Synthetic Methods Based on Electron Transfer Reactions using *tertiary* N-Arylamine Donors

A Thesis

Submitted for the Degree of

DOCTOR OF PHILOSOPHY

By

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Abbreviations

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

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

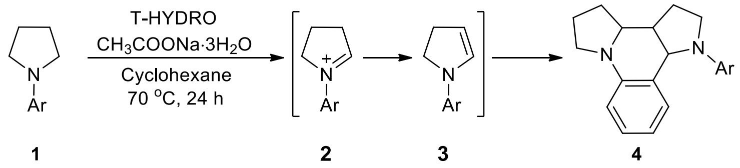
Abstract

This thesis describes the enlargement of "**Synthetic Methods Based on Electron Transfer Reactions using *tertiary* N-Arylamine Donors**" comprises of four chapters. Each chapter is subdivided 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 studies on the oxidation of α C-H bond adjacent to the nitrogen atom of tertiary amines by using *tert*-butyl hydroperoxide and base systems through *in situ* formation of imine and enamine intermediates. In the introductory section, a brief review on the oxidation of tertiary amines using different oxidation systems is presented.

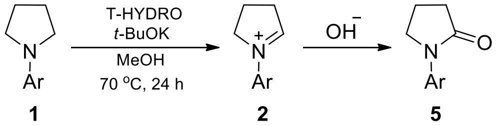
We have observed that the reaction of N-arylpyrrolidine **1** derivatives with 70% aqueous *tert*-butyl hydroperoxide (T-HYDRO) in the presence of $CH_3COONa \cdot 3H_2O$ gives tetracyclic amines **4** in 59-78% yields *via* cycloaddition of the corresponding iminium ion **2** and enamine **3** intermediates formed *in situ* in cyclohexane solvent (Scheme 1).

Scheme 1



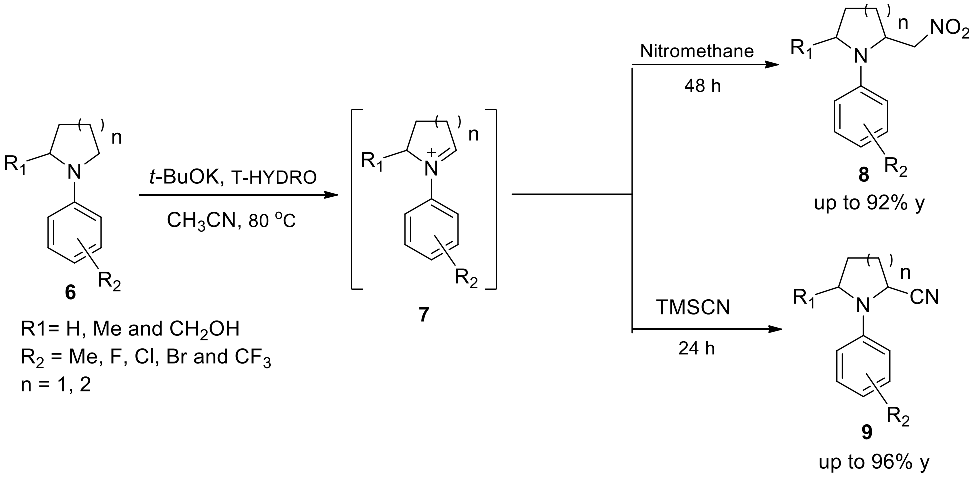
We have also observed that the oxidation of N-phenylpyrrolidines **1** using 70% aqueous *tert*-butyl hydroperoxide and *t*-BuOK in methanol solvent gave the N-phenylpyrrolidones **5** in 77-89% yields (Scheme 2).

Scheme 2



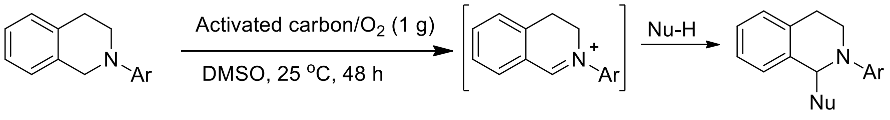
We have developed a metal free C-H functionalization of N-aryl *tert*-amines using nitromethane and TMSCN with the simple oxidizing agent tertiary butyl hydroperoxide (T-HYDRO) and *t*-BuOK. The β-nitroamines **8** and α-aminonitriles **9** were obtained in up to 92% and 96% yields, respectively (Scheme 3).

Scheme 3



In the second chapter, investigations on the methods of synthesis of cross coupled products using N-aryltetrahydroisoquinoline **10** and oxygen adsorbed carbon materials are described (Scheme 4).

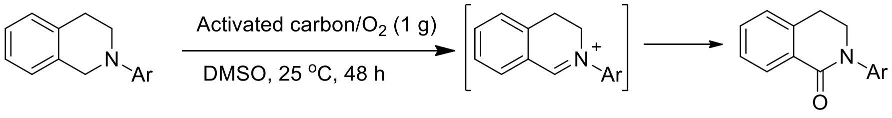
Scheme 4



10 **11** **12**

In the absence of nucleophiles, the corresponding amide derivatives **13** were formed in 65-81% yield (Scheme 5).

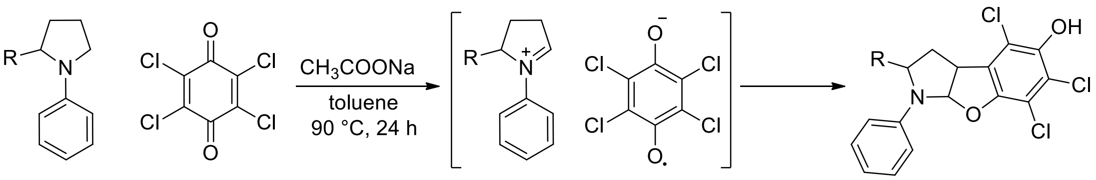
Scheme 5



10 **11** **13**

In the third chapter, results of studies on the electron transfer reactions of tertiary amine derivatives with *p*-chloranil are described. The nature of the intermediates and charge transfer and complexes formed were investigated by UV-Visible and epr spectroscopic methods. Further, we have observed that the coupled products **18** are formed in the reaction of N-arylpyrrolidines **14** and *p*-chloranil **15** in toulene solvent at 90 °C (Scheme 6).

Scheme 6



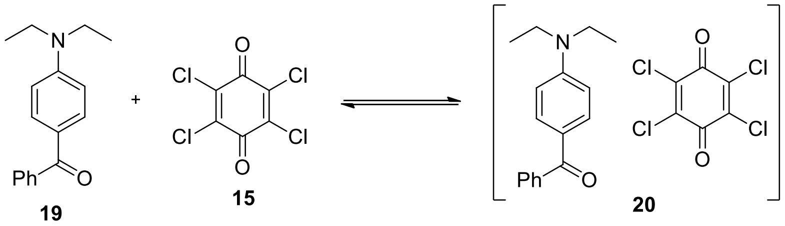
14 **15** **16** **17** **18**

R = H or Me

up to 73% yields

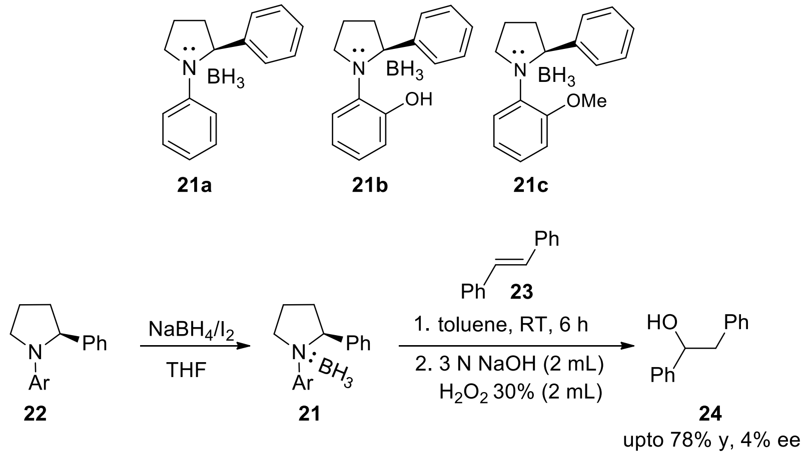
Also, we have observed that the *p*-benzoyl-N,N-diethylaniline **19** reacts with *p*-chloranil to give a weak charge transfer complex as confirmed by UV-visible spectroscopy. Accordingly, we have constructed an electrochemical cell with different configurations (Scheme 7).

Scheme 7



In appendix-I, we have briefly described results of studies on the hydroboration of prochiral olefins with chiral amine borane complexes (Scheme 7).

Scheme 7



In the experimental sections, details of procedures and spectral data are provided.

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

Chapter 1

Electron Transfer Reactions using tert-Butyl Hydroperoxide and N-Arylpyrrolidine System

1.1 Introduction

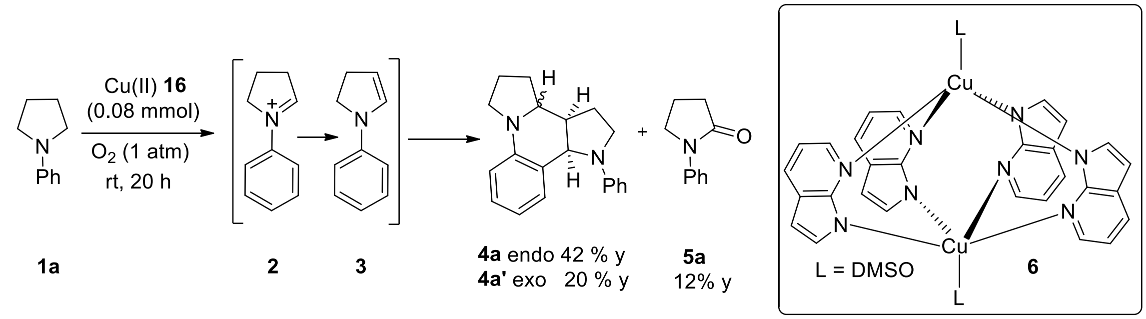
Carbon-Carbon bond formation is the most important class of reactions in organic chemistry. Many metal catalyzed cross coupling reactions have been reported over the years.[1-12] Several oxidative coupling reactions involves amines were also reported by C-H functionalization of tertiary amines at C-H bond adjacent to nitrogen.[13]

We became interested on the synthesis of tetracyclic amines using N-arylpyrrolidine derivatives *via* tertiary butyl hydroperoxide mediated oxidative coupling reaction through the *in situ* formation of iminium and enamine intermediates. A brief review of various methods available for the synthesis of tetracyclic amines will be useful for the discussion.

1.1.1 Synthesis of tetracyclic amines

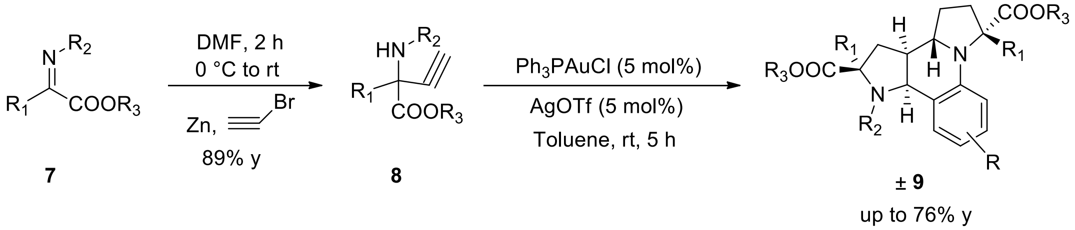
A method for the synthesis of tetracyclic amines was reported using N-phenylpyrrolidine **1a** *via* reaction with binuclear copper (II) complex of 7-azaindole **6** in presence of O_2 (1 atm) to give the cyclic adduct **4** besides the oxygenated product N-phenylpyrrolidone **5a** (Scheme 1).[14]

Scheme 1



An improved method was developed to access tetracyclic framework as a single diastereoisomer using gold catalyst. It involves the use of propargylic α-amino esters **8** as a starting material followed by an intramolecular hydroamination and Aza-Diels–Alder reaction. The overall process leads to the formation of nitrogen-containing tetracyclic amines **9** single diastereoisomer in most cases, through the formation of two C–C bonds, two C–N bonds and five stereo centers (Scheme 2).[15]

Scheme 2



R = 4-OMe, 4-Me, H, 3,5-$(OMe)_2$

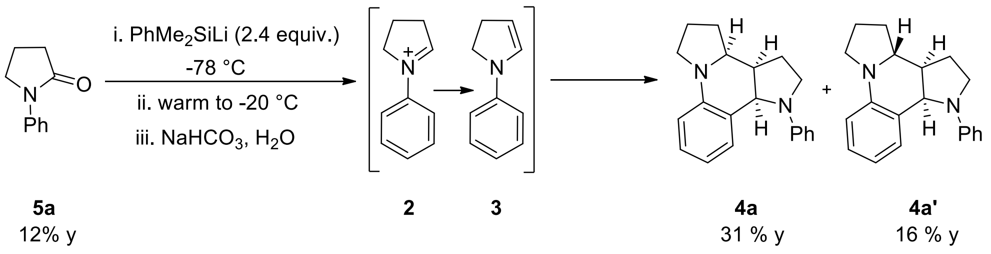
R_1 = CF_3, $ClCF_2$, AllylCF_2, Ph, Me, PMP, 4-Cl-C_6H_4, Allyl, 2-Napthyl

R_2 = PMP, 4-MeC_6H_4, Ph, 3,5-$(MeO)_2C_6H_4$

R_3 = Et, Me, Bn, $(CH_2)_2$TMS

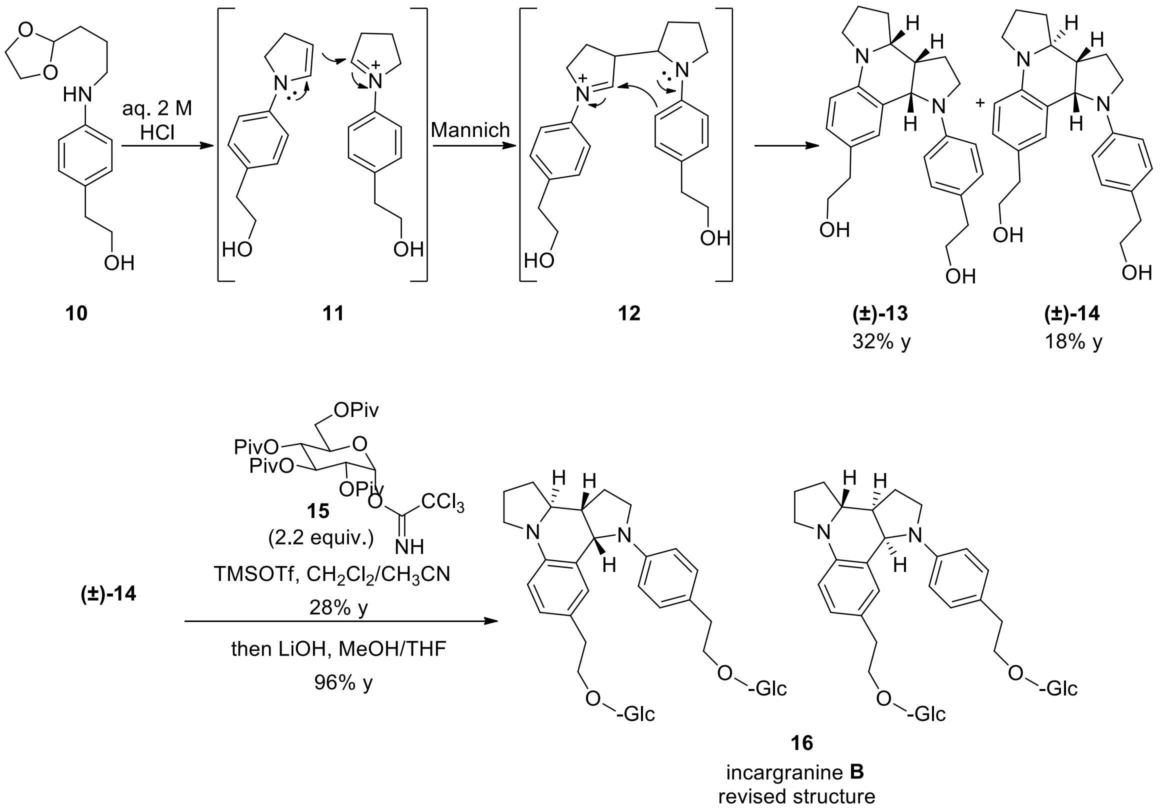
Also, a method was developed for the synthesis of tetracyclic amines by the reaction of N-phenylpyrrolidone **5a** with phenyldimethylsilyllithium at -78 °C. The tetracyclic amines **4a** and **4a′** were formed as major products through the formation of iminium ion and enamine intermediates (Scheme 3).[16]

Scheme 3



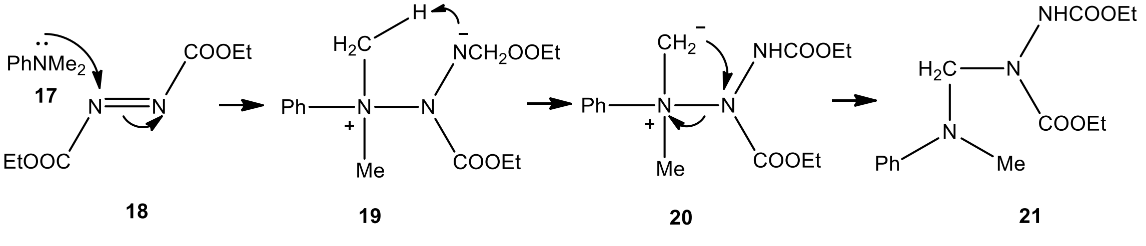
The incargranine B **16** is a biosynthetically important structure synthesized using the glucosyl donor **15** (Scheme 4).[17]

Scheme 4



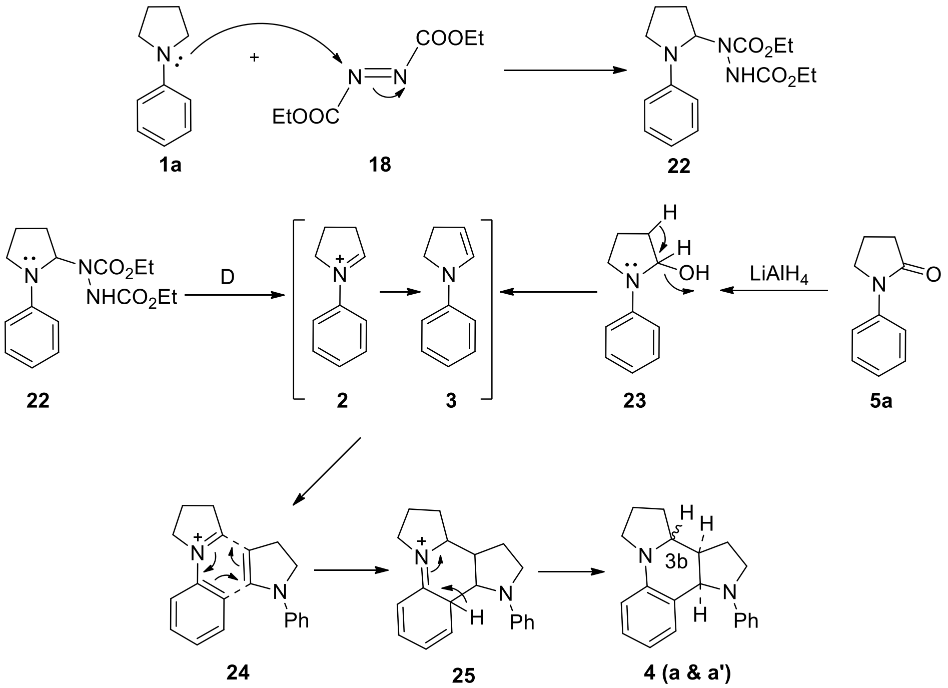
Reaction of N,N-dimethylaniline **17** with diethylazodicarboxylate (DEAD) **18** gave the hydrazine **19** and the process rationalized by Huisgen (Scheme 5).[18,19]

Scheme 5



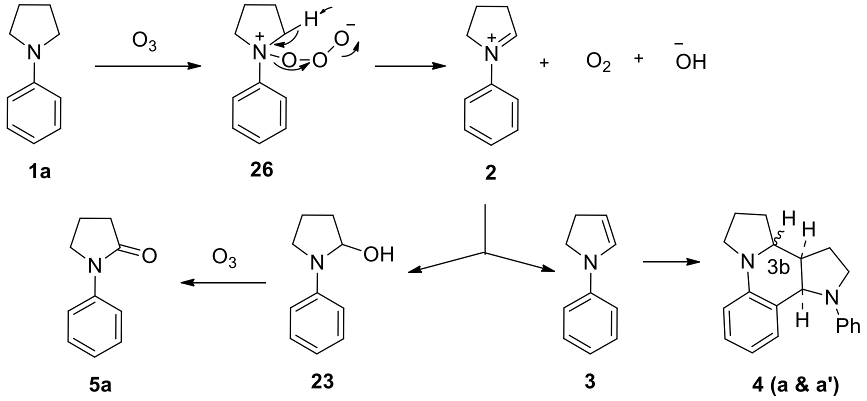
The reaction of N-phenylpyrrolidine **1a** and diethyl azodicarboxylate **18** gave an analogous adduct **22** in high yield, which on heating in xylene, eliminated diethyl hydrazodicarboxylate **18** to form two isomers **4** through the imine **2** and enamine **3** intermediates. Moreover, lithium aluminum hydride reduction of N-phenyl-2-pyrrolidone **5a** also leads to the same two isomers **4**. The mechanisms for formations of two isomers are rationalized by the (4+2) addition reaction as shown in Scheme 6.

Scheme 6



In addition, generation of iminium ions *in situ* was reported by reaction of ozone and tertiary amines.[21] For example, ozonalysis of N-phenylpyrrolidine **1a** gave the dimer **4** along with N-phenyl-2-pyrrolidone **5a**. Also, the formation of the cyclic adduct **4** by γ-irradiation of N-phenylpyrrolidine **1a** was reported (Scheme 7).[21]

Scheme 7



1.1.2 Oxidative C-H functionalization of tertiary amines

The transformation of tertiary amines to the corresponding α-functionalized derivatives is a useful synthetic method. Generally, such transformations involve oxidation of C-H bond adjacent to a nitrogen atom of tertiary amines through iminium ions followed by construction of C-C bond.[22] Recently, several metal-based catalysts were reported for such direct oxidative functionalization of tertiary amines.[23] Also, a few metal-free methods using stoichiometric amount of an oxidant, such as DDQ, I_2, H_2O_2, TBHP, and $PhI(OAc)_2$ were reported.[24] In addition, photoredox catalysts were used for such transformations.[25] We have developed a method for C-H functionalization of N-aryl tertiary amines using nitromethane and TMSCN with the *aq*.TBHP/*t*-BuOK system. A brief review of methods reported will be helpful for the discussion.

1.1.2.1 C-H functionalization of tertiary amines using Cu catalyst

Recent reports highlighted the ability of CuX or CuX_2 as versatile reagent in organic synthesis.[26] Several copper catalyzed cross coupling reactions *via* iminium ion intermediate were reported (Chart 1).[27-37]

Chart 1

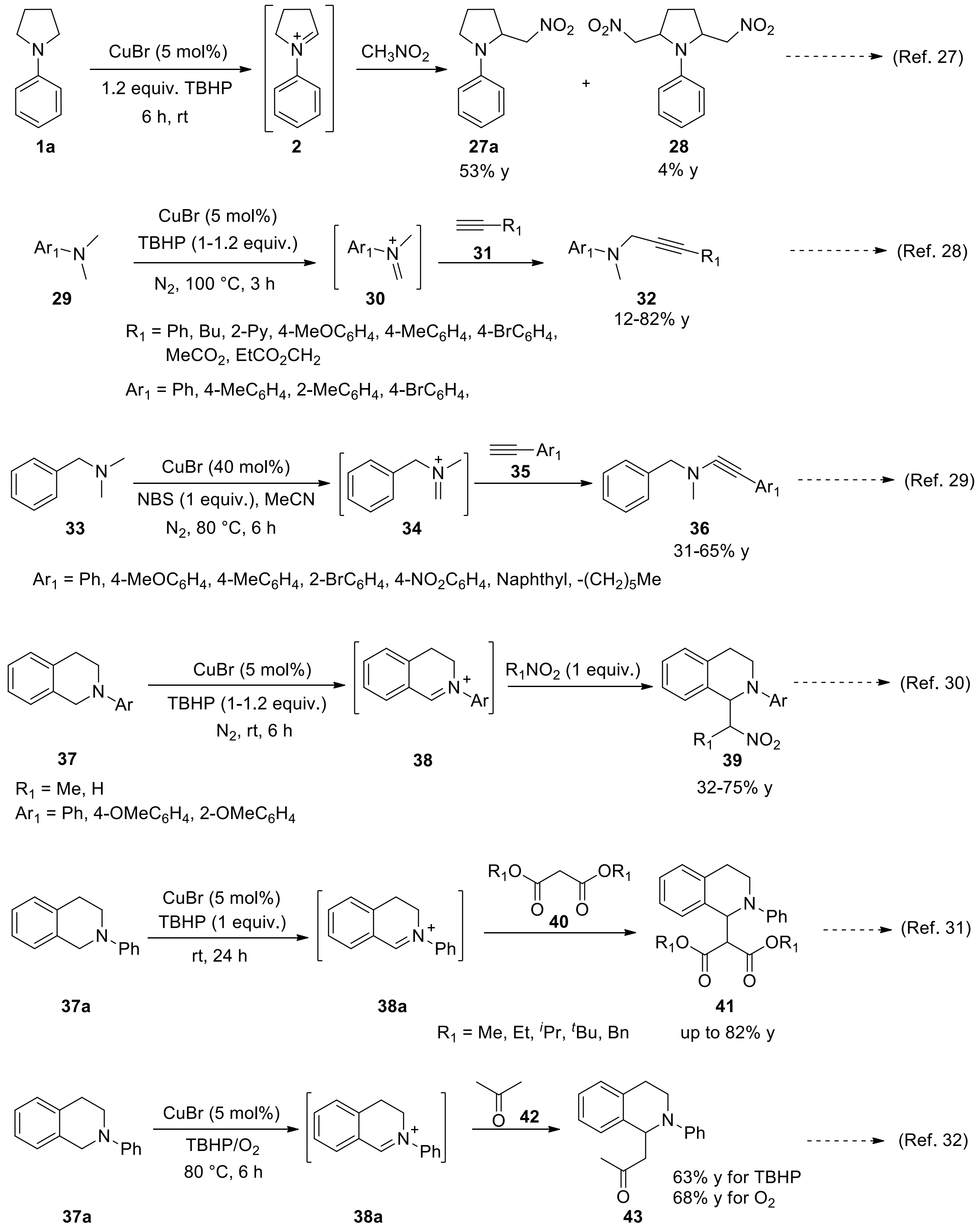
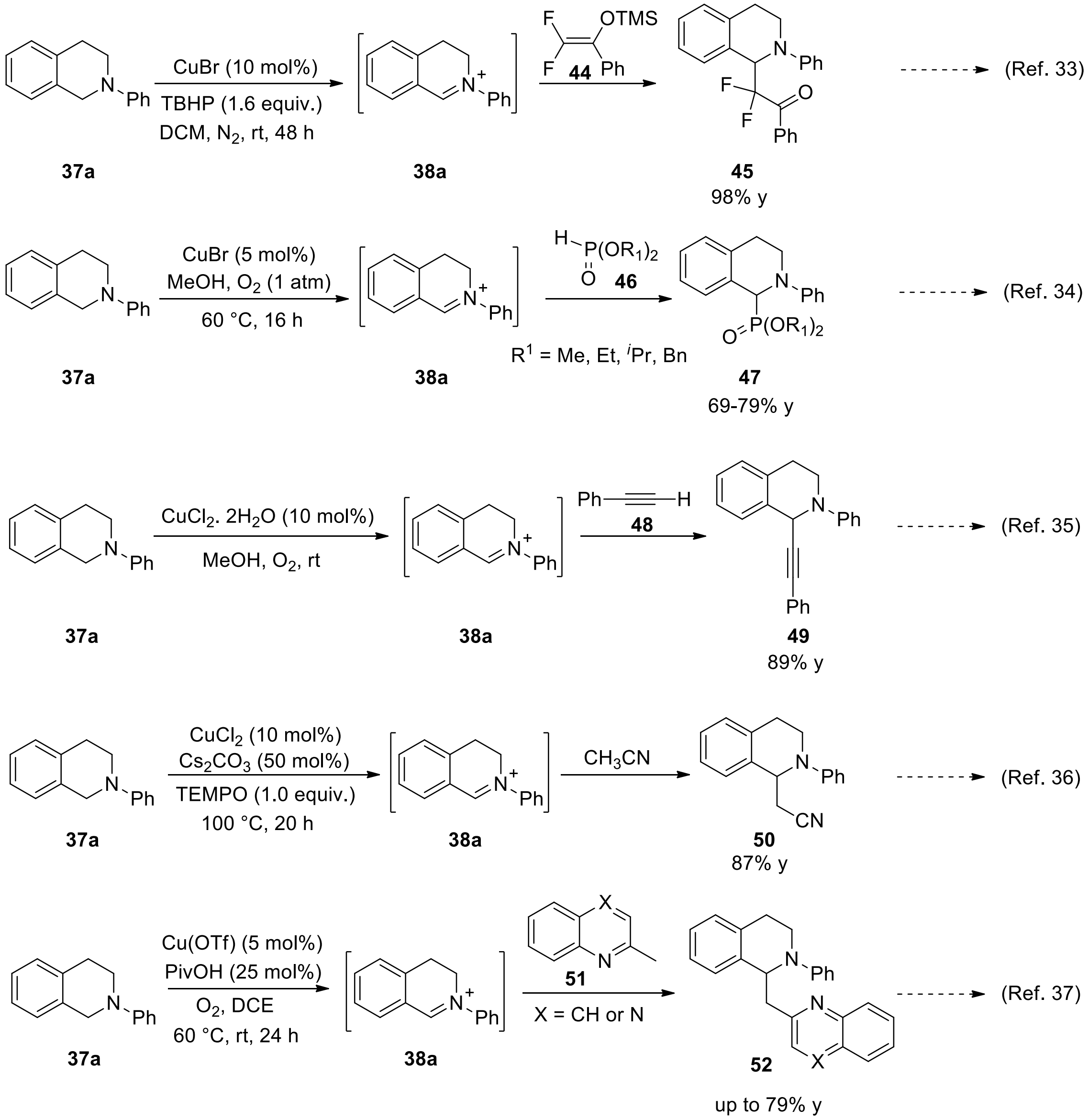
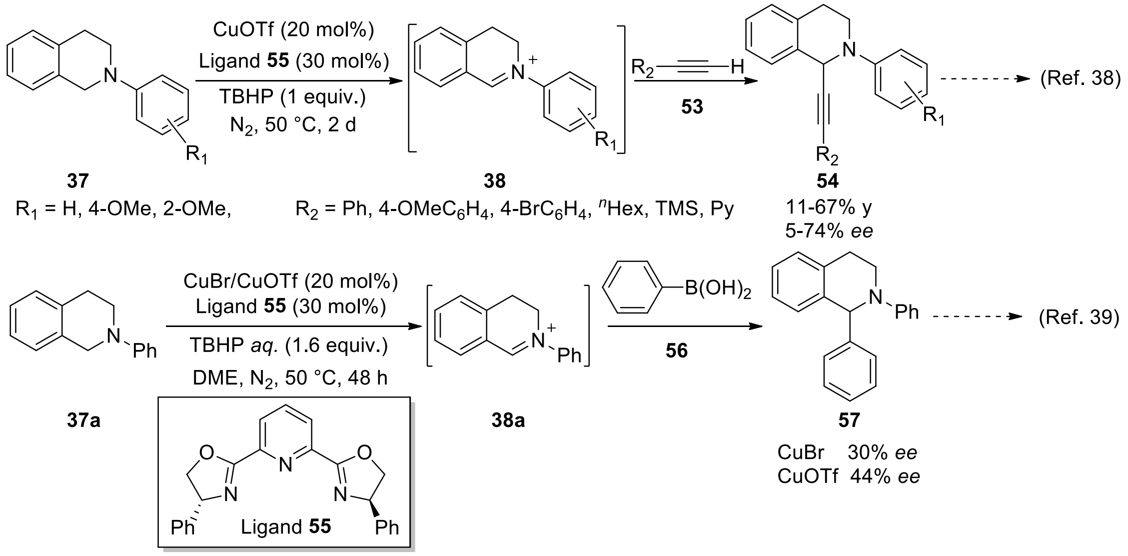

CuBr (5 mol%)
1.2 equiv. TBHP
6 h, rt
CH$_3$NO$_2$
NO$_2$
O$_2$N
+
1a
2
27a
53% y
28
4% y
(Ref. 27)
CuBr (5 mol%)
TBHP (1-1.2 equiv.)
N$_2$, 100 °C, 3 h
Ar$_1$
R$_1$
31
29
30
32
12-82% y
(Ref. 28)
R$_1$ = Ph, Bu, 2-Py, 4-MeOC$_6$H$_4$, 4-MeC$_6$H$_4$, 4-BrC$_6$H$_4$, MeCO$_2$, EtCO$_2$CH$_2$
Ar$_1$ = Ph, 4-MeC$_6$H$_4$, 2-MeC$_6$H$_4$, 4-BrC$_6$H$_4$,
CuBr (40 mol%)
NBS (1 equiv.), MeCN
N$_2$, 80 °C, 6 h
Ar$_1$
35
33
34
36
31-65% y
(Ref. 29)
Ar$_1$ = Ph, 4-MeOC$_6$H$_4$, 4-MeC$_6$H$_4$, 2-BrC$_6$H$_4$, 4-NO$_2$C$_6$H$_4$, Naphthyl, -(CH$_2$)$_5$Me
CuBr (5 mol%)
TBHP (1-1.2 equiv.)
N$_2$, rt, 6 h
R$_1$NO$_2$ (1 equiv.)
Ar
37
38
39
32-75% y
(Ref. 30)
R$_1$ = Me, H
Ar$_1$ = Ph, 4-OMeC$_6$H$_4$, 2-OMeC$_6$H$_4$
CuBr (5 mol%)
TBHP (1 equiv.)
rt, 24 h
R$_1$O
OR$_1$
40
Ph
37a
38a
41
R$_1$ = Me, Et, ^{i}Pr, ^{t}Bu, Bn
up to 82% y
(Ref. 31)
CuBr (5 mol%)
TBHP/O$_2$
80 °C, 6 h
42
Ph
37a
38a
43
63% y for TBHP
68% y for O$_2$
(Ref. 32)

Chart 1 (Continued)



In addition, enantioselective cross dehydrogenative coupling reactions using metal salts and chiral ligand **55** were also reported (Chart 2).[38, 39]

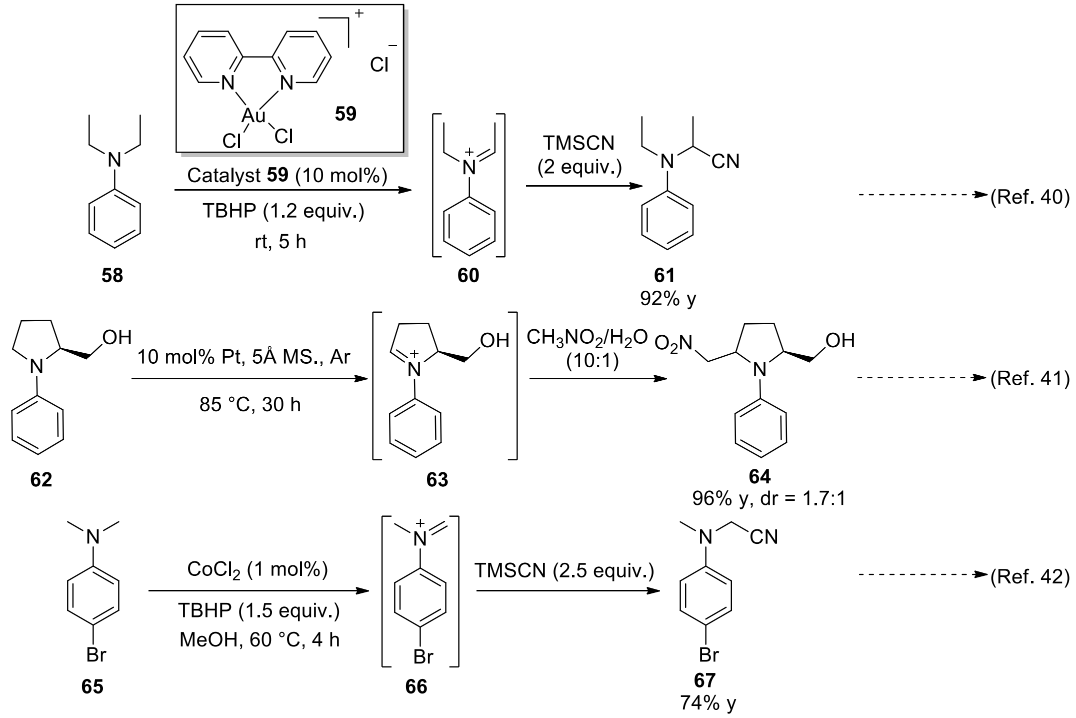
Chart 2



1.1.2.2 C-H functionalization of tertiary amines under metal catalysis

C–H functionalization of tertiary amines by cross dehydrogenative coupling reactions using Au, Pt, and Co metal salts were reported (Chart 3).[40-42]

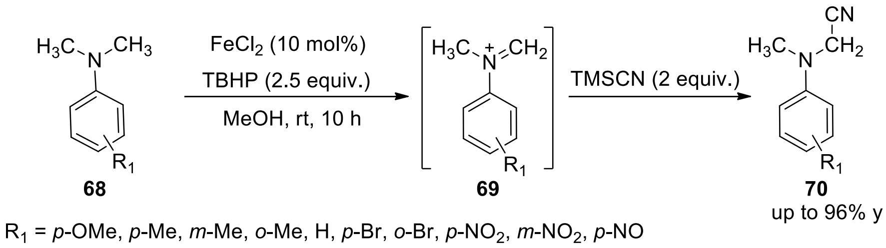
Chart 3



1.1.2.3 Iron catalyzed C-H functionalization of tertiary amines

Iron salts were frequently used as catalysts along with oxidants such as organic peroxides, O_2, or DDQ for C-H bond oxidation.[43] Also, the Iron(II) and iron(III) catalyzed oxidative α-cyanation of tertiary amines were reported by using trimethylsilyl cyanide in the presence of *tert*-butylhydroperoxide under acid-free conditions (Scheme 8).[44]

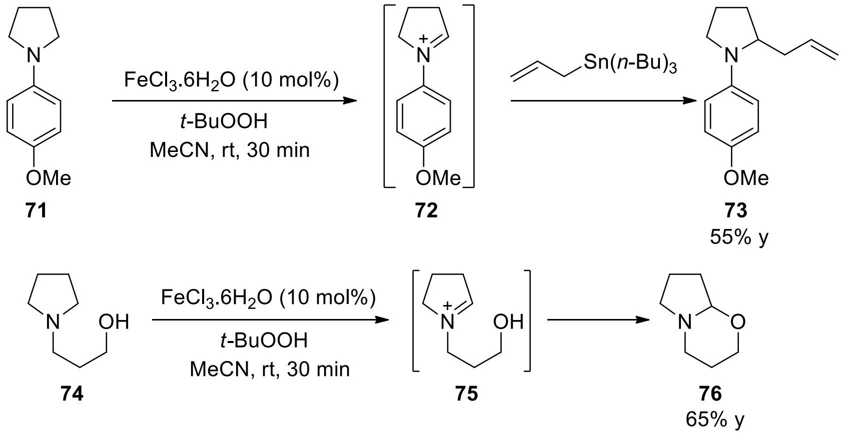
Scheme 8



R_1 = *p*-OMe, *p*-Me, *m*-Me, *o*-Me, H, *p*-Br, *o*-Br, *p*-NO_2, *m*-NO_2, *p*-NO

Furthermore, $FeCl_3$ catalyzed oxidative allylation of tertiary amines was reported by using allyltributyltin and 70% ^{t}BuOOH in H_2O as terminal oxidant in acetonitrile. Also, 1,3-oxazolidines **76** were synthesized (Chart 4).[45]

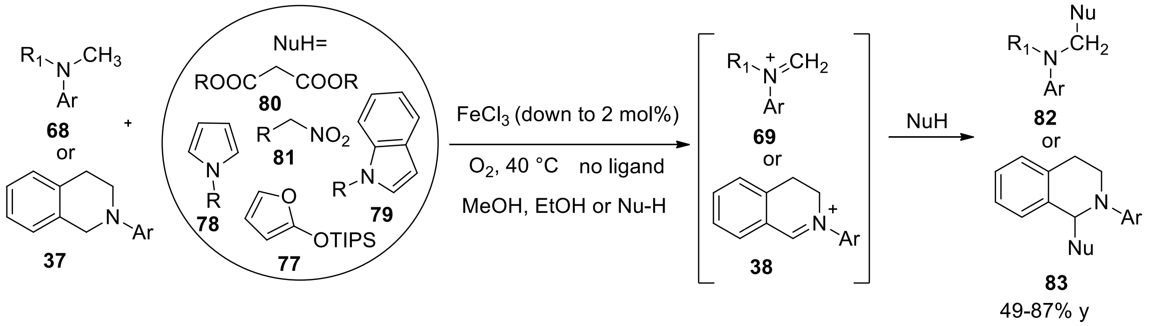
Chart 4



Iron(III) chloride catalyzed aerobic oxidation of tertiary amines, including tetrahydroisoquinolines **37**, gives reactive iminium ion intermediates **69** & **38** that undergo

Mannich reactions with silyloxyfurans, nitroalkanes, and other nucleophiles to give the corresponding butenolides, nitro compounds, and α-substituted tetrahydroisoquinolines **83**, respectively (Scheme 9).[46]

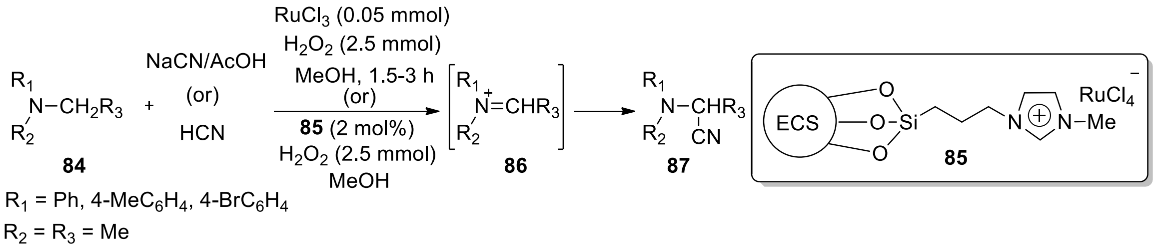
Scheme 9



1.1.2.4 C-H functionalization of tertiary amines using Ru catalyst

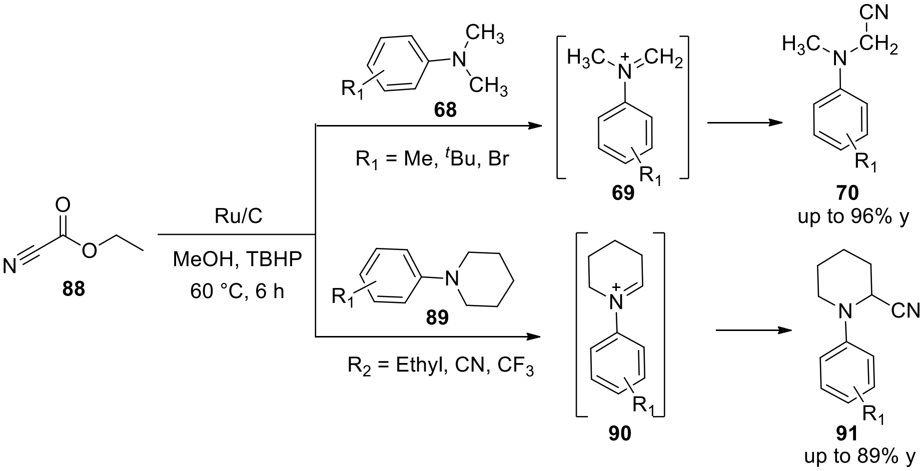
Previously, direct C-H functionalization and C-C bond formation reactions were reported under H_2O_2 oxidation conditions in the presence of $RuCl_3$ as catalyst and sodium cyanide.[47] Later, starch immobilized ruthenium trichloride **85** catalyzed, oxidative cyanation of tertiary amines to α-aminonitriles using hydrogen peroxide and sodium cyanide was reported (Scheme 10).[48]

Scheme 10



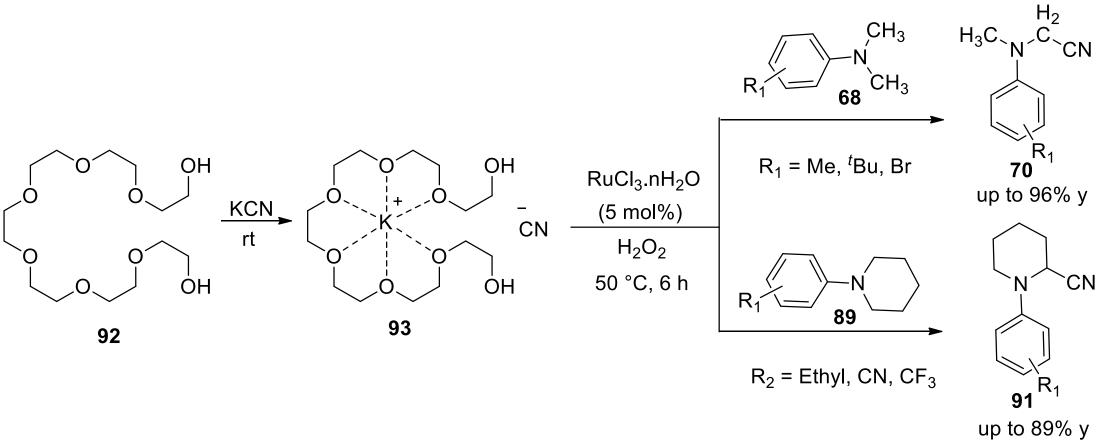
A recyclable Ru/C catalyzed was used in the oxidative α-cyanation of tertiary amines **68** and **89** using ethyl cyanoformate **88** and TBHP under ambient conditions (Scheme 11).[49]

Scheme 11



Potassium PEG-cyanide as a new cyanide source was used in the oxidative cyanation of tertiary amines **68** and **89** to access the corresponding α-aminonitriles using hydrogen peroxide as an oxidant and ruthenium trichloride as catalyst (Scheme 12).[50]

Scheme 12

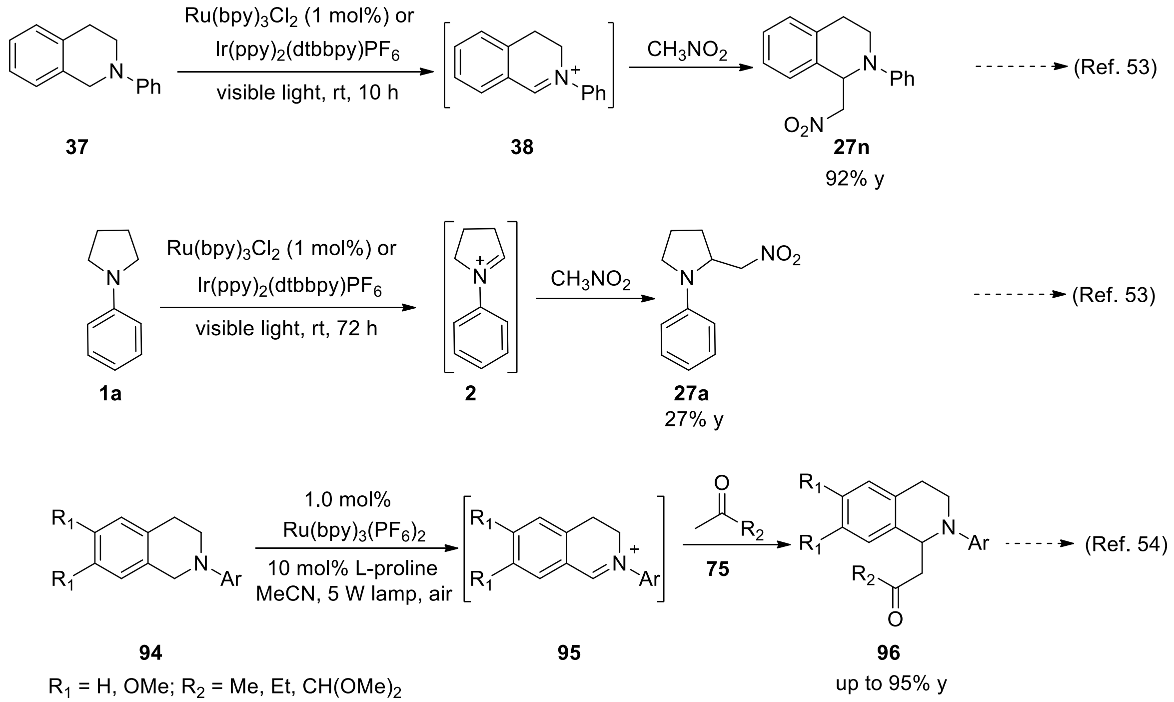


The ruthenium complexes were also used as photoredox catalyst for C-H functionalization of N-aryltertiary amines. Accordingly, a brief review on this topic will be helpful for the discussion.

1.1.2.5 Visible-Light Photoredox Catalysis for C-H functionalization of tertiary amines

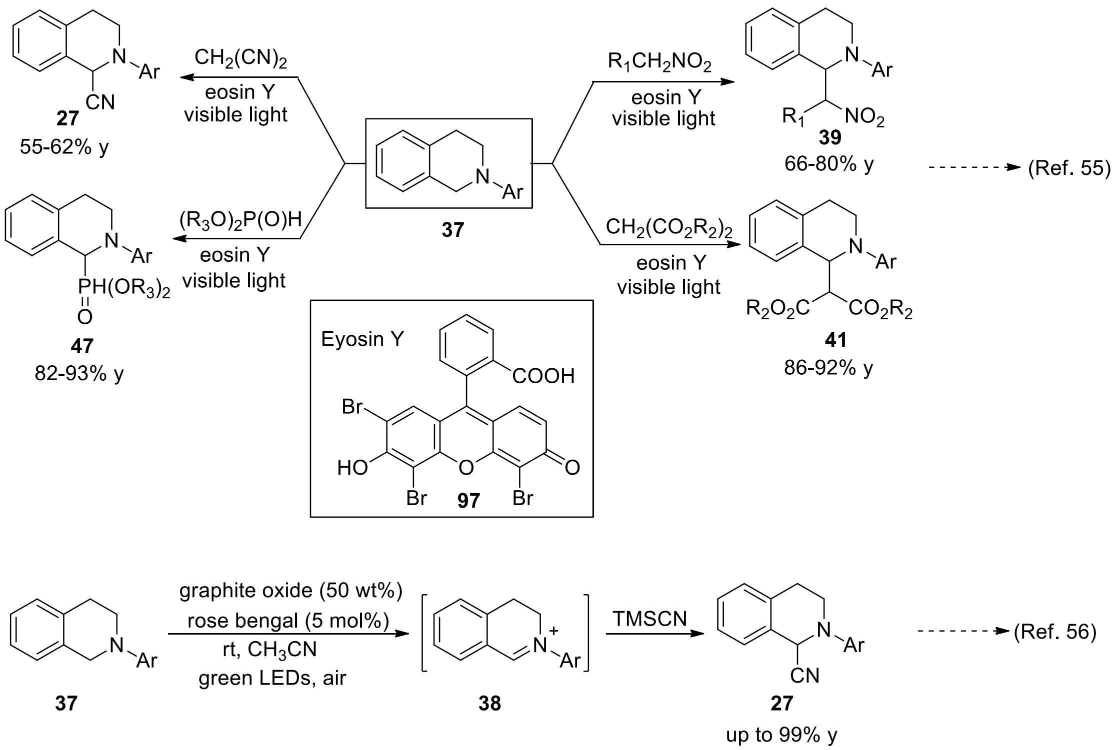
Photoredox Catalysts play an important role for constructing the C-C bonds.[51] In the past decade, tris(bipyridine) ruthenium and iridium complexes were developed as visible light photoredox catalysts in dehalogenation, reduction, oxidation, asymmetric alkylation reactions (Chart 5).[52] Aza-Henry reaction *via* C-H functionalization of tertiary amines was also reported (Chart 5).[53,54]

Chart 5



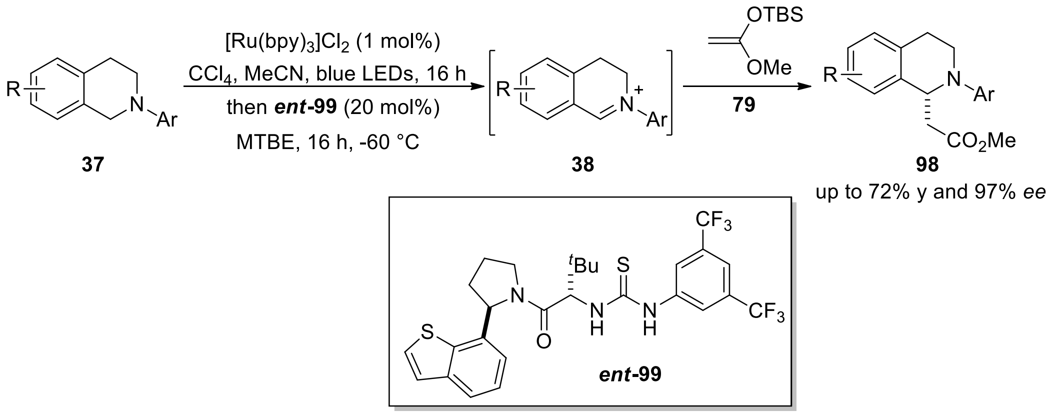
Metal free photoredox catalytic reactions of N-aryltetrahydroisoquinoline were reported using rose bengal and Eyosin Y (Chart 6).[55, 56]

Chart 6



Recently, enantioselective oxidative C-H functionalization of tetrahydroisoquinolilne was reported using photoredox and asymmetric anion-binding catalyst (Scheme 13).[57]

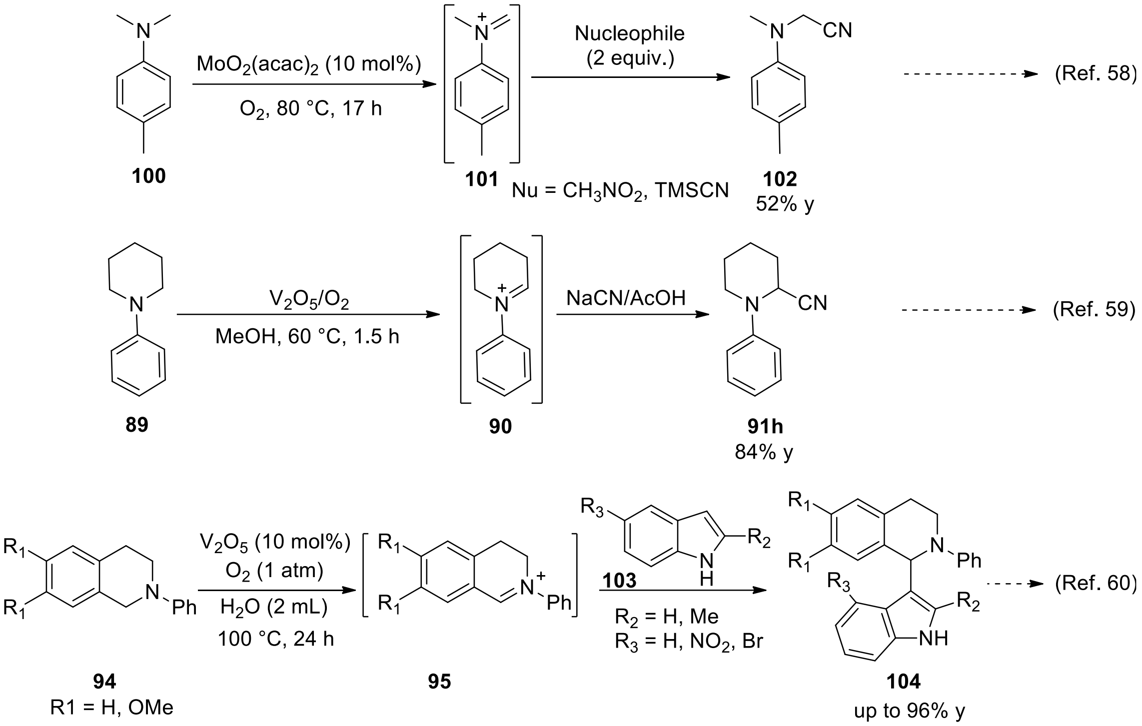
Scheme 13



1.1.2.6 C-H functionalization of tertiary amines using Mo and V metals

Methods were reported for the C-H functionalization of tertiary amines using Mo and V metal salts (Chart 7).[58-60]

Chart 7



1.1.2.7 Transition metal free C-H functionalization of tertiary amines

Several metal free oxidative C-C bond forming reactions between tertiary amines and carbon nucleophiles using peroxides, AIBN, iodine, sulfuryl chloride and acetic acid/O_2 were reported (Chart 8).[61-66]

Chart 8

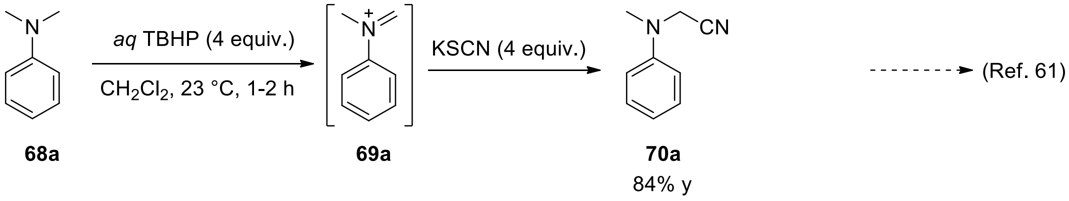
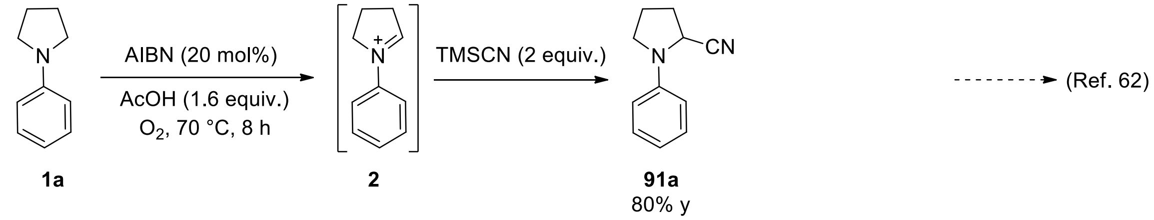
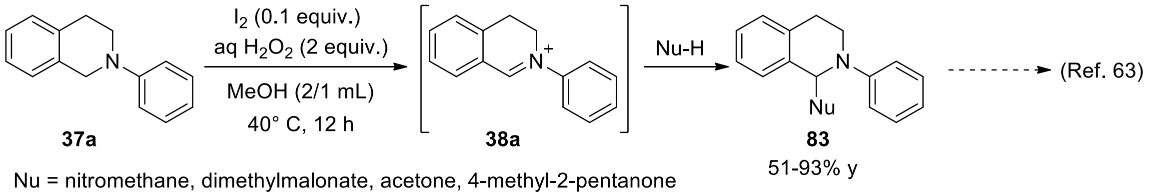
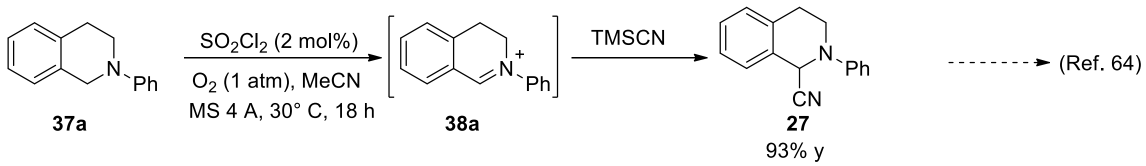


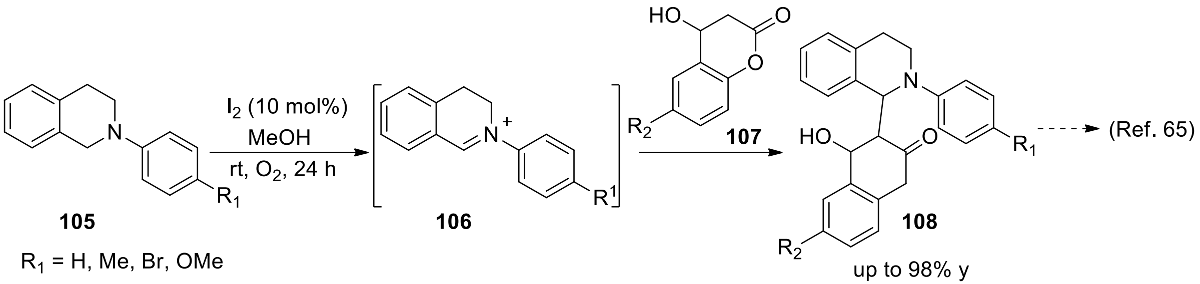
Chart 8 (Continued)



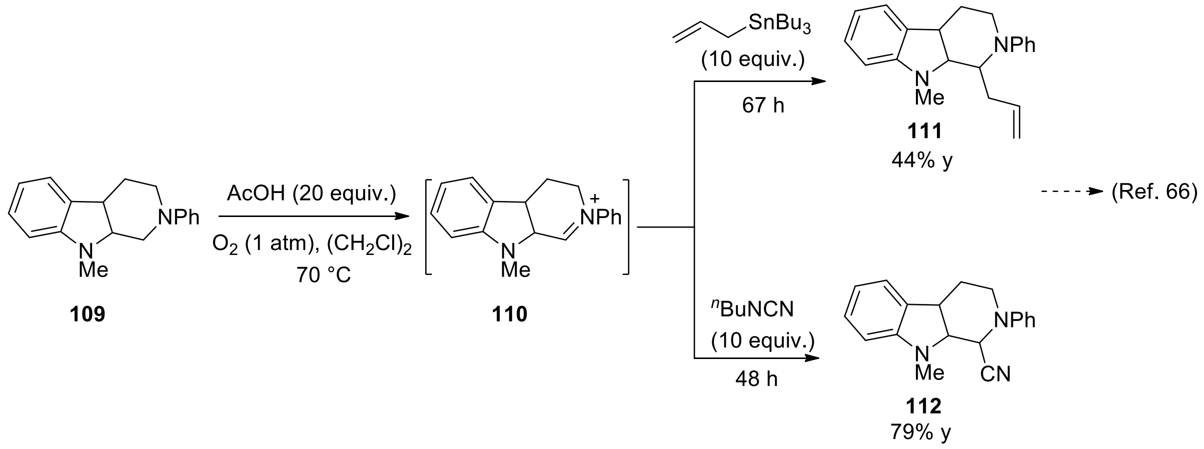


Nu = nitromethane, dimethylmalonate, acetone, 4-methyl-2-pentanone





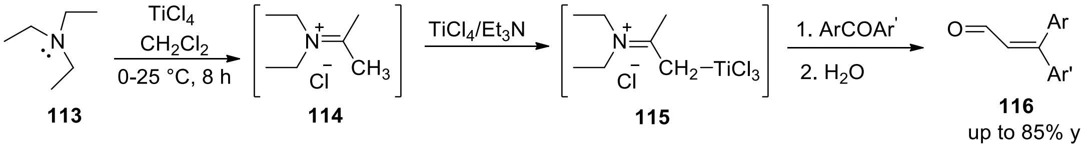
R_1 = H, Me, Br, OMe
R_2 = H, Me



1.1.2.8 Previous work from this laboratory for the generation of iminium ion

The iminium ions produced *in situ* from trialkyl amines **113** and $TiCl_4$ reacts with diaryl ketones to produce the corresponding α, β-unsaturated aldehydes **116** (Scheme 14).[67]

Scheme 14



We have developed several new synthetic methods for constructing the C-C bond *via* the formation of iminium and enamine intermediates using *t*-butylhydroperoxide (T-HYDRO)/*t*-BuOK reagent system. The results are discussed in next section.

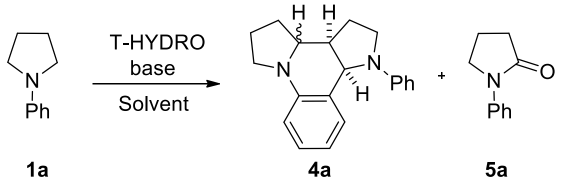
1.2 Results and Discussion

1.2.1 Reactions of N-phenylpyrrolidines with T-HYDRO

As outlined in the introductory section, methods were reported for the synthesis of polycyclic amines, cyclic amides and for oxidative C-H functionalization of tertiary amines *via in situ* preparation of iminium and enamine intermediates. It was of our interest to examine the reaction of N-arylpyrrolidine **1** derivatives with *tert*-butyl hydroperoxide (T-HYDRO) to prepare the corresponding iminium ion and enamine for developing organic synthetic methods.

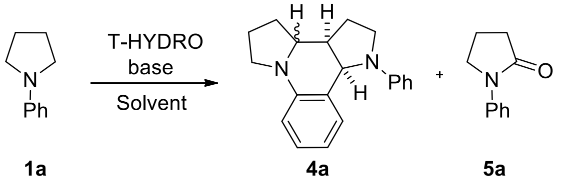
Initially, we have carried out the reaction of N-phenylpyrrolidine **1a** with T-HYDRO under different reaction conditions and observed the formation of tetracyclic amine **4a** and cyclic amide (Scheme 15).

Scheme 15



Whereas the tetracyclic amine **4a** was obtained only in 5% yield without using a base in cyclohexane solvent (Table 1, entry 1), it was observed in 13-45% yields in the presence of bases like K_2CO_3, *t*-BuOK and $CH_3COONa·3H_2O$ in cyclohexane at room temperature for 24 h (Table 1, entries 2-5). The reaction using the base $CH_3COONa·3H_2O$ gave the tetracyclic amine product **4a** in 32% and 45% in toluene and cyclohexane respectively, but in more polar solvents like DCM, CH_3CN, and MeOH, this tetracyclic amine product **4a** was formed in lesser yields (12-21%) besides the amide product **5a** (5-8%) (Table 1, entries 6-8). The reaction in MeOH in the presence of bases gives only the amide **5a** in 33-85% yields (Table 1, entries 9-13). Higher yields were realized at 70 ° C (Table 1, entries 14-17). Whereas the use of MeOH and CH_3CN solvents gave mixture of the tetracyclic amine **4a** (35% and 28%) and the amide **5a** (33% and 21%), the reaction in toluene and cyclohexane solvents was more clean and the tetracyclic amine **4a** product was obtained in 64% and 72% yields, respectively (Table 1, entries 14-17).

Table 1: Optimization for the reaction of N-phenylpyrrolidine with T-HYDRO and $CH_3COONa·3H_2O$.[a-g]



Entry	Base	Solvent	Yield (%)[d] **4a**	Yield (%)[d] **5a**
1[b]	-	Cyclohexane	5[g]	0
2[b]	*t*-BuOK	Cyclohexane	15[g]	21
3[b]	K_2CO_3	Cyclohexane	13[g]	18
4[b]	$CH_3COONa·3H_2O$	Cyclohexane	45[g]	0
5[b]	$CH_3COONa·3H_2O$	Toluene	32[g]	0
6[b]	$CH_3COONa·3H_2O$	DCM	21[f]	7
7[b]	$CH_3COONa·3H_2O$	CH_3CN	18[f]	5
8[b]	$CH_3COONa·3H_2O$	MeOH	12[f]	8

Table 1 (Continued)

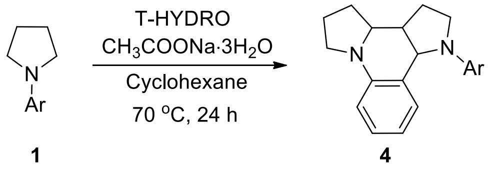
9[b]	K_2CO_3	MeOH	0	33
10[b]	*t*-BuOK	MeOH	0	48
11[c]	*t*-BuOK	MeOH	0	85
12[b]	NaOH	MeOH	0	35
13[c]	NaOH	MeOH	0	78
14[c]	$CH_3COONa{\cdot}3H_2O$	MeOH	35[f]	33
15[c]	$CH_3COONa{\cdot}3H_2O$	CH_3CN	28[f]	21
16[c]	$CH_3COONa{\cdot}3H_2O$	Toluene	64[g]	0
17[c]	$CH_3COONa{\cdot}3H_2O$	Cyclohexane	72[g]	0

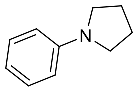
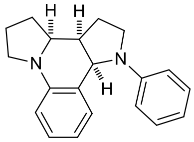
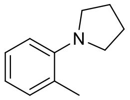
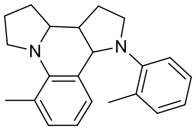
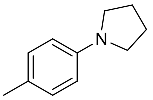
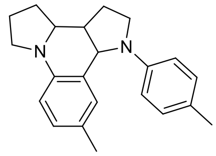
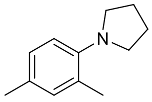
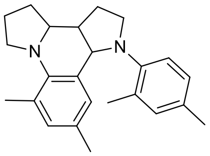
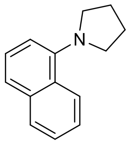
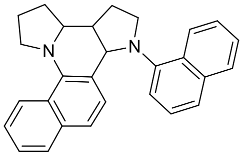
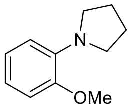
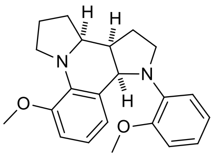
[a] All the reactions were carried out with N-arylpyrrolidine **1** (1 mmol), base (4 mmol), T-HYDRO (4 mmol) for 24 h. [b] Reactions were carried out at room temperature. [c] Reactions were carried out at 70 °C. [d] Isolated yields of **4a** and **5a**. [e] The products were characterized by spectral data (IR, ^{1}H-NMR, ^{13}C-NMR). [f] The product **4a** formed is a mixture of 1:1(approx) of diastereomers. [g] The product **4a** formed is a single diastereomer.

1.2.2 Synthesis of tetracyclic amines using T-HYDRO and $CH_3COONa{\cdot}3H_2O$

Since the use of cyclohexane gave the optimum results, we have carried out reactions using the other aryl amine derivatives in this solvent. The results are summarized in Table 2.

Table 2: Synthesis of tetracyclic amine derivatives **4** by using T-HYDRO.[a-d]

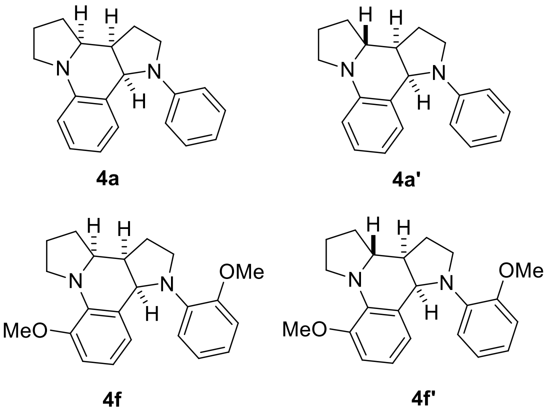


Entry	Substrate	Product	Yeild (%) [c,d]
			4a
1	 **1a**	 **4a**	72
2	 **1b**	 **4b**	69
3	 **1c**	 **4c**	62
4	 **1d**	 **4d**	59
5	 **1e**	 **4e**	78
6	 **1f**	 **4f**	64

[a] All the reactions were carried out with N-phenyl substituted pyrrolidines **1a-1f** (1 mmol), base (4 mmol), T-HYDRO (4 mmol) for 24 h. [b]Reactions were carried out at 70 °C. [c]Isolated yield of **4a-4f**. [d]The products were characterized by spectral data (IR, ^{1}H-NMR, ^{13}C-NMR).

Whereas, the 1-(*o*-tolyl)pyrrolidine **1b** gave the corresponding tetracyclic amine product **4b** in 69% yield, the 1-(*p*-tolyl)pyrrolidine **1c** gave the tetracyclic amine **4c** in 62% yield (Table 2, entries 2 and 3). The reaction using 1-(2,4-dimethylphenyl)pyrrolidine and 1-(naphthalen-1-yl)pyrrolidine derivatives gave the corresponding tetracyclic amines **4d** and **4e** in 59% and 78% yields, respectively (Table 2, entries 4 and 5). The 1-(2-methoxyphenyl)pyrrolidine **1f** gave the tetracyclic amine **4f** in 64% yield.

The tetracyclic amine **4a** was reported to be formed as a minor product along with an isomeric product **4a'** by cycloaddition of the corresponding iminium ion and enamine prepared *in situ* in the reaction of the cyclic amide **5a** with $PhMe_2SiLi$ in THF at -78 °C to -20 °C.[16] We have confirmed that the product obtained in the present transformation has the same stereochemistry as the above-mentioned minor product by comparison of the reported X-ray crystal structure with the X-ray data of the product **4a** formed under the present reaction conditions in cyclohexane. Whereas, the mixture **4a** and **4a'** (1:1) were isolated in polar solvents (Table 1), only product **4a** is obtained in toluene and cyclohexane solvents (Figure 1).



4a **4a'**

4f **4f'**

Figure 1: Possible diastereomeric products.

We have obtained crystals suitable for single crystal X-ray structure analysis by crystallization of the product **4f** from hexane. The X-ray analysis of the product **4f** showed all stereogenic hydrogens have syn stereochemistry as reported earlier (Figure 2).[16]

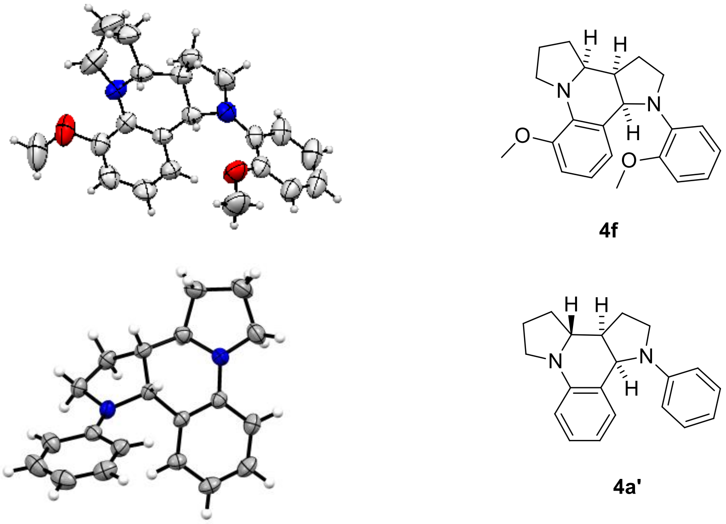


Figure 2: ORTEP Diagram of **4f and 4a'**

The isomeric product **4f'** was not obtained under the present reaction conditions in cyclohexane. Unfortunately, crystals suitable for single crystal X-ray structure analysis were not obtained for the tetracyclic amine products **4b-4e**. However, the ^{13}C-NMR spectral data reveal that only one diasteriomeric product was obtained in these cases but at this stage we cannot assign stereochemistry for these products.

