Final Technical Report

On

"Synthetic Utility of Baylis-Hilman Substrates Towards Synthesis of Heterocycles"

MINOR RESEARCH PROJECT

FINANCIALLY ASSISTED BY

UGC-SERO, HYDERABAD

MRP No: F MRP-7064/16 (SERO/UGC)

(February 2018 – January 2020)

ज्ञान-विज्ञान विमुक्तये

Submitted by

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TELENGANA – 507 002

DECLARATION

I hereby declare that the Minor Research Project No: F MRP-7064/16 (SERO/UGC) entitled **"Synthetic Utility of Baylis-Hilman Substrates Towards Synthesis of Heterocycles"** is based on the original work carried out by me at the Department of Chemistry, SR&BGNR. Govt. Arts & Science College (A), Khammam. The extent and sources of information derived from the existing literature have been indicated throughout the report at appropriate places. I also affirm that this work is original and has not been submitted in part or full, for any other degree or diploma to any University or Institution.

Place: Khammam,

Date: 20-01-2020

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GOVERNMENT OF TELENGANA

EDUCATION DEPARTMENT

CERTIFICATE

I, K S S Ratna Prasad, Principal (FAC), SR & BGNR Government Arts and Science College (A), Khammam hereby certify that Mr. VADIGA SHANTHI KUMAR, Lecturer in Chemistry has carried out this minor research project work No: F MRP-7064/16 (SERO/UGC) entitled **"Synthetic Utility of Baylis-Hilman Substrates Towards Synthesis of Heterocycles"** in this institution during February 2018 - January 2020.

Place: KHAMMAM

Date: 20-01-2020 **PRINCIPAL**

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I pay my devoted thanks to the almighty for giving me strength and the favorable circumstances to make this accomplishment.

Finally I express my sincere thanks to one and all those who have contributed directly or indirectly for bringing out my investigation successfully.

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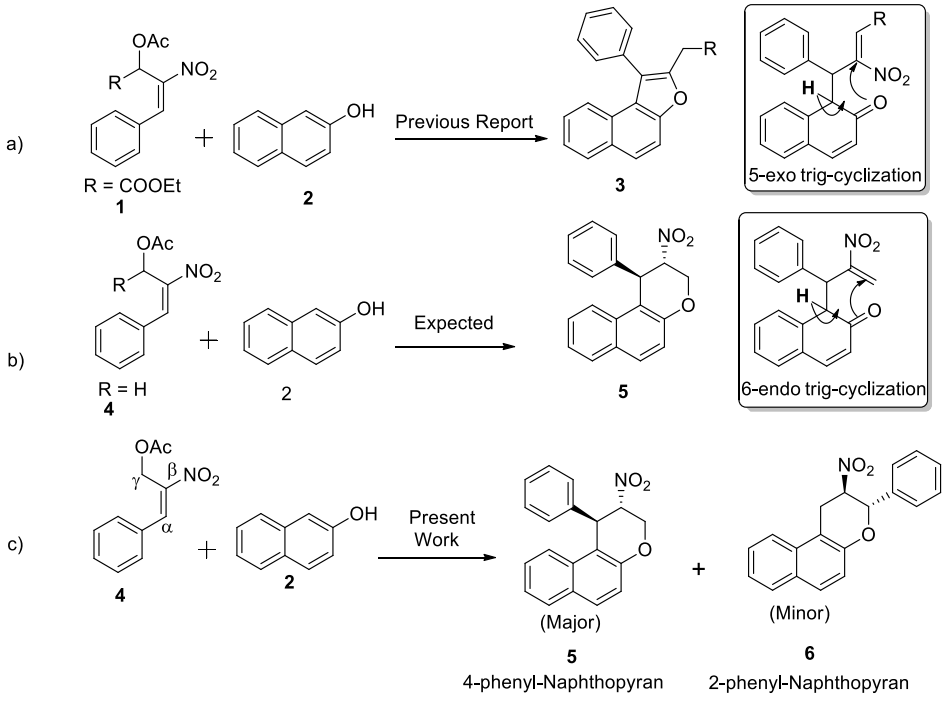
ABSTRACT

The reaction of β-naphthol with β-nitrostyrene derived MBH primary acetates in presence of Cs_2CO_3 as base resulted in the formation of 4-phenyl-naphthopyran as the major isomer. The reaction followed a Friedel-Crafts type alkylation with an initial α-attack on MBH acetate *via* S_N2' process followed by Oxa-Michael ring closure. Due to bis-electrophilic nature of MBH acetates, the minor product 2-phenyl naphthopyran was also obtained presumably due to S_N2 process with γ- attack on MBH acetates. The state of the art density functional theory (DFT) calculations have also been carried out to account for these competitive pathways towards the formation of major Vs minor product

Scheme-1:



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GENERAL REMARKS

- ^{1}H NMR and ^{13}C NMR spectra are recorded on Varian Gemini 200 or Varian Unity 400 or Varian Inova 500 or Bruker Avance 300 MHz Making a solution of samples in $CDCl_3$ solvent using Tetramethylsilane (TMS) as the internal standard unless otherwise mentioned, and are given in the δ scale. The standard abbreviations s, d, t, m, dd refer to singlet, doublet, triplet, multiplet and doublet of a doublet respectively.
- Infrared (IR) spectra are recorded on Perkin-Elmer Infrared–683 or 1310 with NaCl optics. Spectra were calibrated against the polystyrene absorption at $1610cm^{-1}$. Samples were scanned neat, KBr wafers or in chloroform as a thin film.
- Mass spectra recorded on CEC-21-110B, Finnegan Mat 1210 or MICROMASS-7070 spectrometers operating at 70eV using a direct inlet system. If necessary, FABMS is recorded.
- The optical rotations are measured on Jasco Dip 360 digital polarimeter.
- Melting points are determined on an Electro thermal melting point apparatus and are uncorrected.
- All reactions are monitored by thin layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60- F_{254}) with UV light, iodine as probing agents. Acme (India) silica gel (finer than 200 mesh) is used for flash chromatography.
- Column chromatography was performed by using silica gel 60-120 , 100-200 mesh
- The reactions wherever anhydrous conditions needed are carried out under the positive pressure of nitrogen atmosphere using dry and freshly distilled solvents.
- All solvents and reagents were purified by standard techniques. All evaporation of solvents was carried out under reduced pressure on Heidolph rotary evaporator below 45 °C.
- Yield reported are isolated yields of material judged homogeneous by TLC and NMR spectroscopy.
- The names of all compounds given in the experimental section were taken from Chem. ultra, version 11.0

ABBREVATIONS

MBH	:	Morita Baylis Hillman
$SN^{2'}$	:	Substitution Nucleophillic bi molecular prime reaction
SN^2	:	Substitution Nucleophillic bi molecular reaction
OAc	:	Acetate ion
NHC-catalyzed	:	N-Heterocyclic Carbene-Catalyzed
CCDC	:	Cambridge Crystallographic Data Centre code
DFT	:	Density Functional Theory
IRC	:	Intrinsic Reaction Coordinate
DABCO	:	1,4-Di Aza Bi cyclo [2.2.2]Octane
TEA	:	Tri Ethyl Amine
CH2Cl2	:	Di Chloro Methane (DCM)
CHCl3	:	Chloroform (Tri Chloro Methane (TCM))
NaK2PO4	:	Sodium Potassium Phosphate
CH3OH	:	Methanol (Methyl Alcohol)
CsCO3	:	Cesium Carbonate
THF	:	Tetra Hydro Furan
DMF	:	Di Methyl Formamide
CCl4	:	Carbon Tetra Chloride
1,2-DCE	:	1,2- Di Chloro Ethane
CDCl3	:	Carbon tri Chloride (Deuterated)
$CHCl_3$	:	Chloroform
CH_2Cl_2	:	Dichloromethane (DCM)
CH_3OH/MeOH	:	Methanol
DMSO	:	Dimethyl sulphoxide
Et_3N	:	Tri Ethyl Amine(TEA)

Eq : Equivalent(s)

AcOH : Acetic acid

4-Br- : Para-Bromo Substituent

2,4-Cl_2-: Ortho,Para-Di Chloro substituents

4-F- : Para-Fluoro-

4-CH3- : Para Methyl-

4-OBn- : Para Benzyloxy-

3-OCH3- : Meta Methoxy-

4-OCH3- : Para Methoxy-

2,4-(OCH3)2- : Ortho,Para-Di Methoxy-

FTIR : Fourier Transform Infra Red

HRMS : High Resolution Mass Spectroscopy

MHz : Mega hertz

m/z : Mass to charge ratio (in mass spectroscopy)

NCE : New Chemical Entities

NMR : Nuclear Magnetic Resonance spectroscopy

^{1}HNMR : Proton Nuclear Magnetic Resonance spectroscopy

^{13}CNMR : ^{13}Carbon Nuclear Magnetic Resonance spectroscopy

HPLC : High-Performance Liquid Chromatography

HRMS : High Resolution Mass Spectrometry

LCMS : Liquid Chromatography coupled to Mass Spectrometry

ESI : Electronic Supplementary Information

PI : Principal Investigator

TS : Transition State

R*f* : Retention factor (in chromatography)

r.t : Room temperature

hr : Hour

^{o}C : Degree Centigrade

K.Cal/Mol	:	Kilo Calaries/ Mole
TMS	:	Tri Methyl Silane
THF	:	Tetra hydro furan
TLC	:	Thin layer chromatography
µg	:	Microgram
µM	:	Micro molar
nM	:	Nano molar

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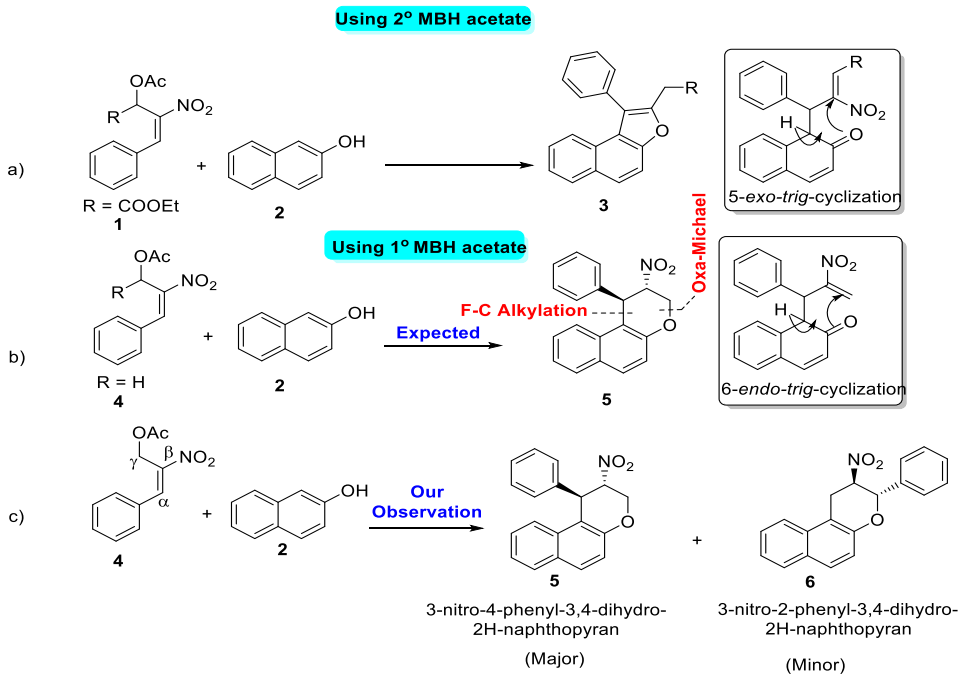
Chapter 1

Introduction

1. Introduction

The efficient construction of multiple bond formation with the control of stereocenters in one-pot operation is a fundamental goal in cascade reaction. The Morita-Baylis-Hillman (MBH) reaction[1] is one of the atom economy protocols for constructing a new C-C bond between an activated olefin and electrophiles in the presence of a tertiary amine/phosphine. MBH adducts are very interesting synthetic targets[2]due to their potential applications as valuable synthons in allylic alkylation,[3]dienamine catalysis[4]as well as construction of various bicyclic skeletons,[5] pyranocoumarins,[6] pyronaphthoquinones[7] and tetrahydro-pyranoquinolinones.[8]Presence of different functional groups in MBH adducts are useful in various regio- and stereoselective transformations through appropriate tuning. The MBH acetate **4** derived from nitrostyrene have been widely employed as starting materials in construction of fused heterocycles[9] and asymmetric reactions.[10]Variuos MBH adducts were used as synthons in organocatalysis and heterocyclic synthesis.[11] Recently, Enders group reported a NHC-catalyzed Michael/Michael/esterification domino reaction of cyclopentane using MBH acetate **4**.[12] Very recently Jin Yu Liu *et al*, established the cascade reactions of 4-hydroxy indole and (*E*)-2-nitro allylic acetates with different electronic and steric properties.[13] Previously, kinetic resolution[14a,b]and synthesis of naphthofuran derivatives (Eqn. a, Scheme-1).[14c-e] were studied extensively using MBH acetates. With our ongoing interest in theexploration of MBH adducts,[15] we were interested in cascade reaction of β-naphthol and MBH acetate **4**. We envisioned that reaction would exclusively yield substituted naphthopyran **5** via *6-endo trig* cyclization (Eqn. b, **Scheme-1).**



Scheme 1. Annulation reactions of nitrostyrene derived MBH acetates

Interestingly, to our observation apart from expected product **5***via* S_N2' we also obtained **6** as a minor product through S_N2 reaction of nitroallylic acetate **4** with naphthol **2** using Cs_2CO_3 (Eqn. c, Scheme-1). The structures of both the products were further confirmed by X-ray crystallography (Fig.1).

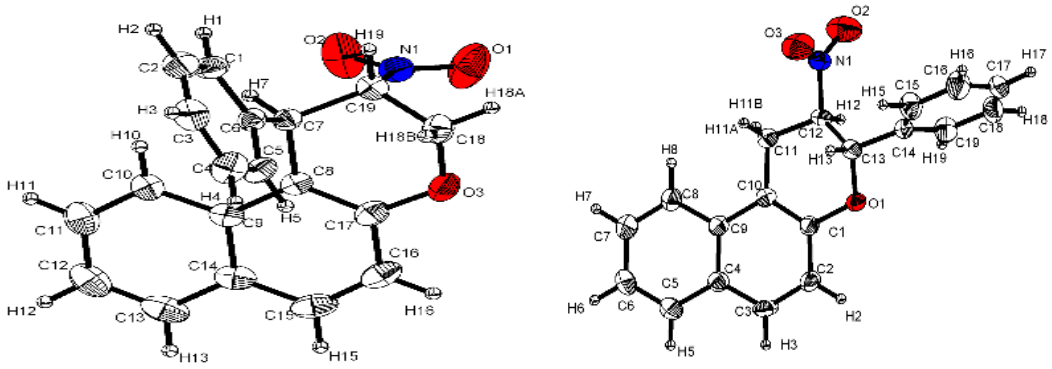


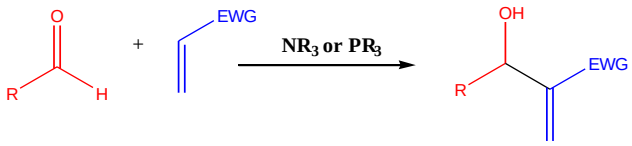
Fig.1. Crystal structure of **5a** (CCDC1860474) and Crystal structure of **6a** (CCDC1863074)

Chapter 2

Origin of the Research Problem

2. Origin of the Research Problem

The **Baylis–Hillman reaction** is a carbon-carbon bond forming reaction between the α-position of an activated alkene and an aldehyde, or generally a carbon electrophile. Employing a nucleophilic catalyst, such as tertiary amine and phosphine, this reaction provides a densely functionalized product (e.g. functionalized allyl alcohol in the case of aldehyde as the electrophile) This reaction is also known as the **Morita–Baylis–Hillman reaction** or **MBH reaction** (Scheme 1) **.**



Scheme 1

MBH reaction has several advantages as a useful synthetic method: 1) It is an atom-economic coupling of easily prepared starting materials. 2) Reaction of a pro-chiral electrophile generates a chiral center, therefore an asymmetric synthesis is possible. 3) Reaction products usually contain multiple functionalities in a proximity so that a variety of further transformations are possible. 4) It can employ a nucleophilic organo-catalytic system without the use of heavy metal under mild conditions. Because the two components of MBH reaction are a general activated alkene and an electrophile, an enormous number of combinations of reaction partners can be generated. Especially, aza-Baylis–Hillman reaction is an important variant of MBH reaction using imines as electrophiles. Although in most cases aldehydes, ketones, or imines are employed as electrophiles, a few reports on the use of allyl halides, alkyl halides, and epoxides have been documented.

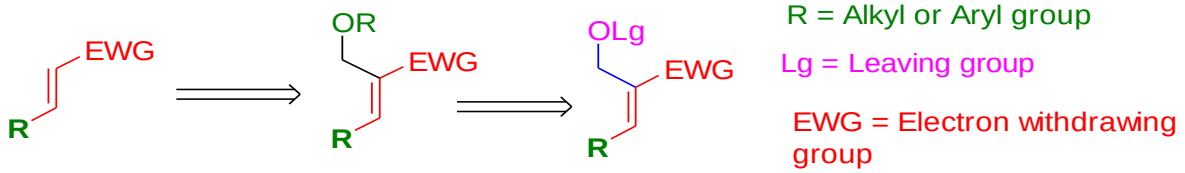
Chapter 3

Review and Development on the Topic

3. Review and Development on the topic

The Baylis–Hillman adducts and their derivatives have been extensively utilized for the generation of heterocycles and other cyclic frameworks.

In light of this, the PI is keen to pursue his research towards synthesis of naphthopyrans and 1,3-oxazines using Baylis-Hillman (B-H) adducts. These Baylis-Hillman (B-H) adducts can be readily accessible by reaction of available bench top chemicals and can be easily prepared by standard protocols. The substrates being prochiral with varied functionality can be synthetically exploited under the appropriate catalytic systems (Scheme 2).



Scheme 2

Chapter 4

Objectives

4. Objectives

The main objective of the proposed program is to utilize Baylis-Hillman adducts (acetates) in various organic transformations. The above main objective is associated with the following sub objectives.

1. To develop cascade reactions for converting simple starting precursors to value added products such as biologically synthetic targets.
2. Avoid use of heavy metals for greener ecosystem.
3. Mild reaction conditions
4. Synthesize a new set of Baylis-Hilman substrates and study their reactivity.
5. To carry out various multicomponent reactions.
6. Synthesis of heterocyclic compounds.
7. To investigate the biological activity as a future plan.


Chapter 5

Experimental Work

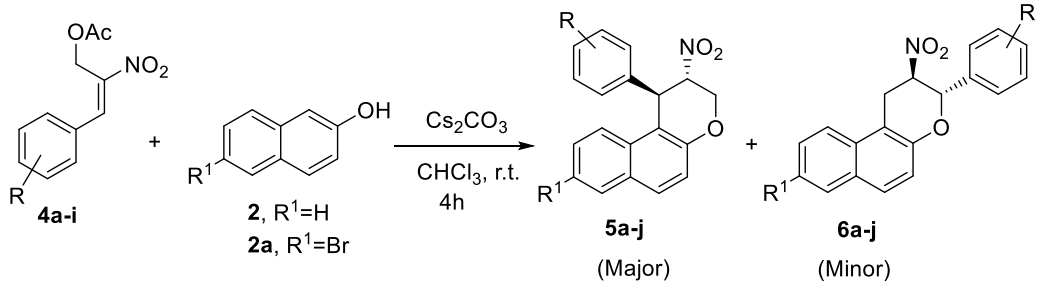
5. Experimental Work

5.1. Materials and methods

All reactions were carried out with dry, freshly distilled solvents in anhydrous conditions. THF was distilled from sodium, while dichloromethane was distilled from CaH_2 immediately prior to use. Thin-layer chromatography (TLC) was performed on silica gel plates (60F-254) using UV-light (254 and 365 nm). Flash chromatography was performed on silica gel (230–400 mesh). NMR (400 MHz for ^{1}H NMR, and ^{13}C NMR) spectra were recorded in $CDCl_3$ with TMS as the internal standard. Chemical shifts are reported in ppm and coupling constants are given in Hz. Data for ^{1}H NMR are recorded as follows: chemical shift (ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quartert; m, multiplet, dd, doublet of doublet), coupling constant (Hz), integration. Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm). High resolution mass spectral (HRMS) analyses were measured using ESI techniques. A variety of (E)-2-nitro-3-phenylallyl acetate were prepared according the reported procedure[1,2]

5.2. Understanding the Mechanism of S_N2' *vs* S_N2 in Cascade Reaction of β-Naphthol and Nitrostyrene Derived MBH Acetates :

General Procedure for the synthesis of 3-nitro-4-phenyl-3,4-dihydro-2H-naphthopyran (5) and 3-nitro-2-phenyl-3,4-dihydro-2H-naphthopyran(6):



To a solution of β- naphthol (1.08 mmol) and cesium carbonate (1.35 mmol) in chloroform (5 mL) MBH acetate (0.90 mmol) at room temperature. The reaction mixture was stirred at room temperature for the given time (i.e. Table 2). The reaction was monitored by using TLC till the completion of starting materials. After the completion of reaction, organic

layer was extracted with dichloromethane, washed with brine solution and dried over Na_2SO_4 and concentrated under reduced pressure. Crude was subjected to flash column chromatography on silica gel by eluting ethylacetate in hexane (0-1%) to afford the desired products.

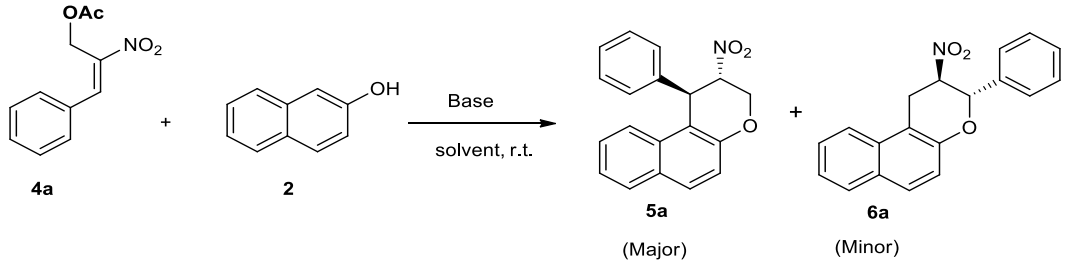
Gram scale preparation of 3-nitro-4-phenyl-3,4-dihydro-2H-naphthopyran (5a) and 3-nitro-2-phenyl-3,4-dihydro-2H-naphthopyran(6a):

To a solution of β- naphthol (0.86 g, 6 mmol) and cesium carbonate (2.44 g, 7.5 mmol) in chloroform (15 mL) MBH acetate (1.11 g, 5 mmol) at room temperature. The reaction mixture was stirred at room temperature for the given time (i.e. Table 2). The reaction was monitored by using TLC till the completion of starting materials. After the completion of reaction, organic layer was extracted with dichloromethane, washed with brine solution and dried over Na_2SO_4 and concentrated under reduced pressure. Crude was subjected to flash column chromatography on silica gel by eluting ethylacetate in hexane (0-1%) to afford the desired products.

5.2.1. Results and discussion:

Intrigued by this observation, we started exploring the optimized condition towards formation of **5** as exclusive product using various bases (Table 1). The initial reactioncarried out using DABCO in DCM gave regioisomers **5a** and **6a** in a ratio of 2:1 with 58 and 29% yield (entry 1, Table 1). Use of triethylamine didn't alter the regioselectivity but decrease in yield for formation of product **5a** and **6a**(entry 2 & 3, Table 1).A shift to inorganic bases such as $NaKPO_4$ retained the yield and regioselectivity (entry 4, Table 1). Changeof base i.e., Cs_2CO_3 in THF retained the overall yield with the drop in regioselectivity (entry 5, Table 1). Change of solvent to methanol also couldn't increase the yield and regioselectivity (entry 6, Table 1). Use of acetonitrile as solvent improved the regioselectivity for the formation of product **5a** and **6a** in 3:1 ratio (entry 7, Table 1). Use of polar aprotic solvent also couldn't lead to improving the regioselectivity (entry 8, Table 1). Among chlorinated solvents, chloroform was the ultimate choice leading to the completion of reaction within 4 hours towards formation of **5a** and **6a** in 65 and 23% yield (entries 9-12, Table 1). Several attempts to further improvise the regioselectivity or exclusive formation of the single product failed. A background reaction was carried out in the absence of base, resulting in <5% of **5a** even after 12 hours.

Table 1. Optimization of reaction conditions[a]



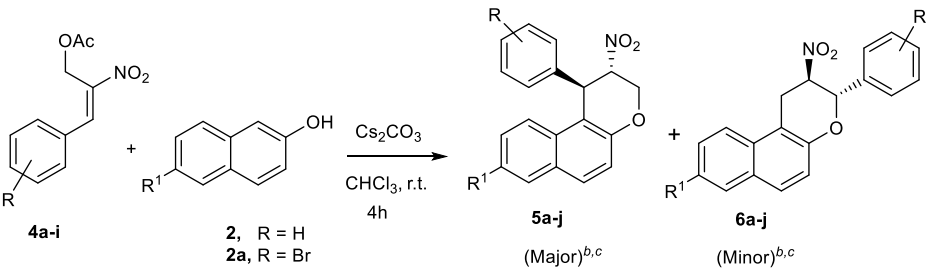
Entry	Base	Solvent	Time (h)	(5a:6a)[b]	Yield (5a)[c]	Yield (6a)[c]
1	DABCO	CH_2Cl_2	4	2:1	58	29
2	TEA	$CHCl_3$	4	2:1	52	22
3	TEA	CH_2Cl_2	4	2:1	52	21
4	NaK_2PO_4	CH_3OH	6	2:1	58	29
5	Cs_2CO_3	THF	24	1:1	45	44
6	Cs_2CO_3	CH_3OH	24	1:1	44	44
7	Cs_2CO_3	CH_3CN	6	3:1	65	22
8	Cs_2CO_3	DMF	6	1:1	43	43
9	Cs_2CO_3	CH_2Cl_2	4	2:1	58	29
10	Cs_2CO_3	CCl_4	8	3:1	65	22
11	Cs_2CO_3	1,2-DCE	6	2:1	59	30
12	Cs_2CO_3	$CHCl_3$	4	4:1	65	23
13	---	$CHCl_3$	12	ND	<5	trace

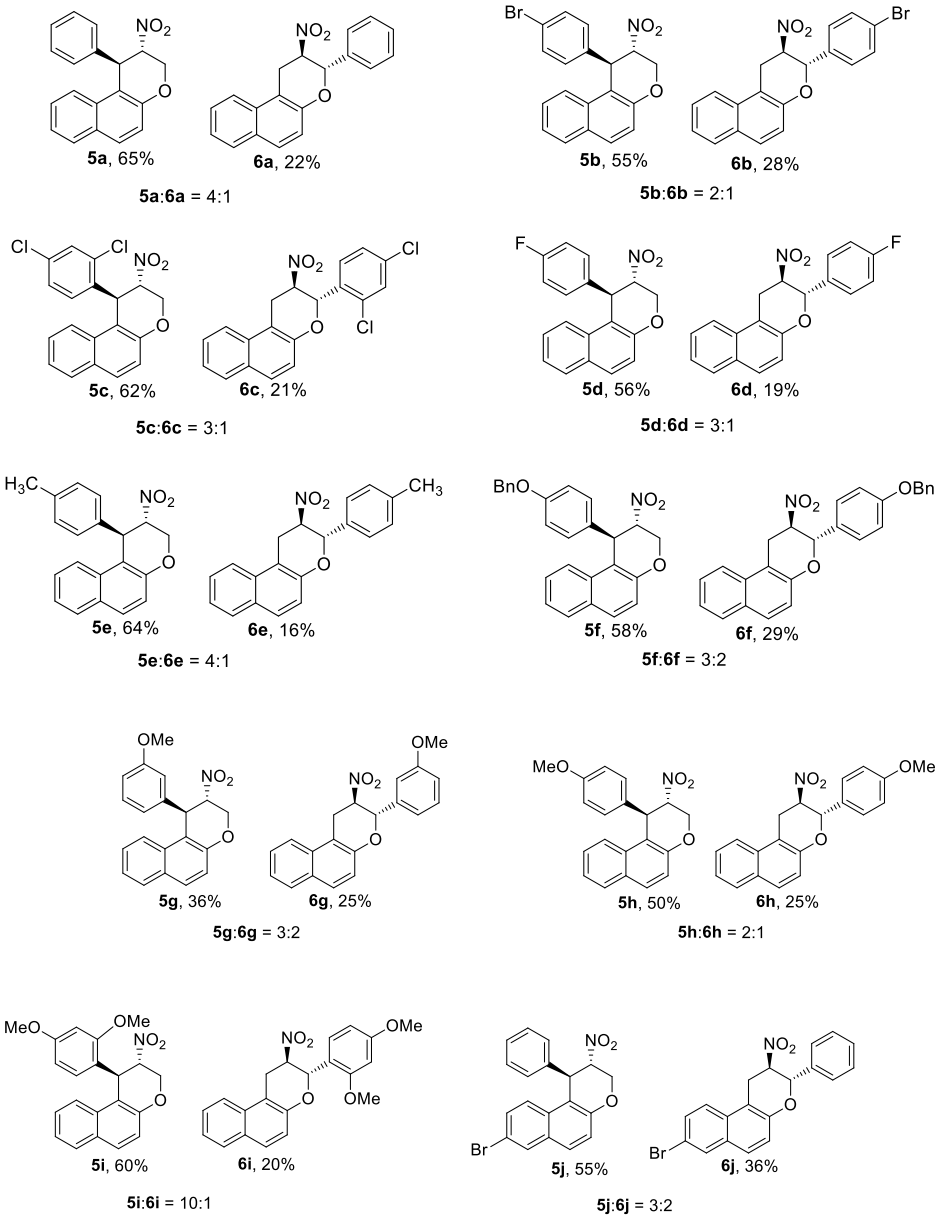
[a] Unless otherwise noted, reactions were carried out with (0.1 mmol) of 4a with (0.12 mmol) of 2 using (0.15 mmol) of a base in 4 mL CHCl3.
[b] Determined by HPLC &1H-NMR analysis of the crude products.
[c] Isolated yield.

