DEVELOPMENT OF NEW AND EFFICIENT METHODS TOWARDS THE SYNTHESIS OF BENZO-FUSED HETEROCYCLES

Thesis Submitted For The Degree Of Doctor Of Philosophy (Science)

BY

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CERTIFICATE FROM THE SUPERVISOR

This is to certify that the thesis entitled **"DEVELOPMENT OF NEW AND EFFICIENT METHODS TOWARDS THE SYNTHESIS OF BENZO-FUSED HETEROCYCLES"** submitted by Sri **SANDIP KUNDAL** who got his name registered on 08.05.2015 [Index. No.: 90/15/Chem./23] for the award of Ph.D. (Science) degree of Jadavpur University is absolutely based upon his own work under the supervision of Dr. Umasish Jana and that neither this thesis nor any part of it has been submitted for either any degree/diploma or any other academic award anywhere before.

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DEDICATED TO

MY PARENTS

Acknowledgement

*The investigations that have been documented in the present dissertation entitled "***DEVELOPMENT OF NEW AND EFFICIENT METHODS TOWARDS THE SYNTHESIS OF BENZO-FUSED HETEROCYCLES***" is a part of more than five years of research work that has been done since I was introduced to Dr. Jana's lab, earlier of year 2014. During my journey, I came in touch with a great number of people whose contribution in assorted ways to the research and the making of the thesis, deserve special mention. It is a pleasure to convey my gratitude to all of them in my humble acknowledgment.*

I feel myself privileged and express my sincere gratitude and respect to my supervisor Dr. Umasish Jana, Organic Chemistry Section, Dept. of Chemistry, Jadavpur University, for introducing me to the engrossing field of "Synthetic Organic Chemistry" and allowing me to work under his supervision and guidance. He always provided me unflinching encouragement and support in various ways. His inspiration, and wise advice throughout the progress of the work and patiently providing me all sort of necessities to proceed with the Doctoral program. Without him it would have been truly impossible to produce this project. His scientific intuition, graceful behavior, dedication, passion of work and oasis of ideas enrich my growth as a student, a researcher and a person with a vision of science inside.

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Ghoshal, Prof. Ranjit Shit, for co-operating me with their valuable support. I am also thankful to Dr. Asok Nath Mondal (microanalyst, JU) for his help in getting NMR spectra.

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Finally, I would like to thank my beloved Mrs. Chandralekha Nandi (Mum) all for her understanding and love for the past few years. Her support and encouragement was in the end what made this dissertation possible. Thanks for being my best friend since when I met you. All of your continued support, suggestion, company and arguing is deeply appreciated. I express my sincere gratitude to my father-in-law Mr. Sanjay Kumar Nandi and

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PREFACE

Investigations embodied in this dissertation entitled **"DEVELOPMENT OF NEW AND EFFICIENT METHODS TOWARDS THE SYNTHESIS OF BENZO-FUSED HETEROCYCLES"** was initiated in March, 2014 under the supervision of Dr. Umasish Jana, Organic Chemistry Section, Dept. of Chemistry, Jadavpur University, Kolkata-700032. The aim of this thesis is to find out more general, efficient and convenient methodologies to synthesize a variety of nitrogen and oxygen containing heterocyclic and selectively substituted benzofused compounds catalyzed by metallic and nonmetallic Lewis acids under environmentally friendly conditions.

The thesis has been divided into three chapters. **Chapter 1** demonstrates the development of an efficient synthesis synthesis of functionalized 3-alkylated indole and benzofuran which are one of the less invaded part of research till date in the region of synthetic organic chemistry. In this pat we have we have reported an iron(III)-catalyzed strategy for the general synthesis of selectively substituted heterocycles via isomerization of 3-(methylene)indoline and 3-methylene-2,3-dihydrobenzofuran derivatives under mild conditions. **Chapter 2** describes a diversity-orientated synthesis of indolo[2,3-*b*]quinolines derivatives which are popular for in medicinal chemistry and hence synthesis of these type of organic moieties becomes major point of interest. In this report we have implemented a unique and competent approach which involves the synthesis of polycyclic heterocycles comprising of palladium-catalyzed intramolecular carbopalladation/Suzuki coupling and successive cycloisomerisation development of C–N bond through DDQ-mediated cross-dehydrogenative (CDC) couplings. **Chapter 3** describes DDQ mediated dehydrogenative oxyfunctionalization of indoles to afford tertiary indole-3- carbinols, which are core compound of the vegetables of *Cruciferae* family and well known for its pharmacological effects over human body. Additionally, the principal synthetic value of such indole based *tert*-carbinols were explored through serving as excellent methylene surrogates to install value added unsymmetrical bis(indolyl)methanes (BIMs), containing all carbon quaternary centre. BIMs are actually the prime metabolite compound produced in our body at certain conditions which are also present in nature and popular for its pharmacological importance and so deserves the attention of the synthetic organic chemists.

Each chapter in this thesis consists of general introduction followed by a brief review of related methodological studies, elaborated description of reactions performed, experimental section containing details of experiments with necessary spectroscopic and analytical data, related references and finally some representative scan picture of NMR spectra.

Appendix consists with List of publications with some of their reprints.

In keeping with the general practice of reporting the scientific observations, I must take the responsibility of any unintentional oversight and error, which might have crept in.

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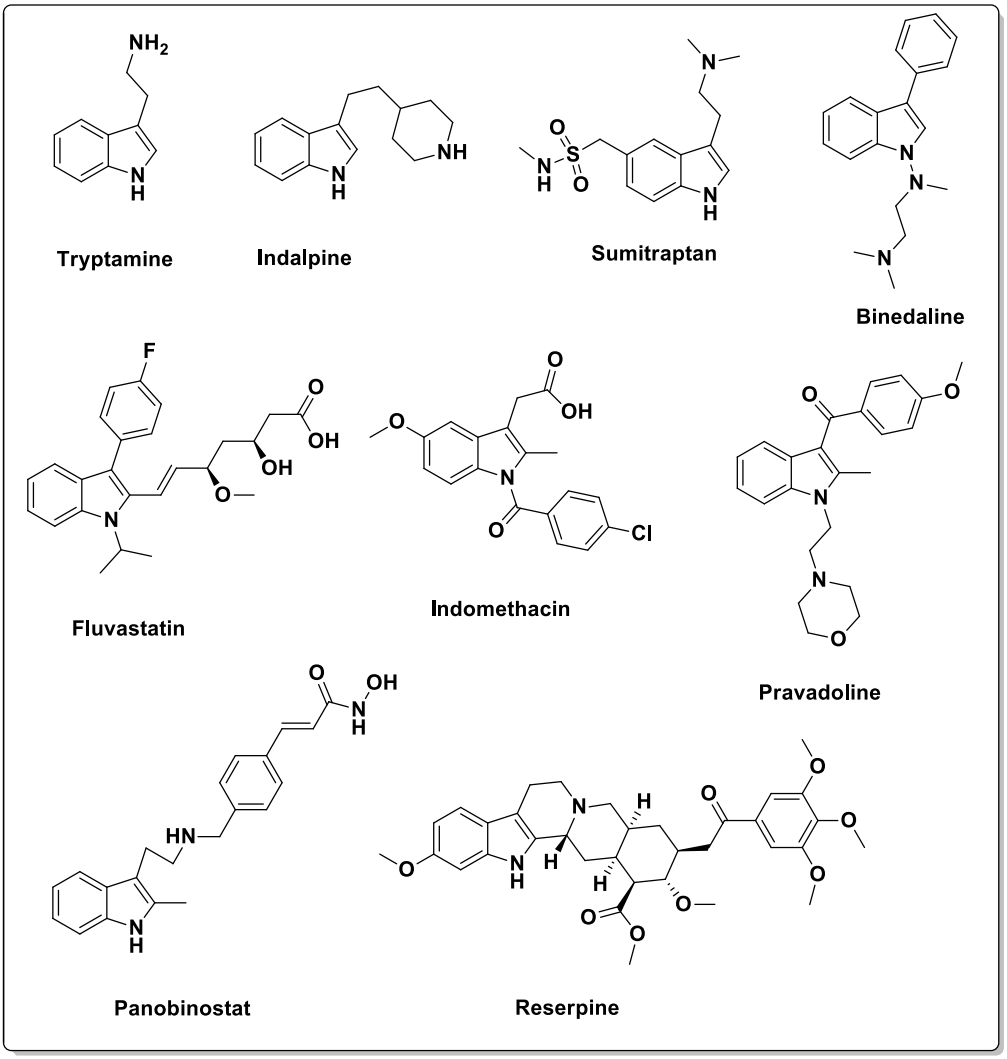
Chapter 1

$Fe(OTf)_3$-Catalyzed Aromatization of Substituted 3-Methyleneindoline and Benzofuran Derivatives: A Selective Route to C-3-Alkylated Indoles and Benzofurans

I.1. Introduction:

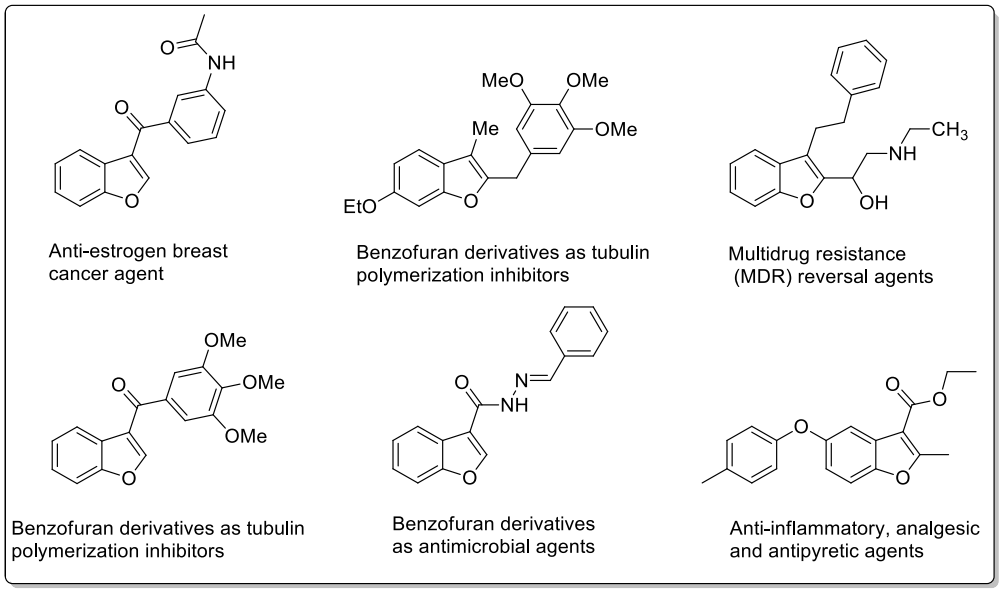
Heterocyclic structural frameworks are the most common as well as highly significant among the organic molecules present in nature, which comprise of the large pool of natural products, agrochemicals, herbicides, pharmaceuticals and biological electrical sensors. Under this umbrella, bicyclic heteroaromatic compounds containing nitrogen atoms, like indoles, quinolines, and isoquinolines occupies a major area, which covers predominant area in the biological and medicinal periphery [1].

Figure 1 : Some bioactive/natural products containing C-3 substituted indole core



Structural motifs containing indole frameworks are one of the most privileged and commonly found motifs which represents large varieties of natural products, biologically active products, agrochemicals etc[2]. Since the date, when indole has been isolated from the naturally occurring compound indigo, for the first time, more than ten thousands of indole derivatives are identified so far to exhibit biological activity. Indole moieties are not only present in biologically active products, but also exhibits importance in pharmaceutical research and material science. Functionalized derivatives of indoles, particularly C-3 substituted indoles shows its high potential in pharmaceuticals and commonly available in a large number promising therapeutic agents [3] (**Figure 1**). Structurally diverse derivatives of indole compounds show noteworthy biological activity such as tryptophan, tryptamine, and serotonin. In the recent years indoles and its bioisosters has been reported for its antimicrobial activity against Gram positive and Gram negative bacteria, such as *Enterobacter, Staphylococcus epidermidis, Pseudomonas aeruginosa and E.coli and* the yeast *Candida albicans.* Indole moieties are ubiquitous in the medicinal chemistry and shows activities in anticancer, antiviral, antiemetic, antihypertensive, antidepressant, antipsychotic, antiasthmatic, opioid agonist, sexual disfunction etc. Furthermore, C-3-substituted indoles are also highly valuable for the production of numerous biologically active compounds [4]. Seeing the significance of this structural motifs, a number of efforts have been made to construct functionalized indoles [5].

Figure 2: Some bioactive/natural products containing C-3 substituted benzofuran core.

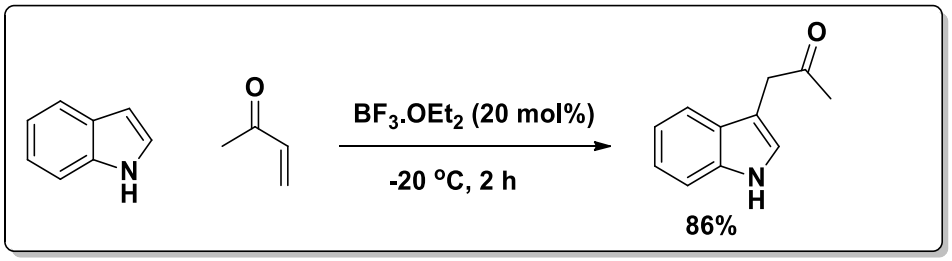


Like indoles C-3 substituted benzofuran derivatives are also considered to be as prominent bioactive compounds present in natural products. Benzofuran derivatives has attracted the attention of the medicinal chemists for the potential of the moiety in broad spectrum pharmalogical (**Figure 2**) and bio-logical activities. Benzofuran derivatives are found to show biological activities including antihyperglycemic, analgesic, antiparasitic, antimicrobial, antitumor activities [6]. Because of the broad spectrum biological and pharmacological activities several attempts has been made for the synthesis of benzoforan derivatives[7].

I. 2. . A brief review on C3-substituted indoles:

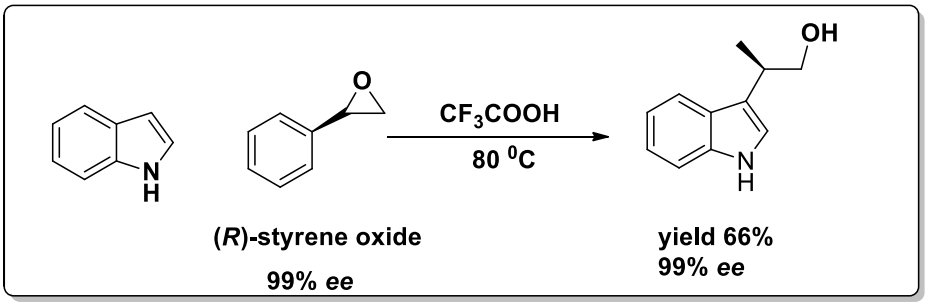
Synthesis of the C-3-substituted indoles structural motifs compounds has become part of great interest for the synthetic organic chemists because of its high importance and severe presence in nature. As a result, various synthetic methods are developed for the contruction of C-3-alkylindoles, such as conjugate addition of indoles to α, β-unsaturated compounds **(Scheme 1)**.[8]

Scheme 1: Lewis acid catalyzed conjugate addition of indole and MVK.



Mayr et.al. described a method of direct substitution of π-activated alcohols where aliphatic and aromatic epoxides undergo regioselective and stereoselective ring opening with and pyrroles

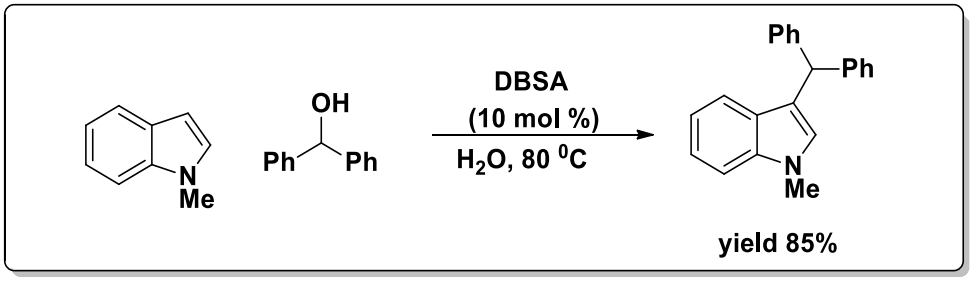
Scheme 2: Ring opening of (*R*)-styrene oxide stereoselectively with indole in CF_3CH_2OH.



indoles in 2,2,2-trifluoroethanol solvent without use of any additive or catalyst. Aromatic epoxides are attacked at benzylic position in selective way. Reaction occurs at the less-substituted position for aliphatic epoxides. Chiral epoxides react with >99% ee=enantiomeric excess **(Scheme 2).**[9].

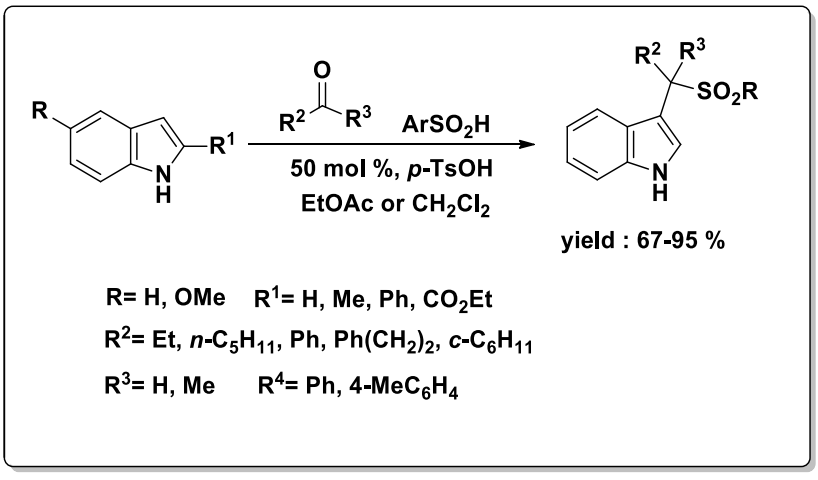
Two independent research groups, Kobayashi[10 a] and Cozzi[10 b,c], reported a catalytic method, using long-chain dodecylbenzenesulfonicacid (DBSA, 10 mol%) as a catalyst, proceeding through in water coupling of indoles with benzyl alcohols to form 3-substituted indole derivatives **(Scheme 3)**.

