Cyclizations of Benzofused 1,6-Enyne/Diyne Systems Towards Synthesis of Diverse Polyaromatic Hydrocarbons and Heterocycles

A Thesis
Submitted for the Degree of

DOCTOR OF PHILOSOPHY

In

CHEMISTRY

By

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(Reg. No. 15CHPH08)

Under the Supervision of

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June, 2022

"If you fail, never give up because F.A.I.L. means 'First Attempt In Learning'. End is not the end; in fact E.N.D. means 'Effort Never Dies'. If you get No as an answer, remember N.O. means 'Next Opportunity'. So Let's be positive."

..... Dr. A. P. J. Abdul Kalam

.....Dedicated to
My Parents

Dear Bapi and Maa,

Thank you for raising me as your "son".

All that I am and all that I hoped to be, I owe to you.

Thank you for all the confidence you gave me to be strong and believing in me in my tough time.

I hope that this achievement will fulfil the dream that you had for me.

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A. Published in the following publications:

M. Mandal and R. Balamurugan, *Adv. Synth. Catal.* **2018**, *360*, 1453-1465.
M. Mandal and R. Balamurugan, *Chemistry Select* **2019**, *4*, 10164-10168.
M. Mandal, S. Sakthivel and R. Balamurugan, *J. Org. Chem.* **2021**, *86*, 333-351.

B. Presented in the following Conferences:

1. 20th CRSI National Symposium-2017; 2. Chemfest-2017; 3. XIII J-NOST Conference-2017; 4. XIV J-NOST Conference-2018; 5. Chemfest-2019; 6. CTCPS International Seminar-2021; 7. XVII J-NOST Conference-2022.

Further the student has passed the following courses towards fulfillment of course work requirement for Ph. D.

Course code	Name	Credits	Pass/Fail
CY-801	Research Proposal	3	Pass
CY-805	Instrumental Methods A	3	Pass
CY-501	Spectroscopic Methods for Structure Elucidation	3	Pass
CY-402	Physical Organic Chemistry	3	Pass

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Acknowledgements

First and foremost, the contribution of my mentor Prof. Rengarajan Balamurugan, for this achievement can never be summoned into words, may be I can start by saying thank you sir. I am indebted to him for his constant guidance, precious advices, care and the freedom that he gave to me for working in different research projects. His progressive thinking and perseverance towards every research problem was admirable and motivating. Throughout my Ph.D tenure, he was always been approachable for any problem and he has helped in all the possible aspect. I am privileged to be a member of his esteemed research group. He has inspired me to have confidence in myself. I am thankful to him for imaparting skills that have shaped my carrier and professional life. Thank you sir, for making me see my achievement in different light. I can never really thank you enough.

I take this opportunity to thank Prof. A. Nangia, Dean, School of Chemistry and former deans for providing the facilities needed for our research. A special thanks to my doctoral committee members Prof. N. Nagarajan and Prof. S. K. Das for their special care and valuable suggestions during my research carrier. It is my pleasure to express my heartfelt thanks to Prof. A. K. Sahoo for his valuable suggestions and generiously providing TNT to carry out my chemosening project. I am thankful to Prof. A. Samanta for helping in fluorescence lifetime measurement study and his valuable suggestions. I extend my sincere thanks all the faculty members, School of Chemistry for their co-operation on various aspects.

I also thank all the non-teaching staff of the School of Chemistry for their assistance on various occasions. I thank DST and UGC for providing the required instruments and UGC-BSR for the financial support during my PhD tenure.

I express my heartfelt gratitude to Shanmu madam for her help, advice and encouragement. Special thanks to Meghalya and Varuksha.

It is my responsibility to thank all my lab members Ramana, Sakthivel, Tamilarasan, Chandrahas, Ramesh, Basha, Arun, Rina, Anjali, Satyajit and Shekar for their encouragement, pleasant company, helpful discussions and cooperation during this tenure. I wish to thank M. Sc project student Soumen and IAS summer project student Supriya.

I would like to thank all my family and in-laws family members for their sacrifice and patience till the completion of my research work. I am very much grateful to my Bapi (father) Dibakar Mandal, and maa (mother) Saradamani Mandal who have struggeled a lot to make me as a first graduate in science from my family. Without their effort I would have not reached at this position. I am grateful to my grandmother Parulbala Mandal, my uncles Nishakar Mandal and Prabir Mandal, my aunts Mira Mandal, Suchitra Mandal, Sumitra Mandal and Anindita Mandal who always bless me for the betterment of my life. I extend my sincere thanks to my brothers Koustuv Kanti Mandal and Sourav Mandal, sister-in-law Sabitri Mandal for their

immense support. From the bottom of my heart, I thank my Dabhai (Koushik Ghosh) for his valuable suggestions and co-operation during my Ph.D tenure. I am indebted to my father-in-law Arun Kumar Saha and mother-in-law Kalpana Saha for their relentless support, blessings and love. My sincere thanks to my sister-in-law Debrupa Saha and brother-in-law Sanjib Saha for their assistance throughout my research carrier. I record my special thanks to my little masters (nephews) Naitik and Shreyansh for making my life enjoyable and memorable.

Especially, a special thanks to my hysband Arijit who sacrificed a lot to support my research carrier and abetted me in all aspect. Through out the ups and downs of life, he never left my side, thank you for being my rock. Without him I would have been like a cut off kite, drifting away aimlessly. Thank you for keeping me safe and showing me direction in life.

I wish to express my sincere thanks to my friends Ankit, Tanmay, Tasnim, Apurba, Chandni, Saddam, Anif, Sankar, Sandeep, Manish, Manjoor and Harilal for their valuable support in the school of chemistry. Also I would like to thank all the research scholar in school of chemistry and special thanks to Narenda, Sutanukadi, Rajada, Rudrada, Sugatada, Prabagar anna, Tamilarasidi, Arpitadi, Navenduda, Sumanda, Majji bhai, Ranjanidi, Suiptada, Rajendra bhai, Kallolda, Snehadi, Sabaridi, Nagamaiah anna, Prabhakar anna, Anjanadi, Anjaneyulu, Kalyani, Mamina, Jotsna, Ishfaq, Subham, Manash, Pritam, Gorachand, Sarada, Soutrik, Joykrushna, Anupam, Nilanjan, Arghyadip, Somratan, Debu, Manoj, Aradhana, Konety, Abhijit.

My hearty thanks to my special friends (my HCU family) Sameeta and Sipra who suppoted me and helped me through out this tenure in every aspect. They were always there to hear me whether I was cracking a stupid joke, complaining about life or just blabbering. Thanks for being a non-judgmental listeners and true friends.

It is my pleasure to express my heartfelt thanks to all my B.Sc and M.Sc friends Atasi, Madhabi, Preeti, Aropita, Moupiya, Snigdha, Ishita, Rohit and Debanjan. It is my pleasure to thank my childhood friends Bidisa, Sudip, Samit, Sudipta, Putul, Amit and Anupam for their support and concern in every stage of my life.

I would like to acknowledge all my teachers throughout my studies. A special and heartfelt thanks to school teachers Nilratan Mandal, Joydeb Jana, Rabindranath Maji, Bsc teachers Dr. Tridib Tripathi, Dr. Mahadev Maity, Prasanna Duley for their special effort during my studies. Especially, I am thankful to my M.Sc teachers Dr. Subhash Banerjee, Dr. V. K. Raman, Dr. Kalpataru Das for inspiring me and encouraging me to start my research carrier. It's my pleasure to thank Dr. Ratnesh Das with whom I have started my research carrier as a project fellow.

Lastly this acknowledgement would be incomplete without express my gratitude to all my family members, lab mates, friends and teachers who have been a constant source of inspiration and support throughout my Ph.D tenure.

University of Hyderabad

June, 2022

Mou Mandal

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List of Acronyms

Å	Angstrom
Ac	acetyl
ACN	acetonitrile
AIBN	azobisisobutyronitrile
Aq.	Aqueous
Ar	aryl
α	alpha
BA	Brønsted acid
Bn	benzyl
Br s	Broad singlet (spectral)
^{n}Bu	n-butyl
^{t}Bu	*tert*-butyl
Bz	benzoyl
β	beta
C	concentration
°C	degree celsius
cat.	catalyst
calcd	calculated
cm^{-1}	Wavenumber(s)
^{13}C NMR	carbon-13 nuclear magnetic resonance spectroscopy
conc.	Concentrated
COPs	covalent organic polymers
CH_3CN	acetonitrile
$CHCl_3$	chloroform
COSY	^{1}H-^{1}H correlation spectroscopy
δ	Chemical shift in parts per million
d	doublet
D-A	DielsAlder
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCC	N,N′-Dicyclohexylcarbodiimide
1,2-DCE	1,2-dichloroethane
DCM	dichloromethane
dd	doublet of doublet
DDQ	2,3-dichloro-5,6-dicyanobenzoquinone
DFT	Density functional theory
dil.	Dilute
DMAP	4-dimethylaminopyridine
DMF	*N*,*N*-dimethylformamide
DMSO	dimethyl sulfoxide
DNT	Dinitrotoluene
dr	Diastereomeric ratio
dt	doublet of triplet

δ	delta
e.g.	exempli gratia
EPR	Electron paramagnetic resonance
Equiv.	equivalent
ESI	electron spray ionization
Et	ethyl
EtOAc	Ethyl acetate
EtOH	Ethyl alcohol
EWG	electron-withdrawing group
FT-IR	fourier transform infrared spectroscopy
FWHM	full width half maxima
E^+	electrophile
ECL	electrogenerated chemiluminescence
FL	Fluorescence
f_k^+	Fukui functions for the nucleophilic attack
f_k^-	Fukui functions for the electrophilic attack
g	gram
γ	gamma
h	hour
HETCOR	^{13}C-^{1}H correlation spectroscopy
HFIP	Hexafluoroisopropanol
^{1}H NMR	proton nuclear magnetic resonance spectroscopy
HOMO	Highest occupied molecular orbital
HRMS	high-resolution mass spectroscopy
Hz	hertz
int	intermediate
IR	Infrared
J	coupling constant in hertz
K	Kelvin (Temperature)
LA	Lewis acid
LUMO	Lowest energy unoccupied molecular orbital
M	Molar (Solution concentration)
m	Multiplet (spectral)
Me	Methyl
MeCN	Acetonitrile
MeOH	Methanol
mg	milligram
MHz	Megahertz
min	Minute(s)
MIPs	molecularly imprinted polymers
mL	milliliter
mmol	millimole
MOFs	metal-organic frameworks
m.p.	melting point
MS	Molecular sieves
µL	microlitre
μ	electronic chemical potential
N_2	nitrogen
NBO	natural bond orbital

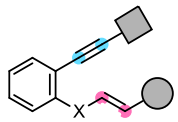
***n*-BuLi**	n-Butyllithium
nM	nanomolar
NMR	Nuclear magnetic resonance
NOE	Nuclear overhauser effect
NOESY	Nuclear overhauser effect spectroscopy
NQR	nuclear quadrupole resonance
Nu	nucleophile
OFET	organic field-effect transistor
OLEDs	organic light emitting diodes
ORTEP	Oak ridge thermal ellipsoid plot
OTf	Trifluoromethanesulfonate
PA	Picric acid
PAHs	Polycyclic aromatic hydrocarbons
PCM	polarisable continuum model
Ph	phenyl
^{i}Pr	isopropyl
^{n}Pr	n-propyl
prc	pre-reaction complex
PTSA/p-TsOH	p-Toluenesulfonic acid
q	Quartet (spectral)
RCI	rate-controlling intermediate
RCTS	rate-controlling transition state
R_f	retention factor
RT	room temperature
Rh	rhodium
s	Singlet (spectral)
SERS	Surface-enhanced Raman spectroscopy
t	Triplet (spectral)
TBAF	tetrabutylammonium fluoride
TBHP	tert-Butyl hydroperoxide
TCSPC	Time Correlated Single Photon Counting
td	Triplet of doublets(spectral)
TEMPO	(2,2,6,6-tetramethylpiperidin-1-yl)oxy
TEOF	triethyl orthoformate
TFA	Trifluoroacetic acid
TFE	2,2,2-Trifluoroethanol
TfOH	Triflic acid
THF	tetrahydrofuran
THP	tetrahydropyran
TLC	thin-layer Chromatography
TMOF	Trimethyl orthoformate
TMS	trimethylsilyl
TNT	Trinitrotoluene
Ts	tosyl
ts	Transition state
UV	Ultraviolet
η	chemical hardness
ω	global electrophilicity index

Synopsis

This thesis entitled "**Cyclizations of Benzofused 1,6-Enyne/Diyne Systems Towards Synthesis of Diverse Polyaromatic Hydrocarbons and Heterocycles** " contains four chapters. The first chapter presents the cyclization possibilities of 1,n-enyne/diyne/diene systems leading to polyaromatic hydrocarbons (PAHs) and heterocycles highlighting selected literature precedents. Chapter 2 describes the cationic cyclizations of 1,6-enyne-3-ones for the synthesis of benzo[*a*]fluorenes and fluorescent benzo[*a*]fluorenones and applications of benzo[*a*]fluorenones as chemosensors. Chapter 3 presents a diversity-oriented synthesis of benzo[*a*]fluorenes, benzo[*b*]fluorenones and naphthyl ketones from aryl-fused 1,6-diyn-3-ones. Chapter 4 deliberates two different cyclization modes of vinylogous amides derived from *o*-alkynylanilines under different reaction conditions. This chapter has two parts. The first part presents the gold-catalyzed cyclization leading to benzo[*b*]azepine framework. In the second part, TfOH-catalyzed synthesis of indoles and benzofurans involving cyclative transposition of vinyl ketone is discussed.

Chapter 1: Diverse Cyclization Cascades of 1,n-Enyne/Diyne/Diene Systems : Access to an Array of Polyaromatic Hydrocarbons and Heterocycles

Polyaromatic hydrocarbons and heterocyclic compounds are extremely versatile class of organic compounds, which has wide application in the field of medicinal chemistry as well as material science. Cycloisomerizations of 1,n-enynes/diynes/dienes have developed as exclusive tools to achieve a diverse range of cyclic compounds, polyaromatic hydrocarbons and heterocyclic compounds in an operationally simple one-pot method. The synthetic possibilities of 1,6-enyne/diyne/diene systems are discussed in this chapter. Also, the 1,6-enynes or diynes precursors **1** used for this thesis work have been introduced in this chapter.



X = C=O or N-R or O

1

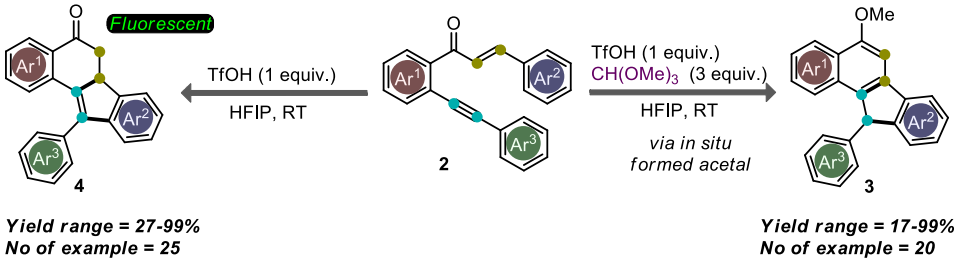
Figure 1. 1,6-Enyne or diyne precursors employed for this thesis work.

Chapter 2: Triflic Acid-Mediated Cyclizations of 1,6-Enyne-3-ones: Synthesis of Benzo[*a*]fluorenes and Fluorescent Benzo[*a*]fluorenones

This chapter presents triflic acid-promoted expedient methodologies for the synthesis of benzo[*a*]fluorene **3** and fluorescent benzo[*a*]fluorenone **4** derivatives from 1,6-enyne-3-ones **2** (Scheme 1). While the formation of benzo[*a*]fluorene **3** involve Brønsted acid-promoted in situ

acetal formation followed by cationic cyclization, fluorescent benzo[*a*]fluorenone **4** formation involve cycloisomerization, encompassing two new C-C bond formations. Alongside, an important application of a selected benzo[*a*]fluorenone in fluorometric detection of nitro-aromatic explosives like TNT has also been investigated.

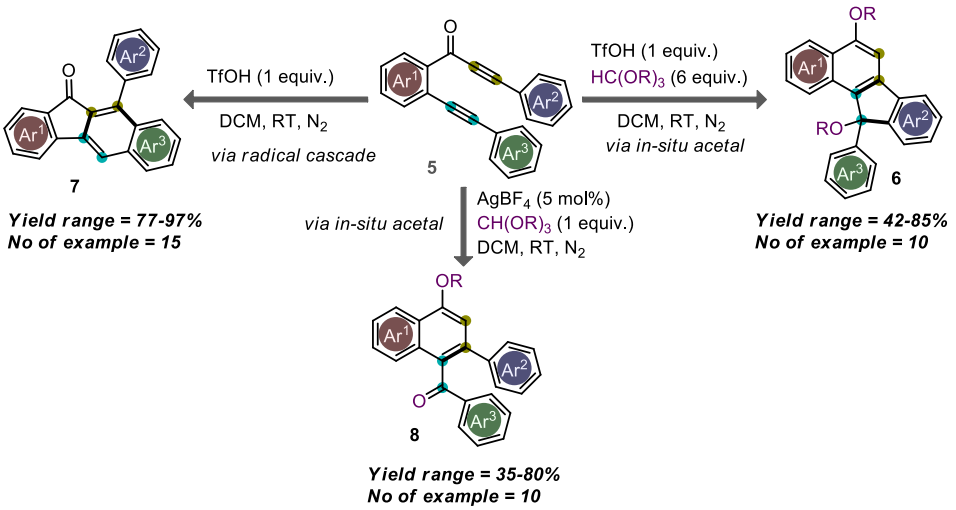
Scheme 1. Brønsted acid-mediated expedient cyclization of 1,6-enyne-3-ones for the synthesis of



benzo[*a*]fluorenes and benzo[*a*]fluorenones.

Chapter 3: Diversity-Oriented Synthesis of Benzo[*a*]fluorenes, Benzo[*b*]fluorenones and Naphthyl Ketones from Aryl-Fused 1,6-Diyn-3-ones

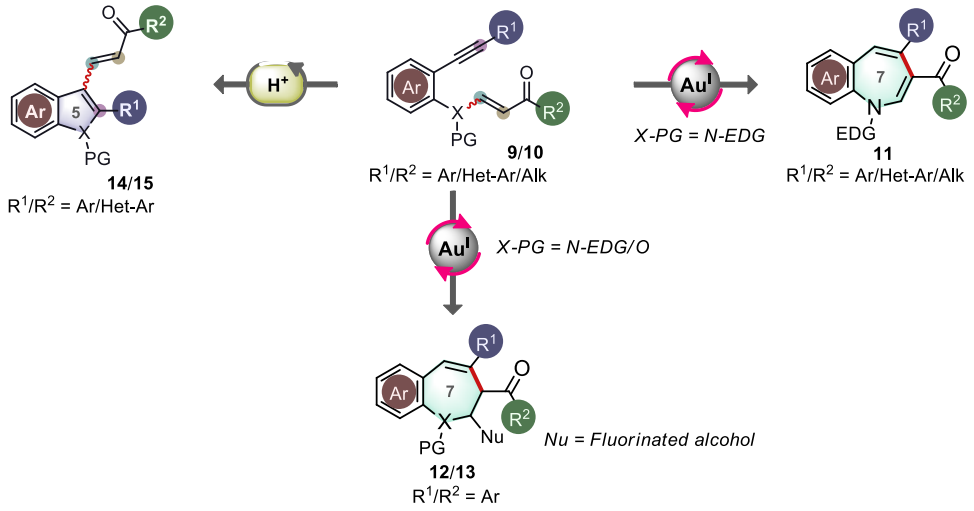
A facile and diversity-oriented approach to access substituted benzo[*a*]fluorenes **6**, benzo[*b*]fluorenones **7** and naphthyl ketones **8** has been developed *via* intramolecular cyclization of aryl fused 1,6-diyn-3-ones **5** (Scheme 2). Benzo[*a*]fluorene and naphthyl ketone synthesis involve in situ formed acetal intermediates. Aryl fused 1,6-diyn-3-one undergo triflic acid-mediated intramolecular cyclization leading to benzo[*b*]fluorene derivatives. Based on EPR study and literature precedents a mechanism involving generation of a biradical intermediate which subsequently transforming into a cyclic allene intermediate has been proposed for the formation of benzo[*b*]fluorenes. A detailed study on substrate scope, mechanistic insight and transformation of the synthesized compounds have been discussed in this chapter.



Scheme 2. Diversity-oriented synthesis of benzo[*a*]fluorenes, benzo[*b*]fluorenones and naphthyl Ketones from 1,6-diyn-3-ones.

Chapter 4: Cyclizations of Vinylogous Amides and Esters Derived from *o*-Alkynylanilines and *o*-Alkynylphenols: Access to an Array of Functionalized Benzo[b]azepines, Benzo[*b*]oxepines, Indoles and Benzofurans

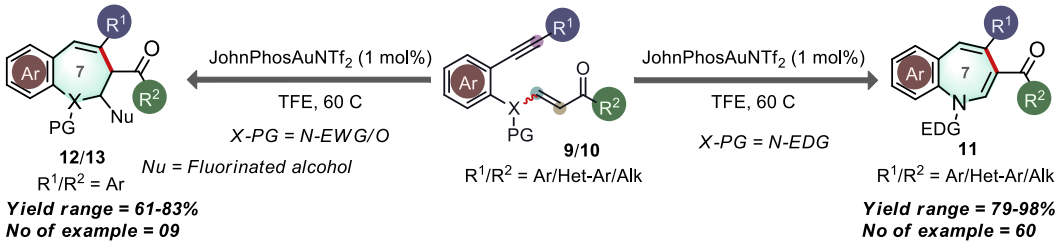
This chapter describes different modes of cyclizations carried out using heteroatom incorporated 1,6-enyne systems to synthesize different types of heterocyclic systems under different reaction conditions. Vinylogous amides **9** derived from *o*-alkynylanilines and vinylogous esters **10** derived from *o*-alkynylphenols have been synthesized and employed in the synthesis of functionalized benzo[*b*]azepines **11**, dihydrobenzo[*b*]azepines **12**, dihydrobenzo[*b*]oxepines **13**, indoles **14** and benzofurans **15**.



Scheme 3. Synthesis of different N- and O-heterocycles

Chapter 4A: Dodging the Conventional Reactivity of *o*-Alkynyl anilines under Gold Catalysis: Synthesis of Benzo[*b*]azepine using Vinylogous Amides Derived from *o*-Alkynylanilines

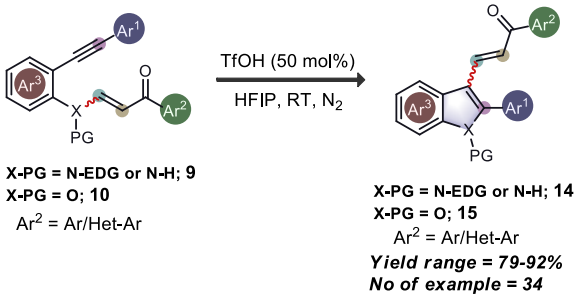
An uncommon 7-*endo*-*dig* carbacyclization of vinylogous amides derived from *o*-alkynylanilines **9** under homogeneous gold catalysis to access a wide array of benzo[*b*]azepines **11** in an atom economical way has been developed (Scheme 4). This cyclization shows excellent functional group compatibility and can also be extended to access fluoroalkoxy incorporated dihydrobenzo[*b*]azepine/oxepine **12/13** derivatives. Control experiments, kinetic studies and DFT calculations have been performed in details to shed light on to the mechanistic aspects of the reaction. Based on these studies, a mechanism that involves deprotonation of a cyclized intermediate mediated by the counter anion followed by protodeauration has been proposed.



Scheme 4. Direct ring-closure for the synthesis of benzo[*b*]azepine, dihydrobenzo[*b*]azepine/oxepine scaffolds under gold catalysis.

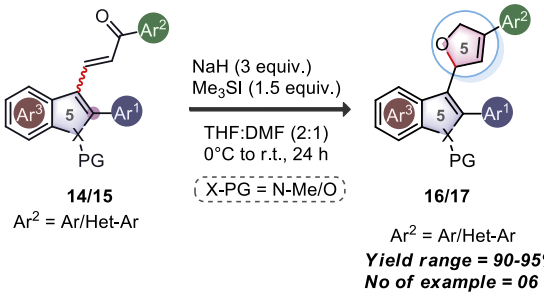
Chapter 4B: TfOH-Catalyzed Synthesis of Indoles and Benzofurans Involving Cyclative Transposition of Vinyl Ketone

A TfOH-catalyzed route for the formation of 3-substituted indoles **14** and benzofurans **15** from vinylogous amides **9** derived from *o*-alkynylanilines and vinylogous esters **10** derived from *o*-alkynylphenols respectively involving Michael, retro-aza/oxa-Michael and amine trapping cascade is described in this chapter (Scheme 5). Excellent stereochemical outcome of the double bond geometry in the products makes this protocol attractive.



Scheme 5. Synthesis of 3-substituted indoles and benzofurans under metal-free conditions.

The synthesized 3-substituted indole and benzofuran derivatives **14** and **15** have also been transformed to 2,4-disubstituted-2,5-dihydrofuran derivatives **16/17** upon treating them with trimethylsulfonium iodide in presence of sodium hydride in THF-DMF (2:1 mixture) (Scheme 6).

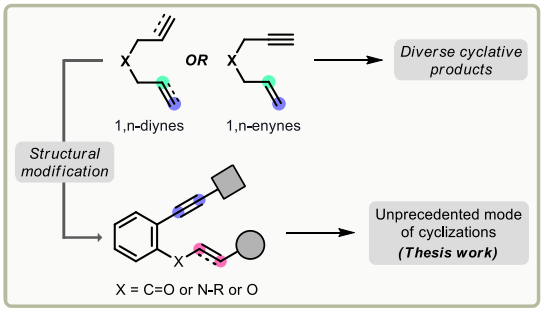


Scheme 6. Late-stage diversification of the synthesized indole and benzofuran derivatives.

Chapter 1

Diverse Cyclization Cascades of 1,n-Enyne/Diyne/Diene Systems : Access to an Array of Polyaromatic Hydrocarbons and Heterocycles

Polycyclic aromatic hydrocarbons (PAHs) and heterocyclic molecules are extremely versatile class of organic compounds having wide application in the field of medicinal chemistry as well as material science. Herein, the synthetic possibilies of 1,6-enyne/diyne systems to access a diverse range of PAHs and heterocycles, have been discussed broadly.



1.1 Introduction:

1.1.1. Background:

Polycyclic aromatic hydrocarbons (PAHs) and heteroaromatic molecules are vital classes of organic compounds with numerous applications in several branches of chemistry. These frameworks have been widely used in the field of materials chemistry,[1] as well as medicinal chemistry.[2] They serve as organic light emitting diodes (OLEDs),[1a-f] especially blue light emitting OLEDs,[1f] organic field-effect transistors,[1g] electrogenerated chemiluminescence (ECL),[1h-m] chemo/bio sensors,[1n] optoelectronic advanced materials,[1o] organic photovoltaic cells,[1q] solar cells [1r-s] and potent photosensitizer in photoconductor devices [1t] etc.

Furthermore, these frameworks also reveal potent biological activities such as antibacterial and antiviral etc.[2] In addition, these structural motifs have also been employed as key building blocks in synthesizing essential drug candidates.[2f]

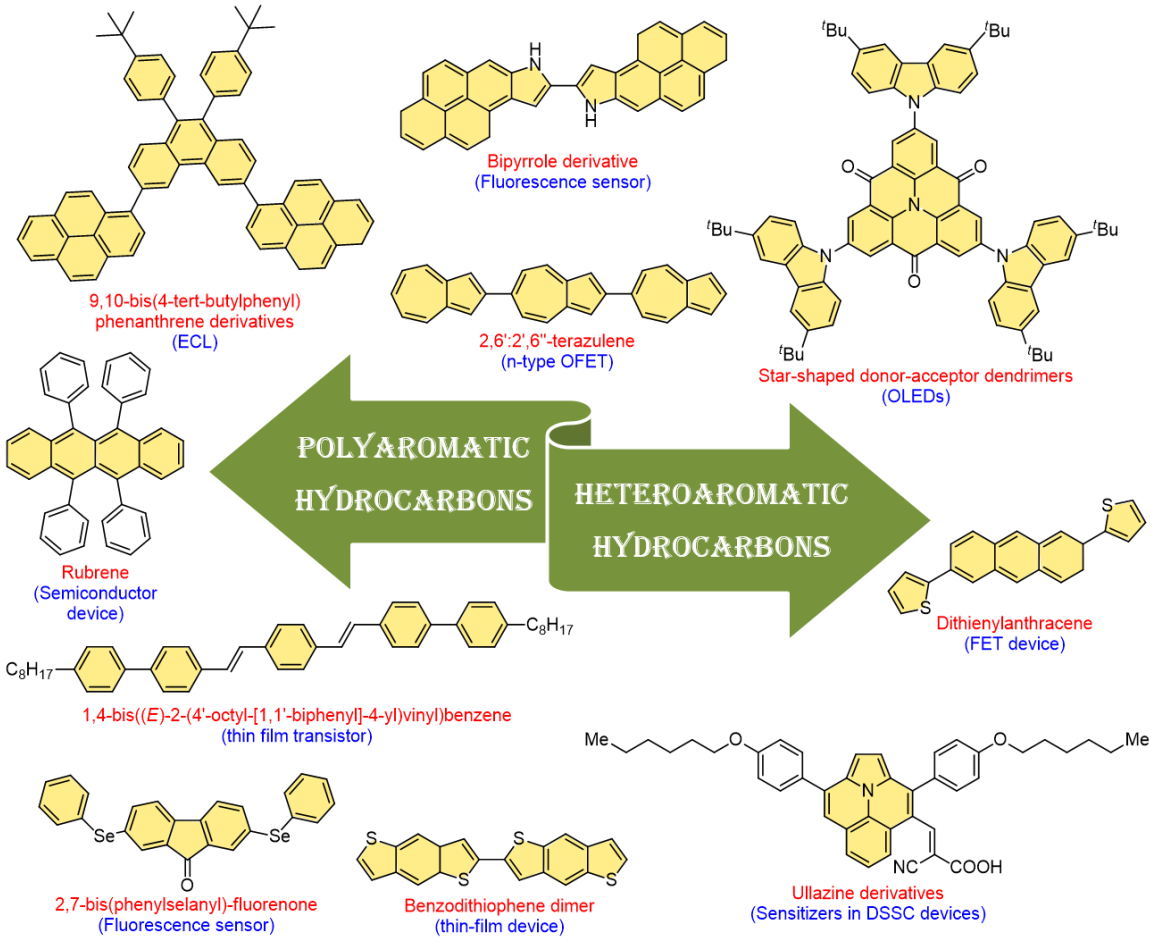


Figure 1.1. Material applications of PAHs and heteroaromatics.

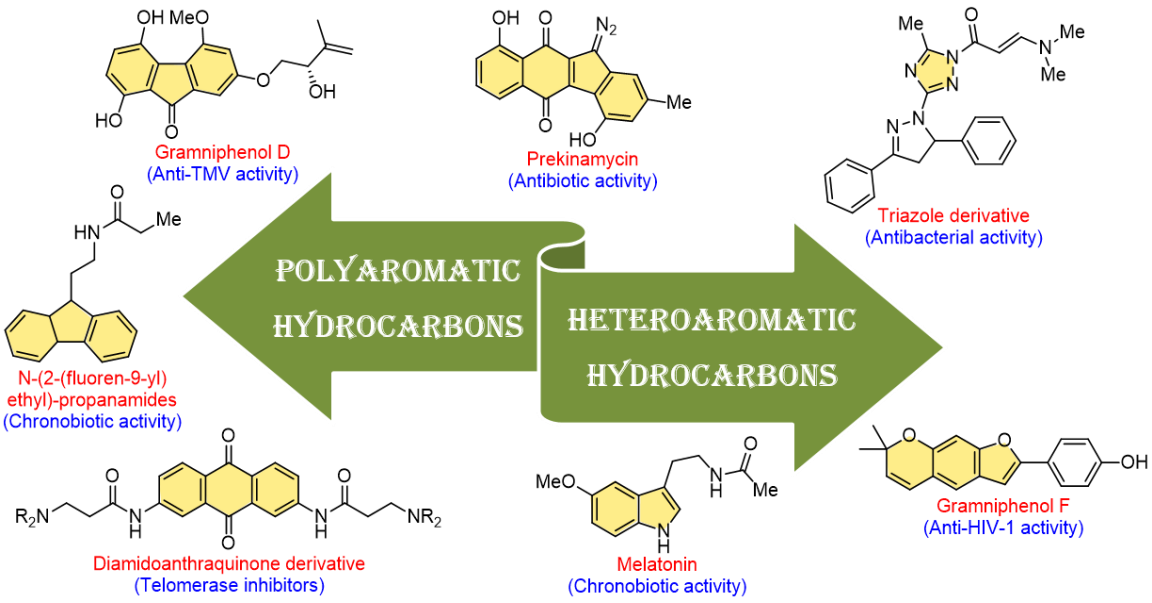


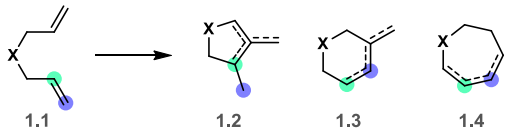
Figure 1.2. Biochemical applications of PAHs and heterocyclicaromatics.

1.1.2. Cyclization Modes of 1,n-Enyne/Diyne/Diene Systems:

With the contributions from different research groups over the past few decades, a number of straightforward routes have been developed for the contruction of PAHs[3] and heteroaromatic molecules [4] having different functionalities. These synthetic routes often involve cyclization of different types of 1,n-enyne/diyne/diene systems.[5]

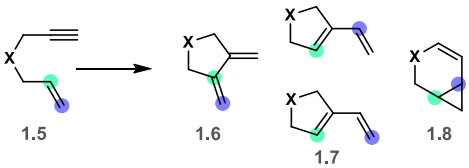
Since the work carried out for this thesis involves use of enynes, diynes and diene systems for the synthesis of PAHs and heteroaromatic compounds, general cyclization modes of such systems are presented below.

1,n-Diene systems could cyclize in a diverse way. The cycloisomerisation of 1,6-dienes (**1.1**) could produce five-, six- or seven-membered cyclic products (**1.2**–**1.4**). Though, the cyclopentane/ene products (**1.2**) are the more favorable ones. The original connectivity of the seven atom acyclic chain in **1.1** is retained in each cases (Scheme 1.1). The isomerisation only includes (formal) migrations of hydrogen and linked bond rearrangements and no carbon–carbon bond cleavage is notied.



Scheme 1.1. Cyclization possibilities of 1,n-diene svstems.

On the other hand, 1,6-enynes (**1.5**) usually form 5-membered rings. These could be the simple cycloisomers of type **1.6**. Skeletal rearrangement is also possible based on the catalytic system used. In these cases, the original connectivity of the 1,6-heptenyne chain (**1.5**) is not retained as shown in **1.7**. In addition, different catalytic systems could be employed to effect the 1,6-enyne cycloisomerisation to

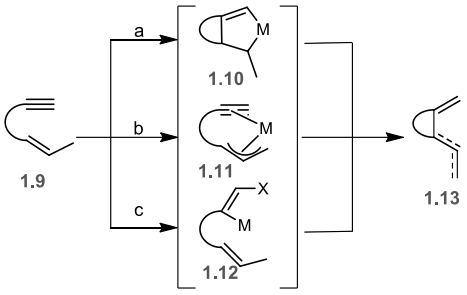


Scheme 1.2. Cyclization possibility of 1,n-enyne systems.

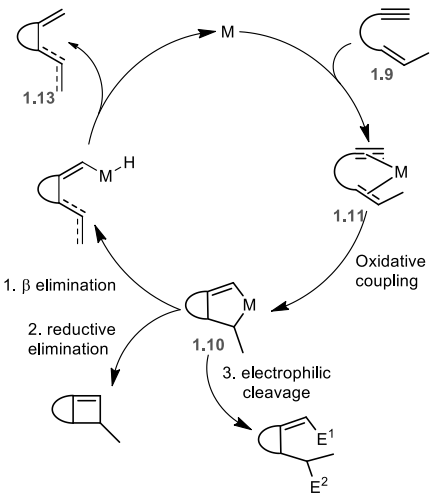
generate six- and seven-membered rings and sometimes bicyclic systems like **1.8** as well (Scheme 1.2).

In this regard, transition-metal-catalyzed cycloisomerizations of 1,n-enynes/diynes/dienes have been developed as exclusive tools to achieve a diverse range of cyclic compounds in an operationally simple manner.

Different pathways can be proposed for the metal-catalyzed cycloisomerization of enynes based on the mechanistic grounds, reaction conditions and choice of the catalyst. Usually the metal coordinate to either the alkene or alkyne or both and activate selectively or both of them. Based on the unsaturation which gets activated, three different mechanistic paths are viable (Scheme 1.3). The metallacycle **1.10** could be formed by the simultaneous coordination of both the unsaturations (path a). Most of the transition metals behave in this way. When a functional group is present at the allylic position, preferentially a π-allyl complex **1.11** (path b) is formed which subsequently react with the triple bond. Lastly, vinylmetal intermediate **1.12** could be formed via the hydrometalation of the alkyne (path c). Now the cyclizations involving the intermediate **1.10**-**1.12** can further be subdivided according to their reactivity. The metallacyclopentene formation is observed commonly in a variety of transition metal-catalyzed reaction of such starting materials. The key steps involved in the catalytic cycle have been described in Scheme 1.4. After the coordination of the metal with both the alkyne and the alkene moities, oxidative coupling produce the metallacyclopentene **1.10**. Now this metallacyclopentene **1.10** could undergo three types of transformations. The most common one is the β-hydride elimination which is the fastest path.



Scheme 1.3. Three possible activations involved in enyne cyclization.

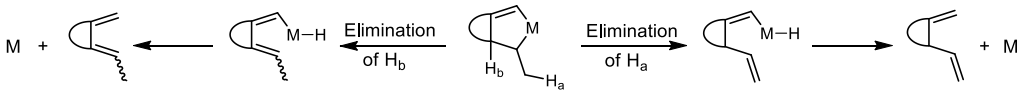


Scheme 1.4. Synthetic opportunities of metallacyclopentene.

It could deliver either one or a mixture of 1,3- and 1,4-dienes after the reductive elimination step. In the second-type, a reductive elimination of the metallacyclopentenes could occur in the case of metals which are not capable of undergoing a β-elimination. In this situation it give bicyclic systems or rearranged compounds. Finally, in presence of an electrophile in the reaction mixture, functionalization of the substrate could be possible via the electrophilic cleavage of the carbon-metal bond (Scheme 1.4).

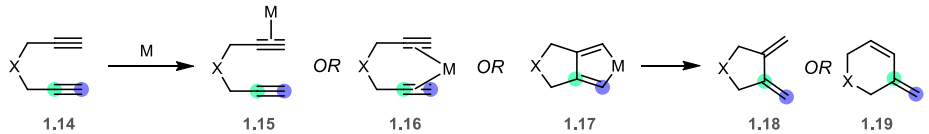
Usually the β-elimination is followed by the reductive elimination of the metal which provides the cycloadduct with the regeneration of the active metal catalyst. A 1,3- diene or 1,4-diene could be achieved based on the regioselectivity of the elimination (H_a or H_b), (Scheme 1.5). Available coordination site on the metal and

a cis stereochemistry between the carbon-metal and carbon-hydrogen bonds for the β-elimination are essential.



Scheme 1.5. Possibilities of β-elimination.

1,n-Diynes have two alkyne bonds, are showing extremely high reactivity and could cyclize in various ways.[6] The metal could activate any one of the alkyne bond and another triple bond can attack it. On the other hand, metal can activate both the alkynes as shown in scheme 1.6. Depending on the mode of cyclization, different types of PAHs could be achieved.



Scheme 1.6. Modes of activation of 1,n-diynes.

The literature study reveals that the cyclization of different types of 1,n-enyne/diyne/diene framework could serve in a diverse way for the development of synthetic strategies to access a series of PAHs and heteroaromatic moities.

1.1.3. Present Work:

In this contest, we have studied in detail the reactivity of 1,6-enynes and diynes precursors **1.20-1.22** under metal catalysts like gold and silver and Brønsted acid promoters. The 1,6-enynes and diynes precursors **1.20-1.22** could be represented as a single precursor as shown in **1.23** (Scheme 1.3). A series of polyaromatic hydrocarbons (PAHs) like benzo[*a*]fluorene, benzo[*a*]fluorenone, benzo[*b*]fluorenone and naphthyl ketones have been synthesized. In addition, a number of heteroaromatic compounds namely benzo[*b*]azepine, benzo[*b*]oxepine, indole and benzofurans have also been prepared.

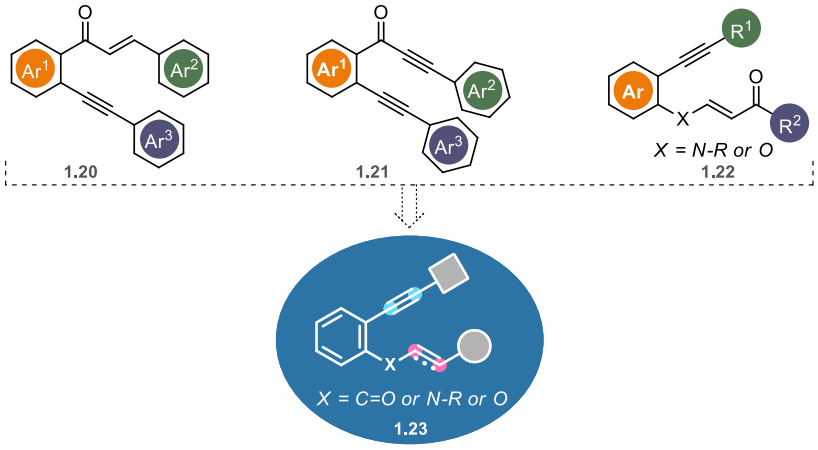


Figure 1.3. 1,6-Enyne or diyne precursors used in this thesis work.

1.2. References:

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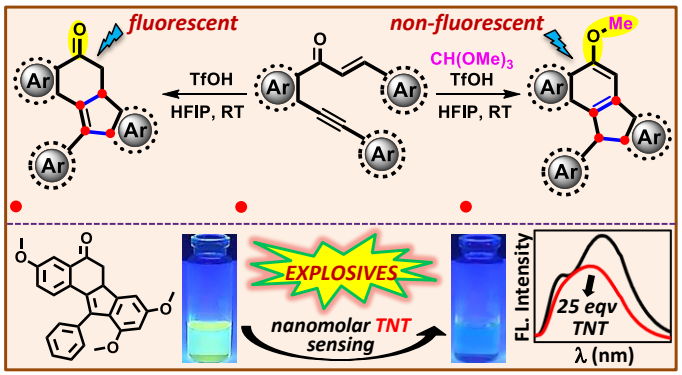
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Chapter 2

Triflic Acid-Mediated Cyclizations of 1,6-Enyne-3-ones: Synthesis of Benzo[a]fluorenes and Fluorescent Benzo[a]fluorenones



Polycyclic aromatic hydrocarbons (PAHs) have engrossed much significance in the field of material due to their interesting optical properties. They find applications in medicinal research as well. In this fortress, benzo-fused fluorenones/fluorenes are one of the most extensively studied entities because of their extended π-conjugation with different structural features. Owing to their importances, development of new, divergent protocol to access these important PAHs are always in high demand. Pleasingly, we have successfully developed triflic acid-promoted expedient methodologies for the synthesis of structurally diverse benzo[*a*]fluorene and fluorescent benzo[*a*]fluorenone derivatives from 1,6-enyne-3-ones. This synthetic pathway involve Brønsted acid promoted *in situ* acetal formation or enolization of chalcone core followed by cationic cycloisomerization, encompasing two new C-C bond formations. Alongside, we exposed an important application of a selected benzo[*a*]fluorenone in fluorometric detection of nitro-aromatic explosives like TNT.

- Mandal, M.; Balamurugan, R. *Adv. Synth. Catal.* **2018**, *360*, 1453-1465.
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2.1. Introduction:

2.1.1. Background of Research:

Polycyclic aromatic hydrocarbons (PAHs), especially, the benzo fused fluorenes/fluorenones, have gathered significant attention in material science[1] as well as medicinal chemistry[2] due to their distinct structural feature where a five-membered ring is sandwiched between arene rings and unusual optical properties due to their extended π-conjugation.[3] The optical properties of these molecules can be tuned by adding different substituents in the cyclopentadiene and arene rings. Subsequently, the functionalized materials were employed in diverse applications, for instance, organic light emitting diodes (OLEDs)[1a-f] organic field-effect transistors (OFET),[1g] electrogenerated chemiluminescence (ECL),[1h-m] chemo/bio sensors,[1n] optoelectronic advanced materials,[1o] organic photovoltaic cells,[1q] solar cells [1r-s] and potent photosensitizer in photoconductor devices [1t] etc (Figure 2.1). Furthermore, these unique functional cores also exhibit potent antibacterial activity,[2a] cytotoxicity,[2a] antiviral[2b] and antibiotic activities.[2c] As well, these structural motifs have also been employed as the key building blocks in developing essential drug candidates,[2d] fluorescent probes for imaging of lysosomes and mitochondria in living cells,[2e] and inhibitors of human telomerase.[2f] Keeping these imperative aspects in mind, the scientific community devotes a copious effort in finding new synthetic approach to access these important structural analogues.

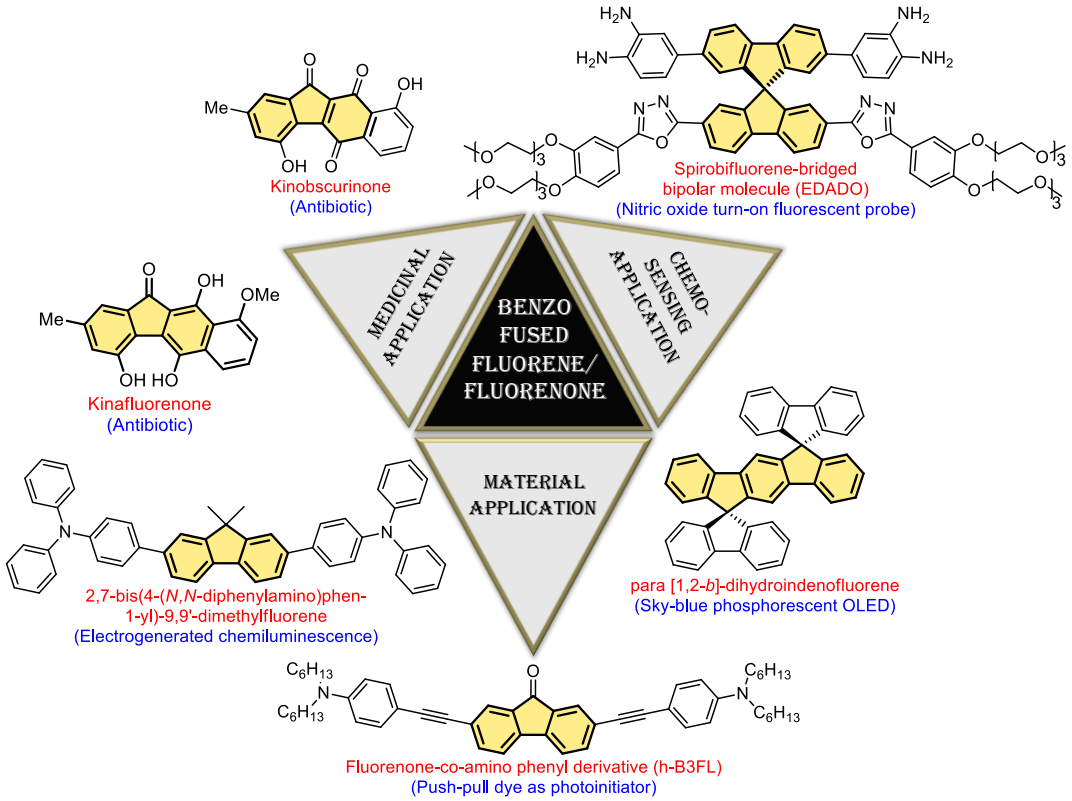


Figure 2.1. Selected novel benzo fused fluorene/fluorenone analogues and their uses.

2.1.2. Literature Reports:

Across the world, several research groups have been working on PAHs which led to the findings of a number of synthetic methods to access benzofluorenes[4]/fluorenones.[5] These protocols involve a variety of synthetic routes, such as, base (*e.g.,* K_2CO_3 or Et_3N)-promoted bicyclization,[5a] radical cyclizations (using DDQ, arylboronic acid, trifluoroborate or Bu_3SnH/AIBN),[5l,5j,5c,4a] thermal Diels-Alder cycloaddition (*via* allene rearrangement or decarbonylation/ dehydrogenation cascades),[5m,5i,4k] intramolecular cyclization *via* C-H activation (through sequential Pd-migration and intramolecular arylation),[5d] metal (*e.g.,* Pd, Cu, Au, Ni, Ru, Rh or Ir)-catalyzed annulations (involving cross-coupling or intramolecular enyne metathesis/ rearrangement or tandem cationic cyclizations),[5e-f,4d-f,4i] and Lewis/Brønsted acid (*e.g.,* $FeCl_3$)-catalyzed intramolecular cyclization[4g-h] etc.

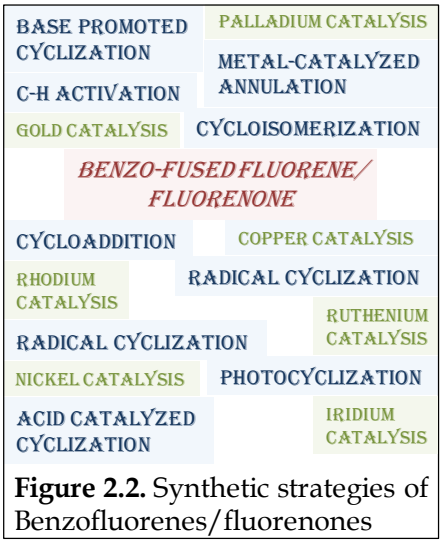


Figure 2.2. Synthetic strategies of Benzofluorenes/fluorenones

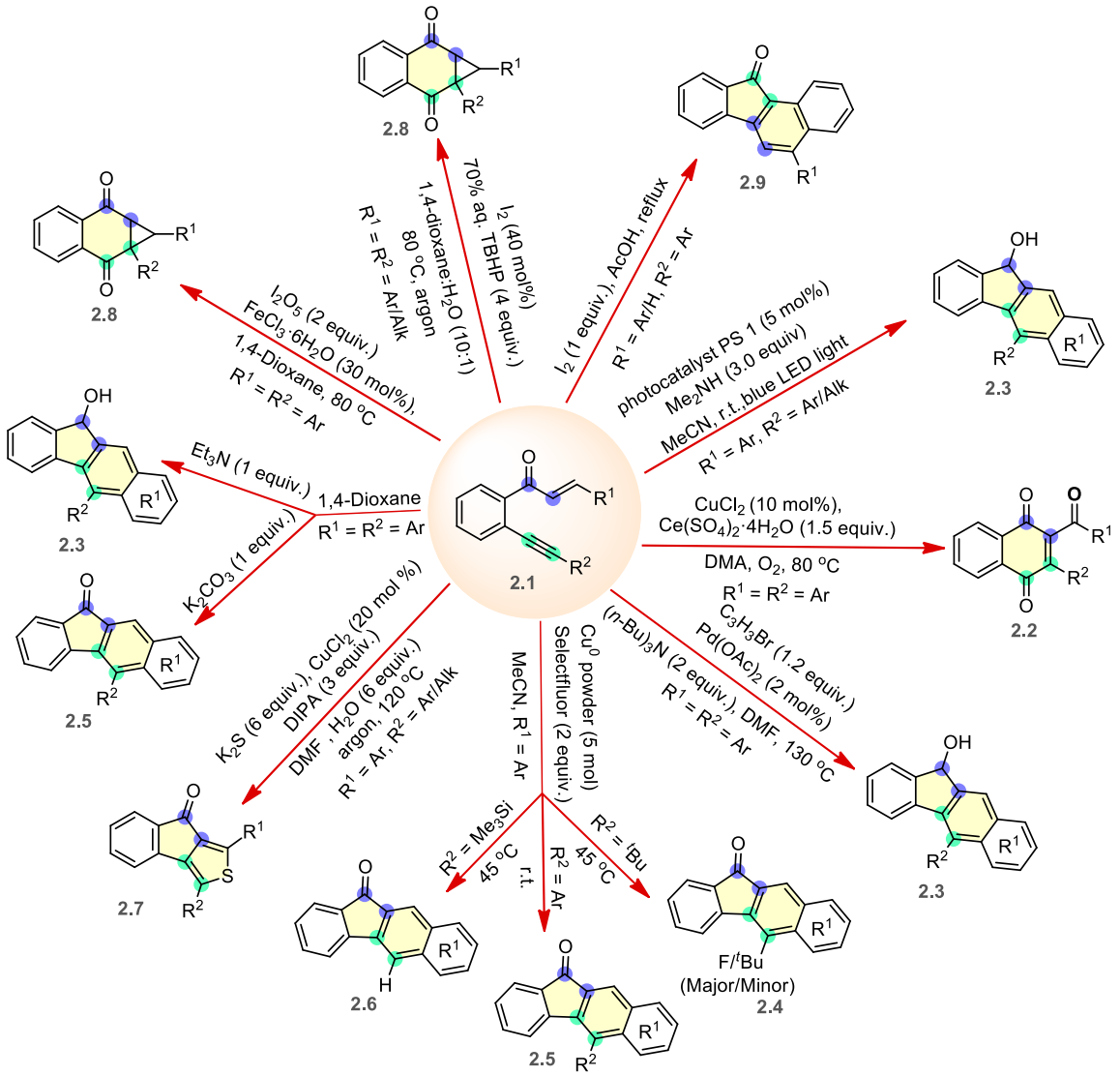
However, 1,6-enyneones are the promising building blocks for the construction of the PAH systems. So, we have demonstrated below some of the existing literature for the cyclization reactions of such types of 1,6-enyneone skeleton,[6]

In 2011, Li and co-workers[6i] demonstrated an intramolecular oxidative carbocyclization of 1,6-enyneone derivative **2.1** under $CuCl_2$ catalysis. In this reaction O_2 has been used as the terminal oxidant as well as a reactant. The reaction follows a 6-*exo-trig* cyclization pathway leading to 1,4-naphthoquinones **2.2** (Scheme 2.1).

In 2012, Hu group[6h] synthesized benzo[*b*]fluorenols **2.3** from 1,6-enyneone derivatives **2.1** and 3-bromoprop-1-yne using $Pd(OAc)_2$ as catalyst. The reaction proceeds through an intramolecular dehydroaromatization and carbonyl reduction (Scheme 2.1).

In 2016, Liu group[6g] has described the synthesis of a diverse range of benzo[*b*]fluorenone moieties *via* a tandem annulation of 1,6-enyneones under Cu^0/Selectfluor catalytic system. When *tert*-butylethynyl-substituted 1,6-enyneones **2.1** were used, the reaction followed a tandem annulation/C–C-bond-cleavage/fluorination process leading to fluorinated benzo[*b*]fluorenones **2.4** as major and *tert*-butyl-substituted benzo[*b*]fluorenones **2.4** as minor products. In the case of arylethynyl-substituted 1,6-enyneones **2.1**, the substrates underwent tandem annulation and 5-aryl-substituted benzo[*b*]fluorenones **2.5** were obtained. In addition, (trimethylsilyl)ethynyl-substituted 1,6-enyneones **2.1** experienced a tandem annulation followed by C–Si bond-cleavage process to provide 11*H*-benzo[*b*]fluoren-11-ones **2.6** (Scheme 2.1).

In 2016, Jiang and co-workers[6f] reported a cascade dehydrobicyclization of 1,6-enyneones in the presence of potassium sulfide as a sulfurating reagent leading to arylated indeno[1,2-*c*]thiophene derivatives **2.7**.



Scheme 2.1. Cyclization cascades of 1,6-enyneone skeleton leading to various PAHs.

The sulfur incorporation pathway comprises of Michael addition followed by 5-*exo-dig*/5-*endo-trig* bicyclization and dehydrogenation. Multiple C–S and C–C bonds have been formed in the course of this reaction (Scheme 2.1).

In the same year, Tu group[6e] described a base-promoted 1,6-enyneone-bicyclization leading to a variety of arylated benzo[*b*]fluorenones **2.5** and benzo[*b*]fluorenols **2.3** depending on the nature of the base (Scheme 2.1). For benzo[*b*]fluorenone synthesis, the reaction proceeded *via* an intramolecular DielsAlder (D-A) reaction/enolization/1,5-H transfer/K_2CO_3-promoted oxidation sequence. Whereas, in the benzo[*b*]fluorenols formation, a similar pathway was followed but the oxidation of alcohol was restricted due to intermolecular hydrogen bonding.

In 2018, Liu group[6d] depicted a radical-triggered tandem cyclization of 1,6-enynones **2.1** for the synthesis of strained 1*H*-cyclopropa[*b*]naphthalene-2,7-diones **2.8** with high level of

stereoselectivity (Scheme 2.1). As indicated by mechanistic studies, water plays a crucial role by producing a hydroxyl radical which initiates a successive Michael addition and ring-closure pathway.

In the same year, Li and co-workers[6c] reported a convenient synthesis of 1*H*-cyclopropa-[*b*]naphthalene-2,7-diones **2.8** under metal-free condition *via* I_2-catalyzed oxidative tandem annulation of 1,6-enynones **2.1**. *tert*-Butyl hydroperoxide (TBHP) has been used as the oxidant as well as the oxygen atom source (Scheme 2.1).

In 2019, Srinivasan group[6b] presented an expedient metal-free procedure for the synthesis of benzo[*a*]fuorenone derivatives **2.9** from 1,6-enynone derivatives **2.1**. Formation of a vinyl indenone intermediate followed by electrocyclic ring-closure and aromatization are the key steps of this protocol. (Scheme 2.1).

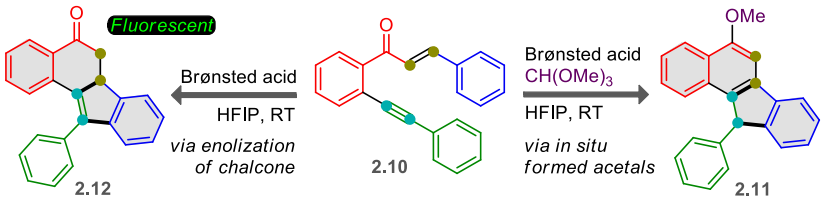
In 2021, Liu group[6a] demonstrated a mild and atom-economical synthesis of benzo[*b*]fluorenols **2.3** from 1,6-enynones **2.1** under photocatalytic conditions. The P/N heteroleptic Cu(I)-photosensitizer could exhibit energy-transfer as well as photoredox catalytic activities in this methodology (Scheme 2.1).

The literature study reveals that the 1,6-enyneones framework could serve in a diverse way for the access of a wide array of cyclized organic molecules.

2.2. Results & Discussion:

2.2.1. Present Work:

Herein, we have demonstrated a Brønsted acid-promoted expedient synthesis of structurally diverse benzo[*a*]fluorene and benzo[*a*]fluorenone derivatives from 1,6-enynone involving two new C-C bond formations under metal-free conditions (Scheme 2.2). The formation of benzo[*a*]fluorenes follows *in situ* formed acetal pathway in presence of trimethyl orthoformate (TMOF) which enables the cationic cycloisomerization. Whereas, without TMOF, the reaction proceeds through enolization of chalcone core leading to the formation of benzo[*a*]fluorenones. Interestingly, all the synthesized benzo[*a*]fluorenones are highly fluorescent. Further we have studied their photo-physical properties and explored their possible application as chemosensor.

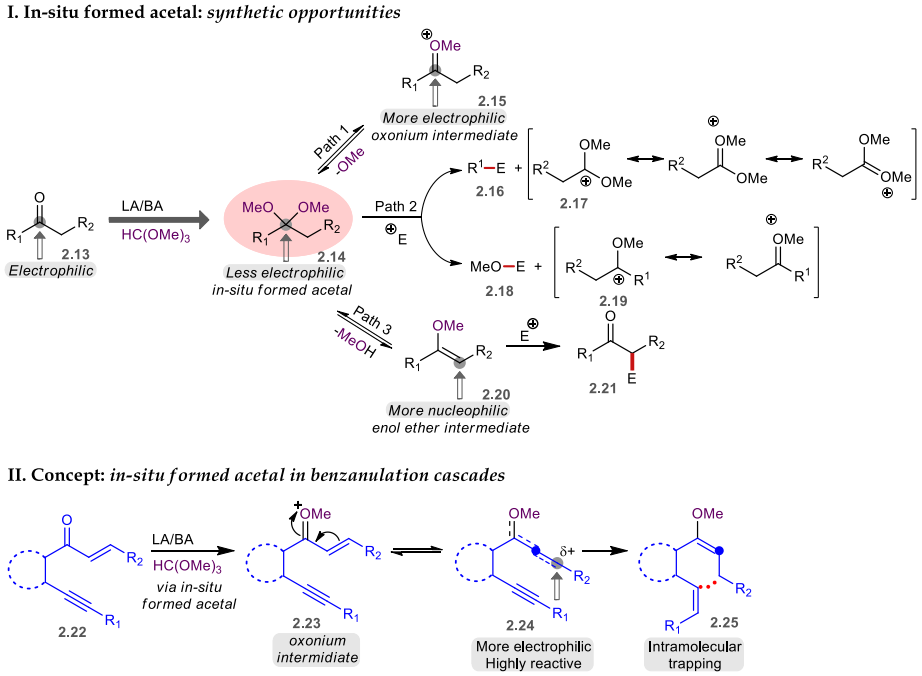


Scheme 2.2. Brønsted acid-mediated expedient bicyclization of 1,6-enynones to access PAHs.

2.2.2. Precedents:

Acetals are frequently used in organic transformations as protecting groups for aldehydes and ketones. The acetals formed *in situ* have been exploited in diverse ways to explore their synthetic potentials as depicted in Scheme 2.3(I). In presence of trialkyl orthoformate (*e.g.,*

TMOF) and Lewis acid (LA)/Brønsted acid (BA) catalyst, the carbonyl compound **2.13** can be converted into the corresponding acetal **2.14**. As described in path 1, acetal **2.14** can be converted into a more electrophilic oxonium intermediate **2.15** upon removal of one of the methoxy groups. This enables further nucleophilic functionalizations. According to path 2, in presence of an electrophile, either the R^1 group or one of the methoxy group can make a new bond with the eletrophile leading to **2.16** or **2.18**. Conversely, as per path 3, more nucleophilic enol ether intermediate **2.20** can be formed which opens up enolate kind of reactivity. Therefore, it is expected that this simple strategy would offer easy access to functionalized organic molecules under metal-free mild conditions Different groups across the world have used acetals formed *in situ* to develop new reactions.[7] Our group has also contributed considerably in these lines.[8]



Scheme 2.3. Reactivity of *in situ* formed acetals and proposed concept.

2.2.3. Optimization of Reaction Conditions for Benzo[*a*]fluorene Synthesis:

To evaluate the feasibility of our hypothesis, first we have synthesized (*E*)-3-phenyl-1-(2-(phenylethynyl)phenyl)prop-2-en-1-one (**2.10a**) as model 1,6-enynone precursor *via* Sonogashira coupling between 2-iodoacetophenone and phenylacetylene followed by aldol condensation with benzaldehyde. Next, the synthesized **2.10a** was treated with 20 mol% of triflic acid (TfOH) in presence of TMOF (2 equiv.) in dichloromethane (DCM) solvent at room temperature under nitrogen atmosphere. After 36 hours of stirring, we obtained a mixture of two products **2.11a** and **2.12a** with 28% and 30% yields respectively (entry 1, Table 2.1). The formation of **2.11a** was primarily confirmed by nuclear magnetic resonance (NMR) spectroscopic (Figure 2.3) and high resolution mass spectroscopic (HRMS) analysis. In ^{1}H NMR spectrum, a peak at 4.09 ppm with an integral value for 3H and the corresponding ^{13}C signal at 53.7 ppm clearly

indicated the presence of one methoxy group in the compound. Additional evidence of the structure comes up from the ^{13}C NMR signal at 156.4 ppm which corresponds to the carbon linked to the methoxy group. In addition, another aliphatic signal at 5.17 ppm in ^{1}H NMR and its corresponding signal at 55.8 ppm were also observed.

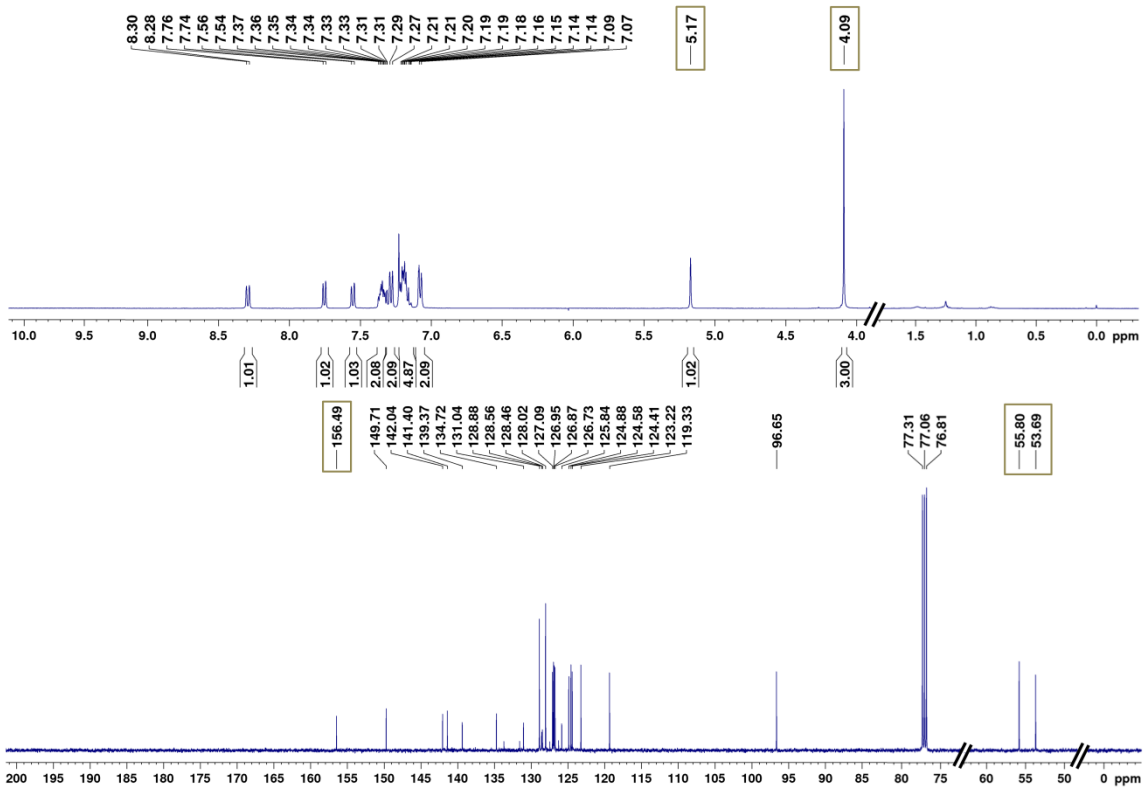


Figure 2.3. ^{1}H and ^{13}C NMR spectra of benzo[*a*]fluorene (**2.11a**).

The structure of **2.11a** was confirmed by single crystal X-ray diffraction studies (Figure 2.4). After getting the confirmed structure in hand, we have started further optimization of the reaction conditions to achieve a better product yield.When we used 3 equivalents of TMOF, we didn't obtain any improved yield of the desired product **2.11a**. But the yield of the other product **2.12a** decreased (entry 2, Table 2.1). So, for further optimizations, we used 3 equivalents of TMOF. The desired product formation was totally nil when TMOF was used as solvent (entry 3, Table 2.1). Next, we have checked the reaction by changing the catalyst loading to 50 mol% and 1 equiv. (entries 4 and 5, Table 2.1) which resulted in 29% and 35% of product yields respectively. Shifting of solvent from DCM to DCE did not have any substantial effect on the product yield (entry 6, Table 2.1), although the yield of **2.12a** was suppressed. Afterwards, we have screened a variety of catalysts. But, unfortunately no reaction was observed when 20 mol% of *p*-toluenesulfonic acid (PTSA), $Cu(OTf)_2$, trifluoroacetic acid (TFA), $AuCl_3$, super acid $HSbF_6.6H_2O$ and $AgSbF_6$, were used instead of TfOH (entries 7-12, Table 2.1). The product yield did not improve upon addition of 10 mol% iodine as an additive (entries 13, Table 2.1). Thus, TfOH was proved to be the efficient

promoter for this transformation. Next, we have decided to alter the solvent in order to improve the product yield. In this regard, we have screened nitromethane (CH_3NO_2), acetonitrile (CH_3CN), 1,4-dioxane, tetrahydrofuran (THF) and trifluoroethanol (TFE) as the solvent (entries 14-18, Table 2.1) but no improvement in the yield was noticed except TFE (54% isolated yield). From this result we guessed that a more fluorinated polar protic solvent could give better result. Finally, we were very much satisfied after noticing a clean reaction in hexafluoroisopropanol (HFIP) solvent with exceptionally high isolated yield (98%, entry 19, Table 2.1) within 2 h. It is anticipated that due to high polarity of HFIP,[9] it stabilizes the polar reaction intermediates for giving best results. Further, loading of 2 equiv. of TMOF yields 75% of the desired products along with 24% of **2.12a** (entry 20, Table 2.1). Decreasing the amount of TMOF and TfOH reduced the yield considerably (entries 20 and 21, Table 2.1). To sum up, a combination of 1 equiv. of TfOH and 3 equiv. of TMOF in HFIP solvent at room temperature under nitrogen atmosphere was considered as the optimized reaction condition (entry 19, Table 2.1).

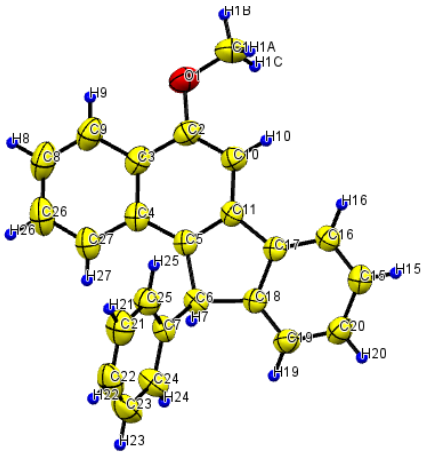
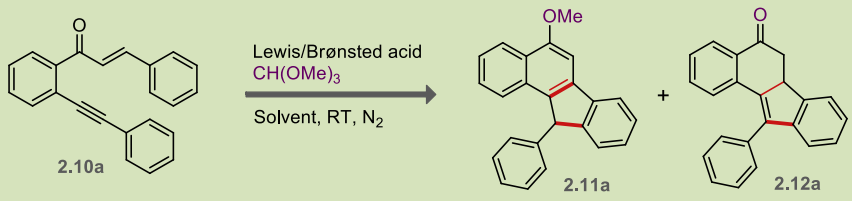


Figure 2.4. ORTEP of **2.11a**.

Table 2.1. Optimization of reaction conditions for the synthesis of benzo[*a*]fluorene (**2.11a**)



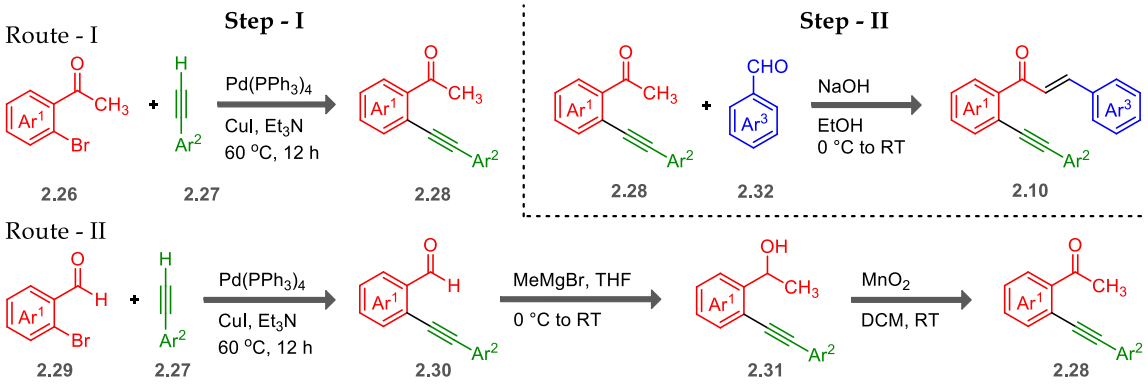
Entry	Solvent	Catalyst (equiv.)	Time (h)	Yield (%) of 2.11a	Yield (%) of 2.12a
1	DCM[a]	TfOH (0.2)	36	28	30
2	DCM	TfOH (0.2)	36	28	12
3	-[b]	TfOH (0.2)	16	-	-
4	DCM	TfOH (0.5)	20	29	9
5	DCM	TfOH (1.0)	20	35	8
6	DCE	TfOH (1.0)	5	33	-
7	DCE	PTSA (0.2)	48	-	-
8	DCE	$Cu(OTf)_2$ (0.2)	48	-	-
9	DCE	TFA (0.2)	48	-	-
10	DCE	$AuCl_3$ (0.2)	48	-	-
11	DCE	$HSbF_6$ (0.2)	48	-	-
12	DCE	$AgSbF_6$ (0.2)	48	-	-
13	CH_3NO_2	TfOH+I_2 (1.0+0.1)	2	14	-
14	CH_3NO_2	TfOH (1.0)	5	29	-
15	CH_3CN	TfOH (1.0)	72	4	-

16	Dioxane	TfOH (1.0)	48	-	-
17	THF	TfOH (1.0)	48	-	-
18	TFE	TfOH (1.0)	48	54	-
19	HFIP	TfOH (1.0)	3	98	-
20	HFIP[a]	TfOH (1.0)	3	75	24
21	HFIP	TfOH (0.5)	3	73	-

Reaction conditions: **2.10a** (0.1 mmol), Lewis/Brønsted acid, TMOF (3.0 equiv.) and solvent (0.5 ml) at rt under N_2 atmosphere, unless otherwise stated. [a]2.0 equiv of TMOF was used. [b]TMOF was used as solvent.

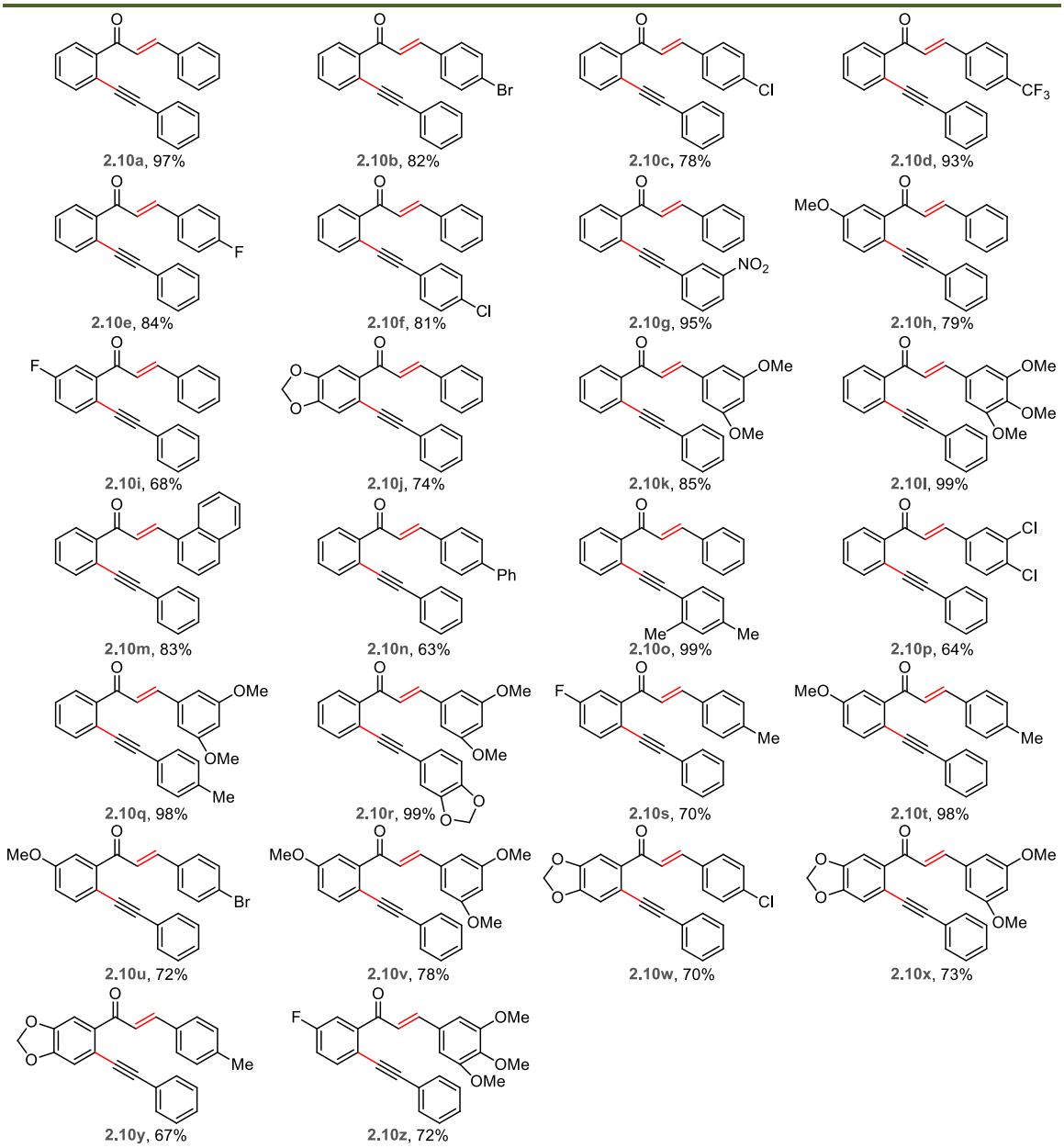
2.2.4. Preparation of 1,6-Enynone Precursors:

To explore the substrate scope of this methodology, first we have synthesized a series of 1,6-enynone derivatives by following known literature reported procedures. Initially Sonogashira coupling has been carried out between 2′-bromoacetophenone and substituted phenylacetylene to get the *o*-alkynylaryl ketone (route-I, Scheme 2.4).[8h] Due to the lack of availability of 2′-bromoacetophenone derivatives, few *o*-alkynylaryl ketones were prepared from 2-bromo benzaldehyde and arylacetylenes followed by Grignard reaction/oxidation (route-II, Scheme 2.4).[8b] Route-II was followed for the synthesis of substrates **2.10h-j** and **2.10s-z**. Finally, *o*-alkynylaryl ketones were condensed with substituted benzaldehyde under basic condition to produce the enynone **2.10** as shown in step-II, Scheme 2.4.[10] The structure of all the synthesized 1,6-enynone derivatives are presented in Table 2.2.



Scheme 2.4. Synthesis of 1,6-enynone derivatives.

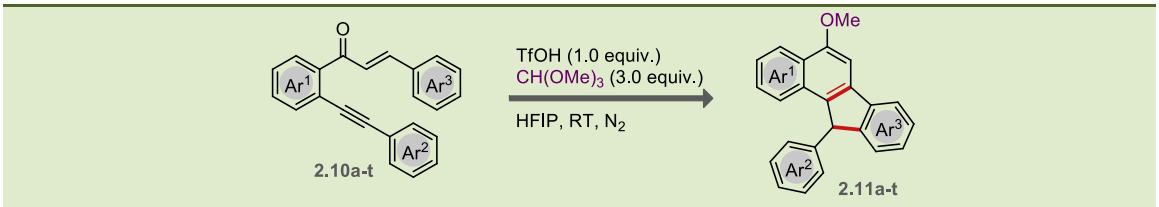
Table 2.2. List of 1,6-enynone derivatives (**2.10**).

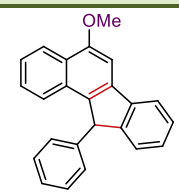


2.2.5. Substrate Scope for the Synthesis of Benzo[*a*]fluorene Derivatives:

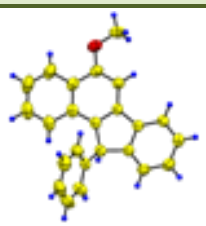
Using the optimized reaction conditions, we explored the scope of this methodology by synthesizing a series of functionalized benzo[*a*]fluorene derivatives using diverse 1,6-enynones (**2.10**). Substrates with different substituents like Cl, Br, F, OMe, Me, Ph, CF_3 and acetal tolerated well the reaction condition and furnished their corresponding desired products with moderate to excellent yields (46-98%) in short time period (1-4 h). The results are compiled in Table 2.3.

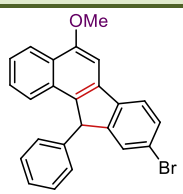
Table 2.3. TfOH-promoted synthesis of benzo[*a*]fluorene derivatives (**2.11**).



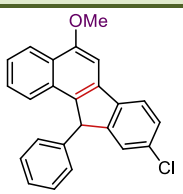


2.11a
98%, 3h

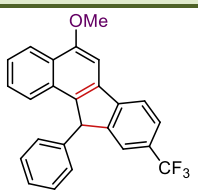




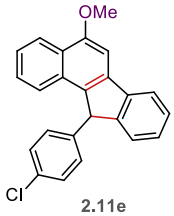
2.11b
75%, 3h



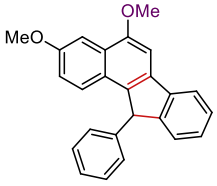
2.11c
70%, 3h



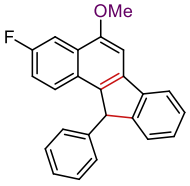
2.11d
17%, 3h



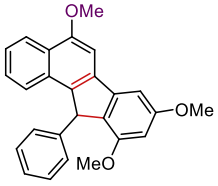
2.11e
84%, 1h



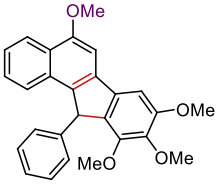
2.11f
54%, 2h



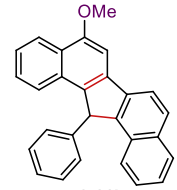
2.11g
87%, 1h



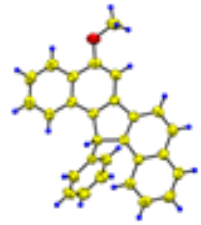
2.11h
98%, 3h

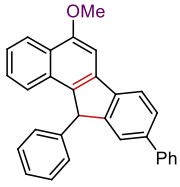


2.11i
99%, 1h

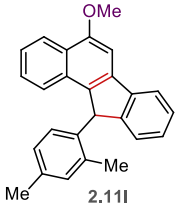


2.11j
67%, 2h

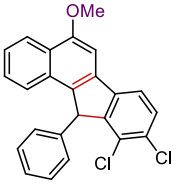




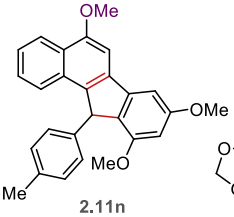
2.11k
73%, 3h



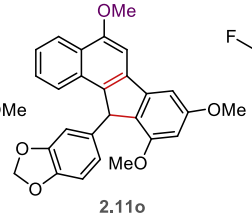
2.11l
76%, 2h



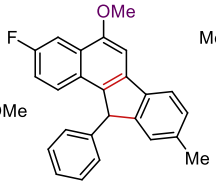
2.11m
59%, 2h



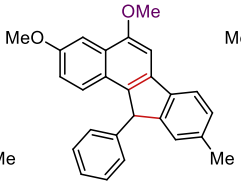
2.11n
98%, 2h



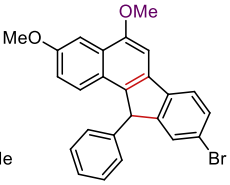
2.11o
84%, 3h



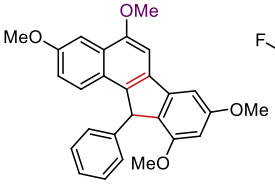
2.11p
83%, 1h



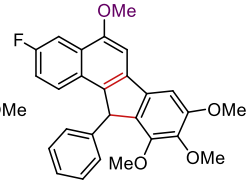
2.11q
77%, 1h



2.11r
46%, 2h



2.11s
75%, 2h



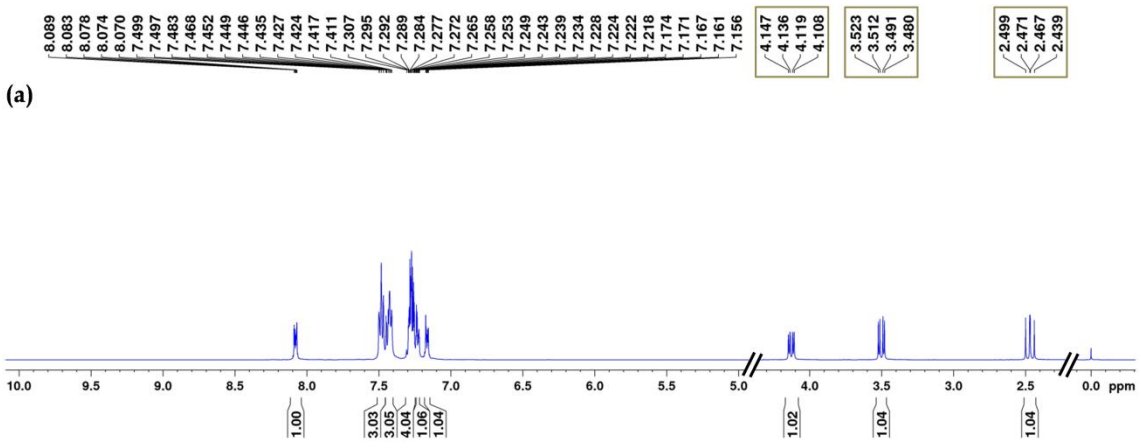
2.11t
68%, 1h

Reaction conditions: **2.10** (0.325 mmol), TfOH (1.0 equiv.), TMOF (3.0 equiv.) and HFIP (1.5 ml) at rt under N_2 atmosphere, unless otherwise stated.

All the products were characterized by NMR, HRMS, FTIR studies. The structures of **2.11a** and **2.11j** were re-confirmed by single crystal X-ray diffraction analysis. The CCDC numbers for these compounds are 1560544 and 1560552 respectively. Yields of benzo[*a*]fluorenes were reduced in presence of electron-withdrawing groups on the aryl rings attached to alkynyl and alkenyl carbons (**2.11c**, **2.11d**, **2.11m** and **2.11r**). This is obvious as this aromatic ring involves in electrophilic aromatic substitution in the course of the reaction and electron withdrawing groups in it will suppress the reactivity. Conversely, electron-withdrawing fluoro group did not have any appreciable negative effect on the product yield when the fluoro group was on the aryl ring of *o*-alkynylaryl ketone segment of the starting material (**2.11g**, **2.11p** and **2.11t**). Whereas, an electron-donating OMe group on the aryl ring of *o*-alkynylaryl ketone decreased the yield of benzo[*a*]fluorenes significantly (**2.11f** *vs* **2.11a**, **2.11r** *vs* **2.11b** and **2.11s** *vs* **2.11h**).

2.2.6. Optimization of Reaction Conditions for Benzo[*a*]fluorenone Synthesis:

As mentioned before when less amount of TMOF was used, a new product (**2.12a**) was also obtained in less yield (entry 1, Table 2.2). We paid some attention to shed some light on this interesting finding. The structure of **2.12a** was established by NMR (Figure 2.5) showed an AMX pattern and HRMS analysis. In ^{1}H NMR spectrum, peaks at 2.48, 3.51 and 4.15 ppm were observed with an approximate integral value for 1H each. In the ^{13}C NMR spectrum only two signals were present in the aliphatic region (43.0 and 49.0 ppm.). This confirms the presence of aliphatic -CH_2 attached to -CH group. In addition, a signal at 197.5 ppm in ^{13}C NMR spectrum confirms the presence of a carbonyl group in the compound. Further, ^{1}H-^{1}H and ^{13}C-^{1}H correlation spectroscopic (COSY and HETCOR), nuclear overhauser effect spectroscopic (NOESY and NOE) analysis were also carried out to evaluate the structure. From HETCOR it was learnt that both the protons corresponding to 2.47 and 3.50 ppm are corollated to a single carbon at 43.0 ppm whereas the proton corresponding to 4.13 ppm is corollated to the carbon at 49.0 ppm. The NOE study shows NOEs between CH_2 (δ = 2.47 and 3.50 ppm) and CH (δ = 4.12 ppm). The structure was confirmed by single crystal X-ray diffraction studies (Figure 2.5f). It was observed that, in the absence of TMOF, the reaction ended up with exclusive formation of benzo[*a*]fluorenone **2.12a**.



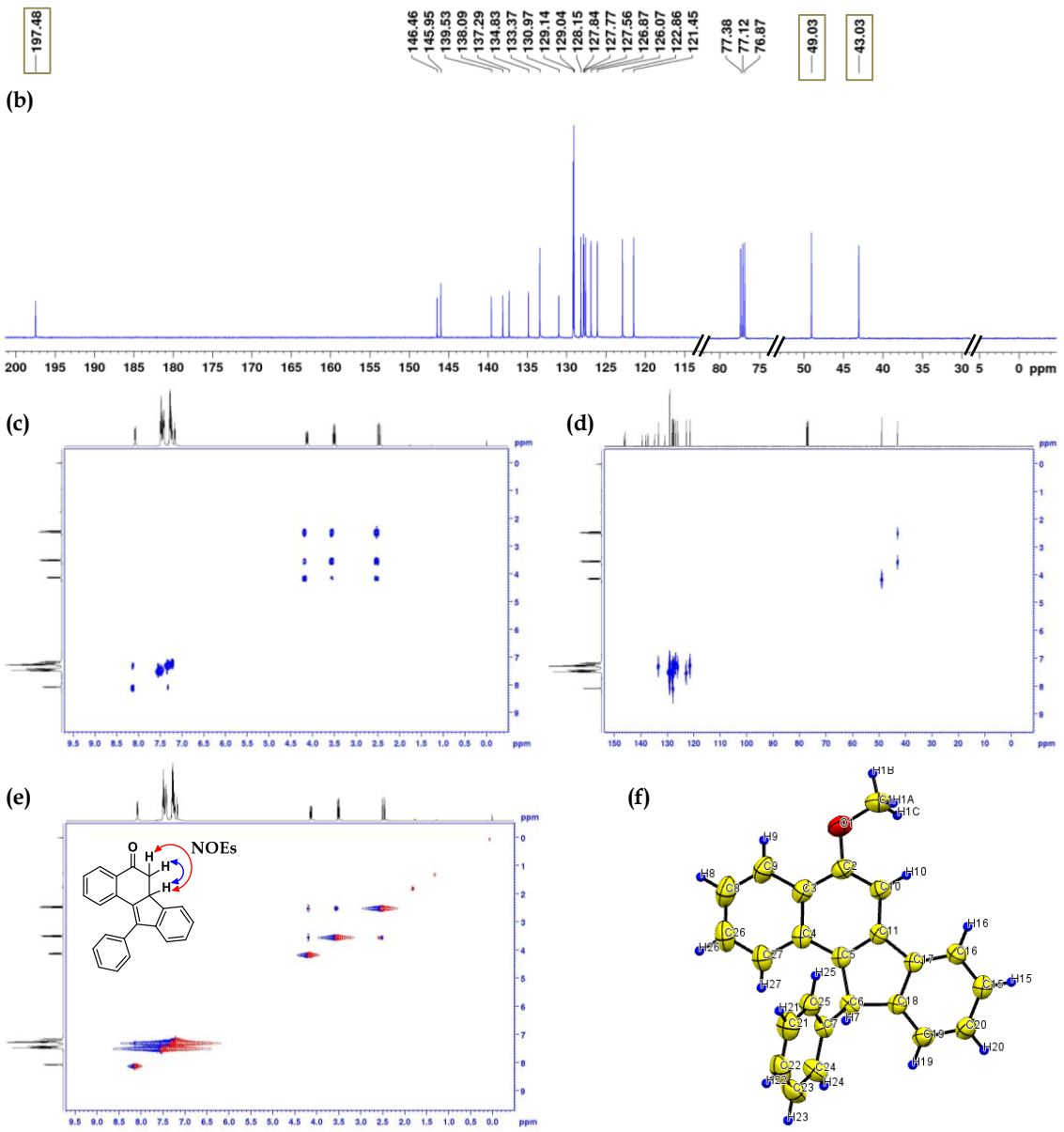
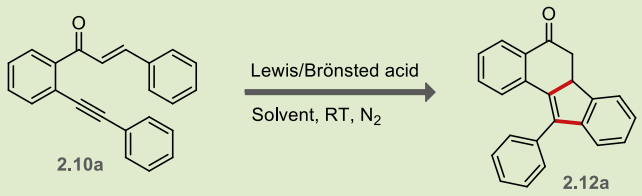


Figure 2.5. (a) ^{1}HNMR; (b) ^{13}C NMR; (c) COSY; (d) HETCOR; (e) NOESY (insight: NOEs) spectra; (f) ORTEP of benzo[*a*]fluorenone (**2.12a**).

By keeping all these aspects in mind, we moved forward to optimize the reaction conditions to obtain best result. The reaction was carried out by treating **2.10a** with 50 mol% of TfOH in dichloromethane (DCM) solvent at room temperature under nitrogen atmosphere for 12 hours. Only 23% of benzo[*a*]fluorenone (**2.12a**) was produced (entry 1, Table 2.4). Next the catalyst loading was increased to 1 equiv. and 53% isolated yield of **2.12a** was obtained (entry 2, Table 2.4). Then various Lewis/Brønsted acids were screened, but, unfortunately, no promising result was found (entry 3-10, Table 2.4). Besides, solvent screening provided low to moderate

yields of **2.12a** (entries 11-18, Table 2.4). To our delight, remarkably high yield (97%) was obtained in HFIP solvent (entry 19, Table 2.4). Decreasing of the amount of TfOH to 50 mol% suppressed the product yield to 80% (entry 20, Table 2.4). So, use of 1 equivalent of TfOH in HFIP solvent was considered as the best reaction condition.

Table 2.4. Optimization of reaction conditions for the synthesis of benzo[*a*]fluorenone (**2.12a**).



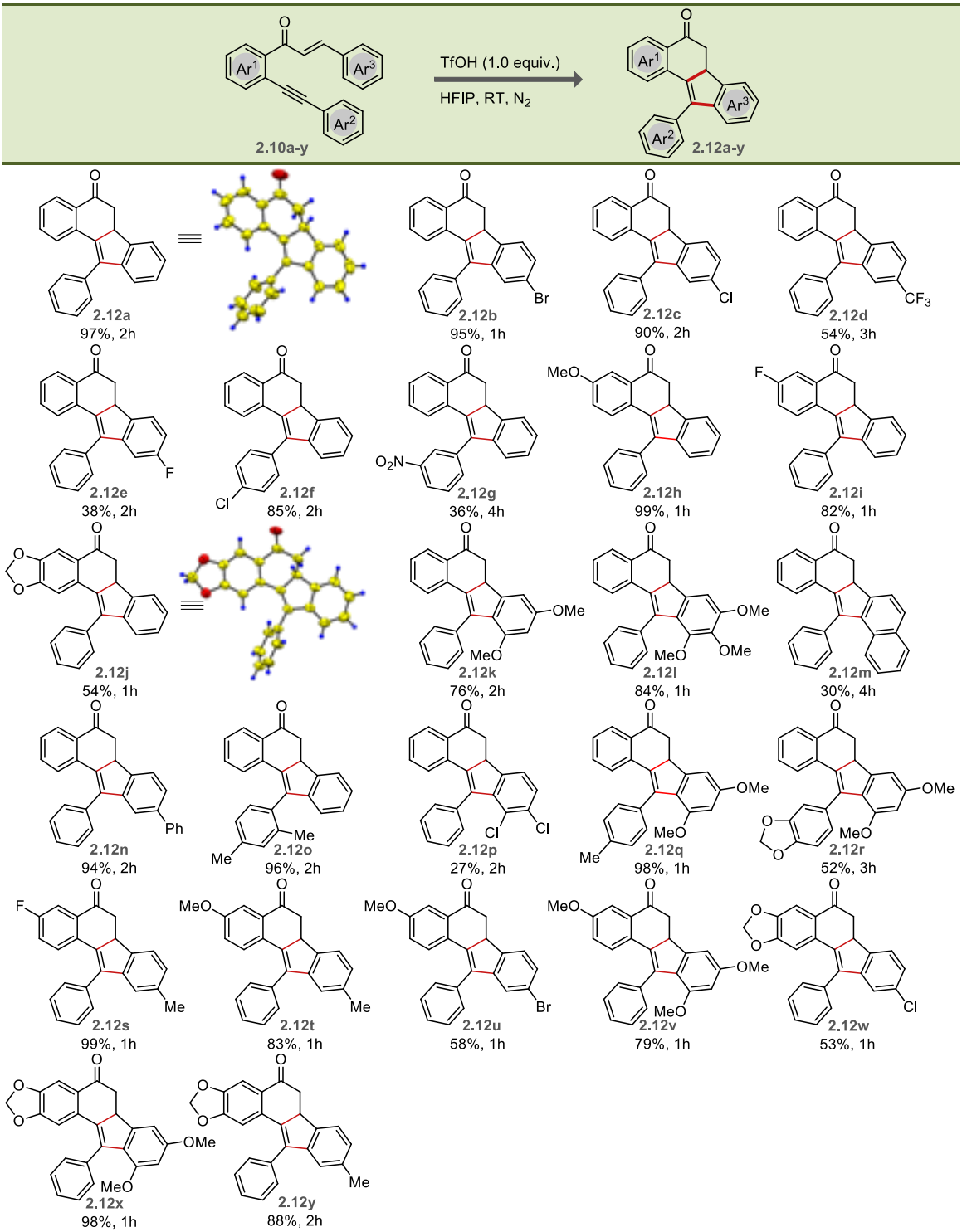
Entry	Solvent	Catalyst (equiv.)	Time (h)	Yield (%) of 2.12a
1	DCM	TfOH (0.5)	12	23
2	DCM	TfOH (1.0)	12	53
3	DCM	TFA (1.0)	24	NR
4	DCM	PTSA (1.0)	24	10
5	DCM	$Cu(OTf)_2$ (1.0)	24	NR
6	DCM	$Fe(OTf)_2$ (1.0)	24	NR
7	DCM	$Yb(OTf)_3$ (1.0)	24	NR
8	DCM	$AuCl_3$ (1.0)	24	-
9	DCM	$AgSbF_6$ (1.0)	24	-
10	DCM	$HSbF_6.6H_2O$ (1.0)	24	6
11	DCE	TfOH (1.0)	3	50
12	CH_3NO_2	TfOH (1.0)	3	45
13	Dioxane	TfOH (1.0)	24	-
14	CH_3CN	TfOH (1.0)	12	5
15	C_2H_5OH	TfOH (1.0)	12	16
16	IPA	TfOH (1.0)	12	18
17	THF	TfOH (1.0)	24	-
18	TFE	TfOH (1.0)	6	39
19	HFIP	TfOH (1.0)	2	97
20	HFIP	TfOH (0.5)	2	80

Reaction conditions: **2.10a** (0.1 mmol), Lewis/Brønsted acid and solvent (0.5 ml) at rt under N_2 atmosphere, unless otherwise stated. 'NR' means no reaction. '-' means complex mixture.

2.2.7. Substrate Scope for the Synthesis of Benzo[*a*]fluorenone Derivatives:

The scope of benzo[*a*]fluorenone synthesis was investigated under the optimized reaction condition using a variety of substrates having different substituents with diverse electronic effects. The outcome is tabulated in Table 2.5.

Table 2.5. TfOH-promoted synthesis of benzo[*a*]fluorenone derivatives (**2.12**).



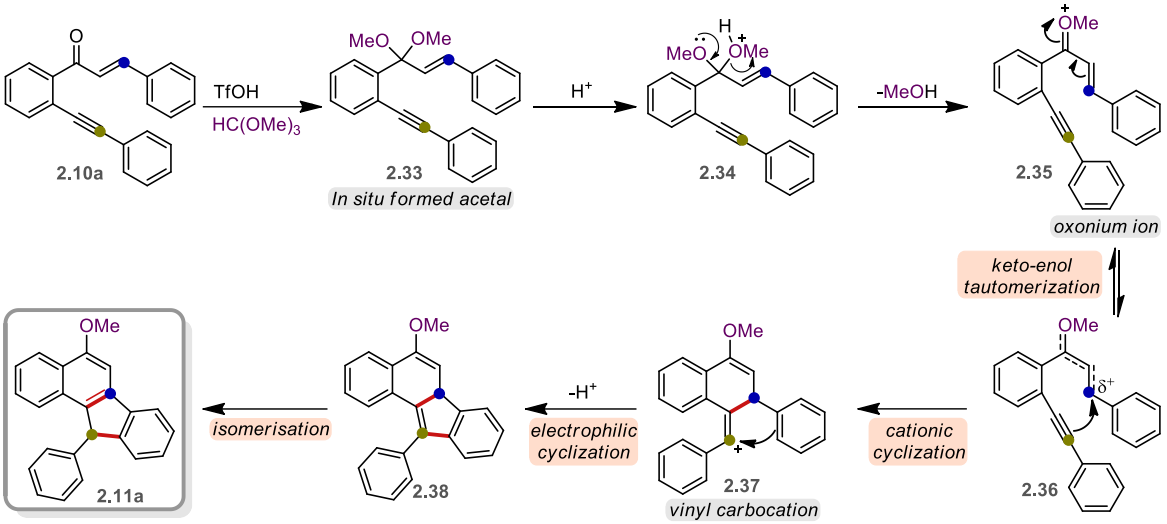
Reaction conditions: **2.10** (0.325 mmol), TfOH (1.0 equiv.), TMOF (3.0 equiv.) and HFIP (1.5 ml) at rt (25 ^{o}C) under N_2 atmosphere, unless otherwise stated.

The yields of these derivatives (**2.12**) were relatively higher in comparison to the analogous benzo[*a*]fluorenes (**2.11**) obtained from the reactions involving *in situ* formed acetals. Similar to benzo[*a*]fluorene synthesis, moderate or poor product yields were noticed whenever electron-withdrawing functionalities were present on the β-aryl ring of the enone moiety (**2.12d**, **2.12p**, **2.12u** and **2.12w**). In a similar fashion, substrate bearing an electron-withdrawing NO_2 substituent in the aryl ring attached to the alkyne moiety resulted in reduced product yield (**2.12g**, 36%), perhaps due to the destabilization of the benzylidene carbocation intermediate **2.41** which is likely to be formed after the first cationic cyclization. Reactions at the *p*- position of PhF are generally prompt than the analogous reactions at a single site of benzene as fluoro group is a *p*-donor.[11] As mentioned from the mechanistic path of this reaction, the second cyclization is happening at the *m*- position of fluoro substitution. So reduced product yield was seen for **2.12e**. With a fluoro substituent present on the aryl ring of *o*-alkynylaryl ketone, the yield of **2.12i** was not affected (82%) much. Alternatively, electron-donating substituents on the aryl ring, accelerated the reaction and afforded promising yields. In this case, methoxy group containing aryl ring of alkynylaryl ketone did not reduce the product yield more, as the oxonium type intermediate was not forming in this case. All the prepared benzo[*a*]fluorenones were characterized by NMR, HRMS, FTIR studies and the structure of **2.12a** and **2.12j** were further confirmed by single crystal X-ray diffraction analysis (CCDC numbers: 1560545 and 1560546 respectively).

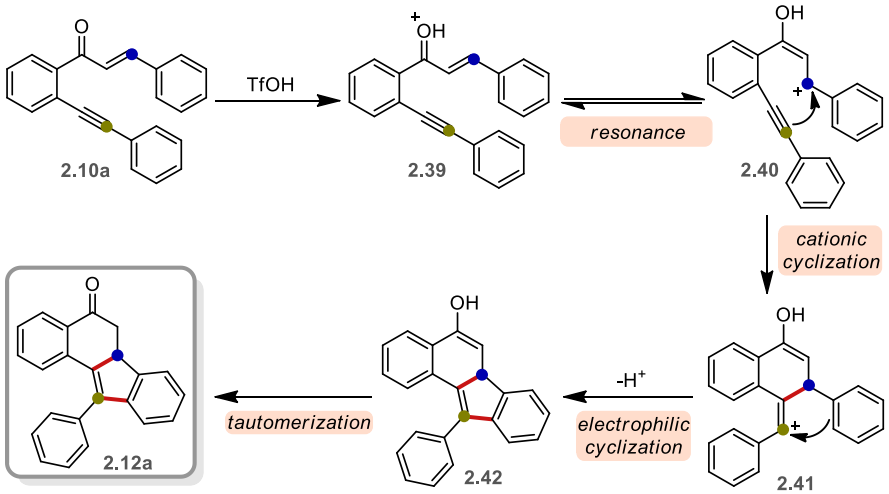
Moreover, both the transformations *i.e.*, benzo[*a*]fluorene and benzo[*a*]fluorenone formations were not feasible in presence of strong electron withdrawing substituents like 4-NO_2, 2-CN etc. Also, these reactions failed to give the desired products from highly substituted (*E*)-3-phenyl-1-(2-(phenylethynyl)phenyl)prop-2-en-1-one derivatives (**2.10**) which may be attributed to the steric effect. In addition, the reaction is not applicable when any of the three aryl moieties was replaced by cyclic/acyclic aliphatic moiety.

2.2.8. Mechanistic Insights of Benzo[*a*]fluorene and Benzo[*a*]fluorenone Formation:

A plausible mechanistic pathway for the formation of benzo[*a*]fluorenes (**2.11**) is illustrated in Scheme 2.5. The acetal **2.33** is formed from **2.10a** in the presence of trimethyl orthoformate and TfOH. The acetal then forms the oxocarbenium ion intermediate **2.35** through protonation of one of the OMe. Now the stage is set for the first cyclization and the intermediate **2.37** could form. This subsequently undergo benzannulation to form the benzofluorene derivative **2.38**. Finally, the intermediate **2.38** could isomerize quickly to the final product, benzo[*a*]fluorene derivative (**2.11a**). Tentative mechanism for benzo[*a*]fluorenone (**2.12a**) formation can be proposed as shown in Scheme 2.6. The 1,6-enynone **2.10a** undergoes protonation to form the intermediate [**2.40**]. Similar to benzo[*a*]fluorene case, first annulation occurs by the intramolecular attack of the alkyne in the intermediate [**2.40**] leading to the vinyl carbocation [**2.41**]. This vinyl carbocation is then trapped by the aryl group *via* aromatic electrophilic substitution reaction to form the intermediate [**2.42**]. Finally, the intermediate [**2.42**] will undergo tautomerization to result in the formation of benzo[*a*]fluorenone derivative (**2.12a**).



Scheme 2.5. Plausible reaction mechanism for the formation of benzo[*a*]fluorenes (**2.11**).

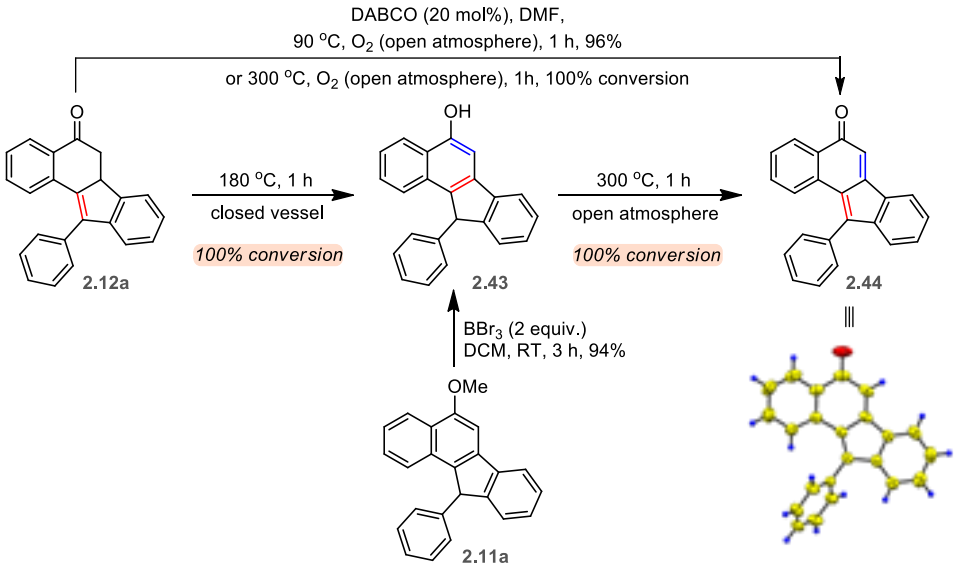


Scheme 2.6. Plausible reaction mechanism for the formation of benzo[*a*]fluorenones (**2.12**).

2.2.9. Late-stage Transformations of Benzo[*a*]fluorenes and Benzo[*a*]fluorenones:

It is surprising that none of the benzo[*a*]fluorenones **2.12a-y** isomerized to their analogous fluorenol derivatives under the reaction conditions. Alongside, we have shown some late-stage conversions of the products benzofluorene/fluorenone. Treatment of benzo[*a*]fluorene **2.11a** with BBr_3 produced the corresponding benzo[*a*]fluorenol **2.43** which is a stable product (Scheme 2.7). Interestingly, the benzo[*a*]fluorenone **2.12a** resulted in exclusive formation of **2.43** upon heating at 180 °C in a closed vessel under nitrogen atmosphere. To our surprise, both **2.12a** and **2.43** converted into a dark red colored solid compound **2.44** at 300 °C in an open atmosphere by dehydrogenation. The structures of **2.43** and **2.44** were arrived by NMR (^1H and ^{13}C), FTIR and

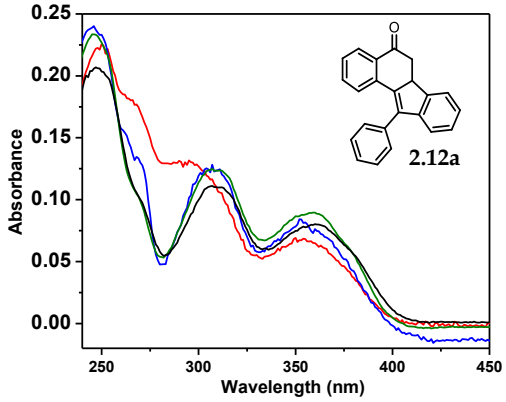
HRMS analysis. The structure of **2.44** was also confirmed by X-ray crystallographic analysis (CCDC number: 1560547).

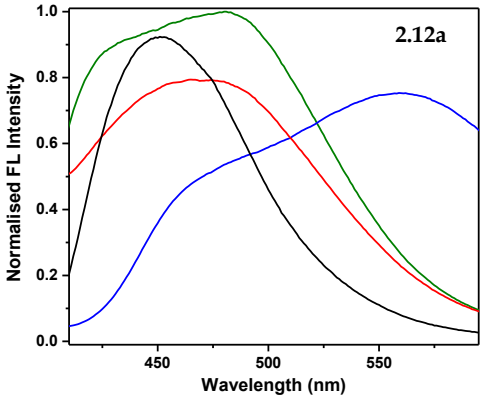


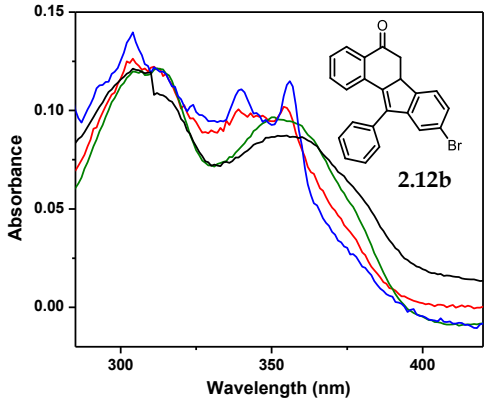
Scheme 2.7. Late-stage conversions of benzo[*a*]fluorene and fluorenone derivatives.

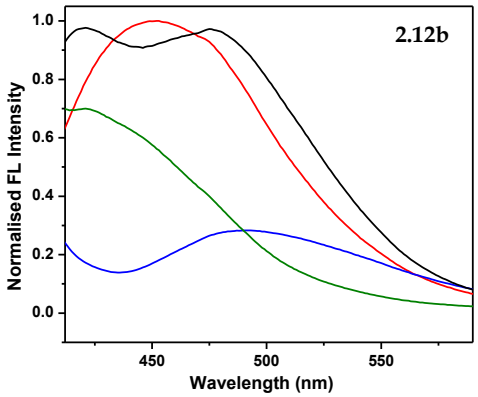
2.2.10. Photophysical Studies on Benzo[*a*]fluorenone Derivatives (2.12)

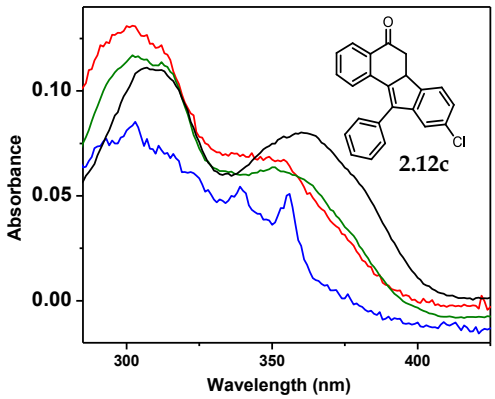
Interestingly all the prepared benzo[*a*]fluorenones (**2.12a-y**) are highly fluorescent in nature. This interesting photophysical property was further investigated by UV-Vis and fluorescent spectroscopic studies in different solvents *i.e.*, $CHCl_3$ (black line), CH_2Cl_2 (green line), CH_3CN (red line) and MeOH (blue line) with a fixed concentration of 10^{-5} M. They are given in figure 2.6. The absorption and fluorescence spectra of each compound is kept left and right respectively.

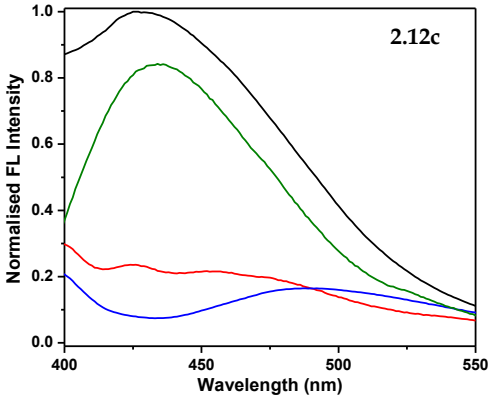


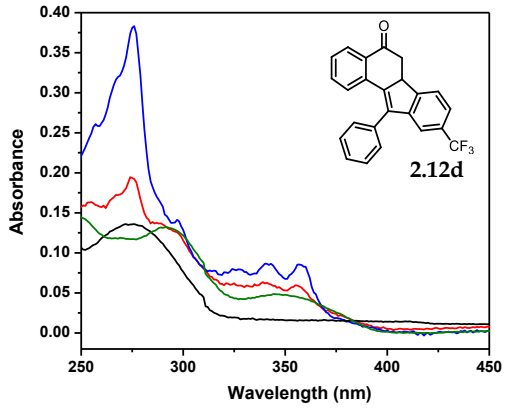


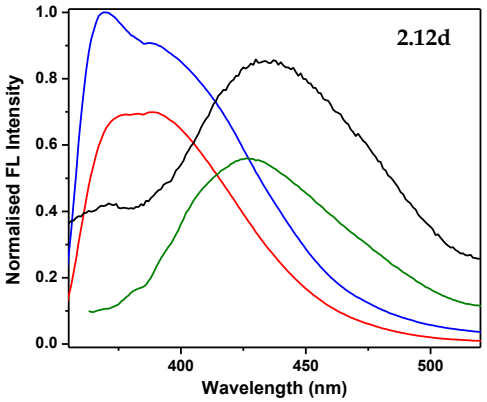

Absorbance
Wavelength (nm)
Br
2.12b

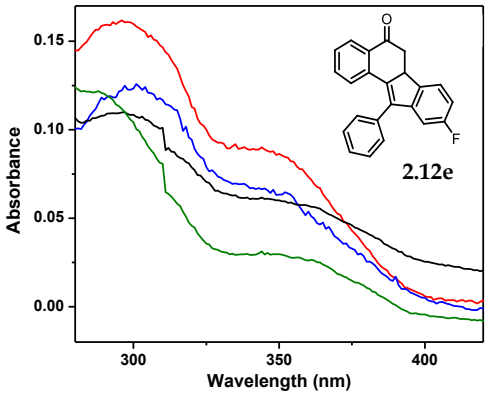

Normalised FL Intensity
Wavelength (nm)
2.12b

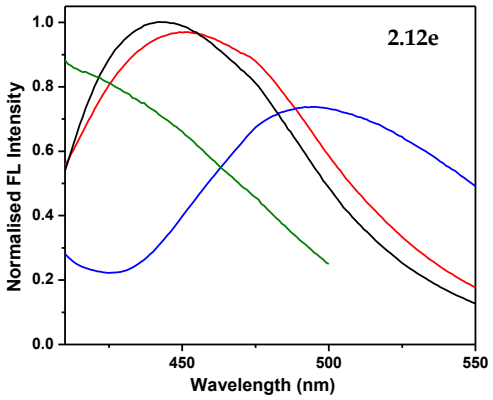

Absorbance
Wavelength (nm)
Cl
2.12c

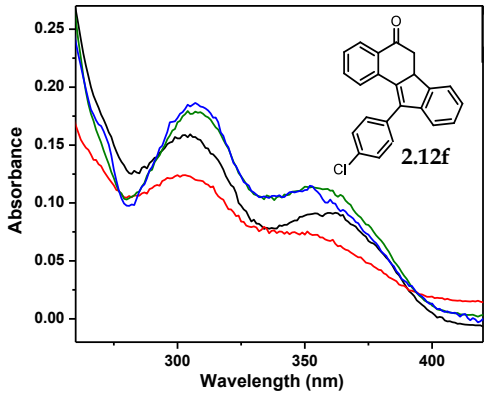

Normalised FL Intensity
Wavelength (nm)
2.12c

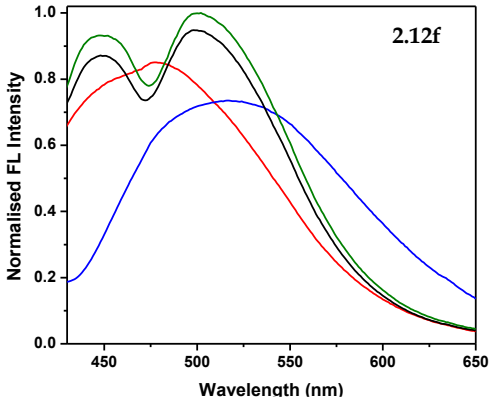

Absorbance
Wavelength (nm)
CF3
2.12d

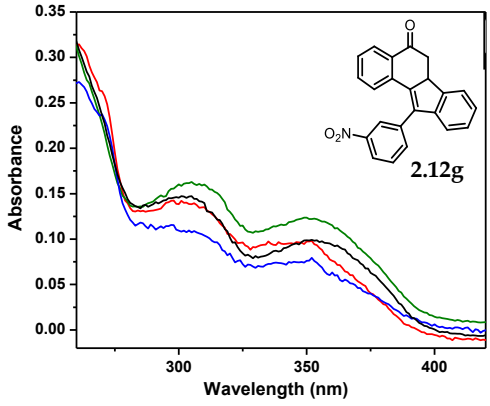

Normalised FL Intensity
Wavelength (nm)
2.12d

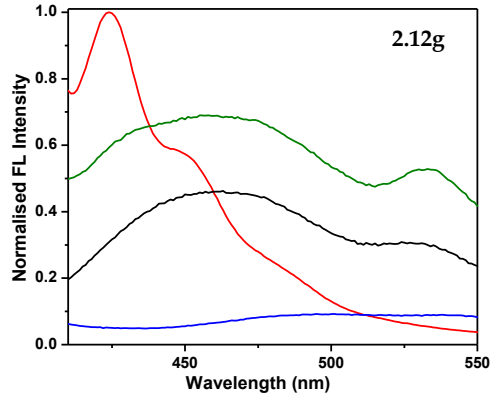

Absorbance
Wavelength (nm)
F
2.12e

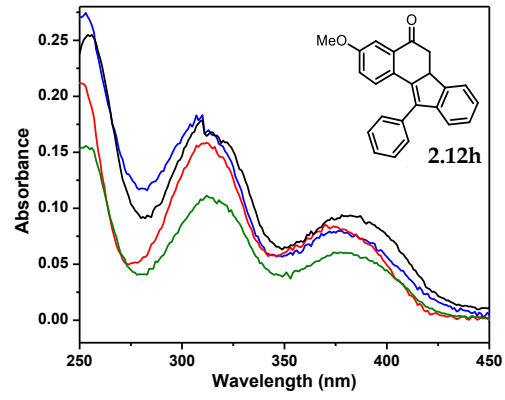

Normalised FL Intensity
Wavelength (nm)
2.12e

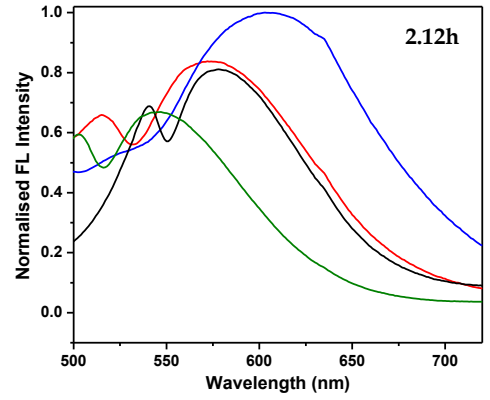

Absorbance
Wavelength (nm)
O
Cl
2.12f

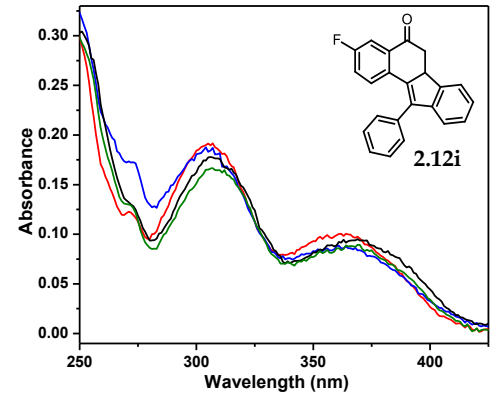

Normalised FL Intensity
Wavelength (nm)
2.12f

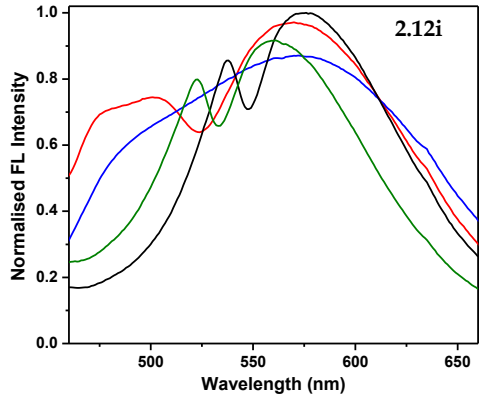

Absorbance
Wavelength (nm)
O
O2N
2.12g

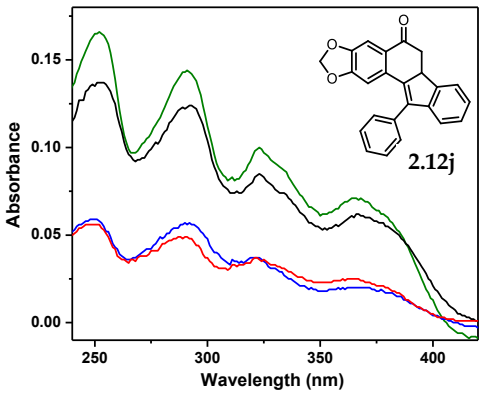

Normalised FL Intensity
Wavelength (nm)
2.12g

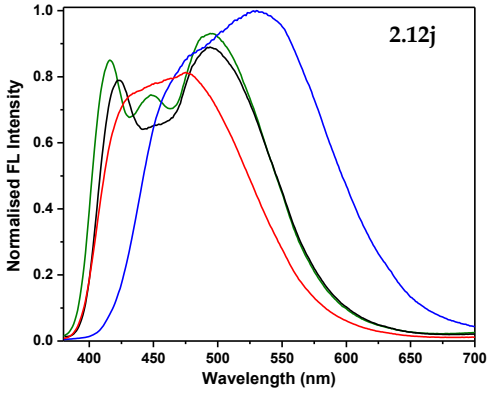

Absorbance
Wavelength (nm)
MeO
O
2.12h

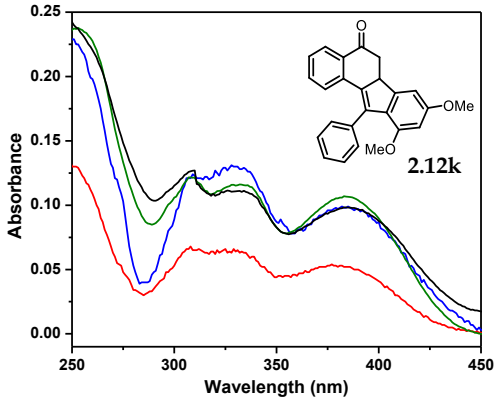

Normalised FL Intensity
Wavelength (nm)
2.12h

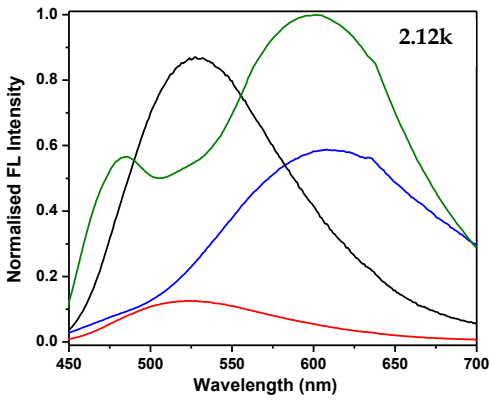

Absorbance
Wavelength (nm)
F
O
2.12i

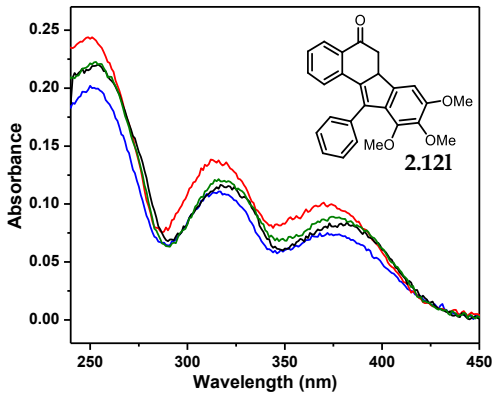

Normalised FL Intensity
Wavelength (nm)
2.12i

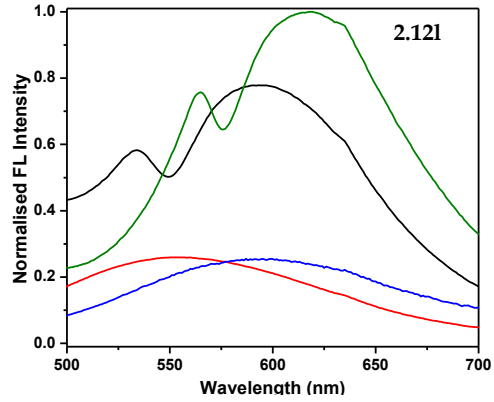

Absorbance
Wavelength (nm)
2.12j

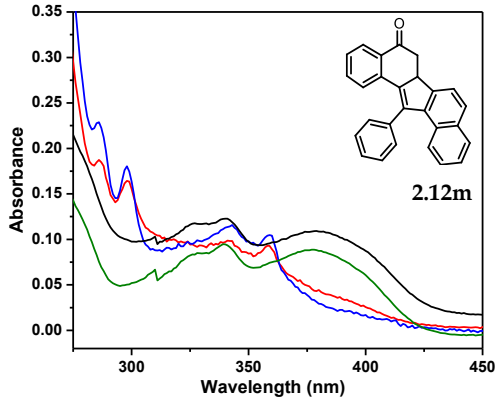

Normalised FL Intensity
Wavelength (nm)
2.12j

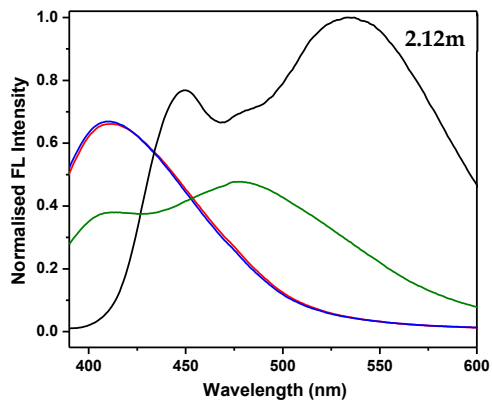

Absorbance
Wavelength (nm)
OMe
MeO
2.12k

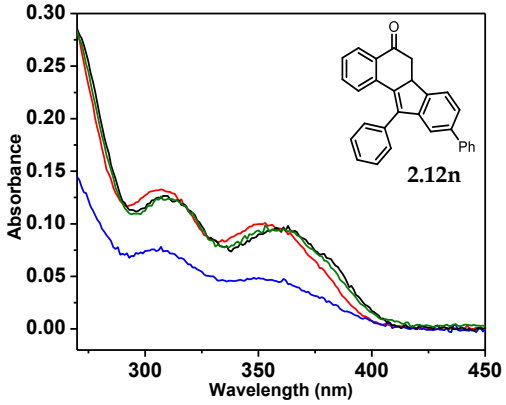

Normalised FL Intensity
Wavelength (nm)
2.12k

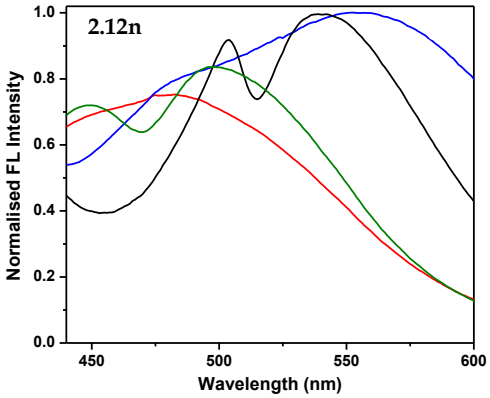

Absorbance
Wavelength (nm)
OMe
MeO
OMe
2.12l

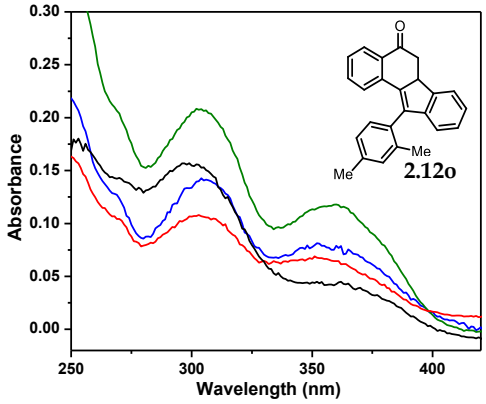

Normalised FL Intensity
Wavelength (nm)
2.12l

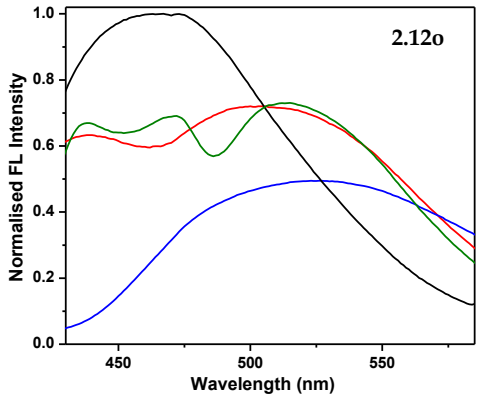

Absorbance
Wavelength (nm)
2.12m

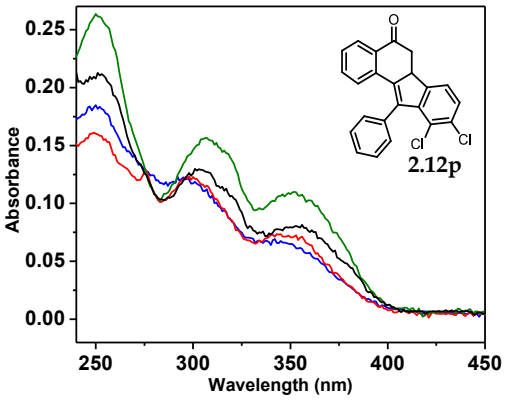

Normalised FL Intensity
Wavelength (nm)
2.12m

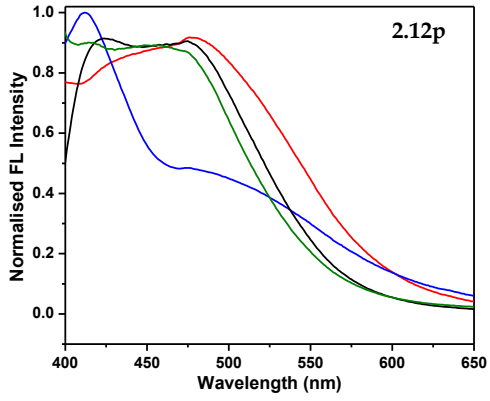

Absorbance
Wavelength (nm)
O
Ph
2.12n

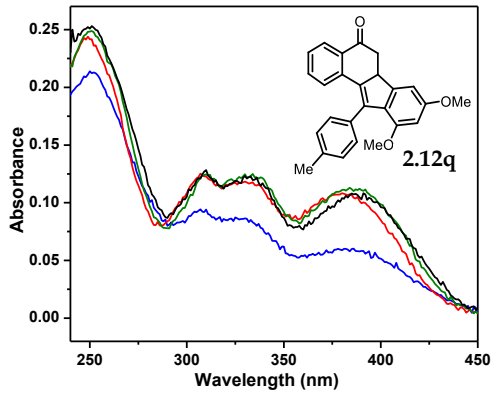

2.12n
Normalised FL Intensity
Wavelength (nm)

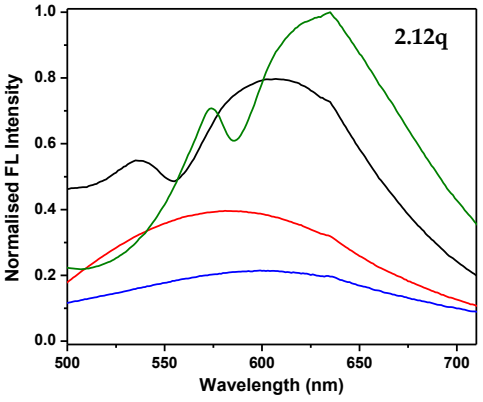

Absorbance
Wavelength (nm)
O
Me
Me
2.12o

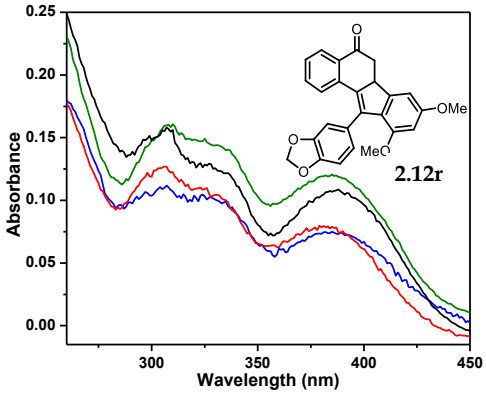

2.12o
Normalised FL Intensity
Wavelength (nm)

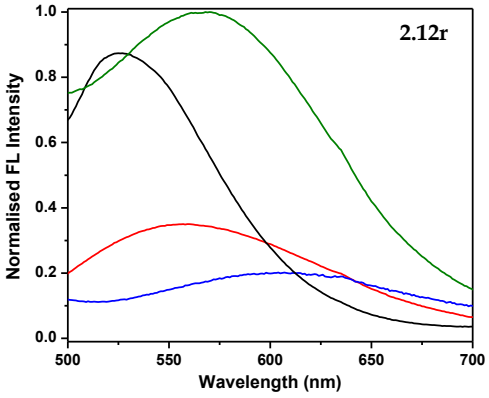

Absorbance
Wavelength (nm)
O
Cl
Cl
2.12p

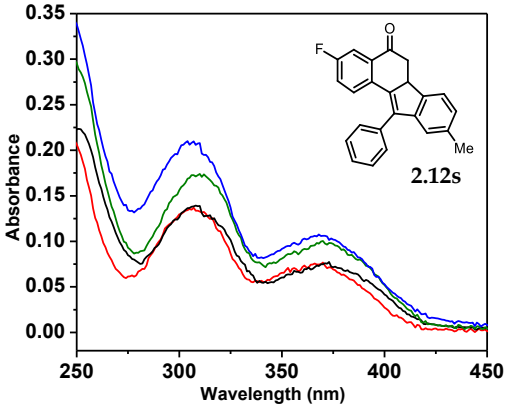

2.12p
Normalised FL Intensity
Wavelength (nm)

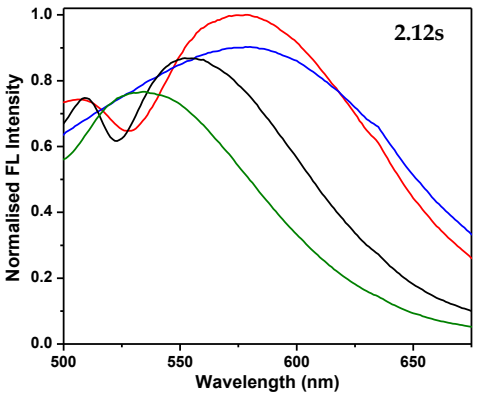

Absorbance
Wavelength (nm)
O
OMe
MeO
Me
2.12q

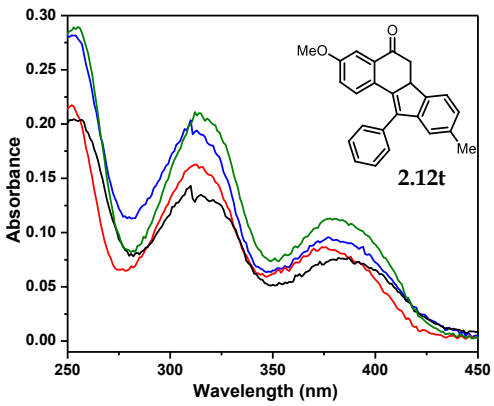

2.12q
Normalised FL Intensity
Wavelength (nm)

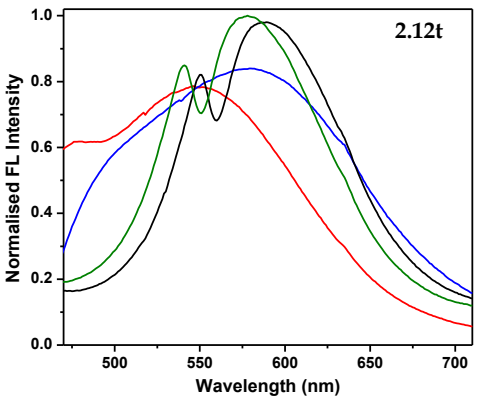

Absorbance
Wavelength (nm)
OMe
MeO
2.12r

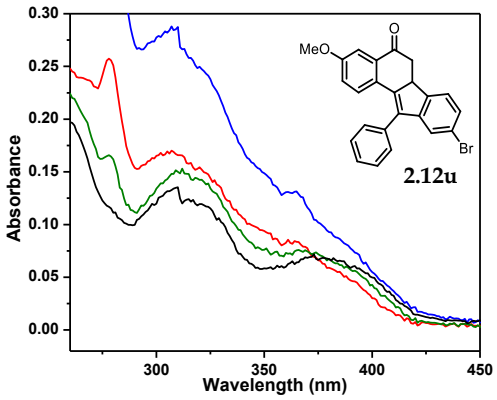

Normalised FL Intensity
Wavelength (nm)
2.12r

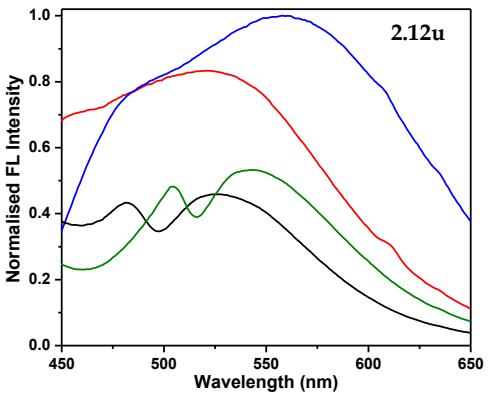

Absorbance
Wavelength (nm)
F
Me
2.12s


Normalised FL Intensity
Wavelength (nm)
2.12s


Absorbance
Wavelength (nm)
MeO
Me
2.12t


Normalised FL Intensity
Wavelength (nm)
2.12t


Absorbance
Wavelength (nm)
MeO
Br
2.12u


Normalised FL Intensity
Wavelength (nm)
2.12u

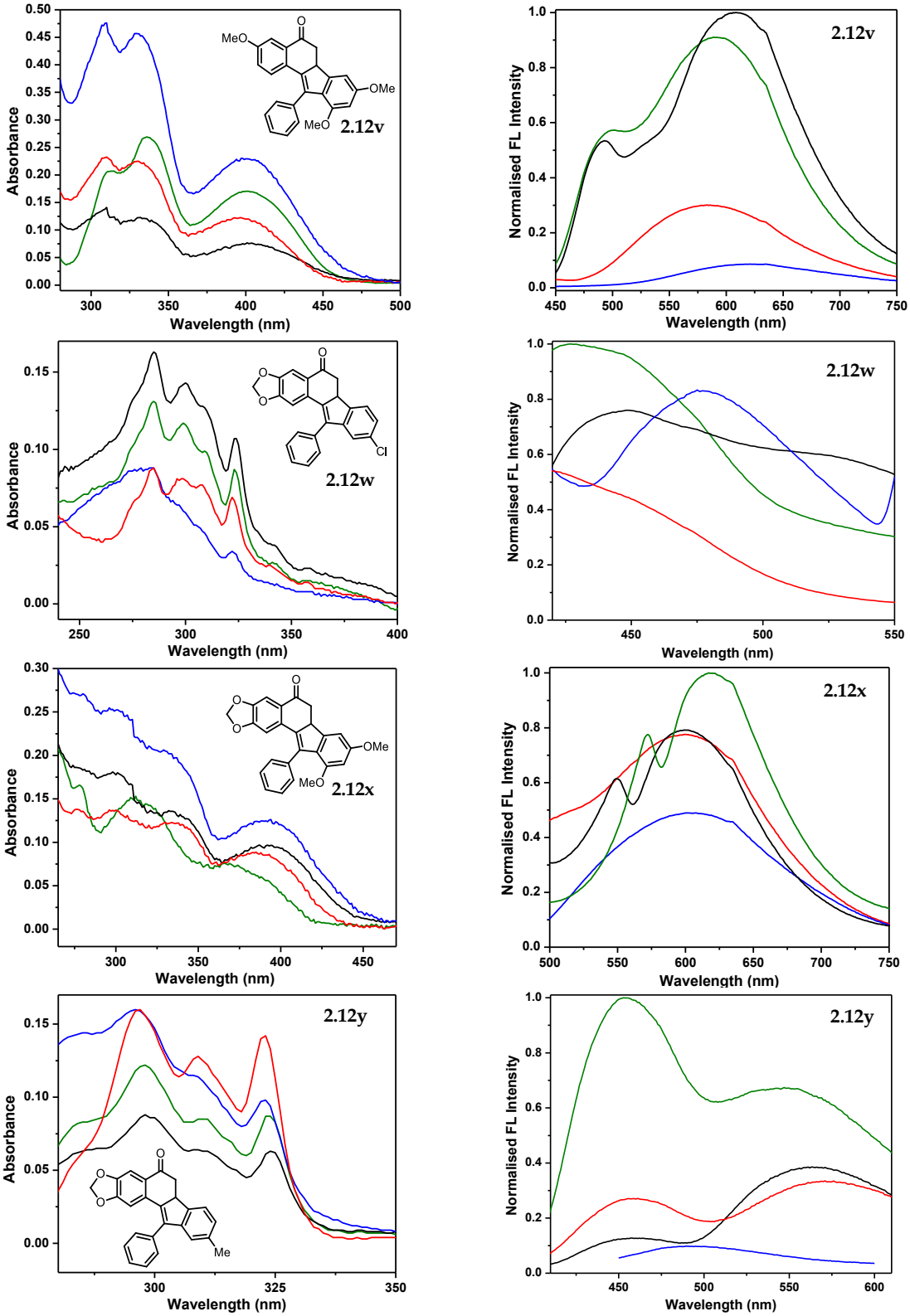


Figure 2.6. UV-Vis absorption and fluorescent spectra of Benzo[*a*]fluorenones(**2.12**).

Table 2.6. Stokes Shifts of the Benzo[*a*]fluorenones (**2.12**) in different solvents

Sl. No.	Pdt. No.	λ_{max} (nm)								Stokes Shift (nm)			
		Absorption				Emission							
		$CHCl_3$	DCM	ACN	MeOH	$CHCl_3$	DCM	ACN	MeOH	$CHCl_3$	DCM	ACN	MeOH
1	2.12a	361	359	354	353	453	481	465	559	92	122	111	206
2	2.12b	355	351	354	356	475	421	453	491	120	70	99	135
3	2.12c	360	351	354	356	426	434	454	492	66	83	100	136
4	2.12d	276	345	355	357	430	426	383	369	154	81	28	12
5	2.12e	359	357	350	348	442	411	449	494	83	54	99	146
6	2.12f	362	359	351	352	498	502	478	517	136	143	127	165
7	2.12g	352	349	352	352	463	455	424	501	111	106	72	149
8	2.12h	382	374	374	378	578	547	572	603	196	173	198	225
9	2.12i	369	369	364	361	576	561	570	572	207	192	206	211
10	2.12j	366	365	363	370	494	494	475	530	128	129	122	160
11	2.12k	384	384	377	382	527	602	528	608	143	218	151	226
12	2.12l	382	375	370	372	593	619	552	595	211	244	182	223
13	2.12m	379	377	358	359	533	478	412	411	154	101	54	52
14	2.12n	363	361	353	350	542	498	482	557	179	137	129	207
15	2.12o	362	360	351	360	467	515	503	523	105	155	152	163
16	2.12p	356	352	353	345	475	460	476	412	119	108	123	67
17	2.12q	385	384	380	383	607	635	581	599	222	251	201	216
18	2.12r	388	385	379	389	525	568	559	607	137	183	180	218
19	2.12s	373	370	370	368	552	535	579	580	179	165	209	212
20	2.12t	387	378	374	377	589	578	546	580	202	200	172	203
21	2.12u	382	374	364	365	525	542	523	558	143	168	159	193
22	2.12v	401	401	397	401	608	592	583	617	207	191	186	216
23	2.12w	323	323	322	322	449	427	420	475	126	104	98	153
24	2.12x	394	366	385	394	599	617	600	602	205	251	215	208
25	2.12y	324	323	323	323	563	453	571	490	239	130	248	167

The fluorescent benzo[*a*]fluorenones **2.12a**-**y** showed high Stokes shifts in all the solvents studied (Table 2.6). For example, when compound **2.12a** was excited at 359, 361, 353 and 354 nms corresponding to the n to π^* transition, it exhibited Stokes shifts of 122, 92, 111 and 206 nms in CH_2Cl_2, $CHCl_3$, CH_3CN and MeOH solvent respectively. In a similar manner all the synthesized benzo[*a*]fluorenones also have high Stokes shifts.[12] The Stokes shifts of magnitude more than 200

nm are highlighted in the table 2.6 for better understanding. Least overlapping of absorption and emission peaks is highly desired for efficient applications which is observed with most of the benzo[*a*]fluorenones synthesized by us. Also, the full width half maxima (FWHM) of the fluorescence peak is quite high. All these findings imply that these compounds are having high fluorescence properties and might find good application in material science. For further study we have chosen **2.12v** because of its high molar extinction coefficient (17,033 $mol^{-1}cm^{-1}$) corresponding to the n to π^* transition band at 401 nm in CH_2Cl_2 when compared with that of other synthesized benzo[*a*]fluorenone derivatives. Excellent fluorescence nature of **2.12v** was accounted by an emission maxima at 592 nm in fluorescence spectra upon excitation at 401 nm with a fluorescent quantum yield (ϕ) of 0.53. In addition, this benzo[*a*]fluorenone **2.12v** shows interesting solvatochromic effects. Figure 2.7 (a) presents an image of fluorescence activity of **2.12v** in different solvents under illumination using a long wavelength 365 nm uv lamp. Though fluorescence persisted in most of the checked solvents, nitromethane and ethanol quenched the fluorescence visibly. We have done paper strip experiments also. Blue dots of approximately 3-5 mm diameter were printed on a white sheet using a laser jet printer. A drop of **2.12v** in CH_2Cl_2 was applied on each drop. The dots showed fluorescence even after the solvent evaporated. (Figure 2.7 (b)). These observations provoked us to test whether we can use this compound **2.12v** as chemosensor for the detection of other nitroaromatic explosives or alcohols by fluorescence quenching. The findings of these experiments are illustrated in the next section.

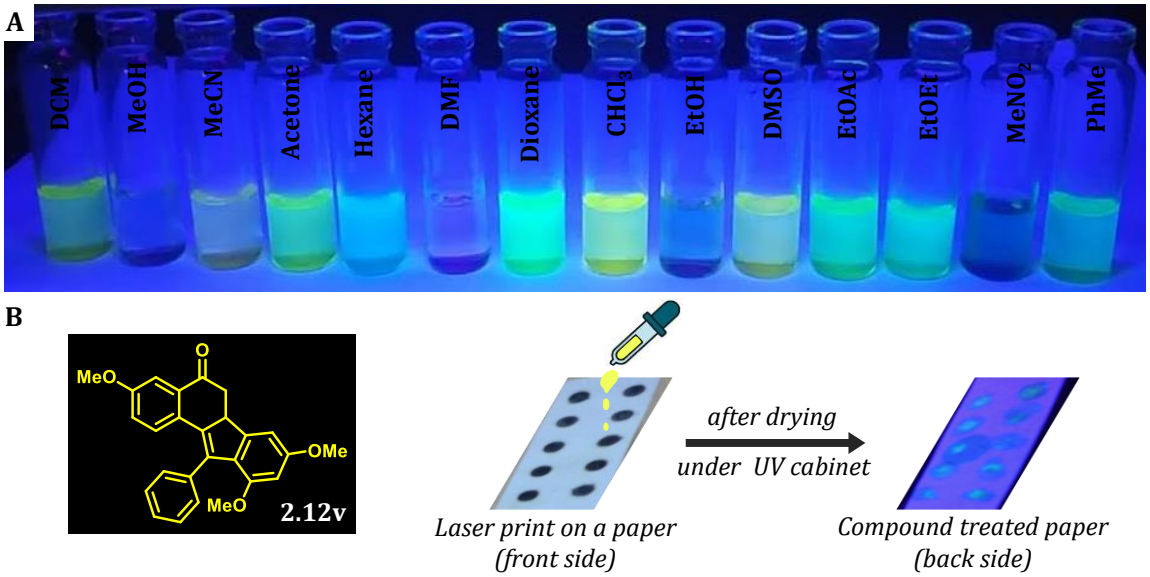


Figure 2.7. (A) Solvetochromic effect (B) Paper strip experiment of fluorescence of benzo[*a*]fluorenone **2.12v**.

2.2.11. Applications of Benzo[*a*]fluorenone Derivatives as Chemosensor:

Chemosensor can be defined as a molecule that signals the existence of matter. To detect such species, a range of analytical methods based on mass spectrometry,[13a] gas and liquid

chromatography,[13a] metal detection,[13a] surface-enhanced Raman spectroscopy (SERS),[13a] X-ray electrochemistry[13a-c] and diffraction and nuclear quadrupole resonance (NQR)[13a,d] etc. have been widely been used. However, the pragmatic application of these methods is restricted owing to several limitations like requirement of expensive equipments, complicated methodology involved such as sophisticated vapor sampling, lack of selectivity, instrument calibration etc. In this regard, fluorescence quenching method has been established as the most suitable and straightforward tool. This strategy commonly implemented in various fields such as biology, pharmacology, physiology and environmental sciences due to its intrinsic sensitivity, quick response, high selectivity, easy sampling and portability etc.[14] Thus, development of new chemosensors is always a sought after technology in sensing.

2.2.11.1. Selective Detection of TNT:

Explosives, typically nitroaromatics are a cause of great concern in recent days for human safety as they can release huge amount of heat as energy by self-oxidation for devastation purposes.[15] Among them, TNT is not only known for its destructive explore properties but also for its grievous environmental pollutions.[16] Thus, selective detection of TNT by means of chemosensors is a promising way to save our society from criminal terrorism. In this perspective, a number of fluorescent chemosensors such as molecularly imprinted polymers (MIPs),[17a] covalent organic polymers (COPs),[17b] conjugated organic/inorganic polymers,[17c-e] organic-inorganic hybrid materials,[17f-g] porous metal-organic frameworks (MOFs),[17h] luminescent gels,[17i] dendrimers,[17j] discrete macrocycles/cages[17k-l] and nano materials[17m-n] etc. have been exploited to sense TNT. Although thsese methods are having good selectivity and low detection limit, the time consuming synthesis of sensor materials with less efficiency severly limit the screening/upscaling probability and realistic applications. Therefore, simple organic molecule based fluorescent sensors were introduced for TNT sensing due to their simple preparation, easy purification, scalability and better reproducibility. But only a handful of systems like fluoroanthene, phosphonate pyrene, phosphonate porphyrins etc. are available for trace detection of TNT.[18] Thus, development of new, efficient chemosensor based on fluorescent organic small molecule is highly

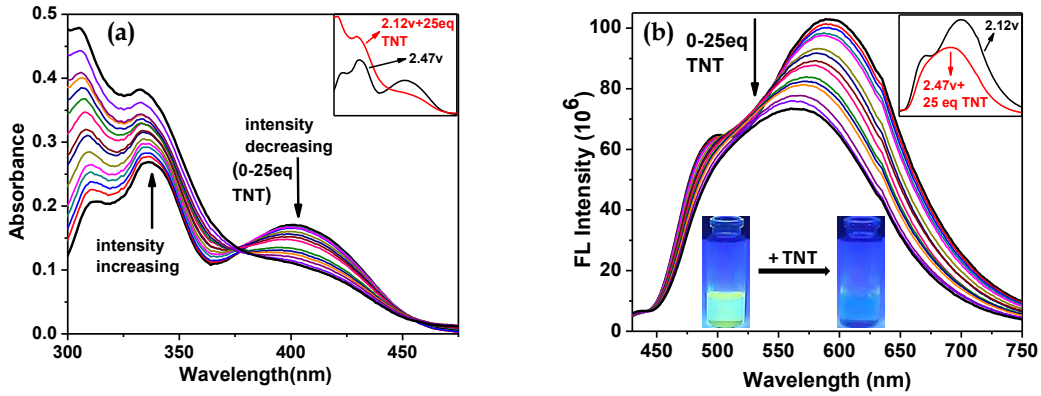


Figure 2.8. Change in UV-Vis spectra and quenching of fluorescence of compound **2.12v** (1 x 10^{-5} M) upon addition of TNT (1 x 10^{-3} M).

desirable from academic and industrial points of view.

Here is an account of how we have developed a new chemosensor based on our synthesized fluorescent benzo[a]fluorenone derivative. As described earlier, fluorescence was quenched almost completely in nitromethane solvent. This finding provoked us to probe the possibility of the detection of explosive nitroaromatics using the prepared benzo[*a*]fluorenone as fluorescent chemosensor. To investigate this finding, we have started with TNT sensing using **2.12v** as model substrate. Sensing of TNT was carried out by analysing the change of absorption and emission behaviour of a 1 x 10^{-5} M solution **2.12v** (1 mL in CH_2Cl_2 solvent) upon periodic addition of calculated amounts of TNT (1 x 10^{-3} M) in CH_2Cl_2 (upto 25 equivalents) as shown in Figure 2.8. All the emission spectra were recorded at an excitation wavelength of 401 nm. Upon gradual addition of TNT, an appreciable decrease in the intensities of absorbance and fluorescence corresponding to n to π^* transition of compound **2.12v** has been observed which infers its ability to act as a fluorescent chemosensor for TNT detection. Nearly 40% of the fluorescence was quenched by 25 equivalents of TNT. To our delight, an isosbestic point was observed at 377 nm as the π to π^* transition intensity increased while the n to π^* transition intensity decreased gradually upon addition of aliquots of TNT. This finding indicates a possibility of interaction between TNT and **2.12v**.[18] To justify this phenomenon, IR spectra were recorded for **2.12v** and **2.12v** treated with TNT seperately. Shifting of the sharp band from 1668 cm^{-1} to 1637 cm^{-1} corresponding to carbonyl stretching frequency in the IR spectra of compound **2.12v** treated with 25 equiv. TNT clearly supports that there is some interaction between **2.12v** and TNT (Figure 2.9).[19] In addition, ^1H NMR spectrum of 25 equiv. of TNT treated **2.12v** was also recorded (Figure 2.10).[19] In the spectrum, there is no shift of peak positions of **2.12v** which suggests no structural change of **2.12v** upon TNT addition. Then the sensitivity of **2.12v** towards TNT sensing was evaluated using Stern-Volmer equation ($(I_o/I) = 1 + K_{sv}C_A = 1 + k_q\tau_0 C_A$), (where I_0 and I are fluorescence intensity of **2.12v** in the absence and presence of TNT respectively, K_{SV} is Stern-Volmer constant, k_q is designated as the bimolecular quenching constant, τ_0 is the lifetime of compound **2.12v** whereas C_A is concentration of quencher). A linear response was observed in fluorescence quenching of **2.12v** in comparison with TNT concentration in the Stern-Volmer plot with a correlation coefficient of 0.971, K_{SV} 1.63 x 10^3 M^{-1} with 0.05% standard error (Figure 2.13a). As k_q depict the efficiency of quenching, it was then calculated and found to be 1.7 x 10^{13} M^{-1} s^{-1}.

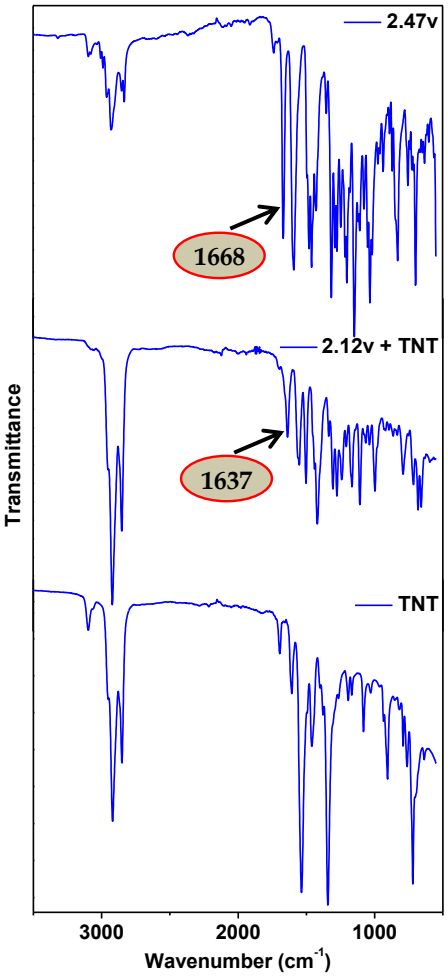


Figure 2.9. FT-IR Studies.

Moreover, the typical value of k_q for diffusion-controlled quenching is usually in the order of 1 x 10^{10} M^{-1} s^{-1}.

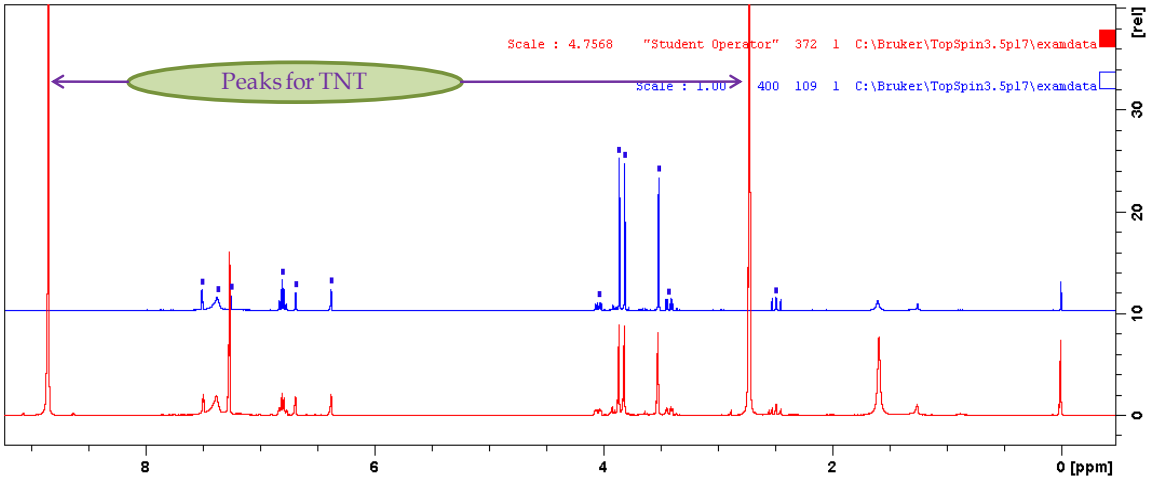


Figure 2.10. ^{1}H NMR studies on TNT sensing mechanism.