Using the current optimized reaction conditions, we carried out the generalization of the present protocol using substituted MBH acetates **4a-i** with β-naphthol **2**&**2a**. The reaction of 4-Bromo substituted acetate **4b** resulted in product **5b** and **6b** in 2:1 in 55 and 28% yield (entry 2, Table 2). Reaction of 2,4-dichloro substituted acetate **4c**

gave corresponding **5c** and **6c** with regioselectivity of 3:1 in 62 and 21% yield (entry 3, Table 2). *p*-Fluoro substituted MBH acetate **4d** gave products **5d** and **6d** in 56 and 19% yield retaining the same regioselectivity (entry 4, Table 2). Electron donating substituents at the *para* position decreased the regioselectivity in the order of Me>OBn>OMe towards the formation of products **5e**/**6e**, **5f**/**6f**, **5g**/**6g** and **5h**/**6h** (entries 5-8, Table 2). Interestingly, the presence of 2,4-$(OMe)_2$ drastically increased the regioselectivity to 10:1 towards formation of products **5i**/**6i** (entry 9, Table 2). Finally, 6-Bromo substituted naphthol on reaction with **4a** gave 55 and 36% yield for formation of **5j** and **6j** (entry 10, Table 2).

Table 2. Substrate Scope towards Cascade Reaction[a]





[a] Unless otherwise noted, reactions were carried out with (0.1 mmol) of **4** with (0.12 mmol) of **2** using (0.15 mmol) of a base in 4 mL $CHCl_3$.

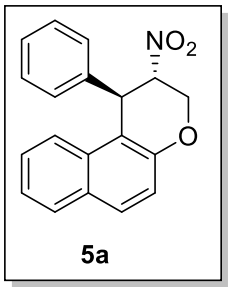
[b] Determined by ^{1}H-NMR analysis of the crude products.

[c] Isolated yield

In order to get a detailed understanding of possible competitive pathways i.e. S_N2' vs S_N2,[16] we have undertaken a comprehensive computational study[17] to analyse the formation of products **5a** and **6a.**

5.2.2. Spectral data:

3-nitro-4-phenyl-3,4-dihydro-2H-naphthopyran (5a)



5a

White solid; Yield: 65% (18.0 mg); mp 93-95 ^{o}C

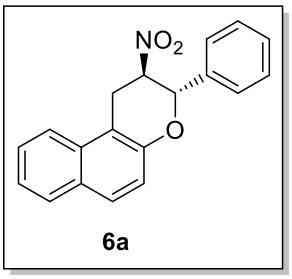
IR (neat, cm^{-1}) 2921 (w), 2856 (m), 1625 (s), 1542 (s), 1468 (s), 1225 (s), 890 (m), 815 (s), 746 (s)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77-7.72 (m, 2H), 7.48- 7.45 (m, 1H), 7.33-7.25 (m, 5H), 7.21 (d, *J* = 7.2 Hz, 2H), 7.14 (d, *J* = 8.8 Hz, 1H), 5.49 (s, 1H), 4.90-4.87 (m, 2H), 4.35 (d, *J* = 11.6 Hz, 1H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 151.4, 141.4, 132.1, 129.9, 129.8, 129.3, 128.6, 128.5, 127.7, 126.8, 123.8, 122.8, 118.3, 110.5, 83.7, 61.4, 40.2.
Anal. Calcd. for $C_{19}H_{15}NO_3$:C, 74.74; H, 4.95; N, 4.59; Found: C, 75.12; H, 5.42; N, 4.34.

HRMS calcd. $C_{19}H_{17}NO_4$, 323.1158; found 323.1272 [M + H_2O]

3-nitro-2-phenyl-3,4-dihydro-2H-naphthopyran(6a):



6a

White solid; Yield: 22% (6.0 mg); mp 97-99 ^{o}C

IR (neat, cm^{-1}) 2936 (w), 2864 (w), 1625 (m), 1542 (s), 1468 (s), 1360 (m), 1225 (m), 741 (s), 697 (s)

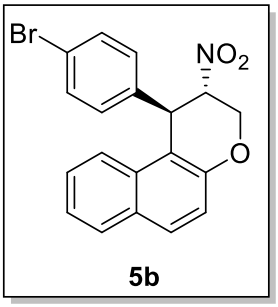
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.0 Hz, 1H), 7.73 (t, *J* = 9.2 Hz, 2H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.44-7.39 (m, 6H), 7.16 (d, *J* = 8.8 Hz, 1H), 5.47 (d, *J*

= 8.4 Hz, 1H), 5.22-5.16 (m, 1H), 3.87 (dd, *J* = 16.4, 8.8 Hz, 1H), 3.65 (dd, *J* = 16.4, 6.0 Hz, 1H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 151.0, 135.4, 132.1, 129.5, 129.4, 129.0, 128.9, 128.6, 127.1, 126.8, 124.2, 121.6, 118.2, 109.8, 84.3, 77.8, 26.9;

Anal. Calcd. for $C_{19}H_{15}NO_3$:C, 74.74; H, 4.95; N, 4.59; Found: C, 74.68; H, 4.91; N, 4.65.

3-nitro-4-(4-bromophenyl)-3,4-dihydro-2H-naphthopyran (5b):



5b

White solid; Yield: 55% (20.9 mg),; mp 97-98 ^{o}C

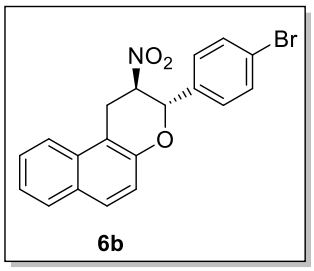
IR (neat, cm^{-1}) 2938 (m), 2921 (w), 1600 (m), 1542 (s), 1225 (m), 1172 (m), 741 (s), 697 (s)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79-7.74 (m, 2H), 7.47-7.38 (m, 3H), 7.35-7.30(m, 2H), 7.17-7.08 (m, 3H), 5.45 (s, 1H), 4.93-4.88 (m, 1H), 4.83-4.82 (m, 1H), 4.32-4.29 (m, 1H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 140.4, 132.5, 131.8, 130.8, 130.1, 130.0, 129.9, 128.7, 127.0, 124.0, 122.6, 118.3, 83.4, 61.3, 39.7

HRMS calcd. $C_{19}H_{15}BrNO_3$, 384.0235; found 384.0058 [M + H]

3-nitro-2-(4-bromophenyl)-3,4-dihydro-2H-naphthopyran(6b):



6b

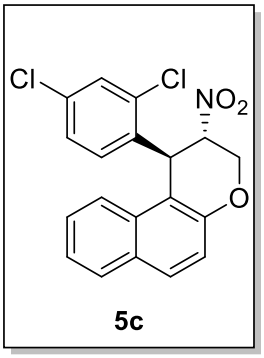
White solid; Yield: 28% (10.6 mg); mp 101-103 ^{o}C

IR (neat, cm^{-1}) 2956 (w), 2921 (w), 1600 (m), 1546 (s), 1228 (m), 741 (s), 697 (s)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.0 Hz, 1H), 7.76-7.72 (m, 2H), 7.58-7.54 (m, 3H), 7.46-7.42 (m, 1H), 7.32 (d, *J* = 8.8 Hz, 2H), 7.15 (d, *J* = 9.2 Hz, 1H), 5.42 (d, *J* = 8.4 Hz, 1H), 5.17-5.11 (m, 1H), 3.87 (dd, *J* = 16.4, 9.2 Hz, 1H), 3.68 (dd, *J* = 16.4, 6 Hz, 1H)

^{13}C NMR (100 MHz, $CDCl_3$,) δ 150.8, 134.5, 132.1, 130.0, 129.5, 129.1, 128.7, 128.6, 127.2, 124.4, 123.7, 121.6, 118.1, 109.8, 84.3, 77.3, 27.1.

3-nitro-4-(2,4-dichlorophenyl)-3,4-dihydro-2H-naphthopyran (5c):



5c

White solid; Yield: 62% (16 mg); mp 85-86 ^{o}C;

IR (neat, cm-1) 2936 (w),1141 (m), 1159 (s), 1225 (s), 1001(s), 1048 (s), 1095 (s), 868 (s), 750 (s)

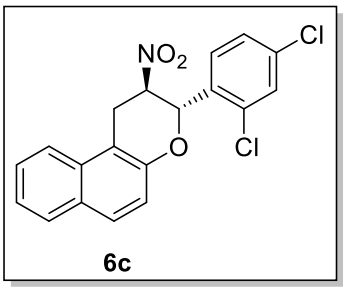
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79-7.74 (m, 2H), 7.55 (d, *J*= 2.4 Hz, 1H), 7.36-7.32 (m, 2H),S7.27 (d, *J* = 2.4 Hz, 1H), 7.13 (d, *J* = 8.8 Hz, 1H), 7.05 (dd, *J* = 8.4 Hz, 2.0 Hz 1H), 6.74(d, *J* = 8.4Hz, 1H), 5.82 (s, 1H), 4.96(dt, *J* = 12.8 Hz, 2.4 Hz, 1H), 4.87-4.85(m, 1H), 4.24(dd, *J* = 12.8, 1.6 Hz, 1H)

^{13}C NMR (100 MHz, $CDCl_3$,) δ 151.8, 136.7, 134.6, 133.7, 132.0, 131.6, 130.2, 130.0, 129.9, 128.8, 127.9, 127.3, 124.1, 122.2, 118.3, 109.5, 80.5, 61.6, 36.8

Anal. Calcd. for $C_{19}H_{13}C_{l2}NO_3$: C, 60.98.; H, 3.50; N, 3.74 5; O, 11.222 Found: C, 60.85; H, 3.45; N, 3.68.

HRMS calcd. $C_{19}H_{14}Cl_2NO_3$, 374.0351; found 374.0179 [M + H]

3-nitro-2-(2,4-dichlorophenyl)-3,4-dihydro-2H-naphthopyran(6c):



6c

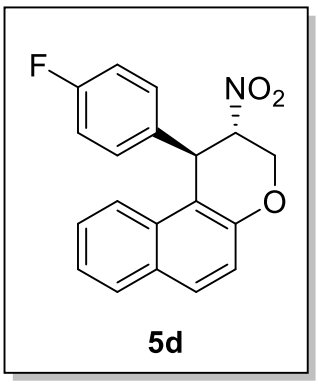
Pale red solid; Yield: 21% (5.5 mg);mp 83-85 ^{o}C

IR (neat, cm^{-1}) 2896 (w), 1625 (m), 1547 (s), 1375 (m), 1240 (m), 868 (m), 750 (s)

^{1}H NMR (400 MHz, $CDCl_3$) 7.83 (d, *J* =8 Hz, 1H), 7.76 (t, *J* = 10.0 Hz, 2H), 7.56 (td, *J* = 8.2, 1.2 Hz, 1H), 7.47-7.42 (m, 2H), 7.34 (d, *J* = 8.4 Hz, 1H) 7.23 (d, *J* = 2.0 Hz, 1H), 7.15 (d, *J* = 8.8 Hz, 1H), 6.11(d, *J* = 6 Hz, 1H), 5.35 (q, *J* = 6.0 Hz, 1H), 3.98 (dd, *J* = 16.8, 6.8 Hz, 1H), 3.44 (dd, *J* = 17.2, 6.0 Hz, 1H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 152.2, 135.8, 133.5, 132.2, 130.1, 129.5, 129.3, 128.9, 128.7, 127.9, 127.2, 124.3, 121.5, 117.9, 109.2, 80.8, 73.7, 29.7
Anal. Calcd. for $C_{19}H_{13}C_{l2}NO_3$: C, 60.98.; H, 3.50; N, 3.74 5; O, 11.222 Found: C, 60.86; H, 3.56; N, 3.71.

3-nitro-4-(4-fluorophenyl)-3,4-dihydro-2H-naphthopyran (5d)



5d

White solid; Yield: 56% (15.1 mg); mp 63-65 ^{o}C

IR (neat, cm^{-1}) 2921 (s), 1623 (m),1545 (s), 1508 (s), 1320 (w), 1223 (s), 1158 (m), 1075 (s),810 (s), 833 (s), 744 (s), 767 (s)

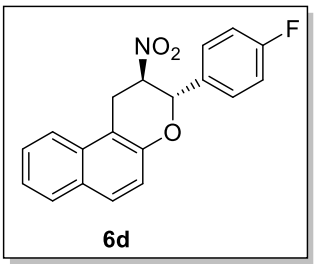
^{1}H NMR (400 MHz, CDCl3) δ 7.77-7.73 (m, 2H), 7.44-7.42 (m, 1H), 7.33-7.31 (m, 2H), 7.20-7.12 (m, 3H), 7.03-6.99 (m, 2H), 5.48 (s, 1H) 4.92-4.89 (m, 1H),4.84-4.83 (m, 1H), 4.34-4.31 (m, 1H)

^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.8,151.4, 137.1, 131.9, 130.1, 130.0, 129.9, 129.9, 128.7, 126.9, 123.9, 122.6, 118.3, 116.4, 116.2, 110.3, 83.6, 61.3, 39.5.

Anal. Calcd. for $C_{19}H_{14}FNO_3$: C, 70.58; H, 4.36; N, 4.33; Found: C, 70.45; H, 4.40; N, 4.38.

HRMS calcd. $C_{19}H_{16}FNO_3$, 325.1114; found 325.1842 [M + 2H]

3-nitro-2-(4-fluorophenyl)-3,4-dihydro-2H-naphthopyran(6d):



Pale pink solid; Yield: 19% (5.1 mg); mp 77-78 ^{o}C

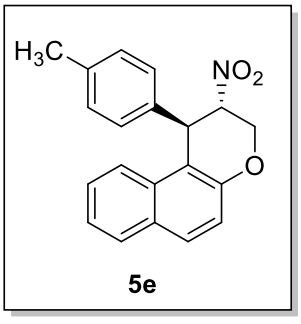
IR (neat, cm^{-1}) 2921 (s), 2853 (m), 1623 (m), 1544 (s), 1320 (m),1220 (s), 1143 (m), 1076 (s), 833 (s), 745 (s)

^{1}H NMR (400 MHz, $CDCl_3$), 7.83 (d, *J* = 8 Hz, 1H), 7.76-7.71 (m, 2H), 7.587.54(m,1H),7.467.42 (m, 3H), 7.16-7.08(m, 3H), 5.41 (d, *J* = 8.8 Hz, 1H), 5.18-5.12 (m, 1H), 3.88 (dd, *J* = 16 Hz, 9.6 Hz, 1H), 3.71 (dd, *J* = 16 Hz, 6.0 Hz, 1H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0, 151.0, 132.1, 131.2, 129.5, 129.1, 129.0, 128.9, 128.7, 127,2, 124.3, 121.6, 118.1, 116.1, 115.9, 109.9, 106.9, 84.5, 77.3, 27.4

Anal. Calcd. for $C_{19}H_{14}FNO_3$: C, 70.58; H, 4.36; N, 4.33; Found: C, 70.48; H, 4.31; N, 4.38.

3-nitro-4-(*p*-tolyl)-3,4-dihydro-2H-naphthopyran(5e):



White solid; Yield: 64% (20.4 mg); mp 58-59 ^{o}C

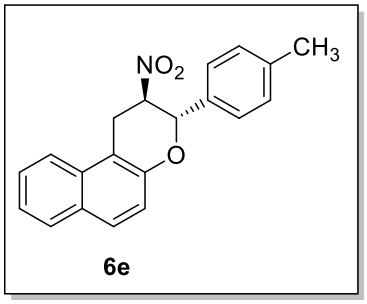
IR (neat, cm^{-1}) 2921 (w), 1546 (s), 1509 (s), 1468 (m), 1353 (m), 1309 (m), 1239 (s), 1223 (s), 1092 (s), 809 (s), 744 (s)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78-7.72 (m, 2H), 7.49-7.47 (m, 1H), 7.32-7.29 (m,2 H), 7.14-7.08 (m, 5H), 5.45 (s, 1H), 4.90-4.85 (m, 2H), 4.37-4.33(m, 1H), 2.36(s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 151.4, 138.5, 129.9, 129.7, 128.6, 128.3, 126.8, 123.8, 122.8, 118.3, 110.8, 83.8, 61.4, 39.9, 20.9.

HRMS calcd. $C_{20}H_{15}NO_3$, 317.1052; found 317.1161 [M - 2H]

3-nitro-2-(*p*-tolyl)-3,4-dihydro-2H-naphthopyran(6e):



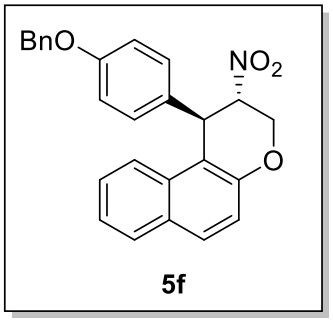
White solid; Yield: 16% (5.1 mg); mp 102-103 ^{o}C

IR (neat, cm^{-1}) 2994 (w), 2920 (w), 1627 (s), 1545 (s), 1462 (s), 1356 (m), 1227 (s), 1204 (s), 1036 (s), 815 (s), 741 (s)

^{1}H NMR (400 MHz, CDCl3) δ 7.82 (d, *J* = 7.6 Hz, 1H), 7.76- 7.71 (m, 2H), 7.55 (t, *J* = 7.2 Hz, 1H), 7.45-7.41 (m, 1H),7.34-7.32 (m, 2H),7.22-7.14 (m, 3 H), 5.43 (d, *J* = 8.4 Hz, 1H), 5.21-5.19 (m, 1H), 3.90-3.84 (m, 1H), 3.70-3.65(m, 1 H), 2.36 (s, 3

^{13}C NMR (100 MHz, $CDCl_3$) δ 151.1, 139.4, 132.3, 132.1, 129.6, 129.4, 128.9, 128.6, 127.1, 126.8, 124.2, 121.6, 118.3, 109.9, 84.3, 77.8, 27.1, 21.2.

3-nitro-4-(4-(benzyloxy)-phenyl)-3,4-dihydro-2H-naphthopyran (5f)



White solid; Yield: 58% (23.7 mg); mp 81-82 ^{o}C

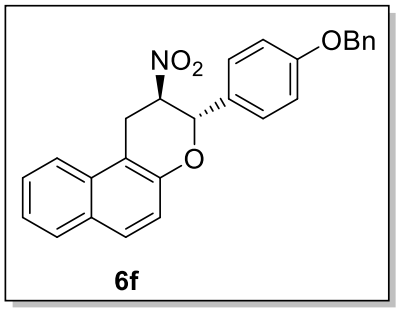
IR (neat, cm^{-1}) 2921 (w), 1625 (m), 1600 (m), 1547 (s), 1466 (s), 1364 (m), 1216 (s), 1002 (s), 859 (m), 823 (s), 790 (s), 740 (s)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77-7.71 (m, 2H), 7.52-7.48 (m, 1H), 7.41-7.28 (m, 7H), 7.16-7.10 (m, 3H), 6.92-6.90 (m, 2H), 5.43 (s, 1H), 5.00 (s, 2H), 4.90-4.83 (m, 2H), 4.36-4.33(m, 1H)
^{13}C NMR (100 MHz, $CDCl_3$) δ 158.2, 151.4, 136.6, 133.6, 132.1, 130.3, 129.9, 129.7, 129.6, 128.6, 128.0, 127.5, 127.4, 127.1, 126.8, 123.8, 122.8, 118.3, 115.5, 115.0, 110.8, 83.8, 70.0, 61.4, 39.5

Anal. Calcd. for $C_{26}H_{21}NO_4$:C, 75.90; H, 5.14; N, 3.40 Found: C, 75.82; H, 5.18; N, 3.36

HRMS calcd. $C_{26}H_{23}NO_5$, 429.1576; found 429.1290 [M + H_2O]

3-nitro-2-(4-(benzyloxy)phenyl-3,4-dihydro-2H-naphthopyran(6f):



6f

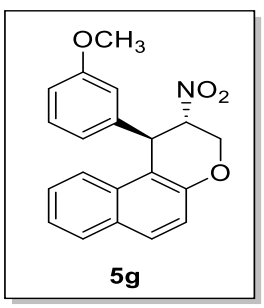
Pale Red solid; Yield: 29% (11.9 mg); mp 85-86 ^{o}C

IR (neat, cm^{-1}) 2920 (w), 1624 (m), 1548 (s), 1467 (s), 1353 (m), 1225 (s), 1177 (s), 842 (s), 740 (s)

^{1}H NMR (400 MHz, CDCl3) δ 7.82 (d, *J* = 8.0 Hz, 1H), 7.76-7.70 (m, 2H), 7.55 (t, *J* = 7.2 Hz, 1H), 7.44-7.31 (m, 8H), 7.14 (d, *J* = 9.2 Hz, 1H), 7.00 (d, *J* = 8.8 Hz, 2H), 5.38 (d, *J* = 8.4 Hz, 1H), 5.21-5.15 (m, 1H), 5.07 (s, 2H), 3.90-3.83 (m, 1H), 3.73-3.68 (m, 1H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 151.2, 136.6, 132.1, 129.4, 129.0, 128.7, 128.6, 128.4, 128.0, 127.5, 127.4, 127.1, 124.2, 121.6, 118.3, 115.2, 109.9, 84.5, 77.7, 70.0, 27.5.

3-nitro-4-(3-methoxyphenyl)-3,4-dihydro-2H-naphthopyran (5g)



5g

White solid; Yield: 36% (9.9 mg); mp 71-73 ^{o}C

IR (neat, cm^{-1}) 2965 (w), 1624 (m), 1547 (s), 1465(m), 1539 (s), 1261 (s), 1157 (s), 1030 (s), 868 (s), 806 (s), 764 (s)

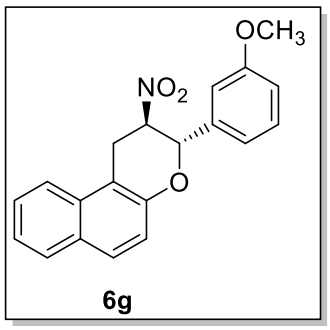
^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.77-7.72 (m, 2H), 7.50-7.48 (m, 1H), 7.33-7.30 (m, 2H), 7.22 (d, *J* = 8.0 Hz, 1H), 7.12 (d, *J* = 9.2 Hz, 1H), 6.81-6.75 (m, 3H), 5.45 (s, 1H), 4.91-4.86 (m, 2H), 4.38 (d, *J* = 11.2 Hz, 1H), 3.74 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 160.2, 151.4, 143.1, 132.2, 130.3, 129.9, 129.8, 128.6, 126.9, 123.8, 122.7, 120.8, 118.3, 114.8, 112.5, 110.5, 83.7, 61.6, 55.2, 40.3.

Anal. Calcd. for $C_{20}H_{17}NO_4$: C, 71.63; H, 5.11; N, 4.18; Found: C, 71.52; H, 5.18; N, 4.09.

HRMS calcd. $C_{19}H_{16}NO_4$, 334.1080; found 334.1079 [M - H]

3-nitro-2-(3-methoxyphenyl)-3,4-dihydro-2H-naphthopyran(6g):



6g

Pale red solid; Yield: 25% (6.7 mg); mp 65-66 ^{o}C

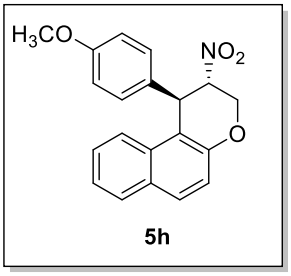
IR (neat, cm^{-1}) 2918 (w), 2849 (w), 1652 (m), 1547 (s), 1465 (m), 1354 (m), 1262 (s), 1157 (s), 1095 (m), 1024 (s), 886 (s), 818 (s), 697 (s)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.0Hz, 1H), 7.76-7.71 (m, 2H), 7.57-7.53 (m, 1H), 7.44-7.41 (m, 1H), 7.33-7.29 (m, 1H), 7.17 (d, *J* = 8.8 Hz, 1H) 7.01-6.97 (m, 2H), 6.93-6.91 (m, 1H), 5.47 (d, *J* = 8.0 Hz, 1H), 5.22-5.17 (m, 1H), 3.87 (dd, *J* = 16.4, 12.0 Hz, 1H), 3.80 (s, 3H), 3.65 (dd, *J* =16.0, 5.6 Hz, 1H)

^{13}C NMR (100 MHz, $CDCl_3$) δ : 159.9, 150.9, 137.0, 132.1, 130.0, 129.4, 129.0, 128.7, 127.1, 124.2, 121.6, 119.0, 118.2, 114.8, 112.5, 109.9, 84.2, 77.6, 55.2, 26.8

Anal. Calcd. for $C_{20}H_{17}NO_4$: C, 71.63; H, 5.11; N, 4.18; Found: C, 71.76; H, 5.09; N, 4.15.

