Trials Towards Visible Light Catalysed Dearomative Spiro-Amidation

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May 2025

“Trials Towards Visible Light Catalysed Dearomative Spiro-Amidation”

Dissertation submitted in partial fulfilment
of the requirements of the degree of
Master of Science

In **Chemistry**

By

Dhrutiman Rout
(Roll Number: 2303131008)

Based on research carried out
Under the supervision of

Dr. Debayan Sarkar
(Associate Professor, IIT Indore)

Department of Chemistry
Indian Institute of Technology Indore

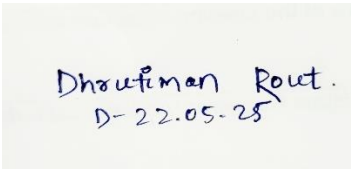
May 2025

INDIAN INSTITUTE OF TECHNOLOGY INDORE

CANDIDATE'S DECLARATION

I hereby certify that the work being presented in the thesis entitled as **Trials Towards Visible Light-Catalyzed Dearomative Spiro-Amidation,** in the Partial fulfilment of the requirements for the award of the degree of **Master of Science** and submitted to the **Department of Chemistry, Indian Institute of Technology Indore**, is an authentic record of my work carried out during the period July 2024 to May 2025 under the supervision of **Dr. Debayan Sarkar** (Associate Professor) Department of Chemistry, Indian Institute of Technology Indore. The matter presented in this thesis has not been submitted by me for the award of any other degree of this or any other institute.

I have not submitted the matter presented in this thesis for the award of any other degree of this or any other institute.



Signature of the student with the date
(Dhrutiman Rout)

This is to certify that the above statement by the candidate is correct to the best of my knowledge.

21-05-2025
Signature of the Supervisor with the date
(Dr. Debayan Sarkar)

Prefatory Notes

Nuclear magnetic resonance spectra

^{1}H and ^{13}C NMR spectra were recorded on a Bruker (500MHz and 126 MHz, respectively). Chemical shifts are reported in delta (δ, chemical shift relative to deuterochloroform (7.26 ppm for ^{1}H NMR & 77.0 for ^{13}C NMR). Data for ^{1}H reported as follows- Chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity is recorded as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets.

Chromatography

Chromatography was performed using (100-200 mesh) silica gel& neutral active aluminium oxide. Analytical TLC was performed with 0.25 mm coated commercial silica gel plates (E. Merck, DC- Kiesel gel 60 F254) and visualized with UV light, iodine, and vanillin stain. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker (500 MHz and 126 MHz, respectively).

General

All reactions were carried out under oven-dried glassware. All solvents were dried over appropriate desiccant before use. All other reagents were purchased from TCI chemicals, Sigma- Aldrich, and HIMEDIA and used without further purification. Na_2SO_4 was dried in an oven & utilized for drying the crude reaction mixture before chromatography.

ACKNOWLEDGEMENT

The research described in this report, entitled **"Trials Towards Visible Light-Catalyzed Dearomative Spiro-Amidation"** was carried out in the Department of Chemistry, Indian Institute of Technology Indore, during the period of my research from July 2024 onwards under the supervision of Dr. Debayan Sarkar.

Firstly, I would like to express my Gratitude and special thanks to my supervisor, **Dr. Debayan Sarkar**, for his sincere guidance, supervision, and advice from the very first day of my research life, as well as for giving me all the valuable experiences throughout my research work. Above all, he encouraged and supported my success and failure throughout my research career.

This journey at IIT Indore has been a memorable time in my life. I extend my heartfelt thanks to my Thesis Evaluator, Dr. Selvakumar Sermadurai, and all the Department of Chemistry, IIT Indore faculty members.

Special thanks to Ph.D. mentor **Priyaranjan Sahoo** and seniors Shantanu Samanta, Sangita Bishi, Bhabani Sankar Lenka, Niladri Sekhar Roy, Rama Kant Mishra, Argha Dey, Subarna Roy, Bhimrao Mohan Hiwarale, and Arindam Bhatta for their kind co-operation and helping nature throughout my research.During this journey, many people helped and encouraged me in various ways. I express my heartiest thanks to my friends. Thanks to all those colleagues whose names are left unwillingly.

I could only have started my research with encouragement and inspiration from my parents, beloved brothers and sisters, and relatives. I dedicate this work to them to honor their love and kind support during this research period.

Dhrutiman Rout
Roll No. 2303131008

Dedicated to My

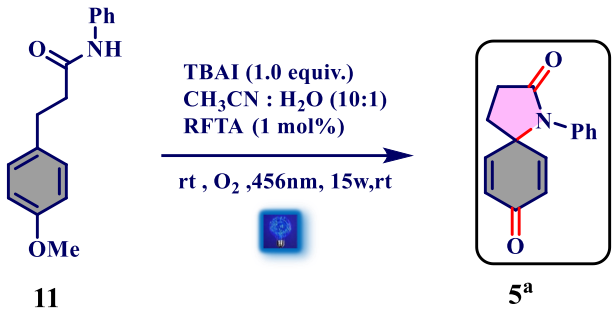
Parents,

Family Members

And Friends.

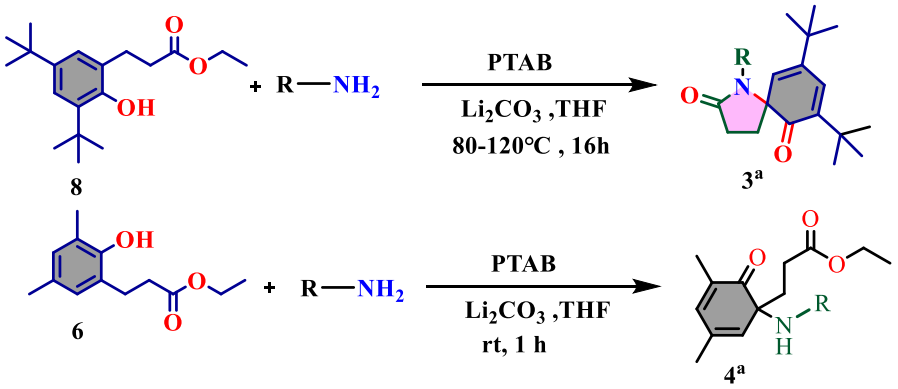
Abstract

As we are trying to synthesize Spiro-Amide from the Phenolic ester using RFTA in an efficient and Sustainable pathway by generating in situ tribromide from ammonium bromide, which was very challenging due to the amide generation is not possible under visible light conditions.



11 5[a]

We synthesize Phenolic amid as a starting material and form a variety of Spiro-Amides using RFTA and iodide source as tetra-butyl ammonium Iodide (TBAI) yield of 27 %.



We are going for the ortho Dearomatization of Ethyl 3-(3,5-di-tert-butyl-2-hydroxyphenyl) propanoate to form 7,9-Di-tert-butyl-1-alkyl-1-azaspiro[4.5]deca-7,9-diene-2,6-dione of 76% yield and Ethyl 3-(2-hydroxy-3,5-dimethylphenyl) propanoate to form Ethyl 3-(3,5-dimethyl-1-(alkylamino)-6-oxocyclohexa-2,4-dien-1-yl)propanoate of 82% yield using Tribromide Source as PTATB, an efficient source of Dearomatisation to form Azaspirodienone and Ethyl 3-(1-alkyllamino)-3,5-dimethyl-6-oxocyclohexa-2,4-dien-1-yl) propanoate respectively.

Table Of Contents

LIST OF FIGURES

ACRONOMYS

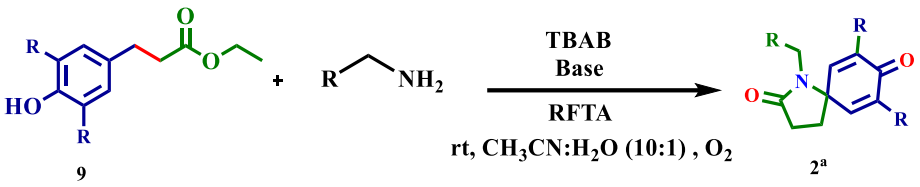
$CDCl_3$	Chloroform-d
$CHCl_3$	Chloroform
THF	Tetrahydrofuran
DCM	Dichloromethane
DMSO	Dimethyl sulfoxide
TBAB	Tetrabutyl ammonium bromide
TBAI	Tetrabutyl ammonium iodide
NIS	N-iodo succinamide
PTATB	Phenyl Trimethyl Ammonium Tri-Bromide
Cs_2CO_3	Cesium Carbonate
K_2CO_3	Potassium carbonate
LCMS	Liquid chromatography-mass spectrometry
EtOH	Ethanol
RFTA	Riboflavin Tetraacetate
MeOH	Methanol
MeCN	Acetonitrile
Na_2SO_4	Sodium sulfate
DBU	1,8-Diazobiclo-[5.4.0]undecen-7-ene
NMR	Nuclear Magnetic Resonance
NH_4Cl	Ammonium chloride
LED	Light Emitting Diode
PPh_3	Triphenylphosphine
NEt_3	Triethyl amine
EtOAc	Ethyl acetate
DMF	Dimethyl formamide
Me	Methyl
TLC	Thin Layer Chromatography
UV	Ultra-violet
UV-Vis	Ultra-violet and visible

NOMENCLATURE

˚C	Degree Celsius
h	hour
Hz	Hertz
M	Molar
mL	Milliliter
mg	Milligrams
MHz	megahertz
mmol	millimole
ppm	Parts per million

OBJECTIVES:

The goal of this research is to develop a visible-light-driven, sustainable methodology for the synthesis of spiro-amides via oxidative dearomatization.



✓ **Background**:

- Oxidative dearomatization is one of the most effective methods for creating stereochemically rich frameworks from phenols and naphthols.
- Historically, hypervalent iodine reagents have been the predominant non-metallic oxidants in such transformations, often used to generate spiro-lactones, spiro-ethers, and spiro-amines.
- However, our group has demonstrated that quaternary ammonium tribromides can serve as cost-effective and bench-stable oxidants for oxidative dearomatization, effectively generating spirocyclic centres through Spiro cyclization reactions.

✓ **Previous Work**

- Our research group has successfully synthesized tribromide-mediated spirolactams from different Phenols and naphthols' cores.
- This has been confirmed by HRMS and Raman Spectroscopy study.

✓ **Current Aim**

- We want to synthesize spiro-amide from the ester using Visible Light catalysis.
- We use Sustainable Catalyst as Riboflavin Tetraacetate (RFTA) as, which operates through a $2e^{-}/2H^{+}$ transfer mechanism.

- The photocatalytic system aims to:
    - Activate Br^- anions, potentially converting them to Br_3^- or enabling C–Br activation,
    - Facilitate radical generation for subsequent aromatic ring activation,
    - Drive the reaction toward the formation of the target spiro-amide products under mild and sustainable conditions

MOTIVATIONS:

Synthesis of Spiro lactams from esters calls for two consecutive steps. Initially, amides need to be formed, followed by arenol oxidation. in 1987, In place of spiro-lactonization, Kita reported hypervalent iodine spiro lactonization as only cyclized product. There have been multiple attempts to develop an appropriate reaction system that would capture a linked amide's direct entry into the Dearomative Spiro lactam production. But none of these have proven effective. Using the oxidative dearomatization of phenol and naphthol derivatives, our research has long been interested in the spiro cyclization caused by TBATB as an advantageous and bench-stable oxidant to generate stereogenic spiro centers. Its mechanistic analysis also highlights me to try something different by using the sustainable visible light photocatalytic process to produce greater efficiency and an environmentally friendly synthesis method &Support green chemistry principles by reducing steps, avoiding toxic metals, and utilizing visible light and air as reagents.

The dearomatization of arenols, an energy and atom-economic process that uses air as the terminal oxidant, has made significant strides and is still in demand. We approached this problem using visible light photocatalysis since it provided a simple, environmentally friendly method of phenol dearomatization. We want to solve this problem using visible light photocatalysis since it provides a simple, ecologically safe catalytic solution for phenol dearomatization, trying to generate a higher percentage of yield and more different

substituted phenols and naphthols. There are many biologically active natural products of Spiro, but the oxidative dearomatisation of Phenols to form Spiro-amide was less explored as compared with others oxidative transformation.

There are a few biologically active Spiro-lactam derivatives:

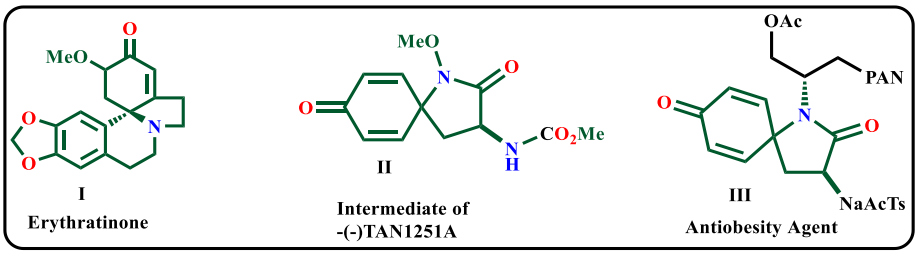


Fig-1 Biologically active Spiro-lactam

LITERATURE SURVEY:

Previous works on spiro-lactam generation[1,2]:

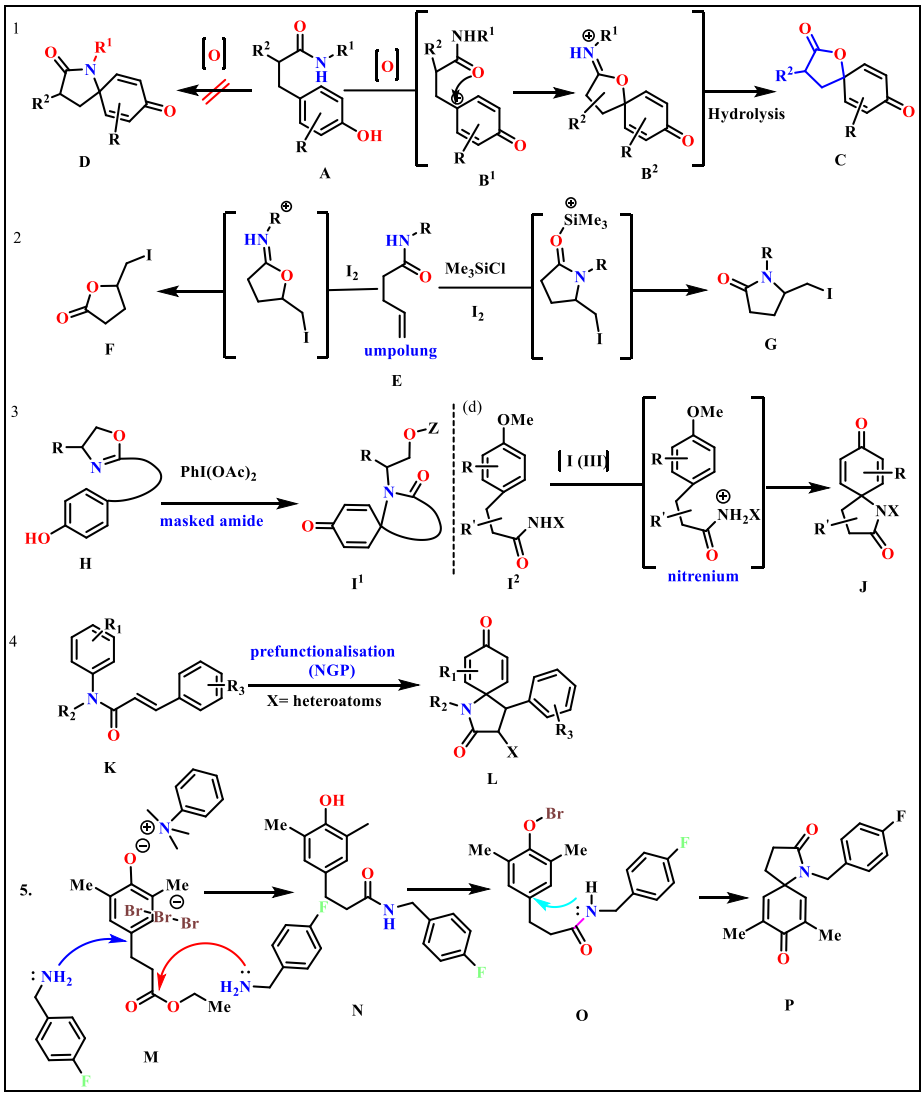
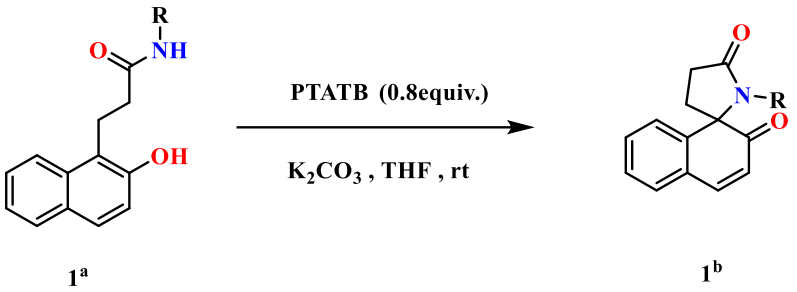


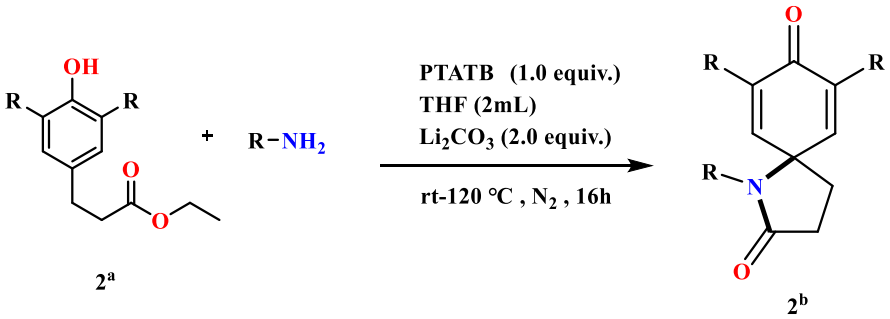
Fig-2: Mechanistic Study of Reported Spirolactams

6-Spiro-Azacycles Through Tri-bromide Mediated Oxidative Dearomatization [3].



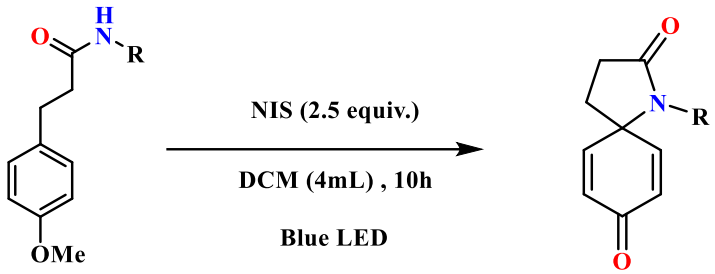
1[a] 1[b]

7-Spirolactams from esters Through Tri-bromide Mediated Oxidative Dearomatization [4].



2[a] 2[b]

8-Visible Light-induced Spiro-amidation [5].



3[a] 3[b]

➢ EXPERIMENTAL SECTION:

✓ Materials & Method

A Bruker Avance 500 MHz spectrometer was set up to capture the ^{1}H and ^{13}C NMR spectra. Chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t-triplet, q = quartet, m = multiplet, dd-doublet of doublets, dt–doublet of triplets), coupling constant (represented as J (Hz), integration, and assignment are the published data for ^{1}H NMR, whereas chemical shift (δ ppm) is provided for ^{13}C.