Scheme 3: Synthesis of 3-substituted indoles by in water catalytic benzhydrylation.



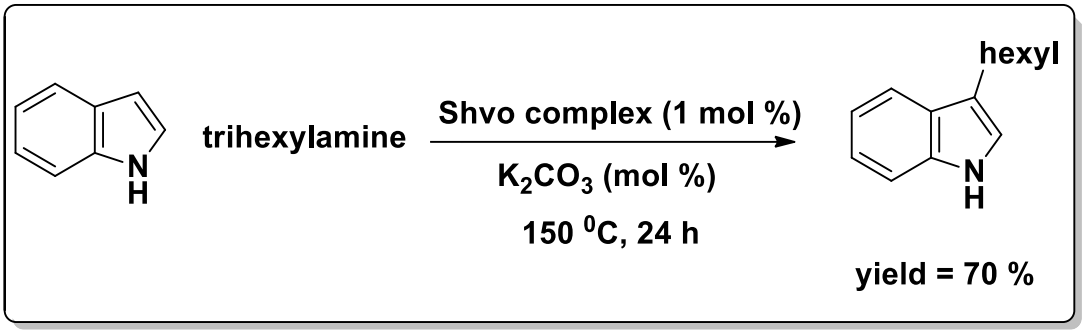
An advanced method including the formation of alkylideneindolenine intermediates followed by selective nucleophilic addition are also developed to generate variety of 3-substituted indoles.[11] Preparation of these compounds can be developed by the reaction of indoles and aldehydes in the presence of *p*-toluenesulfinic acid (**Scheme 4**).

Scheme 4: Synthesis of sulfonyl indoles by three-component coupling.



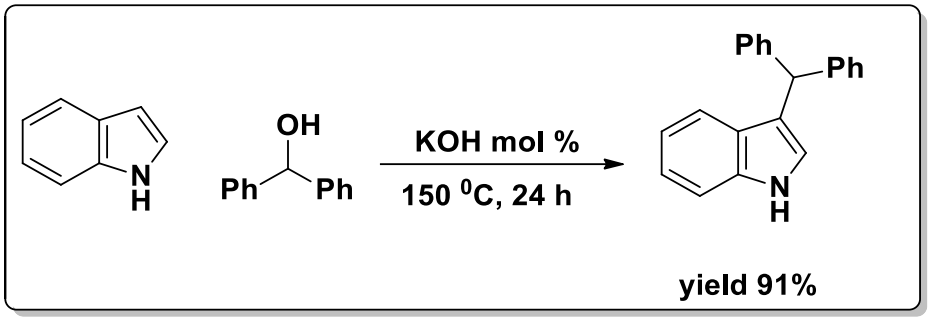
Ruthenium-catalyzed carbon–carbon bond development between indole and benzylic and aliphatic amines was reported by Beller et al. Shvo complex (**Scheme 5**) showed the highest reactivity, producing of 3-hexylindole. To our delight, C-alkylation in the 3-position occurred selectively and no formation of the N-alkylated product took place. [12].

Scheme 5: Alkylation of indole with di-*n*-hexylamine in the presence of different catalysts.



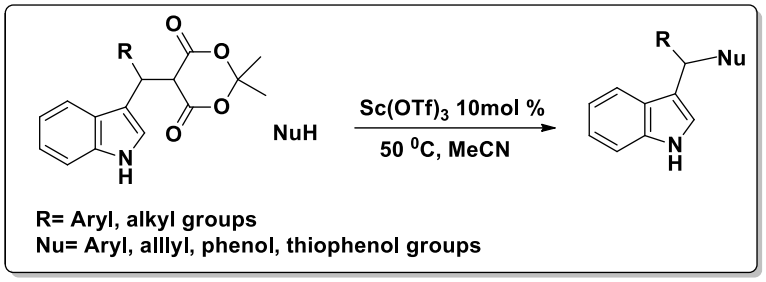
Yus and co-workers developed an environmentally friendly and regioselective method for non-catalytic C-3 alkylation using activated benzyl primary and secondary alcohols via hydrogen-transfer approach by the means of excess amount of KOH (**Scheme 6)**.[13]

Scheme 6: The direct alkylation of indoles using KOH and alcohols in solvent free method



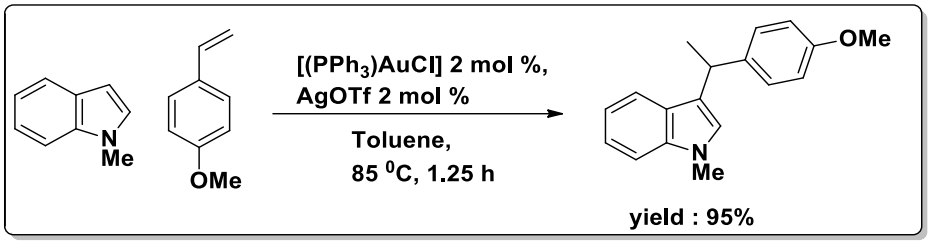
Armstrong et al. proposed nucleophilic substitution of indolylmethyl Meldrum's acids by $Sc(OTf)_3$ catalyst.[14] Variation in the nucleophiles results in the nucleophilic shift of the Meldrum's acid moiety via a gramine-type fragmentation. The reaction is worthwhile for the synthesis of heterocyclic compounds with significant molecular complexity (**Scheme 7**).

Scheme 7: Nucleophilic Additions to Indolylmethyl Meldrum's Acid Derivatives by Scandium Triflate catalyst.



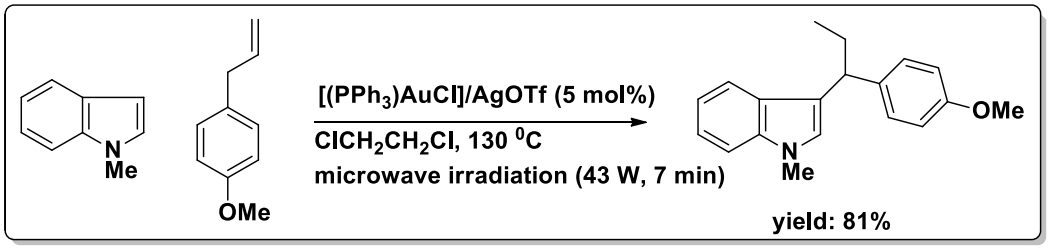
Intermolecular hydroarylation of aryl and aliphatic alkenes with indoles in the presence of [(PPh_3)AuCl]/AgOTf has been reported by Che and co-workers under thermal and microwave assisted conditions **(Scheme 8a, 8b).**[15]

Scheme 8a : Gold(I)-catalyzed coupling of indoles with aryl alkenes under thermal assisted conditions.



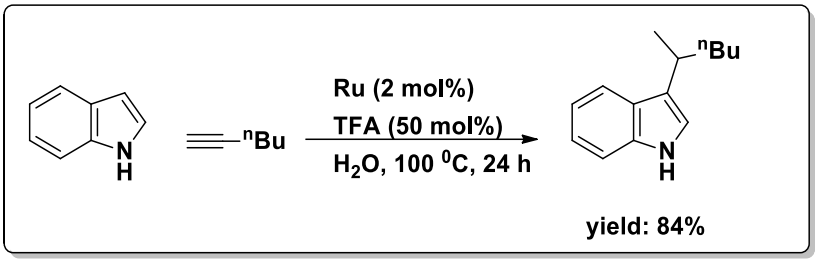
Depending upon the alkynes, different categories of regioselective compounds can be made by this method.This method works good for variety of styrene derivatives having electron-deficient, electron-rich and with bulky substituents. Unactivated aliphatic alkenes also exhibits high efficiency to generate corresponding adduct upto 90 percent yield.

Scheme 8b : Microwave-assisted gold(I)-catalyzed coupling of substituted indoles with aliphatic alkenes



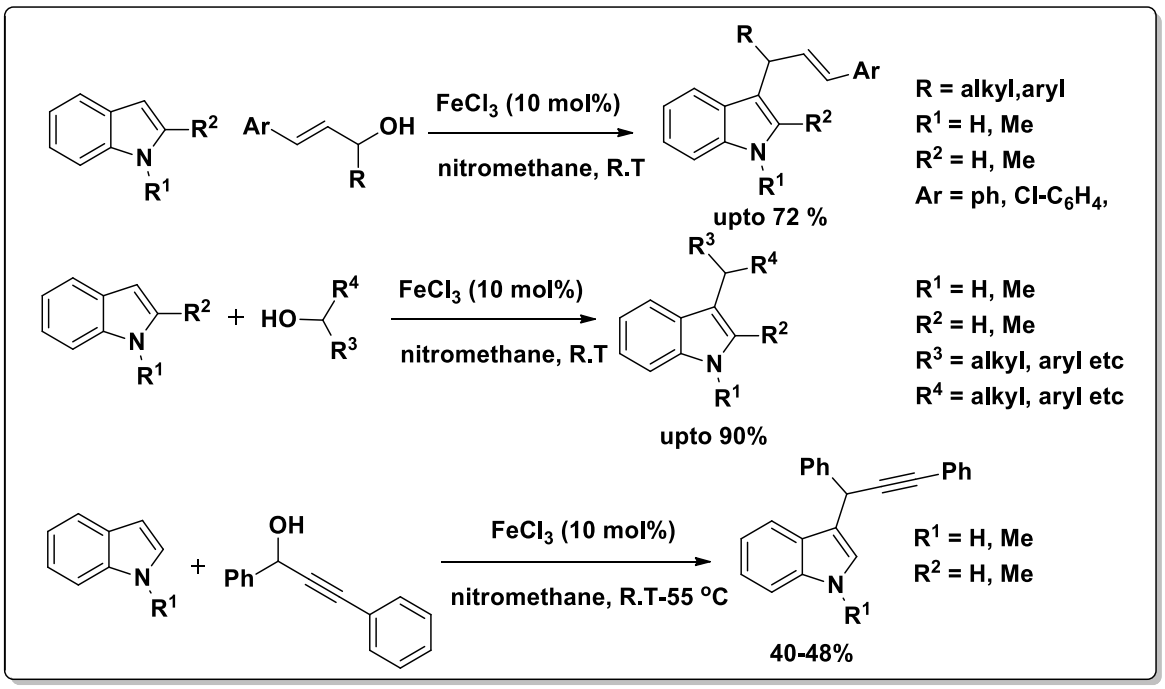
Cadireno et.al. developed C-3-alkylation reaction of indoles with terminal alkynes in aqueous medium using catalytic amounts of ruthenium and trifluoroacetic acid (**Scheme 9**).[16] Studies revealed that alkynes can act as electrophiles and alkylate indoles, via metal-catalyzed hydroarylation of the triple bond, the intermolecular version of this process giving an access to 3-alkenylindoles.

Scheme 9 : In water alkylation reaction of indoles with terminal alkynes catalyzed by complex [{RuCl(μ-Cl)(η^3: η^3-$C_{10}H_{16}$)}$_2$]**.**



In the recent past, some reports[17] have been described the method of direct catalytic substitution of indole with alcohols (**Scheme 10**).

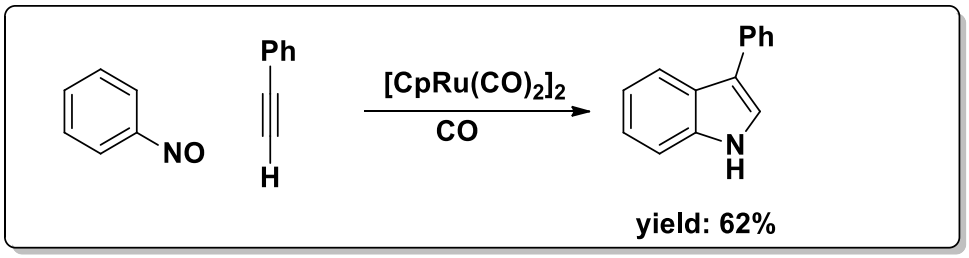
Scheme 10: Friedel–Crafts alkylation between indole and alcohol via iron salt



For an example, Jana *et.al* reported Friedel–Crafts alkylation via iron-catalyzed activation of alcohol between indole and alcohol under mild and environmentally benign conditions. The reaction occurs smoothly and efficiently to produce the 3-allylated indole products with substantial yield in nitromethane as solvent and $FeCl_3$ (10 mol %) at room temperature.[18] The reaction was fair and completed within a time of 2 h without having the need inert atmosphere, and produced the C3-substituted product solely.

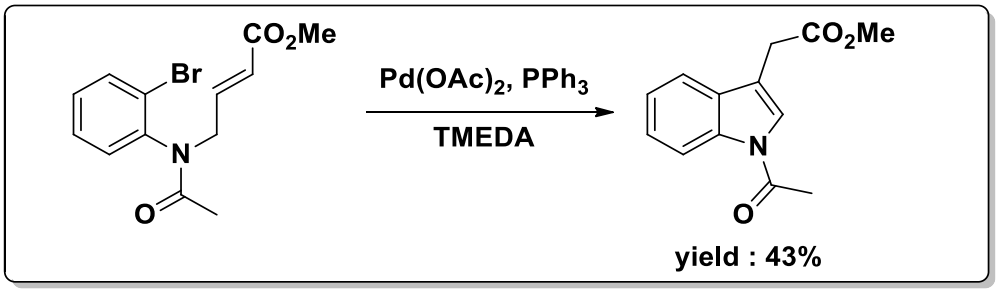
Kenneth M. Nicholas et al reported the Ru-catalyzed reductive coupling of a nitrosoaromatics with alkynes to generate substituted indole[19]. The reaction proceeds in regioselective fashion producing indoles as major product. A series of substituted indoles may be afforded by this method, using differently substituted nitrosoaromatics and alkynes as precursors (**Scheme 11).**

Scheme 11: Reductive Annulation of Nitrosoaromatics with Alkynes



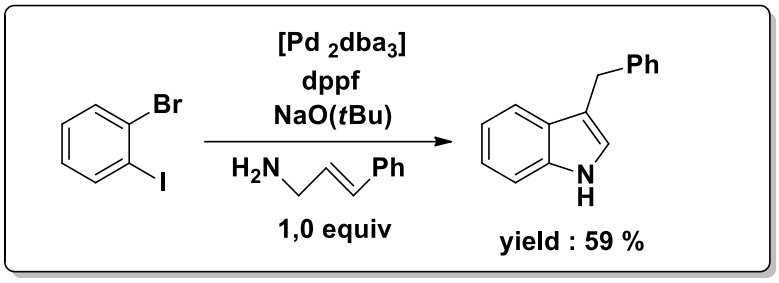
Miwako Mori, et al, utilised Heck cross-coupling reaction for the purpose of intramolecular cyclization to afford heterocyclic compounds, like N-acetyl indole using 2-bromo-*N*-acetylaniline derivatives and methyl 4-bromocrotonate as the starting materials, with a Pd catalyst in suitable conditions (**Scheme 12**). [20]

Scheme 12: Intermolecular reactions of aryl halides with olefinic bonds.



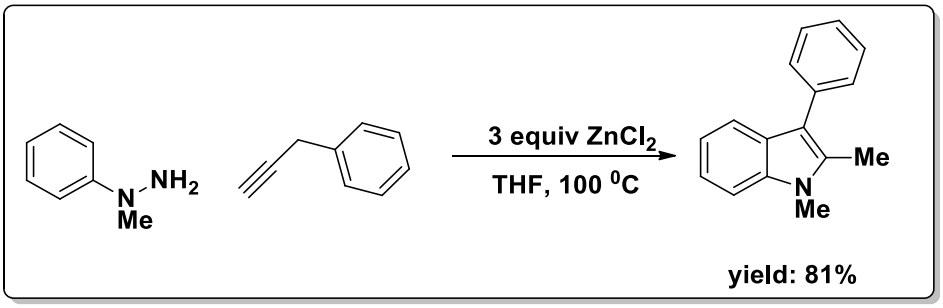
Morten Jørgensen and co-workers, utilised the advantage of the fact that the addition of aryl iodides are more facile over to that of aryl bromides to carry out sequential N-arylation and Heck cyclization, to synthesize 3-alkyl indole (**Scheme 13**). [21]

Scheme 13: One-pot approach to 3-Substituted Indoles through Palladium-catalyzed cascade Aryl Amination–Heck cyclization.



M. Beller and co-workers have developed a convenient one-pot method for the synthesis of substituted indoles starting from commercially available arylhydrazines and terminal alkynes in a reaction promoted by $Zn(OTf)_2$ or $ZnCl_2$ Remarkably, this environmentally friendly process allows the synthesis of free (N-unsubstituted) indoles (**Scheme 14**). [22]

Scheme 14: Domino synthesis of indoles Zinc-promoted hydrohydrazination of terminal alkynes.