We have synthesized the N-arylcyclic amides by using the optimized reaction condition (Table 1, entry 11). Previously, some methods were developed for synthesis of such amides.[68-71] For example, metal salts with different ligand combinations were reported for the synthesis of cyclic amide derivatives.[68] Transition metal catalyzed cross coupling reactions of aryl halides and cyclic amides were also reported for the preparation of N-arylpyrrolidone **5** derivatives (Chart 9).[69-71]

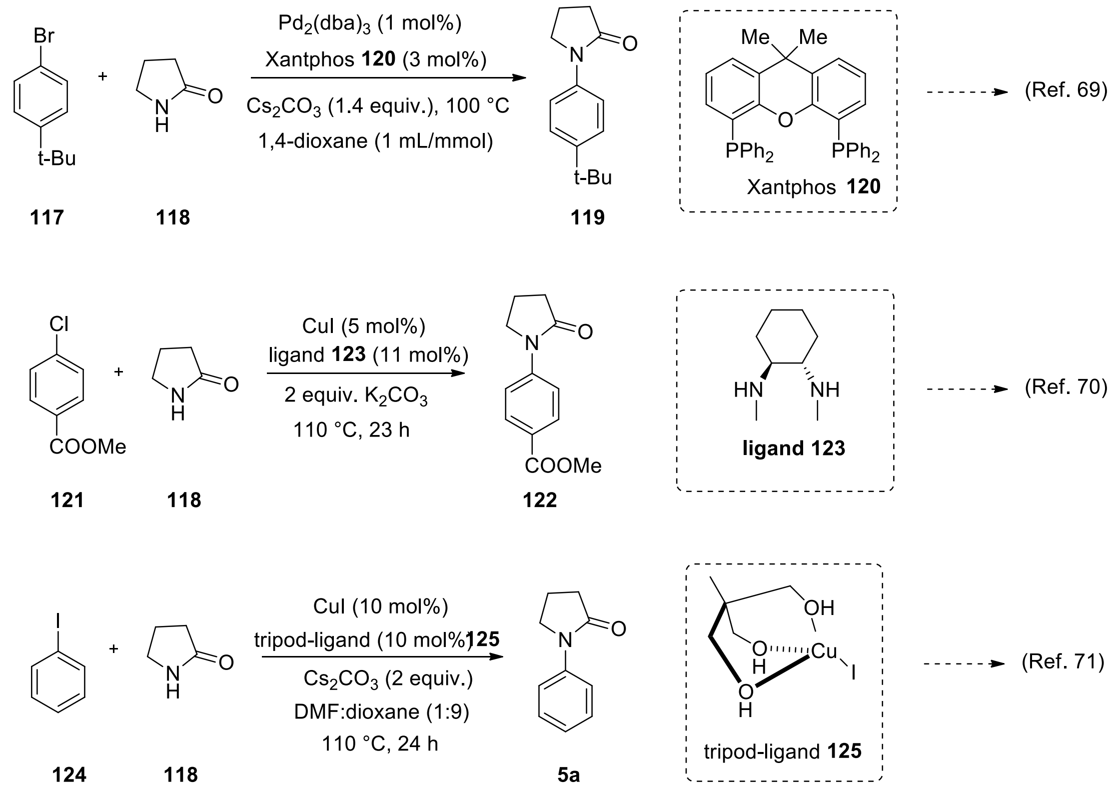
Table 3 Crystal data and structure refinement for compound **4f**.

Identification code	**4f**
Empirical formula	$C_{12}H_{26}N_2O_2$
Formula weight	43.03
Temperature/K	298(2)
Crystal system	triclinic
Space group	P-1
a/Å	7.8794(11)
b/Å	15.1286(18)
c/Å	15.5179(16)
α/°	93.763(9)
β/°	96.324(10)
γ/°	99.219(11)
Volume/Å^3	1808.2(4)
Z	34
ρ_{calc}mg/mm^3	1.343
m/mm^{-1}	0.121
F(000)	748.0
Crystal size/mm^3	0.12 x 0.10 x 0.08 mm^3
Theta range for data collection	5.28 to 58.3°
Index ranges	$-10 \leq h \leq 10$, $-18 \leq k \leq 20$, $-20 \leq l \leq 21$
Reflections collected	13631
Independent reflections	8201[R(int) = 0.0470]
Data/restraints/parameters	8201/0/473
Goodness-of-fit on F^2	0.976
Final R indexes [I>=2σ (I)]	$R_1 = 0.0752$, $wR_2 = 0.1734$
Final R indexes [all data]	$R_1 = 0.1913$, $wR_2 = 0.2581$
Largest diff. peak/hole / e Å^{-3}	0.27/-0.20 Å^{-3}

Table 4 Crystal data and structure refinement for compound **4a’**.

Identification code	**4a’**	
Empirical formula	$C_{20} H_{22} N_2$	
Formula weight	290.39	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 7.4682(9) Å	a= 77.892(11)°.
	b = 7.8925(11) Å	b= 79.666(10)°.
	c = 14.5831(18) Å	g = 69.698(12)°.
Volume	782.88(19) $Å^3$	
Z	2	
Density (calculated)	1.232 Mg/m^3	
Absorption coefficient	0.072 mm^{-1}	
F(000)	312	
Crystal size	0.10 x 0.08 x 0.06 mm^3	
Theta range for data collection	2.877 to 26.372°.	
Index ranges	-8<=h<=9, -8<=k<=9, -18<=l<=17	
Reflections collected	5279	
Independent reflections	3187 [R(int) = 0.0188]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.0000 and 0.85378	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3187 / 0 / 199	
Goodness-of-fit on F^2	0.994	
Final R indices [I>2sigma(I)]	R_1 = 0.0483, wR_2 = 0.1379	
R indices (all data)	R_1 = 0.0640, wR_2 = 0.1590	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.120/-0.180 e. $Å^{-3}$	

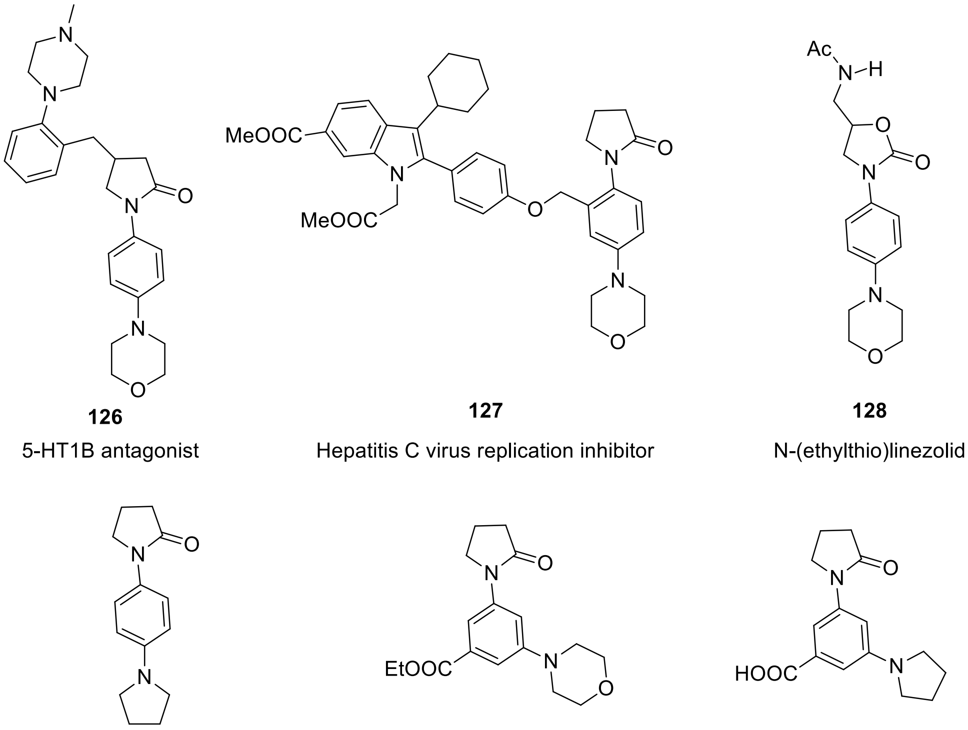
Chart 9



The method reported here is simple and gives the products in comparable yields.

Cyclic amide motifs play an important role in organic synthesis and pharmaceutical chemistry.[72] Also, cyclic amides containing compounds have biological activities like anticancer,[73] antimicrobial,[74] antidiabetic,[75] anti-CNS,[76] anticonvulsants[77] and agrochemicals.[78] Several biologically active molecules and drugs have cyclic amide and amine moieties **126-131** **(**Scheme 16).[79]

Scheme 16



126 5-HT1B antagonist

127 Hepatitis C virus replication inhibitor

128 N-(ethylthio)linezolid

129 Tremogenic activity

130 Precusor of drug against Alzheimer disease

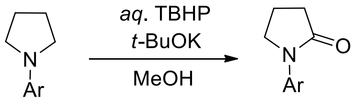
131 BACE-1 inhibitor

Accordingly, the method described here has significant potential for further applications.

1.2.3 Synthesis of N-aryl-2-pyrrolidones by using T-HYDRO and *t*-BuOK in methanol

We have observed that the cyclic amide **5a** was formed in the reaction of N-phenylpyrrolidine **1a** with T-HYDRO (4 equiv.) and *t*-BuOK (4 equiv.) in methanol solvent (Table 2). We have performed the reaction using methyl, methoxy and halogen substituted arylpyrrolidines in methanol to obtain the corresponding cyclic amides **5b-5j** in 35-89% yields (Table 5, entries 2-10).

Table 5: Potassium *tert*-butoxide promoted Oxidation of N-arylpyrrolidine **1** to N-aryl-2-pyrrolidone **5** by using *aq*. TBHP.



1 **5**

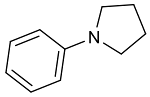
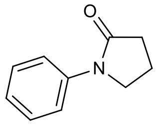
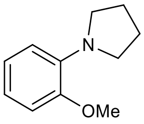
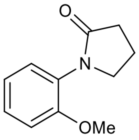
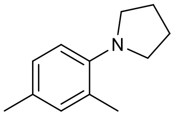
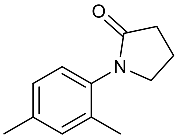
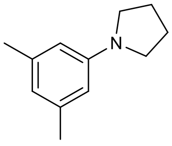
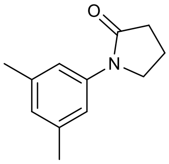
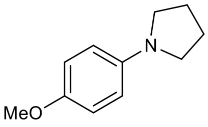
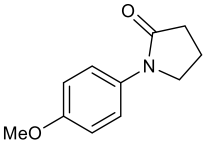
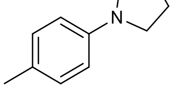
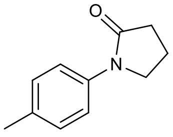
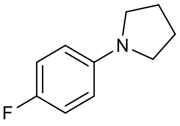
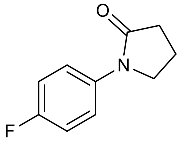
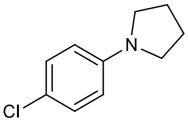
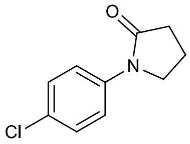
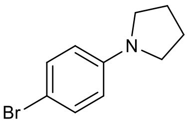
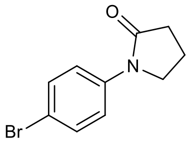
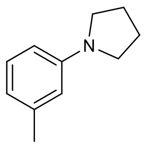
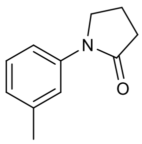
Entry	Substrate	Product	Yeild (%) **5**
1	 **1a**	 **5a**	85
2	 **1b**	 **5b**	89
3	 **1c**	 **5c**	35
4	 **1d**	 **5d**	78
5	 **1e**	 **5e**	86
6	 **1f**	 **5f**	88

Table 5 (Continued)

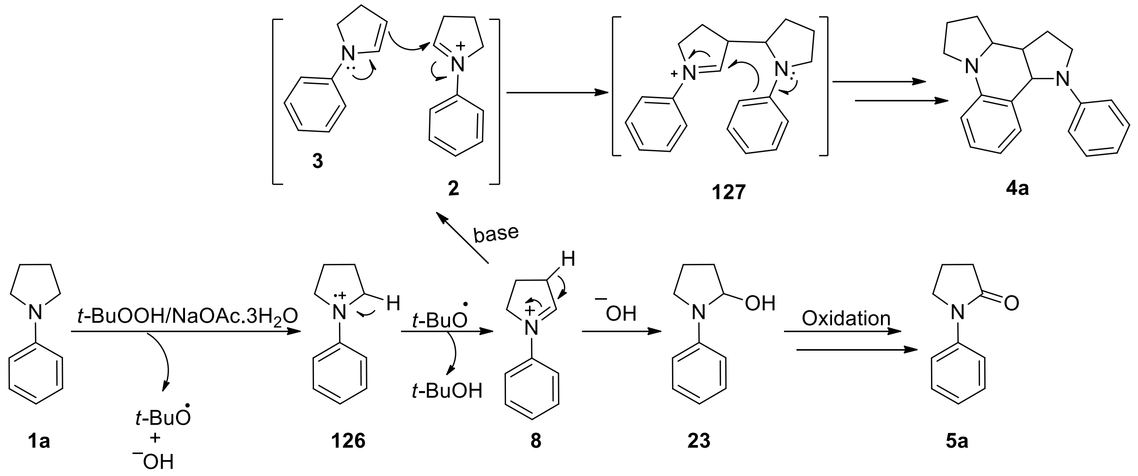
7	 **1g**	 **5g**	81
8	 **1h**	 **5h**	79
9	 **1i**	 **5i**	82
10	 **1j**	 **5j**	77

[a]All the reactions were carried out with N-arylpyrrolidine **1** (1 mmol), base (4 mmol), *aq*. TBHP (4 mmol) for 24 h. [b]Reactions were carried out at 70 °C. [c]Isolated yields of **5a-5j**. [d]The products were characterized by spectral data (IR, ^{1}H-NMR, ^{13}C-NMR).

1.2.4 Plausible mechanism for synthesis of tetracyclic amines 4 and amides 5

Mechanism and intermediates outlined in Scheme 17 may be considered for the formation of products **5a** and **4a**. The reaction may involve activation of the *t*-butyl hydroperoxide by the base[9] followed by the formation of amine radical cation, *tert*-butoxy radical, iminium ion and enamine intermediates (Scheme 17). The iminium ion **2** formed *in situ* could further react with the base to give the corresponding enamine **3** which could undergo Mannich type reaction with the iminium ion **2** followed by cyclization to afford the tetracyclic amine product **4a** (Scheme 17). In methanol solvent, the hydroxyl anion formed *in* *situ* could attack the iminium ion **2** to give the amino alcohol product **142** which after further oxidation could afford the N-phenyl-2-pyrrolidone **5a** (Scheme 17).

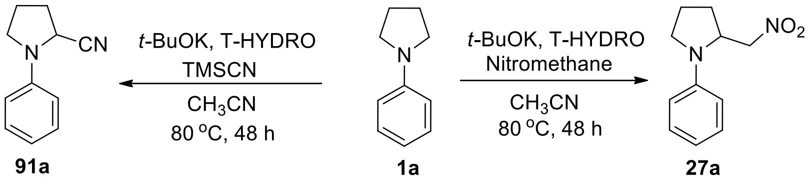
Scheme 17



1.2.5 Functionalization of N-Aryl cyclic tertiaryamines with nitromethane and TMSCN using T-HYDRO/*t*-BuOK system

We have also developed C-H functionalization of N-aryl tertiaryamines using *t*-BuOK/T-HYDRO and nitromethane or trimethylsillylcyanide (Scheme 18).

Scheme 18



1.2.6 Synthesis of β-nitro amines 27 using T-HYDRO and *t*-BuOK

Initially, we have carried out the reaction using N-phenylpyrrolidine **1a**, nitromethane, T-HYDRO, *t*-BuOK, in methanol solvent at room temperature for 48 h and obtained the corresponding β-nitroamine **27a** in 27% yield (Table 6, entry 1).

Table 6: Reaction of N-phenylpyrrolidine and nitromethane using T-HYDRO and *t*-BuOK system.[a-f]

Entry	Base	Solvent	Oxidizing agent	Yield (%)[c] **27a**
1	*t*-BuOK	MeOH	T-HYDRO	27
2	*t*-BuOK	MeOH	T-HYDRO	72
3	K_3PO_4	MeOH	T-HYDRO	59
4	Cs_2CO_3	MeOH	T-HYDRO	61
5	KOH	MeOH	T-HYDRO	65
6	NaOH	MeOH	T-HYDRO	62
7	Et_3N	MeOH	T-HYDRO	48
8	*t*-BuOK	DMSO	T-HYDRO	67
9	*t*-BuOK	DMF	T-HYDRO	63
10	*t*-BuOK	CH_3CN	T-HYDRO	81
11	*t*-BuOK	PEG-400	T-HYDRO	57
12	*t*-BuOK	Toluene	T-HYDRO	70
13	*t*-BuOK	EtOH	T-HYDRO	74
14	-	MeOH	T-HYDRO	5
15	*t*-BuOK	MeOH	-	N R
16	*t*-BuOK	MeOH	O_2	N R
17[c]	*t*-BuOK	MeOH	T-HYDRO	34
18[d]	*t*-BuOK	MeOH	T-HYDRO	51

[a]All the reactions were carried out with N-arylpyrrolidine **1** (1 mmol), base (2 mmol), T-HYDRO (4 mmol) and nitromethane (0.5 mL) for 48 h at 80 °C. [b]Reaction was carried out at room temperature. [c,d]Reaction was carried out at 80 °C for 12 h and 24 h respectively. [e]Isolated yields of **27a**. [f]The products were characterized by spectral data (IR, ^{1}H-NMR, ^{13}C-NMR and HRMS).

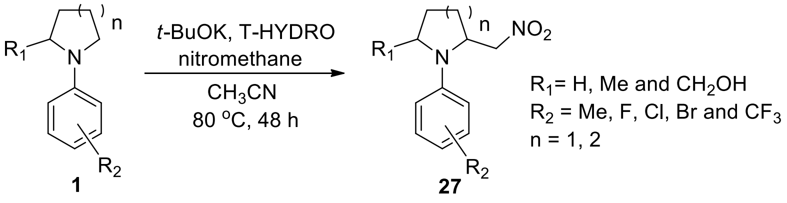
When the reaction was performed at 80 °C, the product was obtained in 72% yield (Table 6, entry 2). Among bases, the *t*-BuOK was the most effective for nitroalkylation of N-phenyl pyrrolidine **1a** (Table 6, entries 2-7). Other solvents like toluene, EtOH, CH_3CN, PEG-400, DMSO and DMF gave the products in 57-81% yields (Table 1, entries 8-13). When the reaction was conducted without the base, the product **27a** was obtained only in 5% yield (Table 6, entry 14). Also, the reaction in the presence of O_2 without the *t*-butyl hydroperoxide (T-HYDRO) did not give product **27a** (Table 6, entries 15 and 16). We have observed that 4 equiv of T-HYDRO as oxidant, 2 equiv of *t*-BuOK as the promoting agent, 0.5 mL of nitromethane as nucleophile in CH_3CN (5 mL) as the solvent at 80 °C for 48 h gave optimum results (Table 6, entry 10). Further, when the reaction was performed for 12 h and 24 h at 80 °C, the products were isolated in 34% and 51% yields, respectively (Table 6, entries 17 and 18).

We have then examined the substrate scope for the nitroalkylation of cyclic tertiary amines. The results are summarized in Table 7. Substituted pyrrolidine and piperidine derivatives were reacted with nitromethane to give the corresponding β-nitro amines **27** in 17-92% yields under the optimal reaction condition (Table 7). Methyl, dimethyl and trifluoromethyl substituents in different positions in the phenyl ring of N-phenylpyrrolidine reacted with nitromethane to give the corresponding β-nitro amines (**27a-27e**) in 77-92% yields (Table 7).

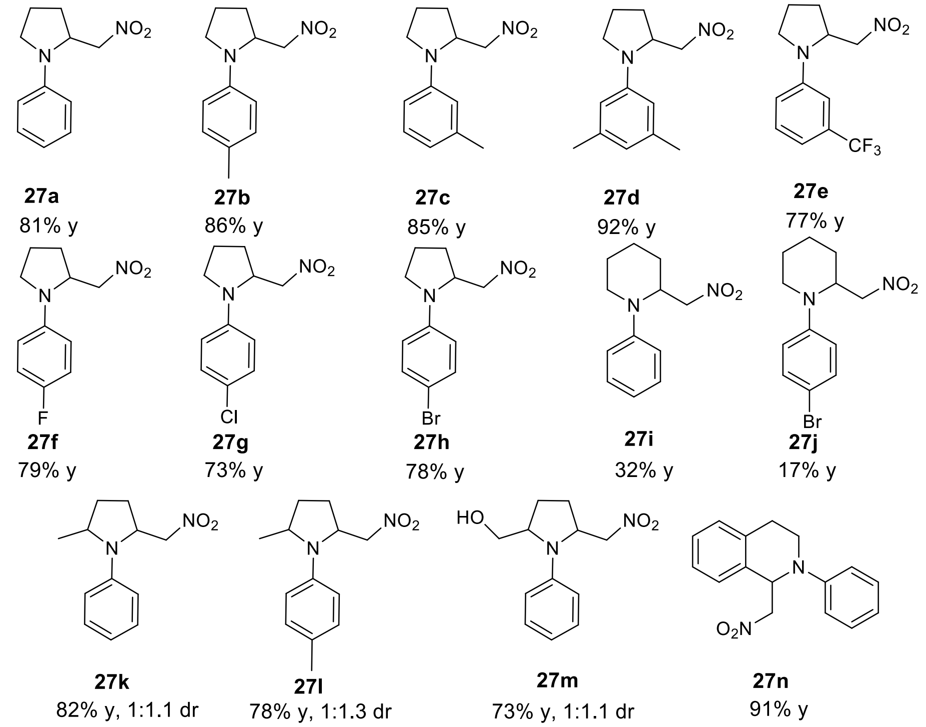
The halogen at the *para* position of N-phenylpyrrolidines furnished the desired products (Table 7, **27f-27h**) in 73-79% yields. However, when the reaction with N-phenylpiperidine and 1-(4-bromophenyl)piperidines were subjected to the functionalization using nitromethane, the yields of the desired products **27i** and **27j** were decreased to 32% and

17% yields, respectively (Table 7). Also, the reaction using 2-methyl-1-phenylpyrrolidine and 2-methyl-1-(*p*-tolyl)pyrrolidines gave the corresponding β-nitro amines **27k** and **27l** in 82% and 78% yields with no selectivity (Table 7).

Table 7: Synthesis of β-nitro amine derivatives using T-HYDRO /*t*-BuOK system.[a-c]



R_1= H, Me and CH_2OH
R_2 = Me, F, Cl, Br and CF_3
n = 1, 2



27a 81% y
27b 86% y
27c 85% y
27d 92% y
27e 77% y
27f 79% y
27g 73% y
27h 78% y
27i 32% y
27j 17% y
27k 82% y, 1:1.1 dr
27l 78% y, 1:1.3 dr
27m 73% y, 1:1.1 dr
27n 91% y

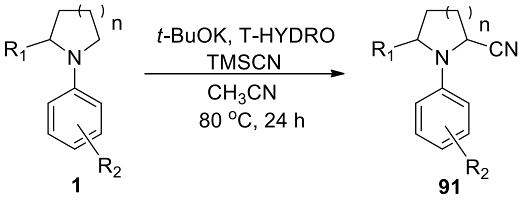
[a]All the reactions were carried out with N-arylamine **1** (1 mmol), *t*-BuOK (0.22 g, 2 mmol), T-HYDRO (4 mmol) and nitromethane (0.5 mL) for 48 h at 80 °C. [b]Isolated yields of **27**. [c]The products were characterized by spectral data (IR, ^{1}H-NMR, ^{13}C-NMR and HRMS).

We have observed that the chiral (1-phenylpyrrolidine-2-yl)methanol gave the corresponding product **27m** in 73% yield without selectivity. The 2-aryl-1,2,3,4-tetrahydroisoquinoline derivative furnished the coupled product **27n** with 91% yield in the reaction with nitromethane. We have also observed that the iminium ion intermediate formed *in situ* readily reacts with TMSCN (1.5 equiv.) to afford the corresponding nitrile in an experiment using T-HYDRO (3 equiv.), *t*-BuOK (1.5 equiv.), at 80 °C in 24 h in CH_3CN solvent (Table 8, entry 1).

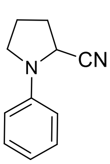
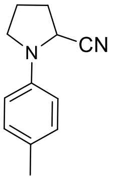
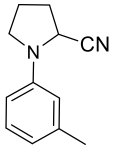
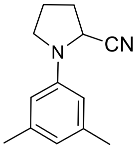
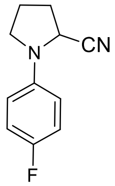
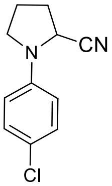
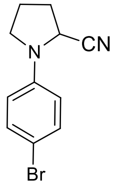
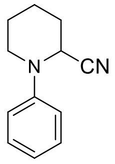
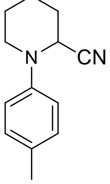
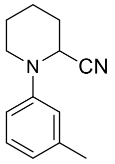
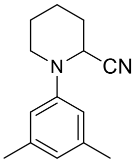
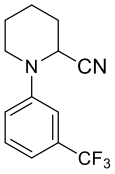
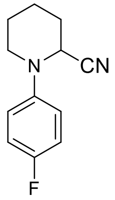
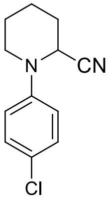
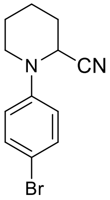
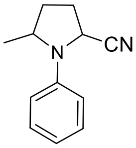
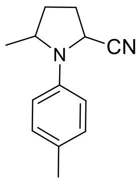
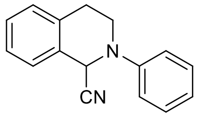
1.2.7 Synthesis of α-aminonitriles 91 using T-HYDRO and *t*-BuOK

We investigated the scope of the reaction using TMSCN. The results are summarized in Table 8.

Table 8: Synthesis of α-aminonitriles using T-HYDRO /*t*-BuOK system.



R_1= H, Me and CH_2OH
R_2 = Me, F, Cl, Br and CF_3
n = 1, 2

 **91a** 89% y	 **91b** 93% y	 **91c** 96% y	 **91d** 95% y	 **91e** 86% y	 **91f** 89% y
 **91g** 90% y	 **91h** 75% y	 **91i** 78% y	 **91j** 73% y	 **91k** 87% y	 **91l** 68% y
 **91m** 71% y	 **91n** 77% y	 **91o** 69% y	 **91p** 79% y, 1:1.1 dr	 **91q** 77% y, 1:1 dr	 **91r** 92% y

[a]All the reactions were carried out with N-arylamine **1** (1 mmol), *t*-BuOK (0.17 g, 1.5 mmol), T-HYDRO (0.41 mL, 3 mmol), and TMSCN (0.19 mL, 1.5 mmol) for 24 h at 80 °C. [b]Isolated yields of **91**. [c]The products were characterized by spectral data (IR, ^1H-NMR, ^{13}C-NMR and HRMS).

A wide variety of substituted N-aryl derivatives containing electron-donating and neutral substances gave the nitrile products in 68-96% yields (Table 8). Methyl, dimethyl, and halogen substituents in different positions on phenyl ring of the N-phenylpyrrolidines and piperidines gave the corresponding α-aminonitriles (**91a-91o**) in 86-96% yields (Table 8). The reaction using 2-methyl-1-phenylpyrrolidine and 2-methyl-1-(*p*-tolyl)pyrrolidines observed the corresponding α-aminonitriles **91p** and **91q** in 79% and 77% yields but there was no selectivity. Also, 2-aryl-1,2,3,4-tetrahydroisoquinoline gave the corresponding coupled product **91r** with 92% yield.The structure of the product **91o** was further confirmed by the single crystal X-ray analysis (Fig. 3).

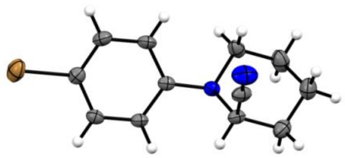


Figure. 3: X-ray crystal structure of **91o**

1.2.8 Plausible mechanism in the reaction of N-phenyl pyrrolidine with T-HYDRO

A tentative mechanism outlined in Scheme 19 may be considered for the transformations to prepare β-nitroamines **27** and α-aminonitriles **91**.

Scheme 19

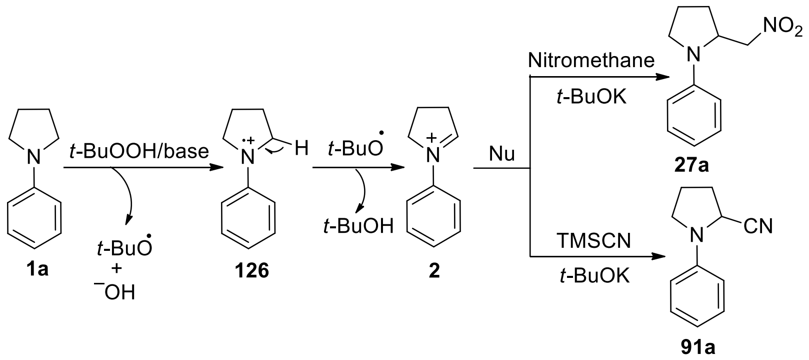


Table 9: Crystal data and structure refinement for compound **91o**.

Identification code	**91o**	
Empirical formula	$C_{12} H_{13} Br N_2$	
Formula weight	265.15	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C2/c	
Unit cell dimensions	a = 19.0509(10) Å	a= 90°.
	b = 5.5565(3) Å	b= 91.295(2)°.
	c = 22.0951(11) Å	g = 90°.
Volume	2338.3(2) Å^3	
Z	8	
Density (calculated)	1.506 Mg/m^3	
Absorption coefficient	3.485 mm^{-1}	
F(000)	1072	
Crystal size	0.18 x 0.16 x 0.14 mm^3	
Theta range for data collection	2.79 to 27.52°.	
Index ranges	-24<=h<=24, -7<=k<=7, -28<=l<=28	
Reflections collected	32595	
Independent reflections	2680 [R(int) = 0.0466]	
Completeness to theta = 27.52°	99.5 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2680 / 0 / 136	
Goodness-of-fit on F^2	1.048	
Final R indices [I>2sigma(I)]	R_1 = 0.0399, wR_2 = 0.0900	
R indices (all data)	R_1 = 0.0562, wR_2 = 0.0982	
Largest diff. peak and hole	0.381 and -0.680 e.Å^{-3}	

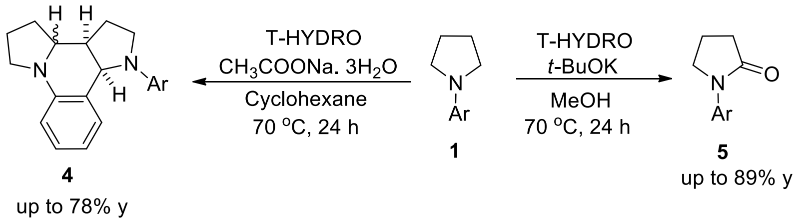
The reaction may proceed through iminium ion intermediate **2.** Subsequently, the Mannich-type reaction with carbon nucleophiles would provide the 2-substituted cyclic tertiary amines **27** and **91**.

Next, we have investigated the electron transfer reactions using oxygen adsorbed activated carbon. The results are described in the next Chapter.

1.3 Conclusions

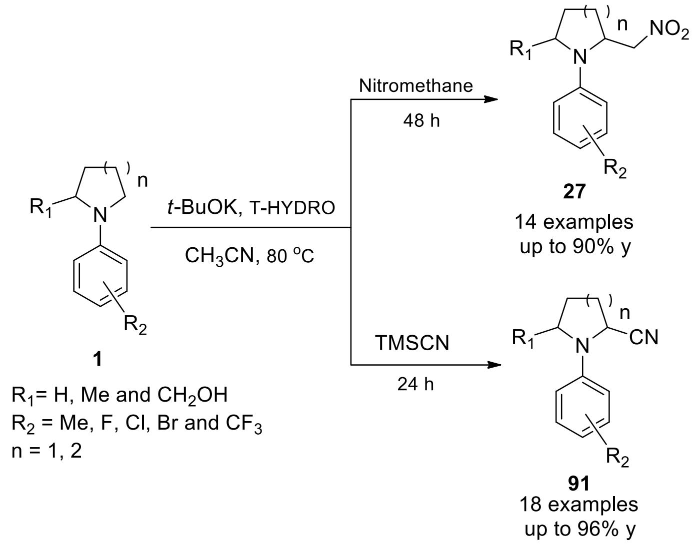
Convenient methods were developed for the synthesis of tetracyclic amines **4** and cyclic amides **5** through *in situ* preparation of iminium and enamine intermediates using aqueous tertiarybutylhydroperoxide (T-HYDRO) and $CH_3COONa·3H_2O$. The tetracyclic amines **4** formed with single diastereoisomers and syn stereochemistry was confirmed by single crystal X-ray structure analysis. The methods developed here involve mild conditions and simple procedures and hence lower potential for further exploitation in organic synthesis (Scheme 20).

Scheme 20



Also, we have developed a *t*-BuOK promoted metal free C-H functionalization of cyclic tertiary amines using T-HYDRO as oxidizing agent and nitromethane or TMSCN as nucleophiles. These methods also involve inexpensive reagents, moderate conditions, and easy synthetic operations (Scheme 21).

Scheme 21



Hence, these methods will be also useful for further applications in organic synthesis.

1.4. Experimental Section

1.4.1 General Information

Melting points reported in this thesis are uncorrected and were determined by using a Superfit capillary point apparatus. IR (KBr) spectra were recorded on JASCO FT-IR spectrophotometer Model 5300. The neat IR spectra were recorded on JASCO FT-IR spectrophotometer Model 5300 and SHIMADZU FT-IR spectrophotometer Model 8300 with polystyrene as reference. ^{1}H-NMR (400 MHz), ^{13}C-NMR (100 MHz) spectra were recorded on Bruker-Avance-400 spectrometers, respectively with chloroform-d as solvent and TMS as reference ($\delta = 0$ ppm). The chemical shifts are expressed in δ downfield from the signal of internal TMS. Mass analysis (HRMS) was performed on SHIMADZU-HRMS by Electro Spray Ionization (ESI) techniques. Analytical thin layer chromatographic tests were carried out on glass plates (3 x 10 cm) coated with 250mμ acme's silica gel-G and GF$_{254}$ containing 13% calcium sulfate as binder. The spots were visualized by short exposure to iodine vapor or UV light. Column chromatography was carried out using SRL India silica gel (100-200) and neutral alumina.

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

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

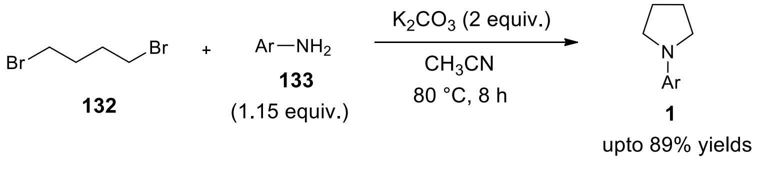
Dichloromethane and chloroform were distilled over CaH_2 and dried over molecular sieves. Methanol and ethanol supplied by Ranbaxy were distilled over CaO before use. Toluene and THF supplied by E-Merck, India were kept over sodium-benzophenone ketyl and freshly distilled before use. Iodine was supplied by Spectrochem, India. All amines, supplied by local Chemicals (P), Ltd., India were distilled or recrystallized from the appropriate solvents before use. $NaBH_4$ was supplied by E-Merck (India).

X-ray reflections were collected using Oxford CCD X-ray diffractometer (Yarnton, Oxford, UK) equipped with Mo-Kα radiation (λ = 0.71073 Å) and Cu-Kα radiation (λ = 1.54184 Å) sources. CrysAlisPro 171.33.55 software was for data reduction. Crystal structures were solved and refined using Olex2-1.0. Hydrogen atoms were experimentally located by the Fourier difference electron density method in all crystal structures. All O–H, and C–H were geometrically fixed by HFIX command in SHELX-TL programme of Bruker-AXS. Bruker SMART-APEX CCD diffractometer (Bruker-AXS, Germany,Karlsruhe) was used for the X-ray reflections. X-ray reflections were collected using Mo-Kα X-radiation (λ = 0.71073 Å) on the single crystal at 298 K. Data reduction was performed using the Bruker SAINT software. Intensities for absorption were corrected by using SADABS and the Siemens detector absorption correction program (Bruker-AXS). All the crystal structures were solved and refined using SHELX-97 with anisotropic displacement for non-hydrogen atoms. Hydrogen atoms on oxygen experimentally located in difference electron density maps.

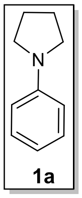
1.4.2. General procedure for the preparation of N-aryl substituted pyrrolydines (6)

To a stirred solution of K_2CO_3 (10 mmol) and KI (5 mol%) in CH_3CN (30 mL) under nitrogen atmosphere, 1,4-dibromobutane **132** (20 mmol) and aryl aniline **133** (25 mmol) were added. The reaction mixture was refluxed for 8 hours. After completion of the reaction, the solvent was evaporated and ethylacetate (EtOAc) 50 mL and water 30 mL were added. The organic layer was separated and extracted with 20 mL of EtOAc. The combined organic layer was washed with brine (50 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography on silica gel (100-200 mesh) using hexane as eluent to isolate the N-aryl substituted pyrrolidines **1** in 82-89% yields (Scheme 22).

Scheme 22



N-Phenylpyrrolidine (1a):

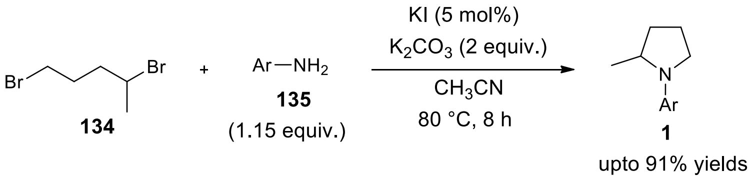

1a

Yield	:	2.44 g (83%); colour less liquid.
IR (Neat)	:	(cm^{-1}) 2961.5, 2822.0, 1592.5, 1515.0, 1365.2, 1179.2, 1153.4, 1034.6, 988.1, 957.1, 910.6, 853.8, 740.1, 688.5.
^{1}H NMR	:	(400 MHz, $CDCl_3$, δ ppm) 7.34-7.30 (m, 2H), 6.75 (t, *J* = 7.32 Hz, 1H), 6.66 (d, *J* = 7.77 Hz, 2H), 3.38-3.35 (m, 4H), 2.10-2.06 (m, 4H).
^{13}C NMR	:	(100 MHz, $CDCl_3$, δ ppm) 148.0, 129.2, 115.5, 111.7, 47.7, 25.5.

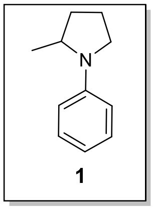
1.4.3. General procedure for the preparation of N-aryl substituted 2-methylpyrrolydines (1)

To a stirred solution of K_2CO_3 (10 mmol), KI (5 mol%) in CH_3CN (30 mL) under nitrogen atmosphere, 1,4-dibromopentane **150** (20 mmol) and arylanilines **149** (25 mmol) were added. The reaction mixture was refluxed for 10 hours. After completion of the reaction, the solvent was evaporated and EtOAc 50 mL and water 30 mL were added. The organic layer was separated and extracted with 20 mL EtOAc. The combined organic layer was washed with brine (50 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography on silica gel (100-200 mesh) using hexane as eluent to isolate the N-aryl substituted 2-methylpyrrolidines **70** in 84-91% yields (Scheme 23).

Scheme 23



N-Phenyl-2-methylpyrrolidine (1)



Yield : 2.77 g (86%); colour less liquid.

IR (Neat) : (cm^{-1}) 2963.5, 2889.0, 1599.4, 1548.2 1403.2, 1189.6, 1144.9, 1054.1, 978.2, 967.5, 883.7, 751.4, 689.3.

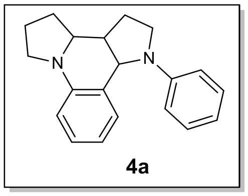
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.30-7.26 (m, 2H), 6.72-6.64 (m, 3H), 3.97-3.90 (m, 1H), 3.51-3.46 (m, 1H), 3.24-3.18 (m, 1H), 2.15-2.00 (m, 3H), 1.80-1.75 (m, 1H), 1.24 (d, *J* = 6.26, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 147.3, 129.2, 115.2, 111.8, 53.6, 48.2, 33.2, 23.3, 19.4.

1.4.4. General procedure for the preparation of Tetracyclic amines (4a-4f)

A mixture of N-arylpyrrolidine **1** (1 mmol), T-HYDRO (4 mmol) and CH_3COONa $3H_2O$ (4 mmol) in cyclohexane (2 mL) was stirred for 24 hours at 70 °C. After completion of the reaction, the solvent was evaporated and EtOAc (10 mL) and water (5 mL) were added. The combined organic layer was washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography on silica gel (100-200 mesh) using EtOAc:Hexane (2:98) as eluent to isolate the tetracyclic amines **4**.

1-Phenyl-2,3,3a,3b,4,5,6,11b-octahydro-1*H*-dipyrrolo[1,2-a:3′,2′-c]quinoline (4a)



4a

Yield : 0.11 g (72%); white solid.

mp : 154-156 ^{o}C.

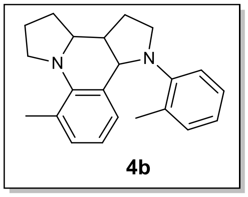
IR (KBr) : (cm^{-1}) 3047, 2970, 2838, 2805, 1611, 1501, 1479, 1358, 740.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.38-7.29 (m, 3H), 7.16-7.13 (m, 1H), 6.87-6.85 (m, 2H), 6.77-6.72 (m, 1H), 6.59-6.54 (m, 1H), 6.46-6.43 (m, 1H), 5.16 (d, J = 6.4 Hz, 1H), 3.79-3.77 (m, 1H), 3.55-3.51 (m, 1H), 3.44-3.29 (m, 3H), 2.59-2.52 (m, 1H), 2.20-2.14 (m, 1H), 2.13-1.95 (m, 3H), 1.92-1.84 (m, 1H), 1.79-1.69 (m, 1H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 148.9, 143.2, 129.4, 128.8, 128.1, 123.0, 115.8, 115.5, 111.3, 110.3, 57.5, 56.6, 47.4, 46.6, 40.1, 30.3, 23.4, 23.3.

HRMS (*m*/*z*) : Calculated for $C_{20}H_{22}N_2$ (M+H): 290.1862, Found (M+H): 290.1860.

8-Methyl-1-(*o*-tolyl)-2,3,3a,3b,4,5,6,11b-octahydro-1*H*-dipyrrolo[1,2-a:3′,2′-c]quinoline (4b)



4b

Yield : 0.11 g (69%); colour less oil.

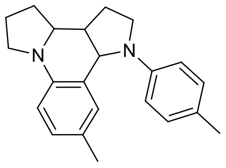
IR (Neat) : (cm^{-1}) 3063, 3024, 2926, 2871, 1599, 1495, 1468, 1254, 1106, 761, 723.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.27-7.17 (m, 2H), 7.01-6.95 (m, 3H), 6.86 (d, *J* = 7.6 Hz, 1H), 6.59 (t, *J* = 7.4 Hz, 1H), 5.03 (d, *J* = 7.6 Hz, 1H), 3.81-3.70 (m, 2H), 3.55-3.42 (m, 2H), 3.01-2.95 (m, 1H), 2.77-2.70 (m, 1H), 2.40 (s, 3H), 2.39 (s, 3H), 2.11-1.89 (m, 6H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 150.6, 145.7, 131.9, 131.2, 130.5, 127.0, 126.8, 126.5, 125.8, 121.8, 120.0, 118.5, 62.0, 58.9, 52.5, 51.5, 41.4, 29.6, 25.0, 24.1, 22.1, 19.6.

HRMS (*m*/*z*) : Calculated for $C_{22}H_{26}N_2$ (M+H): 319.2175, Found (M+H): 319.2174.

10-Methyl-1-(*p*-tolyl)-2,3,3a,3b,4,5,6,11b-octahydro-1*H*-dipyrrolo[1,2-a:3′,2′-c]quinoline (4c)



4c

Yield : 0.099 g (62%); colour less oil.

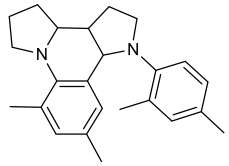
IR (Neat) : (cm^{-1}) 3063, 3014, 2964, 2866, 1600, 1496, 1430, 1293, 1096, 756, 712.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.12 (d, *J* = 8.4 Hz, 2H), 7.06 (t, *J* = 7.8 Hz, 2H), 6.70 (d, *J* = 8.0 Hz, 3H), 4.46 (d, *J* = 9.6 Hz, 1H), 3.72 (t, *J* = 8.2 Hz, 1H), 3.54-3.49 (m, 1H), 3.39-3.33 (m, 1H), 2.90-3.80 (m, 2H), 2.48-2.42 (m, 1H), 2.36 (s, 3H), 2.32-2.17 (m, 6H), 2.08-2.00 (m, 1H), 1.90-1.76 (m, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 147.6, 145.1, 129.7, 128.9, 128.3, 127.7, 127.5, 125.6, 112.9, 112.1, 65.1, 60.2, 49.7, 48.4, 47.6, 32.1, 30.7, 22.4, 21.0, 20.4.

HRMS (*m*/*z*) : Calculated for $C_{22}H_{26}N_2$ (M+H): 319.2175, Found (M+H): 319.2174.

1-(2,4-Dimethylphenyl)-8,10-dimethyl-2,3,3a,3b,4,5,6,11b-octahydro-1*H*-dipyrrolo[1,2-a:3′,2′-c]quinoline (4d)



4d

Yield : 0.10 g (59%); colour less oil.

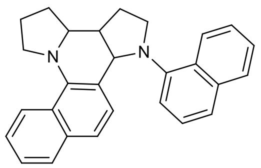
IR (Neat) : (cm^{-1}) 2953, 2915, 2866, 1605, 1496, 1474, 1342, 1288, 866, 816.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.06 (s, 1H), 7.00 (d, *J* = 8.0 Hz, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 6.77 (s, 1H), 6.72 (s, 1H), 4.85 (d, *J* = 7.6 Hz, 1H), 3.79-3.75 (m, 1H), 3.72-3.66 (m, 1H), 3.44-3.40 (m, 2H), 2.93-2.87 (m, 1H), 2.69-2.64 (m, 1H), 2.34 (s, 9H), 2.23-2.17 (m, 1H), 2.10 (s, 3H), 2.06-1.95 (m, 3H), 1.92-1.84 (m, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 149.0, 143.1, 132.7, 131.8, 131.6, 131.2, 127.8, 127.7, 127.4, 127.1, 125.7, 120.6, 62.9, 58.8, 52.7, 52.5, 41.6, 29.7, 25.7, 24.1, 21.8, 20.7, 20.4, 19.2.

HRMS (*m*/*z*) : Calculated for $C_{24}H_{30}N_2$ (M+H): 347.2488, Found (M+H): 347.2483.

3-(Naphthalen-1-yl)-2,3,3a,11,12,13,13a,13b-octahydro-1*H*-benzo[*h*]dipyrrolo[1,2-a:3′,2′-c]quinoline (4e)



4e

Yield : 0.15 g (78%); white solid.

mp : 203-205 °C.

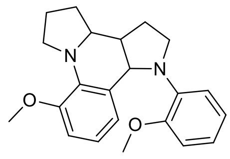
IR (KBr) : (cm^{-1}) 3036, 2953, 2926, 2855, 1556, 1512, 1463, 1397, 1277, 1107, 800, 778, 762.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 8.19 (d, *J* = 8.4 Hz, 1H), 8.01 (d, *J* = 8.4 Hz, 1H), 7.74-7.71 (m, 2H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.57 (t, *J* = 7.6 Hz, 2H), 7.42-7.32 (m, 2H), 7.27 (t, *J* = 7.6 Hz, 1H), 7.05 (t, *J* = 7.6 Hz, 1H), 6.80 (d, *J* = 8.8 Hz, 1H), 6.57 (d, *J* = 8.8 Hz, 1H), 4.46 (d, *J* = 5.6 Hz, 1H), 4.21-4.16 (m, 1H), 3.98-3.93 (m, 1H), 3.59-3.53 (m, 1H), 3.33-3.27 (m, 1H), 3.18-3.13 (m, 1H), 2.53-2.37 (m, 2H), 2.26-2.20 (m, 1H), 2.15-2.00 (m, 3H), 1.94-1.87 (m, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 147.6, 142.8, 134.4, 134.0, 132.9, 128.4, 127.9, 127.3, 125.7, 125.5, 125.2, 125.2, 124.8, 124.6, 124.5, 123.9, 121.6, 119.2, 118.9, 63.2, 59.4, 55.0, 53.8, 36.0, 29.2, 27.5, 23.7.

HRMS (*m*/*z*) : Calculated for $C_{28}H_{26}N_2$ (M+H): 391.2175, Found (M+H): 391.2169.

8-Methoxy-1-(2-methoxyphenyl) 2,3,3a,3b,4,5,6,11b-octahydro-1*H*-dipyrrolo[1,2-a:3′,2′-c]quinoline (4f)



4f

Yield : 0.11 g (64%); white solid.

mp : 120-122 ^{o}C.

IR (KBr) : (cm^{-1}) 3058, 2964, 2960, 2855, 1600, 1507, 1458, 1227, 1036, 789, 734.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 6.90-6.85 (m, 3H), 6.67-6.61 (m, 2H), 6.49-6.44 (m, 2H), 5.66-5.63 (m, 1H), 3.92 (s, 3H), 3.86-3.82 (m, 1H), 3.78 (s, 3H), 3.59-3.51 (m, 2H), 3.20-3.13 (m, 2H), 2.86-2.80 (m, 1H), 2.06-1.88 (m, 5H), 1.79-1.73 (m, 1H).

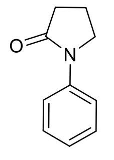
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 150.6, 148.2, 138.6, 137.4, 126.6, 121.8, 121.3, 119.9, 118.3, 117.6, 111.3, 110.9, 59.7, 59.6, 55.9, 55.5, 51.7, 47.8, 41.2, 28.8, 23.7, 23.4.

HRMS (*m*/*z*) : Calculated for $C_{22}H_{26}N_2O_2$ (M+H): 351.2073, Found (M+H): 351.2072.

1.4.5. General procedure for the preparation of cyclic amides (5)

A mixture of the N-arylpyrrolidine **1** (1 mmol), T-HYDRO (4 mmol) and *t*-BuOK (4 mmol) in MeOH (2 mL) was stirred for 24 hours at 70 ^{o}C. After completion of the reaction, the solvent was evaporated and EtOAc (10 mL) and water (5 mL) were added. The organic layer was washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography on silica gel (100-200 mesh) using EtOAc:Hexane (15:100) as eluent to isolate cyclic amides **5**.

1-Phenylpyrrolidin-2-one (5a)


5a

Yield : 0.14 g (85%); white solid.

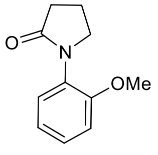
mp : 70-72 ^{o}C.

IR (KBr) : (cm^{-1}) 3419, 3057, 2964, 2937, 1687, 1583, 1539, 1408, 1309 1056, 769, 726.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.59 (d, *J* = 8.4 Hz, 2H), 7.38-7.33 (m, 2H), 7.15-7.11 (m, 1H), 3.83 (t, *J* = 7.0 Hz, 2H), 2.58 (t, *J* = 8.0 Hz, 2H), 2.16-2.09 (m, 2H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 174.1, 139.3, 128.6, 124.3, 119.8, 48.6, 32.6, 17.8.

1-(2-Methoxyphenyl)pyrrolidin-2-one (5b)


5b

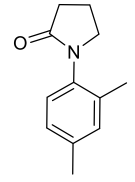
Yield : 0.17 g (89%); light brown oil.

IR (Neat) : (cm^{-1}) 2952, 2925, 2881, 1698, 1602, 1565, 1390, 1301, 1234, 821, 715.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.29-7.24 (m, 2H), 7.01-6.95 (m, 2H), 3.83 (s, 3H), 3.75 (t, *J* = 7.0 Hz, 2H), 2.55 (t, *J* = 8.0 Hz, 2H), 2.21-2.14 (m, 2H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 175.0, 154.6, 128.4, 127.0, 120.7, 111.8, 55.4, 49.7, 31.0, 18.7.

1-(2,4-Dimethylphenyl)pyrrolidin-2-one (5c)



5c

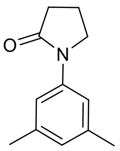
Yield : 0.07 g (35%); light brown oil.

IR (Neat) : (cm^{-1}) 2922, 2887, 1698, 1609, 1552, 1432, 1319, 1215, 976, 837, 718.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.09 (s, 1H), 7.04 (s, 2H), 3.71 (t, *J* = 7.0 Hz, 2H), 2.58 (t, *J* = 8.2 Hz, 2H), 2.33 (s, 3H), 2.24-2.20 (m, 2H).

^{13}C NMR **:** (100 MHz, CDCl$_3$, δ ppm) 174.6, 137.7, 135.2, 134.8, 131.8, 127.6, 126.5, 50.8, 31.2, 21.0, 19.1, 17.8.

1-(3, 5-Dimethylphenyl)pyrrolidin-2-one (5d)



5d

Yield : 0.148 g (78%); white solid.

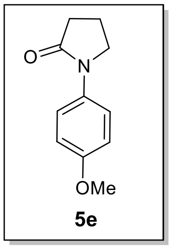
mp : 86-88 °C.

IR (KBr) : (cm^{-1}) 2987, 2854, 1695, 1600, 1524, 1402, 1326, 1234, 817, 739.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.24 (s, 2H), 6.81 (s, 1H), 3.84 (t, *J* = 7.2 Hz, 2H), 2.60 (t, *J* = 8.0 Hz, 2H), 2.34 (s, 6H), 2.18-2.11 (m, 2H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 174.0, 139.2, 138.3, 126.3, 118.0, 49.0, 32.7, 21.4, 18.0.

1-(4-Methoxyphenyl)pyrrolidin-2-one (5e)



5e

Yield : 0.16 g (86%); white solid.

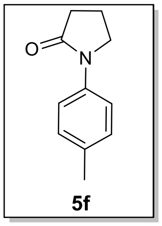
mp : 89-91 ^{o}C.

IR (KBr) : (cm^{-1}) 2983, 2868, 1689, 1607, 1509, 1412, 1306, 1225, 823, 716.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.48 (d, *J* = 9.2 Hz, 2H), 6.88 (d, *J* = 9.2 Hz, 2H), 3.81-3.78 (m, 5H), 2.56 (t, *J* = 8.0 Hz, 2H), 2.16-2.08 (m, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 173.7, 156.3, 132.5, 121.6, 113.8, 55.3, 49.0, 32.3, 17.8.

1-(*p*-Tolyl)pyrrolidin-2-one (5f)



5f

Yield : 0.154 g (88%); white solid.

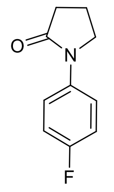
mp : 90-92 ^{o}C.

IR (KBr) : (cm^{-1}) 2964, 2932, 2871, 1693, 1512, 1392, 1304, 1233, 833 724.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.50 (d, *J* = 8.4 Hz, 2H), 7.18 (d, *J* = 8.4 Hz 2H), 3.84 (t, *J* = 7.0 Hz, 2H), 2.60 (t, *J* = 8.2 Hz, 2H), 2.34 (s, 3H), 2.19-2.12 (m, 2H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 173.9, 136.8, 134.1, 129.2, 120.0, 48.8, 32.6, 20.8, 17.9.

1-(4-Fluorophenyl)pyrrolidin-2-one (5g)



5g

Yield : 0.15 g (81%); light brown solid.

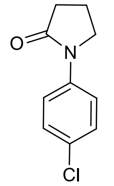
mp : 55-57 °C.

IR (KBr) : (cm^{-1}) 2925, 2868, 1698, 1621, 1583, 1500, 1463, 1319, 1208, 1008 798, 701.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.59-7.55 (m, 2H), 7.07-7.03 (m, 2H), 3.83 (t, J = 7.0 Hz, 2H), 2.60 (t, J = 8.2 Hz, 2H), 2.20-2.12 (m, 2H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 174.1, 160.6, 158.2, 135.5, 121.7, 121.6, 115.6, 115.3, 49.0, 32.5, 17.9.

1-(4-Chlorophenyl)pyrrolidin-2-one (5h)



5h

Yield : 0.15 g (79%); white solid.

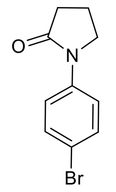
mp : 95-97 °C.

IR (KBr) : (cm^{-1}) 2902, 2879, 1688, 1611, 1571, 1452, 1329, 1236, 998, 845, 716.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.59-7.57 (m, 2H), 7.33-7.31 (m, 2H), 3.83 (t, J = 7.0 Hz, 2H), 2.61 (t, J = 8.2 Hz, 2H), 2.21-2.13 (m, 2H).

^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 174.2, 137.9, 129.4, 128.7, 120.9, 48.6, 32.6, 17.8.

1-(4-Bromophenyl)pyrrolidin-2-one (5i)



5i

Yield : 0.20 g (82%); white solid.

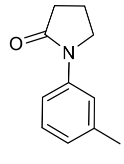
mp : 100-102 °C.

IR (KBr) : (cm^{-1}) 2988, 2862, 1691, 1605, 1564, 1446, 1331, 1245, 834, 726.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.54-7.51 (m, 2H), 7.48-7.45 (m, 2H), 3.82 (t, *J* = 7.0 Hz, 2H), 2.60 (t, *J* = 8.2 Hz, 2H), 2.20-2.12 (m, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 174.2, 138.4, 131.6, 121.1, 117.0, 48.5, 32.6, 17.7.

1-(*m*-Tolyl)pyrrolidin-2-one (5j)



5j

Yield : 0.14 g (77%); light brown solid.

mp : 46-48°C.

IR (KBr) : (cm^{-1}) 2991, 2888, 1691, 1602, 1537, 1416, 1331, 1240, 845, 729.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.46 (s, 1H), 7.39 (d, *J* = 8.4 Hz, 1H), 7.29-7.24 (m, 1H), 7.00 (d, *J* = 7.6 Hz, 1H), 3.85 (t, *J* = 7.0 Hz, 2H), 2.60 (t, *J* = 8.2 Hz, 2H), 2.38 (s, 3H), 2.18-2.11 (m, 2H).

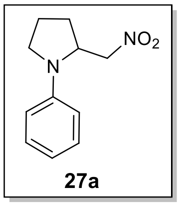
^{13}C NMR **:** (100 MHz, $CDCl_3$, δ ppm) 174.2, 139.3, 138.6, 128.6, 125.4, 120.8, 117.2, 49.0, 32.8, 21.6, 18.1.

1.4.6. General procedure for the preparation of β-nitroamines 27

N-arylpyrrolidine and piperidine derivatives **1** were readily prepared by a recently reported method from our laboratory. A mixture of the arylamine **1** (1 mmol), T-HYDRO (0.55 mL, 4 mmol), *t*-BuOK (0.22 g, 2 mmol) and nitromethane (0.5 mL) in CH_3CN (5 mL) was stirred for 48 h at 80 °C. After completion of the reaction, the solvent was evaporated. EtOAc 10 mL and water 5 mL were added and the organic layer was washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography on silica gel (100-200 mesh) using EtOAc:Hexane (5:95) as eluent to isolate β-nitroamines **27a-27n**.

2-(Nitromethyl)-1-phenylpyrrolidine (27a)

Yield : 0.17 g (81%); yellow oil.



27a

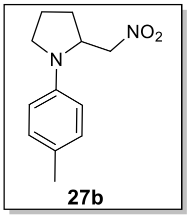
IR (Neat) : (cm^{-1}) 2966, 2914, 2838, 1593, 1541, 1498, 1358, 1260, 1173, 990, 743.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.34-7.27 (m, 2H), 6.83-6.79 (m, 1H), 6.73 (d, *J* = 8.0 Hz, 2H), 4.66-4.63 (m, 1H), 4.46-4.42 (m, 1H), 4.24-4.18 (m, 1H), 3.54-3.49 (m, 1H), 3.27-3.20 (m, 1H), 2.17-2.07 (m, 4H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 145.8, 130.0, 117.4, 112.0, 111.7, 75.8, 57.4, 48.1, 29.3, 22.8.

HRMS (*m/z*) : Calculated for $C_{11}H_{14}N_2O_2$ (M+H): 207.1134, Found (M+H): 207.1134.

2-(Nitromethyl)-1-(*p*-tolyl)pyrrolidine (27b)



27b

Yield : 0.19 g (86%); yellow oil.

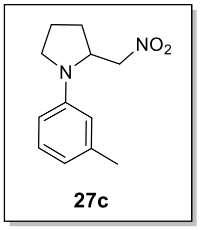
IR (Neat) : (cm^{-1}) 2946, 2896, 2841, 1611, 1541, 1503, 1361, 1228, 1155, 807.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.19-7.07 (m, 2H), 6.71-6.59 (m, 2H), 4.72-4.58 (m, 1H), 4.48-4.53 (m, 1H), 4.29-4.13 (m, 1H), 3.53-3.48 (m, 1H), 3.25-3.19 (m, 1H), 2.31 (s, 3H), 2.19-2.07 (m, 4H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 143.7, 130.2, 126.5, 112.0, 76.0, 57.6, 48.3, 29.3, 22.9, 20.2.

HRMS (*m*/*z*) : Calculated for $C_{12}H_{16}N_2O_2$ (M+H): 221.1291, Found (M+H): 221.1294.

2-(Nitromethyl)-1-(*m*-tolyl)pyrrolidine (27c)



27c

Yield : 0.19 g (85%); yellow oil.

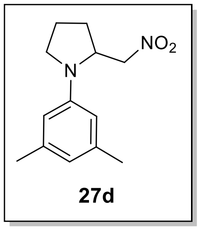
IR (Neat) : (cm^{-1}) 3041, 2964, 2921, 2855, 1600, 1545, 1490, 1364, 1210, 767, 734.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.23-7.19 (m, 1H), 6.65 (d, J = 8.0 Hz, 1H), 6.57-6.54 (m, 2H), 4.67-4.65 (m, 1H), 4.47-4.42 (m, 1H), 4.24-4.19 (m, 1H), 3.54-3.49 (m, 1H), 3.24-3.22 (m, 1H), 2.38 (s, 3H), 2.17-2.05 (m, 4H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 145.9, 139.5, 129.6, 118.3, 112.7, 109.2, 75.9, 57.4, 48.2, 29.3, 22.8, 21.9.

HRMS (*m/z*) : Calculated for $C_{12}H_{16}N_2O_2$ (M+H): 221.1291, Found (M+H): 221.1292.

1-(3,5-Dimethylphenyl)-2-(nitromethyl)pyrrolidine (27d)



27d

Yield : 0.22 g (92%); yellow oil.

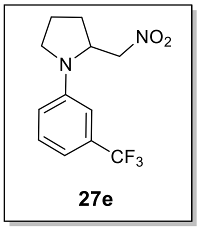
IR (Neat) : (cm^{-1}) 3047, 2948, 2915, 2844, 1600, 1540, 1485, 1425, 1370, 1227, 1118, 811, 685.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 6.49 (s, 1H), 6.36 (s, 2H), 4.69-4.65 (m, 1H), 4.45-4.42 (m, 1H), 4.23-4.18 (m, 1H), 3.52-3.48 (m, 1H), 3.26-3.19 (m, 1H), 2.33 (s, 6H), 2.17-2.06 (m, 4H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 146.0, 139.4, 119.4, 109.9, 75.9, 57.4, 48.2, 29.2, 22.8, 21.8.

HRMS (*m/z*) : Calculated for $C_{13}H_{18}N_2O_2$ (M+H): 235.1447, Found (M+H): 235.1444.

2-(Nitromethyl)-1-(3-(trifluoromethyl)phenyl)pyrrolidine (27e)



27e

Yield : 0.21 g (77%); yellow oil.

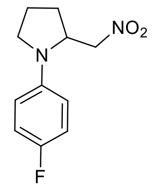
IR (Neat) : (cm^{-1}) 2975, 2921, 2849, 1605, 1545, 1501, 1452, 1370, 1162, 1118, 992, 778, 696.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.42-7.38 (m, 1H), 7.05-7.03 (d, *J* = 7.6 Hz, 1H), 6.89-6.88 (m, 2H), 4.62-4.59 (m, 1H), 4.50-4.46 (m, 1H), 4.29-4.23 (m, 1H), 3.58-3.53 (m, 1H), 3.29-3.26 (m, 1H), 2.22-2.13 (m, 4H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 145.9, 132.1, 131.8 (d, $J_{C\text{-}F}$ = 31.8 Hz), 130.1, 125.6, 122.9 (d, $J_{C\text{-}F}$ = 271.0 Hz), 114.9, 113.79, 113.75, 113.71, 113.67 (q, $J_{C\text{-}F}$ = 4.0 Hz), 108.48, 108.44, 108.40, 108.36 (q, $J_{C\text{-}F}$ = 4.0 Hz), 75.5, 57.4, 48.2, 29.4, 22.7.

HRMS (*m*/*z*) : Calculated for $C_{12}H_{13}F_3N_2O_2$ (M+H): 275.1008, Found (M+H): 275.1006.

1-(4-Fluorophenyl)-2-(nitromethyl)pyrrolidine (27f)



27f

Yield : 0.18 g (79%); yellow oil.

IR (Neat) : (cm^{-1}) 3052, 2964, 2910, 2849, 1605, 1540, 1507, 1386, 1227, 816, 795.

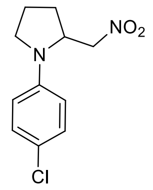
^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.04-7.00 (m, 2H), 6.66-6.62 (m, 2H), 4.62-4.58 (m, 1H), 4.40-4.36 (m, 1H), 4.25-4.20 (m, 1H), 3.51-3.47 (m, 1H), 3.23-3.17 (m, 1H), 2.18-2.06 (m, 4H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 156.9, 154.5 (d, J_{C-F} = 235.9 Hz), 142.5, 116.2, 116.0 (d, J_{C-F} = 22.2 Hz), 112.6, 112.5 (d, J_{C-F} = 7.3 Hz), 76.0, 57.9, 48.6, 29.5, 23.0, 14.2.

HRMS (*m*/*z*) : Calculated for $C_{11}H_{13}FN_2O_2$ (M+H): 225.1040, Found (M+H): 225.1036.

1-(4-Chlorophenyl)-2-(nitromethyl)pyrrolidine (27g)

Yield : 0.18 g (73%); white solid.



27g

mp : 45-47 °C.

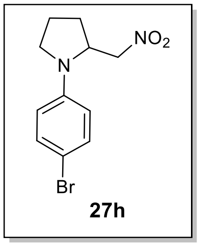
IR (KBr) : (cm^{-1}) 2959, 2921, 2882, 2844, 1595, 1551, 1501, 1364, 1189, 1101, 811, 729.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.24 (d, *J* = 9.2 Hz, 2H), 6.63 (d, *J* = 8.8 Hz, 2H), 4.61-4.57 (m, 1H), 4.41-4.38 (m, 1H), 4.25-4.19 (m, 1H), 3.51-3.47 (m, 1H), 3.24-3.18 (m, 1H), 2.20-2.06 (m, 4H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 144.4, 129.5, 122.2, 113.1, 75.7, 57.5, 48.3, 29.4, 22.9.

HRMS (*m*/*z*) : Calculated for $C_{11}H_{13}ClN_2O_2$ (M+H): 241.0745, Found (M+H): 241.0742.

1-(4-Bromophenyl)-2-(nitromethyl)pyrrolidine (27h)



27h

Yield : 0.22 g (78%); brown solid.

mp : 61-63 °C.

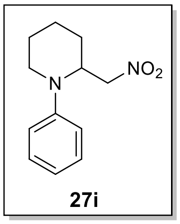
IR (KBr) : (cm^{-1}) 3041, 2970, 2910, 2849, 1595, 1545, 1490, 1359, 1184, 805, 734.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.37 (d, *J* = 9.2 Hz, 2H), 6.58 (d, *J* = 8.8 Hz, 2H), 4.60-4.56 (m, 1H), 4.40-4.37 (m, 1H), 4.24-4.19 (m, 1H), 3.50-3.45 (m, 1H), 3.24-3.16 (m, 1H), 2.19-2.08 (m, 4H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 144.8, 132.3, 113.6, 109.3, 75.6, 57.5, 48.3, 29.4, 22.8.

HRMS (*m*/*z*) : Calculated for $C_{11}H_{13}BrN_2O_2$ (M+Na$^+$): 307.0057, Found (M+ Na$^+$): 307.0061.

2-(Nitromethyl)-1-phenylpiperidine (27i)



27i

Yield : 0.07 g (32%); yellow oil.

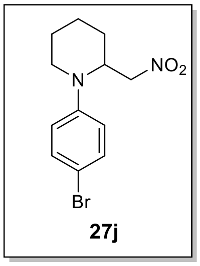
IR (Neat) : (cm^{-1}) 3058, 3041, 2970, 2915, 2844, 1595, 1545, 1501, 1359, 1184, 997, 751, 696.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.34-7.29 (m, 2H), 7.02-7.00 (m, 2H), 6.94-6.90 (m, 1H), 4.62-4.57 (m, 2H), 4.51-4.46 (m, 1H), 3.46-3.43 (m, 1H), 2.96-2.89 (m, 1H), 1.99-1.92 (m, 1H), 1.86-1.64 (m, 5H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 149.3, 129.5, 120.5, 116.9, 73.2, 54.9, 44.6, 26.4, 25.0, 19.1.

HRMS (*m*/*z*) : Calculated for $C_{12}H_{16}N_2O_2$ (M+H): 221.1291, Found (M+H): 221.1291.

1-(4-Bromophenyl)-2-(nitromethyl)piperidine (27j)



27j

Yield : 0.05 g (17%); yellow oil.

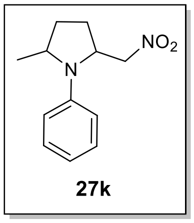
IR (Neat) : (cm^{-1}) 3386, 3058, 2959, 2921, 2877, 1595, 1545, 1501, 1353, 1036, 751, 690.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.41-7.37 (m, 2H), 6.89-6.85 (m, 2H), 4.61-4.55 (m, 2H), 4.51-4.45 (m, 1H), 3.43-3.39 (m, 1H), 2.95-2.88 (m, 1H), 1.98-1.90 (m, 1H), 1.86-1.74 (m, 3H), 1.72-1.59 (m, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 148.4, 132.3, 118.3, 112.5, 73.2, 54.8, 44.2, 26.3, 24.7, 18.9.

HRMS (*m*/*z*) : Calculated for $C_{12}H_{15}BrN_2O_2$ (M+H): 299.0396, Found (M+H): 299.0395.

2-Methyl-5-(nitromethyl)-1-phenylpyrrolidine (27k)



27k

Yield : 0.18 g (82%); yellow oil.

IR (Neat) : (cm^{-1}) 3071, 2960, 2914, 2869, 2223, 1596, 1551, 1505, 1348, 1222, 1157, 1035, 747, 692.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.33-7.28 (m, 4H), 6.84-6.79 (m, 2H), 6.77-6.73 (m, 5H), 4.77-4.73 (m, 1H), 4.68-4.64 (m, 1H), 4.56-4.51 (m, 1H), 4.44-4.38 (m, 1H), 4.31-4.26 (m, 1H), 4.14-4.07 (m, 2H), 3.92-3.85 (m, 1H), 2.36-2.11 (m, 5H), 2.09-2.04 (m, 2H), 1.84-1.74 (m, 2H), 1.31 (d, *J* = 6.0 Hz, 3H), 1.16 (d, *J* = 6.0 Hz, 3H).

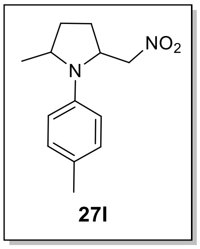
^{13}C NMR **:** (100 MHz, CDCl$_3$, δ ppm) 146.1, 143.5, 129.7, 129.6, 129.2, 117.6, 117.0, 116.5, 115.1, 113.5, 112.4, 111.8, 77.9, 74.8, 59.8, 56.6, 53.6, 53.0, 32.1, 29.8, 28.6, 21.7, 18.0.

HRMS (*m/z*) : Calculated for $C_{12}H_{16}N_2O_2$ (M+H): 221.1291, Found (M+H): 221.1286.

2-Methyl-5-(nitromethyl)-1-(*p*-tolyl)pyrrolidine (27l)

Yield : 0.18 g (78%); yellow oil.

IR (Neat) : (cm^{-1}) 3020, 2970, 2924, 2869, 2227, 1616, 1455, 1343, 1157, 1020, 808, 737.



27l

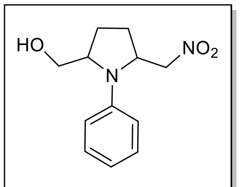
^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.12 (d, *J* = 8.0 Hz, 4H), 6.69-6.64 (m, 4H), 4.75-4.71 (m, 1H), 4.66-4.63 (m, 1H), 4.52-4.48 (m, 1H), 4.39-4.33 (m, 1H), 4.30-4.25 (m, 1H), 4.11-4.05 (m, 2H), 3.87-3.79 (m, 1H), 2.33-2.09 (m, 12H), 2.06-2.02 (m, 2H), 1.82-1.71 (m, 2H), 1.29 (d, *J* = 6.0 Hz, 4H), 1.14 (d, *J* = 6.4 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 144.0, 141.3, 130.2, 130.0, 129.6, 127.0, 126.1, 125.6, 121.4, 113.6, 112.6, 107.8, 78.1, 74.9, 60.1, 56.7, 56.0, 53.0, 32.1, 29.9, 28.5, 26.8, 21.8, 20.3, 20.2, 18.0.