✓ Chemicals Required

- PPh_3
- 2-Bromoethyl acetate
- NaOH
- Toluene
- Salicylaldehyde
- Pd/ C, 10%
- Solvents (EtOAc, Hexane, DCM, MeOH, EtOH)
- Reagents (TBAB, TBAI, KBr, K_2CO_3, Li_2CO_3)
- Na_2SO_4
- TEA
- Acetic Anhydride
- HCOOH
- Riboflavin

✓ Apparatus Required:

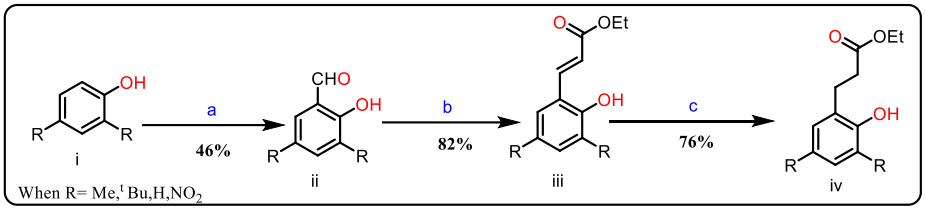
Sealed tube, Magnetic bead, Magnetic stirrer, Glass Syringe. Sealed tube, needles,

Fume Hood, Test tubes, Column, Rotary Evaporator, Spatula, Round bottle flask (RB), Separating Funnel, Glass Funnel. Reaction Vial, sintered funnel

➢ SYNTHETIC PROCEDURE:

A.1. Preparation of Starting Materials:

General Procedure for Synthesis of ethyl 3-(2-hydroxy-3,5-dialkylphenyl) propanoate.



Reagents. (a) $CHCl_3$, 10% aqueous NaOH solution, 80 ºC, 6 h, 49%. (b) Ph_3P=CHCOOEt, DCM, rt, 10h.85 % (c) H_2/ 10% Pd/C, high pressure, 6 h, 82%.

Synthetic procedure a:

10g of the methanolic solution was poured into 40 ml of ethanol in a two-neck RB. Reaction was taken into the heating condition, then a 15M solution of NaOH was added dropwise. After 1 hr, 3 equiv. of $CHCl_3$ (12 ml) was added dropwise over 2-3 h. The reaction was left for another 6 hrs, under reflux conditions at 60-80°C. The reaction was reset to room temperature and quenched with an aqueous HCl (1M) solution. The resulting mixture was then concentrated using a rotary evaporator, and the product was isolated using column chromatography.

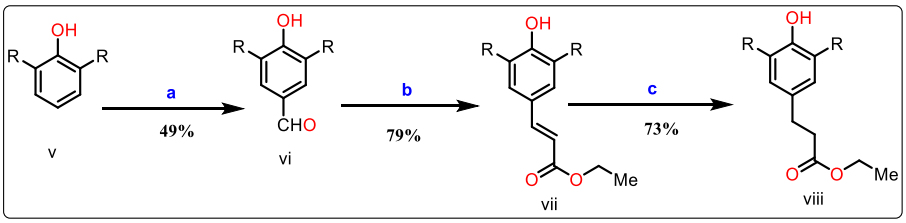
Synthetic procedure b:

Previously prepared substituted salicylaldehyde (1 equiv.) as well as Wittig salt (1.2 equiv.) were dissolved in dry DCM, and stirring was continued for 10 hours at room temperature. Following the completion of the reaction by TLC monitoring, the product was recovered using column chromatography.

Synthetic procedure c:

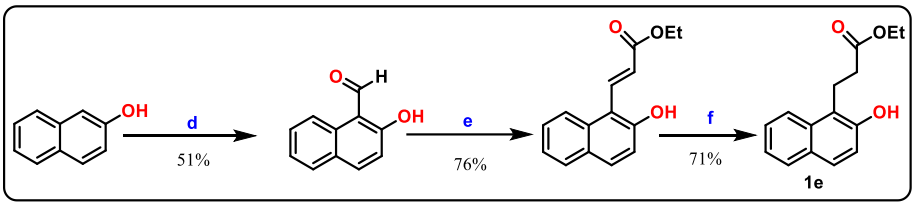
The obtained product as (E)-ethyl 3-(2-hydroxy-3,5-dialkylphenyl) acrylate, was dissolved in dry MeOH, and 10% Pd/C was added to it. The resulting mixture was taken under a 1 atm H_2 atmosphere and agitated for 6-7 hours. The reaction mixture was filtered with the help of Whatman filter paper and concentrated by the help of a rotary evaporator. The crude product was purified by column chromatography on silica gel (15% Hexane /EtOAC) to obtain the desired product.

A.2 Procedure for Synthesis of ethyl 3-(4-hydroxy-3,5-dialkylphenyl) propanoate [6].



This has the same Procedure as previously mentioned, Synthetic Procedure as (a,b,c)

A.3. Procedure for Synthesis of ethyl 3-(2-hydroxynaphthalen-1-yl) propanoate [7].



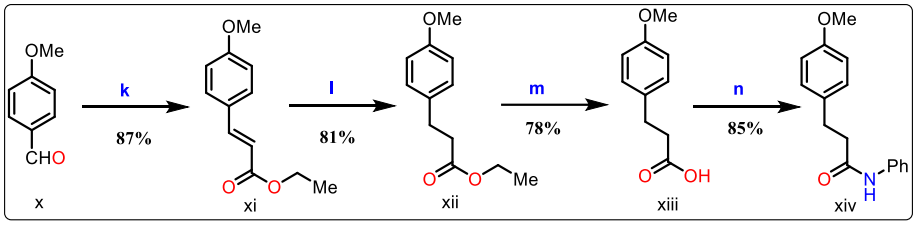
Reagents. (a) $CHCl_3$, 10% aqueous NaOH solution, 80 ºC, 6 h, 49%. (b) Ph_3P=CHCOOEt, DCM, rt, 10h.85 % (c) H_2/ 10% Pd/C, high pressure, 6 h, 82%.

Synthetic procedure d: 10g of naphthalen-2-ol was poured into 40 ml of ethanol in a two-neck RB. Reaction was taken into the heating condition, then a 15M solution of NaOH was added dropwise, slowly. After 1 hr, 3 equiv. of $CHCl_3$ (12 mL) was added dropwise discontinuously, over around 2-3 h. The reaction was left for another 6 hrs, under reflux conditions at 60-80°C. The reaction was cooled to room temperature and quenched with an aqueous HCl (1M) solution. The resulting mixture was then concentrated using a rotary evaporator, and the product was recovered using column chromatography**.**

Synthetic procedure e: Previously prepared, 2-hydroxy naphthaldehyde (1 equiv.) as well as Wittig salt (1.2 equiv.) were dissolved in dry DCM for 10 hours at room temperature while being stirred. Following the completion of the reaction, TLC was monitored. the product was recovered using column chromatography.

Synthetic procedure f: The obtained product (E)-ethyl 3-(2-hydroxynaphthalen-1-yl) acrylate was dissolved in dry MeOH, and 10% Pd/C was added to it. The resulting mixture was taken under a 1 atm H_2 atmosphere and agitated for 6-7 hours. Purify the crude product with Silica gel (15% Hexane /EtOAC) obtain the desired Starting material.

A.3.General Procedure for Synthesis of Phenyl 3-(4-methoxyphenyl) propanamide.



Synthetic procedure k:

4-Methoxy salicylaldehyde (1 equiv.) as well as Wittig salt (1.2 equiv.) were dissolved in dry DCM for 10 hours at room temperature while being stirred. Following the completion of the reaction, TLC was monitored it. the product was recovered using column chromatography.

Synthetic procedure l [8]***:***

The obtained product as (E)-ethyl 3-(2-hydroxy-3,5-dialkylphenyl) acrylate, was dissolved in dry MeOH, and 10% Pd/C was added to it. The resulting mixture was taken under a 1 atm H_2 atmosphere and agitated for 6-7 hours. The reaction mixture was filtered out by help of Whatman paper and concentrated with the help of a rotary evaporator. Purify the crude product with Silica gel (15% Hexane /EtOAC) obtain the desired product.

Synthetic procedure m:

Given, Ester was dissolved in the solvent, dry EtOH, and 5 equivalents. NaOH was added in it then the reaction was set for overnight conditions and observed by TLC to complete the reaction.

Synthetic procedure n [9]***:***

An oven-dried two-neck round-bottom (RB) flask was further dried using a spirit lamp under vacuum to ensure complete removal of moisture. Under an inert atmosphere, 4 mL of dry dichloromethane

(DCM) was added to the flask, followed by the addition of 1.2 equivalents of dicyclohexylcarbodiimide (DCC) and 10 mol% of 4-dimethylaminopyridine (DMAP). The reaction mixture was cooled in an ice bath to 0 °C. Separately, 1.2 equivalents of the previously synthesized carboxylic acid were dissolved in dry DCM and added dropwise to the reaction mixture under stirring. After the addition of the acid, 1 equivalent of the respective aniline was introduced: if the aniline was a liquid, it was added directly; if solid, it was first dissolved in DCM before addition.The progress of the reaction was monitored by thin-layer chromatography (TLC). Upon completion, the reaction mixture was filtered through a plug of silica to remove dicyclohexylurea (DCU) and other insoluble byproducts. The crude product was then purified by column chromatography to afford the desired amide.

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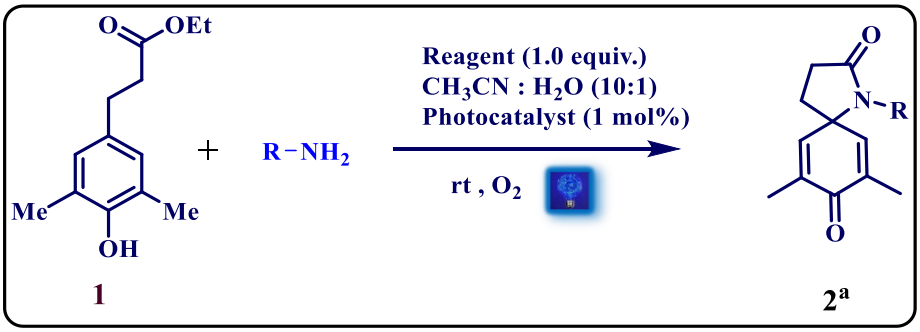
B.1. General Procedure for Synthesis of Azaspirodienone for Phenols.



According to the photocatalyst, we use a different light range for blue LEDs. Varies Light intensity as 0.9w, 5w,9w,15w,27w. Wavelength ranges (370 to 456 nm).

The SM, as Ethyl 3-(4-hydroxy-3,5-alkylphenyl) propanoate, is now set for the final step of the reaction, 40 mg of the substrate, 2 equiv. Of Base was taken in a small dry and clean sample vial with addition of Bromide Source as TBAB and 1 mole % of Photocatalyst then it was dissolved with solvent CH_3CN: $H_2O$and flushed with dioxygen for 2-4 Mins, then respective amine was added to the vial and was taken into visible light of 450 nm in 0.9 w. Monitor the reaction with the help of TLC for 24 hrs.

Optimization Table:

Entry	R	Base	Reagents	Photocatalysts	Solvents	Yield % (2[a])
1	Bn	Li_2CO_3	TBAB	RFTA	CH_3CN: H_2O	0
2	Ph	Li_2CO_3	TBAB	RFTA	CH_3CN: H_2O	0
3	$CH_3(CH_2)_3$	Li_2CO_3	TBAB	RFTA	CH_3CN: H_2O	0
4	Bn	Cs_2CO_3	TBAB	RFTA	CH_3CN: H_2O	0
5	Ph	K_2CO_3	TBAB	RFTA	CH_3CN: H_2O	0
6	Bn	Li_2CO_3	TBAB	RFTA	DCM: H_2O	0
7	Ph	Li_2CO_3	TBAB	RFTA	DCM: H_2O	0
8	$CH_3(CH_2)_3$	Li_2CO_3	TBAB	RFTA	DCM: H_2O	0
9	Ph	Li_2CO_3	TBAB	RFTA	THF: H_2O	0
10	Ph	Li_2CO_3	TBAI	RFTA	CH_3CN: H_2O	0
11	Bn	Li_2CO_3	TBAB	RFTA	THF: H_2O	0
12	Ph	Li_2CO_3	TBAB	RFTA	THF: H_2O	0
13	Ph	K_2CO_3	TBAB	RFTA	CH_3CN: H_2O	0
14	Ph	Li_2CO_3	TBAB	4CzIPN	CH_3CN: H_2O	0
15	Bn	K_2CO_3	TBAB	Rose Bengal	CH_3CN: H_2O	0
16	Ph	K_2CO_3	TBAB	Eosin Y	CH_3CN: H_2O	0
17	Ph	K_2CO_3	TBAB	**$Ru(bpy)_3^{+2}$**	CH_3CN: H_2O	0
18	Bn	K_2CO_3	TBAB	Riboflavin	CH_3CN: H_2O	0

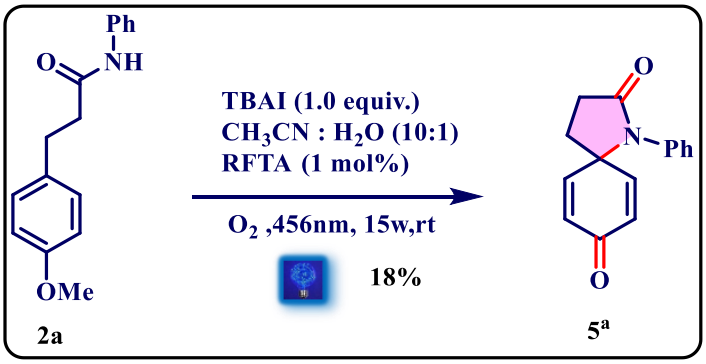
Result and Discussions:

Our research group is working extensively on tribromide (Br_3^-)-mediated dearomatizations, and we aim to generate in situ tribromide from an ammonium bromide source, specifically tetrabutylammonium bromide (TBAB). We employ the organic photocatalyst riboflavin tetraacetate (RFTA) under visible light irradiation to facilitate this transformation. Following the dearomatization step, the conversion of the resulting intermediate ester to the corresponding amide requires thermal conditions.

Observed Problem:

Despite setting up the reaction under these conditions, we observe no substrate consumption, and the amines remain unreacted, as confirmed by TLC analysis. After the reaction, we recover both the starting substrate and amine unchanged via column chromatography

B.2.General Procedure for Synthesis of 1-phenyl-1-azaspiro [4.5] deca-6,9-diene-2,8-dione.



Ethyl 3-(4-methoxyphenyl) propanoate is now set for the final step of the reaction, 30 mg of the substrate taken in a small dry and clean sample vial with addition of TBAI and 1 mole % of Photocatalyst as RFTA then it was dissolved with solvent CH_3CN: H_2O (10:1) and flushed with dioxygen for 2-4 Mins, then the vial and was taken into visible light of 456 nm in 15 w. Monitor the reaction with the help of TLC after 6 hrs. The product was recovered using column chromatography.

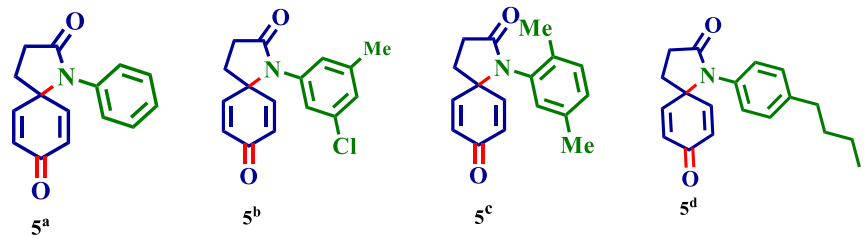
Optimisation Table:

Entry	Reagent	Photocatalysts	Intensity(w)	Solvents	Yield % (5[a])	Recovered % (2a)
1	TBAB	RFTA	9	CH_3CN: H_2O	0	100
2	TBAB	RFTA	18	CH_3CN: H_2O	0	100
3	TBAI	RFTA	9	CH_3CN: H_2O	Trace	>90
4	TBAI	RFTA	18	CH_3CN: H_2O	27	62
5	TBAI	RFTA	36	CH_3CN: H_2O	20	10
6	TBAI	RFTA	18	DCM: H_2O	Trace	100
7	TBAB	RFTA	18	DCM: H_2O	0	100
8	TBAI	RFTA	18	THF: H_2O	0	100
9	TBAI	4CzIPN	18	CH_3CN: H_2O	Trace	>80
10	TBAI	Eosin Y	18	CH_3CN: H_2O	0	100
11	TBAI	Rose Bengal	18	CH_3CN: H_2O	0	100
12	TBAI	$Ru(bpy)_3^{+2}$	18	CH_3CN: H_2O	0	100
13	TBAI	No	18	CH_3CN: H_2O	0	100

Results and Discussions:

As we have used different intensities of Light, 18W is the most suitable, and the wavelength of light is 456nm, but the reaction is going in different wavelengths of Blue LED. We got the Optimum Yield of 27% in CH_3CN: H_2O (10:1) Solvent. we also increased the amount of water, but there is no change in the Product percentage as such. We use Base as K2CO3 and Cs_2CO_3, but there is no use of Base in the reaction because, without the use of Base, the reaction proceeds in the same yield.

