Metal-Mediated Intramolecular Cyclization of Pyridino-alkynes

by

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10CC15J26007

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in
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Under the supervision of
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And under the co-guidance of
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CERTIFICATE

This is to certify that the work presented in this Ph.D. thesis entitled "Metal-Mediated Intramolecular Cyclization of Pyridino-alkynes" submitted by Mr. Ravindra Dattatraya Mule to Academy of Scientific and Innovative Research (AcSIR) in fulfilment of the requirements for the award of the Degree of Doctor of Philosophy in Science, embodies original research work carried-out by the student. We, further certify that this work has not been submitted to any other University or Institution in part or full for the award of any degree or diploma. Research material(s) obtained from other source(s) and used in this research work have been duly acknowledged in the thesis. Image(s), illustration(s), figure(s), table(s) etc., used in the thesis from other source(s), have also been duly cited and acknowledged.

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STATEMENTS OF ACADEMIC INTEGRITY

I Ravindra Dattatraya Mule, a Ph.D. student of the Academy of Scientific and Innovative Research (AcSIR) with Registration No. 10CC15J26007 hereby undertake that, the thesis entitled "Metal-Mediated Intramolecular Cyclization of Pyridino-alkynes'' has been prepared by me and that the document reports original work carried out by me and is free of any plagiarism in compliance with the UGC Regulations on *"Promotion of Academic Integrity and Prevention of Plagiarism in Higher Educational Institutions (2018)"* and the CSIR Guidelines for "*Ethics in Research and in Governance (2020)".*

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Ravindra Dattatraya Mule

Dedicated

to My Beloved Parents

Family

like branches on a tree,
we all grow in different directions,
yet our roots remain as one.

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Abbreviations

ACN	acetonitrile
aq	aqueous
Ar	aryl
BINAP	2,2‘-bis(diphenylphoshino)-1,1‘-binapthyl
br. s.	broad singlet
Bu	butyl
*t*Bu	*tertiary*-butyl
cat	catalyst
calcd	calculated
DCM	dichloromethane
CH_3CN	acetonitrile
DCE	dichloroethane
DMF	dimethylformamide
DMSO	dimethylsulphoxide
DMSO-d_6	deuterated dimethylsulphoxide
DPPF	1,1'-Bis(diphenylphosphino)ferrocene
dppm	bis(diphenylphosphino)methane
dd	doublet of doublet
ddd	doublet of doublet of doublet
ddt	doublet of doublet of triplet
dq	doublet of quartet
e.g.	exempli gratia
ESI	electron spray ionization mass spectroscopy
Et	ethyl
Et_2O	diethyl ether
EtOAc	ethyl acetate
eq	equation
equiv	equivalent
g	gram(s)
GCMS	gas chromatography–mass spectrometry
h	hour(s)
HRMS	high-resolution mass spectrometry

Abbreviations

Hz	hertz
IPr	1,3-bis(2,6-diisopropylphenyl)imidazolium
J	coupling constant (in NMR)
LED	light-emitting diodes
m	multiplet
max	maximum
Me	methyl
min	minute(s)
mL	milliliter(s)
mmol	millimole(s)
m/z	mass to charge ratio
MHz	megahertz
Nap	Naphthalene
N_2	nitrogen
NBS	*N*-bromosuccinimide
NMR	nuclear magnetic resonance
pet. ether	petroleum ether
Ph	phenyl
phen	phenanthroline
ppm	parts per million
Pr	propyl
*i*PrOH	*iso*propyl alcohol
q	quartet
R_f	retention factor
rt	room temperature
s	singlet
sxt	sextet
t	triplet
TBAF	tetra-*n*-butylammonium fluoride
tdd	triplet of doublet of doublet
tert	tertiary
TEA	triethyl amine

Abbreviations

TFA	trifluoroacetic acid
THF	tetrahydrofuran
TfOH	triflic acid
TIPS	triisopropylsilyl
TIPS-EBX	triisopropylsilylethynyl-1,2-benziodoxol-3(1*H*)-one
TLC	thin layer chromatography
TMS	tetramethylsilane
TsOH	*p*-toluenesulfonic acid
W	watt
μM	micromolar

General remarks

All reagents, starting materials and solvents were obtained from commercial suppliers (unless mentioned) and used without further purification. Solvents were dried using standard protocols. Unless otherwise noted, all the reactions were performed in oven-dried glassware under an argon atmosphere with magnetic stirring. Unless otherwise stated, all reactions were carried out under inert atmosphere using Schlenk techniques. Moisture sensitive reagents or solutions were transferred *via* syringe or cannula and were introduced to the apparatus *via* rubber septa. The progress of reactions was monitored by TLC (thin layer chromatography) with 0.25 mm pre-coated silica gel plates (60 F254) or Gas Chromatography. Visualization of TLC was done with UV light, Iodine adsorbed on silica gel or by immersion in ethanolic solution of phosphomolybdic acid (PMA), *p*-anisaldehyde or $KMnO_4$ followed by heating with a heat gun. Flash silica gel column chromatography (100-200 or 230-400 mesh size) or crystallization was performed for the purification of products. All the melting points are uncorrected and were recorded using Büchi B-540. All ^{1}H, ^{13}C, ^{31}P, and ^{19}F spectra were recorded on Bruker AV, 400/500, JEOL 400 MHz spectrometers in appropriate solvents using TMS as internal standard or the solvent signals as secondary standards and the chemical shifts are shown in δ scales. HRMS (ESI) were recorded on ORBITRAP mass analyzer (Q Exactive). UV–visible absorption spectra were measured with a Perkin Elmer LAMBDA 950 UV/Vis Spectrophotometers. Fluorescence spectra were recorded by Photon Technology International, Quanta Master™ 400 Spectro fluorometer and absolute quantum yields were determined using a calibrated integrating sphere system. Time-resolved fluorescence spectra were measured using a Horiba - Lifetime Fluorescence Spectrofluorometers system equipped with a PLP-10 picosecond light pulser (LED wavelengths: 470 or 570 nm). Single-crystal data was collected on a Super Nova Dual source X-ray diffractometer system (Agilent Technologies).

	Synopsis of the Thesis to be Submitted to the Academy of Scientific and Innovative Research for Award of the Degree of Doctor of Philosophy in Chemical Science
Name of the Candidate	**Ravindra Dattatraya Mule**
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CSIR Lab Affiliated With	**Division of Organic Chemistry, CSIR-NCL, Pune**
Title of the Thesis	**Metal-Mediated Intramolecular Cyclization of Pyridino-Alkynes**
Research Supervisor **Research Co-Supervisor**	**Dr. B. Senthil kumar** **Dr. Nitin T. Patil (IISER-Bhopal)**

Key words: *Pyridino-Alkyne, Coinage Metal, Amino-Functionalisation, Ionic Fluorophore, Gold Complex*

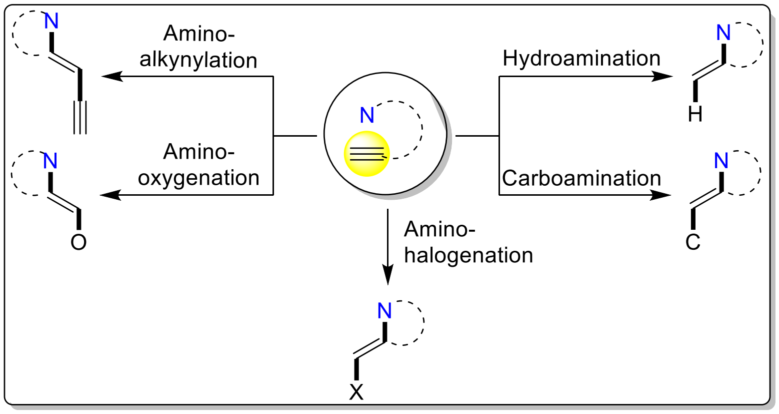
The thesis mainly emphasized on the study of coinage metal mediated intramolecular cyclisation of pyridino-alkynes. The work embodied in this thesis has been divided into four chapters as described below.

Chapter 1: Coinage Metal Catalysed Intramolecular Amino-Functionalisation of Alkynes: A General Introduction

Coinage metals (copper, silver and gold) are extensively used in the field of organic synthesis. These metals mainly act as soft and carbophilic Lewis acids. In general, these metals are the most effective catalysts for the electrophilic activation of alkynes under homogeneous conditions and utilizing this, a broad range of versatile synthetic tools have been developed for the construction of new carbon-carbon or carbon-heteroatom bonds. Thus, the molecular complexity could be afforded from simple starting materials.

In this chapter, literature reports are described in which the coinage metals are used as catalysts to activate the alkynes for synthesis of various molecular scaffolds. Intramolecular amino-functionalization of alkynes is typically focused here which encompasses hydroamination, carboamination, amino-halogenation, amino-alkynylaton and amino-oxygenations.

Scheme 1:

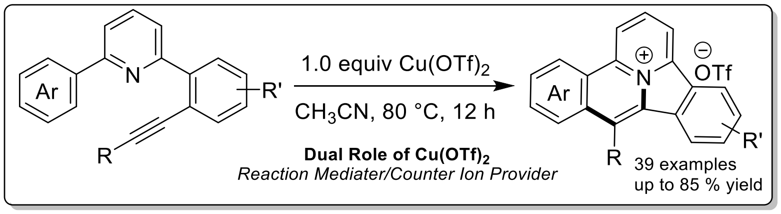


Chapter 2: Copper-Mediated Intramolecular Carboamination of Pyridino-Alkynes: An Access to Ionic Polycyclic Aromatic Hydrocarbons (PAHs)

Polycyclic aromatic hydrocarbons (PAHs) have attracted considerable attention due to their fascinating structural features and wide range of applications in organic, optical and electronic materials. Recently, it has been shown that ionic N-doped PAHs exhibit intriguing optical properties. To access N-doped ionic PAHs, most of the approaches are based on Rh/Ru catalyzed C–H activation between arenes/heteroarenes and alkynes. The major drawbacks of which are the requirement of stoichiometric oxidants, bases or harsh reaction conditions.

In this chapter, synthesis of N-doped ionic polycyclic aromatic hydrocarbons (PAHs) *via* carboamination of alkynes by using copper(II) catalyst has been described. The reaction is proposed to proceed through the intramolecular alkynes/azadienes [4+2]-cycloaddition cascade. Here Cu(II) plays a dual role by not only initiating the cascade transformation but also providing the counterion. The PAHs developed *via* this method exhibit tunable emission wavelengths and good quantum efficiency. The method shows excellent functional group tolerance and proceeds under mild conditions.

Scheme 2:

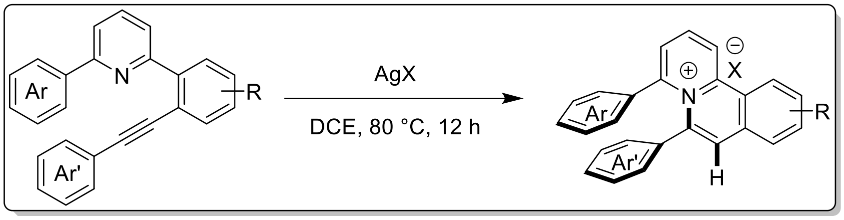


<u>Chapter 3</u>: Silver-Mediated Intramolecular Hydroamination Reactions of Pyridino-Alkynes: An Access to Ionic Solid Light Emitters

Luminescent organic materials have fundamental importance because of their potential application in biology, chemistry, and optoelectronic devices. Additionally these luminescent materials can also hold significant potential in the field of bio-imaging, provided that they do exhibit aggregation-induced emission (AIE) and do not cause aggregation-caused quenching (ACQ) in aqueous biological systems. Molecular packing arrangements play a key role in dominating the photophysical properties of luminophores in aggregated state but fine control of the molecular packing is a great challenge.

In this chapter, an efficient method for accessing ionic solid light emitters *via* silver mediated endo-selective intramolecular cyclisation of pyridino-alkynes has been described. Herein, the silver salt plays dual role, first as a reaction mediator and second as a counter ion provider. The photophysical properties of solid state emitters have been tuned by using different substituents on molecular scaffolds as well as varying the counter ions.

Scheme 3:

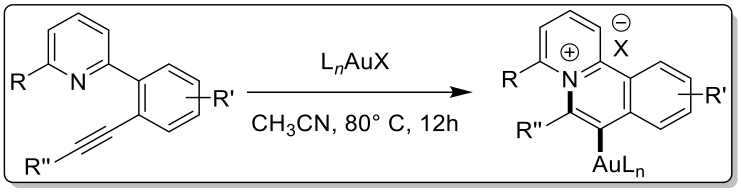


Chapter 4: Accessing a Library of Pyrido-Isoquinoline Based Gold(I) Complexes *via* Intramolecular Aminoauration Reactions of Pyridino-Alkynes

The accidental discovery of the anticancer properties of platinum-based drugs triggered the development of alternative metal-based drugs. However, the platinum-based treatment of tumor diseases is massively hampered by severe side-effects and development of resistance. Therefore, in the twentieth century gold complexes were introduced for the treatment for rheumatoid arthritis, culminating in the introduction of the oral drug Auranofin. Henceforth, further research on new scaffolds for gold complexes which may find appropriate medicinal usage in future is essential.

In this chapter, library based approach to synthesize pyrido-isoquinoline based ionic gold complexes *via* intramolecular aminoauration has been described. The reaction offers an efficient approach to ionic gold complexes. Be noted that the reaction is proceeding equally well with both sterically hindered phosphine and di-phosphine ligands and further screening for their biological activity is going on. Also, functionalization of synthesized gold complexes has been achieved.

Scheme 4:



Noteworthy Findings:

- Developed an efficient method for the constuction of N-doped ionic PAHs through copper(II)-mediated intramolecular carboamination of alkynes
- Developed a route to easily access ionic solid light emitters *via* hydroamination of pyridino-alkynes by using silver (I) salts
- Developed a method for accessing library of pyrido-isoquinoline based gold(I) complexes *via* intramolecular aminoauration reactions of pyridino-alkynes

List of publications:

1) A New Class of N-Doped Ionic PAHs *via* Intramolecular [4 + 2]-Cycloaddition between Arylpyridines and Alkynes;
   Ravindra D. Mule, Aslam C. Shaikh, Amol B. Gade and Nitin T. Patil* *Chem. Commun.*, **2018**, *54*, 11909-11912.

2) Ionic Pyridinium-Oxazole Dyads: Design, Synthesis, and their Application in Mitochondrial Imaging;
   Aslam C. Shaikh, Mokshada E.Varma, **Ravindra D. Mule**, Somsuvra Banerjee, Prasad P. Kulkarni and Nitin T. Patil* *J. Org. Chem.*, **2019**, *84*, 4, 1766-1777.

3) External Oxidant-Dependent Reactivity Switch in Copper-Mediated Intramolecular Carboamination of Alkynes: Access to a Different Class of Fluorescent Ionic Nitrogen-Doped Polycyclic Aromatic Hydrocarbons;
   Aslam C. Shaikh, Somsuvra Banerjee, **Ravindra D. Mule**, Saibal Bera and Nitin T. Patil* *J. Org. Chem.*, **2019**, *84*, 7, 4120-4130.

4) Gold-Catalyzed Alkynylative Meyer-Schuster Rearrangement;
   Somsuvra Banerjee, Shivhar B. Ambegave, **Ravindra D. Mule**, Beeran Senthilkumar* and Nitin T. Patil*, *Org. Lett.*, **2020**, *22*, 4792-4796.

5) Design and Development of a New Class of N-doped Ionic Solid Light Emitters *via* Silver Mediated Endo-Selective Intramolecular Cyclization of 2-(2-alkynylphenyl)Pyridines; **Ravindra D. Mule**, Beeran Senthilkumar* and Nitin T. Patil* *manuscript under preparation.*

6) Accessing Novel Class of Gold(I)-Complexes *via* Aminoauration of Pyridino-Alkynes;
   Ravindra D. Mule, Beeran Senthilkumar* and Nitin T. Patil* *manuscript under preparation.*

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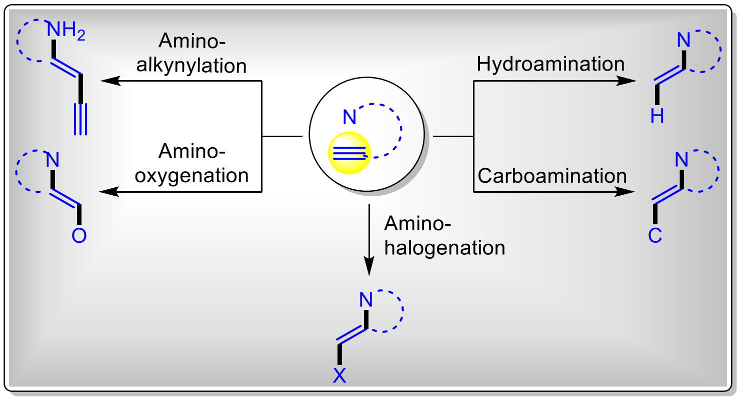
Chapter 1

Coinage Metal-Catalysed Intramolecular Amino-functionalisation of Alkynes: A General Introduction

Literature precedences in which the coinage metals are used as catalysts to activate the alkynes for synthesis of various molecular scaffolds are described here. The reactions explained here are basically intramolecular amino-functionalisation of alkynes, for example, hydroamination, carboamination, amino-halogenation, amino-alkynylation and amino-oxygenations.



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1.1 Introduction:

A catalyst is a chemical coupound that upon addition to a reaction does not affect the thermodynamics but increases the rate of reaction. In periodic table transition metals are well reputed for catalysis in organic synthesis. In particular group 11 consisting of metals (copper, silver, gold) embedded in transition metal (d block) are known as noble metals or coinage metals (Fig.1). Previously it was assumed that these coinage metals are inert, but later it was found that it also possesing excellent chemical reactivity. The current great interest in the photophysics, photochemistry, and catalytic activity of d^{10} complexes of the coinage metals is fully supported in the literature.[1] Coinage metals are among the major players in modern catalysis, they can easily lend and take electrons from other molecules. By taking this advantage of reactivity several reports have emerged in the literature of π-activation.

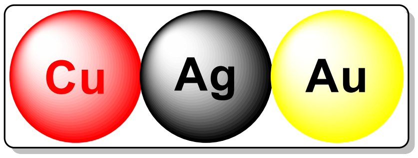


Fig 1.1: Coinage metals

In C-C multiple bonds, particularly alkynes and their derivatives are one of the most commonly encountered and versatile functional groups in organic synthesis because of their abundance and various reactivities.[2] These fundamental functional motifs can serve as molecular building blocks for the design of novel organic transformations and developing functional materials.[3] In particular, as can be understood from the advances in transition metal-catalysed transformations, they can be used to easily access complex molecular scaffolds.[4] Coinage metal salts have demonstrated remarkable alkynophilicity owing to their π-coordination with the carbon-carbon multiple bond, making them ideal catalysts for alkyne-based organic reactions. With the assistance of coinage metals and nucleophile tethered alkynes, molecular complexity can be generated. Mechanistically, the co-ordination of metal catalysts to the π-system renders the alkyne moiety susceptible to nucleophilic attack, thus enabling the intramolecular cyclization.

1.2 Amino-functionalisation:

Amine functionalisation of alkyne is important in many biological systems. The design and development of novel methodologies which enable facile access to valuable heterocycles remain a subject of intensive research in chemical sciences. Among these nitrogen heterocycles are an important class of compounds that occur widely in nature[5] and that display varied and often potent biological activity.[6] Similarly, acyclic amines are extensively used in pharmaceuticals,[7] agrochemicals, and cosmetics, and are considered to be the most crucial intermediates in several industrial processes.[8] These acyclic amines can be prepared by intramolecular amino-functionalisation. The intramolecular amino-functionalisation of C-C multiple bonds has emerged as hot topic of research as it provides biologically and medicinally essential motifs. These cyclization reactions of aminoalkynes have provided numerous modular approaches for the synthesis of such N-heterocycles.

This chapter includes mainly the following topics:

- Hydroamination of Alkynes
- Carboamination of Alkynes
- Amino-halogenation of Alkynes
- Amino-alkynylation of Alkynes and
- Amino-oxygenation of Alkynes

Only selected reports have been discussed here on the above-mentioned categories.

1.2.1 Hydroamination of Alkynes:

Addition of -N and -H across C-C multiple bonds leads to hydroaminated products,[9] and various cyclization reactions of aminoalkynes have been developed to provide various N-containing heterocycles (Fig 1.2).[10] Moreover, hydroamination products of aminoalkynes bearing primary amine moieties rapidly isomerize to afford cyclic imines. In general, hydroamination has been accomplished by the activation of either amine or C–C triple bond aided by acids, bases, transition metals, etc.[11] In this section, hydroamination by coinage metal catalysis is described.

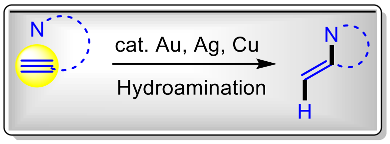
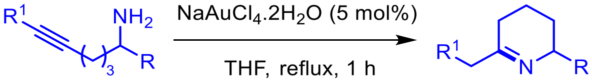


Fig 1.2: Hydroamination of alkynes by coinage metal catalysis

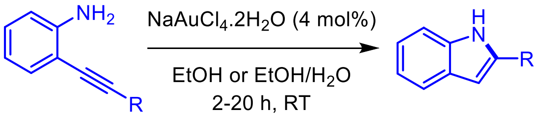
In 1991, Utimoto *et al*. reported Au (III) catalysed cyclization of 5-alkynylamines to afford 2,3,4,5-tetrahydropyridines (Scheme 1.1).[12] The report emphasized on the *anti*-addition of gold and nitrogen in a 6-*exo*-dig fashion to the acetylenic bond to give vinylaurate species which renders the product after protonolysis and isomerization.

Scheme 1.1: Au (III) catalysed hydroamination of 5-alkynylamine



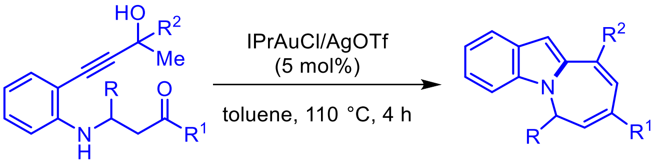
In 2004 Marinelli and co-workers, reported base or acid-free mild and green procedure for annulation reaction of 2-alkynylanilines using gold (III) in ethanol or aqueous ethanol at room temperature to furnish various derivatives of indoles in good yields *via* 5-*endo*-dig cyclization (Scheme 1.2).[13] The step-economic protocol has been reported for the gold-catalysed conversion of 2-alkynylanilines to afford 3-bromo and 3-iodoindoles using appropriate electrophilic halide source.

Scheme 1.2: Au (III) catalysed annulation reaction of 2-alkynylanilines



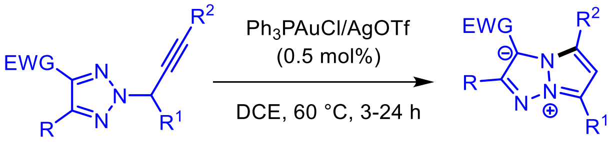
In 2012, Bandini *et al*. achieved an unprecedented gold-catalysed cascade sequence for the synthesis of azepino[1,2-a]indoles (Scheme 1.3).[14] The cascade reaction offers high yields and water as stoichiometric by-product. Experimental studies showed the key role of vinyl gold intermediate in the last step of ring closing.

Scheme 1.3: Gold-catalysed cascade reaction for the synthesis of azepinoindoles



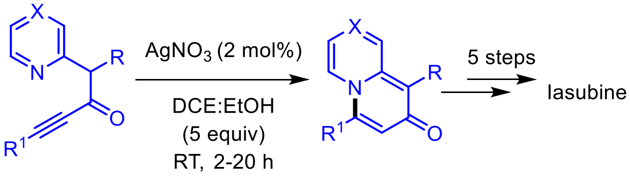
Later, in 2014, Shi *et al*. reported gold catalysed hydroamination of tethered triazole-alkyne in 5-*endo*-dig cyclization to achieve fluorescent active triazapentalene zwitterions (TAPZs) (Scheme 1.4).[15] This strategy provides fair to good yields of expected TAPZs in most of the cases. Moreover, some of the modified TAPZs display outstanding fluorescence highlighting the immense potential of this new disclosed TAPZ synthesis methodology.

Scheme 1.4: Synthesis of fluorescent TAPZs via gold-catalysed hydroamination



Unsworth and Taylor's group developed a series of high-yielding Ag(I)-catalysed cyclization reactions of pyridine-, isoquinoline, and pyrazineynones (Scheme 1.5).[16] This newly reported methodology was undoubtedly a scalable improvement incomparison to the previously reported thermal cyclizations methods. The quinolizinone products were then used to prepare the alkaloid lasubine II.

Scheme 1.5: Silver catalysed dearomative approach to quinolizidine alkaloids



1.2.2 Carboamination of Alkynes:

Carboamination–a formal addition of -C and -N moeties over an unsaturated C-C multiple bond to form new C-C and C-N bonds simultaneously which is undoubtedly a highly potential method for introducing carbon and nitrogen bearing functional group onto organic molecules.[17]

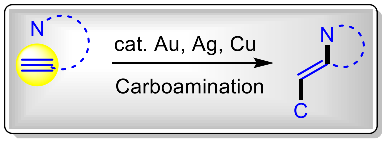
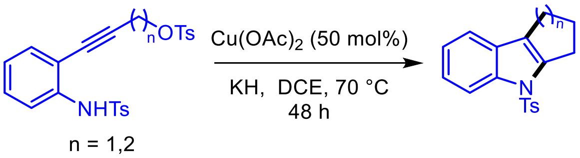


Fig 1.3: Carboamination of alkynes by coinage metal catalysis

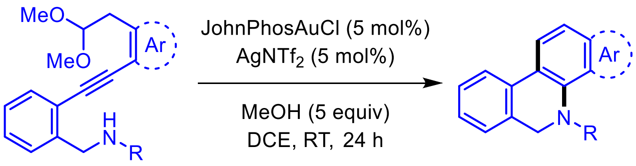
In 2004 Hiroya group reported a base promoted copper-catalysed sequential cyclization reaction by prior treatment of KH with 2-ethynyl aniline derivatives tethered with leaving group which causes for the second cyclization and afford a tricyclic ring system[18] through carboamination. The second cyclization was limited up to five and six members. The key step of this reaction (*i.e.* indole synthesis) has been used for the formal and total synthesis of hippadine.

Scheme 1.6: Copper catalysed sequential cyclization of 2-ethynyl aniline derivatives



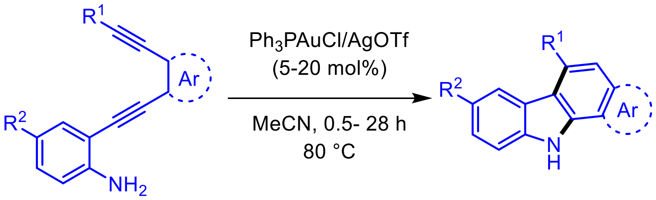
Later, Takemoto *et al.* reported gold(I) catalysed intramolecular carboamination of (2-alkynyl)benzyl carbamates, furthermore, the carboamination of alkynyl carbamates having an acetal or enone was successfully applied for the concise synthesis of tetracyclic heterocycles *via* the tandem cyclization to synthesis dihydroisoquinoline based tetracyclic heterocycles (Scheme 1.7).[19] The methodology was utilized for the formal total synthesis of nitidine.

Scheme 1.7: Gold(I)-catalysed tandem cyclization of alkynyl carbamates



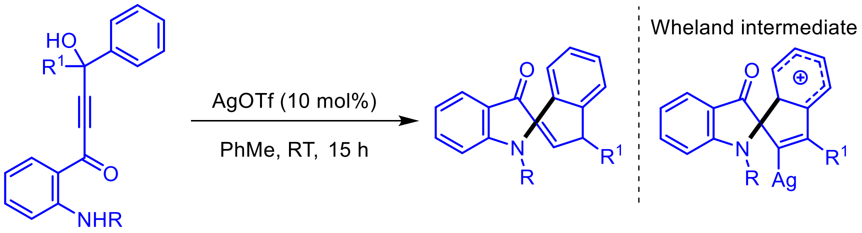
In 2010, Fujii and Ohno achieved novel gold (I) catalysed intramolecular cascade hydroamination-cycloisomerization reaction of novel aniline substituted diethynylarenes for the synthesis of aryl- and heteroaryl-annulated carbazoles (Scheme 1.8).[20] Cascade cyclization achieved *via* $Ph_3PAuCl/AgOTf$ catalysis which renders the polycyclic aromatic compounds under base free condition.

Scheme 1.8: gold (I) catalysed intramolecular cascade to the synthesis of arylated carbazoles



In 2014, Chan and co-workers reported a method for synthesis of spiro-indolines started from 1-(2-(allylamino)phenyl-4-hydroxy-but-2-yn-1-ones *via* silver (AgOTf) catalysis (Scheme 1.9).[21] The proposed mechanistic path involves allenamide and spirocyclic Wheland intermediate. The developed methodology was very robust, general in scope, and efficient to access the novel spirocyclic products in high yield.

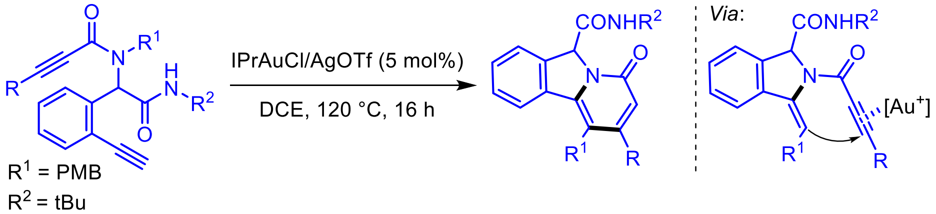
Scheme 1.9: Gold(I)-catalysed efficient access to spiro-indolines



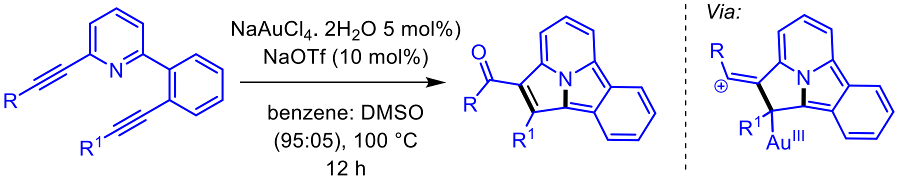
Tian and Eycken coworkers reported cationic gold(I) catalysed cascade *via* nucleophilic cyclization/1,3-migration/cycloisomerization to obtain diverse pyridoisoindolones (Scheme 1.10).[22] Substituent dependant divergence in product formation was obtained, where the electronic effect on the migrating groups and steric effect of the secondary amide moieties plays a crucial role.

Very recently, Patil and coworkers explored an interesting example of gold-catalysed cycloisomerization of pyridine-bridged 1,8-diynes involving carbene/alkyne metathesis (Scheme 1.11).[23] The method offers efficient access to the regioselective synthesis of luminescent cyclazines. DFT calculations of the possible mechanistic pathways highly supported the involvement of a β-gold vinyl cation species over 1,6-carbene transfer process. This methodology was also extended for the synthesis of highly underscored triarylmethanes.

Scheme 1.10: Gold(I)-cyclization/1,3 migration/cycloisomerization reaction



Scheme 1.11: Gold(III)-catalysed synthesis of cyclazines *via* β-gold vinyl cation species



1.2.3 Amino-halogenation of Alkynes:

Addition of –N and –X (halogen) across the C-C triple bond leads to amino-halogenated products. Organic molecules containing both halogen and amine functionalities concurrently have been evident in various bioactive secondary metabolites.[24] Halogen containing compounds are valuable intermediates in organic synthesis as the halogen can serve for cross-coupling and substitution reactions.

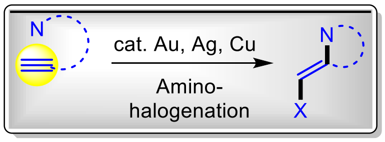
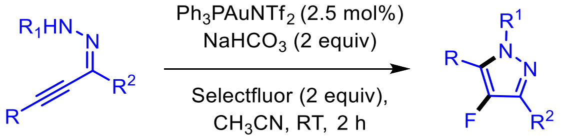


Fig 1.4: Aminohalogenation of alkynes by coinage metal catalysis

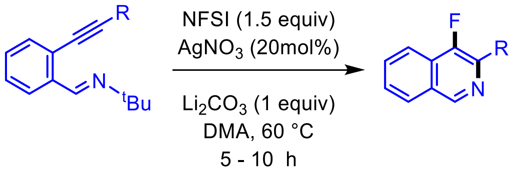
In 2011, , Xu *et al*. disclosed the synthesis of fluorinated pyrazoles *via* gold-catalysed intramolecular tandem amino-fluorinationof alkynes by employing Selectfluor as the halogen source (Scheme 1.12).[25] The method offers an efficient access to numerous fluorinated derivatives of pyrazoles in fair to excellent yield at room temperature. The presence of the Au catalyst was required for the reaction to occur.

Scheme 1.12: Synthesis of fluoropyrazoles



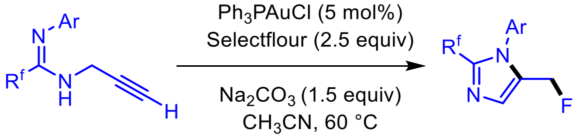
Liu and co-workers demonstrated the Ag-catalysed intramolecular oxidative amino-fluorination of alkynes, in 2012 (Scheme 1.13).[26] Synthesis of 4-fluoroisoquinolines from alkynylimines, via an endo cyclization approach, was reported by employing NFSI. The present strategy was efficient for the modular synthesis of 4-fluoroisoquinolines and 4-fluoropyrrolo[α] isoquinolines.

Scheme 1.13: Silver catalysed oxidative amino-fluorination of alkynes



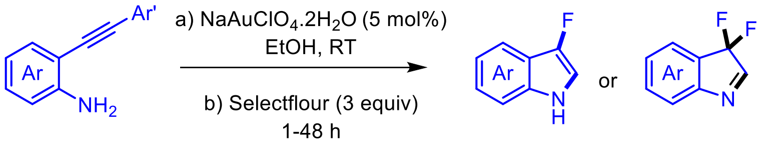
Wu *et al*. reported the synthesis of fluorinated imidazole derivatives starting from propargyl amidines (Scheme 1.14).[27] Fluorinated propargyl amidines under gold(I) catalysis underwent a 5-*exo*-dig-cyclization followed by fluorination cascade in the presence of Selectfluor to sponsor new Csp^3-F bond.

Scheme 1.14: Synthesis of fluorinated imidazole derivatives under gold catalysis



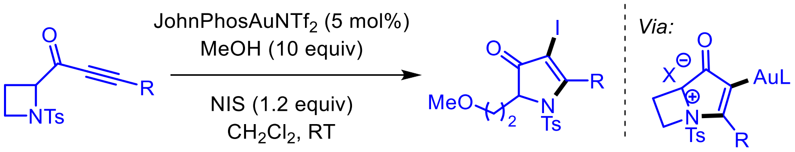
Michelet and co-workers reported one-pot gold(III) catalysed tandem amino-fluorination of unprotected 2-alkynylanilines in two steps. It provided a general method for synthesis of 3,3-difluoro-2-substituted-3H-indoles and the procedure was further employed for the synthesis of 2-aryl-3-fluoro-1H-indoles under mild condition (Scheme 1.15)[28].

Scheme 1.15: Synthesis of fluorinated indole derivatives under gold(III) catalysis



Pale and Blanc *et al*. reported an efficient route to polysubstituted pyrrolin-4-ones via unprecedented gold (I) catalysed cyclization/nucleophilic substitution reaction by using various nucleophiles.[29] For the synthesis of derivatives of 3-iodopyrrolin-4-one NIS was used as a nucleophile (Scheme 1.16). The proposed mechanism includes intramolecular cyclization of N-sulfonylated azetidine on the ynone part followed by a nucleophilic substitution and opening of the so-formed azetidinium ion.

Scheme 1.16: Gold catalysed amino-iodination of alkyne to produce iodo-pyrrolidinone



1.2.4 Amino-alkynylation of Alkynes:

The addition of nitrogen and carbon across C-C triple bond leads to carboamination products,[30] although there exists a large number of reports amino-alkynylation reactions remain scarce. Alkyne moieties are important functional groups and are employed as key substrates in many organic transformations. Recent developments of catalytic aminoalkynylation reactions of alkynes using various transition metal catalysts has been discussed herein.

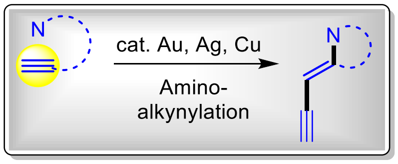
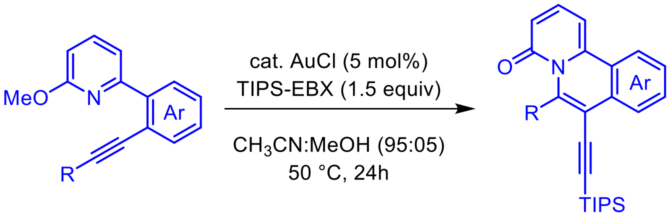


Fig 1.5: Aminoalkynylation of alkynes by coinage metal catalysis

In 2016, our group reported gold (I) catalysed synthesis of alkynylated quinalizinones via aminoalkynylation of pyridine-alkynes (Scheme 1.17),[31] 1-[(triisopropylsilyl)-ethynyl]-1,2-benziodoxol-3(1H)-one (TIPS-EBX) was utilized as alkynylating agent.

Scheme 1.17: Gold(I) catalysed aminoalkynylation of alkyne



1.2.5 Amino-oxygenation of Alkynes:

Amino-oxygenation of alkyne has evolved as an important process which involves the installation of a nitrogen and oxygen atoms simultaneously on alkyne to afford nitrogen-containing heterocycles.[32] In this regard, in 2014, copper[33], gold-catalysed[34] aminooxygenation of alkynes that deals with the condensation of 2-aminopyridines and 3-arylpropiolaldehyde was reported. Similarly, a silver-catalysed intramolecular aminooxygenation of functionalized N-(prop-2-yn-1-yl)pyridin-2- amines to sponsor 3-aroylimidazo[1,2-a]pyridines in good yields was also reported.[35] In all these cases O_2 source was used for oxygen incorporation.

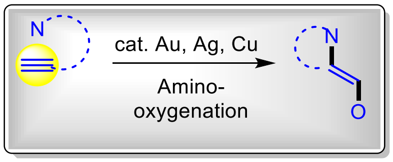
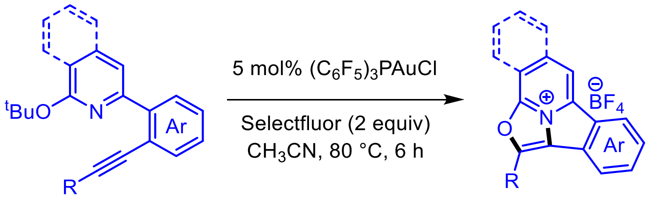


Fig 1.4: Amino-oxygenation of alkynes by coinage metal catalysis

Our continuous efforts on gold catalysis for the amino functionalisation of alkynes brought us on the first report of oxidative gold(I)/gold(III) catalysed intramolecular 1,2-amino-oxygenation of the alkyne (Scheme 1.18).[36] Not only do these reaction present an easy access to a structurally valuable ionic pyridinium-oxazole dyad with modular emission wavelengths; but the application of these fluorophores as potential biomarkers has also been investigated.

Scheme 1.18: Oxidative gold(I)/gold(III) catalysed amino-oxygenation of alkyne



1.3 Conclusion:

In conclusion, this chapter covers the amino-functionalisation of alkyne by using coinage metal catalysis. It provides valuable heterocyclic compounds that are vital in drug and material chemistry. Gold catalysed amino-functionalisation reactions are currently undergoing in our lab to generate new reactivities and selectivities.

1.4 References:

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1 (a) H. H. Patterson, S. M. Kanan, M. A Omary,. *Coord. Chem. Rev*. **2000**, *208*, 227; (b) M. Jansen, *Angew. Chem., Int. Ed*. **1987**, *26*, 1098; (c) P. C Ford,.; A. Vogler,. *Acc. Chem. Res*. **1993**, *26*, 220; (d) A. M. Echavarren, N. Jiao, V. Gevorgyan, *Chem. Soc. Rev*. **2016**, *45*, 4445.

2 (a) D. Habrant, V. Rauhala and A. M. P. Koskinen, *Chem. Soc. Rev*., **2010**, *39*, 2007; (b) J. P. Branda, J. Waser, *Chem. Soc. Rev*., **2012**, *41*, 4165.

3 (a) F. Diederich, P. J. Stang, R. R. Tykwinski, *Acetylene Chemistry. Chemistry, Biology and Material Science*, Wiley-VCH, Weinheim, **2005**; (b) R. Gleiter, D. B. Werz, Alkynes Between Main Group Elements: From Dumbbells *via* Rods to Squares and Tubes, *Chem. Rev*., **2010**, *110*, 4447.

4 (a) B. Godoi, R. F. Schumacher,G. Zeni, *Chem. Rev*., **2011**, *111*, 2937; (b) U. Wille, *Chem. Rev*., **2013**, *113*, 813; (c) I.-T. Trotus, T. Zimmermann, F. Schueth, *Chem. Rev*., **2014**, *114*, 1761.

5 (a) D. O'Hagan, *Nat. Prod. Rep*. **2000**, *17*, 435; (b) A. Mitchinson, A. Nadin, *J. Chem. Soc., Perkin Trans*. **2000**, *1*, 2862; (c) J. W. Daly, H. M. Garraffo, T. F. Spande, The Alkaloids: Chemistry and Pharmacology (Ed.: G. A. Cordell), Academic Press, San Diego, **1993**, 43, 185; (d) A. G. King, J. Meinwald, Chem. Rev. **1996**, *96*, 1105; (e) J. W. Daly, Proc. Natl. Acad. Sci. USA **1995**, *92*, 9; (f) A. Brossi, in The Alkaloids: Chemistry and Pharmacology (Ed.: G. A. Cordell), Academic Press, San Diego, **1993**, vol. *43*, 119.

6 (a) M. Negwer, Organic-Chemical Drugs and Their Synonyms (an International Survey), 7th ed., Akademie Verlag, Berlin, **1994**; (b) J. Ashby, B. M. Elliott, Comprehensive Heterocyclic Chemistry

(Eds.: A. R. Katritzky, C. W. Rees), Pergamon Press, Oxford, **1984**, *1*, 111; (c) J. K. Landquist, in: Comprehensive Heterocyclic Chemistry (Eds.: A. R. Katritzky, C. W. Rees), Pergamon Press, Oxford, **1984**, *1*, 143.

7 (a) J. A. Ellman, T. D. Owens, T. P. Tang, *Acc. Chem. Res*. **2002**, *35*, 984; (b) N. Hermanns, S. Dahmer, C. Bolm, S. Bräse, *Angew. Chem. Int. Ed*. **2002**, *41*, 3692; (c) J. R. Porter, J. F. Traverse, A. H. Hoveyda, M. L. Snapper, *J. Am. Chem. Soc*. **2001**, *123*, 10409; (d) Z. Han, D. Krishnamurthy, P. Grover, Q. K. Fang, D. A. Pflum, C. H. Senanayake, *Tetrahedron Lett*. **2003**, *44*, 4195; (e) E. J. Corey, C. J. Helal, *Tetrahedron Lett*. **1996**, *37*, 4837; (f) R. Bloch, *Chem. Rev*. **1998**, *98*, 1407; (g) F. A. Davis, S. Lee, H. Zhang, D. L. Fanelli, *J. Org. Chem*. **2000**, *65*, 8704.

8 S. A. Lawrence, Amines: Synthesis Properties, and Applications, *Cambridge University Press*, New York, **2004.**

9 (a) K. C. Hultzsch, *Adv. Synth. Catal*., **2005**, *347* 367; (b) P.W. Roesky, T. E. Müller, *Angew. Chem. Int. Ed*., **2003**, *42*, 2708; (c) S. R. Chemler, *Org. Biomol. Chem*., **2009,** *7*, 3009; (d) T. E. Müller, K. C. Hultzsch, M. Yus, F. Foubelo, M. Tada, *Chem. Rev.*, **2008**, *108*, 3795 (e) I. Aillaud, J. Collin, J. Hannedouche, E. Schulz, *Dalton Trans*., **2007**, 5105; (f) R. A. Widenhoefer, X. Han, *Eur. J. Org. Chem*. **2006**, 4555; (g) S. Hong, T. J. Marks, *J. Acc. Chem. Res*. **2004**, *37*, 673; (h) M. Beller, J. Seayad, A. Tillack, H. Jiao, *Angew. Chem. Int. Ed*., **2004**, *43*, 3368; (i) I. Bytschkov, S. Doye, Eur. *J. Org. Chem*. **2003**, 935; (j) M. Beller, C. Breindl, M. Eichberger, C. G. Hartung, J. Seayad, O. R. Thiel, A. Tillack, H. Trauthwein, *Synlett*, **2002**, 1579; (k) M. Nobis, B. Drießen-Hölscher, *Angew. Chem. Int. Ed*. **2001,** *40*, 3983; (l) T. E. Müller, M. Beller, *Chem. Rev*. **1998**, *98*, 675.

10 (a) F. Alonso, I. P. Beletskaya, M. Yus, *Chem. Rev*., **2004**, *104*, 3079; (b) N. T. Patil, R. D. Kavthe, V. S. Shinde, Tetrahedron, **2012**, 8079.

11 R. Severin, S. Doye, *Chem. Soc. Rev*., **2007**, *36*, 1407.

12 Y. Fukuda, K. Utimoto, H. Nozaki, *Heterocycles*, **1987**, *25*, 297.

13 A. Arcadi, G. Bianchi, F. Marinelli, *Synthesis* **2004**, *4*, 610.

14 G. Cera, S. Piscitelli, M. Chiarucci, G. Fabrizi, A. Goggiamani, R. S. Ramn, S. P. Nolan, M. Bandini, *Angew. Chem. Int. Ed*. **2012**, *51*, 9891.

15 R. Cai, D. Wang, Y. Chen, W. Yan, N. R. Geise, S. Sharma, H. Li, J. L. Petersen, M. Li, X. Shi, *Chem. Commun*., **2014**, *50*, 7303.

16 M. J. James, N. D. Grant, P. O’Brien, R. J. K. Taylor, W. P. Unsworth, Org. Lett. **2016**, *18* ,6256.

17 For carbonylation of azides and azetidenes, see: (a) S. Calet, F. Urso, H. Alper, *J. Am. Chem. Soc*. **1989**, *111*, 931; (b) D. Roberto,; H Alper,. *J. Am. Chem. Soc*. **1989**, *111*, 7539; For carbonylation of allylamines, see: (c) S.-I, Murahashi, Y. Imada,; K. Nishimura, *Tetrahedron* **1991**, *50*, 453; (d) For

---

$PtCl_2$-catalysed intramolecular carboamination, see: (e) T. Shimada, I. Nakamura,; Y. Yamamoto, *J. Am. Chem. Soc*. **2004**, *126*, 10546; (f) A. Fürstner,; P. W. Davies, *J. Am. Chem. Soc*. **2005**, *127*, 15024; (g) R. T. Ruck, R. L. Zuckerman, S. W. Krska, R. G. Bergman, *Angew. Chem., Int. Ed*. **2004**, *43*, 5372; (h) Z. Liu,; R. C. Larock, *J. Am. Chem. Soc*. **2005**, *127*, 13112; (i) H. Yoshida, E. Shirakawa, Y Honda, T. Hiyama, *Angew. Chem., Int. Ed*. **2002**, *41*, 3247.

18 K. Hiroya, S. Itoh, T. Sakamoto, *J. Org. Chem*. **2004**, *69*, 1126.

19 T. Enomoto, A.-L. Girard, Y. Yasui, Y. Takemoto, *J. Org. Chem*. **2009**, *74*, 9158.

20 K. Hirano, Y. Inaba, T. Watanabe, S. Oishi, N. Fujii, H. Ohno, *Adv. Synth. Catal*. **2010**, *352*, 368.

21 S. R. Mothe, M. L. Novianti, B. J. Ayers, P. W. H. Chan, *Org. Lett*. **2014**, *16*, 4110.

22 Z. Li, L. Song, L. V. Meervelt, G. Tian, E. V. V.Eycken, *ACS Catal*. **2018**, *8*, 6388.

23 C. C. Chintawar, M. V. Mane, A. G. Tathe, S. Biswas, N. T. Patil, *Org. Lett*. **2019**, *21*, 7109.

24 (a) G. W. Gribble, Occurence of Halogenated Alkaloids. In The Alkaloids; Academic Press: New York, **2012**; Vol. 71, Chapter 1; (b) H. Nakamura, Y. Ohizumi, J. Kobayashi, Y. Hirata, *Tetrahedron Lett*. **1984**, *25*, 2475; (c) A. Nakagawa, Y. Iwai, H. Hashimoto, N. Miyazaki,; R. Oiwa, Y. Takahashi, A. Hirano, N. Shibukawa, Y. Kojima, S. Omura, *J Antibiot*. **1981**, *34*, 1408; (d) R. B. Kinnel, H. -P. Gehrken, P. J. Scheuer, *J. Am. Chem. Soc*. **1993**, *115*, 3376; (e) J. Qiu, R. B. Silverman, *J. Med. Chem*. **2000**, *43*, 706.

25 J. Qian, Y. Liu, J. Zhu, B. Jiang, Z. Xu, *Org. Lett*. **2011**, *13*, 4220.

26 T. Xu, G. Liu, *Org. Lett*. **2012**, *14*, 5416.

27 S. Li, Z. Li, Y. Yuan, Y. Li, L. Zhang, Y. Wu, *Chem. Eur. J*. **2013**, *19*, 1496.

28 A. Arcadi, E. Pietropaolo, A. Alvino,V. Michelet, *Org. Lett*. **2013**, *15*, 2766.

29 S. Miaskiewicz, J.-M. Weibel, P. Pale, and A. Blanc, *Org. Lett*. **2016**, *18*, 844.

30 General reviews: (a) K. Ouyang, W. Hao, W.-X. Zhang , Z. Xi, *Chem. Rev*., **2015**, *115*, 12045; (b) D. Bouyssi, N. Monteiro, G. Balme, Beilstein *J. Org. Chem*., **2011**, *7*, 1387; (c) N. T. Patil, R. D. Kavthe, Y. Yamamoto, *Adv. Heterocycl. Chem*., **2010**, *101*, 75; (d) J. Barluenga, F. Rodrıĝuez, F. J. Fanãnãs, *Chem. – Asian J*., **2009**, *4*, 1036; (e) K. Krüger, A. Tillack, M. Beller, *Adv. Synth. Catal*., **2008**, *350*, 2153; (f) G. Battistuzzi, S. Cacchi, G. Fabrizi, *Eur. J. Org. Chem*., **2002**, 2671.

31 P. S. Shinde, A. C. Shaikh, N. T. Patil, *Chem. Commun*., **2016**, *52*, 8152.

32 a) X. Kou, Y. Li, L. Wu, X. Zhang, G. Yang, W. Zhang, *Org. Lett*. **2015**, *17*, 5566, b) K. K. Toh, S. Sanjaya, S. Sahnoun, S. Y. Chong, S. Chiba., *Org. Lett*. **2012**, *14*, 2290.

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33 H. Cao, X. Liu, J. Liao, J. Huang, H. Qiu, Q. Chen, Y. Chen, *J. Org. Chem*. **2014**, *79*, 11209.

34 H. Zhan, L. Zhao, J. Liao, N. Li, Q. Chen, S. Qiu, H. Cao, *Adv. Synth. Catal*. **2015**, *357*, 46.

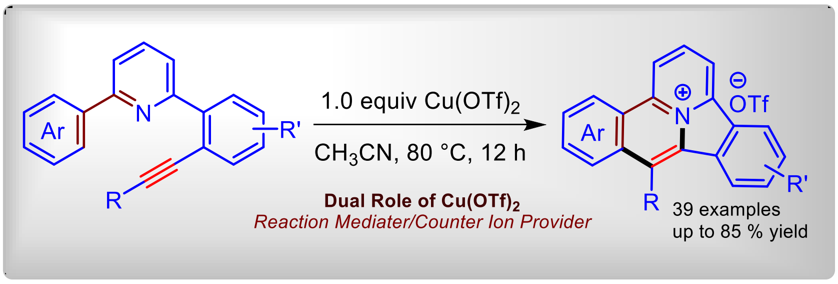
35 D. Chandra Mohan, S. N. Rao, S. Adimurthy, *J. Org. Chem*. **2013**, *78*, 1266.

36 A. C. Shaikh, D. S. Ranade, P. R. Rajamohanan, P. P. Kulkarni, N. T. Patil, *Angew. Chem. Int. Ed.*, **2017**, *56*, 757.

Chapter 2

Copper-Mediated Intramolecular Carboamination of Pyridino-alkynes: An Access to Ionic Polycyclic Aromatic Hydrocarbons (PAHs)

A copper-promoted intramolecular [4+2]-annulation cascade to access ionic N-doped polycyclic aromatic hydrocarbons (PAHs) with tunable emission wavelengths has been discussed here. It is proven that the reaction can also be made catalytic with respect to $Cu(OTf)_2$, when an external oxidant, Selectfluor was used.



Chem. Comm., **2018** *54*, 11909

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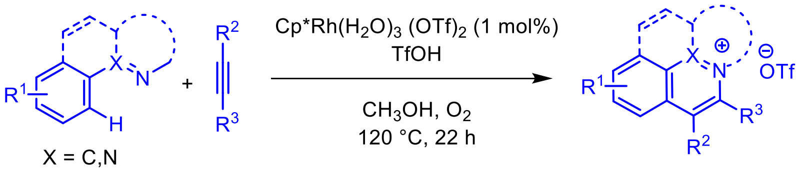
2.1 Introduction:

Polycyclic aromatic hydrocarbons (PAHs) or polyaromatic hydrocarbons are organic compounds which contains only carbon and hydrogen that are composed of multiple aromatic rings with delocalising electrons. PAHs have attracted considerable attention due to their distinctive properties including stacking behavior arising from the nature of planar molecules.[1] The merger of heteroatoms such as boron,[2] nitrogen, phosphorus,[3] oxygen,[4] or sulfur[4] in the aromatic framework of PAHs can tune their supramolecular, physical and chemical properties. As a subset of these compounds, nitrogen-doped PAHs represent an major class of molecules that have applications in the field of optoelectronics, light emitting-diodes, supercapacitors and bio-imaging.[5] Recently, it has been shown that ionic N-doped PAHs exhibit interesting optical and aggregation behavior properties.[6] Successful approaches to access N-doped ionic PAHs are discussed below.

Haung and co-workers reported Rh/O_2 catalytic system to produce isoquinolium salts via oxidative C-H activation annulation reactions from arenes and alkynes (Scheme 2.1).[7] Mechanistic studies reveal the strong evidence of oxidized Rh(III)from Rh(I) facilitated by acid. Similarly, You *et al*. developed rhodium -catalyzed oxidative CH activation/cyclization of azo compounds with alkynes to create cinnoline and cinnolinium frameworks in efficient method.[8] In this report, a stoichiometric metal oxidant was used.

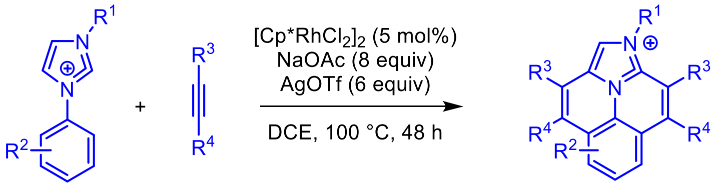
Scheme 2.1: Rhodium catalyzed annulations reaction between alkynes and arynes



Choudhuri *et al*. demonstrated that NHC directed two consecutive sequential reactions to construct benzoimidazo quinolizinium scaffold-containing polycyclic heteroaromatic molecules (Scheme 2.2) *via* Rh−C_{NHC}/Rh−C_{aryl} bond functionalization with internal alkynes.[9] Mechanistic investigation was conducted through series of control studies. Later, similarly Davies and Macgregor synthesized heterocyclic cations by the Rh(III)-catalyzed oxidative C−C and C−N coupling of 1-phenylpyrazole, 2-vinylpyridine, 2-phenylpyridine, with alkynes. The reactions proceed *via* initial heteroatom-directed C−H activation, alkyne insertion, and reductive coupling, it was supported by experimental and

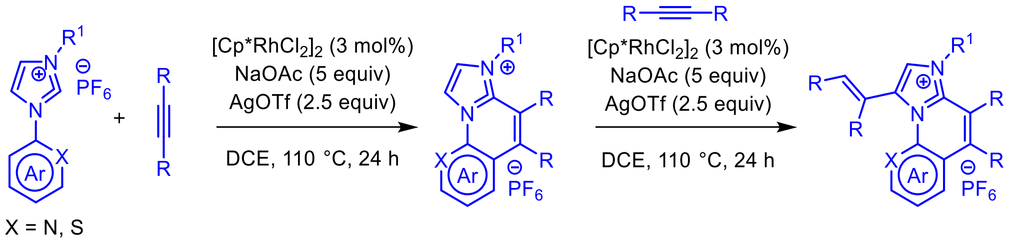
DFT studies. Heteroatom-directed C−H activation step was favored by more polar solvents.[10]

Scheme 2.2: Rhodium catalyzed annulations reaction between alkynes and arynes



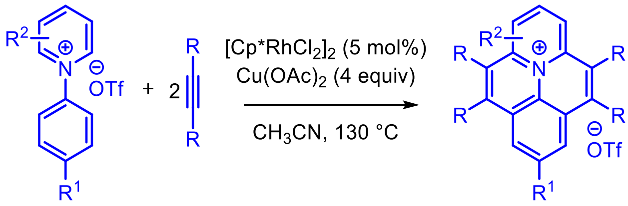
In 2016, Choudhuri *et al*. developed a bimodal C-H activation-functionalization protocol by utilizing chelating organic molecules to explore a novel chemo-divergent rollover pathway for the synthesis of annulated or alkenylated products (Scheme 2.3).[11] C-H activation of rollover pyridine was achieved, within a chelated “NHC−Rh^{III}−pyridine” platform, further annulative functionalization of the resulting cyclometalated species with internal alkynes to produce imidazo-naphthyridinium motifs. In another mode, alkenylated imidazolium compounds were obtained under a similar reaction condition.

Scheme 2.3: Rhodium catalyzed “Rollover Pathway”



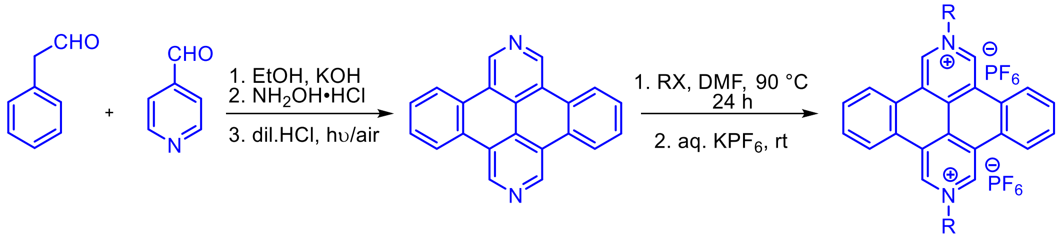
Wang and co-workers developed a one-pot process for synthesis of highly substituted quinolizino-quinolinium- and pyrido-quinolinium-based polyheteroaromatic compounds *via* rhodium(III)-catalyzed multiple C−H bond activation annulations reactions(Scheme 2.4).[12] In similar line, Gao *et al*. reported rhodium(III)-catalyzed C–H annulation of N-arylpyridinium salts with alkynes to access cationic 12-azapyrene salts with fluorescence properties (Scheme 2.4). The obtained aza-pyrene salts were intense fluorescent emissive in solution as well as in the solid state with tunable wavelenth.[13]

Scheme 2.4: Rhodium-catalyzed 1:2 oxidative annulations with alkynes



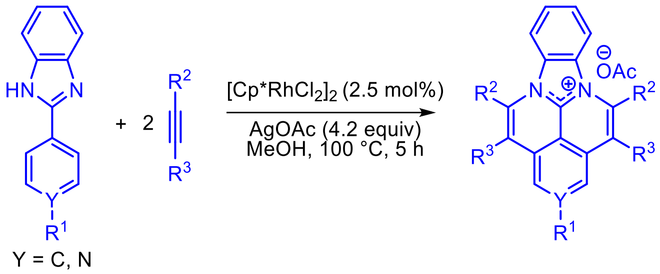
Li and Wei group designed and synthesized a novel family of p-extended viologens from simple and readily available chemicals (Scheme 2.5).[14] Synthesized viologens exhibit excellent electrochemical properties and high thermal stability.

Scheme 2.5: Three-step synthesis of viologens



Saá *et al.* group reported Rh(III) catalyzed synthesis of N-doped benzo-fluoranthenium salts *via* a double oxidative annulation reaction between arylbenzimidazoles and alkynes (Scheme 2.6).[15] The reaction proceeds via double annulation C−H activation and forms two C-N bonds. Reported skeletons showed intense fluorescence.

Scheme 2.6: Rh(III)-catalyzed double- oxidative annulations

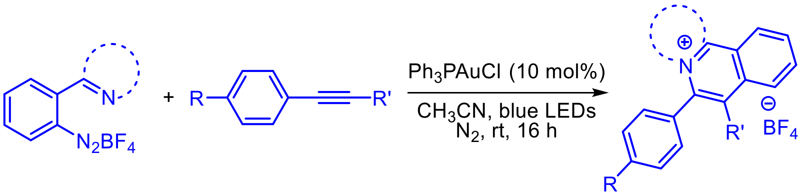


Inagi *et al.* group reported N-cationic doped PAHs with different counterions (Scheme 2.7).[16] The reaction proceeded *via* intramolecular aromatic nucleophilic substitution (S_NAr) reaction of fluoroarenes and pyridine groups, promoted by trimethylsilyl (TMS). Electrochemical properties and optical properties of the obtained nitrogen cation-doped PAHs studies suggested that they have good emission properties and low-lying LUMO levels.

Scheme 2.7: Synthesis of ring-fused bispyridinium salts *via* intramolecular S_NAr reaction

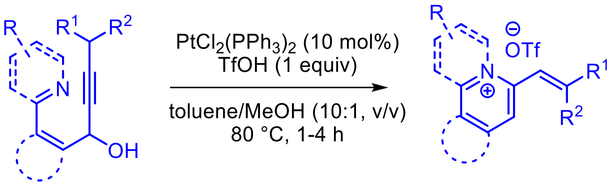
Wong *et al.* reported the synthesis of fluorescent quinolizinium compounds *via* gold-catalyzed photosensitizer-free visible light-mediated cis-difunctionalization reaction. (Scheme 2.8).[17] The reaction showed excellent regioselectivity, good functional group compatibility and chemo-selectivity towards silyl-substituted alkynes. The obtained compounds showed tunable emission properties and large stock shifts, and also it has applied in cellular imaging with subcellular properties. These quinolizinium based fluorophores can utilize as photo-catalysts for photo-oxidative amidation of aldehydes and secondary amines.

Scheme 2.8: Photosensitizer free visible light-mediated gold-catalyzed quinilizinium compounds

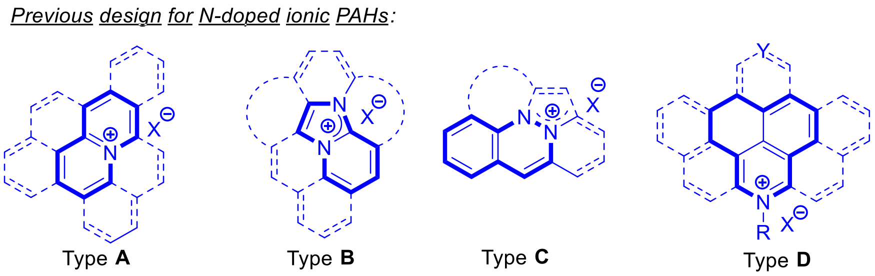


Kim and the group reported Pt metal-activated intramolecular C−N bond formation between the pyridine nitrogen and alkynes for construction of a quinolizinium-type systems (Scheme 2.9).[18] Cyclization and subsequent dehydration step induced by the Pt catalyst and protic acid. Mechanistic studies reveal that reaction proceeds via platinum-carbene intermediate.

Scheme 2.9: Construction of hetero-arenes via Pt catalysis



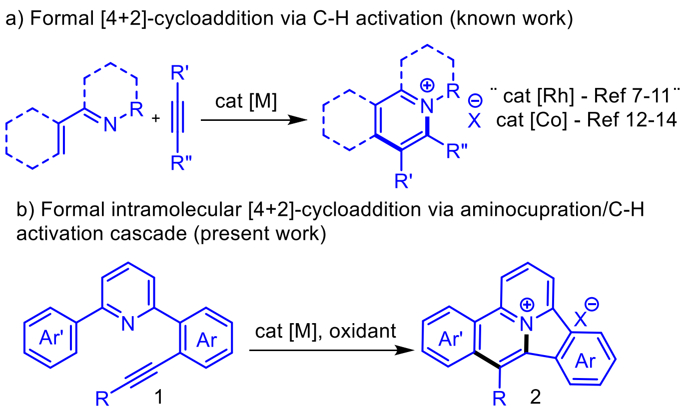
It is noticed that nearly all the reaction to synthesize N-doped PAHs reported between arenes/heteroarenes and alkynes *via* C-H activation, and it requires mainly rhodium catalysis as well as stoichiometric metal oxidant. A representative overview of all the N-doped PAH cores has been given below.



During the last decades, Rh- and Co-catalyzed reactions between alkynes and azadienes, involving C–H activation, have emerged as an important tool for accessing heterocyclic quaternary ammonium salts (Scheme 2.10a). For instance, the groups of Jones,[19] Cheng,[20] Huang,[21] You[22] and Jun[23] showed the utility of Rh-complexes for such reactions. Recently, Pèrez- Temprano,[24] Cheng[25] and Wang,[26] in their independent reports, have successfully demonstrated the use of Co-catalysts for the analogous transformations. In all of these reports, we noted that the reaction conditions which were used are harsh and super stoichiometric amount of oxidant were necessary to complete the reaction. Herein, we envisioned that in the presence of gold catalyst alkyne activates and the subsequent attack of pyridyl nitrogen will lead quaternary ammonium salt which renders the product *via* C-H functionalization and reductive elimination of catalyst.

2.2 Present work

To overcome the limitations of reported methods, we sought our attention in our current interest Au(I)/Au(III) catalysis[27] and inspired by Zhang's report,[28] we envisioned that in the presence of gold catalyst alkyne activates and the subsequent attack of pyridyl nitrogen will lead to vinyl gold(I), subsequently oxidation of Au(I) by Selectfluor to Au(III) which will render the product via C-H functionalization and reductive elimination of the catalyst (Scheme 2.10b).

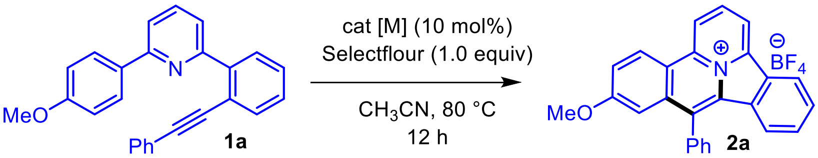


Scheme 2.10: Concept Accessing heterocyclic quaternary ammonium salts *via* formal [4+2]- annulation: Known and present work.

2.2.1 Optimization of the reaction condition:

Based on our previous report on the gold-catalyzed oxidative intramolecular 1,2-amino-oxygenation reaction of alkynes,[27] we envisioned that the substrate of type 1 would undergo intramolecular[4+2]-annulation reactions to produce ionic N-doped PAHs. Towards this end, several metal catalysts/oxidants were screened. At first, we started with the screening of metal catalysis with Selectfluor as an oxidant. Unfortunately, in presence with gold catalysts, we did not observe our expected product. Then, we moved further to copper catalysis, expected product observed in presence with catalyst Cu(OTf)$_2$ (Table 1). After observing Cu(OTf)$_2$ standard catalyst we moved to optimize the oxidants but Selectfluor only gave the prominent result (Table 2).

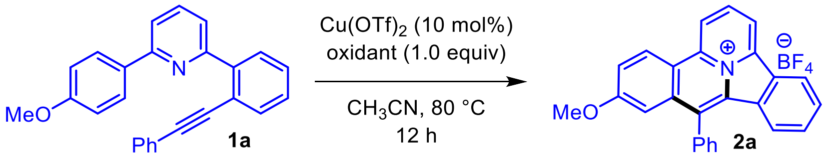
Table 1: Screening of metal catalysts:[a]



Sr. No.	cat [M]	Yield (%)[b]
1.	$(C_6F_5)_3PAuCl$	--
2.	Ph_3PAuCl	--
3.	JohnPhosAuCl	--
4.	$[Cu(OTf)]_2 \cdot C_6H_6$	48
5.	$CuCl_2$	41
6.	$Cu(OAc)_2$	52
7.	$Cu(OTf)_2$	62
8.	$Cu(ACN)_4BF_4$	57

[a]**Reaction conditions**: 0.13 mmol **1a**, 0.13 mmol Selectfluor, 10 mol% cat [M], CH_3CN (2.0 mL), 80 °C, 12 h. [b]Isolated yields.

Table 2: Effect of oxidants: [a]

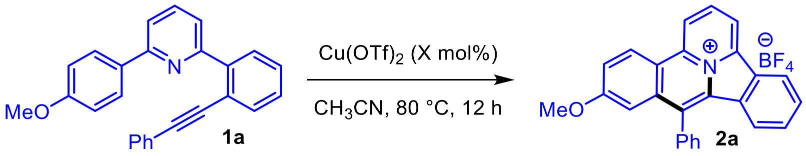


Sr. No.	Oxidant	Yield (%)[b]
1.	Selectfluor	75[c]
2.	$Ph_2I(OTf)$	--
3.	$PhI(OAc)_2$	--
4.	$PhI(CF_3CO_2)_2$	--
5.	AgOAc	16[d]
6.	-	17[d]

[a]**Reaction conditions**: 0.13 mmol **1a**, 0.13 mmol oxidant, 10 mol% Cu(OTf)$_2$, CH$_3$CN (2.0 mL), 80 °C, 12 h. [b]Isolated yields. [c]Counter anion X = BF$_4$. [d]Counter anion X = OTf.

Later the productivity of the reaction was examined by varying the mol% of catalyst Cu(OTf)$_2$. We found that by increasing the mol% of catalyst, the yield of the product also increased as observed from table 3. In order to conceive this transformation catalytically we screened various choose additives. Unfortunately, a catalytic version of this reaction was not realized (*cf*. Table 4).

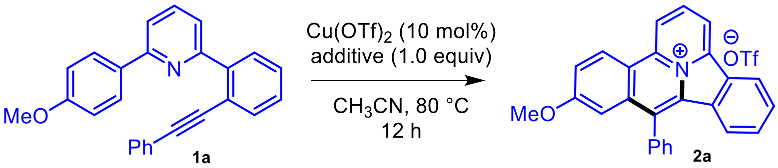
Table 3: Variation in catalyst loading: [a]



Sr. No.	X mol%	Yield (%)[b]
1.	10	17
2.	50	37
3.	**100**	**78**
4.	120	81

[a]**Reaction conditions**: 0.13 mmol **1a**, X mol% Cu(OTf)$_2$, CH$_3$CN (2.0 mL), 80 °C, 12 h. [b]Isolated yields

Table 4: Screening of various additives (1a → 2a): [a]



Sr. No.	Additives	Yield (%)[b]
1.	TfOH	--
2.	NaOTf	15
3.	$Zn(OTf)_2$	36
4.	$Mg(OTf)_2$	25
5.	$Sc(OTf)_3$	28

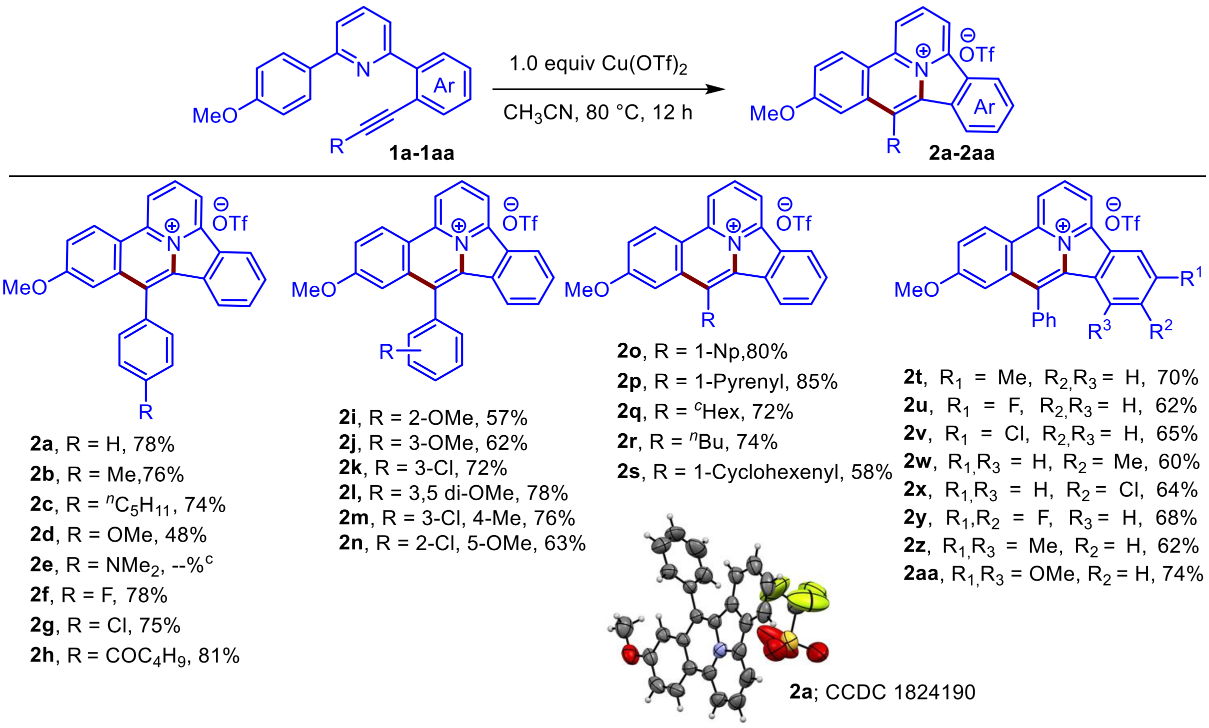
[a]**Reaction conditions**: 0.13 mmol **1a**, 10 mol% $Cu(OTf)_2$, 1.0 equiv additive, CH_3CN (2.0 mL), 80 °C, 12 h. [b]Isolated yields.

Our systematic optimization studies revealed that refluxing **1a** in CH_3CN in the presence of stoichiometric amounts of $Cu(OTf)_2$ is the best condition to achieve the desired PAH (**2a**) in 78% yield. Interestingly, $Cu(OTf)_2$ exhibits a dual role by mediating the cascade transformation as well as providing counter ion. Be noted that the Cu-catalyzed reactions of alkenes, involving the simultaneous formation of C-N and C-C bonds, are known in the literature. However, to the best of our knowledge, the parallel reactions of alkynes have never been reported.

2.2.2 Scope of the reaction:

With the optimized reaction conditions (Table 3 entry 3), we sought to investigate the substrate scope for this reaction. The results are presented in Table 5. In general, substrates with variation in aryl ring at alkyne-terminus with varying functional groups, such as alkyl and OMe were well tolerated (**2b-2d**). However, stronger electron-donating group such as NMe_2 was found to be unsuitable for the reaction. The reaction smoothly tolerated to varying substitution patterns (ortho, meta, para) on the aforementioned aryl moiety to furnish the corresponding PAHs in good yields (**2f-2n**). Next, substrates bearing bulky aromatics or long-chain/cyclic aliphatics at the alkyne terminal position of the pyridino alkynes were screened. For instance, the substrate with sterically demanding 1-Np and pyrenyl aromatic ring efficiently afforded desired PAHs **2o** and **2p** in 80% and 85% yield, respectively. Further, in the cases where aliphatic substituents were placed on the alkyne terminus, the desired PAHs **2q-2s** obtained in good yield. Next, we focused our attention to scrutinize the tolerance of the substituents on the Ar ring. Pleasingly, the introduction of Cl, F and Me substituents on the ring resulted in the formation of desired PAHs **2t-2x** in 60-70% yields. Similarly, the reaction tolerates di-substitutions at Ar ring to offer the products **2y-2aa** in moderate yields.

Table 5: Substrate scope with Ar[a,b]



2a, R = H, 78%
2b, R = Me,76%
2c, R = ^{n}C$_5$H$_{11}$, 74%
2d, R = OMe, 48%
2e, R = NMe$_2$, --%[c]
2f, R = F, 78%
2g, R = Cl, 75%
2h, R = COC$_4$H$_9$, 81%

2i, R = 2-OMe, 57%
2j, R = 3-OMe, 62%
2k, R = 3-Cl, 72%
2l, R = 3,5 di-OMe, 78%
2m, R = 3-Cl, 4-Me, 76%
2n, R = 2-Cl, 5-OMe, 63%

2o, R = 1-Np,80%
2p, R = 1-Pyrenyl, 85%
2q, R = ^{c}Hex, 72%
2r, R = ^{n}Bu, 74%
2s, R = 1-Cyclohexenyl, 58%

2a; CCDC 1824190

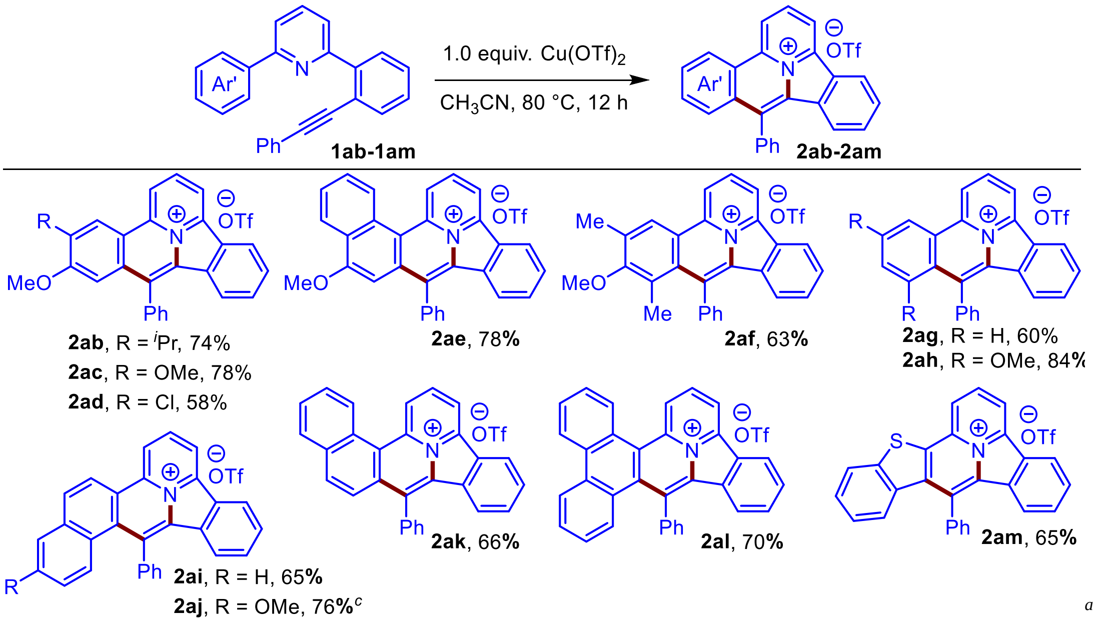
2t, R$_1$ = Me, R$_2$,R$_3$ = H, 70%
2u, R$_1$ = F, R$_2$,R$_3$ = H, 62%
2v, R$_1$ = Cl, R$_2$,R$_3$ = H, 65%
2w, R$_1$,R$_3$ = H, R$_2$ = Me, 60%
2x, R$_1$,R$_3$ = H, R$_2$ = Cl, 64%
2y, R$_1$,R$_2$ = F, R$_3$ = H, 68%
2z, R$_1$,R$_3$ = Me, R$_2$ = H, 62%
2aa, R$_1$,R$_3$ = OMe, R$_2$ = H, 74%

[a]Reaction conditions: 0.13 mmol **1**, 1.0 equiv Cu(OTf)$_2$, CH$_3$CN (2 mL), 80 °C, 12 h. [b]Isolated yield. [c]Complex reaction mixture was obtained.

To understand the tolerance of substituents at Ar′ ring, substrates **1ab-1am** were examined under the optimized reaction conditions (Table 6). It was observed that **1ab-1ah** underwent smooth reactions to provide desired PAHs **2ab-2ah** in good yields (58-84%). Moreover, 1-Np, 2-Np, 9-phenanthryl groups were well tolerated under the present reaction conditions to produce desired PAHs (**2ai-2al**) in good yields.

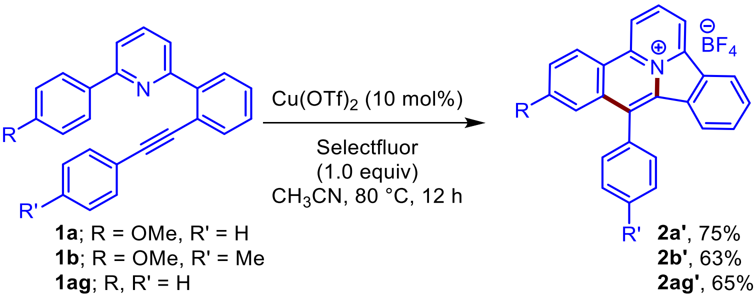
Even, the benzothiophenyl moiety was also well tolerated giving PAH **2am** in 65% yield. The scalability of the methods was demonstrated by the large-scale synthesis employing **1a** (2.7 mmol) as a starting material (**2a**, 76%).

Table 6: Substrate scope with Ar[a,b]



[a]Reaction conditions: 0.13mmol**1**, 1.0 equiv Cu(OTf)$_2$, CH$_3$CN (2 mL), 80 °C, 12 h. [b]Isolated yield. [c]CCDC for **2aj** – 182419.

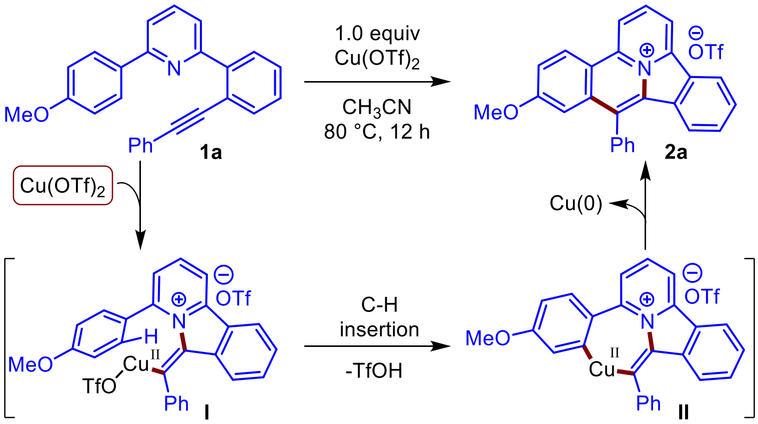
Interestingly, we found that the reaction can be made catalytic with stoichiometric amount oxidant with respect to Cu(OTf)$_2$ (ref. table **2**). When **1a**, **1b** and **1ag** were treated with 10 mol% Cu(OTf)$_2$ in the presence of Selectfluor, the reaction proceeded smoothly to produce **2a′**, **2b′** and **2ag′** in 75, 63 and 65 % yields, respectively.



Scheme 2.11. Catalytic reactions with respect to Cu(OTf)$_2$ in the presence of external oxidant

2.3 Proposed mechanism:

A plausible reaction pathway for the present transformation is depicted in Scheme 2.12. At first, activation of the alkyne by the Cu(OTf)$_2$ would occur to enable nucleophilic attack by the pyridyl nitrogen atom in 5-*exo*-dig fashion to generate vinyl copper intermediate **I**. This intermediate would activate C-H bond of proximal aryl ring and subsequently remove TfOH to generate copper (II) intermediate **II**. Further, reductive elimination would occur to form product **2a**. The fact that the yield of the reaction was not hampered in the presence of the radical scavenger such as 2,2,6,6-tetra-methylpiperidine-1-oxyl (TEMPO) rules out the possibility of radical mechanism.



Scheme 2.12. A plausible reaction mechanism.

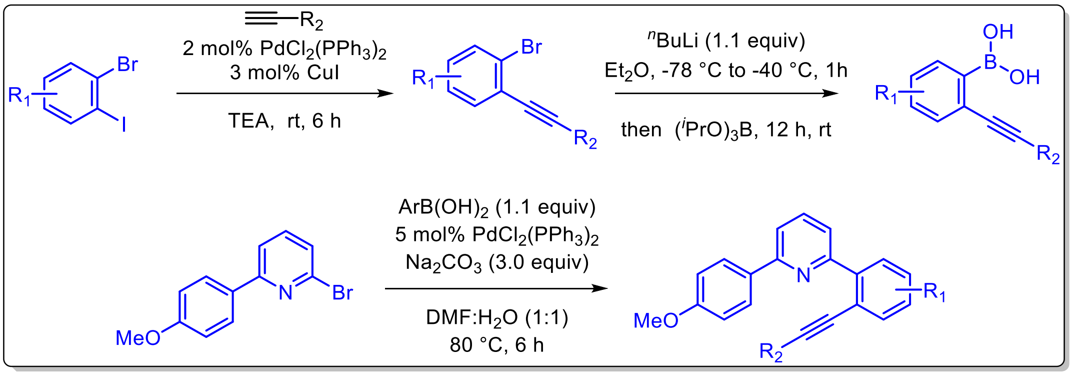
The synthesized PAHs exhibit intense fluorescence and their photophysical properties were studied in CH_2Cl_2 solution (In experimetal procudures). The PL range shields the visible region, offering a palette of colors ranging from violet to orange (λ_{em}: 434-619 nm, Figure 1). These luminogens have good photoluminescence capabilities with Φ_f values (0.06 to 0.88). Next, the PAHs were investigated by cyclic voltammetry and found that PAHs have high electron-accepting abilities and good electrochemical properties.

2.4 Conclusion:

In conclusion, Cu(II)-mediated intramolecular alkynes/azadienes [4+2]-annulation cascade has been disclosed. The reagent $Cu(OTf)_2$ exhibits dual role by mediating the cascade transformation as well as providing counter ion. Further, by employing Selectfluor as an external oxidant, catalytic version of this reaction was realised successfully. The method provided efficient access to ionic N-doped PAHs with tunable emission wavelengths.

2.5 Experimental procedures:

2.5.1 General procedure for preparation of substituted 2-alkynyl-bromobenzenes



The bromo-alkynes **S_1-S_{12}**, **S_{15}-S_{24}**, and **S_{26}-S_{27}** were reported in the literature and prepared according to the literature known procedures.[1] The other analogs of bromo-alkynes **S_{13}-S_{14}** and **S_{25}** were prepared by slightly modified procedures.

Representative procedure for Sonogashira cross-coupling reaction: A suspension of 2-bromoiodobenzene (1.0 gm, 3.55 mmol, 1.0 equiv), $PdCl_2(PPh_3)_2$ (50 mg, 2 mol%), Cu(I) iodide (20 mg, 3 mol%) in 20 mL of triethylamine was degassed with nitrogen for 5 minutes. After 10 min, a solution of phenyl acetylene (0.49 mL, 1.1 equiv) in triethylamine (3.0 mL) was added drop-wise over 5 min via syringe and the reaction mixture was left to stir for 12 h. After complete consumption of the 2-bromoiodobenzene, as monitored by TLC, the reaction mixture was filtered through pad of celite and extracted with ethyl acetate (3 × 10 mL). The organic layer was washed with a saturated solution of NH_4Cl (2 × 10 mL), water (2 × 10 mL), dried over Na_2SO_4 and the organic solvent was removed under vacuo. The reaction mixture was purified by flash chromatography on silica gel, (eluent: petroleum ether) to give the 1-bromo-2-(phenylethynyl) benzene (**S_1**) in 90% yield.

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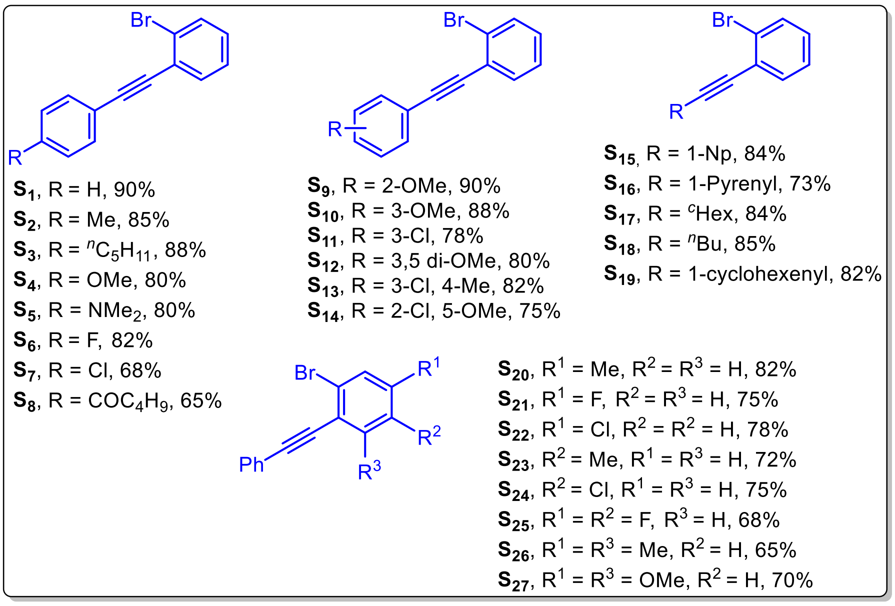
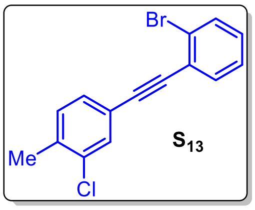
[1] (a) Shaikh, A. C.; Ranade, D. S.; Rajamohanan, P. R.; Kulkarni, P. P.; Patil, N. T. *Angew. Chem. Int. Ed*. **2017**, *56*, 757. (b) Shinde, P. S.; Shaikh, A. C.; Patil, N. T. *Chem. Commun.* **2016**, *52*, 8152. (c) Guo, R.; Li, K.-N.; Liu, B.; Zhu, H.-J.; Fan, Y.-M.; Gong, L.-Z. *Chem. Commun*. **2014**, *50*, 5451.



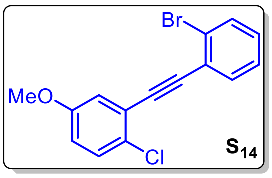
4-((2-bromophenyl)ethynyl)-2-chloro-1-methylbenzene (S_{13}):



S_{13}

Off white solid, 880 mg, 82% yield; mp = 58-60 °C; ***R**$_f$* = 0.80 (petroleum ether/ethyl acetate = 98/02); **^{1}H NMR (400 MHz, $CDCl_3$) δ** = 7.63 (d, *J* = 7.9 Hz, 1 H), 7.59 (s, 1 H), 7.56 (d, *J* = 7.3 Hz, 1 H), 7.38 (d, *J* = 7.3 Hz, 1 H), 7.30 (t, *J* = 7.6 Hz, 1 H), 7.15 - 7.24 (m, 2 H), 2.41 (s, 3 H); **^{13}C NMR (100 MHz, $CDCl_3$) δ** = 136.9, 133.2, 132.4, 131.8, 130.8, 129.8, 129.5, 127.0, 125.6, 125.1, 121.8, 92.5, 88.4, 20.1; **HRMS (ESI)** calcd for $C_{15}H_{11}BrCl$ $(M + H)^+$ 304.9796, found 304.9794.

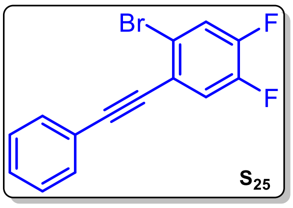
2-((2-bromophenyl)ethynyl)-1-chloro-4-methoxybenzene (S_{14}):



S_{14}

Off white solid, 850 gm, 75% yield; mp = 60-62 °C; ***R**$_f$* = 0.75 (petroleum ether/ethyl acetate = 98/02); **^{1}H NMR (500 MHz, $CDCl_3$) δ** = 7.57 - 7.66 (m, 2 H), 7.27 - 7.35 (m, 2 H), 7.21 (d, *J* = 1.5 Hz, 1 H), 7.13 (d, *J* = 3.1 Hz, 1 H), 6.85 (dd, *J* = 8.8, 3.1 Hz, 1 H), 3.82 (s, 3 H); **^{13}C NMR (125 MHz, $CDCl_3$) δ** = 158.0, 133.8, 132.7, 130.2, 130.0, 127.8, 127.2, 125.8, 125.2, 123.5, 118.0, 116.7, 92.8, 90.8, 55.8; **HRMS (ESI)** calcd for $C_{15}H_{11}BrCl$ (M + H)$^+$ 320.9676, found 320.9674.

1-bromo-4,5-difluoro-2-(phenylethynyl)benzene (S_{25}):



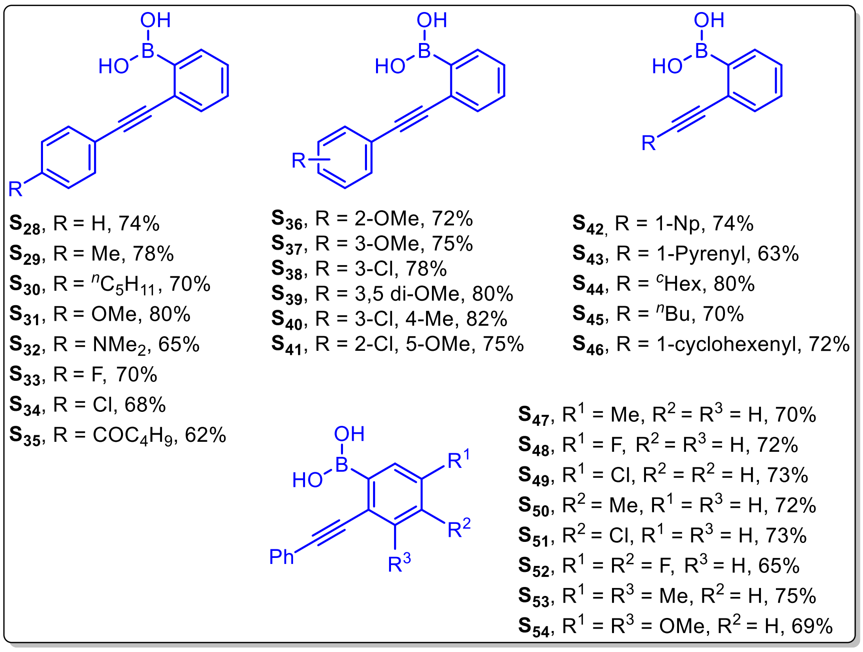
Off white solid, 704 mg, 68% yield; mp = 50-52 °C; $\boldsymbol{R_f}$ = 0.80 (petroleum ether/ethyl acetate = 98/02); **^{1}H NMR (500 MHz, CDCl$_3$) δ** = 7.58 (br.s., 2 H), 7.45 (br.s., 1 H), 7.39 (br.s., 4 H); **^{13}C NMR (125 MHz, CDCl$_3$) δ** = 151.0 - 149.0 (dd, J = 256.5 Hz, 14.3 Hz), 150.2 - 148.2 (dd, J = 249.9, 12.4), 131.7, 129.0, 128.4, 122.3, 122.2 - 122.1 (d, J = 3.8 Hz), 121.6 - 121.5(d, J = 20.0 Hz), 121.3 - 121.1 (d, J = 19.0 Hz), 120.0 - 120.0 (d, J = 2.9 Hz), 94.5, 86.2; **HRMS (ESI)** calcd for $C_{14}H_8BrF_2$ (M + H)$^+$ 292.9786, found 292.9782.

2.5.2 General procedure for preparation of 2-alkynylphenylboronic acids

The boronic acid $\mathbf{S_{28}}$-$\mathbf{S_{39}}$, $\mathbf{S_{41}}$-$\mathbf{S_{51}}$ and $\mathbf{S_{54}}$ were reported in the literature and prepared according to the literature known procedures.[1] The other boronic acids $\mathbf{S_{40}}$ and $\mathbf{S_{52}}$-$\mathbf{S_{53}}$ were prepared from slight modifications in literature known procedures.

Representative procedure for the synthesis of boronic acid: In a two-necked round bottom flask, 1.6 M solution of ^{n}BuLi in ^{n}hexanes (3.1 mL, 1.3 equiv) was added drop-wise to a solution of 2-phenylethynyl bromobenzene ($\mathbf{S_1}$) (1.0 g, 3.92 mmol, 1.0 equiv) in 30 mL of diethyl ether under nitrogen atmosphere at -78 °C. The mixture was stirred at -78 °C for 1 h and then at -40 °C for 1 h then cool back to -78 °C and B(O^{i}Pr)$_3$ (1.1 g, 1.5 equiv) was added drop-wise. The mixture was allowed to warm up gradually to room temperature, while maintaining vigorous stirring for 16 h. Then, the reaction was quenched with 40 mL of 1N HCl for 30 minutes and extracted with ethyl acetate (3 x 20 mL). The combined organic solution was dried over Na_2SO_4 and the organic solvent was removed under vacuo. The product was purified by flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate) followed by recrystallization from petroleum ether to give the (2-(phenylethynyl)phenyl)boronic acid ($\mathbf{S_{28}}$) in 74% yield.

Note: The boronic acid $\mathbf{S_{52}}$-$\mathbf{S_{53}}$ was accompanied with slight impurities and hence used directly for the next reaction without attempting further purification.



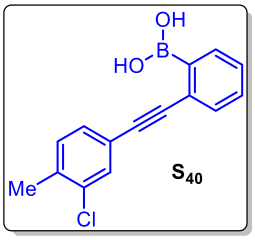
S$_{28}$, R = H, 74%
S$_{29}$, R = Me, 78%
S$_{30}$, R = ^{n}C$_5$H$_{11}$, 70%
S$_{31}$, R = OMe, 80%
S$_{32}$, R = NMe$_2$, 65%
S$_{33}$, R = F, 70%
S$_{34}$, R = Cl, 68%
S$_{35}$, R = COC$_4$H$_9$, 62%

S$_{36}$, R = 2-OMe, 72%
S$_{37}$, R = 3-OMe, 75%
S$_{38}$, R = 3-Cl, 78%
S$_{39}$, R = 3,5 di-OMe, 80%
S$_{40}$, R = 3-Cl, 4-Me, 82%
S$_{41}$, R = 2-Cl, 5-OMe, 75%

S$_{42}$, R = 1-Np, 74%
S$_{43}$, R = 1-Pyrenyl, 63%
S$_{44}$, R = ^{c}Hex, 80%
S$_{45}$, R = ^{n}Bu, 70%
S$_{46}$, R = 1-cyclohexenyl, 72%

S$_{47}$, R^1 = Me, R^2 = R^3 = H, 70%
S$_{48}$, R^1 = F, R^2 = R^3 = H, 72%
S$_{49}$, R^1 = Cl, R^2 = R^2 = H, 73%
S$_{50}$, R^2 = Me, R^1 = R^3 = H, 72%
S$_{51}$, R^2 = Cl, R^1 = R^3 = H, 73%
S$_{52}$, R^1 = R^2 = F, R^3 = H, 65%
S$_{53}$, R^1 = R^3 = Me, R^2 = H, 75%
S$_{54}$, R^1 = R^3 = OMe, R^2 = H, 69%

(2-((3-chloro-4-methylphenyl)ethynyl)phenyl)boronic acid (**S$_{40}$**):

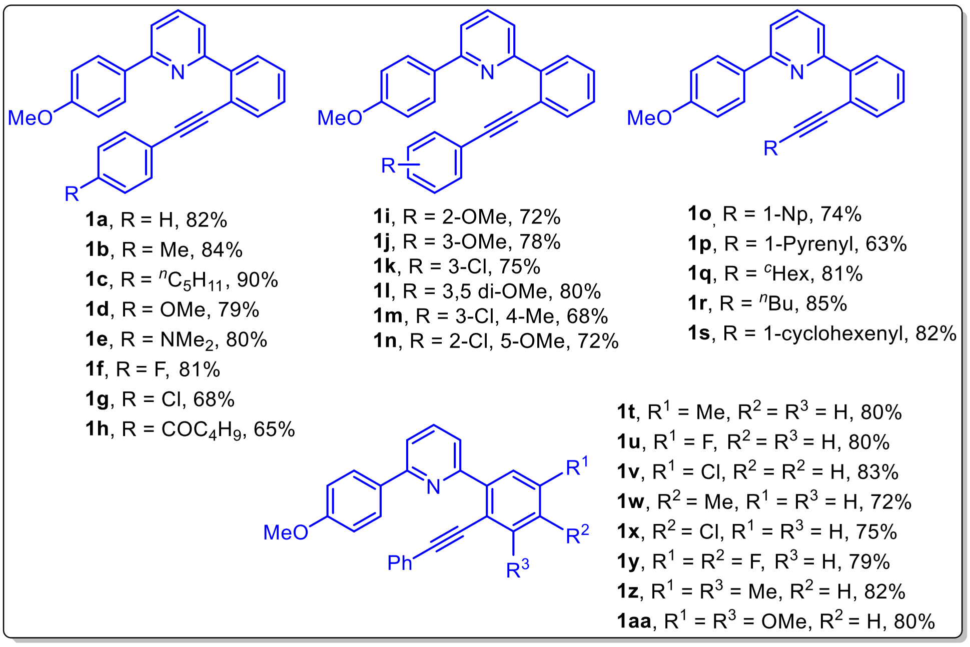


S$_{40}$

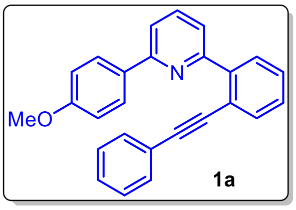
Off white solid, 730 mg, 82% yield; mp = 160-162 °C; ***R$_f$*** = 0.40 (petroleum ether/ethyl acetate = 60/40); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 8.20 (s, 2 H), 7.52 - 7.59 (m, 2 H), 7.47 - 7.52 (m, 1 H), 7.32 - 7.42 (m, 4 H), 2.36 (s, 3 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 136.2, 133.4, 133.0, 131.5, 131.2, 131.0, 129.8, 128.9, 127.8, 124.9, 122.3, 91.8, 88.8, 19.6; **HRMS (ESI)** calcd for $C_{15}H_{13}O_2BCl$ $(M + H)^+$ 271.0692, found 271.0698.

2.5.3 Synthesis of 2-(4-methoxyphenyl)-6-(2(alkynyl)-phenyl)pyridines

Representative procedure for Suzuki cross-coupling reaction:[29] In a sealed tube, 2-bromo-6-(4-methoxyphenyl)pyridine (200 mg, 0.760 mmol, 1.0 equiv) and (2-(phenylethynyl) phenyl)boronic acid (**S$_{28}$**) (203 mg, 1.2 equiv) in DMF/H$_2$O (1:1, 4 mL) was degassed with nitrogen for 5 min. Next, Na$_2$CO$_3$ (240 mg, 3 equiv) and PdCl$_2$(PPh$_3$)$_2$ (27 mg, 5 mol%) were added under nitrogen atmosphere. The reaction mixture was stirred at 80 °C for 6 h. After complete consumption of starting material, as monitored by TLC, the resulting mixture was allowed to bring to room temperature. The reaction mixture was diluted with $NaHCO_3$ (5 mL) and then the product was extracted with ethyl acetate (3 × 5 mL). The combined organic layer was dried over Na_2SO_4 and the organic solvent was removed under vacuo. The crude product was purified on a silica gel column using petroleum ether/ethyl acetate as eluent to afford 2-(4-methoxyphenyl)-6-(2-(phenylethynyl)phenyl)pyridine (**1a**) in 82% yield.

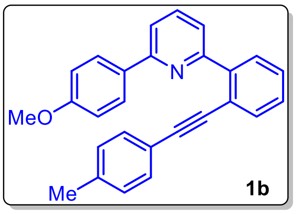


2-(4-methoxyphenyl)-6-(2-(phenylethynyl)phenyl)pyridine (**1a**):



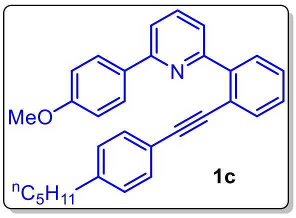
Off white solid, 225 mg, 82% yield; mp = 104-106 °C; ***R_f*** = 0.60 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (500 MHz, $CDCl_3$) δ** = 8.12 (d, *J* = 8.4 Hz, 2 H), 7.94 (d, *J* = 7.6 Hz, 1 H), 7.91 (d, *J* = 7.6 Hz, 1 H), 7.82 (t, *J* = 7.6 Hz, 1 H), 7.67 - 7.73 (m, 2 H), 7.45 - 7.52 (m, 1 H), 7.37 - 7.44 (m, 3 H), 7.28 - 7.34 (m, 3 H), 6.99 (d, *J* = 8.4 Hz, 2 H), 3.87 (s, 3 H); **^{13}C NMR (125 MHz, $CDCl_3$) δ** = 160.4, 157.1, 156.5, 142.5, 136.3, 133.3, 132.1, 131.4, 129.9, 128.6, 128.3, 128.2, 128.1, 128.1, 123.4, 121.8, 121.4, 118.0, 114.0, 92.5, 89.5, 55.3; **HRMS (ESI)** calcd for $C_{26}H_{20}ON$ $(M + H)^+$ 362.1539, found 362.1545.

2-(4-methoxyphenyl)-6-(2-(*p*-tolylethynyl)phenyl)pyridine (**1b**):



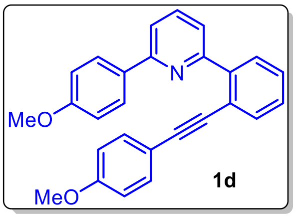
Off white solid, 240 mg, 84% yield; mp = 110-112 °C; ***R_f*** = 0.60 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (400 MHz**, **CDCl$_3$) δ** = 8.12 (d, *J* = 8.5 Hz, 2 H), 7.93 (t, *J* = 8.5 Hz, 2 H), 7.81 (t, *J* = 7.6 Hz, 1 H), 7.64 - 7.73 (m, 2 H), 7.48 (t, *J* = 7.6 Hz, 1 H), 7.41 (t, *J* = 7.3 Hz, 1 H), 7.27 - 7.34 (d, *J* = 7.9 Hz, 2 H), 7.08 - 7.15 (d, *J* = 7.3 Hz, 2 H), 7.00 (d, *J* = 8.5 Hz, 2 H), 3.87 (s, 3 H), 2.36 (s, 3 H); **^{13}C NMR (100 MHz**, **CDCl$_3$) δ** = 160.4, 157.2, 156.5, 142.3, 138.3, 136.3, 133.2, 132.2, 131.3, 129.9, 129.0, 128.4, 128.3, 128.1, 121.9, 121.6, 120.4, 118.0, 114.1, 114.0, 92.7, 88.8, 55.3, 21.5; **HRMS (ESI)** calcd for $C_{27}H_{22}ON$ $(M + H)^+$ 376.1696, found 376.1704.

2-(4-methoxyphenyl)-6-(2-((4-pentylphenyl)ethynyl)phenyl)pyridine (**1c**):



Off white solid, 295 mg, 90% yield; mp = 64-66 °C; ***R_f*** = 0.60 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (400 MHz**, **CDCl$_3$) δ** = 8.13 (d, *J* = 8.5 Hz, 2 H), 7.88 - 7.97 (m, 2 H), 7.82 (t, *J* = 7.6 Hz, 1 H), 7.65 - 7.73 (m, 2 H), 7.45 - 7.52 (m, 1 H), 7.37 - 7.45 (m, 1 H), 7.29 - 7.36 (m, *J* = 7.9 Hz, 2 H), 7.07 - 7.16 (d, *J* = 7.9 Hz, 2 H), 7.00 (d, *J* = 8.5 Hz, 2 H), 3.87 (s, 3 H), 2.61 (t, *J* = 7.6 Hz, 2 H), 1.57 - 1.67 (m, 2 H), 1.30 - 1.40 (m, 4 H), 0.92 (t, *J* = 6.7 Hz, 3 H); **^{13}C NMR (100 MHz**, **CDCl$_3$) δ** = 160.4, 157.2, 156.4, 143.3, 142.3, 136.3, 133.2, 132.2, 131.3, 129.9, 128.4, 128.3, 128.1, 121.9, 121.6, 120.5, 118.0, 114.0, 92.7, 88.8, 55.3, 35.8, 31.4, 30.9, 22.5, 14.0; **HRMS (ESI)** calcd for $C_{31}H_{30}ON$ $(M + H)^+$ 432.2322, found 432.2332.

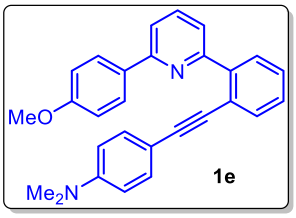
2-(4-methoxyphenyl)-6-(2-((4-methoxyphenyl)ethynyl)phenyl)pyridine (**1d**):



1d

Yellowish solid, 235 mg, 79% yield; mp = 90-92 °C; ***R****f* = 0.55 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (500 MHz**, **$CDCl_3$) δ** = 8.11 (d, *J* = 8.0 Hz, 2 H), 7.88 - 7.96 (m, 2 H), 7.81 (t, *J* = 7.6 Hz, 1 H), 7.61 - 7.70 (m, 2 H), 7.46 (t, *J* = 7.4 Hz, 1 H), 7.40 (t, *J* = 7.4 Hz, 1 H), 7.29 - 7.36 (m, *J* = 8.0 Hz, 2 H), 6.93 - 7.04 (m, *J* = 8.4 Hz, 2 H), 6.83 (d, *J* = 8.4 Hz, 2 H), 3.87 (s, 3 H), 3.81 (s, 3 H); **^{13}C NMR (125 MHz**, **$CDCl_3$) δ** = 160.4, 159.5, 157.3, 156.5, 142.2, 136.3, 133.1, 132.9, 132.2, 129.9, 128.3, 128.2, 128.1, 121.9, 121.7, 118.0, 115.6, 114.0, 113.9, 92.5, 88.2, 55.3, 55.3; **HRMS (ESI)** calcd for $C_{27}H_{22}O_2N$ $(M + H)^+$ 392.1645, found 392.1654.

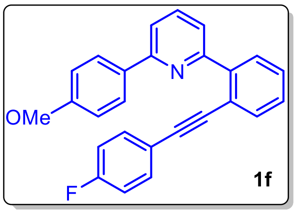
4-((2-(6-(4-methoxyphenyl)pyridin-2-yl)phenyl)ethynyl)-*N*,*N*-dimethylaniline (**1e**):



1e

Brown solid, 247 mg, 80% yield; mp = 122-124 °C; ***R****f* = 0.50 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (500 MHz**, **$CDCl_3$) δ** = 8.08 - 8.16 (d, *J* = 8.8 Hz, 2 H), 7.98 (d, *J* = 7.6 Hz, 1 H), 7.91 - 7.97 (m, 1 H), 7.80 (t, *J* = 7.6 Hz, 1 H), 7.63 - 7.73 (m, 2 H), 7.41 - 7.47 (m, 1 H), 7.38 (td, *J* = 7.5, 1.0 Hz, 1 H), 7.24 - 7.32 (m, *J* = 8.8 Hz, 2 H), 6.93 - 7.04 (d, *J* = 8.8 Hz, 2 H), 6.59 - 6.65 (d, *J* = 8.8 Hz, 2 H), 3.87 (s, 3 H), 2.98 (s, 6 H); **^{13}C NMR (125 MHz**, **$CDCl_3$) δ** = 160.3, 157.3, 156.4, 150.0, 141.8, 136.2, 132.8, 132.5, 132.3, 129.9, 128.3, 128.0, 127.7, 122.2, 122.0, 117.9, 114.0, 111.8, 110.3, 93.9, 87.5, 55.3, 40.2; **HRMS (ESI)** calcd for $C_{28}H_{25}ON_2$ $(M + H)^+$ 405.1961, found 405.1965.

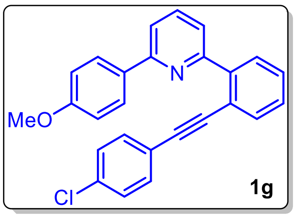
2-(2-((4-fluorophenyl)ethynyl)phenyl)-6-(4-methoxyphenyl)pyridine (**1f**):



1f

Off white solid, 234 mg, 81% yield; mp = 60-62 °C; ***R$_f$*** = 0.65 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (400 MHz, CDCl$_3$) δ** = 8.11 (d, *J* = 9.2 Hz, 2 H), 7.91 (d, *J* = 7.9 Hz, 1 H), 7.87 - 7.75 (m, 2 H), 7.74 - 7.64 (m, 2 H), 7.49 (t, *J* = 7.3 Hz, 1 H), 7.41 (t, *J* = 7.3 Hz, 1 H), 7.35 (dd, *J* = 5.5, 8.5 Hz, 2 H), 7.06 - 6.90 (m, 4 H), 3.87 (s, 3 H); **^{13}C NMR (100 MHz, CDCl$_3$) δ** = 163.6-161.2 (d, *J* = 9.2 Hz), 160.5, 157.2, 156.5, 142.5, 136.4, 133.3, 133.2-133.2 (d, *J* = 3.1 Hz), 132.1, 129.9, 128.6, 128.3, 128.1, 121.7, 121.3, 119.5, 118.0, 115.6-115.4 (d, *J* = 21.8 Hz), 114.0, 91.3, 89.2, 55.3; **HRMS (ESI)** calcd for $C_{26}H_{19}ONF$ $(M + H)^+$ 380.1445, found 380.1450.

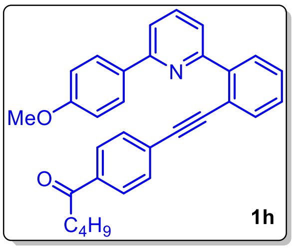
2-(2-((4-chlorophenyl)ethynyl)phenyl)-6-(4-methoxyphenyl)pyridine (**1g**):



1g

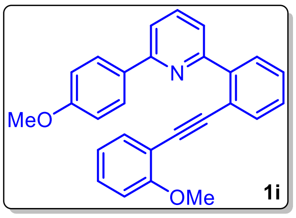
Off white solid, 205 mg, 68% yield; mp = 134-136 °C; ***R$_f$*** = 0.55 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (400 MHz, CDCl$_3$) δ** = 8.13 (d, *J* = 8.5 Hz, 2 H), 7.93 (d, *J* = 7.9 Hz, 1 H), 7.80 – 7.87 (m, 2 H), 7.72 (d, *J* = 7.3 Hz, 2 H), 7.52 (t, *J* = 7.6 Hz, 1 H), 7.44 (t, *J* = 7.3 Hz, 1 H), 7.22 – 7.34 (m, 4 H), 7.01 (d, *J* = 8.5 Hz, 2 H), 3.89 (s, 3 H); **^{13}C NMR (100 MHz, CDCl$_3$) δ** = 160.4, 157.1, 156.5, 142.6, 136.4, 134.1, 133.3, 132.6, 132.0, 129.9, 128.8, 128.6, 128.3, 128.1, 121.9, 121.7, 121.1, 118.1, 114.0, 91.2, 90.5, 55.3; **HRMS (ESI)** calcd for $C_{26}H_{19}ONCl$ $(M + H)^+$ 396.1150, found 396.1161.

1-(4-((2-(6-(4-methoxyphenyl)39yridine-2-yl)phenyl)ethynyl)phenyl)pentan-1-one (**1h**):



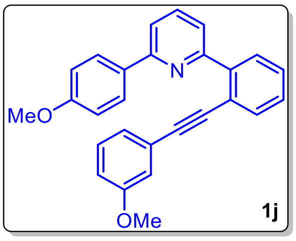
Off white solid, 220 mg, 65% yield; mp = 106-108 °C; ***R*** R_f = 0.50 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (500 MHz, CDCl$_3$) δ** = 8.11 (d, *J* = 8.8 Hz, 2 H), 7.91 (d, *J* = 7.6 Hz, 1 H), 7.85 – 7.89 (m, *J* = 8.4 Hz, 2 H), 7.78 – 7.84 (m, 2 H), 7.66 – 7.74 (m, 2 H), 7.47 – 7.55 (m, 1 H), 7.37 – 7.46 (m, 3 H), 6.91 – 7.03 (d, *J* = 8.8 Hz, 2 H), 3.86 (s, 3 H), 2.94 (t, *J* = 7.4 Hz, 2 H), 1.72 (quin, *J* = 7.5 Hz, 2 H), 1.41 (sxt, *J* = 7.5 Hz, 2 H), 0.96 (t, *J* = 7.2 Hz, 3 H); **^{13}C NMR (125 MHz, CDCl$_3$) δ** = 199.7, 160.4, 157.1, 156.5, 142.8, 136.4, 136.0, 133.4, 132.0, 131.5, 129.9, 129.1, 128.3, 128.2, 128.1, 127.9, 121.7, 120.9, 118.1, 114.0, 92.8, 91.6, 55.3, 38.3, 26.4, 22.4, 13.9; **HRMS (ESI)** calcd for $C_{31}H_{28}O_2N$ $(M + H)^+$ 446.2115, found 446.2125.

2-(4-methoxyphenyl)-6-(2-((2-methoxyphenyl)ethynyl)phenyl)pyridine (**1i**):



Off white solid, 215 mg, 72% yield; mp = 92-94 °C; R_f = 0.55 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (400 MHz, CDCl$_3$) δ** = 8.10 - 8.17 (m, 3 H), 8.00 - 8.06 (m, 1 H), 7.74 - 7.83 (m, 2 H), 7.69 (d, *J* = 7.8 Hz, 1 H), 7.51 (td, *J* = 7.6, 1.4 Hz, 1 H), 7.36 - 7.46 (m, 2 H), 7.25 - 7.33 (m, 1 H), 6.98 - 7.04 (m, 2 H), 6.82 - 6.95 (m, 2 H), 3.87 (s, 3 H), 3.84 (s, 3 H); **^{13}C NMR (100 MHz, CDCl$_3$) δ** = 160.3, 159.9, 156.8, 156.3, 142.0, 136.2, 133.4, 133.3, 132.1, 129.9, 129.6, 128.4, 128.2, 128.0, 122.0, 121.6, 120.3, 117.8, 113.9, 112.6, 110.6, 93.3, 89.2, 55.5, 55.2; **HRMS (ESI)** calcd for $C_{27}H_{22}O_2N$ $(M + H)^+$ 392.1645, found 392.1652.

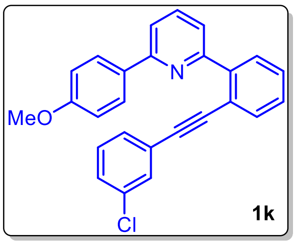
2-(4-methoxyphenyl)-6-(2-((3-methoxyphenyl)ethynyl)phenyl)pyridine (**1j**):



1j

Off white solid, 235 mg, 78% yield; mp = 78-80 °C; ***R****f* = 0.55 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (400 MHz, CDCl$_3$) δ** = 8.07 - 8.18 (m, 2 H), 7.93 (dd, *J* = 7.8, 0.9 Hz, 1 H), 7.86 - 7.91 (m, 1 H), 7.76 - 7.85 (m, 1 H), 7.71 (td, *J* = 7.8, 0.9 Hz, 2 H), 7.50 (td, *J* = 7.8, 1.4 Hz, 1 H), 7.42 (td, *J* = 7.6, 1.4 Hz, 1 H), 7.17 - 7.25 (m, 1 H), 6.95 - 7.04 (m, 3 H), 6.89 - 6.95 (m, 1 H), 6.79 - 6.89 (m, 1 H), 3.87 (s, 3 H), 3.74 (s, 3 H); **^{13}C NMR (100 MHz, CDCl$_3$) δ** = 160.7, 159.5, 157.5, 156.7, 142.8, 136.7, 133.6, 132.4, 130.2, 129.6, 128.9, 128.6, 128.4, 124.7, 124.3, 122.1, 121.6, 118.3, 116.5, 115.1, 114.3, 92.7, 89.6, 55.6, 55.4; **HRMS (ESI)** calcd for $C_{27}H_{22}O_2N$ $(M + H)^+$ 392.1645, found 392.1652.

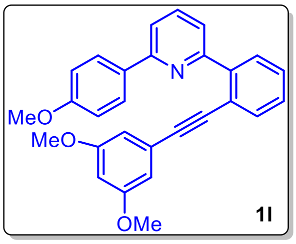
2-(2-((3-chlorophenyl)ethynyl)phenyl)-6-(4-methoxyphenyl)pyridine (**1k**):



1k

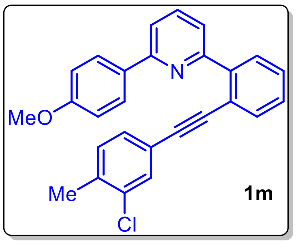
Off white solid, 225 mg, 75% yield; mp = 90-92 °C; ***R****f* = 0.50 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (500 MHz, CDCl$_3$) δ** = 8.06 – 8.19 (m, *J* = 8.8 Hz, 2 H), 7.92 (d, *J* = 7.6 Hz, 1 H), 7.79 – 7.86 (m, 2 H), 7.72 (dt, *J* = 6.0, 3.3 Hz, 2 H), 7.48 – 7.56 (m, 1 H), 7.40 – 7.47 (m, 1 H), 7.38 (s, 1 H), 7.21 – 7.31 (m, 3 H), 6.96 – 7.04 (m, *J* = 8.8 Hz, 2 H), 3.88 (s, 3 H); **^{13}C NMR (125 MHz, CDCl$_3$) δ** = 160.4, 157.1, 156.5, 142.7, 136.4, 134.0, 133.4, 132.0, 131.2, 129.9, 129.5, 129.4, 128.9, 128.3, 128.3, 128.2, 125.2, 121.7, 120.9, 118.1, 114.0, 90.9, 90.7, 55.3; **HRMS (ESI)** calcd for $C_{26}H_{19}ONCl$ $(M + H)^+$ 396.1150, found 396.1155.

2-(2-((3,5-dimethoxyphenyl)ethynyl)phenyl)-6-(4-methoxyphenyl)pyridine (**1l**):



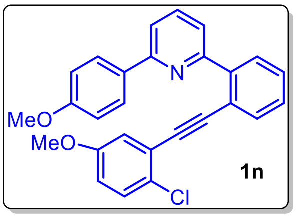
Yellowish solid, 258 mg, 80% yield; mp = 98-100 °C; ***R**$_f$* = 0.50 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (500 MHz**, **CDCl$_3$) δ** = 7.93 (d, *J* = 7.6 Hz, 1 H), 7.84 – 7.89 (m, 1 H), 7.81 (t, *J* = 7.8 Hz, 1 H), 7.73 (d, *J* = 7.2 Hz, 1 H), 7.70 (d, *J* = 7.6 Hz, 1 H), 7.46 – 7.53 (m, 1 H), 7.40 – 7.45 (m, 1 H), 7.00 (d, *J* = 8.8 Hz, 2 H), 6.58 (d, *J* = 2.3 Hz, 2 H), 6.44 – 6.48 (m, 1 H), 3.85 (s, 4 H), 3.73 (s, 6 H); **^{13}C NMR (125 MHz**, **CDCl$_3$) δ** = 160.4, 157.1, 156.2, 142.6, 136.3, 133.2, 131.9, 129.8, 128.6, 128.2, 128.1, 124.6, 121.7, 121.2, 117.8, 113.9, 109.1, 101.6, 92.4, 89.0, 55.2; **HRMS (ESI)** calcd for $C_{28}H_{24}O_3N$ $(M + H)^+$ 422.1751, found 422.1760.

2-(2-((3-chloro-4-methylphenyl)ethynyl)phenyl)-6-(4-methoxyphenyl)pyridine (**1m**):



Off white solid, 212 mg, 68% yield; mp = 136-138 °C; ***R**$_f$* = 0.55 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (500 MHz**, **CDCl$_3$) δ** = 8.07 – 8.15 (d, *J* = 8.8 Hz, 2 H), 7.91 (d, *J* = 8.0 Hz, 1 H), 7.78 – 7.85 (m, 2 H), 7.64 – 7.72 (m, 2 H), 7.45 – 7.52 (m, 1 H), 7.39 – 7.45 (m, 1 H), 7.34 – 7.39 (m, 1 H), 7.10 – 7.19 (m, 2 H), 6.97 – 7.02 (d, *J* = 8.8 Hz, 2 H), 3.87 (s, 3 H), 2.37 (s, 3 H); **^{13}C NMR (125 MHz**, **CDCl$_3$) δ** = 160.4, 157.1, 156.5, 142.5, 136.4, 136.4, 134.1, 133.3, 132.1, 131.6, 130.7, 129.9, 129.6, 128.7, 128.3, 128.1, 122.4, 121.7, 121.2, 118.1, 114.0, 91.1, 89.9, 55.3, 20.0; **HRMS (ESI)** calcd for $C_{27}H_{21}ONCl$ $(M + H)^+$ 410.1306, found 410.1317.

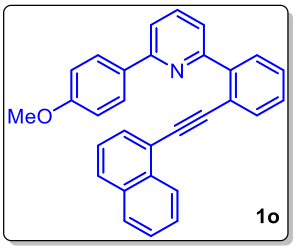
2-(2-((2-chloro-5-methoxyphenyl)ethynyl)phenyl)-6-(4-methoxyphenyl)pyridine (**1n**):



1n

Off white solid, 235 mg, 72% yield; mp = 124-126 °C; ***R_f*** = 0.45 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (400 MHz, CDCl$_3$) δ** = 8.05 – 8.22 (d, *J* = 7.9 Hz, 2 H), 7.95 (d, *J* = 7.3 Hz, 2 H), 7.72 – 7.85 (m, 2 H), 7.68 (d, *J* = 7.9 Hz, 1 H), 7.51 (t, *J* = 7.3 Hz, 1 H), 7.43 (t, *J* = 7.3 Hz, 1 H), 7.25 (s, 1 H), 6.94 – 7.03 (d, *J* = 8.5 Hz, 2 H), 6.89 (br.s., 1 H), 6.78 (d, *J* = 8.5 Hz, 1 H), 3.85 (s, 3 H), 3.67 (s, 3 H); **^{13}C NMR (100 MHz, CDCl$_3$) δ** = 160.3, 157.7, 156.8, 156.3, 142.5, 136.5, 133.7, 132.0, 129.9, 129.8, 128.9, 128.2, 128.1, 127.3, 123.7, 122.0, 120.9, 118.0, 117.5, 116.1, 113.9, 94.1, 89.3, 55.4, 55.2; **HRMS (ESI)** calcd for $C_{27}H_{21}O_2NCl$ $(M + H)^+$ 426.1255, found 426.1267.

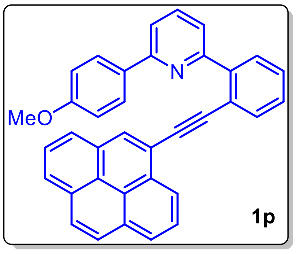
2-(4-methoxyphenyl)-6-(2-(naphthalen-1-ylethynyl)phenyl)pyridine (**1o**):



1o

Off white solid, 235 mg, 74% yield; mp = 110-112 °C; ***R_f*** = 0.60 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (500 MHz, CDCl$_3$) δ** = 8.08 - 8.20 (m, 3 H), 7.91 - 8.00 (m, 2 H), 7.77 - 7.88 (m, 4 H), 7.73 (d, *J* = 8.0 Hz, 1 H), 7.65 (d, *J* = 6.9 Hz, 1 H), 7.52 - 7.58 (m, 1 H), 7.49 (q, *J* = 7.0 Hz, 2 H), 7.42 (td, *J* = 7.6, 2.3 Hz, 2 H), 6.98 (d, *J* = 8.8 Hz, 2 H), 3.85 (s, 3 H); **^{13}C NMR (125 MHz, CDCl$_3$) δ** = 160.4, 157.4, 156.6, 142.6, 136.6, 133.4, 133.1, 133.1, 132.0, 130.3, 129.9, 128.6, 128.6, 128.3, 128.2, 128.1, 126.5, 126.3, 126.3, 125.2, 122.0, 121.6, 121.1, 118.0, 114.0, 94.2, 90.8, 55.3; **HRMS (ESI)** calcd for $C_{30}H_{22}ON$ $(M + H)^+$ 412.1696, found 412.1704.

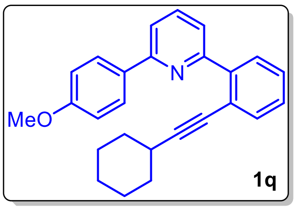
2-(4-methoxyphenyl)-6-(2-(pyren-4-ylethynyl)phenyl)pyridine (**1p**):



1p

Yellow solid, 235 mg, 63% yield; mp = 154-156 °C; R_f = 0.65 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (400 MHz, CDCl$_3$) δ** = 8.35 (d, J = 9.2 Hz, 1 H), 8.12 - 8.21 (m, 4 H), 8.04 - 8.09 (m, 3 H), 7.93 - 8.03 (m, 5 H), 7.91 (dd, J = 7.6, 1.6 Hz, 1 H), 7.85 (t, J = 7.8 Hz, 1 H), 7.77 (dd, J = 7.8, 0.9 Hz, 1 H), 7.46 - 7.59 (m, 2 H), 6.90 - 6.99 (m, 2 H), 3.82 (s, 3 H); **^{13}C NMR (100 MHz, CDCl$_3$) δ** = 160.4, 157.5, 156.7, 142.7, 136.6, 133.4, 132.1, 131.8, 131.2, 131.1, 131.0, 130.0, 129.5, 128.7, 128.4, 128.2, 128.1, 128.0, 127.2, 126.2, 125.6, 125.5, 125.4, 124.4, 124.4, 124.2, 122.1, 121.8, 118.1, 118.0, 114.0, 95.1, 91.9, 55.3; **HRMS (ESI)** calcd for $C_{36}H_{24}ON$ (M + H)$^+$ 486.1852, found 486.1863.

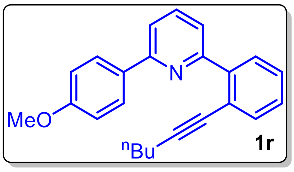
2-(2-(cyclohexylethynyl)phenyl)-6-(4-methoxyphenyl)pyridine (**1q**):



1q

Off white solid, 232 mg, 81% yield; mp = 98-100 °C; R_f = 0.65 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (500 MHz, CDCl$_3$) δ** = 8.13 - 8.05 (m, 2 H), 7.92 - 7.83 (m, 2 H), 7.75 (t, J = 7.8 Hz, 1 H), 7.65 (d, J = 8.0 Hz, 1 H), 7.55 (d, J = 7.6 Hz, 1 H), 7.44 - 7.37 (m, 1 H), 7.36 - 7.30 (m, 1 H), 7.01 (d, J = 8.8 Hz, 2 H), 3.88 (s, 3 H), 2.56 (t, J = 4.0 Hz, 1 H), 1.84 - 1.74 (m, 2 H), 1.71 - 1.62 (m, 2 H), 1.53 - 1.40 (m, 3 H), 1.30 (d, J = 7.2 Hz, 3 H); **^{13}C NMR (125 MHz, CDCl$_3$) δ** = 160.3, 157.3, 156.3, 142.2, 136.0, 133.2, 132.2, 129.8, 128.3, 128.2, 127.9, 127.7, 122.2, 122.0, 117.8, 113.9, 97.7, 80.2, 55.3, 32.3, 29.7, 25.9, 24.7; **HRMS (ESI)** calcd for $C_{26}H_{19}ONF$ (M + H)$^+$ 368.4990, found 368.4996.

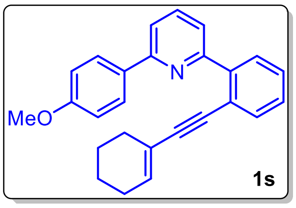
2-(2-(hex-1-yn-1-yl)phenyl)-6-(4-methoxyphenyl)pyridine (**1r**):



1r

Off white solid, 220 mg, 85% yield; mp = 54-56 °C; ***R**$_f$* = 0.70 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (500 MHz**, **CDCl$_3$) δ** = 8.11 - 8.13 (d, *J* = 8.8 Hz, 2 H), 7.86 (d, *J* = 8.0 Hz, 1 H), 7.89 (d, *J* = 8.0 Hz, 1 H), 7.76 (t, *J* = 7.6 Hz, 1 H), 7.66 (d, *J* = 8.0 Hz, 1 H), 7.57 (d, *J* = 7.6 Hz, 1 H), 7.39 - 7.46 (m, 1 H), 7.30 - 7.38 (m, 1 H), 6.99 - 7.06 (m, 2 H), 3.88 (s, 3 H), 2.38 (t, *J* = 7.1 Hz, 2 H), 1.52 (quin, *J* = 7.2 Hz, 2 H), 1.35 - 1.43 (m, 2 H), 0.90 (t, *J* = 7.2 Hz, 3 H); **^{13}C NMR (125 MHz**, **CDCl$_3$) δ** = 160.1, 157.1, 156.0, 142.0, 135.8, 133.0, 132.0, 129.5, 127.9, 127.7, 127.5, 121.9, 121.6, 117.5, 113.7, 93.5, 80.0, 55.0, 30.2, 21.6, 19.0, 13.3; **HRMS (ESI)** calcd for $C_{24}H_{24}ON$ $(M + H)^+$ 342.1852, found 342.1860.

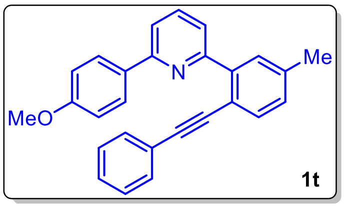
2-(2-(cyclohex-1-en-1-ylethynyl)phenyl)-6-(4-methoxyphenyl)pyridine (**1s**):



1s

Off white solid, 230 mg, 82% yield; mp = 83-85 °C; ***R**$_f$* = 0.70 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (500 MHz**, **CDCl$_3$) δ** = 8.19 – 8.04 (m, *J* = 8.7 Hz, 2 H), 7.87 (d, *J* = 7.8 Hz, 1 H), 7.90 (d, *J* = 7.6 Hz, 1 H), 7.77 (t, *J* = 7.8 Hz, 1 H), 7.65 (d, *J* = 7.8 Hz, 1 H), 7.57 (d, *J* = 7.6 Hz, 1 H), 7.42 (t, *J* = 7.2 Hz, 1 H), 7.35 (t, *J* = 7.2 Hz, 1 H), 7.10 – 6.88 (m, *J* = 8.7 Hz, 2 H), 6.09 (br. S., 1 H), 3.88 (s, 3 H), 2.21 – 1.98 (m, 4 H), 1.68 – 1.56 (m, 4 H); **^{13}C NMR (125 MHz**, **CDCl$_3$) δ** = 160.4, 157.2, 156.4, 142.1, 136.2, 135.0, 133.1, 132.3, 129.8, 128.3, 128.0, 128.0, 121.9, 120.9, 117.9, 114.0, 94.5, 86.8, 55.3, 28.8, 25.7, 22.3, 21.5; **HRMS (ESI)** calcd for $C_{26}H_{23}ON$ $(M + H)^+$ 366.1352, found 366.1355.