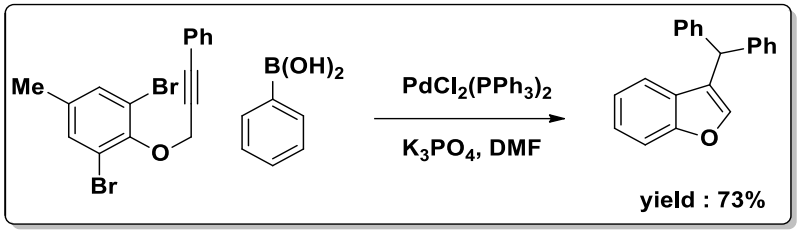
I. 2. 2. A brief review on C3-substituted benzofurans:

Benzofuran framework is an significant heterocyclic core constituent found in numerous natural products and in polymers.[23,24] Specially, 2,3-disubstituted benzofurans are distinguished constructing units in many biologically active and medicinal compounds.[25-30] Additionally, 3-substituted benzofurans have shown the activites as antiviral agents,[31] antimicrobial agents,[32] anticancer agents,[33] antitubercular agents,[34] and anti-inflammatory agents.[35] These compounds also act as enzyme inhibitors,[36,37] ischemic cell death inhibitors,[38] receptor agonist-antagonists[39]

and use as diagnostic imaging agents targeting amyloid plaques in Alzheimer's disease.[40] While it is observed that that the synthesis of 2-substituted or 2,3- disubstituted benzofurans are fairly reported, 3-substituted benzofurans synthesis are quite uncommon.[41-45]

Arcadi et al described a method of synthesis of C-3 functionalized 2-unsubstituted benzofurans applying the policy of cascade cyclocarbopalladation reaction followed by Suzuki-Miyaura coupling reactions of the aryl-substituted propargylic aryl ethers with arylboronic acid and potassium trans-β-styryltrifluoroborate towards the synthesis of benzofurans derivatives (**Scheme 15)**. [46]

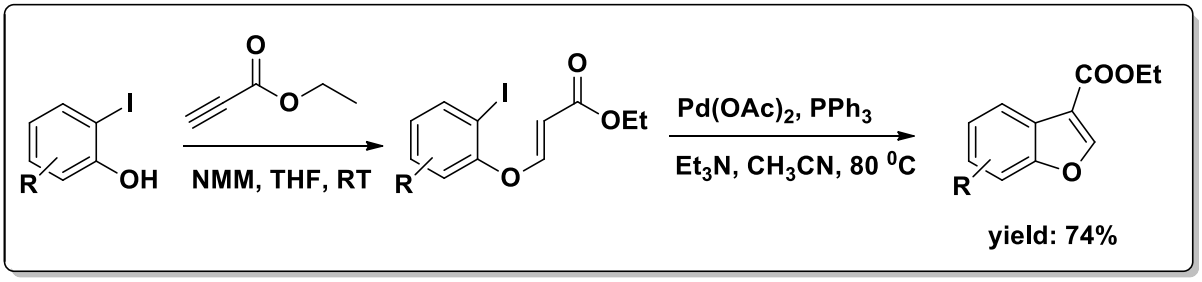
Scheme 15: Synthesis of C-3 alkylated benzofurans from reaction of 1-(3-arylprop-2-ynyloxy)-2-bromo benzene derivatives and organoboron compounds.



During this investigation, several methods for the synthesis of 3-ethoxycarbonyl benzofurans motifs have been reported by a few research groups. Few methods involve transition metal as catalyst where other are transition metal free synthetic methods.

Frontier et al. reported a synthetic approach involving 3-(2-iodophenoxy)acrylic acid ethyl ester for

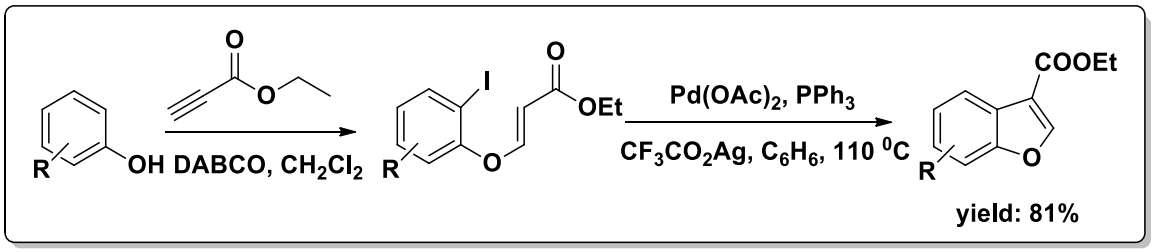
Scheme 16a: Preparation of 3-Ethoxycarbonyl Benzofurans from 2-iodophenol and ethyl propionate



the synthesis of 3-ethoxycarbonyl benzofuran in 74% yield **(Scheme 16a)**.[47] The ester was generated from the reaction of 2-iodophenol and ethyl propionate in the presence of *N*-methylmorpholine (NMM).

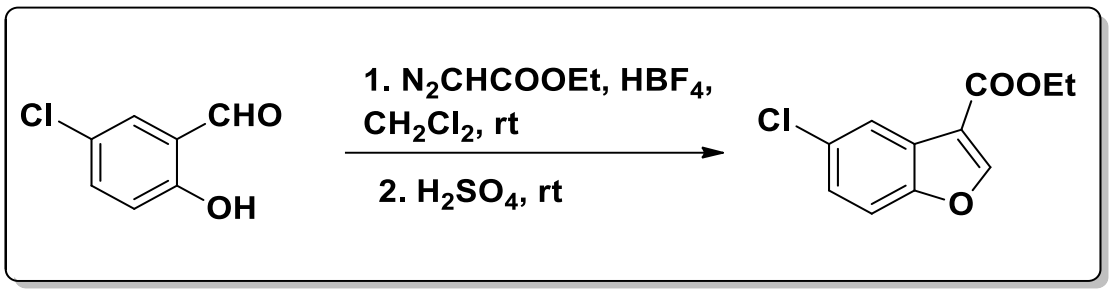
Wang and group established a method of synthesis of 3-ethoxycarbonyl benzofuran by palladium catalyst in 81% yield[48] via the direct oxidative cyclization from (*E*)-3-phenoxyacrylates **(Scheme 16b)** which were prepared from phenol and propynoic acid ethyl ester in the presence of 1,4 -diazabicyclo[2.2.2]octane (DABCO).

Scheme 16b: Preparation of 3-Ethoxycarbonyl Benzofurans from (*E*)-3-phenoxyacrylates.



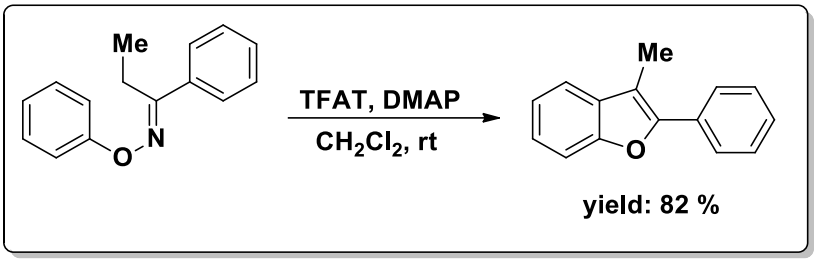
Hossain et. al developed a one-pot synthetic method for the preparation of 3-Ethoxycarbonyl Benzofurans with inexpensive and commercially available starting materials and exhibits several biologically activity **(Scheme 16c)**[49].

Scheme 16c: Synthesis of 3-Ethoxycarbonyl Benzofurans from Salicylaldehydes and Ethyl Diazoacetate.



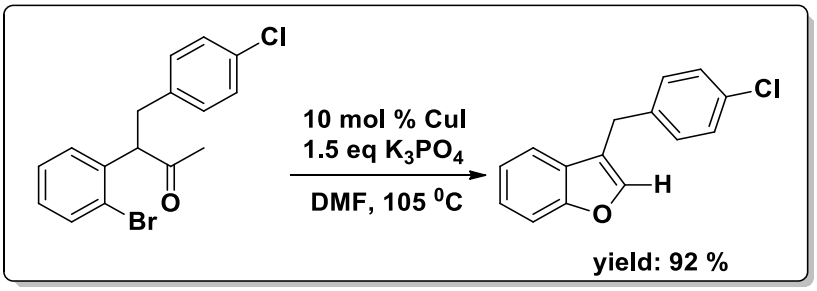
Takeda et al developed a novel method to synthesize a series of 2-aryl 3 substituted benzofuran on the reaction of variety of oxime ethers with TFAT-DMAP which gives a satisfactory yield, which shows biologicals activity **(Scheme 17)**[50].

Scheme 17: Preparation of Benzofurans by the means of [3,3]-Sigmatropic rearrangement prompted by *N*-Trifluoroacetylation of Oxime Ethers.



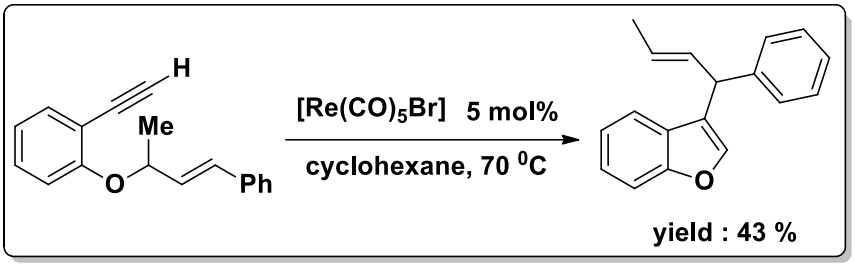
An efficient CuI-catalyzed ring closure method of 2-haloaromatic ketones was established by Chen. et. al., which affords a wide variety of benzo[*b*]furans which includes 2- substituted, 3- substituted and 2,3- disubstituted benzo[*b*]furans. This method is quite appreciable for its excellent tolerance to different functional groups to produce benzofuran.[51] **(Scheme 18)**.

Scheme 18: Synthesis of Benzo[*b*]furans via CuI-Catalyzed Ring Closure.



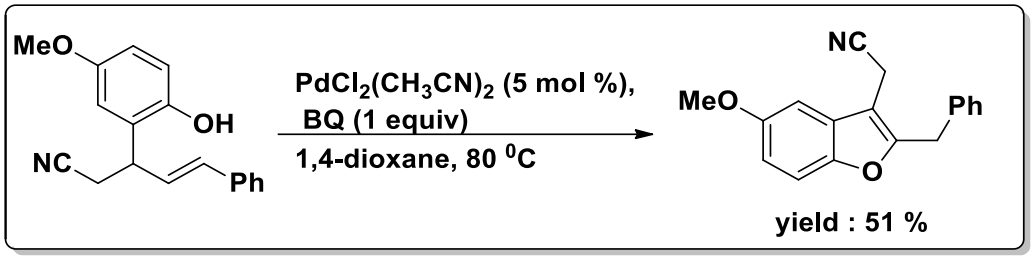
Zi et al. reported rhenium-catalyzed carboalkoxylation of alkyne in moderate to good yields where rhenium acted as a π acid catalyst to facilitate the alkynes, followed by a charge-accelerated [3,3]-sigmatropic rearrangement **(Scheme 19)**.[52]

Scheme 19: Rhenium-Catalyzed Intramolecular Carboalkoxylation of Alkynes for the Synthesis of C3-Substituted Benzofurans



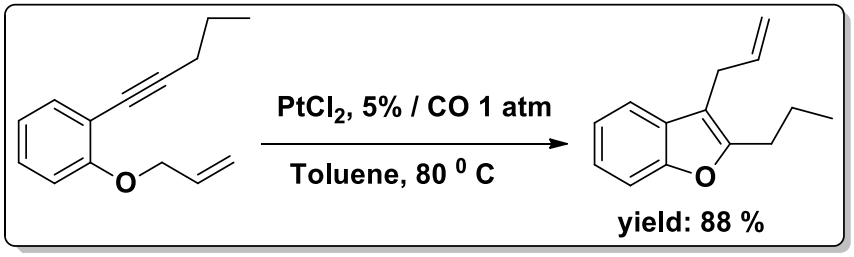
Ghorai et al described a synthetic route for the synthesis of functionalized 2-benzyl benzo[*b*]furans via a regioselective *5-exo-trig* intramolecular oxidative cyclization of *ortho*-cinnamyl phenols using $[PdCl_2(CH_3CN)_2]$ as catalyst and benzoquinone as an oxidant **(Scheme 20)**.[53]

Scheme 20: Synthesis of functionalized Benzo[*b*]furans via Oxidative Cyclization of o-Cinnamyl Phenols.



Furstner et al described an efficient method for the synthesis of the heterocycles by $PtCl_2$-Catalyzed Intramolecular Carboalkoxylation and carboamination of alkynes **(Scheme 21)**.[54]

Scheme 21: Synthesis $PtCl_2$-Catalyzed Benzofuran Synthesis by Intramolecular Carboalkoxylation (Allyl/Benzyl Shift Reactions)



I. 3. Summary:

A number of synthetic strategies were designed for the generation of 3 alkylated indoles and benzofurans. Although few of these above methods are quite efficient, however, many of them suffer from one or more drawbacks; for example, use of large excess of starting materials and expensive and toxic reagents, low yield of the products, complicated reaction assembly, harsh reaction conditions, tedious isolation procedure etc. Some of the methodologies are restricted for the synthesis of the 2 substituted indoles and benzofurans as a secondary product. Few protocols fail to show the versatility of the method of synthesis. Therefore, the development of an efficient, general and environmentally friendly process, which enables a rapid and easy access to 3-

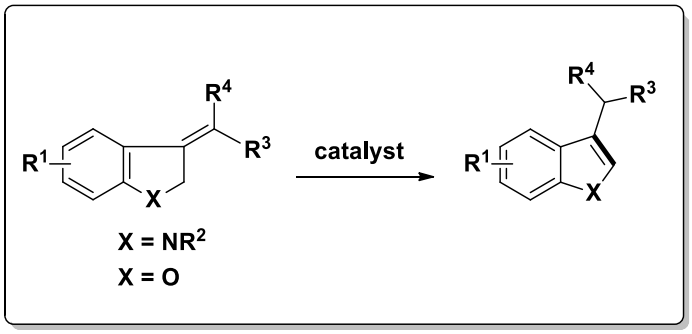
substituted indoles and benzofurans, which are of great importance, is highly desirable in academic interest.

I. 4. Present work:

The synthesis of functionalized 3-alkylated indole and benzofuran types of compounds are an important research topic. Only a few reports has been found in the literature towards the synthesis of 3-alkylated indole derivatives. Specially 3-alkylated benzofurans one of the less invaded part of research till date in the region of synthetic organic chemistry. For this cause, the founding of new, well-organized synthetic methods for the synthesis of 3-alkylated heterocycles derivatives with selective control of substitution patterns from easily obtained starting materials would be highly desirable.

In extension of our current program in emerging environmentally friendly and economical friendly iron-catalyzed synthesis of heterocyclic molecules, we have developped an iron(III)-catalyzed strategy for the synthesis of selectively substituted heterocycles via isomerization of 3-(methylene)indoline and 3-methylene-2,3-dihydrobenzofuran derivatives under mild conditions. During our latest study on the synthesis of benzo[*b*]carbazole derivatives, it was noticed that these reaction conditions are not workable for substituted 3-methyleneindoline derivatives. So, we intended to perform a thorough investigation of this transformation. In this paper, we now report a selective and general synthesis of 3-substituted indoles and benzofurans by aromatization of 3-methyleneindoline and benzofuran derivatives with use of $Fe(OTf)_3$ as catalyst.

Scheme 22: Our present work for the synthesis of 3-substituted indoles and benzofurans

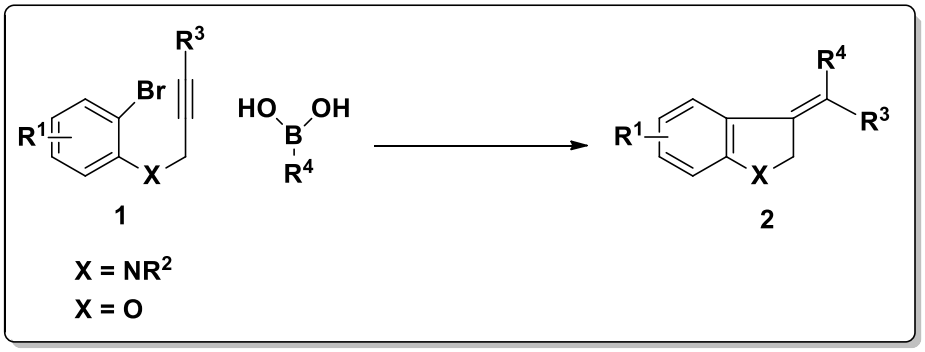


I .5. Result and Discussion:

The required starting material, 3-methyleneindoline derivative, was prepared in high yield by using our previous method involving a domino Heck–Suzuki coupling of 2-bromo-*N*-propargylanilide **1** with arylboronic acid derivatives, as outlined in (**Scheme 23)**. After having a series of 3-methyleneindoline derivatives **2**, we next tried to optimize the reaction conditions for the isomerization of 3-methyleneindoline derivatives.

The domino Heck–Suzuki coupling between substrate **1** and phenylboronic acid was accomplished to afford the 1,5-enyne **2** in 75 % yield using 5 mol % of $Pd(OAc)_2$ and 10 mol % of tricyclohexylphosphine (PCy_3) in the presence of 2.5 M K_2CO_3 in ethanol and toluene at 70°C.

Scheme 23: Synthesis of of 3-methyleneindoline and 3-methylene-2,3-dihydrobenzofuran derivatives

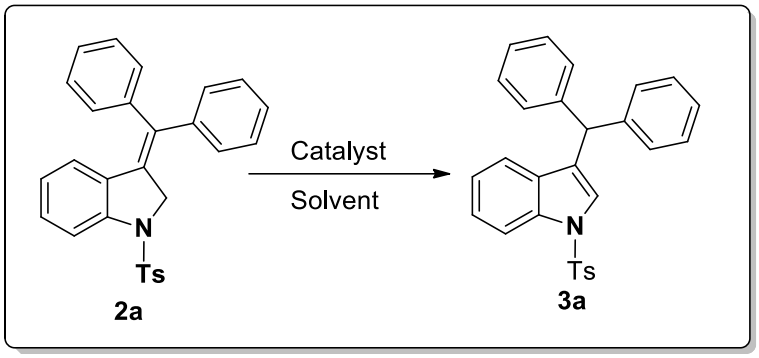


At first, a large number of Lewis and Brønsted acids were screened by using **2a** as the model substrate **(Table 1)**. We first examined the isomerization of **2a** to **3a** in the presence of $FeCl_3$ (10 mol-%) at 80 °C in 1,2-dichloroethane; however, no reaction took place even after prolonged heating **(Table 1, entry 1)**. Interestingly, we noticed that when the reaction mixture was heated to 135 °C in chlorobenzene a trace amount of isomerized product **3a** was formed after heating for 12 h (**Table 1, entry 2**).