HRMS (*m/z*) : Calculated for $C_{13}H_{18}N_2O_2$ (M+Na$^+$): 257.1265, Found (M+ Na$^+$): 257.1267.

(5-(Nitromethyl)-1-phenylpyrrolidin-2-yl)methanol (27m)

Yield : 0.17 g (73%); yellow oil.



27m

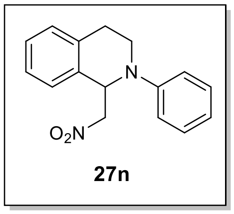
IR (Neat) : (cm^{-1}) 3386, 3058, 2959, 2921, 2877, 1595, 1545, 1501, 1353, 1036, 751, 690.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.32-7.27 (m, 3H), 6.86-6.78 (m, 5H), 4.68-4.56 (m, 2H), 4.48-4.39 (m, 2H), 4.15-4.05 (m, 1H), 3.98-3.95 (m, 2H), 3.82-3.77 (m, 1H), 3.69-3.61 (m, 2H), 3.55-3.51 (m, 1H), 2.51 (s, 2H), 2.35-2.25 (m, 1H), 2.19-2.10 (m, 4H), 2.05-1.97 (m, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 146.5, 143.4, 129.9, 129.6, 118.3, 117.7, 113.9, 112.7, 77.9, 77.5, 77.2, 76.9, 74.5, 62.4, 61.8, 61.5, 60.1, 58.6, 57.1, 28.6, 27.2, 26.4, 26.1.

HRMS (*m/z*) : Calculated for $C_{12}H_{16}N_2O_3$ (M+H): 237.1240, Found (M+H): 237.1243.

1-(Nitromethyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (27n)



27n

Yield : 0.24 g (91%); yellow oil.

IR (Neat) : (cm^{-1}) 3063, 3030, 2964, 2915, 1605, 1545, 1496, 1380, 1003, 899, 756.

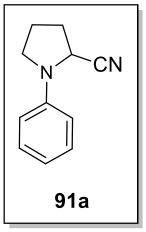
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.29-7.18 (m, 5H), 7.13 (d, *J* = 6.8 Hz 1H), 6.98 (d, *J* = 8.0 Hz, 2H), 6.85 (t, *J* = 7.2 Hz, 1H), 5.55 (t, *J* = 7.0 Hz, 1H), 4.95-4.85 (m, 1H), 4.59-4.54 (m, 1H), 3.79-3.59 (m, 2H), 3.21-3.05 (m, 1H), 2.87-2.78 (m, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 148.5, 135.3, 133.0, 130.0, 129.2, 128.2, 127.0, 126.7, 119.5, 115.2, 78.8, 58.2, 42.1, 26.5.

1.4.7. General procedure for the preparation of α-aminonitriles (91)

A mixture of the N-arylpyrrolidine **1** (1 mmol), T-HYDRO (0.41 mL, 3 mmol), *t*-BuOK (0.17 g, 1.5 mmol) and TMSCN (0.19 mL, 1.5 mmol) in CH_3CN (5 mL) was stirred for 24 h at 80 °C. After completion of the reaction, the solvent was evaporated. EtOAc 10 mL and water 5 mL were added and the organic layer was washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography on silica gel (100-200 mesh) using EtOAc:Hexane (7:93) as eluent to isolate α-aminonitriles **91a-r**.

1-Phenylpyrrolidine-2-carbonitrile (91a)


91a

Yield : 0.15 g (89%); colorless liquid.

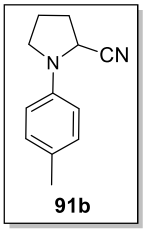
IR (Neat) : (cm^{-1}) 3044, 2951, 2874, 2853, 2227, 1596, 1501, 1359, 1186, 1158, 993.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.35 (t, *J* = 8.0 Hz, 2H), 6.88 (t, *J* = 7.4 Hz, 1H), 6.74 (d, *J* = 8.4 Hz, 2H), 4.48-4.46 (m, 1H), 3.52-3.48 (m, 1H), 3.43-3.38 (m, 1H), 2.48-2.41 (m, 1H), 2.36-2.19 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 145.3, 129.5, 119.3, 118.3, 112.8, 49.1, 47.5, 31.6, 24.0.

HRMS (*m*/*z*) : Calculated for $C_{11}H_{12}N_2$ (M+H): 173.1079, Found (M+H): 173.1071.

1-(*p*-Tolyl)pyrrolidine-2-carbonitrile (91b)


91b

Yield : 0.17 g (93%); colorless liquid.

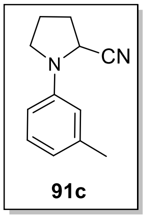
IR (Neat) : (cm^{-1}) 3036, 2926, 2855, 2207, 1616, 1518, 1463, 1364, 1184, 910, 800, 734.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.14-7.12 (m, 2H), 6.65-6.63 (m, 2H), 4.45-4.43 (m, 1H), 3.47-3.35 (m, 2H), 2.46-2.39 (m, 1H), 2.32-2.25 (m, 4H), 2.24-2.19 (m, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 143.1, 130.1, 127.5, 119.4, 112.8, 49.4, 47.6, 31.5, 23.9, 20.3.

HRMS (*m*/*z*) : Calculated for $C_{12}H_{14}N_2$ (M+Na$^+$): 209.1054, Found (M+Na$^+$): 209.1053.

1-(*m*-Tolyl)pyrrolidine-2-carbonitrile (91c)



91c

Yield : 0.18 g (96%); colorless liquid.

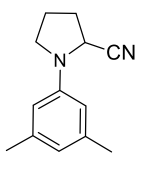
IR (Neat) : (cm^{-1}) 3037, 2919, 2859, 2239, 1603, 1582, 1495, 1455, 1359, 1178, 1023, 837, 767.

^{1}H NMR **:** (400 MHz, $CDCl_3$, δ ppm) 7.26-7.21 (m, 1H), 6.72 (d, *J* = 7.6 Hz, 1H), 6.56 (s, 2H), 4.48-4.46 (m, 1H), 3.52-3.48 (m, 1H), 3.43-3.37 (m, 1H), 2.46-2.44 (m, 1H), 2.41 (s, 3H), 2.36-2.22 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 145.4, 139.3, 129.4, 119.4, 119.2, 113.5, 110.0, 49.1, 47.5, 31.6, 24.1, 21.9.

HRMS (*m*/*z*) : Calculated for $C_{12}H_{12}N_2$ (M+H): 187.1236, Found (M+H): 187.1230.

1-(3,5-Dimethylphenyl)pyrrolidine-2-carbonitrile (91d)



91d

Yield : 0.19 g (95%); colorless liquid.

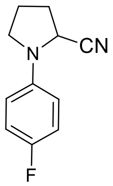
IR (Neat) : (cm^{-1}) 3041, 2975, 2921, 2855, 2230, 1605, 1479, 1381, 1222, 1184, 1036, 822, 685.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 6.55 (s, 1H), 6.38 (s, 2H), 4.46 (d, *J* = 6.0 Hz, 1H), 3.51-3.46 (m, 1H), 3.41-3.38 (m, 1H), 2.44-2.42 (m, 1H), 2.36 (s, 6H), 2.31-2.20 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 145.5, 139.1, 120.3, 119.5, 110.8, 49.2, 47.5, 31.6, 24.0, 21.7.

HRMS (*m*/*z*) : Calculated for $C_{13}H_{16}N_2$ (M+H): 201.1392, Found (M+H): 201.1390.

1-(4-Fluorophenyl)pyrrolidine-2-carbonitrile (91e)



91e

Yield : 0.16 g (86%); colorless liquid.

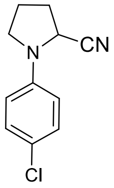
IR (Neat) : (cm^{-1}) 3058, 2975, 2937, 2871, 2225, 1611, 1512, 1463, 1364, 1222, 1162, 964, 816.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.05-7.01 (m, 2H), 6.66-6.63 (m, 2H), 4.41-4.39 (m, 1H), 3.43-3.34 (m, 2H), 2.42-2.26 (m, 4H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 157.4, 155.0 (d, $J_{C\text{-}F}$ = 236.6 Hz), 141.91, 141.90 (d, $J_{C\text{-}F}$ = 1.4 Hz), 119.2, 116.0, 115.8 (d, $J_{C\text{-}F}$ = 22.7 Hz), 113.7, 113.6 (d, $J_{C\text{-}F}$ = 7.4 Hz), 49.6, 47.9, 31.5,24.0.

HRMS (*m*/*z*) : Calculated for $C_{11}H_{11}FN_2$ (M+H): 191.0985, Found (M+H): 191.0981.

1-(4-Chlorophenyl)pyrrolidine-2-carbonitrile (91f)



91f

Yield : 0.18 g (89%); white solid.

mp : 78-80 °C.

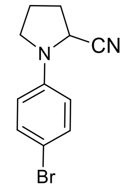
IR (KBr) : (cm^{-1}) 2981, 2948, 2932, 2860, 2205, 1600, 1496, 1364, 1189, 1151, 1096, 970, 811, 718.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.27 (d, *J* = 8.8 Hz, 2H), 6.63 (d, *J* = 8.8 Hz, 2H), 4.43-4.41 (m, 1H), 3.47-3.34 (m, 2H), 2.48-2.43 (m, 1H), 2.41-2.21 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 143.8, 129.3, 123.3, 118.9, 113.9, 49.2, 47.7, 31.6, 24.1.

HRMS (*m*/*z*) : Calculated for $C_{11}H_{11}ClN_2$ (M+H): 207.0690, Found (M+H): 207.0681.

1-(4-Bromophenyl)pyrrolidine-2-carbonitrile (91g)



91g

Yield : 0.23 g (90%); light brown solid.

mp : 75-77 °C.

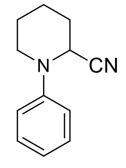
IR (KBr) : (cm^{-1}) 2974, 2861, 2234, 1594, 1492, 1359, 1186, 909, 805, 730.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.41-7.38 (m, 2H), 6.61-6.57 (m, 2H), 4.42-4.41 (m, 1H), 3.47-3.33 (m, 2H), 2.48-2.40 (m, 1H), 2.38-2.21 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 144.2, 132.2, 118.9, 114.4, 110.4, 49.1, 47.7, 31.6, 24.1.

HRMS (*m*/*z*) : Calculated for $C_{11}H_{11}BrN_2$ (M+H): 251.0185, Found (M+H): 251.0187.

1-Phenylpiperidine-2-carbonitrile (91h)



91h

Yield : 0.14 g (75%); colorless liquid.

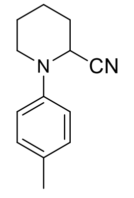
IR (Neat) : (cm^{-1}) 3063, 2942, 2860, 2816, 2225, 1595, 1490, 1447, 1375, 1244, 1162, 1025, 915, 855, 762, 696.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.37-7.33 (m, 2H), 7.05-7.01 (m, 3H), 4.66 (s, 1H), 3.48 (d, *J* = 12.0 Hz, 1H), 3.11-3.04 (m, 1H), 2.09-2.00 (m, 2H), 1.90-1.88 (m, 2H), 1.75-1.70 (m, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 149.8, 129.4, 122.2, 118.3, 117.2, 52.0, 46.6, 29.3, 25.2, 20.2.

HRMS (*m*/*z*) : Calculated for $C_{12}H_{14}N_2$ (M+H): 187.1236, Found (M+H): 187.1231.

1-(*p*-Tolyl)piperidine-2-carbonitrile (91i)



91i

Yield : 0.16 g (78%); colorless liquid.

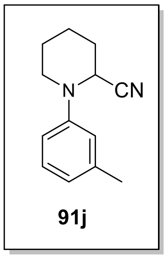
IR (Neat) : (cm^{-1}) 3025, 2939, 2854, 2818, 2224, 1616, 1515, 1444, 1374, 1303, 1247, 1167, 914, 813.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.17-7.15 (m, 2H), 6.98-6.94 (m, 2H), 4.60 (s, 1H), 3.42-3.34 (m, 1H), 3.08-3.03 (m, 1H), 2.34 (s, 3H), 2.07-2.01 (m, 2H), 1.88-1.87 (m, 2H), 1.78-1.70 (m, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 147.6, 131.8, 130.1, 119.1, 118.6, 117.3, 52.7, 46.2, 29.3, 25.2, 20.6, 20.2.

HRMS (*m*/*z*) : Calculated for $C_{13}H_{16}N_2$ (M+H): 201.1392, Found (M+H): 201.1383.

1-(*m*-Tolyl)piperidine-2-carbonitrile (91j)



91j

Yield : 0.15 g (73%); colorless liquid.

IR (Neat) : (cm^{-1}) 2955, 2914, 2855, 2236, 1601, 1581, 1500, 1439, 1253, 1157, 949, 773.

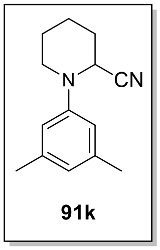
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.24-7.21 (m, 1H), 6.83 (d, *J* = 6.4 Hz, 3H), 4.65 (s, 1H), 3.46 (d, *J* = 12.4 Hz, 1H), 3.07-3.01 (m, 1H), 2.36 (s, 3H), 2.08-1.97 (m, 2H), 1.89-1.86 (m, 2H), 1.75-1.68 (m, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 149.8, 139.1, 129.2, 123.0, 119.1, 117.2, 115.4, 52.1, 46.6, 29.3, 25.2, 21.7, 20.2.

HRMS (*m*/*z*) : Calculated for $C_{13}H_{16}N_2$ (M+H): 201.1392, Found (M+H): 201.1394.

1-(3,5-Dimethylphenyl)piperidine-2-carbonitrile (91k)

Yield : 0.19 g (87%); colorless liquid.



91k

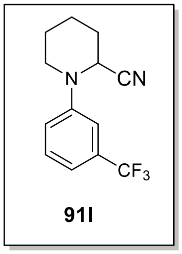
IR (Neat) : (cm^{-1}) 2955, 2919, 2864, 2823, 2228, 1591, 1455, 1374, 1232, 1162, 1070, 955, 919, 843, 737.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 6.67 (d, *J* = 8.0 Hz, 3H), 4.65 (s, 1H), 3.46 (d, *J* = 12.0 Hz, 1H), 3.04 (t, *J* = 11.7 Hz, 1H), 2.33 (s, 6H), 2.08-1.98 (m, 2H), 1.89-1.82 (m, 2H), 1.76-1.68 (m, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 149.9, 138.9, 124.0, 117.3, 116.2, 52.2, 46.6, 29.3, 25.2, 21.6, 20.3.

HRMS (*m*/*z*) : Calculated for $C_{14}H_{18}N_2$ (M+H): 215.1549, Found (M+H): 215.1548.

1-(3-(Trifluoromethyl)phenyl)piperidine-2-carbonitrile (91l)



91l

Yield : 0.17 g (68%); colorless liquid.

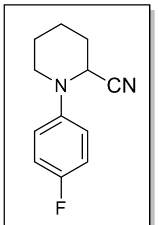
IR (Neat) : (cm^{-1}) 2955, 2859, 2823, 2231, 1616, 1586, 1495, 1455, 1354, 1167, 1121, 939, 793, 692.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.44 (t, *J* = 7.7 Hz, 1H), 7.29-7.18 (m, 3H), 4.70 (s, 1H), 3.52 (d, *J* = 10.8 Hz, 1H), 3.12-3.06 (m, 1H), 2.12-2.01 (m, 2H), 1.93-1.89 (m, 2H), 1.81-1.68 (m, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 150.1, 131.9, 131.6, 130.1, 120.9, 118.53, 118.50 (d, $J_{C\text{-}F}$ = 3.6 Hz), 116.8, 114.9, 114.86 (d, $J_{C\text{-}F}$ = 4.0 Hz), 51.5, 46.4, 29.1, 25.1, 20.0.

HRMS (*m*/*z*) : Calculated for $C_{13}H_{13}F_3N_2$ ($M+Na^+$): 277.0928, Found ($M+Na^+$): 277.0921.

1-(4-Fluorophenyl)piperidine-2-carbonitrile (91m)



91m

Yield : 0.15 g (71%); white solid.

mp : 98-100 °C.

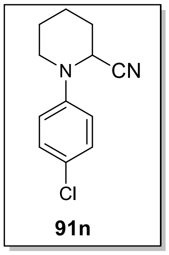
IR (KBr) : (cm^{-1}) 3081, 2945, 2929, 2859, 2227, 1505, 1434, 1343, 1207, 1121, 1030, 924, 828, 727.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.05-6.98 (m, 4H), 4.52 (s, 1H), 3.32-3.29 (m, 1H), 3.07-3.00 (m, 1H), 2.05-2.01 (m, 2H), 1.88-1.86 (m, 2H), 1.75-1.67 (m, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 159.8, 157.3 (d, J_{C-F} = 241.8 Hz), 146.3, 120.6, 120.5 (d, J_{C-F} = 8.0 Hz), 117.0, 116.1, 115.8 (d, J_{C-F} = 22.3 Hz), 53.3, 47.1, 29.3, 25.1, 20.1.

HRMS (*m*/*z*) : Calculated for $C_{12}H_{13}FN_2$ (M+H): 205.1142, Found (M+H): 205.1141.

1-(4-Chlorophenyl)piperidine-2-carbonitrile (91n)



91n

Yield : 0.17 g (77%); white solid.

mp : 112-114 °C.

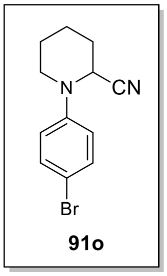
IR (KBr) : (cm^{-1}) 2970, 2950, 2854, 2808, 2231, 1596, 1485, 1384, 1308, 1242, 1217, 1116, 914, 833, 752.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.30-7.27 (m, 2H), 6.96-6.94 (m, 2H), 4.59 (s, 1H), 3.42-3.39 (m, 1H), 3.04-2.98 (m, 1H), 2.07-1.97 (m, 2H), 1.89-1.86 (m, 2H), 1.75-1.67 (m, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 145.6, 126.5, 124.4, 116.8, 114.1, 49.2, 43.8, 26.3, 22.2, 17.2.

HRMS (*m*/*z*) : Calculated for $C_{12}H_{13}ClN_2$ ($M+Na^+$): 243.0664, Found ($M+Na^+$): 243.0658.

1-(4-Bromophenyl)piperidine-2-carbonitrile (91o)



91o

Yield : 0.18 g (69%); white solid.

mp : 109-111 °C.

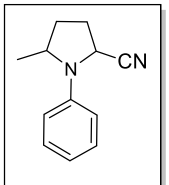
IR (KBr) : (cm^{-1}) 2950, 2919, 2854, 2227, 1591, 1485, 1434, 1404, 1298, 1237, 1126, 995, 813, 798, 742.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.44-7.42 (m, 2H), 6.92-6.89 (m, 2H), 4.61 (s, 1H), 3.43-3.40 (m, 1H), 3.05-2.99 (m, 1H), 2.09-1.98 (m, 2H), 1.89-1.86 (m, 2H), 1.73-1.68 (m, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 148.9, 132.3, 120.1, 116.9, 114.8, 51.8, 46.6, 29.1, 25.0, 20.0.

HRMS (*m/z*) : Calculated for $C_{12}H_{13}BrN_2$ (M+H): 265.0341, Found (M+H): 265.0337.

5-Methyl-1-phenylpyrrolidine-2-carbonitrile (91p)



91p

Yield : 0.15 g (79%); colorless liquid.

IR (Neat) : (cm^{-1}) 3061, 3040, 2970, 2929, 2874, 2232, 1596, 1505, 1465, 1343, 1192, 1040, 747, 692.

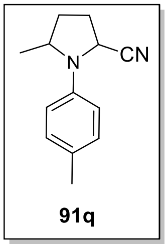
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.35-7.31 (m, 4H), 6.88-6.83 (m, 2H), 6.78-6.72 (m, 4H), 4.57 (d, *J* = 6.8 Hz, 1H), 4.39-4.36 (m, 1H), 4.11-3.97 (m, 2H), 2.31-2.26 (m, 6H), 2.01-1.93 (m, 1H), 1.91-1.87 (m, 1H), 1.37 (d, *J* = 6.4 Hz, 3H), 1.22 (d, *J* = 6.0 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 145.1, 143.8, 129.5, 129.4, 120.4, 119.0, 118.2, 118.1, 113.5, 113.3, 54.6, 53.4, 50.5, 49.4, 32.7, 31.5, 30.2, 29.2, 19.8, 19.3.

HRMS (*m/z*) : Calculated for $C_{12}H_{14}N_2$ (M+H): 187.1236, Found (M+H): 187.1230.

5-Methyl-1-(*p*-tolyl)pyrrolidine-2-carbonitrile (91q)

Yield : 0.15 g (77%); colorless liquid.



91q

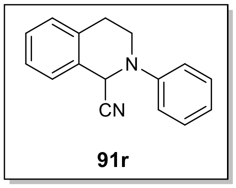
IR (Neat) : (cm^{-1}) 3035, 2970, 2919, 2869, 2229, 1621, 1571, 1515, 1455, 1348, 1157, 1020, 919, 803, 727.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.18 (d, *J* = 8.24 Hz, 4H), 6.75-6.68 (m, 4H), 4.57-4.56 (m, 1H), 4.36-4.34 (m, 1H), 4.07-3.97 (m, 2H), 2.47-2.39 (m, 4H), 2.35 (s, 6H), 2.34-2.27 (m, 2H), 2.01-1.92 (m, 1H), 1.89-1.86 (m, 1H), 1.39-1.37 (m, 3H), 1.25-1.23 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 142.9, 141.7, 130.1, 130.0, 127.4, 127.3, 120.7, 119.2, 113.8, 113.4, 54.8, 53.5, 50.8, 49.9, 32.8, 31.5, 30.2, 29.2, 20.4, 19.8, 19.5.

HRMS (*m/z*) : Calculated for $C_{13}H_{16}N_2$ (M+H): 201.1392, Found (M+H): 201.1384.

2-Phenyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (91r)



91r

Yield : 0.215 g (92%); pale yellow solid.

mp : 94-96 °C.

IR (KBr) : (cm^{-1}) 3041, 2926, 2838, 1742, 1600, 1496, 1463, 1375, 1205, 1145, 1030, 942, 745, 695.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.42-7.38 (m, 2H), 7.35-7.26 (m, 4H), 7.13 (d, *J* = 8.0 Hz, 1H), 7.06 (t, *J* = 7.4 Hz, 1H), 5.55 (s, 1H), 3.83-3.78 (m, 1H), 3.55-3.48 (m, 1H), 3.23-3.14 (m, 1H), 3.02-2.96 (m, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 148.4, 134.7, 129.6, 129.4, 128.8, 127.1, 126.9, 121.9, 117.8, 117.6, 53.2, 44.2, 28.6.

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Chapter 2

Electron Transfer Reactions using Oxygen Doped Carbon Materials

2.1 Introduction

2.1.1 Organic transformations using carbon materials

The carbon materials were widely used as catalytic support for metal species in numerous industrial catalytic processes. For example, aerobic oxidation of benzylic alcohols to ketones was reported using activated carbon.[1] Activated carbon (AC) is widely used as a low-cost adsorbent in the chemical laboratory and industry. Methods were reported for oxidation of benzylic alcohols or alkylarenes (fluorenes, xanthenes and anthrones) to the corresponding carbonyl compounds using the AC/O_2 system.[2]

2.1.1.1 Reactions using activated carbon/ /molecular oxygen system

A variety of heteroaromatic compounds such as substituted pyridines **2**, indoles **4**, 2-substituted imidazoles **6**, 2-arylbenzazoles **9** and pyrimidin-2(1H)-ones **11** were synthesized by oxidative aromatization using activated carbon/molecular oxygen system (Chart 1).[3-8] Also, an environmentally friendly method for oxidative aromatization of several 9,10-dihydroanthracenes **12** was reported using molecular oxygen promoted by inexpensive and readily available activated carbon (Chart 1).[9]

Chart 1

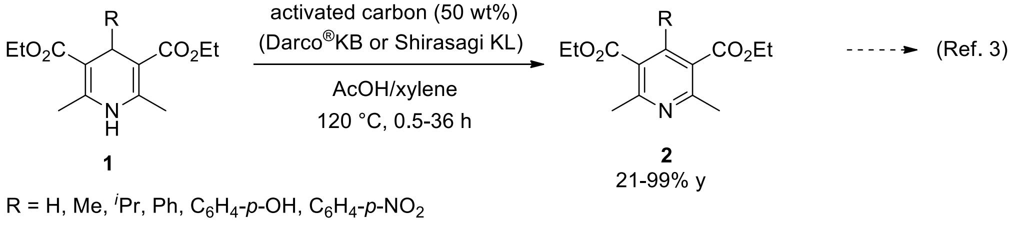
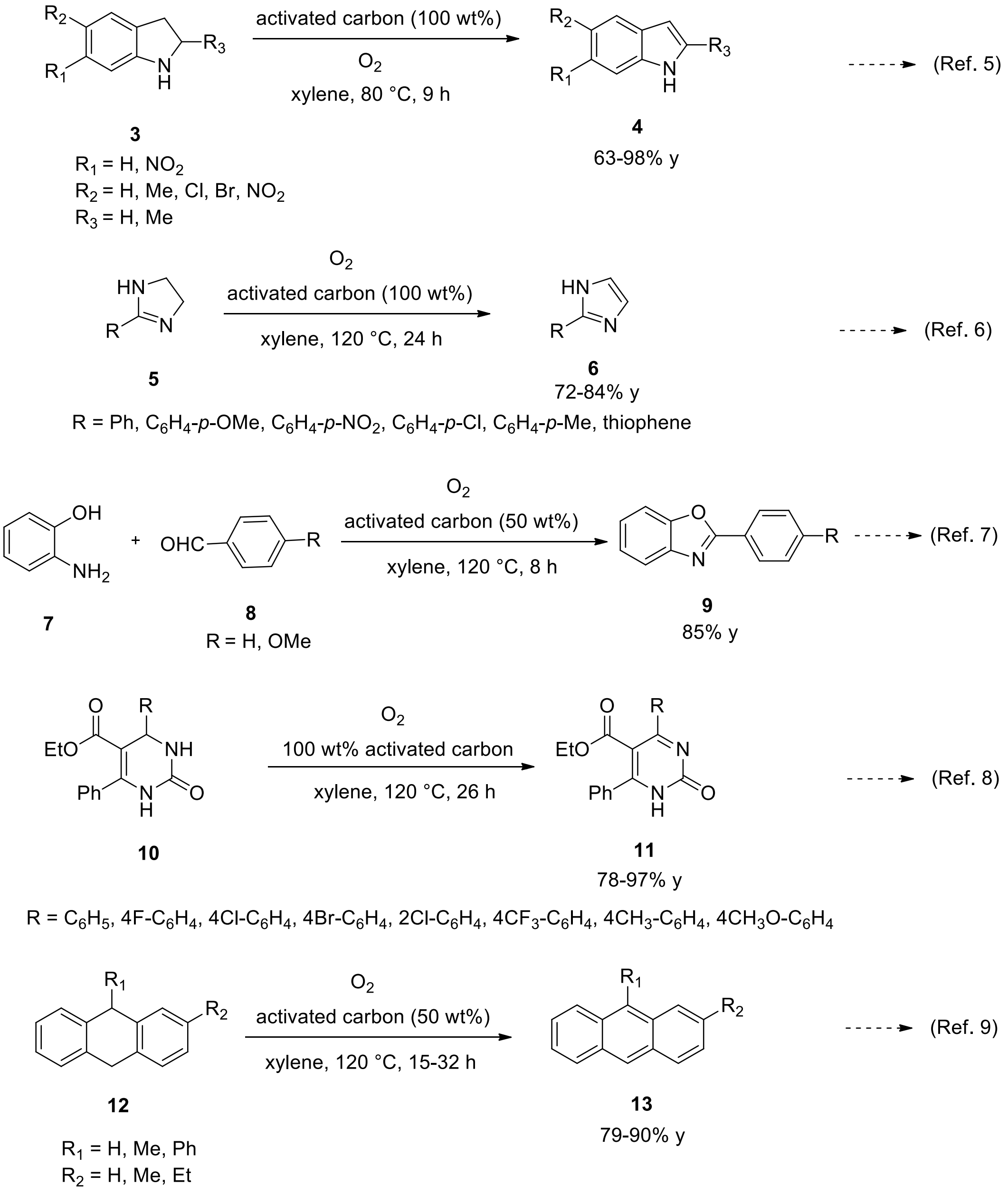
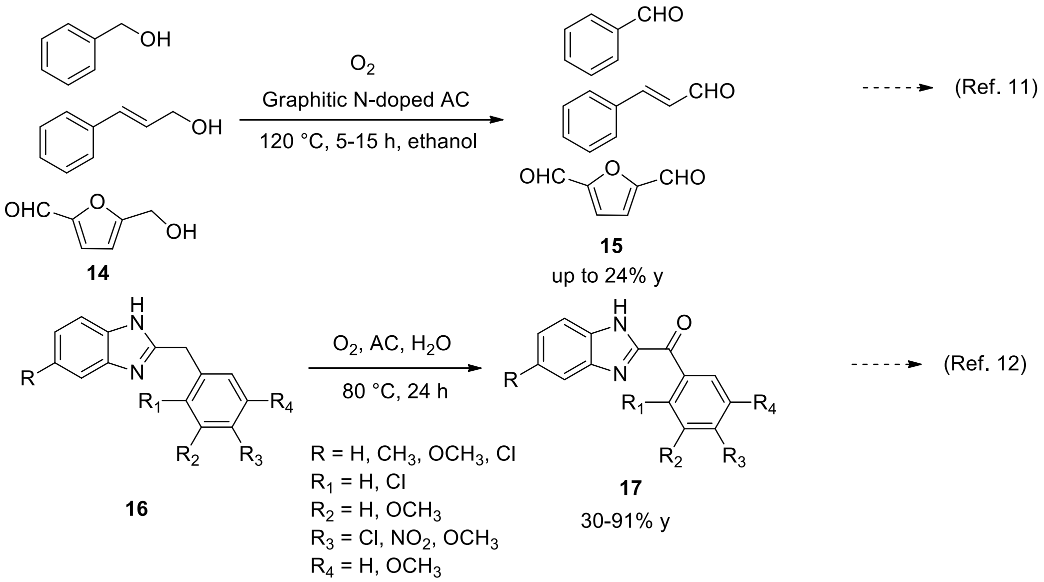


Chart 1 (Continued)



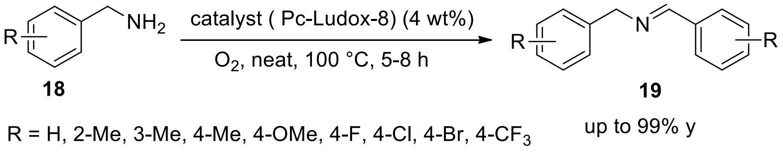
Activated charcoal is also useful in the are aerobic oxidations in the presence of ferrocyanide ($Fe(CN)_6^{4-}$) to ferricyanide ($Fe(CN)_6^{3-}$).[10] Also, a metal free environmentally benign aerobic oxidation of alcohols **14** and benzylic carbon **16** using activated carbon/molecular oxygen was reported (Chart 2).[11,12]

Chart 2



The preparation of mesoporous carbon materials was reported using phthalocyanine or porphyrin as a precursor and silica as a hard template. It exhibits high catalytic activity toward the oxidative coupling of amines. For example, the amines **18** were smoothly transformed into the desired imines **19** in high yields (up to 99%), with molecular oxygen as oxidant under neat conditions (Scheme 1).[13]

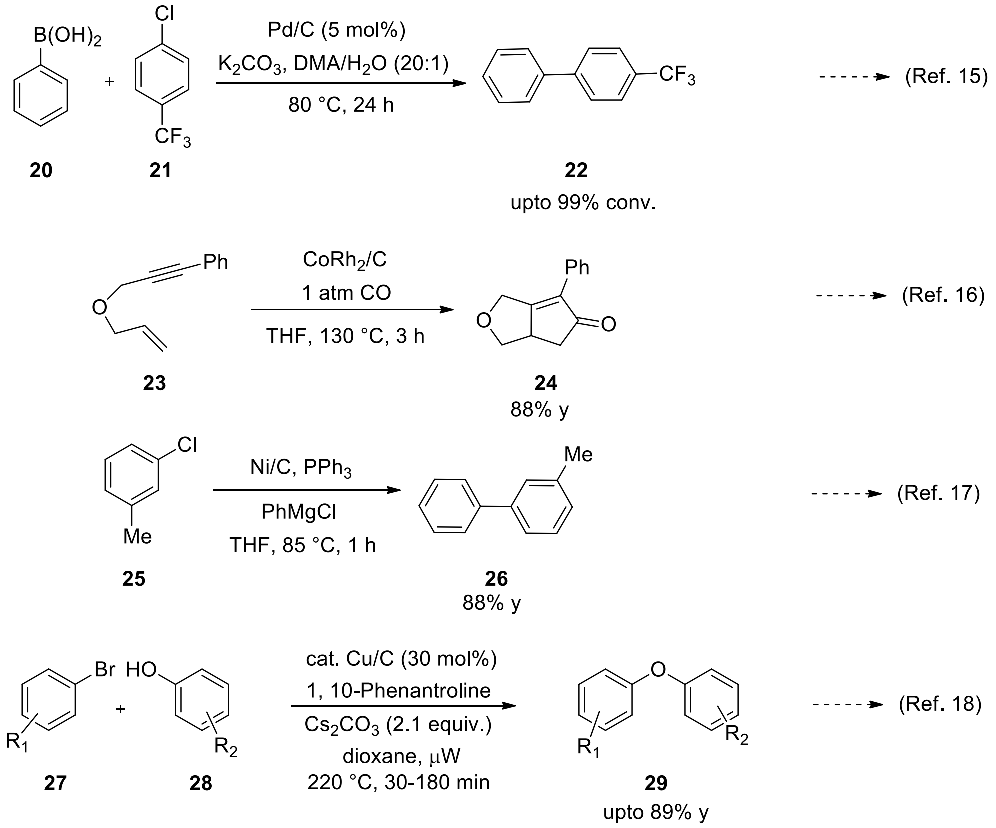
Scheme 1



2.1.1.2 Metal carbon material catalyzed organic transformations

Transition metal clusters (e.g., palladium) immobilized on charcoal is quite common in modern chemistry, especially for use as hydrogenation catalysts. These materials are also useful in a variety of cross-coupling reactions for constructing C-C and C-hetero atom bonds.[14] Some representative metal-carbon material catalyzed organic transformations are outlined in Chart 3.[15-18]

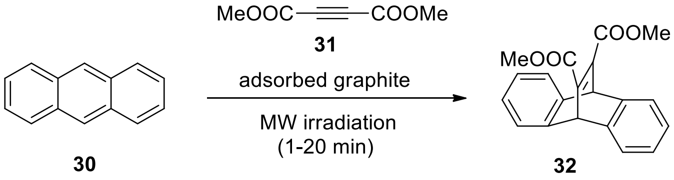
Chart 3



R_1 = 2-CF_3, 4-CHO, 4-$COCH_3$, 4-NO_2, 4-SCH_3
R_2 = 4-^{t}Bu, 2,3-diMe, 4-OMe

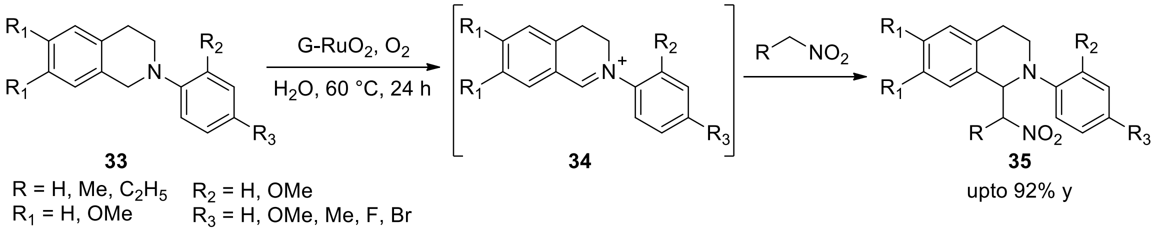
Graphite was used as a solid state thermal conductor due to its high thermal conductivity (19 W cm−1 K−1 at 300 K). After physisorption on graphite, anthracene **30** is susceptible to [4 + 2] cycloaddition reactions with electron-deficient dienophile **31** (e.g., dimethyl but-2-ynedioate) under microwave irradiation to give the cyclic adduct **32** (Scheme 2).[19]

Scheme 2



Recently, it was reported that the graphene-supported RuO_2 nanoparticles are useful for aerobic cross-dehydrogenative coupling reaction between tertiary amines **33** and nitroalkanes **35** in water (Scheme 3).[20]

Scheme 3



2.1.2. Carbon materials: Nature and Properties

In recent years, carbon materials have received considerable attention because of their wide variety of applications such as medical implants, electric and heat conductions (conductor and semi-conductor), energy storage devices (battery anode, super capacitor and gas storage), in environmental protection (activated surface), special materials (mechanical reinforcement, high temperature) and fuel cells.[21] Carbon materials are defined as a family of carbon, and obtained from carbonization of organic raw materials.[22] The carbonization process is conversion of an organic macromolecular system (e.g. coal, wood, nutshell etc.) to a "macro-atomic" network of carbon atoms *via* elimination of small molecules such as water, methanol, carbon dioxide and carbon monoxide by progressive heating.[23]

Recently, investigations were carried out in this laboratory on the production of pyrolysis gas from woody biomass for use in electricity generation sets. The commercially important charcoal is a byproduct in the carbonization process of the woody biomass. This charcoal can be further activated for high end applications by known industrial methods. Here, the development of organic synthetic methods to increase the value of the readily accessible activated charcoal is of our interest. Therefore, a brief review conducted on the nature and properties of activated charcoal for applications in organic transformations.

2.1.3 Characterization and properties of activated carbons

Activated carbon is basically porous and the function originates from the pores on the surface. Pore size, depth and volume are considered as important factors for activated carbon.[24] Substitutional groups on the edge and heteroatoms in the first array of hexagon plane should be also taken into account.[25] The representative structure of activated carbon with surface oxygen groups is shown in Figure 1.

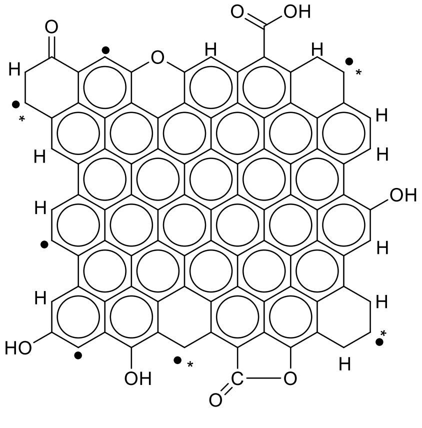
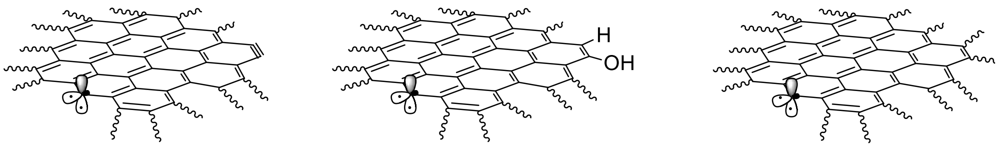


Figure 1: Surface oxygen functional groups of activated carbon fiber.

The characteristics of carbon materials and chemistry of their surface depend on the heteroatom presence, which is further dependent on the nature of the materials and methods used for their preparation.[26] The surface chemistry of the carbon materials are also depend on the nature and presence of graphene edge sites. Further, it was suggested that the heteroatom (like oxygen) free graphene edge sites are neither H terminated nor free radicals. Instead, the edge sites are carbene-like zigzag sites with triplet ground state **38** or aryne-like (arm chair sites) singlet ground state **36** (Figure 2).[27]



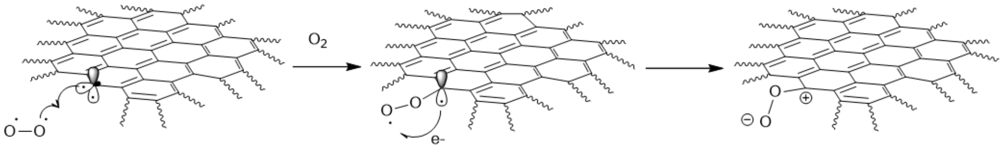
36 37 38

Figure 2. Surface characteristics of the carbon materials

The aryne-like sites are expected to give phenolic groups upon reaction with moisture resulting in phenolic sites like **37** or could undergo trimerization to give benzenoid aggregates like **38** under ambient atmospheric conditions.[25]

It has been reported that chemisorption of molecular oxygen by activated carbon fibre materials lead to the formation of negatively charged oxygen (C-O-O$^{\delta-}$) species **40**.[28-31] Accordingly, we envisaged that the formation of species **40** through electron transfer from the carbon radical site in **39** with molecular oxygen followed by formation of species **40** (Scheme 4).

Scheme 4



38 39 40

It is of our interest to design experiments for practical use of reactive species **40** in the oxygen doped activated charcoal in synthetic transformations (Figure 3).

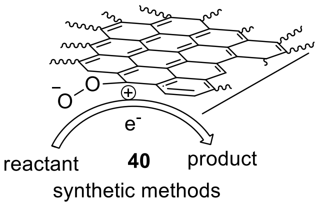
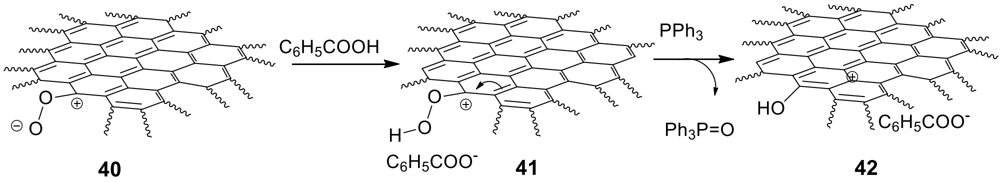


Figure 3

2.1.4 Previous work from our laboratory

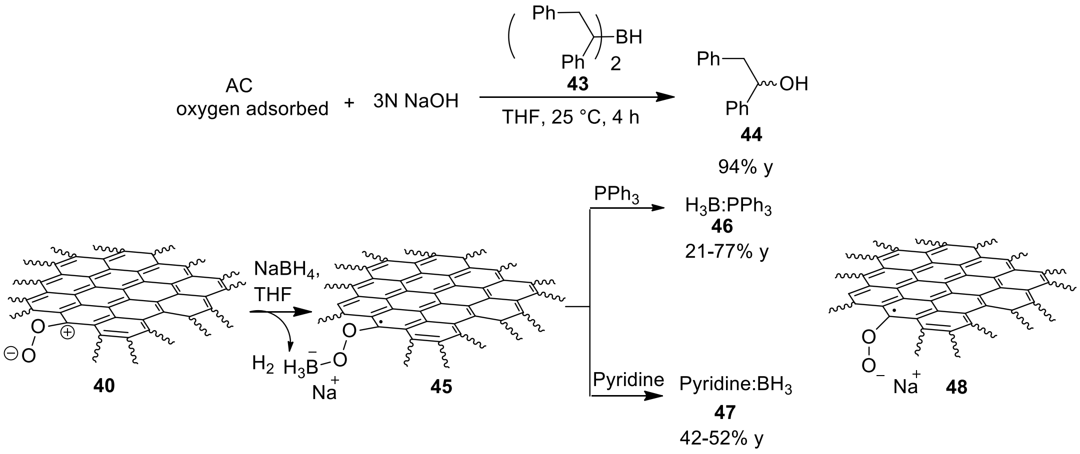
As discussed in previous sections, efforts were undertaken in this laboratory to design experiments for practical utilization of oxygen-adsorbed species like **40** in synthetic transformations. It was found that the carbon materials like activated carbon (AC) undergo chemisorption with O_2 to give species with electron deficiency in the carbon skeleton and negative charge at the oxygen end. Upon reaction with benzoic acid and PPh_3, $Ph_3P{=}O$ was obtained 54% yield (Scheme 5).[32]

Scheme 5



Also, organoboranes oxidation and preparation of Lewis base borane complexes like $Ph_3P{:}BH_3$ **46** and pyridine:BH_3 **47** using readily accessible oxygen adsorbed carbon materials (CM) like activated carbon (AC) and carbon black (CB) were reported from this laboratory (Scheme 6).[33]

Scheme 6



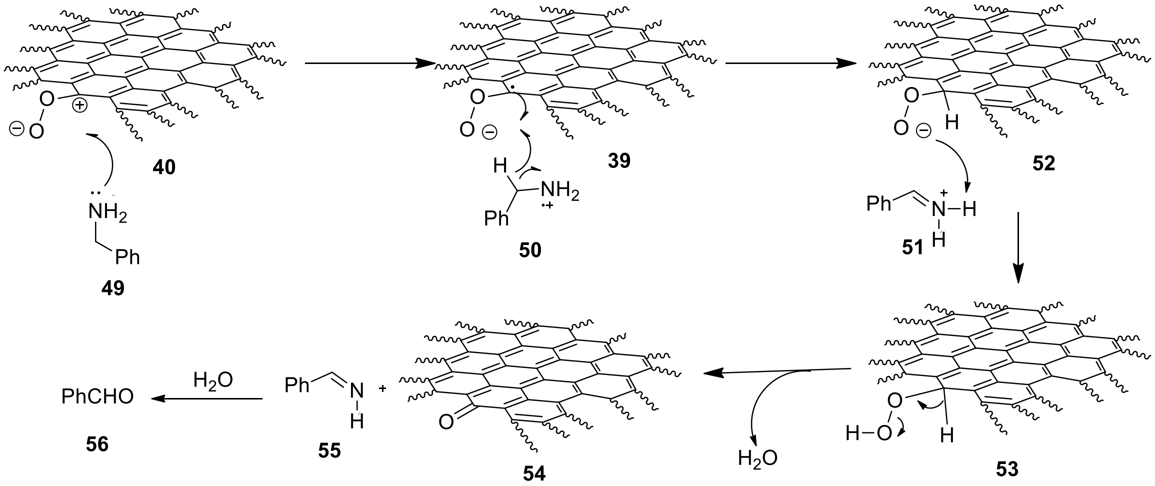
We have observed that oxygen doped carbon materials are useful for cross dehydrogenative coupling of N-aryltetrahydroisoquinoline with different carbon nucleophiles. The results are in the next section.

2.2 Results and Discussion

2.2.1 Dehydrogenative cross coupling (CDC) of N-aryltetrahydroisoquinoline and nitromethane using activated carbon

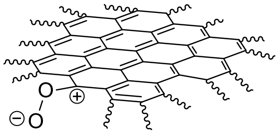
As outlined in the introductory section, carbon materials are useful in organic transformations. Recently, it was reported from this laboratory that the benzaldehyde **56** was obtained in 30% yield when the reaction was carried out with benzylamine **50** and molecular oxygen adsorbed carbon materials **40** (Scheme 7).[32]

Scheme 7



We have undertaken investigations on applications of molecular oxygen-adsorbed carbon materials for the development of new synthetic methods involving reaction with electron rich compounds.

Initially, we have performed several experiments to assess the extent of adsorption of molecular oxygen on carbon materials. One gram of activated charcoal adsorbed 1.06 mmol of molecular oxygen. The results indicated that activated carbon and carbon black samples adsorb molecular oxygen to a greater extent than graphite which was reported to undergo only physisorption.[11] The carbon skeleton of the oxygen-adsorbed intermediate **40** (Figure 4) is expected to behave like an electron acceptor, and hence expected to undergo reaction with electron donors like amines.

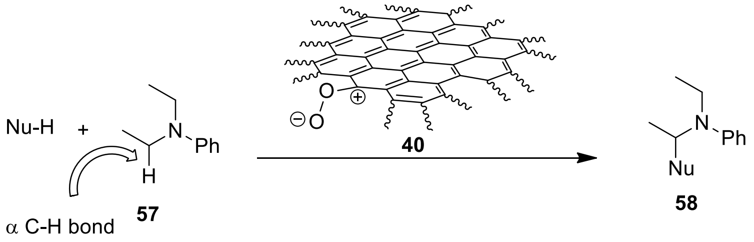


40

Figure 4: carbon skeleton of oxygen-adsorbed intermediate **40**

It was of interest to us, to design experiments for α C-H activation of N-aryl tertiary amines using oxygen adsorbed carbon material **40** (Scheme 8).

Scheme 8



Accordingly, we have selected N-aryl tertiary amines (**59-63**) and carbon materials **40** as reaction partners (Figure 5). Initially, there was no reaction when the reaction was carried out using amines **(59-62)** and carbon nucleophiles in the presence of activated charcoal in THF, DCM, DMSO, dioxane and toluene solvents.

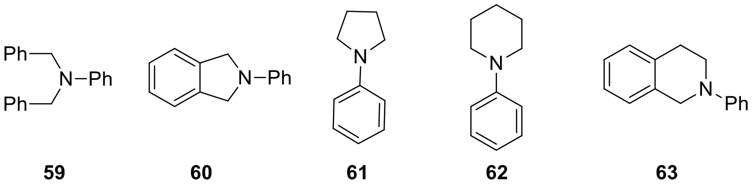
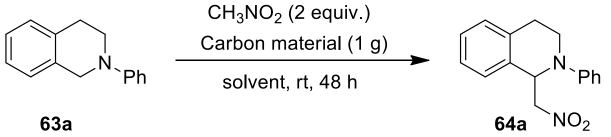


Figure 5

However, when the reaction was carried out with N-phenyltetrahydroisoquinoline **63a** and 2 equiv. of nitromethane and one gram of oxygen adsorbed activated charcoal, the product **64a** was formed in 58% yield in CH_3CN solvent (Table 1, entry 1). Encouraged by these results, the experimental parameters and solvents have been thoroughly screened to improve the yield. The solvent DCM, $CHCl_3$, CCl_4, THF, toluene, dioxoane, DMSO and DMF gave the coupled product **64a** in 35-89% yields (Table 1, entries 2-9).

Table 1: Reaction of N-phenyltetrahydroisoquinoline and nitromethane.[a-d]



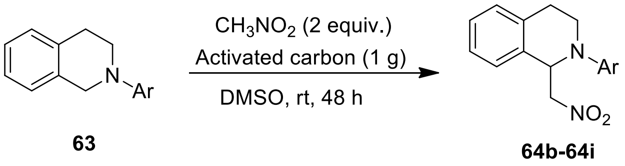
63a **64a**

Entry	Carbon materials (g)	Solvent (3 mL)	Yield (%)[c] **64a**
1	AC(1)	CH_3CN	58
2	AC(1)	DCM	35
3	AC(1)	$CHCl_3$	64
4	AC(1)	CCl_4	55
5	AC(1)	THF	43
6	AC(1)	1,4-Dioxane	41
7	AC(1)	toluene	32
8	AC(1)	DMSO	89
9	AC(1)	DMF	68
10	AC(0.1)	DMSO	43
11	AC(0.3)	DMSO	62
12	AC(0.5)	DMSO	78
13	CB(1)	DMSO	23
14	Graphite(1)	DMSO	15

[a]The carbon material was heated at 200 °C in inert atmosphere under high vaccum (0.001 Hg) for 2 h followed by dry air passed for 1 h. [b]The reactions were carried out by using amine **63a** (0.5 mmol), nitromethane (1 mmol), activated charcoal (1 g) and DMSO (3 mL) at room temperature. [c]Isolated yield. [d]The product **64a** were characterized by spectral data (IR, ^{1}H-NMR and^{13}C-NMR).

Among all solvents DMSO gave the cross coupled product **64a** in higher yield 89% (Table 1, entry 8). The less reactive aryl amines **59**, **60**, **61** and **62** did not undergo reaction under these conditions. Also, we have observed that the reaction of N-phenyltetrahydroisoquinoline **63a** with 2 equiv. of nitromethane using 0.1 g, 0.3 g and 0.5 g of activated charcoal in DMSO, the product **64a** was obtained in 43% to 78% yield (Table 1, entries 10-12).

Table 2: Reaction of different N-substituted THQ with nitroalkanes.[a-d]



Entry	Ar	Yields (%)[c] **64b-64i**
1	*p*-Me-C_6H_4 **(63b)**	86
2	*m*-Me-C_6H_4 **(63c)**	78
3	*p*-MeO-C_6H_4 **(63d)**	92
4	*m*-MeO-C_6H_4 **(63e)**	69
5	*o*-MeO-C_6H_4 **(63f)**	90
6	*p*-F-C_6H_4 **(63g)**	64
7	*p*-Cl-C_6H_4 **(63h)**	63
8	*p*-Br-C_6H_4 **(63i)**	58

[a]The carbon material was heated at 200 °C in inert atmosphere under high vaccum (0.001 Hg) for 2 h followed by dry air passed for 1 h. [b]The reactions were carried out by using amine **63** (0.5 mmol), activated charcoal (1 g), nitromethane (1 mmol) and solvent (3 mL) at room temperature. [c]Isolated yield. [d]The products **64** were characterized by spectral data (IR, ^{1}H-NMR and ^{13}C-NMR).

However, the yield of coupled product **64a** increased to 89% yield when 1 g of activated charcoal was used (Table 1, entry 4). Other carbon materials like carbon black and graphite gave the coupled product **64a** only in 23% and 15% yield, respectively (Table 1, entries 13 & 14).

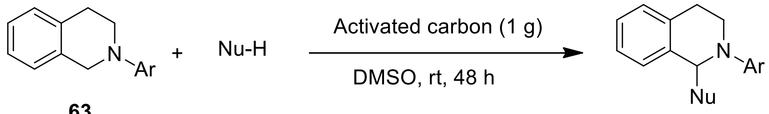
The generality of the reaction was then explored and the results are summarized in Table 2. Both electron donating and electron withdrawing groups on N-aryltetrahydroisoquinolines **63** are compatible under the optimized conditions. The N-aryltetrahydroisoquinoline **63** containing electron donating groups like CH_3 or OMe, reacted with nitromethane to give the corresponding products **64b-64f** in 69-92% yield (Table 2, entry 1-5). Also, electron withdrawing groups F, Cl, and Br substitutions at the *para*-position afforded the corresponding products **64g- 64i** in 58-64% yield (Table 2, entries 6-8).

2.2.2 Reaction of N-aryltetrahydroisoquinoline with different carbon nucleophiles

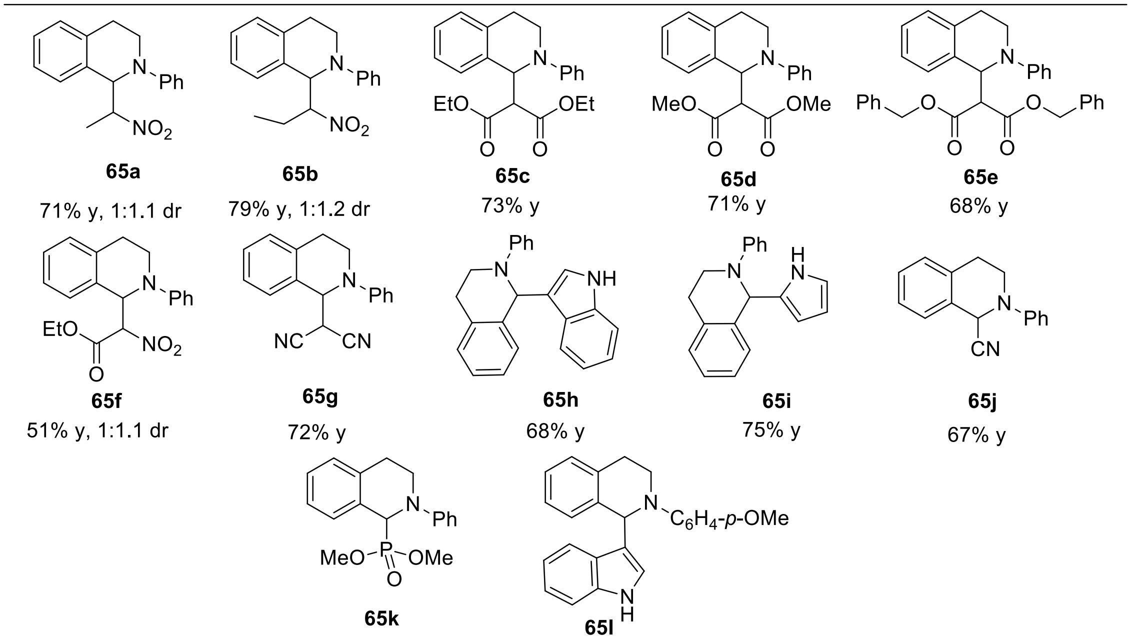
The substrate scope of the reaction was further investigated using different nuclophiles and the results are summarized in Table 3. Different nitroalkanes like nitroethane and nitropropane reacted with N-phenyltetrahydroisoquinoline **63a** to give the corresponding products **65a** and **65b** in 71% and 79% yield, respectively with no selectivity (Table 3). Other carbon nuclophiles such as dialkyl malonates were tolerated in this reaction and the corresponding coupled products **65c-65e** were obtained in 68-73% yield (Table 3). This protocol also was extended to other carbon nuclophiles like ethyl-2-nitroacetate, malononitrile, indoles and pyrrole the corresponding products 6**5f-65i** were isolated in 51-75% yield (Table 3). We have also observed that when N-phenyltetrahydroisoquinoline **63a** was reacted with trimethylsilyl cyanide, the oxidative cyanation product **65j** was isolated in

67% yield (Table 3). In addition to carbon-based nucleophiles, we also carried out reaction with heteroatom based nucleophile, such as dimethyl phosphite and isolated the α-amino phosphonate **65k** in 82% yield (Table 3).

Table 3 Reaction of different Nucleophiles with N-phenyl tetrahydroisoquinoline.[a-d]



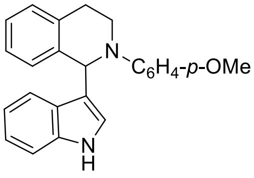
63 **65**



65a 71% y, 1:1.1 dr
65b 79% y, 1:1.2 dr
65c 73% y
65d 71% y
65e 68% y
65f 51% y, 1:1.1 dr
65g 72% y
65h 68% y
65i 75% y
65j 67% y
65k 82% y
65l 79% y

[a]The carbon material was heated at 200 °C in inert atmosphere under high vaccum (0.001 Hg) for 2 h followed by dry air passed for 1 h. [b]The reactions were carried out by using amine **63** (0.5 mmol), nucleophile (1 mmol) and DMSO (3 mL) at room temperature for 48 h. [c]Isolated yield. [d]The product **65** were characterized by spectral data (IR, ^{1}H-NMR and ^{13}C-NMR).

We have also examined the *p*-OMe substituted N-aryltetrahydroisoquinoline and obtained the corresponding product **65l** in 79% yield (Table 3). The structure of the product was confirmed by single crystal X-ray analysis of the compound **65l** (Figure 6).



65l

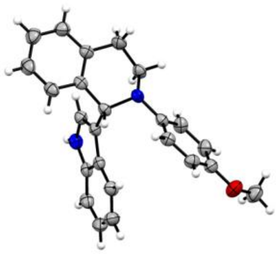


Figure 6: X-ray crystal structure of **65l**

We have also examined the reusability of carbon materials after the reaction. The carbon material remained after reaction was washed with water followed by vaccum drying at 200 ºC for 2 h. This upon reaction with N-phenyl tetrahydroisoquinoline and nitromethane gave the corresponding product **64a** in 82% yield.

2.2.3 Plausible mechanism for dehydrogenative cross coupling reaction

Presumably, the reaction may proceed through the formation of amine radical cation intermediates followed by iminium ion generation as shown in Scheme 9. The iminium ion **67** could react with the nucleophile to form the coupled product **64**.

Scheme 9: Plausible mechanism

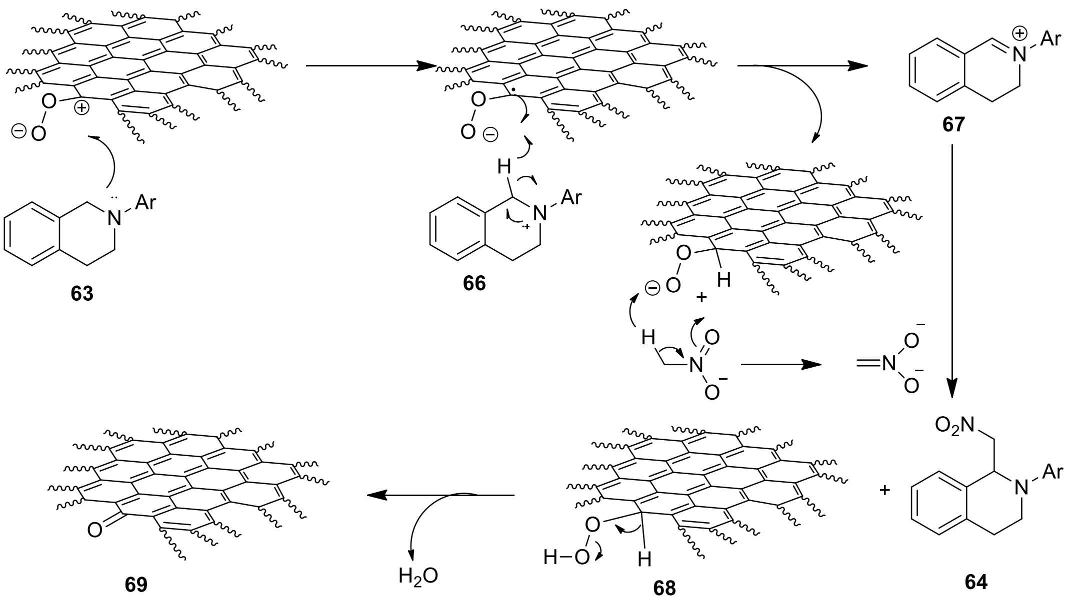


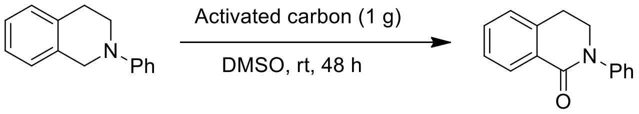
Table 4. Crystal data and structure refinement for compound **65l**.

Identification code	**65l**	
Empirical formula	$C_{24}H_{22}N_2O$	
Formula weight	354.43	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P b c a	
Unit cell dimensions	a = 14.100(3) Å	a= 90°.
	b = 11.200(2) Å	b= 90°.
	c = 23.390(5) Å	g = 90°.
Volume	3693.7(13) $Å^3$	
Z	8	
Density (calculated)	1.275 Mg/m^3	
Absorption coefficient	0.078 mm^{-1}	
F(000)	1504	
Crystal size	0.12 x 0.10 x 0.08 mm^3	
Theta range for data collection	2.263 to 26.128°.	
Index ranges	-17<=h<=17, -13<=k<=13, -28<=l<=28	
Reflections collected	36505	
Independent reflections	3671 [R(int) = 0.0331]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3671 / 0 / 249	
Goodness-of-fit on F^2	1.058	
Final R indices [I>2sigma(I)]	R_1 = 0.0400, wR_2 = 0.0987	
R indices (all data)	R_1 = 0.0473, wR_2 = 0.1043	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.195/-0.236 e.$Å^{-3}$	

2.2.4 Reaction of N-aryltetrahydroisoquinoline without nucleophile (formation of amide)

We have observed that when the reaction of N-phenyltetrahydroisoquinoline **63a** and activated charcoal (1 g) was carried out without nucleophile, the corresponding amide derivative **70a** was obtained in 72% yield (Scheme 10).

Scheme 10

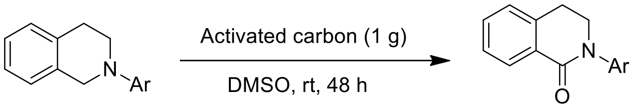


63a

70a
72% y

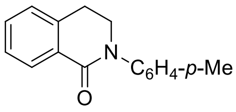
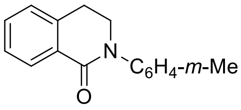
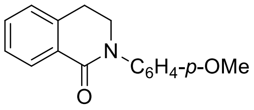
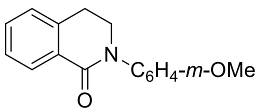
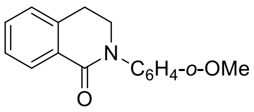
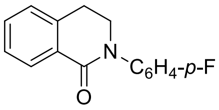
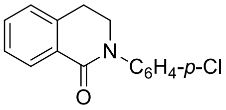
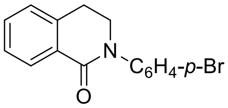
We further tested the generality of this reaction by using different N-aryl substituted tetrahydroisoquinoline **63**. The results are summarized in Table 5**.** Several amide derivatives **70b-70i** containing electron withdrawing as well as electron donating groups were synthesized in 65 to 81% yields (Table 5).

Table 5 Reaction of N-aryl tetrahydroisoquinoline with oxygen adsorbed carbon materials.[a-c]



63

70

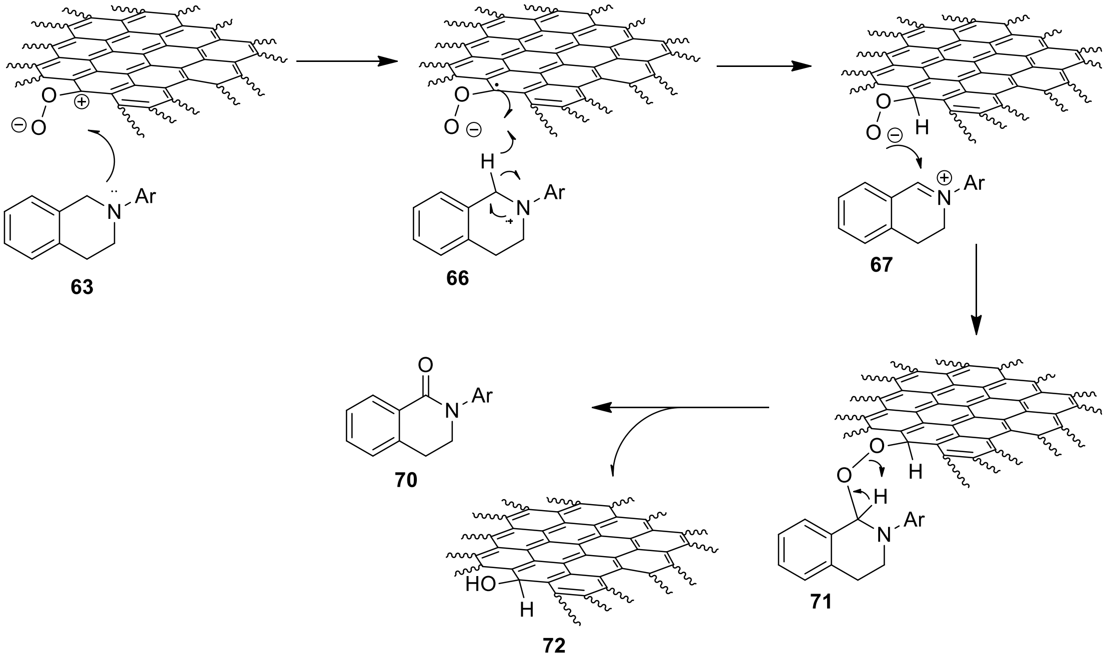
 **70b** 72% y	 **70c** 75% y	 **70d** 69% y	 **70e** 81% y
 **70f** 73% y	 **70g** 68% y	 **70h** 65% y	 **70i** 67% y

[a]The carbon material was heated at 200 °C in inert atmosphere under high vaccum (0.001 Hg) for 2 h followed by dry air passed for 1 h. [b]The reactions were carried out by using amine **63** (0.5 mmol), activated charcoal (1 g) in DMSO (3 mL) at room temperature for 48 h. [c]Isolated yield. [d]The product **70** were characterized by spectral data (IR, ^{1}H-NMR, ^{13}C-NMR and HRMS).

2.2.5 Plausible mechanism for the formation of amide using activated carbon

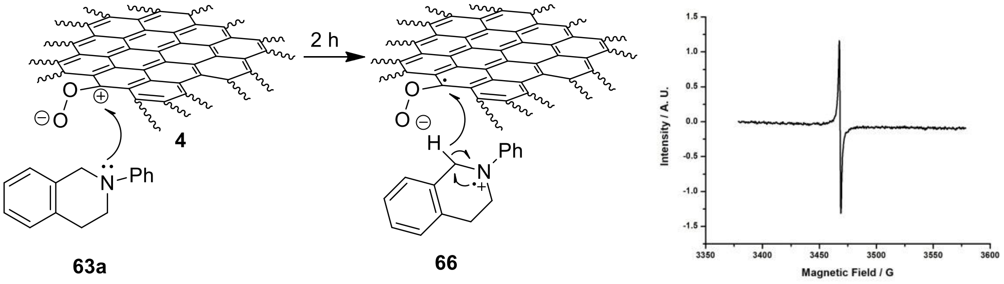
The formation of amide derivatives in this transformation can be explained by considering the mechanism outlined in Scheme 11. Molecular oxygen doped carbon materials could react with N-aryltetrahydroisoquinoline **63** to give the intermediate **66.** Subsequently, proton-coupled electron transfer reaction could take place to generate the iminium ion **67**. Nucleophilic addition by the peroxy anion followed by decomposition of the peroxide would lead to the amide derivative **70**.

Scheme 11: Plausible Mechanism



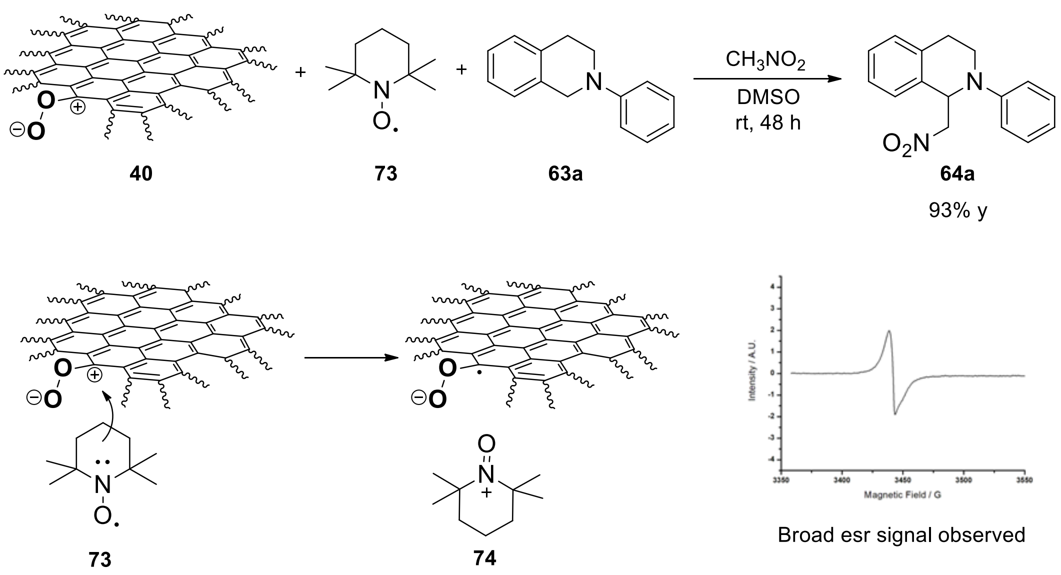
Presence of paramagnetic species (Scheme 9 & 11) upon addition of the amine **63a** was also confirmed by EPR spectral analysis (Scheme 12).

Scheme 12



To examine the effect of the radical scavenger like TEMPO **73**, we performed the reaction of N-phenyltetrahydroisoquinoline **63a** and nitromethane with oxygen-doped carbon materials in the presence of TEMPO **73**. In this case, the coupled product **64a** was isolated in 93% yield. However, it is to be noted that the TEMPO$^+$ **74** intermediate was reported to react with the amine **63a** to give the product **64a**.[34] Accordingly, the results indicate the formation of the TEMPO$^+$ **74** intermediate in the reaction of oxygen-adsorbed activated carbon **40** with the radical scavenger TEMPO **73** (Scheme 13).

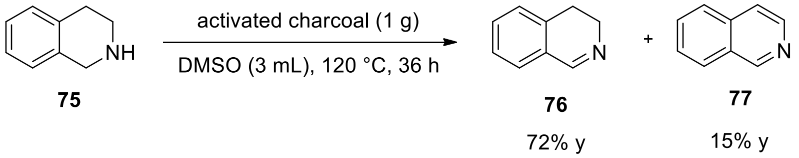
Scheme 13



2.2.6 Synthesis of 3,4-dihydroisoquinoline 76 and isoquinoline 77 using activated carbon

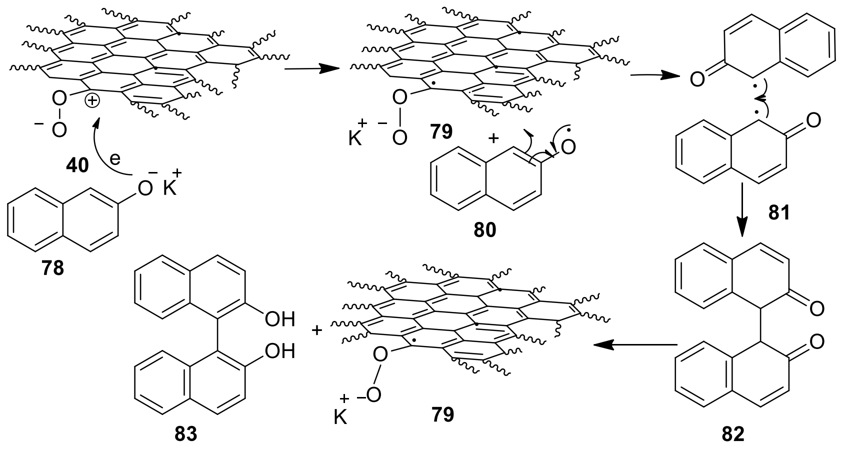
We have also observed that oxidative aromatization of 1,2,3,4-tetrahydroisoquinoline **75** takes place to give the 3,4-dihydroisoquinoline **76** in 72% yield along with isoquinoline **77** in 15% yield using oxygen adsorbed activated charcoal (Scheme 14).