Here, the value of k_q is greater than that of the diffusion controlled limit. This result clearly suggests static quenching due to ground state interactions.

Consequently, to shed more light on the nature of quenching, we have evaluated the fluorescence life time decay by using a Time Correlated Single Photon Counting (TCSPC) technique. A 1 x 10^{-5} M solution of **2.12v** in CH_2Cl_2 gives a impressive τ value of 9.5 ns (Figure 2.11). The measured lifetime is correlated to the radiative and non-radiative electron-hole recombination processes. The radiative rate constant, k_r is associated to ϕ which is the number of photons emitted divided by the total photons absorbed, as $k_r = \Phi/\tau$. For the compound **2.12v** k_r is in the order of 10^9 s^{-1}. This high order of k_r implicits that an optically allowed transition is responsible for the emission in **2.12v**.[16] From the equation $\Phi = k_r/(k_r + k_{nr})$, the non-radiative rate constant k_{nr} of **2.12v** was determined to be in the order of 10^8 s^{-1}. It's clear that both the radiative and non-radiative rate constants are very fast. In addition, there should be a significant change in lifetime if it is a dynamic quenching.[17] But here the lifetime of compound **2.12v** treated with 25 equivalents of TNT was found to be 9.1 ns. This meager change in lifetime (9.1 ns and 9.5 ns) inspite of 40% quenching of fluorescence intensity with 25 equivalents of TNT, clearly suggests static quenching due to ground state interactions. However, from the nearly equal lifetime of **2.12v** before and after

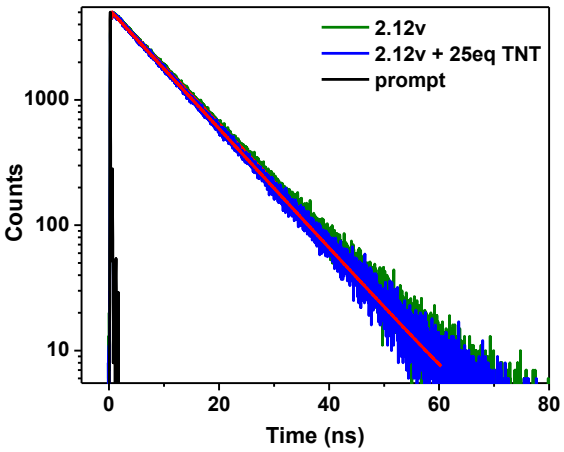


Figure 2.11. Life-time analysis.

TNT addition, it can be inferred that there is no complexation in the excited state or energy transfer between **2.12v** and TNT.

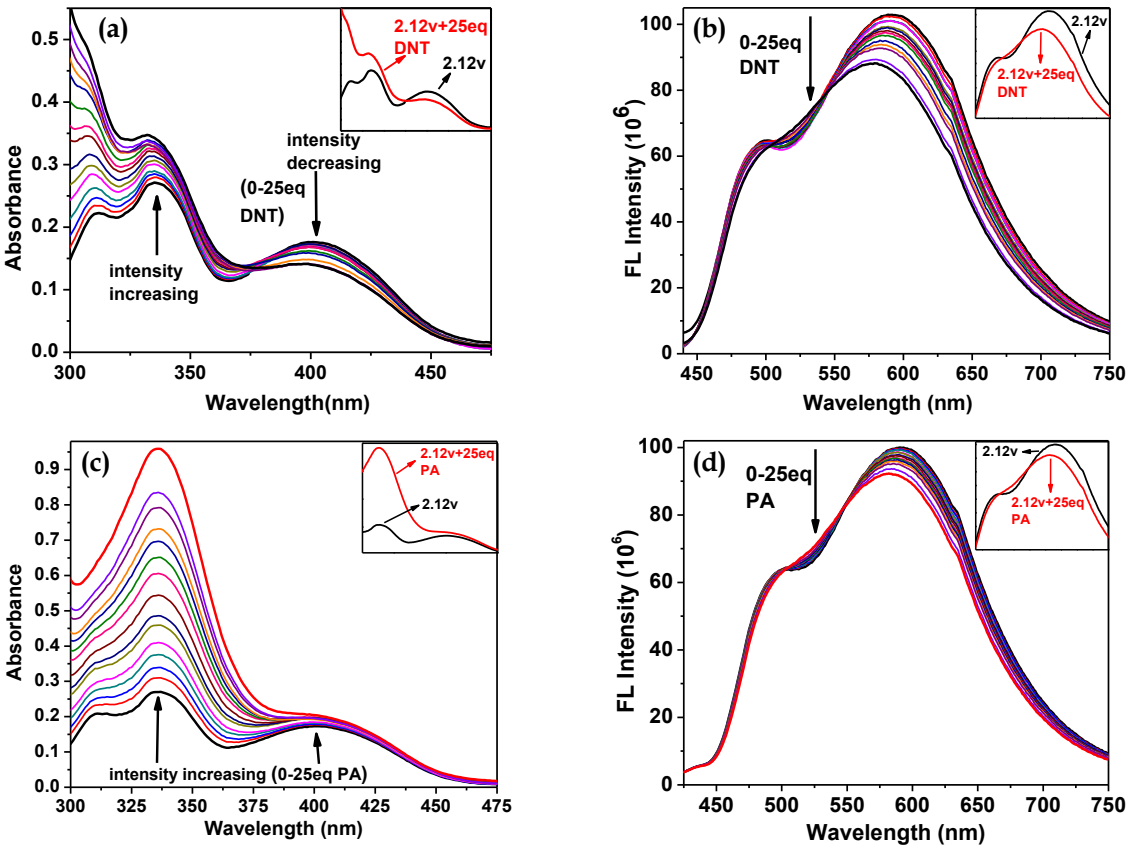


Figure 2.12. Change in UV-Vis spectra and quenching of fluorescence of compound **2.12v** (1 x 10^{-5} M) upon addition of DNT (1 x 10^{-3} M) (a-b) and PA (1 x 10^{-3} M) (c-d).

A similar analysis has been conducted with different nitroaromatics such as dinitrotoluene (DNT) and picric acid (PA) as quencher (Figure 2.12). In all the cases linear response was obtained in their respective Stern-Volmer plots with a correlation coefficient of 0.986 and 0.976 for DNT and PA respectively (Figure 2.13). But in comparison with TNT, considerably lesser K_{SV} was found like 0.648 x 10^3 M^{-1} and 0.341 x 10^3 M^{-1} with 0.03% and 0.04% standard error respectively for DNT and PA (Figure 2.13a). Hence this chemosensor has better sensitivity for TNT sensing. To clearly understand this phenomenon, we have shown a bar graph representing the sensing of different nitroaromatics (Figure 2.13a inset). Next, the stoichiometric ratio of interaction of TNT with compound **2.12v** was calculated using Jobs method and the ratio was found to be 2:8 (Figure 2.13b). In order to find the effect of concentration of compound **2.12v** on the fluorescence quenching property, a lower concentration of **2.12v** (1x 10^{-7} M solution) was treated with 1 x 10^{-6} M solution of TNT and emission spectrum was recorded under the same measurement conditions. Here also quenching of fluorescence was observed with adition of TNT solution (Figure 2.13c). The efficiency of sensing was assessed to determine the lowest

concentration of TNT that can be sensed by our probe **2.12v**. For this, aliquots of 10^{-6} M TNT solution in CH_2Cl_2 was added periodically to 1 mL 10^{-7} M solution of **2.12v** in CH_2Cl_2.

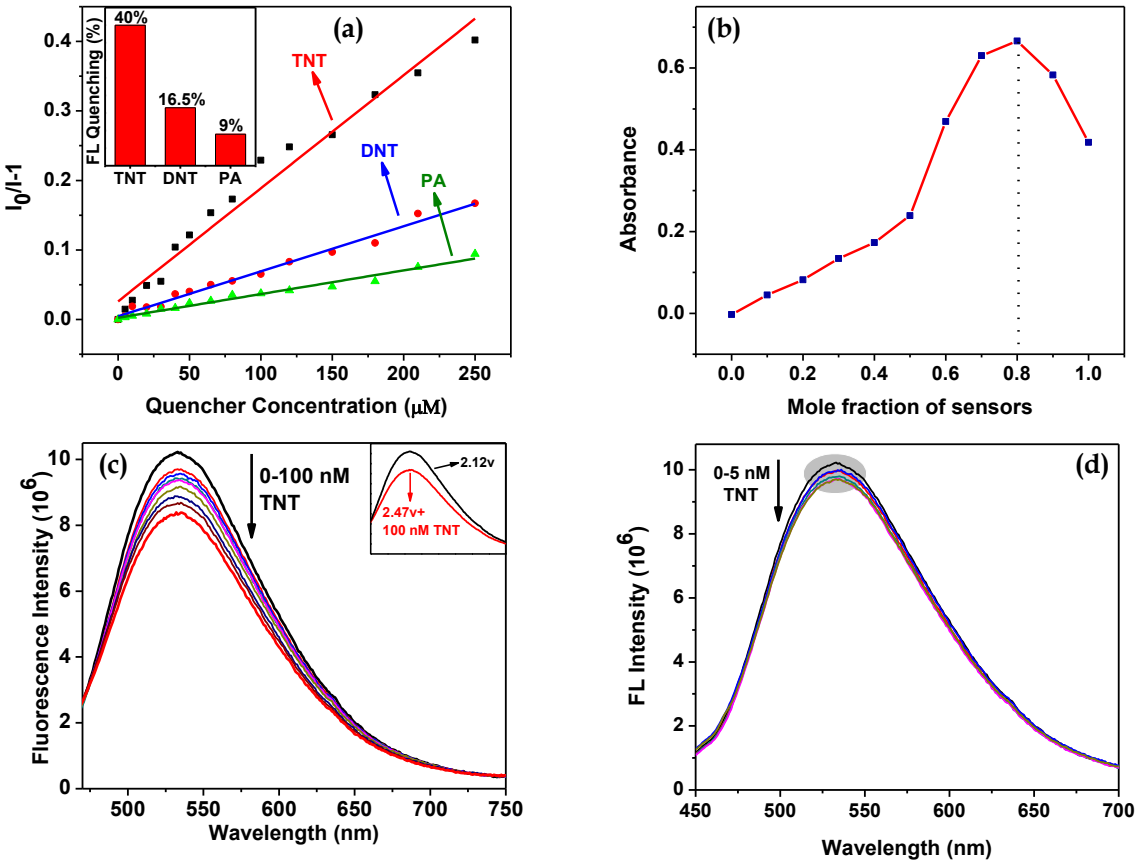


Figure 2.13. (a) Stern-Volmer plot corresponding to the FL quenching of TNT, DNT and PA; (b) Jobs plot to determine the stoichiometric ratio of interaction of TNT with compound **2.12v**; (c) FL spectra of compound **2.12v** (1×10^{-6} M) with nM conc. of TNT. (d) FL spectra for LOD of TNT sensing using compound **2.12v**.

Upon addition of aliquot, the ultimate concentration of TNT becomes nanomolar. The lowest concentration of TNT which reduces the fluorescence intensity by 5% is considered as the limiting concentration.[16f] In this case, a minimum of 4 nM solution of TNT was needed to decrease the fluorescent intensity by 5% (Figure 2.13d).

Additionally, for developing a more realistic application paper strip test has been performed. The bright yellow fluorescence of the paper strip coated with compound **2.12v** was quenched after dropping TNT solution on it (Figure 2.14). After getting this successful manifestation, we were interested to make a comparative study to show the

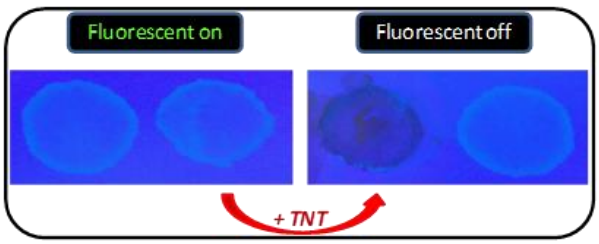


Figure 2.14. Paper strip experiment.

efficiency of our synthesized benzo[*a*]fluorenone moiety for solution phase TNT sensing. Table 2.7 clearly reveals that, in comparison to other reported methods with costly iridium based complex or porphyrine or pyrene-based macromolecules, benzo[*a*]fluorenone **2.12v** prepared by us exhibited outstanding detection limit of 4 nM.

Table 2.7. Comparision of the present vs. earlier reports for solution phase TNT sensing

Sl No.	Sensor	Limit of detection
1.	Benzo[*a*]fluorenone (**2.12v**)[a]	4 nM
2.	$(SBFIQ)_2Ir(acac)$[8a]	5 nM
3.	Phosphonate pyrene[13c]	8.8 nM
4.	Fluoroanthene[13d]	4.8 μM
5.	Phosphonate porphyrin[13b]	5 nM

[a] our work

2.2.11.2. Detection of Alcohol:

Impaired driving is responsible for most of the road accidents around the globe. Development of portable, sensitive and inexpensive chemosensor for alcohol detection[19] has a vital demand not only for safety purpose but also for industries like pharmaceutical industries, alcohol based fuel industries, food and clinical industries. Previously we have briefed about observation of quenching of fluorescence of our synthesized benzo[*a*]fluorenone by ethanol. To consolidate the study, we analysed the quenching of fluorescence of benzo[*a*]fluorenone derivative (**2.12v**) by ethanol solvent using a paper strip experiment. A solution of compound **2.12v** (1 x 10^{-5} M) in ethanol was applied on the dots printed on a paper using a laserjet printer. As seen in figure 2.15, there was no fluorescence of the dot spots as long as ethanol was present.

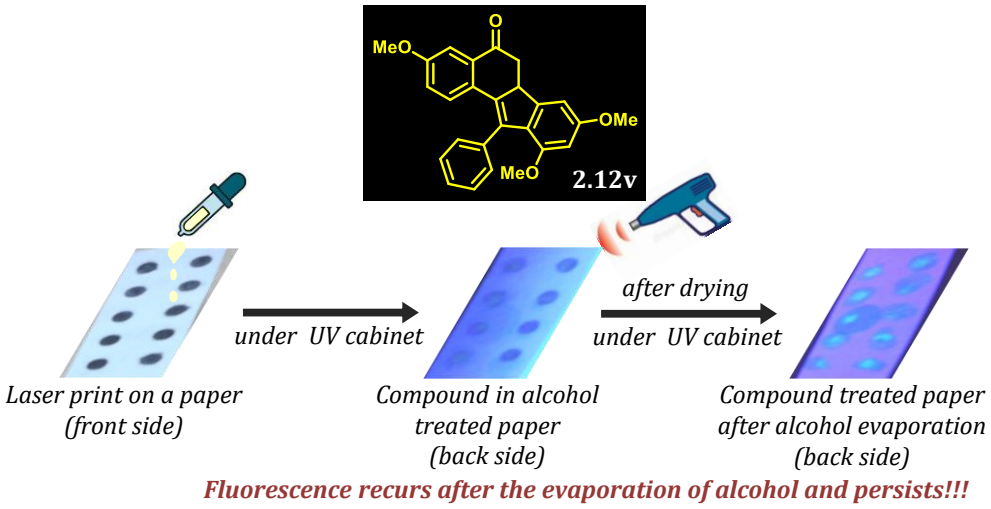


Figure 2.15. Photographs of paper strip experiment for visual detection of alcohol using compound **2.12v**.

It started showing intense fluorescence when the solvent got evaporated. It implies that in presence of alcohol fluorescence is off and after evaporation of alcohol fluorescence is on. The reason of this fluorescence on-off may be due to the keto-enol tautomerization or non bonding interaction of **2.12v** with alcohol. These observations suggest the potential application of these compounds in alcohol sensing.

2.2.11.3. Detection of Fluoride Ion:

Inorganic anions play important roles in a range of biological and chemical systems. It can behave as a nutrient or pollutant based on its concentration and availability. Among the anions, fluoride has engrossed enormous importance due to its vital role in teeth bones development.

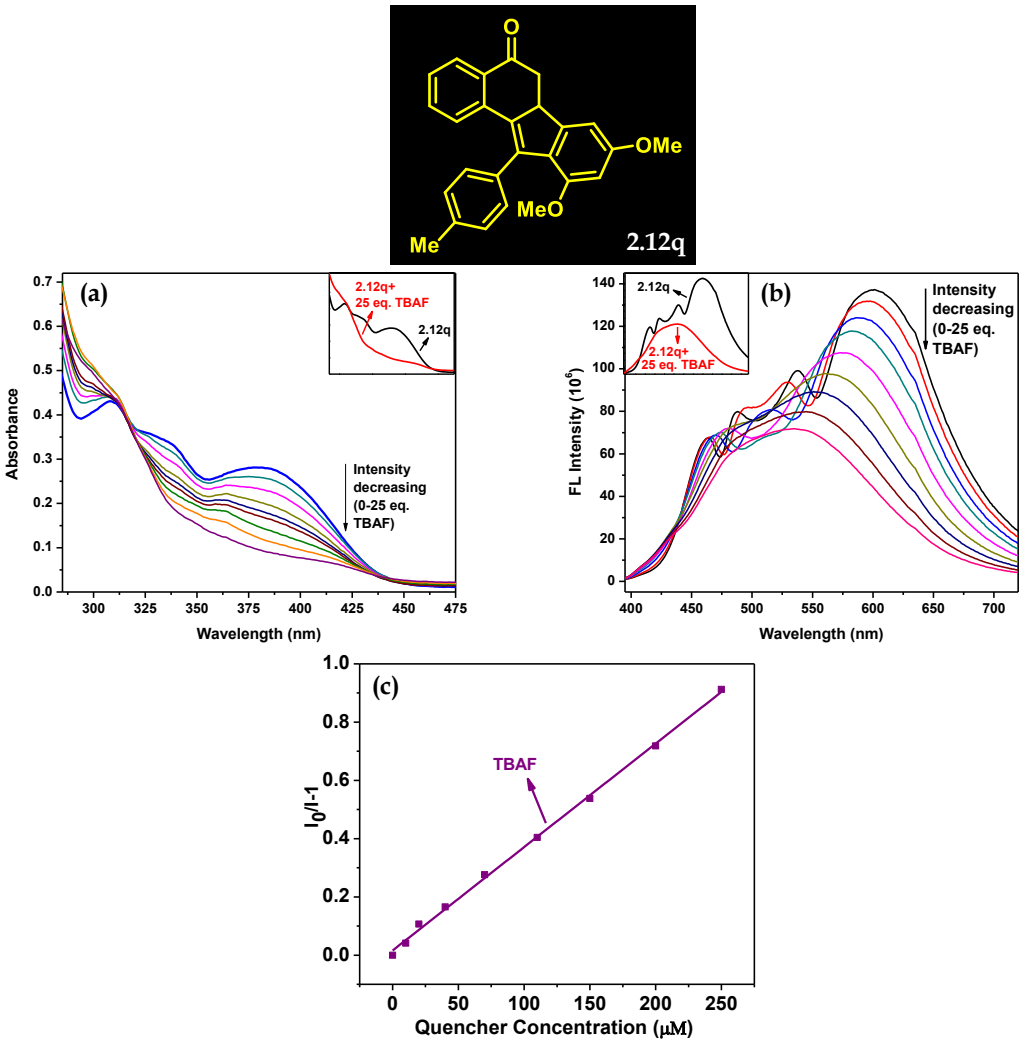


Figure 2.16. Change in UV-Vis spectra (a) and quenching of fluorescence (b) of compound **2.12q** (1 x 10^{-5} M) upon addition of TBAF (1 x 10^{-3} M); (c) Stern-Volmer plot corresponding to the FL quenching activities of TBAF with compound **2.12q**.

But excess consumption of fluoride could be responsible for urolithiasis/fluorosis /cancer.[20] The maximum content of fluoride should ideally be below 4 ppm in drinking water in order to avoid such diseases. Thus, development of chemosensors for fluoride is of high demand over the years.[21] After getting the afore mentioned interesting applications of our synthesized benzo[*a*]fluorenone derivative, we were curious to know whether our compound is capable of detecting any toxic anions like fluoride. With this idea in mind, we have started a few basic photophysical experiments for fluoride sensing with benzo[*a*]fluorenone **2.12q** using tetrabutylammonium fluoride (TBAF) as fluoride source. In this course, we achieved some promising results. In a similar fashion employed in TNT sensing, the absorption and emission spectra of a 1 x 10^{-5} M solution of **2.12q** (1 mL in CH_2Cl_2 solvent) were recorded upon successive addition of calculated amounts of TBAF (1 x 10^{-3} M) in CH_2Cl_2 (upto 25 equivalents) and the results are shown in Figure 2.16 (a) and (b). All the emission spectra were recorded with an excitation wavelength of 635 nm. The UV-Vis spectra revealed that the intensity of peak located at 384 nm corresponding to the n to π^* transition decreased eventually with periodic addition of a solution of fluoride ion. Same phenomenon was reflected in the fluorescence spectra also. As the fluoride ion being added, the fluorecence intensity decreased drastically and with 25 equivalents of TBAF fluorescence was quenched almost 53%. Then the sensitivity of **2.12q** towards TBAF sensing was analyzed by Stern-Volmer equation. Here also a linear response was observed in fluorescence quenching of **2.12q** with respect to the fluoride concentration with a correlation coefficient of 0.998, K_{SV} 3.5 x 10^3 M^{-1} with 0.01% standard error (Figure 2.16c). This fluorescence quenching mechanism may follow tautomerization and hydrogen bonding phenomenon. So our synthesized compound **2.12q** could also be used as chemosensor for fluoride sensing.

2.3. Conclusions:

In conclusion, we have successfully synthesized benzo[*a*]fluorenes and highly fluorescent benzo[*a*]fluorenones *via* cationic cycloisomerization of the enynone moity in presence of triflic acid promoter. The benzo[*a*]fluorenone derivatives have shown very impressing photophysical properties. We have also achieved few promising applications of our synthesized compounds in the field of sensing. The salient features of the work are presented hereafter.

- The methodology is operationally simple, high yielding and has diverse substrate scope.
- This method is more general and direct for the synthesis of benzo[*a*]fluorenone derivatives as two of the three reported methods are for the synthesis of specific derivatives.
- The synthesized benzo[*a*]fluorenone derivatives show solvent dependent fluorescence activity with several compounds having exceptional Stokes shifts.
- Fluorescence quenching by solvent nitromethane and ethanol has advantageously been used for the detection of explosives and alcohols.
- The synthesized benzo[*a*]fluorenone has been shown as an efficient sensor of TNT in solution phase with a sensing efficiency up to 4 nM of TNT. The selectivity for TNT sensing is high in comparison to other nitroaromatic explosives.

- The quenching of fluorescence is due to the ground state interaction of the benzo[*a*]fluorenone with TNT which is proved by lifetime measurements.
- Finally, the synthesized benzo[*a*]fluorenones have also exhibited their capability not only as alcohol detector but also as fluoride sensor.

2.4. Experimental Section:

2.4.1. General Experimental Informations:

All the reactions were performed under nitrogen atmosphere (unless otherwise stated) with oven-dried glasswares. Silica gel plates 60 F_{254} were used for thin layer chromatography (TLC) purpose and compounds were visualized by using UV light and/or by treatment with Seebach solution (phosphomolibdic acid (2.5 g), $Ce(SO_4)_2$ (1 g), Conc. H_2SO_4 (6 mL), H_2O (94 mL) followed by heating. Column chromatography was performed on silica gel (100-200 mesh) using ethyl acetate and hexanes mixture as eluent. ^1H, ^{13}C and ^{19}F spectra were recorded on a 400 MHz or 500 MHz spectrometers. IR spectra were recorded on a FT-IR spectrometer and are reported in cm^{-1}. High-resolution mass spectra (HRMS) were recorded using using ESI-Q-TOF technique. Melting points were determined by using a melting range apparatus and were uncorrected. X-ray data were collected at 293 K on a diffractometer with dual source. Mo-Kα (λ = 0.71073 Å) radiation is used to collect the X-ray reflections of the crystal. All UV-vis absorption spectra were recorded on a UV-Vis spectrophotometer and emission spectra were recorded on a fluorescence spectrometer. UV-Vis Spectra were recorded with a slit width of 1 nm. Slit widths of 3 and 5 nm were used on the excitation and emission monochromators respectively for fluorescence. Time-correlated single photon counting spectrometer was used to measure the time-resolved decays. Pico Brite (400 nm, 1 MHz repetition rate, and 60 ps pulse width) and MCP photomultiplier (Hamamatsu R3809U-50) were used as an excitation source and detector, respectively. The details of the setup including the analysis of the fluorescence decay curve can be found elsewhere.

2.4.2. Materials:

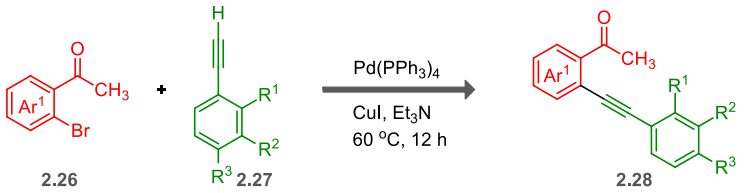
Unless otherwise noted, all the reagents were obtained commercially and used without purification. Dichloromethane (DCM), 1,2-dichloroethane (DCE) and chloroform were distilled over CaH_2. THF was dried over sodium and freshly distilled before use. Trimethyl orthoformate, triflic acid and hexafluoro isopropanol (HFIP), DNT, picric acid and TBAF were purchased from commercially available source, and used as it is. TNT was provided by Advanced Centre for Research in High Energy Materials (ACRHEM), University of Hyderabad, India. All starting materials were prepared by following known literature procedures. The solutions of all the synthesized benzo[*a*]fluorenone compounds for UV-Vis and fluorescence studies were prepared using spectroscopic grade solvents.

2.4.3. Synthesis and Characterization of Enynone Derivatives (2.10):

2.4.3.1. General Synthetic Procedure for the Preparation of 2-(Arylethynyl)acetophenone Derivatives (2.28):

Route 1: 2-Bromoacetophenone **2.26** (1.0 equiv.) and tetrakis(triphenylphosphine) palladium(0) (0.01 equiv.) were dissolved in dry triethylamine in a round bottom flask under nitrogen atmosphere at room temperature. After 5 minutes stirring, CuI (0.02 equiv.) was added and then allowed to stir for further 5 minutes. Next, the corresponding alkyne **2.27** (1.1 equiv.) was added and the reaction mixture was refluxed at 60 °C. After completion of the reaction as indicated by TLC, the reaction mixture was filtered through celite and the solvent was evaporated under reduced pressure. Finally, the crude product was purified by column chromatography (silica gel, hexanes/EtOAc) to get pure 2-(arylethynyl)acetophenone derivatives **2.28**.[8h]

The products were characterized by ^{1}H and ^{13}C NMR studies and the NMR data of all the prepared 2-(arylethynyl)acetophenone were in well accordance with the literature values.[22]



2.27a, $R^1 = R^2 = R^3 = H$
2.27b, $R^1 = R^2 = H; R^3 = Cl$
2.27c, $R_1 = R^3 = H; R^2 = NO_2$
2.27d, $R^2 = H; R_1 = R^3 = Me$
2.27e, $R^1 = R^2 = H; R^3 = Me$
2.27f, $R_1 = H; R^2, R^3 = O\text{-}CH_2\text{-}O$

2.28a, $R^1 = R^2 = R^3 = H$, 95%
2.28b, $R^1 = R^2 = H; R^3 = Cl$, 82%
2.28c, $R_1 = R^3 = H; R^2 = NO_2$, 79%
2.28d, $R^2 = H, R_1 = R^3 = Me$, 83%
2.28e, $R^1 = R^2 = H; R^3 = Me$, 88%
2.28f, $R_1 = H; R^2, R^3 = O\text{-}CH_2\text{-}O$, 78%

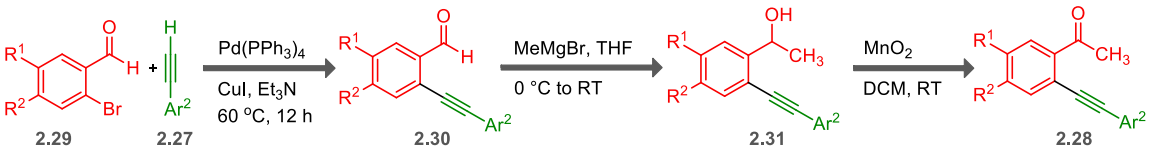
Scheme 2.8. Preparation of 2-(arylethynyl)acetophenones from 2-bromoacetophenones.

Route 2: 2-Bromobenzaldehyde derivative **2.29** (1.0 equiv.) and tetrakis(triphenylphosphine) palladium(0) (0.01 equiv.) were dissolved in dry triethylamine in a round bottom flusk under nitrogen atmosphere at room temperature. After 5 minutes stirring, CuI (0.02 equiv.) was added and then allowed to stir for further 5 minutes. Next, the corresponding alkyne **2.27** (1.1 equiv.) was added and the reaction mixture was refluxed at 60 °C. After completion of the reaction as indicated by TLC, the reaction mixture was filtered through celite and the solvent was evaporated under reduced pressure. Finally, the crude product was purified by column chromatography (silica gel, hexanes/EtOAc) to get pure 2-(arylethynyl)benzaldehyde derivatives **2.30**.[8h] All the products were analyzed by ^{1}H and ^{13}C NMR studies and the NMR data of all the prepared 2-(arylethynyl)benzaldehydes were in well accordance with the literature values.[22]

2-(Arylethynyl)benzaldehyde derivative **2.30** (1.0 equiv.) was then dissolved in dry THF followed by the addition of 1.1 equiv. of methyl magnesium bromide at 0 °C under inert atmosphere. Next, the reaction mixture was allowed to come at room temperature and stirred for 2 hours until completion of the reaction as indicated by TLC. Subsequently, the reaction mixture

was quenched with saturated ammonium chloride solution and then extracted with EtOAc and dried over anhydrous Na_2SO_4. The organic layer was concentrated under reduced pressure and purified by column chromatography (silica gel, hexanes/EtOAc) to afford 1-(2-(arylethynyl)aryl)ethanol derivatives **2.31**.

Compound **2.31** was then dissolved in DCM and MnO_2 (15 equiv.) was added to this solution. The reaction mixture was stirred at room temperature until completion of the reaction as indicated by TLC. Then the reaction mixture was filtered through celite and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (silica gel, hexanes/EtOAc) to get pure 2-(arylethynyl)acetophenone derivatives **2.28**.



2.29 2.27 2.30 2.31 2.28

2.29a, R^1 = F, R^2 = H
2.29b, R^1 = OMe, R^2 = H
2.29c, R^1, R^2 = O-CH_2-O

2.30a, R^1 = F, R^2 = H, 79%
2.30b, R^1 = OMe, R^2 = H, 75%
2.30c, R^1, R^2 = O-CH_2-O, 91%

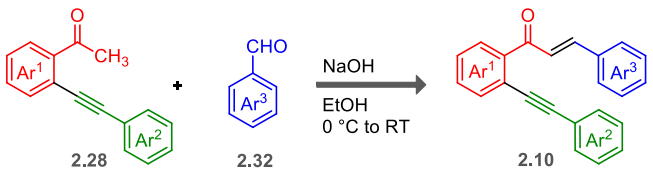
2.31a, R^1 = F, R^2 = H, 97%
2.31b, R^1 = OMe, R^2 = H, 98%
2.31c, R^1, R^2 = O-CH_2-O, 98%

2.28g, R^1 = F, R^2 = H, 97%
2.28h, R^1 = OMe, R^2 = H, 99%
2.28i, R^1, R^2 = O-CH_2-O, 97%

Scheme 2.9. Preparation of 2-(arylethynyl)acetophenones from 2-bromobenzaldehyde.

2.4.3.2. General Synthetic Procedure for the Preparation of 1,6-Enynone Derivatives (2.10):

Arylaldehyde **32** (1.2 equiv.) was slowly added to a solution of 2-(arylethynyl)acetophenone derivative **2.28** (1 equiv.) in ethanol at 0 °C. Subsequently, 15% NaOH solution in ice-cooled water was added very slowly with continuous stirring until turbidity appeared. Then the reaction mixture was allowed to come to room temperature and then stirred for 30 mins. After completion of the reaction, ethanol was evaporated under reduced pressure and then extracted with EtOAc. The organic layer was concentrated under reduced pressure and the residue was purified by column chromatography (silica gel, hexanes/EtOAc) to afford the desired product, enynone derivatives **2.10**.[22] The structure of all the products was confirmed by ^1H, ^{13}C and ^{19}F NMR spectroscopy, HRMS, and IR spectroscopy. Some have already been reported in literature, for which all the NMR data are in well accordance with the literature values.[23]

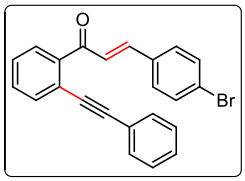


2.28 2.32 2.10

Scheme 2.10. Preparation of 1,6-enynone derivatives from 2-(arylethynyl)acetophenones.

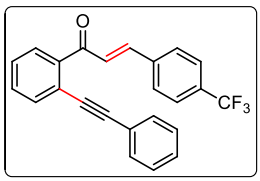
2.4.3.3. Analytical Data of 1,6-Enynone Derivatives (2.10):

(*E*)-3-(4-Bromophenyl)-1-(2-(phenylethynyl)phenyl)prop-2-en-1-one (2.10b, Table 2.2):



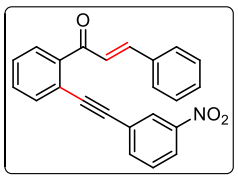
Yellow solid (yield = 82%); M.P. = 46 - 47 °C; R_f value = 0.32 (5% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$): δ7.72 - 7.52 (m, 5H), 7.50 - 7.38 (m, 5H), 7.37 - 7.32 (m, 2H), 7.29 - 7.17 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ193.3, 142.6, 141.7, 136.4, 133.4, 133.2, 131.5, 131.0, 129.6, 129.2, 128.8, 128.7, 128.5, 128.3, 126.3, 122.6, 121.6, 95.7, 88.3; IR (Neat, cm^{-1}): 2920, 1706, 1618, 1587, 1494, 1262, 1066, 1019, 818, 756, 663; HRMS: *m/z* [M+Na]$^+$ calcd for $C_{23}H_{15}BrO$: 409.0198; found: 409.0198.

(*E*)-1-(2-(Phenylethynyl)phenyl)-3-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (2.10d, Table 2.2):



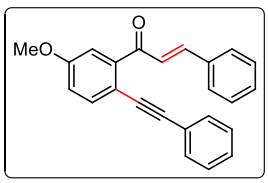
Yellow solid (yield = 93%); M.P. = 82 - 83 °C; R_f value = 0.33 (10% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ7.75 - 7.63 (m, 6H), 7.57 (d, *J* = 8.3 Hz, 2H), 7.52 (td, *J* = 7.5, 1.4 Hz, 1H), 7.45 (td, *J* = 7.5, 1.3 Hz, 1H), 7.32 (d, *J* = 7.0 Hz, 2H), 7.30 - 7.24 (m, 1H), 7.23 - 7.17 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ192.8, 141.4, 139.1, 133.8, 133.3, 132.1, 131.5, 131.3, 129.8, 129.5, 129.0, 128.8, 128.5, 128.3, 128.0, 126.2 (q, *J* = 5.6 Hz), 122.6, 121.7, 95.8, 88.1; ^{19}F NMR (376 MHz, $CDCl_3$): δ-62.9; IR (Neat, cm^{-1}): 3049, 1665, 1603, 1494, 1417, 1324, 1123, 1066, 1014, 761, 689; HRMS: *m/z* [M+Na]$^+$ calcd for $C_{24}H_{15}F_3O$: 399.0967; found: 399.0968.

(*E*)-1-(2-((3-Nitrophenyl)ethynyl)phenyl)-3-phenylprop-2-en-1-one (2.10g, Table 2.2):



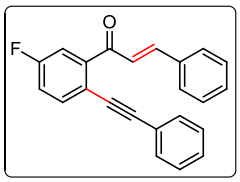
Yellow liquid (yield = 95%); R_f value = 0.16 (5% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ8.20 (s, 1H), 8.08 (d, *J* = 8.1 Hz, 1H), 7.74 - 7.56 (m, 6H), 7.55 - 7.43 (m, 4H), 7.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ192.6, 148.5, 141.14, 141.13, 140.4, 133.4, 131.5, 131.4, 129.3, 129.0, 128.9, 128.6, 128.44, 128.37, 127.3, 124.1, 123.8, 122.4, 121.8, 96.1, 88.0; IR (KBr, cm^{-1}): 3060, 1664, 1595, 1518, 1343, 1207, 1108, 1016, 757, 691; HRMS: *m/z* [M+H]$^+$ calcd for $C_{23}H_{15}NO_3$: 354.1125; found: 354.1125.

(*E*)-1-(5-Methoxy-2-(phenylethynyl)phenyl)-3-phenylprop-2-en-1-one (2.10h, Table 2.2):



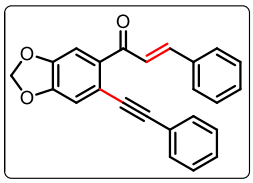
Yellow liquid (yield = 79%); R_f value = 0.61 (5% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ7.72 (d, *J* = 15.9 Hz, 1H), 7.64 - 7.54 (m, 4H), 7.37 - 7.29 (m, 5H), 7.26 - 7.14 (m, 4H), 7.03 (dd, *J* = 2.7, 8.6 Hz, 1H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ193.5, 159.6, 144.4, 143.4, 134.9, 134.7, 131.3, 130.6, 128.9, 128.6, 128.3, 128.2, 125.7, 123.0, 117.6, 113.9, 113.3, 94.2, 88.0, 55.6; IR (Neat, cm^{-1}): 2936, 1660, 1587, 1500, 1422, 1329, 1231, 1024, 973, 823, 756, 689; HRMS: *m/z* [M+H]$^+$ calcd for $C_{24}H_{18}O_2$: 339.1380; found: 339.1381.

(*E*)-1-(5-Fluoro-2-(phenylethynyl)phenyl)-3-phenylprop-2-en-1-one (2.10i, Table 2.2):



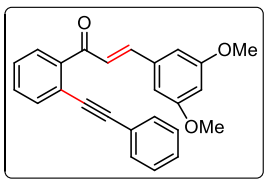
Yellow solid (yield = 68%); M.P. = 92 - 93 °C; R_f value = 0.56 (5% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, J = 15.9 Hz, 1H), 7.64 - 7.53 (m, 4H), 7.42 - 7.35 (m, 3H), 7.33 (d, J = 6.4 Hz, 3H), 7.28 - 7.23 (m, 1H), 7.21 - 7.15 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.2, 163.4, 160.9, 145.1, 143.9 (d, J = 6.6 Hz), 135.2 (d, J = 8.0 Hz), 134.7, 131.5, 130.8, 129.0, 128.7, 128.5 (d, J = 35.2 Hz), 125.2, 122.5, 118.2 (d, J = 22.1 Hz), 117.7 (d, J = 3.7 Hz), 115.9 (d, J = 23.4 Hz), 95.3, 87.0; IR (Neat, cm^{-1}): 3034, 1665, 1593, 1500, 1412, 1262, 1205, 1164, 1045, 823, 766, 689; HRMS: m/z $[M+H]^+$ calcd for $C_{23}H_{15}FO$: 327.1180; found: 327.1183.

(*E*)-3-Phenyl-1-(6-(phenylethynyl)benzo[*d*][1,3]dioxol-5-yl)prop-2-en-1-one (2.10j, Table 2.2):



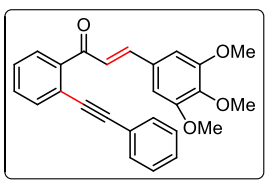
Yellow solid (yield = 74%); M.P. = 161 - 162 °C; R_f value = 0.45 (10% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 - 7.66 (m, 2H), 7.58 (d, J = 6.3 Hz, 2H), 7.36 - 7.28 (m, 5H), 7.26 - 7.21 (m, 2H), 7.19 - 7.13 (m, 2H), 7.03 (s, 1H), 6.04 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.7, 150.0, 148.3, 143.5, 137.1, 135.1, 131.4, 130.4, 128.9, 128.53, 128.51, 128.2, 125.7, 122.7, 116.9, 112.4, 109.2, 102.2, 94.9, 88.3; IR (Neat, cm^{-1}): 2915, 1649, 1593, 1505, 1474, 1376, 1241, 1030, 926, 859, 751, 689; HRMS: m/z $[M+H]^+$ calcd for $C_{24}H_{16}O_3$: 353.1172; found: 353.1176.

(*E*)-3-(3,5-Dimethoxyphenyl)-1-(2-(phenylethynyl)phenyl)prop-2-en-1-one (2.10k, Table 2.2):



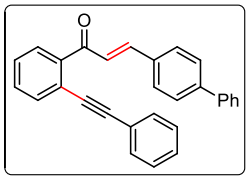
Yellow solid (yield = 85%); M.P. = 103 - 104 °C; R_f value = 0.16 (5% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 - 7.56 (m, 4H), 7.55 - 7.36 (m, 4H), 7.34 - 7.19 (m, 3H), 6.72 (s, 2H), 6.48 (s, 1H), 3.68 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.5, 161.0, 144.3, 141.9, 136.8, 133.2, 131.6, 131.0, 128.9, 128.7, 128.5, 128.3, 126.2, 122.7, 121.6, 106.3, 103.2, 95.6, 88.1, 55.3; IR (Neat, cm^{-1}): 2941, 1580, 1500, 1459, 1417, 1283, 1126, 1020, 758, 690; HRMS: m/z $[M+H]^+$ calcd for $C_{25}H_{20}O_3$: 369.1485; found: 369.1489.

(*E*)-1-(2-(Phenylethynyl)phenyl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (2.10l, Table 2.2):



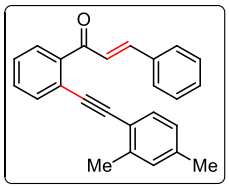
Yellow solid (yield = 99%); M.P. = 119 - 120 °C; R_f value = 0.13 (5% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, J = 7.6 Hz, 1H), 7.66 (s, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.55 (s, 1H), 7.53 - 7.42 (m, 3H), 7.38 (d, J = 7.0 Hz, 2H), 7.23 (d, J = 7.8 Hz, 2H), 6.80 (s, 2H), 3.87 (s, 3H), 3.73 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.3, 153.4, 144.2, 142.0, 140.4, 133.2, 131.6, 130.9, 130.4, 128.9, 128.8, 128.5, 128.3, 125.1, 122.6, 121.5, 105.7, 95.6, 88.2, 61.0, 56.0; IR (Neat, cm^{-1}): 2936, 2843, 1665, 1577, 1500, 1412, 1283, 1247, 1128, 1024, 828, 766, 689; HRMS: m/z $[M+H]^+$ calcd for $C_{26}H_{22}O_4$: 399.1591; found: 399.1594.

(*E*)-3-([1,1'-Biphenyl]-4-yl)-1-(2-(phenylethynyl)phenyl)prop-2-en-1-one (2.10n, Table 2.2):



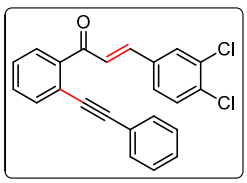
Yellow solid (yield = 63%); M.P. = 92 - 93 ^{o}C; R_f value = 0.34 (5% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 - 7.67 (m, 2H), 7.66 - 7.61 (m, 3H), 7.60 - 7.52 (m, 4H), 7.51 - 7.31 (m, 8H), 7.28 - 7.14 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.6, 143.9, 143.3, 142.0, 140.1, 133.9, 133.3, 131.6, 130.9, 129.1, 129.0, 128.9, 128.7, 128.5, 128.3, 127.9, 127.5, 127.0, 125.7, 122.7, 121.6, 95.6, 88.1; IR (Neat, cm^{-1}): 3054, 1665, 1593, 1484, 1407, 1324, 1205, 983, 833, 756, 694; HRMS: *m/z* [M+H]$^{+}$ calcd for $C_{29}H_{20}O$: 385.1587; found: 385.1589.

(*E*)-1-(2-((2,4-Dimethylphenyl)ethynyl)phenyl)-3-phenylprop-2-en-1-one (2.10o, Table 2.2):



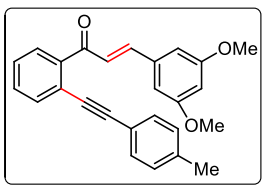
Yellow liquid (yield = 99%); R_f value = 0.27 (5% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 - 7.57 (m, 2H), 7.54 (s, 1H), 7.52 - 7.48 (m, 2H), 7.38 - 7.33 (m, 1H), 7.32 - 7.21 (m, 5H), 6.84 (s, 2H), 6.75 (s, 1H), 1.98 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.6, 147.0, 143.9, 142.0, 140.1, 137.9, 135.0, 133.1, 131.0, 130.6, 129.3, 129.1, 129.0, 128.7, 128.3, 125.8, 125.6, 122.3, 121.8, 96.3, 87.5, 20.9; IR (Neat, cm^{-1}): 2922, 1604, 1448, 1331, 1207, 1056, 978, 851, 759, 691, 528; HRMS: *m/z* [M+H]$^{+}$ calcd for $C_{25}H_{20}O$: 337.1587; found: 337.1587.

(*E*)-3-(3,4-Dichlorophenyl)-1-(2-(phenylethynyl)phenyl)prop-2-en-1-one (2.10p, Table 2.2):



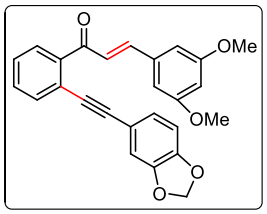
Yellow solid (yield = 64%); M.P. = 148 - 149 ^{o}C; R_f value = 0.69 (5% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, *J* = 7.7 Hz, 1H), 7.54 (s, 2H), 7.49 (s, 2H), 7.44 - 7.32 (m, 2H), 7.30 - 7.26 (m, 4H), 7.22 - 7.11 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ192.8, 141.4, 141.0, 135.0, 134.3, 133.3, 133.25, 131.5, 131.3, 130.9, 129.9, 128.9, 128.8, 128.5, 127.4, 127.2, 122.5, 121.7, 95.9, 88.0; IR (Neat, cm^{-1}): 2925, 1608, 1499, 1323, 1199, 1127, 1013, 817, 755, 683; HRMS: *m/z* [M+H]$^{+}$ calcd for $C_{23}H_{14}Cl_2O$: 377.0494; found: 377.0494.

(*E*)-3-(3,5-Dimethoxyphenyl)-1-(2-(p-tolylethynyl)phenyl)prop-2-en-1-one (2.10q, Table 2.2):



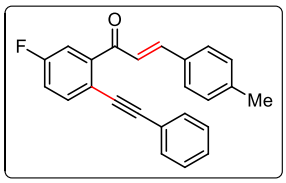
Yellow solid (yield = 98%); M.P. = 95 - 96 ^{o}C; R_f value = 0.13 (5% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, *J* = 7.6 Hz, 1H), 7.65 - 7.53 (m, 3H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.27 (d, *J* = 8.0 Hz, 2H), 7.01 (d, *J* = 7.9 Hz, 2H), 6.71 (s, 2H), 6.47 (s, 1H), 3.67 (s, 6H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ193.5, 161.0, 144.2, 141.7, 138.9, 136.8, 133.2, 131.5, 130.9, 129.1, 128.9, 128.3, 126.2, 121.8, 119.6, 106.2, 103.2, 96.0, 87.5, 55.3, 21.5; IR (Neat, cm^{-1}): 2920, 1660, 1593, 1505, 1453, 1283, 1159, 1061, 1019, 813, 771, 751, 673; HRMS: *m/z* [M+H]$^{+}$ calcd for $C_{26}H_{22}O_3$: 383.1642; found: 383.1643.

(*E*)-1-(2-(Benzo[*d*][1,3]dioxol-5-ylethynyl)phenyl)-3-(3,5-dimethoxyphenyl)prop-2-en-1-one (2.10r, Table 2.2):



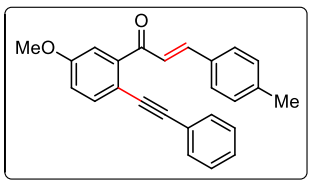
Yellow solid (yield = 99%); M.P. = 135 - 136 °C; R_f value = 0.18 (5% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, J = 7.2 Hz, 1H), 7.54 (d, J = 7.0 Hz, 1H), 7.51 (s, 1H), 7.46 (s, 1H), 7.40 (t, J = 7.5 Hz, 1H), 7.33 (t, J = 7.5 Hz, 1H), 6.82 (dd, J = 1.2, 8.0 Hz, 1H), 6.74 (s, 1H), 6.64 (d, J= 2.0 Hz, 2H), 6.56 (d, J = 8.0 Hz, 1H), 6.40 (s, 1H), 5.85 (s, 2H), 3.65 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ193.6, 161.0, 148.3, 147.4, 144.3, 141.7, 136.8, 133.0, 130.9, 128.8, 128.2, 126.5, 126.2, 121.8, 115.9, 111.5, 108.4, 106.2, 103.2, 101.4, 95.7, 86.6, 55.4; IR (Neat, cm^{-1}): 2935, 1659, 1592, 1489, 1287, 1225, 1158, 1034, 931, 807, 776, 667; HRMS: m/z [M+H]$^+$ calcd for $C_{26}H_{20}O_5$: 413.1384; found: 413.1385.

(*E*)-1-(5-Fluoro-2-(phenylethynyl)phenyl)-3-(*p*-tolyl)prop-2-en-1-one (2.10s, Table 2.2):



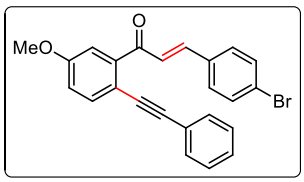
Yellow liquid (yield = 70%); R_f value = 0.45 (5% EtOAc in hexane); ^{1}H NMR (500 MHz, $CDCl_3$): δ7.68 (d, J = 15.9 Hz, 1H), 7.62 - 7.57 (m, 1H), 7.52 - 7.45 (m, 3H), 7.39 - 7.31 (m, 3H), 7.24 (d, J = 7.3 Hz, 1H), 7.21 - 7.11 (m, 5H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.2, 163.2, 161.2, 145.3, 144.1 (d, J = 6.6 Hz), 141.4, 135.2 (d, J = 7.9 Hz), 132.0, 131.5, 129.7, 128.7, 128.5 (d, J = 51.6 Hz), 124.2, 122.6, 118.1 (d, J = 22.3 Hz), 117.7 (d, J = 3.5 Hz), 115.8 (d, J = 23.5 Hz), 95.1, 87.0, 21.5; IR (Neat, cm^{-1}): 3054, 1660, 1587, 1494, 1417, 1329, 1262, 1174, 1045, 756, 648, 513; HRMS: m/z [M+Na]$^+$ calcd for $C_{24}H_{17}FO$: 363.1156; found: 363.1156.

(*E*)-1-(5-Methoxy-2-(phenylethynyl)phenyl)-3-(p-tolyl)prop-2-en-1-one (2.10t, Table 2.2):



Yellow solid (yield = 98%); M.P. = 93 - 94 °C; R_f value = 0.59 (10% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ7.69 (d, J = 15.8 Hz, 1H), 7.54 (dd, J = 3.7, 12.2 Hz, 2H), 7.48 (d, J = 8.1 Hz, 2H), 7.32 (d, J = 6.8 Hz, 2H), 7.25 - 7.11 (m, 6H), 7.01 (dd, J = 8.6, 2.7 Hz, 1H), 3.84 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ193.5, 159.6, 144.6, 143.6, 141.1, 134.7, 132.2, 131.4, 129.7, 128.9, 128.6, 128.2, 124.8, 123.1, 117.4, 113.8, 113.3, 94.1, 88.1, 55.6, 21.5; IR (Neat, cm^{-1}): 3018, 1659, 1592, 1499, 1416, 1323, 1287, 1230, 1174, 1034, 977, 864, 817, 750, 683; HRMS: m/z [M+H]$^+$ calcd for $C_{25}H_{20}O_2$: 353.1536; found: 353.1536.

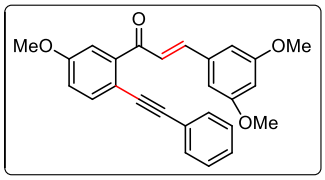
(*E*)-3-(4-Bromophenyl)-1-(5-methoxy-2-(phenylethynyl)phenyl)prop-2-en-1-one (2.10u, Table 2.2):



Yellow solid (yield = 72%); M.P. = 131 - 132 °C; R_f value = 0.59 (10% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ7.63 (d, J = 3.3 Hz, 2H), 7.55 (d, J = 8.6 Hz, 1H), 7.43 (d, J = 1.4 Hz, 4H), 7.32 - 7.28 (m, 2H), 7.26 - 7.16 (m, 4H), 7.03 (dd, J = 8.6, 2.8 Hz, 1H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.0, 159.7, 143.2, 142.6, 134.7, 133.9, 132.1, 131.3, 129.9, 128.4, 128.3, 126.3, 124.8, 122.9, 117.8, 113.9, 113.4, 94.4, 88.1, 55.6; IR (Neat, cm^{-1}): 1654,

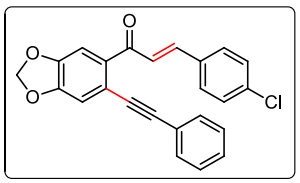
1587, 1494, 1323, 1225, 1168, 1024, 812, 755, 688; HRMS: *m/z* [M+Na]$^+$ calcd for $C_{24}H_{17}BrO_2$: 439.0304; found: 439.0305.

(*E*)-3-(3,5-Dimethoxyphenyl)-1-(5-methoxy-2-(phenylethynyl)phenyl)prop-2-en-1-one (2.10v, Table 2.2):



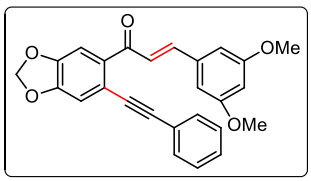
Yellow liquid (yield = 78%); R_f value = 0.42 (10% EtOAc in hexane); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.67 - 7.58 (m, 2H), 7.56 (d, *J* = 8.6 Hz, 1H), 7.36 - 7.33 (m, 2H), 7.26 - 7.17 (m, 4H), 7.03 (dd, *J* = 2.8, 8.6 Hz, 1H), 6.72 (d, *J* = 2.3 Hz, 2H), 6.47 (t, *J* = 2.2 Hz, 1H), 3.87 (s, 3H), 3.67 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.2, 161.0, 159.6, 144.3, 143.3, 136.8, 134.7, 131.4, 128.4, 128.3, 126.0, 122.9, 117.8, 113.8, 113.3, 106.3, 103.3, 94.3, 88.1, 55.6, 55.3; IR (KBr, cm^{-1}): 2935, 1658, 1591, 1417, 1328, 1292, 1229, 1028, 813, 755, 655; HRMS: *m/z* [M+H]$^+$ calcd for $C_{26}H_{22}O_4$: 399.1591; found: 399.1596.

(*E*)-3-(4-Chlorophenyl)-1-(6-(phenylethynyl)benzo[*d*][1,3]dioxol-5-yl)prop-2-en-1-one (2.10w, Table 2.2):



Brown solid (yield = 70%); M.P. = 120 - 121 ^{o}C; R_f value = 0.48 (10% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (s, 2H), 7.49 (d, *J* = 8.6 Hz, 2H), 7.32 - 7.25 (m, 5H), 7.23 (s, 1H), 7.22 - 7.17 (m, 2H), 7.03 (s, 1H), 6.07 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.3, 150.2, 148.3, 141.7, 136.9, 136.2, 133.6, 131.3, 129.6, 129.1, 128.6, 128.3, 126.2, 122.6, 117.0, 112.4, 109.2, 102.2, 95.1, 88.3; IR (Neat, cm^{-1}): 2920, 1591, 1479, 1372, 1240, 1037, 821, 755, 690; HRMS: *m/z* [M+H]$^+$ calcd for $C_{24}H_{15}ClO_3$: 387.0782; found: 387.0781.

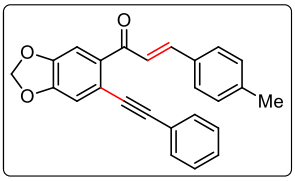
(*E*)-3-(3,5-Dimethoxyphenyl)-1-(6-(phenylethynyl)benzo[*d*][1,3]dioxol-5-yl)prop-2-en-1-one (2.10x, Table 2.2):



Brownish yellow solid (yield = 73%); M.P. = 162 - 163 ^{o}C; R_f value = 0.34 (10% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 - 7.61 (m, 2H), 7.34 (d, *J* = 6.8 Hz, 2H), 7.27 - 7.16 (m, 4H), 7.02 (s, 1H), 6.71 (d, *J* = 2.2 Hz, 2H), 6.45 (t, *J* = 2.2 Hz, 1H), 6.03 (s, 2H), 3.64 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.4, 160.9, 150.1, 148.3, 143.4, 137.0, 136.9, 131.5, 128.6, 128.3, 126.0, 122.6, 116.9, 112.4, 109.2, 106.2, 103.1, 102.2, 95.0, 88.4, 55.2; IR (Neat, cm^{-1}): 2905, 1649, 1598, 1479, 1371, 1236, 1154, 1040, 978, 937, 756, 689; HRMS: *m/z* [M+H]$^+$ calcd for $C_{26}H_{20}O_5$: 413.1384; found: 413.1385.

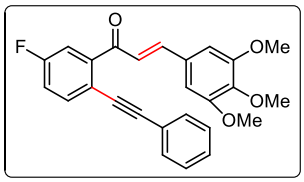
(*E*)-1-(6-(Phenylethynyl)benzo[*d*][1,3]dioxol-5-yl)-3-(*p*-tolyl)prop-2-en-1-one (2.10y, Table 2.2):

Brown solid (yield = 67%); M.P. = 282 - 283 ^{o}C; R_f value = 0.45 (5% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (s, 1H), 7.65 (d, *J* = 8.2 Hz, 1H), 7.52 - 7.47 (m, 3H), 7.28 - 7.07 (m, 5H),



7.04 (s, 1H), 6.99 (s, 1H), 5.81 (s, 2H), 5.53 (s, 1H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.4, 153.1, 148.3, 143.7, 142.4, 139.2, 137.3, 134.8, 132.7, 131.1, 129.8, 128.3, 126.3, 124.3, 112.4, 109.1, 104.5, 102.0, 94.8, 88.3, 22.0; IR (KBr, cm^{-1}): 2912, 1701, 1597, 1477, 1268, 1241, 1035, 935, 811, 702; HRMS: m/z $[M+H]^+$ calcd for $C_{25}H_{18}O_3$: 367.1329; found: 367.1328.

(*E*)-1-(5-Fluoro-2-(phenylethynyl)phenyl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (2.10z, Table 2.2):

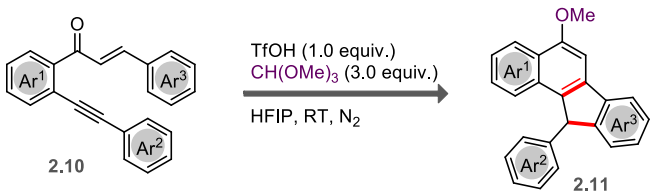


Yellow solid (yield = 72%); M.P. = 237 - 238 ^{o}C; R_f value = 0.15 (5% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 - 7.42 (m, 4H), 7.38 (s, 2H), 7.33 - 7.12 (m, 5H), 6.82 (s, 1H), 3.96 (s, 3H), 3.90 (s, 3H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.2, 153.5 (d, J = 26.8 Hz), 144.9, 140.5, 135.3, 131.7, 131.5, 130.2, 128.6 (d, J = 46.0 Hz), 128.4, 128.1, 124.4, 122.4, 118.4 (d, J = 20.1 Hz), 116.1 (d, J = 23.3 Hz), 106.7, 105.7, 95.4, 87.2, 61.0, 56.3, 56.0; IR (Neat, cm^{-1}): 2936, 1660, 1572, 1505, 1422, 1283, 1128, 999, 828, 756, 689; HRMS: m/z $[M+H]^+$ calcd for $C_{26}H_{21}FO_4$: 417.1497; found: 417.1497.

2.4.4. Synthesis and Characterization of Benzo[*a*]fluorene Derivatives (2.11):

2.4.4.1. General Synthetic Procedure for the Preparation of Benzo[*a*]fluorene Derivatives (2.11):

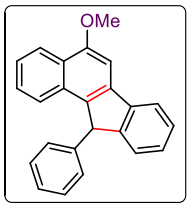
To a solution of 1,6-enynone **2.10** (1.0 equiv.) in hexafluoroisopropanol solvent (5 mL/mmol), trimethyl orthoformate (3 equiv.) followed by triflic acid (1 equiv.) were charged at room temperature (25 ^{0}C) under nitrogen atmosphere. The reaction mixture was stirred at room temperature under nitrogen atmosphere. The progress of the reaction was monitored by TLC. After completion of the reaction (after 3 hrs), it was quenched with a saturated $NaHCO_3$ solution. Then it was extracted using ethyl acetate and water. The combined organic layer was washed with saturated brine solution and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure. The crude product was purified by column chromatography (using silica gel, 2-5% EtOAc/hexanes eluent) to get pure benzo[*a*]fluorene **2.11**.



Scheme 2.11. TfOH-promoted synthesis of benzo[*a*]fluorene derivatives (**2.11**).

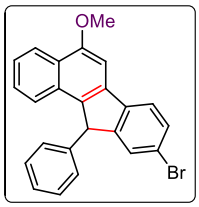
2.4.4.2. Analytical Data of Benzo[*a*]fluorene Derivatives (2.11):

5-Methoxy-11-phenyl-11*H*-benzo[*a*]fluorene (2.11a, Table 2.3):



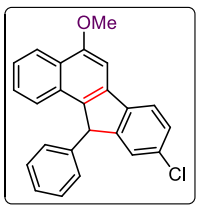
Pale white solid (yield = 98%); M.P. = 194 - 195 °C; R_f value = 0.84 (10% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (d, *J* = 8.2 Hz, 1H), 7.75 (d, *J* = 7.5 Hz, 1H), 7.55 (d, *J* = 8.2 Hz, 1H), 7.38 - 7.31 (m, 2H), 7.28 (d, *J* = 7.3 Hz, 2H), 7.22 - 7.13 (m, 5H), 7.07 (d, *J* = 6.6, 2H), 5.17 (s, 1H), 4.09 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.5, 149.7, 142.0, 141.4, 139.3, 134.7, 131.0, 128.9, 128.0, 127.1, 126.9, 126.8, 126.7, 125.8, 124.9, 124.6, 124.4, 123.2, 119.3, 96.6, 55.8, 53.7; IR (Neat, cm^{-1}): 3023, 1696, 1629, 1587, 1396, 1216, 1148, 1097, 1019, 983, 823, 766, 689; HRMS: *m/z* $[M+H]^+$ calcd for $C_{24}H_{18}O$: 323.1430; found: 323.1433.

9-Bromo-5-methoxy-11-phenyl-11*H*-benzo[*a*]fluorene (2.11b, Table 2.3):



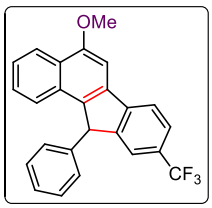
Brownish yellow solid (yield = 75%); M.P. = 230 - 231 °C; R_f value = 0.69 (10% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (d, *J* = 8.1 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.54 (d, *J* = 7.7 Hz, 1H), 7.49 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.42 (s, 1H), 7.40 - 7.36 (m, 1H), 7.35 - 7.30 (m, 1H), 7.26 (s, 2H), 7.24 (s, 1H), 7.23 (s, 1H), 7.09 (dd, *J* = 7.7, 1.6 Hz, 2H), 5.23 (s, 1H), 4.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.6, 151.5, 141.0, 140.4, 138.3, 134.5, 130.8, 130.2, 129.0, 128.1, 127.9, 127.1, 127.0, 125.9, 124.9, 124.3, 123.2, 120.58, 120.57, 96.3, 55.8, 53.6; IR (Neat, cm^{-1}): 1577, 1463, 1407, 1376, 1272, 1216, 1086, 1024, 813, 751, 704; HRMS: *m/z* $[M+Na]^+$ calcd for $C_{24}H_{17}BrO$: 423.0355; found: 423.0359.

9-Chloro-5-methoxy-11-phenyl-11*H*-benzo[*a*]fluorene (2.11c, Table 2.3):



Brownish yellow solid (yield = 70%); M.P. = 208 - 209 °C; R_f value = 0.75 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.29 (d, *J* = 8.1 Hz, 1H), 7.64 (d, *J* = 8.1 Hz, 1H), 7.51 (d, *J* = 8.3 Hz, 1H), 7.40 - 7.35 (m, 1H), 7.33 - 7.29 (m, 2H), 7.25 - 7.19 (m, 4H), 7.17 (s, 1H), 7.05 (dd, *J* = 7.9, 1.5 Hz, 2H), 5.12 (s, 1H), 4.10 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.6, 151.2, 141.1, 139.9, 138.3, 134.6, 132.5, 130.9, 129.0, 127.9, 127.4, 127.1, 127.0, 125.8, 125.3, 124.8, 124.3, 123.3, 120.2, 96.4, 55.8, 53.5; IR (Neat, cm^{-1}): 3049, 2941, 1577, 1463, 1396, 1376, 1262, 1210, 1143, 1092, 1071, 1019, 983, 818; HRMS: *m/z* $[M]^+$ calcd for $C_{24}H_{17}ClO$: 356.0968; found: 356.0967.

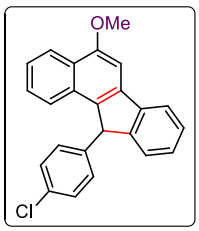
5-Methoxy-11-phenyl-9-(trifluoromethyl)-11*H*-benzo[*a*]fluorene (2.11d, Table 2.3):



Brownish yellow solid (yield = 17%); M.P. = 188 - 189 °C; R_f value = 0.69 (10% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (d, *J* = 7.3 Hz, 1H), 7.85 (s, 1H), 7.74 - 7.51 (m, 5H), 7.49 - 7.31 (m, 4H), 7.10 (s, 2H), 5.29 (s, 1H), 4.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.7, 149.8, 144.9, 140.7, 139.9, 139.2, 137.9, 136.0, 130.8, 129.6, 129.1, 127.9, 127.2, 127.1, 126.3, 125.3, 124.5, 123.3, 121.6 (q, *J* = 3.5 Hz), 119.3, 96.5, 55.8, 53.7; ^{19}F NMR (376 MHz, $CDCl_3$):

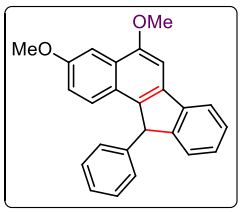
δ -62.9; IR (Neat, cm^{-1}): 3059, 1618, 1582, 1433, 1402, 1329, 1272, 1143, 1117, 1061, 828, 746, 694; HRMS: *m/z* $[M+Na]^+$ calcd for $C_{25}H_{17}F_3O$: 413.1124; found: 413.1125.

11-(4-Chlorophenyl)-5-methoxy-11*H*-benzo[*a*]fluorene (2.11e, Table 2.3):



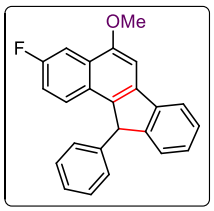
Reddish solid (yield = 84%); M.P. = 190 - 191 °C; R_f value = 0.66 (5% EtOAc in hexanes); ^1H NMR (500 MHz, $CDCl_3$): δ 8.29 (d, *J* = 8.5 Hz, 1H), 7.74 (d, *J* = 7.5 Hz, 1H), 7.49 (d, *J* = 7.7 Hz, 1H), 7.39 - 7.29 (m, 3H), 7.24 (d, *J* = 7.4 Hz, 1H), 7.22 - 7.20 (m, 2H), 7.17 (d, *J* = 8.5 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 2H), 5.11 (s, 1H), 4.09 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.6, 149.2, 141.4, 140.7, 139.4, 134.1, 132.4, 130.9, 129.3, 129.1, 127.3, 127.1, 127.0, 125.9, 124.8, 124.7, 124.2, 123.3, 119.4, 96.6, 55.8, 52.9; IR (Neat, cm^{-1}): 3065, 1624, 1582, 1448, 1402, 1221, 1148, 1097, 1014, 802, 756; HRMS: *m/z* $[M+Na]^+$ calcd for $C_{24}H_{17}ClO$: 379.0860; found: 379.0861.

3,5-Dimethoxy-11-phenyl-11*H*-benzo[*a*]fluorene (2.11f, Table 2.3):



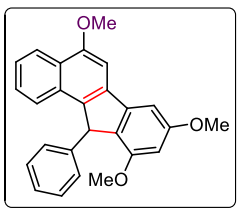
Yellow solid (yield = 54%); M.P. = 249 - 250 °C; R_f value = 0.40 (10% EtOAc in hexanes); ^1H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, *J* = 7.5 Hz, 1H), 7.53 (d, *J* = 2.6 Hz, 1H), 7.41 (d, *J* = 9.1 Hz, 1H), 7.27 (t, *J* = 7.4 Hz, 1H), 7.22 - 7.08 (m, 6H), 7.01 (d, *J* = 6.4 Hz, 2H), 6.91 (dd, *J* = 9.1, 2.7 Hz, 1H), 5.13 (s, 1H), 4.06 (s, 3H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.0, 155.4, 149.3, 142.1, 141.6, 137.1, 135.0, 128.8, 128.0, 127.0, 126.8, 126.7, 126.4, 126.3, 126.0, 124.8, 119.3, 119.0, 101.9, 97.2, 55.8, 55.3, 53.6; IR (Neat, cm^{-1}): 2920, 1587, 1474, 1371, 1210, 1174, 1019, 833, 808, 761, 730; HRMS: *m/z* $[M]^+$ calcd for $C_{25}H_{20}O_2$: 352.1463; found: 352.1461.

3-Fluoro-5-methoxy-11-phenyl-11*H*-benzo[*a*]fluorene (2.11g, Table 2.3):



Off-white solid (yield = 87%); M.P. = 224 - 225 °C; R_f value = 0.69 (10% EtOAc in hexanes); ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.89 (dd, *J* = 10.8, 2.7 Hz, 1H), 7.75 (d, *J* = 7.6 Hz, 1H), 7.53 (dd, *J* = 9.1, 5.6 Hz, 1H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.28 (d, *J* = 7.0 Hz, 1H), 7.26 - 7.17 (m, 5H), 7.10 - 7.04 (m, 3H), 5.17 (s, 1H), 4.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 161.4, 158.9, 155.9 (d, *J* = 5.1 Hz), 149.4, 141.8, 141.2, 138.7 (d, *J* = 2.5 Hz), 134.8, 128.9, 128.0, 127.95, 127.1, 126.9, 126.8, 126.6 (d, *J* = 8.7 Hz), 124.8, 119.3, 116.9 (d, *J* = 25.0 Hz), 107.4 (d, *J* = 22.6 Hz), 97.5, 55.8, 53.7; IR (Neat, cm^{-1}): 2925, 1587, 1520, 1407, 1371, 1205, 1076, 931, 756, 730; HRMS : *m/z* $[M]^+$ calcd for $C_{24}H_{17}FO$: 340.1263; found: 340.1263.

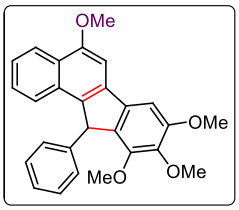
5,8,10-Trimethoxy-11-phenyl-11*H*-benzo[*a*]fluorene (2.11h, Table 2.3):



Brownish-yellow solid (yield = 98%); M.P. = 278 - 279 °C; R_f value = 0.25 (5% EtOAc in hexanes); ^1H NMR (500 MHz, $CDCl_3$): *δ* 8.26 (d, *J* = 8.0 Hz, 1H), 7.61 (d, *J* = 7.7 Hz, 1H), 7.36 - 7.27 (m, 2H), 7.20 (s, 1H), 7.17 - 7.08 (m, 5H), 6.96 (d, *J* = 1.9 Hz, 1H), 6.34 (d, *J* = 1.9 Hz, 1H), 5.28 (s, 1H), 4.13 (s, 3H), 3.92 (s, 3H), 3.66 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 161.4, 156.8, 156.2, 143.7,

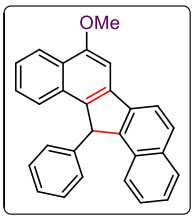
141.5, 138.9, 136.8, 130.8, 129.5, 128.5, 128.1, 126.9, 126.0, 125.8, 124.5, 124.2, 123.1, 98.0, 96.63, 96.55, 55.8, 55.7, 55.5, 51.4; IR (KBr, cm^{-1}): 2930, 1582, 1489, 1447, 1419, 1344, 1246, 1210, 1132, 1075, 1034, 936, 838, 750, 693, 543, 476; HRMS: *m/z* $[M+H]^+$ calcd for $C_{26}H_{22}O_3$: 383.1642; found: 383.1641.

5,8,9,10-Tetramethoxy-11-phenyl-11*H*-benzo[*a*]fluorene (2.11i, Table 2.3):



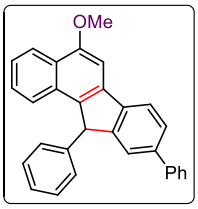
Brownish yellow solid (yield = 99%); M.P. = 278 - 279 °C; R_f value = 0.15 (10% EtOAc in hexanes); ^1H NMR (500 MHz, $CDCl_3$):δ 8.26 (d, *J* = 7.8 Hz, 1H), 7.64 (d, *J* = 7.6 Hz, 1H), 7.36 - 7.28 (m, 2H), 7.22 - 7.16 (m, 3H), 7.16 - 7.11 (m, 4H), 5.32 (s, 1H), 4.14 (s, 3H), 4.02 (s, 3H), 3.87 (s, 3H), 3.29 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.4, 154.2, 150.4, 141.8, 141.7, 138.8, 137.4, 136.0, 134.9, 130.8, 128.5, 128.4, 127.0, 126.4, 125.4, 124.4, 124.0, 123.1, 99.0, 96.3, 60.9, 60.0, 56.4, 55.8, 51.9; IR (KBr, cm^{-1}): 3070, 1603, 1587, 1453, 1412, 1365, 1319, 1247, 1205, 1123, 1035, 983, 823, 756, 699, 570, 513; HRMS: *m/z* $[M+Na]^+$ calcd for $C_{27}H_{24}O_4$: 435.1567; found: 435.1567.

5-Methoxy-13-phenyl-13*H*-dibenzo[*a,i*]fluorene (2.11j, Table 2.3):



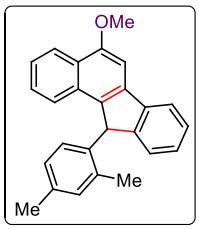
Yellow solid (yield = 67%); M.P. = 250 - 251 °C; R_f value = 0.51 (10% EtOAc in hexanes); ^1H NMR (400 MHz, $CDCl_3$): δ 8.28 - 8.24 (m, 1H), 7.87 (s, 2H), 7.83 (dd,*J* = 8.0, 1.6, Hz, 2H), 7.78 - 7.74 (m, 1H), 7.36 - 7.27 (m, 4H), 7.21 (s, 1H), 7.17 - 7.11 (m, 4H), 7.10 - 7.05 (m, 1H), 5.36 (s, 1H), 4.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.3, 145.3, 142.1, 139.5, 139.1, 136.8, 133.3, 130.8, 130.2, 129.0, 128.8, 128.7, 128.6, 127.0, 126.5, 126.4, 125.5, 125.0, 124.4, 123.9, 123.6, 123.2, 118.2, 96.6, 55.7, 53.6; IR (KBr, cm^{-1}): 3064, 1582, 1515, 1458, 1380, 1220, 1096, 1019, 812, 755, 698, 631, 590, 435; HRMS: *m/z* $[M]^+$ calcd for $C_{28}H_{20}O$: 372.1514; found: 372.1518.

5-Methoxy-9,11-diphenyl-11*H*-benzo[*a*]fluorene (2.11k, Table 2.3):



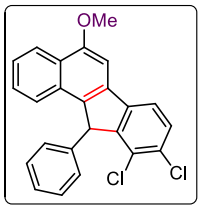
Dull-white solid (yield = 73%); M.P. = 248 - 249 °C; R_f value =0.41 (10% EtOAc in hexanes); ^1H NMR (500 MHz, $CDCl_3$):δ 8.31 (d, *J* = 7.7 Hz, 1H), 7.84 (d, *J* = 7.9 Hz, 1H), 7.61 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.59 - 7.55 (m, 3H), 7.52 (s, 1H), 7.42 - 7.36 (m, 3H), 7.35 - 7.28 (m, 3H), 7.23 (d, *J* = 7.6 Hz, 2H), 7.21 - 7.17 (m, 1H), 7.15 (d, *J* = 6.8 Hz, 2H), 5.31 (s, 1H), 4.16 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.5, 150.3, 141.9, 141.4, 140.7, 140.0, 139.0, 135.0, 131.0, 128.9, 128.7, 128.1, 127.14, 127.06, 127.0, 126.7, 126.3, 125.8, 124.6, 124.4, 123.7, 123.2, 119.5, 96.7, 55.8, 53.8; IR (KBr, cm^{-1}): 1587, 1474, 1396, 1216, 1117, 1092, 828, 756, 694, 632, 503; HRMS: *m/z* $[M+Na]^+$ calcd for $C_{30}H_{22}O$: 421.1563; found: 421.1562.

11-(2,4-Dimethylphenyl)-5-methoxy-11*H*-benzo[*a*]fluorene (2.11l, Table 2.3):



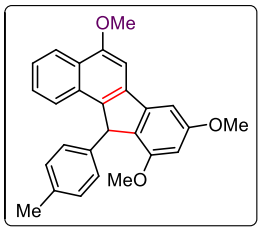
Reddish yellow solid (yield = 76%); M.P. = 171 - 172 °C; R_f value = 0.63 (5% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$):δ 8.30 (d, J = 7.8 Hz, 1H), 7.78 (d, J = 7.5 Hz, 1H), 7.62 (d, J = 7.7 Hz, 1H), 7.40 - 7.29 (m, 4H), 7.28 (s, 1H), 7.24 - 7.19 (m, 1H), 6.82 (s, 1H), 6.71 (s, 2H), 5.16 (s, 1H), 4.14 (s, 3H), 2.19 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$):δ 156.3, 149.9, 141.7, 141.3, 139.2, 138.2, 134.9, 131.1, 128.5, 126.93, 126.9, 126.8, 125.7, 124.8, 124.6, 124.5, 123.1, 119.2, 96.6, 55.8, 53.6, 21.3; IR (Neat, cm^{-1}): 3003, 1587, 1448, 1402, 1371, 1216, 1143, 1102, 1024, 828, 715, 699; HRMS: m/z $[M]^+$ calcd for $C_{26}H_{22}O$: 350.1671; found: 350.1668.

9,10-Dichloro-5-methoxy-11-phenyl-11*H*-benzo[*a*]fluorene (2.11m, Table 2.3):



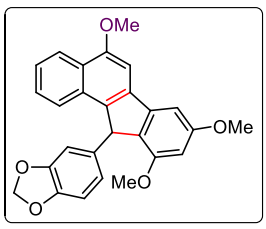
Brownish yellow solid (yield = 59%); M.P. = 187 - 188 °C; R_f value =0.56 (5% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$):δ 8.25 (d, J = 7.9 Hz, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.47 (d, J = 8.0 Hz, 1H), 7.40 - 7.30 (m, 2H), 7.20 - 7.12 (m, 3H), 7.12 - 7.07 (m, 3H), 5.25 (s, 1H), 4.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$):δ 156.6, 148.5, 142.5, 138.8, 137.0, 136.2, 130.8, 130.5, 130.0, 129.6, 129.1, 128.4, 127.3, 126.8, 126.1, 125.1, 123.9, 123.2, 118.1, 96.1, 55.7, 54.4; IR (Neat, cm^{-1}): 2925, 1577, 1453, 1417, 1396, 1221, 1128, 1030, 880, 823, 761; HRMS: m/z $[M+Na]^+$ calcd for $C_{24}H_{16}Cl_2O$: 413.0470; found: 413.0471.

5,8,10-Trimethoxy-11-(p-tolyl)-11*H*-benzo[*a*]fluorene (2.11n, Table 2.3):



Off-white solid (yield = 98%); M.P. = 162 - 163 °C; R_f value = 0.30 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$):δ 8.26 (d, J = 7.9 Hz, 1H), 7.63 (dd, J = 7.5, 1.4 Hz, 1H), 7.36 - 7.28 (m, 2H), 7.21 (s, 1H), 7.01 - 6.93 (m, 5H), 6.34 (d, J = 2.0 Hz, 1H), 5.27 (s, 1H), 4.13 (s, 3H), 3.92 (s, 3H), 3.68 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$):δ 161.3, 156.8, 156.1, 143.7, 138.8, 138.3, 136.9, 135.3, 130.8, 129.6, 128.8, 128.3, 126.8, 125.8, 124.5, 124.3, 123.0, 98.0, 96.6, 96.5, 55.8, 55.7, 55.5, 51.0, 21.1; IR (Neat, cm^{-1}): 2956, 1582, 1453, 1278, 1252, 1200, 1148, 1071, 1040; HRMS: m/z $[M+H]^+$ calcd for $C_{27}H_{24}O_3$: 397.1798; found: 397.1794.

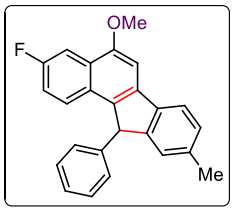
5-(5,8,10-Trimethoxy-11H-benzo[a]fluoren-11-yl)benzo[d][1,3]dioxole (2.11o, Table 2.3):



Brownish yellow solid (yield = 84%); M.P. = 206 - 207 °C; R_f value = 0.21 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$):δ 8.27 (d, J = 7.4 Hz, 1H), 7.68 (d, J = 7.2 Hz, 1H), 7.39 - 7.32 (m, 2H), 7.20 (s, 1H), 6.95 (d, J = 2.0 Hz, 1H), 6.77 (dd, J = 8.0, 1.7 Hz, 1H), 6.65 (d, J = 8.0 Hz, 1H), 6.40 (d, J = 1.6 Hz, 1H), 6.36 (d, J = 2.0 Hz, 1H), 5.83 (dd, J = 8.4, 1.4 Hz, 2H), 5.23 (s, 1H), 4.14 (s, 3H), 3.93 (s, 3H), 3.72 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.4, 156.8, 156.2, 147.2, 145.7, 143.6, 138.8, 136.6, 135.2, 130.8, 129.3, 126.9, 125.8, 124.5, 124.2, 123.1, 121.9, 108.5, 107.9, 100.6, 97.9, 96.6, 96.5, 55.8, 55.7, 55.5, 51.0; IR (Neat, cm^{-1}):

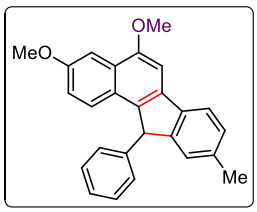
2930, 1582, 1484, 1453, 1247, 1195, 1138, 1035, 926, 828, 735; HRMS: *m/z* $[M+Na]^+$ calcd for $C_{27}H_{22}O_5$: 449.1359; found: 449.1354.

3-Fluoro-5-methoxy-9-methyl-11-phenyl-11*H*-benzo[*a*]fluorene (2.11p, Table 2.3):



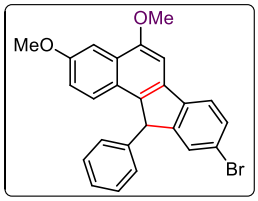
White solid (yield = 83%); M.P. = 209 - 210 °C; R_f value = 0.66 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$):δ 7.93 (d, *J* = 10.8 Hz, 1H), 7.68 (d, *J* = 7.7 Hz, 1H), 7.58 - 7.53 (m, 1H), 7.30 - 7.23 (m, 4H), 7.21 (d, *J* = 7.8 Hz, 1H), 7.15 - 7.08 (m, 4H), 5.18 (s, 1H), 4.15 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$):δ 161.0, 159.0, 155.8 (d, *J* = 5.2 Hz), 149.6, 142.1, 138.6 (d, *J* = 27.1 Hz), 136.8, 134.4, 128.9, 128.1, 128.0, 127.9, 126.8, 126.5 (d, *J* = 8.3 Hz), 126.4, 125.6, 119.0, 116.8 (d, *J* = 25.1 Hz), 107.3 (d, *J* = 22.6 Hz), 97.5, 55.8, 53.5, 21.6; IR (Neat, cm^{-1}): 3008, 1593, 1525, 1484, 1458, 1407, 1195, 1174, 1086, 988, 926, 813, 715; HRMS: *m/z* $[M]^+$ calcd for $C_{25}H_{14}FO$: 354.1420; found: 354.1418.

3,5-Dimethoxy-9-methyl-11-phenyl-11*H*-benzo[*a*]fluorene (2.11q, Table 2.3):



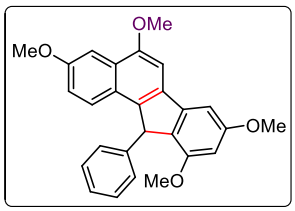
Yellow solid (yield = 77%); M.P. = 260 - 261 °C; R_f value = 0.67 (10% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$):δ 7.63 (d, *J* = 7.7 Hz, 1H), 7.60 (d, *J* = 2.6 Hz, 1H), 7.46 (d, *J* = 9.1 Hz, 1H), 7.22 (d, *J* = 7.3 Hz, 3H), 7.19 (d, *J* = 6.8 Hz, 1H), 7.15 (d, *J* = 8.0 Hz, 1H), 7.10 (d, *J* = 6.3, 3H), 6.97 (dd, *J* = 9.1, 2.6 Hz, 1H), 5.18 (s, 1H), 4.13 (s, 3H), 3.90 (s, 3H), 2.33(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.8, 155.4, 149.5, 142.4, 138.9, 137.2, 136.2, 134.6, 128.8, 128.0, 127.8, 126.6, 126.5, 126.4, 125.9, 125.5, 119.3, 118.7, 97.2, 55.7, 55.3, 53.5, 21.6; IR (Neat, cm^{-1}): 2920, 1593, 1484, 1376, 1272, 1205, 1174, 1102, 839, 808, 678; HRMS: *m/z* $[M]^+$ calcd for $C_{26}H_{22}O_2$: 366.1620; found: 366.1621.

9-Bromo-3,5-dimethoxy-11-phenyl-11*H*-benzo[*a*]fluorene(2.11r, Table 2.3):



Off-white solid (yield = 46%); M.P. = 263 - 264 °C; R_f value =0.74 (10% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$):δ 7.61 (s, 1H), 7.59 (d, *J* = 5.8 Hz, 1H), 7.49 - 7.43 (m, 2H), 7.38 (s, 1H), 7.26 - 7.19 (m, 4H), 7.07 (dd, *J* = 7.7, 1.6 Hz, 2H), 6.99 (dd, *J* = 9.1, 2.6 Hz, 1H), 5.17 (s, 1H), 4.13 (s, 3H), 3.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$):δ 157.2, 155.6, 151.1, 141.2, 140.6, 136.1, 134.8, 130.2, 129.0, 128.0, 127.9, 127.0, 126.97, 126.1, 125.9, 120.2, 120.0, 119.5, 101.9, 96.9, 55.8, 55.3, 53.5; IR (Neat, cm^{-1}): 2920, 1732, 1587, 1458, 1262, 1210, 1185, 1035, 813, 699; HRMS: *m/z* $[M]^+$ calcd for $C_{25}H_{19}BrO_2$: 430.0568; found: 430.0565.

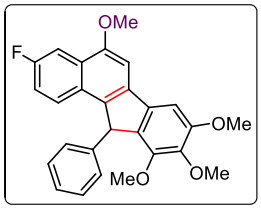
3,5,8,10-Tetramethoxy-11-phenyl-11*H*-benzo[*a*]fluorene(2.11s, Table 2.3):



Brown solid (yield = 75%); M.P. = 237 - 238 °C; R_f value =0.5 (10% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (d, *J* = 2.6 Hz, 1H), 7.53 (d, *J* = 9.1 Hz, 1H), 7.21 (s, 1H), 7.18 - 7.08 (m, 5H), 6.97 (dd, *J* = 9.1, 2.7 Hz, 1H), 6.94 (d, *J* = 2.0 Hz, 1H), 6.32 (d, *J* = 2.0, 1H), 5.26 (s, 1H), 4.14 (s, 3H), 3.92 (s, 3H), 3.89 (s, 3H), 3.66 (s, 3H); ^{13}C NMR (100

MHz, $CDCl_3$): δ 161.3, 157.0, 156.8, 155.2, 143.9, 141.7, 137.1, 136.7, 129.0, 128.5, 128.1, 126.7, 126.1, 126.0, 125.8, 119.3, 101.7, 97.5, 97.2, 96.3, 55.8, 55.7, 55.5, 55.3, 51.3; IR (Neat, cm^{-1}): 3424, 1591, 1460, 1269, 1205, 1138, 988, 844, 734; HRMS: *m/z* $[M]^+$ calcd for $C_{27}H_{24}O_4$: 412.1675; found: 412.1673.

3-Fluoro-5,8,9,10-tetramethoxy-11-phenyl-11*H*-benzo[*a*]fluorene(2.11t, Table 2.3):

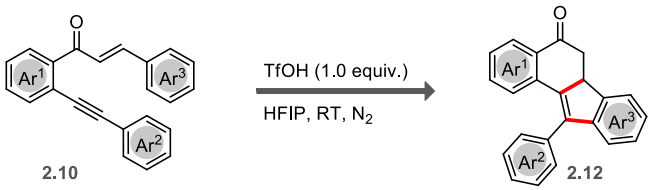


Yellow solid (yield = 68%); M.P. = 231 - 232 °C; R_f value =0.38 (20% EtOAc in hexanes); ^1H NMR (500 MHz, $CDCl_3$):δ 7.85 (dd, *J* = 10.8, 2.7 Hz, 1H), 7.59 (dd, *J* = 9.1, 5.6 Hz, 1H), 7.19 (d, *J* = 7.7 Hz, 2H), 7.17 - 7.13 (m, 2H), 7.12 (d, *J* = 1.5 Hz, 1H), 7.10 (s, 2H), 7.09 - 7.04 (m, 1H), 5.26 (s, 1H), 4.11 (s, 3H), 4.01 (s, 3H), 3.87 (s, 3H), 3.29 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$):δ 161.0, 159.1, 155.8, 154.2, 150.4, 141.7, 138.2 (d, *J* = 2.4 Hz), 137.2, 136.0, 134.6, 128.5 (d, *J* = 8.5 Hz), 127.8, 126.5, 126.3, 126.25 (d, *J* = 8.6 Hz), 126.24, 116.9 (d, *J* = 25.2 Hz), 107.2 (d, *J* = 22.7 Hz), 98.9, 97.2, 60.9, 60.0, 56.4, 55.8, 51.9; IR (Neat, cm^{-1}): 2997, 1593, 1520, 1463, 1407, 1355, 1267, 1112, 1035, 988, 833, 730, 694; HRMS: *m/z* $[M]^+$ calcd for $C_{27}H_{23}FO_4$: 430.1580; found: 430.1576.

2.4.5. Synthesis and Characterization of Benzo[*a*]fluorenone Derivatives (2.12):

2.4.5.1. General Synthetic Procedure for the Preparation of Benzo[*a*]fluorenone Derivatives (2.12):

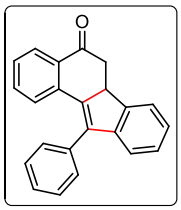
To a solution of 1,6-enynone **2.10** (1.0 equiv.) in hexafluoroisopropanol solvent (5 mL/mmol), triflic acid (1 equiv.) was charged at room temperature (25 °C) under nitrogen atmosphere. The reaction mixture was stirred at room temperature and the progress of the reaction was monitored by TLC. After completion of the reaction (after 2 hrs), it was quenched with saturated $NaHCO_3$ solution. Then it was extracted using ethyl acetate. The combined organic layer was washed with saturated brine solution and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure. The crude was purified by silica gel column chromatography (5% EtOAc/hexanes eluent) to get pure benzo[*a*]fluorenone **2.12**.



Scheme 2.12. TfOH-promoted synthesis of benzo[*a*]fluorenone derivatives (**2.12**).

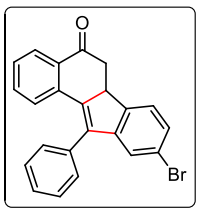
2.4.5.2. Analytical Data of Benzo[*a*]fluorenone Derivatives (2.12):

11-Phenyl-6,6a-dihydro-5*H*-benzo[*a*]fluoren-5-one (2.12a, Table 2.5):



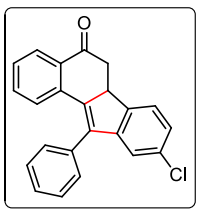
Orange yellow solid (yield = 97%); M.P. = 189 - 190 °C; R_f value = 0.39 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.10 - 8.06 (m, 1H), 7.51 - 7.46 (m, 3H), 7.46 - 7.40 (m, 3H), 7.31 - 7.25 (m, 4H), 7.25 - 7.21 (m, 1H), 7.18 - 7.15 (m, 1H), 4.12 (dd, *J* = 14.1, 5.5 Hz, 1H), 3.50 (dd, *J* = 16, 5.5 Hz, 1H), 2.47 (dd, *J* = 16, 14.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.5, 146.5, 146.0, 139.5, 138.1, 137.3, 134.8, 133.4, 131.0, 129.1, 129.0, 128.2, 127.83, 127.76, 127.6, 126.9, 126.1, 122.9, 121.4, 49.0, 43.0; IR (KBr, cm^{-1}): 1660, 1479, 1443, 1340, 1200, 1097, 1014, 973, 756, 704, 565, 529; HRMS: m/z $[M+H]^+$ calcd for $C_{23}H_{16}O$: 309.1274; found: 309.1271.

9-Bromo-11-phenyl-6,6a-dihydro-5*H*-benzo[*a*]fluoren-5-one (2.12b, Table 2.5):



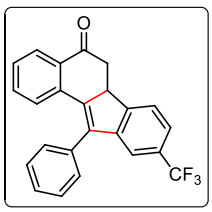
Red solid (yield = 95%); M.P. = 226 - 227 °C; R_f value = 0.69 (10% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (dd, *J* = 7.0, 1.8 Hz, 1H), 7.46 - 7.35 (m, 3H), 7.32 (d, *J* = 7.3 Hz, 3H), 7.27 (d, *J* = 9.8 Hz, 2H), 7.24 - 7.17 (m, 2H), 7.07 (d, *J* = 6.7 Hz, 1H), 4.03 (dd, *J* = 14.2, 5.4 Hz, 1H), 3.41 (dd, *J* = 15.9, 5.4 Hz, 1H), 2.38 (dd, *J* = 15.8, 14.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.0, 148.5, 144.5, 139.6, 138.5, 136.7, 134.1, 133.5, 130.9, 129.3, 128.9, 128.8, 128.4, 128.2, 127.9, 126.9, 124.5, 124.2, 121.7, 48.6, 42.7; IR (Neat, cm^{-1}): 3070, 1680, 1448, 1283, 1241, 1138, 1061, 926, 782, 746, 704; HRMS: *m/z* $[M+Na]^+$ calcd for $C_{23}H_{15}BrO$: 409.0198; found: 409.0194.

9-Chloro-11-phenyl-6,6a-dihydro-5*H*-benzo[*a*]fluoren-5-one (2.12c, Table 2.5):



Red solid (yield = 90%); M.P. = 209 - 210 °C; R_f value = 0.84 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.11 - 8.08 (m, 1H), 7.54 - 7.45 (m, 3H), 7.41 (d, *J* = 7.7 Hz, 2H), 7.35 - 7 .28 (m, 2H), 7.27 - 7.24 (m, 2H), 7.19 (d, *J* = 1.8 Hz, 1H), 7.18 - 7.15 (m, 1H), 4.14 (dd, *J* = 14.0, 5.3 Hz, 1H), 3.50 (dd, *J* = 16, 5.5 Hz, 1H), 2.47 (dd, *J* = 16, 14.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.0, 148.2, 144.0, 139.7, 138.6, 136.8, 134.1, 133.7, 133.5, 130.9, 129.3, 128.9, 128.4, 128.2, 127.9, 126.9, 125.9, 123.8, 121.6, 48.6, 42.8; IR (Neat, cm^{-1}): 3054, 2915, 1680, 1489, 1448, 1283, 1241, 1071, 818, 771, 735, 709; HRMS: *m/z* $[M+H]^+$ calcd for $C_{23}H_{15}ClO$: 343.0884; found: 343.0884.

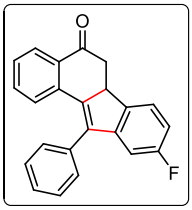
11-Phenyl-9-(trifluoromethyl)-6,6a-dihydro-5*H*-benzo[*a*]fluoren-5-one (2.12d, Table 2.5):



Dark red solid (yield = 54%); M.P. = 171 - 172 °C; R_f value = 0.36 (10% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 - 8.09 (m, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.58 - 7.47 (m, 4H), 7.46 - 7.41 (m, 3H), 7.37 - 7.29 (m, 2H), 7.18 (d, *J* = 7.0 Hz, 1H), 4.21 (dd, *J* = 14.1, 5.5 Hz, 1H), 3.54 (dd, *J* = 16.0, 5.5 Hz, 1H), 2.50 (dd, *J* = 16.0, 14.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ196.8, 149.2, 147.0, 139.7, 138.6, 136.6, 133.9, 133.6, 130.9, 130.4, 129.4, 128.9, 128.5, 128.3,

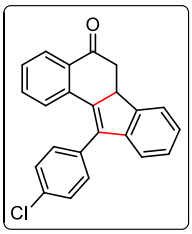
127.9, 126.9, 125.7, 123.0, 122.95, 118.0 (q, J = 4.0 Hz), 48.9, 42.5; ^{19}F NMR (376 MHz, $CDCl_3$):δ -61.9; IR (Neat, cm^{-1}): 3059, 2925, 1686, 1433, 1319, 1278, 1174, 1123, 1055, 895, 844, 771; HRMS: m/z $[M+H]^+$ calcd for $C_{24}H_{15}F_3O$: 377.1148; found: 377.1148.

9-Fluoro-11-phenyl-6,6a-dihydro-5*H*-benzo[*a*]fluoren-5-one (2.12e, Table 2.5):



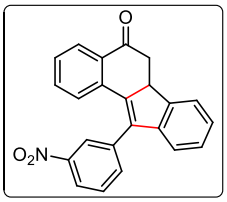
Red solid (yield = 38%); M.P. = 169 - 170 ^{o}C; R_f value = 0.59 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$):δ 8.11 - 8.08 (m, 1H), 7.54 - 7.49 (m, 2H), 7.47 (d, J = 7.3 Hz, 1H), 7.45 - 7.40 (m, 3H), 7.35 - 7.28 (m, 2H), 7.19 - 7.16 (m, 1H), 7.00 - 6.95 (m, 1H), 6.92 (dd, J = 9.1, 2.4 Hz, 1H), 4.13 (dd, J = 14.1, 5.5 Hz, 1H), 3.50 (dd, J = 16.0, 5.5 Hz, 1H), 2.48 (dd, J = 16.0, 14.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$):δ 197.1, 161.9, 148.5 (d, J = 10.1 Hz), 141.2, 140.1, 138.8 (d, J = 2.9 Hz), 136.9, 134.2, 133.4, 130.9, 129.2, 128.9, 128.4, 128.1, 127.8, 126.9, 123.6 (d, J = 9.1 Hz), 112.7 (d, J = 23.2 Hz), 108.5 (d, J = 23.6 Hz), 48.4, 43.0; IR (Neat, cm^{-1}): 2961, 2930, 1686, 1458, 1278, 1138, 1014, 864, 777; HRMS: m/z $[M+H]^+$calcd for $C_{24}H_{15}FO$: 327.1180; found: 327.1180.

11-(4-Chlorophenyl)-6,6a-dihydro-5*H*-benzo[*a*]fluoren-5-one (2.12f, Table 2.5):



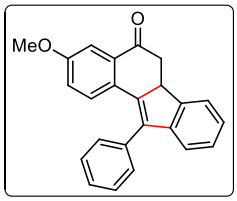
Red solid (yield = 85%); M.P. = 112 - 113 ^{o}C; $R_f$value = 0.71 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$):δ 8.11 - 8.08 (m, 1H), 7.52 (d, J = 5.6 Hz, 1H), 7.48 (d, J = 8.6 Hz, 2H), 7.38 (d, J = 8.1 Hz, 2H), 7.34 - 7.29 (m, 4H), 7.23 - 7.20 (m, 1H), 7.18 - 7.14 (m, 1H), 4.16 (dd, J = 14.0, 5.5 Hz, 1H), 3.52 (dd, J = 16.0, 5.5 Hz, 1H), 2.48 (dd, J = 16.0, 14.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.2, 146.0, 145.9, 138.7, 138.1, 136.9, 134.1, 133.5, 133.3, 131.0, 130.5, 129.5, 128.0, 127.9, 127.6, 126.7, 126.2, 122.9, 121.2, 49.1, 42.9; IR (Neat, cm^{-1}): 2915, 2853, 1680, 1489, 1283, 1241, 1092, 1009, 844, 813, 751; HRMS: m/z $[M+H]^+$ calcd for $C_{23}H_{15}ClO$: 343.0884; found: 343.0880.

11-(3-Nitrophenyl)-6,6a-dihydro-5*H*-benzo[*a*]fluoren-5-one (2.12g, Table 2.5):



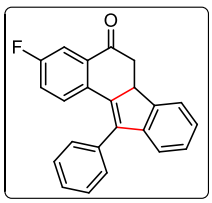
Reddish yellow solid (yield = 36%); M.P. = 207 - 208 ^{o}C; $R_f$value = 0.47 (10% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$):δ 8.36 - 8.32 (m, 2H), 8.12 (dd, J = 7.8, 1.5 Hz, 1H), 7.79 (d, J = 7.6 Hz, 1H), 7.70 (t, J = 8.0 Hz, 1H), 7.57 - 7.53 (m, 1H), 7.39 - 7.29 (m, 4H), 7.21 - 7.17 (m, 1H), 7.05 (d, J = 7.5 Hz, 1H), 4.22 (dd, J = 14.0, 5.5 Hz, 1H), 3.56 (dd, J = 16.1, 5.6 Hz, 1H), 2.51 (dd, J = 16.1, 14.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$):δ 196.8, 149.0, 145.8, 145.4, 140.0, 136.8, 136.6, 136.3, 135.4, 133.6, 131.1, 130.3, 128.5, 128.2, 127.8, 126.6, 126.4, 124.2, 123.2, 123.1, 120.8, 49.3, 42.9; IR (Neat, cm^{-1}): 3070, 2925, 1706, 1531, 1453, 1345, 1278, 1081, 813, 766; HRMS: m/z $[M+Na]^+$ calcd for $C_{23}H_{15}NO_3$: 376.0944; found: 376.0944.

3-Methoxy-11-phenyl-6,6a-dihydro-5*H*-benzo[*a*]fluoren-5-one (2.12h, Table 2.5):



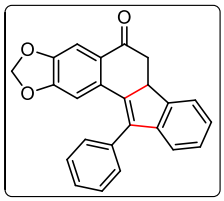
Brownish yellow solid (yield = 99%); M.P. = 230 - 231 °C; R_f value = 0.57 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$):δ 7.56 (d, J = 2.9 Hz, 1H), 7.49 (d, J = 7.1 Hz, 3H), 7.46 - 7.41 (m, 3H), 7.32 - 7.26 (m, 2H), 7.23 - 7.20 (m, 1H), 7.11 (d, J = 8.8 Hz, 1H), 6.87 (dd, J = 8.7, 2.8 Hz, 1H), 4.13 (dd, J = 14.1, 5.4, Hz, 1H), 3.85 (s, 3H), 3.52 (dd, J = 16.0, 5.4 Hz, 1H), 2.49 (dd, J = 16.0, 14.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$):δ 197.5, 159.2, 146.7, 145.5, 138.0, 137.7, 135.0, 132.2, 130.6, 129.09, 129.06, 128.3, 128.0, 127.5, 125.6, 122.7, 121.7, 121.0, 109.8, 55.5, 49.1, 43.0; IR (Neat, cm^{-1}): 2956, 2848, 1680, 1603, 1484, 1453, 1319, 1278, 1221, 1143, 1019, 875, 751, 704; HRMS: m/z [M+H]$^+$ calcd for $C_{24}H_{18}O_2$: 339.1380; found: 339.1384.

3-Fluoro-11-phenyl-6,6a-dihydro-5*H*-benzo[*a*]fluoren-5-one (2.12i, Table 2.5):



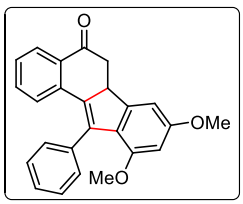
Brownish solid (yield = 82%); M.P. = 185 - 186 °C; R_f value = 0.56 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$):δ 7.73 (dd, J = 9.1, 2.8 Hz, 1H), 7.53 - 7.40 (m, 6H), 7.33 - 7.27 (m, 2H), 7.25 - 7.22 (m, 1H), 7.16 (dd, J = 8.7, 5.2 Hz, 1H), 6.99 (td, J = 8.2, 2.9 Hz, 1H), 4.13 (dd, J = 14.2, 5.4 Hz, 1H), 3.52 (dd, J = 16.1, 5.5 Hz, 1H), 2.47 (dd, J = 16.1, 14.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.5, 163.6, 160.8, 146.3, 145.5, 139.3, 137.0, 134.6, 133.6, 132.9 (d, J = 6.1 Hz), 129.1 (d, J = 26.1 Hz), 129.0, 128.3, 127.6, 126.1, 122.9, 121.4, 120.9 (d, J = 22.6 Hz), 113.8 (d, J = 22.3 Hz), 48.9, 42.8; IR (Neat, cm^{-1}): 3054, 2956, 1660, 1593, 1474, 1293, 1262, 1169, 1019, 926, 740, 704; HRMS: m/z [M+H]$^+$ calcd for $C_{23}H_{15}FO$: 327.1180; found: 327.1180.

11-Phenyl-6,6a-dihydro-5*H*-indeno[2',1':5,6]naphtho[2,3-*d*][1,3]dioxol-5-one (2.12j, Table 2.5):



Dark brown solid (yield = 54%); M.P. = 235 - 236 °C; R_f value = 0.56 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$):δ 7.52 (s, 1H), 7.51 (s, 1H), 7.50 - 7.40 (m, 5H), 7.32 - 7.27 (m, 2H), 7.23 - 7.20 (m, 1H), 6.54 (s, 1H), 5.96 (d, J = 2.9 Hz, 2H), 4.12 (dd, J = 14.0, 5.5 Hz, 1H), 3.47 (dd, J = 16.0, 5.5 Hz, 1H), 2.43 (dd, J = 16.0, 14.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.1, 151.9, 147.8, 146.5, 145.6, 138.7, 138.1, 134.6, 134.3, 129.2, 129.0, 128.2, 127.5, 126.8, 125.9, 122.7, 121.2, 106.8, 106.0, 101.7, 49.3, 42.6; IR (Neat, cm^{-1}): 3337, 1664, 1608, 1470, 1371, 1260, 1034, 931, 751, 699; HRMS: m/z [M+H]$^+$ calcd for $C_{24}H_{16}O_3$: 353.1172; found: 353.1173.

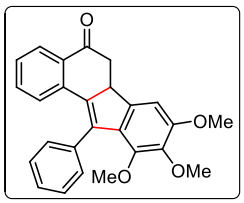
8,10-Dimethoxy-11-phenyl-6,6a-dihydro-5*H*-benzo[*a*]fluoren-5-one (2.12k, Table 2.5):



Yellow solid (yield = 76%); M.P. = 184 - 185 °C; R_f value = 0.45 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$):δ 8.04 - 8.00 (m, 1H), 7.37 (s, 5H), 7.21 - 7.14 (m, 2H), 6.90 - 6.87 (m, 1H), 6.69 (d, J = 1.3 Hz, 1H), 6.37 (d, J = 1.2 Hz, 1H), 4.05 (dd, J = 14.2, 5.4 Hz, 1H), 3.84 (s, 3H), 3.50 (s, 3H), 3.41 (dd, J = 15.9, 5.4 Hz, 1H), 2.47 (dd, J = 15.8, 14.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.6, 160.4, 156.1, 149.7, 139.4, 137.9, 137.2, 135.1, 133.2, 130.6, 129.1, 128.0, 127.6, 127.23, 127.17, 126.8, 126.6, 100.8, 98.5, 55.7, 55.5, 49.2, 43.4; IR (Neat, cm^{-1}): 3059, 2930, 1685,

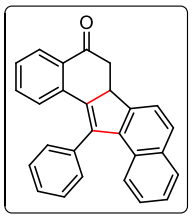
1458, 1292, 1205, 1148, 1101, 827, 765, 693; HRMS: *m/z* $[M+H]^+$ calcd for $C_{25}H_{20}O_3$: 369.1485; found: 369.1483.

8,9,10-Trimethoxy-11-phenyl-6,6a-dihydro-5*H*-benzo[*a*]fluoren-5-one (2.12l, Table 2.5):



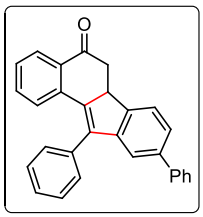
Pale yellow solid (yield = 84%); M.P. = 224 - 225 °C; R_f value =0.09 (10% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$):δ 8.06 - 8.02 (m, 1H), 7.43 (s, 5H), 7.24 - 7.18 (m, 2H), 6.94 - 6.90 (m, 1H), 6.88 (s, 1H), 4.07 (dd, *J* = 14.0, 5.4 Hz, 1H), 3.93 (s, 3H), 3.84 (s, 3H), 3.44 (dd, *J* = 15.9, 5.4 Hz, 1H), 3.35 (s, 3H), 2.50 (dd, *J* = 15.8, 14.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.5, 153.2, 149.4, 142.6, 142.5, 139.1, 137.5, 136.8, 136.5, 133.3, 131.9, 130.6, 129.3, 128.3, 127.6, 127.5, 127.1, 126.6, 103.1, 61.1, 61.0, 56.4, 49.1, 43.4; IR (KBr, cm^{-1}): 2920, 2853, 1675, 1458, 1360, 1334, 1283, 1138, 1102, 1024, 993, 890, 751, 704, 663; HRMS: *m/z* $[M+H]^+$ calcd for $C_{26}H_{22}O_4$: 399.1591; found: 399.1590.

13-Phenyl-6,6a-dihydro-5*H*-dibenzo[*a,i*]fluoren-5-one (2.12m, Table 2.5):



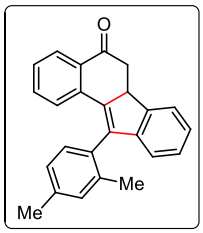
Yellow solid (yield = 30%); M.P. = 123 - 124 °C; R_f value =0.57 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$):δ 8.10 - 8.07 (m, 1H), 7.88 (d, *J* = 8.2, 1H), 7.81 (d, *J* = 8.2 Hz, 1H), 7.72 - 7.65 (m, 3H), 7.57 (tt, *J* = 7.3, 1.5 Hz, 1H), 7.53 - 7.47 (m, 1H), 7.44 - 7.34 (m, 2H), 7.31 (d, *J* = 7.6 Hz, 1H), 7.29 - 7.22 (m, 2H), 7.18 - 7.13 (m, 1H), 6.97 - 6.93 (m, 1H), 4.25 (dd, *J* = 14.1, 5.4 Hz, 1H), 3.62 (dd, *J* = 15.8, 5.5 Hz, 1H), 2.46 (dd, *J* = 15.8, 14.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$):δ 197.5, 145.0, 141.4, 140.7, 139.6, 138.1, 137.4, 134.0, 133.5, 130.7, 130.0, 129.3, 128.9, 128.6, 128.3, 127.8, 127.4, 127.2, 126.5, 125.8, 125.2, 123.8, 120.8, 49.2, 43.0; IR (Neat, cm^{-1}): 3426, 3049, 2920, 1627, 1582, 1463, 1272, 1117, 1081, 735, 699; HRMS: *m/z* $[M+H]^+$ calcd for $C_{27}H_{18}O$: 359.1430; found: 359.1432.

9,11-Diphenyl-6,6a-dihydro-5*H*-benzo[*a*]fluoren-5-one (2.12n, Table 2.5):



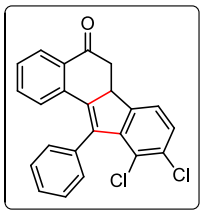
Yellow solid (yield = 94%); M.P. = 147 - 148 °C; R_f value =0.33 (10% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$):δ 8.12 - 8.08 (m, 1H), 7.60 - 7.55 (m, 2H), 7.54 - 7.50 (m, 4H), 7.49 - 7.44 (m, 3H), 7.43 - 7.38 (m, 3H), 7.35 - 7.28 (m, 3H), 7.19 - 7.16 (m, 1H), 4.22 (dd, *J* = 14.0, 5.3 Hz, 1H), 3.55 (dd, *J* = 16.0, 5.5 Hz, 1H), 2.55 (dd, *J* = 16.0, 14.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.4, 147.1, 144.9, 141.4, 141.2, 139.5, 138.8, 137.2, 134.7, 133.4, 131.0, 129.2, 129.0, 128.7, 128.2, 127.82, 127.81, 127.4, 127.3, 126.9, 125.3, 123.0, 120.2, 48.8, 43.1; IR (KBr, cm^{-1}): 2925, 2858, 1680, 1458, 1288, 1138, 1076, 1009, 751, 699; HRMS: *m/z* $[M+H]^+$ calcd for $C_{29}H_{20}O$: 385.1587; found: 385.1580.

11-(2,4-Dimethylphenyl)-6,6a-dihydro-5*H*-benzo[*a*]fluoren-5-one (2.12o, Table 2.5):



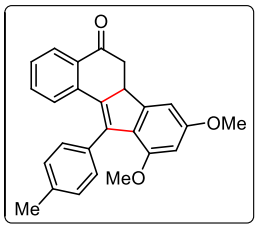
Red solid (yield = 96%); M.P. = 180 - 181 °C; R_f value = 0.45 (10% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$):δ 8.11 - 8.05 (m, 1H), 7.49 (d, *J* = 6.7 Hz, 1H), 7.31 - 7.27 (m, 4H), 7.25 - 7.22 (m, 2H), 7.08 (s, 1H), 7.04 (s, 2H), 4.13 (dd, *J* = 14.2, 5.4 Hz, 1H), 3.50 (dd, *J* = 15.9, 5.4 Hz, 1H), 2.47 (dd, *J* = 16, 14.2 Hz, 1H), 2.36 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.6, 146.7, 145.9, 139.9, 138.6, 137.6, 137.4, 134.7, 133.3, 130.9, 129.7, 128.5, 128.4, 127.7, 127.6, 127.4, 126.9, 126.5, 125.9, 122.7, 121.5, 48.9, 43.0, 21.4; IR (Neat, cm^{-1}): 3023, 2915, 1680, 1463, 1283, 1205, 1014, 978, 849, 756, 694; HRMS: *m/z* $[M+H]^+$ calcd for $C_{25}H_{20}O$: 337.1587; found: 337.1587.

9,10-Dichloro-11-phenyl-6,6a-dihydro-5*H*-benzo[*a*]fluoren-5-one (2.12p, Table 2.5):



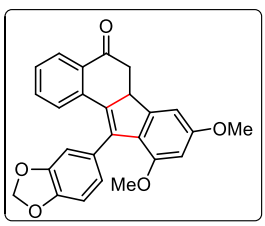
Red solid (yield = 27%); M.P. = 192 - 193 °C; R_f value = 0.38 (5% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.11 - 8.08 (m, 1H), 7.56 (s, 1H), 7.55 - 7.46 (m, 3H), 7.40 (d, *J* = 6.9 Hz, 2H), 7.36 - 7.28 (m, 2H), 7.27 (s, 1H), 7.15 (d, *J* = 7.4 Hz, 1H), 4.15 (dd, *J* = 14.0, 5.5 Hz, 1H), 3.48 (dd, *J* = 16.1,5.6 Hz, 1H), 2.49 (dd, *J* = 16.0, 14.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$):δ 196.4, 146.4, 145.2, 139.8, 138.0, 136.5, 133.8, 133.5, 131.9, 130.9, 130.0, 129.4, 128.8, 128.6, 128.4, 127.9, 126.9, 124.8, 122.9, 48.5, 42.5; IR (Neat, cm^{-1}): 3054, 2915, 1737, 1660, 1598, 1474, 1288, 1262, 1107, 1024, 952, 880, 771; HRMS: *m/z* $[M+H]^+$ calcd for $C_{23}H_{14}Cl_2O$: 377.0494; found: 377.0494.

8,10-Dimethoxy-11-(*p*-tolyl)-6,6a-dihydro-5*H*-benzo[*a*]fluoren-5-one (2.12q, Table 2.5):



Yellow solid (yield = 98%); M.P. = 205 - 206 °C; R_f value = 0.18 (10% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$):δ 8.04 - 8.00 (m, 1H), 7.26 - 7.16 (m, 6H), 6.95 - 6.91 (m, 1H), 6.69 (dd, *J* = 2.0, 0.8 Hz, 1H), 6.38 (d, *J* = 2.0 Hz, 1H), 4.05 (dd, *J* = 14.1, 5.4 Hz, 1H), 3.86 (s, 3H), 3.54 (s, 3H), 3.41 (dd, *J* = 15.9, 5.5 Hz, 1H), 2.48 (dd, *J* = 15.9, 14.2 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$):δ 197.7, 160.3, 156.1, 149.7, 139.4, 138.0, 136.8, 135.0, 134.0, 133.2, 130.6, 128.7, 127.6, 127.2, 126.7, 126.6, 100.7, 98.5, 55.7, 55.5, 49.1, 43.4, 21.4; IR (KBr, cm^{-1}): 1680, 1453, 1355, 1283, 1205, 1154, 1040, 947, 833, 766, 653, 554; HRMS: *m/z* $[M+H]^+$ calcd for $C_{26}H_{22}O_3$: 383.1642; found: 383.1645.

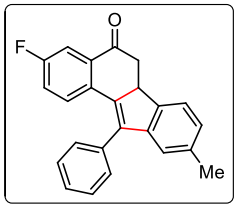
11-(Benzo[*d*][1,3]dioxol-5-yl)-8,10-dimethoxy-6,6a-dihydro-5*H*-benzo[*a*]fluoren-5-one (2.12r, Table 2.5):



Greenish yellow solid (yield = 52%); M.P. = 183 - 184 °C; R_f value = 0.21 (10% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 - 8.01 (m, 1H), 7.25 - 7.19 (m, 2H), 7.02 (d, *J* = 7.5 Hz, 1H), 6.97 - 6.72 (m, 3H), 6.68 (dd, *J* = 2.0, 0.7 Hz, 1H), 6.39 (d, *J* = 2.0 Hz, 1H), 6.04 (s, 2H), 4.04 (dd, *J* = 14.2, 5.4 Hz, 1H), 3.86 (s, 3H), 3.59 (s, 3H), 3.40 (dd, *J* = 15.9, 5.4 Hz, 1H), 2.46 (dd, *J* = 15.9, 14.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$):δ 197.6, 160.4, 156.0, 151.9, 149.6, 147.4, 146.8, 138.8, 137.8, 135.3, 133.3, 130.7, 130.6, 127.6, 127.1, 126.9,

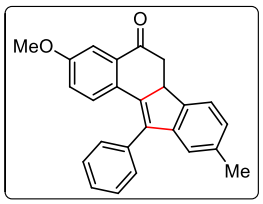
126.6, 110.0, 108.2, 101.0, 100.7, 98.5, 55.7, 55.6, 49.0, 43.3; IR (Neat, cm^{-1}): 2961, 2920, 1675, 1484, 1433, 1324, 1231, 1143, 1097, 1040, 942, 761, 735; HRMS: *m/z* $[M+H]^+$ calcd for $C_{26}H_{20}O_5$: 413.1384; found: 413.1385.

3-Fluoro-9-methyl-11-phenyl-6,6a-dihydro-5*H*-benzo[*a*]fluoren-5-one (2.12s, Table 2.5):



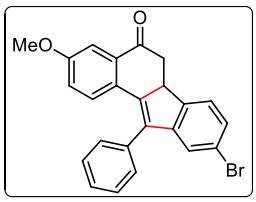
Brownish yellow solid (yield = 99%); M.P. = 140 - 141 °C; R_f value = 0.73 (10% EtOAc in hexanes); ^1H NMR (400 MHz, $CDCl_3$):δ 7.72 (dd, *J* = 9.1, 2.8 Hz, 1H), 7.54 - 7.43 (m, 3H), 7.42 (s, 1H), 7.38 (d, *J* = 7.7 Hz, 2H), 7.16 - 7.09 (m, 2H), 7.03 (s, 1H), 6.97 (td, *J* = 8.3, 2.8 Hz, 1H), 4.09 (dd, *J* = 14.1, 5.4 Hz, 1H), 3.50 (dd, *J* = 16.1, 5.4 Hz, 1H), 2.45 (dd, *J* = 16.1, 14.2 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.6, 163.2, 160.7, 146.6, 142.8, 139.3, 137.5, 137.3, 134.8, 133.7 (d, *J* = 3.1 Hz), 132.9 (d, *J* = 6.3 Hz), 129.1 (d, *J* = 22.9 Hz), 128.9, 128.2, 126.9, 122.6, 122.0, 120.9 (d, *J* = 22.7 Hz), 113.8 (d, *J* = 22.3 Hz), 48.6, 43.0, 21.5; IR (Neat, cm^{-1}): 2961, 2915, 1686, 1603, 1458, 1298, 1262, 1019, 895, 823, 704; HRMS: *m/z* $[M]^+$ calcd for $C_{24}H_{17}FO$: 340.1263; found: 340.1260.

3-Methoxy-9-methyl-11-phenyl-6,6a-dihydro-5*H*-benzo[*a*]fluoren-5-one (2.12t, Table 2.5):



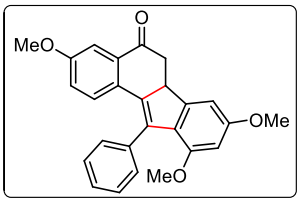
Brownish white solid (yield = 83%); M.P. = 183 - 184 °C; R_f value = 0.58 (10% EtOAc in hexanes); ^1H NMR (400 MHz, $CDCl_3$):δ 7.55 (d, *J* = 2.8 Hz, 1H), 7.53 - 7.40 (m, 5H), 7.37 (d, *J* = 7.5 Hz, 1H), 7.08 (d, *J* = 8.8 Hz, 2H), 7.02 (s, 1H), 6.86 (dd, *J* = 8.8, 2.8 Hz, 1H), 4.09 (dd, *J* = 14.0, 5.4 Hz, 1H), 3.84 (s, 3H), 3.49 (dd, *J* = 16.0, 5.4 Hz, 1H), 2.47 (dd, *J* = 15.9, 14.1 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$):δ 197.7, 159.1, 146.9, 142.7, 138.3, 137.7, 137.3, 135.1, 132.2, 130.7, 129.11, 129.07, 128.3, 127.9, 126.4, 122.4, 121.71, 121.66, 109.7, 55.5, 48.7, 43.2, 21.5; IR (KBr, cm^{-1}): 1685, 1592, 1499, 1468, 1323, 1220, 1153, 1019, 884, 807, 750, 704, 595; HRMS: *m/z* $[M]^+$ calcd for $C_{25}H_{20}O_2$: 352.1463; found: 352.1465.

9-Bromo-3-methoxy-11-phenyl-6,6a-dihydro-5*H*-benzo[*a*]fluoren-5-one (2.12u, Table 2.5):



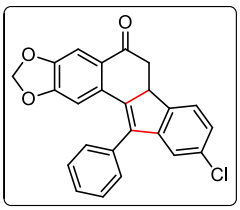
Greenish yellow solid (yield = 58%); M.P. = 202 - 203 °C; R_f value = 0.76 (10% EtOAc in hexanes); ^1H NMR (400 MHz, $CDCl_3$):δ 7.56 (d, *J* = 2.8 Hz, 1H), 7.54 - 7.44 (m, 3H), 7.42 - 7.30 (m, 5H), 7.09 (d, *J* = 8.7 Hz, 1H), 6.88 (dd, *J* = 8.7, 2.9 Hz, 1H), 4.08 (dd, *J* = 14.0, 5.4 Hz, 1H), 3.85 (s, 3H), 3.49 (dd, *J* = 16.0, 5.5 Hz, 1H), 2.47 (dd, *J* = 16.0, 14.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$):δ 197.0, 159.5, 148.8, 144.1, 139.5, 136.7, 134.3, 132.3, 130.0, 129.3, 129.0, 128.4, 128.33, 128.29, 124.1, 124.0, 121.8, 121.7, 109.8, 55.6, 48.7, 42.7; IR (Neat, cm^{-1}): 3018, 2930, 1680, 1587, 1484, 1453, 1319, 1283, 1241, 1210, 1040, 1014, 931, 870, 818, 746, 699; HRMS: *m/z* $[M+H]^+$ calcd for $C_{24}H_{17}BrO_2$: 417.0485; found: 417.0485.

3,8,10-Trimethoxy-11-phenyl-6,6a-dihydro-5*H*-benzo[*a*]fluoren-5-one (2.12v, Table 2.5):



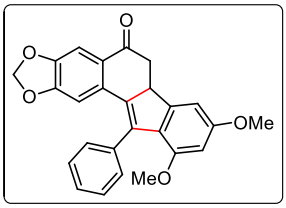
Greenish yellow solid (yield = 79%); M.P. = 208 - 209 °C; R_f value = 0.42 (10% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, J = 2.6 Hz, 1H), 7.38 (s, 5H), 6.84 - 6.76 (m, 2H), 6.69 (d, J = 1.3 Hz, 1H), 6.38 (d, J = 2 Hz, 1H), 4.04 (dd, J = 14.1, 5.4 Hz, 1H), 3.86 (s, 3H), 3.81 (s, 3H), 3.52 (s, 3H), 3.42 (dd, J = 15.9, 5.4 Hz, 1H), 2.49 (dd, J = 15.9, 14.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.7, 160.1, 158.5, 155.8, 149.1, 137.5, 137.3, 135.0, 131.8, 131.3, 128.0, 127.3, 127.1, 121.7, 109.5, 100.8, 98.5, 55.7, 55.5, 55.46, 49.2, 43.3; IR (Neat, cm^{-1}): 2961, 2837, 1675, 1587, 1479, 1309, 1278, 1200, 1143, 1035, 823, 699; HRMS: m/z $[M+H]^+$ calcd for $C_{26}H_{22}O_4$: 399.1591; found: 399.1590.

9-Chloro-11-phenyl-6,6a-dihydro-5*H*-indeno[2',1':5,6]naphtho[2,3-*d*][1,3]dioxol-5-one (2.12w, Table 2.5):



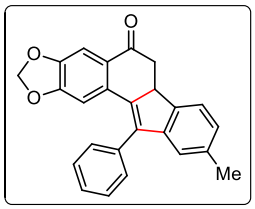
Brown solid (yield = 53%); M.P. = 265 - 266 °C; R_f value = 0.5 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.07 (s, 1H), 7.82 (d, J = 8.6 Hz, 1H), 7.63 - 7.60 (m, 1H), 7.55 - 7.50 (m, 1H), 7.41 - 7.34 (m, 2H), 7.24 (dd, J = 7.9, 1.9 Hz, 1H), 7.17 - 7.15 (m, 1H), 6.53 (s, 1H), 5.97 (s, 2H), 5.67 (s, 1H), 4.09 (dd, J = 13.9, 5.2 Hz, 1H), 3.44 (dd, J = 16.0, 5.6 Hz, 1H), 2.41 (dd, J = 16, 13.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.6, 151.9, 148.6, 143.7, 140.0, 137.7, 133.8, 132.0, 129.7, 129.5, 128.9, 128.5, 126.8, 125.8, 123.6, 121.4, 117.5, 106.9, 106.0, 101.8, 48.9, 42.4; IR (Neat, cm^{-1}): 2920, 1706, 1670, 1593, 1469, 1262, 1035, 942, 839, 813, 746, 699; HRMS: m/z $[M+H]^+$ calcd for $C_{24}H_{15}ClO_3$: 387.0782; found: 387.0783.

8,10-Dimethoxy-11-phenyl-6,6a-dihydro-5*H*-indeno[2',1':5,6]naphtho[2,3-*d*][1,3]dioxol-5-one (2.12x, Table 2.5):



Green solid (yield = 98%); M.P. = 199 - 200 °C; R_f value = 0.22 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.46 (s, 1H), 7.44 - 7.34 (m, 4H), 7.26 (s, 1H), 6.67 (d, J = 1.3 Hz, 1H), 6.37 (d, J = 2 Hz, 1H), 6.26 (s, 1H), 5.90 (q, J = 1.3 Hz, 2H), 4.03 (dd, J = 14.0, 5.5 Hz, 1H), 3.86 (s, 3H), 3.51 (s, 3H), 3.37 (dd, J = 15.9, 5.5 Hz, 1H), 2.42 (dd, J = 15.9, 14.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.1, 160.3, 155.9, 151.7, 149.3, 147.1, 138.5, 137.0, 135.1, 135.0, 128.1, 127.3, 127.1, 126.3, 106.6, 105.7, 101.5, 100.7, 98.5, 55.7, 55.5, 49.4, 42.9; IR (Neat, cm^{-1}): 3054, 2915, 1670, 1613, 1469, 1329, 1257, 1205, 1148, 1035, 931, 839, 735, 699; HRMS: m/z $[M]^+$ calcd for $C_{26}H_{20}O_5$: 412.1311; found: 412.1311.

9-Methyl-11-phenyl-6,6a-dihydro-5*H*-indeno[2',1':5,6]naphtho[2,3-*d*][1,3]dioxol-5-one (2.12y, Table 2.5):

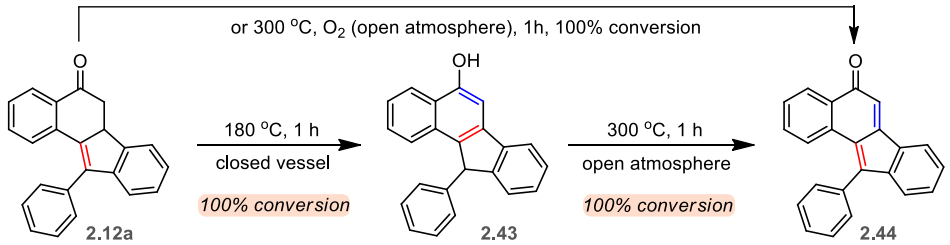


Brown solid (yield = 88%); M.P. = 291 - 292 °C; R_f value = 0.28 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56 - 7.51 (m, 3H), 7.50 - 7.46 (m, 1H), 7.43 (d, J = 6.8 Hz, 2H), 7.39 (d, J = 7.5 Hz, 1H), 7.12 (d, J = 7.5 Hz, 1H), 7.02 (s, 1H), 6.53 (s, 1H), 5.97 (d, J = 2.3 Hz, 2H), 4.11 (dd, J = 13.9, 5.5 Hz, 1H), 3.46 (dd, J = 16.0, 5.5 Hz, 1H), 2.43 (dd, J = 16.0, 13.9 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.2, 151.8, 147.7, 146.7, 142.8, 138.7, 138.4, 137.3, 134.8, 134.4, 129.8, 129.2, 129.0, 128.1, 126.7, 122.4, 121.8, 106.8, 106.0, 101.7, 49.0, 42.8, 21.5; IR (KBr, cm^{-1}): 3385, 1701, 1629, 1484, 1267, 1169, 1035, 870, 808, 766; HRMS: m/z $[M+H]^+$ calcd for $C_{25}H_{18}O_3$: 367.1329; found: 367.1329.

2.4.6. Synthesis and Characterization of Benzo[*a*]fluorenol (2.43) and Benzo[*a*]fluorenone Derivative (2.44):

2.4.6.1. Heating Method for the Preparation of Benzo[*a*]fluorenol Derivative (2.43) and Benzo[*a*]fluorenone Derivative (2.44):

Benzo[*a*]fluorenone **2.12a** was heated under N_2 atmosphere in a closed vessel neatly. After 1 hour, **2.12a** was found to be fully converted into 11-phenyl-11*H*-benzo[*a*]fluoren-5-ol, **2.43**. In an open vessel when **2.12a** was heated at 300 °C, compound 11-phenyl-6,6a-dihydro-5*H*-benzo[*a*]fluoren-5-one (**2.44**) was obtained after 1 hour. The compound **2.43** upon heating at 300 °C in open atmosphere was converted into compound **2.44**.



Scheme 2.13. Synthesis of benzo[*a*]fluorenol (**2.43**) and benzo[*a*]fluorenone (**2.44**).

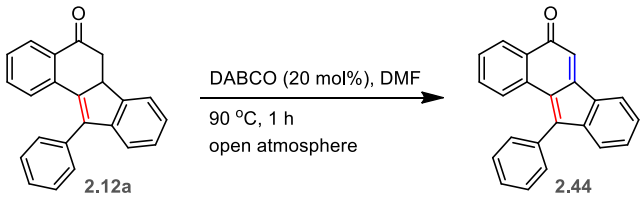
2.4.6.2. Chemical Method for the Preparation of Benzo[*a*]fluorenol Derivative (2.43) and Benzo[*a*]fluorenone Derivative (2.44):

In a round bottom flask, benzo[*a*]fluorene **2.11a** (1 equiv.) was dissolved in CH_2Cl_2 (5ml/mmol) solvent under nitrogen atmosphere at 0 °C. Then BBr_3 (2 equiv.) was added to it and allowed to stir at room temperature for 3 hours. Then the reaction mixture was quenched by a saturated $NaHCO_3$ solution and extracted with EtOAc. Then the organic layer was washed with saturated brine solution, dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. Finally, the crude product was purified by column chromatography (silica gel, hexanes/EtOAc) to get pure 11-phenyl-11*H*-benzo[*a*]fluoren-5-ol **2.43**.



Scheme 2.14. Synthesis of benzo[*a*]fluorenol (**2.43**) by chemical method.

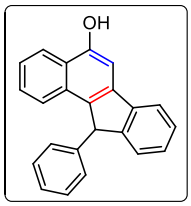
Benzo[*a*]fluorenone **2.12a** (1 equiv.) was dissolved in DMF (5ml/mmol) in a round bottom flask. Then DABCO (20 mol%) was added to the reaction mixture and refluxed at 90 °C for 1 hour in an open atmosphere. After the completion of the reaction water was then added to the reaction mixture. It was extracted with EtOAc. The organic layer was washed with dil. HCl solution followed by saturated $NaHCO_3$ solution. Then the organic layer was washed with saturated brine solution, dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. Finally, the crude product was purified by column chromatography (silica gel, hexaness/EtOAc) to get pure 11-phenyl-5*H*-benzo[*a*]fluoren-5-one **2.44**.



Scheme 2.15. Synthesis of benzo[*a*]fluorenone (**2.44**) by chemical method.

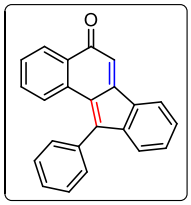
2.4.6.3. Analytical Data of Benzo[*a*]fluorenol Derivative (2.43) and Benzo[*a*]fluorenone Derivative (2.44):

11-Phenyl-11*H*-benzo[*a*]fluoren-5-ol (2.43):



Brown solid (yield = 94% in chemical method); M.P. = 208 - 209 °C; R_f value = 0.20 (10% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ8.25 (d, J = 8.5 Hz, 1H), 7.75 (d, J = 7.6 Hz, 1H), 7.62 (d, J = 8.2 Hz, 1H), 7.45 - 7.32 (m, 5H), 7.27 - 7.21 (m, 4H), 7.14 (d, J = 6.5 Hz, 2H), 5.47 (s, 1H), 5.30 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$):δ152.2, 149.6, 141.9, 140.9, 139.4, 136.1, 131.2, 128.9, 128.0, 127.1, 127.0, 126.7, 125.9, 124.9, 124.59, 124.55, 122.8, 119.8, 119.4, 101.4, 53.7; IR (Neat, cm^{-1}): 2930, 1660, 1587, 1417, 1293, 1102, 1014, 864, 751, 663; HRMS:*m/z* $[M+Na]^+$ calcd for $C_{23}H_{16}O$: 331.1093; found: 331.1092.

11-Phenyl-5*H*-benzo[*a*]fluoren-5-one (2.44):



Dark red solid (yield = 96% in chemical method); M.P. = 190 - 191 °C; R_f value =0.31 (10% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$):δ8.10 (d, J = 8.0 Hz, 1H), 7.60 - 7.55 (m, 2H), 7.55 - 7.51 (m, 2H), 7.49 (d, J = 1.6 Hz, 1H), 7.48 - 7.46 (m, 1H), 7.27 (s, 1H), 7.26 (s, 1H), 7.22 - 7.16 (m, 3H), 6.88 (t, J = 4.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ186.4, 153.0, 149.0, 146.0, 135.7, 134.3, 133.4, 132.3, 130.8, 130.5, 129.3, 129.2, 128.2, 127.84, 127.78, 127.5, 125.2, 122.4, 122.0, 121.3; IR (Neat, cm^{-1}): 2956, 1644, 1593, 1407, 1262, 1097, 1014, 802, 704; HRMS:m/z $[M+H]^+$ calcd for $C_{23}H_{14}O$: 307.1117; found: 307.1118.

2.4.7. *X*-ray *C*rystallography:

Benzo[*a*]fluorenone **2.12a** was heated under N_2 atmosphere in a closed vessel neatly. Single crystal X-ray data for the compound **2.11a**, **2.11j**, **2.12a**, **2.12j** and **2.44** were collected using the detector system [λ (Mo-Kα) = 0.71073 Å] at 293K, graphite monochromator with a ω scan width of 0.3o, crystal-detector distance 60 mm, collimator 0.5 mm. The SMART software[24] was used for the intensity data acquisition and the SAINTPLUS Software[25] was used for the data extraction. In each case, absorption correction was performed with the help of SADABS program,[24] an empirical absorption correction using equivalent reflections was performed with the program. The structure was solved using SHELXS-97[25] and full-matrix least-squares refinement against F2 was carried out using SHELXL-97.[25] All non-hydrogen atoms were refined anisotropically. Aromatic and methyl hydrogens were introduced on calculated positions and included in the refinement riding on their respective parent atoms.

Crystallographic data (including the structure factor) for the structures **2.11a**, **2.11j**, **2.12a**, **2.12j** and **2.44** in this paper have been deposited in the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 1560544, 1560552, 1560545, 1560546 and 1560547. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

2.4.7.1. *X*-ray *C*rystal *S*tructure and *D*ata for *B*enzo[*a*]fluorene *D*erivative (2.11a):

Table 2.8. Crystallographic data for compound **2.11a**

CCDC Number	1560544
Compound identification code	rb 2
Empirical formula	C24 H18 O
Formula weight	322.38
Temperature	296 K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P 21
Unit cell dimensions	a=10.0322(5) alpha=90 b=5.6962(2) beta=97.189(2)

	c=14.9733(7) gamma=90
Volume	848.93(7)Å^3
Z	2
Density (calculated)	1.261 g/cm^3
Absorption coefficient	0.075 mm^{-1}
F(000)	340.0
Reflections collected	3917
Independent reflections	3202
Completeness to theta = 27.539°	0.99
Refinement method	Full-matrix least-squares on F2
Max. and min. transmission	0.996 and 0.995
Goodness-of-fit on F2	1.087
R(reflections)	0.0401 (3202)
wR2(reflections)	0.0974 (3862)
Diffractometer	Xcalibur Gemini Eos CCD

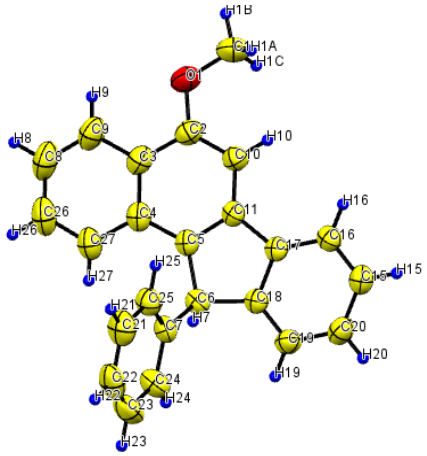


Figure 2.17. ORTEP-drawing of compound **2.11a**.

2.4.7.2. *X*-ray *C*rystal *S*tructure and *D*ata for *B*enzo[*a*]fluorene *D*erivative (2.11j):

Table 2.9. Crystallographic data for compound **2.11j**

CCDC Number	1560552
Compound identification code	rb 23
Empirical formula	C28 H20 O
Formula weight	372.44
Temperature	296 K
Wavelength	0.71073 Å
Crystal system	Orthorhombic

Space group	P b c a
Unit cell dimensions	a=13.703(2) alpha=90 b=8.506(1) beta=90 c=33.133(5) gamma=90
Volume	3861.9(9) Å^3
Z	8
Density (calculated)	1.281 g/cm^3
Absorption coefficient	0.076 mm^{-1}
F(000)	1568.0
Reflections collected	3434
Independent reflections	2394
Completeness to theta = 25.082 °	0.999
Refinement method	Full-matrix least-squares on F2
Max. and min. transmission	0.996 and 0.995
Goodness-of-fit on F2	1.058
R(reflections)	0.0480 (2394)
wR2(reflections)	0.1195 (3429)
Diffractometer	Xcalibur Gemini Eos CCD

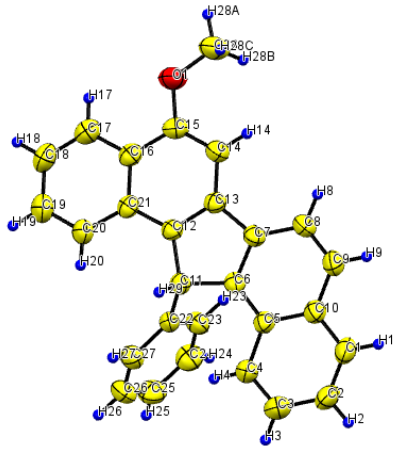


Figure 2.18. ORTEP-drawing of compound **2.11j**.

2.4.7.3. X-ray Crystal Structure and Data for Benzo[a]fluorenone Derivative (2.12a):

Table 2.10. Crystallographic data for compound **2.12a**

CCDC Number	1560545
Compound identification code	rb 7
Empirical formula	C23 H16 O
Formula weight	308.36
Temperature	296 K

Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P -1
Unit cell dimensions	a=5.9202(15) alpha=75.479(15) b=10.539(2) beta=77.92(1) c=13.884(4) gamma=89.397(11)
Volume	819.2(4) $Å^3$
Z	2
Density (calculated)	1.250 g/cm^3
Absorption coefficient	0.075 mm^{-1}
F(000)	324.0
Reflections collected	2889
Independent reflections	2198
Completeness to theta = 25.026 °	0.997
Refinement method	Full-matrix least-squares on F2
Max. and min. transmission	0.995 and 0.993
Goodness-of-fit on F2	1.029
R(reflections)	0.0636 (2198)
wR2(reflections)	0.1637 (2880)
Diffractometer	Xcalibur Gemini Eos CCD

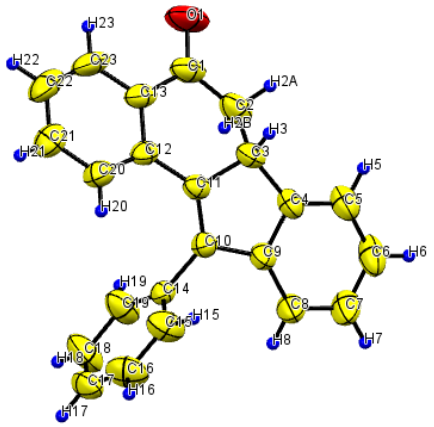


Figure 2.19. ORTEP-drawing of compound **2.12a**.

2.4.7.4. *X*-ray *C*rystal *S*tructure and *D*ata for *B*enzo[*a*]fluorenone *D*erivative (2.12j):

Table 2.11. Crystallographic data for compound **2.12j**

CCDC Number	1560546
Compound identification code	rb 31
Empirical formula	C24 H16 O3

Formula weight	352.37
Temperature	294 K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P -1
Unit cell dimensions	a=10.1506(7) alpha=87.397(4) b=10.1554(8) beta=66.746(3) c=10.1731(8) gamma=64.750(3)
Volume	861.83(12)Å^3
Z	2
Density (calculated)	1.358 g/cm^3
Absorption coefficient	0.089 mm^{-1}
F(000)	368.0
Reflections collected	3036
Independent reflections	2215
Completeness to theta = 25.025°	1.000
Refinement method	Full-matrix least-squares on F2
Max. and min. transmission	0.982 and 0.979
Goodness-of-fit on F2	1.096
R(reflections)	0.0483 (2215)
wR2(reflections)	0.1333 (3036)
Diffractometer	Xcalibur Gemini Eos CCD

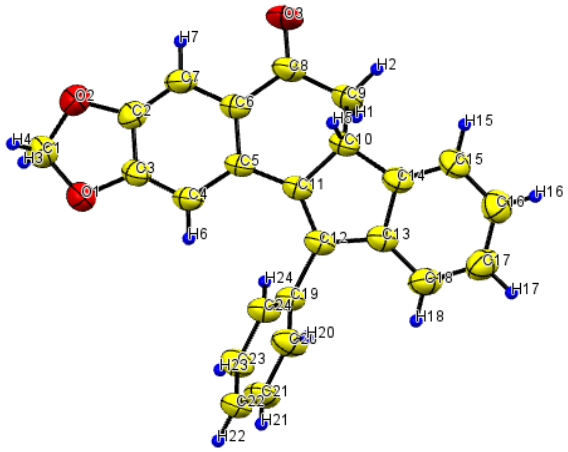


Figure 2.20. ORTEP-drawing of compound **2.11j**.

2.4.7.5. *X*-ray *C*rystal *S*tructure and *D*ata for *B*enzo[*a*]fluorenone *D*erivative (2.44):

Table 2.12. Crystallographic data for compound **2.44**

CCDC Number	1560547

Compound identification code	AKS 65_0m
Empirical formula	C23 H14 O
Formula weight	306.34
Temperature	296 K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P -1
Unit cell dimensions	a=8.821(5) alpha=66.510(13) b=9.504(6) beta=75.253(14) c=10.459(6) gamma=74.826(15)
Volume	764.9(8) $Å^3$
Z	2
Density (calculated)	1.330 g/cm^3
Absorption coefficient	0.080 mm^{-1}
F(000)	320.0
Reflections collected	2470
Independent reflections	1535
Completeness to theta = 24.247 °	1.000
Refinement method	Full-matrix least-squares on F2
Max. and min. transmission	0.996 and 0.995
Goodness-of-fit on F2	1.089
R(reflections)	0.0549 (1535)
wR2(reflections)	0.1258 (2469)
Diffractometer	Xcalibur Gemini Eos CCD

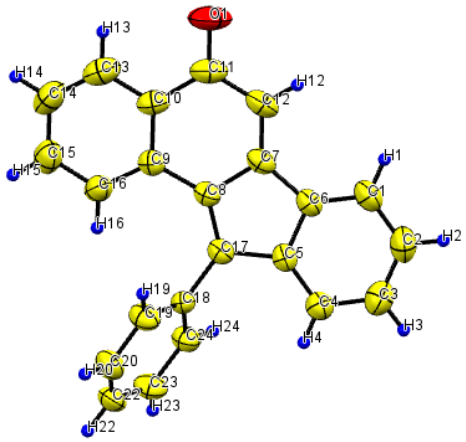


Figure 2.21. ORTEP-drawing of compound **2.44**.

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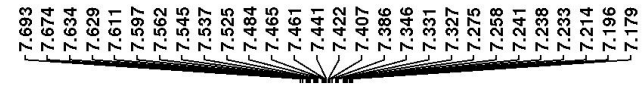
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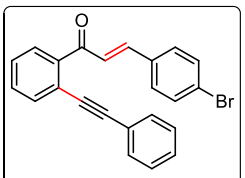
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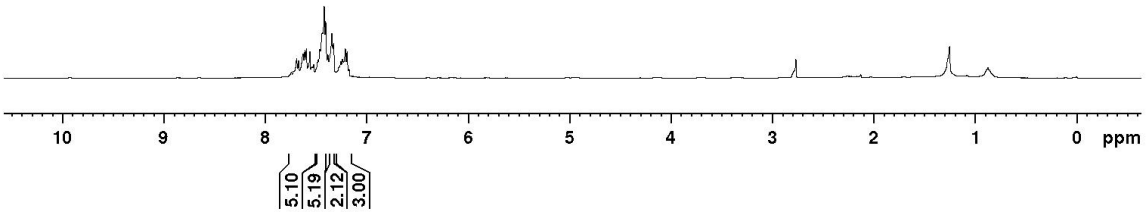
(25) Sheldrick, G. M. *SHELX-97*, Program for Crystal Structure Solution and Analysis; University of Gottingen: Gottingen, Germany, **1997**.