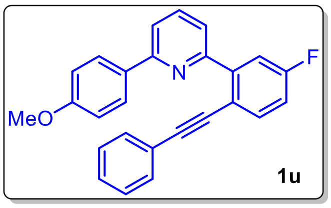
2-(4-methoxyphenyl)-6-(5-methyl-2-(phenylethynyl)phenyl)pyridine (**1t**):



1t

Off white solid, 230 mg, 80% yield; mp = 90-92 °C; ***R**$_f$* = 0.60 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (400 MHz**, **CDCl$_3$) δ** = 8.12 – 8.23 (d, *J* = 8.5 Hz, 2 H), 7.95 (d, *J* = 7.3 Hz, 1 H), 7.77 – 7.89 (m, 2 H), 7.72 (d, *J* = 7.3 Hz, 1 H), 7.66 (d, *J* = 7.9 Hz, 1 H), 7.45 (d, *J* = 3.7 Hz, 2 H), 7.32 – 7.39 (m, 3 H), 7.29 (s, 1 H), 7.01 – 7.08 (d, *J* = 8.5 Hz, 2 H), 3.90 (s, 3 H), 2.52 (s, 3 H); **^{13}C NMR (100 MHz**, **CDCl$_3$) δ** = 160.3, 157.2, 156.4, 142.3, 138.7, 136.2, 133.2, 132.1, 131.3, 130.5, 129.0, 128.3, 128.2, 127.9, 123.6, 121.9, 118.4, 118.0, 113.9, 91.7, 89.6, 55.2, 21.5; **HRMS (ESI)** calcd for $C_{27}H_{22}ON$ (M + H)$^+$ 376.1696, found 376.1702.

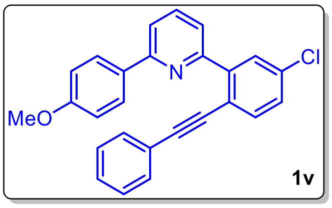
2-(5-fluoro-2-(phenylethynyl)phenyl)-6-(4-methoxyphenyl)pyridine (**1u**):



1u

Off white solid, 232 mg, 80% yield; mp = 60-62 °C; ***R**$_f$* = 0.60 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (400 MHz**, **$CDCl_3$) δ** = 8.12 (d, *J* = 8.5 Hz, 2 H), 7.98 (d, *J* = 7.3 Hz, 1 H), 7.83 (t, *J* = 7.9 Hz, 1 H), 7.63 – 7.76 (m, 3 H), 7.41 (br.s., 2 H), 7.28 – 7.36 (m, 3 H), 7.08 – 7.17 (m, 1 H), 7.01 (d, *J* = 8.5 Hz, 2 H), 3.87 (s, 3 H); **^{13}C NMR (100 MHz**, **$CDCl_3$) δ** = 163.8-161.3 (d, *J* = 249.6 Hz), 160.5, 156.6, 155.7, 144.6-144.6 (d, *J* = 7.7 Hz), 138.8, 136.5, 135.2-135.1(d, *J* = 7.7 Hz), 131.8, 131.3, 128.3, 128.2, 125.4, 123.2, 121.7, 118.5, 118.1, 117.4, 117.0-116.8 (d, *J* = 23.9 Hz), 115.6-115.4 (d, *J* = 22.3 Hz), 114.1, 92.2, 88.5, 55.3; **HRMS (ESI)** calcd for $C_{26}H_{19}ONF$ (M + H)$^+$ 380.1445, found 380.1452.

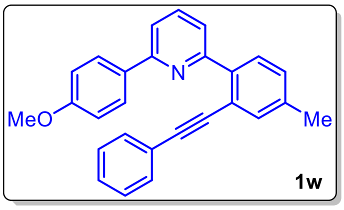
2-(5-chloro-2-(phenylethynyl)phenyl)-6-(4-methoxyphenyl)pyridine (**1v**):



1v

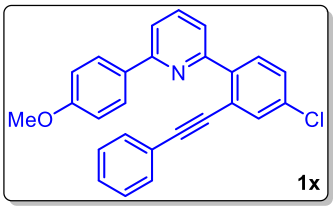
Off white solid, 250 mg, 83% yield; mp = 84-86 °C; ***R**$_f$* = 0.55 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (400 MHz**, **$CDCl_3$) δ** = 8.11 (d, *J* = 8.5 Hz, 2 H), 7.87 – 8.00 (m, 2 H), 7.82 (t, *J* = 7.9 Hz, 1 H), 7.71 (d, *J* = 7.9 Hz, 1 H), 7.58 – 7.66 (m, 1 H), 7.39 (d, *J* = 4.3 Hz, 3 H), 7.27 – 7.34 (m, 3 H), 7.01 (d, *J* = 8.5 Hz, 2 H), 3.87 (s, 3 H); **^{13}C NMR (100 MHz**, **$CDCl_3$) δ** = 160.5, 156.7, 155.7, 143.8, 138.8, 136.5, 134.5, 134.4, 131.8, 131.4, 130.0, 128.4, 128.3, 125.4, 123.1, 121.8, 119.9, 118.5, 118.1, 114.1, 114.1, 93.3, 88.5, 55.3; **HRMS (ESI)** calcd for $C_{26}H_{19}ONCl$ (M + H)$^+$ 396.1150, found 396.1159.

2-(4-methoxyphenyl)-6-(4-methyl-2-(phenylethynyl)phenyl)pyridine (**1w**):



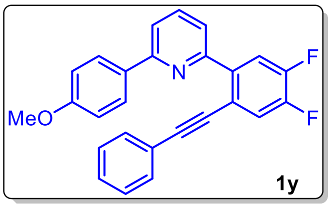
Off white solid, 206 mg, 72% yield; mp = 148-150 °C; ***R**$_f$* = 0.60 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (400 MHz**, **CDCl$_3$) δ** = 8.09 - 8.15 (m, 2 H), 7.90 (d, *J* = 7.8 Hz, 1 H), 7.85 (d, *J* = 7.8 Hz, 1 H), 7.80 (t, *J* = 7.8 Hz, 1 H), 7.67 (dd, *J* = 7.8, 0.9 Hz, 1 H), 7.54 (s, 1 H), 7.37 - 7.43 (m, 2 H), 7.28 - 7.33 (m, 4 H), 6.95 - 7.02 (m, 2 H), 3.87 (s, 3 H), 2.44 (s, 3 H); **^{13}C NMR (100 MHz**, **CDCl$_3$) δ** = 160.3, 157.1, 156.4, 139.7, 138.0, 136.3, 133.7, 132.2, 131.4, 129.9, 129.6, 128.3, 128.2, 128.1, 123.5, 121.7, 121.1, 117.8, 113.9, 92.1, 89.7, 55.3, 21.0; **HRMS (ESI)** calcd for $C_{27}H_{22}ON$ $(M + H)^+$ 376.1696, found 376.1703.

2-(4-chloro-2-(phenylethynyl)phenyl)-6-(4-methoxyphenyl)pyridine (**1x**):



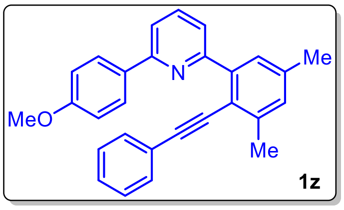
Off white solid, 226 mg, 75% yield; mp = 140-142 °C; ***R**$_f$* = 0.55 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (400 MHz**, **CDCl$_3$) δ** = 8.10 (d, *J* = 9.2 Hz, 2 H), 7.90 (d, *J* = 8.5 Hz, 2 H), 7.81 (t, *J* = 7.6 Hz, 1 H), 7.63 - 7.72 (m, 2 H), 7.46 (dd, *J* = 8.5, 1.8 Hz, 1 H), 7.36 - 7.43 (m, 2 H), 7.27 - 7.36 (m, 3 H), 7.00 (d, *J* = 8.5 Hz, 2 H), 3.87 (s, 3 H); **^{13}C NMR (100 MHz**, **CDCl$_3$) δ** = 160.5, 156.6, 156.0, 140.8, 136.4, 133.9, 132.7, 131.9, 131.5, 131.3, 128.8, 128.5, 128.3, 128.3, 122.9, 121.6, 118.2, 114.0, 93.5, 88.2, 55.3; **HRMS (ESI)** calcd for $C_{26}H_{19}ONCl$ $(M + H)^+$ 396.1150, found 396.1159.

2-(4,5-difluoro-2-(phenylethynyl)phenyl)-6-(4-methoxyphenyl)pyridine (**1y**):



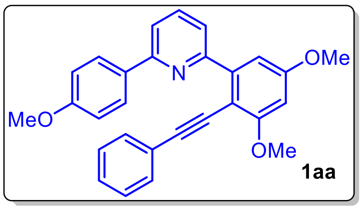
Off white solid, 240 mg, 79% yield; mp = 100-102 °C; ***R**$_f$* = 0.55 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (400 MHz, CDCl$_3$) δ** = 8.09 (d, *J* = 8.5 Hz, 2 H), 7.95 (d, *J* = 7.9 Hz, 1 H), 7.78 - 7.88 (m, 2 H), 7.71 (d, *J* = 7.9 Hz, 1 H), 7.48 (dd, *J* = 10.4, 7.9 Hz, 1 H), 7.37 - 7.43 (m, 2 H), 7.33 (br.s., 3 H), 7.01 (d, *J* = 8.5 Hz, 2 H), 3.88 (s, 3 H); **^{13}C NMR (100 MHz, CDCl$_3$) δ** = 160.6, 156.7, 155.0, 151.8 - 149.1 (dd, *J* = 252.0 Hz, 13.1 Hz), 151.2 - 148.5 (dd, *J* = 250.5 Hz, 13.1 Hz), 139.8, 139.7, 138.9, 136.6, 131.7, 131.4, 128.6, 128.4, 128.3, 128.3, 125.4, 122.8, 121.7 - 121.5 (d, *J* = 18.5 Hz), 121.6, 119.1 - 119.0 (d, *J* = 18.5 Hz), 118.5, 118.1, 117.9, 114.1, 93.0, 87.5, 55.3; **HRMS (ESI)** calcd for $C_{26}H_{18}ONF_2$ $(M + H)^+$ 398.1351, found 398.1358.

2-(3,5-dimethyl-2-(phenylethynyl)phenyl)-6-(4-methoxyphenyl)pyridine (**1z**):



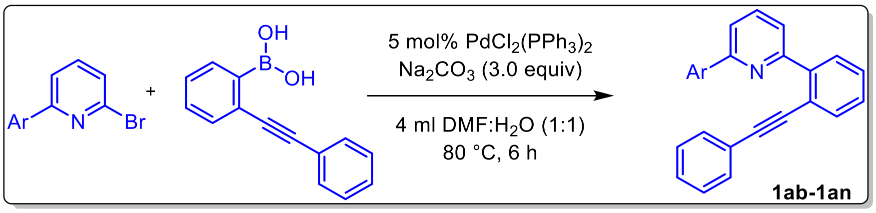
Off white solid, 245 mg, 82% yield; mp = 86-88 °C; ***R**$_f$* = 0.60 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (500 MHz, CDCl$_3$) δ** = 8.07 - 8.17 (d, *J* = 8.8 Hz, 2 H), 7.76 - 7.87 (m, 2 H), 7.68 (d, *J* = 7.2 Hz, 1 H), 7.52 (s, 1 H), 7.34 - 7.41 (m, 2 H), 7.27 - 7.32 (m, 3 H), 7.17 (s, 1 H), 6.95 - 7.03 (d, *J* = 8.8 Hz, 2 H), 3.87 (s, 3 H), 2.62 (s, 3 H), 2.44 (s, 3 H); **^{13}C NMR (125 MHz, CDCl$_3$) δ** = 160.3, 158.0, 156.4, 142.8, 141.0, 138.1, 136.1, 132.3, 131.2, 130.3, 128.4, 128.2, 128.0, 127.8, 123.9, 122.1, 118.4, 117.9, 113.9, 96.4, 88.2, 55.3, 21.5, 21.3; **HRMS (ESI)** calcd for $C_{28}H_{24}ON$ $(M + H)^+$ 390.1852, found 390.1861.

2-(3,5-dimethoxy-2-(phenylethynyl)phenyl)-6-(4-methoxyphenyl)pyridine (**1aa**):

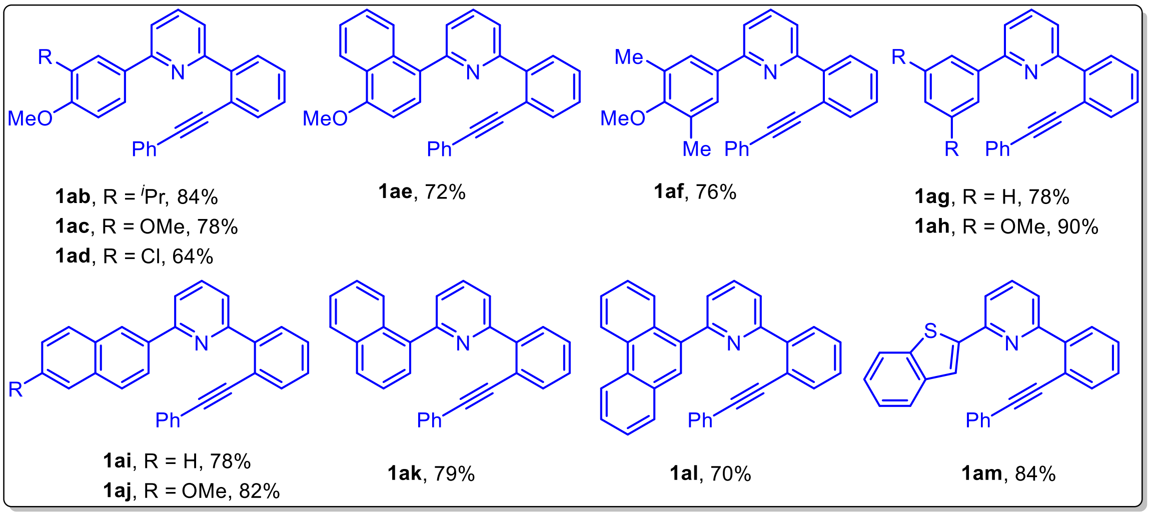


Yellow solid, 258 mg, 80% yield; mp = 102-104 °C; ***R**$_f$* = 0.45 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (500 MHz, CDCl$_3$) δ** = 8.08 - 8.16 (m, 2 H), 7.93 (d, *J* = 7.6 Hz, 1 H), 7.81 (t, *J* = 7.6 Hz, 1 H), 7.70 (d, *J* = 6.9 Hz, 1 H), 7.38 - 7.45 (m, 2 H), 7.25 - 7.33 (m, 3 H), 7.10 (d, *J* = 2.3 Hz, 1 H), 6.96 - 7.03 (m, 2 H), 6.59 (d, *J* = 2.3 Hz, 1 H), 3.97 (s, 3 H), 3.92 (s, 3 H), 3.86 (s, 3 H); **^{13}C NMR (125 MHz, CDCl$_3$) δ** = 161.7, 160.5, 160.3, 157.0, 156.3, 145.3, 136.1, 131.9, 131.1, 128.2, 128.0, 127.5, 124.0, 122.2, 118.2, 113.9, 106.3, 103.8, 98.4, 95.6, 85.5, 56.1, 55.4, 55.2; **HRMS (ESI)** calcd for $C_{28}H_{24}O_3N$ $(M + H)^+$ 422.1751, found 422.1756.

2.5.4 Synthesis of 2-aryl (phenylethynyl)phenyl)pyridines



Representative procedure for Suzuki cross-coupling reaction:[1] In a sealed tube, 2-bromo-6-(3-isopropyl-4-methoxyphenyl)pyridine (200 mg, 0.65 mmol, 1.0 equiv) and aryl boronic acid (**S_{28}**) (174 mg, 1.2 equiv) in DMF/H_2O 1:1 (4 mL) was degassed with nitrogen for 5 min. Next, Na_2CO_3 (204 mg, 3 equiv) and $PdCl_2(PPh_3)_2$ (22.8 mg, 5 mol%) were added under nitrogen atmosphere. The reaction mixture was stirred at 80 °C for 6 h. After complete consumption of starting material, as monitored by TLC, the resulting mixture was allowed to bring to room temperature.



1ab, R = ^{i}Pr, 84%
1ac, R = OMe, 78%
1ad, R = Cl, 64%

1ae, 72%

1af, 76%

1ag, R = H, 78%
1ah, R = OMe, 90%

1ai, R = H, 78%
1aj, R = OMe, 82%

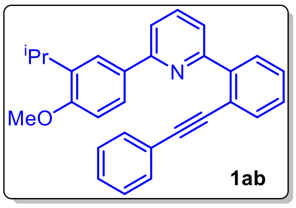
1ak, 79%

1al, 70%

1am, 84%

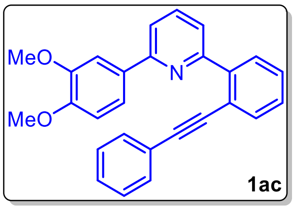
The reaction mixture was diluted with $NaHCO_3$ (5 mL) and then the product was extracted with ethyl acetate (3 × 5 mL). The combined organic layer was dried over Na_2SO_4 and the organic solvent was removed under vacuo. The crude product was purified on a silica gel column using petroleum ether/ethyl acetate as eluent to afford 2-(3-isopropyl-4-methoxyphenyl)-6-(2-(phenylethynyl)phenyl) pyridine (**1ab**) in 84% yield.

2-(3-isopropyl-4-methoxyphenyl)-6-(2-(phenylethynyl)phenyl)pyridine (**1ab**):



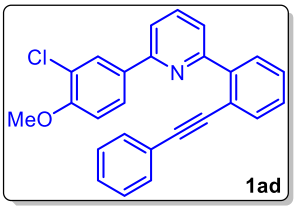
Off white solid, 205 mg, 84% yield; mp = 142-144 °C; ***R*$_f$** = 0.60 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (400 MHz, CDCl$_3$) δ** = 7.92 - 8.03 (m, 3 H), 7.86 - 7.92 (m, 1 H), 7.82 (t, *J* = 7.6 Hz, 1 H), 7.70 (d, *J* = 7.3 Hz, 2 H), 7.45 - 7.53 (m, 1 H), 7.33 - 7.45 (m, 3 H), 7.27 - 7.32 (m, 3 H), 6.93 (d, *J* = 8.5 Hz, 1 H), 3.89 (s, 3 H), 3.36 (dt, *J* = 13.9, 6.8 Hz, 1 H), 1.27 (d, *J* = 6.7 Hz, 6 H); **^{13}C NMR (100 MHz, CDCl$_3$) δ** = 157.8, 157.1, 157.1, 142.6, 137.0, 136.2, 133.2, 132.0, 131.4, 130.0, 128.5, 128.2, 128.1, 128.0, 125.6, 125.0, 123.5, 121.7, 121.4, 118.2, 110.4, 92.4, 89.5, 55.5, 27.2, 22.6; **HRMS (ESI)** calcd for $C_{29}H_{26}ON$ $(M + H)^+$ 404.2009, found 404.2019.

2-(3,4-dimethoxyphenyl)-6-(2-(phenylethynyl)phenyl)pyridine (**1ac**):



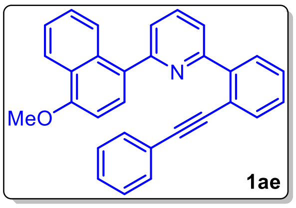
Yellowish solid, 185 mg, 78% yield; mp = 98-100 °C; ***R*$_f$** = 0.55 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (500 MHz, CDCl$_3$) δ** = 7.90 (d, *J* = 7.6 Hz, 1 H), 7.83 - 7.88 (m, 2 H), 7.81 (t, *J* = 7.8 Hz, 1 H), 7.67 - 7.75 (m, 2 H), 7.65 (dd, *J* = 8.4, 1.9 Hz, 1 H), 7.49 (t, *J* = 7.1 Hz, 1 H), 7.40 - 7.44 (m, 1 H), 7.34 - 7.40 (m, 2 H), 7.26 - 7.31 (m, 3 H), 6.94 (d, *J* = 8.4 Hz, 1 H), 3.93 (s, 3 H), 3.88 (s, 3 H); **^{13}C NMR (125 MHz, CDCl$_3$) δ** = 157.1, 156.3, 149.8, 149.0, 142.4, 136.3, 133.2, 132.4, 131.3, 129.7, 128.4, 128.2, 128.1, 128.0, 123.3, 121.8, 121.4, 119.4, 118.1, 110.9, 110.1, 92.3, 89.4, 55.8, 55.6; **HRMS (ESI)** calcd for $C_{27}H_{22}ON$ $(M + H)^+$ 392.1645, found 392.1654.

2-(3-chloro-4-methoxyphenyl)-6-(2-(phenylethynyl)phenyl)pyridine (**1ad**):



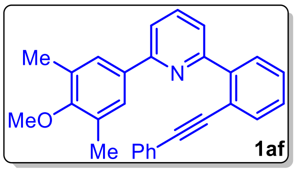
Off white solid, 152 mg, 64% yield; mp = 130-132 °C; $\boldsymbol{R_f}$ = 0.55 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (500 MHz, CDCl$_3$) δ** = 8.24 (d, *J* = 2.3 Hz, 1 H), 8.03 (dd, *J* = 8.6, 2.1 Hz, 1 H), 7.93 (d, *J* = 8.0 Hz, 2 H), 7.82 (t, *J* = 7.8 Hz, 1 H), 7.73 (d, *J* = 7.6 Hz, 1 H), 7.66 (d, *J* = 8.0 Hz, 1 H), 7.48 - 7.54 (m, 1 H), 7.37 - 7.47 (m, 3 H), 7.27 - 7.36 (m, 3 H), 6.97 (d, *J* = 8.8 Hz, 1 H), 3.94(s, 3 H); **^{13}C NMR (125 MHz, CDCl$_3$) δ** = 157.3, 155.5, 155.1, 142.1, 136.4, 133.3, 132.9, 131.4, 129.8, 128.7, 128.6, 128.2, 128.1, 126.3, 123.3, 122.7, 122.3, 121.4, 118.0, 111.8, 92.5, 89.3, 56.1; **HRMS (ESI)** calcd for $C_{26}H_{19}ONCl$ $(M + H)^+$ 396.1150, found 396.1149.

2-(4-methoxynaphthalen-1-yl)-6-(2-(phenylethynyl)phenyl)pyridine (**1ae**):



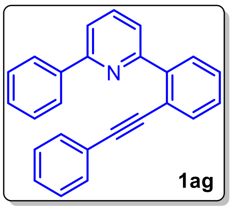
Off white solid, 178 mg, 72% yield; mp = 120-122 °C; $\boldsymbol{R_f}$ = 0.65 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (500 MHz, CDCl$_3$) δ** = 8.41 (d, *J* = 8.0 Hz, 1 H), 8.32 (d, *J* = 8.4 Hz, 1 H), 8.07 (d, *J* = 7.6 Hz, 1 H), 7.97 (d, *J* = 7.6 Hz, 1 H), 7.91 (t, *J* = 7.8 Hz, 1 H), 7.74 (d, *J* = 7.2 Hz, 1 H), 7.69 (d, *J* = 7.6 Hz, 1 H), 7.59 (d, *J* = 7.6 Hz, 1 H), 7.45 - 7.56 (m, 5 H), 7.38 - 7.45 (m, 1 H), 7.28 - 7.37 (m, 3 H), 6.90 (d, *J* = 7.6 Hz, 1 H), 4.05 (s, 3 H); **^{13}C NMR (125 MHz, CDCl$_3$) δ** = 158.9, 157.3, 155.8, 142.4, 135.9, 133.1, 132.1, 131.4, 131.2, 129.9, 128.6, 128.3, 128.2, 128.1, 128.1, 126.8, 125.7, 125.5, 125.1, 123.5, 123.4, 122.1, 122.0, 121.3, 103.3, 92.6, 89.4, 55.5; **HRMS (ESI)** calcd for $C_{30}H_{22}ON$ $(M + H)^+$ 412.1696, found 412.1698.

2-(4-methoxy-3,5-dimethylphenyl)-6-(2-(phenylethynyl)phenyl)pyridine (**1af**):



Off white solid, 178 mg, 76% yield; mp = 122-124 °C; $\boldsymbol{R_f}$ = 0.60 (petroleum ether/ethyl acetate = 90/10); **^{1}H NMR (500 MHz, CDCl$_3$) δ** = 7.91 (d, *J* = 7.6 Hz, 1 H), 7.86 - 7.89 (m, 1 H), 7.82 (t, *J* = 7.8 Hz, 1 H), 7.79 (s, 2 H), 7.65 - 7.74 (m, 2 H), 7.45 - 7.52 (m, 1 H), 7.36 - 7.45 (m, 3 H), 7.24 - 7.34 (m, 3 H), 3.76 (s, 3 H), 2.33 (s, 7 H); **^{13}C NMR (125 MHz, CDCl$_3$) δ** = 157.9, 157.3, 156.8, 142.5, 136.3, 135.0, 133.3, 131.4, 131.0, 129.9, 128.6, 128.2, 128.1, 127.6, 123.5, 122.0, 121.5, 118.6, 92.4, 89.5, 59.7, 16.2; **HRMS (ESI)** calcd for $C_{28}H_{24}ON$ $(M + H)^+$ 390.1852, found 390.1853.

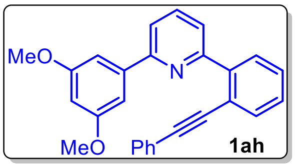
2-phenyl-6-(2-(phenylethynyl)phenyl)pyridine (**1ag**):



1ag

Orange thick liquid, 218 mg, 78% yield; $\boldsymbol{R_f}$ = 0.50 (petroleum ether/EtOAc = 97/03); **^{1}H NMR (500 MHz,CDCl$_3$) δ** = 8.16 (d, *J* = 7.2 Hz, 2 H), 7.96 (t, *J* = 8.6 Hz, 2 H), 7.86 (t, *J* = 7.8 Hz, 1 H), 7.76 (d, *J* = 8.0 Hz, 1 H), 7.72 (d, *J* = 7.2 Hz, 1 H), 7.51 - 7.45 (m, 3 H), 7.41 (d, *J* = 3.4 Hz, 2 H), 7.43 (d, *J* = 5.0 Hz, 2 H), 7.34 - 7.28 (m, 3 H); **^{13}C NMR (125 MHz,CDCl$_3$) δ** = 157.3, 156.9, 142.3, 139.5, 136.4, 133.3, 131.4, 129.9, 128.8, 128.6, 128.6, 128.2, 128.2, 128.2, 127.1, 123.4, 122.5, 121.4, 118.8, 92.5, 89.4; **HRMS (ESI)** calcd for $C_{25}H_{18}N$ $(M + H)^+$ 332.1434, found 332.1434.

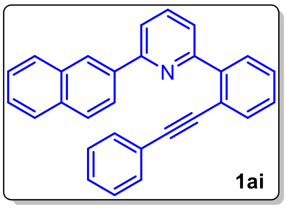
2-(3, 5-dimethoxyphenyl)-6-(2-(phenylethynyl)phenyl)pyridine (**1ah**):



1ah

Off white solid, 238 mg, 90% yield; mp = 145-147 °C; $\boldsymbol{R_f}$ = 0.30 (petroleum ether/EtOAc = 95/05); **^{1}H NMR (400 MHz,CDCl$_3$) δ** = 8.01 - 7.93 (m, 1 H), 7.91 (d, *J* = 7.9 Hz, 1 H), 7.86 (t, *J* = 7.9 Hz, 1 H), 7.72 (t, *J* = 7.3 Hz, 2 H), 7.48 (d, *J* = 6.7 Hz, 1 H), 7.45 - 7.40 (m, 1 H), 7.40 - 7.35 (m, 2 H), 7.34 - 7.27 (m, 5 H), 6.58 - 6.48 (m, 1 H), 3.83 (s, 6 H); **^{13}C NMR (100 MHz,CDCl$_3$) δ** = 161.0, 157.3, 156.5, 142.3, 141.7, 136.5, 133.2, 131.4, 129.9, 128.6, 128.3, 128.2, 123.3, 122.8, 121.5, 119.0, 105.2, 101.2, 92.4, 89.4, 55.4; **HRMS (ESI)** calcd for $C_{27}H_{22}O_2N^+$ $(M + H)^+$ 392.1648, found 392.1645.

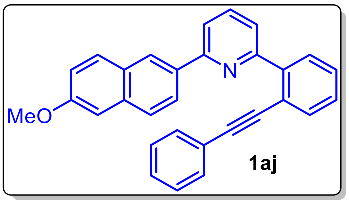
2-(naphthalen-2-yl)-6-(2-(phenylethynyl)phenyl)pyridine (**1ai**):



1ai

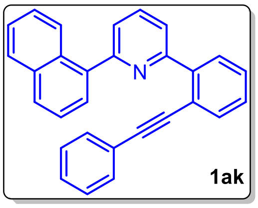
Orange thick liquid, 165 mg, 78% yield; ***R*** R_f = 0.50 (petroleum ether/EtOAc = 97/03); **^{1}H NMR (500 MHz,CDCl$_3$) δ** = 8.65 (s, 1 H), 8.40 - 8.29 (m, 1 H), 8.05 - 7.98 (m, 2 H), 7.95 (d, *J* = 8.8 Hz, 1 H), 7.93 - 7.86 (m, 4 H), 7.77 (d, *J* = 7.6 Hz, 1 H), 7.56 - 7.49 (m, 3 H), 7.49 - 7.41 (m, 3 H), 7.36 - 7.27 (m, 3 H); **^{13}C NMR (125 MHz,CDCl$_3$) δ** = 157.5, 156.7, 142.3, 136.8, 136.5, 133.6, 133.5, 133.3, 131.4, 130.0, 128.7, 128.6, 128.3, 128.2, 128.2, 128.1, 127.6, 126.4, 126.3, 126.1, 124.8, 123.4, 122.6, 121.4, 119.1, 92.6, 89.5; **HRMS (ESI)** calcd for $C_{29}H_{19}N$ $(M + H)^+$ 382.1519, found 382.1523.

2-(6-methoxynaphthalen-2-yl)-6-(2-(phenylethynyl)phenyl)pyridine (**1aj**):



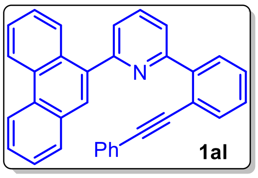
Off white solid, 214 mg, 82% yield; mp = 150-152 °C; R_f = 0.50(petroleum ether/EtOAc = 95/05); **^{1}H NMR (500 MHz,CDCl$_3$) δ** = 8.60 - 8.48 (m, 1 H), 8.25 (dd, *J* = 1.7, 8.6 Hz, 1 H), 7.98 - 7.94 (m, 1 H), 7.94 - 7.89 (m, 1 H), 7.88 - 7.83 (m, 2 H), 7.80 (d, *J* = 8.4 Hz, 1 H), 7.76 (d, *J* = 8.4 Hz, 1 H), 7.73 - 7.67 (m, 1 H), 7.49 (dt, *J* = 1.3, 7.5 Hz, 1 H), 7.42 (dd, *J* = 1.3, 7.4 Hz, 1 H), 7.40 - 7.37 (m, 2 H), 7.28 - 7.24 (m, 3 H), 7.17 - 7.12 (m, 2 H), 3.93 (s, 3 H); **^{13}C NMR (125 MHz,CDCl$_3$) δ** = 158.2, 157.5, 156.9, 142.5, 136.4, 134.9, 134.8, 133.4, 131.5, 130.3, 130.0, 129.0, 128.6, 128.3, 128.2, 127.1, 126.3, 125.3, 123.5, 122.3, 121.5, 119.0, 118.8, 105.7, 92.6, 89.5, 55.3; **HRMS (ESI)** calcd for $C_{30}H_{22}ON^+$ $(M + H)^+$ 412.1693, found 412.1696.

2-(naphthalen-1-yl)-6-(2-(phenylethynyl)phenyl)pyridine (**1ak**):



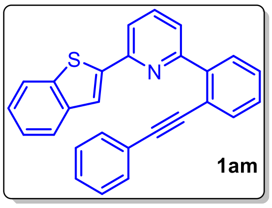
Orange thick liquid, 167 mg, 79% yield; R_f = 0.50 (petroleum ether/EtOAc = 97/03); **^{1}H NMR (500 MHz,CDCl$_3$) δ** = 8.24 (d, *J* = 8.4 Hz, 2 H), 7.97 (t, *J* = 6.9 Hz, 2 H), 7.90 - 7.84 (m, 1 H), 7.83 - 7.78 (m, 1 H), 7.74 - 7.69 (m, 3 H), 7.67 (d, *J* = 7.2 Hz, 2 H), 7.50 - 7.46 (m, 2 H), 7.42 - 7.36 (m, 3 H), 7.34 - 7.28 (m, 3 H); **^{13}C NMR (125 MHz,CDCl$_3$) δ** = 157.4, 156.4, 142.3, 141.6, 140.7, 138.4, 136.5, 133.3, 131.4, 130.0, 128.8, 128.6, 128.3, 128.2, 128.2, 127.5, 127.4, 127.1, 123.4, 122.6, 121.4, 118.7, 92.5, 89.4; **HRMS (ESI)** calcd for $C_{29}H_{19}N$ $(M + H)^+$ 382.1519, found 382.1520.

2-(phenanthren-9-yl)-6-(2-(phenylethynyl)phenyl)pyridine (**1al**):



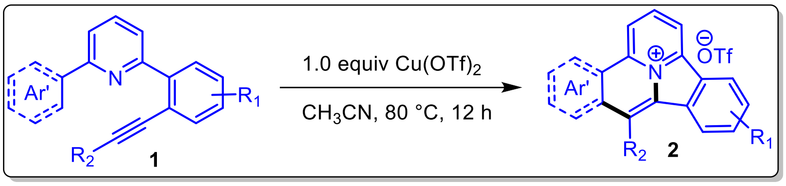
Off white solid, 180 mg, 70% yield; mp = 112-114 °C; ***R****f* = 0.50 (petroleum ether/EtOAc = 97/03); **^{1}H NMR (500 MHz,CDCl$_3$) δ** =8.78 (d, *J* = 8.0 Hz, 1 H), 8.73 (d, *J* = 8.4 Hz, 1 H), 8.21 (d, *J* = 8.0 Hz, 1 H), 8.09 (d, *J* = 7.6 Hz, 1 H), 7.99 - 7.94 (m, 2 H), 7.94 - 7.90 (m, 1 H), 7.83 (d, *J* = 8.0 Hz, 1 H), 7.73 - 7.66 (m, 3 H), 7.66 - 7.62 (m, 1 H), 7.62 - 7.57 (m, 1 H), 7.55 - 7.50 (m, 1 H), 7.49 - 7.43 (m, 3 H), 7.43 - 7.38 (m, 1 H), 7.35 - 7.29 (m, 3 H); **^{13}C NMR (125 MHz,CDCl$_3$) δ** = 159.0, 157.6, 142.3, 137.4, 136.1, 133.2, 131.5, 130.8, 130.5, 130.4, 130.0, 129.0, 128.7, 128.7, 128.4, 128.3, 128.2, 126.9, 126.7, 126.6, 126.5, 123.6, 123.4, 122.9, 122.7, 122.5, 121.5, 92.7, 89.4; **HRMS (ESI)** calcd for $C_{33}H_{21}N^+$ $(M + H)^+$ 432.1750, found 432.1756.

2-(benzo[*b*]thiophen-2-yl)-6-(2-(phenylethynyl)phenyl)pyridine (**1am**):



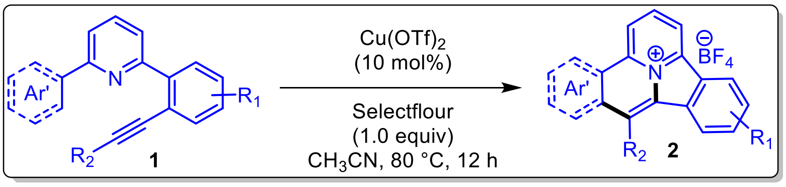
Off white solid, 223 mg, 84% yield; mp = 115-117 °C; ***R****f* = 0.50(petroleum ether/EtOAc = 95/05); **^{1}H NMR (500 MHz,CDCl$_3$) δ** = 8.00 (d, *J* = 8.0 Hz, 1 H), 8.03 (d, *J* = 7.6 Hz, 1 H), 7.94 (s, 1 H), 7.86 (d, *J* = 8.4 Hz, 1 H), 7.84 – 7.76 (m, 3 H), 7.71 (d, *J* = 7.6 Hz, 1 H), 7.55 – 7.50 (m, 1 H), 7.46 – 7.40 (m, 3 H), 7.38 – 7.34 (m, 2 H), 7.33 – 7.28 (m, 3 H); **^{13}C NMR (125 MHz,CDCl$_3$) δ** = 157.3, 152.2, 145.2, 141.6, 140.8, 140.5, 136.3, 133.3, 131.4, 130.1, 128.7, 128.4, 128.3, 128.2, 124.9, 124.5, 124.4, 124.2, 124.1, 123.4, 123.2, 122.5, 121.3, 121.1, 118.0, 92.8, 89.3; **HRMS (ESI)** calcd for $C_{27}H_{18}SN^+$ $(M + H)^+$388.1154, found 388.1154.

2.5.5 Copper-promoted intramolecular formal [4+2] annulation of alkynes with azadiene



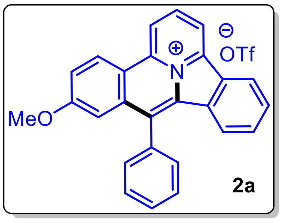
Representative procedure: To a screw-cap vial containing a stir bar were added 2-(4-methoxyphenyl)-6-(2-(phenylethynyl)phenyl)pyridine (**1a**) (50 mg, 0.13 mmol, 1.0 equiv), Cu(Otf)$_2$ (50 mg, 1.0 equiv) and CH_3CN (4 mL). The reaction vial was fitted with a cap, evacuated and back filled with N_2 and heated at 80 °C for 12 h. When the reaction time was completed, the reaction mixture was allowed to cool at ambient temperature. The mixture was diluted with CH_2Cl_2 (10 mL) and the combined mixture was concentrated in vacuo and the resulting residue was purified by column chromatography on silica (CH_2Cl_2/MeOH; 95:05) to afford the product **2a** in 78% yield.

General procedure for catalytic formal [4+2] annulation reaction



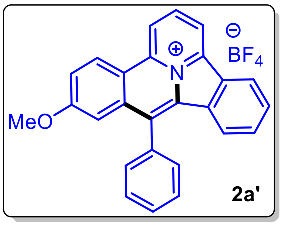
Representative procedure: To a screw-cap vial containing a stir bar were added 2-(4-methoxyphenyl)-6-(2-(phenylethynyl)phenyl)pyridine (**1a**) (50 mg, 0.13 mmol, 1.0 equiv), Cu(OTf)$_2$ (5.0 mg, 10 mol%), Selectfluor (49 mg, 1.0 equiv.) and CH_3CN (4 mL). The reaction vial was fitted with a cap, evacuated and back filled with N_2 and heated at 80 °C for 12 h. When the reaction time was completed, the reaction mixture was allowed to cool at ambient temperature. The mixture was diluted with CH_2Cl_2 (10 mL) and the combined mixture was concentrated in vacuo and the resulting residue was purified by column chromatography on silica (CH_2Cl_2/MeOH; 95:05) to afford the product **2a'** in 75% yield.

6-methoxy-8-phenylbenzo[1,2]indolizino[5,4,3-*ab*]isoquinolin-13-ium trifluoromethanesulfonate (**2a**):



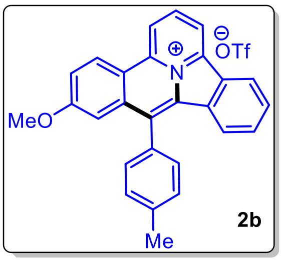
Off white solid, 52 mg, 78% yield; mp = 312-314 °C; ***R**_f_* = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.79 (d, *J* = 8.8 Hz, 1 H), 9.55 (d, *J* = 9.2 Hz, 1 H), 9.34 (d, *J* = 7.6 Hz, 1 H), 9.07 (t, *J* = 8.2 Hz, 1 H), 8.86 (d, *J* = 7.6 Hz, 1 H), 8.02 - 7.92 (m, 2 H), 7.88 (br. s., 3 H), 7.75 (t, *J* = 7.6 Hz, 1 H), 7.70 (d, *J* = 3.4 Hz, 2 H), 7.24 - 7.14 (m, 1 H), 6.88 (d, *J* = 8.0 Hz, 1 H), 3.91 (s, 3 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 163.0, 141.1, 138.9, 138.2, 134.9, 134.4, 132.5, 132.1, 132.0, 131.0, 130.5, 130.3, 130.0, 129.3, 128.4, 123.4, 123.2, 121.3, 120.7, 118.7, 118.1, 108.2, 56.0; **^{19}F NMR** (**376.5 MHz, DMSO-d$_6$)δ** = 77.75; **HRMS (ESI)** calcd for $C_{26}H_{18}ON^+$ (M - OTf)$^+$ 360.1381, found 360.1383.

6-methoxy-8-phenylbenzo[1,2]indolizino[5,4,3-*ab*]isoquinolin-13-ium tetrafluoroborate (2a'):



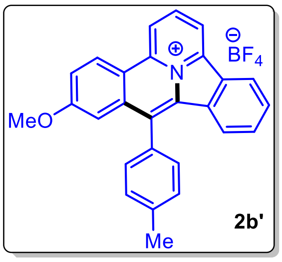
Off white solid, 44 mg, 75% yield; mp = 240-242 °C; ***R**_f_* = 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (400 MHz,DMSO-d$_6$) δ** = 9.79 (d, *J* = 8.5 Hz, 1 H), 9.55 (d, *J* = 9.2 Hz, 1 H), 9.34 (d, *J* = 7.3 Hz, 1 H), 9.07 (t, *J* = 7.9 Hz, 1 H), 8.86 (d, *J* = 7.9 Hz, 1 H), 8.04 - 7.91 (m, 2 H), 7.91 - 7.82 (m, 3 H), 7.75 (t, *J* = 7.6 Hz, 1 H), 7.70 (d, *J* = 3.1 Hz, 2 H), 7.29 - 7.10 (m, 1 H), 6.88 (d, *J* = 7.9 Hz, 1 H), 3.91 (s, 3 H); **^{13}C NMR (100 MHz,DMSO-d$_6$) δ** = 163.0, 141.1, 138.9, 138.2, 134.9, 134.4, 132.5, 132.1, 132.0, 131.0, 130.4, 130.3, 130.0, 129.3, 128.4, 123.4, 123.2, 121.3, 120.7, 118.7, 118.1, 108.2, 56.0; **^{19}F NMR** (**376.5 MHz, DMSO-d$_6$)δ** = -148.26; **HRMS (ESI)** calcd for $C_{25}H_{16}ON^+$ (M - BF_4)$^+$ 360.1383, found 360.1380.

6-methoxy-8-(*p*-tolyl)benzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate(**2b**):



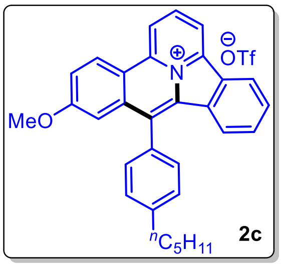
Off white solid, 52 mg, 76% yield; mp = 278-280 °C; ***R*$_f$** = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (400 MHz**, **DMSO-d$_6$) δ** = 9.78 (d, *J* = 8.5 Hz, 1 H), 9.55 (d, *J* = 9.2 Hz, 1 H), 9.33 (d, *J* = 7.3 Hz, 1 H), 9.06 (t, *J* = 7.9 Hz, 1 H), 8.86 (d, *J* = 7.3 Hz, 1 H), 8.02 - 7.89 (m, 2 H), 7.78 (t, *J* = 7.3 Hz, 1 H), 7.72 - 7.63 (m, *J* = 7.3 Hz, 2 H), 7.62 - 7.48 (m, *J* = 7.3 Hz, 2 H), 7.23 (s, 1 H), 6.97 (d, *J* = 7.9 Hz, 1 H), 3.91 (s, 3 H), 2.61 (s, 3 H); **^{13}C NMR (100 MHz**, **DMSO-d$_6$) δ** = 163.0, 141.0, 140.0, 138.8, 138.1, 135.1, 134.6, 132.5, 132.0, 131.0, 130.6, 130.4, 130.3, 129.2, 129.1, 128.4, 123.4, 123.3, 121.2, 120.6, 118.7, 118.0, 108.3, 56.1, 21.2; **HRMS (ESI)** calcd for $C_{27}H_{20}ON^+$ (M - OTf)$^+$ 374.1515, found 374.1537

6-methoxy-8-(*p*-tolyl)benzo[1,2]indolizino[5,4,3-*ab*]isoquinolin-13-ium tetrafluoroborate (2b'):



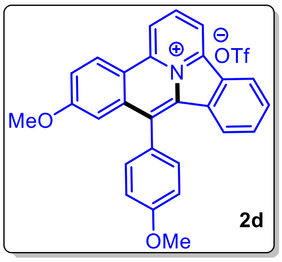
Off white solid, 37 mg, 63% yield; mp = 230-232 °C; ***R*$_f$** = 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (400 MHz**,**DMSO-d$_6$) δ** = 9.77 (d, *J* = 8.5 Hz, 1 H), 9.54 (d, *J* = 9.2 Hz, 1 H), 9.33 (d, *J* = 7.3 Hz, 1 H), 9.14 - 8.98 (m, 1 H), 8.86 (d, *J* = 7.9 Hz, 1 H), 8.05 - 7.85 (m, 2 H), 7.77 (t, *J* = 7.6 Hz, 1 H), 7.68 (d, *J* = 7.9 Hz, 2 H), 7.63 - 7.51 (m, 2 H), 7.23 (d, *J* = 2.4 Hz, 1 H), 6.97 (d, *J* = 7.9 Hz, 1 H), 3.91 (s, 3 H), 2.61 (s, 3 H); **^{13}C NMR (100 MHz**,**DMSO-d$_6$) δ** = 163.0, 141.0, 140.0, 138.8, 138.1, 135.1, 134.6, 132.5, 132.0, 131.0, 130.6, 130.4, 130.3, 129.2, 129.1, 128.4, 123.4, 123.3, 121.2, 120.6, 118.7, 118.0, 108.3, 56.1, 21.2; **HRMS (ESI)** calcd for $C_{25}H_{16}ON^+$ (M - BF_4)$^+$ 374.1539, found 374.1537.

6-methoxy-8-(4-pentylphenyl)benzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (2c):



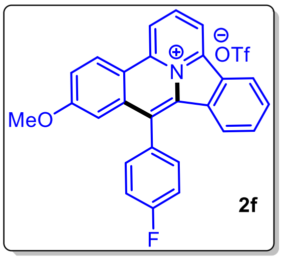
Off white solid, 50 mg, 74% yield; mp = 220-222 °C; ***R*** R_f = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.78 (d, *J* = 8.8 Hz, 1 H), 9.55 (d, *J* = 9.2 Hz, 1 H), 9.33 (d, *J* = 7.6 Hz, 1 H), 9.06 (t, *J* = 8.0 Hz, 1 H), 8.86 (d, *J* = 7.6 Hz, 1 H), 8.01 - 7.90 (m, 2 H), 7.73 (t, *J* = 7.6 Hz, 1 H), 7.71 - 7.66 (m, *J* = 7.6 Hz, 2 H), 7.63 - 7.52 (m, *J* = 8.0 Hz, 2 H), 7.22 (d, *J* = 1.9 Hz, 1 H), 6.91 (d, *J* = 8.0 Hz, 1 H), 3.91 (s, 3 H), 2.87 (t, *J* = 7.4 Hz, 2 H), 1.80 (t, *J* = 6.9 Hz, 2 H), 1.47 - 1.37 (m, 4 H), 0.94 (t, *J* = 6.5 Hz, 3 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 163.0, 144.8, 141.0, 138.8, 138.2, 135.1, 134.6, 132.5, 131.9, 131.0, 130.4, 130.3, 129.9, 129.4, 129.2, 128.5, 123.4, 123.2, 121.2, 120.7, 118.7, 118.1, 108.4, 56.0, 35.0, 30.9, 30.3, 22.0, 14.0; **HRMS (ESI)** calcd for $C_{31}H_{28}ON^+$ (M - OTf)$^+$ 430.2165, found 430.2165.

6-methoxy-8-(4-methoxyphenyl)benzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (2d):



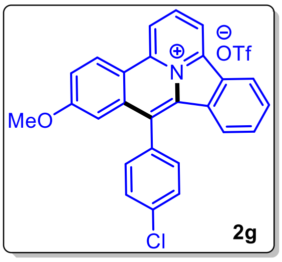
Off white solid, 33 mg, 48% yield; mp = 218-220 °C; R_f = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.77 (d, *J* = 8.5 Hz, 1 H), 9.53 (d, *J* = 9.3 Hz, 1 H), 9.32 (d, *J* = 7.6 Hz, 1 H), 9.05 (t, *J* = 8.2 Hz, 1 H), 8.86 (d, *J* = 7.8 Hz, 1 H), 8.02 - 7.91 (m, 2 H), 7.82 - 7.75 (m, 1 H), 7.67 - 7.59 (m, 2 H), 7.47 - 7.39 (m, *J* = 8.7 Hz, 2 H), 7.27 (d, *J* = 2.6 Hz, 1 H), 7.04 (d, *J* = 7.9 Hz, 1 H), 3.99 (s, 3 H), 3.93 (s, 3 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 163.0, 160.6, 141.0, 138.7, 138.1, 135.3, 134.5, 132.6, 132.0, 131.0, 130.9, 130.4, 130.2, 128.4, 123.8, 123.4, 121.2, 120.6, 118.7, 118.0, 115.5, 108.3, 56.1, 55.5; **HRMS (ESI)** calcd for $C_{27}H_{20}O_2N^+$ (M - OTf)$^+$ 390.1489, found 390.1484.

8-(4-fluorophenyl)-6-methoxybenzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (**2f**):



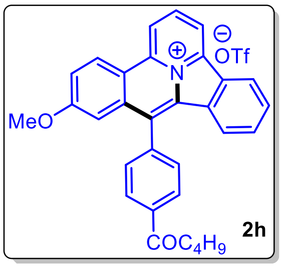
Off white solid, 54 mg, 78% yield; mp = 348-350 °C; $\boldsymbol{R_f}$ = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (400 MHz, DMSO-d$_6$) δ** = 9.79 (d, *J* = 8.5 Hz, 1 H), 9.56 (d, *J* = 9.2 Hz, 1 H), 9.34 (d, *J* = 7.9 Hz, 1 H), 9.08 (t, *J* = 8.2 Hz, 1 H), 8.87 (d, *J* = 7.9 Hz, 1 H), 8.03 - 7.91 (m, 2 H), 7.86 - 7.69 (m, 5 H), 7.19 (br. s., 1 H), 6.96 (d, *J* = 7.9 Hz, 1 H), 3.93 (s, 3 H); **^{13}C NMR (100 MHz, DMSO-d$_6$) δ** =163.2 (d, *J* = 247.4 Hz), 163.1, 141.1, 139.0, 138.2, 135.1, 133.5, 132.7, 132.2, 131.9, 131.8, 131.1, 130.3, 130.2 128.4, 128.4 (d, *J* = 3.08 Hz) 123.4 (d, *J* = 13.10 Hz), 121.4, 120.7, 118.7, 118.1, 117.3(d, *J* = 22.35 Hz), 108.1, 56.1; **HRMS (ESI)** calcd for $C_{26}H_{17}FON^+$ (M - OTf)$^+$ 378.1340, found 378.1345.

8-(4-chlorophenyl)-6-methoxybenzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (**2g**):



Off white solid, 51 mg, 75% yield; mp = 285-287 °C; $\boldsymbol{R_f}$ = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ =** 9.79 (d, *J* = 8.5 Hz, 1 H), 9.56 (d, *J* = 9.3 Hz, 1 H), 9.35 (d, *J* = 7.6 Hz, 1 H), 9.08 (t, *J* = 8.1 Hz, 1 H), 8.88 (d, *J* = 7.8 Hz, 1 H), 8.07 - 7.90 (m, 4 H), 7.82 (t, *J* = 7.6 Hz, 1 H), 7.74 (d, *J* = 8.2 Hz, 2 H), 7.18 (d, *J* = 2.1 Hz, 1 H), 6.99 (d, *J* = 8.1 Hz, 1 H), 3.93 (s, 3 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 163.1, 141.1, 139.0, 138.3, 135.3, 134.8, 133.1, 132.6, 132.2, 131.4, 131.2, 131.0, 130.3, 130.3, 130.2, 128.5, 123.5, 123.3, 121.4, 120.7, 118.7, 118.1, 108.0, 56.2; **HRMS (ESI)** calcd for $C_{26}H_{17}ClON^+$ (M - OTf)$^+$ 394.0993, found 394.0998.

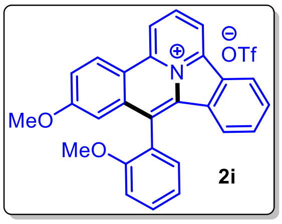
6-methoxy-8-(4-pentanoylphenyl)benzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (2h):



2h

Off white solid, 53 mg, 81% yield; mp = 240-242 °C; $\boldsymbol{R_f}$ = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.81 (d, *J* = 8.5 Hz, 1 H), 9.58 (d, *J* = 9.3 Hz, 1 H), 9.36 (d, *J* = 7.5 Hz, 1 H), 9.10 (t, *J* = 8.2 Hz, 1 H), 8.89 (d, *J* = 7.9 Hz, 1 H), 8.48 - 8.42 (m, *J* = 8.2 Hz, 2 H), 8.02 - 7.95 (m, 2 H), 7.90 - 7.83 (m, *J* = 8.2 Hz, 2 H), 7.80 - 7.71 (m, 1 H), 7.15 (d, *J* = 2.4 Hz, 1 H), 6.93 (d, *J* = 8.1 Hz, 1 H), 3.92 (s, 3 H), 3.27 (t, *J* = 7.2 Hz, 2 H), 1.74 (quin, *J* = 7.4 Hz, 2 H), 1.47 (sxt, *J* = 7.4 Hz, 2 H), 0.99 (t, *J* = 7.3 Hz, 3 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 199.8, 163.1, 141.1, 139.1, 138.3, 138.0, 136.5, 134.6, 133.4, 132.4, 132.2, 131.2, 130.4, 130.1, 129.9, 129.5, 128.5, 123.5, 123.3, 121.3, 120.8, 118.7, 118.1, 108.2, 56.1, 37.9, 25.8, 21.8, 13.9; **HRMS (ESI)** calcd for $C_{31}H_{26}O_2N^+$ (M - OTf)$^+$ 444.1925, found 444.1925.

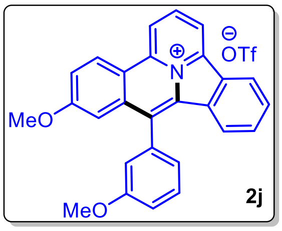
6-methoxy-8-(2-methoxyphenyl)benzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (2i):



2i

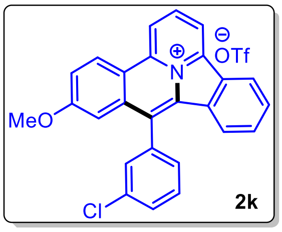
Pale yellow solid, 39 mg, 57% yield; mp = 220-222 °C; $\boldsymbol{R_f}$ = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.78 (d, *J* = 8.4 Hz, 1 H), 9.54 (d, *J* = 9.3 Hz, 1 H), 9.32 (d, *J* = 7.6 Hz, 1 H), 9.06 (t, *J* = 8.1 Hz, 1 H), 8.86 (d, *J* = 7.9 Hz, 1 H), 8.02 - 7.93 (m, 2 H), 7.91 - 7.84 (m, 1 H), 7.78 (t, *J* = 7.6 Hz, 1 H), 7.56 (d, *J* = 8.5 Hz, 1 H), 7.53 - 7.46 (m, 1 H), 7.41 (t, *J* = 7.4 Hz, 1 H), 7.18 (d, *J* = 2.4 Hz, 1 H), 7.01 (d, *J* = 7.9 Hz, 1 H), 3.91 (s, 3 H), 3.69 (s, 3 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 163.1, 156.8, 141.0, 138.9, 138.2, 134.8, 132.6, 132.5, 132.2, 131.9, 131.1, 130.8, 130.3, 130.2, 128.5, 123.5, 122.9, 122.0, 121.3, 120.8, 120.0, 118.6, 118.1, 112.8, 107.9, 56.1, 55.9; **HRMS (ESI)** calcd for $C_{27}H_{20}O_2N^+$ (M - OTf)$^+$ 390.1489, found 390.1474.

6-methoxy-8-(3-methoxyphenyl)benzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (**2j**):



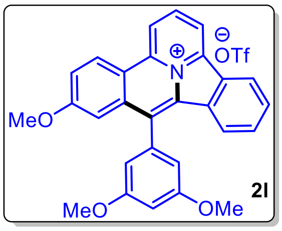
Off white solid, 42 mg, 62% yield; mp = 285-287 °C; ***R_f*** = 0.40 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.79 - 9.69 (m, 1 H), 9.52 (dt, *J* = 3.1, 6.1 Hz, 1 H), 9.36 - 9.25 (m, 1 H), 9.08 - 8.97 (m, 1 H), 8.84 (t, *J* = 6.1 Hz, 1 H), 8.00 - 7.89 (m, 2 H), 7.82 - 7.69 (m, 2 H), 7.43 (dd, *J* = 2.3, 8.4 Hz, 1 H), 7.28 - 7.20 (m, 3 H), 6.97 (d, *J* = 8.0 Hz, 1 H), 3.92 (s, 3 H), 3.86 (s, 3 H); **^{13}C NMR (100 MHz, DMSO-d$_6$) δ** = 163.1, 160.3, 141.1, 138.9, 138.2, 134.9, 134.1, 133.4, 132.4, 132.1, 131.4, 131.1, 130.3, 128.4, 123.4, 121.3, 120.7, 118.7, 118.1, 116.0, 114.6, 108.3, 56.1, 55.5; **HRMS (ESI)** calcd for $C_{27}H_{20}O_2N^+$ (M - OTf)$^+$ 390.1484, found 390.1489.

8-(3-chlorophenyl)-6-methoxybenzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (2k):



Off white solid, 49 mg, 72% yield; mp = 258-260 °C; ***R_f*** = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ**9.81 (d, *J* = 8.7 Hz, 1 H), 9.57 (d, *J* = 9.3 Hz, 1 H), 9.36 (d, *J* = 7.6 Hz, 1 H), 9.09 (t, *J* = 8.2 Hz, 1 H), 8.89 (d, *J* = 7.9 Hz, 1 H), 8.02 - 7.97 (m, 2 H), 7.96 (dd, *J* = 1.1, 2.1 Hz, 1 H), 7.95 - 7.88 (m, 1 H), 7.84 - 7.79 (m, 2 H), 7.70 (d, *J* = 7.5 Hz, 1 H), 7.18 (d, *J* = 2.6 Hz, 1 H), 6.93 (d, *J* = 8.1 Hz, 1 H), 3.94 (s, 3 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 163.2, 141.1, 139.2, 138.3, 134.7, 134.6, 134.2, 132.6, 132.3, 132.1, 131.2, 130.6, 130.4, 130.1, 129.2, 128.5, 128.2, 123.6, 123.2, 121.4, 120.8, 118.7, 118.2, 108.1, 56.2; **HRMS (ESI)** calcd for $C_{26}H_{17}ClON^+$ (M - OTf)$^+$ 394.0993, found 394.0977.

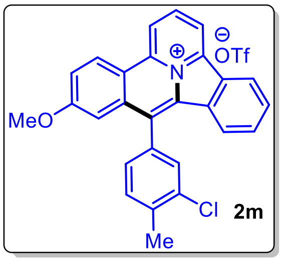
8-(3,5-dimethoxyphenyl)-6-methoxybenzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (**2l**):



2l

Pale yellow solid, 52 mg, 78% yield; mp = 198-200 °C; ***R**$_f$* = 0.60 (CH_2Cl_2/MeOH = 90/10); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.79 (d, *J* = 8.5 Hz, 1 H), 9.55 (d, *J* = 9.2 Hz, 1 H), 9.34 (d, *J* = 7.8 Hz, 1 H), 9.07 (t, *J* = 8.1 Hz, 1 H), 8.87 (d, *J* = 7.8 Hz, 1 H), 8.00 - 7.95 (m, 2 H), 7.84 (t, *J* = 7.7 Hz, 1 H), 7.31 (d, *J* = 2.4 Hz, 1 H), 7.11 (d, *J* = 7.9 Hz, 1 H), 6.97 (t, *J* = 2.1 Hz, 1 H), 6.83 (d, *J* = 2.1 Hz, 2 H), 3.95 (s, 3 H), 3.85 (s, 6 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 163.1, 161.6, 141.1, 138.9, 138.1, 134.8, 134.1, 134.0, 132.3, 132.2, 131.1, 130.2, 130.2, 128.4, 123.5, 123.4, 121.3, 120.7, 118.6, 118.1, 108.3, 107.1, 101.8, 56.2, 55.7; **HRMS (ESI)** calcd for $C_{28}H_{22}O_3N^+$ (M - OTf)$^+$ 420.1594, found 420.1566.

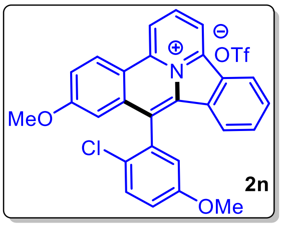
8-(3-chloro-4-methylphenyl)-6-methoxybenzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (**2m**):



2m

Off white solid, 51 mg, 76% yield; mp = 264-266 °C; ***R**$_f$* = 0.60 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.79 (d, *J* = 8.5 Hz, 1 H), 9.56 (d, *J* = 9.3 Hz, 1 H), 9.34 (d, *J* = 7.6 Hz, 1 H), 9.08 (t, *J* = 8.1 Hz, 1 H), 8.88 (d, *J* = 7.8 Hz, 1 H), 8.04 - 7.93 (m, 2 H), 7.86 (d, *J* = 7.8 Hz, 1 H), 7.82 (t, *J* = 7.5 Hz, 1 H), 7.77 (d, *J* = 1.4 Hz, 1 H), 7.60 (dd, *J* = 1.5, 7.6 Hz, 1 H), 7.21 (d, *J* = 2.4 Hz, 1 H), 6.99 (d, *J* = 8.1 Hz, 1 H), 3.94 (s, 3 H), 2.62 (s, 3 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 163.1, 141.1, 139.1, 138.2, 138.0, 134.8, 134.8, 132.9, 132.7, 132.7, 132.2, 131.4, 131.2, 130.3, 130.2, 129.6, 128.5, 128.2, 123.5, 123.3, 121.3, 120.7, 118.6, 118.1, 108.2, 56.2, 19.8; **HRMS (ESI)** calcd for $C_{27}H_{19}ClON^+$ (M - OTf)$^+$ 408.1150, found 408.1141.

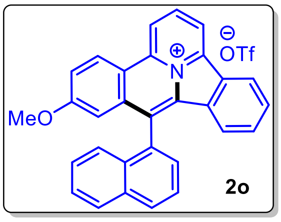
8-(2-chloro-5-methoxyphenyl)-6-methoxybenzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (**2n**):



2n

Off white solid, 42 mg, 63% yield; mp = 210-212 °C;***R**$_f$* = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.82 (d, *J* = 8.5 Hz, 1 H), 9.59 (d, *J* = 9.3 Hz, 1 H), 9.36 (d, *J* = 7.8 Hz, 1 H), 9.10 (t, *J* = 8.2 Hz, 1 H), 8.90 (d, *J* = 7.8 Hz, 1 H), 8.04 - 7.98 (m, 2 H), 7.92 (d, *J* = 9.0 Hz, 1 H), 7.86 (t, *J* = 7.6 Hz, 1 H), 7.49 (dd, *J* = 3.1, 9.0 Hz, 1 H), 7.29 (d, *J* = 2.9 Hz, 1 H), 7.15 (d, *J* = 2.4 Hz, 1 H), 6.99 (d, *J* = 8.1 Hz, 1 H), 3.96 (s, 3 H), 3.83 (s, 3 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 163.4, 159.2, 141.2, 139.4, 138.4, 134.0, 132.7, 132.6, 131.7, 131.5, 131.0, 130.4, 129.7, 128.7, 123.6, 123.6, 122.9, 121.4, 121.0, 118.6, 118.4, 116.5, 107.8, 56.3, 55.9; **HRMS (ESI)** calcd for $C_{27}H_{19}ClO_2N^+$ (M - OTf)$^+$424.1099, found 424.1099.

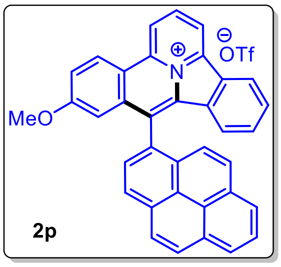
6-methoxy-8-(naphthalen-1-yl)benzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (**2o**):



2o

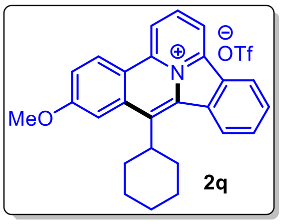
Off white solid, 54 mg, 80% yield; mp = 303-305 °C; ***R**$_f$* = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.85 (d, *J* = 8.5 Hz, 1 H), 9.62 (d, *J* = 9.2 Hz, 1 H), 9.36 (d, *J* = 7.3 Hz, 1 H), 9.16 - 9.04 (m, 1 H), 8.85 (d, *J* = 7.9 Hz, 1 H), 8.44 (d, *J* = 7.9 Hz, 1 H), 8.25 (d, *J* = 8.5 Hz, 1 H), 8.03 - 7.92 (m, 2 H), 7.91 - 7.79 (m, 2 H), 7.64 (t, *J* = 7.3 Hz, 1 H), 7.56 (t, *J* = 7.6 Hz, 1 H), 7.42 (d, *J* = 7.9 Hz, 1 H), 7.34 (t, *J* = 7.6 Hz, 1 H), 6.94 (br. s., 1 H), 6.45 (d, *J* = 7.9 Hz, 1 H), 3.74 (s, 3 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 163.0, 141.2, 139.0, 138.7, 135.4, 133.5, 133.4, 132.7, 132.0, 131.1, 131.0, 130.7, 130.5, 130.1, 129.4, 128.8, 128.6, 128.2, 127.5, 127.1, 126.4, 125.0, 123.4, 123.0, 120.9, 120.8, 119.0, 118.0, 108.4, 56.0; **HRMS (ESI)** calcd for $C_{30}H_{20}ON^+$ (M - OTf)$^+$ 410.1539, found 410.1544.

6-methoxy-8-(pyren-1-yl)benzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (**2p**):



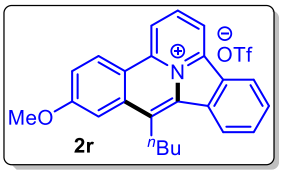
Yellow solid, 55 mg, 85% yield; mp = 337-339 °C; ***R****f* = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.90 (d, *J* = 8.8 Hz, 1 H), 9.66 (d, *J* = 9.2 Hz, 1 H), 9.39 (d, *J* = 7.6 Hz, 1 H), 9.15 (t, *J* = 8.2 Hz, 1 H), 8.86 (d, *J* = 7.6 Hz, 1 H), 8.74 (d, *J* = 8.0 Hz, 1 H), 8.58 - 8.40 (m, 3 H), 8.31 (d, *J* = 7.6 Hz, 1 H), 8.34 (d, *J* = 7.2 Hz, 1 H), 8.18 (t, *J* = 7.4 Hz, 1 H), 8.06 (d, *J* = 9.2 Hz, 1 H), 7.98 (d, *J* = 9.2 Hz, 1 H), 7.82 (t, *J* = 7.6 Hz, 1 H), 7.71 (d, *J* = 9.2 Hz, 1 H), 7.39 (t, *J* = 7.6 Hz, 1 H), 7.05 - 6.85 (m, 1 H), 6.19 (d, *J* = 8.0 Hz, 1 H), 3.64 (s, 3 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 163.1, 141.2, 139.0, 138.7, 135.7, 133.7, 133.1, 132.2, 132.0, 131.0, 130.9, 130.4, 130.4, 130.1, 129.3, 129.1, 128.9, 128.6, 127.5, 127.0, 126.3, 126.2, 126.1, 126.0, 124.2, 124.0, 123.7, 123.4, 122.9, 121.1, 120.8, 119.0, 118.0, 108.5, 55.9; **HRMS (ESI)** calcd for $C_{36}H_{22}ON^+$ (M - OTf)$^+$ 484.1696, found 484.1700.

8-cyclohexyl-6-methoxybenzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (**2q**):



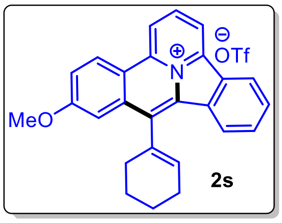
White solid, 50 mg, 72% yield; mp = 280-282 °C; ***R****f* = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (400 MHz, DMSO-d$_6$) δ** = 9.65 (d, *J* = 8.5 Hz, 1 H), 9.45 (d, *J* = 9.2 Hz, 1 H), 9.26 (d, *J* = 7.3 Hz, 1 H), 9.03 - 8.86 (m, 2 H), 8.73 (d, *J* = 7.9 Hz, 1 H), 8.25 (br. s., 1 H), 8.18 - 8.10 (m, 1 H), 8.10 - 8.01 (m, 1 H), 7.92 (d, *J* = 9.2 Hz, 1 H), 4.48 (br. s., 1 H), 4.18 (br. s., 3 H), 2.59 (d, *J* = 10.4 Hz, 2 H), 2.06 (d, *J* = 9.8 Hz, 4 H), 1.99 - 1.90 (m, 1 H), 1.79 (d, *J* = 10.4 Hz, 2 H), 1.71 - 1.57 (m, 1 H); **^{13}C NMR (100 MHz, DMSO-d$_6$) δ** = 162.1, 140.6, 138.2, 137.7, 133.5, 132.8, 130.7, 130.4, 130.2, 128.6, 125.0, 123.5, 121.0, 120.4, 118.9, 117.4, 108.9, 56.3, 30.1, 26.5, 25.4; **HRMS (ESI)** calcd for $C_{26}H_{24}ON^{+}$ (M - OTf)$^{+}$ 366.1852, found 366.1852.

8-butyl-6-methoxybenzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (**2r**):



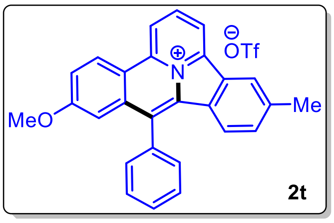
Off white solid, 53 mg, 74% yield; mp = 209-211 °C; ***R$_f$*** = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (400 MHz, DMSO-d$_6$) δ** = 9.64 (d, *J* = 8.5 Hz, 1 H), 9.42 (d, *J* = 9.2 Hz, 1 H), 9.24 (d, *J* = 7.9 Hz, 1 H), 9.02 - 8.81 (m, 2 H), 8.69 (d, *J* = 7.9 Hz, 1 H), 8.16 - 8.08 (m, 1 H), 8.08 - 7.99 (m, 2 H), 7.90 (d, *J* = 9.2 Hz, 1 H), 4.17 (s, 3 H), 3.93 (t, *J* = 7.6 Hz, 2 H), 1.87 (d, *J* = 6.7 Hz, 2 H), 1.76 - 1.62 (m, 2 H), 1.02 (t, *J* = 7.3 Hz, 3 H); **^{13}C NMR (100 MHz, DMSO-d$_6$) δ** = 163.3, 140.5, 138.0, 137.5, 137.0, 134.2, 132.8, 132.2, 130.8, 130.1, 130.0, 128.4, 124.6, 123.4, 121.6, 120.5, 118.4, 117.5, 106.7, 56.5, 40.1, 31.5, 27.1, 22.3, 14.0; **HRMS (ESI)** calcd for $C_{24}H_{22}ON^{+}$ (M - OTf)$^{+}$ 340.1696, found 340.1698.

8-(cyclohex-1-en-1-yl)-6-methoxybenzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (**2s**):



Off white solid, 40 mg, 58% yield; mp = 228-230 °C; ***R$_f$*** = 0.60 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (400 MHz, DMSO-d$_6$) δ** = 9.71 (d, *J* = 8.4 Hz, 1 H), 9.48 (d, *J* = 9.2 Hz, 1 H), 9.29 (d, *J* = 7.3 Hz, 1 H), 9.00 (t, *J* = 8.2 Hz, 1 H), 8.89 (d, *J* = 7.5 Hz, 1 H), 8.52 (d, *J* = 7.8 Hz, 1 H), 8.16 - 7.99 (m, 2 H), 7.95 (dd, *J* = 2.5, 9.1 Hz, 1 H), 7.74 (d, *J* = 2.6 Hz, 1 H), 6.22 (br. s., 1 H), 4.13 (s, 3 H), 2.49 - 2.46 (m, 4 H), 2.14 - 1.94 (m, 4 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 163.1, 140.9, 138.5, 137.9, 136.6, 134.2, 132.6, 132.2, 131.3, 130.9, 130.3, 130.2, 128.4, 123.9, 123.4, 121.5, 120.5, 118.8, 117.9, 107.4, 56.2, 28.5, 25.1, 22.4, 21.3; **HRMS (ESI)** calcd for $C_{26}H_{22}ON^{+}$ (M - OTf)$^{+}$ 364.1696, found 364.1719.

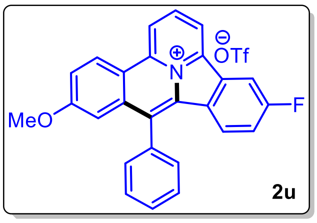
6-methoxy-11-methyl-8-phenylbenzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (**2t**):



2t

Off white solid, 50 mg, 70% yield; mp = 287-289 °C; ***R**_f_* = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz**, **DMSO-d$_6$) δ** = 9.75 (d, *J* = 8.5 Hz, 1 H), 9.52 (d, *J* = 9.2 Hz, 1 H), 9.24 (d, *J* = 7.3 Hz, 1 H), 9.03 (t, *J* = 7.9 Hz, 1 H), 8.66 (s, 1 H), 7.94 (dd, *J* = 1.8, 9.2 Hz, 1 H), 7.87 (br. s., 3 H), 7.68 (d, *J* = 3.7 Hz, 2 H), 7.56 (d, *J* = 7.9 Hz, 1 H), 7.23 - 7.11 (m, 1 H), 6.74 (d, *J* = 7.9 Hz, 1 H), 3.90 (s, 3 H), 2.56 (s, 3 H); **^{13}C NMR (125 MHz**, **DMSO-d$_6$) δ** = 163.0, 141.6, 141.0, 138.8, 138.2, 134.9, 133.6, 133.1, 132.5, 132.2, 130.5, 130.4, 130.0, 129.3, 128.4, 127.9, 123.2, 123.0, 121.1, 120.6, 118.5, 117.9, 108.1, 56.0, 21.4; **HRMS (ESI)** calcd for $C_{27}H_{20}ON^+$ $(M - OTf)^+$ 374.1538, found 374.1539.

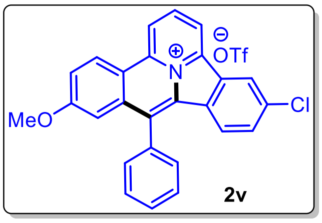
11-fluoro-6-methoxy-8-phenylbenzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (**2u**):



2u

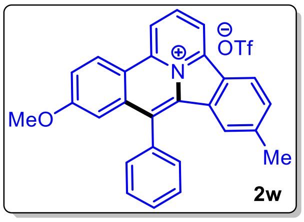
Off white solid, 43 mg, 62% yield; mp = 247-249 °C; ***R**_f_* = 0.60 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (400 MHz**, **DMSO-d$_6$) δ** = 9.84 (d, *J* = 8.8 Hz, 1 H), 9.56 (d, *J* = 9.3 Hz, 1 H), 9.34 (d, *J* = 7.8 Hz, 1 H), 9.10 (t, *J* = 8.3 Hz, 1 H), 8.83 (dd, *J* = 2.1, 8.4 Hz, 1 H), 7.98 (dd, *J* = 2.4, 9.1 Hz, 1 H), 7.92 - 7.83 (m, 3 H), 7.75 - 7.64 (m, 3 H), 7.20 (d, *J* = 2.5 Hz, 1 H), 6.87 (dd, *J* = 4.8, 8.8 Hz, 1 H), 3.91 (s, 3 H); **^{13}C NMR (125 MHz**, **DMSO-d$_6$) δ** = 163.2 (d, *J* = 249.7 Hz), 163.2, 140.2 (d, *J* = 4.5 Hz), 138.8, 138.3, 135.0, 134.1, 132.4, 132.3, 131.9, 131.8, 130.6, 130.1, 129.3, 128.5, 126.8 (d, *J* = 1.8 Hz), 125.5 (d, *J* = 10 Hz), 121.4 (d, *J* = 7.27 Hz), 120.2(d, *J* = 24.5 Hz), 118.7 (d, *J* = 21.8 Hz), 110.3, 110.1, 108.2, 56.1; **HRMS (ESI)** calcd for $C_{26}H_{17}FON^+$ $(M - OTf)^+$ 378.1289, found 378.1302.

11-chloro-6-methoxy-8-phenylbenzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (**2v**):



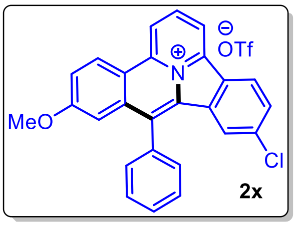
Off white solid, 44 mg, 65% yield; mp = 303-305 °C; ***R*** R_f = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.84 (d, *J* = 8.4 Hz, 1 H), 9.57 (d, *J* = 9.2 Hz, 1 H), 9.37 (d, *J* = 7.6 Hz, 1 H), 9.16 - 9.01 (m, 2 H), 8.00 (dd, *J* = 2.3, 9.2 Hz, 1 H), 7.92 - 7.80 (m, 4 H), 7.69 (d, *J* = 3.4 Hz, 2 H), 7.20 (d, *J* = 2.3 Hz, 1 H), 6.84 (d, *J* = 8.8 Hz, 1 H), 3.91 (s, 3 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 163.2, 140.0, 139.0, 138.2, 135.8, 134.9, 134.7, 132.1, 131.9, 130.6, 130.1, 129.3, 128.9, 128.5, 124.6, 123.4, 121.6, 121.4, 118.8, 108.3, 56.1; **HRMS (ESI)** calcd for $C_{26}H_{17}ClON^+$ (M - OTf)$^+$ 394.1254, found 394.1054.

6-methoxy-10-methyl-8-phenylbenzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (**2w**):



Off white solid, 41 mg, 60% yield; mp = 300-302 °C; R_f = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (400 MHz, DMSO-d$_6$) δ** = 9.74 (d, *J* = 8.5 Hz, 1 H), 9.54 (d, *J* = 9.2 Hz, 1 H), 9.25 (d, *J* = 7.3 Hz, 1 H), 9.03 (t, *J* = 7.9 Hz, 1 H), 8.73 (d, *J* = 7.9 Hz, 1 H), 7.96 (dd, *J* = 2.4, 9.2 Hz, 1 H), 7.88 (d, *J* = 3.7 Hz, 3 H), 7.78 (d, *J* = 7.9 Hz, 1 H), 7.69 (d, *J* = 3.7 Hz, 2 H), 7.26 - 7.15 (m, 1 H), 6.59 (s, 1 H), 3.90 (s, 3 H), 2.33 (s, 3 H); **^{13}C NMR (100 MHz, DMSO-d$_6$) δ** = 163.0, 142.3, 141.2, 138.9, 138.2, 134.9, 134.3, 132.4, 132.2, 132.2, 130.7, 130.4, 130.0, 129.3, 128.4, 128.0, 123.3, 123.2, 121.3, 120.2, 118.7, 117.6, 108.2, 56.1, 21.9; **HRMS (ESI)** calcd for $C_{27}H_{20}ON^+$ (M - OTf)$^+$ 374.1540, found 374.1539.

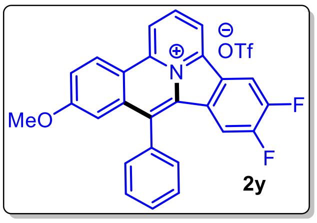
10-chloro-6-methoxy-8-phenylbenzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (2x):



2x

Off white solid, 42 mg, 64% yield; mp = 308-310 °C; $\boldsymbol{R_f}$ = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.82 (d, J = 8.5 Hz, 1 H), 9.58 (d, J = 9.4 Hz, 1 H), 9.36 (d, J = 7.7 Hz, 1 H), 9.09 (t, J = 8.1 Hz, 1 H), 8.92 (d, J = 8.5 Hz, 1 H), 8.06 (dd, J = 1.9, 8.3 Hz, 1 H), 8.01 (dd, J = 2.6, 9.2 Hz, 1 H), 7.94 - 7.87 (m, 3 H), 7.74 - 7.67 (m, 2 H), 7.23 (d, J = 2.5 Hz, 1 H), 6.68 (d, J = 1.7 Hz, 1 H), 3.92 (s, 3 H); **^{13}C NMR (100 MHz, DMSO-d$_6$) δ** = 163.2, 140.3, 139.1, 138.2, 136.4, 135.2, 134.8, 131.8, 131.5, 131.1, 130.7, 130.2, 129.3, 129.0, 128.6, 125.3, 122.7, 121.8, 121.0, 119.0, 118.5, 108.4, 56.2; **HRMS (ESI)** calcd for $C_{26}H_{17}ClON^+$ (M - OTf)$^+$ 394.0988, found 394.0993.

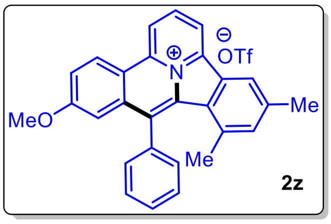
10,11-difluoro-6-methoxy-8-phenylbenzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (2y):



2y

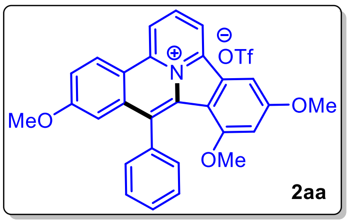
White solid, 47 mg, 68% yield; mp = 238-240 °C; $\boldsymbol{R_f}$ = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.85 (d, J = 8.4 Hz, 1 H), 9.59 (d, J = 9.2 Hz, 1 H), 9.31 (d, J = 7.6 Hz, 1 H), 9.12 (q, J = 7.5 Hz, 2 H), 8.02 (d, J = 8.8 Hz, 1 H), 7.91 (s, 3 H), 7.77 - 7.65 (m, 2 H), 7.24 (s, 1 H), 6.62 - 6.42 (m, 1 H), 3.92 (s, 3 H); **^{13}C NMR (100 MHz, DMSO-d$_6$) δ** = 163.5, 153.1 (d, J = 14 Hz), 153.0 (d, J = 14.6 Hz), 150.6 (d, J = 14.6 Hz), 150.4 (d, J = 13.8 Hz), 140.0, 139.2, 138.5, 135.3, 135.0, 131.7, 131.5, 130.5, 129.8 (d, J = 228.8 Hz), 129.5, 127.5 (d, J = 10 Hz), 127.4 (d, J = 7 Hz), 122.0, 120.0 (d, J = 239.6 Hz), 119.1, 112.9 (d, J = 21.5 Hz), 111.8 (d, J = 21.5 Hz), 108.6, 56.4; **HRMS (ESI)** calcd for $C_{26}H_{16}F_2ON^+$ (M - OTf)$^+$ 396.1194, found 396.1190.

6-methoxy-9,11-dimethyl-8-phenylbenzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (**2z**):



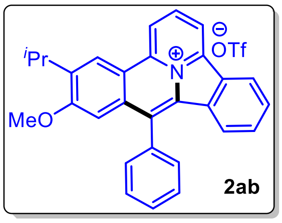
Off white solid, 42 mg, 62% yield; mp = 268-270 °C; **R_f** = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz**, **DMSO-d$_6$) δ** = 9.67 (d, *J* = 8.0 Hz, 1 H), 9.46 (d, *J* = 8.8 Hz, 1 H), 9.20 (d, *J* = 7.2 Hz, 1 H), 8.98 (t, *J* = 7.4 Hz, 1 H), 8.53 (s, 1 H), 7.90 (d, *J* = 8.4 Hz, 1 H), 7.83 – 7.66 (m, 5 H), 7.43 (s, 1 H), 7.23 (s, 1 H), 3.87 (s, 3 H), 2.54 (s, 3 H), 1.56 (s, 3 H); **^{13}C NMR (125 MHz**, **DMSO-d$_6$) δ** = 162.9, 141.5, 141.3, 138.7, 138.3, 137.0, 135.4, 135.2, 135.2, 134.6, 134.2, 131.9, 131.9, 130.1, 128.8, 128.1, 127.1, 120.7, 120.4, 118.0, 117.0, 109.0, 55.9, 21.0, 20.9; **HRMS (ESI)** calcd for $C_{28}H_{22}ON^+$ (M – Otf)$^+$ 388.1699, found 388.1696.

6,9,11-trimethoxy-8-phenylbenzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (**2aa**):



Yellow solid, 50 mg, 74% yield; mp = 263-265 °C; **R_f** = 0.40 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz**, **DMSO-d$_6$) δ** = 9.67 (d, *J* = 8.4 Hz, 1 H), 9.40 (d, *J* = 9.2 Hz, 1 H), 9.24 (d, *J* = 7.6 Hz, 1 H), 8.97 (t, *J* = 8.0 Hz, 1 H), 7.99 (s, 1 H), 7.83 (d, *J* = 8.4 Hz, 1 H), 7.74 – 7.59 (m, 3 H), 7.50 (d, *J* = 6.9 Hz, 2 H), 7.06 (br. S., 1 H), 6.76 (s, 1 H), 3.98 (s, 3 H), 3.83 (s, 3 H), 3.21 (s, 3 H; **^{13}C NMR (125 MHz**, **DMSO-d$_6$) δ** = 163.7, 162.7, 155.9, 141.2, 138.4, 138.2, 136.0, 135.8, 133.4, 133.1, 132.9, 130.2, 128.7, 128.1, 127.6, 120.8, 120.1, 117.9, 117.5, 111.7, 108.9, 102.4, 98.6, 56.4, 55.8; **HRMS (ESI)** calcd for $C_{28}H_{22}O_3N^+$ (M – Otf)$^+$ 420.1591, found 420.1594.

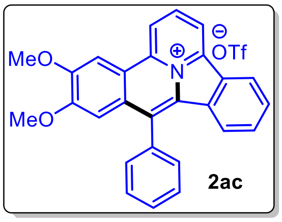
5-isopropyl-6-methoxy-8-phenylbenzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (**2ab**):



2ab

white solid, 51 mg, 74% yield; mp = 270-272 °C; $\boldsymbol{R_f}$ = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.97 (d, *J* = 8.4 Hz, 1 H), 9.41 - 9.30 (m, 2 H), 9.06 (t, *J* = 8.0 Hz, 1 H), 8.88 (d, *J* = 7.6 Hz, 1 H), 7.95 (t, *J* = 7.4 Hz, 1 H), 7.88 (br. s., 3 H), 7.76 (t, *J* = 7.6 Hz, 1 H), 7.71 (br. s., 2 H), 7.21 (s, 1 H), 6.89 (d, *J* = 8.0 Hz, 1 H), 3.85 (s, 3 H), 3.67 - 3.53 (m, 1 H), 1.45 (d, *J* = 6.5 Hz, 6 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 160.8, 143.6, 140.8, 138.2, 137.8, 134.4, 133.3, 132.3, 131.9, 131.8, 130.8, 130.4, 130.4, 130.2, 130.0, 129.3, 123.1, 119.0, 105.7, 56.0, 27.4, 22.3; **HRMS (ESI)** calcd for $C_{29}H_{24}ON^+$ (M - OTf)$^+$ 402.1850, found 402.1852.

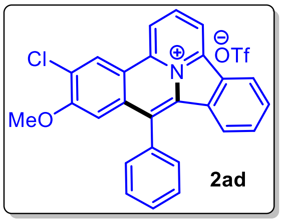
5,6-dimethoxy-8-phenylbenzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (**2ac**):



2ac

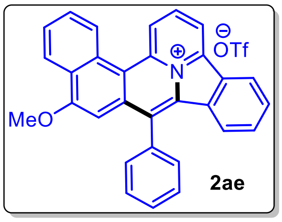
Yellow solid, 54 mg, 78% yield; mp = 295-297 °C; $\boldsymbol{R_f}$ = 0.40 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.94 (d, *J* = 8.4 Hz, 1 H), 9.38 (d, *J* = 7.2 Hz, 1 H), 9.05 (t, *J* = 7.4 Hz, 1 H), 8.89 (br. s., 1 H), 8.87 (d, *J* = 8.0 Hz, 1 H), 7.98 - 7.83 (m, 4 H), 7.79 - 7.65 (m, 3 H), 7.19 (br. s., 1 H), 6.87 (d, *J* = 7.6 Hz, 1 H), 4.23 (br. s., 3 H), 3.82 (br. s., 3 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 154.2, 152.9, 140.5, 137.2, 136.6, 134.4, 132.4, 131.8, 130.6, 130.4, 130.0, 129.7, 129.4, 128.9, 123.3, 122.7, 121.3, 120.6, 118.3, 106.3, 105.9, 57.1, 56.0; **HRMS (ESI)** calcd for $C_{27}H_{20}O_2N^+$ (M - OTf)$^+$ 390.1486, found 390.1489.

5-chloro-6-methoxy-8-phenylbenzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (**2ad**):



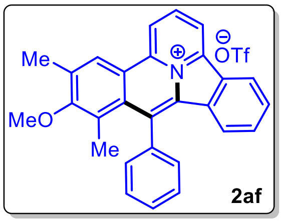
Off white solid, 40 mg, 58% yield; mp = 303-305 °C; ***R**$_f$* = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz**, **DMSO-d$_6$) δ** = 9.87 (d, *J* = 8.7 Hz, 1 H), 9.83 (s, 1 H), 9.40 (d, *J* = 7.6 Hz, 1 H), 9.11 (t, *J* = 8.2 Hz, 1 H), 8.89 (d, *J* = 7.8 Hz, 1 H), 7.97 (t, *J* = 7.5 Hz, 1 H), 7.89 (br. s., 3 H), 7.77 (t, *J* = 7.7 Hz, 1 H), 7.72 (d, *J* = 3.5 Hz, 2 H), 7.31 (s, 1 H), 6.88 (d, *J* = 8.1 Hz, 1 H), 3.92 (s, 3 H); **^{13}C NMR (125 MHz**, **DMSO-d$_6$) δ** = 158.0, 141.2, 139.1, 137.3, 134.1, 133.6, 132.7, 132.1, 131.8, 131.2, 130.6, 130.3, 130.2, 130.1, 129.4, 127.8, 127.6, 123.5, 123.3, 121.2, 119.2, 118.7, 107.5, 56.8; **HRMS (ESI)** calcd for $C_{26}H_{17}ClON^+$ (M - OTf)$^+$388.1696, found 388.1695.

5-methoxy-7-phenylbenzo[h]benzo[1,2]indolizino[5,4,3-ab]isoquinolin-15-ium trifluoromethanesulfonate (**2ae**):



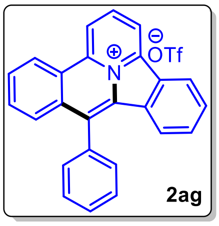
Yellowish solid, 53 mg, 78% yield; mp = 288-290 °C; ***R**$_f$* = 0.40 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz**, **DMSO-d$_6$) δ** = 9.82 (d, *J* = 8.8 Hz, 1 H), 9.43 (d, *J* = 7.6 Hz, 1 H), 9.23 (d, *J* = 8.4 Hz, 1 H), 9.05 (t, *J* = 8.0 Hz, 1 H), 8.93 (d, *J* = 7.6 Hz, 1 H), 8.62 (d, *J* = 8.0 Hz, 1 H), 8.20 - 8.14 (m, 1 H), 8.11 - 8.05 (m, 1 H), 8.00 (t, *J* = 7.6 Hz, 1 H), 7.91 (br. s., 3 H), 7.83 - 7.73 (m, 3 H), 7.07 (s, 1 H), 6.91 (d, *J* = 8.0 Hz, 1 H), 3.99 (s, 3 H); **^{13}C NMR (100 MHz**, **DMSO-d$_6$) δ** = 158.9, 140.6, 137.8, 136.5, 135.9, 133.9, 133.5, 132.6, 131.9, 131.2, 130.5, 130.4, 130.1, 129.9, 129.6, 129.5, 129.4, 129.2, 127.1, 125.4, 123.4, 123.3, 123.0, 119.4, 118.0, 117.7, 99.9, 56.3; **HRMS (ESI)** calcd for $C_{30}H_{20}ON^+$ (M - OTf)$^+$ 410.1535, found 410.1539.

6-methoxy-5,7-dimethyl-8-phenylbenzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (**2af**):



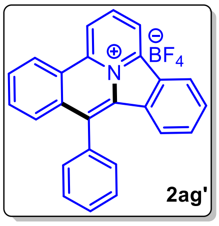
Off white solid, 43 mg, 63% yield; mp = 245-247 °C; ***R**_f* = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.84 (d, *J* = 8.5 Hz, 1 H), 9.49 (s, 1 H), 9.37 (d, *J* = 7.6 Hz, 1 H), 9.08 (t, *J* = 8.1 Hz, 1 H), 8.84 (d, *J* = 7.6 Hz, 1 H), 7.93 - 7.78 (m, 4 H), 7.71 (d, *J* = 7.0 Hz, 2 H), 7.65 (t, *J* = 7.6 Hz, 1 H), 6.32 (d, *J* = 8.1 Hz, 1 H), 3.80 (s, 3 H), 2.70 (s, 3 H), 2.11 (s, 3 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 161.8, 140.7, 138.6, 138.0, 137.2, 136.5, 136.4, 132.5, 131.8, 131.0, 130.7, 130.6, 130.2, 130.1, 129.9, 129.6, 129.3, 126.5, 123.5, 123.3, 122.3, 121.1, 118.5, 60.5, 17.2, 15.1; **HRMS (ESI)** calcd for $C_{28}H_{22}ON^+$ (M - OTf)$^+$ 388.1696, found 388.1695.

8-phenylbenzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (**2ag**):



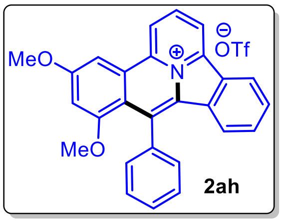
White solid, 43 mg, 60% yield; mp = 288-290 °C; ***R**_f* = 0.60 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.94 (d, *J* = 8.5 Hz, 1 H), 9.64 (d, *J* = 8.3 Hz, 1 H), 9.48 (d, *J* = 7.7 Hz, 1 H), 9.17 (t, *J* = 8.3 Hz, 1 H), 8.91 (d, *J* = 8.0 Hz, 1 H), 8.37 - 8.30 (m, 1 H), 8.30 - 8.24 (m, 1 H), 8.02 - 7.94 (m, 2 H), 7.92 - 7.84 (m, 3 H), 7.81 - 7.74 (m, 1 H), 7.73 - 7.63 (m, 2 H), 6.91 (d, *J* = 8.0 Hz, 1 H); **^{13}C NMR (100 MHz, DMSO-d$_6$) δ** = 141.6, 139.4, 138.5, 135.5, 133.9, 132.3, 132.2, 131.6, 131.0, 130.4, 130.4, 130.2, 130.0, 129.4, 127.5, 126.1, 124.6, 123.6, 123.2, 121.3, 119.5; **HRMS (ESI)** calcd for $C_{25}H_{16}N^+$ (M - OTf)$^+$ 330.1312, found 330.1315.

8-phenylbenzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium tetrafluoroborate (**2ag'**):



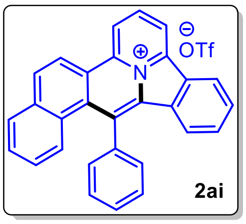
White solid, 35 mg, 65% yield; mp = 288-290 °C; ***R**$_f$* = 0.60 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz**, **DMSO-d$_6$) δ** = = 9.94 (d, *J* = 8.5 Hz, 1 H), 9.64 (d, *J* = 8.2 Hz, 1 H), 9.48 (d, *J* = 7.6 Hz, 1 H), 9.18 (t, *J* = 8.2 Hz, 1 H), 8.91 (d, *J* = 7.9 Hz, 1 H), 8.38 – 8.31 (m, 1 H), 8.31 – 8.22 (m, 1 H), 8.02 – 7.93 (m, 2 H), 7.92 – 7.84 (m, 3 H), 7.78 (t, *J* = 7.6 Hz, 1 H), 7.74 – 7.62 (m, 2 H), 6.91 (d, *J* = 8.1 Hz, 1 H); **^{13}C NMR (100 MHz**, **DMSO-d$_6$) δ** = 141.6, 139.4, 138.5, 135.5, 133.9, 132.3, 132.2, 131.6, 131.0, 130.4, 130.4, 130.2, 130.0, 129.4, 127.5, 126.1, 124.6, 123.6, 123.2, 121.3, 119.5; **HRMS (ESI)** calcd for $C_{25}H_{16}N^+$ $(M – BF_4)^+$ 330.1311, found 330.1315.

5,7-dimethoxy-8-phenylbenzo[1,2]indolizino[5,4,3-ab]isoquinolin-13-ium trifluoromethanesulfonate (**2ah**):



Yellow solid, 58 mg, 84% yield; mp = 302-304 °C; ***R**$_f$* = 0.40 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz**, **DMSO-d$_6$) δ** = 9.90 (d, *J* = 8.4 Hz, 1 H), 9.39 (d, *J* = 7.6 Hz, 1 H), 9.01 (t, *J* = 8.0 Hz, 1 H), 8.80 (d, *J* = 8.0 Hz, 1 H), 8.48 (d, *J* = 1.9 Hz, 1 H), 7.83 (t, *J* = 7.6 Hz, 1 H), 7.75 – 7.66 (m, 3 H), 7.62 (t, *J* = 7.6 Hz, 1 H), 7.56 – 7.44 (m, 2 H), 7.26 (d, *J* = 1.9 Hz, 1 H), 6.35 (d, *J* = 8.0 Hz, 1 H), 4.16 (s, 3 H), 3.54 (s, 3 H); **^{13}C NMR (125 MHz**, **DMSO-d$_6$) δ** = 163.0, 159.5, 140.7, 137.7, 137.0, 136.8, 135.5, 131.7, 130.9, 130.0, 129.9, 129.1, 128.6, 128.4, 127.5, 123.1, 122.9, 121.8, 119.5, 117.5, 105.0, 99.4, 56.8, 56.5; **HRMS (ESI)** calcd for $C_{27}H_{20}O_2N^+$ $(M – OTf)^+$ 390.1488, found 390.1489.

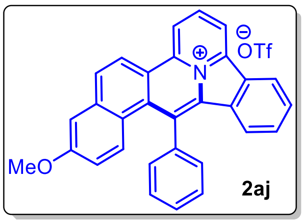
10-phenylbenzo[f]benzo[1,2]indolizino[5,4,3-ab]isoquinolin-15-ium trifluoromethanesulfonate (**2ai**):



2ai

Yellow solid, 45 mg, 65% yield; mp = 306-308 °C; R_f = 0.60 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz**, **DMSO-d$_6$) δ** = 10.08 (d, *J* = 8.4 Hz, 1 H), 9.60 - 9.50 (m, 2 H), 9.21 - 9.12 (m, 1 H), 8.94 (d, *J* = 7.6 Hz, 1 H), 8.76 (d, *J* = 8.8 Hz, 1 H), 8.39 (d, *J* = 7.6 Hz, 1 H), 8.01 - 7.93 (m, 5 H), 7.86 (t, *J* = 7.4 Hz, 1 H), 7.78 (d, *J* = 6.9 Hz, 2 H), 7.73 (t, *J* = 7.8 Hz, 1 H), 7.48 (t, *J* = 7.8 Hz, 1 H), 6.50 (d, *J* = 8.4 Hz, 1 H); **^{13}C NMR (125 MHz**, **DMSO-d$_6$) δ** = 140.1, 138.1, 137.1, 136.8, 136.0, 135.2, 133.8, 131.9, 131.0, 131.0, 130.6, 130.4, 130.0, 130.0, 129.6, 129.1, 128.7, 127.8, 127.3, 125.7, 123.8, 123.3, 122.5, 121.6, 119.7; **HRMS (ESI)** calcd for $C_{29}H_{18}N^+$ (M - OTf)$^+$ 380.1429, found 380.1434.

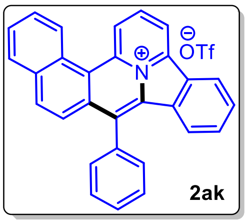
7-methoxy-10-phenylbenzo[f]benzo[1,2]indolizino[5,4,3-ab]isoquinolin-15-ium trifluoromethanesulfonate (**2aj**):



2aj

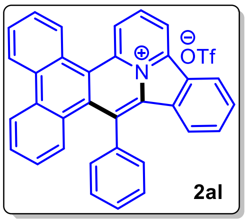
Yellow solid, 52 mg, 76% yield; mp = 294-296 °C; R_f = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz**, **DMSO-d$_6$) δ** = 9.97 (d, *J* = 8.0 Hz, 1 H), 9.59 - 9.36 (m, 2 H), 9.13 (br. s., 1 H), 8.92 (d, *J* = 6.9 Hz, 1 H), 8.62 (d, *J* = 8.0 Hz, 1 H), 7.97 (br. s., 4 H), 7.81 (br. s., 2 H), 7.79 - 7.69 (m, 3 H), 7.09 (d, *J* = 8.4 Hz, 1 H), 6.48 (d, *J* = 7.2 Hz, 1 H), 3.94 (s, 3 H); **^{13}C NMR (125 MHz**, **DMSO-d$_6$) δ** = 159.5, 140.0, 137.9, 137.7, 137.1, 136.8, 135.4, 133.7, 133.1, 131.8, 131.1, 130.9, 130.9, 130.7, 130.0, 129.0, 128.7, 124.0, 123.8, 123.4, 123.3, 122.1, 119.1, 118.3, 109.8, 55.7; **HRMS (ESI)** calcd for $C_{30}H_{20}ON^+$ (M - OTf)$^+$ 410.1537, found 410.1539.

7-phenylbenzo[h]benzo[1,2]indolizino[5,4,3-ab]isoquinolin-15-ium trifluoromethanesulfonate (**2ak**):



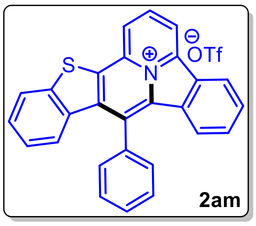
Off white solid, 46 mg, 66% yield; mp = 278-280 °C; ***R**$_f$* = 0.60 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (400 MHz, DMSO-d$_6$) δ =** 9.97 (d, *J* = 8.5 Hz, 1 H), 9.71 (d, *J* = 8.5 Hz, 1 H), 9.47 (d, *J* = 7.3 Hz, 1 H), 9.17 (t, *J* = 8.2 Hz, 1 H), 8.91 (d, *J* = 7.9 Hz, 1 H), 8.65 (d, *J* = 8.5 Hz, 1 H), 8.07 (s, 1 H), 7.98 (t, *J* = 7.3 Hz, 1 H), 7.90 (br. s., 3 H), 7.76 (d, *J* = 6.7 Hz, 3 H), 7.62 - 7.53 (m, 2 H), 7.53 - 7.45 (m, 1 H), 6.92 (d, *J* = 7.9 Hz, 1 H); **^{13}C NMR (100 MHz, DMSO-d$_6$) δ** = 145.0, 141.6, 139.5, 138.3, 138.0, 135.4, 132.9, 132.6, 132.2, 132.0, 131.1, 130.6, 130.4, 130.3, 130.3, 130.1, 129.5, 129.5, 129.3, 127.5, 127.1, 124.4, 123.7, 123.6, 123.3, 121.4, 119.4; **HRMS (ESI)** calcd for $C_{29}H_{18}N^+$ (M - OTf)$^+$ 380.1440, found 380.1445.

9-phenyldibenzo[f,h]benzo[1,2]indolizino[5,4,3-ab]isoquinolin-17-ium trifluoromethanesulfonate (**2al**):



Yellow solid, 47 mg, 70% yield; mp = 307-309 °C; ***R**$_f$* = 0.60 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.63 (d, *J* = 8.8 Hz, 1 H), 9.56 (d, *J* = 7.6 Hz, 1 H), 9.10 - 9.05 (m, 2 H), 9.03 (d, *J* = 8.0 Hz, 1 H), 8.99 (d, *J* = 8.0 Hz, 1 H), 8.71 (d, *J* = 8.0 Hz, 1 H), 8.09 - 8.05 (m, 1 H), 8.02 (t, *J* = 7.8 Hz, 2 H), 7.94 (d, *J* = 8.8 Hz, 1 H), 7.93 - 7.83 (m, 4 H), 7.83 - 7.75 (m, 3 H), 7.40 (t, *J* = 7.6 Hz, 1 H), 6.86 (d, *J* = 8.4 Hz, 1 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 139.3, 137.1, 136.5, 135.1, 134.1, 133.9, 132.4, 131.9, 131.6, 131.1, 130.7, 130.6, 130.5, 130.5, 130.4, 129.8, 128.9, 128.4, 127.3, 127.2, 127.0, 126.2, 124.6, 124.4, 123.8, 123.4, 119.5; **HRMS (ESI)** calcd for $C_{33}H_{20}N^+$ (M - OTf)$^+$ 430.1588, found 430.1590.

8-phenylbenzo[4,5]thieno[2,3-a]isoindolo[1,2,3-de]quinolizin-14-ium trifluoromethanesulfonate (**2am**):

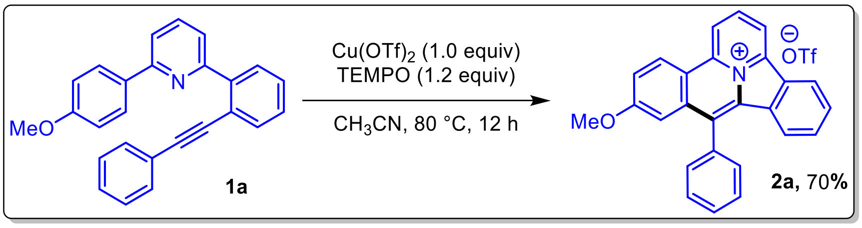


Yellowish solid, 45 mg, 65% yield; mp = 268-270 °C; ***R**$_f$* = 0.40 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.55 (d, *J* = 7.6 Hz, 1 H), 9.51 (d, *J* = 8.4 Hz, 1 H), 9.08 (t, *J* = 8.0 Hz, 1 H), 8.95 (d, *J* = 7.8 Hz, 1 H), 8.56 (d, *J* = 8.1 Hz, 1 H), 8.03 - 7.93 (m, 4 H), 7.85 - 7.75 (m, 4 H), 7.49 (t, *J* = 7.8 Hz, 1 H), 7.08 (d, *J* = 8.4 Hz, 1 H), 6.90 (d, *J* = 8.1 Hz, 1 H); **^{13}C NMR (100 MHz, DMSO-d$_6$) δ** = 141.3, 140.1, 137.7, 137.6, 135.8, 134.0, 133.7, 133.4, 132.8, 132.7, 132.1, 131.0, 130.7, 130.5, 130.0, 129.8, 128.4, 126.4, 125.4, 124.5, 123.6, 123.1, 122.9, 120.2; **HRMS (ESI)** calcd for $C_{27}H_{16}SN^+$ (M - OTf)$^+$ 386.1010, found 386.1014.

Gram Scale Synthesis of 2a: In a round bottom flask, equipped with magnetic stir bar, were added 2-(4-methoxyphenyl)-6-(2-(phenylethynyl)phenyl)pyridine (**1a**) (1g, 2.7 mmol, 1.0 equiv), $Cu(OTf)_2$ (997 mg, 2.7 mmol, 1.0 equiv) and CH_3CN (40 mL) under inert atmosphere. The reaction mixture was heated at 80 °C for 12 h. The mixture was diluted with CH_2Cl_2 (10 mL) and the combined mixture was concentrated in vacuo and the resulting residue was purified by column chromatography on silica (CH_2Cl_2/MeOH; 95:05) to afford the product **2a** (1.05 g) in 76% yield.

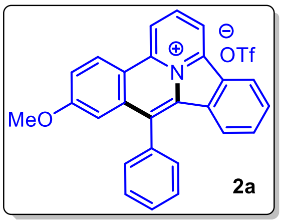
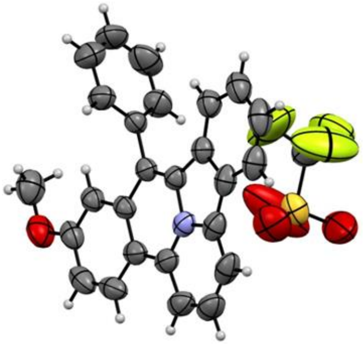
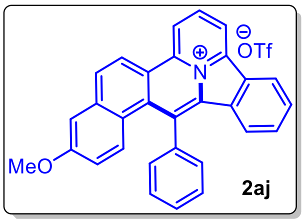
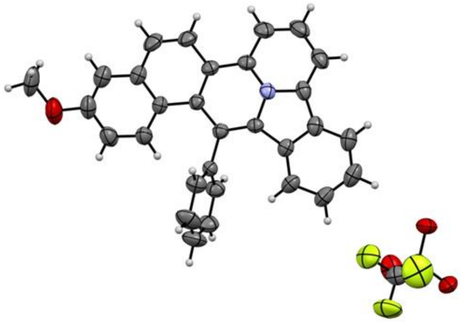
2.6 Control experiments:

2.6.1 Reaction of 1a with TEMPO under standard reaction conditions



To a stirred solution of **1a** (20 mg, 0.055 mmol) in CH_3CN (1 ml) was added $Cu(OTf)_2$, (20 mg, 0.055 mmol), TEMPO (11 mg, 0.066 mmol) at rt. The resulting mixture was stirred at 80 °C for 12 h. The mixture was diluted with CH_2Cl_2 and the reaction mixture was concentrated in vacuo. The resulting residue was purified by column chromatography on silica (CH_2Cl_2/MeOH; 95:05) to afford the product **2a** (18 mg) in 70% yield.

2.7 ORTEP diagrams:

Sr. No	Compound Structure	ORTEP Diagram
1	 **2a** **CCDC No 1824190**	
2	 **2aj** **CCDC No 1824191**	

2.8 Photophysical data of the representative ionic PAHs

Table S1. Spectral properties of selected ionic PAHs in CH_2Cl_2 at RT (10^{-5}M)

Comp	λ_{abs} (nm)[a]	λ_{em} (nm)[b]	ΔStoke's (nm)[c]	ϕ_f[d]	τ_f (ns)[e]
2a	388	444	56	0.86	6.52
2p	386	619	233	0.06	10.48
2aa	417	482	65	0.38	2.38
2ag	385	434	49	0.74	0.46
2ah	454	507	53	0.88	4.89
2ai	428	470	42	0.54	2.58
2aj	346	495	149	0.73	4.37
2al	415	490	75	0.57	7.52

[a]The maximum absorption bands more than 300 nm; Excited at the longest maximum absorption band in CH_2Cl_2; [b]Excited wavelength; [c]Stokes shift = λ_{em} - λ_{abs}; [d]Quinine

sulfate and fluorescein was used as the standard for calculation of quantum yield; [e]Fluorescent lifetime.

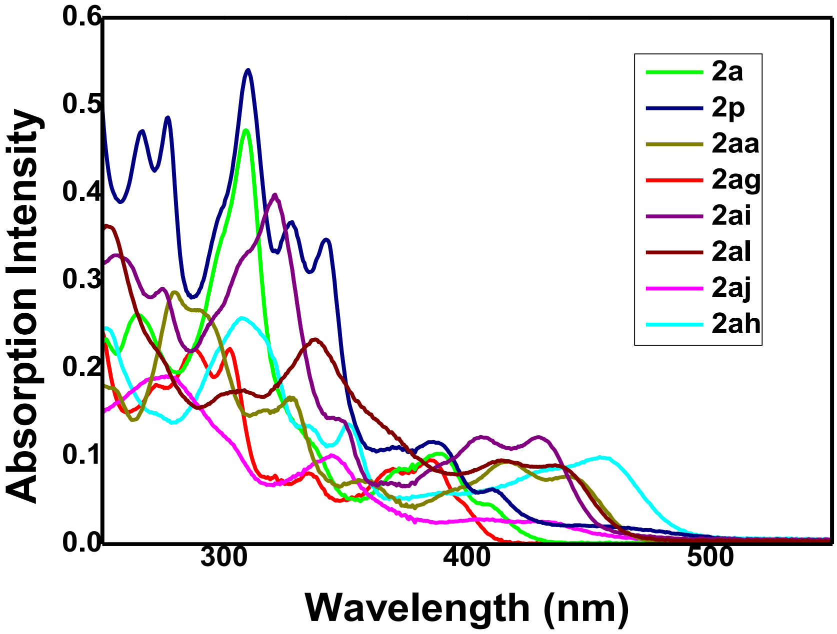


Figure S1. Absorption spectra of selected ionic PAHs in CH_2Cl_2 at RT

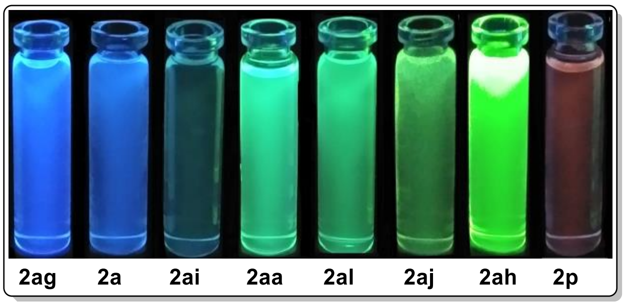


Figure S2. Photographs of selected ionic PAHs in CH_2Cl_2 at RT under UV light (λ_{exc} = 365nm)

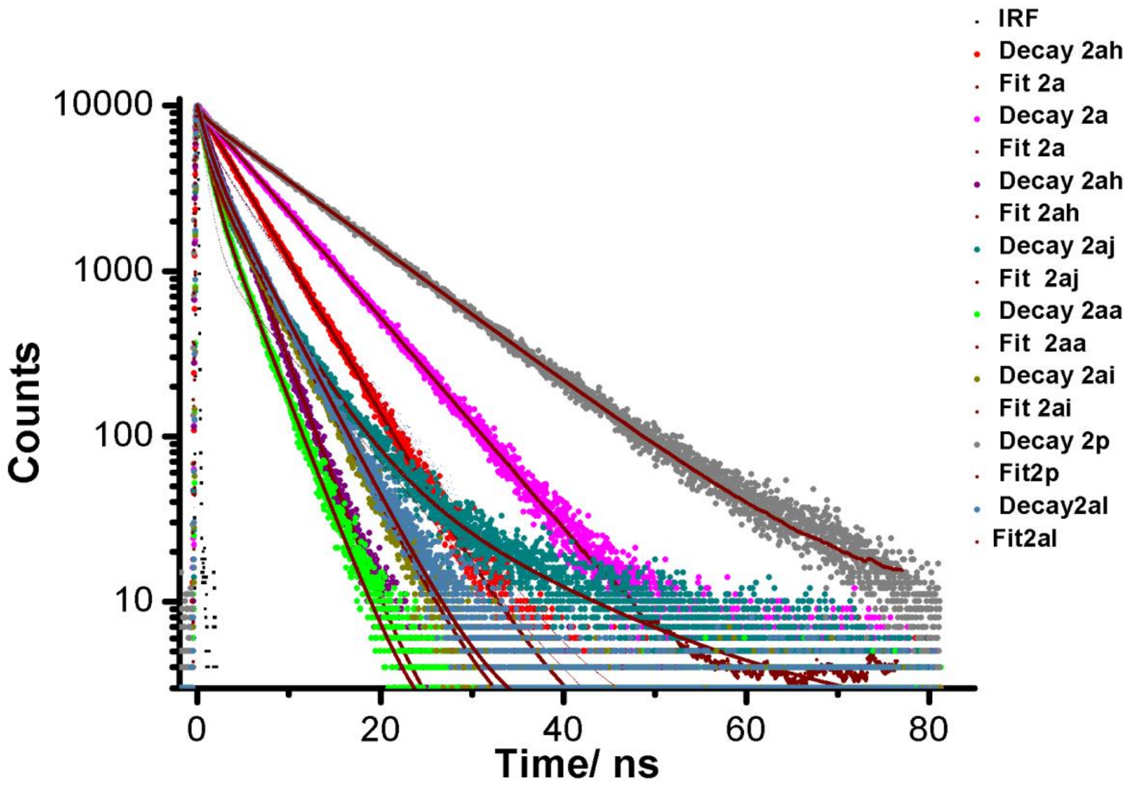


Figure S3: Emission decay profile of selected PAHs

Discussion on the photophysical data of the selected ionic PAHs:

Most of these compounds display bright fluorescence. These PAHs appear to be a new class of fluorescent materials and their photo- physical properties of selected ionic PAHs were studied in CH_2Cl_2 at RT. The absorption and excitation maxima, the photoluminescence (PL) maxima and quantum yields (ϕ_f), as well as the excited state lifetimes (τ_f) of these compounds in CH_2Cl_2 solution are listed in Tables 1, whereas the corresponding absorption, emission, excitation spectra are depicted in Figures S1, S2 and S3. The photoluminescence spectra of fluorophore show intense peaks between λ_{em}: 434–619 nm (Table S1) with Stokes shifts varies between (50-233 nm) which reveals violet-to-red fluorescence emissions depending on the functional group present. Substituent's like methoxy and plain phenyl core had only a modest effect on the fluorescent properties (**2ag** and **2a,** Table S1). Extension of the π-conjugated systems leads to significant bathochromic shifts in emission (**2p**, Table S1). These fluorophores have good photoluminescence capabilities with Φ_f values ranging between 0.40 to 10.48. The life time τ_f values are consistent with a doublet multiplicity.

2.9 Cyclic voltammetry

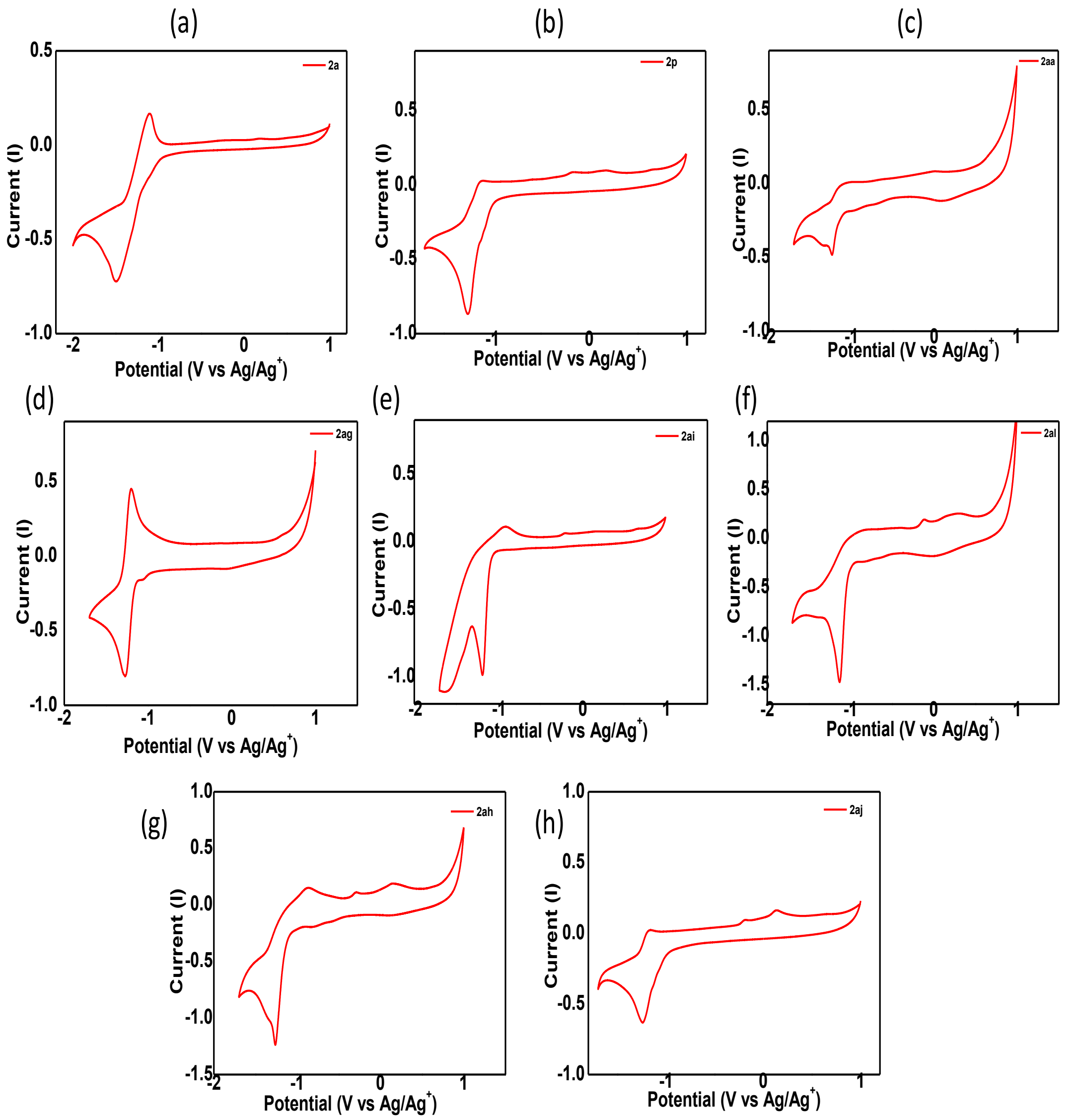


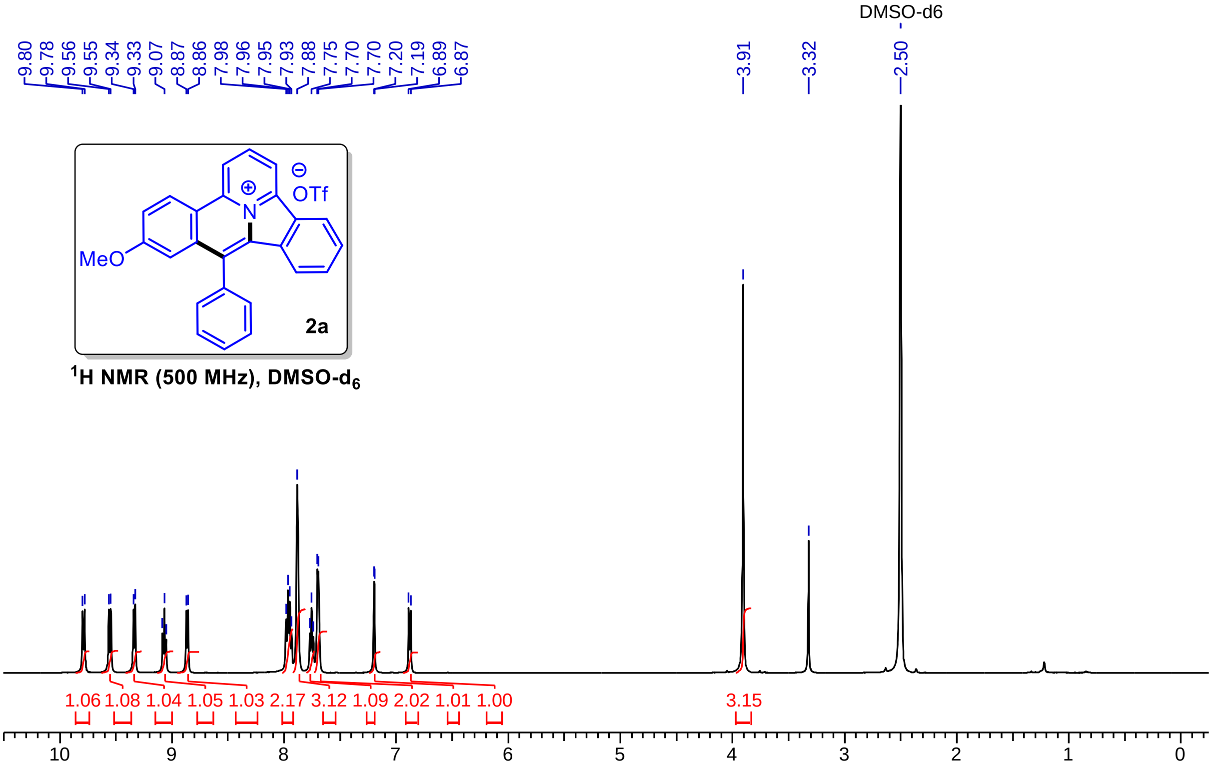
Figure S22. Cyclic voltammograms recorded for **2a**(a), **2p**(b), **2aa**(c), **2ag**(d), **2ai**(e), **2al**(f), **2ah**(g), **2aj**(h) in acetonitrile and 0.1 M TBAP using Pt disc as working electrode. Scan rate – 100 mV/s.

Table S2. Electrochemical data of representative ionic PAHs:

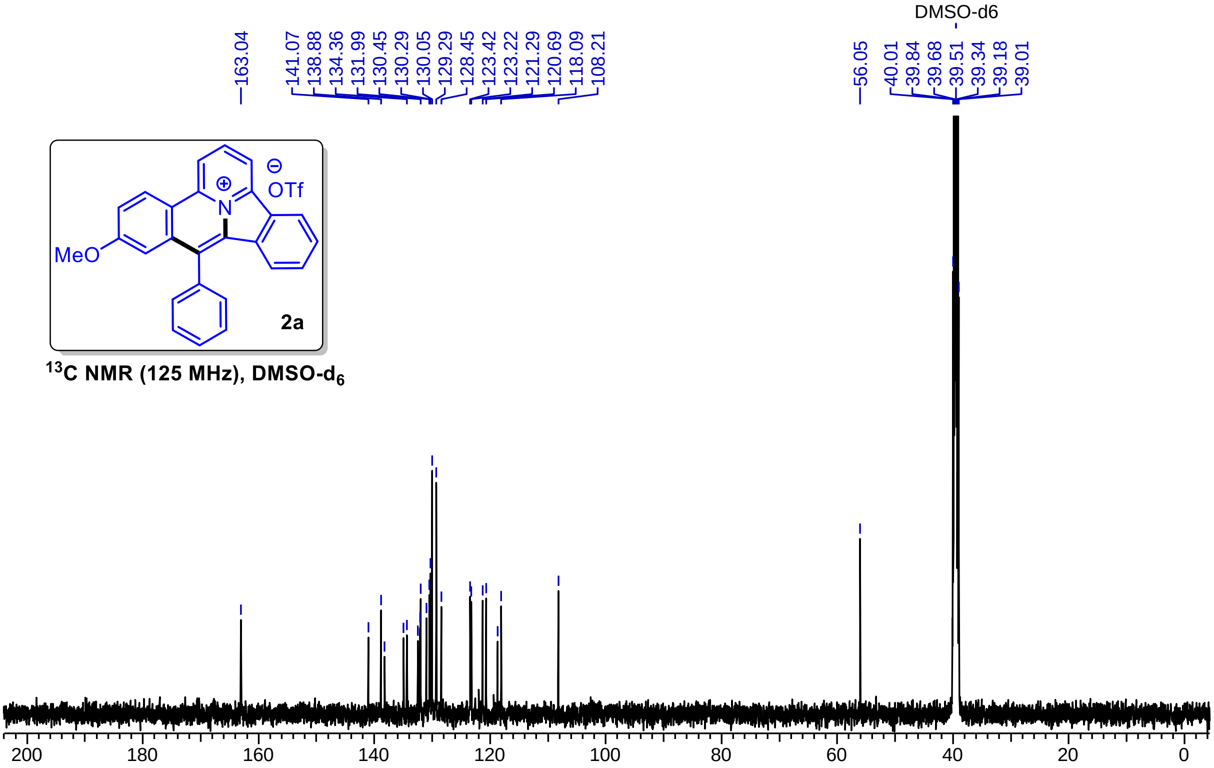
Comp	**λ(nm) onset**	**E_g opt (eV)**	**E_{red} (V)**	**LUMO (eV)**	**HOMO (eV)**
2a	410	3.03	-1.57	-2.83	-5.86
2p	526	2.36	-1.32	-3.08	-5.44
2aa	457	2.71	-1.29	-3.11	-5.82
2ag	400	3.10	-1.34	-3.06	-6.16
2ai	428	2.90	-1.25	-3.15	-6.05
2al	453	2.74	-1.21	-3.19	-5.93
2ah	474	2.62	-1.33	-3.07	-5.69
2aj	448	2.77	-1.32	-3.08	-5.85

HOMO level is calculated using electrochemically determined LUMO level and energy gap as obtained spectro-photometrically.