Encouraged by these results, we then screened other commonly used iron salts such as $FeBr_3$ and $Fe(OTf)_3$ for this transformation. We found that $FeBr_3$ did not initiate the reaction, whereas $Fe(OTf)_3$ (10 mol-%) gave 90% yield at 60 °C within 3 h. Moreover, we also observed that the reaction was sluggish when we reduced the amount of $Fe(OTf)_3$, and further increasing the amount of catalyst

did not improve the yield. Next, we also screened other metal salts such as $In(OTf)_3$, AgOTf, and $AgSbF_6$; we found that $In(OTf)_3$ did not work under similar conditions, but the isomerization took place with AgOTf (10 mol-%) and $AgSbF_6$ (10 mol-%) at 60 °C and gave product **3a** in 73% and 76% yields, respectively **(Table 1, entries 6 and 7)**.

Table 1. Optimization of reaction conditions for the isomerization of 2a to indole derivative 3a.[a]



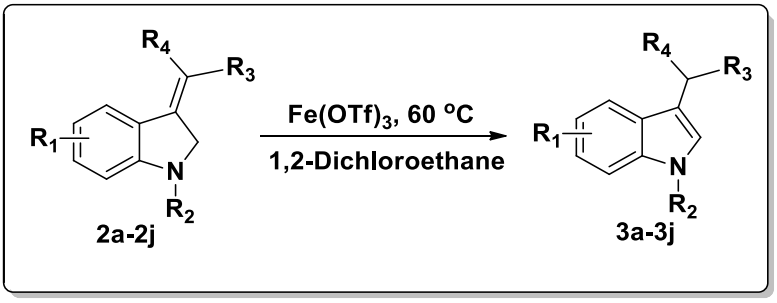
Entry	Catalyst	Solvent	T(°C)	Time (h)	Yield (%)[b]
1	$FeCl_3$	1,2-dicholoethane	80	10	n.r.
2	$FeCl_3$	Cholorobenzene	135	10	15
3	$FeBr_3$	1,2-dichloroethane	80	6	n.r.
4	$Fe(OTf)_3$	1,2-dicholoroethane	60	3	90
5	$In(OTf)_3$	1,2-dichloroethane	60	6	n.r.
6	AgOTf	1,2-dicholroethane	60	6	73
7	$AgSbF_6$	1,2-dicholroethane	60	4	76
8	$PTSA.H_2O$	1,2-dicholroethane	60	5	74
9	TfOH	1,2-dicholroethane	60	3	82

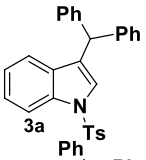
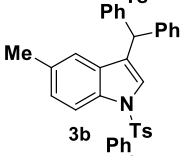
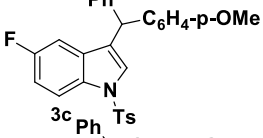
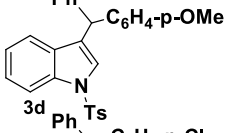
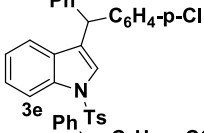
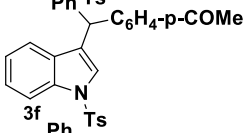
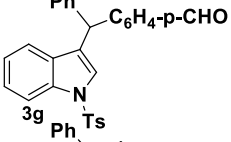
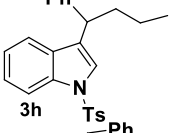
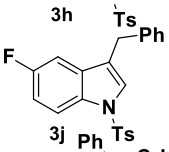
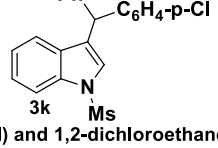
[a]Reaction conditions: Substrate **2a** (0.23 mmol), 1,2-dichloroethane (2 ml), $Fe(OTf)_3$ (0.023 mmol).
[b]isolated pure yield.

Brønsted acids such as *p*-toluenesulfonic acid monohydrate (PTSA·H2O) and triflic acid (TfOH) also afforded the desired products, but not in higher yields (74% and 82%) **(Table 1, entries 8 and 9)**. Finally, we also tested this isomerization with stoichiometric amounts of bases such as K_3PO_4 in DMF at 100 °C **(Table 1, entry 10)**. Although, this strategy has been reported for the synthesis of 3-substituted benzofuran derivatives, it did not work for the synthesis of indole derivative **3a**. These results demonstrated that $Fe(OTf)_3$ has higher catalytic activity for this transformation. A moderately strong Lewis acid is probably more efficient for this transformation. Thus, $Fe(OTf)_3$ (10 mol-%) in 1,2-dichloroethane at 60 °C was defined as the optimal reaction conditions for further study.Next, the isomerization of a large array of 3-methyleneindoline derivatives **2a**–**2j** was investigated under these reaction conditions; the results are presented in Table 2. We were pleased to observe that this isomerization process was quite general and smoothly afforded a variety of disubstituted and monosubstituted alkylideneindole derivatives in very good to excellent yields. The reaction was not markedly affected by the substituents on any of the aryl rings. For example, aryl rings (R^4) including those bearing an electron-donating group such as *p*-OMe **(Table 2, entries 3 and 4)** and electron-withdrawing groups such as *p*-Cl and *p*-COMe **(Table 2, entries 5, 6 and 7)** were compatible, and all gave the corresponding C-3-substituted indoles in good to excellent yields. Functional groups such as –CHO, –COMe, and –Cl are very useful for further synthetic transformations to construct a library of C-3-substituted indole derivatives for biological studies. Similarly, both substituted and unsubstituted aryl rings (R^3) were also tolerated and gave high yields of the desired products.

Moreover, aryl- and alkyl-substituted alkylideneindole derivative **2h (Table 2, entry 8)** was also smoothly converted into the desired C-3-substituted indole derivative **3h** in good yield. In addition,

Table 2. $Fe(OTf)_3$-catalyzed isomerisation of **2a-2j** to C-3 substituted indoles **3a-3j**.[a]



Entry	R_1	R_2	R_3	R_4	Time	Product	Yield(%)[b]
1	H	Ts	Ph	Ph	3	 3a	90
2	p-Me	Ts	Ph	Ph	3	 3b	89
3	p-F	Ts	Ph	p-OMe-C_6H_4	3	 3c	96
4	H	Ts	Ph	p-OMe-C_6H_4	2.5	 3d	97
5	H	Ts	p-Cl-C_6H_4	Ph	5	 3e	82
6	H	Ts	p-COMe-C_6H_4	Ph	4	 3f	83
7	H	Ts	Ph	p-CHO-C_6H_4	4	 3g	81
8	H	Ts	n-Pr	Ph	7	 3h	72
9	p-F	Ts	H	Ph	3.5	 3j	75
10	H	Ms	p-Cl-C_6H_4	Ph	2.5	 3k	99

[a]Reaction conditions: Substrate (0.23 mol), Fe(OTf)3 (0.023 mmol) and 1,2-dichloroethane (2 mL).
[b]pure isolated yield.

Mono-substituted alkylideneindole derivative **2i (Table 2, entry 9)** could also be aromatized to 3-benzyl indole derivative **3i** in 75% yield in the presence 10 mol-% $Fe(OTf)_3$. Further study shows

that, instead of *N*-Ts derivative **2j (Table 2, entry 10)**, the substrate containing *N*-Ms also worked smoothly and gave the desired 3- alkylindole derivative **3j** in quantitative yield.

Furthermore, we also applied this methodology to the synthesis of 3-alkylbenzofurans. To our delight, the reactions proceeded smoothly in the presence of 10 mol-% $Fe(OTf)_3$, affording the corresponding 3-alkylbenzofurans **5a**–**5d (Table 3)** in good to excellent yields. This aromatization was not affected by the presence of a variety of functional groups such as *p*-OMe, *m*-CF_3, and *m*-NO_2 on aryl ring R^1. This method was also very efficient for the synthesis of naphthyl-substituted benzofuran derivative **4e** in 92% yield **(Table 3, entry 5).** Compared to a recently developed method for the aromatization of 2,3-dihydro-methylenebenzofuran derivatives in basic medium that required stoichiometric amounts of bases such as K_3PO_4 in DMF solvent at 100 °C, the present method is superior as only catalytic amounts (10 mol-%) of an environmentally friendly iron salt is required and it works at lower temperature (60 °C).

Table 3: $Fe(OTf)_3$-catalyzed isomerization of **4a**–**4d** to C-3-substituted benzofurans **5a**–**5d**.[a]

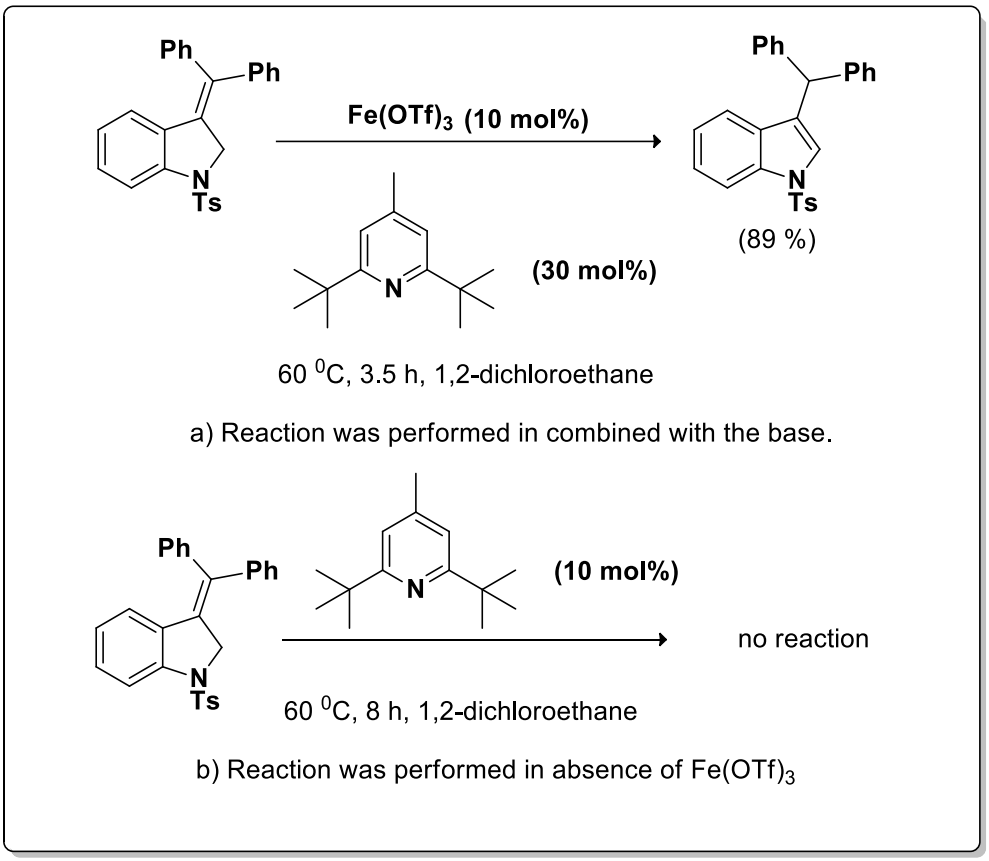
Entry	R_1	Temp (°C)	Time(h)	Products	Yield(%)[b]
1	Ph **4a**	60	3	**5a**	
2	*p*-OMe-Ph **4b**	60	2.5	**5b**	
3	*m*-CF_3-Ph **4c**	80	6	**5c**	
4	*m*-NO_2-Ph **4d**	80	4	**5d**	
5	1-Naphthyl **4e**	60	3	**5e**	

[a]Reaction conditions: Substrate (0.230 mol), $Fe(OTf)_3$ (0.023 mmol) and 1,2-dchloroethane (2 mL). [b]pure isolated yield.

Therefore, an $Fe(OTf)_3$-catalyzed isomerization of 3-methyleneindoline and benzofuran derivatives to corresponding 3-substituted indoles and benzofuran derivatives is very straightforward. $Fe(OTf)_3$ was found to be the best among the catalysts studied. $Fe(OTf)_3$ was prepared from $FeCl_3$ (99.5%) and TfOH according to a literature procedure.[16] Moreover, we noticed that TfOH was also effective for this transformation and gave 82% yield (Table 1,entry 9); hence, there was a chance that this reaction may also be catalyzed by in situ generated TfOH. To check this, we carried out this reaction

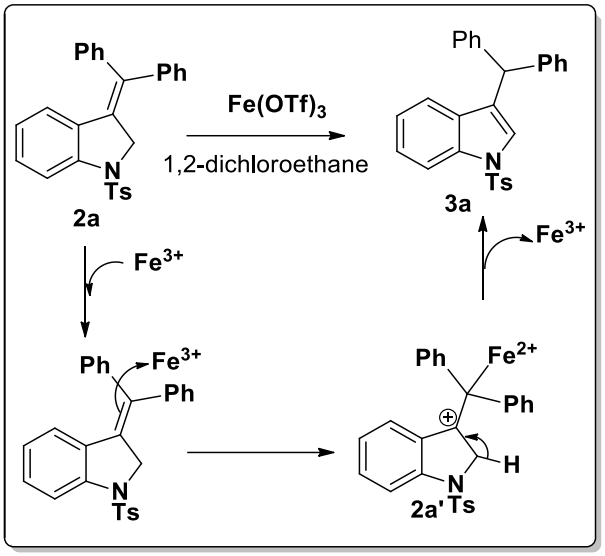
in the presence of a sterically hindered non-nucleophilic base such as 2,6-di-*tert*-butyl-4-methylpyridine (Scheme 3). We observed that no significant changes occur when we added pyridine as base in combination with $Fe(OTf)_3$. The combination of catalysts also gave a high yield of the desired product, but no such isomerization took place in the presence of pyridine base. So, we concluded that possibly TfOH was not generated during the course of the reaction and $Fe(OTf)_3$ was the real catalyst for this transformation.

Scheme 24. Study of the reaction in the presence of a combination of $Fe(OTf)_3$ and base.



A plausible mechanism for the isomerization, based on the above experimental observations, is shown in **Scheme 25**. We believe that iron (III) triflate coordinates to the double bond of **2a** and thus polarizes the alkene double bond. This activation triggers the deprotonation of the $–CH_2–$ group, leads to the isomerization of the double bond, and affords iron-bound product **2a**. Then, demetalation of **2a** by rapid protonolysis releases indole derivative **3a** and regenerates $Fe(OTf)_3$ for the next catalytic cycle.

Scheme 25: Plausible mechanism for the isomerization of **2a**.



I. 6. Conclusions

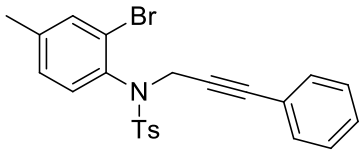
We have developed an $Fe(OTf)_3$-catalyzed synthesis of 3-alkylindole and 3-alkylbenzofuran derivatives in good to high yields under mild conditions from 3-methyleneindoline and benzofuran derivatives. A variety of functionalized 3-alkylidene indole and benzofuran derivatives could easily be prepared by a palladium-catalyzed domino Heck–Suzuki coupling reaction. The advantages of this methodology are easily available starting materials, toleration of various functional groups, excellent regioselectivity, and the use of an environmentally friendly and inexpensive iron catalyst. In view of the mild reaction conditions and broad functional group tolerance, we expect that this reaction will be useful for the synthesis of biologically significant 3-substituted indoles and benzofurans.

I. 7. Experimental Section :

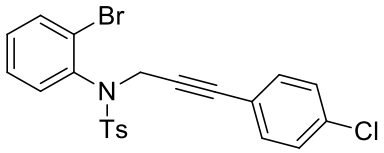
Representative experimental procedure for the synthesis of (1a)–(1j):

Compounds 1a, 1c, 1d, 1f, 1g, 1h, 1i, 1j were made following previous methods and consequently these compounds are already known.[1]

Representative experimental procedure for the synthesis of 2-bromo-*N*,4-dimethyl-N-(3-phenylprop-2-yn-1-yl)aniline (1b):

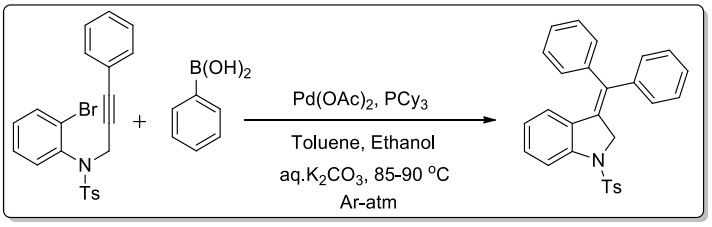


Light yellow semisolid (yield 92%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ2.32 (s, 3H), 2.40 (s, 3H), 4.31 (d, *J* = 18 Hz, 1H), 4.96 (d, *J* = 18 Hz, 1H), 7.01–7.09 (m, 2H), 7.16–7.19 (m, 2H), 7.21–7.27 (m, 5H), 7.48 (s, 1H), 7.75 (d, *J* = 5.4 Hz, 8.4 Hz, 2H) ppm.^{13}C NMR ($CDCl_3$, 75 MHz): δ20.8, 21.5, 41.3, 83.3, 85.5, 122.4, 125.6, 128.1, 128.2, 128.6, 128.8, 129.4, 131.5, 134.3, 134.9, 137.1, 140.8, 143.7 ppm. HRMS (ESI) : calcd for $C_{23}H_{21}BrNO_2S$ $[M+H]^+$ 454.0476; found 454.0475. ***N*-(2-bromophenyl)-*N*-(3-(4-chlorophenyl)prop-2-yn-1-yl)-4-methylbenzenesulfonamide (1e):**



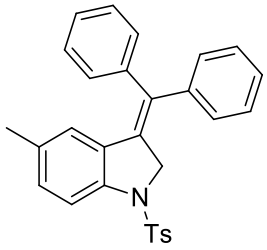
Yellow semisolid (yield 89%). ^{1}H NMR ($CDCl_3$, 300 MHz):δ2.42 (s, 3H), 4.36 (d, *J* = 15 Hz, 1H), 4.94 (d, *J* = 15 Hz, 1H), 7.09–7.17 (m, 1H), 7.22–7.23 (m, 1H), 7.24–7.31 (m, 8H), 7.61–7.69 (m, 1H), 7.74 (d, *J* = 8.1 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ21.6, 41.2, 84.2, 84.6, 120.8, 125.9, 127.8, 128.1, 128.6, 129.5, 130.3, 131.9, 132.7, 133.9, 134.5, 136.9, 137.6, 143.9 ppm. HRMS (ESI) : calcd for $C_{22}H_{18}BrClNO_2S$ $[M+H]^+$ 473.9930; found 473.9931.