Substrates Scope:



5^a

1-phenyl-1-azaspiro[4.5]deca-6,9-diene-2,8-dione

5^b

1-(3-chloro-5-methylphenyl)-1-azaspiro[4.5]deca-6,9-diene-2,8-dione

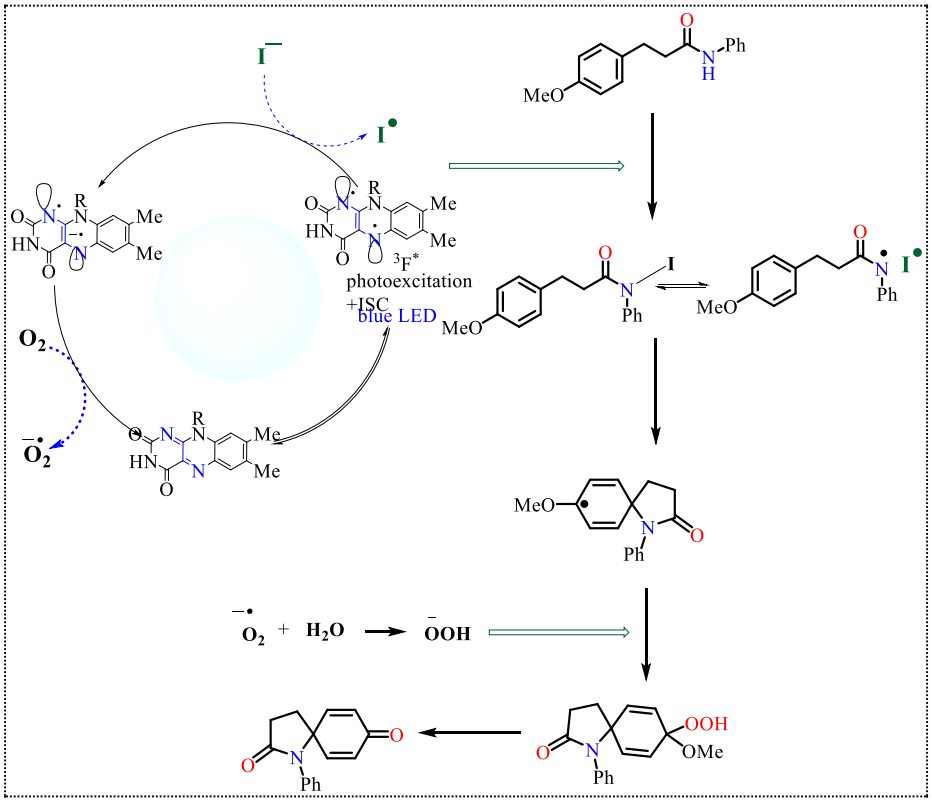
5^c

1-(2,5-dimethylphenyl)-1-azaspiro[4.5]deca-6,9-diene-2,8-dione

5^d

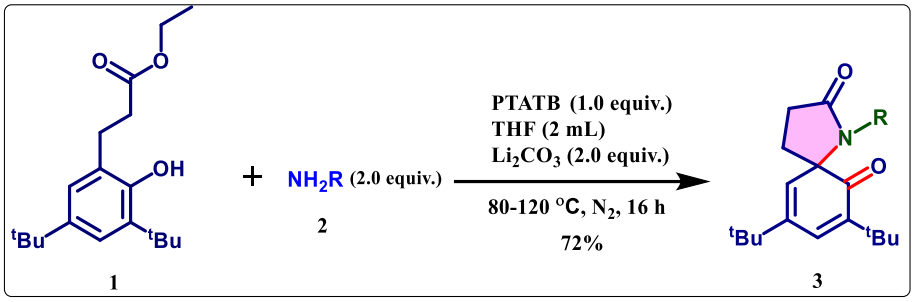
1-(4-butylphenyl)-1-azaspiro[4.5]deca-6,9-diene-2,8-dione

Plausible Mechanism [10]**:**



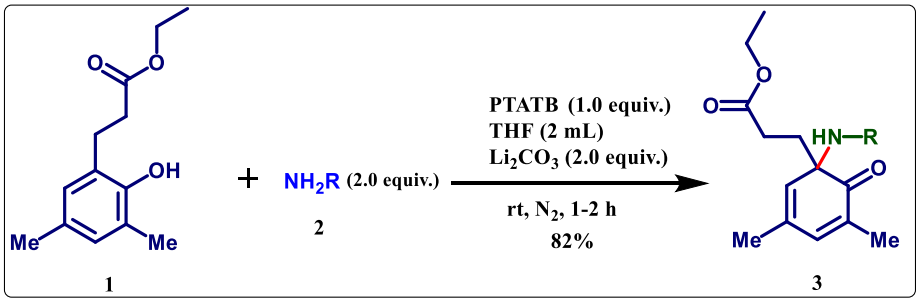
Reaction Scheme-2

B.3. General Procedure for Synthesis of Azaspirodienone for Phenols.

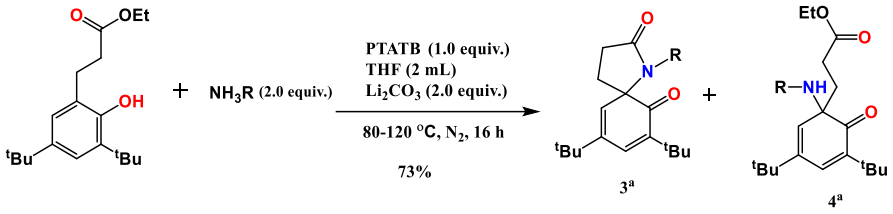


Ethyl 3-(2-hydroxy-3,5-di-tert-butylphenyl) propanoate was used as the starting material and added to a clean, dry reaction vial. To this, 2 mL of anhydrous tetrahydrofuran (THF) was added, followed by the addition of 2 equivalents of lithium carbonate (Li_2CO_3) as the base. The respective amine was then added to the reaction mixture, and the solution was stirred under a nitrogen atmosphere for 5–10 minutes. Subsequently, 1 equivalent of PTATB was introduced. The reaction mixture was then heated under thermal conditions at 80–120 °C for 12–16 hours. The reaction was monitored by thin-layer chromatography (TLC) to ensure complete consumption of the starting material. Upon completion, the reaction mixture was purified by column chromatography to isolate the desired product.

B.4. General Procedure for Synthesis of Ethyl 3-(1-alkyllamino)-3,5-dimethyl-6-oxocyclohexa-2,4-dien-1-yl) propanoate.



Ethyl 3-(2-hydroxy-3,5-dimethylphenyl) propanoate was used as the starting material and added to a clean, dry reaction vial. To this, 2 mL of anhydrous tetrahydrofuran (THF) was added, followed by the addition of 2 equivalents of lithium carbonate (Li_2CO_3) as the base. The respective amine was then introduced to the reaction mixture, and the solution was stirred under a nitrogen atmosphere for 5–10 minutes. Subsequently, 1 equivalent of PTATB was added. The reaction was allowed to proceed for 1–2 hours, during which the consumption of the starting material was monitored by thin-layer chromatography (TLC). Upon completion, the reaction mixture was purified by column chromatography to isolate the desired product.



Optimisation Table:

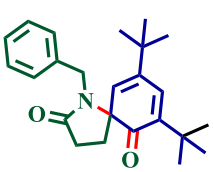
Entry	R	Base	Time(hrs)	Solvent	Temp. (°C)	Yield(3ª)	Yield(4ª)
1.	Bn	K_2CO_3	16	**CH_3CN**	80	0	0
2.	Bn	K_2CO_3	16	**Acetone**	80	0	0
3.	Bn	K_2CO_3	16	**DMF**	120	0	0
4.	Bn	K_2CO_3	16	**THF**	100	0	0
5.	Bn	Li_2CO_3	16	**DCM**	50	Nil	85%
6.	**Bn**	**Li_2CO_3**	**16**	**THF**	**100**	**76%**	**0%**
7.	Ph	**Li_2CO_3**	16	THF	100	0%	0%
8.	Bu	**Li_2CO_3**	5	THF	100	20%	60%
9.	Bn	**Cs_2CO_3**	16	THF	100	78%	0%
10.	Bn	**Cs_2CO_3**	16	THF	100	Nil	85
11.	Bn	**NaOH**	16	THF	100	0	0
12.	Bn	**KOH**	16	THF	100	0	0
13.	Bn	**DBU**	16	THF	100	0	0
14.	Bn	**DBN**	16	THF	100	0	0
15	Bn	Li_2CO_3	5	THF	100	0	60
16	Bn	Li_2CO_3	1	THF	100	0	30
17.	Bn	Li_2CO_3	16	THF	100	76	0
18.	Bn	Li_2CO_3	16	THF	50	0	78
19.	Bn	Li_2CO_3	16	THF	rt	0	78

Results & Discussions:

B.3

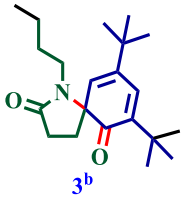
We have tried with different organic Bases and inorganic Bases, Li_2CO_3 acts as the most suitable base for the formation of the 3^a after 16 hrs. of the reaction at 100 ° C. In the case of K_2CO_3 base, the formation of amid is at 100 °C. The reaction undergone by the intermediate 4^a is elaborately discussed in the Reaction Mechanism.

Substrates Scope:



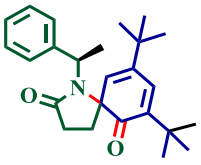
3^a

100 °C , 73%



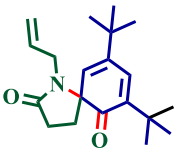
3^b

100 °C ,71 %



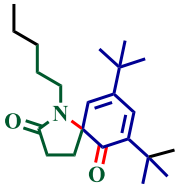
3^c

120°C , 72 %



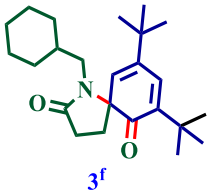
3^d

80°C , 56.6%



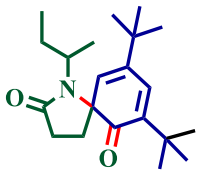
3^e

120 °C , 65%



3^f

80 °C , 65%

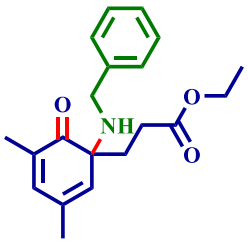


3^g

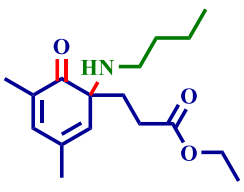
100 °C ,68%

B.4

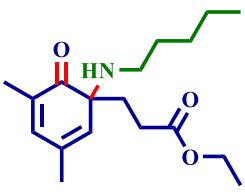
In case of **Ethyl 3-(2-hydroxy-3,5-dimethylphenyl) propanoate,** we observed that there is dearomatization occurs but there is no further formation of Spiro-Amide, as we have earlier mentioned in the case of **Ethyl 3-(3,5-di-tert-butyl-2-hydroxyphenyl) propanoate.**



4^a , 85%

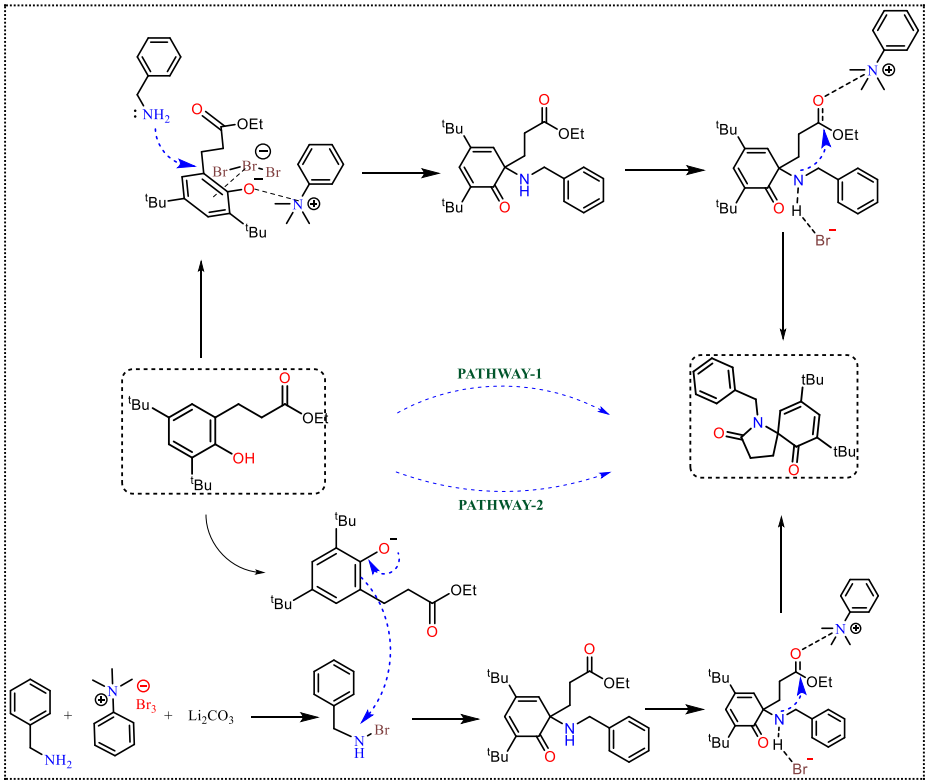


4^b , 82 %

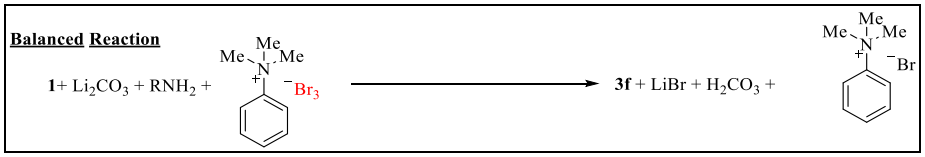


4^c , 78 %

Plausible Mechanism:

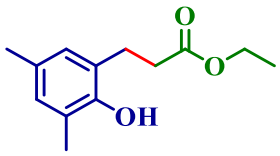


Mechanism Proved by HRMS and Raman Spectroscopy Study.



SUPPORTING DATA:

Ethyl 3-(2-hydroxy-3,5-dimethylphenyl)propanoate



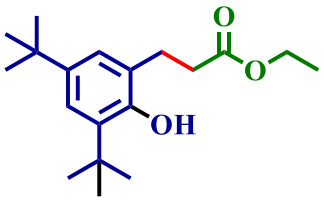
6

Slightly Yellow Liquid Compound. Yield is 71%. R_f value 0.5 (EtOH/ Hexane 25%). Red Char taken in Valine Solution after some time; Colour disappears.

^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 7.00 (s, 1H), 6.74 (d, *J* = 1.5 Hz, 1H), 6.66 (d, *J* = 2.2 Hz, 1H), 4.06 (q, *J* = 7.1 Hz, 2H), 2.79 – 2.75 (m, 2H), 2.64 – 2.60 (m, 2H), 2.15 (s, 6H), 1.15 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ(ppm): 175.89, 150.30, 129.94, 129.34, 128.48, 126.78, 125.79, 77.32, 77.06, 76.81, 61.33, 35.50, 24.55, 20.44, 16.33, 14.09.

Ethyl 3-(3,5-di-*tert*-butyl-2-hydroxyphenyl)propanoate



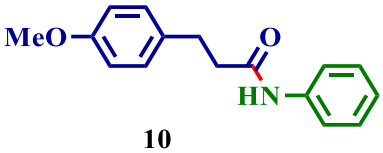
8

Yellow Viscous Liquid Compound. Yield is 65 %. R_f value 0.5 (EtOH/ Hexane 5%). No Char taken in Valine Solution after some time.

^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 7.47 (s, 1H), 7.12 (d, *J* = 2.5 Hz, 1H), 6.87 (d, *J* = 2.5 Hz, 1H), 4.05 (q, *J* = 7.2 Hz, 2H), 2.83 – 2.77 (m, 2H), 2.69 – 2.63 (m, 2H), 1.35 (s, 9H), 1.21 (s, 9H), 1.16 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ(ppm): 175.24, 149.84, 141.20, 136.25, 126.37, 123.93, 121.44, 76.24, 75.99, 75.74, 60.41, 34.77, 34.07, 33.19, 30.61, 28.87, 23.59, 13.00.

3-(4-methoxyphenyl)-*N*-phenylpropanamide



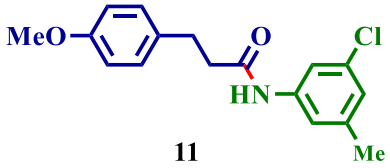
10

White amorphous Compound. Yield is 85 %. R_f value 0.3 (EtOH/ Hexane 30%). Yellow Char taken in Valine Solution.

^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 7.36 (d, *J* = 7.9 Hz, 2H), 7.23 (t, *J* = 7.7 Hz, 2H), 7.09 (d, *J* = 8.2 Hz, 2H), 7.02 (t, *J* = 7.4 Hz, 1H), 6.95 (s, 1H), 6.77 (d, *J* = 8.5 Hz, 2H), 3.72 (s, 3H), 2.93 (t, *J* = 7.5 Hz, 2H), 2.56 (t, *J* = 7.5 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ(ppm): 170.41, 158.19, 137.75, 132.64, 129.39, 128.98, 124.29, 119.87, 114.07, 77.28, 77.03, 76.78, 55.30, 39.83, 30.73.

***N*-(3-chloro-5-methylphenyl)-3-(4-methoxyphenyl)propanamide**



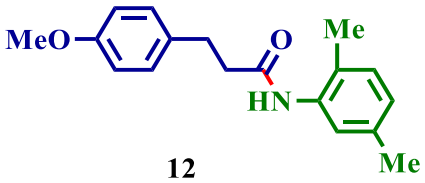
11

White amorphous Compound. Yield is 88 %. R_f value 0.25 (EtOH/ Hexane 40%). Light Yellow Char taken in Valine Solution.

^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 7.32 (d, *J* = 1.9 Hz, 2H), 7.07 – 7.05 (m, 2H), 7.00 (t, *J* = 1.9 Hz, 1H), 6.77 (d, *J* = 8.6 Hz, 2H), 3.72 (s, 3H), 2.90 (t, *J* = 7.4 Hz, 2H), 2.55 (t, *J* = 7.4 Hz, 2H), 2.10 (s, 1H), 1.20 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ(ppm): 170.69, 158.29, 139.50, 135.18, 132.24, 129.36, 124.19, 118.01, 114.15, 77.29, 77.04, 76.78, 55.31, 39.71, 31.24, 30.53.

***N*-(2,5-dimethylphenyl)-3-(4-methoxyphenyl)propanamide**



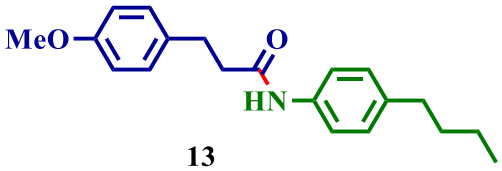
12

White crystalline compound. Yield is 86 %. R_f value 0.2 (EtOH/ Hexane 40%). White Char taken in Valine Solution.

^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 7.49 (s, 1H), 7.10 (d, *J* = 8.0 Hz, 2H), 6.94 (d, *J* = 7.7 Hz, 1H), 6.78 (dd, *J* = 11.7, 8.1 Hz, 4H), 3.71 (s, 3H), 2.93 (t, *J* = 7.4 Hz, 2H), 2.59 (t, *J* = 7.4 Hz, 2H), 2.22 (s, 3H), 1.95 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ(ppm): 170.51, 158.22, 136.46, 135.30, 132.62, 130.20, 129.40, 129.26, 125.97, 123.82, 114.10, 77.30, 77.05, 76.79, 55.31, 39.57, 30.89, 24.91, 17.11.

***N*-(4-butylphenyl)-3-(4-methoxyphenyl)propanamide**



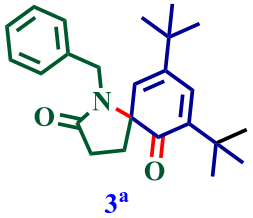
13

White crystalline compound. Yield is 82 %. R_f value 0.5 (EtOH/ Hexane 30%). Deep Yellow Char taken in Valine Solution.

^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm):7.25 (d, *J* = 8.1 Hz, 2H), 7.07 (d, *J* = 8.5 Hz, 2H), 7.02 (d, *J* = 8.2 Hz, 2H), 6.76 (d, *J* = 8.6 Hz, 2H), 3.71 (s, 3H), 2.91 (t, *J* = 7.5 Hz, 2H), 2.53 (t, *J* = 7.6 Hz, 2H), 2.48 (t, *J* = 7.7 Hz, 2H), 1.49 (p, *J* = 7.5 Hz, 2H), 1.26 (q, *J* = 7.4 Hz, 2H), 0.84 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ(ppm): 170.37, 158.15, 139.03, 135.35, 132.73, 129.38, 128.83, 120.01, 114.04, 77.30, 77.04, 76.79, 55.29, 39.74, 35.05, 33.66, 30.78, 22.29, 13.95.

1-Benzyl-7,9-di-*tert*-butyl-1-azaspiro[4.5]deca-7,9-diene-2,6-dione



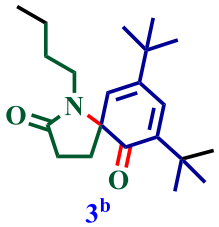
3[a]

Liquid compound. Yield is 73 %. R_f value 0.2 (EtOH/ Hexane 30%). White Char taken in Valine Solution.