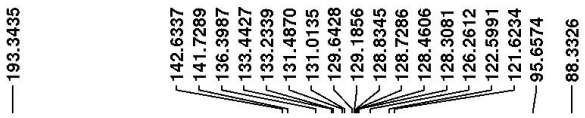
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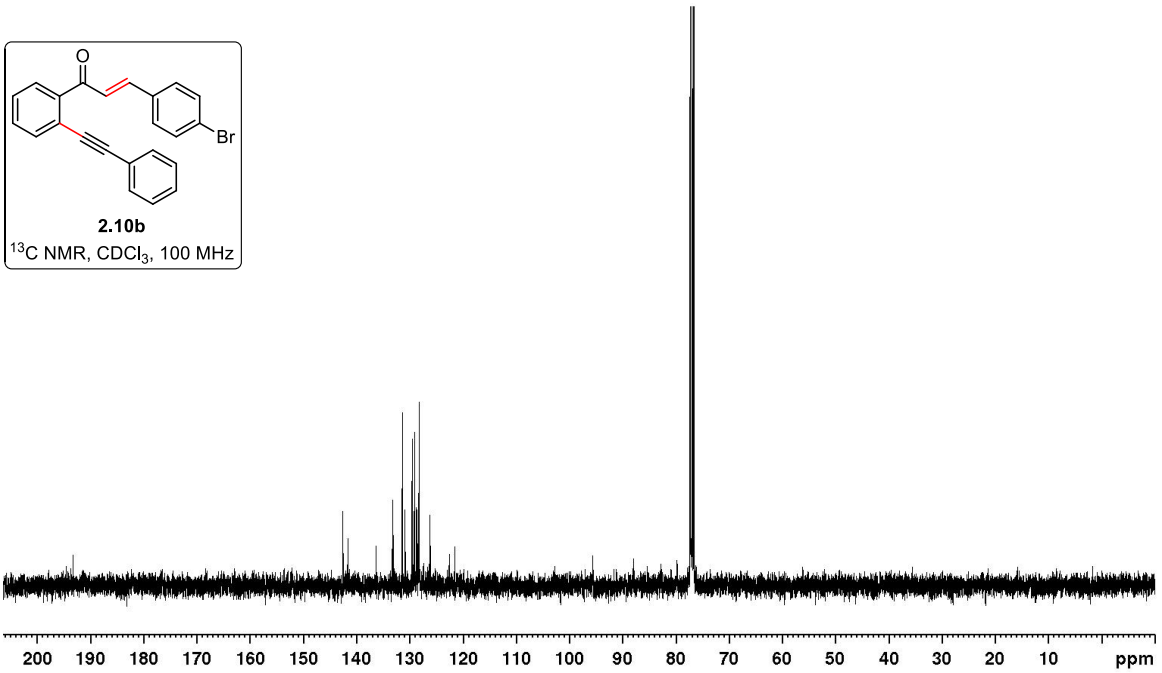


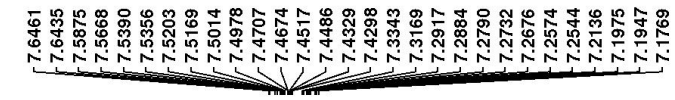
2.10b
^{1}H NMR, $CDCl_3$, 400 MHz

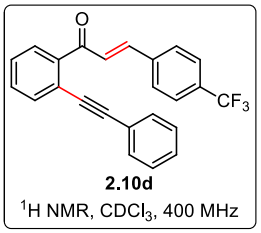




2.10b
^{13}C NMR, $CDCl_3$, 100 MHz

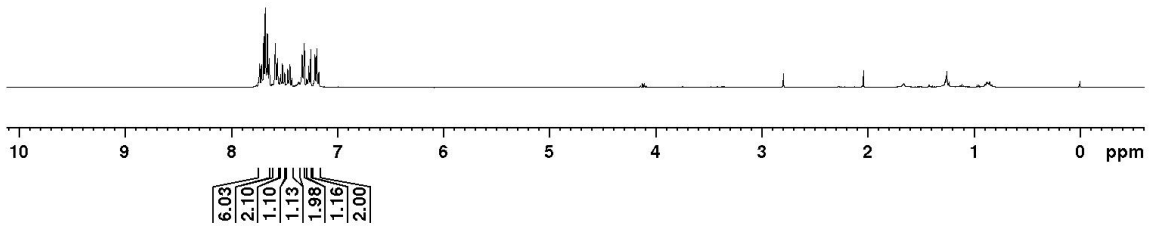


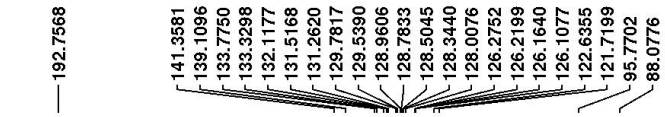


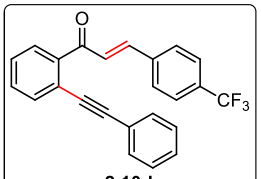


2.10d

^{1}H NMR, $CDCl_3$, 400 MHz

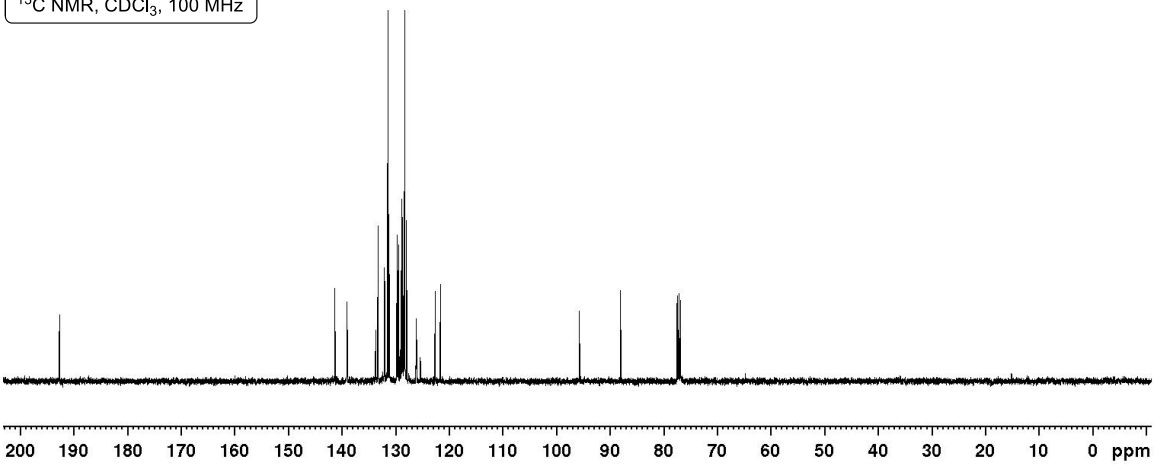


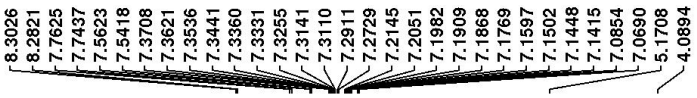


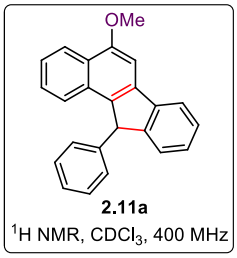


2.10d

^{13}C NMR, $CDCl_3$, 100 MHz

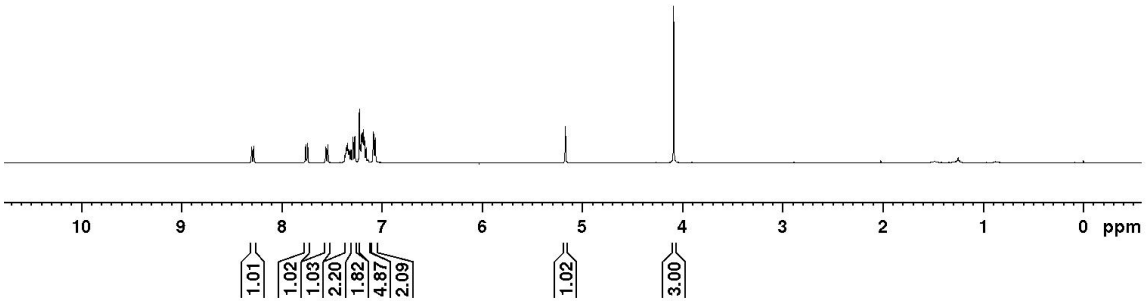


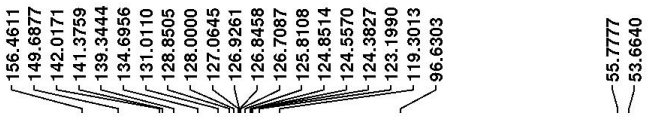


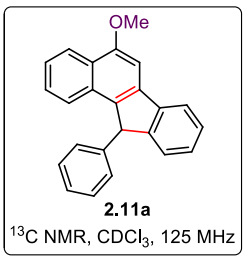


2.11a

^{1}H NMR, $CDCl_3$, 400 MHz

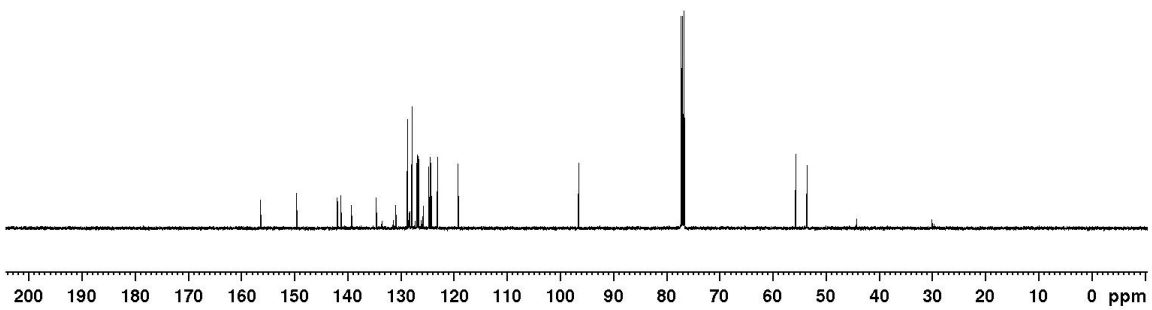


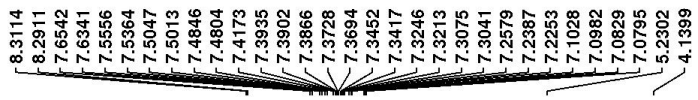


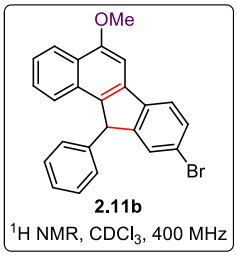


2.11a

^{13}C NMR, $CDCl_3$, 125 MHz

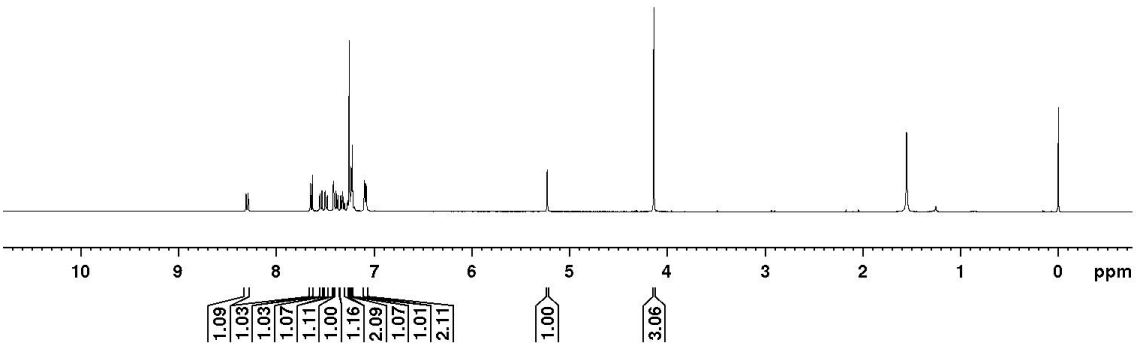


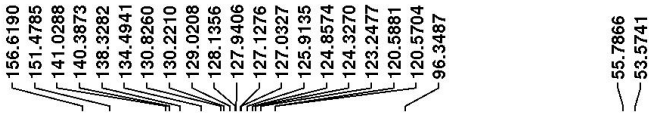




2.11b

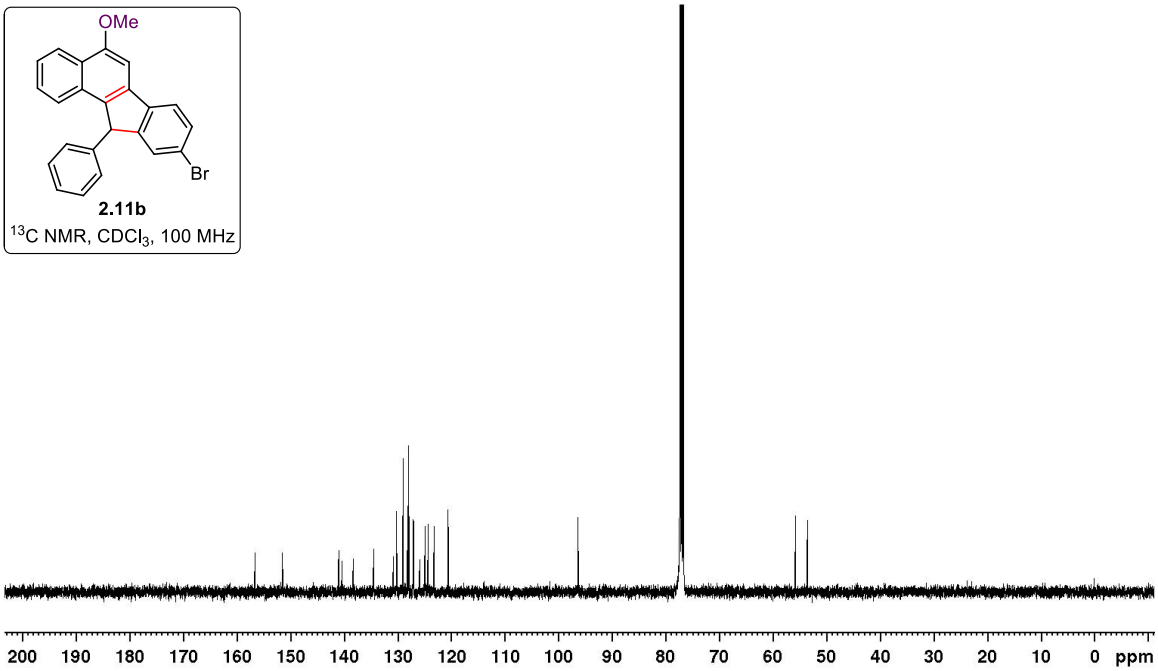
^{1}H NMR, $CDCl_3$, 400 MHz



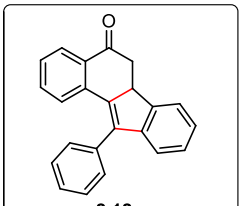


2.11b

^{13}C NMR, $CDCl_3$, 100 MHz

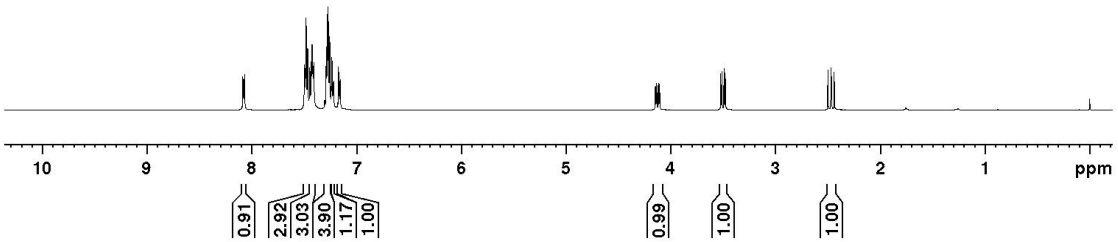


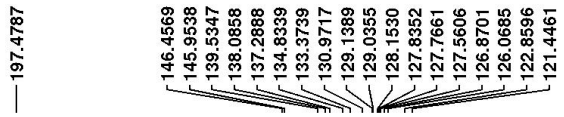


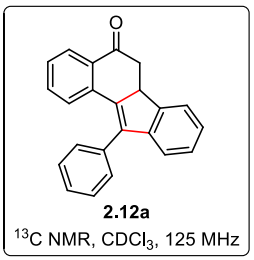


2.12a

^{1}H NMR, $CDCl_3$, 500 MHz

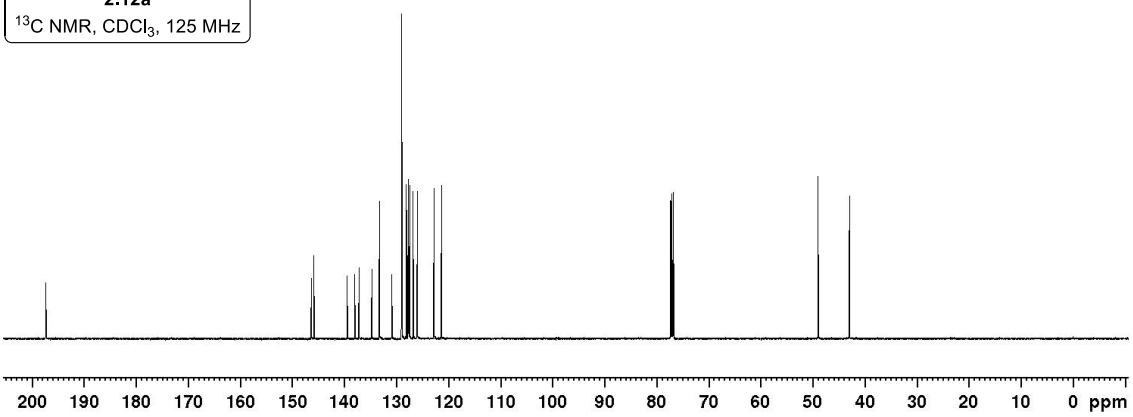


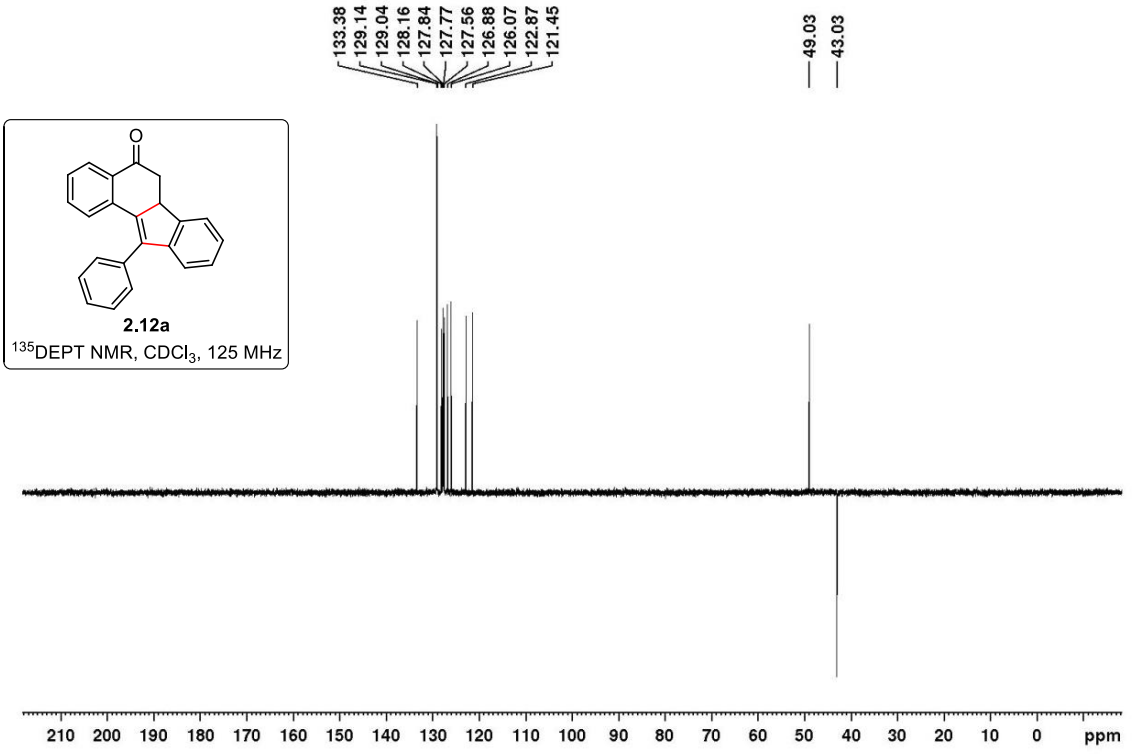


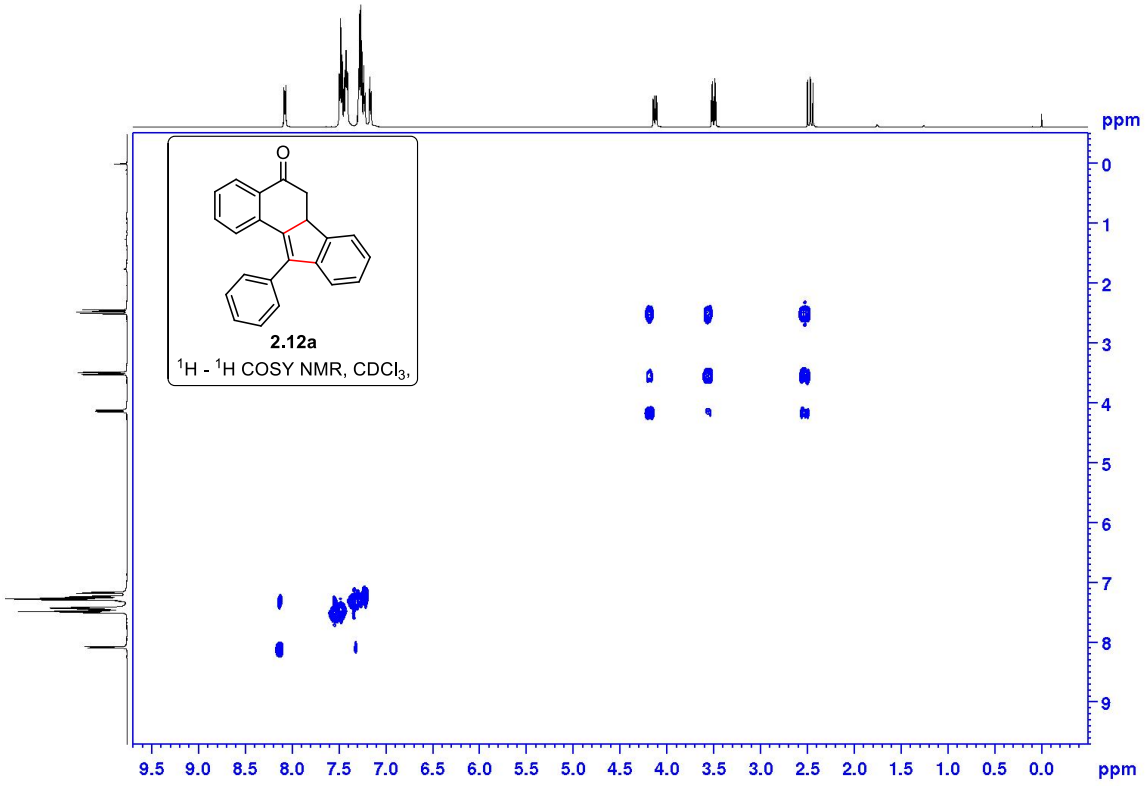


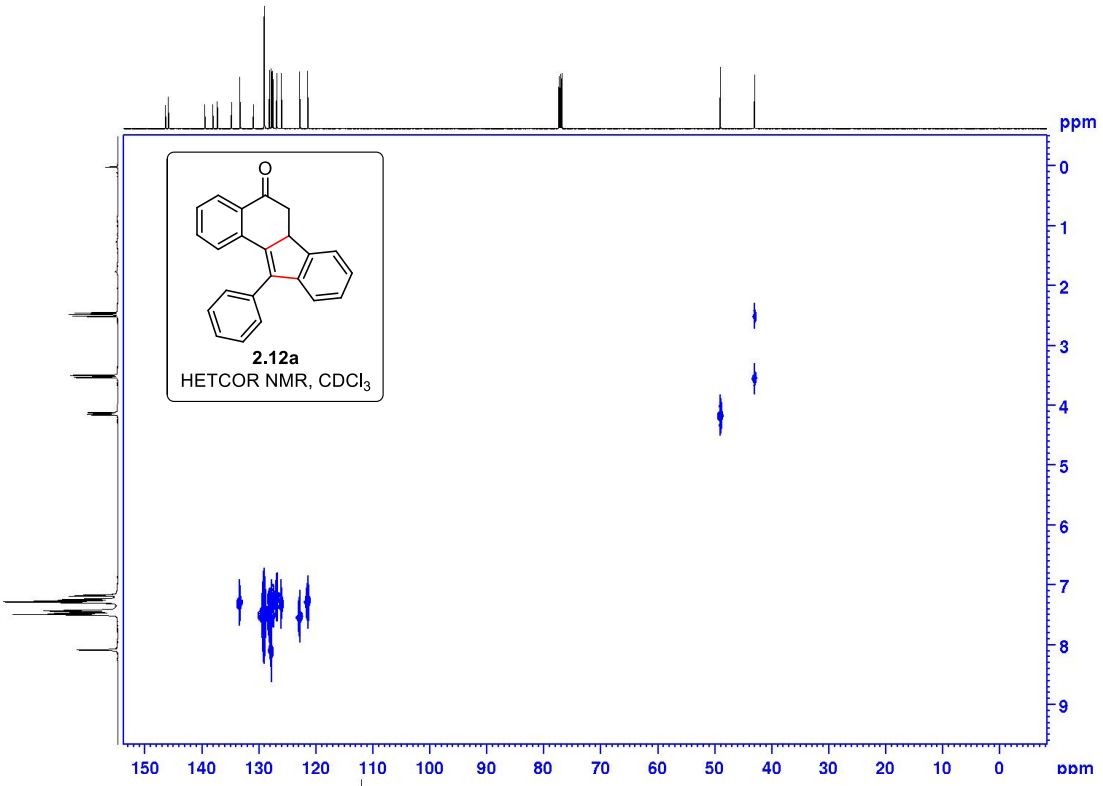
2.12a

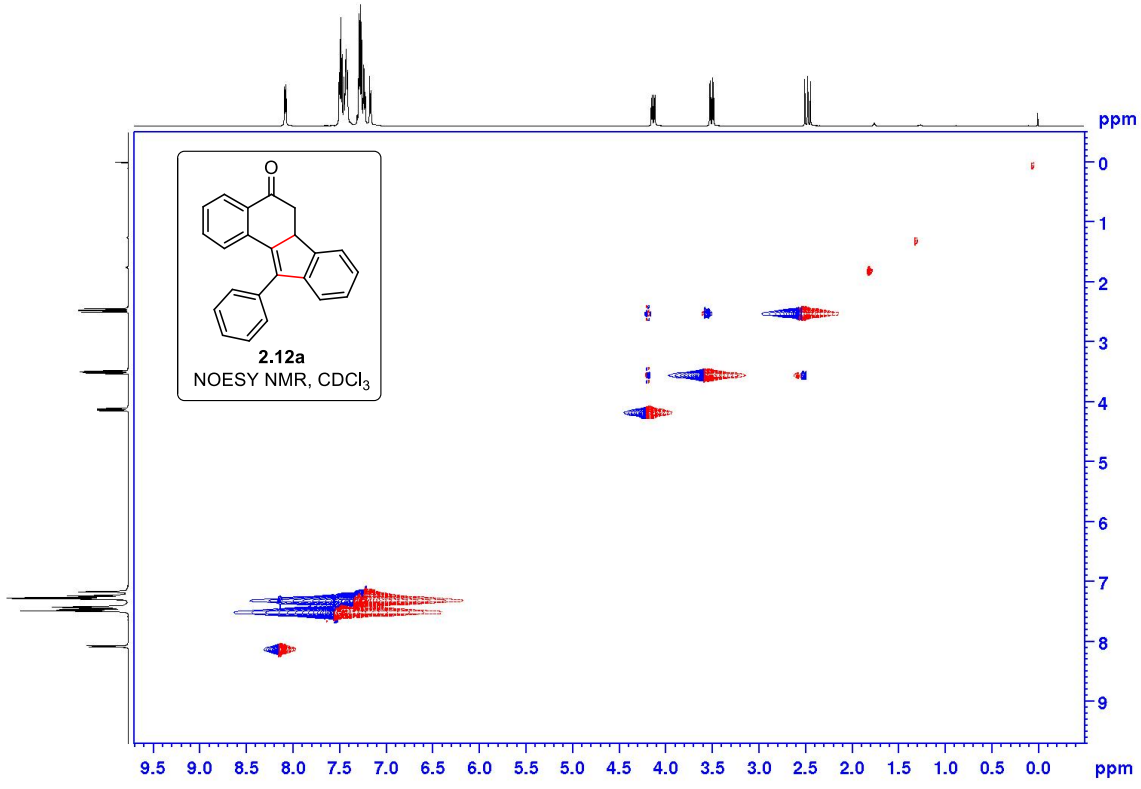
^{13}C NMR, $CDCl_3$, 125 MHz

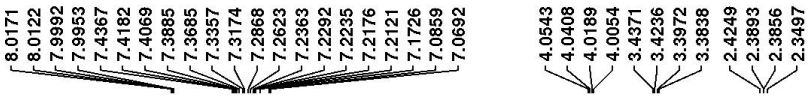


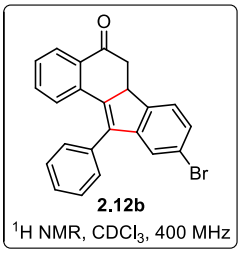

133.38
129.14
129.04
128.16
127.84
127.77
127.56
126.88
126.07
122.87
121.45
49.03
43.03
O
2.12a
135DEPT NMR, CDCl3, 125 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


O
2.12a
1H - 1H COSY NMR, CDCl3,
ppm
0 1 2 3 4 5 6 7 8 9
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm


O
2.12a
HETCOR NMR, CDCl3
ppm
0
1
2
3
4
5
6
7
8
9
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

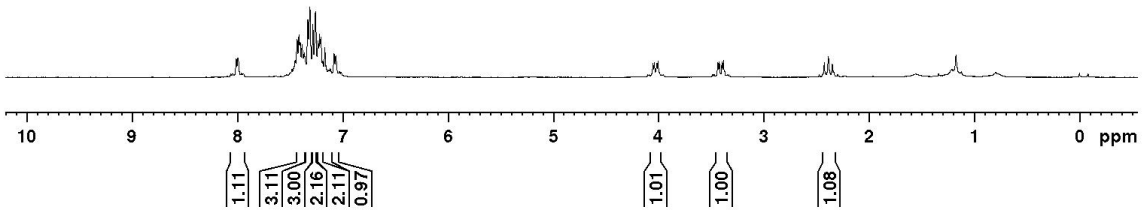

O
2.12a
NOESY NMR, CDCl3
ppm
0
1
2
3
4
5
6
7
8
9
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

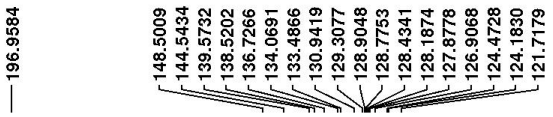


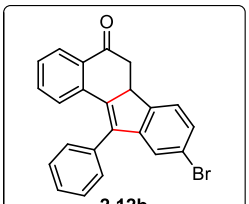


2.12b

^{1}H NMR, $CDCl_3$, 400 MHz

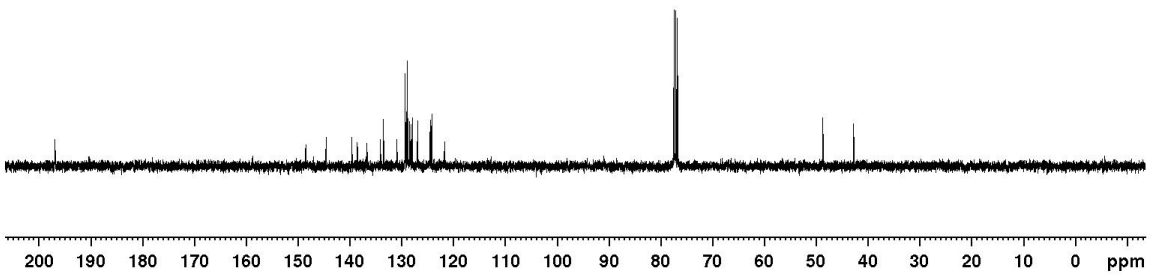


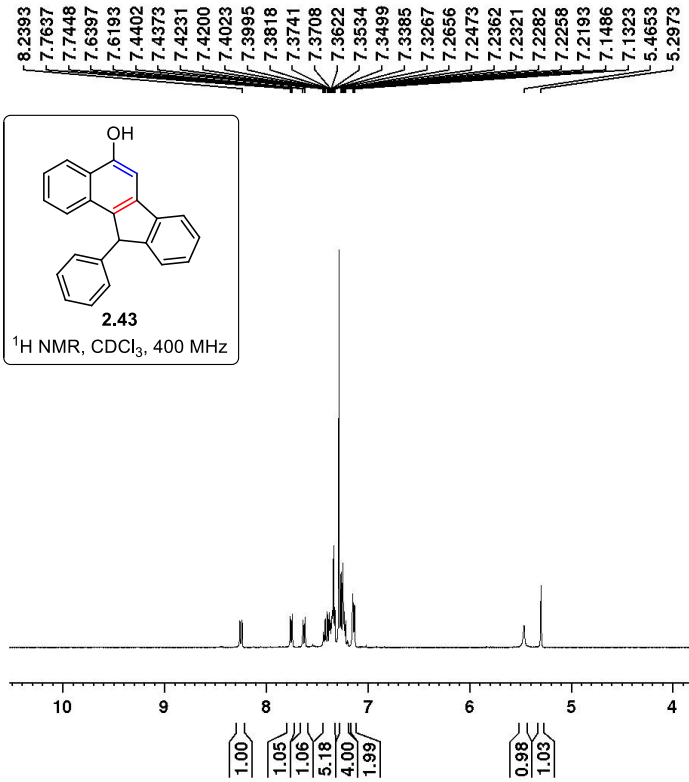


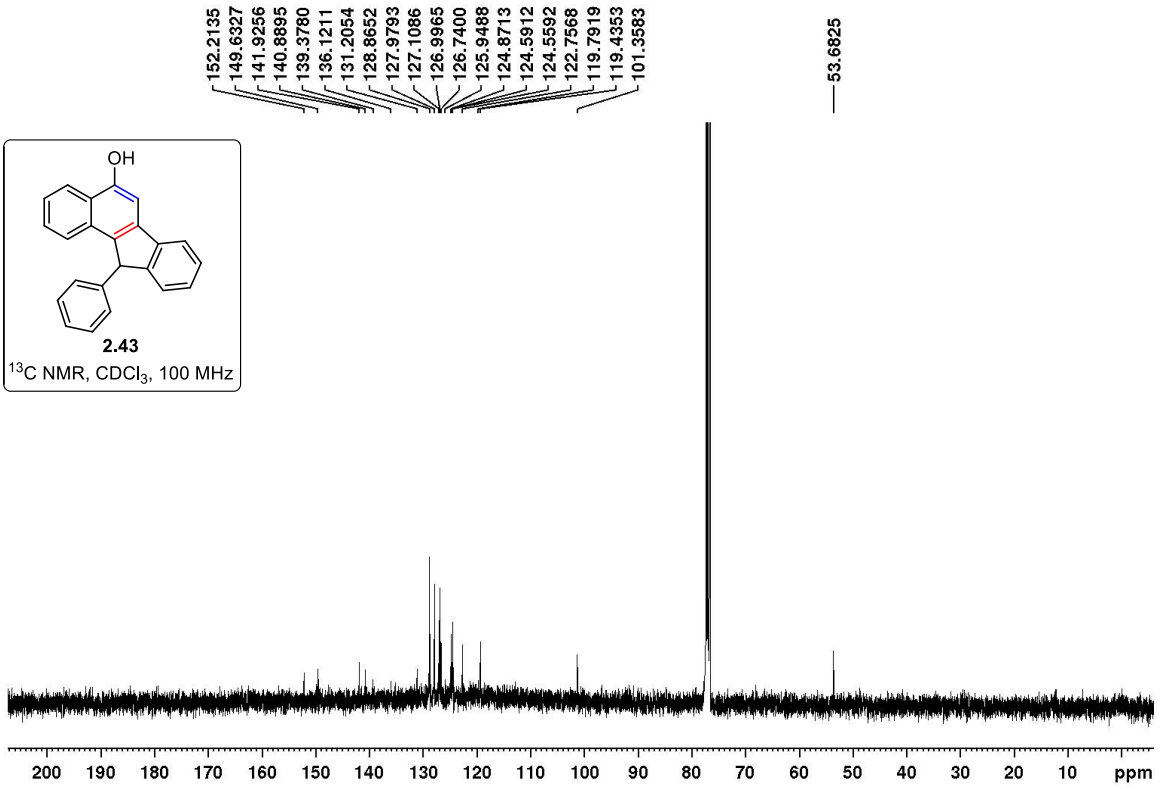


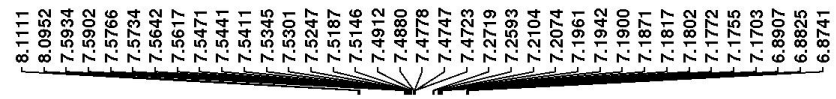
2.12b

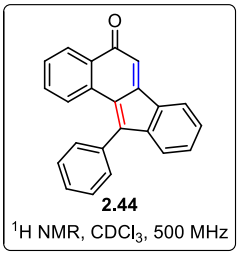
^{13}C NMR, $CDCl_3$, 100 MHz




8.2393
7.7637
7.7448
7.6397
7.6193
7.4402
7.4373
7.4231
7.4200
7.4023
7.3995
7.3818
7.3741
7.3708
7.3622
7.3534
7.3499
7.3385
7.3267
7.2656
7.2473
7.2362
7.2321
7.2282
7.2258
7.2193
7.1486
7.1323
5.4653
5.2973
OH
2.43
1H NMR, CDCl3, 400 MHz
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.05
1.06
5.18
4.00
1.99
0.98
1.03

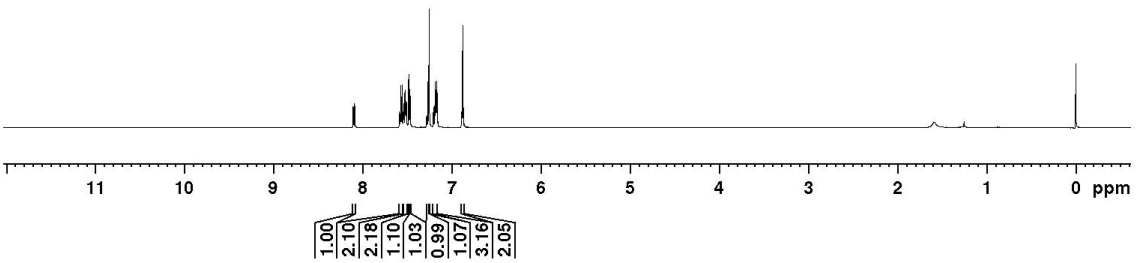

152.2135
149.6327
141.9256
140.8895
139.3780
136.1211
131.2054
128.8652
127.9793
127.1086
126.9965
126.7400
125.9488
124.8713
124.5912
124.5592
122.7568
119.7919
119.4353
101.3583
53.6825
OH
2.43
13C NMR, CDCl3, 100 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

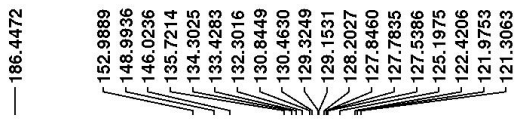




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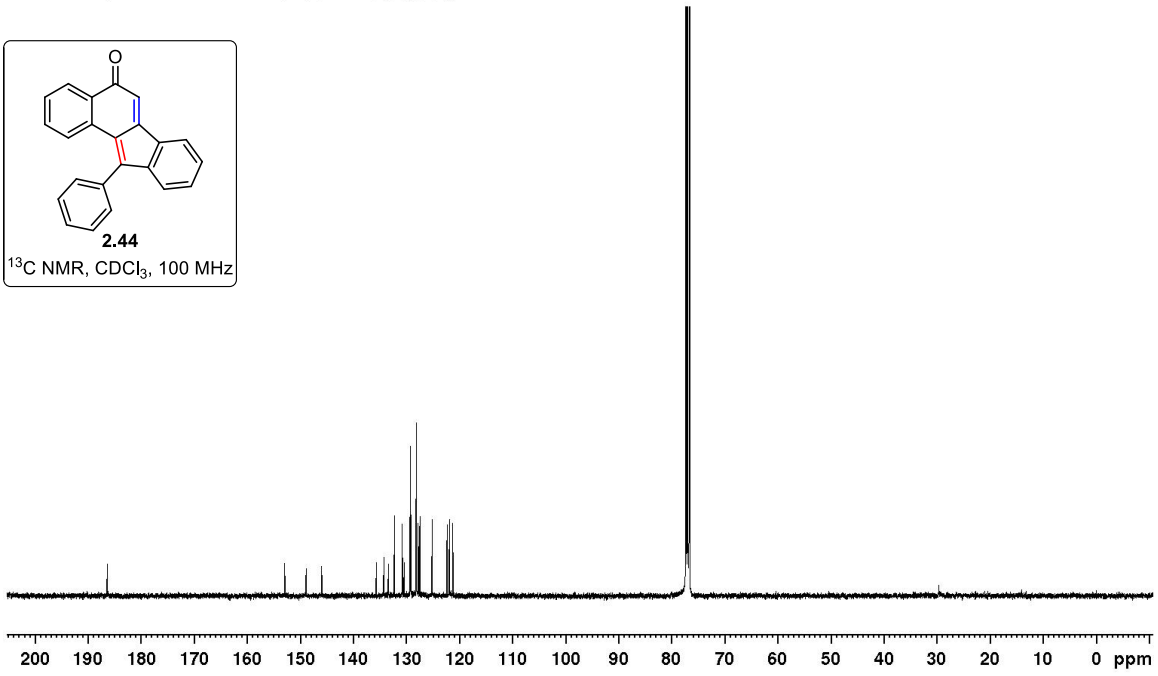
^{1}H NMR, $CDCl_3$, 500 MHz





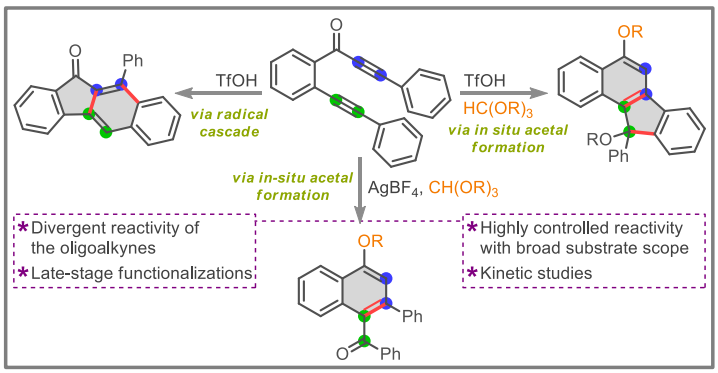
2.44

^{13}C NMR, $CDCl_3$, 100 MHz



Chapter 3

Diversity-Oriented Synthesis of Benzo[a]fluorenes, Benzo[b]fluorenones and Naphthyl Ketones from Aryl-Fused 1,6-Diyn-3-ones



*H*erein, a facile and diversity-oriented approach to access substituted benzo[*a*]fluorenes, benzo[*b*]fluorenones and naphthyl ketones has been presented *via* intramolecular cyclization of aryl fused 1,6-diyn-3-one. Benzo[*a*]-fluorene and naphthyl ketone formation involves *in situ* formed acetal intermediates. Aryl fused 1,6-diyn-3-one undergo triflic acid-mediated intramolecular cyclization leading to benzo[*b*]fluorene derivative.

Mandal, M.; Sakthivel, S.; Balamurugan, R. *J. Org. Chem.* **2021**, *86*, 333-351.

3.1 Introduction:

3.1.1. Background of the Present Work:

Polycyclic aromatic hydrocarbons have engrossed extensive interest due to their electrochemical and photochemical properties, and their utility as π-conjugated functional materials such as organic semiconductors and luminescent materials.[1] Polyarylated derivatives bearing aromatic cores are of particular interest because of their stability, immense ability to transport charge, and fluorescent properties due to the presence of the aryl groups.[2] Over the past decades, the craving interest towards polycyclic aromatic hydrocarbons (PAHs) evoked us to add some new findings using the chemistry of acetals. Accordingly, syntheses of novel PAHs namely, benzo[*a*]fluorenes,[3] benzo[*b*]fluorenones[4] and naphthalene cores[5] have been developed. In the previous chapter, we have discussed elaborately about the important features of benzo-fused fluorene and fluorenones. Naphthyl ketone moiety is also found in many natural products and constitute the core of many pharmaceutical agents[6] too (Figure 3.1). In addition, they have copious applications in material science.[7] For instance, these imperative frameworks have been used in organic field effect transistors, organic electroluminescence devices, semiconductors and solar cells etc (Figure 3.1).[7,8] Since last few decades, benzo[*a*]fluorene, benzo[*b*]fluorenone and naphthyl ketone moities have grabbed immense importance due to their widespread applications. With regard to their extensive scientific and commercial values, construction of new analogues is still a subject of consistent interest to the organic as well as material researchers from academic and industrial points of view.

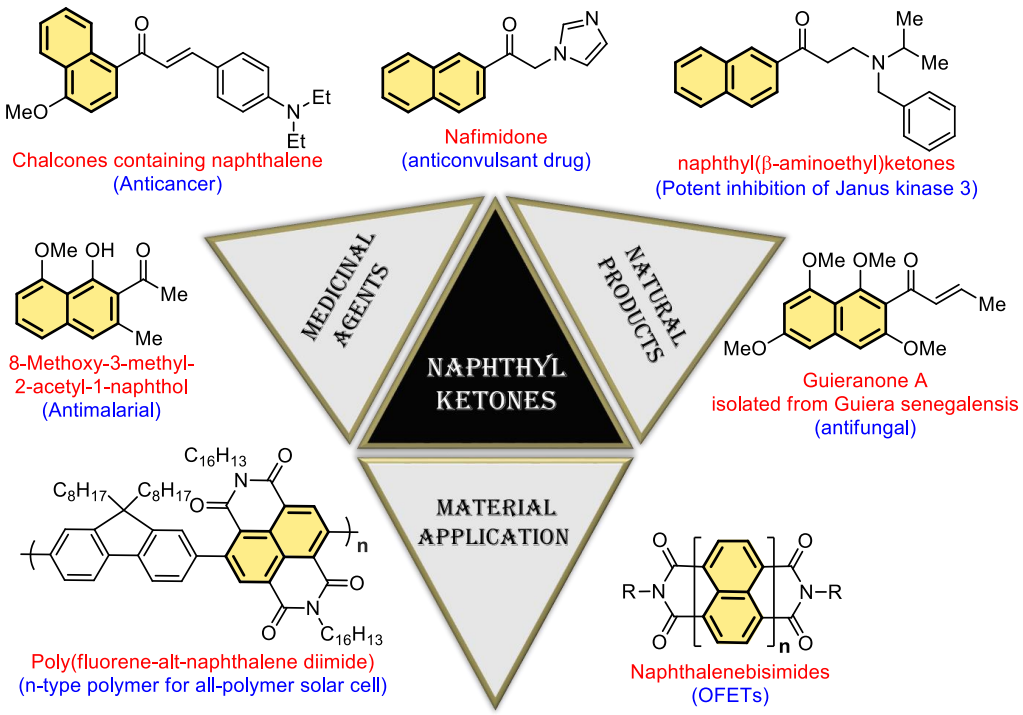


Figure 3.1. Selected novel naphthyl ketone analogues.

3.1.2 Literature Reports:



Figure 3.2. Synthetic strategies of naphthyl ketones

With the contributions from several research groups over the past few decades, a number of synthetic routes leading to benzo[*a*]fluorenes, benzo[*b*]fluorenones and naphthyl ketones have been developed. The methods for the synthesis of benzo-fused fluorenes/fluorenones are depicted in Figure 2.1.2. In addition, different research groups have added alternate protocols to the existing methodologies for the access of naphthyl ketone cores. These methods comprise of a number of synthetic routes like transition metal (*e.g.,* Pd, Zn, Au or Ag)-catalyzed benzannulation reactions (involving dehydrogenation/ [4+2] cycloaddition or Myers-Saito cyclization or hydrative carbocyclization),[5a,j,l-p] Lewis acid-catalyzed [4+2] cycloaddition reactions,[5s-t] iodine-mediated halocyclization/cycloaddition reactions[5k,q] and intramolecular hetero alkyne metathesis via *in situ* acetal incorporation/ alkyne–carbonyl metathesis.[5g,i]

In this regard, 1,6-diyn-3-one/diynes are prominent building blocks for the construction of the PAH systems. So, we have demonstrated some of the existing methods for the cyclization reactions of such types of 1,6-diyn-3-one/1,6-diyne skeleton below,[5h,l,n-p, 8]

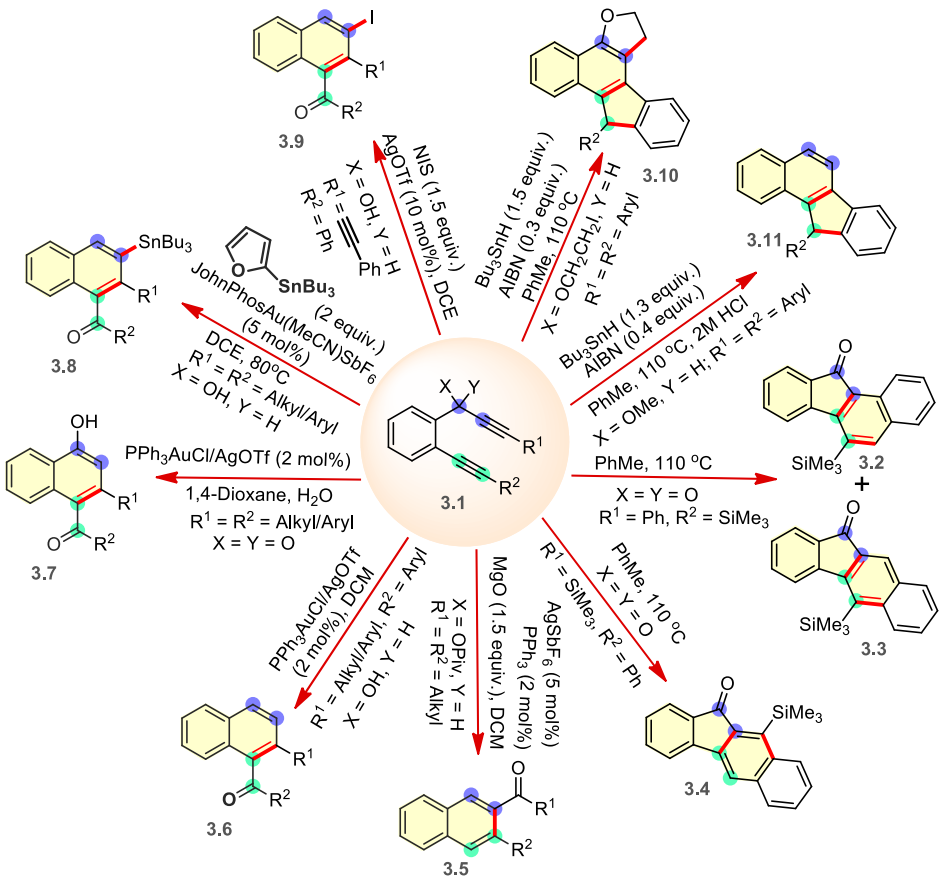
In 2001, Echavarren group[8d] have reported thermal cyclization of 1-[2-(trimethylsilylethynyl)-phenyl]-3-aryl propinones for the selective synthesis of benzo[*a*]- and benzo[*b*]fluorenones **3.2** and **3.3** (Scheme 3.1). The ring-closure was likely to proceed through a less stable diradical species followed by strained cyclic allene intermediate. As well, the benzo[*a*]fluorenone was expected to form *via* a new rearrangement.

In 2004, Saá and co-workers[8c] have reported a thermal intramolecular [4 + 2] cycloaddition of 1-[2-(arylethynyl)phenyl]-3-trimethylsilylpropynones leading to benzo[*b*]fluorenone derivative **3.4**. The reaction involves a similar kind of mechanism as reported by Echavarren.[8d]

In 2006, Toste group[5p] have developed silver-catalyzed synthesis of naphthyl ketones (**3.5**) from propargyl pivaloate. The reaction follows tandem [3,3]-sigmatropic rearrangement/formal Myers-Saito cyclization.

In 2007, Liu group[5o] have demonstrated a gold-catalyzed cyclization of 1,6-diyne-3-ols producing naphthyl ketone derivatives **3.6**. The cyclization proceeds via the formation of a OH-chelated Au(I)–π-alkyne species, which prompts the cyclization by an 6-*endo-dig* attack of the second alkyne moiety.

In 2008, Liu and co-workers[5n] have reported the synthesis of 4-hydroxyl-1-naphthyl ketones **3.7** from 1,6-diyn-3-ones catalyzed by PPh_3AuOTf. This hydrative carbocyclization involves a π-alkyne-assisted oxygen transfer to produce the key oxonium and gold-enolate intermediates.



Scheme 3.1. Cyclization cascades of 1,6-diyn-3-one/1,6-diyne skeletons leading to various PAHs.

Liu group[5l] in 2012, has depicted a gold-catalyzed domino cycloisomerization/stannylation cascade reaction of 1,6-diyne-4-en-3-ols. 2-Tributylstannylfuran has been used as the source of stannyl group. The mechanistic investigations revealed the involvement of a gold to tin transmetalation and destannylation reaction producing the stannyl naphthalenes **3.8**.

In 2014, Wu and co-workers[5h] have reported an electrophilic cyclization reaction of acyclic triynols with NIS, catalyzed by silver triflate. Multiple functional groups like a carbonyl, an alkyne, and a halogen, could be stiched at the C1, C2, and C3 positions of the product naphthalene **3.9**. Even more complex aromatic products could be generated from these trisubstituted naphthalenes.

In 2014, Alabugin group[8b] have developed an atom-economical approach to access functionalized benzo[*a*]fluorene analogues via intramolecular radical cascade cyclization of "skipped" oligoalkynes using Bu_3SnH (as reagent)/AIBN (as radical initiator) system. The reaction involves construction of three new rings through a sequential 5-*exo-dig* and 6-*exo-dig* ring closures of 1,6-diyenes followed by the attack of pendant arene ring and subsequent rearomatization.

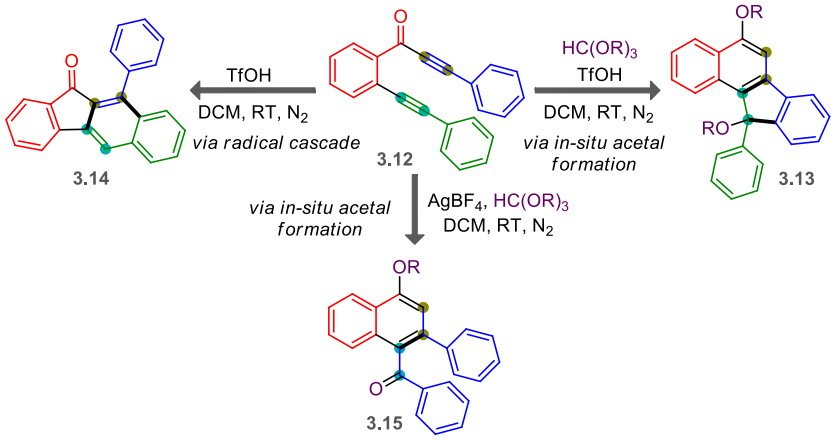
In 2015, the same group[8a] have reported the concept of traceless directing group in radical cascade to access the important class of fused helicenes from "skipped" oligoalkynes without the requirement of tethered initiator.

Therefore, it is evident that 1,6-diyne-3-ones/diynes are good starting material for the synthesis of diverse PAHs. Here we describe our contribution to make different PAHs using 1,6-diyne-3-ones.

3.2. Results & Discussion:

3.2.1. Present Work:

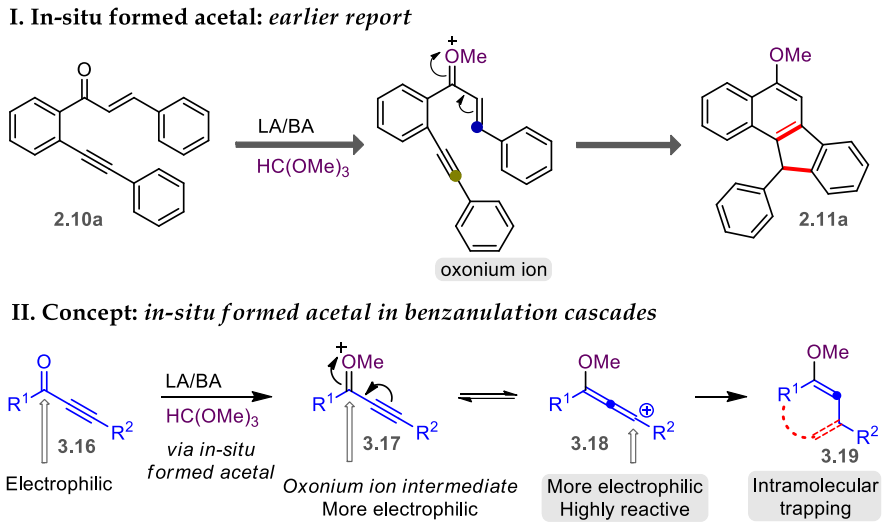
In this contest, we have developed a diversity-oriented synthetic approach towards benzo[*a*]fluorenes, benzo[*b*]fluorenones and naphthyl ketones from aryl fused 1,6-diyne-3-ones (Scheme 3.2). Benzo[*a*]fluorenes and benzo[*b*]fluorenones were obtained using TfOH promoter in the presence and absence of TMOF respectively. On the other hand, naphthyl ketones have been synthesized from the same aryl fused 1,6-diyn-3-one *via* a $AgBF_4$-catalyzed reaction in presence of trimethyl orthoformate. Formation of both benzo[*a*]fluorene and naphthyl ketone moieties are following *in situ* formed acetal pathway. Whereas benzo[*b*]fluorene derivative was achieved via intramolecular cyclization reaction of aryl fused 1,6-diyn-3-one mediated by triflic acid via a radical intermediate as supported by the EPR studies.



Scheme 3.2. Diversity-oriented cycloaromatizations of 1,6-diyn-3-one leading to different PAHs.

3.2.2. Concept:

Acetals are frequently used in organic transformations as protecting groups for aldehydes and ketones. Apart from this they have been used as substrates for developing some reactions. When acetals are formed *in situ*, they can be utilized in a diverse way to develop new reactions as shown in the Scheme 2.3. In the previous chapter, we had decribed the reactions of *o*-alkynyl aryl alkenones. We were curious about the reactivity of *o*-alkynyl aryl alkynones, as it is expected to generate an allenyl cation *via in situ* formed acetal as shown in Scheme 3.3(II). Intramolecular trapping of the intermediates would offer ways to make different PAHs.



Scheme 3.3. Conceptualisation of present work.

3.2.3. Optimization of Reaction Conditions for Benzo[*a*]fluorene, Benzo[*b*]fluorenone and Naphthyl Ketone Synthesis:

To check the viability of our hypothesis, we synthesized 3-phenyl-1-(2-(phenylethynyl)phenyl)prop-2-yn-1-one (**3.12a**) as a model 1,6-diyn-3-one precursor *via* Sonogashira coupling between 2-bromobenzaldehyde and phenylacetylene followed by phenylacetylide addition and oxidation. This substrate **3.12a** was treated with 1 equiv. of triflic acid (TfOH) in the presence of 2 equiv. of trimethyl orthoformate (TMOF) in dichloromethane (DCM) solvent at room temperature under nitrogen atmosphere. After 3 hours of stirring, it led to the formation of benzo[*a*]fluorene derivative **3.13a** in 31% isolated yield (entry 1, Table 3.1). The structure of **3.13a** was confirmed by nuclear magnetic resonance (NMR) spectroscopic (Figure 3.4) and high resolution mass spectroscopic (HRMS) analysis. In ^{1}H NMR spectrum, peaks at 4.16 and 2.90 ppm with integral value for 3H each and the corresponding ^{13}C signals at 55.8 and 51.2 ppm clearly indicated the presence of two methoxy group in the compound. Additional evidence of the structure comes up from the ^{13}C NMR signal at 157.7 ppm which corresponds to the *ipso* carbon linked to the methoxy group. Encouraged by this preliminary observation, we started further optimization to find out the best reaction condition for the formation of **3.13a**. When we took 4 equivalent of TMOF, we noticed an improved product yield (79%) of the desired product **3.13a** (entry 2, Table 3.1). The alkynone is quite stable in DCM as there was no reaction in the absence of TfOH and TMOF (entry 3, Table 3.1). Next, solvent screening was done using a variety of svolvents like hexafluoroisopropanol (HFIP), acetonitrile (CH_3CN), nitromethane (CH_3NO_2), dichloroethane (DCE), 1,4-dioxane, DCM:CH_3CN(1:1) mixture, DCM:HFIP(6:1) mixture, toluene and chloroform (entries 4-8 and 13-17, Table 3.1). We have not noted any improved product yield when TMOF was used as solvent (entry 10, Table 3.1). Though the solvent screening did not translate into improving the product yield of benzo[*a*]fluorene derivative **3.13a**, it opened up an opportunity to find a new reaction as a polar product was obtained in some of the reactions.

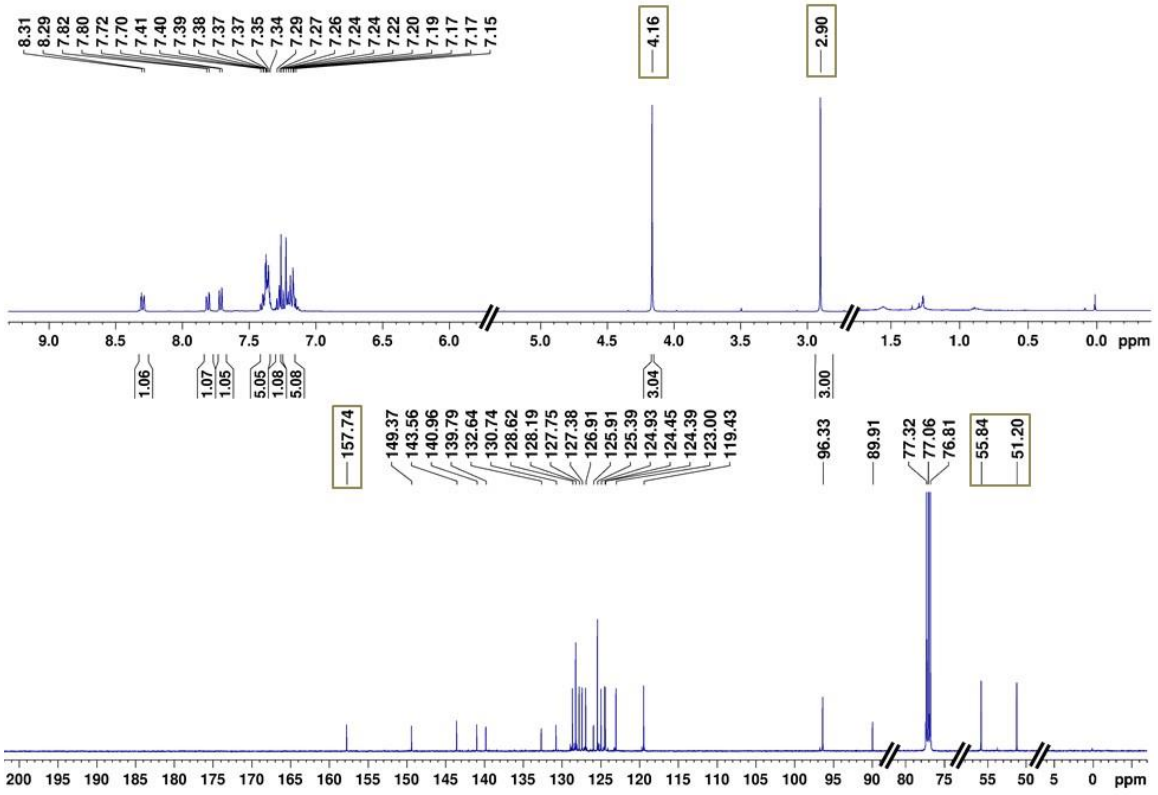


Figure 3.3. ^{1}H and ^{13}C NMR spectra of benzo[*a*]fluorene (**3.13a**).

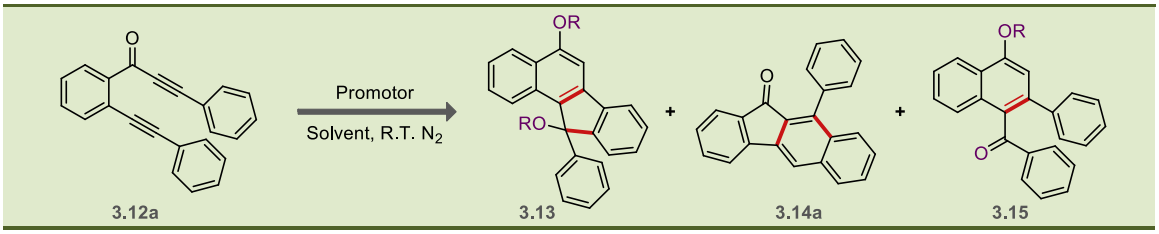
This product was found to be **3.14a** based on spectroscopic analysis. Triflamide (50 mol%) as a promoter was not effective as a mixture of products were obtained (entry 11, Table 3.1). Surprisingly, when the reaction was conducted using 1 equiv. of TfOH, 6 equiv. of TMOF in DCM solvent at room temperature, a maximum yield of 85% of benzo[*a*]fluorene derivative **3.13a** was obtained. The reaction was considerably sluggish if the amount of TfOH was decreased to 0.5 equiv. (entry 9, Table 3.1).

Next, we started to tune the reaction condition to find out the most apropriate condition for the synthesis of benzo[*b*]fluorenone **3.14a**. As there is no OMe in the structure of **3.14a**, we have performed a rection using 1 equiv. of TfOH alone in DCM solvent thinking that TMOF might not have any role in its formation. To our delight, benzo[*b*]fluorenone **3.14a** was obtained in 93% isolated yield within 1 hour (entry 18, Table 3.1). Here also, less amount of catalyst decreased the productivity (entry 19, Table 3.1).

We were curious to know the fate of the reaction in the presence of a Lewis acid. Pleasingly, the treatmentof the same aryl-fused 1,6-diyn-3-one derivative **3.12a** with TMOF in presence of 5 mol% $AgBF_4$ catalyst provided a different PAH, naphthyl ketone **3.15a**, in 70% isolated yield (entry 20, Table 3.1). When triethyl orthoformate (TEOF) was used in the place of trimethyl orthoformate, the yield of the product **3.15b** increased to 79% (entry 21, Table 3.1). Varying the amount of TEOF decreased the the product yield (entries 22-24, Table 3.1). The

reaction ended up with the formation of benzofluorenone derivative **3.14a** only in the absence of TEOF (entry 25, Table 3.1). Extensive screening of diverse Lewis acids indeed failed to render a better result (entries 26-38, Table 3.1). Molecular iodine and (+)-10-camphorsulfonic acid also promoted the formation of benzofluorenone derivative **3.14a** (entries 39-40, Table 3.1). Changing the solvent in the $AgBF_4$-catalyzed reaction was found to be less efficient for the formation of naphthyl ketone derivative **3.15b**. Thus, $AgBF_4$ catalyst in DCM was proved to be the efficient system for this transformation. To sum up, the conditions described in the entries 12, 18 and 21 were considered as the optimized reaction conditions for the synthesis of benzo[*a*]fluorene, benzo[*b*]fluorenone and napthyl ketone derivatives respectively.

Table 3.1. Optimization of reaction conditions for the synthesis of benzo[*a*]fluorene (**3.13a**), benzo[*b*]fluorenone (**3.14a**) and naphthyl ketone (**3.15a**).



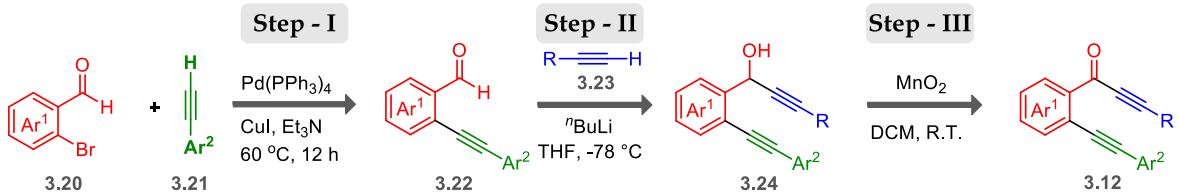
Entry	Solvent	Catalyst (equiv.)	$CH(OR)_3$ (equiv.)	Time (h)	Yield (%)		
					3.13a	3.14a	3.15a
1	DCM	TfOH (1)	TMOF (2)	3	31	-	-
2	DCM	TfOH (1)	TMOF (4)	2	79	-	-
3	DCM	-	-	24	-	-	-
4	HFIP	TfOH (1)	TMOF (4)	4	14	-	-
5	CH_3CN	TfOH (1)	TMOF (4)	4	26	19	-
6	CH_3NO_2	TfOH (1)	TMOF (4)	3	-	89	-
7	DCE	TfOH (1)	TMOF (4)	4	55	-	-
8	Dioxane	TfOH (1)	TMOF (4)	4	17	51	-
9	DCM	TfOH (0.5)	TMOF (6)	4	37	31	-
10	TMOF	TfOH (1)	-	5	30	-	-
11	DCM	Tf_2NH (0.5)	TMOF (4)	3	11	60	-
12	DCM	TfOH (1)	TMOF (6)	3	85	-	-
13	CH_3CN^a	TfOH (1)	TMOF (4)	2	-	90	-
14	DCM:CH_3CN (1:1)	TfOH (1)	TMOF (6)	2	77	17	-
15	DCM:HFIP (6:1)	TfOH (1)	TMOF (6)	4	17	-	-
16	Toluene	TfOH (1)	TMOF (6)	4	34	57	-
17	$CHCl_3$	TfOH (1)	TMOF (6)	4	9	-	-
18	DCM	TfOH (1)	-	1	-	93	-
19	DCM	TfOH (0.5)	-	4	-	76	-
20	DCM	$AgBF_4$ (0.05)	TMOF (1)	24	-	-	70

21	DCM	$AgBF_4$ (0.05)	TEOF (1)	24	-	-	79
22	DCM	$AgBF_4$ (0.05)	TEOF (2)	16	-	-	69
23	DCM	$AgBF_4$ (0.05)	TEOF (3)	24	-	-	22
24	DCM	$AgBF_4$ (0.05)	TEOF (0.5)	26	-	-	75
25	DCM	$AgBF_4$ (0.05)	-	24	-	48	-
26	DCM	AgOTf (0.05)	TEOF (1)	12	-	-	56
27	DCM	$Ag(NTf_2)$ (0.05)	TEOF (1)	11	-	-	68
28	DCM	$AgClO_4$ (0.05)	TEOF (1)	19	-	-	72
29	DCM	$AgSbF_6$ (0.05)	TEOF (1)	11	-	-	68
30	DCM	$Cu(OTf)_2$ (0.05)	TEOF (1)	24	-	-	34
31	DCM	$In(OTf)_3$ (0.05)	TEOF (1)	24	-	87	-
32	DCM	$Sn(OTf)_2$ (0.05)	TEOF (1)	24	-	88	-
33	DCM	$Sc(OTf)_3$ (0.05)	TEOF (1)	24	-	87	-
34	DCM	$BiBr_3$ (0.05)	TEOF (1)	24	-	79	-
35	DCM	$FeCl_3$ (0.05)	TEOF (1)	24	-	74	-
36	DCM	$AuCl_3$ (0.05)	TEOF (1)	24	-	88	-
37	DCM	PPh_3AuCl (0.05)	TEOF (1)	24	-	86	-
38	DCM	IprAuCl (0.05)	TEOF (1)	24	-	78	-
39	DCM	I_2 (0.05)	TEOF (1)	24	-	85	-
40	DCM	CSA (0.05)[b]	TEOF (1)	24	-	87	-
41	Dioxane	$AgBF_4$ (0.05)	TEOF (1)	24	-	22	15
42	CH_3NO_2	$AgBF_4$ (0.05)	TEOF (1)	24	-	79	-
43	DCE	$AgBF_4$ (0.05)	TEOF (1)	24	-	-	63
44	CH_3CN	$AgBF_4$ (0.05)	TEOF (1)	24	-	75	-

Reaction conditions: **3.12a** (0.1 mmol), Lewis/Brønsted acid and solvent (0.5 ml) at rt under N_2 atmosphere, unless otherwise stated. '-': No Reaction. [a]Reaction conducted at 60 °C. [b]10-(+) Camphor sulphonic acid

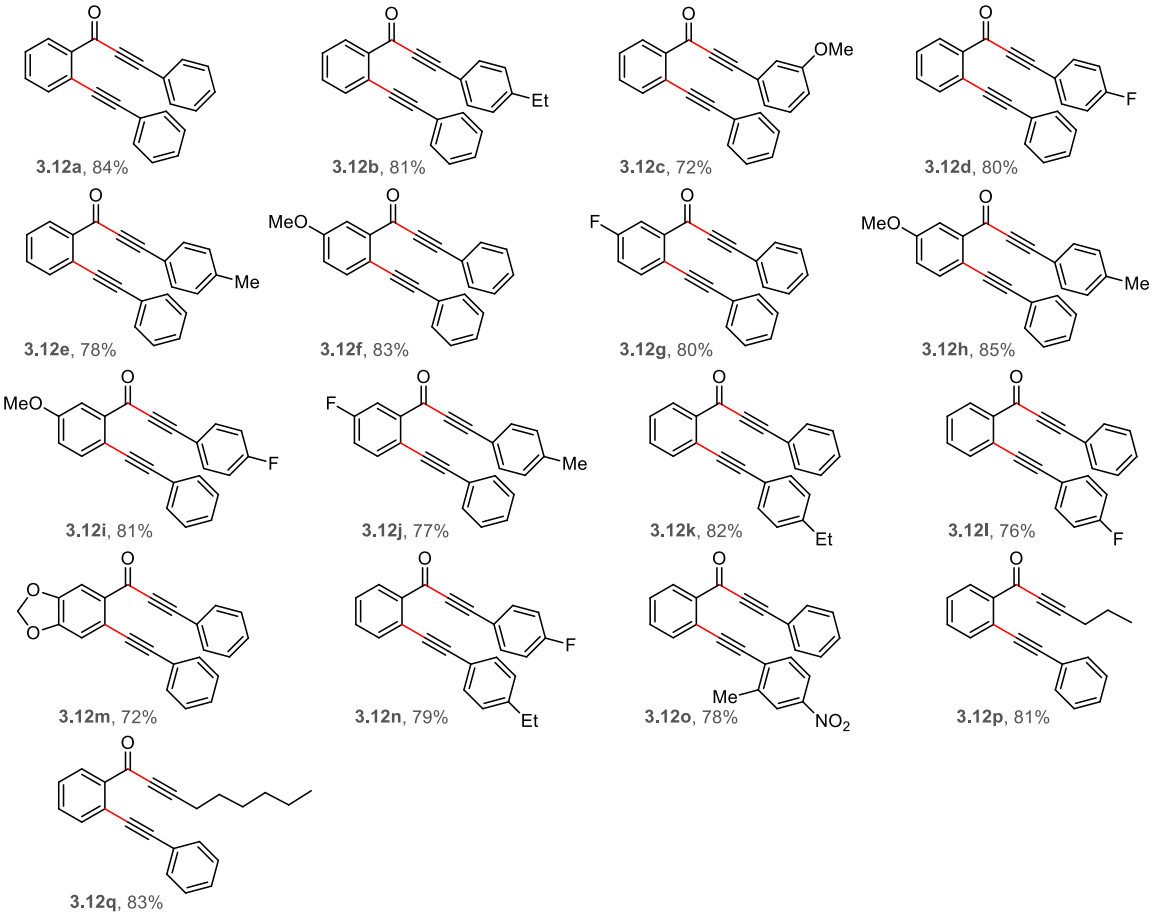
3.2.4. Preparation of 1,6-Diyn-3-one Precursors:

To check the generality of this methodology, a number of 1,6-diyn-3-one derivatives were synthesized using known literature reported procedures. Sonogashira coupling between 2'-bromobenzaldehyde and substituted phenylacetylene afforded the *o*-alkynylbenzaldehydes **3.22** (Scheme 3.4).[9a] Addition of alkynyl lithium generated under the reaction condition with **3.22** yielded 1,6-diyne-3-ols **3.24**.[10]



Scheme 3.4. Synthesis of 1,6-diyn-3-one derivatives.

Table 3.2. Structures of synthesized of 1,6-diyn-3-ones (**3.12**).

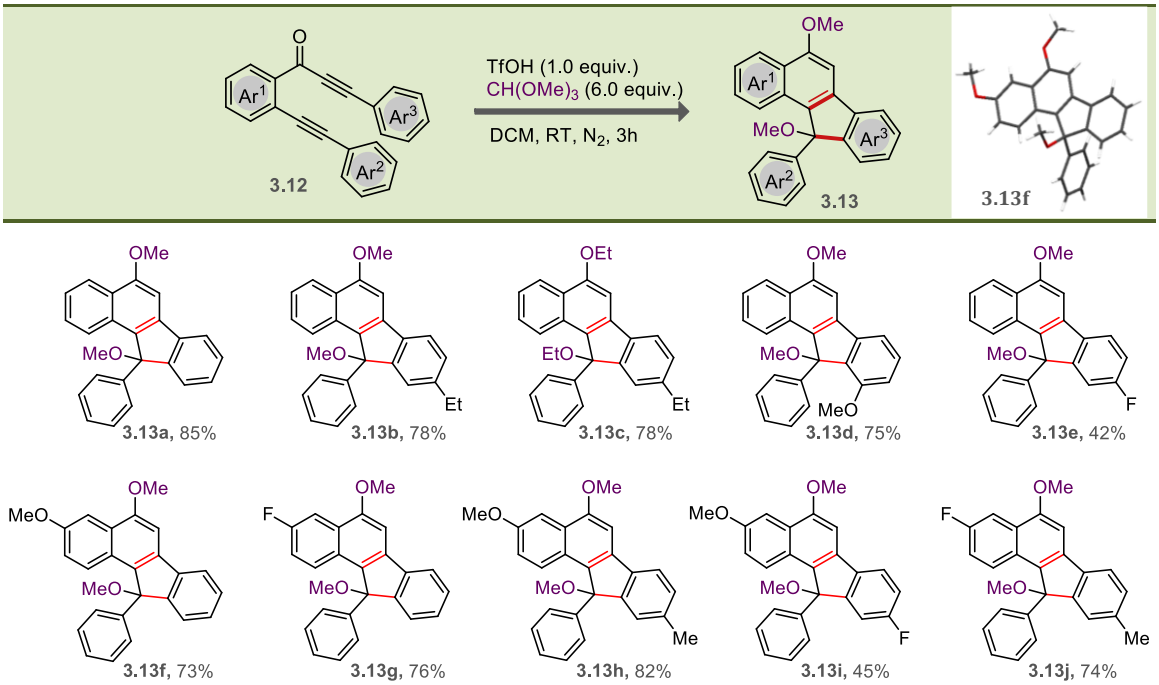


The 1,6-diyn-3-one derivatives **3.12** were obtained by MnO_2 oxidation of 1,6-diyne-3-ol **3.24**. The structure of the synthesized 1,6-diyn-3-one derivatives are presented in Table 3.2.

3.2.5. Substrate Scope for the Synthesis of Benzo[*a*]fluorene Derivatives:

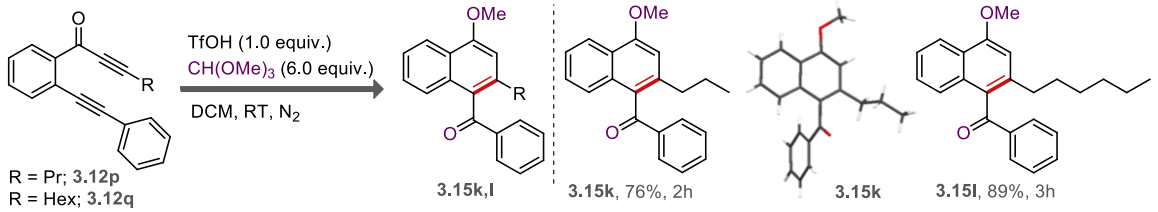
Using the optimized reaction conditions, we explored the scope of this methodology to synthesize a series of functionalized benzo[*a*]fluorene derivatives using diverse 1,6-diyn-3-ones (**3.12**). The results are depicted in Table 3.3. Substrates with different substituents tolerated well the optimized reaction condition and the corresponding products were formed with moderate to good yields (42-85%) in 3 hours (Table 3.3). There was not much of electronic and steric effects of substituents on the reaction outcome, except when fluorine was on Ar^3. It should be noted that fluorine in Ar^3 ring reduced the yields of the products (**3.13e** and **3.13i**). A fluorine substituent in an aryl ring is known to stabilize a cationic intermediate and facilitate the reaction. In the formation of products **3.13e** and **3.13i**, particularly during second cyclization , the carbon meta to fluoro substitution is involved. Thus less yields of **3.13e** and **3.13i** were noticed.

Table 3.3. TfOH-promoted synthesis of benzo[*a*]fluorene derivatives (**3.13**).



Reaction conditions: **3.12** (0.325 mmol), TfOH (1.0 equiv.), TMOF (6.0 equiv.) and DCM (1.5 ml) at rt (25 °C) under N_2 atmosphere, unless otherwise stated.

However, a fluoro substitution on the Ar^1 ring did not affect the yield of the corresponding products **3.13g** (76%) and **3.13j** (74%). While Ar^3 is replaced by an aliphatic substituent, it resulted in naphthyl ketones. Accordingly, products **3.15k** and **3.15l** were obtained from **3.12p** and **3.12q** (Scheme 3.5). This suggests that benzo[*a*]fluorene formation from **3.12** could have taken place via the initial formation of the naphthyl ketone. To evaluate this, the naphthyl ketone (**3.15a**) was treated with 6 equiv. of TMOF and 1 equiv. of TfOH expecting the formation of benzo[*a*]fluorene derivative **3.13a**. But, even after 24 hours, no product formation was observed and the starting material remained unreacted. So, it can be concluded that benzo[*a*]fluorene formation is not going via naphthyl ketone intermediate. The scalability of the reaction has been checked by performing a gram scale reaction using 1 g of **3.12a** which led to 911 mg of **3.13a** (79% yield).



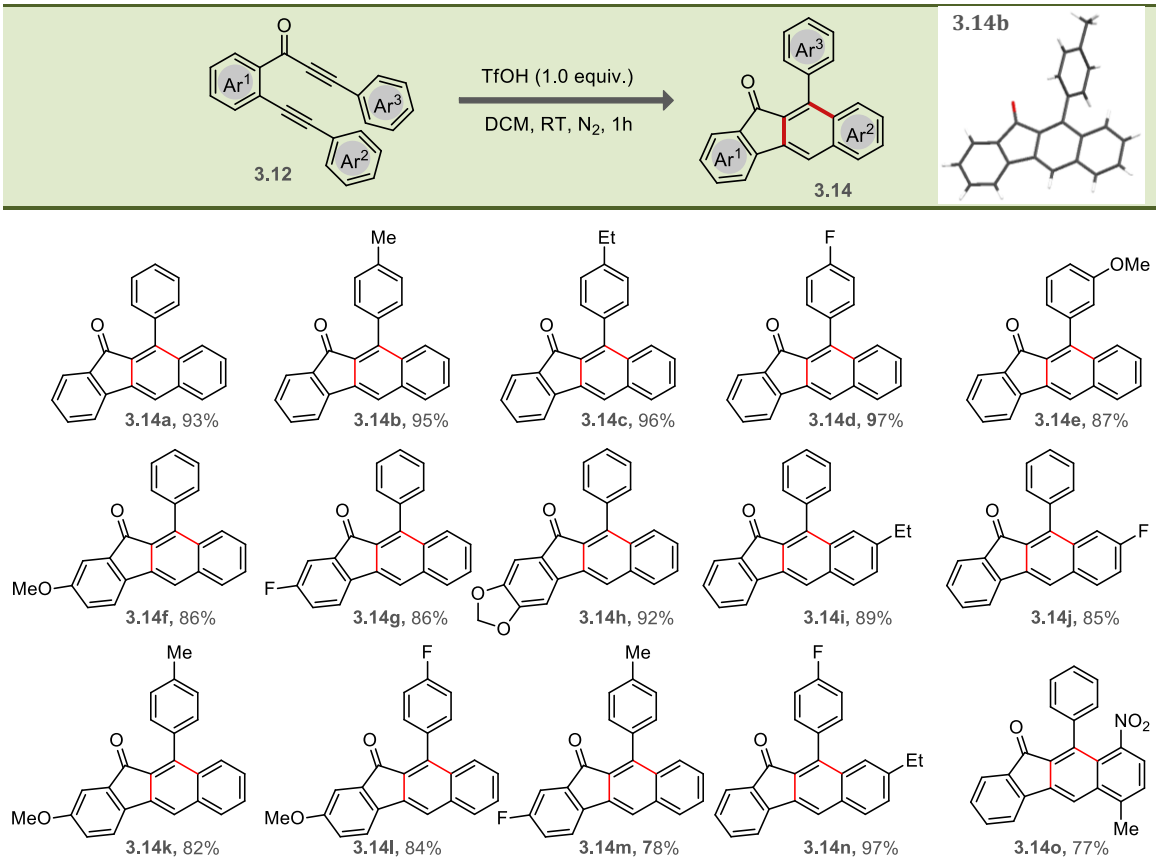
Scheme 3.5. Reaction of aryl fused 1,6-diyn-3-one having aliphatic chain.

So, the applicability and robustness of this transformation has been proved. All the prepared compounds were characterized by NMR, HRMS and FTIR studies. The structure of **3.13f** and **3.15k** were further re-confirmed by single crystal X-ray diffraction analysis (CCDC numbers: 1998442 (**3.13f**) and 1998445 (**3.15k**)).

3.2.6. Substrate Scope for the Synthesis of Benzo[*b*]fluorenone Derivatives:

The scope of benzo[*b*]fluorenone synthesis was also investigated under the optimized reaction conditions using a variety of 1,6-diyn-3-one substrates having different substituents with different electronic effects. The outcome is tabulated in Table 3.4. With regard to the present TfOH-promoted synthesis synthesis of benzo[*b*]fluorenones, it is worth mentioning that Saá and co-workers reported a mixture of two regioisomeric benzo[*b*]fluorenones in almost quantitative combined yield from diarylacetylenes.[8c] But, in our methodology, solely one isomer of benzo[*b*]fluorenone was obtained in excellent yield. No noteworthy electronic and steric effects were experienced in this reaction.

Table 3.4. TfOH-promoted synthesis of benzo[*b*]fluorenone derivatives (**3.14**)



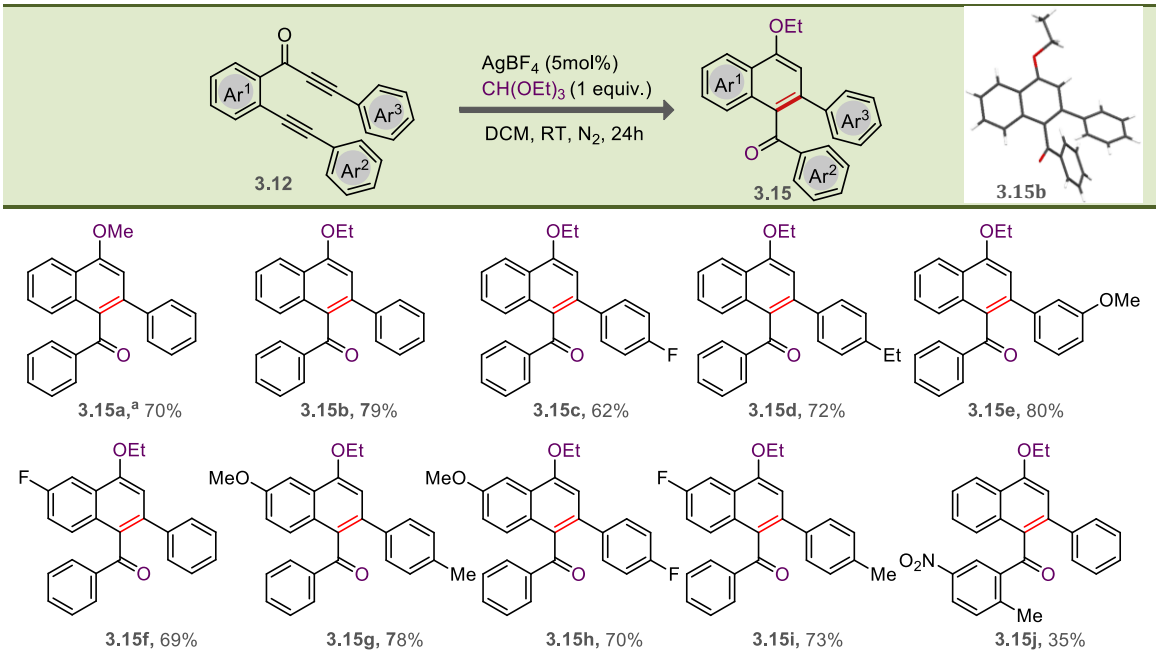
Reaction conditions: **3.12** (0.325 mmol), TfOH (1.0 equiv.) and DCM (1.5 ml) at rt (25 °C) under N_2 atmosphere, unless otherwise stated.

Exceptional yields were obtained for all the substrates studied. This reaction failed to produce the desired product when any of the benzene ring is replaced by an aliphatic group. Instead, complex mixture of products were obtained in the aliphatic group containing substrates. This reaction was also performed using 1 g of **3.12a** and pleasingly, 90% isolated yield (904 mg) of **3.14a** was obtained. All the prepared benzo[*b*]fluorenones were also characterized by NMR, HRMS, FTIR studies and the structure of **3.14b** was further confirmed by single crystal analysis (CCDC number 1998443).

3.2.7. Substrate Scope for the Synthesis of Naphthyl Ketone Derivatives:

Next, we explored the scope of naphthyl ketone synthesis using a number of aryl fused 1,6-diyn-3-one **3.12** under the optimized reaction conditions. The range of substituents consist of both electron-withdrawing and donating groups in all the three benzene rings. The reaction showed decent functional group compatibility for all types of substituents (62–80%) indicating the generality and robustness of this cyclization reaction. Following the same trend of the previous two transformations, this protocol also failed to produce the desired product when aliphatic group was present in the place of any of the benzene ring. The scalability of the reaction was checked by doing the reaction on 1 g of **3.12a** and the product **3.15b** was obtained in 72% yield (823 mg). All the naphthyl ketone derivatives prepared using this protocol were characterized by NMR, HRMS, FTIR studies and the structure of **3.15b** was further confirmed by single crystal X-ray diffration analysis (CCDC number 1998444).

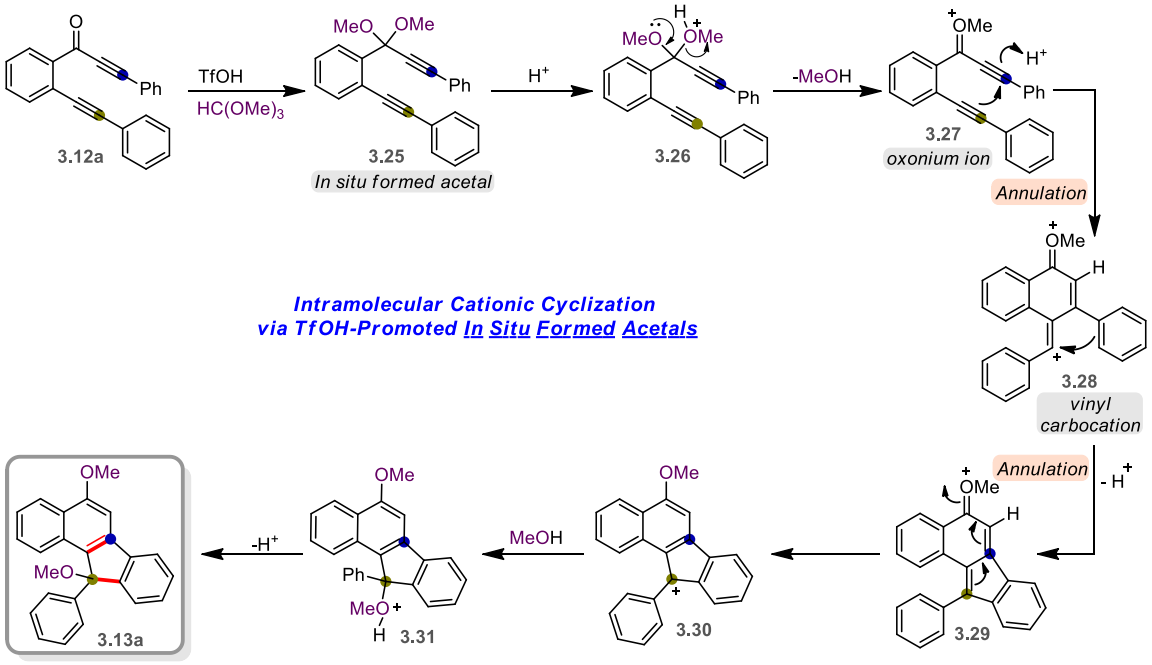
Table 3.5. $AgBF_4$-catalyzed synthesis of naphthyl ketone derivatives (**3.15**).



Reaction conditions: **3.12** (0.325 mmol), $AgBF_4$ (5 mol%), TEOF (1.0 equiv.) and DCM (1.5 ml) at rt (25 °C) under N_2 atmosphere, unless otherwise stated. [a]TMOF was used instead of TEOF

3.2.8. Mechanistic Insights for Benzo[*a*]fluorene, Benzo[*b*]fluorenone and Naphthyl Ketone Synthesis:

A plausible mechanistic pathway for the formation of benzo[*a*]fluorene (**3.13a**) from the starting material **3.12a** is illustrated in Scheme 3.6. In the presence of acid promoter and TMOF, the substrate **3.12a** is expected to generate the oxonium ion intermediate **3.27** via the formation of the acetal **3.25**. Next, an intramolecular cyclization of the alkyne happens on the proton activated alkyne as presented in intermediate **3.27**. This cyclization may be assisted by the electron-withdrawing nature of the oxocarbenium ion. Thus generated intermediate **3.28** will undergo aromatic electrophilic substitution on the vinyl carbocation to form **3.29**. Lastly benzo[*a*]fluorene derivative (**3.13a**) is formed by isomerization of intermediate **3.29** followed by quenching with methanol. When an aliphatic group is present at the β-carbon of the enynone, second cyclization is not possible due to the absence of aryl moiety and the reaction ended up with the formation of naphthyl ketone (Scheme 3.5).



Scheme 3.6. Plausible reaction mechanism for the formation of benzo[*a*]fluorenes (**3.13**).

Next, for understanding the reaction mechanism involved in the synthesis of benzo[*b*]fluorenone, EPR experiments were carried out on the reaction mixture at different time interval. The outcome of all the experiments remained same. An EPR signal with a G value of 2.0129 (Figure 3.4) was obtained. Moreover, upon addition of triflic acid to **3.12a**, the color of the reaction mass changed from pale yellow to greenish yellow instantly and lastly to dark yellow. The oxidation of the substrate to form radical intermediates may be promoted by the Brønsted acid.[12] Based on the outcome of EPR study and the previous reports,[4h,12] a plausible mechanistic path has been proposed as shown in Scheme 3.7. First, triflic acid can promote the cyclization of the aryl

fused 1,6-diyn-3-one **3.12a** producing the biradical intermediate **3.32**. This intermediate **3.32** undergoes a fast intramolecular radical coupling to form a strained cyclic allene intermediate **3.33**. The aromatic product **3.14a** could form from the strained allene intermediate **3.33** in the acidic medium.

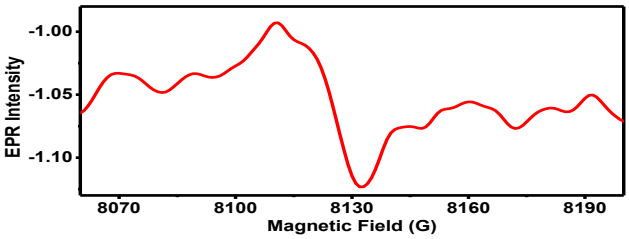
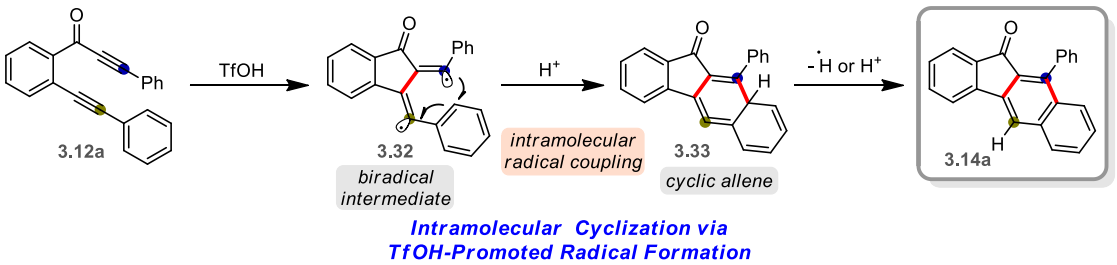
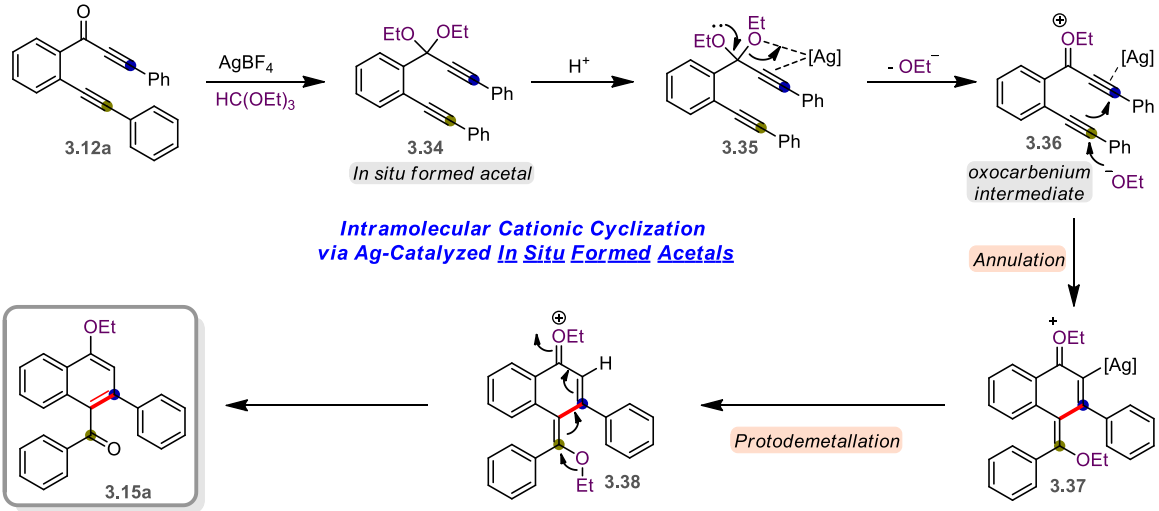


Figure 3.4. EPR study of crude reaction mixture for the preparation of **3.14a**.



Scheme 3.7. Plausible reaction mechanism for the formation of benzo[*b*]fluorenones (**3.14**).

Next, in a similar way, a mechanism for the formation of naphthyl ketone (**3.15a**) can be proposed as shown in Scheme 3.8. Acetal **3.34** will from *in situ* in the presence of TEOF and $AgBF_4$. Coordination of [Ag] catalyst to alkyne as well as acetal oxygen as shown in the intermediate **3.35** might assist the elimination of OEt^- to generate the oxocarbenium ion intermediate **3.36**. Next, attack of OEt^- on the alkyne and subsequent cyclization on the silver activated alkyne will form the intermediate **3.37**. This on protodemetallation would form intermediate **3.38** which on aromatization will lead to the naphthyl ketone product **3.15a**. It has to be noted that Yamamoto group reported a silver-catalyzed reaction of same title compounds with alcohols leading to the formation of 1-allenylisochromes through a different mechanistic pathway.[13]

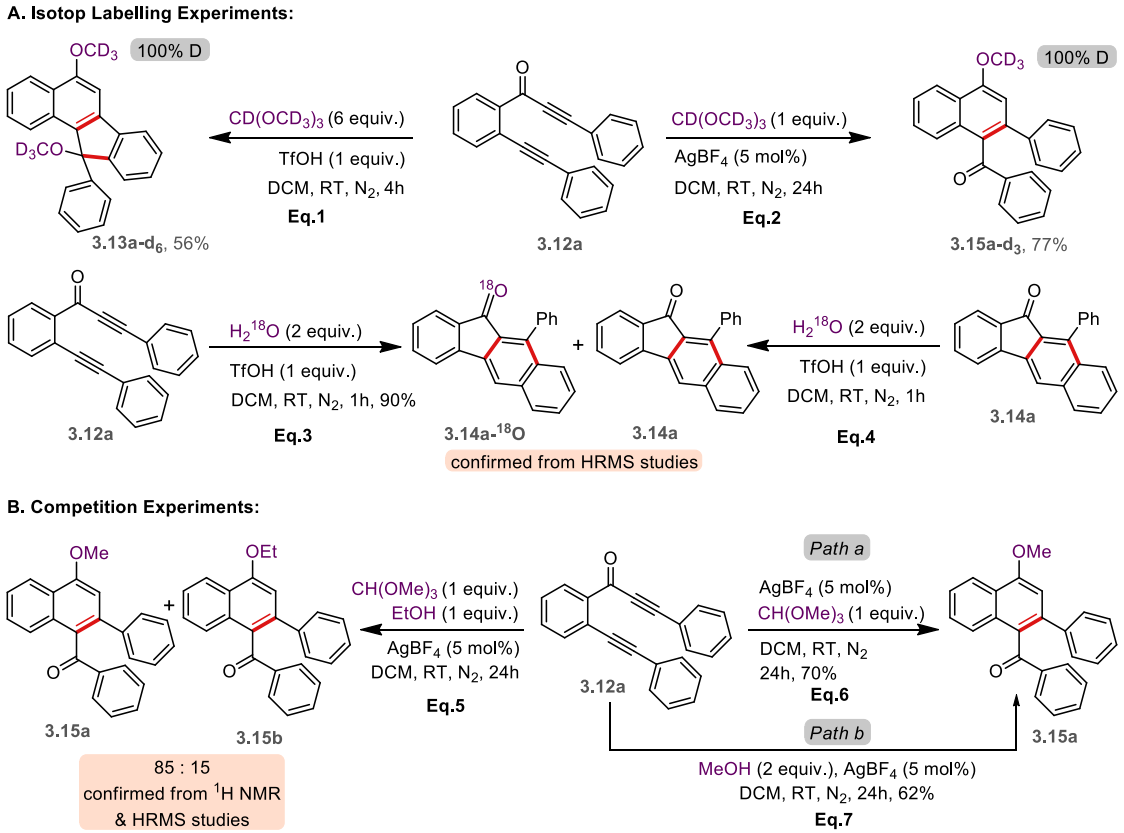


Scheme 3.8. Plausible reaction mechanism for the formtion of naphthyl ketones (**3.15**).

But, the spectral characteristics of the napthyl ketone derivative **3.15a** obtained in our reaction perfectly matched with that of the product reported by them. This indicates that naphthyl ketone is formed in their study as well, at least with this particular substrate.

3.2.9. Control Experiments:

Few control experiments have been carried out to support the proposed mechanisms involved in the synthesis of benzo[*a*]fluorene, benzo[*b*]fluorenone and naphthyl ketone derivatives. Initially, following a literature report[14] a fully deuterated trimethyl orthoformate ($DC(OCD_3)_3$) was prepared. Then, aryl fused 1,6-diyn-3-one (**3.12**) was treated under the standard reaction conditions employed for the synthesis of benzo[*a*]fluorene **3.13a** and naphthyl ketone **3.15a** using $DC(OCD_3)_3$ (Scheme 3.9A). Incorporation of $-OCD_3$ in **3.13a-d$_6$** and **3.15a-d$_3$** were confirmed from ^{1}H NMR spectrum of the respective products (Figures 3.5 and 3.6). The singlets at 4.14 and 2.90 ppm corresponding to the two $-OCH_3$ protons of **3.13a** disappeared in the ^{1}H NMR spectra of **3.13a-d$_6$** and the singlet at 4.02 ppm corresponding to the $-OCH_3$ protons of **3.15a** disappeared in the ^{1}H NMR spectra of **3.15a-d$_3$**. Then, all the three reactions of **3.12a** were carried out in presence of $H_2{}^{18}O$. But no ^{18}O labelling was noticed in benzo[*a*]fluorene **3.13a** and naphthyl ketone **3.15a**. Pleasingly, we got benzo[*b*]fluorenone **3.14a** with ^{18}O incorporation which was confirmed from HRMS analysis.



Scheme 3.9. Isotop labelling experiments and comptition experiments.

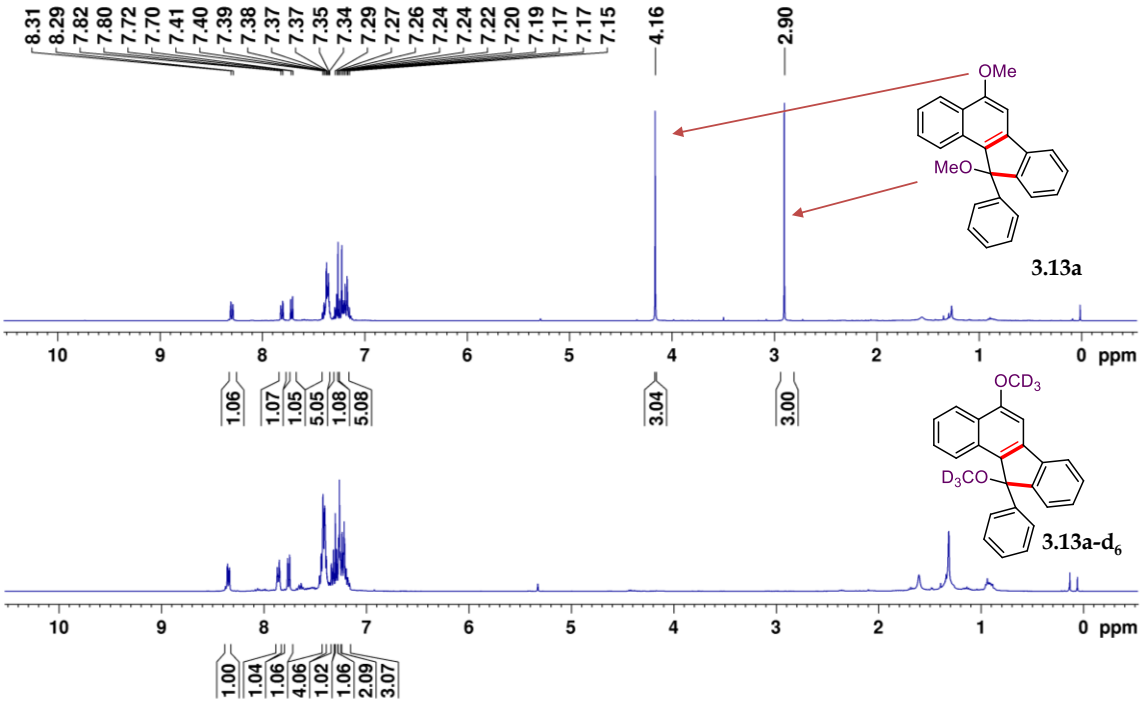


Figure 3.5. Comparison of ^{1}H NMR spectra of **3.13a** and **3.13a-d$_6$**.

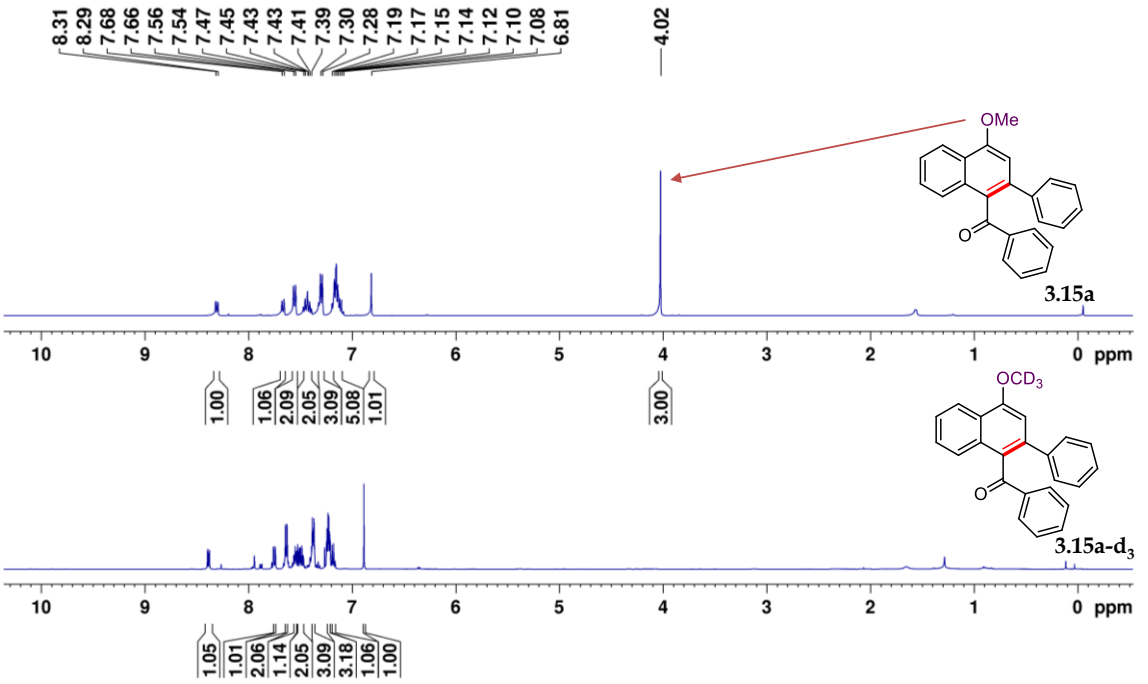


Figure 3.6. Comparison of ^{1}H NMR spectra of **3.15a** and **3.15a-d$_3$**.

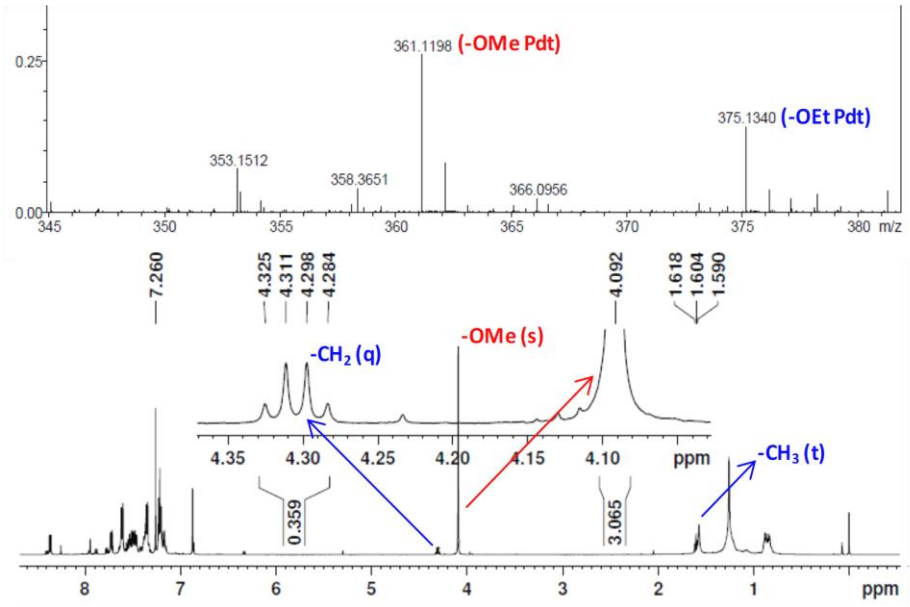
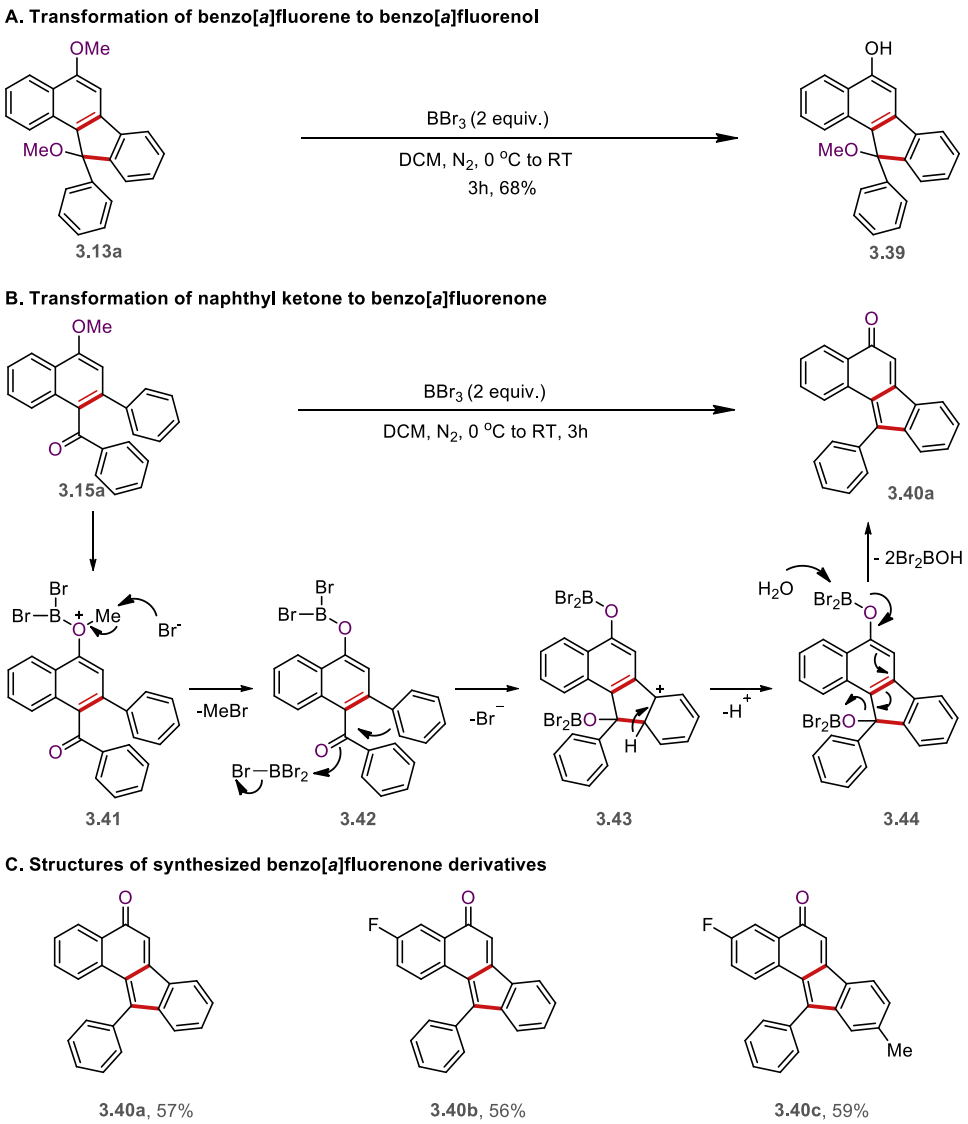


Figure 3.7. HRMS and ^{1}H NMR spectrum of crude product of **eq. 5**.

Benzo[*b*]fluorenone **3.14a** was seperately reacted with 1 equiv. of TfOH in presence of 2 equiv. of $H_2{}^{18}O$ in DCM solvent to know whether the incorporation of ^{18}O happened during the reaction or after the product formation. HRMS spectra of this reaction mixture is same as the earlier. Hence the ^{18}O incorporation in **3.14a** is happening through hydration of the ketone in **3.14a**. Thus, the isotop labelling experiments support the proposed mechanisms. Then a competition experiment was performed to prove whether naphthyl ketone synthesis is following in situ acetal formation path or not. First, a reaction was performed under the optimized condition where 2 equivalents of MeOH was used instead of TMOF. The naphthyl ketone was isolated in 62% yield only (Scheme 3.9B). Another reaction was carried out in the presence of 1 equiv. of TMOF and 1 equiv. of EtOH keeping other parameters unchanged. Both the OMe and OEt incorporated naphthyl ketone (**3.15a** and **3.15b**) derivatives involving TMOF and EtOH respectively were formed. Interestingly, the ratio of OMe and OEt incorporated napthyl ketones (**3.15a** and **3.15b**) was found to be 85:15 (Scheme 3.9B) as discerned from the ^{1}H NMR spectrum of the product mixture (Figure 3.7). This proves clearly that the reaction occures *via* the formation of acetal as a ketone function would form acetal readily with trimethyl orthoformate than with an alcohol. With these findings, it can be concluded that the reaction is going *via in situ* formed acetal only.

3.2.10. Late-stage Transformations of Benzo[*a*]fluorene and Naphthyl Ketone:

Then, a few interesting transformations of the synthesized compounds were achieved. When benzo[*a*]fluorene **3.13a** was treated with BBr_3, it produced the analogous benzo[*a*]fluorenol **3.39** without affecting the benzylic OMe group (Scheme 3.10A). Interestingly, the naphthyl ketone derivative **3.15a** formed a new class of benzo[*a*]fluorenone **3.40a** upon treatment with BBr_3. We have also studied the scope of this conversion with a few more substrates and the product structures are presented in Scheme 3.10C.

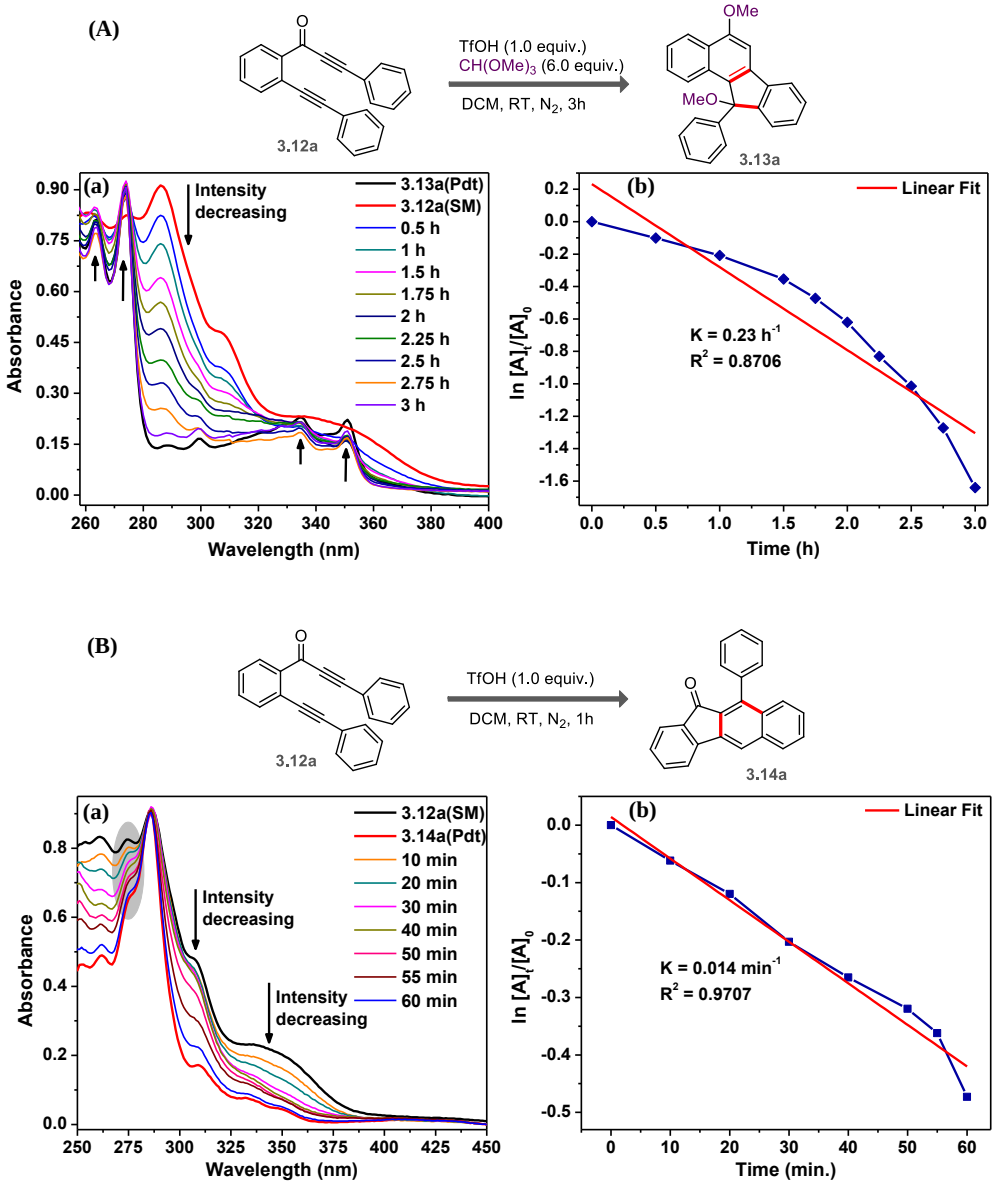


Scheme 3.10. Transformations of the synthesized benzo[*a*]fluorene and naphthyl ketone.

We have also shown a plausible mechanism for the formation of benzo[*a*]fluorenone **3.40a** in Scheme 3.10B. Two equivalents of BBr_3 are required for this transformation. First equivalent BBr_3 reacts with the OMe group to form the intermediate **3.41**. The generated Br^- will attack methyl and the intermediate **3.42** will be generated. Activation at the carbonyl by another molecule of BBr_3 effects the electrophilic cyclization leading to the intermediate **3.43**. Finally, aqueous work-up will produce the benzo[*a*]fluorenone with the removal of two molecules of boronic acid. The structures of all the as prepared compounds were confirmed by NMR, IR and high resolution mass spectroscopic analysis.

3.2.11. Reaction Kinetics by UV-Vis Experiments for the Formation of Benzo[*a*]fluorene, Benzo[*b*]fluorenone and Naphthyl Ketone:

As the starting material and all the three products are aromatic with characteristic absorption maxima, all the transformations have been monitored by UV-Visible spectroscopy to get more insight into the reactions. For every reaction, the UV spectra were recorded at regular intervals of time. Absorbance vs wavelength plot clearly indicated the gradual decrease in the intensity of starting material's absorbance with a smooth increase in the intensity of the product's absorbance. Plot of ln $[A]_t/[A]_o$ for the starting material vs time resulted a linear fit in each case suggesting a first order reaction kinetics (Figure 3.8).



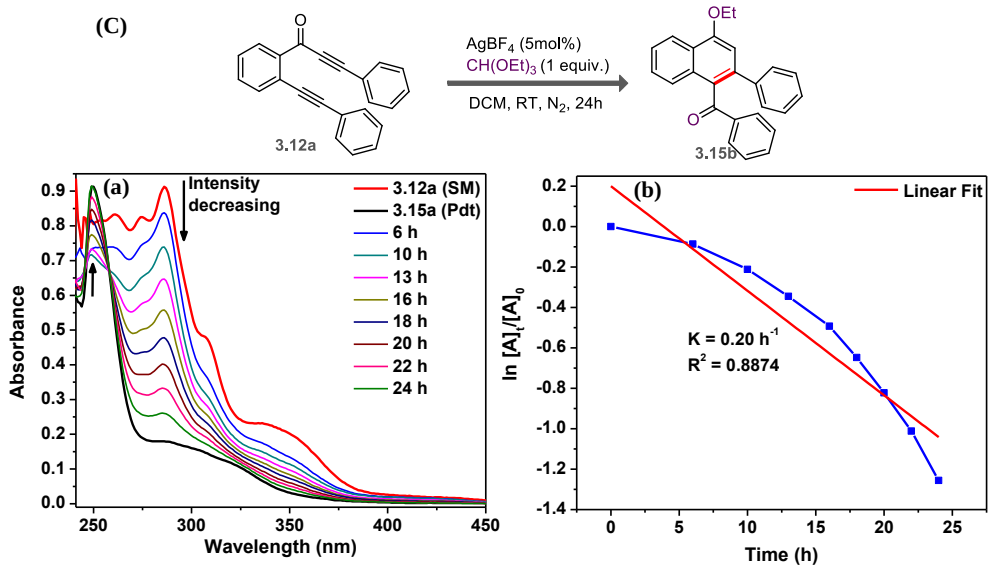


Figure 3.8. (a) Reaction profile (b) Reaction kinetics for the formation of benzo[*a*]fluorene, benzo[*b*]fluorenone and naphthyl ketone respectively in (A), (B) and (C).

3.3. Conclusions:

In conclusion, we have demonstrated synthetic methods for the construction of three polyaromatic hydrocarbons such as benzo[*a*]fluorenes, benzo[*b*]fluorenones and naphthyl ketones from aryl-fused 1,6-diyn-3-ones. In situ acetal formation using trialkyl orthoformate changes the reactivity of the title substrate under different Lewis or Brønsted acid conditions. Further, it has been shown that a different benzo[*a*]fluorenone derivative can be synthesized from the 4-methoxy napthyl ketones. The salient features of the work are presented hereafter.

- The methodology is operationally simple, high yielding and has diverse substrate scope.
- This method is more general and regeospecific for the synthesis of benzo[*b*]fluorenone derivatives.
- The synthesized benzo[*a*]fluorenes, benzo[*b*]fluorenones and naphthyl ketones have the potential to find new applications in the field of material and medicinal chemistry.
- 4-Methoxy napthyl ketones can be converted to a different benzo[*a*]fluorenone derivative.

3.4. Experimental Section:

3.4.1. General Experimental Informations:

All the reactions were performed under nitrogen atmosphere (unless otherwise stated) with oven-dried glasswares. Silica gel plates 60 F_{254} were used for thin layer chromatography (TLC) purpose and compounds were visualized by using UV light and/or by treatment with Seebach solution (phosphomolibdic acid (2.5 g), $Ce(SO_4)_2$ (1 g), Conc. H_2SO_4 (6 mL), H_2O (94 mL) followed by heating. Column chromatography was performed on silica gel (100-200 mesh) using ethyl acetate and hexanes mixture as eluent. ^1H, ^{13}C and ^{19}F spectra were recorded on a 400 MHz

or 500 MHz spectrometers. IR spectra were recorded on a FT-IR spectrometer and are reported in cm^{-1}. High-resolution mass spectra (HRMS) were recorded using using ESI-Q-TOF technique. Melting points were determined by using a melting range apparatus and were uncorrected. X-ray data were collected at 293 K on a diffractometer with dual source. Mo-Kα (λ = 0.71073 Å) radiation is used to collect the X-ray reflections of the crystal. All UV-vis absorption spectra were recorded on a UV-Vis spectrophotometer. UV-Vis Spectra were recorded with a slit width of 1 nm.

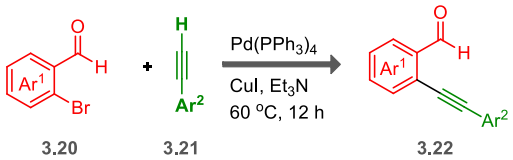
3.4.2. Materials:

Unless otherwise noted, all the reagents were obtained commercially and used without purification. Dichloromethane (DCM), 1,2-dichloroethane (DCE) and chloroform were distilled over CaH_2. THF was dried over sodium and freshly distilled before use. Trimethyl orthoformate, triethyl orthoformate, triflic acid and hexafluoro isopropanol (HFIP) were purchased from commercially available source, and used as it is. All aryl-fused 1,6-diyn-3-ones were prepared by following known literature procedures.

3.4.3. Synthesis and Characterization of Diynone Derivatives (3.12):

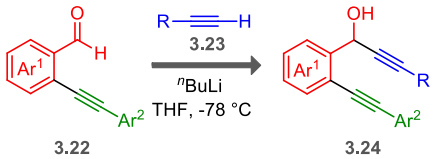
3.4.3.1. General Synthetic Procedure for the Preparation of Aryl-Fused 1,6-Diyn-3-One Derivatives (3.12):

2′-Bromobenzaldehyde derivative **3.20** (1.0 equiv.), $Pd(PPh_3)_2Cl_2$ (2 mol%) and CuI (4 mol%) were dissolved in dry THF:Et_3N (1:1) in a round bottom flask under nitrogen atmosphere at room temperature. After 5 minutes of stirring, the corresponding terminal alkyne **3.21** (1.2 equiv.) was added and the reaction mixture was refluxed at 60 °C using oil bath. After the completion of the reaction as indicated by TLC, the reaction mixture was filtered through celite and the solvents were evaporated under reduced pressure. Finally, the crude product was purified by column chromatography (silica gel, hexanes/EtOAc) to get pure 2-(arylethynyl)benzaldehyde derivatives **3.22**.[9a]



Scheme 3.11. Preparation of 2-(arylethynyl)benzaldehyde from 2-bromobenzaldehyde.

To a solution of alkyne **3.23** (1.2 equiv.) in dry THF at –78 °C, *n*-BuLi (2.5 M in hexanes, 1.2 equiv.) was added slowly and stirred for 45 mins at –78 °C and then a solution of *o*-alkynylaldehyde **3.22** (1 equiv.) in THF was added slowly. The resulting mixture was allowed to stirr for 2h at room temperature. After completion of the reaction as mentioned by TLC, the reaction mixture was quenched by aqueous NH_4Cl solution and the organic layer was extracted with EtOAc and dried over anhydrous Na_2SO_4. The organic layer was concentrated under reduced pressure and it was directly used for further reaction.[10]



Scheme 3.12. Preparation of aryl-fused 1,6-diyn-3-ols.

MnO_2 (15 equiv.) was added in portions to a solution of the alcohol derivative **3.24** in DCM and stirred at room temperature. After completion of the reaction as indicated by TLC, the reaction mixture was filtered through celite and concentrated under reduced pressure. The residue was purified by column chromatography to yield the corresponding 1,6-diyn-3-ones **3.12**.

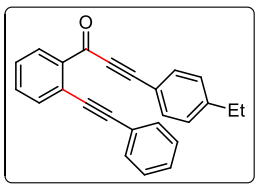


Scheme 3.13. Preparation of aryl-fused 1,6-diyn-3-ones.

3.4.3.2. Analytical Data of Aryl-Fused 1,6-Diyn-3-One Derivatives (3.12):

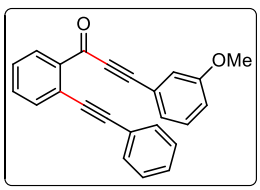
The aryl-fused 1,6-diyn-3-ones **3.12a**, **3.12d**, **3.12e**, **3.12g**, **3.12l**, **3.12p** are reported in literature and the analytical data of the synthesized compounds are in well accordance with that of the literature data. [5n,10]

3-(4-Ethylphenyl)-1-(2-(phenylethynyl)phenyl)prop-2-yn-1-one (3.12b, Table 3.2):



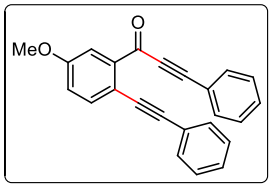
Yellow gummy (yield = 81%); R_f value = 0.44 in 5% EtOAc/hexanes; ^1H NMR (400 MHz, $CDCl_3$): δ 8.23 (d, *J* = 6.9 Hz, 1H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.64-7.60 (m, 2H), 7.56 (d, *J* = 8.2 Hz, 3H), 7.48 (t, *J* = 7.6 Hz, 1H), 7.35-7.32 (m, 3H), 7.19 (d, *J* = 8.0 Hz, 2H), 2.67 (q, *J* = 7.6 Hz, 2H), 1.25 (t, *J* = 7.6 Hz, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 177.5, 147.6, 138.4, 134.2, 133.2, 132.3, 131.9, 131.5, 128.5, 128.2, 128.1, 127.9, 123.1, 122.9, 117.2, 95.4, 94.0, 88.3, 88.0, 28.9, 15.1; IR (KBr, cm^{-1}): υ 2929, 1697, 1598, 1307, 1188, 760, 726, 598; HRMS: m/z $[M + H]^+$ Calcd for $C_{25}H_{19}O$: 335.1430; found: 335.1430.

3-(3-Methoxyphenyl)-1-(2-(phenylethynyl)phenyl)prop-2-yn-1-one (3.12c, Table 3.2):



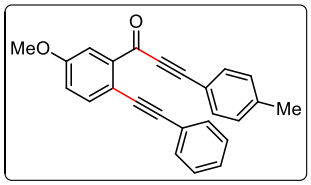
Yellow gummy (yield = 402 mg, 72%); R_f = 0.31 in 10% EtOAc/hexanes; ^1H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, *J* = 7.7 Hz, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.59-7.51 (m, 3H), 7.47-7.42 (m, 1H), 7.30 (s, 3H), 7.26-7.20 (m, 2H), 7.10 (s, 1H), 6.96 (d, *J* = 7.7 Hz, 1H), 3.71 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 177.5, 159.3, 138.2, 134.3, 132.5, 131.9, 131.5, 129.6, 128.6, 128.2, 128.0, 125.6, 123.1, 123.0, 121.0, 117.6, 117.3, 95.5, 93.3, 88.2, 87.8, 55.2; IR (KBr, cm^{-1}): υ 2995, 1703, 1580, 1463, 1245, 1032, 756, 698, 529; HRMS: m/z $[M + H]^+$ Calcd for $C_{24}H_{17}O_2$: 337.1223; found: 337.1229.

1-(5-Methoxy-2-(phenylethynyl)phenyl)-3-phenylprop-2-yn-1-one (3.12f, Table 3.2):



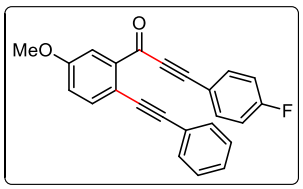
Yellow gummy (yield = 83%); R_f value = 0.28 in 10% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, *J* = 2.7 Hz, 1H), 7.63 (d, *J* = 8.2 Hz, 2H), 7.61 (s, 1H), 7.56-7.53 (m, 2H), 7.45 (t, *J* = 7.4 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.31-7.28 (m, 3H), 7.12 (dd, *J* = 8.6, 2.8 Hz, 1H), 3.94 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 177.6, 159.2, 139.7, 135.7, 133.2, 131.7, 130.8, 128.6, 128.3, 128.2, 123.4, 120.2, 118.9, 115.9, 115.4, 94.0, 93.8, 88.2, 88.0, 55.7; IR (KBr, cm^{-1}): υ 2995, 1699, 1607, 1484, 1275, 1029, 747, 700, 549; HRMS: m/z [M + H]$^+$ Calcd for $C_{24}H_{17}O_2$: 337.1223; found: 337.1226.

1-(5-Methoxy-2-(phenylethynyl)phenyl)-3-(*p*-tolyl)prop-2-yn-1-one (3.12h, Table 3.2):



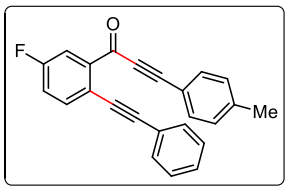
Yellow gummy (yield = 85%); R_f value = 0.47 in 5% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70-7.48 (m, 6H), 7.31 (s, 3H), 7.18-7.10 (m, 3H), 3.94 (s, 3H), 2.40 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 177.5, 159.2, 141.5, 139.9, 135.7, 133.2, 131.7, 129.4, 128.2, 123.5, 118.7, 117.1, 115.9, 115.3, 94.5, 93.9, 88.2, 88.1, 85.6; IR (KBr, cm^{-1}): υ 3006, 1632, 1554, 1292, 1163, 1003, 756, 692; HRMS: m/z [M + H]$^+$ Calcd for $C_{25}H_{19}O_2$: 351.1380; found: 351.1379.

3-(4-Fluorophenyl)-1-(5-methoxy-2-(phenylethynyl)phenyl)prop-2-yn-1-one (3.12i, Table 3.2):



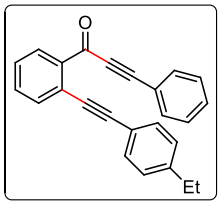
Yellow gummy (yield = 81%); R_f value = 0.50 in 10% EtOAc/hexanes; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63 (d, *J* = 2.7 Hz, 1H), 7.62-7.55 (m, 3H), 7.54-7.51 (m, 2H), 7.30-7.26 (m, 3H), 7.09 (d, *J* = 8.6 Hz, 1H), 7.01 (t, *J* = 8.5 Hz, 2H), 3.89 (s, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$): δ 177.3, 163.9 (d, *J* = 253.7 Hz), 159.2, 139.7, 135.7, 135.4 (d, *J* = 8.9 Hz), 131.6, 128.2 (d, *J* = 6.9 Hz), 123.4, 118.8, 116.3 (d, *J* = 3.5 Hz), 116.1, 115.9, 115.7, 115.4, 94.1, 92.7, 88.2, 88.0, 55.6; IR (KBr, cm^{-1}): υ 2835, 1649, 1594, 1500, 1191, 1005, 831, 745, 522; HRMS: m/z [M + H]$^+$ Calcd for $C_{24}H_{16}O_2F$: 355.1129; found: 355.1130.

1-(5-Fluoro-2-(phenylethynyl)phenyl)-3-(*p*-tolyl)prop-2-yn-1-one (3.12j, Table 3.2):



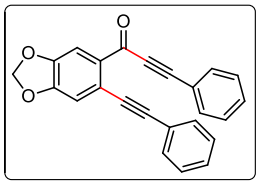
Yellow gummy (yield = 77%); R_f value = 0.58 in 10% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, *J* = 8.8 Hz, 1H), 7.67-7.57 (m, 3H), 7.49 (d, *J* = 7.8 Hz, 2H), 7.32 (s, 3H), 7.26-7.21 (m, 1H), 7.13 (d, *J* = 7.7 Hz, 2H), 2.34 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 175.9, 161.5 (d, *J* = 251.7 Hz), 141.8, 140.1 (d, *J* = 6.4 Hz), 136.2 (d, *J* = 7.5 Hz), 133.2, 131.8, 129.4, 128.6, 128.3, 123.0, 119.8 (d, *J* = 22.0 Hz), 119.1, 118.0 (d, *J* = 23.7 Hz), 116.7, 95.2, 94.8, 87.7, 87.3, 21.7; IR (KBr, cm^{-1}): υ 2919, 1706, 1604, 1478, 1262, 828, 753, 585; HRMS: m/z [M + H]$^+$ Calcd for $C_{24}H_{16}OF$: 339.1180; found: 339.1185.

1-(2-((4-Ethylphenyl)ethynyl)phenyl)-3-phenylprop-2-yn-1-one (3.12k, Table 3.2):



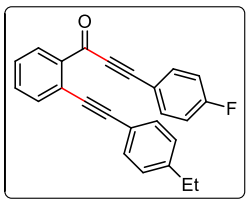
Yellow gummy (yield = 82%); R_f value = 0.47 in 10% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88-7.78 (m, 1H), 7.73 (d, *J* = 6.8 Hz, 1H), 7.67-7.54 (m, 5H), 7.53-7.40 (m, 4H), 7.38-7.17 (m, 2H), 2.69 (q, *J* = 4.1 Hz, 2H), 1.26 (t, *J* = 6.5 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 177.6, 147.6, 138.3, 134.3, 133.2, 132.4, 131.9, 131.5, 128.5, 128.2, 128.15, 127.9, 123.1, 122.9, 117.2, 95.3, 94.1, 88.3, 88.0, 29.0, 15.1; IR (KBr, cm^{-1}): υ 2961, 1701, 1600, 1468, 1075, 759, 724, 601; HRMS: m/z [M + H]$^+$ Calcd for $C_{25}H_{19}O$: 335.1430; found: 335.1436.

3-Phenyl-1-(6-(phenylethynyl)benzo[*d*][1,3]dioxol-5-yl)prop-2-yn-1-one (3.12m, Table 3.2):



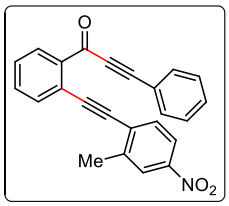
Yellow gummy (yield = 72%); R_f value = 0.31 in 10% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 (s, 1H), 7.91 (d, *J* = 7.0 Hz, 1H), 7.64-7.60 (m, 2H), 7.54 (s, 1H), 7.45-7.38 (m, 4H), 7.16 (s, 1H), 6.10 (d, *J* = 12.2 Hz, 1H), 5.97 (s, 2H), 5.71 (s, 1H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 177.6, 164.0, 161.5, 138.3, 134.2, 133.9, 133.1, 132.6, 131.7, 130.8, 128.6, 128.1, 122.9, 120.2, 119.3, 115.7, 115.5, 94.4, 93.4, 88.1, 88.0; IR (KBr, cm^{-1}): υ 2920, 1699, 1500, 1421, 1264, 1029, 699; HRMS: m/z [M + H]$^+$ Calcd for $C_{24}H_{15}O_3$: 351.1016; found: 351.1021.

1-(2-((4-Ethylphenyl)ethynyl)phenyl)-3-(4-fluorophenyl)prop-2-yn-1-one (3.12n, Table 3.2):



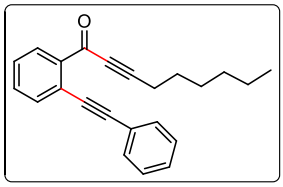
Yellow gummy (yield = 79%); R_f value = 0.73 in 10% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (s, 1H), 7.75 (d, *J* = 8.3 Hz, 1H), 7.68 (d, *J* = 7.4 Hz, 1H), 7.58 (d, *J* = 7.4 Hz, 1H), 7.5 (t, *J* = 7.4 Hz, 1H), 7.43-7.35 (m, 2H), 7.34-7.28 (m, 2H), 7.28-7.20 (m, 3H), 2.66 (q, *J* = 7.6 Hz, 2H), 1.20 (t, *J* = 7.6 Hz, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$): δ 177.1, 147.2 (d, *J* = 300.9 Hz), 138.1, 134.8, 133.1, 132.7, 132.2, 130.9, 130.3, 128.72, 128.7, 127.2, 124.6, 123.2, 121.1(d, *J* = 263.7 Hz), 94.1, 93.5, 91.6, 87.8, 29.7, 21.2; IR (KBr, cm^{-1}): υ 2959, 1699, 1600, 1507, 1220, 874, 759, 556; HRMS: m/z [M + H]$^+$ Calcd for $C_{25}H_{18}OF$: 353.1336; found: 353.1345.

1-(2-((2-Methyl-5-nitrophenyl)ethynyl)phenyl)-3-phenylprop-2-yn-1-one (3.12o, Table 3.2):



Reddish yellow solid (yield = 78%); M.P. = 159 - 160 °C; R_f value = 0.47 in 10% EtOAc/hexanes; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.34 (d, *J* = 2.3 Hz, 1H), 8.28 (d, *J* = 7.8 Hz, 1H), 8.04 (dd, *J* = 8.4, 2.3 Hz, 1H), 7.71 (d, *J* = 7.4 Hz, 1H), 7.63 (d, *J* = 7.1 Hz, 2H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.37 (t, *J* = 8.5 Hz, 3H), 2.70 (s, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$): δ 177.0, 148.4, 146.0, 138.0, 134.8, 133.1, 132.7, 132.2, 130.9, 130.3, 128.7, 128.67, 127.1, 124.5, 123.2, 122.1, 120.0, 94.1, 93.5, 91.7, 87.7, 21.2; IR (KBr, cm^{-1}): υ 3103, 1646, 1512, 1350, 1270, 1009, 751, 677; HRMS: m/z [M + H]$^+$ Calcd for $C_{24}H_{16}O_3N$: 366.1125; found: 366.1125.

1-(2-(Phenylethynyl)phenyl)non-2-yn-1-one (3.12q, Table 3.2):

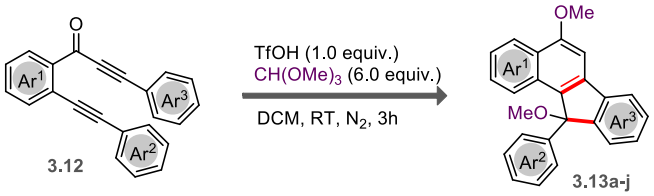


Yellow gummy (yield = 83%); R_f value = 0.63 in 5% EtOAc/hexanes; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.12 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.64-7.60 (m, 3H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.41 (t, *J* = 7.7 Hz, 1H), 7.36-7.33 (m, 3H), 2.42 (t, *J* = 7.2 Hz, 2H), 1.62-1.55 (m, 2H), 1.43-1.36 (m, 2H), 1.32-1.22 (m, 4H), 0.88 (t, *J* = 7.0 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 177.6, 138.3, 134.2, 132.2, 131.9, 131.7, 128.6, 128.3, 127.8, 123.3, 122.8, 97.1, 95.1, 88.3, 80.7, 31.2, 28.6, 27.7, 22.4, 19.3, 14.0; IR (KBr, cm^{-1}): υ 2927, 1707, 1646, 1492, 1242, 1069, 754, 690; HRMS: m/z [M + H]$^+$ Calcd for $C_{23}H_{23}O$: 315.1743; found: 315.1745.

3.4.4. Synthesis and Characterization of Benzo[*a*]fluorene Derivatives (3.13):

3.4.4.1. General Synthetic Procedure for the Preparation of Benzo[*a*]fluorene Derivatives (3.13):

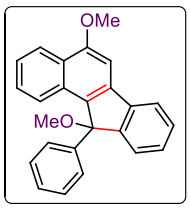
To a solution of aryl-fused 1,6-diyn-3-ones **3.12a** (1.0 equiv.) in dichloromethane solvent (5 mL/mmol), trimethyl orthoformate (6 equiv.) followed by triflic acid (1 equiv.) were charged at room temperature (25 °C) under nitrogen atmosphere. The reaction mixture was allowed to stir at room temperature under nitrogen atmosphere. The progress of the reaction was monitored by TLC. After completion of the reaction, it was quenched with a saturated $NaHCO_3$ solution. Then it was extracted using ethyl acetate. The combined organic layers were washed with saturated brine solution and dried over anhydrous Na_2SO_4. The solvents were evaporated under reduced pressure. The crude product was purified by column chromatography (using silica gel, EtOAc/hexanes eluent) to get pure benzo[*a*]fluorene **3.13**.



Scheme 3.14. TfOH catalyzed synthesis of benzo[*a*]fluorene derivatives.

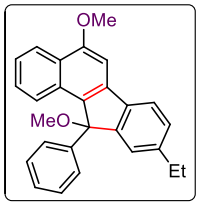
3.4.4.2. Analytical Data of Benzo[*a*]fluorene Derivatives (3.13):

5,11-Dimethoxy-11-phenyl-11*H*-benzo[*a*]fluorene (3.13a, Table 3.3):



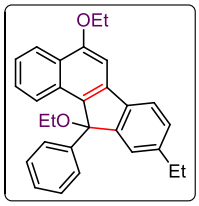
Red solid (yield = 97.4 mg, 85%); M.P. = 152 - 153 °C; R_f value = 0.63 in 10% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (d, *J* = 7.7 Hz, 1H), 7.81 (d, *J* = 7.4 Hz, 1H), 7.71 (d, *J* = 7.5 Hz, 1H), 7.42-7.33 (m, 5H), 7.28 (d, *J* = 7.0 Hz, 1H), 7.25-7.14 (m, 5H), 4.14 (s, 3H), 2.90 (s, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$): δ 157.7, 149.4, 143.6, 141.0, 139.8, 132.6, 130.7, 128.6, 128.2, 127.8, 127.4, 126.9, 125.9, 125.4, 124.9, 124.4, 124.39, 123.0, 119.4, 96.3, 89.9, 55.8, 51.2; IR (KBr, cm^{-1}): υ 2927, 1620, 1584, 1449, 1215, 1156, 757; HRMS: m/z [M + H]$^+$ Calcd for $C_{25}H_{21}O_2$: 353.1536; found: 353.1536.

9-Ethyl-5,11-dimethoxy-11-phenyl-11*H*-benzo[*a*]fluorene (3.13b, Table 3.3):



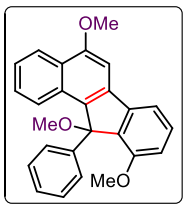
Yellow solid (yield = 78%); M.P. = 178 - 179 °C; R_f value = 0.64 in 10% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30-8.27 (m, 1H), 7.81-7.77 (m, 1H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.39-7.32 (m, 4H), 7.23-7.15 (m, 5H), 7.11 (s, 1H), 4.15 (s, 3H), 2.90 (s, 3H), 2.64 (q, *J* = 7.6 Hz, 2H), 1.22 (t, *J* = 7.6 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 157.6, 149.5, 144.2, 143.7, 139.9, 138.6, 132.4, 130.7, 128.2, 128.1, 127.3, 126.8, 125.6, 125.4, 124.7, 124.2, 124.0, 123.0, 119.2, 96.3, 89.8, 55.8, 51.2, 29.0, 15.6; IR (KBr, cm^{-1}): υ 2927, 1618, 1581, 1456, 1215, 1098, 863, 691; HRMS: m/z [M + H]$^+$ Calcd for $C_{27}H_{25}O_2$: 381.1849; found: 381.1849..

5,11-Diethoxy-9-ethyl-11-phenyl-11*H*-benzo[*a*]fluorene (3.13c, Table 3.3):



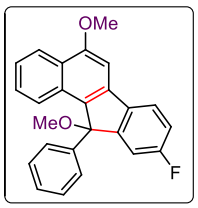
Off-white solid (yield = 78%); M.P. = 169 - 170 °C; R_f value = 0.77 in 10% EtOAc/hexanes; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.31 (d, *J* = 7.7 Hz, 1H), 7.84 (d, *J* = 7.5 Hz, 1H), 7.58 (d, *J* = 7.7 Hz, 1H), 7.38 (d, *J* = 7.0 Hz, 2H), 7.36-7.30 (m, 2H), 7.20-7.13 (m, 5H), 7.11 (s, 1H), 4.36 (q, *J* = 7.0 Hz, 2H), 3.06-2.99 (m, 1H), 2.97-2.90 (m, 1H), 2.62 (q, *J* = 7.6 Hz, 2H), 1.62 (t, *J* = 7.0 Hz, 3H), 1.21 (t, *J* = 7.6 Hz, 3H), 1.08 (t, *J* = 7.0 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 156.8, 150.4, 144.1, 139.6, 138.4, 133.1, 130.8, 128.1, 127.9, 127.1, 126.7, 125.7, 125.5, 124.5, 124.3, 123.9, 123.0, 121.9, 119.1, 96.9, 89.2, 64.0, 58.7, 29.0, 15.7, 15.6, 14.9; IR (KBr, cm^{-1}): υ 2923, 1582, 1446, 1209, 1069, 863, 761; HRMS: m/z [M + H]$^+$ Calcd for $C_{29}H_{29}O_2$: 409.2162; found: 409.2163.

5,10,11-Trimethoxy-11-phenyl-11*H*-benzo[*a*]fluorene (3.13d, Table 3.3):



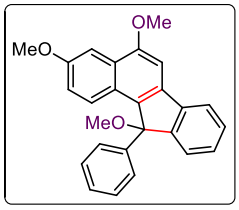
Brown solid (yield = 127.2 mg, 75%); M.P. = 169 - 170 °C; R_f value = 0.65 in 10% EtOAc/hexanes; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.26 (d, *J* = 7.6 Hz, 1H), 7.87 (d, *J* = 7.7 Hz, 1H), 7.40-7.31 (m, 6H), 7.18 (s, 1H), 7.16-7.08 (m, 3H), 6.76 (d, *J* = 6.9 Hz, 1H), 4.14 (s, 3H), 3.68 (s, 3H), 2.97 (s, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$): δ 157.5, 156.5, 143.0, 142.4, 139.0, 134.8, 133.9, 130.8, 130.4, 127.5, 127.3, 126.4, 126.1, 126.0, 124.9, 124.2, 122.9, 112.3, 111.4, 96.3, 90.6, 55.8, 51.3; IR (KBr, cm^{-1}): υ 2923, 1583, 1458, 1262, 1041, 765; HRMS: m/z [M + H]$^+$ Calcd for $C_{26}H_{23}O_3$: 383.1642; found: 383.1642.

9-Fluoro-5,11-dimethoxy-11-phenyl-11*H*-benzo[*a*]fluorene (3.13e, Table 3.3):



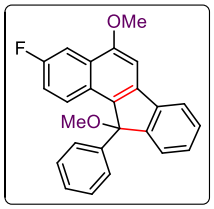
Brown solid (yield = 53.9 mg, 42%); M.P. = 152 - 153 °C; R_f value = 0.85% in 10 EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (d, *J* = 7.6 Hz, 1H), 7.76 (d, *J* = 7.9 Hz, 1H), 7.63 (s, 1H), 7.39-7.32 (m, 5H), 7.91 (d, *J* = 6.4 Hz, 2H), 7.16 (s, 1H), 7.04 (t, *J* = 8.1 Hz, 1H), 6.98 (d, *J* = 8.2 Hz, 1H), 4.15 (s, 3H), 2.91 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 169.1, 157.9, 151.9, 142.9, 139.0, 136.7, 132.4, 130.7, 129.7, 128.3, 127.5, 127.2, 125.5, 125.3, 125.0, 124.2, 123.0, 120.4 (d, *J* = 8.6 Hz), 115.4 (d, *J* = 22.7 Hz), 112.2 (d, *J* = 23.3 Hz), 96.1, 55.8, 51.4; IR (KBr, cm^{-1}): υ 2926, 1707, 1582, 1397, 1219, 1072, 738, 696; HRMS: m/z [M + H]$^+$ Calcd for $C_{25}H_{20}FO_2$: 371.1442; found: 371.1442.

3,5,11-Trimethoxy-11-phenyl-11*H*-benzo[*a*]fluorene (3.13f, Table 3.3):



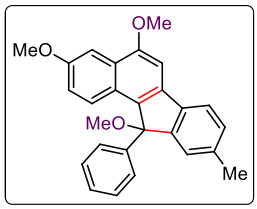
Pale yellow solid (yield = 73%); M.P. = 204 - 205 °C; R_f value = 0.68 in 10% EtOAc/hexanes; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72 (d, *J* = 9.1 Hz, 1H), 7.66 (d, *J* = 7.5 Hz, 1H), 7.59 (d, *J* = 2.6 Hz, 1H), 7.36-7.31 (m, 3H), 7.25 (d, *J* = 6.2 Hz, 1H), 7.21-7.13 (m, 5H), 7.02 (dd, *J* = 9.2, 2.7 Hz, 1H), 4.15 (s, 3H), 3.91 (s, 3H), 2.88 (s, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$): δ 157.3, 156.6, 148.9, 143.7, 141.2, 137.5, 133.0, 128.6. 128.2, 127.3, 127.0, 126.9, 126.1, 126.0, 125.4, 124.4, 119.8, 119.1, 101.7, 96.9, 89.8, 55.8, 55.3, 51.2; IR (KBr, cm^{-1}): υ 2929, 1586, 1478, 1211, 1081, 829, 752, 696; HRMS: m/z $[M + H]^+$ Calcd for $C_{26}H_{23}O_3$: 383.1642; found: 383.1642.

3-Fuoro-5,11-dimethoxy-11-phenyl-11*H*-benzo[*a*]fluorene (3.13g, Table 3.3):



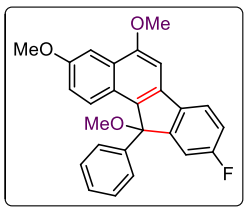
Yellow solid (yield = 76%); M.P. = 206 - 207 °C; R_f value = 0.75 in 5% EtOAc/hexanes; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70 (d, *J* = 9.2 Hz, 1H), 7.59 (d, *J* = 2.6 Hz, 1H), , 7.55 (d, *J* = 7.6 Hz, 1H), 7.42-7.33 (m, 5H), 7.28 (d, *J* = 7.0 Hz, 1H), 7.25-7.14 (m, 5H), 4.14 (s, 3H), 2.90 (s, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$): δ 157.7, 149.4, 143.6, 141.0, 139.8, 132.6, 130.7, 128.6, 128.2, 127.8, 127.4, 126.9, 125.9, 125.4, 124.9, 124.4, 124.39, 123.0, 119.4, 96.3, 89.9, 55.8, 51.2; IR (KBr, cm^{-1}): υ 2911, 1589, 1452, 1170, 1069, 920, 745, 693; HRMS: m/z: $[M + H]^+$ Calcd for $C_{25}H_{20}FO_2$: 371.1442; found: 371.1441.

3,5,11-Trimethoxy-9-methyl-11-phenyl-11*H*-benzo[*a*]fluorene (3.13h, Table 3.3):



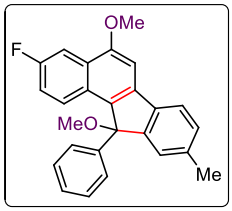
Brown solid (yield = 82%); M.P. = 255 - 256 °C; R_f value = 0.61 in 5% EtOAc/hexanes; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70 (d, *J* = 9.2 Hz, 1H), 7.59 (d, *J* = 2.6 Hz, 1H), 7.55 (d, *J* = 7.6 Hz, 1H), 7.35 (d, *J* = 7.0 Hz, 1H), 7.21-7.13 (m, 5H), 7.07 (s, 1H), 7.01 (dd, *J* = 9.1, 2.6 Hz, 1H), 4.15 (s, 3H), 3.91 (s, 3H), 2.89 (s, 3H), 2.33 (s, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$): δ 157.1, 156.6, 149.1, 143.9, 138.6, 137.6, 137.2, 132.6, 129.3, 128.2, 126.8, 126.7, 126.2, 125.9, 125.4, 125.1, 119.7, 118.8, 101.7, 96.9, 89.7, 55.8, 55.3, 51.2, 21.6; IR (KBr, cm^{-1}): υ 2921, 1581, 1461, 1207, 1079, 816, 695, 556; HRMS: m/z $[M + H]^+$ Calcd for $C_{27}H_{25}O_3$: 397.1798; found: 397.1799.

9-Fluoro-3,5,11-trimethoxy-11-phenyl-11*H*-benzo[*a*]fluorene (3.13i, Table 3.3):



Off-white solid (yield = 45%); M.P. = 254 - 255 °C; R_f value = 0.50 in 5% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): 7.66 (d, *J* = 9.1 Hz, 1H), 7.56 (dd, *J* = 8, 4.8 Hz, 2H), 7.33-7.28 (m, 2H), 7.20-7.14 (m, 3H), 7.12 (s, 1H), 7.00 (d, *J* = 9.2 Hz, 2H), 6.94 (d, *J* = 8.2 Hz, 1H), 4.11 (s, 3H), 3.87 (s, 3H), 2.88 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 164.0, 161.6, 157.3, 156.8, 151.4 (d, *J* = 27.6 Hz), 143.1, 137.0, 136.7, 132.7, 128.3, 127.2, 126.7, 126.1, 125.8, 125.3, 119.9 (d, *J* = 21.2 Hz), 115.4 (d, *J* = 90.7 Hz), 112.1 (d, *J* = 93.1 Hz), 101.7, 96.7, 89.5, 55.8, 55.3, 51.3; IR (KBr, cm^{-1}): υ 2930, 1583, 1481, 1217, 1074, 815, 695; HRMS: m/z $[M + H]^+$ Calcd for $C_{25}H_{20}FO_2$: 401.1547; found: 401.1532.

3-Fluoro-5,11-dimethoxy-9-methyl-11-phenyl-11*H*-benzo[*a*]fluorene (3.13j, Table 3.3):

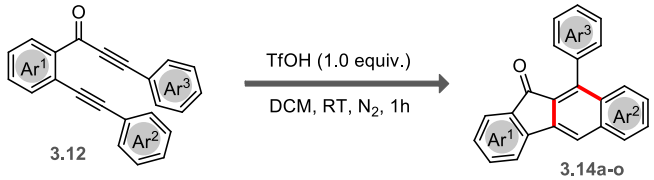


Brown solid (yield = 74%); M.P. = 203 - 204 °C; R_f value = 0.64 in 5% EtOAc/hexanes; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.92-7.84 (m, 2H), 7.81-7.77 (m, 1H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 3.8 Hz, 2H), 7.20-7.17 (m, 2H), 7.15-7.10 (m, 1H), 7.09 (s, 1H), 4.15 (s, 3H), 2.90 (s, 3H), 2.34 (s, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$): δ 161.2, 159.2, 157.0, 149.5 (d, *J* = 99.8 Hz), 143.6, 139.2, 138.0 (d, *J* = 44.7 Hz), 132.5, 129.3 (d, *J* = 18.4 Hz), 128.2 (d, *J* = 7.3 Hz), 127.7, 126.9, 126.8, 126.5 (d, *J* = 8.1 Hz), 125.3, 125.2, 119.2, 117.4 (d, *J* = 25.1 Hz), 107.3, 97.2, 89.7, 58.8, 55.8, 51.2, 21.7, 15.7; IR (KBr, cm^{-1}): υ 2924, 1591, 1457, 1202, 1072, 989, 808, 697; HRMS: m/z [M + H]$^+$ Calcd for $C_{26}H_{22}FO_2$: 385.1598; found: 385.1597.

3.4.5. Synthesis and Characterization of Benzo[*b*]fluorenone Derivatives (3.14):

3.4.5.1. General Synthetic Procedure for the Preparation of Benzo[*b*]fluorenone Derivatives (3.14):

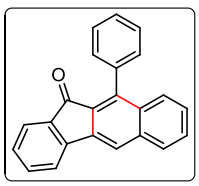
To a solution of aryl-fused 1,6-diyn-3-ones **3.12a** (1.0 equiv.) in dichloromethane solvent (5 mL/mmol), triflic acid (1 equiv.) was charged at room temperature (25 °C) under nitrogen atmosphere. The reaction mixture was allowed to stir at room temperature under nitrogen atmosphere until the completion of the reaction. The progress of the reaction was monitored by TLC. After that, it was quenched with a saturated $NaHCO_3$ solution. Then it was extracted using ethyl acetate and water. The combined organic layers was washed with saturated brine solution and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure. The crude product was purified by column chromatography (using silica gel, EtOAc/hexanes eluent) to get pure benzo[*b*]fluorenone derivatives **3.14**.



Scheme 3.15. TfOH catalyzed synthesis of benzo[*b*]fluorenone derivatives (**3.14a-o**).

3.4.5.2. Analytical Data of Benzo[*b*]fluorenone Derivatives (3.14):

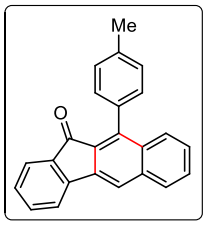
10-Phenyl-11*H*-benzo[*b*]fluoren-11-one (3.14a, Table 3.4):



Yellow solid (yield = 93%); M.P. = 216 - 217 °C; R_f value = 0.60 in 10% EtOAc/hexanes; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.93 (s, 1H), 7.87 (d, *J* = 8.1 Hz, 1H), 7.76 (d, *J* = 7.5 Hz, 1H), 7.64 (d, *J* = 4.4 Hz, 1H), 7.62 (d, *J* = 3.4 Hz, 1H), 7.58-7.52 (m, 5H), 7.39-7.35 (m, 3H), 7.32 (td, *J* = 7.4, 0.8 Hz, 1H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$): δ 192.2, 144.1, 141.3, 138.5, 136.7, 136.4, 135.6, 134.7, 133.9, 129.7, 129.3, 129.25, 129.1, 128.8, 128.7, 128.1, 128.05, 126.9, 124.2, 120.7, 118.8; IR (KBr, cm^{-1}):

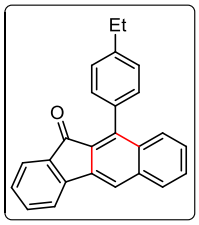
υ 2920, 1697, 1620, 1599, 1443, 1187, 1158, 951, 757, 719, 699; HRMS: m/z $[M + H]^+$ Calcd for $C_{23}H_{15}O$: 307.1117; found: 307.1117.

10-(*p*-Tolyl)-11*H*-benzo[*b*]fluoren-11-one (3.14b, Table 3.4):



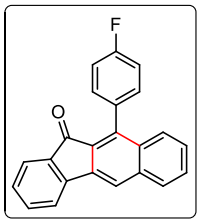
Yellow solid (yield = 95%); M.P. = 286 - 287 °C; R_f value = 0.56 in 10% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (s, 1H), 7.87 (d, *J* = 8.1 Hz, 1H), 7.76 (d, *J* = 7.6 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 1H), 7.63 (d, *J* = 7.4 Hz, 1H), 7.55 (q, *J* = 7.4 Hz, 2H), 7.40-7.30 (m, 4H), 7.29 (s, 1H), 7.26 (d, *J* = 1.8 Hz, 1H), 2.50 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 192.3, 144.0, 141.5, 138.5, 137.7, 136.7, 136.4, 134.7, 134.0, 132.4, 129.7, 129.5, 129.3, 129.2, 129.1, 128.9, 128.8, 128.7, 128.6, 126.7, 124.1, 120.7, 118.6, 21.5; IR (KBr, cm^{-1}): υ 2915, 1797, 1621, 1601, 1468, 1108, 884, 866, 756, 718, 597; HRMS: m/z $[M + H]^+$ Calcd for $C_{24}H_{17}O$: 321.1274; found: 321.1275.

10-(4-Ethylphenyl)-11*H*-benzo[*b*]fluoren-11-one (3.14c, Table 3.4):



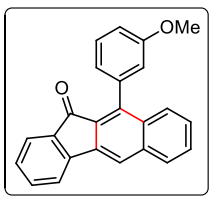
Yellow solid (yield = 96%); M.P. = 208 - 209 °C; R_f value = 0.45 in 10% EtOAc/hexanes; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.92 (s, 1H), 7.86 (d, *J* = 8.1 Hz, 1H), 7.76 (d, *J* = 7.5 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.63 (d, *J* = 7.4 Hz, 1H), 7.55 (q, *J* = 7.6 Hz, 2H), 7.40-7.35 (m, 3H), 7.34-7.29 (m, 3H), 2.81 (q, *J* = 7.6 Hz, 2H), 1.37 (t, *J* = 7.6 Hz, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$): δ 192.4, 144.1, 143.9, 141.6, 138.5, 136.7, 136.4, 134.7, 134.1, 132.6, 129.6, 129.2, 128.8, 128.7, 127.6, 126.8, 124.2, 120.7, 118.6, 28.8, 15.4; IR (KBr, cm^{-1}): υ 2958, 1692, 1620, 1579, 1467, 1334, 1186, 1160, 955, 832, 760, 752, 597; HRMS: m/z $[M + H]^+$ Calcd for $C_{25}H_{19}O$: 335.1430; found: 335.1430.

10-(4-Fluorophenyl)-11*H*-benzo[*b*]fluoren-11-one (3.14d, Table 3.4):



Yellow solid (yield = 97%); M.P. = 192 - 193 °C; R_f value = 0.47 in 10% EtOAc/hexanes; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.95 (s, 1H), 7.89 (d, *J* = 8.1 Hz, 1H), 7.77 (d, *J* = 7.6 Hz, 1H), 7.65-7.60 (m, 2H), 7.60-7.54 (m, 2H), 7.42-7.38 (m, 1H), 7.38-7.32 (m, 3H), 7.26-7.22 (m, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$): δ 192.3, 163.7, 161.8, 144.1, 140.2, 138.5, 136.8, 136.3, 134.9, 131.5, 131.4 (d, *J* = 31.8 Hz), 131.2 (d, *J* = 14.1 Hz), 129.3, 128.9, 128.85, 128.8, 127.0, 124.3, 120.8, 119.0, 115.2 (d, *J* = 86.1 Hz); IR (KBr, cm^{-1}): υ 2922, 1701, 1623, 1597, 1499, 1208, 1093, 952, 839, 760, 720, 595; HRMS: m/z $[M + H]^+$ Calcd for $C_{23}H_{14}FO$: 325.1023; found: 325.1025.

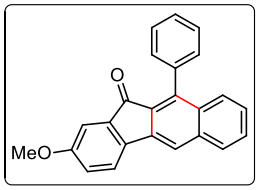
10-(3-Methoxyphenyl)-11*H*-benzo[*b*]fluoren-11-one (3.14e, Table 3.4):



Yellow solid (yield = 87%); M.P. = 238 - 239 °C; R_f value = 0.47 in 10% EtOAc/hexanes; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.93 (s, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 7.5 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 1H), 7.63 (d, *J* = 7.4 Hz, 1H), 7.60-7.52 (m, 2H), 7.46 (t, *J* = 7.9 Hz, 1H), 7.40-7.36 (m, 1H), 7.33 (t, *J* = 7.5 Hz, 1H), 7.08-7.05 (m, 1H), 6.96 (d, *J* = 7.5 Hz, 1H), 6.92 (s, 1H), 3.85 (s, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$): δ 192.1, 159.5, 144.1, 141.0, 138.5, 137.0, 136.7, 136.4, 134.7, 133.8, 129.2, 129.18, 129.1, 128.8, 128.76, 128.6, 126.9, 124.3, 122.0, 120.7, 118.8, 115.3, 113.6,

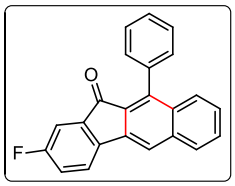
55.3; IR (KBr, cm^{-1}): υ 2916, 1701, 1622, 1581, 1466, 1335, 1248, 1173, 1032, 957, 762, 700; HRMS: m/z $[M + H]^+$ Calcd for $C_{24}H_{17}O_2$: 337.1223; found: 337.1225.

2-Methoxy-10-phenyl-11*H*-benzo[*b*]fluoren-11-one (3.14f, Table 3.4):



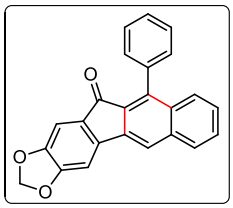
Yellow solid (yield = 86%); M.P. = 240 - 241 °C; R_f value = 0.55 in 10% EtOAc/hexanes; ^1H NMR (500 MHz, $CDCl_3$): δ 8.17 (s, 1H), 7.92-7.89 (m, 1H), 7.62-7.56 (m, 3H), 7.44-7.38 (m, 5H), 7.24 (d, *J* = 2.6 Hz, 1H), 6.72 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.22 (d, *J* = 8.5 Hz, 1H), 3.81 (s, 3H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$): δ 193.2, 160.4, 138.3, 138.1, 137.6, 137.2, 135.6, 133.2, 133.1, 132.9, 130.8, 129.8, 129.3, 129.0, 128.3, 126.9, 126.5, 125.3, 124.9, 121.5, 108.1, 55.7; IR (KBr, cm^{-1}): υ 2921, 1703, 1602, 1485, 1277, 1118, 1017, 820, 745, 698, 591; HRMS: m/z $[M + H]^+$ Calcd for $C_{24}H_{17}O_2$: 337.1223; found: 337.1224.

2-Fluoro-10-phenyl-11*H*-benzo[*b*]fluoren-11-one (3.14g, Table 3.4):



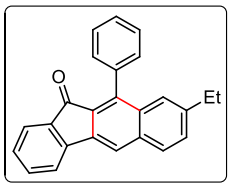
Yellow solid (yield = 86%); M.P. = 294 - 295 °C; R_f value = 0.47 in 10% EtOAc/hexanes; ^1H NMR (500 MHz, $CDCl_3$): δ 7.88 (s, 1H), 7.86 (d, *J* = 8.1 Hz, 1H), 7.73 (dd, *J* = 8.3, 4.4 Hz, 1H), 7.62 (d, *J* = 8.5 Hz, 1H), 7.57-7.51 (m, 4H), 7.40-7.35 (m, 3H), 7.28 (dd, *J* = 7.4, 2.4 Hz, 1H), 7.26-7.22 (m, 1H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$): δ 190.9, 164.8, 162.8, 141.9, 140.0, 138.5 (d, *J* = 29.4 Hz), 137.8, 136.8, 135.4, 133.6, 129.6, 129.2, 129.1, 128.9, 128.8, 128.2, 127.0, 122.2 (d, *J* = 31.0 Hz), 121.5 (d, *J* = 94.3 Hz), 118.5, 111.3 (d, *J* = 91.7 Hz); IR (KBr, cm^{-1}): υ 2923, 1698, 1603, 1476, 1261, 1149, 1032, 924, 811, 777, 700, 581; HRMS: m/z $[M + H]^+$ Calcd for $C_{23}H_{14}FO$: 325.1023; found: 325.1025.

10-Phenyl-11*H*-benzo[6,7]fluoreno[2,3-*d*][1,3]dioxol-11-one (3.14h, Table 3.4):



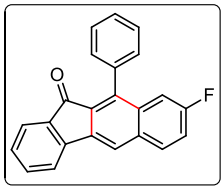
Yellow solid (yield = 92%); M.P. = 291 - 292 °C; R_f value = 0.27 in 10% EtOAc/hexanes; ^1H NMR (400 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.89 (d, *J* = 6.9 Hz, 1H), 7.63-7.57 (m, 3H), 7.47-7.36 (m, 5H), 7.14 (s, 1H), 5.95 (s, 2H), 5.69 (s, 1H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 191.5, 153.2, 148.4, 142.6, 137.2, 136.9, 134.6, 133.3, 133.1, 131.8, 130.6, 129.7, 129.4, 128.8, 128.4, 127.0, 126.7, 124.5, 104.5, 104.3, 102.1; IR (KBr, cm^{-1}): υ 2918, 1693, 1621, 1493, 1451, 1298, 1269, 1028, 927, 818, 747, 727, 554; HRMS: m/z $[M + H]^+$ Calcd for $C_{24}H_{15}O_3$: 351.1016; found: 351.1017.

