water (5 mL) and DCM (15 mL) were added. The DCM layer was washed with saturated NaCl solution, dried with Na_2SO_4 and concentrated. The residue was chromatographed on silica gel (100-200 mesh) using hexane and ethyl acetate as eluent to isolate the propargylamine derivatives (**56-58**). The yields and the spectral data of the are given below.

2.4.2 Procedure for the synthesis of propargylamine 56a from the Michael adduct intermediate 59

A mixture of amine **8a** (2 mmol), methyl vinyl ketone **55a** (3 mmol) and PEG 400 (5 g) was placed in 25 mL round bottomed flask. The contents were stirred at room temperature until the reaction was complete. The crude mixture was extracted with ether. The ether layer was concerted and purified on silica gel (100-200 mesh) using hexane and ethylacetate (50:50) as an eluent to obtain the adduct in excellent yield.[52b] To a stirred solution of freshly

prepared Michael adduct **59** (0.157 g, 1 mmol) in toluene (3 mL), phenyl acetylene **10a** (0.16 mL, 1.5 mmol) and CuCl (0.010 g, 0.1 mmol) were added and contents were stirred at 100 ^{o}C for 12 h. Toluene was removed, water (5 mL) and DCM (10 mL) were added. The DCM layer was washed with saturated NaCl solution, dried with Na_2SO_4 and concentrated. The residue was chromatographed on silica gel (100-200 mesh) using hexane and ethylacetate (80:20) as eluent to isolate the propargylamine **56**.

4-(3-phenylprop-2-yn-1-yl) morpholine



56a

Yield : 0.369 g, 92%; yellow liquid.

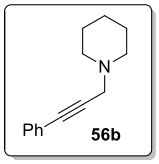
IR (neat) : 2956, 2925, 2853, 2755, 1598, 1479, 1453, 1391, 1324, 1288, 1236, 1112, 1066, 1019, 911, 854, 751, 694 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.46-7.44 (m, 2H) 7.32-7.31 (m, 3H), 3.80-3.78 (m, 4H), 3.53 (s, 2H), 2.68-2.67(m, 4H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 131.7, 128.2, 128.1, 123.0, 85.5, 84.1, 66.9, 52.4, 48.1.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{13}H_{15}NO$: 202.1232; found: 202.1232.

1-(3-phenylprop-2-yn-1-yl) piperidine



56b

Yield : 0.238 g, 60%; yellow liquid.

IR (neat) : 3054, 3028, 2930, 2858, 2796, 2750, 1644, 1593, 1489, 1433, 1371, 1345, 1298, 1257, 1159, 1007, 1066, 1040, 999, 911, 859, 771, 684 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.46-7.44 (m, 2H) 7.32-7.29 (m, 3H), 3.49

(s, 2H), 2.59 (s, 4H), 1.66 (qt, *J* = 6.0 Hz, 4H), 1.46 (s, 2H).

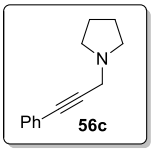
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 131.7, 128.2, 127.9, 123.3, 85.0, 84.9, 53.4, 48.4, 25.9, 23.9.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{14}H_{17}N$: 200.1439: found: 200.1439.

1-(3-phenylprop-2-yn-1-yl) pyrrolidine

Yield : 0.196 g, 53%; yellow liquid.

IR (neat) : 3054, 2959, 2910, 2854, 2814, 2761, 1597, 1489, 1449, 1347, 1329, 1289, 1269, 1116, 1071, 1006, 916, 861, 757, 692 cm^{-1}.



^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.46-7.44 (m, 2H) 7.32-7.30 (m, 3H), 3.80-3.78 (m, 4H), 3.54-3.52 (m, 2H), 2.67-2.66 (m, 2H).

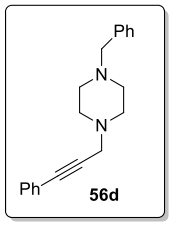
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 131.7, 128.2, 128.1, 122.9, 85.5, 84.0, 66.9, 52.4, 48.0.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{13}H_{15}N$: 186.1282; found: 186.1284.

1-benzyl-4-(3-phenylprop-2-yn-1-yl) piperizine

Yield : 0. 423 g, 73%; yellow liquid.

IR (neat) : 3059, 3028, 2930, 2806, 2765, 2693, 1686, 1598, 1494, 1443, 1329, 1293, 1143, 1071, 1019, 911, 828, 756, 694 cm^{-1}.



^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.46-7.44 (m, 2H) 7.35-7.33 (m, 4H),

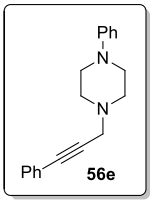
7.32-7.28 (m, 4H), 3.58 (s, 2H), 3.55 (s, 2H), 2.73 (s, 4H) 2.60 (s, 4H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 138.0, 131.7, 129.2, 128.2, 128.0, 127.0, 123.1, 85.2, 84.6, 63.0, 52.9, 52.1, 47.7.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{20}H_{22}N_2$: 291.1861; found: 291.1860.

1-phenyl-4-(3-phenylprop-2-yn-1-yl) piperizine

Yield : 0. 353 g, 64%; yellow liquid.



IR (neat) : 3028, 2941, 2905, 2817, 1598, 1489, 1448, 1391, 1345, 1226, 1138, 1004, 926, 756, 699 cm^{-1}.

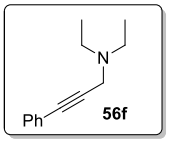
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.48-7.46 (m, 2H), 7.33-7.27 (m, 5H), 6.99-6.97 (m, 2H), 6.91-6.88 (m, 1H), 3.61-3.60 (m, 2H), 3.30-3.28 (m, 4H), 2.85-2.83 (m, 4H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 151.2, 131.7, 129.1, 128.2, 128.1, 123.0, 119.8, 116.1, 85.5, 84.2, 52.1, 49.1, 47.8.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{19}H_{20}N_2$: 277.1704; found: 277.1704.

N,N-diethyl-3-phenylprop-2-yn-1-amine

Yield : 0. 194 g, 52%; yellow liquid.



IR (neat) : 2967, 2930, 2874, 2812, 1562, 1489, 1458, 1371, 1319, 1200, 1117, 1066, 1030, 983, 761, 684 cm^{-1}.

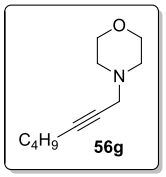
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.45-7.32 (m, 5H) 3.68 (s, 2H), 2.67-2.60 (m, 4H), 1.15-1.08 (m, 6H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 131.7, 128.2, 127.9, 123.3, 84.9, 84.3, 47.3, 41.4, 12.6.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{13}H_{17}N$:188.1439; found: 188.1435.

4-(hept-2-yn-1-yl) morpholine

Yield : 0.238 g, 66%; yellow liquid.



IR (neat) : 2956, 2925, 2853, 2755, 1448, 1376, 1293, 1241, 1123, 1009, 916, 859, 777 cm^{-1}.

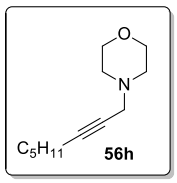
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.74 (t, *J* = 4.6 Hz, 4H), 3.24 (t, *J* = 2.25 Hz, 2H), 2.55 (s, 4H), 2.21-2.18 (m, 2H), 1.51-1.46 (m, 2H), 1.42-1.36 (m, 2H), 0.90 (t, *J* = 7.35 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 85.8, 74.3, 66.8, 52.3, 47.6, 30.8, 21.9, 18.3, 13.5.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{11}H_{19}NO$: 182.1545; found: 182.1540.

4-(oct-2-yn-1-yl) morpholine

Yield : 0.273 g, 70%; yellow liquid.



IR (neat) : 2956, 2930, 2858, 2817, 1448, 1329, 1283, 1236, 1112, 1071, 999, 911, 864, 797 cm^{-1}.

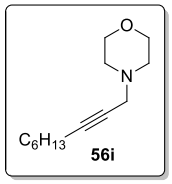
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.75 (t, *J* = 4.48 Hz, 4H), 3.25(t, *J* = 2.20 Hz, 2H), 2.57-2.56 (m, 3H), 2.22-2.17 (m, 2H), 1.51 (qt, *J* = 7.0 Hz, 2H), 1.41-1.26 (m, 5H), 0.90 (t, *J* = 7.04 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 85.9, 74.3, 66.8, 52.3, 47.6, 31.0, 28.5, 22.1,

18.6, 13.9.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{12}H_{21}NO$: 196.1701; found: 196.1702.

4-(non-2-yn-1-yl) morpholine



56i

Yield : 0.342 g, 82%; yellow liquid.

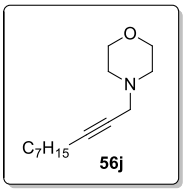
IR (neat) : 2956, 2925, 2848, 2806, 1448, 1350, 1288, 1241, 1117, 1004, 921, 859, 792 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.74 (t, *J* = 3.6 Hz, 4H) 3.24 (t, *J* = 1.76 Hz, 2H), 2.55 (s, 3H), 2.21-2.17 (m, 2H), 1.53-1.47 (m, 2H), 1.41-1.36 (m, 2H), 1.31-1.25 (m, 5H), 0.88 (t, *J* = 5.48, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 85.9, 74.3, 66.8, 52.3, 47.7, 31.3, 28.7, 28.5, 22.5, 18.7, 14.0.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{13}H_{23}NO$: 210.1858; found: 210.1858.

4-(dec-2-yn-1-yl) morpholine



56j

Yield : 0.231 g, 52%; yellow liquid.

IR (neat) : 2951, 2920, 2853, 2806, 1458, 1329, 1293, 1241, 1112, 1066, 999, 916, 859, 792 cm^{-1}.

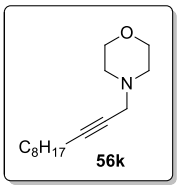
^{1}H NMR : (500 MHz, $CDCl_3$, δ ppm) 3.75 (t, *J* = 4.65, 4H) 3.25 (t, *J* = 2.25 Hz, 2H), 2.57-2.56 (m, 3H), 2.21-2.18 (m, 2H), 1.54-1.48 (m, 2H), 1.41-1.36 (m, 2H), 1.32-1.26 (m, 7H), 0.89 (t, *J* = 6.75 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 85.8, 74.3, 66.8, 52.3, 47.6, 31.7, 28.9, 28.8, 28.7, 28.5, 18.6, 14.0.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{14}H_{25}NO$: 224.2014; found: 224.2015.

4-(undec-2-yn-1-yl) morpholine

Yield : 0.350 g, 74%; yellow liquid.



IR (neat) : 2961, 2925, 2853, 2812, 2765, 1453, 1329, 1262, 1117, 1066, 1004, 911, 864, 797 cm^{-1}.

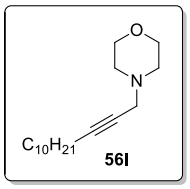
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.74 (t, *J* = 4.6 Hz, 4H), 3.23 (t, *J* = 2.2 Hz, 2H), 2.56-2.55 (m, 3H), 2.21-2.16 (m, 2H), 1.49 (qt, *J* = 6.72 Hz, 2H), 1.41-1.35 (m, 2H), 1.33-1.27 (m, 9H), 0.87 (t, *J* = 6.64 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 85.9, 74.3, 66.8, 52.3, 47.7, 31.8, 29.1, 29.0, 28.9, 28.8, 22.6, 18.6, 14.0.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{15}H_{27}NO$: 238.2171; found: 238.2172.

4-(tridec-2-yn-1-yl) morpholine

Yield : 0.243 g, 46%; yellow liquid..



IR (neat) : 2925, 2848, 1453, 1376, 1288, 1236, 1117, 1014, 911, 870, 797, 720 cm^{-1}.

^{1}H NMR : (500 MHz, $CDCl_3$, δ ppm) 3.74 (t, *J* = 4.55 Hz, 4H), 3.24 (t, *J* = 2.1 Hz, 2H), 2.55 (s, 3H), 2.20-2.17 (m, 2H), 1.49 (qt, *J* = 6.95 Hz, 2H), 1.38-1.34 (m, 2H), 1.29-1.26 (m, 13H), 0.88 (t, *J* = 6.75 Hz, 3H).

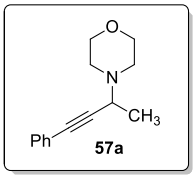
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 85.9, 74.3, 66.8, 52.3, 47.7, 31.9, 29.6, 29.5, 29.3, 29.1, 28.9, 28.8, 22.6, 18.7, 14.1.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{31}NO$: 266.2484; found: 266.2486.

4-(4-phenylbut-3-yn-2-yl) morpholine

Yield : 0.421 g, 98%; yellow liquid.

IR (neat) : 2956, 2894, 2853, 2822, 2755, 1598, 1489, 1443, 1376, 1324, 1298, 1262, 1179, 1123, 1066, 1035, 957, 911, 849, 766 cm^{-1}.



57a

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.46-7.44 (m, 2H), 7.32-7.28 (m, 3H), 3.83-3.75 (m, 4H), 3.72-3.67 (m, 1H), 2.80-2.76 (m, 2H), 2.62-2.59 (m, 2H), 1.48-1.44 (m, 3H).

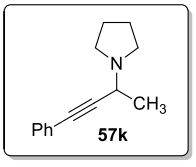
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 131.7, 128.2, 128.0, 123.0, 87.7, 85.4, 67.1, 52.6, 49.5, 19.0.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{14}H_{17}NO$: 216.1388; found: 216.1387.

1-(4-phenylbut-3-yn-2-yl)pyrrolidine

Yield : 0.258 g, 65%; yellow liquid.

IR (neat) : 2965, 2930, 2875, 2809, 1673, 1598, 1489, 1444, 1370, 1313, 1250,1216, 1158, 1132, 1069, 1025, 913, 750, 716, 690, 663 cm^{-1}.



57k

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.44-7.43 (m, 2H), 7.31-7.28 (m, 3H), 3.90-3.85 (m, 1H), 2.87-2.75 (m, 4H), 1.85 (s, 4H) 1.53-1.48 (m, 3H).

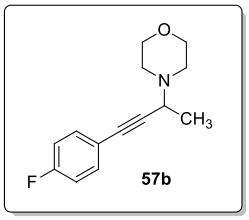
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 131.7, 128.2, 127.9, 123.2, 88.6, 84.6, 49.8, 49.7, 23.5, 21.0.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{14}H_{17}N$: 200.1439; found: 200.1441.

4-(4-(4-fiuorophenyl)but-3-yn-2-yl) morpholine

Yield : 0.377 g, 81%; yellow liquid.

IR (neat) : 2956, 2894, 2853, 2822, 1603, 1505, 1453, 1376, 1324, 1226, 1107, 1071, 1035, 968, 921, 890, 833, 808, 751 cm^{-1}.



57b

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.43-7.38 (m, 2H), 7.02-6.96 (m, 2H), 3.82-3.72 (m, 4H), 3.65 (q, *J* = 7.04 Hz, 1H), 2.77-2.72 (m, 2H) 2.59-2.54 (m, 2H), 1.45-1.41 (m, 3H).

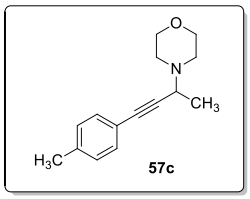
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 163.5, 161.0, 133.5, 133.4, 119.2, 119.1, 115.5, 115.3, 87.4, 84.4, 67.0, 52.6, 49.5, 18.9.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{14}H_{16}FNO$: 234.1294; found: 234.1293.

4-(4-(*p*-tolyl)but-3-yn-2-yl) morpholine

Yield : 0.448 g, 98%; yellow liquid.

IR (neat) : 2951, 2920, 2853, 2812, 1505, 1453, 1371, 1324, 1252, 1185, 1112, 1071, 1030, 968, 916, 859,



57c

818, 761 cm^{-1}.

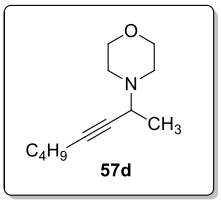
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.35-7.33 (m, 2H), 7.13-7.11 (m, 2H), 3.83-3.75 (m, 4H), 3.70-3.65 (m, 1H), 2.80-2.76 (m, 2H), 2.62-2.58 (m, 2H), 2.36 (s, 3H), 1.47-1.43 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 138.0, 131.5, 128.9, 120.0, 86.9, 85.5, 67.0, 52.6, 49.5, 21.4, 19.0.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{15}H_{19}NO$: 230.1545; found: 230.1546.

4-(oct-3-yn-2-yl) morpholine

Yield : 0.308 g, 79%; yellow liquid.



57d

IR (neat) : 2956, 2925, 2853, 2817, 1453, 1376, 1324, 1252, 1185, 1112, 1071, 1014, 916, 859, 777, 751 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.79-3.69 (m, 4H,) 3.44-3.38 (m, 1H), 2.68-2.62 (m, 2H), 2.50-2.45 (m, 2H), 2.20 (dt, *J* = 7.04 Hz, 1.92 Hz, 2H), 1.53-1.38 (m, 4H), 1.33-1.29 (m, 3H), 0.91 (t, *J* = 7.24 Hz, 3H).

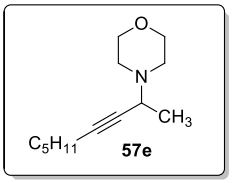
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 85.4, 78.0, 67.0, 52.2, 49.4, 31.1, 21.9, 19.2, 18.2, 13.5.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{12}H_{21}NO$: 196.1701; found: 196.1703.

4-(non-3-yn-2-yl) morpholine

Yield : 0.401 g, 96%; yellow liquid.

IR (neat) : 2956, 2930, 2853, 2822, 1458, 1376, 1324,1252, 1190, 1123, 1071, 1045, 1004, 947, 916, 859, 771 cm^{-1}.



57e

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.79-3.70 (m, 4H), 3.44-3.39 (m, 1H), 2.68-2.63 (m, 2H), 2.51-2.46 (m, 2H), 2.23-2.18 (m, 2H), 1.53-1.37 (m, 5H), 1.34-1.26 (m, 4H), 0.92 (t, *J* = 7.2 Hz, 3H).

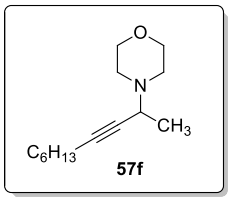
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 85.5, 78.1, 67.0, 52.2, 49.4, 31.0, 28.7, 22.1, 19.2, 18.5, 13.9.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{13}H_{23}NO$: 210.1858; found: 210.1859.

4-(dec-3-yn-2-yl) morpholine

Yield : 0.428 g, 96%; yellow liquid.

IR (neat) : 2956, 2925, 2853, 2822, 1458, 1376, 1324, 1252, 1185, 1112, 1071, 1045, 999, 952, 916, 864 cm^{-1}.



57f

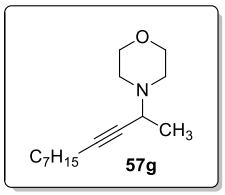
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.79-3.71 (m, 4H), 3.45-3.40 (m, 1H), 2.69-2.65 (m, 2H), 2.52-2.48 (m, 2H), 2.20 (dt, J= 7.0 Hz, 2.5 Hz, 2H), 1.54-1.48 (m, 2H), 1.42-1.36 (m, 2H), 1.32-1.30 (m, 5H), 1.28-1.26 (m,2H), 0.90 (t, *J* = 6.90 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 85.5, 78.1, 67.0, 52.2, 49.4, 31.3, 28.9, 28.5, 22.5, 19.2, 18.6, 14.0.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{14}H_{25}NO$: 224.2014; found: 224.2016.

4-(undec-3-yn-2-yl) morpholine

Yield : 0.331 g, 70%; yellow liquid.



IR (neat) : 2956, 2925, 2853, 2817, 1448, 1376, 1324, 1252, 1190, 1117, 1076, 1045, 1009, 947, 921, 864 cm^{-1}.

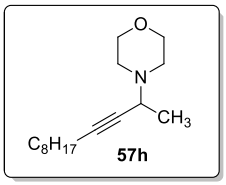
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.78-3.70 (m, 4H), 3.44-3.38 (m, 1H), 2.68-2.63 (m, 2H), 2.51-2.46 (m, 2H), 2.20 (dt, J= 7.2 Hz, 2.0 Hz, 2H), 1.54-1.47 (m, 2H), 1.40-1.36 (m, 2H), 1.32-1.28 (m, 9H), 0.89 (t, *J* = 6.6 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 85.5, 78.1, 67.0, 52.2, 49.4, 31.7, 29.0, 28.8, 28.7, 22.5, 19.2, 18.6, 14.0.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{15}H_{27}NO$: 238.2171; found: 238.2170.

4-(dodec-3-yn-2-yl) morpholine

Yield : 0.381 g, 76%; yellow liquid.



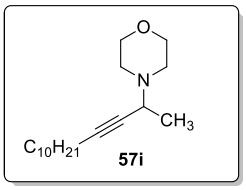
IR (neat) : 2956, 2930, 2843, 1458, 1371, 1324, 1257 1179, 1123, 1071, 1045, 957, 911, 864 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.80-3.70 (m, 4H), 3.45-3.39 (m, 1H), 2.69-2.64 (m, 2H), 2.52-2.47 (m, 2H), 2.20 (dt, *J* = 7.2 Hz, 2.0 Hz, 2H), 1.54-1.47 (m, 2H), 1.40-1.36 (m, 2H), 1.32-1.28 (m, 11H), 0.88 (t, *J* = 6.6 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 85.6, 78.0, 67.0, 52.2, 49.3, 31.8, 29.2, 29.1. 29.0, 28.8, 22.6, 19.2, 18.6, 14.1.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{16}H_{29}NO$: 252.2327; found: 252.2328.

4-(tetradec-3-yn-2-yl) morpholine



57i

Yield : 0.412 g, 74%; yellow liquid.

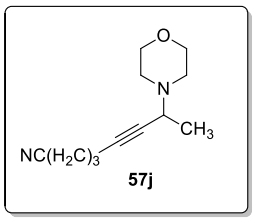
IR (neat) : 2956, 2925, 2853, 1458, 1376, 1319, 1252, 1185, 1117, 1076, 1045, 999, 957, 911, 849 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.80-3.71 (m, 4H), 3.45-3.40 (m, 1H), 2.70-2.65 (m, 2H), 2.53-2.48 (m, 2H), 2.23-2.19 (m, 2H), 1.55-1.48 (m, 2H), 1.39 (s, 2H), 1.33-1.29 (m, 15H), 0.90-0.88 (t, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 85.5, 78.1, 67.1, 52.2, 49.4, 31.9, 29.6, 29.5, 29.3, 29.1, 29.0, 28.8, 22.6, 19.2, 18.6, 14.1.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{18}H_{33}NO$: 280.2640; found: 280.2641.

7-morpholinooct-5-ynenitrile



57j

Yield : 0.337 g, 82%; yellow liquid.

IR (neat) : 2951, 2853, 2822, 2248, 1711, 1453, 1329, 1261, 1184, 1112, 1070, 1013, 967, 910, 858, 760 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.76-3.67 (m, 4H), 3.44-3.39 (m, 1H), 2.65-2.59 (m, 2H), 2.49-2.43 (m, 4H), 2.40-2.36 (m, 2H). 1.84 (qt, J = 6.96 Hz, 2H), 1.32-1.28 (m, 3H).

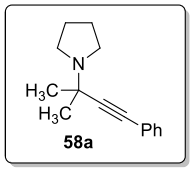
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 119.1, 82.5, 80.1, 66.8, 52.1, 49.3, 24.7, 19.0, 17.7, 16.1.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{12}H_{18}N_2O$: 207.1497; found: 207.1500.

1-(2-methyl-4-phenylbut-3-yn-2-yl)pyrrolidine

Yield : 0.298 g, 70%; yellow liquid.

IR (neat) : 2961, 2868, 2806, 1686, 1587, 1484, 1438, 1360, 1257, 1179, 1117, 1071, 1019, 911, 844, 756, 694 cm^{-1}.



58a

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.45-7.42 (m, 2H), 7.31-7.29 (m, 3H), 2.84-2.82 (m, 4H) 1.85-1.84 (m, 4H), 1.53-1.51 (m, 6H).

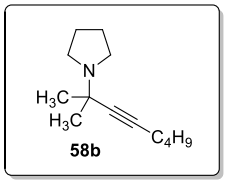
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 131.7, 128.2, 127.7, 123 .4, 91.4, 83.8, 54.2, 48.2, 29.7, 23.8.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{15}H_{19}N$: 214.1595; found: 214.1594.

1-(2-methyloct-3-yn-2-yl)pyrrolidine

Yield : 0.281 g, 73%; yellow liquid.

IR (neat) : 2956, 2926, 2871, 2802, 1706, 1649, 1597, 1458, 1379, 1354, 1324, 1225, 1181, 1126, 1071, 1007, 868, 792 cm^{-1}.



58b

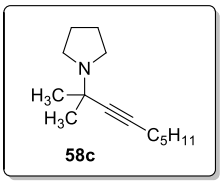
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 2.72-2.69 (m, 4H), 2.19 (t, J = 6.84 Hz, 2H), 1.80-1.76 (m, 4H), 1.52-1.40 (m, 4H), 1.37 (s, 6H), 0.91 (t, J = 7.16 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 83.6. 81.2. 53.8. 47.9. 31.3. 29.8. 23.7. 21.8. 18.2. 13.5.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{13}H_{23}N$: 194.1908; found: 194.1909.

1-(2-methylnon-3-yn-2-yl)pyrrolidine

Yield : 0.190 g, 46%; yellow liquid.



58c

IR (neat) : 2956, 2930, 2874, 2806, 1639, 1556, 1453, 1381, 1221, 1185, 1117, 1019, 916, 859 cm^{-1}.

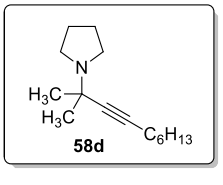
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 3.77-3.74 (m, 4H), 2.64-2.63 (m, 4H), 2.23-2.17 (m, 2H), 1.58-1.46 (m, 2H), 1.39-1.32 (m, 10H), 0.92-0.89 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 84.2, 81.3, 67.3, 54.1, 47.2, 31.0, 28.7, 27.6, 22.1, 18.5, 13.9.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{13}H_{23}N$: 208.2066; found: 208.2066.

1-(2-methyldec-3-yn-2-yl)pyrrolidine

Yield : 0.221 g, 50%; yellow liquid.



58d

IR (neat) : 2956, 2930, 2863, 2811, 1463, 1385, 1354, 1323, 1220, 1184, 1112, 1065, 1013 cm^{-1}.

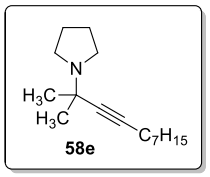
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 2.70-2.67 (m, 4H), 2.18 (t, J= 6.8 Hz, 2H), 1.80-1.75 (m, 4H), 1.51-1.45 (m, 2H), 1.44-1.38 (m, 3H), 1.35 (s, 6H), 1.29-1.26 (m, 3H), 0.88 (t, J = 6.68 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 83.6, 81.3, 53.7, 47.9, 31.2, 29.9, 29.1, 28.4, 23.7, 22.5, 18.5, 13.9.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{15}H_{27}N$: 222.2221; found: 222.2222.

1-(2-methylundec-3-yn-2-yl)pyrrolidine

Yield : 0.263 g, 56%; yellow liquid.



58e

IR (neat) : 2954, 2925, 2854, 2806, 1454, 1383, 1354, 1321, 1221, 1183, 1116, 1073, 1011 cm^{-1}.

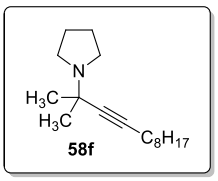
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 2.72-2.71 (m, 4H), 2.19 (t, *J* = 6.88 Hz, 2H), 1.80-1.77 (m, 4H), 1.52-1.45 (m, 2H), 1.42-1.39 (m, 2H), 1.37-1.36 (m, 6H), 1.33-1.28 (m, 6H), 0.90-0.87 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 83.6, 81.4, 53.7, 47.9, 31.7, 29.9, 29.1, 28.8, 28.7, 23.7, 22.5, 18.5, 14.0.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{16}H_{29}N$: 236.2378; found: 236.2375.

1-(2-methyldodec-3-yn-2-yl)pyrrolidine

Yield : 0.383 g, 77%; yellow liquid.



58f

IR (neat) : 2956, 2920, 2853, 2806, 1458, 1376, 1360, 1329, 1220, 1181, 1111, 1066, 1007 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 2.71-2.68 (m, 4H), 2.18 (t, *J* = 6.90 Hz, 2H), 1.79-1.76 (m, 4H), 1.51-1.45 (m, 2H), 1.41-1.38 (m, 2H), 1.36 (s, 6H), 1.31-1.27 (m, 8H), 0.88 (t, *J* = 6.75 Hz, 3H).

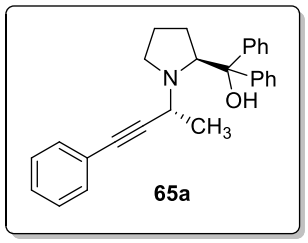
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 83.6, 81.4, 53.7, 47.9, 31.8, 29.9, 29.2, 29.1, 29.0, 28.7, 23.7, 22.6, 18.5, 14.0.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{31}N$: 250.2535; found: 250.2536.

General procedure for the synthesis of chiral propargylamines 65

In a 5 mL RB flask CuCl (0.010 g, 0.1 mmol), amine **64** (1.0 mmol), 3-pentene-2-one **55b** (1.0 mmol) and 1-alkyne **10** (1.2 mmol) were taken in 3 mL toluene at 25 ^oC under N_2 atmosphere and the contents were stirred at 100 ^oC for 12 h. Toluene was removed, water (5 mL) and DCM (10 mL) were added. The DCM layer was washed with saturated NaCl solution, dried with Na_2SO_4 and concentrated. The residue was chromatographed on silica gel (100-200 mesh) using hexane and ethylacetate (98:2) as eluent to isolate the chiral propargylamines **65.** The optical rotations of chiral propargylamine derivatives reported here for freshly prepared samples.

diphenyl((*S*)-1-((*R*)-4-phenylbut-3-yn-2-yl)pyrrolidin-2-yl)methanol



65a

Yield : 0.457 g, 60%; yellow liquid.

$[\alpha]_D^{25}$: -257.39 (*c* 0.20, $CHCl_3$).

IR (neat) : 3057, 3028, 2977, 2872, 1597, 1489, 1447, 1371, 1309, 1250, 1175, 1115, 1069, 996, 891, 754, 695 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.72-7.70 (m, 2H), 7.62-7.60 (m, 2H), 7.50-7.49 (m, 1H), 7.48-7.47 (m, 1H), 7.38-7.37 (m, 1H), 7.36-7.35 (m, 3H), 7.33-7.32 (m, 2H), 7.31-7.28 (m, 1H), 7.21-7.18 (m, 2H), 4.72 (s, 1H)

4.28-4.24 (m, 1H), 3.12-3.07 (m, 1H), 3.06-3.00 (m, 1H), 2.95 (q, *J* = 7.08 1H), 1.94-1.87 (m, 1H), 1.80-1.74 (m, 3H), 1.16 (d, *J* =7.08 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 148.6, 146.4, 131.7, 128.3, 128.1, 128.0, 127.9, 126.4, 126.2, 125.6, 125.3, 123.3, 89.0, 84.3, 77.6, 68.9, 49.2, 48.6, 29.7, 24.4, 21.4.

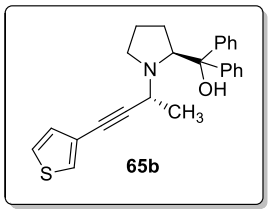
HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{27}H_{27}NO$: 382.2171; found: 382.2173

diphenyl((S)-1-((R)-4-(thiophene-3-yl) but-3-yn-2-yl)pyrrolidin-2-yl)methanol

Yield : 0.270 g, 35%; yellow liquid.

$[\alpha]_D^{25}$: -254.19 (*c* 0.30, $CHCl_3$).

IR (neat) : 3105, 3057, 3028, 2977, 2936, 2863, 1660, 1597, 1491, 1447, 1359, 1307, 1181, 1116, 1067, 1036, 996, 872, 841, 782, 747, 701, 628 cm^{-1}.



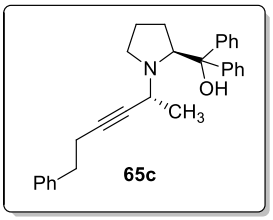
65b

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.69-7.67 (m, 2H), 7.60-7.58 (m, 2H), 7.44-7.43 (m, 1H), 7.33-7.28 (m, 5H), 7.20-7.13 (m, 3H), 4.69 (s, 1H) 4.23-4.20 (m, 1H), 3.10-3.05 (m, 1H), 3.02-2.96 (m, 1H), 2.90 (q, *J* = 7.12 Hz, 1H), 1.92-1.86 (m, 1H), 1.78-1.70 (m, 3H) 1.14-1.12 (m, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 147.9, 146.3, 130.1, 128.2, 128.1, 128.0, 126.4, 126.2, 125.6, 125.3, 125.2, 122.3, 88.6, 79.2, 77.6, 68.9, 49.3, 48.6, 29.6, 24.4, 21.4.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{25}H_{25}NOS$: 388.1735; found: 388.1736

diphenyl((*S*)-1-((*R*)-6-phenylhex-3-yn-2-yl)pyrrolidin-2-yl)methanol



Yield : 0.343 g, 42%; yellow liquid.

$[\alpha]_D^{25}$: -203.64 (*c* 0.18, $CHCl_3$).

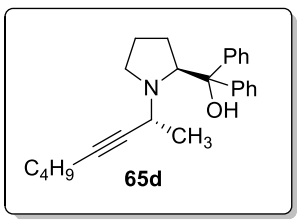
IR (neat) : 3060, 3028, 2927, 2853, 1950, 1891, 1806, 1739, 1660, 1599, 1493, 1450, 1372, 1310, 1265, 1180, 1118, 1031, 892, 864, 809, 742, 699, 668, 639 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.57-7.54 (m, 2H), 7.52-7.50 (m, 2H), 7.39-7.35 (m, 2H), 7.31-7.29 (m, 3H), 7.28-7.27 (m, 2H), 7.25-7.23 (m, 2H), 7.16-7.13 (m, 2H), 4.71 (s, 1H), 3.97-3.94 (m, 1H), 2.95-2.91 (m, 1H), 2.89 -2.85 (m, 2H), 2.80-2.74 (m, 1H), 2.65-2.61 (m, 1H), 2.59-2.56 (m, 2H), 1.63-1.58 (m, 5H), 0.99 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 148.0, 146.5, 140.7, 128.5, 128.3,128.0, 127.9, 126.3, 126.2, 126.1, 125.6, 125.2, 83.2, 80.0, 77.4, 68.4, 48.6, 48.2, 35.2, 29.5, 24.2, 21.5, 20.4.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{29}H_{31}NO$: 410.2484; found: 410.2484.

((*S*)-1-((*R*)-oct-3-yn-2-yl)pyrrolidin-2-yl)diphenylmethanol



Yield : 0.252g, 35%; yellow liquid.

$[\alpha]_D^{25}$: -152.54 (*c* 0.26, $CHCl_3$).

IR (neat) : 3059, 3028, 2957, 2929, 2856, 1598, 1492, 1449, 1373, 1310, 1171, 1117, 1037, 992, 891, 866, 746, 701, 638 cm^{-1}.

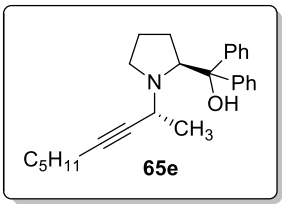
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.65-7.63 (m, 2H), 7.58-7.56 (m, 2H), 7.31-7.29 (m, 2H), 7.28-7.26 (m, 2H), 7.18-7.13 (m, 2H), 4.78 (s, 1H) 4.16-4.13 (m, 1H), 3.01-2.96 (m, 1H), 2.93-2.87(m, 1H), 2.70 -2.65 (m, 1H), 2.25-2.22 (m, 2H), 1.86-1.80 (m, 1H), 1.72-1.67 (m, 3H), 1.58-1.53(m, 2H), 1.52-1.49 (m, 2H), 1.03-1.01 (m, 3H), 1.00-0.96 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 148.0, 146.5, 128.0, 127.9, 126.2, 126.1, 125.6, 125.3, 84.1, 79.1, 77.5, 68.6, 48.7, 48.3, 31.2, 29.7, 24.3, 21.9, 21.7, 18.3, 13.6.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{25}H_{31}NO$: 362.2484; found: 362.2483.

((*S*)-1-((*R*)-non-3-yn-2-yl)pyrrolidin-2-yl)diphenylmethanol

Yield : 0.352 g, 47%; yellow liquid.



65e

[α]$_D^{25}$: -124.85 (*c* 0.32, $CHCl_3$).

IR (neat) : 3059, 3025, 2956, 2928, 2856, 1665, 1598, 1491, 1449, 1373, 1310, 1175, 1117, 1034, 889, 859, 806, 747, 701, 636 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.66-7.64 (m, 2H), 7.58-7.56 (m, 2H), 7.31-7.28 (m, 4H), 7.18-7.15 (m, 2H), 4.75 (s, 1H) 4.17-4.15 (m, 1H), 3.01-2.98 (m, 1H), 2.93-2.89 (m, 1H), 2.69 -2.67 (m, 1H), 2.25-2.22 (m,

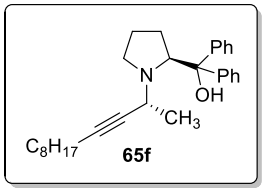
2H), 1.86-1.81 (m, 1H), 1.72-1.69 (m, 2H), 1.58-1.54 (m, 2H), 1.48-1.39 (m, 3H), 1.03-1.01 (m, 3H), 0.99-0.95 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 148.0, 146.5, 128.0, 127.9, 126.2, 126.1, 125.6, 125.3, 84.2, 79.1, 77.6, 68.6, 48.7, 48.3, 31.0, 29.7, 28.8, 24.3, 22.2, 21.6, 18.6, 14.1.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{26}H_{33}NO$: 376.2640; found: 376.2642.

((*S*)-1-((*R*)-non-3-yn-2-yl)pyrrolidin-2-yl)diphenylmethanol

Yield : 0.183 g, 22%; yellow liquid.



65f

$[\alpha]_D^{25}$: -110.17 (*c* 0.22, $CHCl_3$).

IR (neat) : 3060, 2926, 2853, 1661, 1593, 1489, 1449, 1372, 1310, 1173, 1117, 1038, 892, 864, 746, 701 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.65-7.63 (m, 2H), 7.57-7.55 (m, 2H), 7.31-7.29 (m, 2H), 7.28-7.26 (m, 2H), 7.18-7.13 (m, 2H), 4.16-4.13 (m, 1H), 3.01-2.96 (m, 1H), 2.93-2.86 (m, 1H), 2.70 -2.65 (m, 1H), 2.25-2.21 (m, 2H), 1.85-1.79 (m, 1H), 1.71-1.67 (m, 3H), 1.57-1.51 (m, 2H), 1.48-1.46 (m, 2H), 1.35-1.33 (m, 8H), 1.02 (d, *J* =7.04 Hz, 3H), 0.93-0.90 (m, 3H).

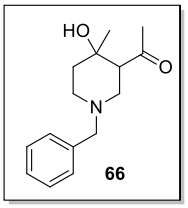
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 148.0, 146.5, 128.0, 127.9, 126.2, 126.1, 125.6, 125.3, 84.2, 79.1, 77.5, 68.6, 48.7, 48.3, 31.8, 29.7, 29.3, 29.2, 29.1, 28.8, 24.3, 22.6, 21.6, 18.6, 14.1.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{29}H_{39}NO$: 418.3110; found: 418.3110.

2.4.3 General procedure for the synthesis of 1-(1-benzyl-4-hydroxy-4-methylpiperidin-3-yl) ethanone 66

In a 10 mL RB flask CuCl (0.010 g, 0.1 mmol), benzylamine **13a** (0.1 mL, 1.0 mmol), methyl vinyl ketone **55a** (0.16 mL, 2.0 mmol) were taken in 4 mL toluene at 25 ^oC under N_2 atmosphere and contents were stirred at 100 ^oC for 3 h. Toluene was removed, water (5 mL) and DCM (15 mL) were added. The DCM layer was washed with saturated NaCl solution, dried with Na_2SO_4 and concentrated. The residue was chromatographed on silica gel (100-200 mesh) using hexane and ethylacetate (50:50) as eluent to isolate the product substituted piperidine product **66**.

1-(1-benzyl-4-hydroxy-4-methylpiperidin-3-yl)ethanone



66

Yield : 0.210 g, 85%; brown liquid.

IR (neat) : 3375, 2927, 2821, 1695, 1569, 1494, 1453, 1360, 1238, 1185, 1150, 1075, 1011, 922, 802, 738, 699, 653, 617 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$) δ 7.33 (s, 5H), 3.73-3.71 (m, 1H), 3.07-2.99 (m, 2H), 2.81-2.78 (m, 1H), 2.64-2.55 (m, 1H), 2.22 (s, 3H), 2.17-2.05 (m, 2H), 1.67-1.62 (m, 2H); 1.23 (s, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$) δ 213.5, 134.9, 129.9, 128.0, 68.0, 61.9, 55.3, 50.1, 48.2, 36.9, 31.6, 28.2.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{15}H_{21}NO_2$: 247.1572; found: 247.1577.

2.5 References

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Chapter 3

Electron Transfer Reactions of Amine Donors with Various Electron Acceptors

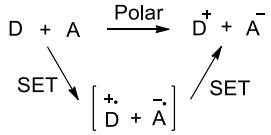
3.1 Introduction

3.1.1 Electron transfer reactions using donors and acceptors

Amine radical cations are useful synthons for applications in organic chemistry.[1-8] Generally, amine radical cations are prepared by removing an electron from the corresponding amines by electrochemical methods,[9-11] using oxidizing agents,[12-14] transition metal-catalyzed oxidation,[15-18] or UV-visible light mediated photochemistry.[7,19-23] Recently, the photolytic approach has become a major research area in organic chemistry.

Generally, organic reactions, which produce charges can take place through single electron transfer (SET) or polar mechanism. In the single electron transfer (SET) method, two sequential electron transfers take place and the polar process proceeds through a concerted mechanism (Scheme 1).

Scheme 1



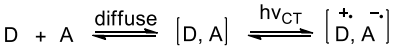
Electron transfer reactions were rationalized by R. S. Mulliken's charge transfer theory,[24] Taube's outer sphere/inner sphere mechanism[25] and Marcus two state non adiabatic theory.[26] In biological processes, reaction between molecules takes place via noncovalent Interactions, like electrostatic, charge transfer, dispersion (Vander Walls), hydrophobic interactions.

Electron transfer can take place between the two molecules i.e donor to the acceptor,

to give a charge transfer complex. Electron donor should have low ionization potential and electron acceptor should have high electron affinities for electron transfer to take place.

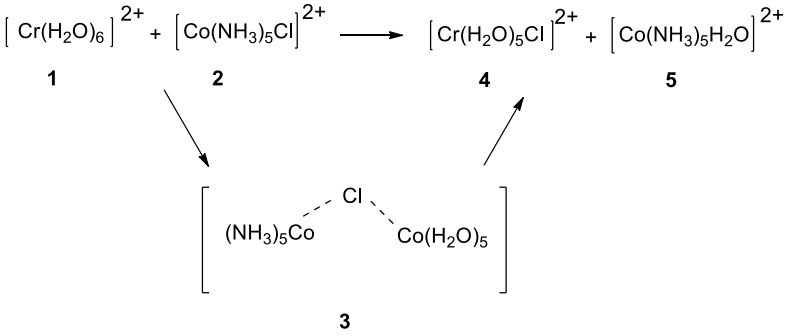
Mulliken *et al.* reported[27] that the electron donors (D) react with electron acceptors (A) in a diffusive manner to give a reversible complex [D, A] with light absoption properties different from the reactants (Scheme 2).

Scheme 2



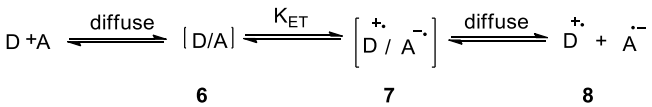
Taube *et al.*[28] reported that the reaction of Cr(II) and Co(III) complexes takes place by inner-sphere electron transfer mechanism through bridged ligands to give the green chromium complex **4** and cobalt complex **5** (Scheme 3).

Scheme 3



Marcus reported[29] that donor (D) and acceptor (A) react with each other to give the outer-sphere precursor complex (D/A) **6** followed by a successor complex ($D^{+\cdot}/A^{-\cdot}$) **7** which further gives the paramagnetic species (Scheme 4).

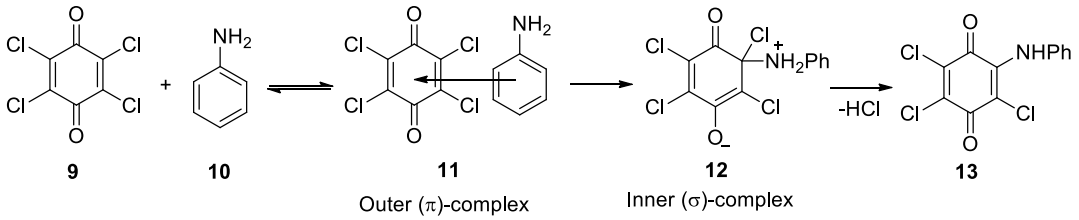
Scheme 4



3.1.2 Charge transfer and electron transfer reactions of quinones

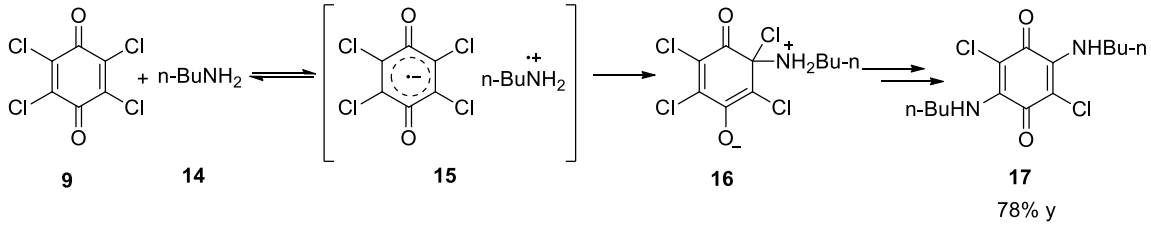
Amines are electron donors and can react with electron acceptors like quinones. For example, Nagakura and coworkers reported[30] that the aniline derivatives react with *p*-chloranil **9** to form the corresponding amino quinone product **13** via the outer (π)-complex **11** and inner (σ)-complex **12** (Scheme 5).

Scheme 5



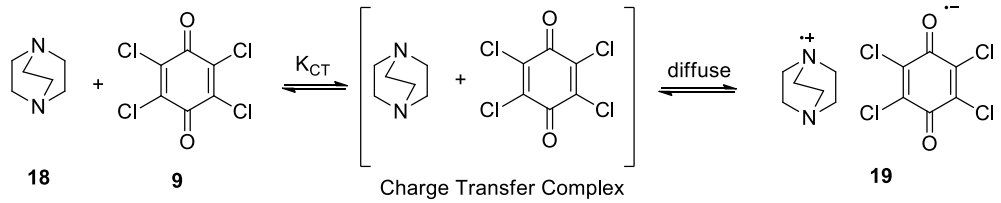
Yamaoka and Nagakura also reported that the reaction of *p*-chloranil **9** with *n*-butyl amine gave the electron transfer complex **15**, which subsequently resulted in the substitution product **17** in 78% yield (Scheme 6).[31,32]

Scheme 6



Sersen et al. observed the charge transfer complex and paramagnetic species, in the reaction between the DABCO **18** and *p*-chloranil or *p*-bromonil in benzene or THF solvent (Scheme 7).[33]

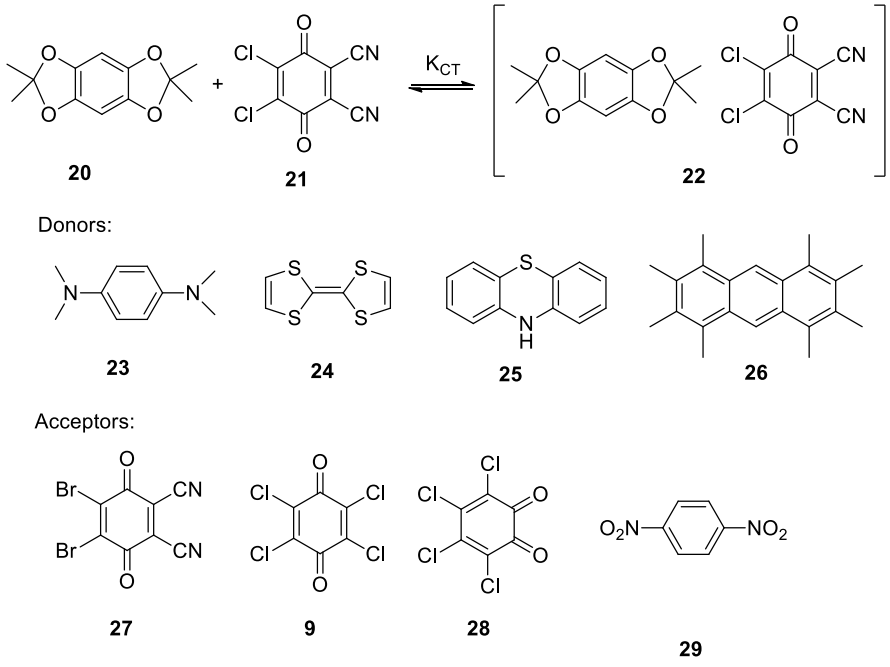
Scheme 7



18 9 19

Kochi and coworkers reported that the reaction of 2,2,6,6-tetramethylbenzo[1,2-*d*;4,5-*d'*]bis[1,3]dioxole (TMDO) **20** with 2,3-dichloro-5,6-dicynao-*p*-benzoquinone (DDQ) **21** gave bright green complex **22** in dichloromethane solvent. They have also studied the reactions of different donors with acceptors (Scheme 8).[34]

Scheme 8



20 21 22

23 24 25 26

27 9 28 29

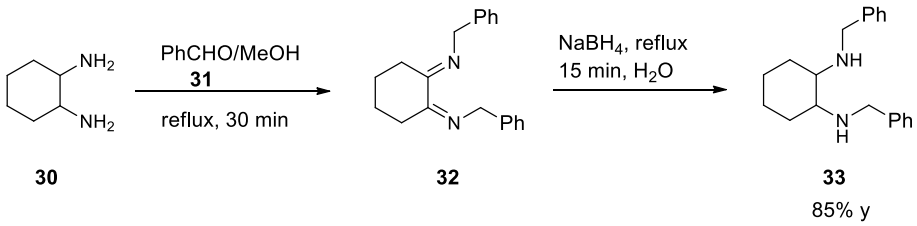
It is of interest to us to prepare amine radical cations in the ground state from the readily available amine systems containing 1,2-diamino-cyclohexane moiety using various electron acceptors like activated charcoal, viologens and dihalomethane. These results are described in the next section.

3.2 Results and Discussions

3.2.1 Synthesis of 1,2-diaminocyclohexane derivatives

We have synthesized several amine systems containing 1,2-diamino-cyclohexane moiety following reported procedures for developing electron transfer reactions using different acceptors in organic transformations.[35-39] For example, the N^1,N^2-dibenzylcyclohexane-1,2-diamine **33** was synthesized by the reaction between 1,2-diaminocyclohexane **30** and benzaldehyde **31** followed by $NaBH_4$ reduction of the intermediate imine (Scheme 9).[35]

Scheme 9

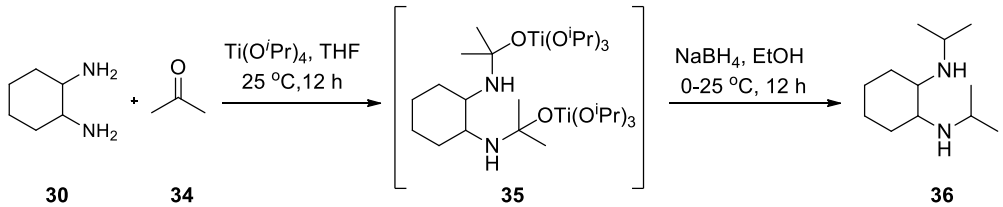


30 **32** **33**

85% y

Reductive *N*-alkylation of 1,2-diaminocyclohexane **30** with acetone **34** using the $Ti(^iOPr)_4/NaBH_4$ system following a reported method yielded the product **36** (Scheme 10).[36]

Scheme 10

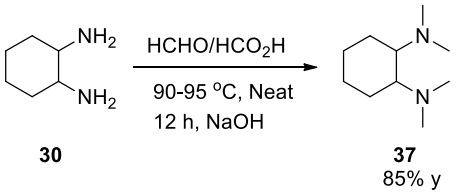


30 **34** **35** **36**

46% y

The N^1,N^1,N^2,N^2-tetramethylclohexane-1,2-diamine **37** was prepared in 85% yield by Eschweiler-Clarke methylation using cyclohexane-1,2-diamine, excess formic acid and formaldehyde *via* a reductive amination approach (Scheme 11).[37]

Scheme 11



3.2.2 Electron transfer reactions of amines with various acceptors at room temperature

3.2.3 Reactions of 1,2-diaminocyclohexane derivatives with activated charcoal.

Previously, it was observed in this laboratory that readily accessible oxygen adsorbed carbon materials (e.g. activated carbon) undergo chemisorption to give $AC^{\delta+}$-O-$O^{\delta-}$ species. The $Ph_3P{=}O$ was obtained in reactions using activated carbon, carboxylic acids and PPh_3. In addition, N-phenyltetrahydroisoquinoline undergoes cross-dehydrogenative coupling reaction with nucleophiles through amine radical cation intermediates. Also, 2-naphthoxide gave oxidative coupling to afford the bi-2-naphthol,[40] upon reaction with oxygen adsorbed activated carbon.

It is of interest to us to examine the reactions of 1,2-diaminocyclohexane derivatives **38** with oxygen adsorbed activated charcoal **39** (Scheme 12).

Scheme 12

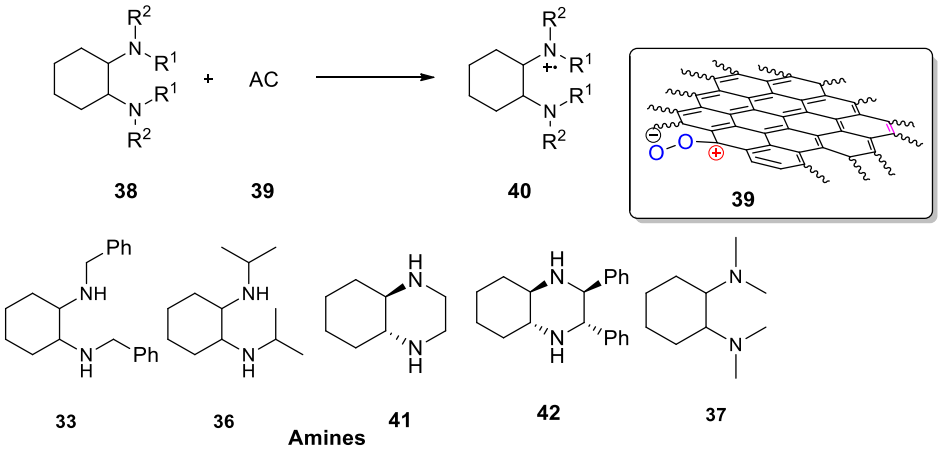
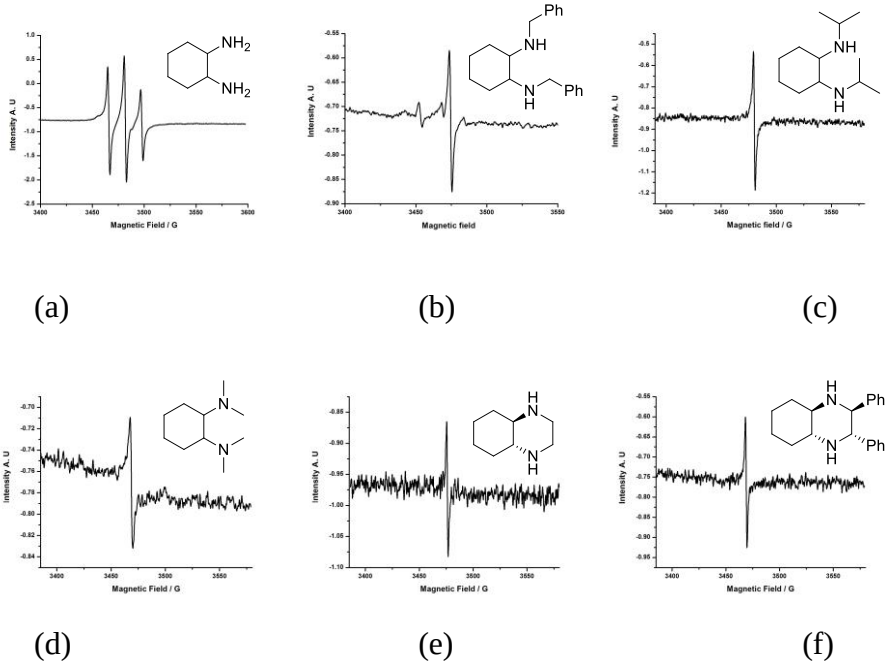


Figure 1: ESR spectra of of 1,2-diaminocyclohexane derivatives with activated charcoal **39** at 5 ms interval in DCM solvent [a]



(a) (b) (c)

(d) (e) (f)

[a]All the experiments were carried out in the ESR tube by mixing amine derivatives (0.01 mmol) with AC (20 mg) in DCM solvent.