^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 7.23 (s, 4H), 7.15 (dt, *J* = 8.8, 4.3 Hz, 1H), 6.52 (d, *J* = 4.9 Hz, 2H), 3.45 (d, *J* = 13.3 Hz, 1H), 3.36 (d, *J* = 13.4 Hz, 1H), 2.57 (qt, *J* = 14.4, 7.2 Hz, 2H), 2.42 (t, *J* = 7.3 Hz, 2H), 1.12 (s, 9H), 0.91 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ(ppm): 185.45, 173.12, 147.82, 146.70, 145.97, 141.50, 140.58, 128.33, 127.92, 126.91, 77.30, 77.04, 76.79, 60.37, 48.44, 39.09, 34.94, 33.36, 29.40, 25.79, 14.23.

7,9-Di-*tert*-butyl-1-butyl-1-azaspiro[4.5]deca-7,9-diene-2,6-dione



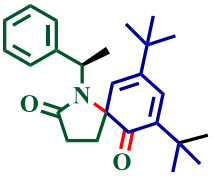
3[b]

Liquid compound. Yield is 71 %. R_f value 0.3 (EtOH/ Hexane 30%). White Char taken in Valine Solution.

^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 6.50 (d, *J* = 4.7 Hz, 2H), 4.03 (q, *J* = 7.2 Hz, 2H), 2.57 (dt, *J* = 12.7, 7.3 Hz, 2H), 2.44 (t, *J* = 7.2 Hz, 2H), 2.22 – 2.14 (m, 2H), 1.17 (d, *J* = 1.7 Hz, 9H), 0.88 (s, 9H), 0.86 – 0.75 (m, 5H).

^{13}C NMR (126 MHz, $CDCl_3$) δ(ppm): 188.25, 172.10, 156.31, 149.17, 131.56, 131.41, 77.28, 77.03, 76.77, 60.36, 35.39, 34.97, 33.42, 32.24, 29.48, 29.23, 25.57, 25.00, 20.37, 14.22

7,9-Di-*tert*-butyl-1-((*R*)-1-phenylethyl)-1-azaspiro[4.5]deca-7,9-diene-2,6-dione



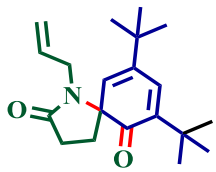
3[c]

Liquid compound. Yield is 72 %. R_f value 0.2 (EtOH/ Hexane 30%). White Char taken in Valine Solution.

^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 7.25 – 7.09 (m, 5H), 6.97 (d, *J* = 2.4 Hz, 1H), 6.88 (d, *J* = 2.6 Hz, 1H), 4.07 (d, *J* = 7.2 Hz, 1H), 2.90 – 2.88 (m, 1H), 2.81 (dd, *J* = 7.2, 4.9 Hz, 1H), 2.70 – 2.66 (m, 2H), 1.35 (s, 9H), 1.24 (s, 9H), 1.22 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ(ppm): 175.25, 167.87, 149.83, 147.39, 145.48, 141.23, 136.28, 127.25, 126.37, 125.40, 123.94, 121.74, 76.24, 75.99, 75.74, 60.43, 33.95, 30.61, 30.46, 29.02, 28.87, 24.69, 23.57, 13.02.

1-Allyl-7,9-di-*tert*-butyl-1-azaspiro[4.5]deca-7,9-diene-2,6-dione



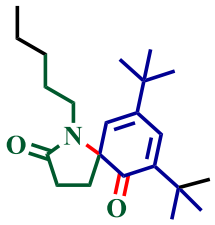
3[d]

Liquid compound. Yield is 56 %. R_f value 0.3 (EtOH/ Hexane 30%). White Char taken in Valine Solution.

^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 6.51 (d, *J* = 4.1 Hz, 2H), 5.79 (ddddd, *J* = 15.7, 7.3, 5.7, 4.6, 1.7 Hz, 1H), 5.07 (d, *J* = 17.2 Hz, 1H), 4.97 (d, *J* = 10.2 Hz, 1H), 4.03 (d, *J* = 5.8 Hz, 2H), 2.62 – 2.56 (m, 2H), 2.44 (d, *J* = 13.9 Hz, 2H), 1.17 (s, 9H), 0.90 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ(ppm): 184.40, 172.08, 146.80, 145.73, 144.98, 139.47, 136.67, 114.31, 76.26, 76.01, 75.75, 59.34, 45.93, 37.93, 33.96, 32.37, 28.68, 28.44, 24.76, 24.56, 13.20.

7,9-Di-*tert*-butyl-1-pentyl-1-azaspiro[4.5]deca-7,9-diene-2,6-dione



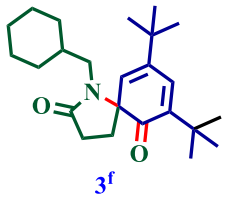
3[e]

Liquid compound. Yield is 65 %. R_f value 0.3 (EtOH/ Hexane 40%). White Char taken in Valine Solution.

^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 6.50 (q, *J* = 3.1 Hz, 1H), 4.03 (q, *J* = 7.2 Hz, 1H), 2.57 (dt, *J* = 12.7, 7.3 Hz, 1H), 2.44 (t, *J* = 7.2 Hz, 1H), 2.24 – 2.13 (m, 1H), 1.33 (dt, *J* = 17.3, 8.1 Hz, 2H), 1.17 (s, 5H), 0.88 (s, 5H), 0.81 (t, *J* = 6.8 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ(ppm): 185.55, 173.13, 147.63, 140.29, 77.28, 77.03, 76.77, 60.34, 44.16, 38.90, 34.94, 33.45, 31.24, 29.50, 29.47, 25.78, 25.58, 22.58, 14.23.

7,9-Di-*tert*-butyl-1-(cyclohexylmethyl)-1-azaspiro[4.5]deca-7,9-diene-2,6-dione



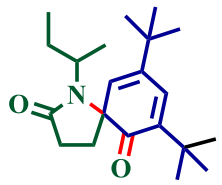
3[f]

Liquid compound. Yield is 68 %. R_f value 0.3 (EtOH/ Hexane 25%). White Char taken in Valine Solution.

^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 6.56 (d, *J* = 3.1 Hz, 1H), 6.52 (d, *J* = 3.0 Hz, 1H), 4.04 (d, *J* = 7.2 Hz, 2H), 2.68 (dtd, *J* = 9.3, 5.0, 2.6 Hz, 1H), 2.43 (dd, *J* = 7.3, 1.5 Hz, 2H), 1.90 (t, *J* = 4.3 Hz, 2H), 1.24 – 1.20 (m, 10H), 1.16 (s, 9H), 0.86 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ(ppm): 185.76, 174.20, 147.26, 146.80, 146.19, 139.49, 104.09, 62.48, 60.36, 52.53, 40.48, 38.83, 36.43, 34.82, 34.36, 33.07, 29.22, 25.60, 14.23.

1-(*sec*-butyl)-7,9-di-*tert*-butyl-1-azaspiro[4.5]deca-7,9-diene-2,6-dione



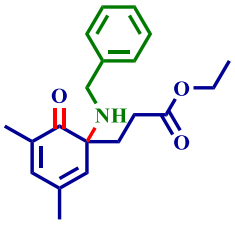
3[g]

Liquid compound. Yield is 72 %. R_f value 0.4 (EtOH/ Hexane 40%). White Char taken in Valine Solution.

^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 6.66 – 6.58 (m, 2H), 4.04 (d, *J* = 7.2 Hz, 1H), 2.60 – 2.49 (m, 2H), 2.43 (td, *J* = 7.1, 2.5 Hz, 2H), 1.18 (d, *J* = 7.2 Hz, 6H), 1.16 (s, 9H), 0.91 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ(ppm): 185.09, 173.02, 145.94, 143.84, 143.38, 138.61, 77.28, 77.03, 76.78, 73.61, 60.45, 39.36, 34.78, 33.15, 29.70, 29.32, 25.43, 25.39, 14.23.

Ethyl 3-(1-(benzylamino)-3,5-dimethyl-6-oxocyclohexa-2,4-dien-1-yl)propanoate



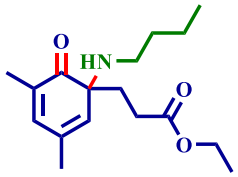
4[a]

Liquid compound. Yield is 82 %. R_f value 0.2 (EtOH/ Hexane 30%). Yellow Char taken in Valine Solution.

^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 7.24 – 7.16 (m, 5H), 6.48 (d, *J* = 15.9 Hz, 2H), 4.02 (qd, *J* = 7.2, 2.0 Hz, 2H), 3.46 (s, 2H), 2.56 (d, *J* = 2.9 Hz, 2H), 2.42 (t, *J* = 7.1 Hz, 2H), 1.82 (s, 3H), 1.25 (s, 3H), 1.15 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ(ppm): 186.15, 173.00, 150.41, 149.69, 137.58, 137.53, 135.51, 128.45, 128.15, 127.16, 77.32, 77.06, 76.81, 60.36, 55.16, 48.81, 33.10, 27.14, 25.25, 15.99, 14.25.

Ethyl 3-(1-(butylamino)-3,5-dimethyl-6-oxocyclohexa-2,4-dien-1-yl)propanoate



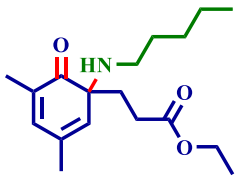
4[b]

Liquid compound. Yield is 80 %. R_f value 0.3 (EtOH/ Hexane 30%). No Char taken in Valine Solution.

^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 6.53 – 6.41 (m, 2H), 4.04 (q, *J* = 7.1 Hz, 2H), 2.56 (td, *J* = 7.3, 3.0 Hz, 2H), 2.44 (t, *J* = 7.4 Hz, 2H), 2.31 (t, *J* = 7.3 Hz, 2H), 1.83 (s, 3H), 1.38 – 1.33 (m, 2H), 1.26 (s, 3H), 1.17 (t, *J* = 7.1 Hz, 5H), 0.81 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ(ppm): 186.08, 172.94, 137.56, 135.53, 77.29, 77.03, 76.78, 60.35, 55.13, 44.07, 33.12, 32.59, 26.94, 25.25, 20.36, 15.96, 14.25, 13.93.

Ethyl 3-(3,5-dimethyl-6-oxo-1-(pentylamino)cyclohexa-2,4-dien-1-yl)propanoate



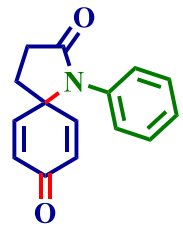
4[c]

Liquid compound. Yield is 76 %. R_f value 0.3 (EtOH/ Hexane 30%). No Char taken in Valine Solution.

^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 6.44 (ddt, *J* = 12.9, 3.1, 1.4 Hz, 2H), 4.04 (q, *J* = 6.9 Hz, 2H), 2.59 – 2.52 (m, 2H), 2.44 (t, *J* = 7.1 Hz, 2H), 2.27 (t, *J* = 7.3 Hz, 2H), 1.82 (d, *J* = 1.6 Hz, 3H), 1.33 (t, *J* = 7.0 Hz, 2H), 1.21 (s, 5H), 1.17 (t, *J* = 7.1 Hz, 5H), 0.80 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ(ppm): 186.21, 172.97, 150.78, 150.02, 137.23, 135.19, 77.30, 77.05,76.79, 60.31, 54.85, 44.40, 33.15, 30.52, 29.42, 27.14, 25.24, 22.55, 15.95, 14.23, 13.98.

1-Phenyl-1-azaspiro[4.5]deca-6,9-diene-2,8-dione



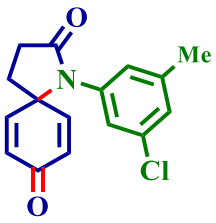
5[a]

Yellow crystalline compound. Yield is 27 %. R_f value 0.2 (EtOH/ Hexane 50%). Light Orange Char taken in Valine Solution.

^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm):7.25 (d, *J* = 8.1 Hz, 2H), 7.19 (s, 1H), 7.10 (d, *J* = 8.5 Hz, 2H), 6.91 (d, *J* = 10.2 Hz, 2H), 6.20 (d, *J* = 10.2 Hz, 2H), 2.72 (t, *J* = 8.0 Hz, 2H), 2.27 (t, *J* = 8.0 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ(ppm): 184.27, 174.01, 149.77, 136.24, 129.85, 129.20, 127.80, 126.11, 77.30, 77.05, 76.79, 63.95, 31.70, 29.88.

1-(3-chloro-5-methylphenyl)-1-azaspiro[4.5]deca-6,9-diene-2,8-dione



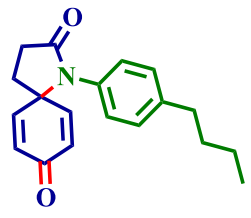
5[b]

Yellow crystalline compound. Yield is 24 %. R_f value 0.3 (EtOH/ Hexane 40%). Yellow Char taken in Valine Solution.

^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm):7.18 (t, *J* = 1.8 Hz, 1H), 7.07 (d, *J* = 1.8 Hz, 2H), 6.92 – 6.85 (m, 2H), 6.28 (d, *J* = 10.1 Hz, 2H), 2.70 (d, *J* = 10.7 Hz, 5H), 2.28 (t, *J* = 8.1 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ(ppm): 183.76, 177.41, 173.83, 149.00, 138.23, 135.31, 130.38, 127.75, 124.10, 77.31, 77.06, 76.80, 63.91, 31.99, 29.73, 29.59.

1-(4-butylphenyl)-1-azaspiro[4.5]deca-6,9-diene-2,8-dione



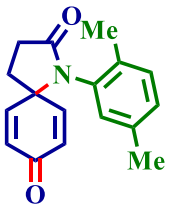
5[c]

Yellow crystalline compound. Yield is 19 %. R_f value 0.2 (EtOH/ Hexane 50%). White Char taken in Valine Solution.

^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm):7.05 (d, *J* = 8.4 Hz, 2H), 6.98 (d, *J* = 8.4 Hz, 2H), 6.93 – 6.89 (m, 2H), 6.19 (d, *J* = 10.1 Hz, 2H), 2.72 – 2.69 (m, 2H), 2.51 – 2.47 (m, 2H), 2.26 (t, *J* = 8.1 Hz, 2H), 1.65 (p, *J* = 7.7 Hz, 2H), 1.26 (d, *J* = 7.5 Hz, 2H), 0.84 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ(ppm): 184.39, 174.08, 149.85, 142.76, 133.60, 129.79, 129.14, 126.09, 77.29, 77.04, 76.78, 63.95, 35.21, 33.31, 31.54, 24.34, 22.37, 13.86.

1-(2,5-dimethylphenyl)-1-azaspiro[4.5]deca-6,9-diene-2,8-dione



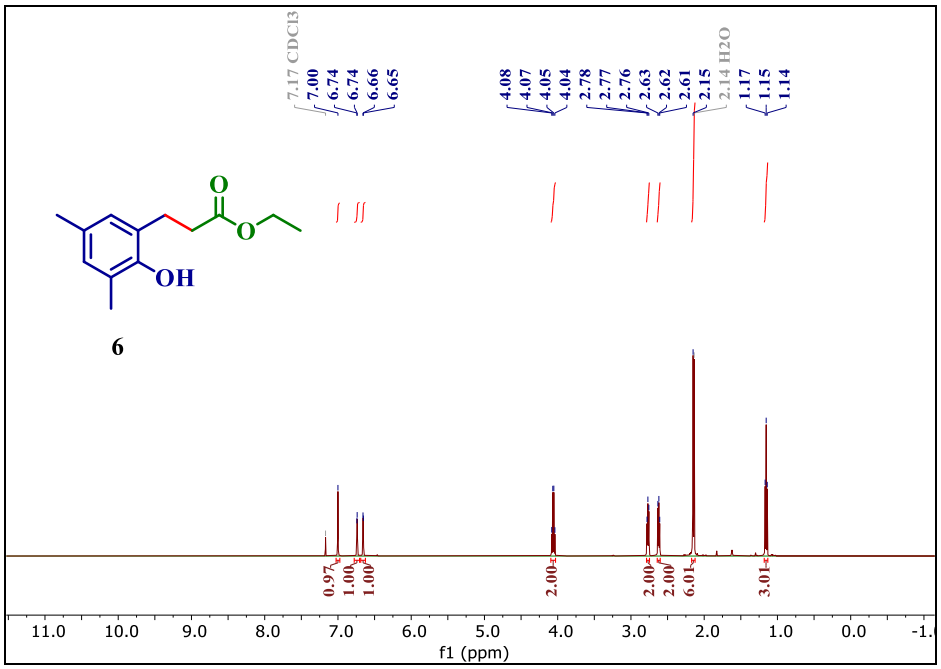
5[d]

Yellow crystalline compound. Yield is 26 %. R_f value 0.3 (EtOH/ Hexane 60%). White Char taken in Valine Solution.

^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm):7.12 (dd, *J* = 10.2, 3.1 Hz, 1H), 7.06 (d, *J* = 7.8 Hz, 1H), 6.95 (dd, *J* = 7.8, 1.8 Hz, 1H), 6.72 – 6.66 (m, 2H), 6.25 (dd, *J* = 10.1, 2.0 Hz, 1H), 6.07 (dd, *J* = 10.1, 2.0 Hz, 1H), 2.70 (d, *J* = 9.4 Hz, 2H), 2.37 (dt, *J* = 13.2, 9.6 Hz, 1H), 2.25 (ddd, *J* = 13.1, 8.8, 4.1 Hz, 1H), 2.15 (d, *J* = 3.7 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ(ppm): 184.39, 173.47, 149.39, 148.19, 136.40, 134.26, 133.01, 131.21, 130.57, 129.79, 129.17, 127.87, 77.29, 77.04, 76.78, 64.35, 31.87, 29.55, 20.85, 18.27.