8-Ethyl-10-phenyl-11*H*-benzo[*b*]fluoren-11-one (3.14i, Table 3.4):



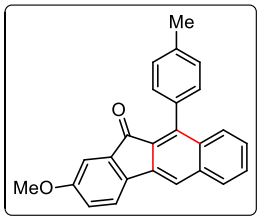
Yellow solid (yield = 89%); M.P. = 193 - 194 °C; R_f value = 0.52 in 10% EtOAc/hexanes; ^1H NMR (400 MHz, $CDCl_3$): δ 7.89 (s, 1H), 7.80 (d, *J* = 8.9 Hz, 1H), 7.74 (d, *J* = 7.5 Hz, 1H), 7.61 (d, *J* = 7.4 Hz, 1H), 7.58-7.52 (m, 4H), 7.44-7.37 (m, 4H), 7.33-7.28 (m, 1H), 2.67 (q, *J* = 7.5 Hz, 2H), 1.21 (t, *J* = 7.6 Hz, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 192.4, 144.2, 143.2, 140.9, 137.7, 136.3, 135.7, 135.1, 134.7, 134.0, 129.7, 129.6, 129.0, 128.8, 128.7, 128.1, 127.9, 127.1, 124.2, 120.6, 118.6, 29.1, 15.5; IR (KBr, cm^{-1}): υ 2962, 1702, 1599, 1468, 1231, 1023, 958, 888, 762, 700, 600; HRMS: m/z $[M + H]^+$ Calcd for $C_{25}H_{19}O$: 335.1430; found: 335.1432.

8-Fluoro-10-phenyl-11*H*-benzo[*b*]fluoren-11-one (3.14j, Table 3.4):



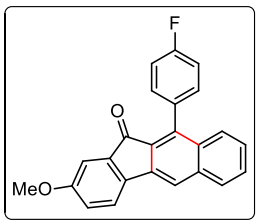
Yellow solid (yield = 85%); M.P. = 220 - 221 °C; R_f value = 0.45 in 10% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (s, 1H), 7.86 (dd, *J* = 8.9, 5.7 Hz, 1H), 7.75 (d, *J* = 7.6 Hz, 1H), 7.63 (d, *J* = 7.4 Hz, 1H), 7.59-7.53 (m, 4H), 7.37-7.24 (m, 5H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 192.1, 161.3 (d, *J* = 245.8 Hz), 144.0, 140.5, 140.4, 138.0, 137.99, 136.1, 135.2 (d, *J* = 8.3 Hz), 135.0, 134.9, 133.5, 130.8 (d, *J* = 8.8 Hz), 129.5, 129.4, 129.3, 128.3, 124.3, 120.7, 118.6 (d, *J* = 24.6 Hz), 112.9 (d, *J* = 22.2 Hz); IR (KBr, cm^{-1}): υ 3052, 1698, 1599, 1514, 1468, 1226, 1102, 875, 810, 758, 722, 597; HRMS: m/z [M + H]$^+$ Calcd for $C_{23}H_{14}FO$: 325.1023; found: 325.1021.

2-Methoxy-10-(p-tolyl)-11*H*-benzo[*b*]fluoren-11-one (3.14k, Table 3.4):



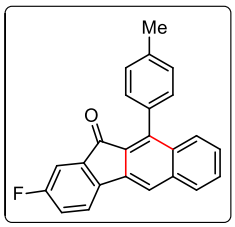
Yellow solid (yield = 82%); M.P. = 265 - 266 °C; R_f value = 0.38 in 5% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, *J* = 8.1 Hz, 1H), 7.77 (s, 1H), 7.66-7.62 (m, 2H), 7.53-7.49 (m, 1H), 7.36-7.31 (m, 3H), 7.26 (s, 2H), 7.12 (d, *J* = 2.3 Hz, 1H), 7.09 (dd, *J* = 8.3, 2.5 Hz, 1H), 3.85 (s, 3H), 2.49 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 192.2, 161.0, 141.6, 138.7, 138.2, 137.7, 137.1, 137.0, 133.5, 132.5, 129.6, 129.2, 129.15, 128.9, 128.8, 128.5, 126.4, 121.9, 121.6, 117.4, 108.0, 55.7, 21.5; IR (KBr, cm^{-1}): υ 2918, 1688, 1576, 1485, 1438, 1277, 1026, 1010, 792, 764, 586; HRMS: m/z [M + H]$^+$ Calcd for $C_{25}H_{19}O_2$: 351.1380; found: 351.1380.

10-(4-Fluorophenyl)-2-methoxy-11*H*-benzo[*b*]fluoren-11-one (3.14l, Table 3.4):



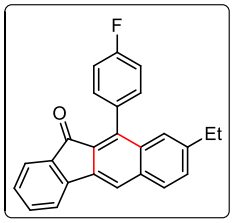
Yellow solid (yield = 84%); M.P. = 281 - 282 °C; R_f value = 0.42 in 5% EtOAc/hexanes; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.83 (d, *J* = 8.1 Hz, 1H), 7.79 (s, 1H), 7.65 (d, *J* = 8.3 Hz, 1H), 7. 57 (d, *J* = 8.4 Hz, 1H), 7.55-7.51 (m, 1H), 7.37-7.32 (m, 3H), 7.23 (t, *J* = 8.8 Hz, 2H), 7.14-7.09 (m, 2H), 3.85 (s, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$): δ 192.2, 163.7, 161.5 (d, *J* = 334.3 Hz), 140.2, 138.4 (d, *J* = 332.6 Hz), 137.0, 133.2 (d, *J* = 107.1 Hz), 131.5, 129.8, 129.4 (d, *J* = 76.6 Hz), 128.8 (d, *J* = 58.3 Hz), 126.6, 125.0, 121.8 (d, *J* = 51.2 Hz), 121.5, 117.7, 115.3, 115.1, 111.3, 108.0, 55.8; IR (KBr, cm^{-1}): υ 2993, 1686, 1573, 1486, 1438, 1294, 1217, 1154, 1011, 837, 766, 574; HRMS: m/z [M + H]$^+$ Calcd for $C_{24}H_{16}FO_2$: 355.1129; found: 355.1128.

2-Fluoro-10-(p-tolyl)-11*H*-benzo[*b*]fluoren-11-one (3.14m, Table 3.4):



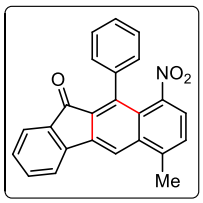
Yellow solid (yield = 78%); M.P. = 284 - 285 °C; R_f value = 0.48 in 5% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (s, 1H), 7.78 (d, *J* = 8.2 Hz, 1H), 7.61-7.57 (m, 2H), 7.37 (dd, *J* = 7.7, 1.7 Hz, 2H), 7.28 (d, *J* = 1.5 Hz, 1H), 7.13 (s, 2H), 5.94 (s, 2H), 5.64 (s, 1H), 2.36 (s, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$): δ191.5, 150.7 (d, *J* = 605.5 Hz), 142.5, 139.2, 137.4, 137.0, 134.9, 132.8, 132.5, 131.9, 131.2, 130.5, 129.8, 129.5, 129.3, 128.7, 128.4, 125.3 (d, *J* = 256.1 Hz), 117.4, 104.4 (d, *J* = 33 Hz), 102.0, 22.0; IR (KBr, cm^{-1}): υ 2915, 1691, 1592, 1262, 1031, 772, 568; HRMS: m/z [M + Na]$^+$ Calcd for $C_{24}H_{15}FONa$: 361.0999, found: 361.0998.

10-(4-Fluorophenyl)-2-methoxy-11*H*-benzo[*b*]fluoren-11-one (3.14n, Table 3.4):



Yellow solid (yield = 97%); M.P. = 234 - 235 °C; R_f value = 0.48 in 10% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (s, 1H), 7.79 (d, *J* = 8.2 Hz, 1H), 7.72 (d, *J* = 7.4 Hz, 1H), 7.60 (d, *J* = 7.4 Hz, 1H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.41 (d, *J* = 8.3 Hz, 1H), 7.37-7.27 (m, 4H), 7.25-7.20 (m, 2H), 7.67 (q, *J* = 7.5 Hz, 2H), 1.20 (t, *J* = 7.6 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 192.4, 162.8 (d, *J* = 245 Hz), 144.2, 143.3, 139.7, 137.7, 136.2, 135.1, 134.8, 134.0, 131.41 (d, *J* = 8.2 Hz), 131.39, 129.8, 129.0, 128.9, 128.8, 126.7, 124.2, 120.6, 118.8, 115.2 (d, *J* = 21.3 Hz), 29.1, 15.5; IR (KBr, cm^{-1}): υ 2959, 1700, 1599, 1508, 1468, 1185, 957, 886, 759, 725, 599; HRMS: m/z [M + H]$^+$ Calcd for $C_{25}H_{18}FO$: 353.1336, found: 353.1337.

6-Methyl-9-nitro-10-phenyl-11*H*-benzo[*b*]fluoren-11-one (3.14o, Table 3.4):

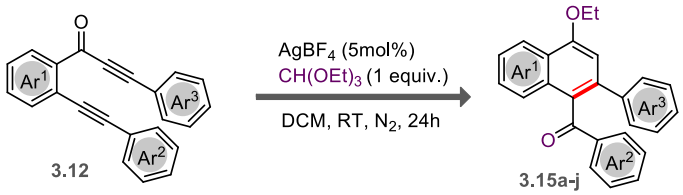


Pale yellow solid (yield = 77%); M.P. = 262 - 263 °C; R_f value = 0.26 in 10% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (dd, *J* = 8.5, 2.5 Hz, 1H), 8.32 (s, 1H), 8.22 (d, *J* = 2.4 Hz, 1H), 8.01 (d, *J* = 7.7 Hz, 1H), 7.79 (d, *J* = 7.0 Hz, 1H), 7.69 (d, *J* = 8.5 Hz, 1H), 7.58-7.48 (m, 2H), 7.33-7.22 (m, 3H), 6.22 (d, *J* = 7.5 Hz, 1H), 2.17 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 192.7, 147.1, 145.6, 144.3, 138.4, 136.5, 135.7, 135.2, 133.6, 132.6, 131.7, 131.3, 130.9, 129.7, 129.3, 127.4, 126.1, 125.9, 125.2, 124.7, 123.7, 122.7, 20.0; IR (KBr, cm^{-1}): υ 2921, 1705, 1513, 1343, 1110, 901, 731; HRMS: m/z [M + H]$^+$ Calcd for $C_{24}H_{16}NO_3$: 366.1125; found: 366.1126.

3.4.6. Synthesis and Characterization of Naphthyl Ketone Derivatives (3.15):

3.4.6.1. General Synthetic Procedure for the Preparation of Naphthyl Ketone Derivatives (3.15):

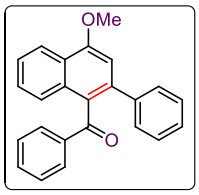
To a solution of aryl-fused 1,6-diyn-3-ones **3.12** (1.0 equiv.) in dichloromethane solvent (5 mL/mmol), trimethyl orthoformate (1.0 equiv.) followed by $AgBF_4$ (5 mol%) were charged at room temperature (25 °C) under nitrogen atmosphere. The reaction mixture was allowed to stir at room temperature under nitrogen atmosphere until the completion of the reaction. The progress of the reaction was monitored by TLC. After that, solvent was removed under reduced pressure and the naphthyl ketone **3.15** was isolated by column chromatography (using silica gel, EtOAc/hexanes eluent).



Scheme 3.16. $AgBF_4$ catalyzed synthesis of naphthyl ketone derivatives (**3.15**).

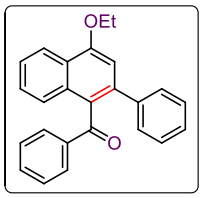
3.4.6.2. Analytical Data of Naphthyl Ketone Derivatives (3.15):

(4-Methoxy-2-phenylnaphthalen-1-yl)(phenyl)methanone (3.15a, Table 3.5):



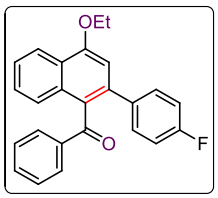
Yellow solid (yield = 70%); M.P. = 133 - 134 °C; R_f value = 0.41 in 10% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (d, *J* = 8.2 Hz, 1H), 7.67 (d, *J* = 8.2 Hz, 1H), 7.55 (d, *J* = 8.2 Hz, 2H), 7.48-7.38 (m, 2H), 7.29 (d, *J* = 7.9 Hz, 3H), 7.20-7.08 (m, 5H), 6.81 (s, 1H), 4.02 (s, 3H); IR (KBr, cm^{-1}): υ 2964, 1658, 1581, 1445, 1383, 1220, 1097, 866, 775, 695, 628; HRMS: m/z [M + Na]$^+$ Calcd for $C_{24}H_{18}O_2Na$: 361.1199; found: 361.1199.

(4-Ethoxy-2-phenylnaphthalen-1-yl)(phenyl)methanone (3.15b, Table 3.5):



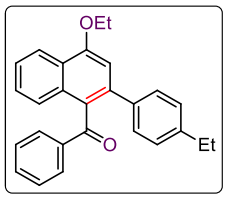
Yellow solid (yield = 79%); M.P. = 235 - 236 °C; R_f value = 0.5 in 10% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (d, *J* = 9 Hz, 1H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.62 (d, *J* = 7.4 Hz, 1H), 7.54-7.45 (m, 2H), 7.40-7.33 (m, 3H), 7.25-7.15 (m, 5H), 6.87 (s, 1H), 4.30 (q, *J* = 7.0 Hz, 2H), 1.61 (t, *J* = 6.9 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 199.9, 155.5, 140.9, 138.6, 132.9, 132.0, 129.6, 129.4, 128.2, 128.15, 127.7, 127.4, 125.5, 125.3, 124.6, 122.3, 106.3, 64.0, 14.9; IR (KBr, cm^{-1}): υ 2970, 1655, 1586, 1473, 1380, 1223, 1094, 866, 759, 690, 632; HRMS: m/z [M + Na]$^+$ Calcd for $C_{25}H_{20}O_2Na$: 375.1356; found: 375.1356.

(4-Ethoxy-2-(4-fluorophenyl)naphthalen-1-yl)(phenyl)methanone (3.15c, Table 3.5):



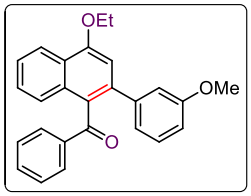
Yellow solid (yield = 62%); M.P. = 165 - 166 °C; R_f value = 0.52 in 10% EtOAc/hexanes; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.39 (d, *J* = 7.3 Hz, 1H), 7.69 (d, *J* = 7.6 Hz, 1H), 7.59 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.53-7.45 (m, 2H), 7.41-7.37 (m, 1H), 7.31-7.27 (m, 2H), 7.23 (t, *J* = 7.8 Hz, 2H), 6.89 (t, *J* = 8.8 Hz, 2H), 6.80 (s, 1H), 4.30 (q, *J* = 13.9, 6.9 Hz, 2H), 1.61 (t, *J* = 7.0 Hz, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$): δ 199.8, 155.6, 138.6, 137.4, 137.0, 133.1, 132.0, 131.1 (d, *J* = 32.3 Hz), 129.7, 129.6, 128.4, 128.3, 127.9, 125.5 (d, *J* = 187.5 Hz), 124.7, 122.4, 115.1 (d, *J* = 85.9 Hz), 106.2, 100.0, 64.1, 14.9; IR (KBr, cm^{-1}): υ 2922, 1656, 1591, 1507, 1381, 1219, 1093, 834, 721, 692; HRMS: m/z [M + H]$^+$ Calcd for $C_{25}H_{20}FO_2$: 371.1442; found: 371.1443.

(4-Ethoxy-2-(4-ethylphenyl)naphthalen-1-yl)(phenyl)methanone (3.15d, Table 3.5):



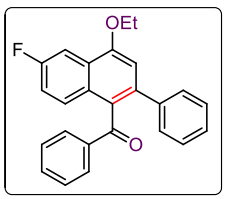
Yellow solid (yield = 72%); M.P. = 155 - 156 °C; R_f value = 0.65 in 10% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (d, *J* = 7.8 Hz, 1H), 7.70 (d, *J* = 8.1 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 2H), 7.48-7.39 (m, 2H), 7.31 (t, *J* = 7.4 Hz, 1H), 7.25 (d, *J* = 8.1 Hz, 2H), 7.17 (t, *J* = 7.7 Hz, 2H), 7.01 (d, *J* = 6.2 Hz, 2H), 6.85 (s, 1H), 4.25 (q, *J* = 6.9 Hz, 2H), 2.51 (q, *J* = 7.5 Hz, 2H), 1.55 (t, *J* = 6.9 Hz, 3H), 1.12 (t, *J* = 7.6 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 199.9, 155.4, 143.4, 138.7, 138.6, 138.2, 132.7, 132.0, 129.5, 129.3, 128.1, 127.6, 127.56, 125.3, 125.2, 124.5, 122.3, 122.2, 106.4, 164.0, 28.4, 15.3, 14.8; IR (KBr, cm^{-1}): υ 2924, 1662, 1592, 1386, 1174, 1140, 856, 797, 724, 626; HRMS: m/z [M + H]$^+$ Calcd for $C_{27}H_{25}O_2$: 381.1849; found: 381.1849.

(4-Ethoxy-2-(3-methoxyphenyl)naphthalen-1-yl)(phenyl)methanone (3.15e, Table 3.5):



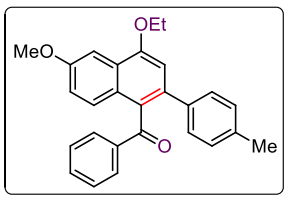
Brown solid (yield = 80%); M.P. = 203 - 204 °C; R_f value = 0.58 in 10% EtOAc/hexanes; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.35 (d, *J* = 8.3 Hz, 1H), 7.58 (d, *J* = 8.1 Hz, 1H), 7.37 (t, *J* = 7.0 Hz, 1H), 7.32 (d, *J* = 7.0 Hz, 1H), 7.30 (d, *J* = 2.5 Hz, 1H), 7.24 (s, 1H), 7.22 (d, *J* = 7.6 Hz, 2H), 7.19 (d, *J* = 7.7 Hz, 2H), 7. 10 (d, *J* = 6.9 Hz, 2H), 6.77 (dd, *J* = 8.2, 2.4 Hz, 1H), 5.21 (s, 1H), 4.38 (q, *J* = 7.0 Hz, 2H), 3.90 (s, 3H), 1.63 (t, *J* = 7.0 Hz, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$): δ 159.5, 155.7, 142.7, 142.4, 142.1, 139.2, 135.6, 131.0, 128.8, 127.9, 126.8, 126.6, 126.0, 125.3, 124.5, 124.3, 123.3, 112.7, 104.8, 97.3, 64.1, 55.6, 52.9, 14.9; IR (KBr, cm^{-1}): υ 2979, 1606, 1583, 1476, 1425, 1234, 1204, 1136, 1029, 739, 701, 626; HRMS: m/z [M + H]$^+$ Calcd for $C_{26}H_{23}O_3$: 383.1642; found: 383.1643.

(4-Ethoxy-6-fluoro-2-phenylnaphthalen-1-yl)(phenyl)methanone (3.15f, Table 3.5):



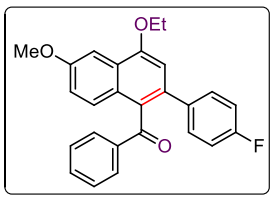
Yellow solid (yield = 69%); M.P. = 154 - 155 °C; R_f value = 0.75 in 10% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (dd, *J* = 10.4, 2.7 Hz, 1H), 7.72 (dd, *J* = 9.3, 5.3 Hz, 1H), 7.58 (dd, *J* = 4.3, 1.3 Hz, 2H), 7.39-7.34 (m, 1H), 7.34-7.30 (m, 2H), 7.25-7.15 (m, 5H), 6.88 (s, 1H), 4.29 (q, *J* = 7.0 Hz, 2H), 1.60 (t, *J* = 7.0 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 199.5, 161.8, 159.4, 154.9 (d, *J* = 20 Hz), 140.6, 138.5, 138.0, 133.1, 129.6, 129.4, 129.0, 128.23, 128.2, 127.9 (d, *J* = 34.6 Hz), 127.5, 125.9(d, *J* = 44.2 Hz), 117.7 (d, *J* = 124.4 Hz), 107.1, 106 (d, *J* = 89.6 Hz), 64.2, 14.8; IR (KBr, cm^{-1}): υ 2979, 1645, 1592, 1508, 1460, 1222, 1191, 1022, 872, 792, 715, 584; HRMS: m/z [M + Na]$^+$ Calcd for $C_{25}H_{19}FO_2Na$: 393.1261; found: 393.1261.

(4-Ethoxy-6-methoxy-2-(*p*-tolyl)naphthalen-1-yl)(phenyl)methanone (3.15g, Table 3.5):



Yellow solid (yield = 78%); M.P. = 148 - 149 °C; R_f value = 0.74 in 10% EtOAc/hexanes; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.35 (d, *J* = 8.3 Hz, 1H), 7.56 (d, *J* = 2.6 Hz, 1H), 7.51 (t, *J* = 9.3 Hz, 3H), 7.25 (t, *J* = 7.4 Hz, 1H), 7.14-7.08 (m, 4H), 7.00 (dd, *J* = 9.2, 2.6 Hz, 1H), 6.90 (d, *J* = 8.0 Hz, 2H), 6.75 (s, 1H), 4.19 (q, *J* = 6.9 Hz, 2H), 3.84 (s, 3H), 2.13 (s, 3H), 1.48 (t, *J* = 7.0 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 200.0, 157.4, 134.4, 138.6, 138.0, 136.9, 136.1, 132.9, 129.6, 129.2, 128.9, 128.1, 128.08, 127.3, 127.0, 125.8, 119.8, 107.0, 100.8, 64.0, 55.4, 21.1, 14.9; IR (KBr, cm^{-1}): υ 2917, 1651, 1593, 1506, 1384, 1280, 1219, 1052, 1024, 814, 724, 629; HRMS: m/z [M + Na]$^+$ Calcd for $C_{22}H_{24}O_3Na$: 419.1618; found: 419.1618.

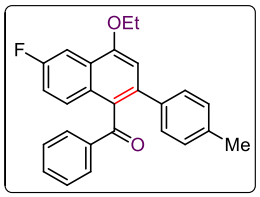
(4-Ethoxy-2-(4-fluorophenyl)-6-methoxynaphthalen-1-yl)(phenyl)methanone (3.15h, Table 3.5):



Yellow solid (yield = 70%); M.P. = 146 - 147 °C; R_f value = 0.39 in 5% EtOAc/hexanes; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65 (d, *J* = 2.7 Hz, 1H), 7.59 (d, *J* = 9.2 Hz, 1H), 7.56 (d, *J* = 7.2 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.28-7.23 (m, 2H), 7.20 (t, *J* = 7.8 Hz, 2H), 7.11 (dd, *J* = 9.2, 2.7 Hz, 1H), 6.86 (t, *J* = 8.7 Hz, 2H), 6.78 (s, 1H), 4.28 (q, *J* = 7.0 Hz, 2H), 3.94 (s, 3H), 1.59 (t, *J* = 7.0 Hz, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$): δ 199.8, 163.1, 161.1, 157.7, 154.6, 138.6, 137.01 (d, *J* = 13.3 Hz), 135.0, 133.1, 131.0 (d, *J* = 32.3 Hz), 129.6, 128.3, 127.9 (d, *J* = 556.0 Hz), 127.0,

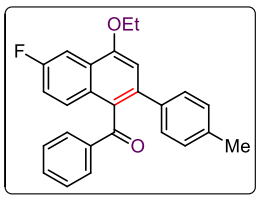
126.0, 120.1, 115.1 (d, J = 85.8 Hz), 106.8, 100.9, 64.1, 55.4, 14.9; IR (KBr, cm^{-1}): υ 2933, 1662, 1592, 1506, 1382,1218, 1163, 1051, 841, 741, 623; HRMS: m/z $[M + Na]^+$ Calcd for $C_{26}H_{21}FO_3Na$: 423.1367; found: 423.1368.

(4-Ethoxy-6-fluoro-2-(p-tolyl)naphthalen-1-yl)(phenyl)methanone (3.15i, Table 3.5):



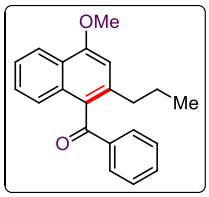
Yellow solid (yield = 73%); M.P. = 172 - 173 °C; R_f value = 0.78 in 10% EtOAc/hexanes; ^1H NMR (500 MHz, $CDCl_3$): δ 7.90 (dd, J = 10.4, 2.6 Hz, 1H), 7.61 (dd, J = 9.2, 5.4 Hz, 1H), 7.52 (d, J = 8.1 Hz, 2H), 7.28 (t, J = 7.4 Hz, 1H), 7.16-7.09 (m, 5H), 6.92 (d, J = 7.9 Hz, 2H), 6.78 (s, 1H), 4.19 (q, J = 7.0 Hz, 2H), 2.15 (s, 3H), 1.49 (t, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$): δ 199.6, 161.5, 159.5, 154.8 (d, J = 19.6 Hz), 138.4, 137.9 (d, J = 8.6 Hz), 137.7, 137.3,133.0, 129.6, 129.2, 129.0, 128.2, 128.0, 127.8 (d, J = 33.8 Hz), 125.7 (d, J = 35.7 Hz), 117.6 (d, J = 99.6 Hz), 107.3, 106.4 (d, J = 89.4 Hz), 64.1, 21.1, 14.8; IR (KBr, cm^{-1}): υ 2920, 1696, 1651, 1600, 1509, 1447, 1224, 1186, 1025, 873, 746, 713, 659; HRMS: m/z $[M + Na]^+$ Calcd for $C_{26}H_{21}FO_2Na$: 407.1418; found: 407.1417.

(4-Ethoxy-2-phenylnaphthalen-1-yl)(2-methyl-5-nitrophenyl)methanone (3.15j, Table 3.5):



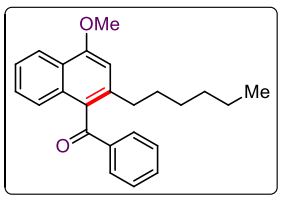
Yellow solid (yield = 35%); M.P. = 164 - 165 °C; R_f value = 0.71 in 10% EtOAc/hexanes; ^1H NMR (400 MHz, $CDCl_3$): δ 8.47-8.44 (m, 1H), 8.07-8.03 (m, 1H), 7.92 (dd, J = 8.4, 2.5 Hz, 1H), 7.83 (d, J = 2.4 Hz, 1H), 7.63-7.55 (m, 2H), 7.17-7.09 (m, 6H), 6.77 (s, 1H), 4.30 (q, J = 7.0 Hz, 2H), 2.47 (s, 3H), 1.61 (t, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 198.9, 156.5, 146.5, 145.4, 141.3, 140.8, 140.2, 132.2, 129.0, 128.5, 128.2, 127.9, 127.7, 125.9, 125.4, 125.2, 125.0, 124.8, 122.6, 106.2, 64.2, 29.7, 21.4, 14.8; IR (KBr, cm^{-1}): υ 2926, 1655, 1509, 1340, 1216, 1092, 750, 638; HRMS: m/z $[M + H]^+$ Calcd for $C_{26}H_{22}FO_2$: 412.1543; found: 412.1543.

(4-Methoxy-2-propylnaphthalen-1-yl)(phenyl)methanone (3.15k, Scheme 3.5):



Yellow solid (yield = 76%); M.P. = 133 - 134 °C; R_f value = 0.72 in 10% EtOAc/hexanes; ^1H NMR (400 MHz, $CDCl_3$): δ 8.27 (d, J = 7.8 Hz, 1H), 7.82 (d, J = 7.1 Hz, 2H), 7.59-7.53 (m, 1H), 7.44-7.32 (m, 5H), 6.73 (s, 1H), 4.06 (s, 3H), 2.54 (t, J = 7.8 Hz, 2H), 1.68-1.59 (m, 2H), 0.86 (t, J = 7.3 Hz, 2H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 200.4, 156.0, 138.5, 138.2, 133.6, 131.9, 129.8, 128.7, 128.3, 127.2, 125.0, 124.8, 124.0, 122.1, 105.2, 55.6, 36.4, 24.6, 14.2; IR (KBr, cm^{-1}): υ 2952, 1657, 1619, 1591, 1448, 1250, 1115, 903, 769, 613; HRMS: m/z $[M + Na]^+$ Calcd for $C_{21}H_{20}O_2Na$: 327.1356; found: 327.1355.

(2-Hexyl-4-methoxynaphthalen-1-yl)(phenyl)methanone (3.15l, Scheme 3.5):



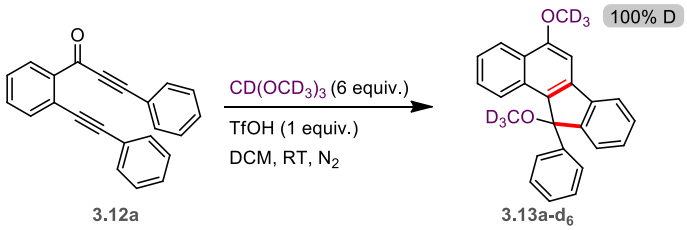
Yellow solid (yield = 89.3%); M.P. = 156 - 157 °C; R_f value = 0.66 in 5% EtOAc/hexanes; ^1H NMR (500 MHz, $CDCl_3$): δ 8.27 (d, J = 8.6 Hz, 1H), 7.82 (d, J = 7.2 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.44-7.39 (m, 4H), 7.37-7.33 (m, 1H), 6.73 (s, 1H), 4.06 (s, 3H), 2.55 (t, J = 8.0 Hz, 2H), 1.61-1.54 (m, 3H), 1.26-1.16 (m, 5H), 0.82 (t, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 200.4, 156.0, 138.5, 138.4, 133.5, 131.9, 129.8, 128.7, 128.2, 127.2, 124.9, 124.8,

123.9, 122.1, 105.1, 55.6, 34.4, 31.5, 31.3, 29.2, 22.5, 14.1; IR (KBr, cm^{-1}): υ 2924, 1663, 1582, 1376, 1242, 1107, 718, 688; HRMS: m/z $[M + H]^+$ Calcd for $C_{24}H_{27}O_2$: 347.2006; found: 347.2006.

3.4.7. Synthesis and Characterization of Deuterated Benzo[*a*]fluorene (3.13a-d_6) and Deuterated Naphthyl Ketone Derivative (3.15a-d_3):

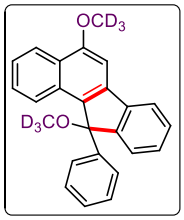
3.4.7.1. Synthesis and Characterization of Deuterated Benzo[*a*]fluorene (3.13a-d_6):

To a solution of aryl-fused 1,6-diyn-3-ones **3.12a** (1.0 equiv.) in dichloromethane solvent (5 mL/mmol), $CD(OCD_3)_3$ (6 equiv.) followed by triflic acid (1 equiv.) were charged at room temperature (25 °C) under nitrogen atmosphere. The reaction mixture was allowed to stir at room temperature under nitrogen atmosphere for 4 hours. After that, it was quenched with a saturated $NaHCO_3$ solution. Then it was extracted using ethyl acetate. The combined organic layers were washed with saturated brine solution and dried over anhydrous Na_2SO_4. The solvents were evaporated under reduced pressure. The crude product was purified by column chromatography (using silica gel, EtOAc/hexanes eluent) to get pure deuteriated benzo[*a*]fluorene **3.13a-d_6** in 56% isolated yield.



Scheme 3.17. Synthesis of deuteriated benzo[*a*]fluorene **3.13a-d_6**.

5,11-Dimethoxy-11-phenyl-11*H*-benzo[*a*]fluorene (3.13a-d_6, Scheme 3.9):

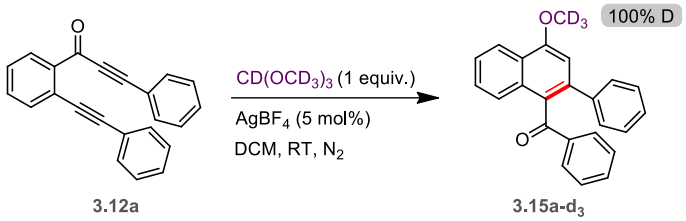


Yellow gummy (yield = 56%); R_f value = 0.58 in 5% EtOAc/hexanes; ^1H NMR (400 MHz, $CDCl_3$): δ 8.34 (d, *J* = 6.8 Hz, 1H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.75 (d, *J* = 7.5 Hz, 1H), 7.45-7.39 (m, 4H), 7.33 (d, *J* = 8.6 Hz, 1H), 7.29 (d, *J* = 5.1 Hz, 1H), 7.27-7.25 (m, 2H), 7.24-7.19 (m, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 157.7, 149.4, 143.5, 140.9, 139.7, 132.6, 130.7, 128.6, 128.2, 127.7, 127.4, 126.9, 125.9, 125.4, 124.9, 124.4, 124.35, 123.0, 119.4, 96.3, 89.8; IR (KBr, cm^{-1}): υ 2922, 1583, 1446, 1110, 757, 698; HRMS: m/z $[M + Na]^+$ Calcd for $C_{25}H_{14}D_6O_2Na$: 381.1732; found: 381.1736.

3.4.7.2. Synthesis and Characterization of Deuterated Naphthyl Ketone Derivative (3.15a-d_3):

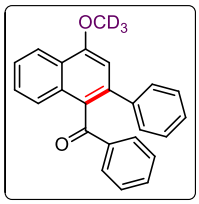
To a solution of aryl-fused 1,6-diyn-3-ones **3.12a** (1.0 equiv.) in dichloromethane solvent (5 mL/mmol), $CD(OCD_3)_3$ (1.0 equiv.) followed by $AgBF_4$ (5 mol%) were charged at room temperature (25 °C) under nitrogen atmosphere. The reaction mixture was allowed to stir at room temperature under nitrogen atmosphere for 24 hours. The progress of the reaction was monitored by TLC. After that, solvent was removed under reduced pressure and the deuteriated naphthyl

ketone **3.15a-d$_3$** was isolated (77%) by column chromatography (using silica gel, EtOAc/hexanes eluent).



Scheme 3.18. Synthesis of deuteriated naphthyl ketone **3.15a-d$_3$**.

(4-Methoxy-2-phenylnaphthalen-1-yl)(phenyl)methanone (3.15a-d$_3$, Scheme 3.9):

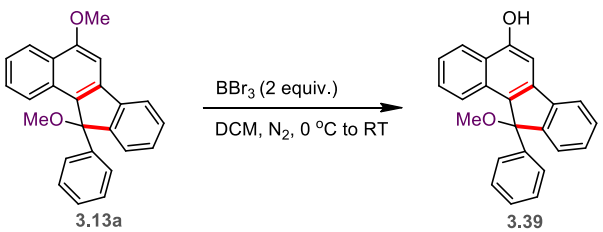


Off-white solid (yield = 77%); M.P. = 227 - 228 °C; R_f value = 0.49 in 5% EtOAc/hexanes; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.38 (d, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 8.1 Hz, 1H), 7.63 (d, *J* = 7.1 Hz, 2H), 7.57-7.53 (m, 1H), 7.53-7.46 (m, 2H), 7.40-7.36 (m, 3H), 7.25-7.20 (m, 3H), 7.20-7.15 (m, 1H), 6.89 (s, 1H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 199.8, 156.1, 140.8, 138.6, 134.7, 132.9, 132.0, 129.6, 129.4, 128.8, 128.2, 127.8, 127.5, 125.7, 125.3, 124.6, 122.2, 120.7, 118.8, 105.6; IR (KBr, cm^{-1}): υ 2922, 1658, 1580, 1499, 1390, 1225, 1101, 773, 693, 610; HRMS: m/z [M + Na]$^+$ Calcd for $C_{24}H_{15}D_3O_2Na$: 364.1387; found: 364.1386.

3.4.8. Synthesis and Characterization of Benzo[*a*]fluorenol (3.39) and Benzo[*a*]fluorenone Derivatives (3.40):

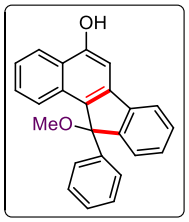
3.4.8.1. Synthesis and Characterization of Benzo[*a*]fluorenol (3.39):

To a solution of benzo[*a*]fluorene **3.13a** (1 equiv.) in CH_2Cl_2 (5 mL/mmol) solvent under nitrogen atmosphere at 0 °C, BBr_3 (2 equiv., 1M BBr_3 in CH_2Cl_2) was added and allowed the reaction for stirring at room temperature for 3 hours. Then the reaction mixture was quenched using saturated $NaHCO_3$ solution and extracted with EtOAc. After that the combined organic layer was washed with saturated NaCl solution and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure and finally, the crude product was purified by column chromatography (silica gel, hexanes/EtOAc) to get pure 11-methoxy-11-phenyl-11*H*-benzo[*a*]fluoren-5-ol **3.39** (68%).



Scheme 3.19. Synthesis of benzo[*a*]fluorenol **3.39**.

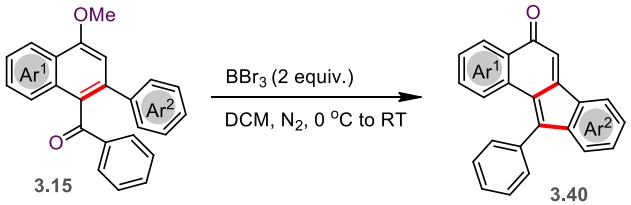
11-Methoxy-11-phenyl-11*H*-benzo[*a*]fluoren-5-ol (3.39, Scheme 3.10):



Red solid (yield = 68%); M.P. = 212 - 213 °C; R_f value = 0.20 in 5% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 (d, *J* = 7.7 Hz, 1H), 7.75 (d, *J* = 7.5 Hz, 1H), 7.68 (d, *J* = 7.5 Hz, 1H), 7.41(d, *J* = 6.8 Hz, 2H), 7.38-7.31 (m, 5H), 7.24 (d, *J* = 7.5 Hz, 2H), 7.21 (s, 1H), 7.17 (s, 1H), 4.13 (s, 3H), 2.49 (bs, 1H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 157.7, 152.8, 143.1, 139.7, 138.3, 136.0, 130.1, 128.7, 128.4, 128.0, 127.3, 127.0, 126.2, 125.1, 124.9, 124.5, 124.0, 123.1, 119.6, 96.4, 84.2, 55.9; IR (KBr, cm^{-1}): υ 2923, 1661, 1584, 1448, 1219, 1141, 756, 699; HRMS: m/z [M - H]$^+$ Calcd for $C_{24}H_{17}O_2$: 337.1229; found: 337.1225.

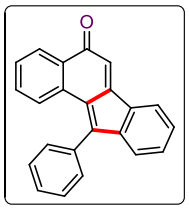
3.4.8.2. Synthesis and Characterization of Benzo[*a*]fluorenone Derivatives (3.40):

To a solution of naphthyl ketone (**3.15**) (1 equiv.) in CH_2Cl_2 (5 mL/mmol) solvent under nitrogen atmosphere at 0 °C, BBr_3 (2equiv., 1M BBr_3 in CH_2Cl_2) was added and allowed the reaction for stirring at room temperature. Completion of the reaction was monitored by TLC and the reaction mixture was quenched using saturated $NaHCO_3$ solution and extracted with EtOAc. After that the combined organic layer was washed with saturated NaCl solution and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure and finally, the crude product was purified by column chromatography (silica gel, hexanes/EtOAc) to get pure benzo[*a*]fluorenone derivatives **3.40**.



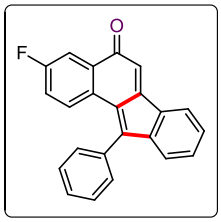
Scheme 3.20. Synthesis of benzo[*a*]fluorenone **3.40**.

11-Phenyl-5*H*-benzo[*a*]fluoren-5-one (3.40a, Scheme 3.10):



Dark red solid (yield = 57%); M.P. = 190 - 191 °C; R_f value = 0.31 in 10% EtOAc/hexanes; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.02 (d, *J* = 7.8 Hz, 1H), 7.52-7.48 (m, 2H), 7.47-7.43 (m, 2H), 7.42-7.39 (m, 2H), 7.22-7.18 (m, 2H), 7.14-7.09 (m, 3H), 6.80 (s, 2H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$): δ 186.5, 153.0, 149.0, 146.1, 135.8, 134.4, 133.5, 132.3, 130.9, 130.5, 129.4, 129.2, 128.2, 127.9, 127.6, 125.2, 122.4, 122.0, 121.3; IR (KBr, cm^{-1}): υ 2921, 1583, 1446, 1374, 1217, 1096, 1026, 741, 700; HRMS: m/z [M + H]$^+$ Calcd for $C_{23}H_{15}O$: 307.1117; found: 307.1118.

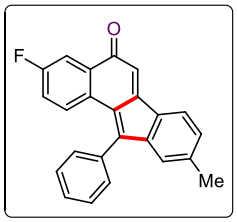
3-Fluoro-11-phenyl-5*H*-benzo[*a*]fluoren-5-one (3.40b, Scheme 3.10):



Dark red solid (yield = 56%); M.P. = 216 - 217 °C; R_f value = 0.51 in 10% EtOAc/hexanes; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.56-7.48 (m, 3H), 7.46-7.44 (m, 1H), 7.42 (d, *J* = 8.1 Hz, 2H), 7.23-7.18 (m, 1H), 7.13 (dd, *J* = 5.3, 3.1 Hz, 2H), 6.88-6.81 (m, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 185.4, 163.2, 161.2, 153.4, 149.0, 145.9, 135.5, 134.0, 132.6 (d, *J* =

6.8 Hz), 131.0, 129.8 (d, *J* = 3.4 Hz), 129.4, 129.3, 128.4, 128.2, 127.4 (d, *J* = 7.2 Hz), 127.1, 122.5, 122.1, 121.0, 119.8 (d, *J* = 22.3 Hz), 113.6 (d, *J* = 22.7 Hz); IR (KBr, cm^{-1}): υ 2920, 1627, 1553, 1439, 1303, 1272, 1049, 758, 700, 576; HRMS: m/z $[M + H]^+$ Calcd for $C_{23}H_{14}FO$: 325.1023; found: 325.1022.

3-Fluoro-9-methyl-11-phenyl-5*H*-benzo[*a*]fluoren-5-one (3.40c, Scheme 3.10):



Dark red solid (yield = 59%); M.P. = 222 - 223 °C; R_f value = 0.47 in 10% EtOAc/hexanes; ^1H NMR (500 MHz, $CDCl_3$): δ 7.73 (dd, *J* = 9.3, 2.9 Hz, 1H), 7.62-7.53 (m, 3H), 7.47-7.43 (m, 2H), 7.36 (d, *J* = 7.4 Hz, 1H), 7.20 (dd, *J* = 8.9, 5.2 Hz, 1H), 6.95 (d, *J* = 7.5 Hz, 1H), 6.91-6.85 (m, 1H), 6.79 (s, 1H), 6.65 (s, 1H), 2.26 (s, 3H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 185.4, 163.4, 160.9, 153.5, 148.9, 146.2, 141.6, 134.2, 132.7, 132.6 (d, *J* = 5.9 Hz), 129.9, 129.4, 129.3, 128.7, 128.2, 127.3 (d, *J* = 7.3 Hz), 123.6, 122.1, 120.4, 119.7 (d, *J* = 22.7 Hz), 113.5 (d, *J* = 22.7 Hz), 21.8; IR (KBr, cm^{-1}): υ 2919, 1629, 1601, 1476, 1262, 921, 697; HRMS: m/z $[M + H]^+$ Calcd for $C_{24}H_{16}FO$: 339.1180; found: 339.1178.

3.4.9. *X*-ray *C*rystallography:

Single crystal X-ray data for the compound **3.13f**, **3.14b**, **3.15b** and **3.15k** were collected using the detector system [λ (Mo-Kα) = 0.71073 Å] at 293K, graphite monochromator with a ω scan width of 0.3o, crystal-detector distance 60 mm, collimator 0.5 mm. The SMART software[15] was used for the intensity data acquisition and the SAINTPLUS Software[16] was used for the data extraction. In each case, absorption correction was performed with the help of SADABS program,[15] an empirical absorption correction using equivalent reflections was performed with the program. The structure was solved using SHELXS-97[16] and full-matrix least-squares refinement against F2 was carried out using SHELXL-97.[16] All non-hydrogen atoms were refined anisotropically. Aromatic and methyl hydrogens were introduced on calculated positions and included in the refinement riding on their respective parent atoms.

Crystallographic data (including the structure factor) for the structures **3.13f**, **3.14b**, **3.15b** and **3.15k** in this paper have been deposited in the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 1998442, 1998443, 1998444 and 1998445. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

3.4.9.1. *X*-ray *C*rystal *S*tructure and *D*ata for *B*enzo[*a*]fluorene *D*erivative (3.13f):

Table 3.6. Crystallographic data for compound **3.13f**.

CCDC Number	1998442
Compound identification code	ss
Empirical formula	C26 H22 O3
Formula weight	382.44
Temperature	298 K
Wavelength	0.71073 Å

Crystal system	Orthorombic
Space group	P b c a
Unit cell dimensions	a=9.5559(16) alpha=90 b=21.991(5) beta=90 c=23.251(5) gamma=90
Volume	4886.1(17)Å^3
Z	8
Density (calculated)	1.040g/cm^3
Absorption coefficient	0.067 mm^{-1}
F(000)	1616.0
Reflections collected	5624
Independent reflections	2588
Completeness to theta = 27.539°	0.996
Refinement method	Full-matrix least-squares on F2
Max. and min. transmission	0.988 and 0.987
Goodness-of-fit on F2	1.083
R(reflections)	0.1337(2588)
wR2(reflections)	0.3796(5604)
Diffractometer	Xcalibur Gemini Eos CCD

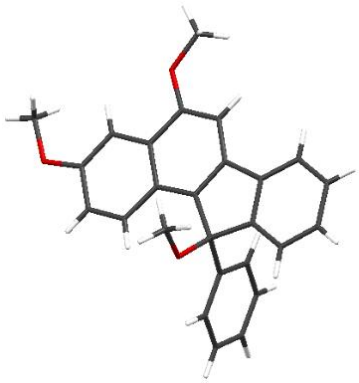


Figure 3.9. ORTEP-drawing of compound **3.13f**.

3.4.9.2. *X*-ray *C*rystal *S*tructure and *D*ata for *B*enzo[*b*]fluorenone *D*erivative (3.14b):

Table 3.7. Crystallographic data for compound **3.14b**.

CCDC Number	1998443
Compound identification code	rb 51A
Empirical formula	C24 H16 O
Formula weight	320.37
Temperature	297 K
Wavelength	0.71073 Å

Crystal system	Monoclinic
Space group	P 21/n
Unit cell dimensions	a=12.3849(7) alpha=90 b=6.9466(6) beta= 96.279(3) c=19.3338(16) gamma=90
Volume	1653.4(2) Å3
Z	4
Density (calculated)	1.287 g/cm3
Absorption coefficient	0.077 mm-1
F(000)	672.0
Reflections collected	3393
Independent reflections	2274
Completeness to theta = 25.082 °	0.981
Refinement method	Full-matrix least-squares on F2
Max. and min. transmission	0.986 and 0.984
Goodness-of-fit on F2	1.069
R(reflections)	0.0555 (2274)
wR2(reflections)	0.1411(3330)
Diffractometer	Xcalibur Gemini Eos CCD

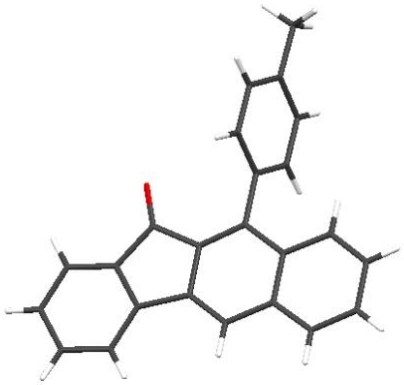


Figure 3.10. ORTEP-drawing of compound **3.14b**.

3.4.9.3. X-ray Crystal Structure and Data for Naphthyl Ketone Derivative (3.15b):

Table 3.8. Crystallographic data for compound **3.15b**.

CCDC Number	1998444
Compound identification code	rb 80a
Empirical formula	C25 H20 O2
Formula weight	352.41
Temperature	298 K
Wavelength	0.71073 Å
Crystal system	Monoclinic

Space group	P 21/n
Unit cell dimensions	a= 12.0254(19) alpha=90 b= 11.2730(19) beta= 102.398(5) c= 14.254(2) gamma=90
Volume	1887.2(5) Å3
Z	4
Density (calculated)	1.240 g/cm3
Absorption coefficient	0.077 mm-1
F(000)	644.0
Reflections collected	3621
Independent reflections	3097
Completeness to theta = 25.026 °	0.980
Refinement method	Full-matrix least-squares on F2
Max. and min. transmission	0.985 and 0.984
Goodness-of-fit on F2	1.043
R(reflections)	0.0419(3097)
wR2(reflections)	0.1186(3549)
Diffractometer	Xcalibur Gemini Eos CCD

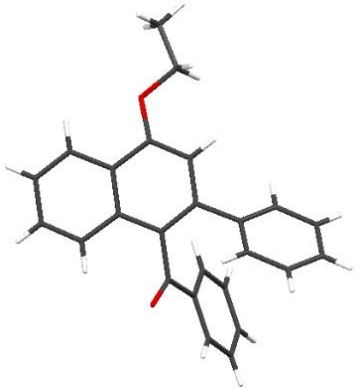


Figure 3.11. ORTEP-drawing of compound **3.15b**.

3.4.9.4. X-ray Crystal Structure and Data for Naphthyl Ketone Derivative (3.15k):

Table 3.9. Crystallographic data for compound **3.15k**.

CCDC Number	1998445
Compound identification code	rb 8
Empirical formula	C21 H20 O2
Formula weight	304.37
Temperature	273 K
Wavelength	0.71073 Å
Crystal system	Monoclinic

Space group	P 2/c
Unit cell dimensions	a= 14.769(5) alpha=90 b= 8.044(3) beta= 114.118(3) c= 15.742(5) gamma=90
Volume	1706.9(10) Å3
Z	4
Density (calculated)	1.184 g/cm3
Absorption coefficient	0.075 mm-1
F(000)	648.0
Reflections collected	4064
Independent reflections	3013
Completeness to theta = 25.025°	0.954
Refinement method	Full-matrix least-squares on F2
Max. and min. transmission	0.987 and 0.984
Goodness-of-fit on F2	1.039
R(reflections)	0.0565(3013)
wR2(reflections)	0.1612(3879)
Diffractometer	Xcalibur Gemini Eos CCD

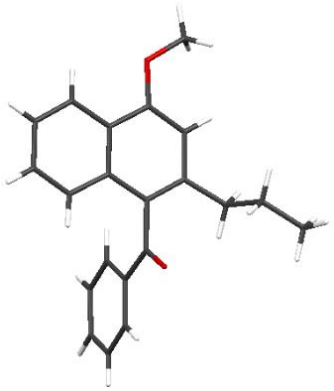


Figure 3.12. ORTEP-drawing of compound **3.15k**.

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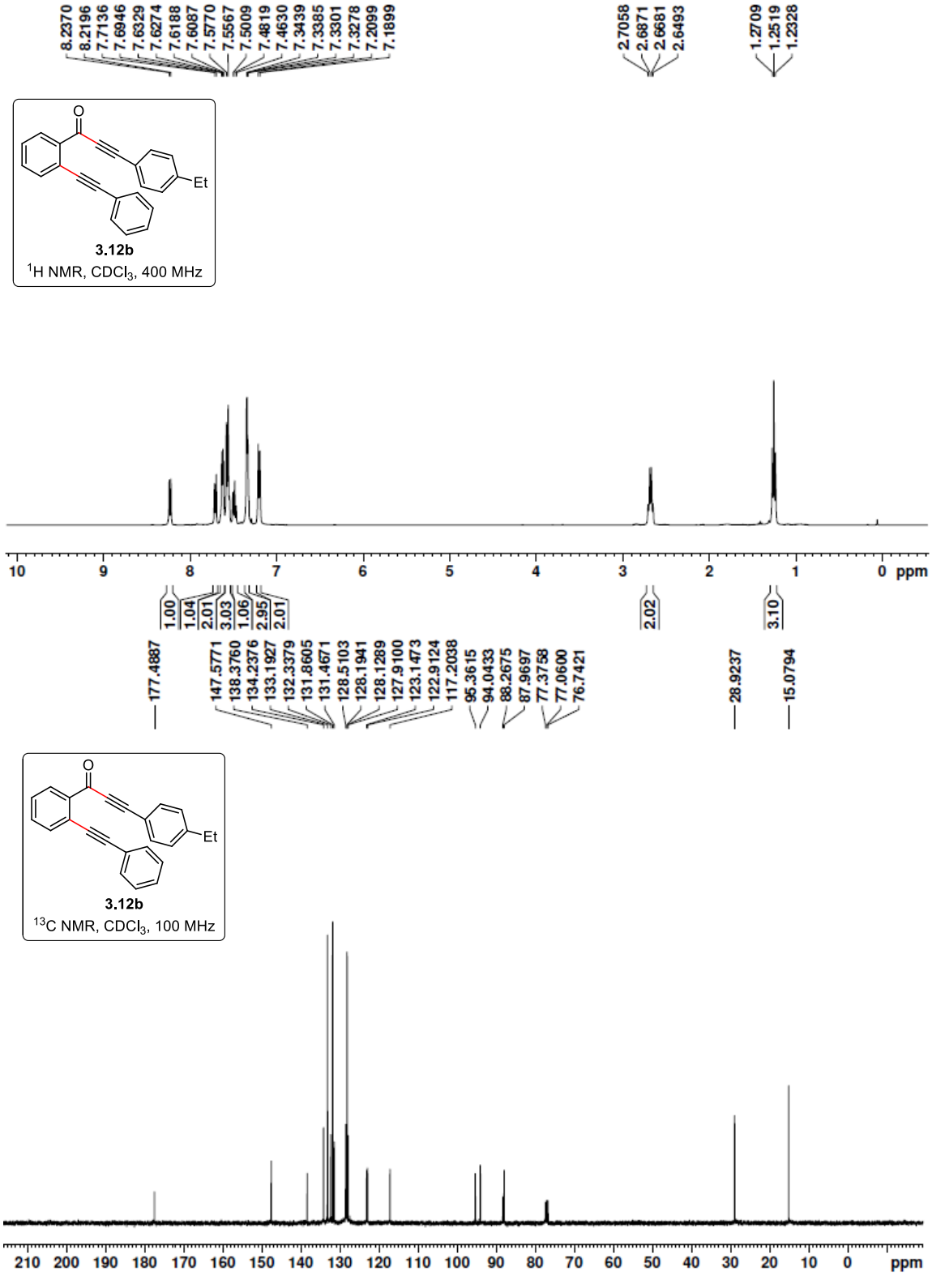
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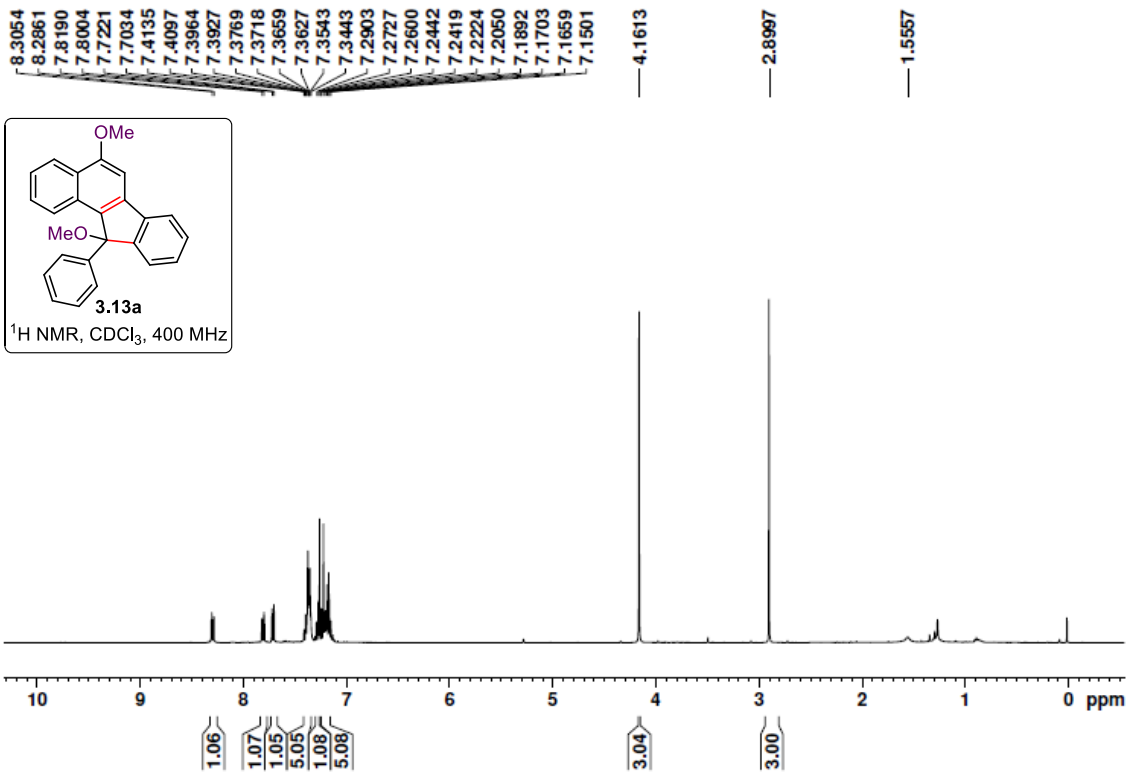
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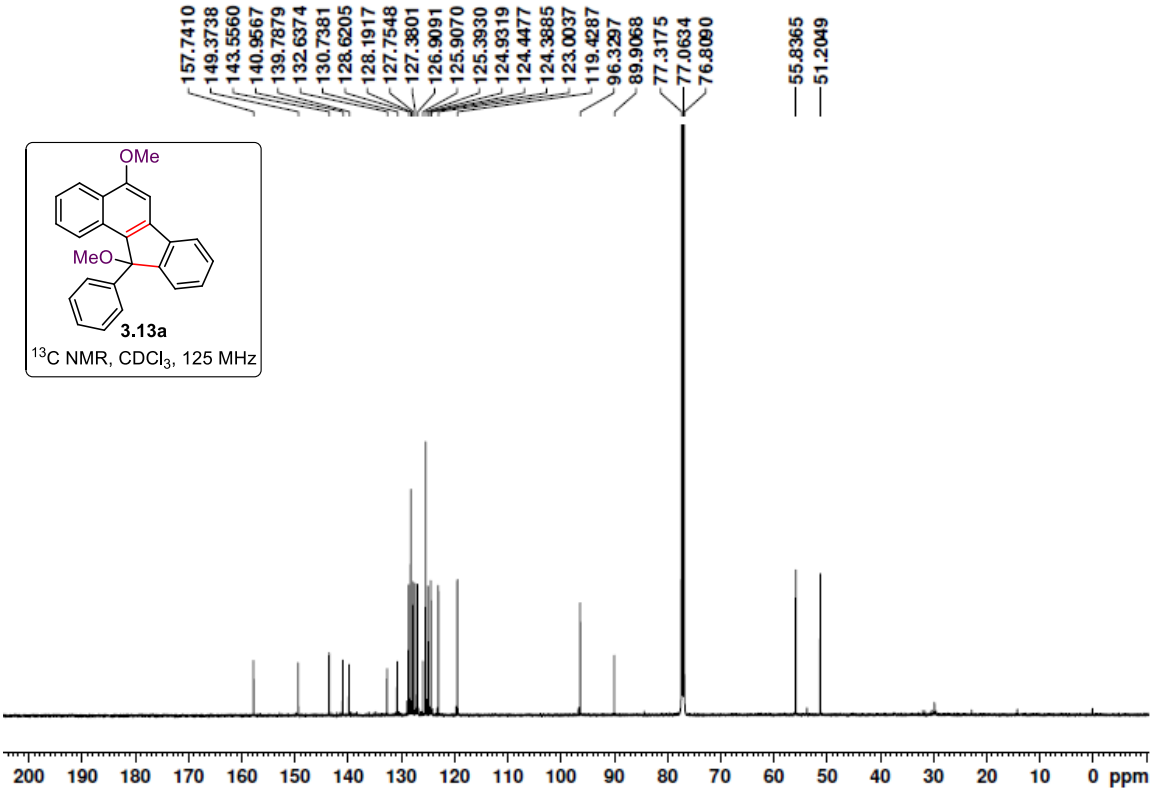
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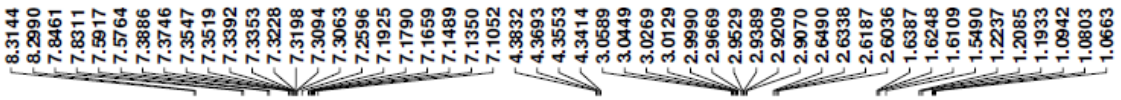
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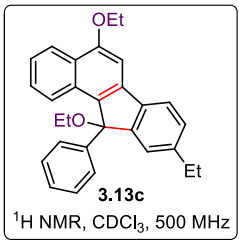
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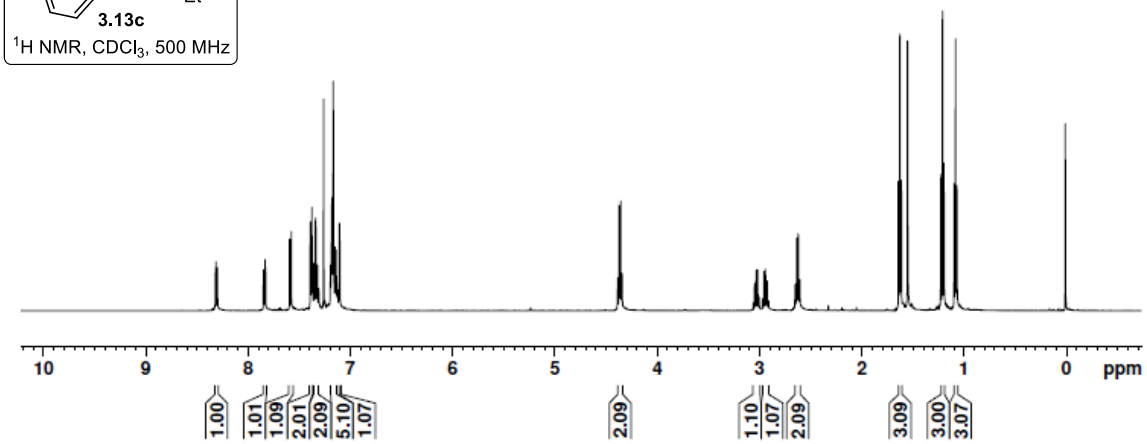


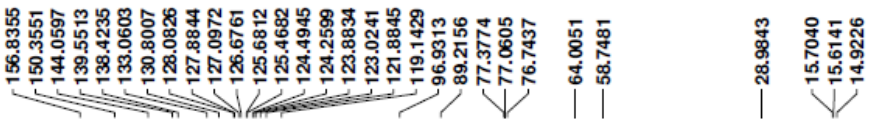

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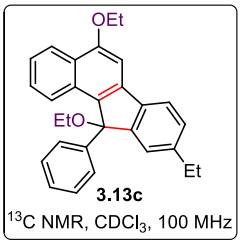

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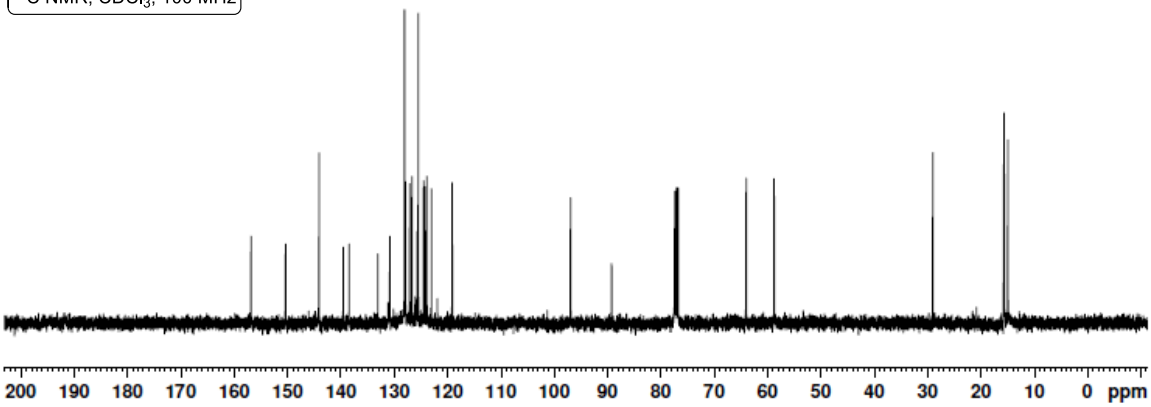

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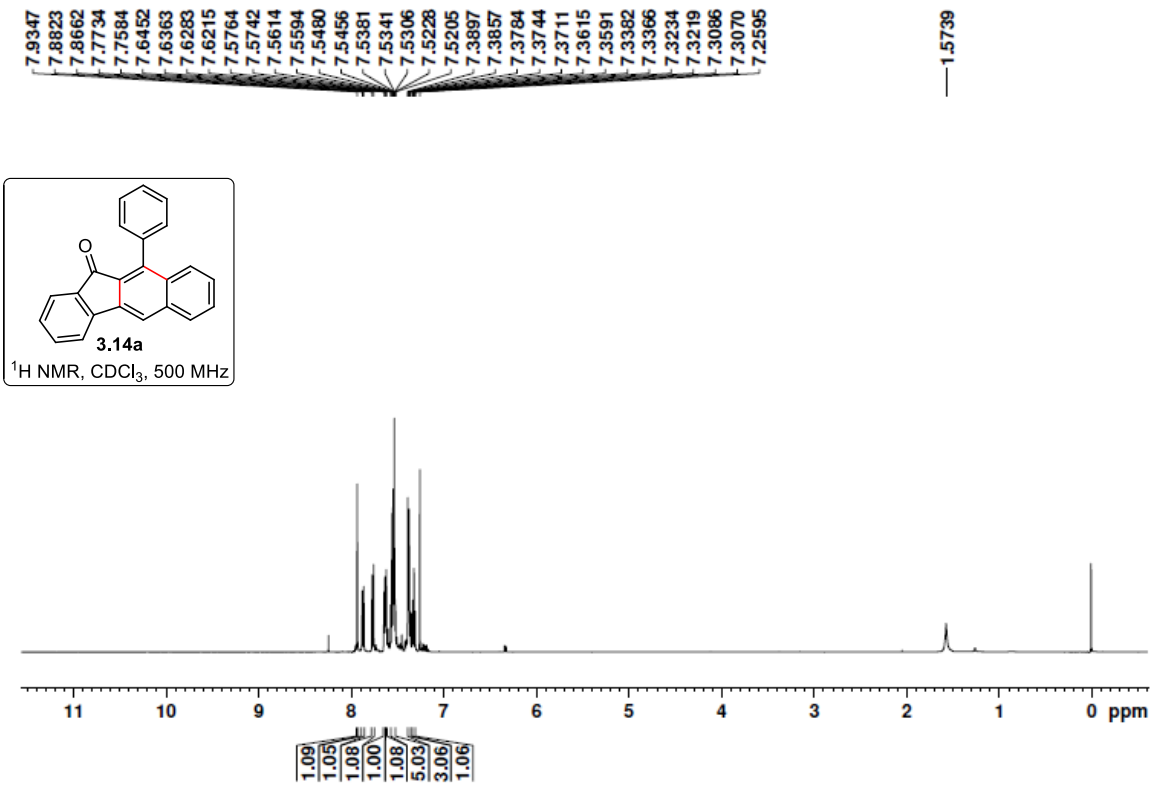

OEt
EtO
Et
3.13c
^{1}H NMR, $CDCl_3$, 500 MHz

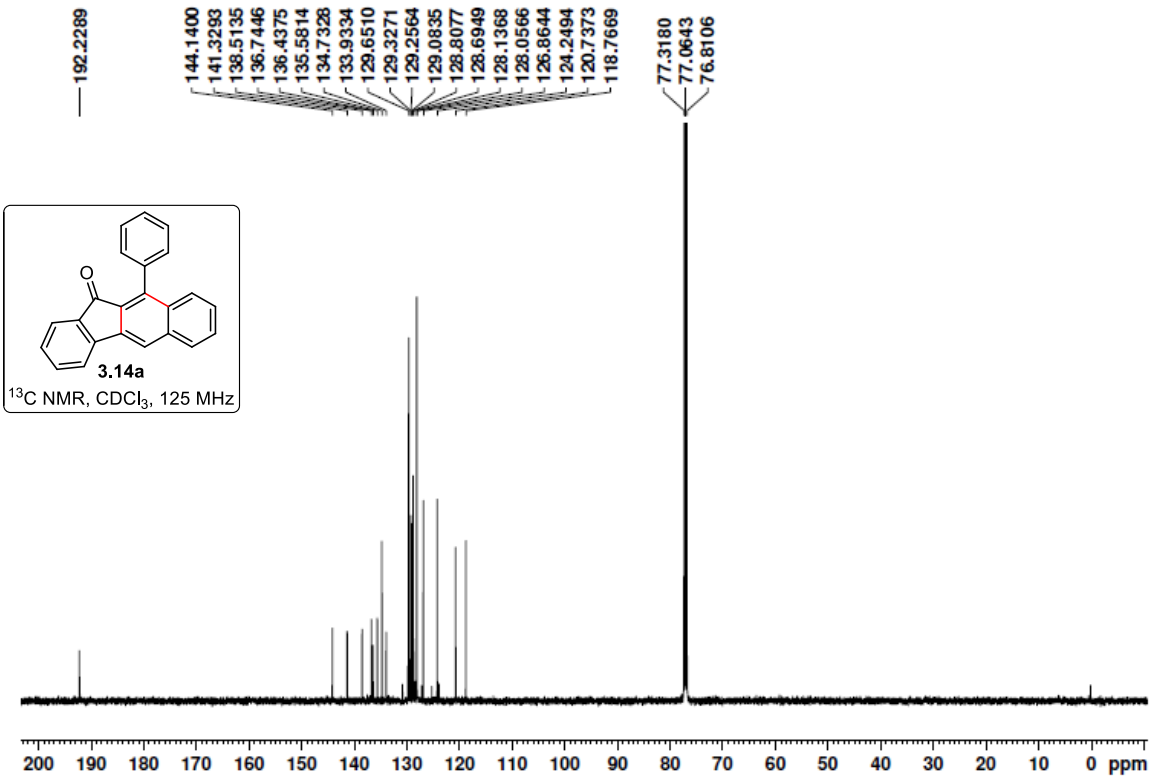

10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.01
1.09
2.01
2.09
5.10
1.07
2.09
1.10
1.07
2.09
3.09
3.00
3.07

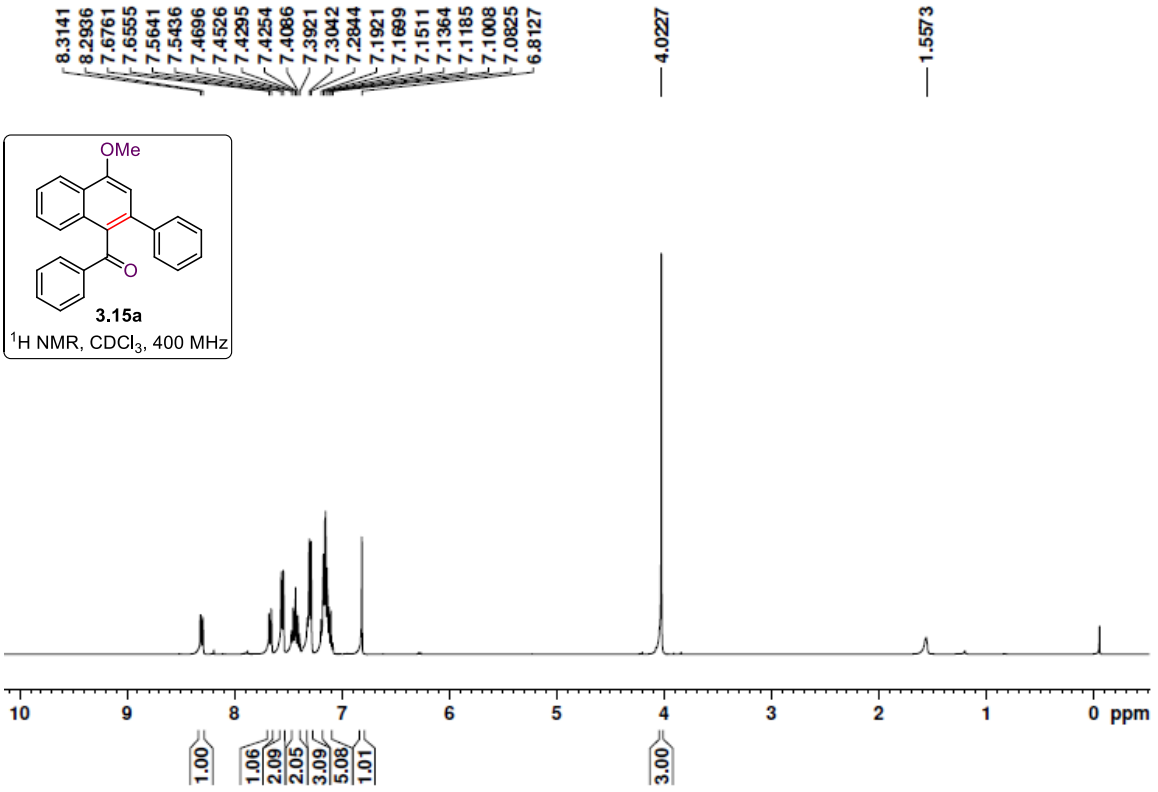

156.8355
150.3551
144.0597
139.5513
138.4235
133.0603
130.8007
128.0826
127.8844
127.0972
126.6761
125.6812
125.4682
124.4945
124.2599
123.8834
123.0241
121.8845
119.1429
96.9313
89.2156
77.3774
77.0605
76.7437
64.0051
58.7481
28.9843
15.7040
15.6141
14.9226

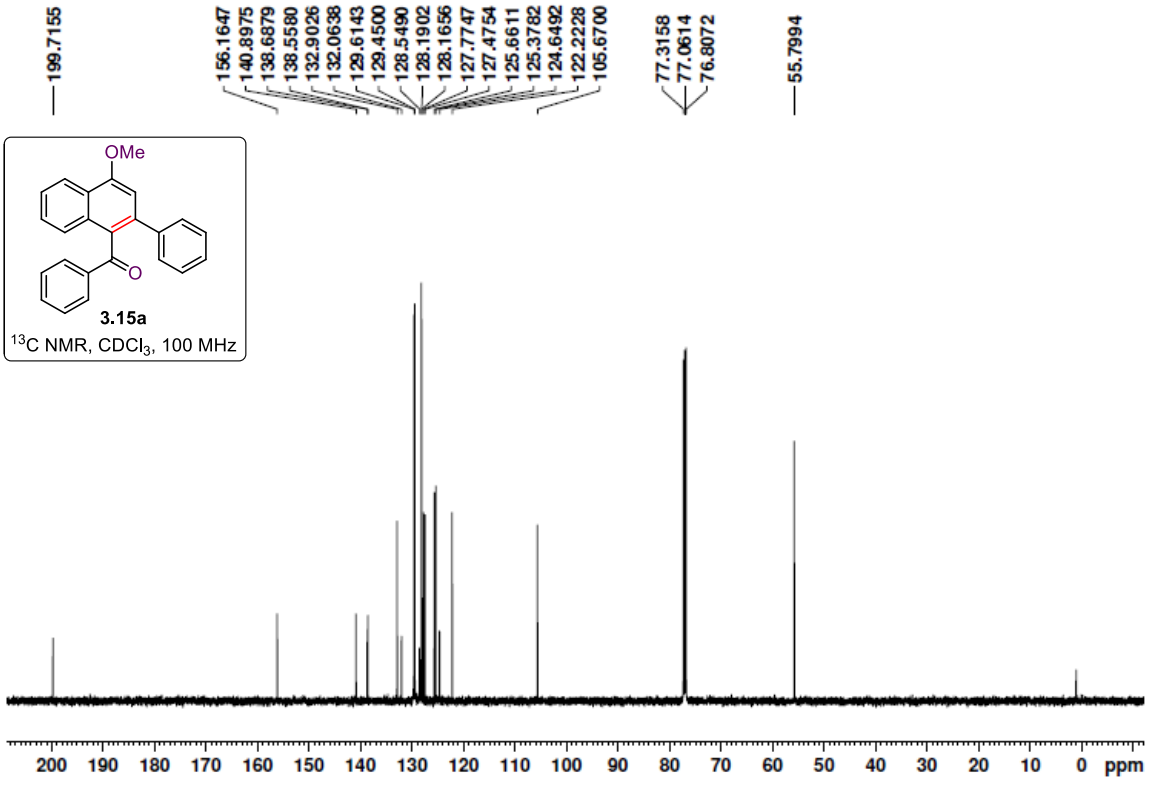

OEt
EtO
Et
3.13c
^{13}C NMR, $CDCl_3$, 100 MHz


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


7.9347
7.8823
7.8662
7.7734
7.7584
7.6452
7.6363
7.6283
7.6215
7.5764
7.5742
7.5614
7.5594
7.5480
7.5456
7.5381
7.5341
7.5306
7.5228
7.5205
7.3897
7.3857
7.3784
7.3744
7.3711
7.3615
7.3591
7.3382
7.3366
7.3234
7.3219
7.3086
7.3070
7.2595
1.5739
3.14a
1H NMR, CDCl3, 500 MHz
11
10
9
8
7
6
5
4
3
2
1
0 ppm
1.09
1.05
1.08
1.00
1.08
5.03
3.06
1.06


192.2289
144.1400
141.3293
138.5135
136.7446
136.4375
135.5814
134.7328
133.9334
129.6510
129.3271
129.2564
129.0835
128.8077
128.6949
128.1368
128.0566
126.8644
124.2494
120.7373
118.7669
77.3180
77.0643
76.8106
3.14a
13C NMR, CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm

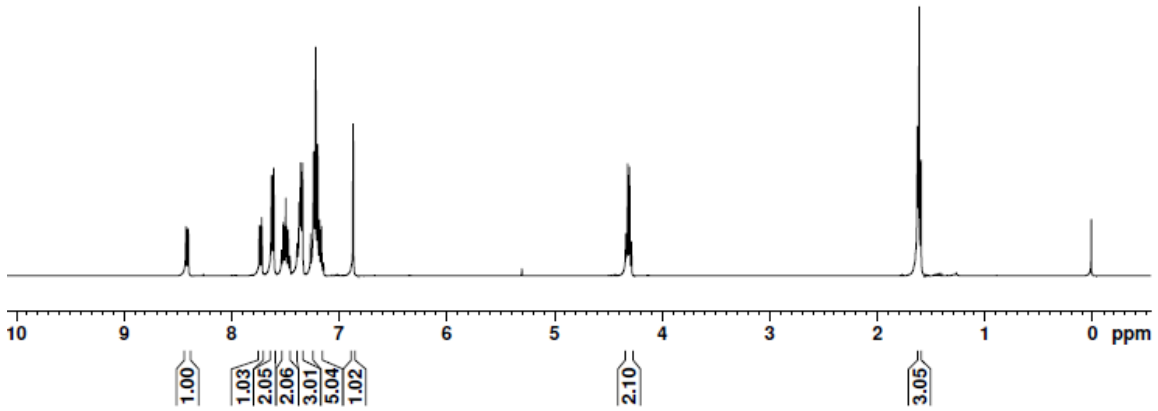

8.3141
8.2936
7.6761
7.6555
7.5641
7.5436
7.4696
7.4526
7.4295
7.4254
7.4086
7.3921
7.3042
7.2844
7.1921
7.1699
7.1511
7.1364
7.1185
7.1008
7.0825
6.8127
4.0227
1.5573
OMe
O
3.15a
^{1}H NMR, CDCl$_3$, 400 MHz
10
9
8
7
6
5
4
3
2
1
0 ppm
1.00
1.06
2.09
2.05
3.09
5.08
1.01
3.00

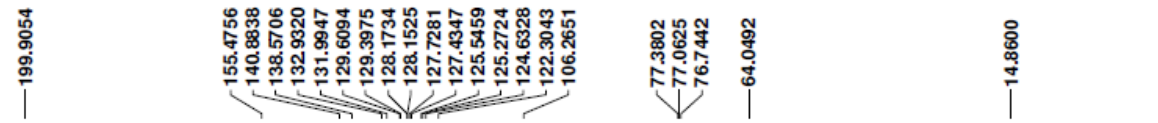

199.7155
156.1647
140.8975
138.6879
138.5580
132.9026
132.0638
129.6143
129.4500
128.5490
128.1902
128.1656
127.7747
127.4754
125.6611
125.3782
124.6492
122.2228
105.6700
77.3158
77.0614
76.8072
55.7994
OMe
O
3.15a
^{13}C NMR, CDCl$_3$, 100 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm

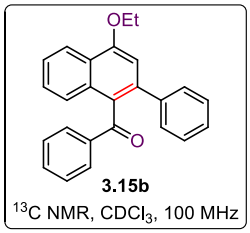


3.15b

^{1}H NMR, $CDCl_3$, 400 MHz

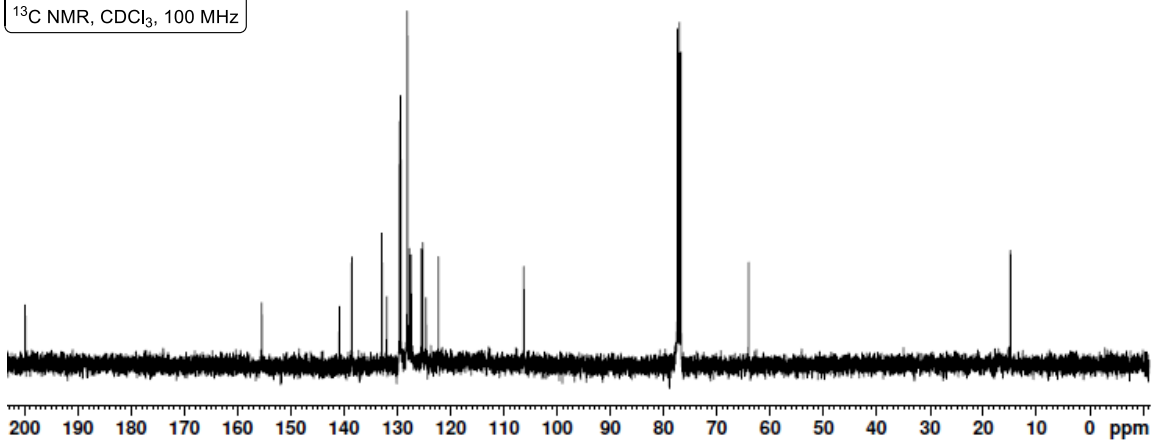


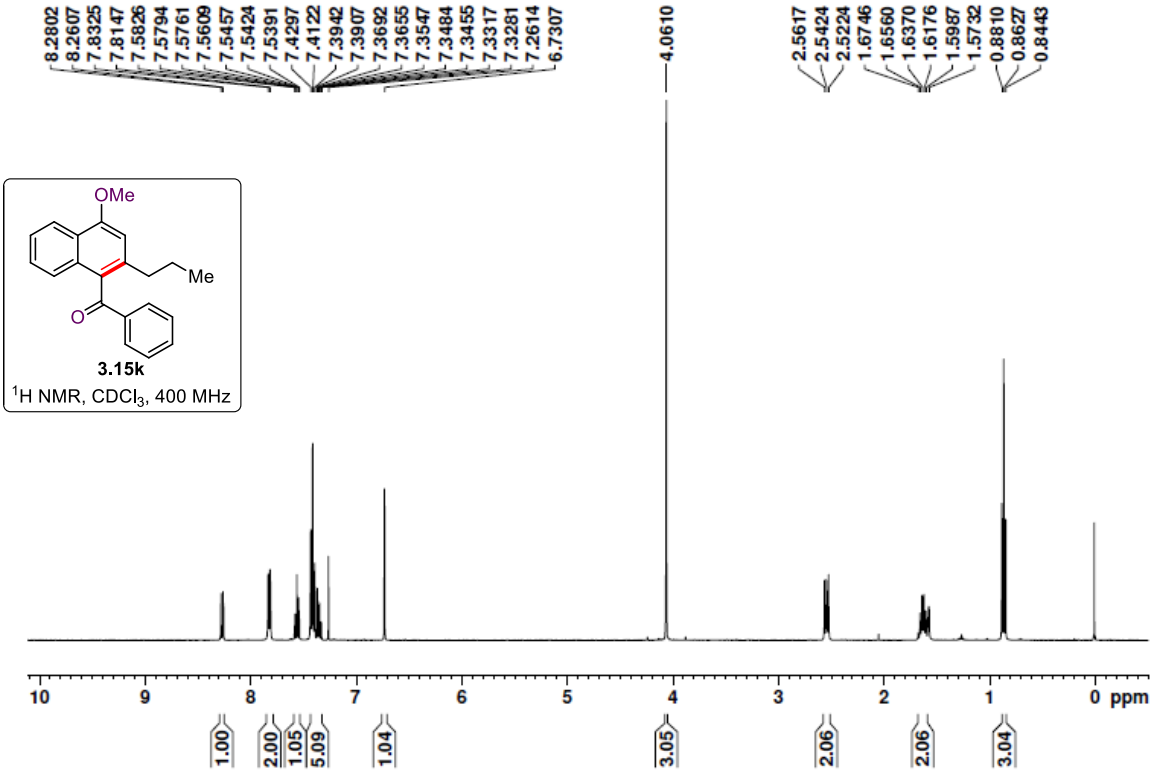


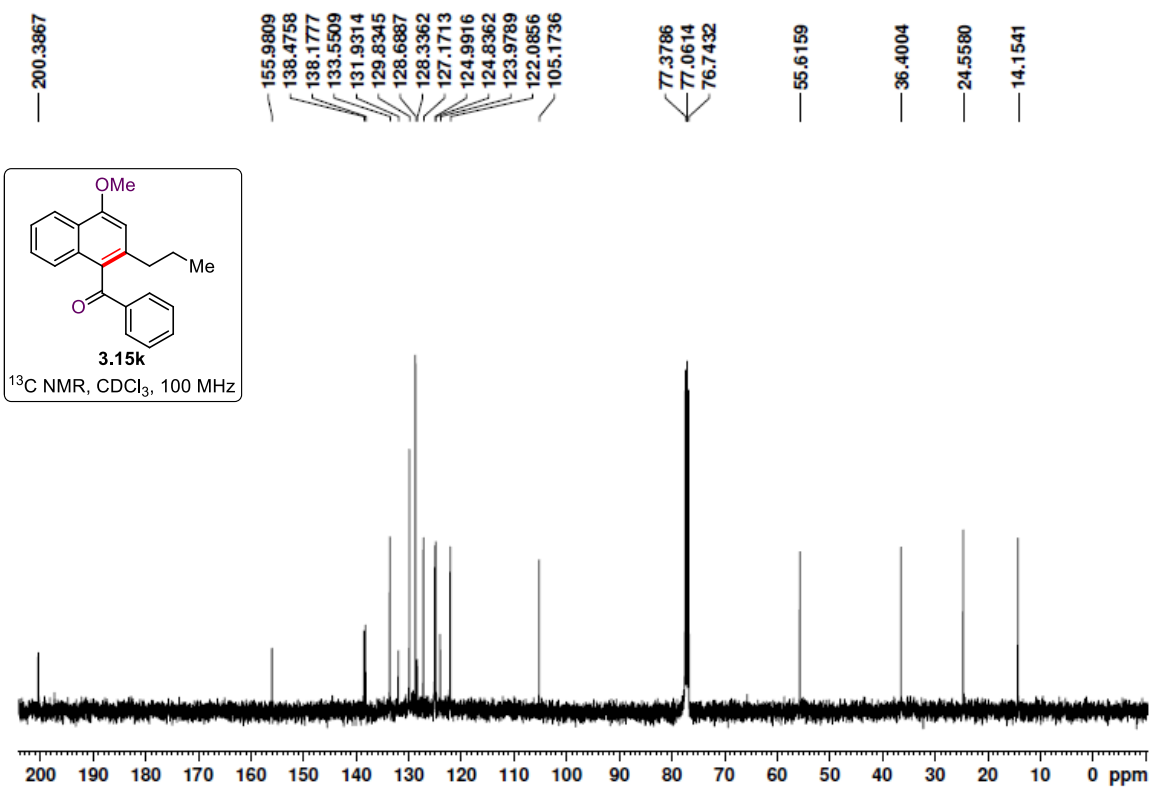


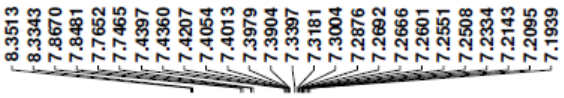
3.15b

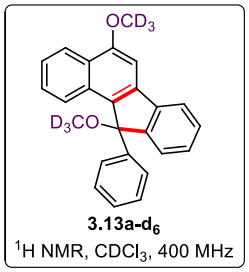
^{13}C NMR, $CDCl_3$, 100 MHz




8.2802
8.2607
7.8325
7.8147
7.5826
7.5794
7.5761
7.5609
7.5457
7.5424
7.5391
7.4297
7.4122
7.3942
7.3907
7.3692
7.3655
7.3547
7.3484
7.3455
7.3317
7.3281
7.2614
6.7307
4.0610
2.5617
2.5424
2.5224
1.6746
1.6560
1.6370
1.6176
1.5987
1.5732
0.8810
0.8627
0.8443
OMe
Me
O
3.15k
1H NMR, CDCl3, 400 MHz
10
9
8
7
6
5
4
3
2
1
0 ppm
1.00
2.00
1.05
5.09
1.04
3.05
2.06
2.06
3.04

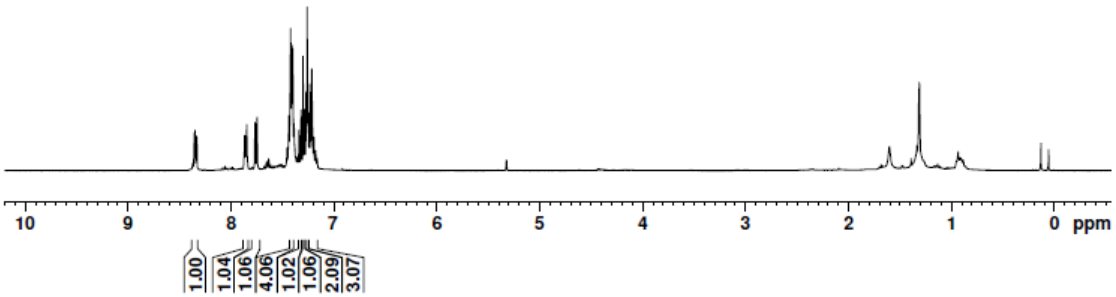

200.3867
155.9809
138.4758
138.1777
133.5509
131.9314
129.8345
128.6887
128.3362
127.1713
124.9916
124.8362
123.9789
122.0856
105.1736
77.3786
77.0614
76.7432
55.6159
36.4004
24.5580
14.1541
OMe
Me
O
3.15k
13C NMR, CDCl3, 100 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm



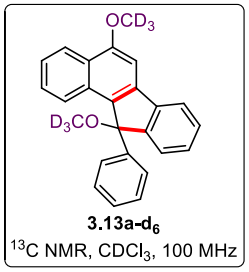


3.13a-d_6

^{1}H NMR, $CDCl_3$, 400 MHz

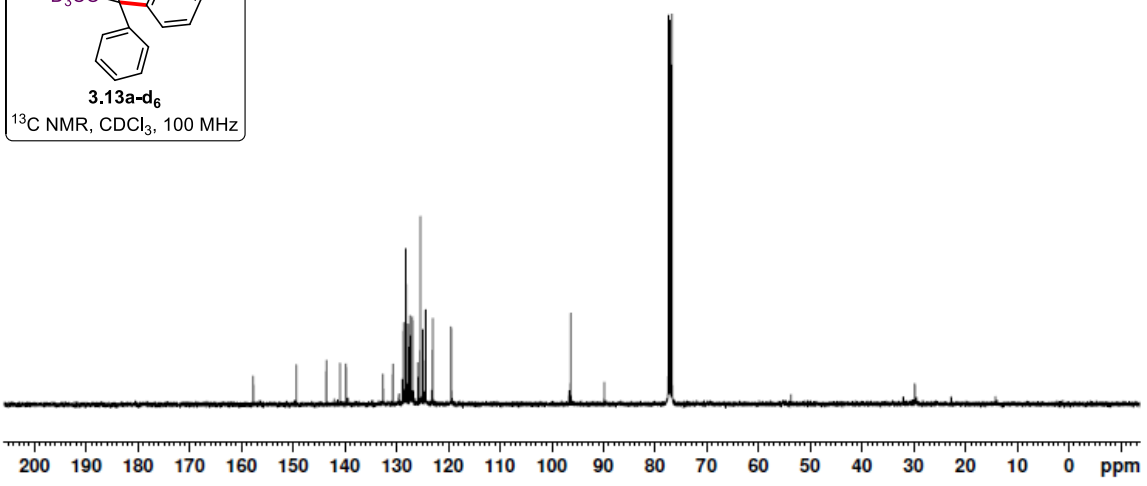


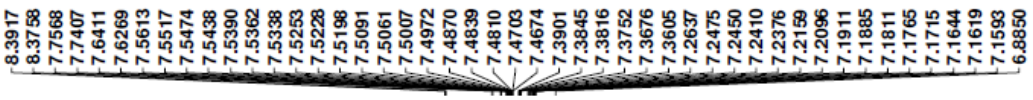


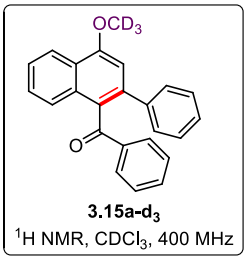


3.13a-d_6

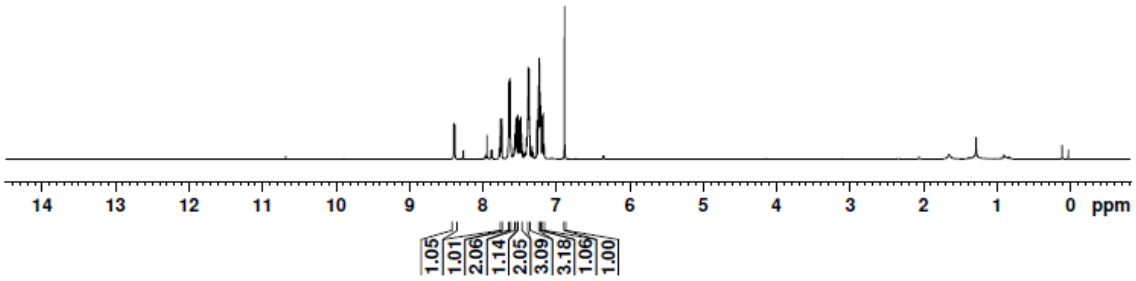
^{13}C NMR, $CDCl_3$, 100 MHz

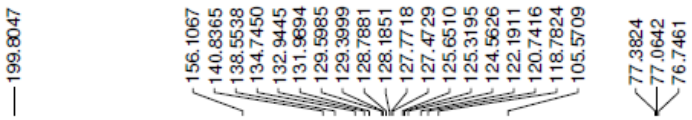


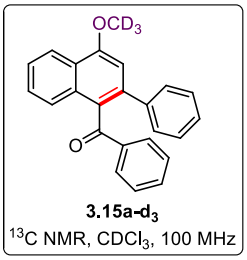




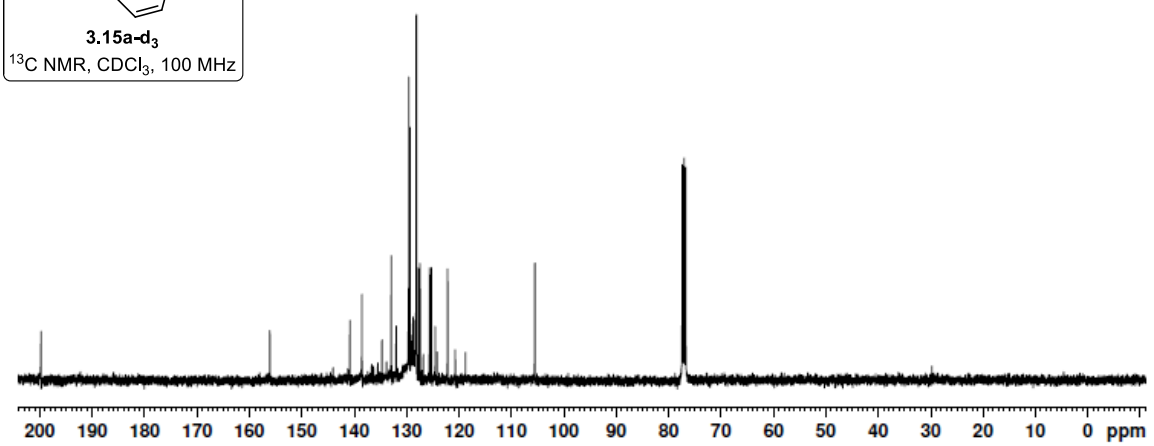
3.15a-d$_3$
^{1}H NMR, $CDCl_3$, 400 MHz

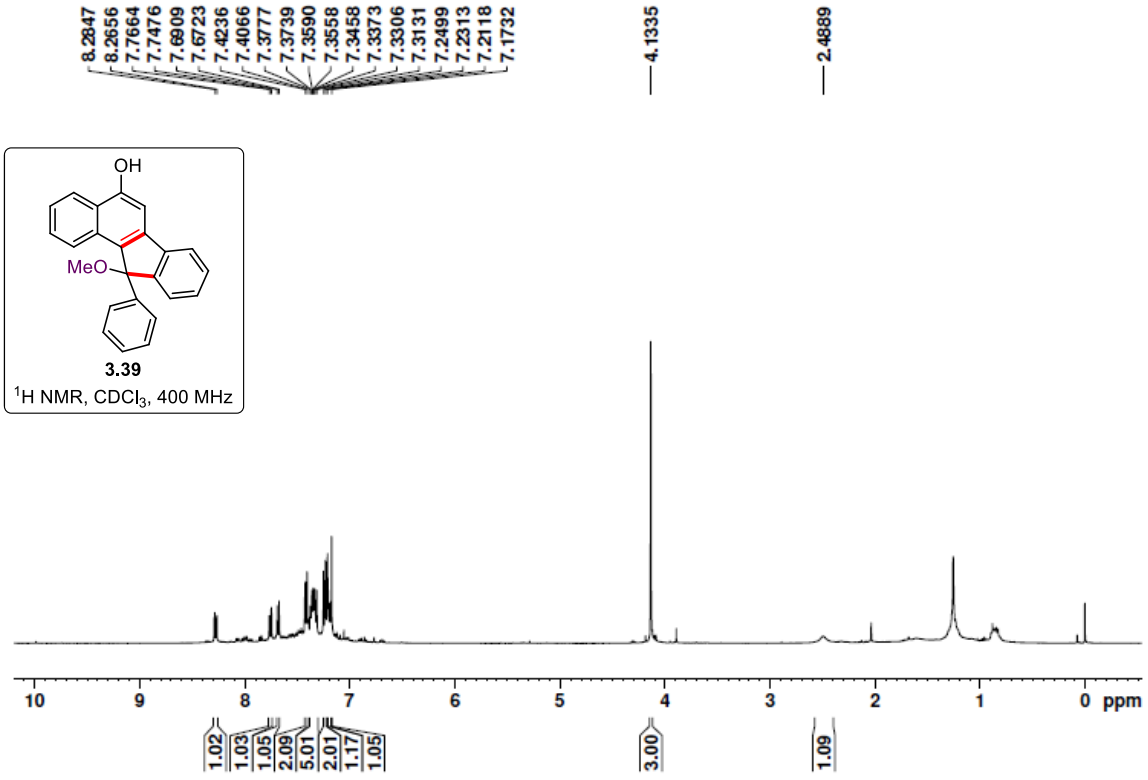


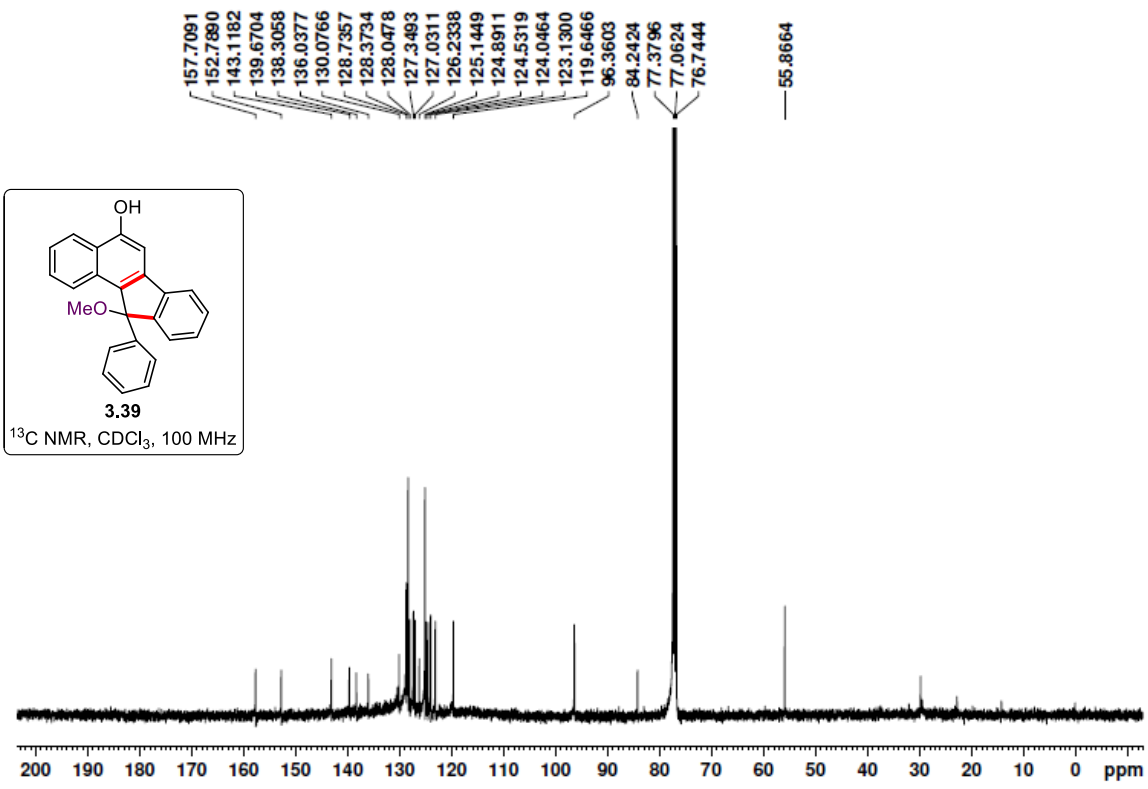




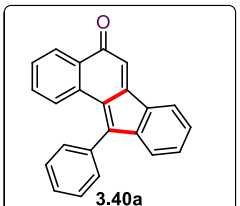
3.15a-d$_3$
^{13}C NMR, $CDCl_3$, 100 MHz




8.2847
8.2656
7.7664
7.7476
7.6909
7.6723
7.4236
7.4066
7.3777
7.3739
7.3590
7.3558
7.3458
7.3373
7.3306
7.3131
7.2499
7.2313
7.2118
7.1732
4.1335
2.4889
OH
MeO
3.39
1H NMR, CDCl3, 400 MHz
10
9
8
7
6
5
4
3
2
1
0 ppm
1.02
1.03
1.05
2.09
5.01
2.01
1.17
1.05
3.00
1.09

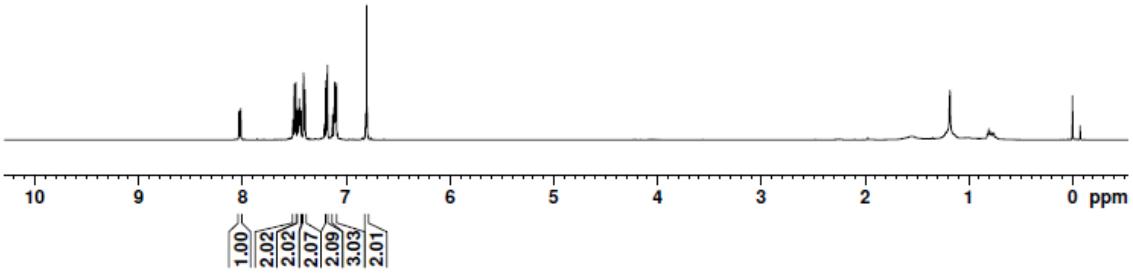

157.7091
152.7890
143.1182
139.6704
138.3058
136.0377
130.0766
128.7357
128.3734
128.0478
127.3493
127.0311
126.2338
125.1449
124.8911
124.5319
124.0464
123.1300
119.6466
96.3603
84.2424
77.3796
77.0624
76.7444
55.8664
OH
MeO
3.39
13C NMR, CDCl3, 100 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm





3.40a

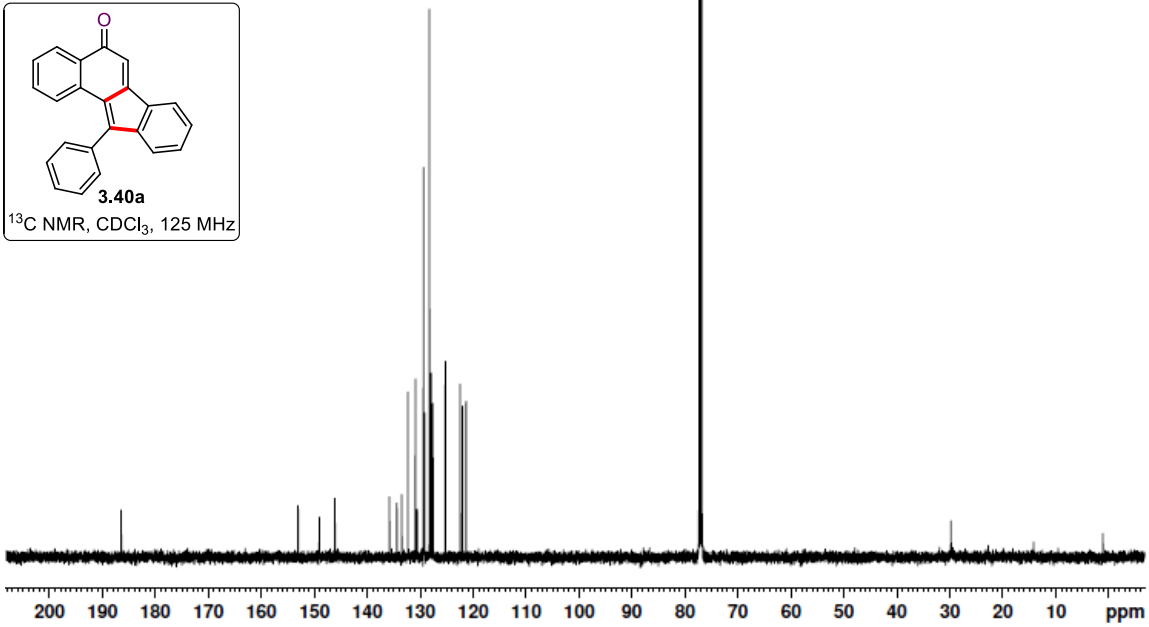
^{1}H NMR, $CDCl_3$, 500 MHz





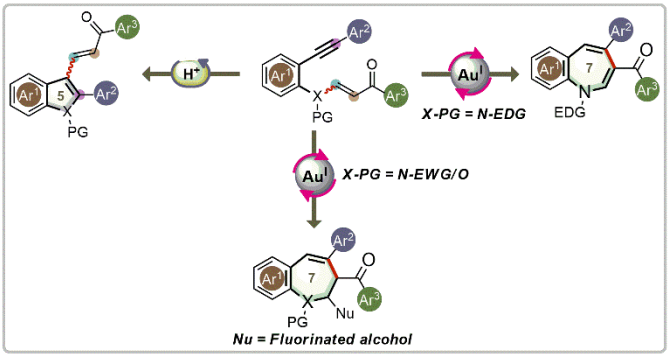
3.40a

^{13}C NMR, $CDCl_3$, 125 MHz



Chapter 4

Cyclizations of Vinylogous Amides and Esters Derived from o-Alkynylanilines and o-Alkynylphenols: Access to an Array of Functionalized Benzo[b]azepines, Benzo[b]oxepines, Indoles and Benzofurans



*H*erein, the synthetic possibilies of vinylogous amides and esters derived from *o*-alkynylanilines and *o*-alkynylphenols have been studied broadly under different metal catalysts and even in metal-free conditions. A diverse synthetic routes to access functionalized benzo[*b*]-azepines, benzo[*b*]oxepines, indoles and benzofurans from vinylogous amides and esters derived from *o*-alkynylanilines and *o*-alkynylphenols have been disclosed. Benzo[*b*]azepines and benzo[*b*]oxepines have been synthesized *via* a gold-catalyzed direct ring-closing strategy following 7-*endo-dig* cyclization. Interestingly, in presence of triflic acid, vinylogous amides derived from *o*-alkynylanilines form indole derivative with the transposition of vinyl ketone whereas the vinylogous esters derived from *o*-alkynylphenols provided the vinyl ketone transpositioned benzofuran.

- Mandal, M.; Balamurugan, R. *Manuscript to be submitted*.
- Mandal, M.; Pradhan, R.; Lourderaj, U.; Balamurugan, R. *Manuscript to be submitted*.

4.1. Introduction:

4.1.1. Background of Research:

Heterocycles are dominant in the research fields of medicinal chemsitry, natural products, and bioactive molecules and show a widespread range of pharmacological activities.[1] They also have a wide range of material applications.[2] Hence a variety of synthetic methodologies have been developed including some of the classical name reactions to produce the heterocyclic systems. *o*-Alkynylaniline derivatives have been used extensively for the construction of various N-heterocyclic moieties.[3] The cycloisomerization of 2-alkynylanilines has widely been studied as it is one of the most direct and atom-economical way to assemble indoles.[4] Several groups, have reported diverse types of cyclization of 2-alkynylanilines armed with different functionalities, followed by migration[5] under transition metal catalysis.

4.1.2. Literature Reports:

With the contributions from several research groups over the past few decades, a number of routes have been developed for the construction of heterocyclic systems from 2-alkynylanilines armed with different functionalities.

So, we have demonstrated below some of the existing literature for the cyclization reactions of such types of 2-alkynylanilines armed with different functionalities,

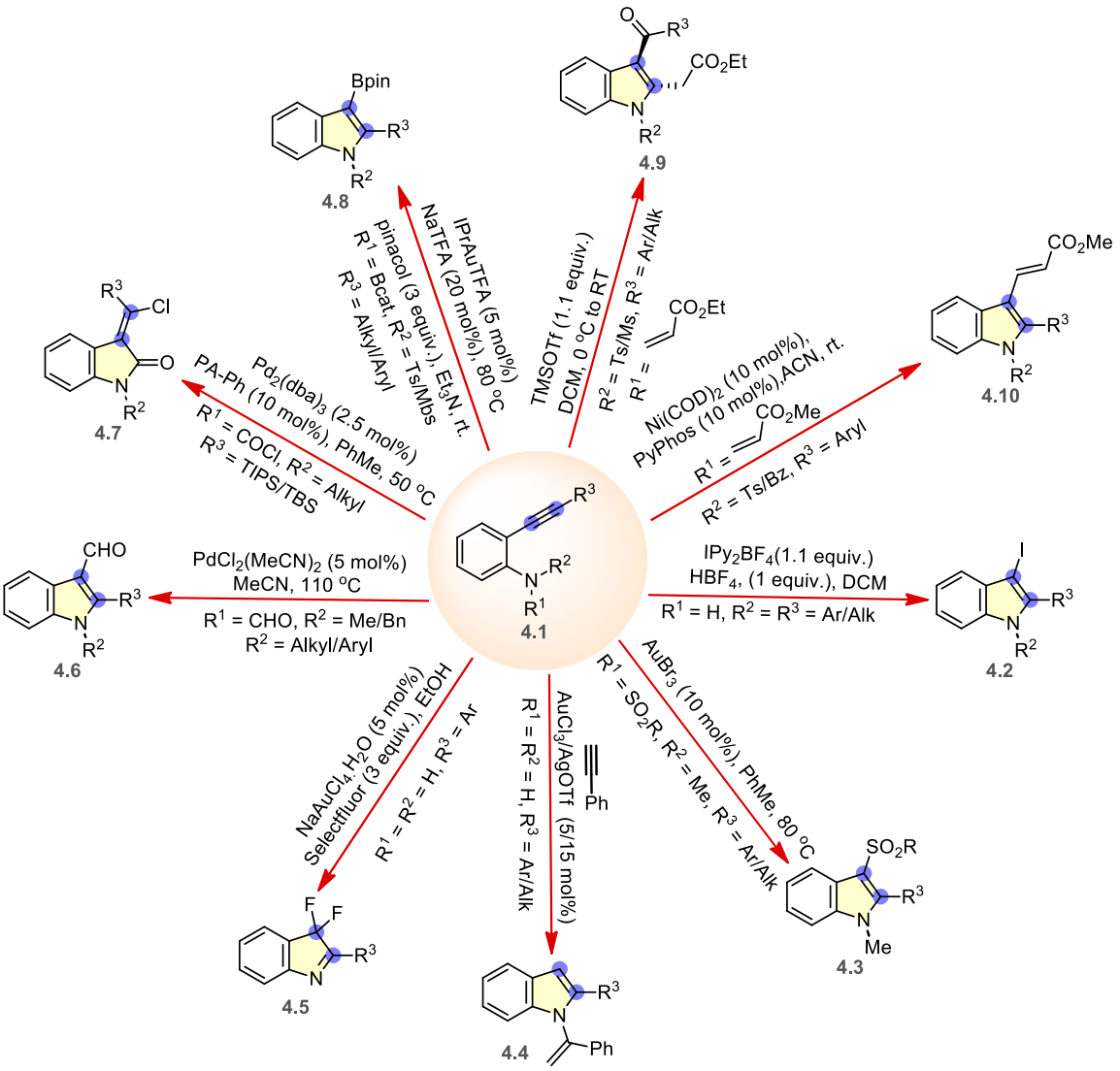
In 2003, González group[4g] has reported solution-phase as well as solid-phase approaches for an addition reaction of nitrogen to alkynes and these reactions have been used for the construction of the biologically relevant indole frame. N-protected 2-alkynylanilines **4.1** delivered N-protected 3-iodoindoles **4.2** upon reaction with IPy_2BF_4. HBF_4 was required for this reaction to activate the iodinating agent IPy_2BF_4.

In 2007, Yamamoto and co-workers[4f] have demonstrated the reactions of the 2-alkynyl-N-sulfonylanilines **4.1** leading to the corresponding 3-sulfonylindoles **4.3** in promising yields under gold catalysis. This reaction is proceeding by the formal addition of a N–S bond to an alkyne bond i.e., the so-called aminosulfonylation.

In the same year, Li group[4f] have developed an efficient double-hydroamination of o-alkynylanilines with terminal alkynes producing N-vinylindoles. 5 mol% $AuCl_3$ and 15 mol% AgOTf could be able to deliver N-vinylindoles **4.4** in a one-pot manner without solvent.

In 2013, Michelet and his group[4d] have reported the $NaAuCl_4.2H_2O$-catalyzed aminofluorination of unprotected 2-alkynylanilines. 3,3-Difluoroindole derivatives **4.5** have been achieved by an one-pot, two-step gold-catalyzed cyclization followed by electrophilic fluorination. This method has also been extended to the synthesis of 2-aryl-3-fluoro-1H-indoles. Base, acid or N-protecting groups are not required for this reaction.

In 2014, Liu and co-workers[5d] have disclosed a palladium-catalyzed intramolecular C–N and S–N bond addition to alkynes using 2-alkynylanilines **4.1** armed with different functional groups like acyl, pyruvoyl, amide, and sulfonyl. Highly functional indoles **4.6** could be synthesized by this approach with the migration of the aforementioned functionalities.



Scheme 4.1. Cyclization cascades of 2-alkynylaniline moieties.

In 2015, Lautens group[4b] have depicted the synthesis of methylene oxindoles **4.7** under palladium(0)-catalysis via intramolecular chlorocarbamoylation reaction of alkynes using 2-alkynylaniline **4.1** with an acyl choride as R^1. A comparatively unexplored class of caged phosphine ligands like aryl phosphaadamantane ligands were used for this reaction and it provided excellent trans selectivity.

In 2015, Blum and co-workers[5c] have reported the catalytic aminoboration which added B–N σ bonds to C–C π bonds using 2-alkynylaniline **4.1** with catecholborane (Bcat) as R^1. They have revealed that the unreactive B–N σ bond could be used for this addition reaction showing a new bond disconnection strategy leading to 3-borylated indoles **4.8**. The functional groups that are either incompatible with or hard to prepare by the existing protocols, well tolerated in presence of the carbophilic gold catalyst and slightly basic trifluoroacetate.

In 2015, Gharpure group[1d] have described the synthesis of indoline derivatives **4.9** via iminium ion trapping by alkyne in an intramolecular fashion using vinylogous carbamates derived from *o*-alkynylanilines **4.1** in a stereoselective manner. This whole process of synthesis of the nitrogen heterocycle **4.9** could also be achieved using 2-iodoaniline in a one-pot manner.

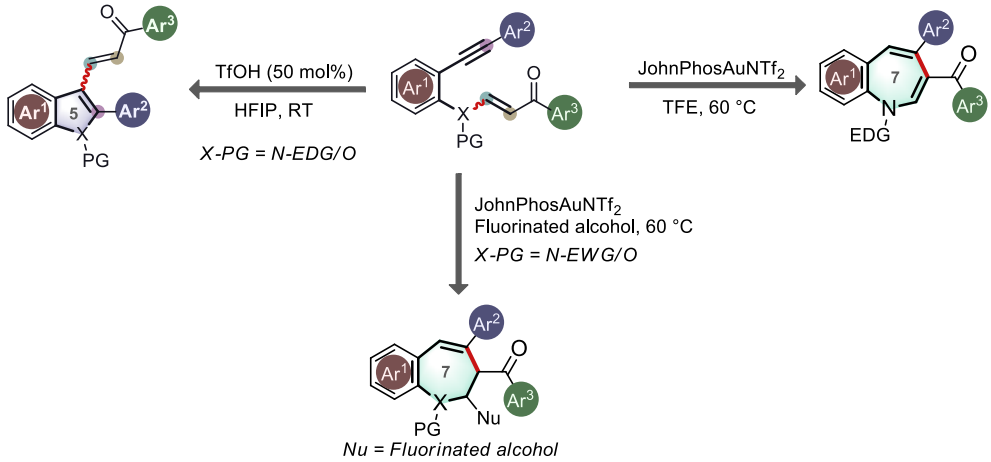
In 2020, Cho and his group[5a] have disclosed a synthetic route to achieve multifunctionalized indoles **4.10** by a Ni-catalyzed transcarboamination using 2-alkynylaniline derivative **4.1** with alkenylester group as R^1. The key steps of this transcarboamination are C–N bond cleavage of the nickelacycle intermediate and syn/anti-rotation of the alkenyl-Ni intermediate.

The literature study reveals that the 2-alkynylaniline framework could serve in a diverse way for the development of a series of heterocyclic moity.

4.2. Results & Discussion:

4.2.1. Present Work:

In this contest, we have presented a diversity-oriented synthetic route to functionalized benzo[*b*]azepines and benzo[*b*]oxepines via gold(I)-catalysis whereas, vinyl ketone transpositioned indole and benzofuran derivatives have been synthesized from the same vinylogous amides and esters derived from *o*-alkynylanilines and *o*-alkynylphenols respectively in a metal-free way.

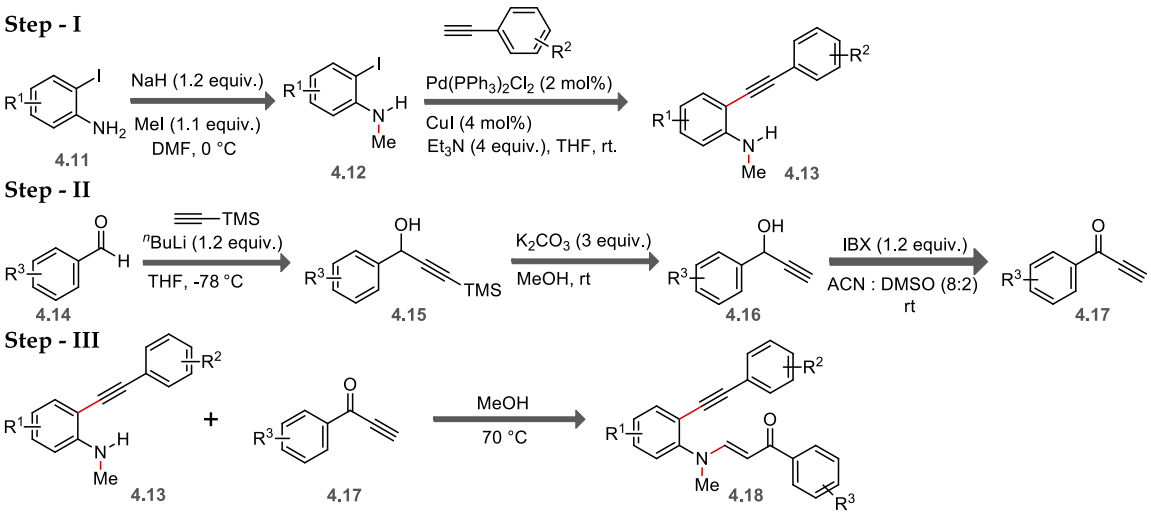


Scheme 4.2. Reactions of vinylogous amides and esters derived from *o*-alkynylanilines and *o*-alkynylphenols leading to benzo[*b*]azepines, benzo[*b*]oxepines, indoles and benzofurans.

4.2.2. Preparation of Vinylogous Amide Precursors Derived from o-Alkynylanilines (4.18):

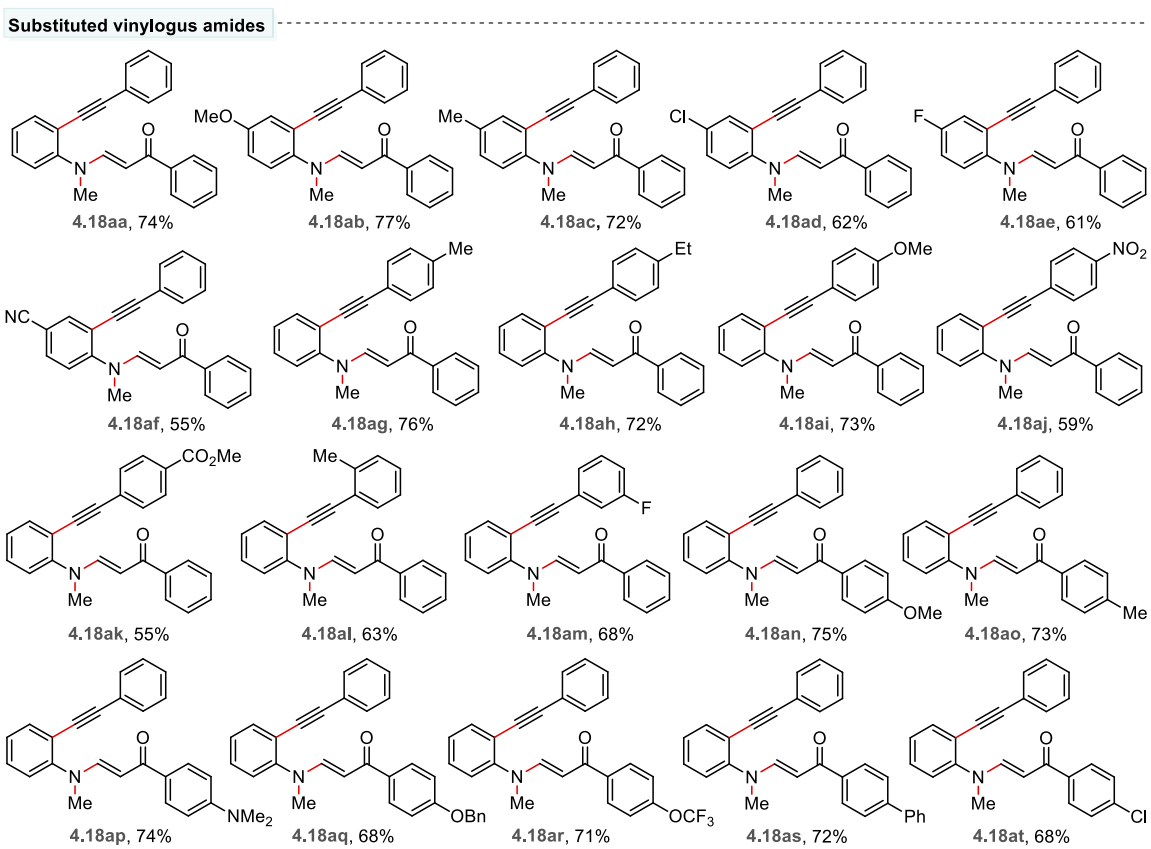
We have first synthesized a number of vinylogous amides derived from *o*-alkynylanilines **4.18**. 2-Alkynyl-N-methylaniline **4.13** was prepared from 2-iodoaniline and reacted with alkynone **4.17**

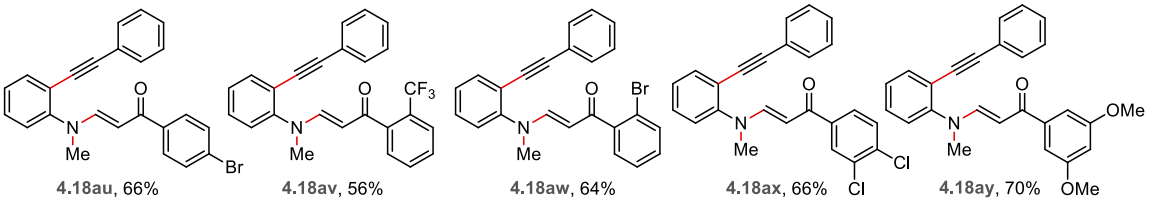
to achieve the synthesis of the desired vinylogous amides derived from *o*-alkynylanilines **4.18** (Scheme **4.3**). Stuctures of all the synthesized starting materials are presented in table **4.1**.

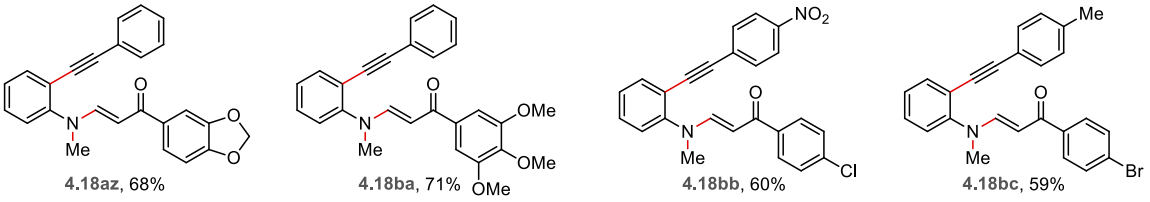


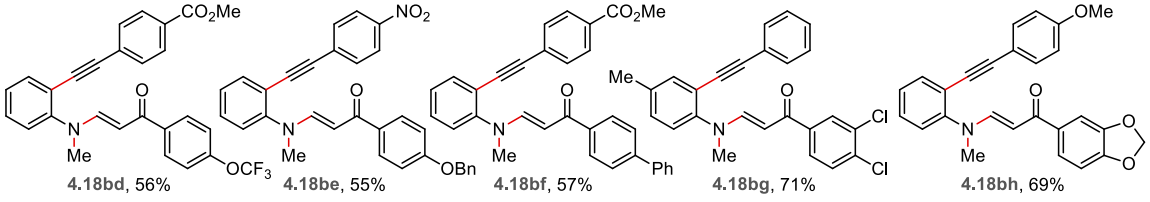
Scheme 4.3. Synthesis of vinylogous amides derived from *o*-alkynylanilines.

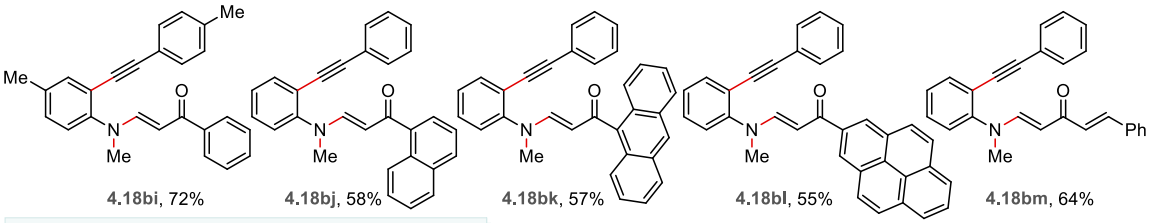
Table 4.1. Structures of synthesized vinylogous amides derived from *o*-alkynylanilines (**4.18**)



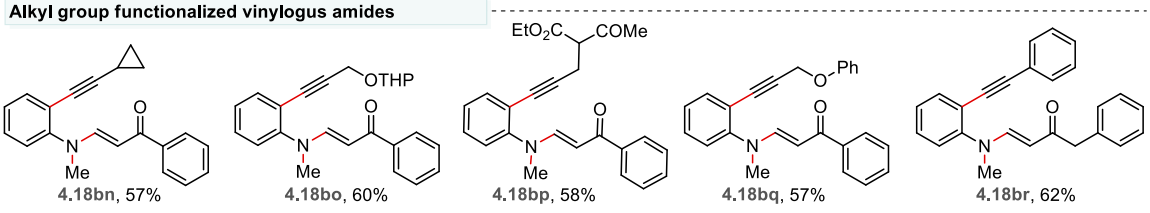




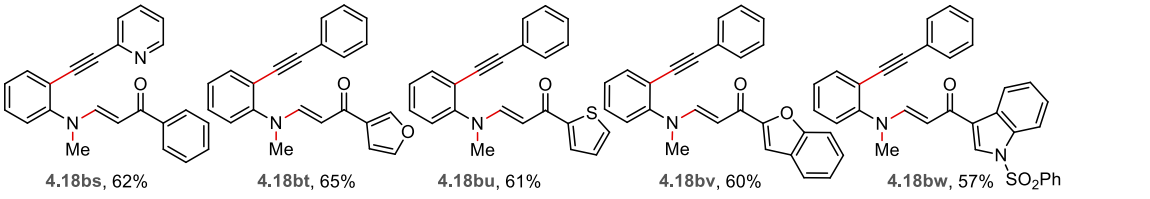




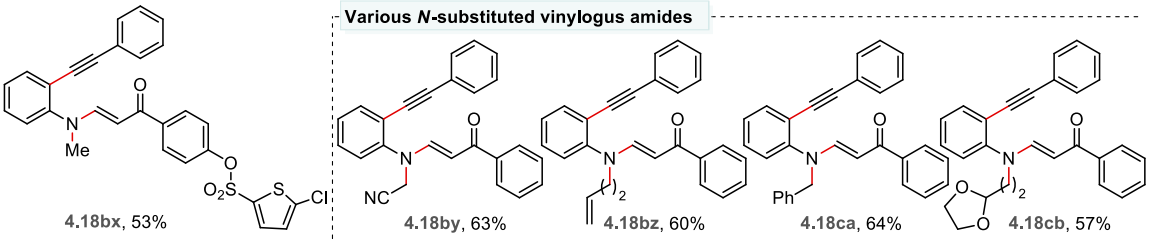
Alkyl group functionalized vinylogus amides

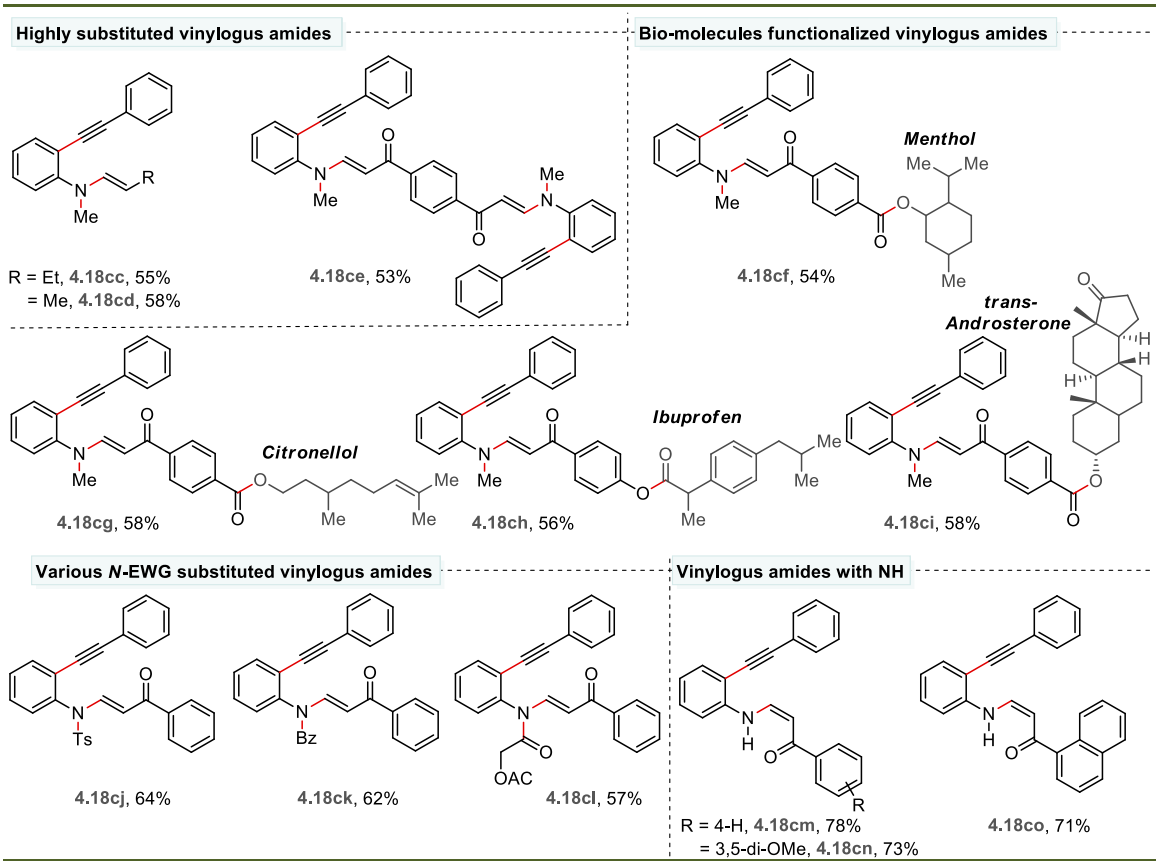


Hetero aryl group functionalized vinylogus amides



Various *N*-substituted vinylogus amides

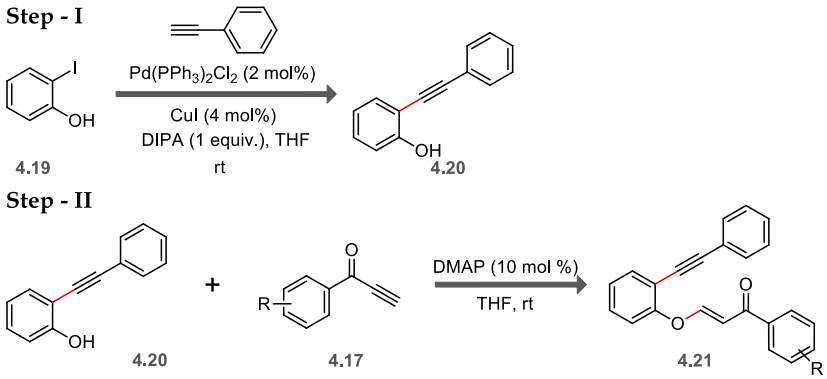




Yield represents the overall yield.

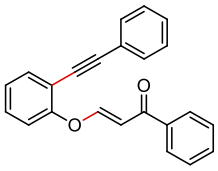
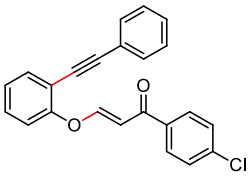
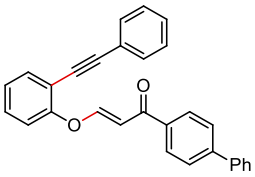
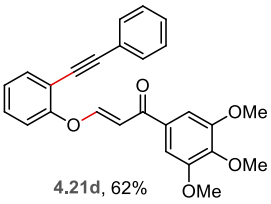
4.2.3. Preparation of Vinylogous Ester Precursors Derived from *o*-Alkynylphenols (4.21):

The vinylogous esters derived from *o*-alkynylphenols **4.21** could be prepared from the reaction of 2-alkynylphenol and alkynone in presence of DMAP in THF solvent. Structures of all the synthesized derivatives **4.21** are presented in table 4.2.



Scheme 4.4. Synthesis of vinylogous esters derived from *o*-alkynylphenols.

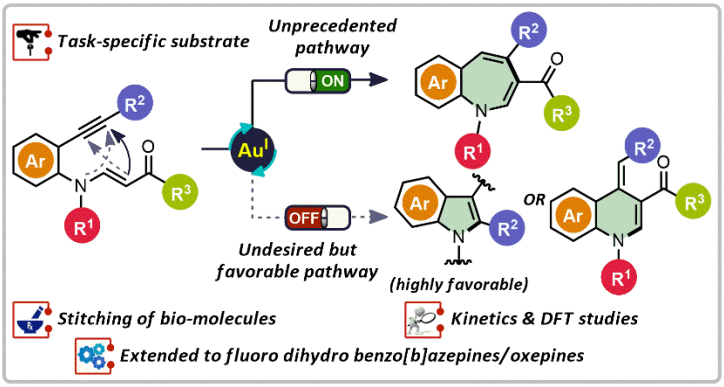
Table 4.2. Structures of synthesized vinylogous esters derived from *o*-alkynylphenols (**4.21**)

			
4.21a, 64%	**4.21b**, 65%	**4.21c**, 61%	**4.21d**, 62%

Yield represents the overall yield.

Chapter 4A

Dodging the Conventional Reactivity of o-Alkynylanilines under Gold Catalysis: Synthesis of Benzo[b]azepine using Vinylogous Amides Derived from o-Alkynylanilines



Multifaceted gold catalysis has become an appealing synthetic tool for direct assembly of nitrogenous heterocycles which are ubiquitous in nature having wide biological activities. In this context, while advances have been made for the construction of biologically active benzo[*b*]azepines, a direct ring-closing strategy involving *o*-alkynylaniline derivatives remains less explored and is highly challenging due to the high nucleophilicity of "N" leading to undesired pathways. Herein, we present an interesting 7-*endo*-*dig* carbacyclization of vinylogous amides derived from *o*-alkynylanilines under homogeneous gold catalysis to access a wide array of benzo[*b*]azepines in an atom economical way. This cyclization shows excellent functional group compatibility and can also be extended to access fluoroalkoxy incorporated dihydrobenzo[*b*]-azepines/oxepines. Deuterium scrambling experiments and DFT studies favor a mechanism that involves deprotonation of a cyclized intermediate followed by protodeauration mediated by the counter anion.

Mandal, M.; Pradhan, R.; Lourderaj, U.; Balamurugan, R. *Manuscript to be submitted.*

4a.1. Introduction:

4a.1.1. Background of Research:

Medium-sized carbocyclic or heterocyclic structures are important entities due to their existence in many bioactive molecules, pharmaceuticals and natural products.[6] Among them, benzo-fused, seven-membered aza heterocycles i.e., benzoazepines, are found in a variety of biologically active synthetic compounds.[7] Based on the extent of unsaturation and the place of the nitrogen atom, benzoazepines are further classified. In this context, benzo[*b*]azepine is found in many alkaloids like goniomine, kopsiyunnanine L and drug molecules like anafranil, tienopramine, imipramine and benazepril etc. In addition, these molecules are specifically relevant as they exhibit diverse medicinal activities to treat diseases such as hypertension, depression, Alzheimer's disease, and heart attacks etc.[8]

With regard to their extensive scientific and commercial values, construction of the benzo[*b*]azepine core to synthesize new analogues is still a subject of consistent interest from academic and industrial points of view.

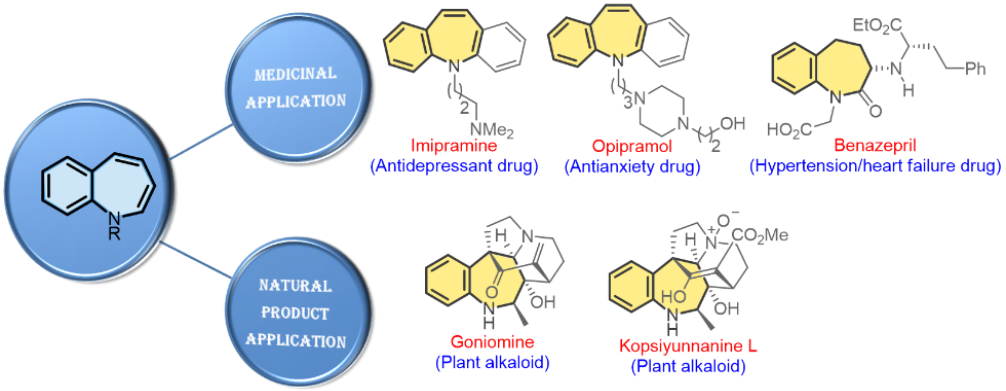


Figure 4a.1. Selected novel benzo[*b*]azepine analogues.

4a.1.2. Literature Reports:

The importance of benzo[*b*]azepines has drawn close attention of synthetic organic chemists to diversify its core structure. A handful of reports are available in literature for the synthesis of benzo[*b*]azepine scaffolds.[9-11] Most of the reports developed so far for the synthesis of benzo[*b*]azepine depend on thermal[9a,b] or oxidative[9c,d] ring-expansion strategies. Other approaches employ multi-step processes[10] and convergent protocols[11] via organocatalysis,[11a] cross-coupling/[2+2] cycloadditions,[11b] and oxidative [5+2] annulations.[11c] We have summerized the methods available for the synthesis of benzo[*b*]azepines in Figure 4a.2.

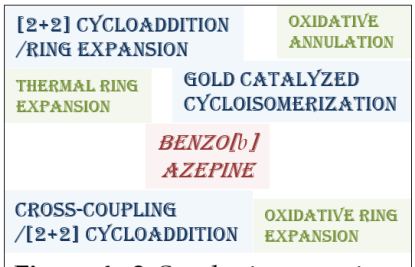
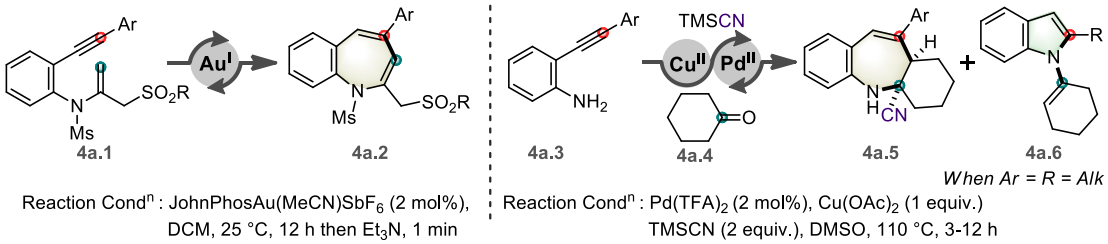


Figure 4a.2. Synthetic strategies towards Benzo[*b*]azepine

However, the ring-expansion strategies have substrate dependency and thereby restrict their generality. The limitations demands the development of strategies that can be applied to a variety of substrates. Direct cyclization is one such approach to synthesize benzo[*b*]azepines in an efficient manner.

In 2016, Menon group[12] have reported a regioselective Au(I)-catalyzed cycloisomerization of N-(*o*-alkynylaryl)-N-vinyl sulfonamides **4a.1** leading to 1-benzoazepine **4a.2**. The reaction proceeds through a 7-*endo-dig* cyclization (Scheme 4a.1). This reaction is highly substrate specific. The success of the reaction requires the presence of an electron-withdrawing group on 'N' and an aryl group on the alkyne. In addition, the sulfonyl group and base Et_3N play crucial roles.

In 2018, Wang and co-workers[11d] have developed an one-pot, three-component cascade reaction for the preparation of 1-benzoazepine carbonitriles **4a.5** from *o*-alkynylanilines **4a.3**, cyclohexanone **4a.4** and trimethylsilyl cyanide using palladium(II)trifluoroacetate and copper(II)acetate in dimethyl sulfoxide. This methodology involves an imination followed by annulation and subsequent cyanation strategy (Scheme 4a.1). Here, aliphatic substituent on the alkyne instead of aromatic ring, lead to the formation of the 5-membered cyclic product **4a.6**. The reaction is unsuccessful when the cyclohexanone is replaced with other cyclic or acyclic ketones. The presence of TMSCN is compulsory to keep this methodology operational.



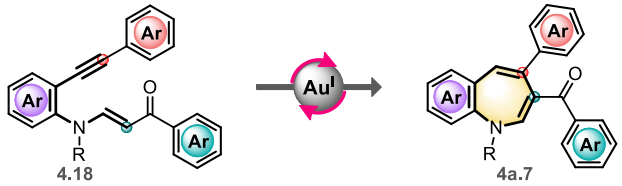
Scheme 4a.1. Ealier approaches involving direct ring closing strategy.

Thus, it could be concluded that the afore-mentioned two protocols are highly substrate dependent and exhibit restricted substrate scope. So, a more generalized direct ring-closing approach for the synthesis of benzo[*b*]azepine moiety is highly desirable.

4a.2. Results & Discussion:

4a.2.1. Present Work:

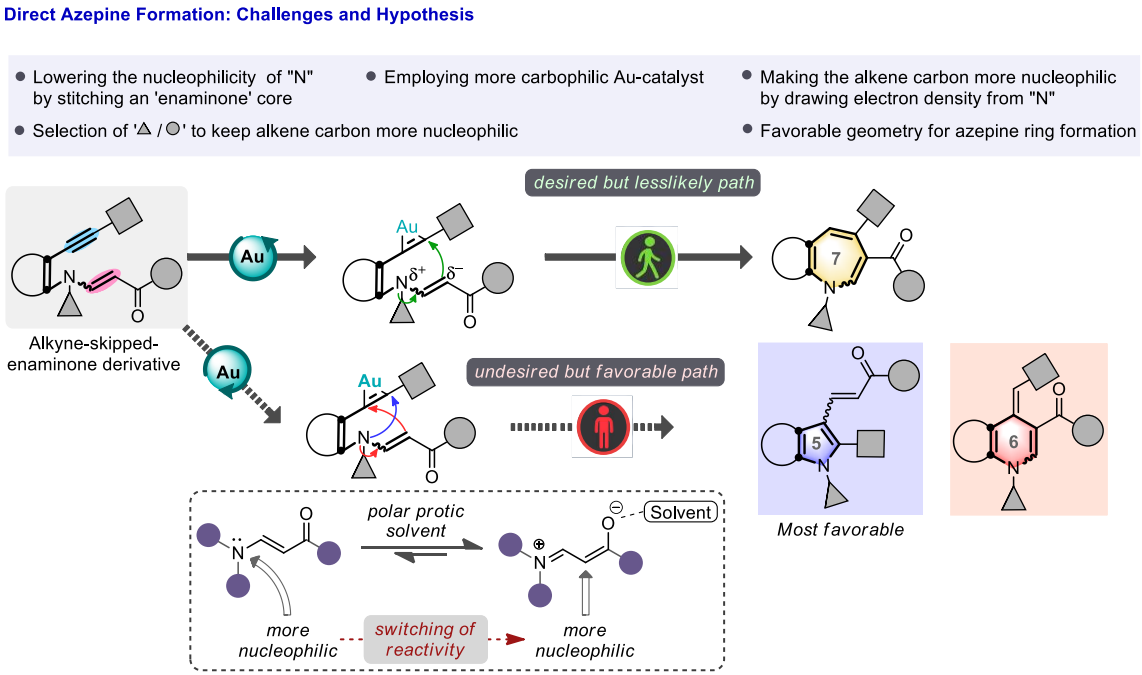
In this contest, we have developed a more generalized direct ring-closing strategy for the synthesis of benzo[*b*]azepine derivatives using vinylogous amides derived from *o*-alkynylanilines under gold catalysis. Here 7-*endo-dig* cyclization is favored over the 5-*endo-dig* aza- and 6-*exo-dig* carba-cyclization modes. Moreover, this strategy can be extended to access fluoroalkoxy incorporated benzo[*b*]azepine/oxepine motifs under the same reaction condition.



Scheme 4a.2. Direct ring-closure for the synthesis of benzo[*b*]azepine moity under gold catalysis.

4a.2.2. Concept:

We envisioned a strategy involving bifunctional substrates bearing an alkyne core prompt to electrophilic activation and a judiciously positioned 'N'-tethered alkene as an internal nucleophile. We anticipated that a polarized alkenyl substituent on the nitrogen would reduce the nucleophilicity of nitrogen and, at the same time, make the alkenyl carbon nucleophilic to facilitate the cyclization to form benzo[*b*]azepines.



Scheme 4a.3. Key challenges and our concept design for benzo[*b*]azepine synthesis involving a direct ring-closure under gold catalysis.

4a.2.3. Optimization of Reaction Conditions for Benzo[*b*]azepine Synthesis:

To check the viability of our hypothesis, we used vinylogous amide derived from *o*-alkynylaniline (**4.18aa**) as a model substrate. **4.18aa** was treated with **Au1** (5 mol%)/$AgSbF_6$ (10 mol%) catalytic system in dichloromethane (DCM) at 60 °C. The desired benzo[*b*]azepine (**4a.7aa**) was obtained in 38% yield (entry 1, Table 4a.1).

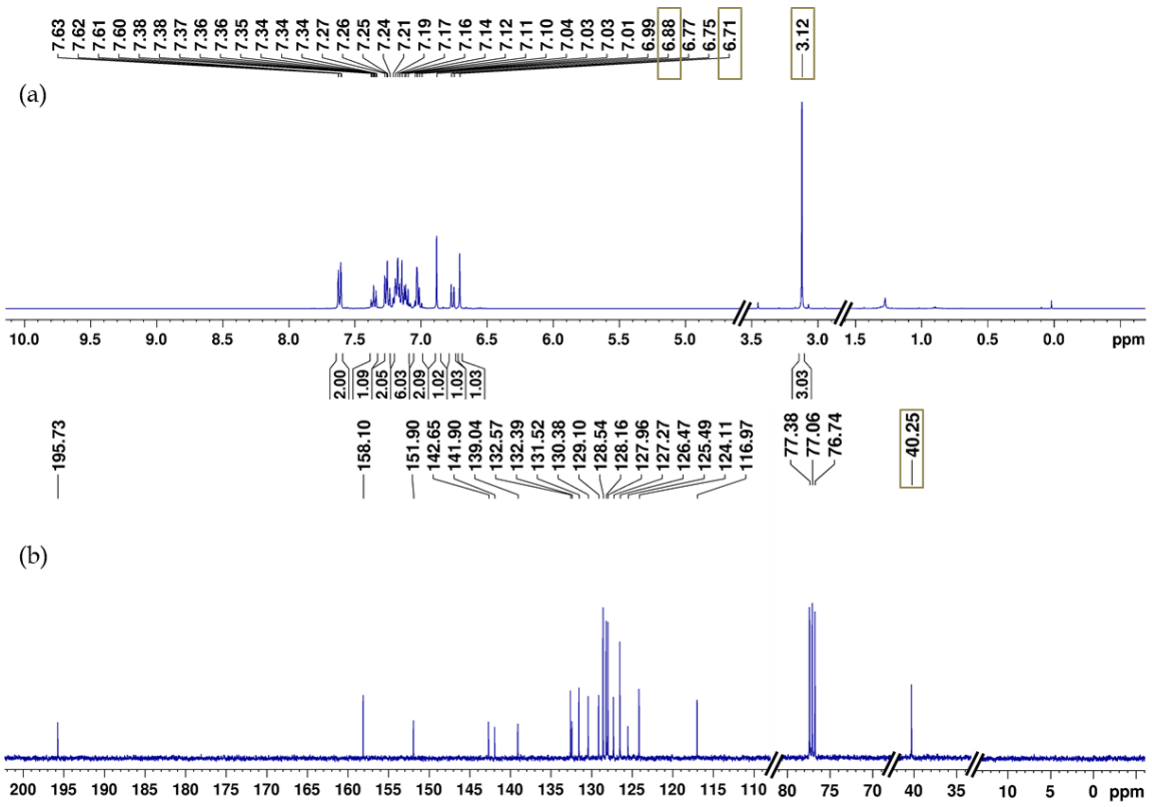


Figure 4a.3. ^{1}H and ^{13}C NMR spectra of benzo[*b*]azepine (**4a.7aa**).

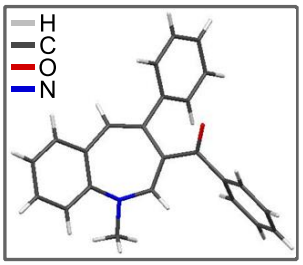
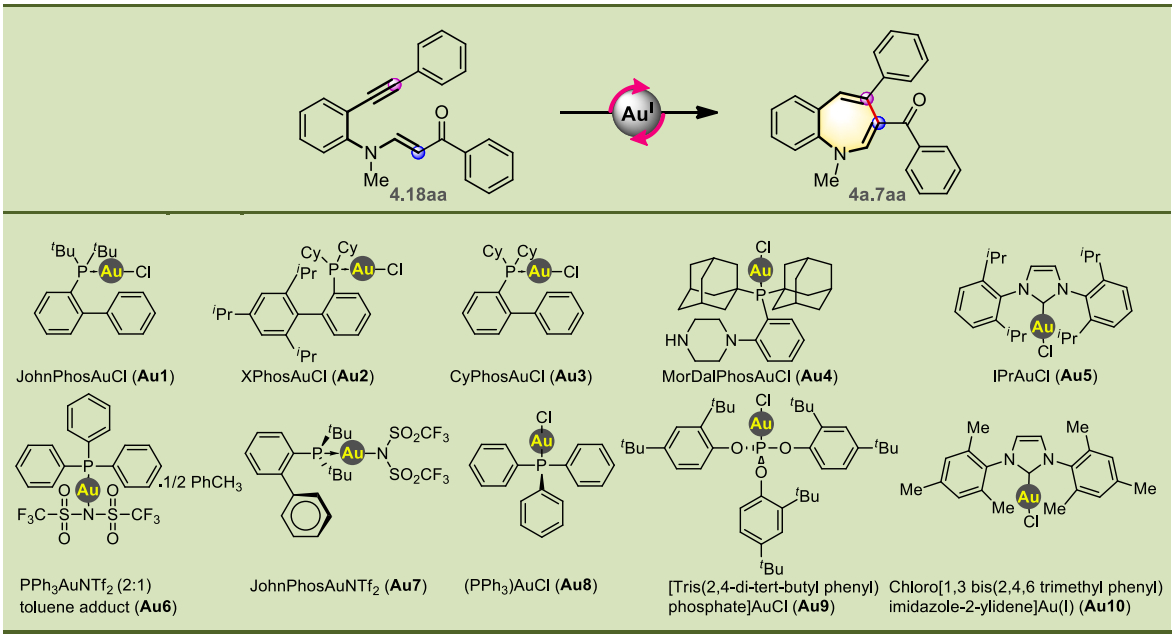


Figure 4a.4. ORTEP diagram of **4a.7aa**.

The structure of **4a.7aa** was confirmed by nuclear magnetic resonance (NMR) spectroscopic (figure 4a.3) and high resolution mass spectroscopic (HRMS) analysis. In ^{1}H NMR spectrum, a peak at 3.12 ppm with integral value for 3H and the corresponding ^{13}C signals at 40.3 ppm clearly indicated the presence of N-methyl group. Singlet at 6.71 and 6.88 ppm in ^{1}H NMR correspond to the protons linked to the C5 and C2 carbons of the product benzo[*b*]azepine **4a.7aa**. The structure of the compound was confirmed by SC-XRD analysis also. We then went ahead with further optimization to find out the best reaction conditions. A variety of solvents (TFE, THF, dioxane, HFIP, acetone, Et_2O, $CHCl_3$, CCl_4, MeOH etc.) were tested. An improved yield (51%) was observed in TFE solvent which prompted that TFE as the solvent of choice (entries 2-10, Table 4a.1). Change of silver co-catalysts intriguingly enhanced the reactivity of **Au1** catalyst. A yield of 78% of **4a.7aa** was noted in presence of $AuNTf_2$ (entry 11, Table 4a.1) with a nearly complete substrate consumption. Whereas the other silver catalysts ($AgBF_4$, AgOTf and AgTFA) were found to be less competent (entries 12-15, Table 4a.1). The reaction was typically sluggish in the absence of a silver co-catalyst, affording 27% yield after 24 h (entry 16). Extensive screening of diverse gold(I) catalysts (**Au2**-**Au5**, **Au8**-**Au11** entries 17-24, Table 4a.1) indeed failed to render a better result.

Surprisingly, $(PPh_3)AuNTf_2$ 2:1 toluene adduct (**Au6**) improved the product yield to 82% in 6 h (entry 25, Table 4a.1). Pleasingly, employment of JohnPhosAuNTf$_2$ (**Au7**) afforded 95% of isolated yield in 5 h (entry 26, Table 4a.1). Even 1 mol% of **Au7** could furnish the reaction with 98% yield in 22 h at 60 °C (entry 30, Table 4a.1). Further, decrease of catalyst loading made the reaction sluggish with a slight erosion of the yield (entry 31). The optimal condition comprising of 1 mol% of **Au7** in TFE solvent at 60 °C was utilized to access benzo[*b*]azepines.

Table 4a.1. Optimization of reaction conditions for the synthesis of benzo[*b*]azepine (**4a.7aa**).



Entry	Solvent	Catalyst (mol%)	LA (mol%)	Time (h)	Yield (%) of 4a.7aa
1	DCM	JohnPhosAuCl (**Au1**) (5)	$AgSbF_6$ (10)	8	38
2	TFE	JohnPhosAuCl (**Au1**) (5)	$AgSbF_6$ (10)	8	51
3	Dioxane	JohnPhosAuCl (**Au1**) (5)	$AgSbF_6$ (10)	8	34
4	THF	JohnPhosAuCl (**Au1**) (5)	$AgSbF_6$ (10)	8	30
5	HFIP	JohnPhosAuCl (**Au1**) (5)	$AgSbF_6$ (10)	8	32
6	Acetone	JohnPhosAuCl (**Au1**) (5)	$AgSbF_6$ (10)	8	30
7	Et_2O	JohnPhosAuCl (**Au1**) (5)	$AgSbF_6$ (10)	8	41
8	$CHCl_3$	JohnPhosAuCl (**Au1**) (5)	$AgSbF_6$ (10)	8	35
9	CCl_4	JohnPhosAuCl (**Au1**) (5)	$AgSbF_6$ (10)	8	20
10	MeOH	JohnPhosAuCl (**Au1**) (5)	$AgSbF_6$ (10)	8	46
11	TFE	JohnPhosAuCl (**Au1**) (5)	$AgNTf_2$ (10)	8	78
12	TFE	JohnPhosAuCl (**Au1**) (5)	$AgBF_4$ (10)	8	47

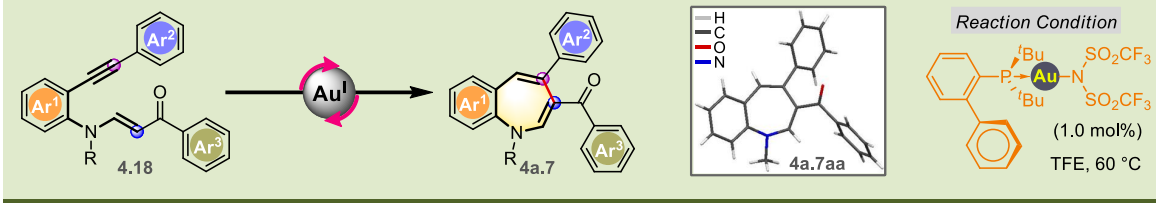
13	TFE	JohnPhosAuCl (**Au1**) (5)	AgOTf (10)	8	28
14	TFE	JohnPhosAuCl (**Au1**) (5)	AgTFA (10)	8	26
15	TFE	JohnPhosAuCl (**Au1**) (5)	$AgSCF_3$ (10)	8	23
16	TFE	JohnPhosAuCl (**Au1**) (5)	-	24	27
17	TFE	XPhosAuCl (**Au2**) (5)	$AgNTf_2$ (10)	8	71
18	TFE	CyclohexylJohnPhosAuCl (**Au3**) (5)	$AgNTf_2$ (10)	8	74
19	TFE	MorDalPhosAuCl (**Au4**) (5)	$AgNTf_2$ (10)	8	59
20	TFE	IprAuCl (**Au5**) (5)	$AgNTf_2$ (10)	8	75
21	TFE	(PPh_3)AuCl (**Au8**) (5)	$AgNTf_2$ (10)	10	64
22	TFE	[Tris(2,4-di-tert-butyl phenyl)phosphate]AuCl (**Au9**) (5)	$AgNTf_2$(10)	10	57
23	TFE	Chloro[1,3 bis(2,4,6 trimethyl phenyl)imidazole-2-ylidene]Au(I) (**Au10**) (5)	$AgNTf_2$(10)	10	65
24	TFE	AuCl (**Au11**) (5)	$AgNTf_2$(10)	10	55
25	TFE	$(PPh_3)AuNTf_2$ 2:1 Toluene adduct (**Au6**) (5)	-	6	82
26	TFE	JohnPhosAu NTf_2 (**Au7**) (5)	-	5	95
27	TFE[b]	JohnPhosAuNTf_2 (**Au7**) (5)	-	3	98
28	TFE[b]	JohnPhosAuNTf_2 (**Au7**) (3)	-	10	97
29	TFE[b]	JohnPhosAuNTf_2 (**Au7**) (2)	-	16	97
30	TFE[b]	JohnPhosAuNTf_2 (**Au7**) (1)	-	22	98
31	TFE[b]	JohnPhosAuNTf_2 (**Au7**) (0.5)	-	26	97

Reaction conditions: All the reactions were carried out using **4.18aa** (1 equiv.) at rt under N_2 atmosphere unless otherwise stated. '-': No Reaction. [b]Reaction conducted at 60 °C.