Representative experimental procedure for the synthesis of 3-(diphenylmethylene)-1-tosylindoline (2a) :



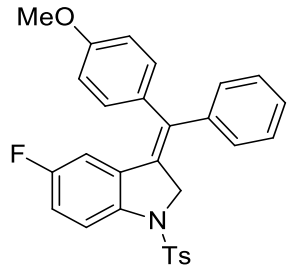
To a solution of **1a** (220 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), phenyl boronic acid (92 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively. The resulting solution was stirred at 85-90 °C under argon atmosphere for 2 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with EtOAc. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **2a** as a yellow semisolid (164 mg, 0.37 mmol, 75%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.40 (s, 3H), 4.65 (s, 2H), 6.27 (d, *J* = 7.8Hz, 1H), 6.68 (t, *J* = 7.8 Hz,1H), 7.00–7.16(m, 5H), 7.22–7.36 (m, 8H), 7.64 (dd, *J* = 8.1, 13.5 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 56.0, 115.7, 123.4, 124.7, 126.2, 127.4, 127.6, 128.1, 128.6, 128.9, 129.2, 129.6, 130.2, 133.8, 135.5, 140.9, 141.8, 144.2, 144.9 ppm. HRMS (ESI) calcd for $C_{28}H_{23}NNaO_2S$ $[M+Na]^+$ 460.1347; found 460.1346.

3-(diphenylmethylene)-5-methyl-1-tosylindoline (2b) :



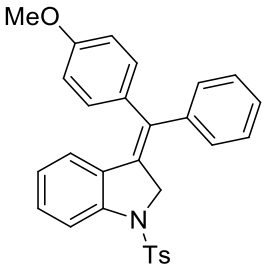
To a solution of **1b** (227mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL) were added, phenylboronic acid (92 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively and the process was followed as described in **2a** to afford the product **2b** as a yellow solid (173mg, 0.38 mmol, 77%), m.p. 162 °C. ^{1}H NMR ($CDCl_3$, 300MHz) δ 1.98(s, 3H), 2.40 (s, 3H), 4.64 (s, 2H), 6.02 (s, 1H), 6.94–7.01 (m, 7H), 7.07–7.09 (m, 2H), 7.22–7.44 (m, 7H), 7.58 (dd, *J* = 3.6Hz, 4.5Hz, 3H), 7.65–7.73 (m, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.9, 21.5, 56.2, 115.7, 125.3, 127.5, 127.6, 128.1, 128.5, 128.8, 129.2, 129.6, 129.9, 130.4, 130.5, 133.0, 133.7, 135.3, 140.9, 141.8, 142.7, 144.0 ppm. HRMS (ESI) calcd for $C_{29}H_{25}NO_2S$ $[M+H]^+$ 451.1606; found 451.1606.

(*E*)-5-fluoro-3-((4-methoxyphenyl)(phenyl)methylene)-1-tosylindoline (2c) :



To a solution of **1c** (229mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), *p*-methoxyphenylboronic acid (114 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively and the process was followed as described in **2a** to afford the product **2c** as a yellow solid (174 mg, 0.36 mmol, 72%), m.p. 142 °C. ^{1}H NMR ($CDCl_3$, 300MHz) δ 2.41 (s, 3H), 3.83 (s, 3H), 4.71 (s, 2H), 6.78–7.05 (m, 7H), 7.23–7.40 (m, 6H), 7.54 (d, J = 8.1 Hz,2H), 7.61 (q, J = 2.4 Hz,1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 55.3, 56.8, 111.3 (d, J_{C-F} = 25.8 Hz), 113.9, 115.4 (d, J_{C-F}= 24.0 Hz), 117.3 (d, J_{C-F}= 8.7 Hz), 127.1, 127.5, 128.0, 129.0, 129.1, 129.5, 129.6, 133.4, 133.7, 136.8, 140.3, 140.7, 144.3, 160.7 (d, J_{C-F}= 238.7 Hz) ppm. HRMS (ESI) calcd for $C_{29}H_{25}FNO_3S$ $[M+H]^+$ 486.1539; found 486.1537.

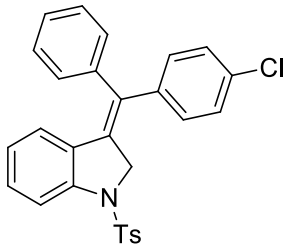
(*E*)-3-(4-methoxyphenyl)(phenyl)methylene)-1-tosylindoline (2d) :



To a solution of **1a** (220 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), *p*-methoxyphenylboronic acid (114 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively and the process was followed as described in **2a** to afford the product **2d** as a yellow solid (170 mg, 0.36 mmol, 73%), as a very slight mixture of non–separable isomers (*E:Z*) where *E* isomer is the major product, m.p. 124 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.42 (s, 3H), 3.84 (s, 3H), 4.70 (s, 2H), 6.24 (d, J = 7.8Hz, 1H), 6.68 (t, J = 7.8 Hz, 1H), 6.81–6.96 (m, 2H), 7.01–7.07 (m, 2H), 7.13 (t, J = 7.8 Hz, 1H), 7.24–7.33 (m, 8H), 7.66 (dd, J = 8.1 Hz, 9.9 Hz, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 55.3, 56.2, 113.8, 115.8,

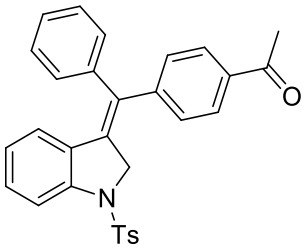
123.4, 124.6, 127.4, 127.6, 128.9, 129.3, 129.5, 129.6, 130.7, 132.9, 133.8, 134.2, 135.3, 141.1, 144.2, 144.7 ppm. HRMS (ESI) calcd for $C_{29}H_{25}NNaO_3S$ $[M+Na]^+$ 490.1453; found 490.1452.

(*Z*)-3-((4-chlorophenyl)(phenyl)methylene)-1-tosylindoline (2e) :



To a solution of **1e** (237 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), phenylboronic acid (92 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively and the process was followed as described in **2a** to afford the product **2e** as a yellow solid (160 mg, 0.34 mmol, 68%), m.p. 168 °C. ^{1}H NMR ($CDCl_3$, 300MHz) δ 2.40 (s, 3H), 4.61 (s, 2H), 6.26 (d, J = 7.8 Hz, 1H), 6.67 (t, J = 7.8 Hz, 1H), 6.96 – 7.03 (m, 3H), 7.12–7.42(m, 9H), 7.64 (dd, J = 8.4, 12.6 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$,75 MHz) δ 21.5, 55.8, 115.7, 123.5, 124.8, 127.9, 128.8, 129.0, 129.2, 129.5, 129.7, 130.0, 130.8, 133.4, 133.7, 134.1, 140.2, 140.5, 144.3, 145.0 ppm. HRMS (ESI) calcd for $C_{28}H_{23}ClNO_2S$ $[M+H]^+$ 472.1138; found 472.1136.

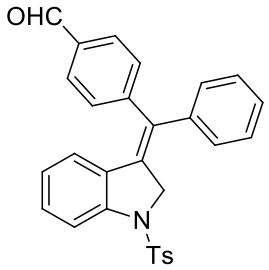
(*Z*)-1-(4-(phenyl(1-tosylindolin-3-ylidene)methyl)phenyl)ethanone (2f) :



To a solution of **1f** (241 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), phenylboronic acid (92 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively and the process was followed as described in **2a** to afford the product **2f** as a yellow solid (180 mg, 0.37 mmol, 75%), m.p. 92 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.43 (s, 3H), 2.64 (s, 3H), 4.66 (s, 2H), 6.30 (d, J = 8.1 Hz, 1H), 6.71 (t, J = 7.2 Hz, 1H), 7.03–7.06 (m, 2H), 7.16–7.37 (m, 8H), 7.67 (dd, J = 8.1 Hz, 17.1 Hz, 3H), 7.96 (d, J = 8.4 Hz, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75MHz) δ 21.5, 26.6, 55.8, 115.6, 123.5, 125.0, 126.7, 127.4, 128.0, 128.4, 128.7, 131.7,

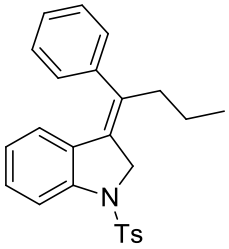
133.6, 134.2, 136.0, 140.2, 144.3, 145.1, 146.5, 197.4 ppm. HRMS (ESI) calcd for $C_{29}H_{23}NNaO_3S$ $[M+Na]^+$ 488.1296; found 488.1296.

(*E*)-4-(phenyl(1-tosylindolin-3-ylidene)methyl)benzaldehyde (2g) :



To a solution of **1a** (220 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), *p*–formylphenylboronic acid (113 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively and the process was followed as described in **2a** to afford the product **2g** as an orange solid (172mg, 0.37 mmol, 74%), m.p. 162 °C. ^{1}H NMR ($CDCl_3$, 300MHz) δ 2.41 (s, 3H), 4.65 (s, 2H), 6.31 (d, *J* = 7.8 Hz, 1H), 6.96 (t, *J* = 7.8 Hz, 1H), 7.06 (d, *J* = 6.9 Hz, 2H), 7.12–7.42 (m, 8H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.70 (d, *J* = 8.1 Hz, 1H), 7.84 (d, *J* = 7.8 Hz, 2H), 10.02 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75MHz) δ 21.5, 56.0, 115.9, 123.5, 124.6, 127.4, 128.0, 128.2, 128.8, 129.5, 129.7, 130.0, 130.2, 130.3, 131.5, 133.7, 133.9, 135.5, 140.9, 144.3, 145.3, 147.4, 191.7 ppm. HRMS (ESI) calcd for $C_{29}H_{24}NO_3S$ $[M+H]^+$ 466.1477; found 466.1476.

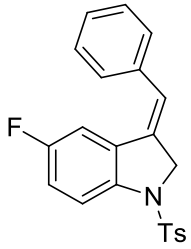
(*E*)-3-(1-phenylbutylidene)-1-tosylindoline(2h) :



To a solution of **1h** (203mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), phenylboronic acid (92 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively and the process was followed as described in **2a** to afford the product **2h** as off white solid (115mg, 0.29 mmol, 57%), m.p. 98 °C. ^{1}H NMR ($CDCl_3$, 300MHz) δ 0.88 (t, *J* = 7.2 Hz, 3H), 1.31 (m, 3H), 2.25 (t, *J* = 7.5 Hz, 2H), 2.38 (s, 3H), 4.66 (s, 3H), 6.02 (d, *J* = 7.8Hz, 1H), 6.58 (d, *J* = 7.5 Hz, 1H), 7.03–7.08 (m, 3H), 7.23–7.39 (m, 5H), 7.67 (dd, *J* = 8.1 Hz, 8.7

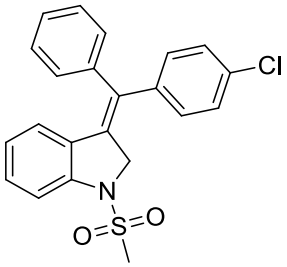
Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.8, 19.9, 21.5, 39.2, 54.2, 114.6, 123.1, 123.9, 127.2, 127.6, 128.1, 128.4, 128.9, 129.6, 129.7, 134.1, 134.8, 144.1, 144.7 ppm. HRMS (ESI) calcd for $C_{25}H_{25}NO_2S$ $[M+H]^+$ 403.1606; found 403.1605.

(*E*)-3-benzylidene-5-fluoro-1-tosylindoline (2i) :



To a solution of **1i** (191 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), phenylboronic acid (92 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively and the process was followed as described in **2a** to afford the product **2i** as a yellow semisolid (118 mg, 0.31 mmol, 62%). ^{1}H NMR ($CDCl_3$, 300MHz) δ 2.41 (s, 3H), 4.69 (s, 2H), 6.55 (s, 1H), 6.75 (dd, J = 2.7 Hz, 6.6 Hz, 1H), 6.92 (dt, J = 2.4 Hz, 1H), 7.17–7.46 (m, 7H), 7.67–7.75 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 56.6, 110.6, 111.8 (d, J_{C-F}= 25.4 Hz), 116.4 (d, J_{C-F}= 8.6 Hz), 116.6 (d, J_{C-F}= 24.15 Hz), 122.6, 127.4, 127.8, 128.1, 128.7, 129.8, 132.5, 133.5, 135.9, 142.0, 144.4, 158.9 (d, J_{C-F}= 240 Hz). HRMS (ESI) calcd for $C_{22}H_{19}FNO_2S$ $[M+H]^+$ 380.1121 ; found 380.1119.

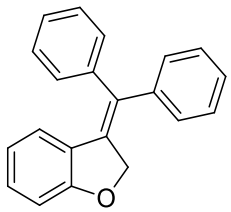
(*Z*)-3-((4-chlorophenyl)(phenyl)methylene)-1-(methylsulfonyl)indoline(2j) :



To a solution of **1j** (199mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), phenylboronic acid (92 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively and the process was followed as described in **2a** to afford the product **2j** as a light yellow semisolid (160 mg, 0.40 mmol, 80%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.90 (s, 3H), 4.69 (s, 2H), 6.84 (d, J = 7.8 Hz, 1H), 6.72 (t, J = 7.8Hz, 1H), 7.13–7.47 (m, 11H) ppm. ^{13}C

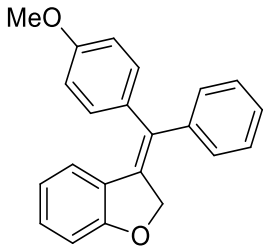
NMR ($CDCl_3$, 75 MHz) δ 35.0, 55.9, 113.8, 123.2, 125.2, 128.0, 128.9, 129.2, 129.5, 129.7, 130.3, 133.5, 134.5, 140.1, 140.6, 144.9 ppm. HRMS (ESI) calcd for $C_{22}H_{19}ClNO_2S$ $[M+H]^+$ 396.0825; found 396.0824.

3-(diphenylmethylene)-2,3-dihydrobenzofuran (4a) :



To a solution of 1-iodo-2-((3-phenylprop-2-yn-1-yl)oxy)benzene (167mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), phenylboronic acid (92 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively. The resulting solution was stirred at 60 °C under argon atmosphere for 2.5 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with EtOAc. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **4a** as a yellow solid (111 mg, 0.39 mmol, 78%), m.p. 116 °C. ^1H NMR ($CDCl_3$, 300 MHz) δ 5.28 (s, 2H), 6.33 (d, J = 7.8 Hz, 1H), 6.58 (t, J =7.5 Hz, 1H), 6.83 (d, J = 8.1 Hz, 1H), 7.09 (t, J =7.5 Hz, 1H), 7.18–7.45 (m, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 75.4, 110.3, 120.1, 124.3, 125.7, 127.2, 127.5, 128.0, 128.5, 129.0, 129.4, 129.8, 132.6, 133.9, 141.2, 142.0, 164.1 ppm. HRMS (ESI) calcd for $C_{21}H_{17}O$ $[M+H]^+$ 285.1279; found 285.1278.

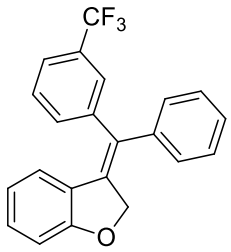
(*E*)-3-((4-methoxyphenyl)(phenyl)methylene)-2,3-dihydrobenzofuran (4b) :



To a solution of 1-iodo-2-((3-phenylprop-2-yn-1-yl)oxy)benzene (167 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), *p*-methoxyphenylboronic acid (114 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively and

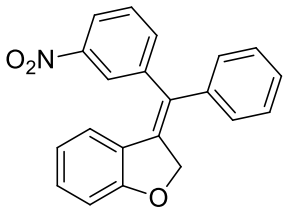
the process was followed as described in **4a** to afford the product **4b** as a yellow solid (126 mg, 0.40 mmol, 80%), as a mixture of non–separable isomers (*E:Z* = 3:1) m.p. 114 °C. ^{1}H NMR of major isomer ($CDCl_3$, 300 MHz) δ 3.86 (s, 3H), 5.27 (s, 2H), 6.48 (d, *J* = 7.8 Hz, 1H), 6.62 (t, *J* = 7.5 Hz, 1H), 6.84 (dd, *J* = 3 Hz, 5.1 Hz, 1H), 6.93–7.01 (m, 3H), 7.07–7.14 (m, 1H), 7.18–7.36 (m, 6H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 55.2, 75.5, 110.3, 114.3, 120.1, 124.3, 125.9, 127.1,127.7, 128.1, 128.4, 129.7, 130.7, 132.4, 133.7, 142.4, 159.0, 164.1 ppm. HRMS (ESI) calcd for $C_{22}H_{19}O_2$ $[M+H]^+$ 314.1307; found 314.1305.