Fig -3 ^{1}H and ^{13}C NMR of - 6



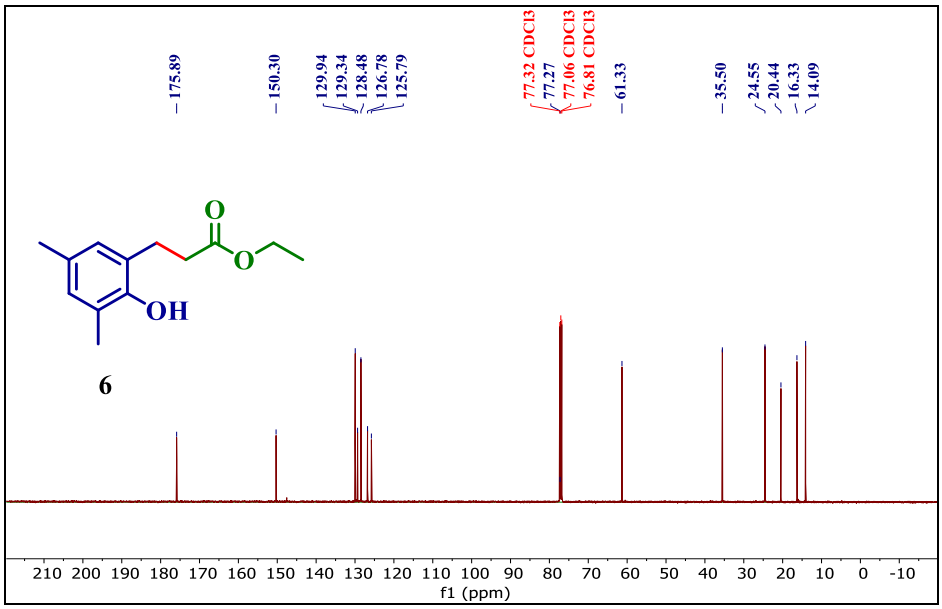
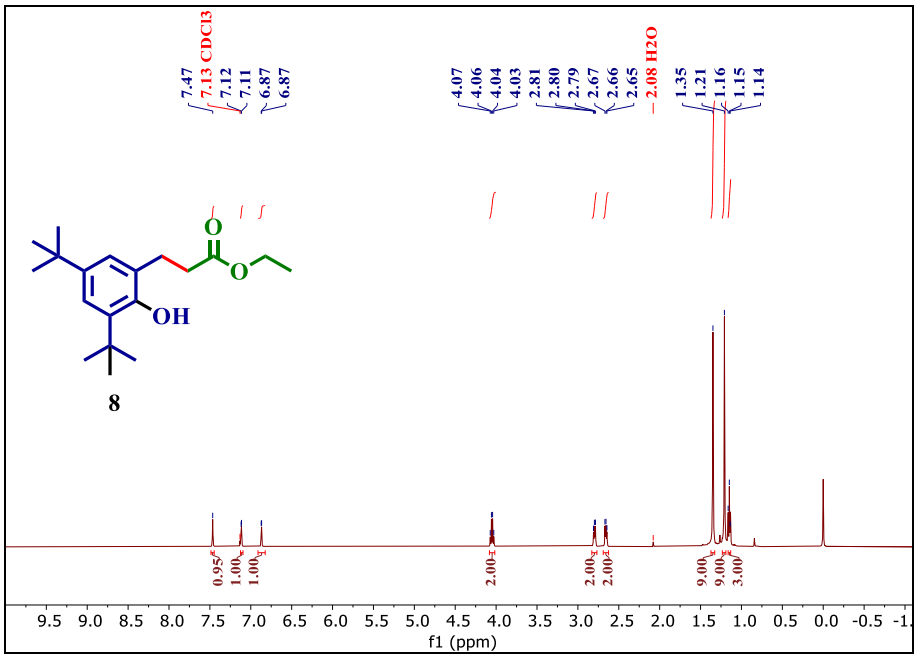


Fig-4 ^{1}H and ^{13}C NMR of - 8



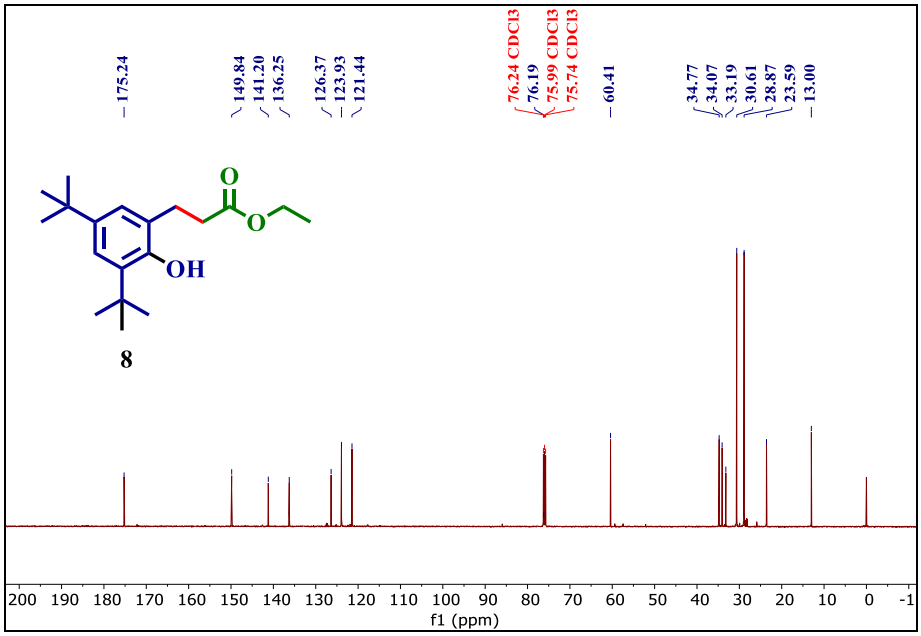
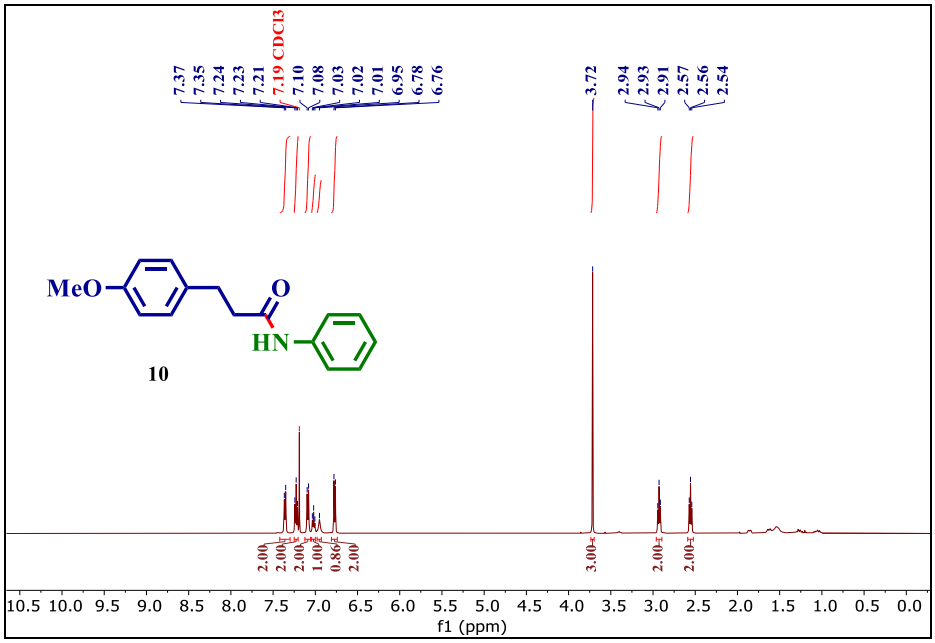


Fig-5 ^{1}H and ^{13}C NMR of -10



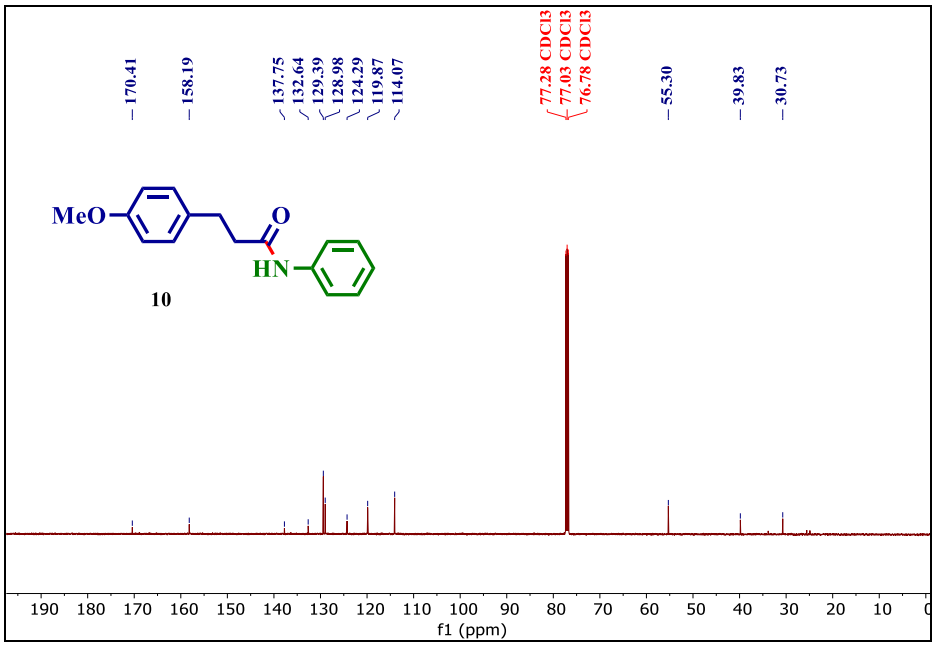
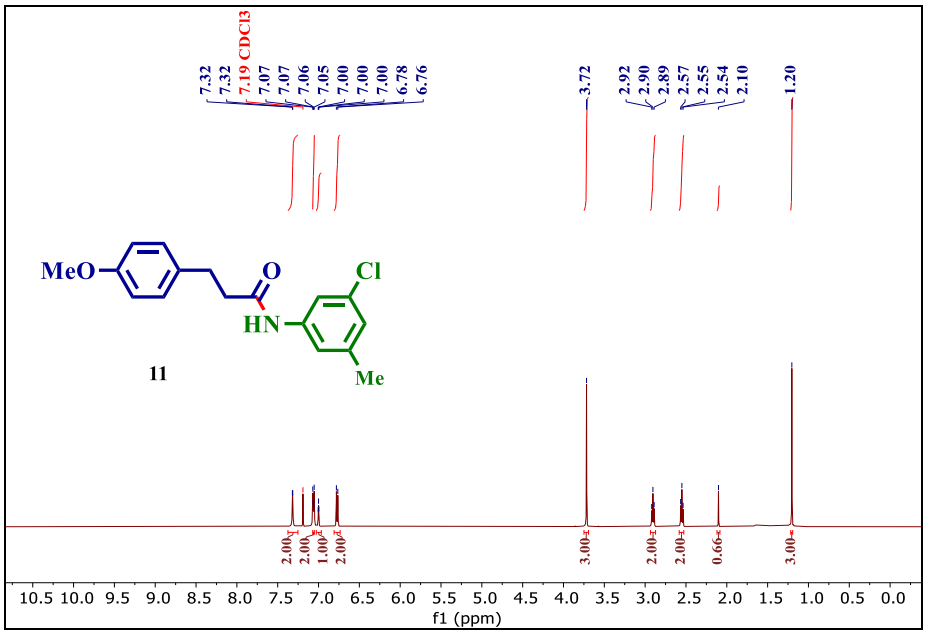


Fig-6 ^{1}H and ^{13}C NMR of- 11



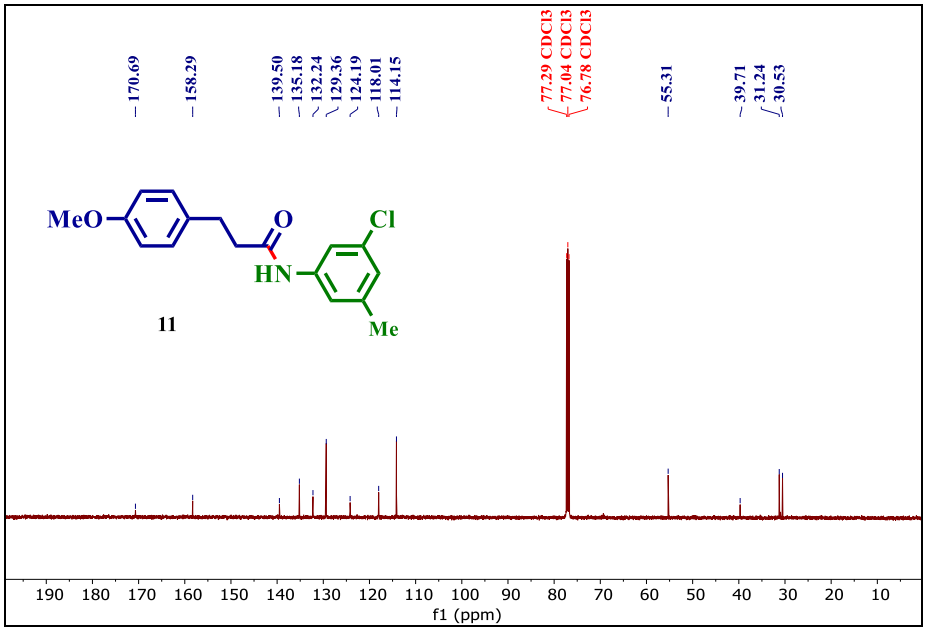
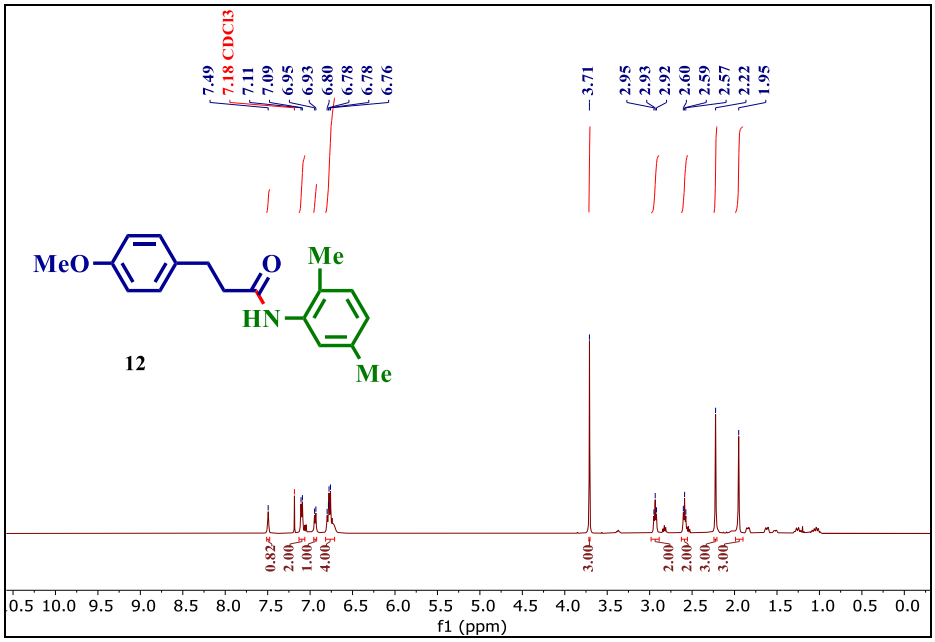


Fig-7 ^{1}H and ^{13}C NMR of -12



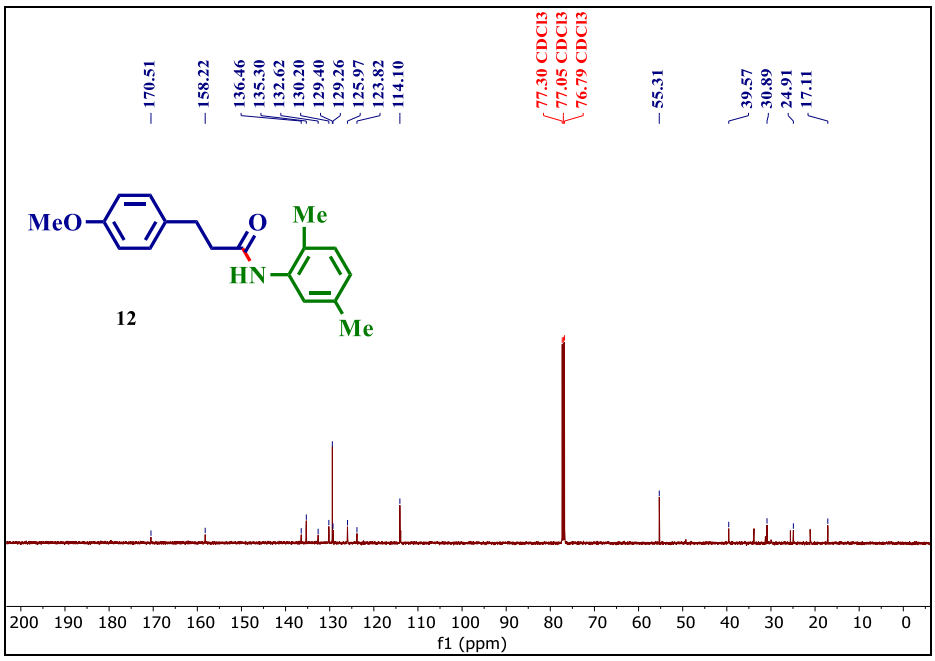
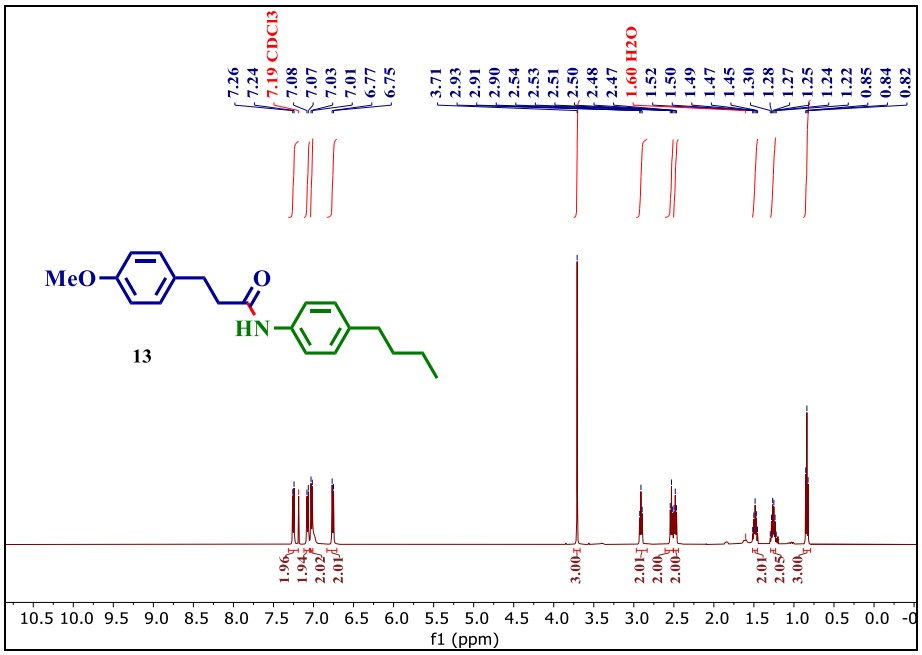