Scheme 14



Moreover, it was found in this laboratory that 2-naphthol gives bi-2-naphthol **83** (BINOL) in 95% yield in the oxidative coupling reaction using molecular oxygen adsorbed activated charcoal and *t*-BuOK (Scheme 15).

Scheme 15



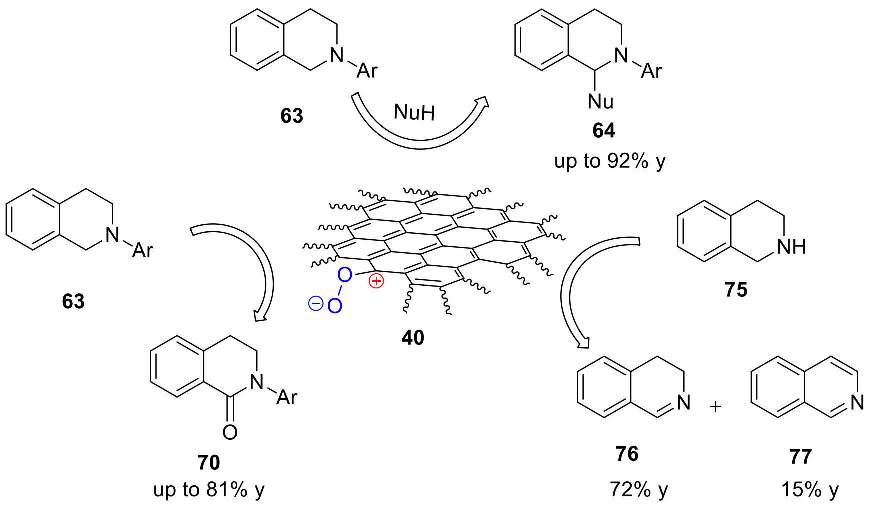
Therefore, further systematic studies on the reaction of oxygen adsorbed activated carbon and other readily accessible carbon materials like carbon black (CB) and graphite (Gr) with electron donors are expected to give fruitful results.

Next, we have explored the reaction of tertiary N-aryl cyclic amines with *p*-chloranil. We have also constructed organic electrochemical cells using tertiary amines and *p*-chloranil. The results are discussed in the Chapter 3.

2.3 Conclusions

Metal free dehydrogenative cross coupling reactions using environmental and eco-friendly molecular oxygen adsorbed carbon materials were developed with N-aryl-1,2,3,4-tetrahydroisoquinolines to provide the corresponding cross coupling products in moderate to excellent yields. Also, we have observed the formation of amide up to 81% yields without using nucleophiles in this reaction condition. A similar method was developed for the synthesized 3,4-dihydroisoquinoline and isoquinoline using oxygen doped activated carbon from 1,2,3,4-tetrahydroisoquinoline. Further, we have confirmed the reusability of carbon materials; the carbon materials after the reaction were reused without loss of its catalytic activity. Further systematic studies for the development of new synthetic transformations using carbon materials will be undergoing in this laboratory (Scheme 16).

Scheme 16

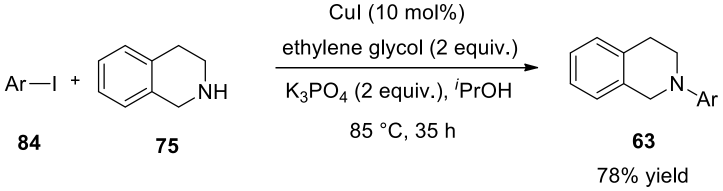


2.4. Experimental Section

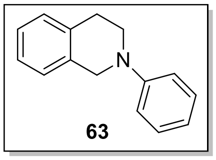
2.4.1 General informations

Several information's given in the section **1.4** are also applicable for the experiments outlined in this section. Analytical grade DMSO, isopropanol, ethylene glycol, aryl iodides and nitromethane were purchased from E-Merk and CuI, 1,2,3,4-tetrahydroisoquinoline and Activated charcoal were purchased from Aigma Aldrich.

2.4.2 General procedure for the preparation of *N*-aryl-1,2,3,4-tetrahydroisoquinolines 63.



To a dried round-bottom flask, equipped with an argon balloon, anhydrous K_3PO_4 (12.65 g, 58 mmol), ^{i}PrOH (30 mL), ethylene glycol (3.72 g, 60 mmol), 1,2,3,4-tetrahydroisoquinoline **67** (6.0 g, 45 mmol), and aryliodide **76** (6.15 g, 30 mmol) were added. Then, CuI (0.57 g, 3 mmol) was added and the reaction mixture was stirred over 35 h at 85 °C. After cooling to room temperature, Et_2O (60 mL) and water (60 mL) was added and extracted with Et_2O (60 mL x 2). Then, the combined organic layer was washed with brine (60 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography on SiO_2 using hexane/EtOAc = 15/1 as an eluent to provide **55** as a white solid (9.46 g, 78%).



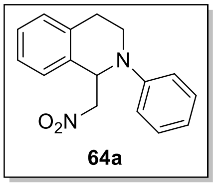
63

Yield	:	(4.893 g) (78%); white solid.
IR (KBr)	:	(cm^{-1}) 3370, 3059, 3024, 2921, 2815, 1662, 1598, 1500, 1459, 1387, 1337, 1293, 1221, 1153, 1112, 1033, 991, 932, 750, 691.
^{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 (m, 2H), 3.04-3.01(m, 2H).
^{13}C NMR	:	(100 MHz, $CDCl_3$, 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.

2.4.3 General procedure for the Reaction of N-phenyltetrahydroisoquinoline dehydrogenative cross coupling using oxygen adsorbed carbon materials and nucleophiles

In a 25 mL RB flask, activated charcoal (1 g) heated at 200 °C under high vacuum (0.001 mm of Hg) for 2 h. After the RB flask was brought to room temperature under nitrogen atmosphere, the contents were saturated with dry air for 1 h. To this N-phenyl tetrahydroisoquinoline (0.5 mmol) and nucleophile (1 mmol) in DMSO were added. The reaction mixture was further stirred for 48 h at room temperature. After that EtOAc (15 mL) was added and stirred for further half an hours. The reaction mixture was filtered, and wash several times with EtOAc and H_2O. The organic layer extracts with EtOAc, washed with brine and then dried over anhyd.Na_2SO_4. Evaporate solvent under vacuum and the crude mixture was chromatographed on silicagel using hexane:ethylacetate (95:5) as an eluent to isolate the pure compound **64**. Without nucleophile 2-phenyl-3,4-dihydroisoquinolin-1(2*H*)-one **70** formed.

1-(Nitromethyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (64a)


64a

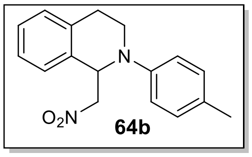
Yield : 0.12 g (89%); yellow oil.

IR (Neat) : (cm^{-1}) 3063, 3030, 2964, 2915, 1605, 1545, 1496, 1380, 1003, 899, 756.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.29-7.18 (m, 5H), 7.14-7.13 (d, *J* = 6.8 Hz 1H), 6.98 (d, *J* = 8.0 Hz, 2H), 6.85 (t, *J* = 7.2 Hz, 1H), 5.55 (t, *J* = 7.0 Hz, 1H), 4.95-4.85 (m, 1H), 4.59-4.54 (m, 1H), 3.79-3.59 (m, 2H), 3.21-3.05 (m, 1H), 2.87-2.78 (m, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 148.5, 135.3, 133.0, 130.0, 129.2, 128.2, 127.0, 126.7, 119.5, 115.2, 78.8, 58.2, 42.1, 26.5.

1-(Nitromethyl)-2-(p-tolyl)-1,2,3,4-tetrahydroisoquinoline (64b)


64b

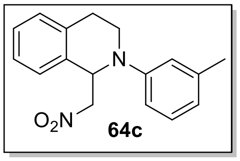
Yield : 0.12 g (86%); yellow oil.

IR (Neat) : (cm^{-1}) 3024, 2915, 2849, 1616, 1550, 1517, 1380, 1210, 1111, 1007, 805, 755.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.27-7.14 (m, 4H), 7.09 (d, *J* = 8.7 Hz, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 5.51 (t, *J* = 7.1 Hz, 1H), 4.89-4.84 (m, 1H), 4.59-4.55 (m, 1H), 3.69-3.56 (m, 2H), 3.11-3.04 (m, 1H), 2.79-2.73 (m, 1H), 2.28 (s, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 146.4, 135.4, 132.9, 129.9, 129.3, 129.1, 128.0, 126.9, 126.7, 115.9, 78.9, 58.4, 42.3, 26.3, 20.4.

1-(Nitromethyl)-2-(*m*-tolyl)-1,2,3,4-tetrahydroisoquinoline (64c)



64c

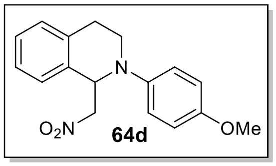
Yield : 0.11 g (78%); yellow oil.

IR (Neat) : (cm^{-1}) 3079, 3047, 2959, 2915, 2849, 1666, 1605, 1529, 1496, 1392, 1260, 1019, 805, 762, 685.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.27-7.14 (m, 5H), 6.80 (d, J = 7.9 Hz, 2H), 6.69 (d, J = 7.1 Hz, 1H), 5.56 (t, J = 7.1 Hz, 1H), 4.90-4.86 (m, 1H), 4.59-4.55 (m, 1H), 3.70-3.58 (m, 2H), 3.14-3.06 (m, 1H), 2.83-2.77 (m, 1H), 2.34 (s, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 148.5, 139.3, 135.3, 133.0, 129.4, 129.2, 128.1, 127.0, 126.7, 120.4, 115.9, 112.3, 78.8, 58.2, 42.2, 26.6, 21.9.

2-(4-Methoxyphenyl)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline (64d)



64d

Yield : 0.14 g (92%); yellow oil.

IR (Neat) : (cm^{-1}) 2959, 2926, 2833, 1556, 1507, 1375, 1244, 1184, 1036, 833, 751.

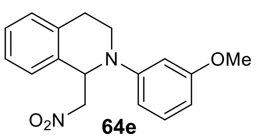
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.27-7.14 (m, 4H), 6.94 (d, *J* = 8.9 Hz, 2H), 6.83 (d, *J* = 9.2 Hz, 2H), 5.43-5.39 (m, 1H), 4.86-4.81 (m, 1H), 4.59-4.55 (m, 1H), 3.76 (s, 3H), 3.59-3.56 (m, 2H), 3.07-2.98 (m, 1H), 2.74-2.68 (m, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 154.0, 143.1, 135.5, 132.9, 129.5, 127.9, 126.9, 126.6, 118.9, 114.7, 78.9, 58.9, 55.6, 43.1, 25.8.

2-(3-Methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (64e)

Yield : 0.10 g (69%); yellow oil.

IR (Neat) : (cm^{-1}) 3030, 2997, 2915, 2833, 1600, 1551, 1496, 1386, 1243, 1211, 1162, 1063, 762.

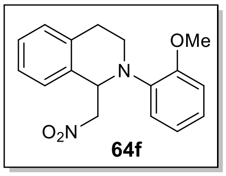


64e

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.26-7.13 (m, 5H), 6.62 (d, *J* = 8.0 Hz, 1H), 6.56 (s, 1H), 6.44 (d, *J* = 7.7 Hz, 1H), 5.56 (t, *J* = 6.9 Hz, 1H), 4.90-4.86 (m, 1H), 4.59-4.54 (m, 1H), 3.82 (s, 3H), 3.69-3.58 (m, 2H), 3.15-3.07 (m, 1H), 2.85-2.78 (m, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 160.9, 149.8, 135.3, 132.9, 130.3, 129.2, 128.2, 127.0, 126.7, 107.6, 104.2, 101.5, 78.9, 58.3, 55.2, 42.1, 26.6.

2-(2-Methoxyphenyl)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline (64f)



64f

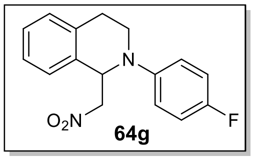
Yield : 0.13 g (90%); yellow oil.

IR (Neat) : (cm^{-1}) 3058, 3019, 2921, 2838, 1595, 1551, 1496, 1452, 1381, 1244, 1118, 1025, 751.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.28-7.25 (m, 2H), 7.20-7.18 (m, 2H), 7.08-7.04 (m, 1H), 6.94-6.85 (m, 3H), 5.55-5.52 (m, 1H), 4.87-4.82 (m, 1H), 4.58-4.54 (m, 1H), 3.85 (s, 3H), 3.66-3.61 (m, 1H), 3.55-3.48 (m, 1H), 3.06-2.97 (m, 1H), 2.76-2.71 (m, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 153.2, 139.0, 135.4, 133.7, 129.6, 127.6, 126.9, 126.5, 124.1, 122.0, 121.1, 112.6, 79.2, 58.3, 55.8, 43.1, 26.9.

2-(4-Fluorophenyl)-1,2,3,4-tetrahydroisoquinoline (64g)



64g

Yield : 0.09 g (64%); yellow oil.

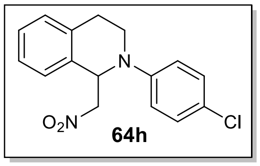
IR (Neat) : (cm^{-1}) 3058, 3025, 2904, 2849, 1551, 1507, 1375, 1233, 1162, 1014, 833, 762.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.24-7.12 (m, 4H), 6.95-6.87 (m, 4H), 5.43-5.39 (m, 1H), 4.84-4.79 (m, 1H), 4.57-4.53 (m, 1H), 3.59-3.56 (m, 2H), 3.05-2.97 (m, 1H), 2.74-2.68 (m, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 158.4, 155.9, 145.4, 145.3, 135.3, 132.6, 129.5, 128.1, 126.9, 126.8, 117.9, 117.9, 115.9, 115.8, 78.9, 58.7, 42.8, 25.8.

2-(4-Chlorophenyl)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline (64h)

Yield : 0.10 g (63%); yellow oil.



64h

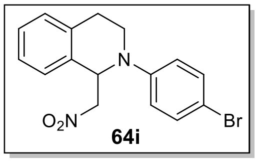
IR (Neat) : (cm^{-1}) 3068, 3041, 2909, 2843, 1594, 1550, 1495, 1380, 1331, 1216, 1127, 1007, 810, 744.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.27-7.14 (m, 6H), 6.90 (d, *J* = 9.3 Hz, 2H), 5.51-5.48 (m, 1H), 4.88-4.83 (m, 1H), 4.60-4.55 (m, 1H), 3.67-3.57 (m, 2H), 3.11-3.03 (m, 1H), 2.82-2.76 (m, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 147.1, 135.1, 132.5, 129.3, 128.3, 126.9, 126.8, 124.5, 116.5, 78.7, 58.2, 42.3, 26.2.

2-(4-Bromophenyl)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline (64i)

Yield : 0.10 g (58%); orange oil.



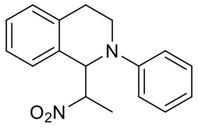
64i

IR (Neat) : (cm^{-1}) 3068, 3029, 2920, 2854, 1583, 1550, 1489, 1380, 1331, 1216, 1117, 1002, 805, 755.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.37-7.33 (m, 2H), 7.29-7.21 (m, 3H), 7.16-7.13 (m, 1H), 6.88-6.83 (m, 2H), 5.53-5.47 (m, 1H), 4.88-4.81 (m, 1H), 4.61-4.54 (m, 1H), 3.67-3.57 (m, 2H), 3.13-3.05 (m, 1H), 2.84-2.76 (m, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 147.5, 135.1, 132.5, 132.3, 129.3, 128.3, 126.9, 116.8, 111.6, 78.6, 58.1, 42.1, 26.2.

1-(1-Nitroethyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (65a)



65a

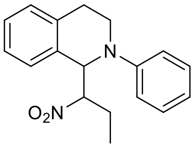
Yield : 0.10 g (71%); yellow oil.

IR (Neat) : (cm^{-1}) 2909, 2844, 1595, 1545, 1512, 1392, 1353, 1216, 1003, 899, 751, 690.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.29-7.10 (m, 6H), 7.01-6.99 (m, 2H), 6.84-6.79 (m, 1H), 5.28-5.22 (m, 1H), 5.05-4.87 (m, 1H), 3.89-3.54 (m, 2H), 3.10-3.04 (m, 1H), 2.95-2.86 (m, 1H), 1.73-1.69 (m, 1H), 1.58-1.53 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 149.2, 148.9, 137.5, 135.6, 134.6, 133.8, 132.0, 130.3, 129.4, 129.3, 129.1, 128.7, 128.4, 128.2, 127.5, 127.3, 126.6, 126.2, 119.3, 118.8, 115.4, 114.5, 88.9, 85.5, 62.8, 61.2, 43.6, 42.7, 26.7, 26.4, 17.4, 16.4.

1-(1-Nitropropyl)-2-(*o*-tolyl)-1,2,3,4-tetrahydroisoquinoline (65b)



65b

Yield : 0.12 g (79%); yellow oil.

IR (Neat) : (cm^{-1}) 3068, 3019, 2969, 2926, 1600, 1551, 1507, 1375, 1315, 1266, 1222, 937, 751, 696.

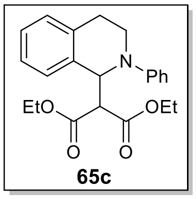
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.34-7.19 (m, 6H), 7.07-6.99 (m, 2H), 6.89-6.83 (m, 1H), 5.32-5.19 (m, 1H), 4.96-4.72 (m, 1H), 3.74-3.45 (m, 2H), 3.17-3.08 (m, 1H), 2.99-2.88 (m, 1H), 2.31-2.13 (m, 1H), 1.94-1.84 (m, 1H), 1.02-0.98 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 149.1, 149.0, 135.6, 134.8, 133.9, 132.6, 129.5, 129.4, 129.2, 128.8, 128.7, 128.3, 127.3, 126.7, 125.9, 119.4, 118.6, 115.9, 114.2, 96.2, 93.1, 62.2, 60.8, 43.6, 42.3, 26.9, 25.8, 25.1, 24.7, 10.7.

Diethyl 2-(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)malonate (65c)

Yield : 0.13 g (73%); colourless oil.

IR (Neat) : (cm^{-1}) 3058, 3025, 2975, 2921, 2849, 1737, 1605, 1507, 1397, 1369, 1151, 1036, 942, 751.

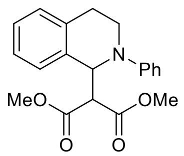


65c

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.27-7.09 (m, 6H), 6.98 (d, *J* = 7.9 Hz, 2H), 6.76 (t, *J* = 7.3 Hz, 1H), 5.73 (d, *J* = 9.2 Hz, 1H), 4.15-3.89 (m, 5H), 3.75-3.61 (m, 2H), 3.12-3.04 (m, 1H), 2.92-2.85 (m, 1H), 1.17 (t, *J* = 7.2 Hz, 3H), 1.09 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 167.9, 167.2, 148.9, 135.9, 134.8, 129.1, 128.9, 127.5, 127.2, 126.0, 118.5, 115.1, 61.6, 59.6, 57.9, 42.3, 29.7, 26.1, 13.9, 13.8.

Dimethyl 2-(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)malonate (65d)



65d

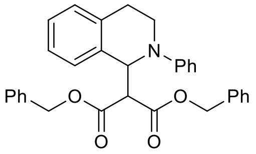
Yield : 0.12 g (71%); colourless oil.

IR (Neat) : (cm^{-1}) 3030, 2953, 2915, 2844, 1737, 1595, 1512, 1430, 1395, 1271, 1150, 1019, 948, 756, 701.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.24-7.12 (m, 6H), 7.00-6.98 (m, 2H), 6.79-6.75 (m, 1H), 5.72 (d, *J* = 9.4 Hz, 1H), 3.98-3.95 (m, 1H), 3.74-3.69 (m, 1H), 3.67 (s, 3H), 3.64-3.61 (m, 1H), 3.56 (s, 3H), 3.12-3.04 (m, 1H), 2.92-2.85 (m, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 168.3, 167.4, 148.8, 135.7, 134.8, 129.1, 128.9, 127.6, 127.1, 126.1, 118.6, 115.2, 59.1, 58.2, 52.6, 42.2, 26.1.

2-(2-Phenyl-1,2,3,4-tetrahydro-isoquinolin-1-yl)-malonic acid dibenzyl ester (65e):



65e

Yield : 0.17 g (68%); white solid.

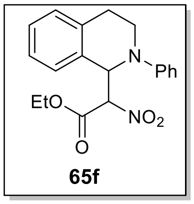
mp : 114-116 °C.

IR (KBr) : (cm^{-1}) 3074, 3036, 2975, 2932, 1737, 1595, 1512, 1397, 1238, 1173, 1145, 1003, 751, 696.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.35-7.25 (m, 8H), 7.21-7.11 (m, 8H), 6.94 (d, *J* = 8.6 Hz, 2H), 6.77 (t, *J* = 7.2 Hz, 1H), 5.75 (d, *J* = 9.1 Hz, 1H), 5.19 (s, 1H), 5.09-5.05 (m, 2H), 4.88 (d, *J* = 12.1 Hz, 1H), 4.04 (d, *J* = 9.2 Hz, 1H), 3.66-3.53 (m, 2H), 3.07-2.99 (m, 1H), 2.84-2.78 (m, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 167.7, 166.9, 148.8, 135.6, 135.2, 135.1, 134.8, 129.1, 128.9, 128.6, 128.5, 128.4, 128.3, 128.2, 127.6, 127.2, 126.1, 118.7, 115.4, 67.4, 59.4, 58.2, 42.3, 26.0.

1-(1-Nitropropyl)-2-(*o*-tolyl)-1,2,3,4-tetrahydroisoquinoline (65f)



65f

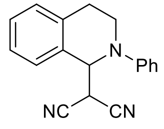
Yield : 0.09 g (51%); colourless oil.

IR (Neat) : (cm^{-1}) 3058, 3025, 2981, 2915, 1748, 1605, 1562, 1501, 1315, 1260, 1216, 1019, 942, 756, 690.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.18-7.04 (m, 6H), 6.88 (d, *J* = 6.9 Hz, 2H), 6.76-6.71 (m, 1H), 5.86-5.79 (m, 1H), 5.45-5.29 (m, 1H), 4.08-3.91 (m, 2H), 3.61-3.41 (m, 2H), 3.01-2.71 (m, 2H), 1.24-0.97 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 163.2, 162.8, 148.6, 148.1, 135.6, 134.9, 133.3, 131.5, 129.4, 128.9, 128.7, 128.5, 127.6, 127.0, 126.9, 126.3, 120.2, 119.3, 116.4, 114.7, 92.5, 91.6, 63.1, 59.8, 58.9, 43.5, 42.6, 26.7, 25.9, 13.7.

2-(2-Phenyl-1,2,3,4-tetrahydro-isoquinolin-1-yl)-malononitrile (65g)



65g

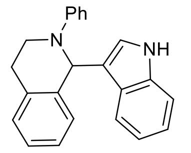
Yield : 0.10 g (72%); light brown liquid.

IR (Neat) : (cm^{-1}) 3036, 2953, 2921, 2855, 2230, 1600, 1501, 1397, 1266, 1233, 1151, 1030, 756, 696.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.49-7.48 (m, 1H), 7.39-7.27 (m, 6H), 7.03-7.00 (m, 2H), 5.38 (d, J = 4.5 Hz, 1H), 4.21 (d, J = 4.5 Hz, 1H), 3.86-3.79 (m, 1H), 3.56-3.50 (m, 1H), 3.22-3.15 (m, 1H), 3.10-3.00 (m, 1H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 147.7, 135.6, 130.7, 129.7, 129.3, 129.3, 127.4, 127.0, 121.2, 116.5, 61.6, 43.5, 29.6, 27.7.

1-(1*H*-Indol-3-yl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (65h)



65h

Yield : 0.11 g (68%); white solid.

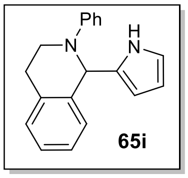
mp : 166-168 ^{o}C.

IR (KBr) : (cm^{-1}) 3446, 3063, 3029, 2915, 2827, 1599, 1501, 1380, 1221, 1084, 1024, 931, 755, 728.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.85 (s, 1H), 7.59 (d, J = 8.3 Hz, 1H), 7.34-7.27 (m, 4H), 7.24-7.18 (m, 4H), 7.09-7.06 (m, 3H), 6.83 (t, J = 7.2 Hz, 1H), 6.62 (s, 1H), 6.22 (s, 1H), 3.68-3.64 (m, 2H), 3.15-3.07 (m, 1H), 2.88-2.81 (m, 1H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 149.8, 137.5, 136.6, 135.6, 129.3, 128.9, 128.1, 126.7, 126.5, 125.8, 124.2, 122.1, 120.1, 119.7, 119.3, 118.2, 115.9, 111.1, 56.7, 42.3, 26.7.

2-Phenyl-1-(1*H*-pyrrol-2-yl)-1,2,3,4-tetrahydroisoquinoline (65i)



65i

Yield : 0.10 g (75%); pale yellow solid.

mp : 175-177 °C.

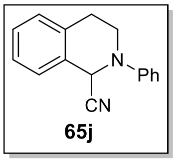
IR (KBr) : (cm^{-1}) 3408, 3058, 2915, 2838, 1704, 1589, 1501, 1452, 1348, 1222, 932, 740.

^{1}H NMR : (400 MHz, $CDCl_3$ δ ppm) 7.85 (s, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.34-7.27 (m, 4H), 7.23-7.18 (m, 4H), 7.09-7.06 (m, 3H), 6.83 (t, *J* = 7.2 Hz, 1H), 6.62 (s, 1H), 6.22 (s, 1H), 3.68-3.65 (m, 2H), 3.15-3.07 (m, 1H), 2.88-2.81 (m, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm) 149.8, 137.5, 136.6, 135.6, 129.3, 128.9, 128.1, 126.7, 126.5, 125.8, 124.2, 122.1, 120.1, 119.7, 119.3, 118.2, 115.9, 111.1, 56.7, 42.3, 26.7.

2-Phenyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (65j)

Yield : 0.08 g (67%); pale yellow solid.



65j

mp : 94-96 °C.

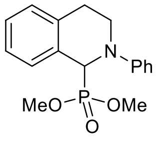
IR (KBr) : (cm^{-1}) 3041, 2926, 2838, 1742, 1600, 1496, 1463, 1375, 1205, 1145, 1030, 942, 745, 695.

^{1}H NMR : (400 MHz, $CDCl_3$ δ ppm) 7.42-7.38 (m, 2H), 7.35-7.26 (m, 4H), 7.13 (d, J = 8.0 Hz, 1H), 7.06 (t, J = 7.4, 1H), 5.55 (s, 1H), 3.83-3.78 (m, 1H), 3.55-3.48 (m, 1H), 3.23-3.14 (m, 1H), 3.02-2.96 (m, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm) 148.4, 134.7, 129.6, 129.4, 128.8, 127.1, 126.9, 121.9, 117.8, 117.6, 53.2, 44.2, 28.6.

Dimethyl (2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)phosphonate (65k)

Yield : 0.13 g (82%); colourless oil.



65k

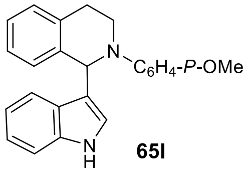
IR (Neat) : (cm^{-1}) 3057, 2942, 2854, 1599, 1501, 1391, 1347, 1319, 1243, 1067, 1007, 832, 744, 684, 569.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.39-7.37 (m, 1H), 7.30-7.26 (m, 2H), 7.23-7.18 (m, 3H), 7.00 (d, J = 8.2 Hz, 2H), 6.83 (t, J = 7.3 Hz, 1H), 5.24 (d, J = 19.8 Hz, 1H), 4.07-4.00 (m, 1H), 3.69-3.65 (m, 6H), 3.13-2.97 (m, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 149.3, 149.2, 136.5, 136.4, 130.4, 129.3, 128.9, 128.0, 127.9, 127.6, 127.6, 126.1, 118.7, 114.8, 59.6, 57.9, 54.0, 53.9, 53.0, 52.9, 43.6, 26.7.

1-(*1H*-Indol-3-yl)-2-(4-methoxy-phenyl)-1,2,3,4-tetrahydro-isoquinoline (65l)

Yield : 0.15 g (79%); white solid.



65l

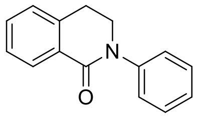
mp : 140-142 °C.

IR (KBr) : (cm^{-1}) 3145, 2959, 2909, 2849, 2833, 1610, 1512, 1451, 1249, 1112, 1035, 914, 816, 734, 640.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 10.02 (bs, 1H), 7.46-7.44 (m, 1H), 7.34-7.33 (m, 1H), 7.23-7.21 (m, 1H), 7.18-7.09 (m, 3H), 7.06-7.02 (m, 3H), 6.92-6.88 (m, 1H), 6.79-6.72 (m, 3H), 6.04 (s, 1H), 3.68 (s, 3H), 3.59-3.44 (m, 2H), 2.06-2.04 (m, 2H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 153.3, 144.7, 138.2, 137.0, 135.2, 128.6, 128.2, 126.2, 125.5, 124.7, 121.2, 119.9, 119.1, 118.7, 118.3, 114.2, 111.2, 57.7, 54.8, 43.0, 26.9.

2-Phenyl-3,4-dihydroisoquinoline-1(2*H*)-one (70a)



70a

Yield : 0.08 g (72%), white solid.

mp : 76-78 °C.

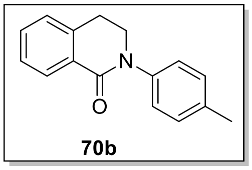
IR (KBr) : (cm^{-1}) 3063, 3041, 2964, 2931, 1660, 1599, 1490, 1408, 1325, 1254, 1029, 739, 690.

^{1}H NMR : (400 MHz, CDCl$_3$ δ ppm) 8.18 (d, *J* = 7.6 Hz, 1H), 7.45-7.34 (m, 5H), 7.27 (t, *J* = 7.0 Hz, 3H), 4.01 (t, *J* = 6.4 Hz, 2H), 3.16 (t, *J* = 6.4 Hz, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$ δ ppm) 164.2, 143.1, 138.3, 132.0, 129.7, 128.9, 128.8, 127.2, 127.0, 126.3, 125.3, 49.4, 28.7.

HRMS (*m*/*z*) : Calculated for $C_{15}H_{13}NO$ (M+H): 224.1075, Found (M+H): 224.1073.

2-(*p*-Tolyl)-3,4-dihydroisoquinolin-1(2*H*)-one (70b)


70b

Yield : 0.09 g (72%); white solid.

mp : 108-110 ^{o}C.

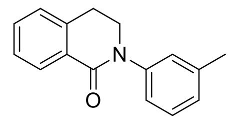
IR (KBr) : (cm^{-1}) 3058, 3041, 2969, 2948, 1655, 1512, 1468, 1408, 1326, 1227, 1167, 1112, 1068, 833, 745, 701, 647.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 8.19 (d, *J* = 7.6 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 1H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.31-7.24 (m, 5H), 3.99 (t, *J* = 6.7 Hz, 2H), 3.16 (t, *J* = 6.7 Hz, 2H), 2.39 (s, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 164.2, 140.6, 138.3, 136.0, 131.9, 129.8, 129.6, 128.7, 127.2, 126.9, 125.2, 49.5, 28.6, 21.1.

HRMS (*m*/*z*) : Calculated for $C_{16}H_{15}NO$ (M+Na): 260.1046, Found (M+Na): 260.1042.

2-(*m*-Tolyl)-3,4-dihydroisoquinolin-1(2*H*)-one (70c)


70c

Yield : 0.09 g (75%); white solid.

mp : 121-123 °C.

IR (KBr) : (cm^{-1}) 2975, 2931, 2898, 2871, 1659, 1605, 1489, 1462, 1413, 1259, 1227, 1172, 783, 739, 695, 470.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 8.20 (d, *J* = 7.6, 1H), 7.49 (t, *J* = 7.6 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.27-7.19 (m, 3H), 7.10 (d, *J* = 7.3 Hz, 1H), 3.98 (t, *J* = 6.3 Hz, 2H), 3.15 (t, *J*= 6.4 Hz, 2H), 2.41 (s, 3H).

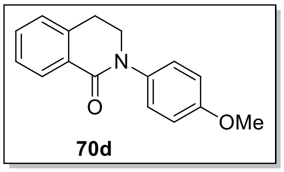
^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 164.2, 143.1, 138.8, 132.0, 129.8, 128.8, 128.7, 127.2, 127.0, 126.2, 122.4, 49.5, 28.6, 21.5.

HRMS (*m*/*z*) : Calculated for $C_{16}H_{15}NO$ (M+Na): 260.1046, Found (M+Na): 260.1043.

2-(4-Methoxyphenyl)-3,4-dihydroisoquinolin-1(2*H*)-one (70d)

Yield : 0.09 g (69%); white solid.

mp : 127-129 °C.



70d

IR (KBr) : (cm^{-1}) 3063, 2932, 2838, 1644, 1600, 1512, 1402, 1332, 1255, 1173, 1036, 833, 739.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 8.18 (d, *J* = 7.7 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.41-7.25 (m, 5H), 6.96 (d, *J* = 8.8, 2H), 3.96 (t, *J* = 6.6, 2H), 3.84 (s, 3H), 3.16 (t, *J* = 6.2 Hz, 2H).

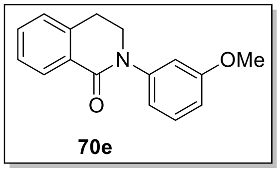
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 164.5, 157.9, 138.4, 136.2, 132.0, 128.8, 128.0, 127.3, 127.0, 126.8, 114.4, 55.6, 49.8, 28.8.

HRMS (*m/z*) : Calculated for $C_{16}H_{15}NO_2$ (M+H): 254.1181, Found (M+H): 254.1183.

2-(3-Methoxyphenyl)-3,4-dihydroisoquinolin-1(2*H*)-one (70e)

Yield : 0.10 g (81%); white solid.

mp : 110-102 ^{o}C.



70e

IR (KBr) : (cm^{-1}) 3079, 3036, 2948, 2860, 2838, 1649, 1611, 1589, 1496, 1419, 1332, 1222, 1162, 1047, 932, 789, 707.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 8.19 (d, *J* = 7.5 Hz, 1H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.7 Hz, 1H), 7.34 (t, *J* = 7.7 Hz, 1H), 7.26 (d, *J* = 7.7 Hz, 1H), 6.99 (s, 2H), 6.85-6.82 (m, 1H), 3.99 (t, *J* = 6.3Hz, 2H), 3.84 (s, 3H), 3.15 (t, *J* = 6.3 Hz, 2H).

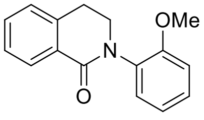
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 164.2, 160.0, 144.3, 138.3, 132.1, 129.7, 129.6, 128.7, 127.2, 126.9, 117.5, 112.2, 111.4, 55.4, 49.5, 28.6.

HRMS (*m/z*) : Calculated for $C_{16}H_{15}NO_2$ (M+H): 254.1181, Found (M+H): 254.1179.

2-(2-Methoxyphenyl)-3,4-dihydroisoquinolin-1(2*H*)-one (70f)

Yield : 0.09 g (73%); white solid.

mp : 119-121 °C.



70f

IR (KBr) : (cm^{-1}) 3024, 2920, 2843, 1599, 1501, 1407, 1331, 1199, 903, 749, 695.

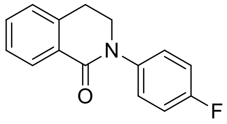
^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 8.19 (d, *J* = 7.7 Hz, 1H), 7.46 (t, *J* = 7.4 Hz, 1H), 7.39-7.29 (m, 3H), 7.25 (d, *J* = 7.6 Hz, 1H), 7.02 (t, *J* = 8.7 Hz, 2H), 3.82 (s, 5H), 3.14 (s, 2H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 164.3, 154.7, 138.9, 131.9, 131.5, 129.8, 129.1, 128.7, 128.6, 127.1, 126.9, 120.8, 112.2, 55.7, 49.1, 28.7.

HRMS (*m/z*) : Calculated for $C_{16}H_{15}NO_2$ (M+H): 254.1181, Found (M+H): 254.1178.

2-(4-Fluorophenyl)-3,4-dihydroisoquinolin-1(2*H*)-one (70g)

Yield : 0.08 g (68%); white solid.



70g

mp : 158-160 °C.

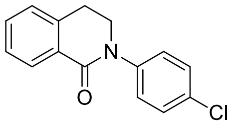
IR (KBr) : (cm^{-1}) 3058, 3024, 2953, 1649, 1606, 1501, 1468, 1425, 1332, 1222, 1156, 1096, 926, 833, 745.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 8.17 (d, *J* = 7.7 Hz, 1H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.42-7.36 (m, 3H), 7.28-7.26 (m, 1H), 7.12 (t, *J* = 8.5 Hz, 2H), 3.98 (t, *J* = 6.5 Hz, 2H), 3.17 (t, *J* = 6.4 Hz, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 164.4, 161.9, 159.5, 139.1, 139.1, 138.3, 132.2, 129.5, 128.7, 127.3, 127.2, 127.1, 127.0, 115.8, 115.6, 49.6, 28.6.

HRMS (*m*/*z*) : Calculated for $C_{15}H_{12}FNO$ (M+H): 242.0981, Found (M+H): 242.0984.

2-(4-Chlorophenyl)-3,4-dihydroisoquinolin-1(2*H*)-one (70h)



70h

Yield : 0.08 g (65%); white solid.

mp : 129-131 °C.

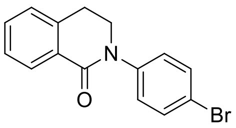
IR (KBr) : (cm^{-1}) 2959, 2921, 2904, 2860, 1648, 1627, 1594, 1495, 1413, 1325, 1166, 1095, 1008, 827, 749.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 8.17 (d, J = 7.5 Hz, 1H), 7.52-7.48 (m, 1H), 7.42-7.35 (m, 5H), 7.29-7.26 (m, 1H), 3.99 (t, J = 6.5 Hz, 2H), 3.17 (t, J = 6.5 Hz, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 164.3, 141.7, 138.4, 132.4, 131.7, 129.6, 129.1, 128.9, 127.4, 127.1, 126.7, 49.4, 28.7.

HRMS (*m*/*z*) : Calculated for $C_{15}H_{12}ClNO$ (M+H): 258.0985, Found (M+H): 258.0984.

2-(4-Bromophenyl)-3,4-dihydroisoquinolin-1(2*H*)-one (70i)



70i

Yield : 0.10 g (67%); white solid.

mp : 168-170 ^{o}C.

IR (KBr) : (cm^{-1}) 2953, 2909, 2838, 1655, 1589, 1490, 1408, 1326, 1293, 1227, 1161, 893 751, 690.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 8.17 (d, *J* = 7.7 Hz, 1H), 7.56-7.49(m, 3H), 7.43-7.35 (m, 2H), 7.32-7.26 (m, 3H), 3.99 (t, *J* = 6.3 Hz, 2H), 3.17 (t, *J* = 6.4 Hz, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 164.2, 142.1, 138.2, 132.3, 131.9, 129.4, 128.8, 127.3, 126.9, 119.5, 49.3, 28.5.

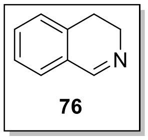
HRMS (*m/z*) : Calculated for $C_{15}H_{12}BrNO$ (M+H): 302.0180, Found (M+H): 302.0142.

2.4.4 General procedure for the formation of 3,4-dihydroisoquinoline 76 and isoquinolone 77

In a 25 mL RB flask, activated charcoal (1 g) heated at 200 °C under high vacuum (0.001 mm of Hg) for 2 h. After the RB flask was brought to room temperature under nitrogen atmosphere, the contents were saturated with dry air for 1 h. To this 1,2,3,4-tetrahydroisoquinoline (1 mmol) in DMSO were added. The reaction mixture was further stirred for 36 h. After that 30 mL EtOAc was added and stirred for further half an hours. The reaction mixture was filtered, and washes several times with EtOAc and H_2O. the organic layer extracts with EtOAc, washes with brine and then dried over anhydrous Na_2SO_4. Evaporate solvent under vacuum and the crude mixture was chromatographed on silicagel using hexane:ethylacetate (90:10) as an eluent to isolate the pure compound **77** and using hexane:ethylacetate (70:30) as an eluent to isolate the pure compound **76**.

3,4-Dihydroisoquinoline (76)

Yield : 0.19 g (72%); yellow oil.



76

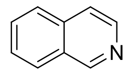
IR (Neat) : (cm^{-1}) 3058, 2958, 2921, 2867, 1595, 1545, 1511, 1352, 1036, 751, 690.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 8.34 (t, *J* = 2.0 Hz, 1H), 7.36-7.27 (m, 3H), 7.16 (d, *J* = 7.3 Hz, 1H), 3.80-3.75 (m, 2H), 2.75 (t, *J* = 7.9 Hz, 2H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 160.4, 136.3, 131.1, 128.5, 127.4, 127.2, 127.1, 47.4, 25.0.

Isoquinoline (77)

Yield : 0.04 g (15%); yellow oil.



77

IR (Neat) : (cm^{-1}) 2959, 2921, 2877, 1601, 1533, 1501, 1353, 1036, 751.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 9.22 (s, 1H), 8.49 (d, *J* = 5.7 Hz, 1H), 7.92-7.90 (m, 1H), 7.78-7.75 (m, 1H), 7.66-7.53 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 152.5, 142.9, 135.8, 130.4, 128.7, 127.6, 127.2, 126.4, 120.5.

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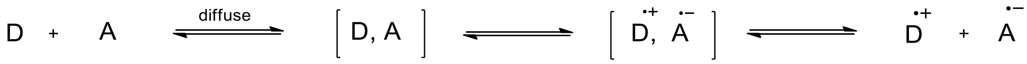
Chapter 3

Electron Transfer Reactions of tertiary N-Aryl Cyclic Amines and p-Chloranil

3. 1 Introduction

The chemistry of quinones has been continuously attracting the attention of chemists over the years.[1] The awareness of oxidizing properties of quinones increased significantly in the early 20th century.[2] Quinones also play an important role in biological[3] and electrochemical[4] processes. In the 1970's and 1980's, there were several reports on the formation of radical cation and radical anion pair intermediates in popular organic reactions like S_N2 reaction, Cannizaro reaction, Aldol condensation, Meervein Pondorf Verly reduction and Michael reaction.[5] The quinones are electron acceptors and their electron transfer reactions with amines were reported extensively.[6] Molecular interactions between electron donors and acceptors have been also widely reported.[7] The role of electron donor acceptor complexes or charge-transfer (CT) complexes in chemical reactions were also widely reported.[8] The pioneering work of Mulliken,[9] Taube,[10] Marcus,[11] and Bijl[12] on the formation of charge transfer complexes (CT) and electron transfer reactions played important roles in the overall understanding of the donor-acceptor processes (Scheme 1).

Scheme 1



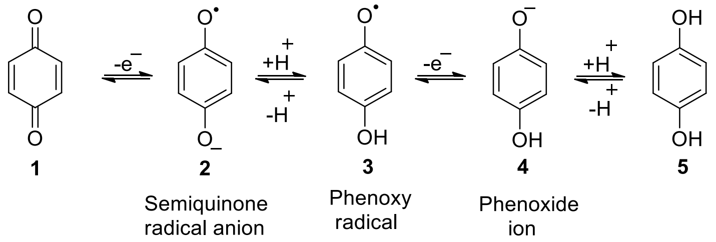
$$D + A \xrightleftharpoons{\text{diffuse}} \left[D, A \right] \rightleftharpoons \left[\overset{\bullet+}{D}, \overset{\bullet-}{A} \right] \rightleftharpoons \overset{\bullet+}{D} + \overset{\bullet-}{A}$$

In 2008, J. K. Kochi *et. al.* summarized the reports on various electron-transfer reactions of electron donors and acceptors.[13] The outer-sphere/inner-sphere mechanism was extended to organic electron-transfer reactions. Kochi *et. al.*[14] proposed an alternative, distance dependence model, based on the van der Waals radii of electron donors and acceptors. The molecular interactions in outer-sphere processes are viewed as between donor and acceptor separated beyond their van der Waals radii. Whereas, in inner-sphere complexes, the distance between donor and acceptor is likely to be less than their van der Waals radii and in these complexes the donor/acceptor are packed closely with enhanced interactions.[15] Therefore, sterically hindered donor/acceptor complexes are expected to form outer-sphere complexes, while less sterically hindered donor and acceptor complexes would prefer to form inner-sphere complexes.[16]

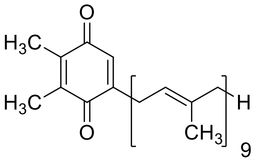
3.1.1 Quinones in biology

Quinone moieties are important structural motifs in many natural, unnatural and heterocyclic products that have a wide range of biological activities such as antitumoral, antiprotozoan, and antibiotic activities.[17] Many of these molecules possess chemotherapeutic properties.[18] The most important reversible redox process of quinone **1** and hydroquinone **5** is a sequence of proton and electron transfers (Scheme 2).

Scheme 2



In addition, quinones play important role in biochemical process of living cells.[19] Anthracyclines, a class of anthraquinones are used as medicine in several types of human cancers[20] where it has been observed that their biological activities are associated with their redox behavior. Derivatives of benzoquinone/hydroquinone play an essential role in many biological systems, including photosystem II (PSII)[21] and their related bacterial reaction center (bRC).[22] The redox reaction, an important example appears in photosynthesis, where the reduction of plastoquinone **6** (PQ, Figure 1) takes place to give the mobile redox carrier plastoquinol.



6

Figure 1. The structue of plastoquinone (PQ).

In this process plastoquinone **6** (PQ) serves as the terminal electron acceptor in a chain of electron transfer events.

3.1.2 Electrochemical aspects of Quinones

The most basic principle in a rechargeable battery is that a compound undergoes reversible redox process. The general reversible redox process can be written as in eq. 1.

$$Ox + Ze^{-} \rightleftharpoons Red \qquad \dashrightarrow (1)$$

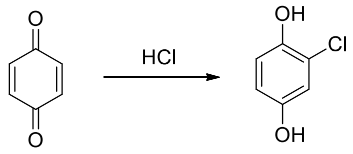
Where z is the number of transferred electrons

The electrochemistry of quinone/hydroquinone redox has been investigated for over a century,[23] and remains as one of the most systematically studied groups of electroactive compounds.[24] This is primarily due to the fact that quinone compounds are biologically relevant, being involved in various cell processes in human including the electron transport chain.[25] The electron and proton transfer steps would occur in different sequences and the pathways will depend on parameters such as the pH of the electrolyte, the electrochemical method used and the substituents on the quinone.

3.1.3 Quinones in Organic Synthesis

The first addition reaction of hydrogen chloride to benzoquinone **1** was reported by Wöhler in 1844 (Scheme 3).[26]

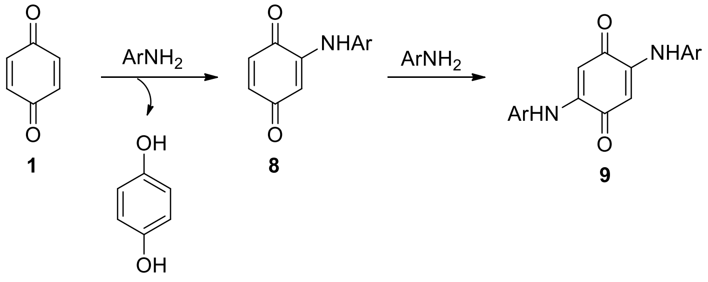
Scheme 3



1 **7**

Many nitrogen containing compounds were found to undergo Michael addition with a variety of quinones. Addition products of 1,4-benzoquinone **1** and substituted anilines were reported. The aryl amine addition product **8** is the result of a sequence of two additions followed by oxidation (Scheme 4).[27]

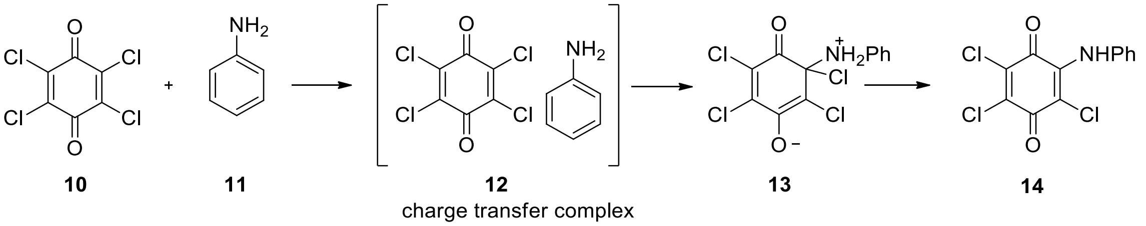
Scheme 4



1 **5** **8** **9**

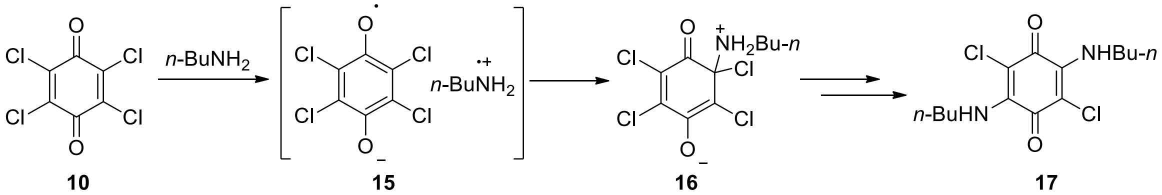
Mulliken presented the well-known theory of the charge-transfer interaction between electron donors and electron acceptors. It has been successfully and widely applied to many processes.[28] It was reported that the reaction of *p*-chloranil **10** with aniline **11** gave the charge transfer (CT) complex **12** (Scheme 5).[29] Subsequently, the ionic diamagnetic intermediate **13** is formed before formation of the aminoquinone product **14** (Scheme 5).

Scheme 5



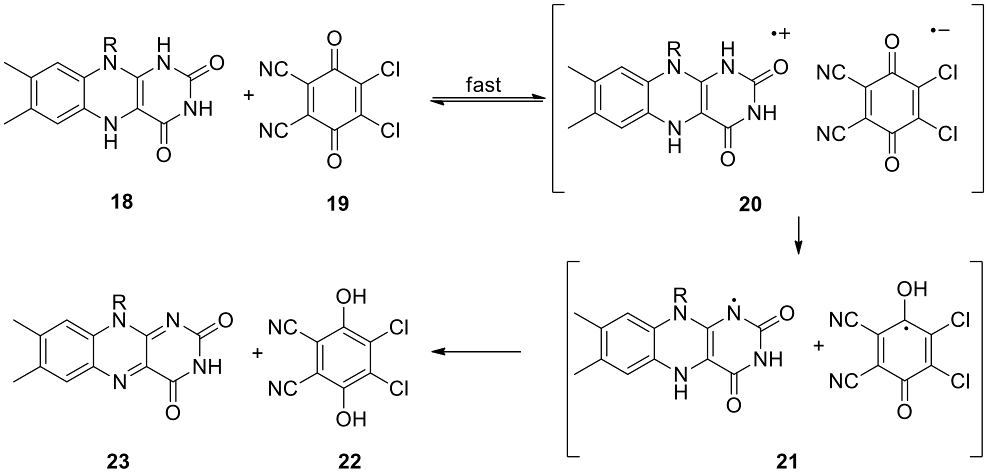
The reaction of *n*-butylamine with *p*-chloranil **10** gave the corresponding electron transfer complex **15**, which subsequently lead to the formation of 1,4-addition product **16** (Scheme 6).[30]

Scheme 6



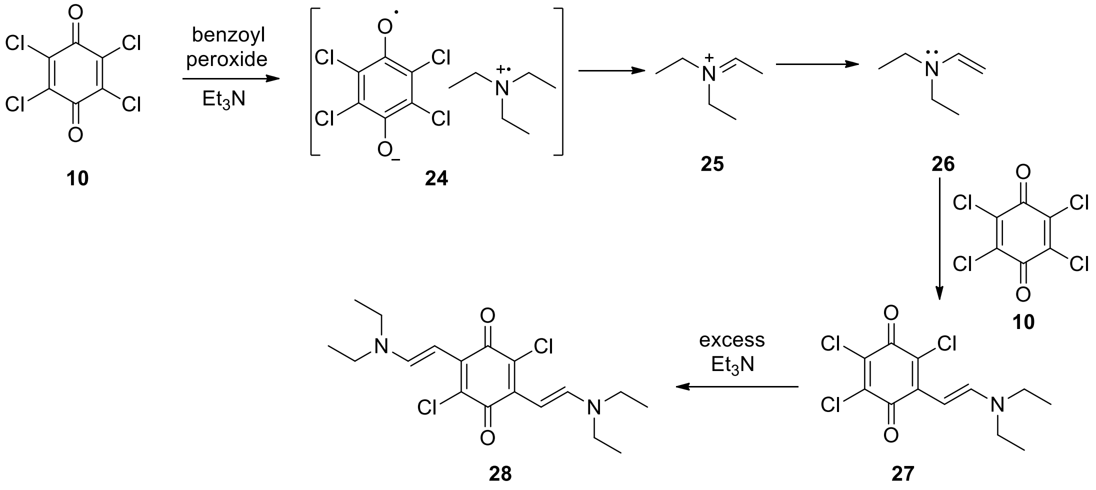
Electron transfer mechanism for hydrogen transfer from dihydroflavins **18** to quinones **19** was reported (Scheme 7).[31]

Scheme 7:



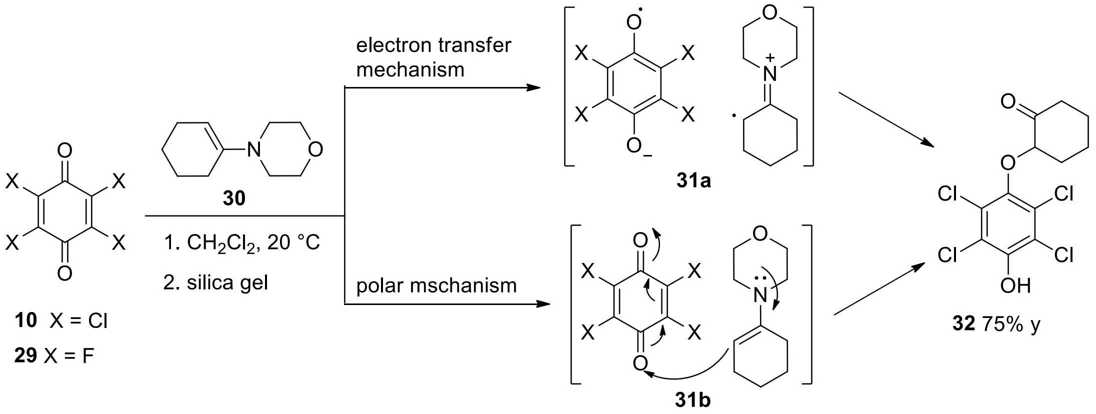
The reaction of *p*-chloranil **10** and triethylamine in the presence of benzoyl peroxide in benzene solvent gave the diethylaminovinylquinone **27** (Scheme 8). When excess of triethylamine was used, the bisdiethylaminovinylquinone **28** formed (Scheme 8).[32]

Scheme 8



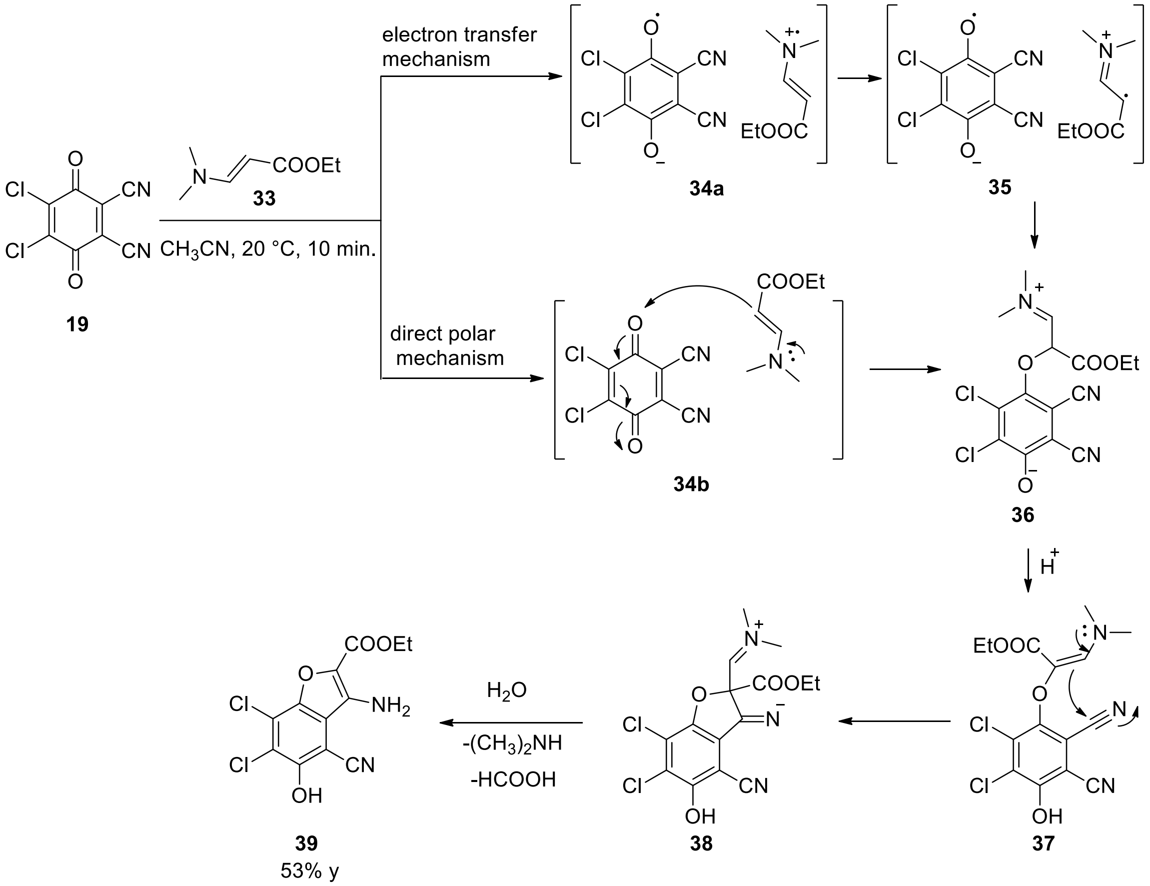
The reactions of *p*-quinones **10** and **29** with an enamine **30** were reported to give 1,2-addition products.[33] Kinetic studies of the *p*-quinones with the π-nucleophiles were also reported (Scheme 9).[34] These authors favored polar mechanism but electron transfer mechanism cannot be ruled out in these cases.

Scheme 9



Formation of benzofuran from 2,3-dichloro-5,6-dicyano-1,4-benzoquinone **19** and tertiary enaminoesters **33** was reported.[35] These authors explained the results by a polar mechanism instead of electron transfer mechanism. Here also, operation of electron transfer mechanism cannot be ruled out (Scheme 10).

Scheme 10

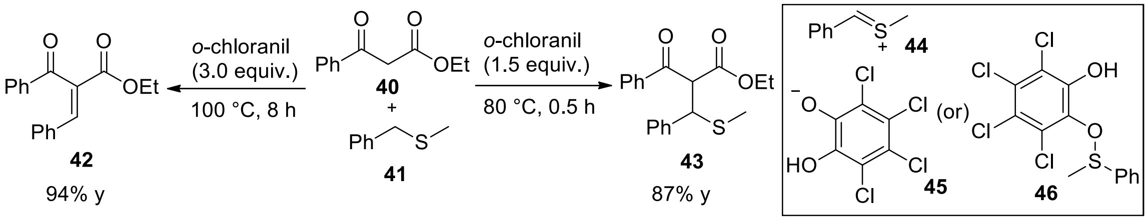


Althrough, Mayr *et. al*. reported[34,35] the reaction between quinone and tertiary amines take place by the direct polar mechanism, mixing of primary, secondary, tertiary amines and quinones gave paramagnetic intermediates and hence operation of electron transfer mechanism in these reactions cannot be ruled out.

3.1.4 Quinones as oxidizing agents

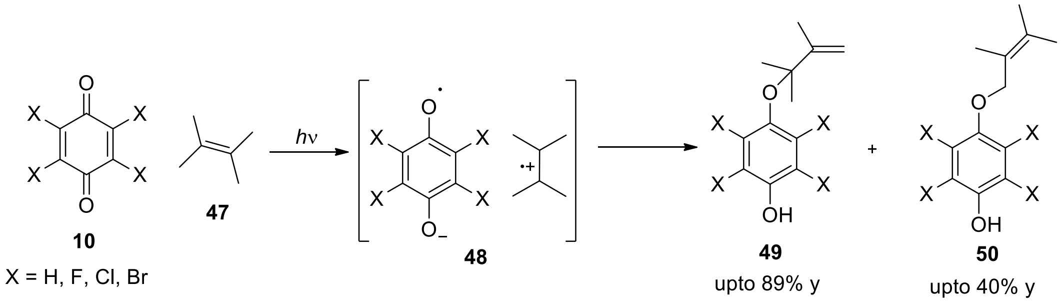
Quinones are important class of oxidizing reagents in organic chemistry.[36] Recently, interesting C-H bond oxidations of benzyl sulfide **41** and 1,3-dicarbonyl compounds **40** using *o*-chloranil to sulfide derivatives **43** were reported (Scheme 11).[37]

Scheme 11



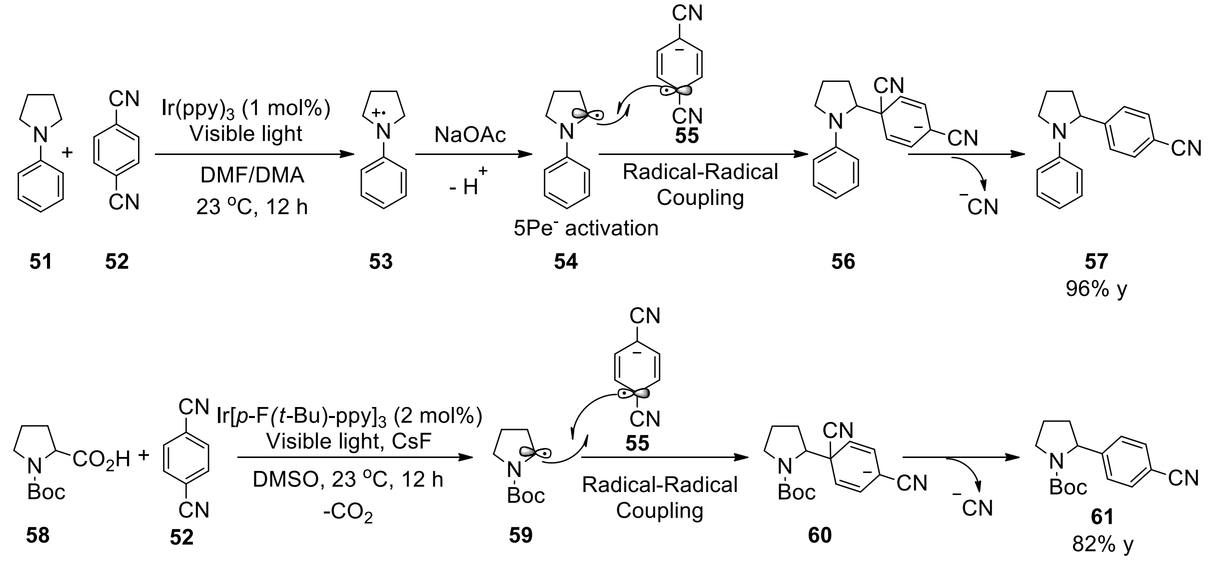
Furthermore, the photo induced electron transfer reaction of halogenated 1,4-benzoquinones **10** with 2,3-dimethyl-2-butene **47** to allyl ethers of hydroquinones **49** and **50** were reported (Scheme 12).[38]

Scheme 12



MacMillan *et. al.*[39] reported a series of photoredox catalytic reactions using transition metal (Ru, Ir, Pd, Cu) complexes using organic electron donors and acceptors (Chart 1).

Chart 1



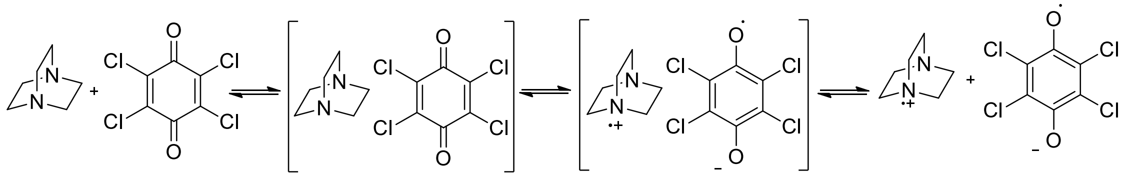
We have decided to investigate the reaction of tertiary amine donors and with *p*-chloranil. The results are described in the next section.

3.2 Results and Discussion

3.2.1 Reactions of DABCO with *p*-chloranil

As early as in 1965, it was reported[40] that the 1,4-diazabicyclo[2.2.2] octane (DABCO) **62** forms stable radical cation due to through space interaction of nitrogen orbitals.[41] In 1977, the reaction of DABCO **62** with *p*-chloranil **10** was reported[42] to give paramagnetic intermediates and the charge transfer (CT) complex **63** was considered to be in equilibrium with the electron transfer (ET) complex **64** and radical cation (**65**)-anion (**66**) pair (Scheme 13). The strength of the esr signals were stronger in a more polar solvent such as THF compared to that in benzene.

Scheme 13

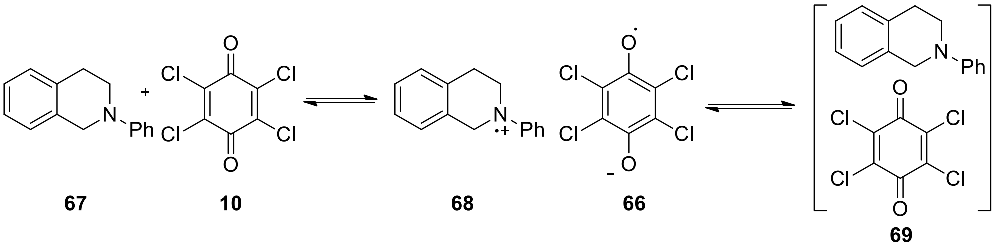


62 10 63 64 65 66

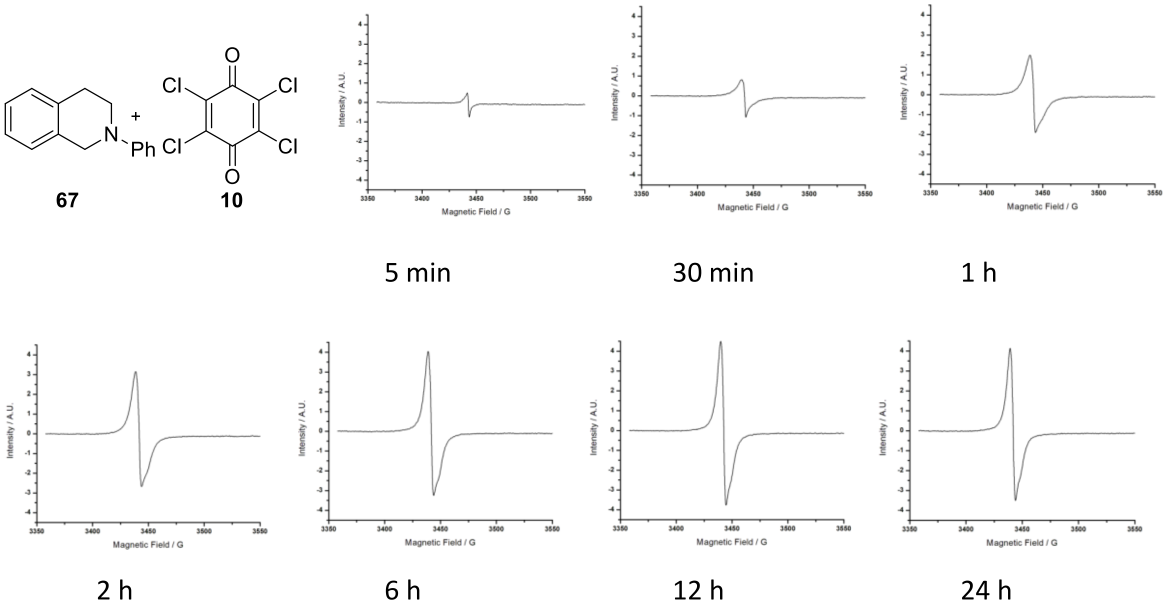
3.2.2 Electron transfer complex of 2-phenyl-1,2,3,4-tetrahydroisoquinoline with *p*-chloranil

We have observed that mixing of 2-phenyl-1,2,3,4-tetrahydroisoquinoline **67** and the electron acceptor *p*-chloranil **10** under neat condition and in propylene carbonate (PC) solvent gave paramagnetic intermediates detected by epr spectral analysis with g value 2.00571 and 2.00617 (Figure 2 and 3). However, the single epr signals observed in these reactions are due to the chloranil radical anion and the triplet signal expected for the amines radical cation was not observed due to fast exchange with neutral amines (Scheme 14).

Scheme 14



The strength of the epr signal was relatively weak and increased with time under neat condition (Figure 2). We made attempts to crystallize the charge transfer complex using solvents such as CH_2Cl_2, PC, dimethylformamide (DMF) and N-methyl-2-pyrrolidone (NMP) but these effords were not successful.

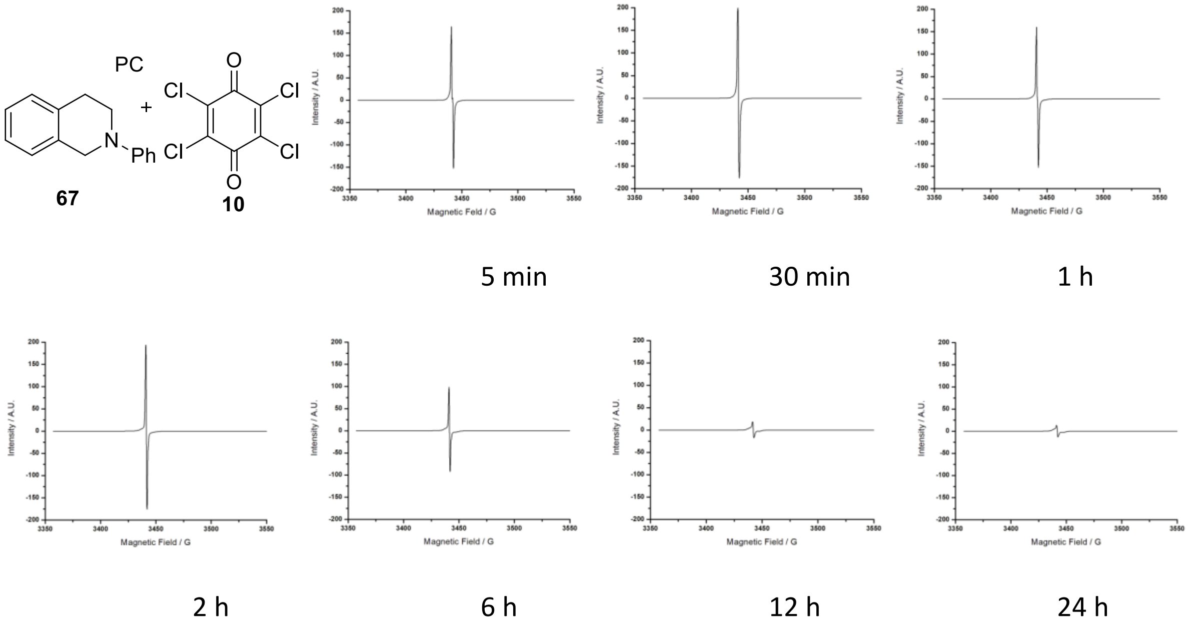


5 min 30 min 1 h

2 h 6 h 12 h 24 h

Figure 2: ESR spectra of 2-phenyl-1,2,3,4-tetrahydroisoquinoline **67** (0.02 mmol) with chloranil **10** (0.02 mmol) in neat condition.

The epr spectra of the donor **67** and *p*-chloranil **10** were initially strong (5 min to 2 h) and then became weak (Figure 3).



5 min 30 min 1 h

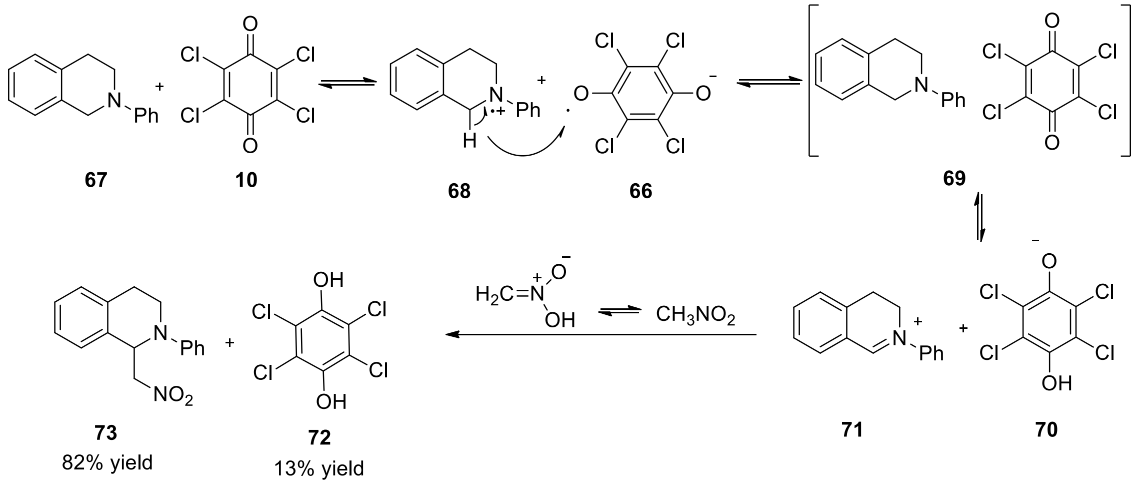
2 h 6 h 12 h 24 h

Figure 3: ESR spectra of 2-phenyl-1,2,3,4-tetrahydroisoquinoline **67** (0.02 mmol) with chloranil **10** (0.02 mmol) in PC solvent.