(*E*)-3-(phenyl(3-(trifluoromethyl)phenyl)methylene)-2,3-dihydrobenzofuran (4c) :



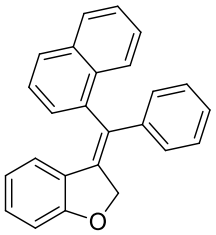
To a solution of 1-iodo-2-((3-phenylprop-2-yn-1-yl)oxy)benzene (167 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), *m*-trifluoromethylphenylboronic acid (142 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively and the process was followed as described in **4a** to afford the product **4c** as a white solid (155 mg, 0.44 mmol, 75%), m.p. 96 °C. ^{1}H NMR ($CDCl_3$, 300MHz) δ 5.28 (s, 2H), 6.29 (d, *J* = 7.5 Hz, 1H), 6.60 (t, *J* = 7.5 Hz, 1H), 6.86 (d, *J* = 8.1 Hz, 1H), 7.15 (dd, *J* = 7.2 Hz, 11.4 Hz, 3H), 7.26–7.39 (m, 3H), 7.47–7.66 (m, 4H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 75.4, 110.6, 120.3, 123.9, 124.4 (q, $J_{C–F}$= 3.7 Hz), 125.0, 126.5 (q, $J_{C–F}$= 3.7 Hz), 127.1, 127.6, 128.1, 128.7, 129.5, 130.3, 131.4 (q, $J_{C–F}$= 32.1 Hz), 133.1, 135.3, 141.3, 141.9, 164.4 ppm. HRMS (ESI) calcd for $C_{22}H_{15}F_3O$ $[M+H]^+$ 352.1075; found 352.1075.

(*Z*)-3-((3-nitrophenyl)(phenyl)methylene)-2,3-dihydrobenzofuran (4d) :



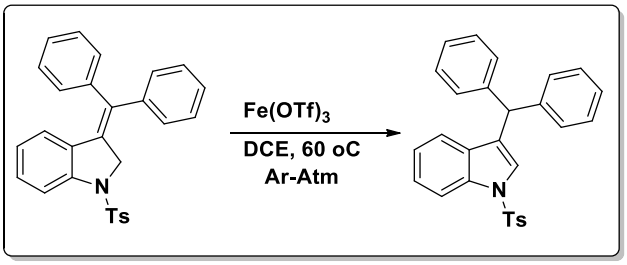
To a solution of 1-iodo-2-((3-phenylprop-2-yn-1-yl)oxy)benzene (167 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), *m*-nitrophenylboronic acid (125 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively and the process was followed as described in **4a** to afford the product **4d** as a yellow solid (122 mg, 0.37 mmol, 74%), m.p. 88 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.27 (s, 2H), 6.32 (d, J = 7.8 Hz, 1H), 6.60 (t, J = 7.8 Hz, 1H), 6.87 (d, J = 8.1 Hz, 1H), 7.11–7.18 (m, 3H), 7.25–7.40 (m, 6H), 7.60 (t, J = 7.8 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 75.4, 120.4, 122.6, 123.8, 124.7, 127.4, 127.8, 128.1, 128.4, 128.8, 129.6, 129.9, 130.7, 136.0, 140.9, 142.9, 148.9, 164.6 ppm. HRMS (ESI) calcd for $C_{21}H_{15}NO_3$ $[M+H]^+$ 329.1052; found 329.1051.

(*E*)-3-(naphthalen-1-yl(phenyl)methylene)-2,3-dihydrobenzofuran (4e):



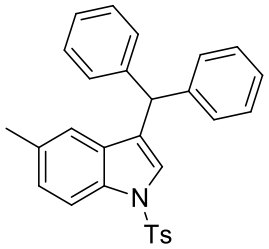
To a solution of 1-iodo-2-((3-phenylprop-2-yn-1-yl)oxy)benzene (167 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), 1-napthylboronic acid (129 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively and the process was followed as described in **4a** to afford the product **4e** as a yellow solid (135 mg, 0.41 mmol, 82%), m.p. 118 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.45–5.68 (m, 3H), 6.37 (t, J =7.5 Hz, 1H), 6.84 (d, J = 8.1 Hz, 1H), 7.02 (t, J =8.1 Hz,1H), 7.24–7.33 (m, 4H), 7.37–7.40 (m, 2H), 7.46–7.51 (m,2H), 7.55–7.60 (m,1H), 7.92–7.97 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 75.3, 110.2, 120.3, 124.5, 125.4, 125.6, 125.8, 126.1, 126.5, 127.2, 127.5, 128.0, 128.3, 128.4, 128.5, 129.8, 130.3, 131.7, 134.2, 135.8, 138.7, 141.6 ppm. HRMS (ESI) calcd for $C_{25}H_{18}NaO$ $[M+Na]^+$ 357.1255; found 357.1253.

3-benzhydryl-1-tosyl-1H-indole (3a) :



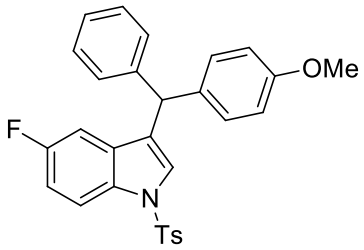
To a solution of **2a** (100 mg, 0.23 mmol) in dry DCE (2mL) anhydrous $Fe(OTf)_3$ (12 mg, 0.023 mmol) was added. The mixture was stirred at 60 °C under an argon atmosphere for 3 h. After completion of the reaction (monitored by TLC), the solvent was evaporated and the product was purified by column chromatography (silica gel 60–120 mesh), eluting with pet ether/EtOAc 97:3 (v/v) to afford the product **3a** as a yellow solid (90 mg, 0.20 mmol, 90%), m.p. 132 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.38 (s, 3H), 5.51 (s, 1H), 6.92 (s, 1H), 7.07–7.16 (m, 5H), 7.20–7.30 (m, 10H), 7.67 (d, J = 8.1 Hz, 2H), 7.96 (d, J = 8.4 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 48.5, 113.9, 120.5, 123.2, 124.7, 125.8, 126.8, 128.5, 128.8, 129.8, 130.5, 135.1, 135.8, 142.1, 144.8 ppm. HRMS (ESI) calcd for $C_{28}H_{23}NNaO_2S$ $[M+Na]^+$ 460.1347; found 460.1345.

3-benzhydryl-5-methyl-1-tosyl-1H-indole (3b) :



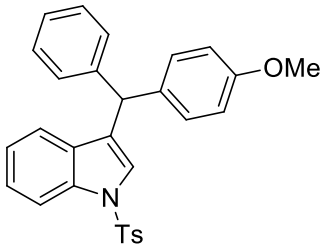
Compound **2b** (104 mg,0.23 mmol) was treated with anhydrous $Fe(OTf)_3$ (12 mg,0.23 mmol)under an argon atmosphere at 60 ˚C as described for synthesis of **3a** for 3 h to afford **3b** as yellow solid (93 mg, 0.20 mmol, 89%), m.p. 110 ˚C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.27 (s,3H), 2.36 (s, 3H), 5.49 (s, 1H), 6.88 (s, 2H), 7.07–7.13 (m, 5H), 7.19–7.30 (m, 8H), 7.65 (d, J = 8.1 Hz, 2H), 7.85 (d, J = 8.4 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.3, 21.5, 48.3, 113.6, 120.2, 126.0, 126.2, 126.7, 128.5, 128.8, 129.7, 130.7, 132.8, 134.0, 135.1, 142.1, 144.6 ppm. HRMS (ESI) calcd for $C_{29}H_{26}NO_2S$ $[M+H]^+$ 452.1684; found 452.1683.

5-fluoro-3-((4-methoxyphenyl)(phenyl)methyl)-1-tosyl-1H-indole (3c) :



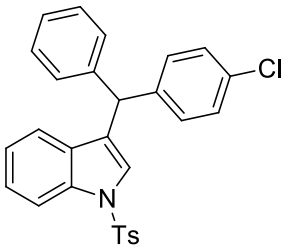
Compound **2c** (112 mg, 0.23 mmol) was treated with anhydrous $Fe(OTf)_3$ (12 mg, 0.023 mmol) under an argon atmosphere at 60 °C as described for synthesis of **3a** for 3 h to afford **3c** as yellow semisolid (107 mg, 0.22 mmol, 96%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.38 (s, 3H), 3.80 (s, 3H), 5.39 (s, 1H), 6.72 (d, J = 9 Hz, 1H), 6.82 (d, J = 8.7 Hz, 2H), 6.96–7.12 (m, 8H), 7.22–7.35 (m, 3H), 7.65 (d, J = 8.4 Hz, 2H), 7.91 (q, J = 7.5 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 47.6, 55.2, 106.2 (d, $J_{C–F}$= 23.8 Hz), 112.7 (d, $J_{C–F}$= 25.3 Hz), 114.0, 115.0 (d, $J_{C–F}$= 9.4 Hz), 126.7, 126.8, 127.1, 127.3, 128.6, 129.6, 129.8, 131.5, 131.7, 132.1, 133.7, 134.9, 142.0, 144.9, 159.7 (d, $J_{C–F}$= 193.5 Hz) ppm. HRMS (ESI) calcd for $C_{29}H_{24}FNO_3S$ $[M+H]^+$ 485.1461; found 485.1459.

3-((4-methoxyphenyl)(phenyl)methyl)-1-tosyl-1H-indole (3d) :



Compound **2d** (107 mg, 0.23 mmol) was treated with anhydrous $Fe(OTf)_3$ (12 mg, 0.023 mmol) under an argon atmosphere at 60 °C as described for synthesis of **3a** for 2.5 h to afford **3d** as white solid (104 mg, 0.22 mmol, 97%), m.p. 121 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.38 (s, 3H), 3.82 (s, 3H), 5.48 (s, 1H), 6.83 (d, J = 8.1 Hz, 2H), 6.93 (s, 1H), 7.04–7.15 (m, 6H), 7.22–7.28 (m, 6H), 7.69 (d, J = 7.8 Hz, 2H), 7.98 (d, J = 8.4 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 47.7, 55.2, 113.9, 120.5, 123.1, 124.7, 125.7, 126.7, 127.1, 128.5, 128.7, 129.7, 130.5, 134.2, 135.1, 135.8, 142.4, 144.7, 158.3 ppm. HRMS (ESI) calcd for $C_{29}H_{26}NO_3S$ $[M+H]^+$ 467.1555; found 467.1554.

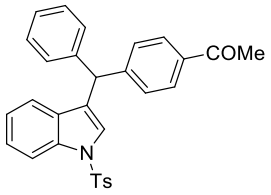
3-((4-chlorophenyl)(phenyl)methyl)-1-tosyl-1H-indole (3e) :



Compound **2e** (108 mg,0.23 mmol) was treated with anhydrous $Fe(OTf)_3$ (12 mg, 0.023 mmol) under an argon atmosphere at 65 °C as described for synthesis of **3a** for 5 h to afford **3e** as yellow semisolid

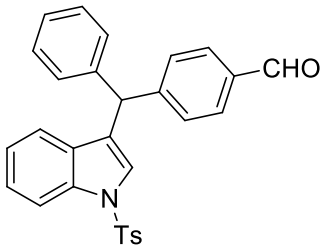
(89 mg, 0.19 mmol, 82%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.39 (s, 3H), 5.50 (s, 1H), 6.93 (s, 1H), 7.06–7.13 (m, 6H), 7.19–7.32 (m, 8H), 7.69 (d, J = 8.4 Hz, 2H), 7.98 (d, J = 8.1 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 47.8, 113.9, 120.4, 123.2, 124.8, 125.7, 126.2, 126.7, 127.0, 128.7, 129.8, 130.1, 132.6, 135.1, 135.7, 140.6, 141.5, 144.8 ppm. HRMS (ESI) calcd for $C_{28}H_{22}ClNO_2S$ $[M+H]^+$ 471.1060; found 471.1058.

1-(4-(phenyl(1-tosyl-1H-indol-3-yl)methyl)phenyl)ethanone (3f) :



Compound **2f** (110 mg, 0.23 mmol) was treated with anhydrous $Fe(OTf)_3$ (12 mg, 0.023 mmol) under an argon atmosphere at 60 °C as described for synthesis of **3a** for 4 h to afford **3f** as yellow semisolid (91 mg, 0.19 mmol, 83%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.39 (s, 3H), 2.61 (s, 3H), 5.59 (s, 1H), 6.95 (s, 1H), 7.09–7.19 (m, 3H), 7.24–7.33 (m, 9H), 7.69–7.77 (m, 2H), 7.95 (dd, J = 8.4, 19.8 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 26.5, 48.4, 113.9, 119.6, 120.3, 123.2, 124.1, 124.9, 125.7, 126.7, 127.1, 128.7, 128.8, 129.0, 129.8, 130.1, 135.1, 135.8, 141.2, 144.9, 147.6, 197.6 ppm. HRMS (ESI) calcd for $C_{30}H_{25}NNaO_3S$ $[M+Na]^+$ 502.1453; found 502.1453.

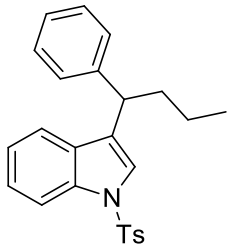
4-(phenyl(1-tosyl-1H-indol-3-yl)methyl)benzaldehyde (3g) :



Compound **2g** (107 mg, 0.023 mmol) was treated with anhydrous $Fe(OTf)_3$ (12 mg, 0.023 mmol) under an argon atmosphere at 60 °C as described for synthesis of **3a** for 4 h to afford **3g** as white solid (87 mg, 0.18 mmol, 81%), m.p. 186 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.37 (s, 3H), 5.59 (s, 1H), 6.94 (s, 1H), 7.05–7.14 (m, 4H), 7.22–7.32 (m, 7H), 7.68 (d, J = 8.1 Hz, 2H), 7.81 (d, J = 8.4 Hz, 2H), 7.98 (d, J = 8.4 Hz, 1H), 10.00 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.6, 48.6, 113.9, 120.2, 123.3,

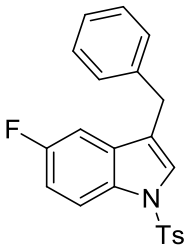
125.0, 125.5, 125.7, 126.8, 127.2, 128.8, 129.5, 129.8, 130.0, 135.0, 135.1, 135.7, 140.9, 144.9, 149.2, 191.8 ppm. HRMS (ESI) calcd for $C_{29}H_{24}NO_3S$ $[M+H]^+$ 466.1477; found 466.1476.

3-(1-phenylbutyl)-1-tosyl-1H-indole (3h) :



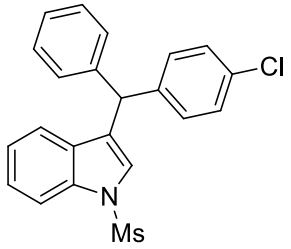
Compound **2h** (93 mg, 0.23 mmol) was treated with anhydrous $Fe(OTf)_3$ (12 mg, 0.023 mmol) under an argon atmosphere at 80 °C as described for synthesis of **3a** for 7 h to afford **3h** as yellow semisolid (67 mg, 0.17 mmol, 72%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.96 (t, J = 7.2 Hz, 3H), 1.33 (m, 2H), 2.03 (m, 2H), 2.36 (s, 3H), 4.05 (t, J = 7.5 Hz, 1H), 7.10 (t, J = 7.5 Hz, 1H), 7.16–7.28 (m, 9H), 7.48 (s,1H), 7.75 (d, J = 8.1 Hz, 2H), 7.96 (d, J = 8.1 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.0, 20.9, 21.5, 37.7, 42.3, 113.7, 120.1, 122.7, 123.0, 124.5, 126.3, 126.7, 127.0, 127.8, 128.4, 129.7, 130.7, 135.2, 135.6, 143.5, 144.7 ppm. HRMS (ESI) calcd for $C_{25}H_{26}NO_2S$ $[M+H]^+$ 403.1606; found 403.1605.

3-benzyl-5-fluoro-1-tosyl-1H-indole (3i) :



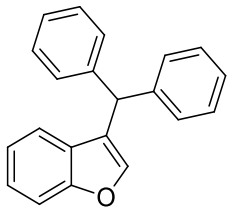
Compound **2i** (87 mg, 0.23 mmol) was treated with anhydrous $Fe(OTf)_3$ (12 mg, 0.023 mmol) under an argon atmosphere at 60 °C as described for synthesis of **3a** for 3.5 h to afford **3b** as white solid (65 mg, 0.17 mmol, 75%), m.p. 100 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.35 (s, 3H), 3.95 (s, 2H), 7.01 (t, J = 8.4 Hz, 2H), 7.16–7.31 (m, 8H), 6.70 (d, J = 8.1 Hz, 2H), 7.92 (q, J = 4.2 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 31.3, 105.5 (d, J_{C-F}= 23.7 Hz), 112.6 (d, J_{C-F}= 25.4 Hz), 114.9 (d, J_{C-F}= 9.3 Hz), 122.4, 125.7, 126.5, 126.7, 128.6, 129.8, 131.9, 135.0, 138.5, 144.9, 159.5 (d, J_{C-F}= 239.2 Hz). HRMS (ESI) calcd for $C_{22}H_{19}FNO_2S$ $[M+H]^+$ 380.1121; found 380.1120.

3-((4-chlorophenyl)(phenyl)methyl)-1-(methylsulfonyl)-1H-indole (3j) :



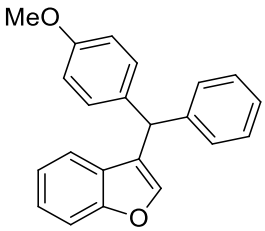
Compound **2j** (91 mg, 0.23 mmol) was treated with anhydrous $Fe(OTf)_3$ (12 mg, 0.023 mmol) under an argon atmosphere at 60 °C as described for synthesis of **3a** for 2.5 h to afford **3j** as white solid (90 mg, 0.22 mmol, 99%), m.p. 112 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.07 (s, 3H), 5.54 (s, 1H), 6.81 (s, 1H), 7.12–7.18 (m, 7H), 7.23–7.37 (m, 5H), 7.90 (d, J = 8.1 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 40.6, 48.0, 113.2, 120.8, 123.4, 125.1, 125.2, 125.6, 127.0, 128.7, 130.0, 130.1, 132.6, 135.7, 140.6, 141.5 ppm. HRMS (ESI) calcd for $C_{22}H_{18}ClNO_2S$ $[M+H]^+$ 395.0747; found 395.0747.