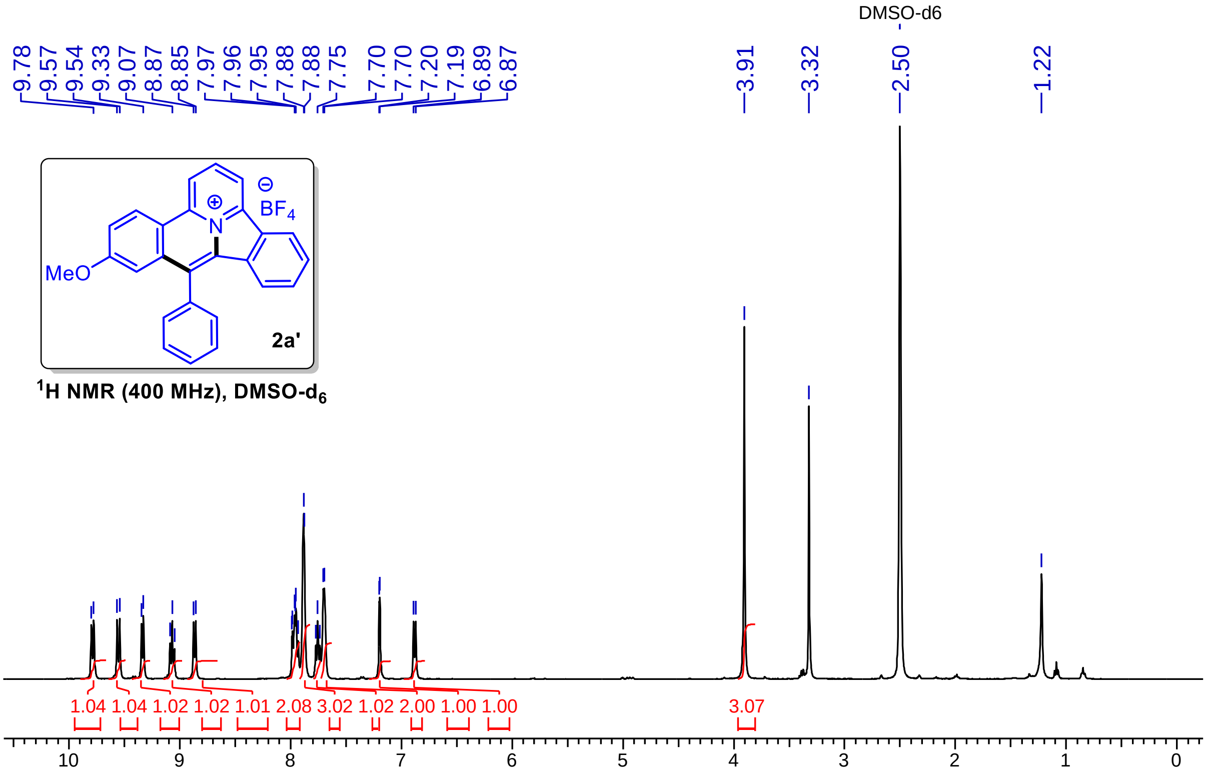
2.10 Selected NMR spectra:

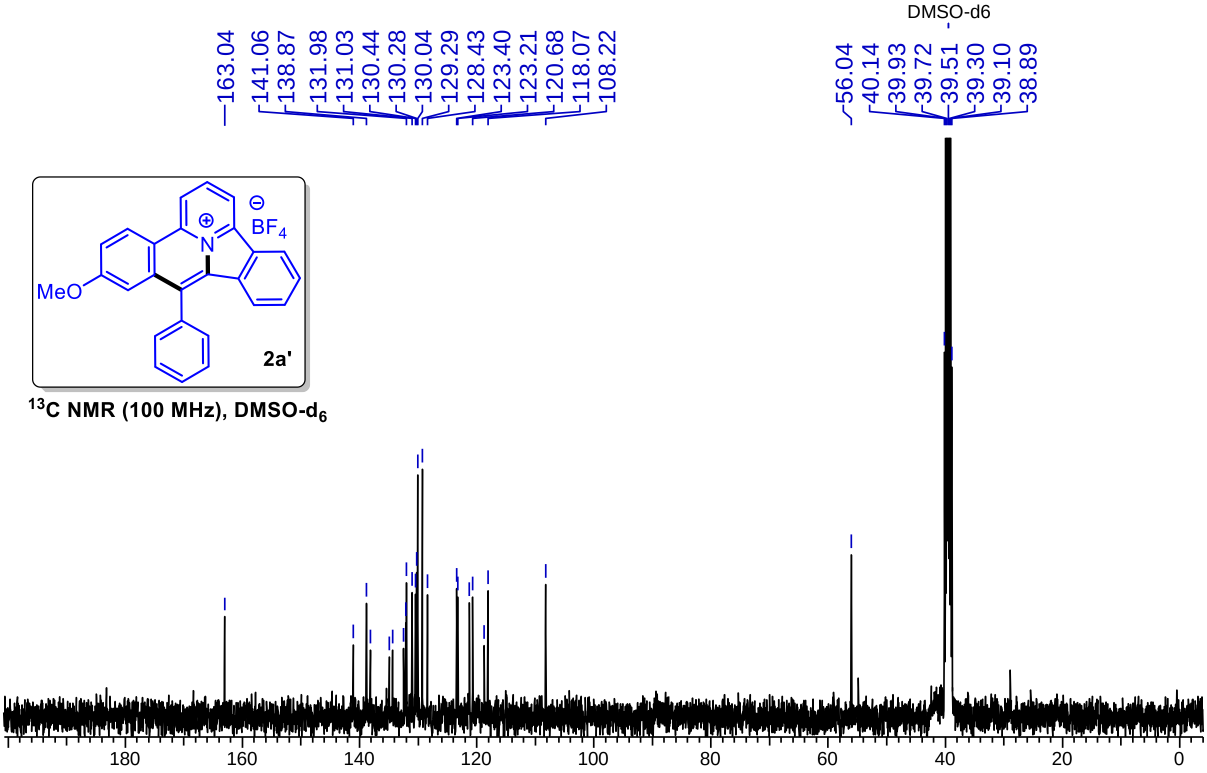


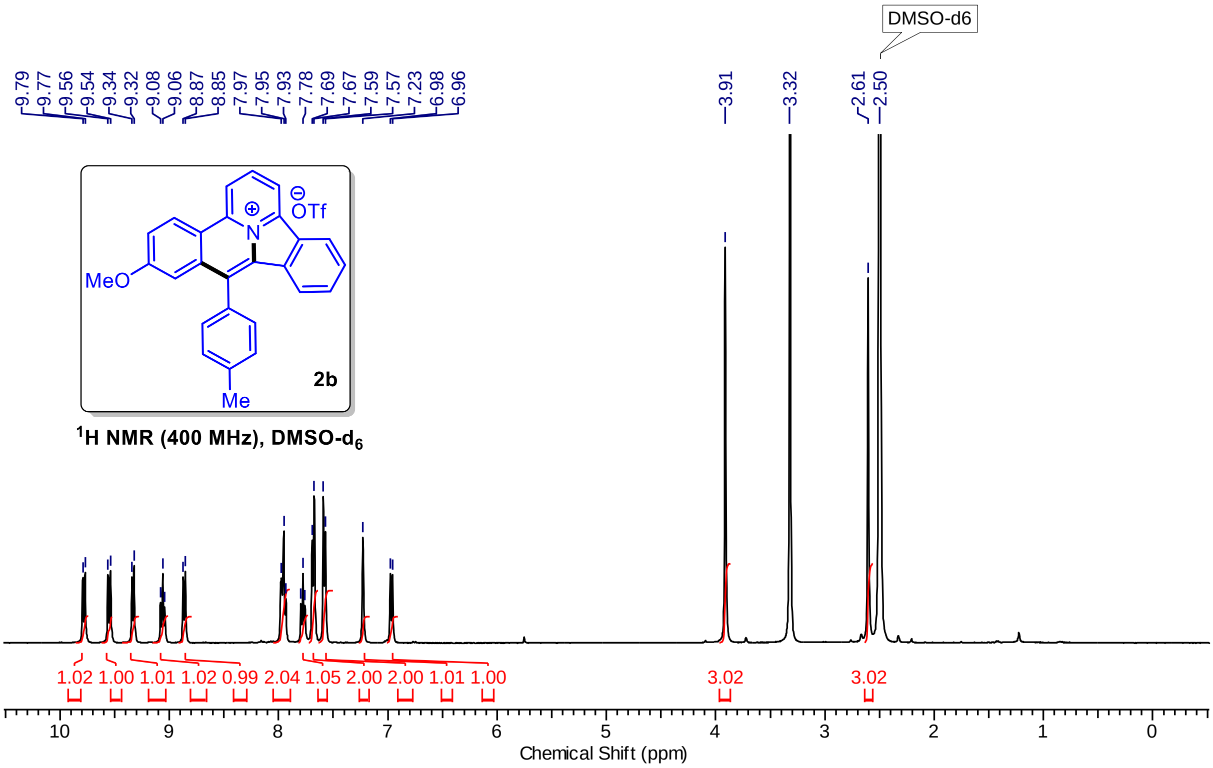
^{1}H NMR (500 MHz), DMSO-d$_6$



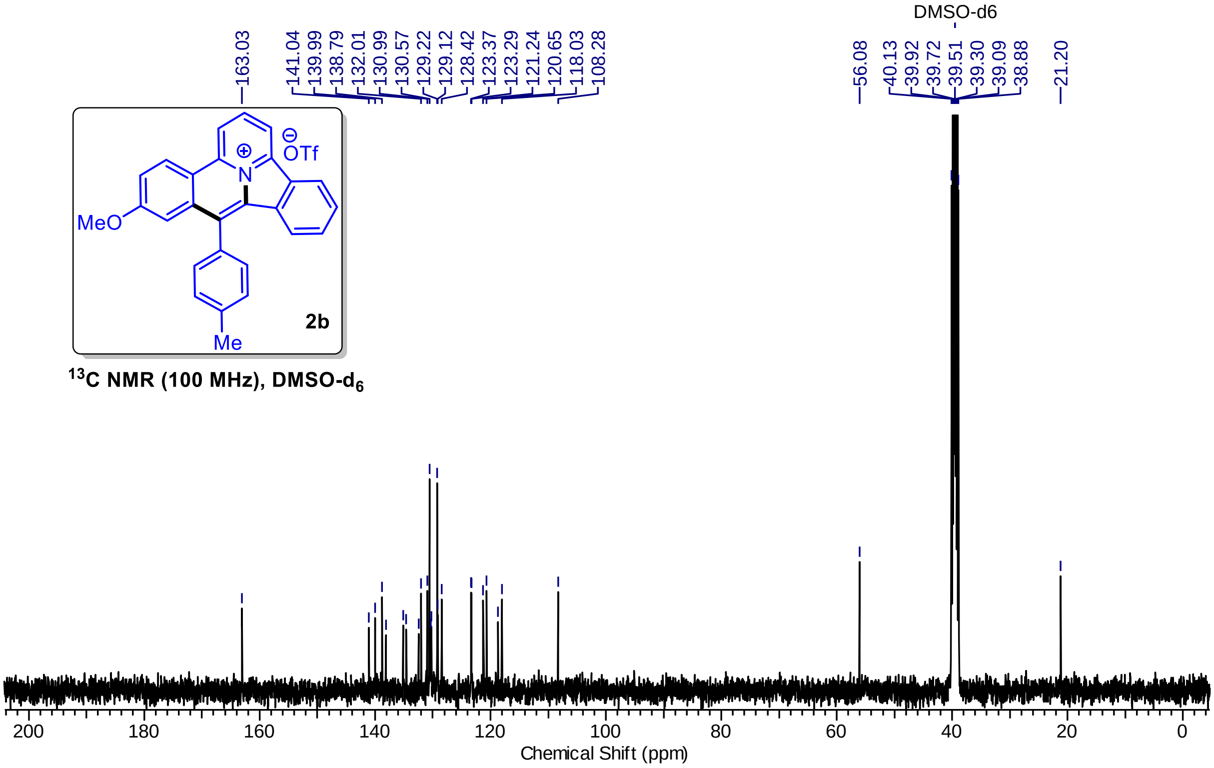
^{13}C NMR (125 MHz), DMSO-d$_6$


DMSO-d6
9.78 9.57 9.54 9.33 9.07 8.87 8.85 7.97 7.96 7.95 7.88 7.88 7.75 7.70 7.70 7.20 7.19 6.89 6.87
3.91
3.32
2.50
1.22
MeO
BF4
N
2a'
¹H NMR (400 MHz), DMSO-d6
1.04 1.04 1.02 1.02 1.01 2.08 3.02 1.02 2.00 1.00 1.00
3.07
10
9
8
7
6
5
4
3
2
1
0

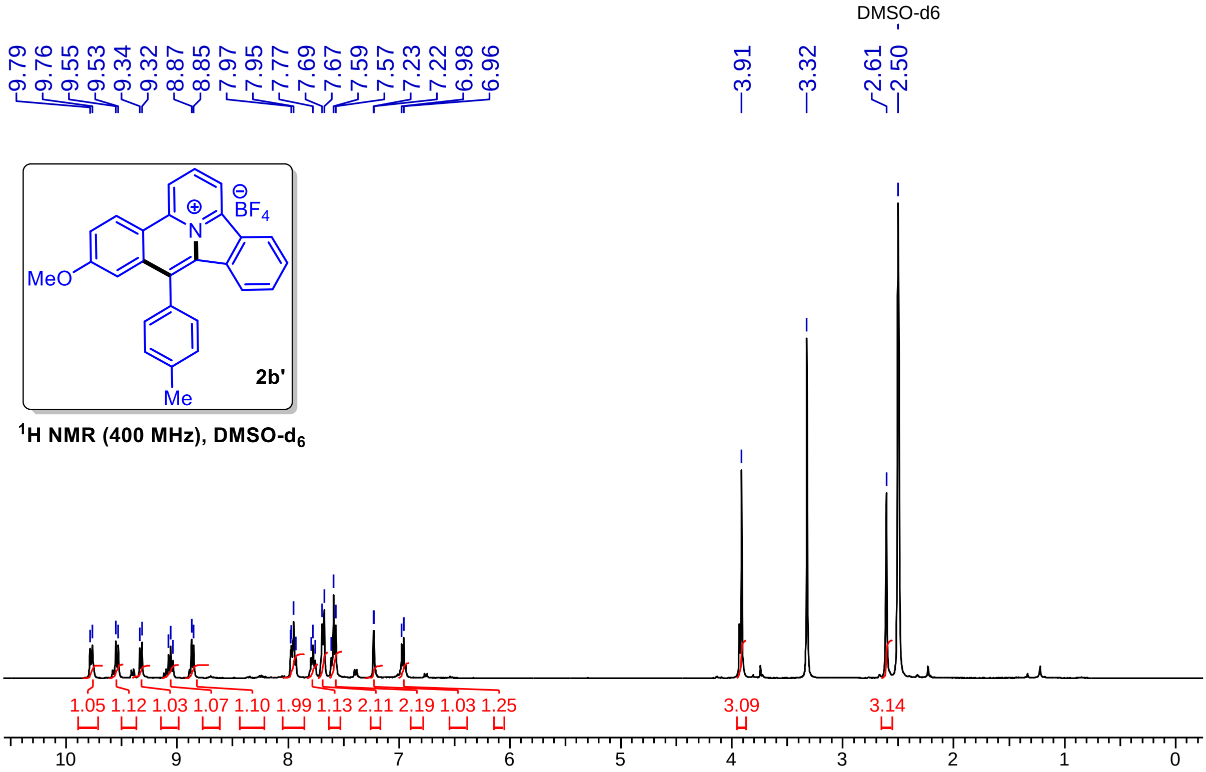

DMSO-d6
163.04
141.06 138.87 131.98 131.03 130.44 130.28 130.04 129.29 128.43 123.40 123.21 120.68 118.07 108.22
56.04
40.14 39.93 39.72 39.51 39.30 39.10 38.89
MeO
BF4
N
2a'
¹³C NMR (100 MHz), DMSO-d6
180
160
140
120
100
80
60
40
20
0



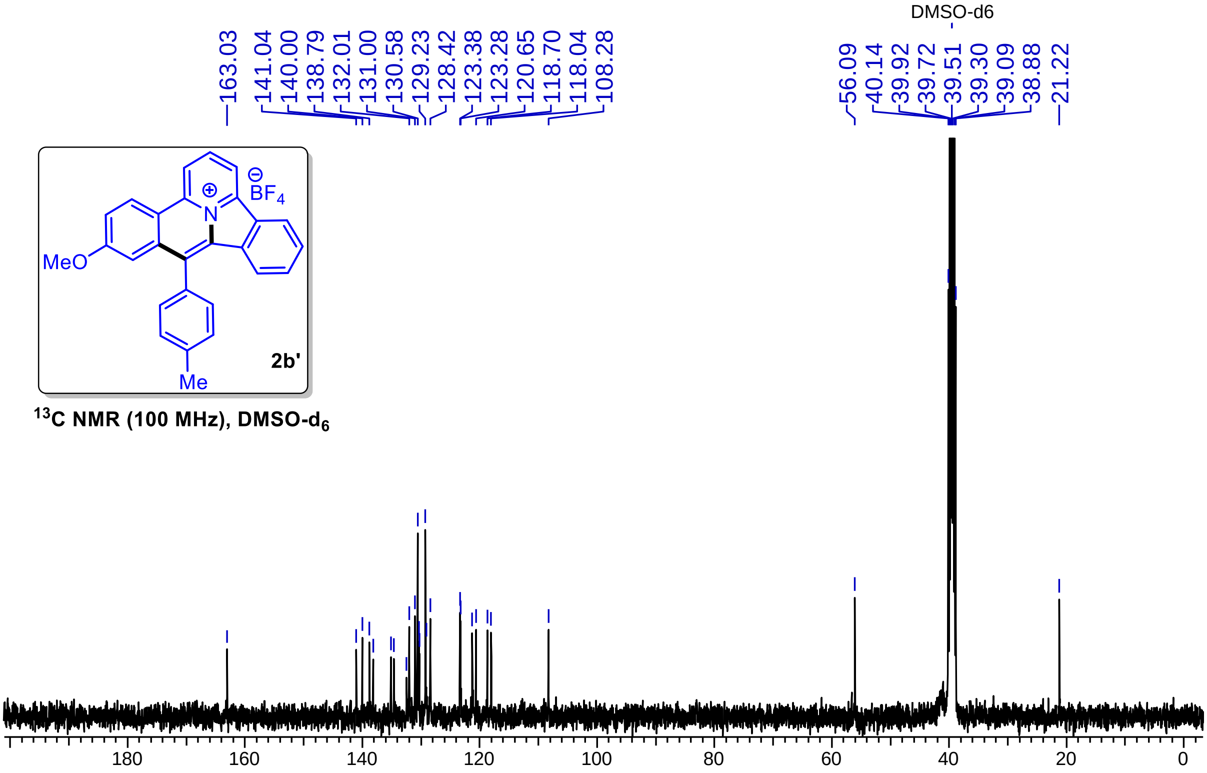
^{1}H NMR (400 MHz), DMSO-d_6



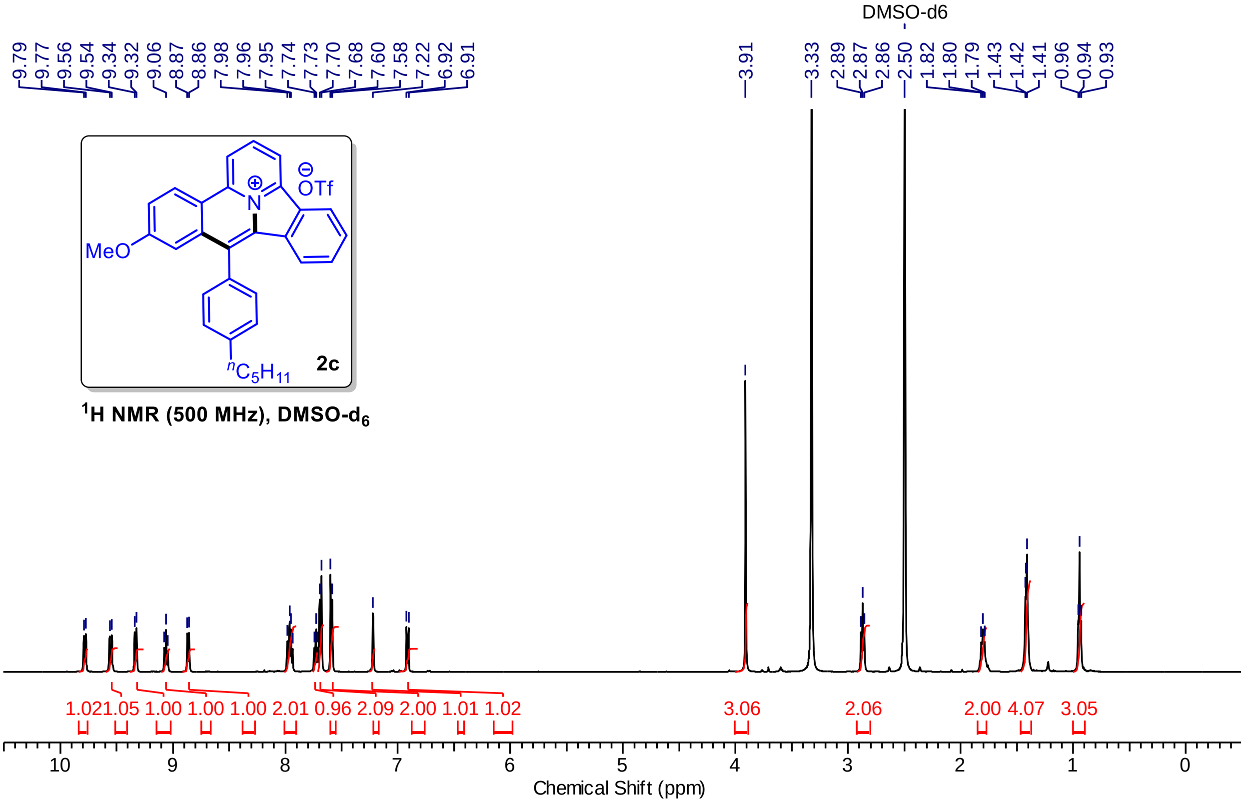
^{13}C NMR (100 MHz), DMSO-d_6



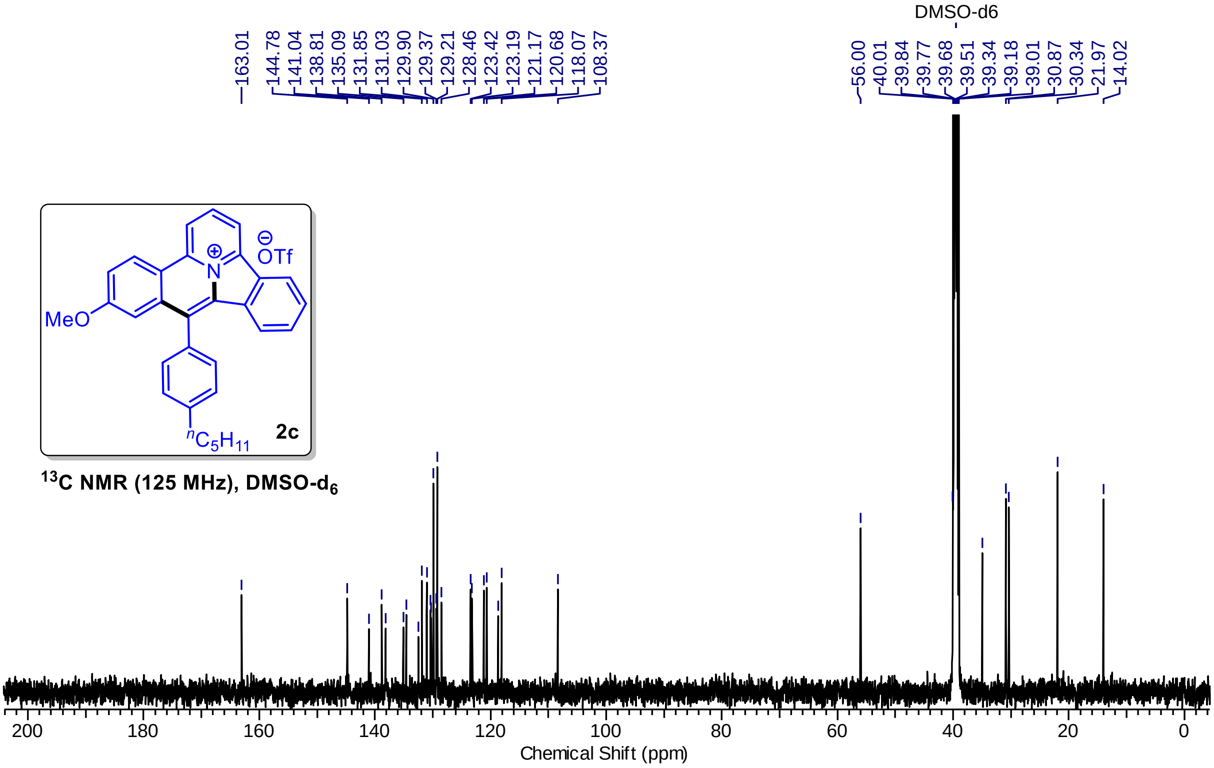
^{1}H NMR (400 MHz), DMSO-d$_6$



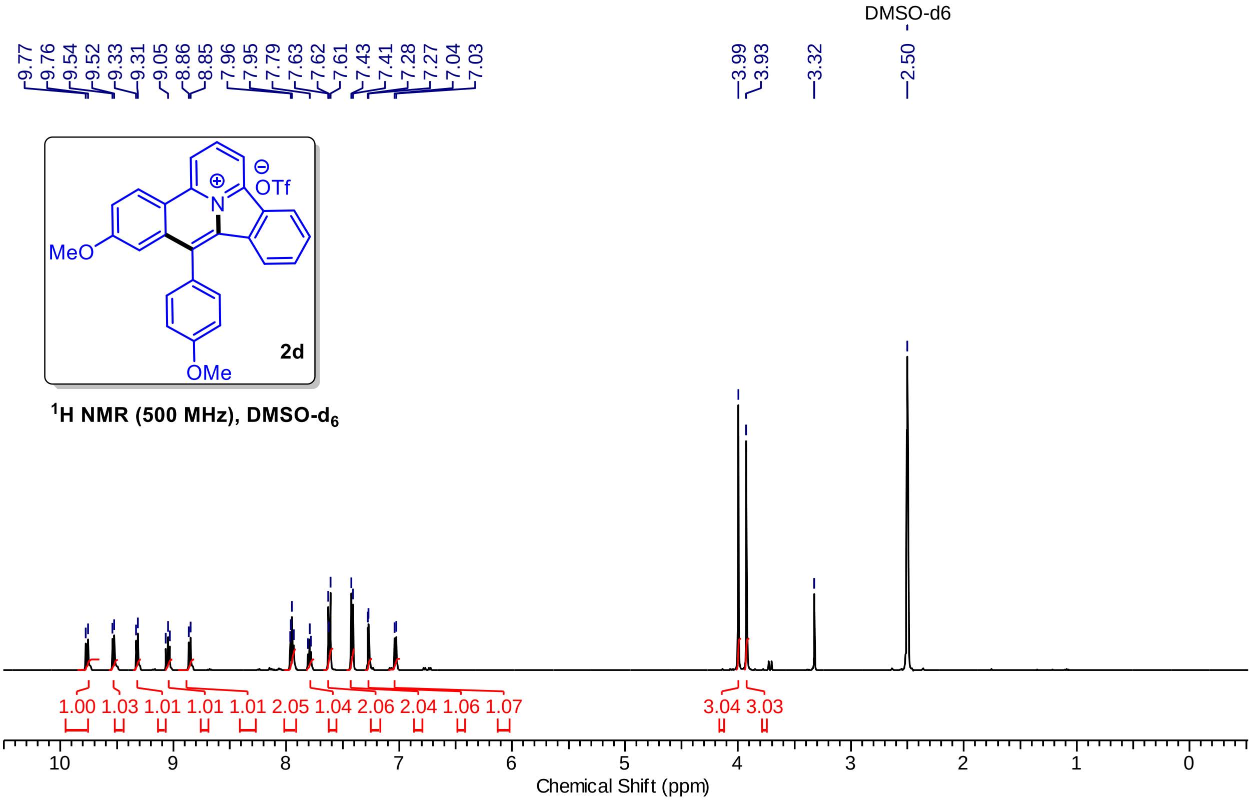
^{13}C NMR (100 MHz), DMSO-d$_6$



^{1}H NMR (500 MHz), DMSO-d$_6$



^{13}C NMR (125 MHz), DMSO-d$_6$


DMSO-d6
9.77
9.76
9.54
9.52
9.33
9.31
9.05
8.86
8.85
7.96
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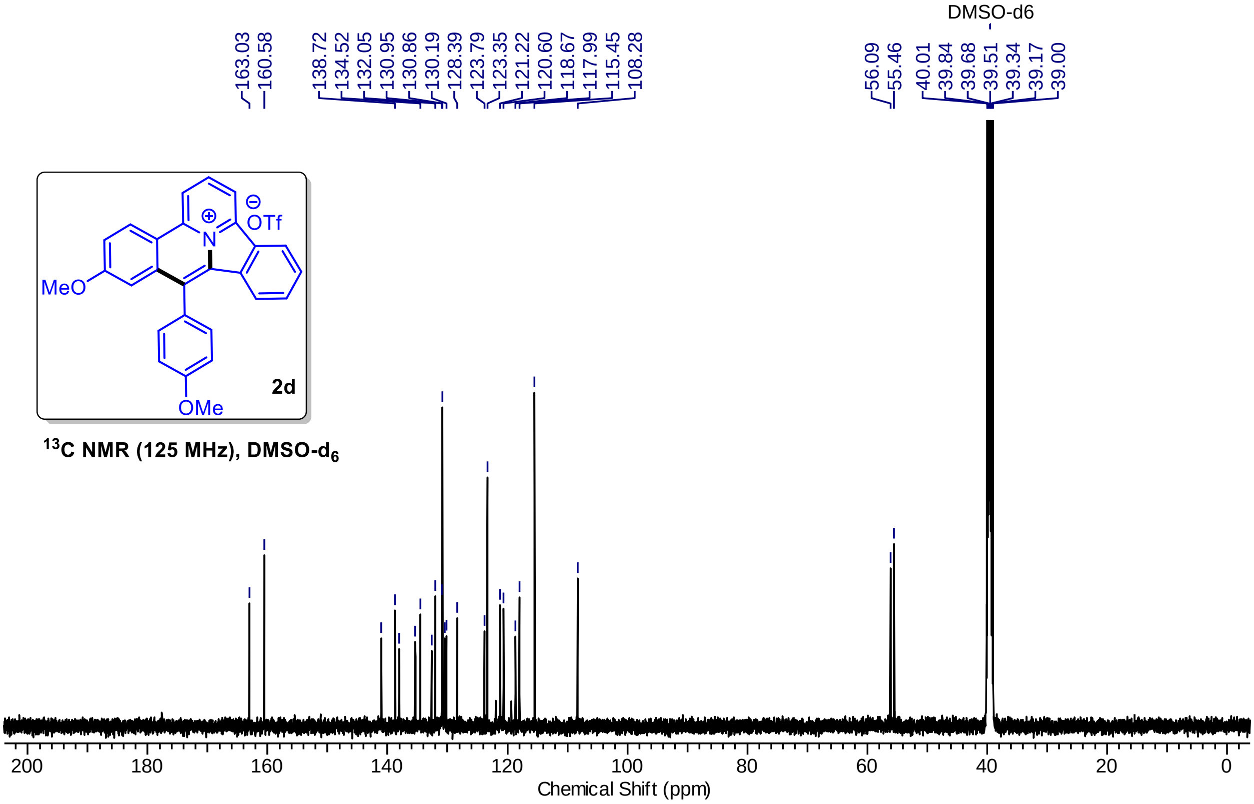
7.63
7.62
7.61
7.43
7.41
7.28
7.27
7.04
7.03
3.99
3.93
3.32
2.50
MeO
N
OTf
OMe
2d
^{1}H NMR (500 MHz), DMSO-d$_6$
1.00
1.03
1.01
1.01
1.01
2.05
1.04
2.06
2.04
1.06
1.07
3.04
3.03
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


DMSO-d6
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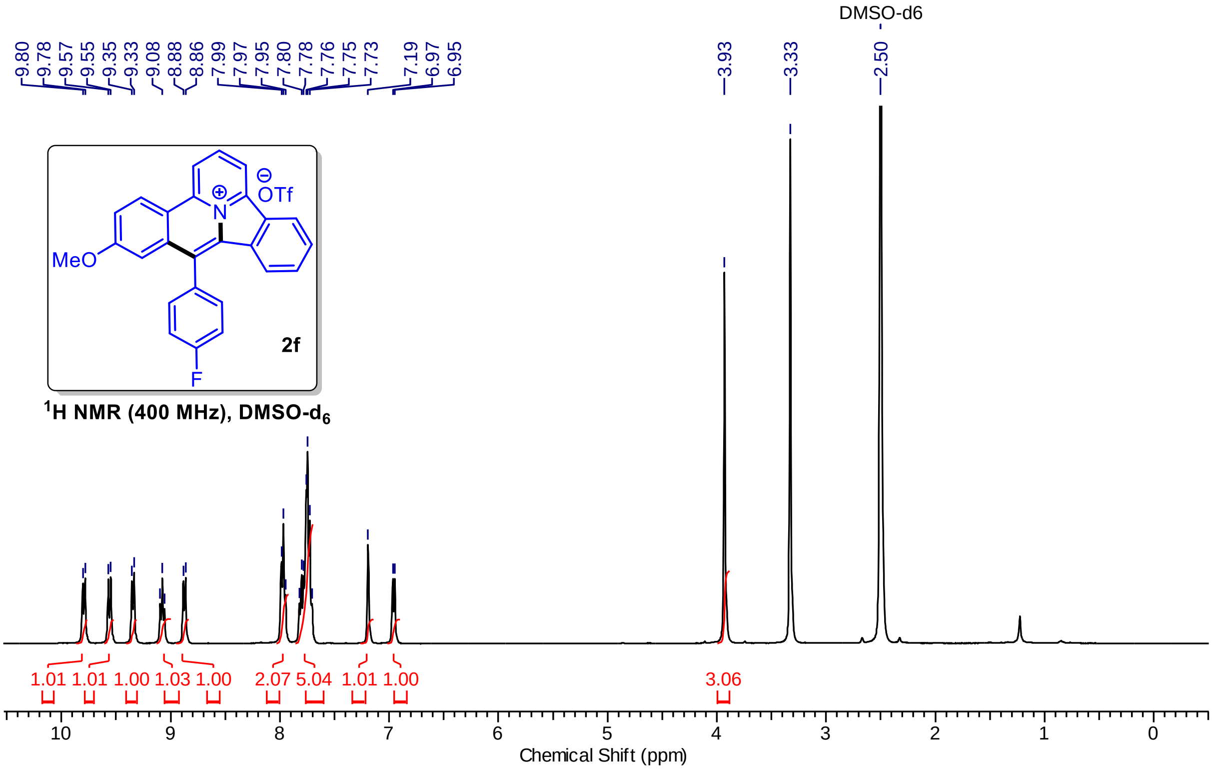
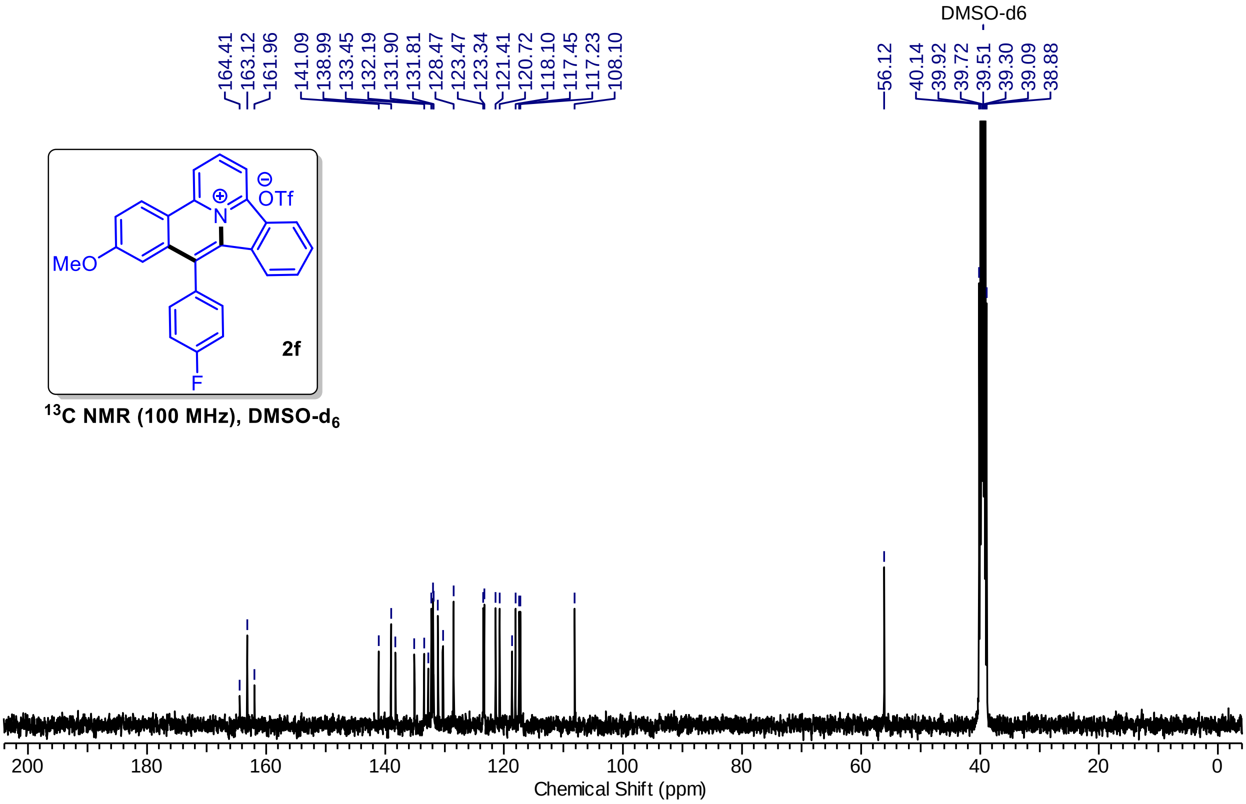
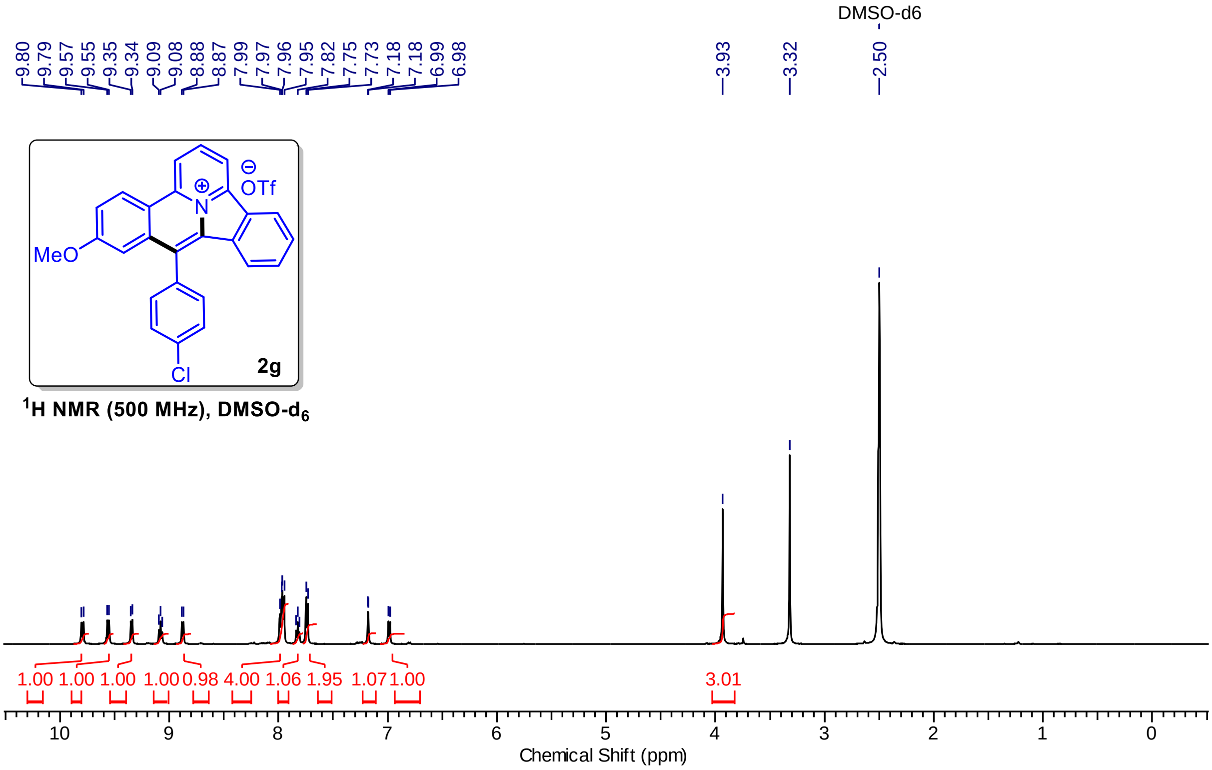
138.72
134.52
132.05
130.95
130.86
130.19
128.39
123.79
123.35
121.22
120.60
118.67
117.99
115.45
108.28
56.09
55.46
40.01
39.84
39.68
39.51
39.34
39.17
39.00
MeO
N
OTf
OMe
2d
^{13}C NMR (125 MHz), DMSO-d$_6$
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)



^{1}H NMR (400 MHz), DMSO-d$_6$

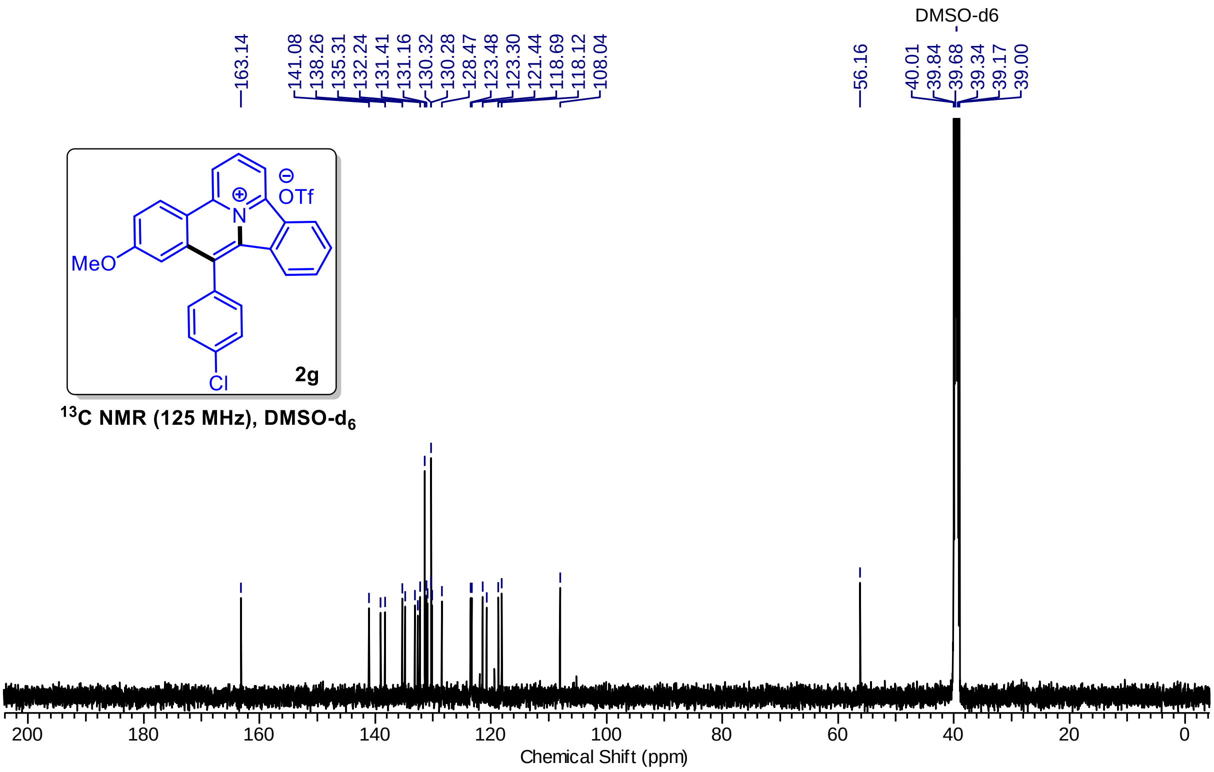


^{13}C NMR (100 MHz), DMSO-d$_6$



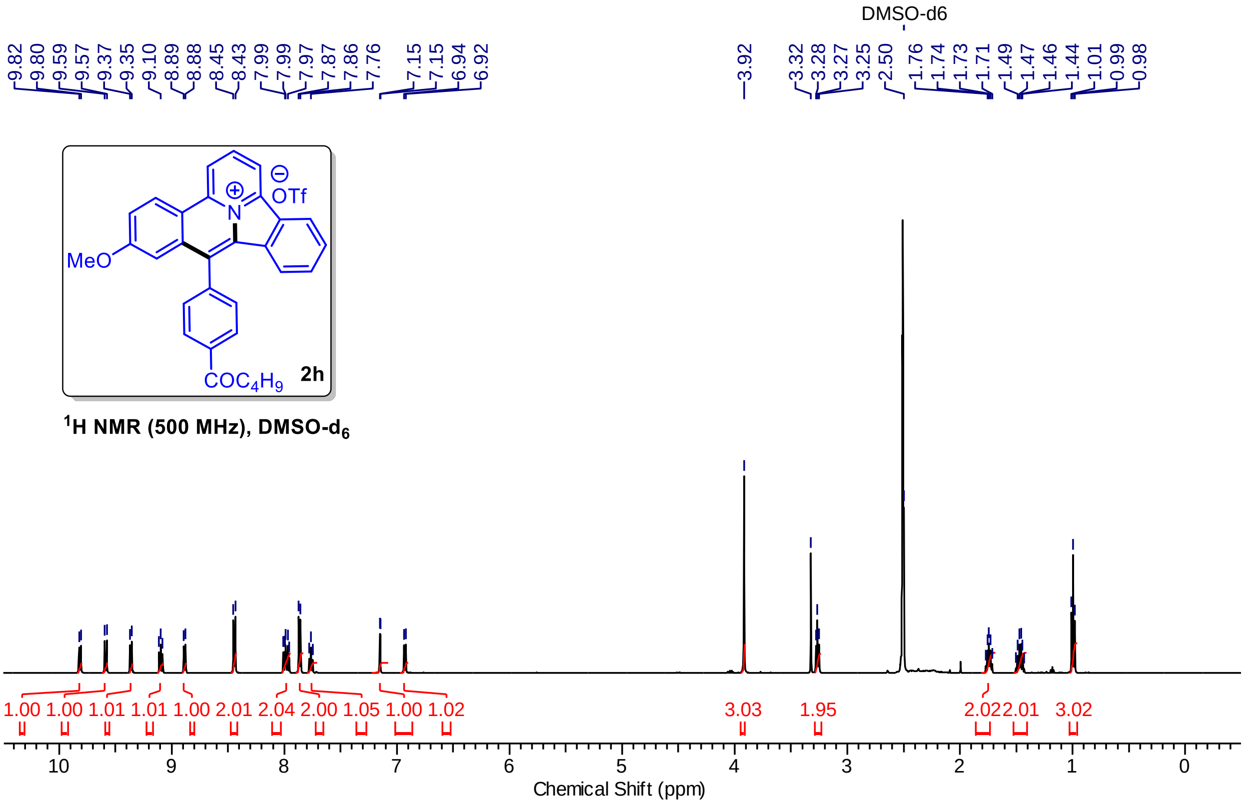
2g

^{1}H NMR (500 MHz), DMSO-d_6

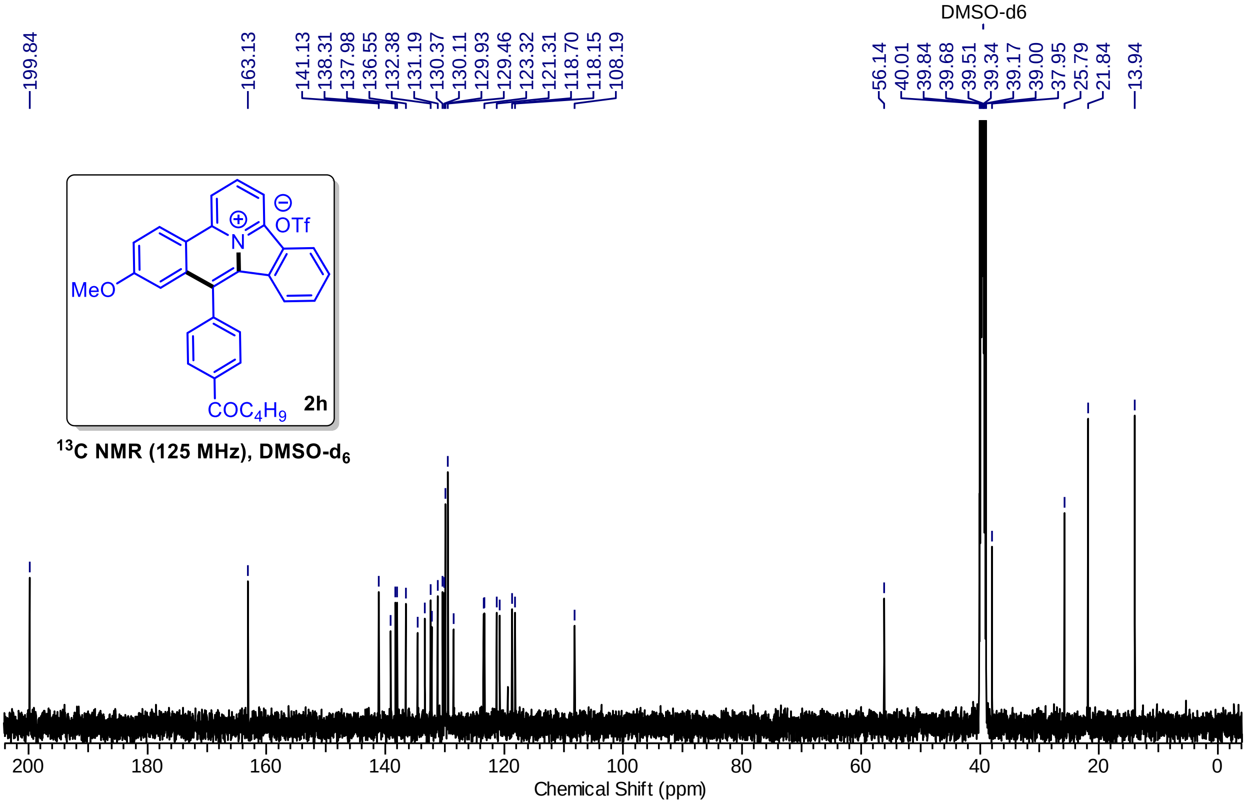


2g

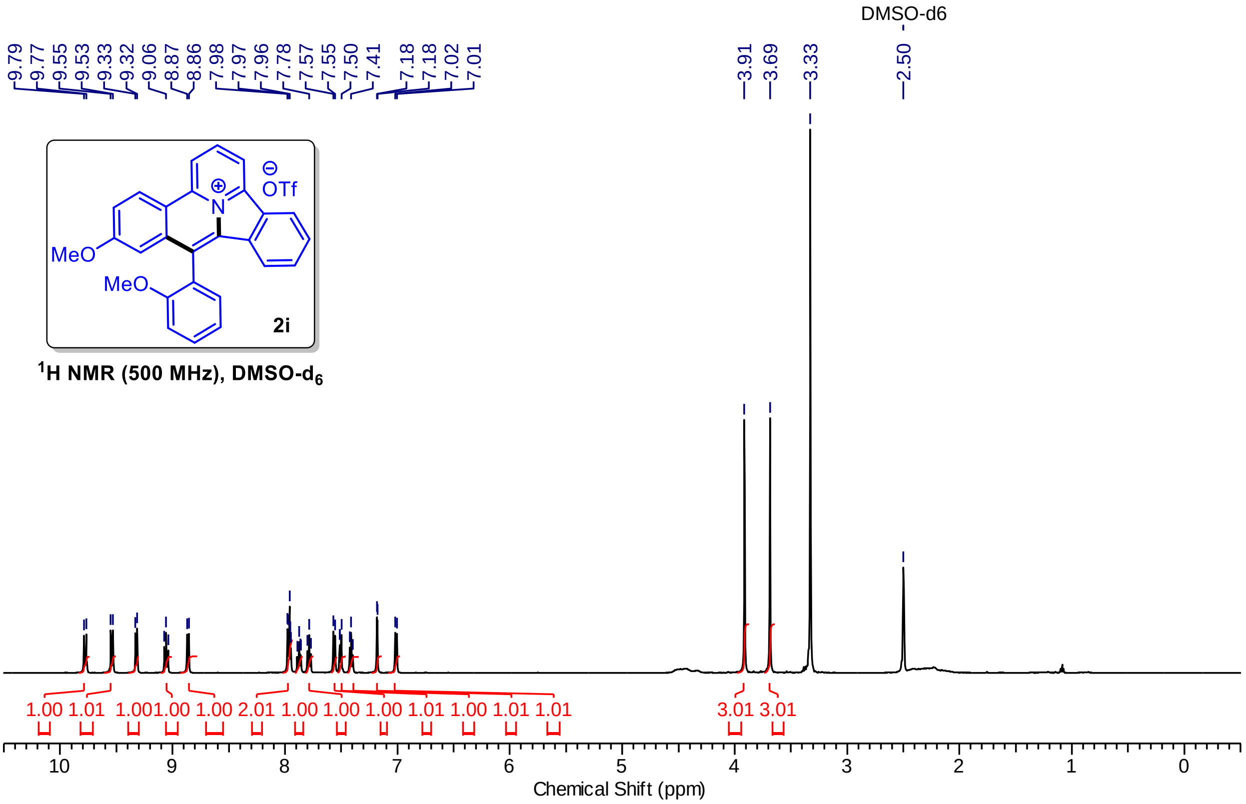
^{13}C NMR (125 MHz), DMSO-d_6



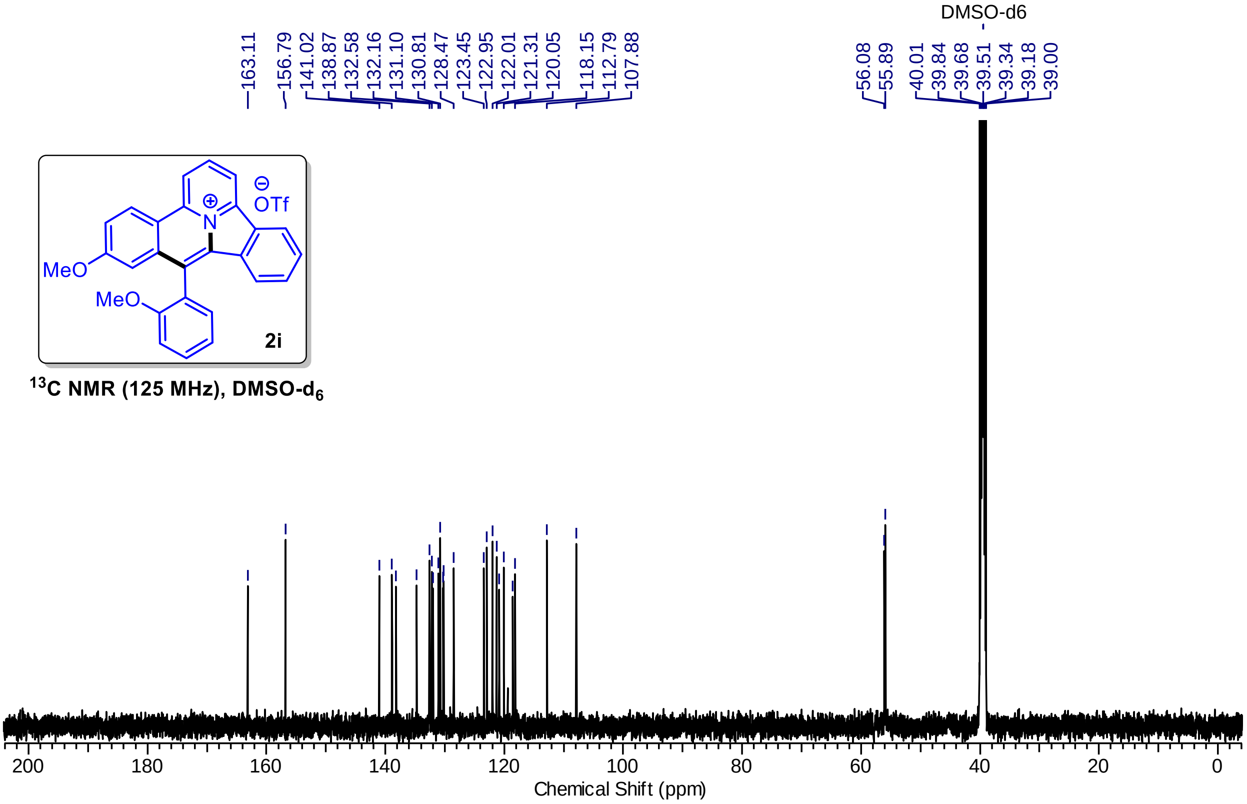
^{1}H NMR (500 MHz), DMSO-d$_6$



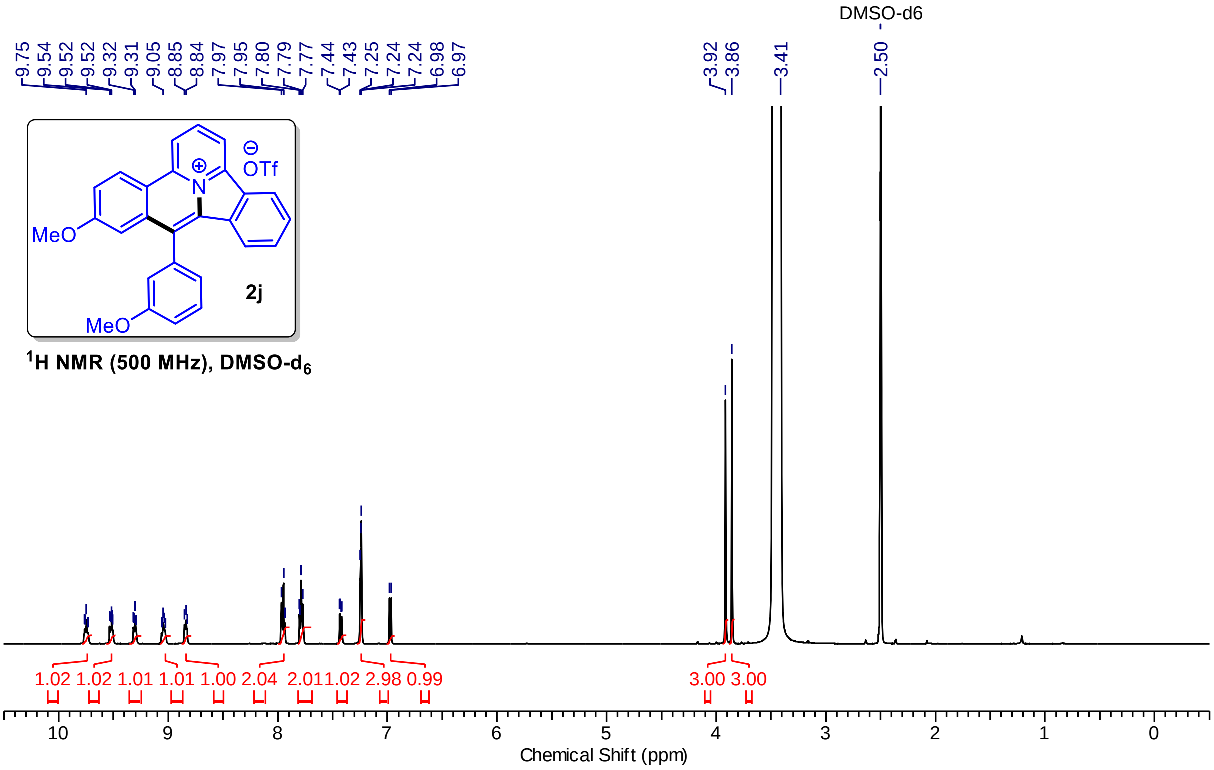
^{13}C NMR (125 MHz), DMSO-d$_6$



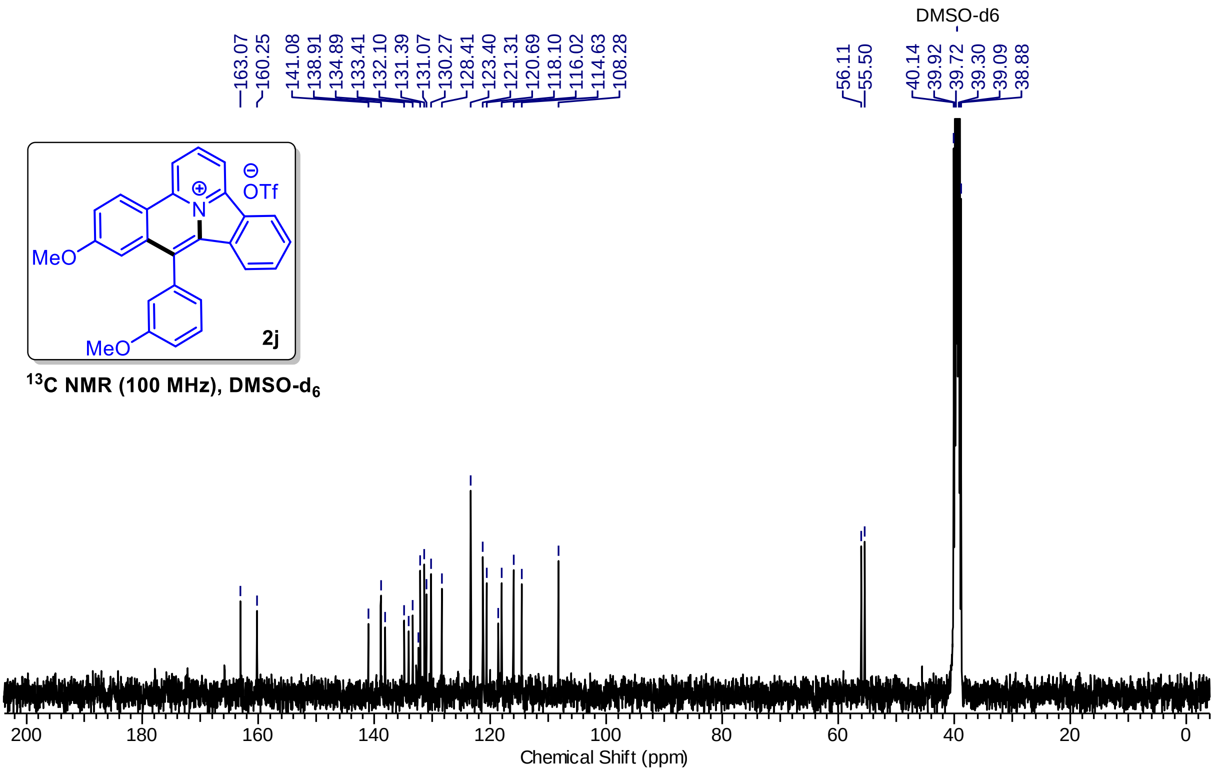
^{1}H NMR (500 MHz), DMSO-d_6



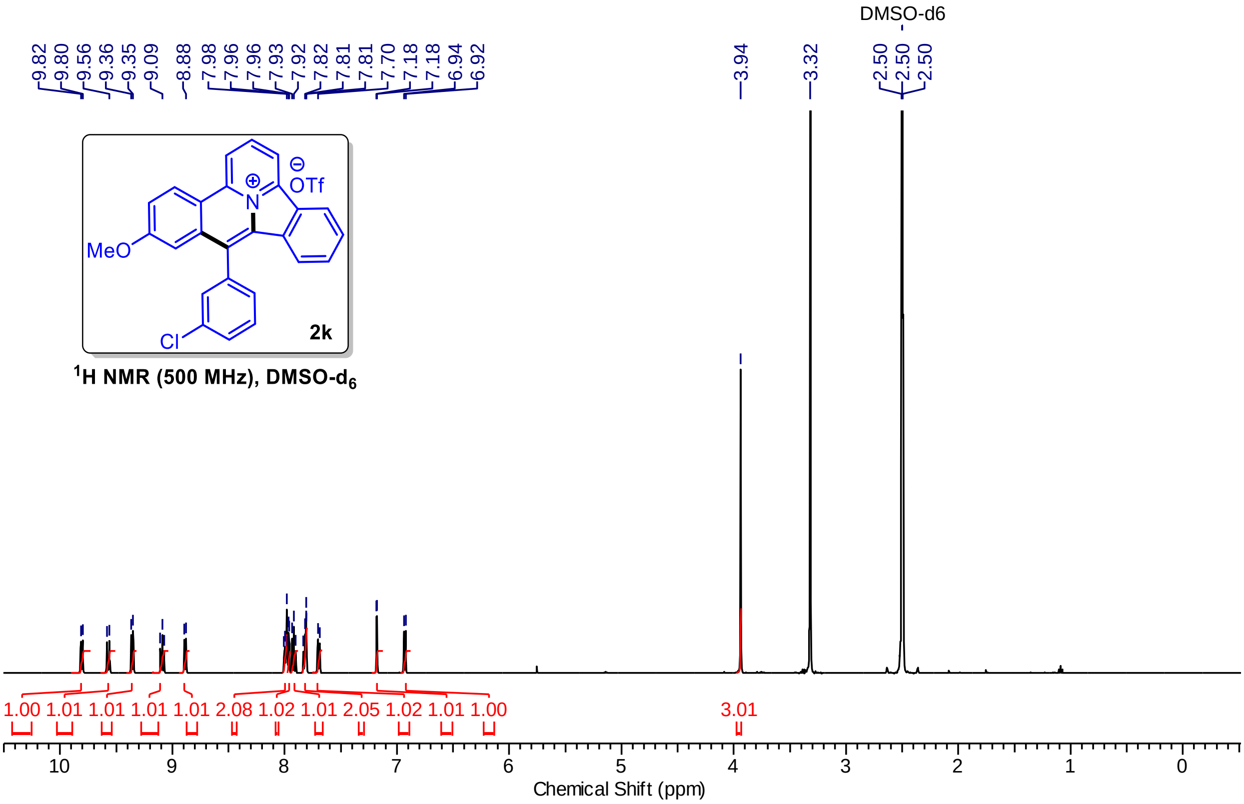
^{13}C NMR (125 MHz), DMSO-d_6

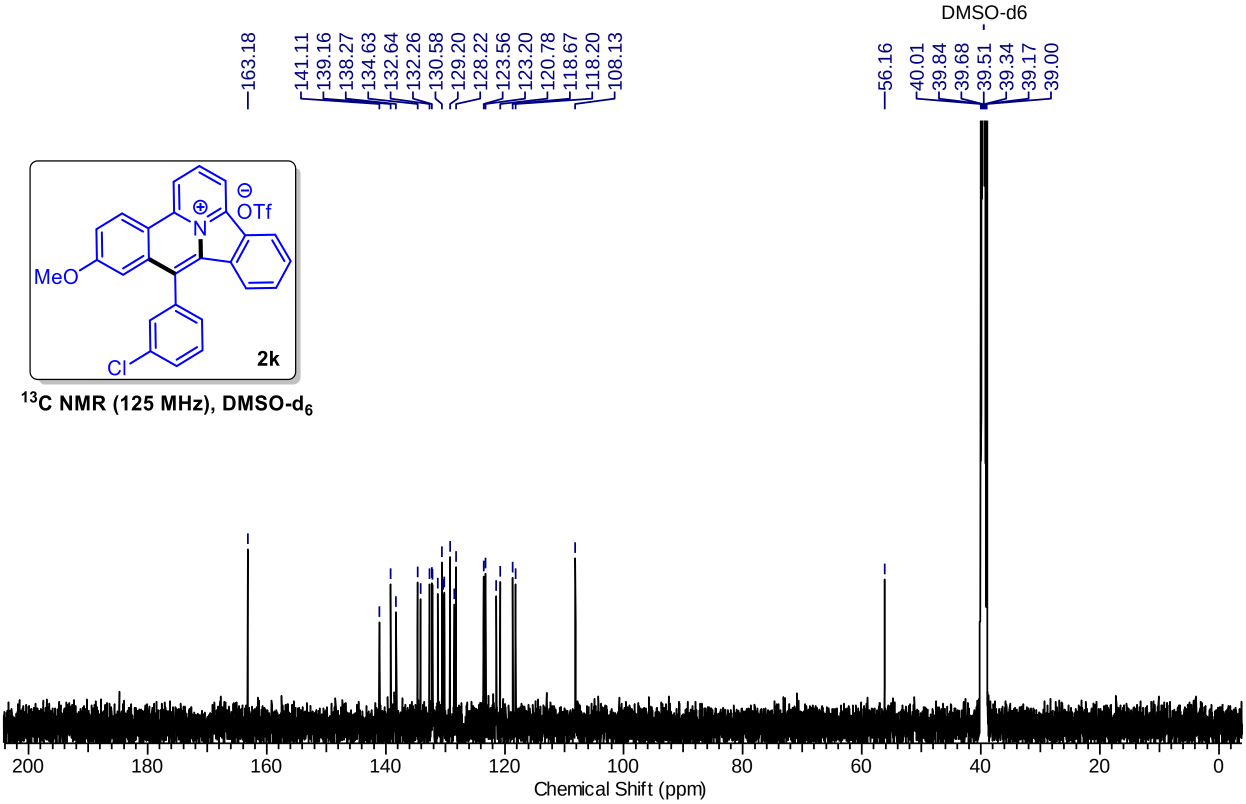


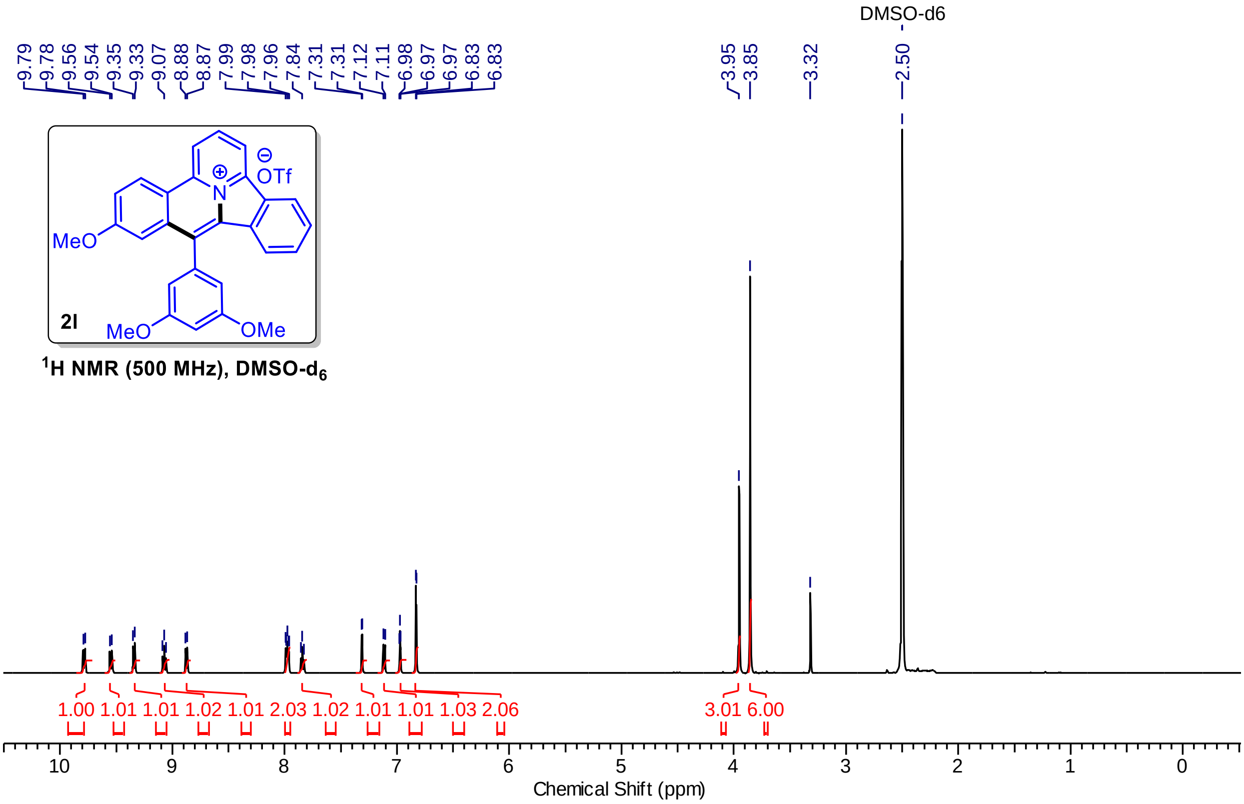
^{1}H NMR (500 MHz), DMSO-d$_6$



^{13}C NMR (100 MHz), DMSO-d$_6$

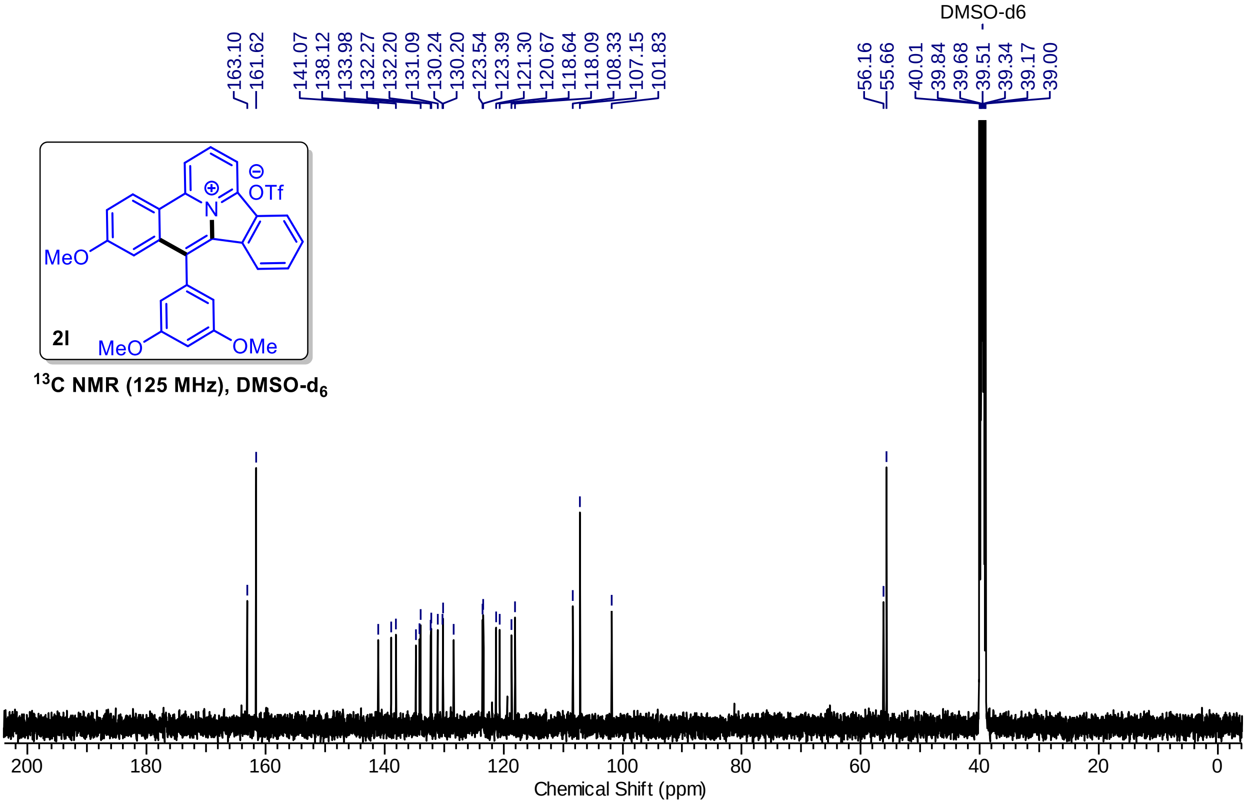

9.82
9.80
9.56
9.36
9.35
9.09
8.88
7.98
7.96
7.96
7.93
7.92
7.82
7.81
7.70
7.18
7.18
6.94
6.92
3.94
3.32
DMSO-d6
2.50
2.50
2.50
OTf
MeO
N
Cl
2k
^{1}H NMR (500 MHz), DMSO-d_6
1.00 1.01 1.01 1.01 1.01 2.08 1.02 1.01 2.05 1.02 1.01 1.00
3.01
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


163.18
141.11
139.16
138.27
134.63
132.64
132.26
130.58
129.20
128.22
123.56
123.20
120.78
118.67
118.20
108.13
56.16
DMSO-d6
40.01
39.84
39.68
39.51
39.34
39.17
39.00
OTf
MeO
N
Cl
2k
^{13}C NMR (125 MHz), DMSO-d_6
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)



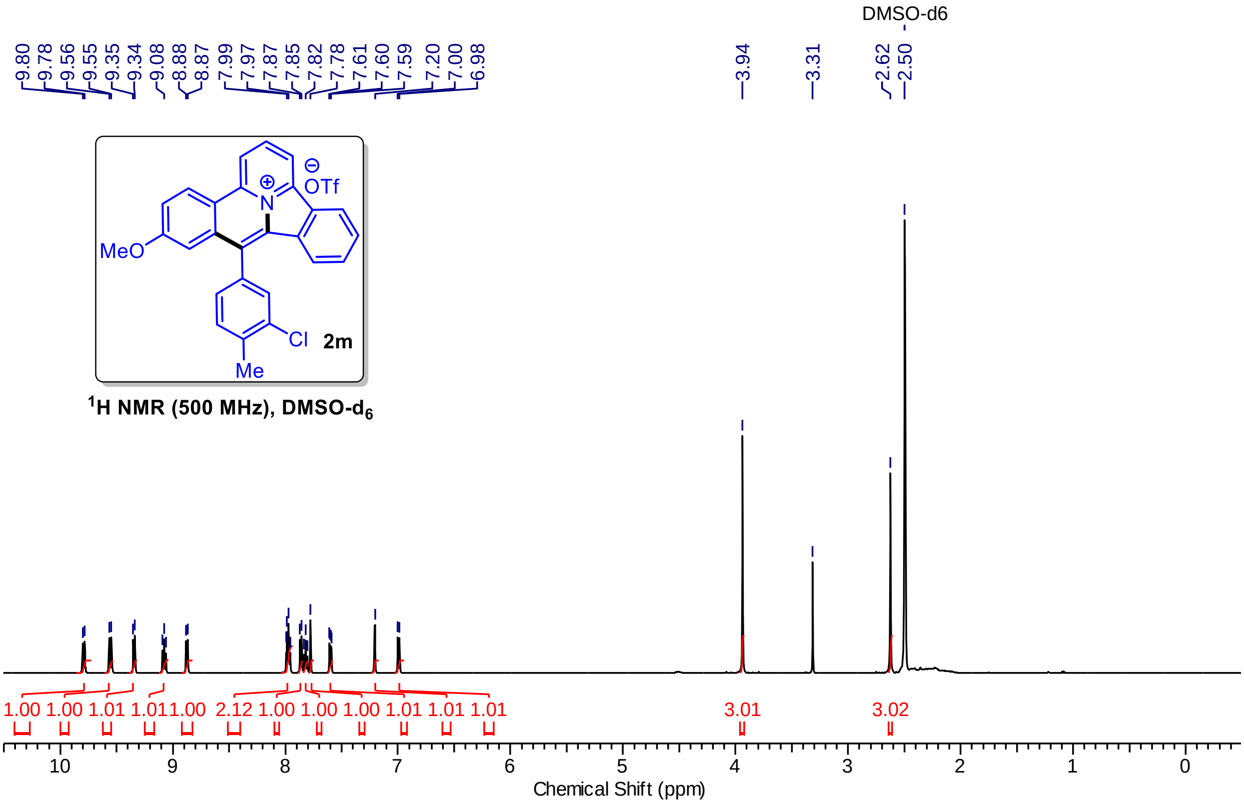
2l

^{1}H NMR (500 MHz), DMSO-d_6

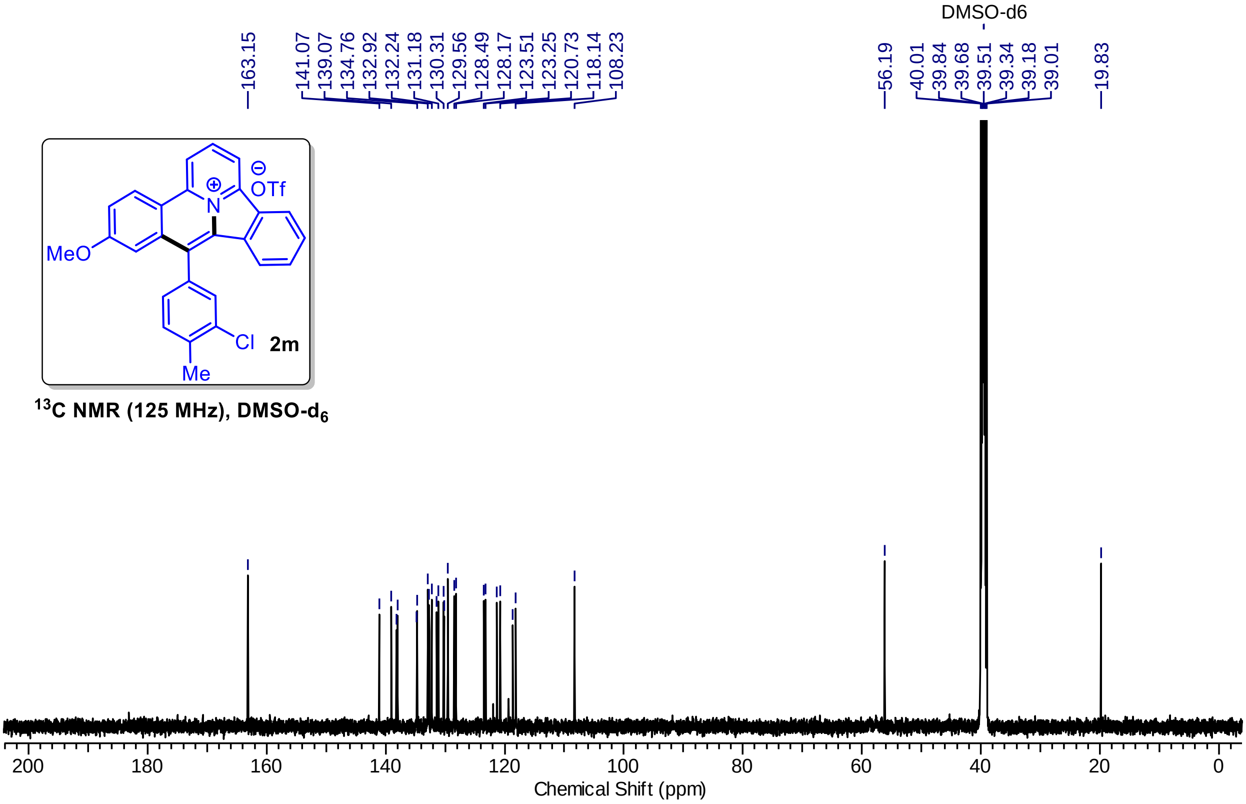


2l

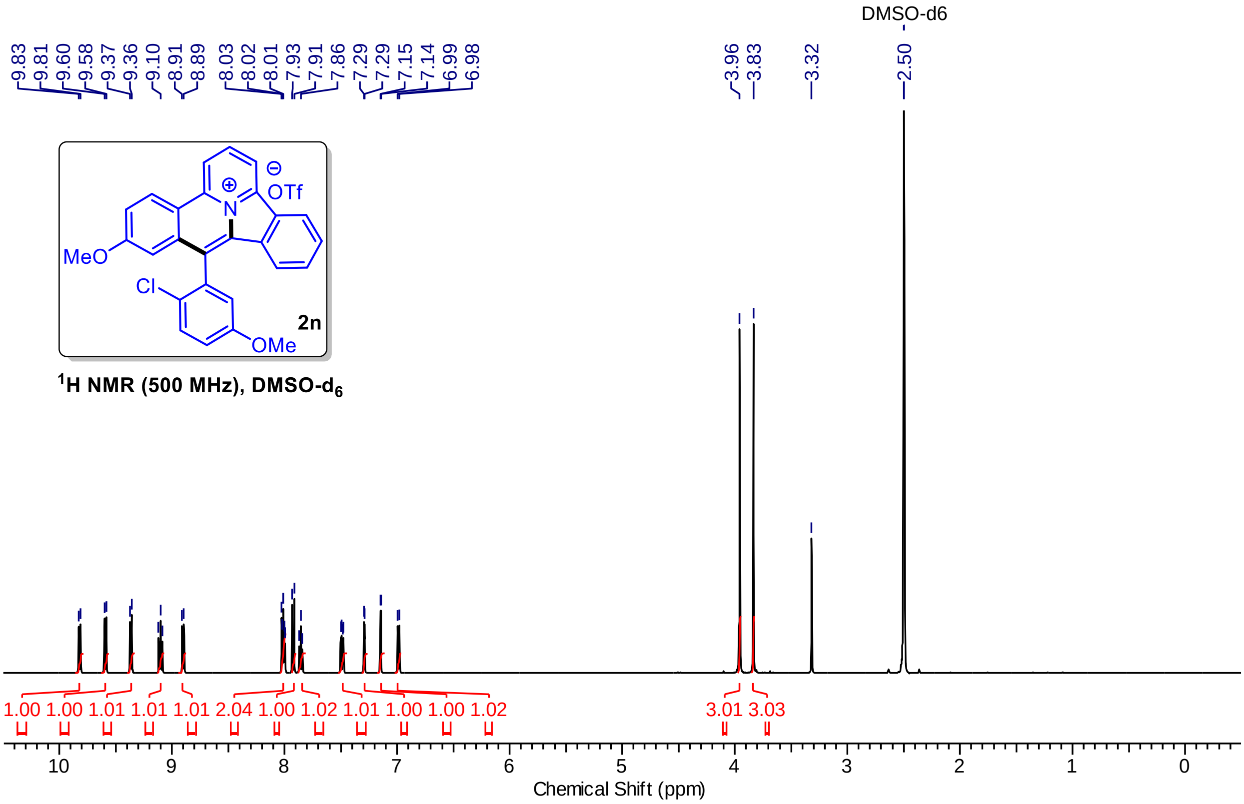
^{13}C NMR (125 MHz), DMSO-d_6



^{1}H NMR (500 MHz), DMSO-d_6

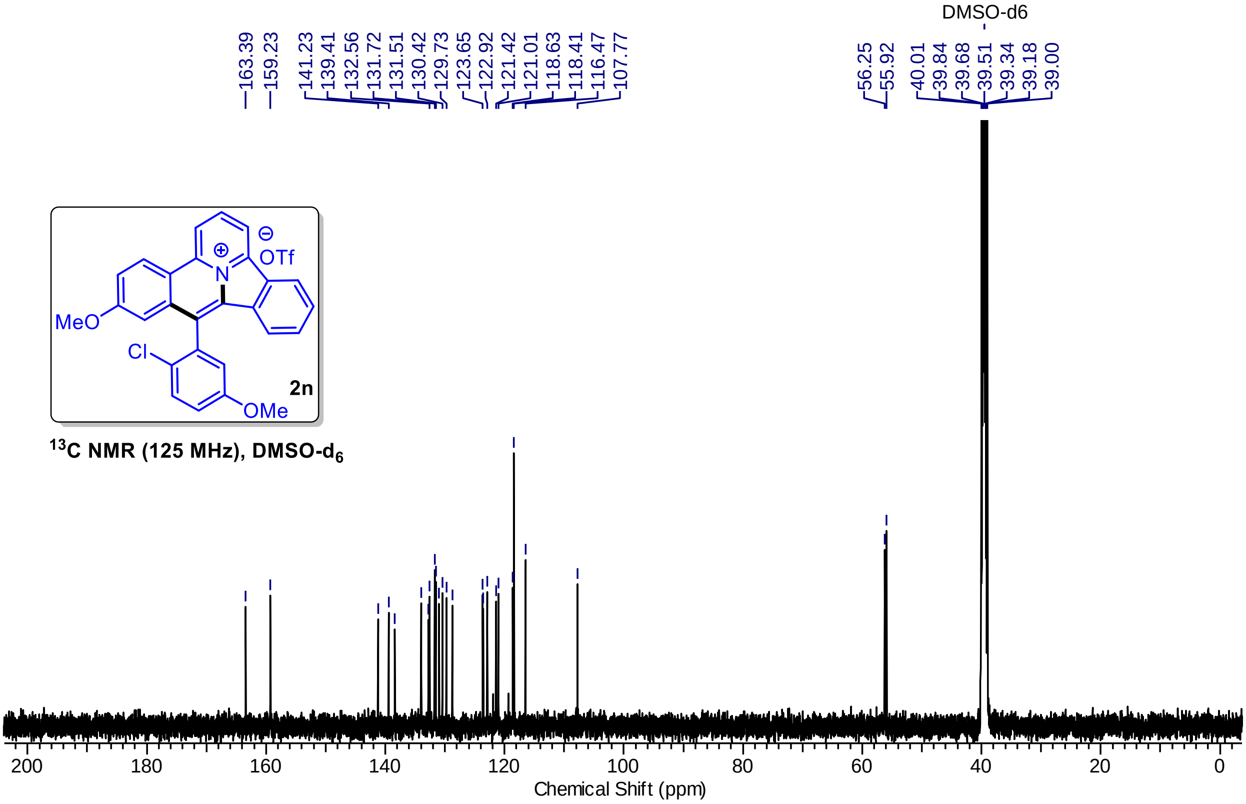


^{13}C NMR (125 MHz), DMSO-d_6



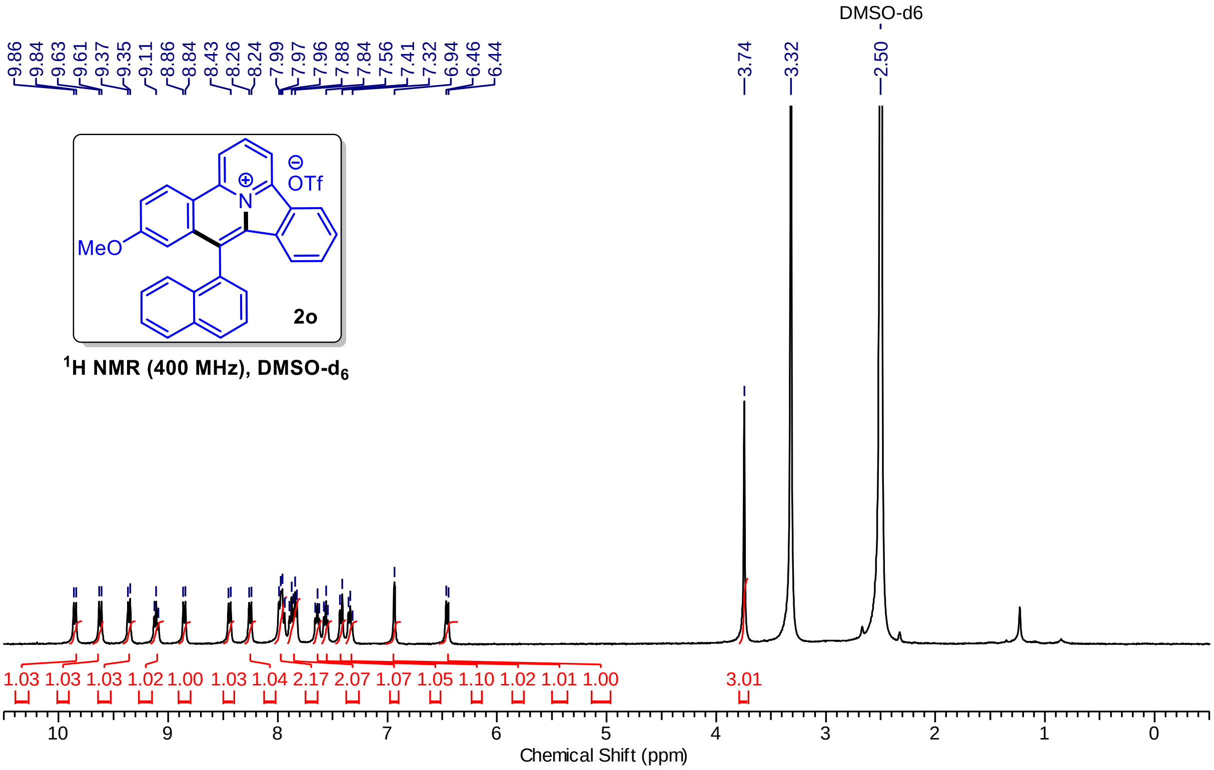
2n

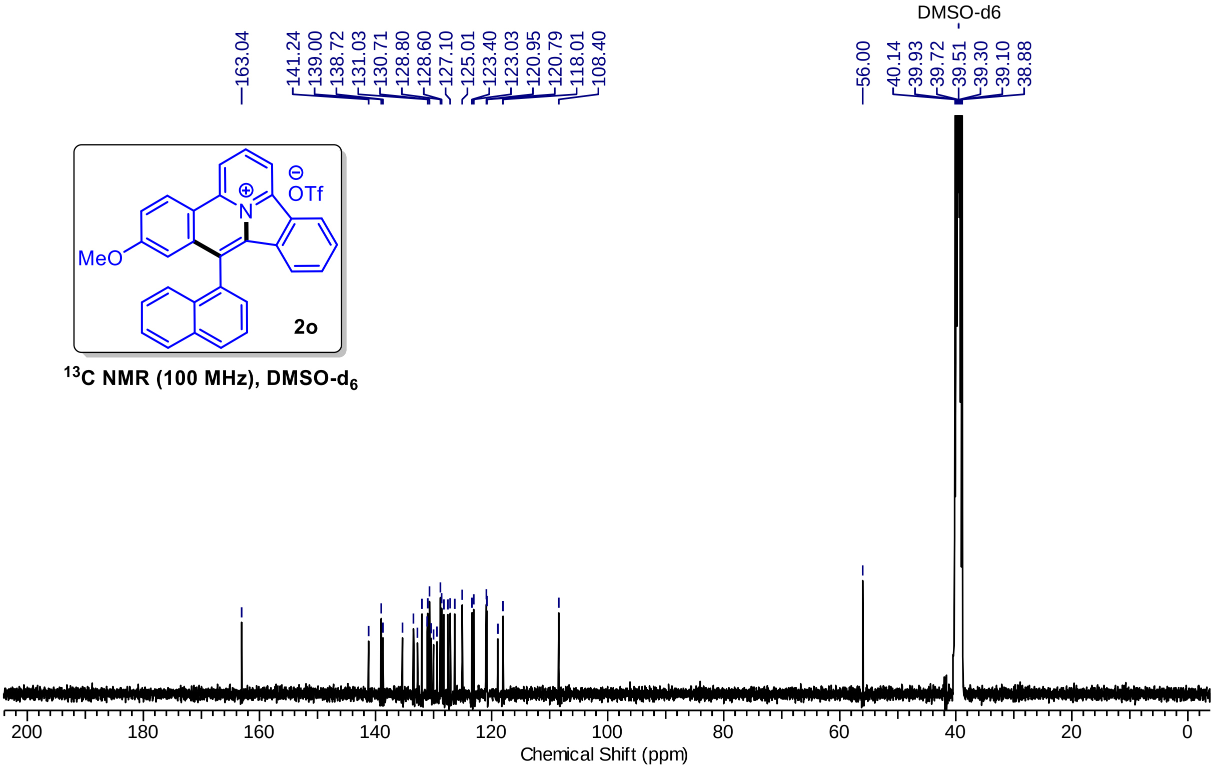
^{1}H NMR (500 MHz), DMSO-d_6

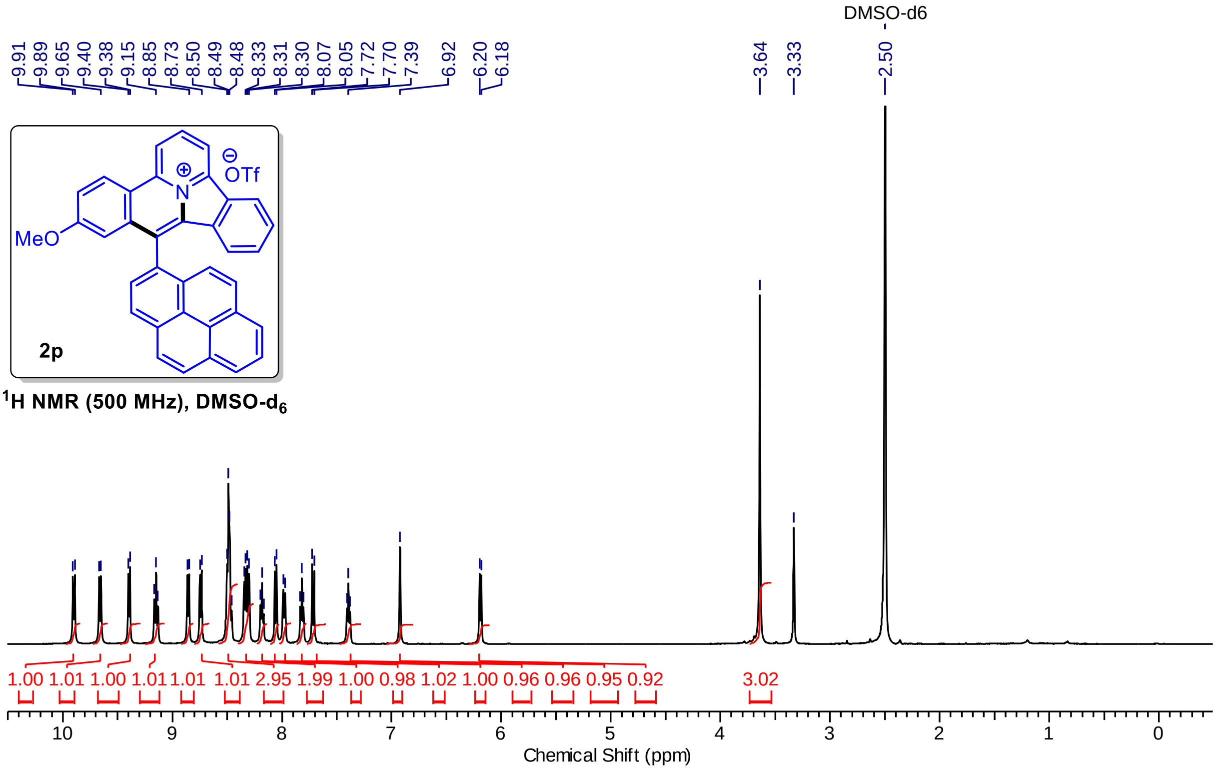


2n

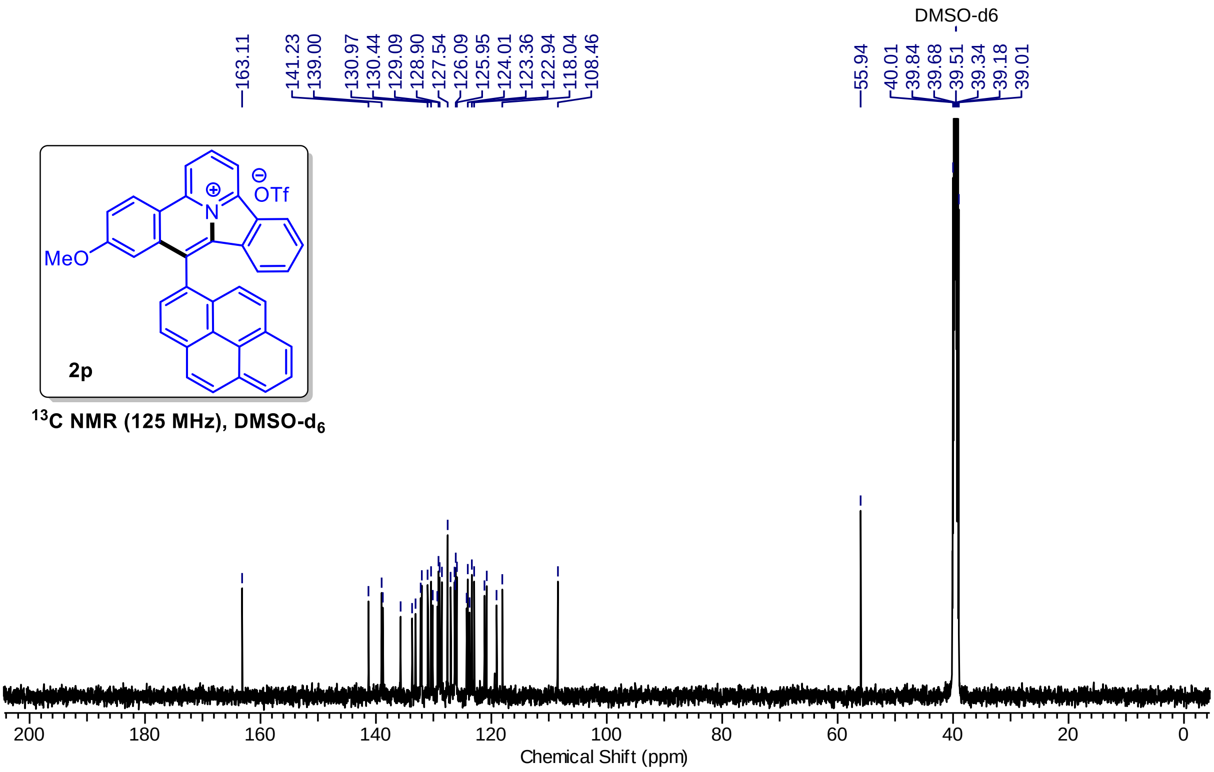
^{13}C NMR (125 MHz), DMSO-d_6


DMSO-d6
9.86
9.84
9.63
9.61
9.37
9.35
9.11
8.86
8.84
8.43
8.26
8.24
7.99
7.97
7.96
7.88
7.84
7.56
7.41
7.32
6.94
6.46
6.44
3.74
3.32
2.50
MeO
OTf
N
2o
^{1}H NMR (400 MHz), DMSO-d$_6$
1.03
1.03
1.03
1.02
1.00
1.03
1.04
2.17
2.07
1.07
1.05
1.10
1.02
1.01
1.00
3.01
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

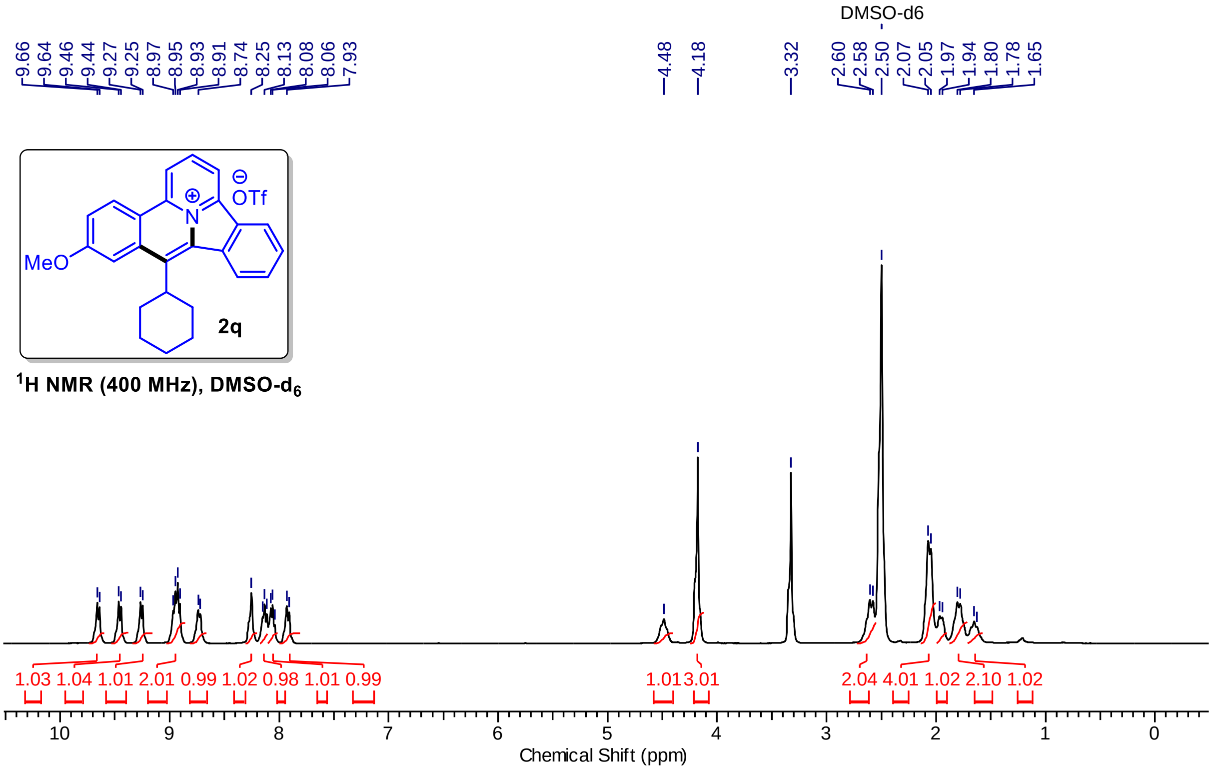

DMSO-d6
163.04
141.24
139.00
138.72
131.03
130.71
128.80
128.60
127.10
125.01
123.40
123.03
120.95
120.79
118.01
108.40
56.00
40.14
39.93
39.72
39.51
39.30
39.10
38.88
MeO
OTf
N
2o
^{13}C NMR (100 MHz), DMSO-d$_6$
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

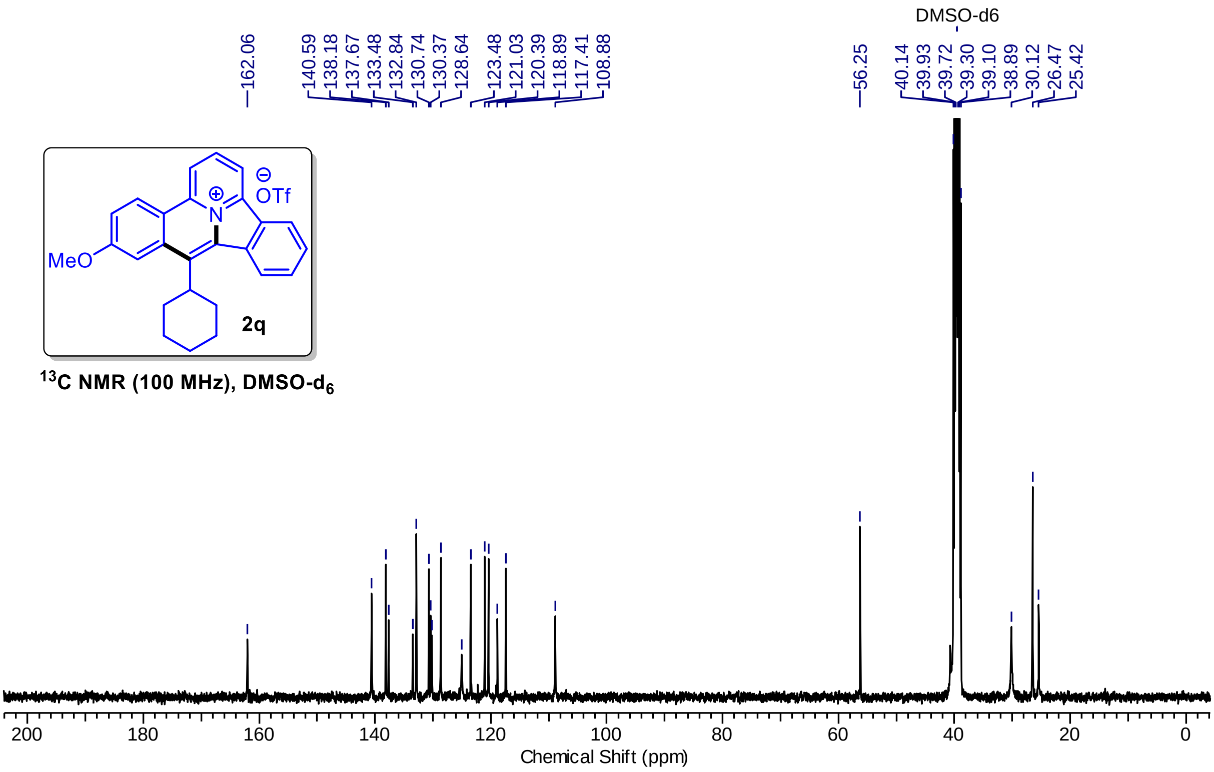


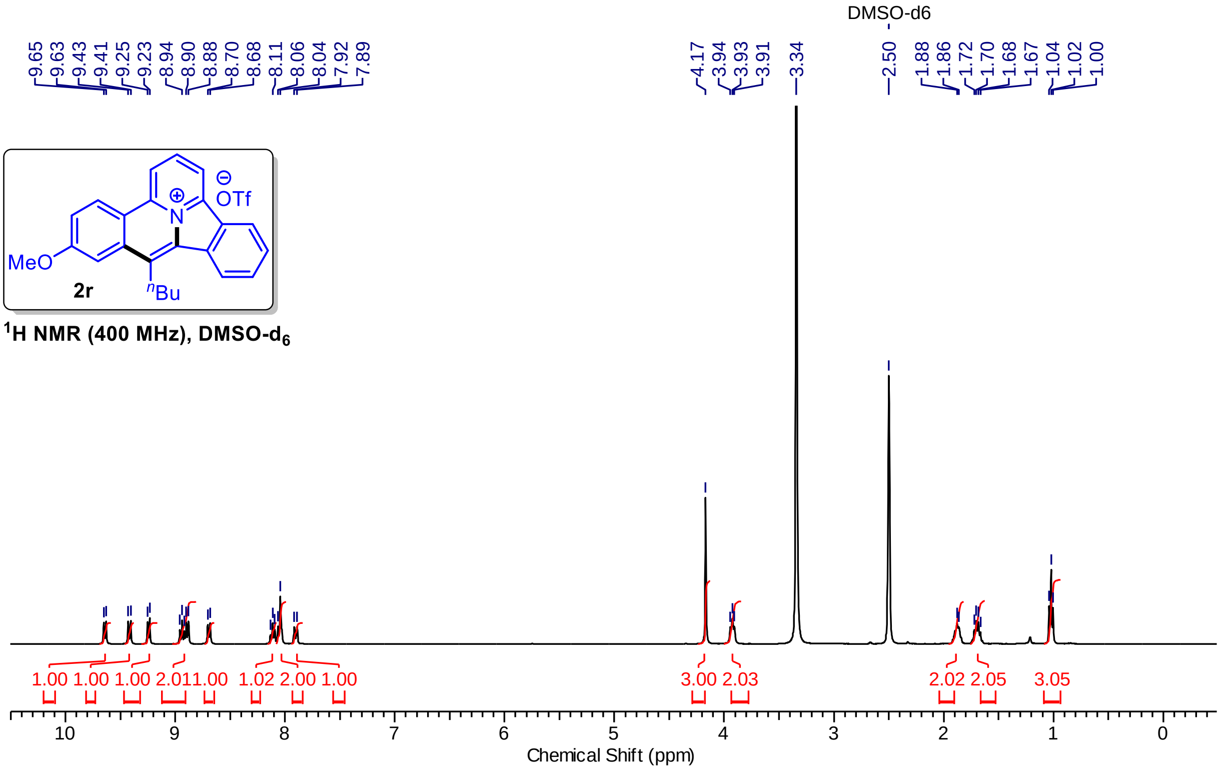
^{1}H NMR (500 MHz), DMSO-d_6



^{13}C NMR (125 MHz), DMSO-d_6

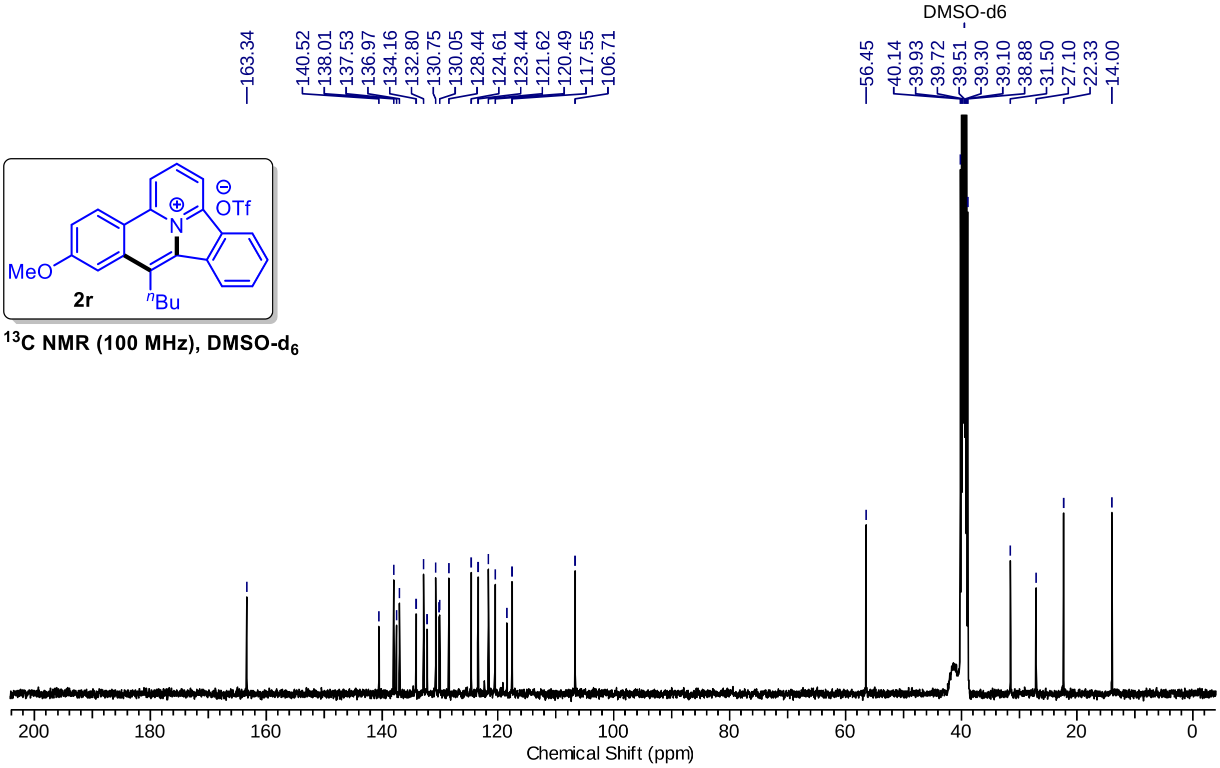

DMSO-d6
9.66
9.64
9.46
9.44
9.27
9.25
8.97
8.95
8.93
8.91
8.74
8.25
8.13
8.08
8.06
7.93
4.48
4.18
3.32
2.60
2.58
2.50
2.07
2.05
1.97
1.94
1.80
1.78
1.65
MeO
OTf
N
2q
^{1}H NMR (400 MHz), DMSO-d$_6$
1.03
1.04
1.01
2.01
0.99
1.02
0.98
1.01
0.99
1.01
3.01
2.04
4.01
1.02
2.10
1.02
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


DMSO-d6
162.06
140.59
138.18
137.67
133.48
132.84
130.74
130.37
128.64
123.48
121.03
120.39
118.89
117.41
108.88
56.25
40.14
39.93
39.72
39.30
39.10
38.89
30.12
26.47
25.42
MeO
OTf
N
2q
^{13}C NMR (100 MHz), DMSO-d$_6$
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)



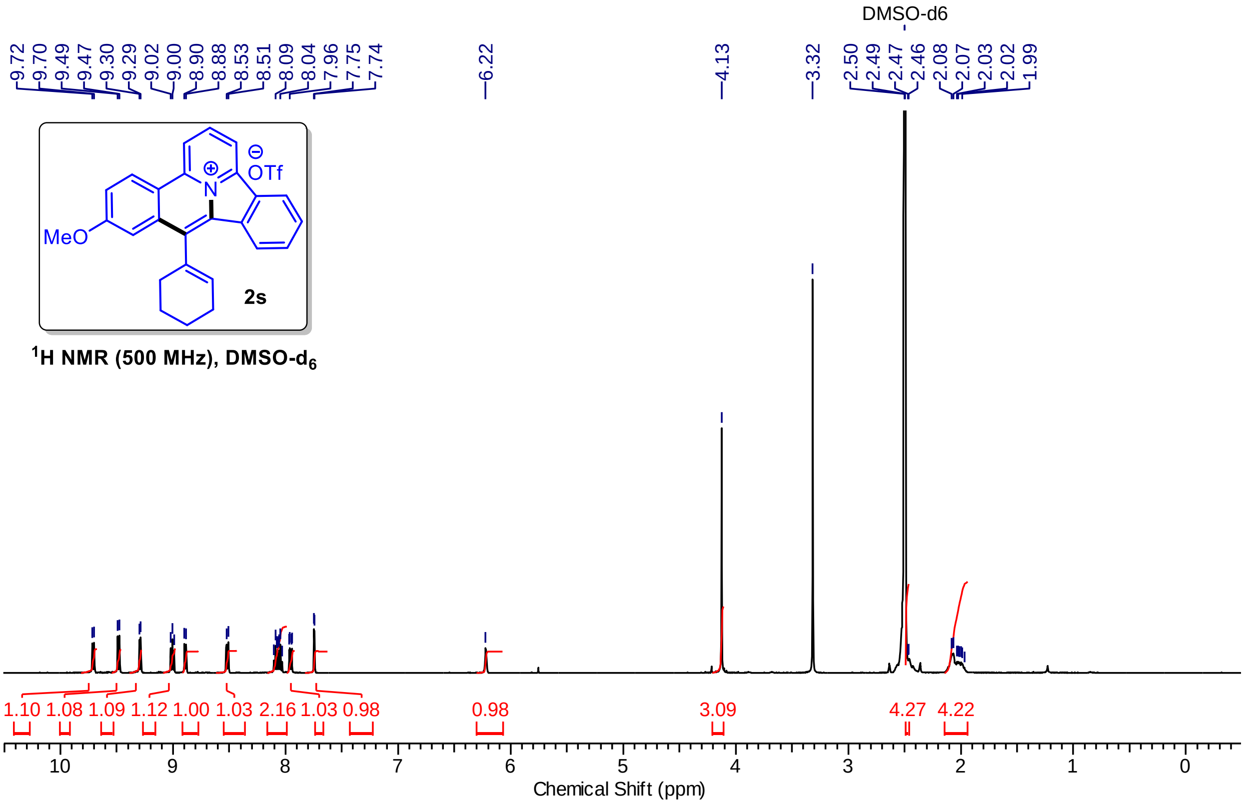
2r

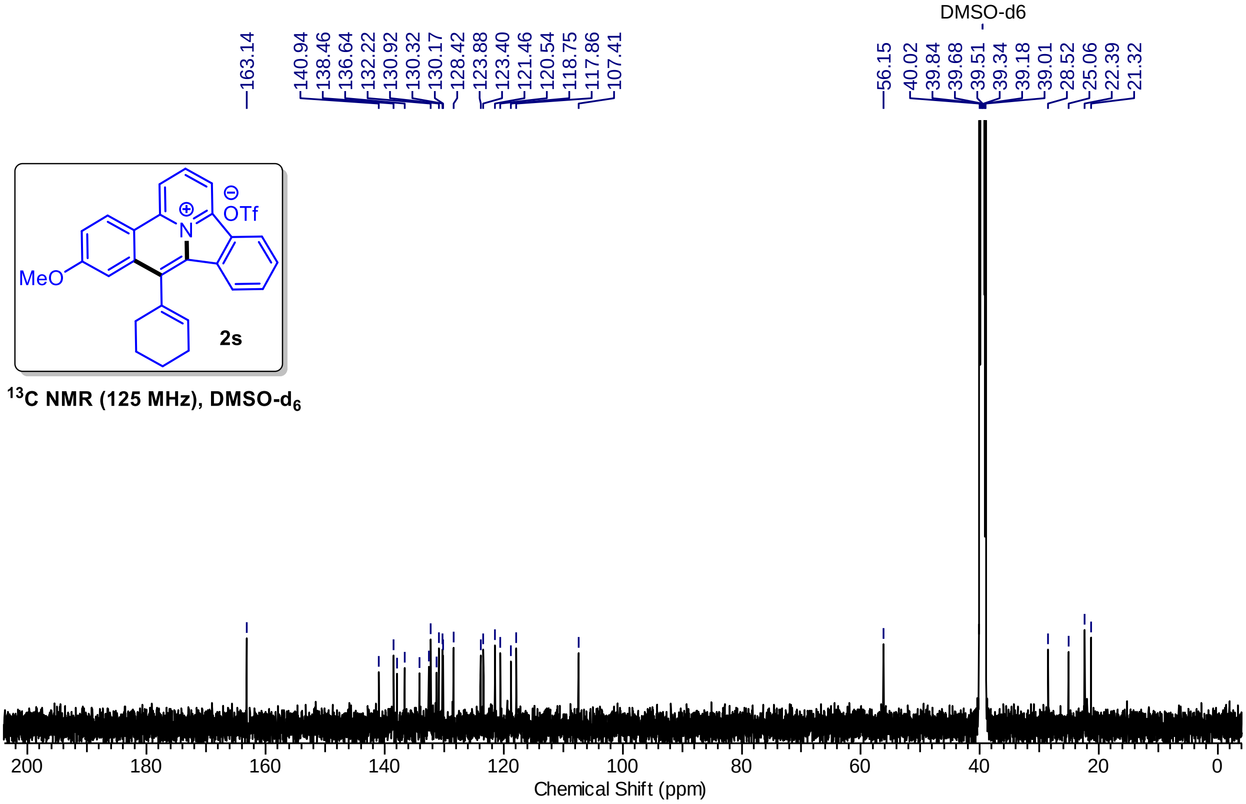
^{1}H NMR (400 MHz), DMSO-d_6

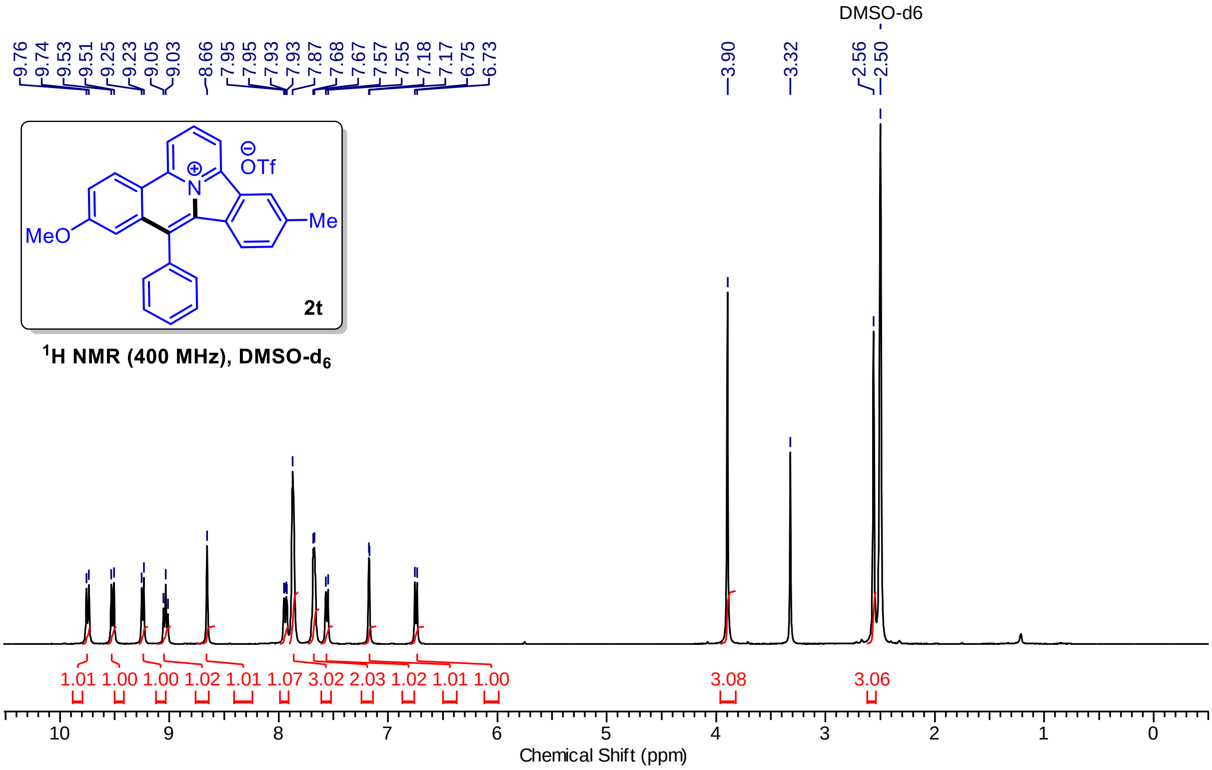


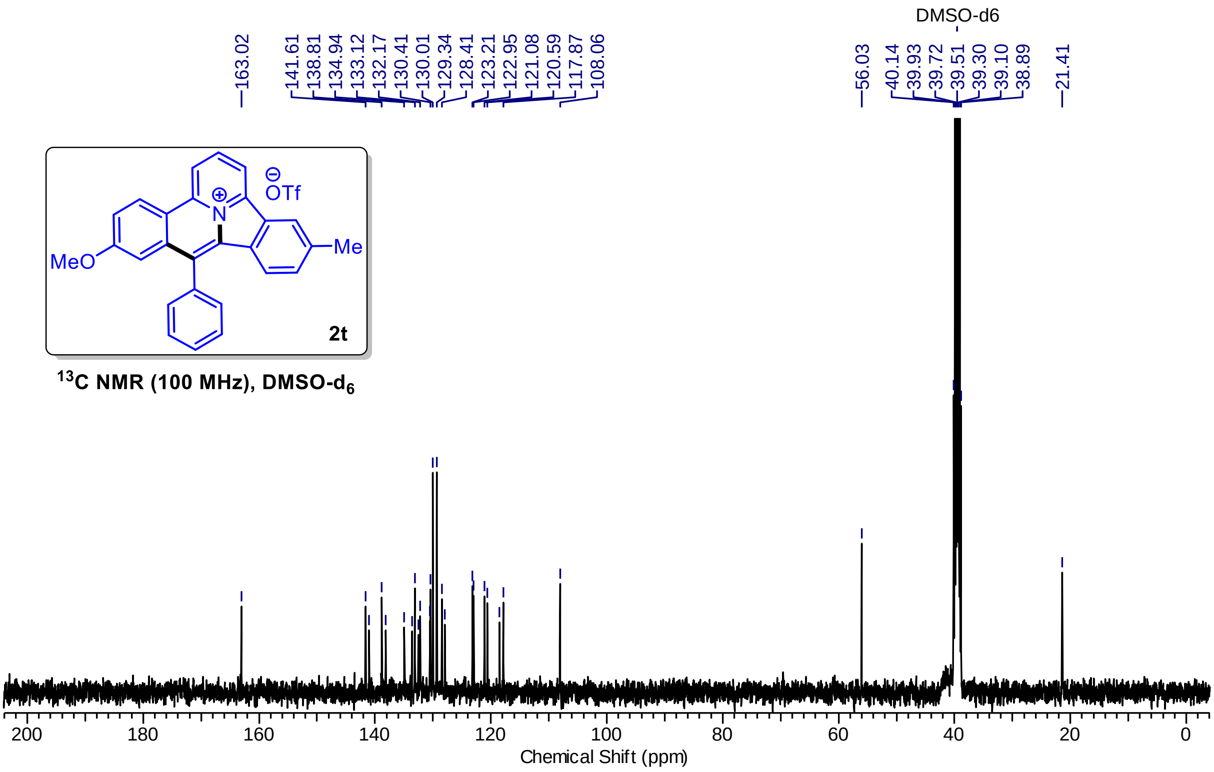
2r

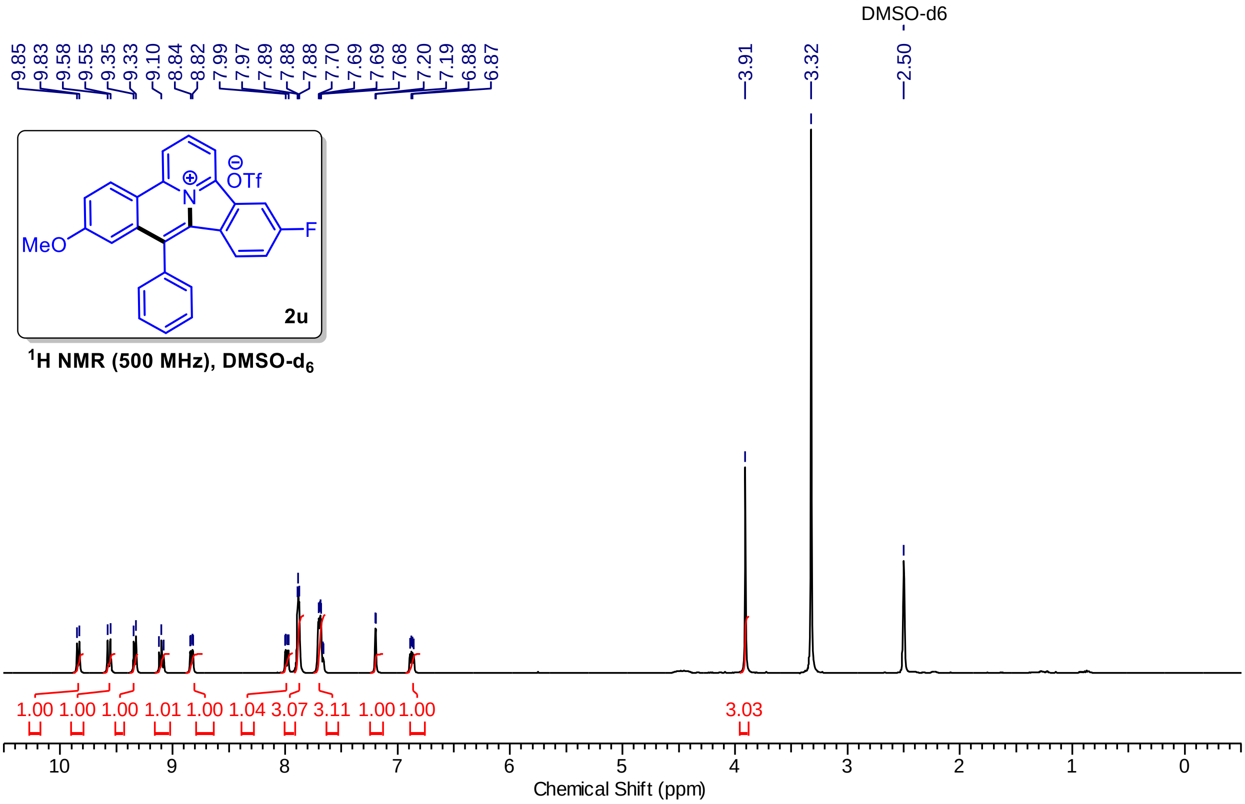
^{13}C NMR (100 MHz), DMSO-d_6

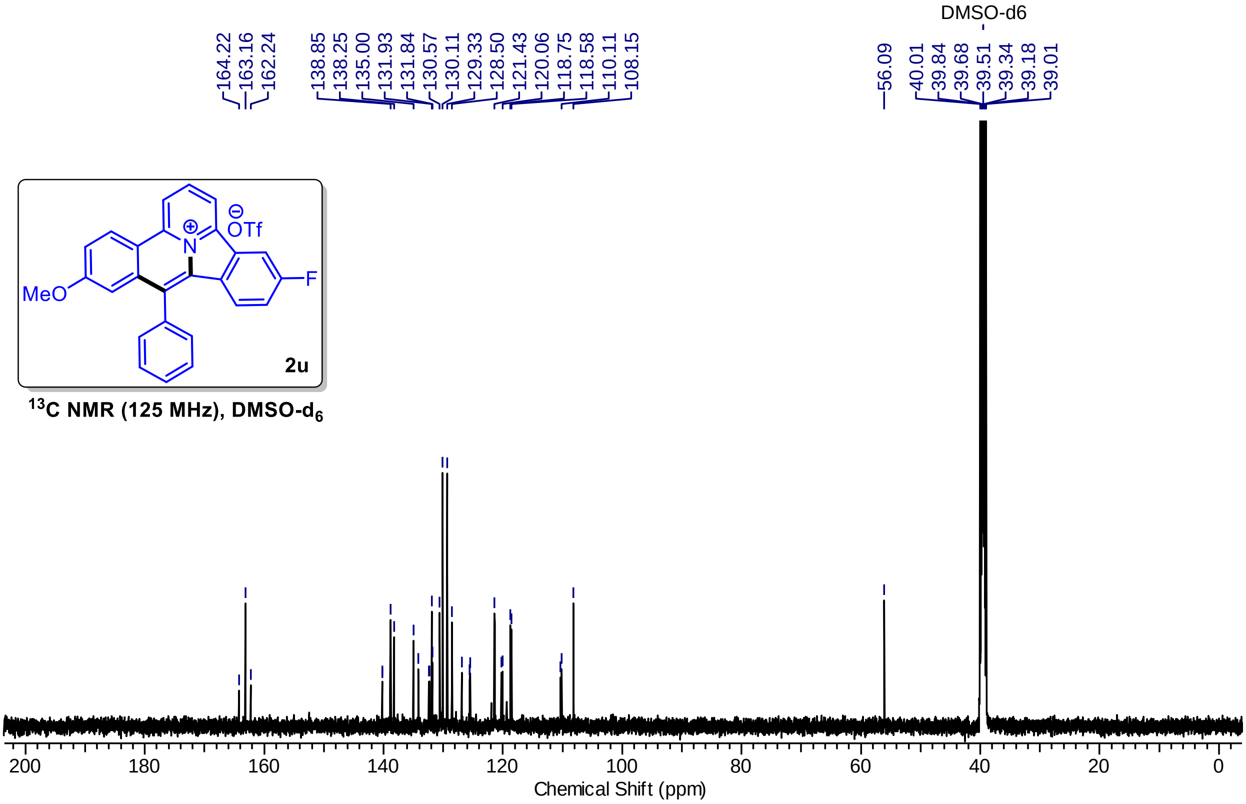

DMSO-d6
9.72
9.70
9.49
9.47
9.30
9.29
9.02
9.00
8.90
8.88
8.53
8.51
8.09
8.04
7.96
7.75
7.74
6.22
4.13
3.32
2.50
2.49
2.47
2.46
2.08
2.07
2.03
2.02
1.99
OTf
MeO
N
2s
^{1}H NMR (500 MHz), DMSO-d$_6$
1.10
1.08
1.09
1.12
1.00
1.03
2.16
1.03
0.98
0.98
3.09
4.27
4.22
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

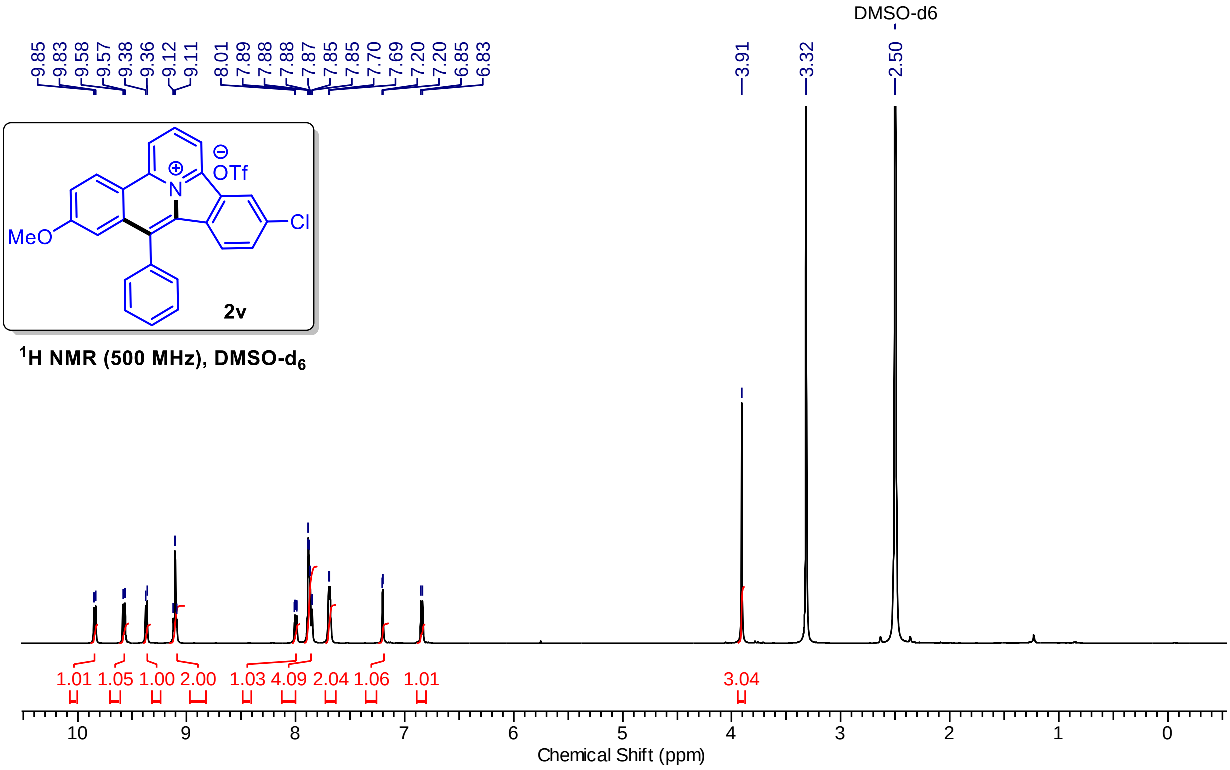

DMSO-d6
163.14
140.94
138.46
136.64
132.22
130.92
130.32
130.17
128.42
123.88
123.40
121.46
120.54
118.75
117.86
107.41
56.15
40.02
39.84
39.68
39.51
39.34
39.18
39.01
28.52
25.06
22.39
21.32
OTf
MeO
N
2s
^{13}C NMR (125 MHz), DMSO-d$_6$
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)


DMSO-d6
9.76 9.74 9.53 9.51 9.25 9.23 9.05 9.03 8.66 7.95 7.95 7.93 7.93 7.87 7.68 7.67 7.57 7.55 7.18 7.17 6.75 6.73
3.90
3.32
2.56 2.50
OTf
N
MeO
Me
2t
^{1}H NMR (400 MHz), DMSO-d$_6$
1.01 1.00 1.00 1.02 1.01 1.07 3.02 2.03 1.02 1.01 1.00
3.08
3.06
10 9 8 7 6 5 4 3 2 1 0
Chemical Shift (ppm)

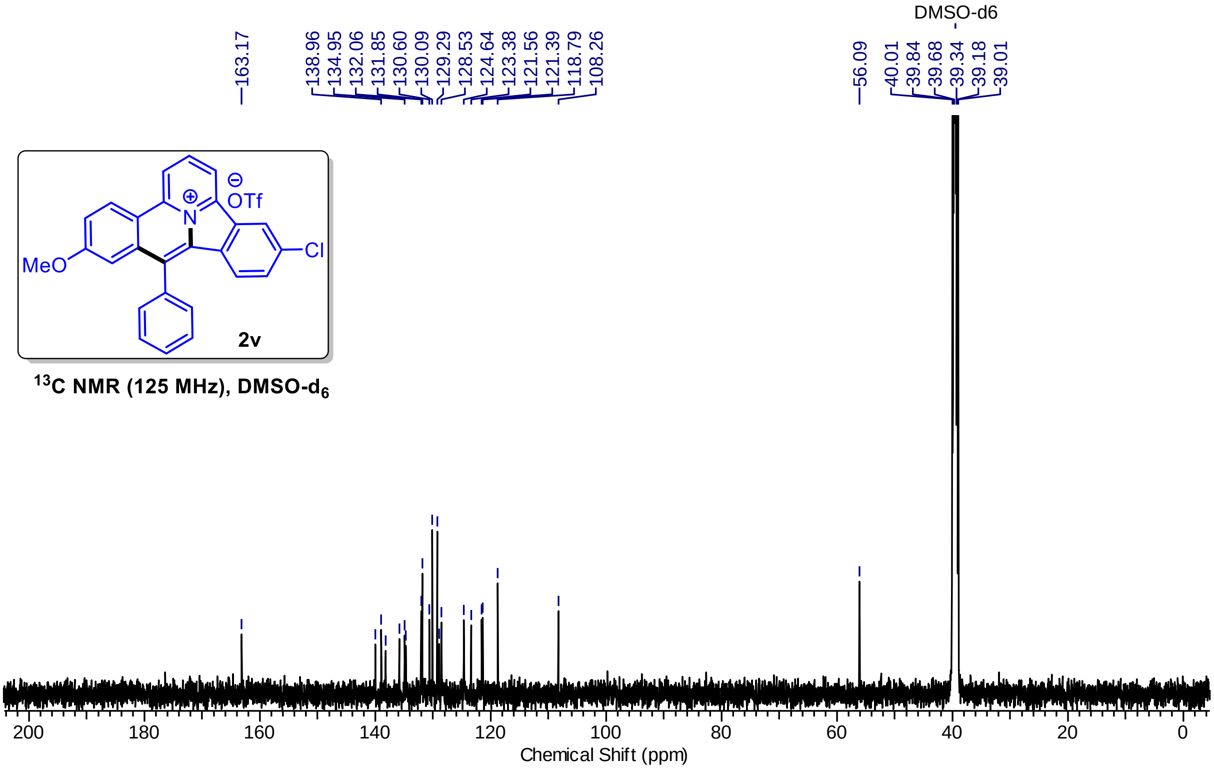

DMSO-d6
163.02
141.61 138.81 134.94 133.12 132.17 130.41 130.01 129.34 128.41 123.21 122.95 121.08 120.59 117.87 108.06
56.03
40.14 39.93 39.72 39.51 39.30 39.10 38.89
21.41
OTf
N
MeO
Me
2t
^{13}C NMR (100 MHz), DMSO-d$_6$
200 180 160 140 120 100 80 60 40 20 0
Chemical Shift (ppm)


DMSO-d6
9.85
9.83
9.58
9.55
9.35
9.33
9.10
8.84
8.82
7.99
7.97
7.89
7.88
7.88
7.70
7.69
7.69
7.68
7.20
7.19
6.88
6.87
3.91
3.32
2.50
MeO
N
OTf
F
2u
^{1}H NMR (500 MHz), DMSO-d$_6$
1.00
1.00
1.00
1.01
1.00
1.04
3.07
3.11
1.00
1.00
3.03
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