Previously, line broadening of esr spectra of naphthalenide ion was observed in 1957, by adding excess naphthalene.[43] The reported rate constants for electron transfer between naphthalene negative ion and naphthalene are in the range 10^7-10^9 liter mole^{-1}sec.$^{-1}$ In 2008, Kochi reported the line broadening in the case of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) radical anion with DDQ with fast exchange rate constant 2.5 x 10^9 M^{-1} S^{-1} and activation energy of 1.6 kcal mol^{-1} at 23 °C.[13] Accordingly, the line-broadening in the esr spectra observed for the 2-phenyl-1,2,3,4-tetrahydroisoquinoline **67** and *p*-chloranil **10** under neat condition can be explained by considering such electron exchange phenomenon. The decrease in the intensity of the paramagnetic species can be explained by the formation of charge transfer complexes with time (Scheme 14).

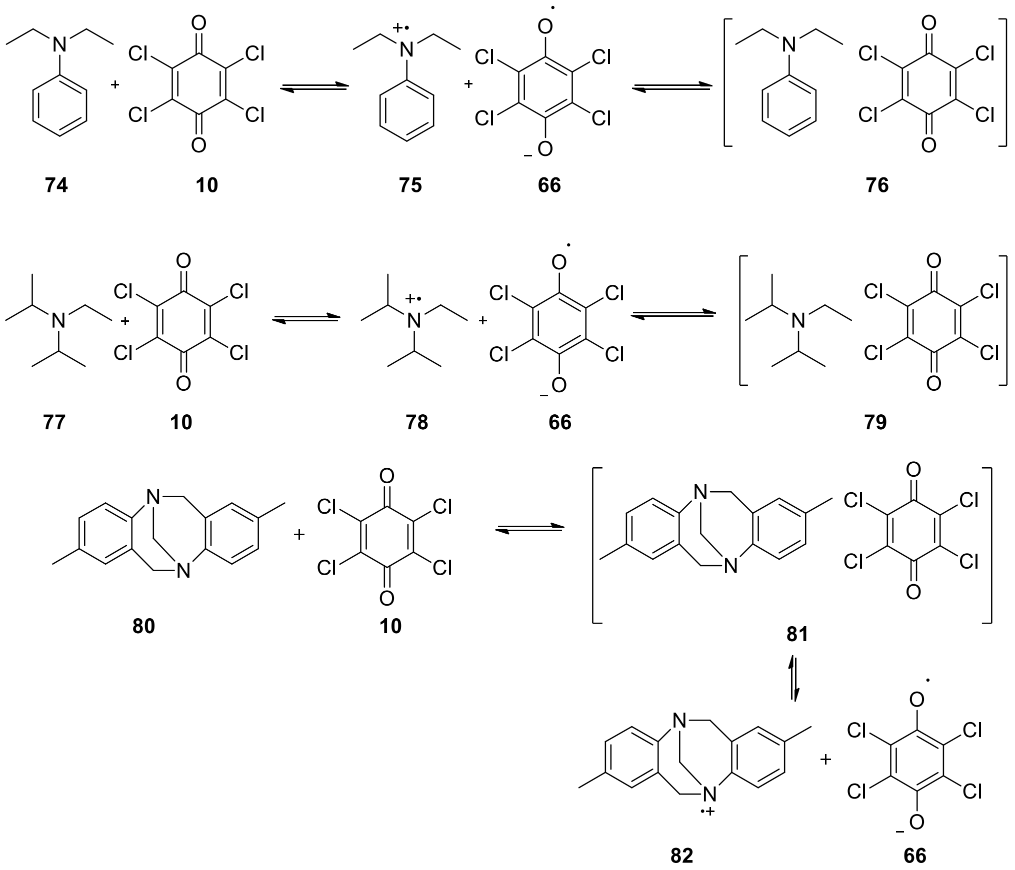
It was thought that the paramagnetic species would participate in further reactions through the formation of the corresponding iminium ions. Hence, we have performed the reaction of 2-phenyl-1,2,3,4-tetrahydroisoquinoline **67**, *p*-chloranil **10** and nitromethane in CH_2Cl_2 solvent at room temperature and obtained the coupled product **73** in 82% yield along with the hydroquinone **72** in 13% yield. Clearly, the amine radical cation **68** formed *in situ* could react the radical anion to give the iminium ion **71** which upon subsequent attack by carbon nucleophile (nitromethane) gives the product **73** (Scheme 15).

Scheme 15



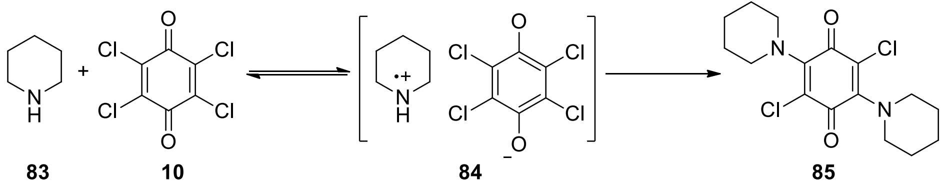
Previously, it was observed in this laboratory that the tertiary amines **74**, **77** and **80** gave paramagnetic species and charge transfer complexes upon reaction with *p*-chloranil **10** in PC solvent. For example, the reaction of amine **77** with *p*-chloranil **10** gave very strong esr signals and the strength of the signal decreased with time (Chart 2).[44,45]

Chart 2



It was also observed in this laboratory that the reaction of *p*-chloranil **10** with secondary amine **83** in DCM or PC solvent gave an esr signal. The strength of the signal decreased with time and disappears within 24 h with the formation of the diamagnetic 1,4-addition product **85** (Scheme 16).

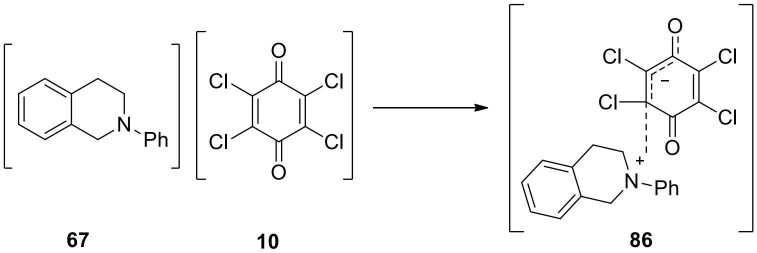
Scheme 16



As the reactivities of the tertiary amines and secondary amines are expected to be similar, the decrease in intensity can be rationalized by initial formation of paramagnetic species followed by formation of diamagnetic charge transfer complexes in equilibrium with initially formed paramagnetic species (Chart 2).

Another possibility is that the reaction of 2-phenyl-1,2,3,4-tetrahydroisoquinoline **67** with *p*-chloranil **10** would lead to initial formation of radical ions (Scheme 14) which could give the outer sphere and inner-sphere complexes with time (Scheme 17). The decrease of esr signal intensity could be explained by considering the closed shell structure **86**.

Scheme 17



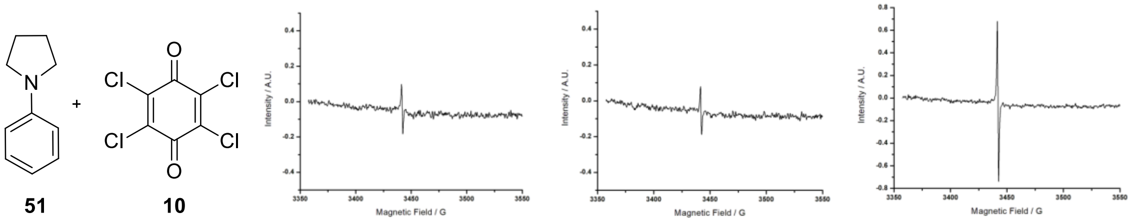
67 **10**
outer-sphere

86
inner-sphere closed shell

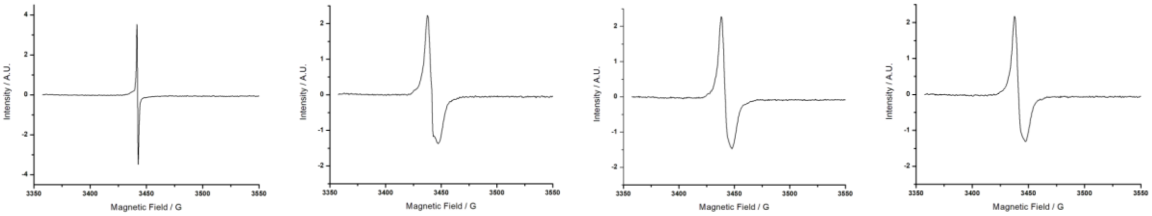
Unfortunately, such complexes could not be crystallized under the present reaction conditions. Hence, the nature of the complexes is not clearly understood.

3.2.3 Electron transfer complex of N-phenylpyrrolidine with *p*-chloranil

Previously, we have reported the formation of N-phenylpyrrolidine radical cation, iminium ion and enamine intermediates using *tert*-butylhydroperoxide (70% in water) at 70 °C (Chapter 1).[46] Hence, we became interested to examine further reaction of radical ions formed in the reaction between N-phenylpyrrolidine **51** and *p*-chloranil **10**. Therefore, we have analyzed mixture of N-phenylpyrrolidine **51** with *p*-chloranil **10** by esr spectroscopy in neat, CH_2Cl_2 and PC solvent conditions. The results are presented in Figure 4 & 5.

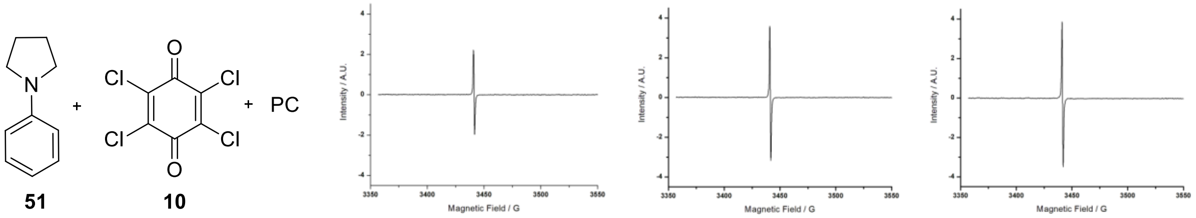


5 min 30 min 1 h

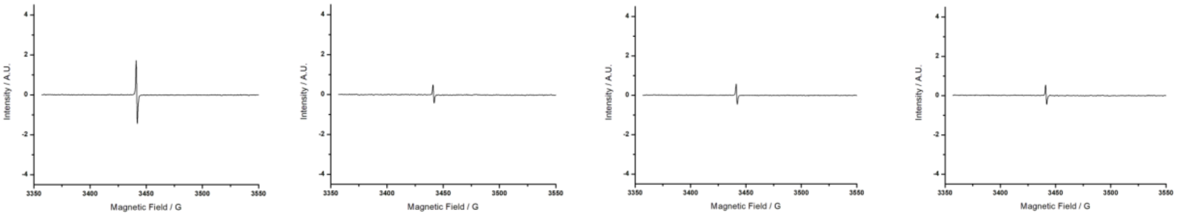


2 h 6 h 12 h 24 h

Figure 4: ESR spectra of N-phenylpyrrolidine **51** (0.02 mmol) with *p*-chloranil **10** (0.02 mmol) in neat condition.



5 min 30 min 1 h



2 h 6 h 12 h 24 h

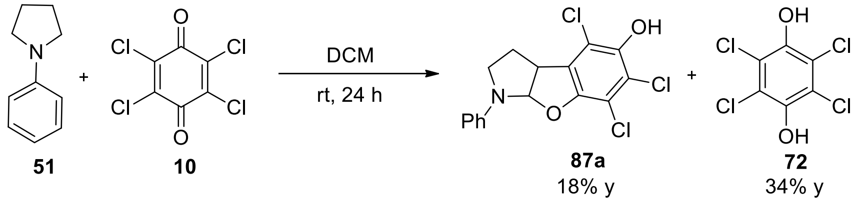
Figure 5: ESR spectra of N-phenylpyrrolidine **51** (0.02 mmol) with *p*-chloranil **10** (0.02 mmol) in PC solvent.

The paramagnetic intermediates formed by the reaction of N-phenylpyrrolidine **51** with *p*-chloranil **10** gave esr signals with g value 2.00585 in neat condition and 2.00598 in PC solvent. Only the signals due to *p*-chloranil radical anion were observed. The triplet signals expected for the amine radical cation were not detected as it would undergo fast exchange with the neutral amine.

3.2.4 Synthesis of benzofuropyrrolidine using N-arylpyrrolidines and *p*-chloranil

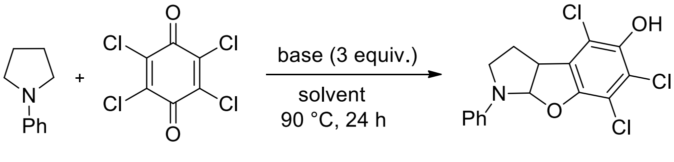
We have observed that the strength of the esr signals in PC solvent decreased with time and disappeared in 48 h. Presumably, the paramagnetic intermediate may give diamagnetic charge transfer complex and would also undergo further reaction. Hence, we have performed the reaction using N-phenylpyrrolidine **51** (1 mmol), *p*-chloranil **10** (1 mmol) in dichloromethane solvent at room temperature for 24 h and isolated the corresponding 4,6,7-trichloro-1-phenyl-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-b]pyrrol-5-ol **87a** in 18% yield (Table 1, entry 1). Also, we have observed the formation of the 2,3,5,6-tetrachlorobenzene-1,4-diol **72** in 34% yield (Scheme 18).

Scheme 18



Clearly, the reaction of N-phenylpyrrolidine **51** and *p*-chloranil **10** results in oxidative cyclization to give the product **87**. Further, we have observed that the product **87a** was obtained in 23% yield as single diastereomer (Table 1, entry 2) along with 42% yield of 2,3,5,6-tetrachlorobenzene-1,4-diol **72** when the reaction time was increased to 24 h.

Table 1: Base promoting reaction of N-phenylpyrrolidine and chloranil.[a-d]



51 **10** **87a**

Entry	Base	Solvent	Yield (%)[c] **87**
1[b]	-	DCM	18
2[b]	-	Toluene	23
3	-	Toluene	49
4	K_2CO_3	Toluene	53
5	*t*-BuOK	Toluene	57
6	NaOH	Toluene	29
7	CH_3COONH_4	Toluene	64
8	CH_3COONa	Toluene	71
9	CH_3COONa	CH_3CN	56
10	CH_3COONa	MeOH	51
11	CH_3COONa	EtOH	53
12	CH_3COONa	PEG-400	54
13	CH_3COONa	Cyclohexane	61

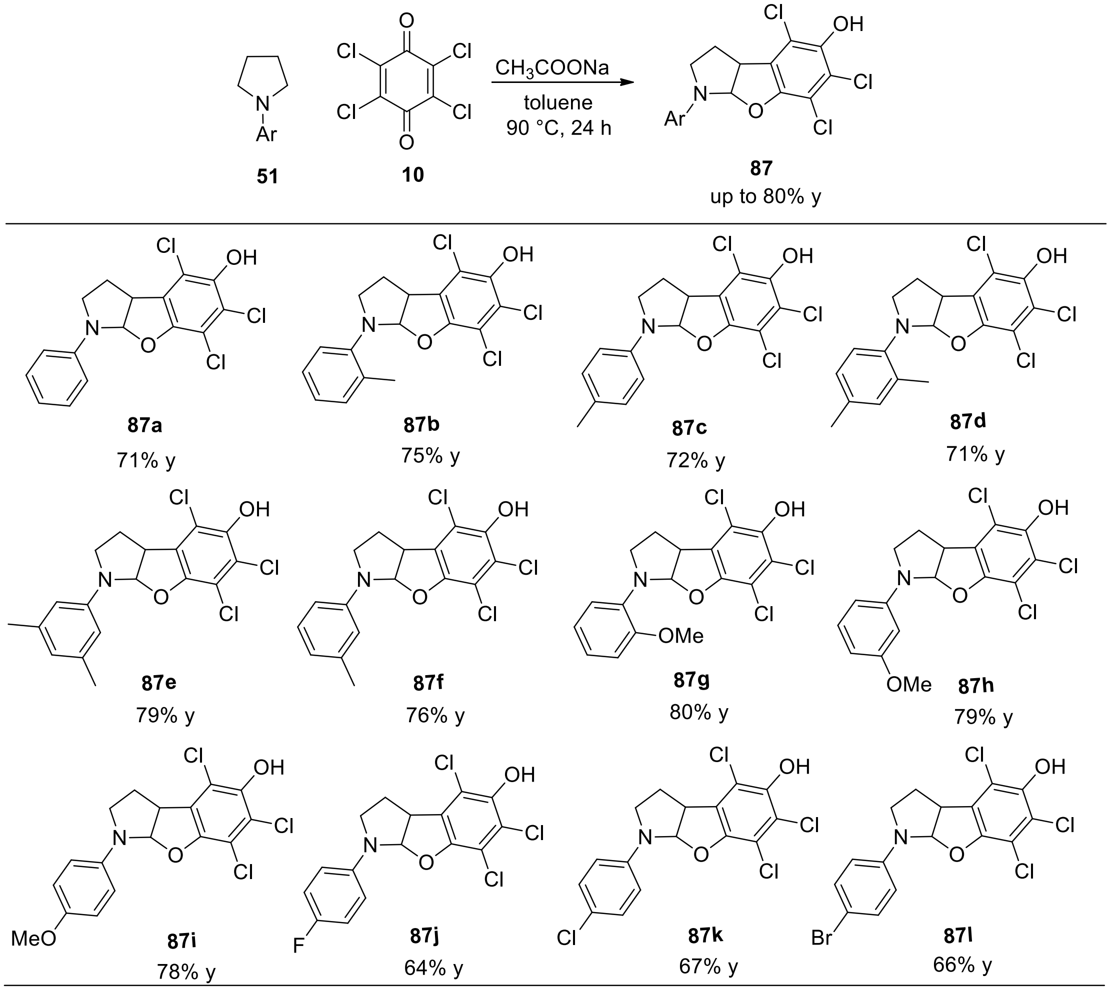
[a]All the reactions were carried out with N-phenylpyrrolidine **51** (1 mmol), *p*-chloranil **10** (1 mmol), base (3 mmol) and solvent (5 mL) for 24 h at 90 °C. [b]Reaction was performed at room temperature. [c]Isolated yields of **87a.** [d]The products were characterized by spectral data (IR, ^{1}H NMR, ^{13}C-NMR and HRMS).

Also, when the reaction was performed at higher temperature 90 °C in toluene solvent for 24 h, the product **87a** was obtained in 49% yield (Table 1, entry 3). The yield of product **87a** was improved to 71% by performing the reaction using 3 equiv. of anhydrous CH_3COONa (Table 1, entry 4). We have screened the reaction using different bases such as

K_2CO_3, *t*-BuOK, NaOH, and CH_3COONH_4 and obtained the product **87a** in 29-71% yields (Table 1, entries 4-7). Also, use of different solvents like CH_3CN, MeOH, EtOH, PEG-400 and cyclohexane gave the coupled product **87a** in 51% to 71% yields (Table 1, entries 9-13).

We have then examined the substrate scope for the synthesis of the tricyclic products **87a-87l.** The results are summarized in Table 2.

Table 2: Synthesis of benzofuropyrrolidine derivatives **87** using N-arylpyrrolidine **51** and *p*-chloranil **10**.[a-d]



87a 71% y; **87b** 75% y; **87c** 72% y; **87d** 71% y; **87e** 79% y; **87f** 76% y; **87g** 80% y; **87h** 79% y; **87i** 78% y; **87j** 64% y; **87k** 67% y; **87l** 66% y

[a]All the reactions were carried out with N-phenylpyrrolidine **51** (1 mmol), *p*-chloranil **10** (1 mmol) and CH_3COONa (3 mmol) in toluene (5 mL) for 24 h at 90 °C. [b]Isolated yields of **87a-87l.** [c]The products were characterized by spectral data (IR, ^1H NMR, ^{13}C-NMR and HRMS).

Methyl substituted N-arylpyrrolidine derivatives **87** reacted with *p*-chloranil **10** to give the corresponding tricyclic products **87b-87f** in 71-79% yields (Table 2). Also, substrates with methoxy and halogen substituents in different positions on the phenyl ring of N-arylpyrrolidines reacted with *p*-chloranil **10** to give the corresponding tricyclic products **87g-87l** in 64-80% yields (Table 2).

The structure of the product **87a** was further confirmed by single crystal X-ray analysis (Figure 6). The newly formed coupled products have two chiral centers, which are *syn* to each other as confirmed by single crystal X-ray analysis. All the products were formed as single diastereomers as indicated by spectral analysis.

Figure 6: X-ray crystal structure of **87a**

3.2.5 Synthesis of benzofuropyrrolidines using 2-methyl-N-arylpyrrolidine and *p*-chloranil

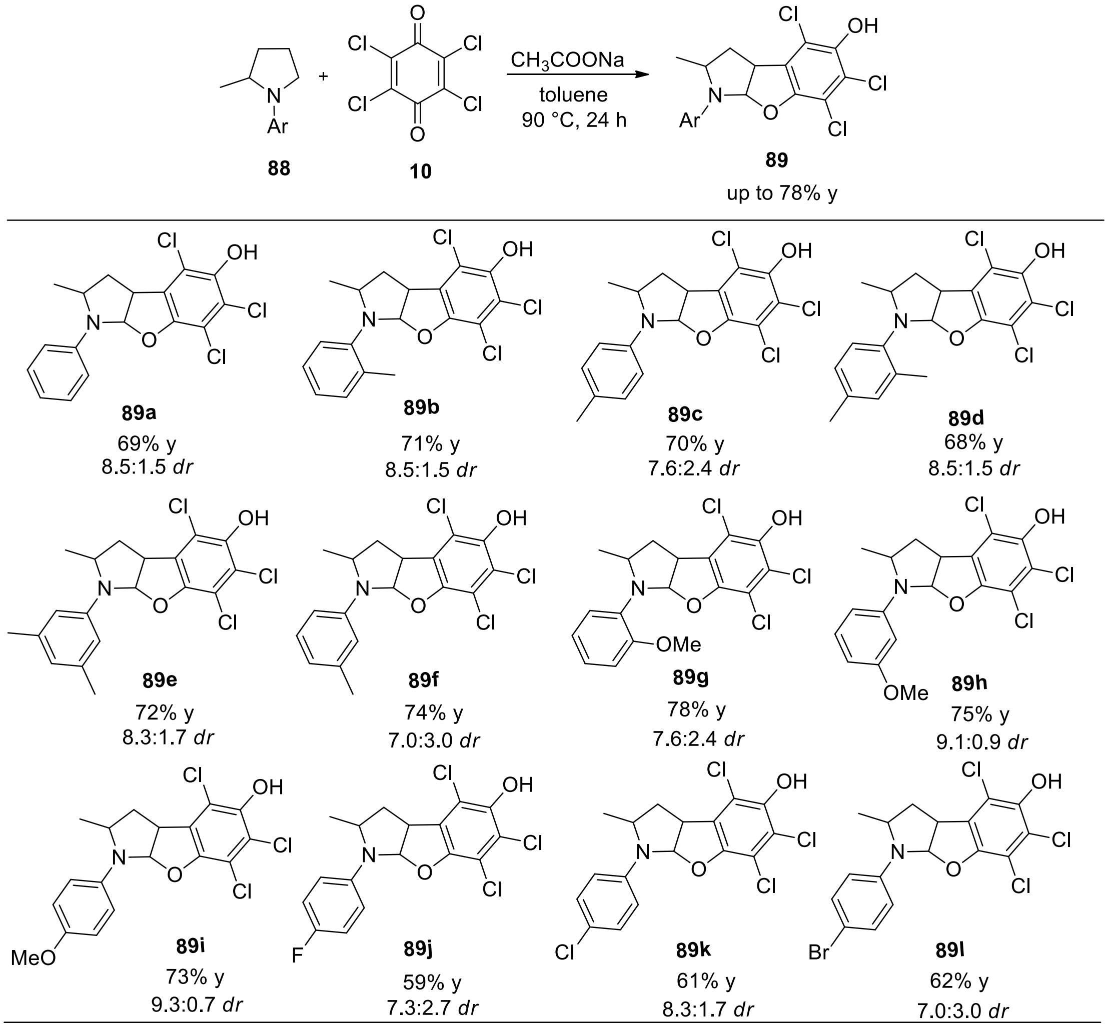
We have also investigated the scope of this reaction using 2-methyl-1-phenylpyrrolidine **88** (1 mmol), *p*-chloranil **10** (1mmol) and CH_3COONa (3 equiv.). The tricyclic product 2-methyl-benzofuropyrrolidine **89** was obtained in 69% yield with the diastereomeric ratio of 8.5:1.5. *p*-Chloranil **10** reacted with other methyl substituted N-arylpyrrolidine to give the coupled products **89a-89f** in 68-74% yields with up to 8.5:1.5 diastereomeric ratio (Table 4, entries **89a-89f**).

Table 3. Crystal data and structure refinement for compound **87a**.

Identification code	**87a**	
Empirical formula	$C_{16}H_{12}C_{l3}NO_2$	
Formula weight	356.62	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 16.3563(9) Å	a= 90°.
	b = 13.7593(7) Å	b= 97.498(2)°.
	c = 13.5111(6) Å	g = 90°.
Volume	3014.7(3) $Å^3$	
Z	8	
Density (calculated)	1.571 Mg/m^3	
Absorption coefficient	0.613 mm^{-1}	
F(000)	1456	
Crystal size	0.12 x 0.10 x 0.08 mm^3	
Theta range for data collection	2.363 to 28.399°.	
Index ranges	-21<=h<=21, -18<=k<=18, -15<=l<=18	
Reflections collected	74411	
Independent reflections	7543 [R(int) = 0.1258]	
Completeness to theta = 25.242°	99.9 %	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7543 / 0 / 399	
Goodness-of-fit on F^2	1.050	
Final R indices [I>2sigma(I)]	$R_1 = 0.0706$, $wR_2 = 0.1183$	
R indices (all data)	$R_1 = 0.1442$, $wR_2 = 0.1403$	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.311 and -0.327 $e.Å^{-3}$	

The reaction between *p*-chloranil **10** and methoxy substituted N-arylpyrrolidine also gave the coupled products **89g-89i** in 73-78% yields with up to 9.3:0.7 diastereomeric ratios (Table 4, entries **89g-89i**). The tricyclic products **89j-89l** were formed in 59-62% yields with up to 8.3:1.7 diastereomeric ratio in the reaction of halogen substituted N-arylpyrrolidines with *p*-chloranil **10** (Table 4, entries **89j-89l**).

Table 4: Synthesis of benzofuropyrrolidine **89** derivatives using N-aryl-2-methylpyrrolidine **88** and *p*-chloranil **10**.[a-c]



88 **10** **89** up to 78% y

89a 69% y 8.5:1.5 *dr*

89b 71% y 8.5:1.5 *dr*

89c 70% y 7.6:2.4 *dr*

89d 68% y 8.5:1.5 *dr*

89e 72% y 8.3:1.7 *dr*

89f 74% y 7.0:3.0 *dr*

89g 78% y 7.6:2.4 *dr*

89h 75% y 9.1:0.9 *dr*

89i 73% y 9.3:0.7 *dr*

89j 59% y 7.3:2.7 *dr*

89k 61% y 8.3:1.7 *dr*

89l 62% y 7.0:3.0 *dr*

[a]All the reactions were carried out with N-aryl-2-methylpyrrolidine **88** (1 mmol), *p*-chloranil **10** (1 mmol) and CH_3COONa (3 mmol) in toluene (5 mL) for 24 h at 90 °C. [b]Isolated yields of **89a-89l.** [c]The products were characterized by spectral data (IR, ^{1}H NMR, ^{13}C-NMR and HRMS).

We have also carried out the reaction using the racemic N-aryl-2-methylpyrrolidine **88** with *p*-chloranil **10** and obtained the tricyclic derivative **89**. The newly formed stereogenic centers are *syn* to each other as confirmed by single crystal X-ray analysis of the major diastereomer of the compound **89g** (Figure 7).

89g

Figure 7: X-ray crystal structure of **89g**

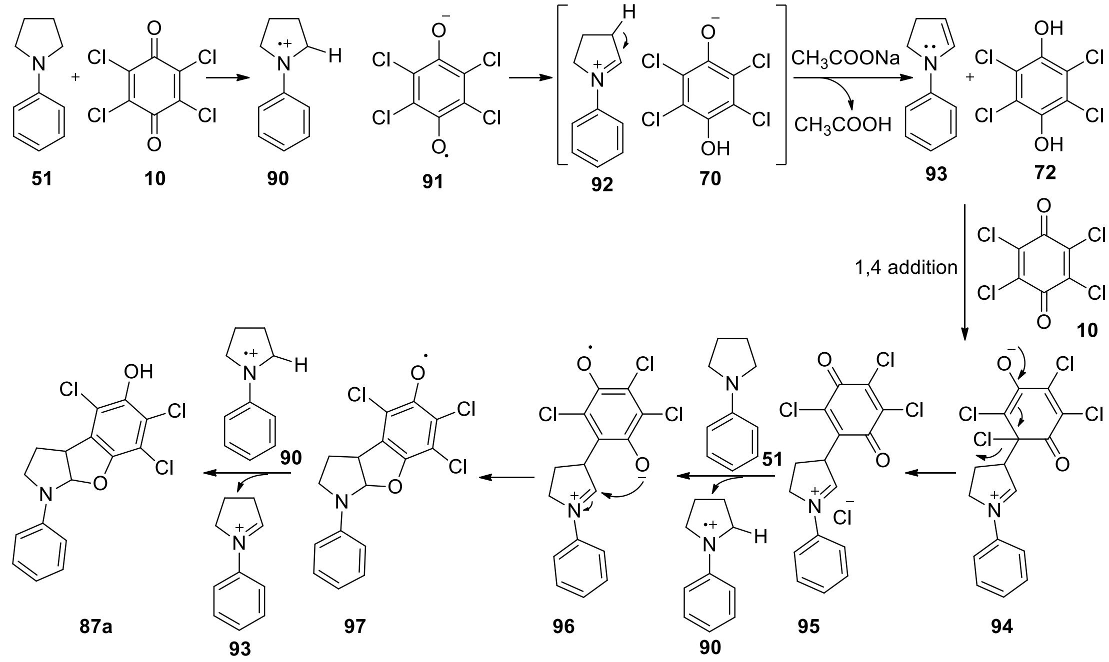
3.2.6 Plausible mechanism for the synthesis of fused benzofuropyrrolidine

A plausible mechanism for the formation of fused benzofuropyrrolidine **87a** is outlined in Scheme 19. The reaction of N-phenylpyrrolidine **51** and *p*-chloranil **10** would give the corresponding paramagnetic species **90** and **91** which subsequently could give the iminium ion **92** and hydroquinone anion **70**. The iminium ion **92** after further reaction with the base would give the corresponding enamine **93** which could undergo reaction with another *p*-chloranil molecule **10** to give the intermediate **94** subsequent elimination of chloride anion could give the intermediate **95** which could act as electron acceptor and accepts electron from parent amine to give the intermediate **96** that could cyclize to afford the tricyclic product **87a**.

Table 5. Crystal data and structure refinement for compound **89g**.

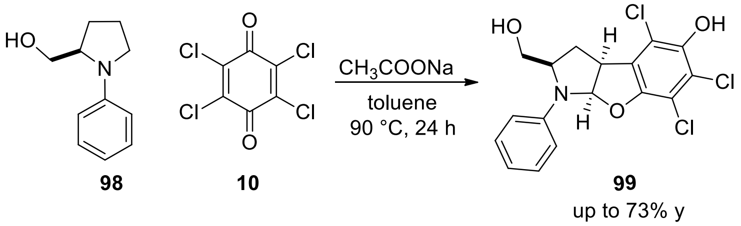
Identification code	Compound **89g**	
Empirical formula	$C_{18}H_{16}Cl_{3}NO_{3}$	
Formula weight	400.67	
Temperature	278(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C 2/c	
Unit cell dimensions	a = 25.625(3) Å	a= 90°.
	b = 6.9502(9) Å	b= 100.060(2)°.
	c = 20.061(3) Å	g = 90°.
Volume	3517.9(8) Å^{3}	
Z	8	
Density (calculated)	1.513 Mg/m^{3}	
Absorption coefficient	0.539 mm^{-1}	
F(000)	1648	
Crystal size	0.12 x 0.10 x 0.08 mm^{3}	
Theta range for data collection	1.614 to 26.457°.	
Index ranges	-32<=h<=32, -8<=k<=8, -25<=l<=24	
Reflections collected	17868	
Independent reflections	3626 [R(int) = 0.0281]	
Completeness to theta = 25.242°	100.0 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F^{2}	
Data / restraints / parameters	3626 / 0 / 228	
Goodness-of-fit on F^{2}	1.141	
Final R indices [I>2sigma(I)]	R_1 = 0.0578, wR_2 = 0.1299	
R indices (all data)	R_1 = 0.0635, wR_2 = 0.1334	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.358 and -0.317 e.Å^{-3}	

Scheme 19



We have also examined the reaction of chiral (1-phenylpyrrolidine-2-yl)methanol **98** and *p*-chloranil **10**. The corresponding coupled product **99** was obtained in 73% yield as a single diastereomer (Scheme 20).

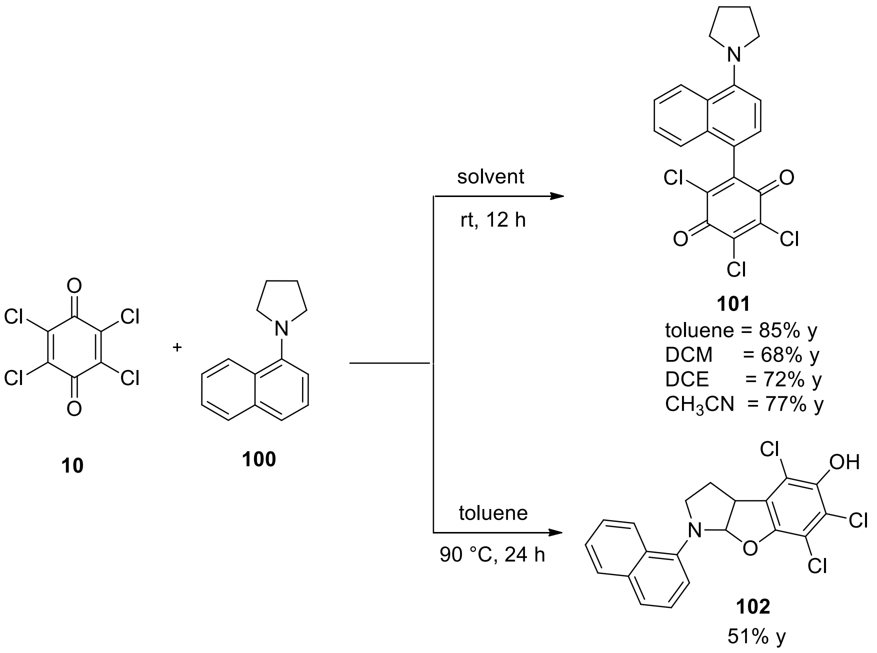
Scheme 20



3.2.7 Reaction of N-napthylpyrrolidine and *p*-chloranil

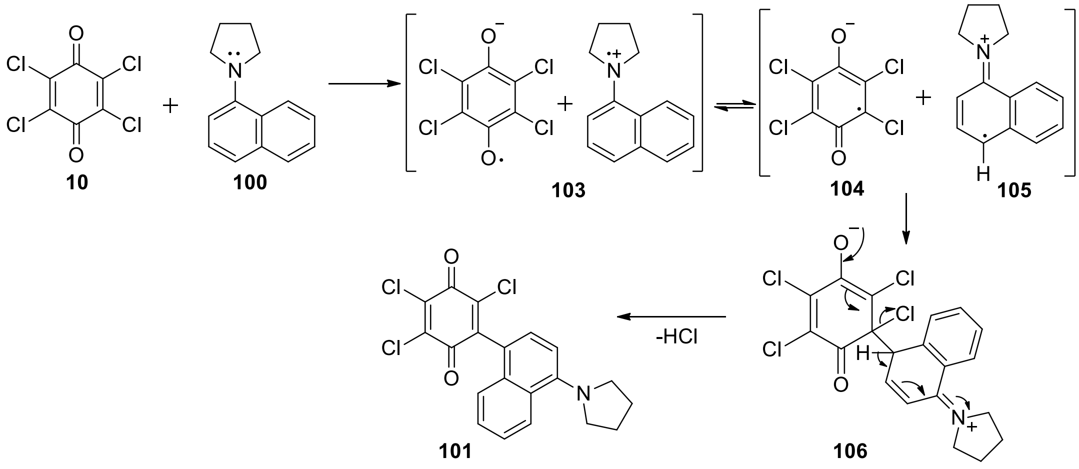
Interestingly, the N-napthylpyrrolidine **100** reacted with *p*-chloranil **10** to give the product **101** in 85% yield (Scheme 21). Also, the reaction in DCM, DCE and acetonitrile also gave the substituted product **101** in 68-85% yields (Scheme 21). However, the reaction in toluene at 90 °C for 24 h gave the tricyclic product **102** in 51% yield (Scheme 21).

Scheme 21



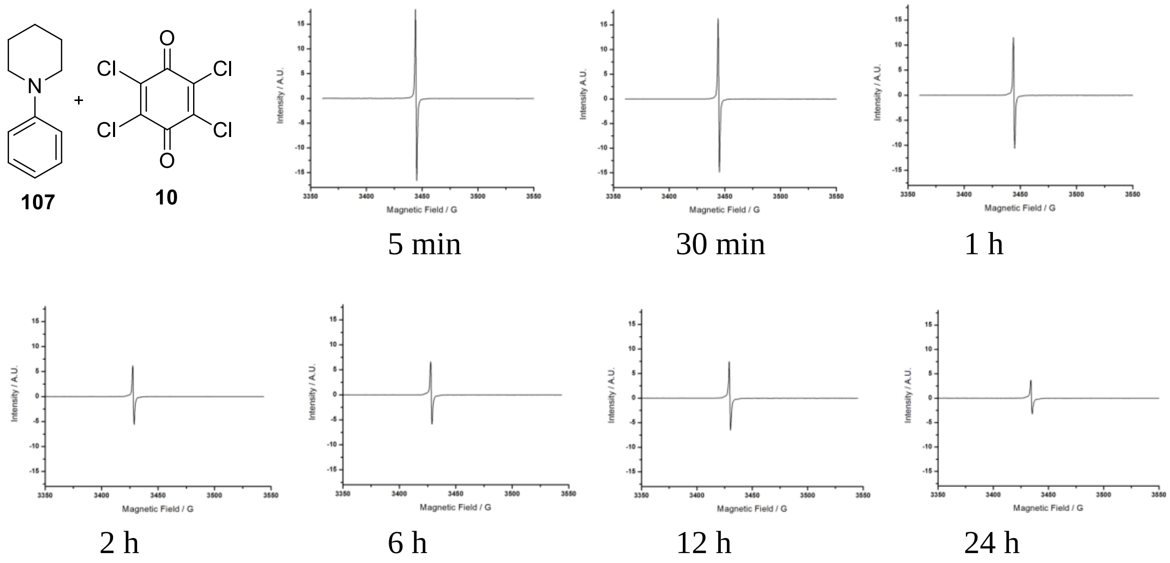
Whereas the reaction at room temperature may give the aromatic substitution product **101** by the mechanism outlined in Scheme 22, the reaction at 90 °C in toluene solvent may give the tricyclic product **102** through a mechanism similar to that outlined in Scheme 19.

Scheme 22



3.2.8 Electron transfer complex of N-phenylpiperidine with *p*-chloranil

We have also recorded the epr spectra of 1:1 mixture of N-phenylpiperidine **107** and *p*-chloranil **10** in neat, and PC solvent. The results are presented in Figure 8 & 9.

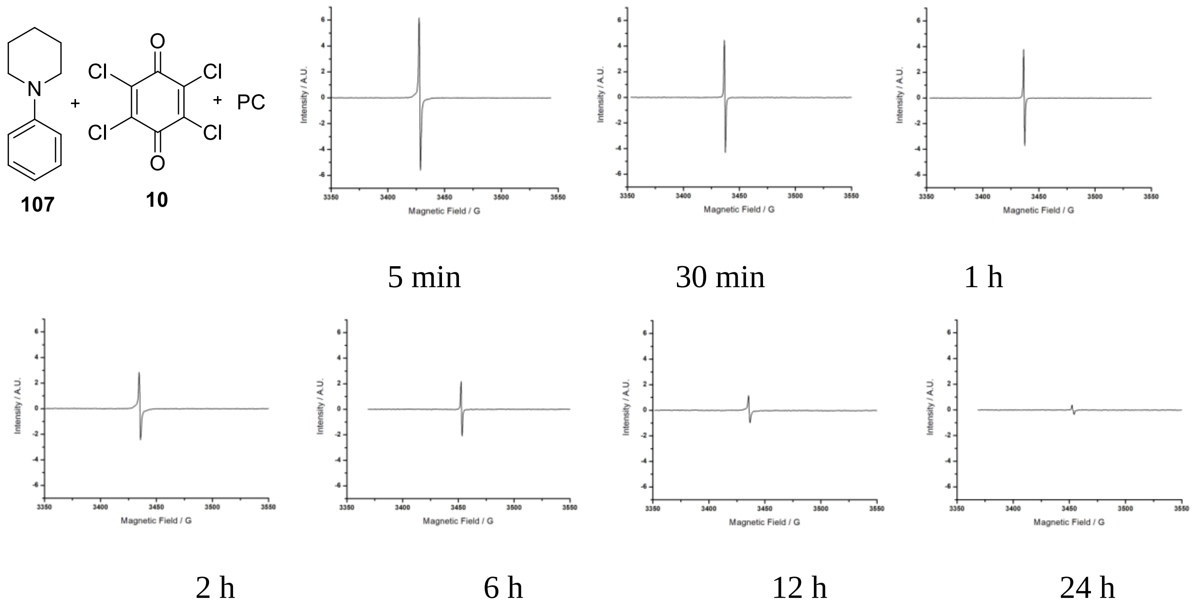


107 **10**

5 min 30 min 1 h

2 h 6 h 12 h 24 h

Figure 8: ESR spectra of N-phenylpiperidine **107** (0.02 mmol) with *p*-chloranil **10** (0.02 mmol) in neat condition.



107 **10**

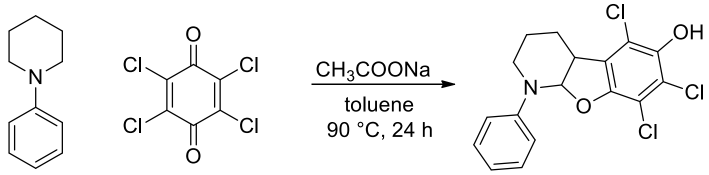
5 min 30 min 1 h

2 h 6 h 12 h 24 h

Figure 9: ESR spectra of N-phenylpiperidine **107** (0.02 mmol) with *p*-chloranil **10** (0.02 mmol) in PC solvent.

The strength of the signals decreases with time. After 24 h at room temperature the corresponding tetrahydrobenzofuropyridine **108** was obtained in 5% yield along with 2,3,5,6-tetrachlorobenzene-1,4-diol **72** in 37% yield. Presumably, the signal strength decreased as covalent intermediates and products are formed from the initially formed paramagnetic intermediates. When the reaction was carried out using CH_3COONa at 90 °C for 24 h in toluene, the corresponding tricyclic product **108** was obtained in 45% yield (Scheme 23).

Scheme 23



107 **10** **108**

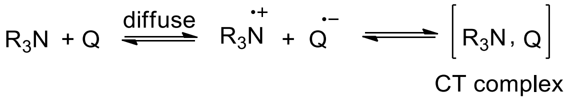
45% y

The tricyclic products obtained in the reaction of *p*-chloranil with aryl pyrrolidines and piperidines have potential for further exploitation in organic synthesis.

3.2.9 Electricity harvesting organic electrochemical cell using tertiary amine donors and *p*-chloranil

Tertiary amines readily undergo electron transfer reactions with acceptors to give the radical cation–anion pair in dipolar aprotic solvent like PC (propylene carbonate) in equilibrium with the corresponding diamagnetic and paramagnetic charge transfer (CT) complexes (Scheme 24).[13]

Scheme 24



$$R_3N + Q \underset{}{\overset{\text{diffuse}}{\rightleftharpoons}} R_3\overset{\bullet+}{N} + \overset{\bullet-}{Q} \rightleftharpoons \left[R_3N, Q\right]$$

CT complex

These reversible electron transfer reactions take place at ambient temperature in the ground state of the amine donors and *p*-chloranil acceptor and the barriers are overcome by ambient heat (Figure 10).

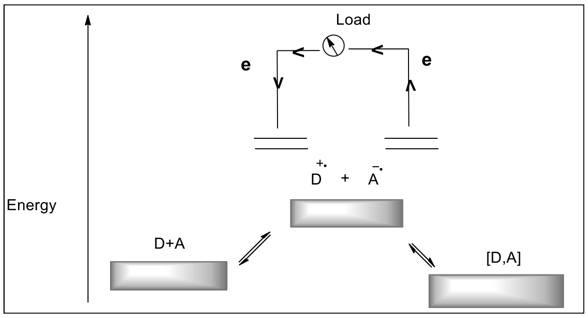


Figure 10. Schematic energy level diagram of donor-acceptor system at ambient temperature

We have envisaged construction of an electrochemical cell so as to transport the charge carriers, i.e. electron in $Q^{-\cdot}$ and the hole (+ve charge) in $R_3N^{+\cdot}$ formed in such reactions under ambient temperature conditions to produce electricity (Fig. 4.1). Accordingly, a brief review of reports on the organic solar cells would facilitate the discussion.

3.2.10 Organic solar cell: Donor acceptor solar cells

An organic solar cell device is an emerging class of photovoltaic cell device that converts the energy of light directly into electricity by the photovoltaic effect. Although, several inorganic materials are available for the conversion of sunlight into electrical energy, there has been sustained efforts to develop organic solar cells in the last four decades.[47-53] The small organic molecules (pigments),[47,48,53] and semiconducting polymers were incorporated into organic solar cells resulting in remarkable improvements in the recent years.[49,52,54] The semiconducting organic materials transport electric current and absorb light in the ultraviolet

(UV)-visible portion of the solar spectrum due to expanded conjugation of the π-bonds. The donor polymers and acceptors used in the heterojunction solar cells are shown in Figure 11.

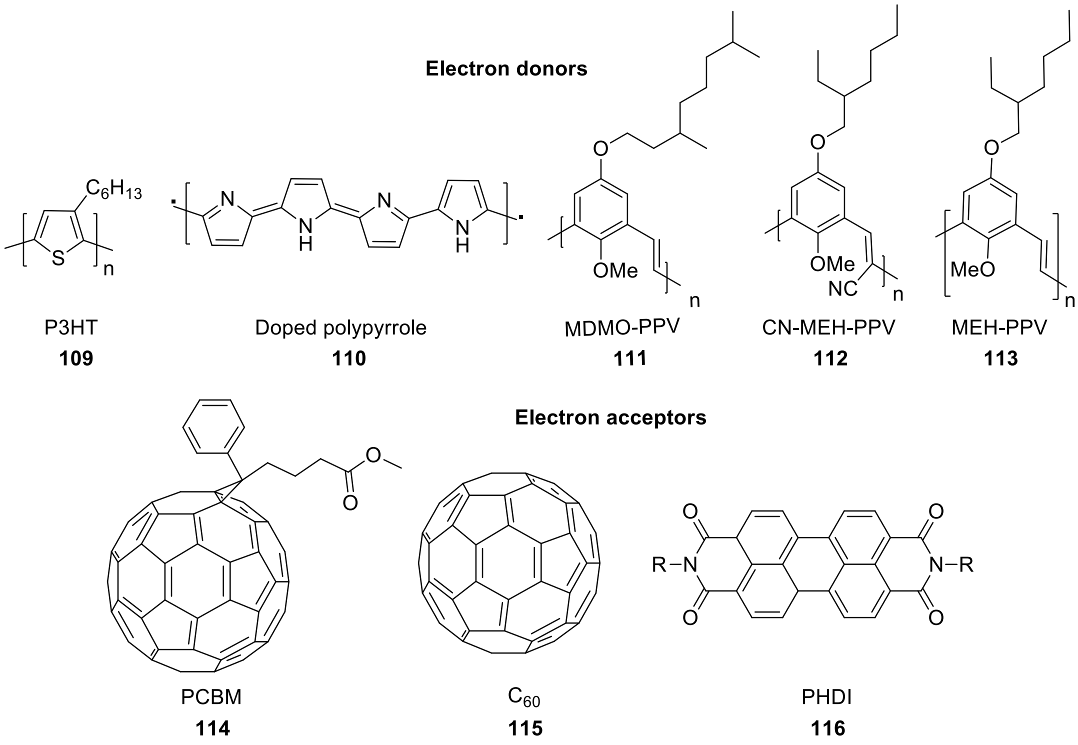


Figure 11: Major donor polymers and acceptors used in the organic solar cells.

As shown in Figure 12, the excitation of the D molecule by light elevates an electron on the HOMO (D) to the LUMO (D) and the electron transfer takes place to the LUMO (A), giving the D$^+$ and A$^-$ states. These charges are transported to the cathode and anode to produce electric power.

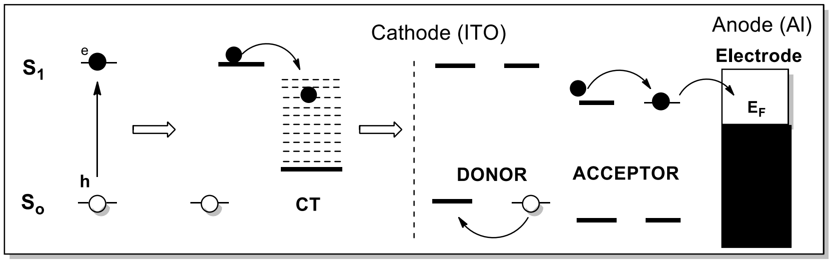


Figure 12: Molecular orbital diagram of photoinduced electron transfer for donor and acceptor.

Previously, electrochemical cells were constructed in two layer and multiple layer configurations in this laboratory. These electrochemical cells were constructed using different amines and amides as donors, *p*-chloranil **10** and benzoquinone are as acceptors in PC solvent with TiO_2/PEO (polyethylene oxide) support using graphite and aluminum electrodes. The cell was characterized by current (I)-voltage (v) measurements.

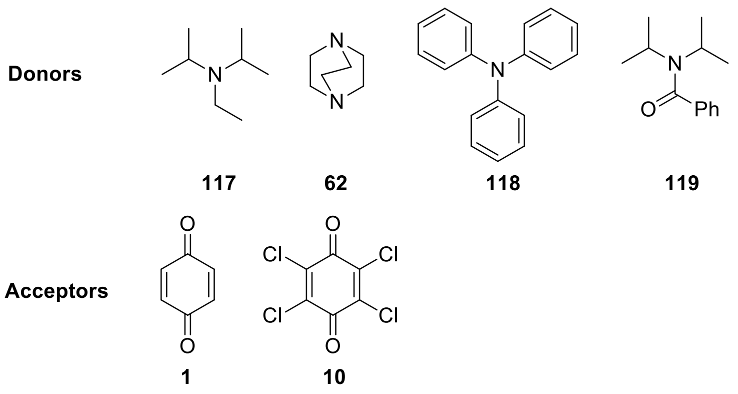
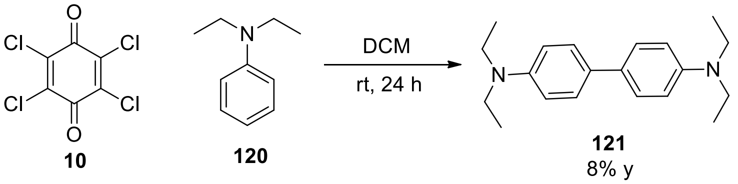


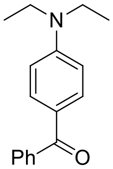
Figure 13: Eelectron donors and acceptors for use in electrochemical cell studies.

It was of interest to us, to utilize the aromatic tertiary amines for electron donors and *p*-chloranil as acceptor for the construction of the electricity harvesting organic electrochemical cell. Also, we have observed that of benzidine **121** was formed in the reaction of N,N-diethylaniline **120** and *p*-chloranil **10** in dichloromethane solvent and this side reaction would decrease the power produced by the cell with time (Scheme 25).

Scheme 25



Therefore, we have prepared the p-benzoyl N,N-diethylaniline **122** to construct the electricity harvesting organic electrochemical cell (Figure 14).



122

Figure 14: Eelectron donor for use in electrochemical cell studies.

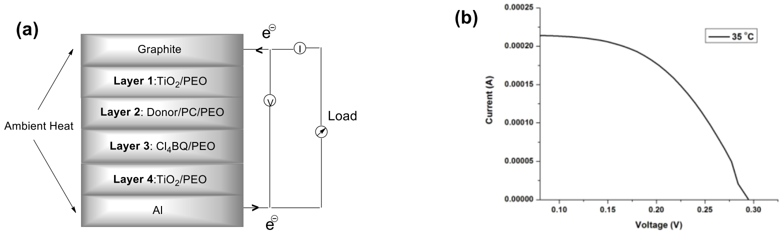
We have observed change upon mixing amine and *p*-chloranil. However, paramagnetic intermediates were not formed in solvents such as DCM and PC But week charge transfer complexes were formed as indicated UV-Visible spectral analysis (Figure 15).

(a) (b)

Figure 15: UV-Visible spectra of a mixuture of amine **122** (1 X 10^{-4} mol L^{-1}) and *p*-chloranil **10** (1 X 10^{-4} mol L^{-1}) in PC at 25 °C. (b) Expanded UV-Visible spectra.

3.2.11 Donor-Acceptor organic electrochemical cell

The cells can be easily constructed by making donor and acceptor pastes with TiO_2, polyethylene oxide (PEO) and propylene carbonate (PC) and coating on commercially available Al (0.2mm x 5cm x 5cm) and graphite sheet (0.4mm x 5cm x 5cm) following previous work from this laboratory.[55] Initially, we have constructed a simple four layer cell using Al foil and graphite sheet. The mixture of TiO_2 (rutile), *p*-chloranil, and polyethylene oxide (PEO) past prepared using DCM was coated on Al foil and the mixture of TiO_2 (rutile), 4-(diethylamino)phenyl)(phenyl)methanone, PC and PEO past prepared using DCM was coated on graphite sheet. The foils were then sandwiched to construct the electrochemical cell. The four layer electrochemical cell produced power (Pmax) of 0.67 mWwith fill factor (FF) of 0.247 at 35 °C but there was very little power after 48 h (Figure 16).



After 1 h		**After 48 h**
Donor:	**Pmax/mW/FF(35 °C)**	**Pmax/mW/FF(35 °C)**
Ph-CO-C_6H_4-NEt_2	0.670/0.247	0.029/0.469

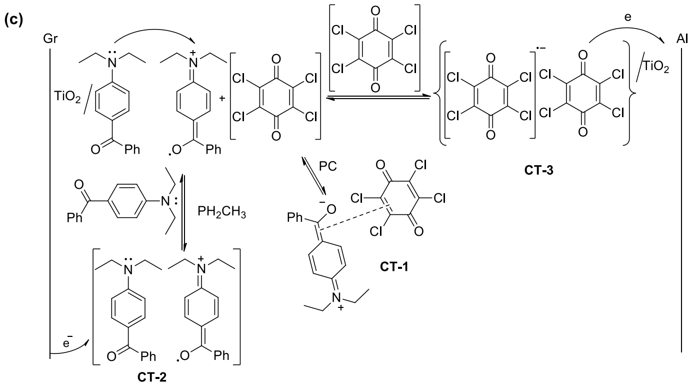
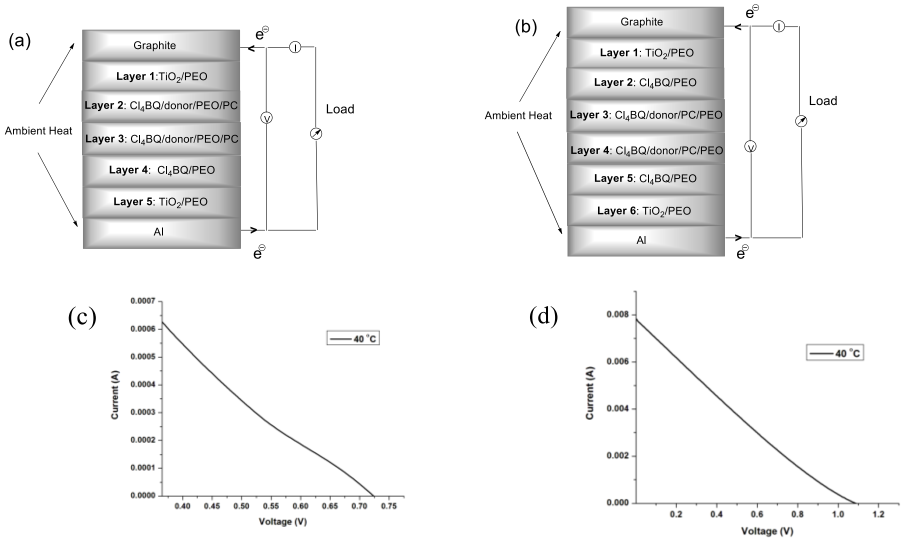


Figure 16. (a) Schematic diagram of multi-layer cell configuration with acceptor and donor layer (b) Representative IV curve for the cell (ES, Table 6, entry 1). (c) Tentative mechanism for electron transport.

A tentative mechanism for electron transport from cathode to anode side is shown in Figure 16(c). The *p*-chloranil would accept an electron from *p*-benzoyl N,N-diethylaniline to give the paramagnetic intermediates of radical anion and radical cation, which will be in equilibrium with the CT-1, CT-2 and CT-3 complexes. The formation of the charge transfer complexes especially the complex CT-1 would lower the conductance if it precipitates out of the solution (Figure 16 (c)).

We have also constructed multi-layer cell in two different configurations 17a and 17b (Figure 17). There was improvement in performance by increasing layers as shown in Figure 17(a) & 17(b).



After 1 h		**After 1 h**
Donor:	**Pmax/mW/FF(40 °C)**	**Pmax/mW/FF(40 °C)**
Ph-CO-C_6H_4-NEt_2	1.898/0.248	2.496/0.198
After 48 h		**After 48 h**
Donor:	**Pmax/mW/FF(40 °C)**	**Pmax/mW/FF(40 °C)**
Ph-CO-C_6H_4-NEt_2	0.096/0.221	1.882/0.221

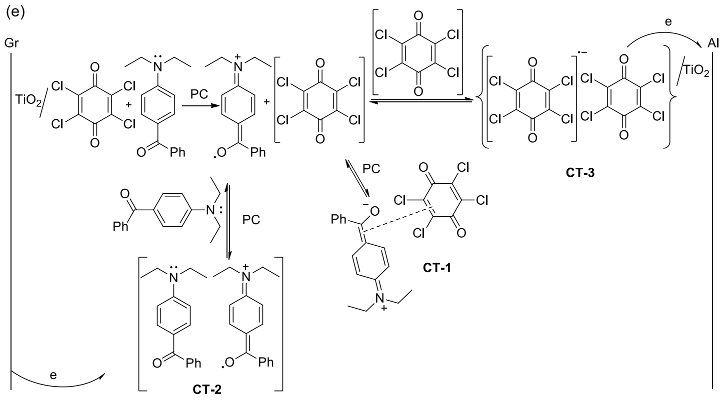
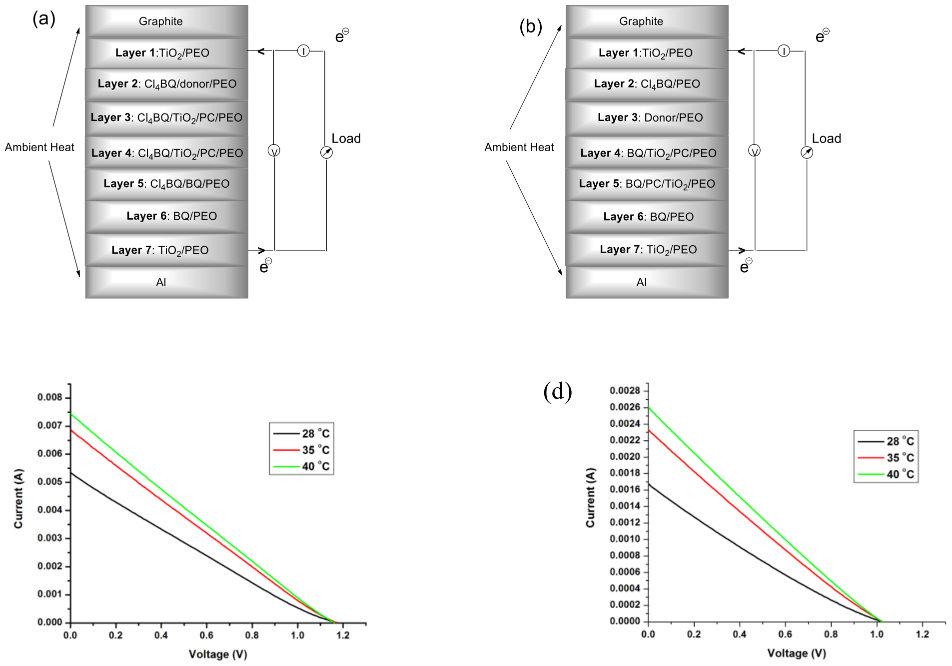


Figure 17. (a) & (b) Schematic diagram of multi-layer cell configuration with acceptor and donor layer. (c) & (d) Representative IV curve for the cell (ES, Table 6, entries 2 & 3, TiO_2 donor). (e) Tentative mechanism for electron transport.

Whereas the cell constructed using the *p*-chloranil, amine donor and PC closer to the Gr gave very little power after 1 h (Figure 17a and 17c), the cell constructed using the *p*-

chloranil, amine and PC in the middle layer and *p*-chloranil also in the layer 2 and layer 5 gave relatively higher power even after 48 h (Figure 17).

It was reported that the radical anion produced from *p*-chloranil with high electron affinity (EA = 2.4 eV) was reported to be stabilized to lesser extent compared to the anion radical of BQ (EA = 1.4 eV). Therefore, we have also constructed the cell using BQ in layer closer to Al electrode to examine whether the *p*-chloranil radical anion could transfer electron to BQ in two configurations (Figure 18). The IV data of these cell are listed in Figure 18(a) & 18(b).



After 1 h		**After 1 h**
Donor:	**Pmax/mW/FF(40 °C)**	**Pmax/mW/FF(40 °C)**
Ph-CO-C_6H_4-NEt_2	1.492/0.237	1.606/0.241
After 48 h		**After 48 h**
Donor:	**Pmax/mW/FF(40 °C)**	**Pmax/mW/FF(40 °C)**
Ph-CO-C_6H_4-NEt_2	1.512/0.226	0.627/0.236

Figure 18 (continued)

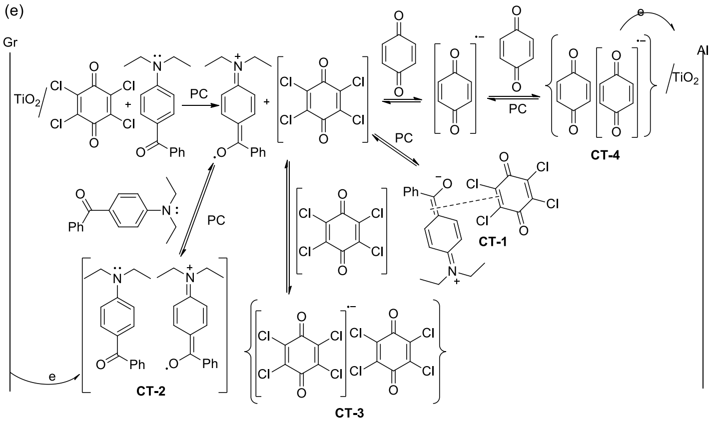


Figure 18. (a) and (b) Schematic diagram of multi-layer cell configuration with acceptor and donor layer (c) and (d) Representative IV curve for the cell (ES, Table 7, entry 1, TiO_2 donor) and (ES, Table 8, entry 1, TiO_2 donor) (e) Tentative mechanism for electron transport.

In these configurations, the Pmax at 40 °C realized after 1 h and 48 h are almost the same in the configuration 18a but becomes lower in the configuration 18b (Figure 18).

The dialkylsulphones are also electron acceptors. We have also constructed cells in different configurations using BQ and Me_2SO_2 both with electron affinity lesser than *p*-chloranil. We have observed that the performance of the cells using Me_2SO_2 was better than cells using BQ as revealed by the IV data (Figure 19a and 19b).

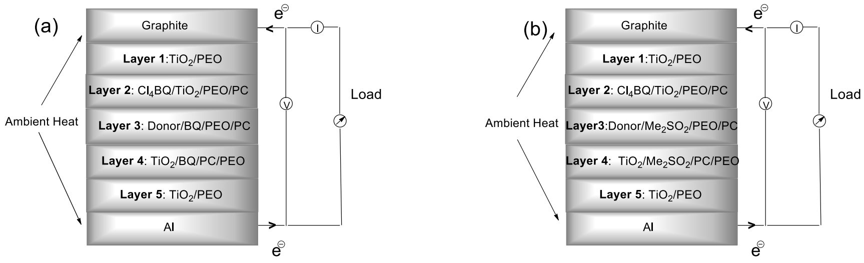
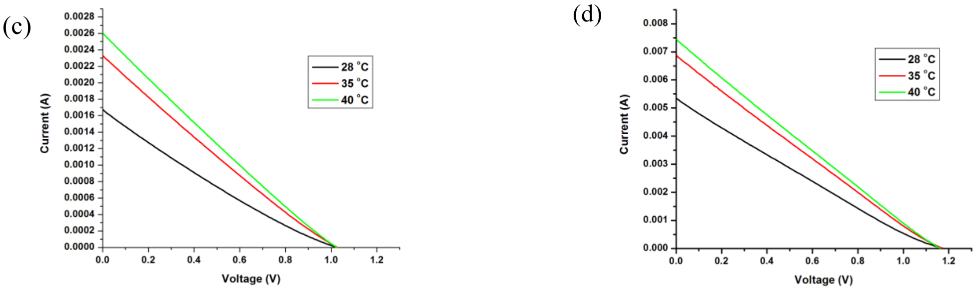


Figure 19 (continued)



After 1 h
Donor: Pmax/mW/FF(40 °C)
Ph-CO-C_6H_4-NEt_2 1.203/0.259
After 48 h
Donor: Pmax/mW/FF(40 °C)
Ph-CO-C_6H_4-NEt_2 0.718/0.200

After 1 h
Pmax/mW/FF(40 °C)
2.85/0.255
After 48 h
Pmax/mW/FF(40 °C)
1.683/0.251

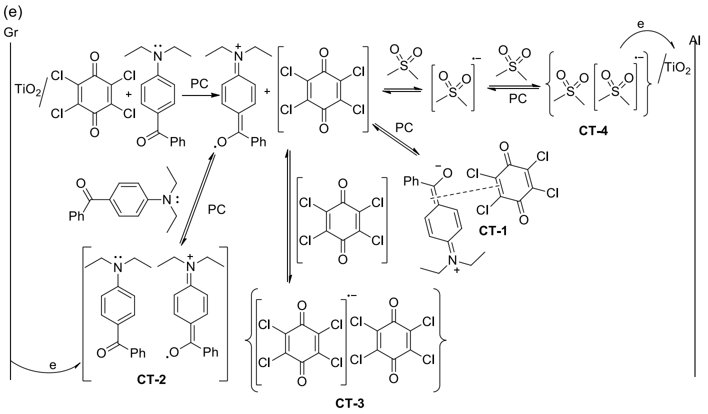


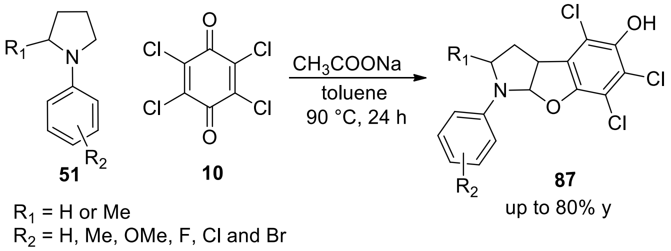
Figure 19. (a) and (b) Schematic diagram of multi-layer cell configuration with acceptor and donor layer. (c) and (d) Representative IV curve for the cell (ES, Table 9, entry 1, TiO_2 donor) and (ES, Table 9, entry 2, TiO_2 donor) (e) Tentative mechanism for electron transport when using Me_2SO_2.

Although, the performance of the cells improved using the BQ or Me_2SO_2 as additional electron transfer, the power produced by the more simple amines like N,N-diisopropylethyl amine were much higher under similar conditions.[55] Accordingly, use of stronger donors and reagents to stabilize the quinone radical aniones may lead to more fruitful results for practical applications of these electricity harvesting cells.

3.3 Conclusions

Systematic studies on the reaction of tertiary amines (N-phenyl-1,2,3,4-tetrahydroisoquinoline, N-phenylpyrrolidine and N-phenylpiperidine) with *p*-chloranil gave paramagnetic intermediates but the esr signals intensity decreased with time, indicating that the initially formed paramagnetic intermediates participate in further reactions. Accordingly, we have developed the method for cross coupling of N-phenyl-1,2,3,4-tetrahydroisoquinoline with nitromethane to obtain the product in 82% yield. Also, we have developed a method for the synthesis of tricyclic product **87** using *p*-chloranil **10** and N-phenylpyrrolidines **51** *via* the formation of iminium ion and enamine intermediates. The method described here is metal free, ecofriendly and requires readily accessible starting materials Hence, this method has good synthetic potential for further exploitations (Scheme 26).

Scheme 26



Also, we have constructed electricity harvesting electrochemical cell using *p*-benzoyl N,N-diethylaniline and *p*-chloranil with different configurations, which also has potential for the development of electricity harvesting cell devices for practical applications.

3.4 Experimental Section

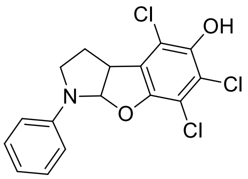
3.4.1 General information

Several informations given in the section **1.4** are also applicable for the experiments outlined in this section. Procedures for synthesis of N-arylpyrrolidines were given in the Chaptor 1 (Section **1.4**). *p*-Chloranil, sodiumacetate, *P*-benzoquinone (BQ) and TiO_2 were purchased from Avra chemicals (India). Propylene carbonate (PC), and polyethylene oxide (PEO) were purchased from Sigma Aldrich. PC and EC were always kept under molecular sieves. Graphite sheet (0.4mm thickness, 5cm x 5cm, Resistivity, $\rho = 2x10^{-4}\Omega.m$) was purchased from Falcon Graphite Industries, Hyderabad, India. Aluminium Foil (0.2mm thickness, 5cm x 5cm, Resistivity, $\rho = 2x10^{-5}\Omega.m$) was purchased from Aluminium Enterprises and Rasik Metals, Hyderabad, India. EPR spectra was recorded on a Bruker-ER073 instrument equipped with an EMX micro X source for X band measurement using Xenon 1.1b.60 software provided by the manufacturer. Electrical measurements were carried out by ZAHNER instrument using CIMPS software. The current-voltage curve was drawn using Origin software.

3.4.2 General procedure for the Synthesis of benzofuropyrrolidine derivatives

A mixture of N-arylpyrrlidine **51** (1 mmol), Chloranil **10** (1 mmol) and anhydrous CH_3COONa (3 mmol) in toluene (5 mL) was stirred for 24 hours at 90 °C. After completion of the reaction, the solvent was evaporated and ethylacetate (10 mL) and water (5 mL) were added the combined organic layer was washed with brine (10 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography on silica gel (100-200 mesh) using EtOAc:hexane (5:95) as an eluent to get benzofuropyrrolidines **87**.

4,6,7-Trichloro-1-phenyl-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-b]pyrrol-5-ol (87a)



87a

Yield **:** 0.22 g (62%); white solid

mp : 119-202 °C

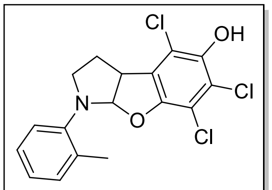
IR (KBr) : (cm^{-1}) 3504, 2978, 2855, 1595, 1575, 1458, 1380, 1195, 1003, 877, 751.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.37-7.33 (m, 2H), 7.01 (d, *J* = 7.88, Hz 2H), 6.94 (t, *J* = 7.32 Hz, 1H), 6.54 (d, *J* = 6.72 Hz, 1H), 5.56 (s, 1H), 4.26-4.20 (m, 1H), 3.71-3.66 (m, 1H), 3.50-3.44 (m, 1H), 2.62-2.52 (m, 1H), 2.36-2.29 (m, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 149.6, 144.4, 142.7, 129.4, 127.3, 119.5, 119.3, 115.4, 114.2, 112.7, 99.4, 47.4, 46.6, 29.3.

HRMS (*m/z*) : Calculated for $C_{16}H_{12}Cl_3NO_2$ (M+H): 356.0013, Found (M+H): 356.0011.

4,6,7-Trichloro-1-(*o*-tolyl)-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-b]pyrrol-5-ol (87b)



87b

Yield **:** 0.27 g (73%); white solid.

mp : 164-166 °C.

IR (KBr) : (cm^{-1}) 3422, 2952, 2822, 1603, 1500, 1423, 1376, 1180, 1113, 886, 818, 762, 674.

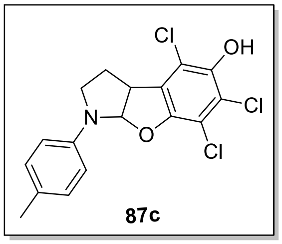
^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.36-7.34 (m, 1H), 7.22 (t, *J* = 6.94Hz 2H), 7.12-7.08 (m, 1H), 6.41 (d, *J* = 6.2 Hz, 1H), 5.52 (s, 1H), 4.25-4.21 (m, 1H), 3.47-3.40 (m, 1H), 3.37-3.33 (m, 1H), 2.48-2.38 (m, 1H), 2.35 (s, 3H), 2.20-2.16 (m, 1H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 150.7, 142.8, 142.4, 132.4, 131.2, 127.3, 126.5, 124.6, 123.5, 118.9, 115.6, 111.9, 102.2, 48.5, 47.5, 30.6, 18.7.

HRMS (*m/z*) : Calculated for $C_{17}H_{14}Cl_3NO_2$ (M+H): 370.0169, Found (M+H): 370.0165.

4,6,7-Trichloro-1-(*p*-tolyl)-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-b]pyrrol-5-ol (87c)

Yield **:** 0.24 g (64%); white solid.



87c

mp : 205-208 °C.