Where as the 1,2-diaminocyclohexane and N^1,N^2-dibenzylcyclohexane-1,2-diamine gave triplet signals in esr spcectra indicating the due to the presence of amine radical cation, other derivatives gave single line in esr spectra due to delocalized carbon radical in activated carbon.

3.2.4 Reactions of 1,2-diaminocyclohexane derivatives with viologens.

Viologens are 1,1'-disubstituted-4,4'-bipyridinium salts **43** and act as electron acceptors. Viologens have been widely used as herbicides, in photosynthesis,[41] electrochromic devices,[42] organic conductive polymers,[43] electrochemical conductors,[44] photocatalytic reduction of water to hydrogen[44] and in storing solar energy.[45] Viologen derivatives are also used as indicators in biological studies. The electrochemically reversible nature and the

noticeable colour change between the oxidation states made viologens to be chosen for electrochemical display devices and also as alternative to LEDs and LCDs.[41] The viologens exist in three major oxidation states as shown in Figure 2.

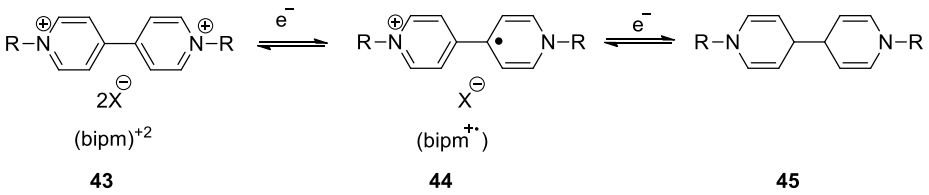


Figure 2: Three bipyridinium oxidation states.

The reductive transfer of electron to viologen derivatives form stable radical cations, due to the delocalization of π-scaffold electron of the bipyridyl moiety. In general, viologen salts are not coloured, but viologen radical cations are intensely coloured due to the charge transfer between the positive and neutral nitrogen atoms. Electron transfer and charge transfer takes place between amines and viologen derivatives with a rapid color change and hence viologens are useful for the detection of amines.[46] Hence, we became interested to investigate the electron transfer reaction between viologen acceptor and 1,2-diaminocyclohexane derivatives.

We have prepared the benzylviologen salt **48** by the reaction of 4,4'-bipyridyl **46** with benzoyl chloride **47** in DMF solvent following a reported procedure (Scheme 13).[47] We have investigated the reaction of the benzyl viologen salt **48** with various readily accessible donor amines like 1,2-diaminocyclohexane derivatives **38** to examine the electron transfer by epr spectral analysis (Figure 3). We have chosen dichloromethane as solvent for these studies.

Scheme 13

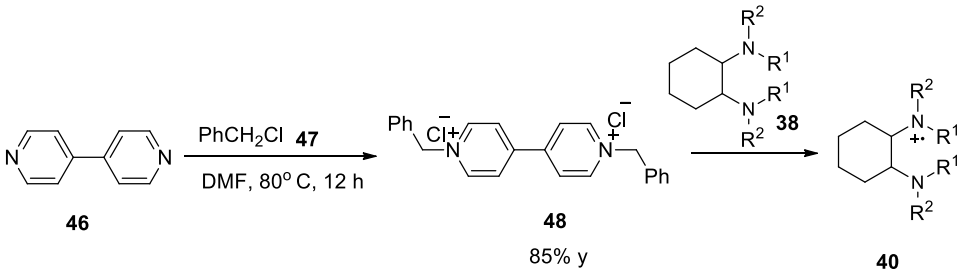
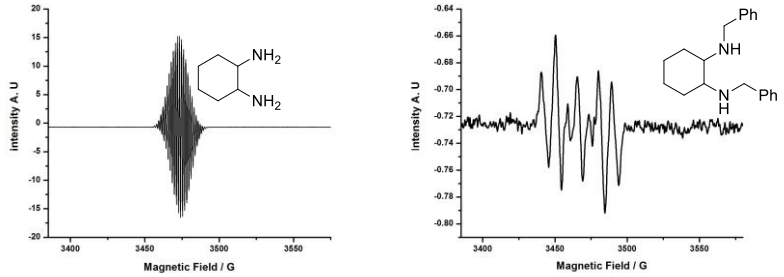
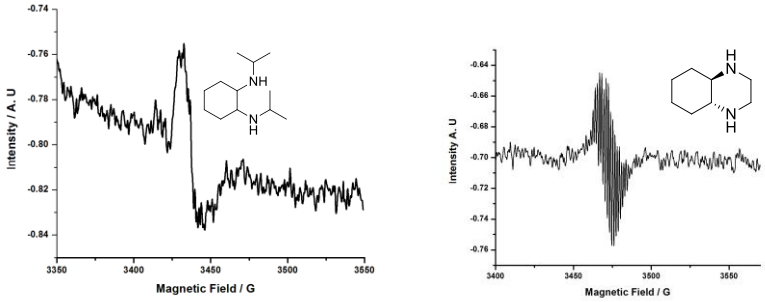


Figure 3: ESR spectra of of 1,2-diaminocyclohexane derivatives with benzyl viologen **48** at 5 ms interval in DCM solvent [a]



(a) 5 ms, DCM (b) 5 ms, DCM



(c) 5 ms, DCM (d) 5 ms, DCM

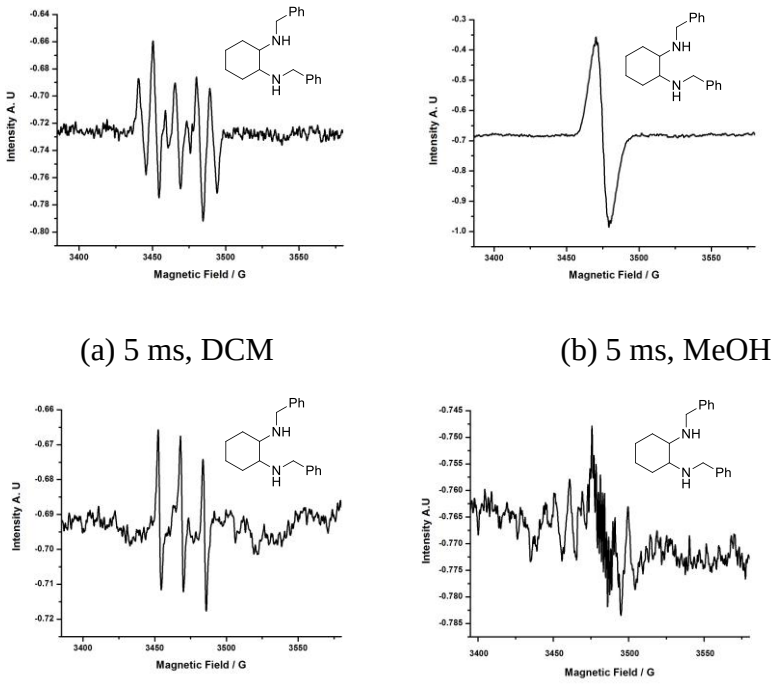
[a]All the experiments were carried out in the ESR tube by mixing amine derivatives (0.01 mmol) with benzyl violozen (0.01 mmol) in DCM solvent.

The 1,2-diaminocyclohexane **30** gave strong esr signal with hyperfine splitting with benzyl viologen. In the case of N^1,N^2-dibenzylcyclohexane-1,2-diamine **33** and N^1,N^2-diisopropyl-1,2-diaminocyclohexane **36** somewhat weaker epr signals were obtained due to

steric hindrance in the vicinity of the nitrogen atoms in the amine. Strong hyperfine splitting of the epr signal was observed when the reaction was carried out using piperizine **41** and benzyl viologen **48**. Finally, we have observed that the reaction of N^1,N^1,N^2,N^2-tetramethylcyclohexane-1,2-diamine **37** and 2,3-diphenyldecahydroquinoxaline **42** did not give epr signals with benzyl viologen, indicating that crowded tertiary amines do not react with viologens (Figure 3).

We have also recorded the epr spectra of N^1,N^2-dibenzylcyclohexane-1,2-diamine **33** with benzylviologen **48** in different solvents (Figure 4).

Figure 4: ESR spectra of of N^1,N^2-dibenzylcyclohexane-1,2-diamine **30** with benzylviologen **48** in different solvents at 5 minutes after mixing [a]



(a) 5 ms, DCM (b) 5 ms, MeOH

(c) 5 ms, DMF (d) 5 ms, PC

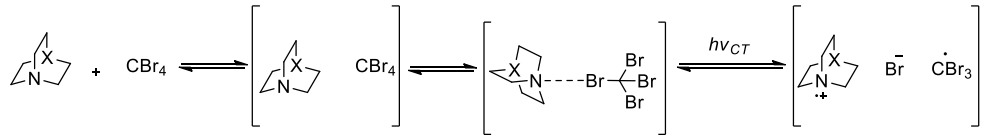
[a]All the experiments were carried out in the ESR tube by mixing amine derivatives (0.01 mmol) with BV (0.01 mmol) in different solvents.

Whereas the N^1,N^2-dibenzylcyclohexane-1,2-diamine gave broad signal with less hyperfine splitting in DCM solvent, different patterns were obtained in protic polar methanol solvent and in the dipolar aprotic solent PC. More detailed studies are required to understand this pattern.

3.2.5 Attempt towards the reactions of tertiary amines with dihalomethanes

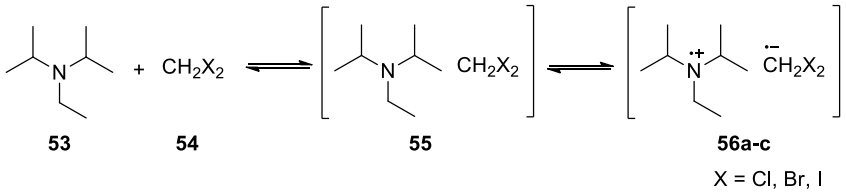
Electron donor acceptor complexes and charge transfer interactions of amines with tetrahalomethanes were also reported by Kochi *et al.*[48] For instance, DABCO **49a** and quinuclidine **49b** afforded 1:l electron-donor-acceptor (EDA) complexes with tetrahalomethanes. In crystal structures of 1:l complexes of DABCO and quinuclidine with CBr_4, N···Br (51) bonding was reported. A mechanism with initial formation of charge transfer complex followed by photochemical reaction of DABCO-CBr_4 complex was proposed (Scheme 14).

Scheme 14



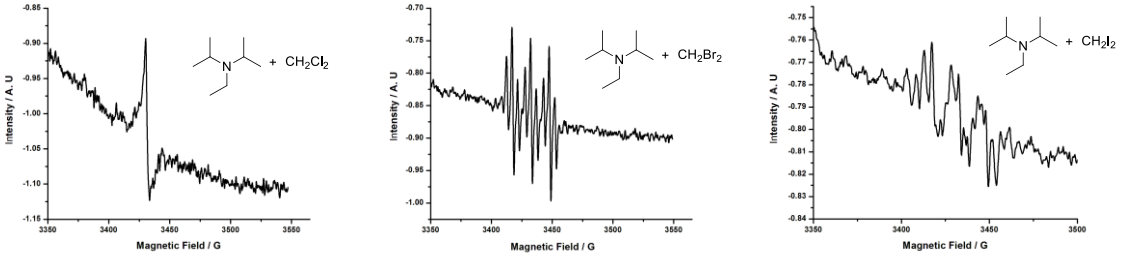
We have also briefly studied the interaction of tertiary amines with dihalomethane acceptors. We have carried out the epr spectral studies of diisopropylethylamine (DIPEA) **53** with various dihalomethane derivatives **54** under neat condition (Scheme 15).

Scheme 15



In the case of CH_2Cl_2 and CH_2Br_2, hyperfine splittings were observed and in the case of CH_2I_2 only a weak esr signal was observed (Figure 5).

Figure 5 ESR spectra of DIPEA with CH_2Cl_2, CH_2Br_2, CH_2I_2 [a]



(a) 5 ms, neat (b) 5 ms, neat c) 5 ms, neat

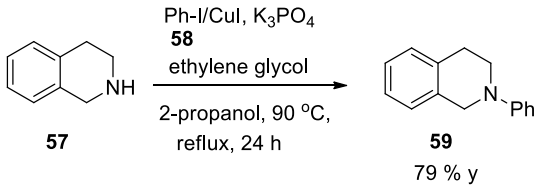
[a]All the experiments were carried out in the ESR tube by mixing DIPEA **53** with CH_2X_2 in neat condition.

The epr signals were mainly due to the corresponding amine radical cations as the radical anions $(CH_2X_2)^{\bullet-}$ may undergo fast exchange reaction with neutral CH_2X_2 species and hence may not give epr signals.

3.2.6 Reaction of *N*-phenyltetrahydroisoquinoline with dibromomethane

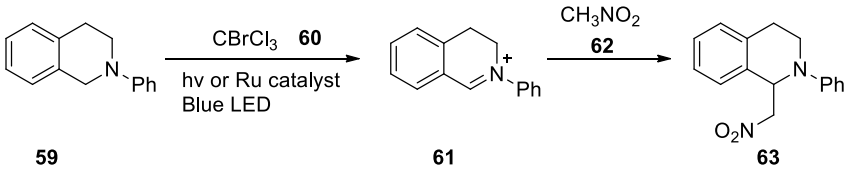
The *N*-phenyl tetrahydroisoquinoline **59** was prepared by *N*-phenylation using 1,2,3,4-tetrahydroisoquinoline **57** and iodobenzene **58** with potassium phosphate in the presence of copper (I) iodide catalyst in isopropanol solvent (Scheme 16).[49]

Scheme 16



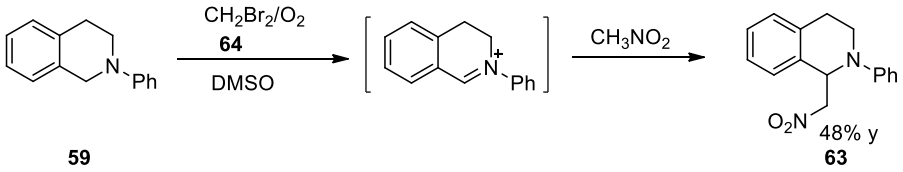
Several methods have been reported for the synthesis of aza-Henry reaction product **63** by using *N*-phenyl-tetrahydroisoquinoline **59**, CH_3NO_2 and $CBrCl_3$ as an oxidant under photolytic (or) photoredox condition (Scheme 17).[50]

Scheme 17



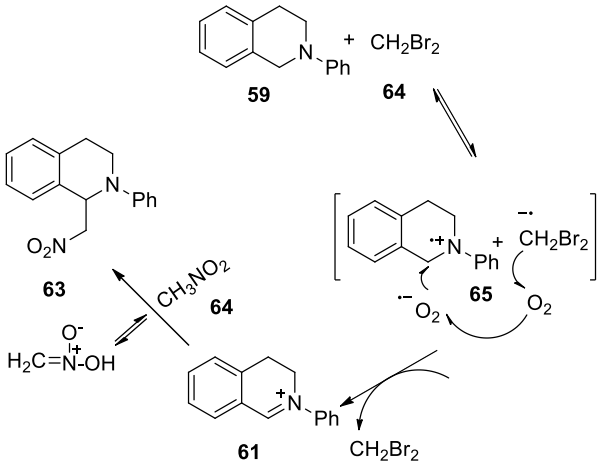
We have carried out the reaction of the 1-(nitromethyl)-2-phenyl 1,2,3,4-tetrahydroisoquinoline **63** synthesized with CH_2Br_2 in the presence of oxygen and obtained the aza-Henry reaction product **63** in 48 % yield (Scheme 18).

Scheme 18



Formation of the product **63** may be explained by the mechanism outlined in Scheme 19. Probably, *N*-phenyltetrahydroisoquinoline and CH_2Br_2 may react to give the corresponding radical cation-radical anion complex **65**, which upon reaction with oxygen could give the superoxide anion, that could extract the proton to give the iminium species **61**. Further reaction with CH_3NO_2 would give the product **63 (**Scheme 19**)**.

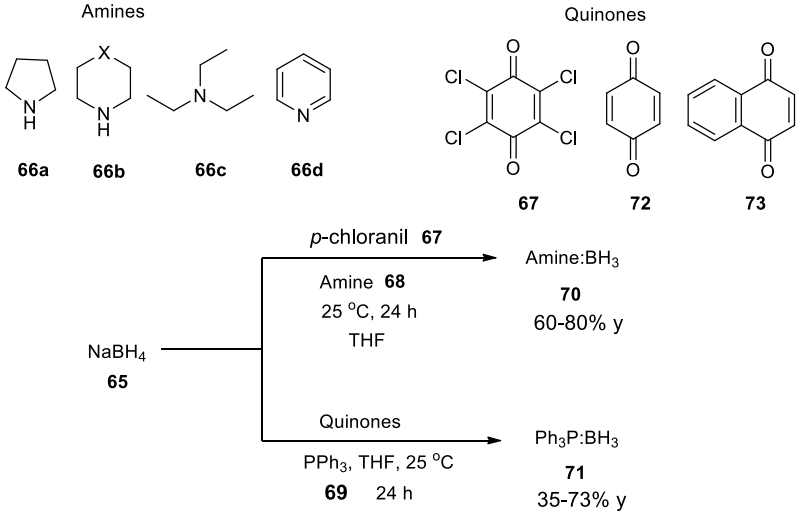
Scheme 19



3.2.7 Reactions of primary and secondary amine moieties containing 1,2-diaminocyclohexane derivatives with quinones

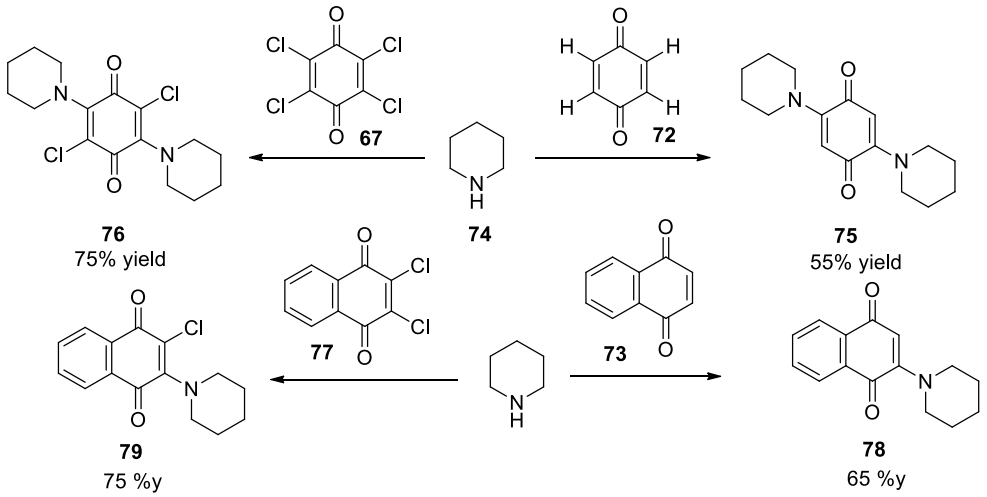
Previously, simple and convenient methods were developed in this laboratory for the generation of borane complexes of amines and PPh_3 (**70** and **71**) using $NaBH_4$/*p*-Chloranil **67** reagent system. The amine:BH_3 **70** and Ph_3:BH_3 **71** complexes were obtained in moderate to good yields (Scheme 20).[51]

Scheme 20



Also, it was reported in this laboratory that the reaction of quinones with secondary amines in DCM or PC solvent gives esr signal. The intensity of the signal decreased with time with the formation of aminoquinone products **75**, **76, 78** and **79** were observed (Chart 1).[51]

Chart 1



We have also studied the electron transfer reactions of donor primary and secondary amine moieties containing 1,2-diaminocyclohexane derivatives with the quinones **67**, **72** and **73** (Figure 6). The reactions were monitored by epr spectroscopic method. We have observed that mixing of the amine derivatives with quinones in DCM solvent led to the formation of paramagnetic intermediates, as detected by epr signals (Table 1).

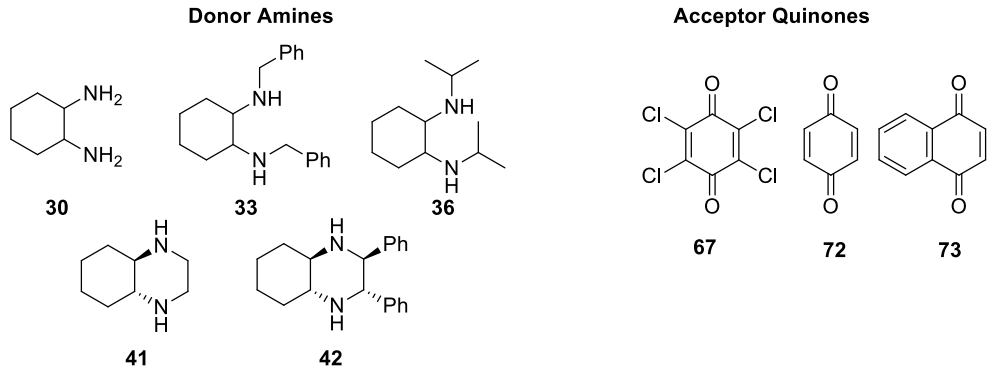
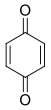
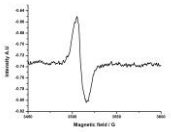
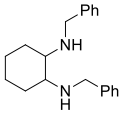
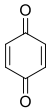
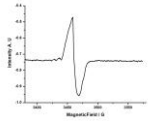
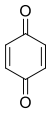
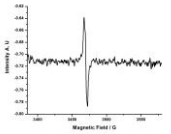
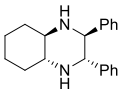
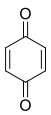
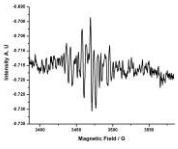


Figure 6 Donor amines and Acceptor quinones

Mixing of the 1,2-diaminocyclohexane **30** with benzoquinone **72** in DCM solvent gives the paramagnetic intermediates as detected by epr spectroscopy with g value 2.00605 (entry 1, Table 1). Similarly, N^1,N^2-dibenzylcyclohexane-1,2-diamine **33** and chiral decahydroquinoxaline **41** also gave epr signals with benzoquinone. In the case of chiral 2,3-diphenylquinoxaline **42**, the strength of the signal was very weak as the steric crowding in the amine would make it difficult to react with benzoquinone. Hence, the compound **42** gave weak esr signal with low intensity (entry 4, Table 1).

Table 1 EPR spectra of 1,2-diaminocyclohexane derivatives with benzoquinone at 5 ms interval in DCM solvent [a]

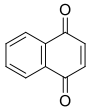
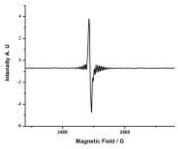
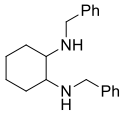
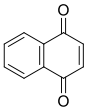
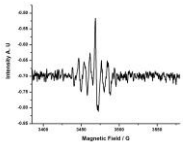
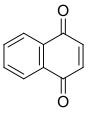
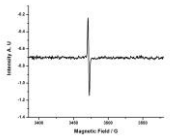
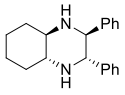
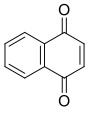
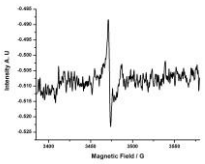
Entry	Donor	Acceptor	Solvent	Time (min)	ESR spectra
1			DCM	5	
2			DCM	5	
3			DCM	5	
4			DCM	5	

[a]All the experiments were carried out in the ESR tube by mixing amine derivatives (0.01 mmol) with benzoquinone (0.01 mmol) in DCM solvent.

We have also performed the reactions of naphthaquinone **73** with various 1,2- diamino

aminocyclohexane derivatives in DCM solvent and recorded the epr spectra 5 minutes after mixing. The 1,2-diaminocyclohexane **30** gave a strong esr signal with hyperfine fine splitting. The N^1,N^2-dibenzylcyclohexane-1,2-diamine **33** gave weak signal with hyperfine splitting because of more steric hindrance in the vicinity of the nitrogen atom in the amine. The reaction of chiral decahydroquinoxaline **41** and 2,3-diphenylquinoxaline **42** with naphthaquinone gave relatively weak esr signal with g value 2.00585 and 2.00598. Again, this may be due to weaker interactions between the donor amines with acceptor naphthaquinone (Table 2).

Table 2 ESR spectra of of 1,2-diaminocyclohexane derivatives with naphthaquinone at 5 ms interval in DCM solvent [a]

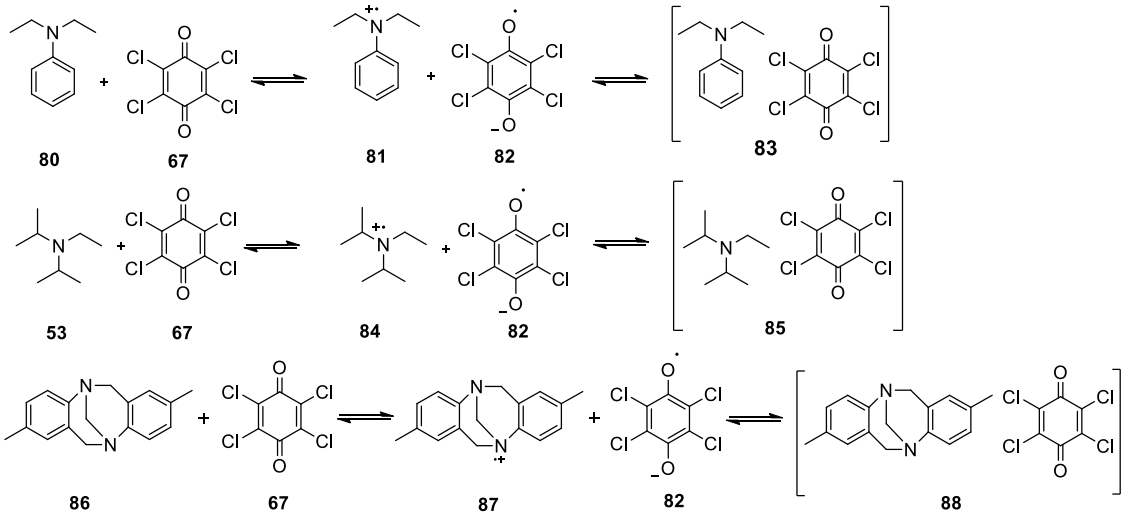
Entry	Donor	Acceptor	Solvent	Time (min)	ESR spectra
1			DCM	5	
2			DCM	5	
3			DCM	5	
4			DCM	5	

[a]All the experiments were carried out in the ESR tube by mixing amine derivatives (0.01 mmol) with naphthaquinone (0.01 mmol) in DCM solvent

3.2.8 Reactions of tertiary amine containing 1,2-diaminocyclohexane moiety with quinones

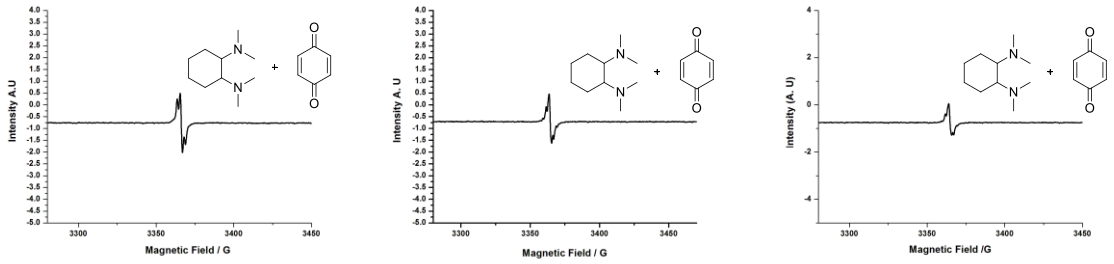
Previously, it was observed in this laboratory that the reaction of tertiary amines with *p*-chloranil initially gave strong esr signals, which became weak with time. (Chart 2).[52]

Chart 2



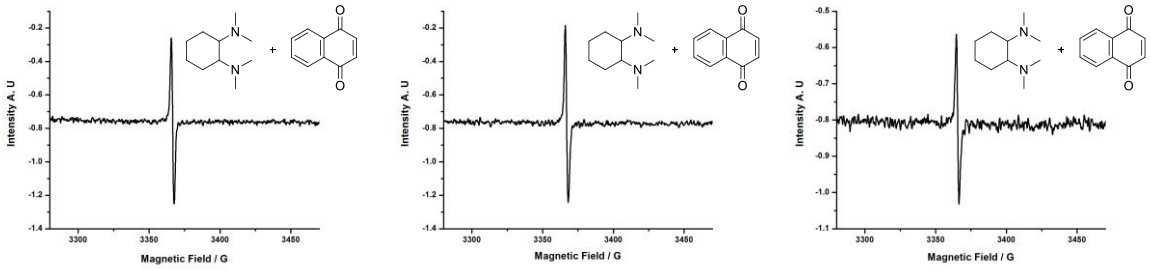
It was of interest to us to examine whether the nitrogen of N^1,N^1,N^2,N^2-tetramethyl moiety **37** of the 1,2-diaminocyclohexane undergoes electron transfer reaction with quinones. We have recorded the esr spectra of of N^1,N^1,N^2,N^2-tetramethylclohexane-1,2-diamine **37** with different quinones in 1:1 ratio in PC solvent.

Figure 7 ESR spectra of N^1,N^1,N^2,N^2-tetramethylclohexane-1,2-diamine **37** with quinones in PC solvent.[a]

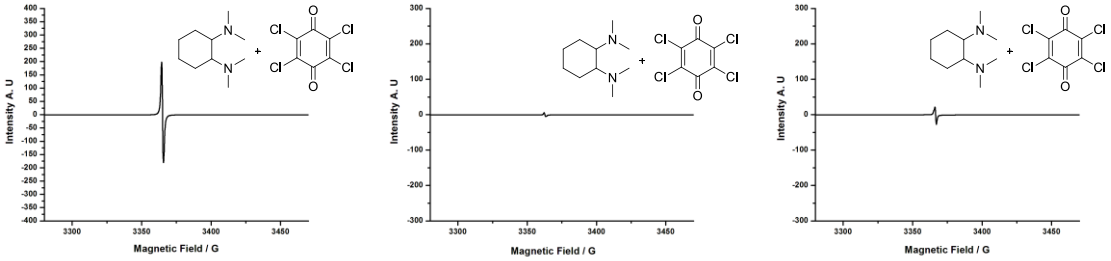


(a) 5 ms (b) 12 h (c) 24 h

Figure 7 (continued)



(a) 5 ms (b) 7 h (c) 24 h

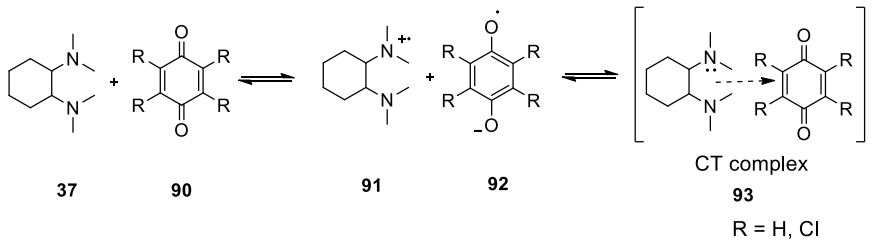


(a) 5 ms (b) 12 h (c) 24 h

[a]All the experiments were carried out in the ESR tube by mixing amine derivatives (0.01 mmol) with naphthaquinone (0.01 mmol) in PC solvent at 5 ms interval.

In the case of N^1,N^1,N^2,N^2-tetramethylclohexane-1,2-diamine and *p*-benzoquinone, only weak epr signal was observed and the strength of the epr signal decreased with time. The N^1,N^1,N^2,N^2-tetramethylclohexane-1,2-diamine also reacted with1,4-naphthaquinone to give only very weak signal but the strength did not change with time. Interestingly, the N^1,N^1,N^2,N^2-tetramethylclohexane-1,2-diamine initially gave a very strong epr signal with *p*-chloranil but the strength decreased with time. Presumably, the *p*-chloranil with very high electron affinity (EA = 2.78eV) reacts fast with the diamine to give the radical ions, which recombine to give the corresponding charge transfer complex (Scheme 21).

Scheme 21



We have also attempted to get crystals of the charge transfer complex from PC, CH_2Cl_2, N-methyl-2-pyrrolidone (NMP) and dimethylformamide (DMF) solvents for x-ray analysis, but these efforts were not successful.

It should be pointed out that the epr signals observed here are only for the *p*-chloranil radical anion as there will be fast intramolecular exchange of electron with the neutral amine site in the molecule. We have then examined the reaction of propargylamines with *p*-chloranil. The results are described in the next chapter.

3.3 Conclusions

Simple and convenient methods were developed to generate paramagnetic species by using donor amines and various acceptors at room temperature. The 1-(nitromethyl)-2-phenyl 1,2,3,4-tetrahydroisoquinoline was obtained in the reaction of *N*-phenyltetrahydroisoquinoline, CH_3NO_2 and dibromomethane in the presence of oxygen. The results described are expected to be useful for further exploitation in organic chemistry.

3.4 Experimental Section

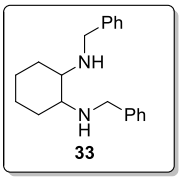
3.4.1 General information

IR (neat) spectra were recorded on JASCO FT-IR spectrophotometer model-5300. ^{1}H (400 MHz), ^{13}C (100 MHz) NMR spectra were recorded on Bruker-Avance-400 spectrometers chloroform-d as solvent. Chemical shifts were determined with tetramethylsilane (TMS) as internal reference (δ = 0 ppm). Coupling constants *J* are in Hz. High-resolution mass spectra (HRMS) were recorded on micromass ESI-TOF. ESR spectra were recorded on Bruker-X band

All the glasswares were pre-dried at 100-120 °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 reagent were carried out using standard syringe-septum technique recommended for handling air sensitive reagents and organometallic compounds.

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

3.4.2 General procedure for the synthesis of N^1,N^2-dibenzylcyclohexane-1,2-diamine 33



33

To a stirred suspension of 1,2-diaminocyclohexane (0.60 mL, 5 mmol) in 10 mL MeOH, benzaldehyde (1.1 mL, 10 mmol) was added slowly over aperiod of 2 min under N_2 atmosphere at 25 ^{o}C and refluxed for 3 h. The reaction mixture was allowed to room temparature and $NaBH_4$ (0.37 g, 10 mmol) was added portion wise at 0 ^{o}C and refluxed for 1 h. The reaction was then quenched by the water (10

mL) and the aqueous phase extracted with DCM (3 x 10 mL). The organic layer was separated, concerted, dried over anhydrous Na_2SO_4 and purified on silica gel (100-200 mesh) using hexane/EtoAc (90:10) as eluent to obtain the desire product.

Yield **:** 1.10 g, 85%; colorless liquid.

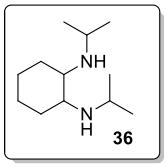
IR (neat) **:** 3450, 2890, 2860, 1630, 1465, 1435, 1360, 1234, 1102, 1091, 972 cm^{-1}.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.37-7.34 (m, 8H), 7.30-7.27 (m, 2H), 3.81-3.76 (m, 2H), 3.70-3.63 (m, 2H), 2.80 (s, br, 4H), 1.18-1.72 (m, 4H), 1.38 (s, br, 4H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 141.3, 128.3, 128.2, 126.7, 55.8, 51.2, 27.9, 22.4.

3.4.3 General procedure for the synthesis of *N*^{1},*N*^{2}-diisopropylcyclohexane-1,2-diamine 36

To a stirred suspension of 1,2-diaminocyclohexane (0.60 mL, 5 mmol) in 10 ml THF, acetone (0.45 mL, 10 mmol), Ti(O^{i}Pr)$_4$ (6 mL, 20 mmol) were added under N_2 atmosphere at 25 ^{o}C and stirred for 12 h. To this, absolute EtOH (20 mL) and $NaBH_4$ (0.76 g, 20 mmol) were added under N_2 atmosphere at 0 ^{o}C and stirred for 12 h at room temperature. The reaction mixture was quenched with water (5 mL) and the solvent was evaporated. To this resulting inorganic precipitate, ether (20 mL) and water (10 mL) were added. The combined oganic layer was washed with brine (20 mL), dried over anhydrous Na_2SO_4, filtered and concerted. The crude product was isolated on silica gel (100-200 mesh) using hexane/EtoAc (50:50) as elutent to obtain the desire product.



36

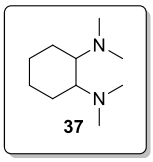
Yield **:** 0.490 g, 50%; colorless liquid.

IR (neat) **:** 3459, 2866, 2862, 1642, 1590, 1485, 1444, 1380, 1392, 1264, 1152, 1065, 960 cm^{-1}.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 2.87-2.83 (m, 2H), 2.12-2.02 (m, 4H), 1.67-1.65 (m, 2H), 1.40-1.16 (m, 6H), 1.03-0.95 (m, 12H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 59.0, 45.4, 32.5, 25.1, 24.8, 22.6.

3.4.4 General procedure for the synthesis of *N*^{1},*N*^{1},*N*^{2},*N*^{2}-tetramethylcyclohexane-1,2-di amine 37



37

To a stirred suspension of 1,2-diaminocyclohexane (5 mmol, 0.60 mL), formaldehyde (37% solution, 5.4 mL, 30 mmol) and formic acid (3 mL, 30 mmol) were slowly added at 25 ^{o}C under N_2 atmosphere in neat condition. The contents were refluxed for 12 h. The solvent was removed under reduced pressure and 20 mL DCM was added to residue at 0 ^{o}C. The NaOH solution (3N, 20 mL) was added to the mixture untill it becomes slightly basic. The organic layer washed with water (2 x 10 mL), brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The crude residue was purified by column chromatography on basic alumina using hexane/EthylAcetate (95:5) as eluent to obtain the desire product. [12]

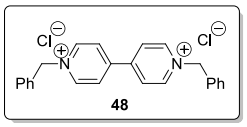
Yield **:** 0.85 g, 89%; colorless liquid.

IR (neat) **:** 3383, 2933, 2861, 1648, 1593, 1455, 1393, 1268, 1065, 960, 606 cm^{-1}.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 1.54-1.49 (m, 6H), 1.49-1.48 (m, 6H), 1.45-1.39 (m, 2H), 1.05 (s, br, 2H), 0.88-0.86 (m, 2H), 0.70-0.68 (m, 2H), 0.53-0.49 (m, 2H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 64.6, 43.5, 25.9, 22.4.

3.4.5 General Procedure for the preparation of viologen salt 48



48

4,4'-Bipyridyl **5** (5 mmol) was dissolved in DMF (50 mL) solvent and benzyl chloride (12 mmol) was slowly added (5 min). The contents were heated at 80 ^{0}C for 24 h. Then, the reaction mixture was cooled to room temperature and the resulting yellowish solid was filtered out and poured into dehydrated diethyl ether for washing. The powdered product was collected and dried. After washing twice with diethyl ether, the resulting viologen salt was dried in vacuum at room temperature.

Yield **:** 0.220 g, 86%; colorless solid.

IR (KBr) **:** 3101, 2958, 1627, 1506, 1172, 832 cm^{-1}.

^{1}H NMR **:** (400 MHz, D_2O, δ ppm) 9.07-9.05 (d, 4H), 8.49-8.47 (d, 4H), 7.46-7.44 (m, 4H), 7.32-7.22 (m, 6H), 3.56 (s, 4H).

^{13}C NMR **:** (100 MHz, D_2O δ ppm) δ: 150.0, 144.2, 131.7, 128.0, 128.1, 125.4, 122.9, 62.0.

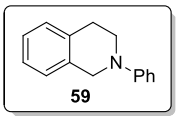
3.4.6 General procedure for the synthesis of *N*-phenyl-1,2,3,4-tetrahydroisoquinoline 59

To a solution of 1,2,3,4-tetrahydroisoquinoxaline (1.26 g, 10 mmol) in 2-PrOH (10 ml), iodobenzene (1.12 ml, 10 mmol), potassium phosphate (4.43 g, 20 mmol), copper(I)iodide (0.19 g, 10 mmol), ethylene glycol (1 mL) were added to this and stirred for 24 h at 90 ^{o}C. After the reaction mixture allowed to cool to room temperature, diethyl ether (10 mL) and water (5 mL) were added to the reaction mixture. The combined organic phases were washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure and purified on silica (100-200 mesh) using hexane/EtoAc (98:2) as eluent to obtain *N*-phenyl-1,2,3,4- tetrahydroisoquinoline.

2-Phenyl-1,2,3,4-tetrahydroisoquinoline

Yield **:** 0.347 g, 83%; colorless liquid.

IR (KBr) **:** 3370, 3059, 3024, 2921, 2815, 1662, 1598, 1500, 1459, 1387, 1337, 1293, 1221, 1153, 1112, 1033, 991, 932, 750, 691 cm^{-1}.



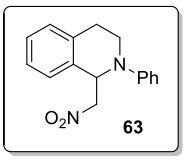
59

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.35-7.31 (m, 2H), 7.23-7.18 (m, 4H), 7.04-7.01 (m, 2H), 6.89-6.85 (m, 1H), 4.45 (s, 2H), 3.62-3.59. (t, 2H), 3.04-3.01(t, 2H).

^{13}C NMR **:** (100MHz, $CDCl_3$, δ ppm) 150.5, 134.8, 134.4, 129.1, 128.4, 126.4, 126.2, 125.9, 118.6, 115.1, 50.6, 46.4, 29.0.

3.4.7 General Procedure for the synthesis of 1-(nitromethyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline 63

To a solution of N-phenyl tetrahydroisoquinoline (0.10 g, 0.5 mmol) in DMSO (10 ml), dibromomethane (0.4 mL) and nitromethane (0.4 mL) were added to this and stirred for 48 h in the presence of oxygen. Afterwards, ethylacetate (10 mL), water (5 mL) were then added to the reaction mixture. The organic layer was washed with brine and dried over Na_2SO_4. The solvent was removed under vacuum and purified on silica (100-200 mesh) using ethyl acetate and hexane (96:4) as eluent to obtain desired product.



63

1-(Nitromethyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline

Yield **:** 0.129 g, 48%; colorless liquid.

IR (Neat) **:** 3023, 2956, 2917, 2848, 1657, 1597, 1550, 1500, 1425, 1378, 1326, 1260, 1218, 1113, 1030, 799, 751, 693 cm^{-1}.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.32-7.28 (m, 3H), 7.26-7.22 (m, 2H), 7.17-7.15 (m, 1H), 7.02-7.00 (m, 2H), 6.89-6.86 (m, 1H), 5.59-5.56 (t, 1H), 4.92-4.87 (m, 1H), 4.61-4.56 (m, 1H), 3.72-3.61 (m, 2H), 3.15-3.08 (m, 1H), 2.85-2.79 (m, 1H).

^{13}C NMR **:** (100MHz, $CDCl_3$, δ ppm) 148.4, 135.2, 132.9, 129.2, 128.1, 127.0, 126.7, 119.4, 115.1, 78.8, 58.2, 42.0, 26.4.

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Chapter 4

Electron Transfer Reactions using Propargylamines and *p*-Chloranil

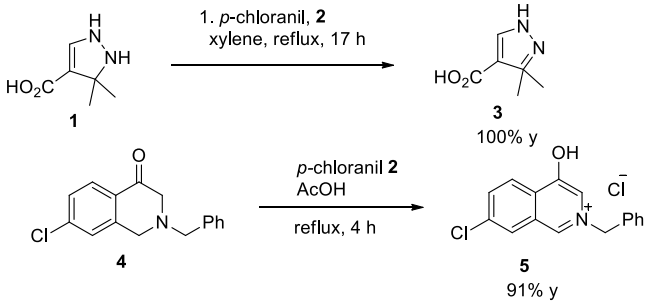
4.1 Introduction

4.1.1 Dehydrogenation reactions using *p*-chloranil

p-Chloranil is a tetrachloro-1,4-benzoquinone planar molecule widely used as a mild oxidant as well as hydrogen acceptor.[1] For example, *p*-chloranil is useful for aromatization reactions, like conversion of cyclohexadienes to benzene derivatives.[2] Secondary amines react with *p*-chloranil to give the charge transfer complexes leading to the formation of amino quinone products by electron transfer mechanism.[3]

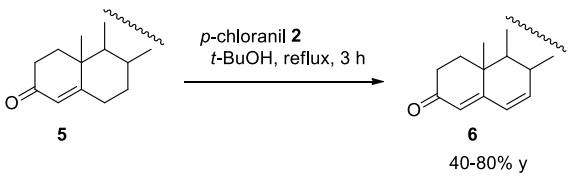
Oxidation of *gem*-dialkylpyrazolidines **1** using *p*-chloranil **2** was reported to give pyrazoles **3**.[4,5] *p*-Chloranil was also used in the synthesis of quinolinium and isoquinolinium salts **5** from the corresponding *N*-substituted dihydroquinolines and isoquinolines **4** via dehydrogenation (Chart 1). [6-7]

Chart 1



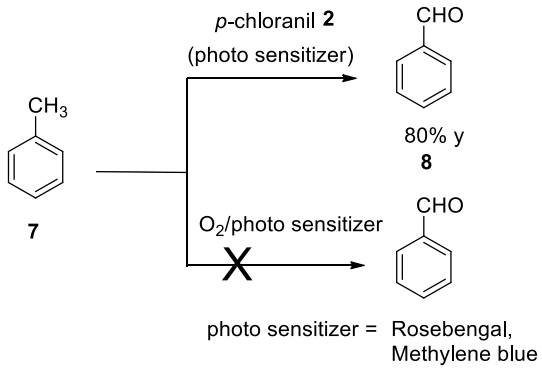
The formation of 4,6-dien-3-ones **6** from the corresponding 4-en-3-one **5** using *p*-chloranil **2** was reported (Scheme 1).[8-11]

Scheme 1



In addition to dehydrogenation, quinones with high E_0 values are useful in various oxidation reactions.[12] For instance, *p*-chloranil is a valuable photosensitizer for the oxidation of toluenes to benzaldehydes, where other usual photosensitizers failed (Scheme 2).[13]

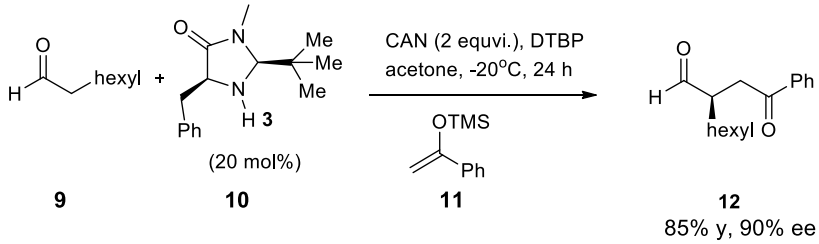
Scheme 2



4.1.2 Synthetic methods based on electron transfer reactions using CAN and under photo catalytic processes

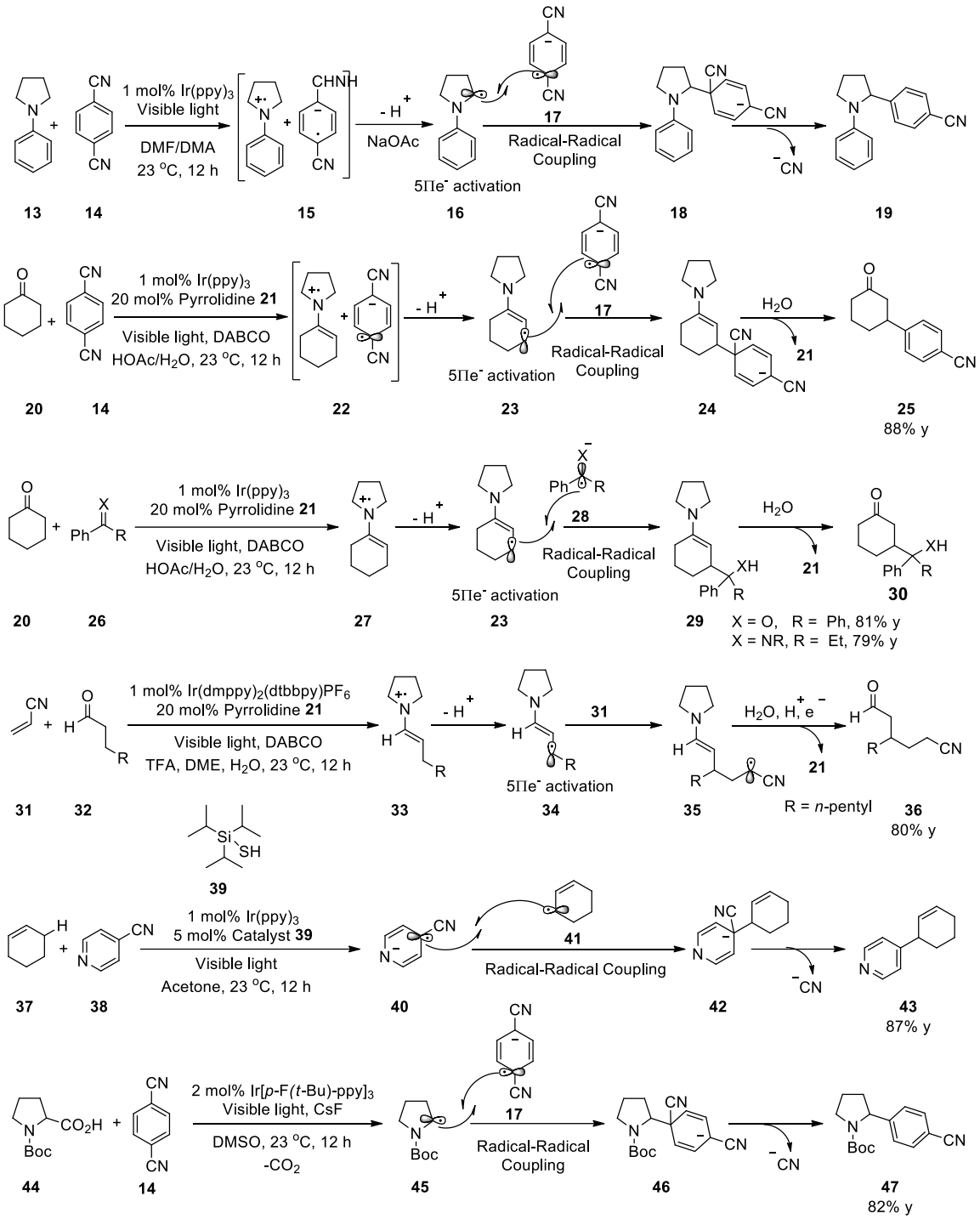
Recently, enantioselective α-enolation of aldehydes using oxidizing agent like ceric ammonium nitrate (CAN) was reported (Scheme 3).[14]

Scheme 3



There have been several synthetic methods reported using tertiary amines under photolytic conditions to produce α-amino alkyl radicals that can be added to various double bonds and nuceophiles (Chart 2).[15]

Chart 2


1 mol% Ir(ppy)3
Visible light
DMF/DMA
23 °C, 12 h
- H+
NaOAc
17
Radical-Radical Coupling
5Πe- activation
13 14 15 16 18 19
1 mol% Ir(ppy)3
20 mol% Pyrrolidine 21
Visible light, DABCO
HOAc/H2O, 23 °C, 12 h
H2O
21
20 14 22 23 24 25
88% y
1 mol% Ir(ppy)3
20 mol% Pyrrolidine 21
Visible light, DABCO
HOAc/H2O, 23 °C, 12 h
28
20 26 27 23 29
X = O, R = Ph, 81% y
X = NR, R = Et, 79% y
30
1 mol% Ir(dmppy)2(dtbbpy)PF6
20 mol% Pyrrolidine 21
Visible light, DABCO
TFA, DME, H2O, 23 °C, 12 h
31
H2O, H, e
31 32 33 34 35 36
R = n-pentyl
80% y
39
1 mol% Ir(ppy)3
5 mol% Catalyst 39
Visible light
Acetone, 23 °C, 12 h
41
Radical-Radical Coupling
37 38 40 42 43
87% y
2 mol% Ir[p-F(t-Bu)-ppy]3
Visible light, CsF
DMSO, 23 °C, 12 h
-CO2
44 14 45 46 47
82% y

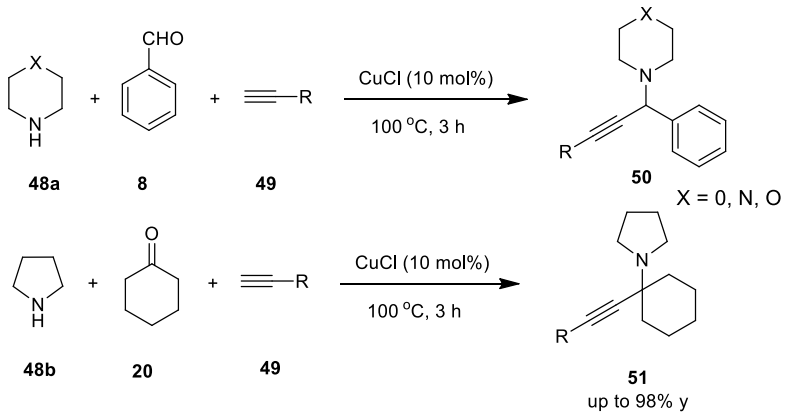
In the previous chapter, we have described that N^1,N^1,N^2,N^2-tetramethylclohexane-1,2-diamine reacts with *p*-chloranil at room temperature to give paramagnetic radical ion intermediates. We have undertaken efforts to explore the utility of the donor propargylamines with acceptor *p*-chloranil for the development of new synthetic methods. The results are discussed in the next section.

4.2 Results and Discussion

4.2.1 Synthesis of propargylamines

Propargylamine derivatives (**50, 51)** have been prepared via A^3 (or) KA^2 coupling reactions using amine, aldehyde (or) ketone, 1-alkynes following a reported procedure (Chart 3).[16]

Chart 3



4.2.2 Electron transfer reactions of propargylamines (tertiary amines) with *p*-chloranil

Over the years, several methods have been developed for the synthesis of heterocyclic compounds from the corresponding propargylamines.[17] Recently, convenient methods to access chiral propargylamines and chiral allenes have been developed from this laboratory.[18,19] We have briefly examined the electron transfer reactions using donor propargylamines[16a] (**50** and **51**) with acceptor *p*-chloranil **2** (Figure. 1). The results are discussed here.

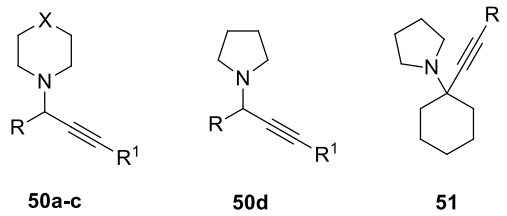
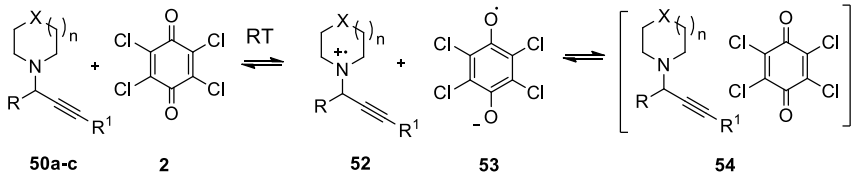


Figure 1

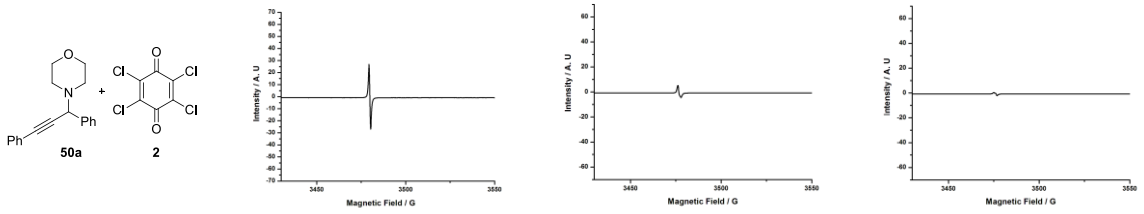
We have observed that addition of propargylamines (**50**-**51**) to *p*-chloranil **2** in propylene carbonate (PC) solvent gives paramagnetic intermediates as detected by epr spectroscopy (Scheme 4).

Scheme 4



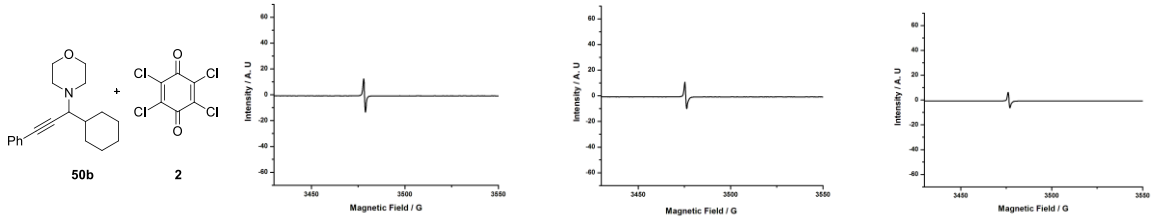
n = 0, 1 X = O, *N*-Ph
R = Ph
R^1 = Ph, *c*-hexyl

The signals were due to the chloranil radical anion and the amine radical cations did not give signal due to fast exchange with neutral amine. The strength of the signal was strong initially, but decreased with the time (Figure 2-4).