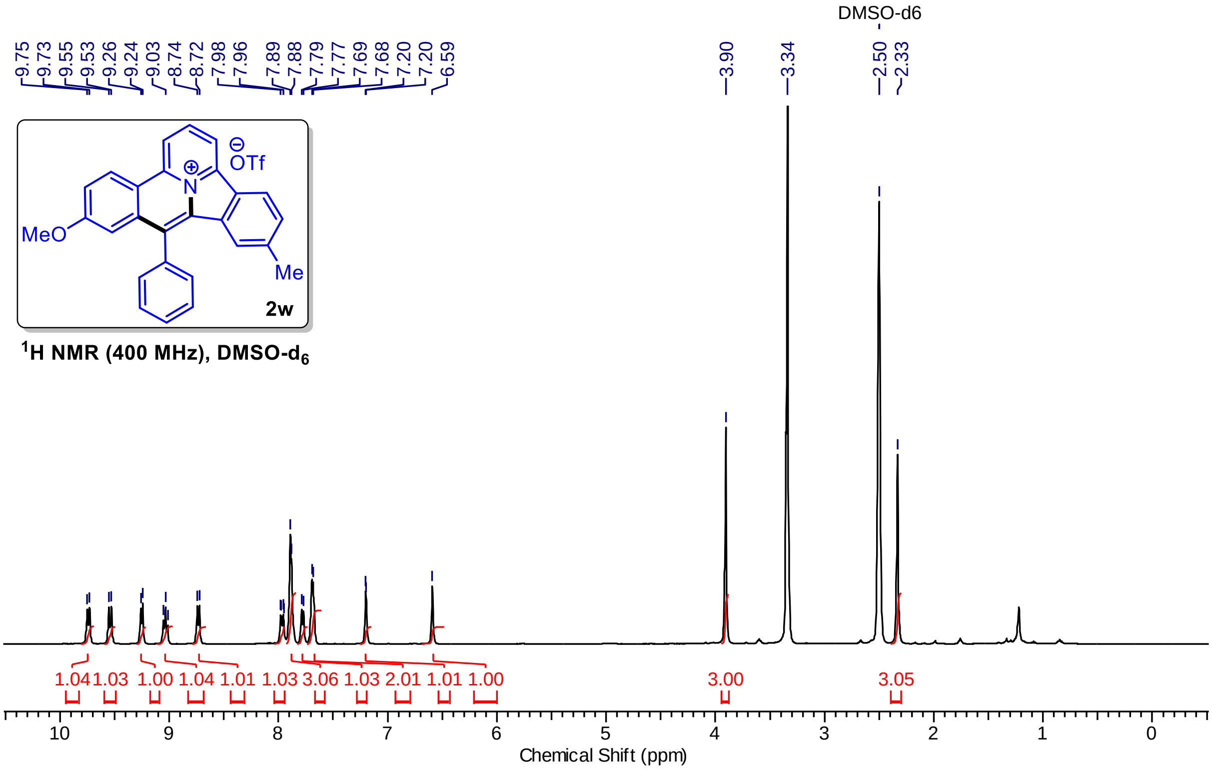

DMSO-d6
164.22
163.16
162.24
138.85
138.25
135.00
131.93
131.84
130.57
130.11
129.33
128.50
121.43
120.06
118.75
118.58
110.11
108.15
56.09
40.01
39.84
39.68
39.51
39.34
39.18
39.01
MeO
N
OTf
F
2u
^{13}C NMR (125 MHz), DMSO-d$_6$
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)



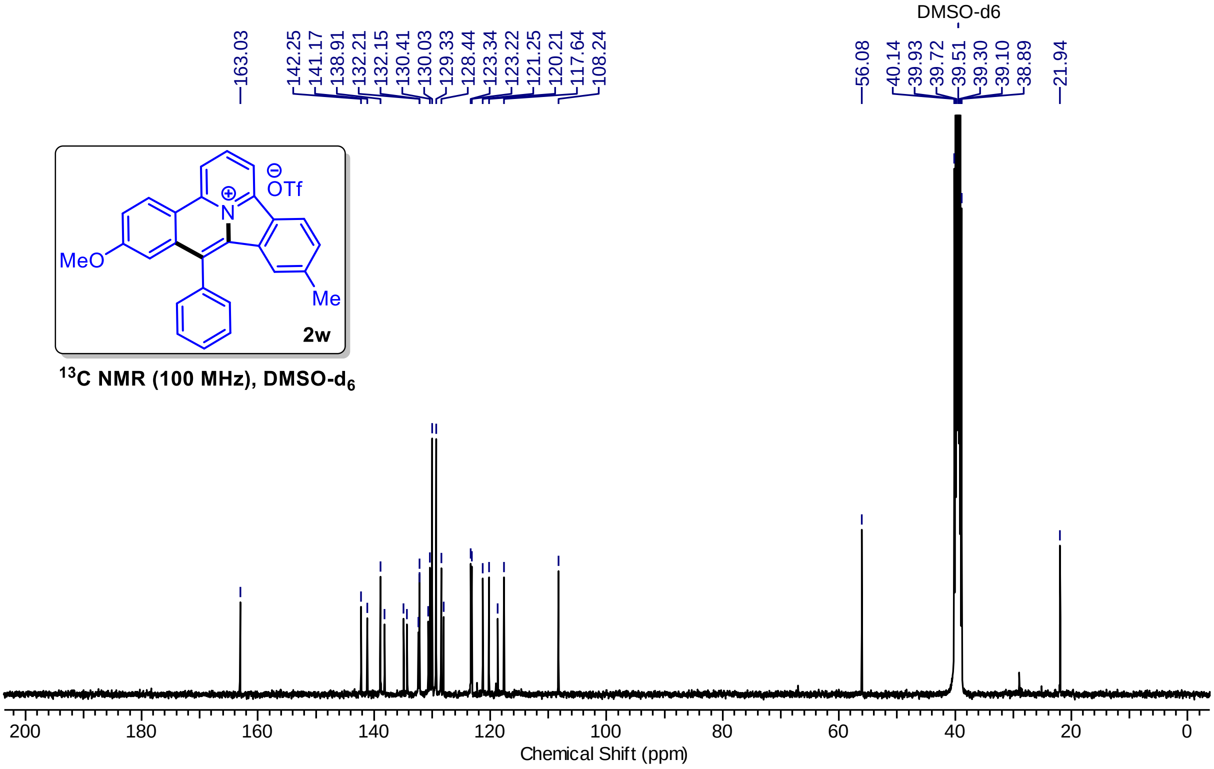
^{1}H NMR (500 MHz), DMSO-d$_6$



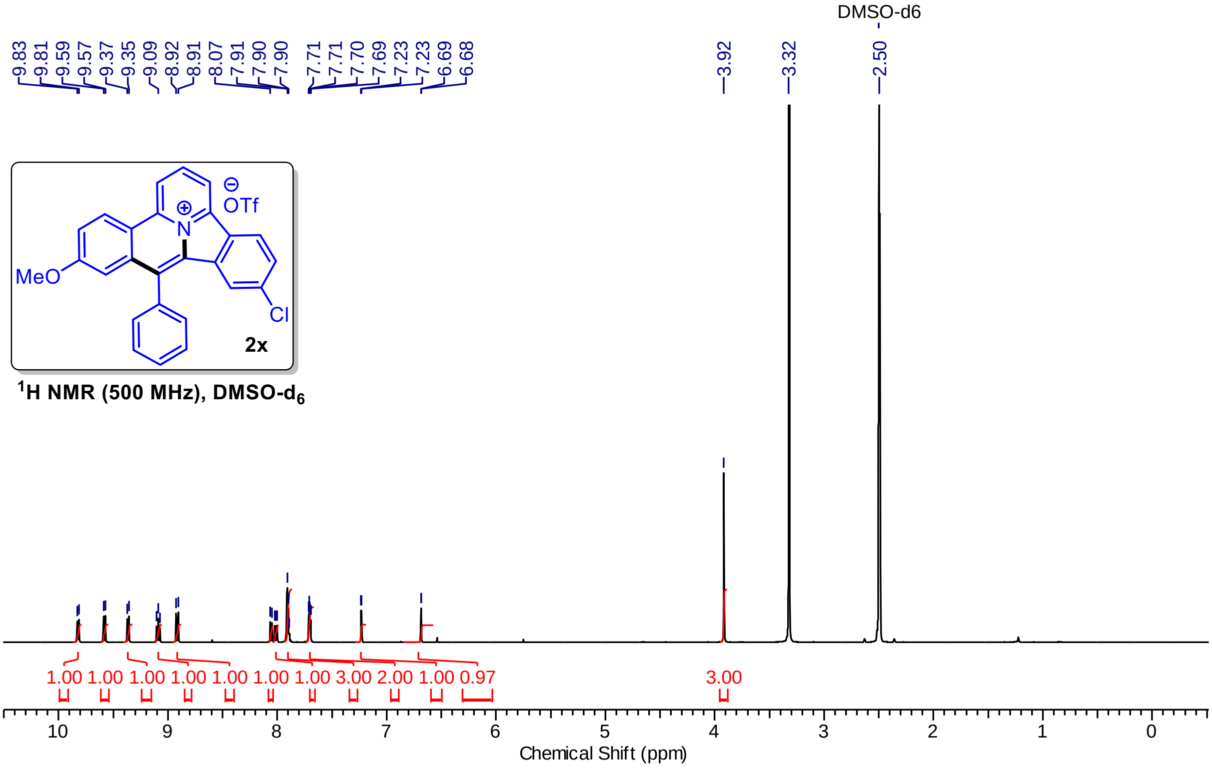
^{13}C NMR (125 MHz), DMSO-d$_6$



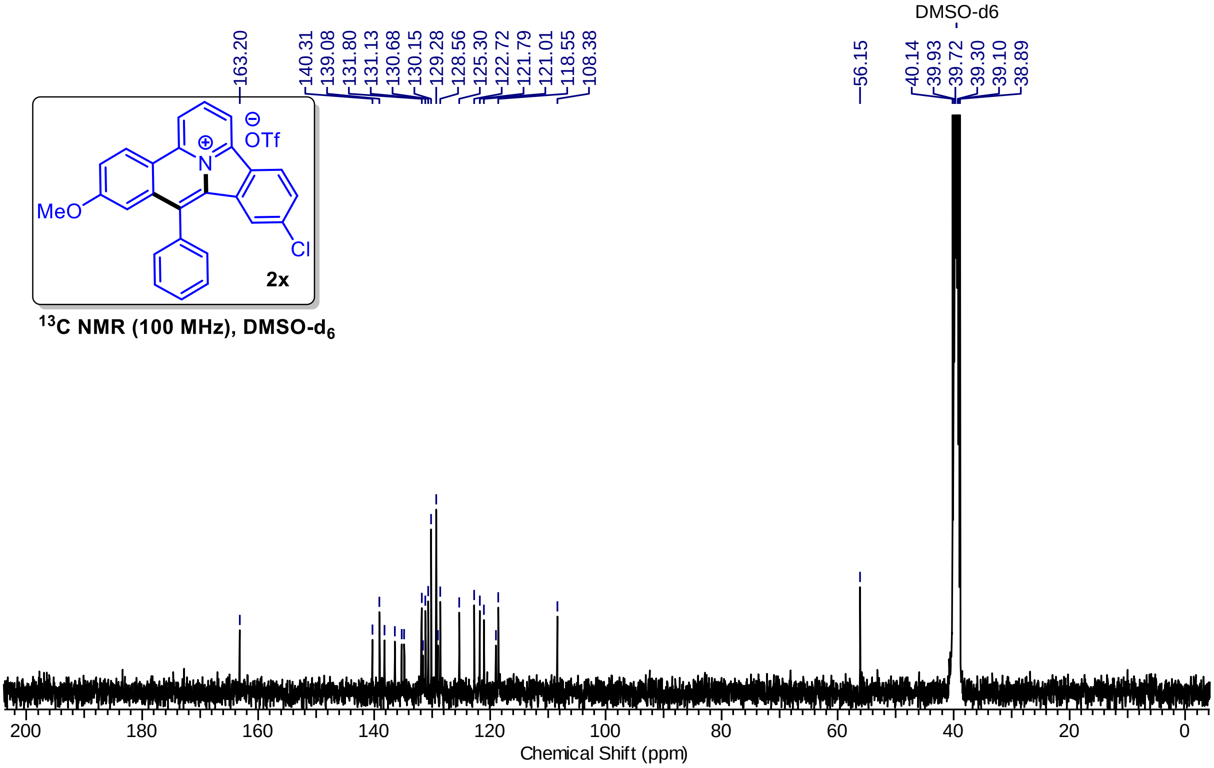
^{1}H NMR (400 MHz), DMSO-d_6



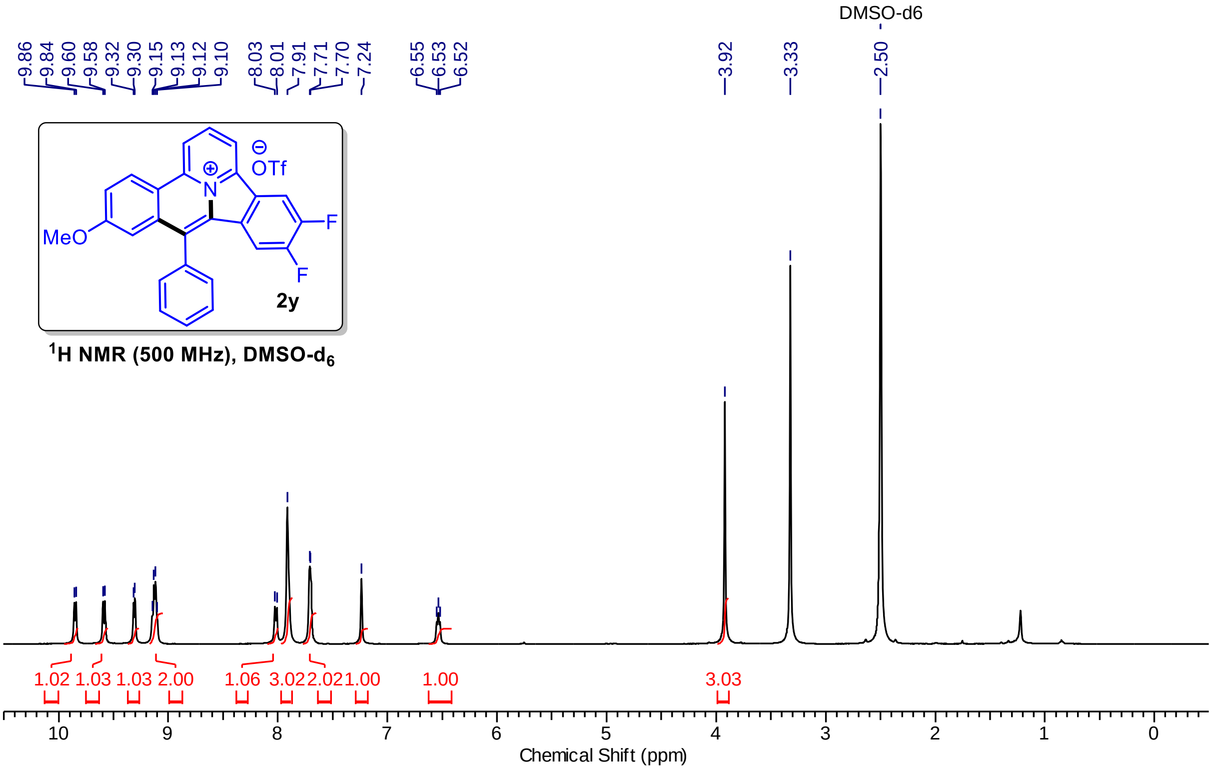
^{13}C NMR (100 MHz), DMSO-d_6



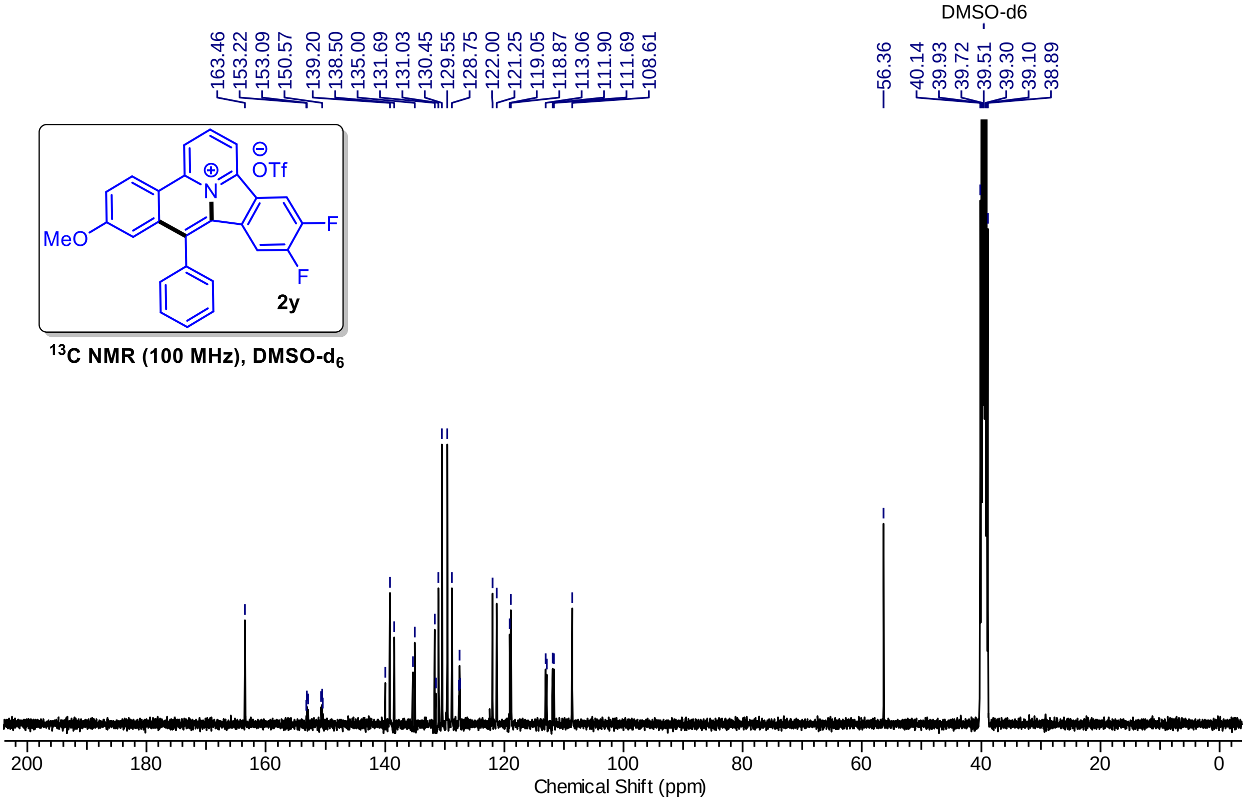
^{1}H NMR (500 MHz), DMSO-d$_6$



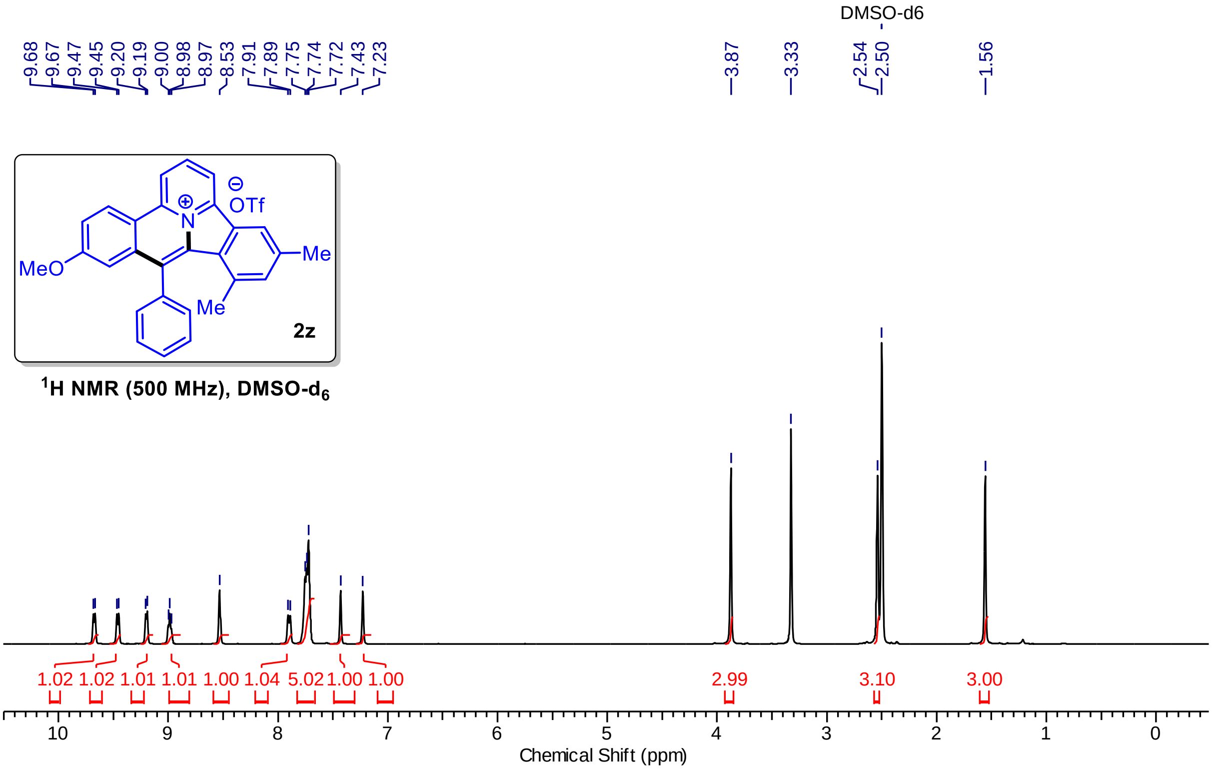
^{13}C NMR (100 MHz), DMSO-d$_6$



^{1}H NMR (500 MHz), DMSO-d$_6$

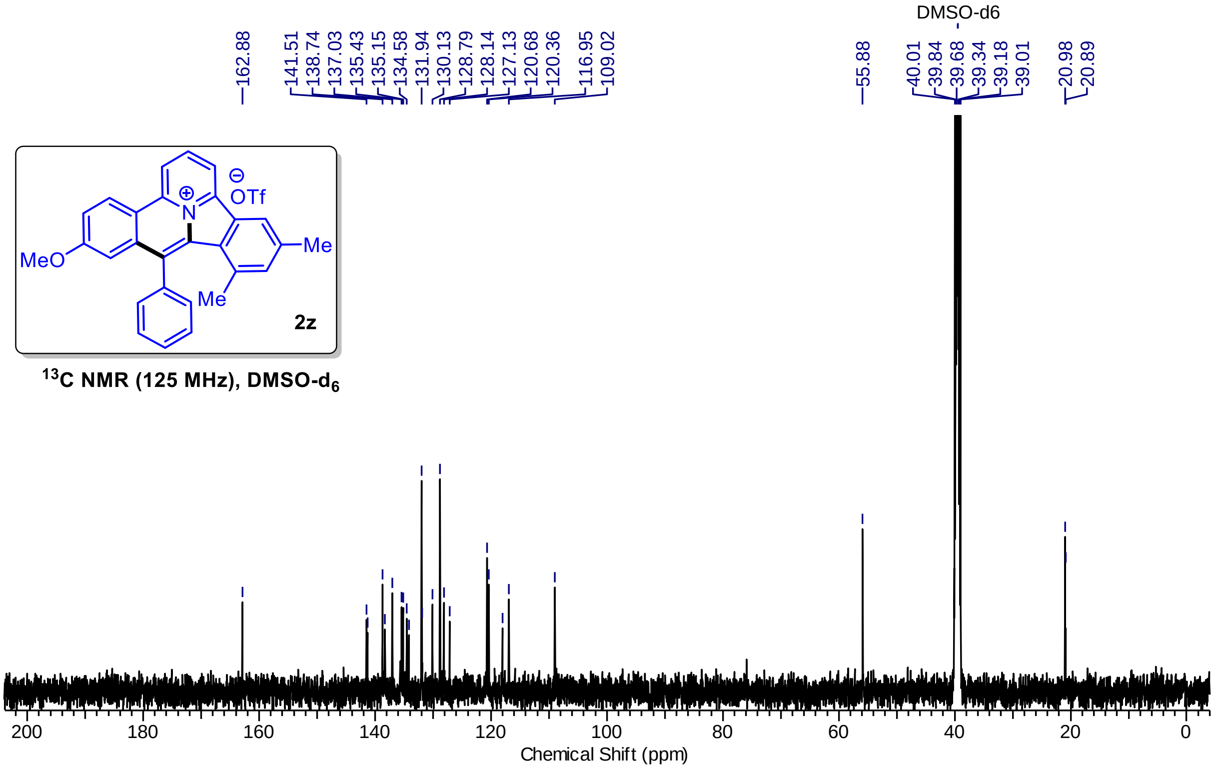


^{13}C NMR (100 MHz), DMSO-d$_6$



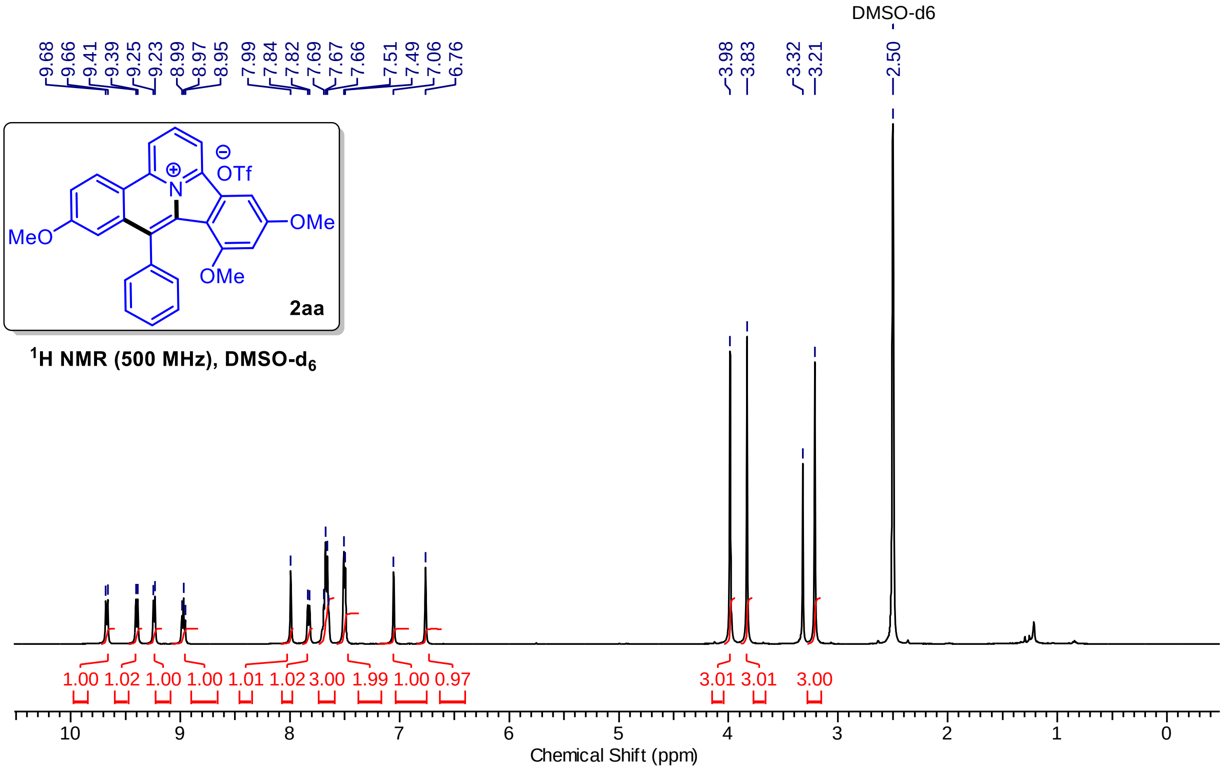
2z

^{1}H NMR (500 MHz), DMSO-d_6

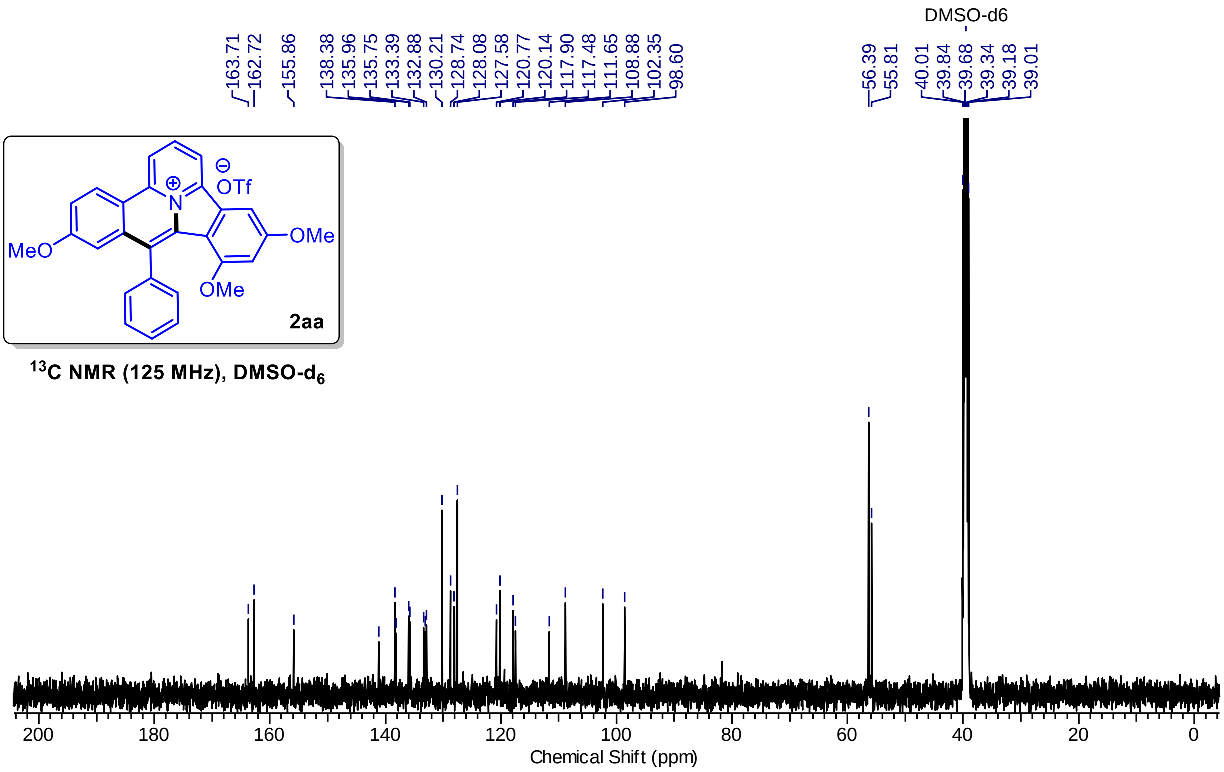


2z

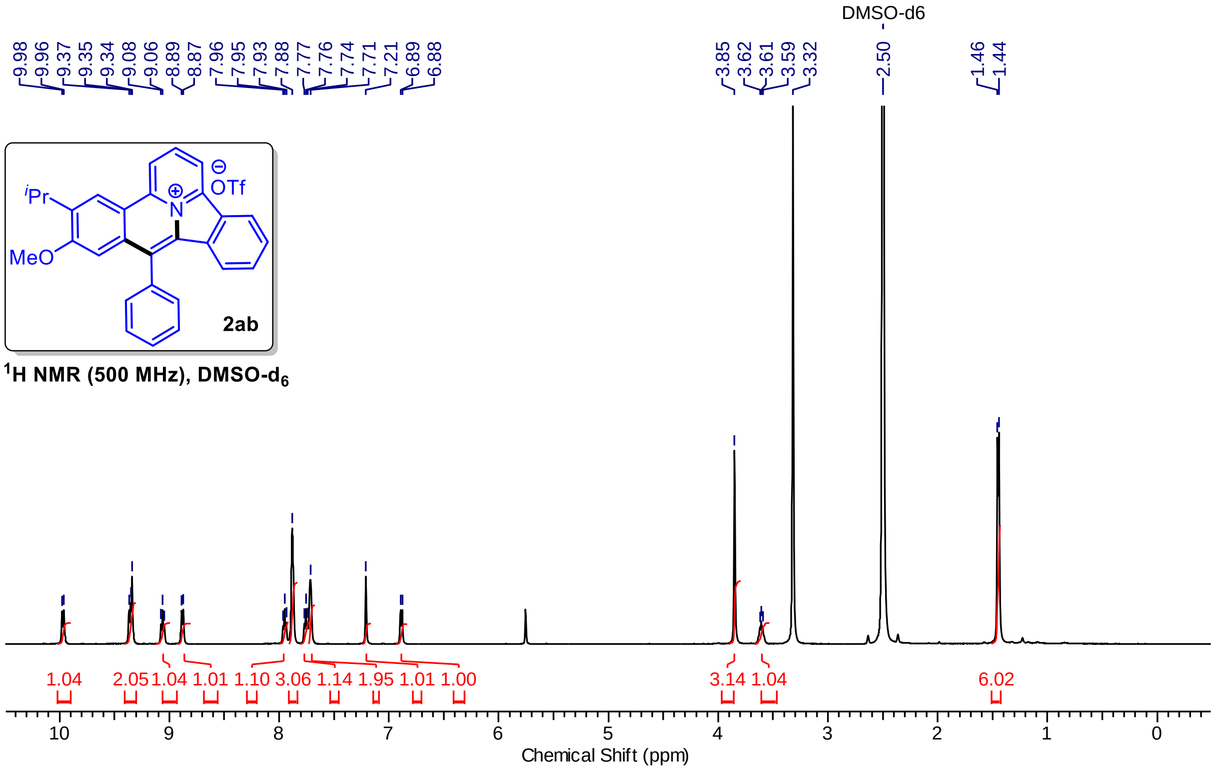
^{13}C NMR (125 MHz), DMSO-d_6



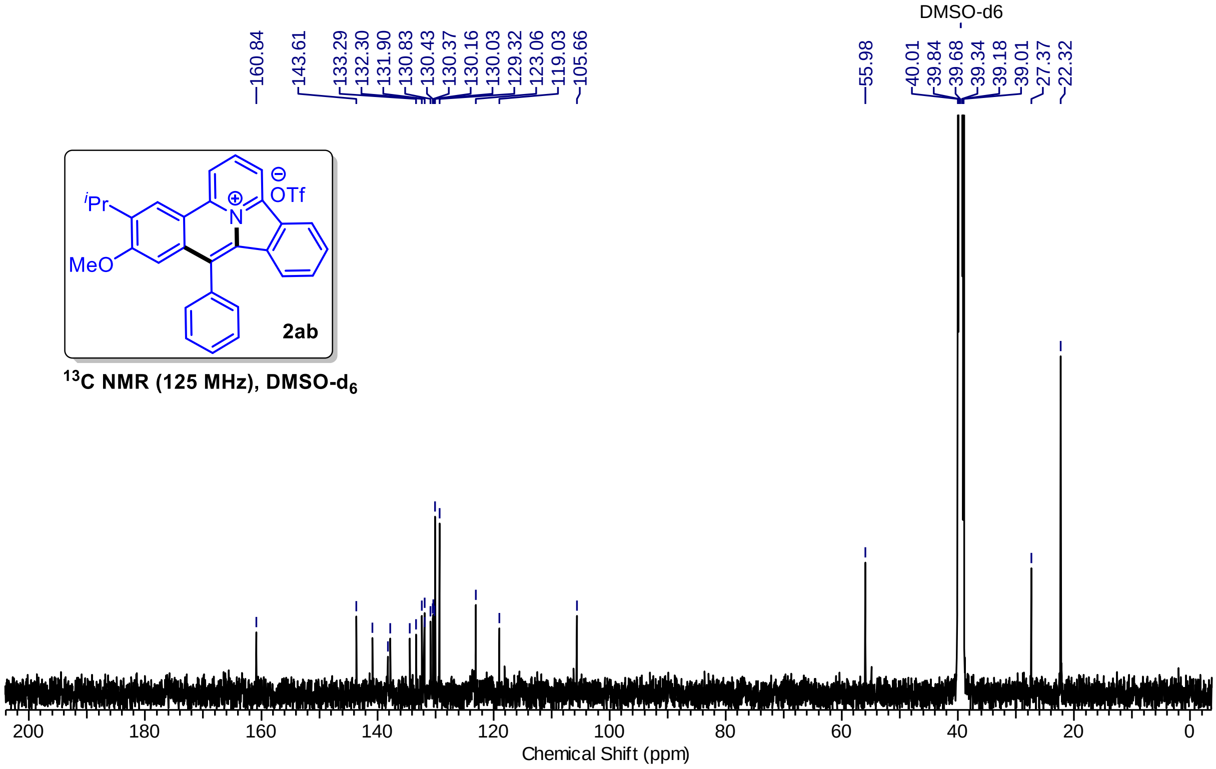
^{1}H NMR (500 MHz), DMSO-d_6



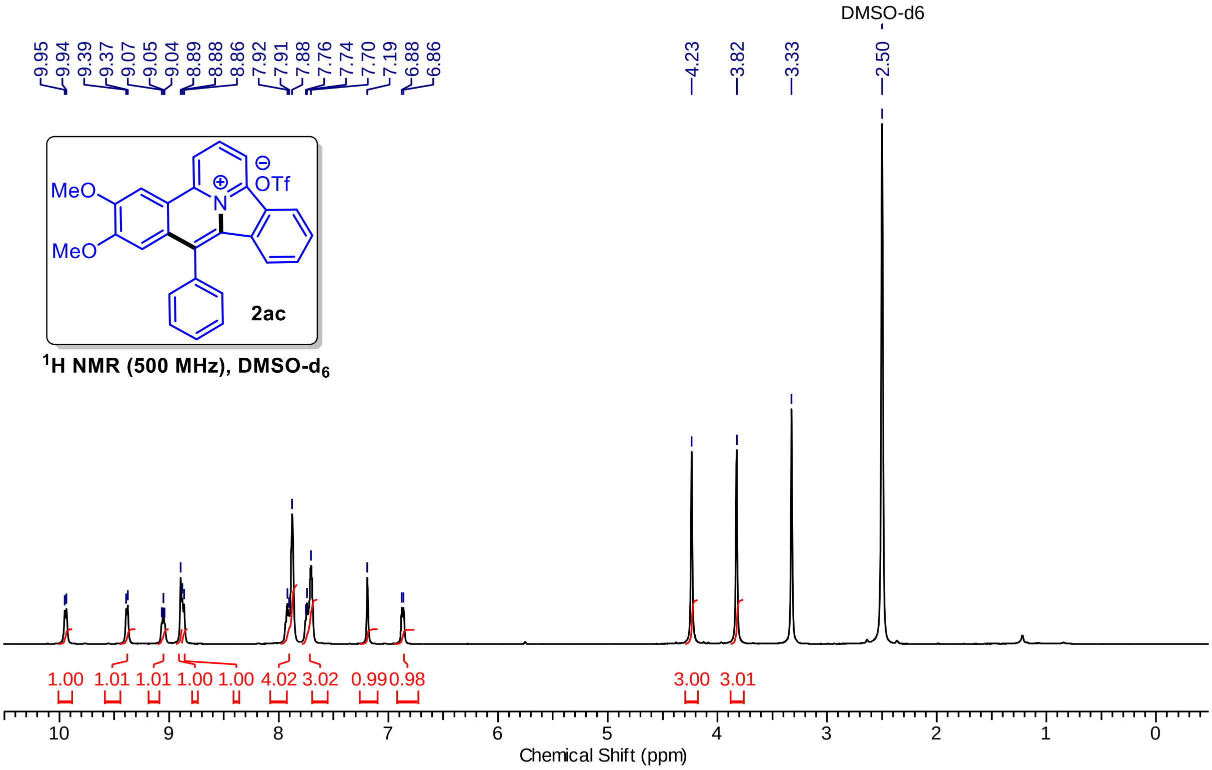
^{13}C NMR (125 MHz), DMSO-d_6



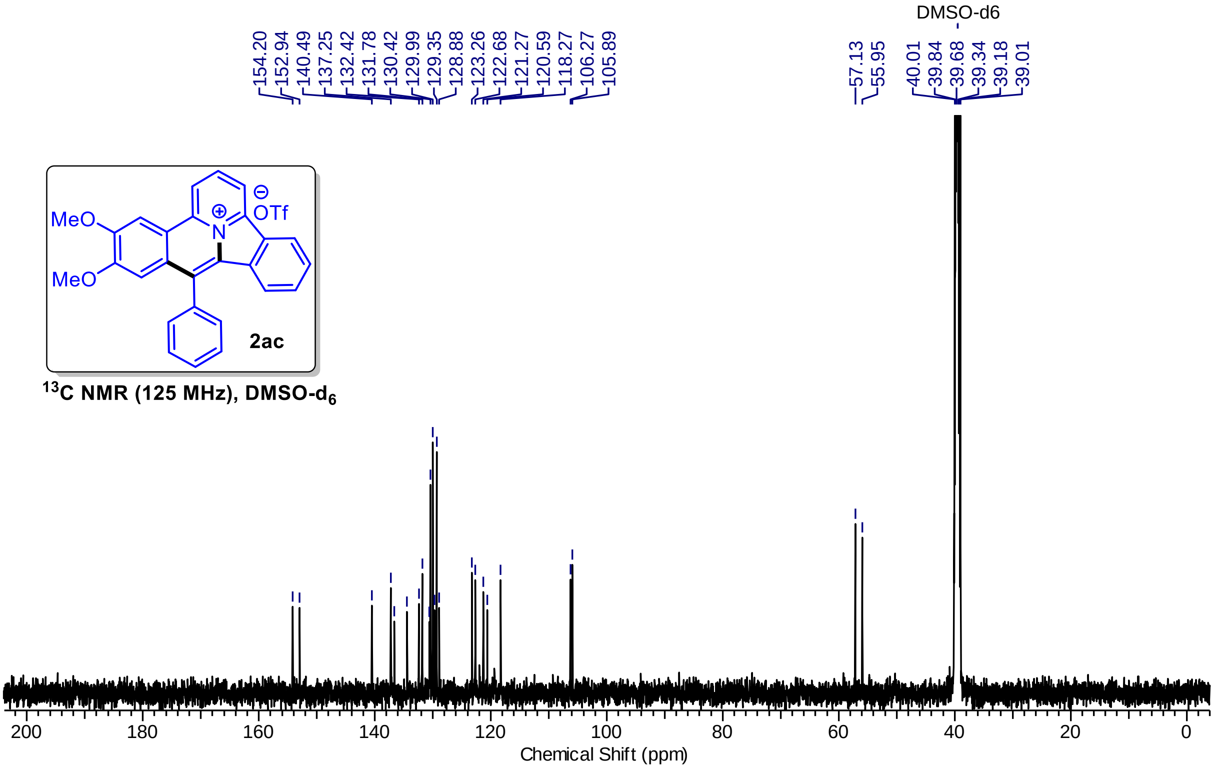
^{1}H NMR (500 MHz), DMSO-d$_6$



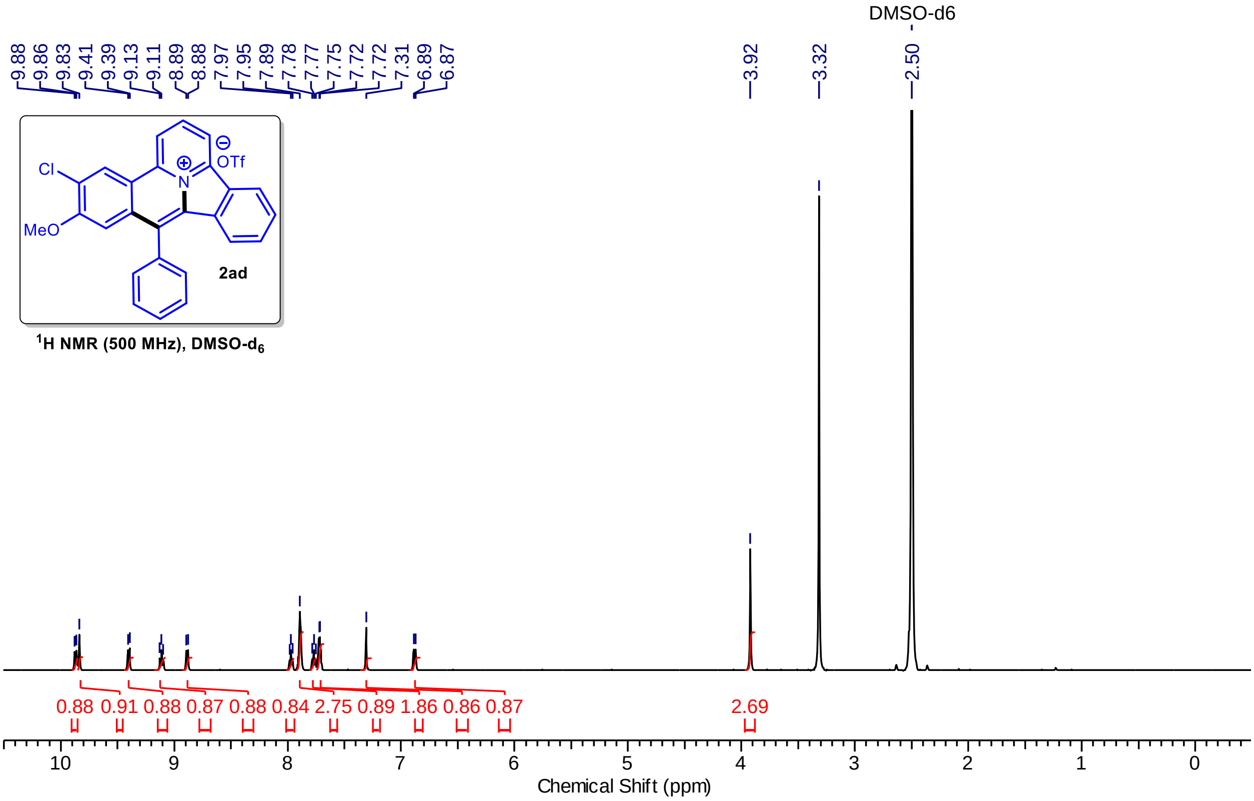
^{13}C NMR (125 MHz), DMSO-d$_6$

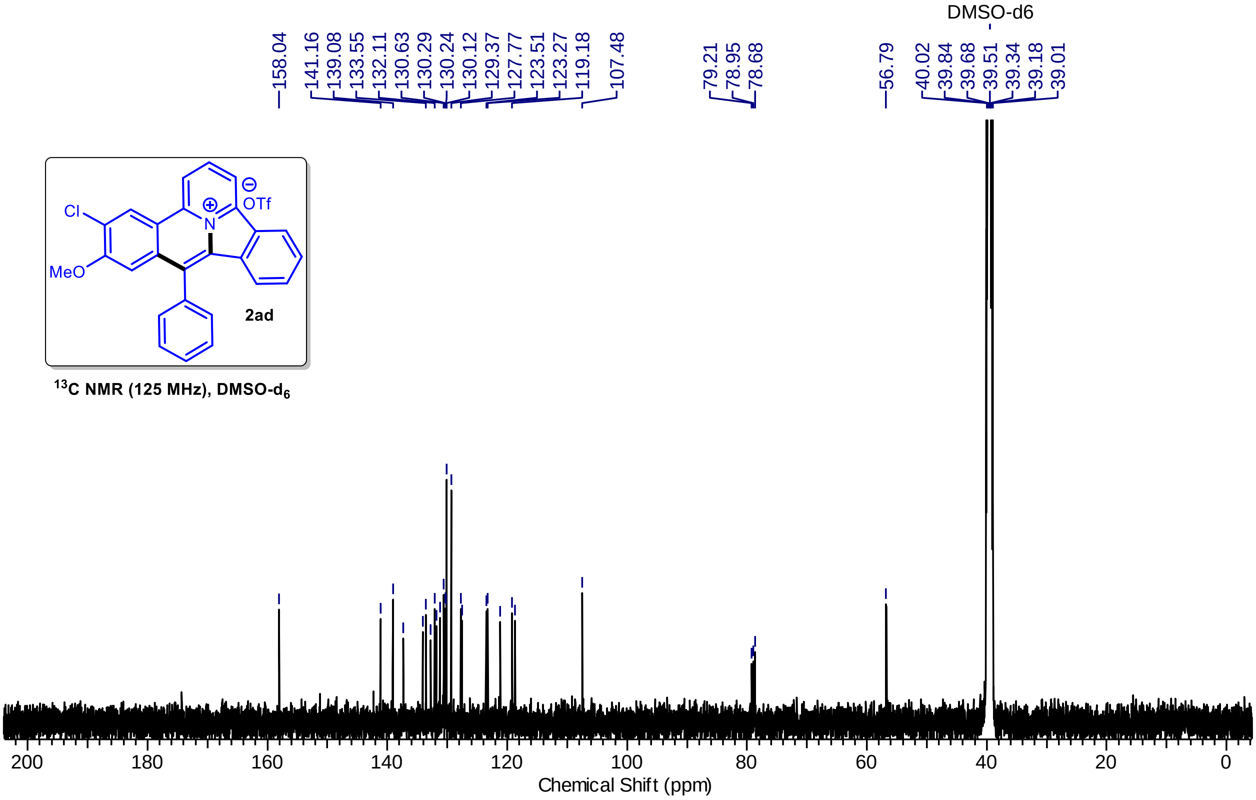


^{1}H NMR (500 MHz), DMSO-d_6



^{13}C NMR (125 MHz), DMSO-d_6


DMSO-d6
9.88
9.86
9.83
9.41
9.39
9.13
9.11
8.89
8.88
7.97
7.95
7.89
7.78
7.77
7.75
7.72
7.72
7.31
6.89
6.87
3.92
3.32
2.50
Cl
MeO
N
OTf
2ad
^{1}H NMR (500 MHz), DMSO-d_6
0.88
0.91
0.88
0.87
0.88
0.84
2.75
0.89
1.86
0.86
0.87
2.69
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)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123.27
119.18
107.48
79.21
78.95
78.68
56.79
40.02
39.84
39.68
39.51
39.34
39.18
39.01
Cl
MeO
N
OTf
2ad
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180
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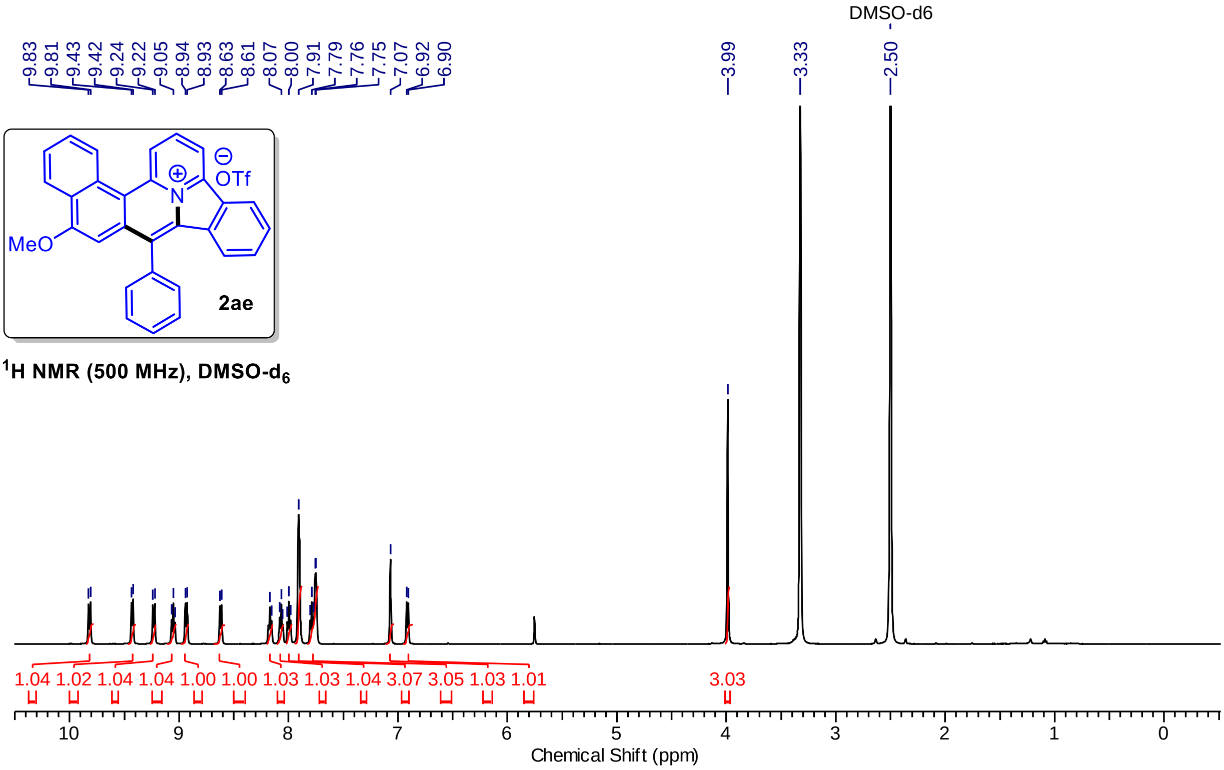
140
120
100
80
60
40
20
0
Chemical Shift (ppm)



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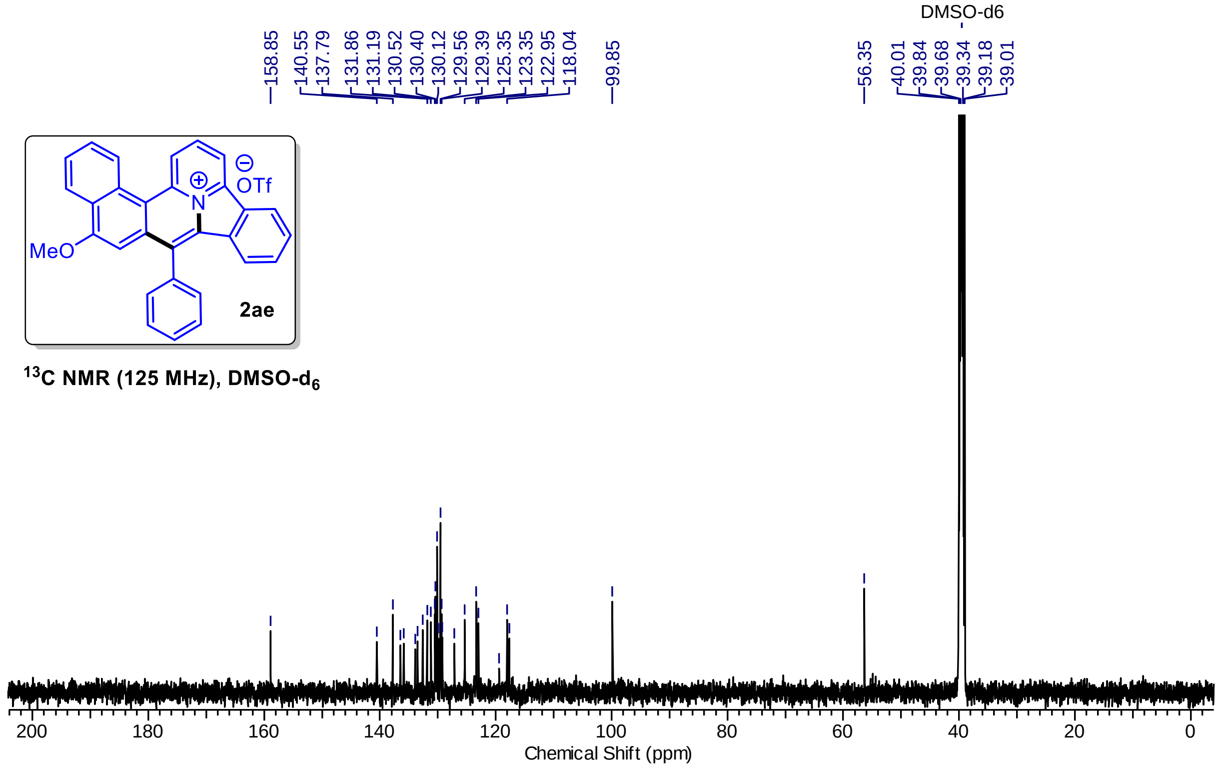

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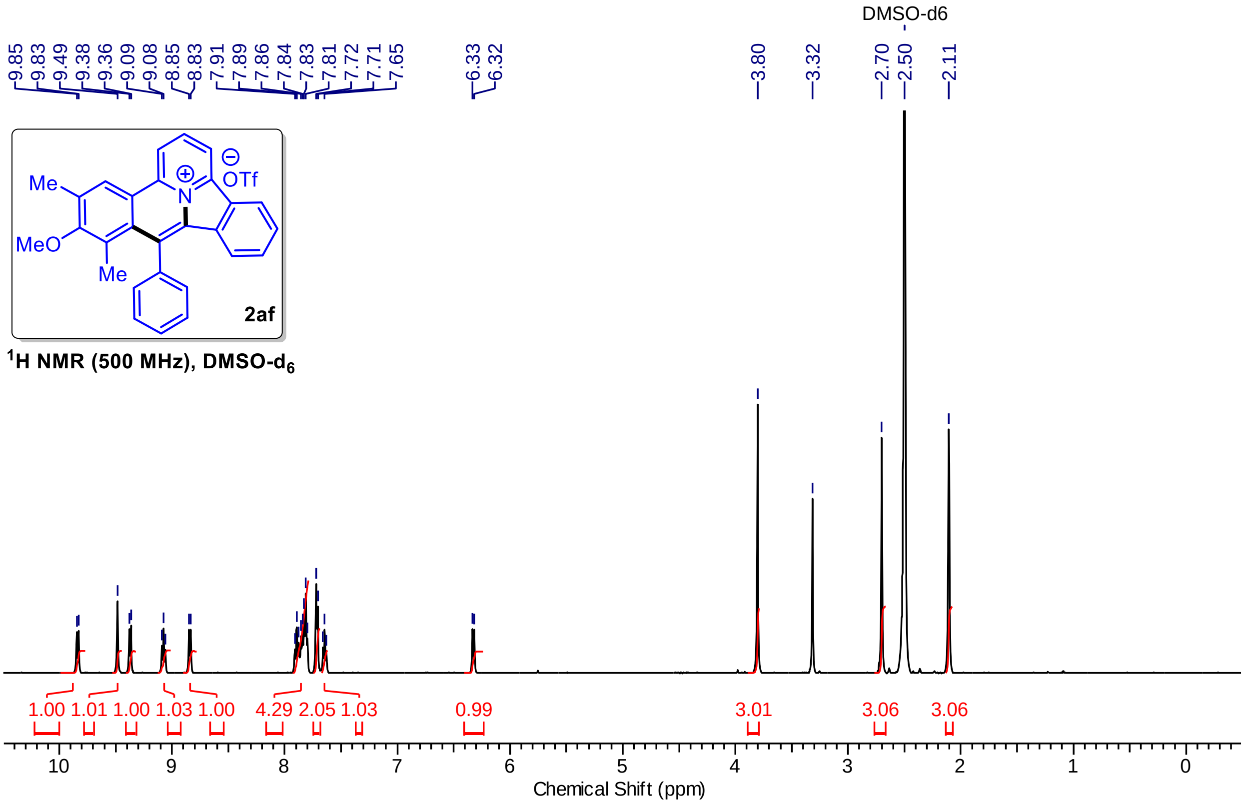

2af

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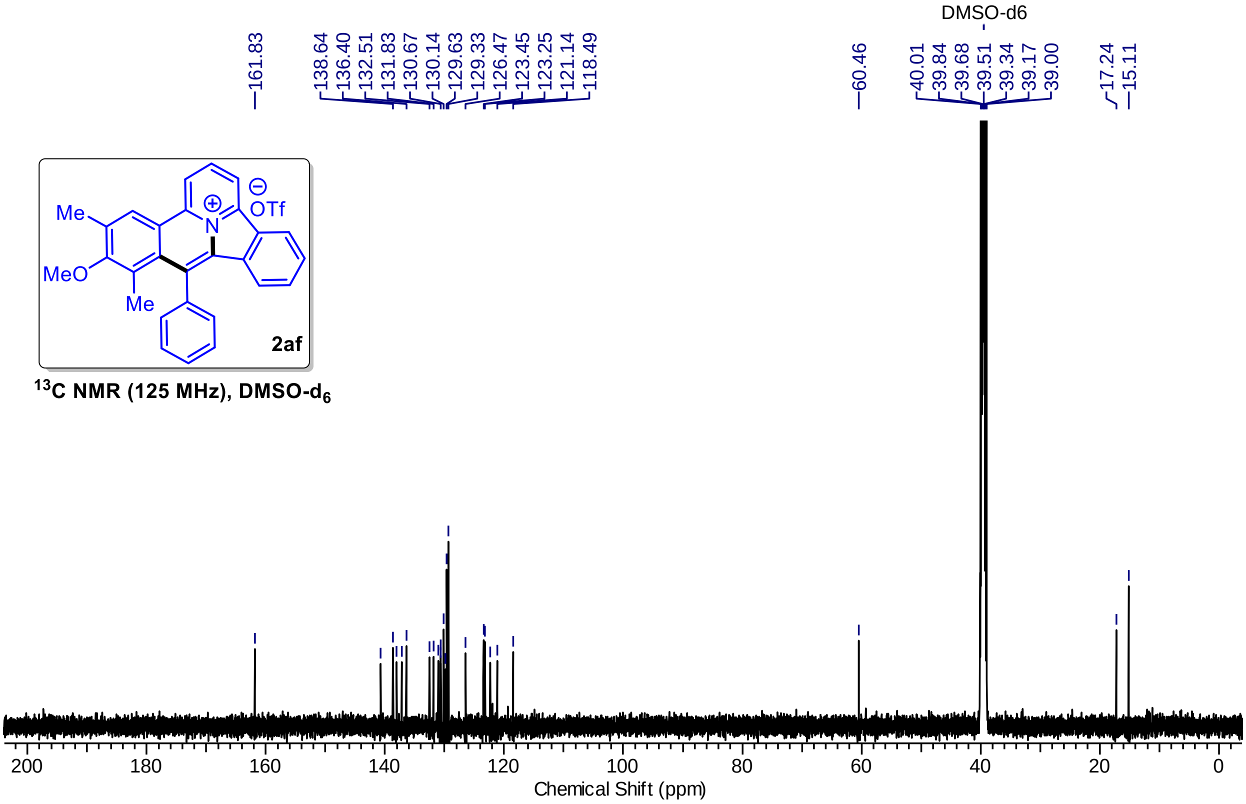

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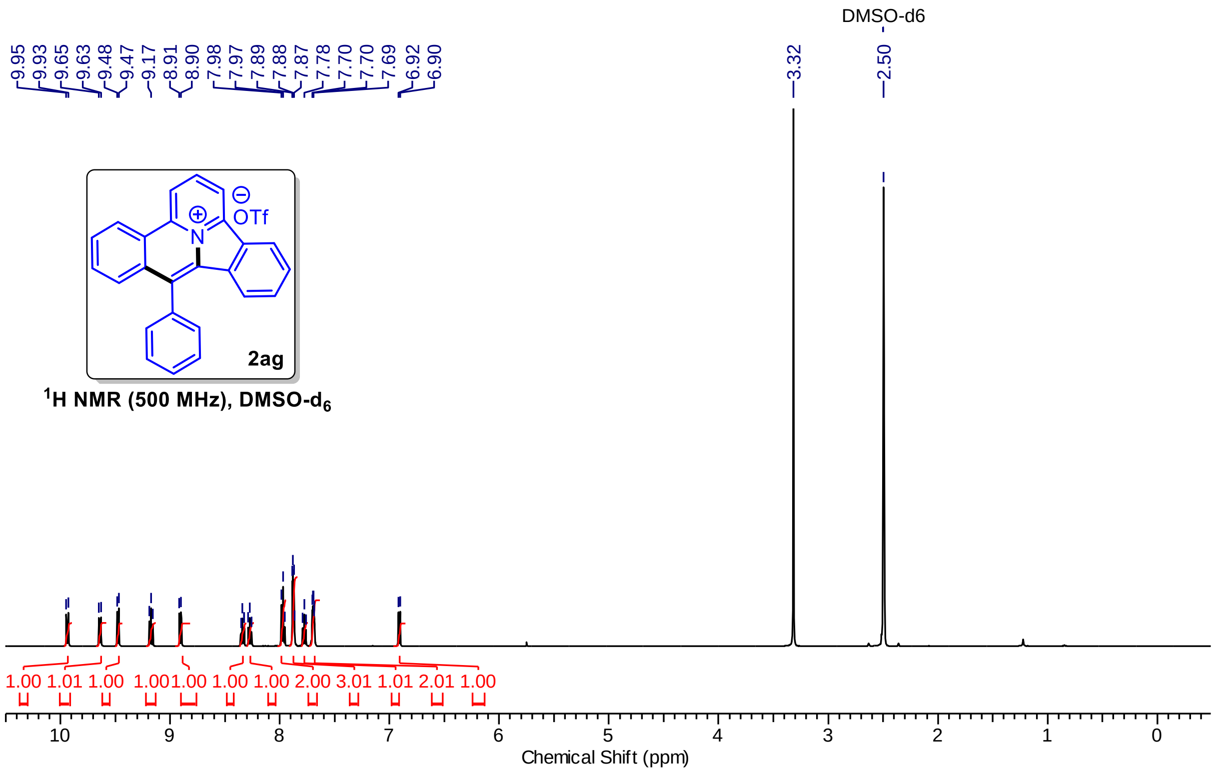
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7.89
7.88
7.87
7.78
7.70
7.70
7.69
6.92
6.90
3.32
2.50
OTf
N
2ag
^{1}H NMR (500 MHz), DMSO-d_6
1.00 1.01 1.00 1.00 1.00 1.00 1.00 2.00 3.01 1.01 2.01 1.00
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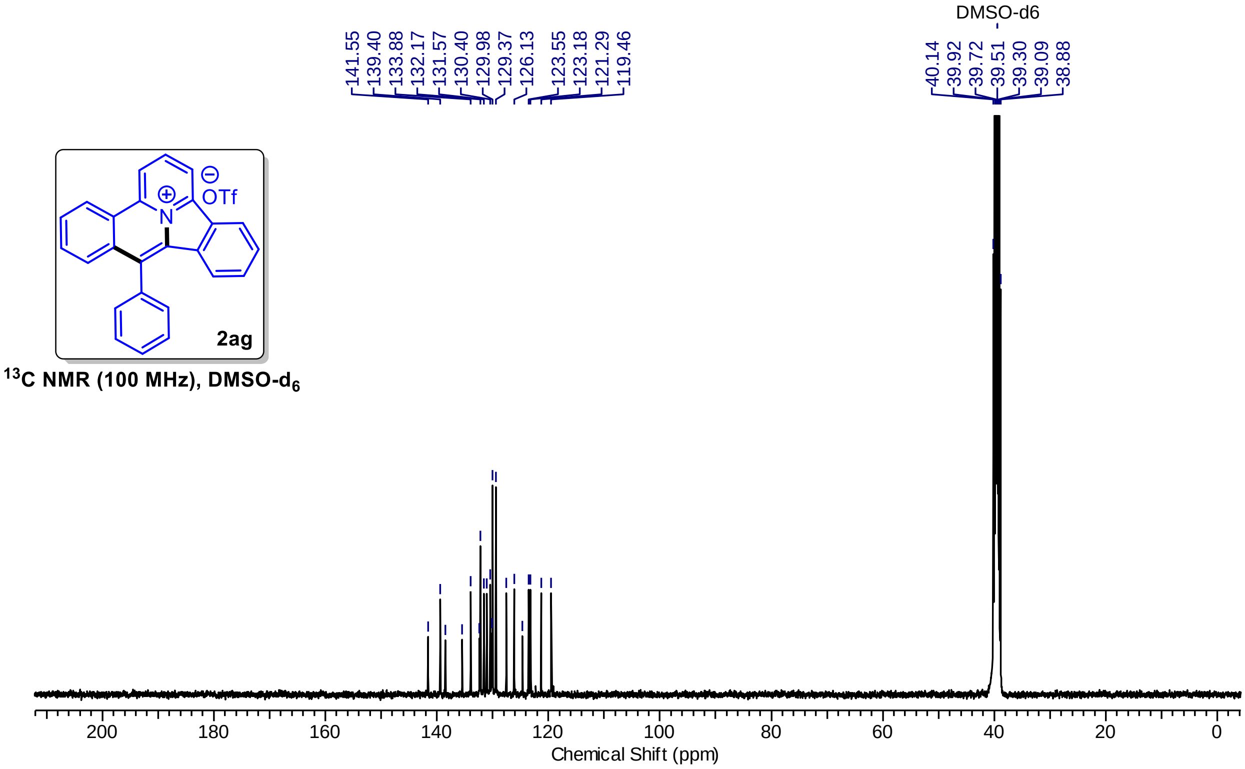
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)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119.46
40.14
39.92
39.72
39.51
39.30
39.09
38.88
OTf
N
2ag
^{13}C NMR (100 MHz), DMSO-d_6
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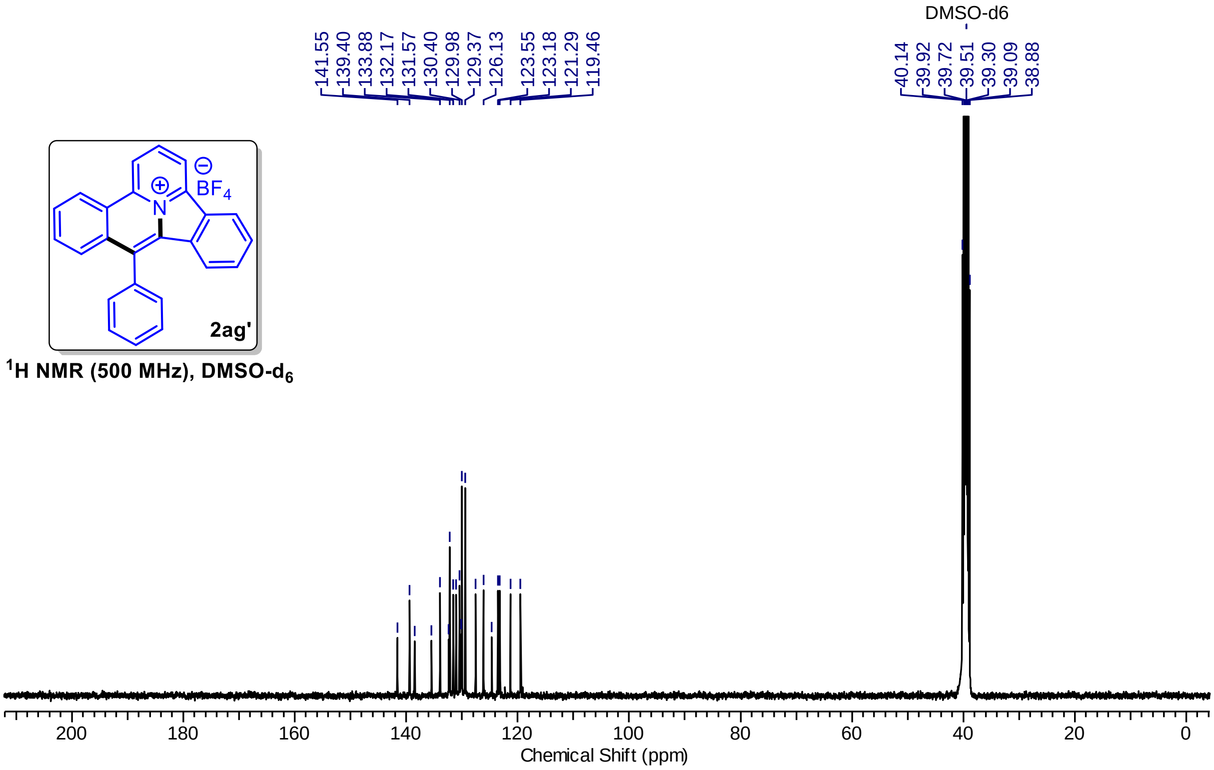
140
120
100
80
60
40
20
0
Chemical Shift (ppm)



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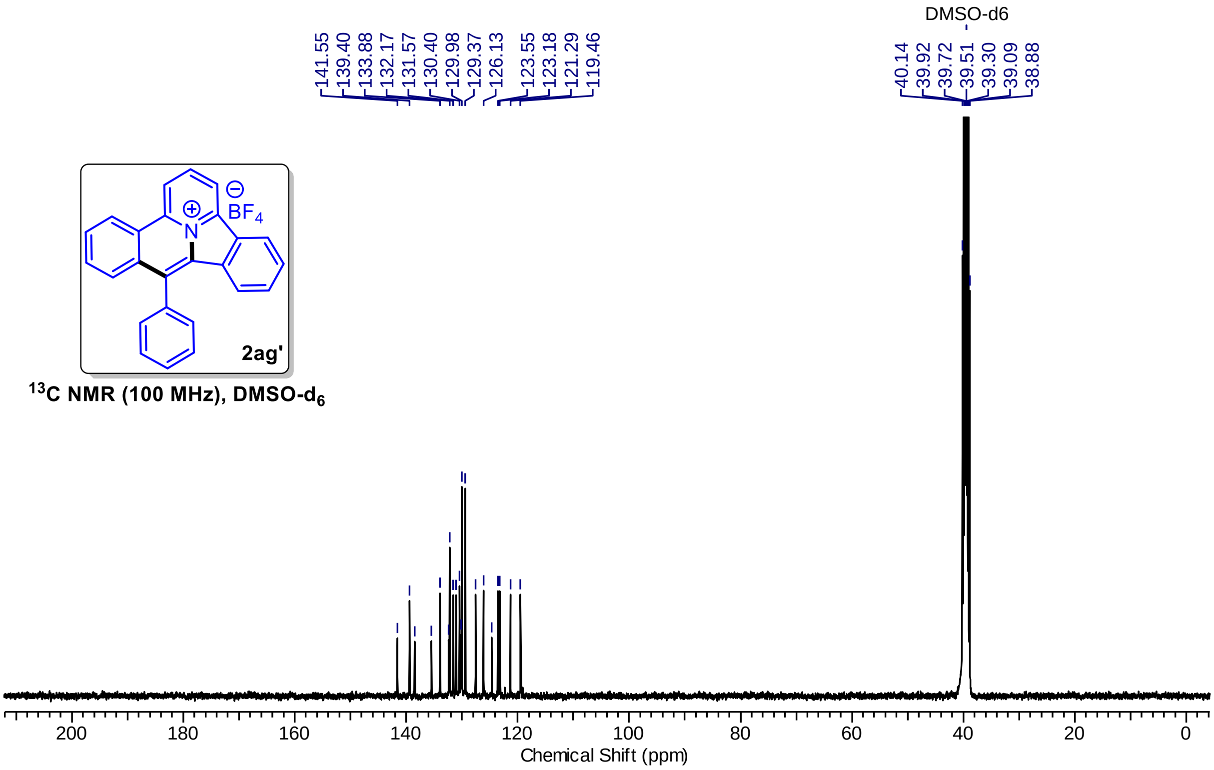

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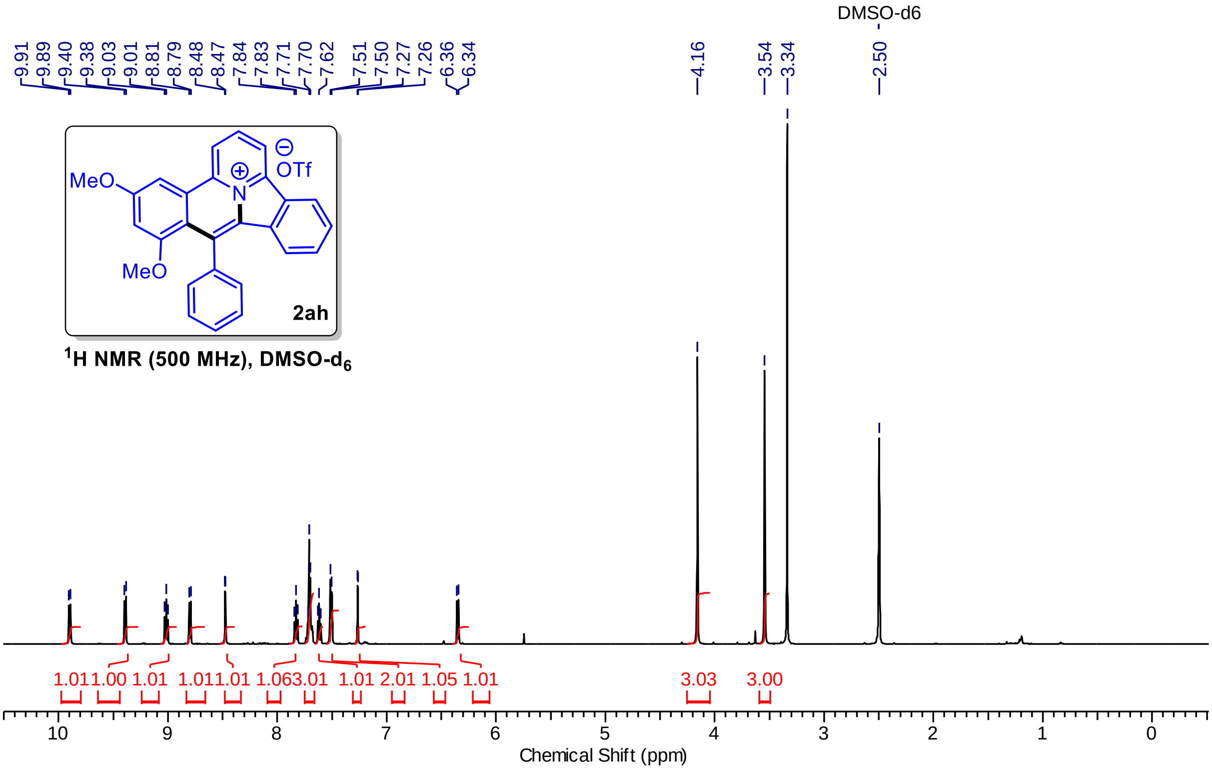

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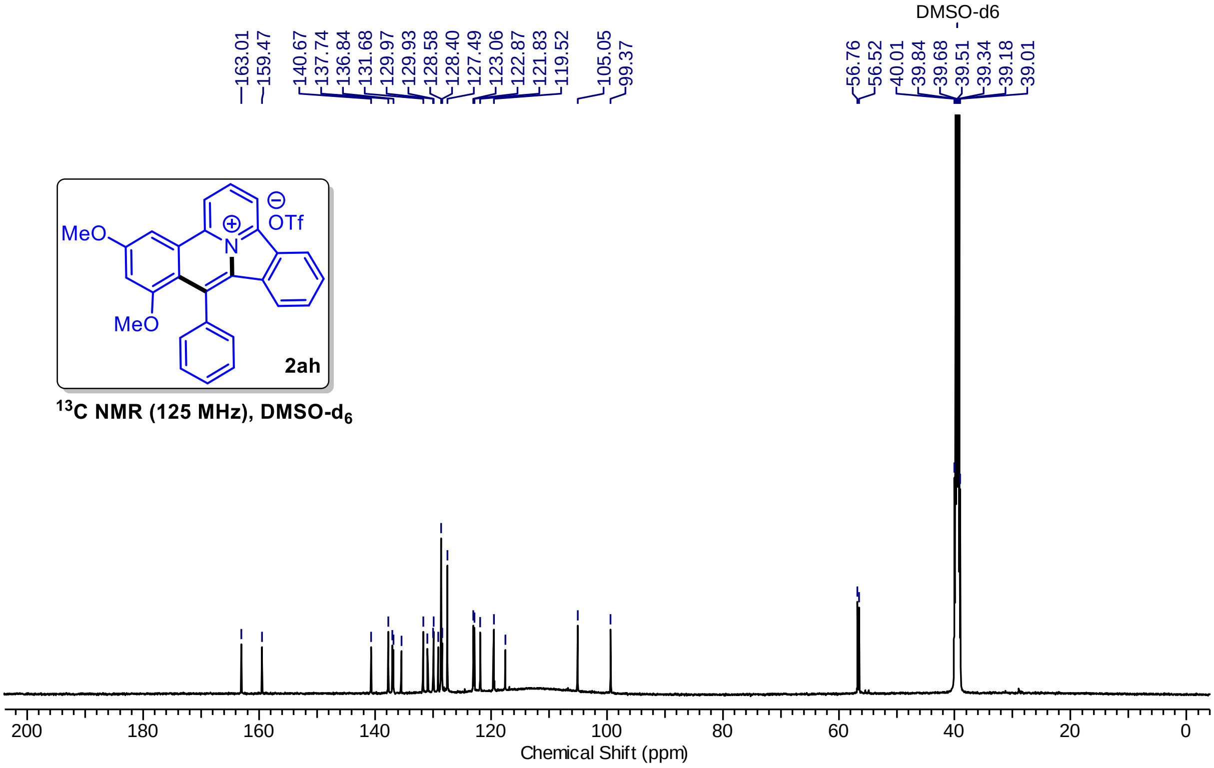

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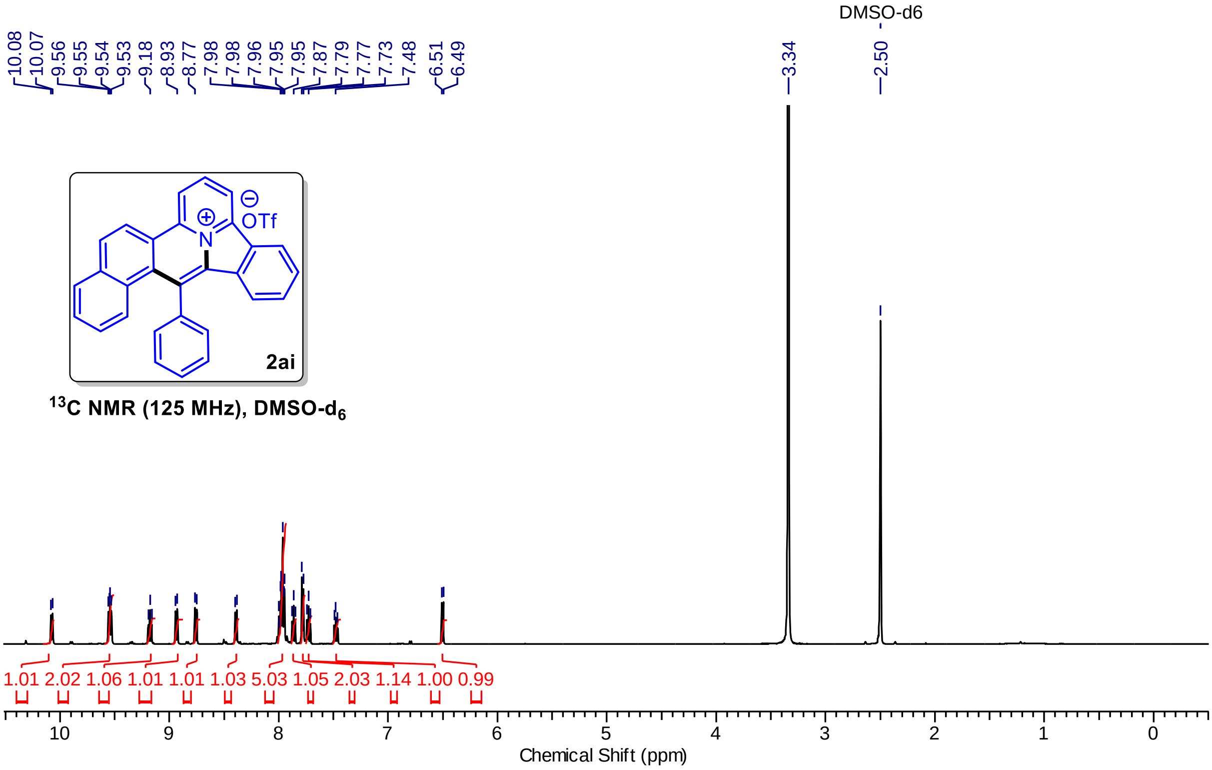
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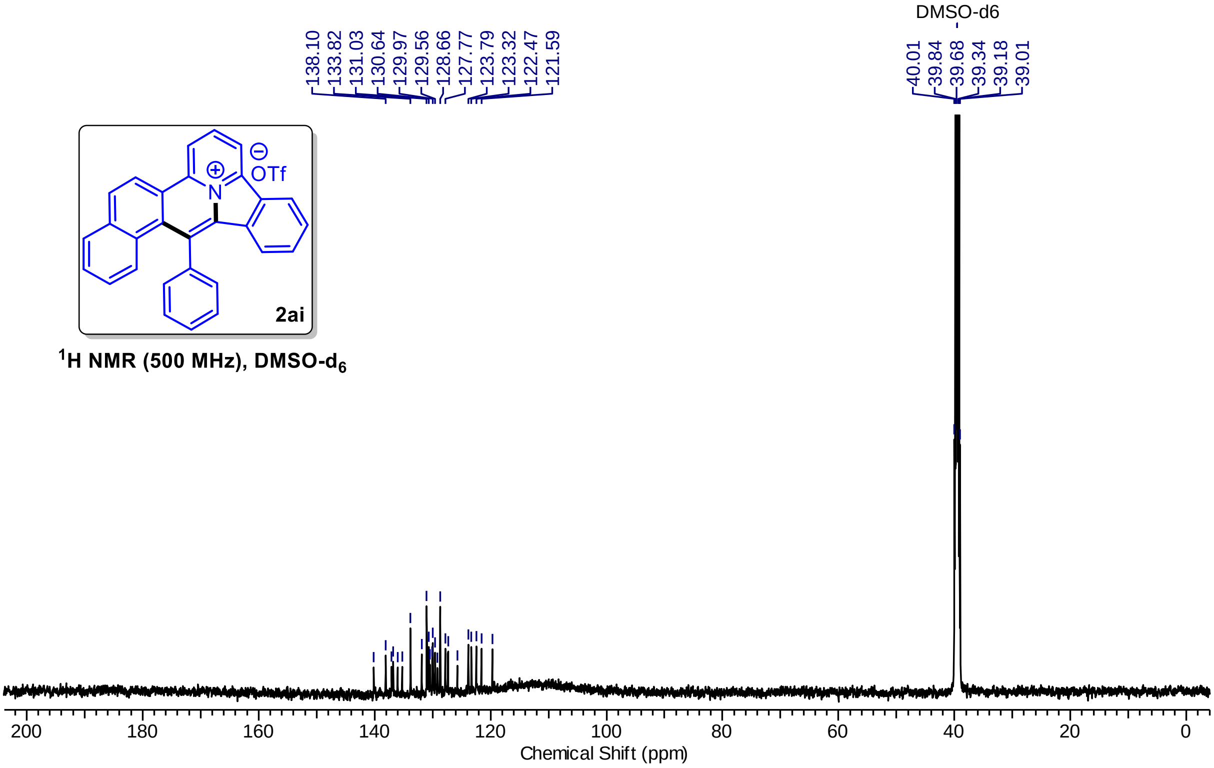
9.55
9.54
9.53
9.18
8.93
8.77
7.98
7.98
7.96
7.95
7.95
7.87
7.79
7.77
7.73
7.48
6.51
6.49
3.34
2.50
OTf
N
2ai
^{13}C NMR (125 MHz), DMSO-d$_6$
1.01 2.02 1.06 1.01 1.01 1.03 5.03 1.05 2.03 1.14 1.00 0.99
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)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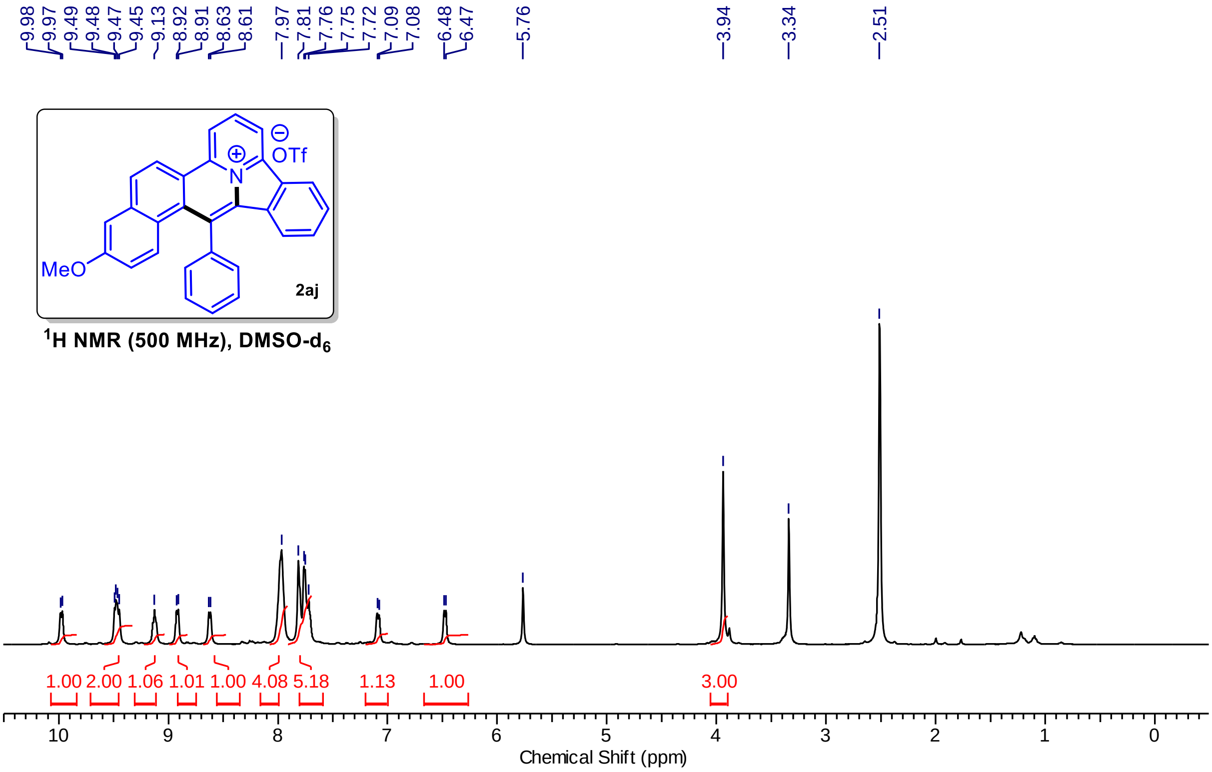
122.47
121.59
40.01
39.84
39.68
39.34
39.18
39.01
OTf
N
2ai
^{1}H NMR (500 MHz), DMSO-d$_6$
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)



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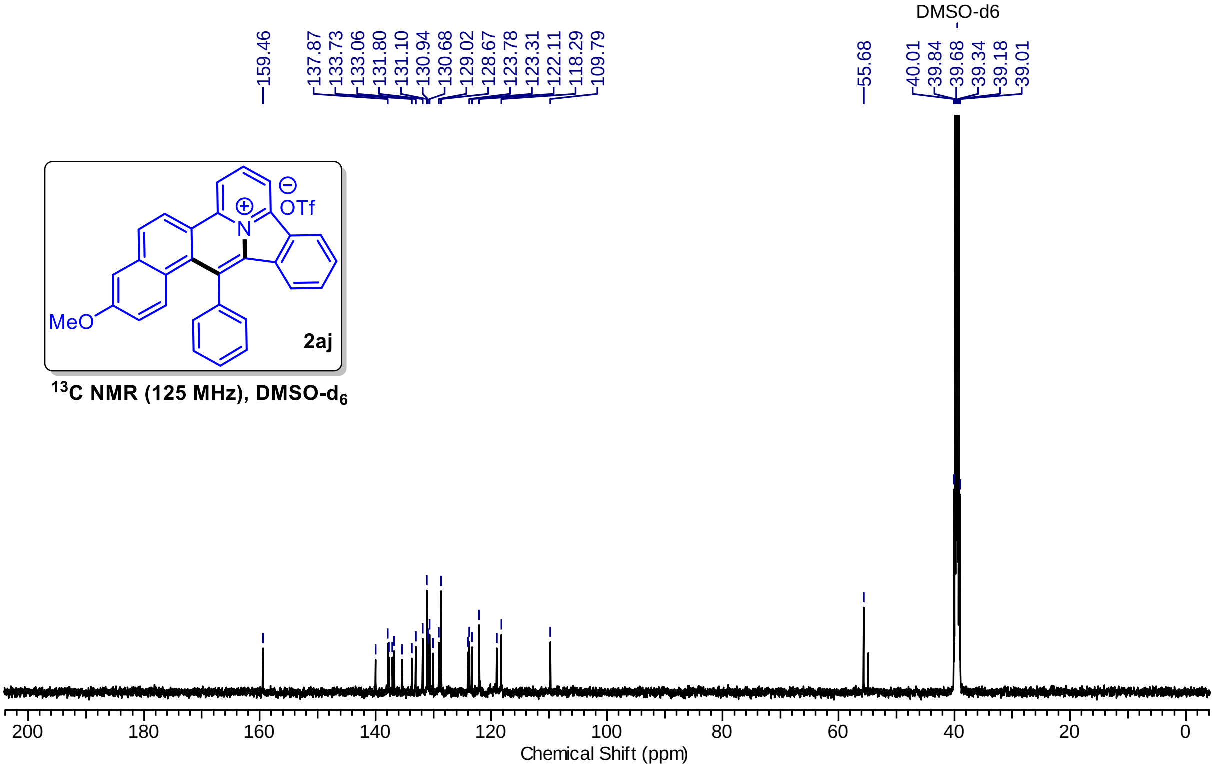

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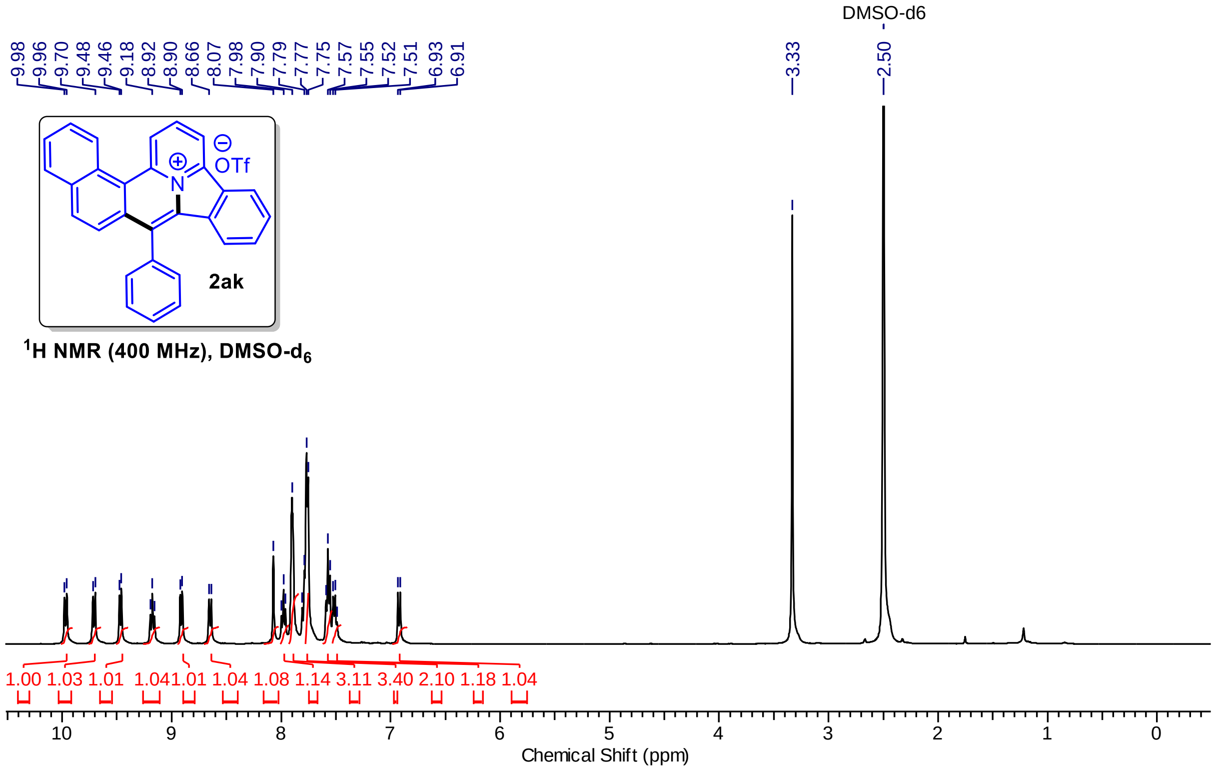
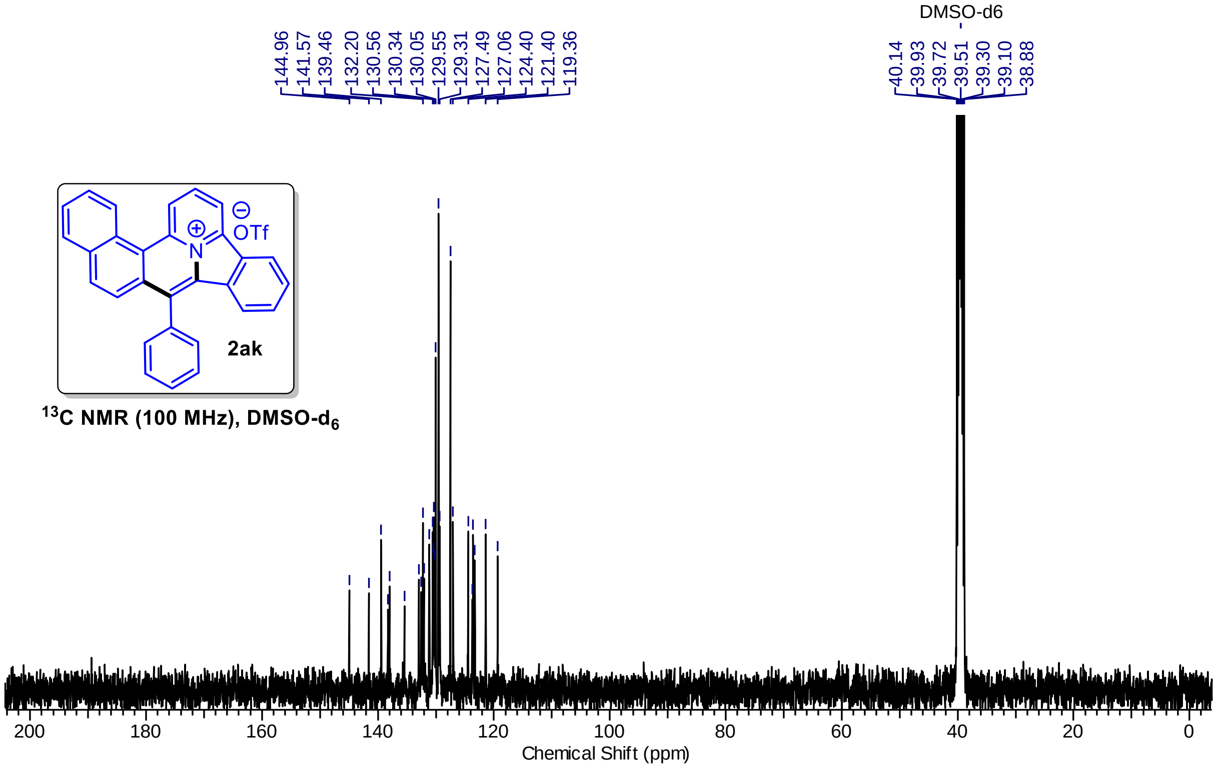
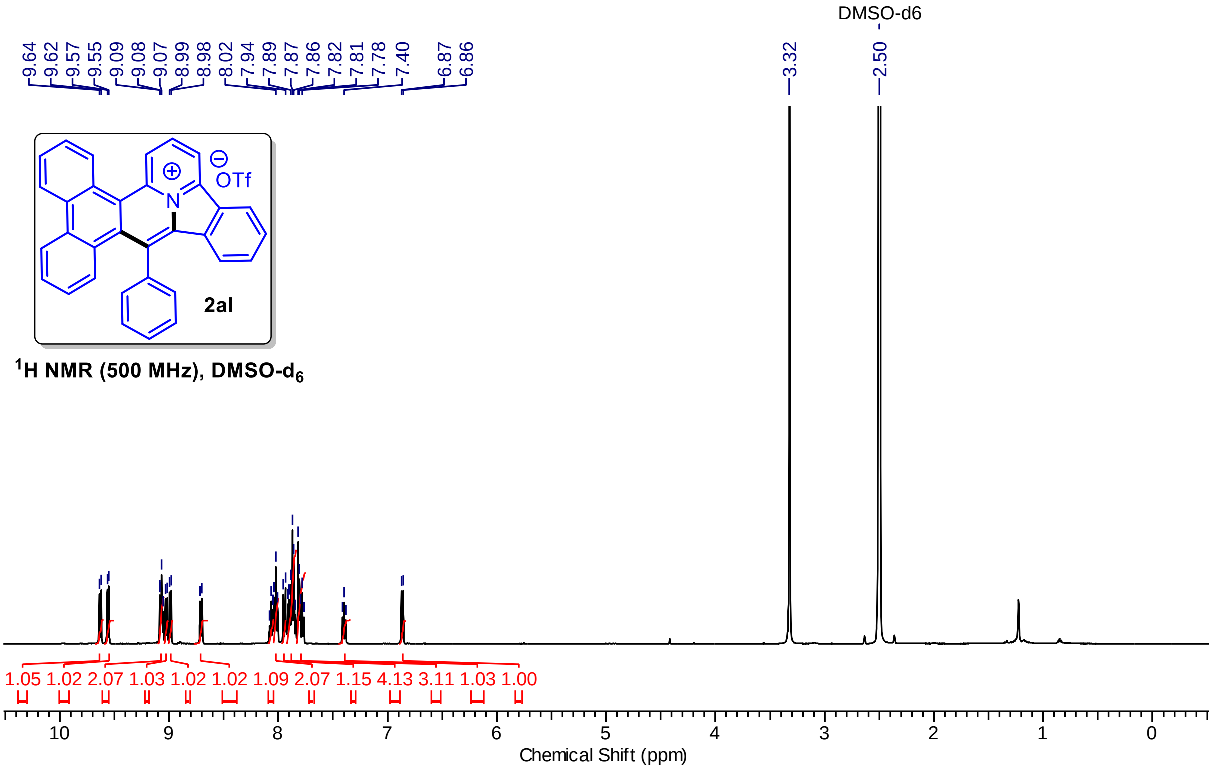
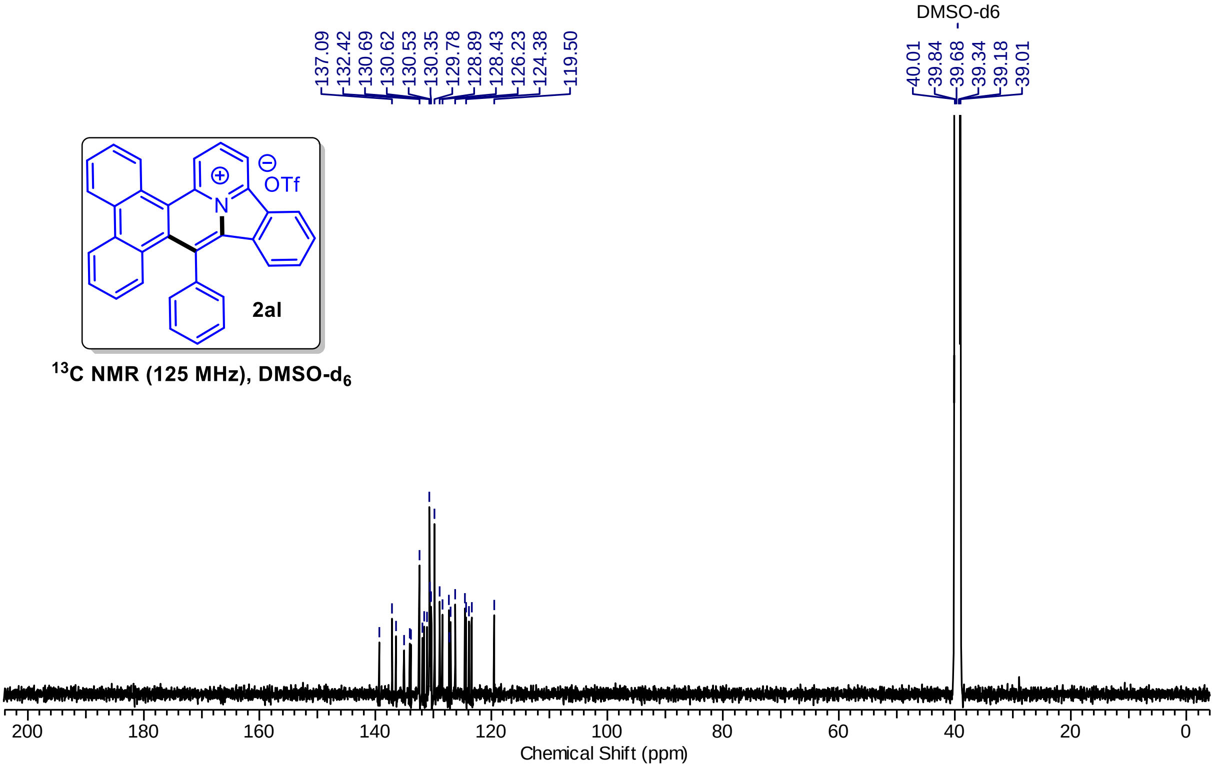

DMSO-d6
9.98 9.96 9.70 9.48 9.46 9.18 8.92 8.90 8.66 8.07 7.98 7.90 7.79 7.77 7.75 7.57 7.55 7.52 7.51 6.93 6.91
3.33
2.50
OTf
N
2ak
^{1}H NMR (400 MHz), DMSO-d_6
1.00 1.03 1.01 1.04 1.01 1.04 1.08 1.14 3.11 3.40 2.10 1.18 1.04
10 9 8 7 6 5 4 3 2 1 0
Chemical Shift (ppm)


DMSO-d6
144.96 141.57 139.46 132.20 130.56 130.34 130.05 129.55 129.31 127.49 127.06 124.40 121.40 119.36
40.14 39.93 39.72 39.51 39.30 39.10 38.88
OTf
N
2ak
^{13}C NMR (100 MHz), DMSO-d_6
200 180 160 140 120 100 80 60 40 20 0
Chemical Shift (ppm)


DMSO-d6
9.64
9.62
9.57
9.55
9.09
9.08
9.07
8.99
8.98
8.02
7.94
7.89
7.87
7.86
7.82
7.81
7.78
7.40
6.87
6.86
3.32
2.50
OTf
N
2al
¹H NMR (500 MHz), DMSO-d₆
1.05
1.02
2.07
1.03
1.02
1.02
1.09
2.07
1.15
4.13
3.11
1.03
1.00
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


137.09
132.42
130.69
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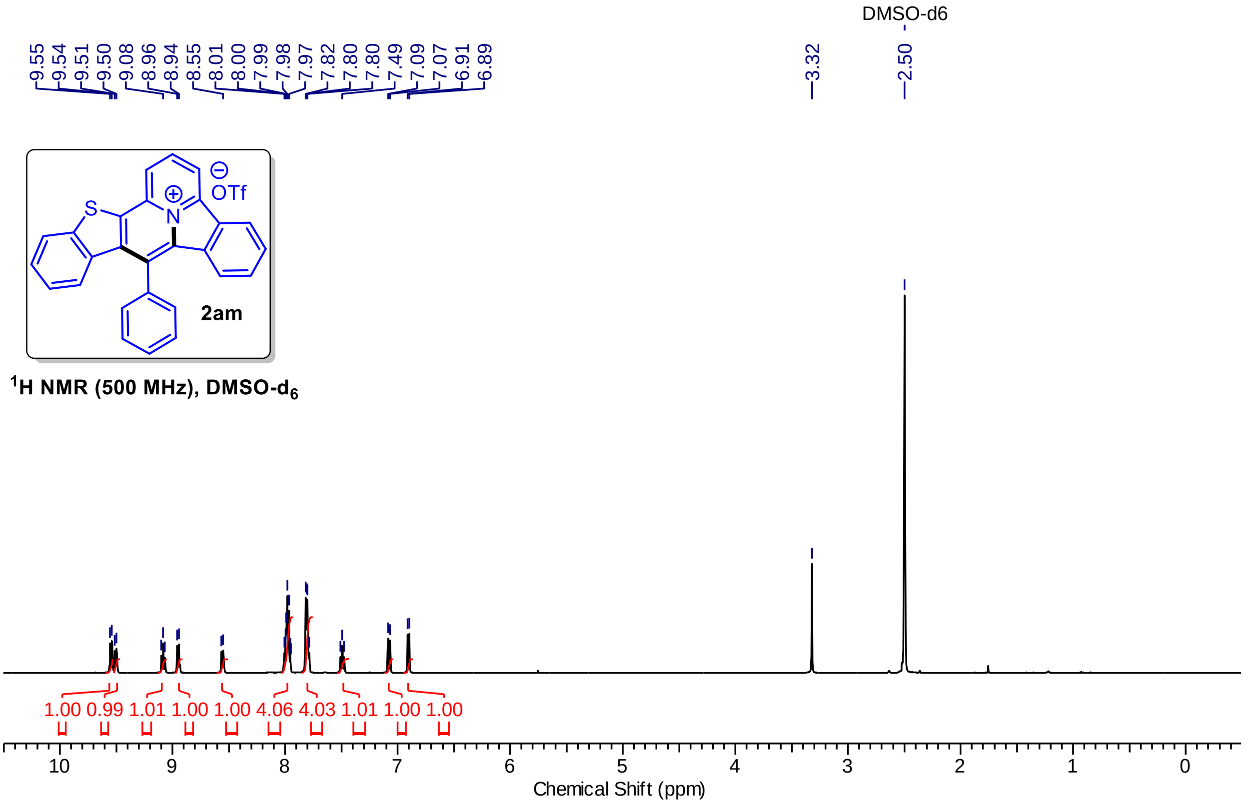
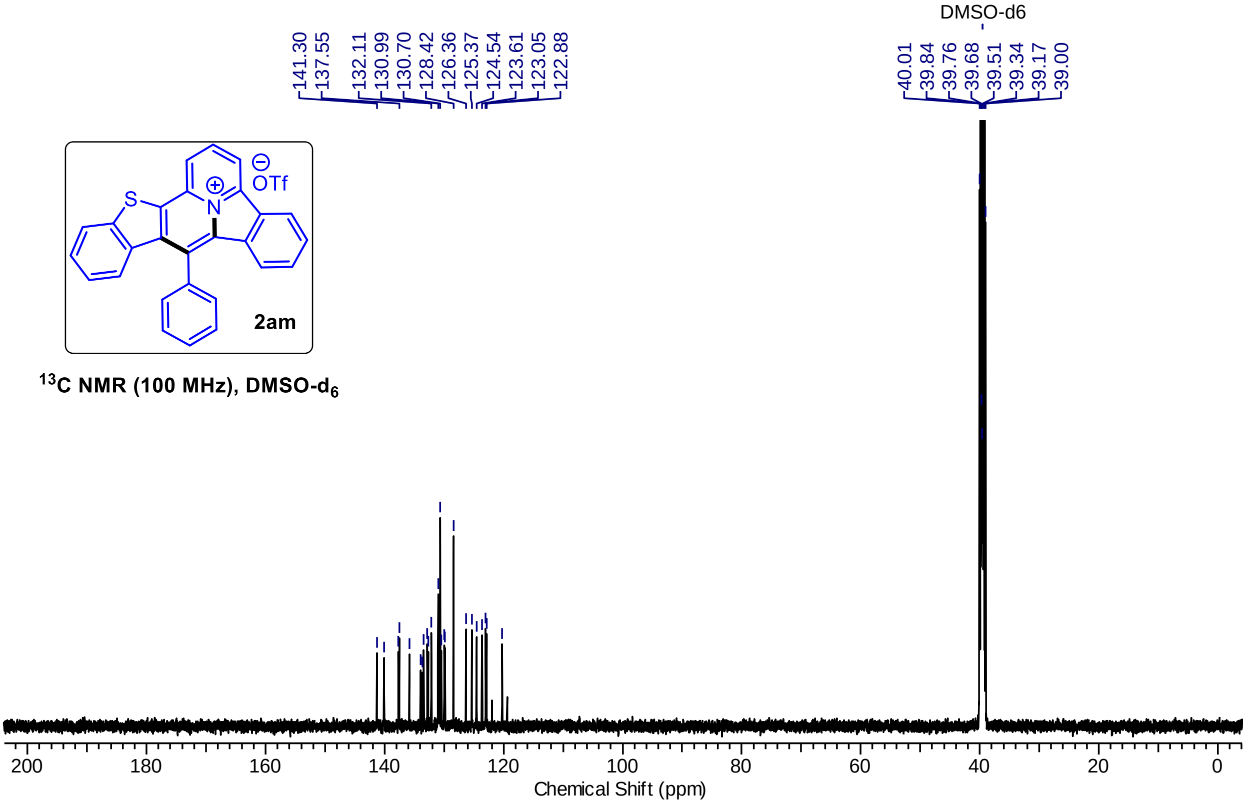
130.53
130.35
129.78
128.89
128.43
126.23
124.38
119.50
DMSO-d6
40.01
39.84
39.68
39.34
39.18
39.01
OTf
N
2al
¹³C NMR (125 MHz), DMSO-d₆
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)



2am

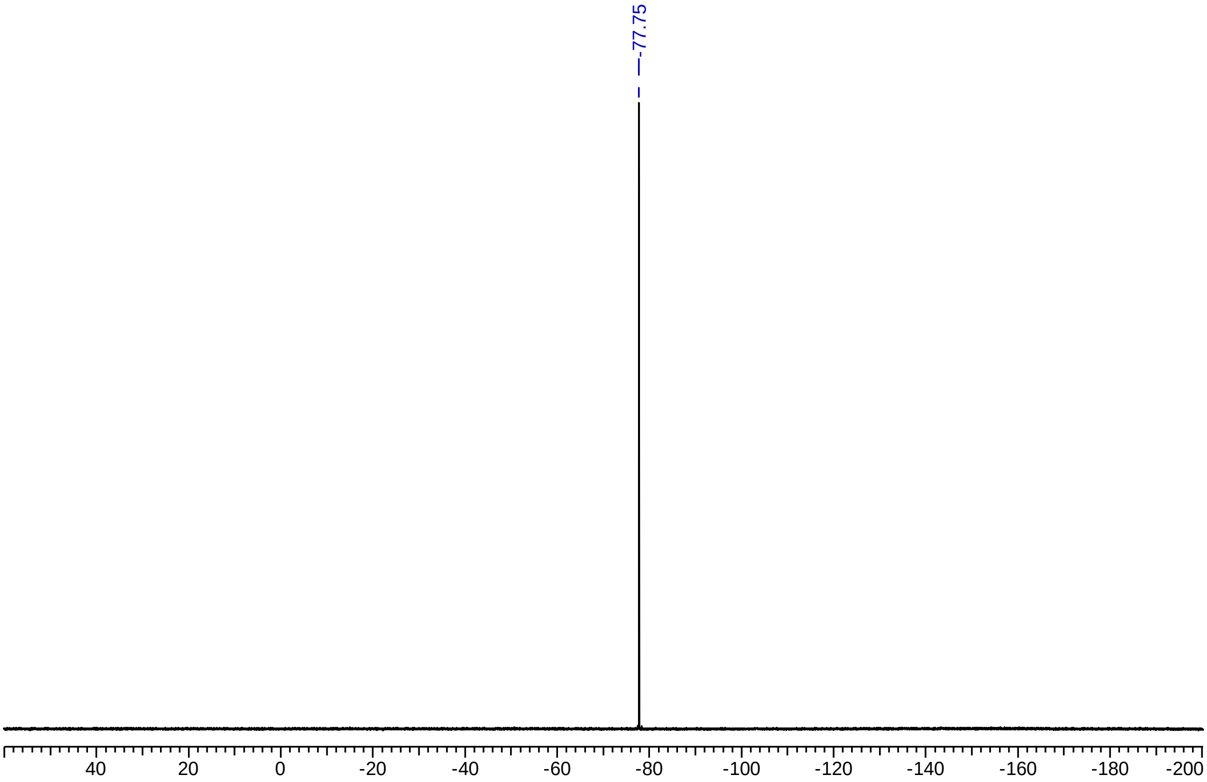
^{1}H NMR (500 MHz), DMSO-d_6



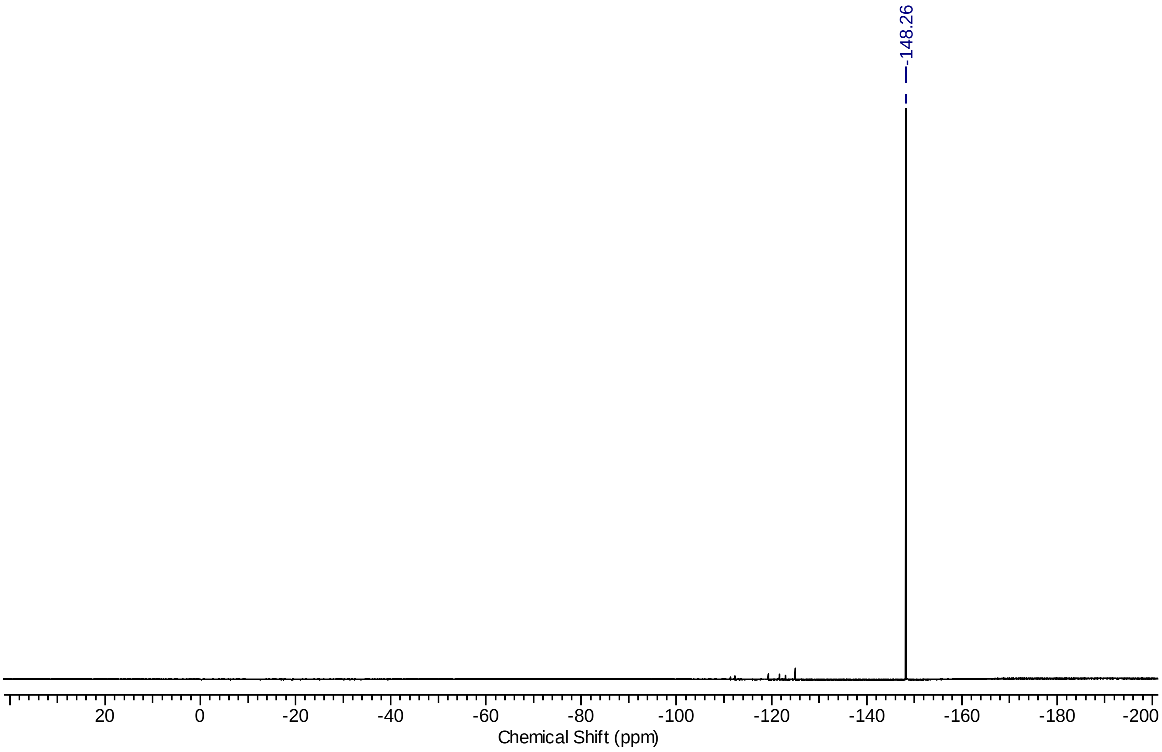
2am

^{13}C NMR (100 MHz), DMSO-d_6

^{19}F NMR (376.5 MHz, DMSO-d_6) of 2a for OTf anion



^{19}F NMR (376.5 MHz, DMSO-d_6)of 2a' for BF_4 anion



2.9 References:

1 Wu, J.; Pisula, W.; Müllen, K. *Chem. Rev*. **2007**, *107*, 718.

2 (a) C. Dou, S. Saito, K. Matsuo,; I. Hisaki, S. Yamaguchi, *Angew. Chem., Int. Ed*. **2012**, *51*, 12206; (b) A. Escande, M. J Ingleson, *Chem. Commun*. **2015**, *51*, 6257; (c) F. Miyamoto, S. Nakatsuka, K. Yamada, K.-i. Nakayama, T. Hatakeyama, *Org. Lett*. **2015**, *17*, 6158; (d) V. M. Hertz, M. Bolte, H.-W Lerner, M. Wagner, *Angew. Chem., Int. Ed*. **2015**, *54*, 8800.

3 T. Baumgartner, *Acc. Chem. Res*. **2014**, *47*, 1613.

4 (a) D. Wu, W. Pisula, M. C. Haberecht, X. Feng, K. Müllen, *Org. Lett*. **2009**, *11*, 5686; (b) L. Zhang, S. M. Fakhouri, F.Liu, J. C Timmons, N. A. Ran, A. L Briseno,. *J. Mater. Chem*. **2011**, *21*, 1329.

5 Reviews: (a) Y. Deng, Y. Xie, K. Zhou and X. Ji, *J. Mater. Chem. A*, **2016**, *4*, 1144; (b) A. Mateo-Alonso, *Chem. Soc. Rev*., **2014**, *43*, 6311; (c) U. H. F. Bunz, J. U. Engelhart, B. D. Lindner and M. Schaffroth, *Angew. Chem., Int. Ed*., **2013**, *52*, 3810; For selected examples, see: (d) A. Skabeev, U. Zschieschang, Y. Zagranyarski, H. Klauk, K. Müllen, C. Li, *Org. Lett*., **2018**, *20*, 1409; (e) X.-Y. Wang, M. Richter, Y. He, J. Björk, A. Riss, R. Rajesh, M. Garnica, F. Hennersdorf, J. J. Weigand, A. Narita, R. Berger, X. Feng, W. Auwärter, J. V. Barth, C.-A. Palma K. Müllen, *Nat. Commun*., **2017**, *8*, 1948; (f) S. Boldt, S. Parpart, A. Villinger, P. Ehlersand P. Langer, *Angew. Chem., Int. Ed*., **2017**, *56*, 4575; (g) C.-F. Liu, C. Cheng, Y. Jiang, W.-Y. Lai, W. Huang, *New J. Chem*., **2017**, *41*, 13619; (h) M. Richter, K. S. Schellhammer, P. Machata, G. Cuniberti, A. Popov, F. Ortmann, R. Berger, K. Müllen, X. Feng, *Org. Chem. Front*., **2017**, *4*, 847.

6 (a) K. Xu, Y. Fu, Y. Zhou, F. Hennersdorf, P. Machata, I. Vincon, J. J. Weigand, A. A. Popov, R. Berger X. Feng, *Angew. Chem., Int. Ed*., **2017**, *56*, 15876; (b) D. Wu, R. Liu, W. Pisula, X. Feng, K. Müllen, *Angew. Chem., Int. Ed*., **2011**, *50*, 2791; (c) J. Fortage, F. Tuyèras, P. Ochsenbein, F. Puntoriero, F. Nastasi, S. Campagna, S. Griveau, F. Bedioui, I. Ciofini P. P. Laine, *Chem. –Eur. J*., **2010**, *16*, 11047; (d) J. Fortage, C. Peltier, F. Nastasi, F. Puntoriero, F. Tuyèras, S. Griveau, F. Bedioui, C. Adamo, I. Ciofini, S. Campagna P. P. Laine, *J. Am. Chem. Soc*., **2010**, *132*, 16700; (e) D. Wu, W. Pisula, V. Enkelmann, X. Feng, K. Müllen, *J. Am. Chem. Soc*., **2009**, *131*, 9620; (f) D. Wu, L. Zhi, G. J. Bodwell, G. Cui, N. Tsao, K. Müllen, *Angew. Chem., Int. Ed*., **2007**, *46*, 5417.

7 G. Zhang, L. Yang, Y. Wang, Y. Xie, H. Huang, *J. Am. Chem. Soc*., **2013**, *135*, 8850.

8 D. Zhao, Q. Wu, X. Huang, F. Song, T. Lv, J. You, *Chem. –Eur. J*., **2013**, *19*, 6239.

9 D. Ghorai, J. Choudhury, *ACS Catal*., 2015, 5, 2692.

10 D. L. Davies, C. E. Ellul, S. A. Macgregor, C. L. McMullin, K. Singh, *J. Am. Chem. Soc*., **2015**, *137*, 9659.

11 D. Ghorai, C. Dutta, J. Choudhury, *ACS Catal*., **2016**, *6*, 709.

12 Q. Ge, Y. Hu, B. Li, B. Wang, *Org. Lett*., **2016**, *18*, 2483.

13 B. Feng, D. Wan, L. Yan, V. D. Kadam, J. You, G. Gao, *RSC Adv*., **2016**, *6*, 66407.

14 Y. Yang, D. Liu, M. Song, D. Shi, B. Liu, K. Cheng, Y. Lu, H. Liu, M. Yang, W. Wang, J. Li, J. Wei, *Chem. – Eur. J*., **2017**, *23*, 7409.

15 J. M. Villar, J. Suárez, J. A. Varela, C. Saá, *Org. Lett*., **2017**, *19*, 1702.

16 Y. Asanuma, H. Eguchi, H. Nishiyama, I. Tomita, S. Inagi, Org. Lett., 2017, 19, 1824.

17 J.-R. Deng, C.-S. Tsang, W.-C. Chan, B. C.-B. Ko, N. C.-H. Lai, S. L.-F. Chan, B. Yang, M.-K. Wong, *Chem. Sci*., **2017**, *8*, 7537.

18 F. Li, J. Cho, S. Tan, S. Kim, *Org. Lett*., **2018**, *20*, 824.

19 L. Li, W. W. Brennessel, W. D. Jones *J. Am. Chem. Soc*. 2008, **130**, 12414.

20 (a) C.-Z. Luo, J. Jayakumar, P. Gandeepan, Y.-C. Wu, C.-H. Cheng, *Org. Lett*.**2015**, *17*, 924; (b) C.-Z. Luo, P. Gandeepan, J. Jayakumar, K. Parthasarathy, Y.-W. Chang, C.-H. Cheng, *Chem. – Eur. J*. **2013**, *19*, 14181.

21 G. Zhang, L. Yang, Y. Wang, Y. Xie, H.Huang, *J. Am. Chem. Soc*. **2013**, *135*, 8850.

22 J. Tang, S. Li, Z. Liu, Y. Zhao, Z. She, V. D. Kadam, G. Gao, J. Lan, J. You, *Org. Lett*., **2017**, *19*, 604.

23 Y. R. Han, S.-H. Shim, D.-S. Kim, C.-H. Jun, *Org. Lett.***2017**, *19***,** 2941.

24 J. Sanjosé-Orduna, D. Gallego, A. Garcia-Roca, E. Martin, J. Benet-Buchholz, M. H. Pérez-Temprano, *Angew. Chem., Int. Ed.*, **2017**, *56***,** 12137.

25 S. Prakash, K. Muralirajan, C.-H. Cheng, *Angew. Chem., Int. Ed.*, **2016**, *55*, 1844.

26 Y.-X. Lao, S.-S. Zhang, X.-G. Liu, C.-Y. Jiang, J.-Q. Wu, Q. Li, Z.-S. Huang, H. Wang, *Adv. Synth. Catal.* **2016**, *358,* 2186.

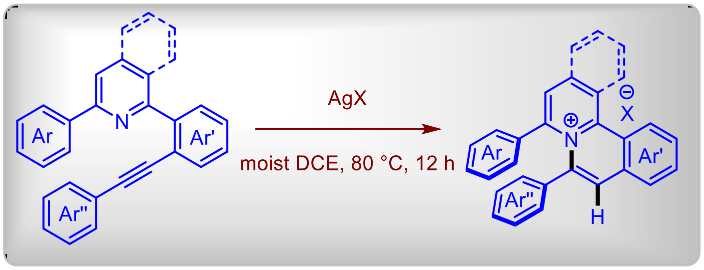
27 A. C.Shaikh, D. S Ranade, P. R. Rajamohanan, P. P. Kulkarni, N. T. Patil, *Angew. Chem. Int. Ed*. **2017**, *56*, 757.

28 G. Zhang, Y. Luo, Y. Wang, L. Zhang, *Angew. Chem., Int. Ed*. **2011**, *50*, 4450.

Chapter 3

Silver-Mediated Intramolecular Hydroamination Reactions of Pyridino-alkynes: An Access to Ionic Solid Light Emitters

Silver(I) salts promoted intramolecular *endo*-selective hydroamination reactions of 2-(2-alkynylphenyl)pyridines to access a new class of N-doped ionic solid light emitters is described. Interestingly, AgOTf exhibits a dual role by mediating the hydroamination reaction as well as providing a counter ion



Manuscript under preparation

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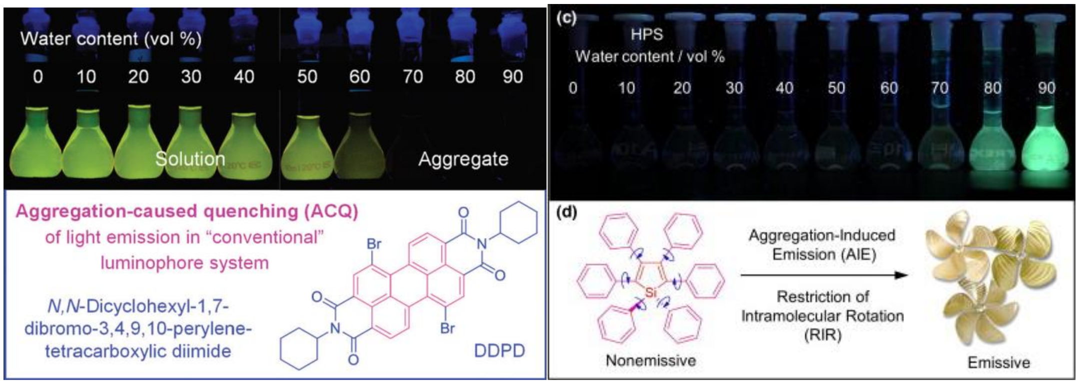
3.1 Introduction

Design and development of luminescent organic materials is of prime importance due to their immense application in biology, chemistry, and optoelectronic device.[1] In general, these fluorophores have been observed to operate most efficiently under high-dilution conditions; whereas the fluorescence quenching (Aggregation Caused Quenching-Fig 3.1a) is studied under highly concentrated conditions and in solid state. As a consequence, the effective application of these luminescent molecules remains limited to narrow range of conditions.

In recent years, ionic solid fluorophores been in the limelight due to their typical properties such as high thermal stabilities, phase tunabilities and water solubilities.[2] However, ionic solid fluorophores display an interesting phenomenon, wherein, compounds exhibit little or no fluorescence in dilute solution, but become remarkably fluorescent once aggregated in the solid state. This remarkable increase in fluorescence was due to restricted intramolecular rotation (RIR) and has been termed as aggregation induced emission (AIE).[3] Hexaphenylsilole (HPS) is one of the first silole derivatives which displayed the AIE phenomenon and hence, HPS can be considered as an archetypal AIE luminogen[4] HPS was discovered to be a propeller-shaped non-planar molecule after structural inspections unlike other conventional luminophores for instance the disc-like planar perylene.



(a) **(b)**

Fig 3.1: a) Conventional luminophore system (ACQ); b) Aggregation induced emission (AIE).

Tang group proposed, the RIR process is responsible for the AIE effect. To understand this effect, they conducted a number of control experiments, activated the RIR process externally and fastened the covalent bonds of aryl rotors to set off the RIR process at the molecular level internally.The luminogens became emissive in response to both the external and internal controls providing strong experimental evidence to support RIR mechanistic hypothesis.[5]

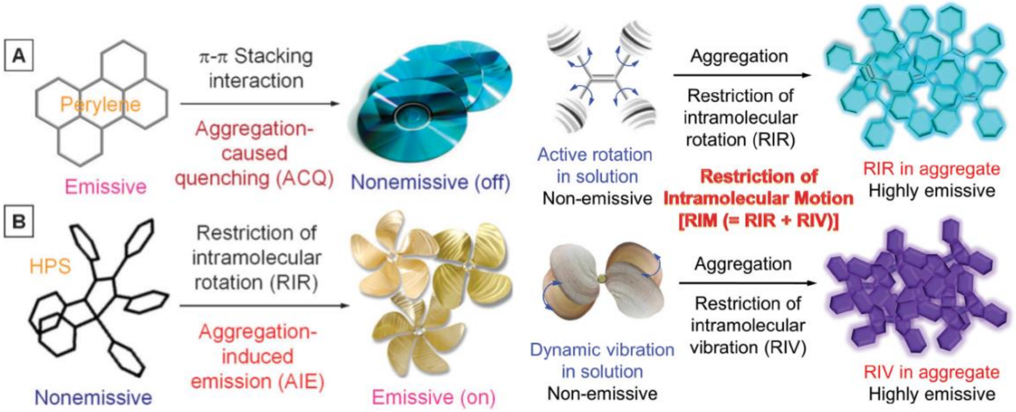


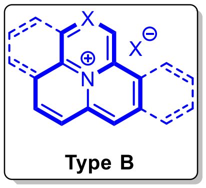
Fig 3.2: Factors which governs the AIE.

Inspired by these features their application are mounting several fields including material science and biology. As a subset, quaternary nitrogen-containing aromatic heterocycles represent an important class of molecules that have interesting applications in the field of optoelectronics, light emitting-diodes, supercapacitors and bio-imaging (Fig 1a).[6] In this chapter reports on pyridinium solid light emitters have been discussed.

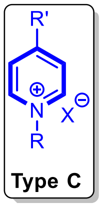
In recent years a series of conjugated polymers have been developed, which showed enhanced light emissions in the solid state because of aggregation of compounds. A structural generality that is commonly found in these polymers is that each of their repeating units bear phenyl rotor(s) and an olefin stator;[7] which also resembles the tetraphenylethene (TPE), a well-known AIE luminogen.[8] In case of TPE, phenyl rotors surround the olefin stator and AIE effect is accounted by the RIR process. Taking this inherent property of TPE in account, pyridinium based AIEgens has been reported.

Based on the strategy discussed above, Tang *et al.* reported the synthesis of a new yellow-emissive AIE dye by attaching a pyridinium unit to TPE through vinyl functionality. Some of the multifunctional properties for instance morpho- and mechano-chromism, optical waveguide and imaging of mitochondrion have been studied.[9] Further, they extended this TPE-Py into TPE-DPy. Interestingly, TPE-DPy molecules also exhibits aggregation-induced emission enhancement properties and irreversible mechanochromic behavior.[10] In 2015, D. Zhang and G. Zhang *et al*. reported salts of highly solid-state emissive pyridinium-substituted tetraphenylethylene with different anions. The emission colors had tuned by the counter anions.[11] Again Tang *et al*. reported a dual functional aggregation-enhanced emission (AEE) molecule, TPE-isoquinoline (TPE-IQ), which targets and illuminates mitochondria in live and fixed cells. More interestingly, TPE-IQ have been found to be good photosensitizer employed to generate reactive oxygen species (ROS) in mitochondria region in order to induce cell apoptosis.[12] Further modification in TPE-IQ to electron-donating methoxy group TPE-IQ-2O gave excellent activity towards selective staining and killing of cancer cells using white light irradiation.[13] The same group in 2018 reported an efficient synthesis to develop three new double bond-free AIEgens that displayed high stability and tolerated multiple functionalities. By the placement of various electron donor groups to the electron-deficient isoquinolinium core,[14] their emission colors were modulated with both visible one-photon and near-infrared two-photon excitations. General representation of all the above discussed Type A solid light emitters has been presented.

polysubstituted cationic 12-azapyrene salts by employing rhodium(III)-catalyzed C–H annulation of alkynes with N-arylpyridinium salts. Thus obtained substituted salts exhibited intense and tunable fluorescent emission in solid as well as in the solution state[15] Recently, Patel *et al.* reported Ru(II)-catalyzed synthesis of multifunctional AEEgens series with tunable emission via quinoxaline- directed oxidative annulation of 2-arylqoinoxalines. The synthesized annulated quaternary ammonium salt possesses aggregation enhanced emission *via* RIR mechanism and donor-π-acceptor interaction. These compounds exhibit mechanochromic property and have an anticancer effect on cells.[16] These reports are summarized in type B design.