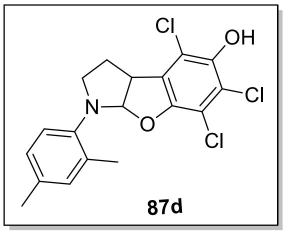
IR (KBr) : (cm^{-1}) 3473, 2962, 2921, 2828, 1603, 1583, 1438, 1350, 1283, 1154, 1004, 973, 875, 802, 767.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.15 (d, *J* = 8.5 Hz 2H), 6.91 (d, *J* = 8.4 Hz, 2H), 6.52 (d, *J* = 6.72 Hz, 1H), 5.64 (bs, 1H), 4.24-4.19 (m, 1H), 3.68-3.62 (m, 1H), 3.47-3.41 (m, 1H), 2.61-2.51 (m, 1H), 2.33 (s, 1H), 2.31-2.26 (m, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 149.7, 143.3, 142.6, 142.1, 129.9, 128.8, 127.4, 119.2, 118.9, 115.4, 114.3, 112.7, 99.8, 47.4, 46.7, 29.4, 20.5.

HRMS (*m/z*) : Calculated for $C_{17}H_{14}Cl_3NO_2$ (M+H): 370.0169, Found (M+H): 370.0164.

4,6,7-Trichloro-1-(2,4-dimethylphenyl)-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-b]pyrrol-5-ol (87d)



Yield **:** 0.26 g (68%); brown solid.

mp : 136-138 °C.

IR (KBr) : (cm^{-1}) 3380, 2977, 2921, 2843, 1598, 1510, 1464, 1433, 1350, 1221, 1180, 978, 875, 798, 668, 581.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.29-7.26 (m, 1H), 7.04 (d, J = 10.84 Hz 2H), 6.36 (d, J = 6.2 Hz, 1H), 5.53 (s, 1H), 4.24-4.20 (m, 1H), 3.44-3.38 (m, 1H), 3.33-3.29 (m, 1H), 2.48-2.38 (m, 1H), 2.33 (s, 3H), 2.31 (s, 3H), 2.19-2.14 (m, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 150.7, 142.3, 140.2, 134.3, 132.5, 131.8, 127.4, 127.1, 123.8, 118.8, 115.5, 111.9, 102.6, 48.7, 47.5, 30.7, 20.8, 18.5.

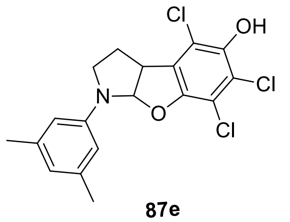
HRMS (*m/z*) : Calculated for $C_{18}H_{16}Cl_3NO_2$ (M+H): 384.0326, Found (M+H): 384.0321.

4,6,7-Trichloro-1-(3,5-dimethylphenyl)-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-b]pyrrol-5-ol (87e)

Yield **:** 0.27 g (71%); white solid.

mp : 198-201 °C.

IR (KBr) : (cm^{-1}) 3401, 2983, 2916, 2848, 1593, 1402, 1304, 1195, 1030, 984, 886, 705, 632.



87e

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 6.63 (s, 2H), 6.59 (s, 1H), 6.53 (d, *J* = 6.72 Hz 1H), 5.55 (s, 1H), 4.22-4.17 (m, 1H), 3.68-3.63 (m, 1H), 3.47-3.41 (m, 1H), 2.58-2.49 (m, 1H), 2.34 (s, 6H), 2.32-2.25 (m, 1H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 149.7, 144.4, 142.6, 139.0, 127.4, 121.5, 119.2, 115.4, 112.7, 112.2, 99.6, 47.3, 46.7, 29.3, 21.7.

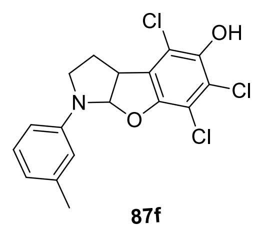
HRMS (*m/z*) : Calculated for $C_{18}H_{16}Cl_3NO_2$ (M+H): 384.0326, Found (M+H): 384.0326.

4,6,7-Trichloro-1-(*m*-tolyl)-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-b]pyrrol-5-ol (87f)

Yield **:** 0.24 g (65%); white solid.

mp : 175-178 °C.

IR (KBr) : (cm^{-1}) 3405, 2955, 2845, 2831, 1602, 1496, 1412, 1350, 1124, 999, 872, 746, 671.



87f

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.23 (t, *J* = 7.98 Hz 1H), 6.82 (d, *J* = 7.24 Hz, 2H), 6.76 (t, *J* = 7.56 Hz, 1H), 6.54 (d, *J* = 6.68 Hz, 1H), 5.57 (s, 1H), 4.24-4.19 (m, 1H), 3.70-3.65 (m, 1H), 3.49-3.43 (m, 1H), 2.60-2.51 (m, 1H), 2.39 (s, 3H), 2.35-2.28 (m, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 149.6, 144.4, 143.3, 142.7, 139.2, 129.2, 127.3, 120.4, 119.2, 118.9, 115.4, 114.9, 112.7, 111.5, 99.5, 47.4, 46.7, 29.3, 21.8;

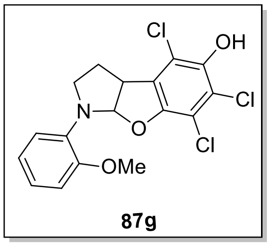
HRMS (*m/z*) : Calculated for $C_{17}H_{14}Cl_3NO_2$ (M+H): 370.0169, Found (M+H): 370.0161.

4,6,7-Trichloro-1-(2-methoxyphenyl)-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-b]pyrrol-5-ol (87g)

Yield **:** 0.23 g (59%); white solid.

mp : 159-162 °C.

IR (KBr) : (cm^{-1}) 3520, 3065, 2946, 2833, 1598, 1505, 1423, 1361, 1304, 1257, 1232, 1113, 1020, 994, 880, 741.



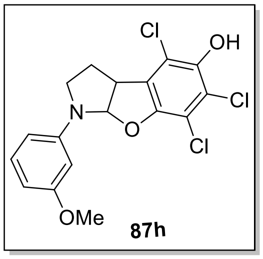
87g

1H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.10-7.05 (m, 2H), 7.00-6.94 (m, 3H), 5.54 (s, 1H), 4.25 (t, *J* = 7.74 Hz, 1H), 3.93 (s, 3H), 3.54 (t, *J* = 8.22 Hz, 1H), 3.42-3.35 (m, 1H), 2.49-2.38 (m, 1H), 2.23-2.19 (m, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 151.2, 150.7, 142.5, 133.4, 127.3, 123.1, 121.0, 120.3, 118.9, 115.6, 111.9, 111.5, 100.5, 55.5, 47.3, 29.8.

HRMS (*m/z*) : Calculated for $C_{17}H_{14}Cl_3NO_3$ (M+H): 386.0118, Found (M+H): 370. 386.0110.

4,6,7-Trichloro-1-(3-methoxyphenyl)-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-b]pyrrol-5-ol (87h)



Yield **:** 0.24 g (67%); white solid.

mp : 135-138 °C.

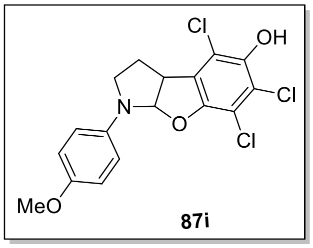
IR (KBr) : (cm^{-1}) 3380, 2941, 2838, 1598, 1495, 1459, 1423, 1350, 1221, 1159, 1056, 875, 751, 674, 570.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.24 (t, *J* = 8.16 Hz 1H), 6.63-6.60 (m, 1H), 6.53 (t, *J* = 4.52 Hz, 1H), 6.50-6.47 (m, 2H), 5.65 (bs, 1H), 4.22-4.17 (m, 1H), 3.85 (m, 3H), 3.67-3.61 (m, 1H), 3.48-3.42 (m, 1H), 2.60-2.50 (m, 1H), 2.33-2.26 (m, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 160.6, 149.5, 145.8, 142.7, 130.1, 127.3, 119.3, 115.5, 112.7, 107.2, 104.3, 101.1, 99.4, 55.3, 47.4, 46.8, 29.2.

HRMS (*m/z*) : Calculated for $C_{17}H_{14}Cl_3NO_3$ (M+H): 386.0118, Found (M+H): 386.0112.

4,6,7-Trichloro-1-(4-methoxyphenyl)-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-b]pyrrol-5-ol (87i)


87i

Yield : 0.30 g (78%); white solid.

mp : 164-166 °C

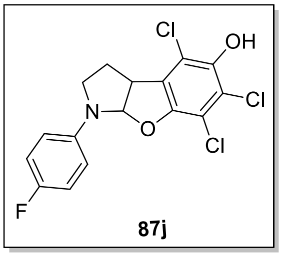
IR (KBr) : (cm^{-1}) 3303, 2946, 2859, 1600, 1505, 1428, 1376, 1356, 1237, 1030, 989, 875, 813, 720, 627.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 6.96-6.90 (m, 4H), 6.47 (d, 1H), 5.63 (s, 1H), 4.21-4.17 (m, 1H), 3.81 (s, 1H), 3.63-3.59 (m, 1H), 3.44-3.39 (m, 1H), 2.59-2.51 (m, 1H), 2.29-2.23 (m 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 153.4, 149.7, 142.6, 138.5, 127.4, 119.2, 115.5, 115.4, 114.9, 112.6, 100.3, 55.7, 47.4, 47.0, 29.5.

HRMS (*m/z*) : Calculated for $C_{17}H_{14}Cl_3NO_3$ (M+H): 386.0118, Found (M+H): 386.0110.

4,6,7-Trichloro-1-(4-fluorophenyl)-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-b]pyrrol-5-ol (87j)


87j

Yield : 0.19 g (51%); white solid.

mp : 179-182 °C.

IR (KBr) : (cm^{-1}) 3504, 2953, 2843, 1608, 1516, 1458, 1422, 1381, 1304, 1211, 1164, 994, 880, 818, 684, 627.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.06-7.01 (m, 2H), 6.94-6.91 (m, 2H), 6.47-6.45 (m, 1H), 5.55 (bs, 1H), 4.26-4.20 (m, 1H), 3.65-3.59 (m, 1H), 3.46-3.40 (m, 1H), 2.61-2.52 (m, 1H), 2.34-2.27 (m, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 158.2, 155.8, 149.5, 142.8, 140.8, 127.2, 119.3, 116.0, 115.7, 115.4, 115.3, 115.2, 112.7, 99.7, 47.5, 47.1, 29.4.

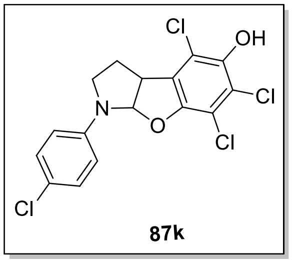
HRMS (*m/z*) : Calculated for $C_{16}H_{14}FCl_3NO_2$ (M+H): 389.9623, Found (M+H): 389.9614.

4,6,7-Trichloro-1-(4-chlorophenyl)-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-b]pyrrol-5-ol (87k)

Yield **:** 0.22 g (55%); white solid.

mp : 207-210 °C.

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



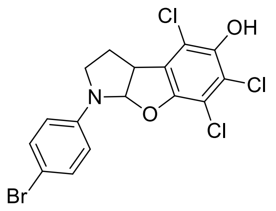
87k

^{1}H NMR : (400 MHz, DMSO-D_6, δ ppm) 9.90 (s, 1H), 7.33 (d, *J* = 7.16 Hz, 2H), 6.96 (d, *J* = 7.2 Hz, 2H), 6.66 (d, *J* = 5.4 Hz, 1H), 4.32-4.28 (m, 1H), 3.63-3.59 (m, 1H), 3.30-3.25 (m, 1H), 2.49-2.44 (m, 1H), 2.18-2.13 (m, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 148.6, 144.0, 143.3, 128.8, 127.6, 122.6, 120.7, 118.1, 115.7, 111.0, 98.9, 46.9, 46.3, 28.8.

HRMS (*m/z*) : Calculated for $C_{16}H_{14}Cl_4NO_2$ (M+H): 373.9918, Found (M+H): 373.9913.

1-(4-Bromophenyl)-4,6,7-trichloro-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-b]pyrrol-5-ol (87l)



87l

Yield **:** 0.29 g (66%); brown solid.

mp : 151-153 °C.

IR (KBr) : (cm^{-1}) 3494, 2913, 2803, 1601, 1526, 1428, 1419, 1354, 1256, 1121, 1064, 977, 855, 805, 761, 618.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 9.90 (s, 1H), 7.43 (d, *J* = 8.70 Hz, 2H), 6.89 (d, *J* = 8.70 Hz, 2H), 6.65 (d, *J* = 6.96 Hz, 1H), 4.32-4.27 (m, 1H), 3.62-3.56 (m, 1H), 3.28-3.23 (m, 1H), 2.49-2.42 (m, 1H), 2.19-2.12 (m, 1H).

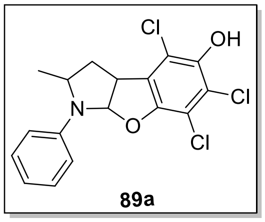
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 149.9, 145.3, 144.9, 132.9, 128.8, 122.0, 119.4, 117.4, 112.3, 111.7, 100.1, 48.3, 48.2, 30.1.

HRMS : (*m/z*): Calculated for $C_{16}H_{14}Cl_4NO_2$ (M+H): 433.9118, Found (M+H): 433.9120.

4.4.3 General procedure for the Synthesis of methyl benzofuropyrrolidine derivatives

A mixture of N-arylpyrrlidine **88** (1 mmol), Chloranil **10** (1 mmol), and anhydrous CH_3COONa (3 mmol) in toluene (5 mL) was stirred for 24 hours at 90 °C. After completion of the reaction, the solvent was evaporated and EtOAc (10 mL) and Water (5 mL) were added the combined organic layer was washed with brine (10 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography on silica gel (100-200 mesh) using EtOAc:Hexane (5:95) as an eluent to get methyl benzofuropyrrolidines **89**.

4,6,7-Trichloro-2-methyl-1-phenyl-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-b]pyrrol-5-ol (89a)



89a

Yield : 0.26 g (69%); white solid.

mp : 123-125 °C.

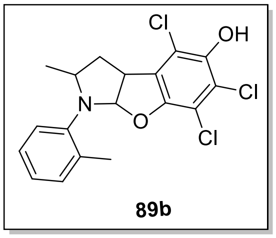
IR (KBr) : (cm^{-1}) 3432, 2987, 2895, 1605, 1556, 1463, 1401, 1213, 1125, 1059, 867, 761.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.38-7.34 (m, 2H), 7.05-7.02 (m, 2H), 6.95-6.92 (m, 1H), 6.53 (d, *J* = 7.04 Hz, 1H), 5.60 (s, 1H), 4.38-4.33 (m, 1H), 4.23-4.17 (m, 1H), 2.74-2.66 (m, 1H), 2.21-2.16 (m, 1H), 1.12 (d, *J* = 6.44 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 149.4, 143.3, 142.6 129.5, 129.3, 128.6, 119.3, 116.5, 115.3, 114.4, 100.4, 53.9, 46.6, 36.5, 20.5.

HRMS (*m/z*) : Calculated for $C_{17}H_{14}Cl_3NO_2$ (M+H): 370.0169, Found (M+H): 370.0163.

4,6,7-Trichloro-2-methyl-1-(*o*-tolyl)-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-b]pyrrol-5-ol (89b)


89b

Yield **:** 0.27 g (71%); white solid.

mp : 129-131 °C.

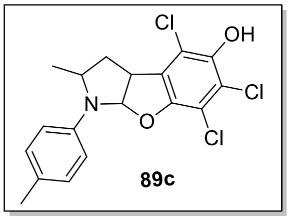
IR (KBr) : (cm^{-1}) 3473, 3962, 2920, 2828, 1603, 1582, 1489, 1417, 1350, 1252, 1154, 1112, 1066, 1004, 875, 767.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.27-7.13 (m, 4H), 6.29-6.27 (m, 1H), 5.6 (s, 1H), 4.21-4.16 (m, 1H), 3.91-3.79 (m, 1H), 2.39-2.32 (m, 4H), 2.09-1.98 (m, 1H), 1.02-1.00 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 150.7, 142.4, 140.8, 135.5, 130.8, 127.6, 126.7, 126.3, 125.6, 118.8, 115.7, 111.9, 102.9, 53.9, 45.8, 39.1, 18.2.

HRMS (*m/z*) : Calculated for $C_{18}H_{16}Cl_3NO_2$ (M+H): 384.0326, Found (M+H): 384.0317.

4,6,7-Trichloro-2-methyl-1-(*p*-tolyl)-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-b]pyrrol-5-ol (89c)


89c

Yield **:** 0.27 g (70%); white solid.

mp : 125-127 °C.

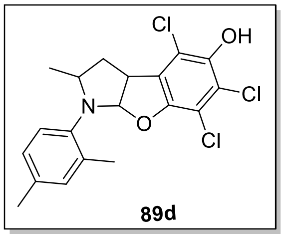
IR (KBr) : (cm^{-1}) 3465, 2972, 2821, 2805, 1603, 1587, 1408, 1356, 1275, 1164, 1015, 963, 875, 832, 759.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.16 (d, *J* = 8.15 Hz, 2H), 6.96-6.93 (m, 2H), 6.50 (d, *J* = 6.93 Hz, 1H), 5.61 (s, 1H), 4.34-4.28 (m, 1H), 4.19-4.15 (m, 1H), 2.73-2.66 (m, 1H), 2.33 (s, 3H), 2.17-2.12 (m, 1H), 1.09 (d, *J* = 6.37 Hz, 3H).

^{13}C NMR : 100 MHz, $CDCl_3$, δ ppm) 149.4, 142.6, 140.9, 129.9, 129.8, 128.7, 128.6, 119.1, 117.6, 114.6, 100.8, 54.1, 46.5, 36.6, 20.5, 20.4.

HRMS (*m/z*) : Calculated for $C_{17}H_{14}Cl_3NO_2$ (M+H): 384.0326, Found (M+H): 384.0315.

4,6,7-Trichloro-1-(2,4-dimethylphenyl)-2-methyl-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-b]pyrrol-5-ol (89d)



89d

Yield **:** 0.27 g (68%); white solid.

mp : 120-122 °C.

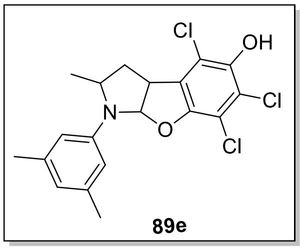
IR (KBr) : (cm^{-1}) 3379, 2968, 2901, 2850, 1607, 1535, 1478, 1425, 1386, 1251, 1179, 965, 886, 785, 669, 588.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.14-7.04 (m, 3H), 6.25-6.24 (m, 1H), 5.56 (s, 1H), 4.19-4.15 (m, 1H), 3.88-3.78 (m, 1H), 2.35 (s, 3H), 2.31 (s, 3H), 2.081.98 (m, 1H), 1.00-0.99 (m, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 150.7, 142.4, 138.1, 135.3, 135.1, 131.7, 131.5, 127.7, 126.9, 126.7, 118.7, 115.6, 111.8, 103.3, 54.0, 45.8, 39.2, 20.9, 18.2, 17.9.

HRMS (*m/z*) : Calculated for $C_{19}H_{18}Cl_3NO_2$ (M+H): 398.0482, Found (M+H): 398.0482.

4,6,7-Trichloro-1-(3,5-dimethylphenyl)-2methyl-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-b]pyrrol-5-ol (89e)



Yield **:** 0.29 g (72%); white solid.

mp : 119-121 °C.

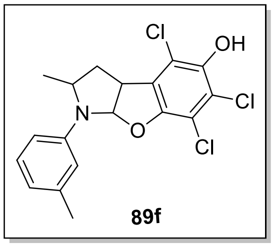
IR (KBr) : (cm^{-1}) 3494, 2972, 2921, 2868, 1598, 1458, 1423, 1386, 1205, 1164, 1040, 875, 823, 793, 704, 612.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 6.68 (s, 2H), 6.61 (s, 1H), 6.53 (d, *J* = 6.96 Hz, 1H), 5.6 (s, 1H), 4.37-4.30 (m, 1H), 4.19-4.14 (m, 1H), 2.72-2.65 (m, 1H), 2.38 (s, 6H), 2.19-2.14 (m, 1H), 1.13 (d, *J* = 6.4 Hz, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 149.4, 143.4, 142.6, 139.1, 128.7, 121.3, 119.2, 115.4, 114.7, 112.3, 100.6, 53.9, 46.5, 36.5, 21.8, 20.7.

HRMS (*m/z*) : Calculated for $C_{19}H_{18}Cl_3NO_2$ (M+H): 398.0482, Found (M+H): 398.0476.

4,6,7-Trichloro-2-methyl-1-(*m*-tolyl)-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-b]pyrrol-5-ol (89f)



89f

Yield **:** 0.28 g (74%); white solid.

mp : 122-124 °C.

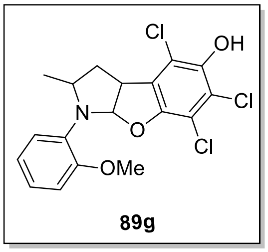
IR (KBr) : (cm^{-1}) 3415, 2964, 2871, 2826, 1606, 1507, 1412, 1357, 1124, 989, 874, 743, 674.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.24 (t, *J* = 7.6, 1H), 6.85 (s, 2H), 6.79-6.75 (m, 1H), 6.53 (d, *J* = 6.08, 1H), 5.56 (s, 1H), 4.36-4.33 (m, 1H), 4.21-4.16 (m, 1H), 2.73-2.65 (m, 1H), 2.40 (s, 3H), 2.24-2.15 (m, 1H), 1.12 (d, *J* = 6.37, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 149.4, 143.3, 142.6, 139.3, 129.3, 128.6, 120.3, 117.4, 115.3, 115.1, 113.9, 111.6, 100.5, 53.9, 46.6, 36.5, 21.8, 20.6.

HRMS (*m/z*) : Calculated for $C_{18}H_{16}Cl_3NO_2$ (M+H): 384.0326, Found (M+H): 384.0319.

4,6,7-Trichloro-1-(2-methoxyphenyl)-2-methyl-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-b]pyrrol-5-ol (89g)



89g

Yield **:** 0.31 g (78%); white solid.

mp : 131-133 °C.

IR (KBr) : (cm^{-1}) 3416, 2941, 2843, 1608, 1499, 1453, 1427, 1375, 1225, 1168, 1091, 1050, 874, 760, 678.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.14-7.11 (m, 1H), 7.01-6.94 (m, 3H), 6.74 (d, *J* = 6.49 Hz, 1H), 5.53 (s, 1H), 4.19-4.17 (m, 1H), 3.90 (s, 3H), 3.87-3.83 (m, 1H), 2.41-2.38 (m, 1H), 2.11-2.04 (m, 1H), 1.13 (d, *J* = 5.77 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 153.9, 150.7, 142.4, 131.5, 127.6, 124.6, 124.3, 120.6, 118.8, 115.6, 111.7, 105.8, 101.9, 55.6, 52.6, 45.5, 38.6, 18.2.

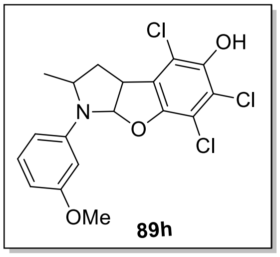
HRMS (*m/z*) : Calculated for $C_{18}H_{16}Cl_3NO_3$ (M+H): 400.0275, Found (M+H): 400.0265.

4,6,7-Trichloro-1-(3-methoxyphenyl)-2-methyl-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-b]pyrrol-5-ol (89h)

Yield **:** 0.30 g (75%); white solid.

mp : 127-129 °C.

IR (KBr) : (cm^{-1}) 3447, 2957, 2827, 1598, 1505, 1458, 1422, 1381, 1288, 1210, 1040, 983, 880, 766, 689.



89h

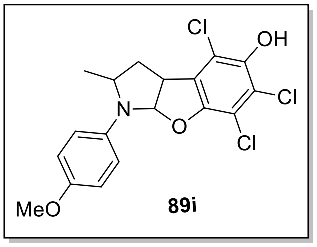
^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.28-7.24 (m, 1H), 6.66-6.64 (m, 1H), 6.59-6.58 (m, 1H), 6.51-6.49 (m, 2H), 5.61 (s, 1H), 4.34-4.27 (m, 1H), 4.21-

4.16 (m, 1H), 3.86 (s, 3H), 2.73-2.65 (m, 1H), 2.19-2.15 (m, 1H), 1.11 (d, *J* = 6.34, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 160.8, 149.4, 144.7, 142.7, 130.2, 128.5, 119.2, 115.3, 107.4, 104.1, 101.2, 100.3, 55.3, 54.2, 46.6, 36.4, 20.6.

HRMS (*m/z*) : Calculated for $C_{18}H_{16}Cl_3NO_3$ (M+H): 400.0275, Found (M+H): 400.0263.

4,6,7-Trichloro-1-(4-methoxyphenyl)-2-methyl-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-b]pyrrol-5-ol (89i)



89i

Yield **:** 0.29 g (73%); white solid.

mp : 138-140 °C.

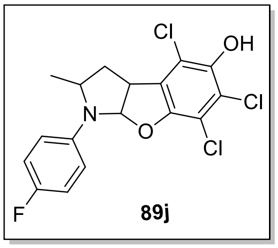
IR (KBr) : (cm^{-1}) 3378, 2941, 2839, 1608, 1515, 1459, 1423, 1345, 1221, 1162, 1075, 897, 754, 674, 579.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.00-6.98 (m, 2H), 6.95-6.92 (m, 2H), 6.45 (d, *J* = 6.90, 1H), 5.55 (s, 1H), 4.29-4.25 (m, 1H), 4.17-4.13 (m, 1H), 3.81 (s, 3H), 2.74-2.68 (m, 1H), 2.12-2.08 (m, 1H), 1.10 (d, *J* = 6.40 Hz, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 153.4, 149.4, 142.5, 137.4, 128.8, 119.1, 116.0, 115.3, 114.9, 114.6, 112.8, 101.7, 55.7, 54.5, 46.5, 36.9, 20.5.

HRMS (*m/z*) : Calculated for $C_{18}H_{16}Cl_3NO_3$ (M+H): 400.0275, Found (M+H): 400.0273.

4,6,7-Trichloro-1-(4-fluorophenyl)-2-methyl-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-b]pyrrol-5-ol (89j)



89j

Yield **:** 0.23 g (59%); brown solid.

mp : 144-146 °C.

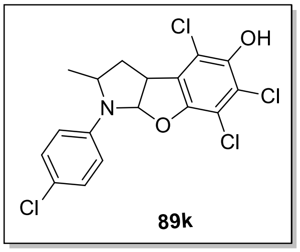
IR (KBr) : (cm^{-1}) 3447, 2977, 2843, 1609, 1516, 1438, 1376, 1288, 1221, 1040, 973, 880, 699.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.06-6.94 (m, 4H), 6.43 (d, J = 7.03 Hz, 1H), 5.62 (s, 1H), 4.28-4.13 (m, 2H), 2.75-2.67 (m, 1H), 2.15-2.08 (m, 1H), 1.09 (d, J = 6.37 Hz, 3H)

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 158.1, 155.7, 149.2, 142.7, 139.7, 139.7, 128.6, 119.2, 116.0, 115.8, 115.7, 115.3, 112.9, 101.0, 54.5, 46.6, 36.7, 20.4.

HRMS (*m/z*) : Calculated for $C_{17}H_{13}FCl_3NO_2$ (M+H): 388.0075, Found (M+H): 388.0064.

4,6,7-Trichloro-1-(4-chlorophenyl)-2-methyl-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-b]pyrrol-5-ol (89k)



89k

Yield **:** 0.25 g (61%); white solid.

mp : 161-163 °C.

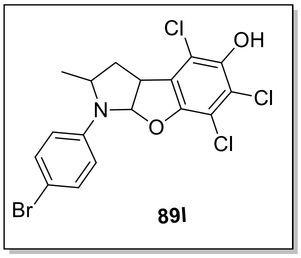
IR (KBr) : (cm^{-1}) 3499, 3044, 2966, 2853, 1597, 1489, 1463, 1298, 1199, 1101, 1019, 983, 874, 817, 740, 698.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.29-7.27 (m, 2H), 6.95-6.92 (m, 2H), 6.45 (d, *J* = 7.01 Hz, 1H), 5.64 (s, 1H), 4.29-4.18 (m, 2H), 2.74-2.66 (m, 1H), 2.20-2.17 (m, 1H), 1.08 (d, *J* = 6.45, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 149.2, 142.8, 141.9, 129.3, 129.2, 128.4, 124.3, 119.3, 115.6, 115.4, 100.1, 54.2, 46.6, 36.4, 20.4.

HRMS (*m/z*) : Calculated for $C_{17}H_{13}Cl_4NO_2$ (M+H): 403.9779, Found (M+H): 403.9760.

1-(4-Bromophenyl)-4,6,7-trichloro-2-methyl-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-b]pyrrol-5-ol (89l)



89l

Yield : 0.28 g (62%); brown solid.

mp : 167-169 °C.

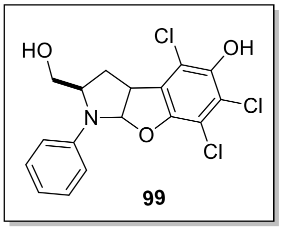
IR (KBr) : (cm^{-1}) 3485, 2923, 2813, 1604, 1536, 1428, 1419, 1361, 1256, 1135, 1067, 979, 858, 815, 751, 638.

^{1}H NMR : (400 MHz, CDCl$_3$, δ ppm) 7.41 (d, *J* = 8.60 Hz, 2H), 6.88 (d, *J* = 8.90 Hz, 2H), 6.44 (d, *J* = 7.37 Hz, 1H), 5.68 (s, 1H), 4.28-4.14 (m, 2H), 2.73-2.65 (m, 1H), 2.18 (d, *J* = 13.08 Hz, 1H), 1.07 (d, *J* = 6.93 Hz, 3H).

^{13}C NMR : (100 MHz, CDCl$_3$, δ ppm) 149.2, 142.8, 142.4, 132.2, 128.3, 120.1, 119.3, 118.1, 116.1, 111.5, 99.9, 54.2, 46.7, 36.3, 20.3.

HRMS : (*m/z*): Calculated for $C_{16}H_{14}Cl_4NO_2$ (M+H): 447.9274, Found (M+H): 447.9271.

(2*R*)-4,6,7-Trichloro-2-(hydroxymethyl)-1-phenyl-2,3,3a,8a-tetrahydro-1*H*-benzofuro[23-*b*]pyrrol-5ol (99)



99

Yield **:** 0.28 g (73%); brown solid.

mp : 149-151 °C.

IR (KBr) : (cm^{-1}) 3486, 2942, 2823, 1605, 1541, 1430, 1413, 1351, 1258, 1151, 1067, 978, 844, 805, 751, 638.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.35 (t, J = 7.85 Hz, 3H), 7.07 (d, J = 8.12 Hz, 2H), 6.96 (t, J = 7.41 Hz, 1H), 6.51 (d, J = 7.06 Hz, 1H), 6.03 (bs, 1H), 4.47-4.46 (m, 1H), 4.21-4.17 (m, 1H), 3.59-3.49 (m, 2H), 2.76-2.69 (m, 1H), 2.44-2.39 (m, 1H).

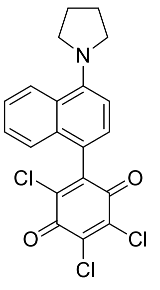
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 148.9, 143.1, 143.0, 129.5, 128.8, 128.3, 120.1, 119.3, 115.5, 114.5, 101.3, 62.5, 60.1, 46.4, 31.8.

HRMS (*m/z*) : Calculated for $C_{17}H_{14}Cl_3NO_3$ (M+H): 386.0118, Found (M+H): 386.0118.

3.4.4 General procedure for 2,3,5-trichloro-6-(4-(pyrrolidin-1-yl)napthalen-1-yl)cyclohexa-2,5-diene-1,4-dione

To a stirred solution of chloranil **10** (2 mmol) in toluene solvent under nitrogen atmosphere, napthyl amines **100** (2 mmol) were added. The reaction mixture was stirred for 12 h at room temparature. After completion of the reaction, the solvent (toluene) was evaporated and ethylacetate (30 mL) and water (15 mL) were added. The organic layer was separated and extracted with 10 mL ethylacetate. The combined organic layer was washed with brine (15 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography on silica gel (100-200 mesh) using hexane as eluent to isolate the compound **101** upto 85% yields.

2,3,5-Trichloro-6-(4-(pyrrolidin-1-yl)napthalen-1-yl)cyclohexa-2,5-diene-1,4-dione (101)



101

Yield : 0.69 g (85%); brown solid.

mp : 171-173 °C.

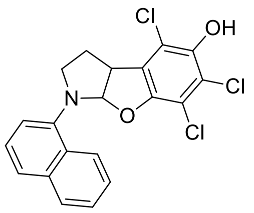
IR (KBr) : (cm^{-1}) 3014, 2966, 2835, 2765, 1678, 1561, 1509, 1449, 1376, 1321, 1239, 1205, 1100, 946, 892, 756.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 8.31-8.29 (m, 1H), 7.44-7.41 (m, 2H), 7.37-7.31 (m, 1H), 7.20 (d, *J* = 8.05 Hz, 1H), 6.92 (d, *J* = 8.05 Hz, 1H), 3.57-3.55 (m, 4H), 2.07-2.05 (m, 4H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 175.7, 171.7, 150.2, 144.3, 141.6, 141.1, 140.6, 131.9, 128.8, 126.9, 126.5, 125.9, 125.1, 124.0, 119.6, 108.9, 52.8, 25.5.

HRMS : (*m/z*): Calculated for $C_{20}H_{14}Cl_3NO_2$ (M+H): 405.0168, Found (M+H): 405.0167.

4,6,7-Trichloro-1-(naphthalen-1-yl)-2,3,3a,8a-tetrahydro-1*H*-benzofuro[2,3-*b*]pyrrol-5-ol (102)



102

Yield **:** 0.21 g (51%); white solid.

mp : 159-161 °C.

IR (KBr) : (cm^{-1}) 3479, 2911, 2826, 1609, 1551, 1430, 1429, 1373, 1242, 1165, 1089, 965, 875, 763.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.97-7.95 (m, 1H), 7.80-7.78 (m, 1H), 7.62-7.58 (m, 1H), 7.49-7.38 (m, 4H), 6.48-6.46 (m, 1H), 5.48 (s, 1H), 4.25-4.21 (m, 1H), 3.45-3.42 (m, 2H), 2.56-2.46 (m, 1H), 2.15-2.11 (m, 1H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 150.7, 142.5, 140.6, 134.6, 129.2, 128.6, 127.4, 126.0, 125.9, 125.8, 125.4, 123.0, 120.5, 118.9, 115.6, 111.9, 103.1, 49.4, 47.6, 30.9.

HRMS : (*m/z*): Calculated for $C_{20}H_{14}Cl_3NO_2$ (M+H): 405.0168, Found (M+H): 405.0157.

3.4.5 Preparation of Electrochemical Cells

Simple solution processing and casting techniques were followed for the construction of the cell device.

Table 6: **Cell configuration 1 with four layers**

The PEO was dissolved in dichloromethane and mixed with TiO_2 powder. DCM was removed to obtain a paste for coating on Al and Graphite foils. After 1 h, (4-(diethylamino)phenyl)(phenyl)methanone/PC/PEO mixed in DCM for drop coated on Graphite foils and dried. The Cl_4BQ/PEO slurry was prepared in DCM and casted above the coated layer on Al and dried in air at room temperature for overnight. The cell was prepared by sandwiching the coated Al/Gr layers. The rim of the cell was sealed all around using a commercial adhesive paste and covered with cellophane tape.

Table 6: **Cell configuration 2 with five layers**

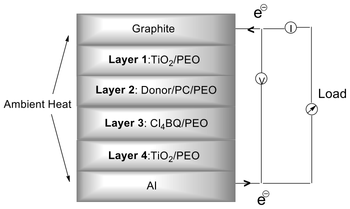
The PEO was dissolved in dichloromethane and mixed with TiO_2 powder. DCM was removed to obtain a paste for coating on Al and Graphite foils. After 1 h, Cl_4BQ/PEO in DCM was drop coated on TiO_2/PEO/Al and dried. Then after, (4-(diethylamino)phenyl)(phenyl)methanone/Cl_4BQ/PC/PEO slurry was prepared for drop coated on Graphite foil and on casted above the coated layer on Al and dried in air at room temperature for overnight. The cell was prepared by sandwiching the coated Al/Gr layers. The rim of the cell was sealed all around using a commercial adhesive paste and covered with cellophane tape.

Table 6: Cell configuration 3 with six layers

The PEO was dissolved in dichloromethane and mixed with TiO_2 powder. DCM was removed to obtain a paste for coating on Al or Graphite foils. After 1 h, Cl_4BQ/PEO in DCM was drop coated on TiO_2/PEO/Al and TiO_2/PEO/Gr dried for 1 h. The Cl_4BQ/(4-(diethylamino)phenyl)(phenyl)methanone /PC/PEO slurry was prepared and casted above the coated layer on Al and Graphite and dried in air at room temperature overnight. The cell was prepared by sandwiching the coated Al/Gr layers. The rim of the cell was sealed all around using a commercial adhesive paste and covered with cellophane tape.

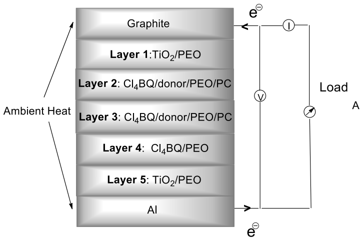
Table 6. Cell Experiments – Four, five and six layer configurations

Cell Configuration 1



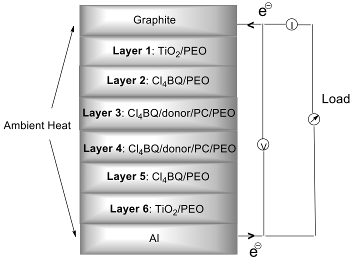
Entry-1

Cell Configuration 2

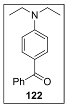
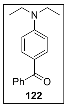


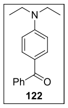
Entry-2

Cell Configuration 3



Entry-3

Entry	Gr/Layers/Al	Time after packing	T ºC[c]	Voc (V)	Isc (mA)	Vmax (V)	Imax (mA)	Pmax (mW)	Fill Factor
1[a]  122	Gr---------- **Layer1**: TiO_2(0.5 g) + PEO(0.05 g) **Layer2**: (4-(diethylamino)phenyl)(phenyl)methanone (0.2 g) + PC (1 mL) + PEO (0.05 g) **Layer3**: Cl_4BQ (0.2 g) + PEO (0.05 g) **Layer4**: TiO_2 (0.5 g) + PEO (0.05 g) Al----------	1 h	28 ºC	0.754	2.332	0.386	1.17	0.452	0.257
			35 ºC	0.847	3.205	0.431	1.558	0.670	0.247
		48 h	35 ºC	0.299	0.213	0.188	0.158	0.029	0.469
2[b]  122	Gr----------------- **Layer1**: TiO_2 (0.75 g) + PEO (0.05 g) **Layer2**: (4-(diethylamino)phenyl)(phenyl)methanone (0.125 g) + Cl_4BQ (0.05 g) + PC (0.5 mL) + PEO (0.05 g) **Layer3**: (4-(diethylamino)phenyl)(phenyl)methanone (0.125 g) + Cl_4BQ (0.05 g) + PC (0.5 mL) + PEO (0.05 g) **Layer4**: Cl_4BQ (0.15 g) + PEO (0.05 g) **Layer5**: TiO_2 (0.5 g) + PEO (0.05 g) Al------------------	1 h	28 ºC	1.077	6.186	0.545	3.08	1.679	0.252
			35 ºC	1.064	7.347	0.526	3.535	1.859	0.238
			40 ºC	1.059	7.241	0.539	3.525	1.898	0.248
		48 h	40 ºC	0.729	0.629	0.334	0.290	0.096	0.211

3[c]  122	Gr----------------- **Layer1**: TiO_2 (0.5 g) + PEO (0.05 g) **Layer2**: Cl_4BQ (0.15 g) + PEO (0.05 g) **Layer3**: (4-(diethylamino)phenyl)(phenyl)methanone (0.125 g) + Cl_4BQ (0.05 g) + PC (0.5 mL) + PEO (0.05 g) **Layer4**: (4-(diethylamino)phenyl)(phenyl)methanone (0.125 g) + Cl_4BQ (0.05 g) + PC (0.5 mL) + PEO (0.05 g) **Layer5**: Cl_4BQ (0.15 g) + PEO (0.05 g) **Layer6**: TiO_2 (0.5 g) + PEO (0.05 g) Al------------------	1 h	28 °C	1.028	9.834	0.422	4.153	1.752	0.173
			35 °C	1.068	12.42	0.464	5.36	2.484	0.187
			40 °C	1.042	12.09	0.469	5.32	2.496	0.198
		48 h	40 °C	1.089	7.81	0.491	3.834	1.882	0.221

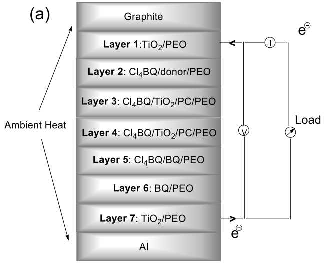
[a]**Four layer configuration:** Layer 1 was coated above Graphite electrode, Layer 2 was coated over Layer 1. Layer 3 was coated above Layer 2 and Layer 4 was coated above Al. [b]**Five layer configuration:** Layer 1 was coated above Graphite electrode, Layer 2 was coated over Layer 1. Layer 3 was coated above Layer 2 and Layer 4 was coated above Layer 5. Layer 5 was coated above Al. [c]**Six layer configuration:** Layer 1 was coated above Graphite electrode, Layer 2 was coated over Layer 1. Layer 3 was coated above Layer 2 and Layer 4 was coated above Layer 3. Layer 5 was coated above Layer6 and Layer6 was coated above Al. [d]All the cells were characterized by IV curve measurement.

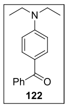
Table 7: Cell configuration 4 with seven layers

The PEO was dissolved in dichloromethane and mixed with TiO_2 powder. DCM was removed to obtain a paste for coating on Al or Graphite foils. After 1 h, Cl_4BQ/Amine donor/PEO in DCM was drop coated on TiO_2/PEO/Gr and dried. The Cl_4BQ/BQ/PEO and BQ/PEO layers were coated on TiO_2/PEO/Al. The Cl_4BQ/TiO_2/PC/PEO slurry was prepared and casted above the coated layer on Al and Graphite and dried in air at room temperature overnight. The cell was prepared by sandwiching the coated Al/Gr layers. The rim of the cell was sealed all around using a commercial adhesive paste and covered with cellophane tape.

Table 7. Cell Experiments – Seven layer configurations

Cell Configuration 4



Entry	Al/Layers/Gr/Layers/Al	Time after packing	T ºC^{c}	Voc (V)	Isc (mA)	Vmax (V)	Imax (mA)	Pmax (mW)	Fill Factor
1  122	Gr----------------- **Layer 1**: TiO_2 (0.5 g) + PEO (0.05 g) **Layer 2**: (4-(diethylamino)phenyl)(phenyl)methanone (0.253 g) + Cl_4BQ (0.25 g) + PEO (0.05 g) **Layer 3**: Cl_4BQ (0.025 g) + TiO_2 (0.25 g) +PC (0.5 g) + PEO (0.05 g) **Layer 4**: Cl_4BQ (0.025 g) + TiO_2 (0.25 g) +PC (0.5 g) + PEO (0.05 g) **Layer 5**: Cl_4BQ (0.1 g) +BQ (0.1 g) + PEO (0.05 g) **Layer 6**: BQ (0.2 g) + PEO (0.05 g) **Layer 7**: TiO_2 (0.5 g) + PEO (0.05 g) Al------------------	1 h	28 ºC	1.165	4.66	0.546	2.218	1.210	0.223
			35 ºC	1.153	5.584	0.559	2.659	1.485	0.231
			40 ºC	1.156	5.451	0.574	2.598	1.492	0.237
		48 h	28 ºC	1.176	3.460	0.549	1.592	0.874	0.215
			35 ºC	1.181	4.662	0.562	2.223	1.249	0.227
			40 ºC	1.179	5.668	0.562	2.689	1.512	0.226

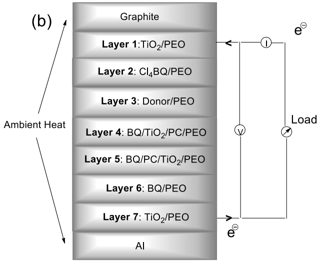
The device was constructed by using simple solution processing and casting techniques. Layer 1 was coated above Graphite electrode, Layer 2 was coated over Layer 1, and Layer 3 was coated above Layer 2. Layer 4 was coated above Layer 5, Layer 5 was coated over Layer 6 and Layer 6 was coated above Layer 7. Layer 7 was coated on the Al electrode.

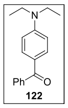
Table 8: **Cell configuration 5 with seven layers using additional acceptor BQ**

The PEO was dissolved in dichloromethane and mixed with TiO_2 powder. DCM was removed to obtain a paste for coating on Al or Graphite foils. After 1 h, BQ/PEO in DCM was drop coated on TiO_2/PEO/Al and dried. The Cl_4BQ/PEO and Amine donor/PEO layers were coated on TiO_2/PEO/Gr and dried over 1 h. The BQ/TiO_2/PC/PEO slurry was prepared and casted above the coated layer on Al and Graphite and dried in air at room temperature overnight. The cell was prepared by sandwiching the coated Al/Gr layers. The rim of the cell was sealed all around using a commercial adhesive paste and covered with cellophane tape.

Table 8. Cell Experiments – Seven layer configurations with additional BQ

Cell Configuration 5



1  **122**	Gr----------- **Layer 1**: TiO_2 (0.5 g) + PEO (0.05 g) **Layer 2**: Cl_4BQ (0.25 g) + PEO (0.05 g) **Layer 3**: (4-(diethylamino)phenyl)(phenyl)methanone (0.253 g) + PEO (0.05 g) **Layer 4**: BQ (0.11 g) + PC (0.5 g) + TiO_2 (0.25 g + PEO (0.05 g) **Layer 5**: BQ (0.11 g) + PC (0.5 g) + TiO_2 (0.25 g + PEO (0.05 g) **Layer 6**: BQ (0.22 g) + PEO (0.05 g) **Layer 7**: TiO_2 (0.5 g) + PEO (0.05 g) Al----------	1 h	28 °C	1.134	5.313	0.538	2.598	1.396	0.232
			35 °C	1.139	5.790	0.536	2.717	1.455	0.221
			40 °C	1.135	5.872	0.571	2.813	1.606	0.241
		48 h	28 °C	1.023	1.672	0.457	0.810	0.369	0.216
			35 °C	1.027	2.332	0.476	1.162	0.553	0.231
			40 °C	1.024	2.602	0.497	1.263	0.627	0.236

[a]The device was constructed by using simple solution processing and casting techniques. Layer 1 was coated above Graphite electrode, Layer 2 was coated over Layer 1, Layer 3 was coated above Layer 2. Layer 4 was coated above Layer 3, Layer 5 was coated over Layer 6 and Layer 6 was coated above Layer 7. Layer 7 was coated on the Al electrode. [b]All the cells were characterized by IV curve measurement.

Table 9: **Cell configuration 6 with five layers using Me2SO2**

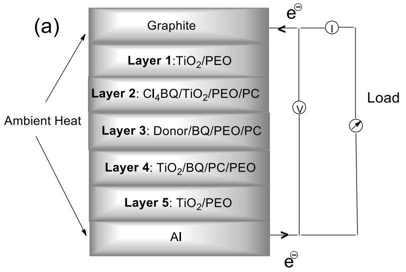
The PEO was dissolved in dichloromethane and mixed with TiO_2 powder. DCM was removed to obtain a paste for coating on Al or Graphite foils. After 1 h, TiO_2/Me_2SO_2/PC/PEO in DCM was drop coated on TiO_2/PEO/Al and dried. The Cl_4BQ/PC/TiO_2/PEO layer was coated on TiO_2/PEO/Gr and dried over 1 h. The amine donor/Me_2SO_2/PC/PEO slurry was prepared and casted above the heat coated layer on Al side before packing. The cell was prepared by sandwiching the coated Al/Gr layers. The rim of the cell was sealed all around using a commercial adhesive paste and covered with cellophane tape.

Table 9: **Cell configuration 7 with five layers using BQ**

The PEO was dissolved in dichloromethane and mixed with TiO_2 powder. DCM was removed to obtain a paste for coating on Al or Graphite foils. After 1 h, TiO_2/BQ/PC/PEO in DCM was drop coated on TiO_2/PEO/Al and dried. The Cl_4BQ/PC/TiO_2/PEO layer was coated on TiO_2/PEO/Gr and dried over 1 h. The amine donor/BQ/PC/PEO slurry was prepared and casted above the heat coated layer on Al side before packing. The cell was prepared by sandwiching the coated Al/Gr layers. The rim of the cell was sealed all around using a commercial adhesive paste and covered with cellophane tape.

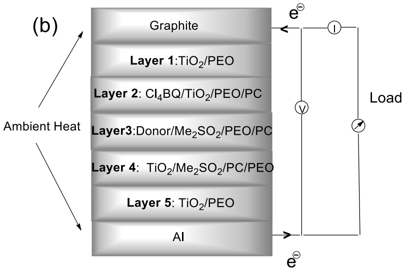
Table 9. Cell Experiments – Five layer configurations with comparition of BQ and Me2SO2

Cell Configuration 6

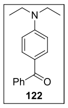
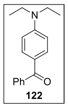


Entries-1&2

Cell Configuration 7



Entries-3&4

Entry	Al/Layers/Gr/Layers/Al	Time after packing	T ºC[c]	Voc (V)	Isc (mA)	Vmax (V)	Imax (mA)	Pmax (mW)	Fill Factor
1  122	Gr----------------- **Layer1**: TiO_2 (0.5 g) + PEO (0.05 g) **Layer2**: TiO_2 (0.5 g) + Cl_4BQ (0.25 g) + PC (0.5 g) + PEO (0.05 g) **Layer3**: (4-(diethylamino)phenyl)(phenyl)methanone (0.253 g) + Me_2SO_2 (0.094 g)+ PC (0.5 g) + PEO (0.1 g) **Layer4**: TiO_2 (0.5 g) +Me_2SO_2 (0.188 g) + PC (0.5 g) +PEO (0.05 g) **Layer5**: TiO_2 (0.5 g) + PEO (0.05 g) Al------------------	1 h	28 ºC	1.054	9.107	0.514	4.506	2.317	0.242
			35 ºC	1.075	10.39	0.527	5.239	2.762	0.247
			40 ºC	1.085	10.29	0.528	5.401	2.850	0.255
		48 h	40 ºC	1.021	6.568	0.486	3.463	1.683	0.251
2  122	Gr----------------- **Layer1**: TiO_2 (0.5 g) + PEO (0.05 g) **Layer2**: TiO_2 (0.5 g) + Cl_4BQ (0.25 g) + PC (0.5 g) + PEO (0.05 g) **Layer3**: (4-(diethylamino)phenyl)(phenyl)methanone (0.253 g) + BQ (0.11 g)+ PC (0.5 g) + PEO (0.1 g) **Layer4**: TiO_2 (0.5 g) +BQ (0.44 g) + PC (0.5 g) +PEO (0.05 g) **Layer5**: TiO_2 (0.5 g) + PEO (0.05 g) Al------------------	1 h	28 ºC	1.101	3.890	0.554	2.007	1.111	0.260
			35 ºC	1.078	4.153	0.544	2.141	1.164	0.260
			40 ºC	1.111	4.188	0.565	2.130	1.203	0.259
		48 h	40 ºC	1.068	3.354	0.459	1.565	0.712	0.200

Five layer configuration: Layer 1 was coated above Graphite electrode, Layer 2 was coated over Layer 1. Layer 3 was coated above Layer 2 and Layer 4 was coated above Layer 5. Layer 5 was coated above Al.

3.5 References

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Appendix-I

Studies on Hydroboration of Olefins with Chiral 2S-phenyl-N-(aryl)pyrrolidine-Borane Complexes

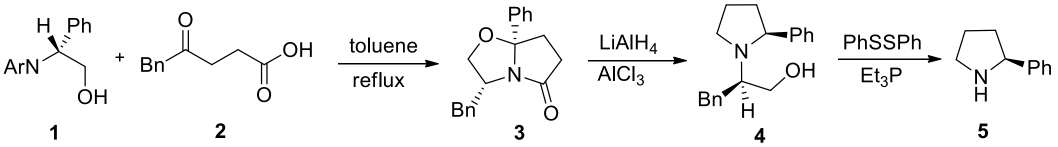
I.1 Introduction

Enantiomerically pure tertiary amines are commonly used in organic synthesis as chiral auxiliaries/chiral bases[1] and also as catalysts for asymmetric synthesis.[2] In addition, chiral tertiary amines are valuable intermediates in the synthesis of pharmaceuticals and agrochemicals.[3] There have been numerous reports on the syntheses of substituted pyrrolidines and other heterocycles.[4] Previously, a few methods have been reported from this laboratory for the preparation of enantiomerically pure tertiary amines.[5,6]

I.1.1 Synthesis and applications of chiral C_1-symmetric nitrogen heterocyclic systems

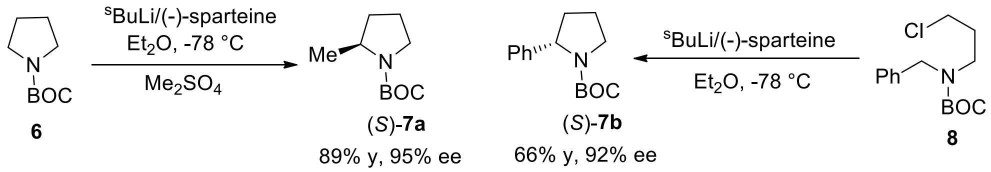
Synthesis of enantiomerically pure 2-substituted pyrrolidines from γ-keto acid **2** and (*R*)-phenylglycinol **1** was reported.[7] The *N*-substituted pyrrolidinone **3** obtained was reduced to the *N*-glycinolpyrrolidine derivative **4** using alane which upon reaction with diphenyldisulfide and triethylphosphine gave the 2-phenylpyrrolidine **5** (Scheme1).

Scheme1



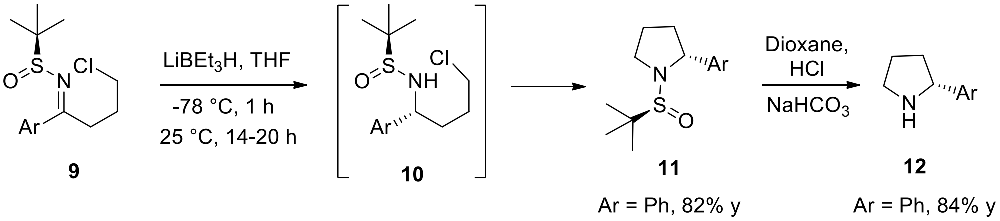
A method for the synthesis of chiral C_1-symmetric 2-substituted pyrrolidines **7** was reported *via* asymmetric deprotonation of *N*-boc-pyrrolidines **6** and arylmethyl-3-chloro propyl-boc-amines **8** using ^{S}BuLi/(-)-sparteine with high enantioselectivity (Scheme2).[8]

Scheme2



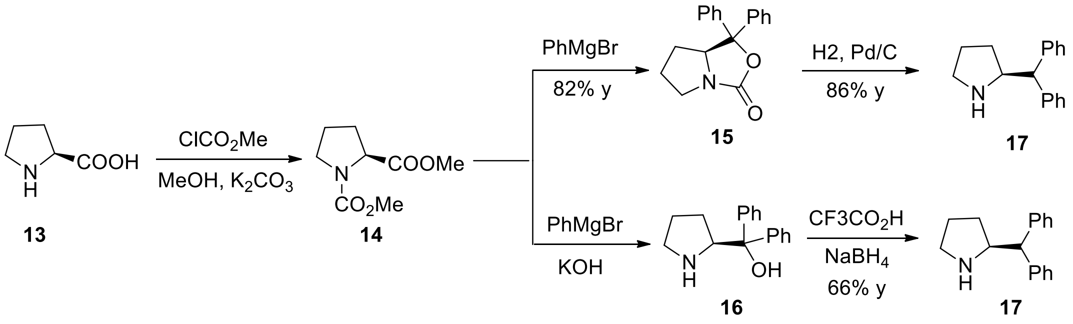
Enantioselective reductive cyclization of γ-chloro *N*-(tert-butanesulfinyl)ketimines **9** using LiBEt3H gives (S_S,R)-2-aryl-1-(^{t}butanesulfinyl)pyrrolidines **11** which after deprotection using HCl afforded the 2-arylpyrrolidine **12** in 84% yield (Scheme3).[9]

Scheme3



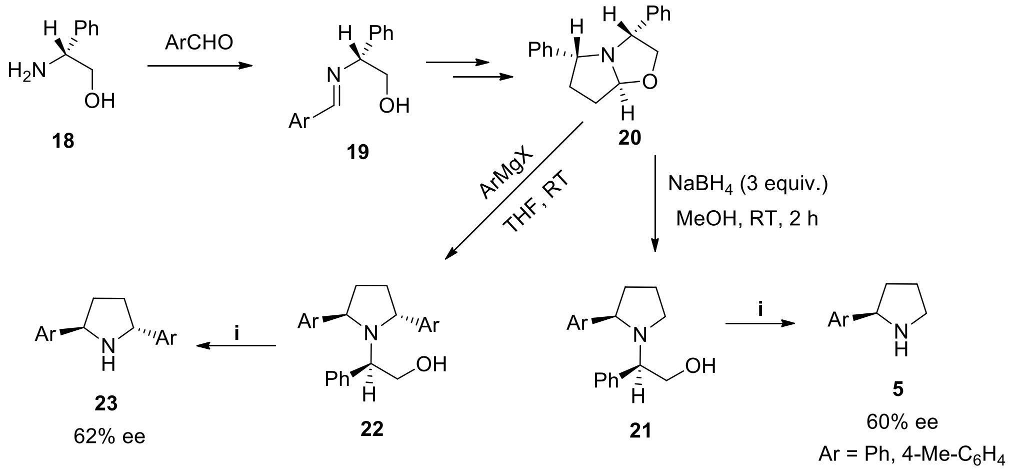
The (*S*)-2-(diphenylmethyl)pyrrolidine **17** was used as achiral solvating agent for NMR spectral analysis of chiral carboxylic acids and some secondary alcohols.[10] The synthesis of **17** involves the hydrogenation of **15** on Pd/C. In this laboratory, a slightly different method involving NaBH4/CF3CO2H was followed for the reduction of (*S*)-α,α'-diphenylprolinol **16** to obtain the chiral amine **17** in 66% yield (Scheme4).[11]

Scheme4



Synthesis of substituted pyrrolidines from chiral aromatic imines derived from (*R*)-phenylgylcinol was reported. Thus, diastereoselective addition of Grignard reagent to the chiral imines and 1,3-oxazolines gave substituted pyrrolidines **19** and **20** in moderate yields (Scheme 5).[12]

Scheme 5



i. a. PhSSPh (5 equiv.), Et_3P (5 equiv.), THF, RT, 16 h
b. LiDBB (3.6 equiv.), THF, -60 °C, 15 min., 0 °C, 16 h

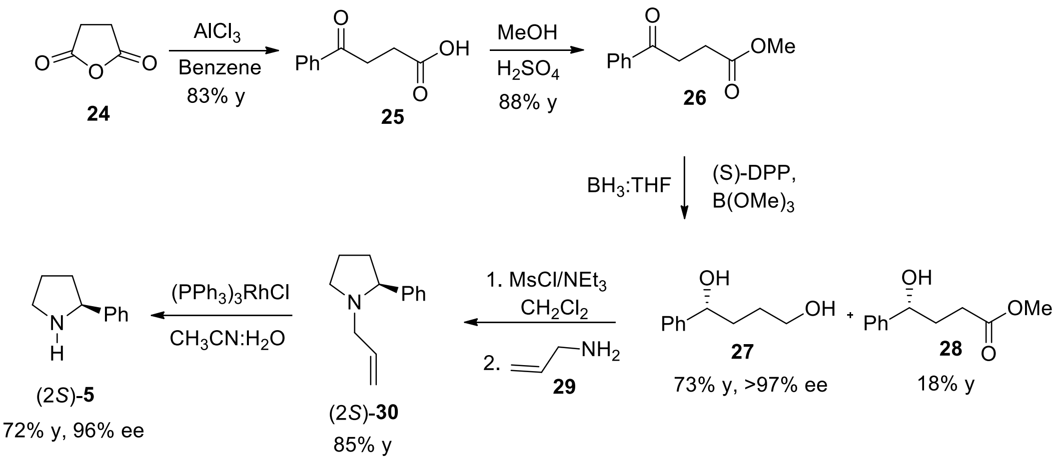
We have followed a method developed for the synthesis of 2-phenylpyrrolidine in this laboratory for the preparation of the corresponding BH_3 complexes for the hydroboration of prochiral olefins. The results are discussed in the next section.

I.2 Result and discussion

I.2.1 Synthesis of (-)-(2*S*)-phenylpyrrolidine

As outlined in the introductory section, several methods were reported for the preparation of (2*S*)-phenylpyrrolidine **5**. We have followed the CBS reduction of methyl 4-benzoylpropionate **26** to get the chiral (1*R*)-phenylbutan-1,4-diol **27** using THF**:**BH3 (2M). We have observed that the chiral diol **27** is formed in 73% yield with 97% ee along with the (4*R*)-hydroxy-4-phenylmethylbutyrate **28** in 18% yield. This hydroxy ester **28** was converted to the chiral diol **27** in 94% yield using THF**:**BH3 (2M). Subsequent mesylation using MsCl/NEt3 followed by cyclization using allylamine **29** gave the (2*S*)-*N*-allyl-2-phenylpyrrolidine **30** in 88% yield. After *N*-deallylation using the Wilkinson's catalyst, the (2*S*)-phenylpyrrolidine **5** was obtained in 82% yield with 96% ee (Scheme6).

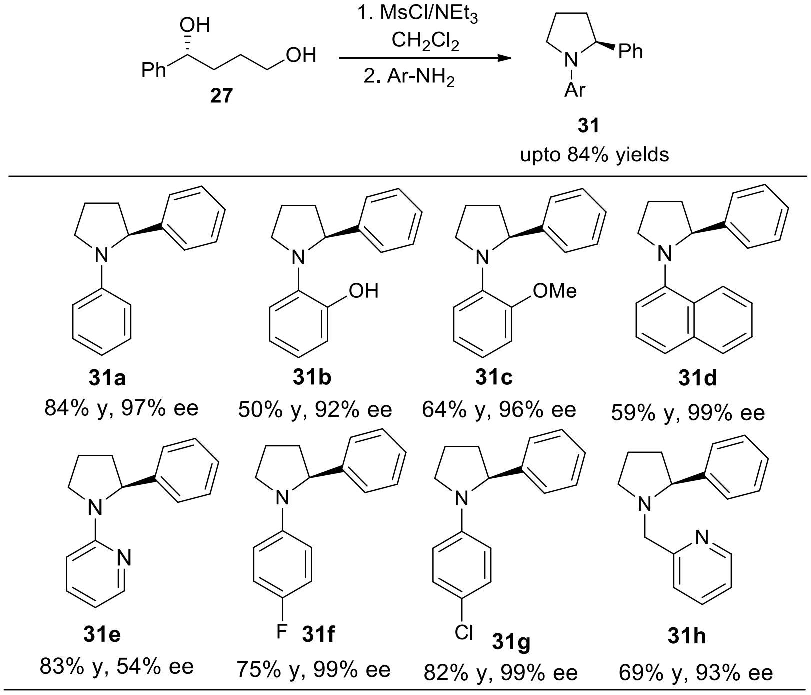
Scheme 6



I.2.2 Synthesis of (-)-(*S*)-1-aryl-2-phenylpyrrolidines 54

Previously, a few methods have been reported from this laboratory for the preparation of enantiomerically pure tertiary amines.[5,6] We have followed a method discussed in Scheme 6 to access the products **31**. The results are summerised in Table 1.

Table 1: Synthesis of Chiral (2*S*)-*N*-aryl-2-phenylpyrrolidines



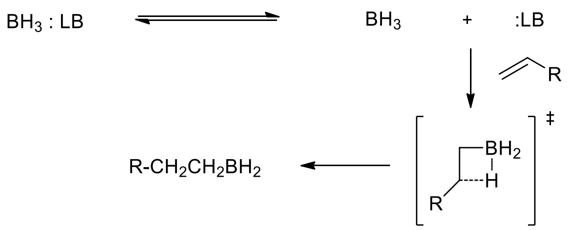
[a]All reactions were carried out using chiral (1*R*)-phenylbutan-1,4-diol **27** (5 mmol), triethylamine (2.8 mmol), methanesulfonyl chloride (1.2 mmol), aromatic amines (100 mmol) at -20 °C for 24 h [b]The yields are isolated products. [c]The products were characterized by spectral data (IR, ^{1}H-NMR and ^{13}C-NMR).

I.2.3 Hydroboration of prochiral olefins using chiral amine borane complexes

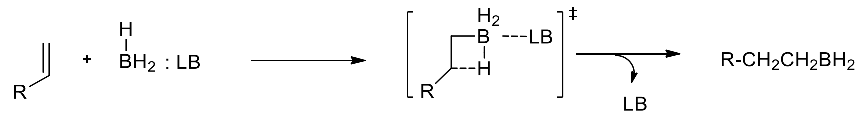
Three types of mechanisms were proposed for the hydroboration of olefins (Scheme 7).[13]

Scheme 7

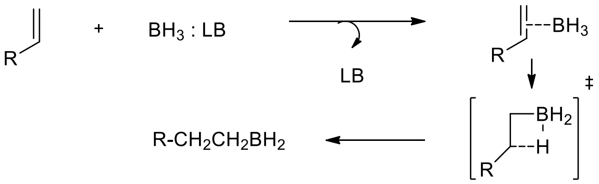
SN1 type mechanism



SN2 type mechanism

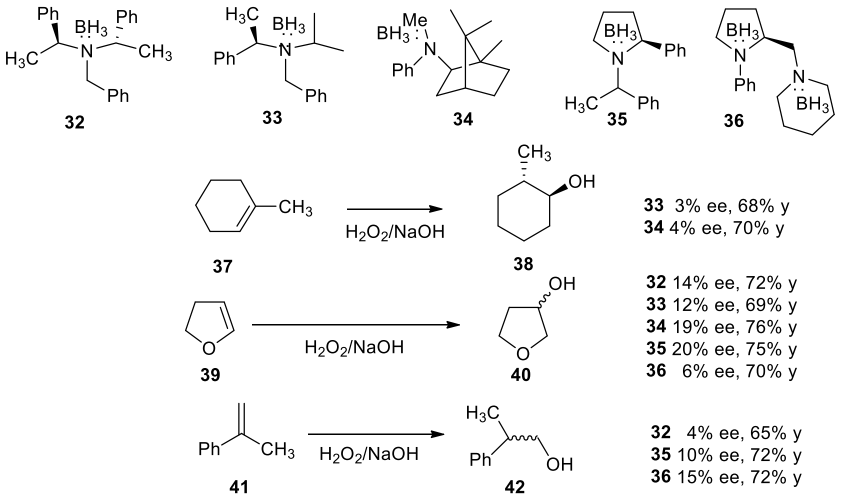


SN2-type mechanism with πcomplex intermediate



Previous efforts from this laboratory indicated that the SN2 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).[14] Poor enantioselectivity realized may be due to operation of a spectrum of mechanisms (Scheme 6).[13] 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.

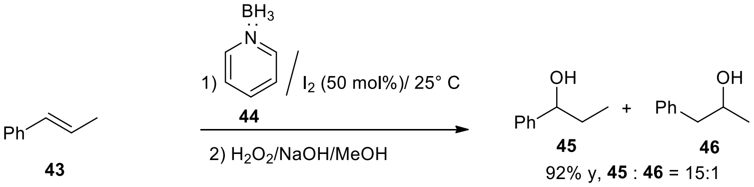
Chart 1



I.2.3.1.Iodine activation of chiral amine borane complexes

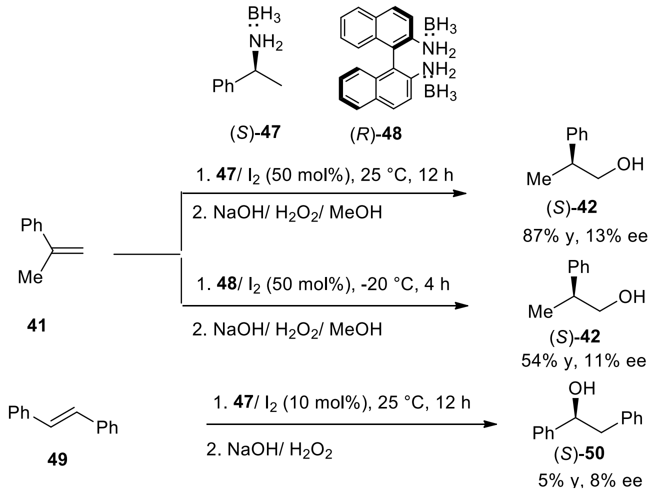
The hydroboration by iodine activation of strong amine-BH_3 complexes offers new opportunities for the asymmetric hydroboration as the BH_2I moiety is expected to be bonded with amines during the reaction with iodide behaving like a leaving group. Vedejs *et. al.*[15] reported the hydroboration reaction of β-methylstyrene **43** under iodine activation of pyridine borane complex **44** at 25 ˚C (Scheme 8).

Scheme 8



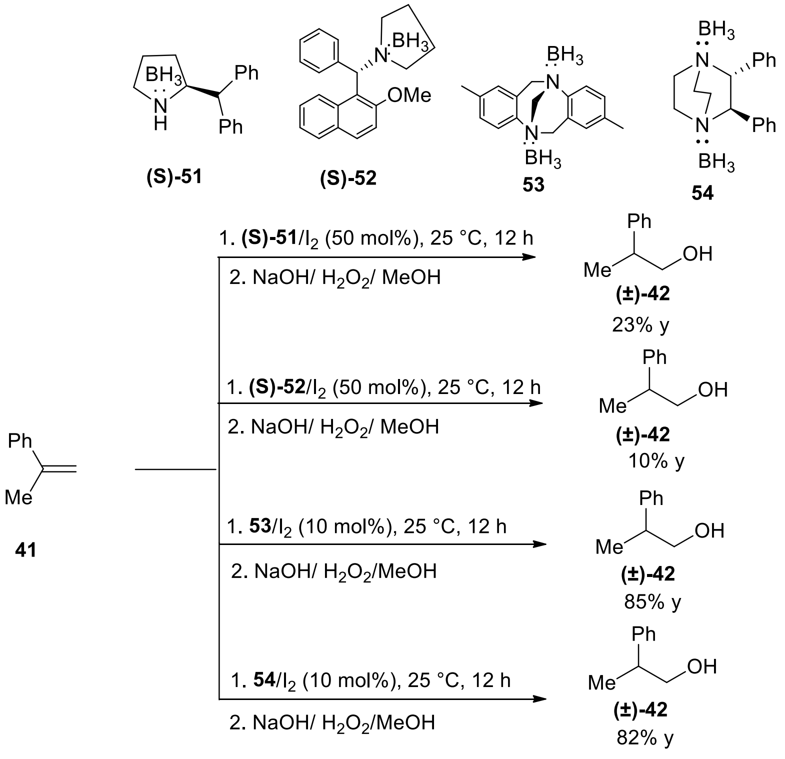
Chiral primary amine borane complexes such as α-methylbenzylamine **47** and (*R*)-BINAM **48** were found to give the product **42** in 13% and 11% ee respectively, under iodine activation (Chart 2).[16] Also, the hydroboration reaction of *trans*-stilbene **49** using α-methylbenzylamine-borane complex **47** with catalytic amount of iodine was reported to give the alcohol **50** in 5% yield and 8% ee (Chart 2).[16]

Chart 2



The hydroborations of α-methylstyrene **41** using the secondary amine **51** and tertiary amine **52-54** borane complexes were reported to give only racemic alcohols under iodine activation. (Chart 3).[16, 17]

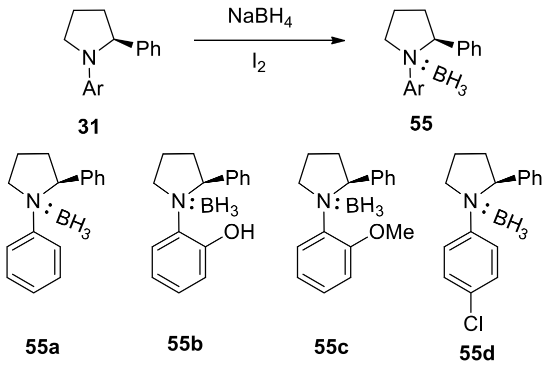
Chart 3



I.2.3.2 Hydroboration of prochiral olefins using chiral (-)-(*S*)-1-aryl-2 phenylpyrrolidine-borane complexes

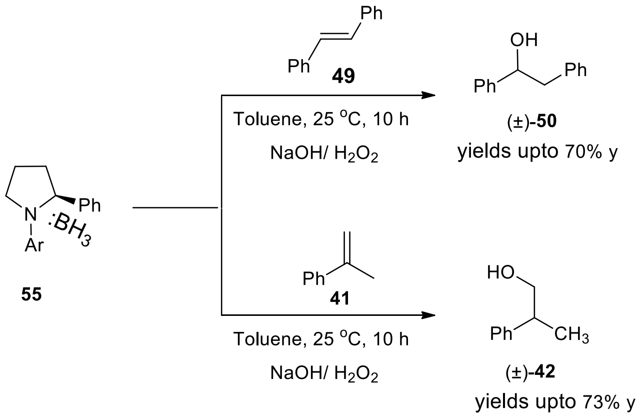
We have prepared the borane complex by passing the B_2H_6 gas generated from the reaction of $NaBH_4$ with I_2 in toluene (Scheme 9).[18]

Scheme 9



The corresponding boranecomplex **55a** showed a characteristic boron signal at -7.976 ppm. We have carried out the hydroboration of prochiral olefins **49** and **41** using the amine borane complexes **55a**, **55b**, **55c** and **55d** at 25 °C. Hence, the corresponding alcohols isolated after oxidation were found to be only racemic mixtures (Scheme 10).