Fig-8 ^{1}H and ^{13}C NMR of -13



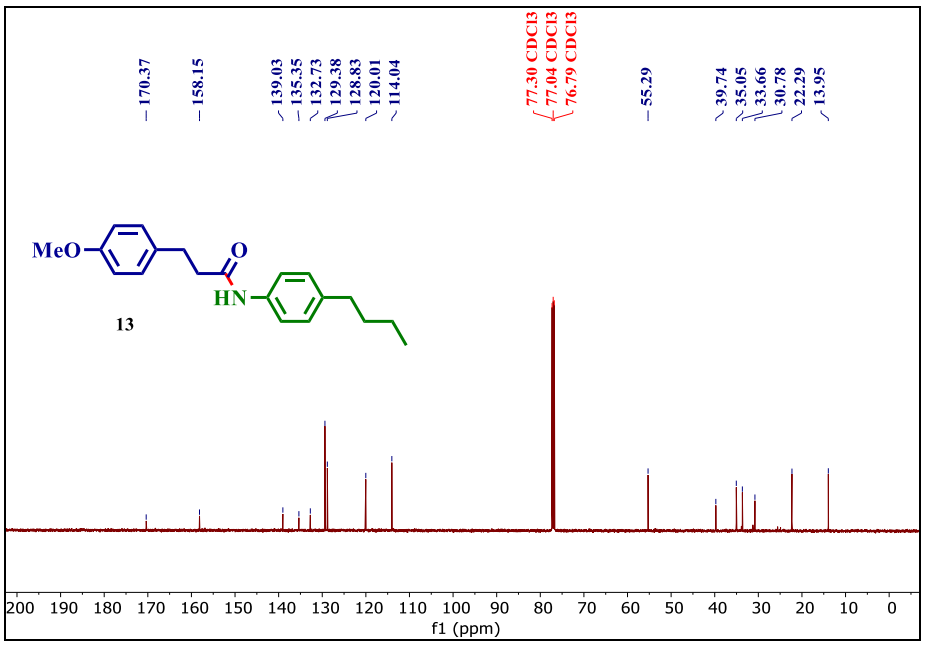
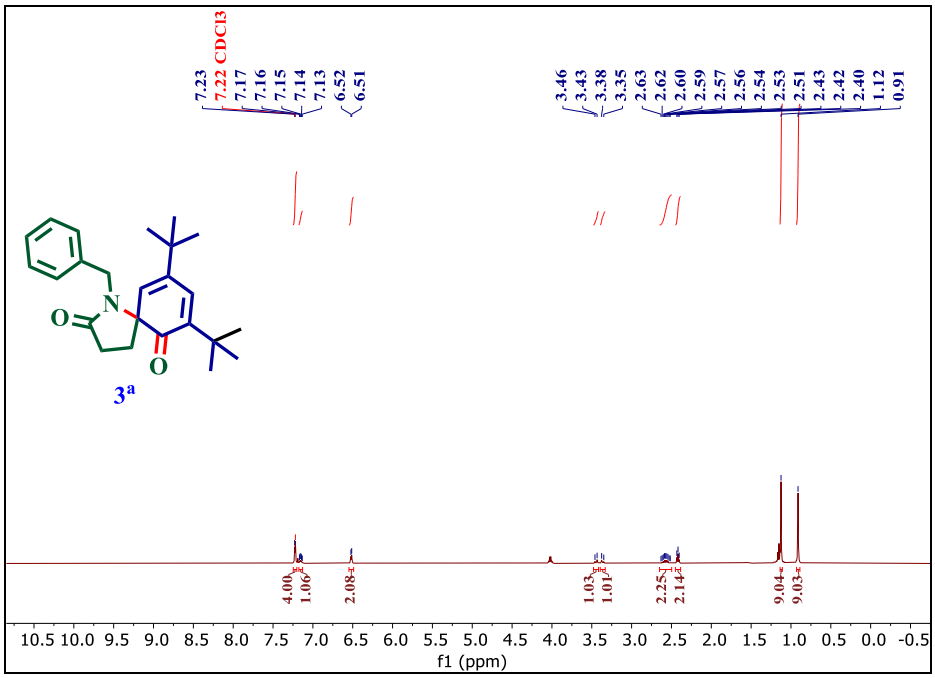


Fig-9 ^{1}H and ^{13}C NMR of 3[a]



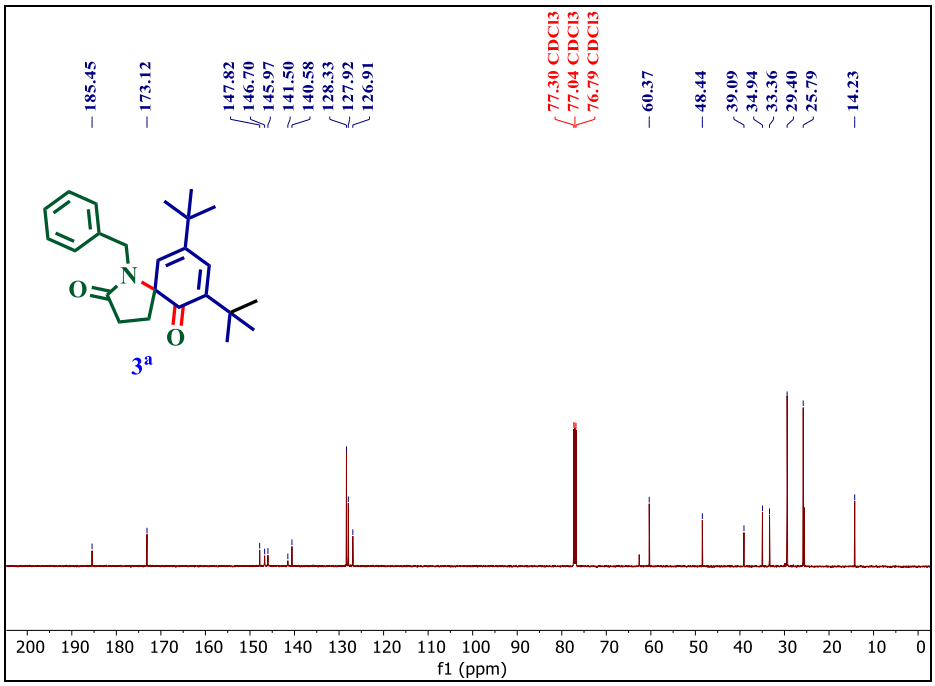
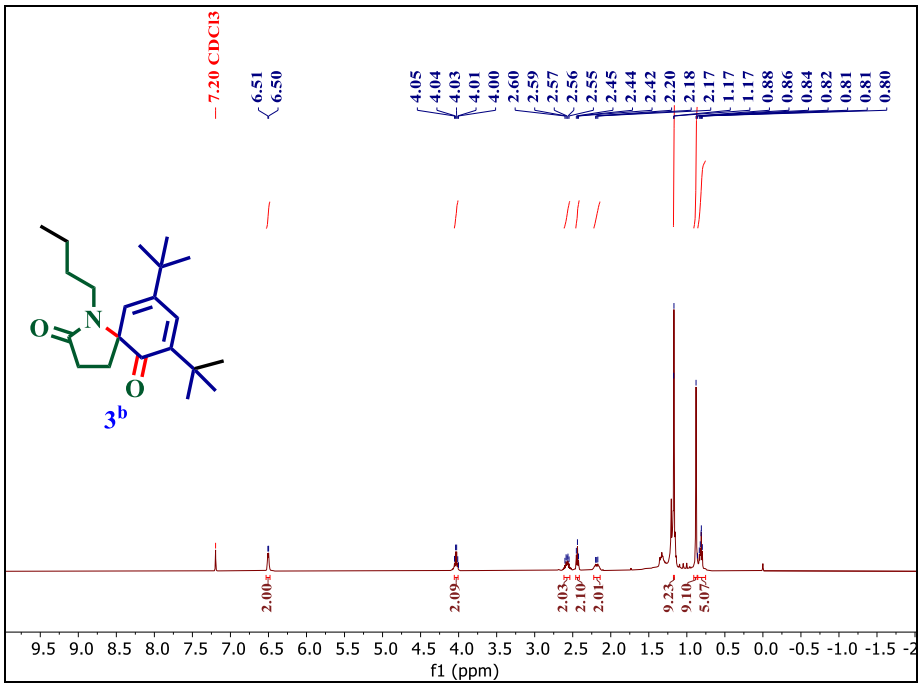


Fig-10 ^{1}H and ^{13}C NMR of 3^{b}



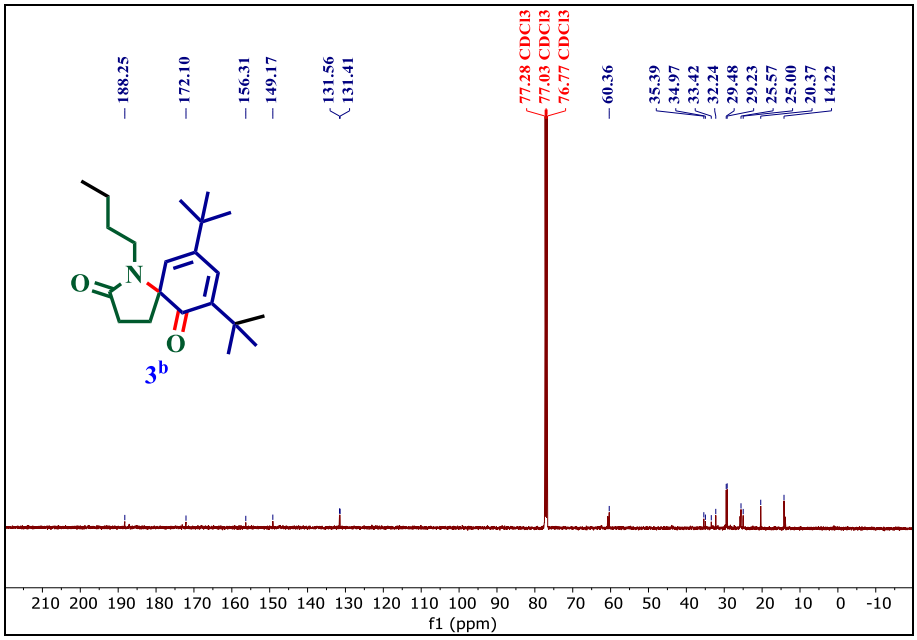
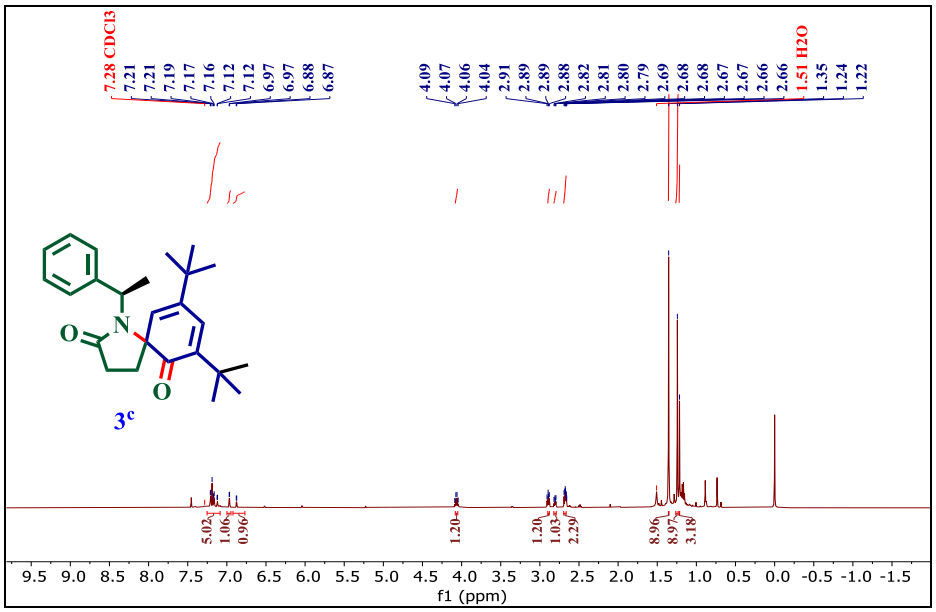


Fig-11 ^{1}H AND ^{13}C NMR OF 3^{c}



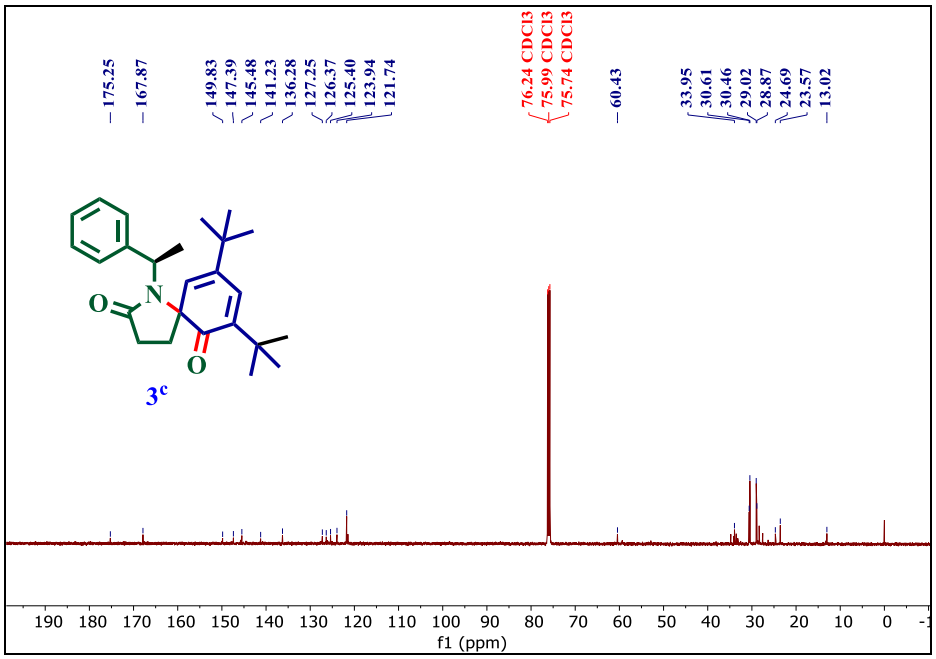
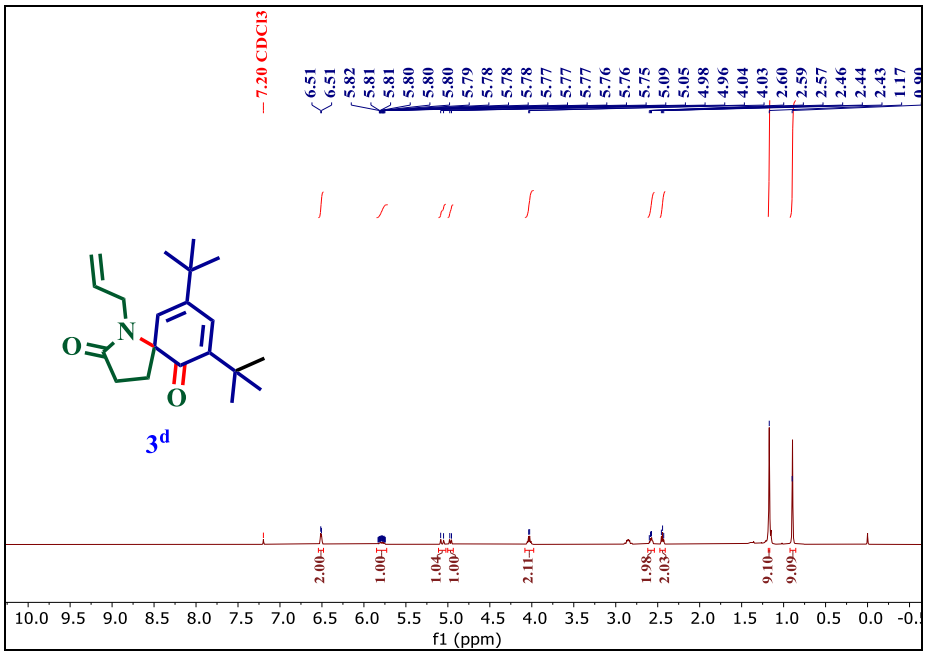


Fig-12 ^{1}H and ^{13}C NMR of 3^{d}



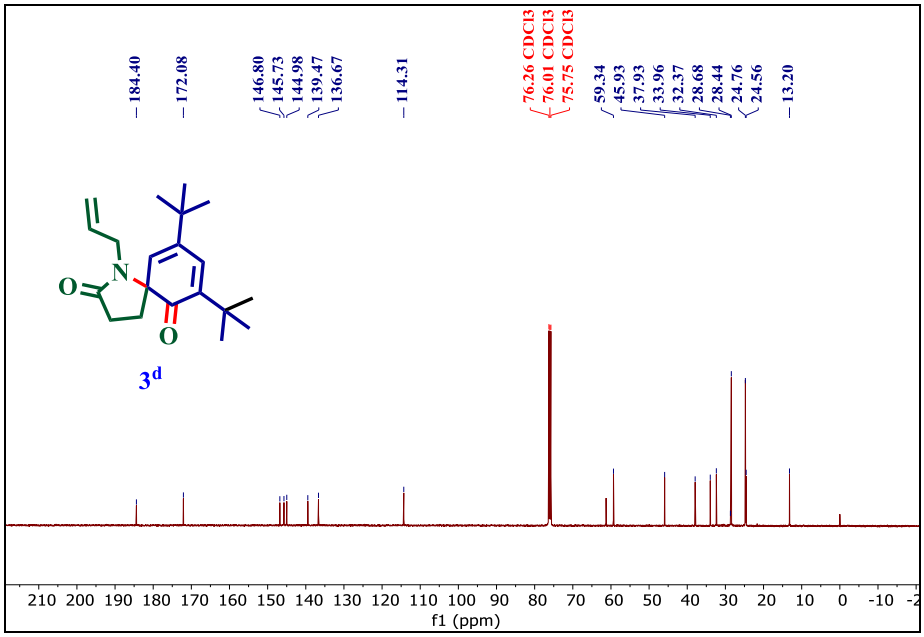
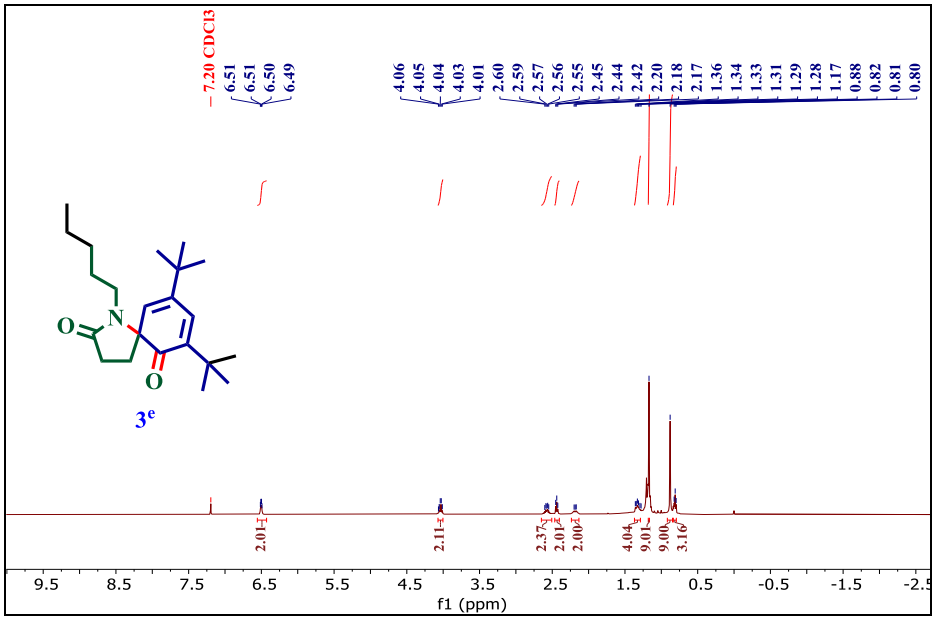