Pyridinium molecules being electron-deficient in nature, could form intermolecular charge transfer complexes with other donor molecules.[17] In this regard, Jie Zhang *et al.* reported the synthesis of pyridinium molecules which have bright white light emission through aggregation of molecules. Intramolecular charge transfer has been studied *via* single-crystal, photophysical and computational studies. It has been demonstrated that the

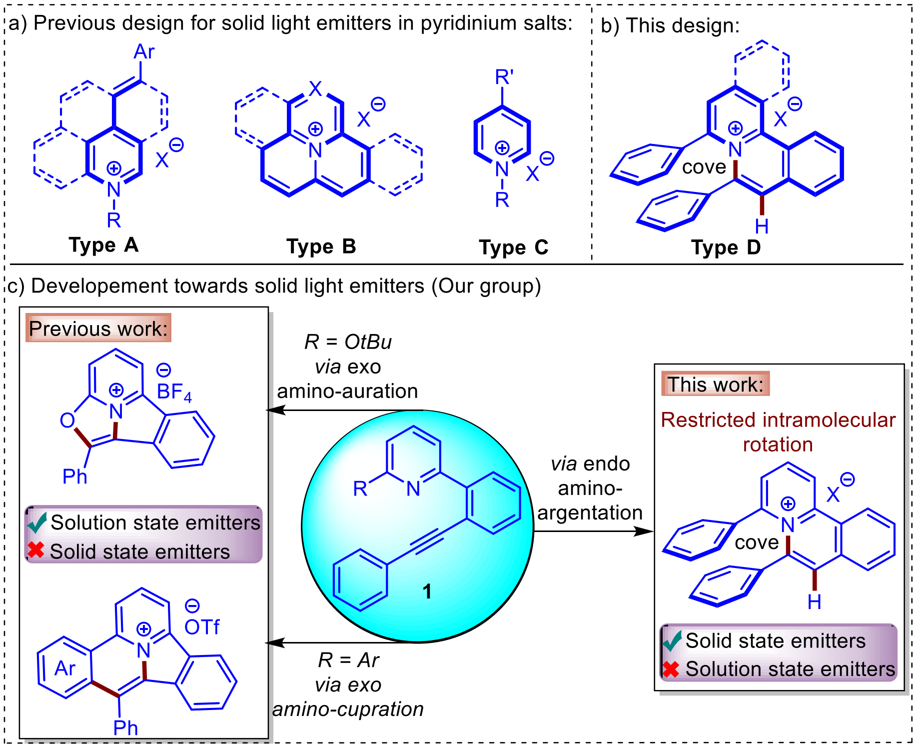


excitation of a newly generated intermolecular charge transfer band at the ground state that cooperates with the non-quenched high-energy monomer emission to produce white light was responsible for the additional low-energy emission.[18] Recently Suna *et al*. reported aggregation-induced emission by pyridinium-pyridinium interactions through non-covalent intermolecular interactions between Py^+ subunits.[19] Later, they also showed an innovative approach to furnish AIEgens by exploiting the non-covalent intermolecular π^+-π interactions in-between the quaternary Py^+ or Im^+ (imidazolium) cations and aromatic π systems.[20] Building on to these reports, we wanted to develop such kind of solid fluorophore which will merge the concept intermolecular charge transfer and RIR in one frame; and our experimental investigation in this regard have been disclosed herein.

3.2 Present Work

As far as our prior reports in this direction are concerned, we have developed gold-catalysed oxidative intramolecular 1,2-amino-oxygenation reactions of alkynes to produce structurally unique ionic pyridinium-oxazole dyad with tunable emission wavelengths (Scheme 1c).[21] Soon after, we reported the Cu(II)-mediated intramolecular alkynes/azadienes [4+2]-formal annulation cascade to provide efficient access to ionic N-doped PAHs with tunable emission wavelengths (Scheme 1c).[22] Unfortunately, all the developed molecules are solution state emitter (ACQ) only, and do not display any significant emission in solid state.

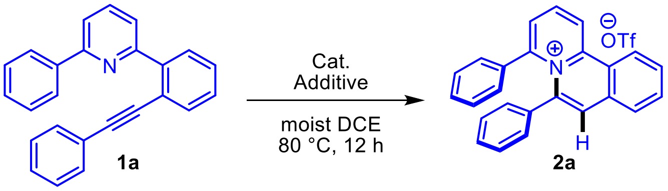
We surmised that the substrate of type **1** (R = Ar) in the presence of appropriate metal catalysts would produce cove shaped 4,6-diarylated isoquinolopyridinium (IQP) salts (Type D) *via* endo-selective hydroamination (Scheme 1c). The approximation was based on the thinking that flat disk-like aromatic molecules at the 2nd and 6th position of IQP will disrupt the planarity thereby hampering[23] the intramolecular rotation (IMR) which is the main requirement for the molecule to be a solid emitter. Herein, we disclose an AgOTf promoted intramolecular hydroamination reactions of 2-(2-alkynylphenyl)pyridines to access a new class of N-doped ionic solid light emitters. In these reactions, AgOTf played a dual role by mediating the hydroamination reaction as well as providing a counter ion.



Scheme 1. Design of *N*-doped ionic solid light emitters

3.3 Optimization table

Table 1. Optimization of reaction conditions[a,b]



Sr. No.	Cat	Additives	Yield (%)[b]
1.	$Ph_3PAuOTf$	NaOTf	--
2.	$Ph_3PAuOTf$	$Mg(OTf)_2$	--
3.	$Ph_3PAuOTf$	$Sc(OTf)_3$	--
4.	$Ph_3PAuOTf$	TfOH	--
5.	$(C_6F_5)_3PAuOTf$	NaOTf	--
6.	AgOTf	NaOTf	09
7.	AgOTf	TfOH	09
8.	AgOTf	--	09

9.	AgOTf	--	45[c]
10.	**AgOTf**	**--**	**94[d]**
11.	AgOTf	--	90[d,e]
12.	AgOTf	--	88[d,f]

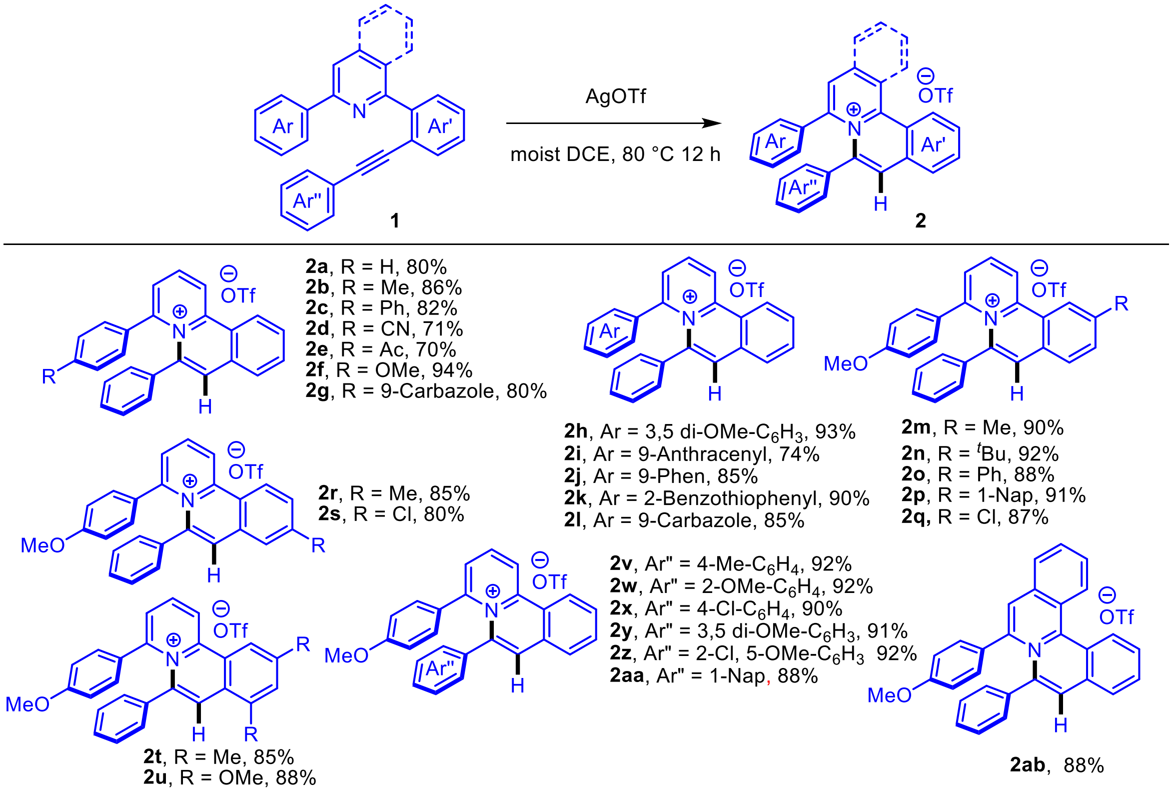
[a]Reaction conditions: **1a** (0.1 mmol), metal catalyst (0.01 mmol, 10 mol%), moist DCE (2.0 mL), 12h. [b]Isolated yields; [c]0.5 equiv. catalyst was used, [d]1.0 equiv. catalyst was used, [e]Solvent $CHCl_3$ was used. [f]Solvent CH_3CN was used. (moist DCE : dry DCE with 0.200 mmol of water was used)

To validate the above-mentioned hypothesis, our study commenced by using 2-(2-alkynylphenyl)pyridine (**1a**) as model substrate, which has been efficiently prepared by Pd-catalyzed cross-coupling reactions. To begin with, the effect of various carbophilic activator were studied, for example the Au(I) salts which would coordinate to the alkyne subsequently triggering an intramolecular attack of pyridyl nitrogen in 6-*endo-dig* fashion to generate vinyl-gold intermediate and subsequent protodeauration leads to product. To test the hypothesis, the reaction of 2-phenyl-6-(2-(phenylethynyl)phenyl)pyridine (**1a**) in the presence of $Ph_3PAuOTf$ with various counter ion providers like NaOTf, MgOTf, $Sc(OTf)_3$ and TfOH was tested. Unfortunately, the the desired product was not obtained in either of the entries (Table 1, entries 1-5). Pleasingly, the desired hydroamination product **2a**, albeit in 9% yield, was obtained when 10 mol% of AgOTf was used in combination with additive (entry 6-7). From these result, we conclude additives are inert in reaction condition, hence by exceeding the mol% AgOTf (1 equiv) and interestingly yield of the product enhanced up to 94%. Next, the various other solvents were examined (entries 11-12), however, a detrimental effect in the yield was observed.

3.4 Substrate scope

With the optimized reaction conditions in hand, we explored the generality of the reaction. The results are summarized in Table 2. At first, substrates with variation at *-para* position of aryl ring (Ar) at the C-2 position of pyridine (**1a-1g**) were put to test. Substrates bearing electron-withdrawing and electron-donating groups were well-tolerated to furnish the corresponding product in good to excellent yields (**2a-2g**). To understand the tolerance of the substituents at the Ar' ring on the same position at the C-2 position, substrates **1h-1j** was examined under the optimized reaction conditions. It was observed that **1h-1j** underwent smooth reactions to provide the desired products **2h-2j** in good yields (74–93%). Even the hetero-aromatic 2-benzothiophenyl and 9-carbazolyl moieties were also well-tolerated giving the desired product 90% and in 85% yield respectively.

Table 2: Substrate Scope[a,b]



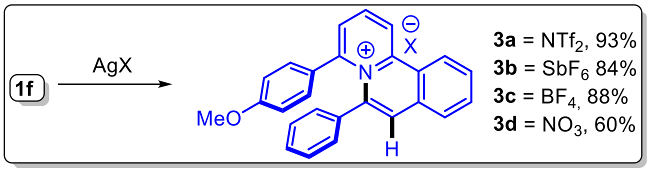
[a]Reaction conditions: **1** (0.1 mmol), 1.0 equiv. AgOTf, moist DCE (2.0 mL), 80 °C, 12h. [b]Isolated yields.

Next, our efforts were directed to examine the tolerance of substitution of the C-6 phenyl ring of pyridinyl scaffold. Introduction of Me, ^{t}Bu, Ph, 1-Nap and Cl, at *meta*-position to the aforementioned phenyl ring resulted in good to excellent yield of the reaction (**2m-2q**). Additionally, the substitution of Me and Cl at para position on the same ring, resulted in good yield of expected products (**2r** and **2s**). Also, the reaction tolerates di-substitutions at the phenyl ring to offer the products **2t**, and **2u** in 85% and 88% yields, respectively.

It was further noted that various substitution patterns on the aryl (Ar") ring of alkynes, such as 4-Me, 2-OMe, 4-OMe and di-substitution are also well tolerated under the standard reaction conditions, and the corresponding products (**2v**-**2z**) were isolated in excellent yields (90-92%). Also, the alkyne tethered aryl ring with 1-Nap also resulted in good yield (**2aa**). Switching the pyridyl ring with an isoquinoline ring did not hamper the reaction and **2ab** was isolated in 88% yield. The scalability of the method was demonstrated by the large-scale synthesis employing **1a** (1.0 mmol) as a starting material (**2a**, 76%). In this reaction the Lewis acidic character of silver complexes allows the π activation of C-C triple bond in pyridine-alkyne core triggering a 6-endo-dig attack from the N-center to generate a vinyl-argentum species which undergo proto-deargentation to afford our observed product.

Various groups found that the effect of the counter ion could change the emission behavior and molecular crystal packing of the salts.[24] Different counter ion bearing isoquinolopyridinium (IQP) salts were synthesized by using corresponding silver salts under optimized reaction condition (Table 3).

Table 3. Variation of counter-ions [b]



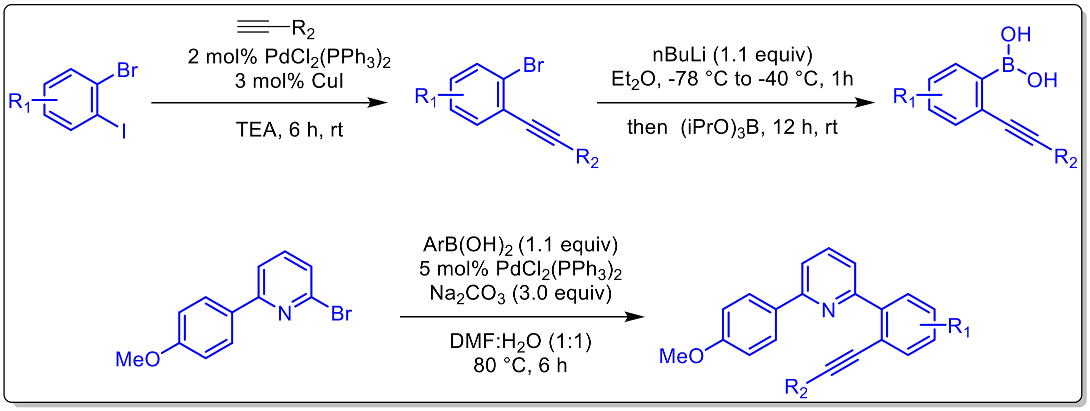
[a]Reaction conditions: **1c** (0.1 mmol), 1.0 equiv. AgX, moist DCE (2.0 mL), 80 °C, 12h. [b]Isolated yields.

3.5 Conclusion

In conclusion, a novel silver mediated color-tunable N-doped series of highly emissive luminogens in solid state has been designed and developed. The reagent AgOTf exhibits a dual role by mediating the cascade transformation as well as providing a counter ion. Excellent photo-physical properties and their crystallography studies indicate that this class of compounds could have potential application in optoelectronic devices.

3.6 Experimental procedures

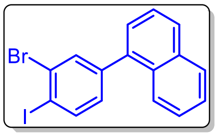
3.6.1 Synthesis of starting materials



Synthesis of 1-(3-bromo-4-iodophenyl)naphthalene (S_1)

To a solution of 2-bromo-4-(naphthalen-1-yl)aniline (2 g, 6.70 mmol) dissolved in CH_3CN (40 mL) was added *p*-toluenesulfonic acid (3.46 g, 20.12 mmol), then the mixture was cooled to 0 °C, and it was added a solution of $NaNO_2$ (0.69 g, 10.05 mmol) in water (10 mL). After addition, the reaction was kept at the temperature lower than 5 °C for 30 min and it was added a solution of KI (1.66 g, 10.05 mmol) in water (10 mL). After addition, the reaction was kept at room temperature overnight, poured into water (300 mL) and extracted with CH_2Cl_2. The organic phase was dried over Na_2SO_4.

1-(3-bromo-4-iodophenyl)naphthalene (S_1):

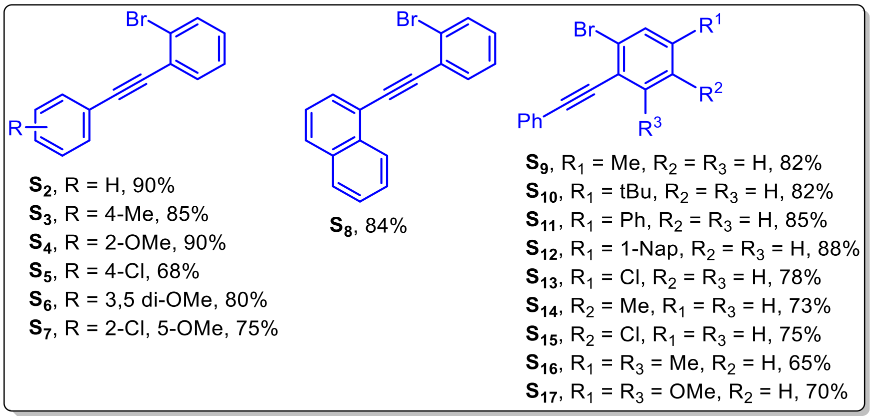


White solid, 2.20 gm, 80% yield; ***Rf*** = 0.50(Hexane/EtOAc = 95/05); **^{1}H NMR (700 MHz, $CDCl_3$) δ** = 7.98 (d, *J* = 8.0 Hz, 1 H), 7.93 (d, *J* = 8.2 Hz, 1 H), 7.90 (d, *J* = 8.2 Hz, 1 H), 7.83 (d, *J* = 8.4 Hz, 1 H), 7.79 (s, 1 H), 7.53 (t, *J* = 7.5 Hz, 2 H), 7.50 - 7.46 (m, 1 H), 7.39 (d, *J* = 6.9 Hz, 1 H), 7.18 - 7.13 (m, 1 H); **^{13}C NMR (175 MHz, $CDCl_3$) δ** = ^{13}C NMR (176MHz ,CHLOROFORM-d) **δ** = 142.5, 140.0, 137.5, 134.0, 133.7, 131.1, 130.2, 129.7, 128.5, 128.4, 126.9, 126.5, 126.1, 125.3, 125.3, 99.7, 77.2, 76.8; **HRMS (ESI)** calcd for $C_{16}H_{10}BrI$ $(M + H)^+$ 408.9012, found 408.9015.

3.6.2 General procedure for preparation of substituted 2-alkynyl-bromobenzenes

The bromo-alkynes **S_2-S_9** and **S_{13}-S_{17}** were reported in the literature and prepared according to the literature known procedure.[1] The other bromo-alkynes **S_{10}-S_{12}** were prepared from the literature known procedure by slightly modified procedure.

Representative procedure for Sonogashira cross-coupling: A suspension of 2-bromo-4-(tert-butyl)-1-iodobenzene (2 gm, 5.89 mmol, 1.0 equiv), $PdCl_2(PPh_3)_2$ (83 mg, 0.11 mmol, 2 mol%), Cu(I) iodide (33.5 mg, 0.17 mmol, 3 mol%) in 20 mL of triethylamine was degassed three times. After 10 min a solution of phenylacetylene (0.71 mL, 6.48 mmol, 1.1 equiv) in triethylamine (3 mL) was added drop-wise over 5 min via syringe and the reaction mixture was left to stir for 12 h. After the total consumption of the 2-bromo-4-(tert-butyl)-1-iodobenzene, as monitored by TLC, the reaction mixture was filtered through celite and extracted with ethyl acetate (3 × 10 mL). The organic layer was washed with a saturated solution of NH_4Cl (2 × 10 mL), water (2 × 10 mL), dried over Na_2SO_4 and the solvent was removed under vacuo. The reaction mixture was purified by flash chromatography on silica gel, (eluent: petroleum ether) to give the 2-bromo-4-(tert-butyl)-1-(phenylethynyl)benzene (**S_{11}**) in 88% yield. **Note**: The Aryl bromo alkyne **S_{10}** was accompanied with slight impurity and hence used directly for next reaction without attempting further purification.



S_2, R = H, 90%
S_3, R = 4-Me, 85%
S_4, R = 2-OMe, 90%
S_5, R = 4-Cl, 68%
S_6, R = 3,5 di-OMe, 80%
S_7, R = 2-Cl, 5-OMe, 75%

S_8, 84%

S_9, R_1 = Me, R_2 = R_3 = H, 82%
S_{10}, R_1 = tBu, R_2 = R_3 = H, 82%
S_{11}, R_1 = Ph, R_2 = R_3 = H, 85%
S_{12}, R_1 = 1-Nap, R_2 = R_3 = H, 88%
S_{13}, R_1 = Cl, R_2 = R_3 = H, 78%
S_{14}, R_2 = Me, R_1 = R_3 = H, 73%
S_{15}, R_2 = Cl, R_1 = R_3 = H, 75%
S_{16}, R_1 = R_3 = Me, R_2 = H, 65%
S_{17}, R_1 = R_3 = OMe, R_2 = H, 70%

3-bromo-4-(phenylethynyl)-1,1'-biphenyl (**S_{11}**):

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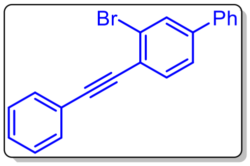
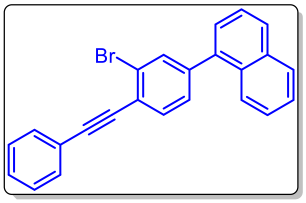
[1] (a) Shaikh, A. C.; Ranade, D. S.; Rajamohanan, P. R.; Kulkarni, P. P.; Patil, N. T. *Angew. Chem. Int. Ed*. **2017**, *56*, 757. (b) Shinde, P. S.; Shaikh, A. C.; Patil, N. T. *Chem. Commun*. **2016**, *52*, 8152. (c) Guo, R.; Li, K.-N.; Liu, B.; Zhu, H.-J.; Fan, Y.-M.; Gong, L.-Z. *Chem. Commun*. **2014**, *50*, 5451. (d) Yoo, W.-J.; Nguyen, T. V. Q.; Kobayashi, S. *Angew. Chem., Int. Ed*. **2014**, *53*, 10213. (e) Körner, C.; Starkov, P.; Sheppard, T. D. *J. Am. Chem. Soc*. **2010**, *132*, 5968.



Off white solid, 1.57 gm, 85% yield; mp = 74-76 °C; ***Rf*** = 0.50 (Hexane/EtOAc = 98/02); **^{1}H NMR (700 MHz, CDCl$_3$) δ** = 7.90 (s, 1 H), 7.64 (d, *J* = 7.3 Hz, 3 H), 7.60 (d, *J* = 7.5 Hz, 2 H), 7.55 (d, *J* = 8.0 Hz, 1 H), 7.49 (t, *J* = 7.3 Hz, 2 H), 7.44 - 7.39 (m, 4 H); **^{13}C NMR (175 MHz, CDCl$_3$) δ** = 142.4, 138.9, 133.4, 131.7, 130.8, 128.9, 128.6, 128.4, 128.1, 127.0, 126.0, 125.7, 124.0, 122.9, 94.4, 88.0; **HRMS (ESI)** calcd for $C_{20}H_{13}Br$ (M + Na)$^+$ 355.0093, found 355.0075.

1-(3-bromo-4-(phenylethynyl)phenyl)naphthalene (**S$_{12}$**):



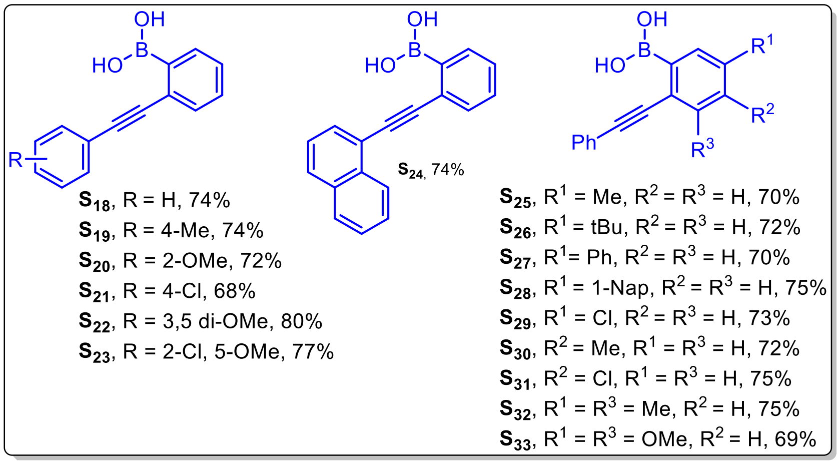
Off white solid, 1.64 gm, 88% yield; mp = 75-77 °C; ***Rf*** = 0.60 (Hexane/EtOAc = 95/05); **^{1}H NMR (500 MHz, CDCl$_3$) δ** = 7.99 - 7.91 (m, 3 H), 7.87 - 7.83 (m, 1 H), 7.76 - 7.67 (m, 3 H), 7.60 - 7.50 (m, 3 H), 7.50 - 7.41 (m, 5 H); **^{13}C NMR (125 MHz, CDCl$_3$) δ** = 142.2, 137.9, 133.7, 132.8, 131.7, 131.1, 128.8, 128.6, 128.4, 128.4, 126.9, 126.4, 126.0, 125.5, 125.4, 125.3, 124.2, 122.9, 94.3, 88.0; **HRMS (ESI)** calcd for $C_{24}H_{15}Br$ (M + H)$^+$ 383.0412, found 383.0415.

3.6.3 General procedure for preparation of 2-alkynylphenylboronic acids

The boronic acid **S$_{18}$-S$_{25}$**, and **S$_{29}$-S$_{33}$** were reported in the literature and prepared according to the literature known procedure. The other boronic acids **S$_{26}$-S$_{28}$** were prepared from literature known procedure with slight modifications.

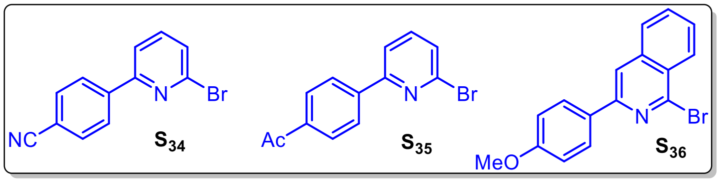
Representative procedure for lithiation/borylation: In a two-necked round bottom flask, 1.6 M solution of ^{n}BuLi in n hexanes (4.5 mL, 7.18 mmol, 1.5 equiv) was added drop-wise to a solution of 2-bromo-4-(tert-butyl)-1-(phenylethynyl)benzene (1.5 g, 4.78 mmol, 1.0 equiv) in 45 mL of diethyl ether under nitrogen atmosphere at -78 °C. The mixture was stirred at -78 °C for 1 h and then at -40 °C for 1 h then cool back to -78 °C and B(O^{i}Pr)$_3$

(1.65 g, 8.78 mmol, 1.5 equiv) was added drop-wise. The mixture was allowed to warm up gradually to room temperature, while maintaining vigorous stirring for 16 h. Then, the reaction was quenched with 40 mL of 1N HCl for 30 minutes and extracted with ethyl acetate (3 x 20 mL). The combined organic solution was dried over Na_2SO_4 and the solvent was removed under vacuo. The product was purified by flash chromatography on silica gel, (eluent: petroleum ether/ethyl acetate) followed by recrystallization from petroleum ether to give the product (5-(tert-butyl)-2-(phenylethynyl)phenyl)boronic acid (**S$_{26}$**) in 80% yield. **Note**: All the boronic acids were carried forward for the next reaction without purification.



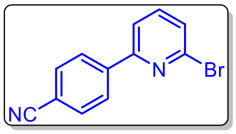
3.6.4 Synthesis of 2-(aryl)-6-(2(alkynyl)-phenyl)pyridines

Representative procedure for Suzuki cross-coupling reaction: In a sealed tube 2,6-di-Bromopyridine (200 mg, 0.84 mmol, 1.0 equiv) and 4-Acetylphenyl boronic acid (**S$_{28}$**) (139 mg, 1.0 equiv) in DMF/H_2O (1:1, 4 mL) was degassed with nitrogen for 5 min. Next, Na_2CO_3 (265 mg, 3 equiv) and $PdCl_2(PPh_3)_2$ (30 mg, 5 mol%) were added under nitrogen atmosphere. The reaction mixture was stirred at 80 °C for 4 h. After complete consumption of starting material, as monitored by TLC, the resulting mixture was allowed to bring to room temperature. The reaction mixture was diluted with $NaHCO_3$ (5 mL), and then the product was extracted with ethyl acetate (3 × 5 mL). The combined organic layer was dried over Na_2SO_4 and the organic solvent was removed under vacuo. The crude product was purified on a silica gel column using petroleum ether/ethyl acetate as eluent to afford 1-(4-(6-bromopyridin-2-yl)phenyl)ethan-1-one (**S$_{35}$**)in 70% yield. Note:



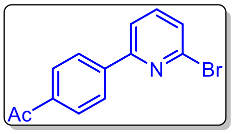
S_{34} S_{35} S_{36}

4-(6-bromopyridin-2-yl)benzonitrile (S_{34}):



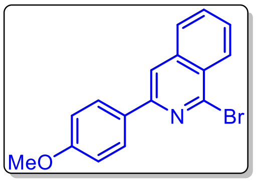
white solid, 131 mg, 65% yield; mp = 95-97 °C; ***Rf*** = 0.30 (Hexane/EtOAc = 95/05); **^{1}H NMR (400 MHz, CDCl$_3$) δ** = 8.12 (d, *J* = 8.3 Hz, 2 H), 7.79 - 7.72 (m, 3 H), 7.70 - 7.64 (m, 1 H), 7.51 (d, *J* = 7.7 Hz, 1 H); **^{13}C NMR (100 MHz, CDCl$_3$) δ** = 156.2, 142.5, 141.6, 139.3, 132.6, 127.7, 127.5, 119.5, 118.5, 113.1; **HRMS (ESI)** calcd for $C_{12}H_7BrN_2$ $(M + H)^+$ 258.9865, found 258.9855.

1-(4-(6-bromopyridin-2-yl)phenyl)ethan-1-one (S_{35}):



White solid, 163 mg, 70% yield; mp = 98-100 °C; ***Rf*** = 0.50(EtOAc/Hexane = 90/10); **^{1}H NMR (700 MHz, CDCl$_3$) δ** = 8.11 - 8.07 (m, *J* = 8.2 Hz, 2 H), 8.06 - 8.02 (m, *J* = 8.4 Hz, 2 H), 7.75 (d, *J* = 7.5 Hz, 1 H), 7.64 (t, *J* = 7.7 Hz, 1 H), 7.47 (d, *J* = 7.7 Hz, 1 H), 2.65 (s, 3 H); **^{13}C NMR (175 MHz, CDCl$_3$) δ** = 197.7, 157.1, 142.3, 141.6, 139.1, 137.6, 128.8, 127.2, 127.1, 119.5, 26.8; **HRMS (ESI)** calcd for $C_{13}H_{10}BrON$ $(M + Na)^+$ 297.9838, found 297.9858.

1-bromo-3-(4-methoxyphenyl)isoquinoline (S_{36}):



White solid, 164 mg, 75% yield; mp = 104-106 °C; ***Rf*** = 0.30 (EtOAc/Hexane = 95/05); **^{1}H NMR (400 MHz, CDCl$_3$) δ** = 8.17 - 8.09 (m, 1 H), 7.84 (s, 1 H), 7.79 (d, *J* = 8.2 Hz, 1 H), 7.73 - 7.63 (m, 3 H), 7.54 (ddd, *J* = 1.2, 7.0, 8.4 Hz, 1 H), 7.11 - 7.01 (m, 2 H), 3.91 (s, 3

H); **^{13}C NMR (100 MHz, CDCl$_3$) δ** = 161.3, 160.4, 139.0, 135.0, 131.5, 130.7, 130.7, 127.9, 127.4, 126.1, 125.6, 122.4, 113.9, 55.4; **HRMS (ESI)** calcd for $C_{16}H_{12}BrON$ (M + Na)$^+$ 335.9994, found 336.0021.

3.6.5 Synthesis of 2-aryl 6-(2(alkynyl)-aryl) pyridines

The 2-aryl 6-(2(alkynyl)-aryl) pyridines **1a-1ab**, **1f, 1h-1k, 1m,** and **1q-1aa** were reported in the literature and prepared according to the literature known procedures.[2] The other 2-aryl 6-(2(alkynyl)-aryl) pyridines **1c-1e**, **1g 1l**, **1n-1p** and **1ab** were prepared from slight modifications in literature known procedures.

***Representative procedure for Suzuki cross-coupling reaction**:*In a sealed tube 2-bromo-6-(4-methoxyphenyl)pyridine (200 mg, 0.757 mmol, 1.0 equiv) and (5-(tert-butyl)-2-(phenylethynyl)phenyl)boronic acid (229 mg, 0.825 mmol, 1.1 equiv) in DMF/H_2O 1:1 (4 mL) was degassed with nitrogen for 5 min. Next, Na_2CO_3 (260 mg, 2.47 mmol, 3 equiv) and $PdCl_2(PPh_3)_2$ (27mg, 0.038 mmol, 5 mol%) were added under nitrogen atmosphere. The reaction mixture was stirred at 80 °C for 6 h. After complete consumption of starting material, as monitored by TLC, the resulting mixture was allowed to bring to room temperature. The reaction mixture was diluted with $NaHCO_3$ (5 mL), and then the product was extracted with ethyl acetate (3 × 5 mL). The combined organic layer was dried over Na_2SO_4 and the organic solvent was removed under vacuo. The crude product was purified on a silica gel column using petroleum ether/ethyl acetateas eluent to afford 2-(5-(tert-butyl)-2-(phenylethynyl)phenyl)-6-(4-methoxyphenyl)pyridine (**1n**) in 80% yield. **Note**: The aryl pyridine alkyne **1ab** was accompanied with slight impurity and hence used directly for next reaction without attempting further purification

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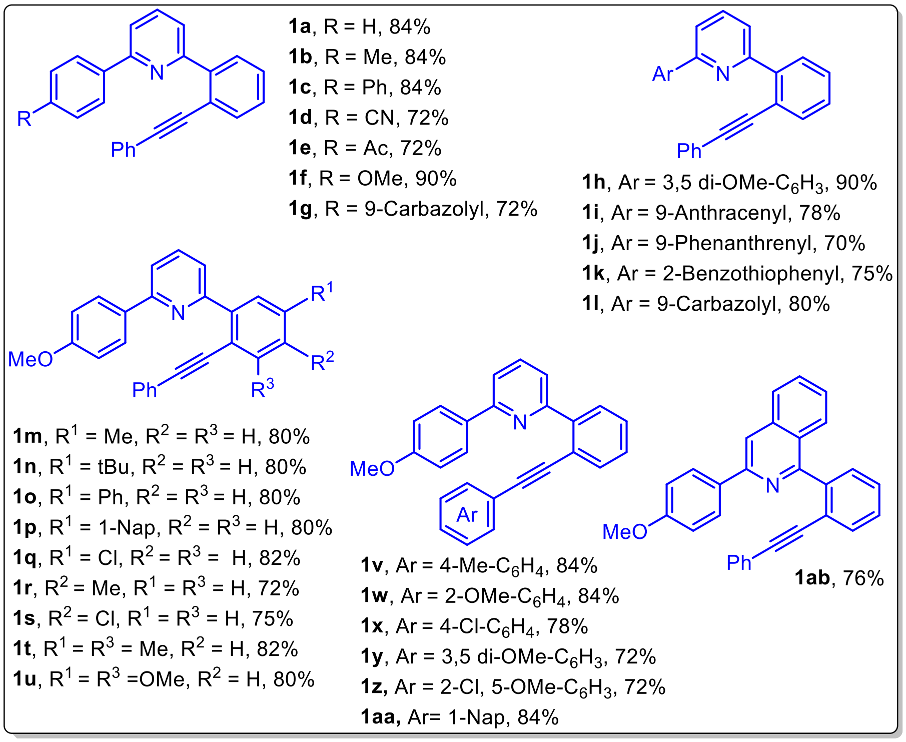
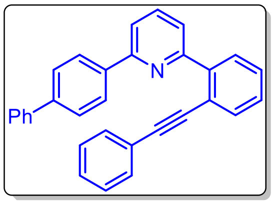
[2] Mule R. D.; Shaikh A. C.; Gade A. B.; Patil N. T. *Chem. Commun*. **2018**, *54*, 11909.

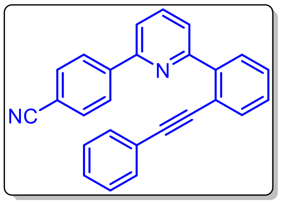


2-([1,1'-biphenyl]-4-yl)-6-(2-(phenylethynyl)phenyl)pyridine (**1c**):



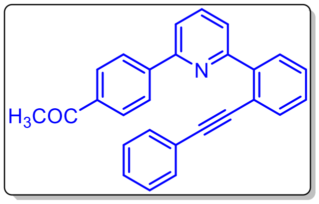
Off white solid, 197 mg, 75% yield; mp = 138-140 °C; ***Rf*** = 0.30 (Hexane/EtOAc = 95/05); **^{1}H NMR (500 MHz, CDCl$_3$) δ** = 8.27 - 8.21 (m, 2 H), 8.01 - 7.94 (m, 2 H), 7.88 (t, *J* = 7.8 Hz, 1 H), 7.81 (dd, *J* = 0.8, 7.9 Hz, 1 H), 7.75 - 7.69 (m, 3 H), 7.69 - 7.65 (m, 2 H), 7.55 - 7.43 (m, 4 H), 7.43 - 7.36 (m, 3 H), 7.33 - 7.28 (m, 3 H); **^{13}C NMR (125 MHz, CDCl$_3$) δ** = 157.4, 156.4, 142.3, 141.6, 140.7, 138.4, 136.5, 133.3, 131.4, 129.9, 128.8, 128.6, 128.3, 128.2, 128.2, 127.4, 127.4, 127.1, 123.4, 122.6, 121.4, 118.7, 92.5, 89.4; **HRMS (ESI)** calcd for $C_{31}H_{21}N$ $(M + H)^+$ 408.1747, found 408.1767.

4-(6-(2-(phenylethynyl)phenyl)142yridine-2-yl)benzonitrile (**1d**):



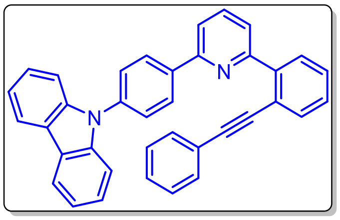
White solid, 165 mg, 60% yield; mp = 104-106 °C; ***Rf*** = 0.40 (Hexane/EtOAc = 85/15); **^{1}H NMR (700 MHz**, **CDCl$_3$) δ** = 8.25 (d, *J* = 8.2 Hz, 2 H), 8.02 (d, *J* = 8.0 Hz, 1 H), 7.94 – 7.87 (m, 2 H), 7.77 (d, *J* = 7.7 Hz, 1 H), 7.74 – 7.70 (m, 3 H), 7.50 (t, *J* = 7.5 Hz, 1 H), 7.45 (t, *J* = 7.5 Hz, 1 H), 7.40 – 7.36 (m, 2 H), 7.35 – 7.28 (m, 3 H); **^{13}C NMR (175 MHz, CDCl$_3$) δ** = 157.7, 154.4, 143.4, 141.6, 136.8, 133.4, 132.5, 132.4, 131.3, 129.7, 128.6, 128.5, 128.3, 127.5, 127.4, 123.6, 123.1, 121.4, 119.4, 119.2, 118.8, 112.2, 92.6, 89.2; **HRMS (ESI)** calcd for $C_{26}H_{16}N_2$ $(M + Na)^+$ 379.1206, found 379.1203.

1-(4-(6-(2-(phenylethynyl)phenyl)142yridine-2-yl)phenyl)ethan-1-one (**1e**):



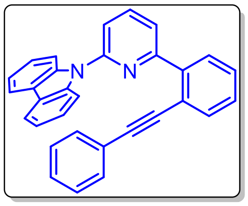
White solid, 205 mg, 76% yield; mp = 125-127 °C; ***Rf*** = 0.30 (Hexane/EtOAc = 90/10); **^{1}H NMR (700 MHz**, **CDCl$_3$) δ** = 8.28 – 8.23 (m, *J* = 8.2 Hz, 2 H), 8.07 – 8.03 (m, *J* = 8.2 Hz, 2 H), 8.01 (d, *J* = 7.7 Hz, 1 H), 7.93 (d, *J* = 7.5 Hz, 1 H), 7.90 (dt, *J* = 2.3, 7.8 Hz, 1 H), 7.81 (d, *J* = 7.7 Hz, 1 H), 7.72 (d, *J* = 7.5 Hz, 1 H), 7.51 (t, *J* = 7.5 Hz, 1 H), 7.44 (t, *J* = 7.5 Hz, 1 H), 7.41 – 7.36 (m, 2 H), 7.34 – 7.28 (m, 3 H), 2.65 (s, 3 H); **^{13}C NMR (175 MHz, CDCl$_3$) δ** = 197.9, 157.7, 155.5, 143.7, 142.0, 137.0, 136.6, 133.3, 131.4, 129.9, 128.7, 128.7, 128.4, 128.3, 128.3, 127.1, 123.4, 123.3, 121.4, 119.3, 92.6, 89.2, 26.7; **HRMS (ESI)** calcd for $C_{27}H_{19}ON$ $(M + Na)^+$ 396.1359, found 396.1359.

9-(4-(6-(2-(phenylethynyl)phenyl)pyridin-2-yl)phenyl)-9H-carbazole (**1g**):



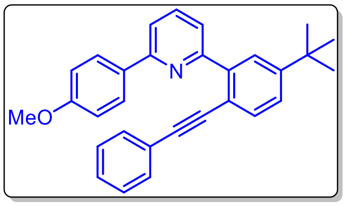
White solid, 159 mg, 64% yield; mp = 151-153 °C; ***Rf*** = 0.30 (Hexane/EtOAc = 85/15); **^{1}H NMR (400 MHz**, **CDCl$_3$) δ** = 8.44 - 8.36 (m, 2 H), 8.22 - 8.15 (m, *J* = 7.8 Hz, 2 H), 8.02 - 7.90 (m, 3 H), 7.89 - 7.83 (m, 1 H), 7.75 (dd, *J* = 1.2, 7.6 Hz, 1 H), 7.70 - 7.65 (m, *J* = 8.6 Hz, 2 H), 7.55 - 7.49 (m, 2 H), 7.49 - 7.41 (m, 7 H), 7.36 - 7.29 (m, 5 H); **^{13}C NMR (175 MHz**,**DMSO-d$_6$) δ** = 157.6, 155.9, 142.2, 140.7, 138.4, 138.2, 136.7, 133.4, 131.4, 129.9, 128.7, 128.5, 128.3, 128.3, 128.2, 127.0, 126.0, 123.4, 123.4, 122.7, 121.5, 120.3, 120.0, 118.8, 109.8, 92.5, 89.4; **HRMS (ESI)** calcd for $C_{37}H_{24}N_2$ (M + H)$^+$ 497.2012, found 497.1990.

9-(6-(2-(phenylethynyl)phenyl)pyridin-2-yl)-9*H*-carbazole (**1l**):



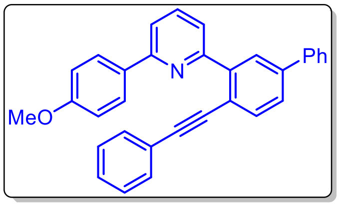
Off white solid, 208 mg, 80% yield; mp = 128-130 °C; ***Rf*** = 0.30 (Hexane/EtOAc = 95/05); **^{1}H NMR (700 MHz**, **CDCl$_3$) δ** = 8.16 - 8.10 (m, 3 H), 8.04 (t, *J* = 7.7 Hz, 1 H), 7.97 (d, *J* = 8.2 Hz, 3 H), 7.73 (d, *J* = 7.7 Hz, 1 H), 7.65 (d, *J* = 7.7 Hz, 1 H), 7.52 - 7.48 (m, 1 H), 7.46 - 7.41 (m, 5 H), 7.35 - 7.30 (m, 5 H); **^{13}C NMR (175 MHz**, **CDCl$_3$) δ** = 157.7, 151.4, 141.3, 139.6, 138.1, 133.4, 131.4, 129.9, 128.8, 128.5, 128.4, 128.4, 126.1, 124.3, 123.2, 121.7, 121.3, 120.8, 120.1, 117.5, 111.4, 93.0, 89.2; **HRMS (ESI)** calcd for $C_{31}H_{20}N_2^+$ (M + Na)$^+$ 443.1519, found 443.1521.

2-(5-(tert-butyl)-2-(phenylethynyl)phenyl)-6-(4-methoxyphenyl)pyridine (**1n**):



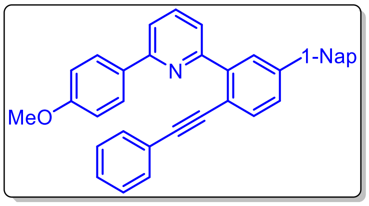
White solid, 240 mg, 76% yield; mp = 116-118 °C; ***Rf*** = 0.40 (Hexane/EtOAc = 95/05); **^{1}H NMR (700 MHz**, **CDCl$_3$) δ** = 8.14 – 8.11 (m, 2 H), 7.92 (d, *J* = 1.9 Hz, 1 H), 7.87 (dd, *J* = 0.9, 7.7 Hz, 1 H), 7.82 (t, *J* = 7.7 Hz, 1 H), 7.71 – 7.68 (m, 1 H), 7.63 (d, *J* = 8.2 Hz, 1 H), 7.45 (dd, *J* = 2.0, 8.1 Hz, 1 H), 7.40 – 7.35 (m, 2 H), 7.28 (dd, *J* = 2.7, 3.8 Hz, 3 H), 7.02 – 6.97 (m, 2 H), 3.87 (s, 3 H), 1.41 (s, 9 H); **^{13}C NMR (175 MHz**, **CDCl$_3$) δ** = 160.4, 157.7, 156.4, 151.8, 142.1, 136.3, 133.0, 132.2, 131.4, 128.3, 128.2, 127.9, 126.9, 125.4, 123.7, 121.9, 118.6, 117.9, 114.0, 91.7, 89.6, 55.3, 34.9, 31.2; **HRMS (ESI)** calcd for $C_{30}H_{27}NO$ $(M +H)^+$ 418.2165, found 418.2180.

2-(4-methoxyphenyl)-6-(4-(phenylethynyl)-[1,1'-biphenyl]-3-yl)pyridine (**1o**):



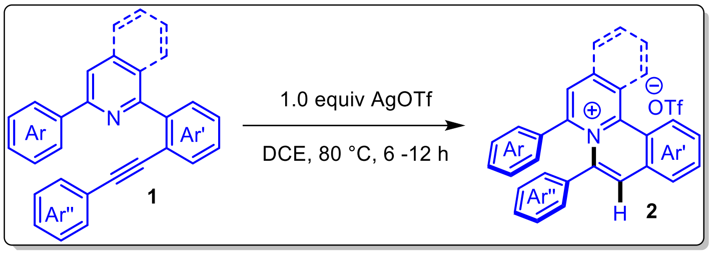
White solid, 285 mg, 86% yield; mp = 113-115 °C; ***Rf*** = 0.40 (Hexane/EtOAc = 95/05); **^{1}H NMR (700 MHz**, **CDCl$_3$) δ** = 8.15 (s, 1 H), 8.13 (d, *J* = 8.2 Hz, 2 H), 7.93 (d, *J* = 7.7 Hz, 1 H), 7.84 (t, *J* = 7.7 Hz, 1 H), 7.77 (d, *J* = 8.0 Hz, 1 H), 7.74 – 7.68 (m, 3 H), 7.66 (d, *J* = 8.0 Hz, 1 H), 7.49 (t, *J* = 7.3 Hz, 2 H), 7.43 – 7.36 (m, 3 H), 7.31 (br. S., 3 H), 6.99 (d, *J* = 8.2 Hz, 2 H), 3.87 (s, 3 H); **^{13}C NMR (175 MHz**, **CDCl$_3$) δ** = 160.4, 157.2, 156.6, 142.9, 141.3, 140.3, 136.4, 133.7, 132.1, 131.4, 128.8, 128.6, 128.3, 128.3, 128.1, 127.7, 127.2, 126.7, 123.5, 122.0, 120.4, 118.2, 114.0, 93.1, 89.4, 55.3; **HRMS (ESI)** calcd for $C_{32}H_{23}NO$ $(M + H)^+$ 438.1856, found 438.1857.

2-(4-methoxyphenyl)-6-(5-(naphthalen-1-yl)-2-(phenylethynyl)phenyl)pyridine (**1p**):



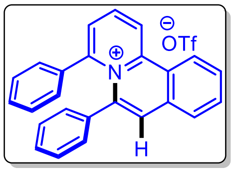
White solid, 226 mg, 83% yield; mp = 108-110 °C; ***Rf*** = 0.50 (Hexane/EtOAc = 95/05); **^{1}H NMR (700 MHz, CDCl$_3$) δ** = 8.11 - 8.05 (m, 4 H), 7.94 (d, *J* = 8.0 Hz, 1 H), 7.97 (d, *J* = 7.7 Hz, 1 H), 7.91 (d, *J* = 8.0 Hz, 1 H), 7.86 - 7.82 (m, 2 H), 7.71 (d, *J* = 7.7 Hz, 1 H), 7.60 - 7.52 (m, 4 H), 7.51 - 7.47 (m, 1 H), 7.44 (br. s., 2 H), 7.32 (br. s., 3 H), 6.95 (d, *J* = 7.7 Hz, 2 H), 3.84 (s, 3 H); **^{13}C NMR (175 MHz, CDCl$_3$) δ** = 160.4, 157.0, 156.5, 142.4, 141.0, 139.4, 136.5, 133.8, 133.3, 132.0, 131.6, 131.5, 131.4, 129.9, 128.3, 128.3, 128.2, 128.0, 127.0, 126.2, 126.0, 125.9, 125.4, 123.5, 121.9, 120.4, 118.1, 114.0, 92.9, 89.5, 55.3; **HRMS (ESI)** calcd for $C_{36}H_{25}NO$ $(M + H)^+$ 488.2009, found 488.2000.

3.6.5 Copper-promoted intramolecular carboamination of alkynes



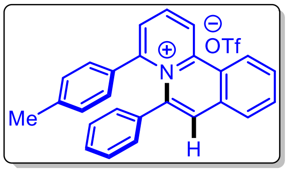
Representative procedure: To a screw-cap vial containing a stir bar were added 2-phenyl-6-(2-(phenylethynyl)phenyl)pyridine (**1a**) (50 mg, 0.15mmol, 1.0 equiv), AgOTf (39 mg, 0.15mmol, 1.0 equiv) and moist DCE (4 mL). The reaction vial was fitted with a cap, evacuated and backfilled with N_2 and heated at 80 °C for 6-12 h. When the reaction time was completed, the reaction mixture was allowed to cool at ambient temperature. The mixture was diluted with CH_2Cl_2 (10 mL) and the combined mixture was concentrated in vacuo and the resulting residue was purified by column chromatography on silica (CH_2Cl_2/MeOH; 95:05) to afford the product **2a** in **80**% yield.

4,6-diphenylpyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (**2a**):



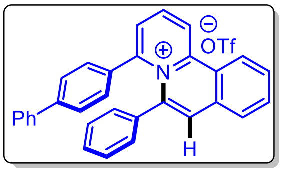
Yellow solid, 57 mg, 80% yield; mp = 210-212 °C; ***Rf*** = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz**, **DMSO-d$_6$) δ** = 9.62 (dd, *J* = 1.1, 8.8 Hz, 1 H), 9.23 (d, *J* = 8.4 Hz, 1 H), 8.74 (dd, *J* = 7.5, 8.5 Hz, 1 H), 8.29 (d, *J* = 7.2 Hz, 1 H), 8.25 (s, 1 H), 8.19 - 8.15 (m, 1 H), 8.14 - 8.08 (m, 2 H), 7.32 - 7.28 (m, 2 H), 7.27 - 7.22 (m, 1 H), 7.22 - 7.18 (m, 2 H), 7.18 - 7.12 (m, 5 H); **^{13}C NMR (125 MHz,DMSO-d$_6$) δ** = 150.8, 148.3, 141.2, 139.9, 137.0, 136.8, 134.2, 131.7, 130.9, 129.8, 128.6, 128.5, 128.4, 128.3, 128.3, 128.1, 127.5, 127.4, 125.8, 125.3, 122.3, 120.6(d, J = 322.43); **HRMS (ESI)** calcd for $C_{25}H_{18}N^+$ $(M - OTf)^+$ 332.1434, found 332.1421.

6-phenyl-4-(p-tolyl)pyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (**2b**):



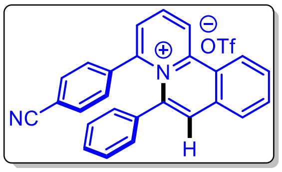
Yellow solid, 62 mg, 86% yield; mp = 238-240 °C; ***Rf*** = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz**, **CD$_3$CN) δ** = 9.28 (d, *J* = 8.7 Hz, 1 H), 8.96 (d, *J* = 8.4 Hz, 1 H), 8.60 (dd, *J* = 7.6, 8.4 Hz, 1 H), 8.22 - 8.14 (m, 1 H), 8.14 - 8.09 (m, 1 H), 8.09 - 8.04 (m, 1 H), 7.98 (s, 1 H), 7.94 (dd, *J* = 1.3, 7.4 Hz, 1 H), 7.20 - 7.12 (m, 3 H), 7.12 - 7.03 (m, 4 H), 7.00 (d, *J* = 8.1 Hz, 2 H), 2.24 (s, 3 H); **^{13}C NMR (125 MHz**, **CD$_3$CN) δ** = 153.2, 149.6, 142.8, 142.0, 141.0, 138.0, 135.7, 135.1, 132.9, 132.4, 132.1, 130.4, 130.0, 129.7, 129.6, 129.5, 129.5, 129.3, 128.9, 128.7, 126.7, 126.4, 123.5, 123.0, 122.8, 121.0, 118.7, 21.4; **HRMS (ESI)** calcd for $C_{26}H_{20}N^+$ $(M - OTf)^+$ 346.1590, found 346.1614.

4-([1,1'-biphenyl]-4-yl)-6-phenylpyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate(2c):



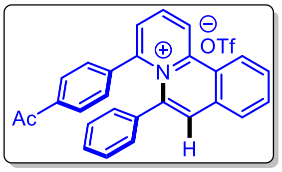
Yellow solid, 56 mg, 82% yield; mp = 203-205 °C; ***Rf*** = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz**, **CD_3CN) δ** = 99.32 (dd, *J* = 1.1, 8.6 Hz, 1 H), 8.99 (d, *J* = 8.2 Hz, 1 H), 8.63 (dd, *J* = 7.6, 8.5 Hz, 1 H), 8.23 - 8.17 (m, 1 H), 8.17 - 8.06 (m, 2 H), 8.05 - 7.99 (m, 2 H), 7.60 - 7.52 (m, 2 H), 7.52 - 7.45 (m, 2 H), 7.45 - 7.38 (m, 3 H), 7.31 - 7.25 (m, 2 H), 7.18 - 7.11 (m, 5 H); **^{13}C NMR (125 MHz**, **CD_3CN) δ** = 152.5, 149.6, 143.6, 142.7, 140.8, 140.5, 138.0, 136.7, 135.6, 132.9, 132.1, 130.1, 130.0, 129.5, 129.2, 128.9, 128.8, 128.2, 128.0, 126.5, 126.4, 123.1, 120.9, 119.0; **HRMS (ESI)** calcd for $C_{31}H_{22}N^+$ (M - OTf)$^+$ 408.1747, found 408.1756.

4-(4-cyanophenyl)-6-phenylpyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (2d):



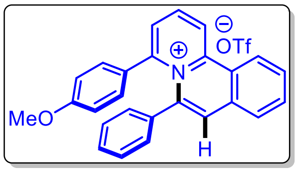
Yellow solid, 50 mg, 71% yield; mp = 232-234 °C; ***Rf*** = 0.40 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz**, **CD_3CN) δ** = 9.37 (d, *J* = 8.5 Hz, 1 H), 9.02 (d, *J* = 8.2 Hz, 1 H), 8.64 (t, *J* = 8.0 Hz, 1 H), 8.26 - 8.20 (m, 1 H), 8.17 (t, *J* = 7.2 Hz, 1 H), 8.15 - 8.06 (m, 2 H), 7.96 (d, *J* = 6.9 Hz, 1 H), 7.60 - 7.47 (m, *J* = 8.4 Hz, 2 H), 7.40 - 7.30 (m, *J* = 8.2 Hz, 2 H), 7.27 - 7.17 (m, 3 H), 7.13 (d, *J* = 7.0 Hz, 2 H); **^{13}C NMR (175 MHz**, **CD_3CN) δ** = 150.1, 149.8, 142.2, 141.5, 140.8, 137.7, 135.9, 133.5, 133.1, 132.4, 130.4, 130.1, 130.0, 129.9, 129.5, 129.4, 129.1, 126.6, 126.4, 124.1, 123.1, 121.2, 118.8, 114.0; **HRMS (ESI)** calcd for $C_{26}H_{17}N^+$ (M - OTf)$^+$ 357.1386, found 357.1407.

4-(4-acetylphenyl)-6-phenylpyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (2e):



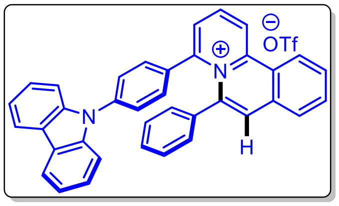
Greenish solid, 49 mg, 70% yield; mp = 236-238 °C; ***Rf*** = 0.20 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, CD_3CN) δ** = 9.36 (d, *J* = 8.5 Hz, 1 H), 9.01 (d, *J* = 8.2 Hz, 1 H), 8.63 (t, *J* = 7.9 Hz, 1 H), 8.25 - 8.18 (m, 1 H), 8.16 (t, *J* = 7.4 Hz, 1 H), 8.13 - 8.08 (m, 1 H), 8.06 (s, 1 H), 7.98 (d, *J* = 7.3 Hz, 1 H), 7.76 - 7.68 (m, *J* = 7.9 Hz, 2 H), 7.35 - 7.28 (m, *J* = 8.1 Hz, 2 H), 7.19 - 7.09 (m, 5 H), 2.51 (s, 3 H); **^{13}C NMR (125 MHz, CD_3CN) δ** = 198.2, 151.3, 149.7, 142.5, 141.4, 140.9, 138.6, 137.8, 135.8, 133.1, 132.4, 130.2, 129.8, 129.8, 129.6, 129.4, 129.3, 129.1, 129.0, 126.6, 126.4, 123.7, 119.2, 117.0, 27.1; **HRMS (ESI)** calcd for $C_{27}H_{20}ON^+$ (M - OTf)$^+$ 374.1539, found 374.1541.

4-(4-methoxyphenyl)-6-phenylpyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (2f)



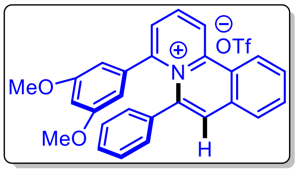
Yellow solid, 66 mg, 94% yield; mp = 200-202 °C; ***Rf*** = 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d_6) δ** = 9.55 (dd, *J* = 1.0, 8.6 Hz, 1 H), 9.19 (d, *J* = 8.2 Hz, 1 H), 8.71 (dd, *J* = 7.6, 8.4 Hz, 1 H), 8.27 (d, *J* = 7.5 Hz, 1 H), 8.20 (s, 1 H), 8.15 (t, *J* = 7.5 Hz, 1 H), 8.12 - 8.06 (m, 2 H), 7.28 - 7.24 (m, 2 H), 7.20 - 7.13 (m, 5 H), 6.79 - 6.72 (m, 2 H), 3.71 (s, 3 H); **^{13}C NMR (125 MHz,DMSO-d_6) δ** = 160.5, 151.1, 148.1, 141.2, 139.8, 137.0, 134.0, 133.7, 132.3, 131.5, 130.8, 130.0, 129.7, 129.4, 128.6, 128.3, 128.2, 128.2, 127.2, 127.2, 125.7, 125.3, 122.0, 121.7, 119.4, 114.0, 55.4; **HRMS (ESI)** calcd for $C_{26}H_{20}NO^+$ (M - OTf)$^+$ 362.1539, found 362.1521.

4-(4-(9H-carbazol-9-yl)phenyl)-6-phenylpyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (2g)



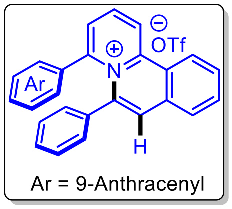
Yellow solid, 52 mg, 80% yield; mp = 230-232 °C; ***Rf*** = 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (700 MHz, CD_3CN) δ** = 9.37 (dd, *J* = 0.9, 8.6 Hz, 1 H), 9.02 (d, *J* = 8.4 Hz, 1 H), 8.68 (t, *J* = 8.0 Hz, 1 H), 8.22 (d, *J* = 7.5 Hz, 1 H), 8.19 (d, *J* = 7.7 Hz, 2 H), 8.15 (t, *J* = 7.4 Hz, 1 H), 8.12 - 8.07 (m, 3 H), 7.53 - 7.46 (m, 4 H), 7.45 - 7.41 (m, 2 H), 7.37 - 7.32 (m, 4 H), 7.31 - 7.26 (m, 5 H); **^{13}C NMR (125 MHz, CD_3CN) δ** = 151.7, 149.7, 142.5, 141.2, 140.9, 140.1, 138.1, 136.5, 135.6, 133.0, 132.3, 131.2, 130.3, 130.0, 129.9, 129.4, 129.3, 129.2, 129.0, 127.9, 127.3, 126.6, 126.4, 124.4, 123.4, 123.1, 121.6, 121.5, 121.2, 110.7; **HRMS (ESI)** calcd for $C_{37}H_{25}N_2^+$ $(M - OTf)^+$ 497.2012, found 497.2005.

4-(3,5-dimethoxyphenyl)-6-phenylpyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (2h)



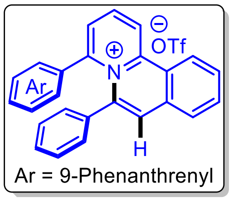
Yellow solid, 74 mg, 93% yield; mp = 178-180 °C; ***Rf*** = 0.30 (CH_2Cl_2/MeOH = 93/07); **^{1}H NMR (500 MHz, CD_3CN) δ** = 9.35 (d, *J* = 8.7 Hz, 1 H), 9.02 (d, *J* = 8.2 Hz, 1 H), 8.67 - 8.61 (m, 1 H), 8.24 - 8.19 (m, 1 H), 8.18 - 8.14 (m, 1 H), 8.12 (dd, *J* = 1.3, 8.3 Hz, 1 H), 8.04 (s, 1 H), 8.02 (dd, *J* = 1.3, 7.4 Hz, 1 H), 7.28 - 7.21 (m, 3 H), 7.20 - 7.15 (m, 2 H), 6.38 (d, *J* = 2.1 Hz, 2 H), 6.33 (t, *J* = 2.2 Hz, 1 H), 3.69 (s, 6 H); **^{13}C NMR (125 MHz, CD_3CN) δ** = 162.0, 152.5, 149.5, 142.9, 140.8, 139.4, 137.8, 135.6, 133.1, 132.2, 129.9, 129.5, 129.5, 129.1, 128.9, 126.6, 126.5, 123.5, 123.4, 121.0, 107.8, 103.3, 56.4; **HRMS (ESI)** calcd for $C_{27}H_{22}O_2N^+$ $(M - OTf)^+$ 392.1645, found 392.1623.

4-(anthracen-9-yl)-6-phenylpyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (2i):



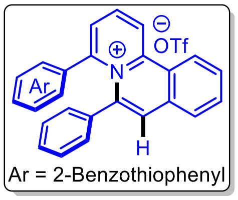
Orangish yellow solid, 50 mg, 74% yield, mp = 280-282 °C; ***Rf*** = 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, CD_3CN) δ** = 9.61 (d, *J* = 8.7 Hz, 1 H), 9.14 (dd, *J* = 3.4, 5.7 Hz, 1 H), 8.77 (t, *J* = 8.0 Hz, 1 H), 8.48 (s, 1 H), 8.23 (d, *J* = 7.3 Hz, 1 H), 8.20 - 8.07 (m, 3 H), 8.07 - 7.96 (m, *J* = 8.4 Hz, 2 H), 7.75 (s, 1 H), 7.52 (t, *J* = 7.5 Hz, 2 H), 7.40 (t, *J* = 7.6 Hz, 2 H), 7.28 - 7.13 (m, *J* = 8.7 Hz, 2 H), 6.60 - 6.43 (m, 1 H), 6.37 (t, *J* = 7.6 Hz, 2 H), 6.24 (d, *J* = 7.5 Hz, 2 H); **^{13}C NMR (175 MHz, CD_3CN) δ** = 149.3, 148.6, 141.9, 140.5, 135.7, 135.5, 133.3, 132.7, 132.4, 132.3, 131.8, 130.1, 130.0, 129.7, 129.4, 129.1, 129.0, 128.3, 127.9, 127.4, 127.0, 126.8, 126.7, 124.7, 124.5, 123.1, 121.2; **HRMS (ESI)** calcd for $C_{33}H_{22}N^+$ $(M - OTf)^+$ 432.1725, found 432.1728.

4-(phenanthren-9-yl)-6-phenylpyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (2j):



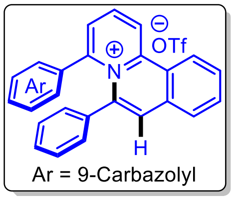
Yellow solid, 57 mg, 85% yield; mp = 268-270 °C; ***Rf*** = 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, CD_3CN) δ** = 9.48 (d, *J* = 8.7 Hz, 1 H), 9.07 (d, *J* = 8.1 Hz, 1 H), 8.71 (t, *J* = 8.1 Hz, 1 H), 8.65 (d, *J* = 8.5 Hz, 1 H), 8.68 (d, *J* = 8.5 Hz, 1 H), 8.22 (dd, *J* = 1.8, 5.6 Hz, 1 H), 8.19 - 8.08 (m, 3 H), 7.89 (s, 1 H), 7.82 - 7.73 (m, 2 H), 7.72 - 7.62 (m, 3 H), 7.52 - 7.46 (m, 1 H), 7.40 (d, *J* = 8.1 Hz, 1 H), 6.90 (d, *J* = 7.6 Hz, 1 H), 6.65 (t, *J* = 7.6 Hz, 1 H), 6.61 - 6.50 (m, 2 H), 6.46 (d, *J* = 7.5 Hz, 1 H); **^{13}C NMR (125 MHz, CD_3CN) δ** = 150.8, 149.2, 142.6, 140.7, 136.8, 135.7, 133.3, 132.8, 132.4, 132.2, 131.8, 131.4, 131.3, 131.2, 130.4, 129.9, 129.5, 129.3, 129.2, 129.0, 128.7, 128.6, 128.6, 128.5, 128.4, 128.3, 127.9, 126.7, 126.7, 125.8, 124.4, 124.0, 123.6, 123.5, 121.0; **HRMS (ESI)** calcd for $C_{33}H_{22}N^+$ (M - OTf)$^+$ 432.1747, found 432.1750.

4-(benzo[b]thiophen-2-yl)-6-phenylpyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (2k)



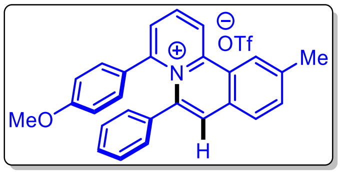
Yellow solid, 62 mg, 90% yield, mp = 208-210 °C; ***Rf*** = 0.40 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, CD_3CN) δ** = 9.32 (dd, *J* = 1.2, 8.7 Hz, 1 H), 8.98 (d, *J* = 8.4 Hz, 1 H), 8.61 (dd, *J* = 7.5, 8.5 Hz, 1 H), 8.22 (d, *J* = 7.3 Hz, 1 H), 8.15 (dt, *J* = 1.1, 7.6 Hz, 2 H), 8.12 - 8.05 (m, 2 H), 7.85 - 7.76 (m, 1 H), 7.75 - 7.69 (m, 1 H), 7.39 (tt, *J* = 5.6, 7.3 Hz, 2 H), 7.35 (s, 1 H), 7.28 (dd, *J* = 1.4, 8.0 Hz, 2 H), 7.12 - 7.00 (m, 3 H); **^{13}C NMR (125 MHz, CD_3CN) δ** = 150.0, 146.1, 142.7, 141.7, 140.7, 139.7, 137.5, 137.3, 135.9, 133.2, 132.4, 130.7, 130.2, 129.9, 129.5, 129.5, 129.4, 128.4, 127.6, 126.7, 126.5, 126.3, 126.0, 123.9, 123.5, 123.3, 121.0,; **HRMS (ESI)** calcd for $C_{27}H_{18}NS^+$ (M - OTf)$^+$ 388.1154, found 388.1182.

4-(9H-carbazol-9-yl)-6-phenylpyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (2l)



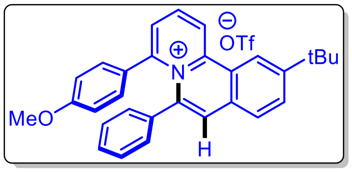
Yellow solid, 57 mg, 85% yield; mp = 290-298 °C; ***Rf*** = 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, CD_3CN) δ** = 9.44 (d, *J* = 8.7 Hz, 1 H), 9.05 (d, *J* = 8.1 Hz, 1 H), 8.80 (t, *J* = 8.2 Hz, 1 H), 8.38 (d, *J* = 7.8 Hz, 1 H), 8.22 - 8.10 (m, 3 H), 7.99 - 7.84 (m, 3 H), 7.43 - 7.31 (m, 4 H), 7.00 (d, *J* = 8.1 Hz, 2 H), 6.68 (qd, *J* = 4.3, 8.5 Hz, 1 H), 6.60 (d, *J* = 4.4 Hz, 4 H); **^{13}C NMR (125 MHz, CD_3CN) δ** = 149.0, 143.4, 142.2, 140.6, 139.1, 135.8, 134.6, 132.4, 129.6, 129.4, 129.3, 128.0, 127.6, 127.0, 126.9, 126.7, 125.9, 125.5, 124.0, 123.4, 121.6, 111.6; **HRMS (ESI)** calcd for $C_{31}H_{22}N_2^+$ (M - OTf)$^+$ 421.1699, found 421.1697.

4-(4-methoxyphenyl)-10-methyl-6-phenylpyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (2m):



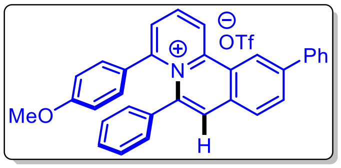
Yellow solid, 63 mg, 90% yield; mp = 190-192 °C; ***Rf*** = 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (400 MHz, DMSO-d$_6$) δ** = 9.53 (d, *J* = 8.5 Hz, 1 H), 9.04 (br. s., 1 H), 8.68 (t, *J* = 7.9 Hz, 1 H), 8.27 - 8.12 (m, 2 H), 8.08 - 7.96 (m, 2 H), 7.30 - 7.22 (m, *J* = 8.3 Hz, 2 H), 7.21 - 7.12 (m, 5 H), 6.80 - 6.70 (m, *J* = 8.5 Hz, 2 H), 3.71 (s, 3 H), 2.71 (s, 3 H) ; **^{13}C NMR (100 MHz, DMSO-d$_6$) δ** = 160.4, 150.9, 147.8, 141.3, 140.5, 139.5, 137.0, 135.5, 129.9, 129.6, 129.5, 128.5, 128.2, 128.1, 128.1, 127.2, 127.1, 125.3, 125.1, 122.3, 121.6, 119.1, 114.0, 55.4, 21.7; **HRMS (ESI)** calcd for $C_{27}H_{22}NO^+$ $(M - OTf)^+$ 376.1696, found 376.1692.

10-(tert-butyl)-4-(4-methoxyphenyl)-6-phenylpyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (2n):



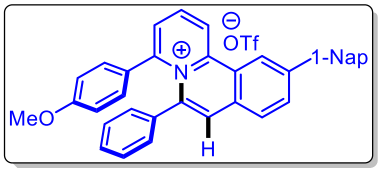
Yellow solid, 62 mg, 92% yield; mp = 245-247 °C; ***Rf*** = 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, CD_3CN) δ** = 9.35 (dd, *J* = 1.2, 8.7 Hz, 1 H), 8.84 (s, 1 H), 8.55 (dd, *J* = 7.5, 8.5 Hz, 1 H), 8.23 (dd, *J* = 1.7, 8.4 Hz, 1 H), 8.11 (d, *J* = 8.4 Hz, 1 H), 7.94 (s, 1 H), 7.91 (dd, *J* = 1.3, 7.4 Hz, 1 H), 7.26 – 7.12 (m, 5 H), 7.12 – 7.06 (m, 2 H), 6.76 – 6.61 (m, 2 H), 3.74 (s, 3 H), 1.55 (s, 9 H); **^{13}C NMR (125 MHz, CD_3CN) δ** = 162.2, 156.0, 153.0, 149.5, 142.4, 140.4, 138.1, 134.0, 131.1, 131.0, 130.5, 129.9, 129.6, 129.3, 129.2, 128.5, 128.4, 126.3, 123.5, 122.7, 122.2, 121.0, 118.7, 115.3, 56.3, 36.8, 31.4; **HRMS (ESI)** calcd for $C_{30}H_{28}ON^+$ $(M – OTf)^+$ 418.2165, found 418.2172.

4-(4-methoxyphenyl)-6,10-diphenylpyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (2o):



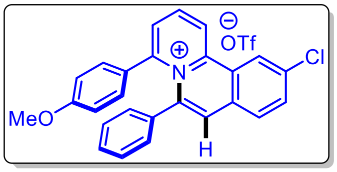
Yellow solid, 59 mg, 88% yield; mp = 250-252 °C; ***Rf*** = 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, CD_3CN) δ** = 9.41 (d, *J* = 8.5 Hz, 1 H), 9.12 (s, 1 H), 8.59 (t, *J* = 8.0 Hz, 1 H), 8.40 – 8.35 (m, 1 H), 8.27 – 8.21 (m, 1 H), 8.01 – 7.98 (m, 1 H), 7.98 – 7.93 (m, 3 H), 7.63 (t, *J* = 6.9 Hz, 2 H), 7.58 – 7.51 (m, 1 H), 7.22 – 7.16 (m, 5 H), 7.15 – 7.10 (m, 2 H), 6.72 (d, *J* = 8.9 Hz, 2 H), 3.75 (s, 3 H); **^{13}C NMR (125 MHz, CD_3CN) δ** = 162.3, 157.5, 153.2, 149.6, 144.6, 142.8, 140.7, 140.1, 138.0, 134.5, 131.9, 131.2, 130.5, 130.4, 130.0, 130.0, 129.6, 129.6, 128.9, 128.5, 128.4, 127.0, 124.3, 122.9, 121.0, 115.3, 56.3; **HRMS (ESI)** calcd for $C_{32}H_{24}NO^+$ $(M – OTf)^+$ 438.1852, found 438.1825.

4-(4-methoxyphenyl)-10-(naphthalen-1-yl)-6-phenylpyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (2p):



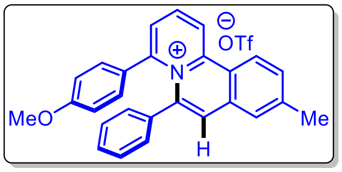
Yellow solid, 59 mg, 91% yield; mp = 221-223 °C; ***Rf*** = 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, CD_3CN) δ** = 9.29 - 9.24 (m, 1 H), 9.05 (s, 1 H), 8.54 (dd, *J* = 7.6, 8.4 Hz, 1 H), 8.29 (d, *J* = 8.2 Hz, 1 H), 8.23 (dd, *J* = 1.4, 8.1 Hz, 1 H), 8.11 - 8.04 (m, 3 H), 7.95 (dd, *J* = 1.1, 7.4 Hz, 1 H), 7.88 (d, *J* = 8.4 Hz, 1 H), 7.73 - 7.67 (m, 2 H), 7.65 - 7.60 (m, 1 H), 7.56 (ddd, *J* = 1.1, 6.9, 8.3 Hz, 1 H), 7.24 - 7.18 (m, 5 H), 7.18 - 7.14 (m, 2 H), 6.78 - 6.70 (m, 2 H), 3.76 (s, 3 H); **^{13}C NMR (125 MHz, CD_3CN) δ** = 162.3, 153.2, 149.5, 144.5, 142.9, 140.7, 139.0, 138.0, 137.3, 134.9, 132.1, 131.9, 131.1, 130.4, 130.0, 129.7, 129.6, 129.3, 129.0, 128.4, 128.0, 127.4, 127.3, 126.7, 126.7, 126.0, 123.4, 122.7, 115.3, 56.3; **HRMS (ESI)** calcd for $C_{36}H_{26}ON^+$ $(M - OTf)^+$ 489.2042, found 489.2070.

10-chloro-4-(4-methoxyphenyl)-6-phenylpyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (2q):



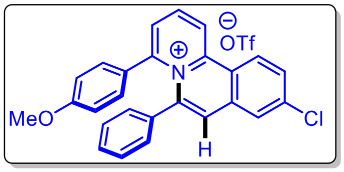
Yellow solid, 60 mg, 87% yield; mp = 227-229 °C ***Rf*** = 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz**, **CD_3CN) δ** = 9.21 (dd, *J* = 1.2, 8.5 Hz, 1 H), 8.98 (d, *J* = 1.5 Hz, 1 H), 8.61 (dd, *J* = 7.6, 8.4 Hz, 1 H), 8.14 (d, *J* = 8.4 Hz, 1 H), 8.06 (dd, *J* = 1.9, 8.5 Hz, 1 H), 7.98 (dd, *J* = 1.4, 7.5 Hz, 1 H), 7.95 (s, 1 H), 3.74 (s, 3 H); **^{13}C NMR (125 MHz**, **CD_3CN) δ** = 162.3, 153.4, 148.4, 143.1, 141.1, 137.7, 137.6, 135.5, 131.3, 131.2, 131.1, 130.2, 130.1, 130.1, 129.5, 128.4, 128.0, 127.7, 125.9, 123.4, 122.8, 120.9, 115.3, 56.3; **HRMS (ESI)** calcd for $C_{26}H_{19}ClON^+$ (M - OTf)$^+$ 396.1150, found 396.1130.

4-(4-methoxyphenyl)-9-methyl-6-phenylpyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (2r):



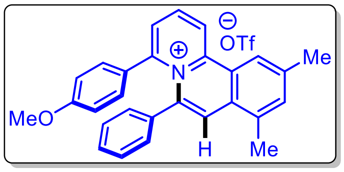
Yellow solid, 59 mg, 85% yield; mp = 190-192 °C, ***Rf*** = 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz**, **CD_3CN) δ** = 9.17 (d, *J* = 8.5 Hz, 1 H), 8.82 (d, *J* = 8.7 Hz, 1 H), 8.53 (dd, *J* = 7.6, 8.5 Hz, 1 H), 7.95 (s, 1 H), 7.92 – 7.85 (m, 3 H), 7.19 – 7.14 (m, 5 H), 7.12 – 7.08 (m, 2 H), 6.74 – 6.68 (m, 2 H), 3.74 (s, 3 H), 2.67 (s, 3 H); **^{13}C NMR (125 MHz, CD_3CN) δ** = 162.2, 152.7, 149.6, 147.3, 143.0, 140.5, 138.1, 133.9, 133.1, 131.1, 130.5, 130.0, 129.6, 128.9, 128.8, 128.5, 128.4, 126.5, 124.3, 123.5, 122.3, 121.0, 115.3, 56.3, 22.1; **HRMS (ESI)** calcd for $C_{27}H_{22}ON^+$ (M – OTf)$^+$ 376.1696, found 376.1672.

9-chloro-4-(4-methoxyphenyl)-6-phenylpyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (2s):



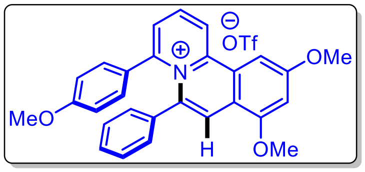
Yellow solid, 55 mg, 80% yield; mp = 219-221 °C, ***Rf*** = 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz**, **CD_3CN) δ** = 9.18 (dd, *J* = 0.9, 8.5 Hz, 1 H), 8.90 (d, *J* = 9.0 Hz, 1 H), 8.59 (dd, *J* = 7.6, 8.5 Hz, 1 H), 8.17 (d, *J* = 2.1 Hz, 1 H), 8.02 (dd, *J* = 2.1, 8.9 Hz, 1 H), 7.95 (dd, *J* = 1.2, 7.5 Hz, 1 H), 7.88 (s, 1 H), 7.20 – 7.15 (m, 5 H), 7.12 – 7.09 (m, 2 H), 6.74 – 6.70 (m, 2 H), 3.74 (s, 3 H); **^{13}C NMR (125 MHz**, **CD_3CN) δ** = 162.4, 157.0, 153.4, 151.9, 149.2, 148.0, 144.0, 142.2, 141.3, 141.1, 141.1, 137.7, 134.0, 132.4, 131.2, 130.2, 129.7, 129.6, 128.6, 128.4, 127.5, 125.1, 123.5, 122.6, 121.2, 115.3, 56.4; **HRMS (ESI)** calcd for $C_{26}H_{19}ClON^+$ $(M – OTf)^+$ 396.1150, found 396.1128.

4-(4-methoxyphenyl)-8,10-dimethyl-6-phenylpyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (2t):



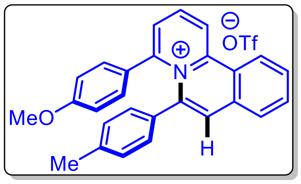
Yellow solid, 59 mg, 85% yield; mp = 214-216 °C, ***Rf*** = 0.40 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz**, **CD_3CN) δ** = 9.21 (d, *J* = 8.5 Hz, 1 H), 8.63 (s, 1 H), 8.53 (t, *J* = 8.1 Hz, 1 H), 7.93 (s, 1 H), 7.89 (dd, *J* = 1.1, 7.4 Hz, 1 H), 7.81 (s, 1 H), 7.20 – 7.10 (m, 7 H), 6.71 (d, *J* = 8.7 Hz, 2 H), 3.74 (s, 3 H), 2.74 (s, 3 H), 2.68 (s, 3 H); **^{13}C NMR (125 MHz**, **CD_3CN) δ** = 162.1, 152.6, 149.4, 142.9, 141.8, 140.3, 138.3, 137.8, 137.3, 131.0, 130.4, 129.9, 129.8, 129.5, 129.0, 128.6, 126.8, 125.6, 123.7, 123.5, 122.6, 120.9, 115.2, 56.3, 22.1, 19.0; **HRMS (ESI)** calcd for $C_{28}H_{24}NO$+ $(M – OTf)^+$ 390.1852, found 390.1864.

8,10-dimethoxy-4-(4-methoxyphenyl)-6-phenylpyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (2u):



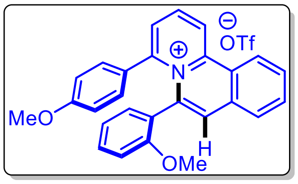
Yellow solid, 60 mg, 88% yield; mp = 217-219 °C; R*f* = 0.50 (CH_2Cl_2/MeOH = 90/10); **^{1}H NMR (500 MHz, CD_3CN) δ** = 9.25 – 9.19 (m, 1 H), 8.51 (dd, *J* = 7.6, 8.5 Hz, 1 H), 8.01 (s, 1 H), 7.90 (dd, *J* = 1.2, 7.5 Hz, 1 H), 7.80 (d, *J* = 1.7 Hz, 1 H), 7.18 – 7.11 (m, 6 H), 7.09 – 7.05 (m, 2 H), 6.73 – 6.67 (m, 2 H), 4.12 (s, 3 H), 4.07 (s, 3 H), 3.74 (s, 3 H); **^{13}C NMR (125 MHz, CD_3CN) δ** = 164.0, 162.2, 158.1, 152.6, 148.3, 140.5, 139.8, 138.4, 131.1, 130.6, 129.7, 129.6, 129.5, 128.8, 128.5, 123.5, 123.3, 123.1, 121.0, 119.4, 115.2, 105.5, 105.5, 98.7, 57.6, 57.4, 56.3; **HRMS (ESI)** calcd for $C_{28}H_{24}O_3N^+$ (M – OTf)$^+$ 422.1751, found 422.1760.

4-(4-methoxyphenyl)-6-(p-tolyl)pyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (2v):



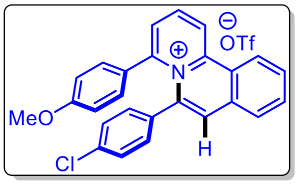
Yellow solid, 57 mg, 82% yield; ; mp = 257-259 °C; ***Rf*** = 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, CD_3CN) δ** = 9.22 (d, *J* = 8.7 Hz, 1 H), 8.93 (d, *J* = 8.4 Hz, 1 H), 8.56 (t, *J* = 8.0 Hz, 1 H), 8.19 – 8.12 (m, 1 H), 8.10 (t, *J* = 7.5 Hz, 1 H), 8.07 – 8.01 (m, 1 H), 7.94 (s, 1 H), 7.91 (dd, *J* = 1.1, 7.4 Hz, 1 H), 7.17 – 7.09 (m, 2 H), 6.98 (s, 4 H), 6.76 – 6.68 (m, 2 H), 3.75 (s, 3 H), 2.23 (s, 3 H); **^{13}C NMR (125 MHz, CD_3CN) δ** = 162.2, 153.1, 149.5, 143.0, 140.6, 140.3, 135.3, 135.2, 132.9, 132.0, 131.0, 130.4, 130.0, 129.3, 129.3, 128.4, 128.2, 126.4, 126.3, 123.5, 122.4, 115.1, 56.3, 21.2; **HRMS (ESI)** calcd for $C_{27}H_{22}ON^+$ (M – OTf)$^+$ 376.1696, found 376.1677.

6-(2-methoxyphenyl)-4-(4-methoxyphenyl)pyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (2w)



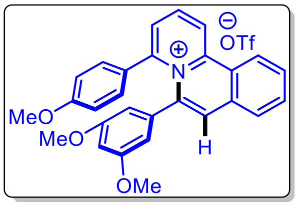
Yellow solid, 63 mg, 92% yield; ; mp = 278-280 °C; ***Rf*** = 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, CD_3CN) δ** = 9.25 (dd, *J* = 1.3, 8.6 Hz, 1 H), 8.95 (d, *J* = 8.2 Hz, 1 H), 8.57 (dd, *J* = 7.6, 8.4 Hz, 1 H), 8.19 – 8.13 (m, 1 H), 8.10 (dt, *J* = 1.1, 7.4 Hz, 1 H), 8.08 – 8.03 (m, 1 H), 8.00 (s, 1 H), 7.94 (dd, *J* = 1.4, 7.5 Hz, 1 H), 7.31 – 7.24 (m, 1 H), 7.22 – 7.15 (m, 2 H), 7.09 – 6.96 (m, 1 H), 6.85 – 6.78 (m, 1 H), 6.75 – 6.65 (m, 3 H); **^{13}C NMR (125 MHz, CD_3CN) δ** = 162.4, 156.0, 153.1, 148.0, 140.5, 140.4, 135.2, 132.6, 132.2, 132.1, 131.7, 131.1, 130.4, 129.5, 129.3, 129.1, 128.6, 126.6, 126.2, 125.7, 123.5, 122.6, 121.8, 121.0, 115.4, 114.9, 111.3, 56.3, 56.1; **HRMS (ESI)** calcd for $C_{27}H_{22}O_2N^+$ (M – OTf)$^+$ 392.1645, found 392.1675.

6-(4-chlorophenyl)-4-(4-methoxyphenyl)pyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (2x):



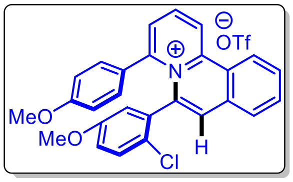
Yellow solid, 55 mg, 80% yield; mp = 218-220 °C; ***Rf*** = 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, CD_3CN) δ** = 9.29 – 9.20 (m, 1 H), 8.95 (d, *J* = 8.2 Hz, 1 H), 8.67 – 8.51 (m, 1 H), 8.20 – 8.14 (m, 1 H), 8.14 – 8.09 (m, 1 H), 8.09 – 8.04 (m, 1 H), 7.97 (s, 1 H), 7.94 (dd, *J* = 1.4, 7.5 Hz, 1 H), 7.24 – 7.12 (m, 4 H), 7.12 – 7.05 (m, 2 H), 6.82 – 6.70 (m, 2 H), 3.78 (s, 3 H): **^{13}C NMR (125 MHz, CD_3CN) δ** = 162.4, 152.8, 149.5, 141.5, 140.9, 136.6, 135.5, 135.2, 132.6, 132.3, 131.2, 130.3, 130.2, 129.5, 129.5, 129.4, 128.8, 126.5, 123.4, 122.6, 120.9, , 115.3, 56.4; **HRMS (ESI)** calcd for $C_{26}H_{19}ClNO^+$ (M – OTf)$^+$ 396.1150, found 396.1136.

6-(3,5-dimethoxyphenyl)-4-(4-methoxyphenyl)pyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (2y):



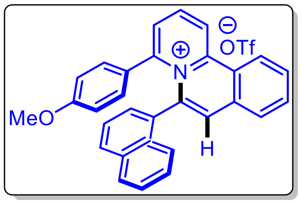
Yellow solid, 62 mg, 91% yield; mp = 222-224°C; ***Rf*** = 0.30 (CH_2Cl_2/MeOH = 97/03); **^{1}H NMR (500 MHz, CD_3CN) δ** = 9.24 (dd, *J* = 1.3, 8.6 Hz, 1 H), 8.95 (d, *J* = 8.2 Hz, 1 H), 8.57 (dd, *J* = 7.5, 8.5 Hz, 1 H), 8.18 – 8.14 (m, 1 H), 8.11 (dt, *J* = 1.1, 7.5 Hz, 1 H), 8.09 – 8.04 (m, 1 H), 8.01 (s, 1 H), 7.93 (dd, *J* = 1.4, 7.5 Hz, 1 H), 7.21 – 7.15 (m, 2 H), 6.81 – 6.73 (m, 2 H), 6.29 – 6.19 (m, 3 H), 3.77 (s, 3 H), 3.67 (s, 6 H); **^{13}C NMR (125 MHz, CD_3CN) δ** = 162.2, 161.9, 153.2, 149.4, 142.5, 140.9, 139.7, 135.5, 132.7, 132.3, 131.4, 130.3, 129.4, 129.4, 128.3, 126.6, 126.5, 123.5, 122.6, 115.1, 107.2, 102.0, 56.4, 56.3; **HRMS (ESI)** calcd for $C_{28}H_{24}O_3N^+$ $(M - OTf)^+$ 422.1751, found 422.1775.

6-(2-chloro-5-methoxyphenyl)-4-(4-methoxyphenyl)pyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (2z):



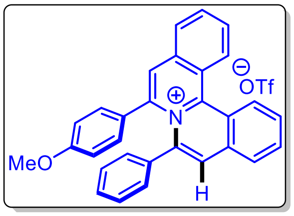
Yellow solid, 62 mg, 92% yield; mp = 175-177 °C, ***Rf*** = 0.30 (CH_2Cl_2/MeOH = 94/06); **^{1}H NMR (500 MHz, CD_3CN) δ** = 9.31 (d, *J* = 8.5 Hz, 1 H), 8.98 (d, *J* = 7.9 Hz, 1 H), 8.60 (t, *J* = 8.1 Hz, 1 H), 8.22 - 8.17 (m, 1 H), 8.16 - 8.09 (m, 2 H), 8.05 (s, 1 H), 7.99 (dd, *J* = 1.2, 7.5 Hz, 1 H), 7.27 (dd, *J* = 2.4, 8.6 Hz, 1 H), 7.13 (dd, *J* = 2.4, 8.6 Hz, 1 H), 7.09 - 7.02 (m, 1 H), 6.83 (dd, *J* = 2.6, 8.7 Hz, 1 H), 6.79 - 6.68 (m, 3 H), 3.78 (s, 3 H), 3.73 (s, 3 H); **^{13}C NMR (125 MHz, CD_3CN) δ** = 162.6, 159.5, 152.7, 148.4, 141.0, 139.6, 136.2, 135.6, 132.8, 132.3, 131.5, 131.2, 130.7, 130.3, 129.8, 129.6, 129.3, 126.8, 126.5, 124.0, 123.3, 121.0, 118.0, 116.0, 114.9, 56.6, 56.4; **HRMS (ESI)** calcd for $C_{27}H_{21}ClO_2N$+ $(M - OTf)^+$ 426.1255, found 426.1276.

4-(4-methoxyphenyl)-6-(naphthalen-1-yl)pyrido[2,1-a]isoquinolin-5-ium trifluoromethanesulfonate (2aa)



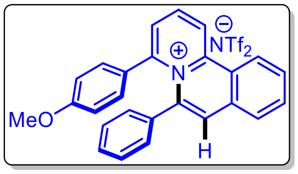
Yellow solid, 60 mg, 88% yield; ; mp = 181-183 °C; ***Rf*** = 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, CD_3CN) δ** = 9.35 (d, *J* = 8.7 Hz, 1 H), 9.03 (d, *J* = 8.1 Hz, 1 H), 8.57 (t, *J* = 8.0 Hz, 1 H), 8.22 - 8.17 (m, 2 H), 8.17 - 8.09 (m, 2 H), 7.83 (d, *J* = 8.2 Hz, 1 H), 7.79 (d, *J* = 7.3 Hz, 1 H), 7.75 (d, *J* = 8.2 Hz, 1 H), 7.52 (t, *J* = 7.5 Hz, 1 H), 7.40 (t, *J* = 7.6 Hz, 1 H), 7.34 - 7.28 (m, 2 H), 7.27 - 7.23 (m, 1 H), 6.94 (dd, *J* = 2.4, 8.6 Hz, 1 H), 6.60 - 6.48 (m, 2 H), 6.15 (dd, *J* = 2.6, 8.5 Hz, 1 H), 3.54 (s, 3 H); **^{13}C NMR (125 MHz, CD_3CN) δ** = 161.5, 153.0, 149.2, 140.9, 140.5, 135.5, 134.6, 134.5, 132.7, 132.5, 131.2, 131.2, 130.2, 130.1, 130.0, 129.8, 129.4, 129.1, 128.2, 127.7, 126.7, 126.7, 126.3, 124.8, 123.2, 115.4, 114.0, 56.1; **HRMS (ESI)** calcd for $C_{30}H_{22}NO^+$ (M - OTf)$^+$ 412.1696, found 412.1711.

8-(4-methoxyphenyl)-6-phenylisoquinolino[3,2-a]isoquinolin-7-ium trifluoromethanesulfonate (2ab):



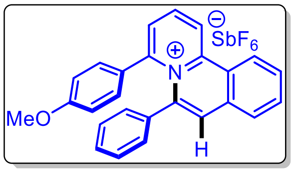
Yellow solid, 60 mg, 89% yield; ***Rf*** = 0.40 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, CD_3CN) δ** = 9.76 (s, 1 H), 8.91 (d, *J* = 7.9 Hz, 1 H), 8.53 (d, *J* = 8.2 Hz, 1 H), 8.25 - 8.15 (m, 1 H), 8.08 (d, *J* = 8.9 Hz, 1 H), 8.05 - 7.94 (m, 3 H), 7.94 - 7.87 (m, 1 H), 7.65 (s, 1 H), 7.27 - 7.08 (m, 5 H), 6.95 - 6.85 (m, 2 H), 6.85 - 6.73 (m, 2 H), 3.83 (s, 3 H); **^{13}C NMR (125 MHz, CD_3CN) δ** = 162.6, 156.3, 142.0, 141.5, 139.3, 138.2, 136.8, 133.7, 133.5, 132.7, 131.9, 130.1, 129.9, 129.5, 129.4, 129.3, 129.1, 128.6, 128.4, 128.4, 127.8, 127.3, 127.1, 125.5, 121.2, 115.5, 56.4; **HRMS (ESI)** calcd for $C_{26}H_{18}ON^+$ (M - OTf)$^+$ 412.1705, found412.1702.

4-(4-methoxyphenyl)-6-phenylpyrido[2,1-a]isoquinolin-5-ium bis((trifluoromethyl)sulfonyl)amide (**3a**):



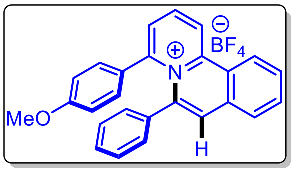
Yellow solid, 82 mg, 93% yield; ***Rf*** = 0.40 (CH_2Cl_2/MeOH = 93/07); **^{1}H NMR (500 MHz, CD_3CN) δ** = 9.23 (dd, *J* = 1.2, 8.7 Hz, 1 H), 8.93 (d, *J* = 8.2 Hz, 1 H), 8.57 (dd, *J* = 7.6, 8.5 Hz, 1 H), 8.19 - 8.14 (m, 1 H), 8.11 (dt, *J* = 1.1, 7.5 Hz, 1 H), 8.08 - 8.03 (m, 1 H), 7.97 (s, 1 H), 7.93 (dd, *J* = 1.4, 7.5 Hz, 1 H), 7.20 - 7.14 (m, 5 H), 7.14 - 7.09 (m, 2 H), 6.75 - 6.68 (m, 2 H); **^{13}C NMR (125 MHz, CD_3CN) δ** = 162.3, 153.1, 149.6, 142.9, 140.8, 138.0, 135.5, 132.9, 132.2, 131.2, 130.4, 130.0, 129.6, 129.5, 129.4, 128.7, 128.5, 126.5, 126.5, 122.5, 122.3, 119.7, 115.3, 56.4.

4-(4-methoxyphenyl)-6-phenylpyrido[2,1-a]isoquinolin-5-ium hexafluorostibate (**3b**):



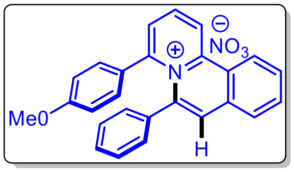
Yellow solid, 75 mg, 86% yield; ***Rf*** = 0.50 (CH_2Cl_2/MeOH = 93/07); **^{1}H NMR (500 MHz, , CD_3CN) δ** = 9.22 (dd, *J* = 1.1, 8.6 Hz, 1 H), 8.93 (d, *J* = 8.2 Hz, 1 H), 8.57 (dd, *J* = 7.6, 8.5 Hz, 1 H), 8.19 - 8.14 (m, 1 H), 8.13 - 8.09 (m, 1 H), 8.08 - 8.03 (m, 1 H), 7.97 (s, 1 H), 7.93 (dd, *J* = 1.2, 7.5 Hz, 1 H), 7.21 - 7.15 (m, 5 H), 7.14 - 7.09 (m, 2 H), 6.75 - 6.68 (m, 2 H), 3.74 (s, 3 H); **^{13}C NMR (125 MHz, , CD_3CN) δ** = 162.3, 153.1, 149.6, 142.9, 140.8, 138.0, 135.5, 132.9, 132.2, 131.2, 130.4, 130.0, 129.6, 129.5, 129.4, 128.7, 128.5, 126.5, 126.5, 122.5, 115.3, 56.4.

4-(4-methoxyphenyl)-6-phenylpyrido[2,1-a]isoquinolin-5-ium tetrafluoroborate (**3c**):



Yellow solid, 54 mg, 87% yield; ***Rf*** = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, CD_3CN) δ** = 9.23 (d, *J* = 8.7 Hz, 1 H), 8.94 (d, *J* = 8.4 Hz, 1 H), 8.58 (t, *J* = 8.0 Hz, 1 H), 8.21 - 8.13 (m, 1 H), 8.11 (t, *J* = 7.5 Hz, 1 H), 8.08 - 8.03 (m, 1 H), 7.97 (s, 1 H), 7.93 (dd, *J* = 1.2, 7.5 Hz, 1 H), 7.22 - 7.13 (m, 5 H), 7.13 - 7.08 (m, 2 H), 6.72 (d, *J* = 8.7 Hz, 2 H), 3.74 (s, 3 H); **^{13}C NMR (125 MHz, CD_3CN) δ** = 162.3, 156.6, 153.1, 149.6, 142.9, 140.9, 138.0, 135.6, 135.3, 132.9, 132.3, 132.0, 131.2, 130.4, 130.0, 129.6, 129.4, 129.2, 128.8, 128.6, 128.5, 126.7, 126.5, 126.3, 122.5, 115.3, 56.3.

4-(4-methoxyphenyl)-6-phenylpyrido[2,1-a]isoquinolin-5-ium nitrate (**3d**):



Yellow solid, 35 mg, 60% yield; ***Rf*** = 0.30 (CH_2Cl_2/MeOH = 90/10); **^{1}H NMR (500 MHz, CD_3CN) δ** = 9.28 (dd, *J* = 1.2, 8.7 Hz, 1 H), 8.97 (d, *J* = 8.2 Hz, 1 H), 8.59 (dd, *J* = 7.6, 8.5 Hz, 1 H), 8.19 - 8.14 (m, 1 H), 8.13 - 8.02 (m, 2 H), 7.97 (s, 1 H), 7.94 (dd, *J* = 1.4, 7.5 Hz, 1 H), 7.21 - 7.14 (m, 5 H), 7.14 - 7.08 (m, 2 H), 6.76 - 6.65 (m, 2 H), 3.74 (s, 3 H); **^{13}C NMR (125 MHz, CD_3CN) δ** = 162.3, 153.1, 149.6, 142.8, 140.9, 138.0, 135.4, 132.9, 132.2, 131.2, 130.4, 130.0, 129.6, 129.5, 129.4, 128.7, 128.5, 126.6, 126.5, 122.6, 115.3, 56.3.

3.6.6 Representative procedure for the synthesis of enyne 2a at 1 mmol scale:

To a screw-cap vial containing a stir bar were added 2-phenyl-6-(2-(phenylethynyl)phenyl)pyridine (**1a**) (330 mg, 1.0mmol, 1.0 equiv), AgOTf (256 mg, 1.0mmol, 1.0 equiv) and moist DCE (4 mL). The reaction vial was fitted with a cap, evacuated and back filled with N_2 and heated at 80 °C for 6-12 h. When the reaction time was completed, the reaction mixture was allowed to cool at ambient temperature. The mixture was diluted with CH_2Cl_2 (10 mL) and the combined mixture was concentrated in vacuo and the resulting residue was purified by column chromatography on silica (CH_2Cl_2/MeOH; 95:05) to afford the product **2a** in 70% yield.

3.7 Photophysical data of the representative ionic solid light emitters

Table S1. Spectral properties of selected ionic solid light emitters

Comp	λ_{abs} (nm)[a]	λ_{em} (nm)[b]	ΔStoke's (nm)[c]	ϕ_f[d]	τ_f (ns)[e]
2f	445	500	55	0.05	10.38
2m	448	506	58	0.12	16.4
2o	450	530	80	0.32	2.6
2r	443	505	62	0.28	14.6
2t	449	542	93	0.34	4.5
2u	460	590	130	0.51	7.2
2y	425	480	55	0.24	18.6
2aa	434	534	100	0.49	5.44

[a]The maximum absorption bands more than 300 nm; Excited at the longest maximum absorption band in CH_2Cl_2; [b]Excited wavelength; [c]Stokes shift = λ_{em} - λ_{abs}; [d]Quinine sulfate and fluorescein was used as the standard for calculation of quantum yield; [e]Fluorescent lifetime

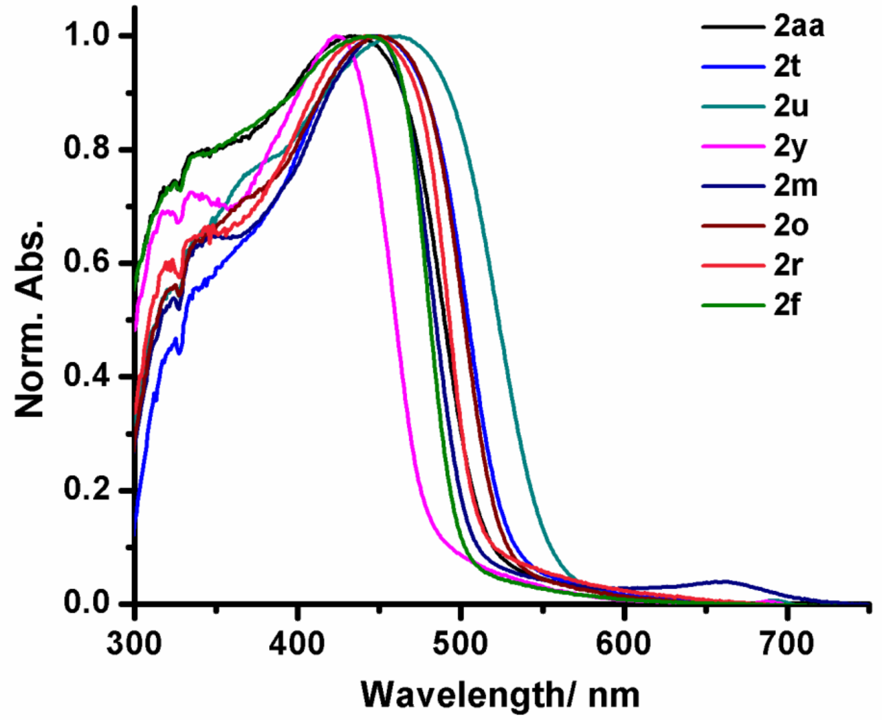


Figure S1. Absorption spectra of selected ionic compounds in solid form

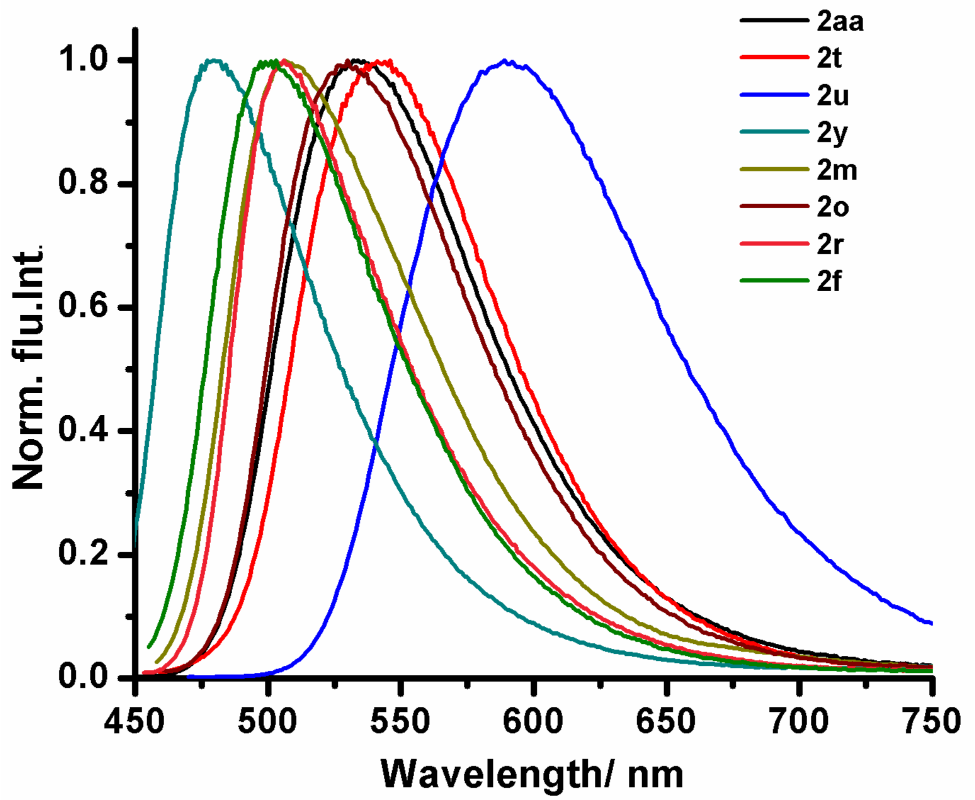


Figure S2. Emission spectra of selected ionic compounds in solid form

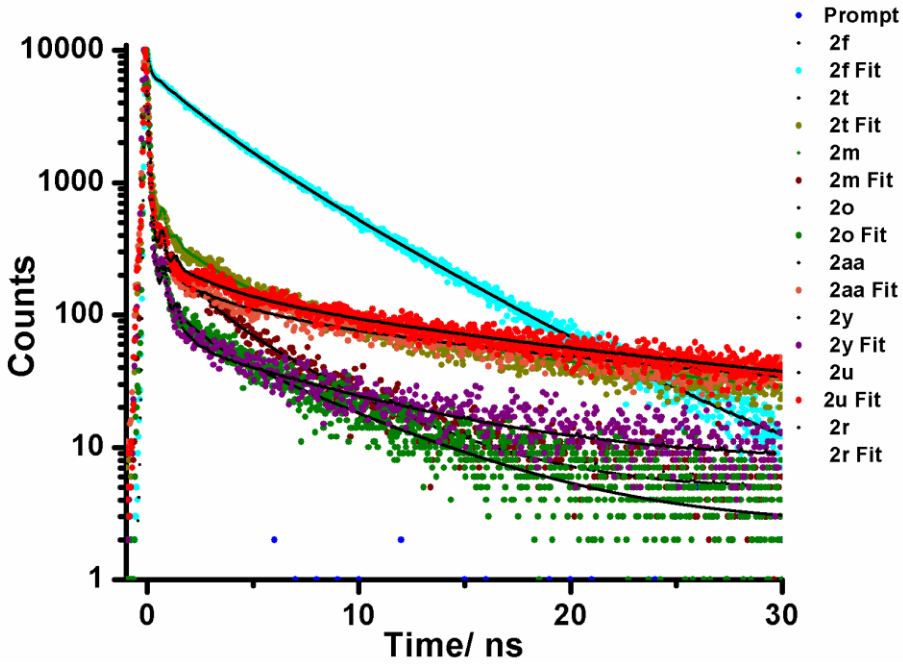
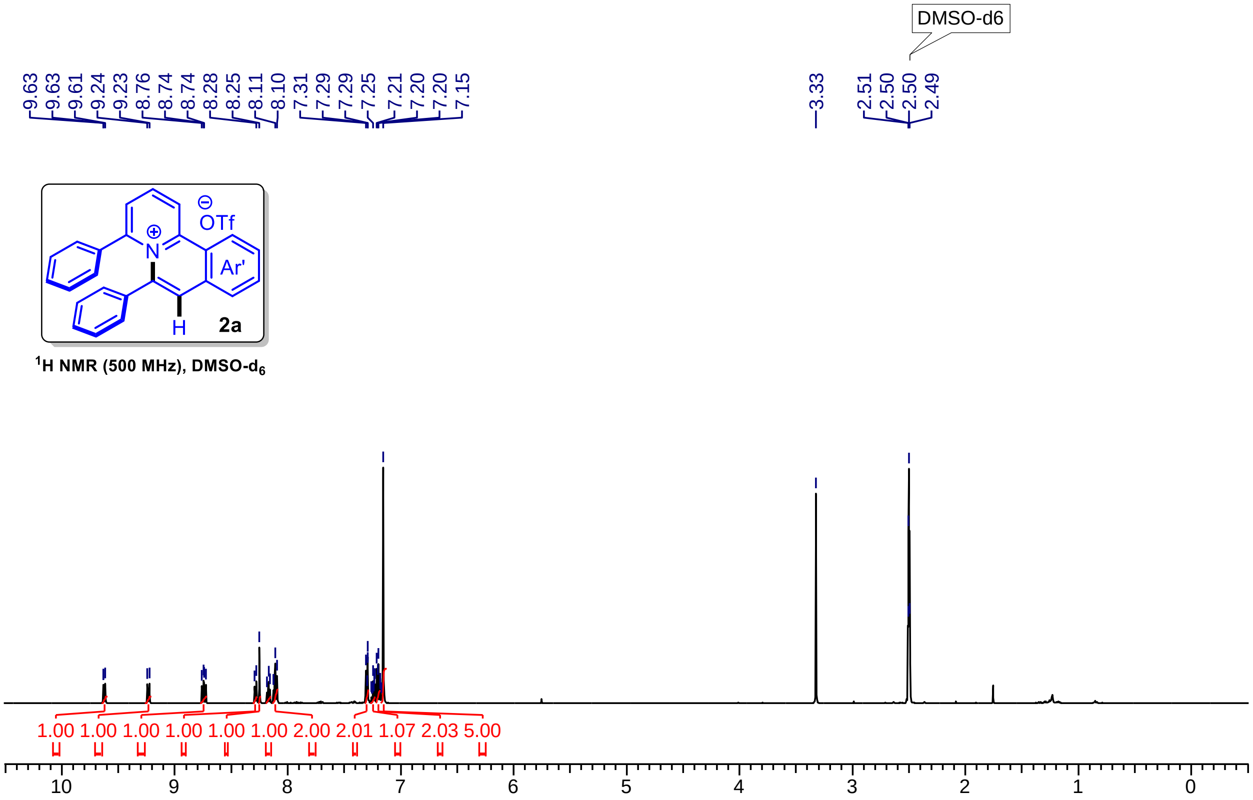


Figure S3: Emission decay profile of selected compounds in solid form

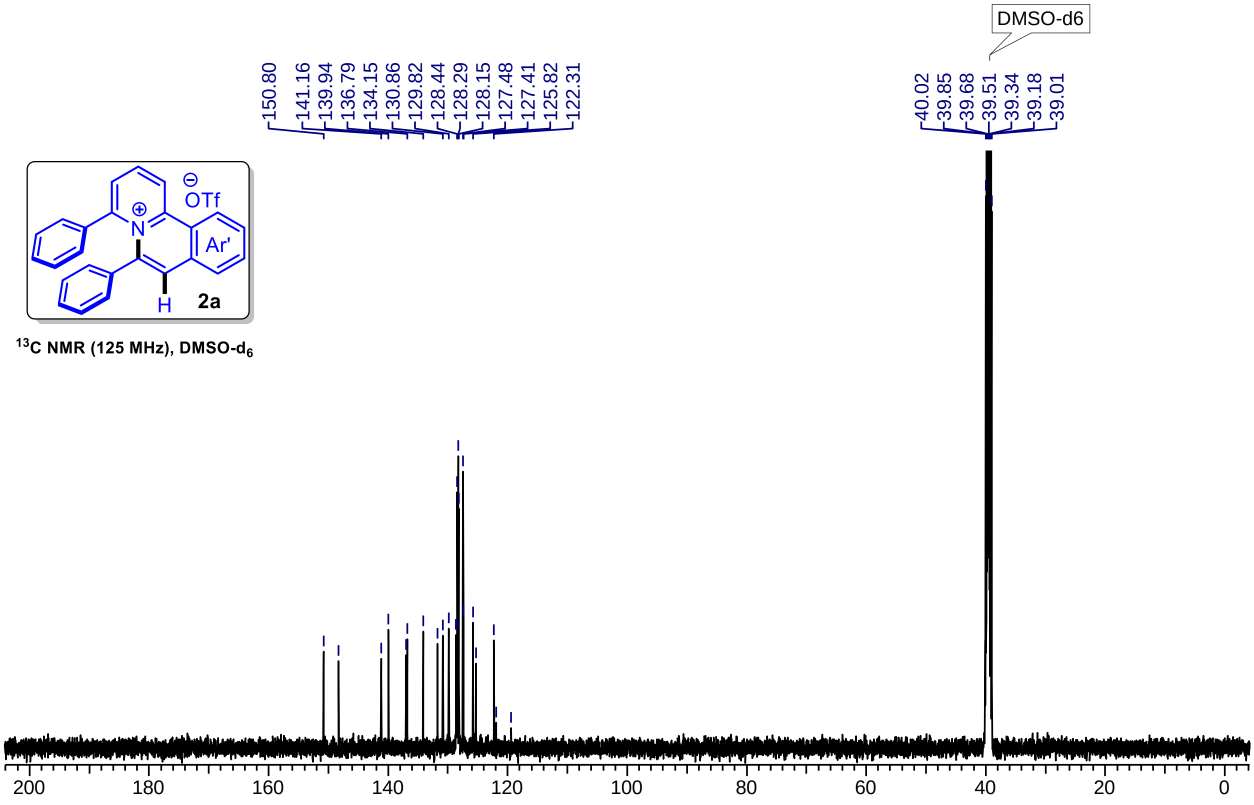
Discussion on the photophysical data of the selected ionic solid light emitters:

Most of these compounds display bright fluorescence. These isoquinolopyridinium (IQP) salts appear to be a new class of fluorescent materials and their photo- physical properties of selected ionic IQP salts were studied. The absorption and excitation maxima, the photoluminescence (PL) maxima and quantum yields (ϕ_f), as well as the excited state lifetimes (τ_f) of these compounds are listed in Tables S1, whereas the corresponding absorption, emission, excitation spectra are depicted in Figures S1, S2 and S3. The photoluminescence spectra of fluorophores show intense peaks between λ_{em}: 434–619 nm (Table S1) with Stokes shifts varies between (55-130 nm) which reveals green-to-yellow fluorescence emissions. These fluorophores have good photoluminescence capabilities with Φ_f values ranging between 0.05 to 0.51. The life time τ_f values are consistent with a doublet multiplicity.