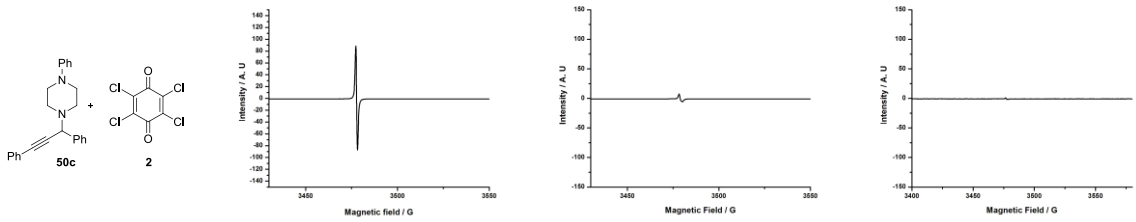
(a) PC, 5 m **(b)** PC, 12 h **(C)** PC, 24 h

Figure 2



(a) PC, 5 m **(b)** PC, 12 h **(C)** PC, 24 h

Figure 3

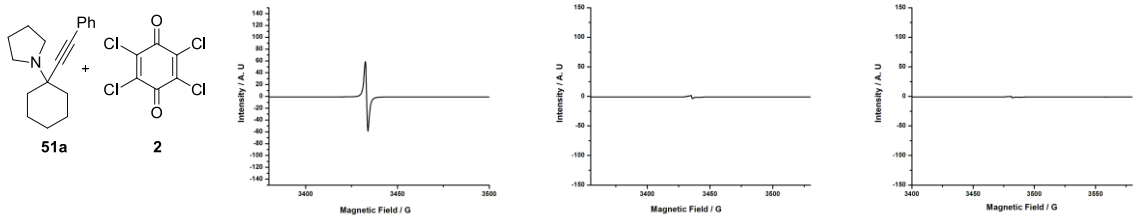


(a) PC, 5 m **(b**) PC, 12 h **(C)** PC, 24 h

Figure 4

All the experiments were carried out in the ESR tube by mixing amine derivatives (0.01 mmol) with *p*-chloranil (0.01 mmol) in PC solvent at 5 ms interval.

When the propargylamine derivative **51a** was reacted with *p*-chloranil in dichloromethane solvent epr signal was observed due to the formation of paramagnetic intermediates. Here also, the mixture gave strong epr signal initially and the strength of intensity decreased with time (Figure 5).



(a) DCM, 5 m (b) DCM, 12 h (c) DCM, 24 h

Figure 5

We have carried out the reaction of propargylamine derivative **51a** with *p*-chloranil in various solvents at diffferent temperatures. The results are summarised in Table 1. We have observed that the reaction gave the corresponding substituted pyrrole product **55a** in 62% yield at 70 ^{o}C in toluene solvent (entry 9, Table 1).

Scheme 5 Synthesis of substituted *N*-propargyl pyrrole **55a** using *N*-propargyl pyrrolidine **51a** and *p*-chloranil

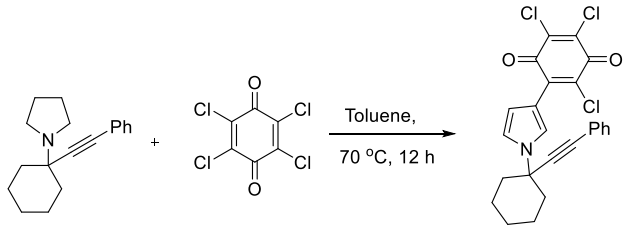


Table 1. Optimized conditions for the synthesis of substituted pyrrole **55a**[a,b]

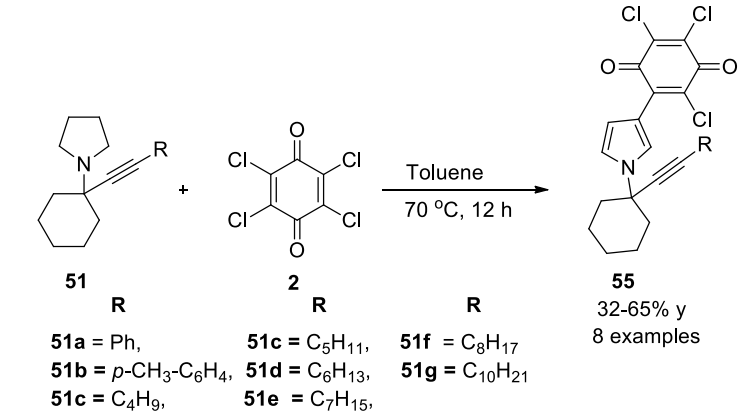
entry	solvent	chloranil (equiv.)	temp (°C)	time (h)	yield (%) [b]
1	DCM	1	25	48	10
2	MeOH	1	25	48	-
3	DMF	1	25	48	-
4	CH_3CN	1	25	48	-
5	Toluene	1	25	12	-
6	Toluene	1	60	12	25
7	Toluene	1.5	70	12	33
8	Toluene	2.0	70	12	46
9	Toluene	3.0	70	12	62

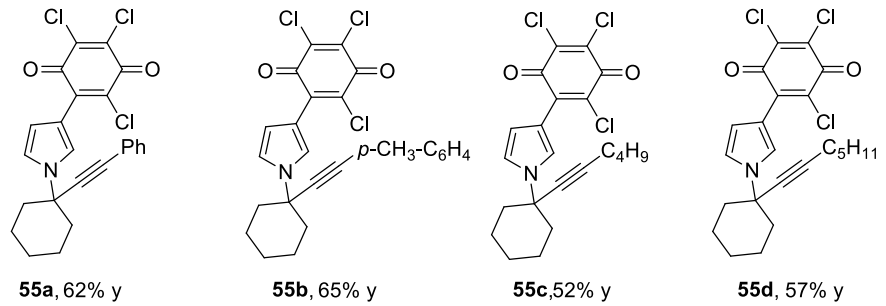
[a] The reactions were carried out by propargylamine **51a (**1.0 mmol) and *p*-chloranil **2** (3.0 mmol) in toluene (4 mL) at 70 °C for 12 h. [b] Isolated yield.

With the optimized conditions (entry 9, Table 1), various propargylamine derivatives **51** were converted to the corresponding pyrrole derivatives **55** (Table 2). For example, the propargylamine containing phenyl group **51a** gives the corresponding pyrrole derivative **55a** in 62% yield and the para methyl phenyl containing propargylamine **51b** gave the

corresponding substituted pyrrole **55b** in 65% yield. The propargylamine containing alkynyl moieties **51c-51e** furnished the corresponding pyrrole derivatives **55c** and **55e** in 52%-60% yield (Table 2**)**. The nonynyl, decynyl and dodecynyl moieties containing propargylamines **51f-51h** also furnished the pyrrole derivatives **55f-55h** in 32%-55% yields (Table 2).

Table 2. Synthesis of *N*-propargyl pyrroles **55** from *N*-propargyl pyrrolidines **51** using *p*-chloranil[a,b]





[a] The reactions were carried out by propargylamine **51 (**1.0 mmol) and *p*-chloranil **2** (3.0 mmol) in toluene (4 mL) at 70 °C for 12 h. [b]Isolated yield.

The pyrrole product **55b** was characterized by X-ray single crystal structural analysis and ORTEP diagram is shown in Figure 6. The crystal structure data of **55b** are summarized in Table A1 and A2 (Appendix II).

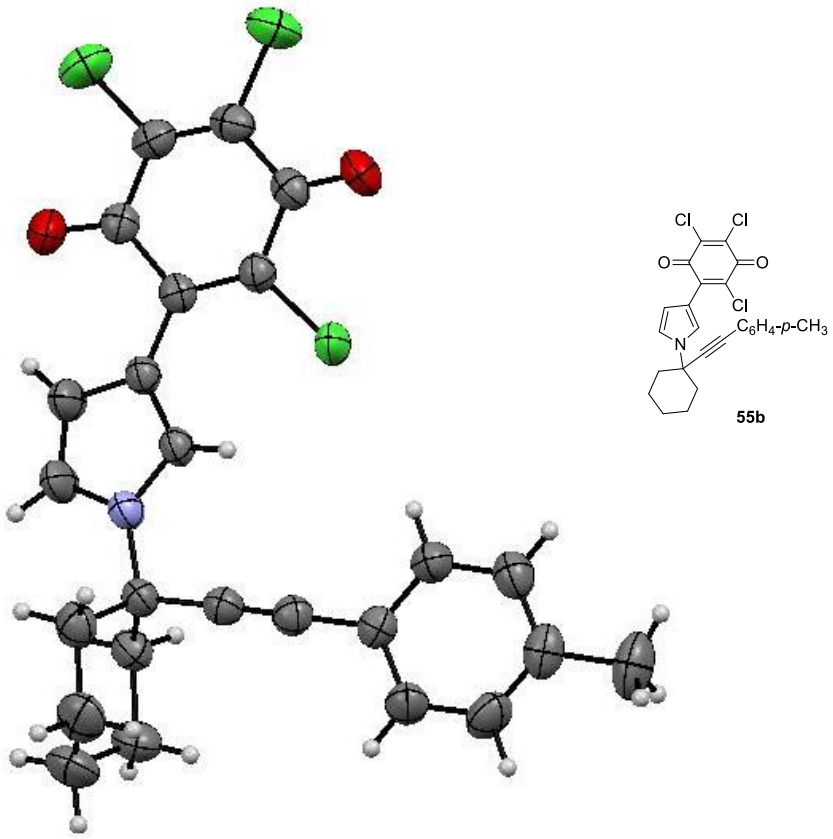
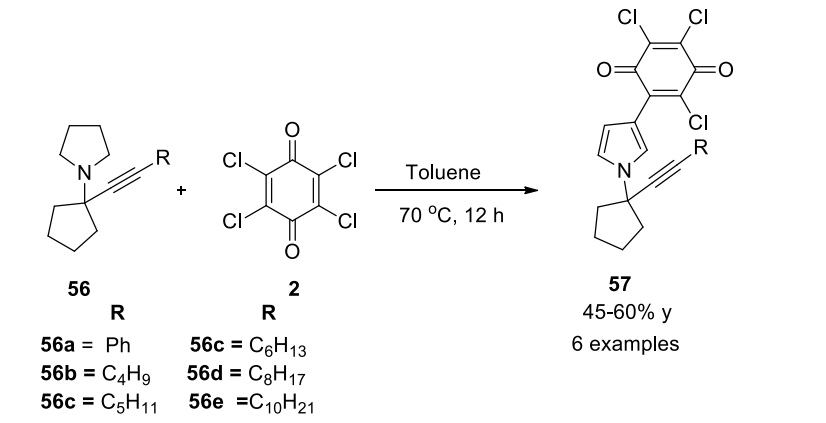


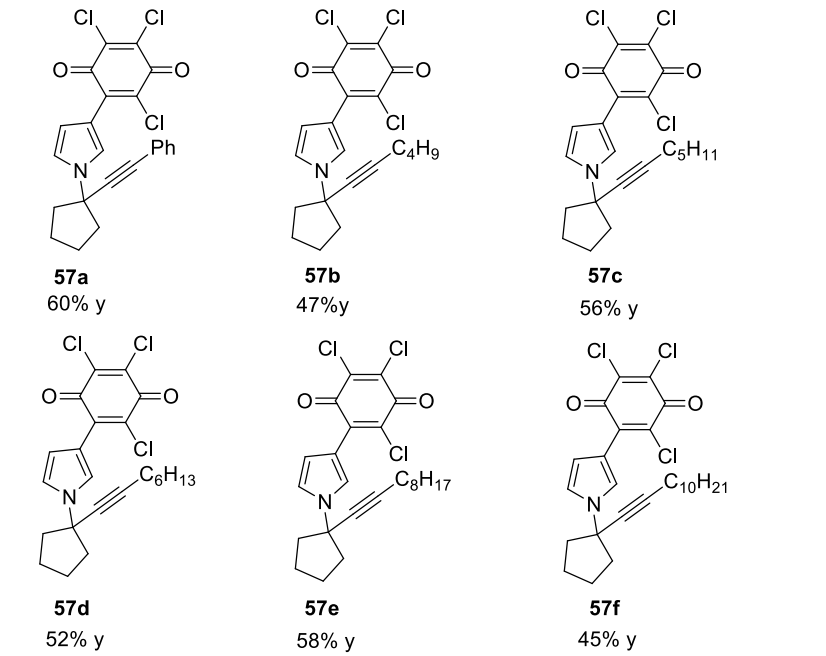
Fig 6. ORTEP representation of compound **55b** and thermal ellipsoids are drawn with 50% probability.

The propargylamine **56a** prepared using pyrrolidine, cyclopentanone and phenylacetylene afforded the pyrrole product **57a** in 60% yield (Table 4). The hexynyl and heptynyl alkynyl moieties containing propargylamines **56b-56c** gave the corresponding pyrrole derivatives **57b-57c** in 47-56% yields. The propargylamines **56d-56f** containing

octynyl, decynyl and dodecynyl moieties also undergo this reaction to give the corresponding substituted pyrroles **57d-57f** in 45%-58% yield (Table 4).

Table 4. Synthesis of substituted pyrroles **57** from *N*-propargyl pyrrolidines **56** using *p*-chloranil[a,b]



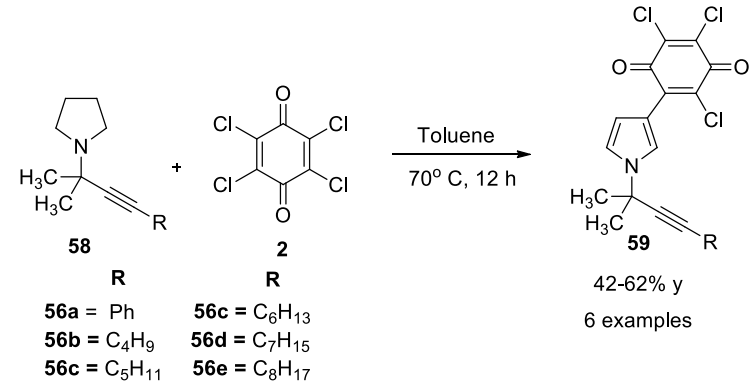


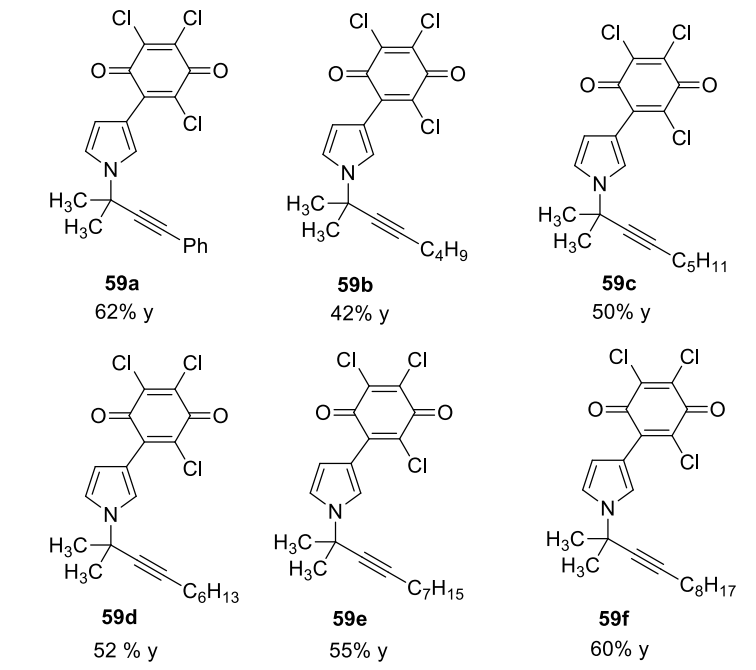
[a]The reactions were carried out by propargylamine **56 (**1.0 mmol) and *p*-chloranil **2** (3.0 mmol) in toluene (4 mL) at 70 °C for 12 h. [b] Isolated yield.

In chapter 2 (Table 4), synthesis of propargylamines **58** using amines, α,β-unsaturated ketones and 1-alkynes was described.[20] We have also examined these propargylamine

derivatives **58** in reactions with the *p*-chloranil acceptor. Interestingly, the propargylamines **58a**-**58f** containing two methyl groups at propargylic carbon also afforded the substituted pyrrole derivatives **59a**-**59f** in 42-62% yields (Table 5).

Table 5. Synthesis of substituted pyrroles **59** from *N*-propargyl pyrrolidines **58** using *p*-chloranil[a,b]





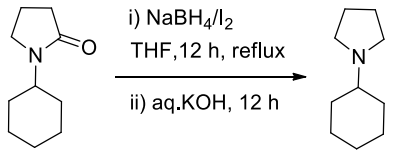
[a] The reactions were carried out by propargylamine **58 (**1.0 mmol) and *p*-chloranil **2** (3.0 mmol) in toluene (4 mL) at 70 °C for 12 h. [b] Isolated yield.

The propargylamine **58a** prepared from pyrrolidine, mesityloxide and phenylacetylene, afforded the pyrrole **59a** in 62% yield (Table 5**)**. Propargylamines **58b**-**58c** containing alkynyl moieties react with *p*-chloranil to give the corresponding pyrrole products **59b** and **59c** in 42% and 50% yield respectively (Table 5). The substituted pyrrole derivatives **59d**, **59e** and **59f** were also obtained in 52%-60% yield (Table 5).

4.2.3 Reactions of *N*-alkyl pyrrolidines with *p*-chloranil

We have also examined whether the alkynyl moiety in the propargylamines is involved in electron transfer reactions resulting in the formation of substituted pyrrole products by performing the reaction using N-alkyl pyrrolidine derivatives **60**. We have prepared the cyclohexylpyrrolidine product **61** in 90% yield by the reduction of 1-cyclohexyl-2-pyrrolidinone **60** with $NaBH_4/I_2$ system following a procedure reported from this laboratory (Scheme 6).[21]

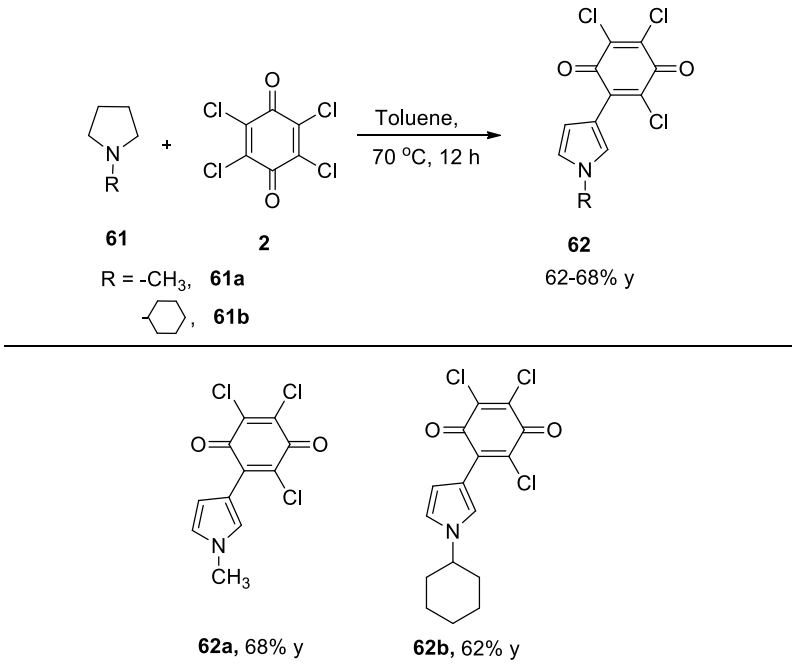
Scheme 6



60 **61**
90% y

We have observed that the reaction of *N*-methylpyrrolidine **61a** with *p*-chloranil **2** in toluene at 70 ^oC gave the corresponding substituted pyrrole product **62a** in 68 % yield (Table 6**)**. We have also examined the cyclohexylpyrrolidine **61b** with *p*-chloranil which gave the substituted pyrrole product **62b** was obtained in 68% yield (Table 6).

Table 6. Synthesis of *N*-alkyl pyrroles **62** from *N*-alkyl pyrrolidines **61**using *p*-chloranil[a,b]



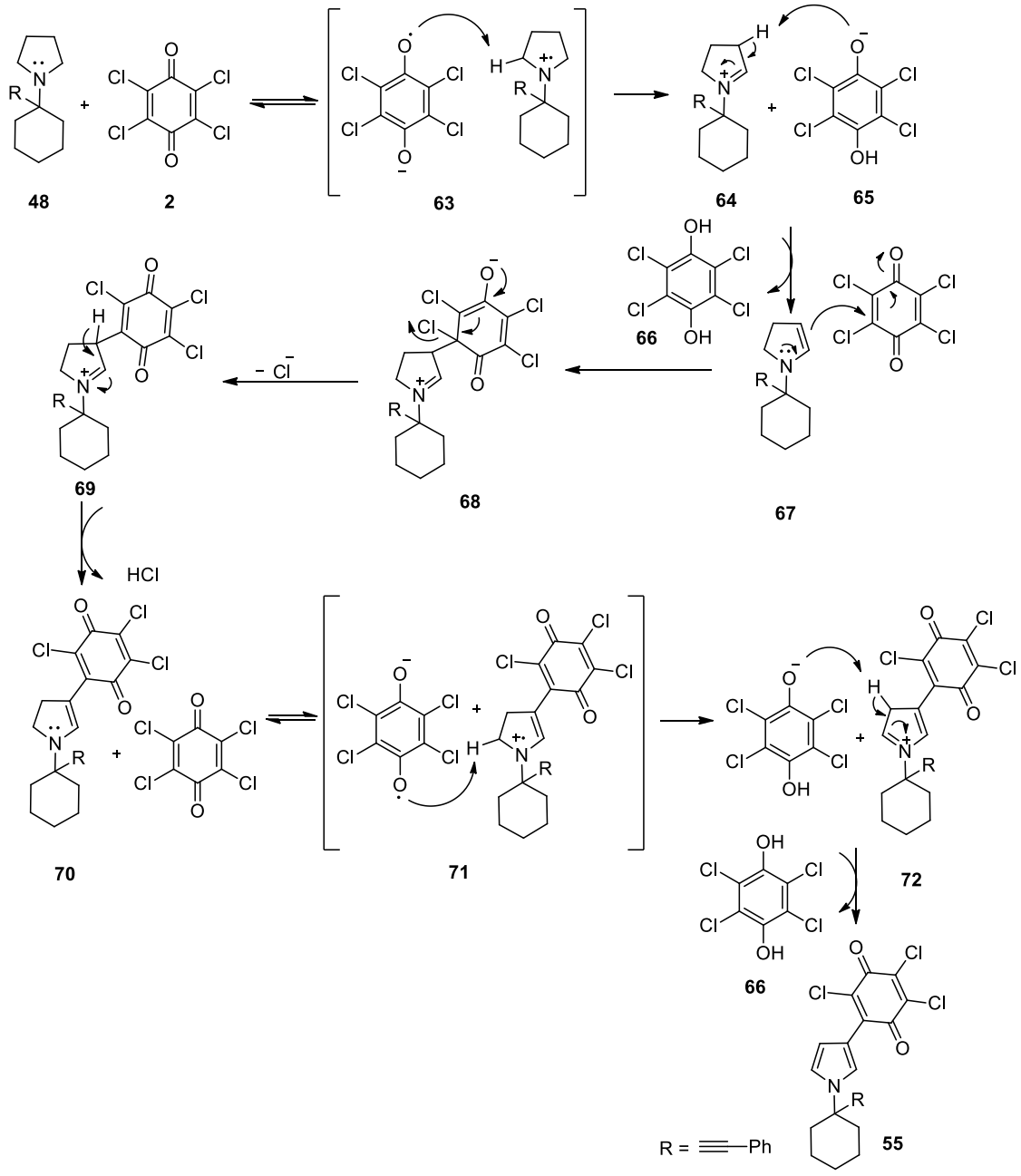
[a]The reactions were carried out by *N*-alkyl pyrrolidines **61 (**1.0 mmol) and chloranil **2** (3.0 mmol) in toluene (4 mL) at 70 °C for 12 h. [b] Isolated yield.

Clearly, the alkynyl group in the propargylamines do not seam to have a role in the reactions using *p*-chloranil.

Tentative mechanism pathway for the formation of substituted pyrrole derivatives

A tentative mechanism outlined in Scheme 7 may be considered for the reaction of the propargylamine and *p*-chloranil. Initially, the amine **48** would react with chloranil **2** to give the radical cation/anion pair intermediate **63**. Then, abstraction of hydrogen atom could give iminium ion **64** followed by deprotonation would give the enamine intermediate **67**, which could react with *p*-chloranil **2** to give the enamine intermediate **70.** Subsequent reaction with *p*-chloranil **2** would give the radical cation/anion pair intermediate **71**, which after abstraction of hydrogen, followed by deprotonation could give the substituted pyrrole product **55**.

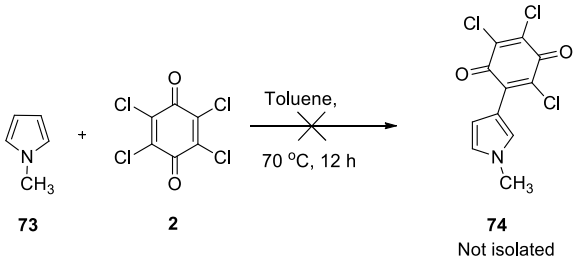
Scheme 7



4.2.4 Reactions of *N*-alkyl pyrrole and *N*-alkyl indole with *p*-chloranil

We have also examined the reaction of *N*-methyl pyrrole **73** with *p*-chloranil **2** under the reaction conditions but in this case no substitution product was obtained (Scheme 8).

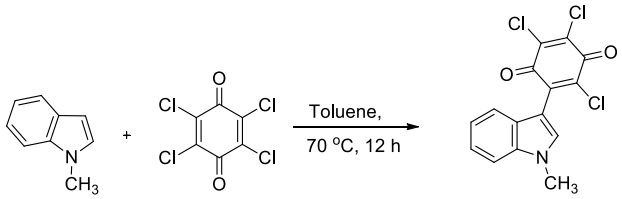
Scheme 8



73 **2** **74**
Not isolated

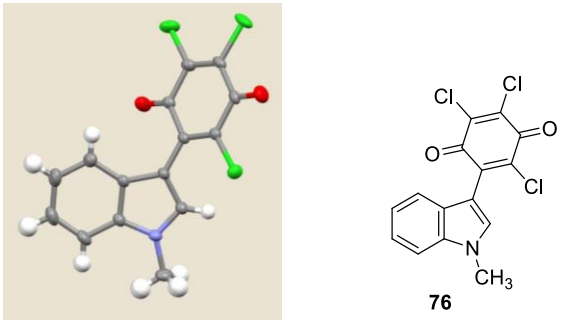
However, we have observed that the *N*-methyl indole **75** reacts with *p*-chloranil to give the substituted indole product **76** in 48% yield (Scheme 9). In this reaction, the indole acts like an enamine like **67** (Scheme 9) and gives the expected product.

Scheme 9 Reaction of *N*-methylindole **75** with *p*-chloranil



75 **2** **76**
48% y

The product **76** was also characterized by X-ray single crystal structural analysis (Figure 7). The crystal structure data of **76** are summarized in Table A3 and Table A4 (Appendix II).

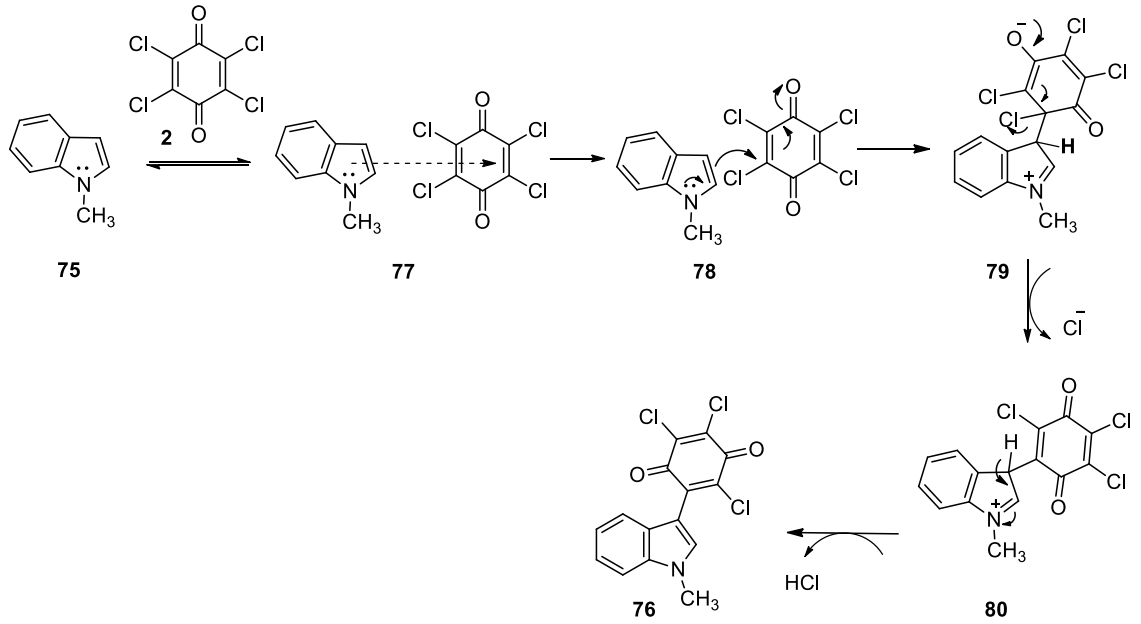


76

Figure 7. ORTEP representation of compound **76** and thermal ellipsoids are drawn with 50% probability.

The formation of substituted indole product can be explained by the mechanism as outlined in Scheme 10. The *N*-methylindole **75** would react with chloranil to give the charge transfer complex **77** which would then undergo 1,4-addition reaction to give the intermediate **79** that after elimination of HCl would give the substituted indole product **76** (Scheme 10).

Scheme 10 Plausible mechanism for the formation of substituted-*N*-methylindole **76**



4.2.5 Reported methods for synthesis of pyrroles

The pyrrole moieties are versatile synthetic intermediates[22] present in a wide variety of useful molecules and materials like pharmaceuticals,[23] conducting polymers,[24] molecular optics[25] and electronic[26] materials and gas sensors,[27] and several physiologically interesting natural products, such as heme, chlorophyll, bile pigments, pyrrolizidines and indolizidines alkaloids[28] and vitamin B_{12}.[29] Pyrrole motif is also present in bioactive compounds,[30-32] nakamuric acid[33] and chiral marinopyrroles.[34] A number of O-methylated analogues of

storniamide have shown potent activity as inhibitors of the multidrug resistance (MDR) phenomenon (Figure 8).[35]

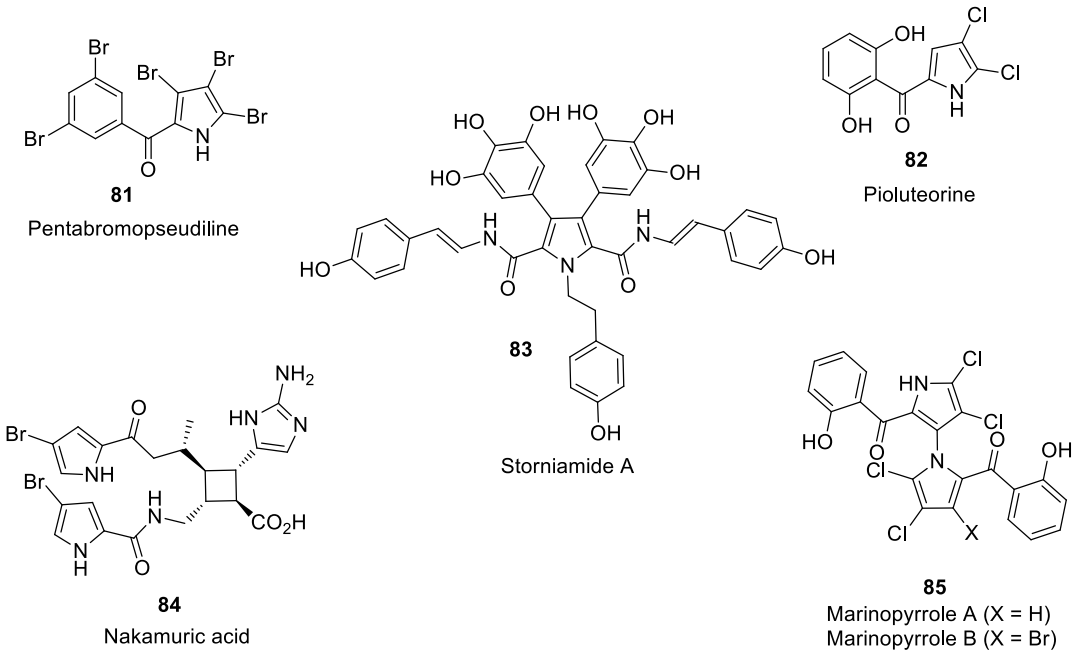


Figure 8. Pyrrole containing bioactive natural compounds

There have been several methods reported for the synthesis of substituted pyrroles using 1,3 and 1,4 carbonyl compounds as well as enamines as outlined in Chart 4.[36-43]

Chart 4

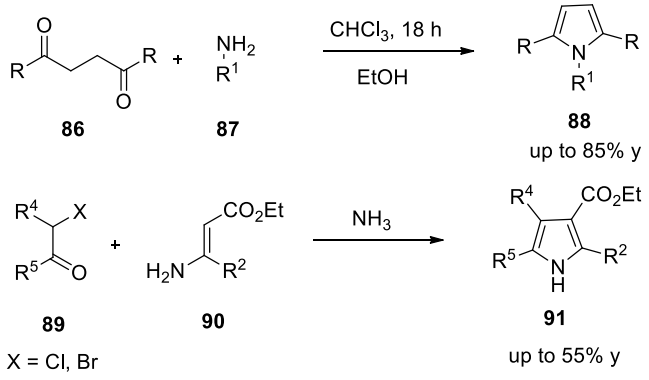
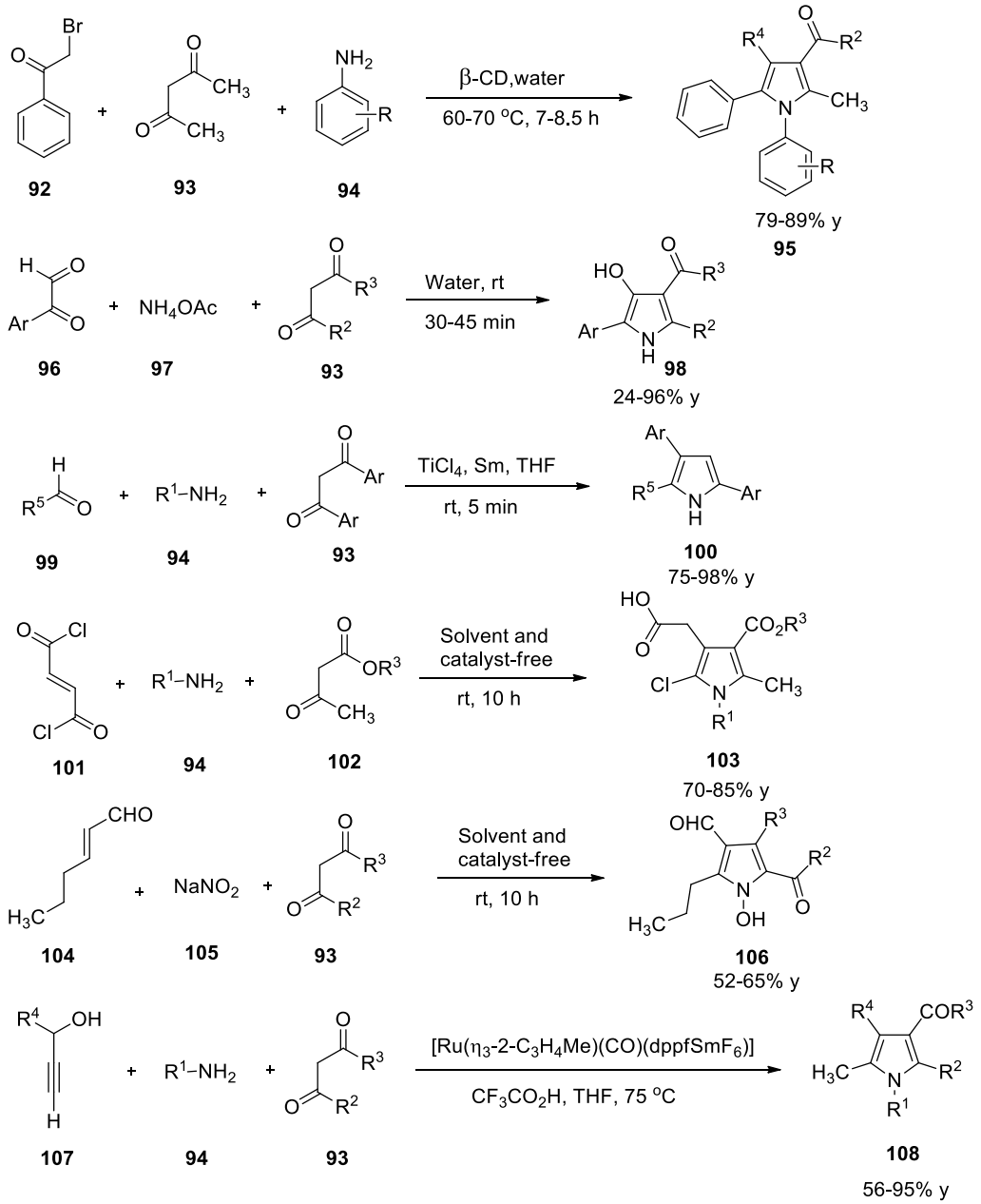
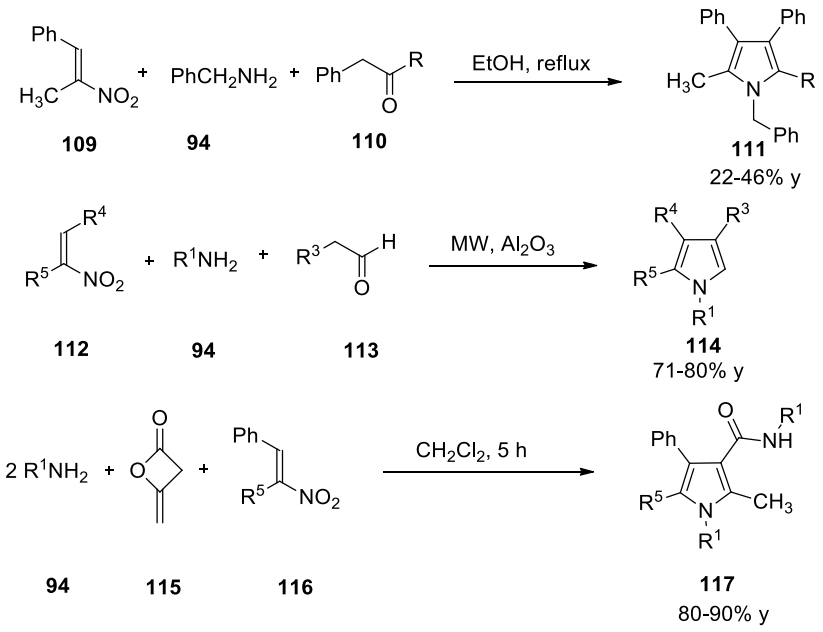


Chart 4 (continued)



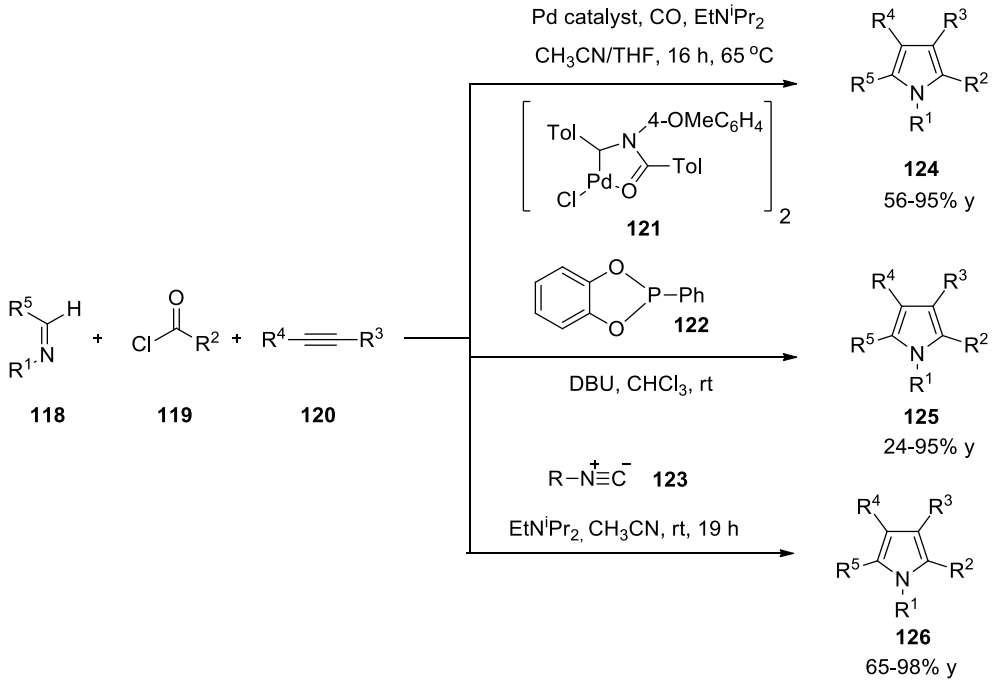
Methods for the synthesis of substituted pyrroles **111**, **114**, **117** through a three-component reaction between an amine **94**, ketone or aldehyde or lactones and a nitroalkene were also reported (Chart 5).[44-46]

Chart 5



The substituted pyrroles were also synthesized by the reaction between the imines **118**, acid chlorides **119** and alkynes **120** under different reaction conditions (Chart 6).[47-50]

Chart 6



Several methods were also reported for the synthesis of substituted pyrrole derivatives using alkynes as starting materials (Chart 7).[51-54] Also, methods were reported for the synthesis of substituted pyrroles (**143**, **145**, **147** and **150**) using *N*-propargylamines as starting materials (Chart 7).[55,56]

Chart 7

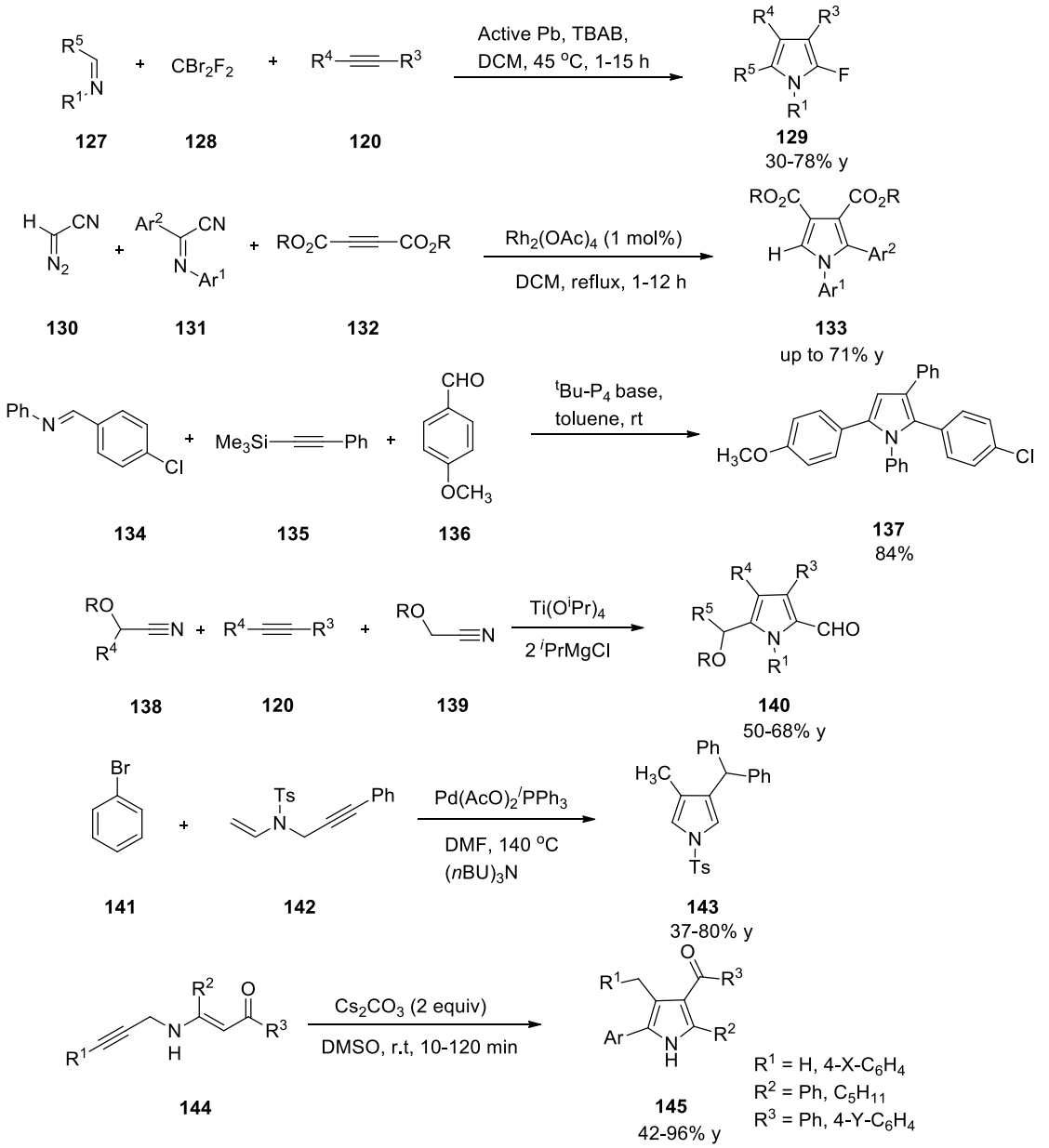
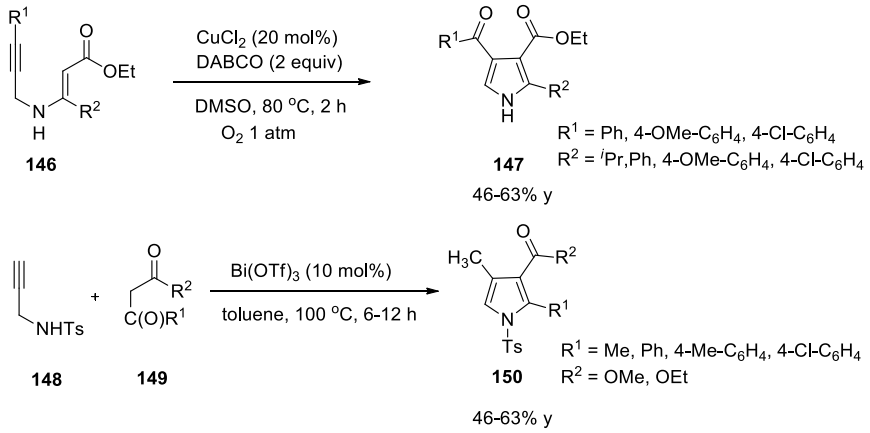
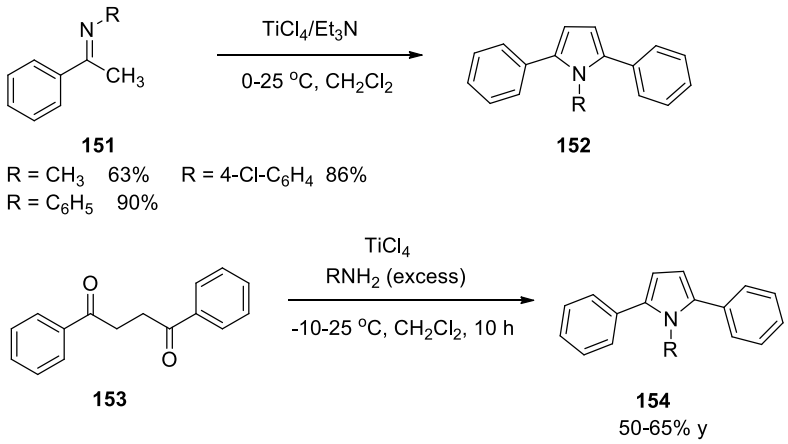


Chart 7 (continued)



Previously, methods were developed for the synthesis of substituted pyrrole derivatives **152** and **154** from this laboratory using aryl methyl ketimines **151** and 1,4-diphenylbutane-1,4-dione **153** with $TiCl_4$ reagent system (Chart 8).[57]

Chart 8



A series of pyrrolochloranil derivatives were synthesized following the method described here. Since, there are methods available to functionalize these derivatives on the pyrrole, quinone and propargyl moieties, this method has good synthetic potential for further synthetic exploitation.

Nex,t we have undertaken efforts towards construction of organic electricity harvesting cells using the radical ions obtained in the reaction of N^1,N^1,N^2,N^2-tetramethylclohexane-1,2-diamine and *p*-chloranil. The results are described in Chapter 5.

4.3 Conclusions

We have developed a new protocol for the synthesis of substituted pyrroles from the corresponding *N*-propargyl as well as *N*-alkyl pyrrolidines by a single pot reaction with *p*-chloranil. To the best of our knowledge, this is the first report on the synthesis of *N*-substituted pyrroles using the oxidizing agent *p*-chloranil through dehydrogenation. We have also observed that the reaction of *N*-methylindole with *p*-chloranil gave the 3-substituted *N*-methylindole containing trichlorobenzoquinone moiety. These transformations have potential for further applications in organic synthesis.

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) and IR (neat) spectra were recorded on JASCO FT-IR spectrophotometer model-5300. ^{1}H (400 MHz), ^{13}C (100 MHz) NMR spectra were recorded on Bruker-Avance-400 spectrometers chloroform-d as solvent. Chemical shifts were determined with tetramethylsilane (TMS) as internal reference (δ = 0 ppm). Coupling constants *J* are in Hz. Liquid chromatography (LC) and mass analysis (LC-MS) were performed on SHIMADZU-LCMS-2010A or HRMS using EI technique.

All the glasswares were pre-dried at 100-120 °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 reagent were carried out using standard syringe-septum technique recommended for handling air sensitive reagents and organometallic compounds.

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 was used. The outlet of the mercury bubbler was connected to the atmosphere by a long tube. All dry solvents and reagents used were distilled from appropriate drying agents. As a routine practice, all organic extracts were washed with saturated NaCl solution (brine) and dried over Na_2SO_4 or K_2CO_3 and concentrated on Heidolph-EL-rotary evaporator. All the yields reported are of isolated materials characterized by IR and NMR.

Dichloromethane and chloroform were distilled over CaH_2 and dried over molecular sieves. Toluene supplied by E-Merck, India was kept over sodium-benzophenone ketyl and freshly distilled before use. All aldehydes, supplied by Loba Chemicals (P), Ltd., India were distilled or recrystallized from the appropriate solvents before use.

Analytical grade of CuCl, CuBr and CuI were purchased from Sigma-Aldrich. Analytical thin layer chromatographic tests were carried out on glass plates (3 x 10 cm) coated with 250 mμ E-Merck and acme's silica gel-G and GF-254 containing 13% calcium sulfate as a 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.

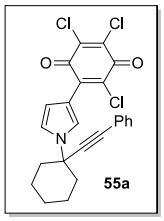
4.4.2 General procedure for the synthesis of substituted pyrrole derivatives

To a stirred suspension of amine (**51, 56**, **58**, 1 mmol) in toluene (3 mL), *p*-chloranil **2** (3.0 mmol) was added at 25 ^oC. The contents were stirred at 70 ^oC for 12 h. Toluene was removed; water (5 mL) and DCM (15 mL) were added. The DCM layer was washed with saturated NaCl solution, dried with Na_2SO_4 and concentrated. The residue was chromatographed on silica gel (100-200 mesh) using hexane and ethyl acetate (98:2) as eluent to isolate the pyrrole. The yields and the spectral data of the substituted pyrrole derivatives are given below.

2,3,5-trichloro-6-(1-(1-(phenylethynyl) cyclohexyl)-1H-pyrrol-3-yl)cyclohexa-2,5-diene-1,4-dione

Yield : 0.285 g, 62%; purple liquid.

IR (neat) **:** 3019, 2925, 2852, 1737, 1679, 1554, 1492, 1463, 1446, 1365, 1350, 1261, 1216, 1163, 1101, 1084, 994, 969, 757, 699, 669, 646, 624 cm^{-1}.



55a

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.94 (t, *J* = 1.96 Hz, 1H), 7.52-7.49 (m, 2H), 7.37-7.36 (m, 2H), 7.29-7.24 (m, 1H), 7.18-7.17 (m, 1H), 6.92-6.91 (m, 1H), 2.37-2.32 (m, 2H), 2.06-1.97 (m, 2H), 1.94-1.93 (m,1H), 1.92-1.88 (m, 2H), 1.593 (s, 1H), 1.35-1.27 (m, 2H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 176.8, 171.8, 140.5, 140.2, 137.7, 131.7, 128.8, 126.0, 122.1, 119.1, 113.4, 112.0, 88.3, 87.9, 59.6, 39.6, 25.0, 23.6.

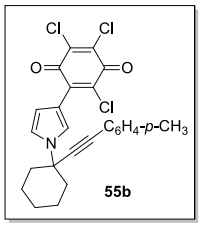
HRMS **:** (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{24}H_{18}Cl_3NO_2$: 458.0481; found: 458.0475.

2,3,5-trichloro-6-(1-(1-(p-tolylethynyl)cyclohexyl)-1H-pyrrol-3-yl)cyclohexa-2,5-diene-1,4-dione

Yield **:** 0.305 g, 65%; purple liquid.

mp **:** 186-188 ^{o}C

IR (KBr) **:** 3020, 2933, 2856, 1677, 1600, 1550, 1509, 1446, 1366, 1349, 1333, 1298, 1261, 1215, 1162, 1100, 1084, 994, 896, 870, 815, 754, 697, 667, 645, 626 cm^{-1}.



55b

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.94 (t, *J* = 2.04, 1H), 7.40-7.38 (m, 2H),

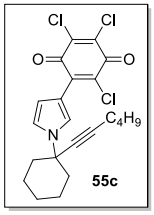
7.18-7.15 (m, 3H), 6.91-6.90 (m, 1H), 2.38 (s, 3H), 2.33-2.30 (m, 2H), 2.02-1.96 (m, 2H), 1.93-1.80 (m, 4H), 1.59-1.27 (s, 1H), 1.36- (m, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 176.8, 171.8, 140.5, 140.2, 138.9, 137.7, 132.1, 131.6, 129.1, 126.1, 119.1, 119.0, 113.4, 111.9, 88.0, 87.6, 59.7, 39.6, 25.0, 23.6, 21.5.

HRMS : (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{25}H_{20}Cl_3NO_2$: 494.0458; found: 494.0457.

2,3,5-trichloro-6-(1-(1-(hex-1-yn-1-yl)cyclohexyl)-1H-pyrrol-3-yl)cyclohexa-2,5-diene-1,4-dione

Yield : 0.228 g, 52%; purple liquid.



IR (neat) : 3020, 2935, 2860, 1678, 1601, 1549, 1498, 1447, 1365, 1349, 1332, 1288, 1215, 1184, 1153, 1101, 1084, 993, 896, 811, 755, 698, 667, 644, 624 cm^{-1}.

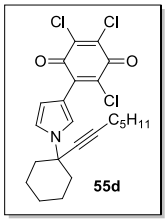
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.89 (t, *J* = 2.0 Hz, 1H), 7.10-7.09 (m, 1H) 6.90-6.88 (m, 1H), 2.32 (t, *J* = 7.0 Hz, 2H), 2.15-2.13 (m, 2H), 1.90-1.85 (m, 2H), 1.84-1.75 (m, 5H), 1.60-1.54 (m, 2H), 1.49-1.44 (m, 2H) 1.26 (s, 1H), 0.95 (t, *J* = 7.35 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 176.8, 171.8, 140.5, 140.2, 137.8, 131.8, 126.3, 119.0, 113.2, 111.8, 88.7, 79.4, 59.4, 39.8, 30.7, 25.1, 23.5, 22.0, 18.3, 13.5.

HRMS : (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{22}H_{22}Cl_3NO_2$: 460.0614; found:

460.0614.

2,3,5-trichloro-6-(1-(1-(hept-1-yn-1-yl)cyclohexyl)-1H-pyrrol-3-yl)cyclohexa-2,5-diene-1,4-dione



Yield : 0.256 g, 57%; purple liquid.

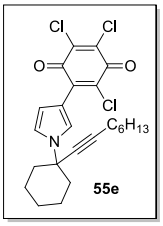
IR (neat) : 3020, 2934, 2859, 1679, 1601, 1548, 1498, 1449, 1366, 1349, 1332, 1288, 1261, 1221, 1184, 1154, 1100, 1083, 993, 896, 811, 757, 723, 698, 667, 644, 623 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.92-7.90 (m, 1H), 7.11-7.09 (m, 1H), 6.90-6.88 (m, 1H), 2.35-2.30 (m, 2H), 2.16-2.14 (m, 2H), 1.91-1.76 (m, 6H), 1.63-1.56 (m, 2H), 1.47-1.36 (m, 4H), 1.27 (s, br, 2H), 0.95-0.91 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 176.8, 171.8, 140.5, 140.2, 137.7, 131.8,126.3, 119.0, 113.2, 111.8, 88.8, 79.4, 59.4, 39.7, 31.1, 28.3, 25.1, 23.5, 22.1, 18.6, 14.0.