3-nitro-4-(4-methoxyphenyl)-3,4-dihydro-2H-naphthopyran (5h)



5h

White solid; Yield: 50% (13.3 mg); mp 71-72 ^{o}C

IR (neat, cm^{-1}) 2998 (w), 2836 (w), 1624 (m), 1552 (s), 1466 (m), 1380 (s), 1235 (s), 852 (m), 838 (s), 805 (s),765 (s), 745 (s)

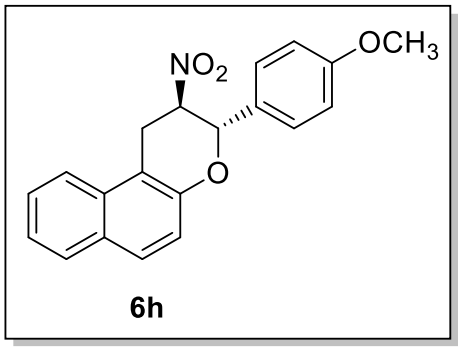
^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.77-7.71 (m, 2H), 7.50-7.47 (m, 1H), 7.32-7.29(m, 2H), 7.14-7.10 (m, 3H), 6.84-6.82 (m, 2H), 5.42 (s, 1H), 4.90-4.83 (m, 2H), 4.35 (dd, *J*= 12.4, 1.6 Hz, 1H), 3.76 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.0, 151.4, 133.4, 132.1, 129.9, 129.6, 129.5, 128.6, 126.8, 123.8, 122.8, 118.3, 114.6, 110.9, 83.9, 61.4, 55.2, 39.5

Anal. Calcd. for $C_{20}H_{17}NO_4$: C, 71.63; H, 5.11; N, 4.18; Found: C, 71.52; H, 5.14; N, 4

HRMS calcd. $C_{20}H_{19}NO_5$, 353.1263; found 353.1406

3-nitro-2-(4-methoxyphenyl)-3,4-dihydro-2H-naphthopyran(6h):



6h

White solid; Yield: 25% (6.7 mg); mp 82-83 ^{o}C

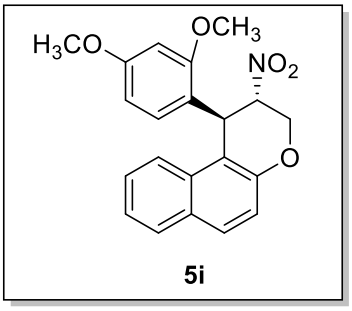
IR (neat, cm^{-1}) 2972 (w), 2889 (w), 1611 (m), 1555 (s), 1509 (s), 1460 (s), 1365 (m), 1227 (s), 826 (s), 754 (s)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.4 Hz, 1H), 7.76-7.70 (m, 2H), 7.57-7.53 (m, 1H), 7.44-7.36 (m, 3H), 7.15 (d, *J* = 8.8 Hz, 1H), 6.95-6.91 (m, 2H), 5.37 (d, *J* = 8.4 Hz, 1H), 5.21-5.15 (m, 1H), 3.89-3.83 (m, 1H), 3.81 (s, 3H), 3.70 (dd, *J* =16.0, 6.0 Hz, 1H)

^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.4, 151.2, 132.1, 129.4, 128.9, 128.6, 128.4, 127.2, 127.1, 124.2, 121.6, 118.3, 114.3, 109.9, 84.5, 77.7, 55.3, 27.5

Anal. Calcd. for $C_{20}H_{17}NO_4$: C, 71.63; H, 5.11; N, 4.18; Found: C, 71.52; H, 5.16; N, 4.23.

3-nitro-4-(2,4-dimethoxyphenyl)-3,4-dihydro-2H-naphthopyran (5i)



5i

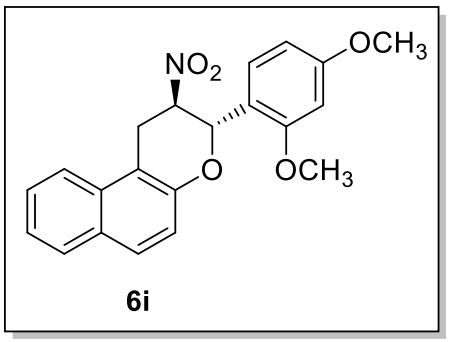
Pale Brown solid; Yield: 60 % (21.9 mg); mp 122-124 ^{o}C

IR (neat, cm-1) 2929 (w), 2853 (w), 1633 (m), 1600 (s), 1560 (s), 1453 (s), 1367 (m), 1262 (s), 881 (s), 793(s)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.90 (d, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 8.8 Hz 1H), 7.68-7.65 (m, 2H), 7.42-7.37 (m, 1H), 7.33-7.28 (m, 2H), 6.65-6.62 (m, 2H), 5.35 (d, *J* = 6.4 Hz, 1H), 5.29 (d, *J* = 6.0 Hz, 1H), 4.76 (d, *J* = 12.4 Hz, 1H), 4.65 (d, *J* = 12.8 Hz, 1H), 3.92 (s, 3H).; 3.65 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.4, 161.3, 158.9, 152.2, 148.7, 132.5, 130.6, 128.6, 126.0, 125.8, 124.1, 123.0, 122.2, 119.6, 113.8, 112.5, 104.3, 98.9, 88.1, 62.1, 55.47, 55.42, 20.9

3-nitro-2-(2,4-dimethoxyphenyl)-3,4-dihydro-2H-naphthopyran(6i):



6i

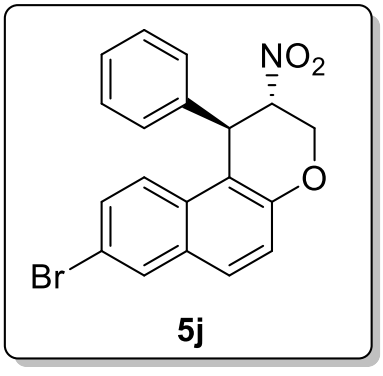
Pale Brown solid; Yield; 20% (7.3mg); mp 117-118 ^{o}C

IR (neat, cm^{-1}) 2944 (w), 2838 (w), 1636 (m), 1542 (s), 1459 (s), 1366 (m), 1237 (s), 867 (s), 792 (s)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77-7.75 (m, 1H), 7.71 (d, J= 8.8Hz, 1H), 7.42-7.39 (m, 1H), 7.33-7.28 (m, 2H), 7.11 (d, *J* = 9.2 Hz, 1H), 6.56 (d, *J* = 2.4 Hz, 1H), 6.52 (d, *J* = 8.4 Hz, 1H), 6.23 (dd, *J* = 8.4, 2.4 Hz, 1H) 5.67 (s, 1H), 4.90-4.84 (m, 2H), 4.31-4.28 (m, 1H), 3.99 (s, 3H), 3.74 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.3, 160.4, 156.8, 151.7, 132.2, 131.1, 129.8, 129.3, 128.5, 126.7, 123.7, 122.9, 121.1, 118.2, 111.1, 104.3, 98.5, 81.3, 62.2, 55.6, 55.3, 33.7

3-nitro-4-phenyl-3,4-dihydro-2H-8-bromo-naphthopyran (5j)



5j

White solid; Yield; 55% (19 mg); mp 76-78 ^{o}C

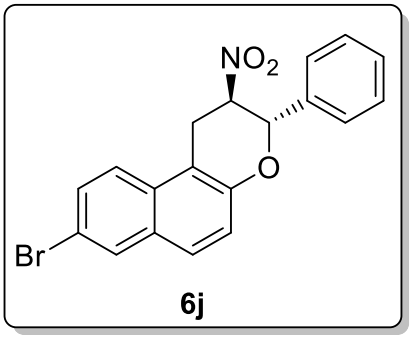
IR (neat, cm^{-1}) 2896 (w), 1618 (w), 1543 (s), 1353 (m), 1310 (s), 1222 (s), 1091 (s), 1073 (s), 868 (s), 804 (s)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 2.0 Hz, 1H), 7.64 (d, *J* = 8.8 Hz, 1H), 7.38-7.28 (m, 5 H), 7.19-7.17 (m, 3H), 5.44 (s, 1H), 4.92-4.86 (m, 2H), 4.34 (d, *J* = 12.4 Hz, 1H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 151.7, 141.0, 131.1, 130.7, 130.6, 130.1, 129.4, 128.8, 128.4, 127.9, 124.5, 119.5, 117.6, 111.0, 83.6, 61.5, 40.2

Anal. Calcd. for $C_{19}H_{14}BrNO_3$:C, 59.39; H, 3.67; N, 3.65; Found: C, 59.45; H, 3.62; N, 3.71
HRMS calcd. $C_{19}H_{16}BrNO_4$, 401.0263; found 401.0167

3-nitro-2-phenyl-3,4-dihydro-2H-8-bromo-naphthopyran(6j):



6j

Pale Brown solid; Yield; 36% (12.6 mg); mp 81-82 ^{o}C

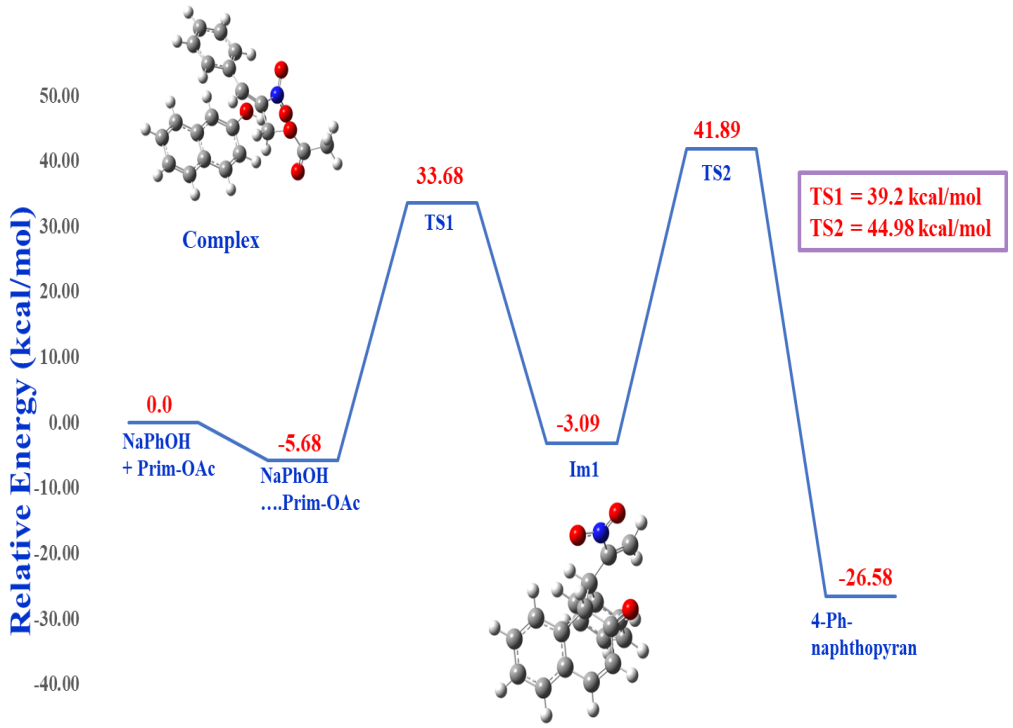
IR (neat, cm-1) 2851 (w), 1624 (m), 1597 (m), 1545 (s), 1350 (m), 1226 (m), 973 (s), 745 (s), 697 (s)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.64-7.61(m, 3H), 7.43-7.39 (m, 5H), 7.17 (d, *J* = 9.2 Hz, 1H), 5.49 (d, *J* = 8.0 Hz, 1H), 5.22-5.16(m, 1H), 3.85 (dd, *J* = 16.4, 8.8 Hz, 1H), 3.61 (dd, *J* = 16.4, 6.0 Hz, 1H)

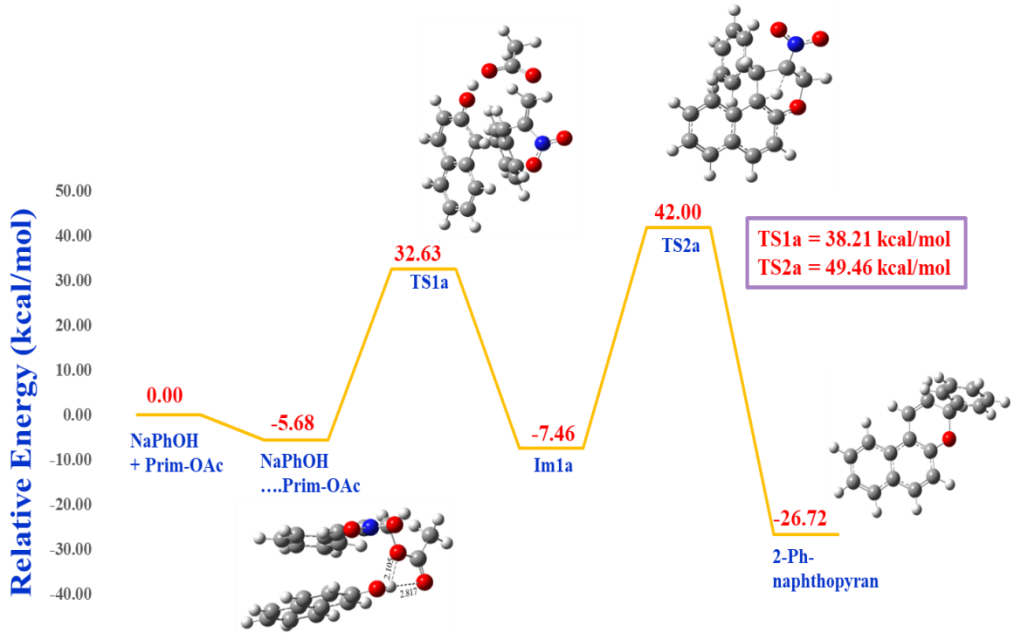
^{13}C NMR (100 MHz, $CDCl_3$) δ 151.3, 139.2, 135.3, 130.7, 130.7, 130.6, 130.3, 129.5, 129.0, 128.1, 126.8, 123.4, 119.4, 118.0, 114.0, 110.2, 84.0, 77.8, 27.0

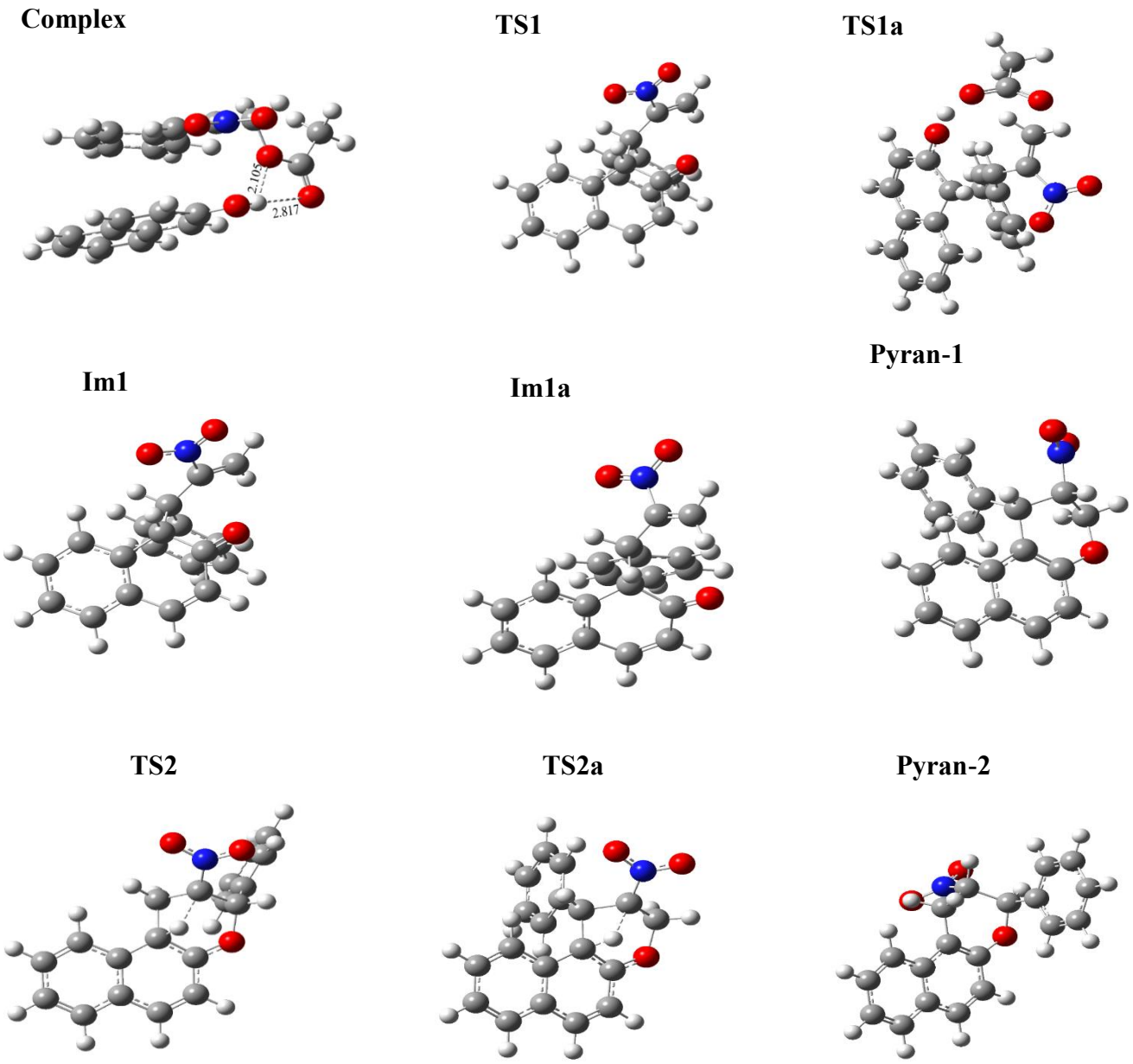
Anal. Calcd. for $C_{19}H_{14}BrNO_3$:C, 59.39; H, 3.67; N, 3.65; Found: C, 59.28; H, 3.72; N, 3.61.

Energy profile diagrams for the formation of 5a



Energy profile diagrams for the formation of 6a





SF-1: The optimized structure of complex, Intermediate, transition state and products.

References

1. C. -L. Cao, Y. -Y. Zhou, J. Zhou, X. -L. Sun, Y. Tang, Y. -X. Li, G. -Y. Li, and J. Sun, 2009, **15**, 11384.

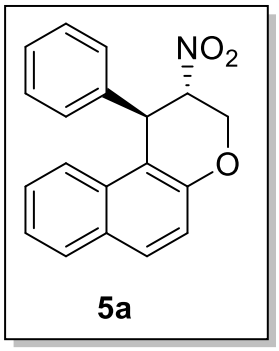
2. P. Basu, R. Sikdar, T. Kumar, I. N. N. Namboothiri, *Eur. J. Org. Chem.*, 2018, **2018**, 5735.

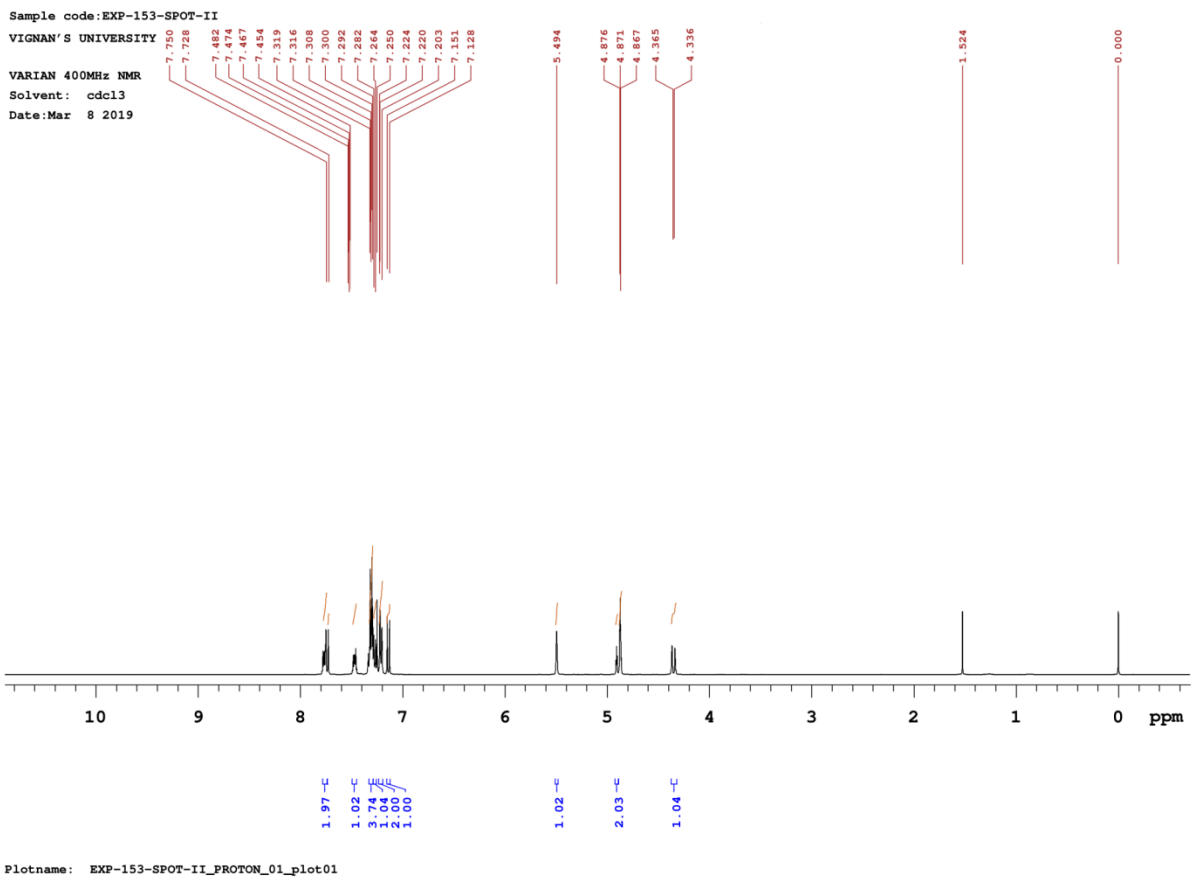
CHAPTER 6.

SUPPORTING INFORMATION

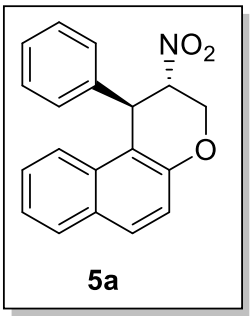
(SPECTRA's &GRAPHICAL DIAGRAMS)