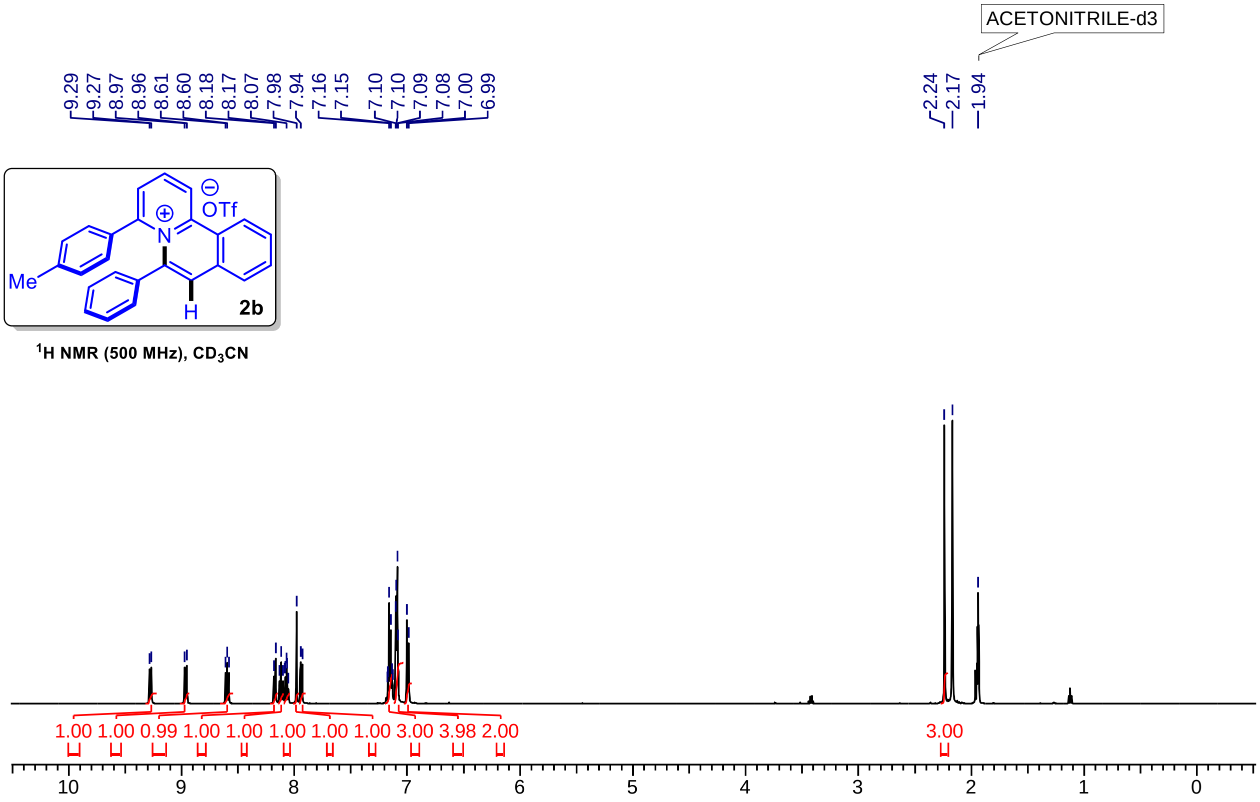
3.8 Selected NMR spectra



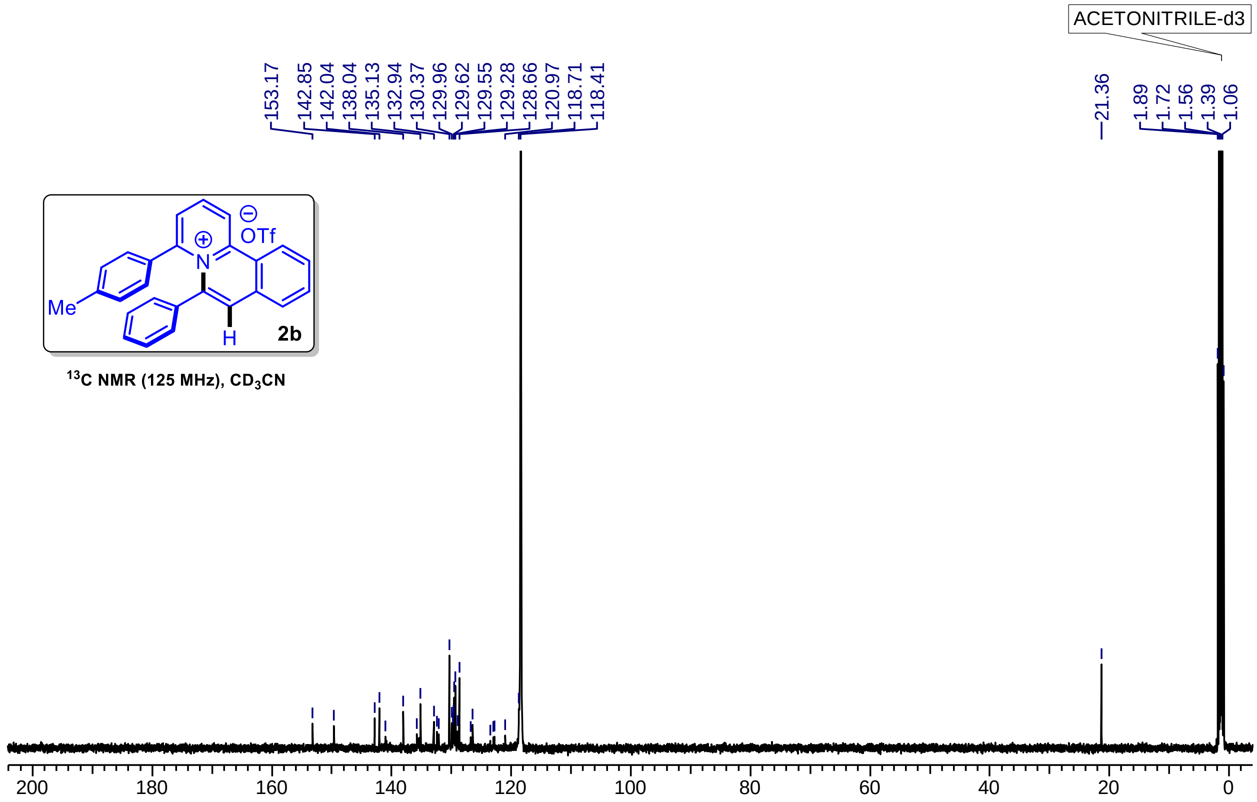
^{1}H NMR (500 MHz), DMSO-d_6



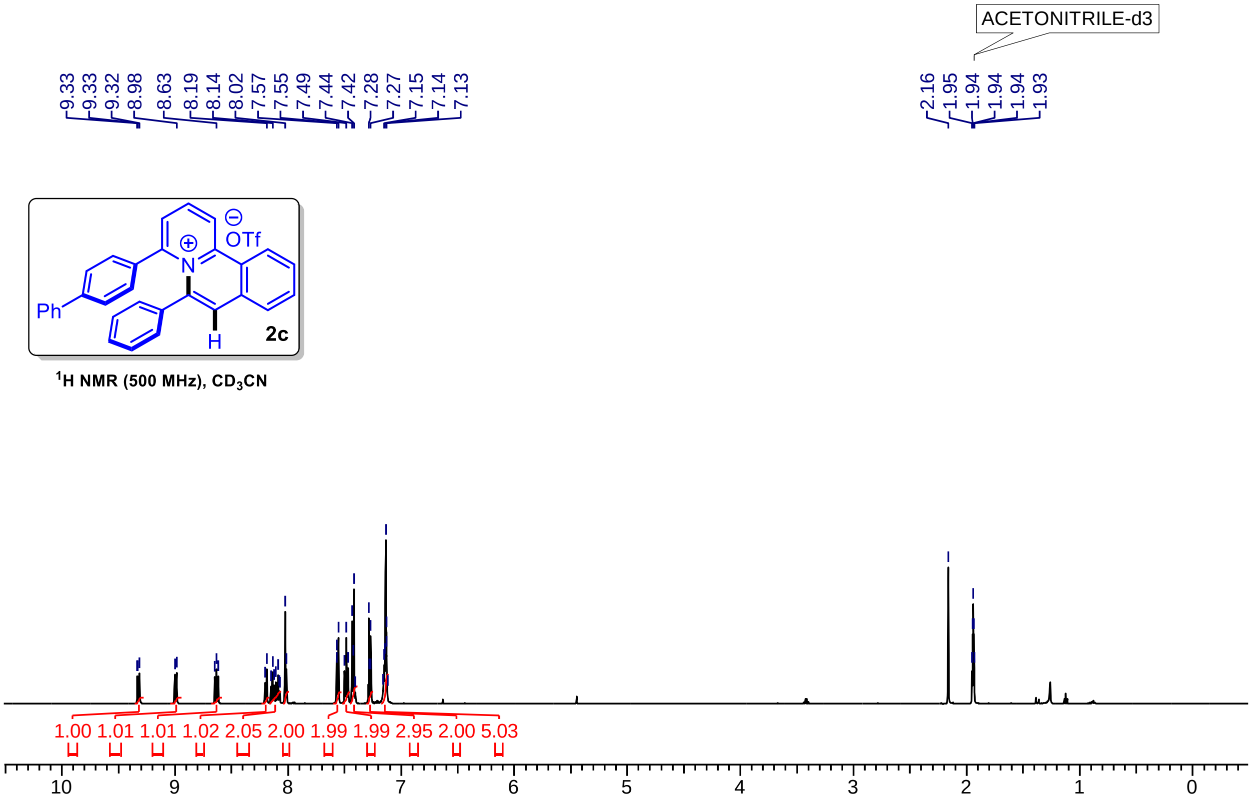
^{13}C NMR (125 MHz), DMSO-d_6

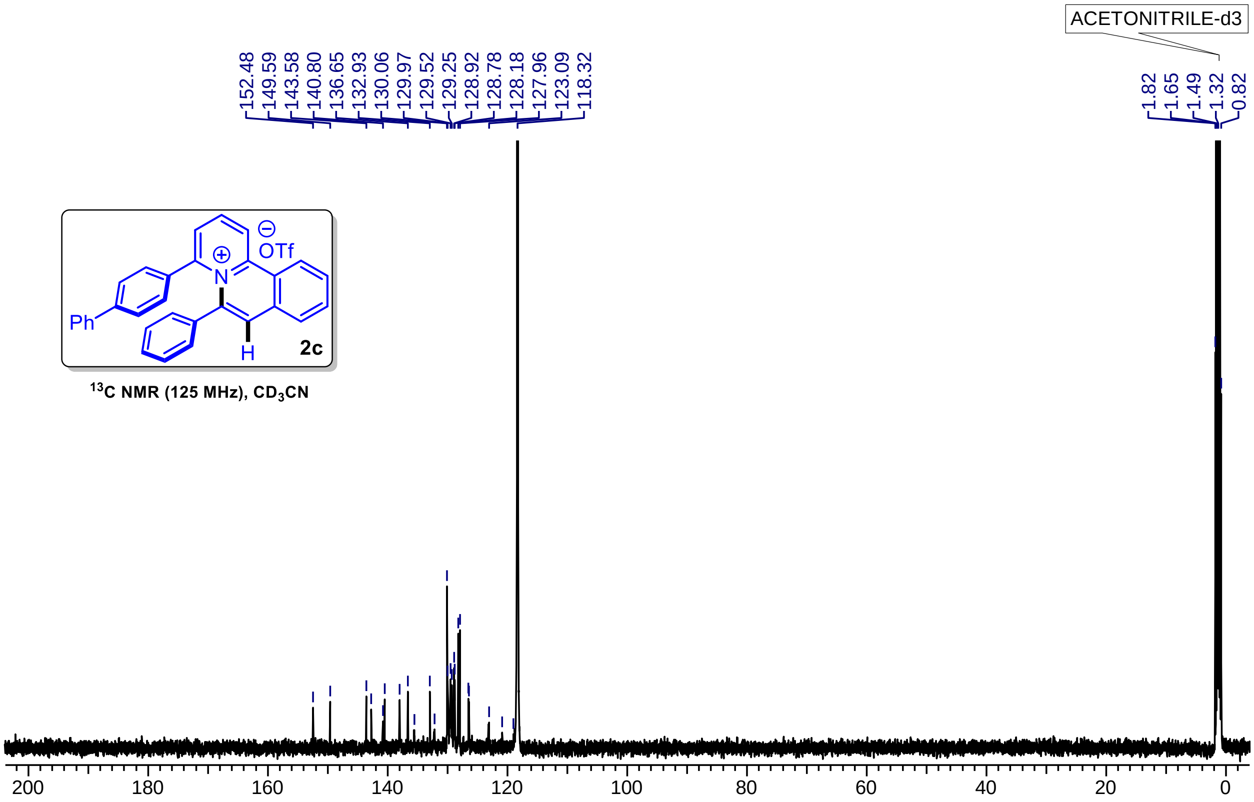


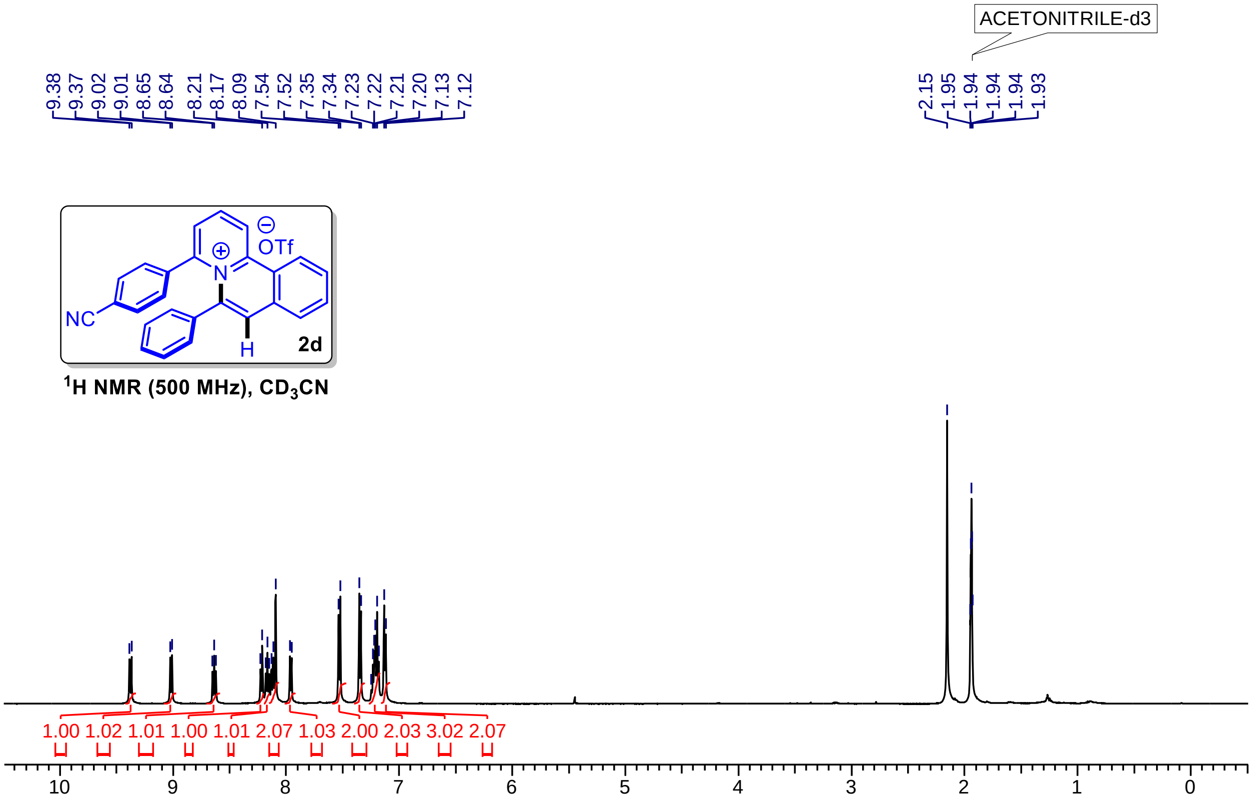
^{1}H NMR (500 MHz), CD_3CN



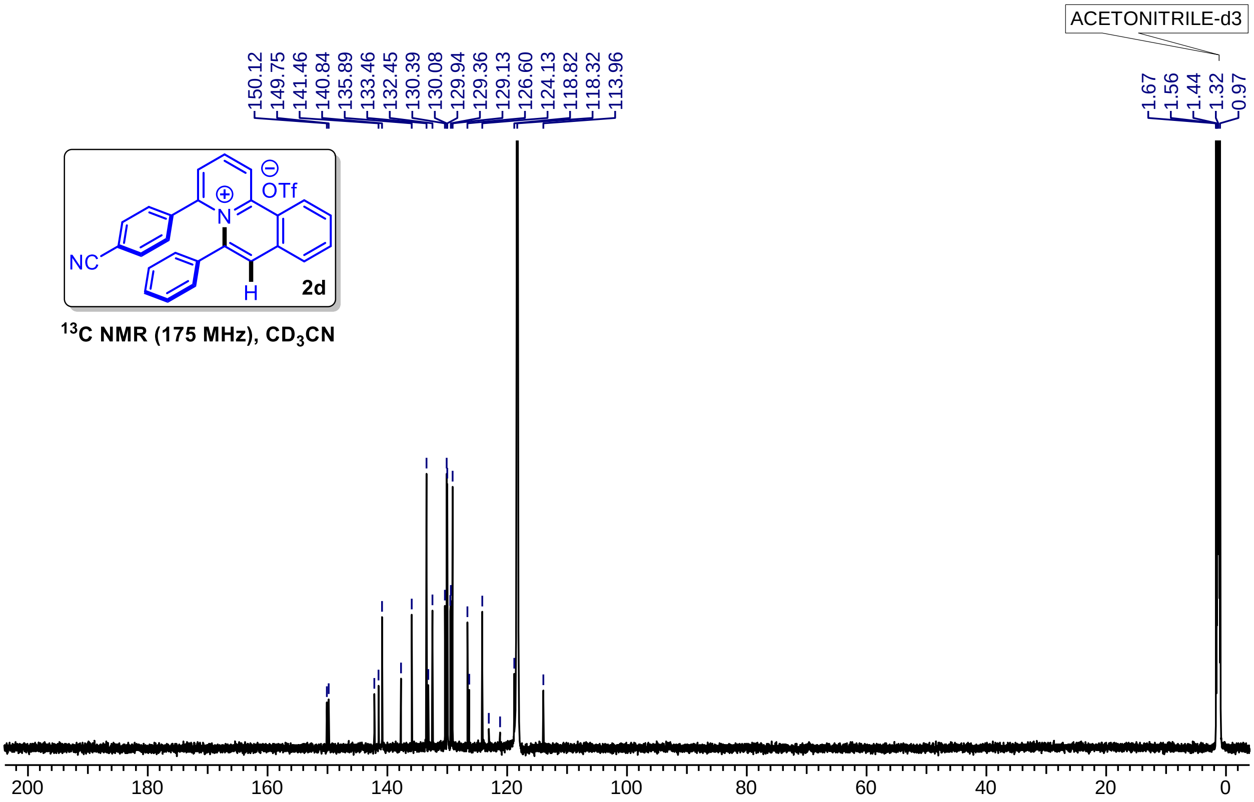
^{13}C NMR (125 MHz), CD_3CN


ACETONITRILE-d3
9.33
9.33
9.32
8.98
8.63
8.19
8.14
8.02
7.57
7.55
7.49
7.44
7.42
7.28
7.27
7.15
7.14
7.13
2.16
1.95
1.94
1.94
1.94
1.93
OTf
N
Ph
H
2c
^{1}H NMR (500 MHz), CD$_3$CN
1.00
1.01
1.01
1.02
2.05
2.00
1.99
1.99
2.95
2.00
5.03
10
9
8
7
6
5
4
3
2
1
0

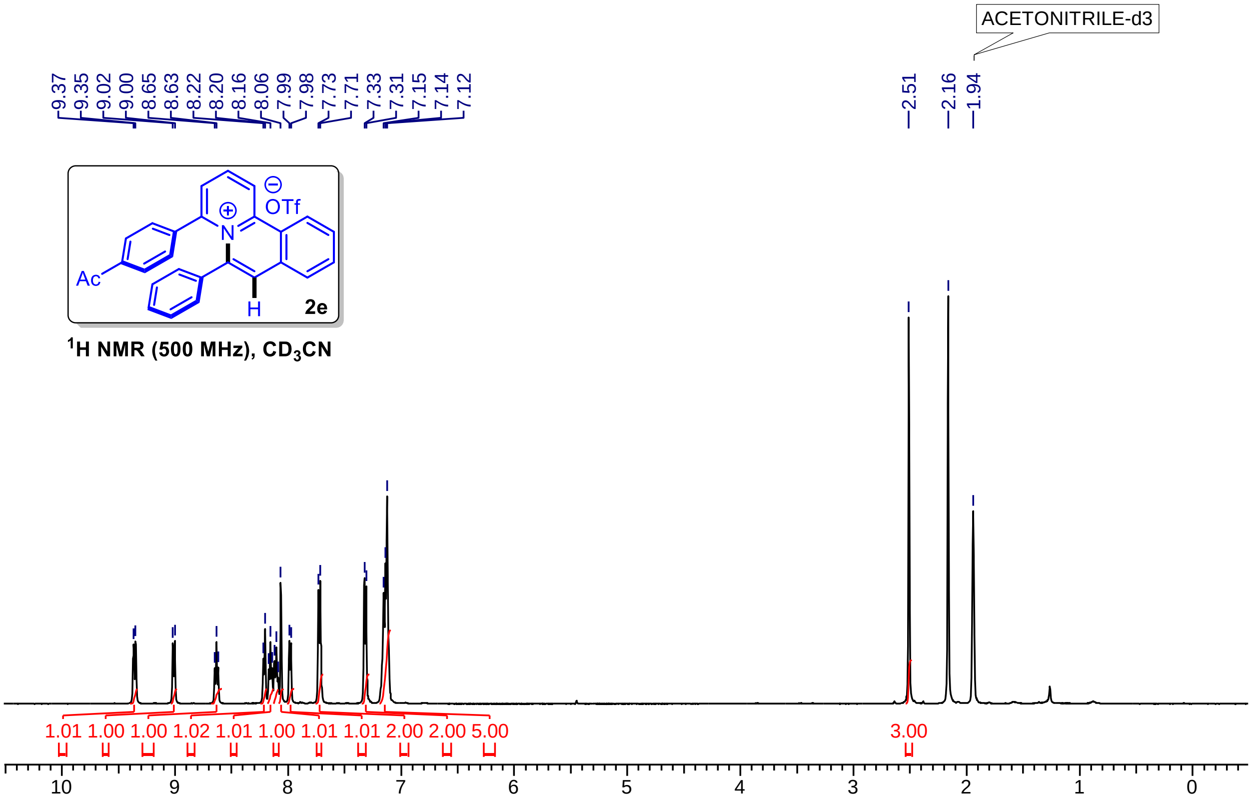

ACETONITRILE-d3
152.48
149.59
143.58
140.80
136.65
132.93
130.06
129.97
129.52
129.25
128.92
128.78
128.18
127.96
123.09
118.32
1.82
1.65
1.49
1.32
0.82
OTf
N
Ph
H
2c
^{13}C NMR (125 MHz), CD$_3$CN
200
180
160
140
120
100
80
60
40
20
0



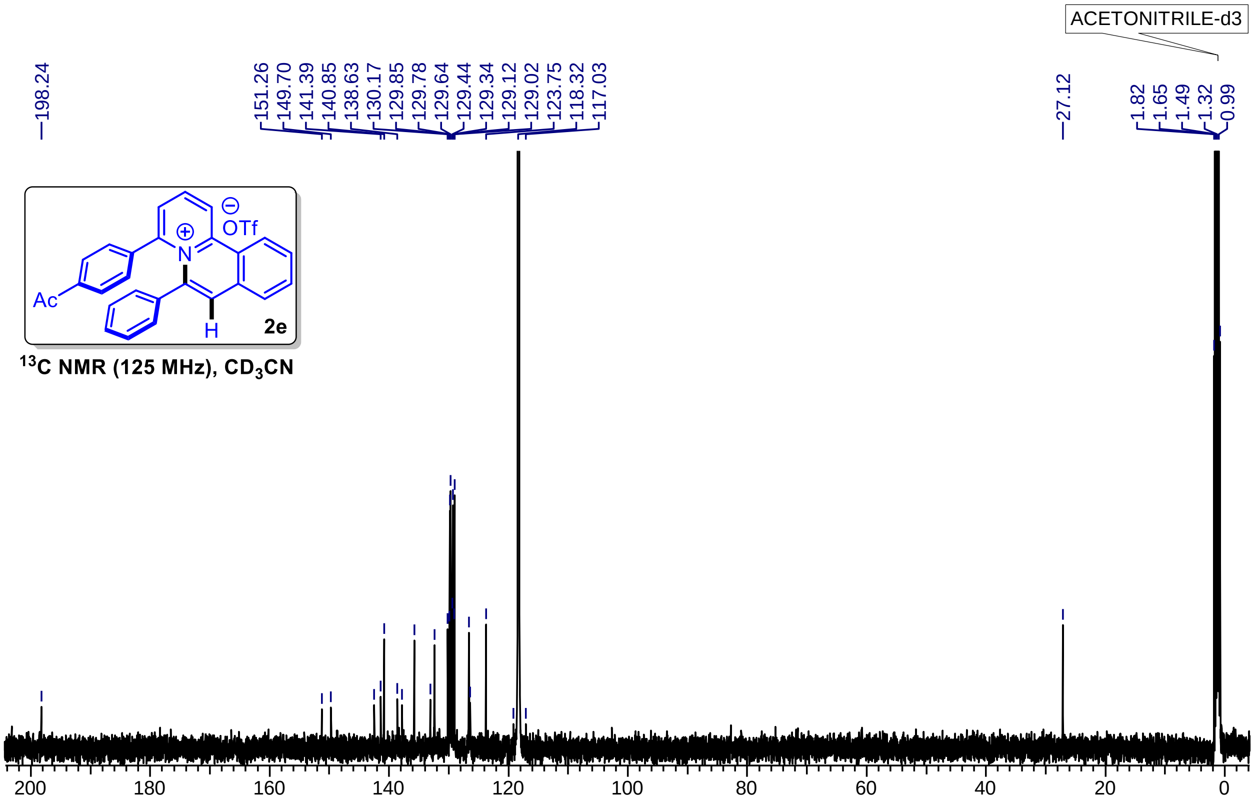
^{1}H NMR (500 MHz), CD_3CN



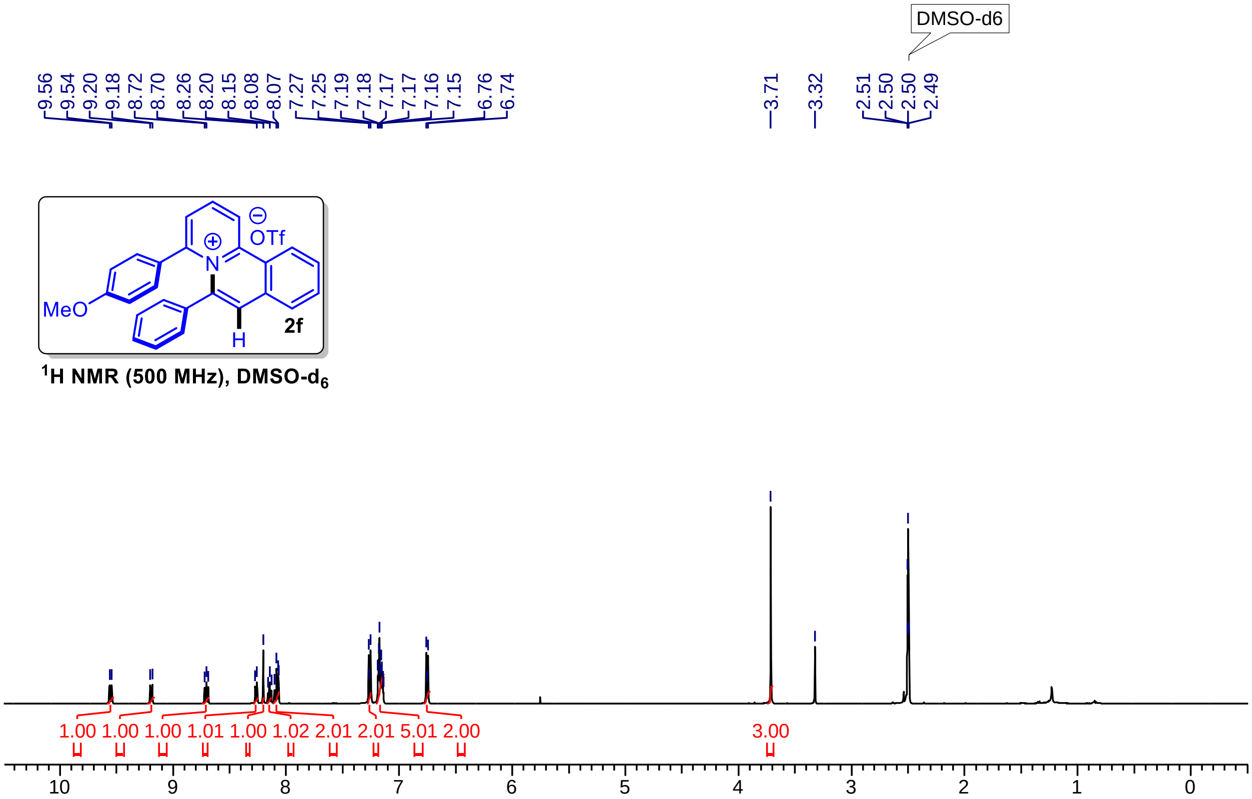
^{13}C NMR (175 MHz), CD_3CN



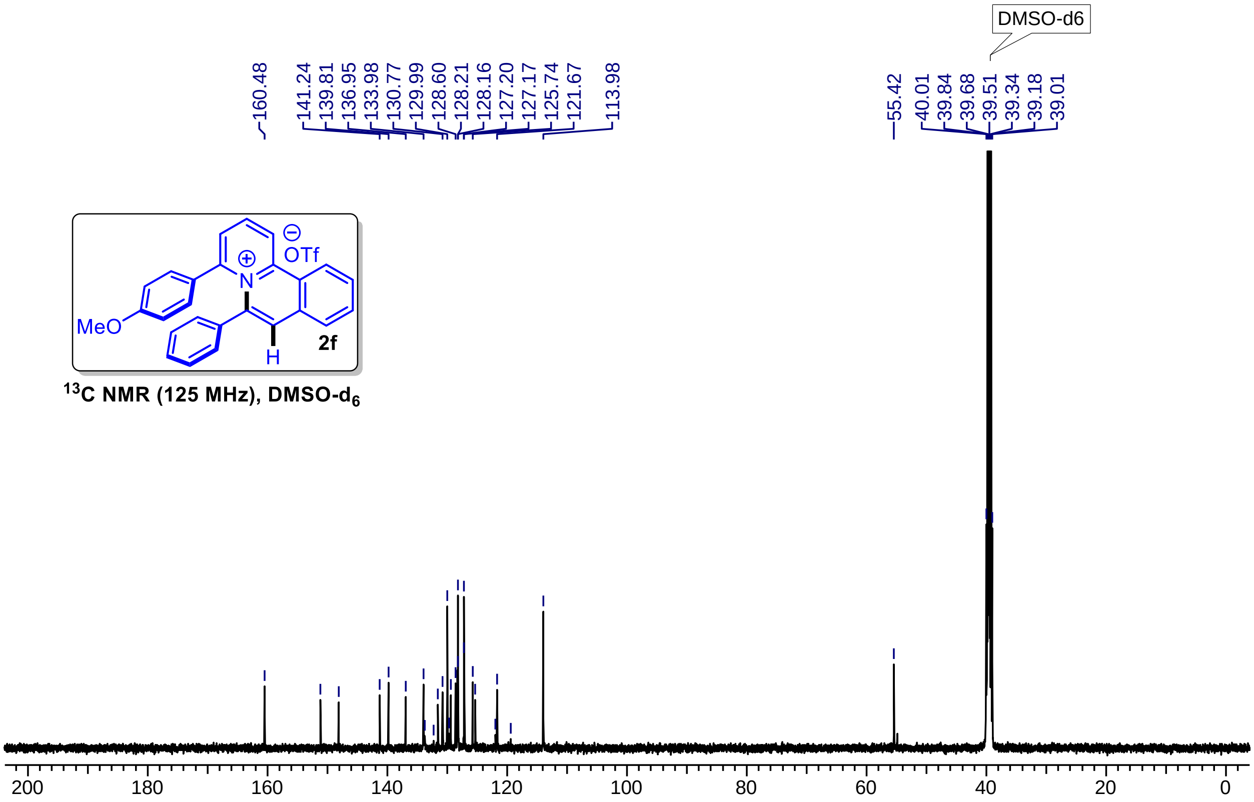
^{1}H NMR (500 MHz), CD$_3$CN



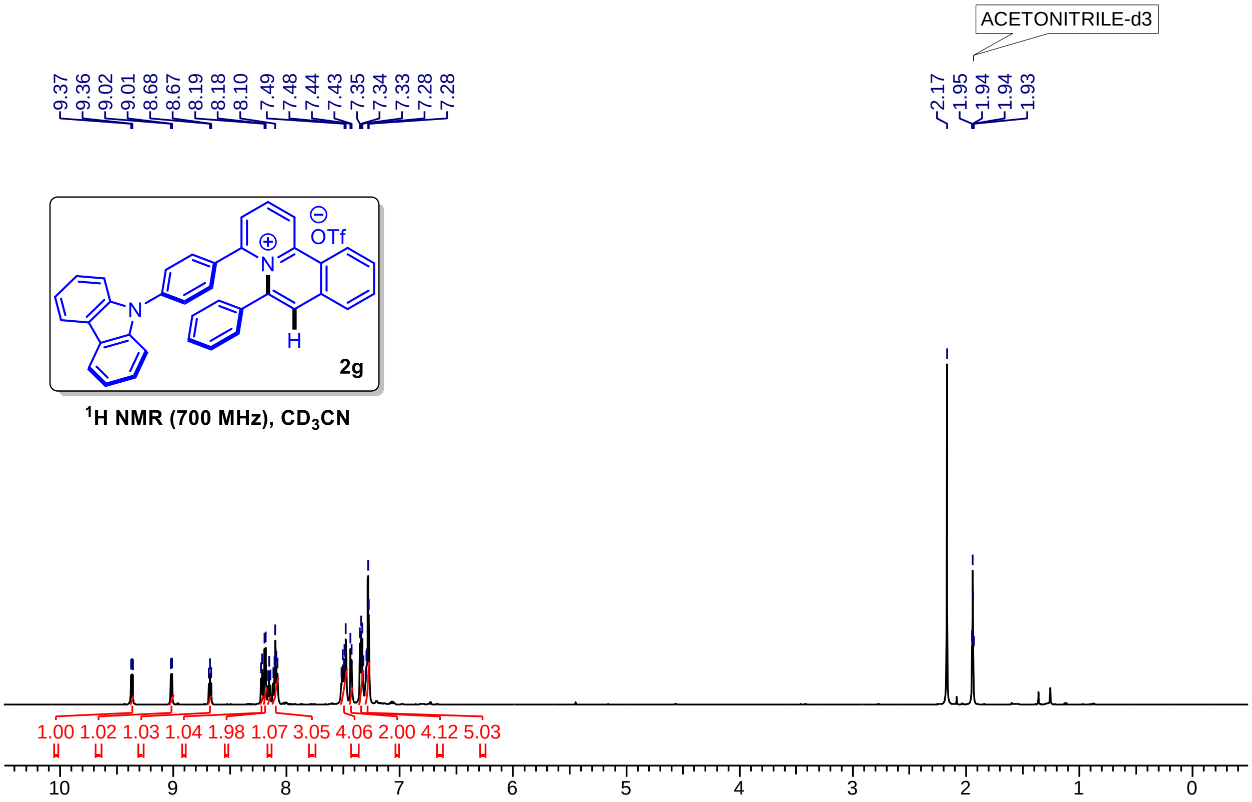
^{13}C NMR (125 MHz), CD$_3$CN

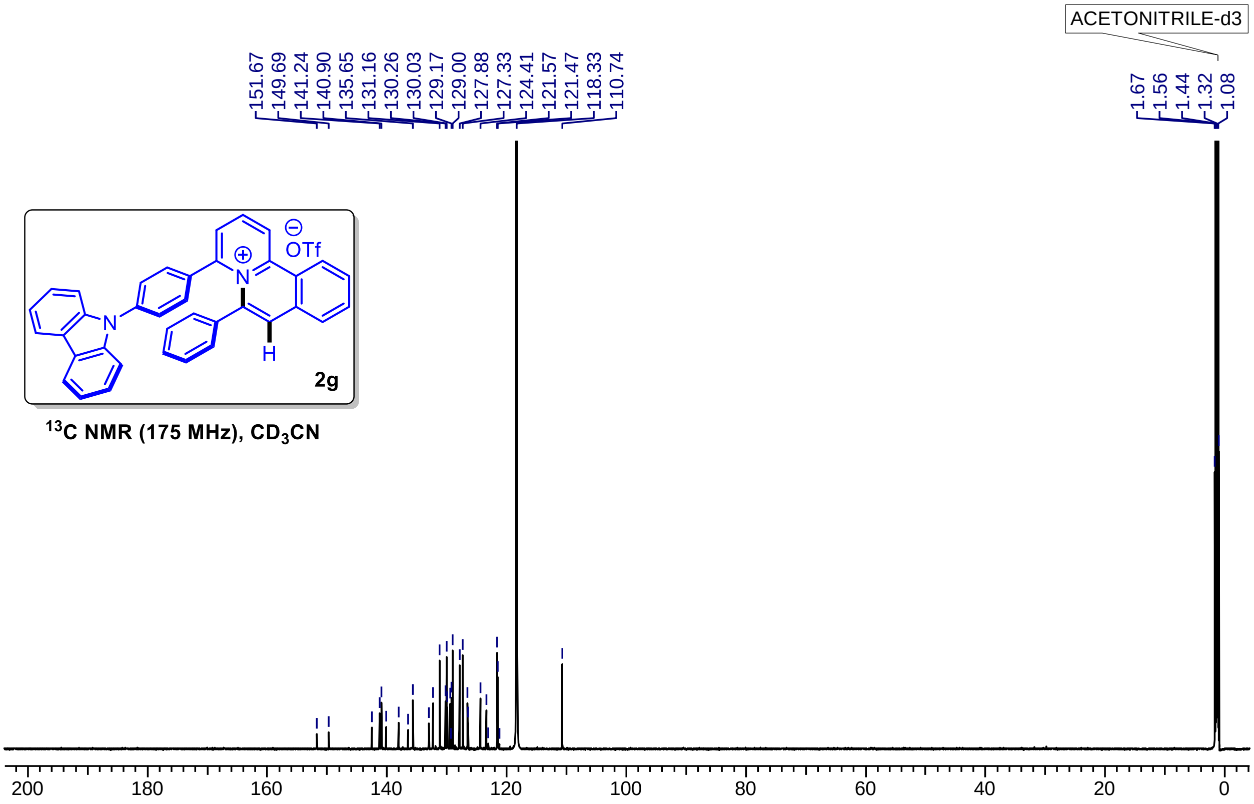


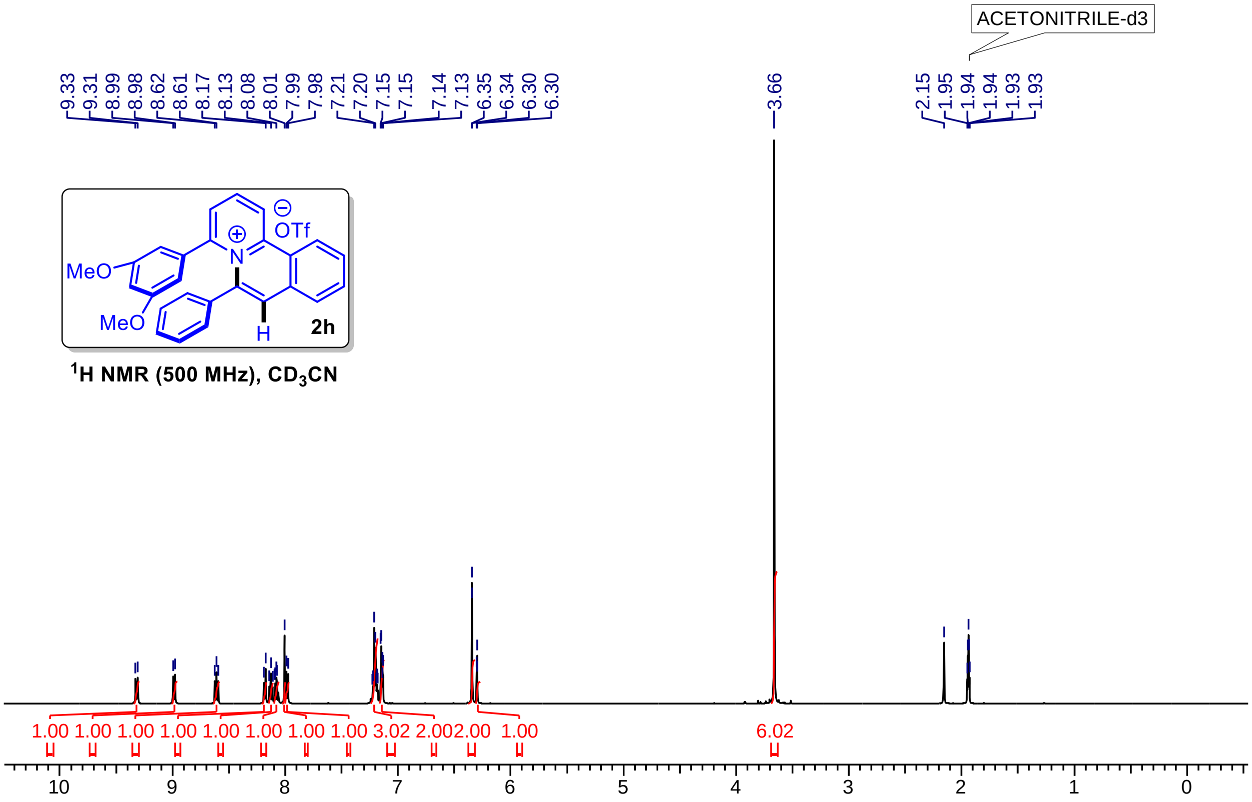
^{1}H NMR (500 MHz), DMSO-d_6

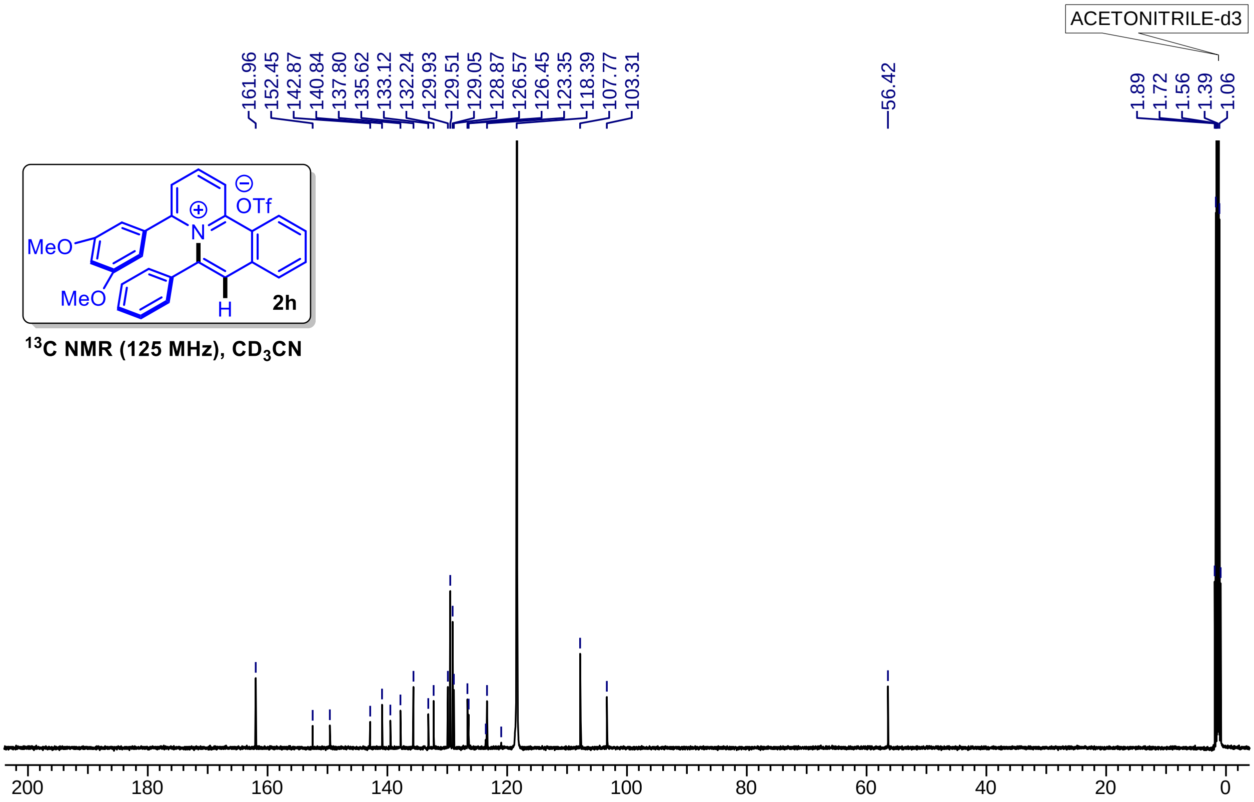


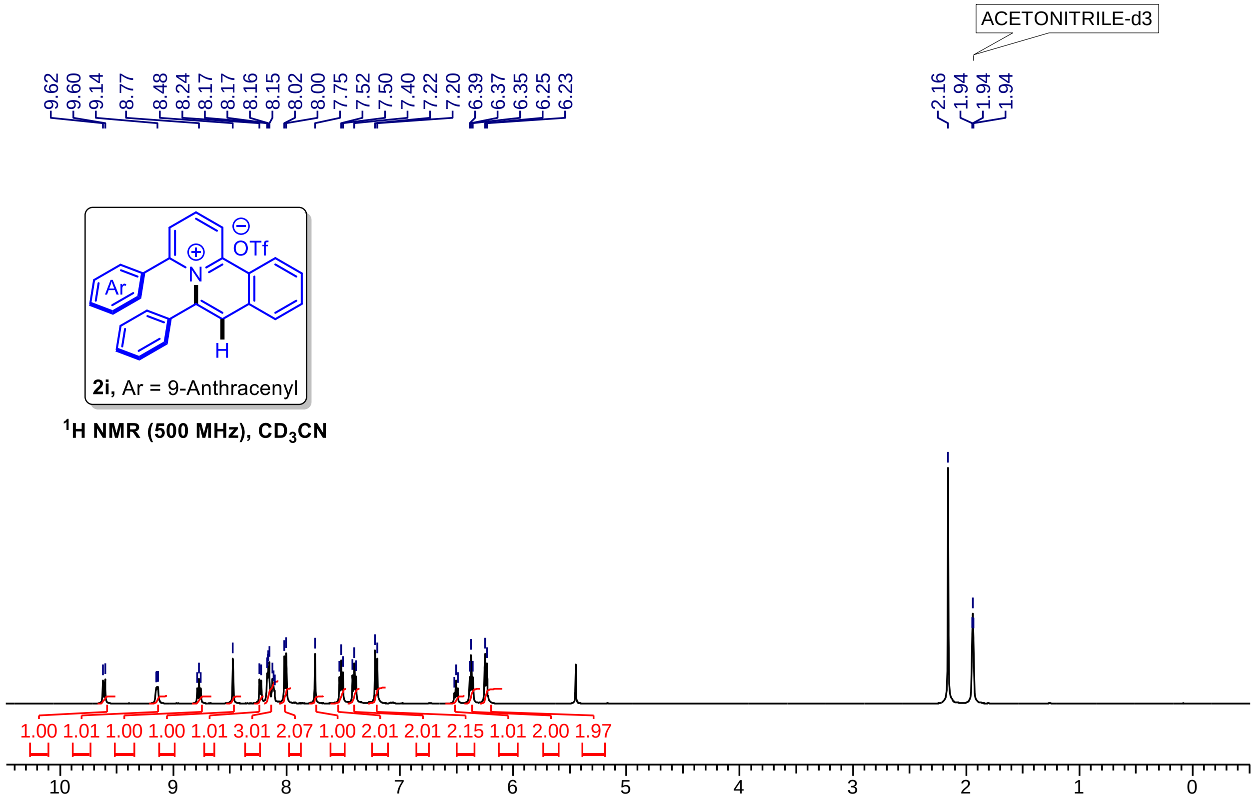
^{13}C NMR (125 MHz), DMSO-d_6

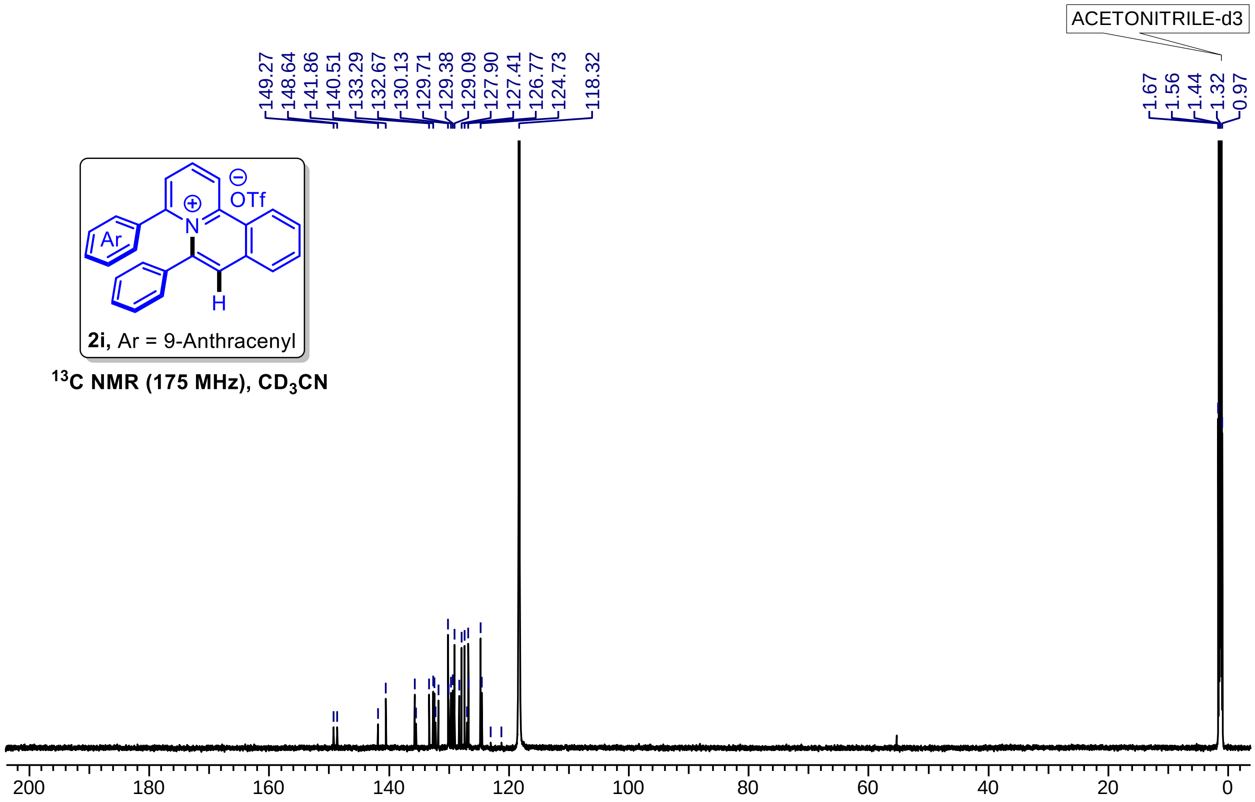

ACETONITRILE-d3
9.37 9.36 9.02 9.01 8.68 8.67 8.19 8.18 8.10 7.49 7.48 7.44 7.43 7.35 7.34 7.33 7.28 7.28
2.17 1.95 1.94 1.94 1.93
OTf
N
H
2g
^{1}H NMR (700 MHz), CD$_3$CN
1.00 1.02 1.03 1.04 1.98 1.07 3.05 4.06 2.00 4.12 5.03
10 9 8 7 6 5 4 3 2 1 0

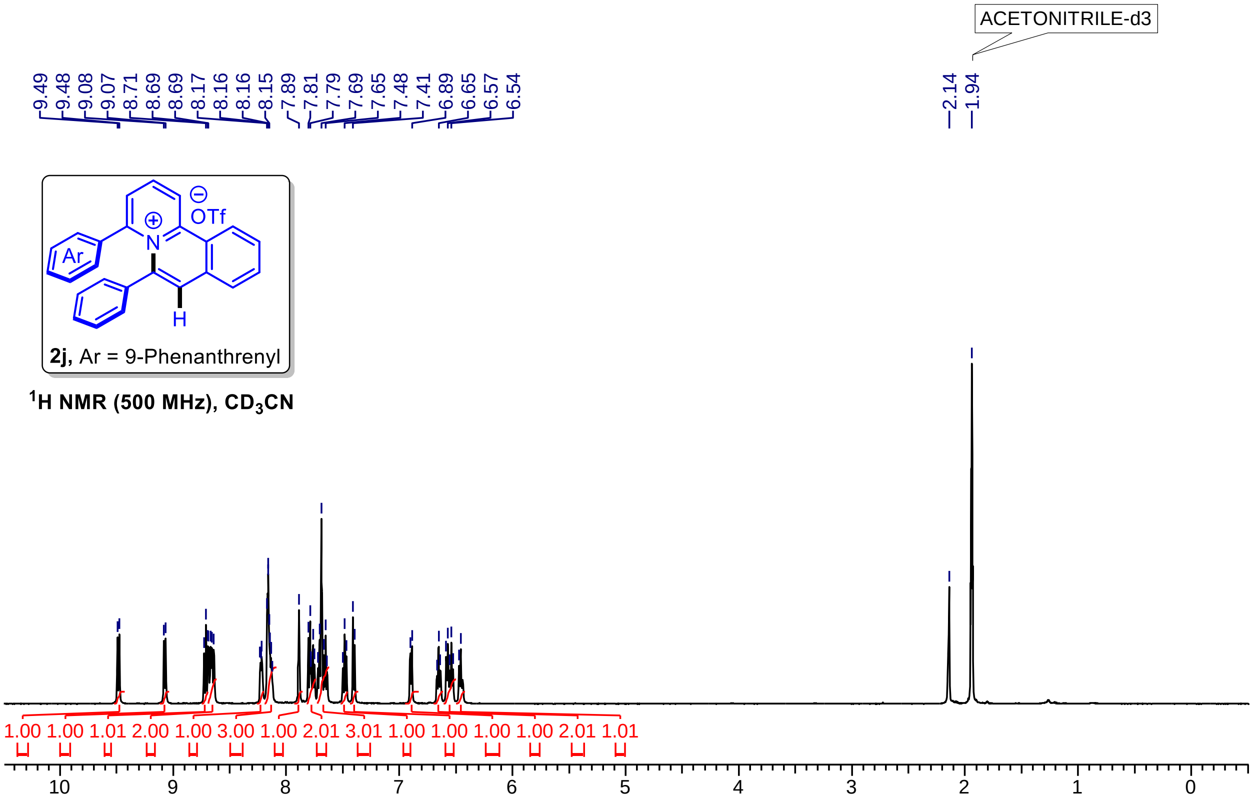

ACETONITRILE-d3
151.67 149.69 141.24 140.90 135.65 131.16 130.26 130.03 129.17 129.00 127.88 127.33 124.41 121.57 121.47 118.33 110.74
1.67 1.56 1.44 1.32 1.08
OTf
N
H
2g
^{13}C NMR (175 MHz), CD$_3$CN
200 180 160 140 120 100 80 60 40 20 0

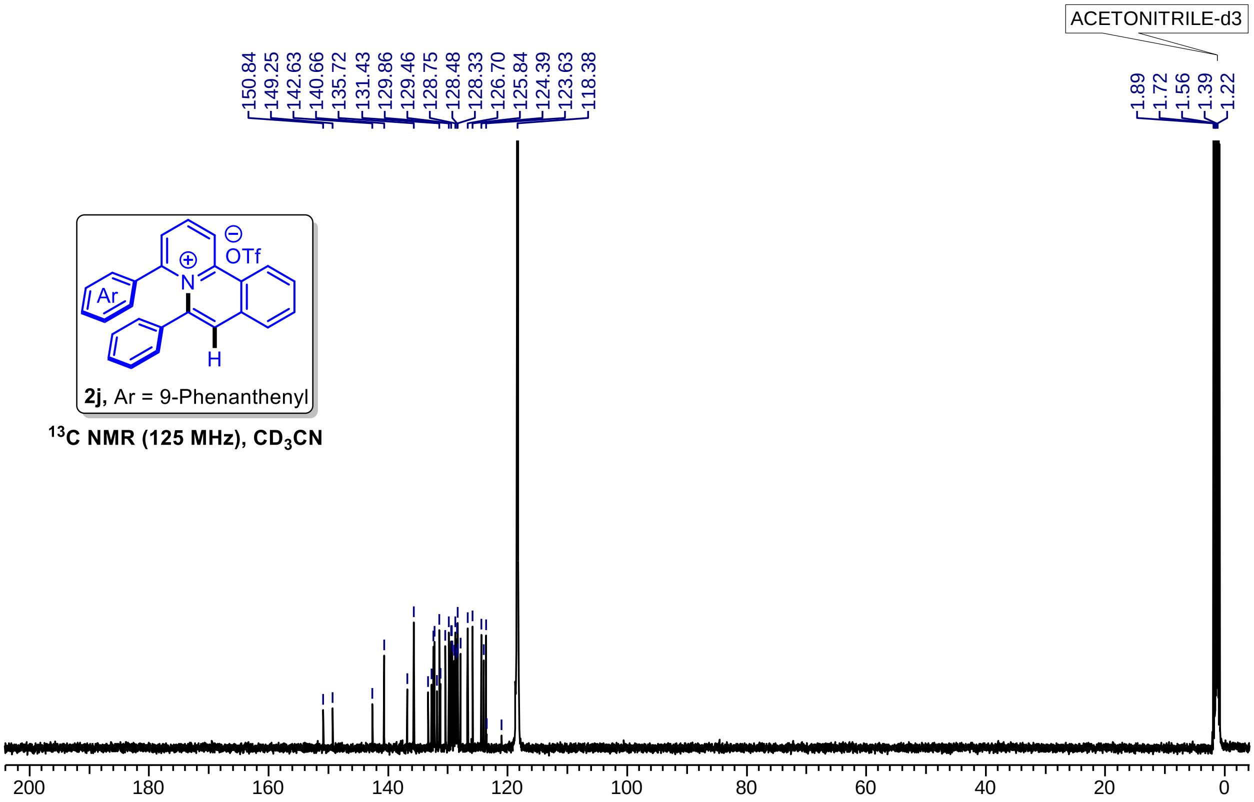

ACETONITRILE-d3
9.33
9.31
8.99
8.98
8.62
8.61
8.17
8.13
8.08
8.01
7.99
7.98
7.21
7.20
7.15
7.15
7.14
7.13
6.35
6.34
6.30
6.30
3.66
2.15
1.95
1.94
1.94
1.93
1.93
MeO
MeO
OTf
N
H
2h
^{1}H NMR (500 MHz), CD$_3$CN
1.00
1.00
1.00
1.00
1.00
1.00
1.00
1.00
3.02
2.00
2.00
1.00
6.02
10
9
8
7
6
5
4
3
2
1
0

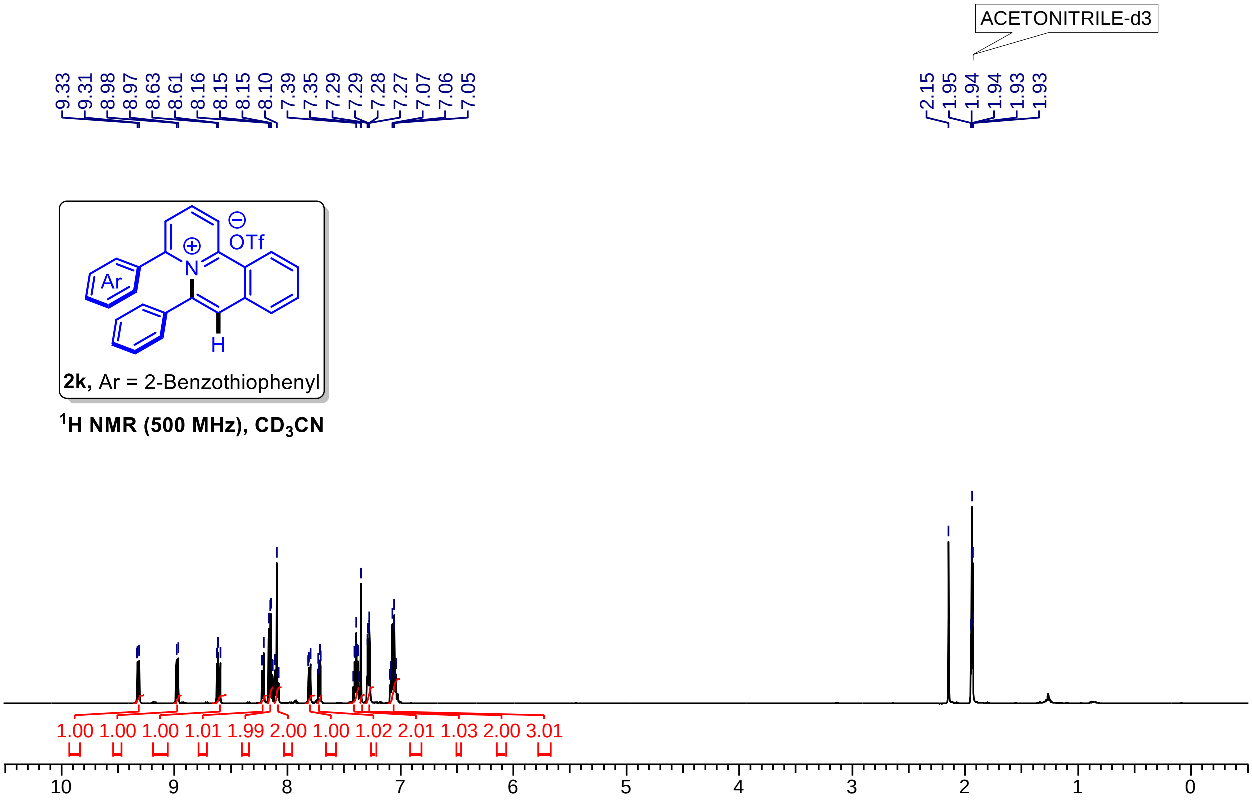

ACETONITRILE-d3
161.96
152.45
142.87
140.84
137.80
135.62
133.12
132.24
129.93
129.51
129.05
128.87
126.57
126.45
123.35
118.39
107.77
103.31
56.42
1.89
1.72
1.56
1.39
1.06
MeO
MeO
OTf
N
H
2h
^{13}C NMR (125 MHz), CD$_3$CN
200
180
160
140
120
100
80
60
40
20
0

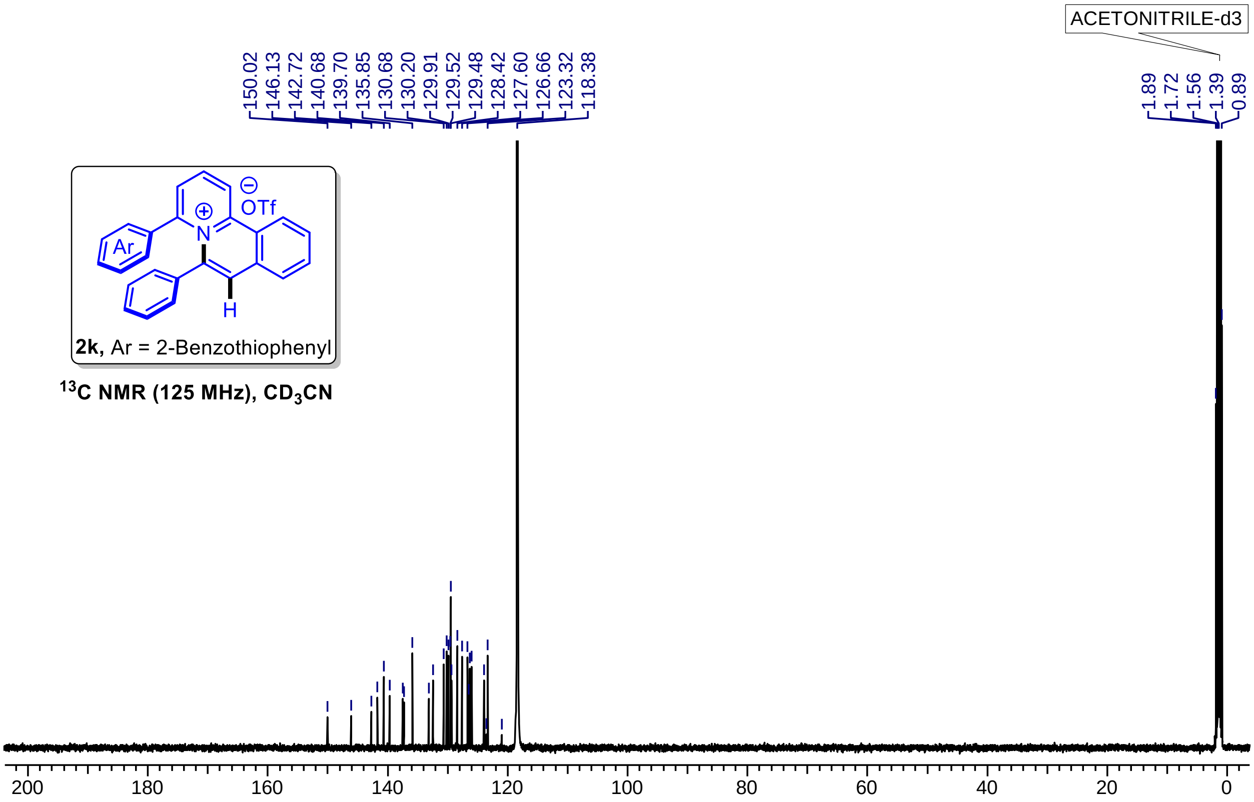

ACETONITRILE-d3
9.62
9.60
9.14
8.77
8.48
8.24
8.17
8.17
8.16
8.15
8.02
8.00
7.75
7.52
7.50
7.40
7.22
7.20
6.39
6.37
6.35
6.25
6.23
2.16
1.94
1.94
1.94
Ar
OTf
N
H
2i, Ar = 9-Anthracenyl
^{1}H NMR (500 MHz), CD$_3$CN
1.00
1.01
1.00
1.00
1.01
3.01
2.07
1.00
2.01
2.01
2.15
1.01
2.00
1.97
10
9
8
7
6
5
4
3
2
1
0

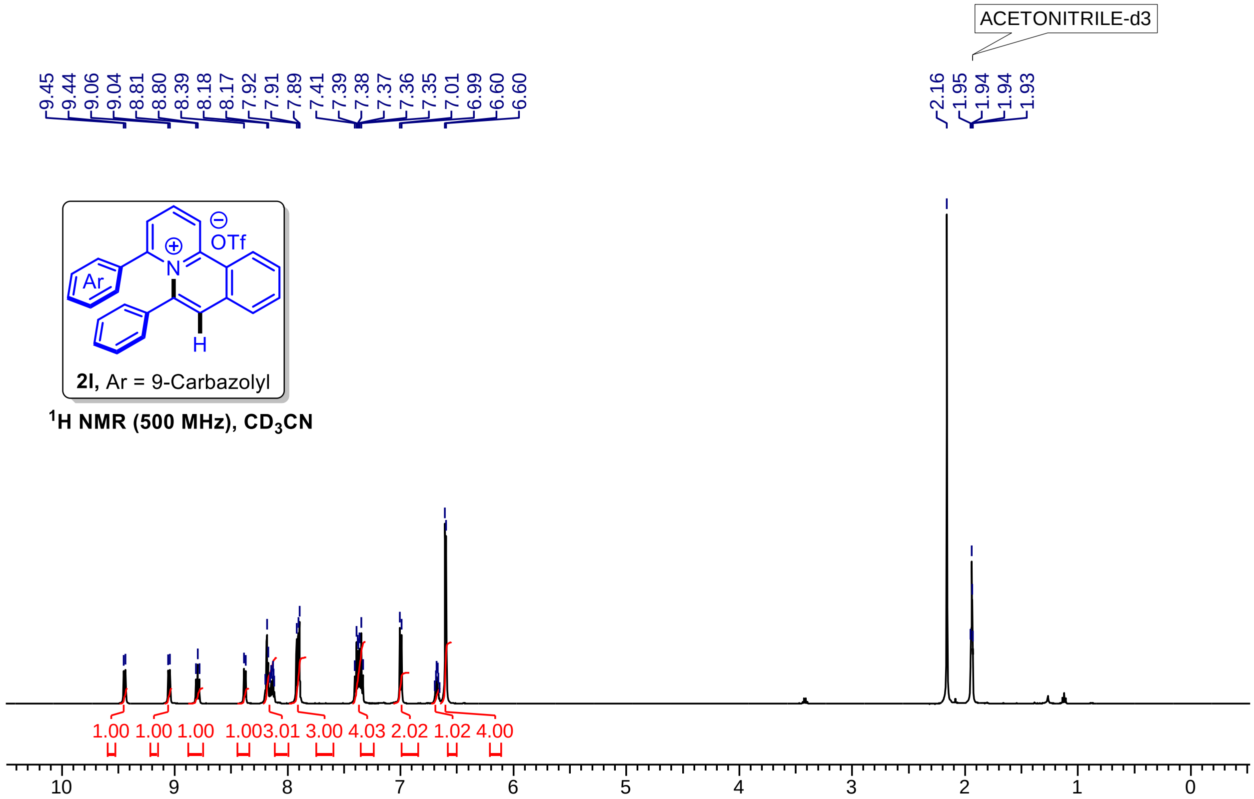

ACETONITRILE-d3
149.27
148.64
141.86
140.51
133.29
132.67
130.13
129.71
129.38
129.09
127.90
127.41
126.77
124.73
118.32
1.67
1.56
1.44
1.32
0.97
Ar
OTf
N
H
2i, Ar = 9-Anthracenyl
^{13}C NMR (175 MHz), CD$_3$CN
200
180
160
140
120
100
80
60
40
20
0


ACETONITRILE-d3
9.49 9.48 9.08 9.07 8.71 8.69 8.69 8.17 8.16 8.16 8.15 7.89 7.81 7.79 7.69 7.65 7.48 7.41 6.89 6.65 6.57 6.54
2.14
1.94
OTf
N
Ar
H
2j, Ar = 9-Phenanthrenyl
^{1}H NMR (500 MHz), CD$_3$CN
1.00 1.00 1.01 2.00 1.00 3.00 1.00 2.01 3.01 1.00 1.00 1.00 1.00 2.01 1.01
10
9
8
7
6
5
4
3
2
1
0


ACETONITRILE-d3
150.84 149.25 142.63 140.66 135.72 131.43 129.86 129.46 128.75 128.48 128.33 126.70 125.84 124.39 123.63 118.38
1.89 1.72 1.56 1.39 1.22
OTf
N
Ar
H
2j, Ar = 9-Phenanthenyl
^{13}C NMR (125 MHz), CD$_3$CN
200
180
160
140
120
100
80
60
40
20
0

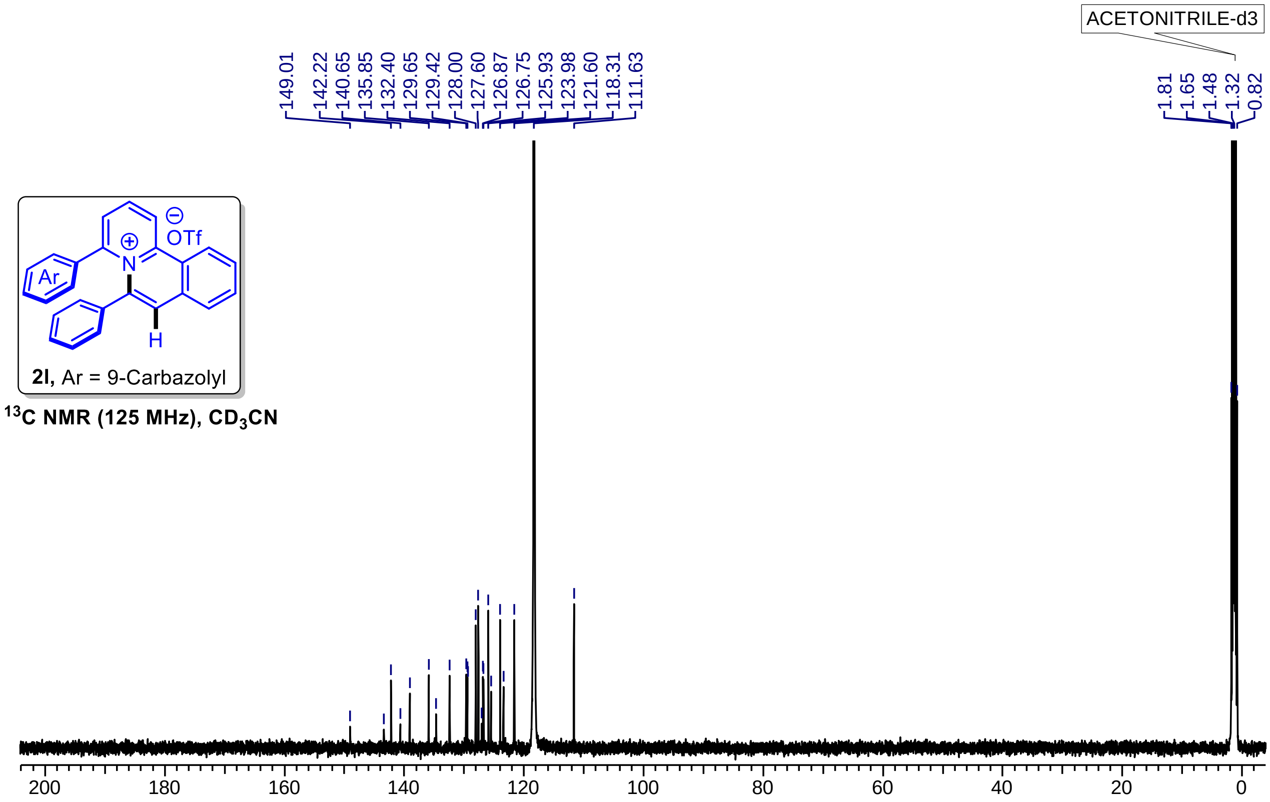

ACETONITRILE-d3
9.33
9.31
8.98
8.97
8.63
8.61
8.16
8.15
8.15
8.10
7.39
7.35
7.29
7.29
7.28
7.27
7.07
7.06
7.05
2.15
1.95
1.94
1.94
1.93
1.93
OTf
Ar
N
H
2k, Ar = 2-Benzothiophenyl
^{1}H NMR (500 MHz), CD$_3$CN
1.00
1.00
1.00
1.01
1.99
2.00
1.00
1.02
2.01
1.03
2.00
3.01
10
9
8
7
6
5
4
3
2
1
0


ACETONITRILE-d3
150.02
146.13
142.72
140.68
139.70
135.85
130.68
130.20
129.91
129.52
129.48
128.42
127.60
126.66
123.32
118.38
1.89
1.72
1.56
1.39
0.89
OTf
Ar
N
H
2k, Ar = 2-Benzothiophenyl
^{13}C NMR (125 MHz), CD$_3$CN
200
180
160
140
120
100
80
60
40
20
0



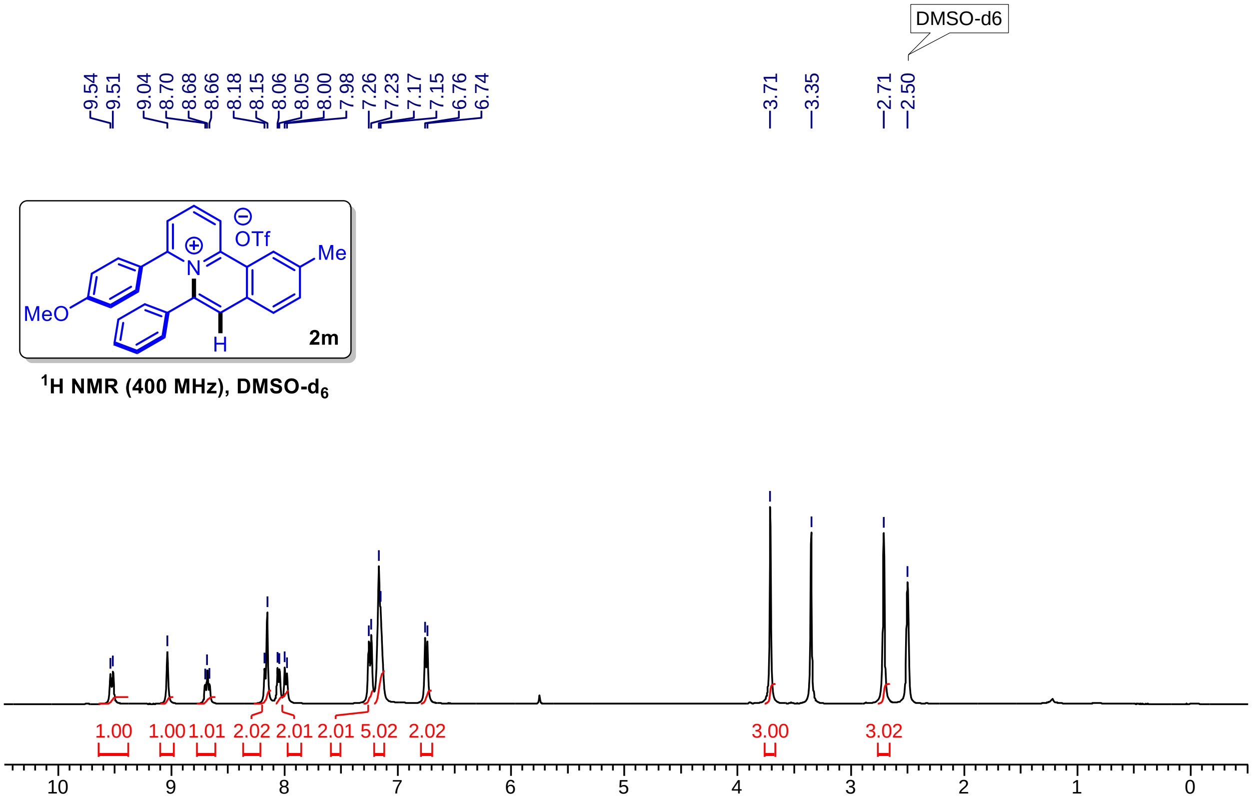
2l, Ar = 9-Carbazolyl

^{1}H NMR (500 MHz), CD$_3$CN

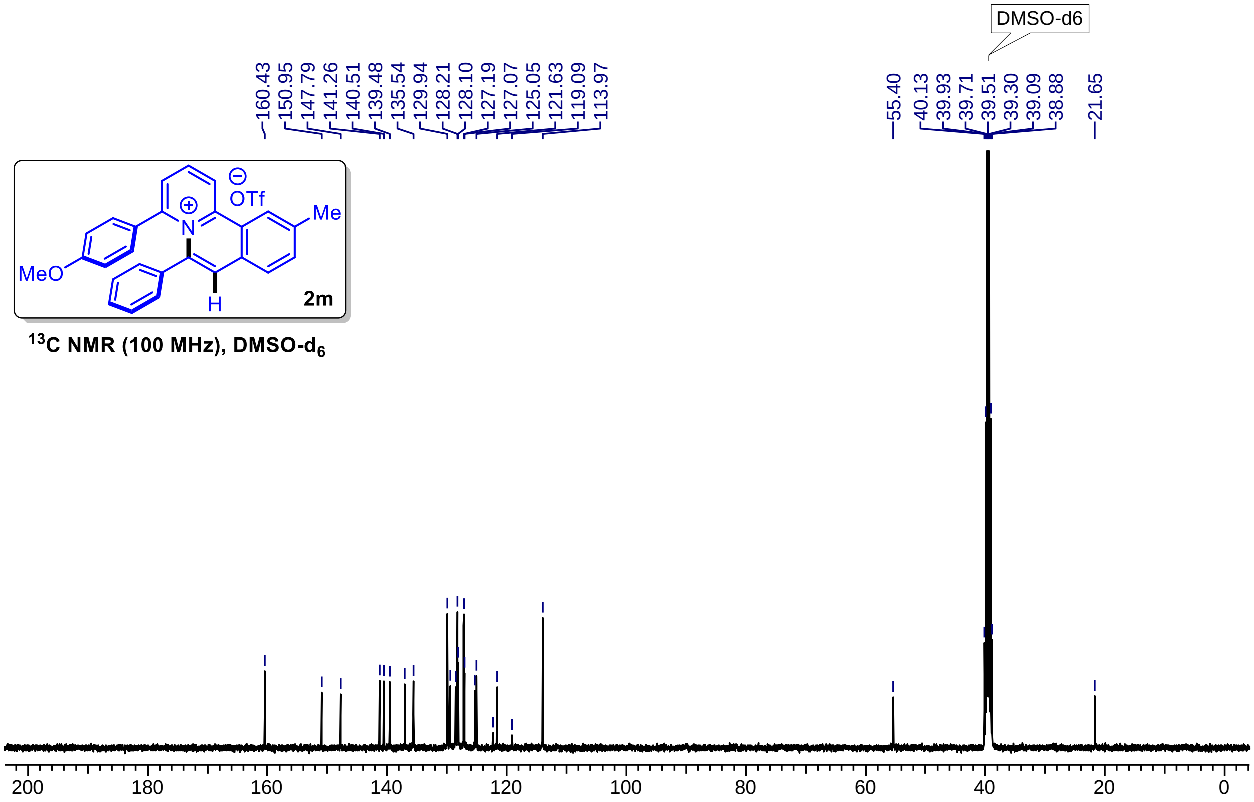


2l, Ar = 9-Carbazolyl

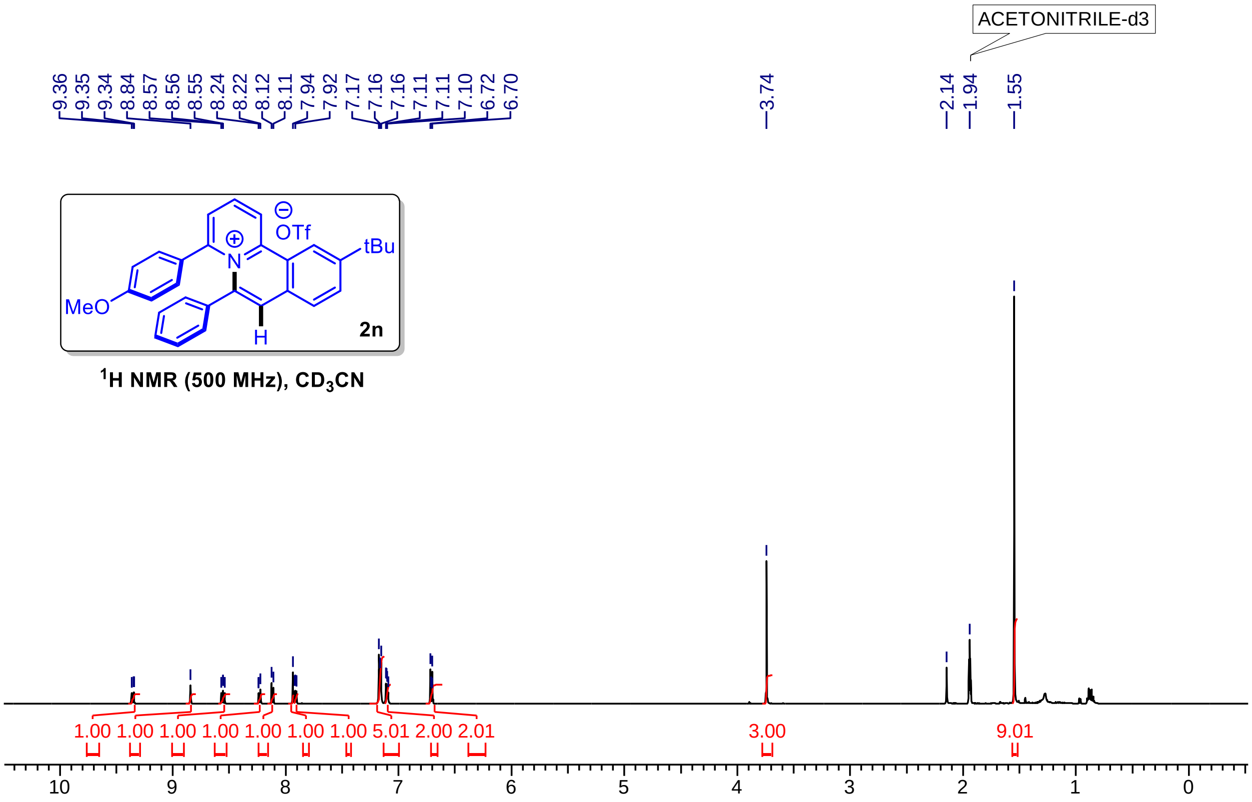
^{13}C NMR (125 MHz), CD$_3$CN



^{1}H NMR (400 MHz), DMSO-d$_6$

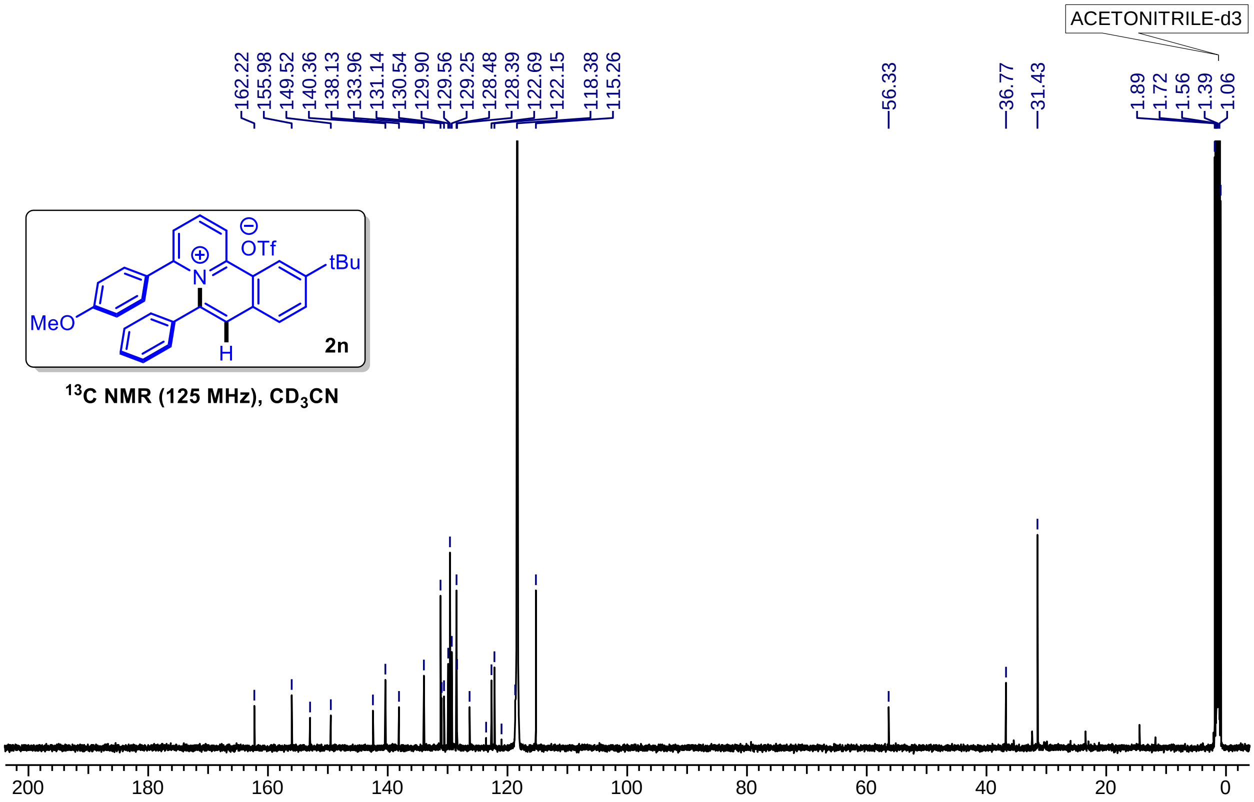


^{13}C NMR (100 MHz), DMSO-d$_6$



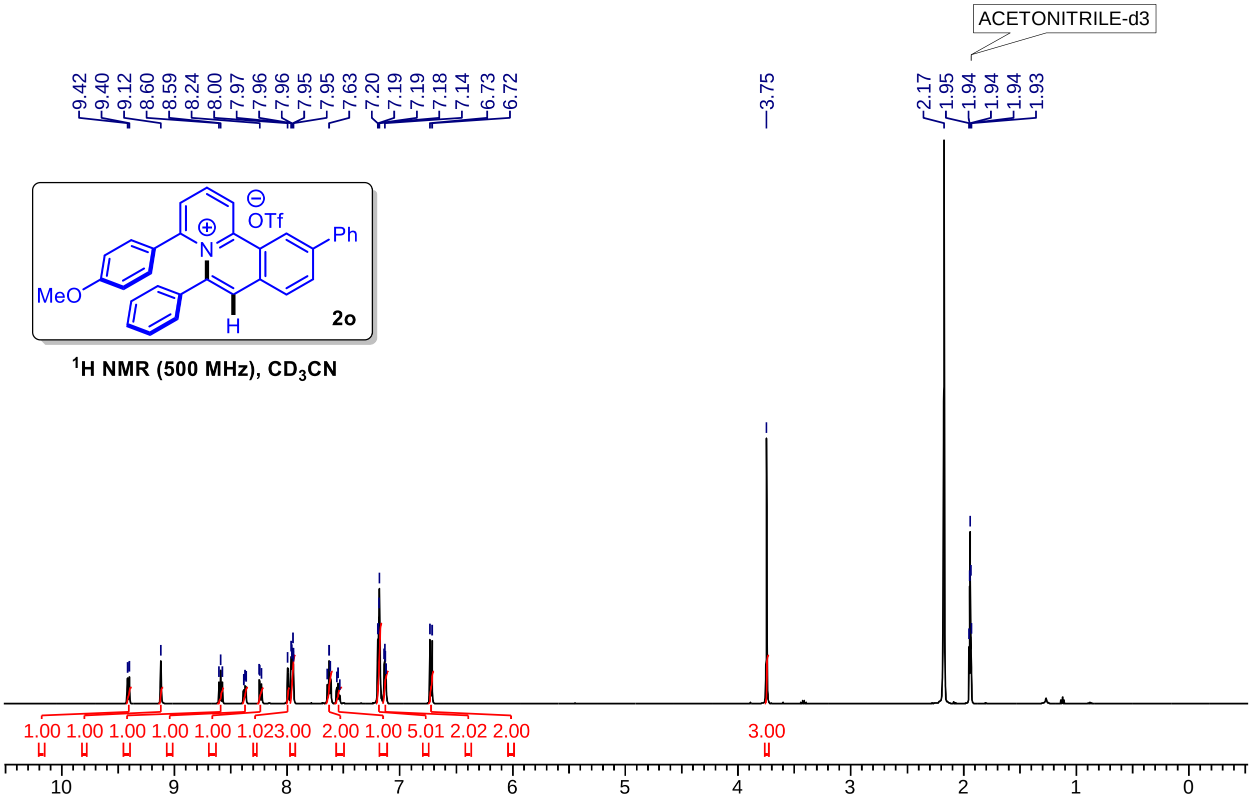
2n

^{1}H NMR (500 MHz), CD$_3$CN

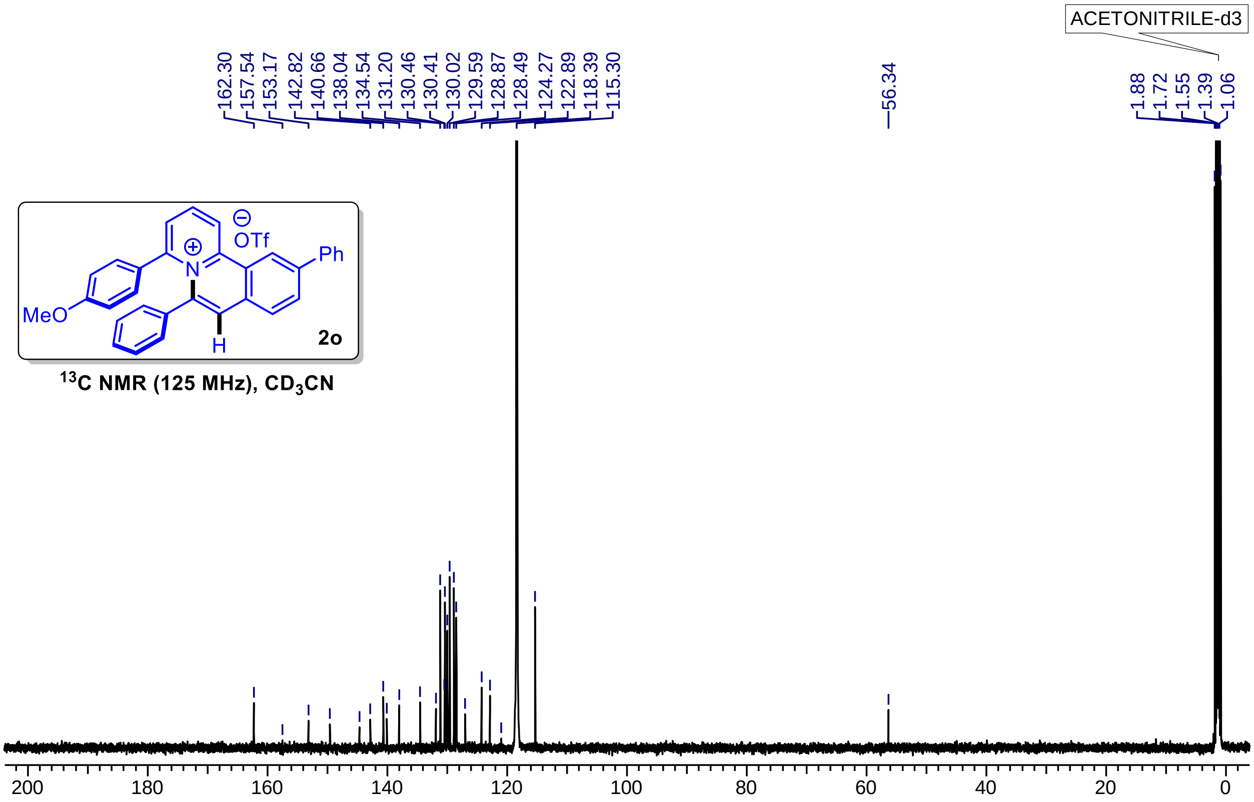


2n

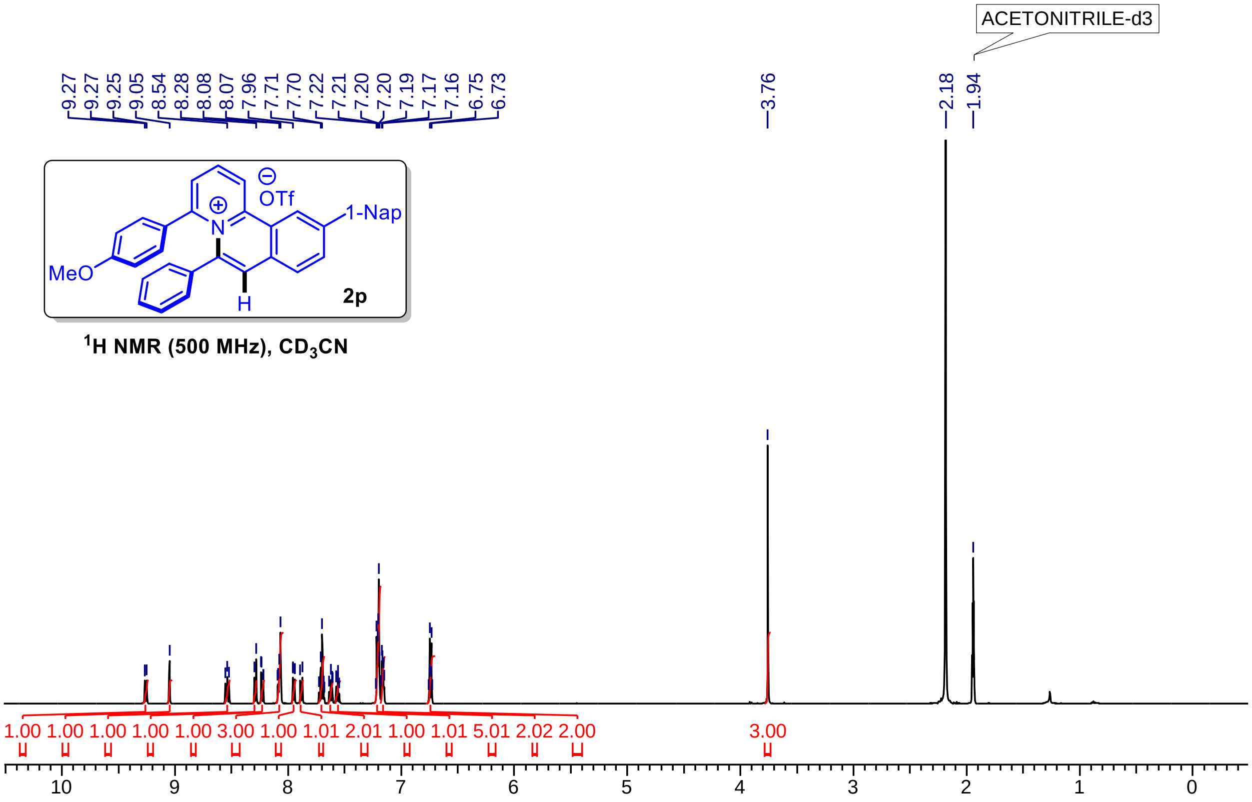
^{13}C NMR (125 MHz), CD$_3$CN



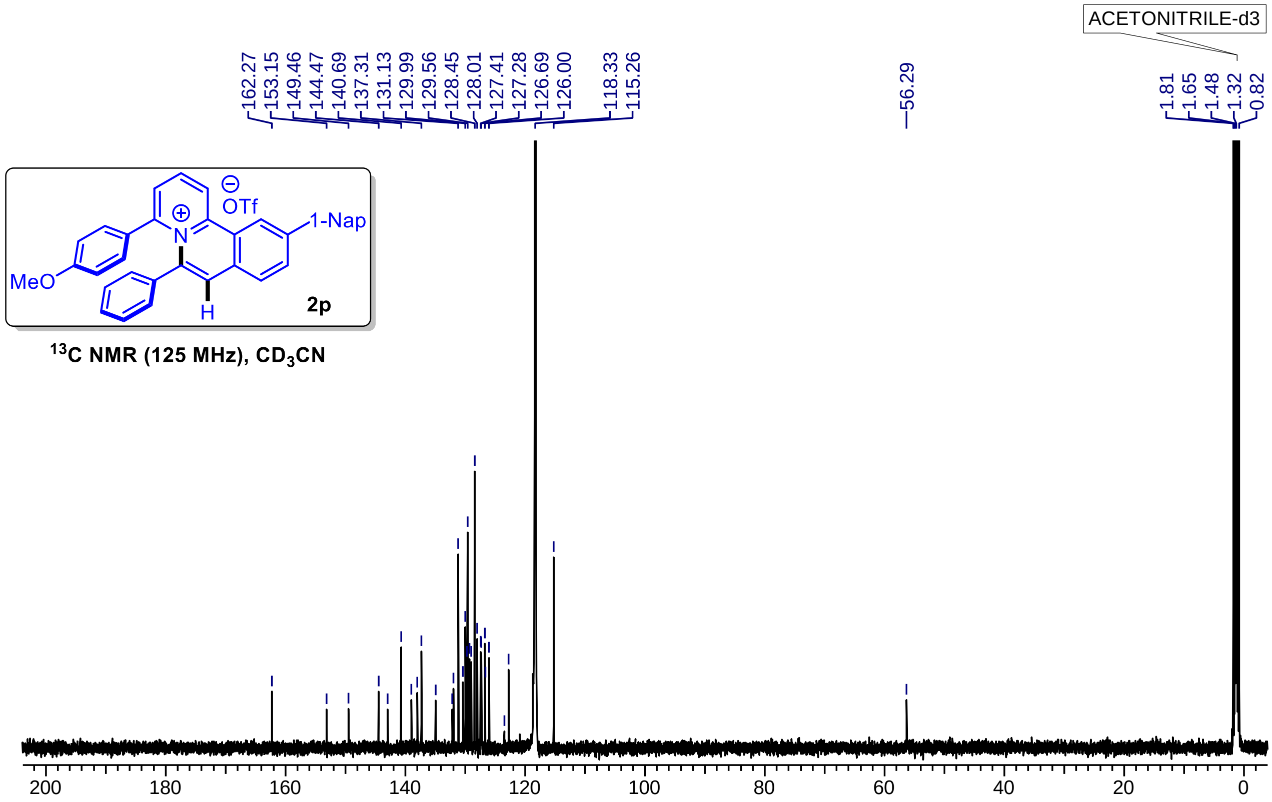
^{1}H NMR (500 MHz), CD_3CN



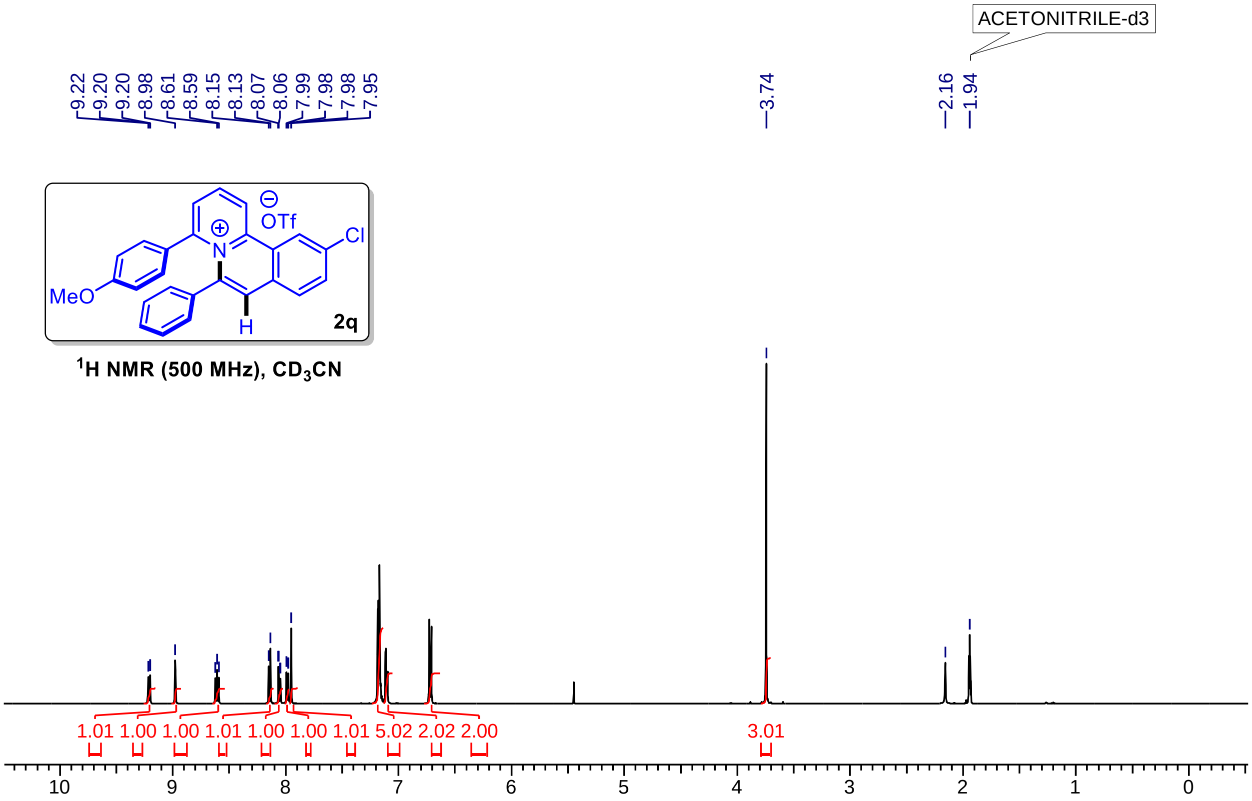
^{13}C NMR (125 MHz), CD_3CN

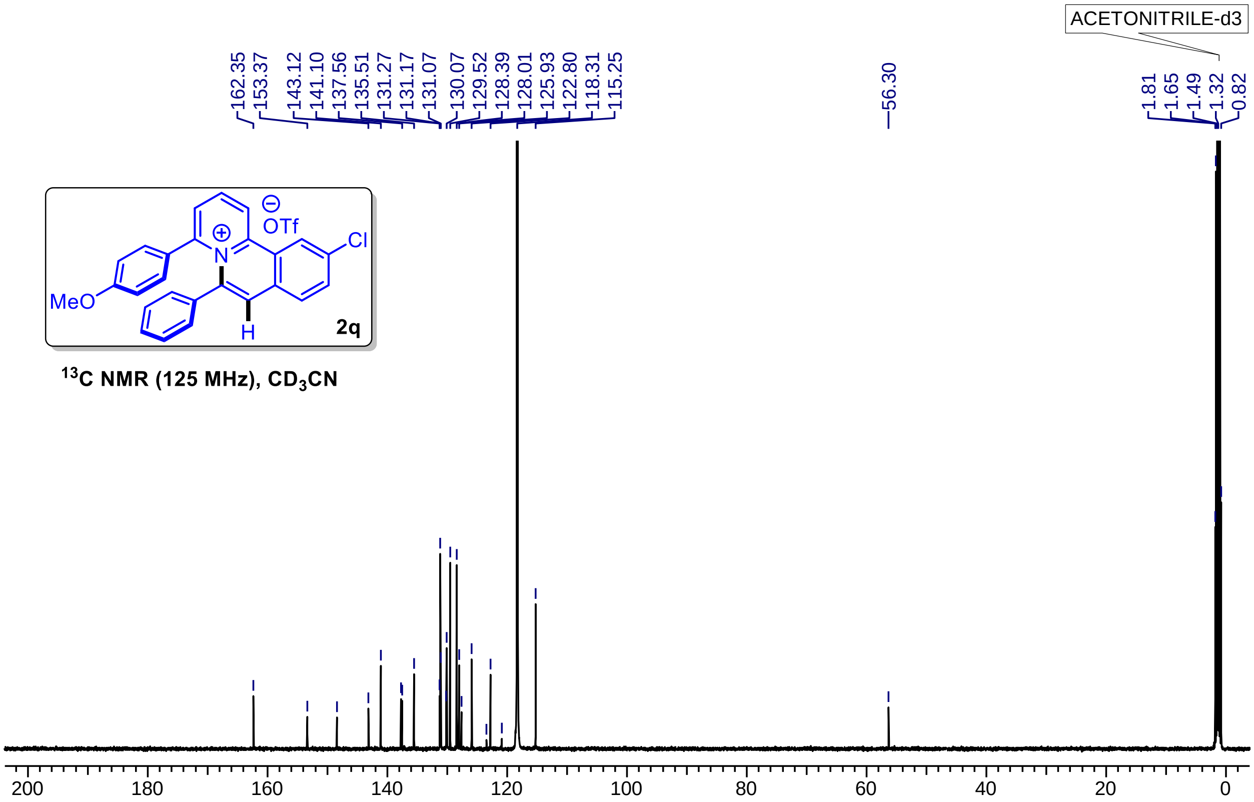


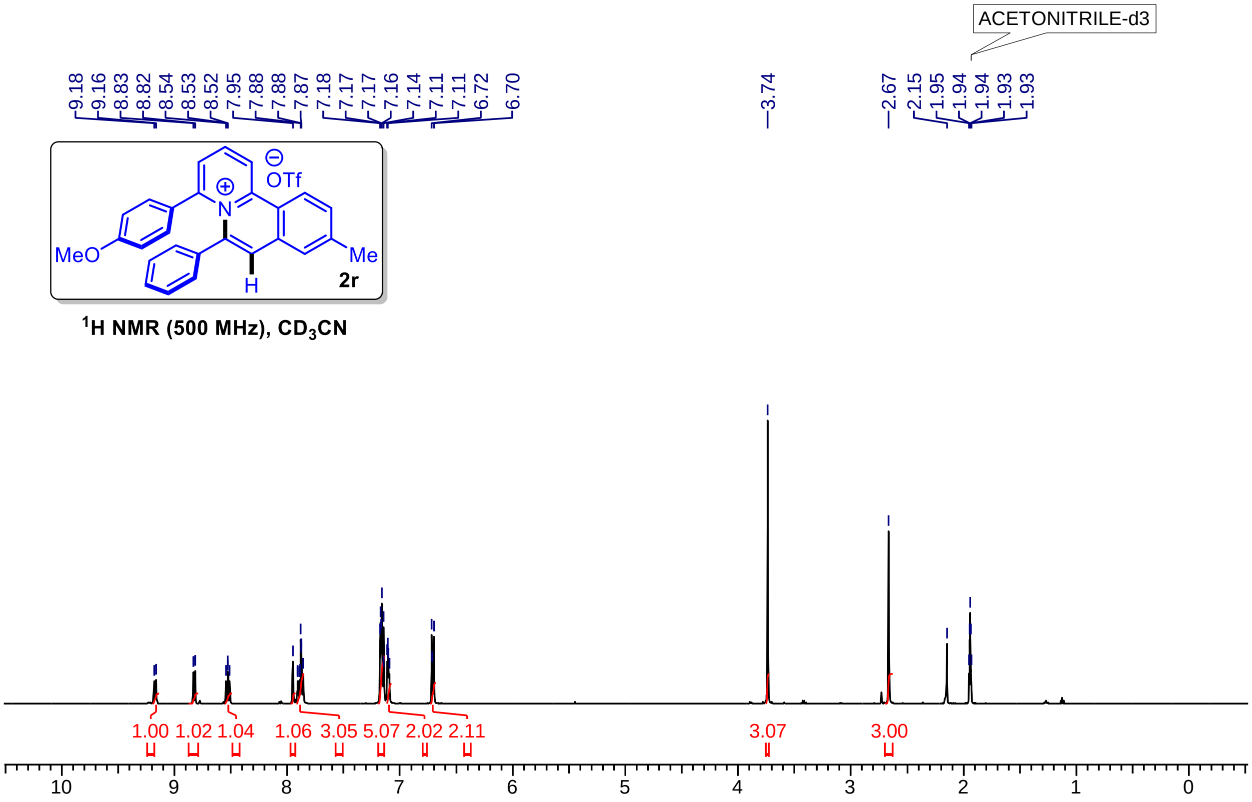
^{1}H NMR (500 MHz), CD$_3$CN

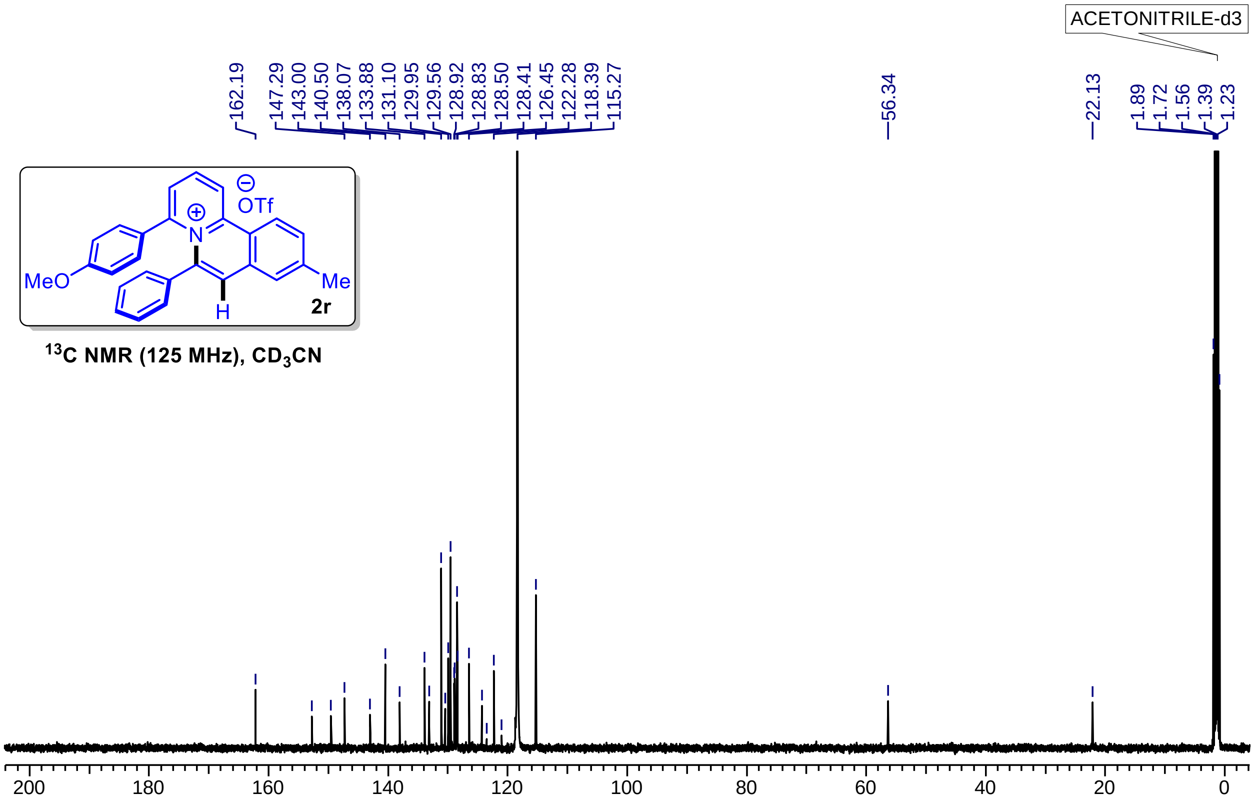


^{13}C NMR (125 MHz), CD$_3$CN


ACETONITRILE-d3
9.22
9.20
9.20
8.98
8.61
8.59
8.15
8.13
8.07
8.06
7.99
7.98
7.98
7.95
3.74
2.16
1.94
OTf
Cl
MeO
N
H
2q
1H NMR (500 MHz), CD3CN
1.01
1.00
1.00
1.01
1.00
1.00
1.01
5.02
2.02
2.00
3.01
10
9
8
7
6
5
4
3
2
1
0


ACETONITRILE-d3
162.35
153.37
143.12
141.10
137.56
135.51
131.27
131.17
131.07
130.07
129.52
128.39
128.01
125.93
122.80
118.31
115.25
56.30
1.81
1.65
1.49
1.32
0.82
OTf
Cl
MeO
N
H
2q
13C NMR (125 MHz), CD3CN
200
180
160
140
120
100
80
60
40
20
0


ACETONITRILE-d3
9.18
9.16
8.83
8.82
8.54
8.53
8.52
7.95
7.88
7.88
7.87
7.18
7.17
7.17
7.16
7.14
7.11
7.11
6.72
6.70
3.74
2.67
2.15
1.95
1.94
1.94
1.93
1.93
OTf
N
MeO
Me
H
2r
^{1}H NMR (500 MHz), CD$_3$CN
1.00
1.02
1.04
1.06
3.05
5.07
2.02
2.11
3.07
3.00
10
9
8
7
6
5
4
3
2
1
0


ACETONITRILE-d3
162.19
147.29
143.00
140.50
138.07
133.88
131.10
129.95
129.56
128.92
128.83
128.50
128.41
126.45
122.28
118.39
115.27
56.34
22.13
1.89
1.72
1.56
1.39
1.23
OTf
N
MeO
Me
H
2r
^{13}C NMR (125 MHz), CD$_3$CN
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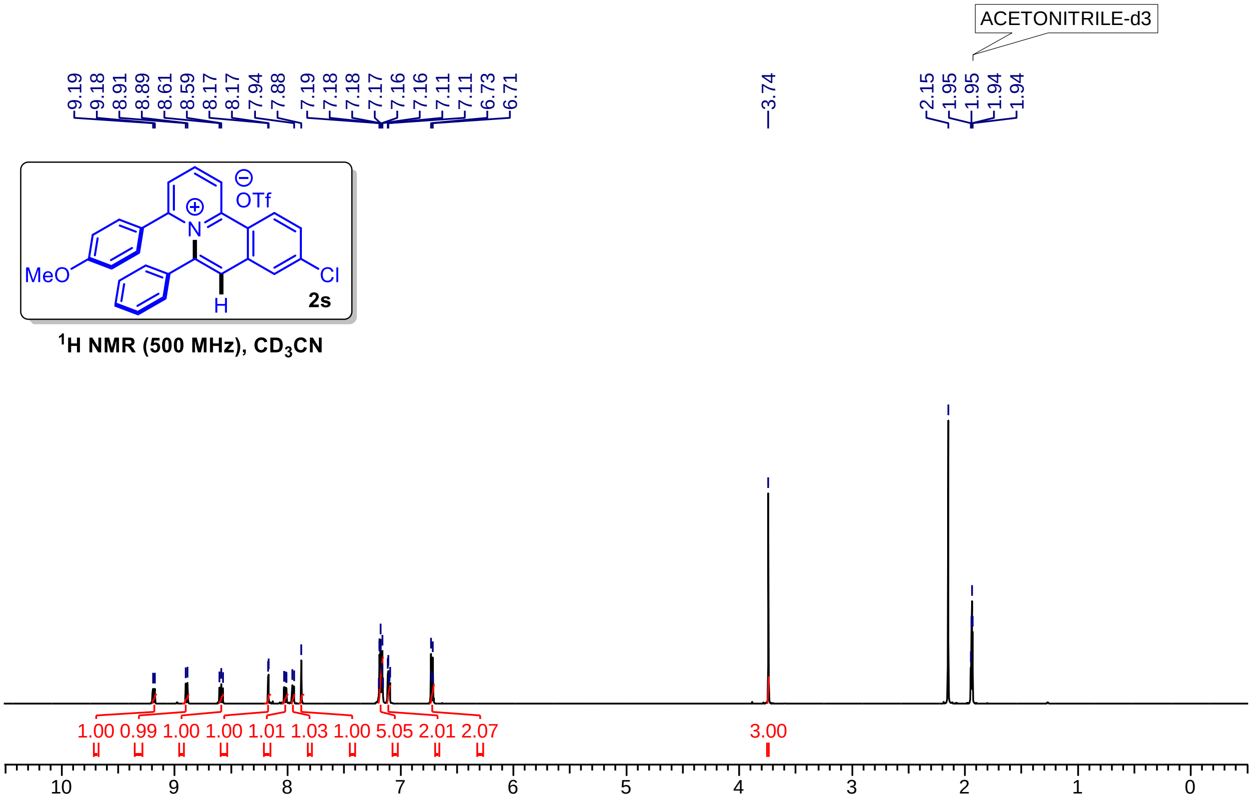
180
160
140
120
100
80
60
40
20
0



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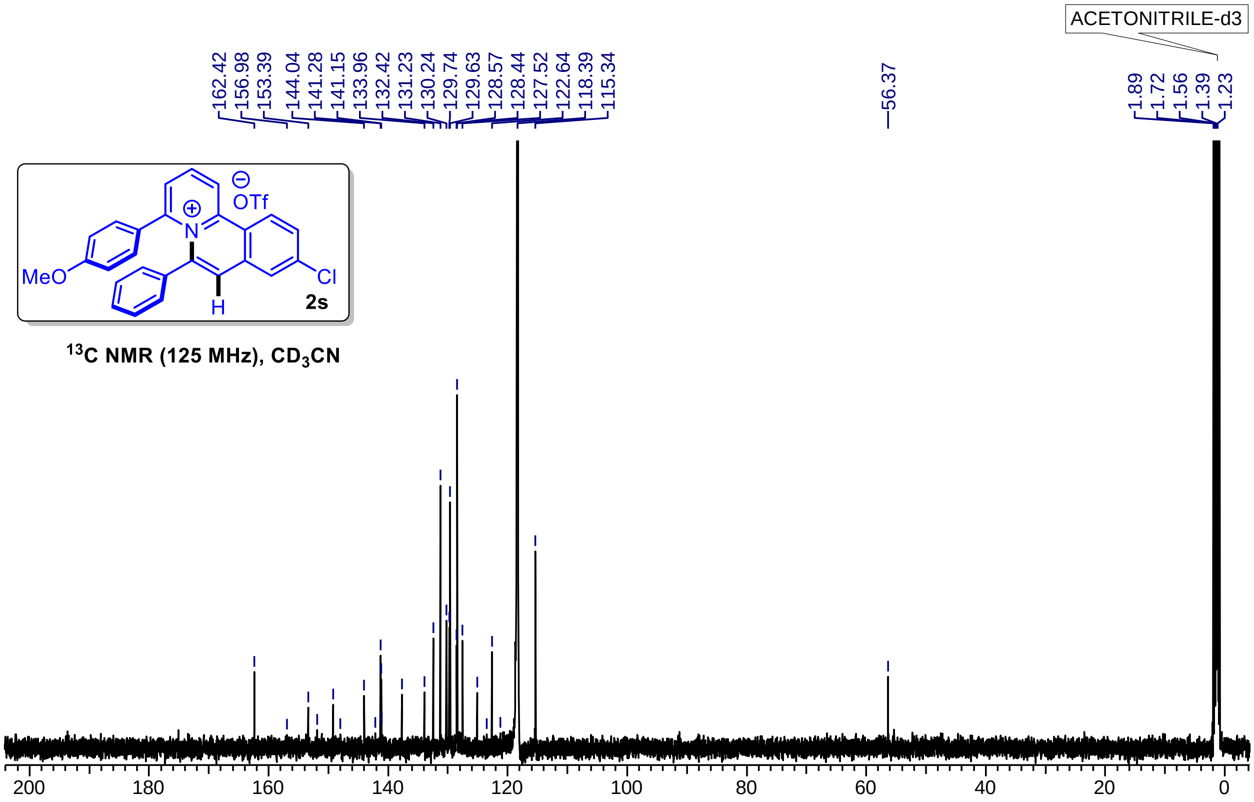

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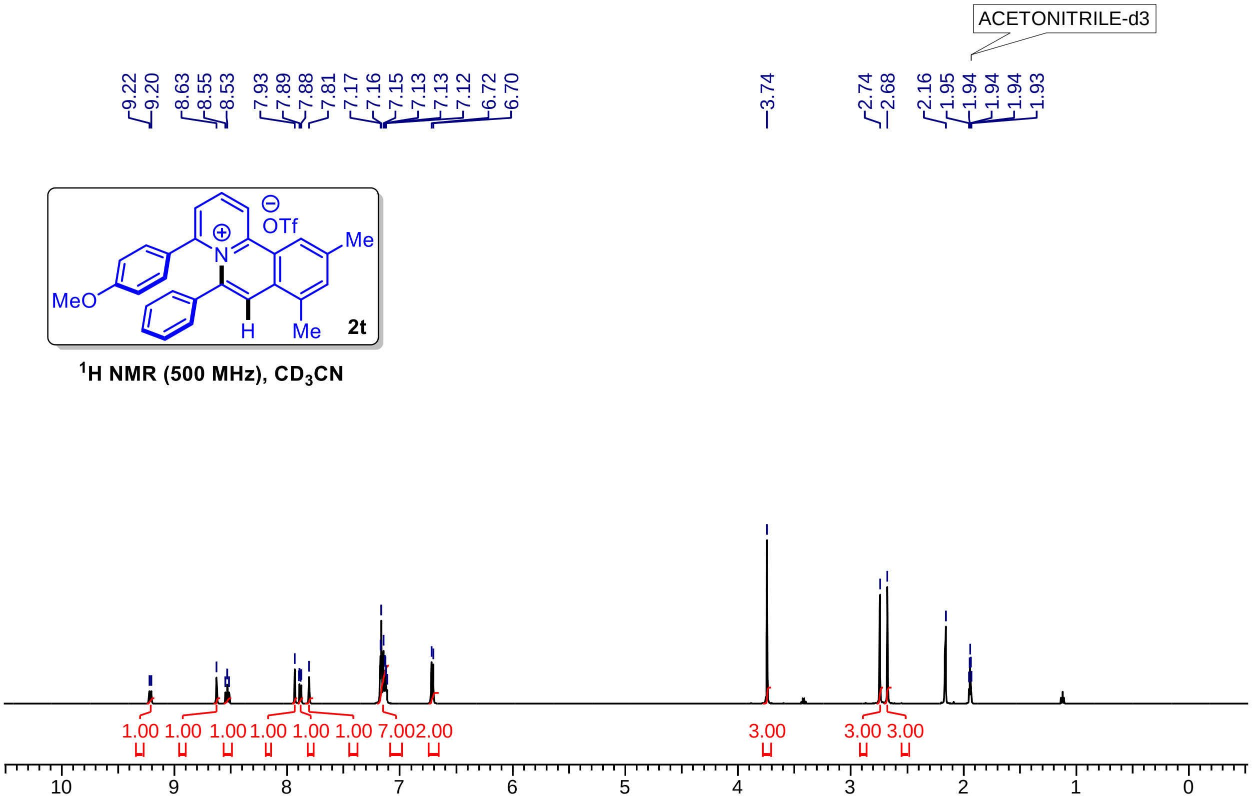

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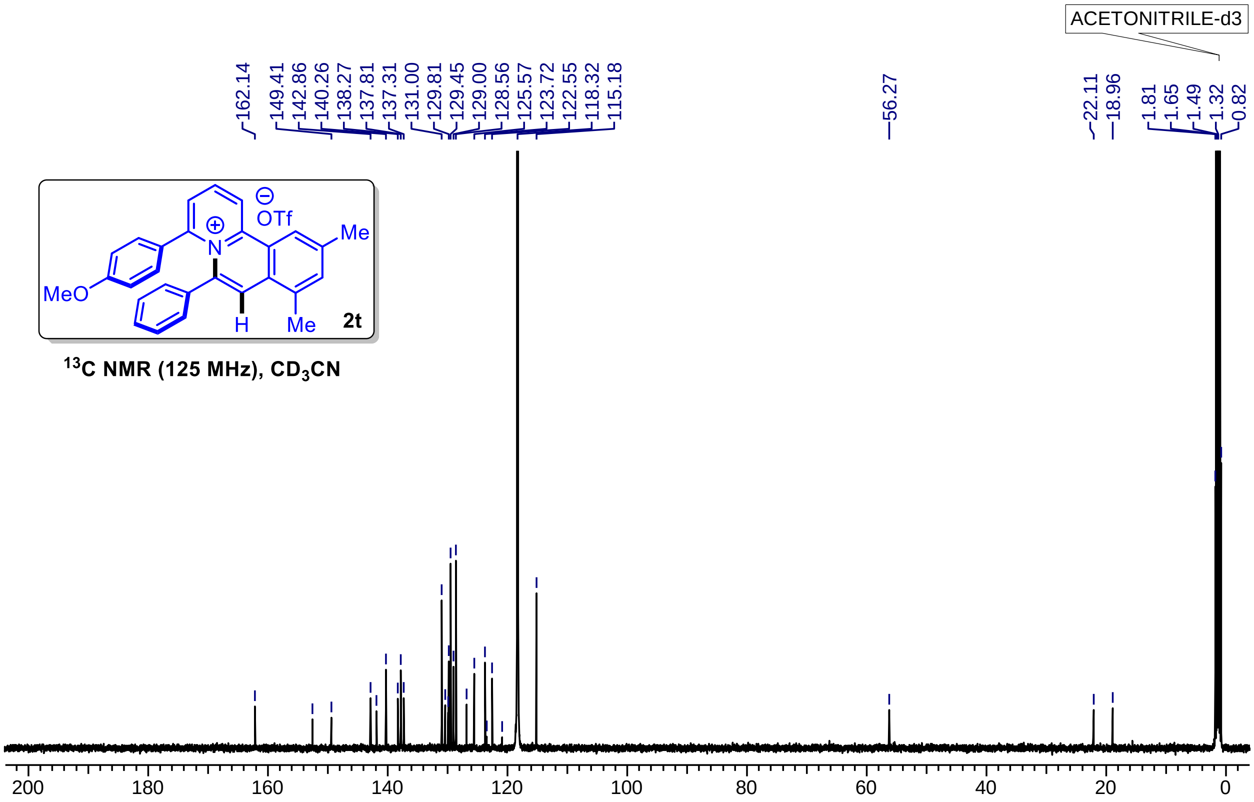

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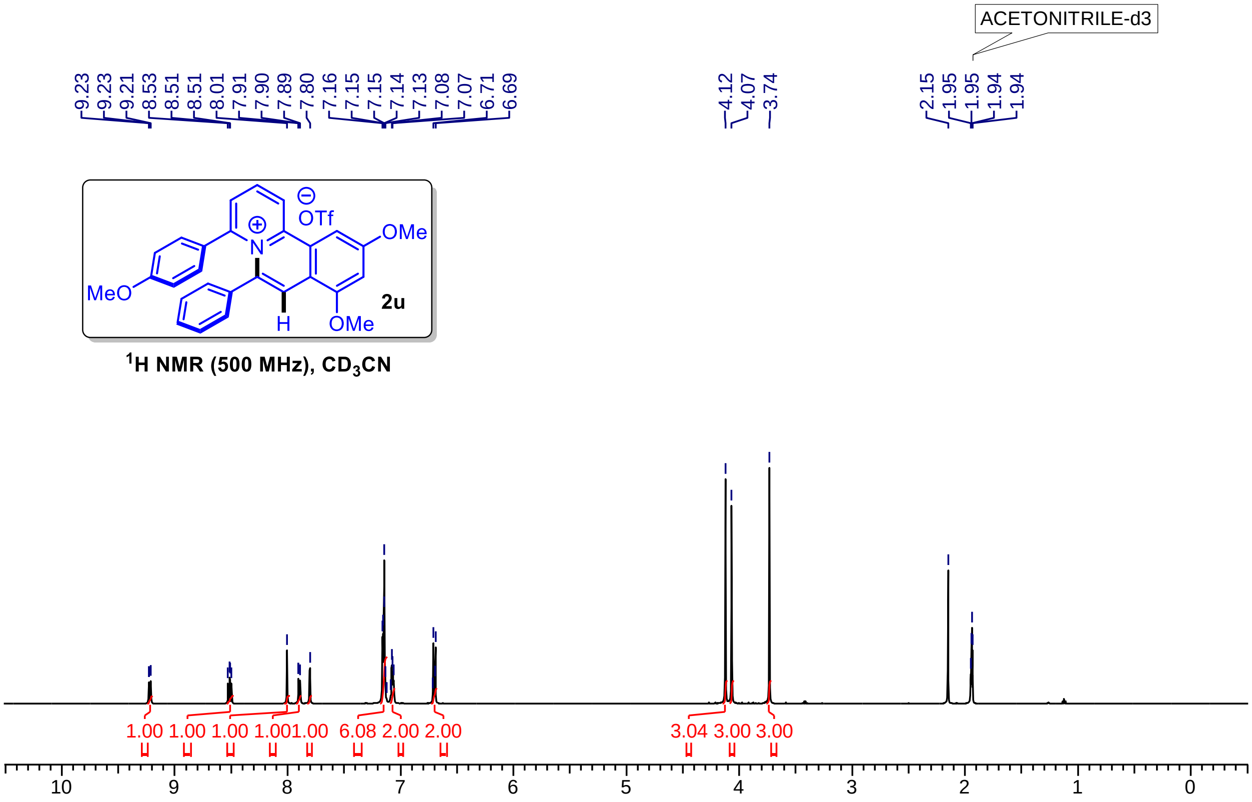

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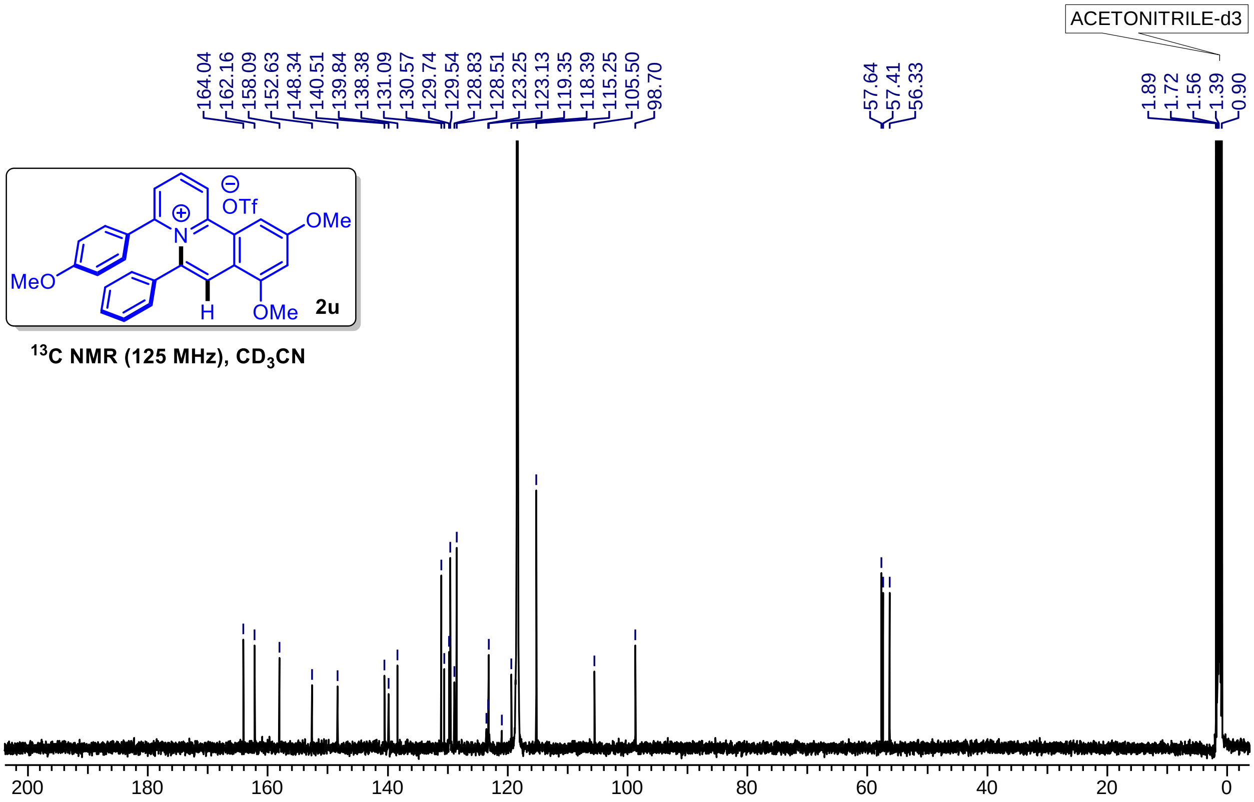

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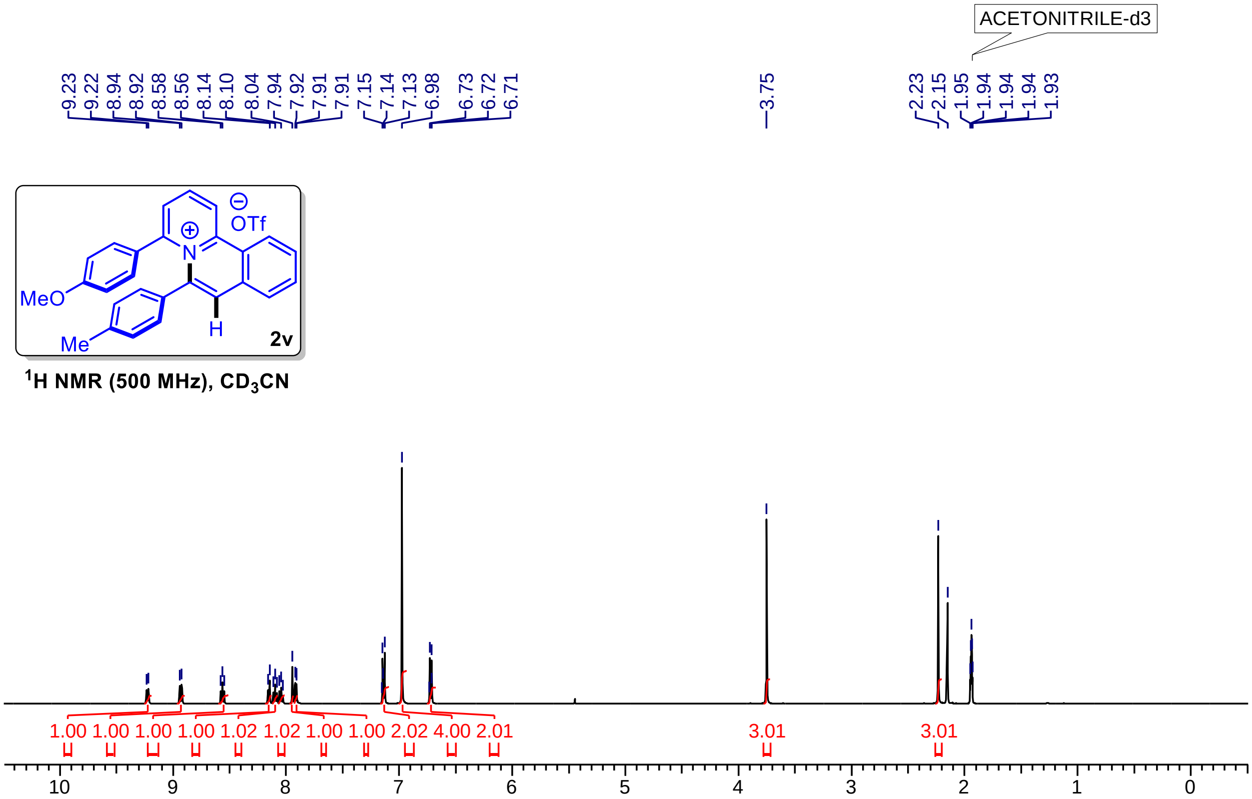

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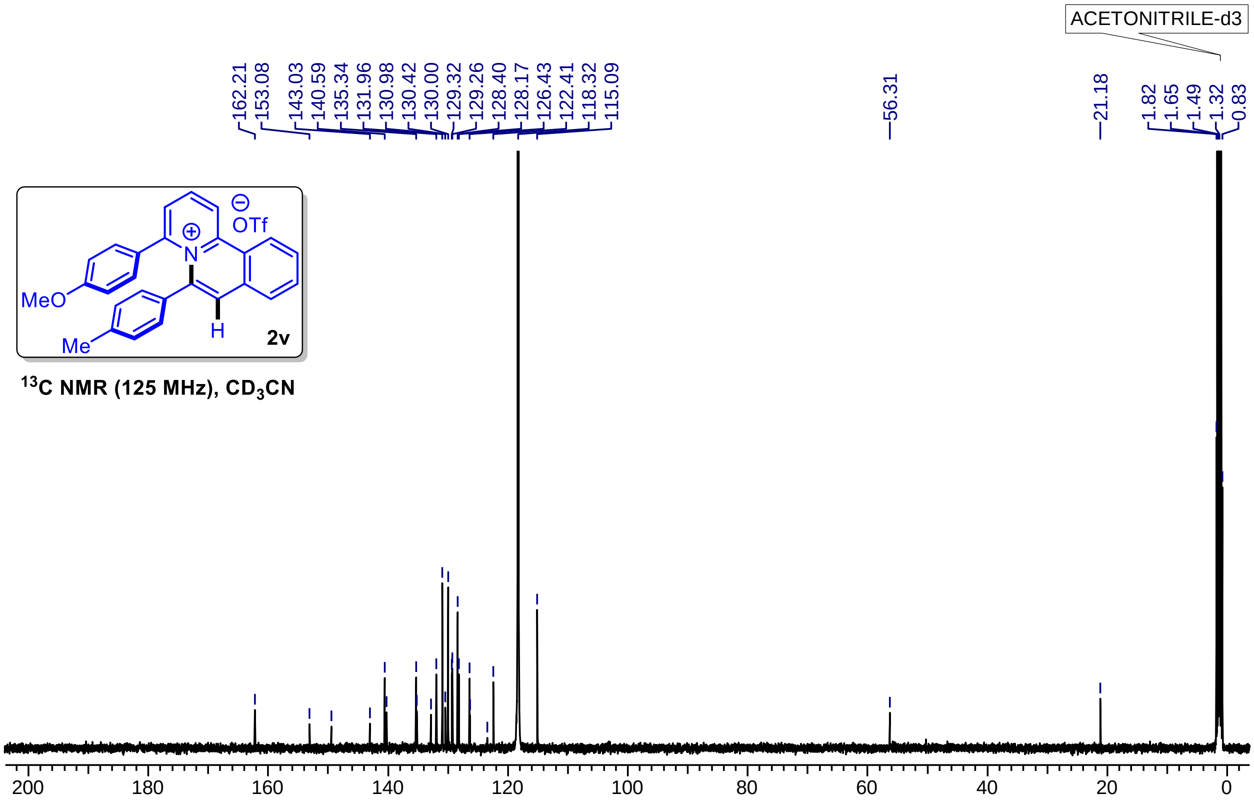

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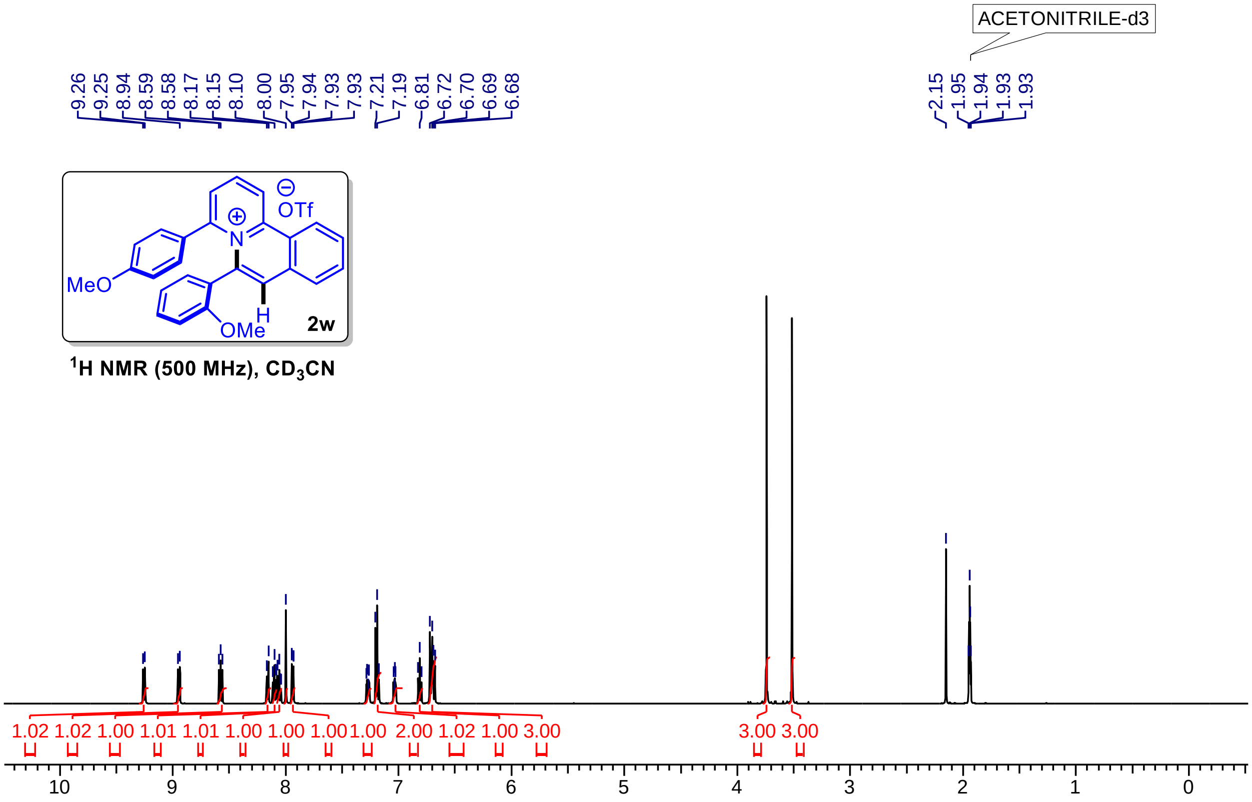
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8.94
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8.17
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7.93
7.93
7.21
7.19
6.81
6.72
6.70
6.69
6.68
2.15
1.95
1.94
1.93
1.93
OTf
N
MeO
H
OMe
2w
^{1}H NMR (500 MHz), CD$_3$CN
1.02
1.02
1.00
1.01
1.01
1.00
1.00
1.00
1.00
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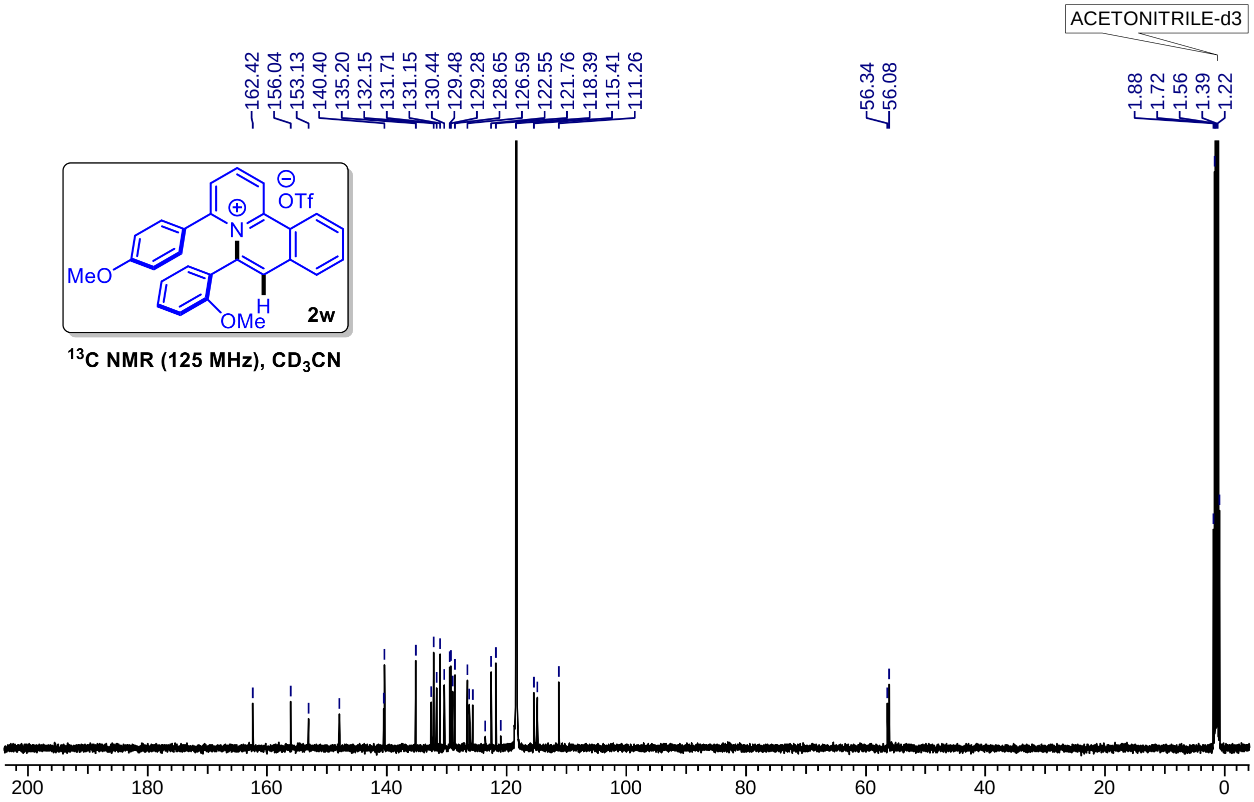
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126.59
122.55
121.76
118.39
115.41
111.26
56.34
56.08
1.88
1.72
1.56
1.39
1.22
OTf
N
MeO
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^{13}C NMR (125 MHz), CD$_3$CN
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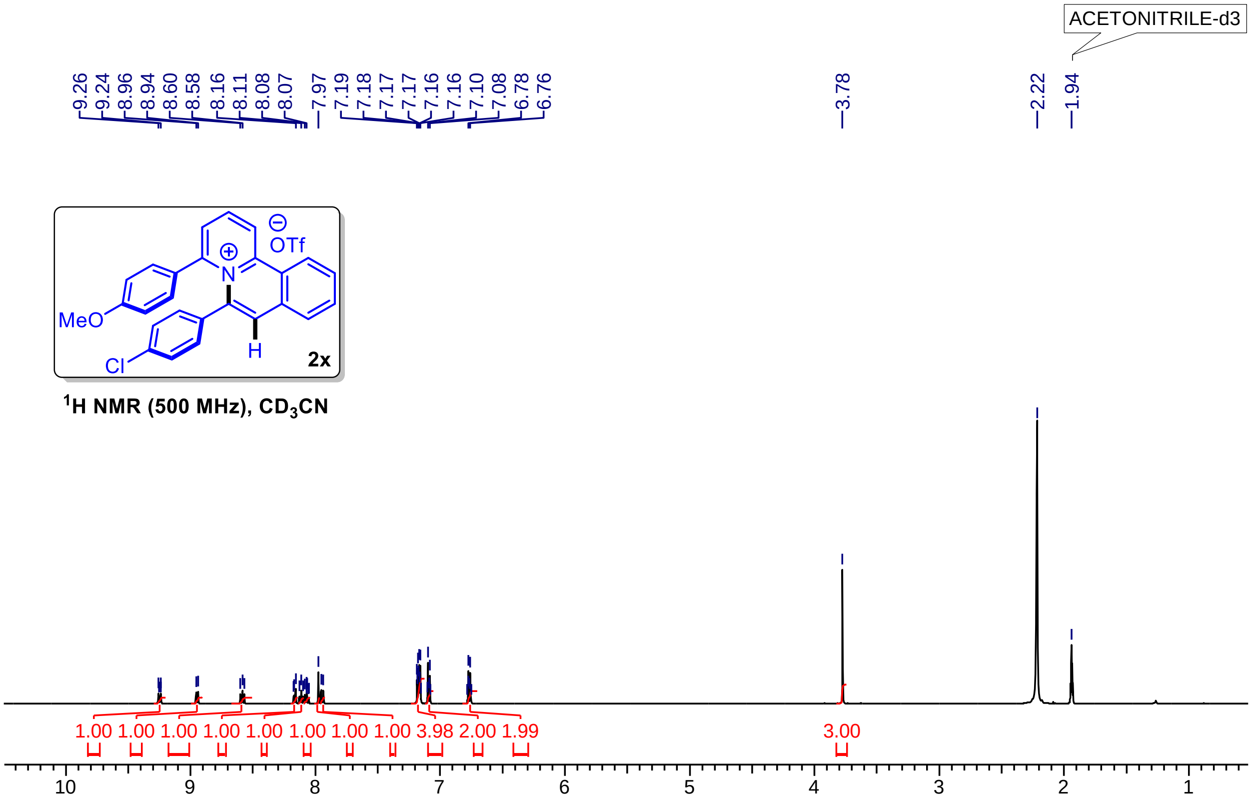
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3.78
2.22 1.94
OTf
N
MeO
H
Cl
2x
^{1}H NMR (500 MHz), CD$_3$CN
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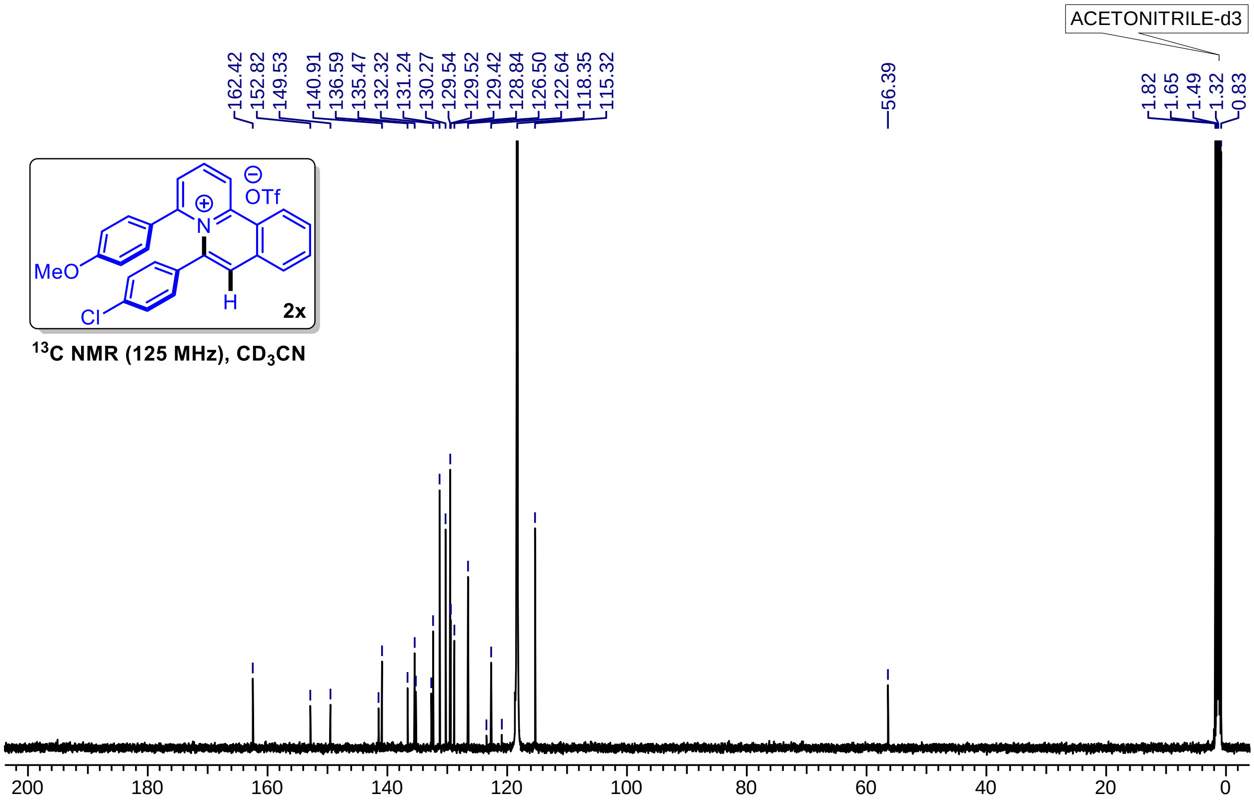
3.00
10 9 8 7 6 5 4 3 2 1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56.39
1.82 1.65 1.49 1.32 0.83
OTf
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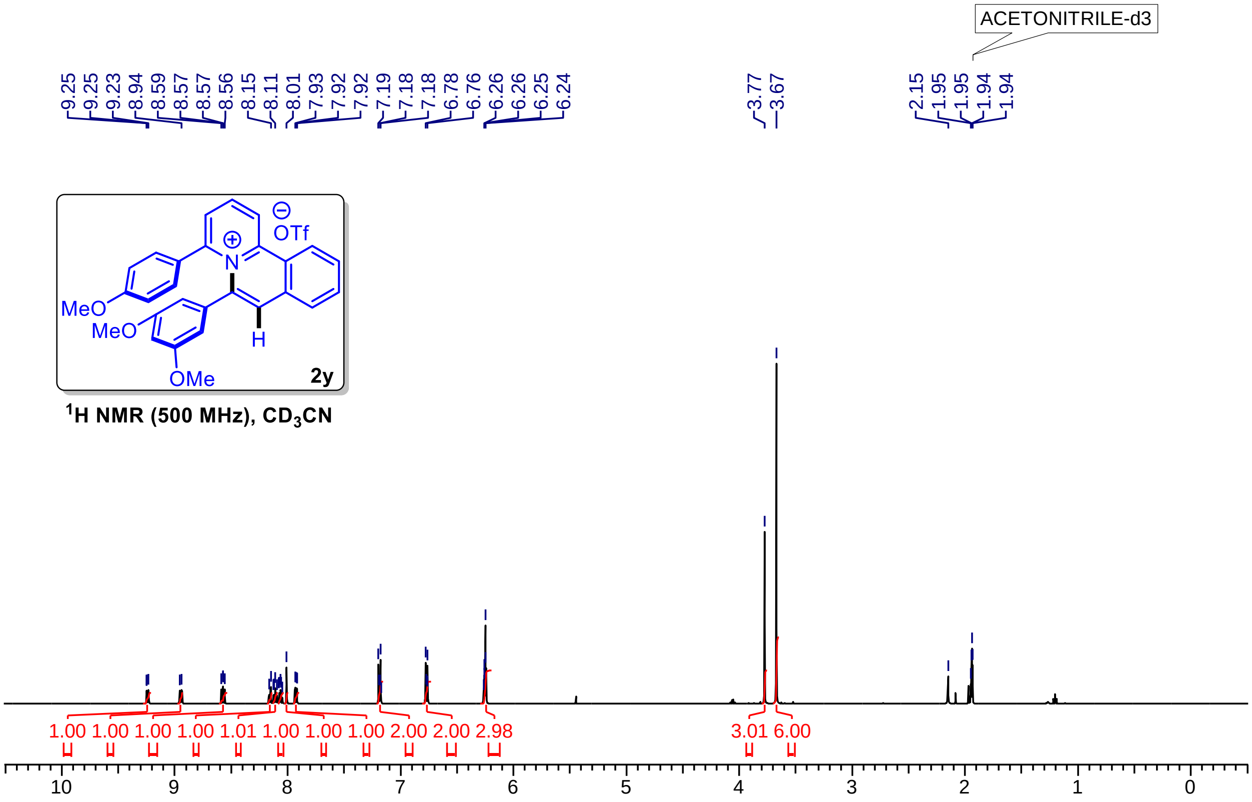
H
Cl
2x
^{13}C NMR (125 MHz), CD$_3$CN
200 180 160 140 120 100 80 60 40 20 0