Fig-13 ^{1}H and ^{13}C NMR of 3^{e}



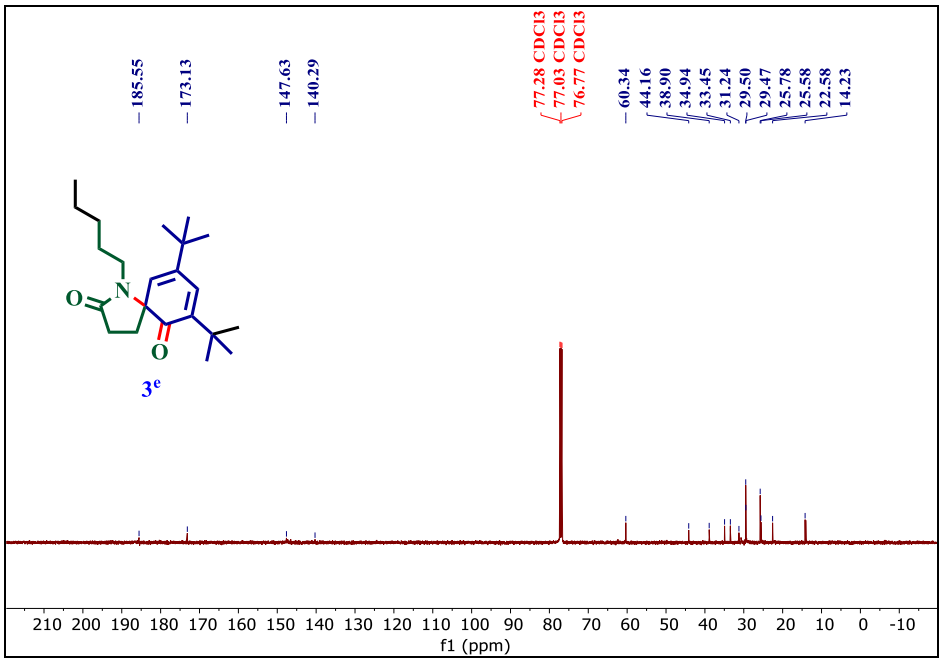
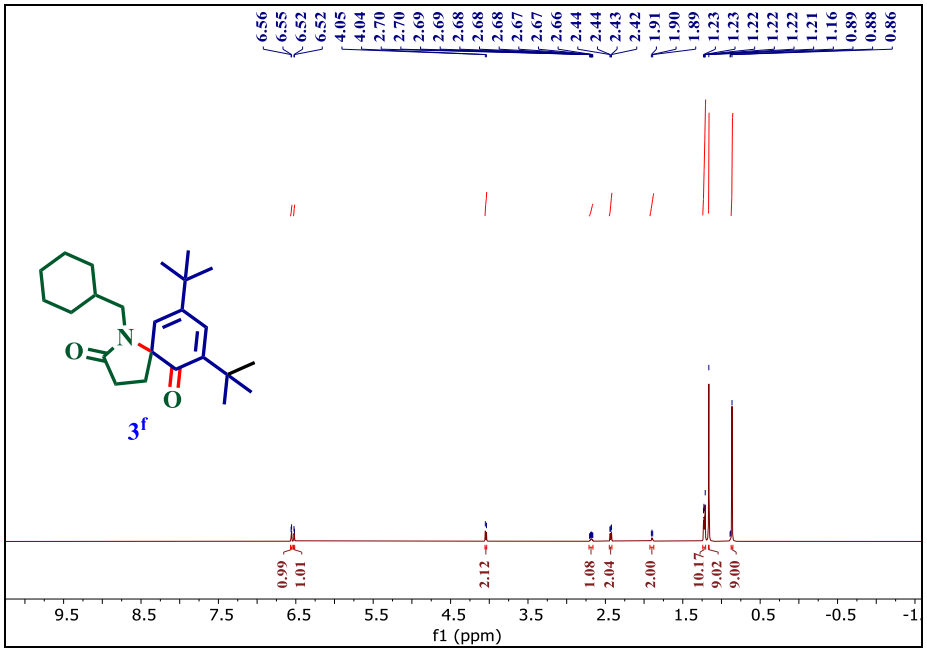


Fig-14 ^{1}H and ^{13}C NMR of 3^{f}



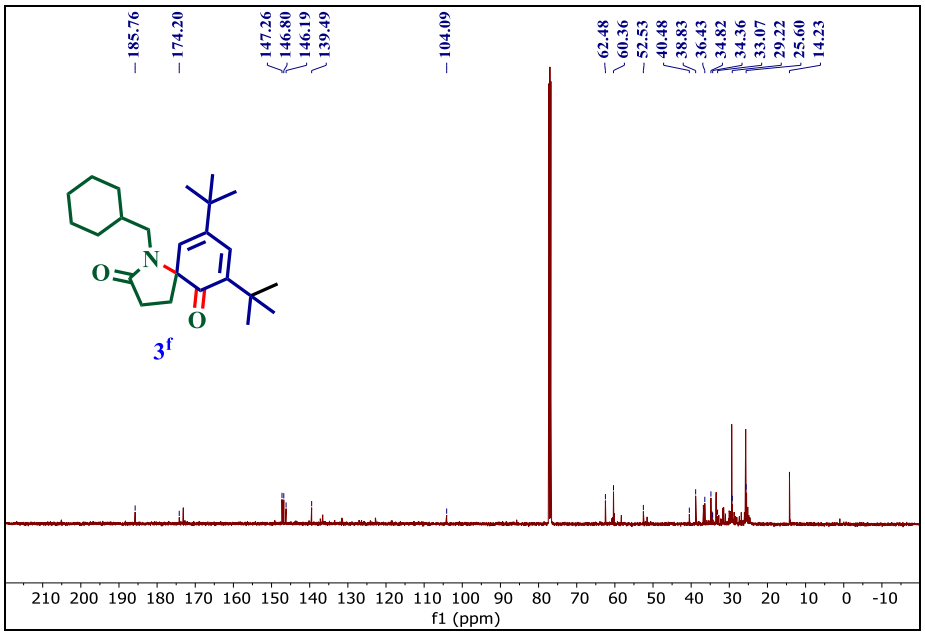
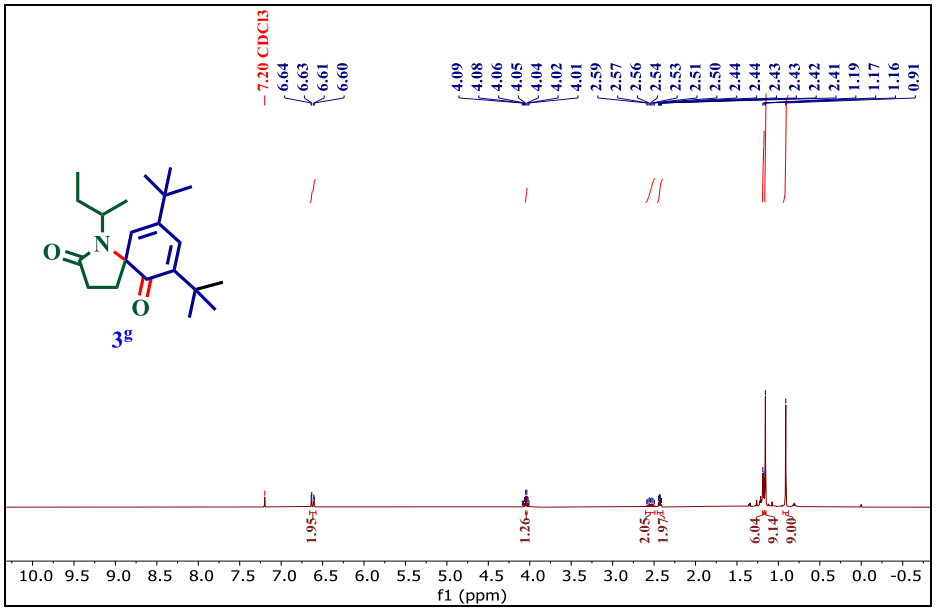


Fig-15 ^{1}H and ^{13}C NMR of 3^{g}



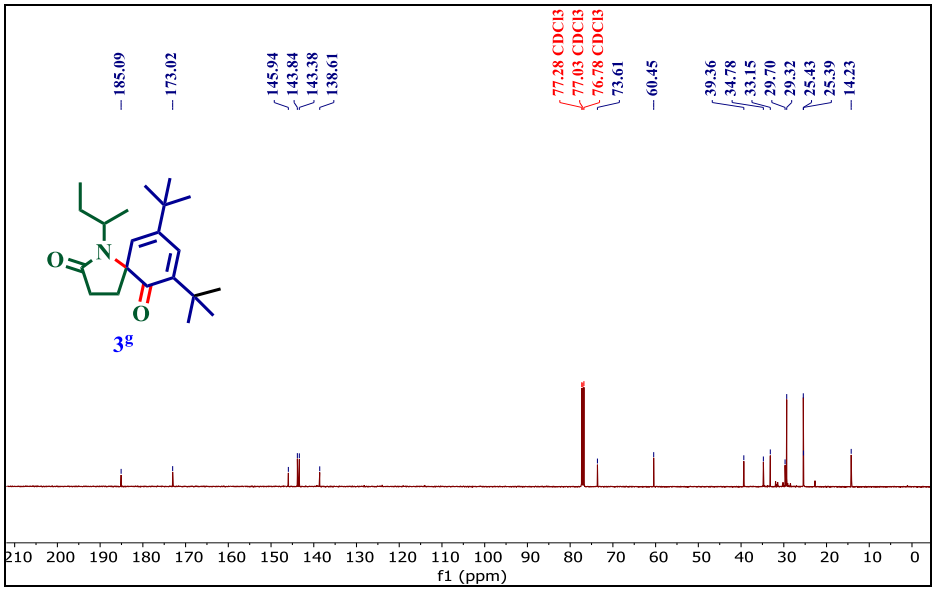
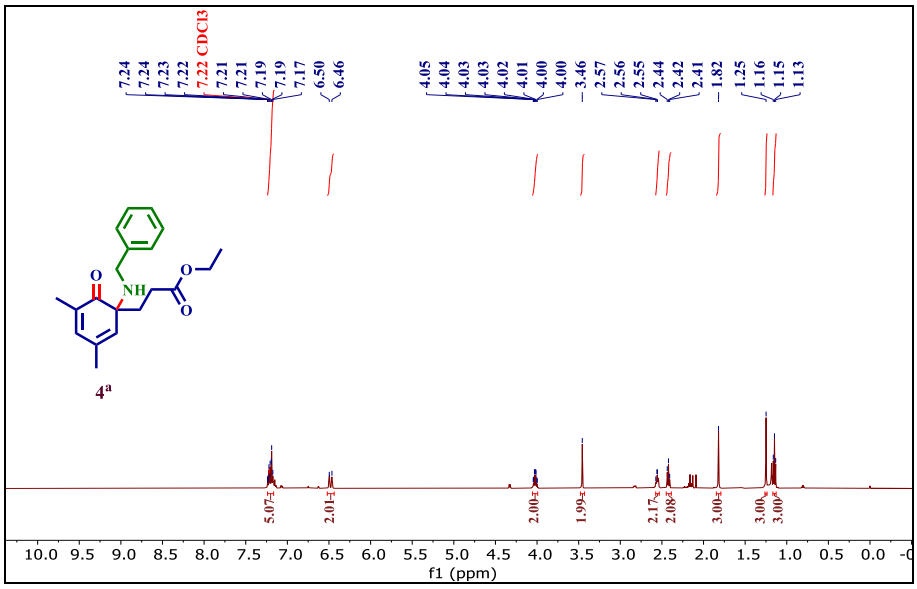


Fig-16 ^{1}H and ^{13}C NMR of 4[a]



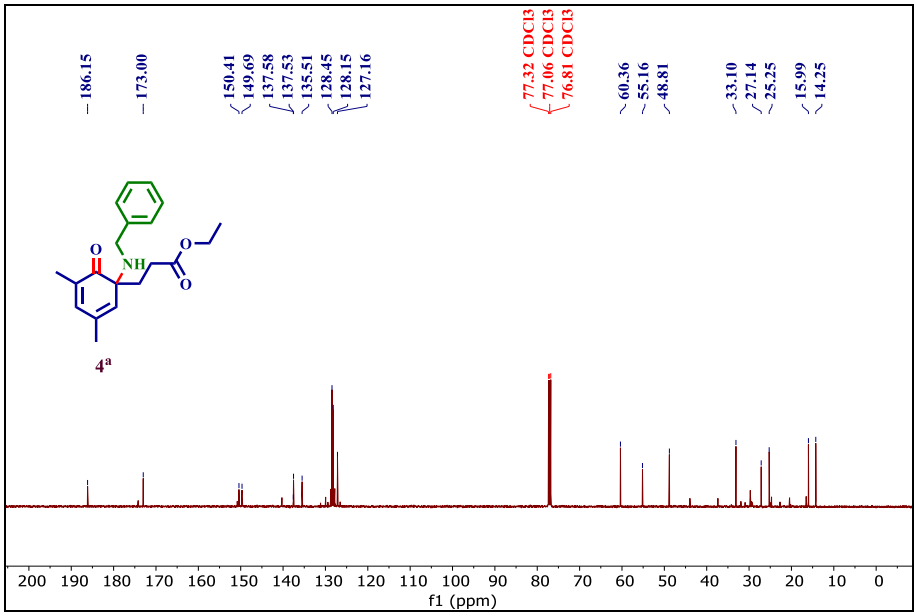
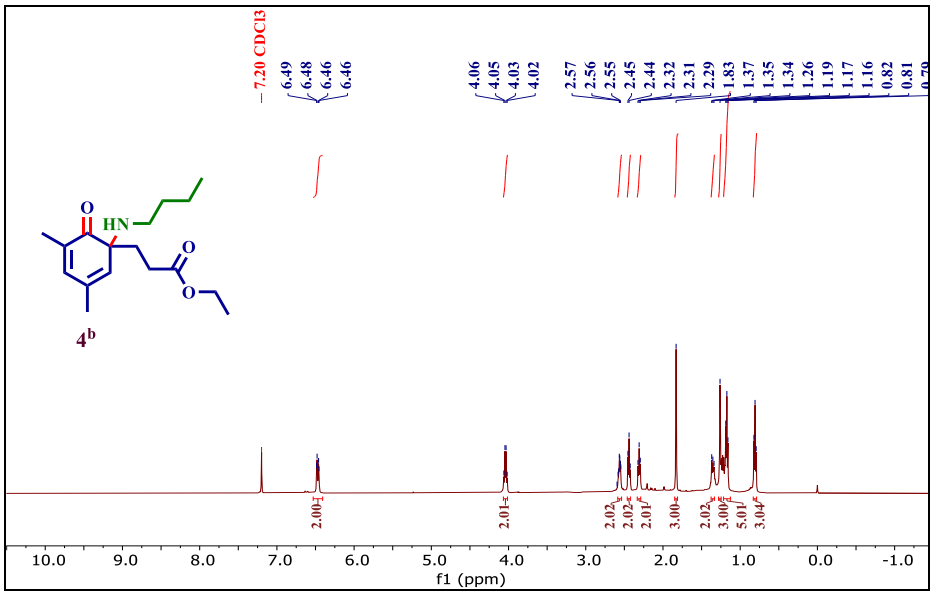


Fig. 17 ^{1}H and ^{13}C NMR of 4^{b}



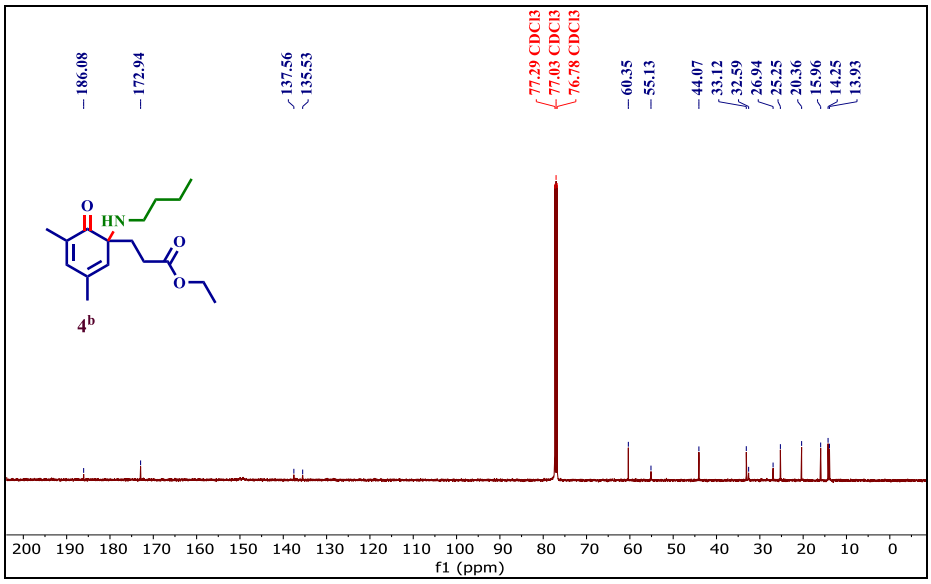
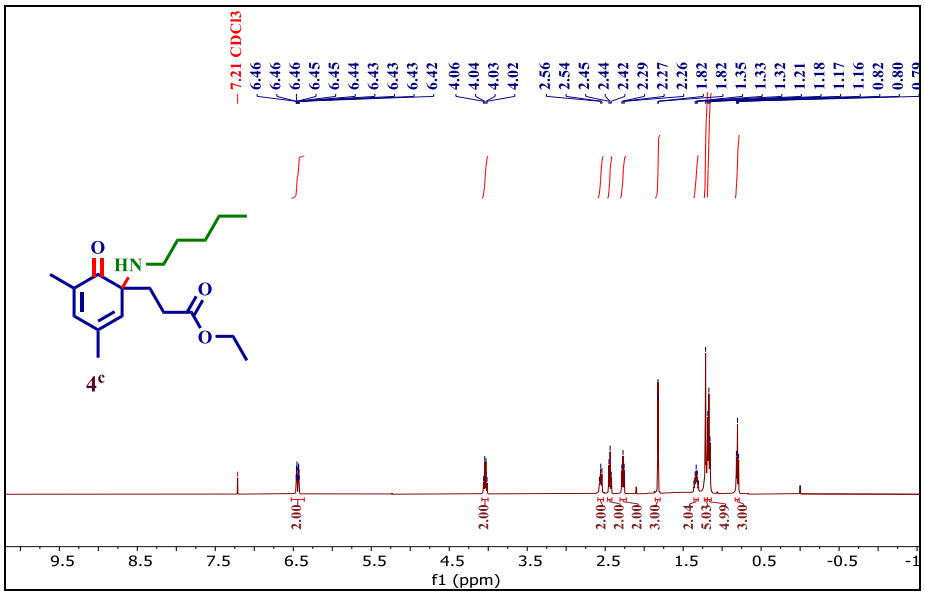