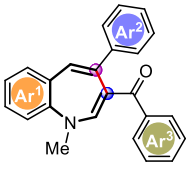
4a.2.4. Substrate Scope for the Synthesis of Benzo[*b*]azepine Derivatives:

We explored the scope of this methodology. For this, a series of vinylogous amides derived from *o*-alkynylanilines (**4.18**) were treated under the optimized reaction condition and the outcome is presented in Table 4a.2. To start with, the electronic effect of the aryl ring Ar^1 was studied by keeping the other two aryl rings (Ar^2 and Ar^3) as phenyl. Substrates having substituents para to the amino group were studied as they will directly affect the electron density on the nitrogen. These substrates furnished their corresponding benzo[*b*]azepines in promising yields. A longer reaction time of 30 h was required for the substrate having *p*-CN substitution which provided relatively lesser yield (79%). Whereas, electron-donating group like *p*-OMe made the cyclization relatively faster leading to **4a.7ab**.

Table 4a.2. Synthesis of diverse benzo[*b*]azepines under gold catalysis (**4a.7**)



Scope of substituted aryl group functionalized benzo[*b*]azepines



Ar¹ = Ar² = Ar³ = Ph

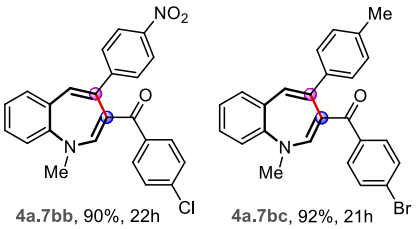
C_6H_4; **4a.7aa**, 98%, 22h
4a.7aa, 82%, 36h[a] (gram scale)
7-OMe-C_6H_3; **4a.7ab**, 95%, 18h
7-Me-C_6H_3; **4a.7ac**, 94%, 22h
7-Cl-C_6H_3; **4a.7ad**, 92%, 22h
7-F-C_6H_3; **4a.7ae**, 91%, 24h
7-CN-C_6H_3; **4a.7af**, 79%, 30h

Ar² = Ar¹ = Ar³ = Ph

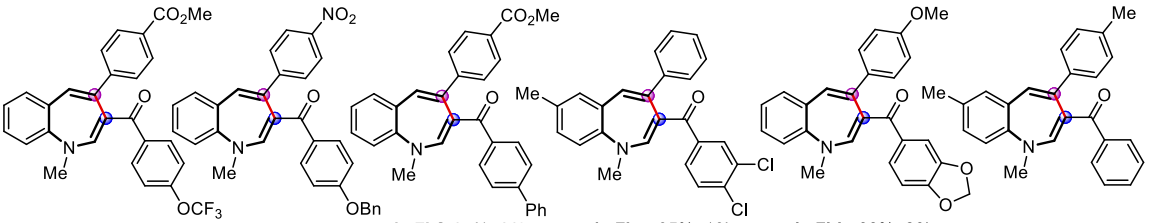
4-Me-C_6H_4; **4a.7ag**, 92%, 22h
4-Et-C_6H_4; **4a.7ah**, 91%, 22h
4-OMe-C_6H_4; **4a.7ai**, 94%, 20h
4-NO_2-C_6H_4; **4a.7aj**, 88%, 21h
4-CO_2Me-C_6H_4; **4a.7ak**, 94%, 20h
2-Me-C_6H_4; **4a.7al**, 90%, 24h
3-F-C_6H_4; **4a.7am**, 90%, 22h

Ar³ = Ar¹ = Ar² = Ph

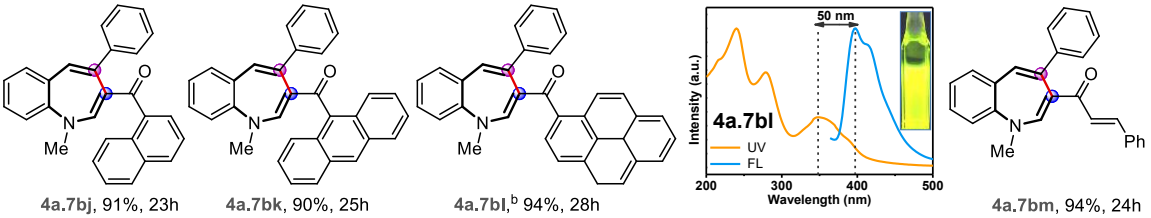
4-OMe-C_6H_4; **4a.7an**, 92%, 22h
4-Me-C_6H_4; **4a.7ao**, 93%, 22h
4-NMe_2-C_6H_4; **4a.7ap**, 89%, 22h
4-OBn-C_6H_4; **4a.7aq**, 94%, 22h
4-OCF_3-C_6H_4; **4a.7ar**, 94%, 22h
4-Ph-C_6H_4; **4a.7as**, 95%, 20h
4-Cl-C_6H_4; **4a.7at**, 95%, 20h
4-Br-C_6H_4; **4a.7au**, 93%, 20h
2-CF_3-C_6H_4; **4a.7av**, 91%, 20h
2-Br-C_6H_4; **4a.7aw**, 92%, 23h
3,4-di-Cl-C_6H_3; **4a.7ax**, 95%, 20h
3,5-di-OMe-C_6H_3; **4a.7ay**, 89%, 23h
3,4-O-CH_2-O-C_6H_3; **4a.7az**, 92%, 24h
3,4,5-tri-OMe-C_6H_2; **4a.7ba**, 88%, 24h



4a.7bb, 90%, 22h **4a.7bc**, 92%, 21h

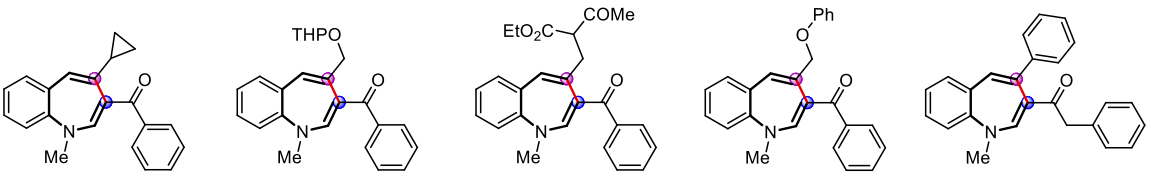


4a.7bd, 94%, 18h **4a.7be**, 88%, 20h **4a.7bf**, 95%, 20h **4a.7bg**, 95%, 18h **4a.7bh**, 93%, 20h **4a.7bi**, 93%, 18h

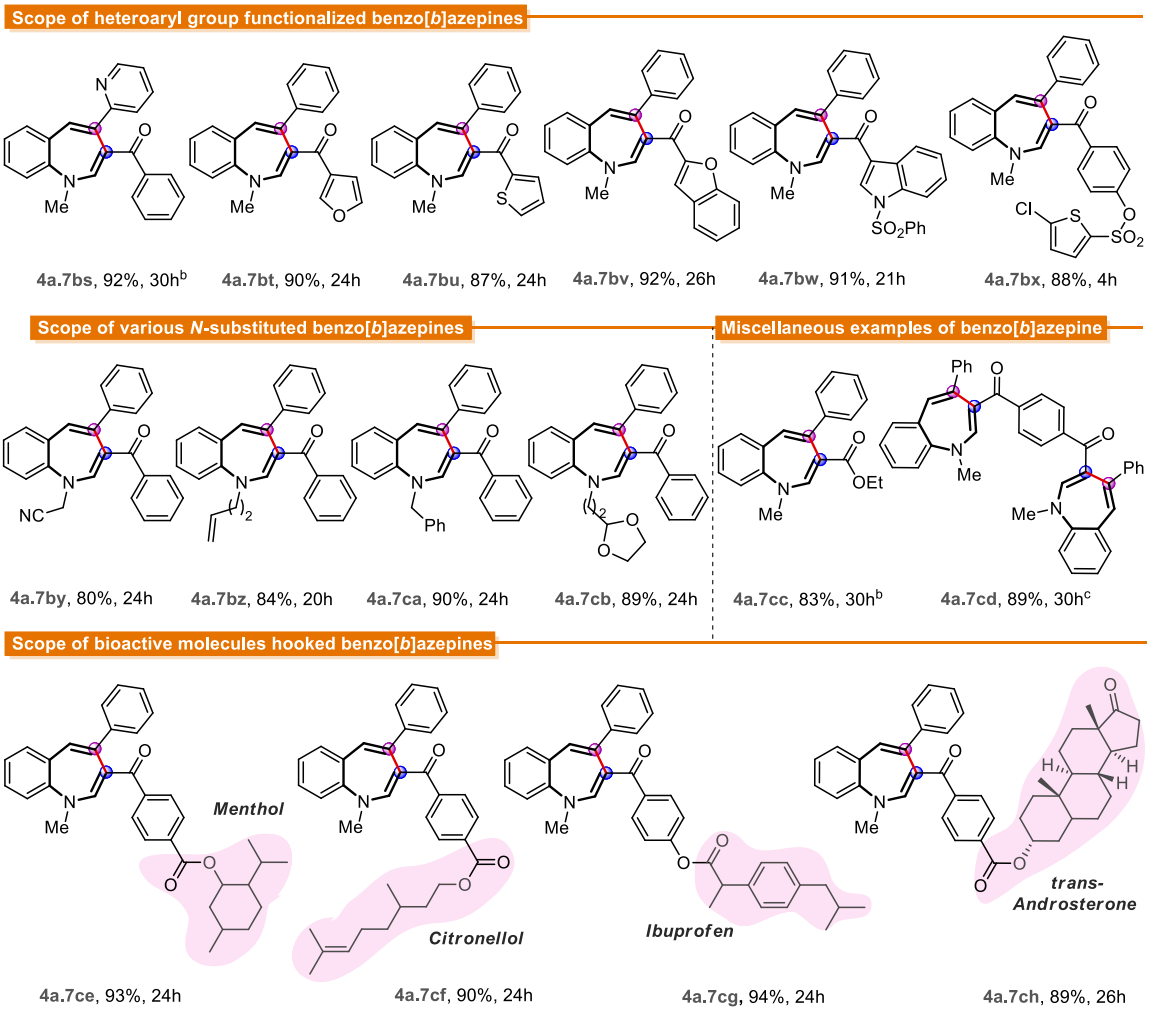


4a.7bj, 91%, 23h **4a.7bk**, 90%, 25h **4a.7bl**,[b] 94%, 28h **4a.7bm**, 94%, 24h

Scope of alkyl group functionalized benzo[*b*]azepines



4a.7bn, 89%, 22h **4a.7bo**, 84%, 20h **4a.7bp**, 88%, 20h **4a.7bq**, 86%, 21h **4a.7br**, 87%, 24h



Reaction condition: **4.18** (0.2 mmol), **Au7** (1 mol%) in TFE (0.5 M) at 60 °C, unless otherwise stated. [a]1g of **4.18aa** and 0.5 mol% of **Au7** were used for a gram scale synthesis. [b]DCM (50 μL) was used as the co-solvent. [c]2 mol% of **Au7** was used.

These observations indeed reveal a certain electronic effect of Ar^1. Substrates bearing Me, Cl and F substituents cyclized efficiently like the unsubstituted one leading to respective benzo[*b*]azepines **4a.7ac-ae**. Pleasingly, different electron-donating groups (Me, Et, OMe) or electron-withdrawing groups (NO_2, CO_2Me) at the *para*-position of the alkyne phenyl ring (Ar^2) were well compatible with this reaction and the corresponding azepine products were obtained in excellent yields (88-94%). Likewise, a Me or F group at either the *ortho*- or *meta*-position on the phenyl ring (Ar^2) had no influence on the reaction, producing compounds **4a.7al** and **4a.7am** respectively without compromising the product yield. So there was no noticeable electronic effect of Ar^2 in this cyclization. Even, cyclizations of a large number of substrates with different functionalities at different positions on Ar^3 showed no electronic effect of the aryl substituents on

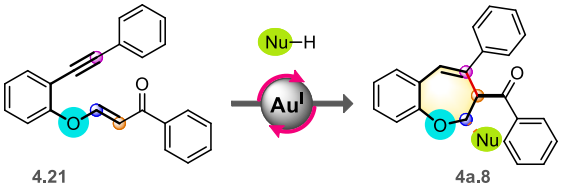
this transformation. Benzo[*b*]azepines **4a.7an-ba** were isolated in these reactions with attractive yields. Notably, efforts towards the access of highly functionalized benzo[*b*]azepines (**4a.7bb-bi**) with diverse electronic variants on Ar^1, Ar^2 and Ar^3 were also successful. Promising yields (88-95%) of the products were noted. Thus, the reaction was proved to be versatile irrespective of any electronic bias at the periphery of vinylogous amides. Since polycyclic aromatic hydrocarbons (PAH) have extensive applications as organic materials, naphthyl, anthracenyl and pyrenyl groups containing substrates were reacted and **4a.7bj-bl** were obtained in very good yields (90-94%). These scaffolds are highly fluorescent in nature and a representative absorption and emission spectra of pyrene anchored derivative **4a.7bl** is provided in Table 4a.2. Alkynyl enaminone having a 2-phenylethenyl group in the place of Ar^3 also cyclized in 7-*endo-dig* fashion giving the benzo[*b*]azepine **4a.7bm** without involving in any side reactions.

Furthermore, the aliphatic functionalities instead of aryl rings Ar^2 and Ar^3 are also compatible in this methodology. Alkyl groups such as benzyl, cyclopropyl, OTHP, keto and ester having substituents in the place of Ar^2 well tolerated the reaction condition and furnished the benzo[*b*]azepines **4a.7bn-bq**. The enaminone having alkyl ketone also worked well in giving **4a.7br**. This strategy offers a facile access to peripherally decorated benzo[*b*]azepines bearing pyridine, furan, thiophene, benzofuran, indole rings **4a.7bs-bx** with promising yields. Switching the substituents at 'N'-center of the enaminone core from methyl to cyanomethyl, homoallyl, benzyl and 2-(2-ethyl)-1,3-dioxolane did not obstruct the reaction progress and the productivity [**4a.7by-cb** (80-90%)]. Pleasingly, an ester containing product **4a.7cc** was also obtained in good yield from the vinylogous carbamate substrate. Bis cyclization to form two benzo[*b*]azepines in a single molecule was achieved efficiently using 2 mol% of **Au7** leading to the product **4a.7cd** from appropriate substrate. We were then interested to install biologically potent motifs in the benzo[*b*]azepine scaffolds in order to integrate their activities. Consequently, access to natural product (menthol), terpenoid (citronellol), non-steroidal anti-inflammatory drug (ibuprofen) and neurosteroid (trans-androsterone) stitched benzo[*b*]azepines **4a.7ce-ch** (90-94%) synthesized by this protocol undoubtably demonstrate the versatility of this method.

All the prepared compounds were characterized by NMR, HRMS and FTIR studies. The structure of **4a.7aa** was further confirmed by single crystal X-ray diffraction analysis (CCDC number 2115137).

4a.2.5. Synthesis of Fluoroalkoxy Incorporated Dihydrobenzo[*b*]oxepine Derivatives:

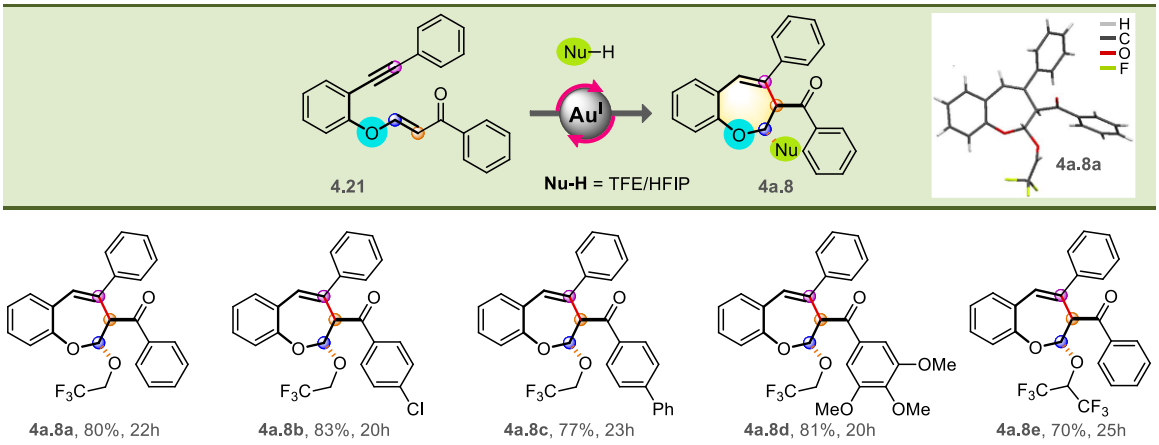
We questioned whether it would be possible to extend this strategy for different heteroatom other than nitrogen. To check this, the vinylogous esters derived from *o*-alkynylphenols **4.21a** was treated under the optimized reaction conditions and found to cyclize in the same 7-*endo-dig* fashion. However, surprisingly, incorporation of the fluorinated solvent at the 2-position of the benzo[*b*]oxepine **4a.8** was noted (Scheme 4a.4). The formation of **4a.8** was confirmed by nuclear magnetic resonance (NMR) spectroscopic and high resolution mass spectroscopic (HRMS) analysis. The structure of **4a.8a** was further confirmed by single crystal X-ray diffraction analysis (CCDC number: 2115138). XRD analysis revealed the exclusive trans geometry of the double bond in the structure.



Scheme 4a.4. Synthesis of fluoroalkoxy incorporated dihydrobenzo[*b*]oxepine analogues under gold catalysis.

The scope of fluoroalkoxy incorporated dihydrobenzo[*b*]oxepine synthesis was also investigated under the optimized reaction conditions using the synthesized substrates having different substituents. The outcome is tabulated in Table 4a.3.

Table 4a.3. Gold-catalyzed synthesis of fluoroalkoxy incorporated dihydrobenzo[*b*]oxepine derivatives (**4a.8**)



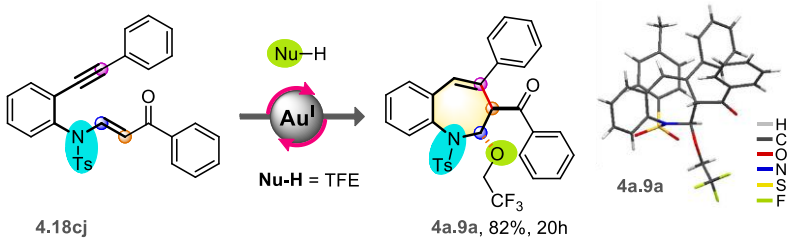
Reaction conditions: **4.21** (0.2 mmol), **Au7** (1.0 mol%) in fluoro-alcohol (0.5 M) solvent at 60 °C unless otherwise stated.

We could able to access TFE incorporated 2,3-dihydro-benzo[*b*]oxepines (**4a.8a-d**) with promising yields (77-81%). Notably, HFIP was also suitable to deliver the corresponding fluorinated oxepine motif **4a.8e** in 70% yield. All the prepared compounds were characterized by NMR, HRMS and FTIR studies and all of them have shown exclusive trans stereochemistry of the substituents.

4a.2.6. Synthesis of Fluoroalkoxy Incorporated Dihydrobenzo[*b*]azepine Derivatives:

We were curious to know whether the higher electronegativity of oxygen compared to that of nitrogen is responsible for this type of behavior. Then, the vinylogous amides derived from *o*-alkynylanilines having a tosyl goup on nitrogen **4.18cj** was treated under the optimized reaction conditions and found to cyclize in the same fashion as that of vinylogous esters derived from *o*-alkynylphenols leading to fluoroalkoxy incorporated dihydrobenzo[*b*]azepine derivative **4a.9a**

having fluroalkoxy and arylketone moieties in trans stereorelationship (Scheme 4a.5). The structure of **4a.9a** was further confirmed by single crystal X-ray diffraction analysis (CCDC number: 2115140).

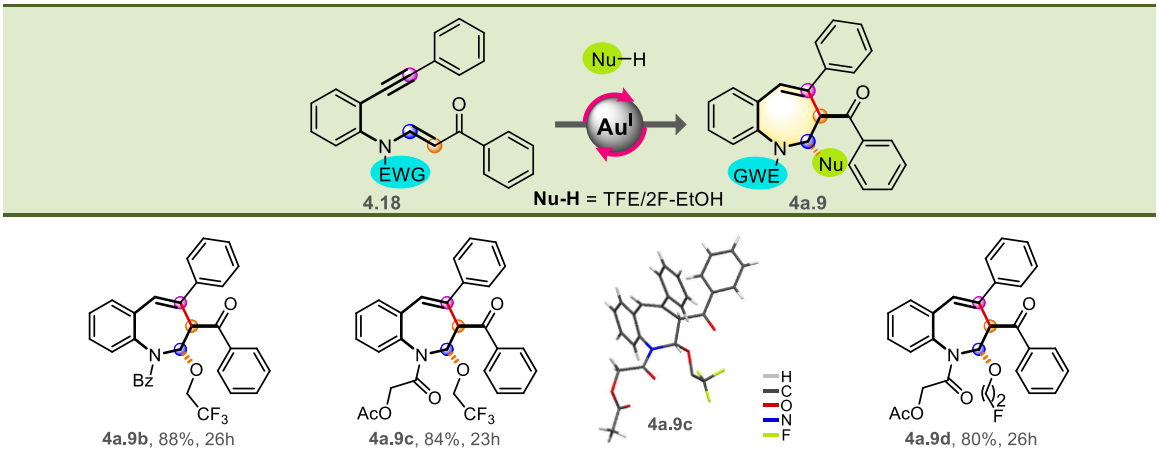


Scheme 4a.5. Synthesis of fluoroalkoxy incorporated dihydrobenzo[*b*]azepine analogues under gold catalysis.

After achieving this cyclization, we have allowed to cyclize few more vinylogous amides derived from *o*-alkynylanilines with different electron-withdrawing groups on nitrogen under the optimized reaction condition.

The scope of fluoroalkoxy incorporated dihydrobenzo[*b*]azepine synthesis was also investigated under the optimized reaction conditions using a variety of vinylogous amides derived from *o*-alkynylanilines having different electron-withdrawing substituents on nitrogen. The results are depicted in Table 4a.4.

Table 4a.4. Gold-catalyzed synthesis of fluoroalkoxy incorporated dihydrobenzo[*b*]azepine derivatives (**4a.9**)



Reaction conditions: **4.18** (0.2 mmol), **Au7** (1.0 mol%) in fluoro-alcohol (0.5 M) solvent at 60 °C unless otherwise stated.

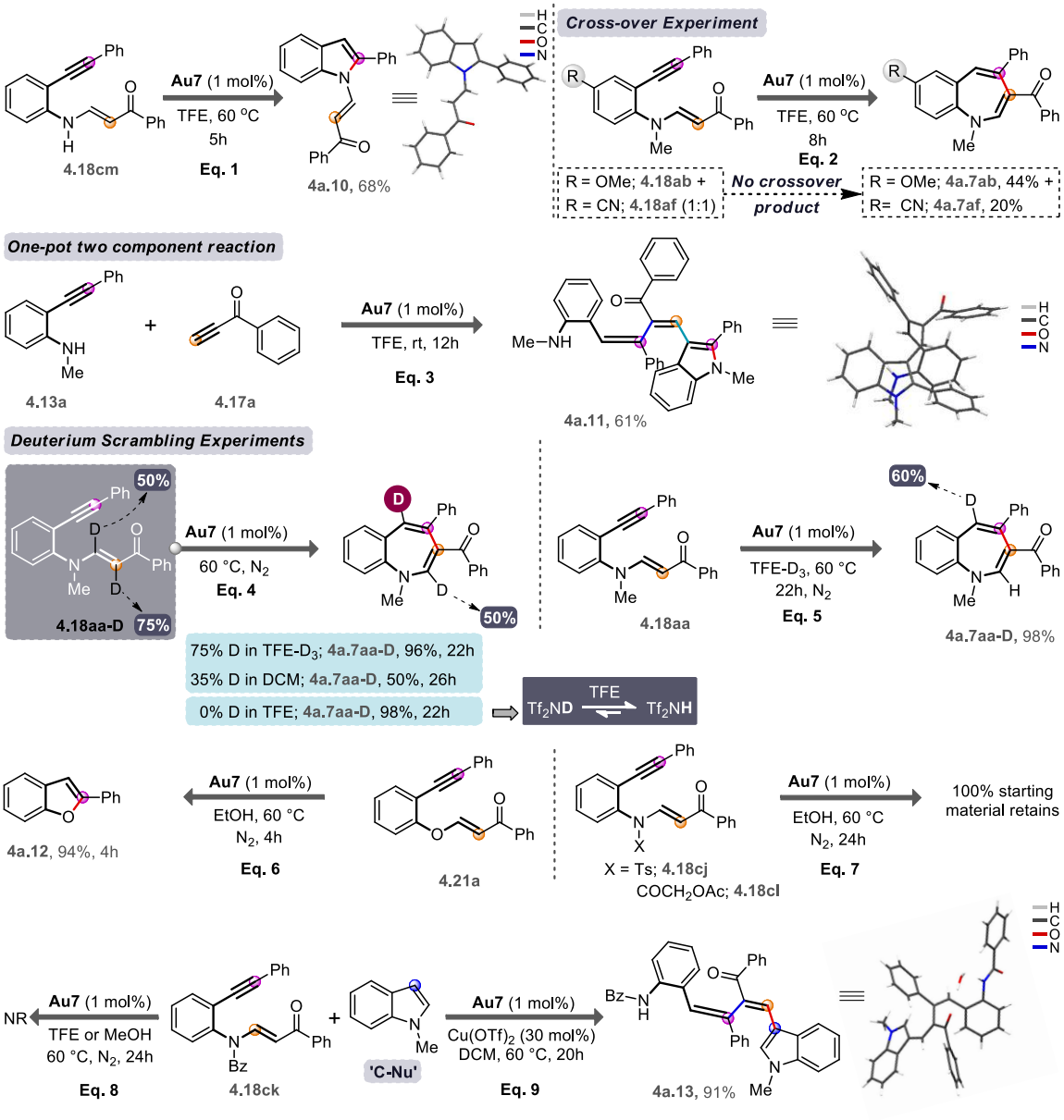
Synthesis of TFE incorporated 2,3-dihydrobenzo[*b*]azepines (**4a.9a-c**) were achieved in promising yields (82-88%). Even, 2-fluoroethanol was also suitable to produce the corresponding fluoroalkoxy incorporated dihydrobenzo[*b*]azepine motif **4a.9d** in 80% yield. All the prepared compounds were characterized by NMR, HRMS and FTIR studies and all of them have shown

exclusive trans stereochemistry. The structure of **4a.9c** was also confirmed by single crystal X-ray analysis (CCDC number: 2062199).

4a.2.7. Control Experiments:

Next, a set of control experiments have been envisaged for mechanistic understanding. Foremost, we were curious to know the reactivity pattern of N-H containing vinylogous amides derived from *o*-alkynylanilines **4.18cm**. The substrate **4.18cm** did not yield the seven-membered product, rather showed the usual reactivity of *o*-alkynylaniline under gold catalysis producing the substituted indole derivative **4a.10** by an 5-*endo-dig* cyclization (eq. 1, Scheme 4a.6). So, the presence of proton on nitrogen makes it available for an effective protodemetallation of indolyl gold species formed after the 5-*endo-dig* cyclization that is the energetically more favorable pathway according to the DFT studies (*vide supra*). Next, to check the nature of this cyclization, a competition reaction of an equimolar mixture of substrates **4.18ab** and **4.18af** was conducted. It lead to **4a.7ab** and **4a.7af** in almost 2:1 ratio after 8 hrs (eq. 2, Scheme 4a.6). This observation confirmed the intramolecular nature of this cyclization. Since the vinylogous amides derived from *o*-alkynylanilines used for this reaction were prepared from the *o*-alkynyl-N-methylanilines and alkynones, we are curious to know wheather this enaminone could be formed in situ or not. Thus an one-pot synthesis of the benzo[*b*]azepine was attempted by reacting N-methyl-2-(phenylethynyl)aniline, **4.13a** and 1-phenylprop-2-yn-1-one, **4.17a** in the presence of **Au7** in TFE. Though there is a probability of gold-catalyzed indole formation from **4.13a** in *5-endo-dig* fashion, the reaction yielded an unusual highly substituted indole derivative **4a.11**. The structure of **4a.11** suggests that the indole formed primarily reacted with the alkynone **4.17a** at the β-position and subsequent addition on the C≡C bond of another molecule of **4.13a** (eq. 3, Scheme 4a.6). Thus the importance of the enaminone core was revealed from this study. The structure of both the substituted indoles **4a.10** and **4a.11** were confirmed by SC-XRD analysis (CCDC numbers: 2115142 and 2062197 respectively).

To get more insight into the reaction mechanism and the source of hydrogen involved in the proto-deauration step during the formation of benzo[*b*]azepine, a few deuterium scrambling experiments were performed. First, the deuterated vinylogous amide derived from *o*-alkynylaniline (**4.18aa-D**) was synthesized by treating 2-alkynyl N-methylaniline (**4.13a**) with alkynone (**4.17a**) in CD_3OD. Notably, 50% and 75% deuterium incorporation were found at β- and α-position of the tethered enaminone. When **4.18aa-D** was allowed to react under the optimized conditions in TFE-D_3 solvent, the desired **4a.7aa-D** was observed in 96% isolated yield with 75% and 50% D at C5 and C2 respectively. Where as, the same reaction in TFE solvent provided **4a.7aa-D** having 0% D at C5 and 50% D at C2 (eq. 4, Scheme 4a.6). Additionally, cyclization of **4.18aa-D** in TFE-D_3 solvent provided 98% of **4a.7aa-D** having 60% deuterium incorporation at C5 (eq. 5, Scheme 4a.6). These observations demonstate that the source of proton taking part in the protodeauration is majorly the solvent.



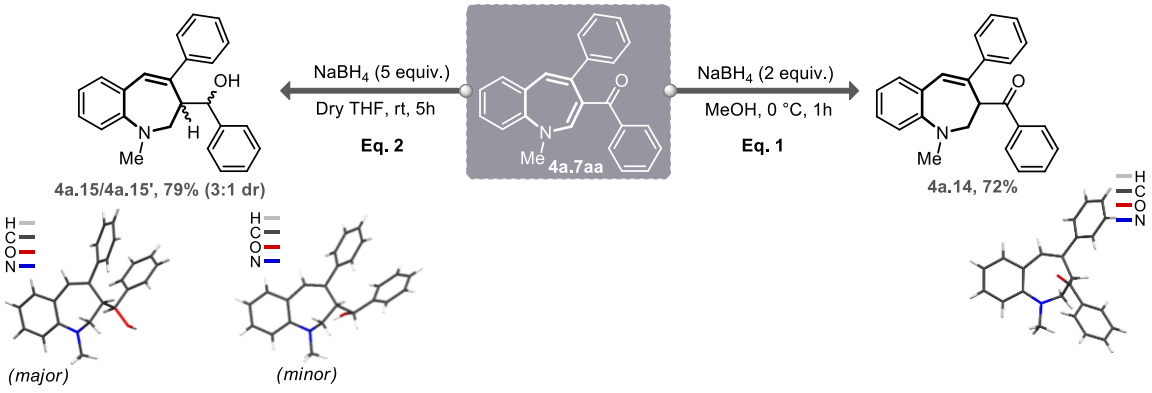
Scheme 4a.6. Control experiments.

The counter anion Tf_2N^- is supposed to be involved in the deprotonation at the C3 position after the cyclization. So, **4.18aa-D** was allowed to cyclize DCM solvent and 35% deuterium incorporation at the C5 of **4a.7aa-D** was noted. Though deuterium from C3 to C5 was not transferred completely in the product, the role of Tf_2N^- counter anion in proton abstraction and delivering it at the time of proto-deauration is clear. When the reactions conducted in protic TFE solvent, Tf_2ND might be experiencing a rapid proton exchange with the solvent to become Tf_2NH before the proto-deauration step. Being a strong acid, Tf_2NH can then involve in the proto-deauration step ahead of the solvent.

To probe the role of fluoroalcohol in the formation of fluoroalkoxy incorporated dihydrobenzo[*b*]azepines/oxepines, we have performed the reactions in ethanol solvent. But no desired product was isolated under the standard reaction condition. Rather, the compound **4.21a** cyclized *via* an 5-*endo-dig* cyclization path with the extrusion of alkenyl ketone moiety providing 2-phenyl benzofuran **4a.12** in 94% yield (eq. 6, Scheme 4a.6) whereas the starting material was recovered totally in case of **4.18cj** and **4.18cl** (eq. 7, Scheme 4a.6). Thus these experiments show certain influence of the fluorinated solvent in effecting this 7-*endo-dig* cyclization.[13] Probably, the fluorinated solvent assists the polarization of the enone *via* hydrogen bonding with the carbonyl oxygen. Conversely, the 'C'-nucleophile such as *N*-methylindole is not capable to furnish the 7-*endo-dig* cyclization when N-methylindole and **4.18ck** were reacted in TFE (eq. 8, Scheme 4a.6). Surprisingly, indole reacted with **4.18ck** to result in **4a.13** when 30 mol% of $Cu(OTf)_2$ was present in addition to the gold catalyst in DCM solvent (eq. 9, Scheme 4a.6). The structure of **4a.13** was confirmed by X-ray crystallographic analysis (CCDC number: 2115141). The structure suggests that the benzo[*b*]azepine ring might have formed first *via* 7-*endo-dig* manner, followed by the 1,4-addition of N-methylindole and subsequent cleavage of C-N bond accompanied with azepine ring-opening.

4a.2.8. Late-stage Transformations of Benzo[*b*]azepine:

A couple of downstream synthetic modifications of these benzo[*b*]azepines were then explored by studying the reduction of **4a.7aa**. The enamine double bond got reduced selectively by $NaBH_4$ in methanol solvent to produce **4a.14** in 72% yield (Eq. 1, Scheme 4a.7). Whereas, both the enamine double bond and the ketone were reduced by $NaBH_4$ in dry THF at room temperature to yield a diastereomeric mixture of **4a.15** and **4a.15'** (Eq. 2, Scheme 4a.7). Five equivalents of $NaBH_4$ was required for this reaction, as a mixture of partially reduced products was resulted with lesser amounts of $NaBH_4$. The structures of **4a.14**, **4a.15** and **4a.15'** were further confirmed by single crystal X-ray crystallographic analysis (CCDC numbers: 2115145, 2115143 and 2115144).



Scheme 4a.7. Late stage transformations of benzo[*b*]azepine.

4a.2.9. Reaction Kinetics for the Formation of Benzo[*b*]azepine:

To probe the mechanistic details further, we embarked into kinetic analysis as picturized in figure 4a.5. First, we have investigated the reaction profile in different intervals of time using **4.18aa** under the optimal set of reaction condition. During the initial period of the reaction, conversion of **4.18aa** was decreasing very slowly. After 4 hrs, the concentration of **4a.7aa** raised significantly upto 17 hrs (84% conversion). At the final stage conversion rate of **4.18aa** was gradually decreasing, with almost full conversion (98% yield) achieved after 22 hrs (plot A). In contrast, the plot B clearly demonstrates the first-order dependency on both the starting material **4.18aa** and the catalyst **Au7**. Then we analogized the reaction rates of vinylogous amides derived from *o*-alkynylanilines (**4.18**) having different *para*-substitution to evaluate the electronic effect in the substrates. Using the results obtained from the kinetic experiments, we have plotted the Hammett graph (plot C). This plot showed a negative reaction constant value ($\rho = -0.34$) which revealed a strong correlation of the first-order rate constant with the σ_p of the Ar^1 group. This indicates the participation of lone pair of electrons on the nitrogen to make the C3 electron rich to effect this 7-*endo-dig* cyclization.

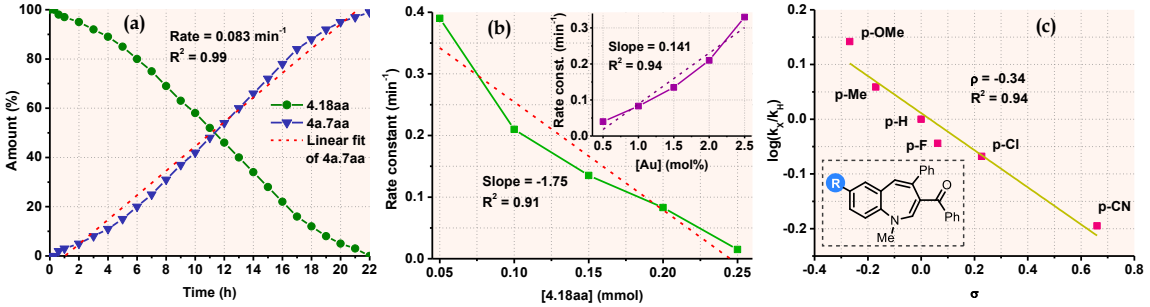


Figure 4a.5. Kinetic studies of the benzo[*b*]azepine (**4a.7aa**) formation.

4a.2.10. Computational Studies:

To understand the mechanism of formation of the seven-membered benzo[*b*]azepines computational studies have been carried out by Ms. Renuka and Prof. Lourderaj of NISER Bhubaneswar in collaboration. DFT calculations were performed using the M062X function with SDD basis set for Au and 6-31G(d,p) for other atoms.[14-16] The calculations were performed using TFE as solvent within the polarisable continuum model (PCM).[17] All the calculations were performed using Gaussian16 software package.[18] The ring-closure of **4.18aa** catalyzed by the catalyst JohnPhosAuNTf$_2$ (**Au7**) that resulted in an excellent yield of 98% of **4a.7aa** was considered in the computational study and the results are summarized in Figure 4a.6. The reaction begins with the approach of the **Au7** catalyst to **4.18aa** to form the active pre-reaction complex, **prc** by a metal---π interaction between Au and C4-C5 alkyne bond. The two similar Au–C bond distances (Au-C5 = 2.36 and Au-C4 = 2.38 Å) indicate a nearly symmetrical coordination of the C4-C5 bond to the gold center. In the **prc**, the counter anion NTf_2^- can have multiple orientations. The formation of **prc** is then followed by the ring-closure which is the crucial step in determining the ring size of the product.

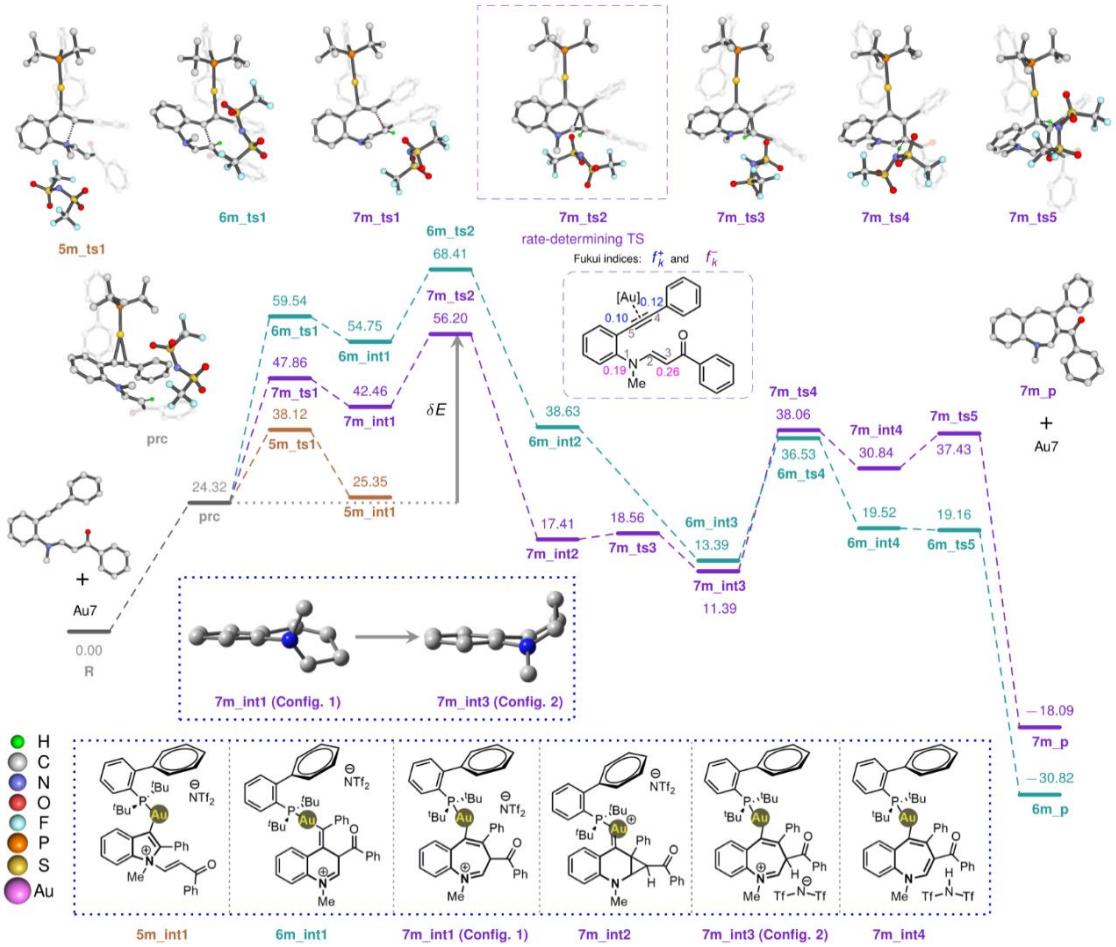


Figure 4a.6. Free energy profile of the various pathways for the cyclization of **4.18aa** by the catalyst **Au7** obtained at the M062X/6-31G(d,p) Au (SDD) level of theory.

In this context, it is of interest to understand the electronic nature of the different carbon and nitrogen centers in **prc**. The condensed Fukui functions and the local electrophilicity calculated from the natural populations (Figure 4a.6) suggest that the C4 and C5 are electrophilic, while C3 and N1 are nucleophilic in nature.[19] Thus, the corresponding ring-closure resulting in five- and six-membered cyclic products can also be expected contrary to the exclusive seven-membered cyclic product observed in the experiments. To understand the mechanism of the selective formation of benzo[*b*]azepine, the complete free energy profile was mapped for different pathways at 333.15 K by identifying the different stationary points on the potential energy surface. The free energy profiles for the various pathways and the geometries of the stationary points are given in Figures 4a.6. As discussed above, after the formation of the **prc**, the ring-closure can happen resulting in five-, six-, or seven-membered cyclic intermediates which is followed by protodeauration to form the products. The specificity of the product formation is thus dictated by the nature of ring-closure. The five-, six-, and seven- membered ring-closure steps result in the intermediates **5m_int1**, **6m_int1** and **7m_int1** via the transition states **5m_ts1**, **6m_ts1** and

7m_ts1 respectively (Figure 4a.6). It can be seen that the formation of the five-membered ring intermediate has the lowest barrier (~14 kcal/mol). However, in **5m_int1** there is no proton available at N1 for abstraction by NTf_2^- and thus the subsequent reaction to form an indole product is arrested. This is supported by the fact that, if the methyl group at N1 is replaced by a proton as in **4.18cm**, exclusive formation of indole derivative **4a.10** was observed via a 5-*endo-dig* cyclization (Eq. 1, Scheme 4a.6). In contrast, the proton abstraction by NTf_2^- is possible in six- and seven-membered ring formation pathways with ring-closure barriers of 35.2 and 23.5 kcal/mol corresponding to the transition states **6m_ts1** and **7m_ts1** respectively.

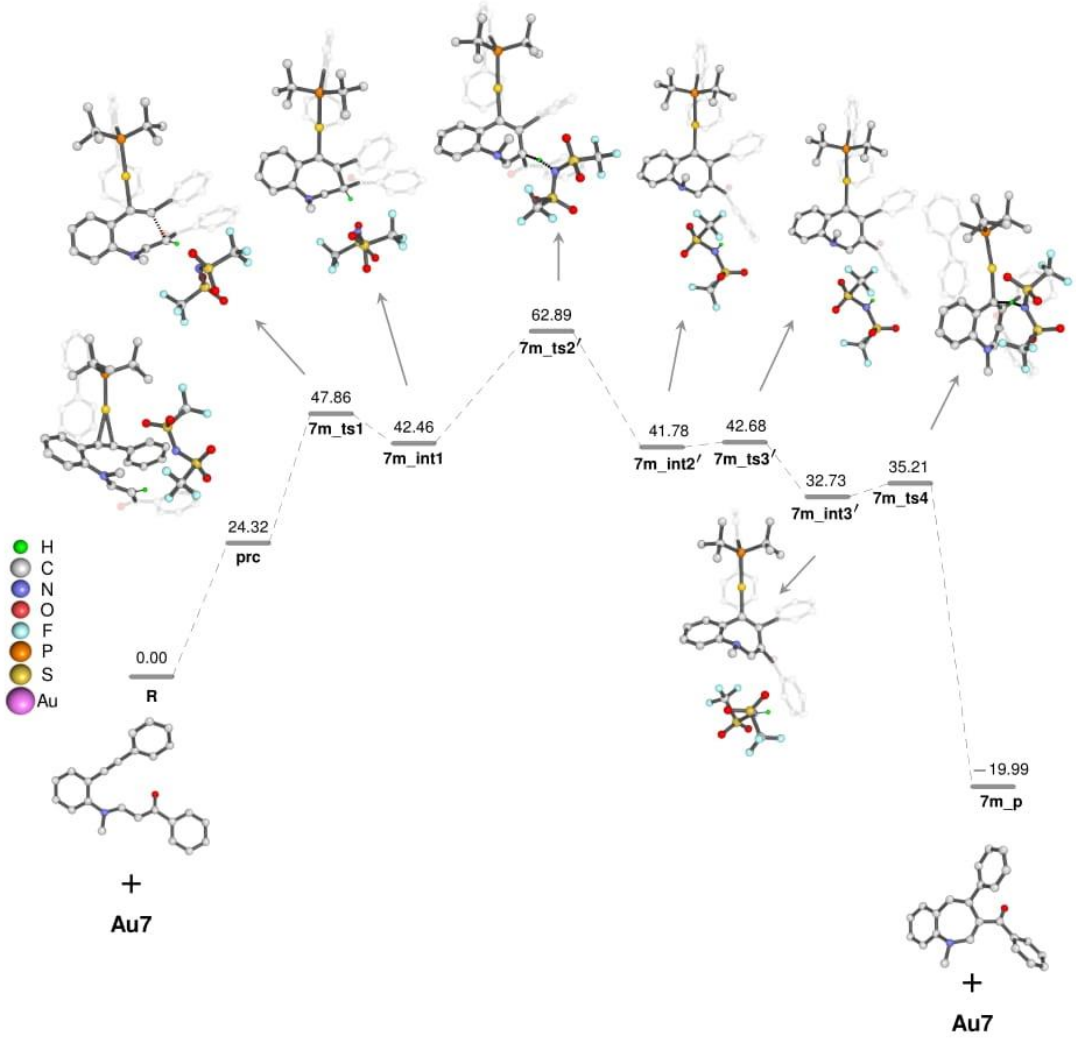


Figure 4a.7. Free energy profile (kcal/mol) for the 7-membered ring formation (alternate path) obtained at the M062X/6-31G(d,p) Au (SDD) level of theory.

Thus, the DFT calculations point that the seven-membered ring formation having a lower barrier is favoured over the six-membered ring formation, consistent with the exclusive 7-*endo-dig* cyclized products observed in the experiments. In the next step of the reaction, the

intermediate **7m_int1** with the N1 group having an envelope geometry undergoes cyclopropanation, resulting in the formation of a cyclopropyl gold carbene intermediate **7m_int2** with a barrier of 13.7 kcal/mol through the transition state **7m_ts2**. Following that, **7m_int2** undergoes the cyclopropane ring-opening via the transition state **7m_ts3** with a barrier of 1.2 kcal/mol, yielding **7m_int3**. It has to be noted that **7m_int1** and **7m_int3** differ in their conformation and **7m_int3** being more stable conformation. From **7m_int3**, a proton is then abstracted at C3 by the NTf_2^- via **7m_ts4** crossing a barrier of 26.7 kcal/mol to result in **7m_int4** and $HNTf_2$. Now, the protodeauration happens at C5 by $HNTf_2$ via the transition state **7m_ts5** with a barrier of 6.6 kcal/mol to form the final product and the active Au(I) catalyst is regenerated. The fastest step in the catalytic cycle for the benzo[*b*]azepine formation is the cyclopropane ring-opening step having a barrier of 1.2 kcal/mol.

To understand the rate-controlling step in the catalytic cycle, the rate-controlling transition state (RCTS) and rate-controlling intermediate (RCI) were evaluated using the energy span model.[20] It was found that the RCTS and the RCI were **7m_ts2** and **prc** respectively with the reaction having an effective free energy barrier of 31.9 kcal/mol.

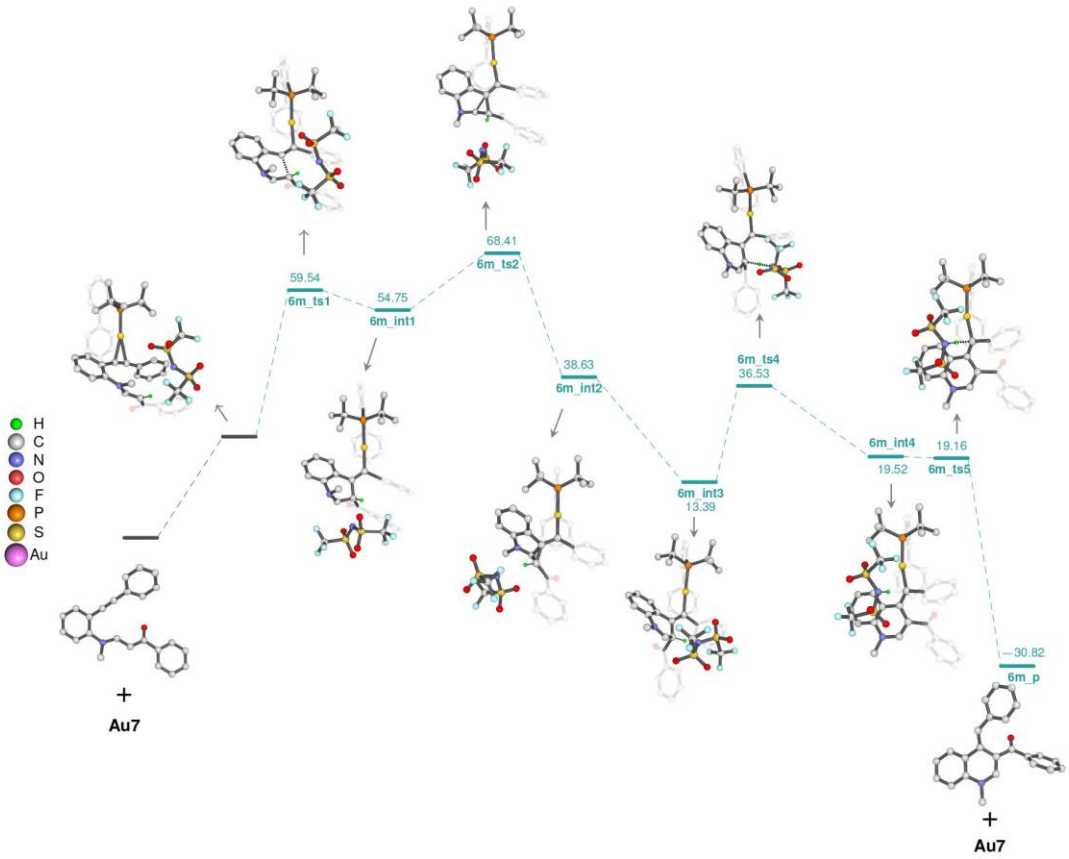
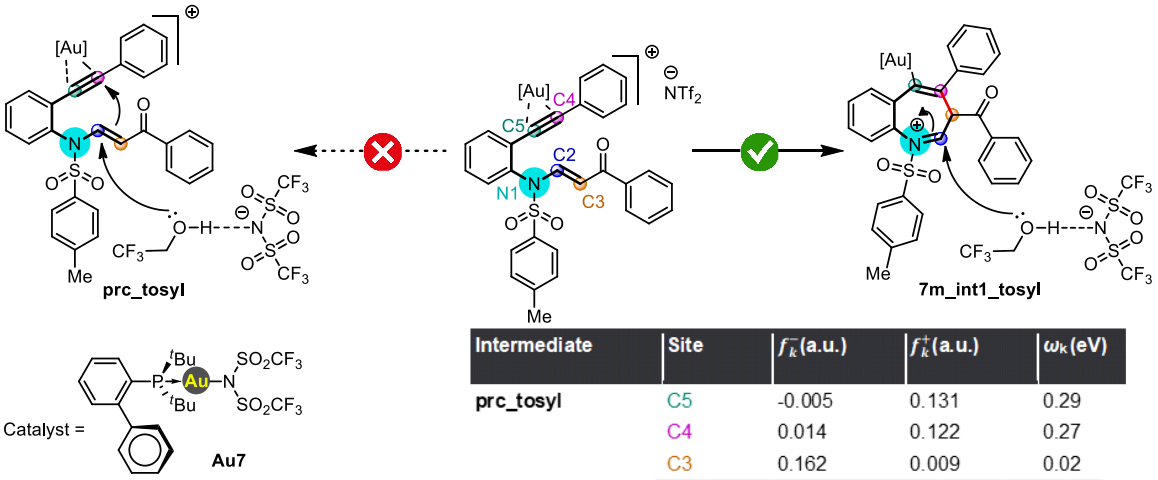


Figure 4a.8. Free energy profile (kcal/mol) for the 6-membered ring formation (when C4 carbon atom of alkene react with the C2 carbon atom of alkyne) obtained at the M062X/6-31G(d,p) Au (SDD) level of theory.

An alternative high energy path that bifurcates from **7m_int1** (effective barrier of 38.6 kcal/mol), following a mechanism where the N1 group in the seven-membered ring retained the envelope geometry without the cyclopropanation step was also identified (Figure 4a.7). To compare the reaction pathways for the seven- and six-membered products formation, the free energy profile for the six-membered pathway was also computed (Figure 4a.8).

This pathway, although closely resembled the seven-membered ring formation path, was higher in energy with an effective barrier of 44.1 kcal/mol. Clearly, the complete mechanism of the catalytic cycle leading to the experimentally observed seven-membered benzo[*b*]azepine is described by the free energy profile obtained from DFT calculations.

Further, to understand the role of tosyl substituent on nitrogen in the solvent insertion at C2 (Scheme 4a.5), the Fukui functions and the local electrophilicity indices (ω_k) were calculated for the tosyl substituted pre-reaction complex (**prc_tosyl**) and the seven-membered cyclic intermediate (**7m_int1_tosyl**) formed after the ring-closure (Figure 4a.9). It can be seen that the f_k^+ and ω_k for the C2 site are nearly zero in **prc_tosyl** and increase to 0.30 and 1.03 respectively in **7m_int1_tosyl**. In addition, the ω_k for C2 in **7m_int1_tosyl** is higher than the value obtained for the methyl substituted **7m_int1** (Table 4.4). These observations reveal that the C2 is more electrophilic in **7m_int1_tosyl** and is susceptible for a nucleophilic attack by the solvent. The calculations not only emphasize the role of tosyl group in solvent insertion but also indicate that the insertion happens after the ring-closure step.

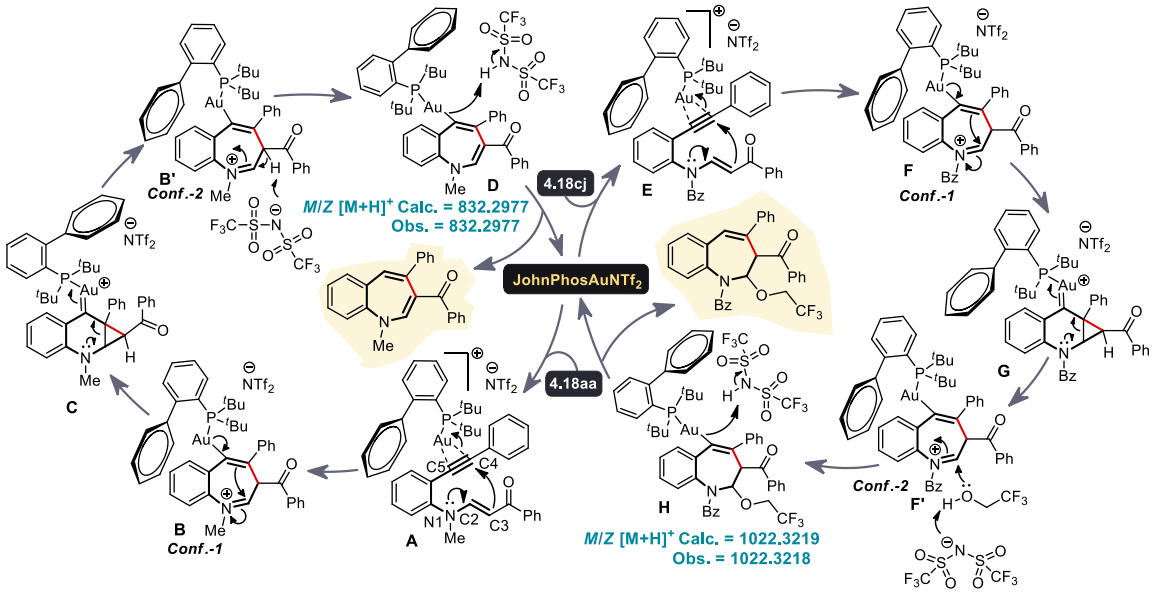


Intermediate	Site	f_k^-(a.u.)	f_k^+(a.u.)	ω_k(eV)
prc_tosyl	C5	-0.005	0.131	0.29
	C4	0.014	0.122	0.27
	C3	0.162	0.009	0.02
	C2	0.022	-0.004	-0.01
7m_int1_tosyl	C5	0.106	0.021	0.09
	C4	0.041	0.007	0.03
	C3	0.002	-0.019	-0.08
	C2	0.011	0.304	1.29

Figure 4a.9. Illustration of the mechanism of solvent insertion at C2 in N-tosyl substituted substrate.

4a.2.11. Mechanism for the Formation of Benzo[*b*]azepine and Fluoroalkoxy Incorporated Dihydrobenzo[*b*]azepine Derivatives:

A plausible mechanistic pathway for the formation of benzo[*b*]azepines and fluoroalkoxy substituted dihydrobeno[*b*]azepines is illustrated in Scheme **4a.8** based on the control experiments and the computational studies. Firstly, Au(I) will interact with the C≡C bond of the vinylogous amide derived from *o*-alkynylaniline **4.18aa** to form intermediates **A** and **E**. As evident from the Hammett plot and Fukui indices, the lone pair of electrons of nitrogen will take part in resonance to polarize the enaminone double bond and nucleophilic attack by C3 on the C4 of the gold-activated alkyne will lead to 7-*endo-dig* cyclization (intermediates **B** and **F**). Next this intermediate will undergo an intramolecular cyclopropanation to form intermediate **C** and **G**. After that, the this intermediate will form interediate **B'** and **F'** having twisted conformation. Then, when a methyl is present on "N", the counter anion Tf_2N^- may abstract the proton from C3 as presented in intermediate **B'** and transfer it at C5 during the protodeauration step to form the desired benzo[*b*]azepine product. HRMS analysis of the reaction mixture after 2h of reaction showed a peak at *m/z* 832.2977. This may be assigned for the $[M+H]^+$ of intermediate **D**. Conversely, when an electron-withdrawing group is present on "N", the C2 of the formed iminium ion **F'** is more electrophilic as revealed by the f_k^+ and ω_k values. This will assist the addition of the fluoroalcohol at C2 leading to intermediate **H**.



Scheme 4a.8. Proposed mechanism for the synthesis of benzo[*b*]azepine and fluoroalkoxy incorporated dihydrobenzo[*b*]azepine.

Finally, protodeauration results in the formation of fluoroalkoxy incorporated dihydrobenzo[*b*]azepine. Formation of intermediate **H** is well-supported by the observance of a peak at *m/z* 1022.3218 corresponding to $[M+H]^+$ in the HRMS of the reaction mixture.

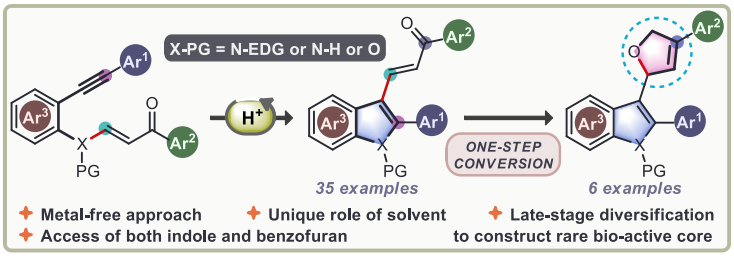
4a.3 Conclusions:

In conclusion, a more generalized direct ring-closing strategy to achieve benzo[*b*]azepines was disclosed by exploiting the multifaceted gold(I)-catalysis. The designed substrate and the fluorinated alcohol solvent preferred the 7-*endo-dig* carbacyclization over the typically expected 5-*endo-dig* cyclization. The detail mechanistic study by deuterium scrambling experiments and DFT calculations endorse the role of fluoro alcohol and the significance of energetically favored cyclopropanation involved in this 7-*endo-dig* cyclization. This approach has shown extensive substrate scope with practically possible substitution patterns including hooking of biologically relevant molecules.

- The methodology is a more generalized direct ring-closing strategy for benzo[*b*]azepine synthesis.
- The formation of 7-*endo-dig* carbacyclization over the most expected 5-*endo-dig* cyclization has been supported by the DFT studies.
- The significance of energetically favored cyclopropanation involved in this 7-*endo-dig* carbacyclization has been disclosed.
- The mild and unique multifaceted gold(I)-catalysis was advantageously exploited in this methodology.
- The methodology is operationally simple, atom economical and high yielding.
- The cyclization has a broad scope and versatility. Even the biologically potent or drug molecules hooked products could also be achieved.
- The synthesized benzo[*b*]azepines and fluoroalkoxy incorporated dihydrobenzo[*b*]-azepine/oxepines could find new applications in the field of medicinal chemistry.
- The role of fluoro alcohol in this 7-*endo-dig* cyclization was proved by the detail mechanistic study like deuterium scrambling experiments and DFT calculations.

Chapter 4B

TfOH-promoted Synthesis of Indoles and Benzofurans Involving Cyclative Transposition of Vinyl Ketone



A metal-free route for the construction of 3-substituted indoles from vinylogous amides derived from *o*-alkynylanilines involving Michael, retro-aza-Michael and amine trapping cascade is described here. The product is essentially the alkenyl ketone migrated product from nitrogen to the C3 carbon of indole which has been reported to form under Ni-catalyzed reactions of similar o-alkynylaniline derivatives. This atom-economical TfOH-promoted transformation has been extended to synthesize benzofuran derivatives using analogous vinylogous esters derived from o-alkynylphenols. Excellent stereochemical outcome of the double bond geometry in the products makes it attractive.

Mandal, M.; Balamurugan, R. *Manuscript submitted*.

4b.1. Introduction:

4b.1.1. Background of Research:

A large number of drugs contain heterocyclic cores because of their distinctive physicochemical properties.[21] Among them, indole/benzofuran/2,5-dihydrofuran scaffolds are found in a variety of biologically active compounds (Figure 4b.1).[22] In addition, indoles serve as key building blocks for the synthesis of numerous natural products such as tryptamine, β-carboline, psilocin, ergoline, bufotenine, pscilocybin and tryptophan etc. Even, it is observed in many plants such as jasmine, robinia pseudacacia, citrus fruits, orange blossoms,[23] animals and marine organisms. Indole core shows vital therapeutic properties on a large number of target diseases like malaria, depression, cancer, inflammatory, hypertension.[24] The marketed drugs such as lurasidone and vilazodone are prominent agents to treat central nervous system disorders. Moreover, this important core is a vital component of many commercially available oils, agrochemicals, flavouring/fragrance agents and photosensitizing compounds.[24d, 25]

On the other hand, benzofuran ring containing heteroaromatic compounds are core structural unit of several bio-active natural proucts and synthetic raw materials.[26] These frameworks have engrossed much attention due to their bio-activities as well as potential applications as drugs.[27-29] Benzofurans are extensively found in higher plants like rutaceae, asteraceae, cyperaceae and liliaceae.

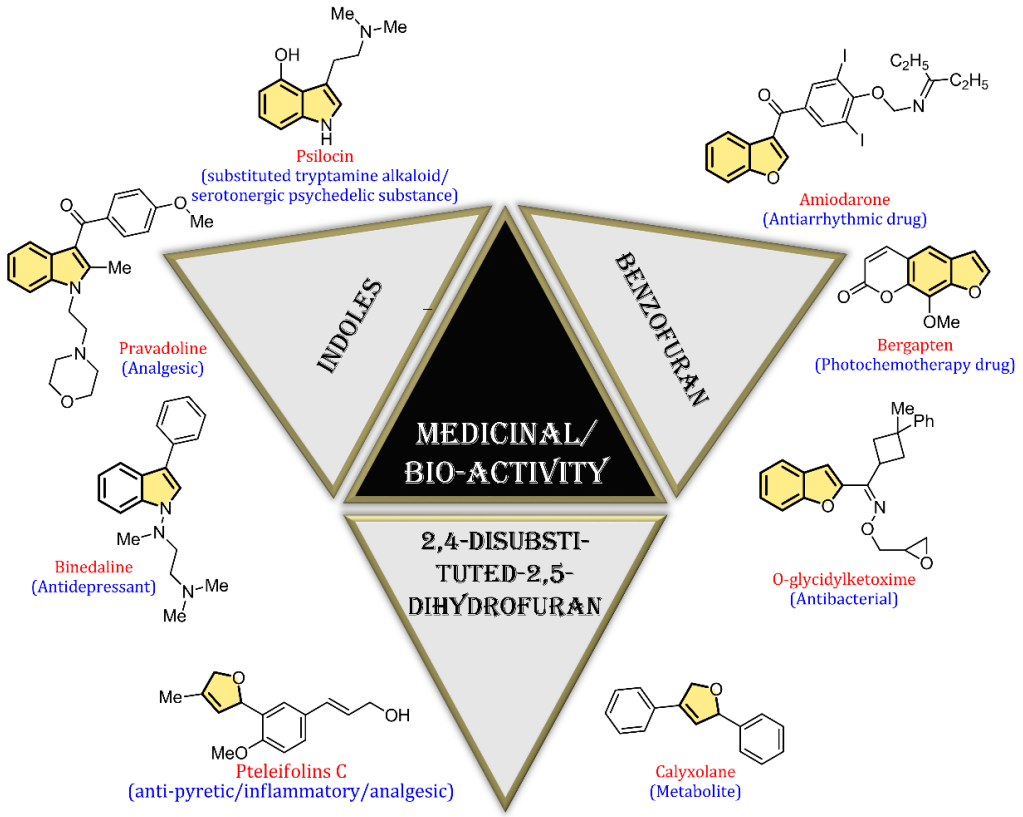


Figure 4b.1. Few novel indole/benzofuran/2,4-disubstituted-2,5-dihydrofuran analogues.

Considering their extensive scientific and commercial values, construction of new analogues of indole/benzofuran/2,5-dihydrofuran is still a subject of consistent interest to the organic researchers from academic and industrial points of view.

4b.1.2. Literature Reports:

The synthetic importance of indole/benzofuran/2,5-dihydrofuran has drawn close attention of organic chemists to diversify its core structure. A handful of reports are available in literature for the synthesis of 3-substituted indole/3-substituted benzofuran/2,4-disubstituted-2,5-dihydrofuran scaffolds.[30-32] Among them, cyclization of 2-alkynyl aniline derivatives constitute a promising strategy.

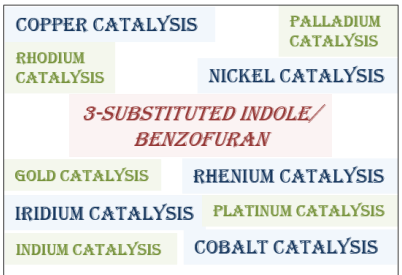
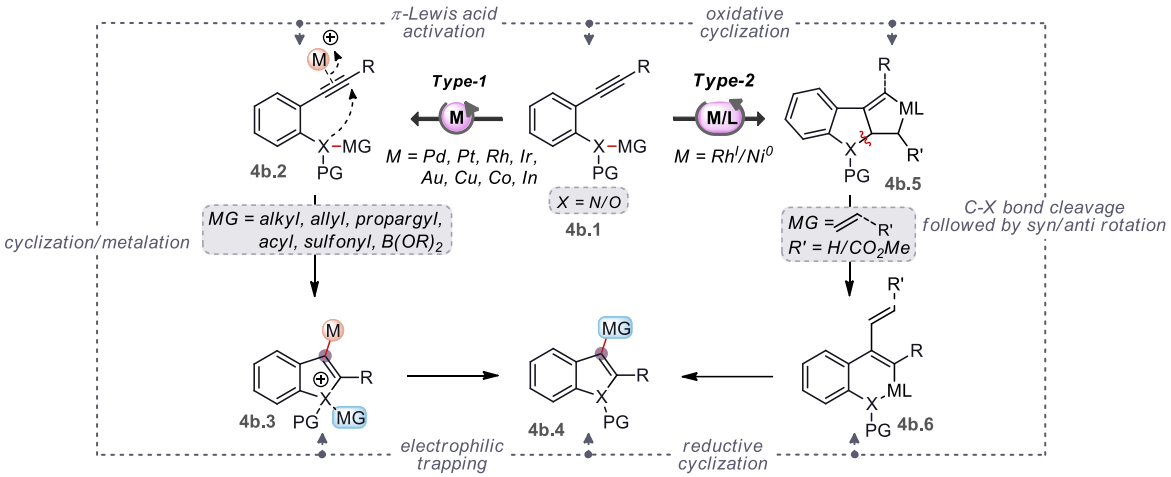


Figure 4b.2. Synthetic strategies of 3-substituted indole/benzofuran

While, significant efforts have been taken towards the synthesis of C2-substituted analogues via direct 5-*endo*-*dig* cyclization of *o*-alkynylanilines using π-philic metal catalysts.[33] The strategies to make C3-substituted indoles from *o*-alkynylanilines requires some trick and are very limited (Figure 4b.2).[34] Few groups have disclosed alkynophilic metals, such as, Pd, Pt, Rh, Ni, Ir, Au, Cu, Co, and In-catalyzed 5-*endo*-*dig* cyclization of 2-alkynylaniline derivatives to afford C3-functionalized indole/benzofuran derivatives (Scheme 4b.1).[30-31] These transformations involve intramolecular migratory cycloisomerization *via* initial alkyne activation, cyclization/C3-metalation followed by 1,3-migration sequences. This phenomenon was found for a variety of N- or O-substituents such as, allyl,[31a] benzyl,[30c] propargyl,[30a] methyl,[30d] α-alkoxyalkyl,[35b] acyl,[30c] sulfonyl,[30e] and $B(OR)_2$[30b,31b] (Scheme 4b.1). These protocols have their own merits and demerits in terms of their synthetic applicability. In this context, Tanaka group disclosed a first report on a difficult vinyl migration to access 2-substituted 3-vinylbenzofurans from naphthol- or phenol-linked 1,6-enynes using Rh(I)/*rac*-binap catalytic system.[35d] Tactically, the reaction proceeds through Rh-catalyzed oxidative cyclization between alkyne and alkene moieties followed by C-O bond cleavage and final reductive cyclative elimination (Scheme 4b.1). Later, Arisawa group[35c] reported a similar strategy to synthesize 2-substituted benzofuran under Ni(0)/terpyridine catalytic system involving transposition of acrylate to the C3 position of benzofuran. Recently, using PyPhos ligand, Cho group[35b] carried out a similar Ni-catalyzed transformation of vinylogous carbamates derived from *o*-alkynylanilines to make C3-acrylated 2-substituted indoles.

Despite the efficacy of these nickel-catalyzed protocols, drawbacks such as formation of E/Z mixtures, limited compatibility of N substituents etc. do exist. Therefore, there is a necessity for developing efficient protocols that avoid the usage of expensive metal catalysts/ligands.

In this manner, a metal-free approach will be the upmost choice for hasselfree access of these important 3-substituted indole/3-substituted benzofuran derivatives.

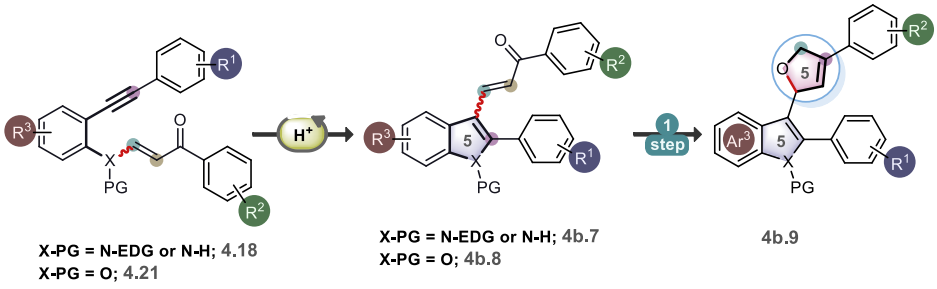


Scheme 4b.1. Ealier approaches for the synthesis of 3-substituted indole or benzofurans using o-alkynyl anilines and phenols.

4b.2. Results & Discussion:

4b.2.1. Present Work:

In this contest, we have developed a metal-free route leading to 3-substituted indole ring formation from vinylogous amides derived from *o*-alkynylanilines via Michael, retro-aza-Michael and amine trapping cascade. Moreover, this strategy can be extended to access benzofuran derivatives using analogous vinylogous esters derived from *o*-alkynylphenols under the same reaction condition. In addition, 3-alkenyl-indoles/benzofurans linked 2,4-disubstituted-2,5-dihydrofuran derivatives could be accomplished from the products in a single step.

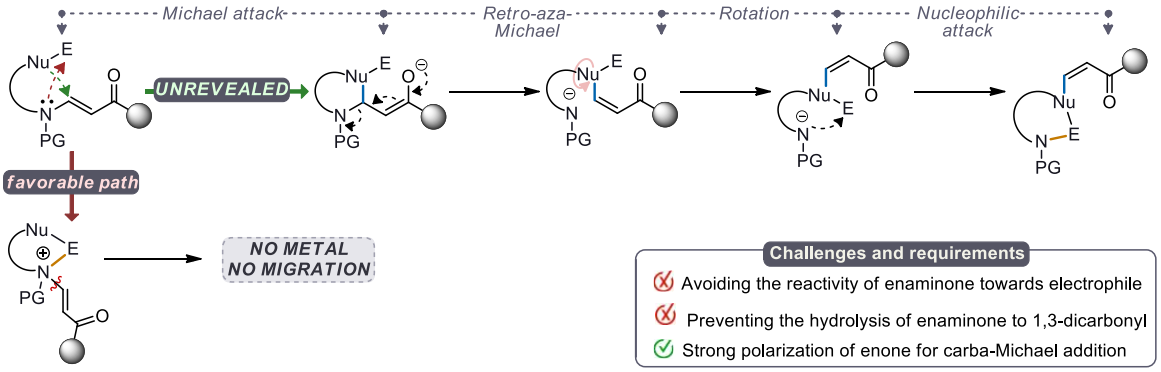


Scheme 4b.2. Synthesis of 3-substituted indoles and benzofurans under metal-free conditions.

4b.2.2. Precedents:

The common feature of the above Rh- and Ni-catalyzed reactions (Scheme 4b.1) is the β-C-O/N bond cleavage after the first cyclization step and subsequent reductive cyclization through the heteroatom. We considered that a C-N bond cleavage could be achieved via a simple retro-aza-Michael reaction[36] after an intramolecular Michael addition on the vinylogous amide derived from *o*-alkynylanilines. Retro oxa-Michael reaction has been reported to happen after the

cyclopropanation of aryloylsilane derived carbene on the *o*-vinylogous carbonates under photochemical conditions.[36a] Also, a related retro-oxa-Michael reaction has been noticed after an intramolecular addition of sulfur ylide on vinylogous carbonates.[36c,d] Carbene and ylide, being strong nucleophiles, added smoothly on the double bond of vinylogous carbonates. In the absence of such a strong nucleophilic center in the *o*-alkynylaniline derived enaminone, activation of the poor Michael acceptor,[37] enaminone for the addition of less nucleophilic alkyne is vital. Thus, use of strong acid such as TfOH was considered for activating the enaminone based on our earlier successful experiences of using TfOH for efficient cyclization reactions.[38] Upon activation of enaminone[39] with TfOH, iminium ion is expected to form which could be trapped by the alkyne.[40]



Scheme 4b.3. Key challenges and our concept design for metal-free synthesis of 3-substituted indole.

4b.2.3. Optimization of Reaction Conditions for 3-Substituted Indole Synthesis:

To check the viability of our hypothesis, the vinylogous amide derived from *o*-alkynylaniline (**4.18aa**) was treated with 50 mol% of TfOH in dichloromethane (DCM) for 12 h. This led to the desired 3-substituted indole (**4b.7aa**), but in 10% yield only (entry 1, Table 4b.1). Formation of **4b.7aa** was confirmed by NMR (Figure 4b.3) and HRMS analysis. In ^{1}H NMR spectrum, a peak at 3.66 ppm with an integral value for 3H and a corresponding ^{13}C signals at 31.3 ppm clearly indicated the presence of methyl group attached to nitrogen in the compound. Signals at 7.97 (dd, 1H) and 7.62 (d, 1H) ppm having a common coupling with a magnitude of 15.5 Hz indicated the presence of two trans olefinic protons. The peak at 190.5 ppm in ^{13}C corrsponds to a ketone group. The structure of the product 3-substituted indole **4b.7aa** was further confirmed by SC-XRD analysis (Figure 4b.4).

We then started further optimization to find out the best reaction conditions. Reactions performed in different solvents such as MeCN, DMF and TFE, resulted in poor yields of the desired product **4b.7aa**. Other solvents like dioxane and acetone did not facilitate the reaction and the unreacted starting material was recovered. To our delight, the target product was isolated in 91% yield with an exclusive *E* geometry of the olefin when the reaction was performed using 50 mol% of TfOH in HFIP at room temperature in 4 hours (entry 9, Table 4b.1).

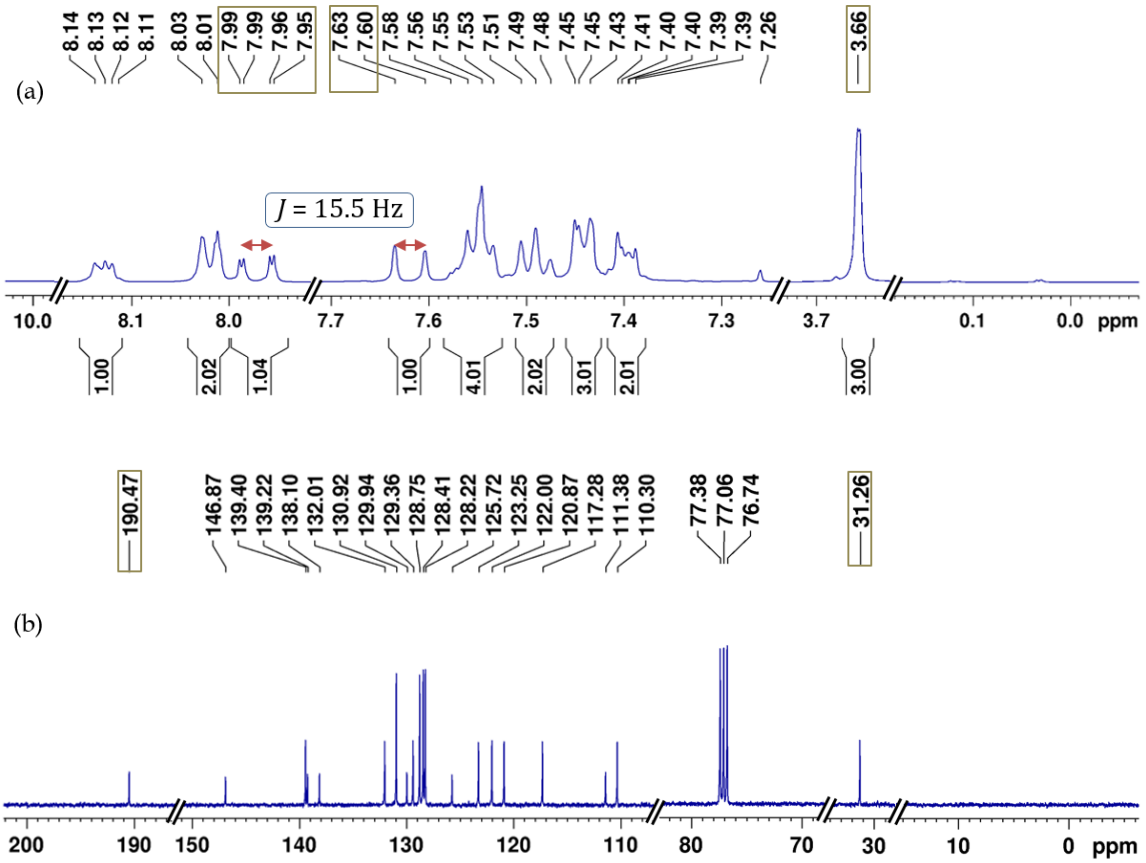


Figure 4b.3. ^{1}H and ^{13}C NMR spectra of 3-substituted indole (**4b.7aa**).

Reducing the amount of TfOH eroded the yield further. Importantly, the reaction did not proceed in the presence of other Lewis/Brønsted acid catalysts (entries 11-24, Table 4b.1). In the presence of catalysts such as AgOTf, $Cu(OTf)_2$, $Bi(OTf)_3$, Rh(I), and $HClO_4$, the reaction resulted in *N*-methyl-2-phenylindole **4b.10** with the extrusion of alkenyl ketone moiety (entries 19-23, Table 4b.1). Other Brønsted acids such as TFA, $MeSO_3H$ and PTSA, though promoted the reaction, resulted in moderate to low yields (entries 25-27, Table 4b.1). The superiority of HFIP as the solvent is overwhelming as it known to polarize the substrates and stabilize the polar intermediates.[41]

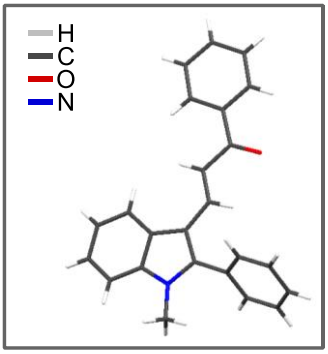
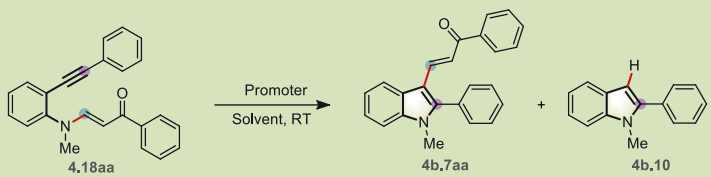


Figure 4b.4. ORTEP of **4b.7aa**.

Table 4b.1. Optimization of reaction conditions for the synthesis of 3-substituted indole (**4b.7aa**).



Entry	Solvent	Promoter (mol%)	Time (h)	Yield (%)	
				4b.7aa	4b.10
1	DCM	TfOH (50)	12	10	0
2	MeCN	TfOH (50)	12	14	0
3	DMF	TfOH (50)	12	12	0
4	Dioxane	TfOH (50)	12	0	0
5	Acetone	TfOH (50)	12	0	0
6	^{i}PrOH	TfOH (50)	12	0	0
7	MeOH	TfOH (50)	12	0	0
8	TFE	TfOH (50)	12	28	0
9	HFIP	TfOH (50)	4	91	0
10	HFIP	TfOH (20)	12	58	0
11	HFIP	$AgBF_4$ (10)	12	0	0
12	HFIP	$AgSbF_6$ (10)	12	0	0
13	HFIP	AuCl (10)	12	0	0
14	HFIP	$AuCl_3$ (10)	12	0	0
15	HFIP	$AlCl_3$ (10)	12	0	0
16	HFIP	$Sc(OTf)_3$ (10)	12	0	0
17	HFIP	$Yb(OTf)_3$ (10)	12	0	0
18	HFIP	$BiCl_3$ (10)	12	0	0
19	HFIP	AgOTf (10)	12	0	26
20	HFIP	$Cu(OTf)_2$ (10)	12	0	24
21	HFIP	$Bi(OTf)_3$ (10)	12	0	48
22	HFIP	$Rh(cod)(MeCN)BF_4$ (10)	12	0	83
23	HFIP	$HClO_4$ (20)	12	0	56
24	HFIP	Tf_2NH (20)	12	0	0
25	HFIP	$MeSO_3H$ (50)	12	63	0
26	HFIP	TFA (5)	12	56	0

27	HFIP	PTSA (5)	12	31	0

Reaction conditions: All the reactions were carried out using **4.18aa** (1 equiv.) and BA/LA at rt under N_2 atmosphere unless otherwise stated.

4b.2.4. Substrate Scope for the Synthesis of 3-Substituted Indole and Benzofuran Derivatives:

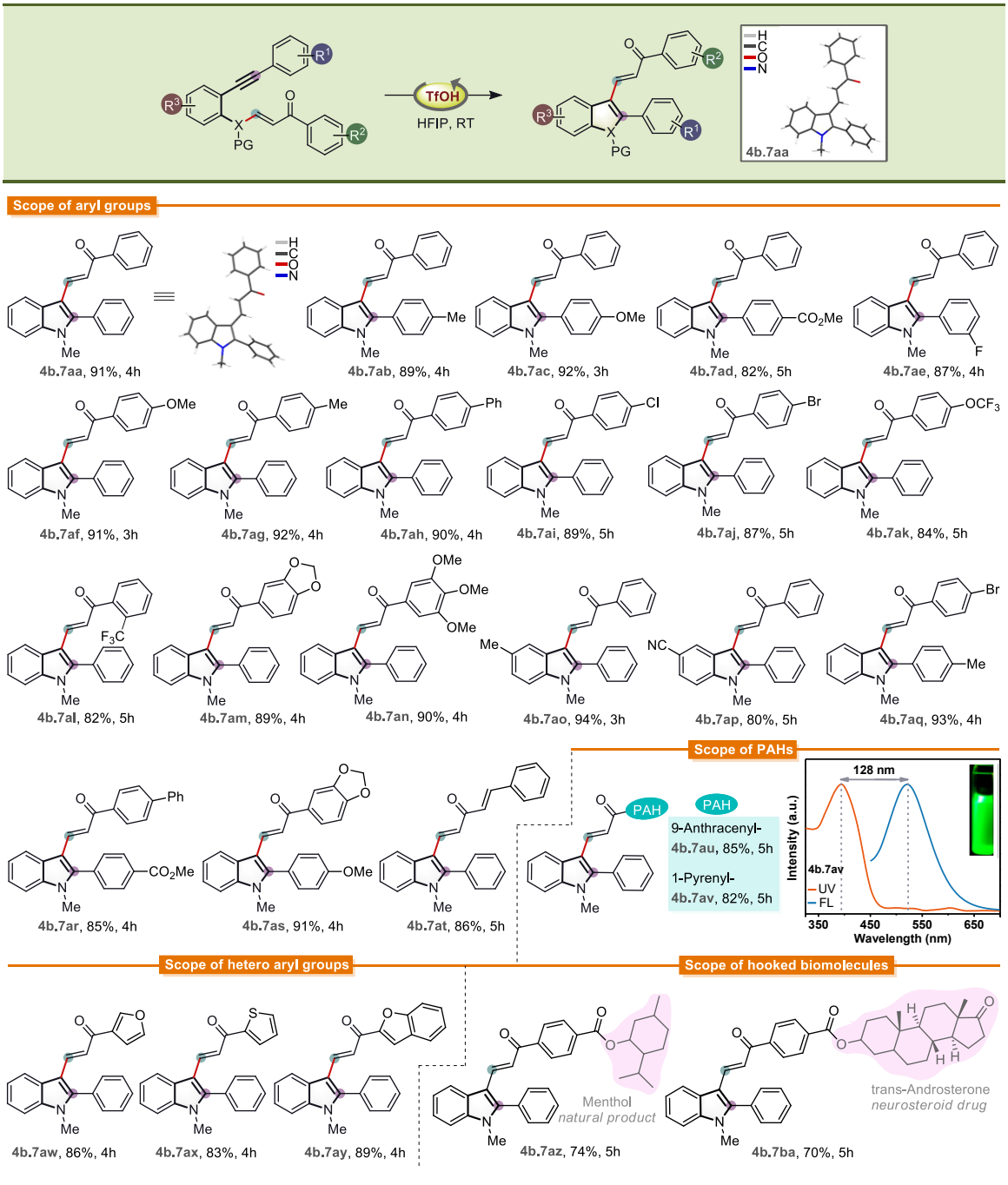
To understand the electronic and structural compatibilities of this transformation, a range of vinylogous amides derived from *o*-alkynylanilines and vinylogous esters derived from *o*-alkynylphenols having practically possible substitution patterns were treated under the optimized conditions. The structures of the starting materials used in this study are presented in Tables 4.1 and 4.2. The synthesis of these derivatives have been already presented in chapter 4. Gratifyingly, all these substrates, irrespective of the electronic demands of their substituents, reacted well and afforded the expected products in high yields (Table 4b.3). Substrates having electron-donating (*e.g.*, *p*-Me, *p*-OMe) groups as R^1 and R^2 when R^3 being hydrogen, efficiently provided compounds **4b.7ab** and **4b.7ac** respectively. Electron-withdrawing substituents such as *p*-CO_2Me and *m*-F did not have any drastic effect on the reaction outcome and the corresponding products **4b.7ad** and **4b.7ae** were obtained in slightly lesser yields 82% and 87% respectively. Then the effect of R^2 was studied employing quite a few numbers of substrates. Here also slight decrease in yield of the product was noticed when electron-withdrawing CF_3 and OCF_3 were present in ortho and para positions respectively. The yields were around 90% with substrates having electron-donating R^2 groups (**4b.7af-aj**) and did not change much with di- or tri-substitution (**4b.7am** and **4b.7an**). A couple of reactions were studied by changing the R^3 group which will have direct influence on the electron density of the vinylogous amide. While an electron-donating methyl group increased the yield of **4b.7ao** to 94%, electron-withdrawing cyano reduced it to 80% (product **4b.7ap**). Substrates having random choice of R^1 and R^2 also underwent smooth reaction to yield their respective indole products. It is pertinent to note that substrates having bromo substituent which is usually labile in the presence of transition metal catalyst tolerated the reaction condition very well. This method could be used to make indole containing diarylideneacetone derivative such as **4b.7at** in 86% yield.

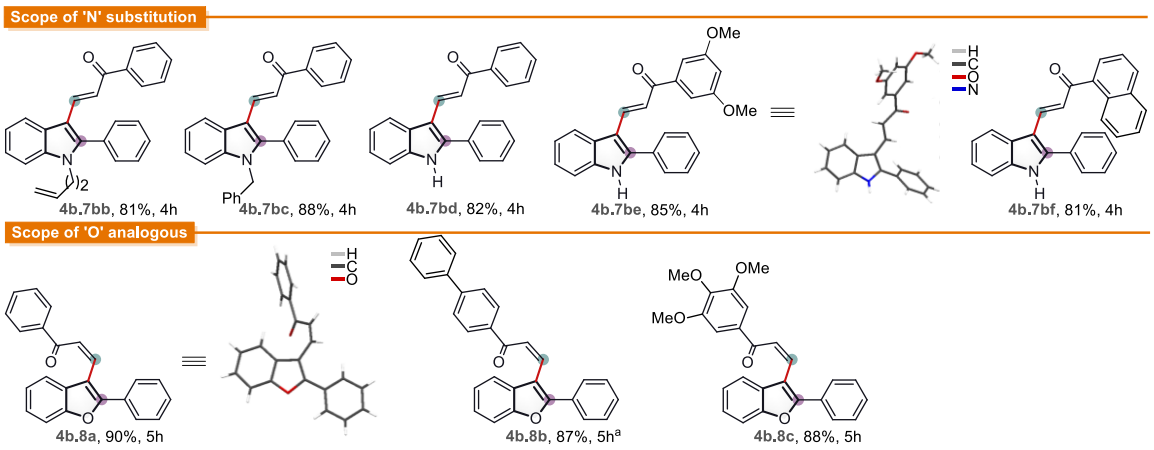
Photophysically interesting PAHs[42] such as anthracenyl and pyrenyl groups conjugated indole derivatives **4b.7au** and **4b.7av** respectively could be obtained in respectable yields. Expectedly, these derivatives exhibit strong fluorescence. Heteroaryl groups which are labile under acidic conditions could also be accommodated (**4b.7aw-ay**).

Hybrid natural products/bioactive compounds have shown tremendous potential in drug development.[43] In this respect, synthesis of natural product conjugated indole derivatives such as **4b.7az** and **4b.7ba** highlight the utility of this protocol.

Next, we evaluated the compatibility of the substituent on nitrogen of the vinylogous amide. Pleasingly, in addition to methyl group, 3-butenyl and benzyl groups were also compatible (**4b.7bb-bc**). Very importantly, this atom-economical indole synthesis could be achieved with great efficiencies on vinylogous amides having free N-H group (**4b.7bd-bf**). Remarkably, the nitrogen did not cyclize on the alkyne directly to afford a different indole derivative.

Table 4b.2. Synthesis of diverse 3-substituted indole (**4b.7**) and 3-substituted benzofuran derivatives (**4b.8**)





Reaction conditions: All the reactions were performed using **4.18**/**4.21** (0.2 mmol), TfOH (50 mol%) in HFIP under N_2 at RT. [a]E/Z = 1:9

Therefore, this method is unique and advantageous from the known metal-catalyzed indole formation accompanied with N to C3 migration as they require mandatory protection of nitrogen. It should also be noted that the olefin geometry in the products **4b.7bd**-**bf** is trans. It reveals that only the product with trans olefin geometry is obtained from both the N-protected/unprotected substrates having the enaminone in trans and cis configurations respectively.

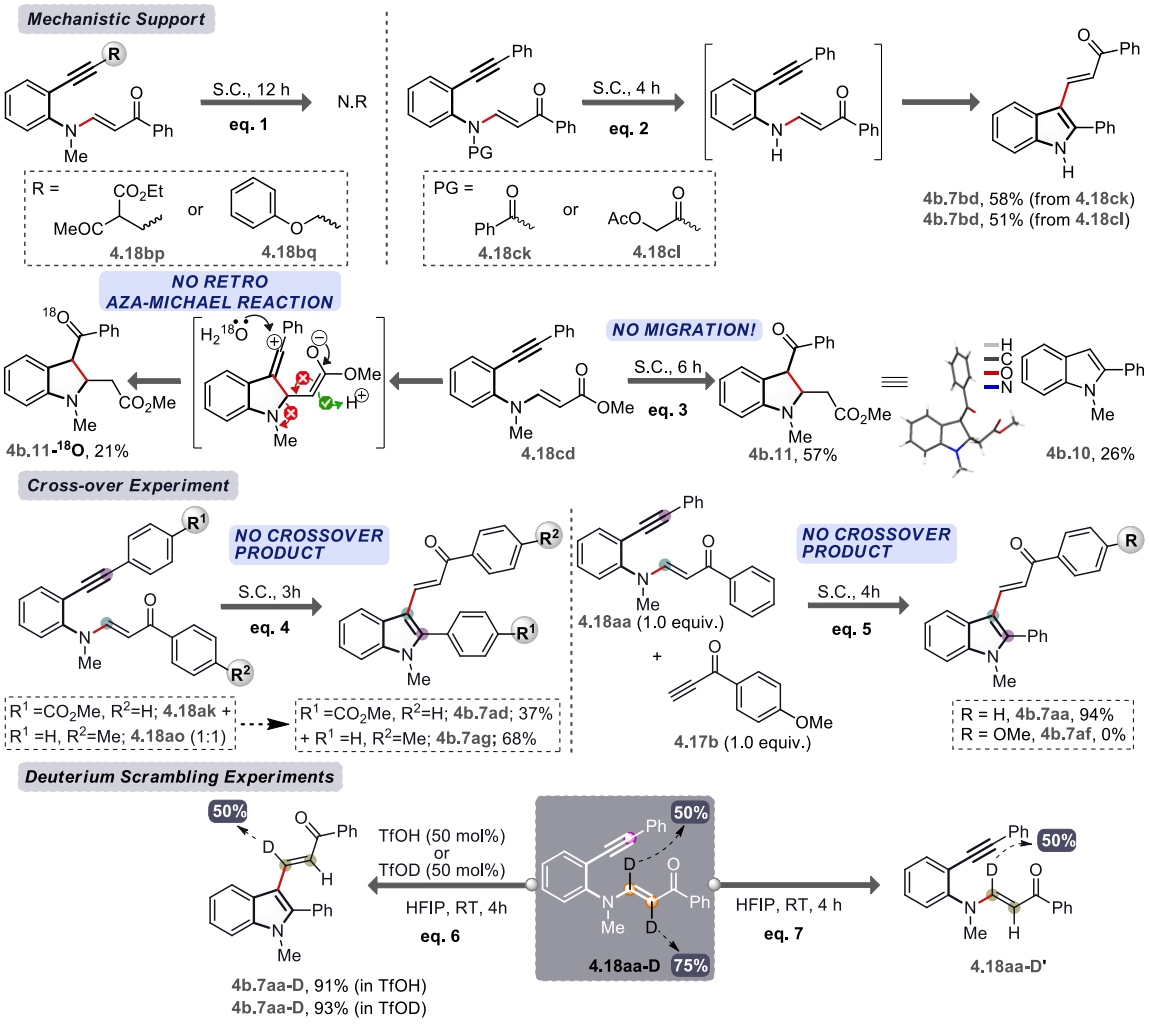
In pursuit of expansion of scope of this methodology, the cyclization of vinylogous esters derived from *o*-alkynylphenols were also studied. Corresponding 3-alkenyl benzofurans (**4b.8a**-**c**) were obtained in promising yields (87-90%). Interestingly, the double bond geometry is mostly cis in the products **4b.8a** and **4b.8c**. The cis/trans ratio in product **4b.8b** was found to be 9:1. Unlike the nitrogen analogues, where exclusive trans geometry of olefin was noticed in the products derived from both trans and cis-enaminones, the trans vinylogous ester resulted in cis olefin geometry in its product. A possible reason for this is provided during the discussion of mechanism.

4b.2.5. Control Experiments:

Next, a set of control experiments have been envisaged for mechanistic investigation (Scheme 4b.4). Substrates **4.18bp** and **4.18bq** which have alkyl substituents on the alkyne, however, did not undergo the cyclization and were recovered after 12 h. Interestingly, the reactions of substrates (**4.18ck** and **4.18cl**) possessing electron-withdrawing groups such as benzoyl and acetoxyacetyl on nitrogen delivered N-H containing 2-alkenylindole derivative **4b.7bd** accompanied with the cleavage of amide bonds. Perhaps, TfOH might have promoted the deprotection as it is known to deprotect N-arylsulfonamides.[44] The vinylogous carbamate derived from 2-phenylaniline, as reported earlier,[40a] did not undergo retro aza-Michael reaction after the initial nucleophilic addition of triple bond on the iminium ion. Substituted indoline **4b.11** was obtained in 57% yield along with 26% of 2-phenyl-N-methylindole **4b.10**. A competition

experiment using equimolar quantities of **4.18ak** and **4.18ao** did not result any cross-over products. Also, the cyclization of **4.18aa**, when conducted along with an equimolar quantity of 1-(4-methoxyphenyl)prop-2-yn-1-one **4.17b**, resulted the product **4b.7aa**. Non participation of **4.17b** in the above reaction and the result of cross-over reaction revealed the intramolecular nature of the reaction.

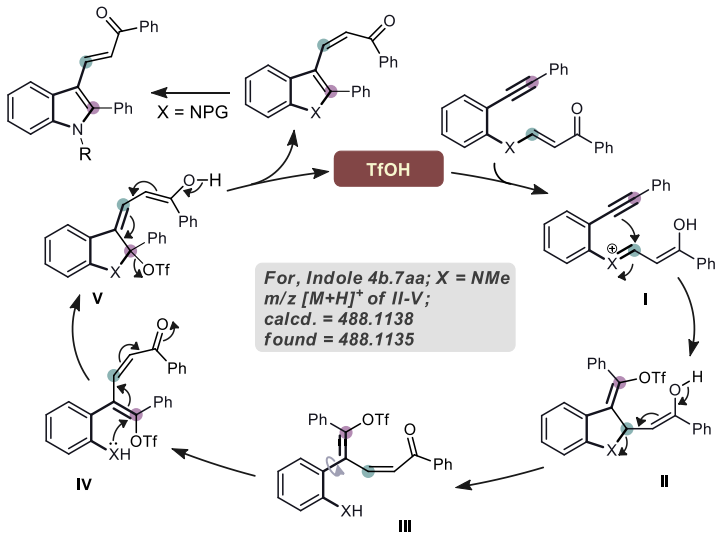
A set of deuterium-scrambling experiments were conducted on substrate **4.18aa-D** having 75% and 50% D contents, respectively, at α- and β- positions of the enaminone moiety. Reaction of **4.18aa-D** separately with TfOH and TfOD resulted in **4b.7aa-D** with 50% and 0% deuterium contents at β- and α- positions of the enone moiety respectively. In another experiment, it was found that the compound **4.18aa-D** completely lost the deuterium at the α- position when stirred in HFIP for 4 h. These two experiments indicates that there is a strong polarization of the enaminone in HFIP solvent leading to the exchange of deuterium at α-position of the enone moiety with hydrogen from HFIP.



Scheme 4b.4. Control experiments.

4b.2.6. Plausible Mechanism for the Formation of 3-Substituted Indole and Benzofuran:

Based on the control experiments, a plausible mechanism is drawn in scheme 4b.5 to explain the mode of cyclization. Protonation of the trans vinylogous amide/ester moiety generates electrophilic iminium/oxocarbenium ion species **I**. Nucleophilic addition of alkyne on the iminium/oxocarbenium ion would generate the vinyl triflate **II**. Retro aza/oxa-Michael reaction would open up the formed ring to result **III** keeping cis configuration of the enone double bond. The C-C bond connecting the aryl and vinyl triflate moieties would rotate to place the double bond for effecting an aza/oxa-Michael addition on the dienone. Thus formed intermediate **V** would eliminate OTf leading to the formation of vinyl ketone trans positioned indole/benzofuran derivatives. The cis geometry of eneone double bond might isomerize to more stable trans in indoles under the acidic reaction condition. Such isomerisations are reported to happen under certain reaction conditions.[35b] The electron push from indole ring nitrogen to C3 might promote it effectively. High electronegativity of oxygen and the consequent less electron density at the C3 of benzofuran does not promote such cis to trans isomerism in benzofuran products. HRMS analysis of the reaction mixture after 30 min. of reaction of **4.18aa** showed a peak at *m/z* 488.1135, which may be assigned for the $[M+H]^+$ of triflate incorporated intermediates **II** – **V** (X = NMe).

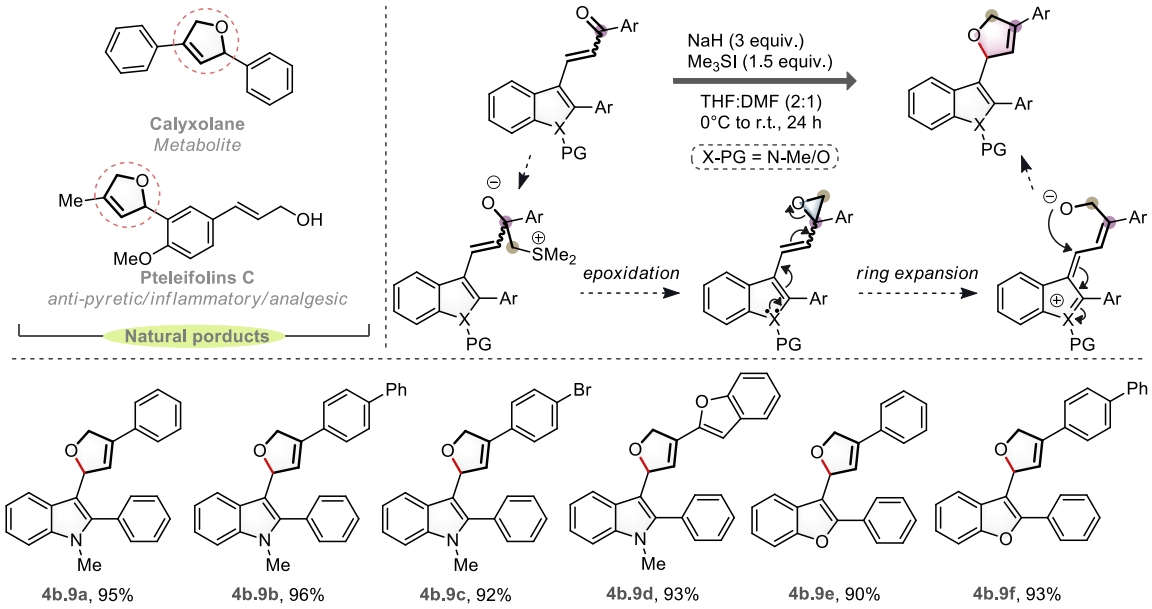


Scheme 4b.5. Proposed mechanism for the synthesis of 3-substituted indole and benzofuran.

4b.2.7. Late-stage Transformations of 3-Substituted Indole and Benzofuran Derivatives:

To explore the synthetic value of the synthesized compounds, a late-stage transformation was performed. Consequently, 2,4-disubstituted-2,5-dihydrofuran derivatives **4b.9a-f** were accomplished upon treating the synthesized 3-alkenyl-indoles/benzofurans with trimethylsulfonium iodide in presence of sodium hydride in THF-DMF (2:1 mixture) (Scheme 4b.6). The aryl-substituted dihydrofuran scaffold is found in many natural products.[45] Pleasingly,

we could able to synthesize a diverse indole and benzofuran linked 2,5-dihydrofuran derivatives **4b.9a-f** in excellent yields (90-96%, Scheme 4b.6).



Scheme 4b.6. Late-stage diversification of the synthesized compounds.

4b.3 Conclusions:

In conclusion, a straightforward triflic acid-promoted synthetic route to access challanging 3-alkenylindole/3-alkenyl benzofuran analogues was uncovered. The effect of triflic acid as promoter and HFIP as solvent is truely noteworthy to accomplish the transformation with excellent productivity and selectivity. Applicability of the products to access an important aryl substituted dihydrofurans undoubtedly enrich the synthetic value. Use of less-expensive triflic acid, high selectivity and atom-economy of the process, together with metal-free mild conditions make this method synthetically significant.

- The methodology is the first metal-free approach for the synthesis of 3-alkenylindole/3-alkenyl benzofuran.
- The role of triflic acid as promoter and HFIP as solvent is highly important for this transformation with excellent productivity and selectivity.
- The methodology is operationally simple, atom economical and high yielding.
- This protocol has a broad scope and versatility. Even the biologically potent or drug molecules hooked products could also be accessed.
- Applicability of the products inaccessing an important aryl substituted 2,4-disubstituted-2,5-dihydrofuran adds value to this protocol.

4.3. Experimental Section:

4.3.1. General Experimental Informations:

All the reactions dealing with air and/or moisture-sensitive compounds were performed under an atmosphere of nitrogen with oven-dried glasswares and standard syringe/septa techniques. The abbreviation "rt" refers to reactions carried out approximately at 25 °C. Silica gel plates 60 F_{254} were used for thin layer chromatography (TLC) purpose and compounds were visualized by using UV light and/or by treatment with Seebach solution (phosphomolibdic acid (2.5 g), $Ce(SO_4)_2$ (1 g), Conc. H_2SO_4 (6 mL), H_2O (94 mL) followed by heating. Column chromatography was performed on silica gel (100-200 mesh) using ethyl acetate and hexanes mixture as eluent. ^1H, ^{13}C and ^{19}F spectra were recorded on a 400 MHz or 500 MHz spectrometers. Chemical shifts are reported in ppm relative to $CDCl_3$ (for ^1H, δ 7.26), and $CDCl_3$ (for ^{13}C, δ 77.06). The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, pent = pentate, sext = sextet, sept = septet and m = multiplet. IR spectra were recorded on a FT-IR spectrometer and are reported in cm^{-1}. High-resolution mass spectra (HRMS) were recorded using an ESI-TOF machine. Melting points were determined by using MR-VIS visual melting range apparatus and are uncorrected. X-ray data were collected at 293 K on a diffractometer with dual source. Mo-Kα (λ = 0.71073 Å) radiation as used to collect the X-ray reflections of the crystal. The UV-vis absorption spectrum was recorded on a UV-Vis spectrophotometer and emission spectrum was recorded on a fluorescence spectrometer. UV-Vis spectrum was recorded with a slit width of 1 nm. Slit widths of 3 and 5 nm were used on the excitation and emission monochromators respectively for fluorescence.

4.3.2. Materials:

Unless otherwise noted, all commercial reagents and solvents were obtained from commercial supplier and used without further purification. Dichloromethane (DCM), 1,2-dichloroethane (DCE) and chloroform were distilled over CaH_2. THF was dried over sodium and freshly distilled before use. Gold catalysts, silver catalysts and triflic acid were purchased from Sigma-Aldrich. TFE and HFIP were purchased from spectrochem.

4.3.3. Synthesis and Characterization of Vinylogous Amide Precursors Derived from *o*-Alkynylaniline (4.18) and Vinylogous Ester Precursors Derived from o-Alkynylphenols (4.21):

4.3.3.1. General Synthetic Procedure for the Preparation of Vinylogous Amide Precursors Derived from *o*-Alkynylaniline (4.18) and Vinylogous Ester Precursors Derived from o-Alkynylphenols (4.21):

General Procedure 1 (GP-1):

Step 1: NaH (1.2 equiv.) was added to an oven-dried RB flask containing dry DMF (3 mL/mmol) under N_2 atmosphere. Then 2-iodo aniline **4.11** (1.0 equiv.) in dry DMF (1 mL/mmol) was added

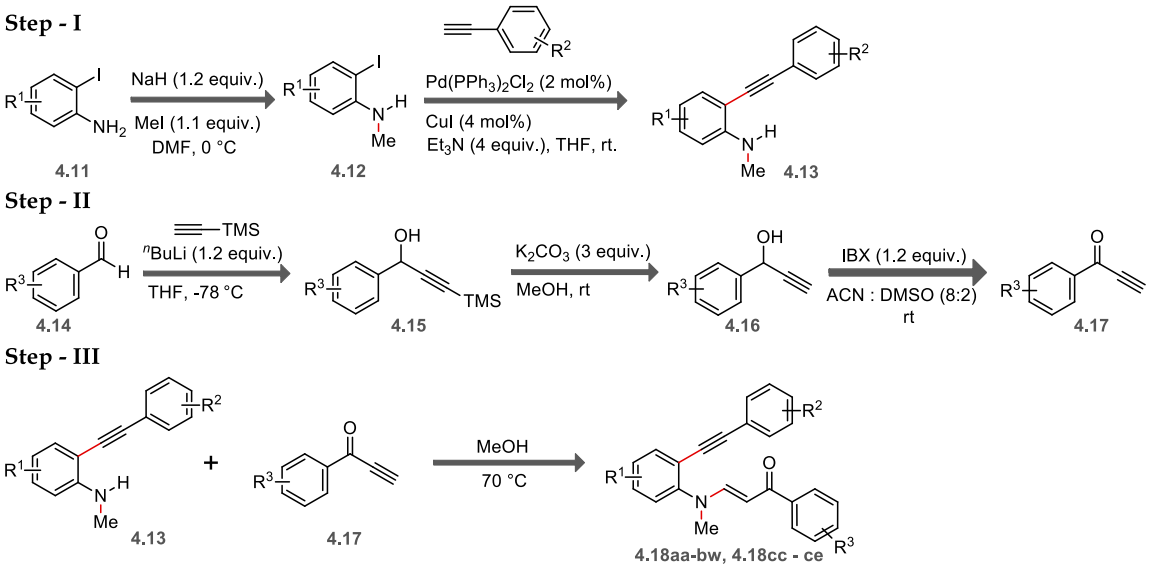
dropwise to it at 0 °C and the mixture was stirred for 30 minutes. Then MeI (1.1 equiv.) in dry DMF (1 mL/mmol) was added slowly and the reaction mixture was warmed to rt and stirred overnight. After that, water was added and the resulting mixture was extracted with ethyl acetate. The combined organic layers were washed with saturate brine solution, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to get the crude product which was purified by column chromatography (silica gel, hexanes/EtOAc) to afford 2-iodo-N-methylaniline derivative (**4.12**).[46]

2-Iodo-N-methylaniline (**4.12**) (1.0 equiv.), $Pd(PPh_3)_2Cl_2$ (0.02 equiv.) and CuI (0.04 equiv.) were dissolved in dry THF (3 mL/mmol) in a round bottom flask under nitrogen atmosphere at rt. Then triethylamine (4 equiv.) was added to the reaction mixture. After 5 minutes of stirring, the corresponding alkyne (1.1 equiv.) in dry THF (1 mL/mmol) was added and the reaction mixture was allowed to stir overnight at rt. After completion of the reaction as indicated by TLC, the reaction mixture was filtered through a pad of celite and the solvent was evaporated under reduced pressure to get the crude product which was purified by column chromatography (silica gel, hexanes/EtOAc) to get the desired 2-alkynyl-N-methyl aniline (**4.13**).[47]

Step 2: To a solution of trimethylsilyl acetylene (1.1 equiv.) in dry THF (3 mL per mmol) at -78 °C under N_2 atmosphere was added ^{n}BuLi (1.2 equiv., 2.5 M solution in hexane). Then it was allowed to stir at -78 °C for 20 minutes. It was brought to rt and the stirring was continued. After 1h, corresponding aldehyde **4.14** (1 equiv.) in dry THF (1 mL/mmol) was added to the reaction mixture at -78 °C. After 15 minutes, it was warmed up to rt and the progress of the reaction was monitored by TLC. After completion of the reaction, the reaction was quenched with saturated aqueous NH_4Cl solution. Then it was extracted using ethyl acetate. The combined organic layers were dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure to get crude TMS protected alkynol (**4.15**).[48]

K_2CO_3 (3 equiv.) was added to the crude 1-phenyl-3-(trimethylsilyl)prop-2-yn-1-ol (**4.15**) (1 equiv.) in MeOH (3 mL/mmol). The reaction mixture was allowed to stir for 2 h at rt. The reaction mixture was filtered through a pad of celite and washed with DCM. The residue was washed with saturated aqueous NH_4Cl solution followed by saturated brine solution and dried over anhydrous Na_2SO_4.The solvent was evaporated under reduced pressure to get crude product alkynol (**4A.14**).[48] The crude alkynol **4.16** was dissolved in DMSO/CH_3CN (2:8) solvent system (3 mL/mmol) and treated with IBX (1.2 equiv.). It was stirred at rt overnight. The reaction mixture was filtered through a pad of celite and the filtrate was washed with water followed by saturated brine solution and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to afford the crude product which was purified by column chromatography (silica gel, hexanes/EtOAc) to get the desired alkynone derivative (**4.17**).[49]

Step 3: 2-Iodo-N-methylaniline (**4.13**) (1.0 equiv.) and alkynone (**4.17**) (1.0 equiv.) were dissolved in MeOH (3 mL/mmol) and the reaction mixture was stirred overnight at 70 °C. After completion of the reaction (as monitored by TLC), the reaction mixture was concentrated under reduced pressure and purified by column chromatography (silica gel, hexanes/EtOAc) to get the desired product vinylogous amides derived from *o*-alkynylanilines (**4.18**).



Scheme 4.5. Preparation of vinylogous amides derived from *o*-alkynylanilines **4.18aa-bw**, **4.18cc - ce**.

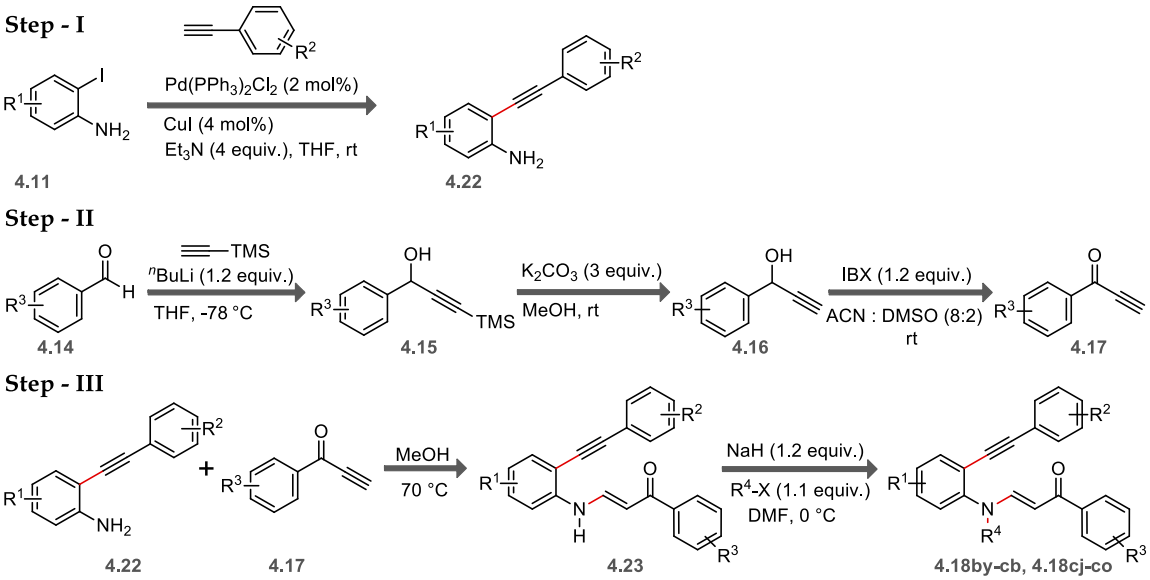
General Procedure 2 (GP-2):

Step 1: 2-Iodo-aniline (**4.11**) (1.0 equiv.) and $Pd(PPh_3)_2Cl_2$ (0.02 equiv.) and CuI (0.04 equiv.) were dissolved in dry THF (3 mL/mmol) in a RB flask under nitrogen atmosphere at rt. Then triethylamine (4 equiv.) was added to the reaction mixture. After 5 minutes of stirring, a solution of the corresponding alkyne (1.1 equiv.) in dry THF (1 mL/mmol) was added and the reaction mixture was allowed to stir overnight at rt. After completion of the reaction as indicated by TLC, the reaction mixture was filtered through a pad of celite and the solvent was evaporated under reduced pressure to get the crude product which was purified by column chromatography (silica gel, hexanes/EtOAc) to get the desired 2-alkynyl aniline (**4.22**).[47]

Step 2: Same as the step 2 of GP-1.

Step 3: 2-Alkynylaniline (**4.22**) (1.0 equiv.) and alkynone (**4.17**) (1.0 equiv.) were dissolved in MeOH (3 mL/mmol) and the reaction mixture was stirred overnight at 70 °C. After completion of the reaction (monitored by TLC), the reaction mixture was concentrated under reduced pressure and purified by column chromatography (silica gel, hexanes/EtOAc) to get the product **4.23**.

NaH (1.2 equiv.) was added to an oven-dried RB flask containing dry DMF (3 mL/mmol) under N_2 atmosphere. Then compound **4.23** (1.0 equiv.) dissolved in dry DMF (1 mL/mmol) was added drop wise to it at 0 °C and the mixture was stirred for 30 minutes. Then R^4X (1.1 equiv.) in dry DMF (1 mL/mmol) was added and the reaction mixture was warmed to room temperature and stirred overnight. After that, water was added and the resulting mixture was extracted with ethyl acetate. The combined organic layers were washed with saturated brine solution, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford vinylogous amides derived from *o*-alkynylanilines **4.18**.[46]



Scheme 4.6. Preparation of vinylogous amides derived from *o*-alkynylanilines **4.18by-cb**, **4.18cj-co**.

General Procedure 3 (GP-3):

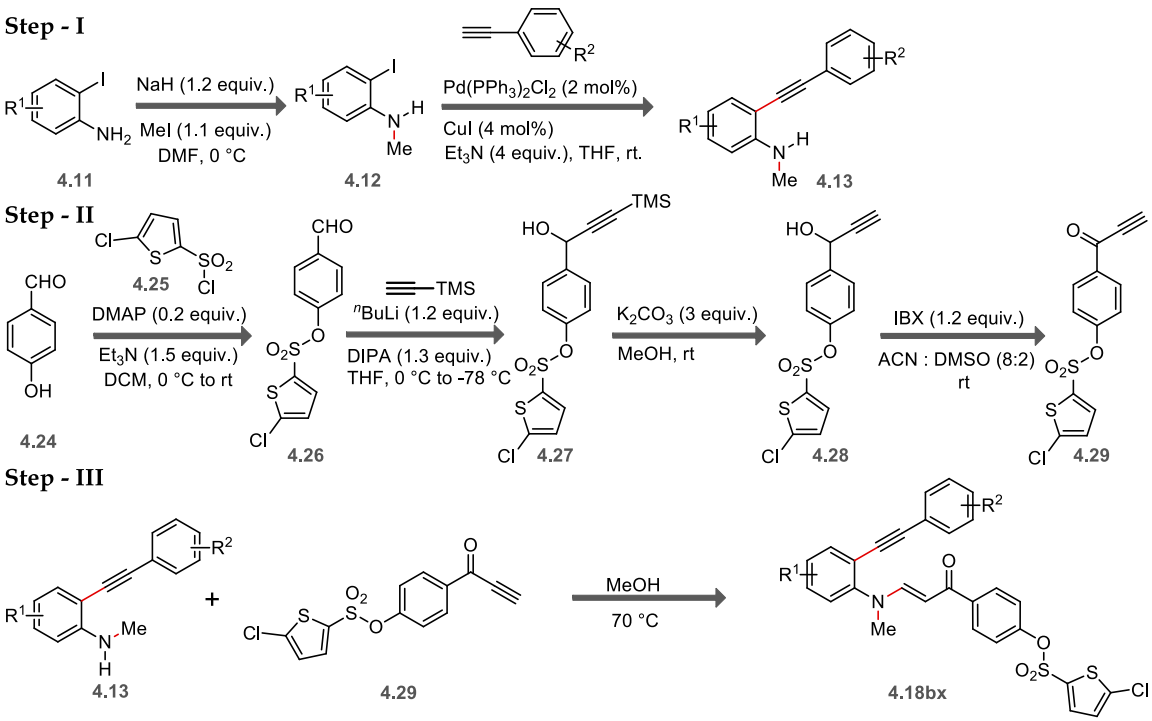
Step 1: Same as the step 1 of GP-1.

Step 2: To a solution of 4-hydroxybenzaldehyde **4.24** (1.2 equiv.) in dry DCM (3 mL/mmol), DMAP (20 mol%) was added. Then Et_3N (1.5 equiv.) was added to the reaction mixture at 0 °C. The mixture was stirred for 30 minutes. Next, a solution of 5-chlorothiophene-2-sulfonyl chloride **4.25** (1 equiv.) in dry DCM (1 mL/mmol) was added slowly to the reaction mixture. After completion of the reaction (monitored by TLC), it was quenched with saturated aqueous $NaHCO_3$ solution. The organic layer was washed with saturated brine solution, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford the crude **4.26**.[50]

To a solution of diisopropylamine (DIPA, 1.3 equiv.) in dry THF (3 mL/mmol), ^{n}BuLi (2.5M solution in hexane, 1.2 equiv.) was added at 0 °C under N_2 atmosphere. The solution was stirred at the same temperature for 1 h. Then the reaction mixture was cooled to -78 °C and trimethylsilyl acetylene (1.1 equiv.) in dry THF (1 mL/mmol) was added. After 1 h, the corresponding aldehyde **4.26** (1 equiv.) in dry THF (1 mL/mmol) was added to the reaction mixture and stirred for 3 h at -78 °C. After completion of the reaction, the reaction mixture was quenched with a saturated aqueous NH_4Cl solution. Then it was extracted using ethyl acetate. The combined organic layers were dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure to get crude product (**4.27**).

TMS deprotection and oxidation follows same method as in step 2 of GP-1.

Step 3: Same as the step 3 of GP-1.



Scheme 4.7. Preparation of vinylogous amide derived from *o*-alkynylaniline **4.18bx**.

General Procedure 4 (GP-4):

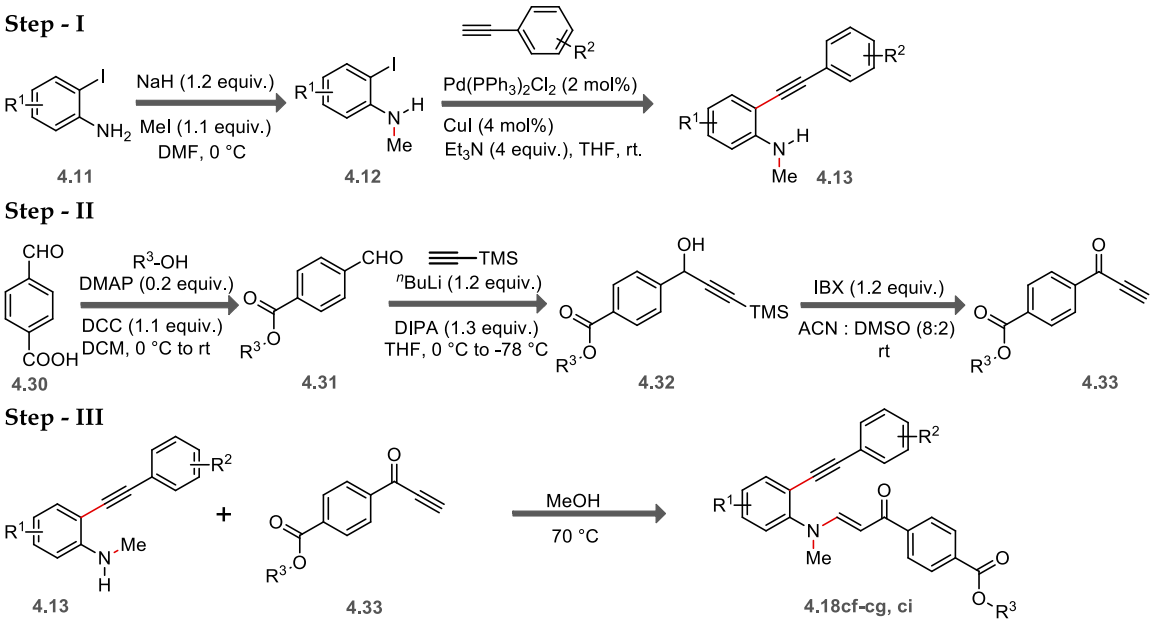
Step 1: Same as the step 1 of GP-1.

Step 2: To a solution of R^3OH (1.2 equiv.) in dry DCM (3 mL/mmol), DMAP (20 mol%) was added followed by 4-carboxybenzaldehyde **4.30** (1 equiv.). Then DCC (1.1 equiv.) was added to the reaction mixture at 0 °C. The mixture was stirred at rt for 24 h. The dicyclohexyl urea formed in the reaction was removed by filtration through silica gel. The organic layer was washed three times with 10% aqueous HCl solution followed by 5% aqueous $NaHCO_3$ solution. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford the crude product **4.31**.

Conversion of **4.31** to **4.32** follows same method as in step 2 of GP 3.

The crude **4.32** (1 equiv.) was dissolved in DMSO/CH_3CN (2:8) solvent system (3 mL/mmol) and treated with IBX (1.2 equiv.). After overnight stirring at room temperature the crude was filtered through a pad of celite and the filtrate was washed with water followed by saturated brine solution and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to afford the crude propargylic ketone which was purified by column chromatography (silica gel, hexanes/EtOAc) to get the pure alkynone **4.33**.

Step 3: Same as the step 3 of GP-1.



Scheme 4.8. Preparation of vinylogous amides derived from *o*-alkynylanilines **4.18cf-cg, ci**.

General Procedure 5 (GP-5):

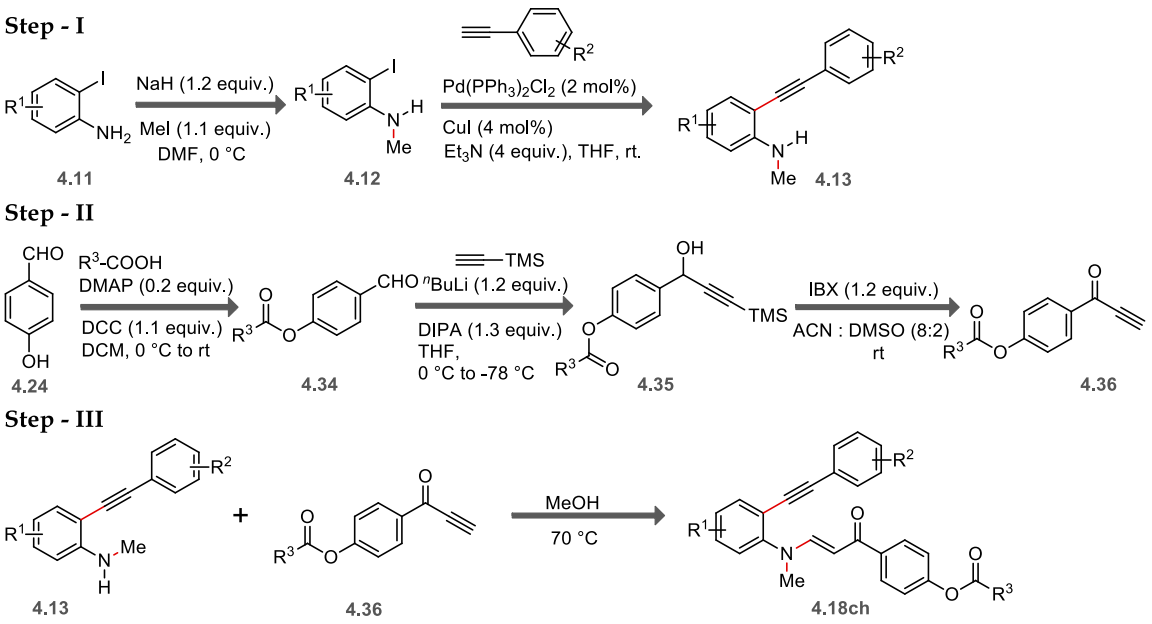
Step 1: Same as the step 1 of GP-1.

Step 2: To a solution of 4-hydroxybenzaldehyde **4.24** (1.2 equiv.) in dry DCM (3 mL/mmol) was added DMAP (20 mol%) followed by R^3COOH (1 equiv.). Then DCC (1.1 equiv.) was added to the reaction mixture at 0 °C. The mixture was stirred at rt for 24 h. The side product dicyclohexyl urea was then removed by filtration through silica gel. The organic layer was washed three times with 10% aqueous HCl solution followed by 5% aqueous $NaHCO_3$ solution. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford the crude product **4.34**.

Conversion of **4.34** to **4.35** follows same method as in step 2 of GP 3.

Conversion of **4.35** to **4.36** follows same method as in step 2 of GP 4.

Step 3: Same as the step 3 of GP-1.



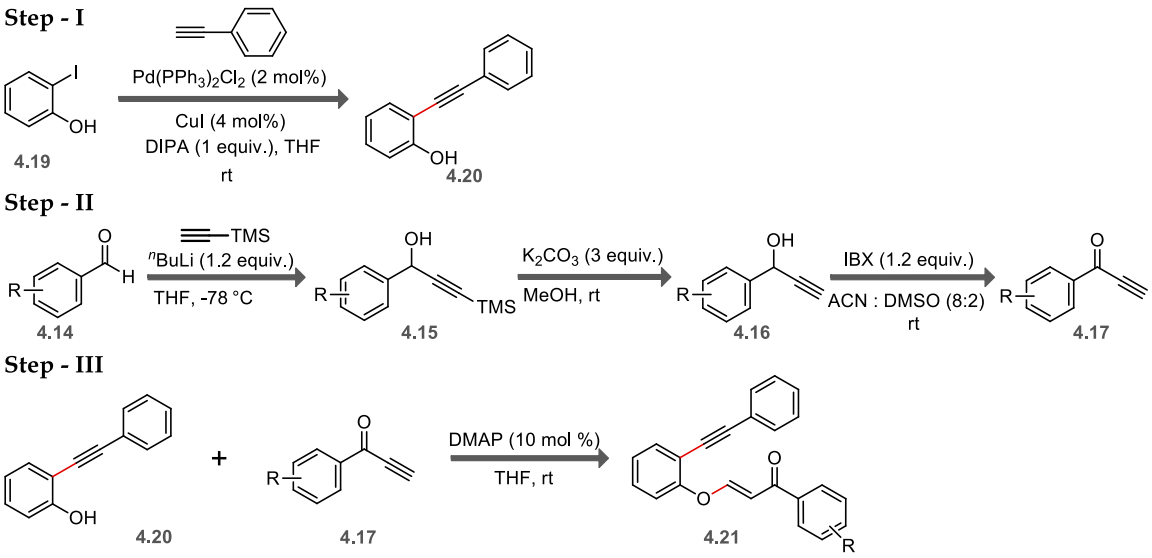
Scheme 4.9. Preparation of vinylogous amide derived from *o*-alkynylaniline **4.18ch**.

General Procedure 6 (GP-6):

Step 1: 2-Iodophenol **4.19** (1.0 equiv.) and $Pd(PPh_3)_2Cl_2$ (0.02 equiv.) and CuI (0.04 equiv.) were dissolved in dry THF (3 mL/mmol) in an oven-dried RB flask under nitrogen atmosphere at rt. Then DIPA (1 equiv.) was added to the reaction mixture. After 5 minutes of stirring, the corresponding alkyne (1.1 equiv.) in dry THF (3 mL/mmol) was added and the reaction mixture was allowed to stir overnight at rt. The reaction mixture was filtered through a pad of celite and the solvent was evaporated under reduced pressure to get the crude product which was purified by column chromatography (silica gel, hexanes/EtOAc) to get the desired 2-alkynyl phenol **4.20**.[51]

Step 2: Same as the step 2 of GP-1.

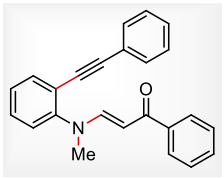
Step 3: 2-Alkynyl phenol **4.20** (1.0 equiv.) and alkynone **4.17** (1.0 equiv.) were dissolved in THF (3 mL/mmol). DMAP (10 mol%) was added to the reaction mixture and allowed to stir at rt. After completion of the reaction (monitored by TLC), the reaction mixture was concentrated under reduced pressure and purified by column chromatography (silica gel, hexanes/EtOAc) to get the desired vinylogous esters derived from *o*-alkynylphenols **4.21**.[52]



Scheme 4.10. Preparation of vinylogous esters derived from *o*-alkynylphenols **4.21**.

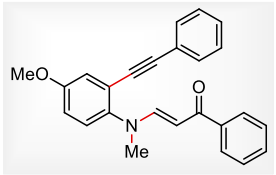
4.3.3.2. Analytical Data of Vinylogous Amide Precursors Derived from *o*-Alkynylaniline (4.18) and Vinylogous Ester Precursors Derived from o-Alkynylphenols (4.21):

(*E*)-3-(Methyl(2-(phenylethynyl)phenyl)amino)-1-phenylprop-2-en-1-one (4.18aa, Table 4.1):



The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as dark yellow gummy liquid (376.5 mg, 74%). R_f value = 0.16 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.13 (d, J = 12.7 Hz, 1H), 7.93 (s, 2H), 7.59 (d, J = 7.4 Hz, 1H), 7.51 – 7.34 (m, 7H), 7.33 – 7.29 (m, 3H), 7.23 (d, J = 7.8 Hz, 1H), 6.09 (s, 1H), 3.46 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 189.6, 152.5, 140.3, 133.7, 131.6, 131.2, 129.5, 128.7, 128.4, 128.2, 127.7, 127.4, 126.5, 125.0, 122.7, 109.1, 96.2, 95.3, 85.8, 38.8. IR (neat): ν/ cm^{-1} = 3061, 1626, 1519, 1446, 1272, 1211, 1052, 921, 751. HRMS: m/z $[M+H]^+$ calcd for $C_{24}H_{20}NO$: 338.1539, found: 338.1540.

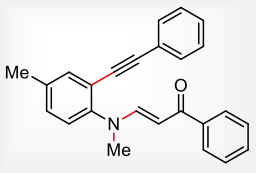
(*E*)-3-((4-Methoxy-2-(phenylethynyl)phenyl)(methyl)amino)-1-phenylprop-2-en-1-one (4.18ab, Table 4.1):



The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as dark yellow gummy liquid (376.5 mg, 74%). R_f value = 0.16 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.13 (d, J = 12.7 Hz, 1H), 7.93 (s, 2H), 7.59 (d, J = 7.4 Hz, 1H), 7.51 – 7.34 (m, 7H), 7.33 – 7.29 (m, 3H), 7.23 (d, J = 7.8 Hz, 1H), 6.09 (s, 1H), 3.46 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 189.6, 152.5, 140.3, 133.7, 131.6, 131.2, 129.5, 128.7, 128.4, 128.2, 127.7, 127.4, 126.5, 125.0, 122.7, 109.1, 96.2, 95.3, 85.8,

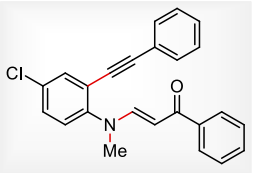
38.8. IR (neat): ν/ cm^{-1} = 3061, 1626, 1519, 1446, 1272, 1211, 1052, 921, 751. HRMS: *m/z* $[M+H]^+$ calcd for $C_{24}H_{20}NO$: 338.1539, found: 338.1540.

(*E*)-3-(Methyl(4-methyl-2-(phenylethynyl)phenyl)amino)-1-phenylprop-2-en-1-one (4.18ac, Table 4.1):



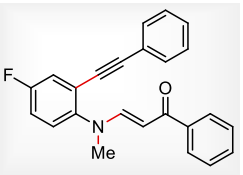
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (382.6 mg, 72%). R_f value = 0.28 (20% EtOAc in hexane). ^1H NMR (400 MHz, $CDCl_3$) *δ*/ ppm = 8.12 (d, *J* = 12.7 Hz, 1H), 7.94 (s, 2H), 7.50 – 7.46 (m, 3H), 7.45 – 7.39 (m, 3H), 7.32 – 7.28 (m, 3H), 7.13 (d, *J* = 15.8 Hz, 2H), 6.09 (s, 1H), 3.43 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*/ ppm = 189.6, 152.7, 146.2, 140.3, 136.4, 133.9, 131.5, 131.1, 130.2, 128.6, 128.4, 128.2, 127.6, 124.9, 122.7, 118.8, 95.8, 94.8, 85.9, 38.9, 20.7. IR (neat): ν/ cm^{-1} = 3054, 1642, 1526, 1484, 1336, 1274, 1207, 1174, 982, 817, 759. HRMS: *m/z* $[M+H]^+$ calcd for $C_{25}H_{22}NO$: 352.1696, found: 352.1699.

(*E*)-3-((4-Chloro-2-(phenylethynyl)phenyl)(methyl)amino)-1-phenylprop-2-en-1-one (4.18ad, Table 4.1):



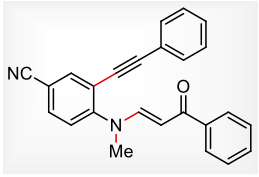
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (346.1 mg, 62%). R_f value = 0.26 (20% EtOAc in hexane). ^1H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 7.93 – 7.65 (m, 6H), 7.48 – 7.34 (m, 7H), 7.20 (s, 1H), 6.07 (s, 1H), 3.28 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 189.4, 152.1, 139.8, 133.7, 131.4, 129.0, 128.2, 127.7, 121.2, 96.2, 38.7. IR (neat): ν/ cm^{-1} = 2919, 1638, 1538, 1333, 1220, 1092, 844, 734. HRMS: *m/z* $[M+Na]^+$ calcd for $C_{24}H_{18}NOClNa$: 394.0969, found: 394.0969.

(*E*)-3-((4-Fluoro-2-(phenylethynyl)phenyl)(methyl)amino)-1-phenylprop-2-en-1-one (4.18ae, Table 4.1):



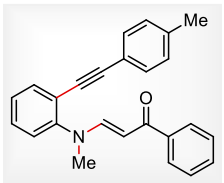
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (324.2 mg, 61%). R_f value = 0.32 (20% EtOAc in hexane). ^1H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 8.06 (d, *J* = 12.6 Hz, 1H), 7.95 (s, 2H), 7.47 – 7.44 (m, 2H), 7.39 (s, 3H), 7.26 – 7.22 (m, 4H), 7.08 (s, 1H), 6.98 (s, 1H), 6.08 (s, 1H), 3.33 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 188.8, 159.8 (d, *J* = 244.7 Hz), 152.0, 144.5, 139.7, 131.3, 130.9, 128.7, 128.1, 127.9, 127.3, 127.0, 126.3, 121.8, 119.3 (d, *J* = 22.8 Hz), 116.3 (d, *J* = 23.5 Hz), 95.8, 95.6, 84.4, 38.4. ^{19}F NMR (470 MHz, $CDCl_3$) *δ*/ ppm = -114.69. IR (neat): ν/ cm^{-1} = 3044, 1639, 1578, 1498, 1272, 1201, 759. HRMS: *m/z* $[M+H]^+$ calcd for $C_{24}H_{19}NOF$: 356.1445, found: 356.1444.

(*E*)-4-(Methyl(3-oxo-3-phenylprop-1-en-1-yl)amino)-3-(phenylethynyl)benzonitrile (4.18af, Table 4.1):



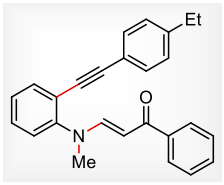
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (301.5 mg, 55%). R_f value = 0.14 (30% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.17 (d, J = 12.8 Hz, 1H), 7.94 (d, J = 7.1 Hz, 2H), 7.84 (s, 1H), 7.57 (d, J = 8.3 Hz, 1H), 7.48 (d, J = 6.9 Hz, 3H), 7.44 (d, J = 7.3 Hz, 2H), 7.33 – 7.27 (m, 4H), 6.18 (d, J = 12.8 Hz, 1H), 3.46 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 189.3, 151.2, 150.4, 139.6, 137.6, 132.4, 131.6, 129.2, 128.4, 128.3, 127.9, 127.7, 124.9, 121.8, 119.5, 117.5, 109.6, 98.3, 97.6, 83.9, 38.8. IR (neat): ν/ cm^{-1} = 2919, 1582, 1539, 1333, 1220, 1092, 734. HRMS: m/z [M+H]$^+$ calcd for $C_{25}H_{19}N_2O$: 363.1492, found: 363.1494.

(*E*)-3-(Methyl(2-(p-tolylethynyl)phenyl)amino)-1-phenylprop-2-en-1-one (4.18ag, Table 4.1):



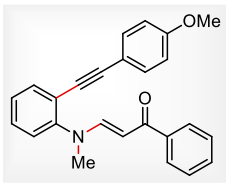
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (398.4 mg, 76%). R_f value = 0.23 (10% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.14 (d, J = 12.4 Hz, 1H), 7.95 (s, 2H), 7.57 (d, J = 6.9 Hz, 1H), 7.48 – 7.42 (m, 3H), 7.39 (d, J = 8.1 Hz, 2H), 7.34 (t, J = 6.9 Hz, 1H), 7.26 – 7.19 (m, 2H), 7.11 (d, J = 7.9 Hz, 2H), 6.10 (s, 1H), 3.44 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 189.5, 152.5, 140.2, 138.8, 133.5, 131.4, 131.1, 129.2, 129.1, 128.1, 127.6, 126.4, 124.9, 119.6, 116.1, 108.9, 96.1, 95.5, 85.1, 38.7, 21.4. IR (neat): ν/ cm^{-1} = 2919, 1640, 1525, 1484, 1336, 1274, 1174, 759. HRMS: m/z [M+H]$^+$ calcd for $C_{25}H_{22}NO$: 352.1696, found: 352.1699.

(*E*)-3-((2-((4-Ethylphenyl)ethynyl)phenyl)(methyl)amino)-1-phenylprop-2-en-1-one (4.18ah, Table 4.1):



The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (396.9 mg, 72%). R_f value = 0.43 (25% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.17 (d, J = 12.2 Hz, 1H), 7.97 (s, 2H), 7.57 (s, 1H), 7.48 – 7.41 (m, 5H), 7.32 (s, 1H), 7.23 (s, 1H), 7.19 (s, 1H), 7.13 (d, J = 7.7 Hz, 2H), 6.11 (s, 1H), 3.43 (s, 3H), 2.62 (q, J = 7.2 Hz, 2H), 1.21 (t, J = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 189.3, 152.4, 145.0, 140.1, 133.4, 131.4, 131.0, 129.1, 128.0, 127.8, 127.5, 126.4, 124.8, 119.7, 116.0, 108.8, 96.0, 95.5, 85.1, 38.6, 28.7, 15.1. IR (neat): ν/ cm^{-1} = 2926, 1646, 1579, 1448, 1278, 1050, 749. HRMS: m/z [M+H]$^+$ calcd for $C_{26}H_{24}NO$: 366.1852, found: 366.1848.

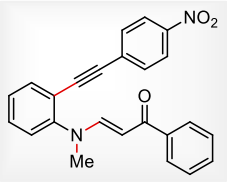
(*E*)-3-((2-((4-Methoxyphenyl)ethynyl)phenyl)(methyl)amino)-1-phenylprop-2-en-1-one (4.18ai, Table 4.1):



The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (404.6 mg, 73%). R_f value = 0.47 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.16 (d, J = 12.5 Hz, 1H), 7.95 (s, 2H), 7.51 (d, J = 5.1 Hz, 1H), 7.41 (d, J = 7.3 Hz, 5H),

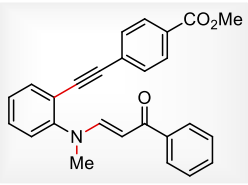
7.26 (s, 1H), 7.16 (d, *J* = 10.8 Hz, 2H), 6.78 (d, *J* = 7.2 Hz, 2H), 6.08 (s, 1H), 3.70 (s, 3H), 3.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 189.1, 159.6, 152.2, 139.9, 133.1, 132.8, 130.9, 128.8, 128.0, 127.4, 126.1, 124.5, 119.0, 115.9, 114.4, 113.8, 108.7, 98.0, 97.7, 95.2, 84.4, 54.9, 38.4. IR (neat): ν/ cm^{-1} = 2931, 1642, 1536, 1335, 1244, 1024, 830, 700. HRMS: *m/z* $[M+Na]^+$ calcd for $C_{25}H_{21}NO_2Na$: 390.1465, found: 390.1461.

(*E*)-3-(Methyl(2-((4-nitrophenyl)ethynyl)phenyl)amino)-1-phenylprop-2-en-1-one (4.18aj, Table 4.1):



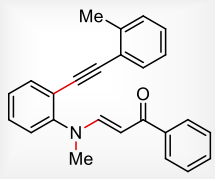
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (336.2 mg, 59%). R_f value = 0.21 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.23 – 8.16 (m, 1H), 8.12 (d, *J* = 8.7 Hz, 2H), 7.94 (s, 2H), 7.60 (d, *J* = 8.9 Hz, 3H), 7.50 – 7.43 (m, 4H), 7.30 – 7.23 (m, 2H), 6.12 (s, 1H), 3.45 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 189.3, 152.2, 147.1, 139.9, 133.9, 132.3, 131.9, 131.5, 130.5, 129.5, 128.3, 127.6, 127.3, 123.6, 123.6, 116.4, 109.3, 98.3, 96.2, 93.1, 90.9, 38.9. IR (neat): ν/ cm^{-1} = 3056, 1649, 1538, 1337, 1208, 1042, 849, 693. HRMS: *m/z* $[M+Na]^+$ calcd for $C_{24}H_{18}N_2O_3Na$: 405.1210, found: 405.1210.

(*E*)-Methyl 4-((2-(methyl(3-oxo-3-phenylprop-1-en-1-yl)amino)phenyl)ethynyl)benzoate (4.18ak, Table 4.1):



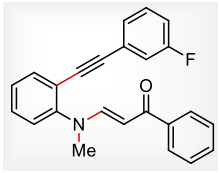
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (324.7 mg, 55%). R_f value = 0.18 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.15 (d, *J* = 12.4 Hz, 1H), 7.95 (d, *J* = 8.3 Hz, 4H), 7.58 (d, *J* = 7.4 Hz, 1H), 7.52 (d, *J* = 8.3 Hz, 2H), 7.47 – 7.36 (m, 4H), 7.25 – 7.20 (m, 2H), 6.09 (s, 1H), 3.88 (s, 3H), 3.43 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 189.4, 166.3, 152.3, 140.0, 133.8, 132.3, 131.4, 131.2, 129.9, 129.8, 129.5, 128.6, 128.2, 127.6, 127.3, 126.4, 124.9, 116.2, 109.1, 96.2, 94.3, 88.6, 52.1, 38.7. IR (neat): ν/ cm^{-1} = 2951, 1720, 1542, 1433, 1272, 1105, 700. HRMS: *m/z* $[M+Na]^+$ calcd for $C_{26}H_{21}NO_3Na$: 418.1414, found: 418.1414.

(*E*)-3-(Methyl(2-(o-tolylethynyl)phenyl)amino)-1-phenylprop-2-en-1-one (4.18al, Table 4.1):



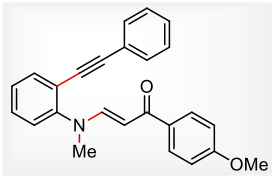
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (334.1 mg, 63%). R_f value = 0.53 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.09 (d, *J* = 12.6 Hz, 1H), 7.92 (s, 2H), 7.61 (d, *J* = 5.5 Hz, 1H), 7.46 (d, *J* = 7.4 Hz, 2H), 7.41 (s, 2H), 7.37 (s, 1H), 7.28 (s, 1H), 7.25 – 7.18 (m, 3H), 7.13 (t, *J* = 7.6 Hz, 1H), 6.07 (s, 1H), 3.46 (s, 3H), 2.47 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 189.6, 152.6, 148.4, 140.2, 140.15, 133.8, 132.1, 131.2, 129.5, 129.4, 128.8, 128.2, 127.7, 126.6, 125.7, 125.3, 122.5, 119.5, 96.2, 94.2, 89.5, 38.9, 20.8. IR (neat): ν/ cm^{-1} = 2936, 1687, 1509, 1242, 1127, 1044, 746. HRMS: *m/z* $[M+H]^+$ calcd for $C_{25}H_{22}NO$: 352.1696, found: 352.1693.

(*E*)-3-((2-((3-Fluorophenyl)ethynyl)phenyl)(methyl)amino)-1-phenylprop-2-en-1-one (4.18am, Table 4.1):



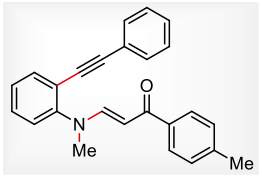
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (362.2 mg, 68%). R_f value = 0.45 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.21 (d, J = 12.2 Hz, 1H), 8.00 (s, 2H), 7.60 (d, J = 7.2 Hz, 1H), 7.51 – 7.44 (m, 3H), 7.38 (t, J = 7.1 Hz, 1H), 7.31 – 7.24 (m, 3H), 7.22 (d, J = 9.6 Hz, 2H), 7.02 (t, J = 8.0 Hz, 1H), 6.14 (s, 1H), 3.45 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 189.5, 162.3 (d, J = 247.2 Hz), 161.4, 152.4, 148.6, 140.2, 133.8, 131.3, 130.1 (d, J = 8.5 Hz), 129.9, 128.3, 127.7, 127.5 (d, J = 2.9 Hz), 126.5, 124.9, 124.5 (d, J = 9.6 Hz), 118.3 (d, J = 22.9 Hz), 116.0 (d, J = 21.1 Hz), 96.2, 93.9, 86.7. ^{19}F NMR (470 MHz, $CDCl_3$) δ/ ppm = -112.60. IR (neat): ν/ cm^{-1} = 3057, 1643, 1535, 1492, 1276, 1047, 759. HRMS: m/z [M+Na]$^+$ calcd for $C_{24}H_{18}NOFNa$: 378.1265, found: 378.1257.

(*E*)-1-(4-Methoxyphenyl)-3-(methyl(2-(phenylethynyl)phenyl)amino)prop-2-en-1-one (4.18an, Table 4.1):



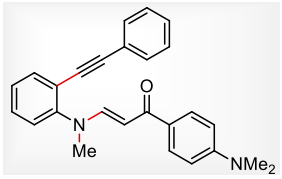
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (411.5 mg, 75%). R_f value = 0.17 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.14 (d, J = 12.7 Hz, 1H), 7.95 (s, 2H), 7.61 – 7.42 (m, 3H), 7.37 – 7.28 (m, 5H), 7.23 (d, J = 11.6 Hz, 1H), 6.92 (d, J = 8.1 Hz, 2H), 6.06 (s, 1H), 3.85 (s, 3H), 3.46 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 188.5, 162.3, 141.5, 133.7, 132.8, 131.6, 129.8, 129.5, 128.7, 128.4, 127.9, 122.8, 116.3, 114.1, 113.4, 109.1, 95.8, 95.3, 85.9, 55.4, 30.4. IR (neat): ν/ cm^{-1} = 2924, 1721, 1645, 1573, 1247, 1166, 1024, 752. HRMS: m/z [M+H]$^+$ calcd for $C_{25}H_{22}NO_2$: 368.1645, found: 368.1644.

(*E*)-3-(Methyl(2-(phenylethynyl)phenyl)amino)-1-(p-tolyl)prop-2-en-1-one (4.18ao, Table 4.1):



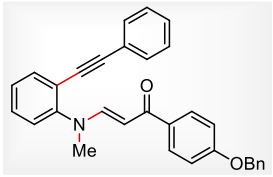
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (386.4 mg, 73%). R_f value = 0.27 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.16 (d, J = 12.8 Hz, 1H), 7.89 (s, 2H), 7.56 (d, J = 7.7 Hz, 1H), 7.51 – 7.47 (m, 2H), 7.30 – 7.26 (m, 3H), 7.24 – 7.16 (m, 5H), 6.10 (s, 1H), 3.41 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 188.9, 151.9, 148.4, 141.4, 137.3, 133.4, 131.3, 129.3, 128.7, 128.5, 128.2, 127.6, 126.2, 124.7, 122.5, 118.8, 95.9, 95.1, 85.7, 38.6, 21.3. IR (neat): ν/ cm^{-1} = 2926, 1737, 1640, 1562, 1278, 1054, 878, 690. HRMS: m/z [M+H]$^+$ calcd for $C_{25}H_{22}NO$: 352.1696, found: 352.1696.

(*E*)-1-(4-(Dimethylamino)phenyl)-3-(methyl(2-(phenylethynyl)phenyl)amino)prop-2-en-1-one (4.18ap, Table 4.1):



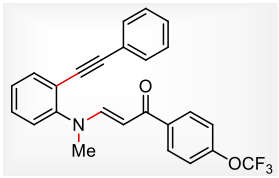
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (419.6 mg, 74%). R_f value = 0.18 (30% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.15 (d, J = 12.7 Hz, 1H), 7.95 (s, 2H), 7.60 – 7.49 (m, 3H), 7.36 – 7.29 (m, 5H), 7.23 (d, J = 7.4 Hz, 1H), 6.67 (d, J = 8.3 Hz, 2H), 6.11 (s, 1H), 3.46 (s, 3H), 3.02 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 188.2, 152.6, 141.2, 133.6, 132.3, 131.5, 131.2, 129.8, 129.4, 128.6, 128.4, 127.7, 127.4, 122.8, 110.8, 95.8, 95.1, 86.0, 40.1, 40.0. IR (neat): ν/ cm^{-1} = 2918, 1719, 1587, 1272, 1166, 1058, 745. HRMS: m/z $[M+H]^+$ calcd for $C_{26}H_{25}N_2O$: 381.1961, found: 381.1960.

(*E*)-1-(4-(benzyloxy)phenyl)-3-(methyl(2-(phenylethynyl)phenyl)amino)prop-2-en-1-one (4.18aq, Table 4.1):



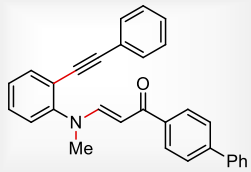
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (455.2 mg, 68%). R_f value = 0.16 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.12 (d, J = 12.7 Hz, 1H), 7.95 (s, 2H), 7.59 (d, J = 7.4 Hz, 1H), 7.51 – 7.47 (m, 2H), 7.45 (d, J = 7.3 Hz, 2H), 7.40 (t, J = 7.1 Hz, 3H), 7.36 (t, J = 7.1 Hz, 3H), 7.31 (d, J = 1.5 Hz, 2H), 7.23 (d, J = 7.8 Hz, 1H), 7.00 (d, J = 8.1 Hz, 2H), 6.07 (s, 1H), 5.12 (s, 2H), 3.45 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 188.2, 161.4, 152.1, 136.6, 133.7, 133.1, 132.7, 131.6, 129.8, 129.5, 128.7, 128.4, 128.1, 127.9, 127.5, 126.4, 125.0, 122.7, 114.3, 95.8, 95.2, 86.0, 70.0. IR (neat): ν/ cm^{-1} = 3030, 1641, 1596, 1243, 1164, 1005, 742. HRMS: m/z $[M+Na]^+$ calcd for $C_{31}H_{25}NO_2Na$: 466.1778, found: 466.1779.

(E)-3-(Methyl(2-(phenylethynyl)phenyl)amino)-1-(4-(trifluoromethoxy)phenyl)prop-2-en-1-one (4.18ar, Table 4.1):



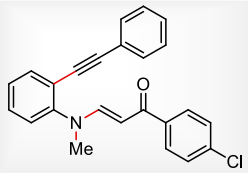
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (446.6 mg, 71%). R_f value = 0.42 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.16 (d, J = 12.4 Hz, 1H), 7.98 (s, 2H), 7.59 (d, J = 6.2 Hz, 1H), 7.50 – 7.46 (m, 2H), 7.37 – 7.23 (m, 8H), 6.05 (d, J = 10.9 Hz, 1H), 3.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 187.7, 152.9, 151.2, 148.4, 138.6, 133.6, 131.5, 129.4, 128.7, 128.4, 125.4 (q, J = 161.1 Hz), 122.6, 120.5, 120.4 (q, J = 258.4 Hz), 120.2, 116.2, 109.0, 95.5, 95.3, 85.7, 38.8. ^{19}F NMR (470 MHz, $CDCl_3$) δ/ ppm = -57.57. IR (neat): ν/ cm^{-1} = 3054, 1635, 1527, 1292, 1166, 1128, 744. HRMS: m/z $[M+H]^+$ calcd for $C_{25}H_{19}NO_2F_3$: 422.1362, found: 422.1369.

(*E*)-1-([1,1'-Biphenyl]-4-yl)-3-(methyl(2-(phenylethynyl)phenyl)amino)prop-2-en-1-one (4.18as, Table 4.1):



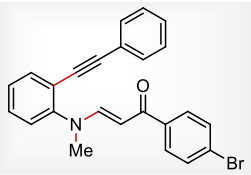
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (449.6 mg, 72%). R_f value = 0.12 (10% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.24 (d, J = 12.2 Hz, 1H), 8.09 (s, 2H), 7.71 – 7.64 (m, 4H), 7.61 (d, J = 7.0 Hz, 1H), 7.56 – 7.52 (m, 2H), 7.47 (t, J = 7.5 Hz, 2H), 7.39 (t, J = 7.4 Hz, 2H), 7.34 – 7.31 (m, 4H), 7.22 (d, J = 6.0 Hz, 1H), 6.18 (s, 1H), 3.46 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 188.7, 152.2, 148.4, 143.7, 140.1, 138.8, 133.5, 131.4, 129.4, 128.7, 128.6, 128.3, 128.2, 127.7, 127.0, 126.8, 124.7, 122.5, 118.7, 116.1, 108.9, 107.1, 95.9, 95.2, 85.8, 38.7. IR (neat): ν/ cm^{-1} = 3055, 1641, 1532, 1275, 1203, 1007, 752. HRMS: m/z $[M+H]^+$ calcd for $C_{30}H_{24}NO$: 414.1852, found: 414.1863.