3-benzhydrylbenzofuran (5a) :



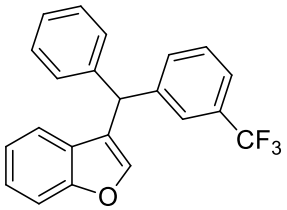
Compound **4a** (65 mg, 0.23 mmol) was treated with anhydrous $Fe(OTf)_3$ (12 mg, 0.023 mmol) under an argon atmosphere at 60 °C as described for synthesis of **3a** for 3 h to afford **5a** as yellow semisolid (61 mg, 0.21 mmol, 94%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.52 (s, 1H), 7.01 (s, 1H), 7.10 (t, J = 6 Hz, 2H), 7.23–7.32 (m, 10H), 7.46 (d, J = 8.1 Hz, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 47.7, 111.4, 120.7, 122.4, 124.0, 124.2, 126.7, 127.6, 128.5, 12.8, 142.2, 144.0, 155.8 ppm. HRMS (ESI) calcd for $C_{21}H_{17}O$ $[M+H]^+$ 285.1279; found 285.1279.

3-((4-methoxyphenyl)(phenyl)methyl)benzofuran (5b) :



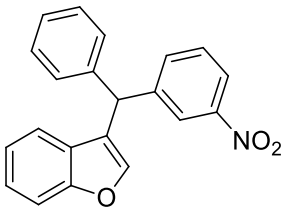
Compound **4b** (72 mg, 0.23 mmol) was treated with anhydrous $Fe(OTf)_3$ (12 mg, 0.023 mmol) under an argon atmosphere at 60 °C as described for synthesis of **3a** for 2.5 h to afford **5b** as yellow semisolid (69 mg, 0.22 mmol, 96%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.82 (s, 3H), 5.51 (s, 1H), 6.88 (dd, J = 2.1 Hz, 4.8 Hz, 2H), 7.05 (s, 1H), 7.10–7.21 (m, 5H), 7.24–7.36 (m, 5H), 7.49–7.53 (m, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 46.8, 55.2, 111.4, 113.9, 120.7, 122.3, 124.2, 124.4, 126.6, 127.6, 128.5, 128.7, 129.8, 134.4, 142.6, 143.9, 155.8, 158.3 ppm. HRMS (ESI) calcd for $C_{22}H_{19}O_2$ $[M+H]^+$ 315.1385; found 315.1384.

3-(phenyl(3-(trifluoromethyl)phenyl)methyl)benzofuran (5c) :



Compound **4c** (81 mg, 0.23 mmol) was treated with anhydrous $Fe(OTf)_3$ (12 mg, 0.023 mmol) under an argon atmosphere at 65 °C as described for synthesis of **3a** for 3 h to afford **5c** as yellow semisolid (71 mg, 0.20 mmol, 88%).^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.60 (s, 1H), 7.02 (s, 1H), 7.11–7.16 (m, 2H), 7.24–7.40 (m, 5H), 7.43–7.44 (m, 2H), 7.49 (s, 1H), 7.52–7.56 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 47.5, 111.6, 120.4, 122.5, 123.3, 123.7 (q, J_{C-F}= 3.7 Hz), 124.5, 125.5 (q, J_{C-F}= 3.7 Hz), 127.1, 128.7, 129.0, 130.9 (q, J_{C-F}= 31.9 Hz), 132.1, 141.2, 143.2, 144.0, 155.8 ppm. HRMS (ESI) calcd for $C_{22}H_{15}F_3O$ $[M+H]^+$ 352.1075; found 352.1075.

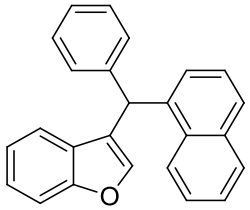
3-((3-nitrophenyl)(phenyl)methyl)benzofuran (5d) :



Compound **4d** (75 mg, 0.23 mmol) was treated with anhydrous $Fe(OTf)_3$ (12 mg, 0.023 mmol) under an argon atmosphere at 70 °C as described for synthesis of **3a** for 4 h to afford **5d** as yellow solid (59 mg, 0.18 mmol, 78 %), m.p. 78 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.65 (s, 1H), 7.05 (s, 1H), 7.09–7.16 (m, 2H), 7.24–7.53 (m, 8H), 7.61 (d, J = 7.8 Hz, 1H), 8.13–8.16 (m, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 47.3, 111.7, 120.3, 122.0, 122.7, 122.8, 123.7, 124.7, 127.0, 127.4, 128.6, 128.9, 129.5,

134.8, 140.7, 144.0, 144.4, 148.5, 155.8 ppm. HRMS (ESI) calcd for $C_{21}H_{15}NO_3$ $[M+H]^+$ 329.1052; found 329.1051.

3-(naphthalen-2-yl(phenyl)methyl)benzofuran (5e) :



Compound **4e** (76 mg, 0.23 mmol) was treated with anhydrous $Fe(OTf)_3$ (12 mg, 0.023 mmol) under an argon atmosphere at 60 °C as described for synthesis of **3a** for 3 h to afford **5e** as yellow semisolid (70 mg, 0.21 mmol, 92%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.31 (s, 1H), 6.94 (s, 1H), 7.09–7.19 (m, 3H), 7.28–7.43 (m, 6H), 7.46–7.52 (m, 3H), 7.81 (d, J = 8.1 Hz, 1H), 7.90–7.98 (m, 1H), 8.10 (d, J = 7.5 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 43.5, 111.5, 120.6, 122.4, 123.9, 124.0, 124.3, 125.4, 125.5, 126.2, 126.8, 127.6, 128.6, 128.8, 129.0, 131.7, 134.1, 137.7, 142.0, 144.7, 155.8 ppm. HRMS (ESI) calcd for $C_{25}H_{18}NaO$ $[M+Na]^+$ 357.1255; found 357.1254.

I. 8. References :

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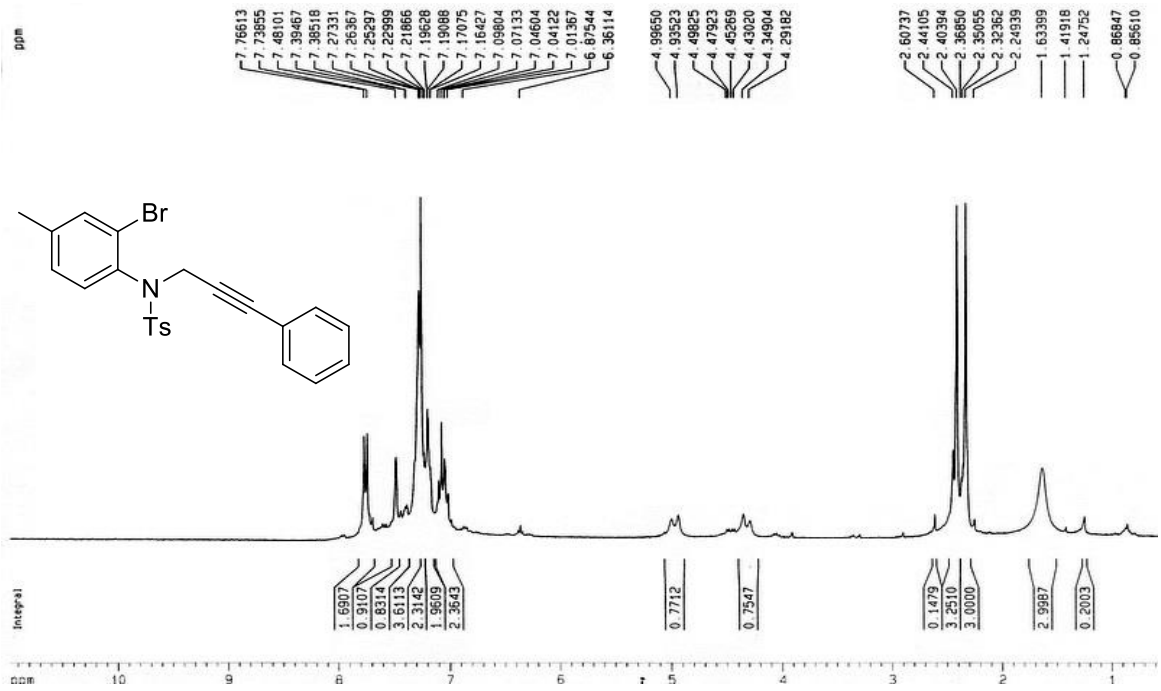
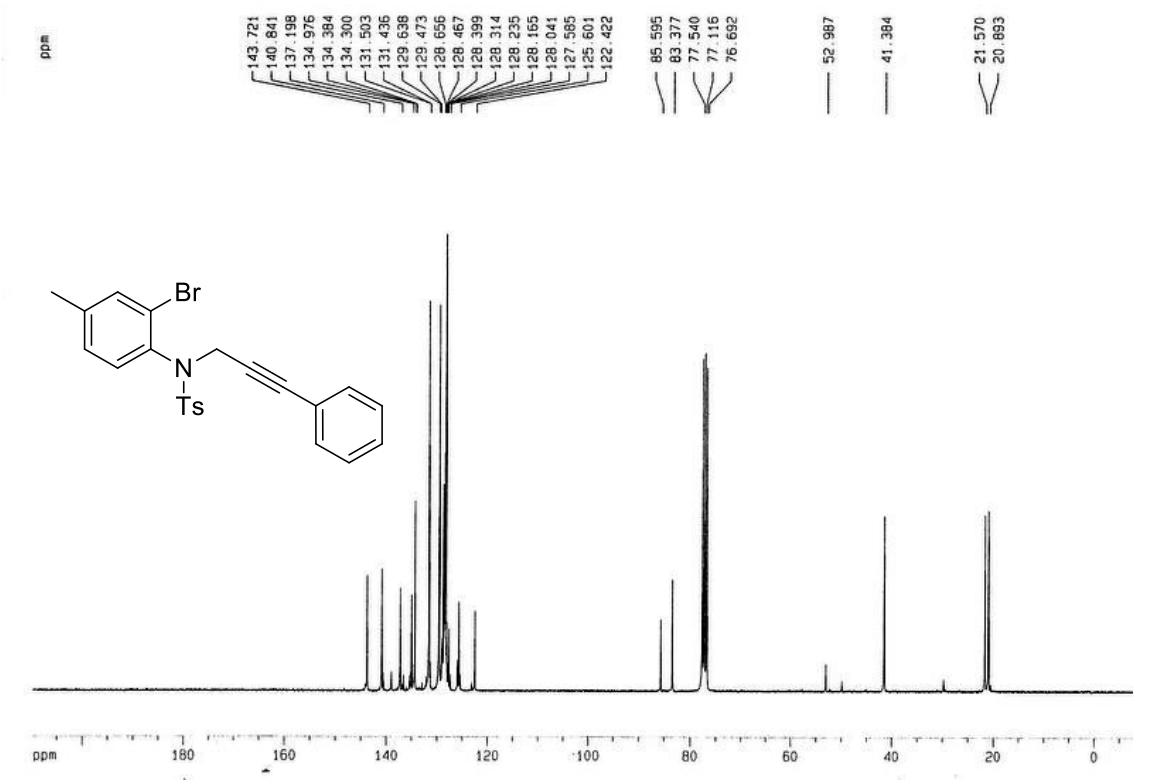
I. 9. Copies of some important ^{1}H and ^{13}C NMR spectra of compounds described in Chapter I

^{1}H NMR of 1b, $CDCl_3$, 300 MHz



^{13}C NMR of 1b, $CDCl_3$, 75 MHz



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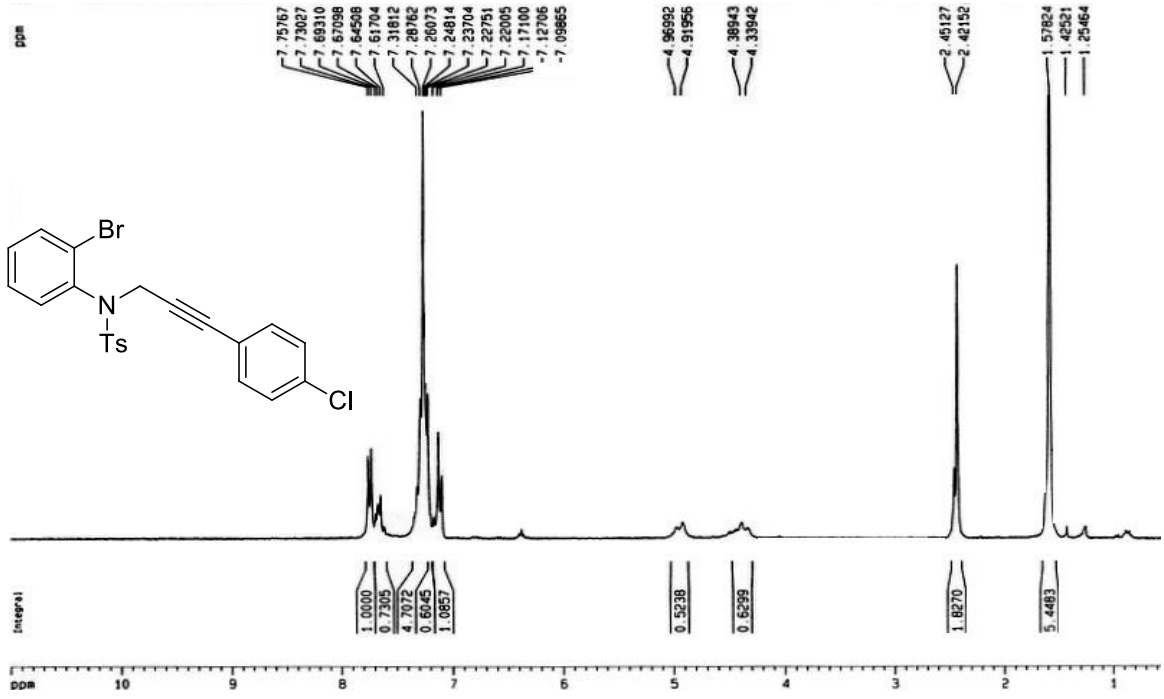

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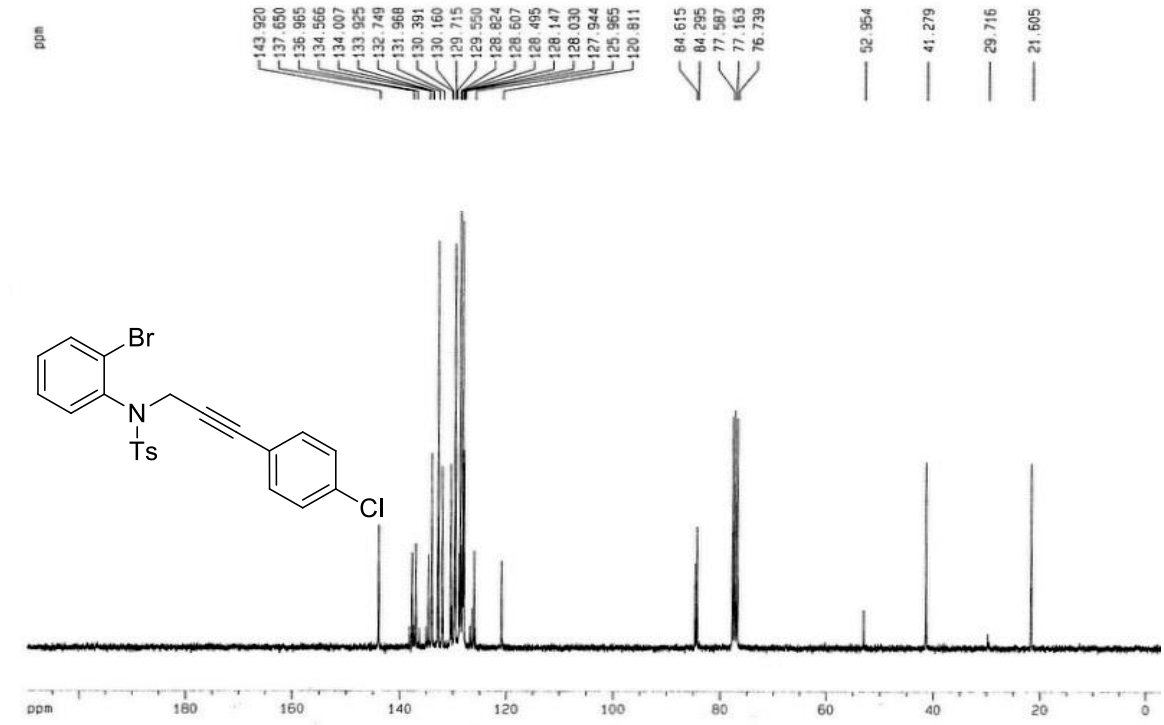