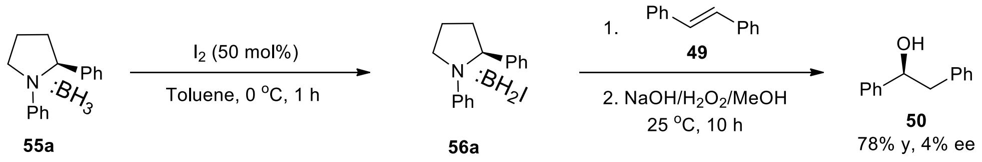
Scheme 10



I.2.3.3 Hydroboration of prochiral olefins using chiral(-)-(*S*)-1-aryl-2-phenylpyrrolidine-borane complexes under iodine activation

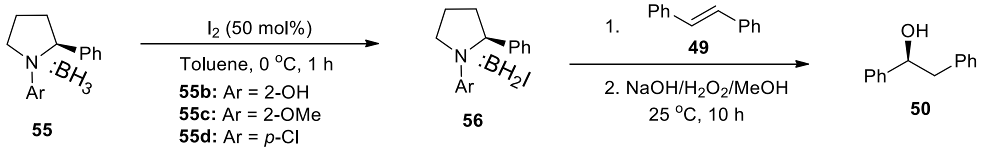
Since the amine moiety is anchored on the boron center in iodo borane complexes, iodide behaving like a leaving group, it was of interest to us to prepare the chiral amine-BH_2I complexes to examine the enantioselectivity in the hydroboration of prochiral olefins. The borane complex **55a** was prepared by preparing the B_2H_6 in the presence of tertiary amines. The complex was then used for the hydroboration of *trans*-stilbene **49** under iodine activation. ^{11}B NMR specral analysis indicated that a new peak appeared at -10.91 ppm. After hydroboration of the olefin **49**, the mixture was oxidized and the corresponding alcohol was obtained only in 4% ee (Scheme 11).

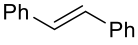
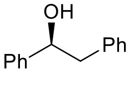
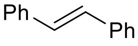
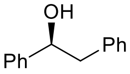
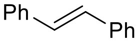
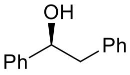
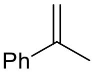
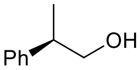
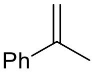
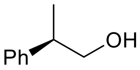
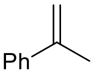
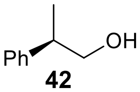
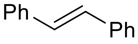
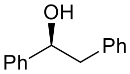
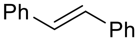
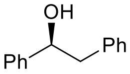
Scheme 11



We have also examined the hydroboration-oxidation reaction of *trans*-stilbene **49** with the borane complexes **55b, 55c** and **55d** under iodine activation and the corresponding alcohols were isolated in 4%, 2% and 3% ee after H_2O_2/NaOH oxidation (Table 2, entries 1-3). Also, hydroboration of α-methylstyrenewas hydroboration-oxidation reaction by using the borans complexes **55b**, **55c** and **55d** under iodine activation, resulted the corresponding alcohol was isolated in 3%, 0% and 2% ee respectively, after H_2O_2/NaOH oxidation (Table 2, entries 4-6). Further, when the hydroboration was carried out using catalytic amount (10 or 20 mol% relative to the chiral amine equivalents) of iodine, the alcohol product was obtained only in up to 2% ee after oxidation (Table 2, entry 7).

Table 2. Hydroboration of prochiral olefins using chiral(-)-(*S*)-1-aryl-2-phenylpyrrolidine borane complexes under iodine activation[a]



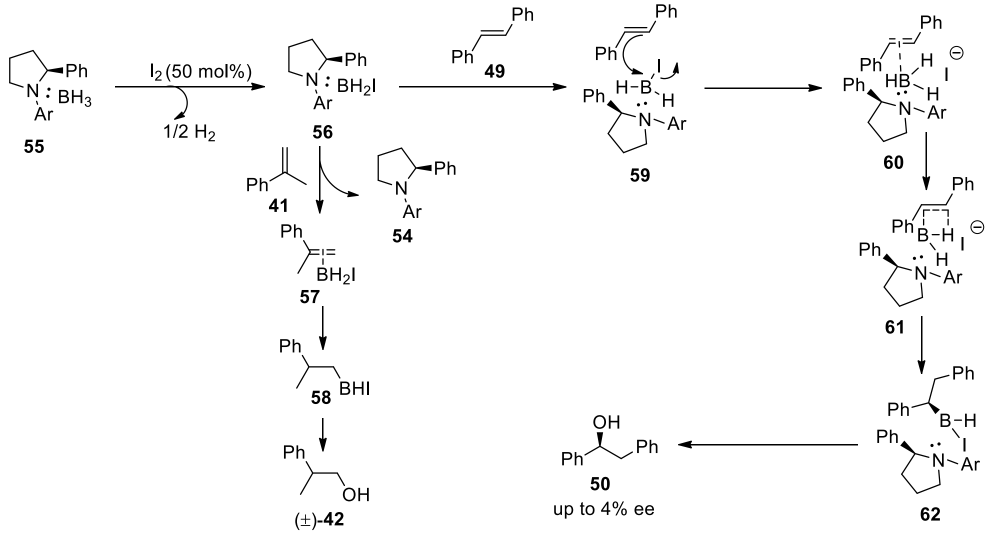
Entry	Substrate	Borane complex	Product	Yield[b]	% ee[c]
1	 **49**	**55b**	 **50**	71	4
2	 **49**	**55c**	 **50**	68	2
3	 **49**	**55d**	 **50**	73	3
4	 **41**	**55b**	 **42**	75	3
5	 **41**	**55c**	 **42**	69	0
6	 **41**	**55d**	 **42**	71	2
7[d]	 **49**	**55a**	 **50**	68	2
8[e]	 **49**	**55a**	 **50**	62	3

[a] All the reactions were carried out in 1 mmol scale at 25 °C for 10 h. [b] Products were isolated after oxidation with NaOH/H_2O_2. [c] HPLC analysis were carried out on chiral column OB-H; *n*-Hexane:*i*-PrOH-97:3, 0.3 mL/min. and OD-H using *n*-Hexane:*i*-PrOH-90:10, 0.5 mL/min. [d] In this case, addition of I_2 (10 and 20 mol%) in dry toluene (5 mL). [e] In this case, after the addition of I_2 (10, 20 and 50 mol%) in dry toluene (5 mL) to chiral (-)-(*S*)-1-aryl-2-phenylpyrrolidine-borane complex **55a**, to the reaction mixture was added *N*,*N*-diethyl aniline (weaker than chiral (-)-(*S*)-1-aryl-2-phenylpyrrolidine **31**) (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 **41** under iodine activation in the presence of *N*,*N*-diethylaniline as additive to examine whether this could lead to better selectivities through formation of complex like $R_3N^+BH_2:N(C_6H_5)Et_2I^-$complex. Unfortunately, the corresponding alcohol product was obtained with only 3% ee after H_2O_2/NaOH oxidation (Table 2, entry 8).

The results obtained in the hydroboration by borane complexes of chiral (-)-(*S*)-1-aryl-2-phenylpyrrolidinederivatives **31** can be rationalized by considering the mechanism as outlined in Scheme 12. The reaction of iodine with chiral (-)-(*S*)-1-aryl-2-phenylpyrrolidine-BH_3 complexes **55** would give the chiral (-)-(*S*)-1-aryl-2-phenylpyrrolidine-BH_2I complex **56** and hydrogen. In the reaction of olefin with chiral (-)-(*S*)-1-aryl-2-phenylpyrrolidine-BH_2I **56**, if the iodide leaves, the chiral (-)-(*S*)-1-aryl-2-phenylpyrrolidine **31** would be attached to the boron in the transition state leading to the optically active product. However, if chiral (-)-(*S*)-1-aryl-2-phenylpyrrolidine **31** acts as a leaving group, the hydroboration reaction would lead to racemic mixtures.

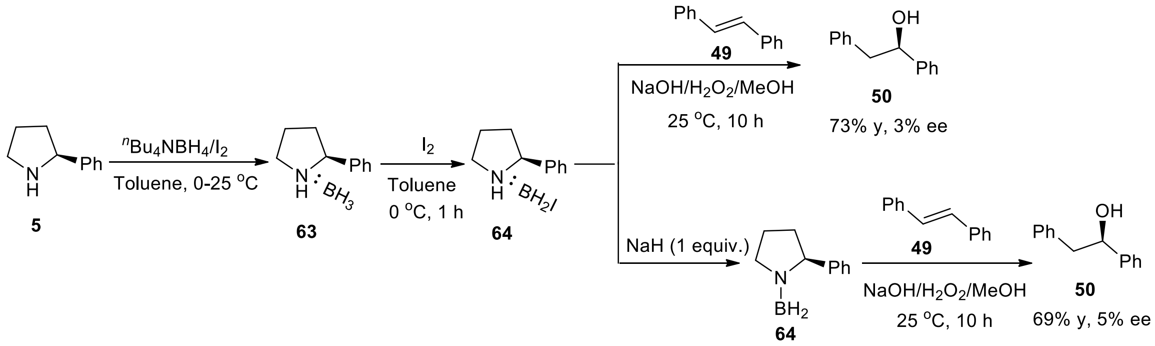
Scheme 12



I.2.3.4 Hydroboration of prochiral olefins using (-)-(2*S*)-phenylpyrrolidine

We have next studied the hydroboration reactions using chiral secondary (-)-(2*S*)-phenylpyrrolidine 1-boran complex **63**. The borane complex **63** was prepared by reaction of B_2H_6 prepared initially by the reaction of ^{n}Bu$_4$NBH$_4$, amine **5** with I_2 in toluene. We have also carried out the hydroboration reaction under iodine activation and also by adding sodium hydride. However, after the NaOH/H_2O_2 oxidation, the corresponding alcohol was obtained only in 3% and 5% ee respectively (Scheme 13).

Scheme 13

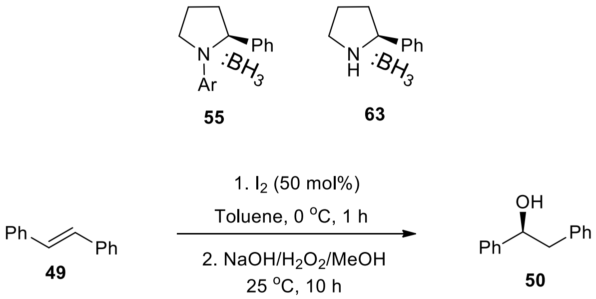


Since only poor selectivity was realized in these reactions, we did not pursue further research efforts on this topic.

I.3 Conclusions

Efforts were undertaken toward the hydroboration of olefins using chiral (-)-(*S*)-1-aryl-2-phenylpyrrolidine-borane complexes **55** and (-)-(2*S*)-phenylpyrrolidine-borane complex **63** (Scheme 14).

Scheme 14



It was found that the borane complexes of (-)-(*S*)-1-aryl-2-phenylpyrrolidine **31** hydroborate olefin **49** to give alcohol **50** with only up to 5% ee by iodine activation, indicating that the olefin may displace the chiral amine before hydroboration because of steric hindrance of the phenyl group at C2 carbon of the chiral amine boranes **55** and **63**.

I. 4 Experimental Section

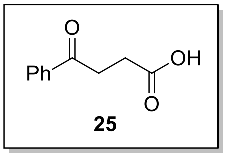
I.4.1 General informations

Several informations given in the section 1.4 are also applicable for the experiments outlined in this section. HPLC analyses were performed on an SCL-10ATVP SHIMADZU instrument. Perkin-Elmer elemental analyzer-240C and Thermo finnigan analyzer Flash EA 1112 were used for the elemental analysis. Rudolph Analytical AUTOPOL-IV (readability ± 0.001°) automatic polarimeter was used for checking optical rotations. 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.

I.4.2 Procedure for the preparation of 3-benzoylpropionicacid (25)

Dry benzene (100 mL) and succinic anhydride (17 g, 170 mmol) were placed in one liter three necked flask equipped with an efficient reflux condenser. The top of the condenser was connected to a calcium chloride guard tube. The mixture was stirred and powdered anhydrous aluminum chloride (50 g, 375 mmol) was added all at once. The reaction started immediately, hydrogen chloride was evolved and the mixture became hot. The reaction mixture was refluxed for 2 h. It was allowed to cool in a bath of cold water and water (50 mL) was slowly added. HCl (13N, 25 mL) was added and the organic layer was separated and the aqueous layer was extracted with ether. The combined organic extracts were washed with water (25 mL), brine (25 mL) and dried over anhydrous Na_2SO_4. After evaporation of the solvent, 3-benzoylpropionicacid **25** was isolated.

Yield : 50 g (83%).



Mp : 113 °C (*Lit.*[19] 115 °C).

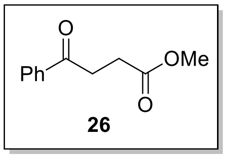
IR(KBr) : (cm^{-1}) 1680, 1600, 760, 680.

^{1}HNMR : (400 MHz, $CDCl_3$, δ ppm) 8.02-7.99 (m, 2H), 7.62-7.58 (m, 1H), 7.51-7.47 (m, 2H), 3.34 (t, *J* = 6.6 Hz, 2H), 2.84 (t, *J* = 6.6 Hz, 2H).

^{13}CNMR : (100 MHz, $CDCl_3$, δ ppm) 197.9, 179.1, 136.4, 133.4, 128.7, 128.1, 33.2, 28.1.

I.4.3 Procedure for the preparation of methyl-4-benzoylpropionate (26)

To a stirred solution of 3-benzoylpropionic acid **25** (17.8 g, 100 mmol) in methanol (80 mL) was added catalytic amount of conc. H_2SO_4 and refluxed for 12 h at 78 °C. Methanol was evaporated and diluted with ether (80 mL), washed successively with satd. $NaHCO_3$ (20 mL), water (20 mL) and brine (15 mL). The organic extract was dried over anhydrous Na_2SO_4. The crude product was distilled out under reduced pressure to afford methyl 4-benzoylpropionate **26**.



Yield : 16.9 g (88%).

IR (Neat) **:** (cm^{-1}) 2953, 1738, 1687, 1597, 1448, 750, 692.

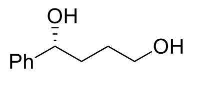
^{1}HNMR : (400 MHz, $CDCl_3$, δ ppm) 7.99 (d, *J* = 8 Hz, 2H), 7.58-7.46 (m, 3H), 3.72 (s, 3H), 3.34 (t, *J* = 8 Hz, 2H), 2.78 (t, *J* =8 Hz, 2H).

^{13}CNMR : (100 MHz, $CDCl_3$, δ ppm) 198.1, 173.4, 136.5, 133.3, 128.6, 128.0, 51.9, 33.4, 28.0.

I.4.4 Procedure for the preparation of (1*R*)-phenyl-butane-1,4-diol (27)

To a stirred solution of (*S*)-α,α-diphenylpyrrolidine methanol (5.06 g, 20 mmol) in THF (20 mL) at 25 °C, trimethylborate (2.8 mL, 25 mmol) was added and stirred for 1 h. To this, THF: BH_3 (100 mL, 2 M) was added at 0 °C. The ketoester **26** (38.4 g, 200 mmol) dissolved in THF (100 mL) was added to this suspension at 0 °C during 1 h. The reaction mixture was further stirred at 25 °C for 1 h. The reaction was carefully hydrolyzed with 2N HCl (20 mL) and the organic layer was separated. The aqueous layer was extracted with ether. The combined organic extract was washed with brine (10 mL) and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure and the crude product was purified on silica gel (100-200 mesh). The solvent mixture hexane:ethylacetate (85:15) elutes the methyl(4*R*)-hydroxy-4-phenyl methylbutyrate and its lactone (yield 39%). The chiral diol(1*R*)-phenyl-butane-1,4-diol **27** was eluted in hexane:ethylacetate (50:50).

Yield : 13.94 g (42%).



27

mp : 83 °C (*Lit.*[20] 82-83°C)

IR(KBr) : (cm^{-1}) 3333, 3036, 1496, 1446, 947

^{1}HNMR : (400 MHz, $CDCl_3$, δ ppm) 7.26-7.34 (m, 5H), 4.67-4.70 (m, 1H), 3.58-3.68 (m, 2H), 3.09 (bs, 2H), 1.86-1.81 (m, 2H), 1.61-1.71 (m, 2H).

^{13}CNMR : (100 MHz, $CDCl_3$, δ ppm) 144.7, 128.3, 127.3, 125.8, 74.1, 62.5, 36.3, 29.1.

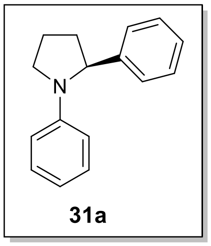
$[\alpha]^{25}_{D}$ = +30.8 (c 1.0, CH_3OH) {*Lit.*^{21}$_{D}$ = $[\alpha]^{25}$ +27.5 for 91% ee, (c 0.75, CH_3OH)}.

HPLC : 97% ee, Chiral cell OB-H Hexane (90):Isopropanol (10). Flow rate 1.0 mL/min t_S (9.6 min), t_R (18.7 min).

I.4.5 Procedure for the preparation of (2*S*)-*N*-Aryl-2-phenylpyrrolidine (31)

To methanesulfonyl chloride (0.6 mL, 6 mmol) in dichloromethane (10 mL) at-15 °C was added a solution of (1*R*)-phenylbutan-1,4-diol **27** (0.498 g, 3 mmol, 97% ee) and triethylamine (1 mL, 9 mmol) in dichloromethane (10 mL). The mixture was stirred for 2 h. at -15 °C and then quenched with saturated NH_4Cl (3 mL). The mixture was warmed to 25 °C. The organic layer was washed with water (5 mL), saturated $NaHCO_3$ (5 mL) and brine solution (10 mL). The organic extract was dried over with anhydrous Na_2SO_4 and concentrated under reduced pressure to approximately 5 mL. The crude dimesylate was added to arylamine (90 mmol) at 0 °C and stirred for 24 h. The reaction mixture was warmed to 25 °C. The residue was dissolved in ether (50 mL) and washed successively with saturated $NaHCO_3$ (10 mL), water (10 mL) and brine (10 mL). The organic extract was dried over with anhydrous Na_2SO_4 and concentrated to afford the residue as yellow oil. The crude product was purified on silicagel (100-200 mesh) using hexane:ethylacetate (95:5) as eluent to obtain the pure product **31** as colourless liquid.

(*S*)-1,2-Diphenylpyrrolidine (31a)



31a

Yield : 0.562 g (84%); white solid.

mp : 74-76 °C.

$[\alpha]_D^{25}$: -61.804 (*c* 0.90, $CHCl_3$).

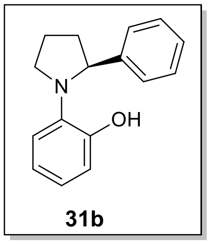
IR (KBr) : (cm^{-1}) 3057, 2969, 2871, 2816, 1599, 1506, 1473, 1441, 1364, 1249, 1167, 1024, 991, 958, 739, 695.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.34-7.30 (m, 2H), 7.26-7.22 (m, 3H), 7.17 (t, *J* = 7.92 Hz, 2H), 6.66 (t, *J* = 7.26 Hz, 1H), 6.52 (d, *J* = 8.13 Hz, 2H), 4.75 (d, *J* = 7.96 Hz, 1H), 3.76-3.71 (m, 1H), 3.47-3.40 (m, 1H), 2.46-2.36 (m, 1H), 2.09-1.94 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 147.2, 144.7, 129.0, 128.5, 126.6, 125.9, 115.8, 112.4, 62.9, 49.1, 36.1, 23.1.

HRMS : (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{17}N$: 224.1439, Found: 224.1438.

(*S*)-2-(2-Phenylpyrrolidin-1-yl)phenol (31b)



31b

Yield : 0.359 g (50%); white solid.

mp : 88-90 °C.

$[\alpha]_D^{25}$: -54.54 (*c* 0.88, $CHCl_3$).

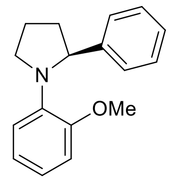
IR (KBr) : (cm^{-1}) 3353, 3287, 3035, 2969, 2854, 2832, 1588, 1484, 1440, 1363, 1265, 1243, 1117, 1084, 821, 760.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.27-7.15 (m, 6H), 6.99-6.95 (m, 1H), 6.84-6.77 (m, 2H), 4.33 (t, *J* = 7.9 Hz, 1H), 3.58-3.53 (m, 1H), 2.97-2.91 (m, 1H), 2.48-2.40 (m, 1H), 2.20-1.95 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 152.5, 142.2, 135.8, 128.5, 128.2, 127.3, 126.9, 125.9, 121.9, 120.1, 114.0, 67.7, 56.0, 35.1, 23.8.

HRMS : (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{17}NO$: 240.1388, Found: 240.1387.

(*S*)-1-(2-Methoxyphenyl)-2-phenylpyrrolidine (31c)



31c

Yield : 0.486 g (64%); colorless oil.

$[\alpha]_D^{25}$: -16.03 (*c* 0.40, $CHCl_3$).

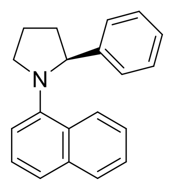
IR (KBr) : (cm^{-1}) 3057, 3018, 2964, 2827, 1599, 1506, 1456, 1330, 1276, 1232, 1182, 1023, 903, 733.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.30-7.24 (m, 4H), 7.19-7.14 (m, 1H), 6.84-6.75 (m, 3H), 6.66-6.64 (m, 1H), 4.84 (t, *J* = 7.12 Hz, 1H), 4.14-4.08 (m, 1H), 3.78 (s, 3H), 3.34-3.28 (m, 1H), 2.44-2.38 (m, 1H), 2.08-1.88 (m, 3H)

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 150.4, 144.6, 138.9, 128.2, 126.4, 126.3, 121.1, 119.2, 116.7, 112.5, 64.2, 55.8, 52.8, 36.9, 24.2.

HRMS : (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{17}H_{19}NO$: 254.1545, Found: 254.1540.

(*S*)-1-(Naphthalene-1-yl)-2-phenylpyrrolidine (31d)



31d

Yield : 0.483 g (59%); white solid.

mp : 101-103 °C.

$[\alpha]_D^{25}$: +303.90 (*c* 0.45, $CHCl_3$).

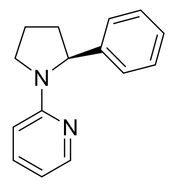
IR (KBr) : (cm^{-1}) 3057, 2964, 2931, 2821, 1583, 1572, 1506, 1490, 1452, 1271, 1095, 1013, 947, 805, 772, 706.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 8.51 (d, *J* = 8.02 Hz, 1H), 7.88-7.86 (m, 1H), 7.62-7.47 (m, 5H), 7.33-7.19 (m, 4H), 6.99 (d, *J* = 7.47 Hz, 1H), 4.85-4.81 (m, 1H), 4.33-4.27 (m, 1H), 3.22-3.16 (m, 1H), 2.59-2.55 (m, 1H), 2.24-2.01 (m, 3H),

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 146.7, 143.4, 134.9, 129.5, 128.6, 128.4, 128.3, 126.8, 126.7, 125.9, 125.6, 124.9, 124.6, 121.9, 113.9, 64.6, 56.7, 36.8, 24.5.

HRMS : (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{20}H_{19}N$: 274.1595, Found: 274.1596.

(*S*)-2-(2-Phenylpyrrolidine-1-yl)pyridine (31e)



31e

Yield : 0.558 g (83%); white solid.

mp : 119-121 °C.

$[\alpha]_D^{25}$: -50.3 (*c* 0.50, $CHCl_3$).

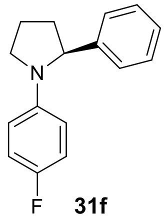
IR (KBr) : (cm^{-1}) 3057, 2969, 2838, 1599, 1561, 1495, 1473, 1441, 1369, 1304, 1243, 1156, 986, 767, 695.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 8.18-8.17 (m, 1H), 7.35-7.18 (m, 6H), 6.52-6.49 (m, 1H), 6.17 (d, *J* = 8.52 Hz, 1H), 4.92 (d, *J* = 8.85 Hz, 1H), 3.94-3.88 (m, 1H), 3.76-3.70 (m, 1H), 2.46-2.38 (m, 1H), 2.08-1.94 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 157.0, 148.2, 144.0, 136.7, 128.5, 126.7, 125.8, 111.6, 107.5, 61.7, 48.1, 36.1, 22.9

HRMS : (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{15}H_{16}N_2$: 225.1391, Found:225.1391.

(*S*)-1-(4-Fluorophenyl)-2-phenylpyrrolidine (31f)



31f

Yield : 0.543 g (75%); white solid.

mp : 120-122 °C.

$[\alpha]_D^{25}$: -60.89 (*c* 0.90, $CHCl_3$).

IR (KBr) : (cm^{-1}) 3063, 2964, 2871, 1583, 1468, 1435, 1315, 1276, 1101, 1057, 750, 695.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.43-7.33 (m, 5H), 6.99-6.93 (m, 2H), 6.53-6.49 (m, 2H), 4.77 (d, *J* = 6.65 Hz, 1H), 3.80-3.54 (m, 1H), 3.50-3.44 (m, 1H), 2.54-2.45 (m, 1H), 2.18-2.04 (m, 3H).

^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 156.2, 153.9, 144.7, 143.9, 128.7, 126.9, 126.0, 115.6, 115.4, 112.9, 112.8, 63.4, 49.7, 36.4, 23.4.

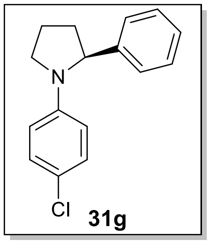
HRMS : (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{16}FN$: 242.1345, Found: 242.1347.

(*S*)-1-(4-Chlorophenyl)-2-phenylpyrrolidine (31g)

Yield : 0.634 g (82%); white solid.

mp : 125-127 °C.

$[\alpha]_D^{25}$: -92.04 (*c* 0.59, $CHCl_3$).



31g

IR (KBr) : (cm^{-1}) 3063, 3030, 2964, 2838, 1594, 1501, 1446, 1364, 1183, 1095, 964, 810, 701.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 7.35-7.32 (m, 2H), 7.27-7.21 (m, 3H), 7.10 (d, *J* = 8.93 Hz, 1H), 6.42 (d, *J* = 8.93 Hz, 2H), 4.73-4.70 (m, 1H), 3.73-3.68 (m, 1H), 3.44-3.38 (m, 1H), 2.46-2.38 (m, 1H), 2.09-1.95 (m, 3H).

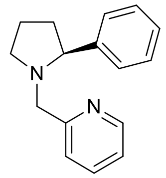
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 145.7, 144.1, 128.8, 128.6, 126.8, 125.9, 120.6, 113.4, 63.0, 49.3, 36.2, 23.1

HRMS : (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{16}ClN$: 258.7657, Found: 258.7649.

(*S*)-2-((2-Phenylpyrrolidin-1-yl)methyl)pyridine (31h)

Yield : 0.493 g (69%); colorless oil.

$[\alpha]_D^{25}$: -67.41 (*c* 1.06, $CHCl_3$).



31h

IR (KBr) : (cm^{-1}) 3068, 2969, 2800, 1600, 1479, 1430, 1353, 1293, 1172, 1041, 898, 761, 701.

^{1}H NMR : (400 MHz, $CDCl_3$, δ ppm) 8.50-8.49 (m, 1H), 7.61 (t, *J* = 7.51 Hz, 1H), 7.48-7.41 (m, 3H), 7.35-7.31 (m, 2H), 7.27-7.22 (m, 1H), 7.12-7.09 (m, 1H), 3.95 (d, *J* = 13.71 Hz, 1H), 3.49-3.45 (m, 1H), 3.32 (d, *J* = 13.83 Hz, 1H), 3.19-3.15 (m, 1H), 2.36-2.30 (m, 1H), 2.24-2.17 (m, 1H), 1.96-1.73 (m, 3H).

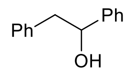
^{13}C NMR : (100 MHz, $CDCl_3$, δ ppm) 160.1, 148.8, 143.7, 136.3, 128.4, 127.6, 127.1, 122.8, 121.7, 69.9, 60.1, 53.8, 35.1, 22.6.

HRMS : (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{18}N_2$: 239.1548, Found: 239.1550.

I.4.6 General procedure for the hydroboration of olefins using chiral (-)-(*S*)-1-aryl-2-phenylpyrrolidines borane complex

The reaction flask cooled under N_2, containing the corresponding borane complex **55** (1 mmol, 8 mL in toluene), was added olefin (1 mmol) at 25 °C. This content was allowed to stir for 10 h at 110 °C. The mixture was brought to 25 °C after the required time. The reaction mixture was quenched with methanol (2 mL) and then oxidation was carried out for 4 h by adding 3N NaOH (4 mL) and H_2O_2 (30%, 4 mL). The organic layer was separated and the aqueous layer was extracted using ethyl acetate (2 x 10 mL). The combined organic layer was successively washed with water, brine and dried over Na_2SO_4. The solvent was evaporated and the crude product was purified by chromatography on silica gel column using hexane/ethyl acetate (90:10) as eluent to isolate the product.

1,2-Diphenylethanol (50)

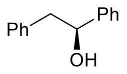

50

Yield	:	70%
mp	:	67-69°C
IR (KBr)	:	(cm^{-1}) 3315, 3024, 2920, 2854, 1030, 701.
^{1}H NMR	:	(400 MHz, $CDCl_3$, δ ppm) 7.32-7.22 (m, 10 H), 4.94-4.90 (m, 1H), 3.00-3.09 (m, 2H), 2.14 (s, 1H).
^{13}C NMR	:	(100 MHz, $CDCl_3$, δ ppm) 143.8, 138.1, 129.5, 128.5, 128.4, 127.6, 126.6, 125.9, 75.3, 46.1.

I.4.7 General procedure for the hydroboration of olefins using chiral (-)-(*S*)-1-aryl-2-phenylpyrrolidines-borane and chiral (-)-(2*S*)-phenylpyrrolidine-borane complexes by iodine activation

The reaction flask cooled under N_2, containing the corresponding borane complex **55** (1 mmol, 8 mL in toluene), was added iodine (0.1 to 0.5 mmol, 0.025 to 0.125 g) in toluene (5 mL) at 0 °C. Then, olefin (1 mmol) was added at 0 °C. The resulting content was allowed to stir for 10 h at 25 °C. The reaction mixture was quenched with methanol (2 mL) and then oxidation was carried out for 4 h by adding 3N NaOH (4 mL) and H_2O_2 (30%, 4 mL). The organic layer was separated and the aqueous layer was extracted using ethyl acetate (2 x 10 mL). The combined organic layer was successively washed with water, brine and dried over Na_2SO_4. The solvent was evaporated and the crude product was purified by chromatography on silica gel column using hexane/ethyl acetate (90:10) as eluent to isolate the product.

1,2-Diphenylethanol (50)



50

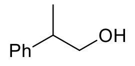
Yield : 68-73%

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

$[\alpha]_D^{25}$: +2.8 (c 0.5, EtOH), {lit.[22] for 100% ee, $[\alpha]_D^{25}$ = +52.8 (c, 1.40, EtOH)} (4% ee, confirmed by HPLC using chiral column, chiralcel OD-H, hexane/*i*-propanol= 90:10, flow rate: 0.3 mL/min., 254 nm, retention times: 26.66 min.(*R*) and 30.27 min. (*S*)).

The spectral data of the corresponding products were showed 1:1 correspondence with the data obtained in the earlier experiments.

2-Phenylpropanol (42)


42

Yield : 69-75%

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.

I. 5 References

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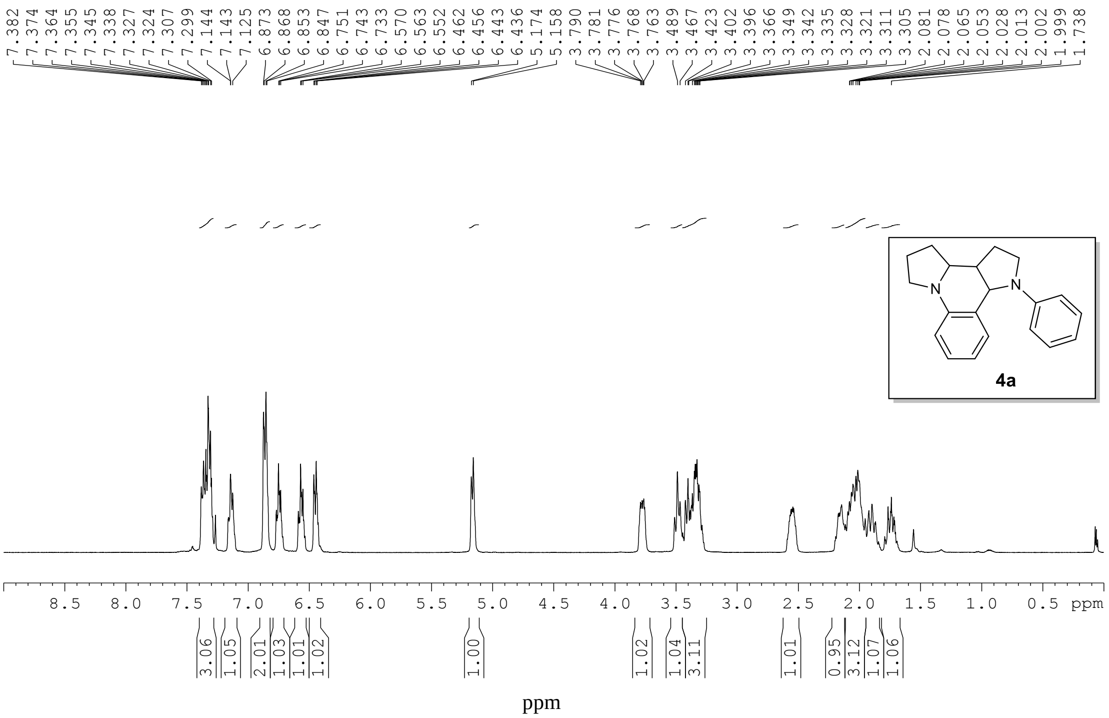
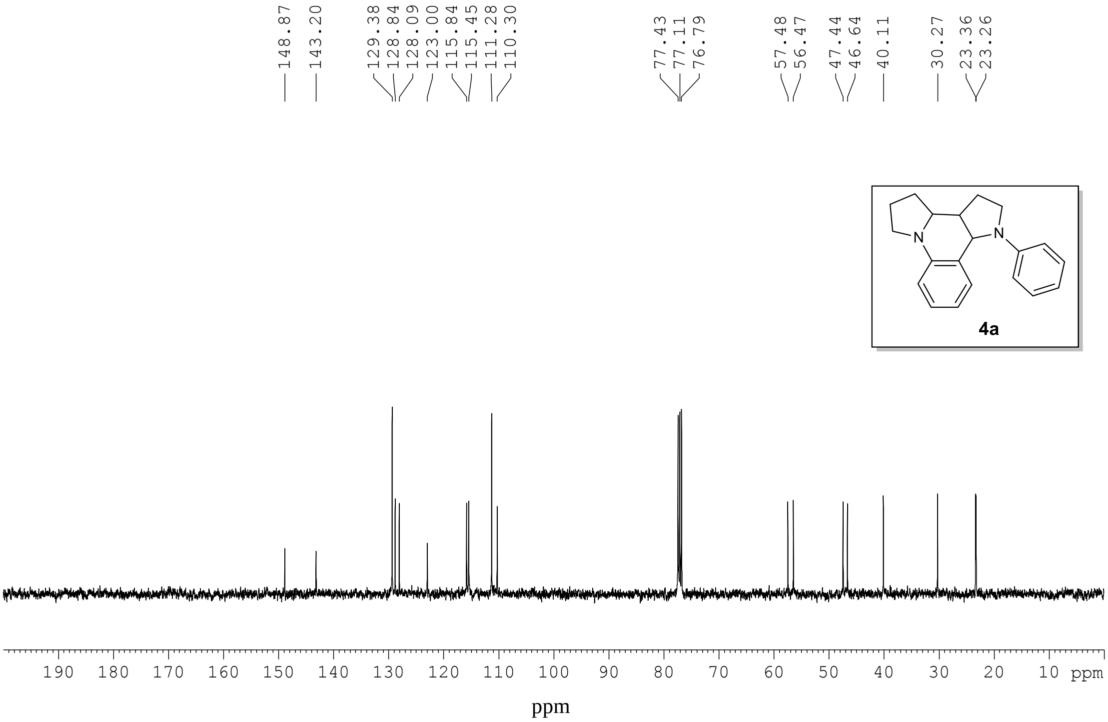
Appendix II

(Representative Spectra)

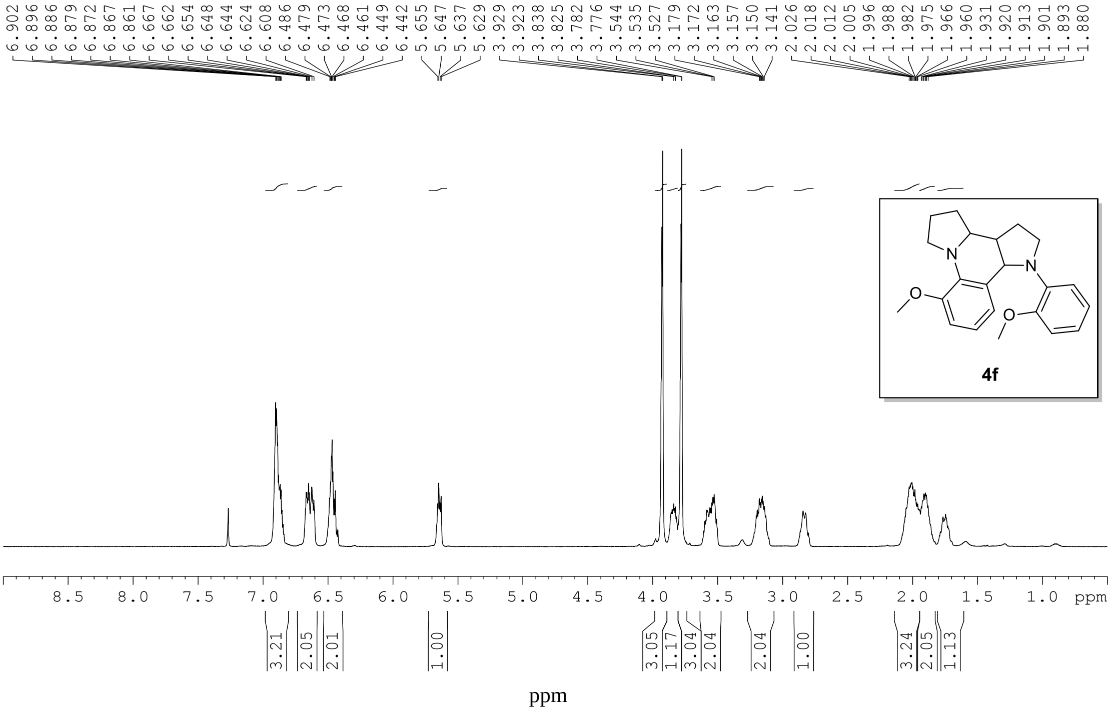
Spectrum No. 1 (Chapter 1, Section 1.2.2), ^{1}H NMR Spectrum (400 MHz, CDCl$_3$)



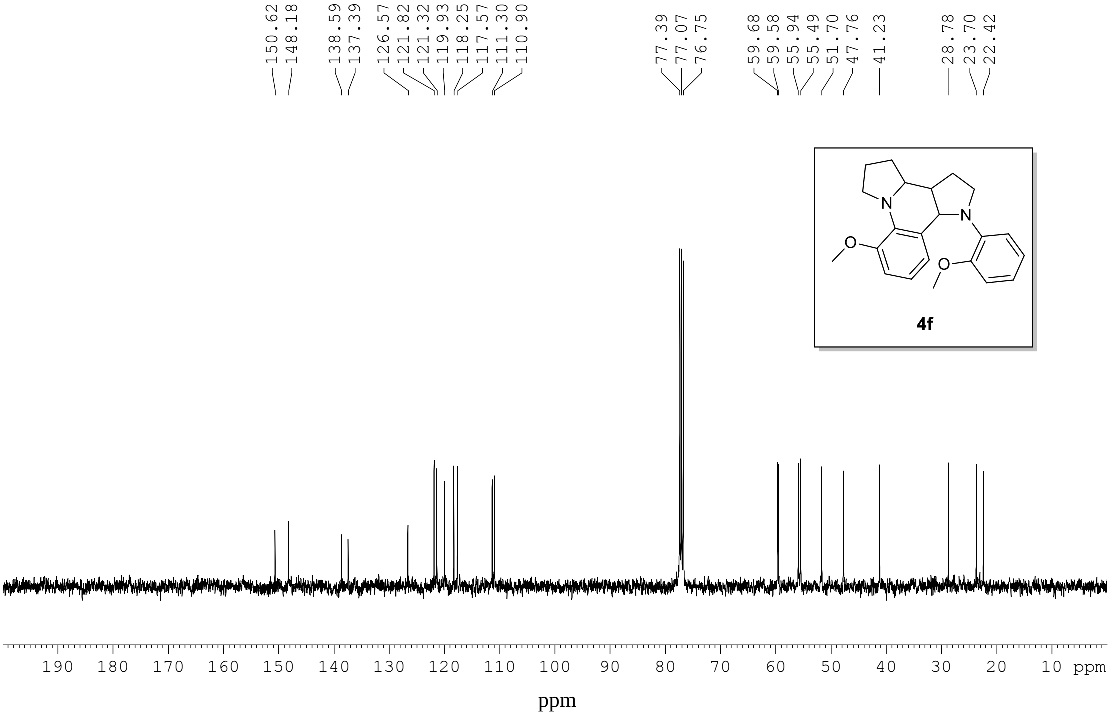
Spectrum No. 2 (Chapter 1, Section 1.2.2), ^{13}C NMR Spectrum (100 MHz, CDCl$_3$)



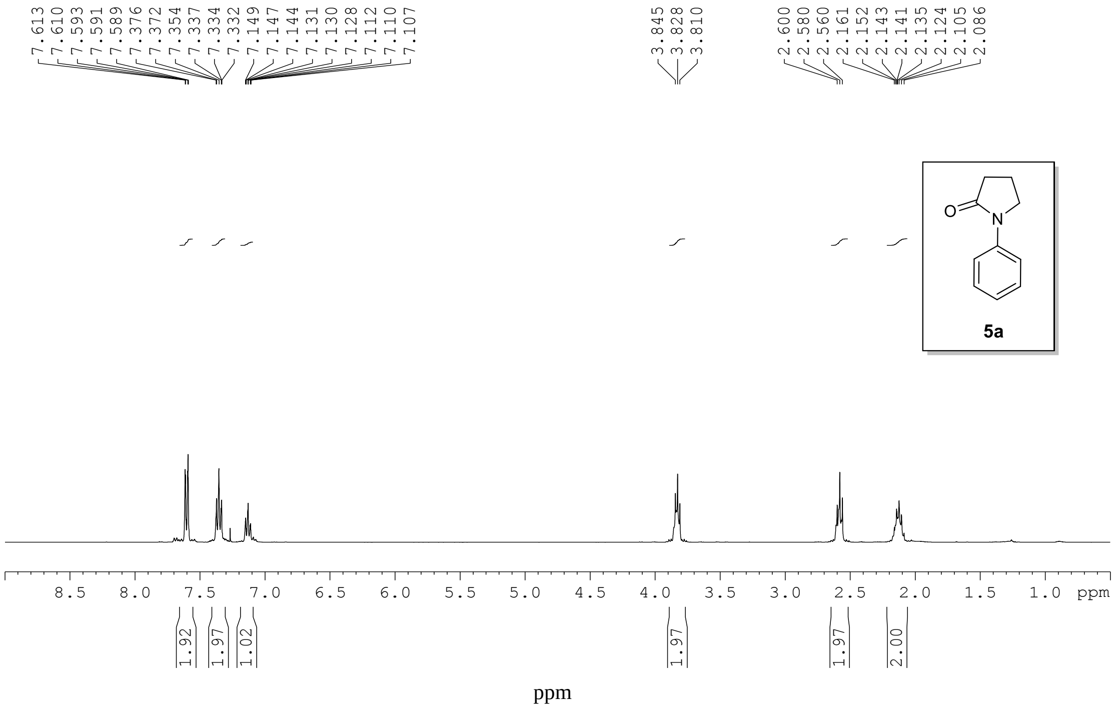
Spectrum No. 3 (Chapter 1, Section 1.2.2), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



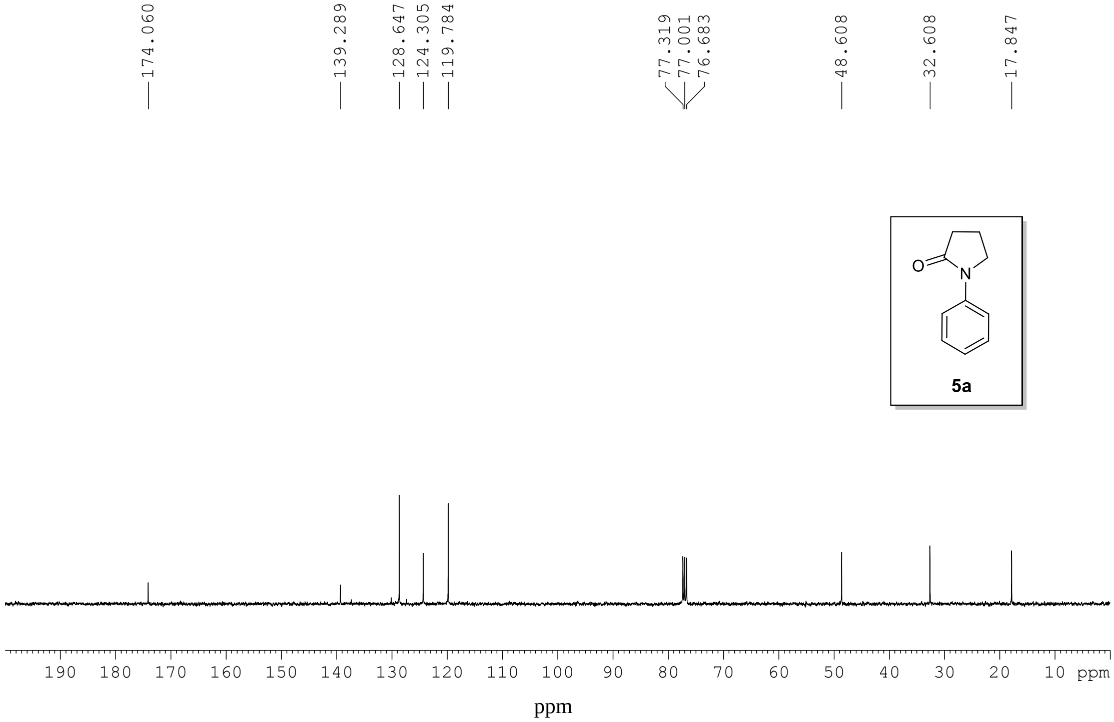
Spectrum No. 4 (Chapter 1, Section 1.2.2), ^{13}C NMR Spectrum (400 MHz, $CDCl_3$)



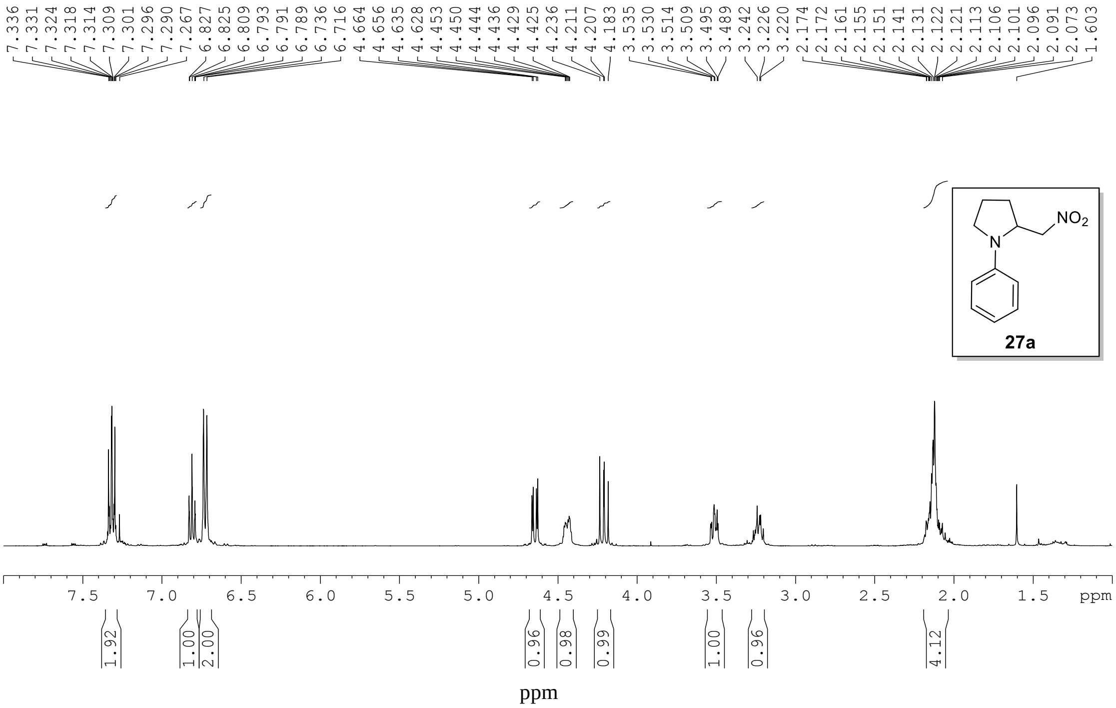
Spectrum No. 5 (Chapter 1, Section 1.2.3), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



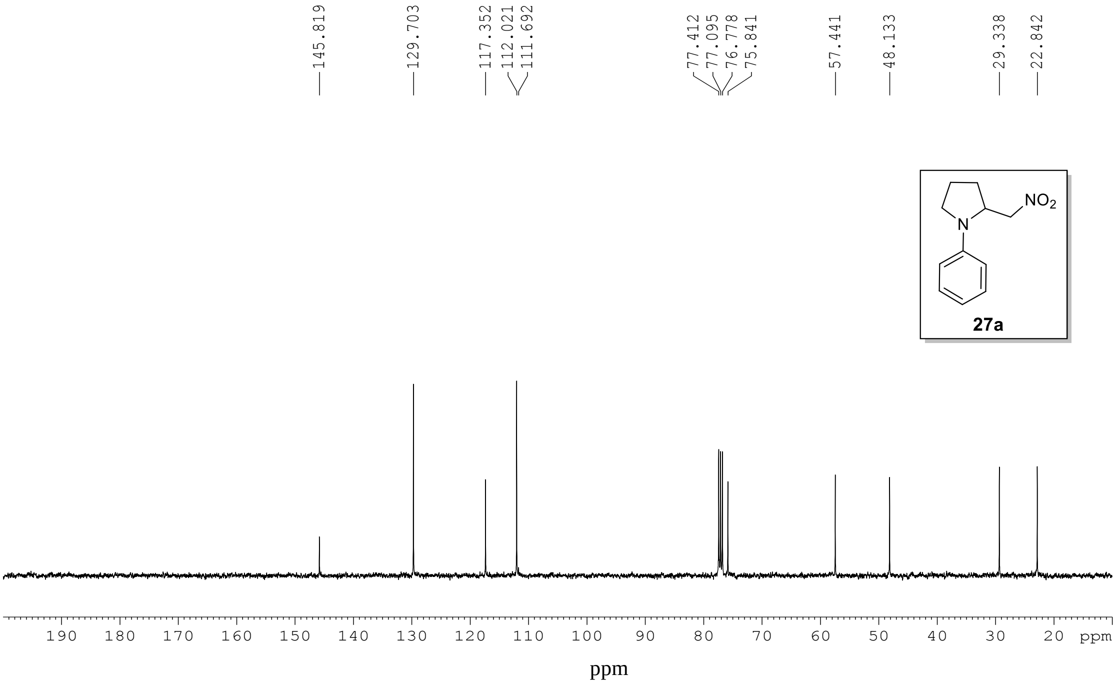
Spectrum No. 6 (Chapter 1, Section 1.2.3), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



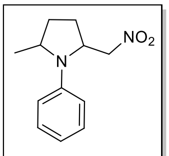
Spectrum No. 7 (Chapter 1, Section 1.2.6), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



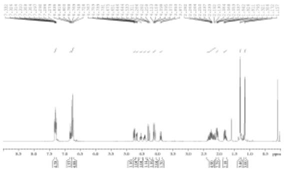
Spectrum No. 8 (Chapter 1, Section 1.2.6), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



Spectrum No. 9 (Chapter 1, Section 1.2.6), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)

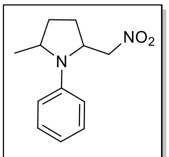


27k

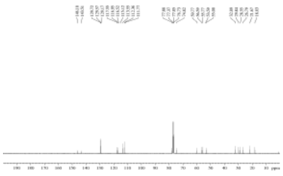


ppm

Spectrum No. 10 (Chapter 1, Section 1.2.6), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)

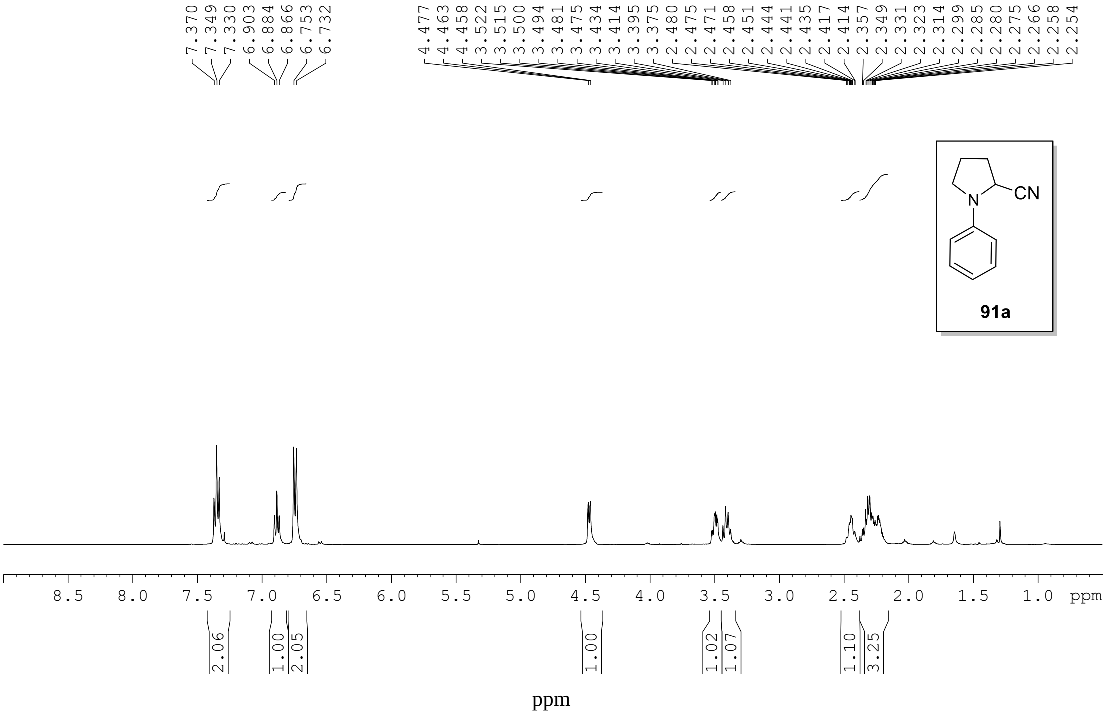


27k

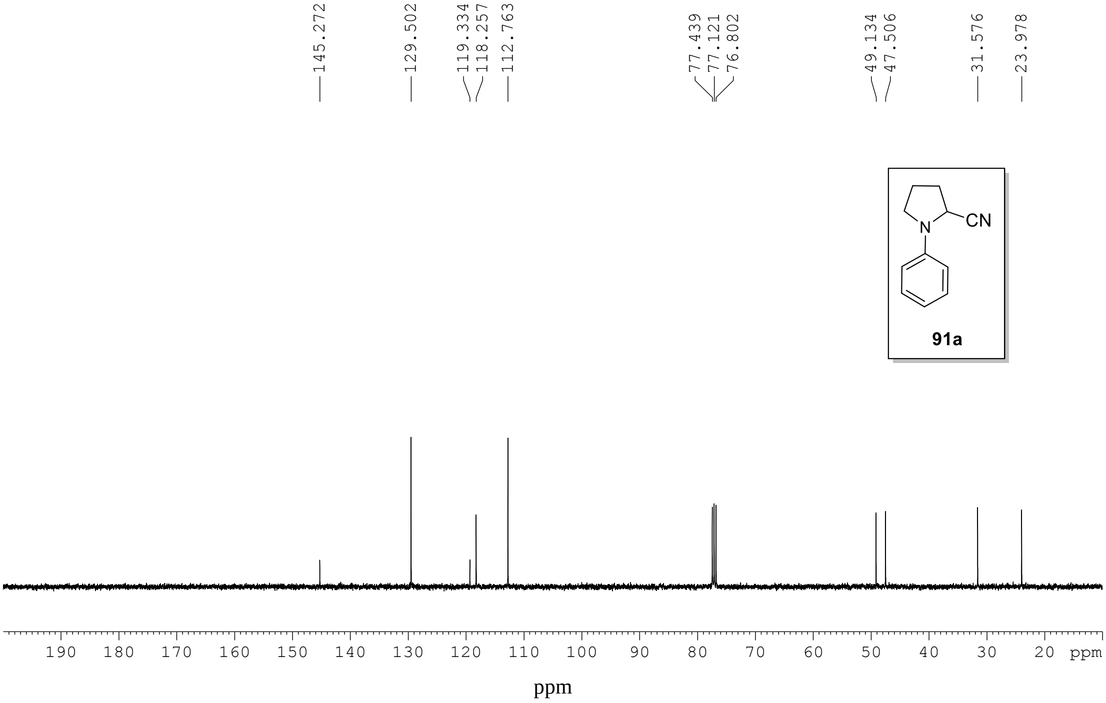


ppm

Spectrum No. 11 (Chapter 1, Section 1.2.7), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



Spectrum No. 12 (Chapter 1, Section 1.2.7), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



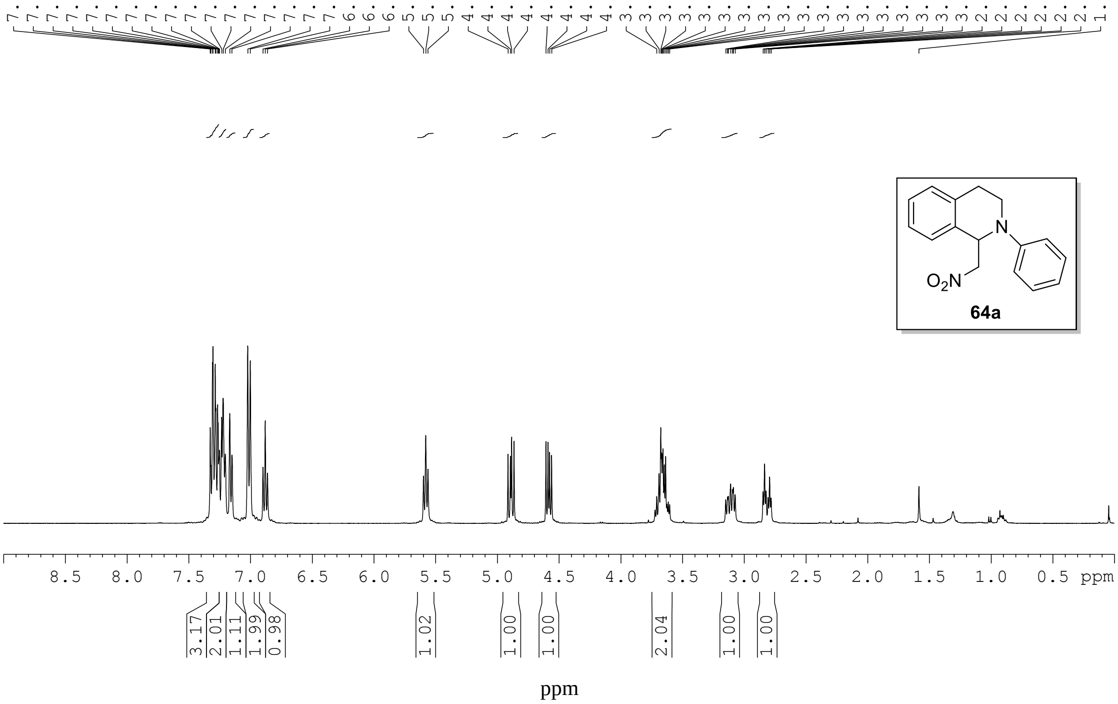
Spectrum No. 13 (Chapter 1, Section 1.2.7), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)

ppm

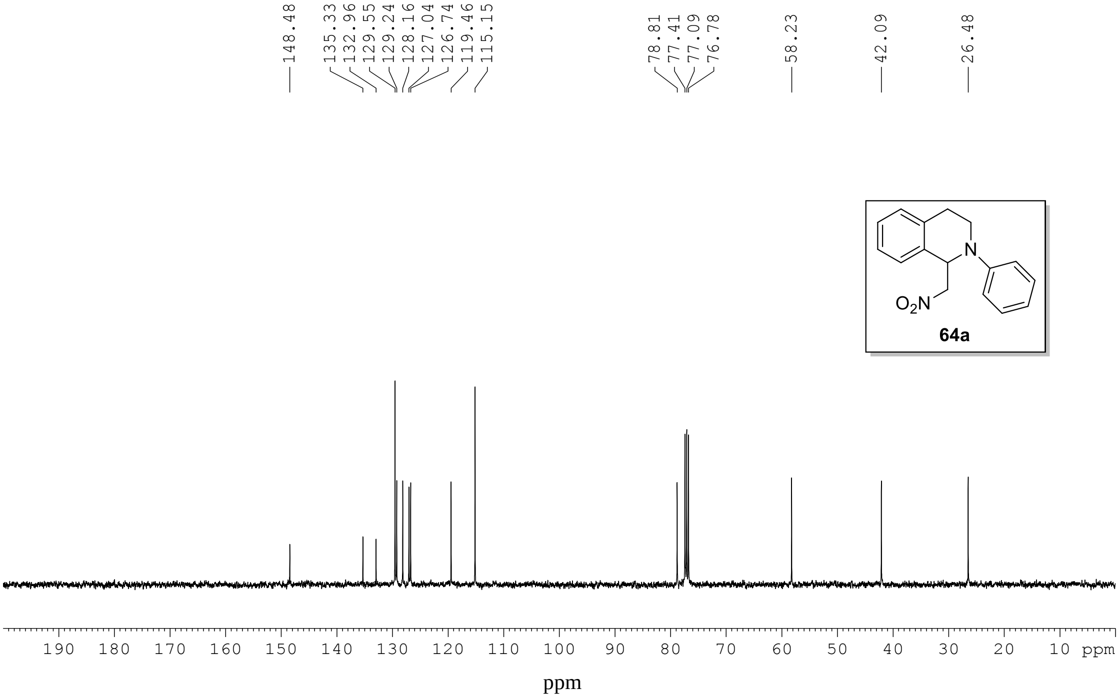
Spectrum No. 14 (Chapter 1, Section 1.2.7), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)

ppm

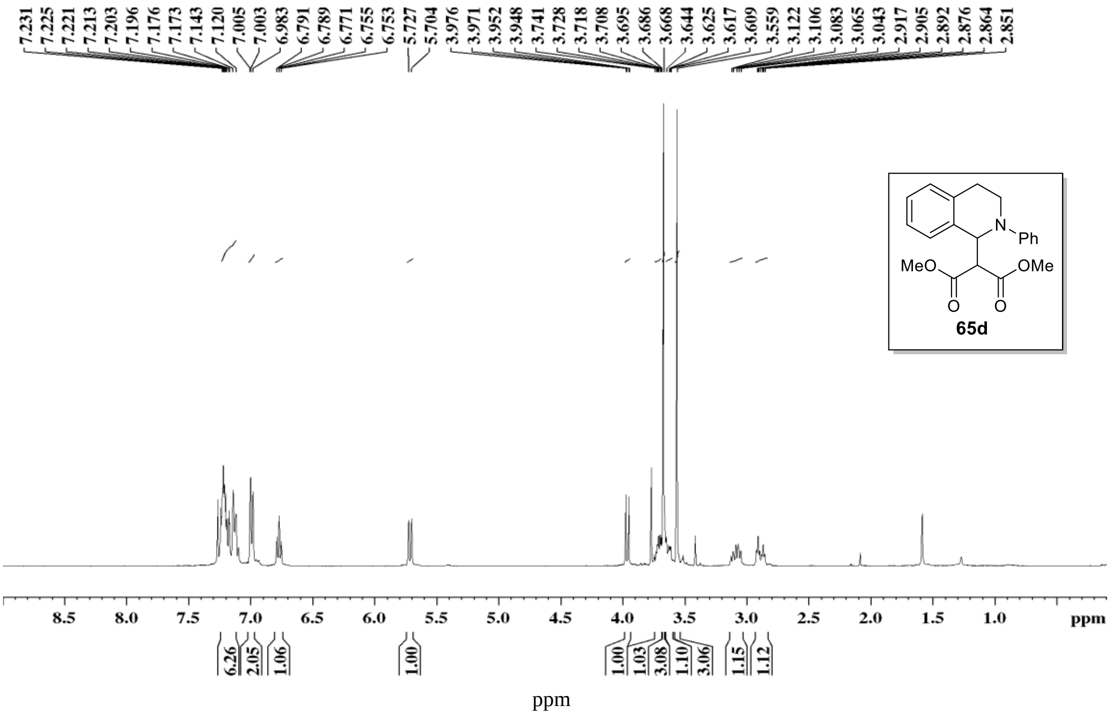
Spectrum No. 15 (Chapter 2, Section 2.2.1), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



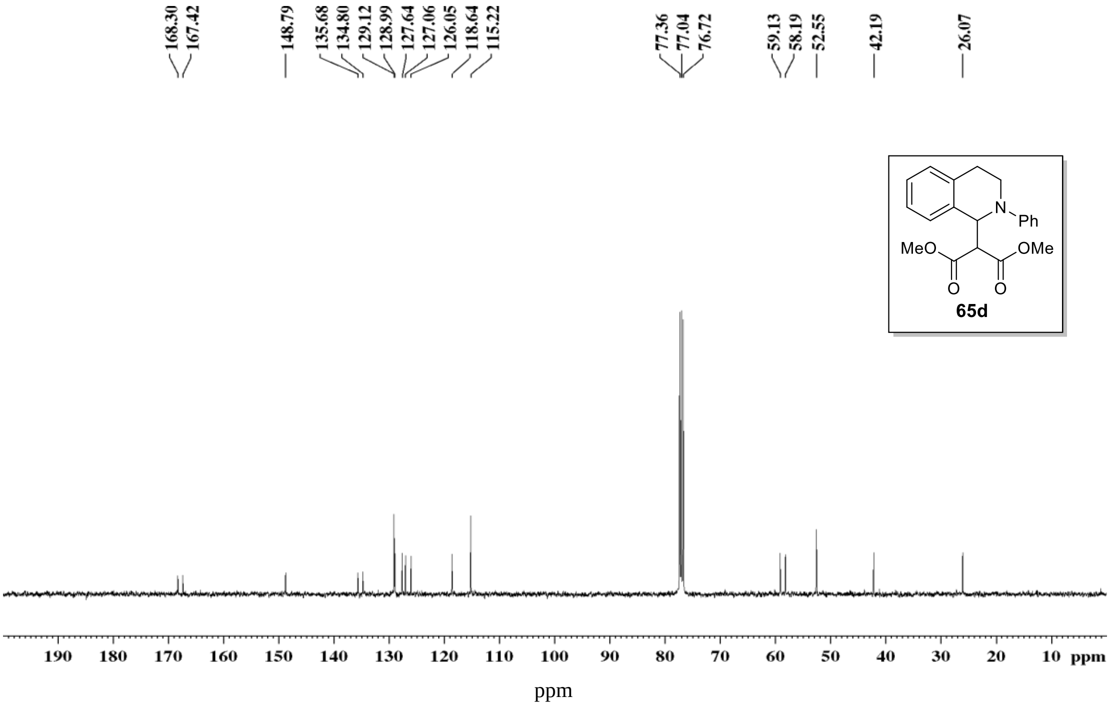
Spectrum No. 16 (Chapter 2, Section 2.2.1), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



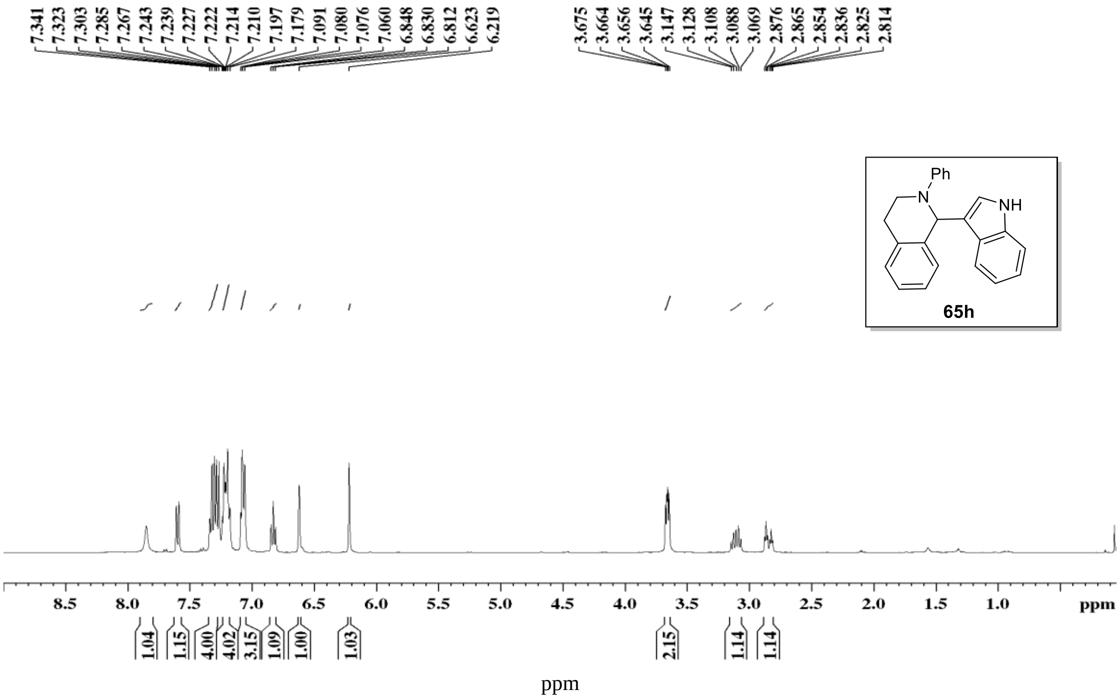
Spectrum No. 17 (Chapter 2, Section 2.2.2), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



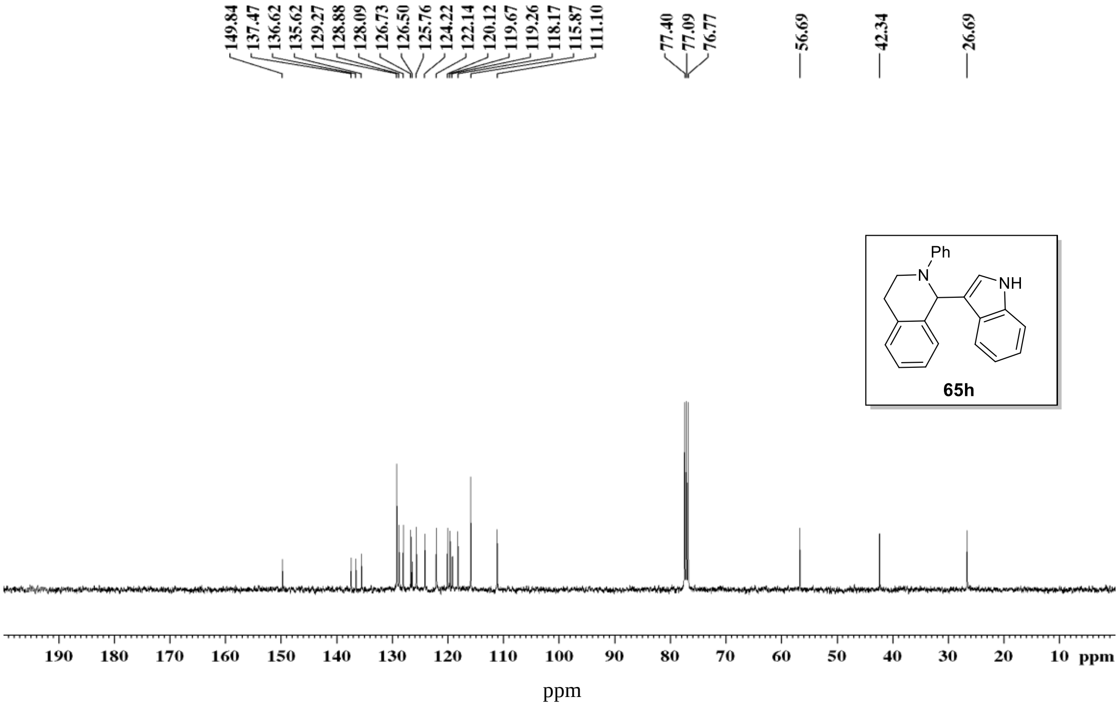
Spectrum No. 18 (Chapter 2, Section 2.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