HRMS : (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{23}H_{24}Cl_3NO_2$: 474.0771; found: 474.0772.

2,3,5-trichloro-6-(1-(1-(oct-1-yn-1-yl)cyclohexyl)-1H-pyrrol-3-yl)cyclohexa-2,5-diene-1,4-dione



Yield : 0. 280 g, 60%; purple liquid.

IR (neat): 3020, 2931, 2857, 1679, 1600, 1549, 1498, 1434, 1349, 1332, 1288, 1261, 1216, 1184, 1154, 1100, 1083, 993,

896, 811, 756, 698, 667, 644, 624 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.89 (t, *J* = 2.0 Hz, 1H) 7.10-7.09 (m, 1H), 6.89-6.88 (m, 1H), 2.31 (t, *J* = 7.05 Hz, 2H), 2.16-2.14 (m, 2H), 1.91-1.85 (m, 2H), 1.84-1.79 (m, 5H), 1.61-1.55 (m, 3H), 1.47-1.43 (m, 2H), 1.33-1.31 (m, 3H), 1.27 (s, 1H), 092-0.89 (m, 3H).

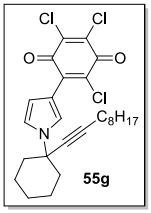
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 176.8, 171.8, 140.5, 140.2, 137.8, 131.8, 126.2, 119.0, 113.2, 111.8, 88.8, 79.4, 59.4, 39.7, 31.2, 28.6, 28.5, 25.1, 23.5, 22.5, 18.7, 14.0.

HRMS : (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{24}H_{26}Cl_3NO_2$: 488.0927; found: 488.0930.

2,3,5-trichloro-6-(1-(1-(dec-1-yn-1-yl)cyclohexyl)-1H-pyrrol-3-yl)cyclohexa-2,5-diene-1,4-dione

Yield : 0.272 g, 55%; purple liquid.

IR (neat) : 3020, 2928, 2855, 1688, 1679, 1572, 1548, 1498, 1448, 1406, 1374, 1365, 1349, 1332, 1288, 1260, 1216, 1154, 1110, 993, 905, 896, 811, 756, 712, 698, 667, 644, 623 cm^{-1}.



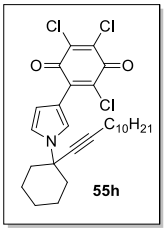
55g

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.89 (t, *J* = 2.0 Hz, 1H), 7.11-7.09 (m, 1H). 6.89-6.88 (m, 1H), 2.31 (t, *J* = 7.05 Hz, 2H), 2.16-2.14 (m, 2H), 1.91-1.86 (m, 2H), 1.84-1.79 (m, 5H), 1.61-1.55 (m, 3H), 1.45-1.42 (m, 2H), 1.33-1.27 (m, 8H), 0.89 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 176.8, 171.8, 140.5, 140.2, 137.8, 131.8, 126.2, 119.0, 113.2, 118.2, 88.8, 79.4, 59.4, 39.8, 31.8, 29.1, 29.0, 28.9, 28.6, 25.1, 23.5, 22.6, 18.6, 14.0.

HRMS : (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{26}H_{30}Cl_3NO_2$: 516.1240; found: 516.1236.

2,3,5-trichloro-6-(1-(1-(dodec-1-yn-1-yl)cyclohexyl)-1H-pyrrol-3-yl)cyclohexa-2,5-diene-1,4-dione



55h

Yield : 0.240 g, 46%; purple liquid.

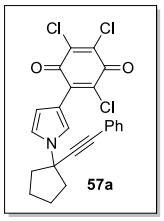
IR (neat) : 3019, 2928, 2855, 1678, 1600, 1549, 1513, 1499, 1464, 1450, 1365, 1349, 1333, 1288, 1261, 1215, 1185, 1154, 1100, 1084, 993, 896, 811, 755, 667, 645, 624 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.89 (s, 1H), 7.10-7.09 (m, 1H), 6.89-6.88 (m, 1H), 2.31 (t, J = 7.05 Hz, 2H), 2.16-2.14 (m, 2H), 1.89-1.86 (m, 2H), 1.84-1.75 (m, 6H), 1.61-1.55 (m, 3H), 1.45-1.42 (m, 2H), 1.28 (s, br, 11H), 0.89 (t, J = 6.5 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 176.8, 171.8, 140.5, 140.2, 137.8, 131.8, 126.2, 119.0, 113.2, 111.8, 88.8, 79.4, 59.4, 39.7, 31.9, 30.0, 29.5, 29.3, 29.0, 28.9, 28.6, 25.1, 23.5, 22.6, 18.6, 14.1.

HRMS : (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{28}H_{34}Cl_3NO_2$: 544.1553; found: 544.1558.

2,3,5-trichloro-6-(1-(1-(phenylethynyl)cyclopentyl)-1H-pyrrol-3-yl)cyclohexa-2,5-diene-1,4-dione



57a

Yield : 0.265 g, 60%; purple liquid.

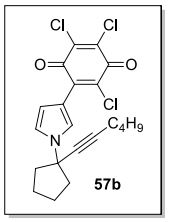
IR (neat) : 2960, 2875, 2930, 1677, 1599, 1550, 1491, 1443, 1405, 1356, 1316, 1260, 1232, 1192, 1162, 1144, 1099, 1081, 992, 895, 808, 757, 697, 644, 628 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.85-7.84 (m, 1H), 7.47-7.44 (m, 2H),7.35-7.34 (m, 3H), 7.10-7.08 (m, 1H), 6.92-6.91 (m, 1H), 2.54-2.49 (m, 2H), 2.41-2.35 (m, 2H), 2.07-2.04 (m, 2H), 1.96-1.94 (m, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 176.7, 171.8, 140.6, 140.2, 137.6, 132.3, 131.7, 128.6, 128.3, 126.8, 122.2, 119.9, 113.5, 112.3, 90.0, 84.9, 63.9, 41.7, 23.2.

HRMS : (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{23}H_{16}Cl_3NO_2$: 466.0145; found: 466.0141.

2,3,5-trichloro-6-(1-(1-(hex-1-yn-1-yl)cyclopentyl)-1H-pyrrol-3-yl)cyclohexa-2,5-diene-1,4-dione



57b

Yield : 0.200 g, 47%; purple liquid.

IR (neat) : 2957, 2927, 2871, 2856, 1679, 1548, 1496, 1356, 1260, 1160, 1110, 1081, 992, 895, 810, 698, 644 cm^{-1}.

^{1}H NMR : (500 MHz, $CDCl_3$, δ ppm) 7.79 (t, J = 2.0 Hz, 1H), 7.01-7.00 (m, 1H), 6.88-6.87 (m, 1H), 2.37-2.31 (m, 2H), 2.25 (t, J = 6.8 Hz, 3H), 1.99-

1.94 (m, 2H), 1.89-1.84 (m, 2H), 1.56-1.50 (m, 2H), 1.49-1.38 (m, 3H), 0.93 (t, *J* = 7.28 Hz, 3H).

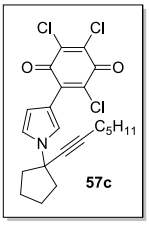
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 176.8, 171.8, 140.5, 140.2, 137.7, 131.9, 127.0, 119.8, 113.3, 112.1, 85.8, 81.2, 63.7, 41.9, 30.6, 23.1, 21.9, 18.3, 13.6.

HRMS : (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{21}H_{20}Cl_3NO_2$: 446.0458; found: 446.0458.

2,3,5-trichloro-6-(1-(1-(hept-1-yn-1-yl)cyclopentyl)-1H-pyrrol-3-yl)cyclohexa-2,5-diene-1,4-dione

Yield : 0.245 g, 56%; purple liquid.

IR (neat) : 2956, 2928, 2856, 1678, 1600, 1549, 1499, 1455, 1356, 1262, 1215, 1161, 1100, 1081, 992, 896, 810, 757, 699, 667, 644, 624 cm^{-1}.



57c

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.79 (t, *J* = 2.05 Hz, 1H), 7.01-7.00 (m, 1H), 6.88-6.87 (m, 1H), 2.37-2.31 (m, 2H), 2.25-2.22 (m, 3H), 1.99-1.94 (m, 2H), 1.90-1.85 (m, 2H), 1.59-1.51 (m, 3H), 1.40-1.31 (m, 4H), 0.91 (t, *J* = 7.15 Hz, 3H).

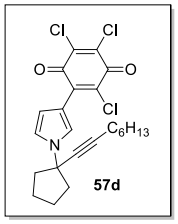
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 176.8, 171.8, 140.5, 140.2, 137.7,132.0, 126.9, 119.8, 113.3, 112.1, 85.9, 81.2, 63.7, 41.9, 31.0, 28.2, 23.1, 22.1, 18.6, 13.9.

HRMS : (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{22}H_{22}Cl_3NO_2$: 460.0614; found:

460.0613.

2,3,5-trichloro-6-(1-(1-(oct-1-yn-1-yl)cyclopentyl)-1H-pyrrol-3-yl)cyclohexa-2,5-diene-1,4-dione

Yield **:** 0.235 g, 52%; purple liquid.



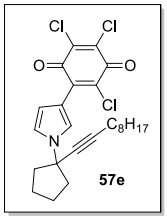
IR (neat) **:** 2957, 2926, 2855, 1679, 1600, 1550, 1498, 1457, 1356, 1262, 1214, 1161, 1111, 1082, 993, 896, 810, 756, 699, 668, 645, 624 cm^{-1}.

^{1}H NMR **:** (500 MHz, $CDCl_3$, δ ppm) 7.79 (t, *J* = 2.05 Hz, 1H), 7.01-7.00 (m, 1H), 6.88-6.87 (m, 1H), 2.36-2.31 (m, 2H), 2.25-2.22 (m, 3H), 1.99-1.93 (m, 2H), 1.91-1.85 (m, 2H), 1.61 (s, 2H), 1.56-1.50 (m, 2H), 1.43-1.36 (m, 2H), 1.31-1.29 (m, 3H), 0.90 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 176.8, 171.8, 140.5, 140.2, 137.7, 132.0, 126.9, 119.8, 113.3, 112.1, 85.9, 81.2, 63.7, 41.8, 31.2, 28.5, 23.1, 23.0 22.5, 18.6, 14.0.

HRMS **:** (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{23}H_{24}Cl_3NO_2$: 474.0771; found: 474.0777.

2,3,5-trichloro-6-(1-(1-(dec-1-yn-1-yl)cyclopentyl)-1H-pyrrol-3-yl)cyclohexa-2,5-diene-1,4-dione



Yield **:** 0.278 g, 58%; purple liquid.

IR (neat) **:** 2958, 2924, 2853, 1678, 1599, 1551, 1491, 1443, 1405, 1357, 1261, 1233, 1193, 1162, 1144, 1099, 1081, 992,

895, 809, 757, 698, 644 cm^{-1}.

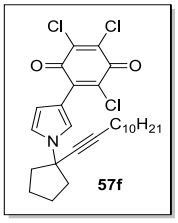
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.79 (t, *J* = 1.96 Hz, 1H), 7.00-6.99 (m, 1H), 6.87-6.86 (m, 1H), 2.36-2.31 (m, 2H), 2.25-2.21 (m, 3H), 1.99-1.93 (m, 2H), 1.92-1.84 (m, 2H), 1.55-1.49 (m, 2H), 1.43-1.36 (m, 2H), 1.29-1.28 (m, 9H), 0.90-0.87 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 176.7, 171.7, 140.5, 140.1, 137.6, 131.9, 127.0, 119.8, 113.3, 112.1, 85.9, 81.2, 63.7, 41.8, 31.8, 29.2, 29.0, 28.8, 28.5, 23.1, 22.6, 18.7, 14.1.

HRMS : (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{25}H_{28}Cl_3NO_2$: 502.1084; found: 502.1084.

2,3,5-trichloro-6-(1-(1-(dodec-1-yn-1-yl)cyclopentyl)-1H-pyrrol-3-yl)cyclohexa-2,5-diene-1,4-dione

Yield : 0.228 g, 45%; purple liquid.



57f

IR (neat) : 2953, 2925, 2854, 1678, 1600, 1548, 1455, 1356, 1261, 1214, 1160, 1099, 1081, 992, 895, 810, 756, 698, 667, 644, 624 cm^{-1}.

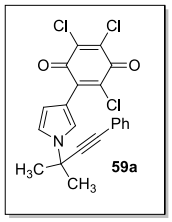
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.79 (t, *J* = 2.0 Hz, 1H), 7.01-7.00 (m, 1H), 6.88-6.87 (m, 1H), 2.36-2.31 (m, 2H), 2.25-2.22 (m, 3H), 1.99-1.93 (m, 2H), 1.90-1.85 (m, 2H), 1.56-1.50 (m, 3H), 1.43-1.36 (m, 2H), 1.27 (s, 12H), 0.89 (t, *J* = 6.80 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 176.7, 171.7, 140.5, 140.2, 137.7, 131.9,

126.9, 119.8, 113.3, 112.1, 85.9, 81.3, 63.7, 41.9, 31.9, 29.6, 29.5, 29.3, 29.0, 28.8, 28.5, 23.1, 22.6, 18.6, 14.1.

HRMS : (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{27}H_{32}Cl_3NO_2$: 530.1397; found: 530.1398.

2,3,5-trichloro-6-(1-(2-methyl-4-phenylbut-3-yn-2-yl)-1H-pyrrol-3-yl)cyclohexa-2,5-diene-1,4-dione



Yield : 0.260 g, 62%; purple liquid.

IR (neat) : 3020, 2989, 2927, 2854, 1677, 1599, 1551, 1491, 1353,1282, 1260,1215, 1177, 1129, 1078, 994, 896, 811, 753, 696, 667, 641 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.88 (t. *J* = 2.0 Hz, 1H), 7.49-7.48 (m, 2H), 7.38-7.33 (m, 3H), 7.13-7.12 (m, 1H), 6.91-6.90 (m, 1H), 1.94 (s, 6H).

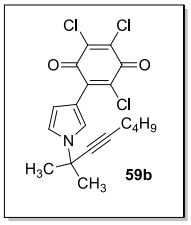
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 176.7, 171.8, 140.6, 140.2, 137.7, 132.4, 131.7, 128.8, 128.4, 126.0, 121.9, 119.1, 113.5, 112.3, 90.0, 84.8, 54.5, 31.3.

HRMS : (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{21}H_{14}Cl_3NO_2$: 418.0168; found: 418.0173.

2,3,5-trichloro-6-(1-(2-methyloct-3-yn-2-yl)-1H-pyrrol-3-yl)cyclohexa-2,5-diene-1,4-dione

Yield : 0.168 g, 42%; purple liquid.

IR (neat) : 2958, 2926, 2854, 1679, 1600, 1550, 1512, 1499,



1463, 1409, 1353, 1262, 1221, 1176, 1130, 1101, 1079, 993, 960, 896, 811, 758, 698, 640 cm^{-1}.

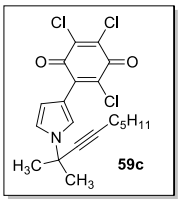
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.83 (t. *J* = 2.05 Hz, 1H), 7.04-7.03 (m, 1H), 6.88-6.87 (m, 1H), 2.28 (t, *J* = 7.0 Hz, 2H), 1.80 (s, 6H), 1.58-1.52 (m, 2H), 1.49-1.43 (m, 2H), 0.95 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 176.8, 171.8, 140.5, 140.2, 137.7, 132.0, 126.3, 119.0, 113.3, 112.1, 85.7, 81.4, 54.2, 31.6, 30.5, 21.9, 18.3, 13.6.

HRMS : (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{19}H_{18}Cl_3NO_2$: 420.0301; found: 420.0302.

2,3,5-trichloro-6-(1-(2-methylnon-3-yn-2-yl)-1H-pyrrol-3-yl)cyclohexa-2,5-diene-1,4-dione

Yield : 0.205 g, 50%; purple liquid.



IR (neat) : 2987, 2957, 2931, 2860, 1678, 1600, 1549, 1499, 1465, 1353, 1262, 1215, 1175, 1130, 1112, 1100, 1079, 993, 896, 812, 753, 698, 667, 642 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.84-7.83 (m, 1H), 7.05-7.03 (m, 1H), 6.88-6.87 (m, 1H), 2.27 (t, *J* = 7.08 Hz, 2H), 1.80 (s, 6H), 1.60-1.53 (m, 2H), 1.43-1.35 (m, 4H), 0.92 (t, *J* = 7.08 Hz, 3H).

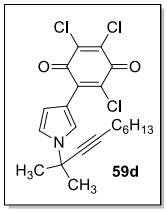
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 176.7, 171.7, 140.5, 140.2, 137.7, 132.0, 126.3, 119.0, 113.3, 112.1, 85.8, 81.4, 54.2, 31.6, 31.0, 28.2, 22.1, 18.5,

13.9.

HRMS **:** (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{20}H_{20}Cl_3NO_2$: 434.0458; found: 434.0462.

2,3,5-trichloro-6-(1-(2-methyldec-3-yn-2-yl)-1H-pyrrol-3-yl)cyclohexa-2,5-diene-1,4-dione

Yield **:** 0.220 g, 52%; purple liquid.



IR (neat) **:** 2985, 2955, 2929, 2857, 1677, 1600, 1546, 1497, 1435, 1352, 1261, 1217, 1173, 1129, 1099, 1078, 992, 895, 884, 811, 753, 697, 667, 640 cm^{-1}.

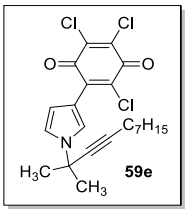
^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.83 (t, *J* = 2.04 Hz, 1H), 7.04-7.03 (m, 1H), 6.88-6.86 (m, 1H), 2.29-2.25 (m, 2H), 1.80 (s, 6H), 1.58-1.52 (m, 2H), 1.44-1.40 (m, 2H), 1.38-1.29 (m, 4H), 0.92-0.88 (m, 3H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 176.6, 171.6, 140.4, 140.1, 137.6, 131.9126.2, 118.9, 113.2, 112.0, 85.7, 81.3, 54.1, 31.5, 31.1, 28.4, 28.3, 22.4, 18.5, 13.9.

HRMS **:** (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{21}H_{22}Cl_3NO_2$: 448.0614; found: 448.0615.

2,3,5-trichloro-6-(1-(2-methylundec-3-yn-2-yl)-1H-pyrrol-3-yl)cyclohexa-2,5-diene-1,4 dione

Yield **:** 0.242 g, 55%; purple liquid.



IR (neat) **:** 2986, 2955, 2928, 2856, 1678, 1601, 1549, 1511,

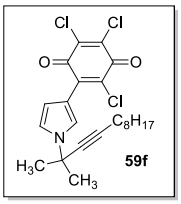
1464, 1353, 1262, 1216, 1176, 1130, 1079, 993, 896, 812, 756, 698, 668, 641 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.83-7.82 (m, 1H), 7.04-7.03 (m, 1H), 6.88-6.87 (m, 1H), 2.26 (t, *J* = 7.1 Hz, 2H), 1.80 (s, 6H), 1.67-1.53 (m, 2H), 1.43-1.38 (m, 2H), 1.35-1.30 (m, 6H), 0.89 (t, *J* = 6.75 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 176.8, 171.8, 140.5, 140.2, 137.7, 132.0, 126.2, 119.0, 133.3, 112.1, 85.8, 81.4, 54.2, 31.7, 31.6, 28.8, 28.7, 28.5, 22.6, 18.6, 14.0.

HRMS : (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{22}H_{24}Cl_3NO_2$: 462.0771 found: 462.0773.

2,3,5-trichloro-6-(1-(2-methyldodec-3-yn-2-yl)-1H-pyrrol-3-yl)cyclohexa-2,5-diene-1,4-dione



Yield : 0.272 g, 60%; purple liquid.

IR (neat) : 3019, 2929, 2856, 1678, 1600, 1501, 1551, 1466, 1430, 1354, 1336, 1214, 1176, 1130, 1079, 994, 928, 897, 745, 667 cm^{-1}.

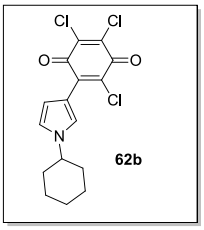
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.83 (t, *J* = 1.95 Hz, 1H), 6.82-6.81 (m, 1H), 6.67-6.66 (m, 1H), 2.26 (t, *J* = 7.05 Hz, 2H), 1.80 (s, 6H), 1.59-1.53 (m, 2H), 1.43-1.40 (m, 2H), 1.31-1.28 (m, 8H), 0.89 (t, *J* = 6.70 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 176.7, 171.7, 140.5, 140.2, 137.7, 132.0, 126.2, 119.0, 113.3, 112.1, 85.8, 81.4, 54.4, 31.8, 31.6, 29.1, 29.0, 28.8,

28.5, 22.6, 18.6, 14.0.

HRMS : (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{23}H_{26}Cl_3NO_2$: 476.0927 found: 476.0928.

2,3,5-trichloro-6-(1-cyclohexyl-1H-pyrrol-3-yl)cyclohexa-2,5-diene-1,4-dione



Yield : 0.221 g, 62%; purple liquid.

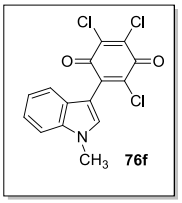
IR (neat) : 3018, 2920, 2848, 1672, 1538, , 1442, 1428, 1332, 1152, 1124, 1038, 992, 928, 872, 735, 667 cm^{-1}.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.43-7.42 (m, 1H), 7.04-7.03 (m, 1H), 6.88-6.87 (m, 1H), 3.72 (s, 1H), 2.14-2.11(m, 1H), 2.09-1.95 (m, 1H), 1.94-1.88 (m, 2H), 1.87-1.79 (m, 1H) 1.77-1.63 (m, 2H), 1.48-1.20 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 176.8, 171.7, 140.5, 140.0, 137.4, 132.1, 122.6, 119.6, 113.7, 112.5, 59.4, 34.2, 25.5, 25.2.

HRMS : (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{23}H_{26}Cl_3NO_2$: 357.0090 found: 379.9984.

2,3,5-trichloro-6-(1-methyl-1H-indol-3-yl)cyclohexa-2,5-diene-1,4-dione



Yield : 0.162 g, 48%; purple solid.

mp : 203-205 ^oC

IR (KBr) : 3019, 2929, 2856, 1678, 1600, 1551, 1501, 1466, 1430, 1354, 1336, 1214, 1176, 1130, 1079, 994, 928, 897, 745, 667 $cm.^{-1}$

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.51 (s, 1H), 7.43-7.40 (m, 2H), 7.35-7.32 (m, 1H), 7.28-7.24 (m, 1H), 3.92 (s, 3H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 176.2, 171.7, 140.8, 140.7, 138.2, 136.9, 134.7, 125.7, 128.8, 122.2, 121.0, 110.1, 105.4, 33.5.

HRMS **:** (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{23}H_{26}Cl_3NO_2$: 339.9699 found: 339.9696.

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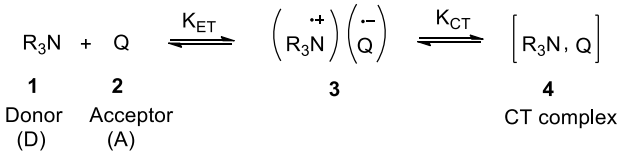
Chapter 5

Studies on Construction of Electricity Harvesting Cells using Organic Amine Donors and Quinone Acceptors

5.1 Introduction

5.1.1 Electricity Harvesting Cells

Electricity harvesting methods are available from various renewable sources like solar energy, thermal energy, wind energy, salinity gradients and potential energy.[1] Among these methods and devices, solar cells are more popular than others in recent years. It was of interest to us to construct an organic electrochemical cell based on the reactions of organic compounds like amines with quinones that could transport the charge carriers, i.e. electron in $Q^{-\cdot}$ and the hole (positive charge) in $R_3N^{+\cdot}$ to the electrodes to produce electricity (Figure 1).[2]



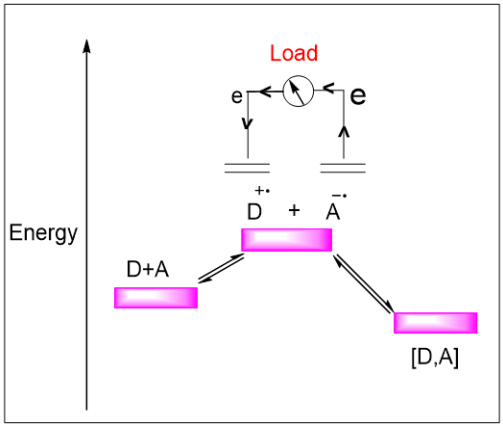


Figure 1: Ground state electricity harvesting Cell

Accordingly, a brief review of the various types of organic solar cells would facilitate the discussion of the present results.

5.1.2 Organic Solar Cell

There have been a sustained efforts to develop organic solar cells in the last three decades.[3–10] Initially, small organic molecules and semiconducting polymers were used in organic solar cells with significant improvements in the recent years.[3-6,9-15] The organic solar cells working principles are similar to the inorganic solar cell mechanism. When the sun light is absorbed by organic materials, excitons (coupled electron and hole pair) are produced. The electric field splits the exciton into charge carriers (separated electron and hole pair) which then moves to the respective electrodes. Some donor polymer and acceptors used in the organic solar cells are shown in Figure 2.

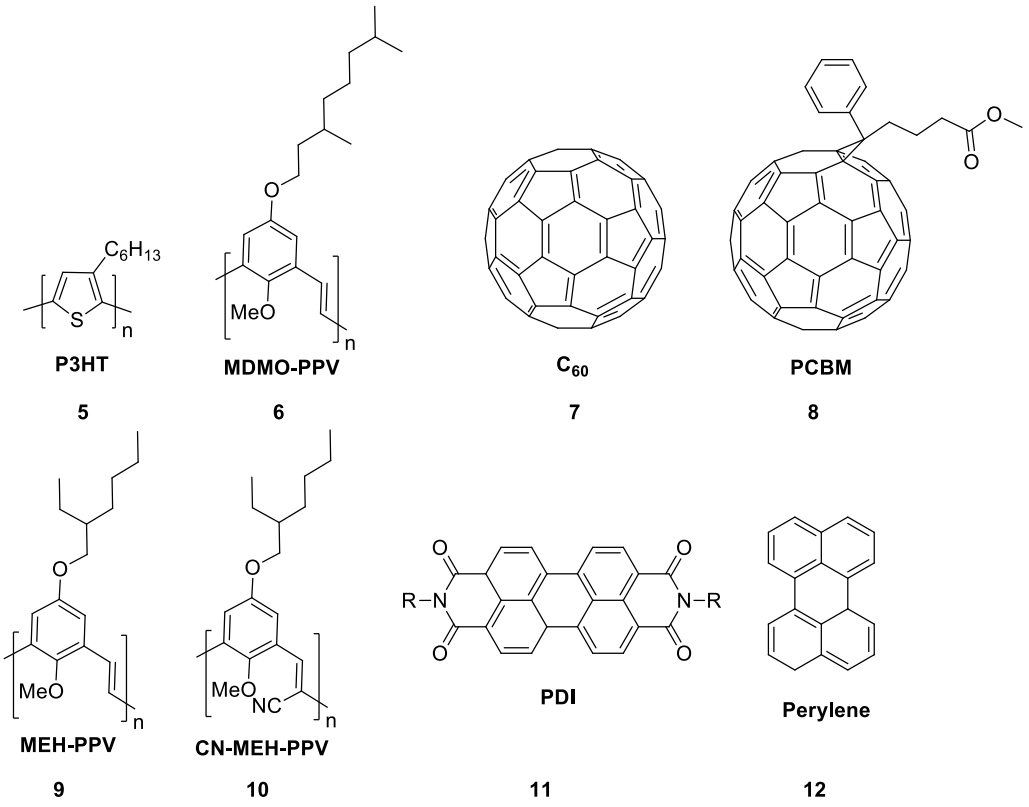


Figure 2: Organic solar cells containing donor polymers and acceptors

Single layer organic solar cells

The first single organic layer cell was constructed by sandwiching of organic material in between the ITO (indium tin oxide) coated on glass and aluminium which have different work funcions (Figure 3).[4,5,17-19] Ghosh and co-workers reported[17] that magnesium phthalocyanine (MgPc) single layer solar cell (Al/MgPc/Ag) produced electric power with 0.01% efficiency. Glenis and co-workers reported[20] that the single layer cell using poly-3-methyl thiophene gave 0.15% power conversion efficiency. Also, the single layer cell using the conjugated polymer polyacetylene gave 0.3% conversion efficiency.[21] These cells gave less than 1% power conversion efficiency.

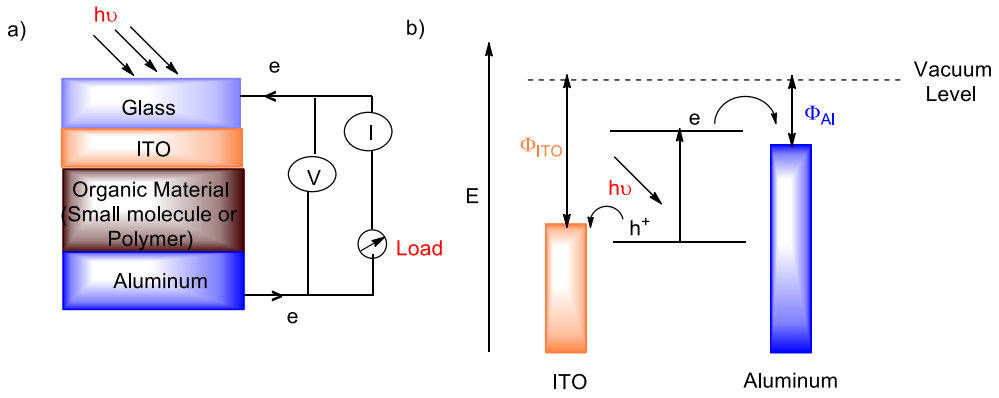


Figure 3: Single layer organic solar cell

Bilayer organic solar cells

The bilayer device was prepared by stacking donor and an acceptor layers between the two electrodes (Figure 4). The work function of the two electrodes sandwiching the two layers should match the energy levels of the donor HOMO and the acceptor LUMO for the effective extraction of the respective charge carriers.[22,23]

Sariciftci and co-workers reported[24] that the double layer cell gave 0.04% power conversion efficiency by using C_{60} as an acceptor and poly (2-methoxy-5-(2'-ethylhexyloxy-1,4-phenylene-vinylene) or MEH-PPV as donor. Tang *et al.*[25] developed a two layer organic cell with electron donor copper phthalocyanine (CuPc) and acceptor perylene tetracarboxylic derivative with 1% power conversion efficiency. Halls *et al.* also reported a bilayer cell using donor polymer poly (p-phenylenevinylene), PPV and acceptor C_{60}. The PPV/C_{60} cell produced 9% power conversion efficiency.[26]

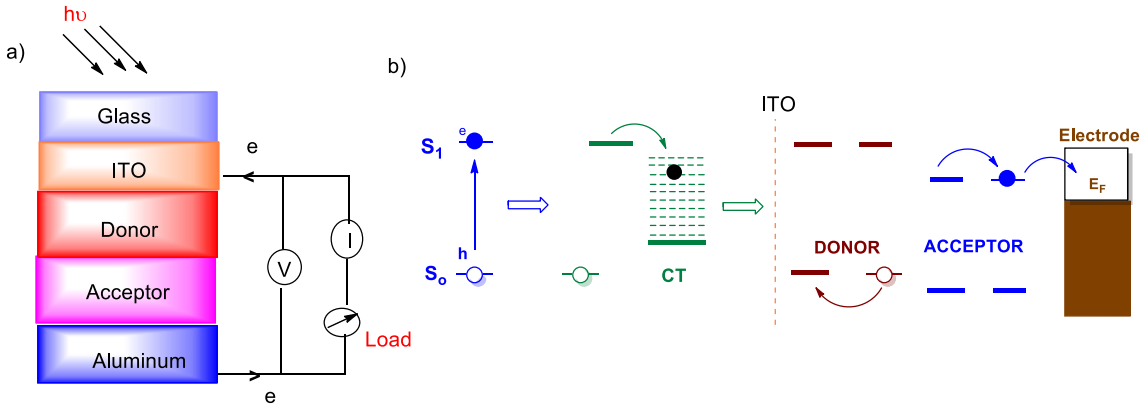


Figure 4: Double layer organic solar cell

Bulk heterojunction solar cell

In bulk-heterojunction cell, the use of electron donor and acceptor mixture decreases the exciton diffusion pathway and improves the light absorption efficiency. Yu *et al.* developed[27] a cell using the mixture of polymer MEH-PPV donor and fullerene based acceptor as the heterojunction. The cell using Ca/MEH-PPV/PCBM/ITO gave 2.9% power conversion efficiency. Later, MEH-PPV polymer was replaced by poly (3-octylthiophene) to produce the power conversion efficiency 4.8%.[28] Recently, He and co-workers reported[29] that the use of thiophene based PTB7-Th polymer and $PC_{71}BM$ as acceptor gave the power

conversion efficiency of 11%. The organic heterojunction cells were further improved by sandwiching the active layer in between the electron (ETL) and hole (HTL) transport materials (Figure 5).[30]

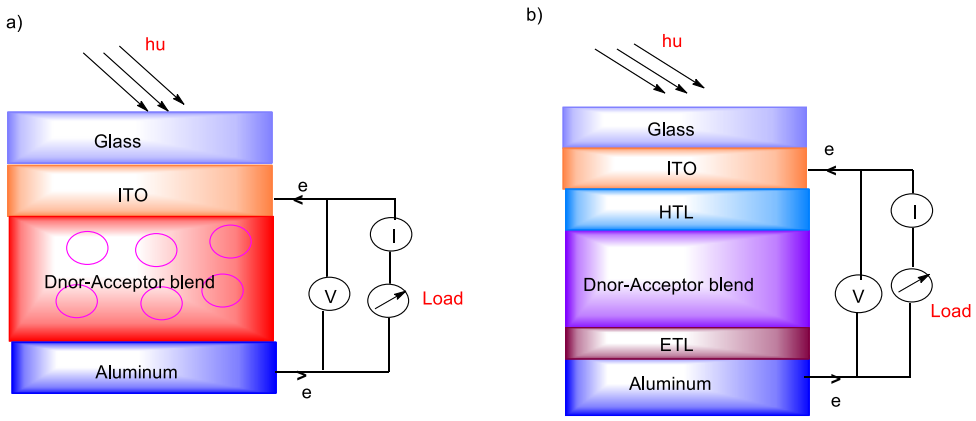


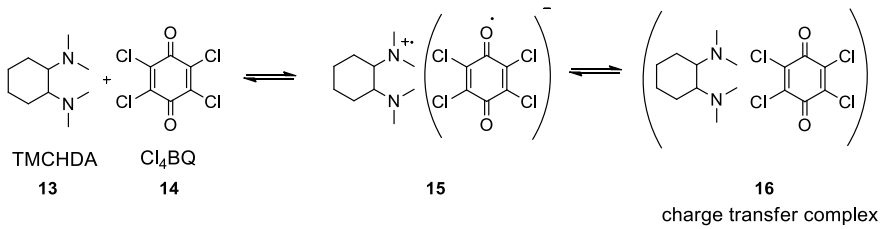
Figure 5: Bulk heterojunction solar cell

It is of interest to us construct electricity harvesting cells using organic donor amines and quinones acceptors. The results are discussed in the next section.

5.2 Results and Discussion

As discussed earlier, the reaction of the donor N^1,N^1,N^2,N^2-tetramethylcyclohexane-1,2-diamine with *p*-chloranil gave the radical cation–anion pair followed by the formation of the corresponding charge transfer complex (Scheme 1).

Scheme 1



We have undertaken efforts to construct electricity harvesting electrochemical cells based on such ground state electron transfer reactions.

5.2.1 Previous reports from our laboratory on the electrochemical cells

Recently, electrochemical cells were constructed in this laboratory based on ground state electron transfer reactions using various donor amines and *p*-chloranil and TiO_2 in different configurations as outlined in Figure 6.[2]

Figure 6. Six layers cells previously constructed in this laboratory

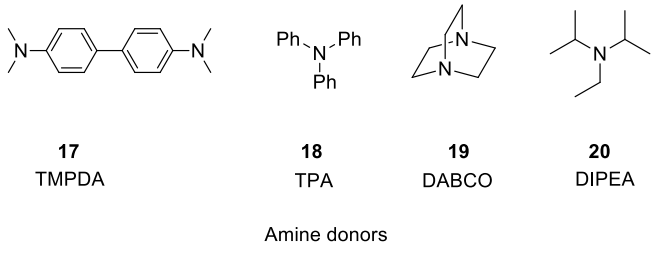
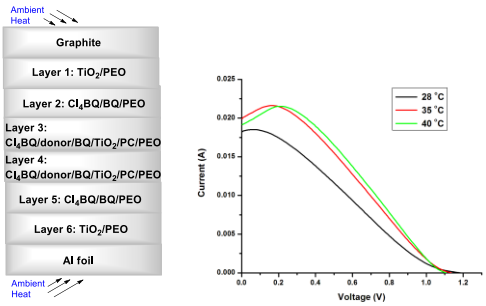


Figure 6 (continued)

(a) (b) (c)



Donor	1 h after packing Pmax(mW)/FF(40 °C)	48 h after packing Pmax(mW)/FF(40 °C)
TMPDA	1.614/0.282	1.299/0.263
TPA	0.939/0.219	0.728/0.219
DABCO	4.806/0.432	3.776/0.434
DIPEA	**11.74/0.296**	**8.338/0.394**

(d)

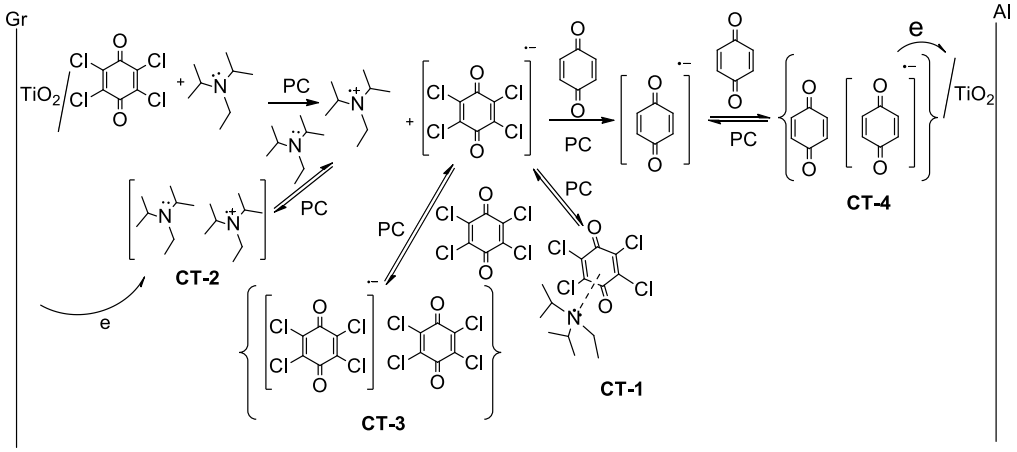


Figure 6. (a) Schematic diagram of six layer cell. (b) Representative IV curve for the DIPEA after 48 h. (c) Representative IV curve data for different amines. (d) Tentative mechanism for electron transport to the electrodes via D/D.+ and A-/A exchange reactions.

It was of interest to us to develop such electrochemical cells using the donor N^1,N^1,N^2,N^2-tetramethylcyclohexane-1,2-diamine (TMCHDA) **13** and *p*-chloranil (Cl_4BQ) **14**.

5.2.2 Efforts for the construction of the electricity harvesting cells using donor N^1,N^2,N^2-tetramethylcyclohexane-1,2-diamine

We have constructed the electrochemical cell by using the readily accessible donor N^1,N^2,N^2-tetramethylcyclohexane-1,2-diamine (TMCHDA) **13** and *p*-chloranil (Cl_4BQ) **14** as

well as electron transporters **21**-**24** to produce electricity at ambient temperature (Figure 7). We have chosen the readily accessible aluminum foil (Al) as anode and graphite sheet as cathode respectively for the construction of the electrochemical cells.

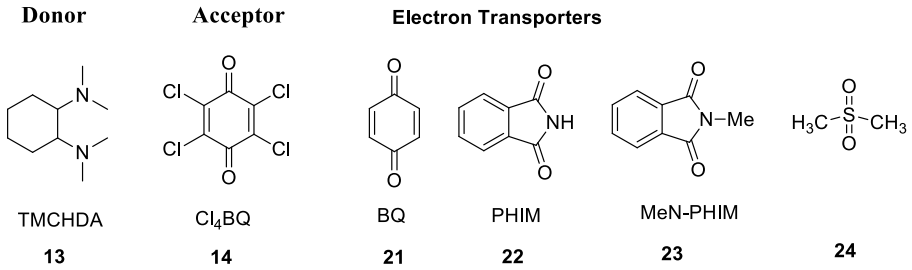


Figure. 7

5.2.3 Multi-layer Cell Configurations

We have initially constructed the cells by making donor and acceptor pastes using TiO_2, polyethylene oxide (PEO) and propylene carbonate (PC) for coating on commercially available Al (0.2mm x 5cm x 5cm) and graphite sheet (0.4mm x 5cm x 5cm) (Figure 8). The TiO_2 was reported to react with electron donors to accept electrons from amines.[31-37] Accordingly, we have initially constructed the cell using the donor N^1,N^2,N^2-tetramethylcyclohexane-1,2-diamine (TMCHDA) **13** and the TiO_2 as acceptor without using Cl_4BQ **14** (Figure 8).

Figure 8. Four layer cell by using TMCHDA without Cl_4BQ

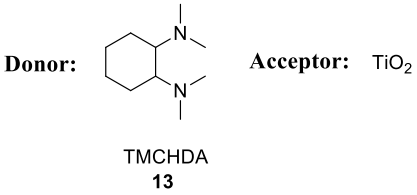
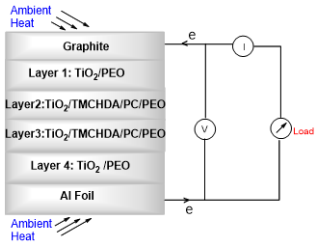
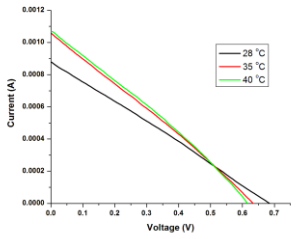


Figure 8 (continued)

(a) (b)





(C)

1**h after packing**	**48 h after packing**
Pmax mW/FF	**Pmax mW/FF**
0.157/0.262 (28°C)	0.168/0.271 (28°C)
0.179/0.268 (35°C)	0.209/0.269 (35°C)
0.185/0.283 (40°C)	**0.221/0.272 (40°C)**

(d)

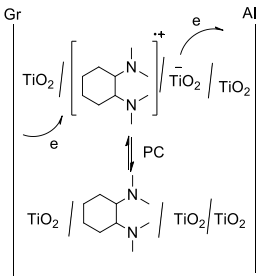


Figure 8. (a) Schematic diagram of cell with four layer configuration. (b) Representative IV curve after 48 h. (c) Representative IV curve data (Table ES1, entry 1, TiO_2 acceptor) (d) Tentative mechanism for electron transport via $D/D^{\cdot+}$ and A^{-}/A exchange reactions.

The current (I)-voltage (V) data recorded 1 h and 48 h after packing at 28 ^{o}C, 35 ^{o}C and 40 ^{o}C respectively. Interestingly, the power produced was low but the performance remained the same for a long time in this cell configuration.

We have then constructed the cell using Cl_4BQ and BQ in four layers using PC solvent as shown in Figure 9.

Figure 9. Six layer cell with BQ as electron transporter in four layer

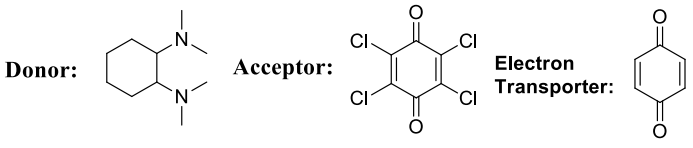
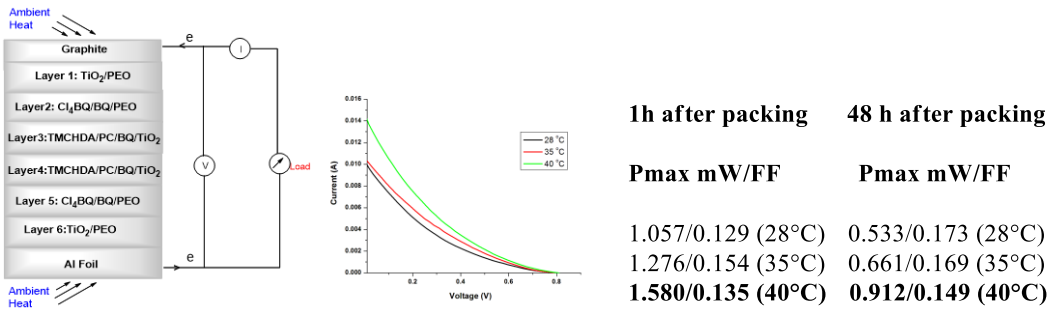


Figure 9 (continued)

(a) (b) (c)



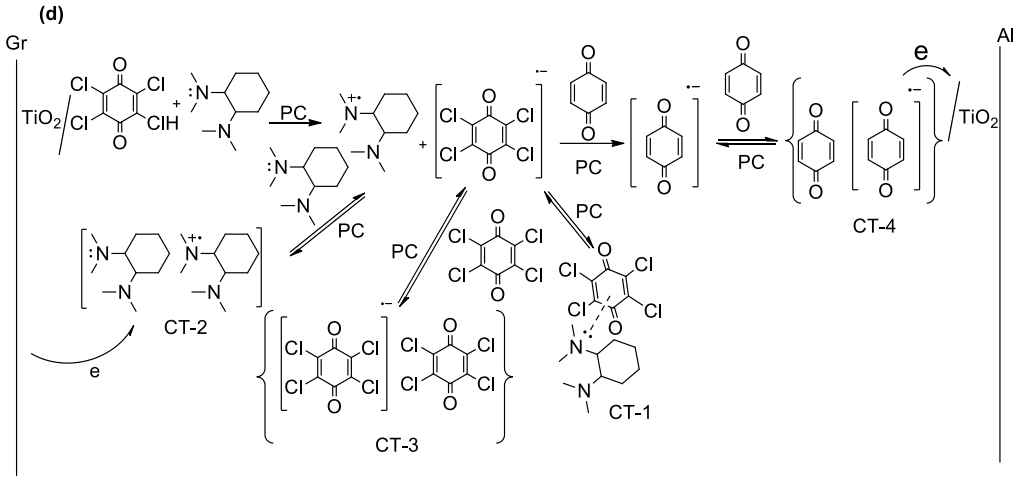


Figure 9. (a) Schematic diagram of cell with six layer configuration. (b) Representative IV curve after 48 h packing. (c) Representative IV curve data (Table ES2, entry 2, BQ-ET). (d) Tentative mechanism for electron transport via $D/D^{\cdot+}$ and A^{-}/A exchange reactions.

This configuration is similar to the configuration of the cell using diisopropyl ethylamine (Figure 6), but the power produced here is lower. Presumably, the N^1,N^1,N^2,N^2-tetramethylcyclohexane-1,2-diamine may form the CT-1 complex in more amounts leading to lower power output.

Then, we have constructed a six layers cell using the Cl_4BQ acceptor and the electron transporters like BQ, Me_2SO_2 and MeN-Phthalimide **23** (MeNPHIM) in one layer in PC solvent in similar configurations (Figure 10-12).

Figure 10. Six layer cell using BQ as electron transporter in one layer

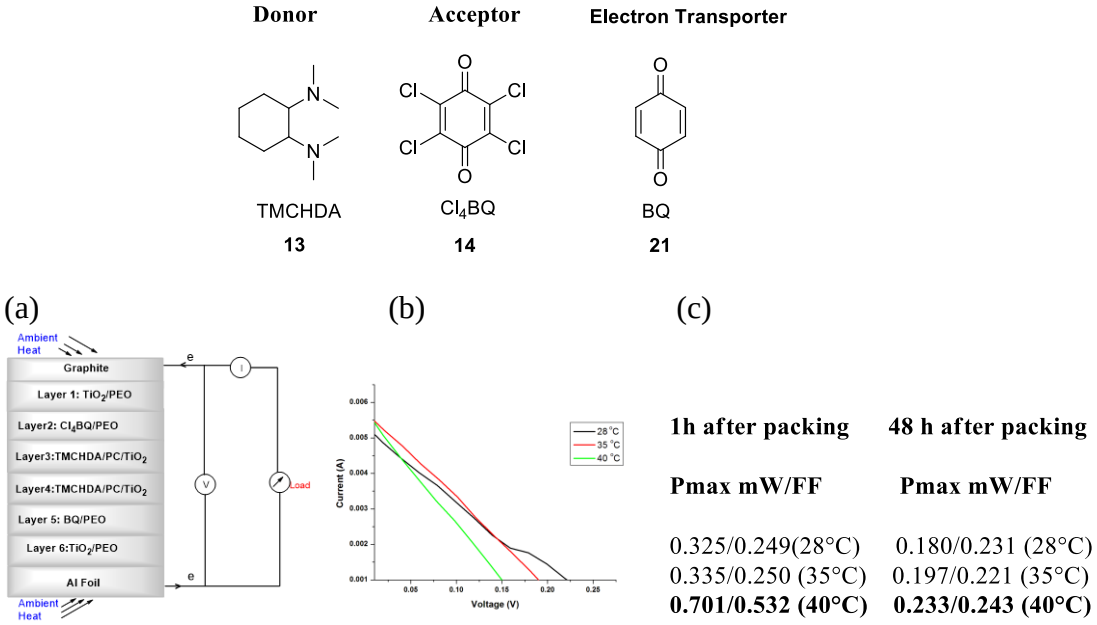
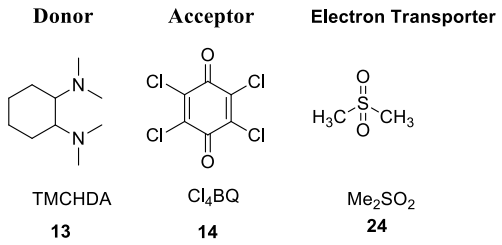


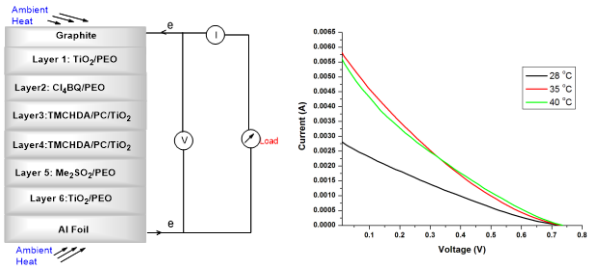
Figure 10. (a) Schematic diagram of cell with six layer configuration. (b) Representative IV curve after 48 h. (c) Representative IV curve data (Table ES2, entry 3, BQ-ET).

We observed that the Pmax values obtained are somewhat low in this configuration. We have also constructed the six layer cell by using dimethyl sulfone in the place of BQ (Figure 11).

Figure 11. Six layer cell using Me_2SO_2 as electron transporter in one layer



(a) (b) (c)

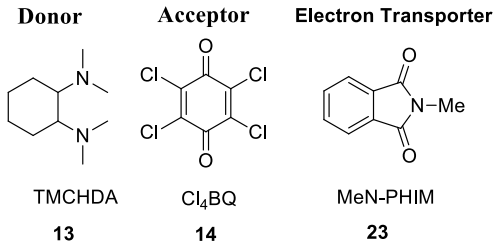


1h after packing	48 h after packing
Pmax mW/FF	**Pmax mW/FF**
0.417/0.204 (28°C)	0.503/0.190 (28°C)
0.759/0.175 (35°C)	0.762/0.195 (35°C)
0.748/0.178 (40°C)	**0.960/0.197 (40°C)**

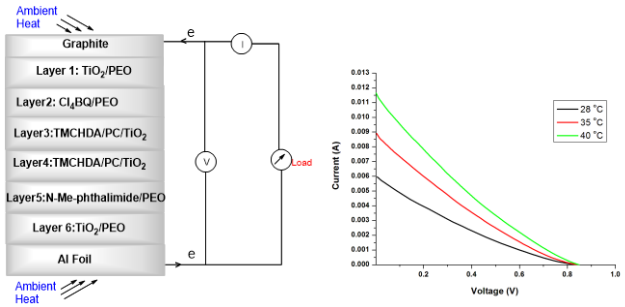
Figure 11. (a) Schematic diagram of cell with six layer configuration. (b) Representative IV curve after 48 h. (c) Representative IV curve data (Table ES2, entry 4, dimethyl sulfone-ET).

In this experiment, there was slight improvement in the power output (Pmax). We have also constructed the cell using Me-N-phthalimide as electron transporter in this configuration (Figure 12).

Figure 12. Six layer cell using MeN-PHIM as electron transporter in one layer



(a) (b) (c)



1h after packing	48 h after packing
Pmax mW/FF	**Pmax mW/FF**
0.944/0.190 (28°C)	0.956/0.182 (28°C)
1.439/0.192 (35°C)	1.034/0.196 (35°C)
1.897/0.192 (40°C)	**1.315/0.203 (40°C)**

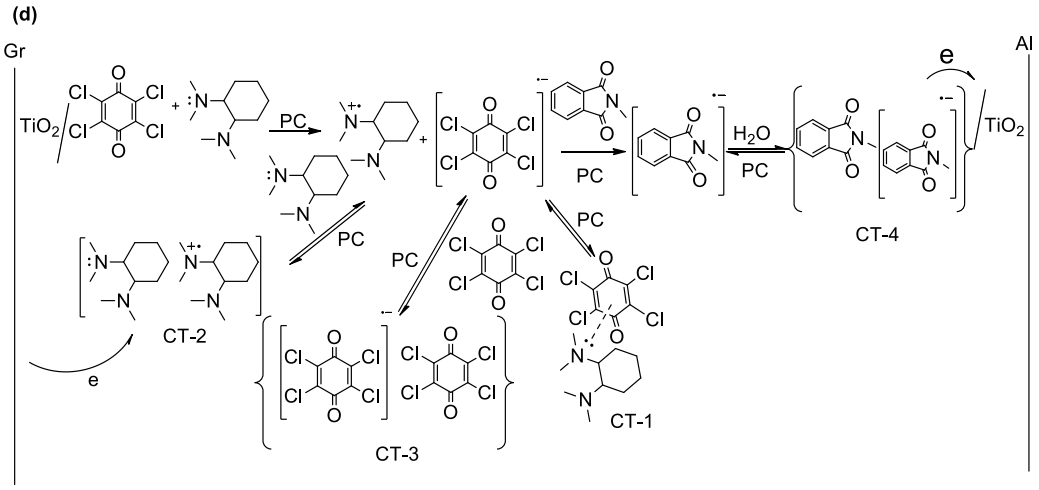


Figure 12. (a) Schematic diagram of cell with six layer configuration. (b) Representative IV curve after 48 h. (c) Representative IV curve data (Table ES2, entry 5, MeN-Phthalimide-ET). (d) Tentative mechanism for electron transport via $D/D^{\cdot+}$ and A^{-}/A exchange reactions.

Interestingly, the MeN-phthalimide gave better power compared to the BQ and Me_2SO_2 electron transporters.

Next, we turned towards the construction of the five layers cell using donor N^1,N^1,N^2,N^2-tetramethylcyclohexane-1,2-diamine and different electron transporters like BQ, Me_2SO_2 in NMP solvent (Figure 13 and 14).

Figure 13. Five layer cell with BQ in two layers

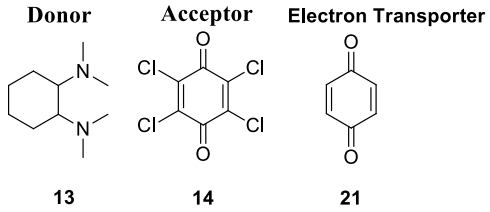
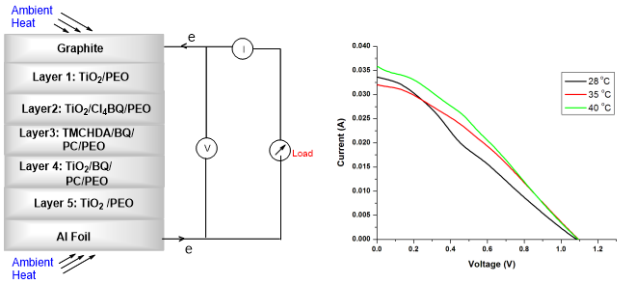


Figure 13 (continued)

(a) (b) (c)

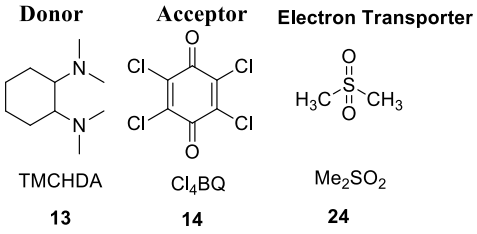


1h after packing	48 h after packing
Pmax mW/FF	**Pmax mW/FF**
3.837/0.262 (28°C)	1.124/0.268 (28°C)
5.094/0.301 (35°C)	1.488/0.254 (35°C)
5.566/0.314 (40°C)	**1.736/0.278 (40°C)**

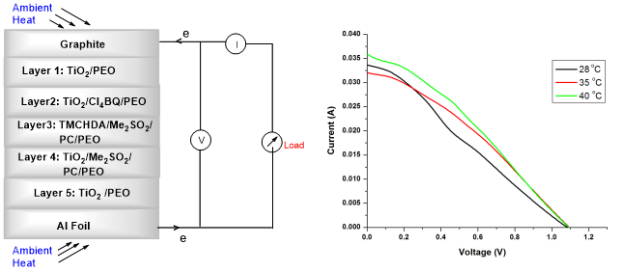
Figure 13. (a) Schematic diagram of cell with five layer configuration. (b) Representative IV curve after 48 h. (c) Representative IV curve data (Table ES3, entry 6, BQ-ET).