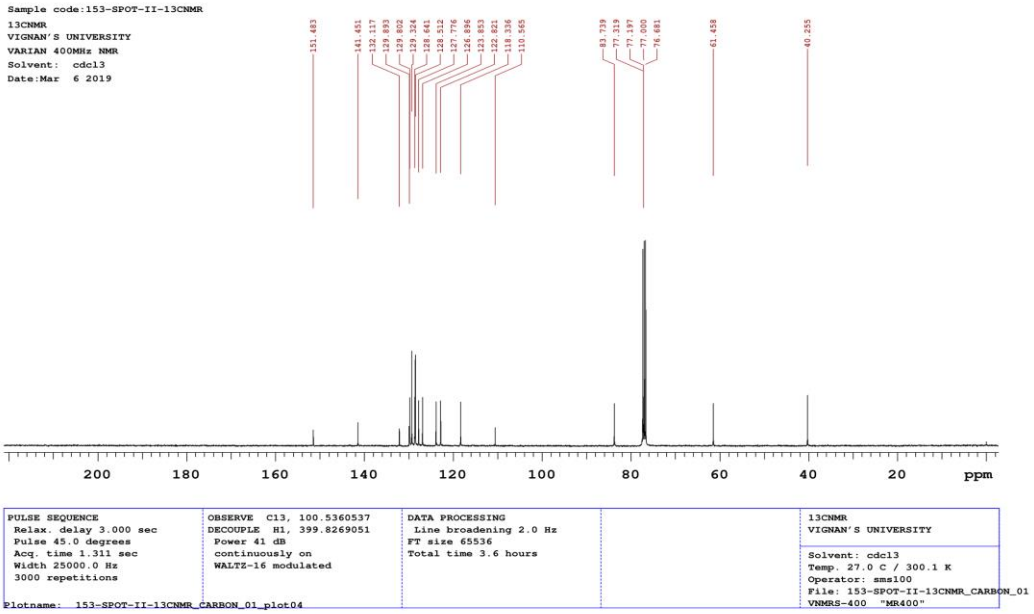
6.Spectral Dat



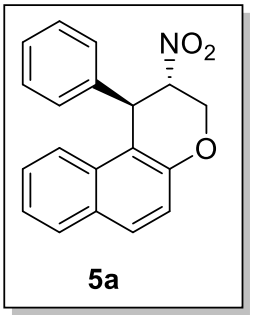


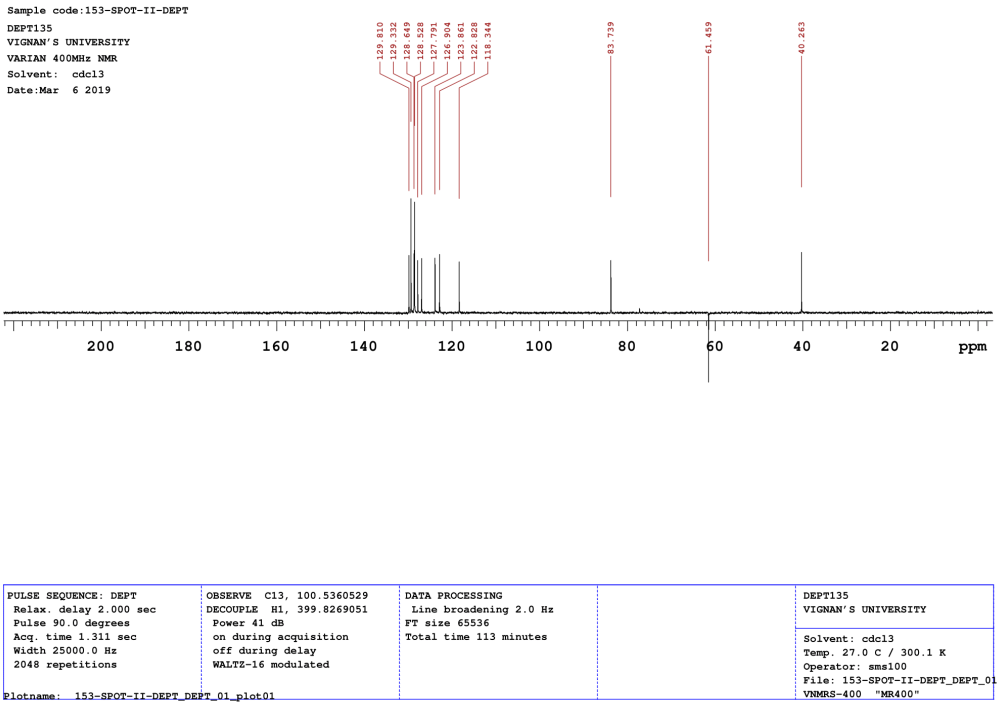
[1] NMR Spectra for compound **5a**



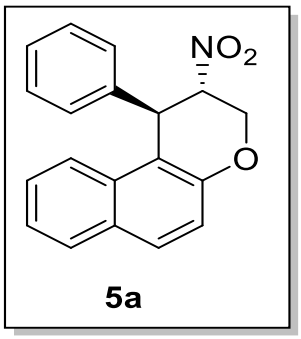


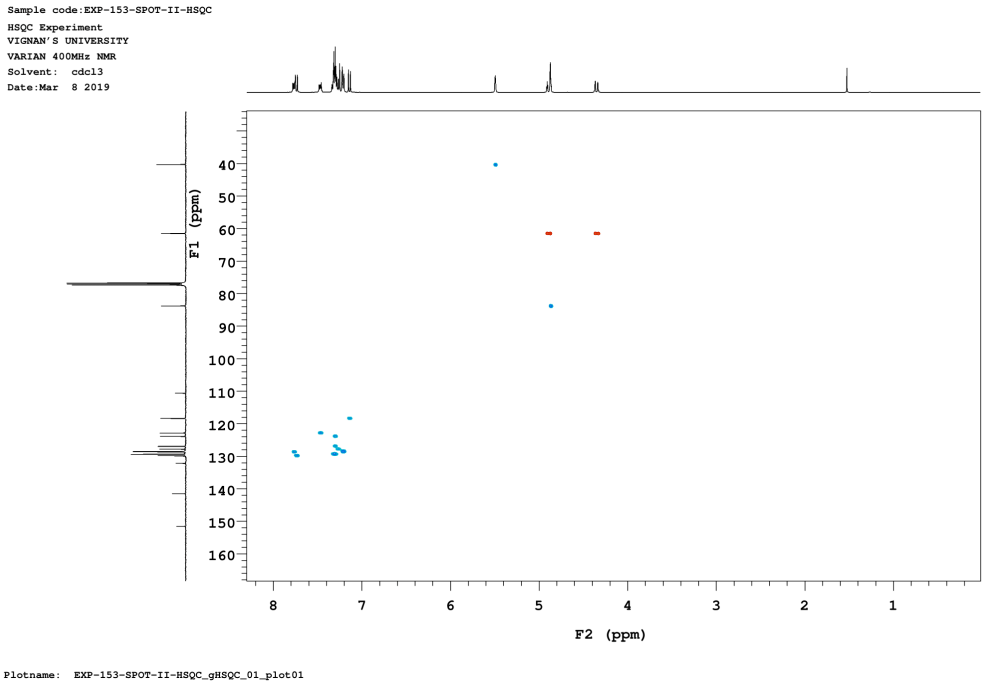
^{13}C NMR Spectra for compound **5a**



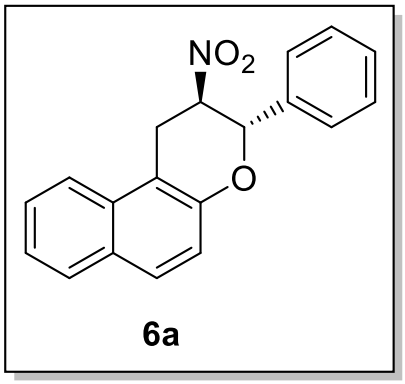


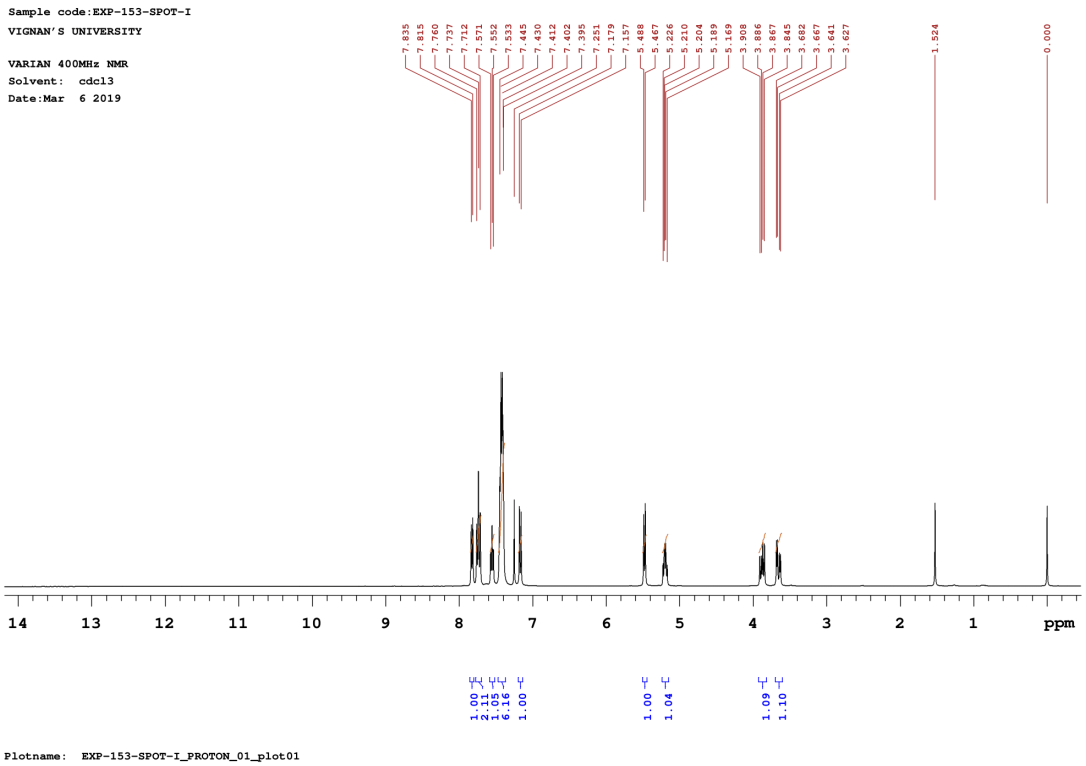
DEPT-135 Spectra for compound **5a**



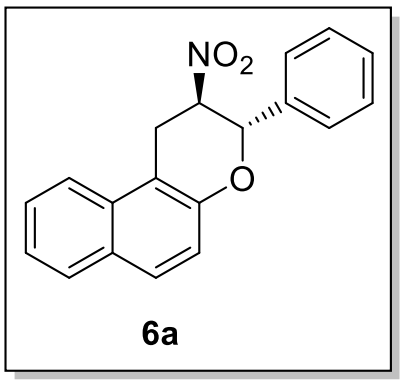


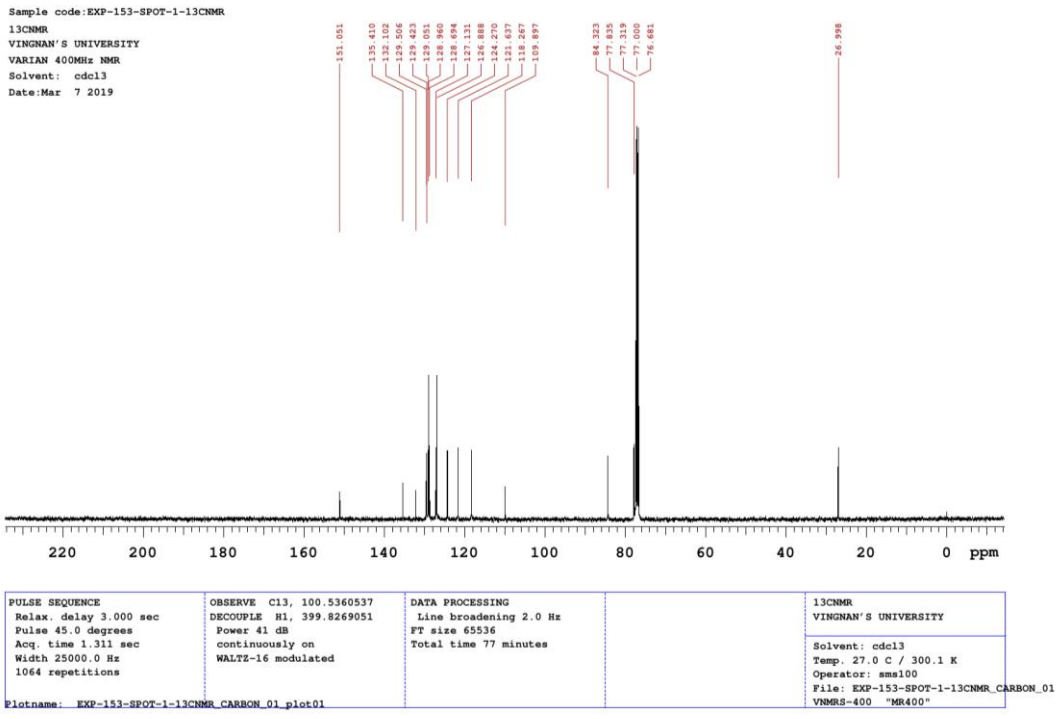
HSQC Spectra for compound **5a**



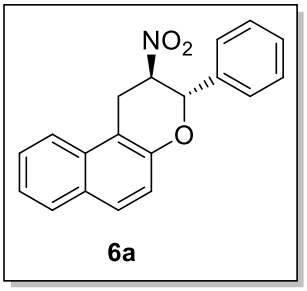


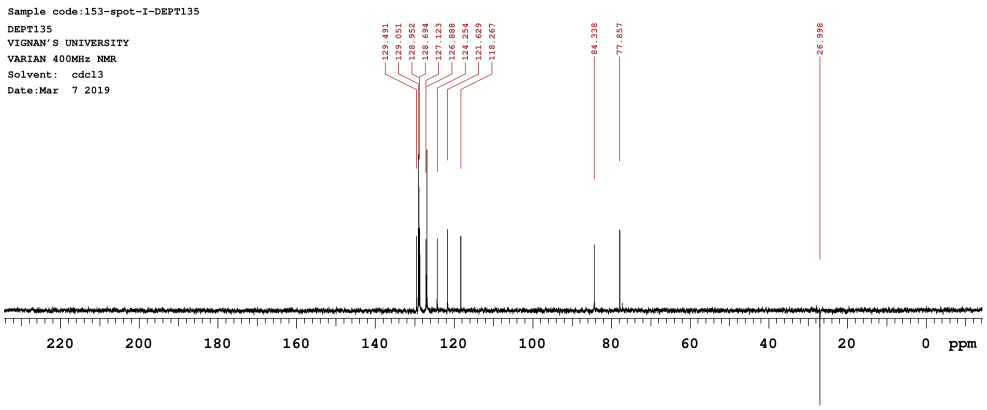
^{1}H NMR Spectra for compound **6a**





^{13}C NMR Spectra for compound **6a**

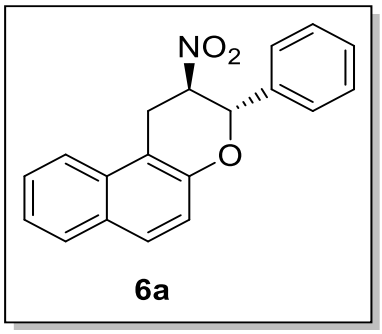


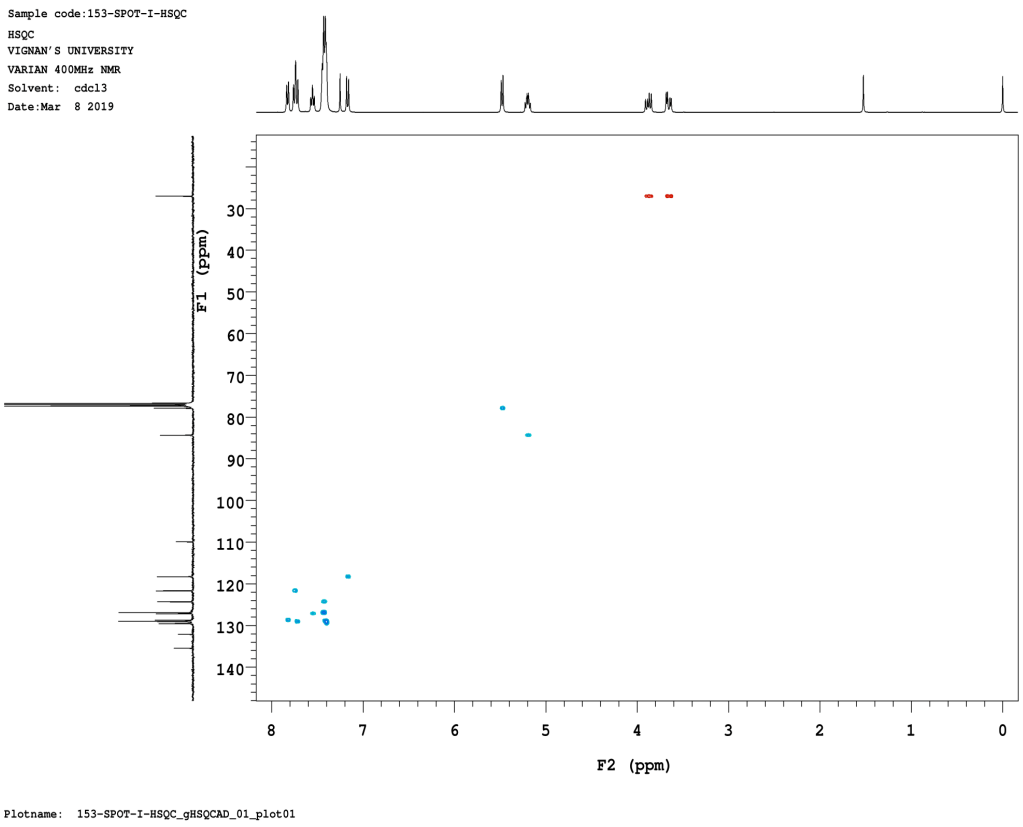


PULSE SEQUENCE: DEPT Relax. delay 2.000 sec Pulse 90.0 degrees Acq. time 1.311 sec Width 25000.0 Hz 1024 repetitions	OBSERVE C13, 100.5360522 DECOUPLE H1, 399.8269051 Power 41 dB on during acquisition off during delay WALTZ-16 modulated	DATA PROCESSING Line broadening 2.0 Hz FT size 65536 Total time 56 minutes		DEPT135 VIGNAN'S UNIVERSITY Solvent: cdcl3 Temp. 27.0 C / 300.1 K Operator: sms100 File: 153-spot-I-DEPT135_DEPT_01 VNMRS-400 "MR400"

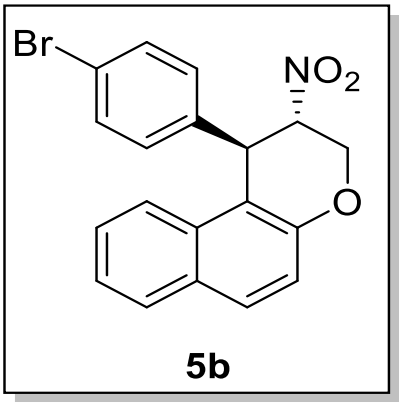
Plotname: 153-spot-I-DEPT135_DEPT_01_plot01