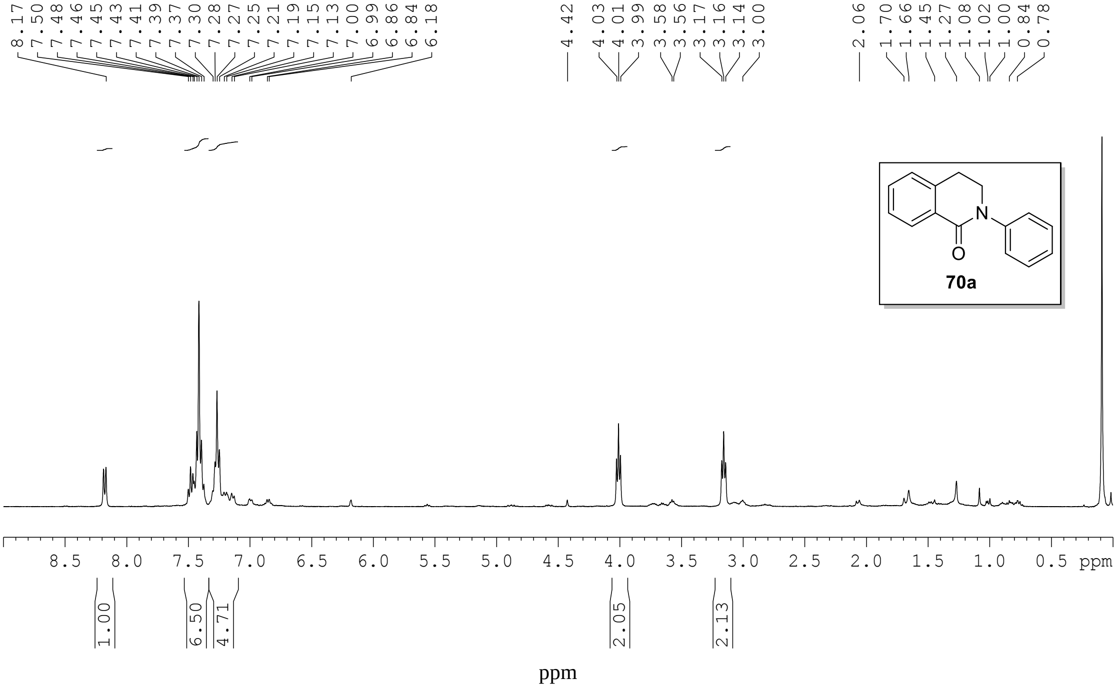
Spectrum No. 19 (Chapter 2, Section 2.2.2), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



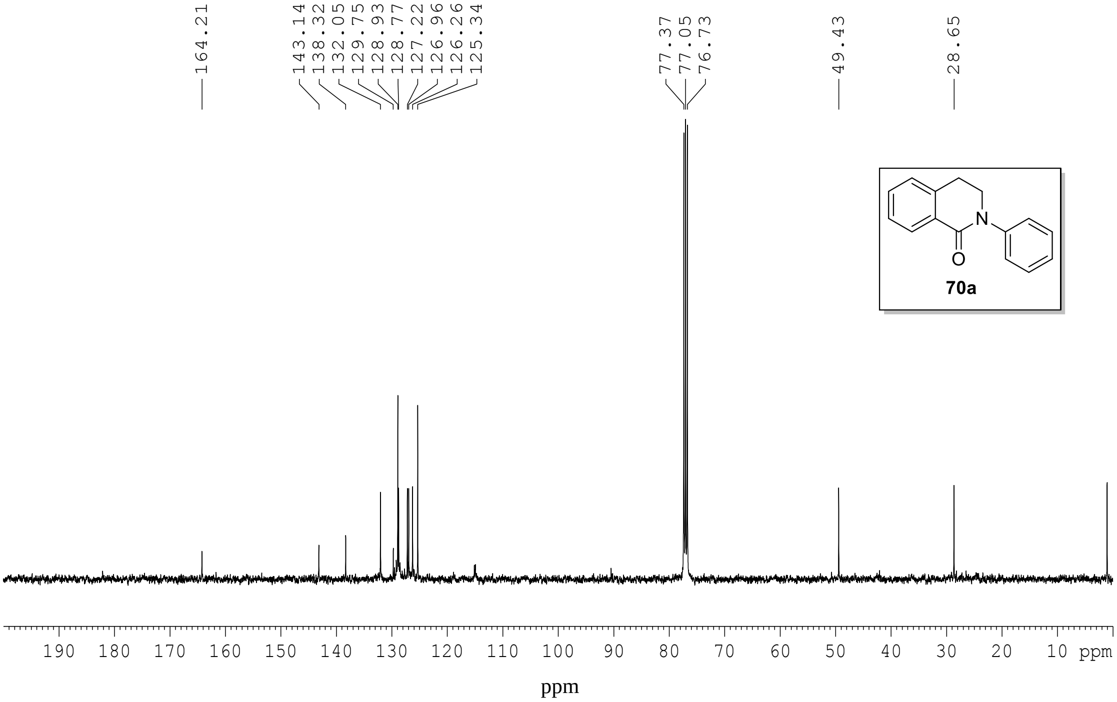
Spectrum No. 20 (Chapter 2, Section 2.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



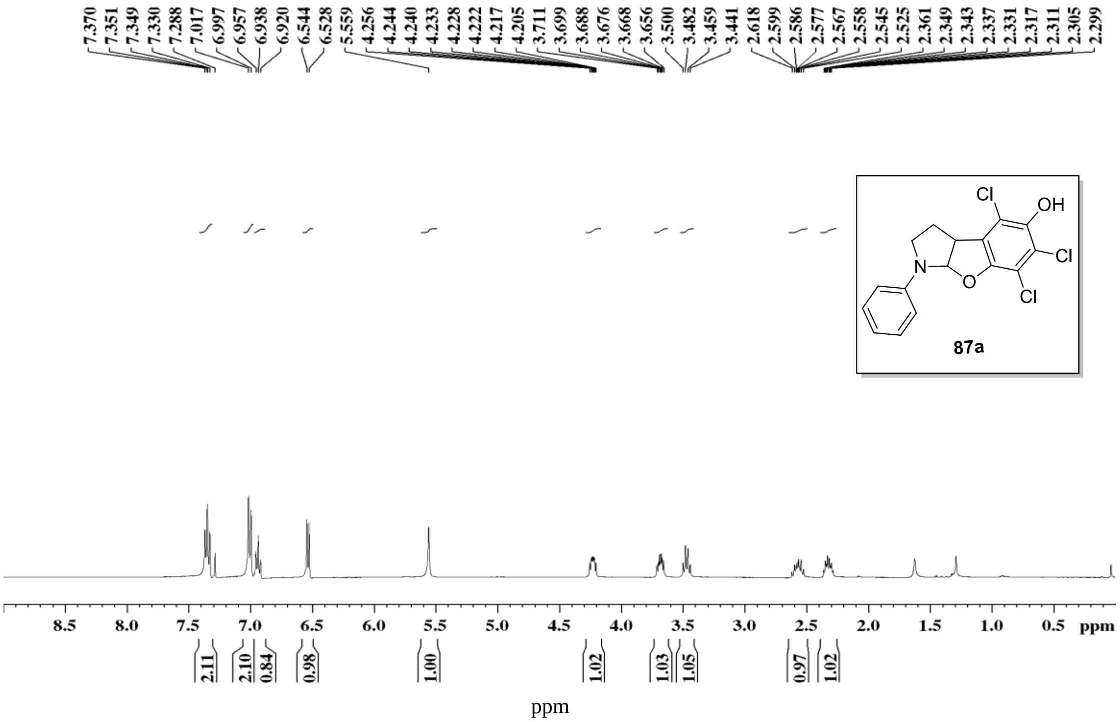
Spectrum No. 21 (Chapter 2, Section 2.2.4), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



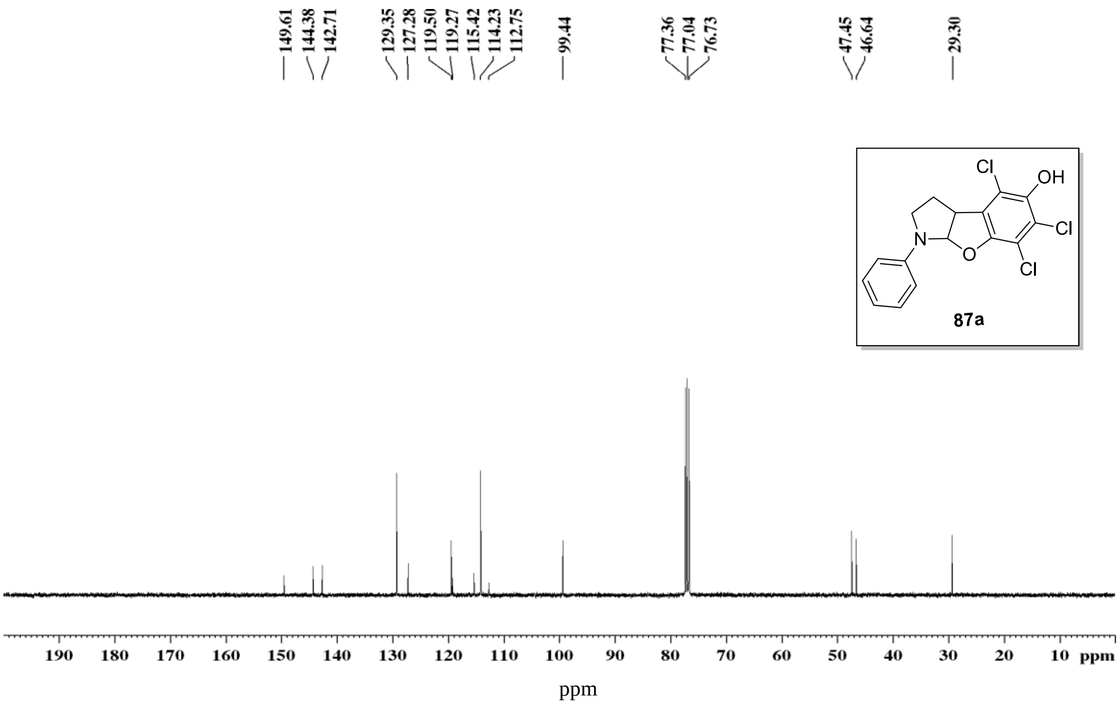
Spectrum No. 22 (Chapter 2, Section 2.2.4), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



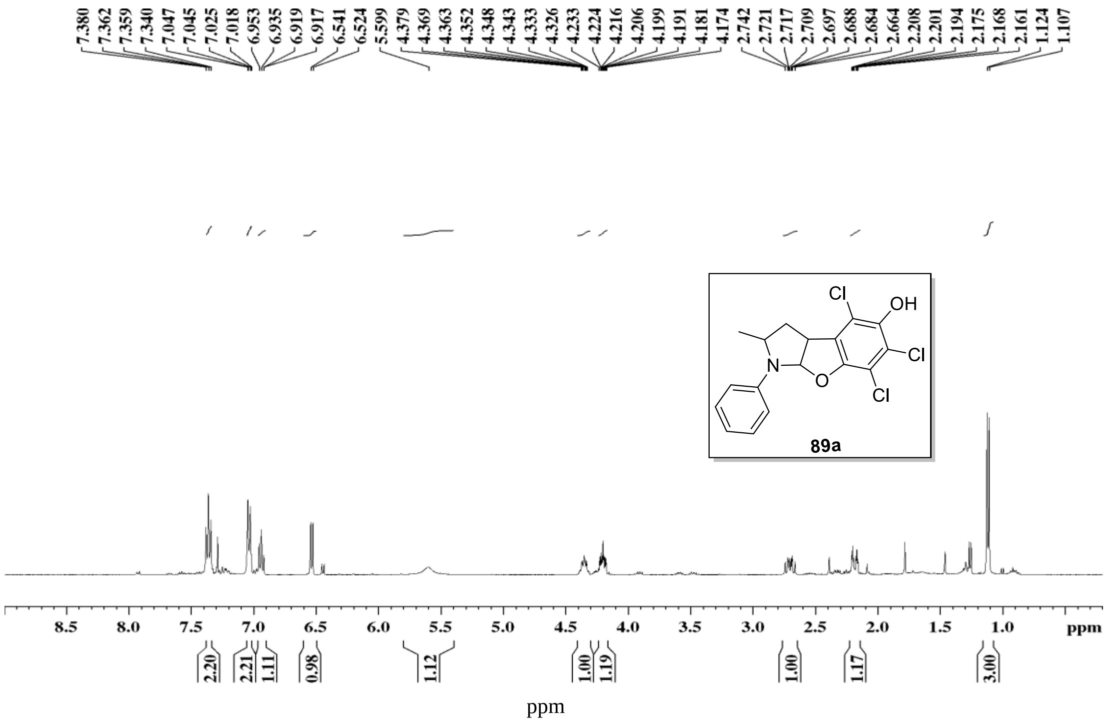
Spectrum No. 23 (Chapter 3, Section 3.2.4), ^{1}H NMR Spectrum (400 MHz, CDCl$_3$)



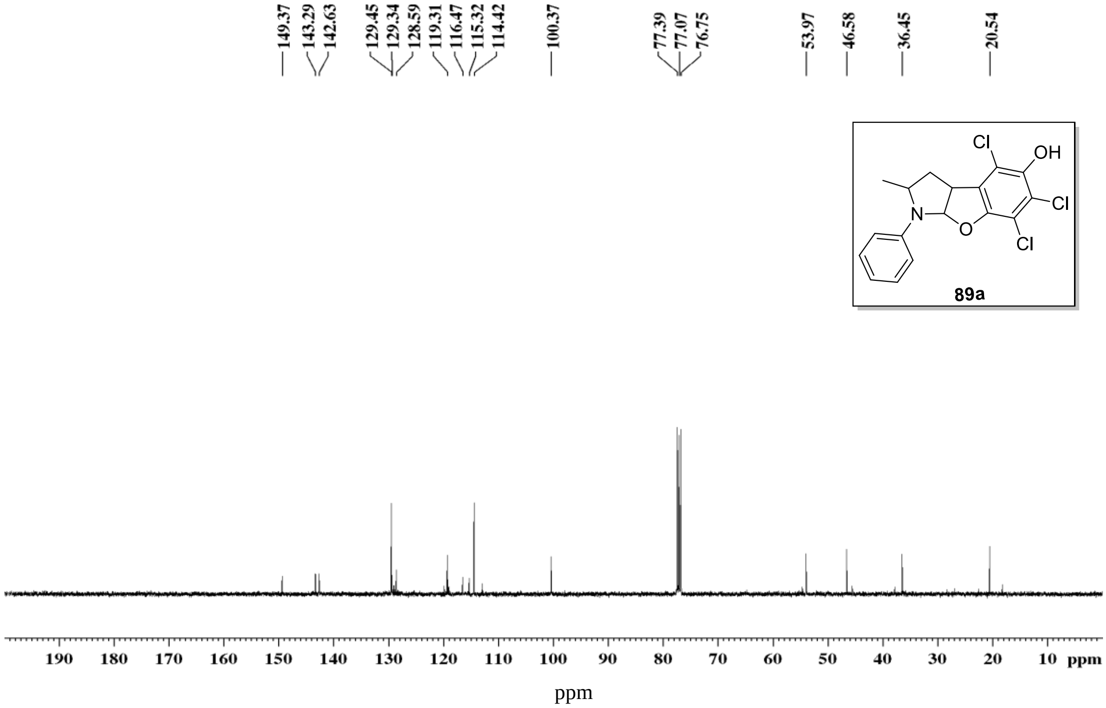
Spectrum No. 24 (Chapter 3, Section 3.2.4), ^{13}C NMR Spectrum (100 MHz, CDCl$_3$)



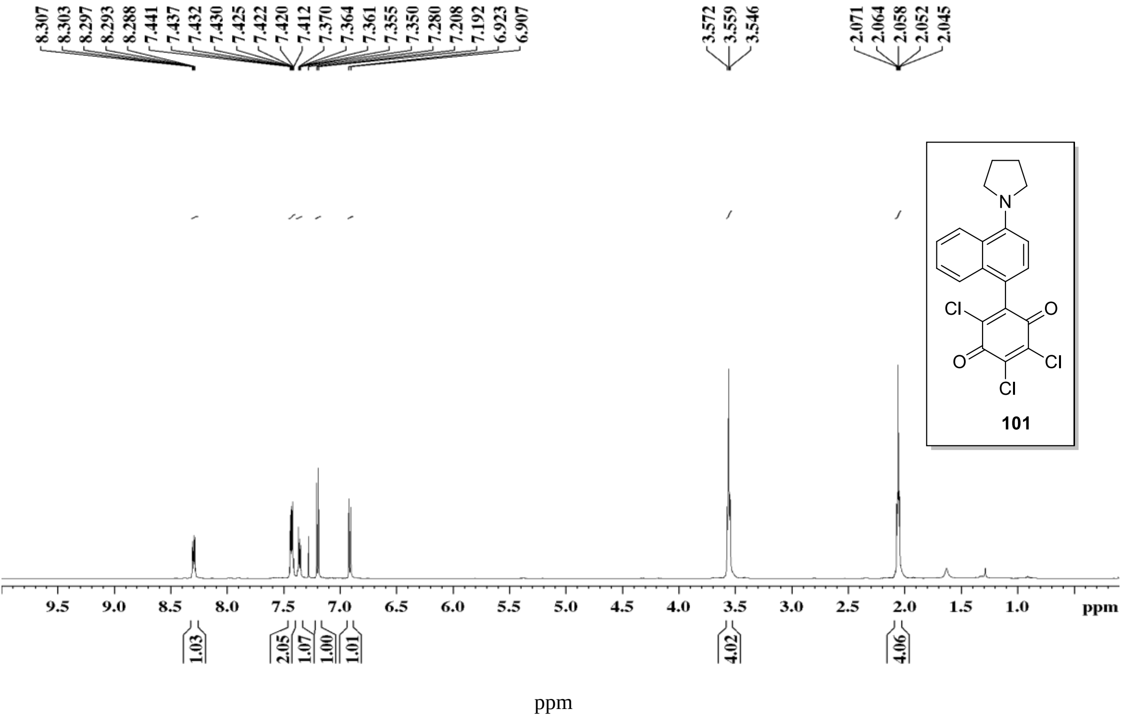
Spectrum No. 25 (Chapter 3, Section 3.2.5), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



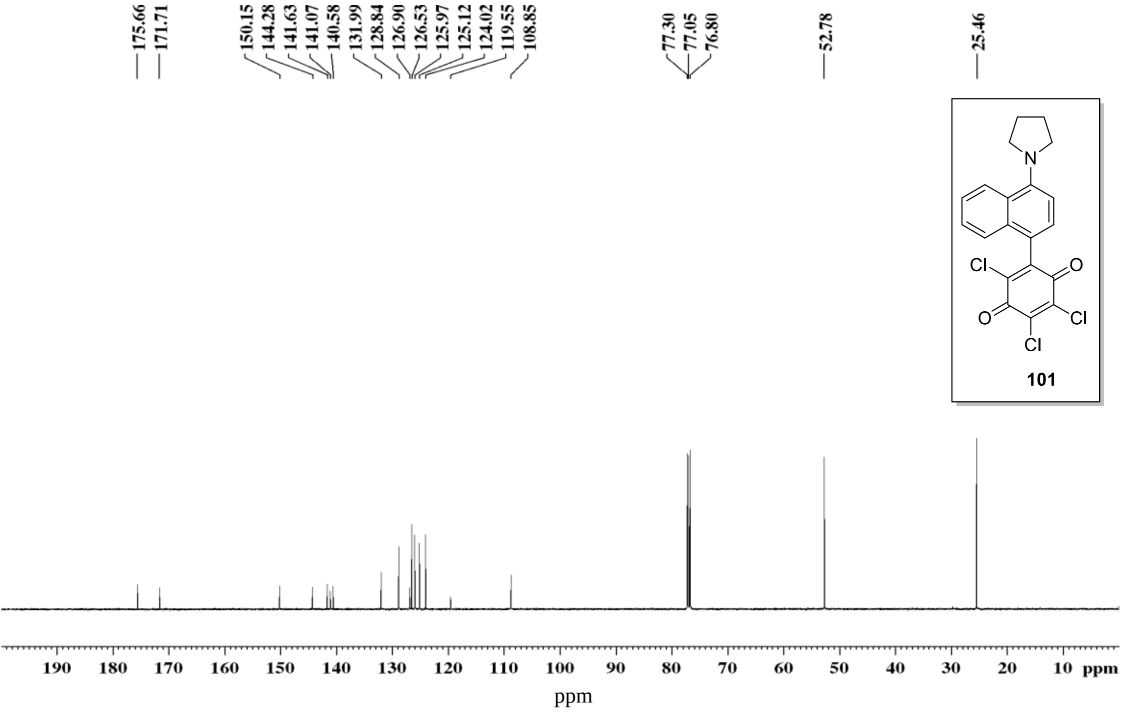
Spectrum No. 26 (Chapter 3, Section 3.2.5), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



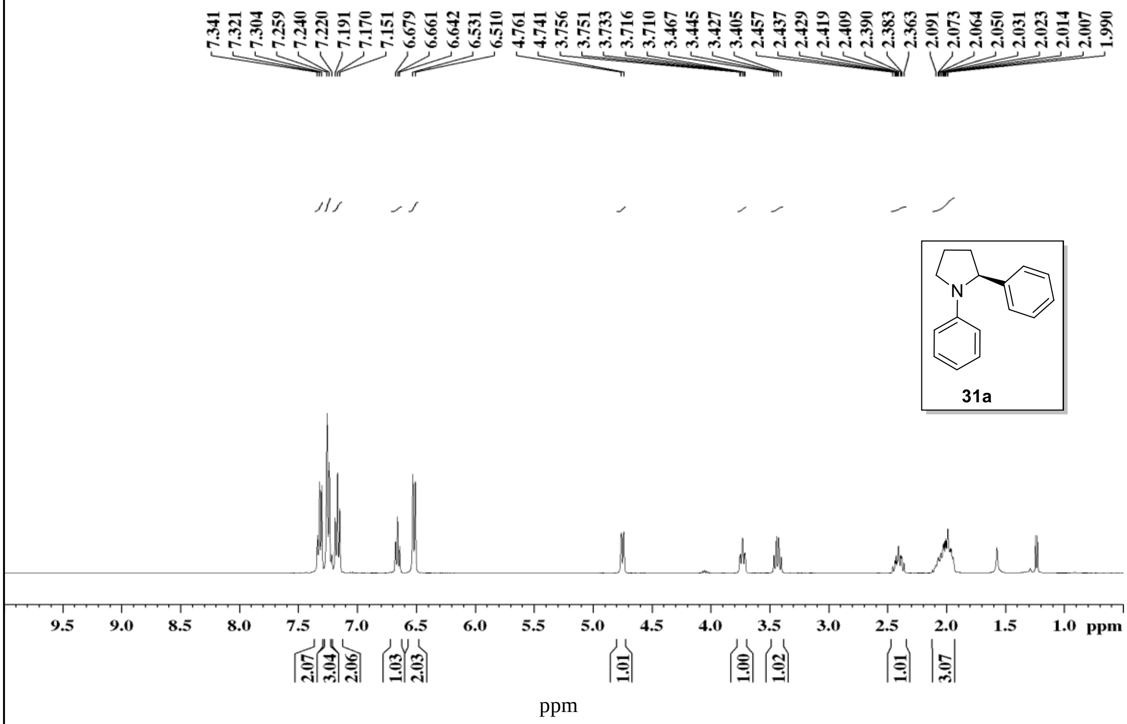
Spectrum No. 27 (Chapter 3, Section 3.2.7), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



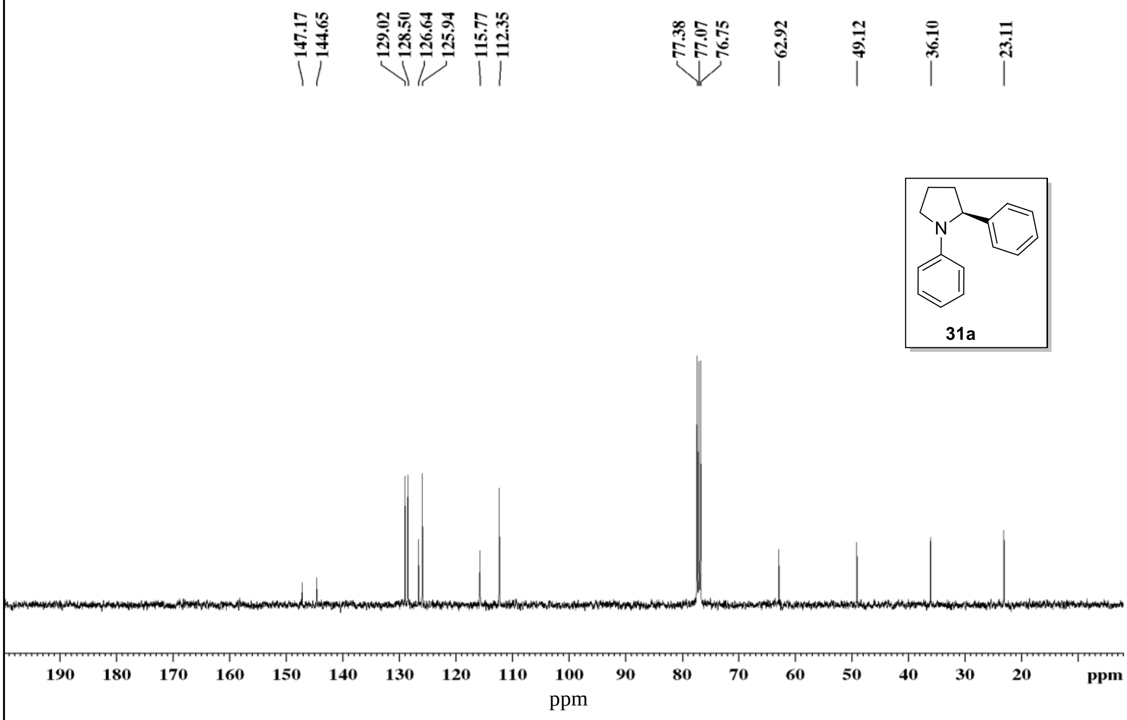
Spectrum No. 28 (Chapter 3, Section 3.2.7), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



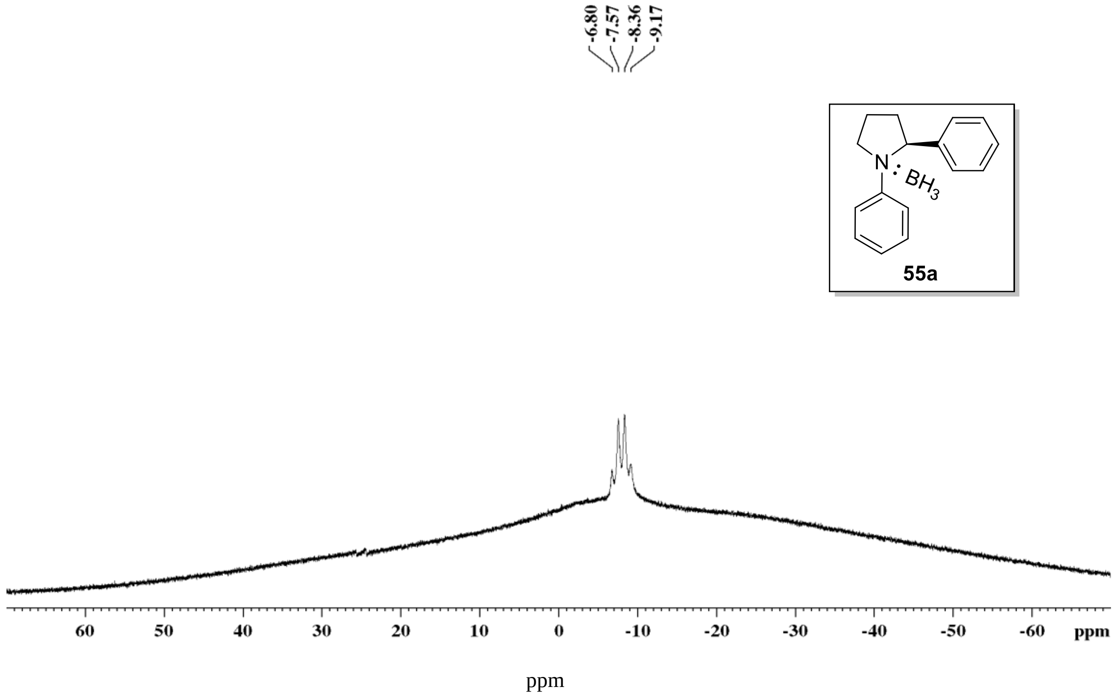
Spectrum No. 29 (Appendix I, Section I.2.2), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



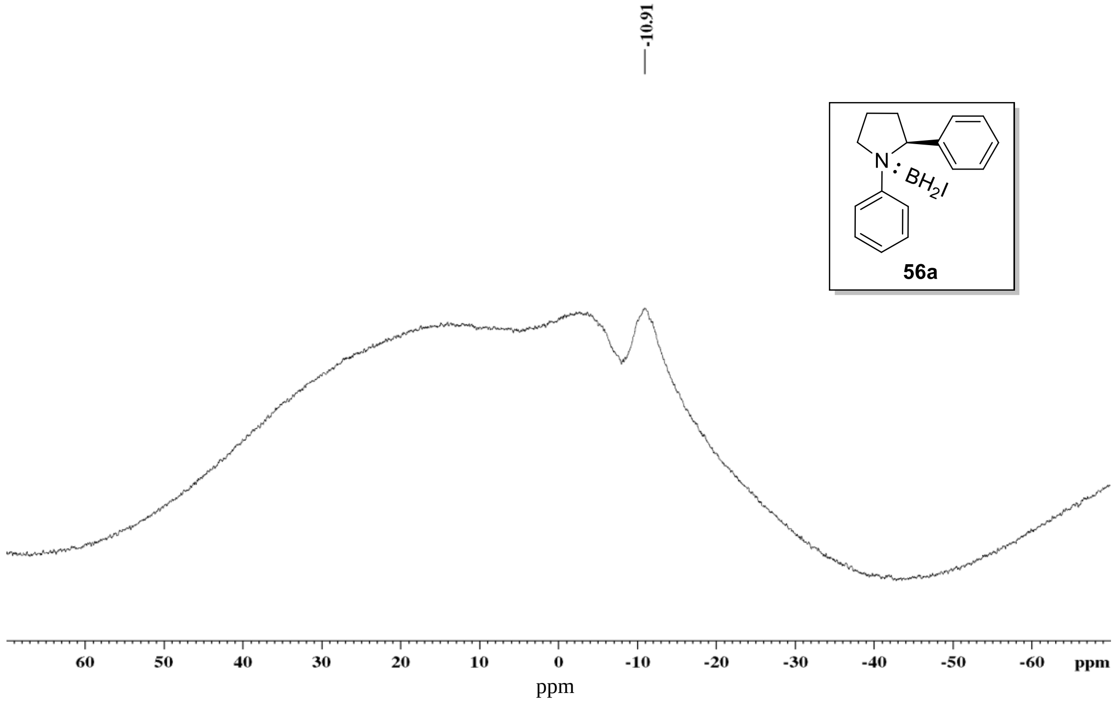
Spectrum No. 30 (Appendix I, Section I.2.2), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



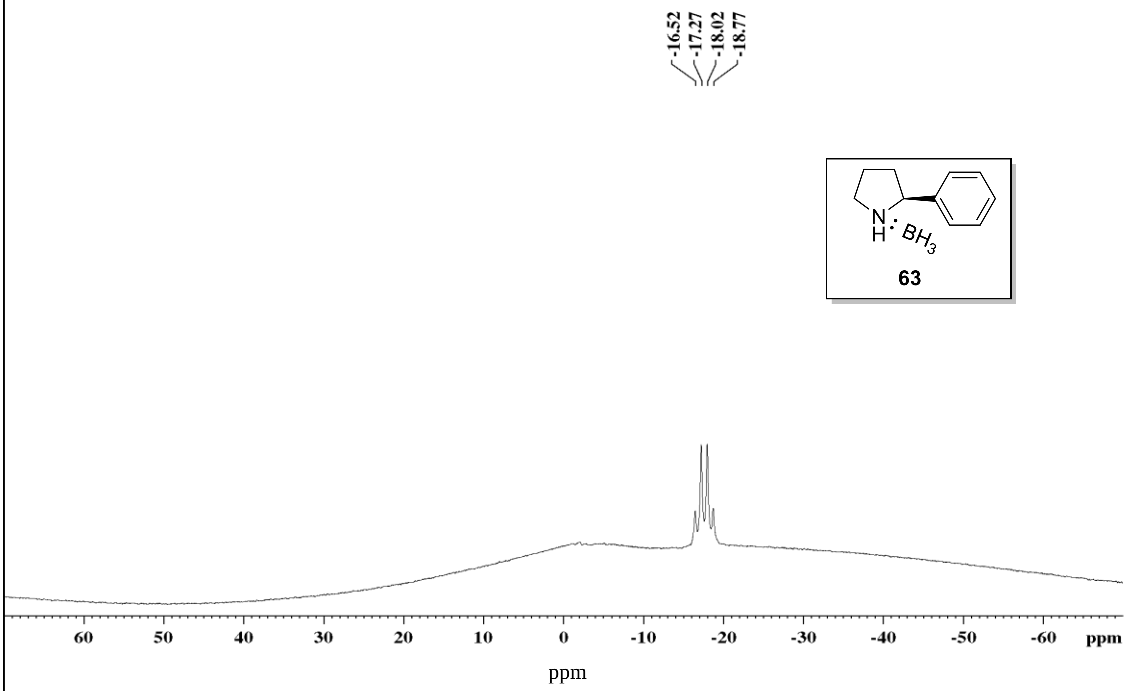
Spectrum No. 31 (Appendix I, Section I.2.3.2), ^{11}B NMR Spectrum (128.3 MHz, Toluene)



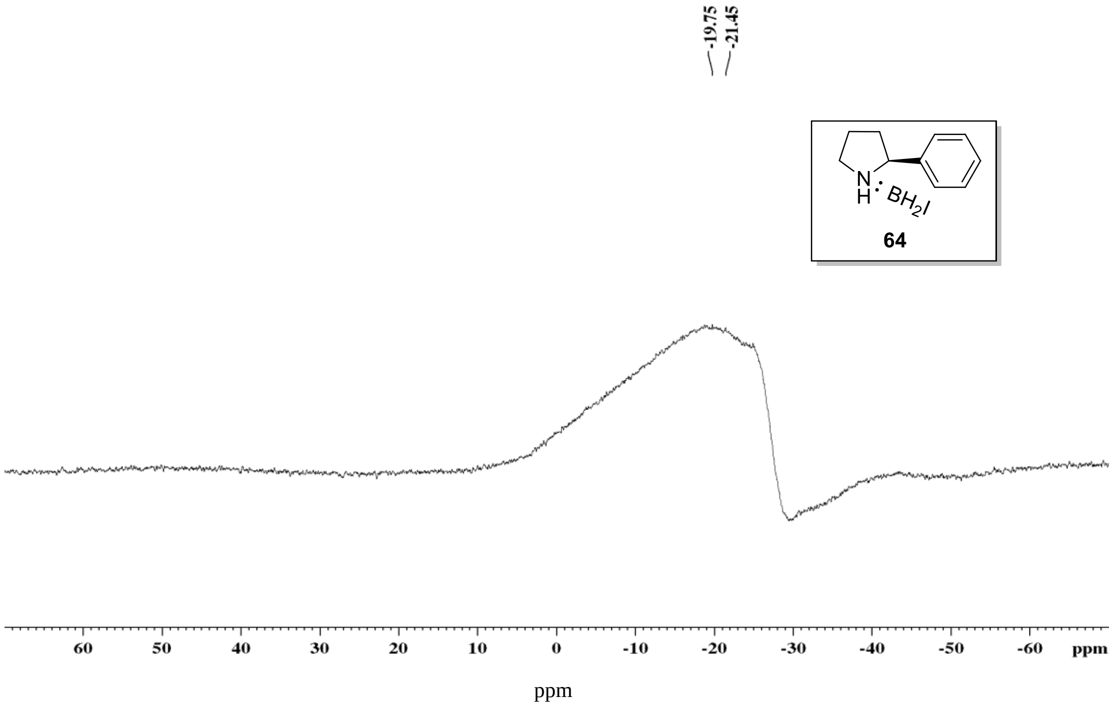
Spectrum No. 32 (Appendix I, Section I.2.3.3), ^{11}B NMR Spectrum (128.3 MHz, Toluene)



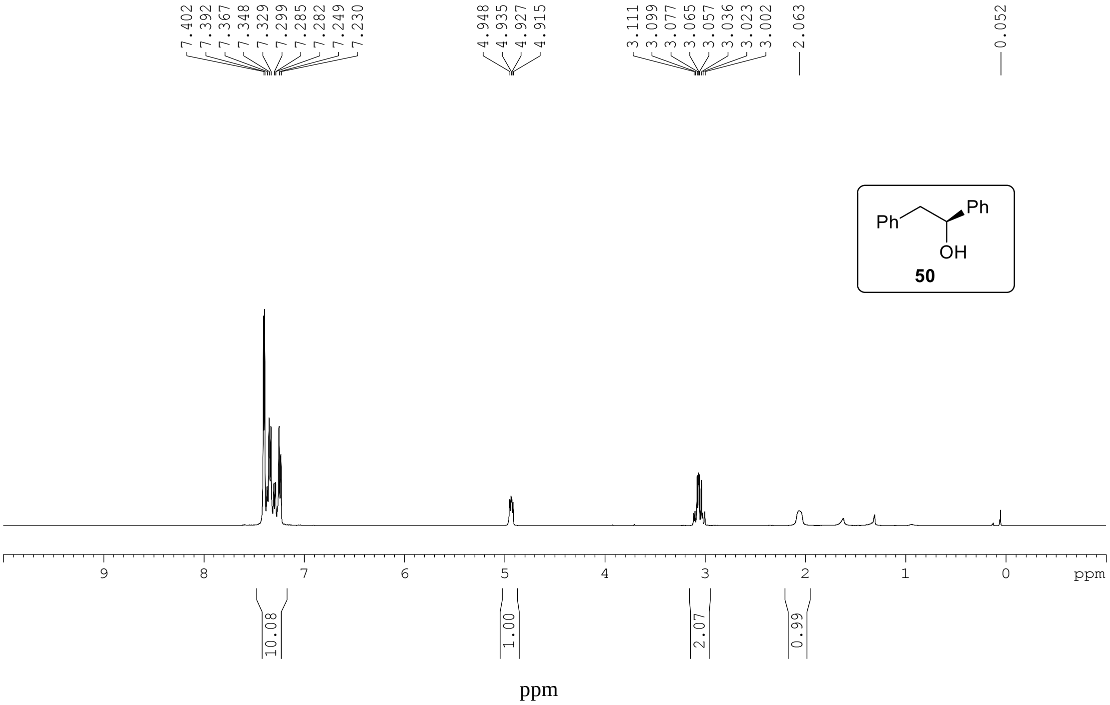
Spectrum No. 33 (Appendix I, Section I.2.3.4), ^{11}B NMR Spectrum (128.3 MHz, Toluene)



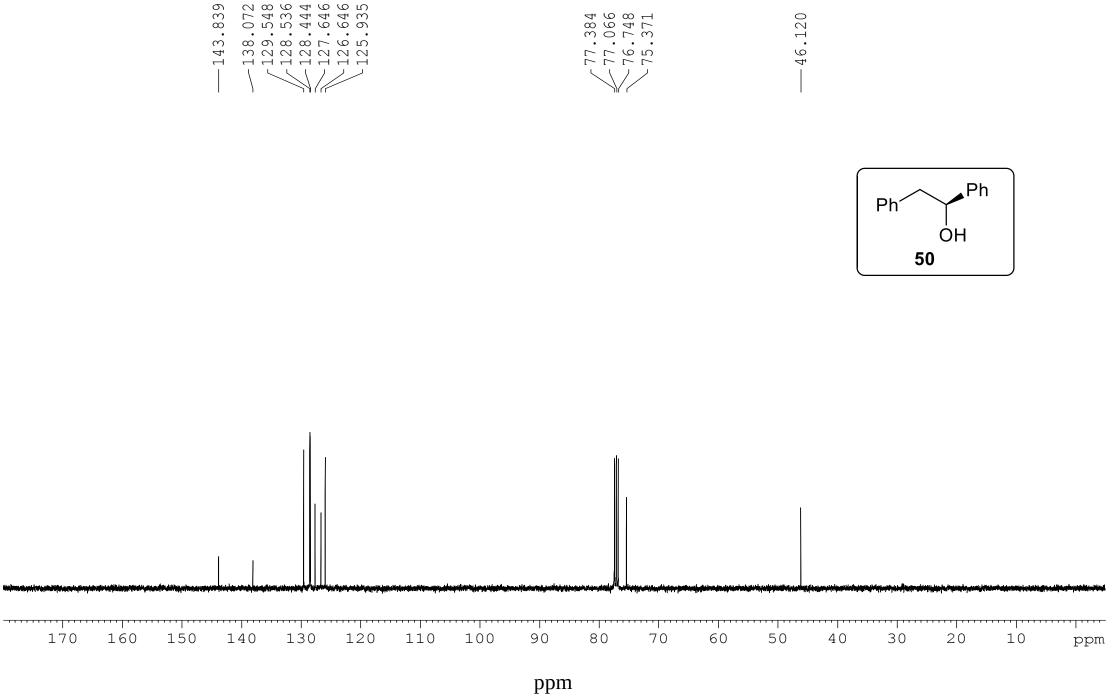
Spectrum No. 34 (Appendix I, Section I.2.3.4), ^{11}B NMR Spectrum (128.3 MHz, Toluene)



Spectrum No. 35 (Appendix I, Section I.2.3.3), ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)

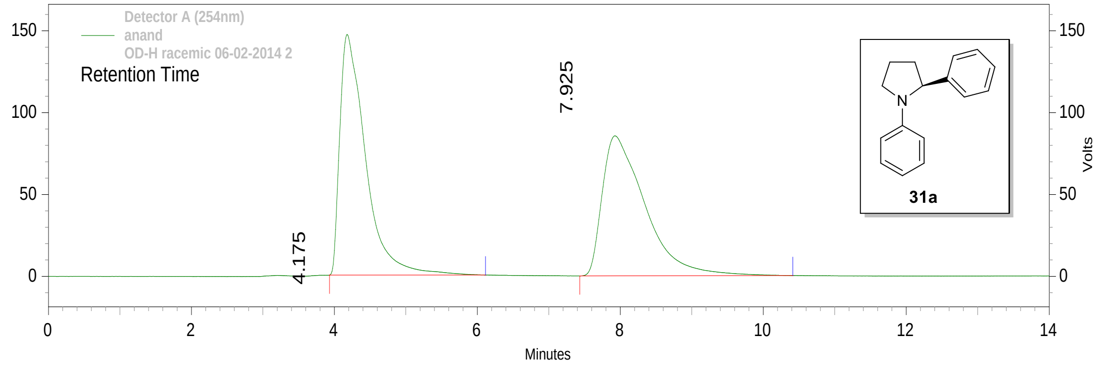


Spectrum No. 36 (Appendix I, Section I.2.3.3), ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



HPLC Profile of 31a: Chiralcel OD-H, hexanes:*i*-PrOH/90:10; flow rate 1 mL/min.

Racemic-31a:

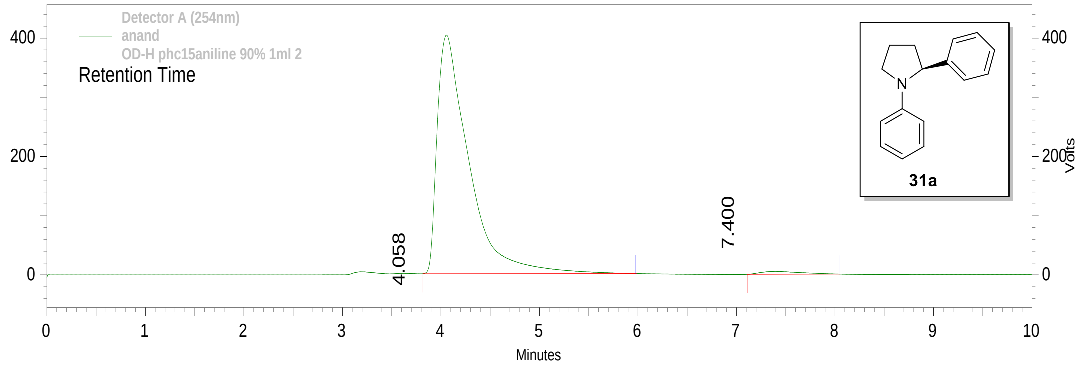


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	4.175	3674210	50.843	146946	63.212
2	7.925	3552353	49.157	85518	36.788

Totals		7226563	100.000	232464	100.000

(-)-(*S*)-31a:



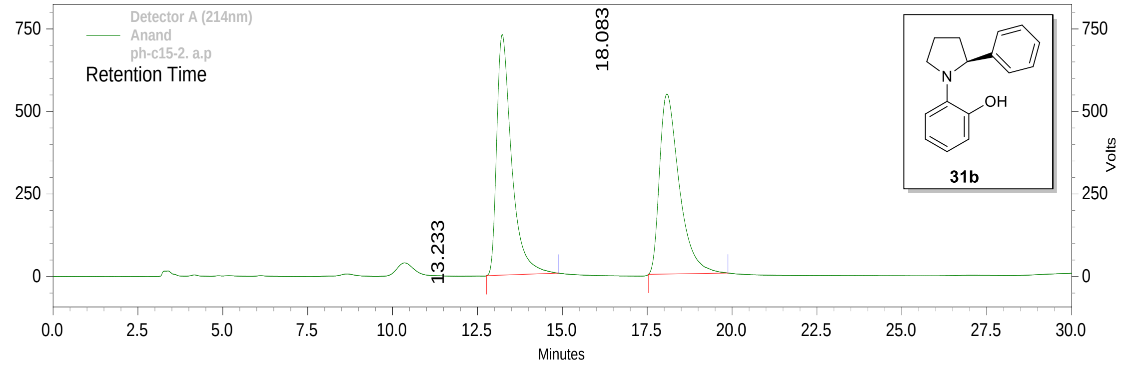
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	4.058	8997934	98.522	403032	98.822
2	7.400	135011	1.478	4806	1.178

Totals		9132945	100.000	407838	100.000

HPLC Profile of 31b: Chiralcel OJ-H, hexanes:*i*-PrOH/90:10; flow rate 1 mL/min.

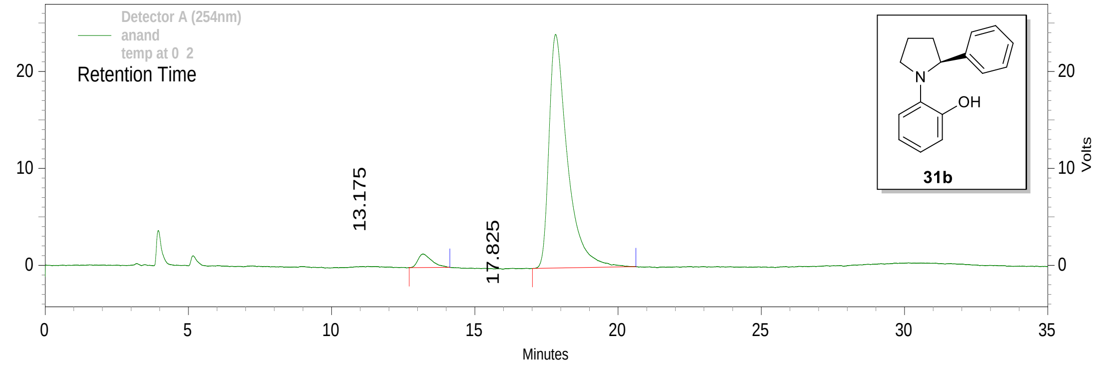
Racemic-31b:



Detector A (214nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	13.233	22250181	50.281	728498	57.198
2	18.083	22001784	49.719	545140	42.802
Totals		44251965	100.000	1273638	100.000

(-)-(*S*)-31b:

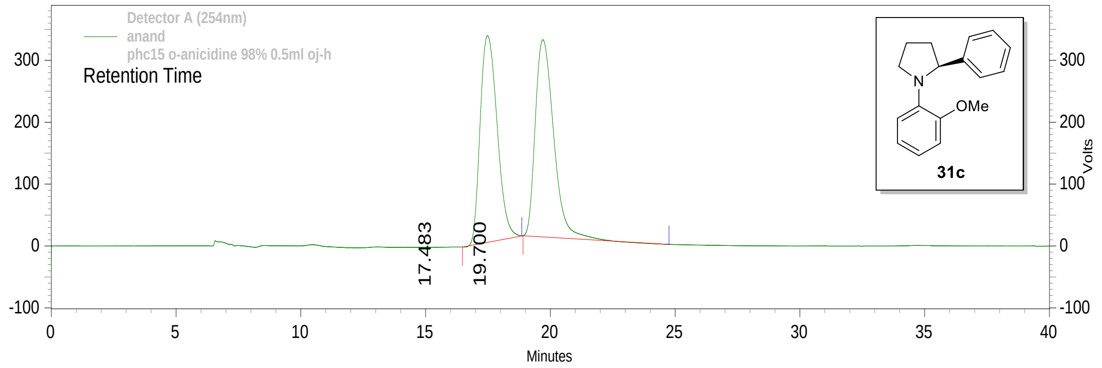


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	13.175	46280	4.129	1395	5.473
2	17.825	1074561	95.871	24092	94.527
Totals		1120841	100.000	25487	100.000

HPLC Profile of 31c: Chiralcel OJ-H, hexanes:*i*-PrOH/98:2; flow rate 0.5 mL/min.

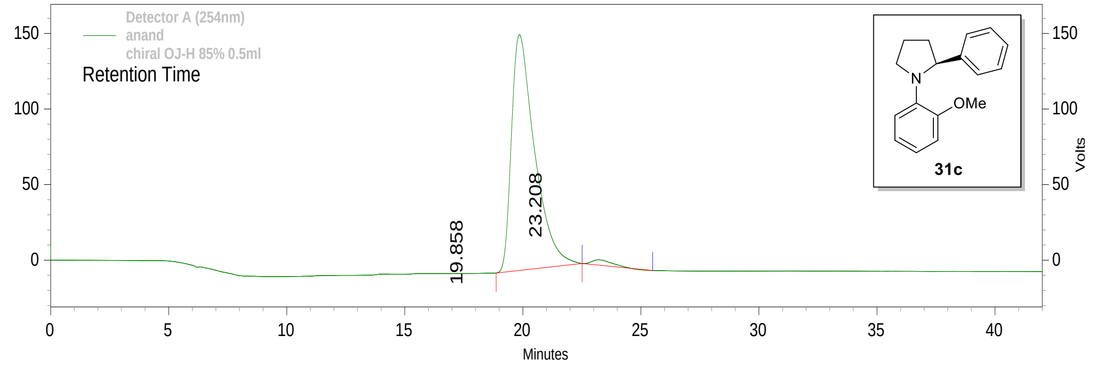
Racemic-31c:



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	17.483	15784461	49.107	333855	51.170
2	19.700	16358506	50.893	318588	48.830
Totals		32142967	100.000	652443	100.000

(-)-(*S*)-31c:

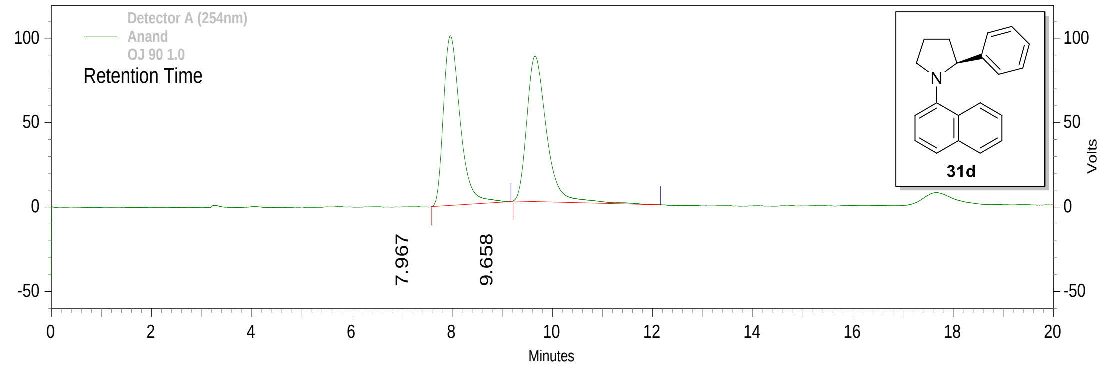


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	19.858	10651642	98.107	156020	97.783
2	23.208	205472	1.893	3538	2.217
Totals		10857114	100.000	159558	100.000

HPLC Profile of 31d: Chiralcel OJ-H, hexanes:*i*-PrOH/90:10; flow rate 1 mL/min.

Racemic-31d:

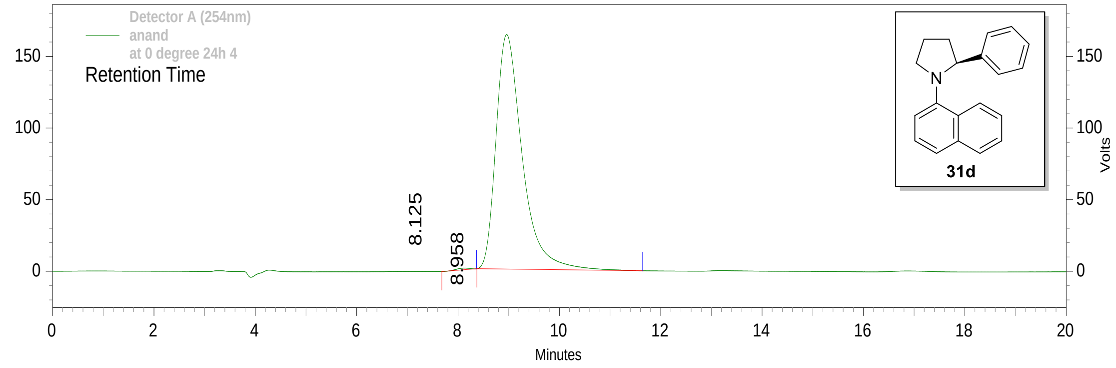


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	7.967	2336554	49.612	100386	53.827
2	9.658	2373127	50.388	86113	46.173

Totals		Area	Area %	Height	Height %
Totals		4709681	100.000	186499	100.000

(-)-(*S*)-31d:



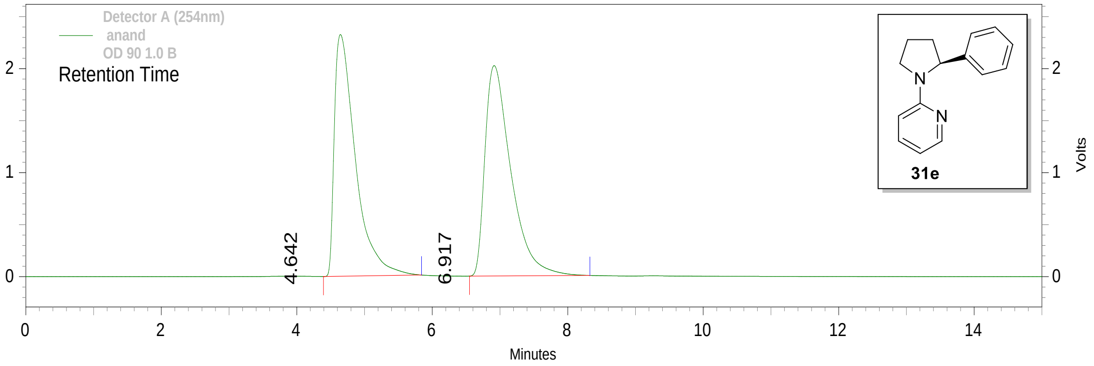
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	8.125	20267	0.343	1153	0.699
2	8.958	5891150	99.657	163694	99.301

Totals		Area	Area %	Height	Height %
Totals		5911417	100.000	164847	100.000

HPLC Profile of 31e: Chiralcel OD-H, hexanes:*i*-PrOH/90:10; flow rate 1 mL/min.

Racemic-31e:

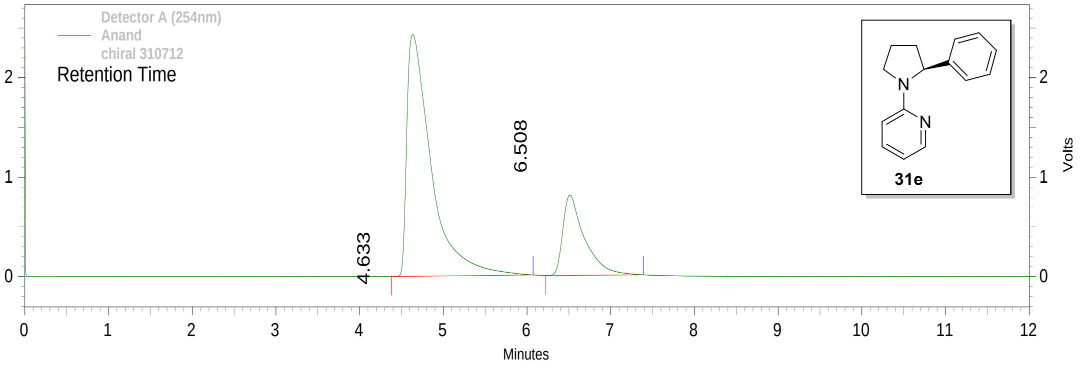


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	4.642	50194521	48.221	2323505	53.460
2	6.917	53898366	51.779	2022742	46.540

Totals		104092887	100.000	4346247	100.000

(-)-(*S*)-31e:



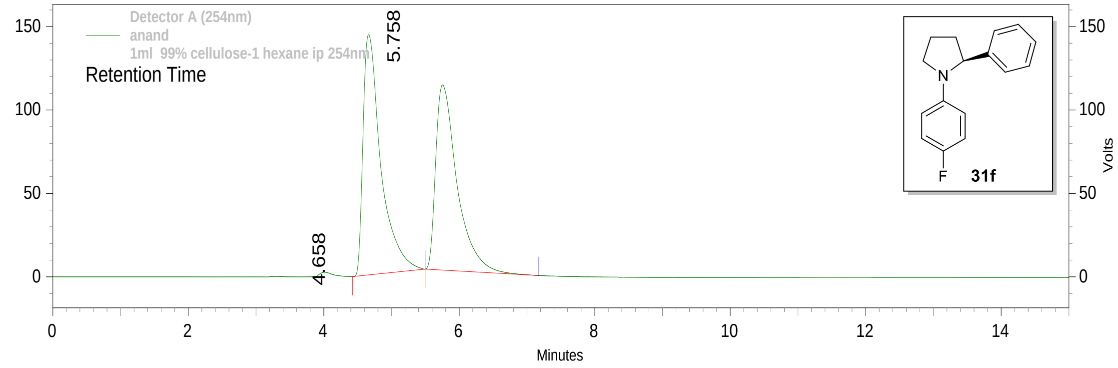
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	4.633	49221280	77.262	2430563	75.056
2	6.508	14485444	22.738	807791	24.944

Totals		63706724	100.000	3238354	100.000

HPLC Profile of 31f: Chiralcel Cellulose-1, hexanes:*i*-PrOH/99:1; flow rate 1 mL/min.

Racemic-31f:

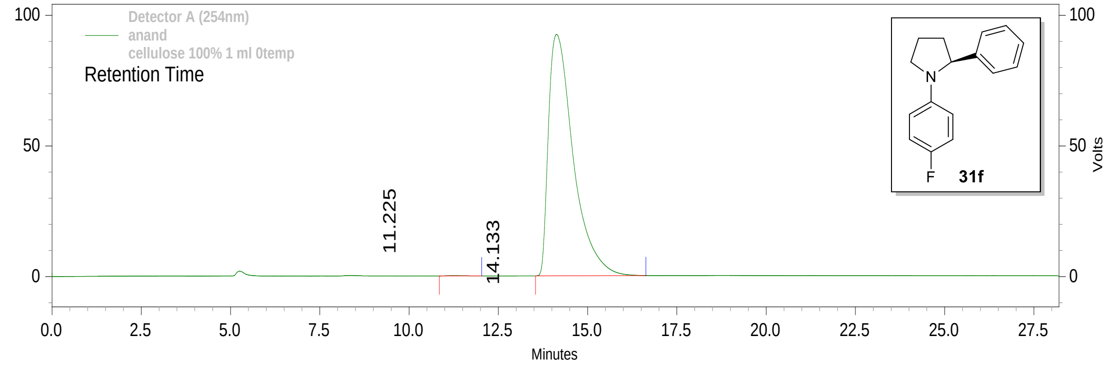


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	4.658	2630988	51.997	144038	56.481
2	5.758	2428919	48.003	110982	43.519

Totals		5059907	100.000	255020	100.000

(-)-(*S*)-31f:



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	11.225	2727	0.061	87	0.094
2	14.133	4460624	99.939	92367	99.906

Totals		4463351	100.000	92454	100.000

Appendix III

(X-Ray Crystallographic Data)

Table 1. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for compound **14f**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

atom	**x**	**y**	**z**	**U(eq)**
N(4)	2976(4)	394(2)	2036(2)	59(1)
C(2)	4332(4)	878(2)	2613(2)	49(1)
N(5)	2285(4)	723(2)	4627(2)	57(1)
C(4)	4066(4)	1190(2)	3450(2)	47(1)
N(3)	-79(4)	3991(2)	6930(2)	59(1)
C(15)	1473(4)	3986(2)	8368(2)	48(1)
O(4)	1885(4)	2522(2)	4813(2)	85(1)
N(1)	-398(4)	3349(2)	9447(2)	64(1)
C(14)	1290(5)	4343(2)	7566(2)	54(1)
O(1)	2225(4)	2299(2)	9672(2)	84(1)
C(11)	2279(4)	1023(2)	3752(2)	50(1)
C(8)	185(4)	3208(2)	8589(2)	54(1)
C(13)	2429(5)	2127(2)	5541(2)	59(1)
C(1)	5450(5)	1660(2)	4009(2)	61(1)
C(3)	2642(4)	1220(2)	5421(2)	54(1)
O(2)	2367(4)	5309(2)	6569(2)	98(1)
O(3)	6129(4)	886(2)	1508(2)	104(1)
C(18)	1124(5)	241(2)	3217(2)	55(1)
C(19)	3159(5)	817(2)	6163(2)	62(1)
C(9)	-1512(4)	3099(2)	7992(2)	59(1)
C(7)	403(5)	3213(2)	10255(2)	60(1)
C(22)	2705(5)	2568(3)	6361(2)	68(1)
C(5)	2572(5)	5033(2)	7395(2)	64(1)
C(24)	1217(5)	304(2)	2261(2)	59(1)
C(25)	5974(5)	1118(2)	2367(2)	63(1)
C(6)	2894(5)	4344(2)	8964(2)	60(1)
C(27)	7077(5)	1840(2)	3765(2)	67(1)
C(28)	3168(5)	2145(3)	7085(2)	73(1)
C(29)	7329(5)	1578(2)	2931(2)	71(1)

C(30)	1696(5)	-563(2)	3622(2)	64(1)
C(31)	2250(5)	-246(2)	4571(2)	61(1)
C(10)	1687(5)	2678(2)	10393(2)	63(1)
C(12)	-1136(5)	3146(2)	7061(2)	61(1)
C(16)	-161(6)	3587(2)	10991(2)	76(1)
C(20)	3948(5)	5390(2)	7998(2)	73(1)
C(36)	3394(5)	1273(3)	6977(2)	73(1)
C(37)	218(5)	-506(3)	1687(2)	82(1)
C(17)	-1845(5)	3833(2)	9363(2)	70(1)
C(1A)	2343(6)	2539(2)	11224(2)	77(1)
C(21)	4098(5)	5047(2)	8795(2)	74(1)
C(1B)	1752(7)	2908(3)	11944(3)	93(2)
C(42)	3125(5)	-327(3)	1410(2)	77(1)
C(23)	-1092(6)	4553(3)	6421(2)	91(2)
C(1C)	-2701(6)	3062(3)	6377(2)	93(1)
C(1D)	-2388(5)	3817(3)	8392(2)	75(1)
C(1E)	489(7)	3421(3)	11815(3)	94(2)
C(47)	1315(6)	-644(3)	991(2)	88(1)
C(1F)	-2914(7)	4003(4)	6265(3)	122(2)
C(49)	7387(6)	1389(3)	1117(2)	104(2)
C(1G)	3670(6)	1875(3)	9762(3)	110(2)
C(51)	1805(7)	3433(2)	4875(3)	108(2)
C(1H)	3673(8)	5958(3)	6343(3)	136(2)

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for compound **14a′**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

atom	**x**	**y**	**z**	**U(eq)**
N(1)	2611(2)	9490(2)	6614(1)	45(1)
C(2)	2051(2)	11761(2)	7679(1)	38(1)
C(3)	896(2)	12576(2)	8441(1)	41(1)

N(4)	-510(2)	11820(2)	8912(1)	47(1)
C(5)	4467(2)	8347(2)	6441(1)	43(1)
C(6)	1804(2)	10018(2)	7533(1)	38(1)
C(7)	3394(2)	12505(2)	7141(1)	45(1)
C(8)	-320(2)	10159(2)	7603(1)	43(1)
C(9)	5797(2)	7915(2)	7084(1)	50(1)
C(10)	2613(2)	14745(2)	8145(1)	59(1)
C(11)	1116(2)	9690(2)	6039(1)	50(1)
C(12)	3670(2)	14013(2)	7371(1)	54(1)
C(13)	5082(2)	7595(2)	5606(1)	57(1)
C(14)	1231(2)	14046(2)	8685(1)	55(1)
C(15)	-1615(2)	11419(2)	8287(1)	47(1)
C(16)	-713(2)	10738(2)	6580(1)	51(1)
C(17)	-3042(2)	10712(3)	9006(1)	61(1)
C(18)	7646(2)	6739(2)	6902(1)	60(1)
C(19)	8211(3)	6001(2)	6086(2)	69(1)
C(20)	-1890(2)	12679(3)	9650(1)	64(1)
C(21)	6922(2)	6430(3)	5441(1)	71(1)
C(22)	-3434(3)	11763(3)	9817(1)	72(1)

Table 3. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for compound **91o**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

atom	**x**	**y**	**z**	**U(eq)**
C(1)	6402(1)	7892(4)	7211(1)	34(1)
C(2)	6136(1)	9677(4)	7587(1)	39(1)
C(3)	6258(1)	9642(4)	8202(1)	42(1)
C(4)	6654(1)	7807(4)	8455(1)	42(1)
C(5)	6934(1)	6050(5)	8096(1)	50(1)
C(6)	6807(1)	6083(4)	7479(1)	44(1)
C(7)	5523(1)	8115(4)	6402(1)	41(1)
C(8)	5421(2)	8783(6)	5735(1)	58(1)

C(9)	5837(2)	7163(6)	5327(1)	66(1)
C(10)	6603(2)	7136(7)	5538(1)	69(1)
C(11)	6669(1)	6390(6)	6195(1)	52(1)
C(12)	5188(1)	5745(5)	6526(1)	49(1)
N(1)	6270(1)	8022(3)	6578(1)	39(1)
N(2)	4968(1)	3908(5)	6622(2)	74(1)
Br(1)	6805(1)	7692(1)	9307(1)	72(1)

Table 4. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for compound **122l**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

atom	**x**	**y**	**z**	**U(eq)**
N(1)	1745(1)	889(1)	7469(1)	40(1)
C(8)	-972(1)	-274(1)	6565(1)	42(1)
C(2)	241(1)	-196(1)	7211(1)	39(1)
N(2)	-1311(1)	116(1)	7081(1)	46(1)
C(18)	1972(1)	1228(1)	6894(1)	41(1)
O(1)	2857(1)	2108(1)	5251(1)	66(1)
C(1)	-581(1)	159(1)	7461(1)	43(1)
C(3)	8(1)	-482(1)	6630(1)	40(1)
C(10)	1079(1)	-606(1)	8121(1)	41(1)
C(23)	1596(1)	2214(1)	6627(1)	50(1)
C(17)	1288(1)	1830(1)	7809(1)	47(1)
C(19)	2625(1)	549(1)	6589(1)	45(1)
C(9)	1197(1)	-246(1)	7503(1)	38(1)
C(7)	-1438(1)	-454(1)	6049(1)	51(1)
C(15)	1058(1)	239(1)	8556(1)	45(1)
C(22)	1866(1)	2530(1)	6078(1)	55(1)
C(4)	519(1)	-899(1)	6159(1)	52(1)
C(11)	919(1)	-1792(1)	8257(1)	53(1)
C(21)	2530(1)	1869(1)	5788(1)	49(1)

C(20)	2906(1)	869(1)	6049(1)	49(1)
C(14)	835(1)	-124(1)	9108(1)	57(1)
C(12)	717(1)	-2137(1)	8808(1)	64(1)
C(6)	-910(1)	-832(1)	5594(1)	60(1)
C(16)	1315(1)	1512(1)	8434(1)	54(1)
C(13)	665(1)	-1297(2)	9235(1)	64(1)
C(5)	58(1)	-1064(2)	5648(1)	63(1)
C(24)	2510(1)	3139(2)	4976(1)	75(1)

Table 5. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for compound **101a**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

atom	**x**	**y**	**z**	**U(eq)**
Cl(4)	3520(1)	7394(1)	7504(1)	49(1)
Cl(5)	3418(1)	7886(1)	9778(1)	48(1)
Cl(1)	8518(1)	7475(1)	8348(1)	51(1)
Cl(2)	8417(1)	6939(1)	10608(1)	49(1)
Cl(6)	559(1)	5917(1)	9555(1)	55(1)
Cl(3)	5667(1)	9077(1)	10516(1)	55(1)
O(3)	2097(1)	6139(2)	6610(1)	31(1)
O(1)	7159(1)	8881(2)	7528(1)	33(1)
O(2)	6965(2)	7829(2)	11404(2)	44(1)
O(4)	1917(2)	7065(2)	10523(2)	44(1)
N(2)	831(1)	5812(2)	5529(2)	32(1)
N(1)	5853(2)	9224(2)	6513(2)	33(1)
C(27)	2108(2)	6432(2)	7581(2)	24(1)
C(11)	7162(2)	8548(2)	8481(2)	27(1)
C(30)	1995(2)	6885(2)	9555(2)	30(1)
C(14)	7045(2)	8026(2)	10443(2)	32(1)
C(16)	6525(2)	8906(2)	8954(2)	29(1)
C(6)	6021(2)	9202(2)	5525(2)	30(1)

C(29)	2654(2)	7213(2)	9090(2)	29(1)
C(32)	1442(2)	6097(2)	8025(2)	26(1)
C(26)	1353(2)	5489(2)	6369(2)	29(1)
C(28)	2712(2)	6991(2)	8095(2)	28(1)
C(22)	1076(2)	5817(2)	4573(2)	30(1)
C(25)	864(2)	5570(2)	7261(2)	30(1)
C(12)	7742(2)	7931(2)	8960(2)	32(1)
C(13)	7687(2)	7684(2)	9952(2)	32(1)
C(15)	6466(2)	8643(2)	9922(2)	30(1)
C(31)	1391(2)	6318(2)	9001(2)	31(1)
C(10)	6424(2)	9555(2)	7308(2)	31(1)
C(24)	77(2)	6133(2)	6861(2)	37(1)
C(1)	5491(2)	8744(2)	4780(2)	43(1)
C(7)	5189(2)	8666(3)	6863(2)	41(1)
C(23)	182(2)	6440(2)	5805(2)	40(1)
C(21)	1778(2)	5329(2)	4370(2)	40(1)
C(9)	5974(2)	9531(2)	8244(2)	34(1)
C(17)	608(2)	6292(2)	3783(2)	40(1)
C(8)	5125(2)	9094(3)	7883(2)	43(1)
C(5)	6720(2)	9651(3)	5257(2)	45(1)
C(18)	833(2)	6262(3)	2833(2)	51(1)
C(2)	5671(2)	8736(3)	3809(3)	54(1)
C(20)	1997(2)	5302(3)	3420(3)	52(1)
C(3)	6359(3)	9174(3)	3552(3)	57(1)
C(19)	1523(3)	5770(3)	2645(3)	55(1)
C(4)	6883(2)	9636(3)	4275(3)	58(1)

Table 6. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for compound **103g**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

atom	**x**	**y**	**z**	**U(eq)**
Cl(1)	7513(1)	6436(1)	7001(1)	80(1)

Cl(2)	8224(1)	496(2)	5694(1)	79(1)
Cl(3)	7042(1)	-998(1)	5261(1)	78(1)
N(1)	5693(1)	2207(3)	6625(1)	34(1)
O(1)	4829(1)	2520(2)	5640(1)	45(1)
O(2)	6257(1)	1576(3)	5801(1)	50(1)
C(14)	6876(1)	3711(4)	6338(1)	41(1)
O(3)	8316(1)	4009(4)	6514(1)	82(1)
C(15)	7390(1)	4364(4)	6518(1)	50(1)
C(7)	5367(1)	574(3)	6443(1)	34(1)
C(8)	6052(1)	2300(4)	7291(1)	38(1)
C(10)	6314(1)	4248(4)	7248(1)	42(1)
C(2)	4915(1)	749(3)	5927(1)	36(1)
C(12)	5952(1)	3037(4)	6122(1)	39(1)
C(3)	4585(1)	-828(4)	5752(1)	45(1)
C(5)	5127(1)	-2744(4)	6593(2)	53(1)
C(6)	5463(1)	-1196(4)	6760(1)	44(1)
C(18)	7181(1)	1031(4)	5748(1)	49(1)
C(11)	6364(1)	4470(4)	6500(1)	40(1)
C(13)	6779(1)	2057(4)	5957(1)	42(1)
C(9)	5755(1)	2168(4)	7880(1)	51(1)
C(16)	7808(1)	3365(5)	6323(1)	54(1)
C(4)	4690(1)	-2556(4)	6089(2)	53(1)
C(1)	4371(1)	2746(4)	5128(1)	56(1)
C(17)	7697(1)	1713(5)	5938(1)	53(1)

List of publications

1. Cycloaddition of enamine and iminium ion intermediates formed in the reaction of N-arylpyrrolidines with T-HYDRO; **Rao, G. A.**; Periasamy, M**.** *Synlett* **2015,** *26,* 2231**.**
2. Synthetic transformations using molecular oxygen-doped carbon materials; Periasamy, M.; Shanmugaraja, M.: Reddy, P. O.; Ramusagar, M.; **Rao, G. A.** *J. Org. Chem*. **2017**, *82*, 4944.
3. Oxidative Functionalization of N-Aryl Cyclic Amines with Nitromethane and TMSCN Using the T-HYDRO/t-BuOK System; **Rao, G. A.**; Periasamy, M**.** *Synthesis* **2017,** *50*, 617**.**
4. Metal free and base promoted cross coupling of N-arylpyrrolidines and chloranil: access to benzofuropyrrolidines; **Rao, G. A.**; Periasamy, M**.** (*to be communicated*)
5. Reaction of 2-arylamines dehydrogenative cross coupling using oxygen doped carbon materials; **Rao, G. A.**; Periasamy, M**.** (*to be communicated*)
6. Synthesis and applications of optically pure C_1-symmetric (2S)-phenyl-N-(aryl)pyrrolidine; **Rao, G. A.**; Periasamy, M**.** (*Manuscript under preparation*).