Fig.18 ^{1}H and ^{13}C NMR of 4^{c}



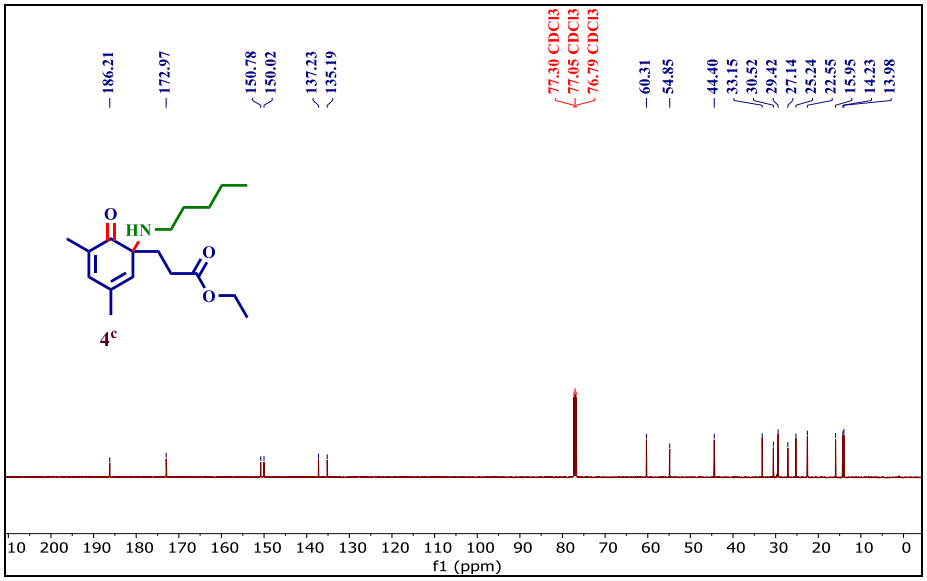
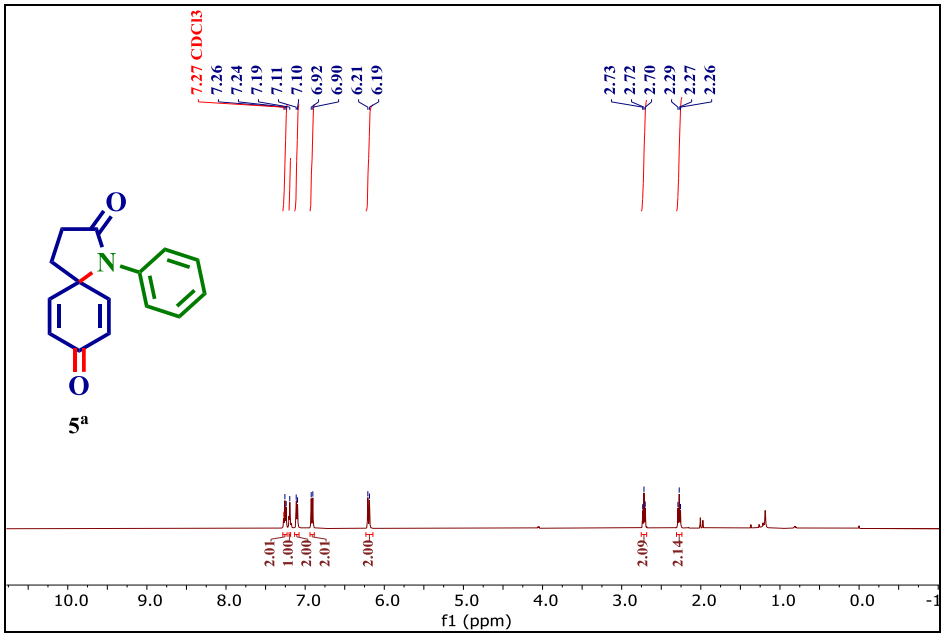


Fig.19 ^{1}H and ^{13}C NMR of 5[a]



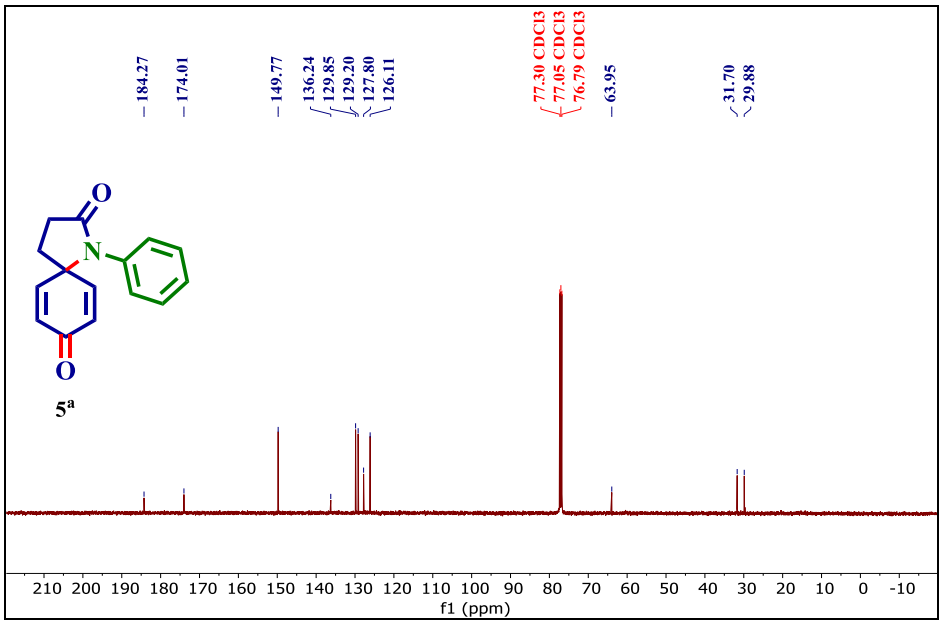
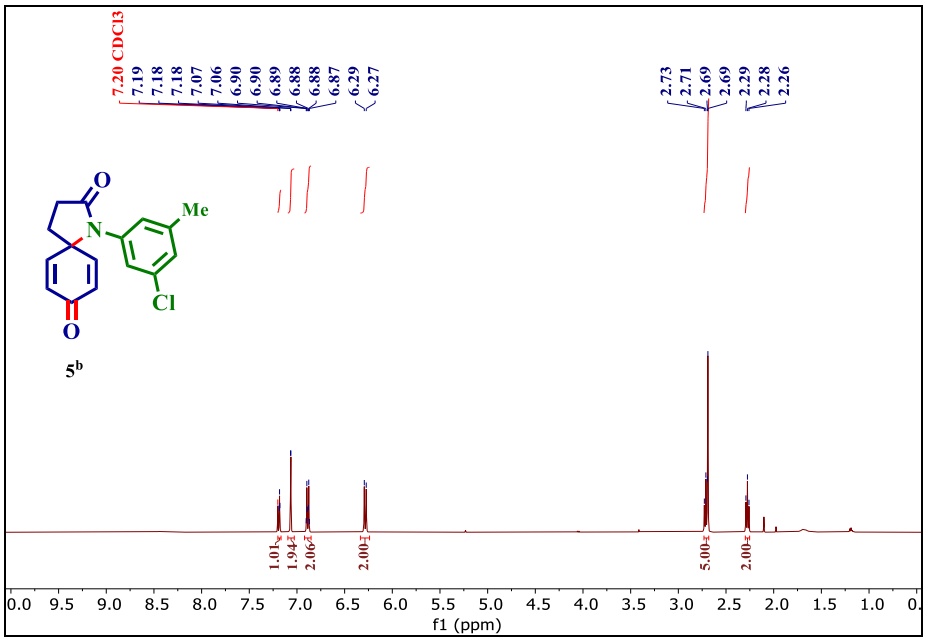


Fig.20 ^{1}H and ^{13}C NMR of 5^{b}



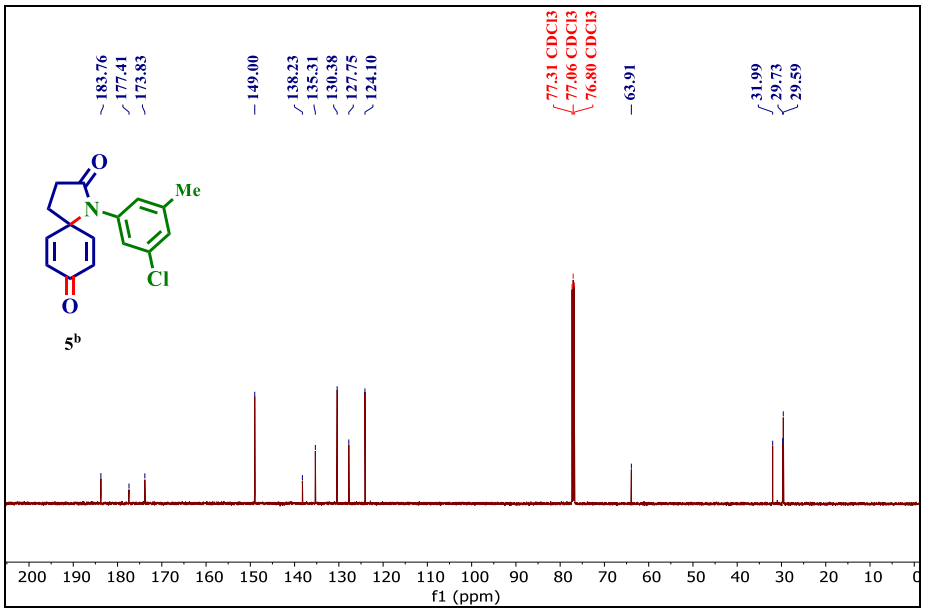
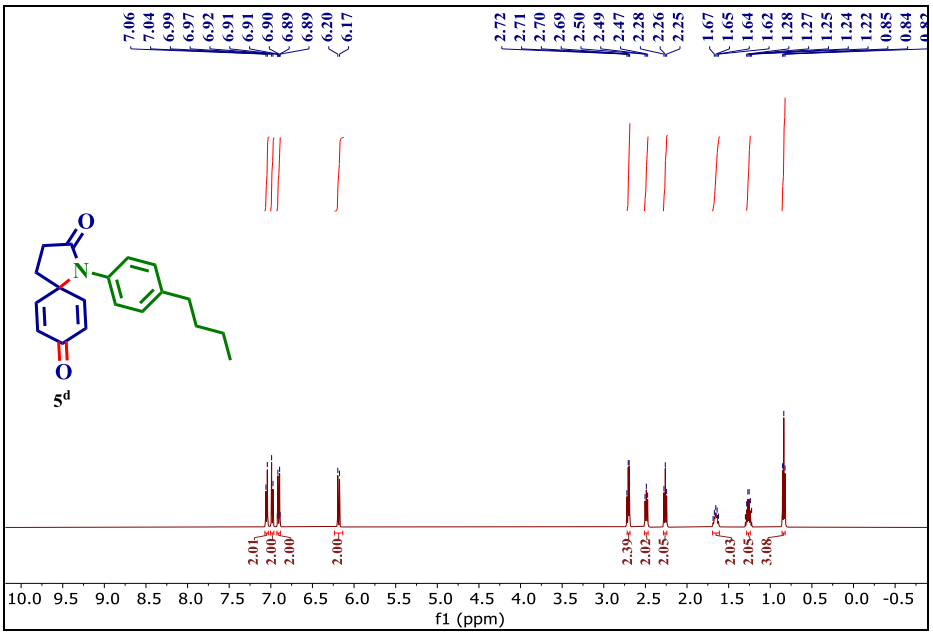


Fig-21 ^{1}H and ^{13}C NMR of 5^{c}



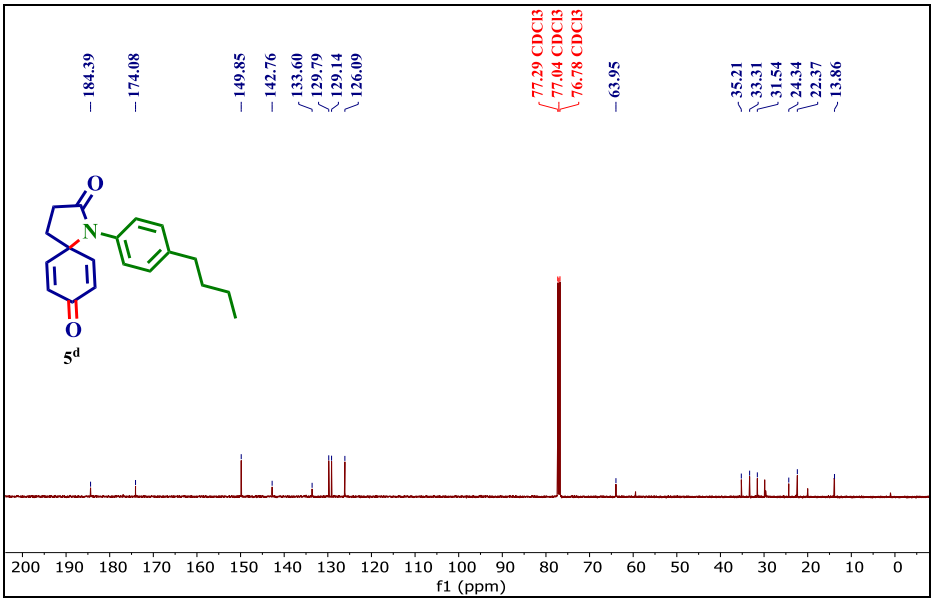
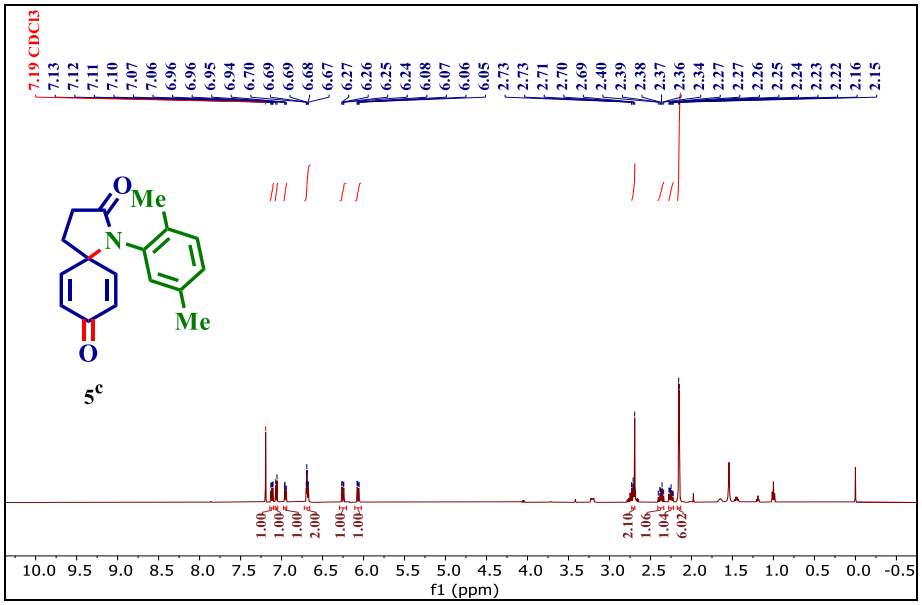
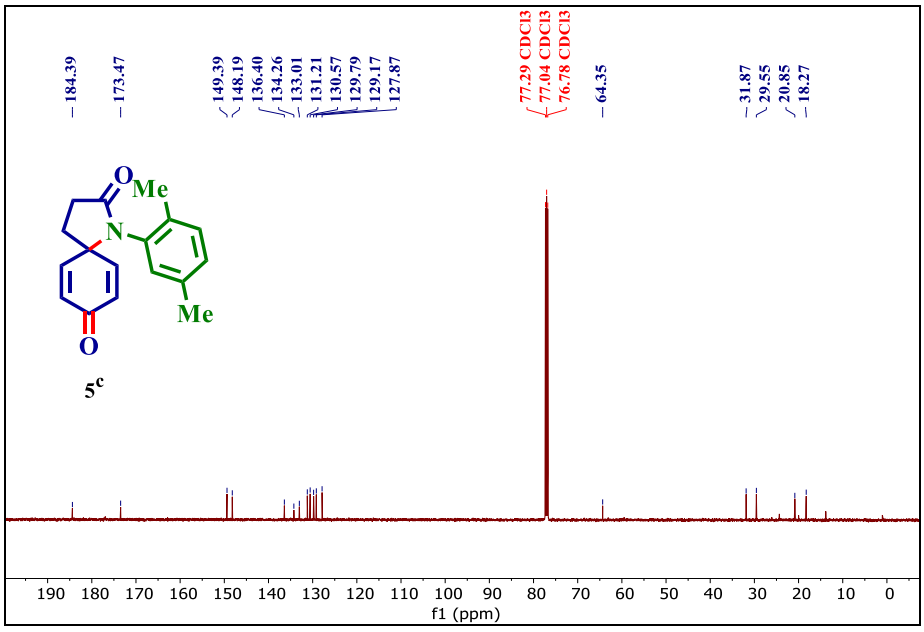


Fig.22 ^{1}H and ^{13}C NMR of 5[d]





CONCLUSION:

The transformation of esters to spiro amides under visible light conditions remains a challenge but a promising area of synthetic chemistry. While ester-to-amide conversions typically require harsher conditions, the use of visible light activation offers a milder, more sustainable alternative. So further we try to synthesise Spiro lactam from Amide as starting material using RFTA as photocatalyst and TBAI as Iodine source, as a result, Iodide forms Iodine radical by RFTA very low productive of the Desired Product was Synthesized.

Further, the successful synthesis of ortho-dearomatized spiro amides using a Tribromide source from esters under thermal conditions marks a significant advancement in synthetic methodology. The transformation leverages the unique reactivity of Tribromides, which, under thermal conditions, facilitate the oxidative dearomatization of phenolic esters, leading to the formation of spiro amides.

REFERENCE:

(1) Mak, C.-P.; Biichi, G.; Cohen, N.; Lopresti, R. J.; Saucy, G.; Chen, C.-P.; Swenton, J. S.; Stewart, R. F.; Miller, L. L.; Buchanan, G. L.; Raphael, R. A.; Taylor, R. *) Deslongchamps*; 1987; Vol. 52.

(2) Roy, B.; Avasare, V.; Sarkar, D. Tribromide Enabled Step-up Generation of Spirolactams from Esters Employing Oxidative Dearomatization of Arenols. *Chemical Communications* **2024**, *60* (69), 9206–9209. https://doi.org/10.1039/d4cc02527j.

(3) Sahoo, S. R.; Sarkar, D. Stereoselective Synthesis of Spiro-Azacycles Through Tri-Bromide Mediated Oxidative Dearomatization. *European J Org Chem* **2020**, *2020* (3), 397–401. https://doi.org/10.1002/ejoc.201901676.

(4) Roy, B.; Avasare, V.; Sarkar, D. Tribromide Enabled Step-up Generation of Spirolactams from Esters Employing Oxidative Dearomatization of Arenols. *Chemical Communications* **2024**, *60* (69), 9206–9209. https://doi.org/10.1039/d4cc02527j.

(5) Wu, L.; Sun, L.; Liu, W.; Cui, J.; Wang, Y.; Xie, L. Visible-Light-Induced Photocatalyst-Free Dearomative Amidation of Phenol Derivatives. *Tetrahedron Lett* **2023**, *128*. https://doi.org/10.1016/j.tetlet.2023.154637.

(6) Roy, B.; Avasare, V.; Sarkar, D. Tribromide Enabled Step-up Generation of Spirolactams from Esters Employing Oxidative Dearomatization of Arenols. *Chemical Communications* **2024**, *60* (69), 9206–9209. https://doi.org/10.1039/d4cc02527j.

(7) Sahoo, S. R.; Sarkar, D. Stereoselective Synthesis of Spiro-Azacycles Through Tri-Bromide Mediated Oxidative Dearomatization. *European J Org Chem* **2020**, *2020* (3), 397–401. https://doi.org/10.1002/ejoc.201901676.

(8) Oyamada, H.; Naito, T.; Miyamoto, S.; Akiyama, R.; Hagio, H.; Kobayashi, S. Development of Polysilane-Supported Palladium/Alumina Hybrid Catalysts and Their Application to Hydrogenation. *Org Biomol Chem* **2008**, *6* (1), 61–65. https://doi.org/10.1039/b715220e.

(9) Gooding, O. W.; Vo, L.; Bhattacharyya, S.; Labadie, J. W. Use of Statistical Design of Experiments in the Optimization of Amide Synthesis Utilizing Polystyrene-Supported N-Hydroxybenzotriazole Resin. *J Comb Chem* **2002**, *4* (6), 576–583. https://doi.org/10.1021/cc0200282.

(10) Bera, N.; Lenka, B. S.; König, B.; Sarkar, D. Riboflavin Photocatalyzed Dearomative Spiro-Etherification of Naphthols. *Journal of Organic Chemistry* **2023**, *88* (13), 7977–7987. https://doi.org/10.1021/acs.joc.2c03037.