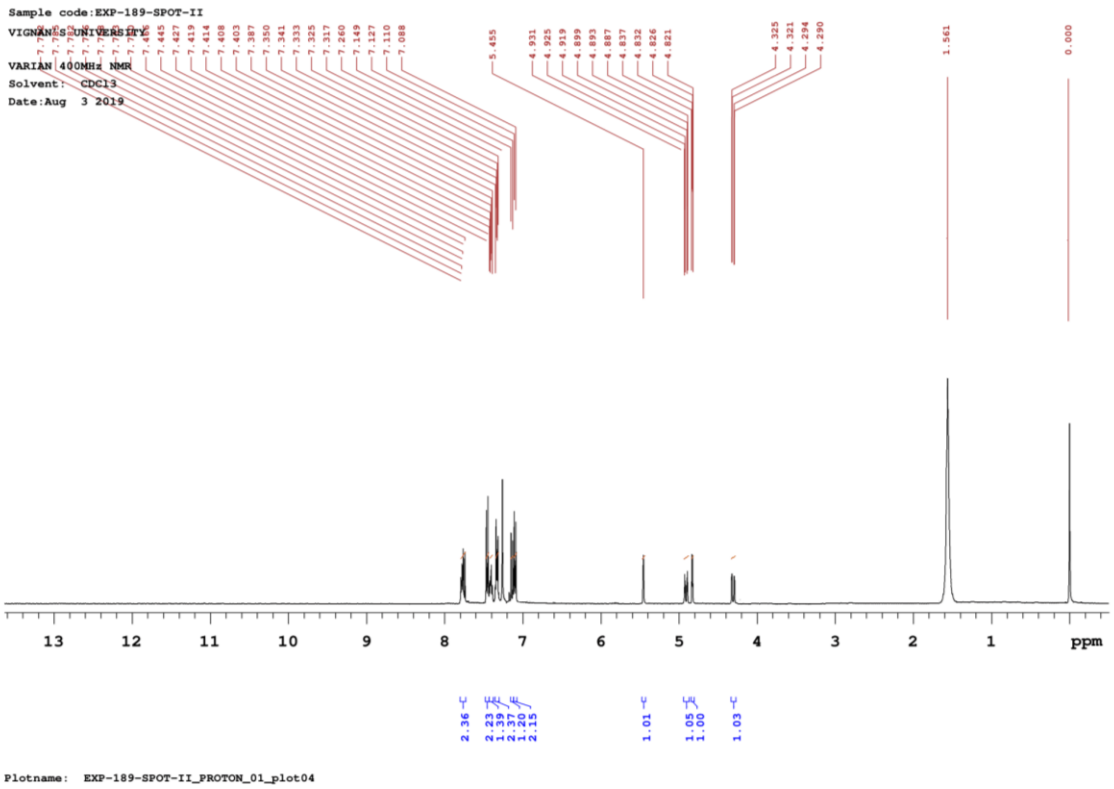
DEPT-135 Spectra for compound **6a**



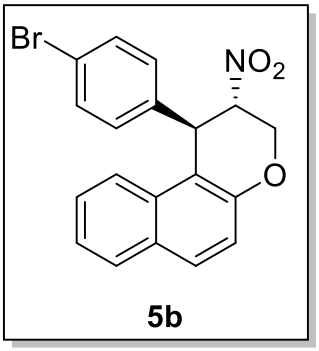


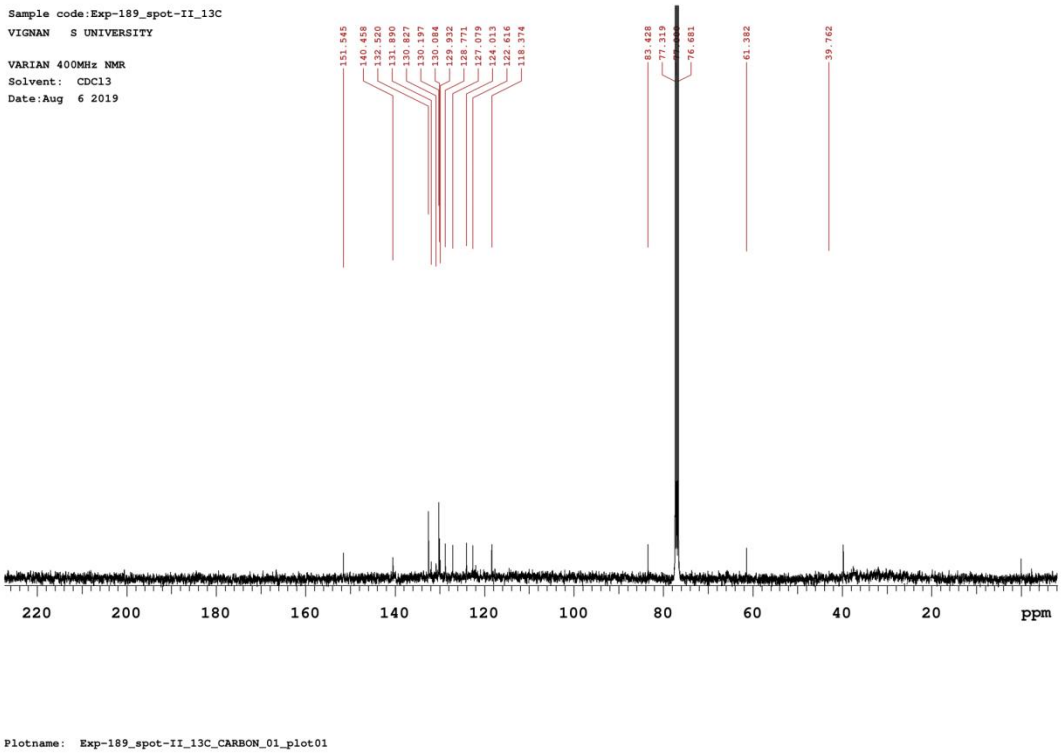
HSQC Spectra for compound **6a**



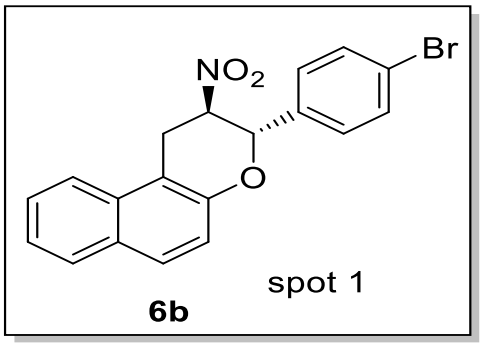


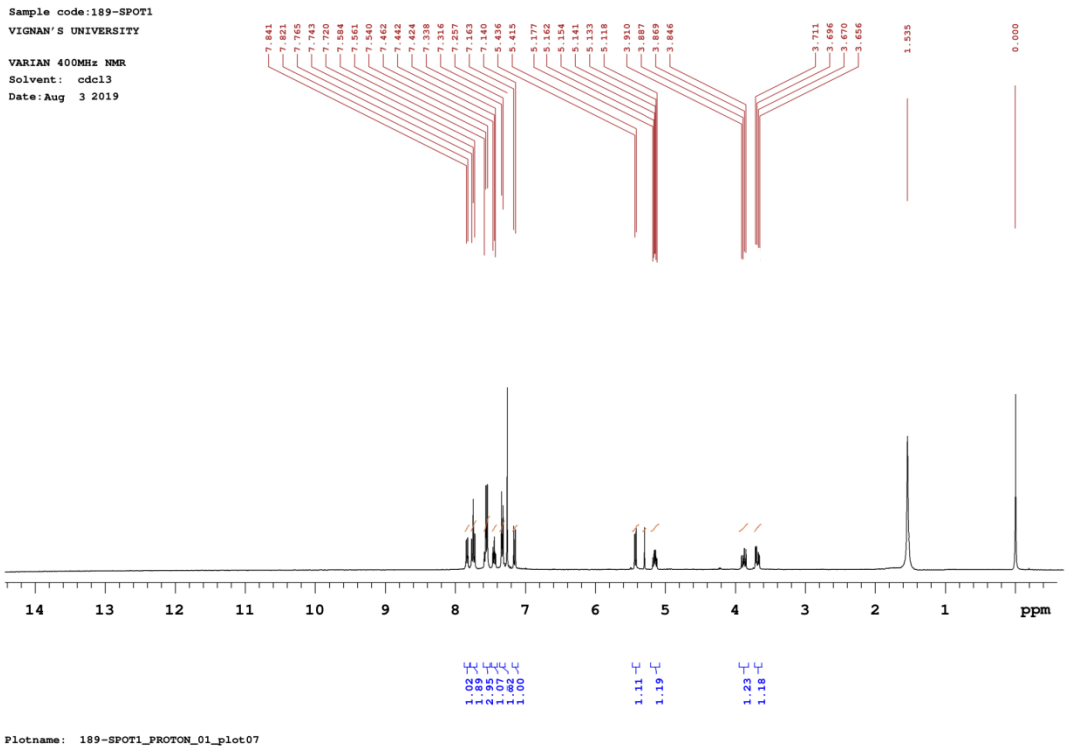
^{1}H NMR Spectra for compound **5b**



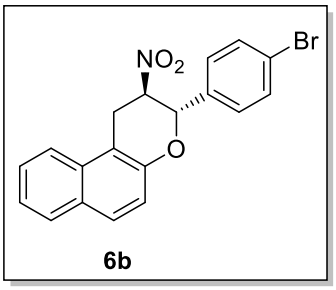


^{13}C NMR Spectra for compound **5b**

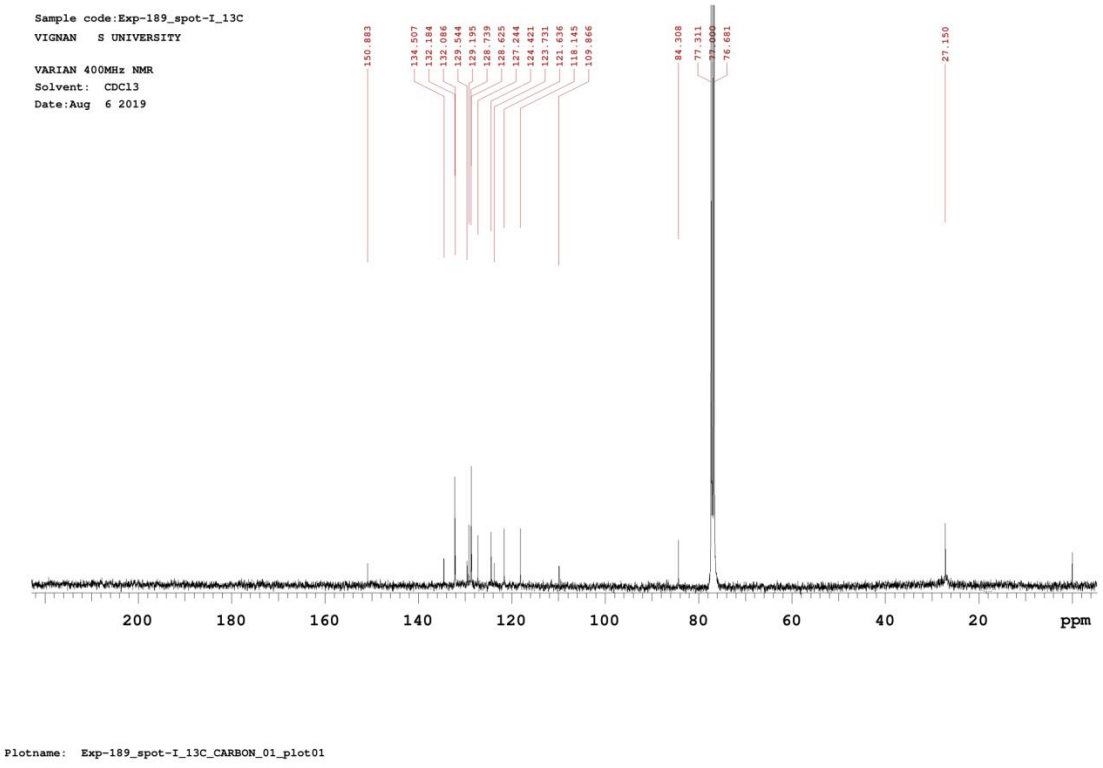




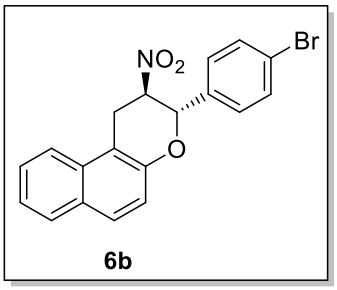
^{1}H NMR Spectra for compound **6b**



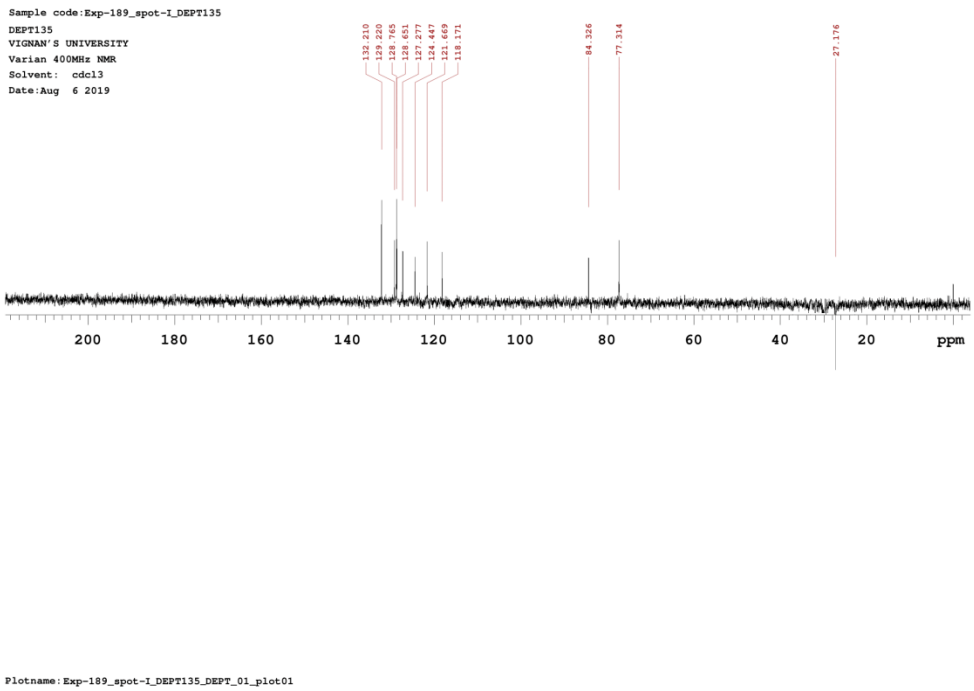
6b



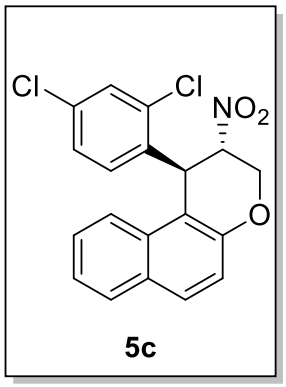
^{13}C NMR Spectra for compound **6b**

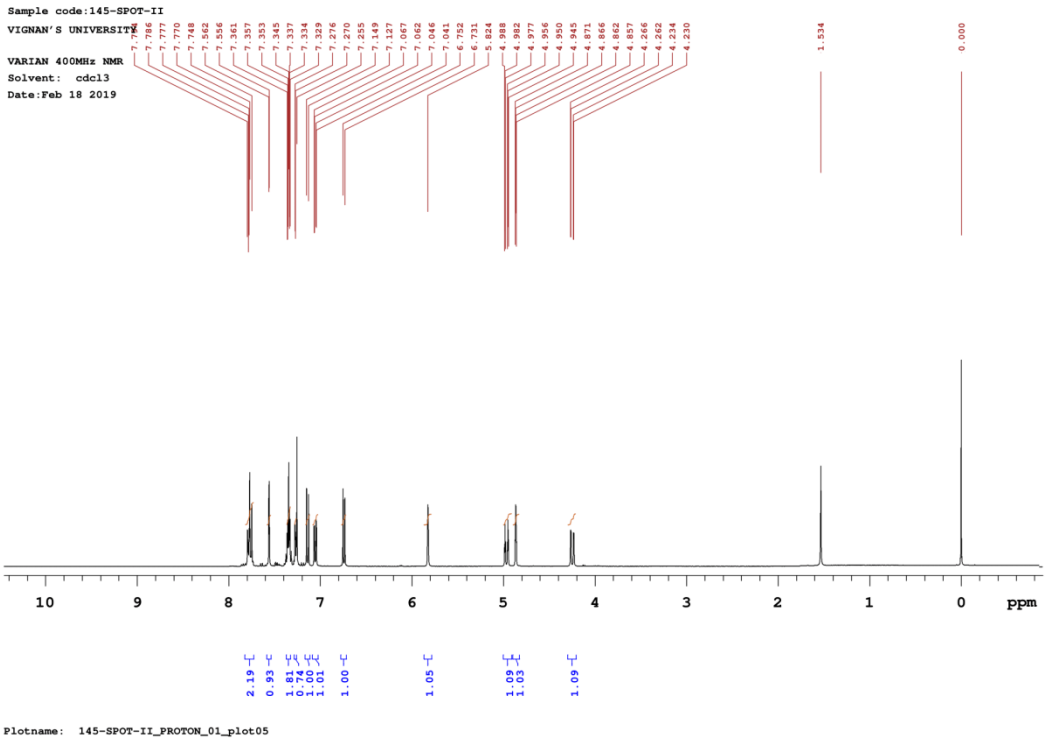


S

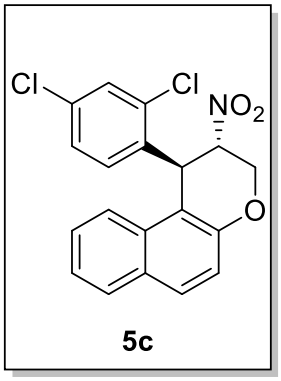


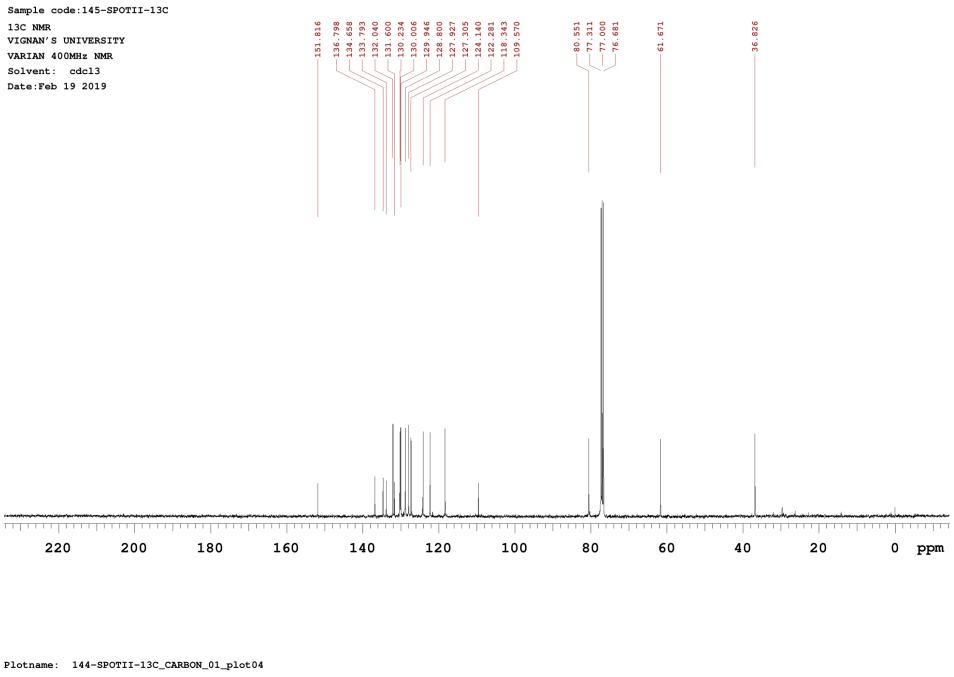
DEPT-135 Spectra for compound **5c**



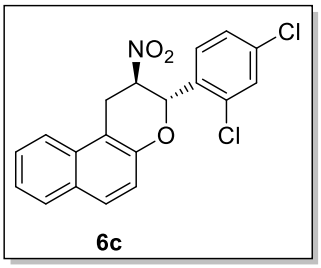


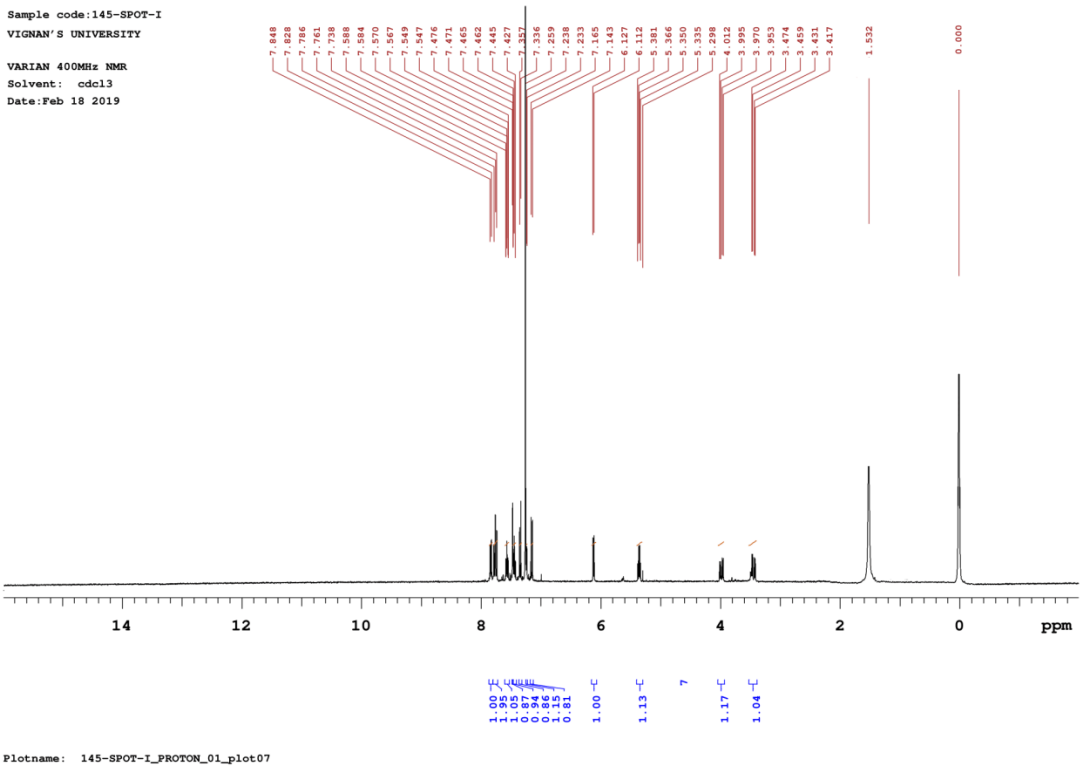
^{1}H NMR Spectra for compound **5c**



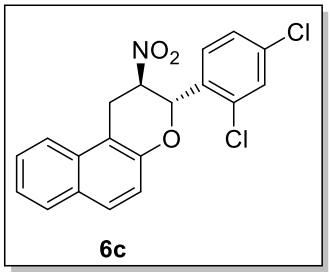


^{13}C NMR Spectra for compound **5c**

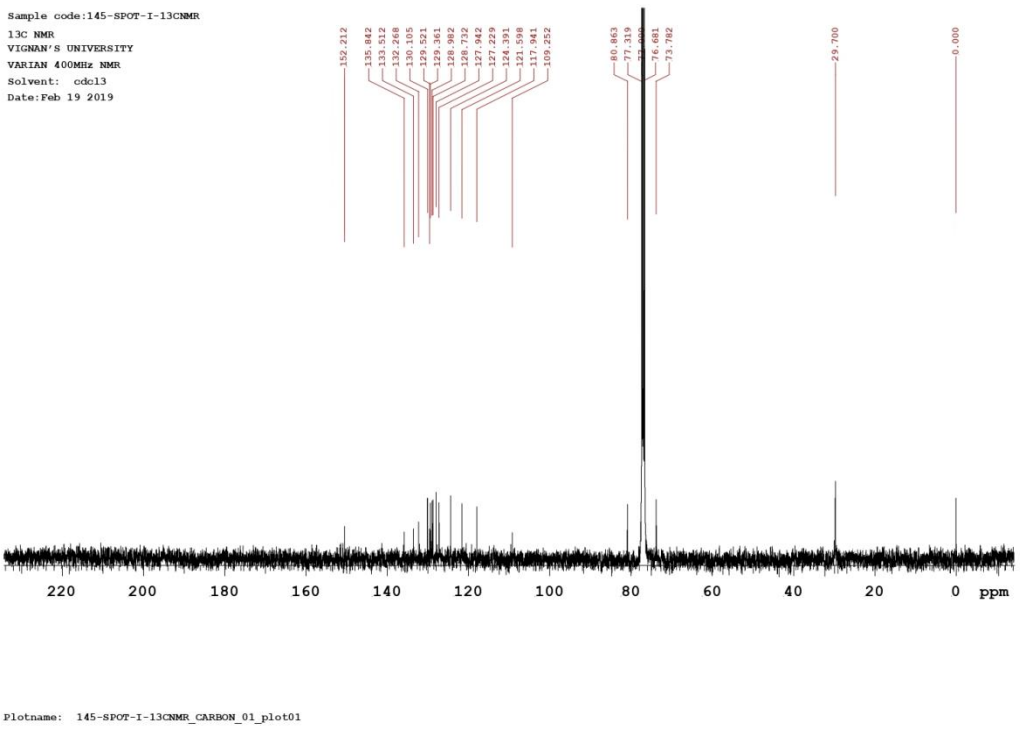




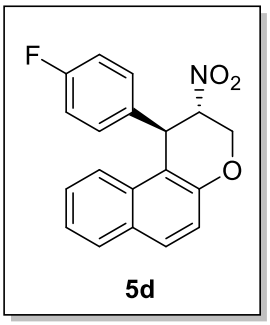
^{1}H NMR Spectra for compound **6c**

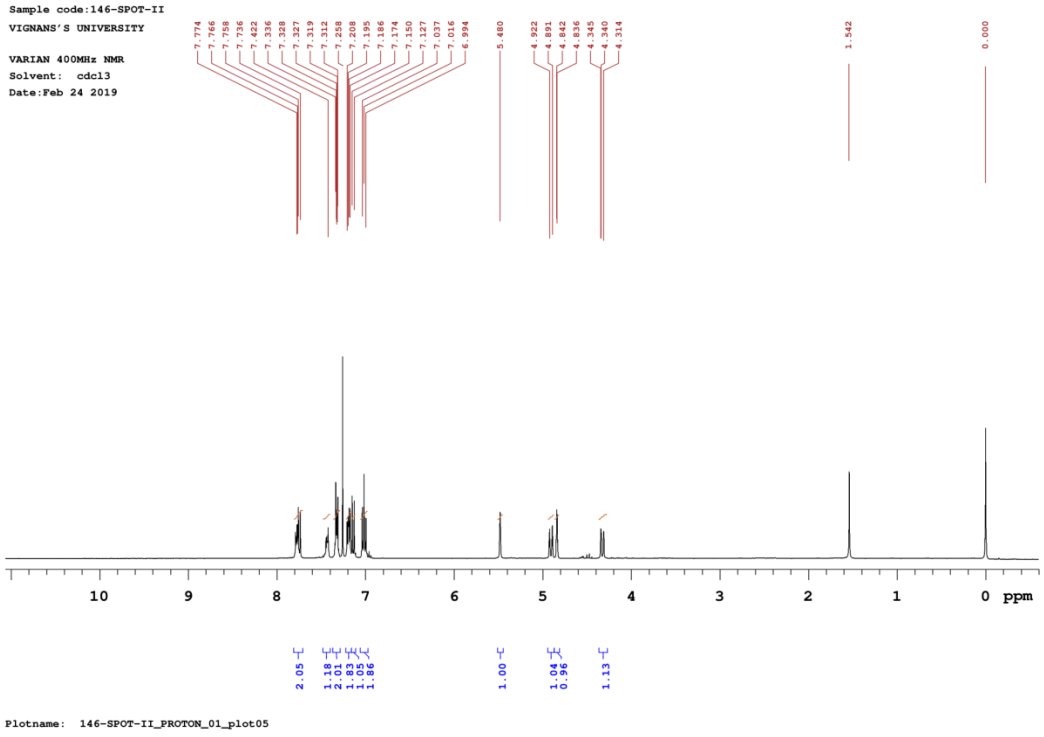


6c

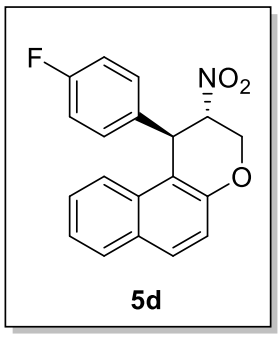


^{13}C NMR Spectra for compound **6c**

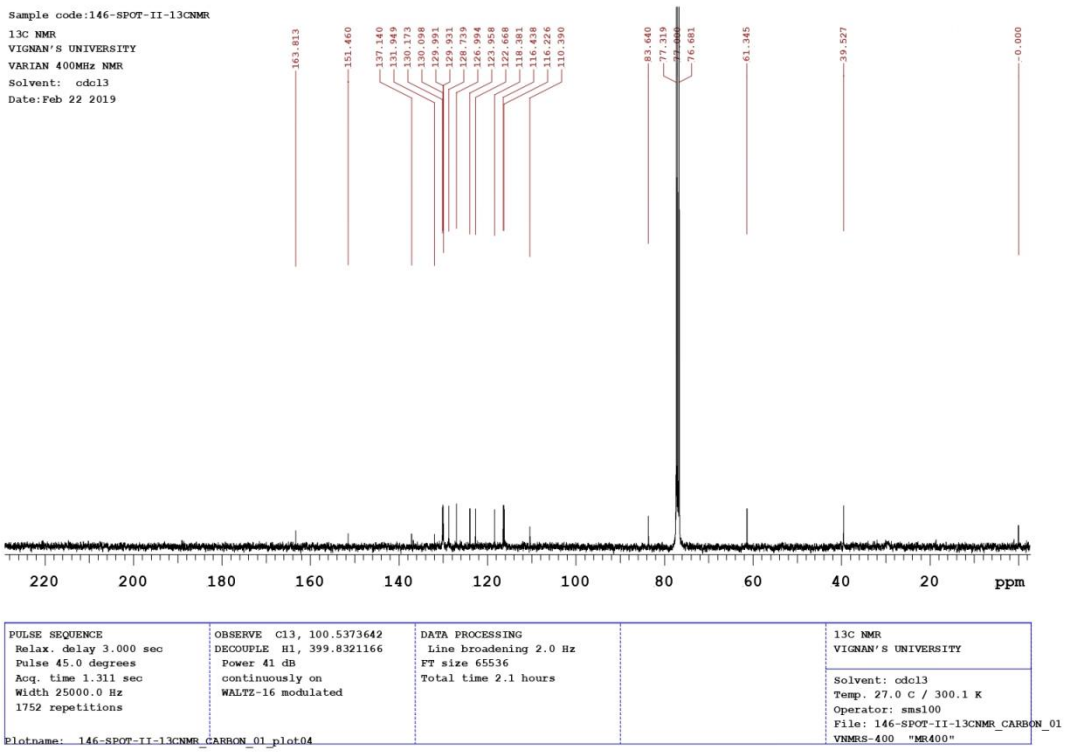




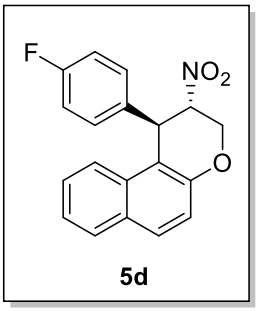
^{1}H NMR Spectra for compound **5d**



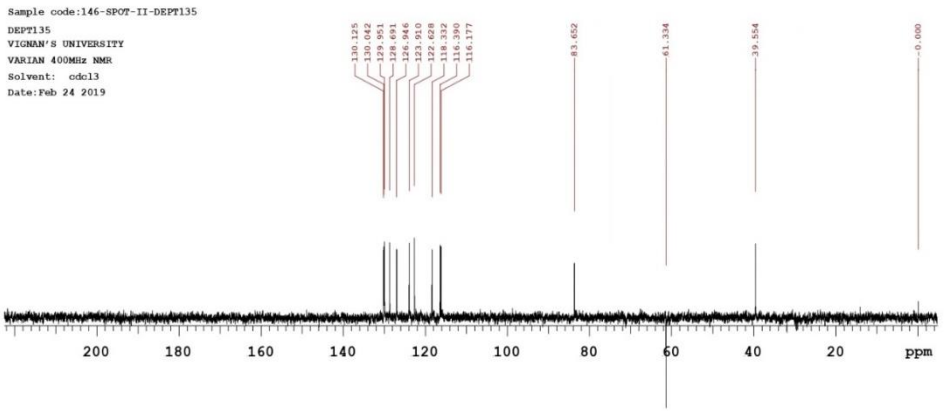
5d



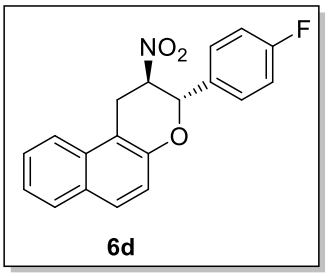
^{13}C NMR Spectra for compound **5d**

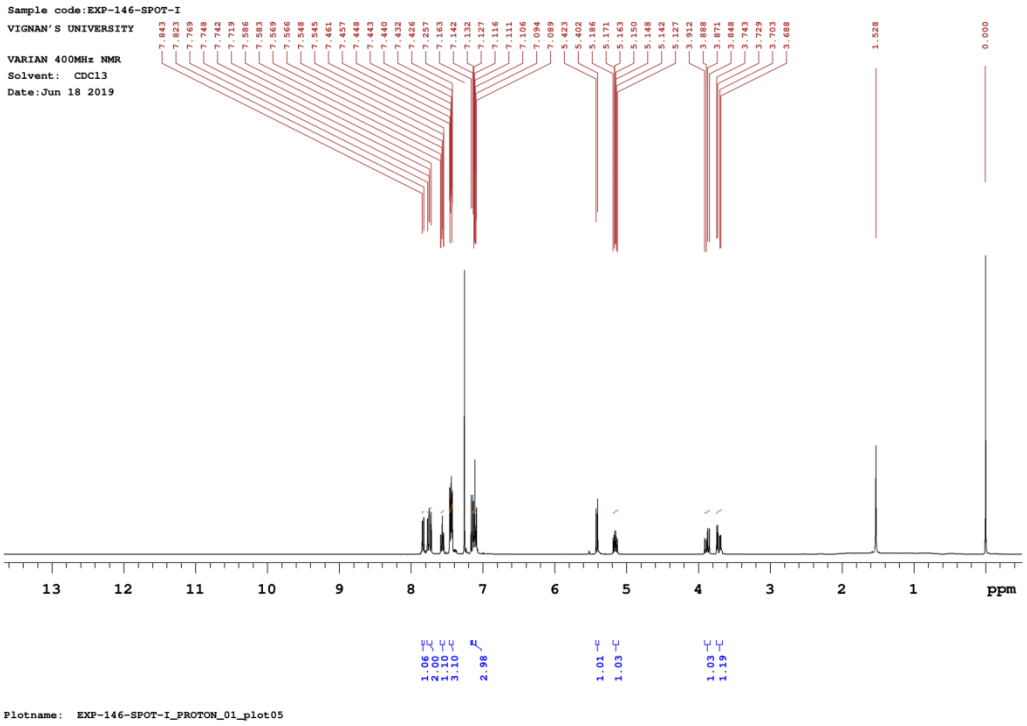


5d

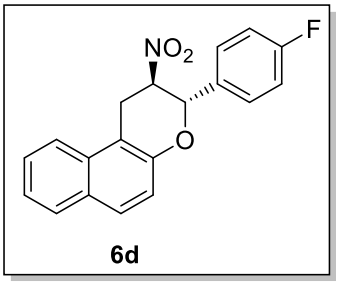


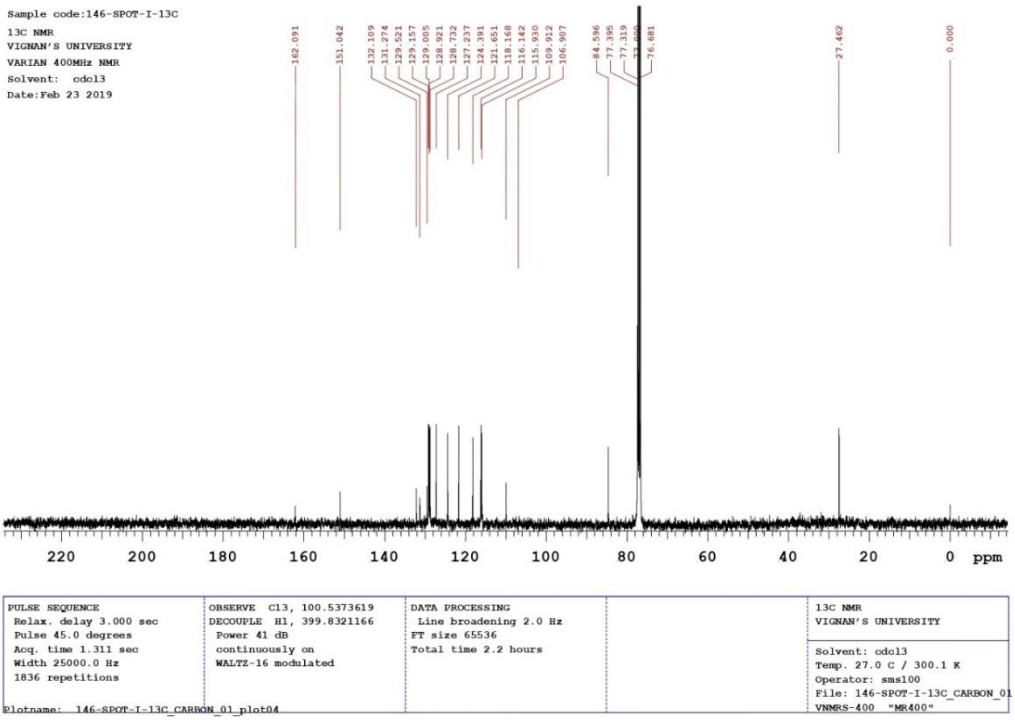
DEPT-135 Spectra for compound **5d**



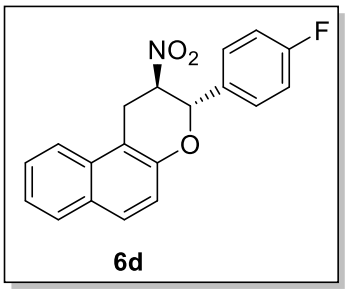


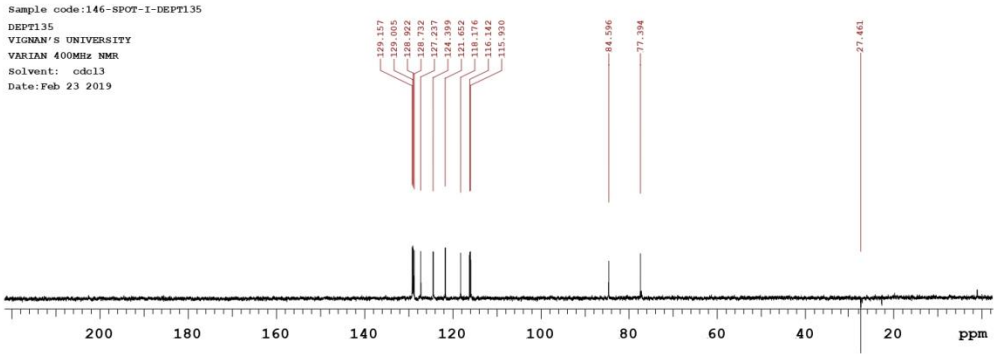
^{1}H NMR Spectra for compound **6d**





^{13}C NMR Spectra for compound **6d**

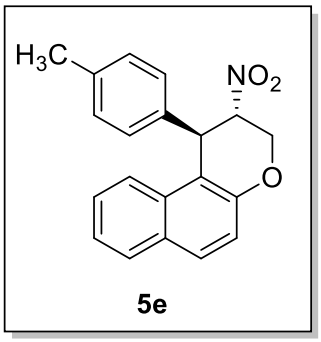




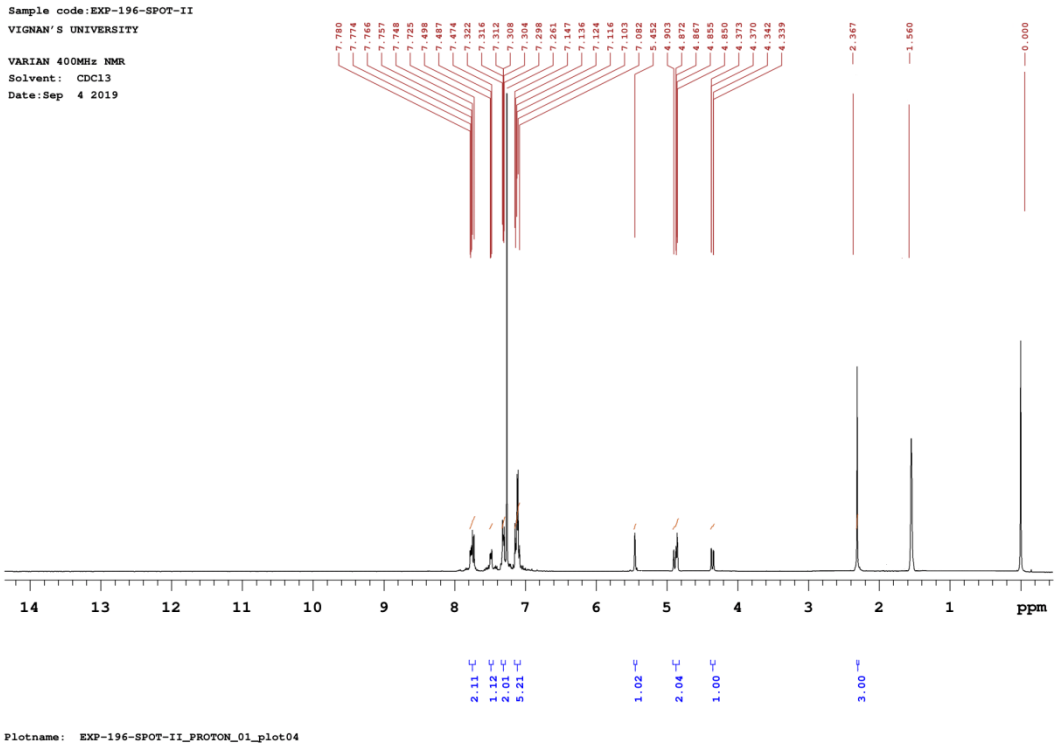
PULSE SEQUENCE: DEPT Relax. delay 2.000 sec Pulse 90.0 degrees Acq. time 1.311 sec Width 25000.0 Hz 3000 repetitions	OBSERVE C13, 100.5360499 DECOUPLE H1, 399.8269051 Power 41 dB on during acquisition off during delay WALTZ-16 modulated	DATA PROCESSING Line broadening 2.0 Hz FT size 65536 Total time 2.8 hours		DEPT135 VIGNAN'S UNIVERSITY Solvent: cdcl3 Temp. 27.0 C / 300.1 K Operator: sms100 File: 146-SPOT-I-DEPT135_DEPT_01 VNMRS-400 "MR400"