(*E*)-1-(4-Chlorophenyl)-3-(methyl(2-(phenylethynyl)phenyl)amino)prop-2-en-1-one (4.18at, Table 4.1):



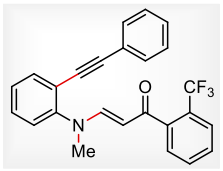
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (378.6 mg, 68%). R_f value = 0.13 (10% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.14 (d, J = 12.4 Hz, 1H), 7.88 (s, 2H), 7.60 (d, J = 6.1 Hz, 1H), 7.50 – 7.46 (m, 2H), 7.39 (d, J = 6.5 Hz, 3H), 7.32 (s, 3H), 7.27 (d, J = 1.0 Hz, 1H), 7.22 (d, J = 6.8 Hz, 1H), 6.03 (s, 1H), 3.46 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 188.0, 152.9, 138.6, 137.3, 133.7, 132.1, 131.6, 129.5, 129.1, 128.8, 128.4, 126.7, 125.1, 122.7, 119.2, 116.3, 109.0, 95.6, 95.4, 85.7, 38.8. IR (neat): ν/ cm^{-1} = 3057, 1640, 1527, 1340, 1277, 1091, 750. HRMS: m/z $[M+H]^+$ calcd for $C_{24}H_{19}NOCl$: 372.1150, found: 372.1156.

(*E*)-1-(4-Bromophenyl)-3-(methyl(2-(phenylethynyl)phenyl)amino)prop-2-en-1-one (4.18au, Table 4.1):



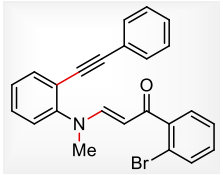
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (412.5 mg, 66%). R_f value = 0.18 (10% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.15 (d, J = 12.0 Hz, 1H), 7.81 (s, 2H), 7.53 (s, 3H), 7.47 (d, J = 7.0 Hz, 2H), 7.28 (s, 4H), 7.22 (s, 1H), 7.16 (s, 1H), 6.02 (s, 1H), 3.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 188.9, 152.6, 148.2, 138.8, 133.5, 131.4, 131.2, 129.4, 129.2, 128.6, 128.3, 126.4, 125.7, 124.7, 122.5, 118.8, 95.4, 95.2, 85.6, 38.7. IR (neat): ν/ cm^{-1} = 3054, 1641, 1533, 1334, 1275, 1007, 752. HRMS: m/z $[M+H]^+$ calcd for $C_{24}H_{19}NOBr$: 416.0645, found: 416.0649.

(*E*)-3-(Methyl(2-(phenylethynyl)phenyl)amino)-1-(2-(trifluoromethyl)phenyl)prop-2-en-1-one (4.18av, Table 4.1):



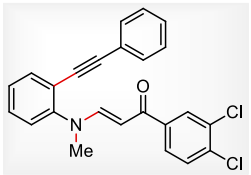
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (343.5 mg, 56%). R_f value = 0.27 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.65 (t, *J* = 7.4 Hz, 1H), 7.56 – 7.50 (m, 4H), 7.42 (s, 2H), 7.36 (t, *J* = 3.0 Hz, 4H), 7.32 (t, *J* = 6.5 Hz, 1H), 7.23 (s, 1H), 7.14 (s, 1H), 5.70 (d, *J* = 12.7 Hz, 1H), 3.37 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 192.7, 153.9, 148.1, 141.0, 133.6, 131.5, 131.4, 129.4, 128.8, 128.7, 128.4, 128.3, 127.6, 127.2 (d, *J* = 31.7 Hz), 126.7, 126.2 (q, *J* = 4.7 Hz), 124.9, 123.9 (q, *J* = 274.1 Hz), 122.5, 119.2, 101.2, 95.3, 85.4, 38.7. ^{19}F NMR (470 MHz, $CDCl_3$) δ/ ppm = -58.01. IR (neat): ν/ cm^{-1} = 2921, 1651, 1542, 1311, 1273, 1115, 1031, 753. HRMS: *m/z* $[M+H]^+$ calcd for $C_{25}H_{19}NOF_3$: 406.1413, found: 406.1415.

(*E*)-1-(2-Bromophenyl)-3-(methyl(2-(phenylethynyl)phenyl)amino)prop-2-en-1-one (4.18aw, Table 4.1):



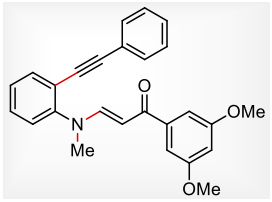
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (398.2 mg, 64%). R_f value = 0.22 (25% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.52 – 7.48 (m, 4H), 7.34 – 7.31 (m, 4H), 7.29 (s, 2H), 7.19 (t, *J* = 7.0 Hz, 2H), 7.16 – 7.11 (m, 2H), 5.71 (d, *J* = 12.8 Hz, 1H), 3.36 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 192.3, 153.7, 148.0, 142.7, 133.4, 132.9, 131.4, 129.9, 129.3, 128.64, 128.6, 128.3, 126.9, 126.5, 124.7, 122.4, 119.1, 118.9, 100.7, 95.2, 85.4, 38.6. IR (neat): ν/ cm^{-1} = 3055, 1648, 1537, 1333, 1277, 1073, 1022, 752. HRMS: *m/z* $[M+H]^+$ calcd for $C_{24}H_{19}NOBr$: 416.0645, found: 416.0644.

(*E*)-1-(3,4-Dichlorophenyl)-3-(methyl(2-(phenylethynyl)phenyl)amino)prop-2-en-1-one (4.18ax, Table 4.1):



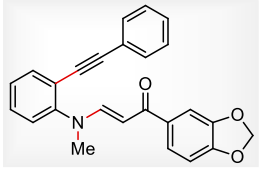
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (401.9 mg, 66%). R_f value = 0.36 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.15 (d, *J* = 12.3 Hz, 1H), 8.02 (s, 1H), 7.77 (d, *J* = 6.9 Hz, 1H), 7.59 (d, *J* = 6.4 Hz, 1H), 7.51 – 7.45 (m, 3H), 7.37 (s, 1H), 7.33 – 7.27 (m, 4H), 7.21 (d, *J* = 7.0 Hz, 1H), 5.99 (d, *J* = 12.2 Hz, 1H), 3.46 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 186.6, 153.3, 148.3, 140.0, 135.4, 133.7, 132.6, 131.6, 130.3, 129.7, 129.5, 128.8, 128.5, 126.9, 125.0, 122.6, 119.2, 95.4, 95.1, 85.6, 39.0. IR (neat): ν/ cm^{-1} = 2922, 1641, 1534, 1276, 1199, 1027, 751. HRMS: *m/z* $[M+H]^+$ calcd for $C_{24}H_{18}NOCl_2$: 406.0760, found: 406.0760.

(*E*)-1-(3,5-Dimethoxyphenyl)-3-(methyl(2-(phenylethynyl)phenyl)amino)prop-2-en-1-one (4.18ay, Table 4.1):



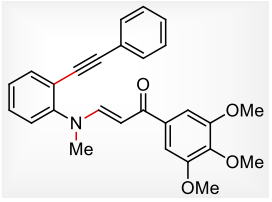
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (416.8 mg, 70%). R_f value = 0.16 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.13 (d, J = 12.3 Hz, 1H), 7.56 (d, J = 6.7 Hz, 1H), 7.49 – 7.46 (m, 2H), 7.29 (s, 4H), 7.24 – 7.17 (m, 2H), 7.10 (s, 2H), 6.58 (s, 1H), 6.05 (s, 1H), 3.80 (s, 6H), 3.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 189.0, 160.5, 152.5, 148.4, 142.4, 133.5, 131.4, 129.4, 128.6, 128.3, 126.3, 124.9, 122.5, 118.9, 105.5, 103.3, 96.0, 95.1, 85.7, 55.4, 38.7. IR (neat): ν/ cm^{-1} = 3055, 1648, 1537, 1333, 1276, 1022, 753. HRMS: m/z [M+H]$^+$ calcd for $C_{26}H_{24}NO_3$: 398.1751, found: 398.1750.

(*E*)-1-(Benzo[*d*][1,3]dioxol-5-yl)-3-(methyl(2-(phenylethynyl)phenyl)amino)prop-2-en-1-one (4.18az, Table 4.1):



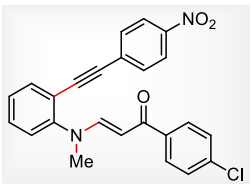
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (391.4 mg, 68%). R_f value = 0.26 (30% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.18 (d, J = 12.3 Hz, 1H), 7.60 (s, 2H), 7.52 (d, J = 3.5 Hz, 3H), 7.38 – 7.32 (m, 4H), 7.23 (s, 2H), 6.85 (d, J = 6.8 Hz, 1H), 6.07 (s, 1H), 6.00 (s, 2H), 3.46 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 187.4, 151.9, 150.1, 147.6, 134.6, 133.4, 131.6, 131.3, 129.3, 128.5, 128.2, 126.2, 124.8, 122.8, 122.5, 118.7, 107.8, 107.4, 101.3, 95.4, 95.1, 85.7, 38.5. IR (neat): ν/ cm^{-1} = 2898, 1639, 1538, 1437, 1238, 1032, 752. HRMS: m/z [M+H]$^+$ calcd for $C_{25}H_{20}NO_3$: 382.1438, found: 382.1440.

(*E*)-3-(Methyl(2-(phenylethynyl)phenyl)amino)-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (4.18ba, Table 4.1):



The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (452.0 mg, 71%). R_f value = 0.19 (40% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.11 (d, J = 12.7 Hz, 1H), 7.56 (d, J = 7.2 Hz, 1H), 7.48 – 7.44 (m, 2H), 7.34 (t, J = 7.0 Hz, 1H), 7.28 (s, 3H), 7.24 – 7.17 (m, 4H), 6.01 (s, 1H), 3.88 (s, 9H), 3.44 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 188.4, 152.8, 141.0, 135.7, 133.5, 131.4, 129.4, 128.6, 128.3, 126.5, 125.0, 122.6, 119.0, 116.1, 108.9, 105.2, 95.7, 95.1, 85.7, 60.7, 56.2, 38.7. IR (neat): ν/ cm^{-1} = 2940, 1632, 1531, 1450, 1296, 1120, 982, 755. HRMS: m/z [M+H]$^+$ calcd for $C_{27}H_{26}NO_4$: 428.1856, found: 428.1864.

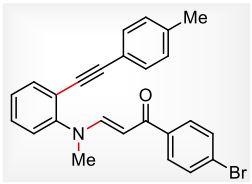
(*E*)-1-(4-Chlorophenyl)-3-(methyl(2-((4-nitrophenyl)ethynyl)phenyl)amino)prop-2-en-1-one (4.18bb, Table 4.1):



The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (376.4 mg, 60%). R_f value = 0.15 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.19 (d, J = 12.8 Hz, 1H), 8.13 (d, J = 8.7 Hz, 2H), 7.88 (s, 3H), 7.59 (d, J =

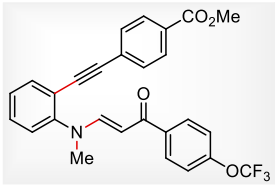
8.9 Hz, 2H), 7.46 – 7.37 (m, 4H), 7.05 (s, 1H), 6.01 (s, 1H), 3.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 187.8, 152.5, 147.2, 138.3, 137.6, 134.0, 132.3, 130.6, 129.5, 129.1, 129.06, 128.5, 128.4, 126.6, 123.6, 95.6, 95.2, 93.1, 90.8, 39.0. IR (neat): ν/ cm^{-1} = 3066, 1642, 1535, 1335, 1274, 1088, 746. HRMS: *m/z* $[M+H]^+$ calcd for $C_{24}H_{18}N_2O_3Cl$: 417.1000, found: 417.1001.

(*E*)-1-(4-bromophenyl)-3-(methyl(2-(p-tolylethynyl)phenyl)amino)prop-2-en-1-one (4.18bc, Table 4.1):



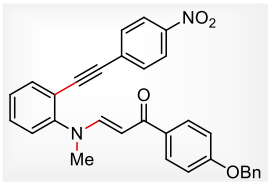
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (380.1 mg, 59%). R_f value = 0.12 (15% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.14 (d, *J* = 12.5 Hz, 1H), 7.81 (s, 2H), 7.54 (s, 3H), 7.37 (d, *J* = 8.1 Hz, 2H), 7.32 (s, 1H), 7.22 (s, 1H), 7.18 (s, 1H), 7.09 (d, *J* = 7.7 Hz, 2H), 6.03 (d, *J* = 11.3 Hz, 1H), 3.42 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 187.9, 152.7, 148.2, 138.9, 133.5, 131.3, 131.27, 129.2, 129.1, 126.4, 125.7, 124.8, 119.4, 119.1, 116.1, 108.8, 98.1, 95.5, 95.4, 85.0, 38.7, 21.4. IR (neat): ν/ cm^{-1} = 2920, 1639, 1521, 1337, 1266, 1057, 759. HRMS: *m/z* $[M+Na]^+$ calcd for $C_{25}H_{20}NOBrNa$: 452.0620, found: 452.0619.

(*E*)-Methyl 4-((2-(methyl(3-oxo-3-(4-(trifluoromethoxy)phenyl)prop-1-en-1-yl)amino)phenyl)ethynyl)benzoate (4.18bd, Table 4.1):



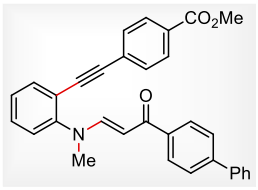
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (405.2 mg, 56%). R_f value = 0.16 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.14 (d, *J* = 12.0 Hz, 1H), 7.96 (s, 2H), 7.91 (d, *J* = 7.8 Hz, 2H), 7.54 (s, 1H), 7.48 (d, *J* = 8.1 Hz, 2H), 7.33 (s, 1H), 7.21 (d, *J* = 5.1 Hz, 4H), 6.05 (s, 1H), 3.84 (s, 3H), 3.41 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 187.4, 166.2, 152.5, 151.2, 148.4, 138.4, 133.7, 131.3, 129.9, 129.7, 129.4, 129.3, 127.1, 126.4, 124.6, 120.3 (q, *J* = 257.5 Hz), 120.1, 118.2, 95.4, 94.2, 88.4, 52.0, 38.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ/ ppm = -57.60. IR (neat): ν/ cm^{-1} = 2952, 1719, 1648, 1538, 1250, 1104, 1053, 754. HRMS: *m/z* $[M+Na]^+$ calcd for $C_{27}H_{20}NO_4F_3Na$: 502.1237, found: 502.1234.

(*E*)-1-(4-(Benzyloxy)phenyl)-3-(methyl(2-((4-nitrophenyl)ethynyl)phenyl)amino)prop-2-en-1-one (4.18be, Table 4.1):



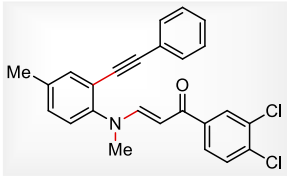
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (399.7 mg, 55%). R_f value = 0.16 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.21 (d, *J* = 12.5 Hz, 1H), 8.11 (d, *J* = 8.8 Hz, 2H), 7.97 (d, *J* = 7.9 Hz, 2H), 7.59 (d, *J* = 8.9 Hz, 2H), 7.46 – 7.36 (m, 8H), 7.23 (d, *J* = 7.8 Hz, 1H), 7.02 (d, *J* = 8.6 Hz, 2H), 6.09 (s, 1H), 5.12 (s, 2H), 3.44 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 187.8, 161.5, 161.3, 151.6, 147.0, 136.4, 133.8, 132.7, 132.2, 130.4, 129.7, 129.5, 128.5, 128.0, 127.4, 126.2, 124.7, 123.5, 114.3, 114.2, 95.8, 95.2, 93.0, 91.0, 69.9, 38.9. IR (neat): ν/ cm^{-1} = 2921, 1595, 1507, 1338, 1244, 1165, 1014, 732. HRMS: *m/z* $[M+H]^+$ calcd for $C_{31}H_{25}N_2O_4$: 489.1809, found: 489.1815.

(*E*)-Methyl 4-((2-((3-([1,1'-biphenyl]-4-yl)-3-oxoprop-1-en-1-yl)(methyl)amino)phenyl)-ethynyl)benzoate (4.18bf, Table 4.1):



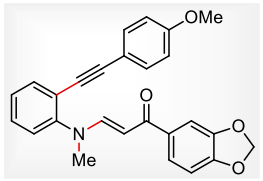
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (402.9 mg, 57%). R_f value = 0.15 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.21 (d, J = 12.5 Hz, 1H), 8.04 (s, 2H), 7.98 (d, J = 8.4 Hz, 2H), 7.69 – 7.59 (m, 6H), 7.55 (d, J = 8.5 Hz, 2H), 7.46 (t, J = 7.5 Hz, 2H), 7.38 (t, J = 7.3 Hz, 2H), 7.24 (d, J = 7.8 Hz, 1H), 6.17 (s, 1H), 3.89 (s, 3H), 3.47 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 188.7, 166.3, 152.2, 143.9, 140.2, 138.7, 133.8, 131.4, 131.2, 130.4, 129.9, 129.8, 129.5, 128.8, 128.2, 127.7, 127.3, 127.1, 126.8, 126.5, 125.0, 96.1, 94.3, 88.6, 52.1, 39.0. IR (neat): ν/ cm^{-1} = 3026, 1720, 1643, 1537, 1273, 1105, 984, 735. HRMS: m/z [M+H]$^+$ calcd for $C_{32}H_{26}NO_3$: 472.1907, found: 472.1897.

(*E*)-1-(3,4-Dichlorophenyl)-3-(methyl(4-methyl-2-(phenylethynyl)phenyl)amino)prop-2-en-1-one (4.18bg, Table 4.1):



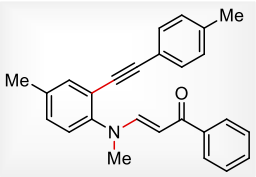
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (446.2 mg, 71%). R_f value = 0.34 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.11 (d, J = 12.5 Hz, 1H), 8.01 (s, 1H), 7.75 (s, 1H), 7.51 – 7.43 (m, 3H), 7.40 (s, 1H), 7.31 (d, J = 6.3 Hz, 3H), 7.17 (s, 1H), 7.11 (s, 1H), 5.95 (d, J = 12.3 Hz, 1H), 3.43 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 186.6, 153.6, 146.0, 140.1, 136.9, 135.3, 133.9, 133.3, 132.6, 131.8, 131.5, 130.3, 129.7, 128.8, 128.5, 126.9, 124.9, 122.7, 118.9, 96.1, 85.8, 39.1, 20.8. IR (neat): ν/ cm^{-1} = 2920, 1608, 1556, 1374, 1273, 1027, 735. HRMS: m/z [M+H]$^+$ calcd for $C_{25}H_{19}NOCl_2Na$: 442.0736, found: 442.0736.

(*E*)-1-(Benzo[d][1,3]dioxol-5-yl)-3-((2-((4-methoxyphenyl)ethynyl)phenyl)(methyl) amino)prop-2-en-1-one (4.18bh, Table 4.1):



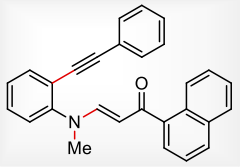
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (423.1 mg, 69%). R_f value = 0.13 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.12 (d, J = 12.4 Hz, 1H), 7.52 (d, J = 4.7 Hz, 2H), 7.46 (s, 1H), 7.39 (d, J = 6.8 Hz, 2H), 7.28 (s, 1H), 7.18 (d, J = 12.5 Hz, 2H), 6.79 (d, J = 5.3 Hz, 3H), 6.00 (s, 1H), 5.94 (s, 2H), 3.72 (s, 3H), 3.39 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 187.3, 175.8, 159.7, 152.0, 150.1, 147.6, 134.6, 133.2, 132.8, 128.9, 126.2, 124.7, 122.8, 119.0, 114.5, 113.9, 107.8, 107.4, 101.3, 97.7, 95.2, 84.5, 55.0, 38.5. IR (neat): ν/ cm^{-1} = 2898, 1639, 1539, 1437, 1240, 1090, 1031, 745. HRMS: m/z [M+H]$^+$ calcd for $C_{26}H_{22}NO_4$: 412.1543, found: 412.1541.

(*E*)-3-(Methyl(4-methyl-2-(p-tolylethynyl)phenyl)amino)-1-phenylprop-2-en-1-one (4.18bi, Table 4.1):



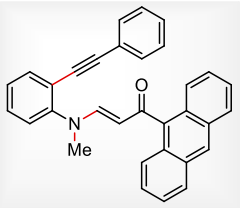
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (396.4 mg, 72%). R_f value = 0.34 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.12 (d, J = 12.5 Hz, 1H), 7.96 (s, 2H), 7.46 (s, 3H), 7.38 (d, J = 7.9 Hz, 3H), 7.11 (d, J = 8.0 Hz, 4H), 6.07 (d, J = 10.4 Hz, 1H), 3.42 (s, 3H), 2.34 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 189.4, 152.7, 146.1, 140.2, 138.7, 136.3, 133.7, 131.3, 131.0, 130.0, 129.6, 129.1, 128.5, 128.2, 128.1, 127.6, 124.8, 119.6, 95.7, 95.0, 85.2, 38.8, 21.4, 20.6. IR (neat): ν/ cm^{-1} = 2918, 1642, 1543, 1492, 1313, 1048, 697. HRMS: m/z [M+H]$^+$ calcd for $C_{26}H_{24}NO$: 366.1852, found: 366.1855.

(*E*)-3-(Methyl(2-(phenylethynyl)phenyl)amino)-1-(naphthalen-1-yl)prop-2-en-1-one (4.18bj, Table 4.1):



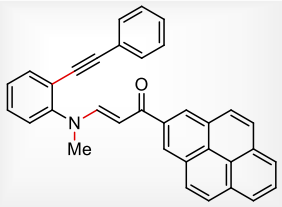
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (334.9 mg, 58%). R_f value = 0.21 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.46 (s, 1H), 8.21 (d, J = 12.4 Hz, 1H), 8.07 (s, 1H), 7.96 – 7.85 (m, 3H), 7.62 – 7.50 (m, 5H), 7.38 – 7.29 (m, 6H), 6.26 (s, 1H), 3.50 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 189.4, 152.6, 145.7, 137.5134.8, 133.7, 132.7, 131.6, 129.5, 129.2, 128.7, 128.4, 128.2, 127.9, 127.7, 127.4, 126.3, 125.5, 124.7, 122.7, 115.6, 105.1, 96.3, 95.3, 85.8. IR (neat): ν/ cm^{-1} = 2924, 1642, 1578, 1538, 1276, 1041, 761. HRMS: m/z [M+H]$^+$ calcd for $C_{28}H_{22}NO$: 388.1696, found: 388.1698.

(*E*)-1-(Anthracen-9-yl)-3-(methyl(2-(phenylethynyl)phenyl)amino)prop-2-en-1-one (4.18bk, Table 4.1):



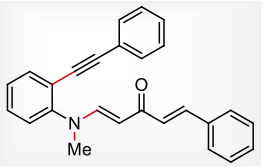
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (337.0 mg, 57%). R_f value = 0.34 (25% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.40 (s, 1H), 8.11 (s, 2H), 7.96 (d, J = 8.1 Hz, 2H), 7.55 (s, 3H), 7.41 (s, 6H), 7.33 (s, 3H), 7.15 (s, 2H), 6.03 (s, 1H), 3.38 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 183.1, 149.8, 148.1, 143.7, 134.1, 133.5, 131.6, 131.2, 129.3, 128.8, 128.5, 128.3, 127.2, 126.8, 26.0, 125.9, 125.2, 122.7, 119.5, 116.2, 109.0, 95.3, 94.9, 85.4, 38.8. IR (neat): ν/ cm^{-1} = 2921, 1640, 1536, 1332, 1220, 1090, 735. HRMS: m/z [M+H]$^+$ calcd for $C_{32}H_{24}NO$: 438.1852, found: 438.1853.

(*E*)-3-(Methyl(2-(phenylethynyl)phenyl)amino)-1-(pyren-2-yl)prop-2-en-1-one (4.18bl, Table 4.1):



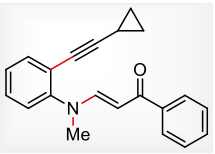
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (384.1 mg, 55%). R_f value = 0.15 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.68 (d, J = 8.1 Hz, 1H), 8.16 (t, J = 7.2 Hz, 3H), 8.12 – 7.96 (m, 6H), 7.63 – 7.59 (m, 2H), 7.50 (s, 1H), 7.40 – 7.37 (m, 3H), 7.22 – 7.08 (m, 3H), 6.13 (d, J = 10.9 Hz, 1H), 3.40 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 194.6, 153.6, 148.1, 136.6, 133.4, 131.9, 131.4, 131.0, 130.6, 129.3, 128.7, 128.4, 128.0, 127.1, 125.9, 125.3, 125.27, 125.2, 125.1, 124.7, 124.4, 124.0, 122.6, 118.9, 102.4, 95.1, 85.6, 38.6. IR (neat): ν/ cm^{-1} = 2921, 1643, 1538, 1337, 1273, 1041, 746. HRMS: *m/z* $[M+H]^+$ calcd for $C_{34}H_{24}NO$: 462.852, found: 462.859.

(1*E*,4*E*)-1-(Methyl(2-(phenylethynyl)phenyl)amino)-5-phenylpenta-1,4-dien-3-one (4.18bm, Table 4.1):



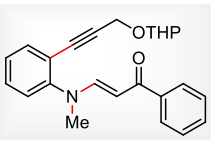
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (350.6 mg, 64%). R_f value = 0.23 (25% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.11 (d, J = 12.8 Hz, 1H), 7.65 (d, J = 15.8 Hz, 1H), 7.55 (d, J = 7.2 Hz, 1H), 7.53 – 7.46 (m, 4H), 7.31 – 7.25 (m, 7H), 7.20 (s, 1H), 7.14 (d, J = 6.0 Hz, 1H), 6.92 (d, J = 14.1 Hz, 1H), 5.65 (s, 1H), 3.36 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 186.7, 151.0, 148.0, 139.1, 135.2, 133.3, 131.2, 129.2, 129.16, 128.4, 128.1, 127.6, 127.1, 126.0, 124.4, 122.3, 118.5, 108.7, 100.1, 95.0, 85.6, 38.3. IR (neat): ν/ cm^{-1} = 3054, 1606, 1531, 1443, 1328, 1083, 976, 734. HRMS: *m/z* $[M+H]^+$ calcd for $C_{26}H_{22}NO$: 364.1696, found: 364.1696.

(*E*)-3-((2-(Cyclopropylethynyl)phenyl)(methyl)amino)-1-phenylprop-2-en-1-one (4.18bn, Table 4.1):



The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (258.5 mg, 57%). R_f value = 0.35 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.03 (d, J = 12.6 Hz, 1H), 7.93 (s, 2H), 7.47 – 7.41 (m, 4H), 7.27 (s, 1H), 7.18 – 7.11 (m, 2H), 6.00 (s, 1H), 3.36 (s, 3H), 1.45 – 1.38 (m, 1H), 0.85 – 0.80 (m, 2H), 0.79 – 0.76 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 189.3, 152.7, 140.3, 133.7, 131.1, 130.0, 128.5, 128.1, 127.6, 126.4, 124.7, 119.9, 99.8, 95.6, 72.1, 38.5, 8.6, 0.30. IR (neat): ν/ cm^{-1} = 2926, 1645, 1543, 1489, 1275, 1043, 761. HRMS: *m/z* $[M+H]^+$ calcd for $C_{21}H_{20}NO$: 302.1539, found: 302.1540.

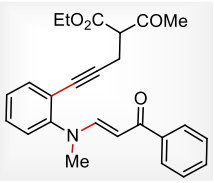
(*E*)-3-(Methyl(2-(3-((tetrahydro-2*H*-pyran-2-yl)oxy)prop-1-yn-1-yl)phenyl)amino)-1-phenylprop-2-en-1-one (4.18bo, Table 4.1):



The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); with a modification like the alkyne used in step 1 was prepared from propargyl alcohol and dihydropyran. **1bo** was obtained as

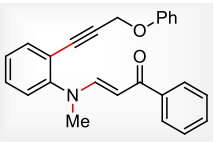
yellow gummy liquid (339.1 mg, 60%). R_f value = 0.33 (10% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.01 (d, J = 12.7 Hz, 1H), 7.92 (s, 2H), 7.51 – 7.40 (m, 4H), 7.33 (s, 1H), 7.22 (t, J = 8.2 Hz, 1H), 7.17 (d, J = 7.4 Hz, 1H), 6.04 (s, 1H), 4.83 (t, J = 3.4 Hz, 1H), 4.47 (d, J = 4.4 Hz, 2H), 3.85 – 3.78 (m, 1H), 3.52 – 3.46 (m, 1H), 3.38 (s, 3H), 1.79 – 1.73 (m, 1H), 1.73 – 1.65 (m, 1H), 1.61 – 1.53 (m, 2H), 1.51 – 1.46 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 189.3, 152.3, 140.1, 134.0, 132.3, 131.2, 130.1, 129.7, 128.7, 128.2, 127.7, 125.2, 115.9, 108.9, 96.9, 96.0, 91.4, 82.1, 62.1, 54.6, 39.2, 30.2, 25.3, 19.0. IR (neat): ν/ cm^{-1} = 2918, 1633, 1523, 1338, 1276, 1023, 761. HRMS: *m/z* [M+Na]$^+$ calcd for $C_{24}H_{25}NO_3Na$: 398.1727, found: 398.1724.

(*E*)-Ethyl 2-acetyl-5-(2-(methyl(3-oxo-3-phenylprop-1-en-1-yl)amino)phenyl)pent-4-ynoate (4.18bp, Table 4.1):



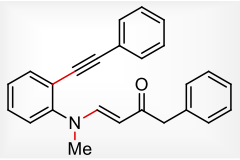
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); with a modification like the alkyne used in step 1 was prepared from propargyl bromide and ethylacetoacetate. **1bp** was obtained as yellow gummy liquid (351.5 mg, 58%). R_f value = 0.29 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.01 (d, J = 11.8 Hz, 1H), 7.92 (s, 2H), 7.38 (s, 4H), 7.25 (s, 1H), 7.13 (s, 1H), 7.09 (s, 1H), 6.03 (s, 1H), 4.16 – 4.08 (m, 2H), 3.76 (s, 1H), 3.29 (s, 3H), 2.88 (t, J = 6.5 Hz, 2H), 2.22 (s, 3H), 1.16 (t, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 200.9, 188.8, 167.8, 152.1, 139.8, 133.5, 131.0, 129.0, 128.0, 127.4, 126.1, 124.6, 118.6, 115.5, 108.5, 98.1, 95.3, 92.1, 61.5, 57.7, 38.4, 29.3, 18.2, 13.8. IR (neat): ν/ cm^{-1} = 2973, 1737, 1642, 1537, 1489, 1335, 1276, 1042, 163. HRMS: *m/z* [M+Na]$^+$ calcd for $C_{25}H_{25}NO_4Na$: 426.1676, found: 426.1674.

(*E*)-3-(Methyl(2-(3-phenoxyprop-1-yn-1-yl)phenyl)amino)-1-phenylprop-2-en-1-one (4.18bq, Table 4.1):



The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); with a modification like the alkyne used in step 1 was prepared from propargyl bromide and phenol. **1bq** was obtained as yellow gummy liquid (312.4 mg, 57%). R_f value = 0.16 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 7.97 (s, 5H), 7.47 (s, 5H), 7.29 (d, J = 7.0 Hz, 2H), 7.02 – 6.93 (m, 3H), 6.00 (s, 1H), 4.92 (s, 2H), 3.22 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 189.1, 157.4, 152.5, 140.2, 140.0, 139.9, 133.8, 131.1, 129.8, 129.4, 128.1, 127.6, 127.2, 121.4, 114.9, 98.2, 95.7, 90.0, 83.4, 56.2, 38.5. IR (neat): ν/ cm^{-1} = 3055, 1642, 1536, 1489, 1333, 1273, 1018, 753. HRMS: *m/z* [M+H]$^+$ calcd for $C_{25}H_{22}NO_2$: 368.1645, found: 368.1649.

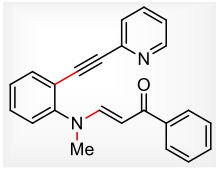
(*E*)-4-(Methyl(2-(phenylethynyl)phenyl)amino)-1-phenylbut-3-en-2-one (4.18br, Table 4.1):



The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (328.5 mg, 62%). R_f value = 0.27 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.95 (d, J = 12.4 Hz, 1H), 7.57 (d, J = 7.5 Hz, 1H), 7.46 (d, J = 7.8 Hz, 2H), 7.35 – 7.31 (m, 5H), 7.28 (s, 3H), 7.24 (s, 2H), 7.12 (d, J = 7.9 Hz, 1H), 5.41

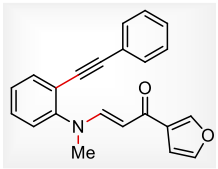
(d, *J* = 7.5 Hz, 1H), 3.74 (s, 2H), 3.29 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 195.8, 151.2, 140.7, 136.5, 133.7, 131.5, 129.4, 129.3, 128.7, 128.5, 128.4, 126.4, 124.8, 122.7, 99.2, 95.2, 85.8, 48.7, 38.5. IR (neat): ν/ cm^{-1} = 3025, 1656, 1545, 1493, 1331, 1275, 1088, 752. HRMS: *m/z* $[M+Na]^+$ calcd for $C_{25}H_{21}NONa$: 374.1515, found: 374.1511.

(*E*)-3-(Methyl(2-(pyridin-2-ylethynyl)phenyl)amino)-1-phenylprop-2-en-1-one (4.18bs, Table 4.1):



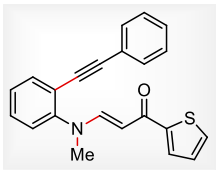
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (316.5 mg, 62%). R_f value = 0.35 (70% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 8.68 (s, 1H), 8.48 (s, 1H), 8.51 (d, *J* = 11.6 Hz, 1H), 7.91 (s, 2H), 7.73 (d, *J* = 7.1 Hz, 1H), 7.56 (d, *J* = 6.4 Hz, 1H), 7.44 – 7.34 (m, 4H), 7.23 (s, 1H), 7.18 (s, 2H), 6.07 (s, 1H), 3.40 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 189.2, 152.1, 151.7, 148.7, 139.9, 138.5, 133.6, 131.2, 129.9, 128.1, 127.5, 126.3, 124.7, 123.0, 119.8, 118.0, 117.1, 96.0, 91.5, 88.9, 38.7. IR (neat): ν/ cm^{-1} = 2920, 1656, 1501, 1440, 1255, 1033, 752. HRMS: *m/z* $[M+Na]^+$ calcd for $C_{23}H_{18}N_2ONa$: 361.1311, found: 361.1310.

(*E*)-1-(Furan-3-yl)-3-(methyl(2-(phenylethynyl)phenyl)amino)prop-2-en-1-one (4.18bt, Table 4.1):



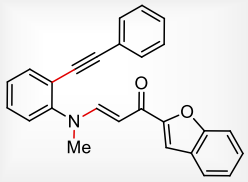
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (321.1 mg, 65%). R_f value = 0.24 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 8.06 (s, 1H), 7.35 (s, 4H), 7.13 (d, *J* = 16 Hz, 4H), 7.03 (s, 3H), 6.32 (s, 1H), 5.95 (s, 1H), 3.22 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 177.3, 154.1, 151.0, 147.3, 144.2, 133.1, 131.0, 129.1, 128.2, 127.9, 126.0, 124.3, 122.1, 120.8, 118.3, 113.7, 111.5, 94.9, 94.8, 85.4, 38.2. IR (neat): ν/ cm^{-1} = 2910, 1639, 1538, 1462, 1278, 1059, 749. HRMS: *m/z* $[M+H]^+$ calcd for $C_{22}H_{18}NO_2$: 328.1332, found: 328.1320.

(*E*)-3-(Methyl(2-(phenylethynyl)phenyl)amino)-1-(thiophen-2-yl)prop-2-en-1-one (4.18bu, Table 4.1):



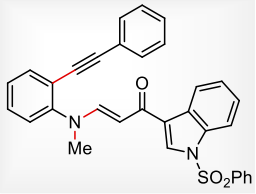
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (316.8 mg, 61%). R_f value = 0.23 (25% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 8.11 (d, *J* = 12.1 Hz, 1H), 7.68 (s, 1H), 7.55 (d, *J* = 6.7 Hz, 1H), 7.47 – 7.43 (m, 3H), 7.31 (d, *J* = 7.0 Hz, 1H), 7.28 – 7.24 (m, 3H), 7.23 (s, 1H), 7.17 (d, *J* = 5.6 Hz, 1H), 7.06 (s, 1H), 5.97 (s, 1H), 3.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*/ ppm = 181.4, 151.7, 148.3, 147.1, 133.6, 131.5, 130.9, 129.4, 129.0, 128.6, 128.4, 127.6, 126.5, 125.0, 122.6, 119.1, 95.6, 95.3, 85.7, 38.8. IR (neat): ν/ cm^{-1} = 2920, 1627, 1534, 1413, 1276, 1054, 759. HRMS: *m/z* $[M+H]^+$ calcd for $C_{22}H_{18}NOS$: 344.1104, found: 344.1107.

(*E*)-1-(Benzofuran-2-yl)-3-(methyl(2-(phenylethynyl)phenyl)amino)prop-2-en-1-one (4.18bv, Table 4.1):



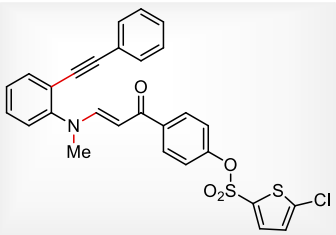
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (342.5 mg, 60%). R_f value = 0.22 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.25 (d, J = 12.0 Hz, 1H), 7.60 (s, 1H), 7.47 (s, 5H), 7.34 (s, 1H), 7.22 (s, 5H), 7.09 (s, 2H), 6.23 (d, J = 10.9 Hz, 1H), 3.38 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 178.6, 154.9, 151.8, 147.9, 133.3, 131.2, 129.2, 128.4, 128.1, 127.5, 126.5, 126.3, 124.5, 123.1, 122.3, 122.26, 118.5, 111.7, 109.5, 95.4, 95.1, 85.4, 38.5. IR (neat): ν/ cm^{-1} = 3085, 1631, 1535, 1452, 1339, 1278, 1071, 743. HRMS: m/z $[M+H]^+$ calcd for $C_{26}H_{20}NO_2$: 378.1489, found: 378.1496.

(*E*)-3-(Methyl(2-(phenylethynyl)phenyl)amino)-1-(1-(phenylsulfonyl)-1*H*-indol-3-yl)prop-2-en-1-one (4.18bw, Table 4.1):



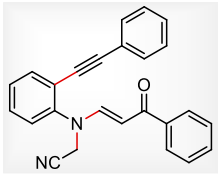
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); with a modification like, N protection of indole followed by 3-formylation has been performed before step-2. **4.18bw** was obtained as yellow gummy liquid (439.4 mg, 57%). R_f value = 0.46 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.40 (d, J = 6.7 Hz, 1H), 8.24 (s, 1H), 8.17 (d, J = 12.6 Hz, 1H), 7.97 (d, J = 7.9 Hz, 1H), 7.91 (d, J = 7.6 Hz, 2H), 7.60 (d, J = 7.0 Hz, 1H), 7.54 – 7.50 (m, 3H), 7.44 – 7.37 (m, 3H), 7.34 (t, J = 7.0 Hz, 3H), 7.29 (d, J = 5.9 Hz, 3H), 7.22 (d, J = 6.7 Hz, 1H), 6.00 (s, 1H), 3.48 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 184.6, 151.3, 137.6, 135.0, 134.2, 133.6, 132.4, 131.5, 131.4, 129.4, 128.8, 128.7, 128.6, 128.3, 126.8, 126.4, 125.3, 124.9, 124.3, 123.5, 123.2, 122.6, 118.8, 113.0, 97.2, 95.2, 85.8, 38.9. IR (neat): ν/ cm^{-1} = 3056, 1635, 1527, 1444, 1292, 1128, 1085, 744. HRMS: m/z $[M+Na]^+$ calcd for $C_{32}H_{24}N_2O_3SNa$: 539.1400, found: 539.1403.

(*E*)-4-(3-(Methyl(2-(phenylethynyl)phenyl)amino)acryloyl)phenyl 5-chlorothiophene-2-sulfonate (4.18bx, Table 4.1):



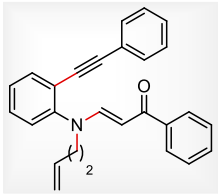
The title compound was prepared following **GP-3** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (428.0 mg, 53%). R_f value = 0.14 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.13 (d, J = 12.6 Hz, 1H), 7.91 (d, J = 6.4 Hz, 2H), 7.59 (d, J = 5.7 Hz, 1H), 7.47 (d, J = 7.8 Hz, 2H), 7.36 – 7.29 (m, 6H), 7.22 (d, J = 7.3 Hz, 1H), 7.13 (d, J = 6.6 Hz, 2H), 6.92 (d, J = 3.7 Hz, 1H), 6.02 (d, J = 11.8 Hz, 1H), 3.46 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 188.0, 153.3, 151.3, 141.5, 140.5, 139.5, 135.2, 133.7, 132.8, 132.1, 132.0, 131.6, 129.5, 128.8, 128.5, 127.9, 127.1, 126.8, 125.0, 122.6, 121.9, 95.6, 95.4, 39.0. IR (neat): ν/ cm^{-1} = 3054, 1628, 1572, 1444, 1281, 1014, 750. HRMS: m/z $[M+H]^+$ calcd for $C_{28}H_{21}NO_4S_2Cl$: 534.0595, found: 534.0600.

(*E*)-2-((3-Oxo-3-phenylprop-1-en-1-yl)(2-(phenylethynyl)phenyl)amino)acetonitrile (4.18by, Table 4.1):



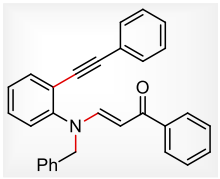
The title compound was prepared following **GP-2** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (342.7 mg, 63%). R_f value = 0.21 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 7.98 – 7.94 (m, 3H), 7.64 (d, *J* = 7.5 Hz, 1H), 7.53 – 7.49 (m, 3H), 7.46 – 7.39 (m, 3H), 7.39 – 7.28 (m, 5H), 6.24 (d, *J* = 12.7 Hz, 1H), 4.67 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 189.3, 149.6, 139.1, 133.9, 131.9, 131.6, 129.9, 129.1, 129.0, 128.4, 128.35, 128.0, 127.8, 127.1, 126.4, 122.0, 121.2, 119.8, 114.1, 99.0, 96.4, 84.7. IR (neat): ν/ cm^{-1} = 2923, 1671, 1596, 1446, 1336, 1210, 1089, 751. HRMS: *m/z* [M+H]$^+$ calcd for $C_{25}H_{19}N_2O$: 363.1492, found: 363.1493.

(*E*)-3-(But-3-en-1-yl(2-(phenylethynyl)phenyl)amino)-1-phenylprop-2-en-1-one (4.18bz, Table 4.1):



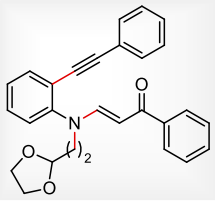
The title compound was prepared following **GP-2** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (340.3 mg, 60%). R_f value = 0.35 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.08 (d, *J* = 12.4 Hz, 1H), 7.91 (s, 2H), 7.58 (d, *J* = 5.6 Hz, 1H), 7.48 – 7.44 (m, 2H), 7.38 – 7.27 (m, 5H), 7.24 (s, 5H), 5.80 – 5.70 (m, 1H), 5.10 – 5.01 (m, 2H), 3.85 (s, 2H), 2.40 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 189.1, 152.4, 139.9, 135.2, 134.0, 133.3, 131.2, 131.0, 130.8, 129.2, 128.4, 128.1, 127.8, 127.3, 122.2, 117.1, 95.2, 95.0, 85.4, 56.6, 50.5, 42.0, 33.1. IR (neat): ν/ cm^{-1} = 3025, 1719, 1537, 1273, 1187, 1105, 1055, 763. HRMS: *m/z* [M+H]$^+$ calcd for $C_{27}H_{24}NO$: 378.1852, found: 378.1860.

(*E*)-3-(But-3-en-1-yl(2-(phenylethynyl)phenyl)amino)-1-phenylprop-2-en-1-one (4.18ca, Table 4.1):



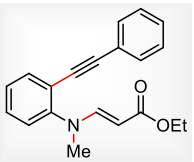
The title compound was prepared following **GP-2** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow gummy liquid (398.9 mg, 64%). R_f value = 0.54 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.26 (d, *J* = 12.8 Hz, 1H), 7.81 (d, *J* = 7.5 Hz, 2H), 7.64 (d, *J* = 6.3 Hz, 1H), 7.50 (d, *J* = 7.2 Hz, 2H), 7.44 (t, *J* = 7.0 Hz, 1H), 7.37 (t, *J* = 7.4 Hz, 4H), 7.34 – 7.26 (m, 8H), 7.20 (s, 1H), 6.12 (s, 1H), 5.05 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 189.6, 152.4, 147.4, 140.0, 135.7, 133.7, 131.5, 131.1, 129.3, 128.6, 128.3, 128.1, 127.6, 127.2, 126.8, 125.3, 122.5, 97.0, 95.4, 85.8, 55.0. IR (neat): ν/ cm^{-1} = 3056, 1643, 1535, 1446, 1281, 1200, 1043, 753. HRMS: *m/z* [M+H]$^+$ calcd for $C_{30}H_{24}NO$: 414.1852, found: 414.1858.

(*E*)-3-((2-(1,3-Dioxolan-2-yl)ethyl)(2-(phenylethynyl)phenyl)amino)-1-phenylprop-2-en-1-one (4.18cb, Table 4.1):



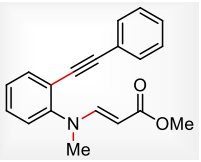
The title compound was prepared following **GP-2** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as off-white gummy liquid (364.4 mg, 57%). R_f value = 0.12 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.04 (d, J = 12.3 Hz, 1H), 7.93 (s, 2H), 7.55 (s, 1H), 7.43 (s, 2H), 7.36 (s, 3H), 7.20 (s, 6H), 6.30 (s, 1H), 4.89 (s, 1H), 3.93 (s, 2H), 3.83 (d, J = 6.9 Hz, 2H), 3.69 (d, J = 7.0 Hz, 2H), 2.04 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 189.0, 152.2, 139.9, 133.2, 131.2, 130.8, 129.2, 128.4, 128.1, 128.0, 127.8, 127.3, 126.7, 125.7, 122.3, 120.2, 101.7, 95.3, 94.8, 85.4, 64.6, 45.9, 30.3. IR (neat): ν/ cm^{-1} = 2882, 1642, 1536, 1494, 1193, 1022, 751. HRMS: m/z $[M+H]^+$ calcd for $C_{28}H_{26}NO_3$: 424.1907, found: 424.1908.

(*E*)-Ethyl 3-(methyl(2-(phenylethynyl)phenyl)amino)acrylate (4.18cc, Table 4.1):



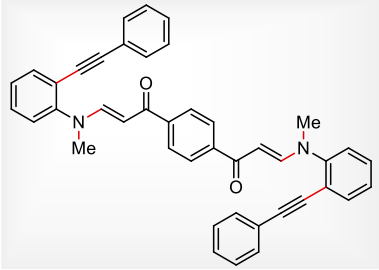
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as gummy liquid (249.7 mg, 55%). R_f value = 0.74 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.90 (d, J = 13.2 Hz, 1H), 7.56 (dd, J = 7.7, 1.5 Hz, 1H), 7.52 – 7.48 (m, 2H), 7.35 – 7.30 (m, 4H), 7.20 (t, J = 7.5 Hz, 1H), 7.15 (d, J = 8.0 Hz, 1H), 4.90 (d, J = 11.5 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 3.30 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 169.1, 150.9, 133.6, 131.4, 129.4, 128.6, 128.3, 125.9, 124.8, 122.8, 118.9, 116.2, 95.1, 89.2, 86.0, 59.1, 38.6, 14.5. IR (neat): ν/ cm^{-1} = 2937, 1688, 1589, 1443, 1243, 1127, 1044, 746. HRMS: m/z $[M+Na]^+$ calcd for $C_{20}H_{19}NO_2Na$: 328.1308, found: 328.1307.

(*E*)-methyl 3-(methyl(2-(phenylethynyl)phenyl)amino)acrylate (4.18cd, Table 4.1):



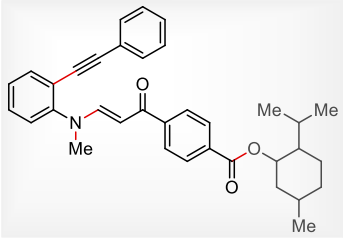
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as gummy liquid (257.8 mg, 59%). R_f value = 0.72 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.90 (d, J = 13.2 Hz, 1H), 7.55 (dd, J = 7.7, 1.5 Hz, 1H), 7.51 – 7.47 (m, 2H), 7.35 – 7.30 (m, 4H), 7.20 (t, J = 7.6 Hz, 1H), 7.14 (d, J = 8.00 Hz, 1H), 4.90 (d, J = 11.5 Hz, 1H), 3.68 (s, 3H), 3.30 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ/ ppm = 169.4, 151.0, 133.6, 131.4, 129.3, 128.6, 128.3, 125.9, 124.8, 122.8, 116.2, 108.9, 95.1, 88.7, 86.0, 50.6, 38.6. IR (neat): ν/ cm^{-1} = 1734, 1562, 1515, 1368, 1218, 1010, 743. HRMS: m/z $[M+Na]^+$ calcd for $C_{19}H_{17}NO_2Na$: 314.1151, found: 314.1155.

(2*E*,2'*E*)-1,1'-(1,4-Phenylene)bis(3-(methyl(2-(phenylethynyl)phenyl)amino)prop-2-en-1-one) (4.18ce, Table 4.1):



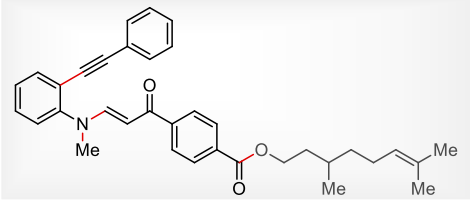
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); with a modification like, 2 equiv. of alkynone has been used in step-3. **1ce** was obtained as reddish yellow gummy liquid (316.4 mg, 53%). R_f value = 0.30 (50% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.13 (d, J = 12.1 Hz, 2H), 7.96 (s, 4H), 7.59 (d, J = 5.6 Hz, 2H), 7.50 – 7.46 (m, 5H), 7.36 (d, J = 6.0 Hz, 3H), 7.31 (s, 6H), 7.23 (s, 2H), 6.09 (s, 2H), 3.47 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 189.1, 152.9, 142.4, 133.7, 132.1, 131.6, 130.0, 129.5, 128.8, 128.4, 127.6, 126.6, 125.1, 122.7, 96.4, 95.4, 85.7, 39.3. IR (neat): ν/ cm^{-1} = 2921, 1635, 1535, 1334, 1273, 1053, 750. HRMS: m/z $[M+H]^+$ calcd for $C_{42}H_{33}N_2O_2$: 597.2537, found: 597.2535.

(*E*)-2-Isopropyl-5-methylcyclohexyl 4-(3-(methyl(2-(phenylethynyl)phenyl)amino)-acryloyl)benzoate (4.18cf, Table 4.1):



The title compound was prepared following **GP-4** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as reddish yellow gummy liquid (278.9 mg, 54%). R_f value = 0.09 (10% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.14 (d, J = 12.3 Hz, 1H), 8.09 (d, J = 5.7 Hz, 2H), 7.97 (s, 2H), 7.58 (d, J = 5.6 Hz, 1H), 7.49 – 7.45 (m, 2H), 7.36 (s, 1H), 7.31 – 7.28 (m, 4H), 7.21 (d, J = 5.9 Hz, 1H), 6.07 (d, J = 10.9 Hz, 1H), 4.98 – 4.92 (m, 1H), 3.45 (s, 3H), 2.13 (d, J = 11.8 Hz, 1H), 1.96 (s, 1H), 1.73 (d, J = 11.8 Hz, 2H), 1.56 (s, 2H), 1.25 (s, 1H), 1.16 – 1.09 (m, 2H), 0.92 (t, J = 4.7 Hz, 6H), 0.80 (d, J = 6.8 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 188.7, 165.6, 153.1, 148.4, 143.9, 133.7, 132.8, 131.5, 129.4, 128.7, 128.4, 127.5, 126.6, 124.9, 122.6, 119.2, 96.2, 95.3, 85.6, 75.1, 47.2, 40.9, 38.9, 34.3, 31.4, 26.5, 23.7, 22.0, 20.7, 16.6. IR (neat): ν/ cm^{-1} = 2919, 1656, 1501, 1440, 1255, 1033, 751. HRMS: m/z $[M+Na]^+$ calcd for $C_{35}H_{37}NO_3Na$: 542.2666, found: 542.2666.

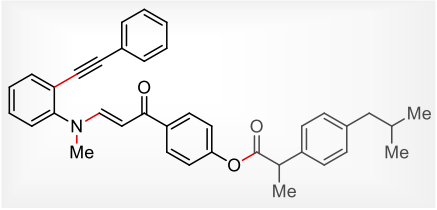
(*E*)-3,7-Dimethyloct-6-en-1-yl 4-(3-(methyl(2-(phenylethynyl)phenyl)amino)acryloyl)-benzoate (4.18cg, Table 4.1):



The title compound was prepared following **GP-4** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as reddish yellow gummy liquid (299.0 mg, 58%). R_f value = 0.30 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.13 (d, J = 12.1 Hz, 1H), 8.06 (s, 2H), 7.97 (s, 2H), 7.54 (s, 1H), 7.45 (s, 2H), 7.30 (s, 1H), 7.26 (s, 4H), 7.17 (s, 1H), 6.06 (d, J = 9.7 Hz, 1H), 5.08 (s, 1H), 4.35 (s, 2H), 3.42 (s, 3H), 2.01 – 1.97 (m, 3H), 1.80 (t, J = 6.0 Hz, 1H), 1.65 (s, 3H), 1.58 (s, 3H), 1.41 – 1.36 (m, 1H), 1.25 – 1.19 (m, 2H), 0.95 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 188.4, 166.0, 152.9, 148.2, 143.8, 133.5, 132.3, 131.4, 131.1, 129.3, 128.6, 128.2, 127.4, 126.5, 124.4, 122.4, 118.9, 95.9, 95.2, 85.6,

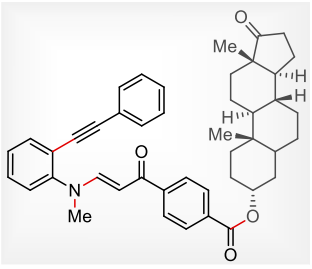
63.5, 38.7, 36.8, 35.3, 29.4, 25.6, 25.2, 19.4, 17.5, 14.0. IR (neat): ν/ cm^{-1} = 2914, 1715, 1643, 1538, 1445, 1265, 1099, 1015, 754. HRMS: *m/z* $[M+H]^+$ calcd for $C_{35}H_{38}NO_3$: 520.2846, found: 520.2850.

(*E*)-4-(3-(Methyl(2-(phenylethynyl)phenyl)amino)acryloyl)phenyl 2-(4-isobutylphenyl)-propanoate (4.18ch, Table 4.1):



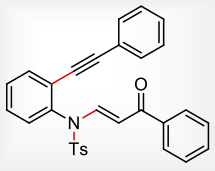
The title compound was prepared following **GP-5** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as reddish yellow gummy liquid (302.3 mg, 56%). R_f value = 0.26 (20% EtOAc in hexane). ^1H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 8.16 (d, *J* = 11.9 Hz, 1H), 7.98 (s, 2H), 7.59 (d, *J* = 6.5 Hz, 1H), 7.51 – 7.48 (m, 2H), 7.34 (d, *J* = 7.7 Hz, 4H), 7.30 (s, 3H), 7.18 (d, *J* = 7.9 Hz, 3H), 7.10 (d, *J* = 6.3 Hz, 2H), 6.07 (s, 1H), 3.97 (q, *J* = 7.0 Hz, 1H), 3.43 (s, 3H), 2.50 (d, *J* = 7.2 Hz, 2H), 1.93 – 1.86 (m, 1H), 1.63 (d, *J* = 7.1 Hz, 3H), 0.95 (s, 3H), 0.93 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 188.0, 172.7, 153.1, 152.5, 140.7, 137.6, 137.0, 133.5, 131.4, 131.3, 129.4, 129.38, 128.9, 128.6, 128.3, 127.1, 126.5, 124.9, 122.6, 121.0, 119.0, 95.7, 95.2, 85.7, 45.2, 44.9, 38.7, 30.0, 22.3, 18.4. IR (neat): ν/ cm^{-1} = 2954, 1754, 1597, 1455, 1200, 1131, 1064, 752. HRMS: *m/z* $[M+H]^+$ calcd for $C_{37}H_{36}NO_3$: 542.2690, found: 542.2694.

(3*R*,8*R*,9*S*,10*S*,13*S*,14*S*)-10,13-Dimethyl-17-oxohexadecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl 4-((*E*)-3-(methyl(2-(phenylethynyl)phenyl)amino)-acryloyl)benzoate (4.18ci, Table 4.1):



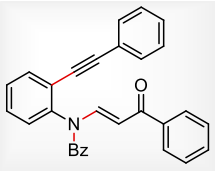
The title compound was prepared following **GP-4** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as reddish yellow gummy liquid (379.4 mg, 58%). R_f value = 0.31 (20% EtOAc in hexane). ^1H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 8.12 (d, *J* = 12.1 Hz, 1H), 8.06 (d, *J* = 5.8 Hz, 2H), 7.94 (s, 2H), 7.59 (d, *J* = 5.5 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 2H), 7.36 (d, *J* = 7.4 Hz, 1H), 7.30 (d, *J* = 6.2 Hz, 4H), 7.22 (s, 1H), 6.06 (d, *J* = 10.1 Hz, 1H), 4.98 – 4.92 (m, 1H), 3.46 (s, 3H), 2.43 (dd, *J* = 19.2, 8.7 Hz, 1H), 2.11 – 2.02 (m, 1H), 1.99 – 1.91 (m, 2H), 1.80 (d, *J* = 14.6 Hz, 4H), 1.67 (d, *J* = 12.0 Hz, 2H), 1.58 – 1.48 (m, 3H), 1.36 (s, 1H), 1.28 (d, *J* = 5.9 Hz, 2H), 1.25 (s, 3H), 1.11 (t, *J* = 12.3 Hz, 1H), 1.04 – 0.95 (m, 1H), 0.90 (s, 3H), 0.86 (s, 3H), 0.75 (t, *J* = 10.4 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 188.8, 165.7, 153.1, 143.9, 133.7, 132.9, 131.6, 132.9, 131.6, 129.5, 128.8, 128.4, 127.5, 126.8, 125.0, 122.7, 96.2, 95.4, 74.4, 54.4, 51.4, 47.8, 44.8, 36.8, 35.9, 35.7, 35.1, 34.1, 31.6, 30.9, 28.3, 27.5, 21.8, 20.5, 13.8, 12.3, 1.02. IR (neat): ν/ cm^{-1} = 2920, 1717, 1540, 1498, 1262, 1012, 753. HRMS: *m/z* $[M+H]^+$ calcd for $C_{44}H_{48}NO_4$: 654.3578, found: 654.3582.

(*E*)-4-Methyl-*N*-(3-oxo-3-phenylprop-1-en-1-yl)-*N*-(2-(phenylethynyl)phenyl) benzenesulfonamide (4.18cj, Table 4.1):



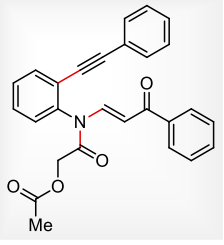
The title compound was prepared following **GP-2** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow solid (456.2 mg, 64%). R_f value = 0.24 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.59 (d, J = 13.4 Hz, 1H), 7.74 (d, J = 7.4 Hz, 2H), 7.63 (d, J = 7.9 Hz, 3H), 7.51 – 7.48 (m, 2H), 7.44 (d, J = 7.5 Hz, 1H), 7.34 (t, J = 7.5 Hz, 3H), 7.31 – 7.26 (m, 3H), 7.23 (d, J = 7.2 Hz, 2H), 7.08 (d, J = 8.1 Hz, 2H), 5.82 (d, J = 13.4 Hz, 1H), 2.21 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 189.7, 144.9, 143.4, 138.5, 136.0, 134.9, 133.5, 132.2, 131.5, 131.0, 129.9, 129.6, 128.8, 128.7, 128.3, 128.1, 127.9, 127.8, 123.8, 122.3, 104.7, 95.1, 84.7, 21.4. IR (neat): ν/ cm^{-1} = 2924, 1656, 1571, 1369, 1168, 1087, 934, 754. HRMS: m/z $[M+H]^+$ calcd for $C_{30}H_{24}NO_3S$: 478.1471, found: 478.1477.

(*E*)-*N*-(3-oxo-3-phenylprop-1-en-1-yl)-*N*-(2-(phenylethynyl)phenyl)benzamide (4.18ck, Table 4.1):



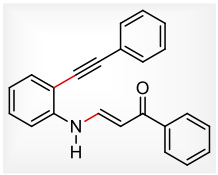
The title compound was prepared following **GP-2** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as reddish yellow gummy liquid (395.4 mg, 62%). R_f value = 0.16 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.86 (d, J = 13.7 Hz, 1H), 7.80 (d, J = 8.3 Hz, 2H), 7.63 (d, J = 7.8 Hz, 1H), 7.58 (d, J = 8.1 Hz, 2H), 7.56 – 7.51 (m, 2H), 7.50 - 7.44 (m, 2H), 7.42 (s, 1H), 7.40 (d, J = 7.7 Hz, 3H), 7.38 – 7.34 (m, 4H), 7.28 (t, J = 7.5 Hz, 2H), 6.09 (d, J = 13.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 190.4, 170.1, 144.1, 139.9, 138.4, 133.9, 133.3, 132.2, 131.6, 131.1, 129.5, 129.1, 129.0, 128.9, 128.7, 128.4, 128.3, 128.0, 127.9, 122.9, 122.1, 107.4, 95.5, 84.8. IR (neat): ν/ cm^{-1} = 3067, 1680, 1560, 1448, 1263, 1160, 1017, 753. HRMS: m/z $[M+Na]^+$ calcd for $C_{30}H_{21}NO_2Na$: 450.1465, found: 450.1467.

(*E*)-2-Oxo-2-((3-oxo-3-phenylprop-1-en-1-yl)(2-(phenylethynyl)phenyl)amino)ethyl acetate (4.18cl, Table 4.1):



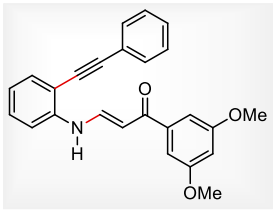
The title compound was prepared following **GP-2** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as reddish yellow gummy liquid (362.8 mg, 57%). R_f value = 0.21 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.77 (d, J = 14.0 Hz, 1H), 7.79 – 7.75 (m, 1H), 7.70 (d, J = 7.2 Hz, 2H), 7.58 – 7.54 (m, 2H), 7.49 – 7.43 (m, 3H), 7.44 – 7.40 (m, 1H), 7.37 – 7.31 (m, 5H), 5.81 (d, J = 14.0 Hz, 1H), 4.52 (dd, J = 34.5, 15.7 Hz, 2H), 2.13 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 190.8, 170.1, 166.2, 141.7, 138.4, 137.3, 133.7, 132.3, 131.9, 130.33, 130.3, 129.2, 129.0, 128.5, 128.4, 128.2, 123.4, 121.7, 108.1, 96.4, 83.3, 61.9, 20.4. IR (neat): ν/ cm^{-1} = 3074, 1631, 1535, 1339, 1278, 1138, 1071, 742. HRMS: m/z $[M+Na]^+$ calcd for $C_{27}H_{21}NO_4Na$: 446.1363, found: 446.1364.

(*E*)-1-Phenyl-3-((2-(phenylethynyl)phenyl)amino)prop-2-en-1-one (4.18cm, Table 4.1):



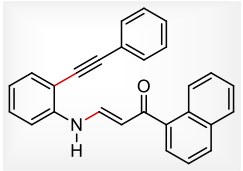
The title compound was prepared following **GP-2** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow solid (378.6 mg, 78%). M.P. = 121 - 122°C. R_f value = 0.84 (25% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 12.74 (d, J = 12.1 Hz, 1H), 7.99 (t, J = 6.7 Hz, 4H), 7.62 – 7.53 (m, 2H), 7.53 – 7.44 (m, 3H), 7.44 – 7.35 (m, 3H), 7.32 (t, J = 7.4 Hz, 1H), 7.22 (d, J = 8.1 Hz, 1H), 7.03 (td, J = 7.5, 0.9 Hz, 1H), 6.13 (d, J = 8.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 190.7, 142.8, 141.7, 139.3, 132.7, 132.3, 131.6, 129.5, 128.5, 128.4, 128.37, 127.5, 123.1, 122.7, 112.6, 112.5, 97.0, 94.9, 84.6. IR (neat): ν/ cm^{-1} = 3050, 1631, 1583, 1456, 1236, 1016, 750. HRMS: *m/z* [M+Na]$^+$ calcd for $C_{23}H_{17}NONa$: 346.1202, found: 346.1200.

(*E*)-1-(3,5-dimethoxyphenyl)-3-((2-(phenylethynyl)phenyl)amino)prop-2-en-1-one (4.18cn, Table 4.1):



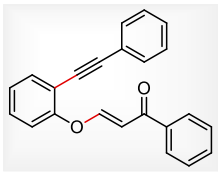
The title compound was prepared following **GP-2** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow solid (465.9 mg, 81%). M.P. = 124 - 125°C. R_f value = 0.72 (25% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 12.82 (d, J = 12.2 Hz, 1H), 8.06 (d, J = 8.0 Hz, 2H), 7.54 (dd, J = 7.7, 1.3 Hz, 1H), 7.50 (dd, J = 12.2, 8.0 Hz, 1H), 7.46 – 7.38 (m, 3H), 7.25 (t, J = 7.8 Hz, 1H), 7.19 (d, J = 2.3 Hz, 2H), 7.14 (d, J = 8.3 Hz, 1H), 7.00 (t, J = 7.5 Hz, 1H), 6.64 (t, J = 2.2 Hz, 1H), 6.04 (d, J = 7.9 Hz, 1H), 3.86 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ/ ppm = 189.7, 160.5, 142.7, 141.4, 141.0, 132.3, 132.1, 129.4, 128.3, 128.1, 122.9, 122.4, 112.3, 112.0, 105.1, 103.6, 96.8, 94.6, 84.6, 55.2. IR (neat): ν/ cm^{-1} = 1640, 1502, 1326, 1194, 1009, 766. HRMS: *m/z* [M+H]$^+$ calcd for $C_{25}H_{22}NO_3$: 384.1594, found: 384.1597.

(*E*)-1-(naphthalen-1-yl)-3-((2-(phenylethynyl)phenyl)amino)prop-2-en-1-one (4.18cn, Table 4.1):



The title compound was prepared following **GP-2** using 2-iodo aniline (330 mg, 1.5 mmol); obtained as yellow solid (442.4 mg, 79%). M.P. = 119 - 120°C. R_f value = 0.77 (25% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 12.81 (d, J = 12.1 Hz, 1H), 8.49 (s, 1H), 8.11 (d, J = 8.5 Hz, 1H), 8.03 (d, J = 7.6 Hz, 2H), 7.97 (d, J = 7.8 Hz, 1H), 7.90 (dd, J = 17.4, 8.5 Hz, 2H), 7.62 (dd, J = 12.2, 8.1 Hz, 1H), 7.57 (d, J = 7.9 Hz, 2H), 7.46 (t, J = 7.3 Hz, 2H), 7.42 – 7.37 (m, 1H), 7.36 – 7.30 (m, 1H), 7.23 (d, J = 8.2 Hz, 1H), 7.04 (t, J = 7.4 Hz, 1H), 6.76 – 6.71 (m, 1H), 6.28 (d, J = 7.9 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ/ ppm = 190.5, 147.8, 142.8, 141.7, 136.6, 135.0, 132.7, 132.3, 131.5, 129.8, 129.6, 129.4, 128.5, 128.4, 128.3, 127.8, 126.4, 124.2, 123.1, 122.7, 118.0, 114.4, 112.6, 108.0, 97.0, 95.1, 85.9, 84.7. IR (neat): ν/ cm^{-1} = 1589, 1468, 1262, 1196, 1069, 730, 698. HRMS: *m/z* [M+H]$^+$ calcd for $C_{27}H_{20}NO$: 374.1539, found: 374.1542.

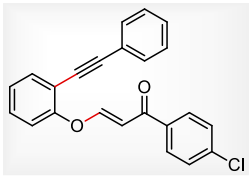
(*E*)-1-Phenyl-3-(2-(phenylethynyl)phenoxy)prop-2-en-1-one (4.21a, Table 4.2):



The title compound was prepared following **GP-6** using 2-iodo phenol (330 mg, 1.5 mmol); obtained as yellow gummy liquid (312.8 mg, 64%). R_f value = 0.59 (15% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.01 (d,

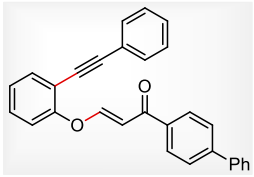
J = 11.8 Hz, 1H), 7.91 (d, *J* = 7.7 Hz, 2H), 7.60 (d, *J* = 7.7 Hz, 1H), 7.57 – 7.50 (m, 3H), 7.45 (t, *J* = 7.4 Hz, 2H), 7.38 (t, *J* = 7.8 Hz, 1H), 7.32 (d, *J* = 5.1 Hz, 3H), 7.23 (t, *J* = 7.5 Hz, 1H), 7.17 (d, *J* = 8.1 Hz, 1H), 6.72 (d, *J* = 11.8 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 190.5, 161.1, 156.3, 138.5, 133.8, 132.6, 131.7, 129.9, 128.7, 128.6, 128.2, 125.4, 122.9, 118.9, 115.6, 106.9, 95.3, 84.0. IR (neat): ν/ cm^{-1} = 3070, 1664, 1561, 1442, 1213, 1014, 746. HRMS: *m/z* $[M+H]^+$ calcd for $C_{23}H_{17}O_2$: 325.1223, found: 325.1222.

(E)-1-(4-Chlorophenyl)-3-(2-(phenylethynyl)phenoxy)prop-2-en-1-one (4.21b, Table 4.2):



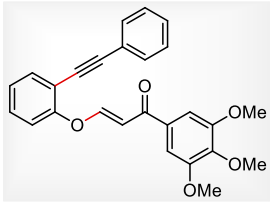
The title compound was prepared following **GP-6** using 2-iodo phenol (330 mg, 1.5 mmol); obtained as yellow gummy liquid (351.0 mg, 65%). R_f value = 0.50 (10% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.02 (d, *J* = 11.8 Hz, 1H), 7.84 (d, *J* = 8.6 Hz, 2H), 7.60 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.53 – 7.49 (m, 2H), 7.41 (d, *J* = 8.6 Hz, 2H), 7.39 – 7.35 (m, 1H), 7.32 (dd, *J* = 5.2, 2.0 Hz, 3H), 7.23 (td, *J* = 7.6, 1.1 Hz, 1H), 7.16 (dd, *J* = 8.2, 1.0 Hz, 1H), 6.68 (d, *J* = 11.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 189.1, 161.3, 156.1, 139.0, 136.6, 133.8, 131.6, 129.9, 129.5, 128.8, 128.7, 128.4, 125.5, 122.7, 118.8, 115.4, 106.3, 95.3, 83.9. IR (neat): ν/ cm^{-1} = 3057, 1662, 1601, 1477, 1204, 1090, 745. HRMS: *m/z* $[M+H]^+$ calcd for $C_{23}H_{15}O_2ClNa$: 381.0653, found: 381.0653.

(*E*)-1-([1,1'-Biphenyl]-4-yl)-3-(2-(phenylethynyl)phenoxy)prop-2-en-1-one (4.21c, Table 4.2):



The title compound was prepared following **GP-6** using 2-iodo phenol (330 mg, 1.5 mmol); obtained as yellow gummy liquid (367.3 mg, 61%). R_f value = 0.50 (10% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.07 (d, *J* = 11.8 Hz, 1H), 8.01 (d, *J* = 8.4 Hz, 2H), 7.68 (d, *J* = 8.5 Hz, 2H), 7.66 – 7.60 (m, 3H), 7.58 – 7.53 (m, 2H), 7.48 (t, *J* = 7.1 Hz, 2H), 7.45 – 7.35 (m, 3H), 7.35 – 7.32 (m, 2H), 7.26 – 7.20 (m, 1H), 7.19 (d, *J* = 8.2 Hz, 1H), 6.81 (d, *J* = 11.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 189.9, 160.8, 156.2, 145.3, 139.9, 137.0, 133.7, 131.6, 129.9, 128.9, 128.7, 128.6, 128.4, 128.1, 127.2, 127.1, 125.3, 122.8, 120.3, 118.7, 115.4, 114.8, 106.7, 95.2, 84.0. IR (neat): ν/ cm^{-1} = 3057, 1661, 1564, 1478, 1194, 1029, 749. HRMS: *m/z* $[M+Na]^+$ calcd for $C_{29}H_{20}O_2Na$: 423.1356, found: 423.1355.

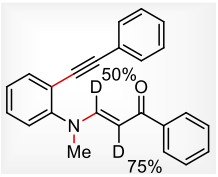
(*E*)-3-(2-(Phenylethynyl)phenoxy)-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (4.21d, Table 4.2):



The title compound was prepared following **GP-6** using 2-iodo phenol (330 mg, 1.5 mmol); obtained as yellow gummy liquid (385.0 mg, 62%). R_f value = 0.22 (15% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.98 (d, *J* = 11.8 Hz, 1H), 7.59 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.52 – 7.48 (m, 2H), 7.41 – 7.35 (m, 1H), 7.34 – 7.28 (m, 3H), 7.25 – 7.20 (m, 2H), 7.17 (s, 2H), 6.74 (d, *J* = 11.8 Hz, 1H), 3.91 (s, 3H), 3.89 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 189.2, 160.7, 156.3, 153.0, 142.2, 133.7, 133.6, 131.6, 129.9, 128.7, 128.3, 125.3, 122.7, 118.7, 115.4, 106.6, 105.6, 95.2, 83.9, 60.9, 56.3. IR (neat): ν/

cm^{-1} = 3056, 1662, 1564, 1477, 1205, 1030, 745. HRMS: *m/z* $[M+Na]^+$ calcd for $C_{26}H_{22}O_5Na$: 437.1359, found: 437.1362.

Deuterated (*E*)-3-(methyl(2-(phenylethynyl)phenyl)amino)-1-phenylprop-2-en-1-one (4.18aa-D):



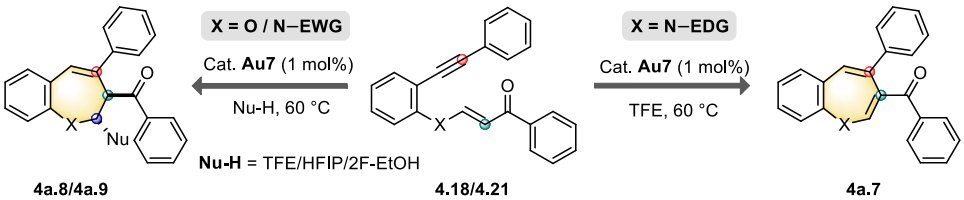
The title compound was prepared following **GP-1** using 2-iodo aniline (330 mg, 1.5 mmol); using methanol-D_4 as solvent in step-3. **4.18aa-D** was obtained as yellow solid (238.5 mg, 70%). M.P. = 118 - 119°C. R_f value = 0.35 (25% EtOAc in hexane). ^1H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.13 (s, 0.5H), 7.94 (s, 2H), 7.59 (d, *J* = 5.3 Hz, 1H), 7.51 – 7.46 (m, 3H), 7.43 (s, 2H), 7.37 (s, 1H), 7.32 – 7.26 (m, 4H), 7.23 (s, 1H), 6.09 (s, 0.25H), 3.46 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 189.6, 152.5, 140.3, 133.7, 131.6, 131.2, 129.5, 128.7, 128.4, 128.2, 127.7, 126.5, 125.2, 122.7, 96.3, 95.3, 85.8, 39.1. IR (neat): ν/ cm^{-1} = 3060, 1626, 1519, 1446, 1272, 1052, 921, 751. HRMS: *m/z* $[M+H]^+$ calcd for $C_{24}H_{17}NOD_2$: 339.1592, found: 339.1595.

4.3.4. Synthesis and Characterization of Benzo[*b*]azepine, Fluoroalkoxy Incorporated Dihydrobenzo[*b*]oxepine/azepine Derivatives (4a.7, 4a.8 and 4a.9):

4.3.4.1. General Synthetic Procedure for the Preparation of Benzo[*b*]azepine, Fluoroalkoxy Incorporated Dihydrobenzo[*b*]oxepine/azepine Derivatives (4a.7, 4a.8 and 4a.9):

General Procedure 7 (GP-7):

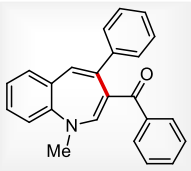
To a mixture of **4.18/4.21** (1 equiv.) and JohnphosAuNTf$_2$ (1 mol%) in a 10 mL dried Pyrex screw-top reaction tube was added TFE (0.1 M). Then the reaction mixture was heated at 60 °C in an oil bath with continuous stirring. After the completion of the reaction as mentioned by the TLC, the reaction mixture was concentrated under reduced pressure and the crude mixture was purified by column chromatography (silica gel, hexanes/EtOAc) to give the corresponding benzo[*b*]azepine or fluoroalkoxy incorporated dihydrobenzo[*b*]oxepine/azepine derivative **4a.7/4a.8/4a.9** in an analytically pure form.



Scheme 4.11. Preparation of benzo[*b*]azepine or fluoroalkoxy incorporated dihydrobenzo[*b*]oxepine/azepine derivatives **4a.7**, **4a.8** and **4a.9**.

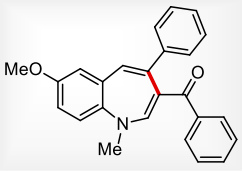
4.3.4.2. Analytical Data of Benzo[*b*]azepine, Fluoroalkoxy Incorporated Dihydrobenzo[*b*]oxepine/azepine Derivatives (4a.7, 4a.8 and 4a.9):

(1-Methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)(phenyl)methanone (4a.7aa, Table 4a.2):



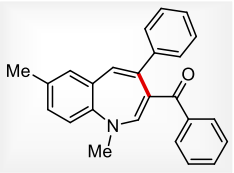
The title compound was prepared following **GP-7** using **4.18aa** (67.5 mg, 0.2 mmol); obtained as yellow solid (65.9 mg, 98%). M.P. = 157 - 158°C. R_f value = 0.53 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 7.61 (dd, J = 8.3, 1.3 Hz, 2H), 7.36 (tt, J = 6.7, 1.3 Hz, 1H), 7.28 – 7.23 (m, 2H), 7.22 – 7.08 (m, 6H), 7.05 – 6.98 (m, 2H), 6.88 (s, 1H), 6.76 (d, J = 8.2 Hz, 1H), 6.71 (s, 1H), 3.12 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 195.7, 158.1, 151.9, 142.7, 141.9, 139.0, 132.6, 132.4, 131.5, 130.4, 129.1, 128.5, 128.2, 128.0, 127.3, 126.5, 125.5, 124.1, 117.0, 40.2. IR (neat): ν/ cm^{-1} = 3023, 1634, 1563, 1445, 1278, 1101, 875, 693. HRMS: m/z [M+H]$^+$ calcd for $C_{24}H_{20}NO$: 338.1539, found: 338.1540.

(7-Methoxy-1-methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)(phenyl)methanone (4a.7ab, Table 4a.2):



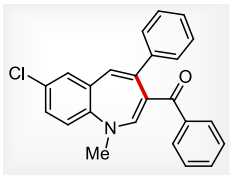
The title compound was prepared following **GP-7** using **4.18ab** (73.5 mg, 0.2 mmol); obtained as yellow solid (69.8 mg, 95%). M.P. = 121- 122°C. M.P. = 163 - 164°C. R_f value = 0.61 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.59 (d, J = 7.0 Hz, 2H), 7.37 – 7.31 (m, 1H), 7.24 (t, J = 7.5 Hz, 2H), 7.19 – 7.08 (m, 5H), 6.97 (s, 1H), 6.71 (dd, J = 8.9, 2.8 Hz, 1H), 6.68 (d, J = 8.9 Hz, 1H), 6.63 (s, 1H), 6.59 (d, J = 2.8 Hz, 1H), 3.79 (s, 3H), 3.10 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 195.6, 159.1, 156.4, 144.8, 143.4, 142.1, 139.2, 133.7, 131.7, 131.4, 128.5, 128.1, 127.9, 127.3, 126.5, 124.4, 117.7, 115.7, 113.5, 55.5, 40.6. IR (neat): ν/ cm^{-1} = 2925, 1642, 1537, 1424, 1276, 1041, 761, 685. HRMS: m/z [M+Na]$^+$ calcd for $C_{25}H_{21}NO_2Na$: 390.1465, found: 390.1464.

(1,7-Dimethyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)(phenyl)methanone (4a.7ac, Table 4a.2):



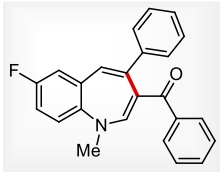
The title compound was prepared following **GP-7** using **4.18ac** (70 mg, 0.2 mmol); obtained as yellow solid (65.8 mg, 94%). M.P. = 160 - 161°C. R_f value = 0.67 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.62 (d, J = 8.4 Hz, 2H), 7.34 (t, J = 7.4 Hz, 1H), 7.27 (t, J = 7.5 Hz, 2H), 7.20 – 7.09 (m, 5H), 7.00 (d, J = 8.3 Hz, 1H), 6.94 (s, 1H), 6.87 (s, 1H), 6.67 (d, J = 8.2 Hz, 2H), 3.13 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 195.8, 158.6, 149.3, 142.7, 142.1, 139.2, 133.6, 132.4, 132.2, 131.4, 131.1, 129.5, 128.5, 128.1, 127.9, 127.2, 126.5, 124.9, 116.8, 40.4, 20.4. IR (neat): ν/ cm^{-1} = 2920, 1634, 1593, 1460, 1279, 1103, 907, 694. HRMS: m/z [M+H]$^+$ calcd for $C_{25}H_{22}NO$: 352.1696, found: 352.1702.

(7-Chloro-1-methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)(phenyl)methanone (4a.7ad, Table 4a.2):



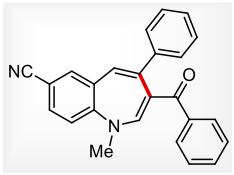
The title compound was prepared following **GP-7** using **4.18ad** (74 mg, 0.2 mmol); obtained as yellow solid (68.1 mg, 92%). M.P. = 169 - 170°C. R_f value = 0.62 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 7.58 (d, *J* = 7.0 Hz, 2H), 7.38 – 7.33 (m, 1H), 7.23 (d, *J* = 7.3 Hz, 2H), 7.16 – 7.11 (m, 6H), 7.00 (d, *J* = 2.4 Hz, 1H), 6.84 (s, 1H), 6.67 (d, *J* = 8.7 Hz, 1H), 6.58 (s, 1H), 3.10 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 195.5, 157.7, 150.7, 144.1, 141.5, 138.9, 134.2, 131.7, 131.0, 130.2, 129.9, 129.5, 128.7, 128.5, 128.3, 128.0, 127.6, 126.6, 125.7, 118.1, 40.4. IR (neat): ν/ cm^{-1} = 2922, 1636, 1595, 1446, 1276, 1205, 1020, 750, 694. HRMS: *m/z* $[M+H]^+$ calcd for $C_{24}H_{19}NOCl$: 372.1150, found: 372.1150.

(7-Fluoro-1-methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)(phenyl)methanone (4a.7ae, Table 4a.2):



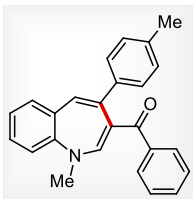
The title compound was prepared following **GP-7** using **4.18ae** (71 mg, 0.2 mmol); obtained as yellow solid (64.6 mg, 91%). M.P. = 160 - 161°C. R_f value = 0.50 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 7.60 (d, *J* = 6.9 Hz, 2H), 7.39 – 7.33 (m, 1H), 7.28 – 7.23 (m, 2H), 7.18 – 7.10 (m, 5H), 6.89 (s, 1H), 6.88 – 6.84 (m, 1H), 6.75 (dd, *J* = 9.1, 3.0 Hz, 1H), 6.69 (dd, *J* = 9.0, 4.8 Hz, 1H), 6.62 (s, 1H), 3.09 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 195.5, 159.6 (d, *J* = 242.7 Hz), 158.2, 147.7 (d, *J* = 2.4 Hz), 144.0, 141.6, 138.9, 134.4 (d, *J* = 7.5 Hz), 131.6, 131.0 (d, *J* = 1.2 Hz), 128.5, 128.2, 128.0, 127.5, 126.5, 125.3, 118.0 (d, *J* = 8.5 Hz), 116.5 (d, *J* = 22.8 Hz), 115.0 (d, *J* = 22.5 Hz), 40.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ/ ppm = -120.61. IR (neat): ν/ cm^{-1} = 2923, 1630, 1496, 1277, 1101, 909, 725, 693. HRMS: *m/z* $[M+Na]^+$ calcd for $C_{24}H_{18}NOFNa$: 378.1265, found: 378.1262.

3-Benzoyl-1-methyl-4-phenyl-1*H*-benzo[*b*]azepine-7-carbonitrile (4a.7af, Table 4a.2):



The title compound was prepared following **GP-7** using **4.18af** (72.5 mg, 0.2 mmol); obtained as yellow solid (57.3 mg, 79%). M.P. = 172 - 173°C. R_f value = 0.26 (30% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.59 (d, *J* = 8.4 Hz, 2H), 7.44 (dd, *J* = 8.5, 2.0 Hz, 1H), 4.40 – 7.35 (m, 1H), 7.28 – 7.24 (m, 4H), 7.15 – 7.11 (m, 4H), 6.76 (d, *J* = 8.5 Hz, 1H), 6.70 (s, 1H), 6.57 (s, 1H), 3.10 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 195.2, 156.7, 155.9, 144.5, 140.8, 138.4, 133.7, 133.4, 133.1, 132.0, 130.8, 128.5, 128.4, 128.1, 127.9, 126.8, 126.4, 118.5, 117.5, 107.6, 40.2. IR (neat): ν/ cm^{-1} = 2923, 1638, 1462, 1210, 1102, 895, 761, 695. HRMS: *m/z* $[M+H]^+$ calcd for $C_{25}H_{19}N_2O$: 363.1492, found: 363.1503.

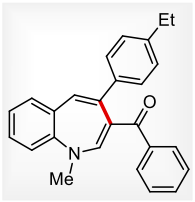
(1-Methyl-4-(*p*-tolyl)-1*H*-benzo[*b*]azepin-3-yl)(phenyl)methanone (4a.7ag, Table 4a.2):



The title compound was prepared following **GP-7** using **4.18ag** (70 mg, 0.2 mmol); obtained as yellow solid (64.4 mg, 92%). M.P. = 161 - 162°C. R_f value = 0.53 (10% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.64 (d, *J* = 7.2 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.28 (t, *J* = 7.7 Hz, 2H), 7.20 – 7.16 (m, 1H),

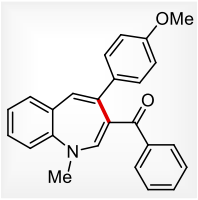
7.10 (d, *J* = 8.0 Hz, 2H), 7.05 – 6.99 (m, 2H), 6.96 (d, *J* = 8.0 Hz, 2H), 6.84 (s, 1H), 6.75 (d, *J* = 8.1 Hz, 1H), 6.71 (s, 1H), 3.11 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 195.7, 157.6, 151.9, 142.5, 139.0, 137.0, 132.5, 132.0, 131.5, 130.3, 128.9, 128.89, 128.6, 127.9, 126.3, 125.8, 124.0, 116.9, 40.2, 21.1. IR (neat): ν/ cm^{-1} = 2921, 1655, 1562, 1444, 1258, 1096, 891, 747, 711. HRMS: *m/z* $[M+H]^+$ calcd for $C_{25}H_{22}NO$: 352.1696, found: 352.1697.

(4-(4-Ethylphenyl)-1-methyl-1*H*-benzo[*b*]azepin-3-yl)(phenyl)methanone (4a.7ah, Table 4a.2):



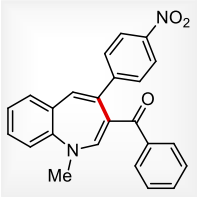
The title compound was prepared following **GP-7** using **4.18ah** (73 mg, 0.2 mmol); obtained as yellow solid (66.4 mg, 91%). M.P. = 162 - 163°C. R_f value = 0.71 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 7.62 (d, *J* = 7.1 Hz, 2H), 7.38 – 7.34 (m, 1H), 7.26 (t, *J* = 7.7 Hz, 2H), 7.20 – 7.15 (m, 1H), 7.10 (d, *J* = 8.1 Hz, 2H), 7.04 – 6.96 (m, 4H), 6.84 (s, 1H), 6.75 (d, *J* = 8.1 Hz, 1H), 6.70 (s, 1H), 3.11 (s, 3H), 2.53 (q, *J* = 7.6 Hz, 2H), 1.14 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 195.8, 157.7, 151.9, 143.3, 142.5, 139.2, 139.1, 132.5, 132.0, 131.5, 130.3, 129.0, 128.6, 127.9, 127.7, 126.4, 125.8, 124.1, 116.9, 40.2, 28.5, 15.4. IR (neat): ν/ cm^{-1} = 2922, 1643, 1444, 1269, 1101, 849, 763, 697. HRMS: *m/z* $[M+H]^+$ calcd for $C_{26}H_{24}NO$: 366.1852, found: 366.1857.

(4-(4-Methoxyphenyl)-1-methyl-*1H*-benzo[*b*]azepin-3-yl)(phenyl)methanone (4a.7ai, Table 4a.2):



The title compound was prepared following **GP-7** using **4.18ai** (73.5 mg, 0.2 mmol); obtained as yellow solid (69.1 mg, 94%). M.P. = 164 - 165°C. R_f value = 0.64 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 7.64 (d, *J* = 7.6 Hz, 2H), 7.40 – 7.35 (m, 1H), 7.27 (t, *J* = 7.6 Hz, 2H), 7.21 – 7.17 (m, 1H), 7.12 (d, *J* = 8.8 Hz, 2H), 7.05 – 6.99 (m, 2H), 6.85 (s, 1H), 6.77 (d, *J* = 8.1 Hz, 1H), 6.69 (d, *J* = 8.6 Hz, 3H), 3.72 (s, 3H), 3.12 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 195.9, 158.9, 157.4, 151.9, 142.1, 139.0, 134.3, 132.5, 131.6, 131.4, 130.2, 128.9, 128.5, 128.0, 127.6, 125.7, 124.0, 116.9, 113.6, 55.1, 40.2. IR (neat): ν/ cm^{-1} = 3001, 1604, 1508, 1243, 1175, 1030, 827, 748, 697. HRMS: *m/z* $[M+H]^+$ calcd for $C_{25}H_{22}NO_2$: 368.1645, found: 368.1648.

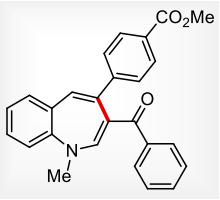
(1-Methyl-4-(4-nitrophenyl)-1*H*-benzo[*b*]azepin-3-yl)(phenyl)methanone (4a.7aj, Table 4a.2):



The title compound was prepared following **GP-7** using **4.18aj** (76.5 mg, 0.2 mmol); obtained as yellow solid (67.3 mg, 88%). M.P. = 186 - 187°C. R_f value = 0.44 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) *δ*/ ppm = 8.02 (d, *J* = 8.9 Hz, 2H), 7.59 (d, *J* = 7.0 Hz, 2H), 7.43 – 7.38 (m, 1H), 7.36 – 7.27 (m, 4H), 7.24 – 7.19 (m, 1H), 7.03 – 7.01 (m, 2H), 6.95 (s, 1H), 6.75 (d, *J* = 8.2 Hz, 1H), 6.72 (s, 1H), 3.13 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*/ ppm = 195.1, 160.4,

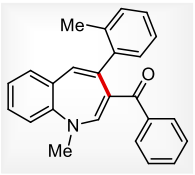
151.5, 149.0, 146.7, 140.7, 138.7, 135.3, 131.9, 131.5, 131.0, 129.9, 128.5, 128.3, 127.0, 124.5, 124.1, 123.6, 117.4, 40.5. IR (neat): ν/ cm^{-1} = 2924, 1591, 1510, 1338, 1274, 1104, 845, 750, 692. HRMS: *m/z* $[M+H]^+$ calcd for $C_{24}H_{19}N_2O_3$: 383.1390, found: 383.1398.

Methyl 4-(3-benzoyl-1-methyl-1*H*-benzo[*b*]azepin-4-yl)benzoate (4a.7ak, Table 4a.2):



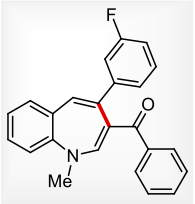
The title compound was prepared following **GP-7** using **4.18ak** (79 mg, 0.2 mmol); obtained as yellow solid (74.3 mg, 94%). M.P. = 182 - 183°C. R_f value = 0.36 (20% EtOAc in hexane). ^1H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 7.82 (d, *J* = 8.5 Hz, 2H), 7.59 (d, *J* = 7.0 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 1H), 7.27 – 7.23 (m, 4H), 7.21 – 7.17 (m, 1H), 7.03 – 6.98 (m, 2H), 6.91 (s, 1H), 6.75 (d, *J* = 8.2 Hz, 1H), 6.72 (s, 1H), 3.84 (s, 3H), 3.11 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 195.3, 166.8, 159.1, 151.7, 146.7, 141.7, 138.8, 134.0, 131.9, 131.7, 130.7, 129.5, 129.49, 128.7, 128.5, 128.1, 126.3, 124.8, 124.3, 117.1, 52.0, 40.3. IR (neat): ν/ cm^{-1} = 2950, 1714, 1604, 1434, 1274, 1101, 880, 698. HRMS: *m/z* $[M+H]^+$ calcd for $C_{26}H_{22}NO_3$: 396.1594, found: 396.1600.

(1-Methyl-4-(*o*-tolyl)-1*H*-benzo[*b*]azepin-3-yl)(phenyl)methanone (4a.7al, Table 4a.2):



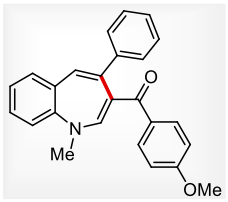
The title compound was prepared following **GP-7** using **4.18al** (70 mg, 0.2 mmol); obtained as yellow solid (63.0 mg, 90%). M.P. = 159 - 160°C. R_f value = 0.76 (20% EtOAc in hexane). ^1H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 7.51 (d, *J* = 8.1 Hz, 2H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.25 (t, *J* = 7.7 Hz, 2H), 7.19 (t, *J* = 7.4 Hz, 1H), 7.01 – 6.92 (m, 6H), 6.74 (d, *J* = 8.1 Hz, 1H), 6.71 (s, 1H), 6.40 (s, 1H), 3.12 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 195.7, 156.6, 151.6, 142.6, 141.5, 139.4, 135.4, 134.2, 132.5, 131.4, 130.3, 130.2, 129.2, 129.0, 128.3, 128.0, 127.1, 126.7, 125.3, 124.1, 117.0, 40.4, 20.0. IR (neat): ν/ cm^{-1} = 2920, 1629, 1445, 1284, 1120, 757, 694. HRMS: *m/z* $[M+H]^+$ calcd for $C_{25}H_{22}NO$: 352.1696, found: 352.1697.

(4-(3-Fluorophenyl)-1-methyl-1*H*-benzo[*b*]azepin-3-yl)(phenyl)methanone (4a.7am, Table 4a.2):



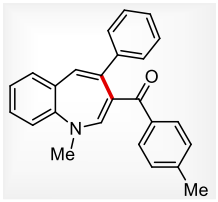
The title compound was prepared following **GP-7** using **4.18am** (71 mg, 0.2 mmol); obtained as yellow solid (63.9 mg, 90%). M.P. = 161 - 162°C. R_f value = 0.71 (20% EtOAc in hexane). ^1H NMR (400 MHz, $CDCl_3$) *δ*/ ppm = 7.60 (d, *J* = 7.1 Hz, 2H), 7.41 – 7.35 (m, 1H), 7.28 (t, *J* = 7.8 Hz, 2H), 7.22 – 7.17 (m, 1H), 7.14 – 7.07 (m, 1H), 7.01 (d, *J* = 4.3 Hz, 2H), 6.96 (d, *J* = 7.8 Hz, 1H), 6.91 – 6.86 (m, 2H), 6.83 – 6.77 (m, 1H), 6.75 (d, *J* = 8.2 Hz, 1H), 6.68 (s, 1H), 3.12 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*/ ppm = 195.4, 162.7 (d, *J* = 245.5 Hz), 158.9, 151.8, 144.4 (d, *J* = 7.5 Hz), 141.5, 139.0, 133.3, 132.0, 131.6, 130.6, 129.6 (d, *J* = 8.6 Hz), 129.4, 128.5, 128.1, 124.9, 124.3, 122.2 (d, *J* = 2.7 Hz), 117.1, 114.1 (d, *J* = 21.3 Hz), 113.4 (d, *J* =22.1 Hz), 40.3. ^{19}F NMR (470 MHz, $CDCl_3$) *δ*/ ppm = -113.57. IR (neat): ν/ cm^{-1} = 2922, 1735, 1579, 1446, 1258, 875, 746, 691. HRMS: *m/z* $[M+H]^+$ calcd for $C_{24}H_{19}NOF$: 356.1445, found: 356.1449.

(4-Methoxyphenyl)(1-methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)methanone (4a.7an, Table 4a.2):



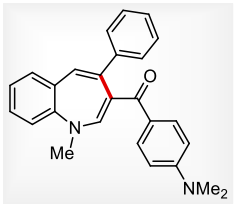
The title compound was prepared following **GP-7** using **4.18an** (73.5 mg, 0.2 mmol); obtained as yellow solid (67.6 mg, 92%). M.P. = 165 - 166°C. R_f value = 0.64 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 7.66 (d, J = 8.9 Hz, 2H), 7.22 – 7.16 (m, 3H), 7.16 – 7.07 (m, 3H), 7.06 – 6.98 (m, 2H), 6.79 – 6.72 (m, 5H), 3.78 (s, 3H), 3.11 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 194.5, 162.5, 156.4, 152.3, 142.9, 141.8, 132.5, 131.7, 131.0, 130.3, 129.1, 128.2, 127.4, 126.6, 126.1, 124.0, 116.9, 113.2, 96.2, 55.4, 40.2. IR (neat): ν/ cm^{-1} = 2925, 1638, 1595, 1463, 1250, 1166, 1023, 753, 696. HRMS: m/z $[M+H]^+$ calcd for $C_{25}H_{22}NO_2$: 368.1645, found: 368.1649.

(1-Methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)(*p*-tolyl)methanone (4a.7ao, Table 4a.2):



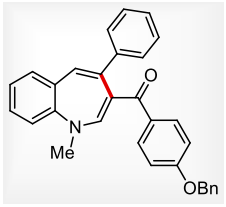
The title compound was prepared following **GP-7** using **4.18ao** (70 mg, 0.2 mmol); obtained as yellow solid (65.1 mg, 93%). M.P. = 160 - 161°C. R_f value = 0.64 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.57 (d, J = 8.0 Hz, 2H), 7.23 – 7.20 (m, 2H), 7.19 – 7.14 (m, 3H), 7.12 (d, J = 6.9 Hz, 1H), 7.08 (d, J = 8.1 Hz, 2H), 7.06 – 6.99 (m, 2H), 6.82 (s, 1H), 6.75 (d, J = 9.3 Hz, 2H), 3.10 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 195.4, 157.3, 151.9, 142.6, 142.2, 141.8, 136.2, 132.6, 132.3, 130.3, 129.1, 128.8, 128.7, 128.1, 127.3, 126.4, 125.9, 124.0, 116.9, 40.2, 21.5. IR (neat): ν/ cm^{-1} = 2924, 1625, 1600, 1568, 1451, 1282, 1206, 1100, 899, 754, 696. HRMS: m/z $[M+H]^+$ calcd for $C_{25}H_{22}NO$: 352.1696, found: 352.1700.

(4-(Dimethylamino)phenyl)(1-methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)methanone (4a.7ap, Table 4a.2):



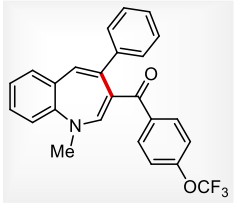
The title compound was prepared following **GP-7** using **4.18ap** (76 mg, 0.2 mmol); obtained as yellow solid (67.6 mg, 89%). M.P. = 161 - 162°C. R_f value = 0.63 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.13 (d, J = 7.8 Hz, 1H), 7.99 (d, J = 8.9 Hz, 2H), 7.91 (d, J = 15.5 Hz, 1H), 7.66 (d, J = 15.5 Hz, 1H), 7.57 – 7.50 (m, 3H), 7.46 – 7.42 (m, 3H), 7.40 – 7.33 (m, 2H), 6.71 (d, J = 8.9 Hz, 2H), 3.66 (s, 3H), 3.07 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 188.2, 153.1, 145.9, 138.1, 137.1, 131.0, 130.5, 129.2, 128.7, 128.2, 126.9, 125.9, 123.0, 121.7, 120.9, 117.8, 111.6, 110.9, 110.2, 40.1, 31.3. IR (neat): ν/ cm^{-1} = 2921, 1589, 1525, 1366, 1281, 1169, 743, 697. HRMS: m/z $[M+H]^+$ calcd for $C_{26}H_{25}N_2O$: 381.1961, found: 381.1967.

(4-(Benzyloxy)phenyl)(1-methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)methanone (4a.7aq, Table 4a.2):



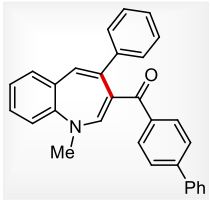
The title compound was prepared following **GP-7** using **4.18aq** (89 mg, 0.2 mmol); obtained as yellow solid (83.7 mg, 94%). M.P. = 160 - 161°C. R_f value = 0.50 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.67 (d, J = 7.2 Hz, 2H), 7.40 (d, J = 4.3 Hz, 4H), 7.37 – 7.33 (m, 1H), 7.22 – 7.10 (m, 6H), 7.06 – 7.00 (m, 2H), 6.83 (d, J = 8.3 Hz, 2H), 6.81 (s, 1H), 6.76 (d, J = 8.2 Hz, 1H), 6.75 (s, 1H), 5.05 (s, 2H), 3.11 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 194.4, 161.6, 156.6, 152.1, 142.7, 141.8, 136.3, 132.5, 132.4, 131.8, 130.9, 130.3, 129.1, 128.6, 128.2, 128.1, 127.4, 127.3, 126.5, 125.9, 123.9, 116.9, 114.1, 69.9, 40.1. IR (neat): ν/ cm^{-1} = 2922, 1595, 1492, 1244, 1167, 1001, 838, 747, 694. HRMS: m/z [M+H]$^+$ calcd for $C_{31}H_{26}NO_2$: 444.1958, found: 444.1967.

(1-Methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)(4-(trifluoromethoxy)phenyl)methanone (4a.7ar, Table 4a.2):



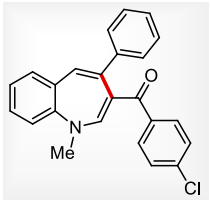
The title compound was prepared following **GP-7** using **4.18ar** (84 mg, 0.2 mmol); obtained as yellow solid (79.0 mg, 94%). M.P. = 159 - 160°C. R_f value = 0.71 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.59 (d, J = 8.3 Hz, 2H), 7.22 – 7.17 (m, 1H), 7.13 – 7.07 (m, 5H), 7.05 – 7.01 (m, 4H), 6.96 (s, 1H), 6.77 (d, J = 8.2 Hz, 1H), 6.63 (s, 1H), 3.15 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 194.3, 158.8, 151.9, 151.2, 142.8, 141.9, 137.7, 132.4, 132.37, 130.4, 130.2, 129.2, 128.2, 127.4, 126.6, 124.6, 124.3, 120.3 (q, J = 260.5 Hz), 120.0, 117.2, 40.3. ^{19}F NMR (470 MHz, $CDCl_3$) δ/ ppm = -57.68. IR (neat): ν/ cm^{-1} = 2925, 1599, 1491, 1248, 1155, 1015, 893, 754, 697. HRMS: m/z [M+H]$^+$ calcd for $C_{25}H_{19}NO_2F_3$: 422.1362, found: 422.1370.

[1,1'-Biphenyl]-4-yl(1-methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)methanone (4a.7as, Table 4a.2):



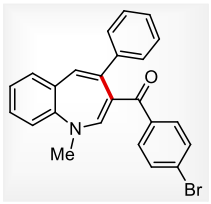
The title compound was prepared following **GP-7** using **4.18as** (83 mg, 0.2 mmol); obtained as yellow solid (78.9 mg, 95%). M.P. = 176 - 177°C. R_f value = 0.41 (10% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.72 (d, J = 8.3 Hz, 2H), 7.57 (d, J = 7.3 Hz, 2H), 7.51 (d, J = 8.3 Hz, 2H), 7.45 (t, J = 7.6 Hz, 2H), 7.38 (t, J = 7.3 Hz, 1H), 7.24 – 7.18 (m, 3H), 7.18 – 7.14 (m, 2H), 7.11 (t, J = 7.0 Hz, 1H), 7.07 – 7.01 (m, 2H), 6.92 (s, 1H), 6.78 (d, J = 8.2 Hz, 1H), 6.74 (s, 1H), 3.14 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 195.3, 157.9, 151.9, 144.2, 142.6, 141.9, 140.1, 137.7, 132.6, 132.4, 130.4, 129.2, 129.1, 128.9, 128.2, 127.9, 127.3, 127.1, 126.6, 126.5, 125.6, 124.1, 117.0, 40.3. IR (neat): ν/ cm^{-1} = 3025, 1599, 1563, 1448, 1274, 1099, 893, 743, 694. HRMS: m/z [M+H]$^+$ calcd for $C_{30}H_{24}NO$: 414.1852, found: 414.1849.

(4-Chlorophenyl)(1-methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)methanone (4a.7at, Table 4a.2):



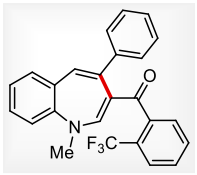
The title compound was prepared following **GP-7** using **4.18at** (74 mg, 0.2 mmol); obtained as yellow solid (70.3 mg, 95%). M.P. = 168 - 169°C. R_f value = 0.50 (10% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 7.55 (d, *J* = 8.5 Hz, 2H), 7.23 – 7.20 (m, 3H), 7.17 – 7.12 (m, 5H), 7.04 (d, *J* = 4.2 Hz, 2H), 6.93 (s, 1H), 6.78 (d, *J* = 8.1 Hz, 1H), 6.69 (s, 1H), 3.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 194.5, 158.5, 151.9, 142.6, 141.8, 137.6, 137.4, 132.4, 132.3, 130.4, 129.8, 129.2, 128.2, 128.18, 127.4, 126.5, 124.8, 124.3, 117.1, 40.3. IR (neat): ν/ cm^{-1} = 2923, 1631, 1566, 1489, 1271, 1087, 874, 761, 696. HRMS: *m/z* $[M+H]^+$ calcd for $C_{24}H_{19}NOCl$: 372.1150, found: 372.1154.

(4-Bromophenyl)(1-methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)methanone (4a.7au, Table 4a.2):



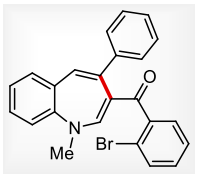
The title compound was prepared following **GP-7** using **4.18au** (83 mg, 0.2 mmol); obtained as yellow solid (77.2 mg, 93%). M.P. = 171 - 172°C. R_f value = 0.48 (10% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.45 (d, *J* = 8.6 Hz, 2H), 7.35 (d, *J* = 8.6 Hz, 2H), 7.21 – 7.17 (m, 1H), 7.15 – 7.09 (m, 5H), 7.04 – 7.00 (m, 2H), 6.90 (s, 1H), 6.76 (d, *J* = 8.1 Hz, 1H), 6.65 (s, 1H), 3.13 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 194.7, 158.5, 151.9, 142.6, 141.8, 137.9, 132.5, 132.4, 131.2, 130.5, 130.0, 129.2, 128.3, 127.5, 126.5, 126.3, 124.8, 124.3, 117.1, 40.3. IR (neat): ν/ cm^{-1} = 2919, 1632, 1568, 1464, 1270, 1065, 873, 741, 694. HRMS: *m/z* $[M]^+$ calcd for $C_{24}H_{19}NOBr$: 416.0645, found: 416.0647.

(1-Methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)(2-(trifluoromethyl)phenyl)methanone (4a.7av, Table 4a.2):



The title compound was prepared following **GP-7** using **4.18av** (81 mg, 0.2 mmol); obtained as yellow solid (73.7 mg, 91%). M.P. = 165 - 166°C. R_f value = 0.74 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 7. 57 (d, *J* = 7.4 Hz, 1H), 7.50 - 7.40 (m, 3H), 7.25 – 7.13 (m, 6H), 7.04 – 6.95 (m, 2H), 6.90 (s, 1H), 6.74 (d, *J* = 8.2 Hz, 1H), 6.55 (s, 1H), 3.08 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 192.6, 164.1, 151.1, 142.4 (d, *J* = 11.5 Hz), 139.1, 133.3, 132.1, 131.1, 130.6, 129.4, 128.9, 128.3, 128.1 (q, *J* = 32.2 Hz), 128.0, 127.1, 126.6 (q, *J* = 4.8 Hz), 126.4, 124.9, 124.7, 124.6, 122.1, 117.2, 40.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ/ ppm = -57.94. IR (neat): ν/ cm^{-1} = 2918, 1610, 1567, 1313, 1106, 1033, 757, 699. HRMS: *m/z* $[M]^+$ calcd for $C_{25}H_{19}NOF_3$: 406.1413, found: 406.1417.

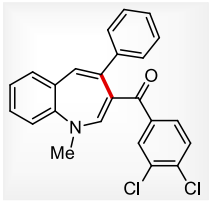
(2-Bromophenyl)(1-methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)methanone (4a.7aw, Table 4a.2):



The title compound was prepared following **GP-7** using **4.18aw** (83 mg, 0.2 mmol); obtained as yellow solid (76.4 mg, 92%). M.P. = 172 - 173°C. R_f value = 0.55 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7. 40 (d, *J* =

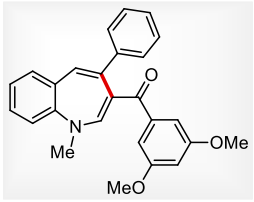
7.9 Hz, 1H), 7.24 - 7.19 (m, 5H), 7.19 – 7.13 (m, 3H), 7.10 (td, *J* = 7.7, 1.8 Hz, 1H), 7.02 (s, 1H), 7.02 – 6.95 (m, 2H), 6.75 (d, *J* = 8.2 Hz, 1H), 6.55 (s, 1H), 3.12 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 193.3, 163.2, 151.2, 142.6, 141.1, 133.2, 133.0, 132.4, 130.6, 129.6, 128.9, 128.2, 127.1, 126.8, 126.3, 124.5, 124.2, 119.8, 117.2, 40.5. IR (neat): ν/ cm^{-1} = 2925, 1604, 1563, 1463, 1290, 1101, 894, 744, 696. HRMS: *m/z* $[M+H]^+$ calcd for $C_{24}H_{19}NOBr$: 416.0645, found: 416.0648.

(3,4-Dichlorophenyl)(1-methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)methanone (4a.7ax, Table 4a.2):



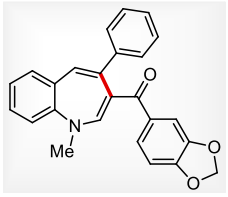
The title compound was prepared following **GP-7** using **4.18ax** (81 mg, 0.2 mmol); obtained as yellow solid (77.0 mg, 95%). M.P. = 167 - 168°C. R_f value = 0.52 (10% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 7.63 (d, *J* = 2.0 Hz, 1H), 7.40 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.27 (d, *J* = 8.3 Hz, 1H), 7.22 – 7.17 (m, 1H), 7.16 – 7.07 (m, 5H), 7.05 – 7.00 (m, 2H), 6.98 (s, 1H), 6.76 (d, *J* = 8.2 Hz, 1H), 6.62 (s, 1H), 3.15 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 193.1, 159.5, 151.8, 142.6, 141.8, 138.9, 135.6, 132.4, 132.37, 132.3, 130.5, 130.3, 130.0, 129.3, 128.4, 127.5, 127.4, 126.5, 124.5, 123.9, 117.2, 40.4. IR (neat): ν/ cm^{-1} = 2923, 1736, 1672, 1451, 1373, 1200, 1027, 753, 698. HRMS: *m/z* $[M+H]^+$ calcd for $C_{24}H_{18}NOCl_2$: 406.0760, found: 406.0761.

(3,5-Dimethoxyphenyl)(1-methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)methanone (4a.7ay, Table 4a.2):



The title compound was prepared following **GP-7** using **4.18ay** (79.5 mg, 0.2 mmol); obtained as yellow solid (70.8 mg, 89%). M.P. = 166 - 167°C. R_f value = 0.47 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 7.21 – 7.15 (m, 5H), 7.14 – 7.10 (m, 1H), 7.00 (s, 1H), 6.995 (d, *J* = 2.3 Hz, 1H), 6.88 (s, 1H), 6.77 – 6.75 (m, 3H), 6.71 (s, 1H), 6.46 (t, *J* = 2.2 Hz, 1H), 3.72 (s, 6H), 3.12 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 195.2, 160.3, 157.9, 151.9, 142.8, 141.9, 141.0, 132.5, 132.4, 130.3, 129.1, 128.2, 127.3, 126.6, 125.7, 124.2, 117.0, 106.5, 104.3, 55.5, 40.3. IR (neat): ν/ cm^{-1} = 2919, 1591, 1562, 1456, 1280, 1152, 1029, 751, 698. HRMS: *m/z* $[M+H]^+$ calcd for $C_{26}H_{24}NO_3$: 398.1751, found: 398.1758.

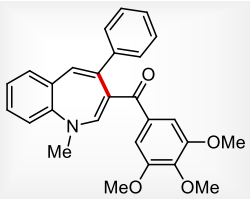
Benzo[*d*][1,3]dioxol-5-yl(1-methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)methanone (4a.7az, Table 4a.2):



The title compound was prepared following **GP-7** using **4.18az** (76 mg, 0.2 mmol); obtained as yellow solid (69.9 mg, 92%). M.P. = 153 - 154°C. R_f value = 0.61 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 7.31 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.21 – 7.10 (m, 6H), 7.10 (d, *J* = 1.6 Hz, 1H), 7.05 – 6.98 (m, 2H), 6.81 (s, 1H), 6.76 (d, *J* = 8.1 Hz, 1H), 6.71 (s, 1H), 6.66 (d, *J* = 8.1 Hz, 1H), 5.93 (s, 2H), 3.11 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 194.0, 156.9, 152.1, 150.6, 147.4, 142.8, 141.8, 133.3, 132.4, 132.39, 130.3, 129.2, 128.2, 127.4, 126.5, 125.6, 124.7, 124.0, 116.9, 108.8, 107.5, 101.5, 40.2. IR (neat): ν/ cm^{-1} = 2922,

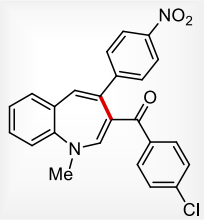
1599, 1485, 1436, 1254, 1033, 748, 696. HRMS: *m/z* $[M+H]^+$ calcd for $C_{25}H_{20}NO_3$: 382.1438, found: 382.1445.

(1-Methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)(3,4,5-trimethoxyphenyl)methanone (4a.7ba, Table 4a.2):



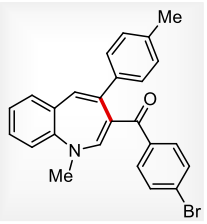
The title compound was prepared following **GP-7** using **4.18ba** (85.5 mg, 0.2 mmol); obtained as yellow solid (75.2 mg, 88%). M.P. = 167 - 168°C. R_f value = 0.69 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.20 – 7.17 (m, 1H), 7.13 (d, *J* = 4.2 Hz, 4H), 7.12 – 7.09 (m, 1H), 6.99 (d, *J* = 4.1 Hz, 2H), 6.88 (s, 2H), 6.86 (s, 1H), 6.78 (d, *J* = 8.1 Hz, 1H), 6.72 (s, 1H), 3.81 (s, 3H), 3.75 (s, 6H), 3.11 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 194.7, 156.6, 152.4, 152.2, 143.1, 141.5, 141.1, 134.0, 132.3, 131.9, 129.9, 129.1, 128.1, 127.3, 126.6, 125.6, 124.1, 117.0, 106.1, 60.7, 56.0, 40.0. IR (neat): ν/ cm^{-1} = 2921, 1656, 1582, 1452, 1328, 1230, 1120, 1003, 815, 766, 707. HRMS: *m/z* $[M+H]^+$ calcd for $C_{27}H_{26}NO_4$: 428.1856, found: 428.1861.

(4-Chlorophenyl)(1-methyl-4-(4-nitrophenyl)-1*H*-benzo[*b*]azepin-3-yl)methanone (4a.7bb, Table 4a.2):



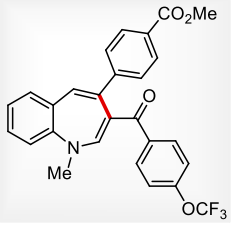
The title compound was prepared following **GP-7** using **4.18bb** (83 mg, 0.2 mmol); obtained as yellow solid (74.7 mg, 90%). M.P. = 187 - 188°C. R_f value = 0.43 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.04 (d, *J* = 8.9 Hz, 2H), 7.54 (d, *J* = 8.6 Hz, 2H), 7.31 (d, *J* = 8.9 Hz, 2H), 7.29 – 7.25 (m, 2H), 7.25 – 7.20 (m, 1H), 7.07 – 7.00 (m, 2H), 6.95 (s, 1H), 6.77 (d, *J* = 8.2 Hz, 1H), 6.70 (s, 1H), 3.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 193.7, 160.6, 151.4, 148.9, 146.8, 140.6, 138.1, 137.1, 135.4, 131.4, 131.0, 130.1, 129.9, 128.6, 127.0, 124.7, 123.7, 123.6, 117.5, 40.5. IR (neat): ν/ cm^{-1} = 2925, 1588, 1512, 1339, 1203, 1088, 839, 746, 693. HRMS: *m/z* $[M+H]^+$ calcd for $C_{24}H_{18}N_2O_3Cl$: 417.1000, found: 417.1003.

(4-Bromophenyl)(1-methyl-4-(*p*-tolyl)-1*H*-benzo[*b*]azepin-3-yl)methanone (4a.7bc, Table 4a.2):



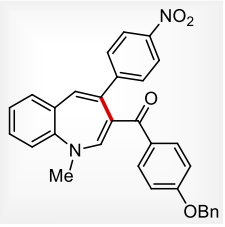
The title compound was prepared following **GP-7** using **4.18bc** (86 mg, 0.2 mmol); obtained as yellow solid (79.1 mg, 92%). M.P. = 172 - 173°C. R_f value = 0.61 (15% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.49 (d, *J* = 8.1 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.21 – 7.15 (m, 1H), 7.04 (d, *J* = 7.9 Hz, 2H), 7.01 (d, *J* = 4.3 Hz, 2H), 6.95 (d, *J* = 8.0 Hz, 2H), 6.86 (s, 1H), 6.75 (d, *J* = 8.2 Hz, 1H), 6.66 (s, 1H), 3.11 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 194.6, 157.9, 151.9, 142.4, 138.9, 137.9, 137.2, 132.5, 131.9, 131.1, 130.3, 130.1, 129.0, 128.97, 126.4, 126.3, 125.1, 124.2, 117.0, 40.2, 21.1. IR (neat): ν/ cm^{-1} = 2915, 1635, 1572, 1470, 1269, 1064, 858, 747. HRMS: *m/z* $[M+H]^+$ calcd for $C_{25}H_{21}NOBr$: 430.0801, found: 430.0801.

Methyl 4-(1-methyl-3-(4-(trifluoromethoxy)benzoyl)-1*H*-benzo[*b*]azepin-4-yl)benzoate (4a.7bd, Table 4a.2):



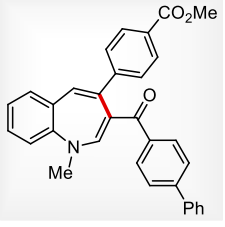
The title compound was prepared following **GP-7** using **4.18bd** (96 mg, 0.2 mmol); obtained as yellow solid (90.2 mg, 94%). M.P. = 181 - 182°C. R_f value = 0.65 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.80 (d, J = 8.4 Hz, 2H), 7.60 (d, J = 8.7 Hz, 2H), 7.22 – 7.16 (m, 3H), 7.05 (d, J = 8.1 Hz, 2H), 7.03 – 6.99 (m, 2H), 6.98 (s, 1H), 6.76 (d, J = 8.2 Hz, 1H), 6.67 (s, 1H), 3.85 (s, 3H), 3.14 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 193.8, 166.7, 159.8, 151.7, 151.3, 146.7, 141.8, 137.4, 133.9, 131.9, 130.7, 130.2, 129.62, 129.6, 128.9, 126.4, 124.5, 123.9, 120.2 (q, J = 259.3 Hz), 120.1, 117.3, 52.0, 40.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ/ ppm = -57.68. IR (neat): ν/ cm^{-1} = 2920, 1717, 1603, 1245, 1153, 1098, 758, 711. HRMS: m/z $[M+H]^+$ calcd for $C_{27}H_{21}NO_4F_3$: 480.1417, found: 480.1425.

(4-(Benzyloxy)phenyl)(1-methyl-4-(4-nitrophenyl)-1*H*-benzo[*b*]azepin-3-yl)methanone (4a.7be, Table 4a.2):



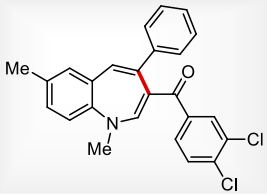
The title compound was prepared following **GP-7** using **4.18be** (98 mg, 0.2 mmol); obtained as yellow solid (86.2 mg, 88%). M.P. = 187 - 188°C. R_f value = 0.61 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.01 (d, J = 8.8 Hz, 2H), 7.62 (d, J = 8.8 Hz, 2H), 7.39 (d, J = 4.4 Hz, 4H), 7.35 – 7.32 (m, 3H), 7.24 – 7.20 (m, 1H), 7.02 (d, J = 4.2 Hz, 2H), 6.87 (s, 1H), 6.85 (d, J = 8.8 Hz, 2H), 6.76 (d, J = 10.3 Hz, 2H), 5.06 (s, 2H), 3.13 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 193.8, 161.9, 158.7, 151.8, 148.9, 146.7, 140.9, 136.2, 135.2, 131.5, 130.9, 130.0, 128.7, 128.2, 127.4, 127.1, 124.3, 123.6, 117.3, 114.4, 170.0, 40.3. IR (neat): ν/ cm^{-1} = 2922, 1592, 1507, 1339, 1167, 1011, 839, 749, 696. HRMS: m/z $[M]^+$ calcd for $C_{31}H_{26}N_2O_4$: 489.1809, found: 489.1817.

Methyl 4-(3-([1,1'-biphenyl]-4-carbonyl)-1-methyl-1*H*-benzo[*b*]azepin-4-yl)benzoate (4a.7bf, Table 4a.2):



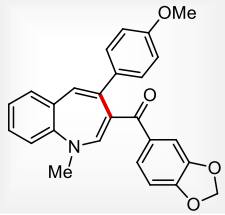
The title compound was prepared following **GP-7** using **4.18bf** (94 mg, 0.2 mmol); obtained as yellow solid (89.3 mg, 95%). M.P. = 183 - 184°C. R_f value = 0.61 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.85 (d, J = 8.2 Hz, 2H), 7.70 (d, J = 8.1 Hz, 2H), 7.56 (d, J = 7.1 Hz, 2H), 7.51 (d, J = 8.3 Hz, 2H), 7.46 – 7.42 (m, 2H), 7.39 – 7.35 (m, 1H), 7.30 (d, J = 8.2 Hz, 2H), 7.23 – 7.18 (m, 1H), 7.06 – 7.00 (m, 2H), 6.94 (s, 1H), 6.76 (t, J = 4.3 Hz, 2H), 3.85 (s, 3H), 3.13 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 194.9, 166.8, 158.9, 151.7, 146.7, 144.4, 141.7, 140.0, 137.5, 134.1, 131.9, 130.7, 129.6, 129.2, 128.9, 128.8, 128.0, 127.1, 126.8, 126.3, 124.9, 124.3, 117.1, 52.0, 40.3. IR (neat): ν/ cm^{-1} = 2950, 1714, 1601, 1487, 1266, 1101, 892, 745, 693. HRMS: m/z $[M+H]^+$ calcd for $C_{32}H_{26}NO_3$: 472.1907, found: 472.1906.

(3,4-Dichlorophenyl)(1,7-dimethyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)methanone (4a.7bg, Table 4a.2):



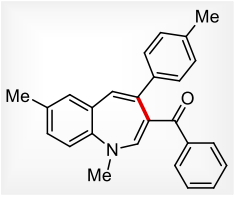
The title compound was prepared following **GP-7** using **4.18bg** (84 mg, 0.2 mmol); obtained as yellow solid (79.8 mg, 95%). M.P. = 167 - 168°C. R_f value = 0.61 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 7.61 (d, J = 1.9 Hz, 1H), 7.40 (dd, J = 8.3, 2.0 Hz, 1H), 7.26 (d, J = 8.3 Hz, 1H), 7.15 – 7.05 (m, 5H), 7.03 (s, 1H), 6.98 (dd, J = 8.3, 1.7 Hz, 1H), 6.82 (d, J = 1.9 Hz, 1H), 6.65 (d, J = 8.3 Hz, 1H), 6.55 (s, 1H), 3.14 (s, 3H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 193.1, 160.1, 149.1, 142.6, 142.1, 139.1, 135.4, 134.1, 132.2, 132.18, 132.1, 131.2, 130.3, 129.9, 129.6, 128.3, 127.44, 127.4, 126.5, 123.2, 117.1, 40.6, 20.4. IR (neat): ν/ cm^{-1} = 2919, 1581, 1494, 1375, 1278, 1102, 1029, 755, 696. HRMS: m/z [M+H]$^+$ calcd for $C_{25}H_{20}NOCl_2$: 420.0916, found: 420.0925.

Benzo[*d*][1,3]dioxol-5-yl(4-(4-methoxyphenyl)-1-methyl-1*H*-benzo[*b*]azepin-3-yl)methanone (4a.7bh, Table 4a.2):



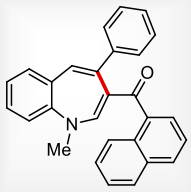
The title compound was prepared following **GP-7** using **4.18bh** (82 mg, 0.2 mmol); obtained as yellow solid (76.3 mg, 93%). M.P. = 158 - 159°C. R_f value = 0.27 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 7.33 (dd, J = 8.1, 1.7 Hz, 1H), 7.21 – 7.15 (m, 1H), 7.11 (d, J = 8.7 Hz, 3H), 7.04 – 6.97 (m, 2H), 6.76 (d, J = 8.5 Hz, 2H), 6.68 (t, J = 9.1 Hz, 4H), 5.94 (s, 2H), 3.72 (s, 3H), 3.10 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 194.1, 158.9, 156.2, 152.2, 150.7, 147.4, 142.3, 134.2, 133.3, 132.5, 131.2, 130.1, 128.9, 127.7, 125.9, 124.7, 124.0, 116.8, 113.6, 108.7, 107.5, 101.5, 55.2, 40.1. IR (neat): ν/ cm^{-1} = 2900, 1602, 1507, 1436, 1238, 1032, 826, 745. HRMS: m/z [M+H]$^+$ calcd for $C_{26}H_{22}NO_4$: 412.1543, found: 412.1543.

(1,7-Dimethyl-4-(*p*-tolyl)-1*H*-benzo[*b*]azepin-3-yl)(phenyl)methanone (4a.7bi, Table 4a.2):



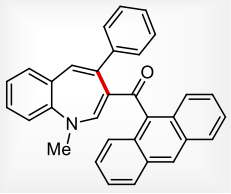
The title compound was prepared following **GP-7** using **4.18bi** (73 mg, 0.2 mmol); obtained as yellow solid (67.9 mg, 93%). M.P. = 161 - 162°C. R_f value = 0.62 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 7.61 (d, J = 7.0 Hz, 2H), 7.36 (t, J = 7.4 Hz, 1H), 7.27 (s, 1H), 7.24 (d, J = 7.3 Hz, 1H), 7.06 (d, J = 8.1 Hz, 2H), 6.98 – 6.92 (m, 3H), 6.86 (s, 1H), 6.83 (d, J = 1.9 Hz, 1H), 6.64 (d, J = 5.9 Hz, 2H), 3.09 (s, 3H), 2.27 (s, 3H), 2.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 195.8, 158.2, 149.3, 142.5, 139.2, 136.9, 133.5, 132.3, 131.9, 131.5, 131.0, 130.8, 129.4, 128.9, 128.6, 127.9, 126.4, 125.3, 116.7, 40.4, 21.1, 20.4. IR (neat): ν/ cm^{-1} = 2921, 1731, 1597, 1447, 1366, 1234, 1176, 794, 695. HRMS: m/z [M+H]$^+$ calcd for $C_{26}H_{24}NO$: 366.1852, found: 366.1855.

(1-Methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)(naphthalen-1-yl)methanone (4a.7bj, Table 4a.2):



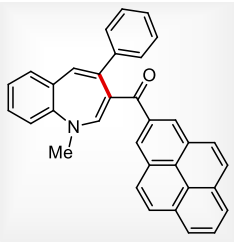
The title compound was prepared following **GP-7** using **4.18bj** (77.5 mg, 0.2 mmol); obtained as yellow solid (70.5 mg, 91%). M.P. = 189 - 190°C. R_f value = 0.74 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.21 (s, 1H), 7.85 (d, J = 7.4 Hz, 1H), 7.78 (d, J = 7.5 Hz, 1H), 7.73 - 7.66 (m, 2H), 7.55 – 7.47 (m, 2H), 7.22 (d, J = 6.9 Hz, 2H), 7.12 – 7.04 (m, 6H), 6.93 (s, 1H), 6.79 – 6.75 (m, 2H), 3.13 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 195.6, 157.9, 152.0, 142.7, 141.9, 136.3, 134.8, 132.6, 132.4, 132.3, 130.4, 129.6, 129.2, 129.1, 128.2, 127.9, 127.7, 127.3, 126.4, 125.7, 125.1, 124.2, 117.0, 40.3. IR (neat): ν/ cm^{-1} = 2923, 1621, 1464, 1279, 1184, 1099, 899, 752, 696. HRMS: m/z $[M+H]^+$ calcd for $C_{28}H_{22}NO$: 388.1696, found: 388.1699.

Anthracen-9-yl(1-methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)methanone (4a.7bk, Table 4a.2):



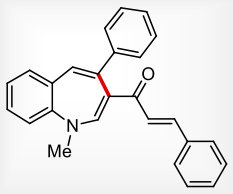
The title compound was prepared following **GP-7** using **4.18bk** (87.5 mg, 0.2 mmol); obtained as yellow solid (78.8 mg, 90%). M.P. = 190 - 191°C. R_f value = 0.47 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.30 (s, 1H), 8.02 (d, J = 8.6 Hz, 3H), 7.88 (d, J = 8.0 Hz, 2H), 7.41 - 7.33 (m, 6H), 7.16 (t, J = 7.4 Hz, 1H), 7.04 (t, J = 7.4 Hz, 2H), 6.94 (d, J = 7.1 Hz, 3H), 6.73 (d, J = 6.0 Hz, 1H), 6.38 (s, 1H), 3.01 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 196.0, 151.3, 143.6, 135.0, 134.1, 133.0, 132.2, 130.9, 130.5, 128.6, 128.5, 128.3, 128.2, 128.1, 127.6, 127.5, 127.2, 127.0, 126.2, 126.0, 125.8, 125.7, 125.1, 124.6, 117.2, 40.5. IR (neat): ν/ cm^{-1} = 2917, 1592, 1447, 1349, 1232, 1101, 880, 734, 696. HRMS: m/z $[M+H]^+$ calcd for $C_{32}H_{24}NO$: 438.1852, found: 438.1857.

(1-Methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)(pyren-2-yl)methanone (4a.7bl, Table 4a.2):



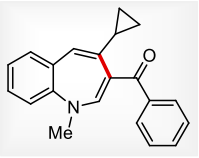
The title compound was prepared following **GP-7** using **4.18bl** (92 mg, 0.2 mmol); obtained as yellow solid (86.5 mg, 94%). M.P. = 193 - 194°C. R_f value = 0.64 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.45 (dd, J = 9.2, 5.1 Hz, 1H), 8.17 (d, J = 7.5 Hz, 2H), 8.11 - 7.98 (m, 6H), 7.19 (d, J = 5.9 Hz, 3H), 7.09 (s, 1H), 7.07 – 7.00 (m, 4H), 6.91 (t, J = 7.5 Hz, 1H), 6.74 (d, J = 8.0 Hz, 1H), 6.62 (s, 1H), 3.08 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 196.5, 160.9, 151.6, 142.9, 142.3, 134.3, 132.8, 132.6, 132.4, 131.0, 130.6, 130.5, 129.2, 129.0, 128.6, 128.1, 128.0, 127.1, 126.9, 126.1, 125.9, 125.6, 125.57, 125.1, 124.6, 124.3, 124.2, 123.7, 117.1, 40.3. IR (neat): ν/ cm^{-1} = 2918, 1731, 1594, 1449, 1237, 1098, 906, 802, 695. HRMS: m/z $[M+H]^+$ calcd for $C_{34}H_{24}NO$: 462.1852, found: 462.1857.

(*E*)-1-(1-methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)-3-phenylprop-2-en-1-one (4a.7bm, Table 4a.2):



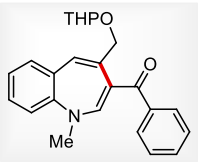
The title compound was prepared following **GP-7** using **4.18bm** (73 mg, 0.2 mmol); obtained as yellow solid (68.6 mg, 94%). M.P. = 161 - 162°C. R_f value = 0.53 (25% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.41 (d, J = 15.7 Hz, 1H), 7.36 (d, J = 7.1 Hz, 2H), 7.30 - 7.23 (m, 7H), 7.21 (s, 1H), 7.20 – 7.14 (m, 2H), 7.02 – 6.97 (m, 2H), 6.79 (s, 1H), 6.76 (d, J = 8.2 Hz, 1H), 6.58 (d, J = 15.7 Hz, 1H), 3.13 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 190.1, 158.5, 152.1, 142.3, 141.9, 141.0, 135.1, 132.8, 132.3, 130.2, 129.7, 128.9, 128.6, 128.0, 127.7, 126.4, 125.7, 125.1, 124.1, 117.0, 40.2. IR (neat): ν/ cm^{-1} = 3060, 1641, 1583, 1450, 1328, 1230, 1123, 1036, 735, 693. HRMS: m/z $[M+H]^+$ calcd for $C_{26}H_{22}NO$: 364.1696, found: 364.1698.

(4-Cyclopropyl-1-methyl-1*H*-benzo[*b*]azepin-3-yl)(phenyl)methanone (4a.7bn, Table 4a.2):



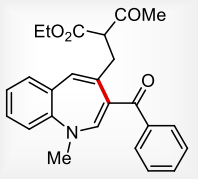
The title compound was prepared following **GP-7** using **4.18bn** (60 mg, 0.2 mmol); obtained as yellow gummy liquid (53.4 mg, 89%). R_f value = 0.75 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 7.77 (d, J = 7.4 Hz, 2H), 7.50 (t, J = 7.5 Hz, 1H), 7.41 (t, J = 7.5 Hz, 1H), 7.10 (t, J = 7.1 Hz, 1H), 6.93 (t, J = 7.4 Hz, 1H), 6.86 (d, J = 7.0 Hz, 1H), 6.66 (d, J = 8.1 Hz, 1H), 6.50 (s, 1H), 6.29 (s, 1H), 3.00 (s, 3H), 1.42 – 1.34 (m, 1H), 0.59 – 0.55 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 196.0, 155.8, 150.8, 144.3, 139.5, 134.1, 133.3, 132.2, 131.9, 129.9, 129.0, 128.8, 128.5, 128.3, 127.1, 123.9, 116.6, 40.3, 17.0, 7.4. IR (neat): ν/ cm^{-1} = 2921, 1669, 1595, 1447, 1242, 1020, 474, 696. HRMS: m/z $[M]^+$ calcd for $C_{21}H_{19}NO$: 301.1467, found: 301.1456.

(1-Methyl-4-(((tetrahydro-2*H*-pyran-2-yl)oxy)methyl)-1*H*-benzo[*b*]azepin-3-yl)(phenyl)-methanone (4a.7bo, Table 4a.2):



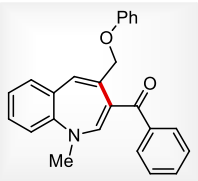
The title compound was prepared following **GP-7** using **4.18bo** (75 mg, 0.2 mmol); obtained as yellow gummy liquid (63.0 mg, 84%). R_f value = 0.67 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.70 (d, J = 6.9 Hz, 2H), 7.49 (t, J = 7.4 Hz, 1H), 7.40 (t, J = 7.7 Hz, 2H), 7.11 (t, J = 8.1 Hz, 1H), 6.92 (td, J = 7.5, 1.0 Hz, 1H), 6.84 (dd, J = 7.6, 1.6 Hz, 1H), 6.64 (d, J = 8.1 Hz, 1H), 6.53 (s, 1H), 6.42 (s, 1H), 4.51 (s, 1H), 4.38 (dd, J = 12.3, 1.2 Hz, 1H), 4.14 (dd, J = 12.3, 1.5 Hz, 1H), 3.80 – 3.74 (m, 1H), 3.47 – 3.42 (m, 1H), 3.00 (s, 3H), 2.04 (s, 2H), 1.68 (s, 1H), 1.52 – 1.46 (m, 2H), 1.41 – 1.36 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 195.8, 157.7, 151.0, 139.1, 131.8, 131.7, 131.65, 130.1, 129.2, 129.1, 128.2, 124.1, 123.9, 116.9, 98.4, 68.9, 61.9, 40.6, 30.3, 25.4, 23.5, 19.1. IR (neat): ν/ cm^{-1} = 2922, 1599, 1436, 1254, 1033, 927, 748, 696. HRMS: m/z $[M+Na]^+$ calcd for $C_{24}H_{25}NO_3Na$: 398.1727, found: 398.1729.

Ethyl 2-((3-benzoyl-1-methyl-1*H*-benzo[*b*]azepin-4-yl)methyl)-3-oxobutanoate (4a.7bp, Table 4a.2):



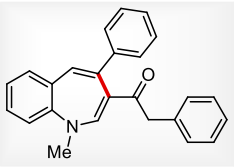
The title compound was prepared following **GP-7** using **4.18bp** (81 mg, 0.2 mmol); obtained as yellow gummy liquid (71.3 mg, 88%). R_f value = 0.47 (30% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 7.73 (d, J = 7.0 Hz, 2H), 7.53 (t, J = 7.4 Hz, 1H), 7.45 (t, J = 7.7 Hz, 2H), 7.16 – 7.11 (m, 1H), 6.95 (t, J = 7.4 Hz, 1H), 6.87 (dd, J = 7.6, 1.4 Hz, 1H), 6.67 (d, J = 8.1 Hz, 1H), 6.63 (s, 1H), 4.23 (q, J = 7.0 Hz, 2H), 3.63 (dd, J = 8.3, 7.3 Hz, 1H), 3.00 (s, 3H), 2.92 (dd, J = 14.4, 7.1 Hz, 1H), 2.81 (dd, J = 14.4, 8.5 Hz, 1H), 2.28 (s, 3H), 1.30 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 202.9, 195.5, 169.2, 160.1, 150.9, 139.1, 138.7, 133.6, 131.8, 131.5, 130.2, 128.9, 128.5, 128.2, 124.4, 124.1, 116.7, 61.4, 58.9, 40.3, 34.8, 29.3, 14.2. IR (neat): ν/ cm^{-1} = 2922, 1612, 1573, 1491, 1368, 1220, 1082, 751, 698. HRMS: m/z $[M]^+$ calcd for $C_{25}H_{26}NO_4$: 404.1856, found: 404.1866.

(1-Methyl-4-(phenoxymethyl)-1*H*-benzo[*b*]azepin-3-yl)(phenyl)methanone (4a.7bq, Table 4a.2):



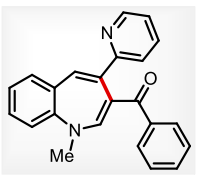
The title compound was prepared following **GP-7** using **4.18bq** (73.5 mg, 0.2 mmol); obtained as yellow solid (63.2 mg, 86%). M.P. = 141 - 142°C. R_f value = 0.56 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.59 (d, J = 6.5 Hz, 2H), 7.40 (t, J = 7.0 Hz, 1H), 7.33 – 7.29 (m, 2H), 7.18 – 7.11 (m, 2H), 7.07 – 7.04 (m, 1H), 6.88 – 6.77 (m, 5H), 6.58 (s, 2H), 6.43 (s, 1H), 4.62 (s, 2H), 2.92 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 195.7, 158.8, 158.5, 151.0, 139.2, 138.2, 132.3, 131.6, 131.59, 130.2, 129.3, 129.27, 129.1, 128.3, 124.2, 123.5, 120.8, 117.1, 114.9, 69.3, 40.6. IR (neat): ν/ cm^{-1} = 2920, 1635, 1595, 1446, 1287, 1235, 1015, 747, 696. HRMS: m/z $[M+Na]^+$ calcd for $C_{25}H_{21}NO_2Na$: 390.1465, found: 390.1470.

1-(1-Methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)-2-phenylethanone (4a.7br, Table 4a.2):



The title compound was prepared following **GP-7** using **4.18br** (70 mg, 0.2 mmol); obtained as yellow solid (60.9 mg, 87%). M.P. = 143 - 144°C. R_f value = 0.70 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.37 – 7.31 (m, 5H), 7.21 -7.16 (m, 4H), 7.06 (s, 1H), 7.02 – 7.00 (m, 2H), 6.92 (d, J = 7.4 Hz, 2H), 6.80 (s, 1H), 6.78 (d, J = 8.2 Hz, 1H), 3.44 (s, 2H), 3.10 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 198.8, 157.6, 152.3, 142.1, 141.6, 134.9, 133.2, 132.1, 130.2, 129.4, 128.9, 128.7, 128.2, 127.8, 126.5, 126.3, 125.6, 124.0, 116.9, 47.2, 40.0. IR (neat): ν/ cm^{-1} = 2919, 1594, 1465, 1277, 1196, 1028, 749, 696. HRMS: m/z $[M+H]^+$ calcd for $C_{25}H_{22}NO$: 352.1696, found: 352.1700.

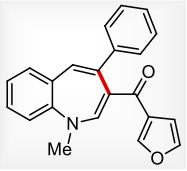
(1-Methyl-4-(pyridin-2-yl)-1*H*-benzo[*b*]azepin-3-yl)(phenyl)methanone (4a.7bs, Table 4a.2):



The title compound was prepared following **GP-7** using **4.18bs** (68 mg, 0.2 mmol); obtained as yellow solid (62.6 mg, 92%). M.P. = 141 - 142°C. R_f value = 0.36 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.43 (s,

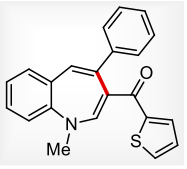
1H), 8.33 (d, *J* = 4.0 Hz, 1H), 7.58 (d, *J* = 7.0 Hz, 2H), 7.47 (dt, *J* = 7.9, 1.9 Hz, 1H), 7.37 (t, *J* = 7.4 Hz, 1H), 7.27 (t, *J* = 7.3 Hz, 2H), 7.21 -7.16 (m, 1H), 7.06 (dd, *J* = 7.8, 4.8 Hz, 1H), 7.00 (d, *J* = 3.8 Hz, 2H), 6.91 (s, 1H), 6.73 (d, *J* = 8.2 Hz, 1H), 6.65 (s, 1H), 3.11 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*/ ppm = 195.1, 159.8, 151.6, 148.2, 147.5, 139.5, 138.8, 137.7, 134.1, 133.6, 131.8, 131.7, 130.6, 129.5, 128.4, 128.2, 124.4, 124.2, 122.9, 117.2, 40.3. IR (neat): ν/ cm^{-1} = 2921, 1632, 1443, 1276, 1123, 1020, 763, 696. HRMS: *m/z* $[M+H]^+$ calcd for $C_{23}H_{19}N_2O$: 339.1492, found: 339.1493.

Furan-3-yl(1-methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)methanone (4a.7bt, Table 4a.2):



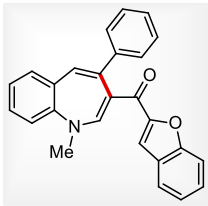
The title compound was prepared following **GP-7** using **4.18bt** (65.5 mg, 0.2 mmol); obtained as yellow solid (59.0 mg, 90%). M.P. = 151 - 152°C. R_f value = 0.74 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) *δ*/ ppm = 7.38 (dd, *J* = 1.6, 0.6 Hz, 1H), 7.29 – 7.26 (m, 2H), 7.22 – 7.11 (m, 4H), 7.05 – 6.98 (m, 4H), 6.76 (d, *J* = 7.6 Hz, 2H), 6.30 (dd, *J* = 3.5, 1.7 Hz, 1H), 3.13 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*/ ppm = 182.1, 157.3, 152.6, 152.1, 145.6, 142.1, 141.6, 132.5, 132.3, 130.2, 129.1, 128.3, 127.4, 126.3, 124.7, 124.1, 118.1, 117.0, 111.7, 40.1. IR (neat): ν/ cm^{-1} = 2927, 1619, 1462, 1310, 1205, 1033, 840, 758, 695. HRMS: *m/z* $[M+H]^+$ calcd for $C_{22}H_{18}NO_2$: 328.1332, found: 328.1333.

(1-Methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)(thiophen-2-yl)methanone (4a.7bu, Table 4a.2):



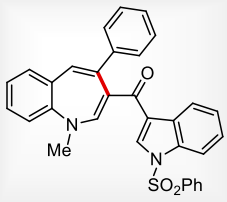
The title compound was prepared following **GP-7** using **4.18bu** (69 mg, 0.2 mmol); obtained as yellow solid (60.0 mg, 87%). M.P. = 153 - 154°C. R_f value = 0.58 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) *δ*/ ppm = 7.61 (dd, *J* = 3.8, 1.1 Hz, 1H), 7.41 (dd, *J* = 5.0, 1.1 Hz, 1H), 7.27 (d, *J* = 7.3Hz, 2H), 7.22 – 7.16 (m, 3H), 7.16 – 7.10 (m, 1H), 7.07 – 6.99 (m, 2H), 6.93 (dd, *J* = 4.9, 3.8 Hz, 1H), 6.90 (s, 1H), 6.81 (s, 1H), 6.77 (d, *J* = 8.2 Hz, 1H), 3.13 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 187.1, 156.3, 152.2, 144.4, 142.1, 141.5, 132.9, 132.7, 132.5, 132.3, 130.3, 129.2, 128.4, 127.5, 127.4, 126.5, 126.0, 124.0, 117.0, 40.1. IR (neat): ν/ cm^{-1} = 3089, 1603, 1567, 1411, 1297, 1202, 1100, 721, 694. HRMS: *m/z* $[M+H]^+$ calcd for $C_{22}H_{18}NOS$: 344.1104, found: 344.1100.

Benzofuran-2-yl(1-methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)methanone (4a.7bv, Table 4a.2):



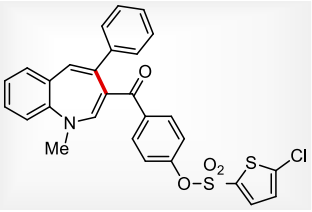
The title compound was prepared following **GP-7** using **4.18bv** (75.5 mg, 0.2 mmol); obtained as yellow solid (69.5 mg, 92%). M.P. = 152 - 153°C. R_f value = 0.61 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) *δ*/ ppm = 7.58 (d, *J* = 7.8 Hz, 1H), 7.48 (d, *J* = 8.9 Hz, 1H), 7.38 (t, *J* = 8.4 Hz, 1H), 7.34 – 7.29 (m, 3H), 7.23 (d, *J* = 7.9 Hz, 1H), 7.22 – 7.17 (m, 2H), 7.15 (t, *J* = 4.2 Hz, 2H), 7.11 – 7.00 (m, 3H), 6.77 (d, *J* = 9.0 Hz, 2H), 3.17 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*/ ppm = 183.5, 158.4, 155.2, 152.9, 151.9, 142.1, 141.7, 132.7, 132.4, 130.4, 129.1, 128.3, 128.2, 127.5, 127.0, 126.3, 124.6, 124.3, 123.5, 122.8, 117.1, 113.7, 112.2, 40.3. IR (neat): ν/ cm^{-1} = 2923, 1611, 1545, 1491, 1279, 1167, 1100, 742, 696. HRMS: *m/z* $[M+H]^+$ calcd for $C_{26}H_{20}NO_2$: 378.1489, found: 378.1494.

(1-Methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)(1-(phenylsulfonyl)-1*H*-indol-3-yl)methanone (4a.7bw, Table 4a.2):



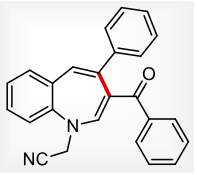
The title compound was prepared following **GP-7** using **4.18bw** (103 mg, 0.2 mmol); obtained as yellow solid (93.7 mg, 91%). M.P. = 151 - 152°C. R_f value = 0.58 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.04 (s, 1H), 8.03 (d, J = 7.7 Hz, 1H), 7.81 – 7.78 (m, 3H), 7.58 (t, J = 7.5 Hz, 1H), 7.45 (t, J = 7.9 Hz, 2H), 7.25 – 7.19 (m, 5H), 7.11 – 7.01 (m, 5H), 6.94 (s, 1H), 6.83 (s, 1H), 6.79 (d, J = 8.2 Hz, 1H), 3.14 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 189.3, 157.1, 152.3, 142.1, 141.7, 137.7, 134.5, 134.4, 133.2, 132.2, 131.4, 130.5, 129.5, 129.3, 128.4, 128.1, 127.4, 127.0, 126.5, 126.3, 125.4, 124.3, 124.25, 122.7, 121.8, 117.0, 112.9, 40.2. IR (neat): ν/ cm^{-1} = 2933, 1536, 1445, 1373, 1283, 1170, 1088, 960, 745, 683. HRMS: m/z [M+H]$^+$ calcd for $C_{32}H_{25}N_2O_3S$: 517.1580, found: 517.1587.

4-(1-Methyl-4-phenyl-1*H*-benzo[*b*]azepine-3-carbonyl)phenyl 5-chlorothiophene-2-sulfonate (4a.7bx, Table 4a.2):



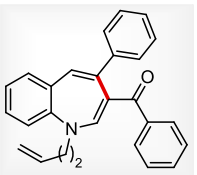
The title compound was prepared following **GP-7** using **4.18bx** (107 mg, 0.2 mmol); obtained as yellow solid (94.2 mg, 88%). M.P. = 150 - 151°C. R_f value = 0.57 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 7.55 (d, J = 6.9 Hz, 2H), 7.24 – 7.18 (m, 2H), 7.15 – 7.06 (m, 5H), 7.03 – 6.98 (m, 3H), 6.92 – 6.87 (m, 3H), 6.77 (d, J = 8.3 Hz, 1H), 6.62 (s, 1H), 3.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 194.3, 159.3, 152.0, 151.3, 142.7, 141.9, 140.5, 138.5, 135.2, 132.4, 132.3, 131.9, 130.5, 130.1, 129.3, 128.3, 127.4, 127.0, 126.6, 124.4, 124.2, 121.7, 117.2, 40.4. IR (neat): ν/ cm^{-1} = 2923, 1637, 1489, 1448, 1276, 1132, 1022, 893, 753, 694. HRMS: m/z [M+H]$^+$ calcd for $C_{28}H_{21}NO_4S_2Cl$: 534.0595, found: 534.0603.

2-(3-Benzoyl-4-phenyl-1*H*-benzo[*b*]azepin-1-yl)acetonitrile (4a.7by, Table 4a.2):



The title compound was prepared following **GP-7** using **4.18by** (72.5 mg, 0.2 mmol); obtained as yellow solid (58.0 mg, 80%). M.P. = 147 - 148°C. R_f value = 0.43 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.72 (d, J = 7.1 Hz, 2H), 7.70 (d, J = 7.8 Hz, 1H), 7.60 (s, 1H), 7.55 (d, J = 7.5 Hz, 1H), 7.50 – 7.46 (m, 4H), 7.46 – 7.40 (m, 3H), 7.39 – 7.34 (m, 1H), 7.29 (t, J = 7.0 Hz, 1H), 7.20 (d, J = 7.6 Hz, 1H), 6.84 (s, 1H), 3.53 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 194.0, 140.9, 140.7, 137.1, 136.6, 132.9, 131.6, 129.6, 129.4, 129.1, 128.9, 128.7, 128.69, 126.1, 123.8, 122.4, 121.7, 115.9, 110.6, 107.0, 16.9. IR (neat): ν/ cm^{-1} = 2921, 1630, 1512, 1338, 1227, 1055, 758, 720. HRMS: m/z [M+H]$^+$ calcd for $C_{25}H_{19}N_2O$: 363.1492, found: 363.1496.

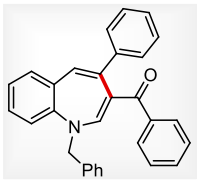
(1-(But-3-en-1-yl)-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)(phenyl)methanone (4a.7bz, Table 4a.2):



The title compound was prepared following **GP-7** using **4.18bz** (75.5 mg, 0.2 mmol); obtained as yellow solid (63.4 mg, 84%). M.P. = 145 - 146°C. R_f value = 0.47 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 7.61 (d, J

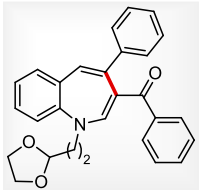
= 7.0 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.28 (t, *J* = 7.7 Hz, 2H), 7.23 – 7.11 (m, 6H), 7.09 – 7.01 (m, 2H), 6.94 (s, 1H), 6.81 (s, 1H), 6.75 (d, *J* = 8.1 Hz, 1H), 5.96 (ddt, *J* = 13.5, 10.3, 6.7 Hz, 1H), 5.23 (dd, *J* = 17.1, 1.7 Hz, 1H), 5.13 (d, *J* = 10.2 Hz, 1H), 3.47 (t, *J* = 7.3 Hz, 2H), 2.56 (q, *J* = 7.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*/ ppm = 195.7, 157.1, 151.2, 142.7, 142.1, 139.2, 134.8, 133.3, 132.4, 131.5, 130.2, 129.0, 128.6, 128.2, 128.0, 127.3, 126.8, 126.5, 124.2, 118.5, 117.2, 52.0, 34.2. IR (neat): ν/ cm^{-1} = 2925, 1646, 1542, 1489, 1335, 1275, 1043, 761, 699. HRMS: *m/z* $[M+H]^+$ calcd for $C_{27}H_{24}NO$: 378.1852, found: 378.1852.

(1-Benzyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)(phenyl)methanone (4a.7ca, Table 4a.2):



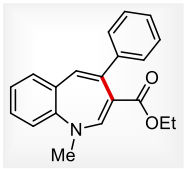
The title compound was prepared following **GP-7** using **4.18ca** (83 mg, 0.2 mmol); obtained as yellow solid (74.7 mg, 90%). M.P. = 150 - 151°C. R_f value = 0.74 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 7.60 (d, *J* = 6.7 Hz, 2H), 7.54 – 7.47 (m, 3H), 7.37 (t, *J* = 7.0 Hz, 1H), 7.27 – 7.23 (m, 8H), 7.17 (d, *J* = 6.5 Hz, 3H), 7.09 (d, *J* = 7.1 Hz, 1H), 6.99 (s, 1H), 6.87 (d, *J* = 7.8 Hz, 1H), 6.62 (s, 1H), 4.59 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 195.3, 157.3, 151.3, 142.1, 142.0, 138.4, 137.5, 133.6, 132.6, 131.6, 130.4, 129.0, 128.4, 128.0, 127.9, 127.7, 127.3, 126.2, 124.1, 117.9, 56.2. IR (neat): ν/ cm^{-1} = 2920, 1641, 1447, 1280, 1174, 1023, 754, 692. HRMS: *m/z* $[M+H]^+$ calcd for $C_{30}H_{24}NO$: 414.1852, found: 414.1852.

(1-(2-(1,3-Dioxolan-2-yl)ethyl)-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)(phenyl)methanone (4a.7cb, Table 4a.2):



The title compound was prepared following **GP-7** using **4.18cb** (85 mg, 0.2 mmol); obtained as yellow solid (75.7 mg, 89%). M.P. = 141 - 142°C. R_f value = 0.55 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 7.62 (d, *J* = 8.1 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 2H), 7.23 (d, *J* = 8.1 Hz, 2H), 7.21 – 7.16 (m, 3H), 7.13 (t, *J* = 7.4 Hz, 1H), 7.08 (d, *J* = 7.4 Hz, 1H), 7.03 (t, *J* = 7.4 Hz, 1H), 6.92 (s, 1H), 6.83 (s, 1H), 6.78 (d, *J* = 8.1 Hz, 1H), 5.14 (t, *J* = 4.6 Hz, 1H), 4.02 – 3.98 (m, 2H), 3.89 – 3.85 (m, 2H), 3.57 (t, *J* = 7.3 Hz, 2H), 2.19 – 2.15 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 195.6, 157.0, 150.9, 142.4, 141.9, 139.0, 133.0, 132.6, 131.5, 130.1, 129.0, 128.6, 128.2, 128.0, 127.2, 126.9, 126.4, 124.1, 118.2, 102.3, 65.0, 47.4, 33.7. IR (neat): ν/ cm^{-1} = 2878, 1638, 1489, 1275, 1133, 1022, 750, 695. HRMS: *m/z* $[M+H]^+$ calcd for $C_{28}H_{26}NO_3$: 424.1907, found: 424.1913.

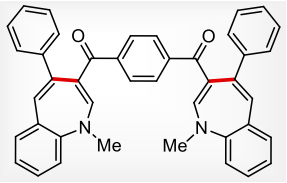
Ethyl 1-methyl-4-phenyl-1*H*-benzo[*b*]azepine-3-carboxylate (4a.7cc, Table 4a.2):



The title compound was prepared following **GP-7** using **4.18cc** (61 mg, 0.2 mmol); obtained as yellow solid (50.6 mg, 83%). M.P. = 139 - 140°C. R_f value = 0.91 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 7.32 – 7.27 (m, 4H), 7.26 - 7.22 (m, 1H), 7.19 – 7.14 (m, 2H), 6.98 (d, *J* = 4.2 Hz, 2H), 6.76 (d, *J* = 8.1 Hz, 1H), 6.67 (s, 1H), 3.84 (q, *J* = 7.1 Hz, 2H), 3.11 (s, 3H), 0.77 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 167.5, 158.1, 152.3, 142.9, 141.7, 132.4, 132.3, 130.3, 128.9, 128.1, 127.1, 126.0, 124.0, 117.0, 116.9, 60.0, 40.0, 13.6. IR (neat): ν/ cm^{-1} = 2976,

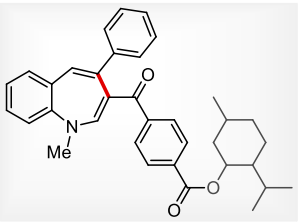
1701, 1468, 1261, 1193, 1090, 751, 698. HRMS: *m/z* $[M+H]^+$ calcd for $C_{20}H_{20}NO_2$: 306.1489, found: 306.1494.

1,4-Phenylenebis((1-methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)methanone) (4a.7cd, Table 4a.2):



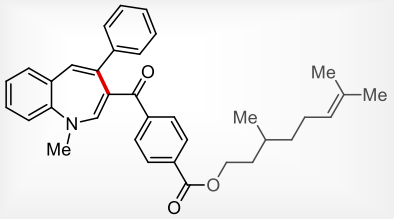
The title compound was prepared following **GP-7** using **4.18ce** (119 mg, 0.2 mmol); obtained as yellow solid (105.9 mg, 89%). M.P. = 156 - 157°C. R_f value = 0.69 (60% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.44 (s, 4H), 7.21 – 7.16 (m, 3H), 7.10 (s, 9H), 7.00 (d, *J* = 6.4 Hz, 4H), 6.81 (s, 2H), 6.75 (d, *J* = 8.2 Hz, 2H), 6.63 (s, 2H), 3.11 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 195.1, 159.0, 151.7, 142.4, 141.9, 141.4, 132.6, 132.4, 130.5, 129.2, 128.2, 128.1, 127.4, 126.5, 125.1, 124.3, 117.1, 40.4. IR (neat): ν/ cm^{-1} = 2918, 1633, 1523, 1487, 1338, 1276, 1023, 760, 698. HRMS: *m/z* $[M+H]^+$ calcd for $C_{42}H_{33}N_2O_2$: 597.2537, found: 597.2549.