Interestingly, the cell this configuration gave higher output (Pmax). We have then constructed the cell in 5 layer configuration using the dimethyl sulfone.

Figure 14. Five layer cell using Me_2SO_2 in two layers



(a) (b) (c)



1h after packing	48 h after packing
Pmax mW/FF	**Pmax mW/FF**
9.416/0.258 (28°C)	2.409/0.267 (28°C)
11.590/0.331 (35°C)	2.909/0.256 (35°C)
12.340/0.316 (40°C)	**3.263/0.309 (40°C)**

Figure 14 (continued)

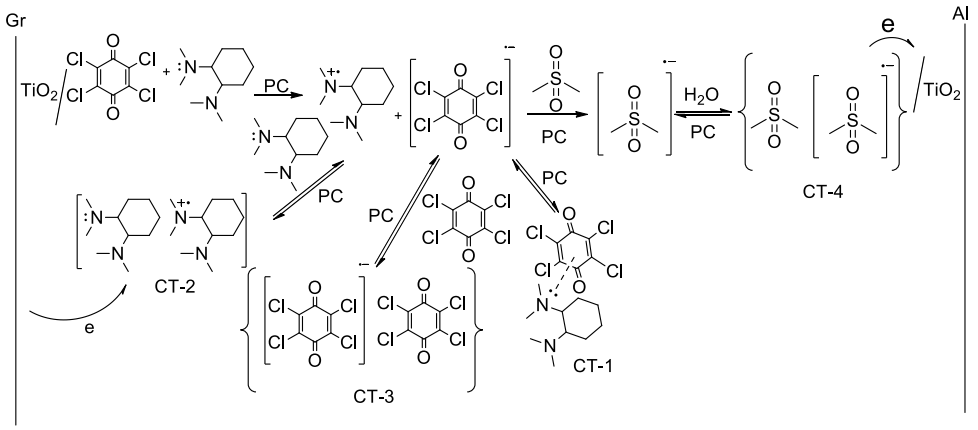


Figure 14. (a) Schematic diagram of cell with five layer configuration. (b) Representative IV curve after 48 h. (c) Representative IV curve data (Table ES3, entry 7, Me_2SO_2-ET). (d) Tentative mechanism for electron transport via $D/D^{\cdot+}$ and A^{-}/A exchange reactions.

Surprisingly, this configuration gave higher power (Pmax 12.340 mW) but after 48 h, the power output decreased (Pmax 3.263 mW). We have also constructed the cell in this configuration using pthalimide as electron transporter in NMP solvent.(Figure 15).

Figure 15. Five layer cell using NMP as solvent and PHIM as electron transporter

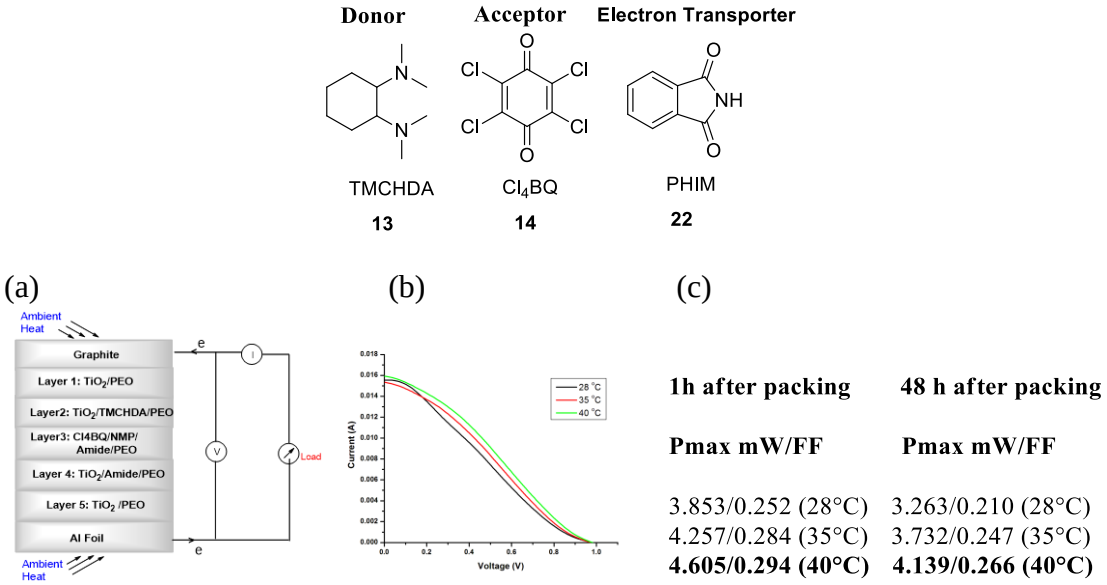


Figure 15 (continued)

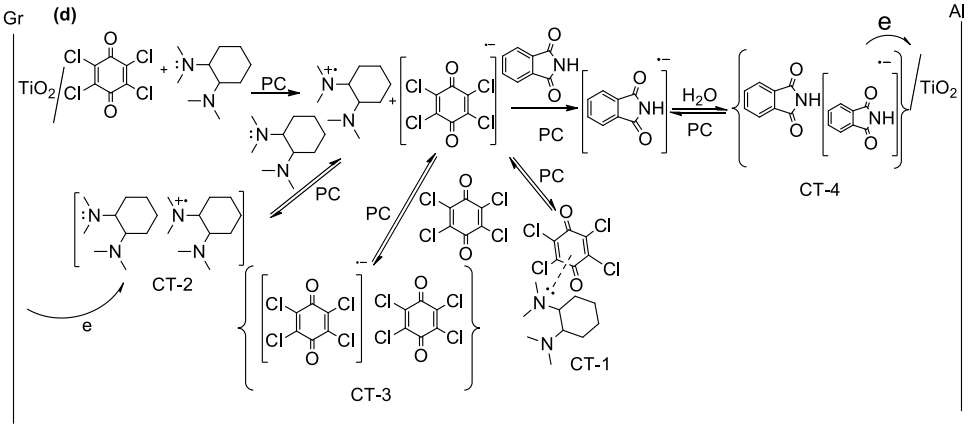


Figure 15. (a) Schematic diagram of cell with five layer configuration. (b) Representative IV curve after 48 h. (c) Representative IV curve data (Table ES3, entry 8, phthalimide-ET). (d) Tentative mechanism for electron transport via $D/D^{\cdot+}$ and A^{-}/A exchange reactions.

In this case, the power output remained approximately the same for 48 h (Figure 15).

Next, we have constructed the cell in seven layer configuration as shown in Figure 16.

Figure 16. Seven layer cell using Cl_4BQ in two layers and BQ in three layers

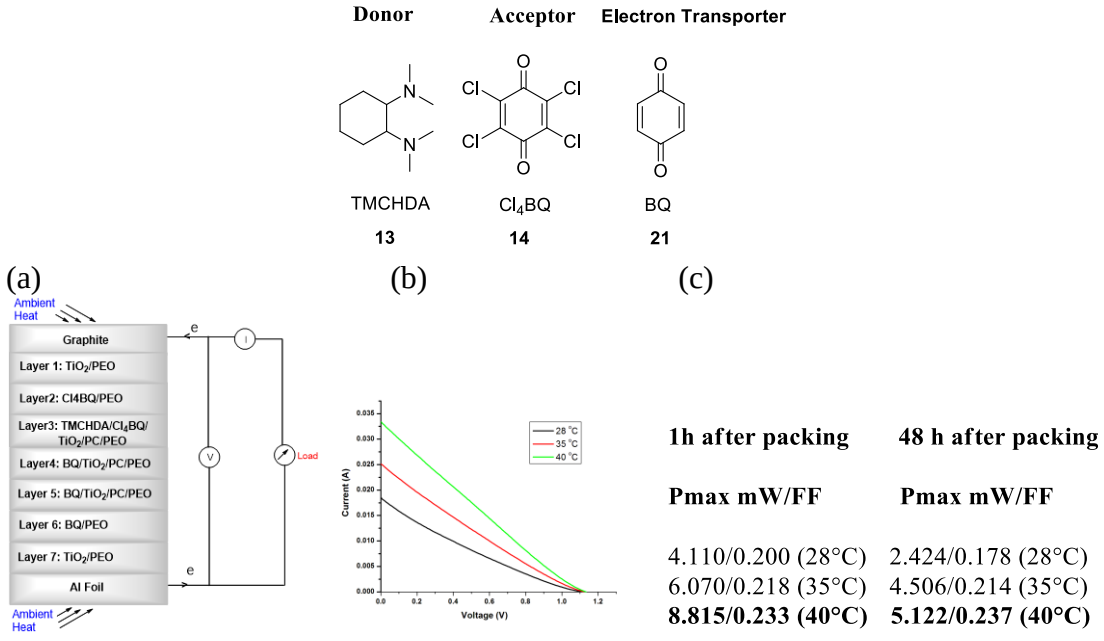


Figure 15. (a) Schematic diagram of cell with seven layer configuration. (b) Representative IV curve after 48 h. (c) Representative IV curve data (Table ES4, entry 9, BQ-ET). (d) Tentative mechanism for electron transport via $D/D^{\cdot+}$ and A^{-}/A exchange reactions.

In this case higher power output was realized initially (Pmax 8.815) but decreased to some extent after 48 h. Finally, we have also constructed the cell by using Cl_4BQ in seven layer configurations as shown in Figure 17.

Figure 17. Seven layer cell using Cl_4BQ in two layers and BQ in three layers

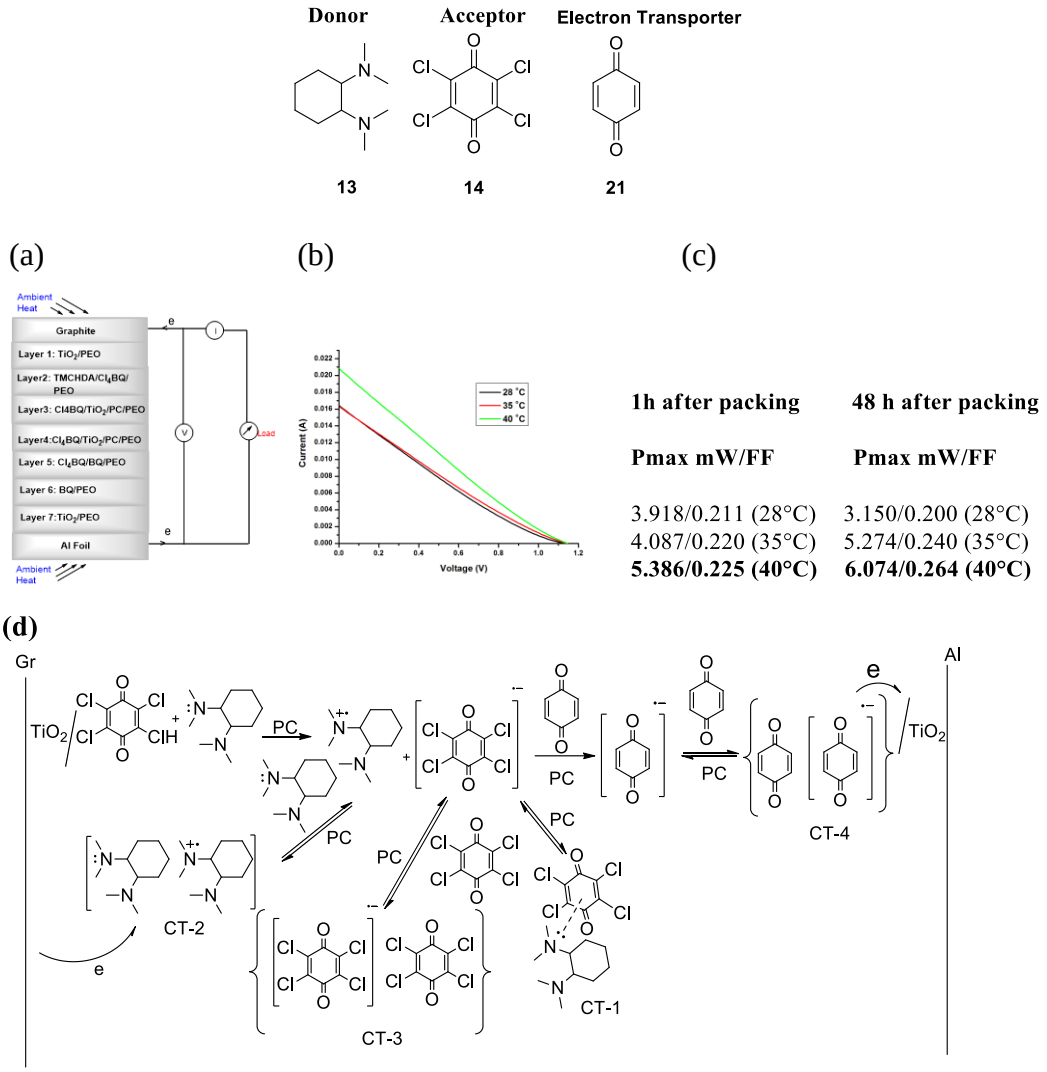


Figure 17. (a) Schematic diagram of cell with seven layer configuration (b) Representative IV curve after 48 h. (c) Representative IV curve data (Table ES4, entry 10, TMCHDA donor). (d) Tentative mechanism for electron transport via $D/D^{\cdot+}$ and A^{-}/A exchange reactions.

Interestingly, in this configuration the initial power output increased (Pmax 6.074 mW) after 48 h. The results obtained here illustrate that the performance of the cells can be improved by using appropriate electron transporters in different configurations. Further, studies using various amines in the configurations as in Figures 16 and 17 would be fruitful in understanding the reactions and electron transport mechanism involved in the functioning of these electrochemical cells.

5.3 Conclusions

We have constructed organic electrochemical cells, based on ground state electron transfer reaction of amine donor and *p*-chloranil acceptor in different configurations. Further efforts to improve the performance of the cells would lead to construction of cells for practical household, grid and automobile applications.

5.4 Experimental Section

5.4.1 General Information

P-Chloranil, *P*-benzoquinone (BQ) and TiO_2 were purchased from Avra chemicals (India). Triphenylamine (TPA), propylene carbonate (PC), ethylene carbonate (EC) and polyethylene oxide (PEO) were purchased from Sigma Aldrich.. 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^1,N^1,N^2,N^2-tetramethylcyclohexylamine was prepared from the literature procedure. Graphite sheet (0.4 mm thickness, 5cm x 5cm, Resistivity, $\rho = 2x10^{-4}$ Ω.m) was purchased from Falcon Graphite Industries, Hyderabad, India. Aluminum foil (0.2 mm thickness, 5 cm x 5 cm, Resistivity, $\rho = 2x10^{-5}$Ω.m) were purchased from Aluminum 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.

5.4.2 Preparation of Electrochemical Cells

Simple solution processing and casting techniques were followed for the construction of the cell device.

Table ES1. Cell Configuration 1 (entry 1)

The PEO (0.75 g) was dissolved in dichloromethane and mixed with TiO_2 (0.05 g) powder. DCM was removed to obtain a paste for coating on Al or graphite foils. After 1 h the

donor amine (0.17 mL)/PC (0.5 mL)/PEO (0.05 g) slurry was prepared and casted above the coated layer on Al and Graphite and dried in air at room temperature overnight. The cell was prepared by sandwiching the coated Al/Gr layers. The rim of the cell prepared in this way was sealed all around using TiO_2/PEO paste, then with commercial adhesive Bondfix (India) and covered with cellophane tape.

Table ES2. Cell Configuration 2 (entry 2)

The PEO (0.05 g) was dissolved in dichloromethane and mixed with TiO_2 (0.5 g) powder. DCM was removed to obtain a paste for coating on Al or Graphite foils. After 1 h Cl_4BQ (0.125 g)/BQ (0.11 g)/PEO (0.05 g) was coated on TiO_2/PEO/Al and TiO_2/PEO/Gr and dried. The donor amine (2 mmol)/PC (0.5 g)/BQ (0.11 g)/TiO_2 (0.25 g) slurry was prepared and casted above the coated layer on Al and Graphite and dried in air at room temperature overnight. The cell was prepared by sandwiching the coated Al/Gr layers. The rim of the cell prepared in this way was sealed all around using TiO_2/PEO paste, then with commercial adhesive Bondfix (India) and covered with cellophane tape.

Table ES2. Cell Configuration 3 (entries 3-5)

The PEO (0.05 g) was dissolved in dichloromethane and mixed with TiO_2 (0.5 g) powder. DCM was removed to obtain a paste for coating on Al or Graphite foils. After 1 h Cl_4BQ (0.250 g)/PEO (0.05 g) was coated on TiO_2/PEO/Al layer and ET (4 mmol)/PEO (0.05 g) was coated on TiO_2/PEO/Gr layer respectively and dried. The donor amine (2 mmol)/PC (0.5 g)/TiO_2 (0.25 g) slurry was prepared and casted above the coated layer on Al and Graphite and dried in air at room temperature overnight. The cell was prepared by sandwiching the coated Al/Gr layers. The rim of the cell prepared in this way was sealed all

around using TiO_2/PEO paste, then with commercial adhesive Bondfix (India) and covered with cellophane tape.

Table ES3. Cell Configuration 4 (entries 6-7)

The PEO (0.05 g) was dissolved in dichloromethane and mixed with TiO_2 (0.5 g) powder. DCM was removed to obtain a paste for coating on Al or Graphite foils. After 1 h TiO_2 (0.5 g)/Cl_4BQ/(0.25 g)/PEO (0.05 g) was coated on TiO_2/PEO/Al layer and TiO_2 (0.5 g)/ET/PC (0.5 g)/PEO (0.05 g) was coated on TiO_2/PEO/Gr layer respectively and dried. The donor amine (1 mmol)/ET (1 mmol)/PC (0.5 g)/PEO (0.05 g) slurry was prepared and heat coated on Al layer and dried in air at room temperature overnight. The cell was prepared by sandwiching the coated Al/Gr layers. The rim of the cell prepared in this way was sealed all around using TiO_2/PEO paste, then with commercial adhesive Bondfix (India) and covered with cellophane tape.

Table ES3. Cell Configuration 5 (entry 8)

The PEO (0.05 g) was dissolved in dichloromethane and mixed with TiO_2 (0.05 g) powder. DCM was removed to obtain a paste for coating on Al or Graphite foils. After 1 h TiO_2(0.5 g)/donor amine (1 mmol)/PEO (0.05 g) slurry was coated on TiO_2/PEO/Al layer and TiO_2(0.5 g)/phthalimide (0.147 g)/PEO (0.05 g) layer was coated on TiO_2/PEO/Gr respectively and dried. The Cl_4BQ (0.25 g)/NMP (1 g)/phthalimide (0.147 g)/PEO (0.05 g) was prepared and heat coated on Al layer and dried in air at room temperature overnight.. The cell was prepared by sandwiching the coated Al/Gr layers. The rim of the cell prepared in this way was sealed all around using TiO_2/PEO paste, then with commercial adhesive Bondfix (India) and covered with cellophane tape.

Table ES4. Cell Configuration 6 (entry 9)

The PEO (0.05 g) was dissolved in dichloromethane and mixed with TiO_2 (0.05 g) powder. DCM was removed to obtain a paste for coating on Al or Graphite foils. After 1 h Cl_4BQ (0.250 g)/ PEO (0.05 g) layer was coated on TiO_2/PEO/Al and BQ (0.11 g)/PEO (0.05 g) layer was coated on TiO_2/PEO/Gr respectively and dried.. The donor amine (1 mmol)/PEO (0.05g) slurry was coated on Cl_4BQ/PEO/Al layer and BQ (0.11 g)/TiO_2 (0.25 g)/PC (0.5 g)/PEO (0.05 g)) layer coated on BQ/PEO/Gr layer and dried. The BQ (0.11 g)/TiO_2 (0.25 g)/PC (0.5 g)/PEO (0.05 g)) layer also coated on amine/PEO/Al and dried in air at room temperature overnight. The cell was prepared by sandwiching the coated Al/Gr layers. The rim of the cell prepared in this way was sealed all around using TiO_2/PEO paste, then with commercial adhesive Bondfix (India) and covered with cellophane tape.

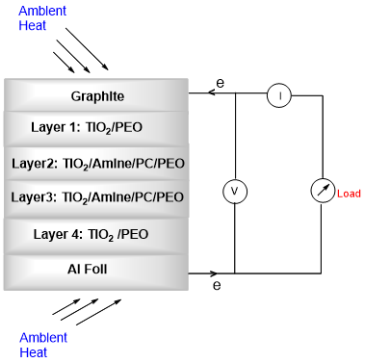
Table ES4. Cell Configuration 7 (entry 10)

The PEO (0.05 g) was dissolved in dichloromethane and mixed with TiO_2 (0.05 g) powder. DCM was removed to obtain a paste for coating on Al or Graphite foils. After 1 h donor amine (0.17 g)/Cl_4BQ (0.125 g)/PEO (0.05 g) layer was coated on TiO_2/PEO/Al and BQ (0.11 g)/PEO (0.05 g) layer was coated on TiO_2/PEO/Gr respectively and dried. The Cl_4BQ (0.250 g)/TiO_2 (0.25 g)/PC (0.5 g)/PEO (0.05 g) was coated on donor amine/Cl_4BQ/PEO/Al layer and Cl_4BQ (0.250 g)/BQ (0.11 g)/PEO (0.05 g) layer coated on BQ/PEO/Gr layer and dried. The Cl_4BQ (0.250 g)/TiO_2 (0.25 g)/PC (0.5 g)/PEO (0.05 g) layer also coated on Cl_4BQ /TiO_2/PC/PEO layer and dried in air at room temperature overnight. The cell was prepared by sandwiching the coated Al/Gr layers. The rim of the cell

prepared in this way was sealed all around using TiO_2/PEO paste, then with commercial adhesive Bondfix (India) and covered with cellophane tape.

Table ES1. Cell Experiments: Four layer cell by using TMCHDA without Cl_4BQ

Cell Configuration 1

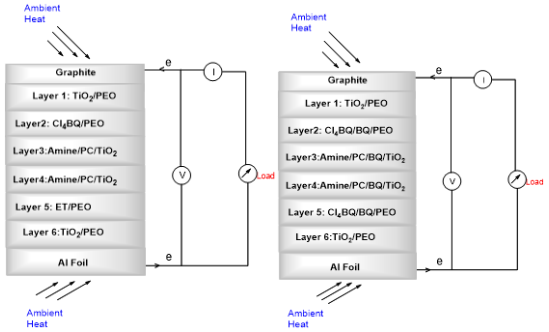


(entry 1)

Entry	Gr/Layers/Al	Time after packing	T °C	Voc (V)	Isc (mA)	Vmax (V)	Imax (mA)	Pmax (mW)	Fill Factor
1	Gr---------- Layer1: TiO_2(0.75g) + PEO(0.05g) Layer2: TiO_2(0.5g) + TMCHDA(0.17ml)+ PC(0.5ml) + PEO(0.05g)+ Layer3: TiO_2(0.5g) + TMCHDA (0.17ml)+ PC(0.5ml) + PEO(0.05g)+ Layer4: TiO_2(0.75g) + PEO(0.05g) Al----------	1 h	28 °C	0.685	0.877	0.348	0.452	0.157	0.262
			35 °C	0.634	1.056	0.338	0.530	0.179	0.268
			40 °C	0.615	1.069	0.346	0.538	0.185	0.283
		48 h	28 °C	0.649	0.956	0.358	0.470	0.168	0.271
			35 °C	0.638	1.224	0.361	0.581	0.209	0.269
			40 °C	0.632	1.284	0.356	0.622	0.221	0.272

Table ES2. Cell Experiments : Six layer cells with TMCHDA, Cl_4BQ and electron transporters

Cell Configuration 2, 3



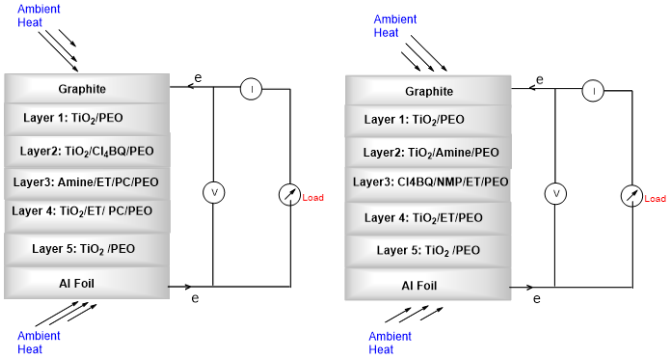
(entry 2) (entries 3-5)

Entry	Gr/Layers/Al	Time after packing	T °C	Voc (V)	Isc (mA)	Vmax (V)	Imax (mA)	Pmax (mW)	Fill Factor
2	Gr---------- Layer1:TiO_2(0.5g) + PEO(0.05g) Layer2: Cl_4BQ(0.125g)+BQ(0.11g)+PEO(0.05g) Layer3: TMCHDA (0.34g)+ PC (0.5g)+ BQ(0.11g) TiO_2 (0.25g) Layer4: : TMCHDA (0.34g)+ PC (0.5g)+ BQ(0.11g) TiO_2 (0.25g Layer5: Cl_4BQ(0.125g)+BQ(0.11g)+PEO(0.05g) Layer6: TiO_2(0.5g) + PEO(0.05g) Al----------	1 h	28 °C	0.802	10.19	0.257	4.117	1.057	0.129
			35 °C	0.802	10.31	0.310	4.118	1.276	0.154
			40 °C	0.810	14.470	0.257	6.148	1.580	0.135
		48 h	28 °C	0.802	3.847	0.534	1.506	0.533	0.173
			35 °C	0.800	4.906	0.322	2.055	0.661	0.169
			40 °C	0.806	7.585	0.323	2.828	0.912	0.149
3	Gr---------- Layer1: TiO_2(0.5g) + PEO(0.05g) Layer2: Cl_4BQ(0. 25g)+ PEO(0.05g) Layer3: TMCHDA (0.34g)+ PC (0.5g)+ TiO_2(0.25g) Layer4: TMCHDA (0.34g)+ PC (0.5g) + TiO_2 (0.25g) Layer5: BQ(0.44g)+ PEO(0.05g) Layer6: TiO_2(0.5g) + PEO(0.05g) Al----------	1 h	28 °C	0.249	5.253	0.119	2.748	0.325	0.249
			35 °C	0.239	5.601	0.101	3.335	0.335	0.250
			40 °C	0.235	5.620	0.235	2.990	0.701	0.532
		48 h	28 °C	0.464	1.682	0.221	0.819	0.180	0.231
			35 °C	0.512	1.752	0.220	0.900	0.197	0.221
			40 °C	0.446	2.153	0.222	1.050	0.233	0.243

4	Gr---------- Layer1: TiO_2(0.5g) + PEO(0.05g) Layer2: Cl_4BQ(0. 25g)+ PEO(0.05g) Layer3: TMCHDA (0.34g)+ PC (0.5g)+ TiO_2(0.25g) Layer4: TMCHDA (0.34g)+ PC (0.5g)+ TiO_2 (0.25g) Layer5: Me_2SO_2(0.376g)+ PEO(0.05g) Layer6: TiO_2(0.5g) + PEO(0.05g) Al----------	1 h	28 ºC	0.726	2.821	0.326	1.279	0.417	0.204
			35 ºC	0.731	5.943	0.276	2.750	0.759	0.175
			40 ºC	0.735	5.729	0.317	2.362	0.748	0.178
		48 h	28 ºC	0.690	3.844	0.291	1.731	0.503	0.190
			35 ºC	0.696	5.623	0.297	2.567	0.762	0.195
			40 ºC	0.696	7.000	0.294	3.272	0.960	0.197
5	Gr---------- Layer1: TiO_2(0.5g) + PEO(0.05g) Layer2: Cl_4BQ(0. 25g)+ PEO(0.05g) Layer3: TMCHDA (0.34g)+ PC(0.5g)+ TiO_2(0.25g) Layer4: TMCHDA $_2$(0.34g)+ PC(0.5g)+ TiO_2 (0.25 g) Layer5: MeN-phthalimide (0.644g)+ PEO(0.05g) Layer6: TiO_2(0.5g) + PEO(0.05g) Al----------	1 h	28 ºC	0.836	5.962	0.343	2.751	0.944	0.190
			35 ºC	0.840	8.899	0.357	4.030	1.439	0.192
			40 ºC	0.849	11.650	0.352	5.386	1.897	0.192
		4 8h	28 ºC	0.725	7.254	0.292	3.275	0.956	0.182
			35 ºC	0.724	7.287	0.303	3.413	1.034	0.196
			40 ºC	0.726	8.921	0.326	4.032	1.315	0.203

Table ES3. Cell Experiments: Five layer cells with TMCHDA, Cl_4BQ and electron transporters

Cell Configuration 4, 5

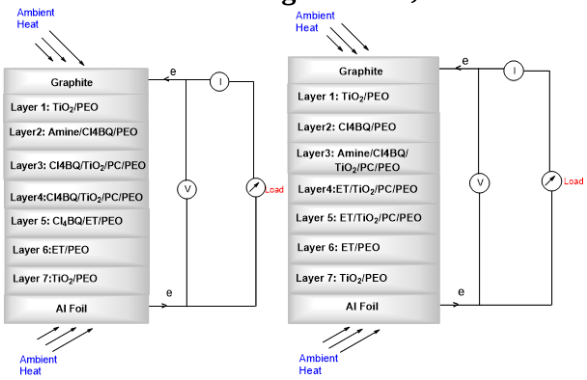


(entries 6-7) (entry 8)

Entry	Cell Configuration	Time after packing	T °C	Voc (V)	Isc (mA)	Vmax (V)	Imax (mA)	Pmax (mW)	Fill Factor
6	Gr---------- Layer1: TiO_2(0.5g) + PEO(0.05g) Layer2: TiO_2(0.5g) + Cl_4BQ(0.25g)+ PEO(0.05g Layer3: TMCHDA (0.17g))+BQ(0.11g)+PC(0.5g) + PEO(0.05g)) Layer4 TiO_2(0.5g)+ BQ(0.44g)+ PC(0.5g)+PEO(0.05g) Layer5: TiO_2(0.5g) + PEO(0.05g) Al----------	1 h	28 °C	1.046	14.000	0.525	7.312	3.837	0.262
			35 °C	1.068	15.840	0.583	8.744	5.094	0.301
			40 °C	1.082	16.370	0.607	9.177	5.566	0.314
		48 h	28 °C	1.069	3.931	0.527	2.132	1.124	0.268
			35 °C	1068	5.488	0.505	2.445	1.488	0.254
			40 °C	1.071	5.828	0.516	3.367	1.736	0.278
7	Gr---------- Layer1: TiO_2(0.5g) + PEO(0.05g) Layer2: TiO_2(0.5g) + Cl_4BQ(0.25g)+ PEO(0.05g Layer3: TMCHDA (0.17g))+Me_2SO_2 (0.094g)+PC(0.5g)+ PEO(0.05g)) Layer4 TiO_2(0.5g)+ Me_2SO_2 (0.188g))+PC(0.5g)+PEO(0.05g) Layer5: TiO_2(0.5g) + PEO(0.05g) Al----------	1 h	28 °C	1.086	33.600	0.564	16.690	9.416	0.258
			35 °C	1.094	31.980	0.598	19.370	11.590	0.331
			40 °C	1.093	35.780	0.576	21.410	12.340	0.316
		48 h	28 °C	0.980	9.206	0.491	5.120	2.409	0.267
			35 °C	0.969	11.740	0.602	4.832	2.909	0.256
			40 °C	0.976	10.830	0.643	5.079	3.263	0.309
8	Gr---------- Layer1: TiO_2(0.5g) + PEO(0.05g) Layer2: TiO_2(0.5g) + TMCHDA (0.17g)+PEO(0.05g Layer3: Cl_4BQ(025g)+NMP(1g) + Pthalamide(0.147)+PEO(0.05g)) Layer4 TiO_2(0.5g)+ Pthalamide(0.147)+PEO(0.05g) Layer5: TiO_2(0.5g) + PEO(0.05g) Al----------	1 h	28 °C	0.985	15.550	0.433	8.903	3.853	0.252
			35 °C	0.978	15.340	0.451	9.434	4.257	0.284
			40 °C	0.985	15.920	0.450	10.080	4.605	0.294
		48 h	28 °C	1.062	14.640	0.443	7.367	3.263	0.210
			35 °C	1.065	14.180	0.467	7.990	3.732	0.247
			40 °C	1.062	14.680	0.528	8.155	4.139	0.266

Table ES4. Cell Experiments: Seven layer cells with TMCHDA, Cl_4BQ and BQ electron transporter

Cell Configuration 6,7



(entry 9) (entry 10)

Entry	Cell Configuration	Time after packing	T °C	Voc (V)	Isc (mA)	Vmax (V)	Imax (mA)	Pmax (mW)	Fill Factor
9	Gr---------- Layer1: TiO_2(0.5g) + PEO(0.05g) Layer2: Cl_4BQ(0.25g)+PEO(0.05g) Layer3 TMCHDA (0.17g)+ PEO(0.05g) Layer4: BQ(0.11g +TiO_2(0.25g) + PC(0.5g)+PEO(0.05g) Layer5: : BQ(0.11g +TiO_2(0.25g) + PC(0.5g)+PEO(0.05g) Layer6: BQ(0.2g+)+ PEO(0.05g) Layer7: TiO_2(0.5g+)+ PEO(0.05g) Al----------	1 h	28 °C	1.115	18.46	0.489	8.406	4.110	0.200
			35 °C	1.126	25.11	0.510	12.070	6.070	0.218
			40 °C	1.134	33.38	0.529	16.680	8.815	0.233
		48 h	28 °C	1.116	12.17	0.443	5.478	2.424	0.178
			35 °C	1.122	18.78	0.465	9.7	4.506	0.214
			40 °C	1.116	19.38	0.487	10.5	5.122	0.237
10	Gr---------- Layer1: TiO_2(0.5g) + PEO(0.05g) Layer2: TMCHDA (0.17 g)+ Cl_4BQ(0.25g)+ PEO(0.05g) Layer3: Cl_4BQ(0.25g +TiO_2(0.25g) + PC(0.5g)+PEO(0.05g) Layer4: Cl_4BQ(0.25g +TiO_2(0.25g) + PC(0.5g)+PEO(0.05g Layer5: Cl_4BQ(0.1g) + BQ(0.1g)+PEO(0.05g) Layer6: BQ(0.2g+)+ PEO(0.05g) Layer7: TiO_2(0.5g+)+ PEO(0.05g) Al----------	1 h	28 °C	1.131	16.43	0.48	8.041	3.918	0.211
			35 °C	1.141	16.28	0.512	7.986	4.087	0.22
			40 °C	1.147	20.83	0.508	10.6	5.386	0.225
		48 h	28 °C	1.146	13.77	0.45	7.003	3.15	0.2
			35 °C	1.15	19.12	0.498	10.58	5.274	0.24
			40 °C	1.147	20.07	0.54	11.24	6.074	0.264

5.5 References

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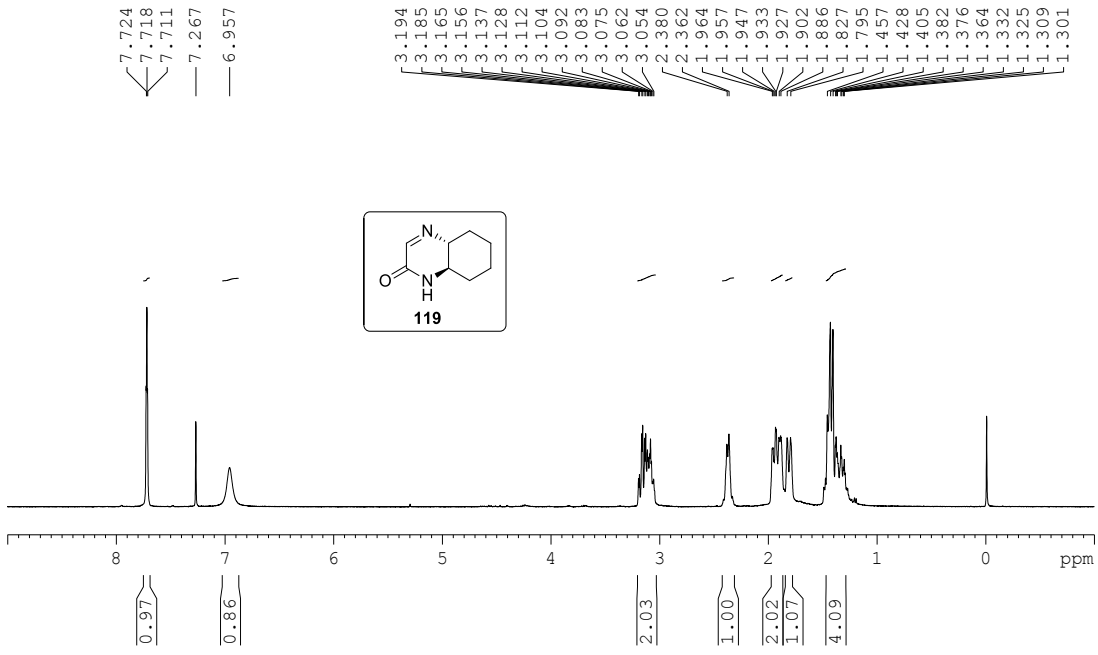
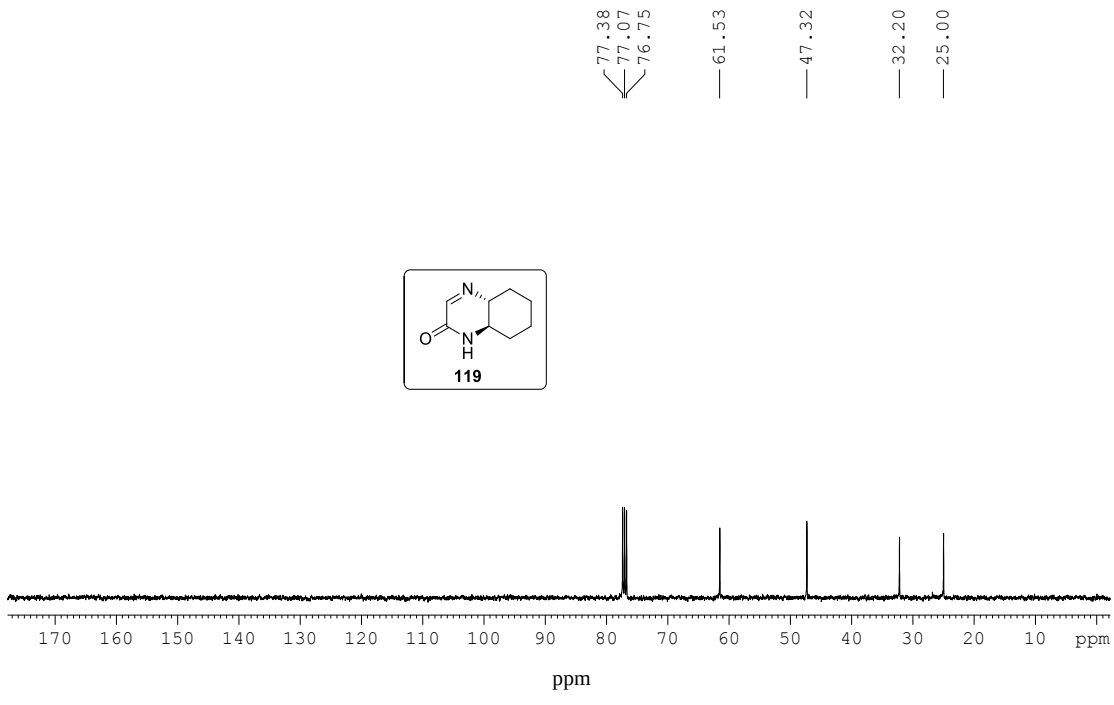
Appendix I

(Representative Spectra)

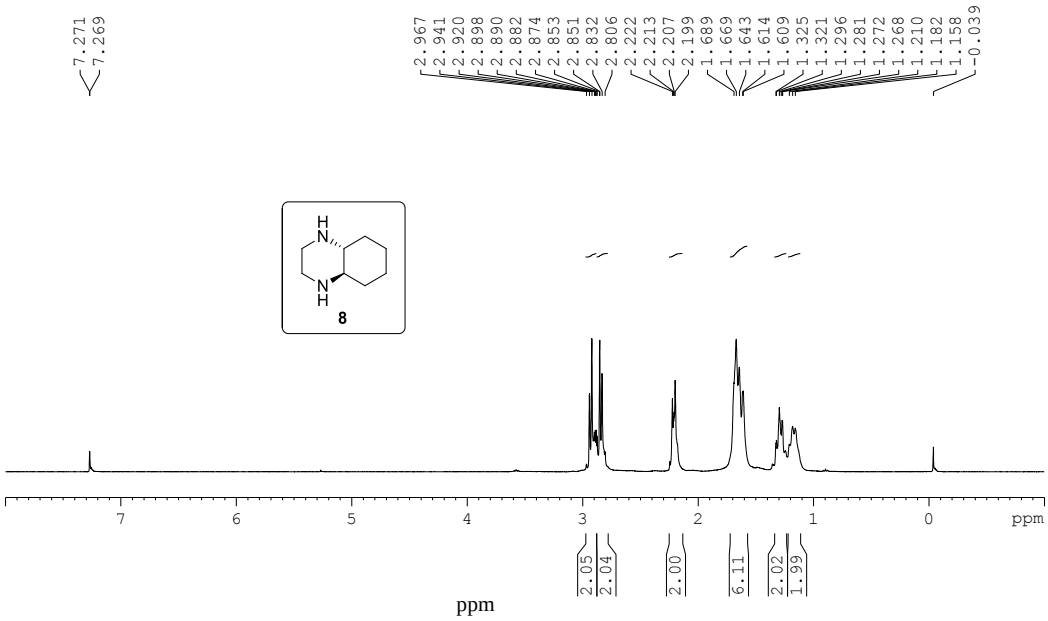
Spectrum No. 1 (Chapter 1, Section 1.2.2), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$) at 25 °C



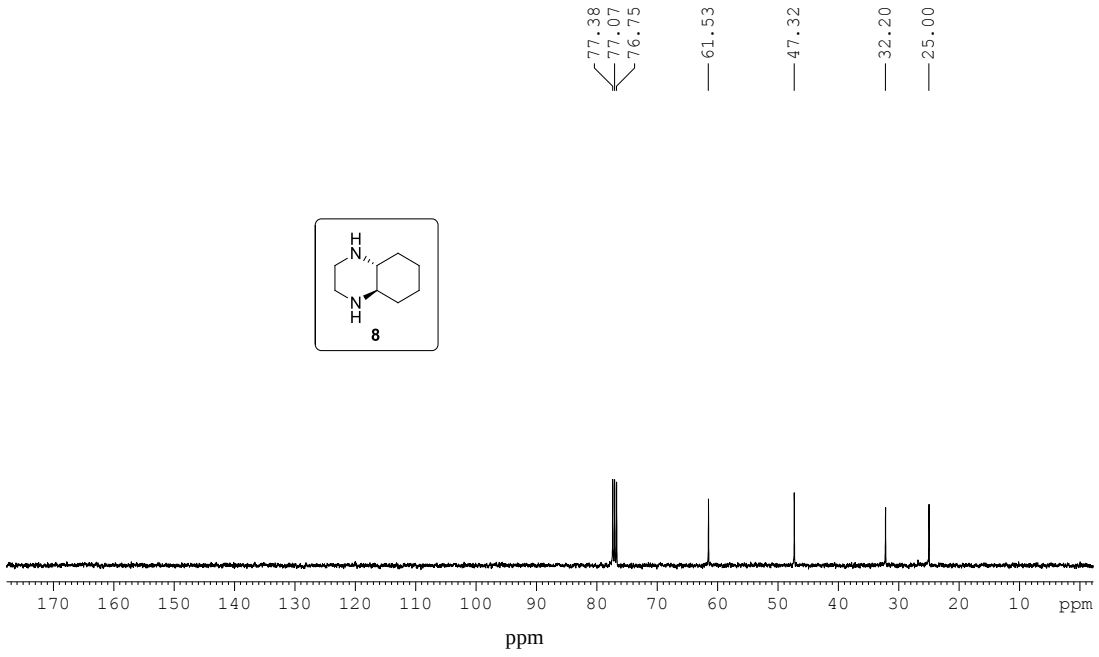
Spectrum No. 2 (Chapter 1, Section 1.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$) at 25 °C



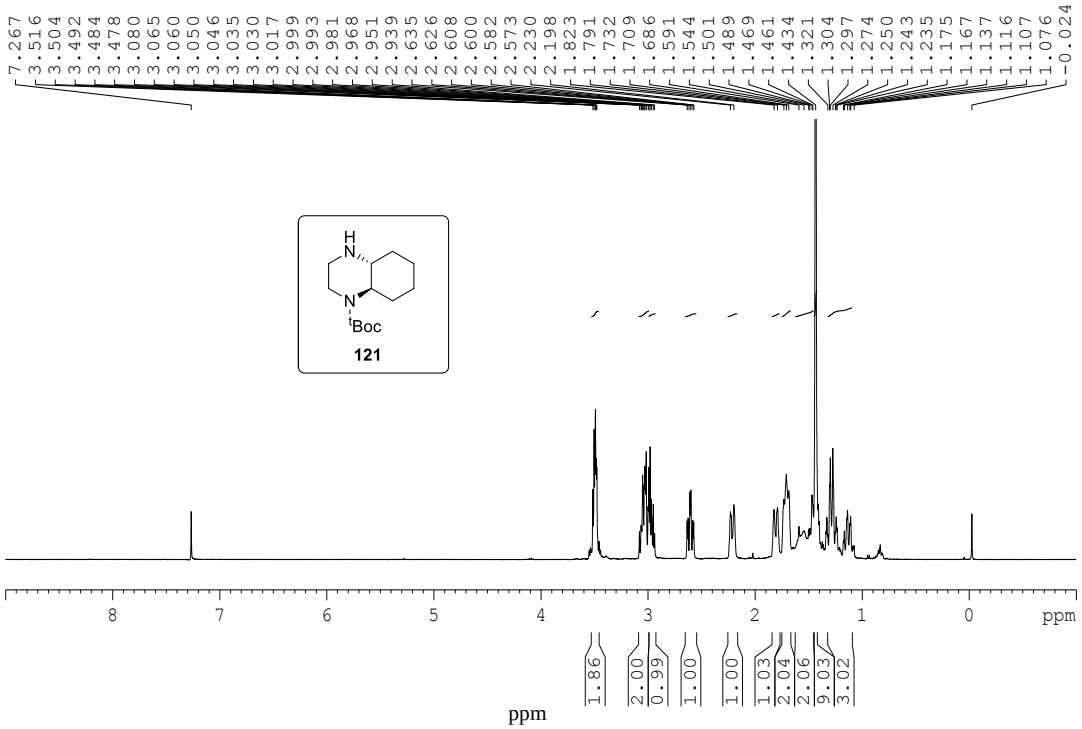
Spectrum No. 3 (Chapter 1, Section 1.2.1), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



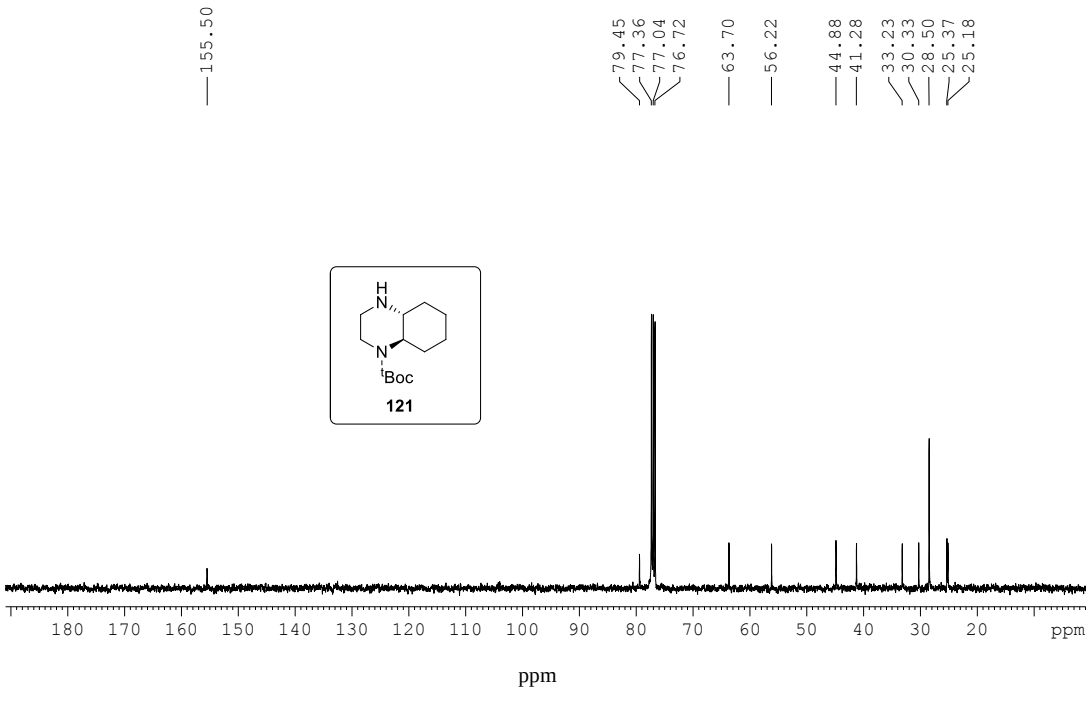
Spectrum No. 4 (Chapter 1, Section 1.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



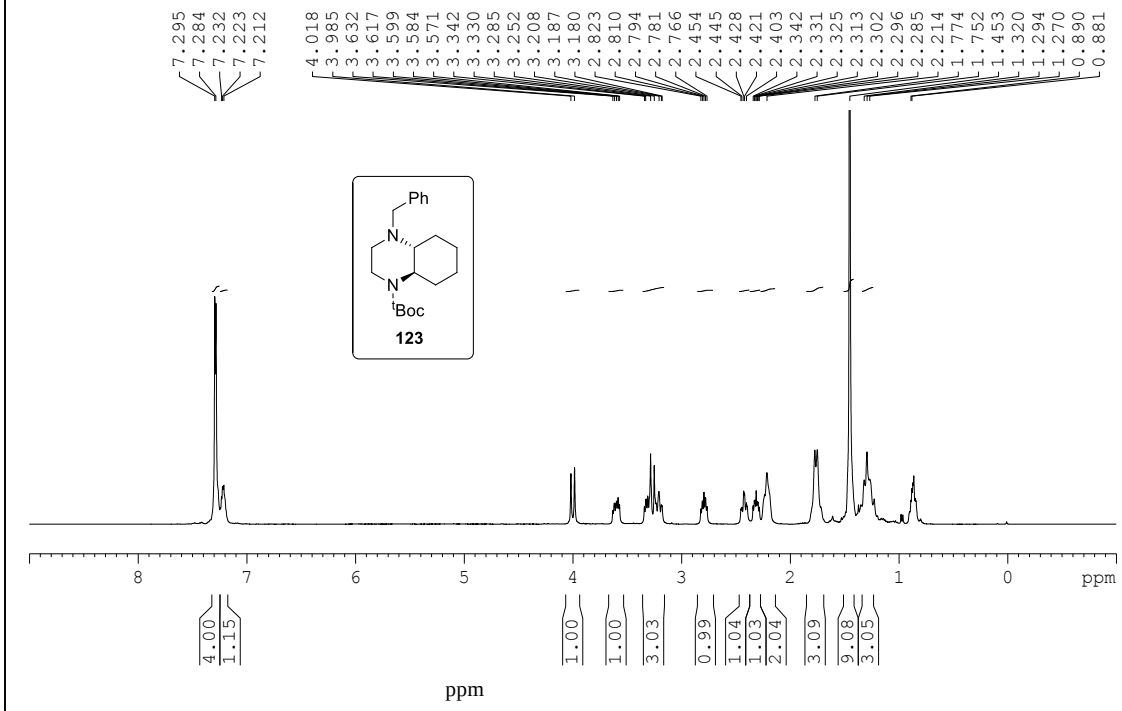
Spectrum No. 5 (Chapter 1, Section 1.2.2), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



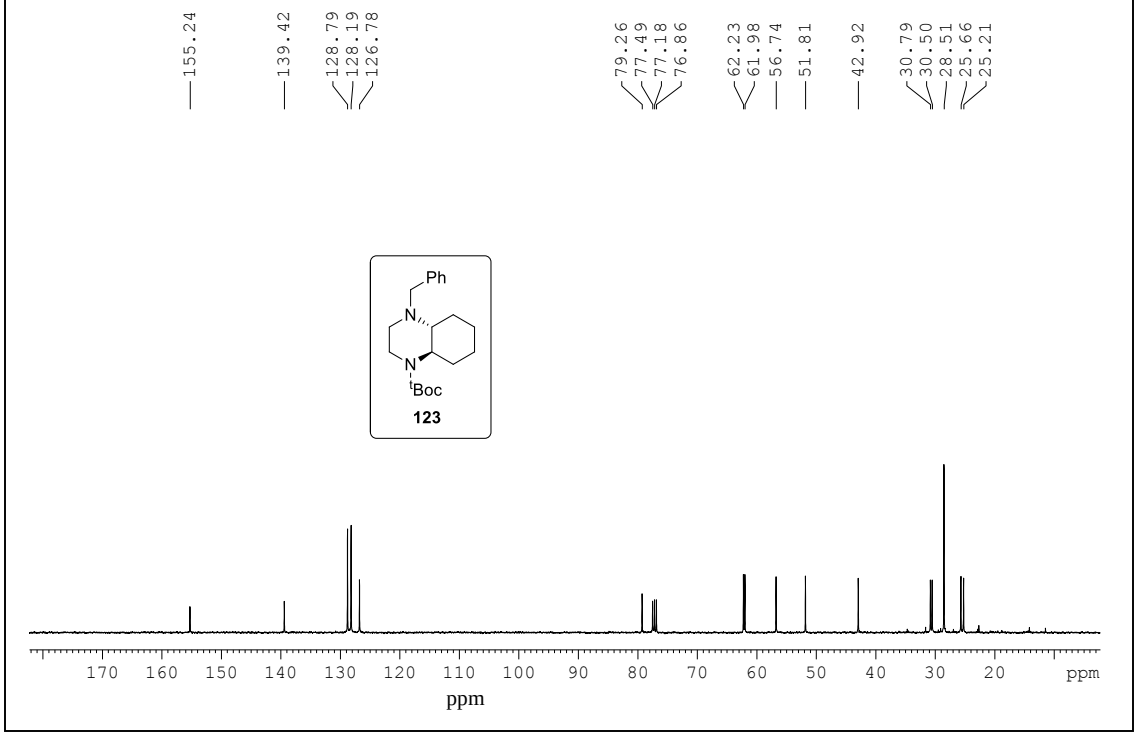
Spectrum No. 6 (Chapter 1, Section 1.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



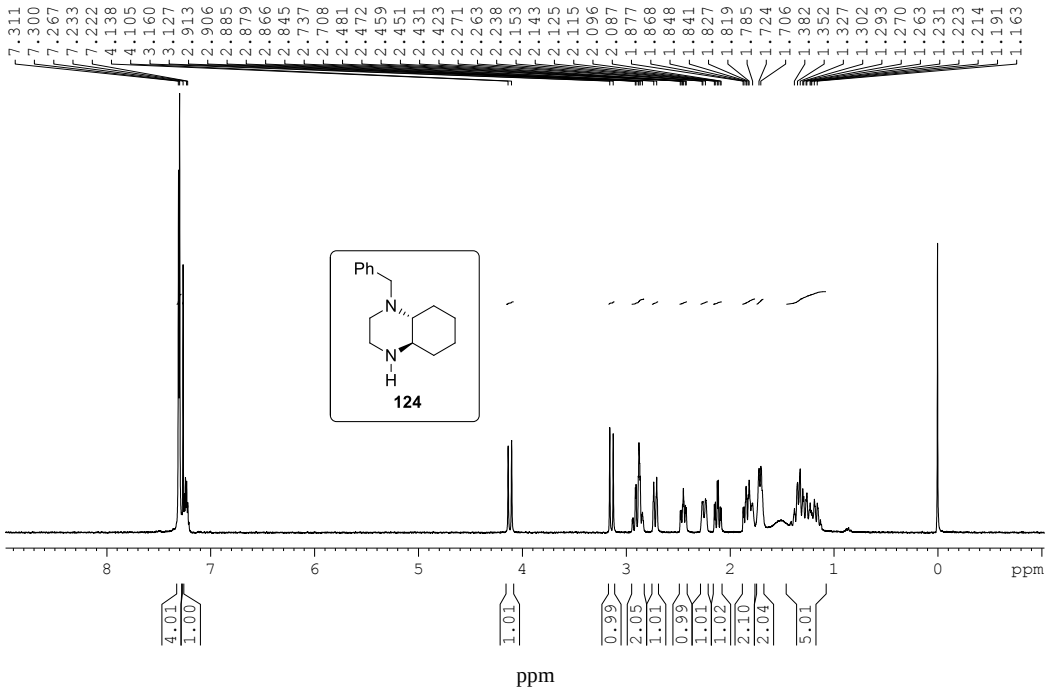
Spectrum No. 7 (Chapter 1, Section 1.1.1), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