Plotname: 146-SPOT-I-DEPT135_DEPT_01_plot01

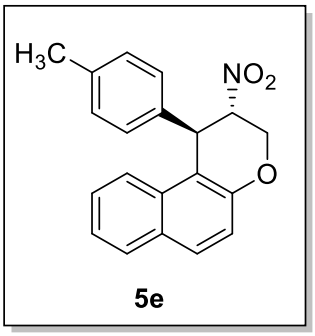
DEPT-135 Spectra for compound **6d**

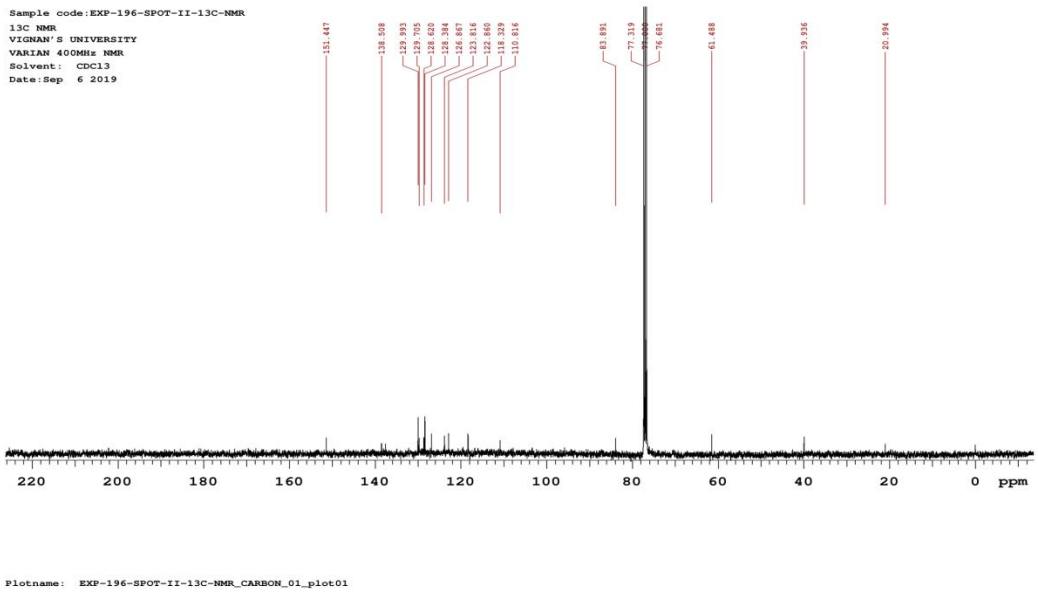


5e

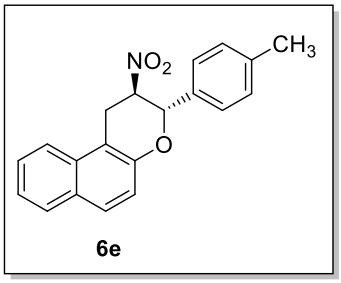


^{1}H NMR Spectra for compound **5e**

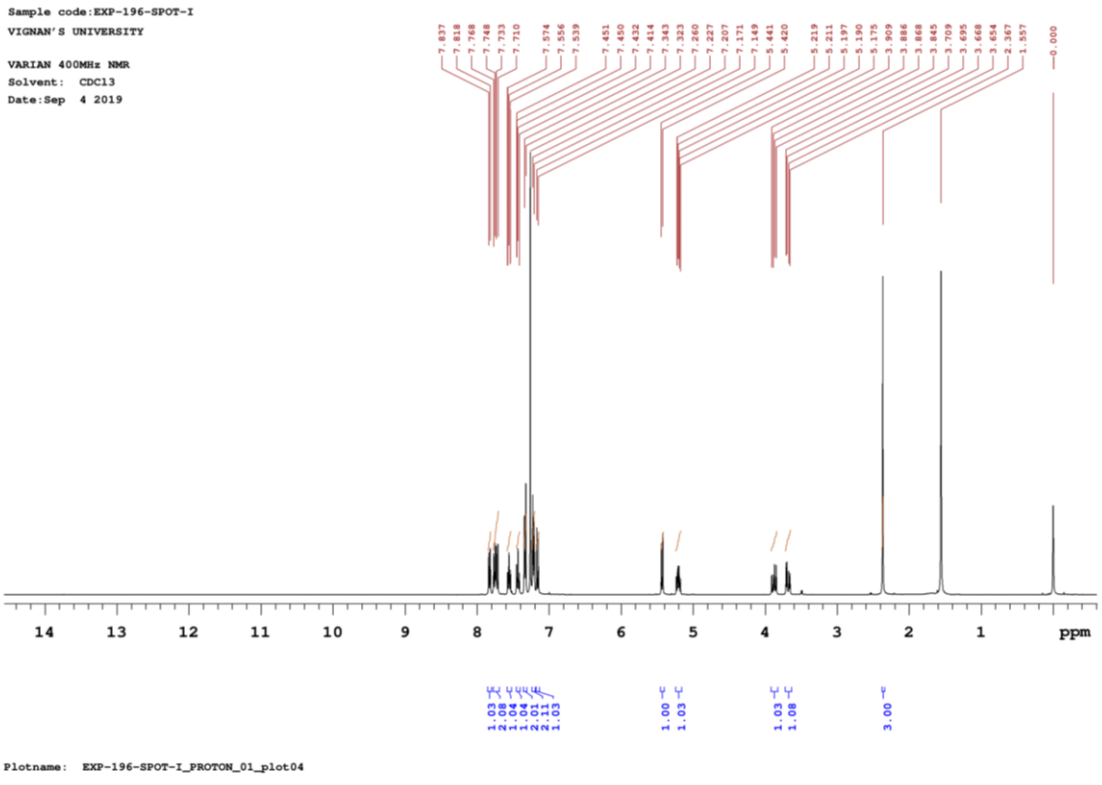




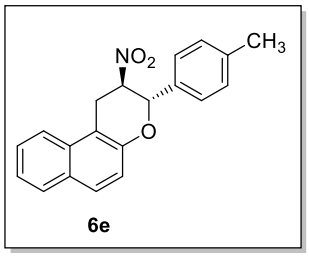
^{13}C NMR Spectra for compound **5e**



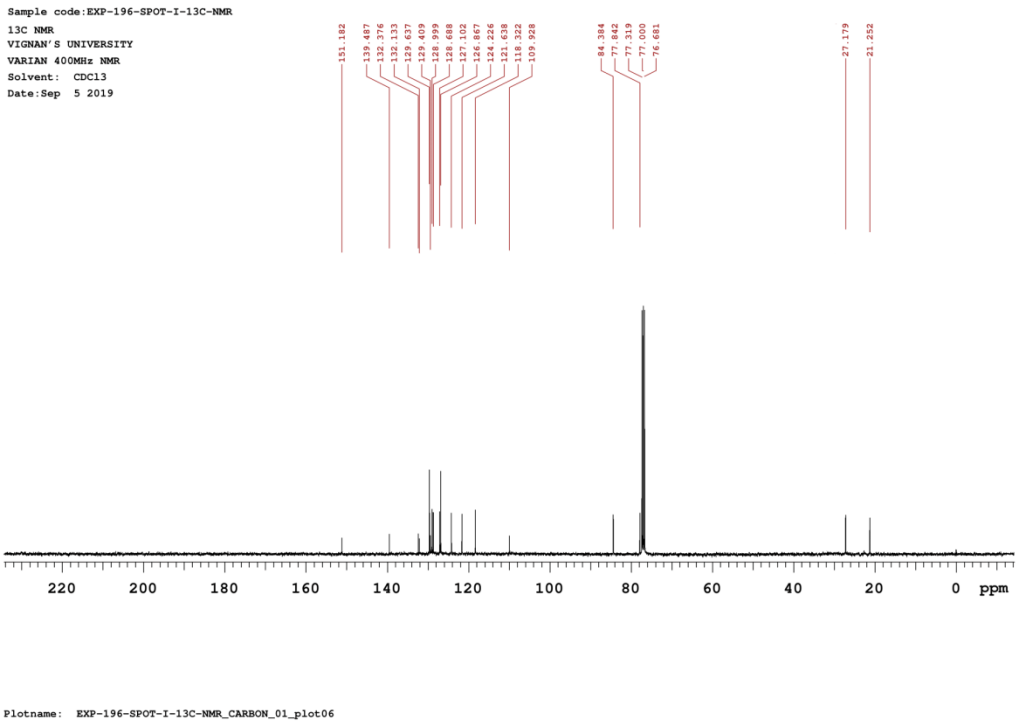
6e



^{1}H NMR Spectra for compound **6e**



6e



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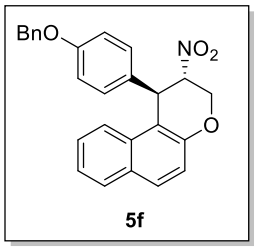
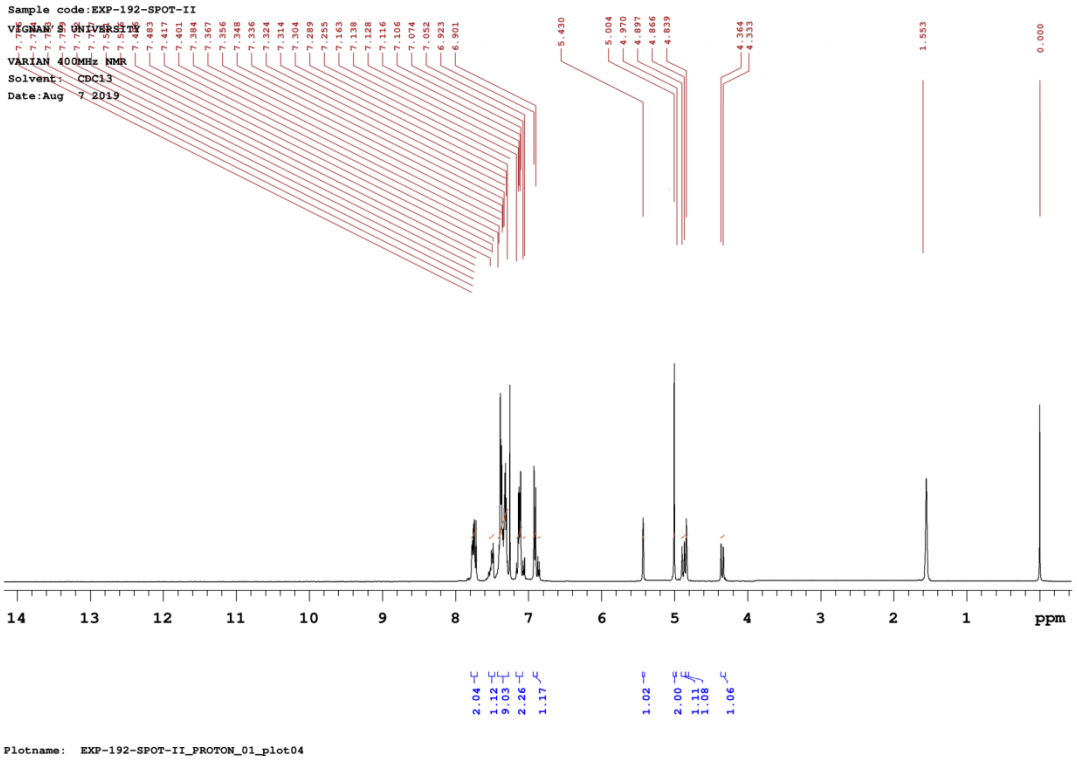
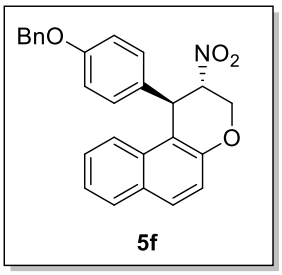
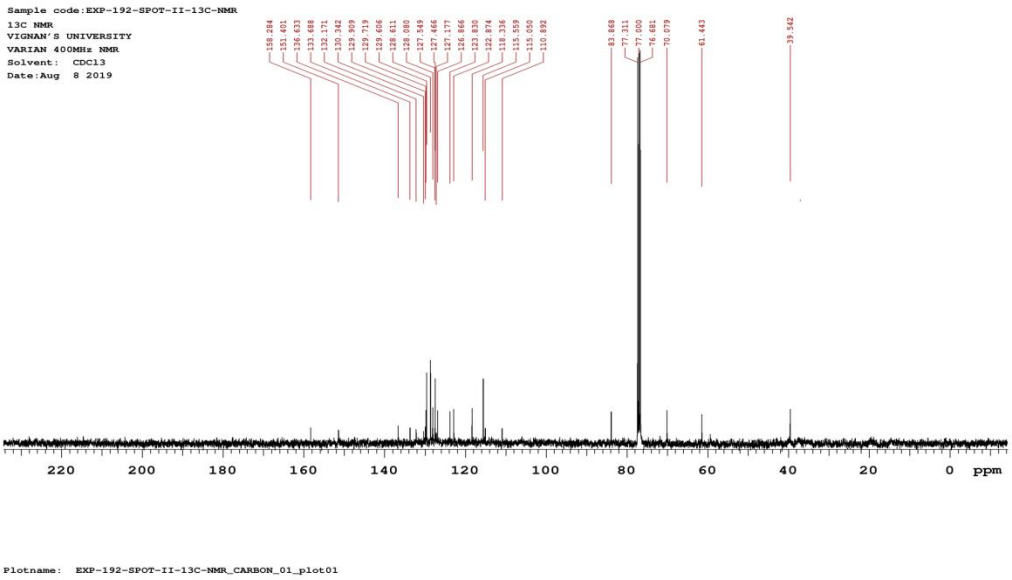