2-Isopropyl-5-methylcyclohexyl 4-(1-methyl-4-phenyl-1*H*-benzo[*b*]azepine-3-carbonyl)-benzoate (4a.7ce, Table 4a.2):



The title compound was prepared following **GP-7** using **4.18cf** (104 mg, 0.2 mmol); obtained as yellow solid (96.7 mg, 93%). M.P. = 169 - 170°C. R_f value = 0.53 (10% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.90 (d, *J* = 8.0 Hz, 2H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.20 – 7.16 (m, 1H), 7.15 – 7.08 (m, 5H), 7.01 (d, *J* = 4.4 Hz, 2H), 6.93 (s, 1H), 3.13 (s, 3H), 2.11 (d, *J* = 12.0 Hz, 1H), 1.93 – 1.89 (m, 1H), 1.73 (d, *J* = 11.4 Hz, 2H), 1.57 – 1.52 (m, 2H), 1.26 (d, *J* = 4.2 Hz, 1H), 1.17 - 1.05 (m, 2H), 0.92 (d, *J* = 7.2 Hz, 6H), 0.79 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 194.9, 165.4, 159.1, 151.7, 142.8, 142.5, 141.8, 133.0, 132.6, 132.3, 130.5, 129.2, 128.21, 128.2, 127.4, 126.5, 124.9, 124.3, 117.1, 75.2, 47.2, 40.9, 40.3, 34.3, 31.4, 26.6, 23.7, 22.0, 20.7, 16.6. IR (neat): ν/ cm^{-1} = 2921, 1709, 1451, 1265, 1100, 1016, 733, 696. HRMS: *m/z* $[M+H]^+$ calcd for $C_{35}H_{38}NO_3$: 520.2846, found: 520.2856.

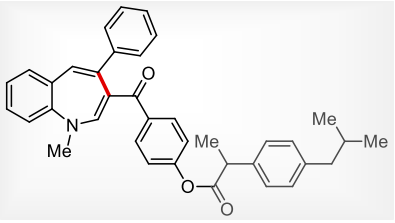
3,7-Dimethyloct-6-en-1-yl-4-(1-methyl-4-phenyl-1*H*-benzo[*b*]azepine-3-carbonyl) benzoate (4a.7cf, Table 4a.2):



The title compound was prepared following **GP-7** using **4.18cg** (104 mg, 0.2 mmol); obtained as yellow solid (93.6 mg, 90%). M.P. = 173 - 174°C. R_f value = 0.61 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.88 (d, *J* = 8.4 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.21 – 7.17 (m, 1H), 7.12 – 7.05 (m, 5H), 7.04 – 7.00 (m, 2H), 6.95 (s, 1H), 6.76 (d, *J* = 8.2 Hz, 1H), 6.64 (s, 1H), 5.09 (t, *J* = 7.1 Hz, 1H), 4.38 – 4.28 (m, 2H), 3.14 (s, 3H), 2.07 – 1.93 (m, 2H), 1.83 – 1.76 (m, 1H), 1.67 (s, 3H), 1.60 (s, 3H), 1.59 – 1.53 (m, 1H), 1.41 (d, *J* = 15.5 Hz, 1H), 0.96 (d, *J* = 6.5 Hz, 3H), 0.91 – 0.83 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 195.0, 166.0, 159.2, 151.9, 143.0, 142.6, 141.9, 132.7, 132.5, 131.5, 130.5, 129.2, 128.3, 128.2, 127.4, 126.6, 124.8,

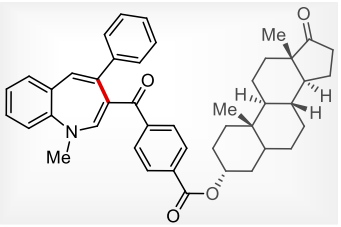
124.6, 124.4, 117.2, 63.8, 40.4, 37.0, 35.5, 29.7, 29.6, 25.7, 25.4, 19.6, 17.7. IR (neat): ν/ cm^{-1} = 2916, 1716, 1565, 1450, 1265, 1200, 1099, 743, 697. HRMS: *m/z* $[M+H]^+$ calcd for $C_{35}H_{38}NO_3$: 520.2846, found: 520.2855.

4-(1-Methyl-4-phenyl-1*H*-benzo[*b*]azepine-3-carbonyl)phenyl-2-(4-isobutylphenyl) propanoate (4a.7cg, Table 4a.2):



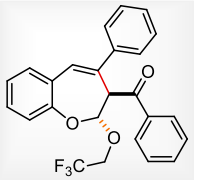
The title compound was prepared following **GP-7** using **4.18ch** (108 mg, 0.2 mmol); obtained as yellow solid (101.5 mg, 94%). M.P. = 171 - 172°C. R_f value = 0.48 (20% EtOAc in hexane). ^1H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 7.61 (d, *J* = 8.6 Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 2H), 7.21 – 7.16 (m, 1H), 7.16 – 7.13 (m, 5H), 7.13 – 7.08 (m, 2H), 7.00 (d, *J* = 4.3 Hz, 2H), 6.90 (d, *J* = 8.6 Hz, 2H), 6.84 (s, 1H), 6.75 (d, *J* = 8.1 Hz, 1H), 6.69 (s, 1H), 3.91 (q, *J* = 7.1 Hz, 1H), 3.11 (s, 3H), 2.48 (d, *J* = 7.2 Hz, 2H), 1.92 – 1.83 (m, 1H), 1.59 (d, *J* = 7.1 Hz, 3H), 0.92 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 190.5, 172.7, 157.8, 153.4, 151.9, 142.6, 141.8, 141.0, 137.0, 136.5, 132.6, 132.4, 130.4, 130.0, 129.6, 129.2, 128.3, 127.4, 127.2, 126.5, 125.5, 124.2, 121.0, 117.0, 45.3, 45.1, 40.3, 30.2, 22.4, 18.5. IR (neat): ν/ cm^{-1} = 2953, 1754, 1597, 1451, 1273, 1199, 1068, 751, 697. HRMS: *m/z* $[M+H]^+$ calcd for $C_{37}H_{36}NO_3$: 542.2690, found: 542.2699.

(3*R*,8*R*,9*S*,10*S*,13*S*,14*S*)-10,13-dimethyl-17-oxohexadecahydro-1*H*-cyclopenta[*a*] phenanthren-3-yl-4-(1-methyl-4-phenyl-1*H*-benzo[*b*]azepine-3-carbonyl)benzoate (4a.7ch, Table 4a.2):



The title compound was prepared following **GP-7** using **4.18ci** (131 mg, 0.2 mmol); obtained as yellow solid (116.6 mg, 89%). M.P. = 173 - 174°C. R_f value = 0.56 (20% EtOAc in hexane). ^1H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 7.87 (d, *J* = 8.4 Hz, 2H), 7.59 (d, *J* = 8.4 Hz, 2H), 7.21 – 7.16 (m, 1H), 7.12 – 7.06 (m, 5H), 7.04 – 6.99 (m, 2H), 6.93 (s, 1H), 6.76 (d, *J* = 8.2 Hz, 1H), 6.64 (s, 1H), 4.94 – 4.87 (m, 1H), 3.13 (s, 3H), 2.43 (dd, *J* = 19.3, 8.7 Hz, 1H), 2.11 – 2.03 (m, 1H), 1.96 – 1.90 (m, 2H), 1.82 – 1.77 (m, 3H), 1.76 – 1.72 (m, 1H), 1.69 – 1.58 (m, 3H), 1.57 – 1.45 (m, 3H), 1.36 – 1.31 (m, 2H), 1.29 – 1.25 (m, 3H), 1.13 – 1.06 (m, 1H), 1.05 – 0.95 (m, 1H), 0.87 (d, *J* = 12.7 Hz, 6H), 0.78 – 0.71 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 195.0, 165.5, 159.1, 151.9, 142.8, 142.6, 141.9, 133.0, 132.5, 132.4, 130.5, 129.2, 129.1, 128.3, 128.2, 127.4, 126.5, 124.9, 124.4, 117.1, 74.5, 54.4, 51.4, 47.8, 44.8, 40.4, 36.8, 35.9, 35.7, 35.1, 34.0, 31.6, 30.9, 28.3, 27.5, 21.8, 20.5, 13.9, 12.3. IR (neat): ν/ cm^{-1} = 2922, 1729, 1614, 1450, 1265, 1101, 1013, 755, 697. HRMS: *m/z* $[M+H]^+$ calcd for $C_{44}H_{48}NO_4$: 654.3578, found: 654.3588.

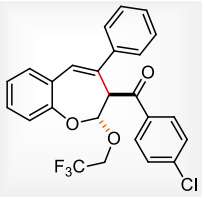
Phenyl((2*S*,3*R*)-4-phenyl-2-(2,2,2-trifluoroethoxy)-2,3-dihydrobenzo[*b*]oxepin-3-yl)methanone (4a.8a, Table 4a.3):



The title compound was prepared following **GP-7** using **4.21a** (65 mg, 0.2 mmol); obtained as off-white solid (68.3 mg, 80%). M.P. = 116 - 117°C. R_f value = 0.62 (10% EtOAc in hexane). ^1H NMR (500 MHz, $CDCl_3$) *δ*/ ppm =

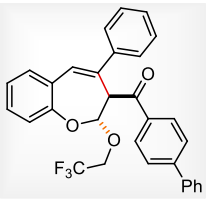
7.80 (d, *J* = 7.2 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 2H), 7.34 – 7.27 (m, 4H), 7.22 – 7.13 (m, 4H), 7.09 (d, *J* = 7.9 Hz, 1H), 6.75 (s, 1H), 5.67 (d, *J* = 6.8 Hz, 1H), 5.33 (dd, *J* = 6.8, 1.0 Hz, 1H), 4.15 (dq, *J* = 12.3, 8.6 Hz, 1H), 3.97 (dq, *J* = 12.3, 8.4 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 196.4, 152.7, 141.9, 137.3, 136.4, 133.1, 132.6, 130.3, 128.9, 128.5, 128.4, 127.7, 127.5, 127.1, 126.9, 124.3, 123.4 (q, *J* = 278 Hz), 120.5, 104.2, 65.7 (q, *J* = 35.4 Hz), 57.8. ^{19}F NMR (470 MHz, $CDCl_3$) *δ*/ ppm = -74.09. IR (neat): ν/ cm^{-1} = 2921, 1672, 1448, 1284, 1129, 1035, 759, 698. HRMS: *m/z* $[M+Na]^+$ calcd for $C_{25}H_{19}O_3F_3Na$: 447.1179, found: 447.1182.

(4-Chlorophenyl)((2*S*,3*R*)-4-phenyl-2-(2,2,2-trifluoroethoxy)-2,3-dihydrobenzo[*b*]oxepin-3-yl)methanone (4a.8b, Table 4a.3):



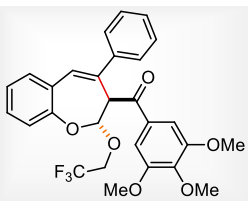
The title compound was prepared following **GP-7** using **4.21b** (72 mg, 0.2 mmol); obtained as yellow solid (75.9 mg, 83%). M.P. = 121 - 122°C. R_f value = 0.52 (10% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) *δ*/ ppm = 7.77 (d, *J* = 8.6 Hz, 2H), 7.41 – 7.34 (m, 3H), 7.33 – 7.27 (m, 3H), 7.26 – 7.17 (m, 4H), 7.14 (d, *J* = 7.9 Hz, 1H), 6.77 (s, 1H), 5.65 (d, *J* = 7.1 Hz, 1H), 5.34 (d, *J* = 7.1 Hz, 1H), 4.23 (dq, *J* = 12.2, 8.6 Hz, 1H), 4.00 (dq, *J* = 12.2, 8.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*/ ppm = 195.6, 152.8, 141.7, 139.6, 136.2, 135.7, 132.6, 130.3, 129.8, 129.0, 128.8, 128.4, 127.6, 127.55, 127.0, 124.5, 123.3 (q, *J* = 278 Hz), 120.4, 104.7, 65.6 (q, *J* = 35.1 Hz), 57.7. ^{19}F NMR (470 MHz, $CDCl_3$) *δ*/ ppm = -74.03. IR (neat): ν/ cm^{-1} = 2917, 1674, 1585, 1490, 1283, 1143, 1039, 760, 699. HRMS: *m/z* $[M+Na]^+$ calcd for $C_{25}H_{18}O_3F_3ClNa$: 481.0789, found: 481.0790.

(4-Chlorophenyl)((2*S*,3*R*)-4-phenyl-2-(2,2,2-trifluoroethoxy)-2,3-dihydrobenzo[*b*]oxepin-3-yl)methanone (4a.8c, Table 4a.3):



The title compound was prepared following **GP-7** using **4.21c** (80 mg, 0.2 mmol); obtained as yellow solid (77.1 mg, 77%). M.P. = 119 - 120°C. R_f value = 0.52 (10% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) *δ*/ ppm = 7.89 (d, *J* = 8.5 Hz, 2H), 7.62 (d, *J* = 8.5 Hz, 4H), 7.47 (t, *J* = 7.1 Hz, 2H), 7.40 (t, *J* = 7.3 Hz, 1H), 7.36 – 7.30 (m, 3H), 7.25 – 7.13 (m, 5H), 7.10 (d, *J* = 8.0 Hz, 1H), 6.78 (s, 1H), 5.70 (d, *J* = 6.8 Hz, 1H), 5.37 (d, *J* = 6.7 Hz, 1H), 4.16 (dq, *J* = 12.3, 8.6 Hz, 1H), 3.99 (dq, *J* = 12.3, 8.4 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 195.9, 152.7, 145.8, 142.0, 139.8, 136.4, 135.9, 132.6, 130.4, 129.1, 129.0, 128.96, 128.4, 128.3, 127.7, 127.5, 127.3, 127.14, 127.1, 124.3, 123.4 (q, *J* = 278 Hz), 120.6, 104.2, 65.7 (q, *J* = 35.1 Hz), 57.8. ^{19}F NMR (470 MHz, $CDCl_3$) *δ*/ ppm = -74.01. IR (neat): ν/ cm^{-1} = 2920, 1540, 1332, 1222, 1092, 815, 733. HRMS: *m/z* $[M+Na]^+$ calcd for $C_{31}H_{23}O_3F_3Na$: 523.1492, found: 523.1492.

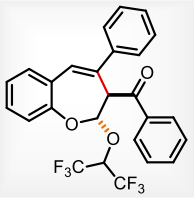
((2*S*,3*R*)-4-phenyl-2-(2,2,2-trifluoroethoxy)-2,3-dihydrobenzo[*b*]oxepin-3-yl)(3,4,5-trimethoxyphenyl)methanone (4a.8d, Table 4a.3):



The title compound was prepared following **GP-7** using **4.21d** (83 mg, 0.2 mmol); obtained as yellow solid (83.5 mg, 81%). M.P. = 120 - 121°C. R_f value = 0.36 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) *δ*/ ppm = 7.30 (d, *J* = 7.8 Hz, 3H), 7.25 – 7.17 (m, 4H), 7.16 – 7.11 (m, 1H),

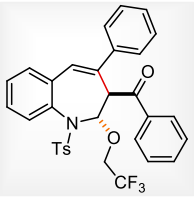
7.09 (d, *J* = 8.0 Hz, 1H), 7.03 (s, 2H), 6.75 (s, 1H), 5.66 (d, *J* = 6.5 Hz, 1H), 5.28 (d, *J* = 6.5 Hz, 1H), 4.17 (dq, *J* = 12.3, 8.7 Hz, 1H), 3.99 (dq, *J* = 12.3, 8.4 Hz, 1H), 3.89 (s, 3H), 3.80 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*/ ppm = 195.3, 152.8, 142.5, 141.9, 136.3, 132.6, 132.5, 130.2, 129.0, 128.4, 127.5, 127.4, 127.0, 126.2, 124.2, 123.5 (q, *J* = 278.5 Hz), 120.4, 105.9, 103.7, 65.5 (q, *J* = 35.0 Hz), 60.9, 58.1, 56.1. ^{19}F NMR (470 MHz, $CDCl_3$) *δ*/ ppm = -73.94. IR (neat): ν/ cm^{-1} = 2936, 1672, 1580, 1413, 1331, 1122, 758, 697. HRMS: *m/z* $[M+Na]^+$ calcd for $C_{28}H_{25}O_6F_3Na$: 537.1495, found: 537.1491.

((2*S*,3*R*)-2-((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)-4-phenyl-2,3-dihydrobenzo[*b*] oxepin-3-yl)(phenyl)methanone (4a.8e, Table 4a.3):



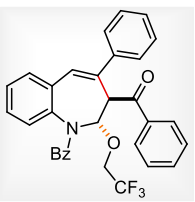
The title compound was prepared following **GP-7** using **4.21a** (65 mg, 0.2 mmol) and HFIP as solvent; obtained as yellow solid (69.3 mg, 70%). M.P. = 117 - 118°C. R_f value = 0.91 (10% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 7.77 (d, *J* = 7.2 Hz, 2H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.38 (t, *J* = 7.8 Hz, 2H), 7.32 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.29 – 7.25 (m, 3H), 7.22 – 7.15 (m, 4H), 7.09 (d, *J* = 8.1 Hz, 1H), 6.73 (s, 1H), 5.81 (d, *J* = 7.1 Hz, 1H), 5.39 (dd, *J* = 7.1, 1.2 Hz, 1H), 4.60 (sept, *J* = 5.9 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 194.8, 151.6, 140.7, 136.2, 135.2, 132.3, 131.7, 129.3, 128.1, 127.5, 127.45, 127.4, 126.6, 126.5 5 (q, *J* = 285 Hz), 126.3, 126.1, 125.9, 123.7, 119.3, 103.9, 71.7 (pent, *J* = 33.2 Hz), 56.4. ^{19}F NMR (470 MHz, $CDCl_3$) *δ*/ ppm = -73.27, -73.30. IR (neat): ν/ cm^{-1} = 2922, 1682, 1597, 1448, 1286, 1192, 1043, 757, 689. HRMS: *m/z* $[M+Na]^+$ calcd for $C_{26}H_{18}O_3F_6Na$: 515.1052, found: 515.1062.

Phenyl((2*R*,3*R*)-4-phenyl-1-tosyl-2-(2,2,2-trifluoroethoxy)-2,3-dihydro-1*H*-benzo[*b*] azepin-3-yl)methanone (4a.9a, Table 4a.4):



The title compound was prepared following **GP-7** using **4.18cj** (95.5 mg, 0.2 mmol); obtained as yellow solid (94.5 mg, 82%). M.P. = 116 - 117°C. R_f value = 0.74 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 7.67 (d, *J* = 7.1 Hz, 1H), 7.51 - 7.45 (m, 2H), 7.44 (d, *J* = 7.4 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 1H), 7.24 (dd, *J* = 7.0, 2.2 Hz, 1H), 7.20 – 7.14 (m, 4H), 7.09 – 7.07 (m, 3H), 6.92 – 6.89 (m, 2H), 6.73 (d, *J* = 8.2 Hz, 2H), 6.67 (d, *J* = 10.3 Hz, 1H), 5.73 (s, 1H), 4.57 (dq, *J* = 11.5, 8.7 Hz, 1H), 4.43 (d, *J* = 10.2 Hz, 1H), 4.33 (dq, *J* = 11.5, 8.6 Hz, 1H), 2.10 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 195.6, 143.6, 139.7, 139.1, 137.2, 136.5, 135.5, 133.9, 133.8, 133.0, 130.2, 129.4, 128.9, 128.8, 128.7, 128.2, 128.15, 127.8, 127.5, 127.45, 127.4, 123.7 (q, *J* = 278 Hz), 97.9, 65.5 (q, *J* = 34.9 Hz), 54.3, 21.3. ^{19}F NMR (470 MHz, $CDCl_3$) *δ*/ ppm = -73.96. IR (neat): ν/ cm^{-1} = 2922, 1686, 1596, 1347, 1280, 1165, 962, 759, 691. HRMS: *m/z* $[M+Na]^+$ calcd for $C_{32}H_{26}NO_4SF_3Na$: 600.1427, found: 600.1434.

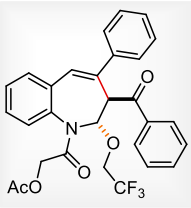
((2*R*,3*R*)-4-phenyl-2-(2,2,2-trifluoroethoxy)-2,3-dihydro-1*H*-benzo[*b*]azepine-1,3-diyl)bis (phenylmethanone) (4a.9b, Table 4a.4):



The title compound was prepared following **GP-7** using **4.18ck** (85.5 mg, 0.2 mmol); obtained as yellow solid (92.7 mg, 88%). M.P. = 119 - 120°C. R_f value = 0.47 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) *δ*/ ppm = 7.58 (d, *J*

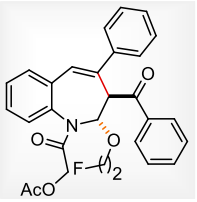
= 7.2 Hz, 2H), 7.47 (d, *J* = 7.7 Hz, 1H), 7.39 (t, *J* = 7.4 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.25 (t, *J* = 7.6 Hz, 3H), 7.22 - 7.10 (m, 10H), 7.10 – 7.04 (m, 1H), 6.93 (s, 1H), 6.89 (d, *J* = 7.9 Hz, 1H), 4.80 – 4.69 (m, 2H), 4.43 (dq, *J* = 11.5, 8.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*/ ppm = 196.1, 171.9, 142.2, 139.5, 138.4, 136.8, 135.5, 135.3, 133.1, 130.1, 129.8, 129.1, 128.5, 128.3, 128.2, 128.17, 128.1, 128.0, 127.8, 127.7, 127.6, 123.8 (q, *J* = 277.6 Hz), 93.3, 68.3 (q, *J* = 34.5 Hz), 54.9. ^{19}F NMR (376 MHz, $CDCl_3$) *δ*/ ppm = -74.54. IR (neat): ν/ cm^{-1} = 2920, 1630, 1513, 1410, 1339, 1227, 1055, 759, 720. HRMS: *m/z* $[M+Na]^+$ calcd for $C_{32}H_{24}NO_3F_3Na$: 550.1600, found: 550.1599.

2-((2*R*,3*R*)-3-benzoyl-4-phenyl-2-(2,2,2-trifluoroethoxy)-2,3-dihydro-1*H*-benzo[*b*]azepin-1-yl)-2-oxoethyl acetate (4a.9c, Table 4a.4):



The title compound was prepared following **GP-7** using **4.18cl** (85 mg, 0.2 mmol); obtained as yellow solid (88.2 mg, 84%). M.P. = 116 - 117°C. R_f value = 0.38 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) *δ*/ ppm = 7.61 – 7.52 (m, 2H), 7.51 – 7.45 (m, 3H), 7.44 (d, *J* = 7.8 Hz, 1H), 7.37 (t, *J* = 7.4 Hz, 1H), 7.22 (t, *J* = 7.8 Hz, 2H), 7.18 (d, *J* = 10.5 Hz, 1H), 7.12 – 7.09 (m, 3H), 7.04 – 7.00 (m, 2H), 6.74 (s, 1H), 4.54 (d, *J* = 15.5 Hz, 1H), 4.46 (dd, *J* = 10.5, 1.3 Hz, 1H), 4.37 (dq, *J* = 11.8, 8.7 Hz, 1H), 4.30 4.57 (dq, *J* = 11.8, 8.8 Hz, 1H), 3.81 (d, *J* = 15.5 Hz, 1H), 2.10 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*/ ppm = 195.4, 170.2, 168.1, 143.0, 138.9, 136.8, 136.5, 135.4, 133.0, 130.3, 129.7, 129.4, 129.3, 129.0, 128.3, 128.1, 128.0, 127.8, 127.6, 123.6 (q, *J* = 277.3 Hz), 94.0, 67.3 (q, *J* = 34.8 Hz), 61.5, 53.8, 20.4. ^{19}F NMR (376 MHz, $CDCl_3$) *δ*/ ppm = -74.35. IR (neat): ν/ cm^{-1} = 2962, 1689, 1488, 1395, 1217, 1080, 769, 692. HRMS: *m/z* $[M+Na]^+$ calcd for $C_{29}H_{24}NO_5F_3Na$: 546.1499, found: 546.1506.

2-((2*R*,3*R*)-3-benzoyl-2-(2-fluoroethoxy)-4-phenyl-2,3-dihydro-1*H*-benzo[*b*]azepin-1-yl)-2-oxoethyl acetate (4a.9d, Table 4a.4):

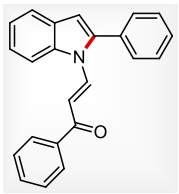


The title compound was prepared following **GP-7** using **4.18cl** (85 mg, 0.2 mmol) and 2F-EtOH as solvent; obtained as yellow solid (78.6 mg, 80%). M.P. = 111 - 112°C. R_f value = 0.56 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 7.58 – 7.50 (m, 2H), 7.50 – 7.44 (m, 4H), 7.35 (t, *J* = 7.4 Hz, 1H), 7.23 – 7.17 (m, 3H), 7.12 – 7.06 (m, 3H), 7.05 – 7.02 (m, 2H), 6.72 (s, 1H), 4.63 – 4.58 (m, 1H), 4.55 (d, *J* = 15.4 Hz, 1H), 4.53 – 4.48 (m, 1H), 4.46 (dd, *J* = 10.3, 1.2 Hz, 1H), 4.27 – 4.16 (m, 1H), 4.15 – 4.02 (m, 1H), 3.77 (d, *J* = 15.4 Hz, 1H), 2.10 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*/ ppm = 195.8, 170.3, 167.7, 143.3, 139.1, 136.9, 136.6, 135.7, 132.9, 130.5, 129.6, 129.3, 129.2, 128.8, 128.2, 128.1, 128.0, 127.8, 127.7, 127.4, 93.4, 82.6 (q, *J* = 169.0 Hz), 68.8 (d, *J* = 19.6 Hz), 61.6, 54.1, 20.5. ^{19}F NMR (376 MHz, $CDCl_3$) *δ*/ ppm = -223.24. IR (neat): ν/ cm^{-1} = 2921, 1642, 1538, 1337, 1273, 1041, 746, 698. HRMS: *m/z* $[M+Na]^+$ calcd for $C_{29}H_{26}NO_5FNa$: 510.1687, found: 510.1689.

4.3.5. Details of Control Experiments for the Synthesis of Benzo[*b*]azepine, Fluoroalkoxy incorporated Dihydrobenzo[*b*]oxeine/azepine (Scheme 4a.6):

4.3.5.1. Analytical Data of 2-Phenyl-N-Subtituteted Indole (4a.10, eq. 1, Scheme 4a.6):

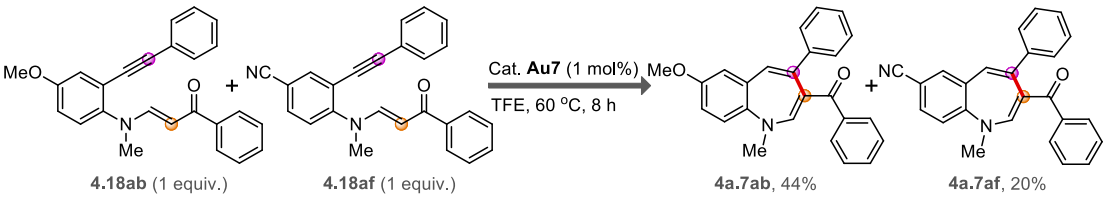
(1-Methyl-4-phenyl-2,3-dihydro-1*H*-benzo[*b*]azepin-3-yl)(phenyl)methanone:



The title compound was prepared following **GP-7** using **4.18cm** (65 mg, 0.2 mmol); obtained as an off-white solid (43.9 mg, 68%). M.P. = 171 - 172°C. R_f value = 0.91 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.41 (d, J = 13.9 Hz, 1H), 7.88 (d, J = 8.0 Hz, 3H), 7.66 (d, J = 7.7 Hz, 1H), 7.58 – 7.51 (m, 5H), 7.51 - 7.44 (m, 3H), 7.41 (t, J = 7.6 Hz, 1H), 7.32 (t, J = 7.4 Hz, 1H), 7.10 (d, J = 13.9 Hz, 1H), 6.75 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 189.6, 141.4, 139.3, 138.4, 137.0, 132.6, 131.6, 130.0, 129.9, 128.9, 128.8, 128.6, 128.1, 124.0, 123.1, 121.3, 112.6, 109.0, 108.2. IR (neat): ν/ cm^{-1} = 2961, 1669, 1566, 1453, 1259, 1008, 795, 767. HRMS: m/z $[M+H]^+$ calcd for $C_{23}H_{18}NO$: 324.1383, found: 324.1386.

4.3.5.2. Method of Cross-over Experiment for the Synthesis of Benzo[*b*]azepine (eq. 2, Scheme 4a.6):

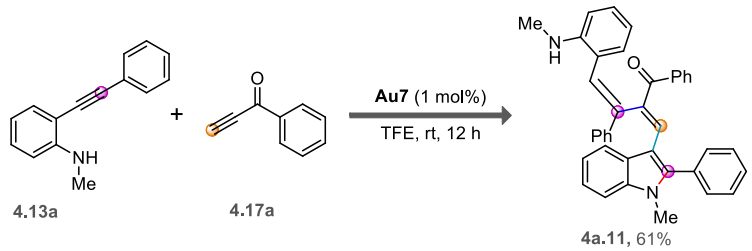
To a equimolar mixture of substrates **4.18ab** (37 mg, 1 equiv.) and **4.18af** (36.5 mg, 1 equiv.) and **Au7** (1mg, 1 mol%) in a 10 mL dried pyrex screw-top reaction tube was added TFE (1 mL, 0.1 M). Then the reaction mixture was heated at 60 °C in an oil bath with continuous stirring for 8 hrs. After that, the reaction mixture was concentrated under reduced pressure and the crude mixture was analyzed by ^{1}H NMR spectra to find out that benzo[*b*]azepines **4a.7ab** and **4a.7af** were formed in almost 2:1 ratio.



Scheme 4.12. Cross-over experiment for the synthesis of Benzo[*b*]azepines **4a.7ab and 4a.7af**.

4.3.5.3. Method of One-pot Two Component Reaction (eq. 3, Scheme 4a.6):

To a mixture of **4.13a** (41.5 mg, 1 equiv.) and **4.17a** (26 mg, 1 equiv.) in TFE solvent (2 mL, 0.1 M), **Au7** (1.6 mg, 1 mol%) was added in a 10 mL RB flask. Then the reaction mixture was allowed to stir at rt. After completion of the reaction as mentioned by the TLC, the reaction mixture was concentrated under reduced pressure and the crude mixture was purified by column chromatography (silica gel, hexanes/EtOAc) to get highly substituted indole **4a.11** (66.5 mg, 61%).

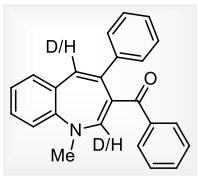


4.13a 4.17a **4a.11**, 61%

Scheme 4.13. One-pot two component reaction for the synthesis of highly substituted indole **4a.11**.

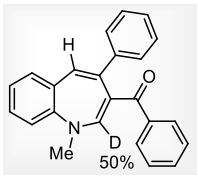
4.3.5.4. Analytical Data of Deuterium Scrambling Experiments for the Synthesis of Benzo[*b*]azepine (eq. 4-5, Scheme 4a.6):

Deuterated (1-methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)(phenyl)methanone (4a.7aa-D from 4.18aa-D in TFE-D_3 solvent, eq. 4, Scheme 4a.6):



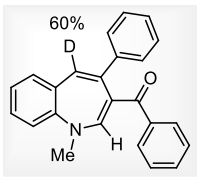
The title compound was prepared following **GP-7** using **4.18aa-D** (68 mg, 0.2 mmol) and TFE-D_3 as solvent; obtained as yellow solid (65.4 mg, 96%). M.P. = 155 - 156°C. R_f value = 0.53 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.61 (d, J = 7.2 Hz, 2H), 7.36 (t, J = 7.4 Hz, 1H), 7.25 (t, J = 7.6 Hz, 2H), 7.20 – 7.09 (m, 6H), 7.05 – 6.99 (m, 2H), 6.87 (s, 0.5H), 6.76 (dd, J = 8.0, 2.4 Hz, 1H), 6.70 (d, J = 5.2 Hz, 0.25H), 3.12 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 195.7, 158.1, 151.9, 142.6, 141.9, 139.1, 132.6, 132.4, 131.5, 130.4, 129.1, 128.5, 128.2, 128.0, 127.3, 126.5, 125.5, 124.1, 117.0, 40.3. IR (neat): ν/ cm^{-1} = 2923, 1633, 1564, 1445, 1276, 1124, 1043, 755, 692. HRMS: m/z [M]$^+$ calcd for $C_{24}H_{17}D_2NO$: 339.1592, found: 339.1589.

Deuterated (1-methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)(phenyl)methanone (4a.7aa-D from 4.18aa-D in TFE solvent, eq. 4, Scheme 4a.6):



The title compound was prepared following **GP-7** using **4.18aa-D** (68 mg, 0.2 mmol); obtained as yellow solid (66.4 mg, 98%). M.P. = 155 - 156°C. R_f value = 0.53 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.64 (d, J = 7.2 Hz, 2H), 7.36 (t, J = 7.4 Hz, 1H), 7.26 (t, J = 7.6 Hz, 2H), 7.22 – 7.08 (m, 6H), 7.06 – 6.99 (m, 2H), 6.89 (s, 0.5H), 6.75 (dd, J = 8.1, 2.5 Hz, 1H), 6.71 (d, J = 5.2 Hz, 1H), 3.11 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 195.6, 158.0, 151.8, 142.6, 141.9, 139.0, 132.5, 132.3, 131.4, 130.3, 129.0, 128.5, 128.1, 127.9, 127.2, 126.4, 125.4, 124.0, 116.9, 40.2. IR (neat): ν/ cm^{-1} = 3023, 1634, 594, 1445, 1278, 1101, 751, 693. HRMS: m/z [M+Na]$^+$ calcd for $C_{24}H_{18}DNONa$: 361.1422, found: 361.1421.

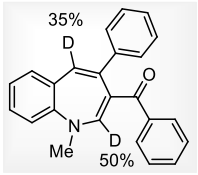
Deuterated (1-methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)(phenyl)methanone (4a.7aa-D from 4.18aa in TFE-D_3 solvent, eq. 5, Scheme 4a.6):



The title compound was prepared following **GP-7** using **4.18aa** (67.5 mg, 0.2 mmol) and TFE-D_3 as solvent; obtained as yellow solid (66.1 mg, 98%). M.P. = 155 - 156°C. R_f value = 0.53 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.61 (d, J = 7.7 Hz, 2H), 7.35 (t, J = 7.4 Hz, 1H), 7.25 (t, J = 7.6

Hz, 2H), 7.21 – 7.07 (m, 6H), 7.05 – 6.99 (m, 2H), 6.88 (s, 1H), 6.76 (d, *J* = 8.2 Hz, 1H), 6.70 (s, 0.4H), 3.12 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*/ ppm = 195.7, 158.0, 151.9, 142.6, 141.9, 139.1, 132.5, 132.4, 131.5, 130.4, 129.1, 128.5, 128.2, 127.9, 127.3, 126.5, 125.5, 124.1, 117.0, 40.2. IR (neat): ν/ cm^{-1} = 3054, 1595, 1446, 1314, 1276, 1175, 751, 694. HRMS: *m/z* $[M]^+$ calcd for $C_{24}H_{18}DNONa$: 361.1422, found: 361.1422.

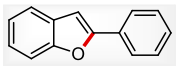
Deuterated (1-methyl-4-phenyl-1*H*-benzo[*b*]azepin-3-yl)(phenyl)methanone (4a.7aa-D from 4.18aa-D in DCM solvent, eq. 4, Scheme 4a.6):



The title compound was prepared following **GP-7** using **4.18aa-D** (68 mg, 0.2 mmol) and DCM as solvent; obtained as yellow solid (33.8 mg, 50%). M.P. = 155 - 156°C. R_f value = 0.53 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) *δ*/ ppm = 7.63 (d, *J* = 7.5 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.26 (t, *J* = 7.8 Hz, 2H), 7.22 – 7.09 (m, 6H), 7.06 – 6.98 (m, 2H), 6.88 (s, 0.5H), 6.75 (d, *J* = 8.2 Hz, 1H), 6.71 (d, *J* = 4.1 Hz, 0.65H), 3.11 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*/ ppm = 195.6, 158.1, 151.8, 142.6, 141.9, 139.0, 132.5, 132.3, 131.5, 130.3, 129.1, 128.5, 128.1, 127.9, 127.2, 126.4, 125.4, 124.1, 116.9, 40.2. IR (neat): ν/ cm^{-1} = 3055, 1642, 1536, 1342, 1279, 1170, 1044, 756, 688. HRMS: *m/z* $[M+Na]^+$ calcd for $C_{24}H_{17}D_2NONa$: 362.1484, found: 362.1465.

4.3.5.5. Analytical Data of 2-Phenylbenzofuran (4a.12, eq. 6, Scheme 4a.6):

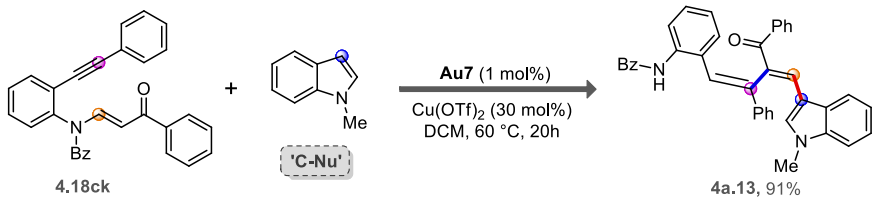
2-Phenylbenzofuran:



The title compound was prepared following **GP-7** using **4.21a** (65 mg, 0.2 mmol) and EtOH as solvent; obtained as an off-white solid (36.5 mg, 94%). M.P. = 38 - 39°C. R_f value = 0.33 (10% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) *δ*/ ppm = 7.88 (d, *J* = 7.2 Hz, 2H), 7.60 (d, *J* = 7.4 Hz, 1H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.39 – 7.33 (m, 1H), 7.29 (td, *J* = 8.0, 1.4 Hz, 1H), 7.40 (td, *J* = 7.3, 1.0 Hz, 1H), 7.04 (d, *J* = 0.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*/ ppm = 156.0, 154.0, 130.5, 129.3, 128.8, 128.6, 125.0, 124.3, 123.0, 120.9, 111.2, 101.3. IR (neat): ν/ cm^{-1} = 2920, 1562, 1453, 1255, 1167, 1018, 805, 739, 688. HRMS: *m/z* $[M+Na]^+$ calcd for $C_{14}H_{10}ONa$: 217.0624, found: 217.0624.

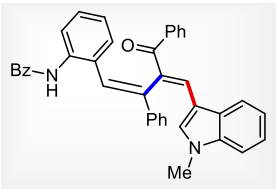
4.3.5.6. Synthesis and Characterization of Highly Subtituteted Indole (4a.13, eq. 9, Scheme 4a.6):

To a mixture of **4.18ck** (85 mg, 1 equiv.) and N-methyl indole (26 mg, 1 equiv.) in TFE solvent (2 mL, 0.1 M), in a 10 mL dried pyrex screw-top reaction tube **Au7** (1.6 mg, 1 mol%) was added. Then $Cu(OTf)_2$ (21.7 mg, 30 mol%) was added to the reaction mixture and the contents were heated at 60 °C in an oil bath with continuous stirring. After the completion of the reaction (20 h) as mentioned by the TLC, the reaction mixture was concentrated under reduced pressure and the crude mixture was purified by column chromatography (silica gel, hexanes/EtOAc) to get the indole derivative **4a.13** (91.2 mg, 82%).



Scheme 4.14. Reaction of vinylogous amide derived from *o*-alkynylaniline **4.18ck** with N-methyl indole as external nucleophile.

(2-(1-Methyl-1*H*-indol-3-yl)-4-phenyl-1*H*-benzo[*b*]azepine-1,3-diyl)bis (phenylmethanone)

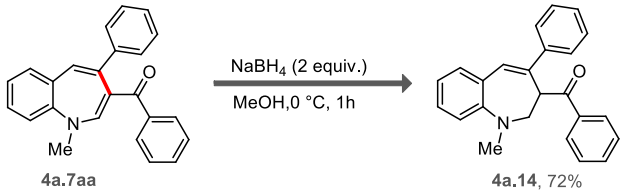


Yellow solid (101.4 mg, 91%). M.P. = 168 – 169 °C. R_f value = 0.25 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.62 (s, 1H), 8.08 (d, *J* = 7.4 Hz, 2H), 7.91 (d, *J* = 8.1 Hz, 1H), 7.84 (s, 1H), 7.67 (d, *J* = 7.5 Hz, 2H), 7.56 (s, 1H), 7.49 (d, *J* = 7.5 Hz, 2H), 7.45 (t, *J* = 7.0 Hz, 3H), 7.36 (d, *J* = 4.3 Hz, 3H), 7.34 (d, *J* = 7.9 Hz, 2H), 7.32 – 7.27 (m, 5H), 7.19 (t, *J* = 7.8 Hz, 1H), 7.14 (d, *J* = 7.5 Hz, 1H), 6.98 (t, *J* = 7.5 Hz, 1H), 3.72 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 197.6, 165.5, 142.4, 139.6, 138.4, 137.9, 136.6, 135.6, 134.6, 132.8, 132.5, 131.6, 131.3, 130.9, 128.9, 128.7, 128.6, 128.4, 128.3, 128.2, 128.1, 128.0, 127.5, 127.2, 126.5, 124.5, 123.9, 123.1, 121.2, 118.4, 110.8, 109.9, 33.5. IR (neat): ν/ cm^{-1} = 3054, 1642, 1526, 1336, 1274, 1048, 759, 700. HRMS: *m/z* $[M+H]^+$ calcd for $C_{39}H_{31}N_2O_2$: 559.2380, found: 559.2391.

4.3.6. Details of Late-stage Transformation of Benzo[*b*]azepine Derivative (Scheme 4a.7):

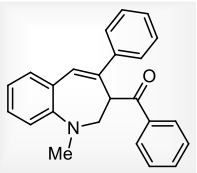
4.3.6.1. Synthetic Procedure and Characterization for the Preparation of 2,3-Dihydrobenzo[*b*]azepine Derivatives (4a.14):

To a mixture of **4a.7aa** (67.5 mg, 1 equiv.) in MeOH (2 mL, 0.1 M), $NaBH_4$ (15.1 mg, 2 equiv.) was added. Then the reaction mixture was continuously stirred for 1 hrs at 0 °C. After the completion of the reaction, it was quenched with water, extracted with ethyl acetate and washed with saturated brine solution. The combined organic layers were then concentrated under reduced pressure and crude was purified and separated by column chromatography (silica gel, hexanes/EtOAc) to get 2,3-dihydrobenzo[*b*]azepine derivative **4a.14** (49 mg, 72%) in an analytically pure form.



Scheme 4.15. Preparation of 2,3-dihydrobenzo[*b*]azepine derivative **4a.14**.

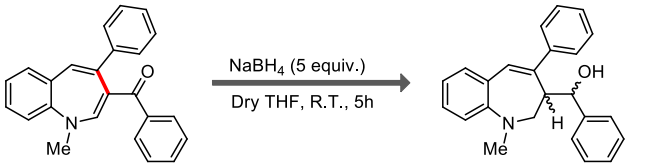
(1-Methyl-4-phenyl-2,3-dihydro-1*H*-benzo[*b*]azepin-3-yl)(phenyl)methanone:



Pale-yellow solid (49 mg, 72%). M.P. = 148 – 149 °C. R_f value = 0.55 (10% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.00 (d, J = 7.2 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.4 Hz, 2H), 7.40 (d, J = 7.2 Hz, 2H), 7.34 (dd, J = 7.7, 1.3 Hz, 1H), 7.27 (t, J = 7.4 Hz, 2H), 7.22 – 7.13 (m, 2H), 7.02 (s, 1H), 6.85 (t, J = 7.3 Hz, 1H), 6.75 (d, J = 8.2 Hz, 1H), 5.18 (dd, J = 4.4, 2.0 Hz, 1H), 3.89 (dd, J = 14.2, 4.5 Hz, 1H), 3.51 (dd, J = 14.2, 2.1 Hz, 1H), 2.74 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 198.5, 150.1, 143.6, 137.1, 136.8, 135.2, 133.3, 133.0, 128.9, 128.4, 128.35, 128.0, 126.9, 126.4, 124.5, 119.0, 113.9, 56.3, 56.0, 41.4. IR (neat): ν/ cm^{-1} = 2962, 1684, 1592, 1499, 1259, 1016, 797, 752, 695. HRMS: m/z [M]$^+$ calcd for $C_{24}H_{22}NO$: 340.1696, found: 340.1700.

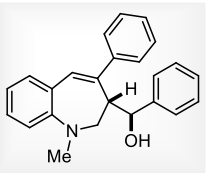
4.3.6.2. Synthetic Procedure and Characterization for the Preparation of 2,3-Dihydrobenzo[*b*]azepinol Derivatives (4a.15 and 4a.15′):

To a mixture of **4a.7aa** (67.5 mg, 1 equiv.) in dry THF (2 mL, 0.1 M), $NaBH_4$ (38 mg, 5 equiv.) was added. Then the reaction mixture was continuously stirred for 5 hrs. After the completion of the reaction, it was quenched with water, extracted with ethyl acetate and washed with saturated brine solution. The combined organic layers were then concentrated under reduced pressure and crude was purified and separated by column chromatography (silica gel, hexanes/EtOAc) to get 2,3-dihydrobenzo[*b*]azepinol derivatives **4a.15** (39 mg, 58%) and **4a.15'** (15 mg, 21%) in an analytically pure form.

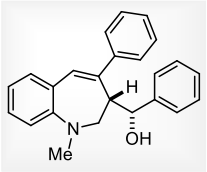


Scheme 4.16. Preparation of benzo[*b*]azepinol derivative **4a.15/4a.15′**.

(1-Methyl-4-phenyl-2,3-dihydro-1*H*-benzo[*b*]azepin-3-yl)(phenyl)methanol:



Major isomer 4a.15 was obtained as pale yellow solid (39 mg, 58%). M.P. = 141 – 142 °C. R_f value = 0.39 (10% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 7.49 (d, J = 7.1 Hz, 2H), 7.45 (d, J = 7.4 Hz, 2H), 7.41 – 7.29 (m, 6H), 7.26 – 7.18 (m, 2H), 6.97 (td, J = 7.4, 1.0 Hz, 1H), 6.91 (d, J = 8.3 Hz, 1H), 6.84 (s, 1H), 4.97 (d, J = 2.9 Hz, 1H), 4.63 (s, 1H), 3.52 (d, J = 2.5 Hz, 1H), 3.35 (dd, J = 13.8, 3.0 Hz, 1H), 3.07 (d, J = 13.8 Hz, 1H), 2.98 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ ppm = 150.4, 144.0, 143.9, 142.0, 134.8, 132.5, 128.5, 128.3, 127.6, 127.3, 127.2, 126.9, 126.1, 125.7, 120.6, 114.3, 74.6, 54.8, 51.5, 41.7. IR (neat): ν/ cm^{-1} = 3367, 2919, 1595, 1494, 1288, 1184, 1016, 749, 695. HRMS: m/z [M+H]$^+$ calcd for $C_{24}H_{24}NO$: 342.1852, found: 342.1852.



Minor isomer 4a.15' was obtained as pale yellow solid (15 mg, 21%). M.P. = 143 - 144°C. R_f value = 0.35 (10% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.32 (d, J = 7.3 Hz, 3H), 7.23 – 7.16 (m, 5H), 7.16 – 7.07 (m, 4H), 6.91 (t, J = 7.3 Hz, 2H), 6.82 (s, 1H), 5.05 (d, J = 4.9 Hz, 1H), 3.78 (s, 1H), 3.48 (dd, J = 13.5, 4.5 Hz, 1H), 3.37 (d, J = 13.1 Hz, 1H), 3.00 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ/ ppm = 149.5, 144.9, 142.4, 140.3, 135.2, 133.3, 129.1, 128.1, 127.9, 127.8, 127.1, 126.8, 126.6, 124.9, 119.3, 113.9, 77.9, 58.1, 52.1, 42.7. IR (neat): ν/ cm^{-1} = 3397, 2919, 1595, 1494, 1288, 1184, 1016, 748, 696. HRMS: m/z $[M+H]^+$ calcd for $C_{24}H_{24}NO$: 342.1852, found: 342.1855.

4.3.7. Details of Kinetic Analysis for the Formation of Benzo[*b*]azepine:

4.3.7.1. Reaction Profile of Benzo[*b*]azepine Synthesis:

The gold catalyzed cyclization of **4.18aa** was conducted for different time periods and the isolated amounts of the starting material, **4.18aa** and the product, **4a.7aa** in each experiment were plotted against time to get insight into the reaction profile. During the initial period of reaction, conversion of **4.18aa** was decreasing very slowly. After 4 hrs, the concentration of **4a.7aa** was raising drastically upto 17 hrs (84% conversion). In the final stage conversion rate of **4.18aa** was gradually decreasing, albeit with almost full conversion (98% yield) after 22 hrs.

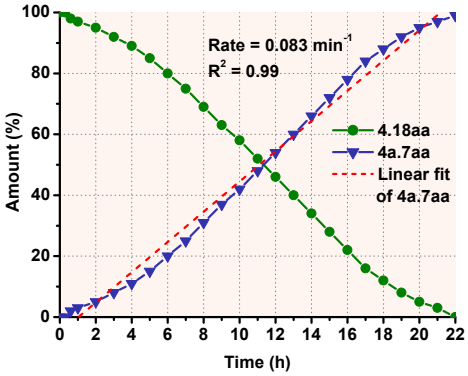
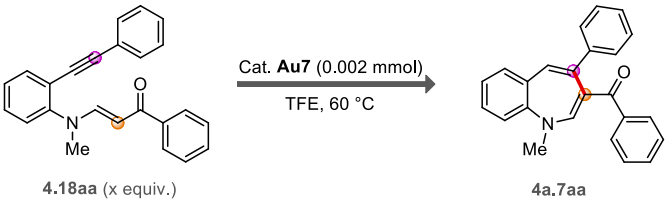


Figure 4.1. Reaction profile of **4.18aa**.

4.3.7.2. Reaction Order for Benzo[*b*]azepine Synthesis:

The dependence of *k* (min^{-1}) on the amount of vinylogous amides derived from *o*-alkynylanilines (4.18aa):



[**4.18aa**] (mmol)	k_{obs} (min^{-1})
0.05	3.9×10^{-1}
0.1	2.1×10^{-1}
0.15	1.35×10^{-1}
0.2	0.83×10^{-1}
0.25	0.15×10^{-1}

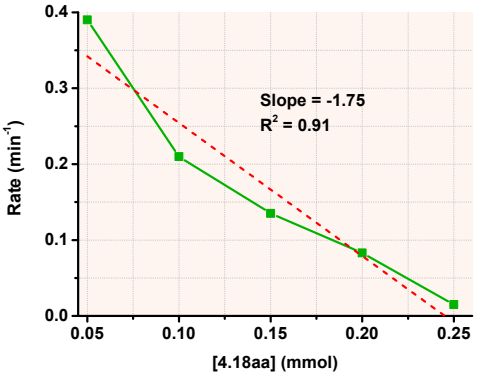
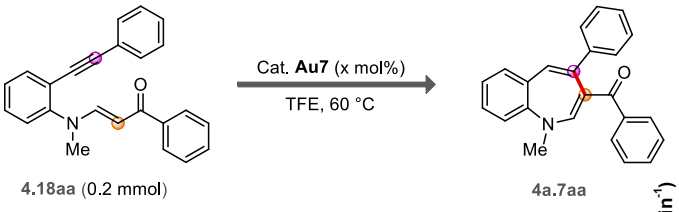


Figure 4.2. Dependence of rate on the amount of **4.18aa**.

The dependence of *k* (min^{-1}) on the amount of catalyst (Au7):



[**Au7**] (mol%)	k_{obs} (min^{-1})
0.5	0.4×10-1
1	0.83×10-1
1.5	1.35×10-1
2	2.1×10-1
2.5	3.3×10-1

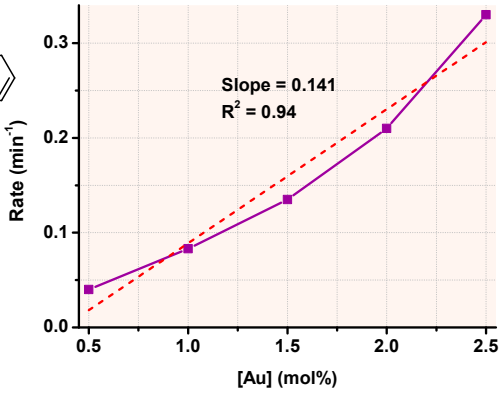
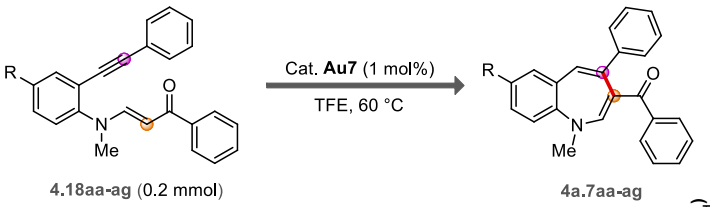


Figure 4.3. Dependence of rate on the amount of **Au7**.

Figure 4.2 and 4.3 shows the first-order dependency on both the starting material **4.18aa** and the catalyst **Au7** which indicates the engagement of **4.18aa** and cat. **Au7**.

4.3.7.3. Details of Hammett Analysis:

We analogized the reaction rates of vinylogous amides derived from *o*-alkynylanilines (**4.18aa**) having different para-substitution to execute the electronic effect in the substrates. With this information we have studied the Hammett plot (figure 4.4) and it was found that the 1st order rate constant correlated strongly with σ_p of the Ar^1 group. The negative reaction constant value (ρ = −0.34) undoubtedly reveals the participation of lone pair of electrons on the nitrogen of enaminone by making C3 electron rich to effect the cyclization.



Substrate	R	σ_p	k_R	Log(k_R/ k_H)
4.18ab	*p*-OMe	-0.268	0.115	0.142
4.18ac	*p*-Me	-0.17	0.095	0.059
4.18aa	*p*-H	0	0.083	0
4.18ae	*p*-F	0.062	0.075	-0.044
4.18ad	*p*-Cl	0.227	0.071	-0.068
4.18af	*p*-CN	0.66	0.053	-0.195

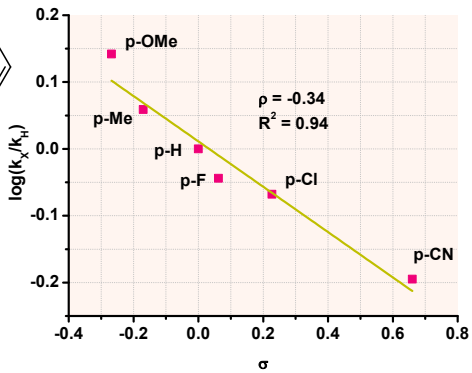


Figure 4.4. Hammett Plot.

4.3.8. HRMS Studies to Support the Proposed Mechanisms for the Formation of Benzo[*b*]azepine and Fluoroalkoxy incorporated Dihydrobenzo[*b*]azepine:

The gold catalyzed cyclization of **4.18aa** and **4.18ck** were conducted separately. After 2 hours, HRMS analysis has been performed for both the reactions to identify few intemediates.

For the synthesis of **4a.7aa**, formation of intemediate **D** was observed in the HRMS spectra (Figure 4.5 - 4.6). Similarly for the synthesis of **4a.9b**, formation of intemediate **H** was detected in the HRMS spectra (Figure 4.7 - 4.8).

For more clarification, we have added **Au7** to the products (**4a.7aa** and **4a.9b**) separately and recorded the HRMS spectra. But both the cases we did not observed the peaks corresponding to the Intermediates (Figure 4.9-4.11).

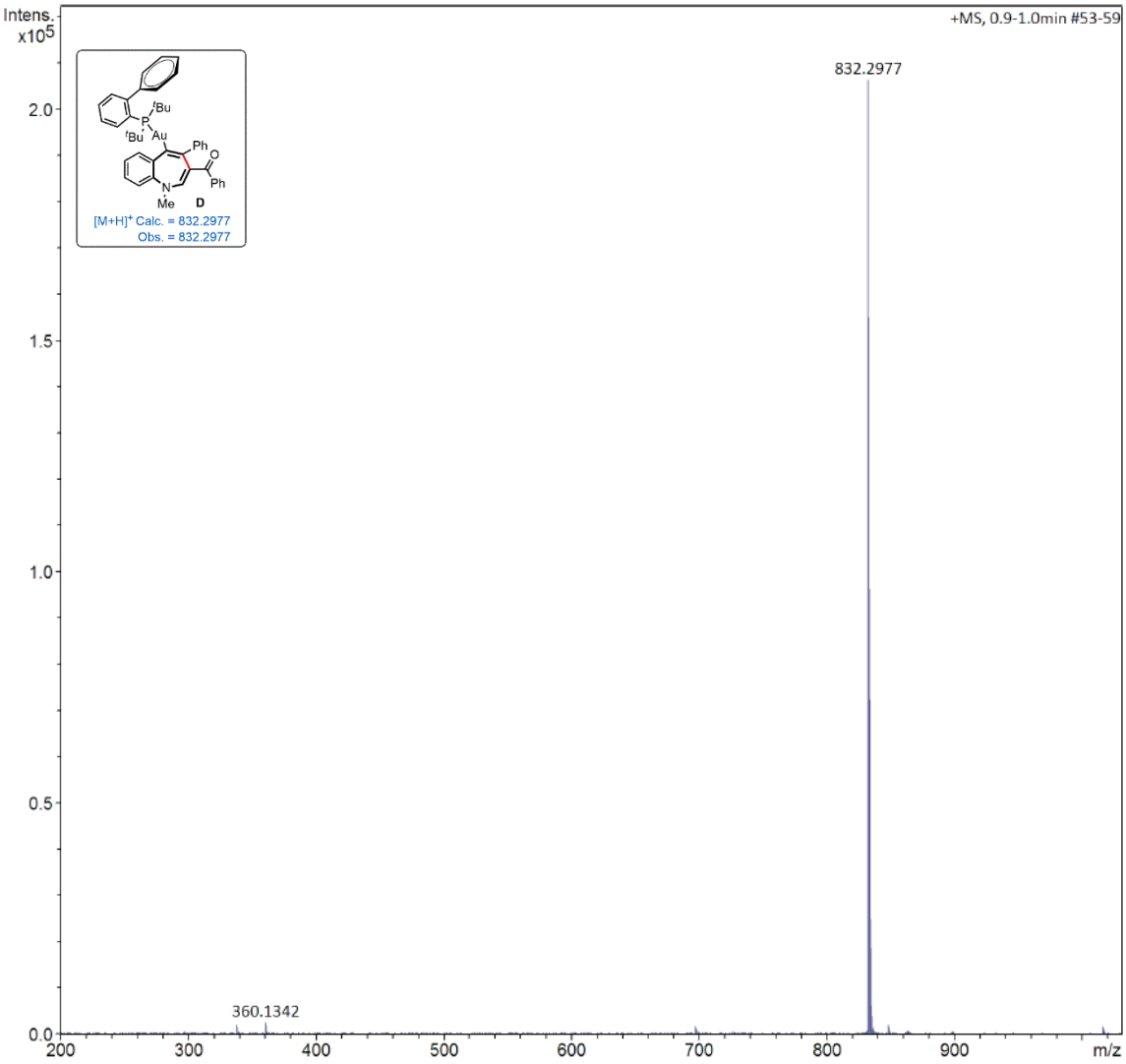


Figure 4.5. Full HRMS spectrum of crude reaction mixture for intermediate **D**.

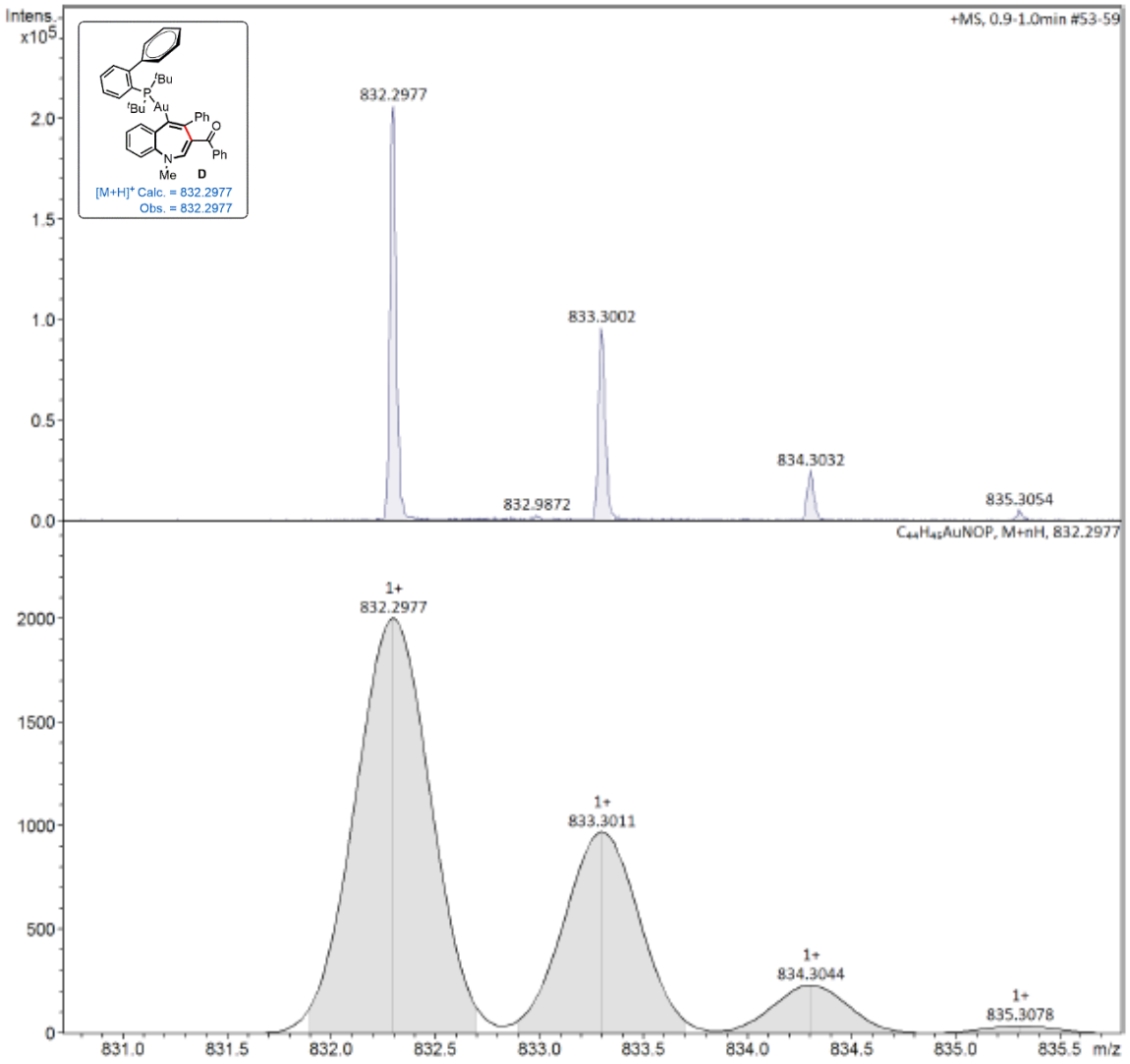


Figure 4.6. Simulated HRMS spectrum of intermediate **D**.

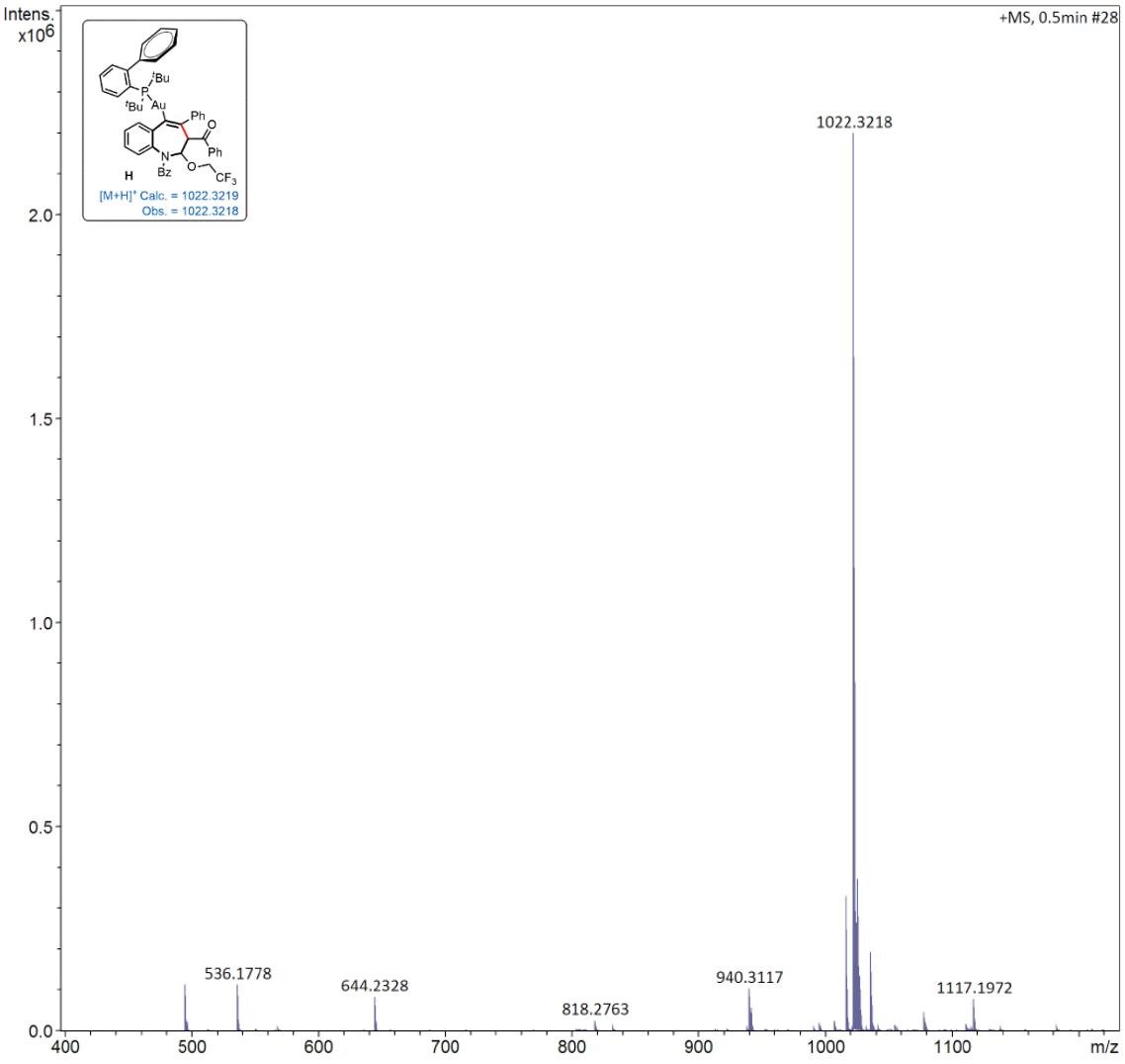


Figure 4.7. Full HRMS spectrum of crude reaction mixture for intermediate **H**.

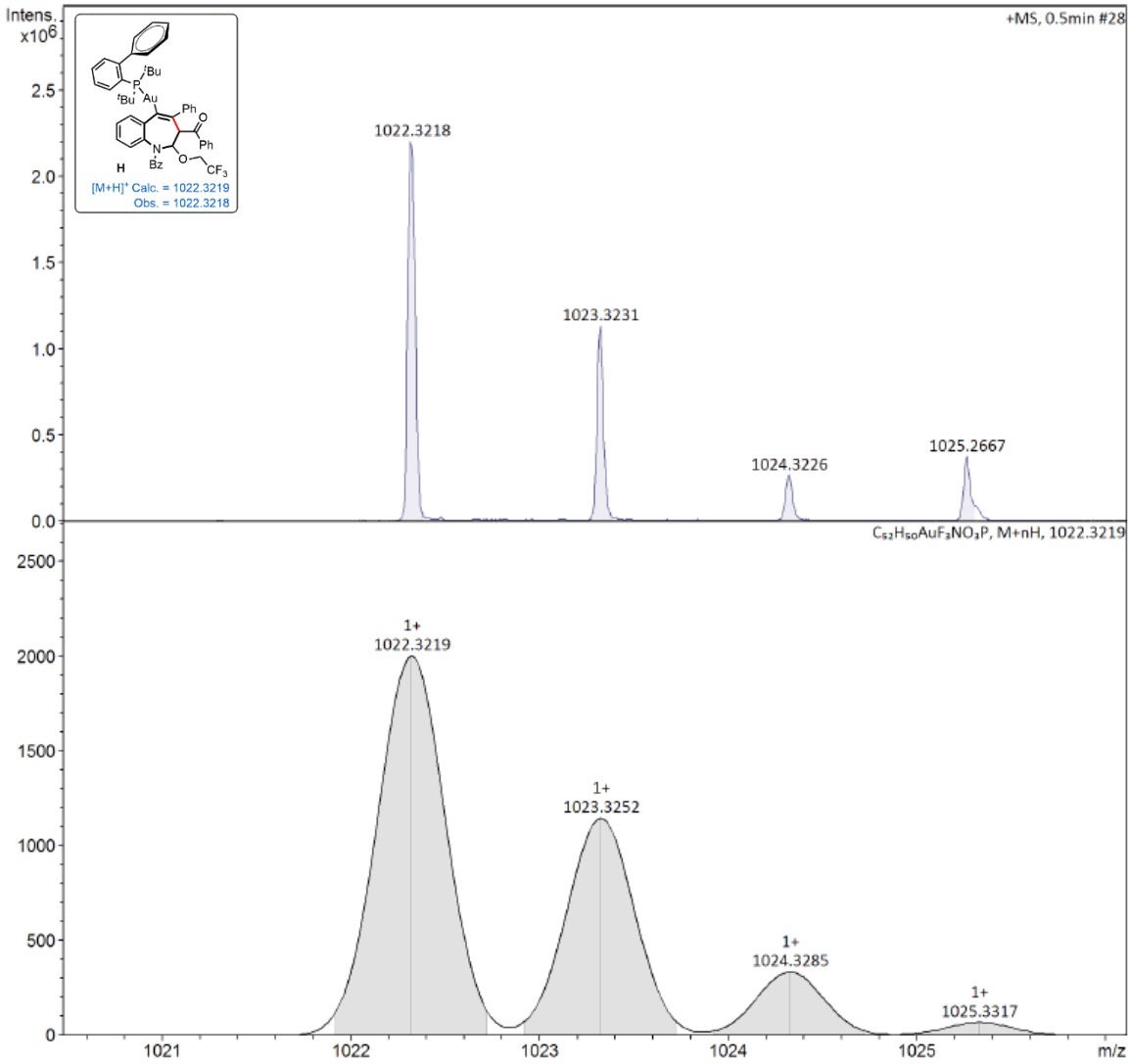


Figure 4.8. Simulated HRMS spectrum of intermediate **H**.

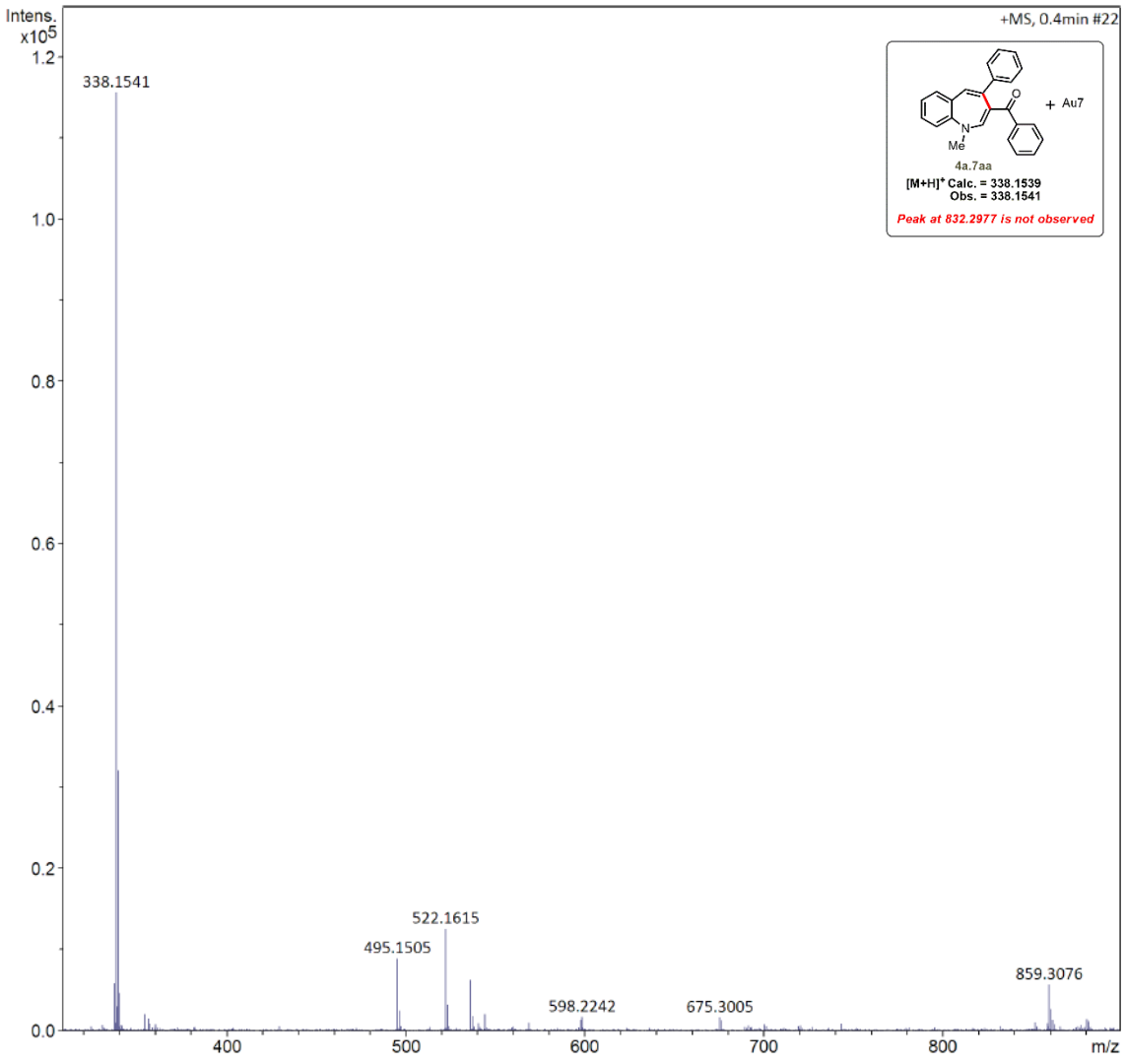


Figure 4.9. Full HRMS spectrum of product **4a.7aa** along with catalyst **Au7**.

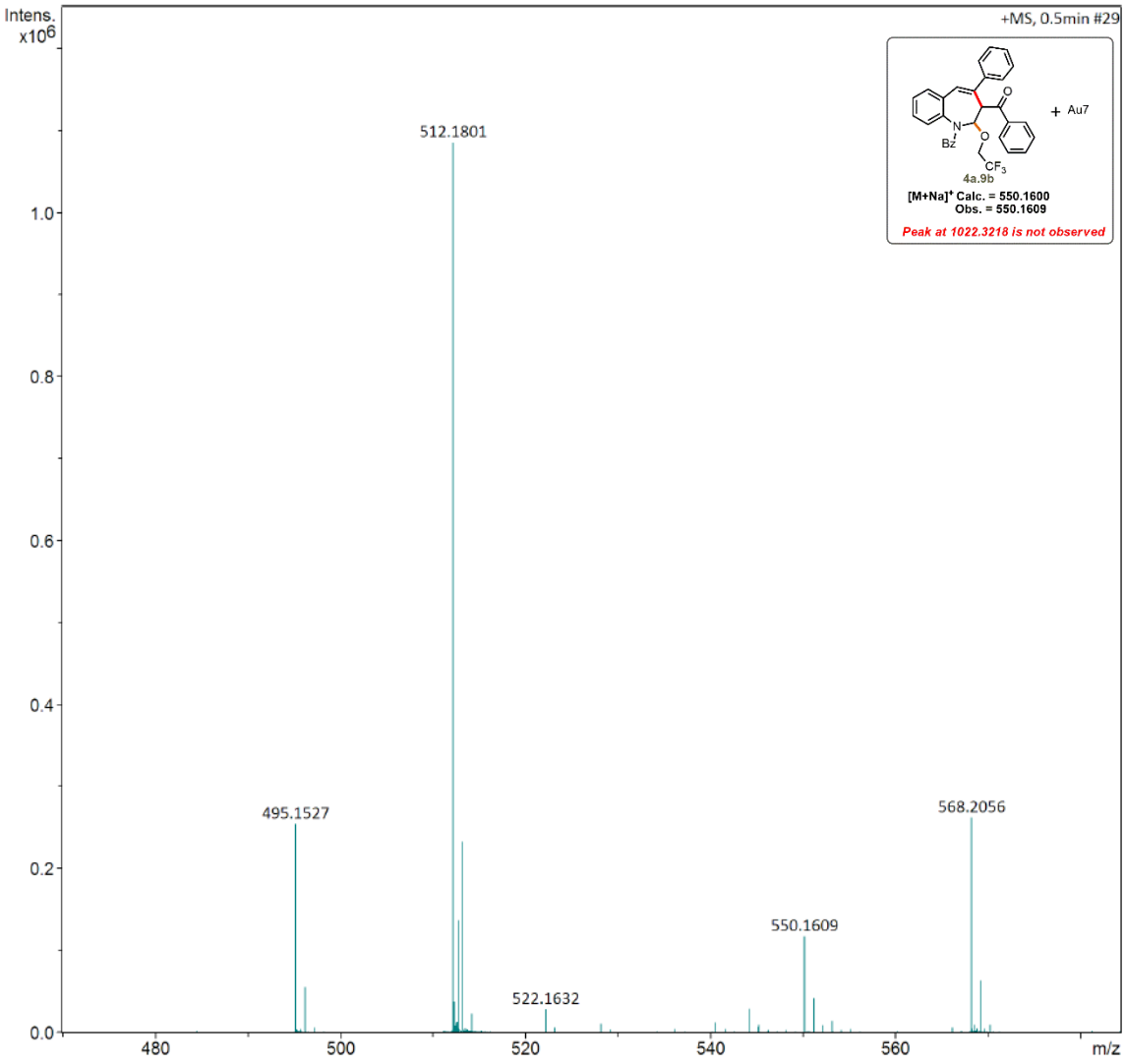


Figure 4.10. HRMS spectrum of product **4a.9b** along with catalyst **Au7**.

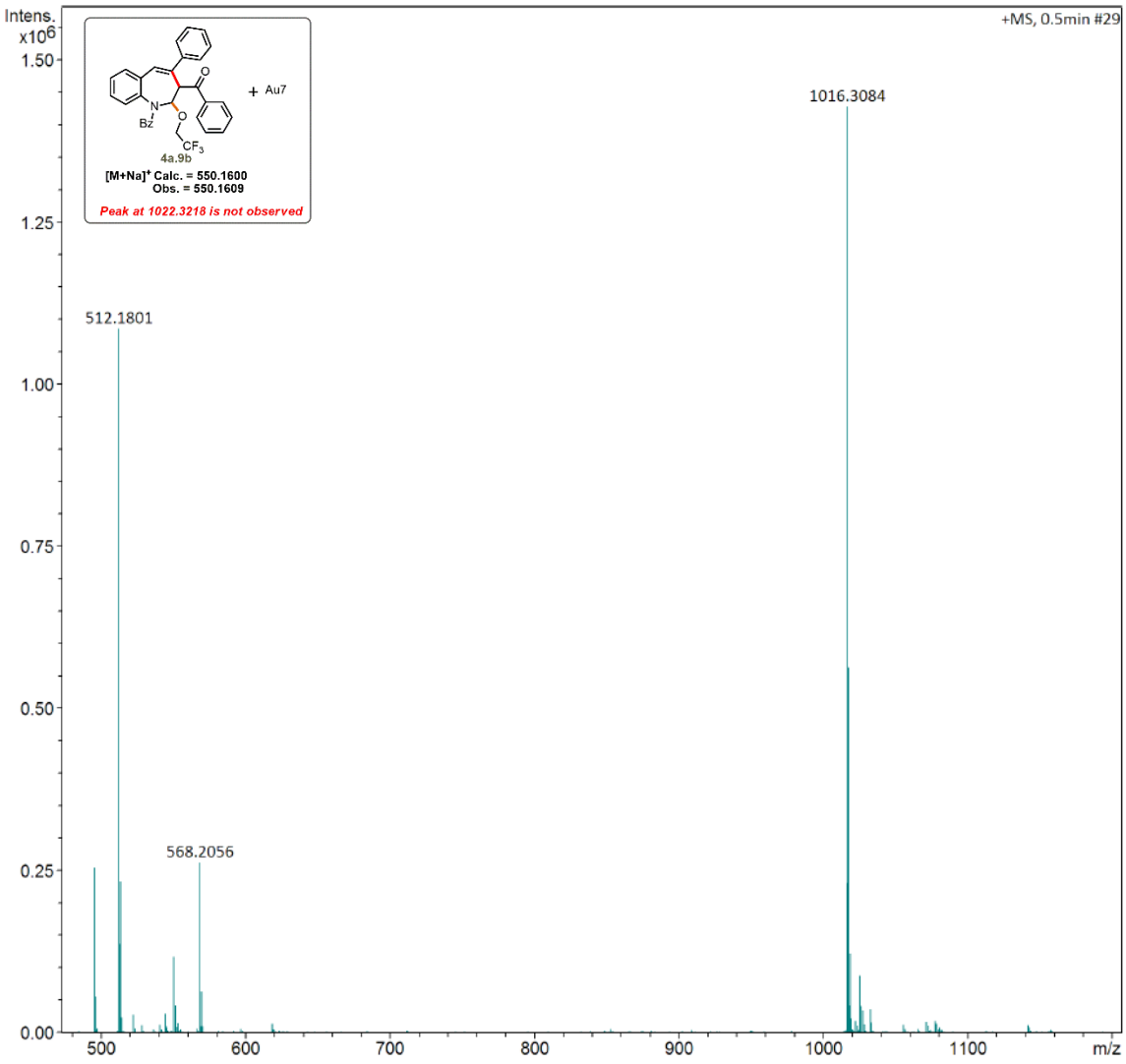
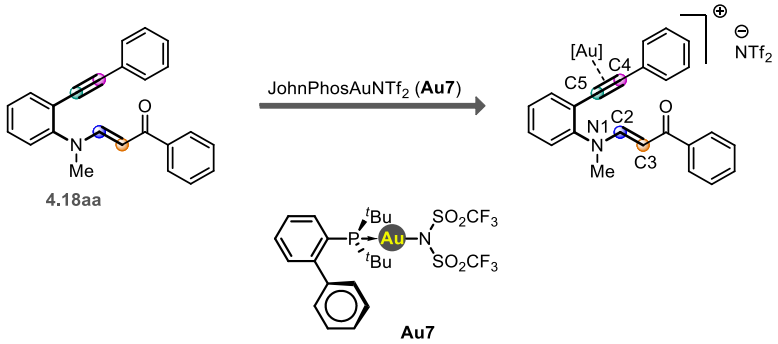


Figure 4.11. HRMS spectrum of product **4a.9b** along with catalyst **Au7**.

4.3.9. DFT Reactivity Indices for the Formation of Benzo[*b*]azepine and Fluoroalkoxy incorporated Dihydrobenzo[*b*]azepine:

The DFT reactivity indices are excellent tools to understand the reactivity of molecules in the ground state. To understand the experimental regioselectivity in the formation of benzo[*b*]azepine, we have calculated the global reactivity indices such as electronic chemical potential (μ), chemical hardness (η), global electrophilicity index (ω) for the pre-reaction complex (**prc**) and the intermediate **7m_int1**. The Fukui functions for the nucleophilic (f_k^+) and electrophilic (f_k^-) attack have been calculated by using natural population obtained from the NBO (natural bond orbital) calculations. To predict the regioselectivity, the electrophilic and nucleophilic Fukui functions and local electrophilicity at the C1, C2, C3, and C4 carbon atoms and

N5 nitrogen atom (Scheme 4.17) of **prc, 7m_int1, prc_tosyl, and 7m_int_tosyl** were calculated at the M062X/6-31G(d,p) Au SDD level of theory.



Scheme 4.17. Schematic diagram of the formation of the pre-reaction complex (**prc**) with important atom numbers labelled to describe the reaction mechanisms.

The electronic chemical potential μ, is the relative measure for the capacity of a molecule to donate electron density and it can be approximated, using Koopmans' theorem as mean value of the HOMO and LUMO orbital energies.[53]

$$\mu = \frac{E_{\mathrm{HOMO}}+E_{\mathrm{LUMO}}}{2}$$

where E_{HOMO} and E_{LUMO} are the HOMO and LUMO orbital energies respectively.

The chemical hardness (η) is the difference between the HOMO and LUMO orbital energies.[53]

$$\eta = E_{\mathrm{HOMO}} - E_{\mathrm{LUMO}}$$

The global electrophilicity index measures the total ability of a system to attract electrons and is given by[54]

$$\omega = \frac{\mu^2}{2\eta}$$

The electrophilic Fukui function (f_k^+) can be expressed as[55]

$$f_k^+ = \rho_k(N+1) - \rho_k(N)$$
$$= q_k(N) - q_k(N+1)$$

The nucleophilic Fukui function (f_k^-) can be expressed as[55]

$$f_k^- = \rho_k(N) - \rho_k(N-1)$$
$$= q_k(N-1) - q_k(N)$$

Where, $\rho_k(N)$, $\rho_k(N+1)$, and $\rho_k(N-1)$ are population at the site k of the neutral, anionic and cationic system and $q_k(N)$, $q_k(N+1)$, and $q_k(N-1)$ are the net charge of the neutral, anionic and cationic system at site k respectively.

The local electrophilicity index,[56] ω_k at site k of the molecule is obtained by multiplying the global electrophilicity index ω with the electrophilic Fukui function (f_k^+)

$$\omega_k = \omega f_k^+$$

Table 4.3. The electronic chemical potential (μ), chemical hardness (η), and global electrophilicity (ω) for **prc**, **7m_int1**, **prc_tosyl**, and **7m_int_tosyl** obtained at the M062X/6-31G(d,p) Au SDD level of theory

Structures	μ (a.u.)	η (a.u.)	ω (eV)
Prc	-0.1363	0.1443	1.75
7m_int1	-0.1574	0.1183	2.85
prc_tosyl	-0.1509	0.1643	1.89
7m_int1_tosyl	-0.1648	0.1081	3.42

Table 4.4. The nucleophilic Fukui function (f_k^-), the electrophilic Fukui function (f_k^+), and the local electrophilicity indices (ω_k) at the C1, C2, C3 and C4 carbon atoms, and N5 nitrogen atom of **prc**, **7m_int1**, **prc_tosyl**, and **7m_int1_tosyl** obtained at the M062X/6-31G(d,p) Au SDD level of theory.

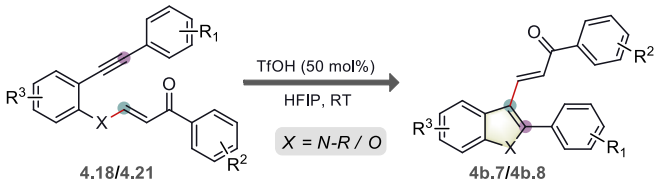
Structure	**Site**	f_-^k (a.u.)	f_+^k (a.u.)	ω_k (eV)
prc	C5	-0 .020	0.097	0.17
	C4	0.021	0.121	0.21
	C3	0.263	0.014	0.02
	C2	-0.007	0.001	0.00
	N1	0.188	-0.004	0.00
7m_int1	C5	0.131	0.015	0.04
	C4	0.075	-0.010	-0.03
	C3	-0.001	-0.021	-0.06
	C2	0.004	0.313	0.89
	N1	0.008	0.120	0.34
prc_tosyl	C5	-0.014	0.039	0.07
	C4	0.010	0.097	0.18
	C3	0.178	0.017	0.03
	C2	0.025	0.041	0.08
	N1	0.128	-0.004	-0.01
7m_int1_tosyl	C5	0.127	0.013	0.05
	C4	0.069	-0.007	-0.02
	C3	-0.002	-0.020	-0.07
	C2	-0.002	0.300	1.03
	N1	0.004	0.079	0.27

4.3.10. Synthesis and Characterization of 3-Substituted Indole and Benzofuran Derivatives (4b.7 and 4b.8):

4.3.10.1. General Synthetic Procedure for the Preparation of 3-Substituted Indole and Benzofuran Derivatives (4b.7 and 4b.8):

General Procedure 8 (GP-8):

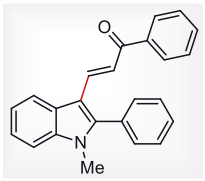
To a mixture of **4.18/4.21** (1 equiv.) in HFIP (0.1 M), 50 mol% TfOH was added under nitrogen atmosphere. Then the reaction mixture was stirred for 3-5 hrs. After the completion of the reaction as mentioned by the TLC, the reaction mixture was quenched with a saturated $NaHCO_3$ solution. Then it was extracted using ethyl acetate and water. The combined organic layers was washed with saturated brine solution and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure. The crude product was purified by column chromatography (using silica gel, EtOAc/hexanes eluent) to get the corresponding functionalized indole/benzofuran **4b.7/4b.8** derivatives in an analytically pure form.



Scheme 4.18. Preparation of 3-substituted indole and benzofuran derivatives (**4b.7** and **4b.8**).

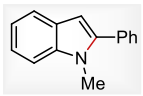
4.3.10.2. Analytical Data of 3-Substituted Indole and Benzofuran Derivatives (4b.7 and 4b.8):

(*E*)-3-(1-methyl-2-phenyl-1*H*-indol-3-yl)-1-phenylprop-2-en-1-one (4b.7aa, Table 4b.2):



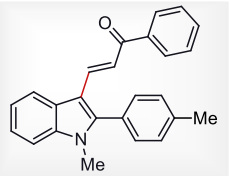
The title compound was prepared following **GP-8** using **4.18aa** (67.5 mg, 0.2 mmol); obtained as yellow solid (61.4 mg, 91%). M.P. = 179 - 180°C. R_f value = 0.44 (10% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.15-8.10 (m, 1H), 8.02 (d, J = 8.1 Hz, 2H), 7.97 (dd, J = 15.2, 2.1 Hz, 1H), 7.62 (d, J = 15.5 Hz, 1H), 7.59 – 7.52 (m, 4H), 7.49 (t, J = 7.6 Hz, 2H), 7.46 – 7.42 (m, 3H), 7.42 – 7.38 (m, 2H), 3.66 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ/ ppm = 190.5, 146.9, 139.4, 139.2, 138.1, 132.0, 130.9, 129.9, 129.4, 128.7, 128.4, 128.2, 125.7, 123.2, 122.0, 120.9, 117.3, 111.4, 110.3, 31.3. IR (neat): ν/ cm^{-1} = 1580, 1560, 1365, 1152, 1128, 1011, 698, 671. HRMS: m/z [M+H]$^+$ calcd for $C_{24}H_{20}NO$: 338.1539, found: 338.1537.

1-methyl-2-phenyl-1*H*-indole (4b.10):



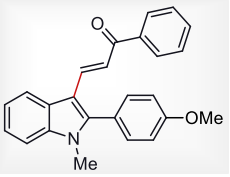
^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.45 – 8.41 (m, 1H), 7.84 – 7.80 (m, 2H), 7.57 – 7.52 (m, 2H), 7.48 (t, J = 7.6 Hz, 2H), 7.39 – 7.33 (m, 3H), 3.85 (s, 3H).

(*E*)-3-(1-methyl-2-(*p*-tolyl)-1*H*-indol-3-yl)-1-phenylprop-2-en-1-one (4b.7ab, Table 4b.2):



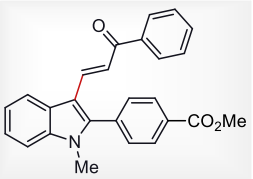
The title compound was prepared following **GP-8** using **4.18ag** (70.3 mg, 0.2 mmol); obtained as yellow solid (62.6 mg, 89%). M.P. = 182 - 183°C. R_f value = 0.31 (10% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.14 – 8.10 (m, 1H), 8.03 (d, *J* = 7.0 Hz, 2H), 7.98 (d, *J* = 15.5 Hz, 1H), 7.62 (d, *J* = 15.5 Hz, 1H), 7.54 (d, *J* = 7.2 Hz, 1H),7.49 (t, *J* = 7.0 Hz, 2H), 7.45 – 7.41 (m, 1H), 7.40 (d, *J* = 2.9 Hz, 1H), 7.39 – 7.30 (m, 5H), 3.66 (s, 3H), 2.48 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ/ ppm = 190.4, 147.3, 139.6, 139.4, 139.3, 139.1, 132.0, 130.8, 129.5, 128.4, 128.2, 126.9, 125.7, 123.1, 121.9, 120.8, 117.0, 111.3, 110.3, 31.2, 21.4. IR (neat): ν/ cm^{-1} = 1652, 1558, 1222, 1176, 1012, 805, 701. HRMS: *m/z* [M+H]$^+$ calcd for $C_{24}H_{22}NO$: 352.1696, found: 352.1696.

(*E*)-3-(2-(4-methoxyphenyl)-1-methyl-1*H*-indol-3-yl)-1-phenylprop-2-en-1-one (4b.7ac, Table 4b.2):



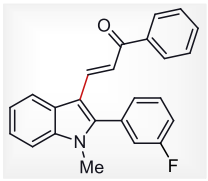
The title compound was prepared following **GP-8** using **4.18ai** (73.5 mg, 0.2 mmol); obtained as yellow solid (67.6 mg, 92%). M.P. = 171 - 172°C. R_f value = 0.59 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.12 – 8.08 (m, 1H), 8.02 (d, *J* = 7.0 Hz, 2H), 7.96 (d, *J* = 15.5 Hz, 1H), 7.60 (d, *J* = 15.5 Hz, 1H), 7.57 – 7.51 (m, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.45 – 7.41 (m, 1H), 7.39 – 7.34 (m,4H), 7.08 (d, *J* = 8.7 Hz, 2H), 3.91 (s, 3H), 3.66 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ/ ppm = 190.5, 160.5, 147.2, 139.7, 139.4, 138.1, 132.3, 132.0, 128.4, 128.3, 125.8, 123.1, 122.0, 121.97, 120.8, 117.0, 114.3, 111.4, 110.3, 55.5, 31.3. IR (neat): ν/ cm^{-1} = 1712, 1557, 1468, 1270, 1115, 1011, 745. HRMS: *m/z* [M+H]$^+$ calcd for $C_{25}H_{22}NO_2$: 368.1645, found: 368.1643.

(*E*)-methyl 4-(1-methyl-3-(3-oxo-3-phenylprop-1-en-1-yl)-1*H*-indol-2-yl)benzoate (4b.7ad, Table 4b.2):



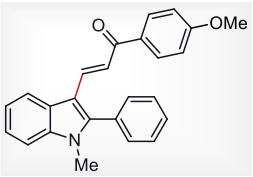
The title compound was prepared following **GP-8** using **4.18ak** (79.1 mg, 0.2 mmol); obtained as yellow solid (64.9 mg, 82%). M.P. = 184 - 185°C. R_f value = 0.34 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.23 (d, *J* = 8.1 Hz, 2H), 8.12 (d, *J* = 7.3 Hz, 1H), 8.00 (d, *J* = 7.5 Hz, 2H), 7.89 (d, *J* = 15.5 Hz, 1H), 7.63 (d, *J* = 15.5 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 3H), 7.51 – 7.44 (m, 3H), 7.44 – 7.36 (m, 2H), 3.99 (s, 3H), 3.68 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ/ ppm = 190.4, 166.5, 145.5, 139.1, 138.7, 138.3, 134.5, 132.2, 131.1, 130.9, 130.0, 128.5, 128.3, 125.6, 123.7, 122.2, 121.1, 118.1, 111.9, 110.4, 52.5, 31.5. IR (neat): ν/ cm^{-1} = 1735, 1562, 1515, 1342, 1219, 1010, 743. HRMS: *m/z* [M+H]$^+$ calcd for $C_{26}H_{22}NO_3$: 396.1594, found: 396.1598.

(*E*)-3-(2-(3-fluorophenyl)-1-methyl-1*H*-indol-3-yl)-1-phenylprop-2-en-1-one (4b.7ae, Table 4b.2):



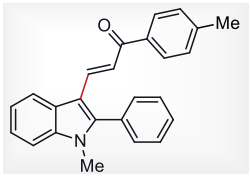
The title compound was prepared following **GP-8** using **4.18am** (71.1 mg, 0.2 mmol); obtained as yellow solid (61.8 mg, 87%). M.P. = 163 - 164°C. R_f value = 0.48 (10% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.11 (d, *J* = 6.9 Hz, 1H), 8.01 (d, *J* = 7.0 Hz, 2H), 7.90 (d, *J* = 15.6 Hz, 1H), 7.62 (d, *J* = 15.6 Hz, 1H), 7.57 - 7.52 (m, 2H), 7.51 – 7.46 (m, 2H), 7.46 – 7.44 (m, 1H), 7.42 – 7.36 (m, 2H), 7.23 (d, *J* = 8.2 Hz, 2H), 7.16 (dt, *J* = 9.1, 2.0 Hz, 1H), 3.67 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ/ ppm = 190.6, 162.7 (d, *J* = 248.2 Hz), 145.0, 138.8, 138.7 (d, *J* = 96.3 Hz), 132.2, 132.0, 130.5 (d, *J* = 8.5 Hz), 128.7, 128.4 (d, *J* = 21.1 Hz), 128.1, 127.0, 125.6, 123.6, 122.2, 121.0, 118.0, 118.0 (d, *J* = 21.8 Hz), 116.6 (d, *J* = 20.8 Hz), 111.7, 110.4, 31.4. ^{19}F NMR (470 MHz, $CDCl_3$) δ/ ppm = -111.6. IR (neat): ν/ cm^{-1} = 1738, 1555, 1444, 1177, 1215, 1012, 741. HRMS: *m/z* $[M+H]^+$ calcd for $C_{24}H_{19}FNO$: 356.1445, found: 356.1446.

(*E*)-1-(4-methoxyphenyl)-3-(1-methyl-2-phenyl-1*H*-indol-3-yl)prop-2-en-1-one (4b.7af, Table 4b.2):



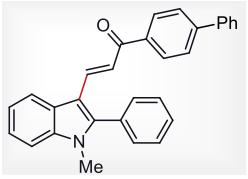
The title compound was prepared following **GP-8** using **4.18an** (73.5 mg, 0.2 mmol); obtained as yellow solid (66.9 mg, 91%). M.P. = 181 - 182°C. R_f value = 0.68 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.14 – 8.10 (m, 1H), 8.03 (d, *J* = 8.6 Hz, 2H), 7.94 (d, *J* = 15.5 Hz, 1H), 7.62 (d, *J* = 15.5 Hz, 1H), 7.58 – 7.51 (m, 3H), 7.44 (d, *J* = 8.0 Hz, 3H), 7.42 - 7.37 (m, 2H), 6.98 (d, *J* = 8.6 Hz, 2H), 3.88 (s, 3H), 3.66 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ/ ppm = 188.8, 162.9, 146.5, 138.5, 138.1, 132.1, 131.0, 130.4, 130.1, 129.3, 128.8, 125.8, 123.2, 121.9, 120.8, 117.3, 113.7, 111.4, 110.3, 55.4, 31.2. IR (neat): ν/ cm^{-1} = 1646, 1598, 1461, 1369, 1282, 1160, 787, 696. HRMS: *m/z* $[M+H]^+$ calcd for $C_{25}H_{22}NO_2$: 368.1645, found: 368.1645.

(*E*)-3-(1-methyl-2-phenyl-1*H*-indol-3-yl)-1-(*p*-tolyl)prop-2-en-1-one (4b.7ag, Table 4b.2):



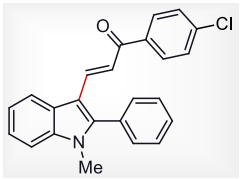
The title compound was prepared following **GP-8** using **4.18ao** (70.3 mg, 0.2 mmol); obtained as yellow solid (64.7 mg, 92%). M.P. = 178 - 179°C. R_f value = 0.61 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.15 – 8.10 (m, 1H), 8.00 – 7.92(m, 3H), 7.62 (d, *J* = 15.5 Hz, 1H), 7.58 – 7.52 (m, 3H), 7.46 – 7.42 (m, 3H), 7.42 – 7.37 (m, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 3.65 (s, 3H), 2.44 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ/ ppm = 189.9, 146.6, 142.7, 138.9, 138.1, 136.6, 130.9, 130.0, 129.3, 129.1, 128.7, 128.3, 125.7, 123.2, 121.9, 120.8, 117.3, 111.4, 110.3, 31.2, 21.6. IR (neat): ν/ cm^{-1} = 1649, 1558, 1362, 1277, 1176, 805, 701. HRMS: *m/z* $[M+H]^+$ calcd for $C_{25}H_{22}NO$: 352.1696, found: 352.1696.

(*E*)-1-([1,1'-biphenyl]-4-yl)-3-(1-methyl-2-phenyl-1*H*-indol-3-yl)prop-2-en-1-one (4b.7ah, Table 4b.2):



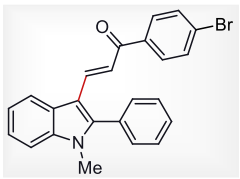
The title compound was prepared following **GP-8** using **4.18as** (82.7 mg, 0.2 mmol); obtained as yellow solid (74.4 mg, 90%). M.P. = 188 - 189°C. R_f value = 0.39 (20% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.19 – 8.15 (m, 1H), 8.12 (d, *J* = 8.2 Hz, 2H), 8.03 (d, *J* = 15.5 Hz, 1H), 7.73 (d, *J* = 8.3 Hz, 2H), 7.71 – 7.66 (m, 3H), 7.60 – 7.54 (m, 3H), 7.53 – 7.41 (m, 8H), 3.66 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ/ ppm = 189.8, 146.9, 144.7, 140.1, 139.3, 138.1, 137.9, 130.9, 129.9, 129.3, 128.9, 128.8, 128.7, 128.0, 127.2, 127.1, 125.7, 123.2, 122.0, 120.9, 117.1, 111.4, 110.3, 31.2. IR (neat): ν/ cm^{-1} = 1652, 1562, 1367, 1283, 1221, 1005, 730, 696. HRMS: *m/z* [M+H]$^+$ calcd for $C_{30}H_{24}NO$: 414.1852, found: 414.1852.

(*E*)-1-(4-chlorophenyl)-3-(1-methyl-2-phenyl-1*H*-indol-3-yl)prop-2-en-1-one (4b.7ai, Table 4b.2):



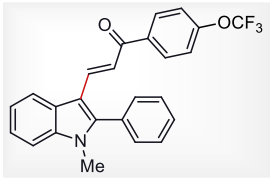
The title compound was prepared following **GP-8** using **4.18at** (74.3 mg, 0.2 mmol); obtained as yellow solid (66.1 mg, 89%). M.P. = 169 - 170°C. R_f value = 0.28 (10% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.11 – 8.07 (m, 1H), 7.99 – 7.91 (m, 3H), 7.56 – 7.50 (m, 4H), 7.46 – 7.37 (m, 7H), 3.64 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ/ ppm = 188.9, 147.1, 139.8, 138.2, 138.1, 137.5, 130.9, 129.8, 129.6, 129.4, 128.7, 128.6, 125.6, 123.3, 122.0, 120.8, 116.4, 111.3, 110.3, 31.2. IR (neat): ν/ cm^{-1} = 1642, 1553, 1363, 1275, 1007, 809, 724, 652. HRMS: *m/z* [M+H]$^+$ calcd for $C_{24}H_{19}ClNO$: 372.1150, found: 372.1151.

(*E*)-1-(4-bromophenyl)-3-(1-methyl-2-phenyl-1*H*-indol-3-yl)prop-2-en-1-one (4b.7aj, Table 4b.2):



The title compound was prepared following **GP-8** using **4.18au** (83.3 mg, 0.2 mmol); obtained as yellow solid (72.4 mg, 87%). M.P. = 173 - 174°C. R_f value = 0.23 (10% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.10 – 8.07 (m, 1H), 7.96 (d, *J* = 15.4 Hz, 1H), 7.85 (d, *J* = 8.3 Hz, 2H), 7.60 (d, *J* = 8.3 Hz, 2H), 7.57 – 7.52 (m, 3H), 7.51 (d, *J* = 15.5 Hz, 1H), 7.44 – 7.37 (m, 5H), 3.65 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ/ ppm = 189.1, 147.1, 139.9, 138.1, 138.0, 131.6, 130.9, 129.9, 129.8, 129.4, 128.8, 126.9, 125.7, 123.3, 122.1, 120.8, 116.6, 111.4, 110.3, 31.3. IR (neat): ν/ cm^{-1} = 1649, 1550, 1283, 1068, 1005, 805, 724, 668. HRMS: *m/z* [M+H]$^+$ calcd for $C_{24}H_{19}BrNO$: 416.0645, found: 416.0645.

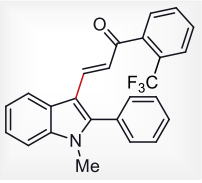
(*E*)-3-(1-methyl-2-phenyl-1*H*-indol-3-yl)-1-(4-(trifluoromethoxy)phenyl)prop-2-en-1-one (4b.7ak, Table 4b.2):



The title compound was prepared following **GP-8** using **4.18ar** (84.3 mg, 0.2 mmol); obtained as yellow solid (70.8 mg, 84%). M.P. = 173 - 174°C. R_f value = 0.58 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.09 (d, *J* = 8.6 Hz, 1H), 8.03 (d, *J* = 8.8 Hz, 2H), 7.94 (d, *J* = 15.5 Hz, 1H), 7.58 – 7.51 (m, 4H), 7.47- 7.42 (m, 3H), 7.42 – 7.36 (m,

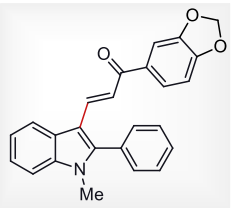
2H), 7.30 (d, *J* = 8.0 Hz, 2H), 3.68 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) *δ*/ ppm = 189.0, 151.8, 147.3, 140.2, 138.2, 137.6, 131.0, 130.1, 129.9, 129.5, 128.8, 125.7, 123.4, 122.2, 120.9, 120.4, 120.4 (q, *J* = 259.7 Hz), 116.7, 111.4, 110.4, 31.4. ^{19}F NMR (376 MHz, $CDCl_3$) *δ*/ ppm = -57.6. IR (neat): ν/ cm^{-1} = 1646, 1556, 1255, 1153, 1012, 802, 697. HRMS: *m/z* $[M+H]^+$ calcd for $C_{25}H_{19}F_3NO_2$: 422.1362, found: 422.138.

(*E*)-3-(1-methyl-2-phenyl-1*H*-indol-3-yl)-1-(2-(trifluoromethyl)phenyl)prop-2-en-1-one (4b.7al, Table 4b.2):



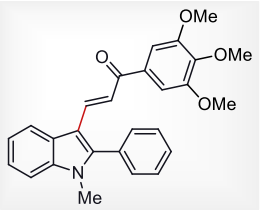
The title compound was prepared following **GP-8** using **4.18av** (81.1 mg, 0.2 mmol); obtained as yellow solid (66.5 mg, 82%). M.P. = 169 - 170°C. R_f value = 0.49 (20% EtOAc in hexane). ^1H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 8.00 (d, *J* = 7.7 Hz, 1H), 7.67 (d, *J* = 7.8 Hz, 1H), 7.53 (t, *J* = 6.8 Hz, 1H), 7.49 (d, *J* = 7.6 Hz, 1H), 7.47 – 7.44 (m, 3H), 7.43 - 7.39 (m, 3H), 7.38 – 7.29 (m, 4H), 7.10 (d, *J* = 16.0 Hz, 1H), 3.66 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) *δ*/ ppm = 195.2, 147.3, 142.6, 140.1, 138.2, 131.4, 130.8, 129.4, 129.38, 129.1, 128.6, 128.2, 127.5 (q, *J* = 32.8 Hz), 126.4, 125.4, 125.1, 123.5, 122.3, 121.8, 120.9, 110.9, 110.3, 31.4. ^{19}F NMR (376 MHz, $CDCl_3$) *δ*/ ppm = -61.3. IR (neat): ν/ cm^{-1} = 1599, 1467, 1368, 1259, 1122, 1031, 699. HRMS: *m/z* $[M+H]^+$ calcd for $C_{25}H_{19}F_3NO$: 406.1413, found: 406.1413.

(*E*)-1-(benzo[*d*][1,3]dioxol-5-yl)-3-(1-methyl-2-phenyl-1*H*-indol-3-yl)prop-2-en-1-one (4b.7am, Table 4b.2):



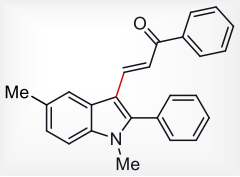
The title compound was prepared following **GP-8** using **4.18az** (76.3 mg, 0.2 mmol); obtained as yellow solid (67.9 mg, 89%). M.P. = 161 - 162°C. R_f value = 0.51 (30% EtOAc in hexane). ^1H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 8.11 – 8.08 (m, 1H), 7.92 (d, *J* = 15.5 Hz, 1H), 7.63 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.57 – 7.50 (m, 5H), 7.46 – 7.42 (m, 3H), 7.41 - 7.35 (m, 2H), 6.88 (d, *J* = 8.1 Hz, 1H), 6.05 (s, 2H), 3.67 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) *δ*/ ppm = 188.5, 151.1, 148.1, 146.7, 138.9, 138.2, 134.1, 131.0, 130.1, 129.4, 128.8, 125.8, 124.1, 123.3, 122.0, 120.9, 117.1, 111.5, 110.3, 108.4, 107.9, 101.7, 31.3. IR (neat): ν/ cm^{-1} = 1738, 1553, 1437, 1237, 1109, 840, 751. HRMS: *m/z* $[M+H]^+$ calcd for $C_{25}H_{20}NO_3$: 382.1438, found: 382.1437.

(*E*)-3-(1-methyl-2-phenyl-1*H*-indol-3-yl)-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (4b.7an, Table 4b.2):



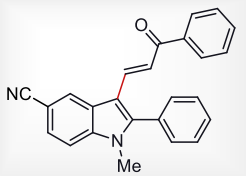
The title compound was prepared following **GP-8** using **4.18ba** (85.5 mg, 0.2 mmol); obtained as yellow solid (76.9 mg, 90%). M.P. = 178 - 179°C. R_f value = 0.35 (40% EtOAc in hexane). ^1H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 8.07 (d, *J* = 8.1 Hz, 1H), 7.95 (d, *J* = 15.5 Hz, 1H), 7.58 – 7.52 (m, 3H), 7.48 - 7.43 (m, 4H), 7.42 – 7.34 (m, 2H), 7.21 (s, 2H), 3.92 (s, 9H), 3.67 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) *δ*/ ppm = 189.6, 153.0, 146.4, 141.8, 139.2, 138.1, 134.7, 130.9, 130.3, 129.4, 128.9, 126.0, 123.3, 122.0, 120.6, 117.4, 111.3, 110.3, 105.9, 61.0, 56.4, 31.3. IR (neat): ν/ cm^{-1} = 1640, 1551, 1326, 1122, 1009, 812, 699. HRMS: *m/z* $[M+H]^+$ calcd for $C_{27}H_{26}NO_4$: 428.1856, found: 428.1856.

(*E*)-3-(1,5-dimethyl-2-phenyl-1*H*-indol-3-yl)-1-phenylprop-2-en-1-one (4b.7ao, Table 4b.2):



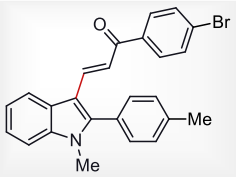
The title compound was prepared following **GP-8** using **4.18ac** (70.3 mg, 0.2 mmol); obtained as yellow solid (66.1 mg, 94%). M.P. = 162- 163°C. R_f value = 0.43 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.00 – 7.96 (m, 2H), 7.92 (d, *J* = 15.5 Hz, 1H), 7.88 (s, 1H), 7.57-7.51 (m, 5H), 7.50 – 7.45 (m, 2H), 7.43 (dd, *J* = 7.5, 1.9 Hz, 2H), 7.33 (d, *J* = 8.3 Hz, 1H), 7.21 (dd, *J* = 8.3, 1.0 Hz, 1H), 3.64 (s, 3H), 2.58 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ/ ppm = 190.9, 147.0, 139.8, 139.4, 136.6, 132.0, 131.6, 131.0, 130.1, 129.4, 128.8, 128.4, 128.3, 126.0, 124.8, 120.8, 117.3, 111.0, 110.0, 31.4, 21.9. IR (neat): ν/ cm^{-1} = 1552, 1530, 1281, 1218, 1013, 736, 699. HRMS: *m/z* [M+H]$^+$ calcd for $C_{25}H_{22}NO$: 352.1696, found: 352.1700.

(*E*)-1-methyl-3-(3-oxo-3-phenylprop-1-en-1-yl)-2-phenyl-1*H*-indole-5-carbonitrile (4b.7ap, Table 4b.2):



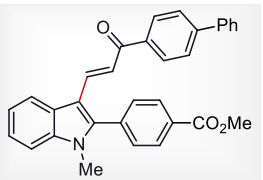
The title compound was prepared following **GP-8** using **4.18af** (72.5 mg, 0.2 mmol); obtained as yellow solid (58 mg, 80%). M.P. = 163 - 164°C. R_f value = 0.33 (30% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.41 (d, *J* = 0.9 Hz, 1H), 8.02 – 7.99 (m, 2H), 7.88 (d, *J* = 15.7 Hz, 1H), 7.63 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.60-7.56 (m, 4H), 7.55 – 7.48 (m, 4H), 7.46 – 7.42 (m, 2H), 3.70 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ/ ppm = 19.1, 148.2, 139.6, 138.7, 137.6, 134.6, 132.6, 130.9, 130.0, 129.1, 128.7, 128.3, 126.2, 126.0, 125.6, 125.4, 120.4, 118.9, 111.7, 111.1, 104.9, 31.6. IR (neat): ν/ cm^{-1} = 1642, 1556, 1255, 1153, 1012, 696. HRMS: *m/z* [M+H]$^+$ calcd for $C_{25}H_{19}N_2O$: 363.1492, found: 363.1494.

(*E*)-1-(4-bromophenyl)-3-(1-methyl-2-(p-tolyl)-1*H*-indol-3-yl)prop-2-en-1-one (4b.7aq, Table 4b.2):



The title compound was prepared following **GP-8** using **4.18bc** (86.1 mg, 0.2 mmol); obtained as yellow solid (80.1 mg, 93%). M.P. = 176 - 177°C. R_f value = 0.29 (15% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.09 – 8.06 (m, 1H), 7.96 (d, *J* = 15.4 Hz, 1H), 7.86 (d, *J* = 8.2 Hz, 2H), 7.60 (d, *J* = 8.3 Hz, 2H), 7.51 (d, *J* = 15.5 Hz, 1H), 7.42 – 7.34 (m, 5H), 7.31 (d, *J* = 7.9 Hz, 2H), 3.65 (s, 3H), 2.48 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ/ ppm = 189.1, 147.6, 140.2, 139.5, 138.1, 138.0, 131.6, 130.8, 129.8, 129.5, 126.8, 126.75, 125.7, 123.2, 122.0, 120.8, 116.2, 111.3, 110.3, 31.3, 21.4. IR (neat): ν/ cm^{-1} = 1642, 1550, 1463, 1282, 1068, 1005, 805, 724. HRMS: *m/z* [M+H]$^+$ calcd for $C_{25}H_{21}BrNO$: 430.0801, found: 430.0801.

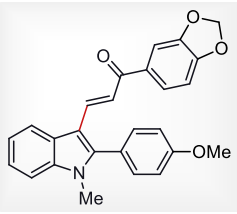
(*E*)-methyl 4-(3-(3-([1,1'-biphenyl]-4-yl)-3-oxoprop-1-en-1-yl)-1-methyl-1*H*-indol-2-yl)benzoate (4b.7ar, Table 4b.2):



The title compound was prepared following **GP-8** using **4.18bf** (94.3 mg, 0.2 mmol); obtained as yellow solid (80.2 mg, 85%). M.P. = 181 - 182°C. R_f value = 0.41 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.24 (d, *J* = 8.1 Hz, 2H), 8.14 (dd, *J* = 6.1, 2.0 Hz, 1H),

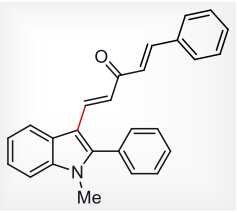
8.08 (d, *J* = 8.2 Hz, 2H), 7.92 (d, *J* = 15.5 Hz, 1H), 7.70 (t, *J* = 8.1 Hz, 2H), 6.67 – 6.63 (m, 3H), 7.55 (d, *J* = 8.1 Hz, 2H), 7.51 – 7.44 (m, 3H), 7.42 – 7.38 (m, 3H), 3.99 (s, 3H), 3.68 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) *δ*/ ppm = 189.9, 166.5, 145.2, 144.9, 140.2, 138.6, 138.4, 137.8, 134.6, 131.1, 131.0, 130.0, 129.0, 128.9, 128.1, 127.3, 127.2, 125.7, 123.7, 122.2, 121.1, 118.1, 112.0, 110.4, 52.4, 31.4. IR (neat): ν/ cm^{-1} = 1716, 1563, 1466, 1274, 1105, 1012,732. HRMS: *m/z* $[M+H]^+$ calcd for $C_{32}H_{26}NO_3$: 472.1907, found: 472.1908.

(*E*)-1-(benzo[*d*][1,3]dioxol-5-yl)-3-(2-(4-methoxyphenyl)-1-methyl-1*H*-indol-3-yl)prop-2-en-1-one (4b.7as, Table 4b.2):



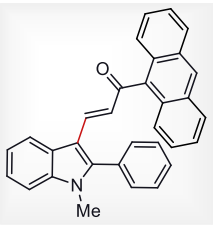
The title compound was prepared following **GP-8** using **4.18bh** (82.3 mg, 0.2 mmol); obtained as yellow solid (74.5 mg, 91%). M.P. = 163 - 164°C. R_f value = 0.46 (10% EtOAc in hexane). ^1H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 8.10 – 8.06 (m, 1H), 7.92 (d, *J* = 15.4 Hz, 1H), 7.64 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.54 (d, *J* = 15.4 Hz, 2H), 7.44 – 7.40 (m, 1H), 7.39 – 7.34 (m, 4H), 7.07 (d, *J* = 8.7 Hz, 2H), 6.89 (d, *J* = 8.1 Hz, 1H), 6.05 (s, 2H), 3.91 (s, 3H), 3.66 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) *δ*/ ppm = 188.4, 160.5, 151.0, 148.1, 146.9, 139.2, 138.1, 134.1, 132.3, 125.8, 124.0, 123.1, 122.0, 121.9, 120.8, 116.6, 114.3, 111.3, 110.2, 108.4, 107.8, 101.7, 55.5, 31.3. IR (neat): ν/ cm^{-1} = 1744, 1552, 1437, 1278,1236, 1030, 840, 735. HRMS: *m/z* $[M+H]^+$ calcd for $C_{26}H_{22}NO_4$: 412.1543, found: 412.1548.

(1*E*,4*E*)-1-(1-methyl-2-phenyl-1*H*-indol-3-yl)-5-phenylpenta-1,4-dien-3-one (4b.7at, Table 4b.2):



The title compound was prepared following **GP-8** using **4.18bm** (72.7 mg, 0.2 mmol); obtained as yellow solid (62.5 mg, 86%). M.P. = 168 - 169°C. R_f value = 0.31 (25% EtOAc in hexane). ^1H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 8.11(d, *J* = 8.6 Hz, 1H), 7.85 (d, *J* = 15.8 Hz, 1H), 7.66 (d, *J* = 15.9 Hz, 1H), 7.60 – 7.53 (m, 5H), 7.46 – 7.43 (m,3H), 7.42 – 7.34 (m, 5H), 7.14 (d, *J* = 15.7 Hz, 1H), 7.01 (d, *J* = 15.9 Hz, 1H), 3.67 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) *δ*/ ppm = 189.0, 146.7, 141.6, 138.2, 138.16, 135.4, 131.0, 130.1, 130.0, 129.5, 128.9, 128.8, 128.3, 126.6, 125.8, 123.3, 122.0, 121.4, 121.0, 111.3, 110.3, 31.3. IR (neat): ν/ cm^{-1} = 1610,1559, 1368, 1269, 1098, 984, 818, 733. HRMS: *m/z* $[M+H]^+$ calcd for $C_{26}H_{22}NO$: 364.1696, found: 364.1697.

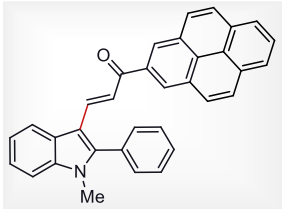
(*E*)-1-(anthracen-9-yl)-3-(1-methyl-2-phenyl-1*H*-indol-3-yl)prop-2-en-1-one (4b.7au, Table 4b.2):



The title compound was prepared following **GP-8** using **4.18bk** (87.5 mg, 0.2 mmol); obtained as yellow solid (74.4 mg, 85%). M.P. = 171 - 172°C. R_f value = 0.53 (25% EtOAc in hexane). ^1H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 8.41(s, 1H), 8.05 (d, *J* = 7.4 Hz, 1H), 8.04 - 7.98 (m, 4H), 7.49 – 7.42 (m, 4H), 7.41 – 7.30 (m, 5H), 7.23 (t, *J* = 7.5 Hz, 1H), 7.07 (d, *J* = 7.8 Hz, 2H), 6.95 (d, *J* = 7.2 Hz, 2H), 3.60 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) *δ*/ ppm = 200.1, 147.0, 143.9, 138.3, 135.5, 131.1, 130.6, 129.0, 128.8, 128.5, 128.4, 128.2, 127.7, 127.3, 126.1,

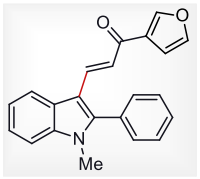
125.9, 125.3, 124.8, 123.5, 122.3, 121.0, 110.9, 110.3, 31.4. IR (neat): ν/ cm^{-1} = 1673, 1589, 1468, 1196, 1069, 821,731, 699. HRMS: *m/z* $[M]^+$ calcd for $C_{32}H_{24}NO$: 438.1852, found: 438.1852.

(*E*)-3-(1-methyl-2-phenyl-1*H*-indol-3-yl)-1-(pyren-2-yl)prop-2-en-1-one (4b.7av, Table 4b.2):



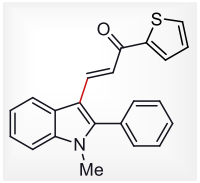
The title compound was prepared following **GP-8** using **4.18bl** (92.3 mg, 0.2 mmol); obtained as yellow solid (75.7 mg, 82%). M.P. = 175 - 176°C. R_f value = 0.38 (20% EtOAc in hexane). ^1H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 8.61 (d, *J* = 9.3 Hz, 1H), 8.20 – 8.14 (m, 2H), 8.12 (d, *J* = 9.3 Hz, 1H), 8.10 – 8.07 (m, 2H), 8.05 (t, *J* = 7.6 Hz, 1H), 7.72 (d, *J* = 15.9 Hz, 1H), 7.52 (d, *J* = 15.9 Hz, 1H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.40 – 7.25 (m, 7H), 3.65 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) *δ*/ ppm = 196.4, 147.1, 141.2, 138.2, 135.6, 132.7, 131.3, 130.8, 130.77, 129.6, 129.2, 129.1, 129.6, 128.5, 128.4, 127.3, 126.2, 126.0, 125.8, 125.7, 125.3, 124.9, 124.6, 124.3, 123.4, 123.0, 122.8, 122.2, 121.0, 111.3, 110.3, 31.4. IR (neat): ν/ cm^{-1} = 1738, 1649, 1563, 1365, 1365, 1253, 1014, 742, 697. HRMS: *m/z* $[M]^+$ calcd for $C_{34}H_{24}NO$: 462.1852, found: 462.1850.

(*E*)-1-(furan-3-yl)-3-(1-methyl-2-phenyl-1*H*-indol-3-yl)prop-2-en-1-one (4b.7aw, Table 4b.2):



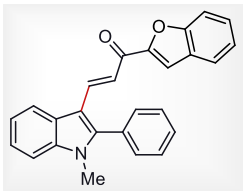
The title compound was prepared following **GP-8** using **4.18bt** (65.5 mg, 0.2 mmol); obtained as yellow solid (56.3 mg, 86%). M.P. = 166 - 167°C. R_f value = 0.57 (20% EtOAc in hexane). ^1H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 8.15 – 8.11 (m, 1H), 7.95 (d, *J* = 15.7 Hz, 1H), 7.61 (d, *J* = 1.6 Hz, 1H), 7.55 (d, *J* = 7.0 Hz, 3H), 7.50 (d, *J* = 15.7 Hz, 1H), 7.44 – 7.41 (m, 3H), 7.40 – 7.36 (m, 2H), 7.22 (d, *J* = 3.5 Hz, 1H), 6.55 (dd, *J* = 3.5, 1.7 Hz, 1H), 3.65 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) *δ*/ ppm = 178.6, 154.4, 147.0, 145.7, 138.5, 138.1, 130.9, 129.9, 129.4, 128.7, 125.7, 123.2, 122.0, 120.9, 116.7, 116.0, 112.2, 111.3, 110.3, 31.3. IR (neat): ν/ cm^{-1} = 1615, 1565, 1462, 1364, 1229, 1067, 872, 711. HRMS: *m/z* $[M+H]^+$ calcd for $C_{22}H_{18}NO_2$: 328.1332, found: 328.1333.

(*E*)-3-(1-methyl-2-phenyl-1*H*-indol-3-yl)-1-(thiophen-2-yl)prop-2-en-1-one (4b.7ax, Table 4b.2):



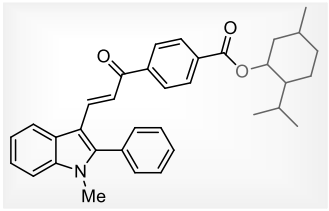
The title compound was prepared following **GP-8** using **4.18bu** (68.7 mg, 0.2 mmol); obtained as yellow solid (57 mg, 83%). M.P. = 162 - 163°C. R_f value = 0.51 (25% EtOAc in hexane). ^1H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 8.11 – 8.09 (m, 1H), 7.94 (d, *J* = 15.4 Hz, 1H), 7.79 (d, *J* = 3.6 Hz, 1H), 7.60 (d, *J* = 7.4 Hz, 1H), 7.58 – 7.52 (m, 3H), 7.48 (s, 1H), 7.46 – 7.42 (m, 3H), 7.41 – 7.36 (m, 2H), 7.16 (t, *J* = 4.2 Hz, 1H), 3.63 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) *δ*/ ppm = 182.4, 146.9, 146.6, 138.6, 138.2, 132.6, 131.0, 130.6, 130.0, 129.5, 128.8, 128.0, 125.9, 123.3, 122.1, 120.8, 117.2, 111.3, 110.3, 31.3. IR (neat): ν/ cm^{-1} = 1639, 1365, 1278, 1061, 735, 703, 640. HRMS: *m/z* $[M+H]^+$ calcd for $C_{22}H_{18}NOS$: 344.1104, found: 344.1104.

(*E*)-1-(benzofuran-2-yl)-3-(1-methyl-2-phenyl-1*H*-indol-3-yl)prop-2-en-1-one (4b.7ay, Table 4b.2):



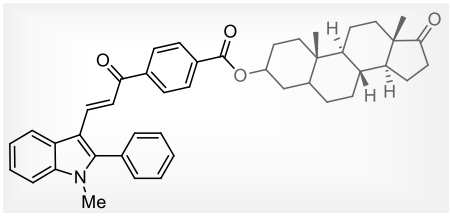
The title compound was prepared following **GP-8** using **4.18bv** (75.5 mg, 0.2 mmol); obtained as yellow solid (67.2 mg, 89%). M.P. = 166 - 167°C. R_f value = 0.47 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.21 – 8.18 (m, 1H), 8.03 (d, *J* = 15.6 Hz, 1H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.66 – 7.61 (m, 2H), 7.59 – 7.53 (m, 4H), 7.49 – 7.40 (m, 6H), 7.31 (t, *J* = 7.2 Hz, 1H), 3.67 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ/ ppm = 180.1, 155.6, 154.7, 147.6, 139.3, 138.2, 131.0, 129.8, 129.5, 128.8, 127.6, 127.5, 125.8, 123.6, 123.4, 123.0, 122.2, 121.1, 116.7, 112.4, 111.7, 111.5, 110.4, 31.4. IR (neat): ν/ cm^{-1} = 1738, 1568, 1368, 1287, 1050, 737. HRMS: *m/z* [M+H]$^+$ calcd for $C_{26}H_{20}NO_2$: 378.1489, found: 378.1486.

(*E*)-2-isopropyl-5-methylcyclohexyl-4-(3-(1-methyl-2-phenyl-1*H*-indol-3-yl)acryloyl) benzoate (4b.7az, Table 4b.2):



The title compound was prepared following **GP-8** using **4.18cf** (103.9 mg, 0.2 mmol); obtained as yellow solid (76.9 mg, 74%). M.P. = 158 - 159°C. R_f value = 0.34 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.15 (d, *J* = 8.2 Hz, 2H), 8.10 (dd, *J* = 5.8, 3.1 Hz, 1H), 8.03 (d, *J* = 8.4 Hz, 2H), 7.96 (d, *J* = 15.5 Hz, 1H), 7.58 – 7.53 (m, 4H), 7.45 – 7.37 (m, 5H), 4.98 (td, *J* = 10.9, 4.4 Hz, 1H), 3.65 (s, 3H), 2.17 (d, *J* = 11.8 Hz, 1H), 2.02 – 1.96 (, 1H), 1.75 (d, *J* = 10.7 Hz, 2H), 1.60 (t, *J* = 11.7 Hz, 2H), 1.29 – 1.10 (m, 3H), 0.96 (d, *J* = 6.7 Hz, 6H), 0.83 (d, *J* = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ/ ppm = 189.8, 165.5, 147.3, 142.7, 140.2, 138.1, 133.5, 130.5, 129.8, 129.6, 129.4, 128.8, 128.0, 125.7, 123.4, 122.1, 120.8, 116.9, 114.4, 110.4, 45.2, 47.2, 40.9, 34.3, 31.4, 31.3, 26.5, 23.6, 22.0, 20.8, 16.5. IR (neat): ν/ cm^{-1} = 1714, 1581, 1367, 1270, 1215, 1113, 710. HRMS: *m/z* [M+H]$^+$ calcd for $C_{35}H_{38}NO_3$: 520.2846, found: 520.2849.

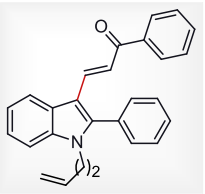
(8*R*,9*S*,10*S*,13*S*,14*S*)-10,13-dimethyl-17-oxohexadecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl-4-((*E*)-3-(1-methyl-2-phenyl-1*H*-indol-3-yl)acryloyl)benzoate (4b.7ba, Table 4b.2):



The title compound was prepared following **GP-8** using **4.18ci** (130.7 mg, 0.2 mmol); obtained as yellow solid (91.5 mg, 70%). M.P. = 162 - 163°C. R_f value = 0.62 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.14 – 8.07 (m, 3H), 8.01 (d, *J* = 8.7 Hz, 2H), 7.95 (d, *J* = 15.5 Hz, 1H), 7.57 – 7.52 (m, 4H), 7.47 – 7.37 (m, 5H), 5.01 – 4.92 (m, 1H), 3.67(s, 3H), 2.44 (dd, *J* = 19.2, 8.7 Hz, 1H), 2.12 – 2.03 (m, 1H), 2.00 – 1.90 (m, 2H), 1.81 (d, *J* = 12.4 Hz, 3H), 1.69(d, *J* = 12.9 Hz, 3H), 1.59 – 1.47 (m, 3H), 1.24 (d, *J* = 15.1 Hz, 1H), 1.40 – 1.31 (m, 2H), 1.29 (d, *J* = 10.8 Hz, 2H), 1.26 (s, 1H), 1.17 – 1.08 (m, 1H), 1.05 – 0.99 (m, 1H), 0.91 (s, 3H), 0.87 (s, 3H), 0.76 (td, *J* = 11.9, 4.1 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ/ ppm = 221.3, 189.9, 165.5, 147.4, 142.7, 140.3, 138.1, 133.6, 130.9, 129.8, 129.6, 129.5, 128.8, 128.0, 125.7, 123.4, 122.2, 120.9, 117.0, 111.4, 110.4, 74.6, 54.3, 51.4, 47.8, 44.7, 36.8, 35.9, 35.7,

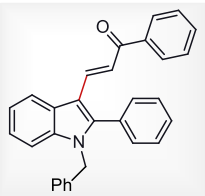
35.1, 34.0, 31.5, 31.4, 30.8, 28.3, 27.5, 21.8, 20.5, 13.8, 12.3. IR (neat): ν/ cm^{-1} = 1712, 1557, 1217, 1011, 745, 701. HRMS: *m/z* $[M+H]^+$ calcd for $C_{44}H_{48}NO_4$: 654.3578, found: 654.3581.

(*E*)-3-(1-(but-3-en-1-yl)-2-phenyl-1*H*-indol-3-yl)-1-phenylprop-2-en-1-one (4b.7bb, Table 4b.2):



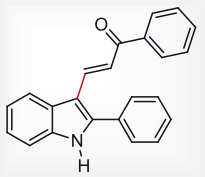
The title compound was prepared following **GP-8** using **4.18bz** (75.5 mg, 0.2 mmol); obtained as yellow solid (61.2 mg, 81%). M.P. = 177 - 178°C. R_f value = 0.59 (20% EtOAc in hexane). ^1H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 8.13 – 8.09 (m, 1H), 7.99 (d, *J* = 7.1 Hz, 2H), 7.88 (d, *J* = 15.6 Hz, 1H), 7.59 – 7.51 (m, 5H), 7.47 (t, *J* = 7.7 Hz, 3H), 7.45 – 7.41 (m, 2H), 7.40 – 7.35 (m, 2H), 5.58 (ddt, *J* = 13.8, 10.2, 6.8 Hz, 1H), 4.99 – 4.91 (m, 2H), 4.13 (t, *J* = 7.5 Hz, 2H), 2.42 (q, *J* = 7.4 Hz, 2H). $^{13}C\{^1H\}$ NMR (126MHz, $CDCl_3$) *δ*/ ppm = 190.5, 146.6, 139.3, 137.2, 133.9, 132.1, 130.9, 130.3, 129.5, 128.8,128.4, 128.3, 126.0, 123.2, 122.0, 121.0, 117.7, 117.4, 111.8, 110.7, 49.0, 46.6, 43.8, 34.0. IR (neat): ν/ cm^{-1} = 1649, 1563, 1364, 1281, 1219, 1014, 742. HRMS: *m/z* $[M+H]^+$ calcd for $C_{27}H_{24}NO$: 378.1852, found: 378.1852.

(*E*)-3-(1-benzyl-2-phenyl-1*H*-indol-3-yl)-1-phenylprop-2-en-1-one (4b.7bc, Table 4b.2):



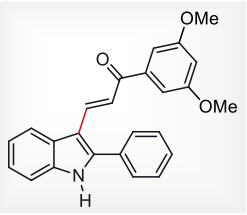
The title compound was prepared following **GP-8** using **4.18ca** (82.7 mg, 0.2 mmol); obtained as yellow solid (72.8 mg, 88%). M.P. = 186 - 187°C. R_f value = 0.71 (20% EtOAc in hexane). ^1H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 8.14 (d, *J* = 8.0 Hz, 1H), 8.00 (d, *J* = 7.1 Hz, 2H), 7.96 (d, *J* = 15.6 Hz, 1H), 7.63 (d, *J* = 15.6 Hz, 1H), 7.57 – 7.52 (m, 1H), 7.51 – 7.44 (m, 5H), 7.40 – 7.33 (m, 3H), 7.30 – 7.27 (m, 2H), 7.26 (s, 1H), 7.25 – 7.23 (m, 2H), 7.97 (d, *J* = 6.3 Hz, 2H), 5.29 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) *δ*/ ppm = 190.5, 147.0, 139.3, 139.2, 137.7, 137.0, 132.1, 130.9, 129.9, 129.5, 128.9, 128.8, 128.5, 128.3, 127.6, 126.1, 126.0, 123.5, 122.2, 121.0, 117.9, 111.9, 111.3, 48.0. IR (neat): ν/ cm^{-1} = 1739, 1652, 1565, 1363, 1219, 1012, 697. HRMS: *m/z* $[M+H]^+$ calcd for $C_{30}H_{24}NO$: 414.1852, found: 414.1857.

(*E*)-1-phenyl-3-(2-phenyl-1*H*-indol-3-yl)prop-2-en-1-one (4b.7bd, Table 4b.2):



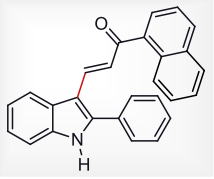
The title compound was prepared following **GP-8** using **4.18cm** (64.7 mg, 0.2 mmol); obtained as yellow solid (53.0 mg, 82%). M.P. = 160 - 161°C. R_f value = 0.93 (25% EtOAc in hexane). ^1H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 8.98 (s, 1H), 8.21 (d, *J* = 15.5 Hz, 1H), 8.09 (d, *J* = 7.3 Hz, 1H), 8.05 (d, *J* = 7.1 Hz, 2H), 7.73 (d, *J* = 15.5 Hz, 1H), 7.56 (d, *J* = 7.3 Hz, 3H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.47 – 7.43 (m, 4H), 7.36 – 7.29 (m, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) *δ*/ ppm = 191.0, 144.2, 139.5, 136.6, 132.3, 131.2, 129.3, 129.27, 129.1, 128.6, 128.4, 126.6, 123.6, 122.0, 121.1, 118.5, 111.8, 110.9. IR (neat): ν/ cm^{-1} = 1738, 1366, 1258, 1228, 1016, 795. HRMS: *m/z* $[M]^+$ calcd for $C_{23}H_{18}NO$: 324.1383, found: 324.1384.

(*E*)-1-(3,5-dimethoxyphenyl)-3-(2-phenyl-1*H*-indol-3-yl)prop-2-en-1-one (4b.7be, Table 4b.2):



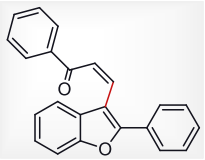
The title compound was prepared following **GP-8** using **4.18cn** (76.7 mg, 0.2 mmol); obtained as yellow solid (65.2 mg, 85%). M.P. = 166 - 167°C. R_f value = 0.85 (25% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 9.60 (s, 1H), 8.23 (d, *J* = 15.5 Hz, 1H), 8.05 (d, *J* = 7.8 Hz, 1H), 7.63 (d, *J* = 15.5 Hz, 1H), 7.48 (d, *J* = 7.5 Hz, 2H), 7.43 (d, *J* = 7.8 Hz, 1H), 7.34 – 7.30 (m, 4H), 7.28 (d, *J* = 7.4 Hz, 1H), 7.19 (d, *J* = 2.2 Hz, 2H), 6.66 (t, *J* = 2.2 Hz, 1H), 3.82 (s, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ/ ppm = 190.9, 160.8, 144.6, 141.2, 140.1, 136.7, 131.0, 129.2, 129.1, 128.9, 126.5, 123.5, 121.9, 120.9, 118.1, 111.9, 110.6, 106.3, 104.4, 55.5. IR (neat): ν/ cm^{-1} = 1741, 1552, 1451, 1292, 1189, 1037, 742. HRMS: *m/z* [M+H]$^+$ calcd for $C_{25}H_{22}NO_3$: 384.1594, found: 384.1599.

(*E*)-1-(naphthalen-1-yl)-3-(2-phenyl-1*H*-indol-3-yl)prop-2-en-1-one (4b.7bf, Table 4b.2):



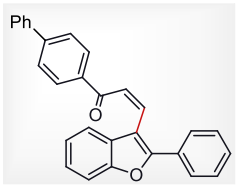
The title compound was prepared following **GP-8** using **4.18co** (74.7 mg, 0.2 mmol); obtained as yellow solid (60.5 mg, 81%). M.P. = 167 - 168°C. R_f value = 0.88 (25% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 9.53 (s, 1H), 8.56 (s, 1H), 8.30 (d, *J* = 15.4 Hz, 1H), 8.13 (t, *J* = 7.1 Hz, 2H), 8.00 (d, *J* = 7.8 Hz, 1H), 7.93 (d, *J* = 8.8 Hz, 1H), 7.90 (d, *J* = 8.3 Hz, 1H), 7.86 (d, *J* = 15.4 Hz, 1H), 7.63 – 7.55 (m, 2H), 7.54 – 7.51 (m, 2H), 7.47 (d, *J* = 7.9 Hz, 1H), 7.40 – 7.28 (m, 5H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ/ ppm = 191.1, 144.5, 139.8, 139.79, 136.7, 136.4, 135.3, 132.6, 131.1, 129.5, 129.3, 129.1, 128.9, 128.4, 128.1, 127.8, 126.6, 124.6, 123.6, 121.9, 121.0, 118.3, 112.0, 110.8. IR (neat): ν/ cm^{-1} = 1739, 1546, 1372, 1214, 1121, 740. HRMS: *m/z* [M+H]$^+$ calcd for $C_{27}H_{20}NO$: 374.1539, found: 374.1541.

(*E*)-1-phenyl-3-(2-phenylbenzofuran-3-yl)prop-2-en-1-one (4b.8a, Table 4b.2):



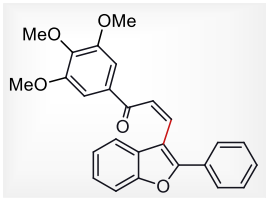
The title compound was prepared following **GP-8** using **4.21a** (64.9 mg, 0.2 mmol); obtained as yellow solid (58.4 mg, 90%). M.P. = 158 - 159°C. R_f value = 0.72 (15% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.93 (d, *J* = 8.0 Hz, 2H), 7.82 (d, *J* = 8.0 Hz, 2H), 7.51 – 7.46 (m, 4H), 7.44 – 7.36 (m, 3H), 7.26 – 7.22 (m, 1H), 7.21 (d, *J* = 12.0 Hz, 1H), 7.14 – 7.11 (m, 2H), 7.10 (d, *J* = 12.0 Hz, 1H). Prominent peaks for minor product, 8.20 (d, *J* = 15.6 Hz, 1H), 8.07 (d, *J* = 8.1 Hz, 2H), 8.00 – 7.96 (m, 1H), 7.79 (d, *J* = 5.1 Hz, 2H), 7.59 (d, *J* = 8.7 Hz, 2H), 7.53 (d, *J* = 7.4 Hz, 3H), 7.51 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ/ ppm = 191.9, 154.1, 137.9, 132.9, 132.8, 130.3, 129.1, 128.7, 128.6, 128.5, 127.8, 127.1, 127.0, 124.7, 122.8, 121.6, 113.7, 111.2. IR (neat): ν/ cm^{-1} = 1710, 1656, 1604, 1446, 1258, 1220, 1004, 734. HRMS: *m/z* [M+H]$^+$ calcd for $C_{23}H_{17}O_2$: 325.1223, found: 325.1221.

(*E*)-1-([1,1'-biphenyl]-4-yl)-3-(2-phenylbenzofuran-3-yl)prop-2-en-1-one (4b.8b, Table 4b.2):



The title compound was prepared following **GP-8** using **4.21c** (80.1 mg, 0.2 mmol); obtained as yellow solid (69.7 mg, 87%). M.P. = 162 - 163°C. R_f value = 0.69 (10% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.03 (d, *J* = 8.3 Hz, 2H), 7.86 (d, *J* = 7.7 Hz, 2H), 7.63 (t, *J* = 8.3 Hz, 4H), 7.54 – 7.40 (m, 8H), 7.30 – 7.26 (m, 1H), 7.25 (d, *J* = 12.8 Hz, 1H), 7.18 – 7.14 (m, 2H). Prominent peaks for minor product, 8.25 (d, *J* = 15.6 Hz, 1H), 8.18 (d, *J* = 8.3 Hz, 2H), 7.78 (d, *J* = 8.3 Hz, 2H), 7.68 (d, *J* = 7.5 Hz, 3H), 7.56 (t, *J* = 7.1 Hz, 5H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ/ ppm = 191.4, 154.2, 145.6, 140.0, 136.7, 132.7, 130.4, 129.3, 129.1, 129.0, 128.95, 128.8, 128.2, 127.8, 127.4, 127.3, 127.1, 125.5, 124.7, 123.9, 122.8, 121.6, 121.1, 113.8, 111.3. IR (neat): ν/ cm^{-1} = 1656, 1578, 1451, 1273, 1070, 744. HRMS: *m/z* [M+H]$^+$ calcd for $C_{29}H_{21}O_2$: 401.1536, found: 401.1538.

(*E*)-3-(2-phenylbenzofuran-3-yl)-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (4b.8c, Table 4b.2):

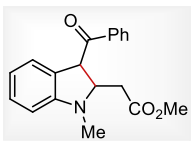


The title compound was prepared following **GP-8** using **4.21d** (82.9 mg, 0.2 mmol); obtained as yellow solid (72.9 mg, 88%). M.P. = 163 - 164°C. R_f value = 0.43 (15% EtOAc in hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ/ ppm = 8.18 (d, *J* = 15.6 Hz, 1H), 7.95 (d, *J* = 8.7 Hz, 1H), 7.82 (d, *J* = 8.2 Hz, 2H), 7.74 (d, *J* = 15.6 Hz, 1H), 7.61 (d, *J* = 8.2 Hz, 1H), 7.57 – 7.49 (m, 3H), 7.45 – 7.38 (m, 2H), 7.32 (s, 2H), 3.96 (s, 6H), 3.95 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ/ ppm = 191.5, 154.0, 153.9, 152.8, 142.4, 133.0, 132.0, 130.3, 129.1, 128.7, 127.6, 127.5, 127.4, 124.8, 122.8, 121.3, 113.6, 111.2, 106.1, 60.9, 56.1. IR (neat): ν/ cm^{-1} = 1740, 1574, 1333, 1217, 1123, 1002, 740, 694. HRMS: *m/z* [M+H]$^+$ calcd for $C_{26}H_{23}O_5$: 415.1540, found: 415.1539.

4.3.11. Details of Control Experiments for the Formation of 3-Substituted Indole Derivatives (Scheme 4b.4):

4.3.11.1. Analytical Data of Methyl 2-(3-benzoyl-1-methylindolin-2-yl)acetate (4b.11, eq. 3, Scheme 4b.4):

Methyl 2-(3-benzoyl-1-methylindolin-2-yl)acetate:

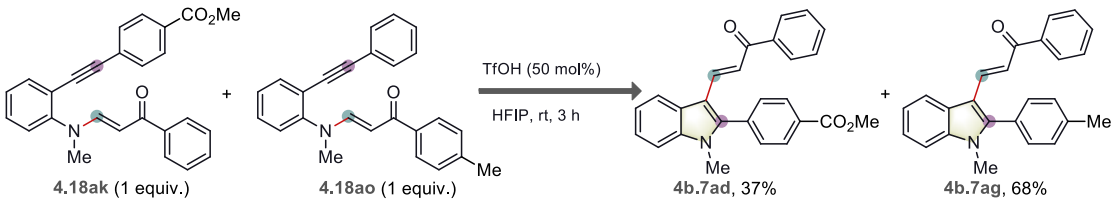


The title compound was prepared following **GP-8** using **4.18cd** (61.9 mg, 0.2 mmol); obtained as yellow solid (35.3 mg, 57%). M.P. = 168 - 169°C. R_f value = 0.81 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ/ ppm = 8.09 (d, *J* = 7.1 Hz, 2H), 7.67 – 7.62 (m, 1H), 7.55 (t, *J* = 7.9 Hz, 2H), 7.10 (t, *J* = 7.7 Hz, 1H), 6.70 (d, *J* = 7.4 Hz, 1H), 6.55 (td, *J* = 7.5, 0.9 Hz, 1H), 6.52 (d, *J* = 7.9 Hz, 1H), 5.12 (d, *J* = 8.7 Hz, 1H), 4.41 (td, *J* = 8.7, 3.9 Hz, 1H), 3.53 (s, 3H), 2.86 (dd, *J* = 14.6, 3.9 Hz, 1H), 2.86 (s, 3H), 2.66 (dd, *J* = 14.6, 8.7 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ/ ppm = 197.3, 171.4, 152.2, 137.3, 133.4, 129.2, 128.9, 128.7, 126.9, 124.0, 118.1, 107.9, 65.1, 54.4, 51.7, 37.9, 34.4. IR (neat): ν/

cm^{-1} = 1716, 1562, 1466, 1274, 1105, 1012, 769. HRMS: *m/z* $[M+H]^+$ calcd for $C_{19}H_{18}NO_3$: 308.1292, found: 308.1302.

4.3.11.2. Method of Cross-over Experiment for the Formation of 3-Substituted Indole Derivatives (eq. 4, Scheme 4b.4):

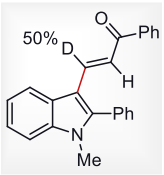
A equimolar mixture of substrates **4.18ak** (15.8 mg, 1 equiv.) and **4.18ao** (14.0 mg, 1 equiv.) were dissolved in HFIP (1 mL, 0.1 M)and TfOH (2µL, 50 mol%) was added to it. Then the reaction mixture was continuous stirring for 3 hrs. After that, the reaction mixture was concentrated under reduced pressure and the mixture of product **4b.7ad** and **4b.7ag** was separated by column chromatography (silica gel, hexanes/EtOAc) and analyzed by ^1H NMR spectra to find out that indoles **4b.7ad** and **4b.7ag** were formed in almost 1:1.8 ratio.



Scheme 4.19. Cross-over experiment for the synthesis of 3-substituted indoles **4b.7ad and 4b.7ag**.

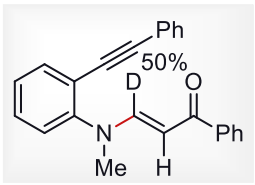
4.3.11.3. Analytical Data of Deuterium Scrambling Experiments for the Formation of 3-Substituted Indole Derivatives (eq. 6-7, Scheme 4b.4):

Deuterated (*E*)-3-(1-methyl-2-phenyl-1*H*-indol-3-yl)-1-phenylprop-2-en-1-one (4b.7aa-D, eq. 6, Scheme 4b.4):



The title compound was prepared following **GP-8** using **4.18aa-D** (67.9 mg, 0.2 mmol); obtained as yellow solid (61.8 mg, 91% using TfOH; 63.1 mg, 93% using TfOD). M.P. = 176 - 177°C. R_f value = 0.44 (10% EtOAc in hexane). ^1H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 8.14 – 8.10 (m, 1H), 8.01 (d, *J* = 7.1 Hz, 2H), 7.95 (d, *J* = 15.5 Hz, 0.5 H), 7.61 (d, *J* = 15.5 Hz, 1H), 7.59 – 7.52 (m, 4H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.46 – 7.42 (m, 3H), 7.42 – 7.36 (m, 2H), 3.67 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) *δ*/ ppm = 190.5, 146.9, 139.4, 139.3, 138.2, 132.0, 131.0, 130.0, 129.4, 128.4, 128.5, 128.3, 125.8, 123.3, 122.0, 120.9, 117.4, 111.5, 110.3, 31.3. IR (neat): ν/ cm^{-1} = 1581, 1560, 1462, 1365, 1285, 1219, 1011, 732. HRMS: *m/z* $[M+H]^+$ calcd for $C_{24}H_{19}DNO$: 339.1602, found: 339.1603.

Deuterated (*E*)-3-(methyl(2-(phenylethynyl)phenyl)amino)-1-phenylprop-2-en-1-one (4.18aa-D', eq. 7, Scheme 4b.4):



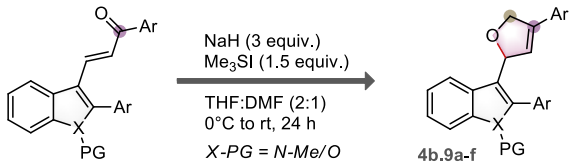
^1H NMR (500 MHz, $CDCl_3$) *δ*/ ppm = 8.13 (d, *J* = 12.2 Hz, 0.5 H), 7.93 (s, 2H), 7.59 (d, *J* = 6.4 Hz, 1H), 6.50 – 6.35 (m, 7H), 7.31 (d, *J* = 5.3 Hz, 3H), 7.23 (d, *J* = 6.8 Hz, 1H), 6.08 (s, 1H), 3.46 (s, 3H). IR (neat): ν/ cm^{-1} = 1640, 1578, 1526, 1277, 1208, 1044, 753. HRMS: *m/z* $[M-H]^+$ calcd for $C_{24}H_{19}NOD$: 339.1602, found: 339.1602.

4.3.12. Details of Late-stage Transformation of 3-Substituted Indole and Benzofuran Derivatives (Scheme 4b.5):

4.3.12.1. Synthetic Procedure for the Preparation of 2,5-Dihydrofuran Derivatives (4b.9):

General Procedure 9 (GP-9):

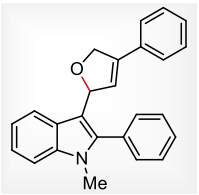
NaH (1.5 equiv.) and Me_3SI (1.5 equiv.) were taken in a 2:1 mixture of dry THF:DMF (0.1 M) and stirred at 0 °C under nitrogen atmosphere for 30 mins. Then the reaction mixture is allowed to bring to room temperature and a solution of the synthesized indole/benzofuran derivatives **4b.7**/**4b.8** in dry THF was added dropwise to it. Then the reaction mixture was continuously stirred for 24 hrs. After the completion of the reaction, it was poured into ice-cooled saturated NH_4Cl solution, extracted with ethyl acetate and washed with saturated brine solution. The combined organic layers were then concentrated under reduced pressure and crude was purified and separated by column chromatography (silica gel, hexanes/EtOAc) to get 2,5-dihydrofuran derivatives (**4b.9a-f**) in an analytically pure form.



Scheme 4.20. Preparation of 2,5-dihydrofuran derivatives (**4b.9a-f**).

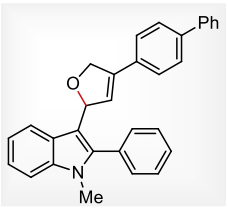
4.3.12.2. Analytical Data of 2,5-Dihydrofuran Derivatives (4b.9):

1-Methyl-2-phenyl-3-(4-phenyl-2,5-dihydrofuran-2-yl)-1*H*-indole (4b.9a, Scheme 4b.5):



The title compound was prepared following **GP-9** using **4b.7aa** (50.6 mg, 0.15 mmol), obtained as off-white gummy (50.1 mg, 95%). R_f value = 0.61 (10% EtOAc in hexane). ^1H NMR (500 MHz, $CDCl_3$) δ/ ppm = 7.68 (d, J = 7.8 Hz, 1H), 7.52 (d, J = 5.3 Hz, 3H), 7.50 – 7.46 (m, 1H), 7.44 – 7.33 (m, 7H), 7.29 – 7.24 (m, 1H), 7.10 (t, J = 7.2 Hz, 1H), 6.33 (d, J = 0.74 Hz, 1H), 6.11 (t, J = 4.5 Hz, 1H), 5.30 (dd, J = 11.9, 5.8 Hz, 1H), 5.15(d, J = 11.8 Hz, 1H), 3.64 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ/ ppm = 139.9, 138.6, 137.7, 132.7, 131.1, 131.0, 128.7, 128.5, 128.4, 128.1, 126.4, 126.0, 124.4, 122.1, 120.1, 120.0, 112.3, 109.6, 82.8, 75.1, 30.8. IR (neat): ν/ cm^{-1} = 1737, 1451, 1202, 1065, 744, 692. HRMS: m/z $[M+H]^+$ calcd for $C_{25}H_{22}NO$: 352.1696, found: 352.1696.

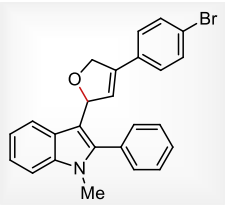
3-(4-([1,1'-biphenyl]-4-yl)-2,5-dihydrofuran-2-yl)-1-methyl-2-phenyl-1*H*-indole (4b.9b, Scheme 4b.5):



The title compound was prepared following **GP-9** using **4b.7ah** (62.0 mg, 0.15 mmol), obtained as off-white gummy (61.6 mg, 96%). R_f value = 0.51 (20% EtOAc in hexane). ^1H NMR (500 MHz, Acetone-D_6) δ/ ppm = 7.69 (d, J = 8.0 Hz, 4H), 7.63 (d, J = 7.8 Hz, 1H), 7.59 – 7.55 (m, 6H), 7.52 – 7.41 (m,

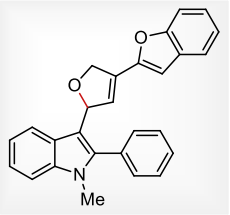
4H), 7.36 (t, *J* = 7.8 Hz, 1H), 7.20 (t, *J* = 7.0 Hz, 1H), 7.01 (t, *J* = 7.7 Hz, 1H), 6.48 (s, 1H), 6.03 (s, 1H), 5.25 (dd, *J* = 11.8, 5.8 Hz, 1H), 5.08 (d, *J* = 11.8 Hz, 1H), 3.63 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, Acetone-D_6) *δ*/ ppm = 141.5, 141.4, 140.4, 139.2, 138.7, 132.8, 132.3, 132.0, 129.9, 129.4, 129.36, 128.5, 128.1, 127.7, 127.5, 125.9, 122.7, 120.9, 120.5, 113.8, 110.7, 83.7, 75.5, 31.2. IR (neat): ν/ cm^{-1} = 1710, 1359, 1219, 1090, 742, 698. HRMS: *m/z* $[M+H]^+$ calcd for $C_{31}H_{26}NO$: 450.1828, found: 450.1821.

3-(4-(4-bromophenyl)-2,5-dihydrofuran-2-yl)-1-methyl-2-phenyl-1*H*-indole (4b.9c, Scheme 4b.5):



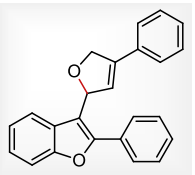
The title compound was prepared following **GP-9** using **4b.7aj** (62.4 mg, 0.15 mmol), obtained as off-white gummy (59.4 mg, 92%). R_f value = 0.46 (10% EtOAc in hexane). ^1H NMR (500 MHz, DMSO-D_6) *δ*/ ppm = 7.59 (d, *J* = 8.6 Hz, 2H), 7.56 (d, *J* = 7.1 Hz, 2H), 7.54 – 7.48 (m, 4H), 7.46 (d, *J* = 7.9 Hz, 1H), 7.43 (d, *J* = 8.5 Hz, 2H), 7.19 (t, *J* = 7.2 Hz, 1H), 7.00 (dt, *J* = 7.9 Hz, 1H), 6.61 (q, *J* = 1.8 Hz, 1H), 5.91 (t, *J* = 5.9 Hz, 1H), 5.12 (ddd, *J* = 12.2, 5.9, 1.9 Hz, 1H), 4.96 (ddd, *J* = 12.2, 4.3, 2.3 Hz, 1H), 3.60 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, DMSO-D_6) *δ*/ ppm = 138.9, 137.0, 136.9, 131.6, 131.4, 130.7, 130.4, 128.5, 128.45, 128.0, 125.9, 125.7, 121.7, 121.2, 119.5, 119.3, 111.9, 110.1, 82.2, 74.1, 30.7. IR (neat): ν/ cm^{-1} = 1737, 1458, 1245, 1019, 776, 697. HRMS: *m/z* $[M+H]^+$ calcd for $C_{25}H_{21}NOBr$: 430.0801, found: 430.0801.