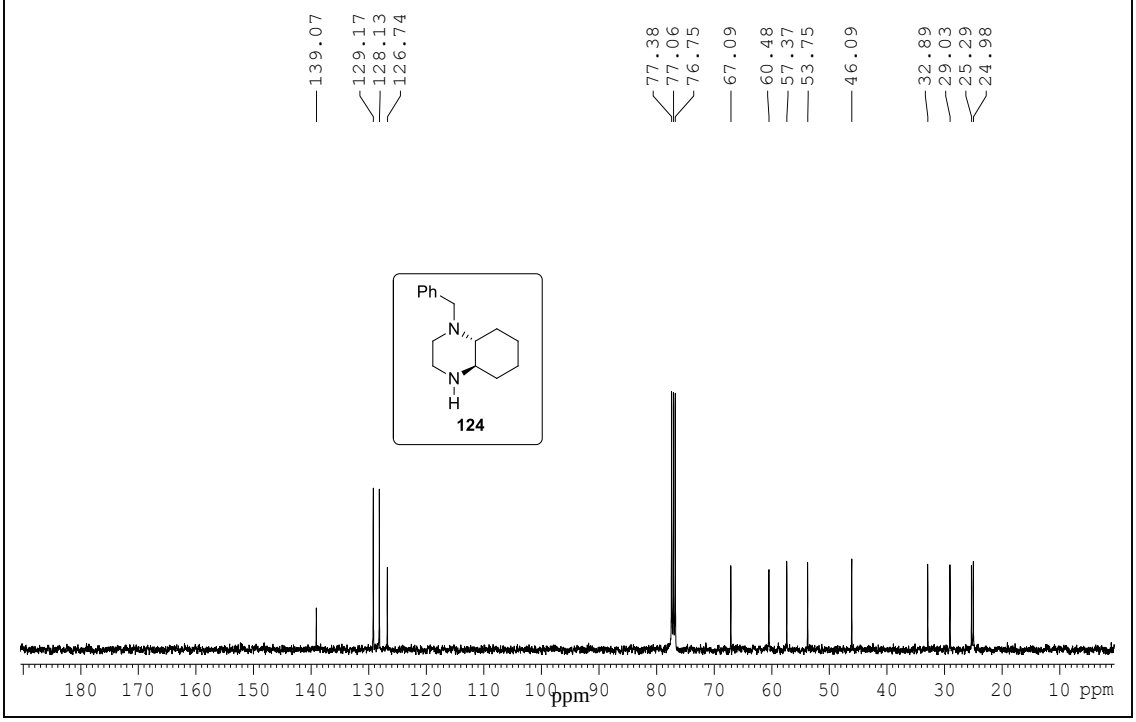
Spectrum No. 8 (Chapter1, Section 1.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



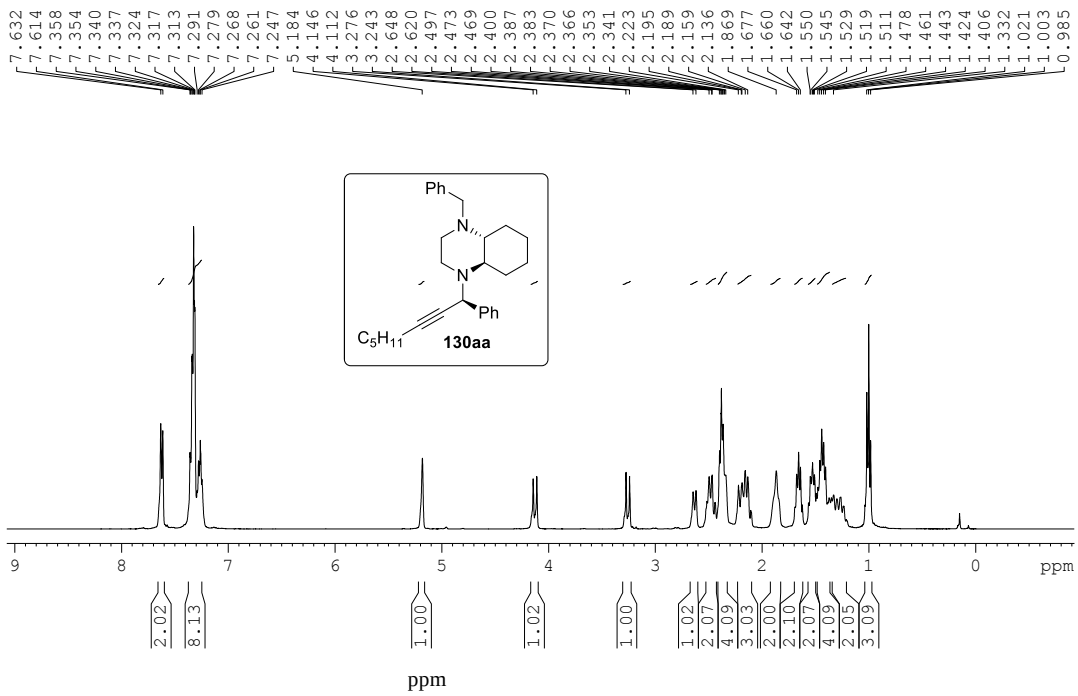
Spectrum No. 9 (Chapter 1, Section 1.2.2), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



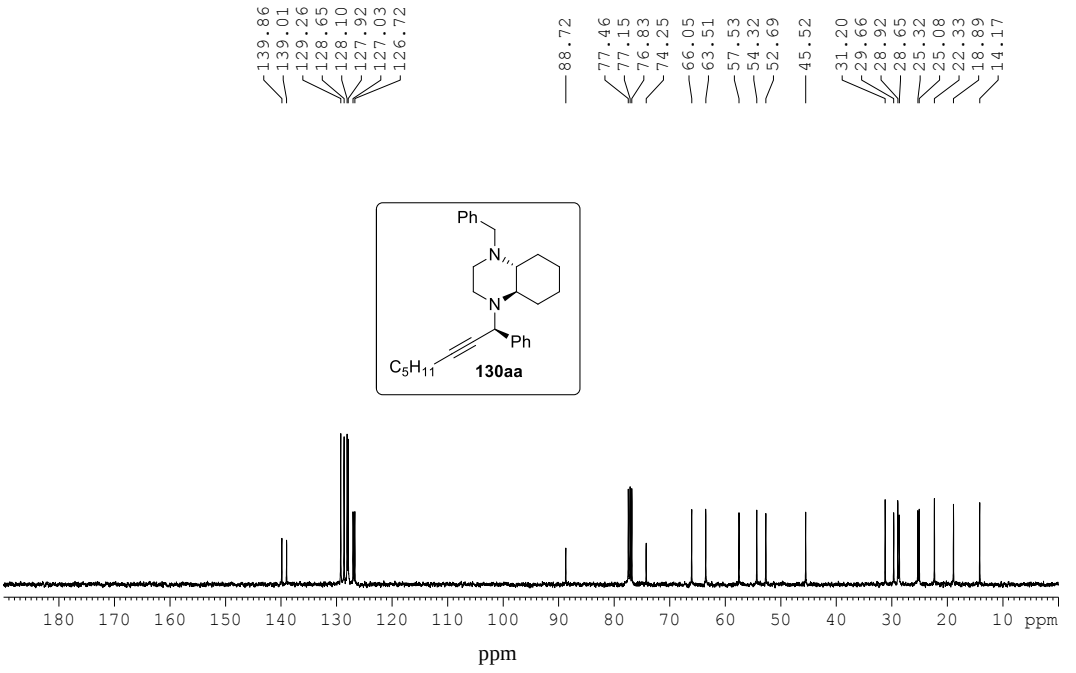
Spectrum No. 10 (Chapter 1, Section 1.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



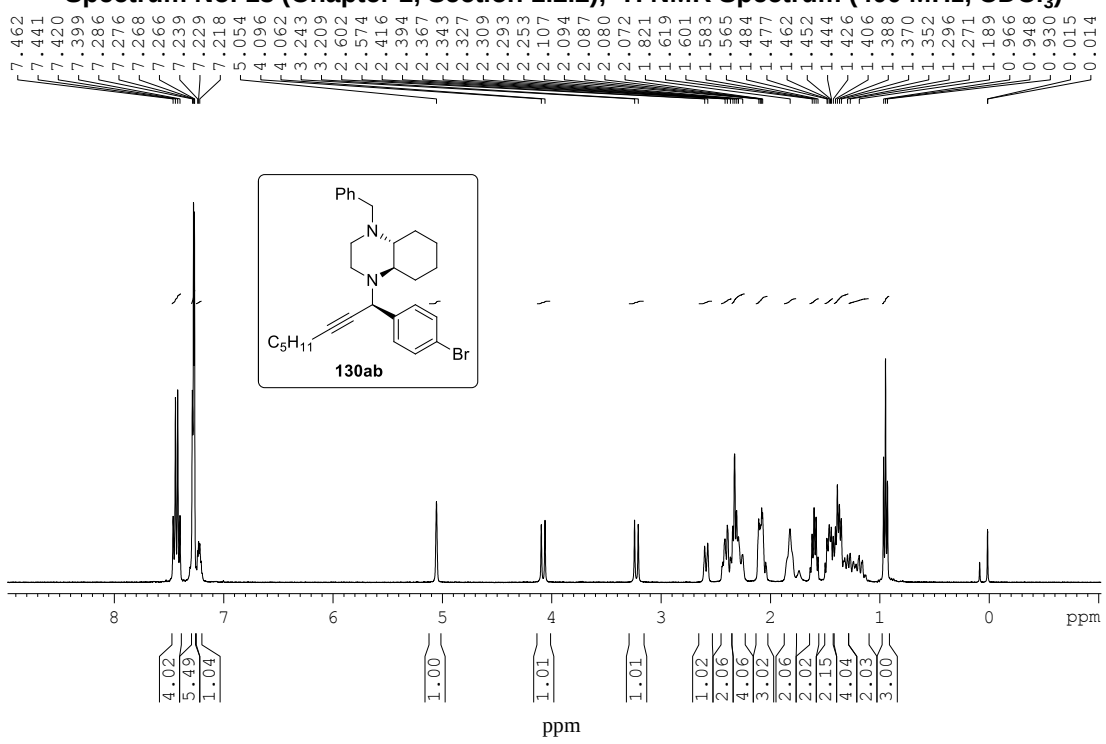
Spectrum No. 11 (Chapter 1, Section 1.2.2), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



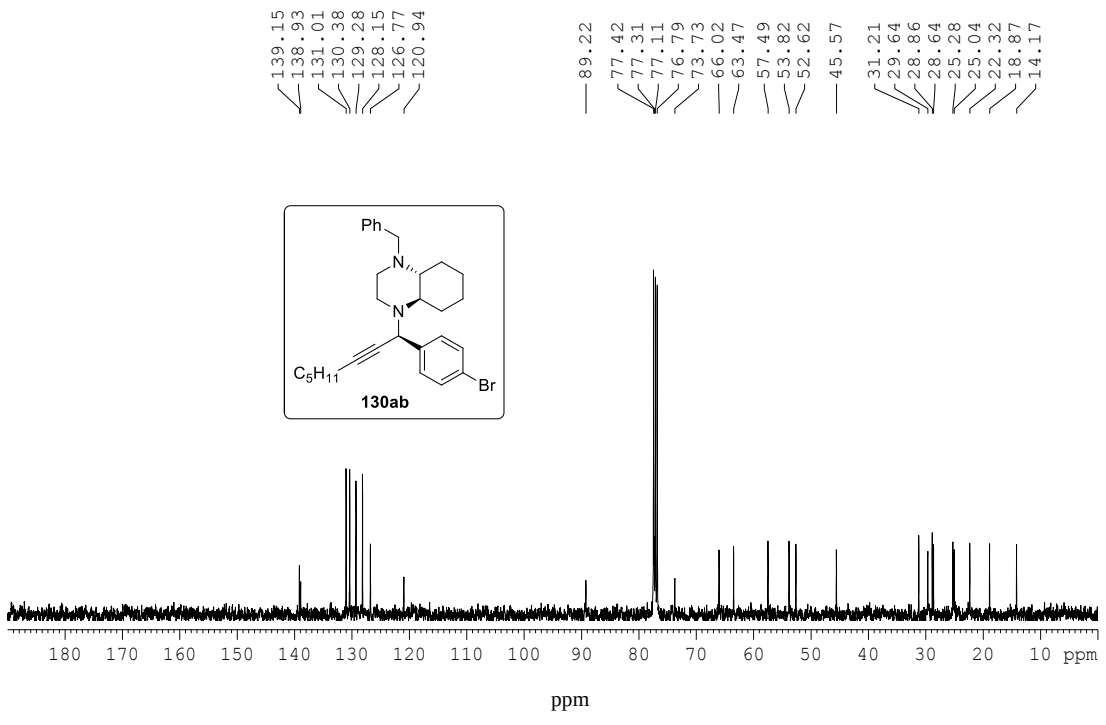
Spectrum No. 12 (Chapter 1, Section 1.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



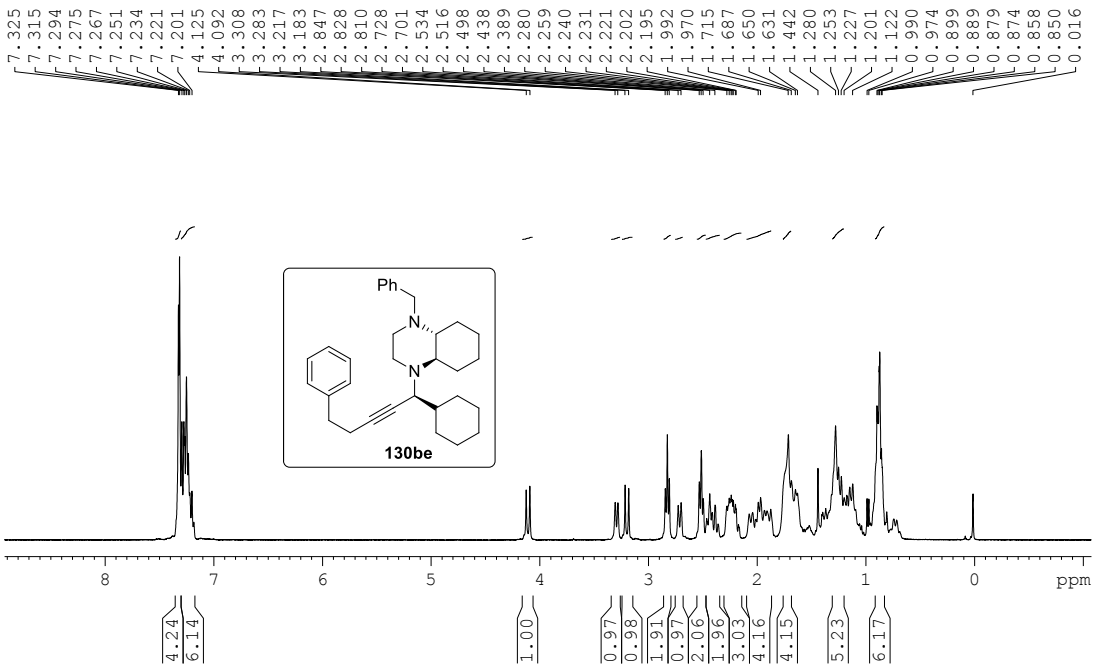
Spectrum No. 13 (Chapter 1, Section 1.2.2), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



Spectrum No. 14 (Chapter 1, Section 1.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)

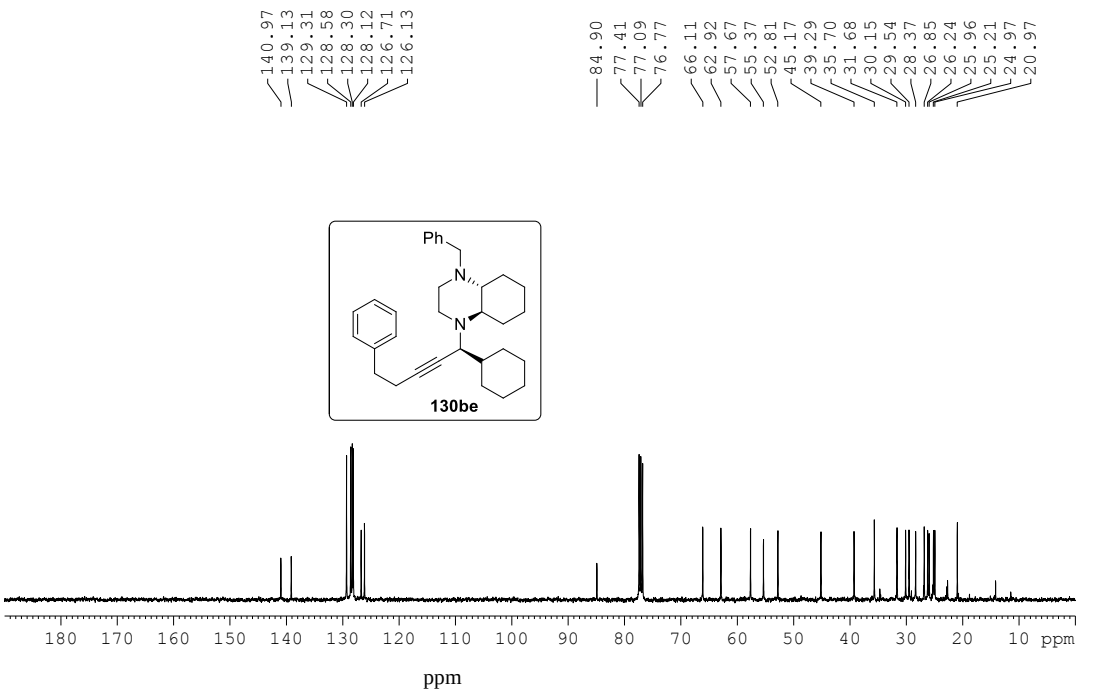


Spectrum No. 15 (Chapter1, Section 1.2.2), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



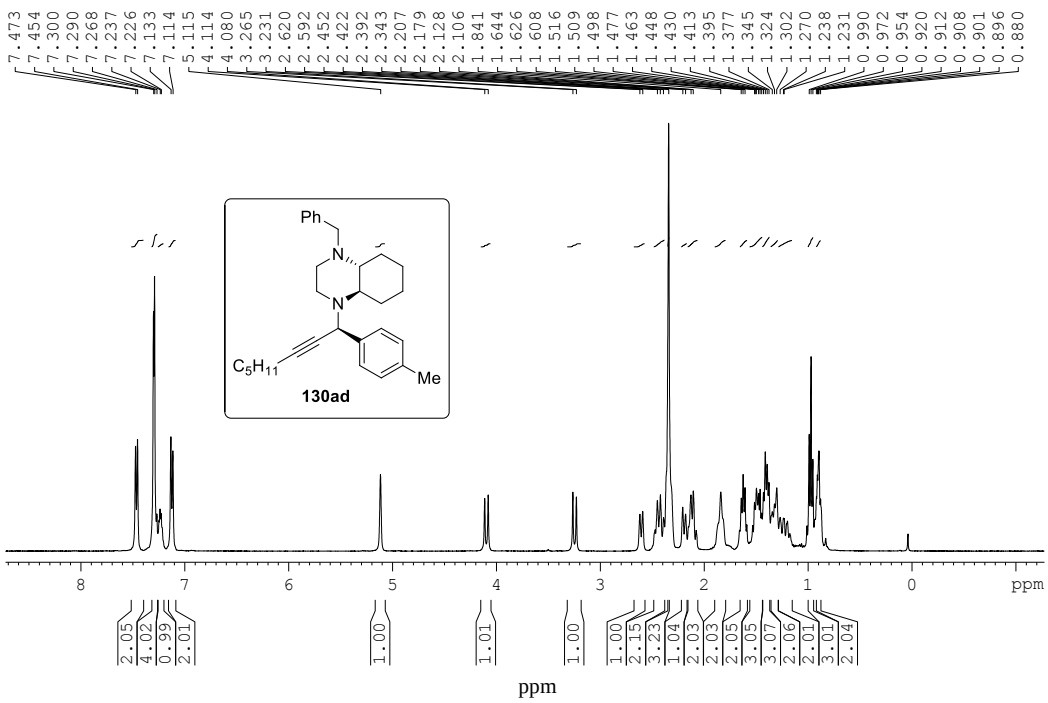
ppm

Spectrum No. 16 (Chapter 1, Section 1.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)

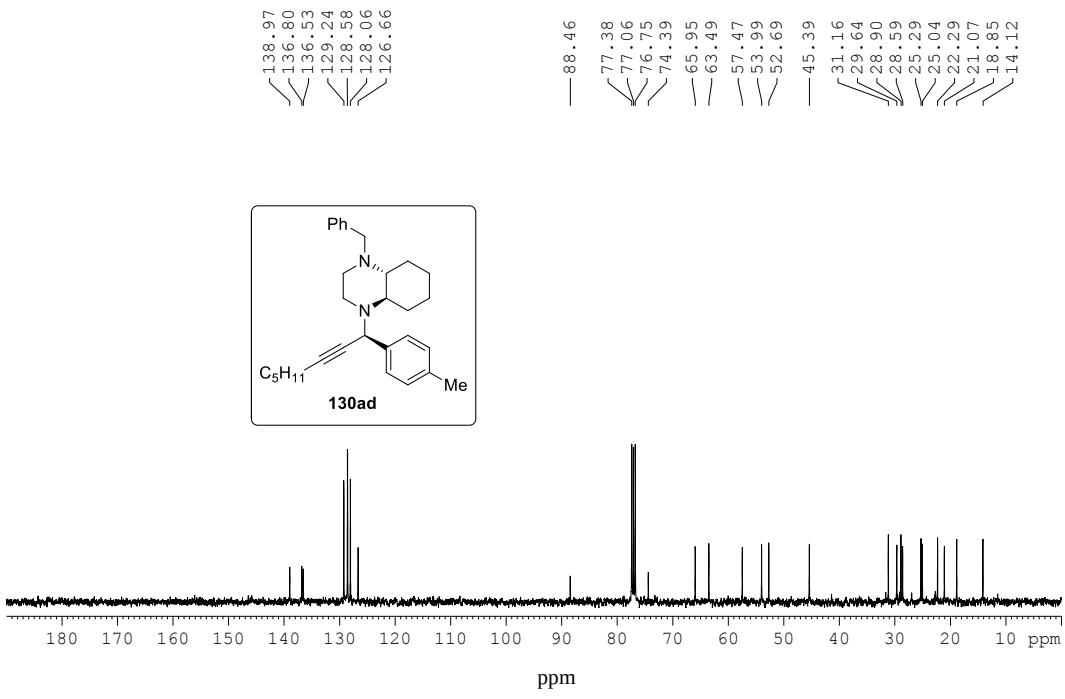


ppm

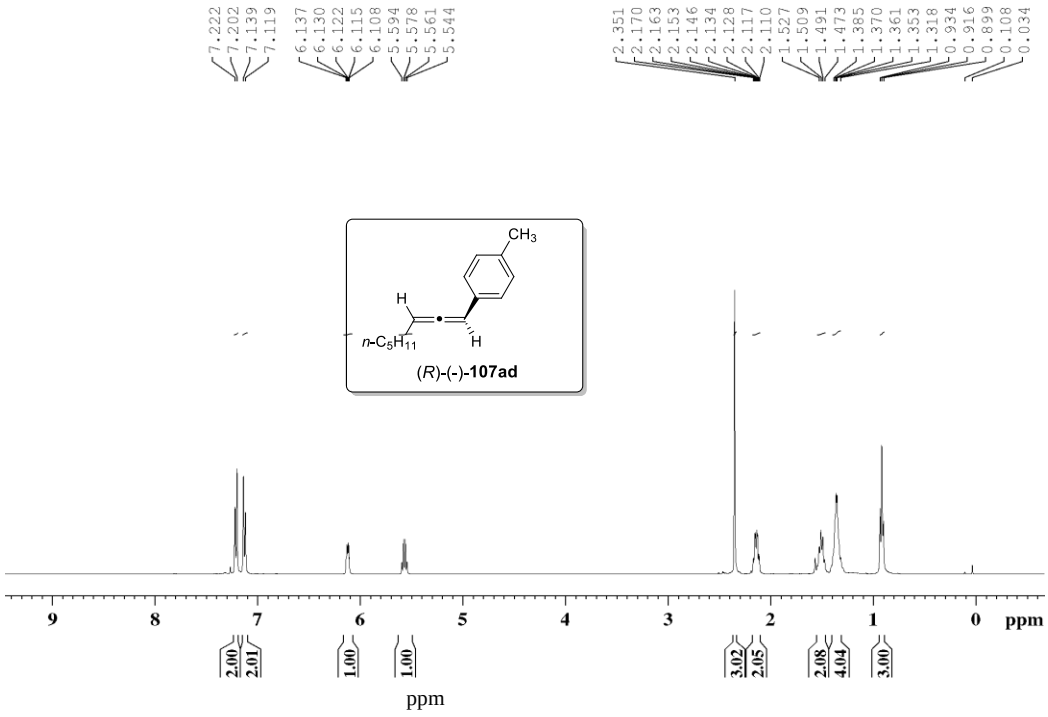
Spectrum No. 17 (Chapter 1, Section 1.2.2), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



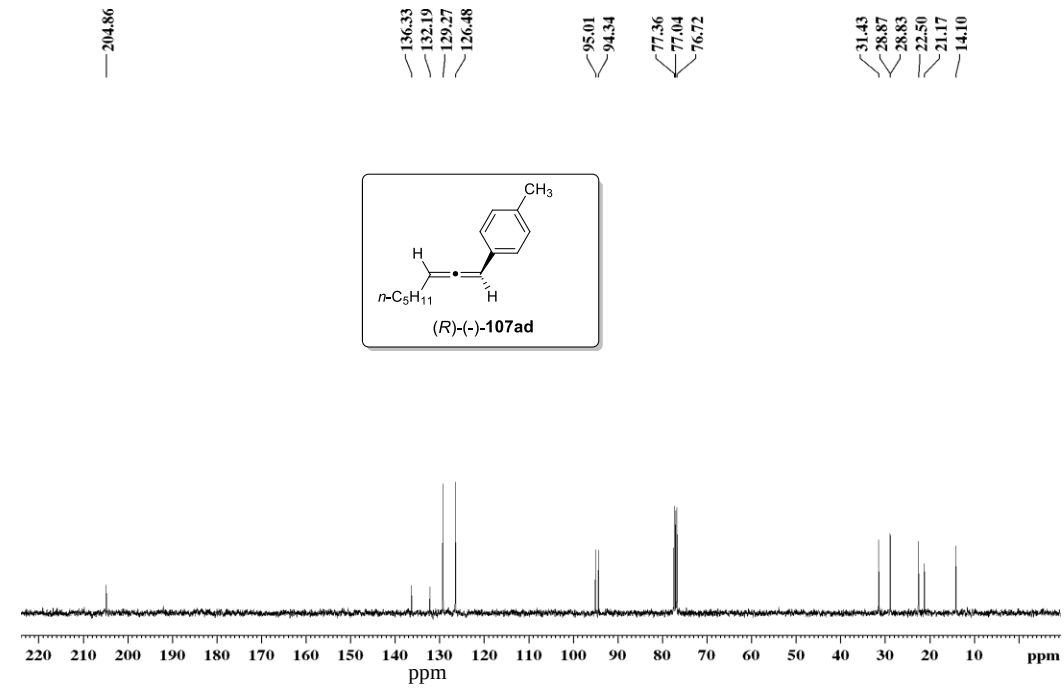
Spectrum No. 18 (Chapter 1, Section 1.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



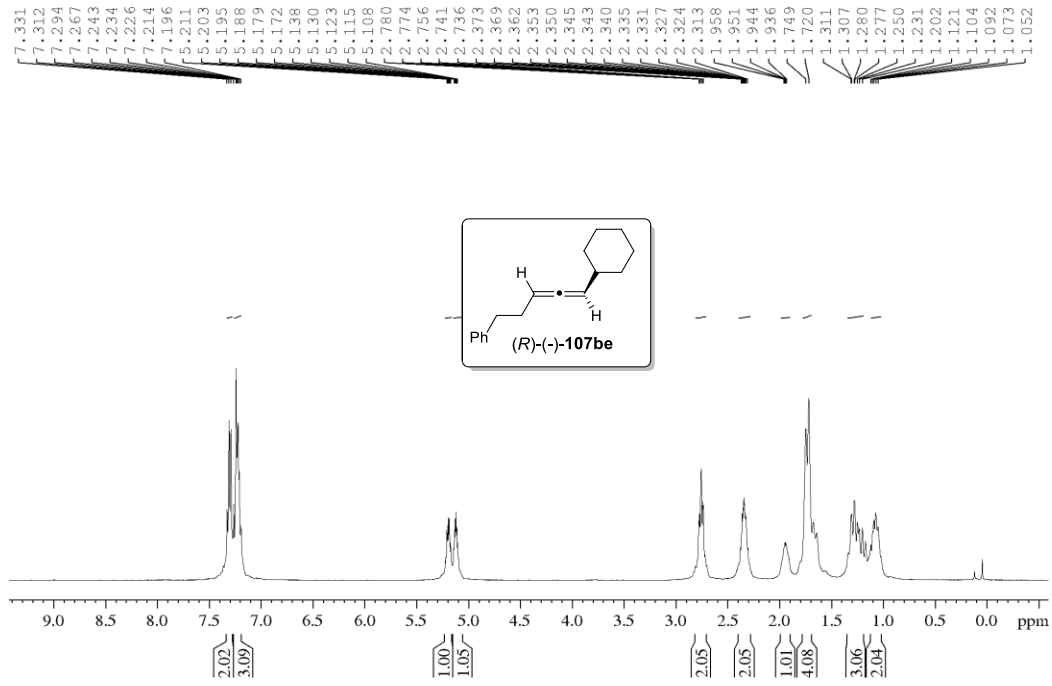
Spectrum No.19 (Chapter 1, Section 1.2.2), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



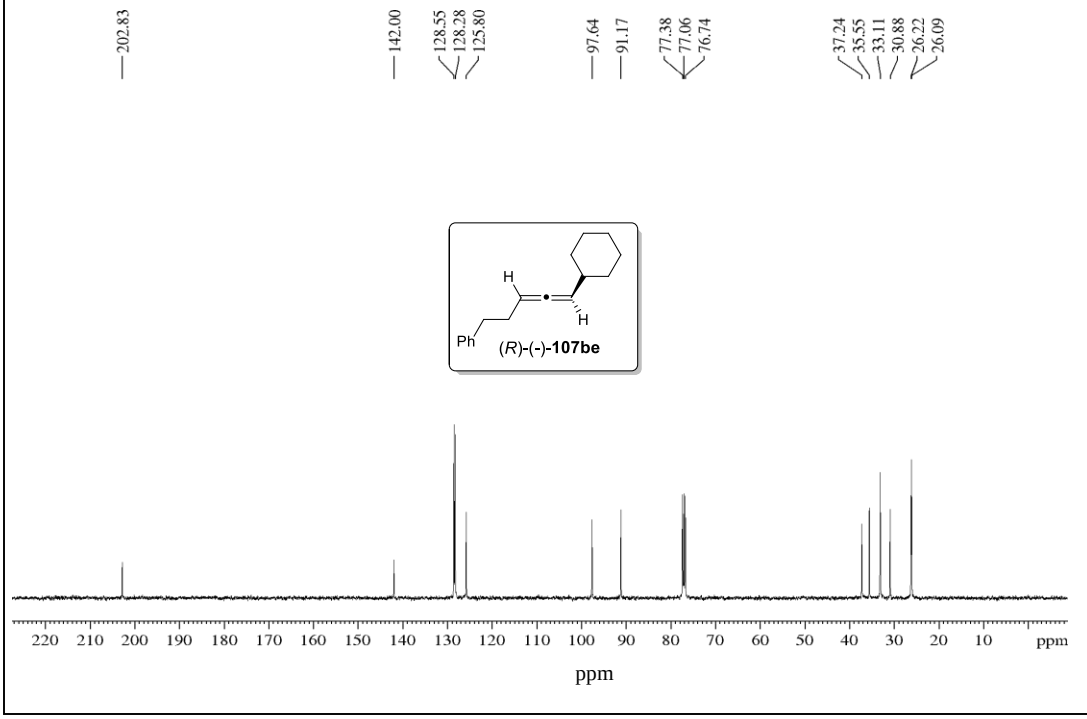
Spectrum No. 20 (Chapter 1, Section 1.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



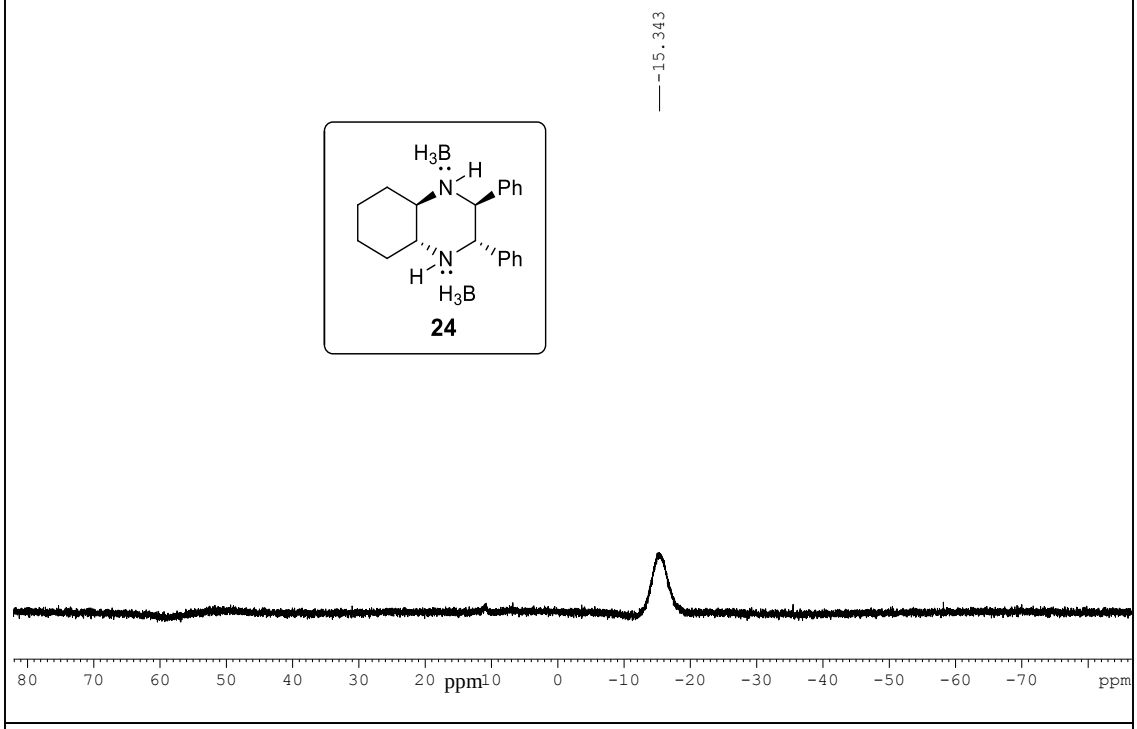
Spectrum No. 21 (Chapter 1, Section 1.2.2), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



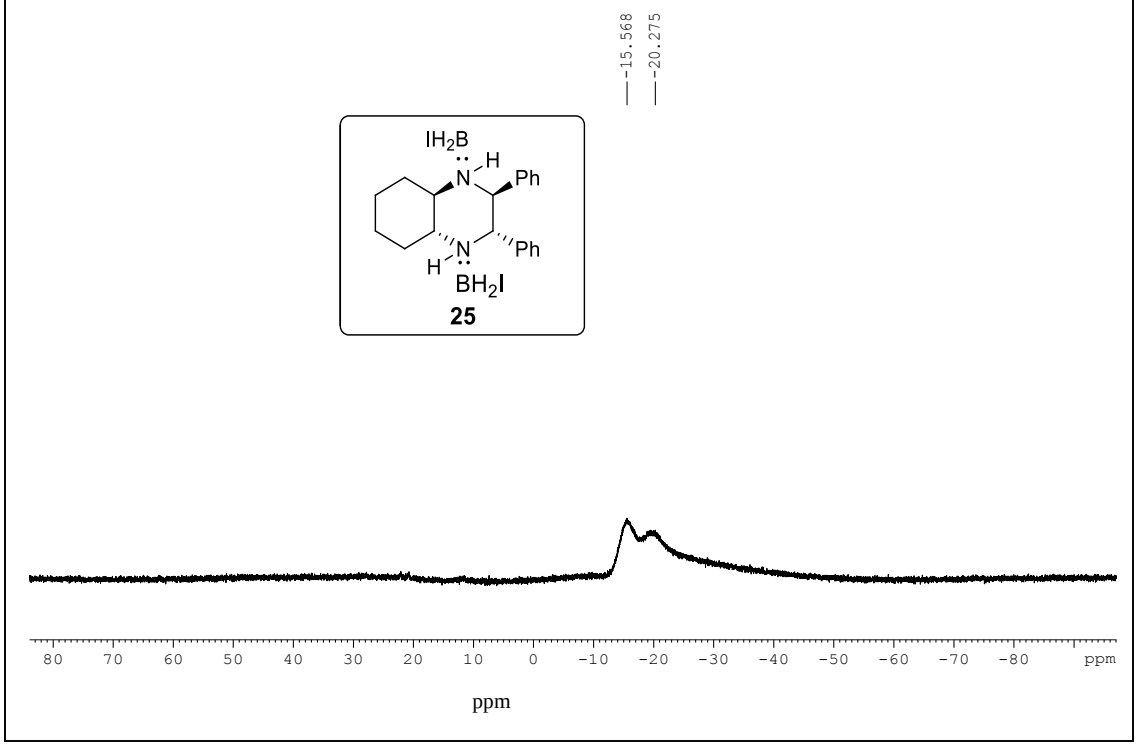
Spectrum No. 22 (Chapter1, Section 1.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



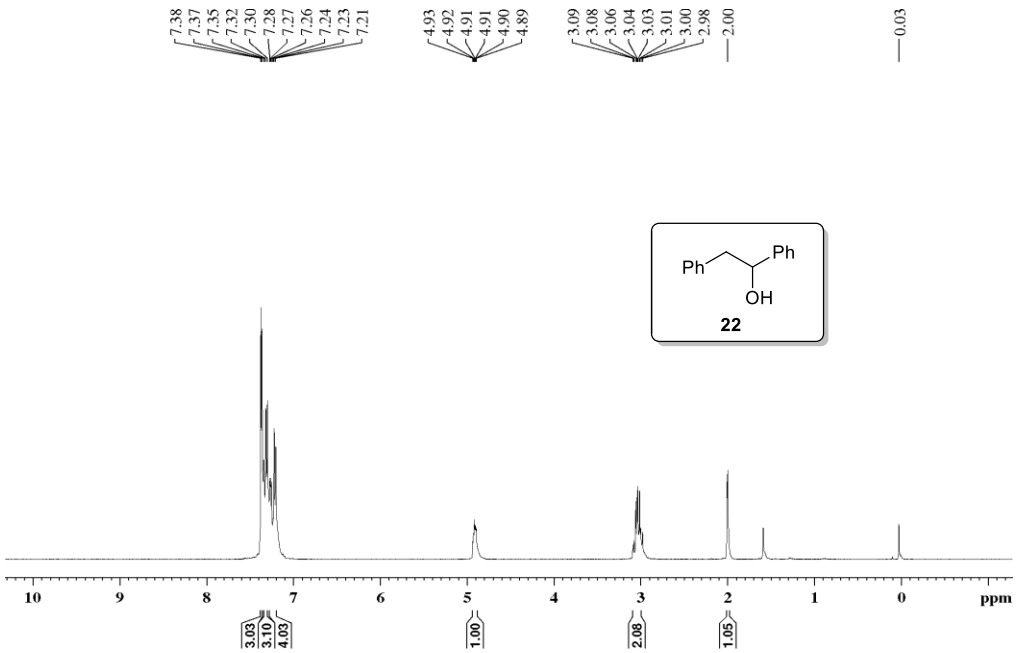
Spectrum No.23 (Annexure III, Section III.2.1), ^{11}B NMR Spectrum (128.3 MHz, Toluene)



Spectrum No. 24 (Annexure III, Section III.2.1), ^{11}B NMR Spectrum (128.3 MHz, Toluene)

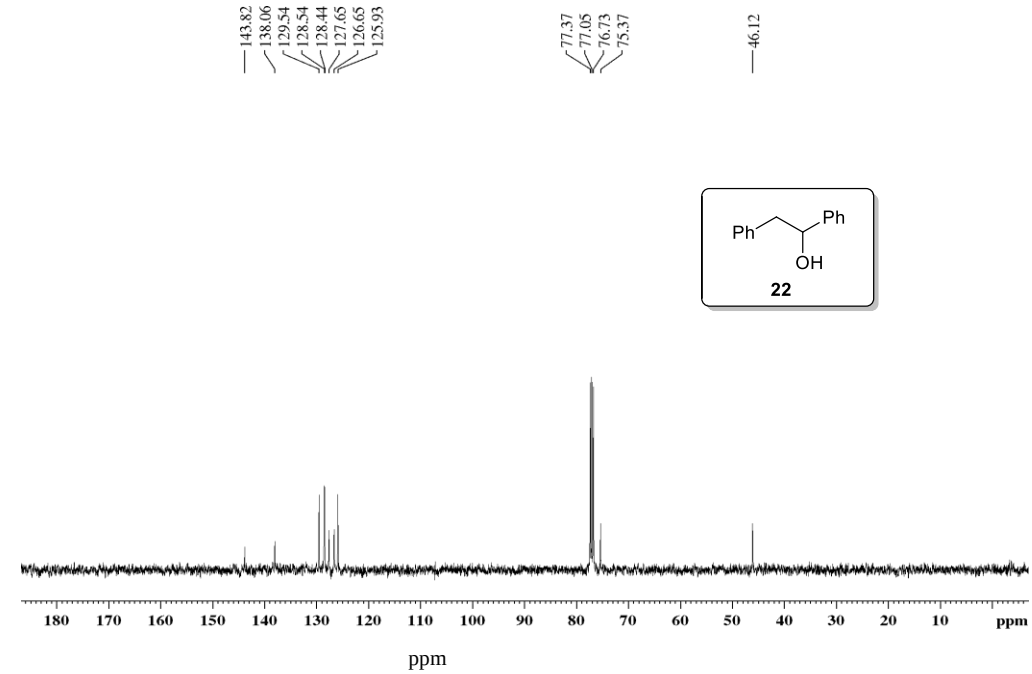


Spectrum No. 25 (Annexure III, Section III.2.1), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



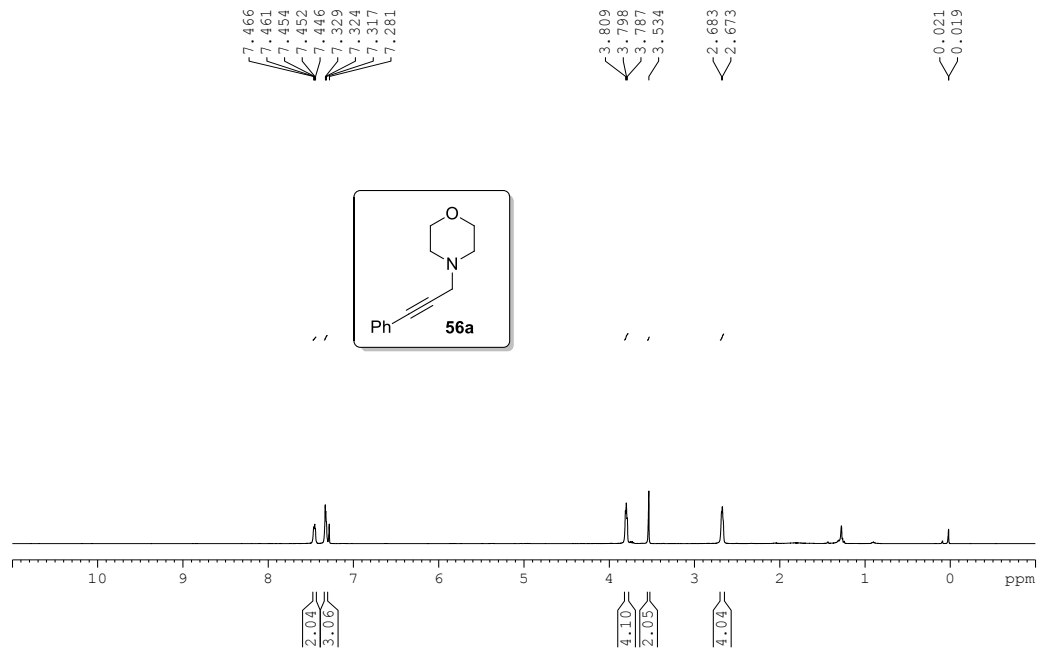
ppm

Spectrum No. 26 (Annexure III, Section III.2.1), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



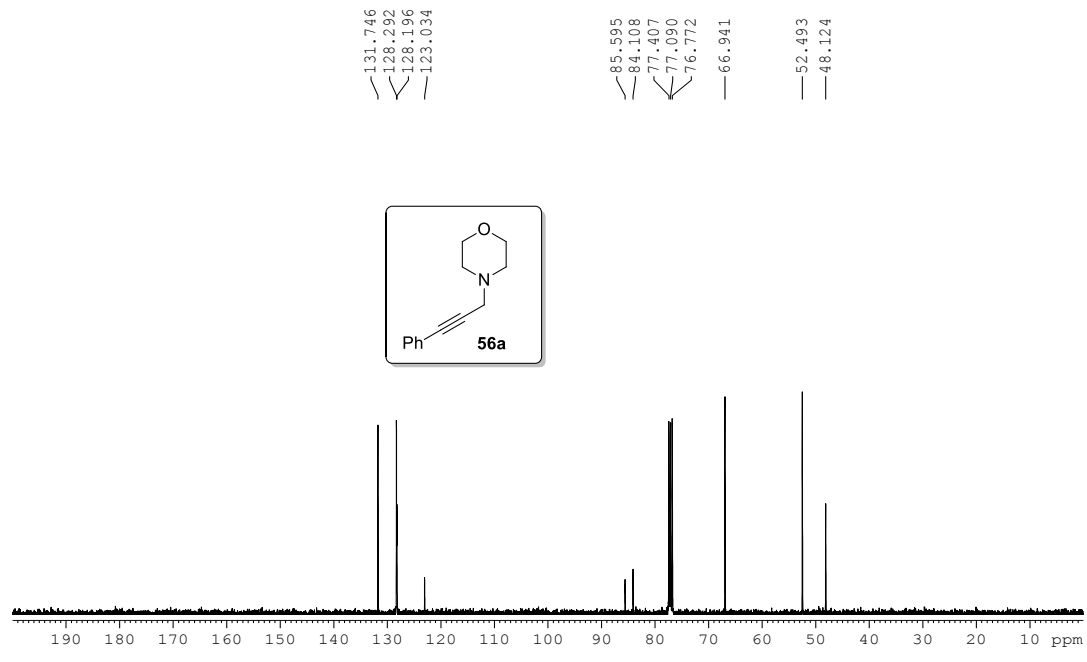
ppm

Spectrum No. 27 (Chapter 2, Section 2.2.1), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



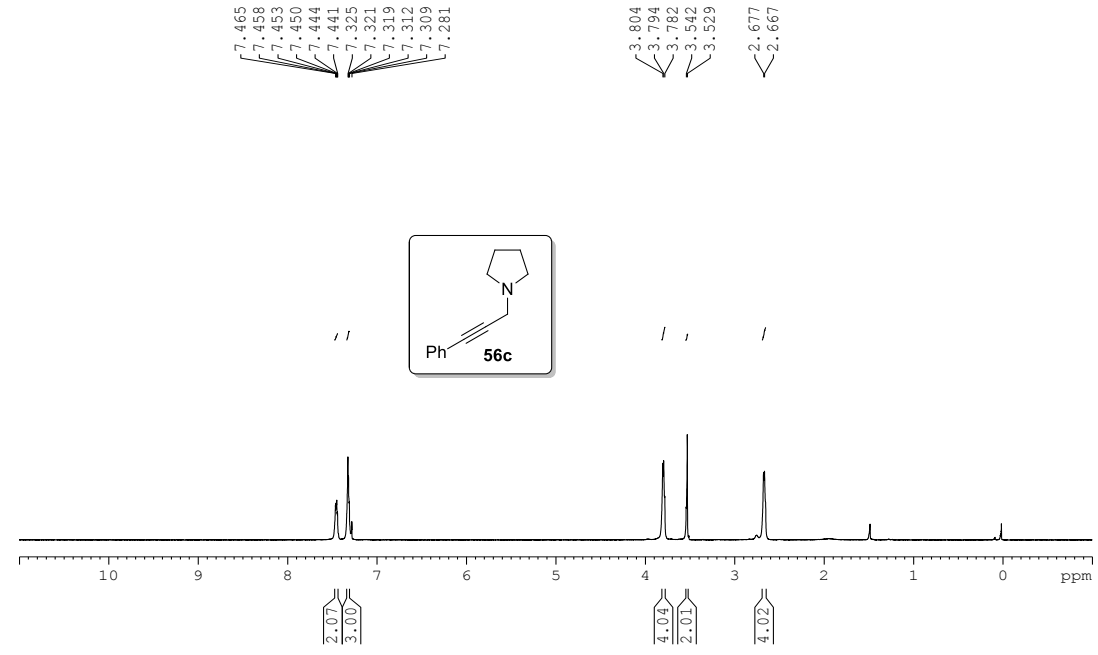
ppm

Spectrum No. 28 (Chapter 2, Section 2.2.1), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



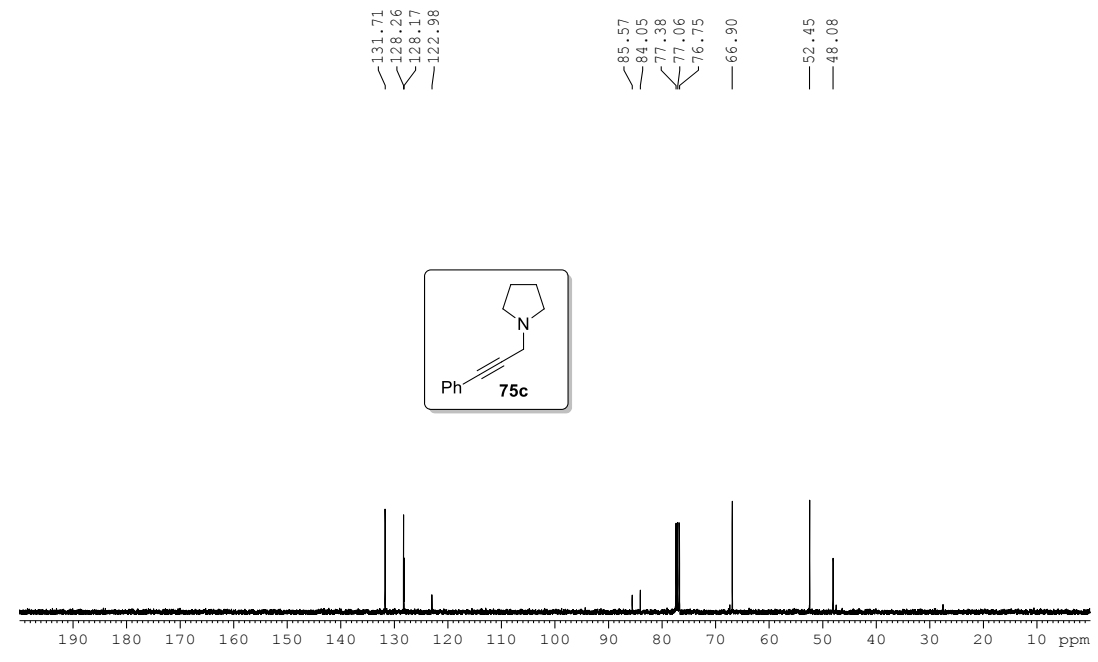
ppm

Spectrum No. 29 (Chapter 2, Section 2.2.1), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



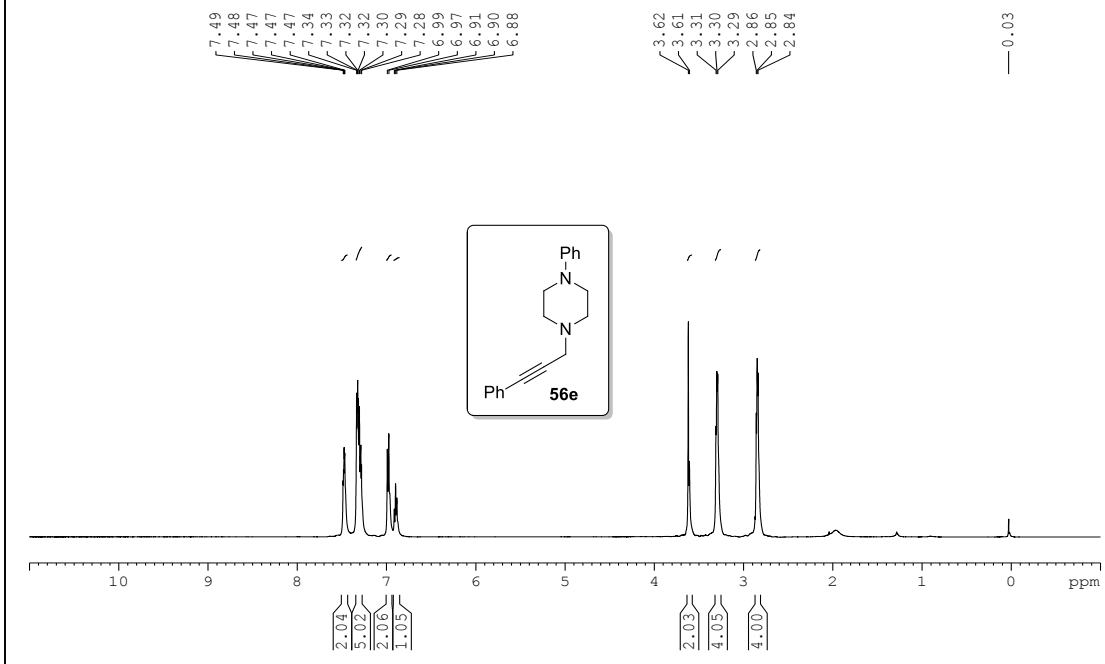
ppm

Spectrum No. 30 (Chapter 2, Section 2.2.1), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



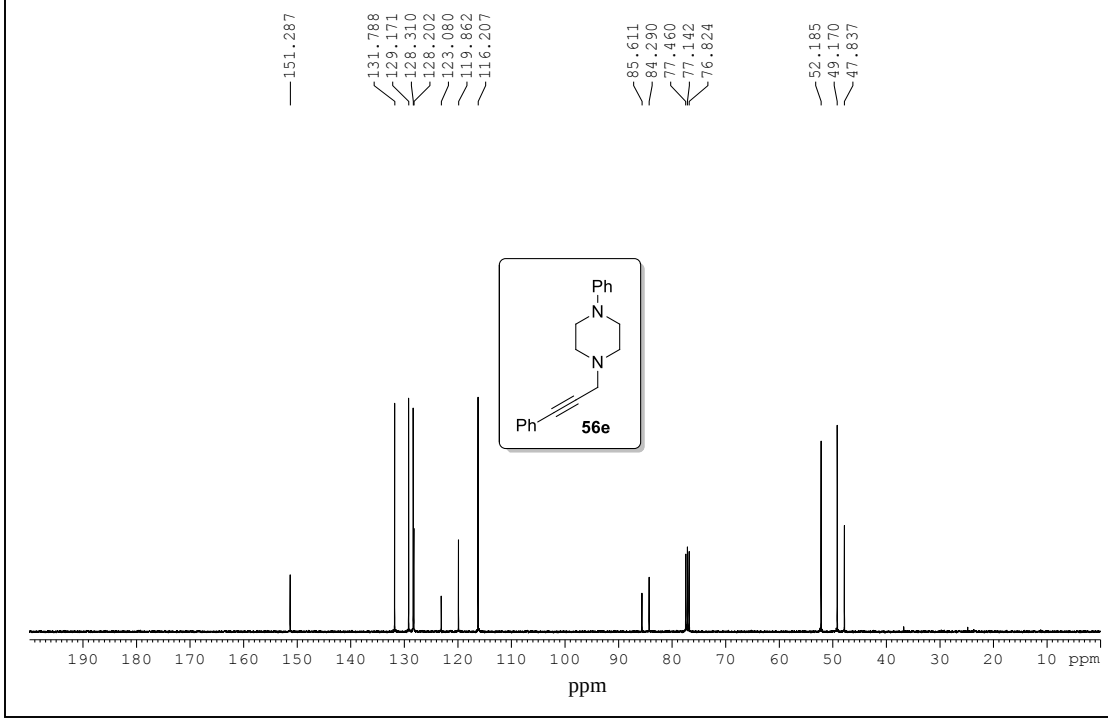
ppm

Spectrum No. 31 (Chapter 2, Section 2.2.1), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