5f

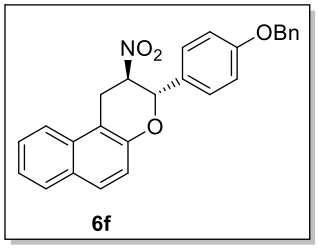


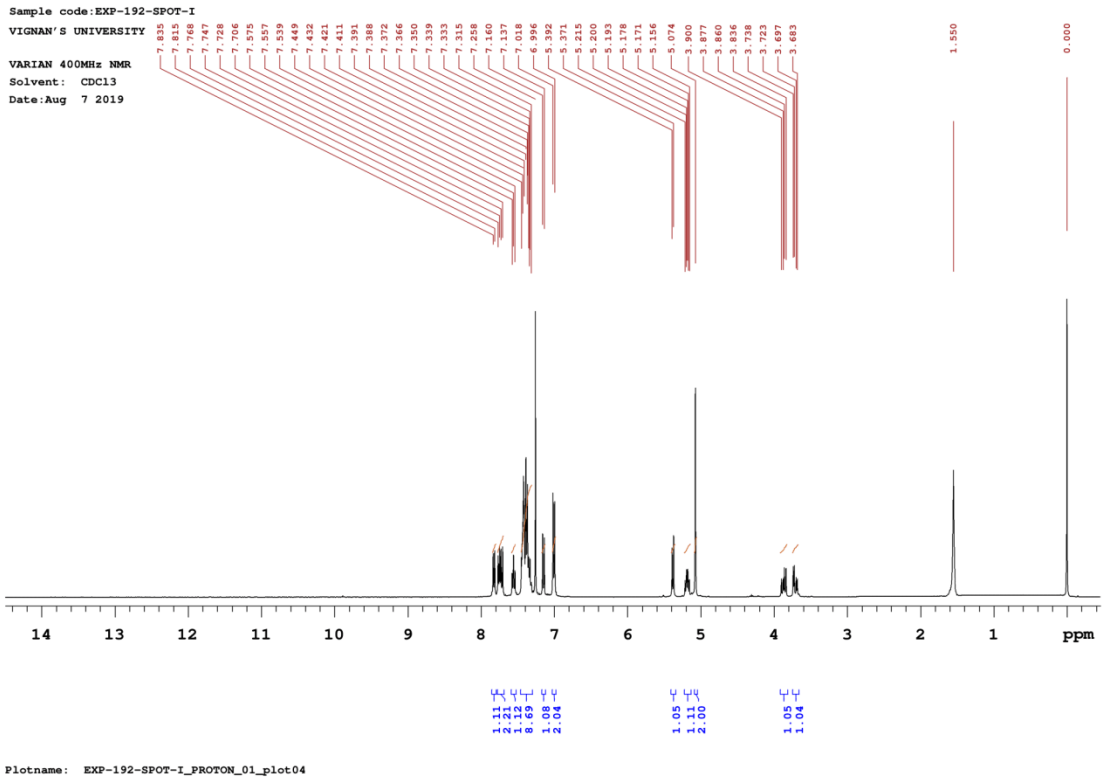
^{1}H NMR Spectra for compound **5f**



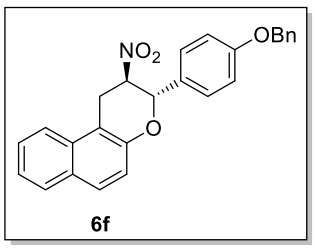


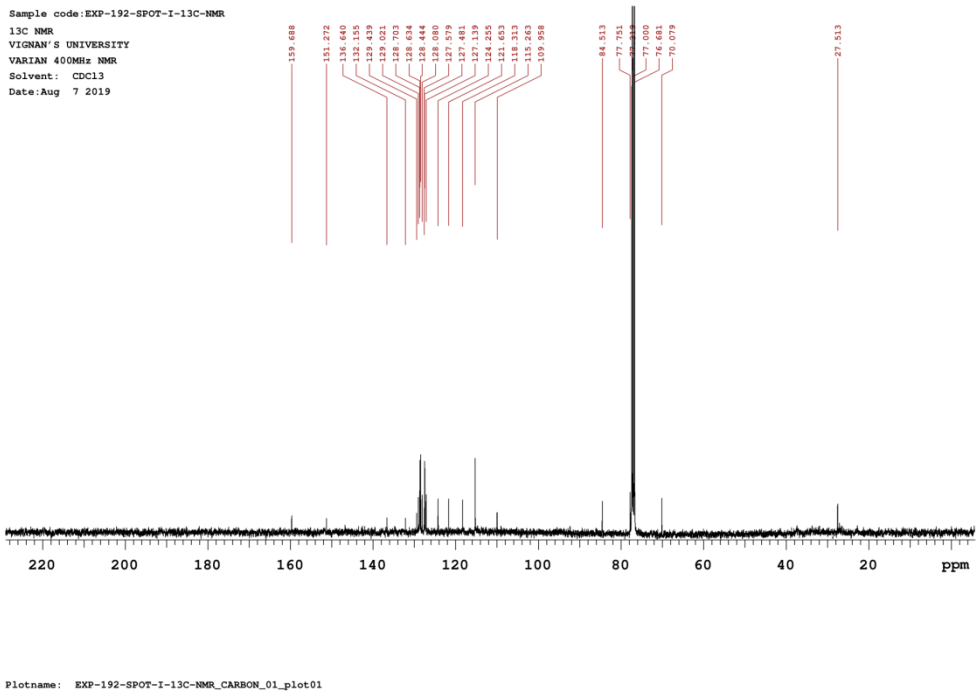
^{13}C NMR Spectra for compound **5f**



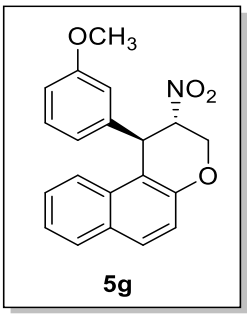


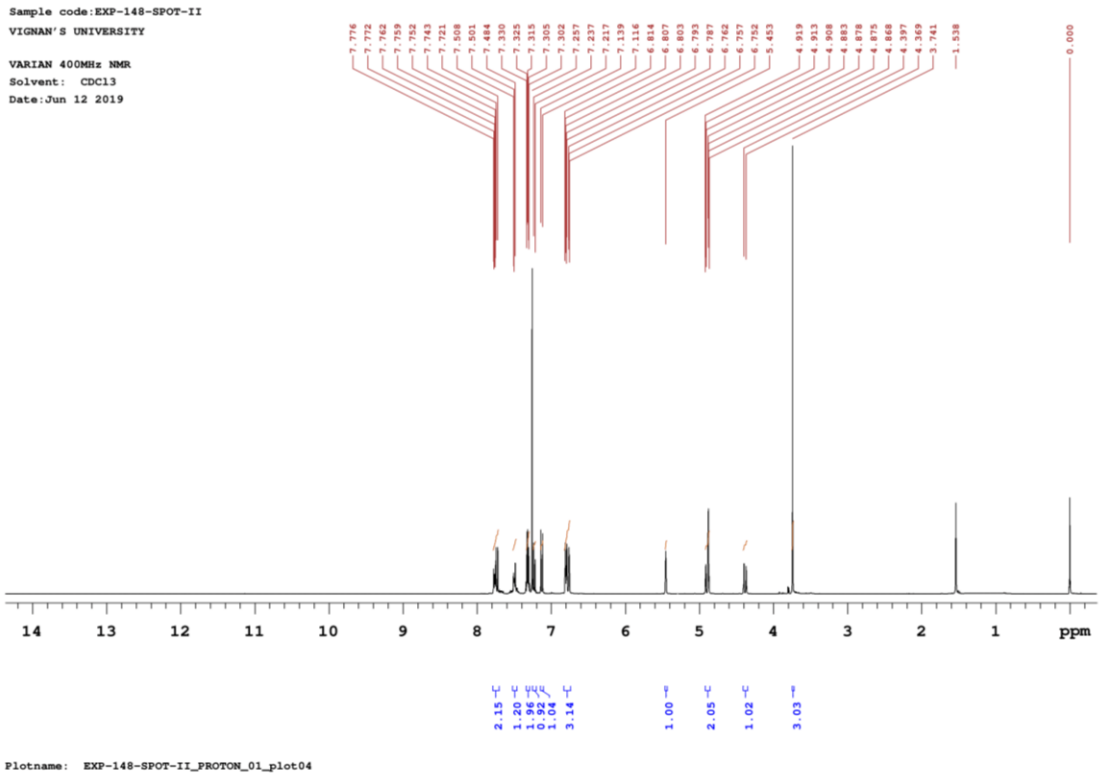
^{1}H NMR Spectra for compound **6f**



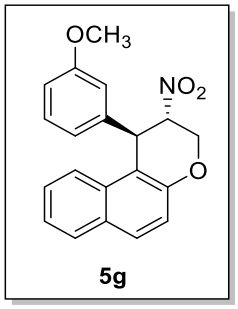


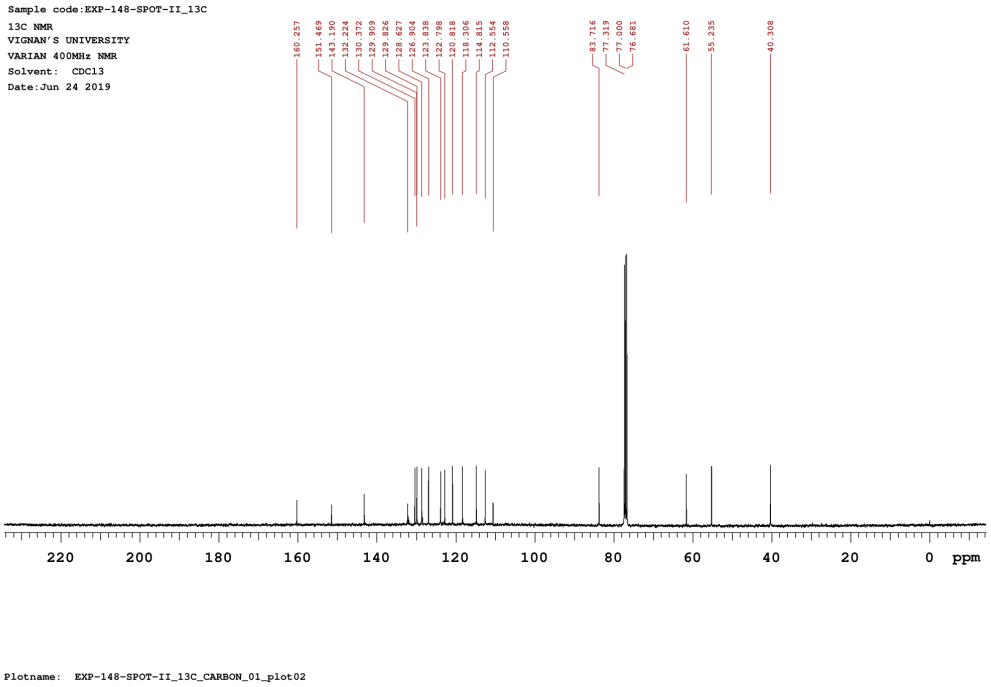
^{13}C NMR Spectra for compound **6f**



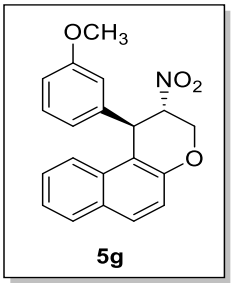


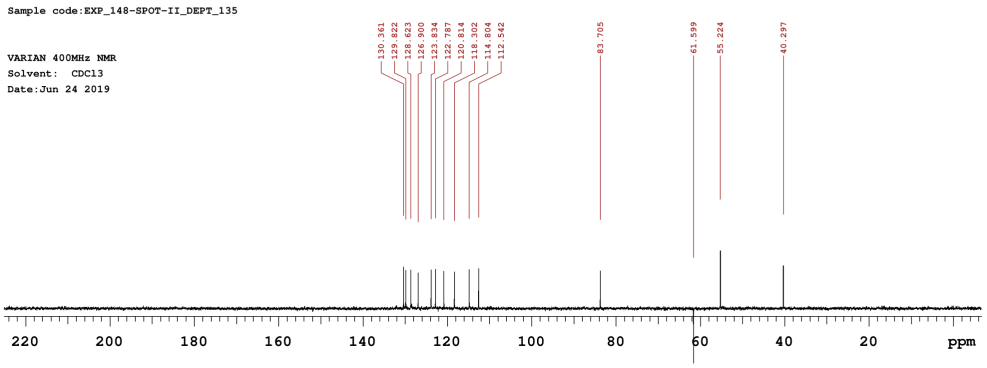
^{1}H NMR Spectra for compound **5g**



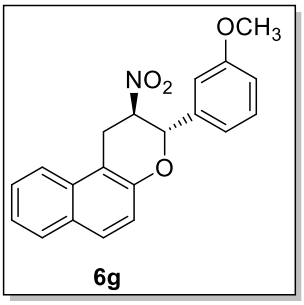


^{13}C NMR Spectra for compound **5g**





DEPT-135 Spectra for compound **5g**



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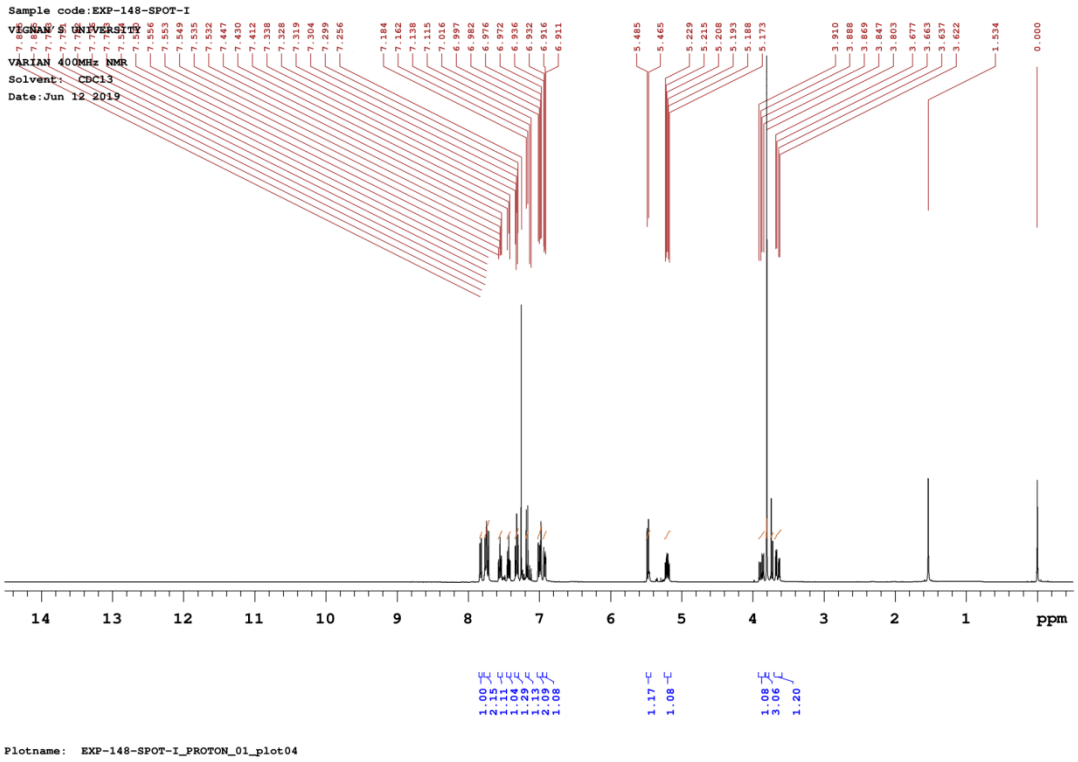
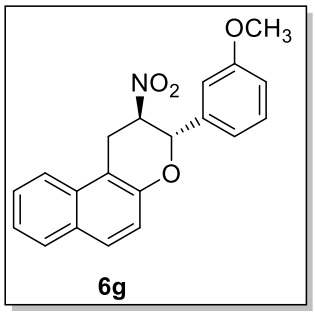
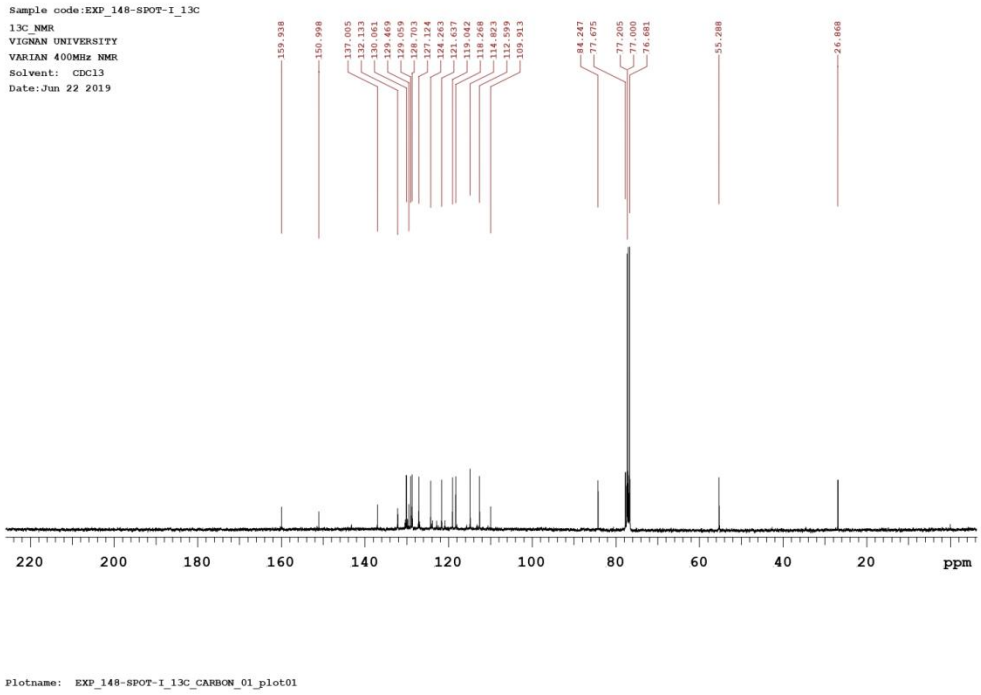
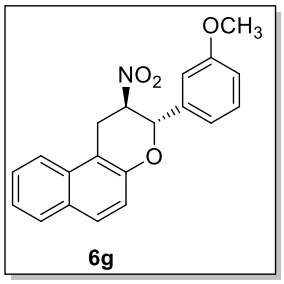