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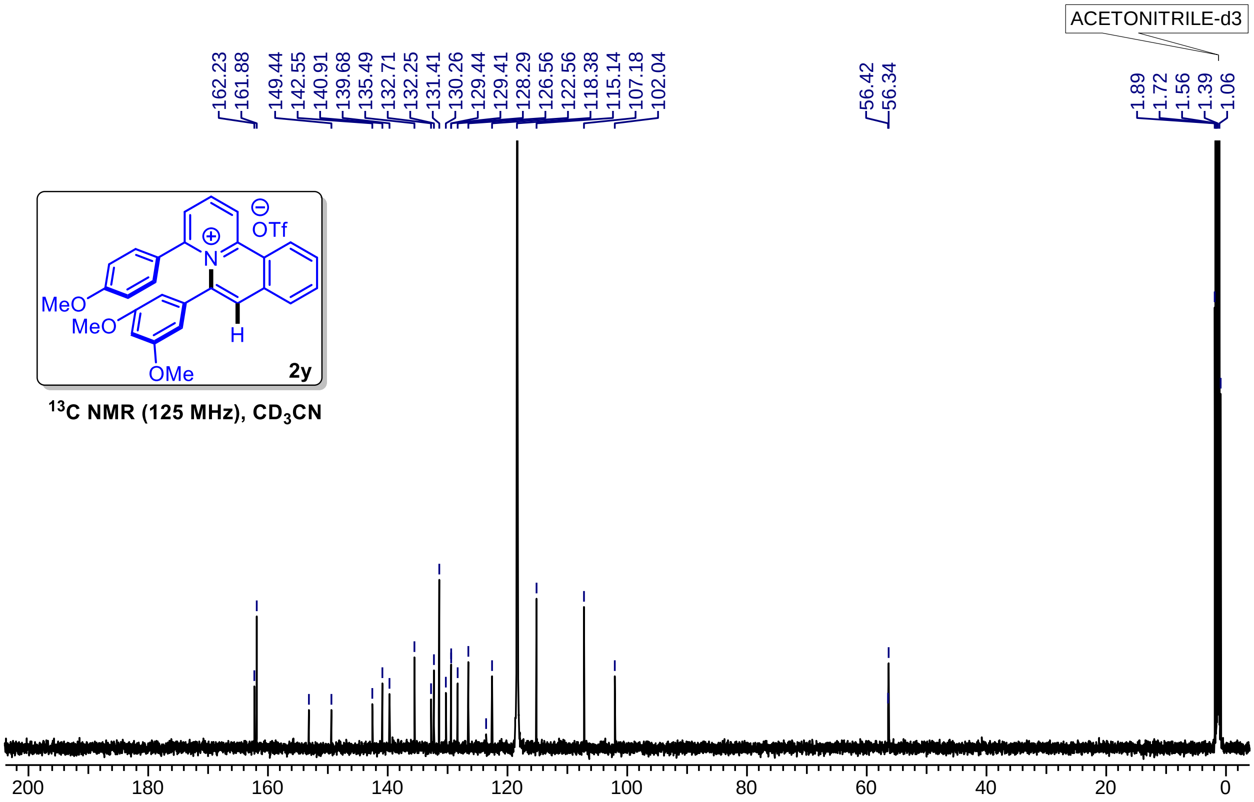

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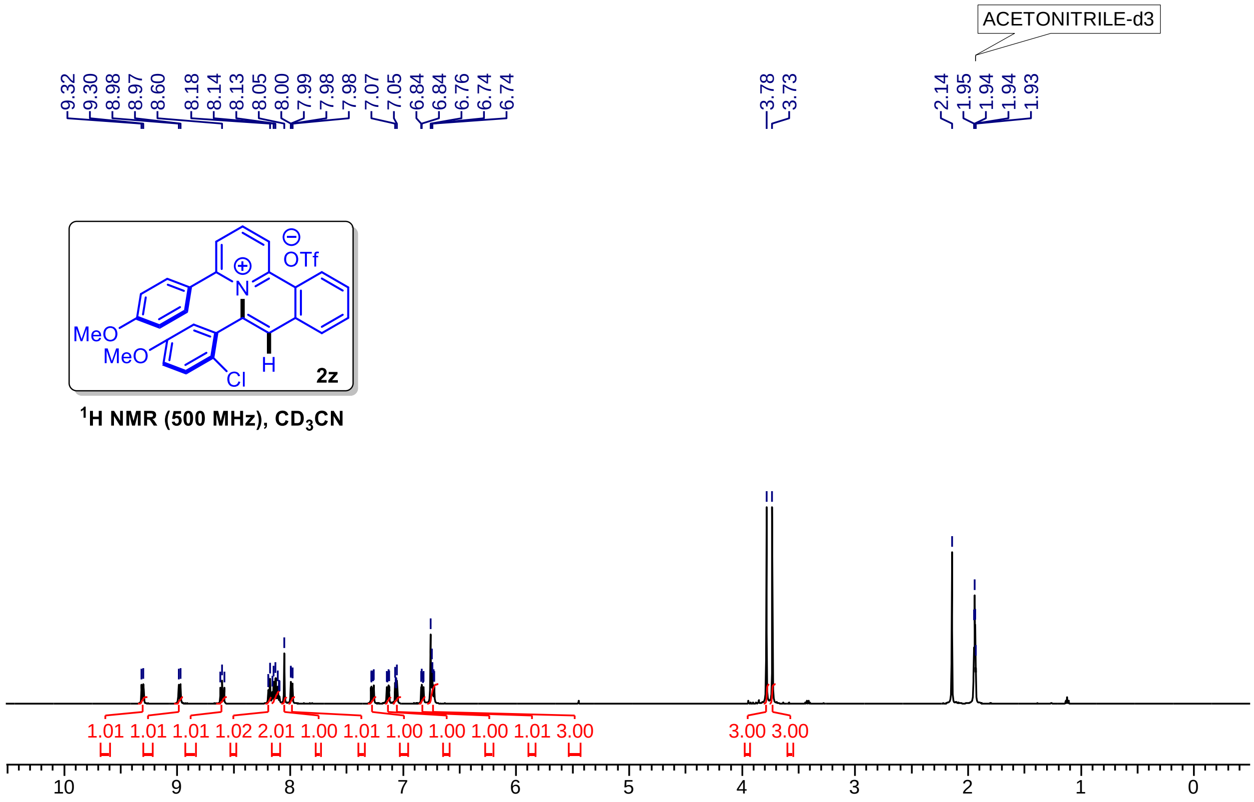

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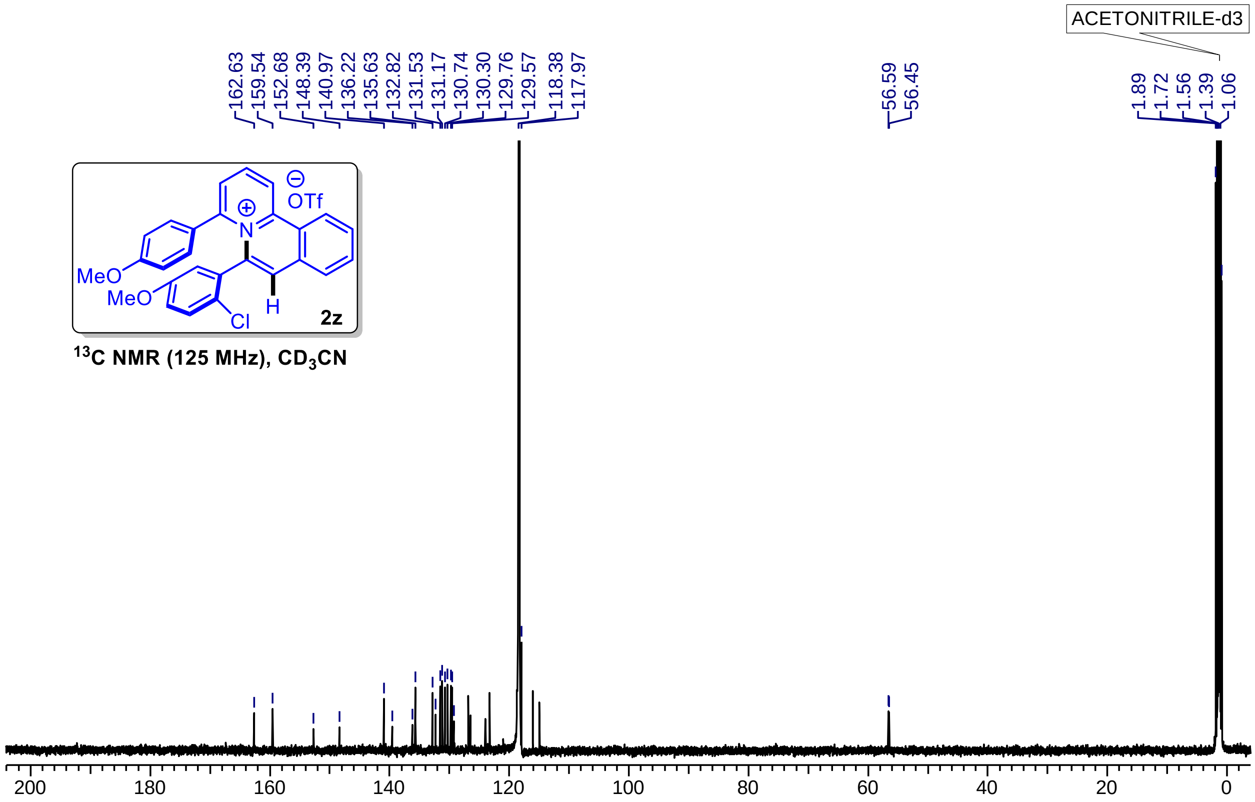

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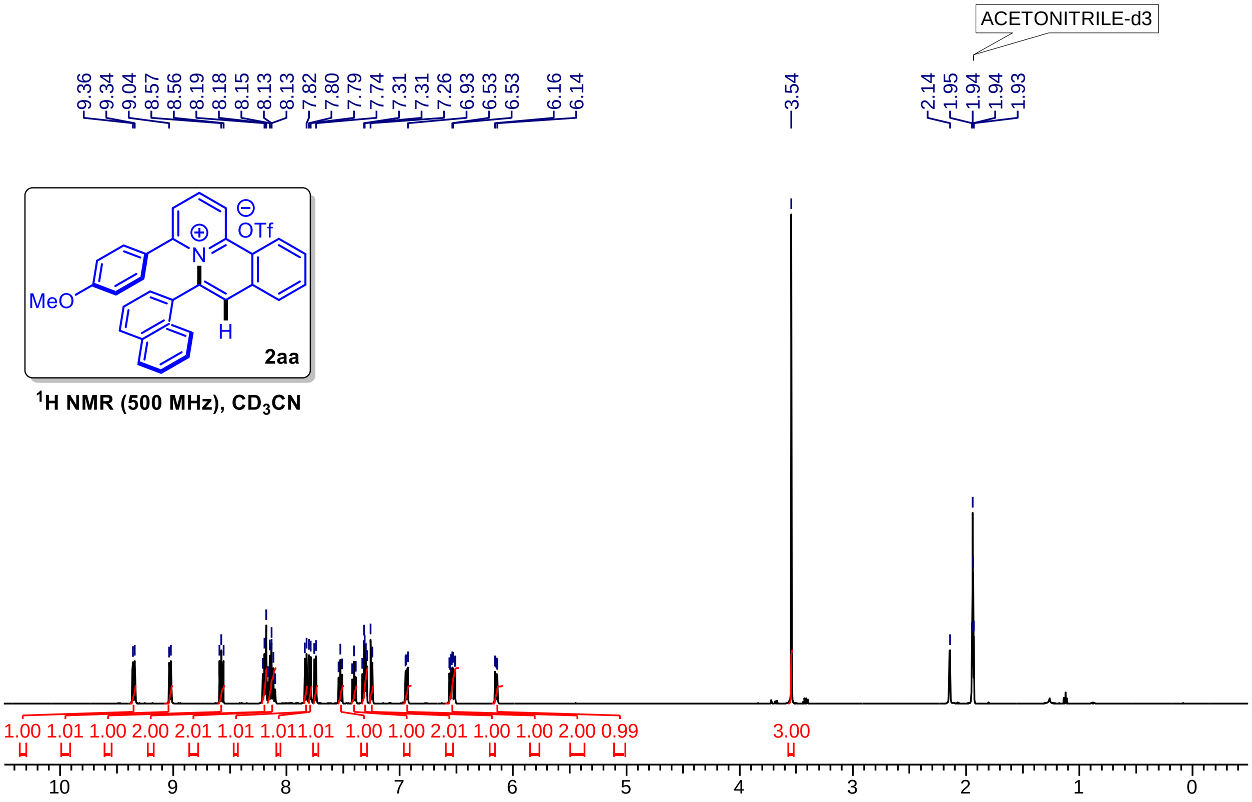

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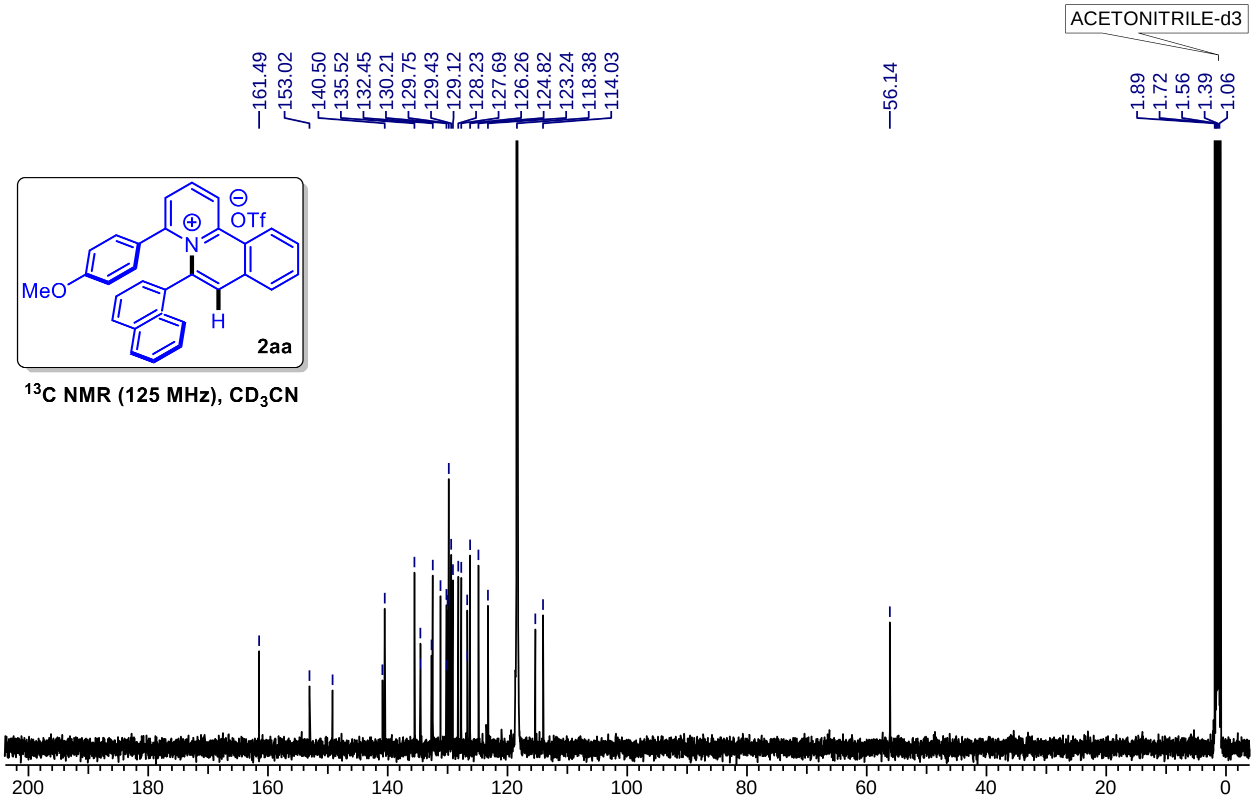

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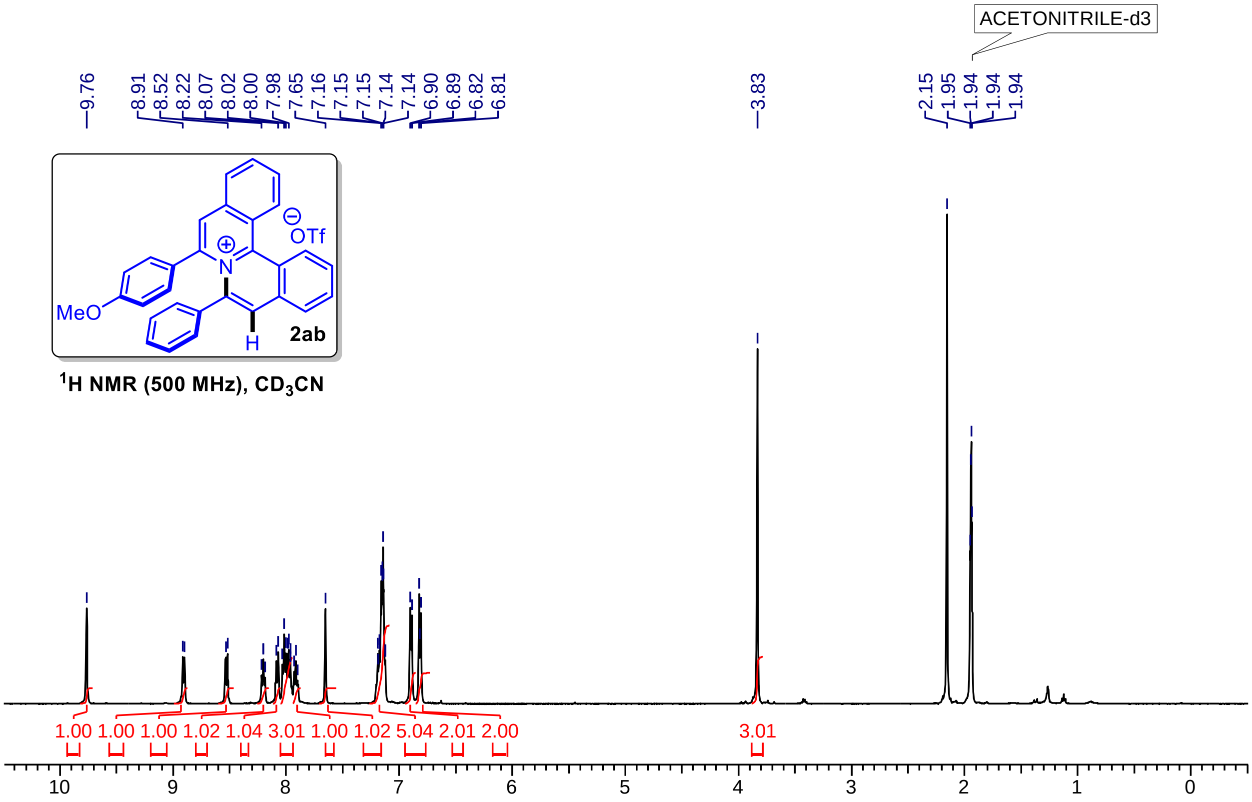

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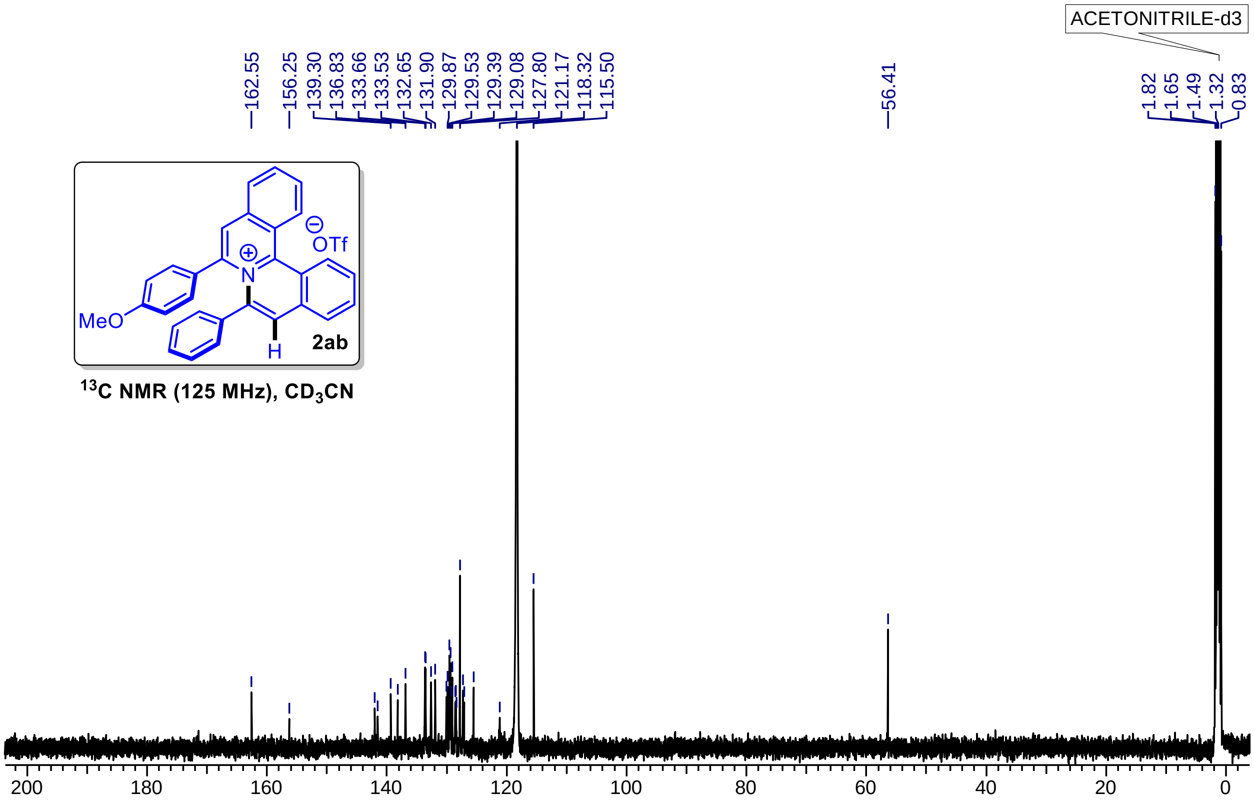

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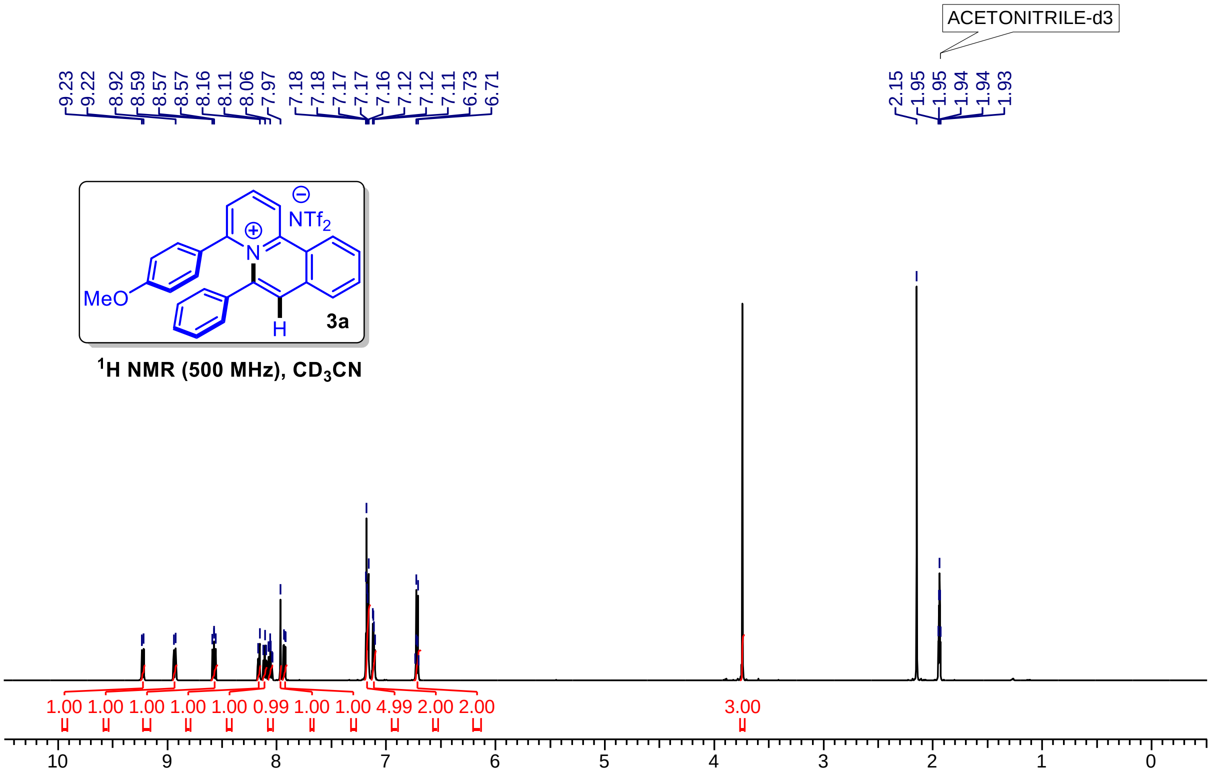

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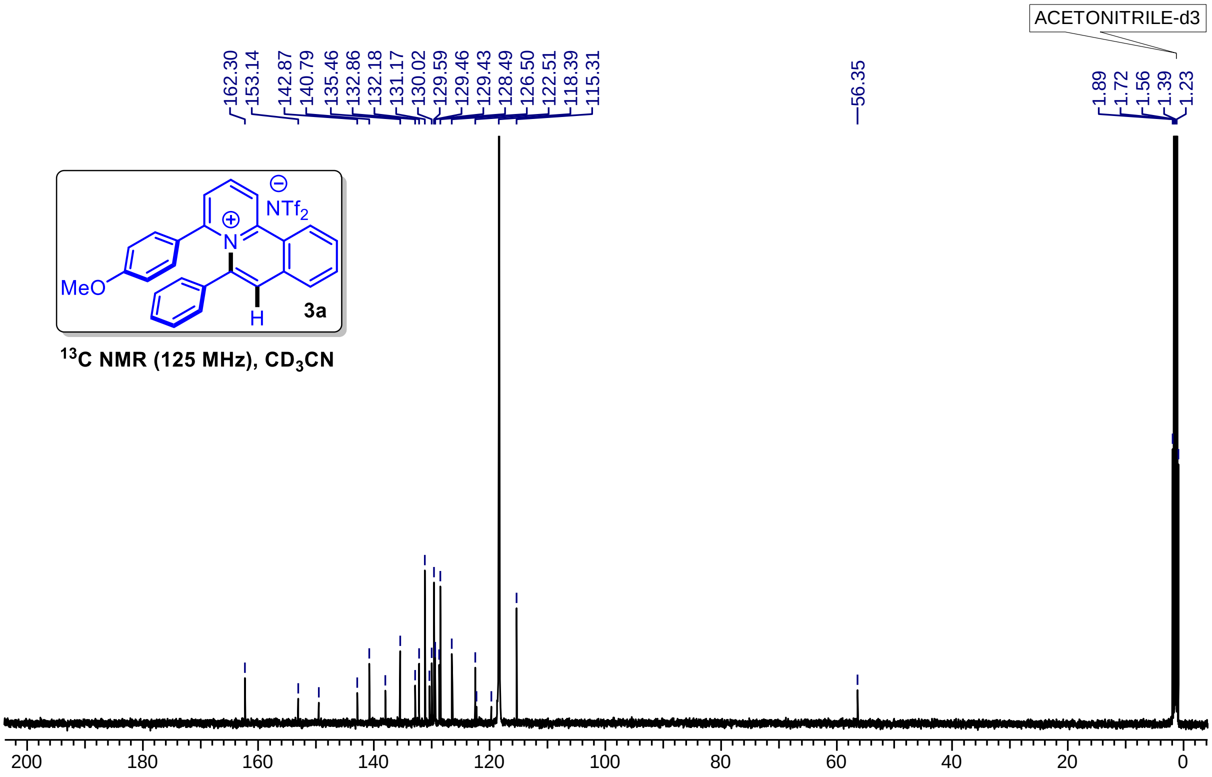

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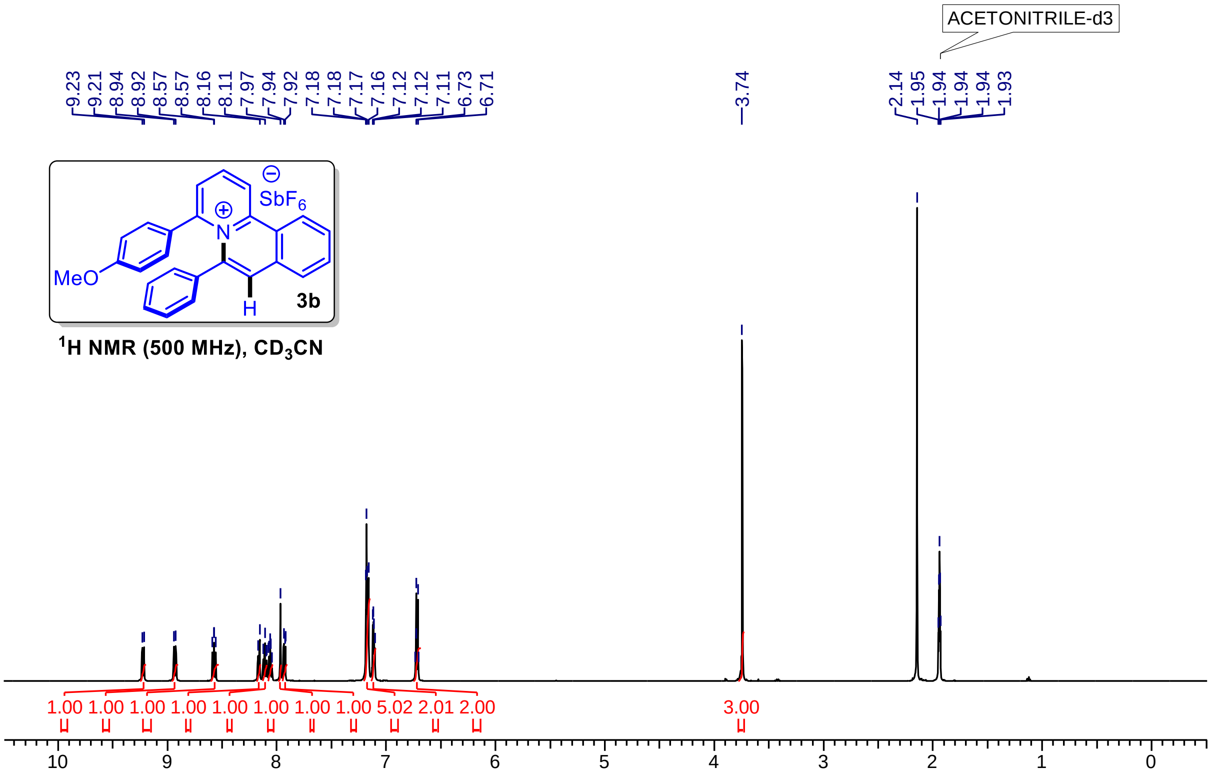

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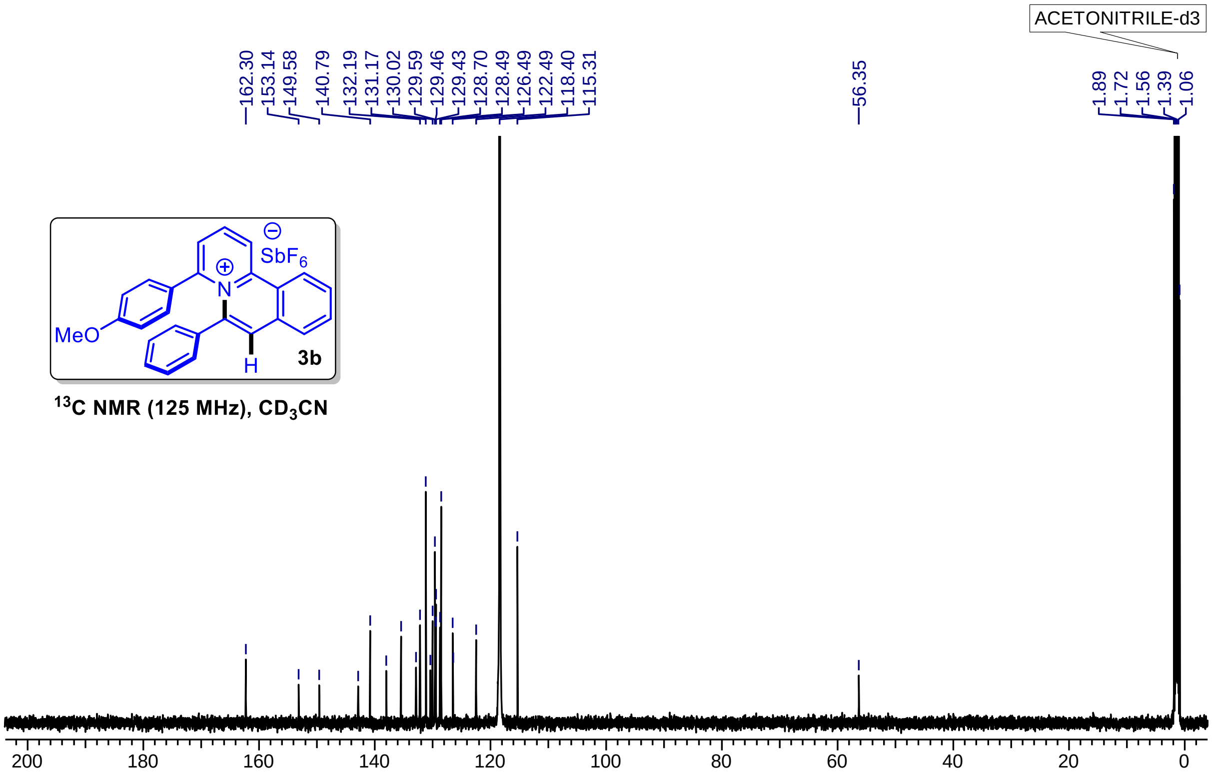

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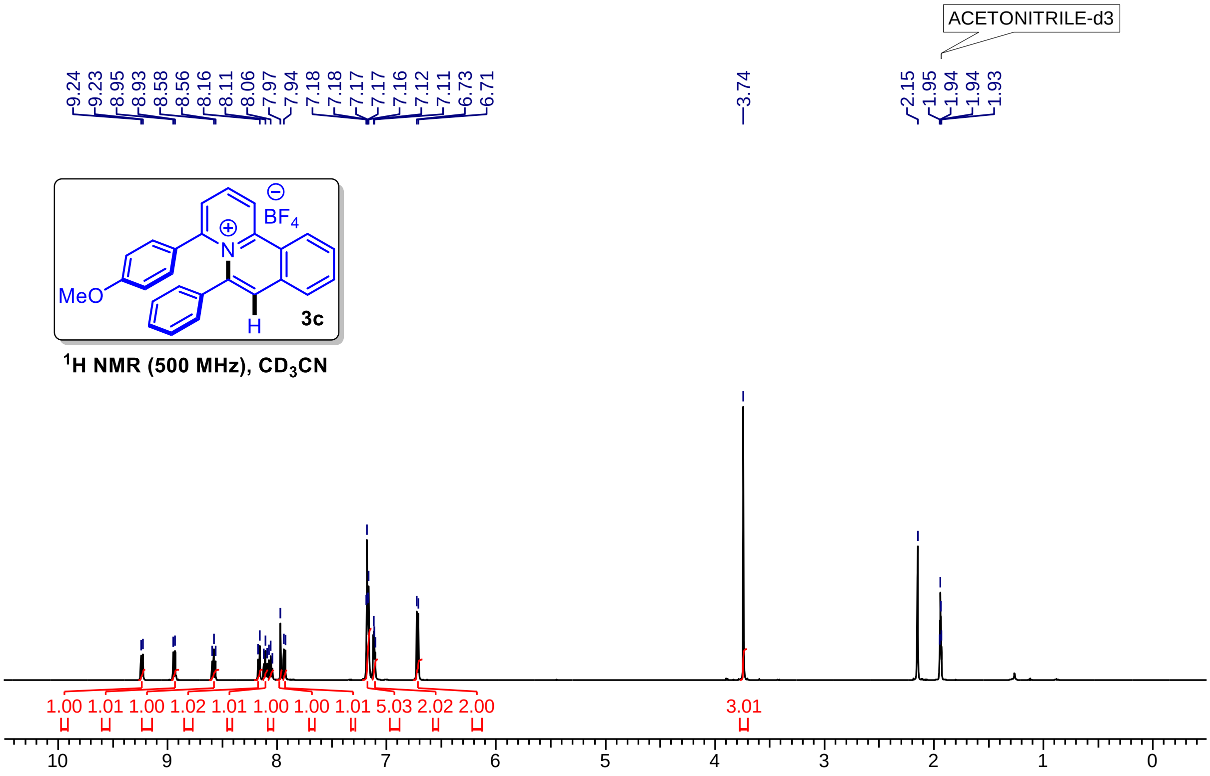

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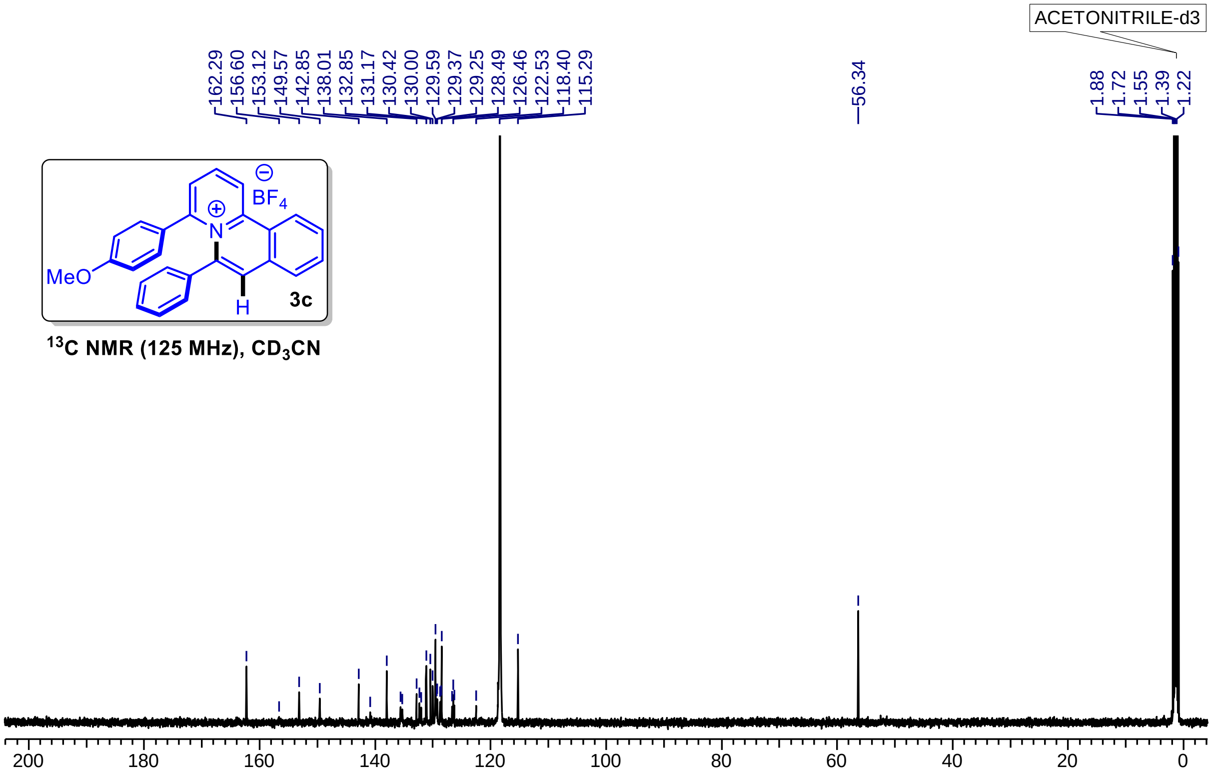

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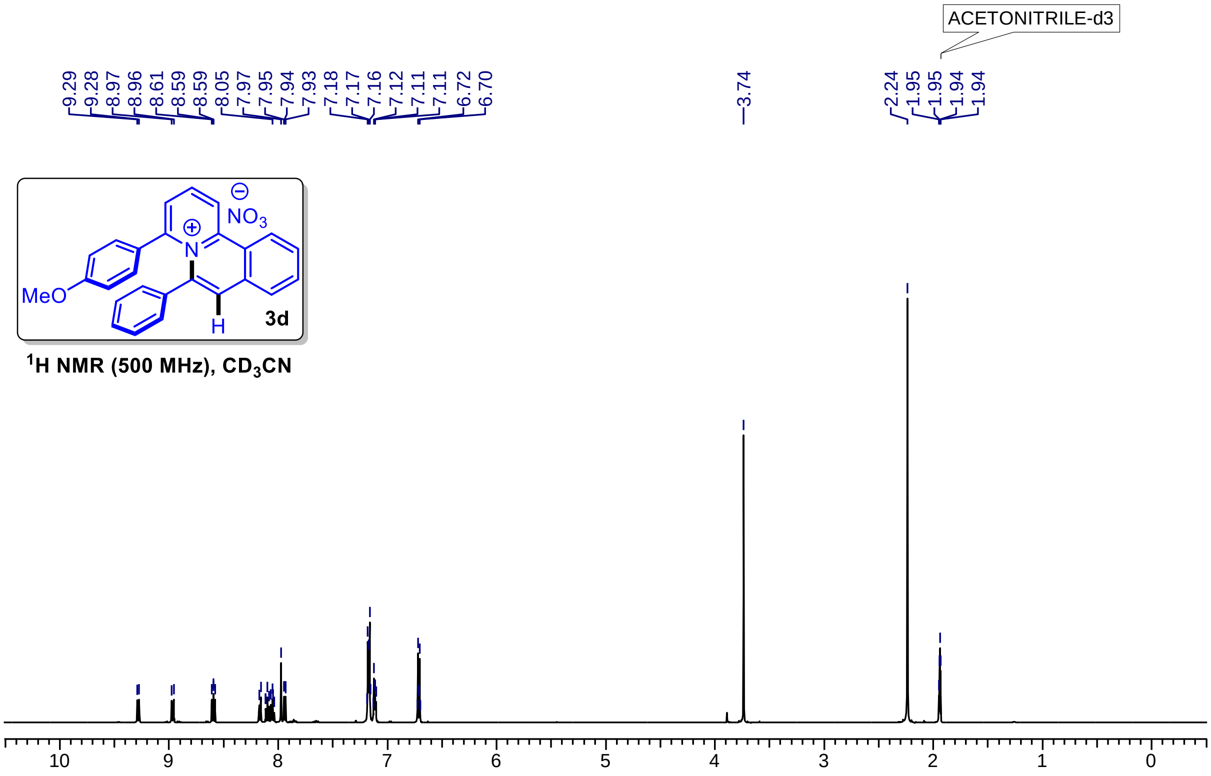

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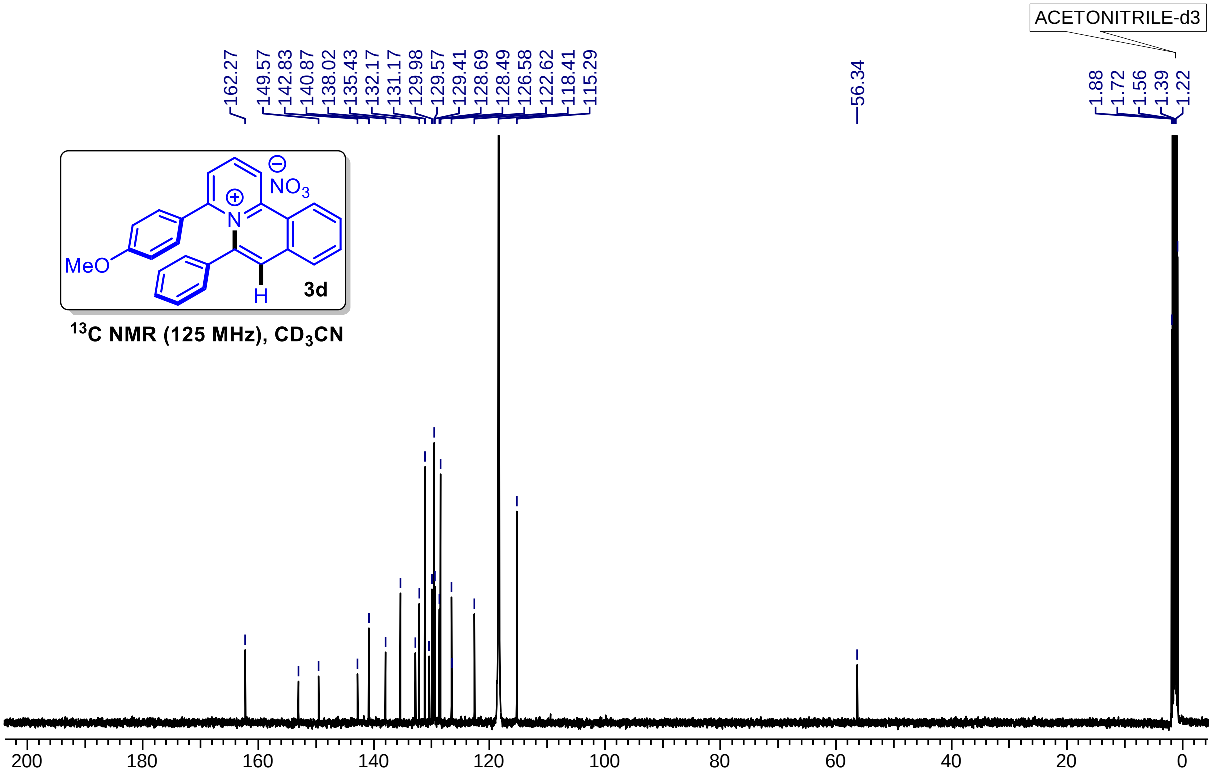

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3.8 References:

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1 Reviews: a) Z. Yang, A. Sharma, J. Qi, X. Peng, D. Y. Lee, R. Hu, D. Lin, J. Qu, J. S. Kim, *Chem. Soc. Rev*. **2016**, *45*, 4651; b) J. Mei, N. L. C. Leung, R. T. K. Kwok, J. W. Y. Lam, B. Z. Tang, *Chem. Rev*. **2015**, *115*, 11718; c) K. M. Dean, A. E. Palmer, *Nat. Chem. Biol*. **2014**, *10*, 512; d) J. Chan, S. C. Dodani, C. J. Chang, *Nat. Chem*. **2012**, *4*, 973; e) T. M. Figueira-Duarte, K. Müllen, *Chem. Rev*., **2011**, *111*, 7260-7314; f) M. L. Tang, Z. N. Bao, *Chem. Mater*., **2011**, *23*, 446; g) J. E. Anthony, *Angew. Chem. Int. Ed*., **2008**, *47*, 452; h) B. W. D'Andrade, S. R. Forrest, *Adv. Mater*., **2004**, *16*, 1585; i) A. P. Kulkarni, C. J. Tonzola, A. Babel, S. A. Jenekhe, *Chem. Mater*., **2004**, *16*, 4556; j) H. Aziz, Z. D. Popovic, N. X. Hu, A. M. Hor, G. Xu, *Science*, **1999**, *283*, 1900.

2 (a) X. Hou, C. Ke, C. J. Bruns, P. R. McGonigal, R. B. Pettman, J. Fraser Stoddart, *Nat. Commun*., **2015**, 6, 6884; (b) A. Goel, A. Sharma, M. Rawat, R. S. Anand, R. Kant, *J. Org. Chem*., **2014**, *79*, 10873; (c) S. Y. Lee, T. Yasuda, Y. S. Yang, Q. Zhang, C. Adachi, *Angew. Chem*., *Int. Ed*., **2014**, *53*, 6402; (d) Y. Kubota, Y. Ozaki, K. Funabiki, M. Matsui, *J. Org. Chem*., **2013**, *78*, 7058; (e) Z. Zhang, B. Xu, J. Su, L. Shen, Y. Xie, H. Tian, *Angew. Chem*., *Int. Ed*., **2011**, *50*, 11654.

3 Y. Chen, J. W. Y. Lam, R. T. K. Kwok, B. Liu, B. Z. Tang, *Mater. Horiz*., **2019**, *6*, 428.

4 J. Luo, Z. Xie., J. W. Y. Lam., L. Cheng, H. Chen, C. Qiu, H. S. Kwok, X. Zhan, Y. Liu, D. Zhu., B. Z. Tang *Chem. Commun*. **2001**, 1740.

5 Y. Hong, J. W. Y. Lam and B. Z. Tang, *Chem. Commun*., **2009**, 4332.

6 For selected examples, see: a), Y. Chen, W. Zhang, Z. Zhao, Y. Cai, J. Gong, R. T. K. Kwok, J. W. Y. Lam, H. H. Y. Sung, I. D. Williams, B. Z. Tang, *Angew. Chem. Int. Ed*. **2018**, *57*, 5011; b) X. Liu, M. Li, T. Han, B. Cao, Z, Qiu, Y. Li, Q Li, Y. Hu, Z. Liu, J. W. Y. Lam, X. Hu,B. Z. Tang, *J. Am. Chem. Soc*. **DOI**: 10.1021/jacs.9b04757; c) C. Gui, E. Zhao,R. T. K. Kwok, A. C. S. Leung, J. W. Y. Lam, M. Jiang, H. Deng, Y. Cai, W. Zhang,H. Su, B. Z. Tang, *Chem. Sci*., **2017**, *8*, 1822.

7 a) J. Liu, J. W. Y. Lam B. Z. Tang, *Chem. Rev*., **2009**, *109*, 5799; b) A. Qin, C. K. W. Jim, Y. Tang, J. W. Y. Lam, J. Liu, F. Mahtab, P. Gao, B. Z. Tang, *J. Phys. Chem. B*, **2008**, *112*, 9281.

8 Y. Hong, J. W. Y. Lam, B. Z. Tang, *Chem. Commun*., **2009**, 4332.

9 N. Zhao, M. Li, Y. Yan, J. W. Y. Lam, Y. L. Zhang, Y. S. Zhao,K. S. Wong. B. Z. Tang, *J. Mater. Chem. C*, **2013**, *1*, 4640.

10 T. Hu, B. Yao, X. Chen, W. Li, Z. Song, A. Qin, J. Z. Sun, B. Z. Tang, *Chem. Commun*., **2015**, *51*, 8849.

11 F. Hu, G. Zhang, C. Zhan, W. Zhang, Y. Yan, Y. Zhao, H. Fu, D. Zhang, *small* **2015**, *11*, 1335.

12 E. Zhao, H. Deng, S. Chen, Y Hong,C. W. T. Leung, J. Wing Y. Lam B. Z. Tang, *Chem. Commun.*, **2014**, *50*, 14451.

13 C. Gui, E. Zhao, R. T. K. Kwok, A. C. S. Leung, J. W. Y. Lam, M. Jiang, H. Deng, Y. Cai, W. Zhang, H. Sub, B. Z. Tang, *Chem. Sci*., **2017**, *8*, 1822.

14 M. Jiang, X. Gu, R. T. K. Kwok, Y. Li, H. H. Y. Sung, X. Zheng, Y. Zhang, J. W. Y. Lam, I. D. Williams, X. Huang, K. S. Wong, B. Z. Tang, *Adv. Funct. Mater*. **2018**, *28*, 1704589.

15 B. Feng, D. Wan, L. Yan, V. D. Kadam, J. You, G. Gao, *RSC Adv*., **2016**, *6*, 66407.

16 S. Ghosh, S. Pal, S. Rajamanickam, R. Shome, P. R. Mohanta, S. S. Ghosh, B. K. Patel, *ACS Omega* **2019**, *4*, 5565;

17 a) S. Aloise, Z. Pawlowska, O. Poizat, G. Buntinx, A. Perrier, F. Maurel, K. Ohkawa, A. Kimoto, J. Abe, *Phys. Chem. Chem. Phys.*, **2014**, *16*, 1460; b) C. Reichardt, S. Asharin-Fard, *Angew. Chem., Int. Ed*., 1991, 30, 558; c) E. M. Kosower, J. A. Skorcz, *J. Am. Chem. Soc*., **1960**, *82*, 2195; d) T. Nagamura, K. Sakai, *Chem. Phys. Lett*., **1987**, *141*, 553.

18 X,-H. Jin, C. Chen, C.-X. Ren, L.-X. Cai, J. Zhang, *Chem. Commun.*, **2014**, *50*, 15878.

19 K. Leduskrasts, E. Suna, *RSC Adv*., **2019**, *9*, 460.

20 K. Leduskrasts, A. Kinens, E. Suna, *Chem. Commun***., 2019**, *55*, 12663.

21 a) A. C. Shaikh, D. S. Ranade, P. R. Rajamohanan, P. P. Kulkarni, N. T. Patil, *Angew. Chem., Int. Ed*. **2017**, *56*, 757; b) A. C. Shaikh, M. E. Varma, R. D. Mule, S. Banerjee, P. P. Kulkarni, N. T. Patil,. *J. Org. Chem*. **2019**, *84*, 1766.

22 a) R. D. Mule, A. C. Shaikh, A. B. Gade, N. T. Patil, *Chem. Commun*. **2018**, *54*, 11909; b) A. C. Shaikh, S. Banerjee, R. D. Mule, S. Bera, N. T. Patil, *J. Org. Chem*. **2019**, *84*, 4120.

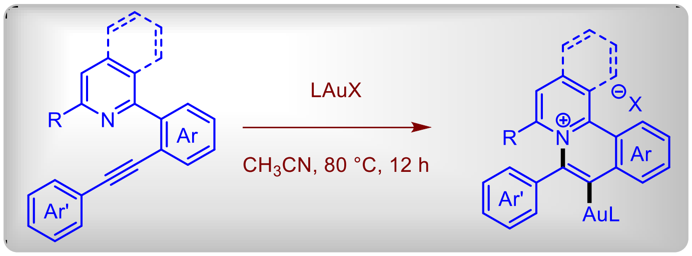
23 A. C. Shaikh, S. Shalini, R. Vaidhyanathan, M. V. Mane, A. K. Barui, C. R. Patra, Y. Venkatesh, P. R. Bangal, N. T. Patil, *Eur. J. Org. Chem*.**, 2015**, *22*, 4860.

24 N. Zhao, J. W. Y. Lam, H. H. Y. Sung, H. M. Su,I. D. Williams, K. S. Wong,B. Z. Tang, *Chem. Eur. J*. **2014**, *20*, 133, b) G. Zhang, X. Zhang, L. Kong, S. Wang, Y. Tian, X. Tao, J. Yang, *Sci. Rep*. **2016**, *6*, 37609.

Chapter 4

Accessing a Library of Pyrido-isoquinoline-based Gold(I) Complexes *via* Intramolecular Aminoauration Reactions of Pyridino-Alkynes

Design and development of library-based approach for the synthesis gold(I) complexes through aminoauration of alkynes has been achieved. Current reaction proceeds under base free and at mild condition with excellent functional group tolerance. NHC, mono and bidented phosphine ligands worked appreciably under the present reaction condition to render desired product.



Manuscript under preparation

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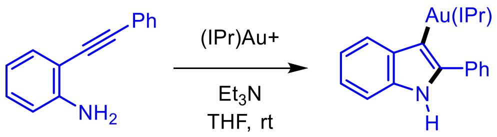
4.1 Introduction

The construction of new carbon–carbon or carbon–heteroatom bonds is key feature in chemistry and it always attracts the interests of organic chemists. In the field of synthetic organic chemistry, the homogeneous gold catalysis has received great attention because of its reactivity and applications.[1] Intra- or intermolecular nucleophilic attack on activated carbon-carbon multiple bonds achieved by gold catalysts, which are known to be extremely mild and effective soft π-acids. In gold-catalysed reactions several organo-gold intermediates have been anticipated to support the advanced mechanisms; mostly in these intermediates gold-carbon bonds were cleaved by electrophiles (often proton) to achieve the products. Although various kinds of organogold compounds have been known in organometallic chemistry.[2]

In homogeneous gold catalysis protodeauration of organogold intermediates was generally known to be fast process. Nowadays, synthetic organic chemists are able to isolate an organogold intermediates under certain conditions. In consequent, various new organogold complexes have been prepared and their existence has assisted mechanisms or emerged as new transformations, selected reports will be discussed in the category of aminoauration of alkynes.

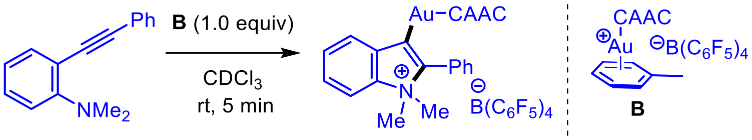
Hashmi *et al*. reported successful isolation and characterisation of two heteroaryl gold(I) compounds with stoichiometric amount of gold (IPrAuOTs) and base.[3] It shows that the conditions using the IPr ligand and base can isolate broad scope for the isolation of the organometallic intermediates in gold-catalysed nucleophilic additions to alkynes (Scheme 4.1).

Scheme 4.1: Au (I) catalysed aminoauration of 2-alkynylaniline



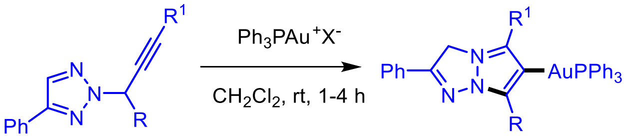
Bertrand and group reported a coincidentle discovery of the catalytic methylamination and hydroammoniumation of alkynes. Aiming to prepare the tricordinated alkynylamine gold complexes, unfortunately it rendered the hydroamination product, to prevent this they prepared N,N-Dimethylated alkynyl aniline and subjected it with stoichiometric amount of **cat. B** and ended with aminoaurated product in excellent yield (Scheme 4.2).[4]

Scheme 4.2: Au (I) catalysed aminoauration of 2-alkynyl N,N-dimehylaniline



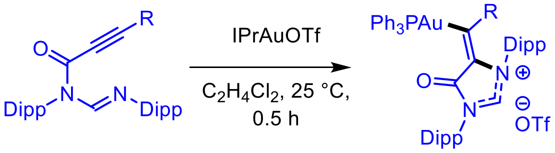
In same year, Shi *et al.* synthesised a new class of ionic organogold complexes from 5-*endo*-dig cyclization of triazole-alkyne. Synthesised Au-C bond showed highly stable character towards air, moisture and acid.[5]

Scheme 4.3: Au (I) catalysed aminoauration of triazole



Zhang and coworkers investigated gold-catalysed cyclization oxidation of imidoalkyne. Stoichiometric amount of PPh_3AuOTf and imidoalkyne offered gold carbene in moderate yield (Scheme 4.4).[6]

Scheme 4.4: Au (I) catalysed aminoauration of 2-imidoalkyne



Literature survey reveals that gold complexes are bioactive and they are applicable in variety of disease models; like, rheumatoid arthritis, cancers, auto-immune diseases, and other chronic inflammatory, as well as viral, fungal and bacterial infections.[7] Gold I/III oxidation states are reasonably stable in aqueous solution to aid their use in biological research. To take this into account, it is essential to design and develop a library of gold complexes which will be utilized in chemistry as well as biology.

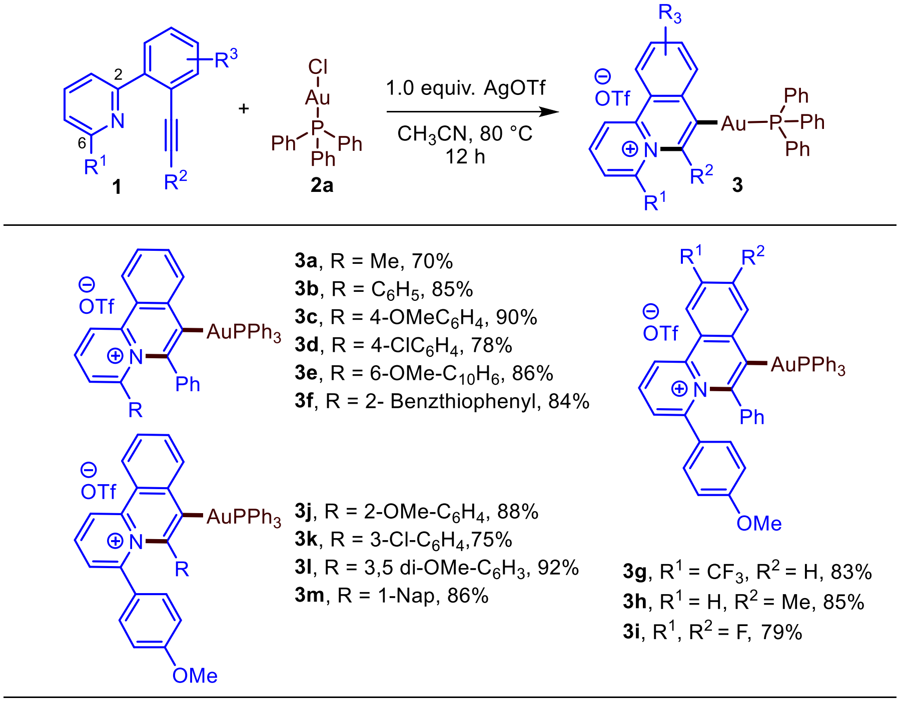
4.2 Present work

As a part of continuing curiosity in Au(I)/Au(III) catalysis[8] and encouraged by importance of gold complexes in biological activity, we envisioned that the substrate of type **1** (R = Ar, alkyl) in the presence of appropriate stoichiometric gold catalyst would produce cove shaped 4,6-diarylated isoquinolopyridinium (IQP) salts *via* endo-selective aminoauration. Herein, a new class of gold complexes synthesized from 2-(2-alkynylphenyl)pyridines *via* LAu^IX promoted intramolecular *endo*-selective aminoauration reaction. In these reactions, LAu^IX played a dual role by mediating the amino-auration reaction as well as providing a counter ion. While prepairing gold complexes protodeauration of organogold intermediates is fast step, to exclude this we designed a substrate **1**. One equivalent of Ph_3PAuCl was observed to be optimal to furnish desired product **3a** in good yield (70%).

4.3 Synthesis of gold complexes:

All Gold Complexes were prepared by treating pyridinoalkynes substrate (**1**) with 1 equiv. of corresponding gold(I) precatalyst and 1 equiv. AgOTf in ACN at 80 °C for 12 hours. At first, we tried methyl substituent at C6 position, it gave the corresponding product in 70 % yield. Later, phenyl substitution was examined and delightfully it provided the product in 85% yield (**3b**). Substitution on phenyl ring such as OMe, Cl provided **3c-3d** in 90% and 78% yield respectively. Notably, polyaromatic and heteroaromatic like 6-OMe-naphthyl and 2-benzothiophenyl gave the corresponding product (**3e** and **3f**) in good yields. Next, we aimed at the tolerance of the substituents on Ar ring at C2 position. Pleasingly, the introduction of $–CF_3$, Me and F substituents on the ring resulted in the formation of desired products **3g-3i** in 79-85% yield. Substrates with variation in aryl ring at alkyne-terminus with varying functional groups, such as OMe, Cl, and 3,5 di-OMe were well tolerated (**3j-3l**). Next, substrates bearing bulky aromatics at the alkyne terminal position of the pyridino alkynes were screened. For instance, the substrate with sterically demanding 1-Np ring efficiently afforded desired product in 86% yield.

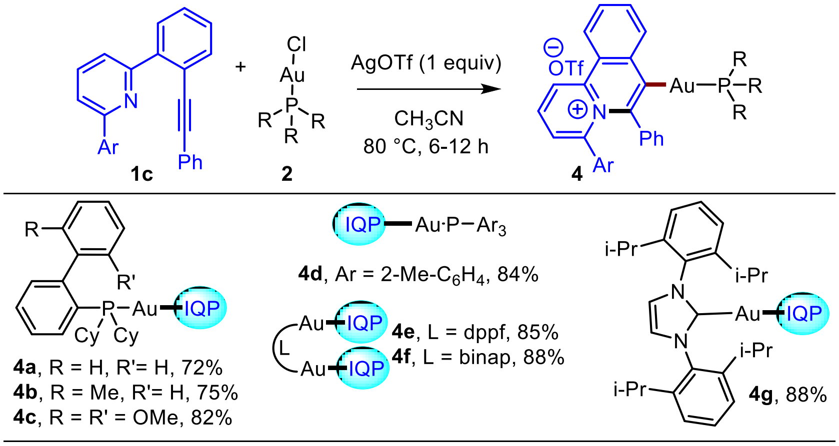
Table 4.1. **Substrate scope** [a,b]



[a]Reaction conditions: 0.20 mmol **1**, 0.20 mmol **2a**, 0.20 mmol AgOTf, CH_3CN (0.1 M), 80 °C, 6-12 h. [b] isolated yield.

After that, the extent of the reaction with respect to a variety of phosphine ligands on gold (I) was examined. As judged from Table 4.2. Changing ligands didn't affect the outcome of the reaction. At first JohnPhos ligand was tried which rendered the product in good yield (72%). Similarly, MePhos, SPhos also resulted in 75% and 82% yield, respectively. Later, *ortho*-substitution on phenyl ring also worked well to give corresponding product in 84% yield. Further, phosphine-based bidented lignads, such as BINAP and DPPF ligands were also found to be compatible with present reaction condition and provided the corresponding product **4e** (85%) and **4f** (88%) in good yield. Besides these phosphine ligands, NHC-based IPr ligand was also tried which provided the product **4g** in 88% yield.

Table 4.2. **Substrate scope**^{a,b}



^{a}Reaction conditions: 0.20 mmol **1**, 0.20 mmol **2a**, 0.20 mmol AgOTf, CH_3CN (0.1 M), 80 °C, 6-12 h. ^{b} isolated yield.

4.4 Conclusion:

In conclusion, we have developed a method to access a library of gold complexes. Electronically variable as well as sterically demanding ligands were found to be compatible with present methodology. Moreover, current reaction proceeds under base free, and mild condition and it shows excellent functional group tolerance.

4.5 Experimental procedures:

All the starting materials were prepared according to literature known procedures.[1] And the characterization data of these compounds has already been provided earlier in chapter 2 and chapter 3.

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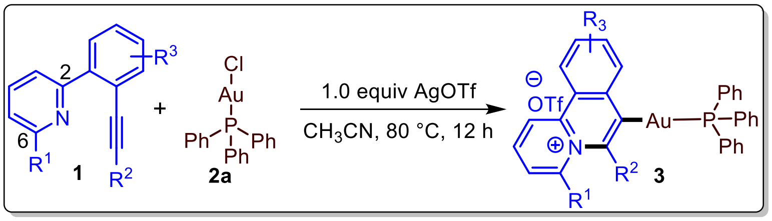
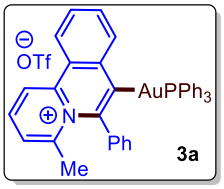
[1] (a) Mule R. D.; Shaikh A. C.; Gade A. B.; Patil N. T. *Chem. Commun*. **2018**, *54*, 11909; (b) Shaikh, A. C.; Ranade, D. S.; Rajamohanan, P. R.; Kulkarni, P. P.; Patil, N. T. *Angew. Chem. Int. Ed*. **2017**, *56*, 757; (c) Shinde, P. S.; Shaikh, A. C.; Patil, N. T. *Chem. Commun.* **2016**, *52*, 8152; (d) Guo, R.; Li, K.-N.; Liu, B.; Zhu, H.-J.; Fan, Y.-M.; Gong, L.-Z. *Chem. Commun*. **2014**, *50*, 5451.

4.5.1 Gold(I)-promoted aminoauration of pyridinoalkynes:



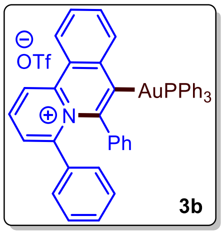
Representative procedure: To a screw-cap vial containing a stir bar were added 2-methyl-6-(2-(phenylethynyl)phenyl)pyridine (**1a**) (30 mg, 0.11 mmol, 1.0 equiv), Ph_3PAuCl (**2a**) (54 mg, 1.0 equiv), AgOTf (28 mg, 1.0 equiv) and CH_3CN (4 mL). The reaction vial was fitted with a cap, evacuated and back filled with N_2 and heated at 80 °C for 12 h. When the reaction time was completed, the reaction mixture was allowed to cool at ambient temperature. The mixture was diluted with CH_2Cl_2 (10 mL) and the combined mixture was concentrated in vacuo and the resulting residue was purified by column chromatography on silica (CH_2Cl_2/MeOH; 95:05) to afford the product **3a** in 68% yield.

(**3a**):



Pale yellow solid, 68 mg, 70% yield; $\boldsymbol{R_f}$ = 0.50 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.43 (d, J = 8.1 Hz, 1 H), 9.11 (d, J = 8.5 Hz, 1 H), 8.75 - 8.64 (m, 1 H), 8.49 (dd, J = 7.5, 8.5 Hz, 1 H), 8.14 - 8.07 (m, 1 H), 7.98 - 7.92 (m, 1 H), 7.90 (d, J = 7.0 Hz, 1 H), 7.76 - 7.70 (m, 2 H), 7.66 - 7.62 (m, 3 H), 7.61 - 7.56 (m, 6 H), 7.46 - 7.38 (m, 7 H), 7.36 - 7.31 (m, 2 H), 2.15 (s, 3 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 173.5, 172.6, 148.0, 145.9, 143.2, 142.7, 142.7, 139.4, 138.0, 133.8, 133.7, 133.6, 132.7, 131.9, 129.6, 129.5, 129.4, 129.1, 129.0, 128.8, 128.5, 127.8, 125.3, 124.5, 124.5, 121.9, 121.1, 119.4, 116.8, 26.1; **HRMS (ESI)** calcd for $C_{38}H_{30}AuPN^+$ (M - OTf)$^+$ 728.1812, found 728.1815.

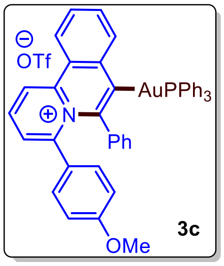
(**3b**):



3b

Yellow solid, 72 mg, 85% yield; ***R*** R_f = 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.48 (d, *J* = 7.8 Hz, 1 H), 9.15 (d, *J* = 8.4 Hz, 1 H), 8.66 (d, *J* = 7.9 Hz, 1 H), 8.56 (dd, *J* = 7.5, 8.4 Hz, 1 H), 8.12 (t, *J* = 7.6 Hz, 1 H), 7.97 (t, *J* = 7.2 Hz, 1 H), 7.91 - 7.83 (m, 1 H), 7.63 - 7.57 (m, 3 H), 7.56 - 7.49 (m, 6 H), 7.31 (d, *J* = 7.2 Hz, 3 H), 7.34 (d, *J* = 7.2 Hz, 3 H), 7.28 - 7.23 (m, 1 H), 7.20 (t, *J* = 7.4 Hz, 2 H), 7.15 - 7.12 (m, *J* = 7.2 Hz, 2 H), 7.12 - 7.08 (m, *J* = 7.2 Hz, 2 H), 7.04 (t, *J* = 7.5 Hz, 1 H), 6.90 (t, *J* = 7.6 Hz, 2 H) ; **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 149.4, 146.8, 144.4, 143.4, 140.4, 137.9, 137.6, 133.7, 133.6, 133.0, 131.8, 129.5, 129.4, 129.4, 129.2, 129.0, 128.9, 128.5, 128.1, 127.6, 127.1, 125.6, 124.1, 121.7; **HRMS (ESI)** calcd for $C_{43}H_{32}AuPN^+$ (M - OTf)$^+$ 790.1940, found 790.1930.

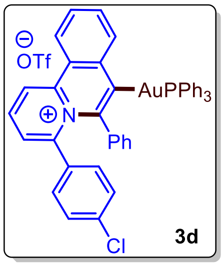
(**3c**):



3c

Yellow solid, 72 mg, 90% yield; R_f = 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.42 (d, *J* = 7.8 Hz, 1 H), 9.12 (d, *J* = 8.4 Hz, 1 H), 8.64 (d, *J* = 7.6 Hz, 1 H), 8.58 - 8.49 (m, 1 H), 8.10 (t, *J* = 7.6 Hz, 1 H), 8.01 - 7.92 (m, 1 H), 7.91 - 7.83 (m, 1 H), 7.62 - 7.57 (m, 3 H), 7.54 (dt, *J* = 1.8, 7.5 Hz, 6 H), 7.32 (d, *J* = 7.3 Hz, 3 H), 7.35 (d, *J* = 7.3 Hz, 3 H), 7.14 (d, *J* = 7.2 Hz, 2 H), 7.09 - 7.03 (m, 3 H), 6.98 - 6.91 (m, 2 H), 6.75 (d, *J* = 8.9 Hz, 2 H), 3.73 (s, 3 H) ; **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 172.2, 171.3, 160.1, 149.7, 146.8, 144.4, 143.5, 140.3, 138.0, 133.7, 133.6, 133.4, 132.9, 131.8, 130.3, 129.5, 129.4, 129.3, 129.0, 128.6, 128.0, 127.4, 127.1, 125.5, 124.1, 122.0, 121.3, 120.9, 119.4, 114.1, 55.4; **HRMS (ESI)** calcd for $C_{44}H_{34}AuPON^+$ (M - OTf)$^+$ 820.2014, found 820.2005.

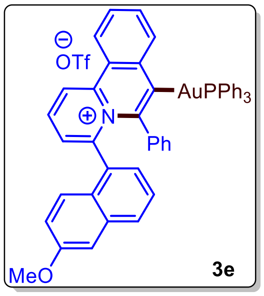
(3d):



3d

Yellow solid, 62 mg, 78% yield; ***Rf* =** 0.40 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.56 - 9.43 (m, 1 H), 9.16 (d, *J* = 8.4 Hz, 1 H), 8.67 (d, *J* = 7.6 Hz, 1 H), 8.56 (dd, *J* = 7.4, 8.5 Hz, 1 H), 8.12 (t, *J* = 7.6 Hz, 1 H), 8.02 - 7.93 (m, 1 H), 7.88 (dd, *J* = 1.1, 7.3 Hz, 1 H), 7.64 - 7.58 (m, 4 H), 7.58 - 7.52 (m, 7 H), 7.38 (br. s., 6 H), 7.28 - 7.24 (m, *J* = 8.5 Hz, 2 H), 7.19 (d, *J* = 7.2 Hz, 2 H), 7.16 - 7.13 (m, *J* = 8.5 Hz, 2 H), 7.13 - 7.07 (m, 1 H), 7.01 - 6.93 (m, 2 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 148.0, 146.9, 144.1, 143.4, 140.5, 137.9, 136.3, 134.0, 133.8, 133.7, 133.6, 133.1, 131.9, 129.6, 129.5, 129.5, 129.3, 129.1, 128.9, 128.5, 128.1, 127.6, 127.4, 125.6, 124.2, 122.1, 122.0, 119.4; **HRMS (ESI)** calcd for $C_{43}H_{31}AuClPN^+$ (M - OTf)$^+$ 824.1554, found 824.1559.

(3e):

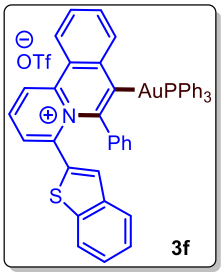


3e

Yellow solid, 64 mg, 86% yield; ***Rf* =** 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.48 (dd, *J* = 1.1, 8.8 Hz, 1 H), 9.16 (d, *J* = 8.5 Hz, 1 H), 8.71 - 8.63 (m, 1 H), 8.58 (dd, *J* = 7.4, 8.5 Hz, 1 H), 8.17 - 8.07 (m, 1 H), 8.05 - 7.93 (m, 2 H), 7.70 (d, *J* = 9.0 Hz, 1 H), 7.65 - 7.60 (m, 2 H), 7.59 - 7.54 (m, 3 H), 7.53 - 7.47 (m, 6 H), 7.35 - 7.25 (m, 7 H), 7.21 (d, *J* = 7.5 Hz, 1 H), 7.18 - 7.12 (m, 2 H), 7.03 (d, *J* = 7.6 Hz, 1 H), 6.90 -

6.81 (m, 1 H), 6.72 (q, *J* = 7.8 Hz, 2 H), 3.88 (s, 3 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 172.7, 171.8, 158.4, 149.8, 146.8, 144.5, 144.4, 143.3, 140.5, 137.9, 134.2, 133.7, 133.6, 133.0, 132.7, 131.8, 129.9, 129.5, 129.4, 129.0, 128.7, 128.6, 127.9, 127.8, 127.7, 127.6, 127.4, 127.1, 127.0, 125.6, 125.1, 124.2, 124.1, 122.0, 121.5, 119.4, 119.3, 105.8, 55.3; **HRMS (ESI)** calcd for $C_{48}H_{36}AuPON^+$ (M - OTf)$^+$ 870.2245, found 870.2259.

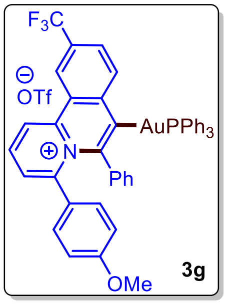
(3f):



3f

Yellow solid, 65 mg, 84% yield; ***Rf*** **=** 0.40 (CH_2Cl_2/MeOH = 96/04); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.52 (d, *J* = 8.9 Hz, 1 H), 9.15 (d, *J* = 8.5 Hz, 1 H), 8.69 (d, *J* = 7.9 Hz, 1 H), 8.61 - 8.51 (m, 1 H), 8.14 (t, *J* = 7.6 Hz, 1 H), 8.11 - 8.05 (m, 1 H), 8.02 - 7.95 (m, 1 H), 7.92 - 7.87 (m, 1 H), 7.80 - 7.74 (m, 1 H), 7.62 - 7.57 (m, 3 H), 7.55 - 7.48 (m, 6 H), 7.41 - 7.27 (m, 11 H), 6.96 (t, *J* = 7.4 Hz, 1 H), 6.80 (t, *J* = 7.8 Hz, 2 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 147.2, 144.5, 142.7, 140.7, 140.1, 138.5, 137.8, 137.5, 133.8, 133.7, 133.3, 131.9, 129.6, 129.5, 129.0, 128.6, 128.0, 127.5, 127.3, 125.9, 125.7, 125.0, 124.8, 124.1, 122.7, 122.4, 122.0, 119.4; **HRMS (ESI)** calcd for $C_{45}H_{32}AuPSN^+$ (M - OTf)$^+$ 846.1788, found 846.1795.

(**3g**):

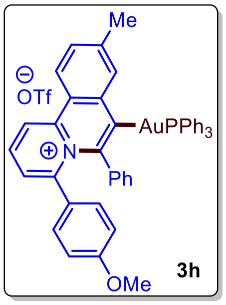


3g

Yellow solid, 60 mg, 83% yield; ***Rf*** **=** 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.67 (d, *J* = 8.4 Hz, 1 H), 9.49 (s, 1 H), 8.81 (d, *J* = 8.2 Hz, 1 H), 8.61 (t, *J*

= 7.9 Hz, 1 H), 8.37 (d, *J* = 8.2 Hz, 1 H), 7.95 (d, *J* = 7.3 Hz, 1 H), 7.65 - 7.58 (m, 3 H), 7.54 (t, *J* = 6.7 Hz, 6 H), 7.33 (d, *J* = 7.5 Hz, 3 H), 7.35 (d, *J* = 7.8 Hz, 3 H), 7.16 (d, *J* = 7.5 Hz, 2 H), 7.11 - 7.05 (m, 3 H), 6.99 - 6.93 (m, 2 H), 6.77 (d, *J* = 8.7 Hz, 2 H), 3.74 (s, 3 H); **^{13}C NMR (125 MHz, DMSO-d_6) δ** = 160.3, 150.3, 146.8, 146.2, 143.2, 142.4, 138.7, 134.9, 133.8, 133.7, 131.9, 130.1, 129.6, 129.5, 129.3, 129.2, 128.9, 128.5, 128.2, 128.0, 127.5, 125.1, 124.5, 123.5, 122.9, 122.0, 121.7, 119.4, 114.2, 55.4, 29.0; **HRMS (ESI)** calcd for $C_{45}H_{33}F_3OPN^+$ (M - OTf)$^+$ 888.1895, found 888.1912.

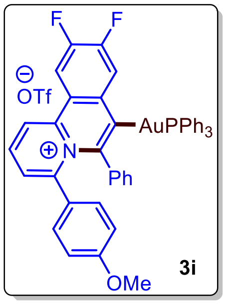
(**3h**):



3h

Yellow solid, 67 mg, 85% yield; ***Rf*** **=** 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d_6) δ** = 9.35 (d, *J* = 8.1 Hz, 1 H), 9.00 (d, *J* = 8.7 Hz, 1 H), 8.51 - 8.45 (m, 1 H), 8.42 (s, 1 H), 7.79 (d, *J* = 7.6 Hz, 2 H), 7.62 - 7.58 (m, 3 H), 7.57 - 7.52 (m, 6 H), 7.41 - 7.32 (m, 6 H), 7.13 (d, *J* = 7.2 Hz, 2 H), 7.07 - 7.02 (m, 3 H), 6.98 - 6.92 (m, 2 H), 6.75 (d, *J* = 8.9 Hz, 2 H), 3.72 (s, 3 H), 2.59 (s, 3 H); **^{13}C NMR (125 MHz, DMSO-d_6) δ** = 160.0, 149.4, 146.7, 144.5, 143.5, 143.4, 140.5, 137.7, 133.7, 133.6, 133.0, 131.8, 130.9, 130.3, 129.5, 129.4, 129.3, 128.5, 127.9, 127.1, 126.9, 125.5, 122.0, 120.9, 119.4, 114.1, 55.4, 21.7; **HRMS (ESI)** calcd for $C_{45}H_{36}AuOPN^+$ (M - OTf)$^+$ 834.2213, found 834.2215.

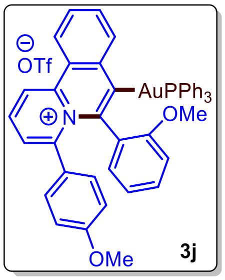
(**3i**):



3i

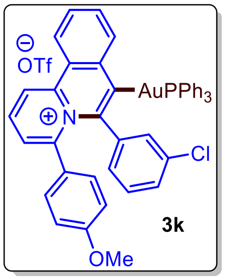
Yellow solid, 60 mg, 79% yield; ***Rf* =** 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.35 (dd, *J* = 1.1, 8.7 Hz, 1 H), 9.29 (dd, *J* = 7.8, 12.1 Hz, 1 H), 8.60 - 8.45 (m, 2 H), 7.89 (dd, *J* = 1.2, 7.3 Hz, 1 H), 7.65 - 7.56 (m, 3 H), 7.56 - 7.46 (m, 6 H), 7.38 - 7.26 (m, 6 H), 7.14 - 7.09 (m, 2 H), 7.09 - 7.02 (m, 3 H), 6.98 - 6.89 (m, 2 H), 6.79 - 6.69 (m, 2 H), 3.73 (s, 3 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 171.0, 170.2, 160.3, 151.4, 151.2, 151.1, 150.0, 149.4, 149.3, 145.9, 145.0, 143.2, 139.0, 138.9, 138.3, 133.8, 133.7, 131.9, 130.2, 129.6, 129.5, 129.5, 129.4, 129.0, 128.7, 128.1, 127.8, 127.5, 122.0, 121.9, 121.7, 120.4, 120.2, 119.4, 114.2, 55.5; **HRMS (ESI)** calcd for $C_{44}H_{32}AuF_2NOP^+$ (M - OTf)$^+$ 856.1790, found 856.1802.

(3j):



Yellow solid, 67 mg, 88% yield; ***Rf* =** 0.30 (CH_2Cl_2/MeOH = 93/07); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.48 - 9.40 (m, 1 H), 9.11 (d, *J* = 8.4 Hz, 1 H), 8.64 (d, *J* = 7.8 Hz, 1 H), 8.58 - 8.49 (m, 1 H), 8.09 (t, *J* = 7.3 Hz, 1 H), 8.00 - 7.93 (m, 1 H), 7.88 (dd, *J* = 1.1, 7.3 Hz, 1 H), 7.65 - 7.57 (m, 3 H), 7.57 - 7.48 (m, 6 H), 7.39 - 7.28 (m, 7 H), 7.13 - 7.06 (m, 2 H), 7.04 (dd, *J* = 2.3, 8.5 Hz, 1 H), 6.79 (dd, *J* = 2.6, 8.5 Hz, 1 H), 6.75 - 6.66 (m, 2 H), 6.44 (t, *J* = 7.4 Hz, 1 H), 3.72 (s, 3 H), 3.34 (s, 3 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 160.5, 155.2, 149.8, 145.9, 142.4, 140.5, 137.9, 134.1, 134.0, 133.7, 133.2, 132.2, 131.1, 129.9, 129.8, 129.6, 129.6, 129.4, 127.5, 125.8, 124.1, 122.8, 121.5, 120.6, 119.3, 114.6, 114.2, 110.5, 55.7, 55.4; **HRMS (ESI)** calcd for $C_{45}H_{36}AuO_2PN^+$ (M - OTf)$^+$ 850.2114, found 850.2116.

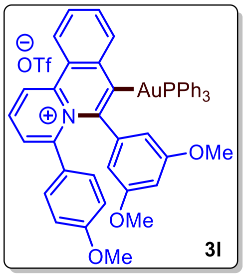
(**3k**):



3k

Yellow solid, 57 mg, 75% yield; ***Rf* =** 0.30 (CH$_2$Cl$_2$/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.44 (d, *J* = 7.9 Hz, 1 H), 9.13 (d, *J* = 8.4 Hz, 1 H), 8.63 (d, *J* = 7.8 Hz, 1 H), 8.55 (t, *J* = 7.9 Hz, 1 H), 8.11 (t, *J* = 7.5 Hz, 1 H), 7.97 (t, *J* = 7.4 Hz, 1 H), 7.90 (d, *J* = 7.2 Hz, 1 H), 7.65 - 7.57 (m, 4 H), 7.57 - 7.51 (m, 7 H), 7.36 (d, *J* = 8.4 Hz, 6 H), 7.23 (s, 1 H), 7.18 - 7.09 (m, 2 H), 7.08 - 6.97 (m, 3 H), 6.88 (dd, *J* = 2.5, 8.6 Hz, 1 H), 6.75 (dd, *J* = 2.5, 8.6 Hz, 1 H), 3.76 (s, 3 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 160.4, 149.4, 146.9, 145.2, 142.7, 140.1, 138.1, 133.7, 133.6, 133.5, 133.1, 133.0, 131.9, 129.9, 129.8, 129.7, 129.6, 129.5, 129.3, 129.0, 127.4, 127.0, 126.9, 125.6, 124.4, 122.0, 121.4, 119.4, 114.6, 113.8, 55.4; **HRMS (ESI)** calcd for C$_{44}$H$_{33}$AuClNOP^{+} (M - OTf)$^{+}$ 854.1652, found 854.1659.

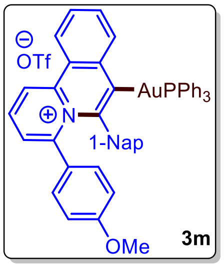
(**3l**):



3l

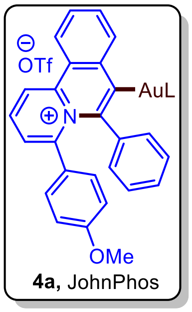
Yellow solid, 67 mg, 92% yield; ***Rf* =** 0.40 (CH$_2$Cl$_2$/MeOH = 92/08); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.42 (d, *J* = 8.2 Hz, 1 H), 9.12 (d, *J* = 8.4 Hz, 1 H), 8.63 (d, *J* = 7.9 Hz, 1 H), 8.53 (t, *J* = 7.9 Hz, 1 H), 8.10 (t, *J* = 7.6 Hz, 1 H), 7.96 (t, *J* = 7.6 Hz, 1 H), 7.85 (d, *J* = 7.2 Hz, 1 H), 7.65 - 7.57 (m, 3 H), 7.52 (t, *J* = 6.7 Hz, 6 H), 7.31 (d, *J* = 7.6 Hz, 3 H), 7.34 (d, *J* = 7.8 Hz, 3 H), 7.14 - 7.06 (m, *J* = 8.7 Hz, 2 H), 6.84 - 6.77 (m, *J* = 8.7 Hz, 2 H), 6.31 (d, *J* = 1.8 Hz, 2 H), 6.26 - 6.20 (m, 1 H), 3.73 (s, 3 H), 3.44 - 3.37 (m, 6 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 160.2, 160.0, 149.8, 146.7, 145.1, 144.2, 140.2, 137.9, 133.7, 133.6, 133.5, 132.9, 131.9, 130.1, 129.8, 129.5, 129.4, 129.3, 129.1, 127.2, 125.5, 124.3, 122.0, 121.2, 119.4, 114.0, 107.1, 100.0, 55.3, 54.9; **HRMS (ESI)** calcd for $C_{46}H_{38}AuPO_3N^+$ (M - OTf)$^+$ 880.2252, found 880.2256.

(**3m**):



Yellow solid, 64 mg, 86% yield; ***Rf* =** 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.52 (d, *J* = 8.5 Hz, 1 H), 9.20 (d, *J* = 8.4 Hz, 1 H), 8.66 (d, *J* = 7.9 Hz, 1 H), 8.57 - 8.46 (m, 1 H), 8.14 (t, *J* = 7.5 Hz, 1 H), 8.01 (t, *J* = 7.7 Hz, 1 H), 7.73 (t, *J* = 7.5 Hz, 3 H), 7.58 - 7.52 (m, 4 H), 7.44 (t, *J* = 7.0 Hz, 6 H), 7.32 - 7.25 (m, 2 H), 7.23 - 7.19 (m, 1 H), 7.15 (t, *J* = 7.6 Hz, 1 H), 7.04 (br. s., 6 H), 6.87 - 6.78 (m, 1 H), 6.64 (d, *J* = 8.5 Hz, 1 H), 6.53 - 6.45 (m, 1 H), 6.18 (d, *J* = 8.5 Hz, 1 H), 3.49 (s, 3 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 159.1, 149.5, 146.6, 142.3, 140.1, 139.5, 137.4, 133.6, 133.5, 133.4, 133.2, 132.9, 131.7, 130.0, 129.6, 129.3, 129.2, 129.1, 129.0, 128.8, 128.7, 128.6, 128.3, 128.0, 127.8, 126.0, 125.8, 125.6, 125.2, 125.1, 124.2, 122.0, 121.9, 119.4, 114.3, 112.8, 55.1; **HRMS (ESI)** calcd for $C_{48}H_{36}AuPON^+$ (M - OTf)$^+$ 870.2215, found 870.2255.

(**4a**):

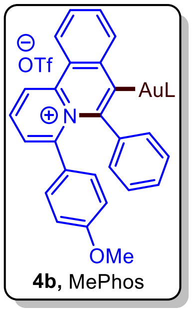


4a, JohnPhos

Yellow solid, 63 mg, 72% yield; ***Rf* =** 0.40 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.35 (dd, *J* = 1.1, 8.7 Hz, 1 H), 9.05 (d, *J* = 8.2 Hz, 1 H), 8.47 (dd, *J* = 7.5, 8.5 Hz, 1 H), 8.24 (d, *J* = 7.5 Hz, 1 H), 8.02 (t, *J* = 7.6 Hz, 1 H), 7.94 (dd, *J* = 3.1, 6.3 Hz, 1

H), 7.92 - 7.85 (m, 1 H), 7.77 (dd, *J* = 1.1, 7.2 Hz, 1 H), 7.64 - 7.56 (m, 2 H), 7.29 - 7.20 (m, 3 H), 7.14 (br. s., 2 H), 7.01 - 6.89 (m, 7 H), 6.89 - 6.80 (m, 4 H), 3.79 (s, 3 H), 1.11 (s, 9 H), 1.14 (s, 9 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 172.9, 172.1, 160.1, 149.4, 149.1, 149.0, 146.3, 143.6, 143.0, 142.8, 140.9, 137.4, 134.8, 134.3, 132.6, 132.6, 131.8, 130.6, 130.4, 129.1, 129.0, 128.7, 128.5, 128.0, 127.4, 127.0, 126.9, 126.7, 126.6, 126.5, 125.1, 123.9, 120.8, 114.1, 55.5, 36.9, 36.7, 30.2, 30.1; **HRMS (ESI)** calcd for $C_{46}H_{46}AuPON^+$ (M - OTf)$^+$ 856.3054, found 856.3075.

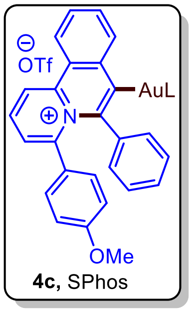
(**4b**):



4b, MePhos

Yellow solid, 66 mg, 75% yield; ***Rf* =** 0.40 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.43 - 9.30 (m, 1 H), 9.07 (d, *J* = 8.4 Hz, 1 H), 8.55 - 8.46 (m, 1 H), 8.25 (d, *J* = 7.8 Hz, 1 H), 8.03 (t, *J* = 7.3 Hz, 1 H), 7.91 (t, *J* = 7.6 Hz, 1 H), 7.84 - 7.74 (m, 2 H), 7.62 - 7.52 (m, 2 H), 7.19 - 7.12 (m, 1 H), 7.06 - 6.94 (m, 7 H), 6.94 - 6.89 (m, 2 H), 6.89 - 6.82 (m, 2 H), 6.80 (d, *J* = 7.3 Hz, 2 H), 6.76 - 6.70 (m, 1 H), 3.78 (s, 3 H), 2.22 - 2.07 (m, 1 H), 1.87 (s, 3 H), 1.73 (br. s., 3 H), 1.64 (br. s., 3 H), 1.57 (br. s., 3 H), 1.33 (s, 1 H), 1.27 - 1.10 (m, 7 H), 1.04 - 0.92 (m, 4 H),; **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 174.0, 173.2, 160.1, 149.5, 147.8, 146.3, 143.4, 143.2, 141.6, 141.6, 141.0, 137.5, 134.8, 134.0, 133.5, 131.7, 130.9, 130.4, 130.3, 129.6, 129.0, 128.8, 128.2, 127.8, 127.7, 127.2, 127.0, 126.7, 126.5, 126.1, 125.6, 125.2, 123.9, 120.8, 119.4, 114.3, 113.9, 55.5, 36.7, 36.4, 34.4, 34.1, 30.4, 28.8, 28.3, 26.1, 26.0, 25.6, 25.5, 25.4, 25.3, 20.6; **HRMS (ESI)** calcd for $C_{51}H_{52}AuOPN^+$ (M - OTf)$^+$ 922.3445, found 922.3449.

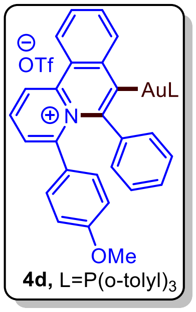
(**4c**):



4c, SPhos

Yellow solid, 76 mg, 82% yield; ***Rf* =** 0.40 (CH_2Cl_2/MeOH = 90/10); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.37 (dd, *J* = 1.1, 8.8 Hz, 1 H), 9.07 (d, *J* = 8.4 Hz, 1 H), 8.49 (dd, *J* = 7.5, 8.5 Hz, 1 H), 8.36 (d, *J* = 7.3 Hz, 1 H), 8.08 - 7.98 (m, 1 H), 7.96 - 7.87 (m, 1 H), 7.79 (dd, *J* = 1.1, 7.4 Hz, 1 H), 7.76 - 7.68 (m, 1 H), 7.49 (t, *J* = 6.9 Hz, 2 H), 7.05 - 6.95 (m, 6 H), 6.95 - 6.91 (m, 2 H), 6.90 - 6.82 (m, 3 H), 6.36 (d, *J* = 8.4 Hz, 2 H), 3.77 (s, 3 H), 3.58 (s, 6 H), 2.37 - 2.23 (m, 2 H), 1.76 (d, *J* = 11.4 Hz, 2 H), 1.66 (d, *J* = 11.7 Hz, 2 H), 1.58 (t, *J* = 12.5 Hz, 4 H), 1.53 - 1.42 (m, 2 H), 1.17 (quin, *J* = 13.2 Hz, 4 H), 1.11 - 0.95 (m, 6 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 174.1, 173.2, 160.0, 156.8, 149.5, 146.3, 143.5, 143.3, 143.3, 141.8, 141.7, 141.1, 137.5, 134.0, 132.8, 132.6, 132.5, 131.7, 130.7, 130.4, 129.2, 129.2, 129.1, 128.9, 128.5, 127.8, 127.4, 127.0, 126.8, 125.2, 123.9, 122.0, 120.9, 119.4, 118.8, 118.8, 114.0, 103.9, 55.5, 55.0, 35.9, 35.7, 30.2, 30.1, 28.8, 26.2, 26.1, 26.0, 25.9, 25.5; **HRMS (ESI)** calcd for $C_{52}H_{54}AuO_3PN^+$ (M - OTf)$^+$ 968.3512, found 968.3517.

(**4d**):

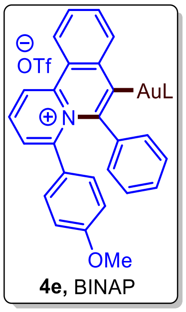


4d, L=P(o-tolyl)$_3$

Yellow solid, 70 mg, 84% yield; ***Rf* =** 0.30 (CH_2Cl_2/MeOH = 95/05); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.44 - 9.32 (m, 1 H), 9.08 (d, *J* = 8.4 Hz, 1 H), 8.51 (dd, *J* = 7.6, 8.3 Hz, 1 H), 8.44 (d, *J* = 7.6 Hz, 1 H), 8.05 (t, *J* = 7.6 Hz, 1 H), 7.98 - 7.90 (m, 1 H), 7.82 (dd, *J* =

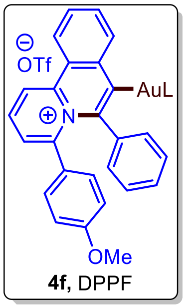
1.1, 7.3 Hz, 1 H), 7.59 - 7.49 (m, 3 H), 7.46 - 7.40 (m, 3 H), 7.30 (t, *J* = 7.6 Hz, 3 H), 7.05 - 6.98 (m, *J* = 8.9 Hz, 2 H), 6.95 (d, *J* = 7.3 Hz, 2 H), 6.86 (t, *J* = 7.4 Hz, 1 H), 6.78 (d, *J* = 7.6 Hz, 2 H), 6.80 (d, *J* = 7.8 Hz, 1 H), 6.75 - 6.69 (m, *J* = 8.7 Hz, 2 H), 6.61 (t, *J* = 7.8 Hz, 2 H), 3.72 (s, 3 H), 2.34 (s, 9 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 169.7, 168.8, 160.1, 149.7, 146.8, 144.3, 144.3, 143.3, 142.1, 142.0, 140.1, 137.9, 133.3, 133.1, 133.0, 132.6, 132.2, 132.2, 131.9, 130.3, 129.3, 128.3, 127.7, 127.3, 127.1, 127.1, 127.0, 125.7, 125.6, 125.3, 124.1, 124.1, 122.0, 121.1, 119.4, 114.0, 55.4, 22.3, 22.2; **HRMS (ESI)** calcd for $C_{47}H_{40}AuPON^+$ (M - OTf)$^+$ 862.2556, found 862.2571.

(**4e**):



Yellow solid, 143 mg, 85% yield; ***Rf* =** 0.50 (CH_2Cl_2/MeOH = 90/10); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.35 (dd, *J* = 1.1, 8.9 Hz, 2 H), 9.03 (d, *J* = 8.5 Hz, 2 H), 8.49 (dd, *J* = 7.6, 8.3 Hz, 2 H), 7.97 (d, *J* = 8.7 Hz, 2 H), 7.92 - 7.81 (m, 4 H), 7.81 - 7.68 (m, 4 H), 7.63 - 7.50 (m, 4 H), 7.44 - 7.28 (m, 10 H), 7.23 (dt, *J* = 2.3, 7.8 Hz, 4 H), 7.15 (d, *J* = 7.3 Hz, 2 H), 7.18 (d, *J* = 7.5 Hz, 2 H), 7.06 (t, *J* = 7.9 Hz, 2 H), 6.98 (d, *J* = 9.2 Hz, 2 H), 6.84 (d, *J* = 7.8 Hz, 2 H), 6.81 - 6.72 (m, 8 H), 6.72 - 6.62 (m, 6 H), 6.54 - 6.48 (m, *J* = 7.6 Hz, 2 H), 6.47 - 6.38 (m, *J* = 7.5 Hz, 2 H), 6.17 (t, *J* = 7.3 Hz, 2 H), 3.76 (s, 6 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 169.7, 168.9, 167.1, 163.1, 160.0, 149.7, 146.5, 143.8, 143.7, 142.7, 142.2, 139.7, 137.9, 134.2, 134.1, 134.0, 133.5, 133.4, 132.9, 132.8, 132.0, 131.6, 131.4, 130.9, 130.4, 130.3, 130.1, 129.6, 129.5, 129.4, 129.1, 129.0, 128.4, 128.2, 127.8, 127.6, 127.4, 127.2, 126.8, 126.4, 125.3, 123.9, 123.9, 122.0, 120.9, 119.4, 114.2, 113.8, 55.5.

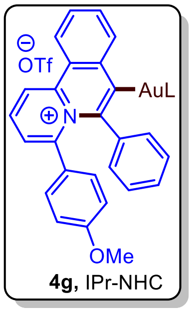
(**4f**):



4f, DPPF

Yellow solid, 86 mg, 72% yield; ***Rf* =** 0.50 (CH_2Cl_2/MeOH = 90/10); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.44 (d, *J* = 8.5 Hz, 2 H), 9.14 (d, *J* = 8.4 Hz, 2 H), 8.74 - 8.60 (m, *J* = 7.9 Hz, 2 H), 8.55 (t, *J* = 7.9 Hz, 2 H), 8.06 (t, *J* = 7.5 Hz, 2 H), 7.95 (t, *J* = 7.6 Hz, 2 H), 7.90 - 7.81 (m, *J* = 7.3 Hz, 2 H), 7.46 (d, *J* = 6.7 Hz, 4 H), 7.45 - 7.37 (m, 8 H), 7.24 (d, *J* = 7.5 Hz, 4 H), 7.26 (d, *J* = 7.8 Hz, 4 H), 7.14 (d, *J* = 7.3 Hz, 4 H), 7.09 - 6.94 (m, 10 H), 6.76 (d, *J* = 8.7 Hz, 4 H), 4.29 (br. s., 4 H), 3.94 (br. s., 4 H), 3.73 (s, 6 H); **^{13}C NMR (125 MHz, DMSO-d$_6$) δ** = 171.9, 171.0, 160.0, 149.7, 146.7, 144.3, 143.5, 140.4, 138.1, 132.9, 132.8, 131.5, 130.8, 130.4, 130.3, 129.1, 129.0, 128.6, 128.1, 127.2, 124.1, 121.9, 119.3, 114.0, 74.3, 74.3, 74.2, 71.2, 70.7, 55.4.

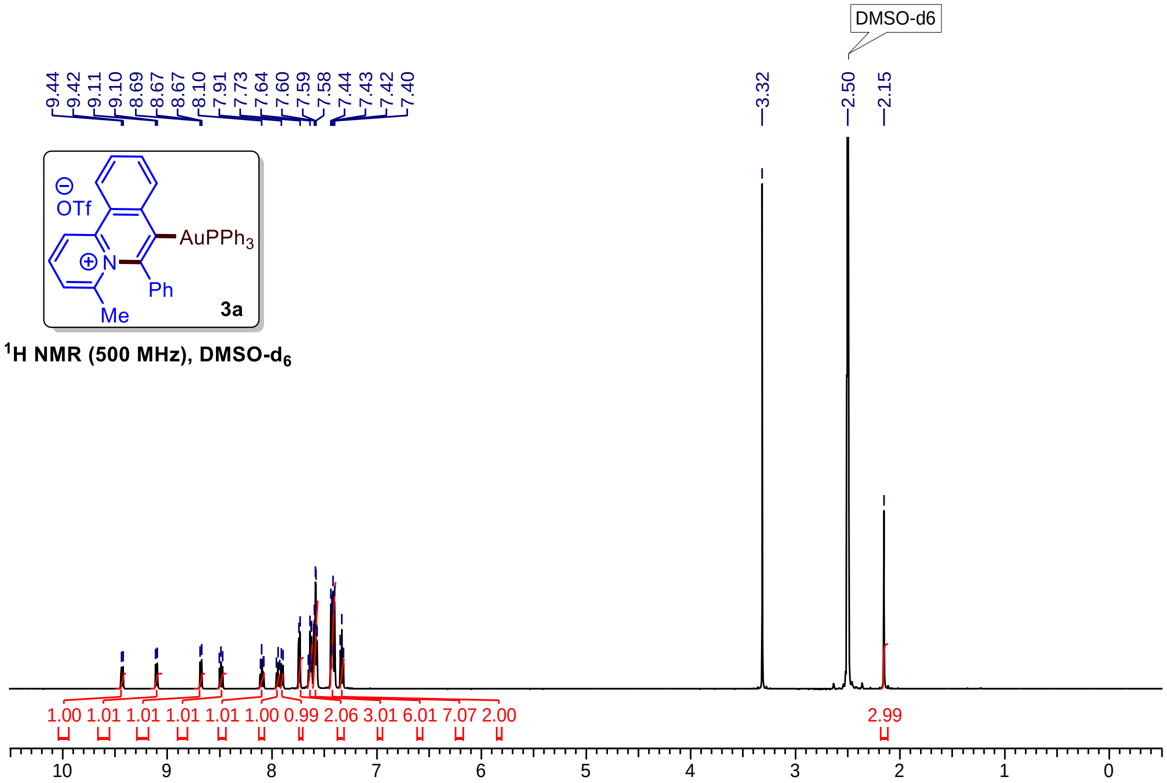
(**4g**):

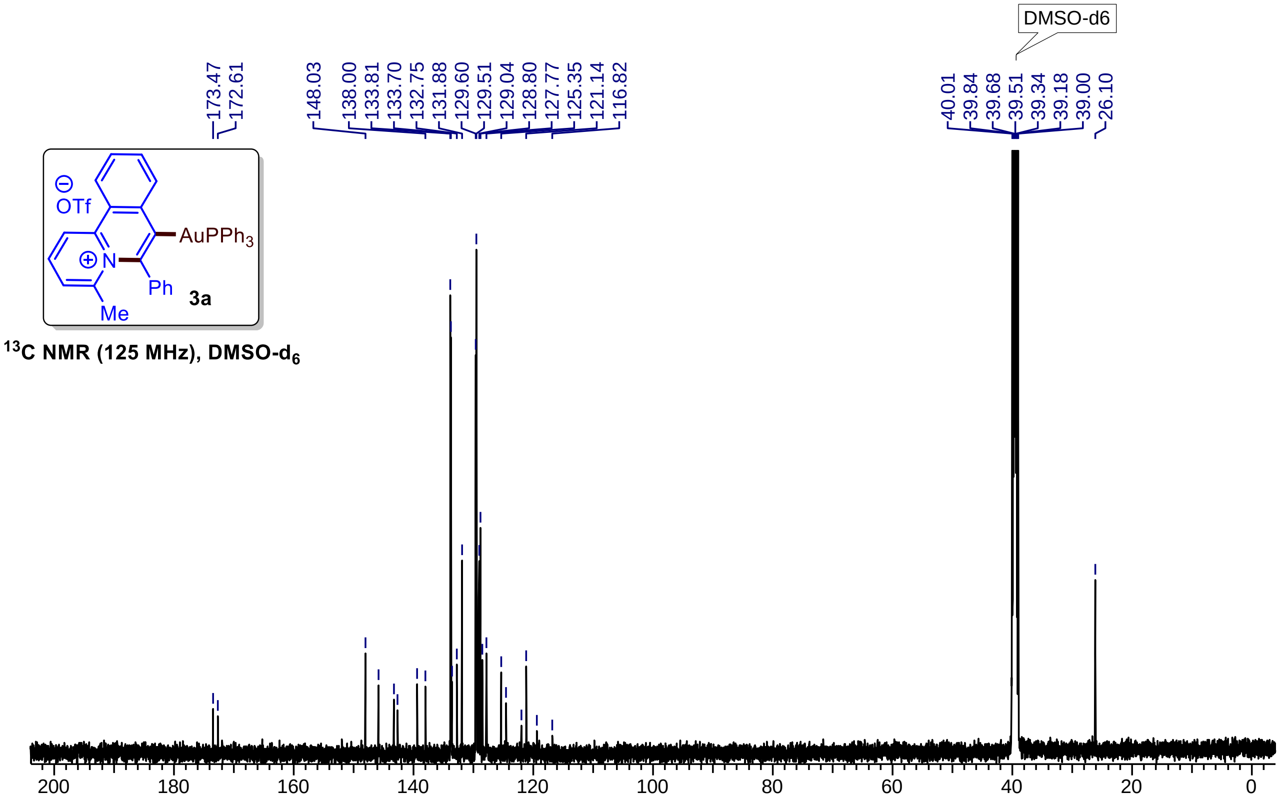


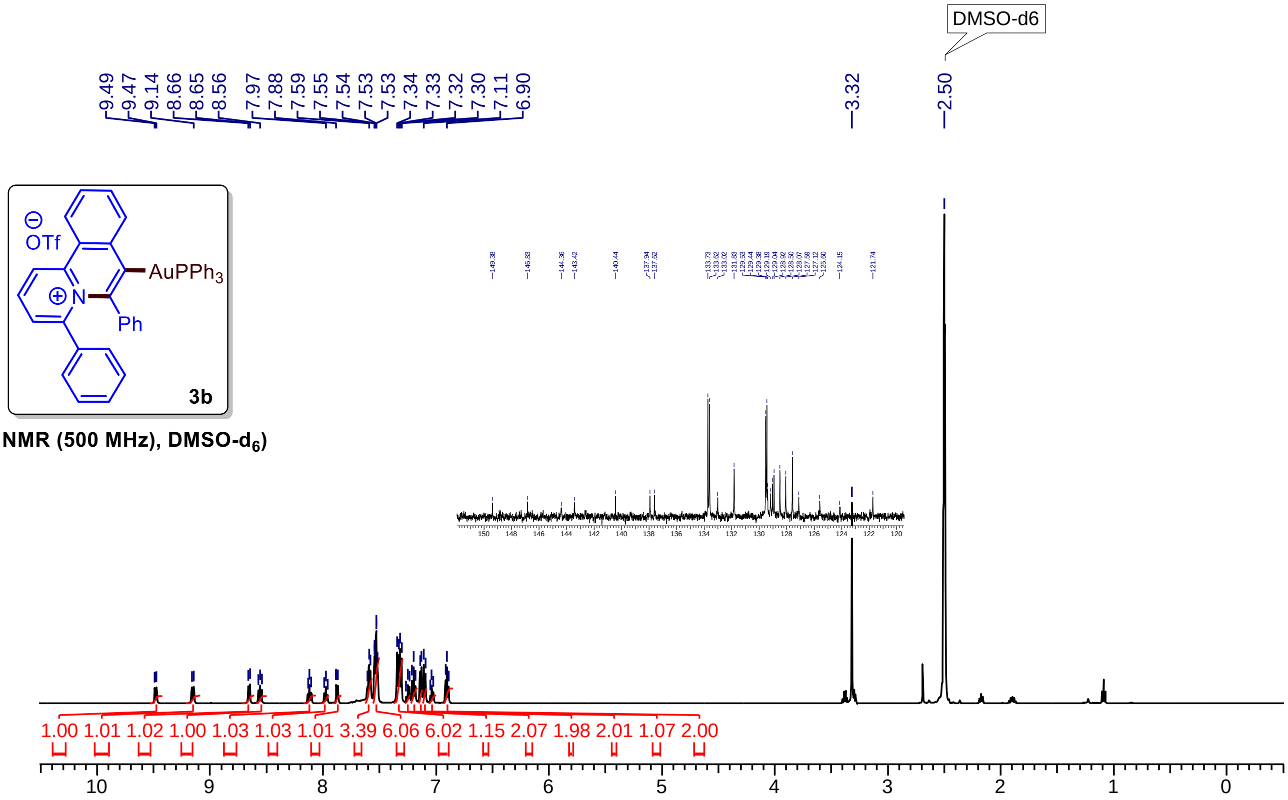
4g, IPr-NHC

Yellow solid, 81 mg, 88% yield; ***Rf* =** 0.40 (CH_2Cl_2/MeOH = 92/08); **^{1}H NMR (500 MHz, DMSO-d$_6$) δ** = 9.20 (dd, *J* = 1.2, 8.9 Hz, 1 H), 8.89 (d, *J* = 8.4 Hz, 1 H), 8.34 (dd, *J* = 7.3, 8.5 Hz, 1 H), 7.92 (s, 2 H), 7.79 - 7.69 (m, 3 H), 7.62 (dd, *J* = 1.2, 7.2 Hz, 1 H), 7.56 - 7.49 (m, 1 H), 7.46 (d, *J* = 7.9 Hz, 4 H), 7.13 (d, *J* = 7.3 Hz, 1 H), 6.85 - 6.77 (m, 2 H), 6.74 (t, *J* = 7.4 Hz, 1 H), 6.65 - 6.59 (m, *J* = 8.9 Hz, 2 H), 6.55 (d, *J* = 7.2 Hz, 2 H), 6.37 (t, *J* = 7.8 Hz, 2 H), 3.73 (s, 3 H), 1.17 (d, *J* = 7.0 Hz, 12 H), 1.05 (d, *J* = 6.7 Hz, 12 H); **^{13}C NMR (125 MHz**, **DMSO-d$_6$) δ** = 189.7, 168.2, 159.7, 149.1, 146.2, 145.2, 144.3, 142.9, 141.7, 137.0, 134.4, 133.7, 131.7, 130.5, 130.4, 128.7, 128.5, 127.4, 127.4, 126.7, 126.3, 124.9, 124.8, 124.1, 123.4, 122.0, 120.8, 119.4, 116.9, 113.7, 55.4, 28.3, 23.9, 23.4; **HRMS (ESI)** calcd for $C_{53}H_{55}AuON_3^+$ (M - OTf)$^+$ 946.4187, found 946.4175.