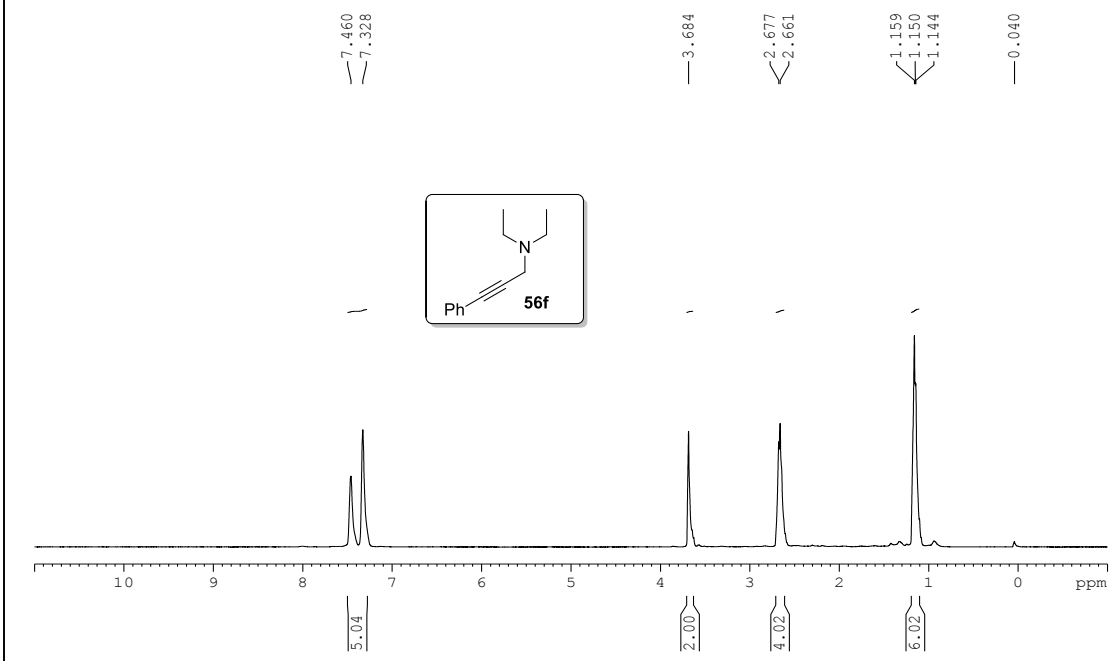
ppm

Spectrum No. 32 (Chapter 2, Section 2.2.1), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



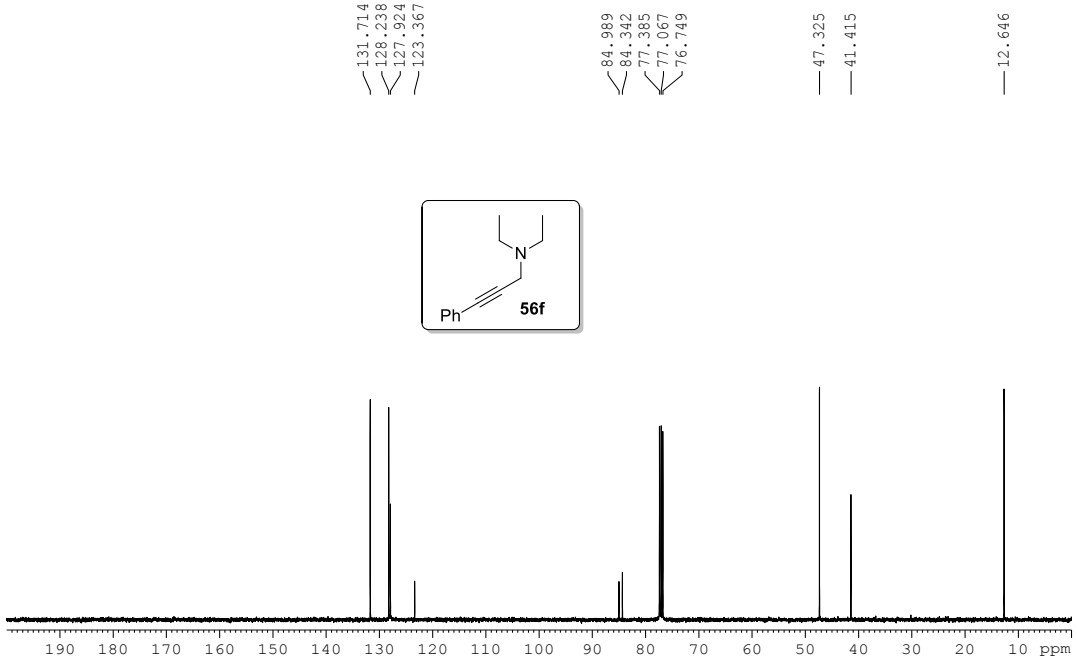
ppm

Spectrum No. 33 (Chapter 2, Section 2.2.1), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



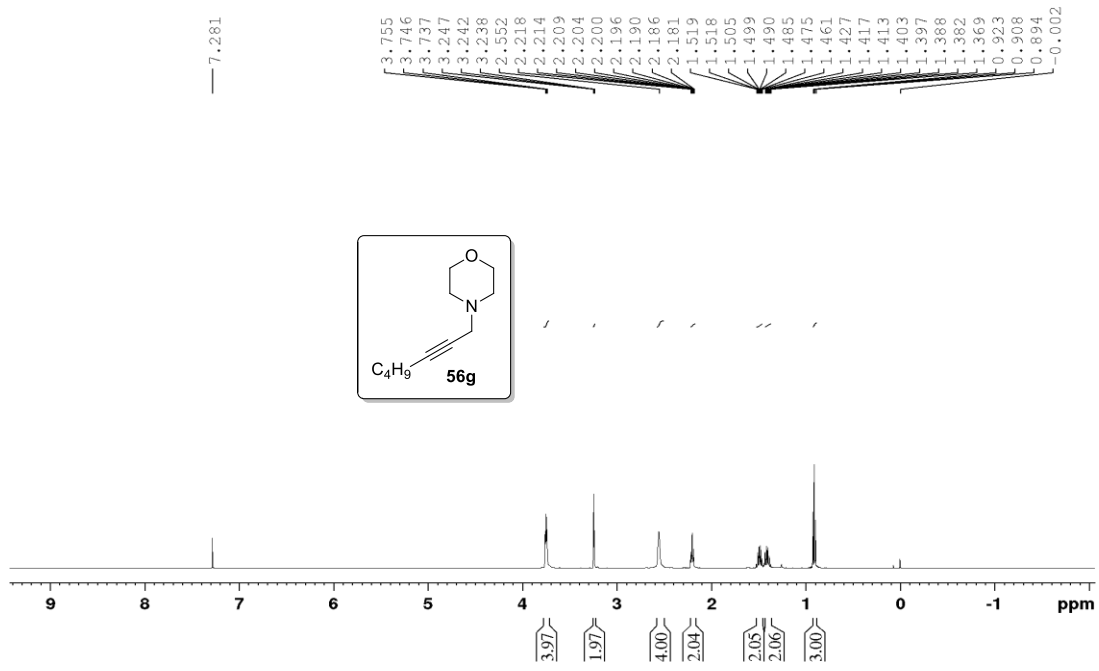
ppm

Spectrum No. 34 (Chapter 2, Section 2.2.1), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



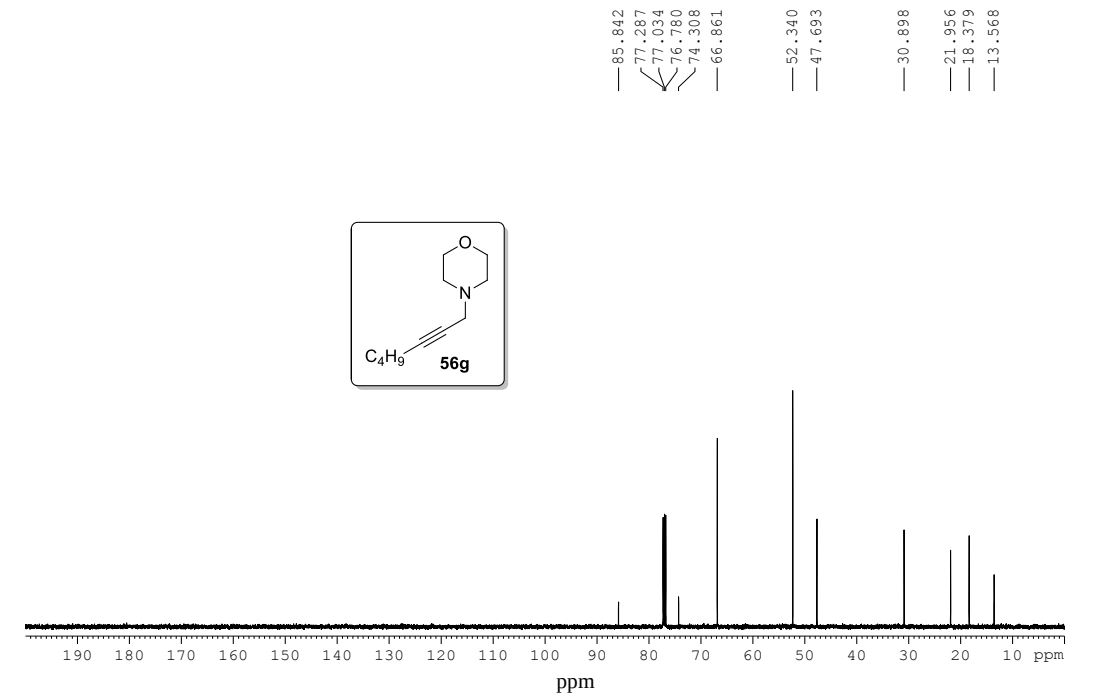
ppm

Spectrum No. 35 (Chapter 2, Section 2.2.1), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



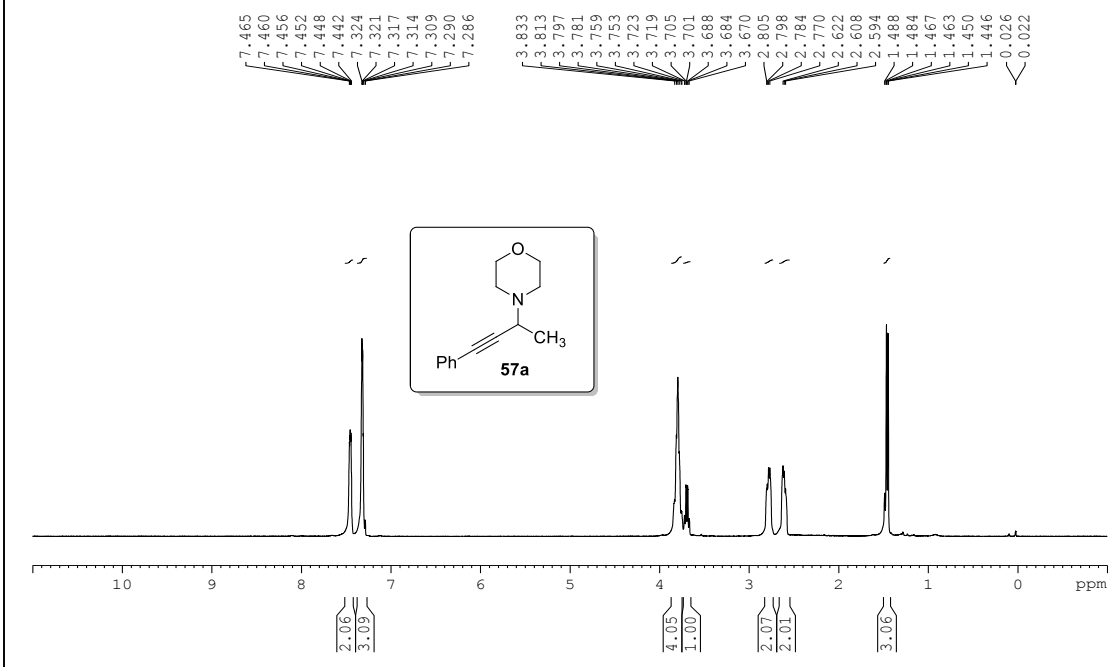
ppm

Spectrum No. 36 (Chapter 2, Section 2.2.1), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



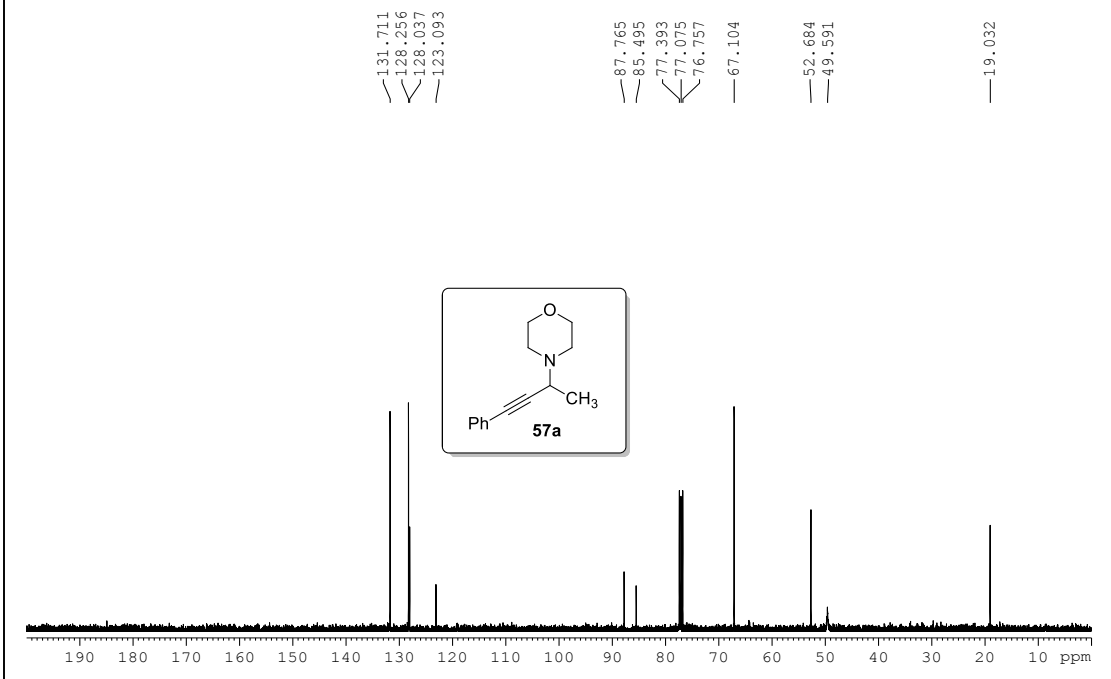
ppm

Spectrum No. 37 (Chapter 2, Section 2.2.1), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



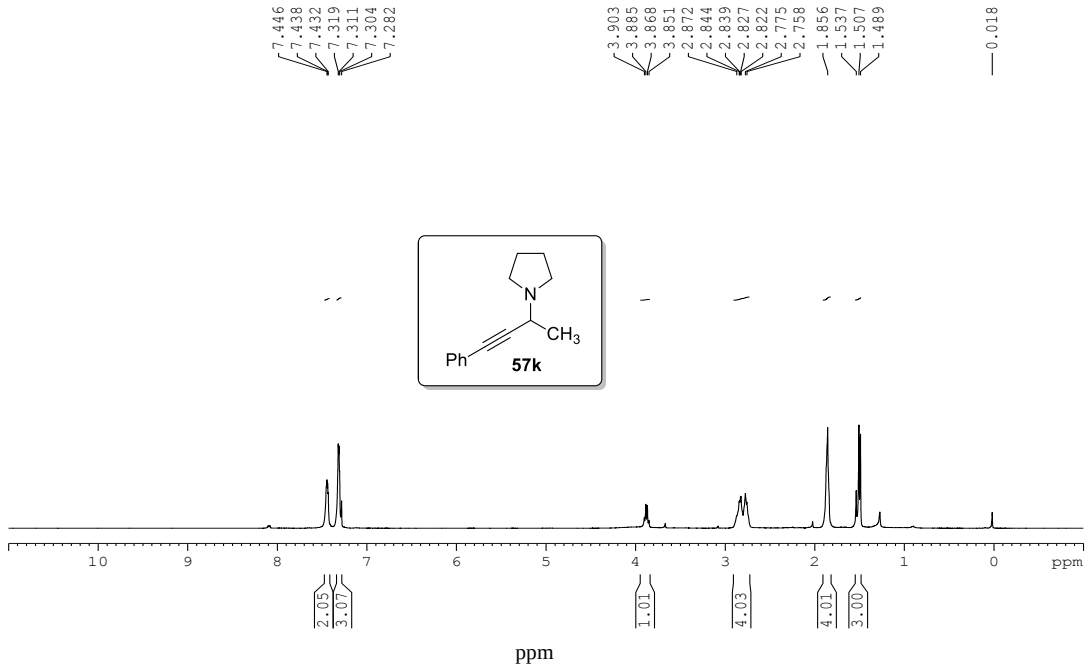
ppm

Spectrum No. 38 (Chapter 2, Section 2.2.1), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)

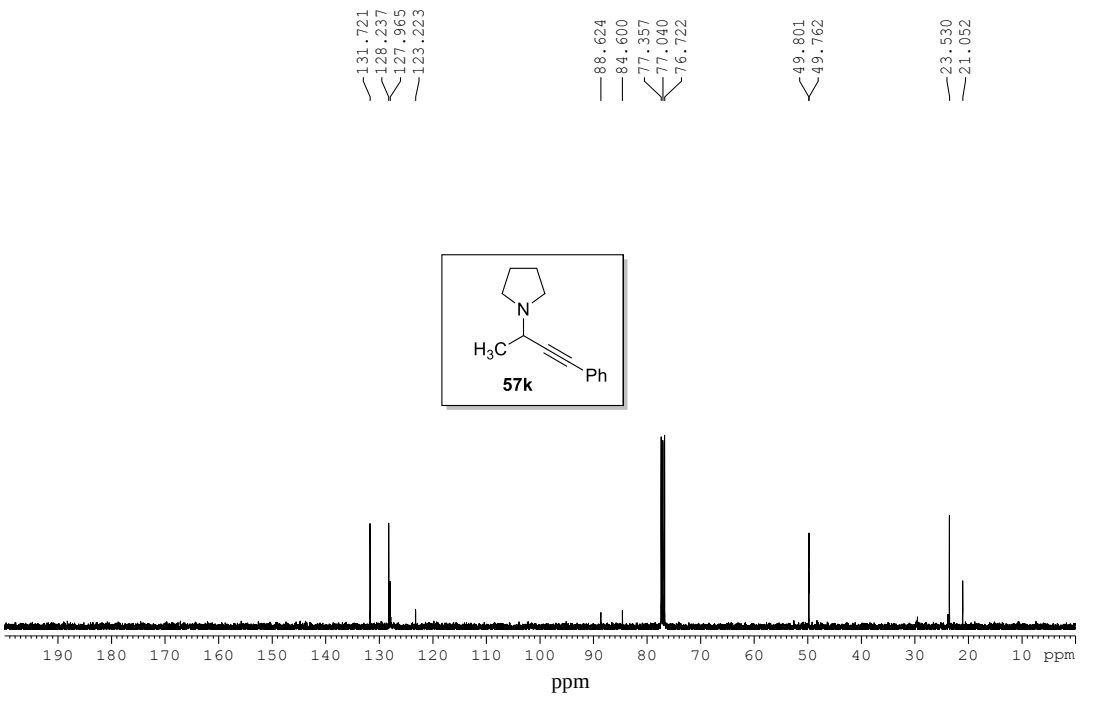


ppm

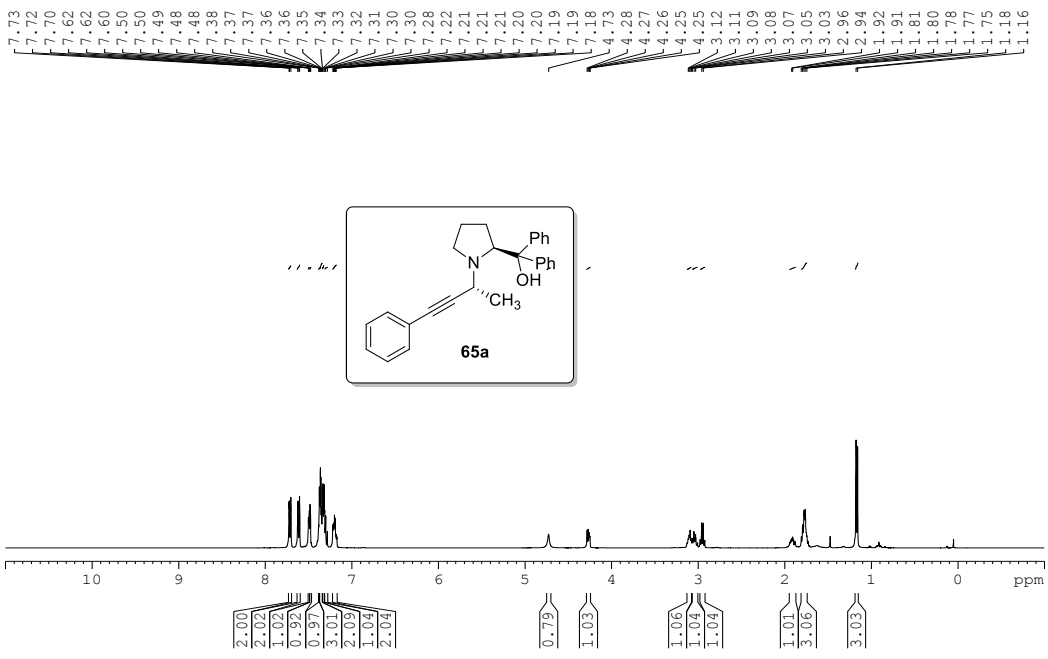
Spectrum No. 39 (Chapter 2, Section 2.2.1), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



Spectrum No. 40 (Chapter 2, Section 2.2.1), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)

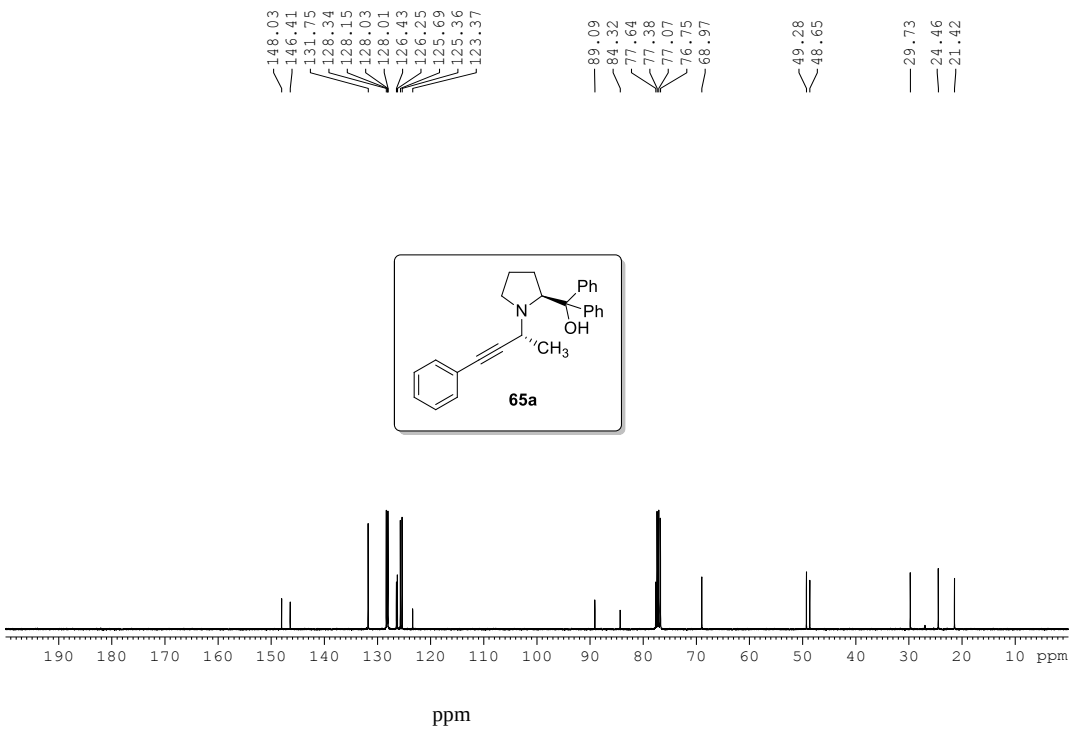


Spectrum No. 41 (Chapter 2, Section 2.2.2), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



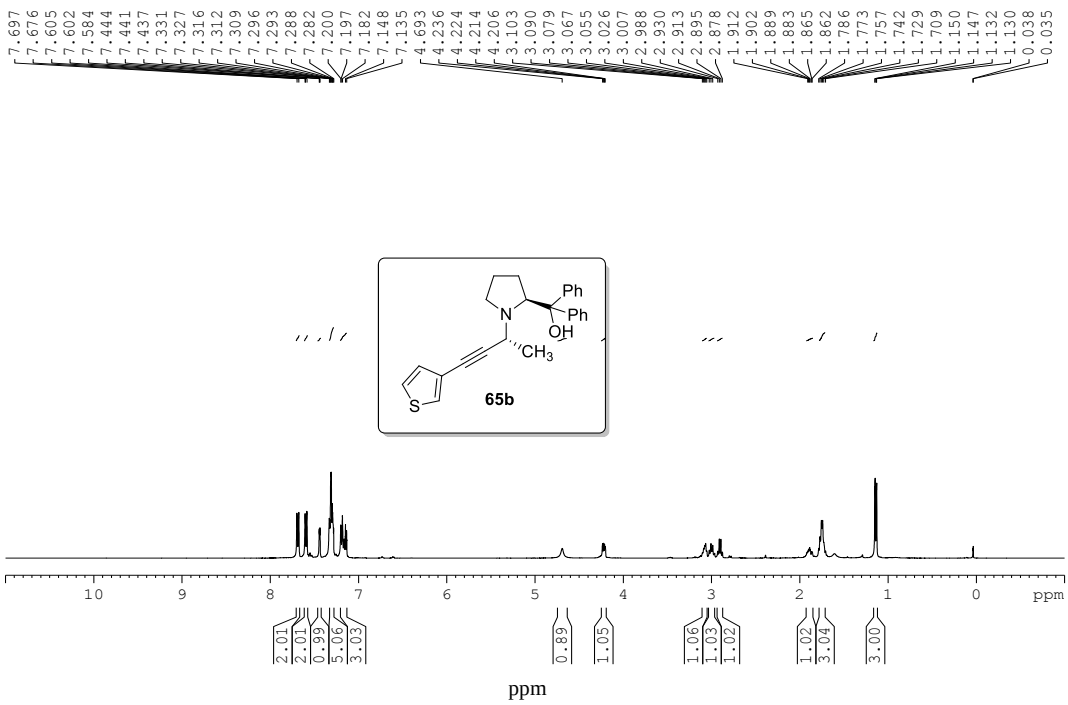
ppm

Spectrum No. 42 (Chapter 2, Section 2.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



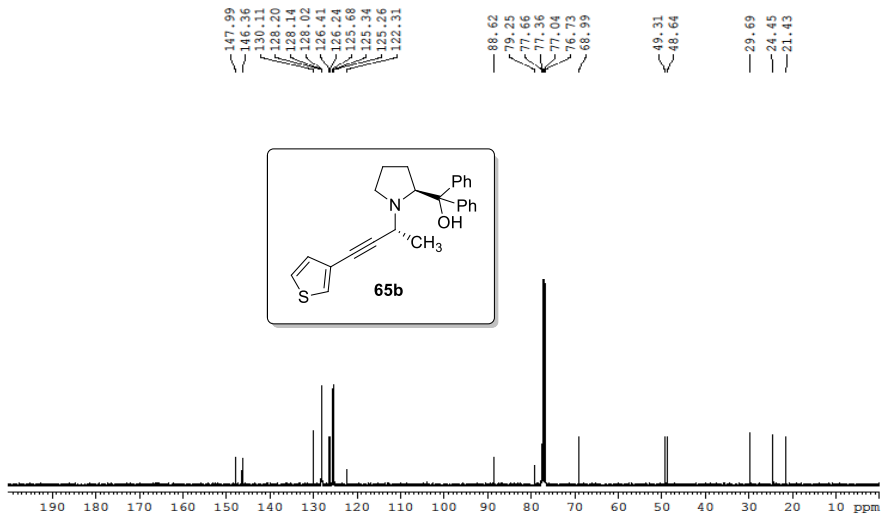
ppm

Spectrum No. 43 (Chapter 2, Section 2.2.2), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



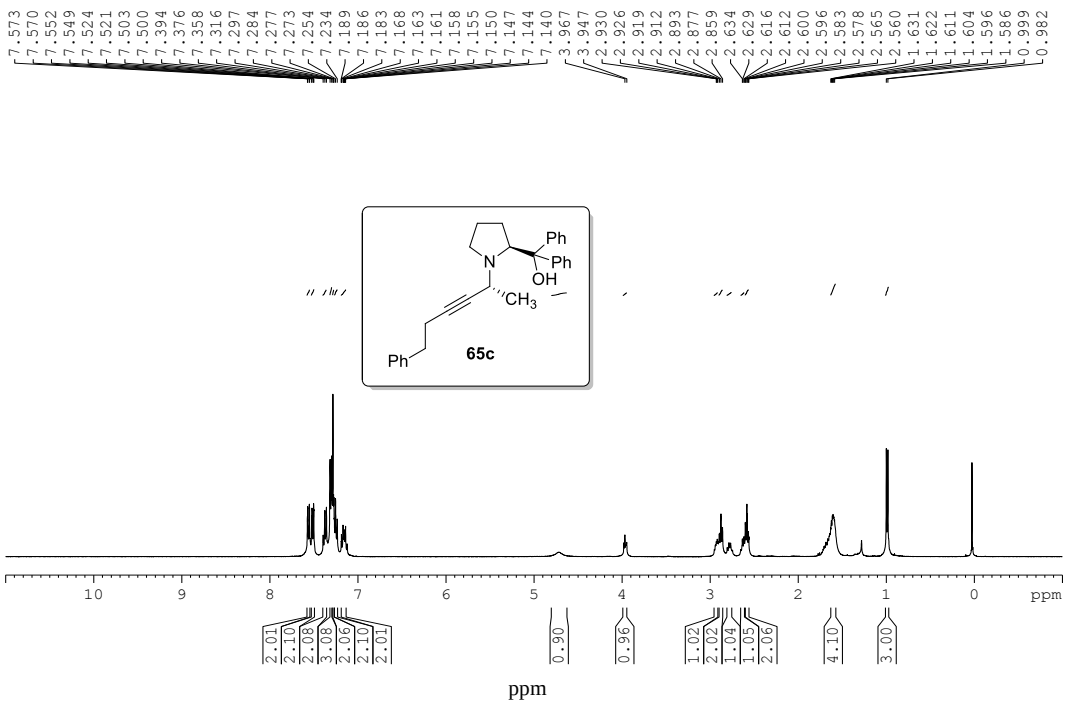
ppm

Spectrum No. 44 (Chapter 2, Section 2.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)

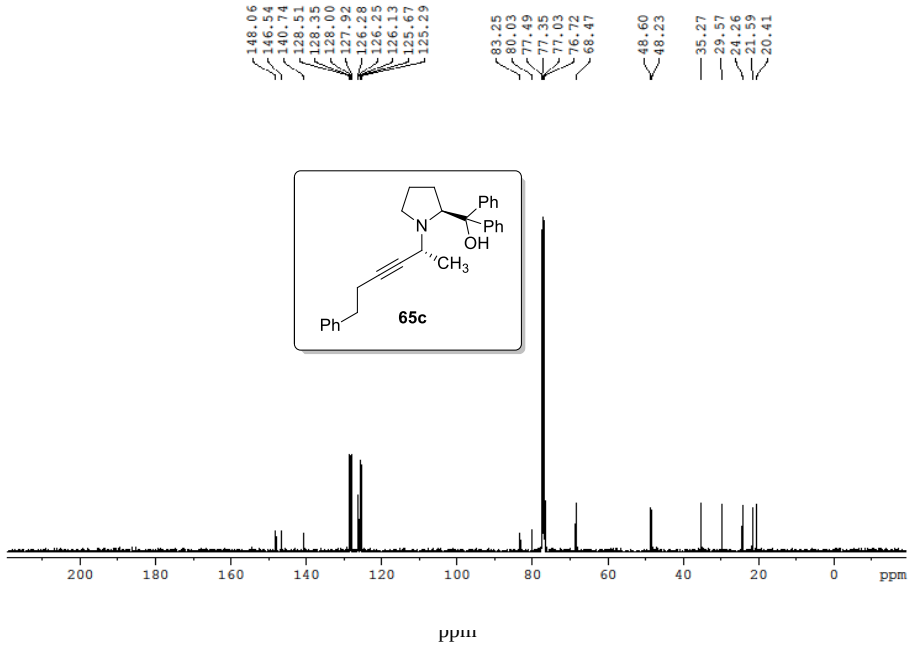


ppm

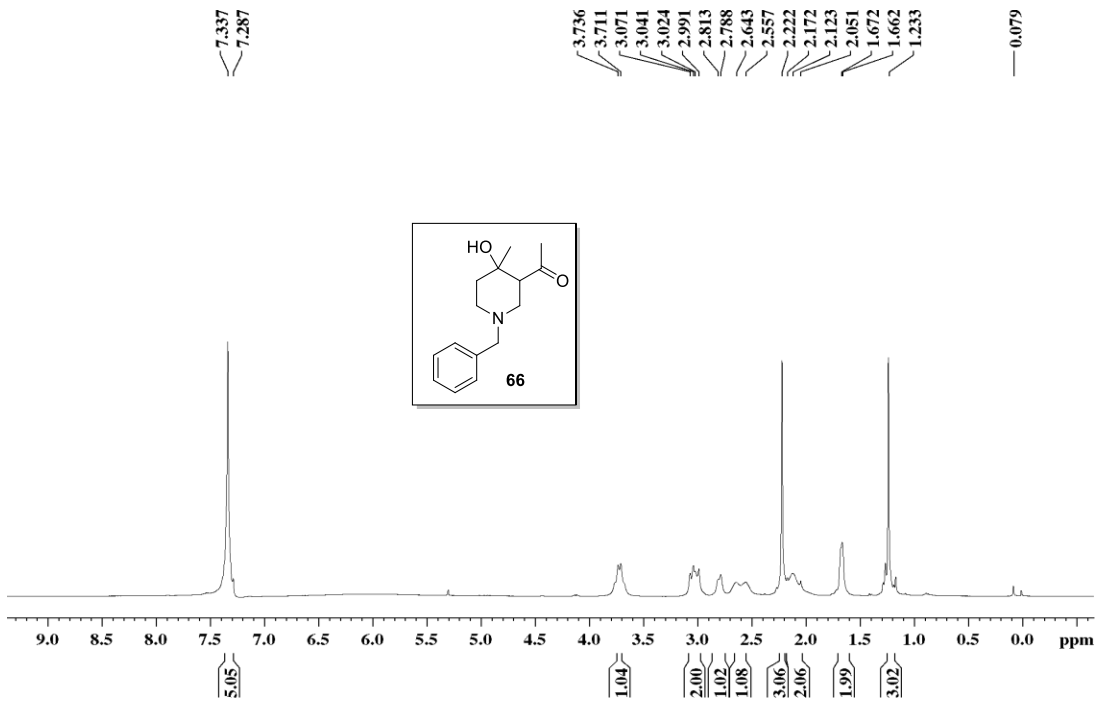
Spectrum No. 45 (Chapter 2, Section 2.2.2), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



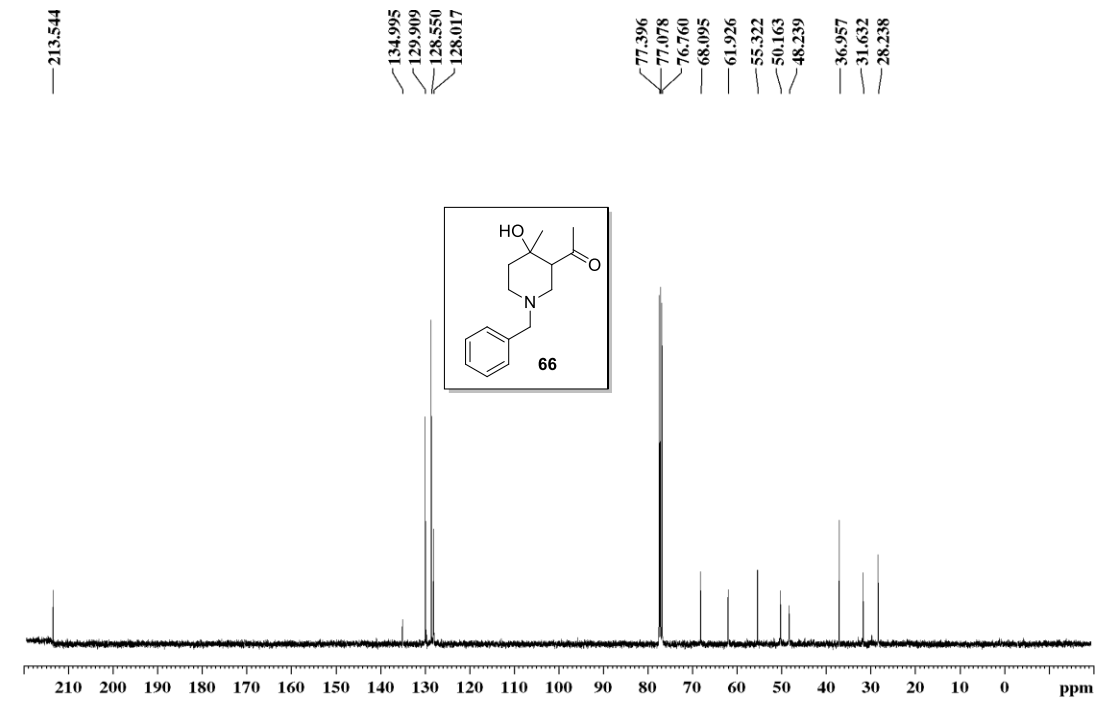
Spectrum No.46 (Chapter 2, Section 2.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



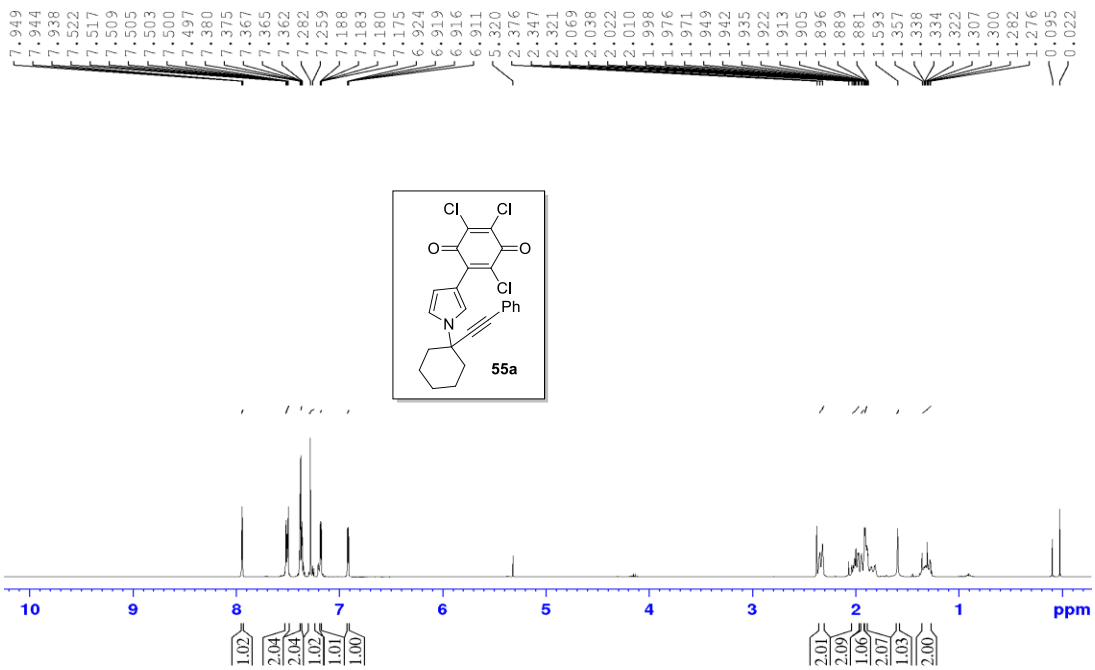
Spectrum No.47 (Chapter 2, Section 2.2.3), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



Spectrum No.48 (Chapter 2, Section 2.2.3), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)

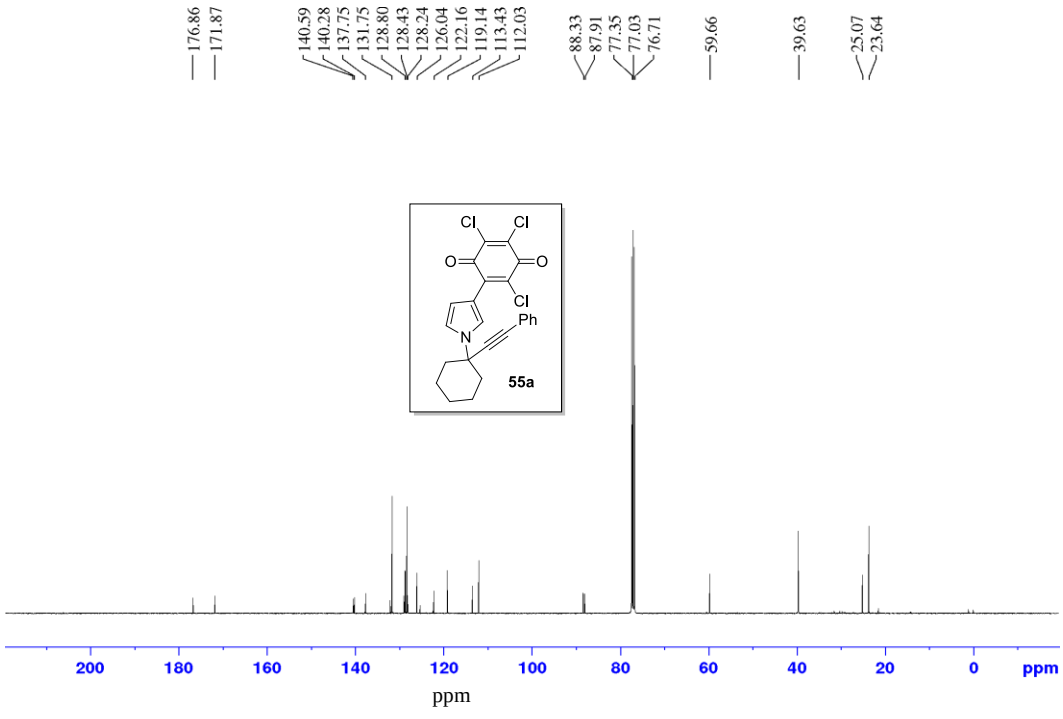


Spectrum No. 49 (Chapter 3, Section 4.2.2), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



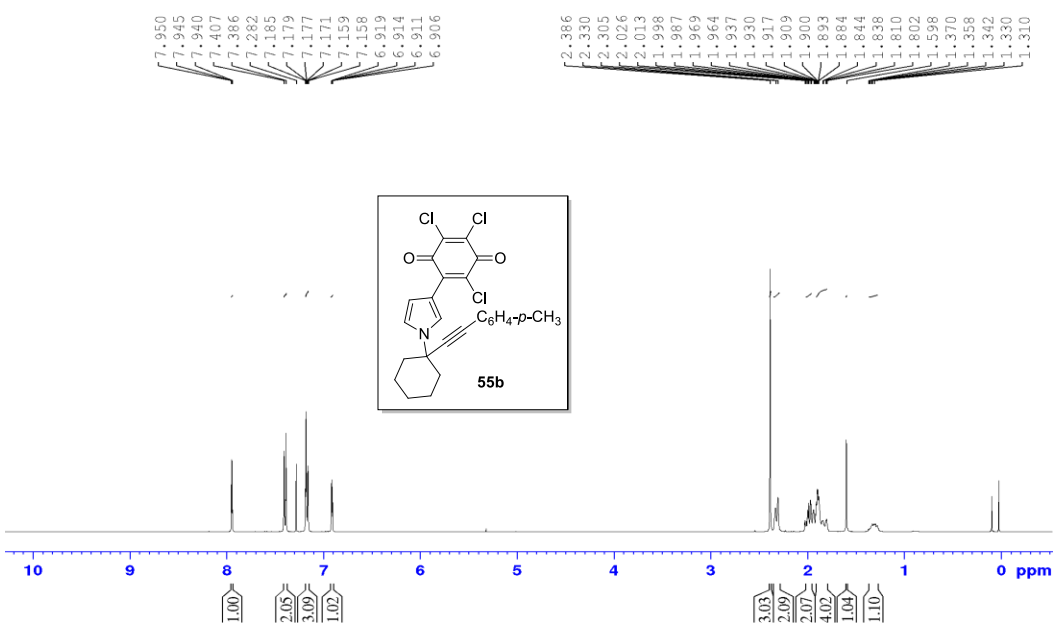
ppm

Spectrum No.50(Chapter 3, Section 4.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



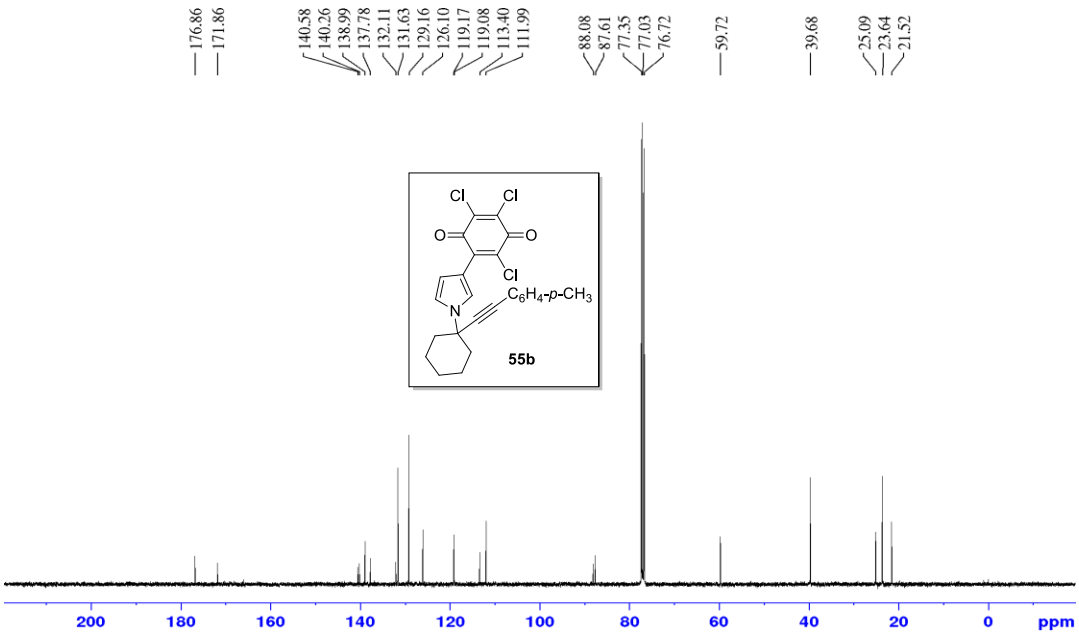
ppm

Spectrum No. 51 (Chapter 3, Section 3.2.1), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



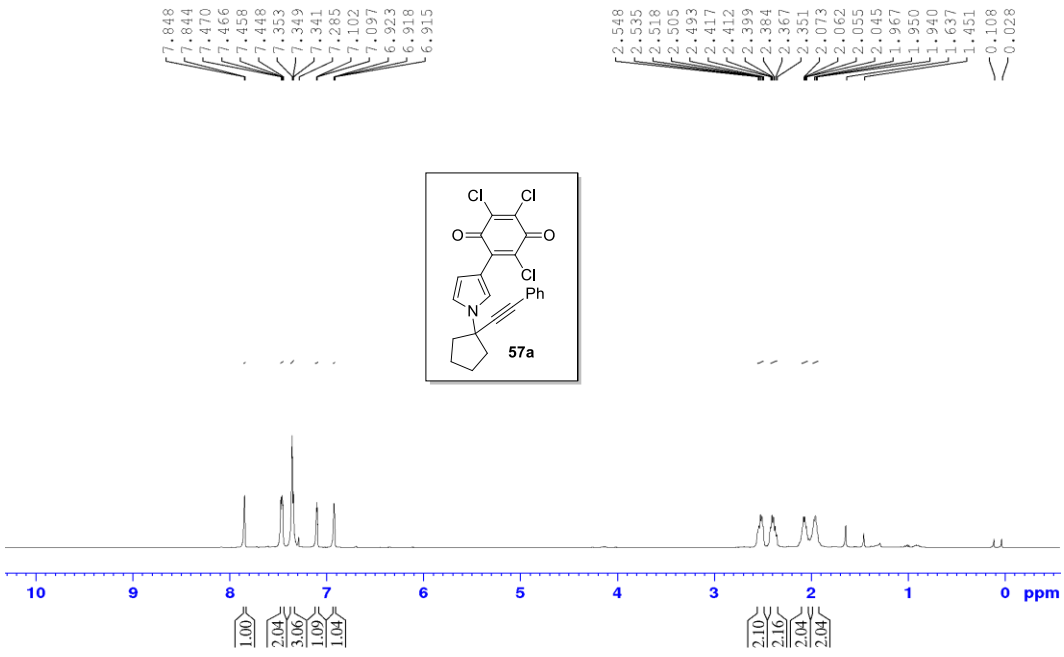
ppm

Spectrum No. 52(Chapter 3, Section 4.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



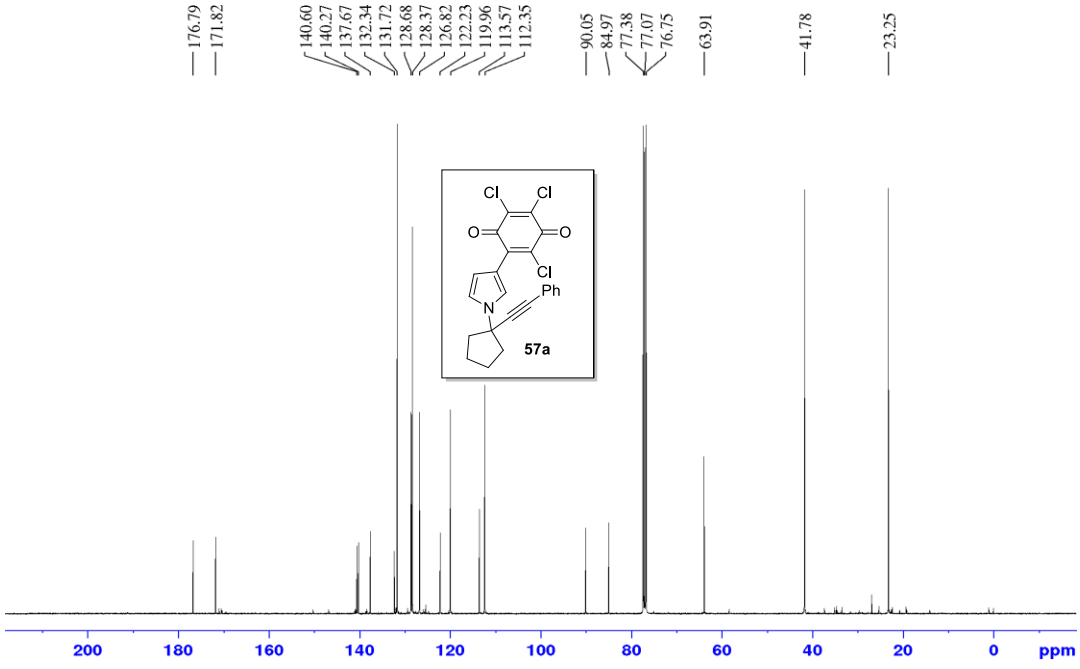
ppm

Spectrum No. 53 (Chapter 3, Section 4.2.2), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



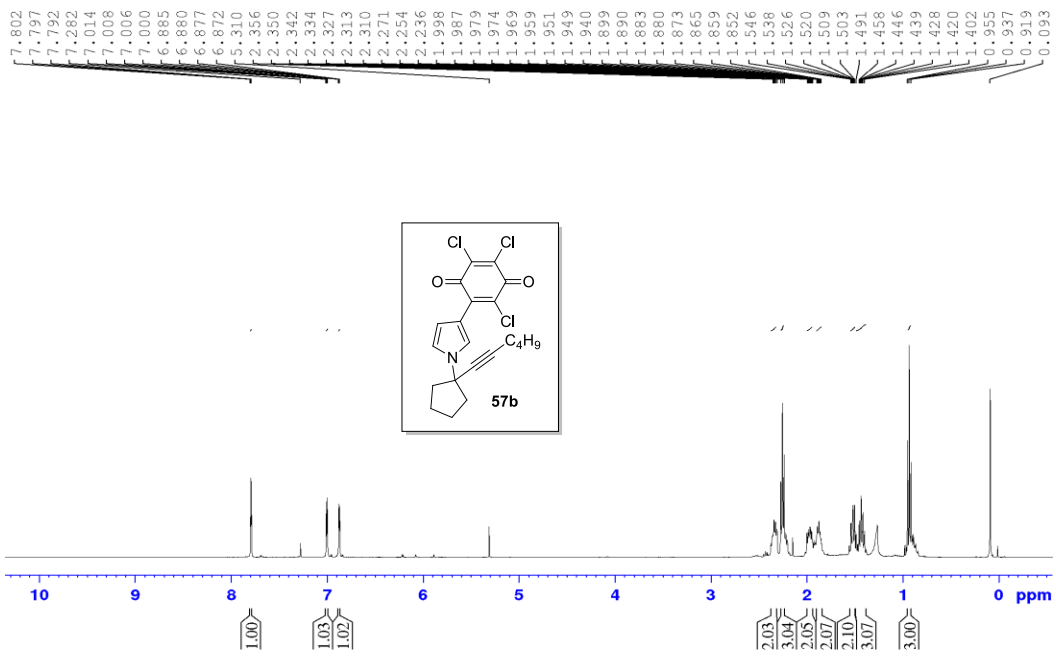
ppm

Spectrum No. 54 (Chapter 3, Section 4.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



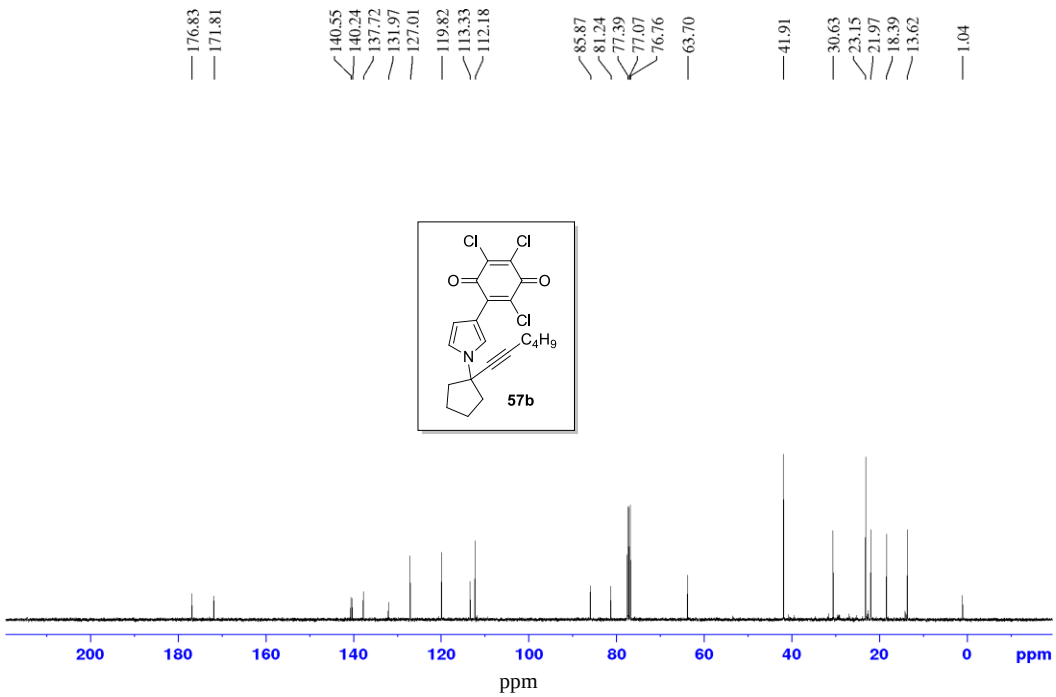
ppm

Spectrum No. 55 (Chapter 3, Section 4.2.2), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