3-(4-(benzofuran-2-yl)-2,5-dihydrofuran-2-yl)-1-methyl-2-phenyl-1*H*-indole (4b.9d, Scheme 4b.5):



The title compound was prepared following **GP-9** using **4b.7ay** (56.6 mg, 0.15 mmol), obtained as off-white gummy (54.6 mg, 93%). R_f value = 0.69 (20% EtOAc in hexane). ^1H NMR (500 MHz, DMSO-D_6) *δ*/ ppm = 7.66 (d, *J* = 7.7 Hz, 1H), 7.59 – 7.53 (m, 5H), 7.50 (dd, *J* = 8.2, 3.4 Hz, 3H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.27 (t, *J* = 7.6 Hz, 1H), 7.19 (t, *J* = 7.8 Hz, 1H), 7.02 (t, *J* = 7.5 Hz, 1H), 6.99 (s, 1H), 6.57 (d, *J* = 1.6 Hz, 1H), 5.97 (t, *J* = 4.0 Hz, 1H), 5.14 (ddd, *J* = 11.8, 5.8, 1.5 Hz, 1H), 4.97 (ddd, *J* = 11.8, 4.0, 2.2 Hz, 1H), 3.61 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-D_6) *δ*/ ppm = 154.2, 149.3, 139.2, 137.0, 130.8, 130.3, 129.1, 128.6, 128.5, 128.3, 126.7, 125.9, 125.2, 123.3, 121.8, 121.4, 119.6, 119.2, 111.3, 111.0, 110.2, 104.8, 82.1, 73.2, 30.7. IR (neat): ν/ cm^{-1} = 1710, 1359, 1219, 1090, 743, 670. HRMS: *m/z* $[M+H]^+$ calcd for $C_{27}H_{22}NO_2$: 392.1645, found: 392.1643.

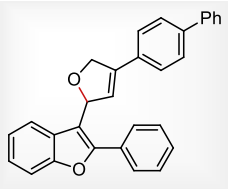
2-Phenyl-3-(4-phenyl-2,5-dihydrofuran-2-yl)benzofuran (4b.9e, Scheme 4b.5):



The title compound was prepared following **GP-9** using **4b.8a** (48.7 mg, 0.15 mmol), obtained as off-white gummy (45.7 mg, 90%). R_f value = 0.39 (20% EtOAc in hexane). ^1H NMR (500 MHz, DMSO-D_6) *δ*/ ppm = 7.80 (d, *J* = 7.1 Hz, 2H), 7.64 (d, *J* = 8.2 Hz, 1H), 7.62 – 7.50 (m, 6H), 7.43 (t, *J* = 7.2 Hz, 2H), 7.37 (t, *J* = 7.3 Hz, 1H), 7.33 (t, *J* = 8.3 Hz, 1H), 7.21 (t, *J* = 8.0 Hz, 1H), 6.72 (d, *J* = 1.9 Hz, 1H), 6.32 (t, *J* = 5.7 Hz, 1H), 5.30 (ddd, *J* = 12.4, 5.8, 2.0 Hz, 1H), 5.14 (ddd, *J* = 12.4, 4.2, 2.3 Hz, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, DMSO-D_6) *δ*/ ppm = 153.7, 152.3, 139.3, 131.7, 129.4, 129.39,

129.1, 128.8, 128.5, 127.9, 127.7, 126.2, 124.8, 123.1, 122.9, 120.8, 115.8, 111.3, 80.9, 75.0. IR (neat): ν/ cm^{-1} = 1737, 1665, 1450, 1202, 1065, 744, 692. HRMS: *m/z* $[M+Na]^+$ calcd for $C_{24}H_{18}O_2Na$: 361.1199, found: 361.1196.

3-(4-([1,1'-biphenyl]-4-yl)-2,5-dihydrofuran-2-yl)-2-phenylbenzofuran (4b.9f, Scheme 4b.5):



The title compound was prepared following **GP-9** using **4b.8b** (60.1 mg, 0.15 mmol), obtained as off-white gummy (57.8 mg, 93%). R_f value = 0.81 (20% EtOAc in hexane). ^1H NMR (500 MHz, DMSO-D_6) *δ*/ ppm = 7.81 (d, *J* = 8.2 Hz, 2H), 7.76 – 7.70 (m, 4H), 7.64 (d, *J* = 8.2 Hz, 3H), 7.60 (t, *J* = 7.3 Hz, 2H), 7.54 (d, *J* = 7.9 Hz, 2H), 7.48 (t, *J* = 8.2 Hz, 2H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.33 (t, *J* = 7.3 Hz, 1H), 7.22 (t, *J* = 7.6 Hz, 1H), 6.77 (s, 1H), 6.34 (s, 1H), 5.34 (dd, *J* = 12.3, 5.7 Hz, 1H), 5.17 (d, *J* = 12.2 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-D_6) *δ*/ ppm = 186.9, 153.7, 152.3, 140.1, 139.5, 138.9, 130.8, 129.4, 129.1, 129.0, 127.9, 127.7, 127.0, 126.8, 126.6, 125.0, 124.8, 123.1, 123.06, 120.8, 115.8, 111.3, 81.0, 75.0. IR (neat): ν/ cm^{-1} = 1710, 1524, 1359, 1219, 1090, 748. HRMS: *m/z* $[M+H]^+$ calcd for $C_{30}H_{23}O_2$: 415.1693, found: 415.1697.

4.3.13. HRMS Studies to Support the Proposed Mechanisms for the Formation of 3-Substituted Indole Derivatives:

The reaction for the formation of indole **4b.7aa** from **4.18aa** was conducted separately in presence of TfOH and $MeSO_3H$. After 30mins, HRMS analysis has been performed for both the reactions to identify few intemediates.

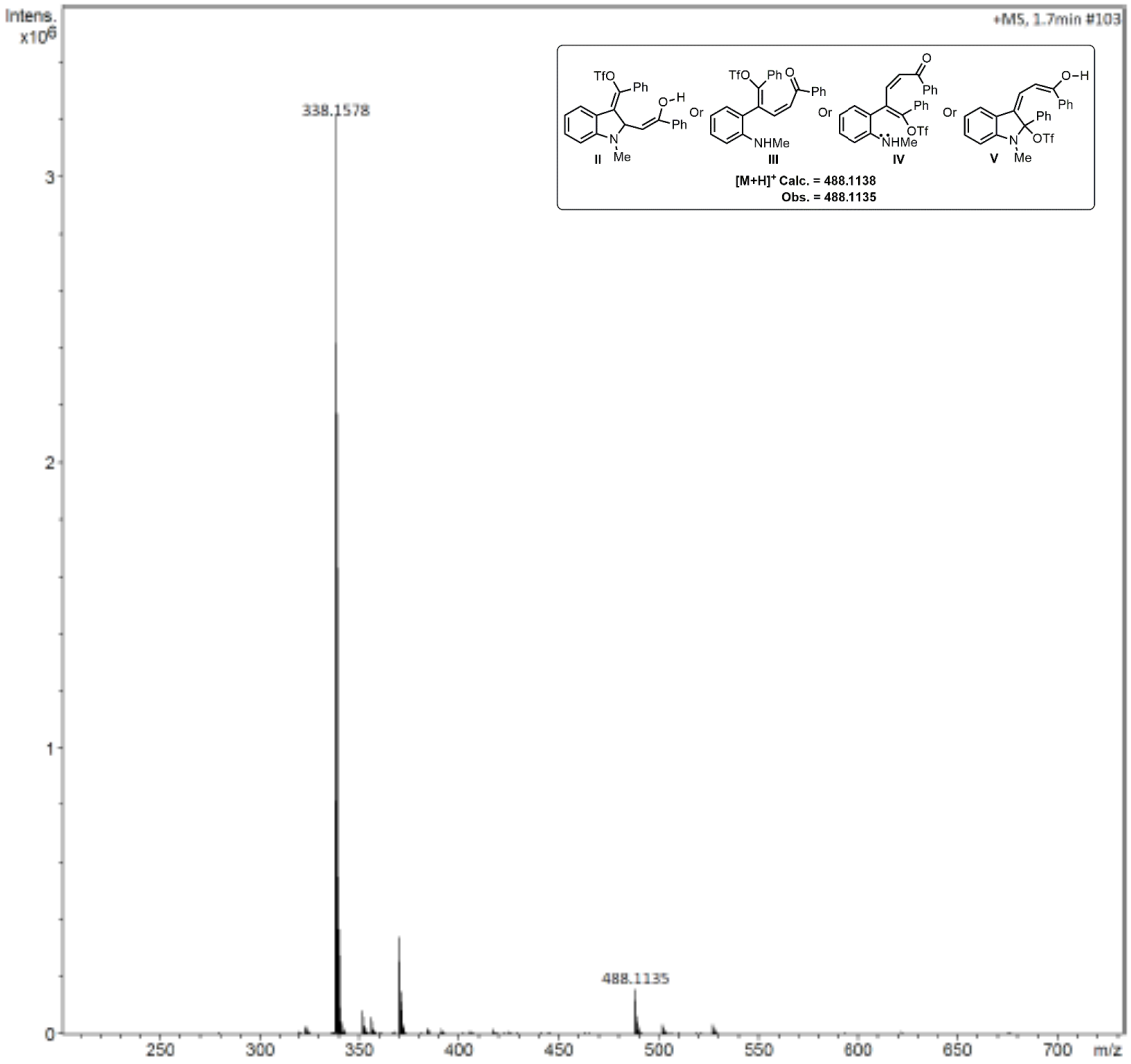


Figure 4.12. Full HRMS spectrum of crude reaction mixture of TfOH catalysis for intermediate **II/III/IV/V**.

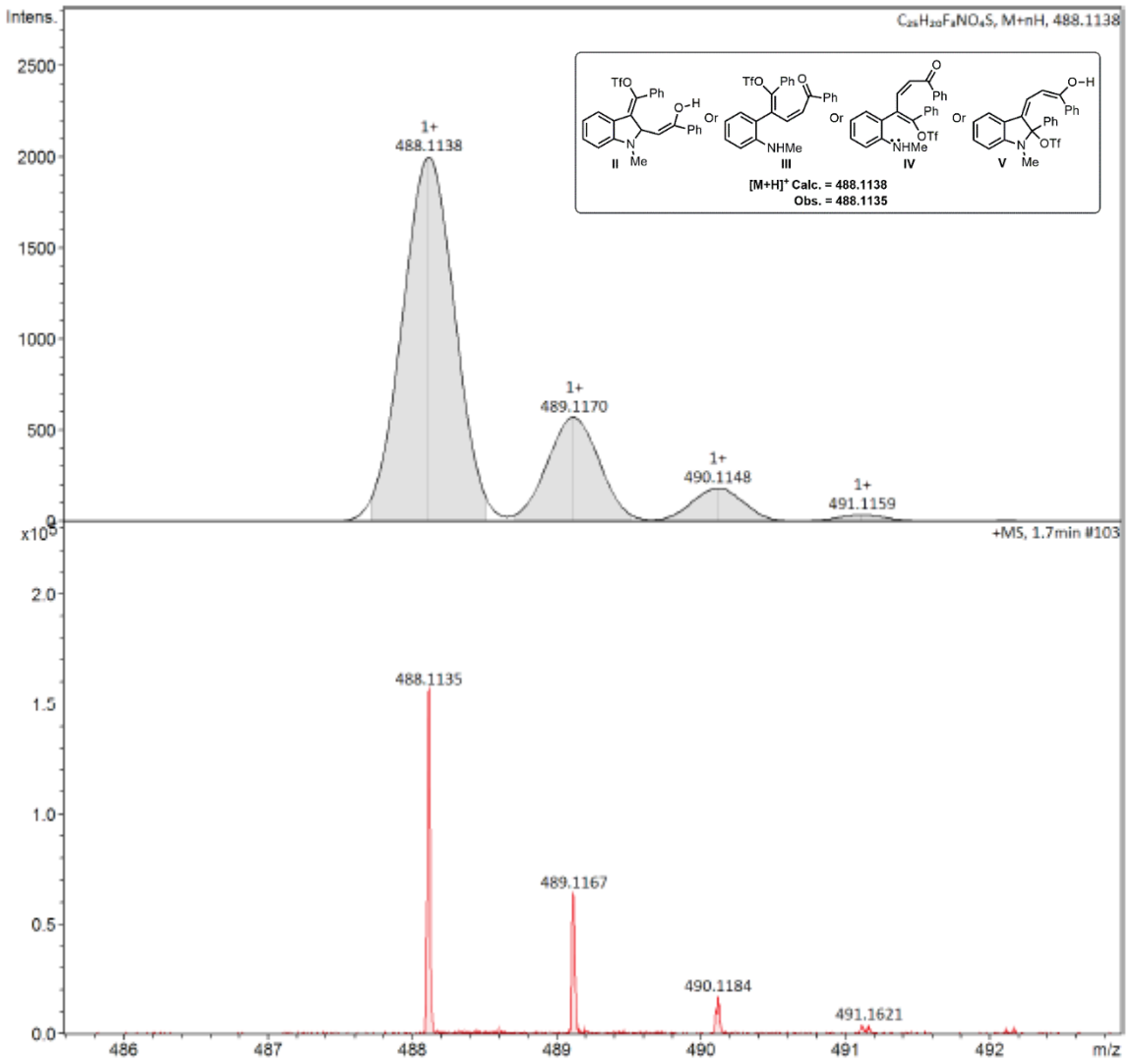


Figure 4.13. Simulated HRMS spectrum of crude reaction mixture of TfOH catalysis for intermediate **II/III/IV/V**.

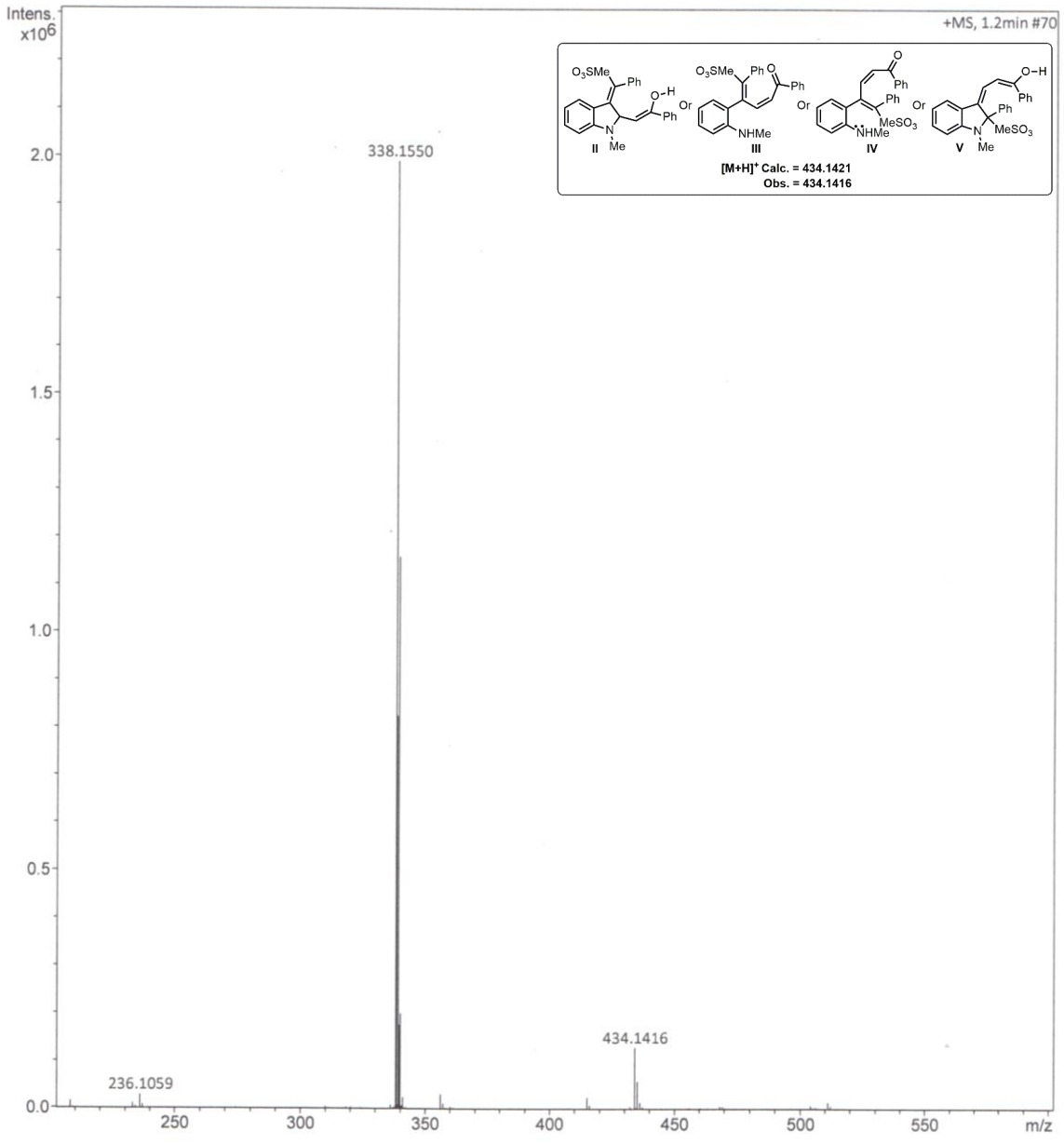


Figure 4.14. Full HRMS spectrum of crude reaction mixture of $MeSO_3H$ catalysis for intermediate **II/III/IV/V**.

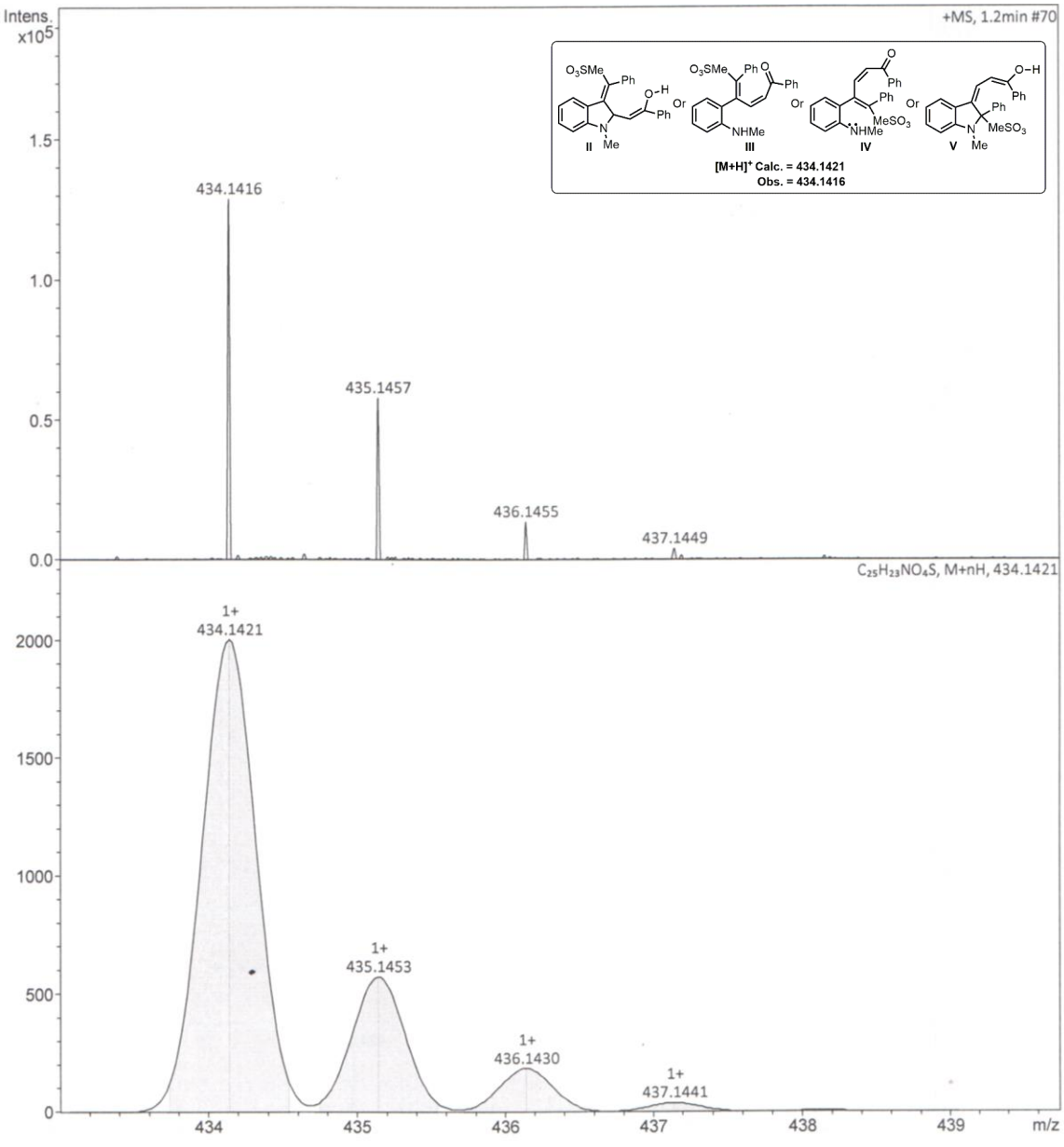


Figure 4.15. Simulated HRMS spectrum of crude reaction mixture of $MeSO_3H$ catalysis for intermediate **II/III/IV/V**.

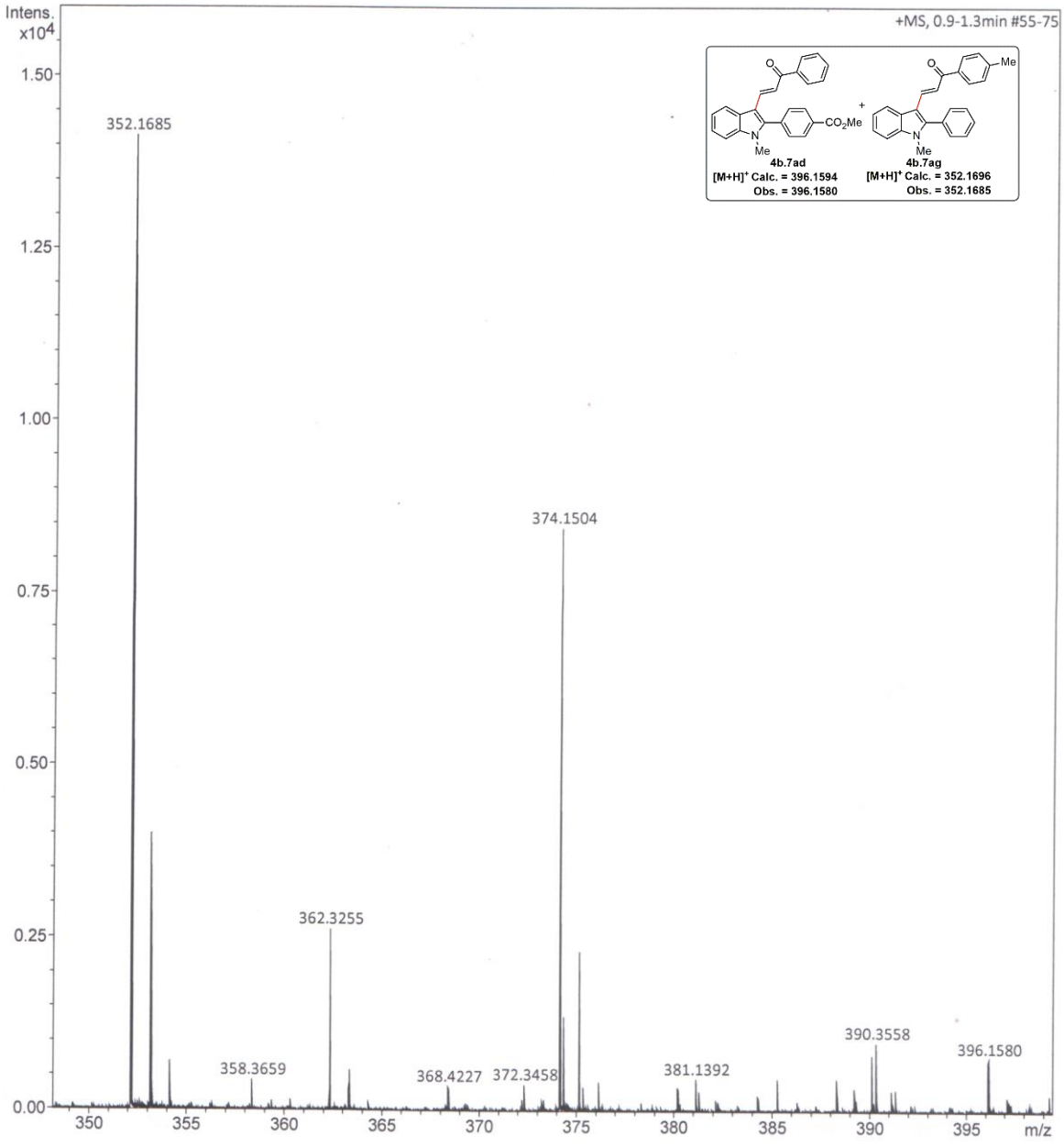


Figure 4.16. HRMS spectrum of cross-over experiment.

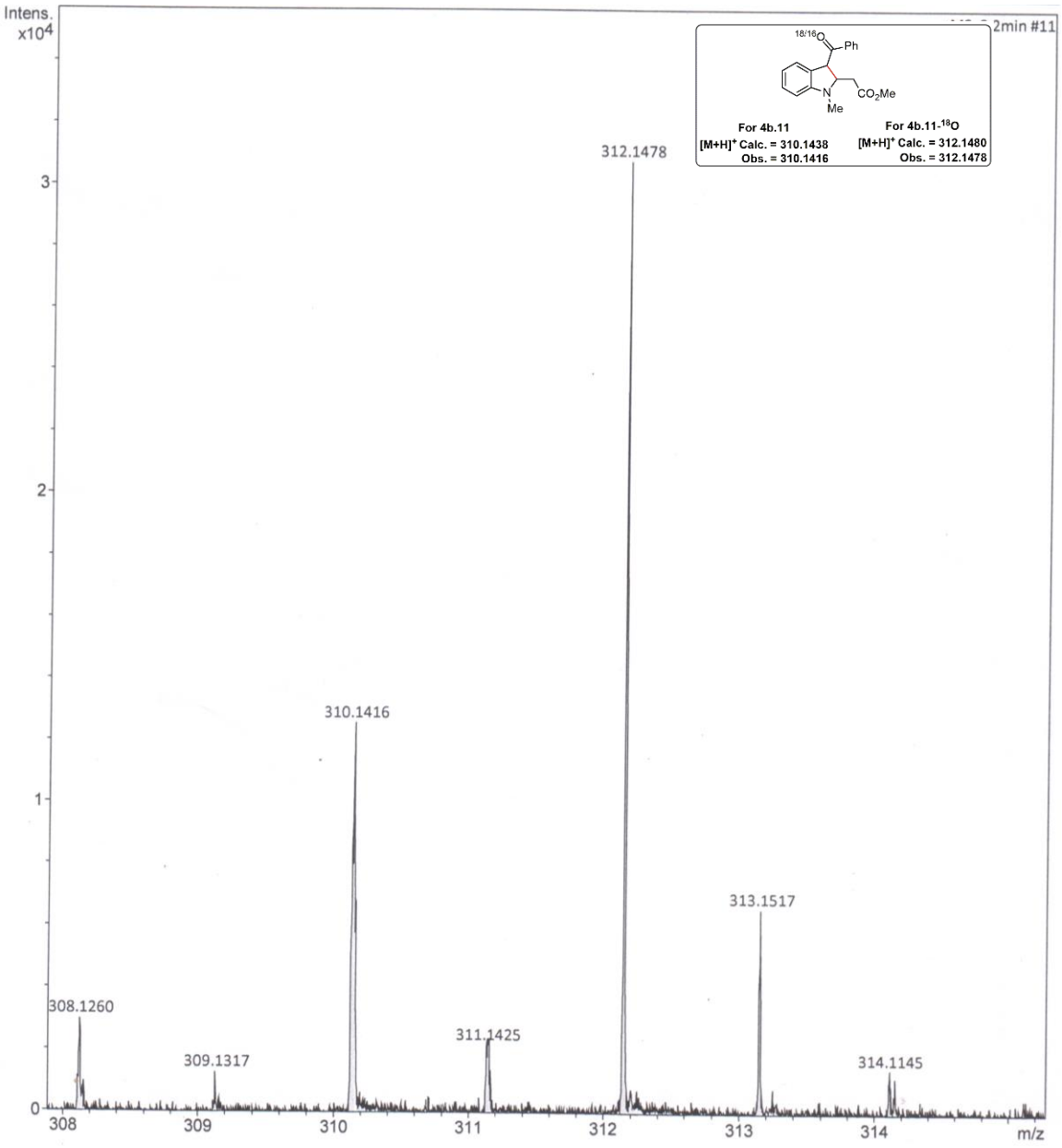


Figure 4.17. HRMS spectrum of ^{18}O levelling experiment.

4.3.14. *X*-ray *C*rystallography:

Single crystal X-ray data for the compounds **4.18ak**, **4.21b**, **4a.7aa**, **4a.8a**, **4a.9a**, **4a.9c**, **4a.10**, **4a.11**, **4a.13**, **4a.14**, **4a.15**, **4a.15'**, **4b.7aa**, **4b.7be**, **4b.8a** and **4b.11** were collected using the detector system [λ (Mo-Kα) = 0.71073 Å] at 293K, graphite monochromator with a ω scan width of 0.3o, crystal-detector distance 60 mm, collimator 0.5 mm. The SMART software[57] was used for the intensity data acquisition and the SAINTPLUS Software[58] was used

for the data extraction. In each case, absorption correction was performed with the help of SADABS program,[57] an empirical absorption correction using equivalent reflections was performed with the program. The structure was solved using SHELXS-97[58] and full-matrix least-squares refinement against F2 was carried out using SHELXL-97.[58] All non-hydrogen atoms were refined anisotropically. Aromatic and methyl hydrogens were introduced on calculated positions and included in the refinement riding on their respective parent atoms.

Crystallographic data (including the structure factor) for the structures **4.18ak**, **4.21b**, **4a.7aa**, **4a.8a**, **4a.9a**, **4a.9c**, **4a.10**, **4a.11**, **4a.13**, **4a.14**, **4a.15**, **4a.15'**, **4b.7aa**, **4b.7be**, **4b.8a** and **4b.11** in this chapter have been deposited in the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 2166460, 2180193, 2115137, 2115138, 2115140, 2062199, 2115142, 2062197, 2115141, 2115145, 2115143, 2115144, 2166456, 2166457, 2166458 and 2166459. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

4.3.14.1. X-ray Crystal Structure and Data for Vinylogous Amide Derived from *o*-Alkynylaniline (4.18ak):

Table 4.5. Crystallographic data for compound **4.18ak**.

CCDC Number	2166460
Compound identification code	Rb38
Empirical formula	C26 H21 N O3
Formula weight	395.44
Temperature	298 K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P 21/n
Unit cell dimensions	a= 19.4449(8) alpha= 90 b= 5.9085(2) beta= 116.246(5) c= 19.6048(8) gamma= 90
Volume	2020.19(16) $Å^3$
Z	4
Density (calculated)	1.300 g/cm^3
Absorption coefficient	0.085 mm^{-1}
F(000)	832.0
Reflections collected	4408
Independent reflections	2574
Completeness to theta = 25.025°	0.958
Refinement method	Full-matrix least-squares on F2
Max. and min. transmission	0.992 and 0.985
Goodness-of-fit on F2	1.053

R(reflections)	0.0514 (2574)
wR2(reflections)	0.1502 (4222)
Diffractometer	Xcalibur Gemini Eos CCD

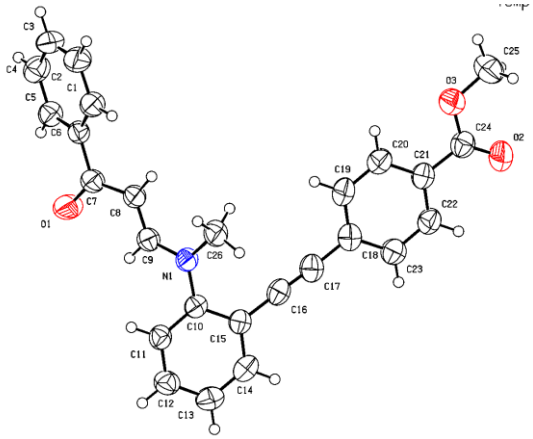


Figure 4.18. ORTEP-drawing of compound **4.18ak**.

4.3.14.2. X-ray Crystal Structure and Data for Vinylogous Ester Precursor Derived from o-Alkynylphenol (4.21b):

Table 4.6. Crystallographic data for compound **4.21b**.

CCDC Number	2180193
Compound identification code	Rb41
Empirical formula	C23 H15 Cl O2
Formula weight	358.80
Temperature	300 K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	I a
Unit cell dimensions	a= 15.1110(6) alpha= 90 b= 5.6328(2) beta= 92.360(3) c= 43.1868(12) gamma= 90
Volume	3672.8(2) $Å^3$
Z	8
Density (calculated)	1.298 g/cm^3
Absorption coefficient	0.221 mm^{-1}
F(000)	1488.0
Reflections collected	6469
Independent reflections	4313
Completeness to theta = 25.025°	0.99

Refinement method	Full-matrix least-squares on F2
Max. and min. transmission	0.978 and 0.961
Goodness-of-fit on F2	1.015
R(reflections)	0.0447 (4313)
wR2(reflections)	0.1165 (6416)
Diffractometer	Xcalibur Gemini Eos CCD

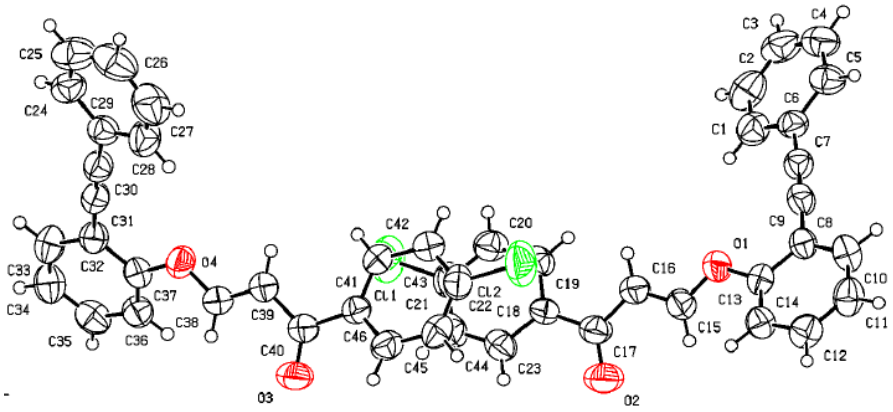


Figure 4.19. ORTEP-drawing of compound **4.21b**.

4.3.14.3. *X*-ray *C*rystal *S*tructure and *D*ata for *B*enzo[*b*]azepine *D*erivative (4a.7aa):

Table 4.7. Crystallographic data for compound **4a.7aa**

CCDC Number	2115137
Compound identification code	ss_a
Empirical formula	C24 H19 N O
Formula weight	337.40
Temperature	100 K
Wavelength	0.71073Å
Crystal system	Triclinic
Space group	P -1
Unit cell dimensions	a=8.8810(17) alpha=68.127(8) b=10.050(2) beta=77.445(8) c=11.676(3) gamma=67.628(7)
Volume	890.8(3) $Å^3$
Z	2
Density (calculated)	1.258 g/cm^3
Absorption coefficient	0.076 mm^{-1}
F(000)	356.0
Reflections collected	4379
Independent reflections	3611

Completeness to theta = 27.539°	0.924
Refinement method	Full-matrix least-squares on F2
Max. and min. transmission	0.985 and 0.983
Goodness-of-fit on F2	1.138
R(reflections)	0.1557 (3611)
wR2(reflections)	0.4838 (4045)
Diffractometer	Xcalibur Gemini Eos CCD

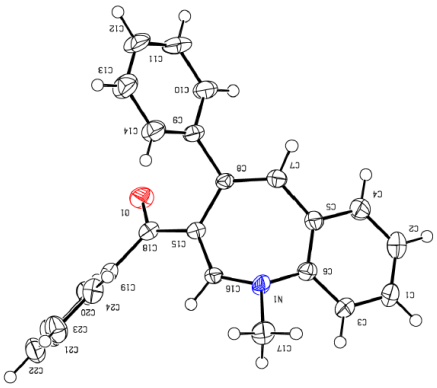


Figure 4.20. ORTEP-drawing of compound **4a.7aa**.

4.3.14.4. *X*-ray Crystal Structure and Data for Fluoroalkoxy Incorporated Dihydrobenzo[*b*]oxepine Derivative (4a.8a):

Table 4.8. Crystallographic data for compound **4a.8a**

CCDC Number	2115138
Compound identification code	Rb 11
Empirical formula	C25 H18 F3 O3
Formula weight	423.39
Temperature	303 K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P -1
Unit cell dimensions	a= 10.0756(7) alpha= 85.039(7) b= 13.9457(14) beta= 74.685(6) c= 15.6585(12) gamma= 85.638(7)
Volume	2110.9(3) $Å^3$
Z	4
Density (calculated)	1.332 g/cm^3
Absorption coefficient	0.104 mm^{-1}
F(000)	876.0

Reflections collected	9273
Independent reflections	1570
Completeness to theta = 25.082 °	0.952
Refinement method	Full-matrix least-squares on F2
Max. and min. transmission	0.998 and 0.996
Goodness-of-fit on F2	0.910
R(reflections)	0.1383 (1570)
wR2(reflections)	0.5011 (8831)
Diffractometer	Xcalibur Gemini Eos CCD

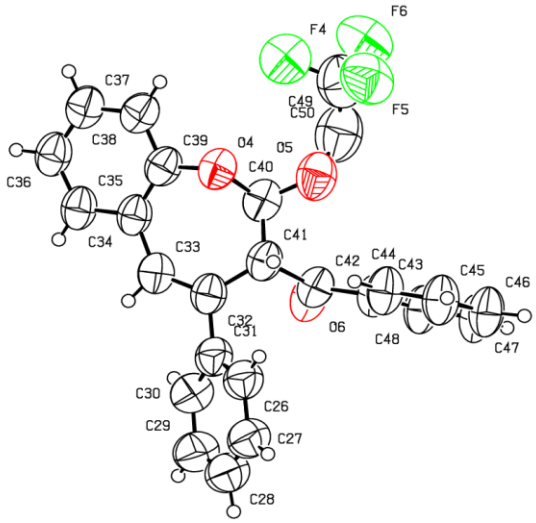


Figure 4.21. ORTEP-drawing of compound **4a.8a**.

4.3.14.5. *X*-ray Crystal Structure and Data for Fluoroalkoxy Incorporated Dihydrobenzo[*b*]azepine Derivative (4a.9a):

Table 4.9. Crystallographic data for compound **4a.9a**

CCDC Number	2115140
Compound identification code	rb06
Empirical formula	C32 H26 F3 N O4 S
Formula weight	577.60
Temperature	297 K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P -1
Unit cell dimensions	a= 12.0657(4) alpha= 76.982(2) b= 14.7620(5) beta= 74.984(2) c= 17.9978(4) gamma= 69.796(3)

Volume	2872.90(16) Å^3
Z	4
Density (calculated)	1.335 g/cm^3
Absorption coefficient	0.170 mm^{-1}
F(000)	1200.0
Reflections collected	12876
Independent reflections	4698
Completeness to theta = 25.026 °	0.953
Refinement method	Full-matrix least-squares on F2
Max. and min. transmission	0.967 and 0.965
Goodness-of-fit on F2	1.032
R(reflections)	0.0789 (4698)
wR2(reflections)	0.2779 (12272)
Diffractometer	Xcalibur Gemini Eos CCD

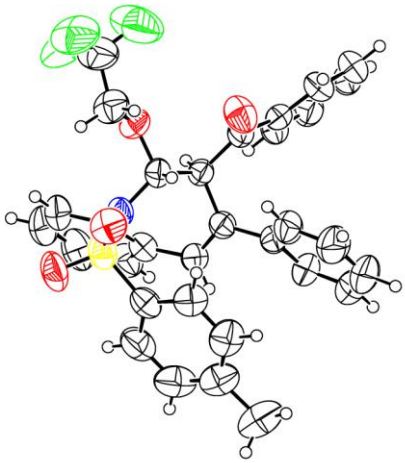


Figure 4.22. ORTEP-drawing of compound **4a.9a**.

4.3.14.6. *X*-ray Crystal Structure and Data for Fluoroalkoxy Incorporated Dihydrobenzo[*b*]azepine Derivative (4a.9c):

Table 4.10. Crystallographic data for compound **4a.9c**

CCDC Number	2062199
Compound identification code	Rb 12
Empirical formula	C29 H22 F3 N O5
Formula weight	521.48
Temperature	304 K
Wavelength	0.71073 Å
Crystal system	Monoclinic

Space group	P 21/c
Unit cell dimensions	a= 8.7984(8) alpha= 90 b= 16.0667(17) beta= 99.989(12) c= 18.773(3) gamma= 90
Volume	2613.6(6) Å^3
Z	4
Density (calculated)	1.325g/cm^3
Absorption coefficient	0.105 mm^{-1}
F(000)	1080.0
Reflections collected	5735
Independent reflections	940
Completeness to theta = 25.025°	0.957
Refinement method	Full-matrix least-squares on F2
Max. and min. transmission	0.998 and 0.995
Goodness-of-fit on F2	1.036
R(reflections)	0.1647 (940)
wR2(reflections)	0.6676 (5486)
Diffractometer	Xcalibur Gemini Eos CCD

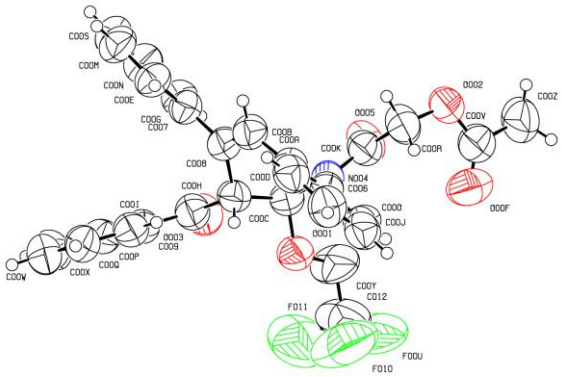


Figure 4.23. ORTEP-drawing of compound **4a.9c**.

4.3.14.7. *X*-ray *C*rystal *S*tructure and *D*ata for 2-*P*henyl-N-*S*ubtituteted *I*ndole *D*erivative (4a.10):

Table 4.11. Crystallographic data for compound **4a.10**

CCDC Number	2115142
Compound identification code	Rb 10
Empirical formula	C23 H17 N O
Formula weight	323.38
Temperature	298 K

Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P 21/n
Unit cell dimensions	a= 5.7352(7) alpha= 90 b= 28.615(3) beta= 103.167(9) c= 10.5446(9) gamma= 90
Volume	1685.0(3) $Å^3$
Z	4
Density (calculated)	1.275 g/cm^3
Absorption coefficient	0.078 mm^{-1}
F(000)	680.0
Reflections collected	3668
Independent reflections	1255
Completeness to theta = 25.025°	0.945
Refinement method	Full-matrix least-squares on F2
Max. and min. transmission	0.998 and 0.997
Goodness-of-fit on F2	0.875
R(reflections)	0.0690 (1255)
wR2(reflections)	0.1889 (3465)
Diffractometer	Xcalibur Gemini Eos CCD

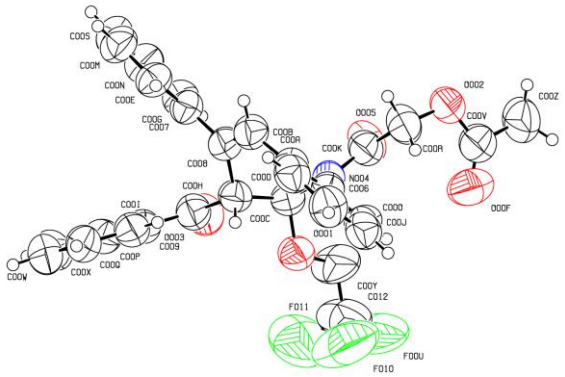


Figure 4.24. ORTEP-drawing of compound **4a.10**.

4.3.14.8. *X*-ray *C*rystal *S*tructure and *D*ata for *S*ubtituteted *I*ndole *D*erivative (4a.11):

Table 4.12. Crystallographic data for compound **4a.11**

CCDC Number	2062197
Compound identification code	mou_628
Empirical formula	C39 H32 N2 O
Formula weight	544.67
Temperature	293 K

Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P 21/n
Unit cell dimensions	a= 9.5362(10) alpha= 90 b= 20.967(2) beta= 103.785(11) c= 15.7993(16) gamma= 90
Volume	3068.0(6) $Å^3$
Z	4
Density (calculated)	1.179 g/cm^3
Absorption coefficient	0.070 mm^{-1}
F(000)	1152.0
Reflections collected	8370
Independent reflections	3019
Completeness to theta = 25.025°	0.850
Refinement method	Full-matrix least-squares on F2
Max. and min. transmission	0.999 and 0.997
Goodness-of-fit on F2	0.941
R(reflections)	0.0762 (3019)
wR2(reflections)	0.2253 (7113)
Diffractometer	Xcalibur Gemini Eos CCD

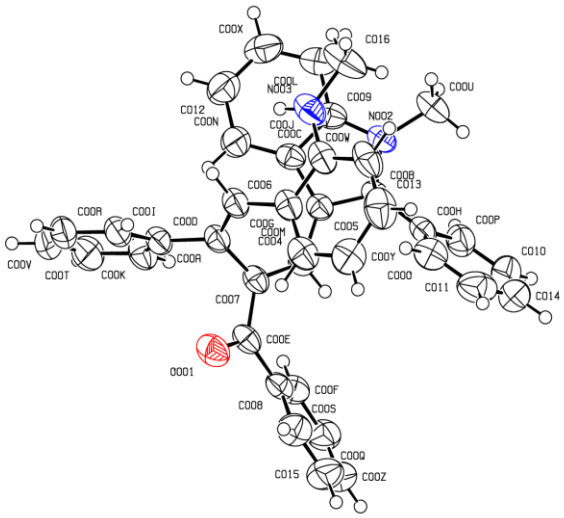


Figure 4.25. ORTEP-drawing of compound **4a.11**.

4.3.14.9. *X*-ray *C*rystal *S*tructure and *D*ata for *S*ubtituteted *I*ndole *D*erivative (4a.13):

Table 4.13. Crystallographic data for compound **4a.13**

CCDC Number	2115141
Compound identification code	rb24a

Empirical formula	C39 H32 N2 O3
Formula weight	576.67
Temperature	113 K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P 21/c
Unit cell dimensions	a= 10.7368(4) alpha= 90 b= 28.8529(13) beta= 101.004(4) c= 9.9567(4) gamma= 90
Volume	3027.8(2) $Å^3$
Z	4
Density (calculated)	1.265 g/cm^3
Absorption coefficient	0.080 mm^{-1}
F(000)	1216.0
Reflections collected	6650
Independent reflections	3449
Completeness to theta = 25.025°	0.956
Refinement method	Full-matrix least-squares on F2
Max. and min. transmission	0.999 and 0.998
Goodness-of-fit on F2	0.995
R(reflections)	0.0616 (3449)
wR2(reflections)	0.1627 (6357)
Diffractometer	Xcalibur Gemini Eos CCD

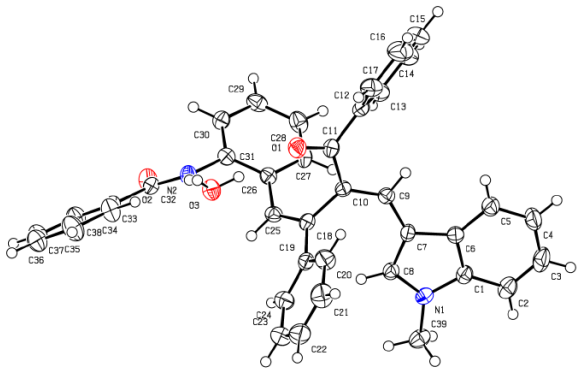


Figure 4.26. ORTEP-drawing of compound **4a.13**.

4.3.13.10. *X*-ray *C*rystal *S*tructure and *D*ata for 2,3-*D*ihydrobenzo[*b*]azepine *D*erivative (4a.14):

Table 4.14. Crystallographic data for compound **4a.14**

CCDC Number	2115145
Compound identification code	RB006_0m_a

Empirical formula	C24 H21 N O
Formula weight	339.42
Temperature	300 K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P 21/c
Unit cell dimensions	a= 14.2410(17) alpha= 90 b= 6.0681(6) beta= 93.855(5) c= 21.122(3) gamma= 90
Volume	1821.2(4) $Å^3$
Z	4
Density (calculated)	1.238 g/cm^3
Absorption coefficient	0.074 mm^{-1}
F(000)	0.075
Reflections collected	4177
Independent reflections	3117
Completeness to theta = 25.025°	1.000
Refinement method	Full-matrix least-squares on F2
Max. and min. transmission	0.987and 0.993
Goodness-of-fit on F2	1.072
R(reflections)	0.0667 (3117)
wR2(reflections)	0.2058 (4176)
Diffractometer	Xcalibur Gemini Eos CCD

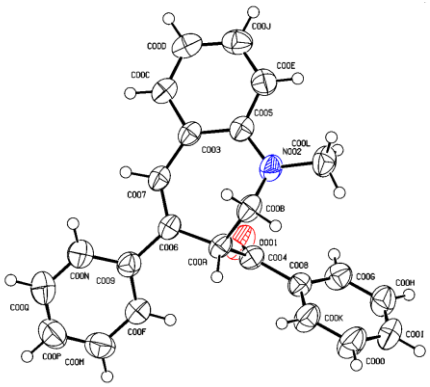


Figure 4.27. ORTEP-drawing of compound **4a.14**.

4.3.14.11. *X*-ray *C*rystal *S*tructure and *D*ata for 2,3-*D*ihydrobenzo[*b*]azepinol *D*erivative (4a.15):

Table 4.15. Crystallographic data for compound **4a.15**

CCDC Number	2115143
Compound identification code	RB27

Empirical formula	C24 H23 N O
Formula weight	341.43
Temperature	298 K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P -1
Unit cell dimensions	a= 12.4670(2) alpha= 93.650(1) b= 12.8335(2) beta= 114.849(2) c= 13.6779(3) gamma= 98.756(1)
Volume	1942.67(7) $Å^3$
Z	4
Density (calculated)	1.167 g/cm^3
Absorption coefficient	0.071 mm^{-1}
F(000)	728.0
Reflections collected	6859
Independent reflections	4310
Completeness to theta = 25.025°	0.999
Refinement method	Full-matrix least-squares on F2
Max. and min. transmission	0.987 and 0.993
Goodness-of-fit on F2	1.057
R(reflections)	0.0519 (4310)
wR2(reflections)	0.1479 (6853)
Diffractometer	Xcalibur Gemini Eos CCD

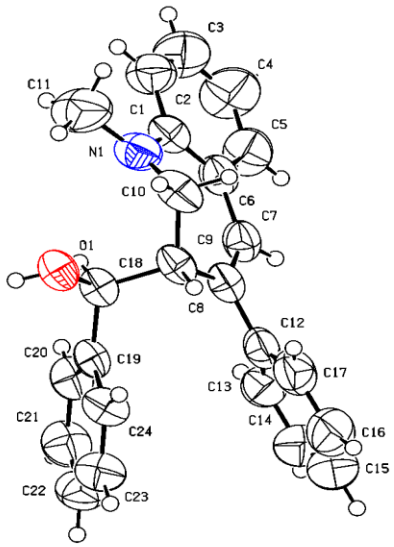


Figure 4.28. ORTEP-drawing of compound **4a.15**.

4.3.14.12. X-ray Crystal Structure and Data for 2,3-Dihydrobenzo[b]azepinol Derivative (4a.15'):

Table 4.16. Crystallographic data for compound **4a.15'**

CCDC Number	2115144
Compound identification code	rb004_0m_a
Empirical formula	C24 H23 N O
Formula weight	341.43
Temperature	296 K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P 21/c
Unit cell dimensions	a= 9.259(3) alpha= 90 b= 25.351(8) beta= 96.559(9) c= 7.934(3) gamma= 90
Volume	1850.1(11) Å3
Z	4
Density (calculated)	1.226 g/cm3
Absorption coefficient	0.074 mm-1
F(000)	728.0
Reflections collected	4251
Independent reflections	3642
Completeness to theta = 25.025°	0.998
Refinement method	Full-matrix least-squares on F2
Max. and min. transmission	0.987and 0.993
Goodness-of-fit on F2	1.204
R(reflections)	0.0750 (3642)
wR2(reflections)	0.1793 (4242)
Diffractometer	Xcalibur Gemini Eos CCD

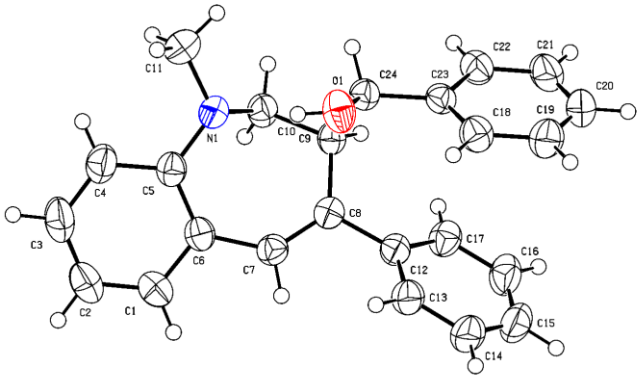


Figure 4.29. ORTEP-drawing of compound **4a.15'**.

4.3.14.13. X-ray Crystal Structure and Data for 3-Substituted Indole Derivative (4b.7aa):

Table 4.17. Crystallographic data for compound **4b.7aa**

CCDC Number	2166456
Compound identification code	rb007_0m_a
Empirical formula	C24 H19 N O
Formula weight	337.40
Temperature	300 K
Wavelength	0.71073Å
Crystal system	Triclinic
Space group	P -1
Unit cell dimensions	a=5.9743(5) alpha=90.934(4) b=10.7749(9) beta=95.031(4) c=14.3140(13) gamma=105.858(3)
Volume	882.17(13) $Å^3$
Z	2
Density (calculated)	1.270 g/cm^3
Absorption coefficient	0.077 mm^{-1}
F(000)	356.0
Reflections collected	4107
Independent reflections	2765
Completeness to theta = 27.539°	0.995
Refinement method	Full-matrix least-squares on F2
Max. and min. transmission	0.992 and 0.986
Goodness-of-fit on F2	1.080
R(reflections)	0.0679 (2765)
wR2(reflections)	0.1896 (4086)
Diffractometer	Xcalibur Gemini Eos CCD

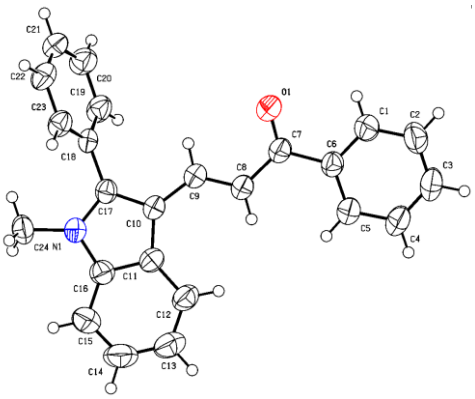


Figure 4.30. ORTEP-drawing of compound **4b.7aa**.

4.3.14.14. X-ray Crystal Structure and Data for 3-Substituted Indole Derivative (4b.7be):

Table 4.18. Crystallographic data for compound **4b.7be**

CCDC Number	2166457
Compound identification code	Rb 32
Empirical formula	C25 H21 N O3
Formula weight	383.43
Temperature	298 K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P -1
Unit cell dimensions	a= 11.0647(2) alpha= 111.413(2) b= 12.8133(2) beta= 91.060(1) c= 15.8157(3) gamma= 102.444(1)
Volume	2026.78(7) $Å^3$
Z	4
Density (calculated)	1.257 g/cm^3
Absorption coefficient	0.082 mm^{-1}
F(000)	808.0
Reflections collected	7179
Independent reflections	5150
Completeness to theta = 25.082 °	0.999
Refinement method	Full-matrix least-squares on F2
Max. and min. transmission	0.992 and 0.985
Goodness-of-fit on F2	1.048
R(reflections)	0.0464 (5150)
wR2(reflections)	0.1279 (7171)
Diffractometer	Xcalibur Gemini Eos CCD

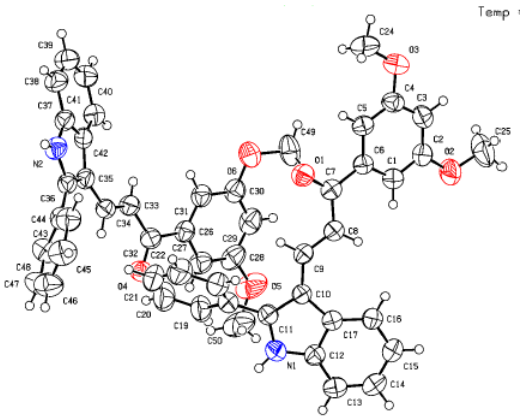


Figure 4.31. ORTEP-drawing of compound **4b.7be**.

4.3.14.15. X-ray Crystal Structure and Data for 3-Substituted Benzofuran Derivative (4b.8a):

Table 4.19. Crystallographic data for compound **4b.8a**

CCDC Number	2166458
Compound identification code	rb016_0ma_a
Empirical formula	C23 H16 O2
Formula weight	324.36
Temperature	300 K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P 21/c
Unit cell dimensions	a= 11.716(6) alpha= 90 b= 14.621(7) beta= 107.26(2) c= 10.413(5) gamma= 90
Volume	1703.4(15) $Å^3$
Z	4
Density (calculated)	1.265 g/cm^3
Absorption coefficient	0.080 mm^{-1}
F(000)	680.0
Reflections collected	3018
Independent reflections	1800
Completeness to theta = 25.026 °	0.914
Refinement method	Full-matrix least-squares on F2
Max. and min. transmission	0.992 and 0.986
Goodness-of-fit on F2	1.313
R(reflections)	0.1195 (1800)
wR2(reflections)	0.3502 (2759)
Diffractometer	Xcalibur Gemini Eos CCD

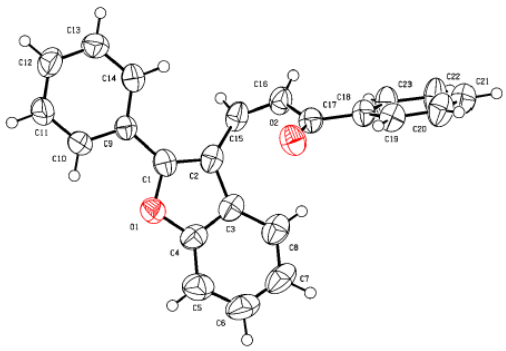


Figure 4.32. ORTEP-drawing of compound **4b.8a**.

4.3.14.16. X-ray Crystal Structure and Data for Substituted Indoline Derivative (4b.11):

Table 4.20. Crystallographic data for compound **4b.11**

CCDC Number	2166459
Compound identification code	RB100
Empirical formula	C19 H19 N O3
Formula weight	309.35
Temperature	297 K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P 21/n
Unit cell dimensions	a= 10.6702(4) alpha= 90 b= 9.9677(4) beta= 109.575(5) c= 15.8095(8) gamma= 90
Volume	1584.28(13) $Å^3$
Z	4
Density (calculated)	1.297 g/cm^3
Absorption coefficient	0.088 mm^{-1}
F(000)	656.0
Reflections collected	3514
Independent reflections	2236
Completeness to theta = 25.025°	0.924
Refinement method	Full-matrix least-squares on F2
Max. and min. transmission	0.996 and 0.995
Goodness-of-fit on F2	1.060
R(reflections)	0.0495 (2236)
wR2(reflections)	0.1437 (3248)
Diffractometer	Xcalibur Gemini Eos CCD

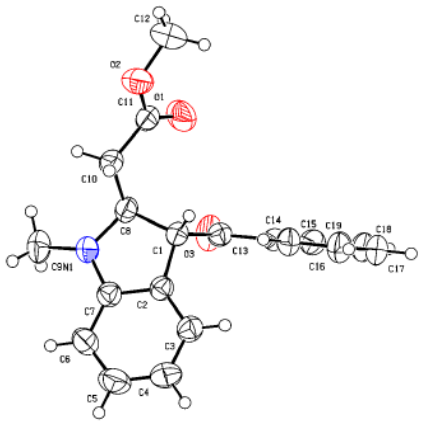


Figure 4.33. ORTEP-drawing of compound **4b.11**.

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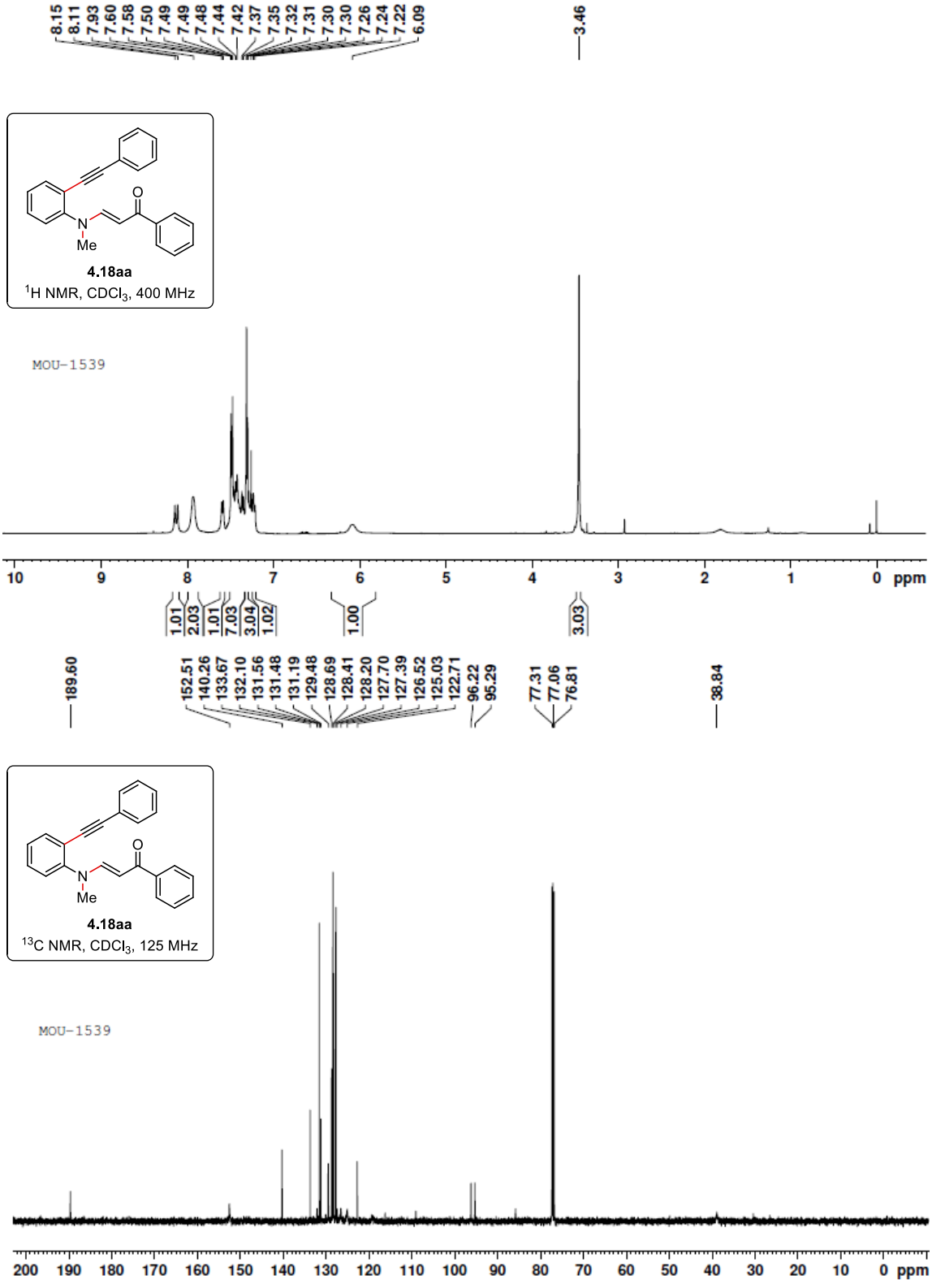
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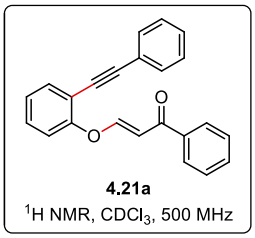
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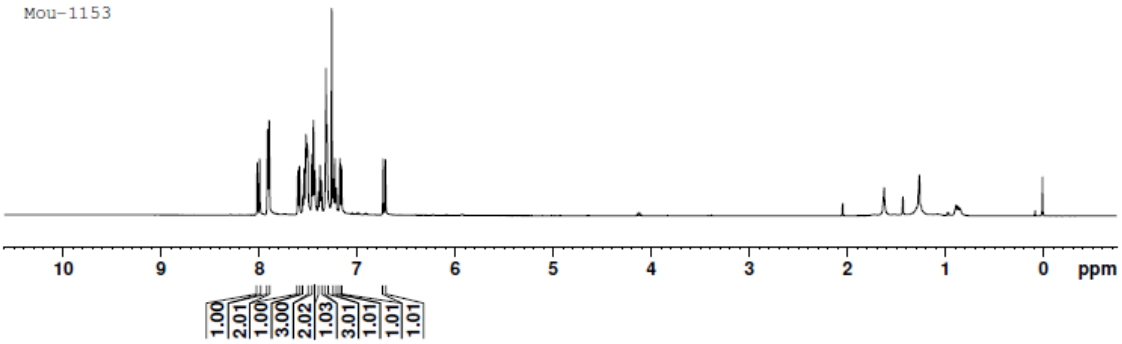


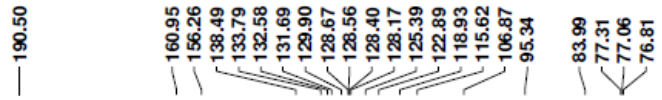


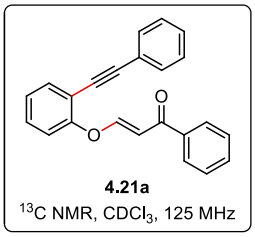


4.21a

^{1}H NMR, $CDCl_3$, 500 MHz

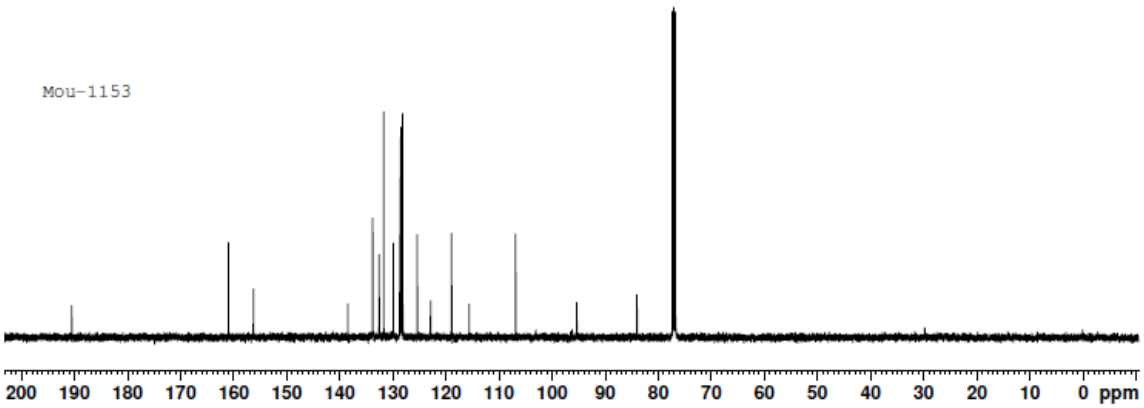




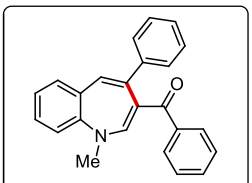


4.21a

^{13}C NMR, $CDCl_3$, 125 MHz

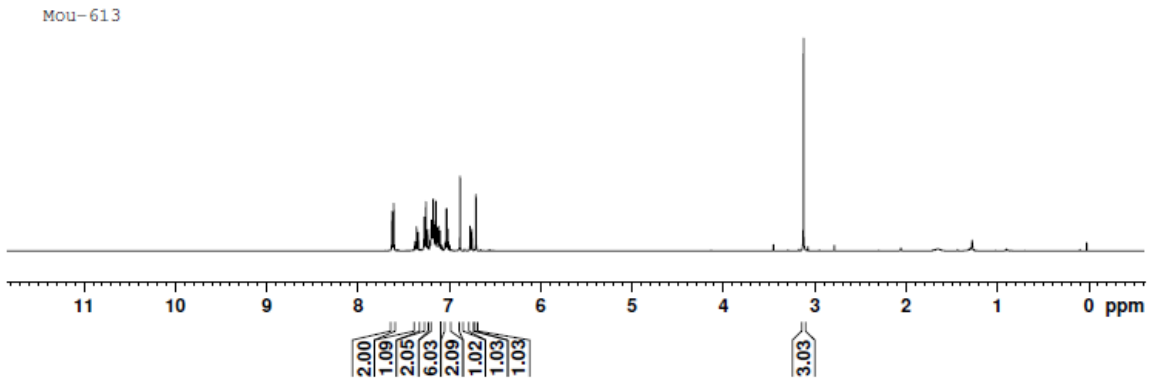


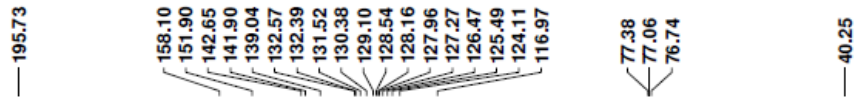


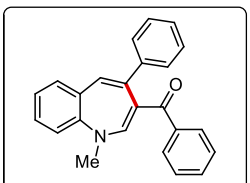


4a.7aa

^{1}H NMR, $CDCl_3$, 400 MHz

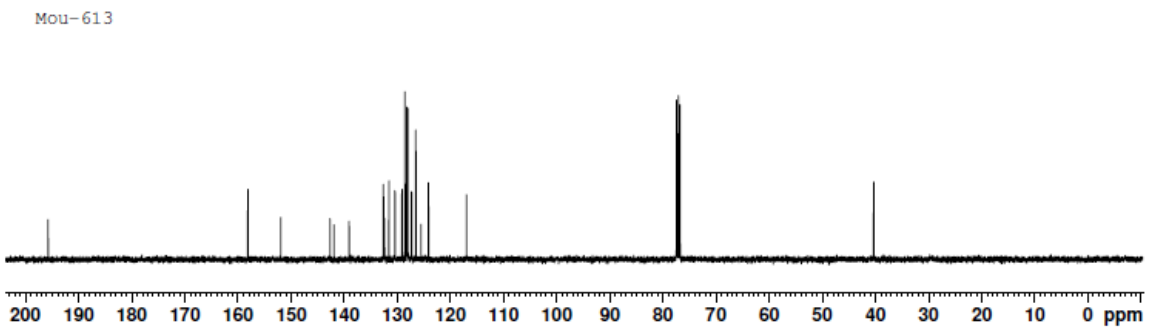


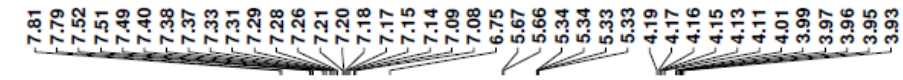


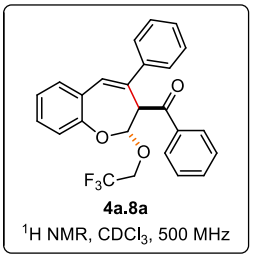


4a.7aa

^{13}C NMR, $CDCl_3$, 100 MHz

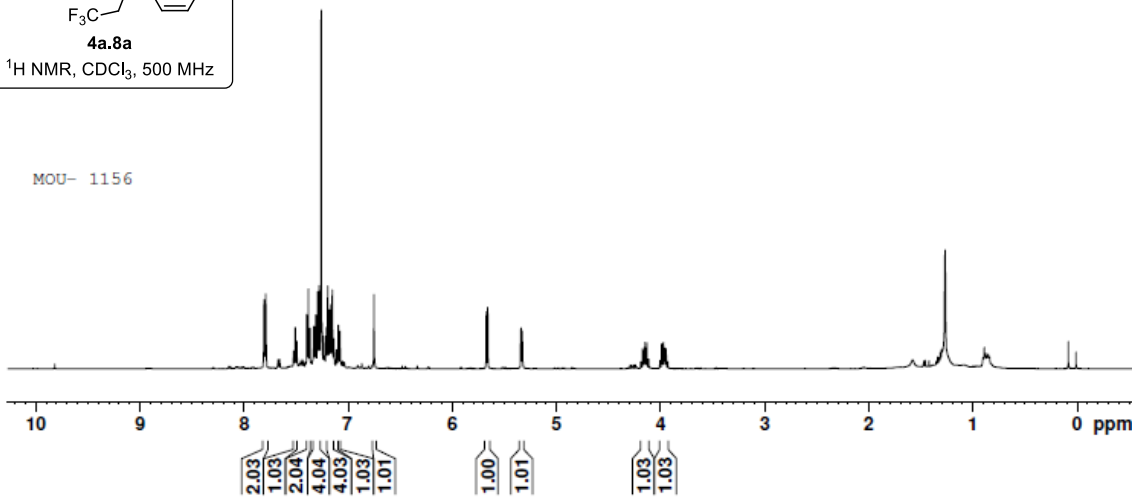


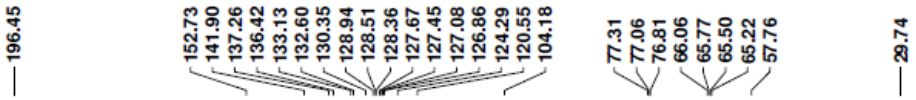


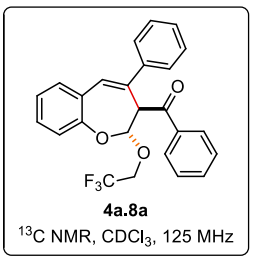


4a.8a

^{1}H NMR, $CDCl_3$, 500 MHz

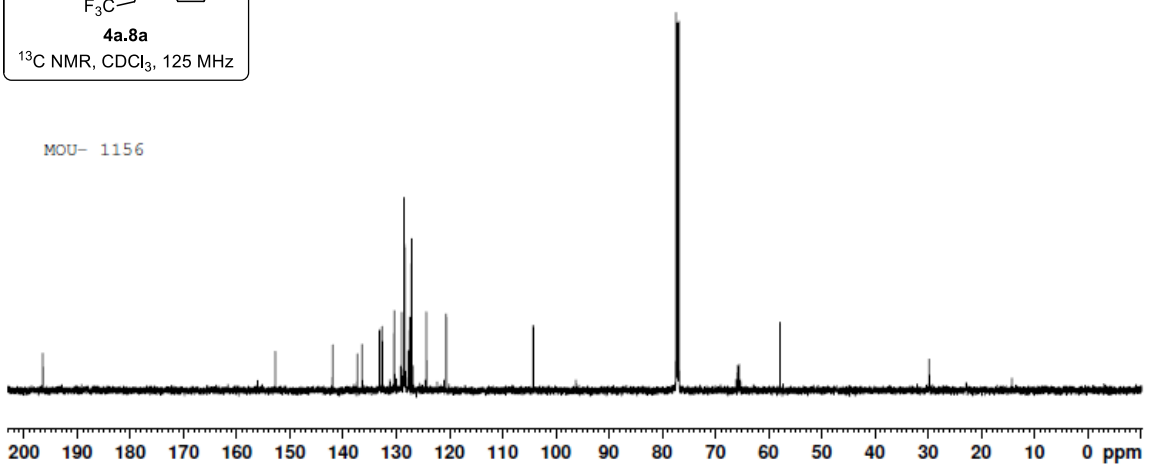




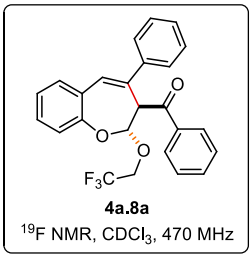


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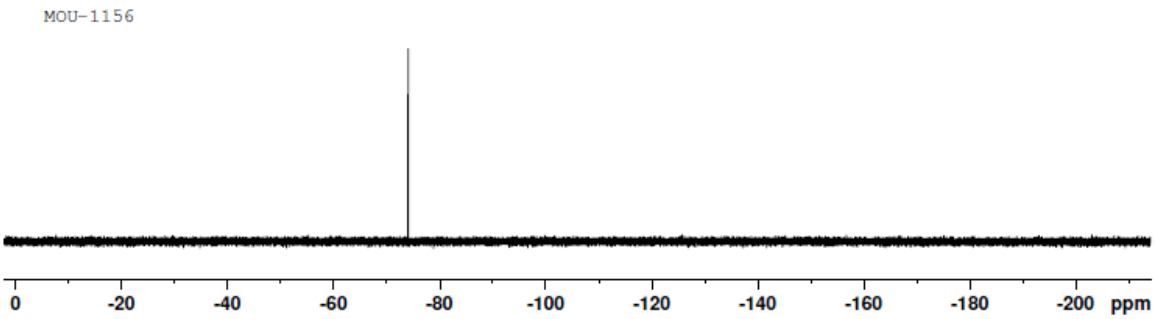
^{13}C NMR, $CDCl_3$, 125 MHz

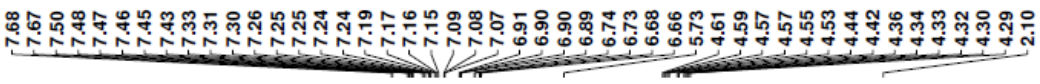


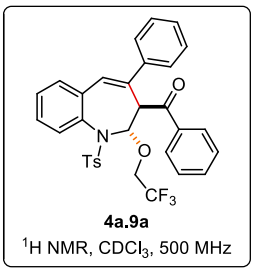




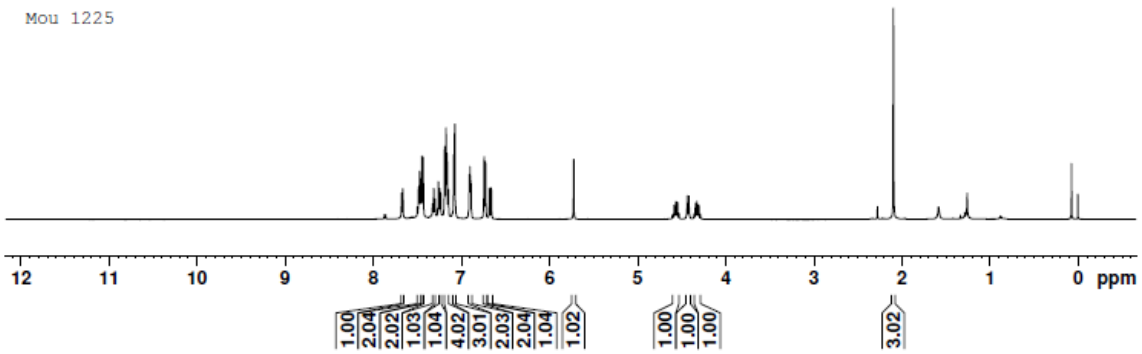
4a.8a
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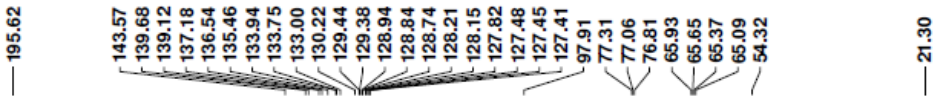


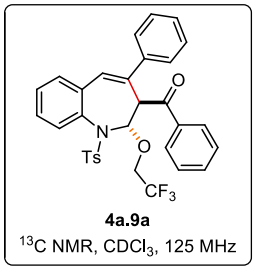




4a.9a
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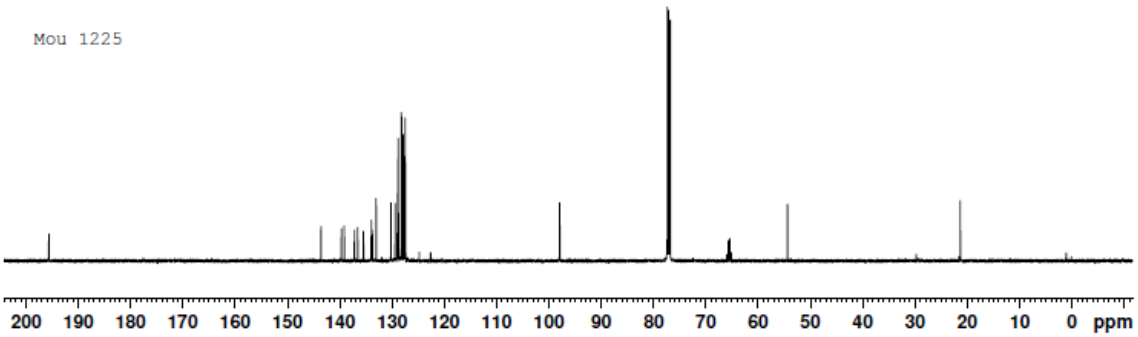




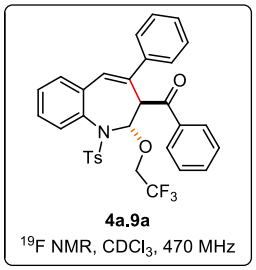


4a.9a

^{13}C NMR, $CDCl_3$, 125 MHz

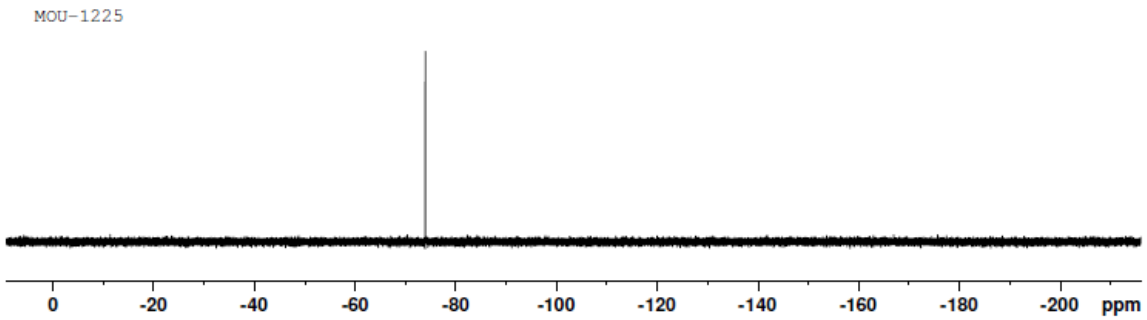




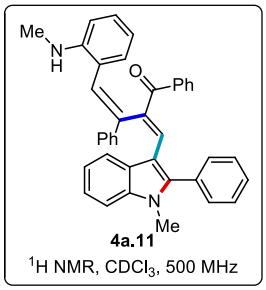


4a.9a

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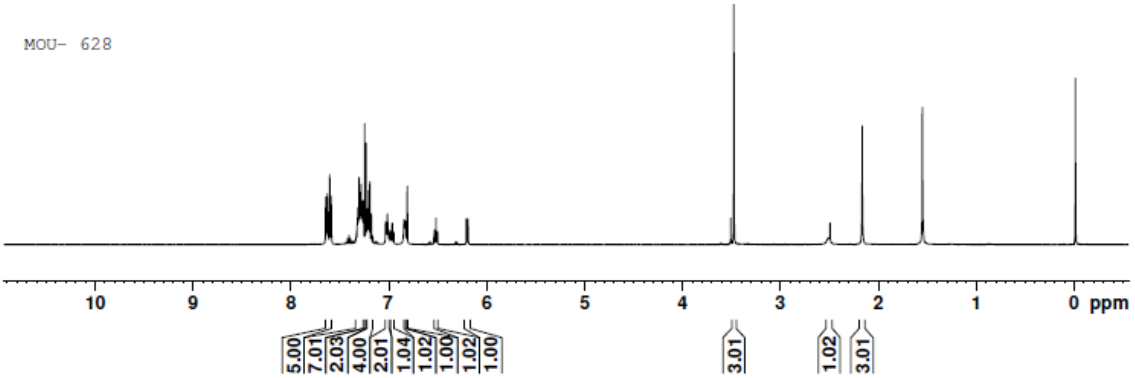




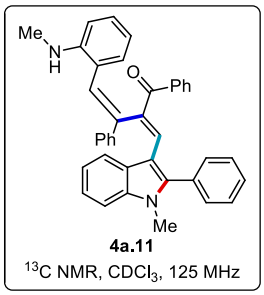


4a.11

^{1}H NMR, $CDCl_3$, 500 MHz

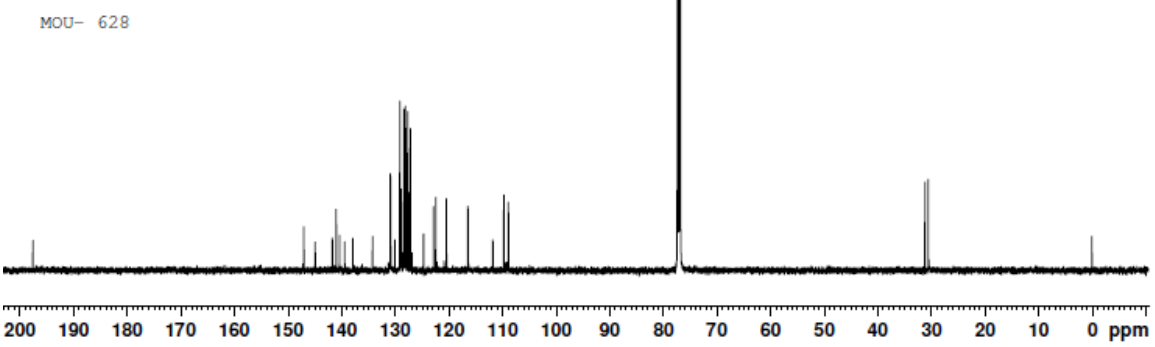


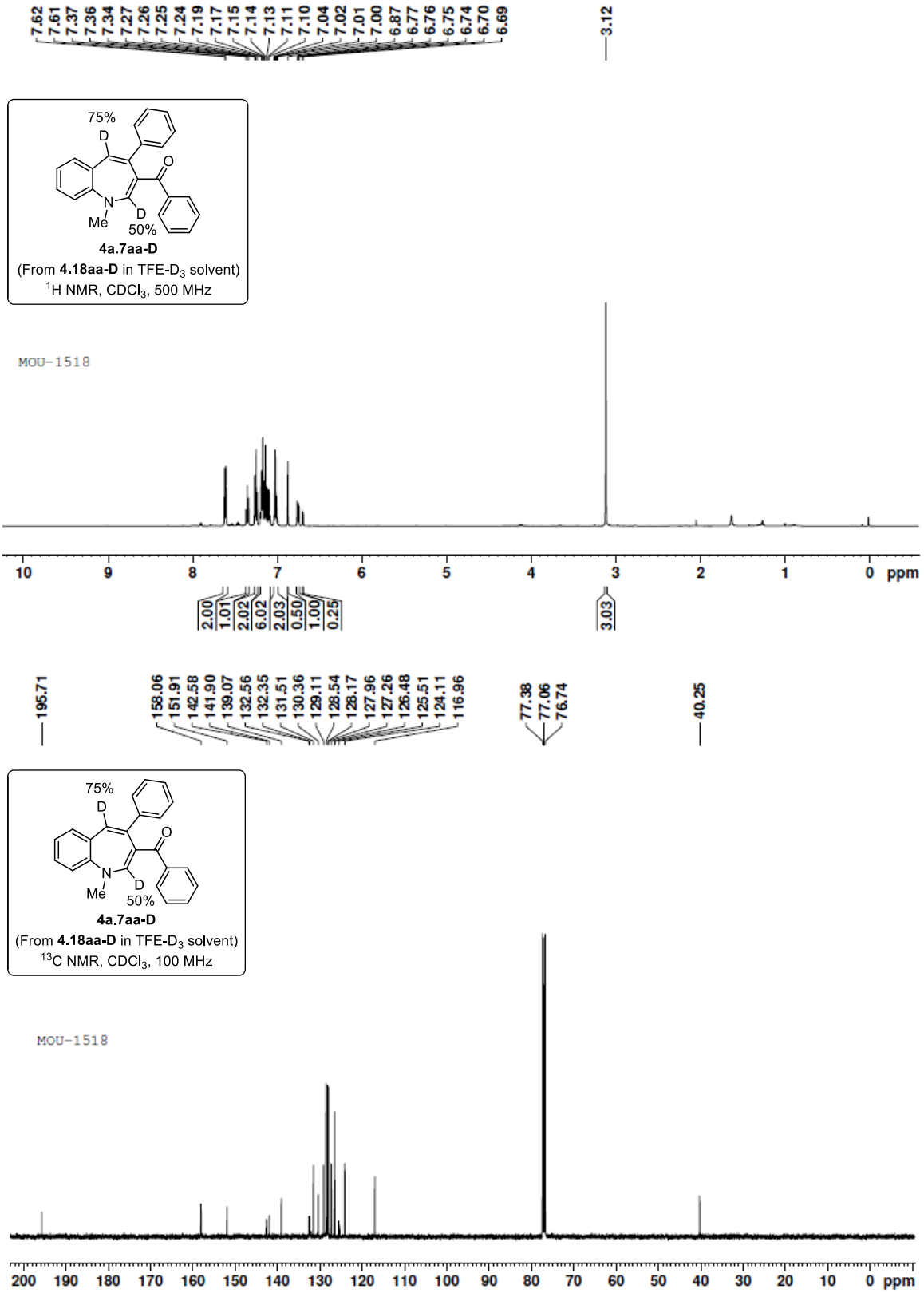


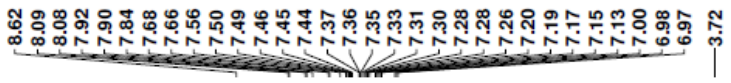


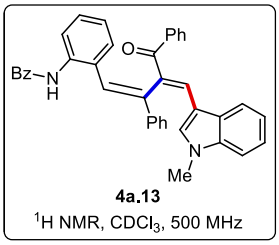
4a.11

^{13}C NMR, $CDCl_3$, 125 MHz



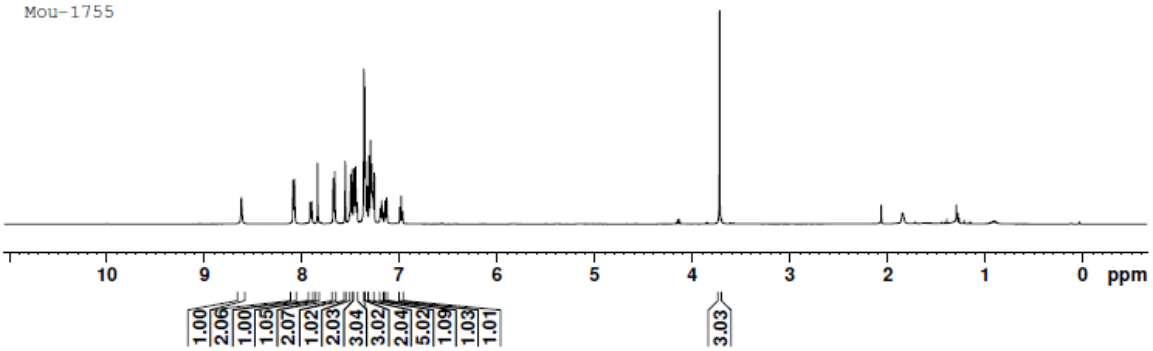

7.62
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7.04
7.02
7.01
7.00
6.87
6.77
6.76
6.75
6.74
6.70
6.69
3.12
75%
D
O
N
Me
D
50%
4a.7aa-D
(From 4.18aa-D in TFE-D3 solvent)
1H NMR, CDCl3, 500 MHz
MOU-1518
10
9
8
7
6
5
4
3
2
1
0 ppm
2.00
1.01
2.02
6.02
2.03
0.50
1.00
0.25
3.03
195.71
158.06
151.91
142.58
141.90
139.07
132.56
132.35
131.51
130.36
129.11
128.54
128.17
127.96
127.26
126.48
125.51
124.11
116.96
77.38
77.06
76.74
40.25
75%
D
O
N
Me
D
50%
4a.7aa-D
(From 4.18aa-D in TFE-D3 solvent)
13C NMR, CDCl3, 100 MHz
MOU-1518
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm

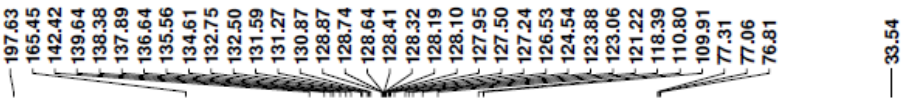


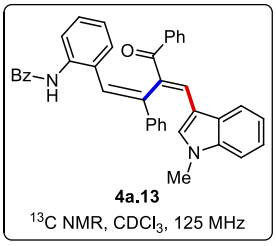


4a.13

^{1}H NMR, $CDCl_3$, 500 MHz

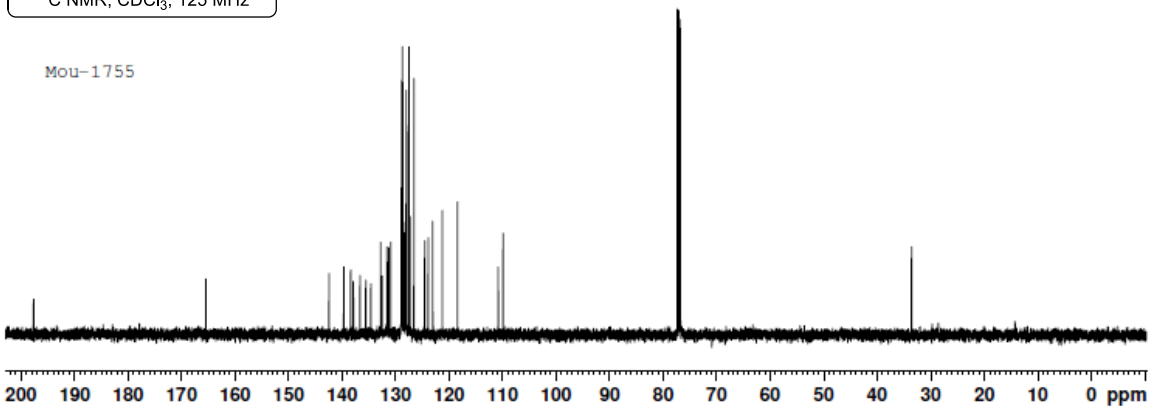


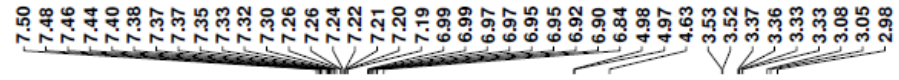


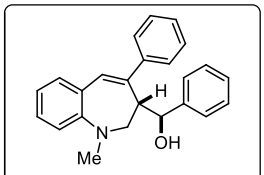


4a.13

^{13}C NMR, $CDCl_3$, 125 MHz

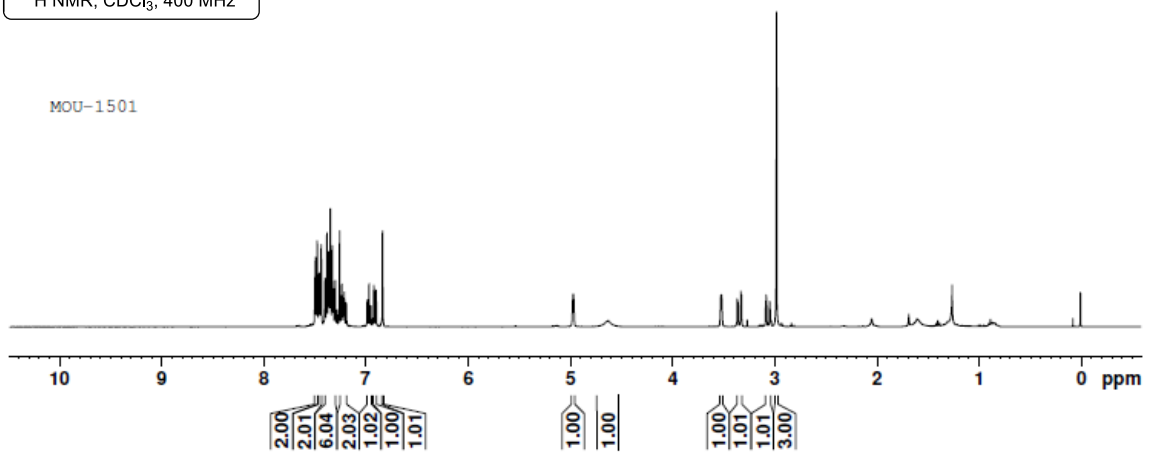


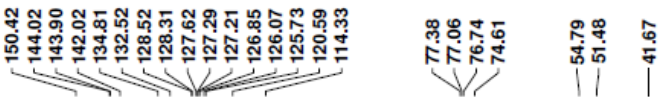




4a.15

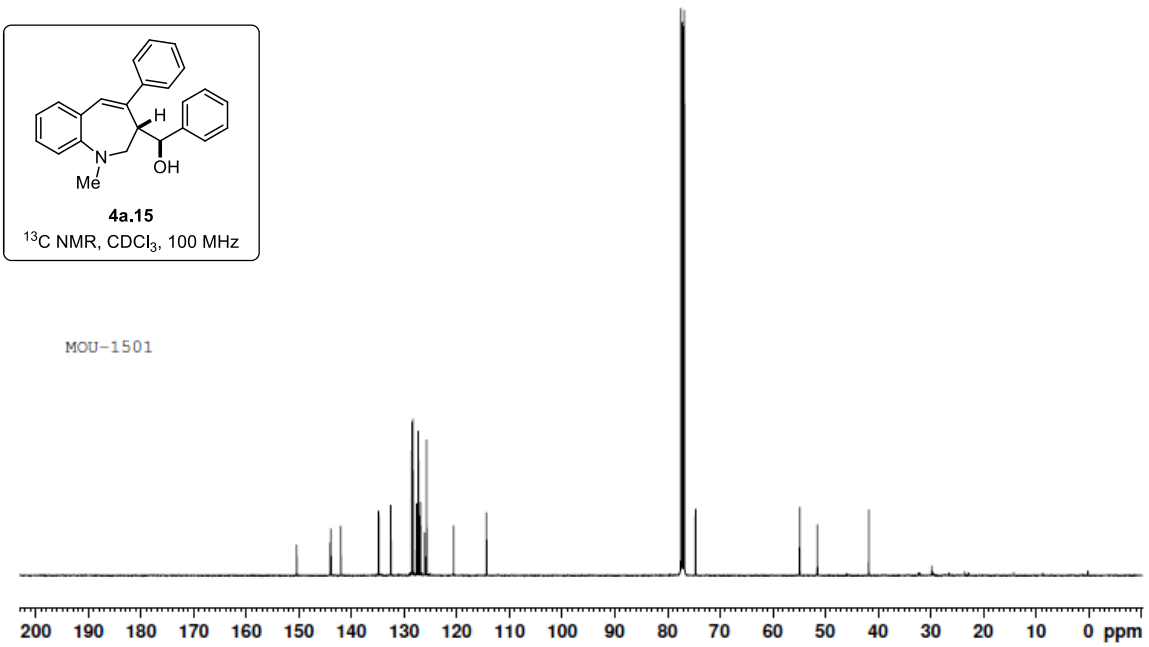
^{1}H NMR, $CDCl_3$, 400 MHz

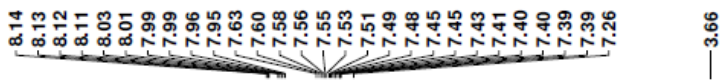


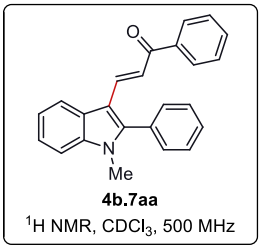


4a.15

^{13}C NMR, $CDCl_3$, 100 MHz

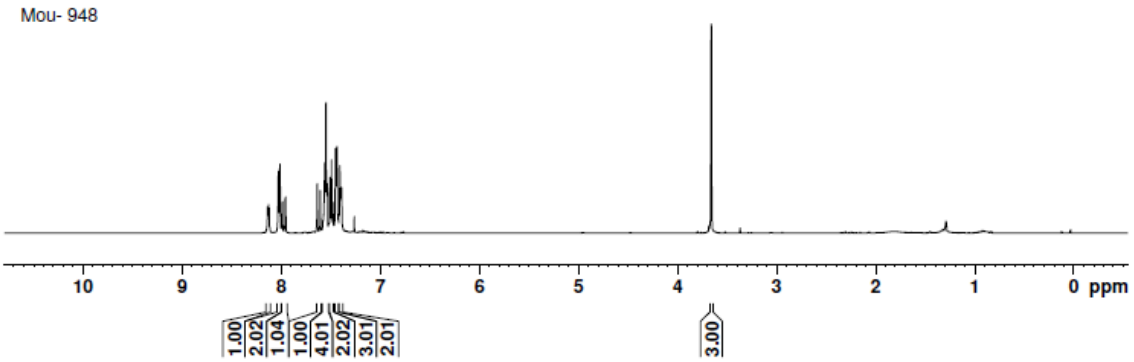


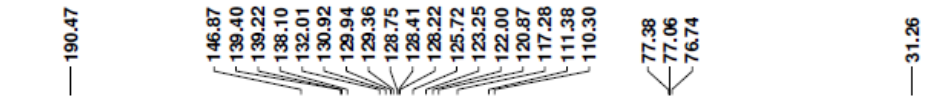


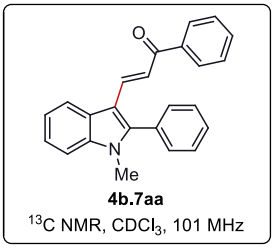


4b.7aa

^{1}H NMR, $CDCl_3$, 500 MHz

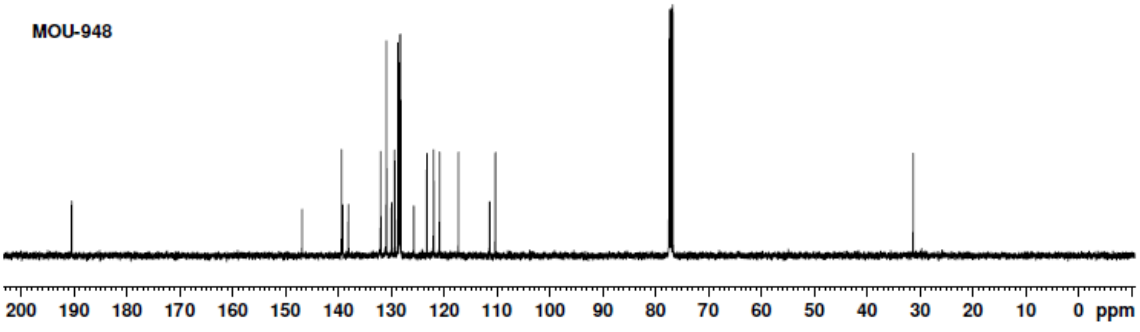


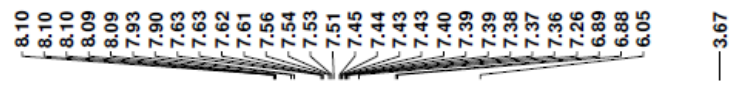


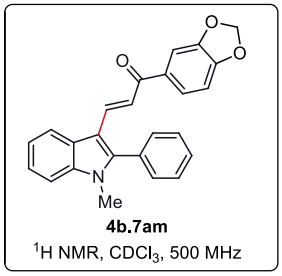


4b.7aa

^{13}C NMR, $CDCl_3$, 101 MHz

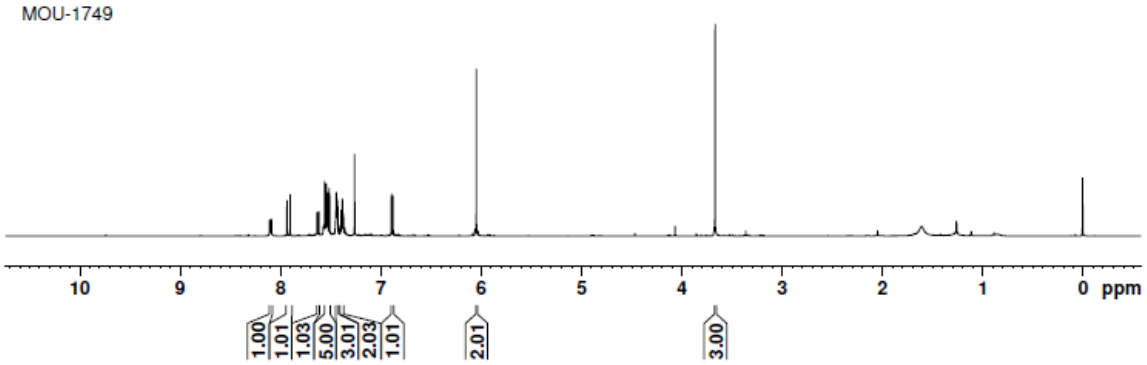


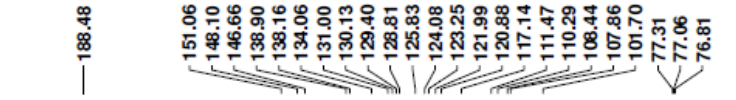




4b.7am

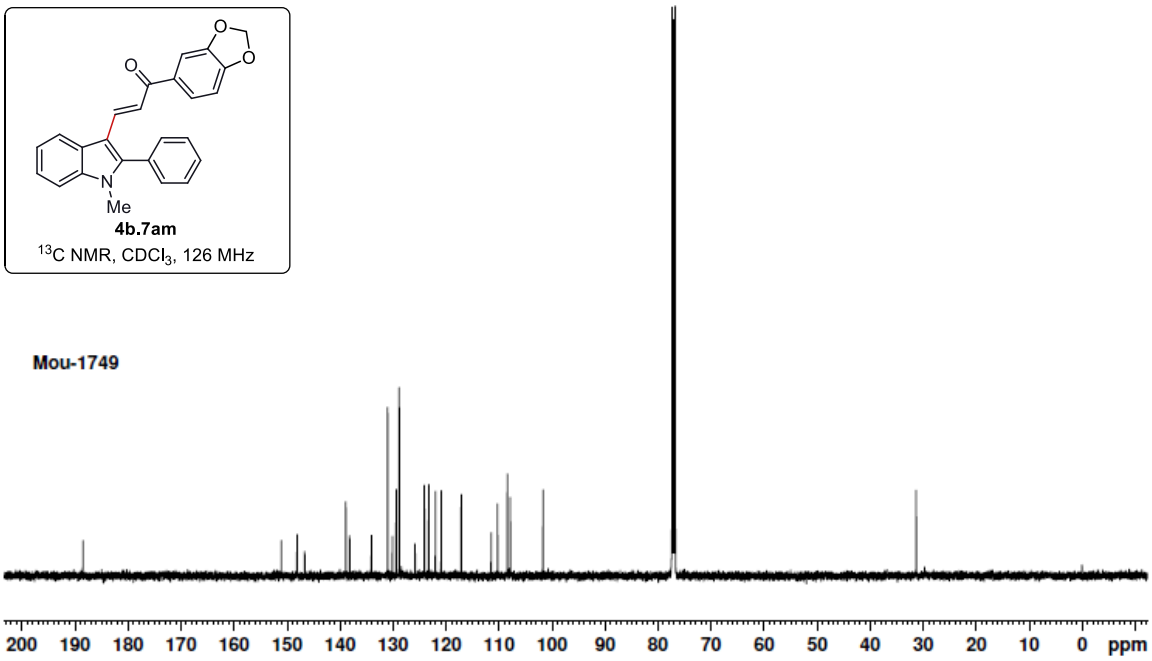
^{1}H NMR, $CDCl_3$, 500 MHz

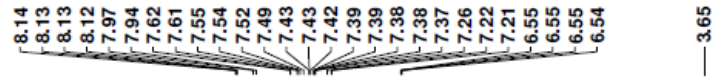


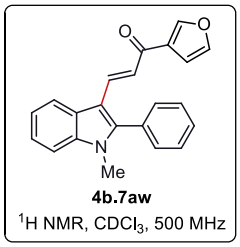


4b.7am

^{13}C NMR, $CDCl_3$, 126 MHz

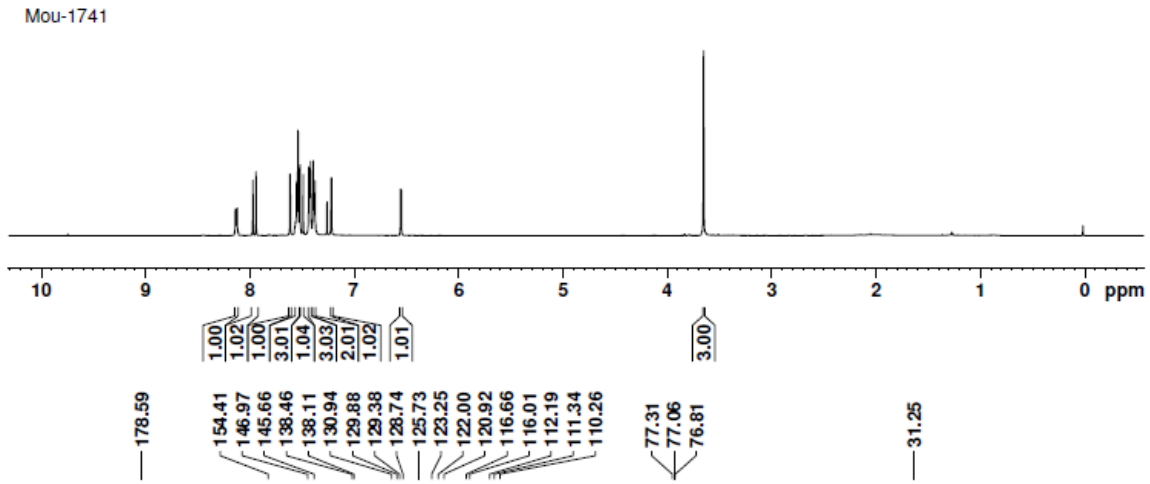


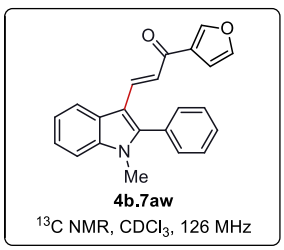




4b.7aw

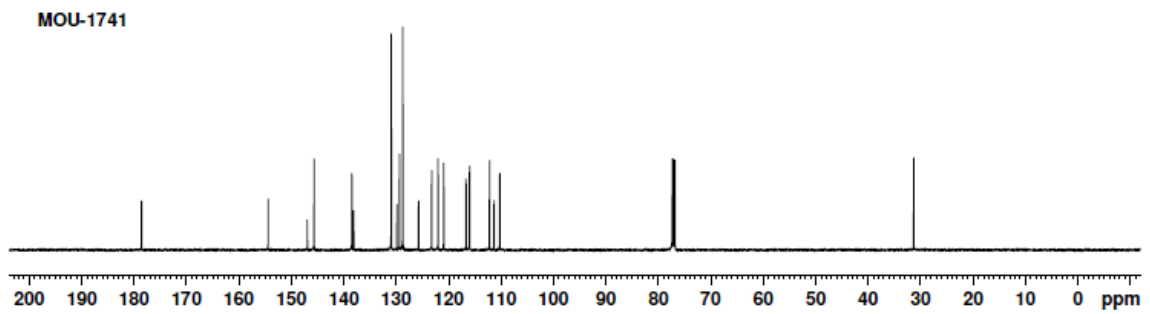
^{1}H NMR, $CDCl_3$, 500 MHz

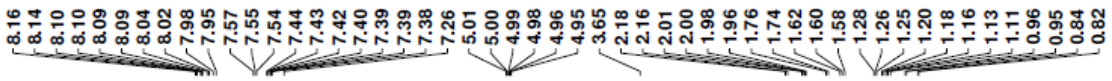


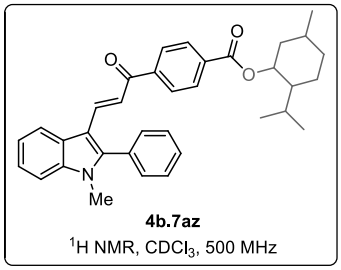


4b.7aw

^{13}C NMR, $CDCl_3$, 126 MHz



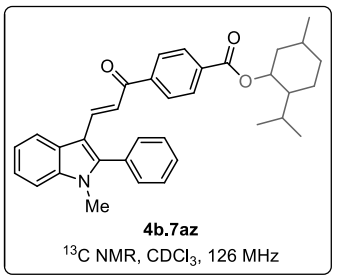




4b.7az

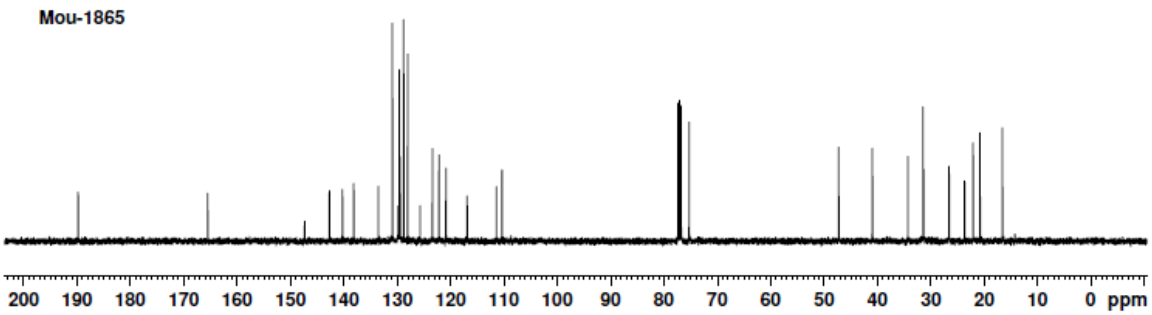
^{1}H NMR, $CDCl_3$, 500 MHz



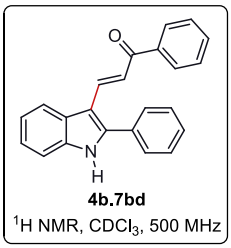


4b.7az

^{13}C NMR, $CDCl_3$, 126 MHz



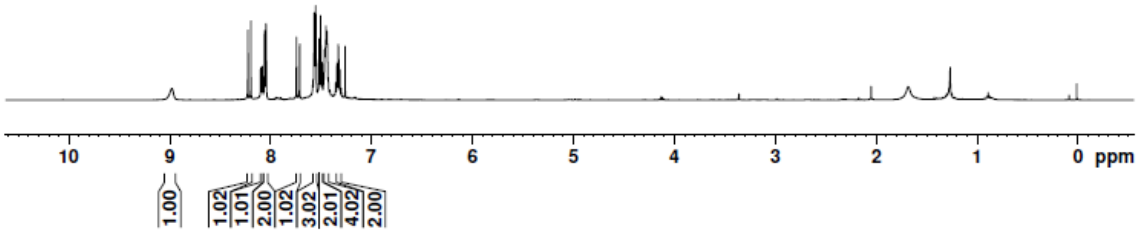


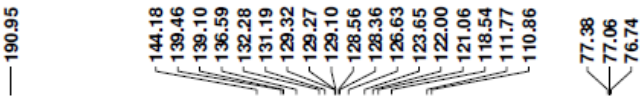


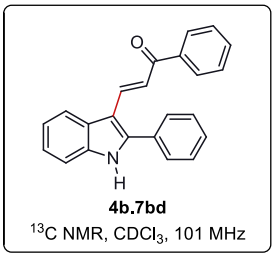
4b.7bd

^{1}H NMR, $CDCl_3$, 500 MHz

Mou-1783



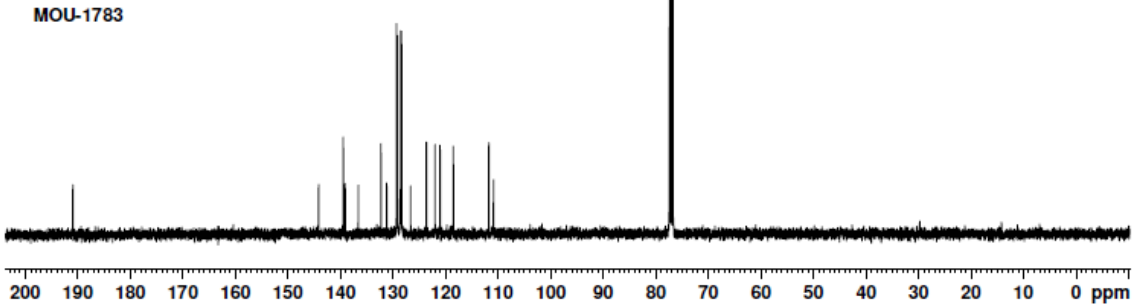




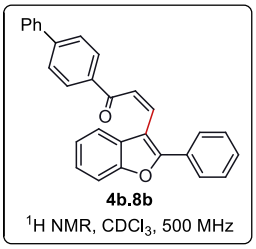
4b.7bd

^{13}C NMR, $CDCl_3$, 101 MHz

MOU-1783



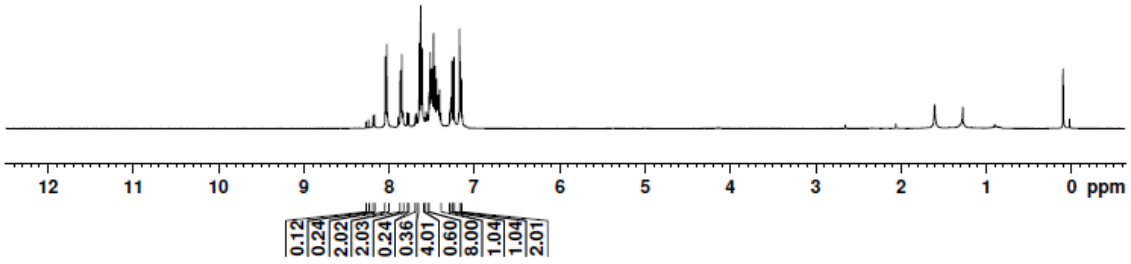




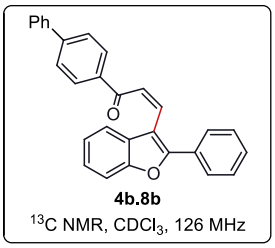
4b.8b

^{1}H NMR, $CDCl_3$, 500 MHz

Mou-1778



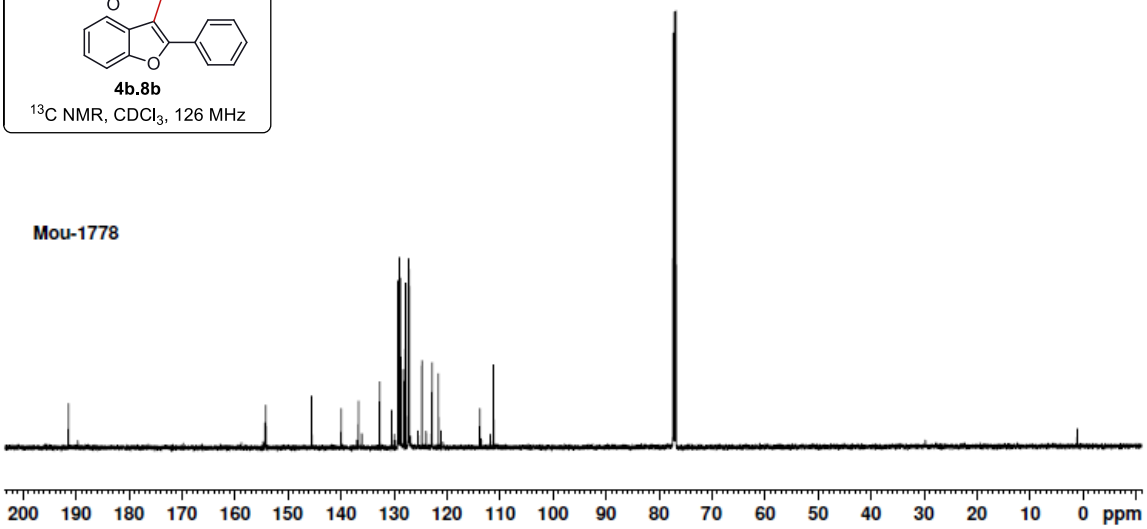


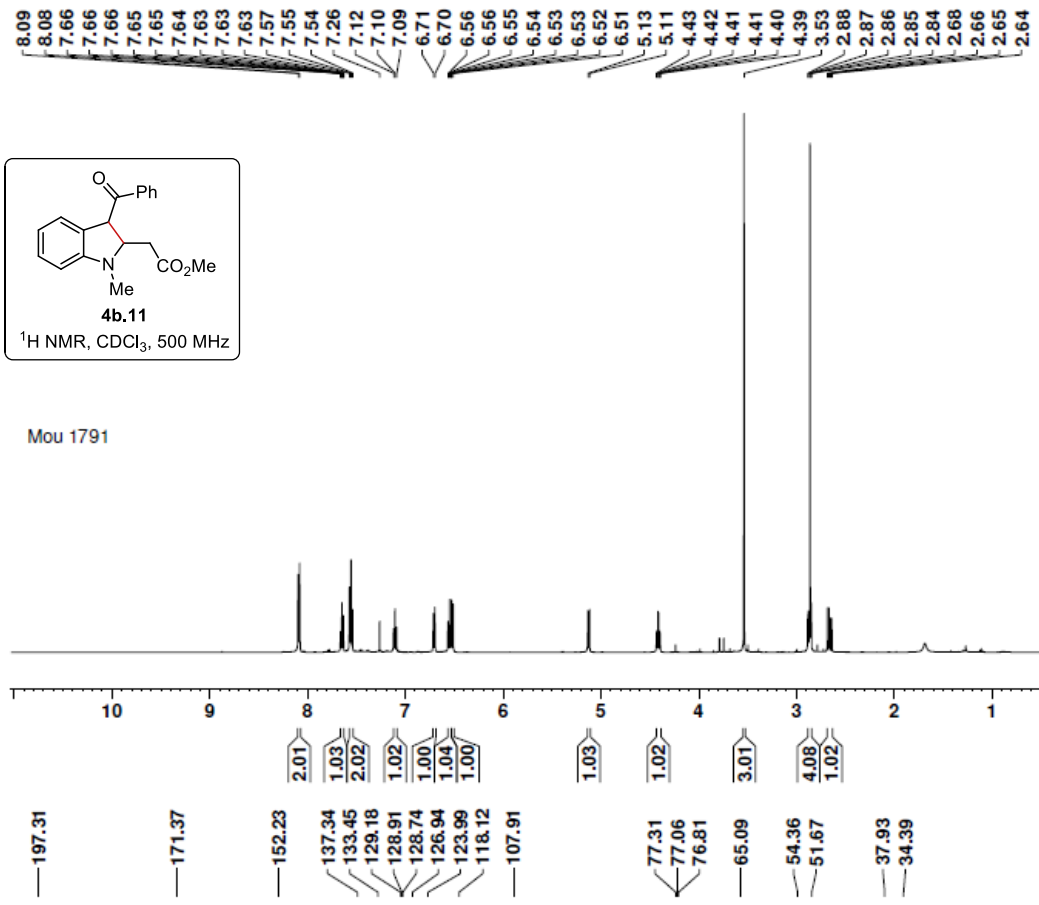


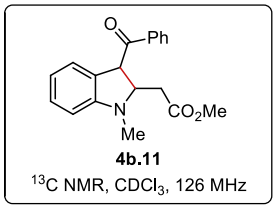
4b.8b

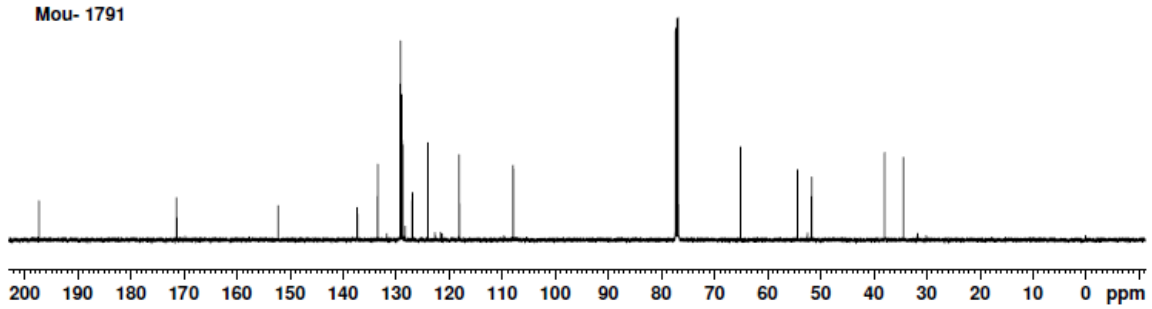
^{13}C NMR, $CDCl_3$, 126 MHz

Mou-1778

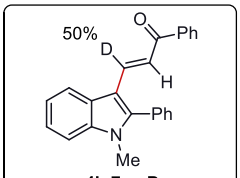



8.09 8.08 7.66 7.66 7.66 7.65 7.65 7.64 7.63 7.63 7.63 7.57 7.55 7.54 7.26 7.12 7.10 7.09 6.71 6.70 6.56 6.56 6.55 6.54 6.53 6.53 6.52 6.51 5.13 5.11 4.43 4.42 4.41 4.41 4.40 4.39 3.53 2.88 2.87 2.86 2.85 2.84 2.68 2.66 2.65 2.64
O
Ph
N
Me
CO2Me
4b.11
1H NMR, CDCl3, 500 MHz
Mou 1791
10 9 8 7 6 5 4 3 2 1 0 ppm
2.01 1.03 2.02 1.02 1.00 1.04 1.00 1.03 1.02 3.01 4.08 1.02
197.31 171.37 152.23 137.34 133.45 129.18 128.91 128.74 126.94 123.99 118.12 107.91 77.31 77.06 76.81 65.09 54.36 51.67 37.93 34.39


O
Ph
N
Me
CO2Me
4b.11
13C NMR, CDCl3, 126 MHz

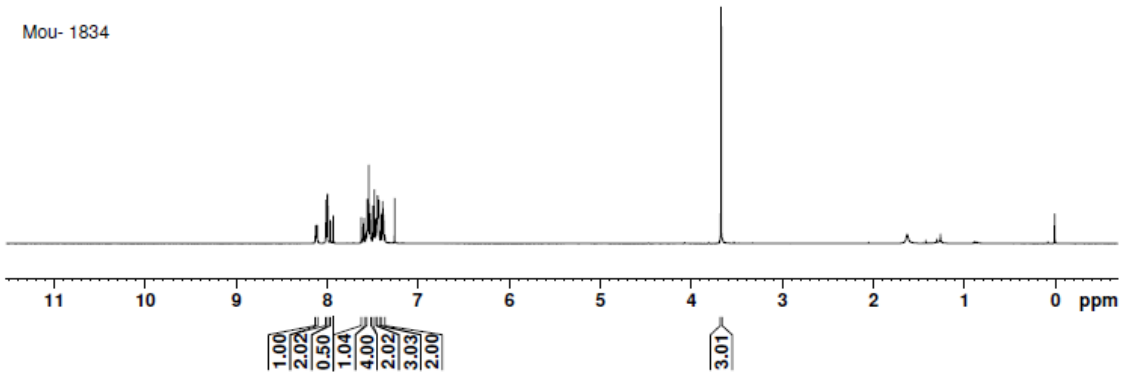

Mou- 1791
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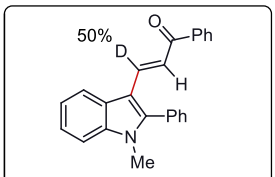


4b.7aa-D

^{1}H NMR, $CDCl_3$, 500 MHz

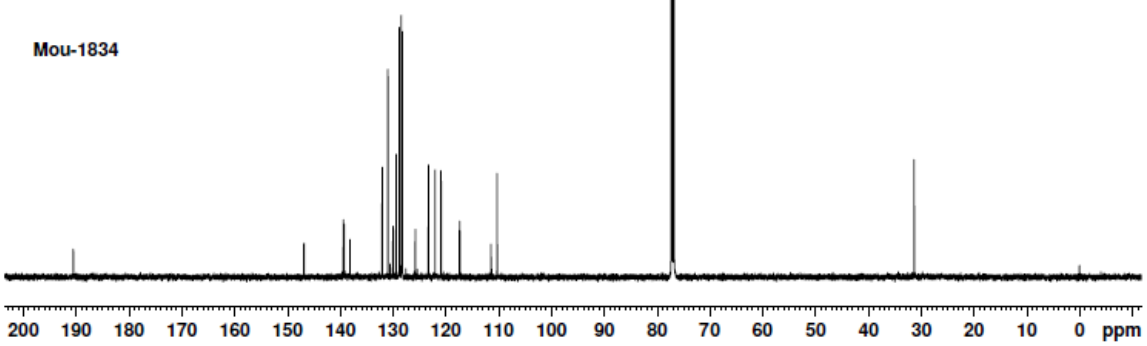


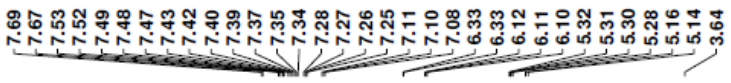


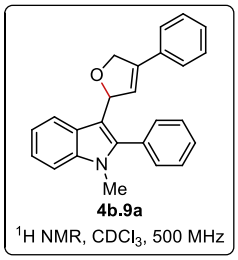


4b.7aa-D

^{13}C NMR, $CDCl_3$, 126 MHz

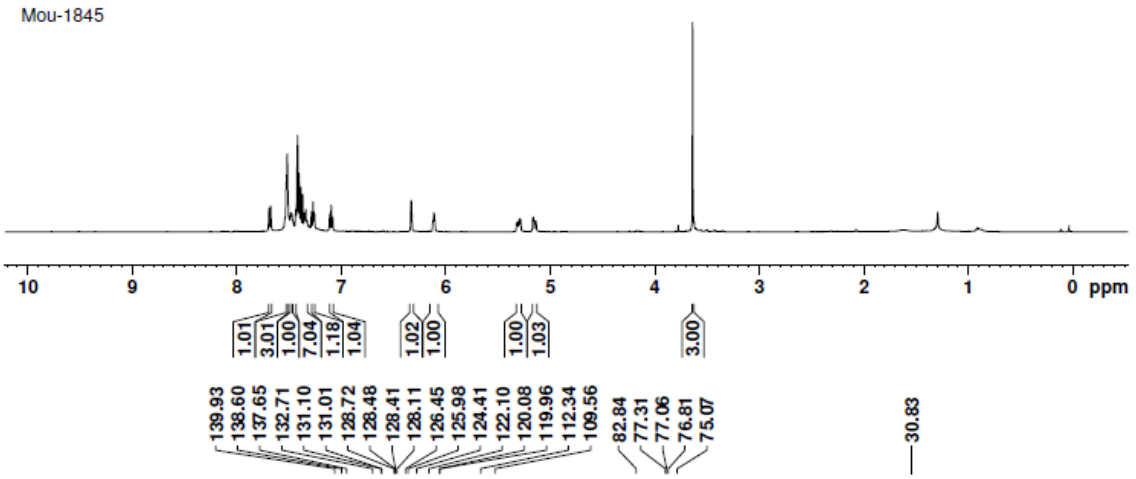


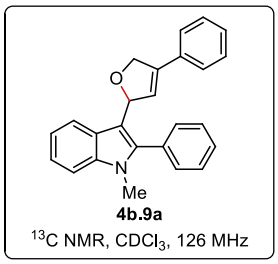




4b.9a

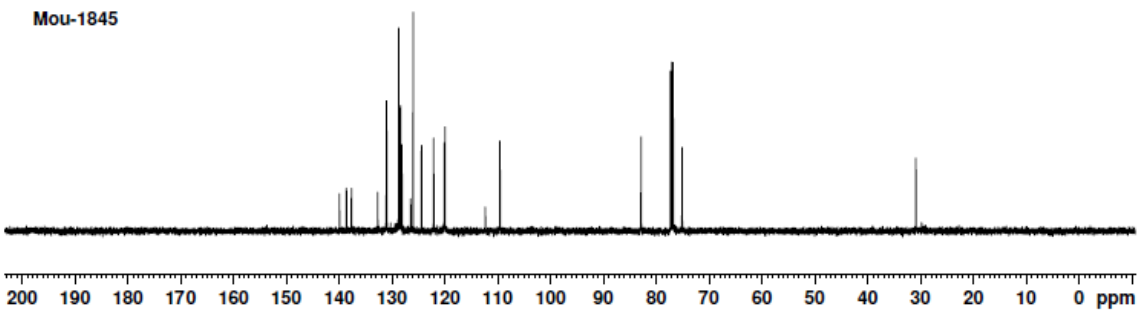
^{1}H NMR, $CDCl_3$, 500 MHz





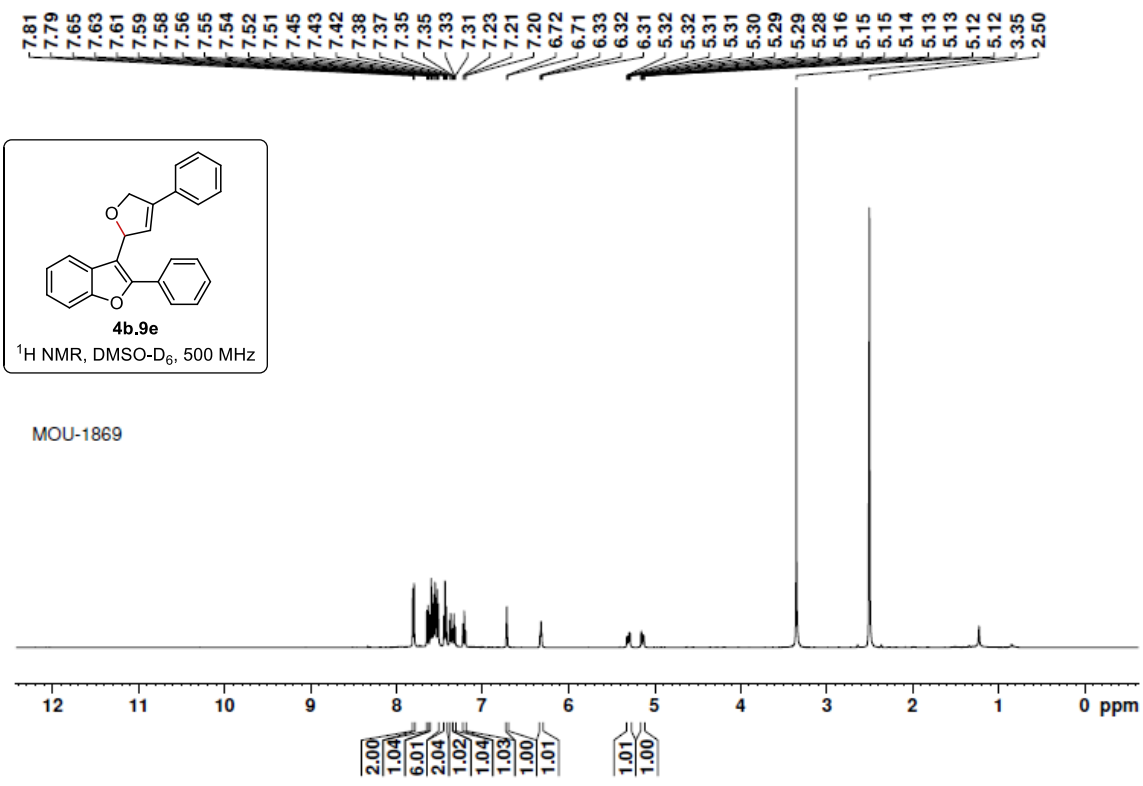
4b.9a

^{13}C NMR, $CDCl_3$, 126 MHz



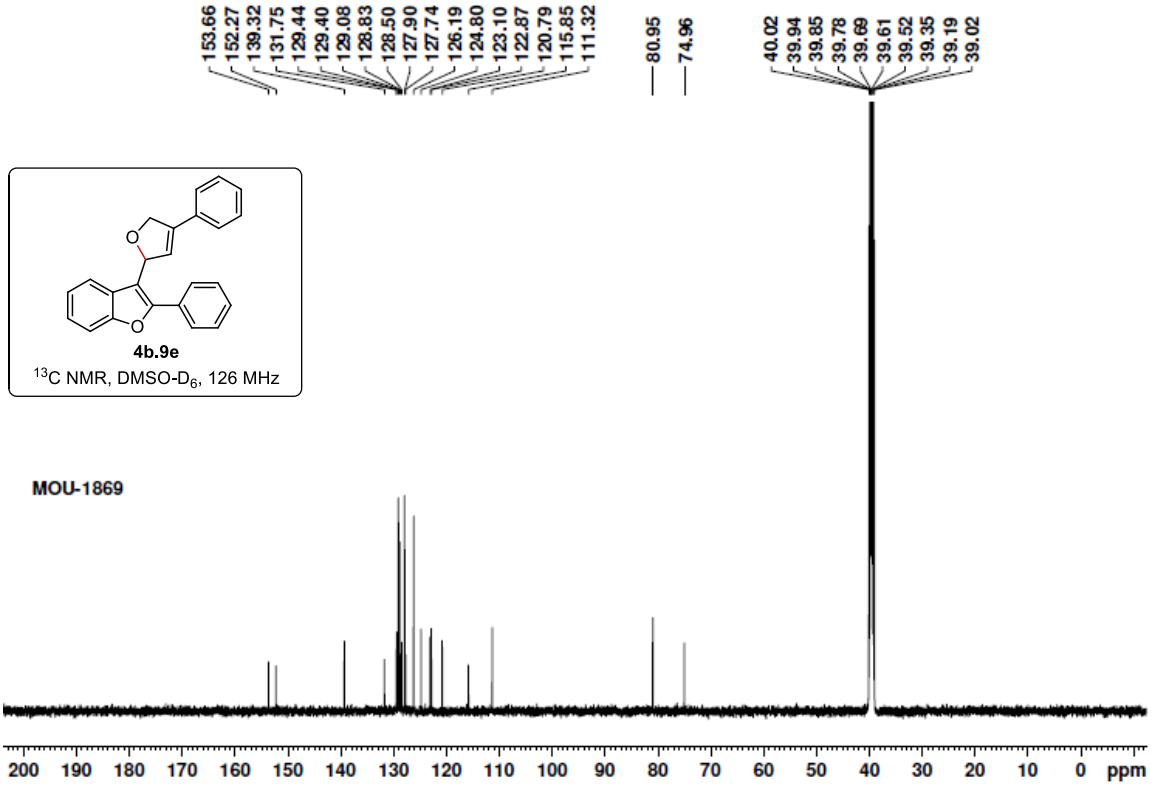
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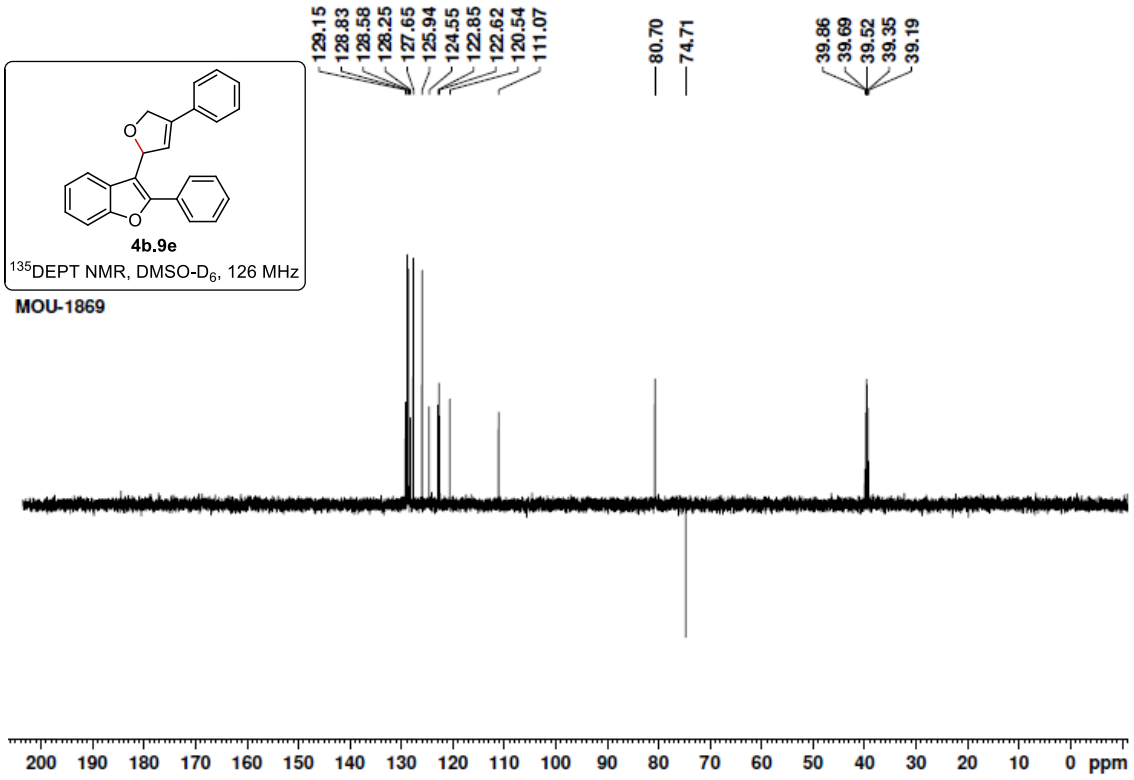
^{1}H NMR, DMSO-D_6, 500 MHz

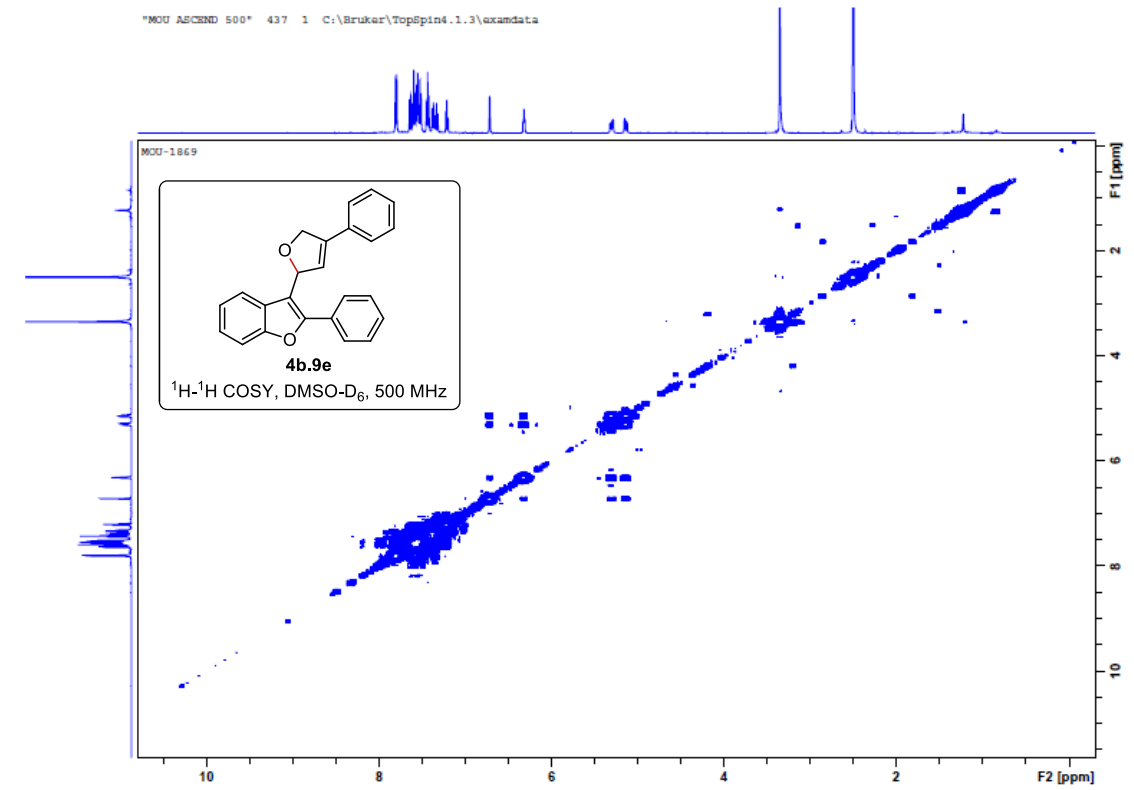


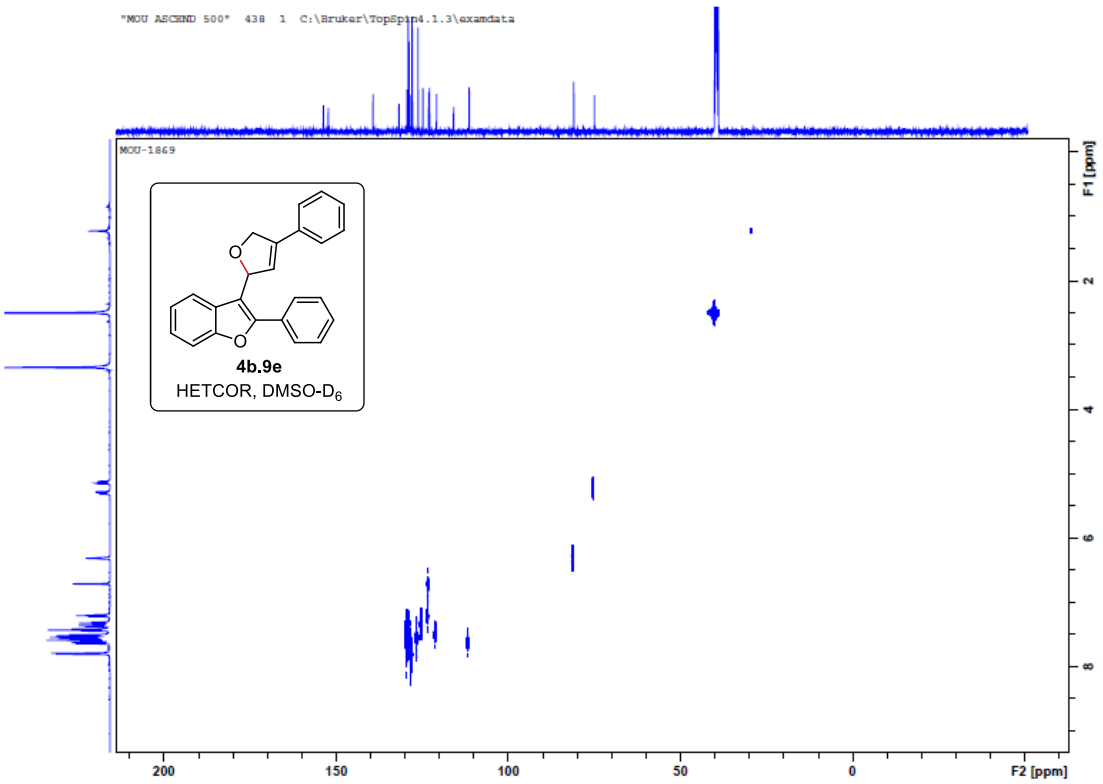
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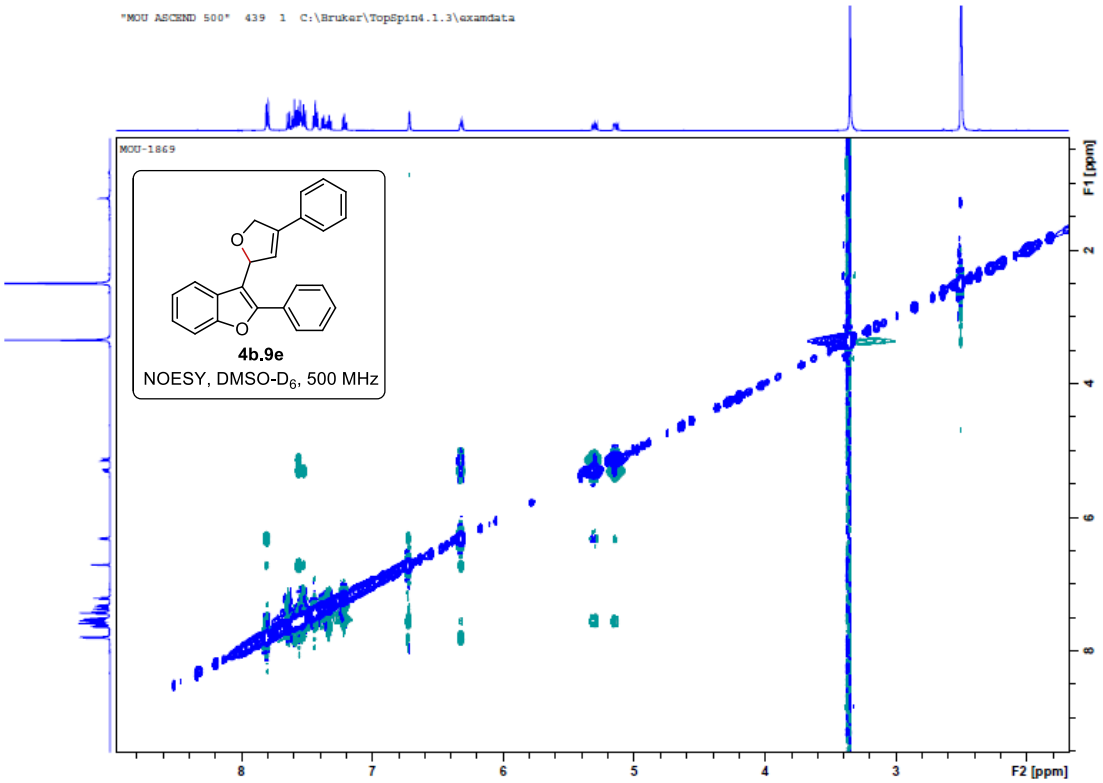
^{13}C NMR, DMSO-D_6, 126 MHz




129.15
128.83
128.58
128.25
127.65
125.94
124.55
122.85
122.62
120.54
111.07
80.70
74.71
39.86
39.69
39.52
39.35
39.19
4b.9e
135DEPT NMR, DMSO-D6, 126 MHz
MOU-1869
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


"MOU ASCEND 500" 437 1 C:\Bruker\TopSpin4.1.3\examdata
MOU-1869
4b.9e
1H-1H COSY, DMSO-D6, 500 MHz
F1 [ppm]
F2 [ppm]
10
8
6
4
2

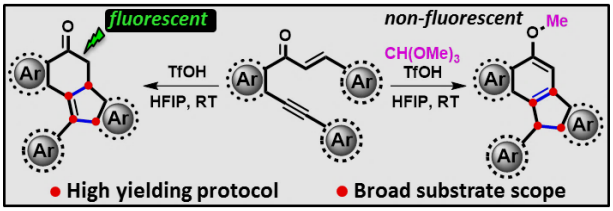

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MOU-1869
4b.9e
HETCOR, DMSO-D6
F1 [ppm]
F2 [ppm]
200
150
100
50
0


"MOU ASCEND 500" 439 1 C:\Bruker\TopSpin4.1.3\examdata
MOU-1869
4b.9e
NOESY, DMSO-D6, 500 MHz
F1 [ppm]
F2 [ppm]
8
7
6
5
4
3

List of Publications

1 Triflic acid-Mediated Expedient Synthesis of Benzo[*a*]fluorenes and Fluorescent Benzo[*a*]fluorenones

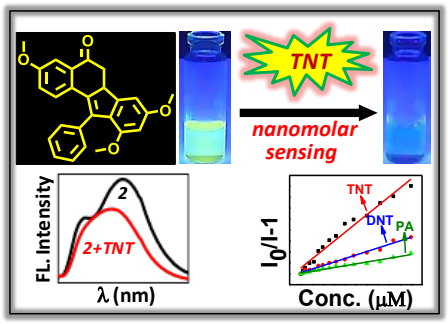
Mou Mandal and Rengarajan Balamurugan*



Adv. Synth. Catal. **2018**, *360*, 1453-1465 (DOI: 10.1002/adsc.201701516)

2 Efficient sensing of explosive TNT using a photoluminescent benzo[a]fluorenone derivative

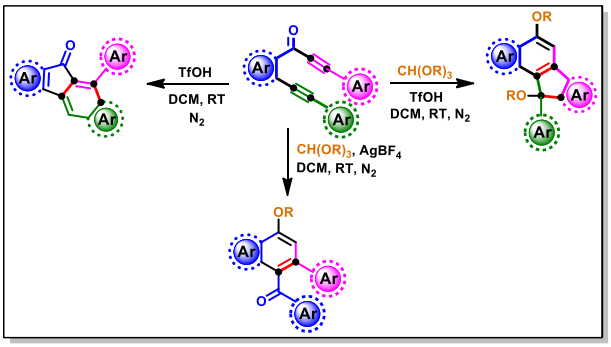
Mou Mandal and Rengarajan Balamurugan*



Chemistry Select **2019**, *4*, 10164-10168 (DOI: 10.1002/slct.201902639)

3 Diversity-Oriented Synthesis of Benzo[*a*]fluorenes, Benzo[*b*]fluorenones and Naphthyl ketones via Intramolecular Cyclization of Aryl Fused 1,6-Diyn-3-one

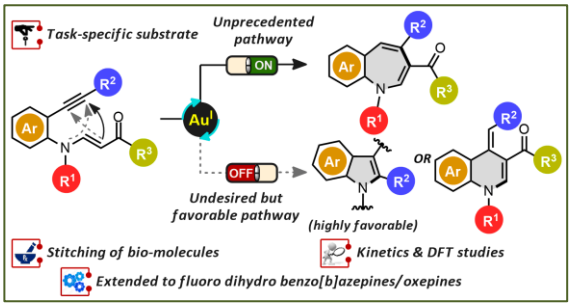
Mou Mandal, Shanmugam Sakthivel and Rengarajan Balamurugan*



J. Org. Chem. **2021**, *86*, 333-351 (DOI: 10.1021/acs.joc.0c02131)

4 Overriding the Conventional Reactivity of *o*-Alkynylanilines under Gold Catalysis using Alkyne-Skipped-Enaminones for Distal 7-*endo-dig* Cyclization

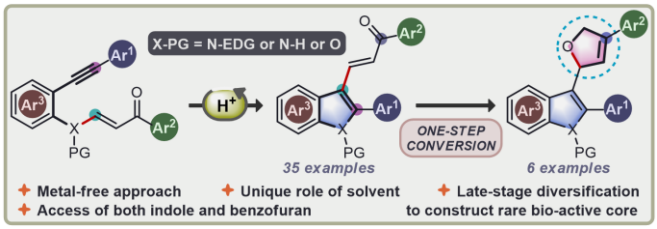
Mou Mandal, Renuka Pradhan, Upakarasamy Lourderaj* and Rengarajan Balamurugan*



Manuscript to be submitted.

5 TfOH-catalyzed synthesis of indoles and benzofurans involving cyclative transposition of vinyl ketone

Mou Mandal and Rengarajan Balamurugan*



Manuscript submitted.

List of Presentations

- Poster presentation on "*Triflic Acid Promoted Synthesis of Fluorescent Active Benzo[a]fluorenone and Benzo[a]fluorene Derivatives*" in the *20th CRSI National Symposiums in Chemistry* at Gauhati University on February 02-05, 2017.
- Poster presentation on "*Synthesis of Fluorescent Active Benzo[a]fluorenone and Benzo[a]fluorene Derivatives*" in *Chemfest-2017 (14th Annual In-House Symposium)* at School of Chemistry, University of Hyderabad on March 3-4, 2017.
- Poster presentation on "*Bronsted Acid Promoted Synthesis of Fluorescent Active Benzo[a]fluorenone Derivatives and Their Application in Sensing of Explosive TNT*" in the *XIII J-NOST* at Banaras Hindu University, Varanasi on November 9-12, 2017.
- Oral presentation on "*Diversity-Oriented Synthesis of Benzo[a]fluorene, Benzo[b]fluorenone and Naphthyl Ketone Derivatives From Aryl Fused 1,6-Diyn-3-ones*" in the *XIV J-NOST* at CSIR-IICT, Hyderabad on November 28-December 1, 2018.
- Oral presentation on "*Diversity-Oriented Synthesis of Benzo[a]fluorenes, Benzo[b]fluorenones and Naphthyl ketones via Intramolecular Cyclization of Aryl Fused 1,6-Diyn-3-one*" in *Chemfest-2019 (16th Annual In-House Symposium)* at School of Chemistry, University of Hyderabad on February 22-23, 2019.
- Attended "*NOST-OCC 2019*" on December 04-07, 2019.
- Oral presentation on "*Intramolecular Divergent Cycloisomerizations of Aryl-Fused 1,6-Diyn-3-ones to Benzo-Fluorenes/Fluorenones and Naphthyl Ketones*" in *CTCPS-2021* at Department of Chemistry, Dr. Harisingh Gour Vishwavidyalaya on February 20-22, 2021. *(Received Best Presentation Award)*
- Oral presentation on "*Dodging the Conventional Reactivity of o-Alkynyl anilines for the Synthesis of Benzo[b]azepine using Alkyne-Skipped-Enaminones under Gold Catalysis*" in the *XIV J-NOST* at UoH, Hyderabad on January 6-9, 2022.

Cyclizations of Benzofused 1,6-Enyne/Diyne Systems Towards the Synthesis of Diverse Polyaromatic Hydrocarbons and Heterocycles

by Mou Mandal

Submission date: 25-Jun-2022 01:42PM (UTC+0530)
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Cyclizations of Benzofused 1,6-Enyne/Diyne Systems Towards the Synthesis of Diverse Polyaromatic Hydrocarbons and Heterocycles

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PRIMARY SOURCES

1	Mou Mandal, Shanmugam Sakthivel, Rengarajan Balamurugan. "Brønsted/Lewis Acid-Promoted Site-Selective Intramolecular Cycloisomerizations of Aryl-Fused 1,6-Diyn-3-ones for Diversity-Oriented Synthesis of Benzo-Fused Fluorenes and Fluorenones and Naphthyl Ketones", The Journal of Organic Chemistry, 2020 Publication	7%
2	Mou Mandal, Rengarajan Balamurugan. " Efficient Sensing of Trinitrotoluene Using a Photoluminescent Benzo[ ]fluorenone Derivative ", ChemistrySelect, 2019 Publication	3%
3	Mou Mandal, Rengarajan Balamurugan. " Triflic acid-Mediated Expedient Synthesis of Benzo[ ]fluorenes and Fluorescent Benzo[ ]fluorenones ", Advanced Synthesis & Catalysis, 2018 Publication	2%
4	Limeng Zheng, Bingwei Zhou, Hongwei Jin, Ting Li, Yunkui Liu. " Radical-Triggered	<1%

Dr. R. Balamurugan
Professor
School of Chemistry
University of Hyderabad
Hyderabad-46, India.

Tandem Cyclization of 1,6-Enynes with H O: A Way to Access Strained 1 -Cyclopropa[ ]naph thalene-2,7-diones ", Organic Letters, 2018
Publication

5	www.ingentaconnect.com Internet Source	<1 %
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8	Undeela, Sridhar, Gurram Ravikumar, Jagadeesh Babu Nanubolu, Kiran Kumar Singarapu, and Rajeev S. Menon. "The facile synthesis of 1-benzoazepine derivatives via gold-catalyzed regioselective cycloisomerization reactions of N-(o-alkynylaryl)-N-vinyl sulfonamides", Chemical Communications, 2016. Publication	<1 %
9	Corinne Aubert, Olivier Buisine, Max Malacria. " The Behavior of 1, -Enynes in the Presence of Transition Metals ", Chemical Reviews, 2002 Publication	<1 %

10	Amol Milind Garkhedkar, Babasaheb Sopan Gore, Wan-Ping Hu, Jeh-Jeng Wang. " Lewis Acid Catalyzed Atom-Economic Synthesis of C2-Substituted Indoles from -Amido Alkynols ", Organic Letters, 2020 Publication	<1 %
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14	Ganesh Kumar Dhandabani, Mohana Reddy Mutra, Jeh-Jeng Wang. " Palladium-Catalyzed Regioselective Synthesis of 1-Benzoazepine Carbonitriles from -Alkynylanilines via 7- -dig Annulation and Cyanation ", Advanced Synthesis & Catalysis, 2018 Publication	<1 %
15	Lian, Jian-Jou, and Rai-Shung Liu. "Gold-catalyzed cyclo-isomerization of 1,6-diyne-4-en-3-ols to form naphthyl ketone derivatives", Chemical Communications, 2007. Publication	<1 %
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Cu(I)-Photosensitizer Enabling Combination of Energy-Transfer and Photoredox Catalysis for the Synthesis of Benzo[ ]fluorenols from 1,6-Enynes ", Organic Letters, 2021
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17 José Barluenga, Mónica Trincado, Eduardo Rubio, José M. González. Angewandte Chemie, 2003 <1 %
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18 Liangbin Huang, Matthias Arndt, Käthe Gooßen, Heinrich Heydt, Lukas J. Gooßen. "Late Transition Metal-Catalyzed Hydroamination and Hydroamidation", Chemical Reviews, 2015 <1 %
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28 Eloísa Jiménez-Núñez, Antonio M. Echavarren. "Gold-Catalyzed Cycloisomerizations of Enynes: A Mechanistic Perspective", Chemical Reviews, 2008
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31 Zhenyu An, Yi Ren, Yafeng Liu, Rulong Yan. " I ‐ Promoted Intramolecular Oxidative Cyclization of Butenyl Anilines: A Facile Route to Benzo[ ]azepines ", Chemistry – An Asian Journal, 2021 <1%
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32 Anand Acharya , S. Vijay Kumar, Hiriyakkanavar Ila. " Diversity-Oriented Synthesis of Substituted Benzo[ ]thiophenes and Their Hetero-Fused Analogues through Palladium-Catalyzed Oxidative C□H Functionalization/Intramolecular Arylthiolation ", Chemistry - A European Journal, 2015 <1%
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