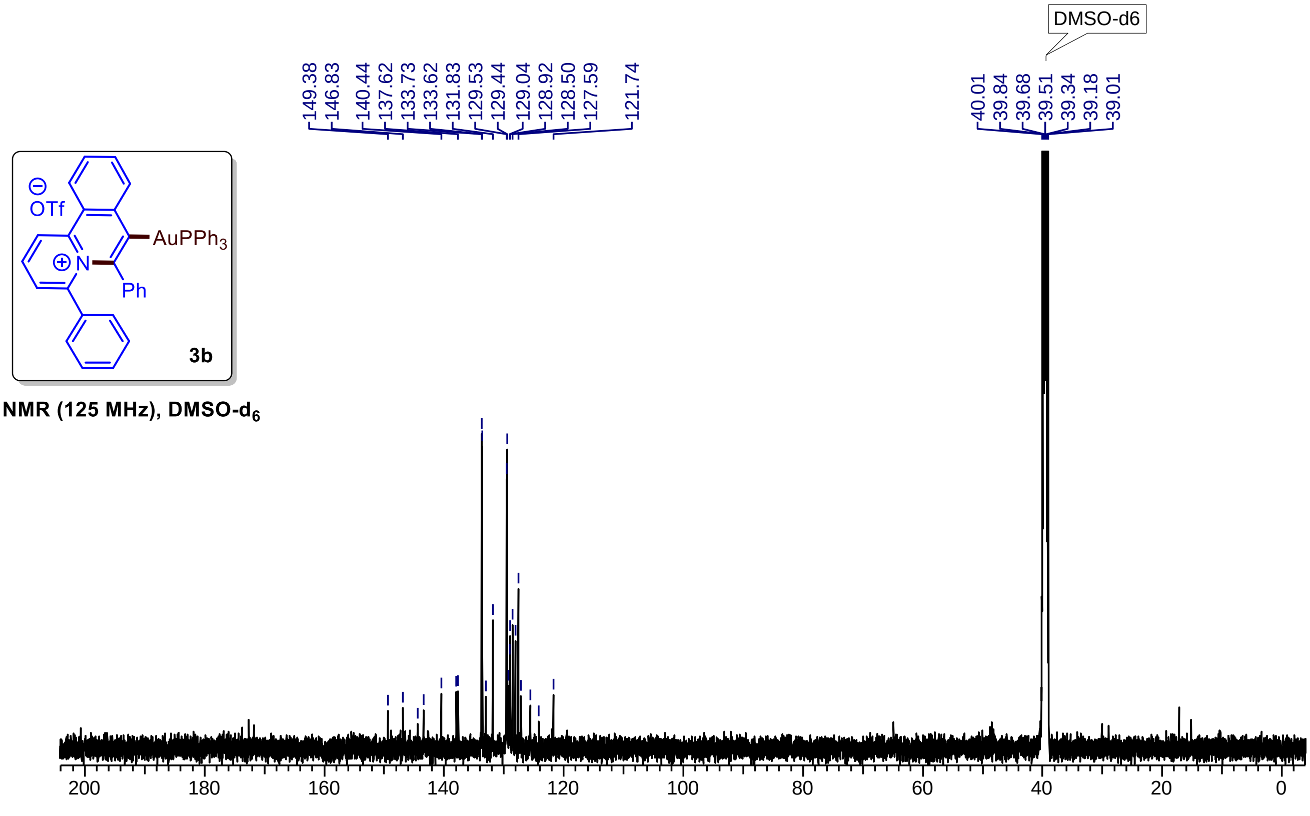
4.6 Selected NMR spectra



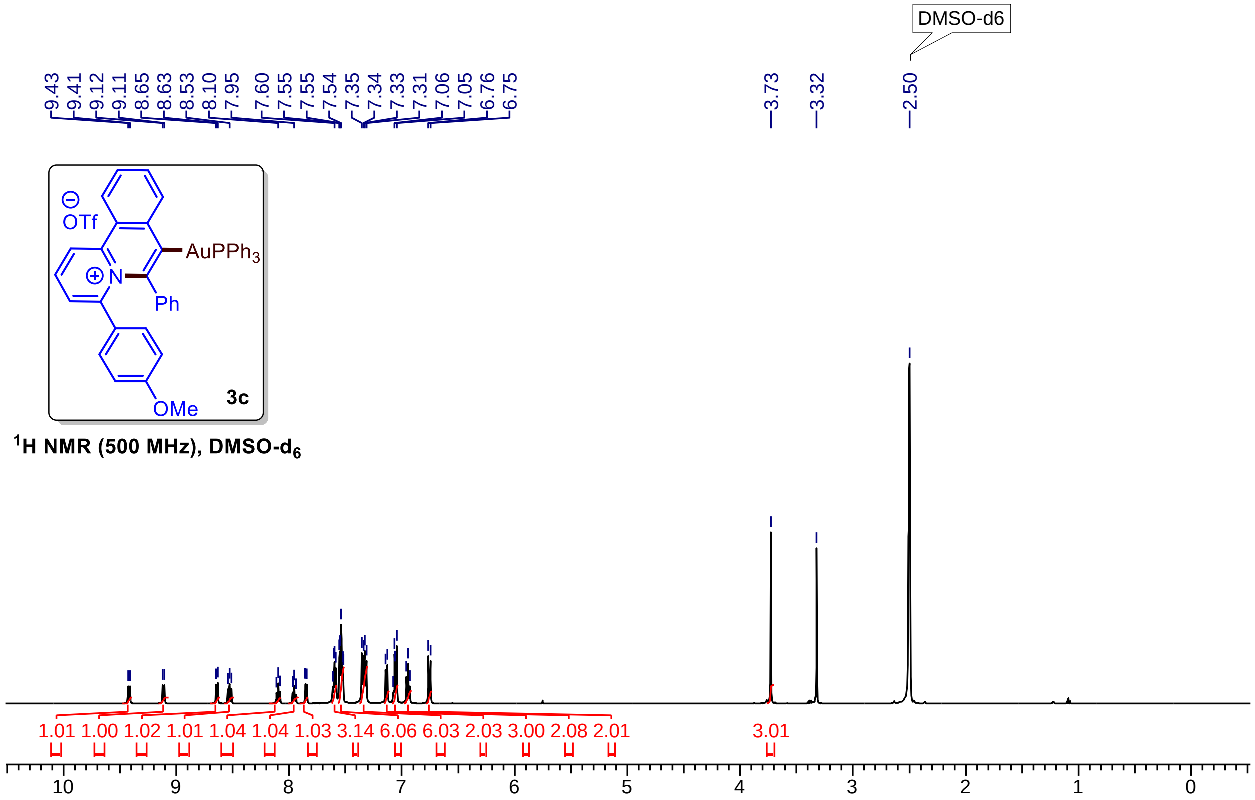




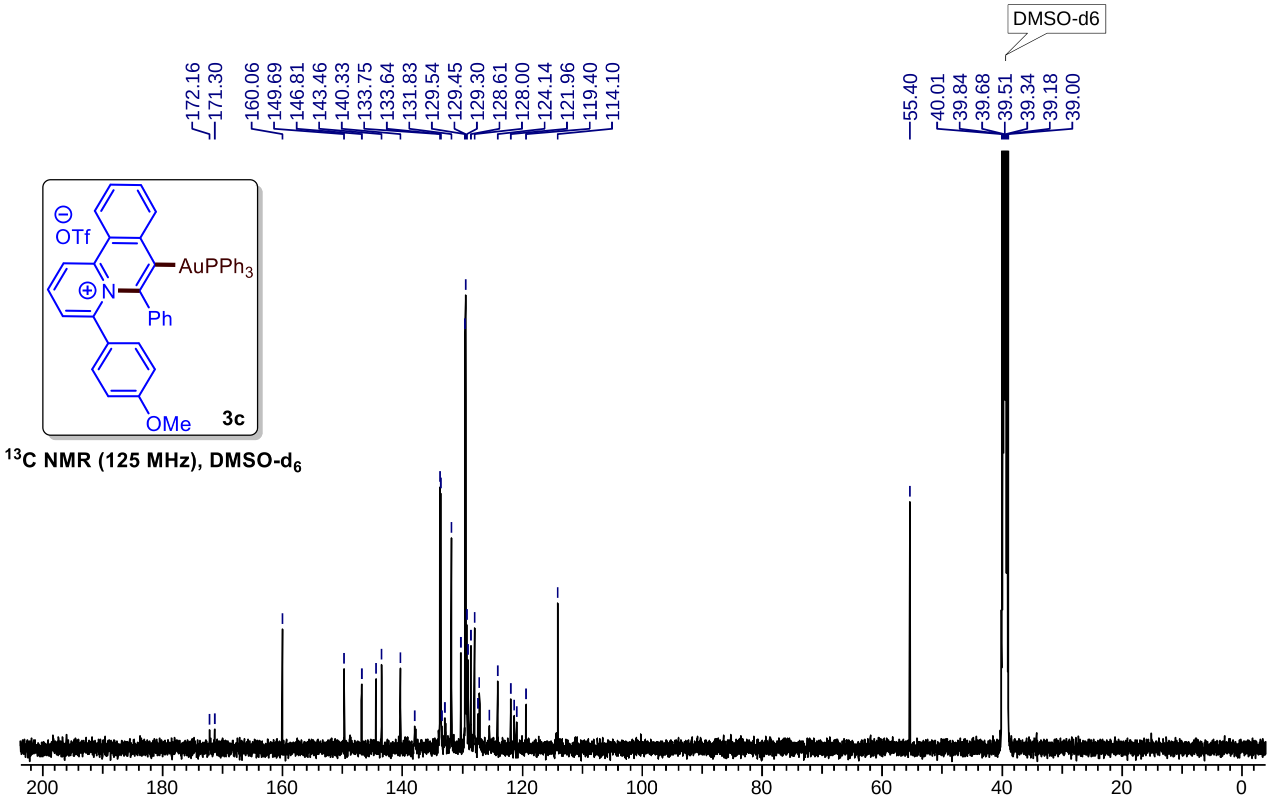
^{1}H NMR (500 MHz), DMSO-d$_6$)



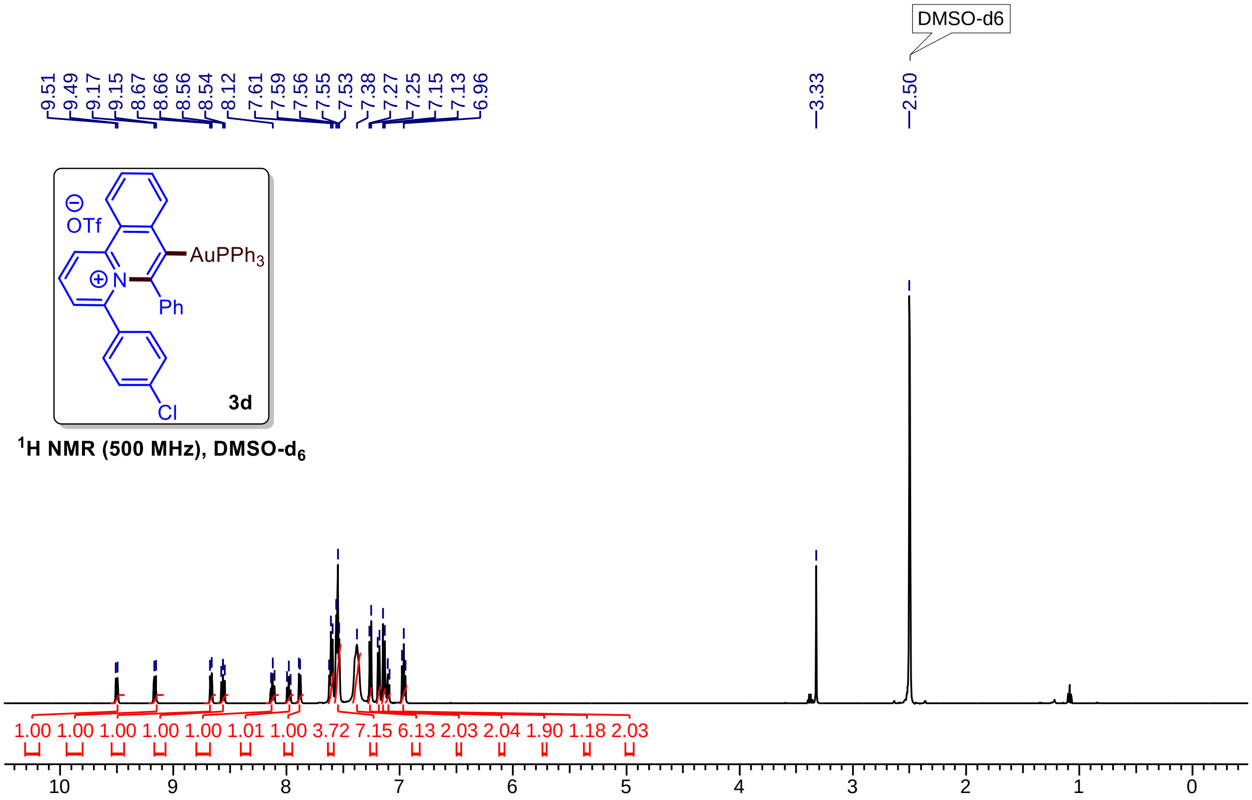
^{13}C NMR (125 MHz), DMSO-d$_6$



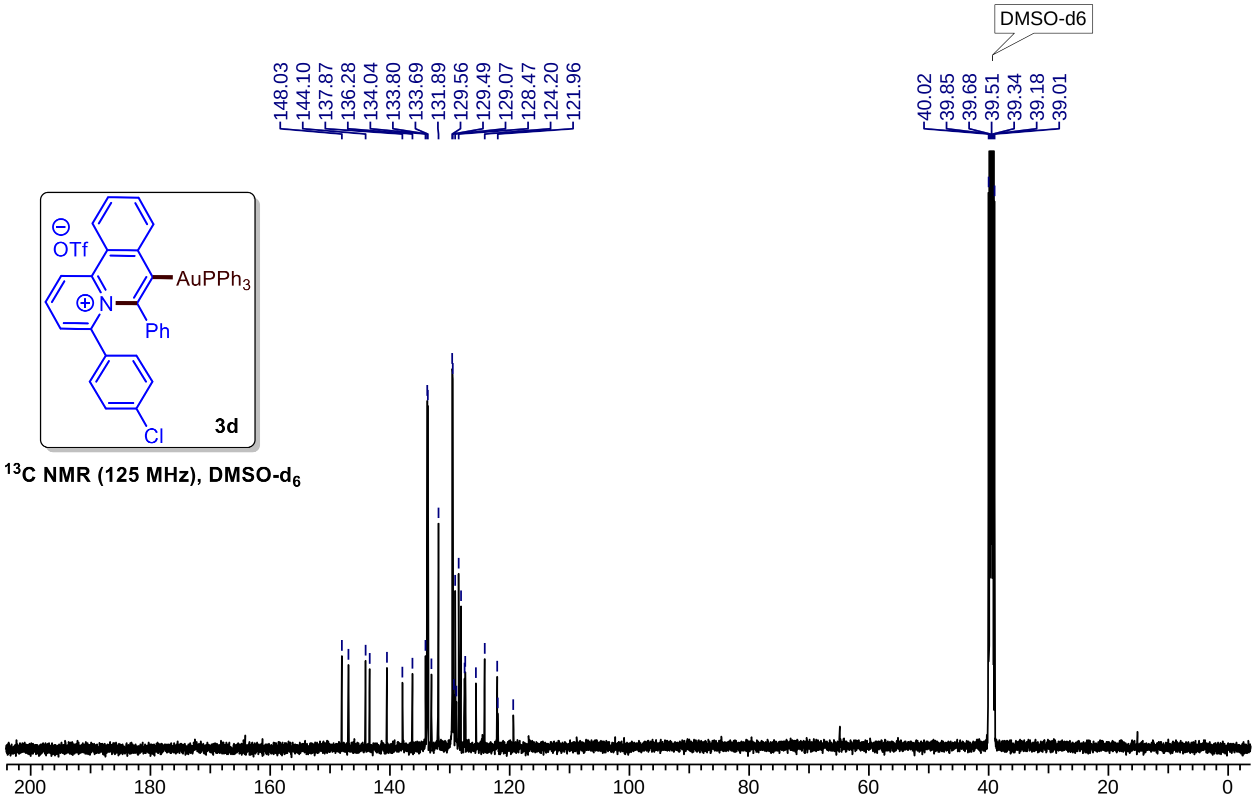
^{1}H NMR (500 MHz), DMSO-d_6



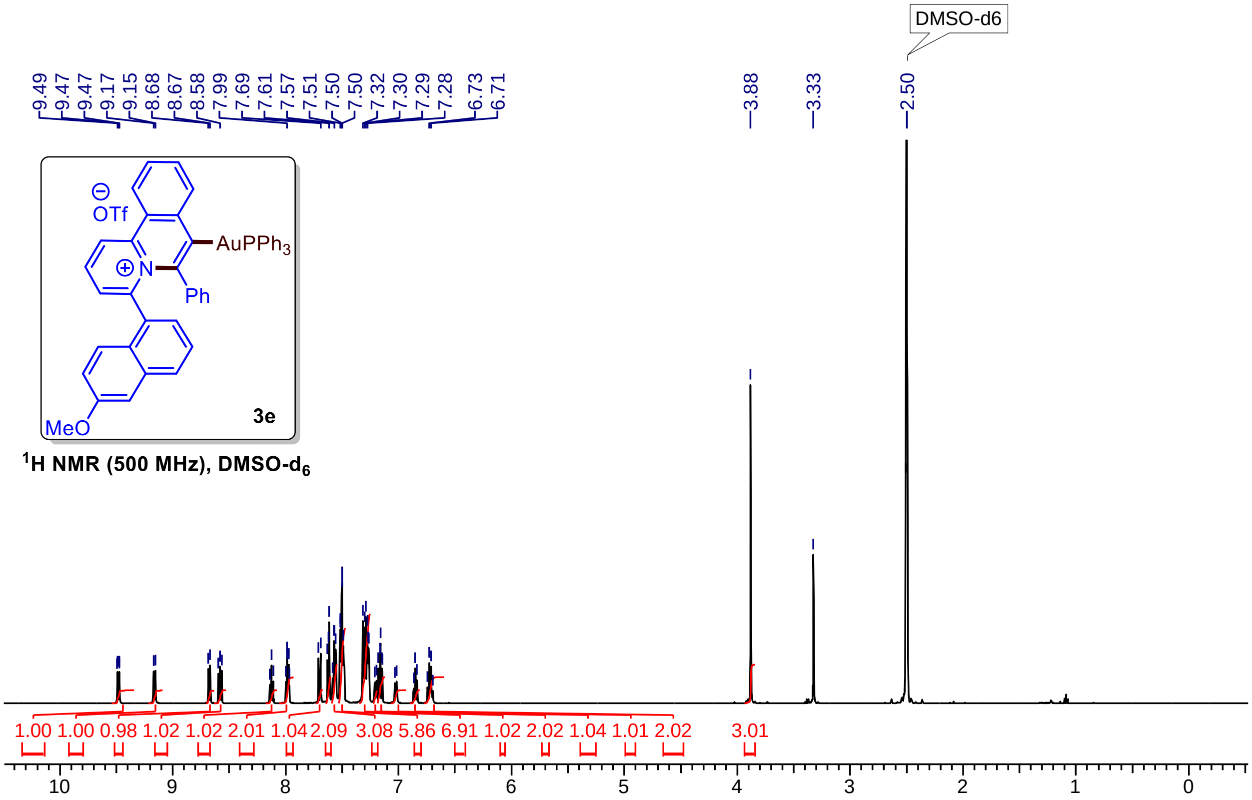
^{13}C NMR (125 MHz), DMSO-d_6



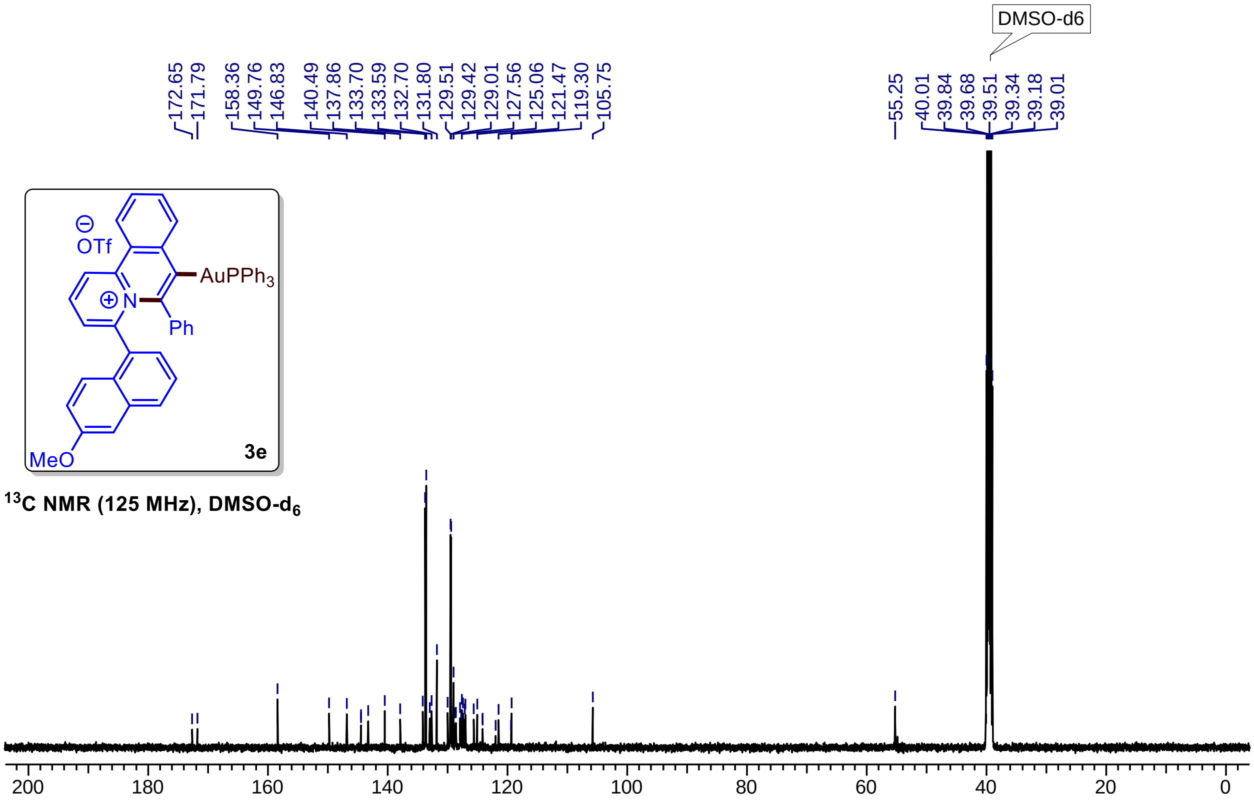
^{1}H NMR (500 MHz), DMSO-d$_6$



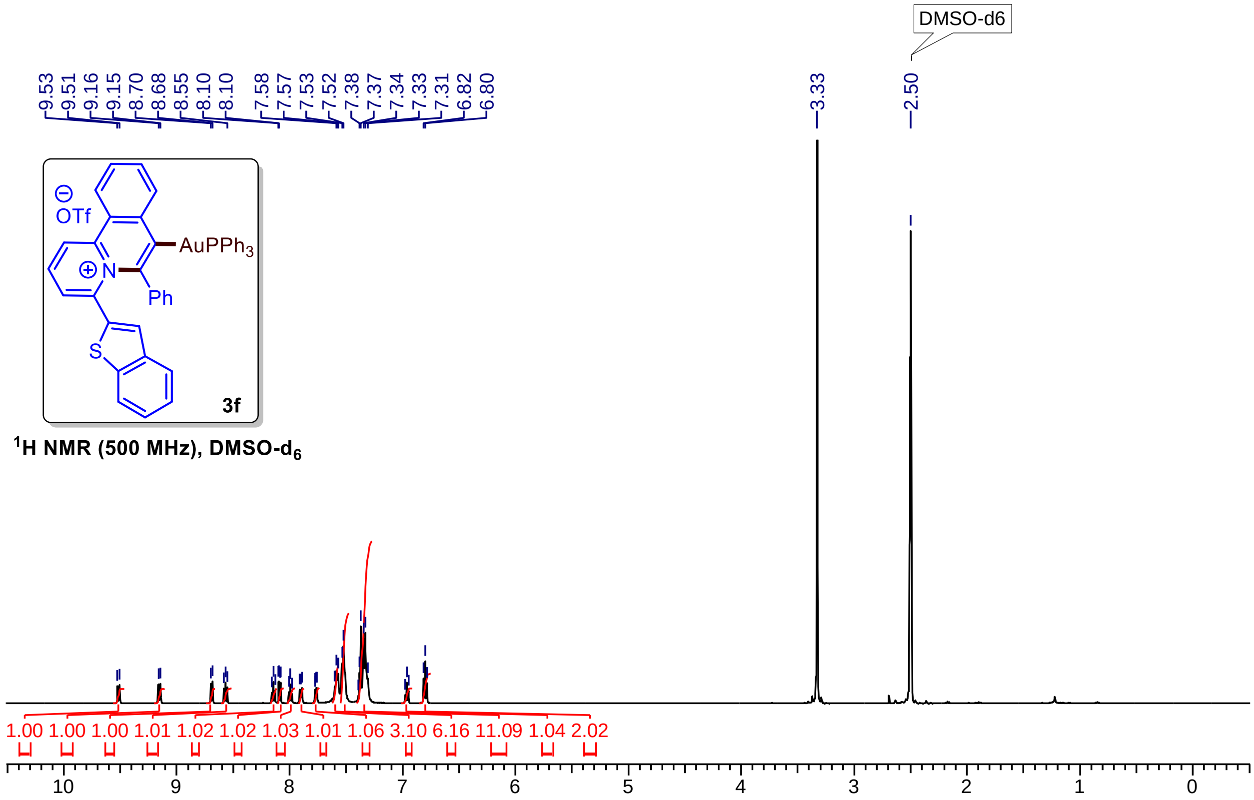
^{13}C NMR (125 MHz), DMSO-d$_6$



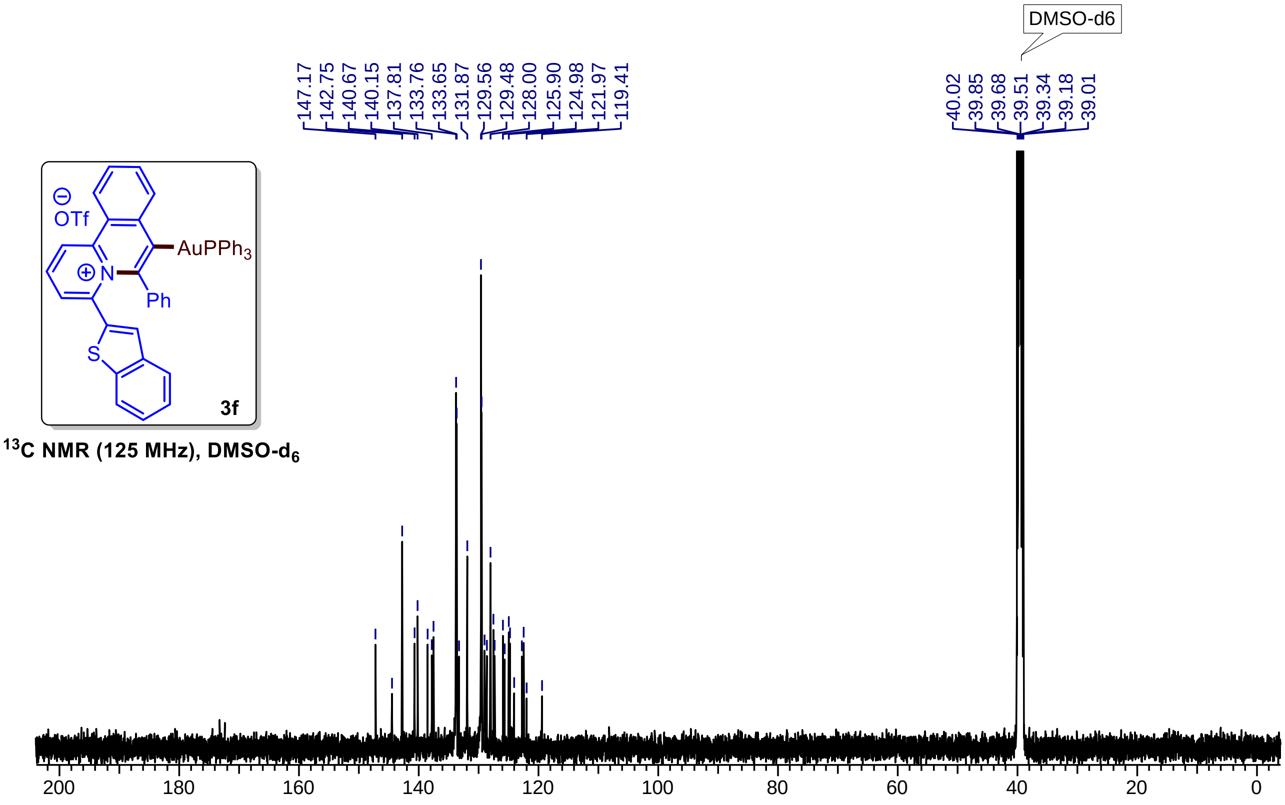
^{1}H NMR (500 MHz), DMSO-d$_6$



^{13}C NMR (125 MHz), DMSO-d$_6$



^{1}H NMR (500 MHz), DMSO-d$_6$



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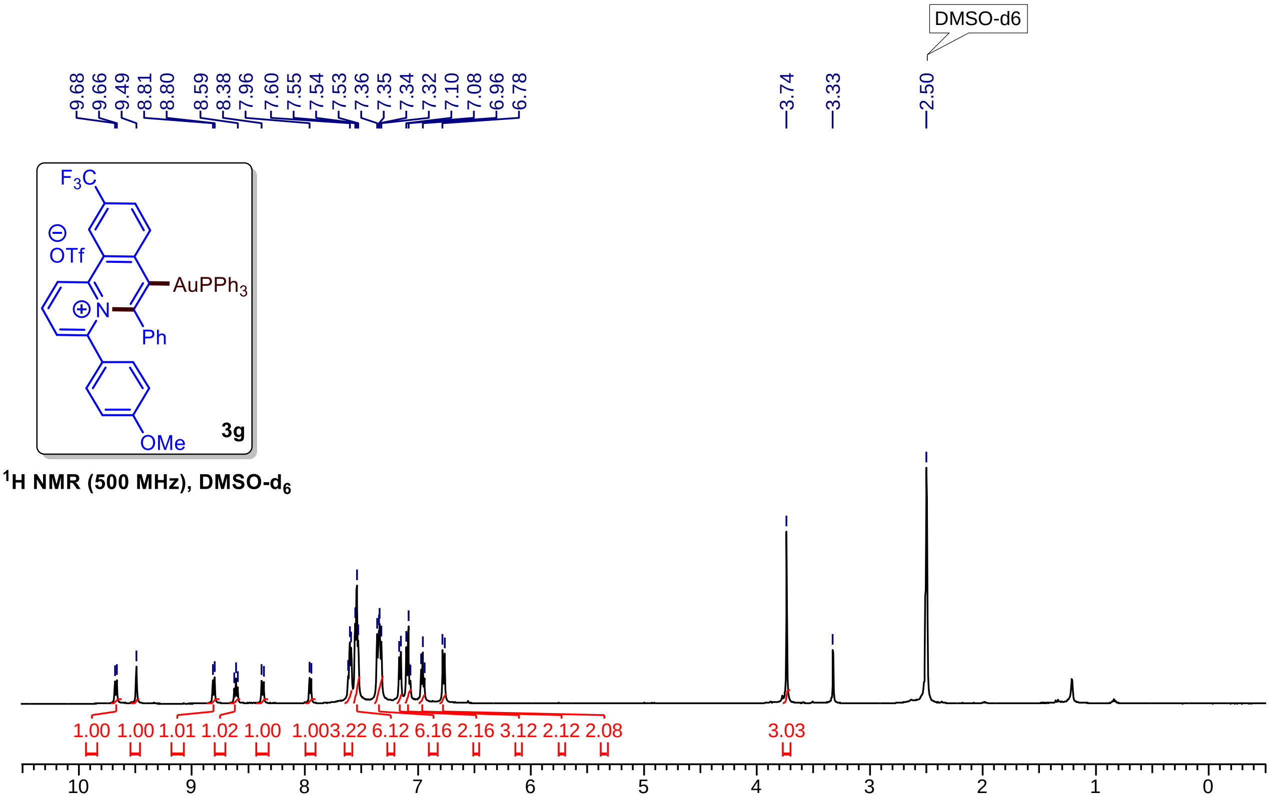

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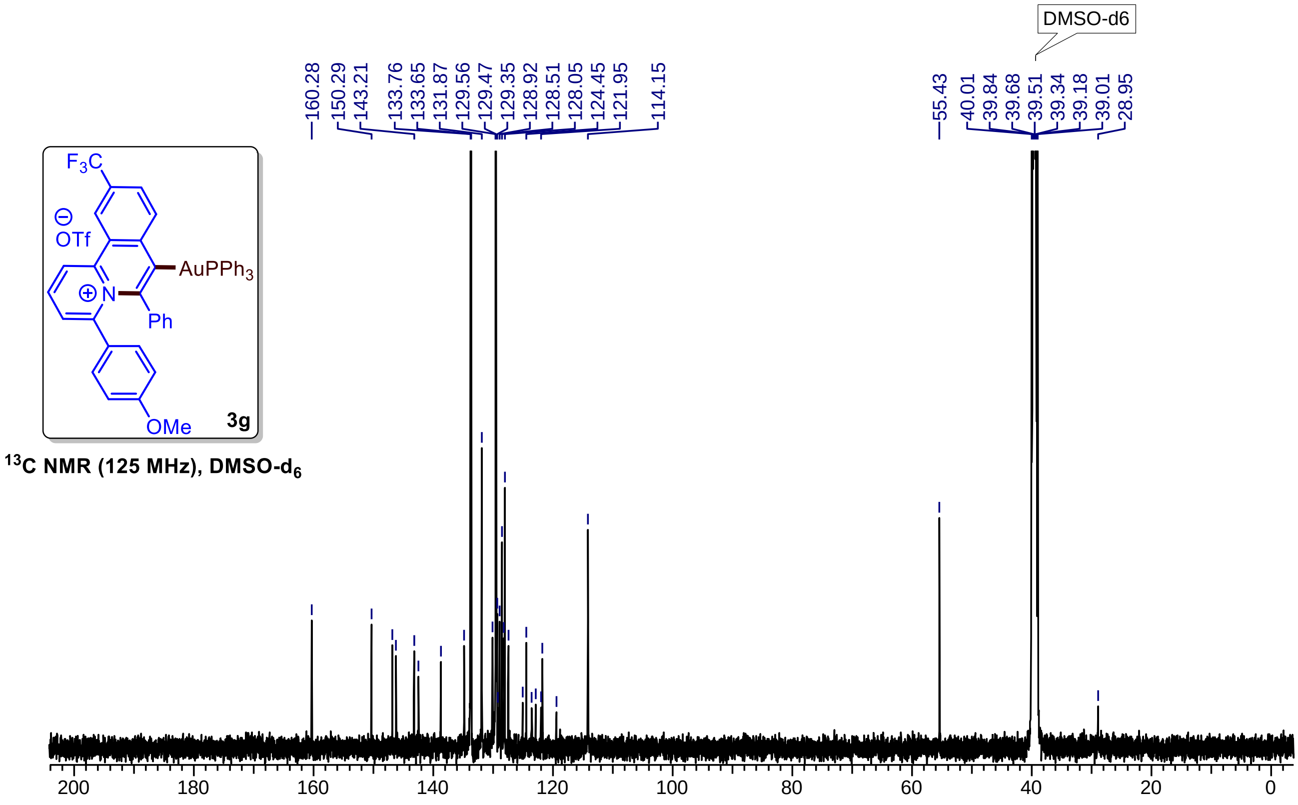

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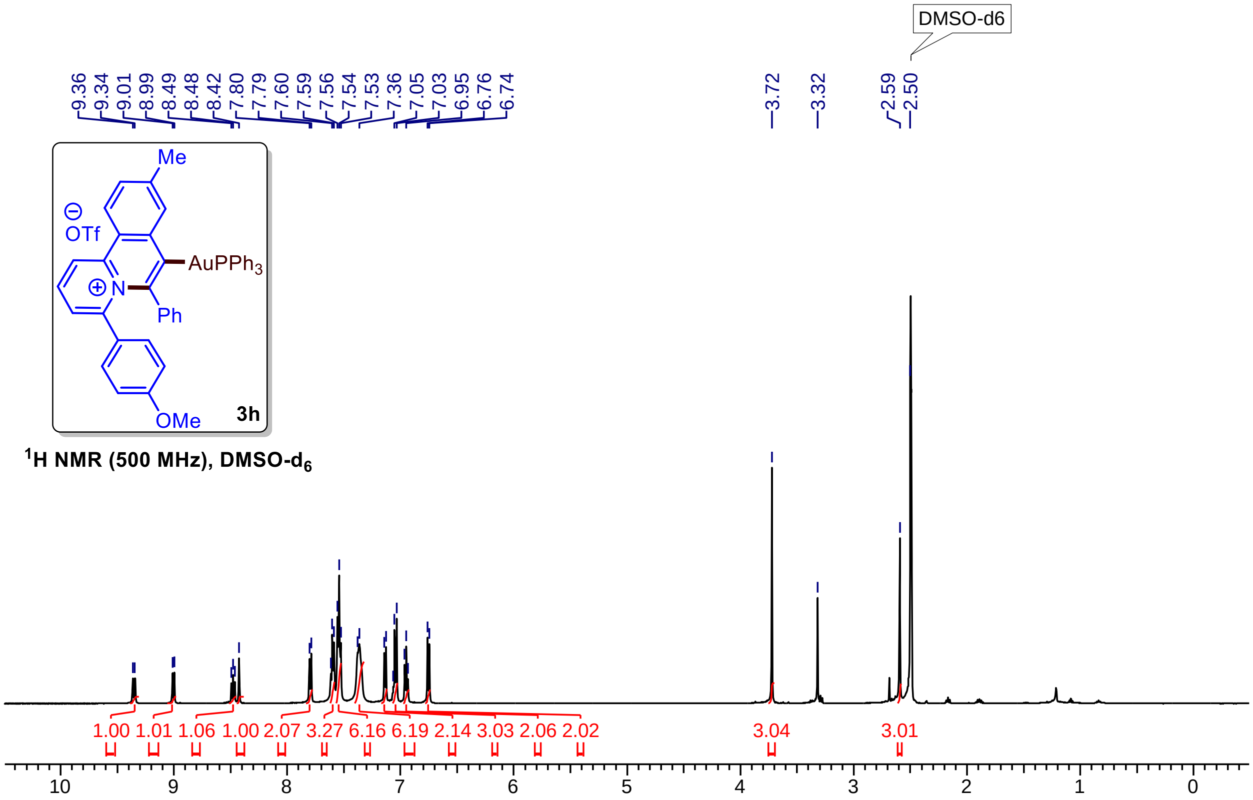

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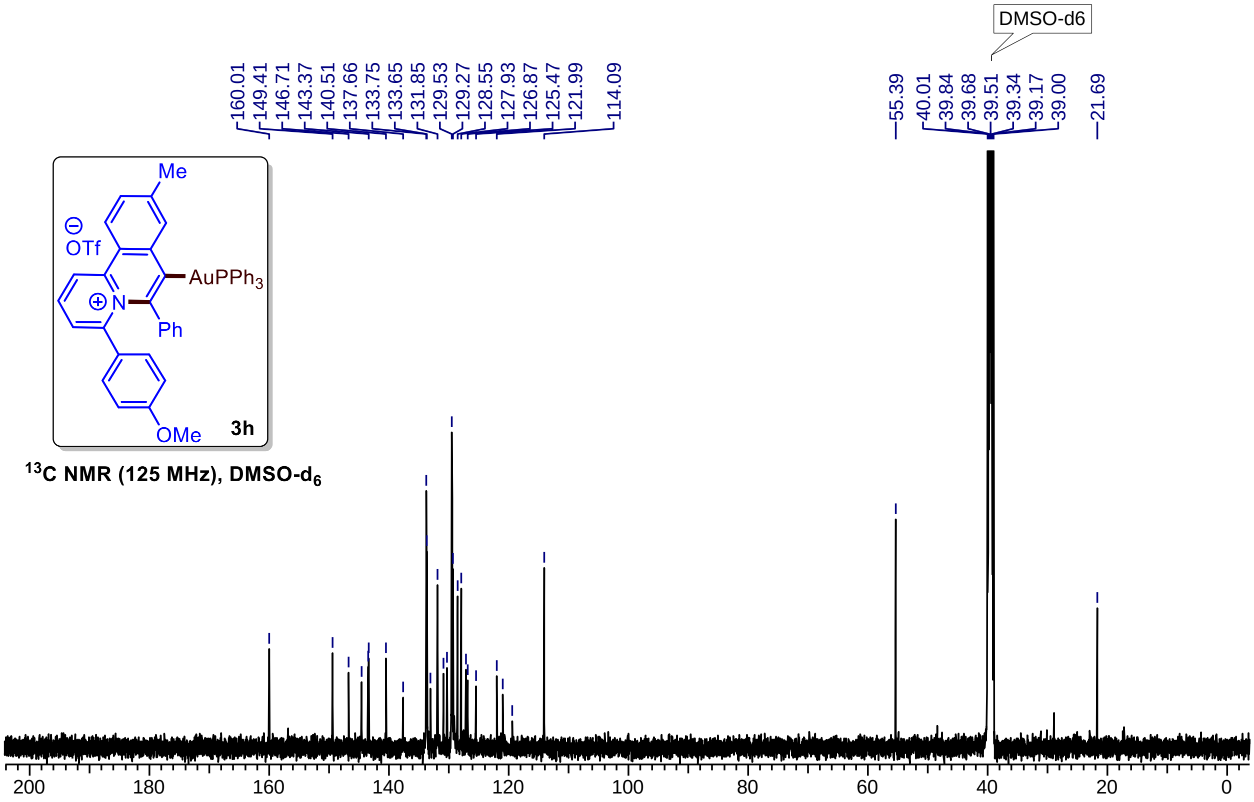

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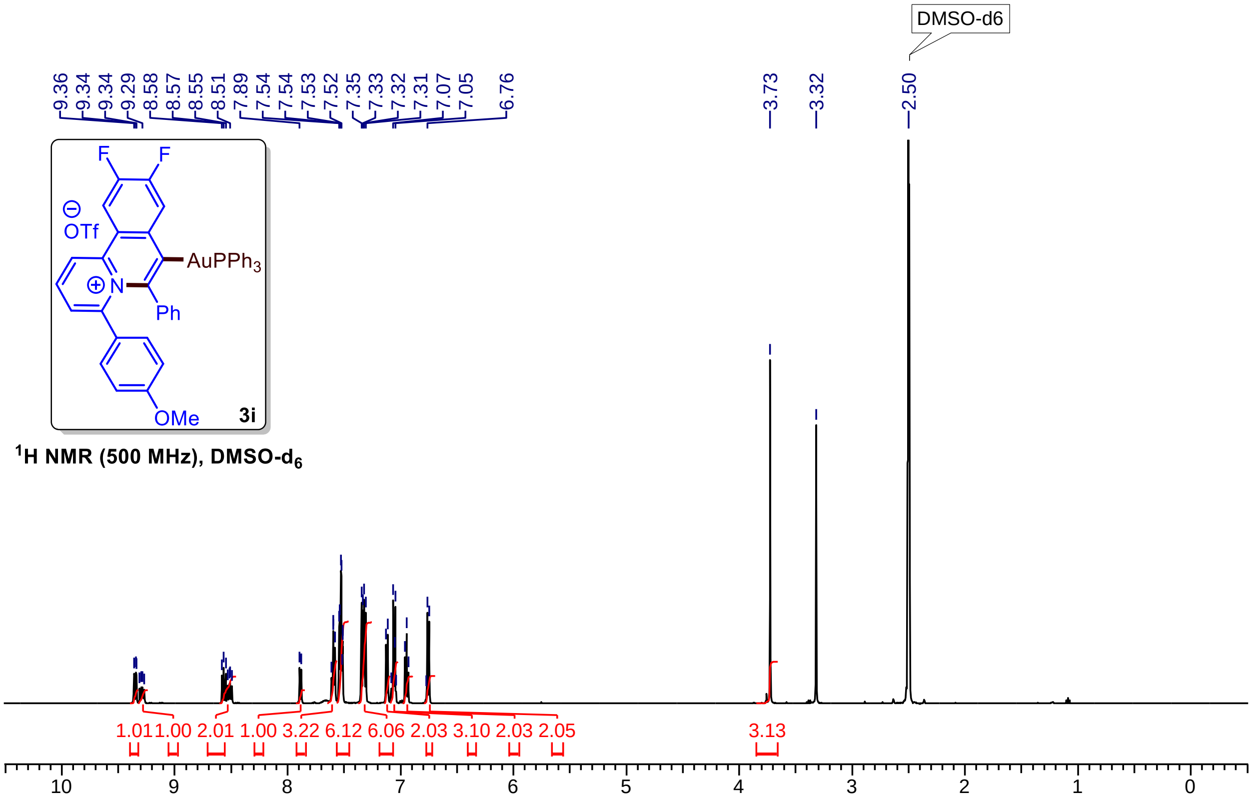

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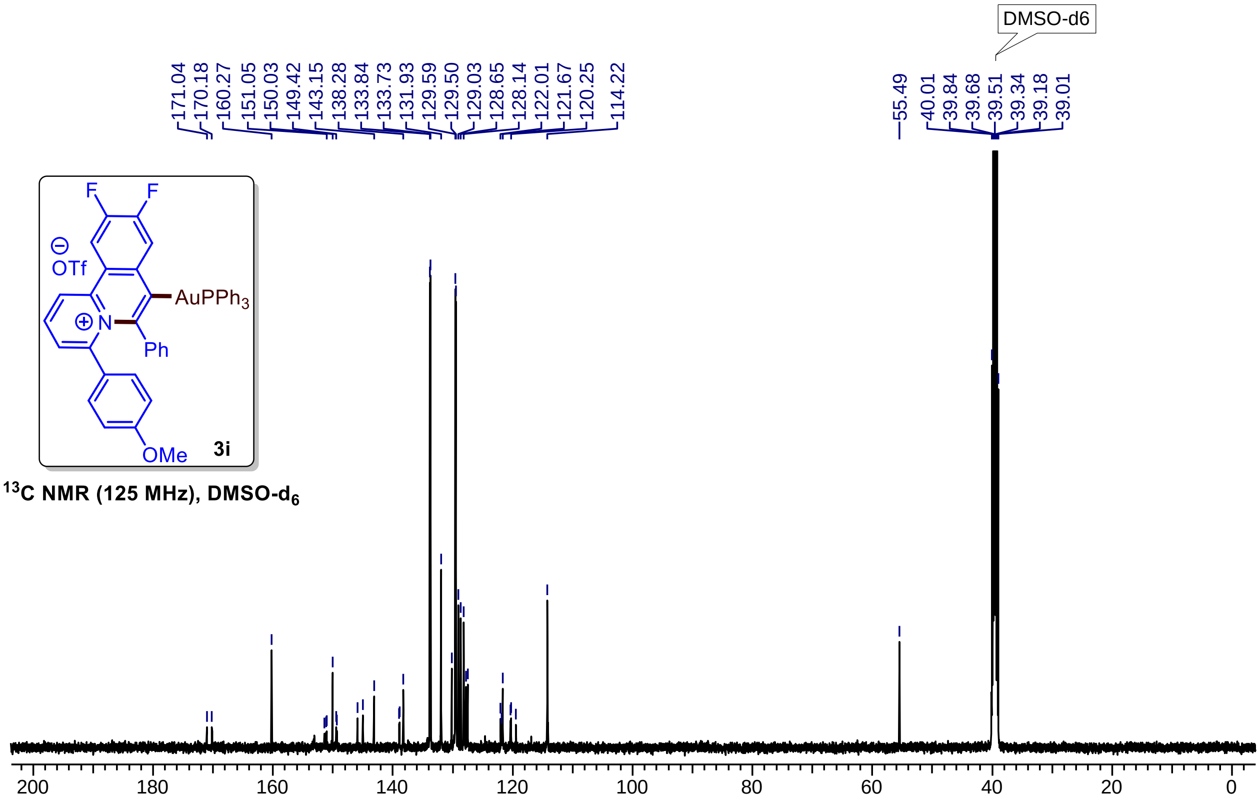

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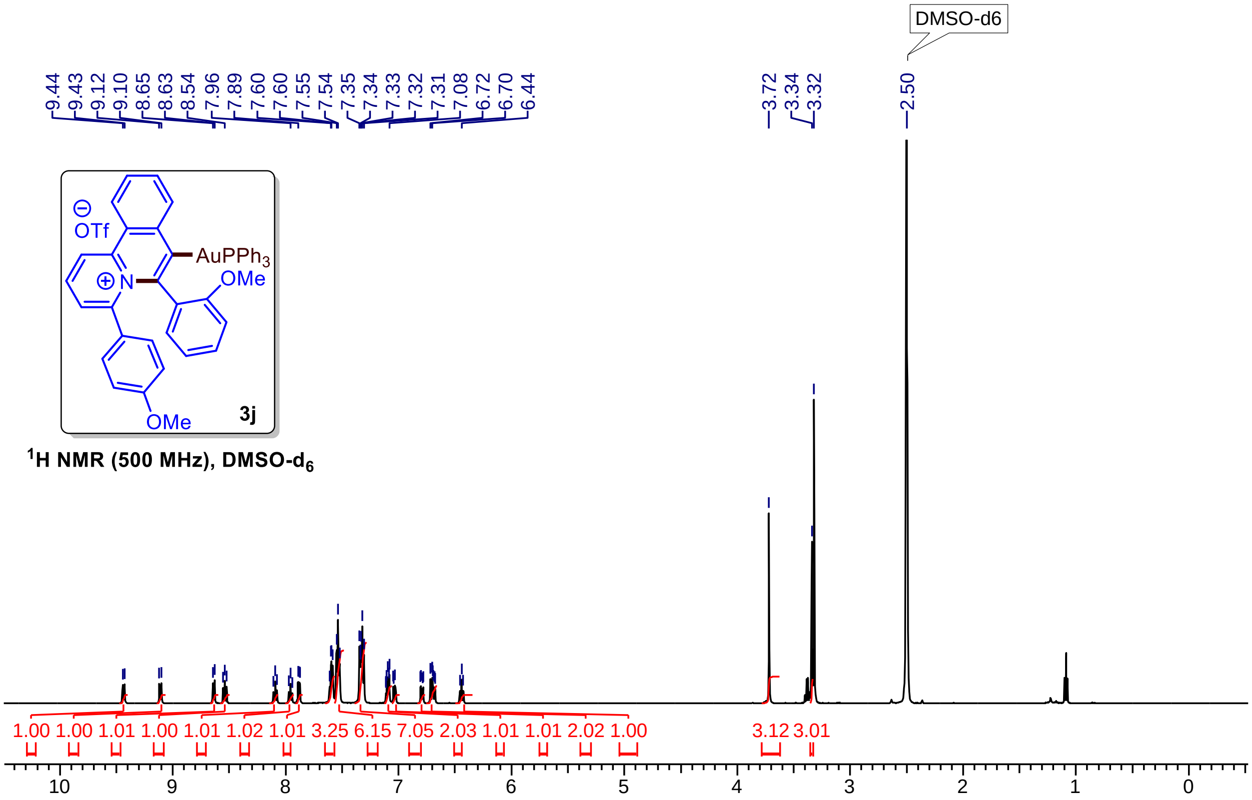
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9.43
9.12
9.10
8.65
8.63
8.54
7.96
7.89
7.60
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7.55
7.54
7.35
7.34
7.33
7.32
7.31
7.08
6.72
6.70
6.44
3.72
3.34
3.32
2.50
OTf
AuPPh3
OMe
N
OMe
3j
1H NMR (500 MHz), DMSO-d6
1.00 1.00 1.01 1.00 1.01 1.02 1.01 3.25 6.15 7.05 2.03 1.01 1.01 2.02 1.00
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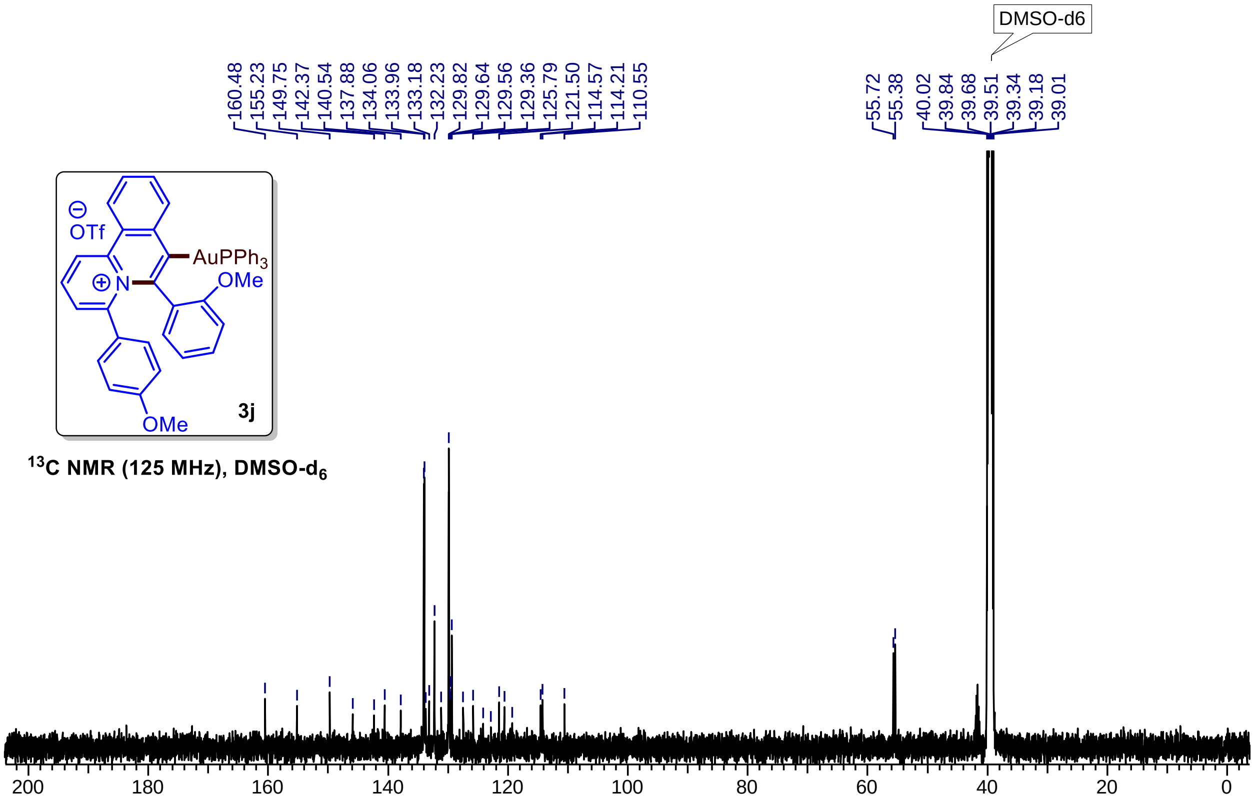
5
4
3
2
1
0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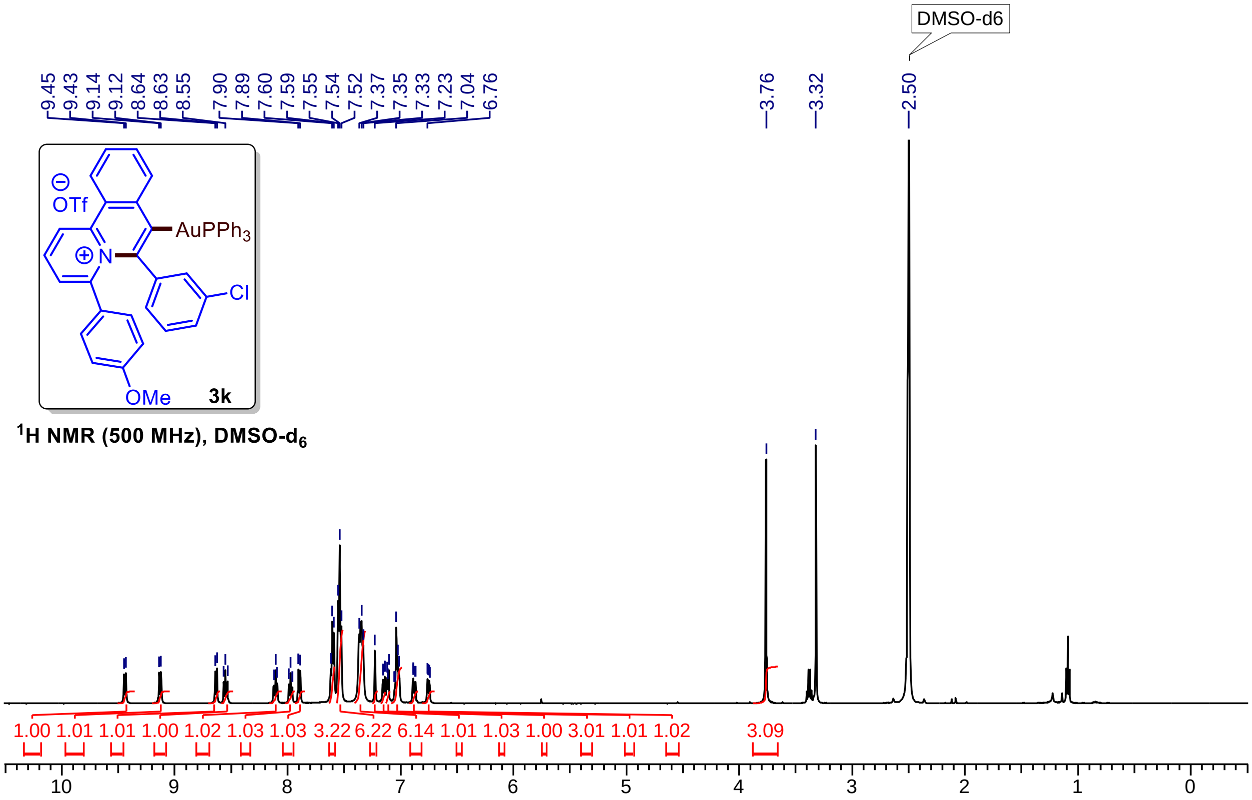
155.23
149.75
142.37
140.54
137.88
134.06
133.96
133.18
132.23
129.82
129.64
129.56
129.36
125.79
121.50
114.57
114.21
110.55
55.72
55.38
40.02
39.84
39.68
39.51
39.34
39.18
39.01
OTf
AuPPh3
OMe
N
OMe
3j
13C NMR (125 MHz), DMSO-d6
200
180
160
140
120
100
80
60
40
20
0



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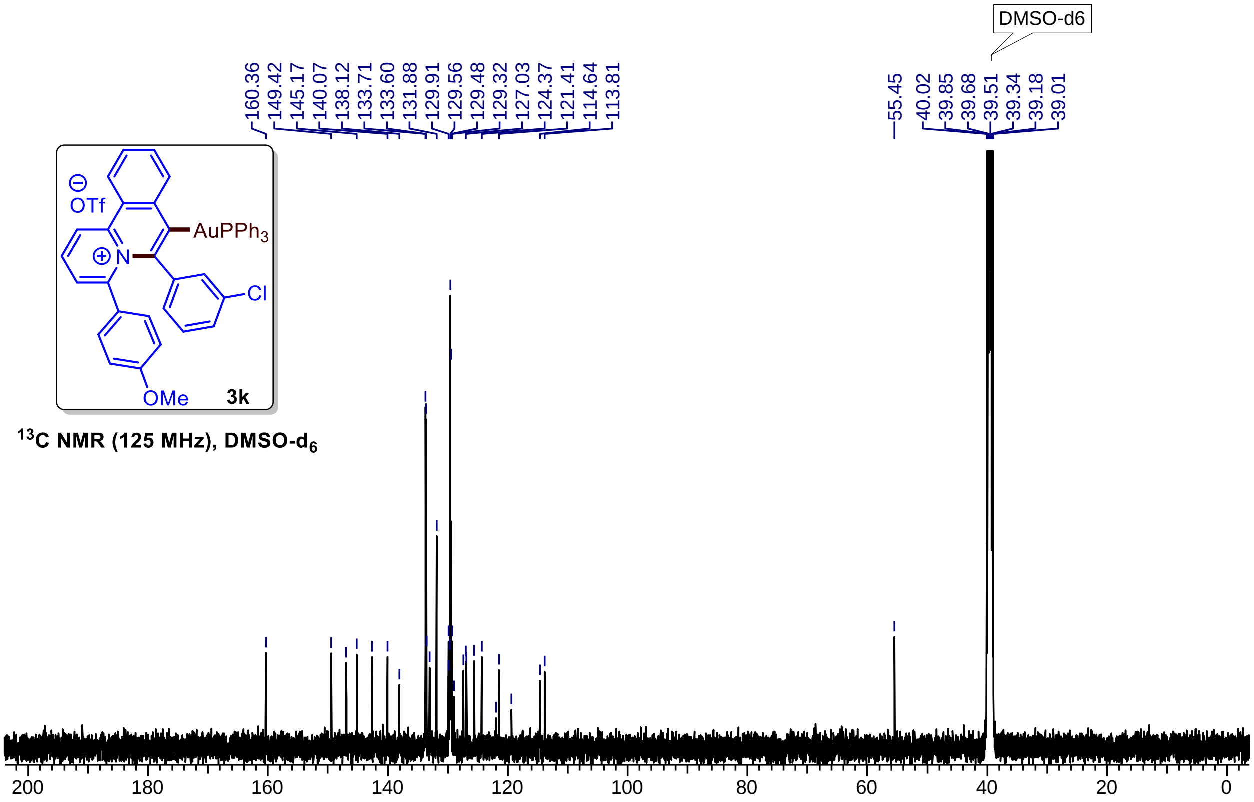

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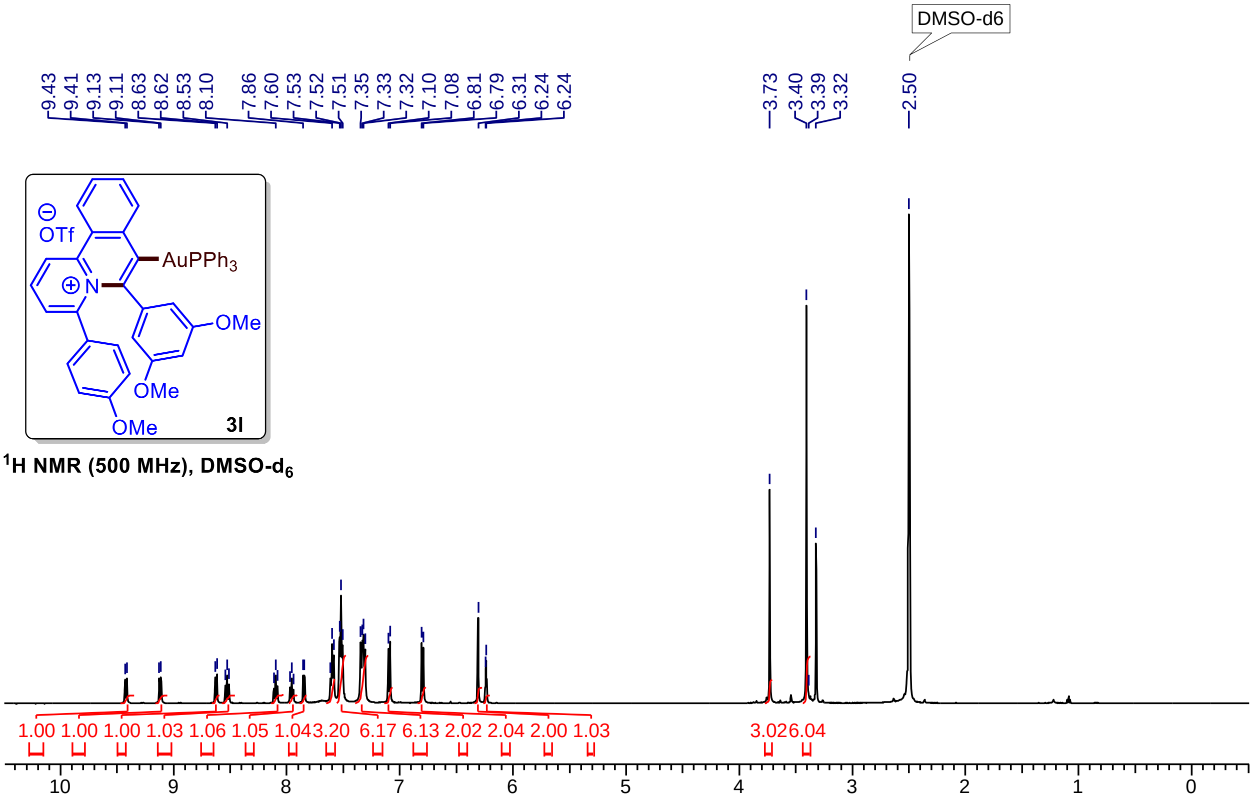

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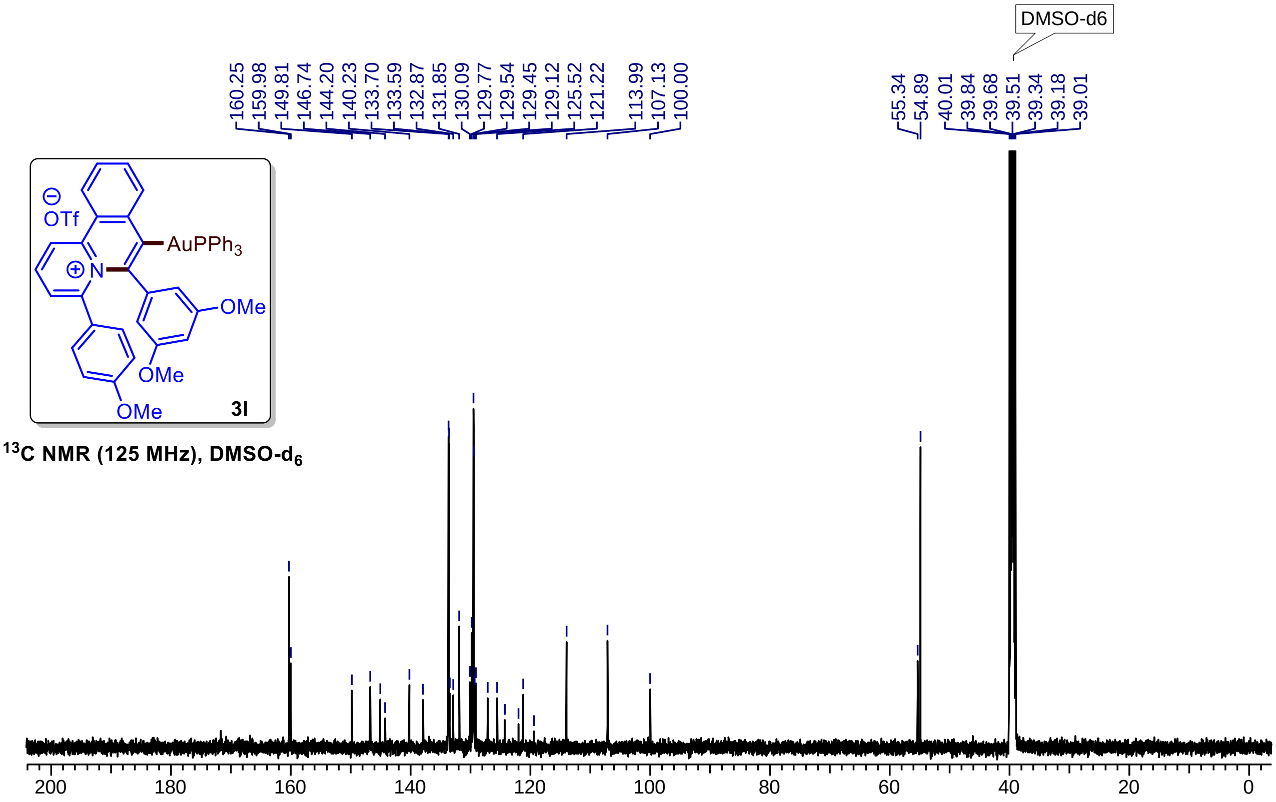

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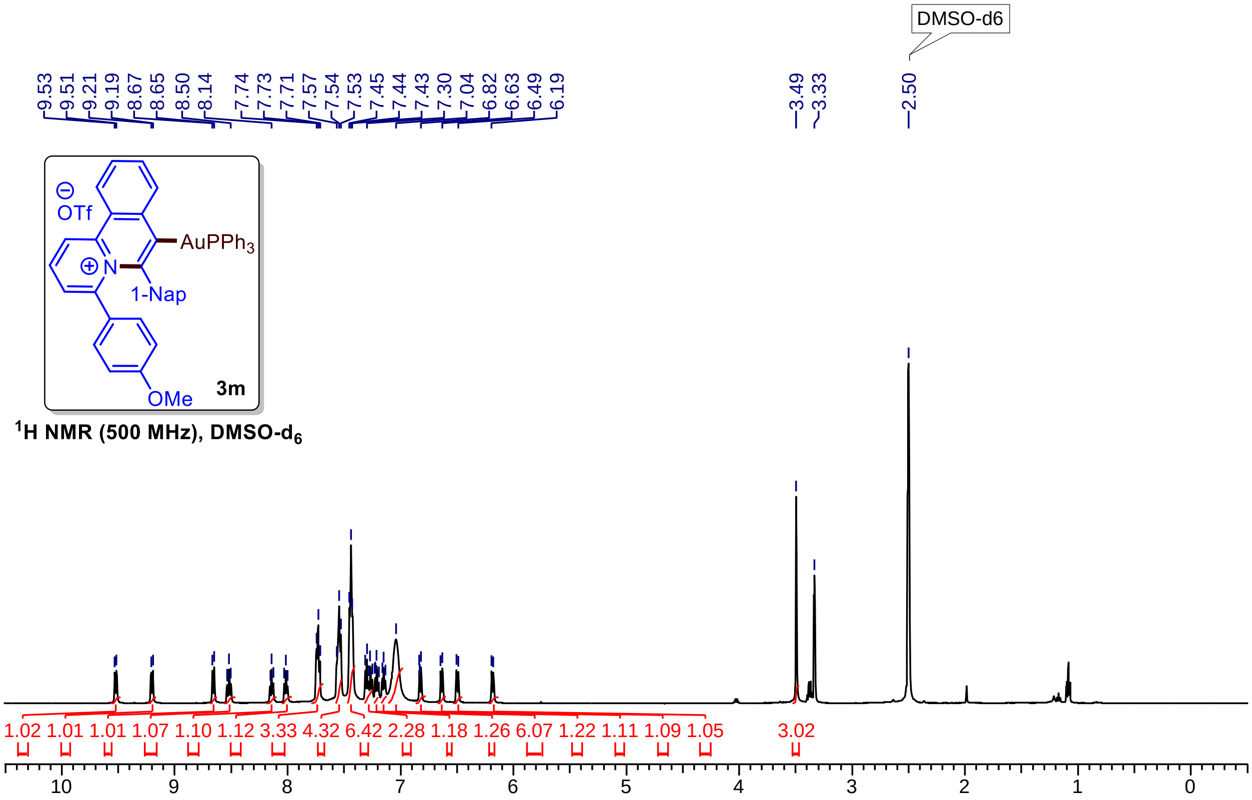

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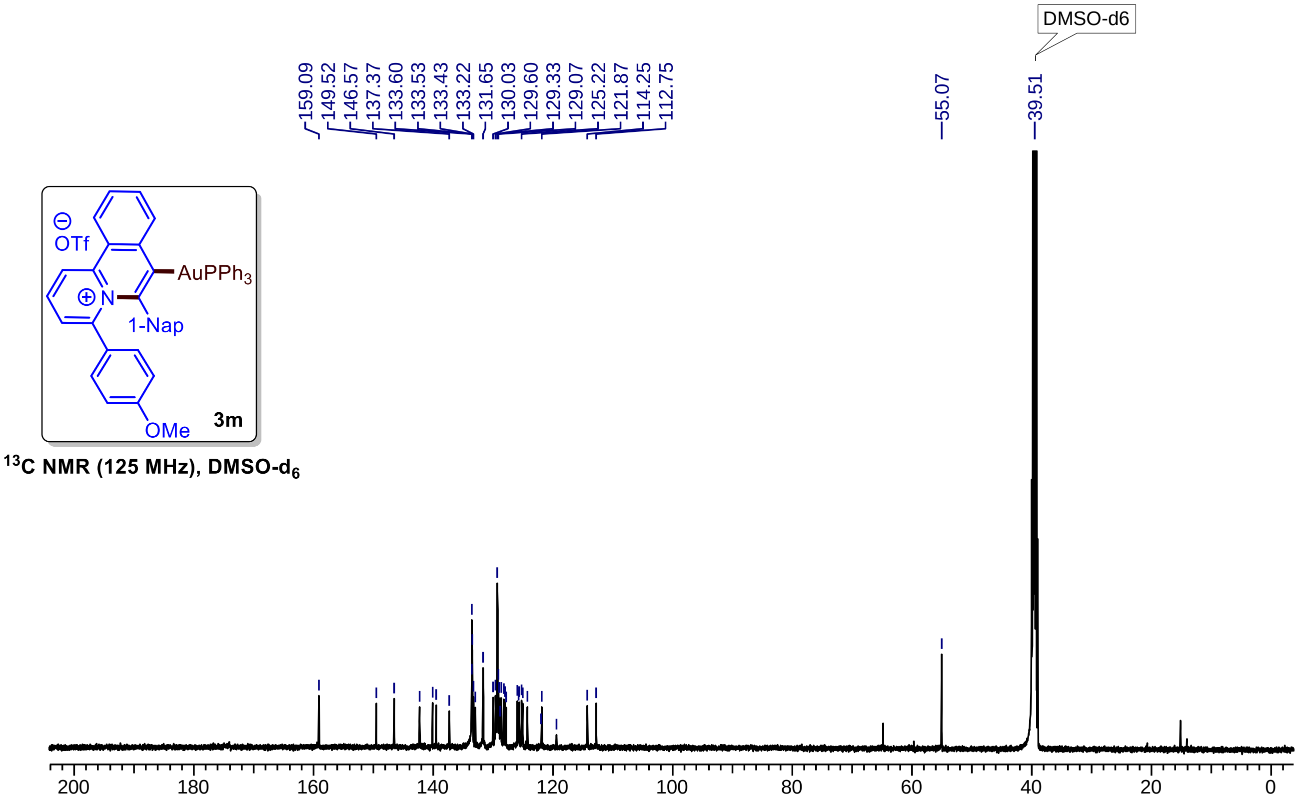

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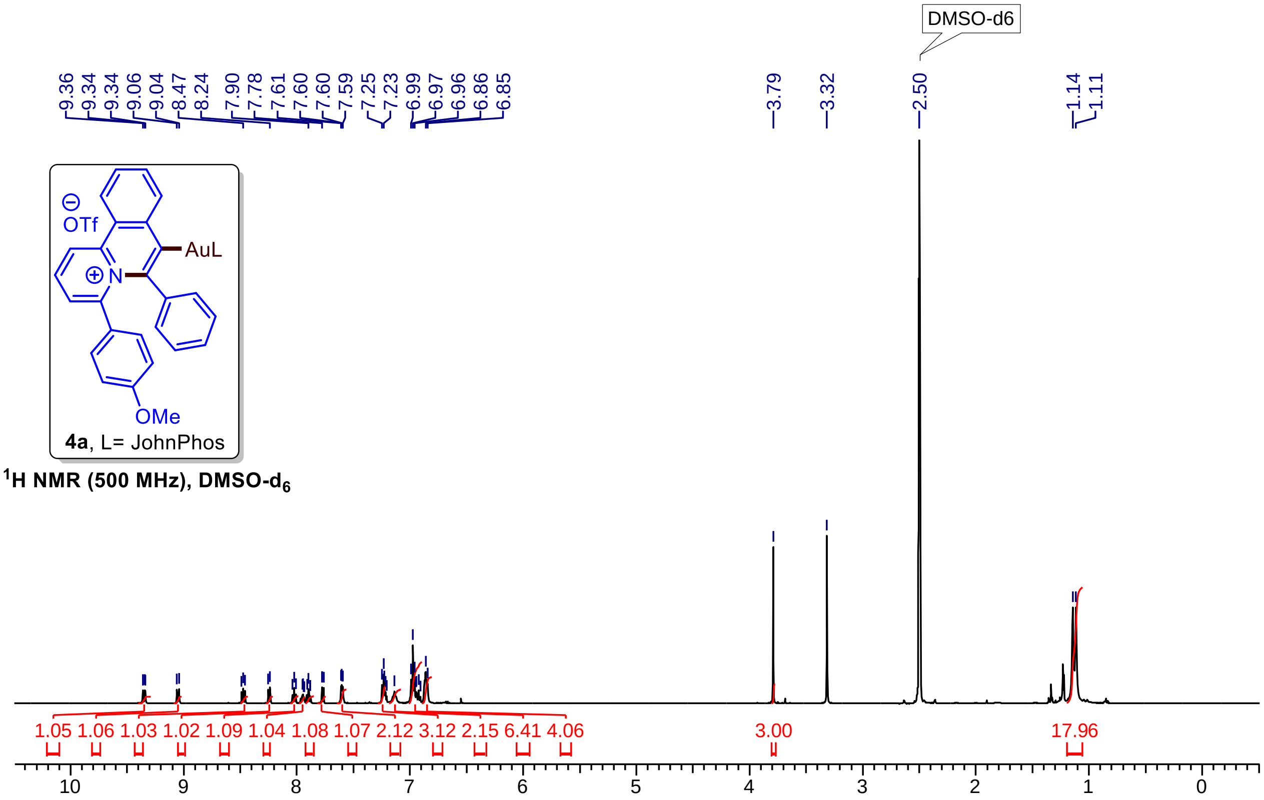

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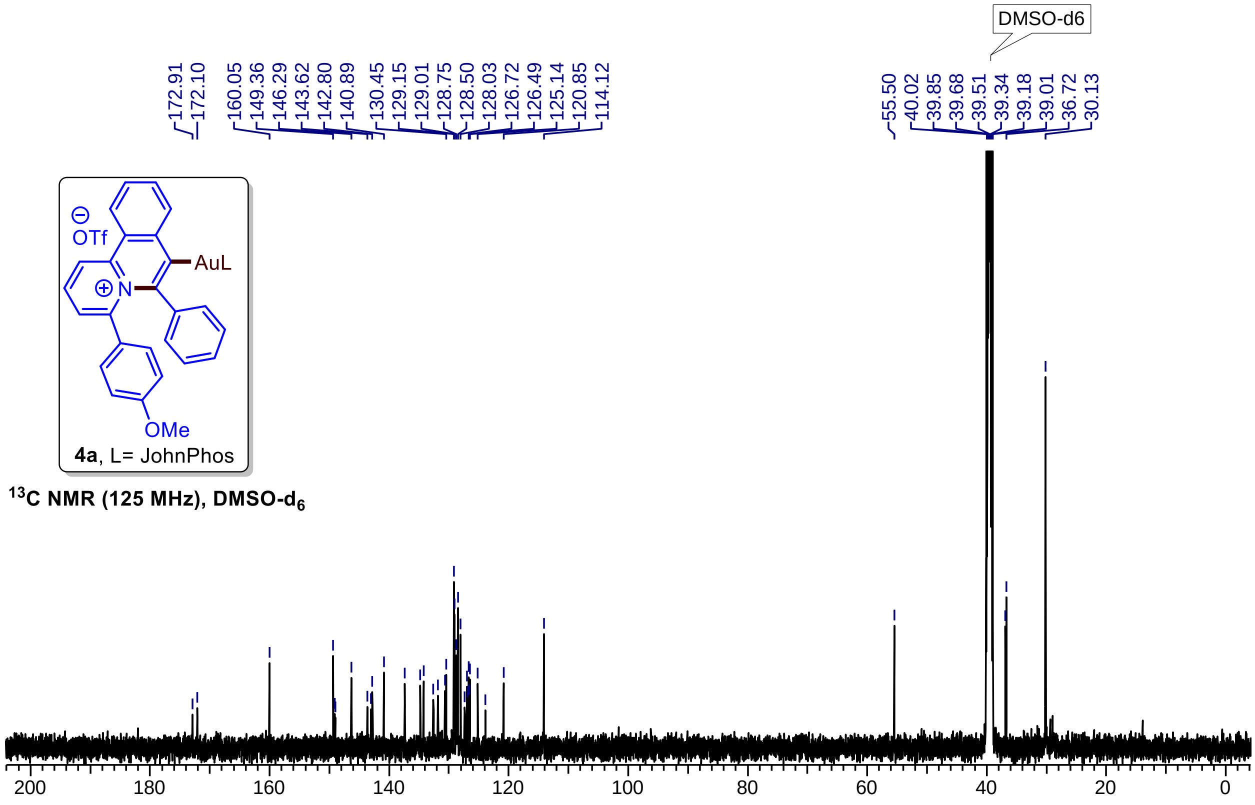

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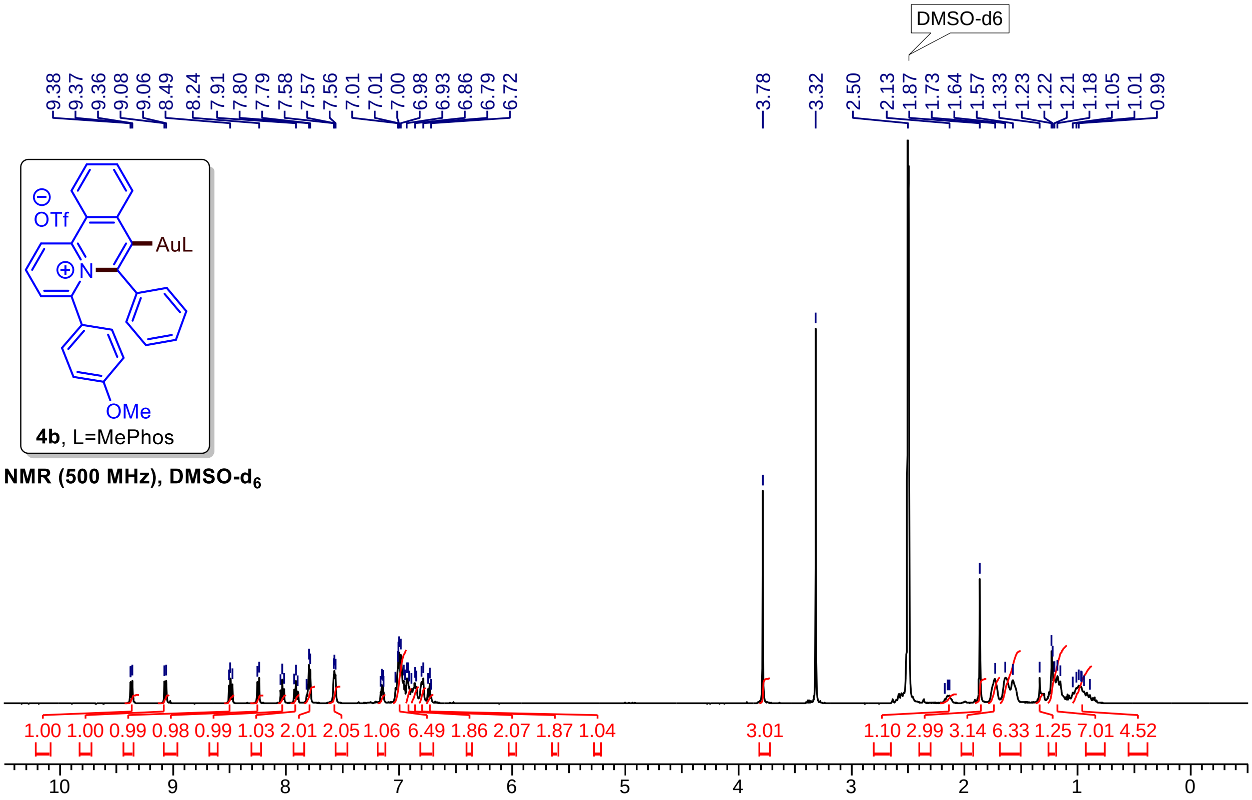

4b, L=MePhos

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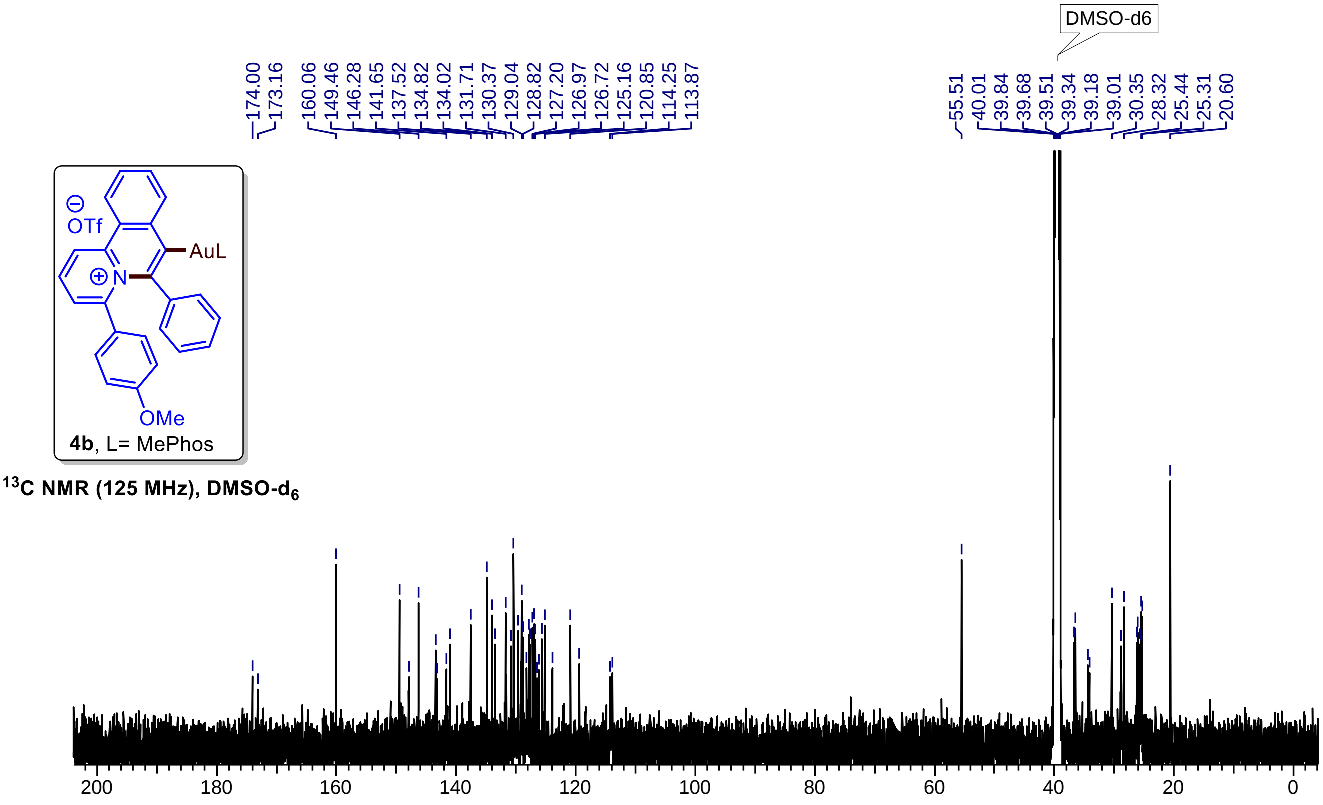
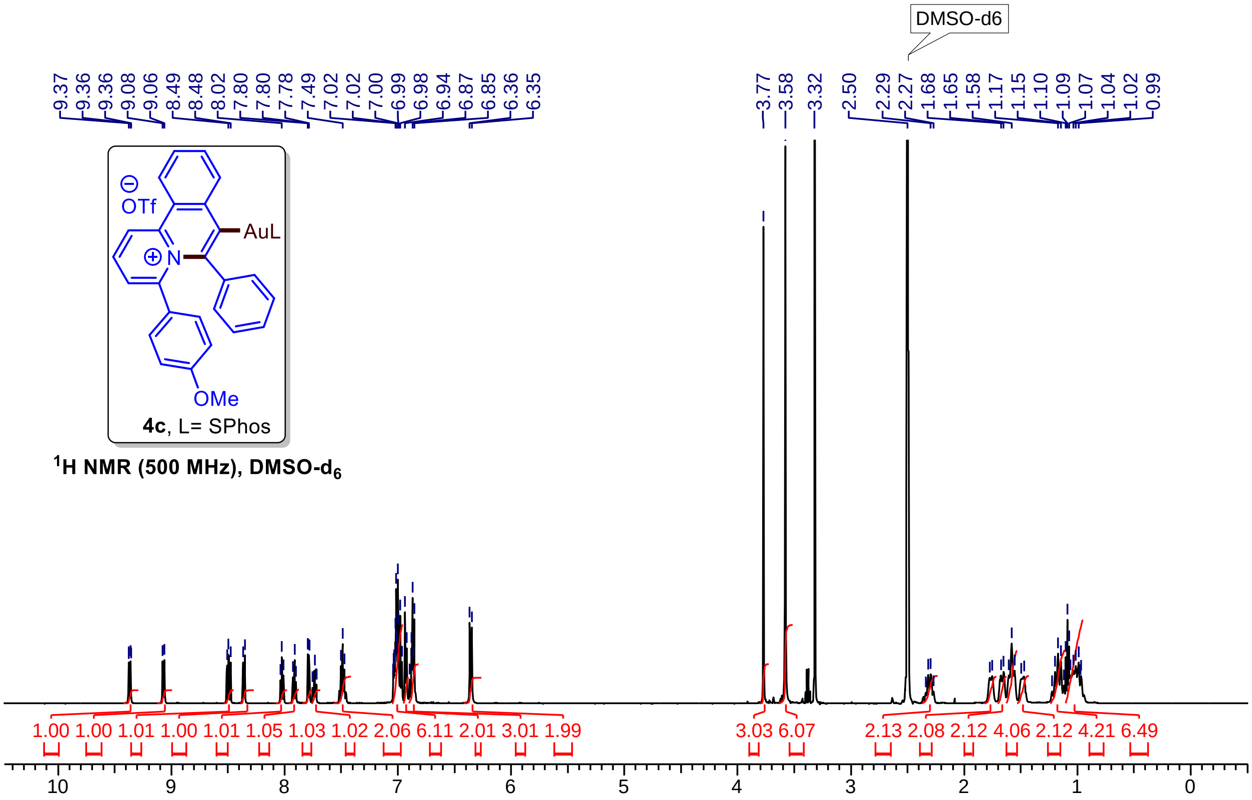


4b, L= MePhos

^{13}C NMR (125 MHz), DMSO-d$_6$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9.36
9.36
9.08
9.06
8.49
8.48
8.02
7.80
7.80
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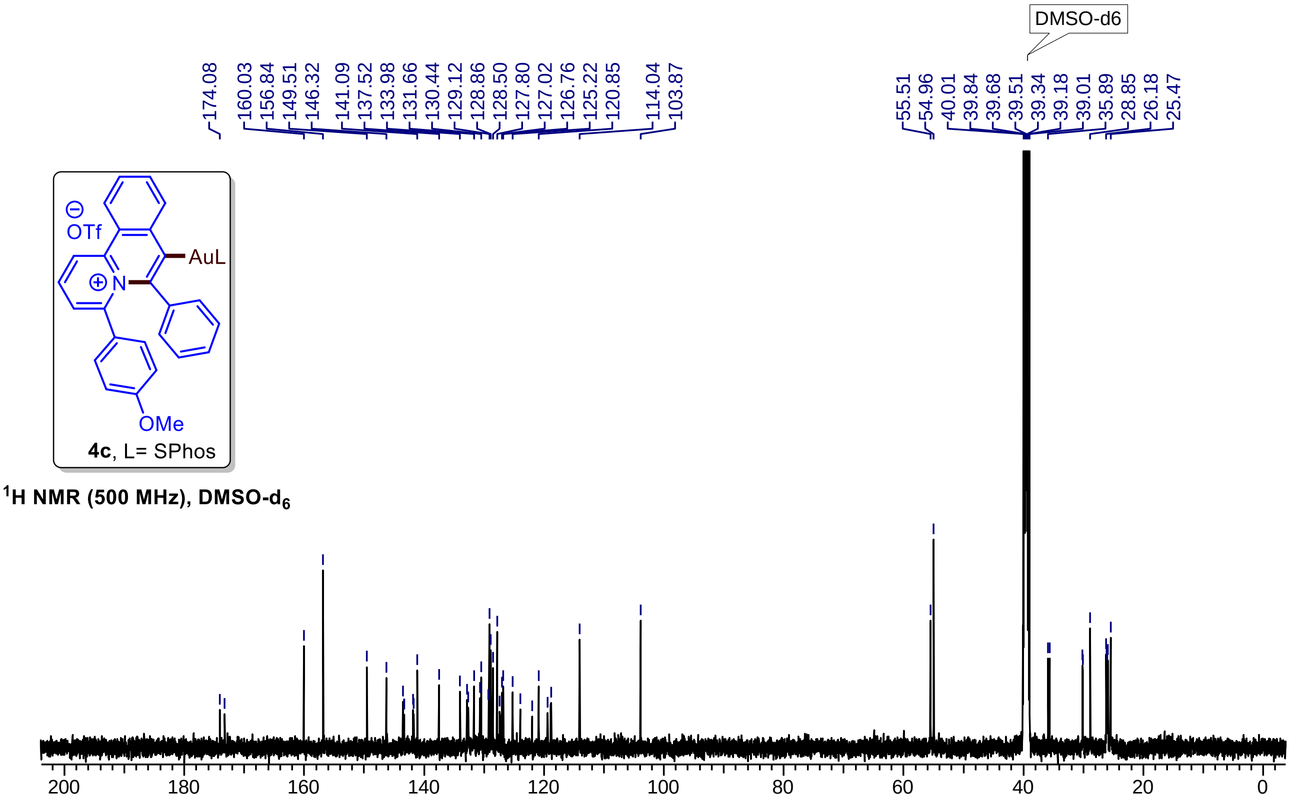
7.02
7.02
7.00
6.99
6.98
6.94
6.87
6.85
6.36
6.35
3.77
3.58
3.32
2.50
2.29
2.27
1.68
1.65
1.58
1.17
1.15
1.10
1.09
1.07
1.04
1.02
0.99
OTf
AuL
N
OMe
4c, L= SPhos
^{1}H NMR (500 MHz), DMSO-d_6
1.00 1.00 1.01 1.00 1.01 1.05 1.03 1.02 2.06 6.11 2.01 3.01 1.99
3.03 6.07
2.13 2.08 2.12 4.06 2.12 4.21 6.49
10
9
8
7
6
5
4
3
2
1
0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149.51
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141.09
137.52
133.98
131.66
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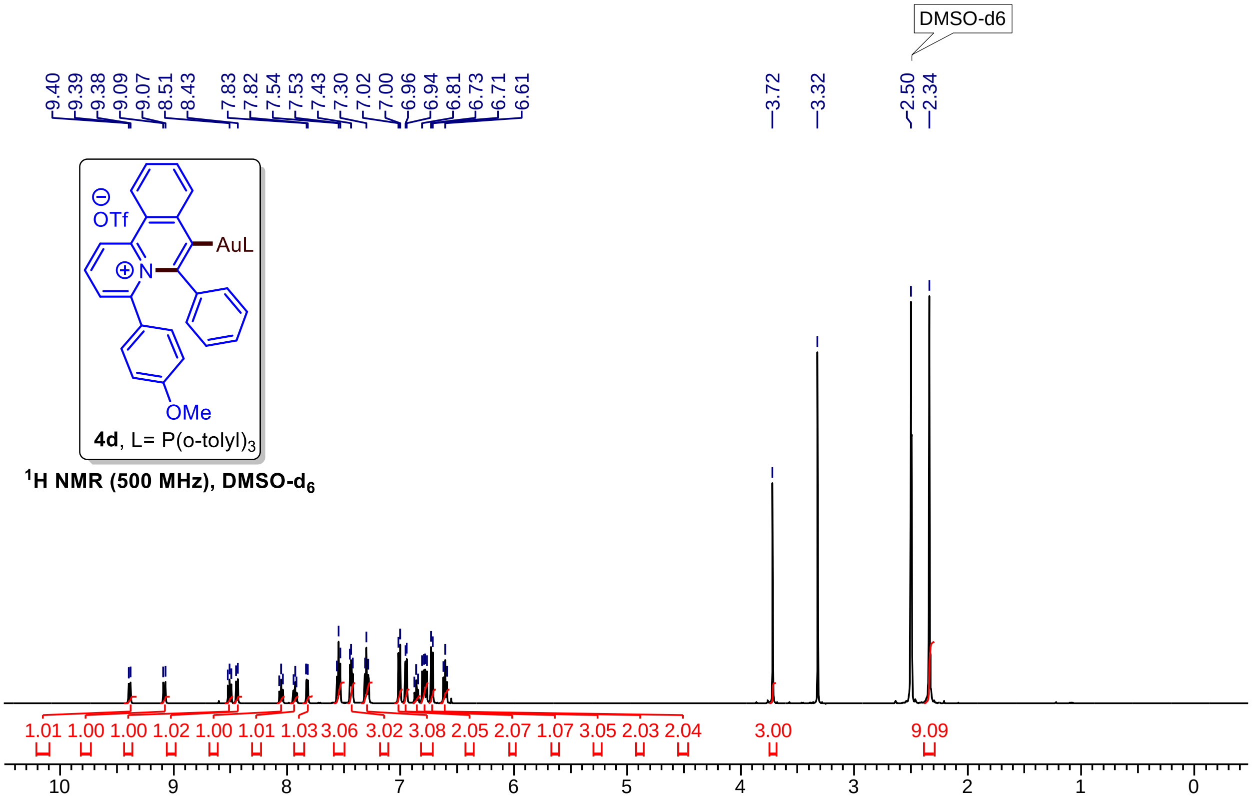
129.12
128.86
128.50
127.80
127.02
126.76
125.22
120.85
114.04
103.87
55.51
54.96
40.01
39.84
39.68
39.51
39.34
39.18
39.01
35.89
28.85
26.18
25.47
OTf
AuL
N
OMe
4c, L= SPhos
^{1}H NMR (500 MHz), DMSO-d_6
200
180
160
140
120
100
80
60
40
20
0



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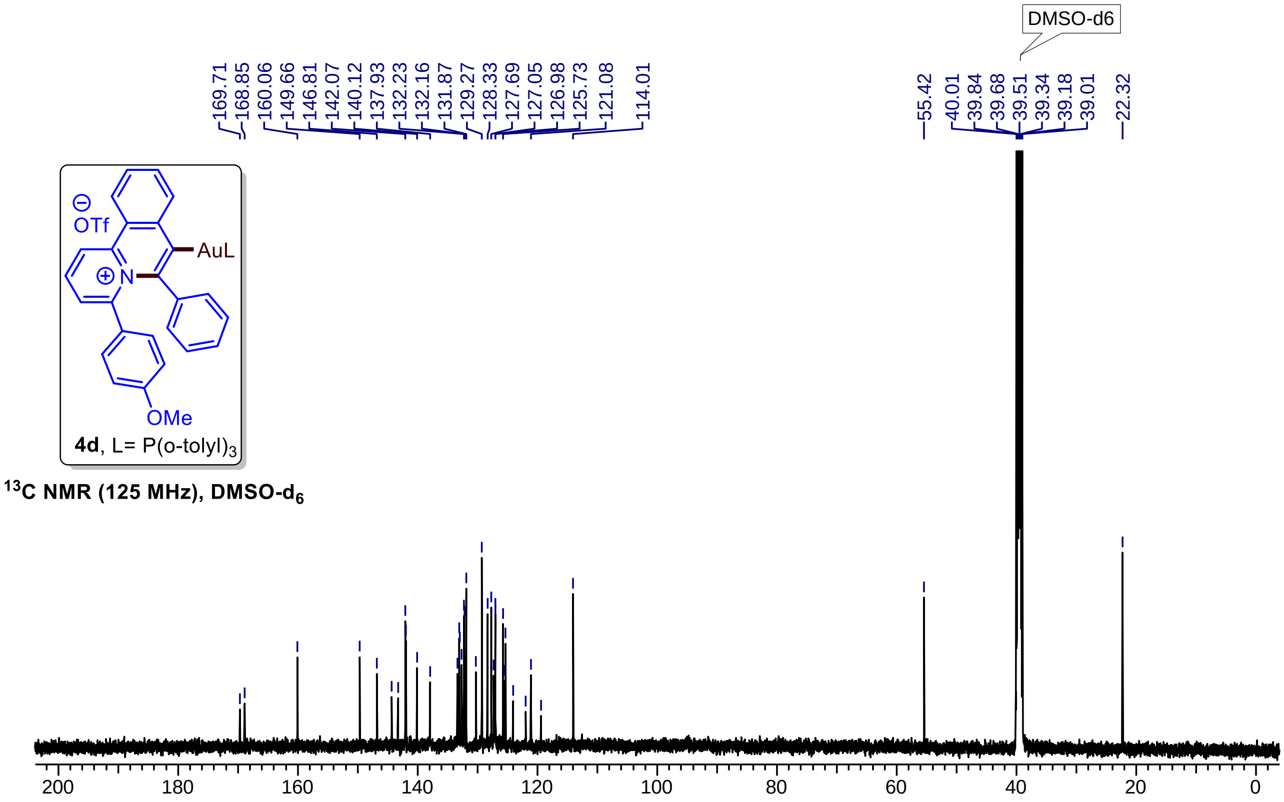
^{1}H NMR (500 MHz), DMSO-d$_6$



4d, L= P(o-tolyl)$_3$

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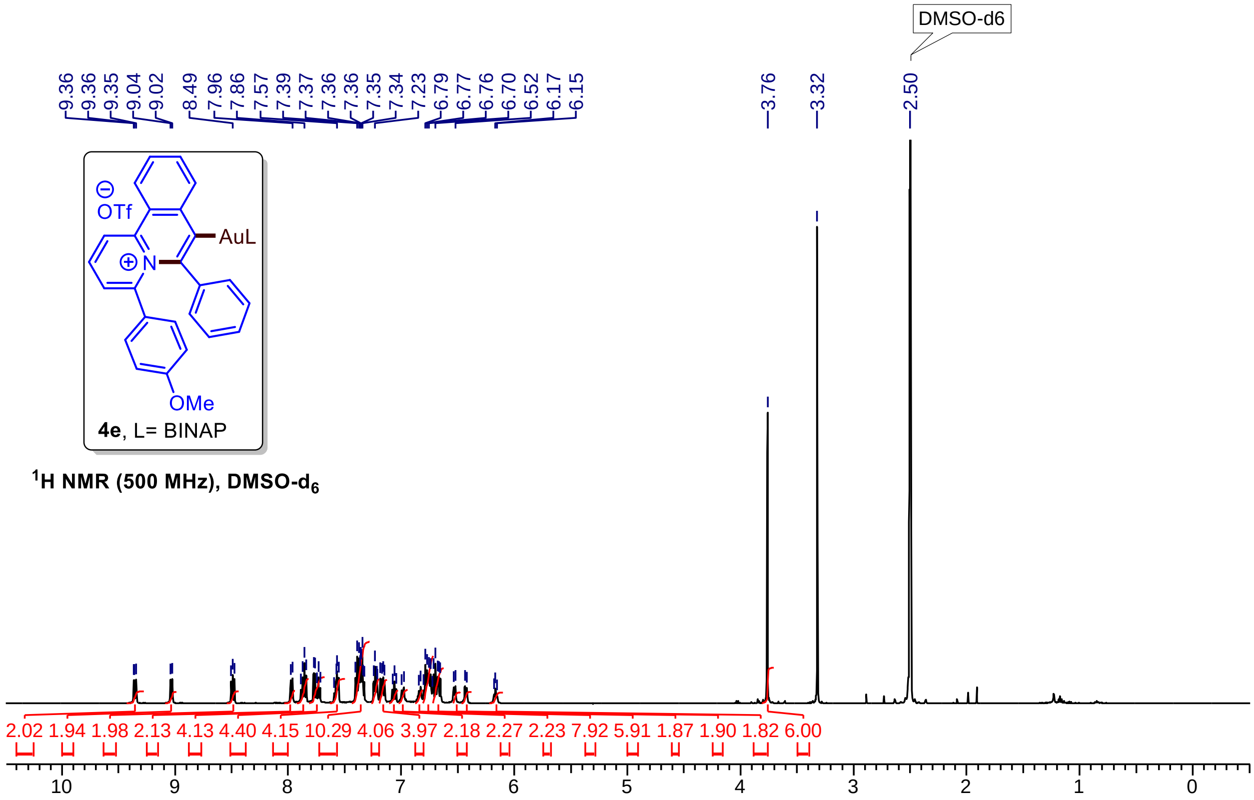
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9.36
9.35
9.04
9.02
8.49
7.96
7.86
7.57
7.39
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7.36
7.36
7.35
7.34
7.23
6.79
6.77
6.76
6.70
6.52
6.17
6.15
3.76
3.32
2.50
OTf
AuL
N
OMe
4e, L= BINAP
^{1}H NMR (500 MHz), DMSO-d$_6$
2.02 1.94 1.98 2.13 4.13 4.40 4.15 10.29 4.06 3.97 2.18 2.27 2.23 7.92 5.91 1.87 1.90 1.82 6.00
10
9
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5
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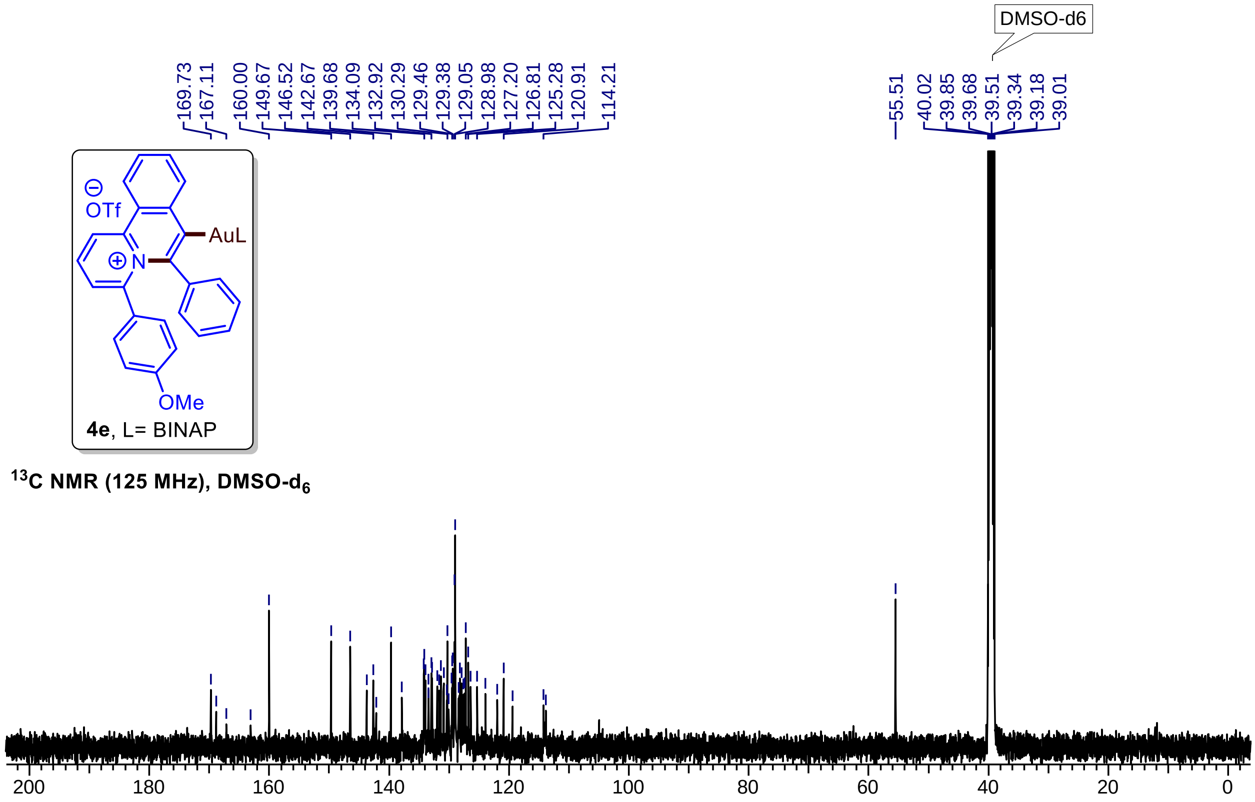
3
2
1
0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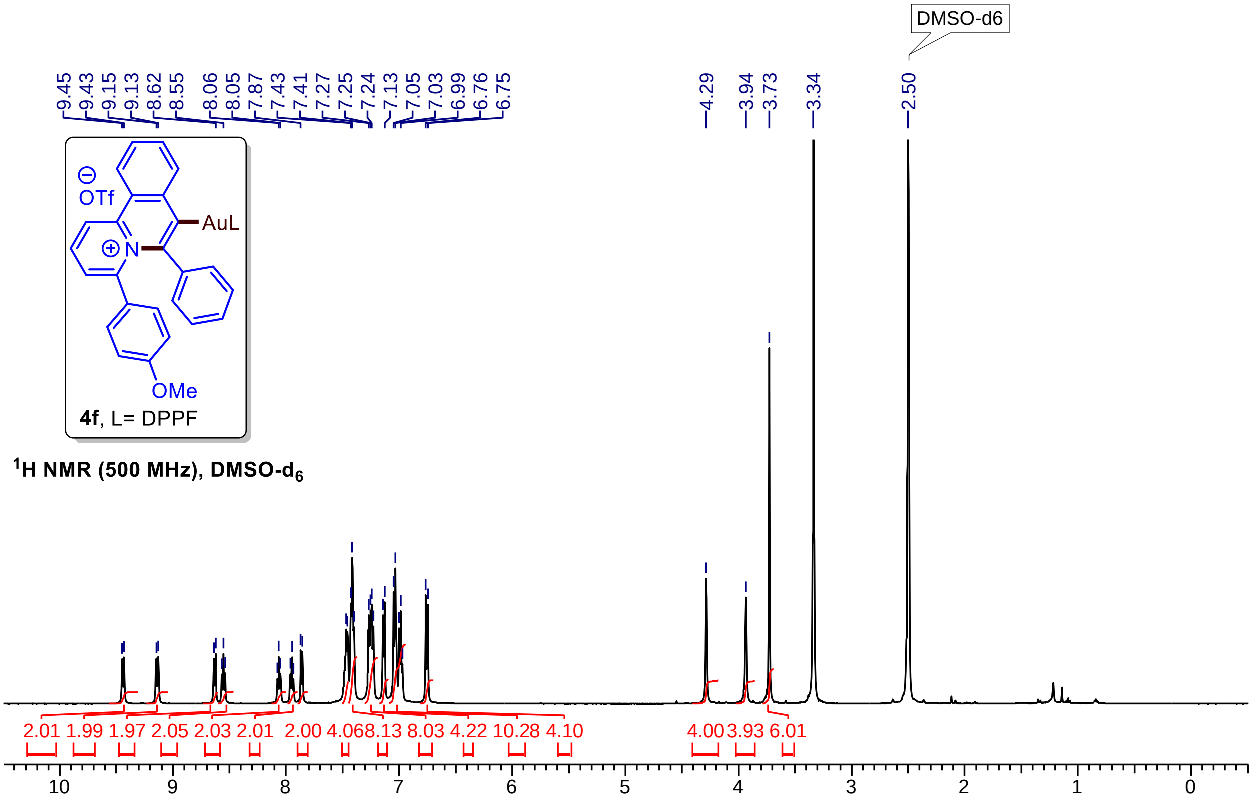
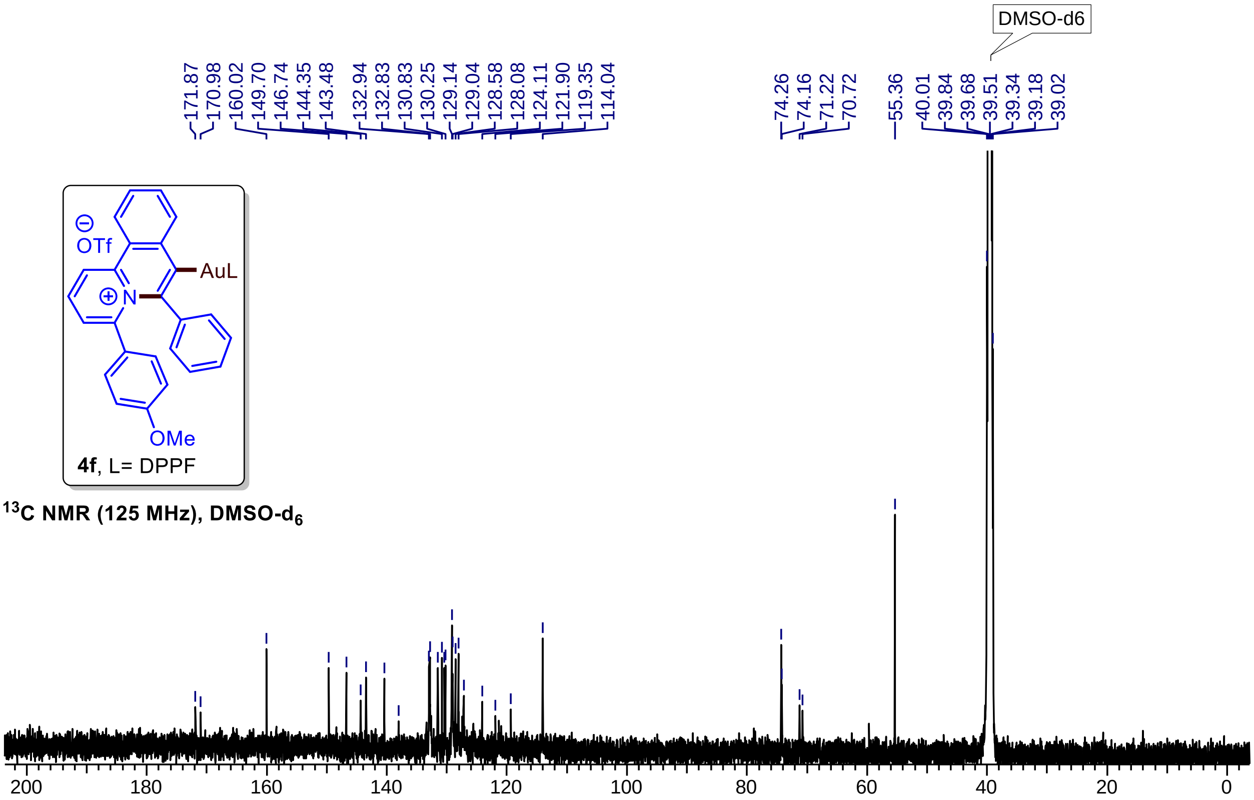
160.00
149.67
146.52
142.67
139.68
134.09
132.92
130.29
129.46
129.38
129.05
128.98
127.20
126.81
125.28
120.91
114.21
55.51
40.02
39.85
39.68
39.51
39.34
39.18
39.01
OTf
AuL
N
OMe
4e, L= BINAP
^{13}C NMR (125 MHz), DMSO-d$_6$
200
180
160
140
120
100
80
60
40
20
0



4f, L= DPPF

^{1}H NMR (500 MHz), DMSO-d$_6$



4f, L= DPPF

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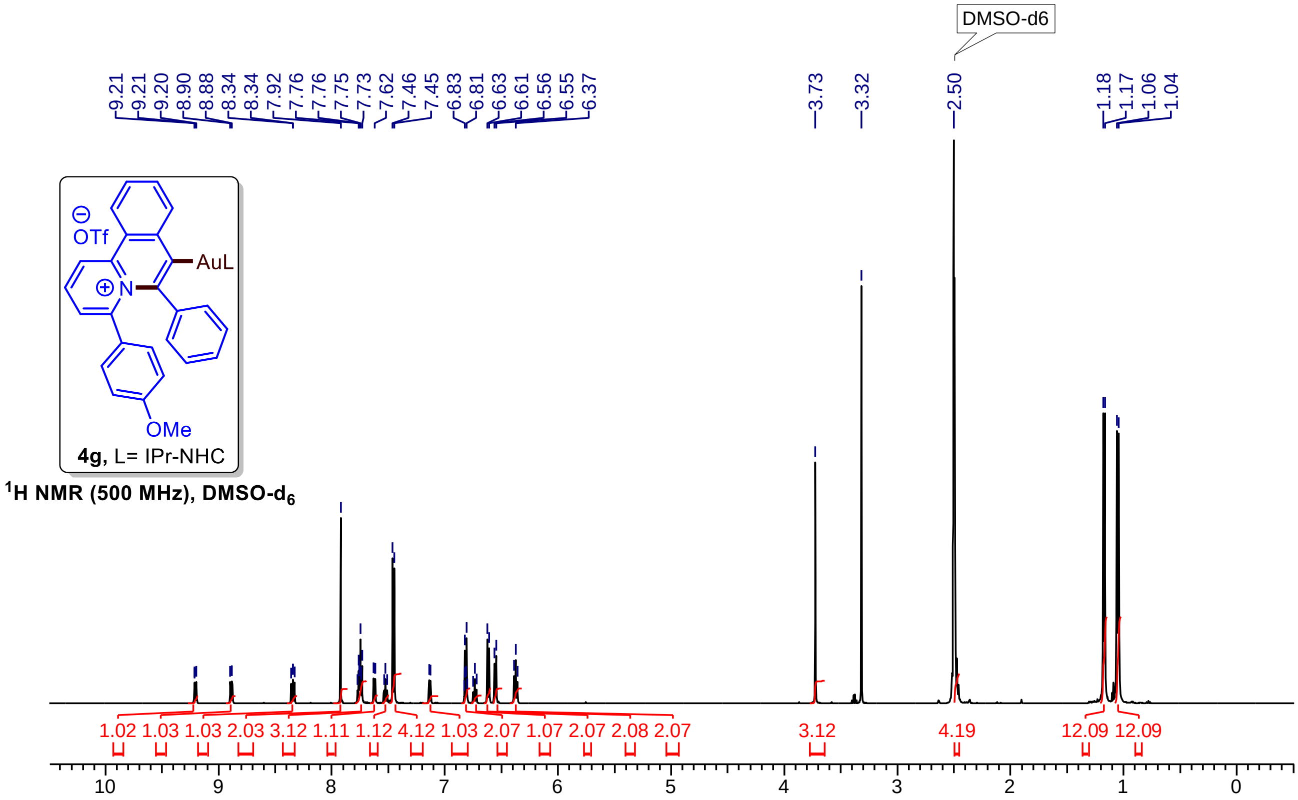

4g, L= IPr-NHC

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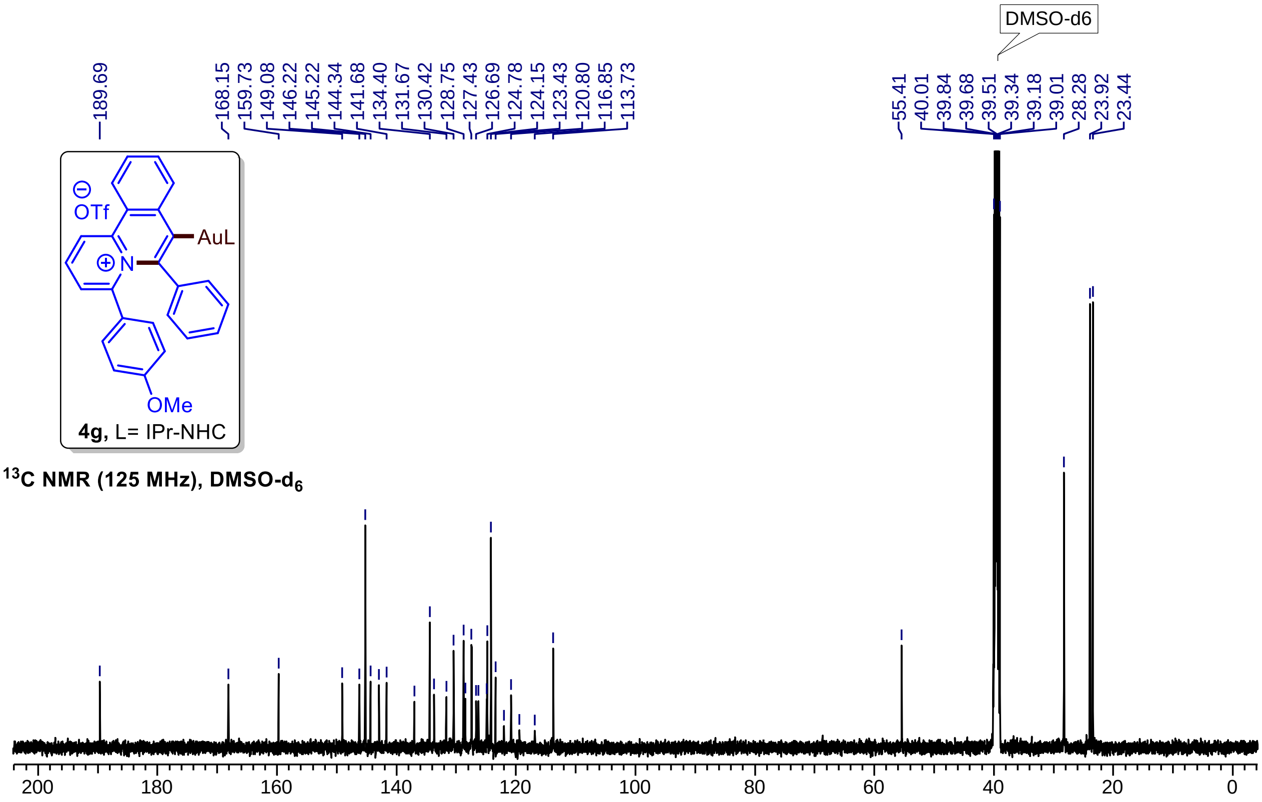

4g, L= IPr-NHC

^{13}C NMR (125 MHz), DMSO-d_6

4.6 References:

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1 a) A. S. K. Hashmi, *Chem. Rev*., **2007**, *107*, 3180; b) A. Arcadi, *Chem. Rev*., **2008**, *108*, 3266;c) D. J. Gorin, B. D. Sherry, F. D. Toste, *Chem. Rev*., **2008**, *108*, 3351; d) A. S. K. Hashmi, M. Rudolph, *Chem. Soc. Rev*., **2008**, *37*,1766; e) E. s. Jimènez- Nùñez and A. M. Echavarren, *Chem. Rev*., **2008**, *108*, 3326; f) Z. Li, C. Brouwer, C. He, *Chem. Rev*., **2008**, *108*, 3239; g) A. Corma, A. Leyva-Pèrez, M. J. Sabater, *Chem. Rev*., **2011**, *111*, 1657.

2 a) E. J. FernLndez, A. Laguna, M. E. Olmos, *Adv. Organomet. Chem*., **2005**, *52*, 77; b) H. Schmidbaur, A. Schier, *Sci. Synth*., **2004**, *3*, 691.

3 A. S. K. Hashmi, T. D. Ramamurthi, F. Rominger, *Adv. Synth. Catal*. **2010**, *352*, 971.

4 Xiaoming Zeng, Rei Kinjo, Bruno Donnadieu, and Guy Bertrand, *Angew. Chem. Int. Ed*. **2010**, *49*, 942.

5 Y. Chen, D. Wang, J. L. Petersen, N. G. Akhmedova, Xiaodong Shi, *Chem. Commun.*, **2010**, *46*, 6147.

6 S. Lv, J. Wang, C. Zhang, S. Xu, M. Shi, J. Zhang, *Angew. Chem. Int. Ed*. **2015**, *54*, 14941; b) J. Wang, X. Cao, S. Lv, C. Zhang, S. Xu, M. Shi, J. Zhang, **DOI**: 10.1038/ncomms14625 |

7 T. Traut-Johnstone, S. Kanyanda, F.H. Kriel, T Viljoen, P.D.R. Kotze, W.E. van Zyl, J. Coates, D.J.G. Rees, M. Meyer, R. Hewer, D.B.G.Williams, *J. Inorg. Biochem*. **2015**, *145*, 108.

8 a) A. C. Shaikh, D. S. Ranade, P. R. Rajamohanan, P. P. Kulkarni, N. T. Patil, *Angew. Chem. Int. Ed.*, **2017**, *56*, 757;b) M. O. Akram, P. S. Mali, N. T. Patil, *Org. Lett*., **2017**, *19*, 3075.

ABSTRACT

Name of the Student: Ravindra Dattatraya Mule **Registration No.: 10CC15J26007**
Facultyof Study: Chemical Science **Year of Submission:** 2020
AcSIR academiccenter/CSIRLab: CSIR-NCL **Name of the Supervisor:** Dr. B. Senthil kumar
Name of the Co-Supervisor: Dr. Nitin T. Patil

Title of the thesis: Metal-Mediated Intramolecular Cyclization of Pyridino-alkynes

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Coinage metals are widely used in the field of organic synthesis. These metals mainly act as soft and carbophilic Lewis acids. Coinage metals are effective as catalyst for the electrophilic activation of alkynes and utilizing this, a broad range of versatile synthetic tools have been developed for the construction of new carbon-carbon or carbon-heteroatom bonds. Thus, the molecular complexity could be afforded from simple starting materials.

Chapter 1, includes the literature reports in which the coinage metals has been used as catalysts to activate the alkynes for synthesis of various molecular scaffolds. Intramolecular amino-functionalization of alkynes is typically focused here. Which mainly encompasses hydroamination, carboamination, amino-halogenation, amino-alkynylaton and amino-oxygenations reactions. In next chapter, synthesis of N-doped ionic polycyclic aromatic hydrocarbons (PAHs) *via* carboamination of alkynes by using copper(II) catalyst has been described. In these reactions Cu(II) played a dual role by not only initiating the cascade transformation but also providing the counterion. The PAHs developed *via* this method exhibit tunable emission wavelengths and good quantum efficiency.

Chapter 3 descibes the silver mediated endo-selective intramolecular cyclisation of pyridino-alkynes to access ionic solid light emitters. Herein, the silver salt plays dual role, first as a reaction mediator and second as a counter ion provider. The photophysical properties of compounds has been tuned by using different substituents on molecular scaffolds as well as varying the counter ions. In last, chapter 4 includes library based approach to synthesize pyrido-isoquinoline based ionic gold complexes *via* intramolecular aminoauration of pyridiono-alkynes. The reaction offers an efficient approach to ionic gold complexes. This reaction is proceeding equally well with both sterically hindered phosphine and di-phosphine ligands.

LIST OF PUBLICATION

1) A New Class of N-Doped Ionic PAHs *via* Intramolecular [4 + 2]-Cycloaddition between Arylpyridines and Alkynes;

   Ravindra D. **Mule**, Aslam C. Shaikh, Amol B. Gade and Nitin T. Patil* *Chem. Commun.*, **2018**, *54*, 11909-11912.

2) Ionic Pyridinium-Oxazole Dyads: Design, Synthesis, and their Application in Mitochondrial Imaging;

   Aslam C. Shaikh, Mokshada E.Varma, **Ravindra D**. **Mule**, Somsuvra Banerjee, Prasad P. Kulkarni and Nitin T. Patil* *J. Org. Chem.*, **2019**, *84*, 4, 1766-1777.

3) External Oxidant-Dependent Reactivity Switch in Copper-Mediated Intramolecular Carboamination of Alkynes: Access to a Different Class of Fluorescent Ionic Nitrogen-Doped Polycyclic Aromatic Hydrocarbons;

   Aslam C. Shaikh, Somsuvra Banerjee, **Ravindra D**. **Mule**, Saibal Bera and Nitin T. Patil* *J. Org. Chem.*, **2019**, *84*, 7, 4120-4130.

4) Gold-Catalyzed Alkynylative Meyer-Schuster Rearrangement;

   Somsuvra Banerjee, Shivhar B. Ambegave, **Ravindra D. Mule**, Beeran Senthilkumar* and Nitin T. Patil*, *Org. Lett.*, **2020**, *22*, 4792-4796.

5) Design and Development of a New Class of N-doped Ionic Solid Light Emitters *via* Silver Mediated Endo-Selective Intramolecular Cyclization of 2-(2-alkynylphenyl)Pyridines; **Ravindra D**. **Mule**, Beeran Senthilkumar* and Nitin T. Patil* *manuscript under preparation.*

6) Accessing Novel Class of Gold(I)-Complexes *via* Aminoauration of Pyridino-Alkynes;

   Ravindra D. **Mule**, Beeran Senthilkumar* and Nitin T. Patil* *manuscript under preparation.*

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LIST OF NATIONAL INTERNATIONAL CONFERENCES

(1) Participated and presented poster in *TRI-2020 National Symposium* held during February 14-15, 2020, at SP College, Pune Pune, India.

(2) Participated and presented poster on *Natioanl Science day -2020* held during February 26-28, 2020, at at CSIR- National Chemical Laboratory, Pune, India.

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rsc.li/chemcomm

A new class of N-doped ionic PAHs *via* intramolecular [4+2]-cycloaddition between arylpyridines and alkynes†

Ravindra D. Mule,[ab] Aslam C. Shaikh,[ab] Amol B. Gade[ab] and Nitin T. Patil*[c]

Reported herein, for the first time, is a copper-promoted intramolecular [4+2]-cycloaddition cascade to access ionic N-doped polycyclic aromatic hydrocarbons (PAHs) with tunable emission wavelengths. It is shown that the reaction can be made catalytic with respect to $Cu(OTf)_2$ when an external oxidant, Selectfluor, was used.

Polycyclic aromatic hydrocarbons (PAHs) with annulated aromatic rings have attracted considerable attention due to their fascinating structural features and wide range of applications in organic, optical and electronic materials.[1] It is known that the incorporation of heteroatoms in the aromatic framework of PAHs can modulate their physical, chemical and supramolecular properties.[2] As a subset of these compounds, nitrogen-doped PAHs represent an important class of molecules that have interesting applications in the field of optoelectronics, light emitting-diodes, supercapacitors and bio-imaging.[3] Recently, it has been shown that ionic N-doped PAHs exhibit interesting optical and aggregation behavior properties.[4] Therefore, it is not surprising that several research groups across the globe are engaged in the design and development of novel ionic N-doped PAHs (Fig. 1a, Type **A**–**D**).[5] However, most of the approaches to access N-doped ionic PAHs are based on Rh/Ru catalyzed C–H activation between arenes/heteroarenes and alkynes.[6]

During the last decades, Rh and Co-catalyzed reactions between alkynes and azadienes, involving C–H activation, have emerged as an important tool for accessing heterocyclic quaternary ammonium salts (Scheme 1a). For instance, the groups of Jones,[7] Cheng,[8] Huang,[9] You[10] and Jun[11] showed the utility of Rh-complexes for such reactions. Recently, Pérez-Temprano,[12] Cheng[13] and Wang,[14] in their independent reports, have successfully demonstrated the use of Co-catalysts for the analogues transformations. Herein, we report the design and development of a new class of ionic N-doped PAHs *i.e.* Type **E** (Fig. 1b) *via* Cu-mediated alkyne/azadiene [4+2]-cycloaddition cascades (Scheme 1b). The reaction was proposed to proceed *via* initial amino-cupration followed by the C–H activation/reductive elimination sequence to produce ionic N-doped PAHs (Scheme 1b).

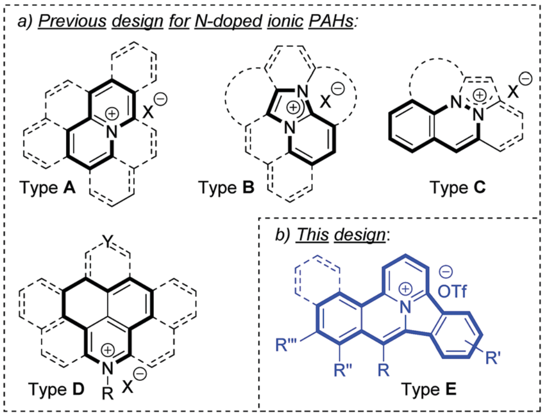

Fig. 1 N-Doped ionic PAHs: known and present design.

Based on our previous report on the gold-catalyzed oxidative intramolecular 1,2-amino-oxygenation reaction of alkynes,[15] we envisioned that the substrate of type **1** would undergo intramolecular [4+2]-cycloaddition reactions to produce ionic N-doped PAHs. Towards this end, several metal catalysts/oxidants were screened.[16] Our systematic optimization studies revealed that refluxing **1a** (Ar′ = 4-OMe-C_6H_4 and R = Ph) in CH_3CN in the presence of stoichiometric amounts of $Cu(OTf)_2$ is the best condition to achieve the desired PAH (**2a**) in 78% yield. Interestingly, $Cu(OTf)_2$ exhibits a dual role by mediating the cascade transformation as well as providing a counter ion. It should be noted that the Cu-catalyzed reactions of alkenes, involving the

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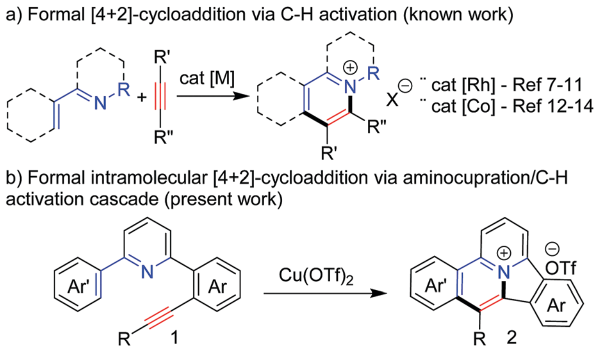
† Electronic supplementary information (ESI) available. CCDC 1824190 and 1824191. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c8cc05743e



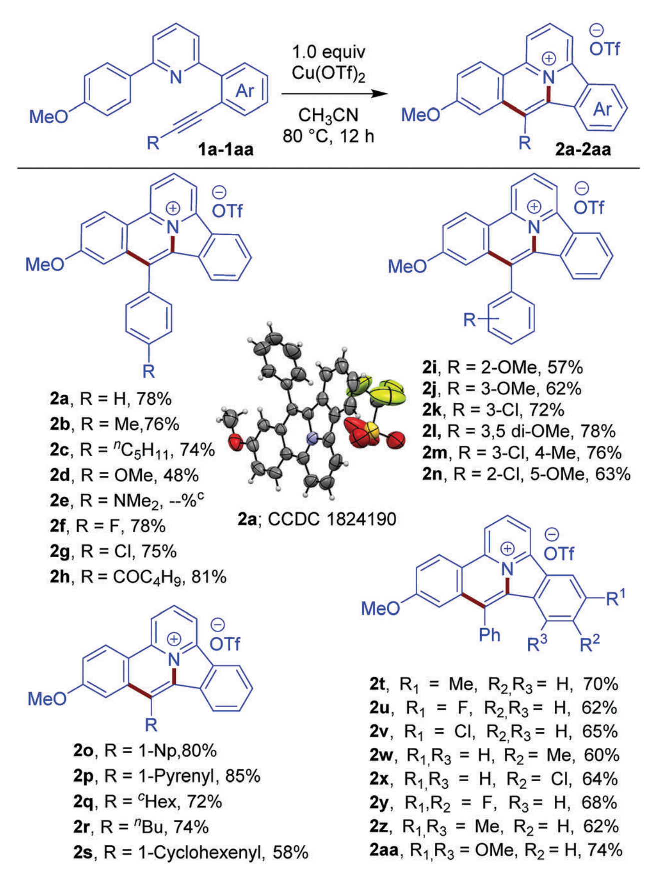
Scheme 1 Concepts for accessing heterocyclic quaternary ammonium salts *via* formal [4+2]-cycloadditions: known and present work.

simultaneous formation of C–C and C–N bonds, are known in the literature.[17] However, to the best of our knowledge, the analogous reactions of alkynes have never been reported.

With the optimized reaction conditions in hand, we sought to explore the substrate scope for this reaction. The results are presented in Table 1. In general, substrates with variation in the aryl ring at the alkyne-terminus with varying functional groups, such as alkyl and –OMe, were well tolerated (**2b**–**2d**). However, a stronger electron donating group, such as $–NMe_2$, was found to be unsuitable for the reaction. The reaction smoothly tolerated varying substitution patterns (*ortho*, *meta* and *para*) on the aforementioned aryl moiety to furnish the corresponding PAHs in good yields (**2f**–**2n**). Next, substrates bearing bulky aromatics or long-chain/cyclic aliphatics at the alkyne terminal position of the pyridino alkynes were screened. For instance, the substrate with sterically demanding 1-Np and a pyrenyl aromatic ring efficiently afforded the desired PAHs **2o** and **2p** in 80 and 85% yields, respectively. Furthermore, in the cases where aliphatic substituents were placed on the alkyne terminus, the desired PAHs **2q**–**2s** were obtained in good yields. Next, we directed our attention to examining the tolerance of the substituents on the Ar ring. Pleasingly, the introduction of the –Me, –F and –Cl substituents on the ring resulted in the formation of the desired PAHs **2t**–**2x** in 60–70% yields. Similarly, the reaction tolerates di-substitutions at the Ar ring to offer the products **2y**–**2aa** in moderate yields.

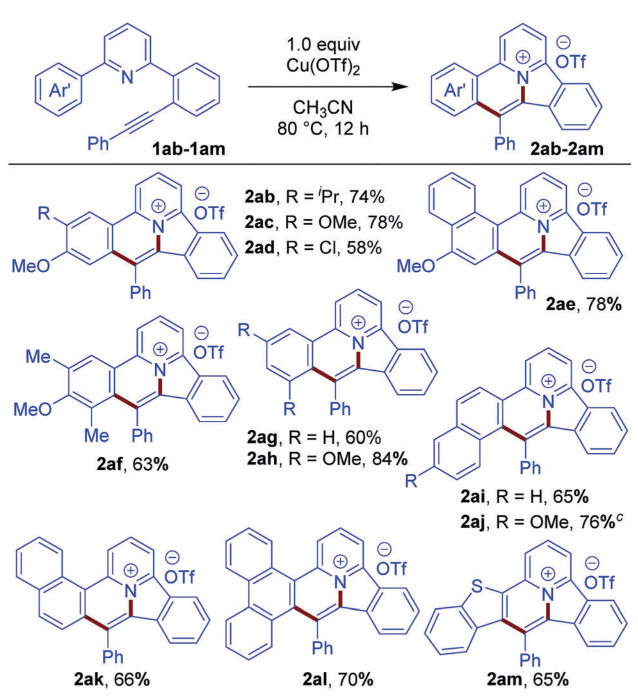
To understand the tolerance of the substituents at the Ar′ ring, substrates **1ab**–**1am** were examined under the optimized reaction conditions (Table 2). It was observed that **1ab**–**1ah** underwent smooth reactions to provide the desired PAHs **2ab**–**2ah** in good yields (58–84%). Moreover, 1-Np, 2-Np and 9-phenanthryl groups were well tolerated under the present reaction conditions to produce the desired PAHs (**2ai**–**2al**) in good yields. Even the benzothiophenyl moiety was also well tolerated giving PAH **2am** in 65% yield. The scalability of the method was demonstrated by the large-scale synthesis employing **1a** (2.7 mmol) as a starting material (**2a**, 76%).[16]

Table 1 Substrate scope with Ar[a,b]

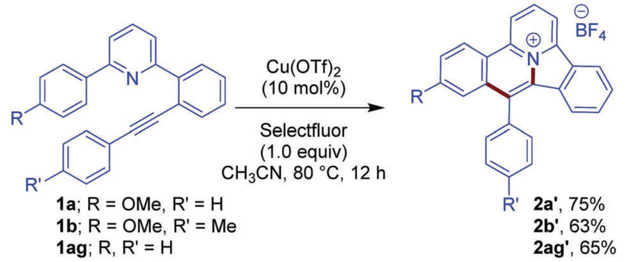


[a] Reaction conditions: 0.13 mmol **1**, 1.0 equiv. $Cu(OTf)_2$, CH_3CN (2 mL), 80 °C, 12 h. [b] Isolated yield. [c] Complex reaction mixture was obtained.

Table 2 Substrate scope with Ar′[a,b]



[a] Reaction conditions: 0.13 mmol **1**, 1.0 equiv. $Cu(OTf)_2$, CH_3CN (2 mL), 80 °C, 12 h. [b] Isolated yield. [c] CCDC for **2aj** – 1824191.



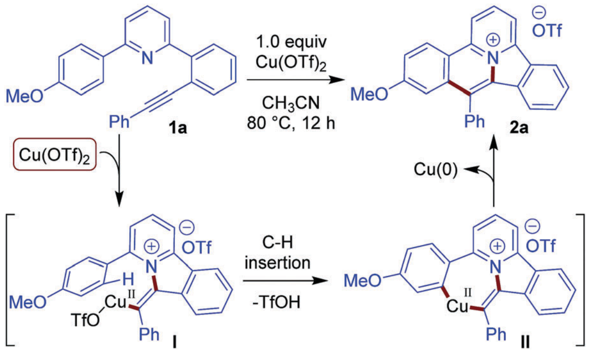
Scheme 2 Catalytic reactions with respect to $Cu(OTf)_2$ in the presence of an external oxidant.

Interestingly, we found that the reaction can be made catalytic with respect to $Cu(OTf)_2$ when a stoichiometric amount of oxidant was used (Scheme 2).[16] When **1a**, **1b** and **1ag** were treated with 10 mol% $Cu(OTf)_2$ in the presence of selectfluor, the reaction proceeded smoothly to produce **2a**′, **2b**′ and **2ag**′ in 75, 63 and 65% yields, respectively.

A plausible reaction pathway for the present transformation is depicted in Scheme 3. At first, the activation of the alkyne by the $Cu(OTf)_2$ would occur to enable nucleophilic attack by the pyridyl nitrogen atom in a 5-*exo*-dig fashion to generate vinyl copper intermediate **I.**[18] This intermediate would activate the C–H bond of the proximal aryl ring and subsequently remove TfOH to generate copper(II) intermediate **II.**[19] Furthermore, reductive elimination would occur to form product **2a**. The fact that the yield of the reaction was not hampered in the presence of a radical scavenger such as 2,2,6,6-*tetra*-methylpiperidine-1-oxyl (TEMPO)[16] rules out the possibility of a radical mechanism.

The synthesised PAHs exhibit intense fluorescence and their photophysical properties were studied in CH_2Cl_2 solution (Table S1, ESI†).[16] The PL range covers the visible region, offering a palette of colors ranging from violet to orange (λ_{em}: 434–619 nm, Fig. 2). These fluorophores exhibit good photoluminescence capabilities with Φ_f values ranging from 0.02 to 0.88. Next, the electrochemical properties of the representative PAHs were investigated by cyclic voltammetry and the results indicated that these PAHs exhibited high electron-accepting abilities.[16]

In conclusion, a Cu(II)-mediated intramolecular alkynes/azadienes [4+2]-cycloaddition cascade has been disclosed. The reagent $Cu(OTf)_2$ exhibits a dual role by mediating the cascade transformation as well as providing a counter ion. Furthermore, it is shown that the reaction can be made catalytic with respect to $Cu(OTf)_2$ in the presence of an external oxidant, Selectfluor. The method provided an efficient access to ionic N-doped PAHs with tunable emission wavelengths.



Scheme 3 A plausible reaction mechanism.

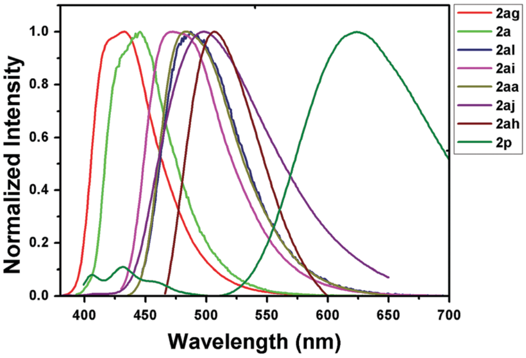


Fig. 2 Emission spectra of the selected ionic PAHs in CH_2Cl_2.

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Conflicts of interest

There are no conflicts to declare.

Notes and references

1 (*a*) R. G. Harvey, *Polycyclic Aromatic Hydrocarbons*, Wiley-VCH, New York, 1997, p. 43; (*b*) A. Narita, X.-Y. Wang, X. Feng and K. Müllen, *Chem. Soc. Rev.*, 2015, **44**, 6616; (*c*) D. Pérez, D. Peña and E. Guitián, *Eur. J. Org. Chem.*, 2013, 5981; (*d*) J. Wu, W. Pisula and K. Müllen, *Chem. Rev.*, 2007, **107**, 718; (*e*) M. D. Watson, A. Fechtenkötter and K. Müllen, *Chem. Rev.*, 2001, **101**, 1267.

2 For recent reviews, see: (*a*) M. Stępien, E. Gońka, M. Żyła and N. Sprutta, *Chem. Rev.*, 2017, **117**, 3479; (*b*) X. Wang, G. Sun, P. Routh, D.-H. Kim, W. Huang and P. Chen, *Chem. Soc. Rev.*, 2014, **43**, 7067; (*c*) W. Jiang, Y. Li and Z. Wang, *Chem. Soc. Rev.*, 2013, **42**, 6113.

3 Reviews: (*a*) Y. Deng, Y. Xie, K. Zhou and X. Ji, *J. Mater. Chem. A*, 2016, **4**, 1144; (*b*) A. Mateo-Alonso, *Chem. Soc. Rev.*, 2014, **43**, 6311; (*c*) U. H. F. Bunz, J. U. Engelhart, B. D. Lindner and M. Schaffroth, *Angew. Chem., Int. Ed.*, 2013, **52**, 3810; For selected examples, see: (*d*) A. Skabeev, U. Zschieschang, Y. Zagranyarski, H. Klauk, K. Müllen and C. Li, *Org. Lett.*, 2018, **20**, 1409; (*e*) X.-Y. Wang, M. Richter, Y. He, J. Björk, A. Riss, R. Rajesh, M. Garnica, F. Hennersdorf, J. J. Weigand, A. Narita, R. Berger, X. Feng, W. Auwärter, J. V. Barth, C.-A. Palma and K. Müllen, *Nat. Commun.*, 2017, **8**, 1948; (*f*) S. Boldt, S. Parpart, A. Villinger, P. Ehlers and P. Langer, *Angew. Chem., Int. Ed.*, 2017, **56**, 4575; (*g*) C.-F. Liu, C. Cheng, Y. Jiang, W.-Y. Lai and W. Huang, *New J. Chem.*, 2017, **41**, 13619; (*h*) M. Richter, K. S. Schellhammer, P. Machata, G. Cuniberti, A. Popov, F. Ortmann, R. Berger, K. Müllen and X. Feng, *Org. Chem. Front.*, 2017, **4**, 847.

4 (*a*) K. Xu, Y. Fu, Y. Zhou, F. Hennersdorf, P. Machata, I. Vincon, J. J. Weigand, A. A. Popov, R. Berger and X. Feng, *Angew. Chem., Int. Ed.*, 2017, **56**, 15876; (*b*) D. Wu, R. Liu, W. Pisula, X. Feng and K. Müllen, *Angew. Chem., Int. Ed.*, 2011, **50**, 2791; (*c*) J. Fortage, F. Tuyèras, P. Ochsenbein, F. Puntoriero, F. Nastasi, S. Campagna, S. Griveau, F. Bedioui, I. Ciofini and P. P. Laine, *Chem. – Eur. J.*, 2010, **16**, 11047; (*d*) J. Fortage, C. Peltier, F. Nastasi, F. Puntoriero, F. Tuyèras, S. Griveau, F. Bedioui, C. Adamo, I. Ciofini, S. Campagna and P. P. Laine, *J. Am. Chem. Soc.*, 2010, **132**, 16700; (*e*) D. Wu,

W. Pisula, V. Enkelmann, X. Feng and K. Müllen, *J. Am. Chem. Soc.*, 2009, **131**, 9620; (*f*) D. Wu, L. Zhi, G. J. Bodwell, G. Cui, N. Tsao and K. Müllen, *Angew. Chem., Int. Ed.*, 2007, **46**, 5417.

5 For general reviews, see: (*a*) D. Sucunza, A. M. Cuadro, J. Alvarez-Builla and J. J. Vaquero, *J. Org. Chem.*, 2016, **81**, 10126; For selected examples, see: (*b*) F. Li, J. Cho, S. Tan and S. Kim, *Org. Lett.*, 2018, **20**, 824; (*c*) N. Toriumi, N. Asano, K. Miyamoto, A. Muranaka and M. Uchiyama, *J. Am. Chem. Soc.*, 2018, **140**, 3858; (*d*) J.-R. Deng, C.-S. Tsang, W.-C. Chan, B. C.-B. Ko, N. C.-H. Lai, S. L.-F. Chan, B. Yang and M.-K. Wong, *Chem. Sci.*, 2017, **8**, 7537; (*e*) Y. Asanuma, H. Eguchi, H. Nishiyama, I. Tomita and S. Inagi, *Org. Lett.*, 2017, **19**, 1824; (*f*) J. M. Villar, J. Suárez, J. A. Varela and C. Saá, *Org. Lett.*, 2017, **19**, 1702; (*g*) Y. Yang, D. Liu, M. Song, D. Shi, B. Liu, K. Cheng, Y. Lu, H. Liu, M. Yang, W. Wang, J. Li and J. Wei, *Chem. – Eur. J.*, 2017, **23**, 7409; (*h*) Q. Ge, Y. Hu, B. Li and B. Wang, *Org. Lett.*, 2016, **18**, 2483; (*i*) B. Feng, D. Wan, L. Yan, V. D. Kadam, J. You and G. Gao, *RSC Adv.*, 2016, **6**, 66407; (*j*) D. Ghorai, C. Dutta and J. Choudhury, *ACS Catal.*, 2016, **6**, 709; (*k*) D. Ghorai and J. Choudhury, *ACS Catal.*, 2015, **5**, 2692; (*l*) D. L. Davies, C. E. Ellul, S. A. Macgregor, C. L. McMullin and K. Singh, *J. Am. Chem. Soc.*, 2015, **137**, 9659; (*m*) D. Zhao, Q. Wu, X. Huang, F. Song, T. Lv and J. You, *Chem. – Eur. J.*, 2013, **19**, 6239; (*n*) G. Zhang, L. Yang, Y. Wang, Y. Xie and H. Huang, *J. Am. Chem. Soc.*, 2013, **135**, 8850.

6 For recent reviews, see: (*a*) J. Jayakumar and C.-H. Cheng, *J. Chin. Chem. Soc.*, 2018, **65**, 11; (*b*) P. Gandeepan and C.-H. Cheng, *Chem. – Asian J.*, 2016, **11**, 448.

7 L. Li, W. W. Brennessel and W. D. Jones, *J. Am. Chem. Soc.*, 2008, **130**, 12414.

8 (*a*) C.-Z. Luo, J. Jayakumar, P. Gandeepan, Y.-C. Wu and C.-H. Cheng, *Org. Lett.*, 2015, **17**, 924; (*b*) C.-Z. Luo, P. Gandeepan, J. Jayakumar, K. Parthasarathy, Y.-W. Chang and C.-H. Cheng, *Chem. – Eur. J.*, 2013, **19**, 14181.

9 G. Zhang, L. Yang, Y. Wang, Y. Xie and H. Huang, *J. Am. Chem. Soc.*, 2013, **135**, 8850.

10 J. Tang, S. Li, Z. Liu, Y. Zhao, Z. She, V. D. Kadam, G. Gao, J. Lan and J. You, *Org. Lett.*, 2017, **19**, 604.

11 Y. R. Han, S.-H. Shim, D.-S. Kim and C.-H. Jun, *Org. Lett.*, 2017, **19**, 2941.

12 J. Sanjosé-Orduna, D. Gallego, A. Garcia-Roca, E. Martin, J. Benet-Buchholz and M. H. Pérez-Temprano, *Angew. Chem., Int. Ed.*, 2017, **56**, 12137.

13 S. Prakash, K. Muralirajan and C.-H. Cheng, *Angew. Chem., Int. Ed.*, 2016, **55**, 1844.

14 Y.-X. Lao, S.-S. Zhang, X.-G. Liu, C.-Y. Jiang, J.-Q. Wu, Q. Li, Z.-S. Huang and H. Wang, *Adv. Synth. Catal.*, 2016, **358**, 2186.

15 A. C. Shaikh, D. S. Ranade, P. R. Rajamohanan, P. P. Kulkarni and N. T. Patil, *Angew. Chem., Int. Ed.*, 2017, **56**, 757.

16 See the ESI† for more details.

17 For general reviews, see: (*a*) X. Zhu and S. Chiba, *Chem. Soc. Rev.*, 2016, **45**, 4504; (*b*) Y. Shimizu and M. Kanai, *Tetrahedron Lett.*, 2014, **55**, 3727; (*c*) J. P. Wolfe, *Top. Heterocycl. Chem.*, 2013, **32**, 1; (*d*) S. R. Chemler, *J. Organomet. Chem.*, 2011, **696**, 150; (*e*) S. R. Chemler and P. H. Fuller, *Chem. Soc. Rev.*, 2007, **36**, 1153; For pertinent reports, see: (*f*) E. S. Sherman and S. R. Chemler, *Adv. Synth. Catal.*, 2009, **351**, 467; (*g*) W. Zeng and S. R. Chemler, *J. Am. Chem. Soc.*, 2007, **129**, 12948; (*h*) P. H. Fuller and S. R. Chemler, *Org. Lett.*, 2007, **9**, 5477; (*i*) E. S. Sherman, P. H. Fuller, D. Kasi and S. R. Chemler, *J. Org. Chem.*, 2007, **72**, 3896.

18 (*a*) L. Ouyang, X. Tang, H. He, C. Qi, W. Xiong, Y. Ren and H. Jiang, *Adv. Synth. Catal.*, 2015, **357**, 2556; (*b*) X. Zhang, R. P. Hsung and H. Li, *Chem. Commun.*, 2007, 2420.

19 For selected reviews, see: (*a*) W.-H. Rao and B.-F. Shi, *Org. Chem. Front.*, 2016, **3**, 1028; (*b*) X.-X. Guo, D.-W. Gu, Z. Wu and W. Zhang, *Chem. Rev.*, 2015, **115**, 1622; (*c*) S. E. Allen, R. R. Walvoord, R. Padilla-Salinas and M. C. Kozlowski, *Chem. Rev.*, 2013, **113**, 6234; (*d*) K. Hirano and M. Miura, *Chem. Commun.*, 2012, **48**, 10704.