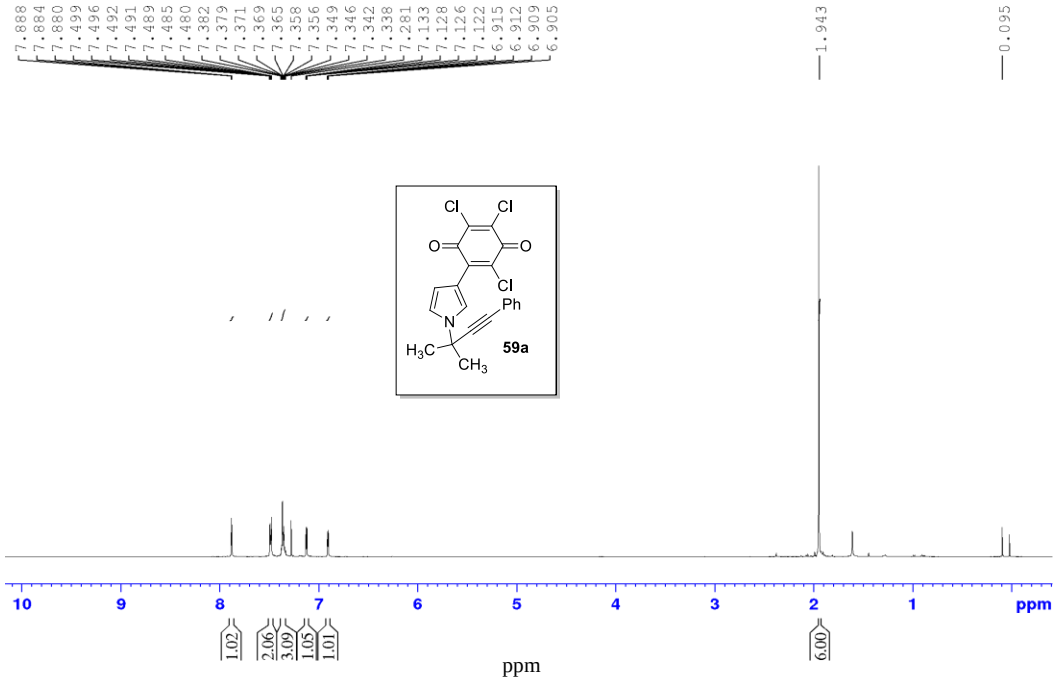
ppm

Spectrum No. 56 (Chapter 3, Section 4.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)

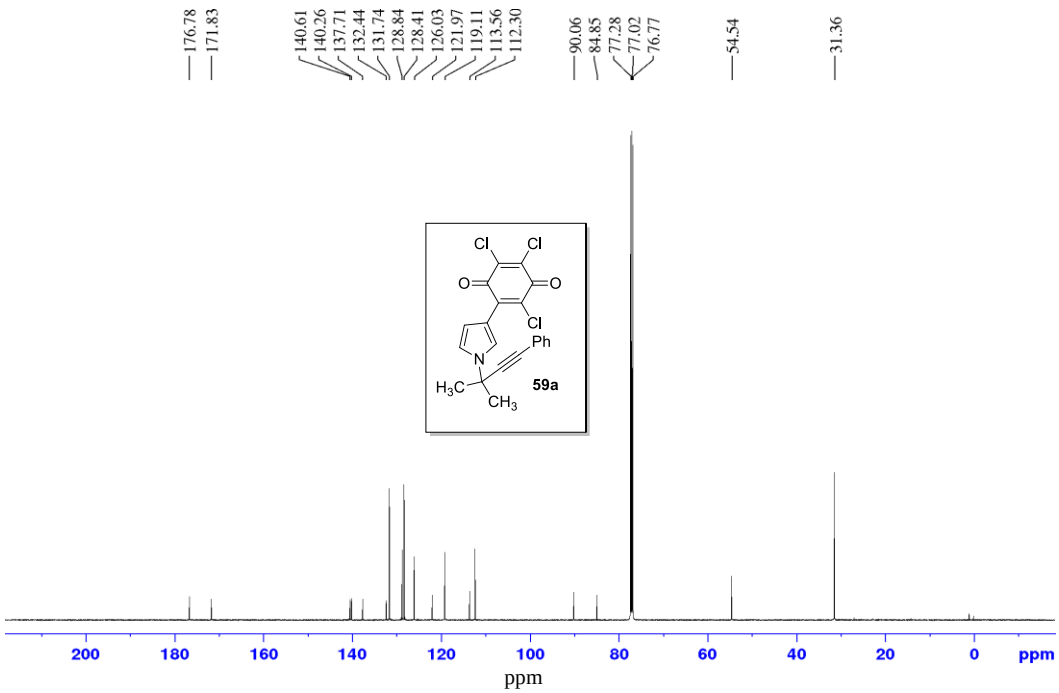


ppm

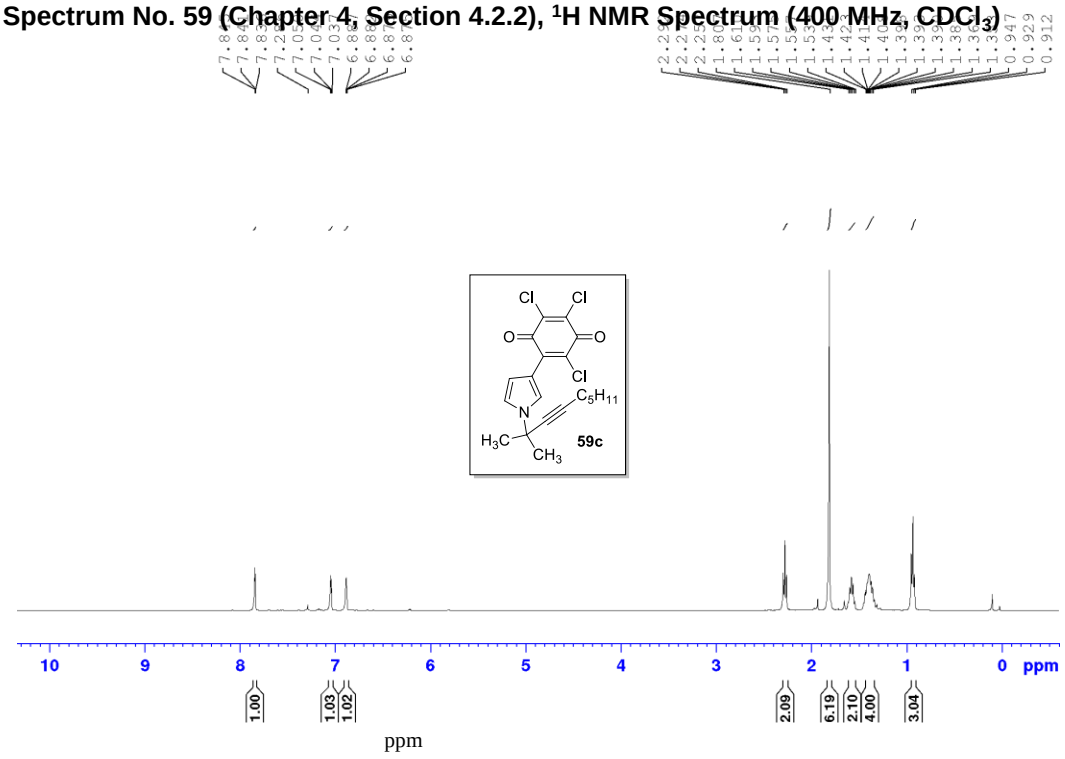
Spectrum No. 57 (Chapter 3, Section 4.2.2), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



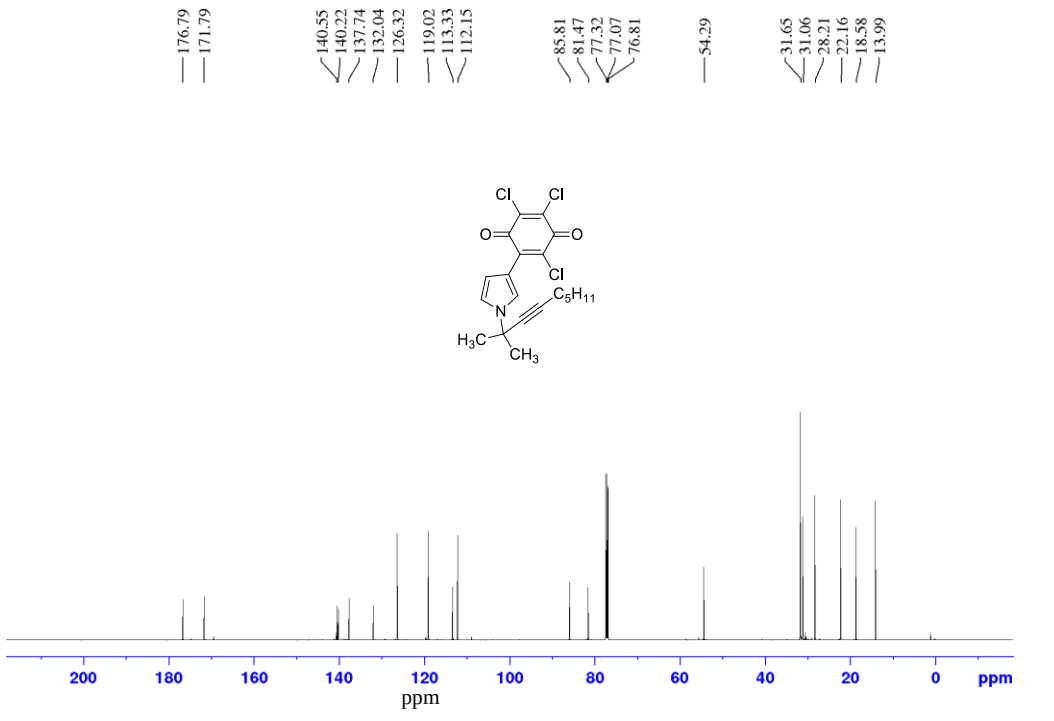
Spectrum No. 58 (Chapter 4, Section 4.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



Spectrum No. 59 (Chapter 4, Section 4.2.2), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)

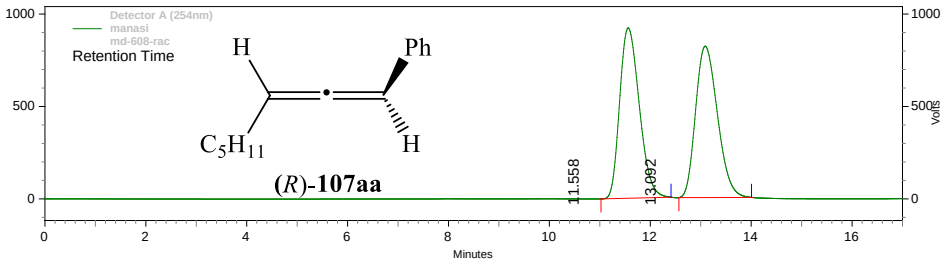


Spectrum No. 60 (Chapter 4, Section 4.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



HPLC Profile of 107aa (Chiralcel OD-H column, 100% Hexane, 0.5 mL/min)

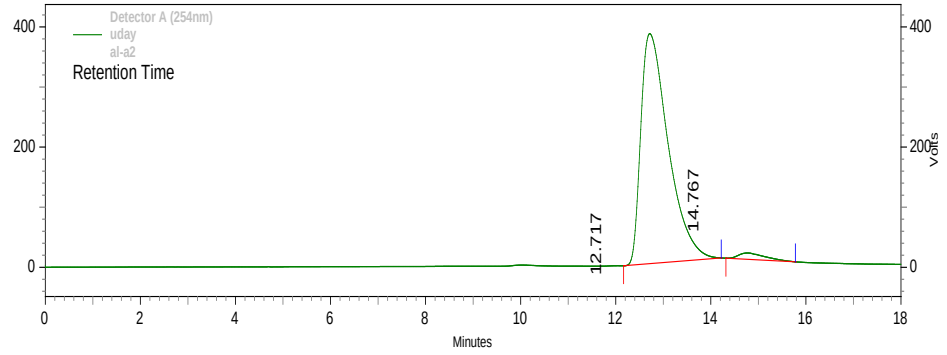
Racemic:



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	11.558	24861251	50.192	921460	52.946
2	13.092	24671532	49.808	818914	47.054
Totals		49532783	100.000	1740374	100.000

(*R*)- **107aa**

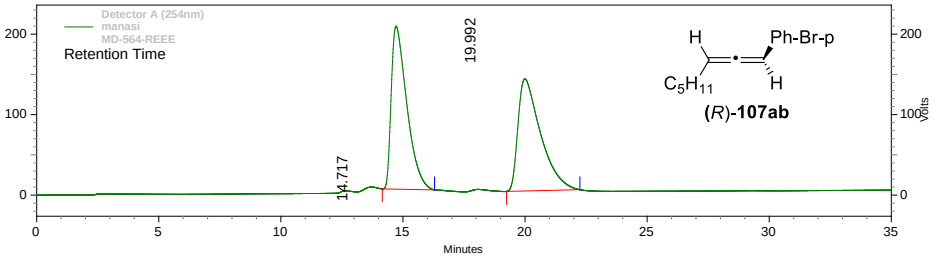


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	12.717	15302340	97.378	382640	97.313
2	14.767	411953	2.622	10566	2.687
Totals		15714293	100.000	393206	100.000

HPLC Profile of 107ab: (Chiralcel OD-H column, 100% Hexane, 0.3 mL/min)

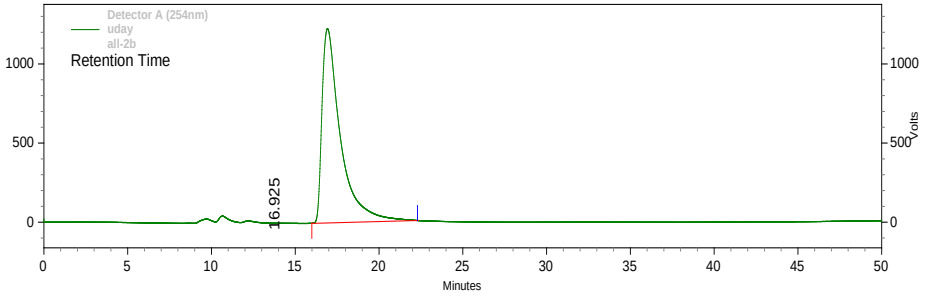
Racemic:



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	14.717	8977007	50.024	202610	59.250
2	19.992	8968342	49.976	139346	40.750
Totals		17945349	100.000	341956	100.000

(*R*)- **107ab**

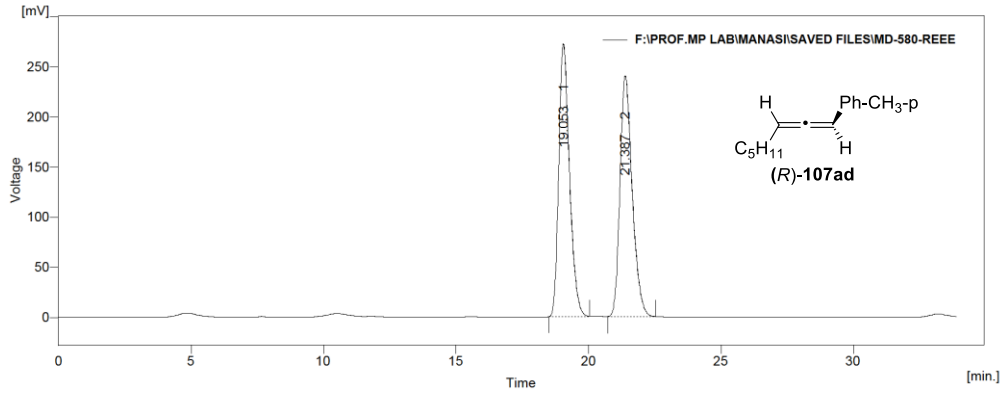


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	16.925	93875732	100.000	1227297	100.000
Totals		93875732	100.000	1227297	100.000

HPLC Profile of 107ad - (Chiralcel OD-H column, 100% Hexane, 0.5 mL/min)

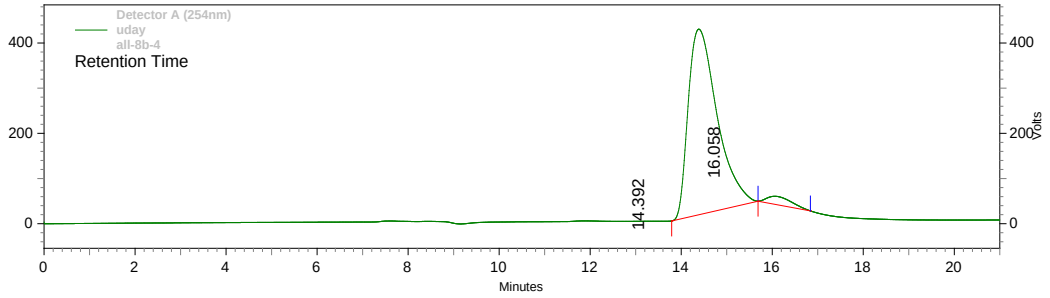
Racemic:



Result Table (Uncal - F:\PROF.MP LAB\MANASI\SAVED FILES\MD-580-REEE)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	19.053	5112.992	181.813	49.8	53.2	0.43
2	21.387	5145.236	160.246	50.2	46.8	0.49
	Total	10258.228	342.058	100.0	100.0	

(R)- **107ad**

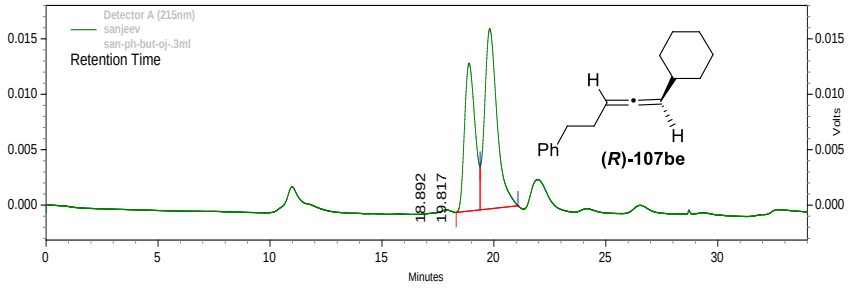


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	14.392	18150076	96.314	410638	95.859
2	16.058	694527	3.686	17738	4.141
Totals		18844603	100.000	428376	100.000

HPLC Profile of 107be: chiral column, chiralcel Oj-H, hexanes:i-PrOH/100:0; flow rate 0.3 mL/min.

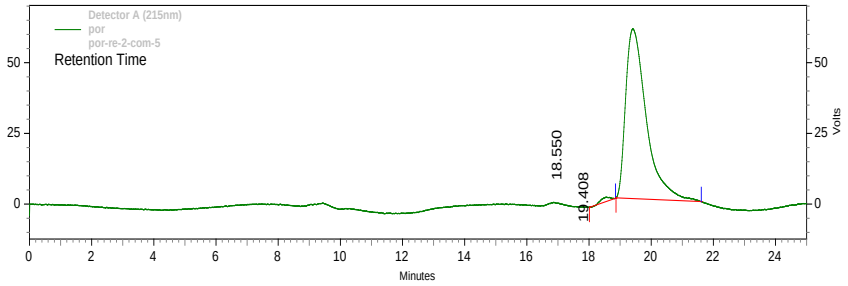
Racemic:



Detector A (215nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	18.892	435292	40.695	13327	45.091
2	19.817	634341	59.305	16229	54.909
Totals		1069633	100.000	29556	100.000

(*R*)- 107be

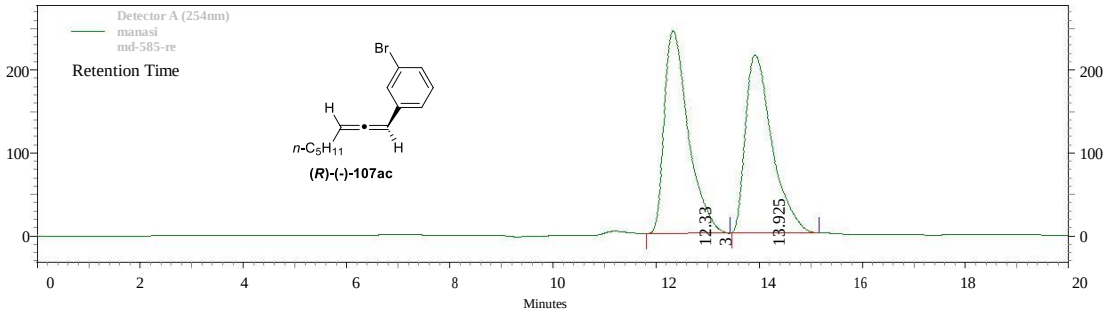


Detector A (215nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	18.550	30278	1.080	1517	2.465
2	19.408	2772119	98.920	60036	97.535
Totals		2802397	100.000	61553	100.000

HPLC Profile of 107ac (Chiralcel OD-H column, 100% Hexane, 0.5 mL/min)

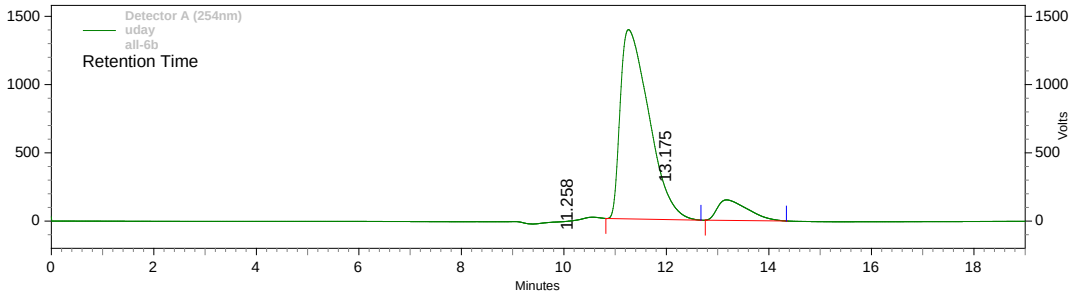
Racemic:



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	12.333	7947474	50.768	244347	53.298
	13.925	7707108	49.232	214111	46.702
Totals		15654582	100.000	458458	100.000

(*R*)- 107ac

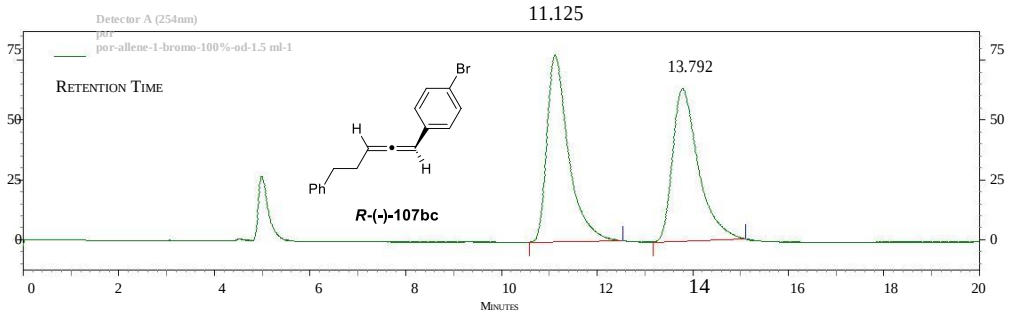


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	11.258	53923319	89.726	1386283	90.209
2	13.175	6174572	10.274	150459	9.791
Totals		60097891	100.000	1536742	100.000

HPLC Profile of 107bc (Chiralcel OD-H column, 100% Hexane, 0.5 mL/min)

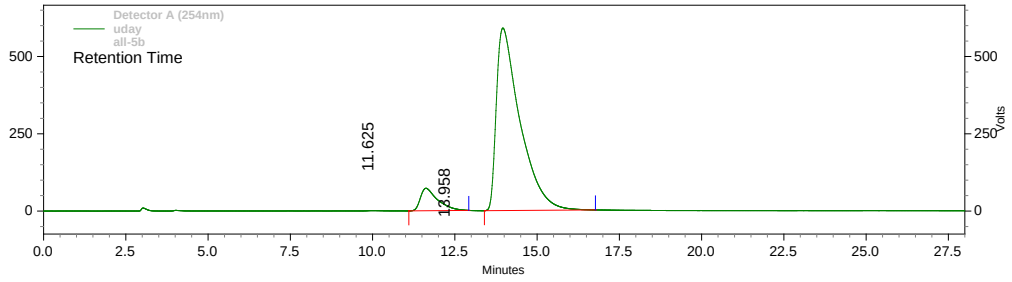
Racemic:



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	11.125	2464658	50.753	77875	55.067
2	13.792	2391563	49.247	63544	44.933
Totals		4856221	100.000	141419	100.000

(*R*)- 107bc



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	11.625	2638513	8.222	72672	10.961
2	13.958	29452730	91.778	590342	89.039
Totals		32091243	100.000	663014	100.000

Appendix II

(X-Ray Crystallographic Data)

Table A1 Crystal data and structure refinement for compound **55b**

Identification code	Compound **55b**	
Empirical formula	C_{25} H_{20} Cl_3 N O_2	
Formula weight	472.77	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 9.7264(7) Å	α= 99.343(3)°.
	b = 10.3197(9) Å	β= 92.395(3)°.
	c = 11.7441(10) Å	γ = 103.029(3)°.
Volume	1129.44(16) $Å^3$	
Z	2	
Density (calculated)	1.390 Mg/m^3	
Absorption coefficient	0.428 mm^{-1}	
F(000)	488	
Crystal size	0.20 x 0.18 x 0.16 mm^3	
Theta range for data collection	2.463 to 25.112°.	
Index ranges	-11<=h<=11, -12<=k<=12, -13<=l<=13	
Reflections collected	23482	
Independent reflections	3947 [R(int) = 0.0289]	
Completeness to theta = 25.112°	98.2 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3947 / 0 / 281	
Goodness-of-fit on F^2	1.027	
Final R indices [I>2sigma(I)]	R1 = 0.0417, wR2 = 0.1144	
R indices (all data)	R1 = 0.0487, wR2 = 0.1210	
Extinction coefficient	n/a	

Largest diff. peak and hole	0.208 and -0.384 e.Å^{-3}

Table A2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **55b_**0m_a. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

atom	x	y	z	U(eq)
Cl(1)	6110(1)	3556(1)	4773(1)	68(1)
Cl(3)	5109(1)	-653(1)	8100(1)	87(1)
Cl(2)	8199(1)	1066(1)	7833(1)	93(1)
O(2)	3083(2)	-282(2)	6422(2)	66(1)
O(1)	8152(1)	2714(2)	6075(2)	66(1)
N(1)	1565(2)	2430(2)	3956(1)	45(1)
C(5)	4352(2)	1606(2)	5670(1)	39(1)
C(17)	2145(2)	3822(2)	2512(2)	47(1)
C(11)	967(2)	3044(2)	3051(2)	44(1)
C(2)	3068(2)	1787(2)	5112(2)	41(1)
C(10)	4189(2)	541(2)	6422(2)	44(1)
C(1)	2941(2)	2442(2)	4184(2)	42(1)
C(19)	4210(2)	5457(2)	1715(2)	44(1)
C(18)	3082(2)	4537(2)	2127(2)	47(1)
C(6)	5701(2)	2301(2)	5587(2)	43(1)
C(7)	6965(2)	2115(2)	6212(2)	46(1)
C(4)	786(2)	1782(2)	4738(2)	61(1)
C(16)	106(2)	4013(2)	3638(2)	52(1)
C(3)	1659(2)	1378(2)	5445(2)	58(1)
C(8)	6725(2)	1170(2)	7047(2)	52(1)
C(9)	5435(2)	457(2)	7160(2)	51(1)
C(12)	2(2)	1928(2)	2146(2)	57(1)
C(24)	5599(2)	5669(2)	2167(2)	57(1)
C(22)	6385(2)	7345(2)	985(2)	58(1)
C(20)	3933(2)	6196(2)	889(2)	59(1)
C(23)	6659(2)	6598(2)	1800(2)	60(1)
C(21)	5011(3)	7122(2)	534(2)	68(1)
C(15)	-669(2)	4589(2)	2773(2)	67(1)
C(13)	-786(3)	2531(3)	1293(2)	75(1)
C(14)	-1623(3)	3477(3)	1908(2)	78(1)
C(25)	7547(3)	8388(3)	607(3)	90(1)

Table A3. Crystal data and structure refinement for compound 76

Identification code	compound **76**	
Empirical formula	$C_{15}\ H_8\ Cl_3\ N\ O_2$	
Formula weight	340.57	
Temperature	299(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 7.691(3) Å	α= 98.321(10)°.
	b = 8.798(3) Å	β= 91.726(11)°.
	c = 11.179(4) Å	γ = 113.282(10)°.
Volume	684.3(4) $Å^3$	
Z	2	
Density (calculated)	1.653 Mg/m^3	
Absorption coefficient	0.671 mm^{-1}	
F(000)	344	
Crystal size	0.2 x 0.18 x 0.14 mm^3	
Theta range for data collection	2.890 to 28.346°.	
Index ranges	-9<=h<=9, -11<=k<=11, -14<=l<=14	
Reflections collected	24463	
Independent reflections	3125 [R(int) = 0.0293]	
Completeness to theta = 25.000°	98.2 %	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3125 / 0 / 190	
Goodness-of-fit on F^2	1.262	
Final R indices [I>2sigma(I)]	R1 = 0.0766, wR2 = 0.1969	
R indices (all data)	R1 = 0.0876, wR2 = 0.2157	
Extinction coefficient	n/a	
Largest diff. peak and hole	1.903 and -2.181 e.$Å^{-3}$	

Table A4. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **76**_0m_a. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

atom	x	y	z	U(eq)
Cl(01)	3288(1)	5936(1)	5027(1)	32(1)
Cl(02)	9133(1)	11905(1)	6492(1)	40(1)
Cl(03)	9951(1)	12212(1)	3733(1)	40(1)
O(004)	7456(3)	9276(2)	2085(2)	36(1)
N(005)	2923(3)	3784(2)	1217(2)	26(1)
O(006)	5819(3)	8876(3)	6641(2)	41(1)
C(007)	3816(3)	4659(3)	2322(2)	25(1)
C(008)	3631(3)	6534(3)	1187(2)	23(1)
C(009)	4311(3)	6367(3)	2364(2)	22(1)
C(00A)	5384(3)	7656(3)	3387(2)	20(1)
C(00B)	5104(3)	7585(3)	4578(2)	22(1)
C(00C)	2779(3)	4902(3)	507(2)	25(1)
C(00D)	3551(3)	7876(3)	675(2)	32(1)
C(00E)	2215(4)	1971(3)	853(2)	37(1)
C(00F)	1934(4)	4560(3)	-681(2)	35(1)
C(00G)	1929(4)	5903(4)	-1177(2)	42(1)
C(00H)	7811(3)	10411(3)	5291(2)	25(1)
C(00I)	8154(3)	10539(3)	4131(2)	25(1)
C(00J)	6216(3)	8929(3)	5594(2)	24(1)
C(00K)	7003(3)	9172(3)	3110(2)	23(1)
C(00L)	2711(4)	7539(4)	-501(3)	40(1)

Annexure III

Hydroboration of Prochiral Olefins using Chiral Amine Borane Complexes under Iodine Activation

1 Introduction

In 1956, H. C. Brown and B. C. SubbaRao discovered the hydroboration reaction.[1] The borane complexes of tetrahydrofuran (THF), dimethyl sulfide (DMS) and sterically crowded amines were reported extensively for the hydroboration reactions of double and triple bonds. The borane adducts were also used for the reduction of aldehydes, ketones, carboxylicacids, amides, lactams and schiff bases. Conversion of prochiral ketones to chiral alcohols were achieved by using oxazaborolidine catalyst in organic synthesis.[2] We have also undertaken efforts on applications of the borane complexes of chiral 2,3-diphenyldecahydroquinoxaline for hydroboration studies using different prochiral olefins.

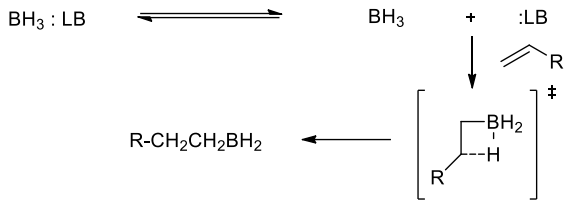
III.1.1 Asymmetric hydroboration using chiral amine-borane complexes

Over the years various borane ether complexes such as H_3B:THF, BH_3:SMe_2 and BH_3:$N(C_2H_5)_2Ph$ were developed and are commercially available.[3] The relatively stable amine-borane complexes are 'easy to handle' carriers of borane. However, due to strong complexation, majorityof amine-boranes complexes hydroborate the olefins only at higher temperatures. For example, the pyridine-borane adduct hydroborates the alkenes in diglyme solvent at 100 °C.[4] The *N*,*N*-diethylaniline-borane adduct hydroborates the olefins at ambient conditions due to weaker strength of the N-B bond by steric or electronic effects.[5]

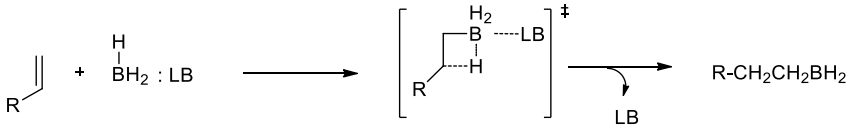
Three types of mechanisms were considered for the hydroboration of olefins (Scheme 1).[6]

Scheme 1

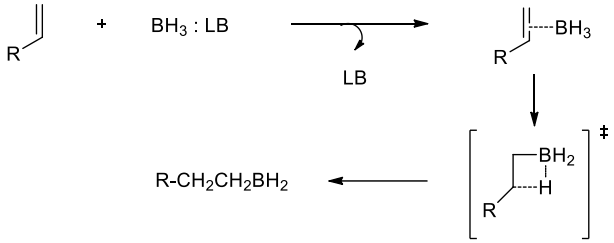
S_N1 type mechanism



S_N2 type mechanism



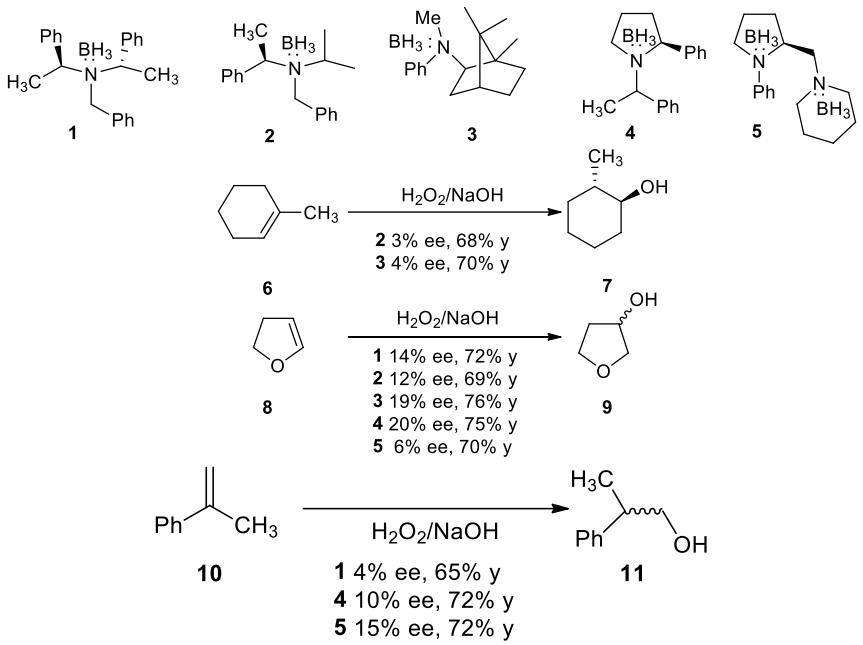
S_N2-type mechanism with π-complex intermediate



Electron rich olefins may follow the S_N2 mechanistic way. The S_N2 reaction occurs with a π-complex intermediate, when the sterically crowded borane complex or olefin involving in reactions. In the S_N1 type reaction the borane complex dissociates in to free BH_3 species before hydroboration (Scheme 1).

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 lead to the corresponding alcohols with 3-20% ee after H_2O_2/NaOH oxidation (Chart 1).[7]

Chart 1

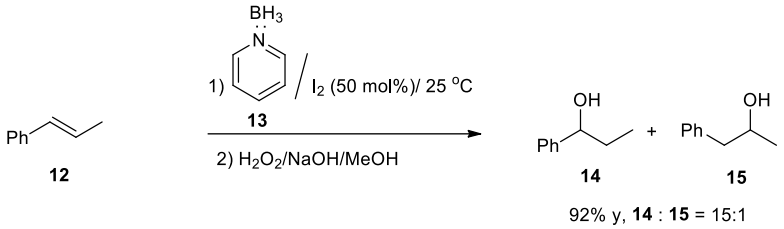


In hydroboration reactions poor enantioselectivity was observed due to may be action of a spectrum of mechanisms possible for the hydroboration reaction (Scheme 1). Also, selectivity of the initial hydroboration by the amine-BH_3 complex and selectivity of further hydroboration by initially formed alkyl boranes (RBH_2 and R_2BH) may be different.

III.1.3 Iodine activation of hydoborations using chiral amine borane complexes

The hydroboration olefins by using iodine with strong amine-BH_3 complexes to give the BH_2I moiety, which may give better enanatioselectivity due to the iodidie behaves as leaving group.[8] Vedejs *et al.*[8] developed the hydroboration reaction of β-methylstyrene **12** with iodine activation of pyridine-borane complex **13** at 25 °C (Scheme 2).

Scheme 2



Chiral α-methylbenzylamine **16** and (*R*)-BINAM **17** gave the corresponding alcohol **11** with 13% and 11% ee respectively, under iodine activation (Chart 2).[9] 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. Tröger base borane complex **20** also gave only the racemic mixture in 85% yield with α-methylstyrene (Chart 2).[9]

Chart 2

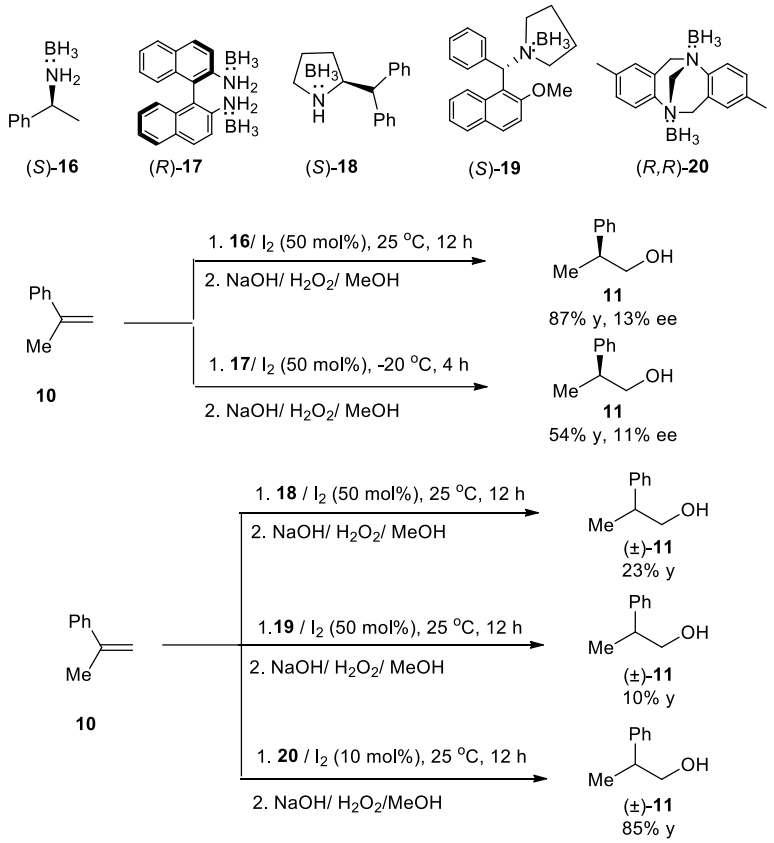
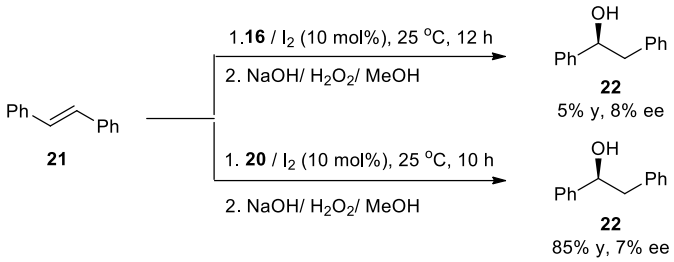


Chart 2 (continued)



Further, the hydroboration reaction of trans-stilbene **21** was reported using Tröger base-borane **20** and α-methylbenzylamine-borane **16** under iodine activation to give the alcohol **22** in 85% yield, 7% ee, and 5% yield, 8% ee respectively (Chart 1).[9]

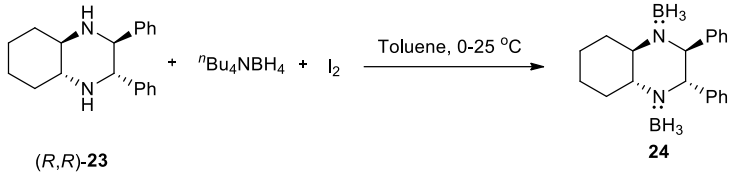
Since chiral 2,3-diphenyldecahydroquinoxaline can be easily accessed *via* the method reported in Chapter 1 (Scheme 5), we became interested to examine the asymmetric hydroboration of prochiral olefins using 2,3-diphenyldecahydroquinoxaline-borane complexes. The results are presented un the next section.

2 Results and Discussions

III.2.1 Hydroboration of olefins using chiral 2,3-diphenyldecahydroquinoxalineborane complex

We have undertaken reaction efforts on the hydroboration reactions using chiral 2,3-diphenyldecahydroquinoxaline-borane complexes. The borane complex **24** was prepared by passing the B_2H_6 gas generated from the reaction of $^nBu_4NBH_4$ **23** with I_2 in toluene (Scheme 3).[9,10]

Scheme 3



(*R*,*R*)-**23** **24**

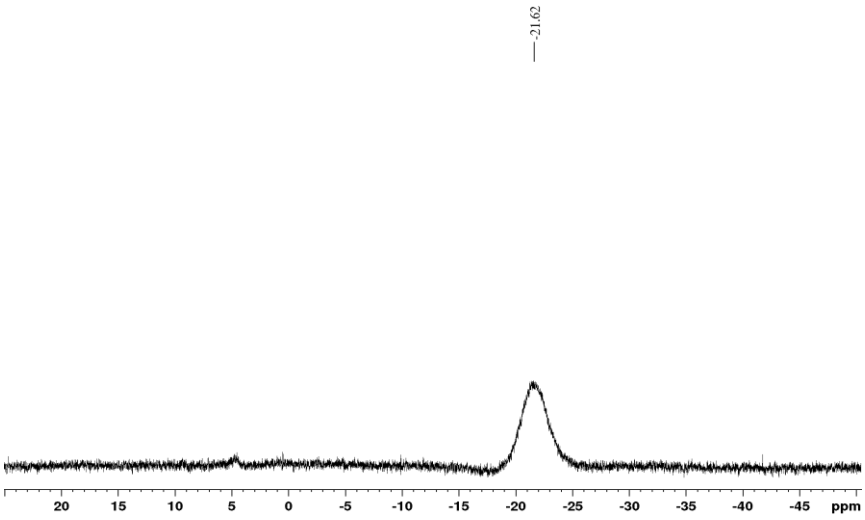
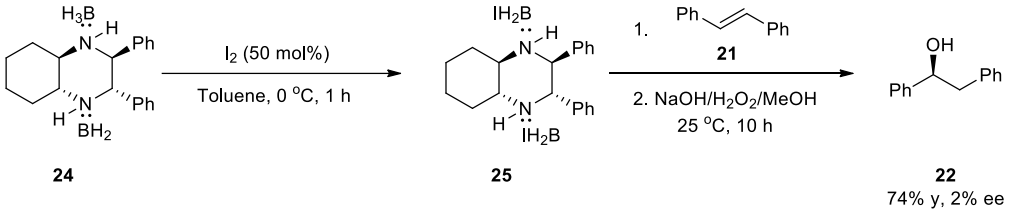


Figure 1 ^{11}B-NMR of the 2,3-diphenyldecahydroquinoxaline-borane complex **24**.

The ^{11}B signal was observed at -21.62 ppm for chiral 2,3-diphenyldecahydroquinoxaline-borane complex **24** (Figure 1). The borane complex **24** was

used for the hydroboration reaction of trans-stilbene in the presence of iodine. The reaction was monitored by ^{11}B NMR. A new peak was observed at -25.83 ppm in the ^{11}B NMR spectrum (Figure 2). After the H_2O_2/NaOH oxidation, the alcohol **22** was observed with 2% ee (Scheme 4, Table 1, entry 1).

Scheme 4



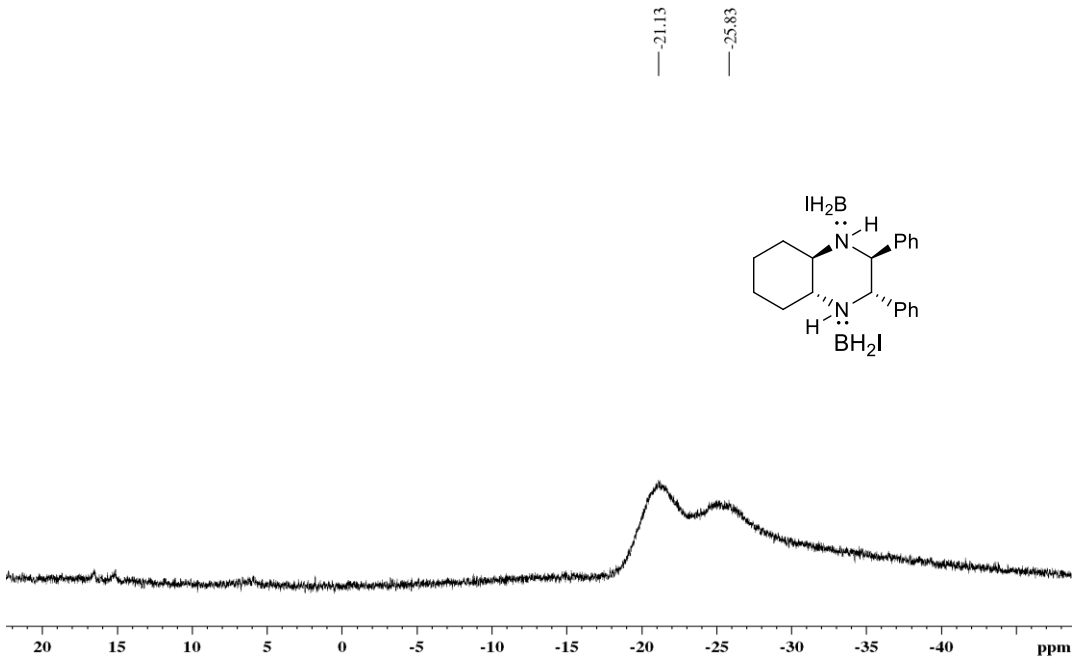
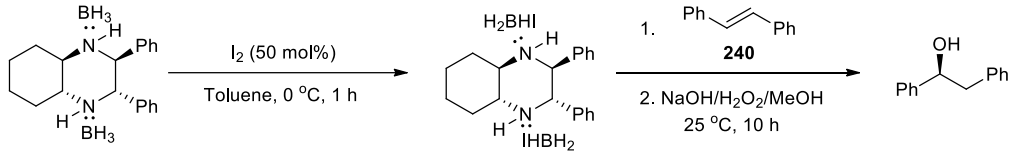


Figure 2 ^{11}B-NMR of the chiral 2,3-diphenyldecahydroquinoxaline-borane complex **25**.

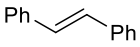
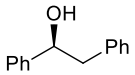
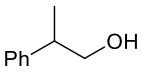
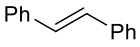
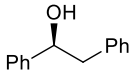
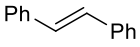
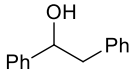
However, hydroboration of α-methylstyrene gave only racemic alcohols by using chiral 2,3-diphenyldecahydroquinoxaline-borane complexe **25** (Table 1, entry 2). The hydroboration was also carried out with catalytic amount (10 or 20 mol% relative to the

piperazine equivalents) of iodine. The alcohol product was observed only in 2% ee after oxidation (Table 1, entry 3).

Table 1. Hydroboration of prochiral olefins using chiral 2,3-diarylpiperazine borane complex under iodine activation[a]



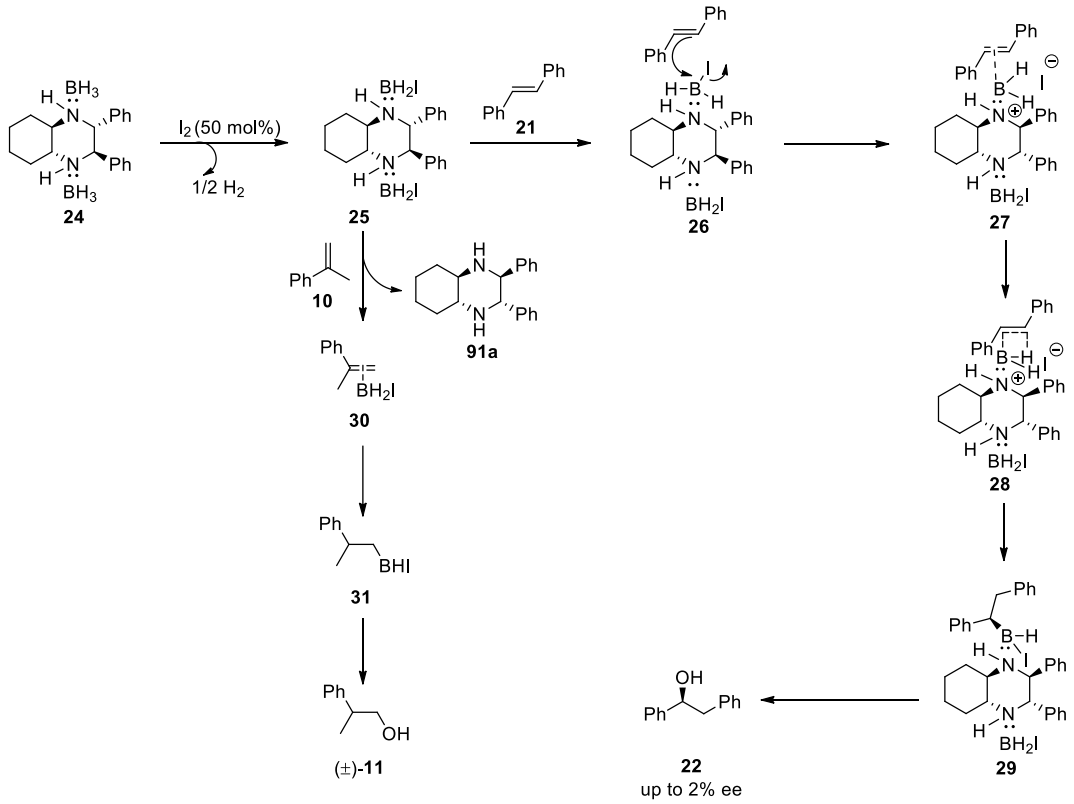
24 **25** **22**
74% y, 2% ee

Entry	Substrate	Borane complex	Product	Yield[b]	% ee[c]
1	 **240**	**25**	 **241**	74	2
2	 **229**	**25**	 **230**	75	0
3[d]	 **240**	**25**	 **241**	70	2
4[e]	 **240**	**25**	 **241**	68	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 OD-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 diarylpiperazine-borane complex **25**, to the reaction mixture was added *N,N*-diethylaniline (weaker than chiral diarylpiperazine) (1 mmol) and allowed to stir for 30 min. Then trans-stilbene (1 mmol) was added and stirred for 10 h.

We have also carried out the hydroboration reaction of trans-stilbene with catalytic amount of iodine using *N*,*N*-diethylaniline as additive to observe whether this could give better selectivities. Unfortunately, these studies did not improve the results (Table 1, entry 4). Presumably, asymmetric induction realized may be poor because the hydroboration reaction takes place after the chiral amine leaves the complex (Scheme 5).

Scheme 5



The hydroboration of olefins by borane complexes of 2,3-diphenyldecahydroquinoxaline-borane complex can be rationalized by considering the mechanism outlined in Scheme 5. The reaction of iodine with chiral 2,3-diphenyldecahydroquinoxaline-BH_3 complex **24** complexes would give the chiral 2,3-diphenyldecahydroquinoxaline-BH_2I complex **25** and hydrogen. During the reaction of olefin

with chiral 2,3-diphenyldecahydroquinoxaline-BH_2I, if the iodide leaves, the chiral 2,3-diphenyldecahydroquinoxaline would be attached to the boron in the transition state leading to the optically active product. However, if chiral 2,3-diphenyldecahydroquinoxaline acts as a leaving group, the hydroboration reaction would lead to racemic mixtures. The results indicate that the chiral 2,3-diphenyldecahydroquinoxaline might leave from chiral 2,3-diphenyldecahydroquinoxaline-BH_2I complex **25** to give the π-complex **30**. Presumably, only a fraction of the product may be formed *via* the iodide displacement mechanism involving the intermediates **26-29** leading to poor ee.

3 Conclusions

Efforts were made for the preparation of BH_3 complexes of chiral diamine containing trans-(*1R,2R*)-diaminocyclohexane moiety for studies on iodine activated hydroboration of α-methyl styrene, trans stilbene and cis stilbene. However, the alcohols were obtained only in poor enantiomer excess after H_2O_2/OH^- oxidation, indicating that the chiral amine may not be present in the transition state of the hydroboration reaction.

4 Experimental Section

III.4.1 General information

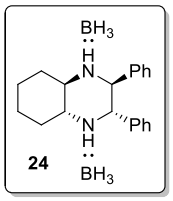
Melting points reported in this thesis are uncorrected and were determined using a superfit capillary point apparatus. IR (KBr) and IR (neat) spectra were recorded on JASCO FT-IR spectrophotometer model-5300. ^{1}H (400 MHz), ^{13}C (100 MHz) NMR spectra were recorded on Bruker-Avance-400 spectrometers chloroform-d as solvent. Chemical shifts were determined with tetramethylsilane (TMS) as internal reference (δ = 0 ppm). Coupling constants *J* are in Hz. High-resolution mass spectra (HRMS) were recorded on micromass ESI-TOF. HPLC analyses were performed on a SCL-10ATVP SHIMADZU instrument. Optical rotations were measured on Rudolph Research Analytical 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-methylbenzylamine $[\alpha]_D^{25}$ = –29.6 (c 0.74, EtOH) supplied by Aldrich.

All the glasswares were pre-dried at 100-120 °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 reagent were carried out using standard syringe-septum technique recommended for handling air sensitive reagents and organometallic compounds.

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

III.4.2 Hydroboration of olefins

III.4.3 Preparation of chiral 2,3-diphenyldecahydroquinoxaline-borane complex



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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 the addition funnel. The diborane gas generated in this way was bubbled through a side arm using bubbler into another reaction flask containing chiral 2,3-diphenyldecahydroquinoxaline **93** (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) -21.62

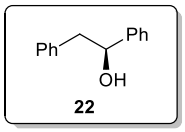
{δ = 0, BF_3:Et_2O (external reference)}

III.4.4 General procedure for the hydroboration of prochiral olefins using chiral 2,3-diphenyldecahydroquinoxaline-borane complexe 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 3 N 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 (10 mL), 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



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Yield : 0.142 g (72%).

mp : 66-68 °C

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

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.38-7.35 (m, 3H), 7.32-7.27 (m, 3H), 7.26-7.21 (m, 4H), 4.93-4.89 (m, 1H), 3.09-2.98 (m, 2H), 2.00 (s, 1H).

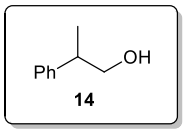
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 143.8, 138.0, 129.5, 128.5, 128.4, 127.6, 126.6, 125.9, 75.3, 46.1.

IR (KBr) : (cm^{-1}) 3320, 3090, 3068, 3024, 2915, 2860, 1605, 1583, 1495, 1457, 1068, 1035, 947, 920, 783, 761, 739, 695, 558.

$[\alpha]_D^{25}$: +1.4 (c, 0.5, EtOH), {lit.[196] for 100% ee, $[\alpha]_D^{25}$ = +52.8 (c, 1.40, EtOH} (2% ee, confirmed by HPLC using chiral column, chiralcel OD-H, hexanes:*i*-PrOH/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



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Yield : 0.103 g (76%).

IR (neat) : (cm^{-1}) 3336, 3030, 2958, 1600, 1495, 1035, 756.

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

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List of publications

1. Zinc salt promoted diastereoselective synthesis of chiral propargylamines using chiral piperazines and their enantioselective conversion to chiral allenes; Periasamy, M.; Reddy, P. O.; Edukondalu, **A**.; Dalai, M.; Alakonda, L. M.; **Udaykumar, B**. *Eur. J. Org. Chem.* **2014**, 6067.

2. Synthesis of propargylamines *via* Michael addition using methyl vinyl ketone derivatives, 1-alkynes and secondary amines catalyzed by copper(I)halides; **Udaykumar, B**.; Periasamy, M. (*communicated).*

3. Synthesis of chiral propargylamines using (*S*)-dpp, α,β-unsaturated ketones and 1-alkynes with Cu(I)Cl; **Udaykumar, B**.; Periasamy, M. (*to be communicated).*

4. Synthesis of substituted pyrroloquinones from the *N*-Propargyl and *N*- alkyl pyrrolidines using *p*-chloranil; **Udaykumar, B**; Periasamy, M. (*to be communicated).*

5. Ambient heat harvesting organic electrochemical cells using N^1,N^1,N^2,N^2-tetramethylcyclohexane-1,2-diamine as donor with *p*-chloranil acceptor; **Udaykumar, B**; Periasamy, M. (*to be communicated).*

Posters presented in symposia

1. Poster presentation in the *Chemfest 2017* (annual in-house symposium) held at School of Chemistry, University of Hyderabad, INDIA, March-**2017**. Title: New synthetic methods based on secondary amines.

2. Poster presentation in the *Chemfest 2018* (annual in-house symposium) held at School of Chemistry, University of Hyderabad, INDIA, March-**2018**. Title: Synthesis of propargylamines and allenes using aldehydes (or) α,β- unsaturated ketones, amines and 1-alkynes.

Synthesis of Allenes and Propargylamines and Development of Electron Transfer Reactions

by Bantu Udaykumar

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Character count: 61459

Synthesis of Allenes and Propargylamines and Development of Electron Transfer Reactions

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2	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	2%

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