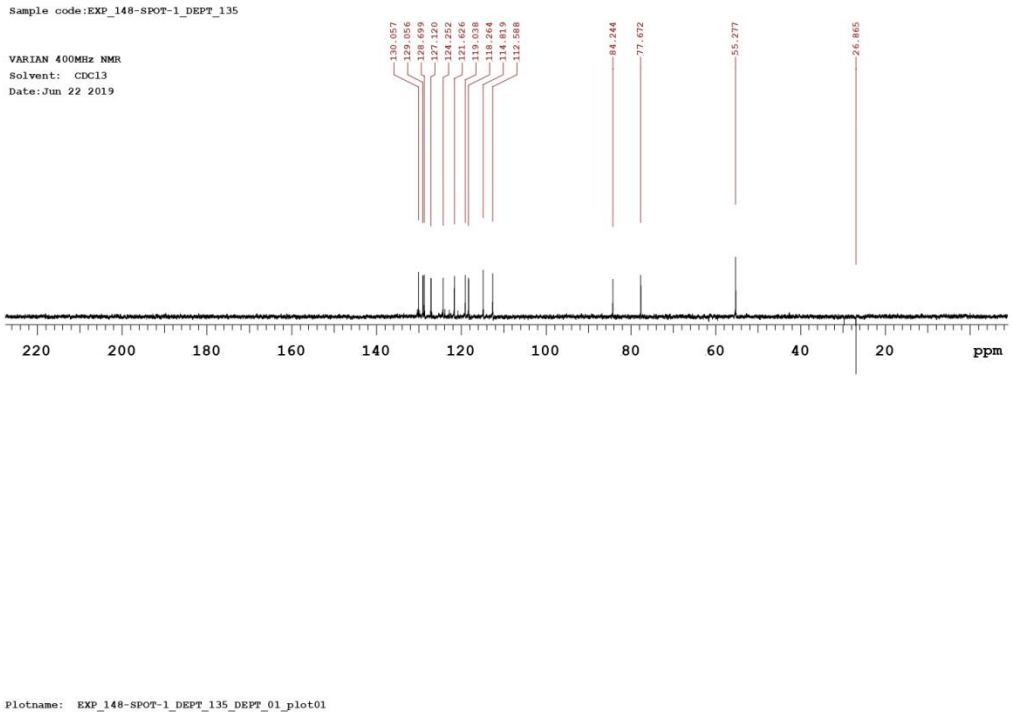
^{1}H NMR Spectra for compound **6g**



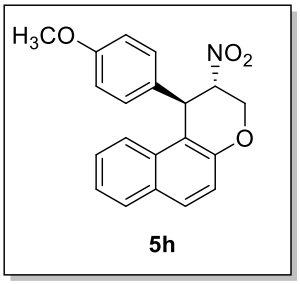


^{13}C NMR Spectra for compound **6g**

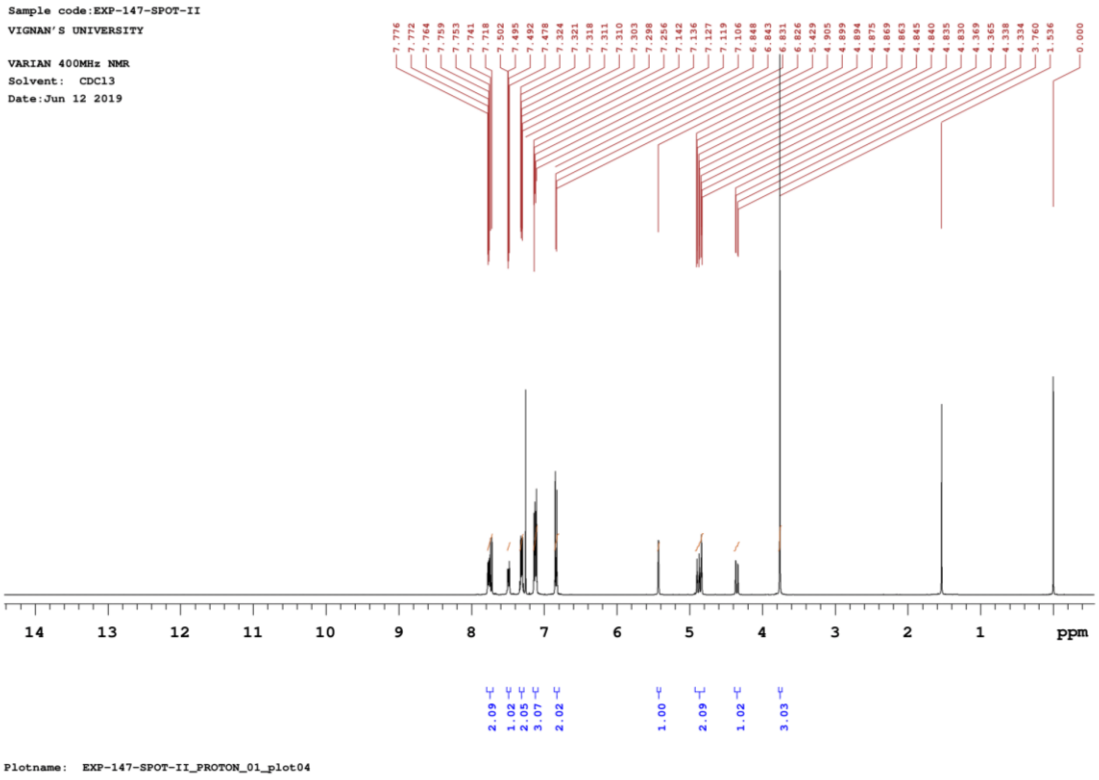




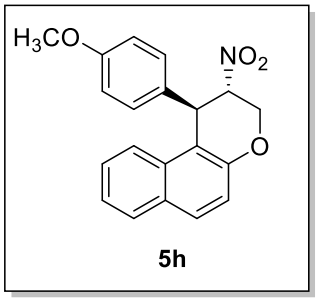
DEPT-135 Spectra for compound **6g**



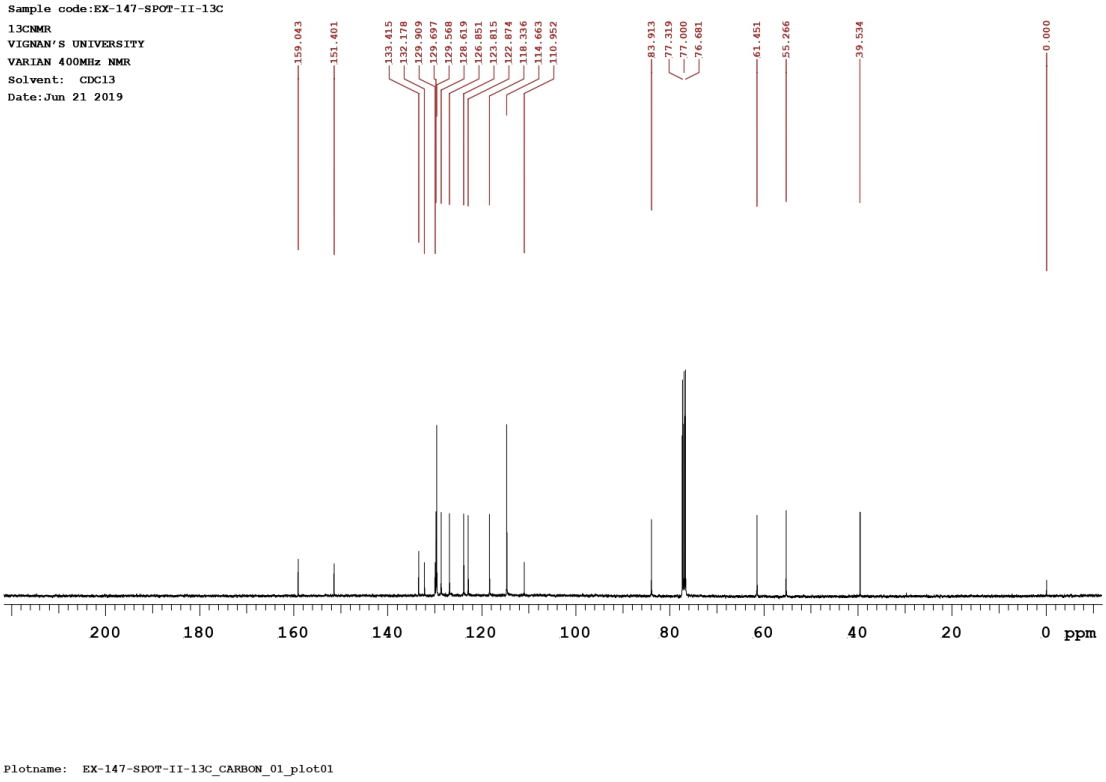
5h



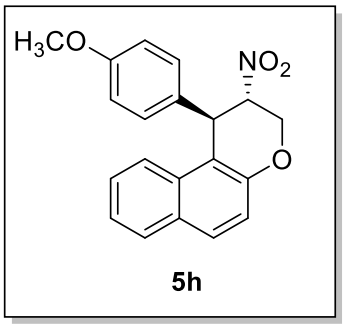
^{1}H NMR Spectra for compound **5h**

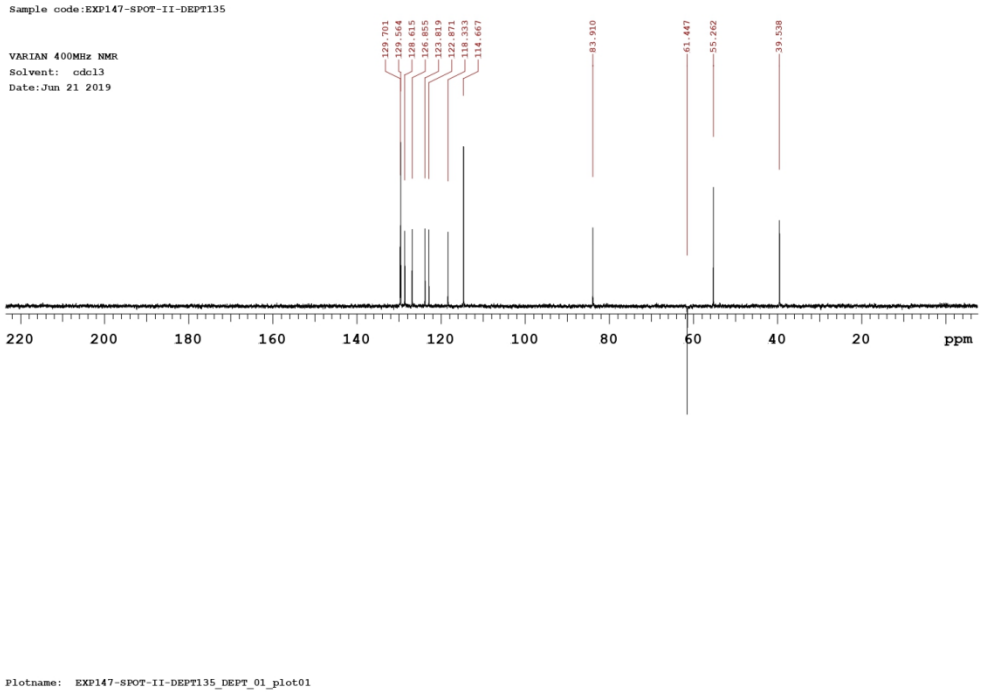


5h

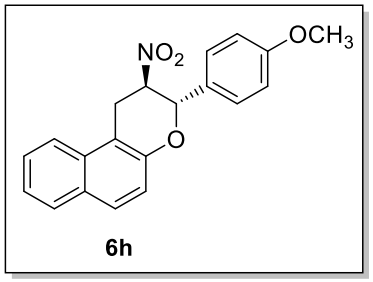


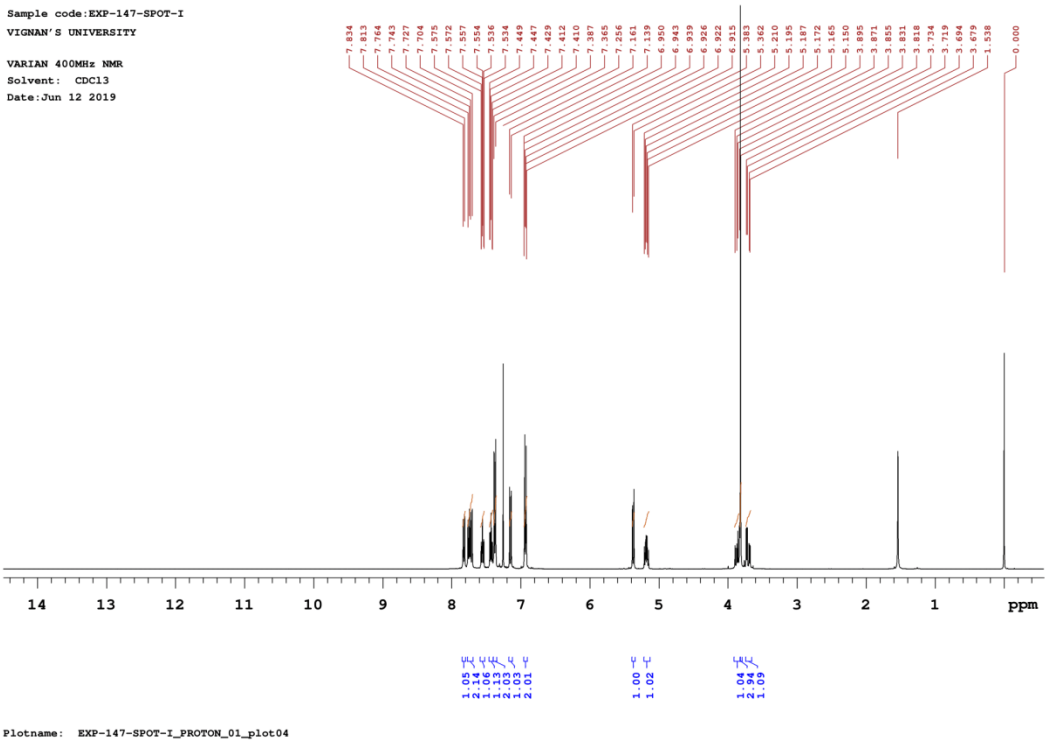
^{13}C NMR Spectra for compound **5h**



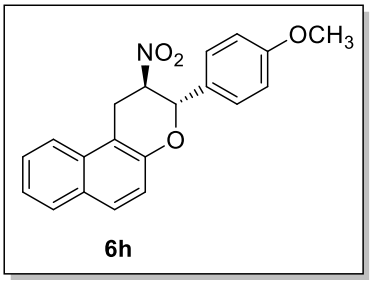


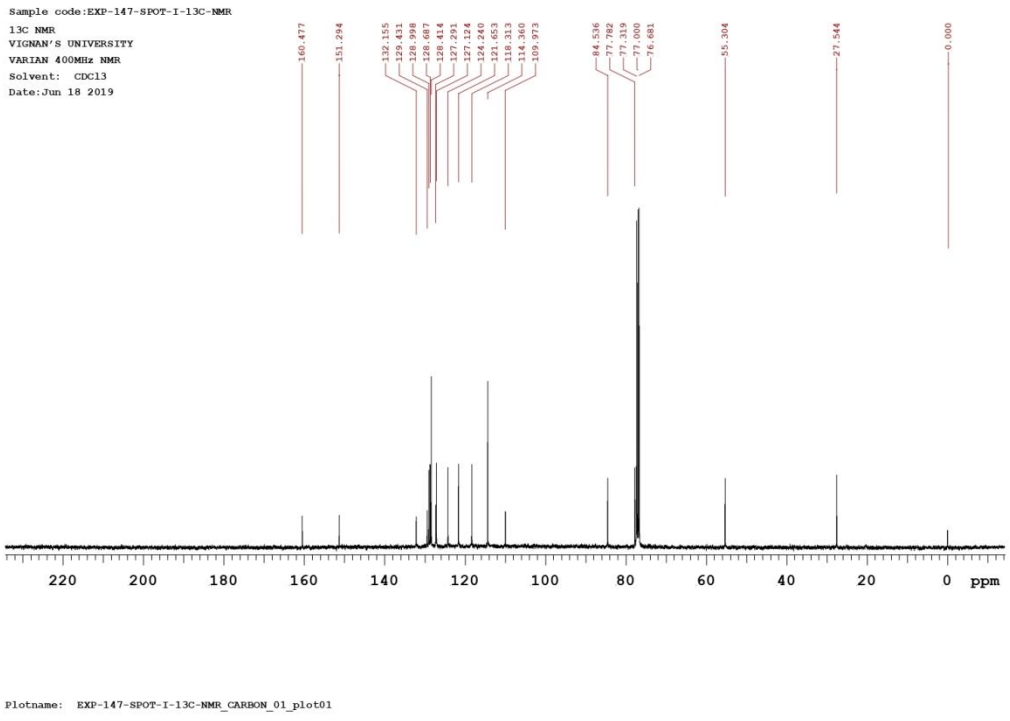
DEPT-135 Spectra for compound **5h**



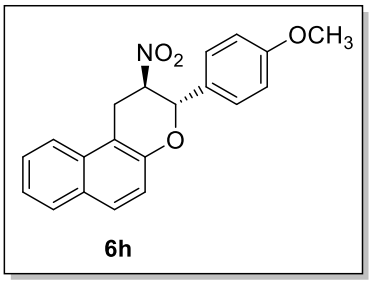


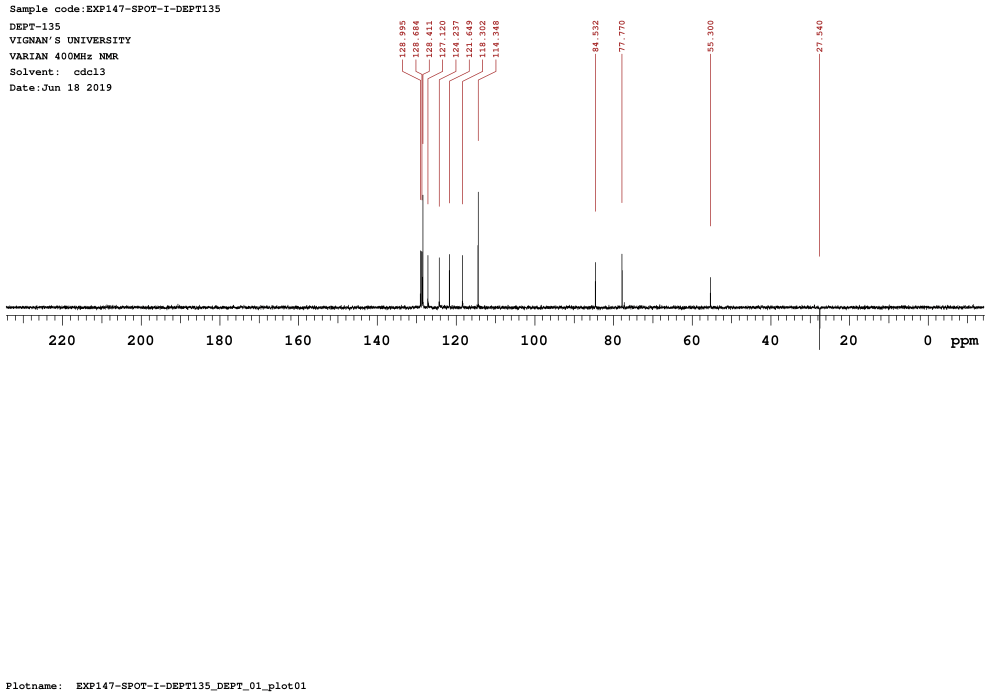
^{1}H NMR Spectra for compound **6h**



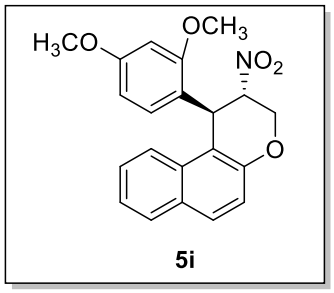


^{13}C NMR Spectra for compound **6h**

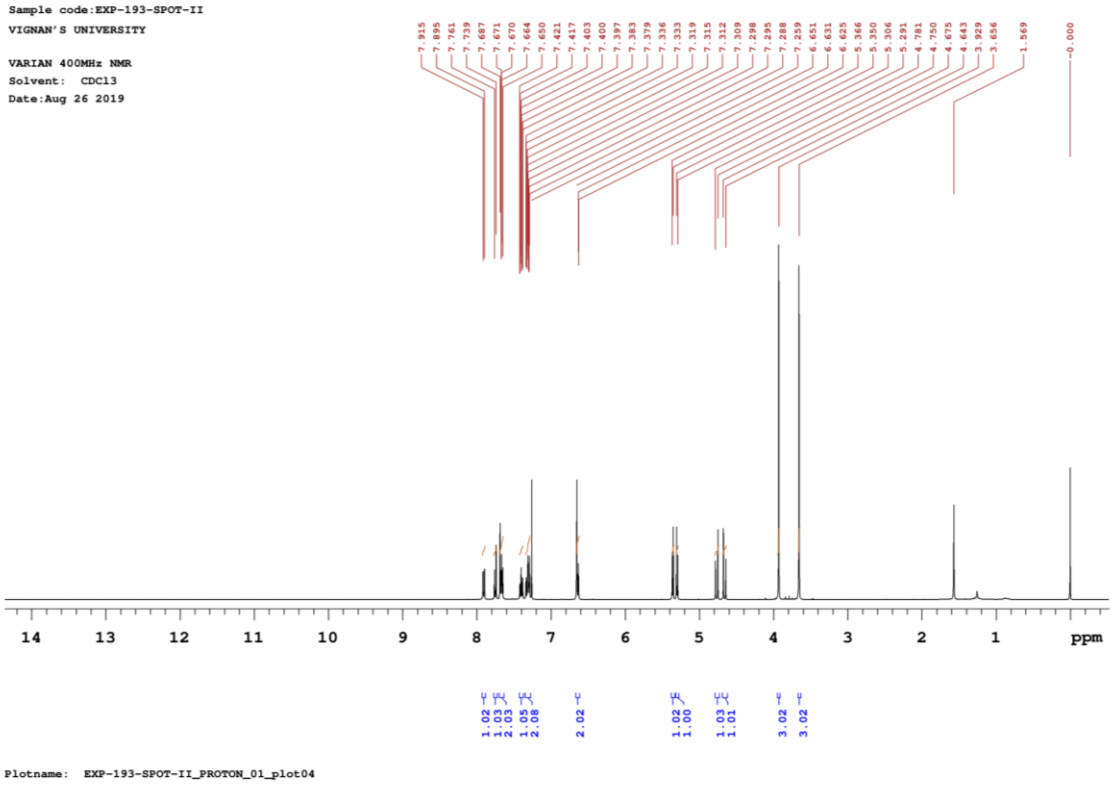




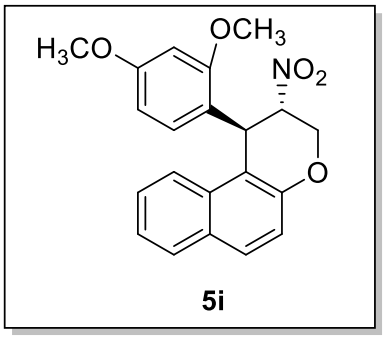
DEPT-135 Spectra for compound **6h**



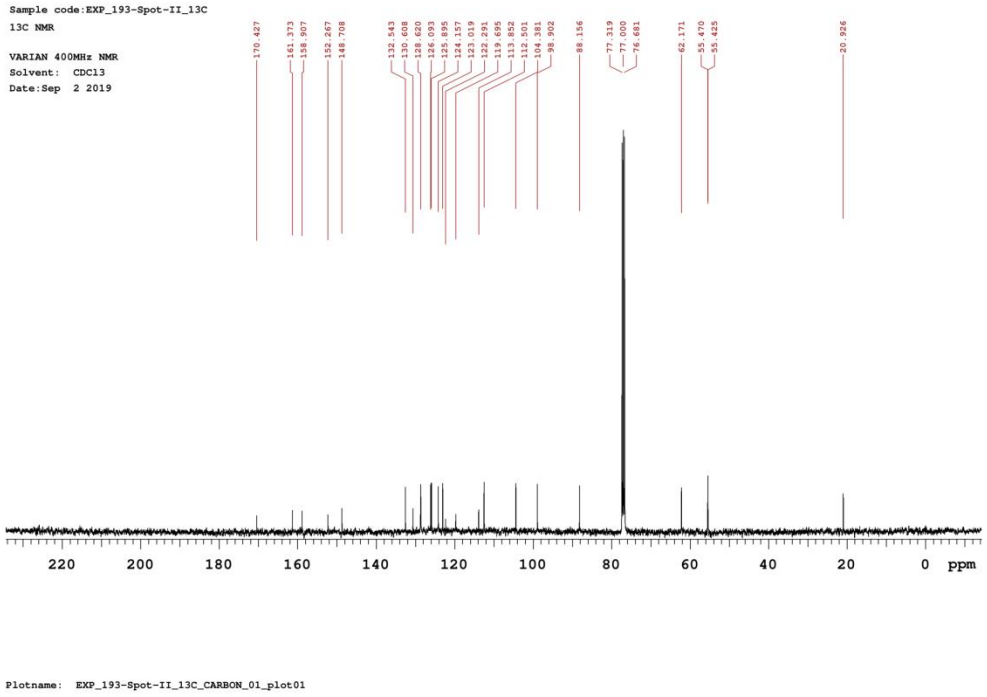
5i



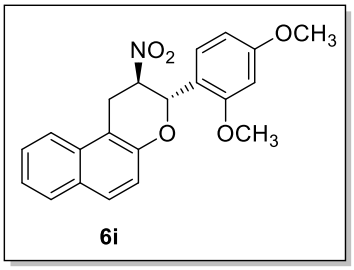
^{1}H NMR Spectra for compound **5i**



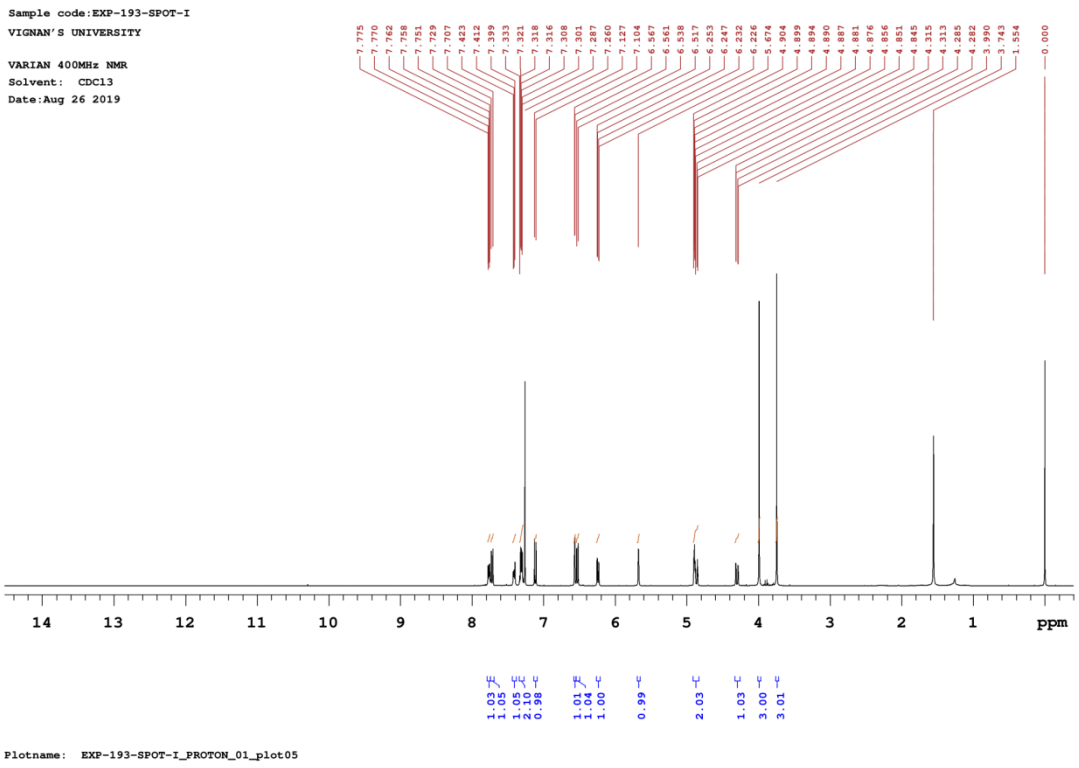
5i



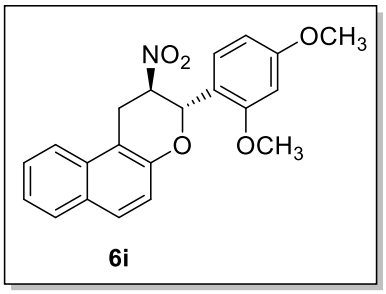
^{13}C NMR Spectra for compound **5i**



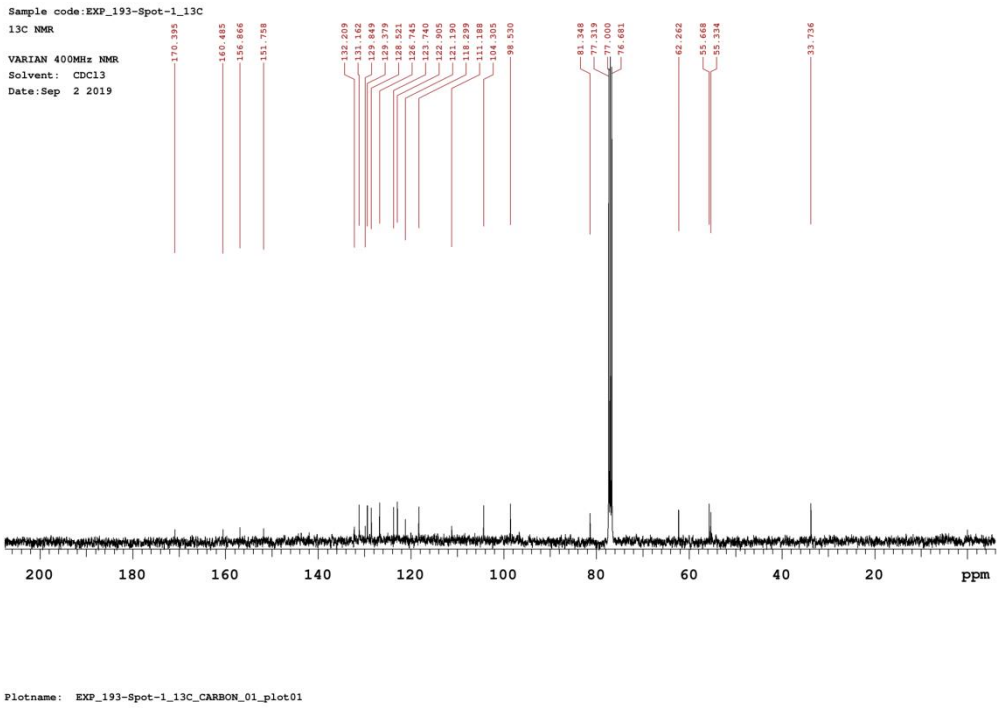
6i



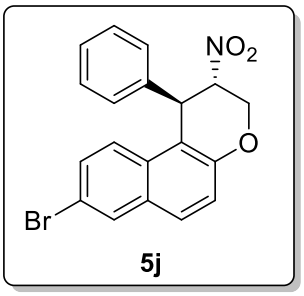
^{1}H NMR Spectra for compound **6i**



6i



^{13}C NMR Spectra for compound **6i**



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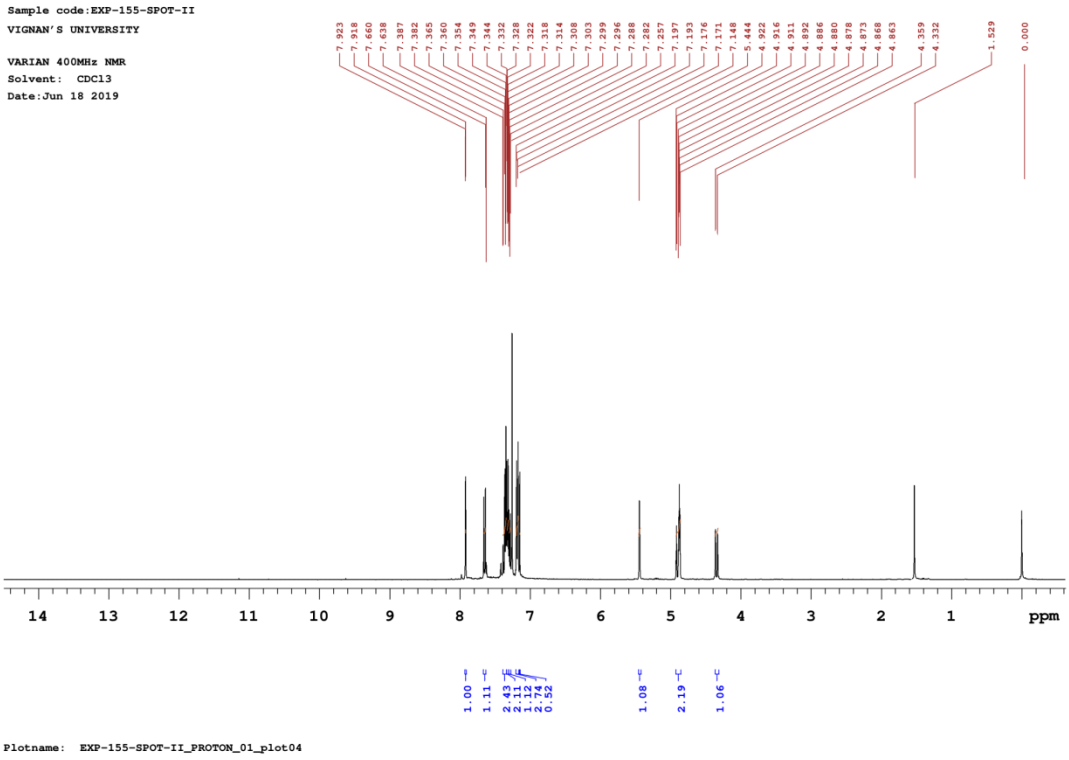

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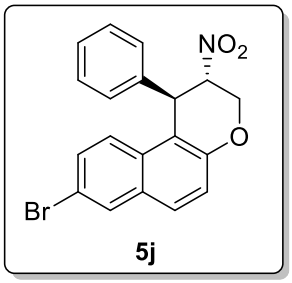
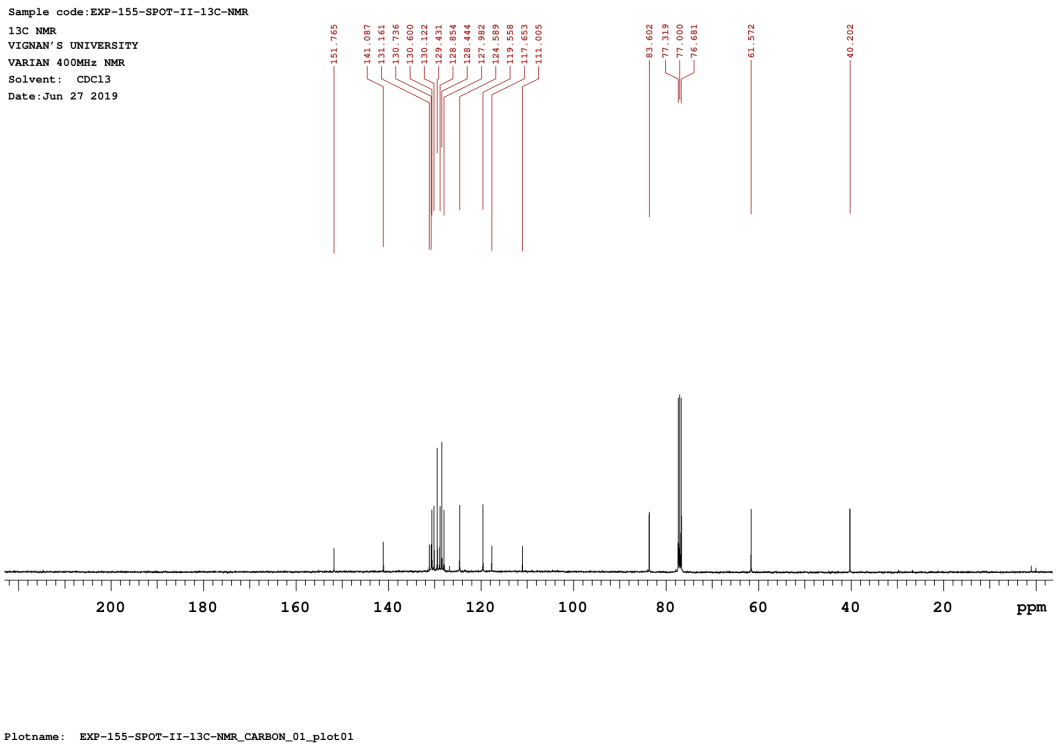


5j



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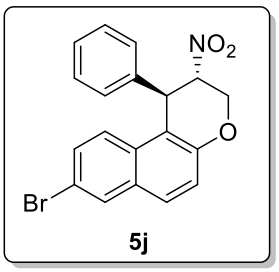
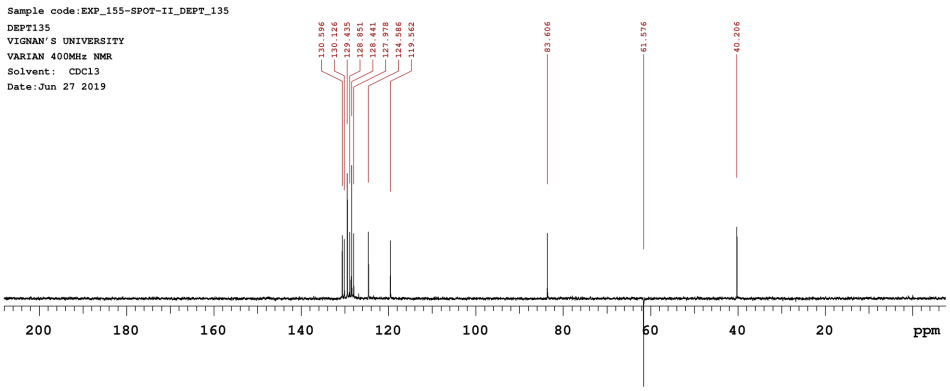
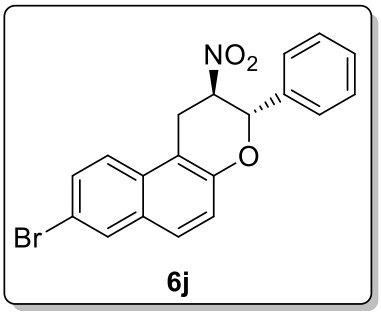




DEPT-135 Spectra for compound **5j**



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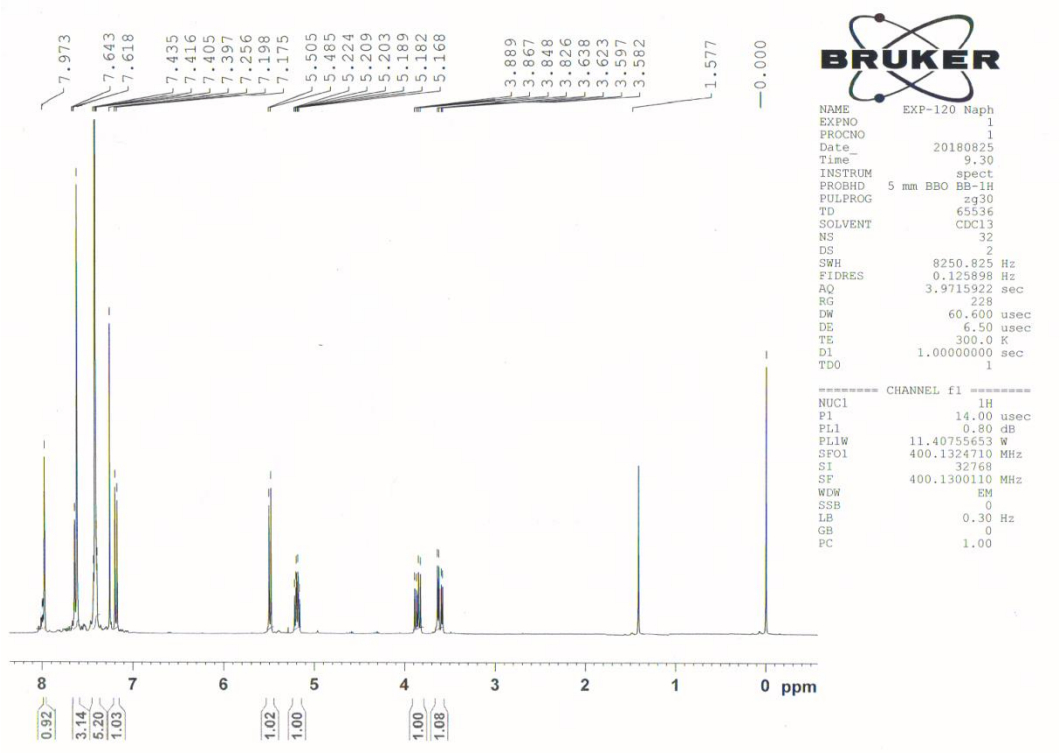
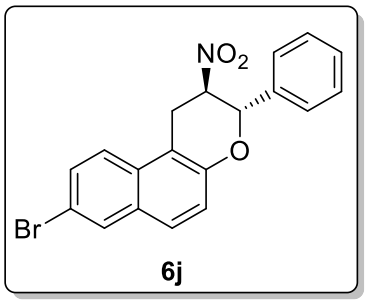


^{1}H NMR Spectra for compound **6j**



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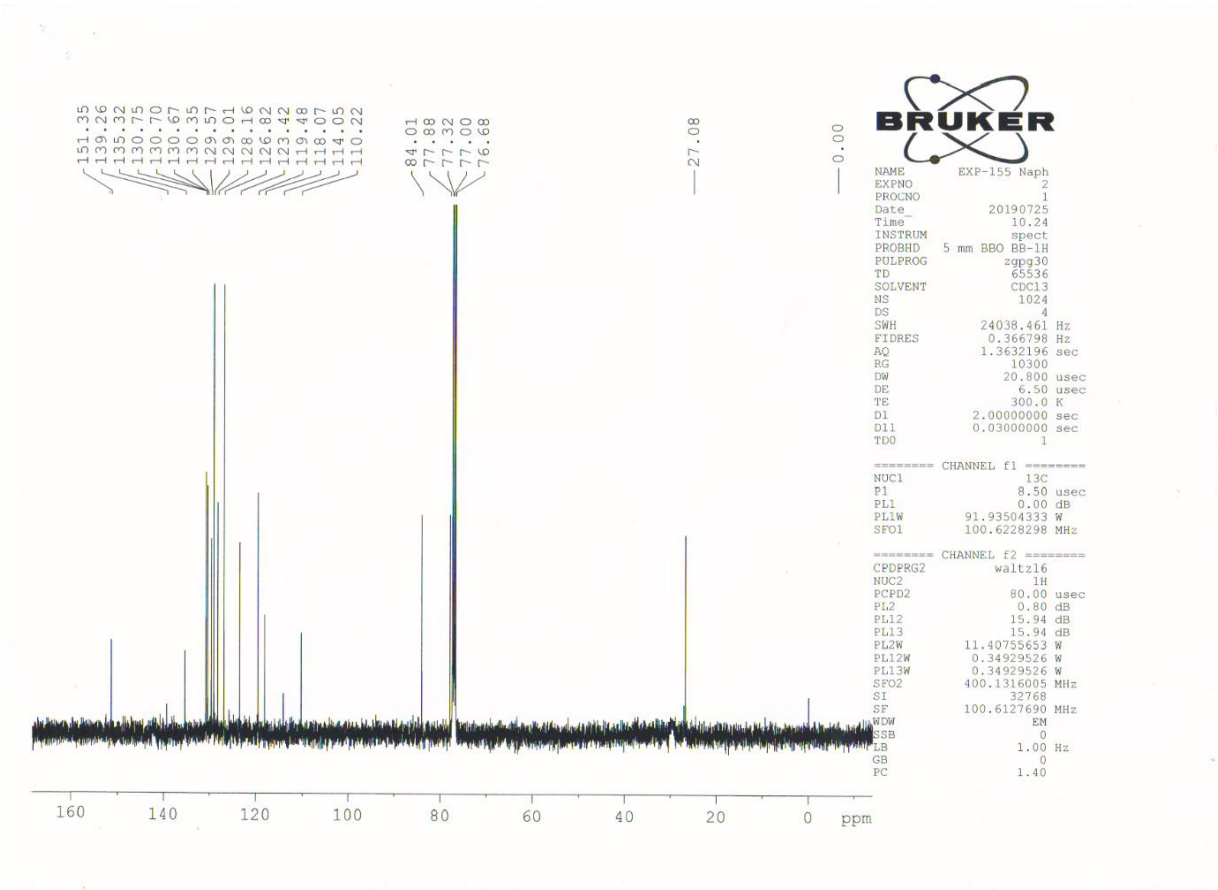
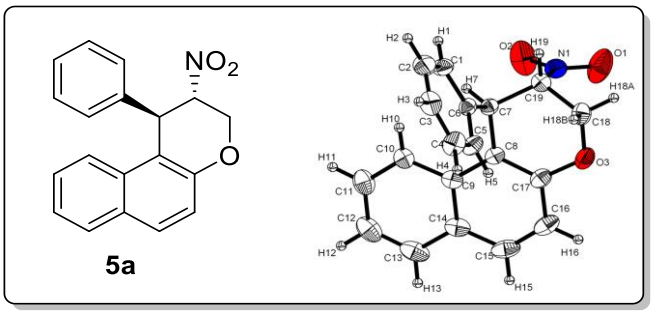


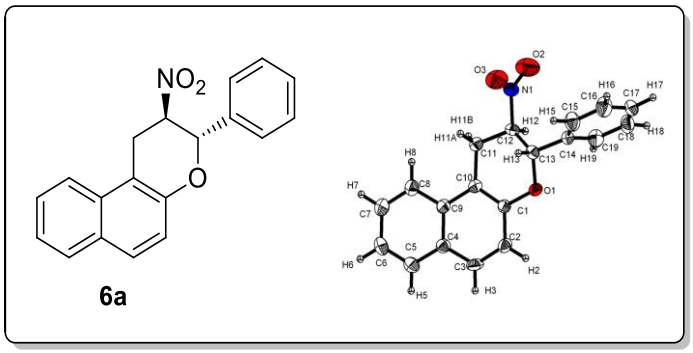
^{13}C NMR Spectra for compound **6j**

Crystal Data and structure refinement for product 5a



1. Identification code	5a
2. Chemical formula moiety	$C_{19}H_{15}NO_3$
3. Chemical formula sum	$C_{19}H_{15}NO_3$
4. Chemical Formula weight	305.32
5. Cell measurement Temperature [K]	296(2)
6. Crystal system	orthorhombic
7. Crystal size/mm^3	0.20 × 0.15× 0.10
8. Space group	*Pna21*
9. Cell formula units	*Z*4
10.Wavelength (Å)	0.71073
11.Cell length *a* [Å]	9.7984(2)
12.Cell Length *b* [Å]	11.7153(2)
13.Cell Length *c* [Å]	13.3345(3)
14.Cell Angle α [°]	90.000
15.Cell Angle β [°]	90.000
16.Cell Angle γ [°]	90.000
17.Cell Volume *V* [Å]^3	1530.68(5)
18.Calculated density [Mg/m^{-3}]	0.090
19.Reflections collected/ unique	32896/ 2665
20.Exptl crystal F(000)	640
21.θ range for data collection[°]	8.106 to 49.986
22.Refinement method	Full-matrix least-squares on F^2
23.Diffrn reflns limit h min	-11
24.Diffrn reflns limit h max	11
25.Diffrn reflns limit k min	-13
26.Diffrn reflns limit k max	13
27.Diffrn reflns limit l min	-15
28.Diffrn reflns limit l max	15
29.Data / restraints / parameters	2665 / 1 / 209
30.Goodness-of-fit on F^2	1.03
31.R_1/wR_2 [I>2sigma(I)]	0.0325/ 0.0819
32.R_1/wR_2 (all data)	0.0359/ 0.0855
33.Largest diff. peak and hole[e.Å^{-3}]	0.15 and -0.17

Crystal Data and structure refinement for product 6a



1. Identification code	6a
2. Chemical formula moiety	$C_{19}H_{15}NO_3$
3. Chemical formula sum	$C_{19}H_{15}NO_3$
4. Chemical Formula weight	305.32
5. Cell measurement Temperature [K]	296(2)
6. Crystal system	triclinic
7. Crystal size/mm^3	0.150 × 0.100× 0.080
8. Space group	*P-1*
9. Cell formula units *Z*	2
10.Wavelength (Å)	0.71073
11.Cell length *a* [Å]	5.368(2)
12.Cell Length *b* [Å]	12.130(4)
13.Cell Length *c* [Å]	12.428(4)
14.Cell Angle α [°]	107.145(16)
15.Cell Angle β [°]	96.128(18)
16.Cell Angle γ [°]	102.496(18)
17.Cell Volume *V* $[Å]^3$	744.7(5)
18.Calculated density $[Mg/m^{-3}]$	1.362
19.Reflections collected/ unique	0.0647/ 3372
20.Exptl crystal F(000)	320.0
21.θ range for data collection[°]	3.488 to 49.654
22.Refinement method	Full-matrix least-squares on F^2
23.Diffrn reflns limit h min	-6
24.Diffrn reflns limit h max	5
25.Diffrn reflns limit k min	-13
26.Diffrn reflns limit k max	14
27.Diffrn reflns limit l min	-14
28.Diffrn reflns limit l max	14
29.Data / restraints / parameters	6648 / 0 / 210
30.Goodness-of-fit on F^2	1.013
31.R_1/wR_2 [I>2sigma(I)]	0.0647/ 0.1322
32.R_1/wR_2 (all data)	0.1378/ 0.1720
33.Largest diff. peak and hole[$e.Å^{-3}$]	0.21 and -0.23

Chapter 7

Summary and Achievements of the Project

7. Summary and achievements of the project

In summary, we have demonstrated the utility of primary MBH acetate towards the formation of substituted naphthopyran derivatives. The formation of major product **5a** is accompanied by nucleophilic attack by 2-naphthol **2** on to α-position of MBH acetate **4a** resulting in C-C bond formation between sp^2-sp^2 carbon atoms. The unusual C-C bond formation between sp^2-sp^3 carbon atoms was also observed leading to formation of minor product **6a**. This is the first of this kind of study where the cascade process of C-C and O-C bond formation *via6- endo-trig* cyclization resulting in two possible products has been reasonably justified. Substituted naphthopyrans were synthesized at room temperature using a variety of primary MBH acetates derived from β-nitrostyrene. DFT calculations was carried out to account for formation of major product **5a** and minor product **6a**.

1. we developed cascade reactions for converting simple starting precursors to value added products such as biologically synthetic targets.
2. We Avoid the use of heavy metals for greener ecosystem.
3. We developed Mild reaction conditions
4. We synthesized a new set of Baylis-Hilman substrates and study their reactivity.
5. we carried out various multicomponent reactions.
6. We synthesized heterocyclic compounds.
7. We investigate the biological activity as a future plan.

Chapter 8

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8. References

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