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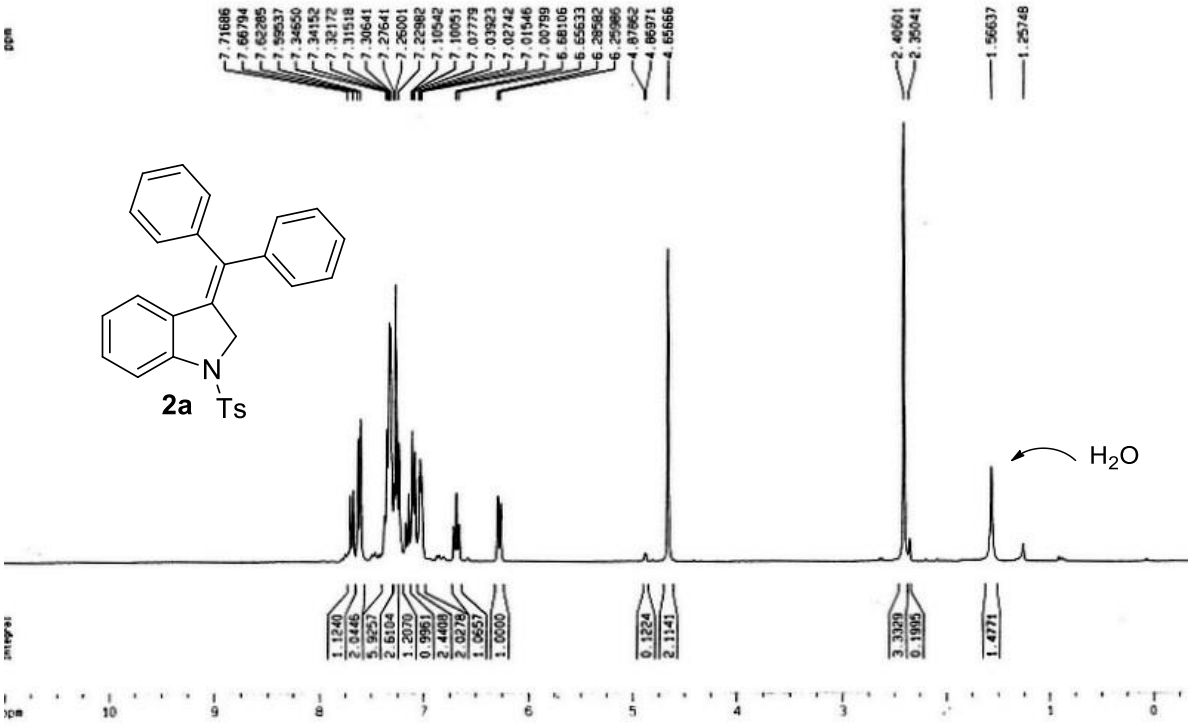

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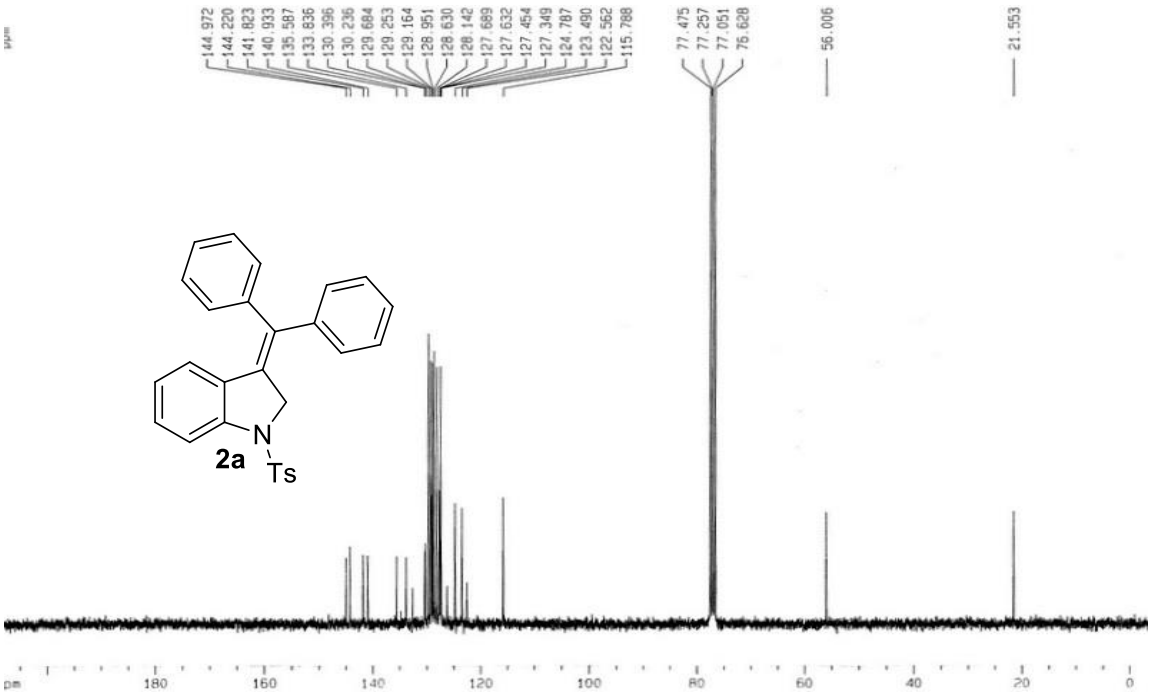

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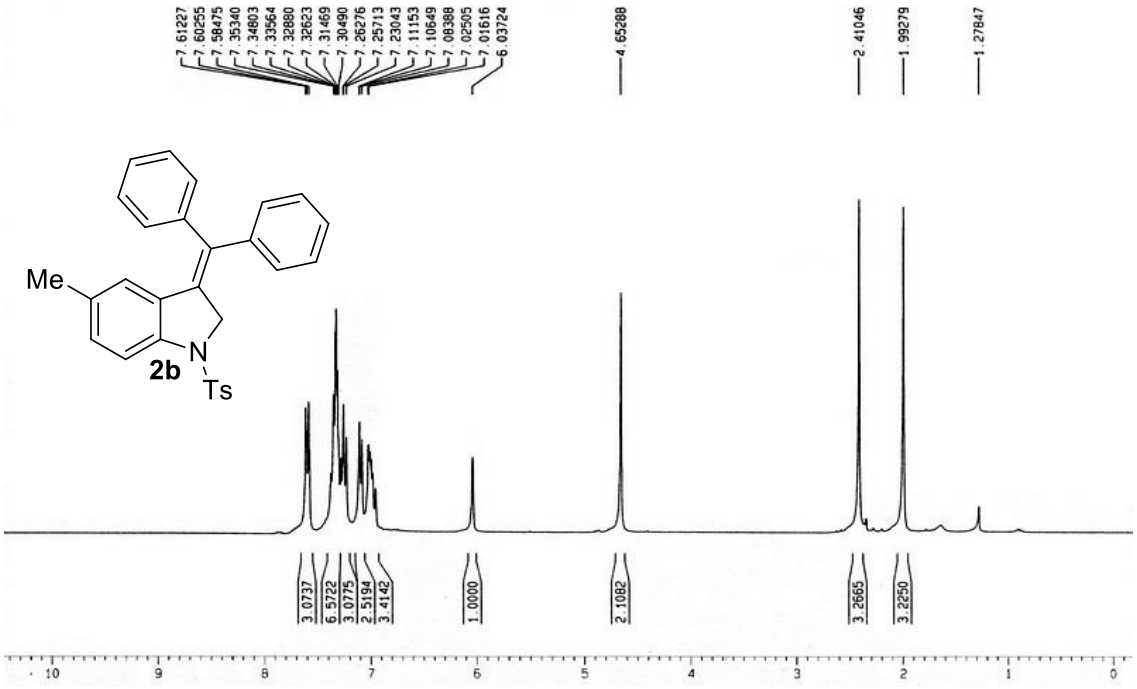

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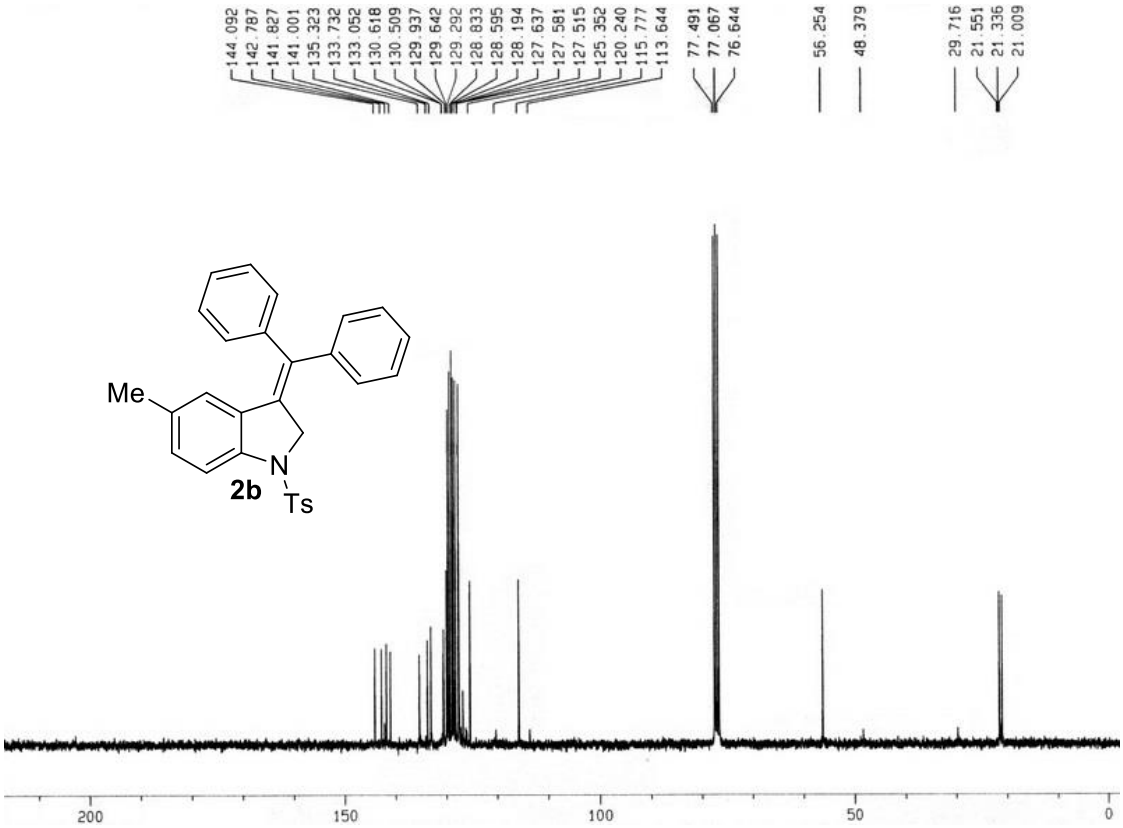

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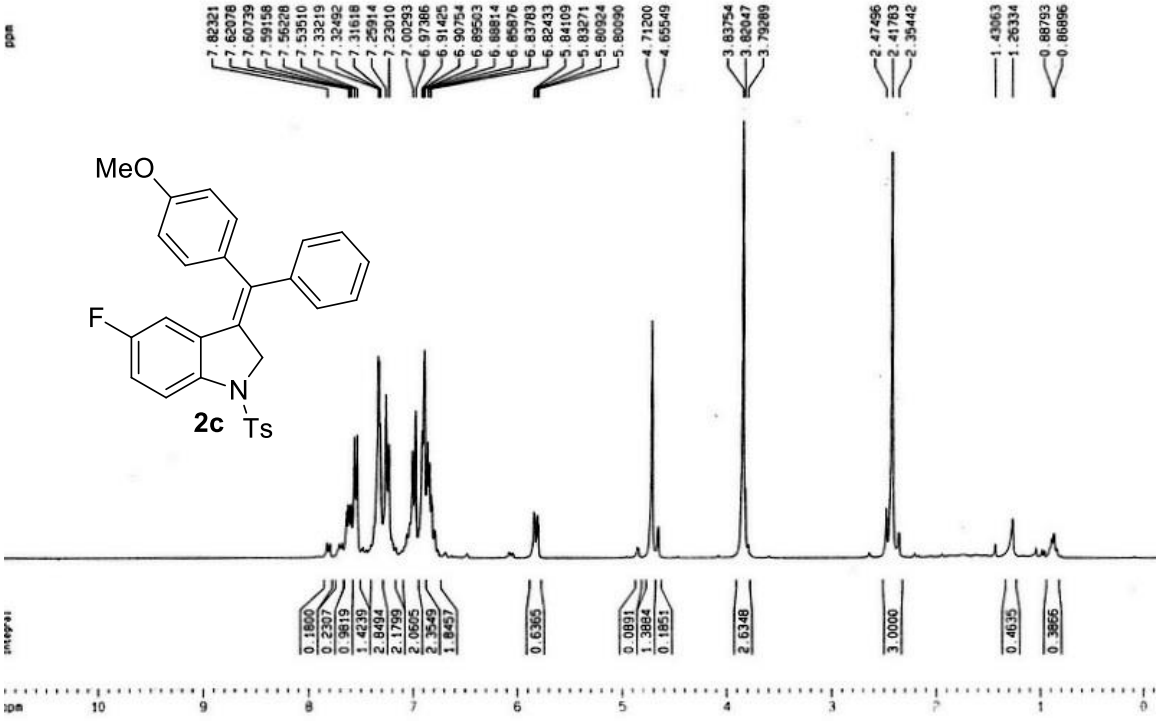

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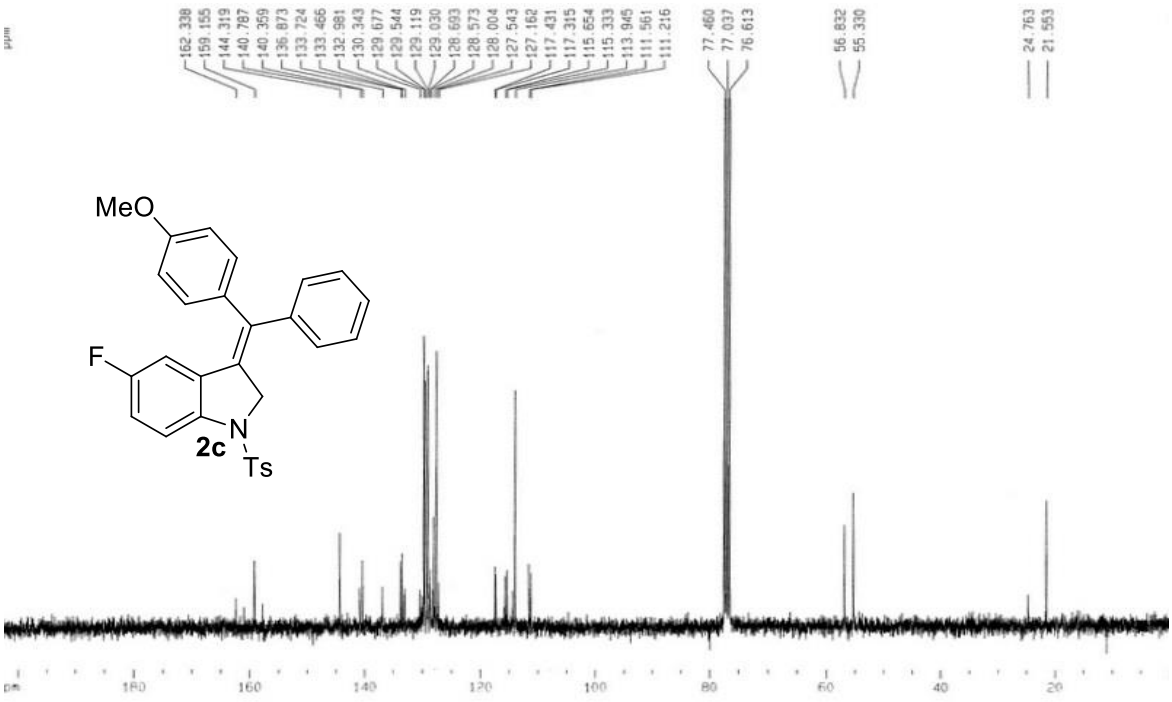

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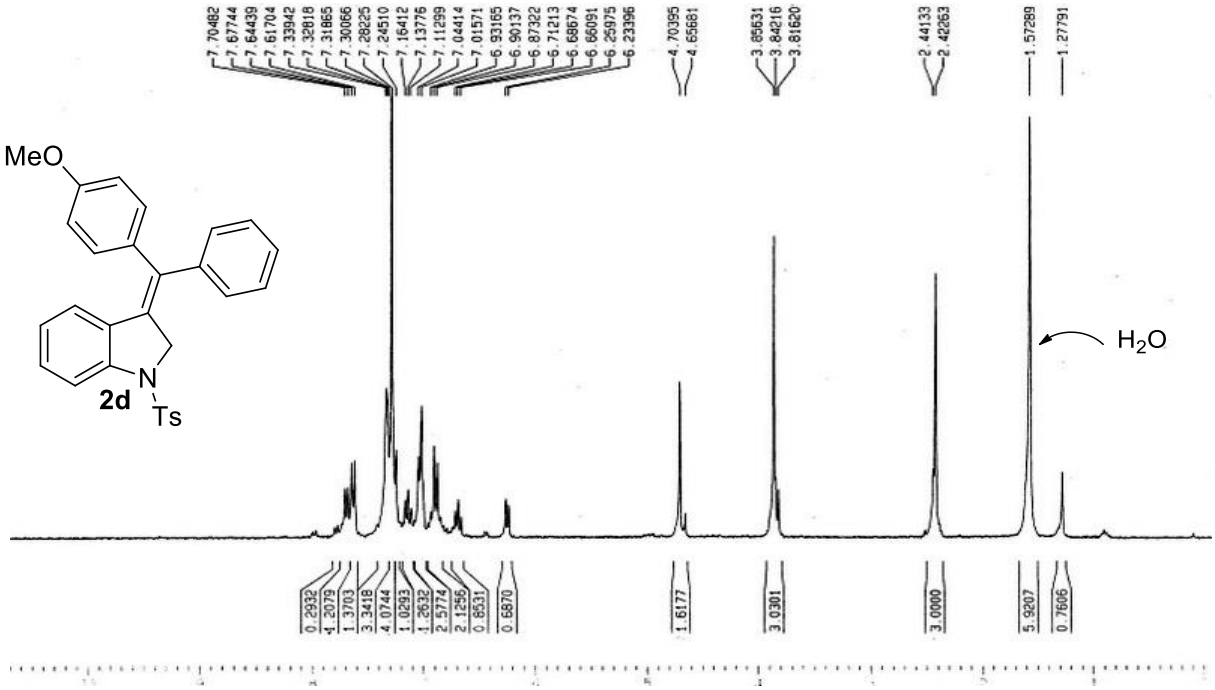

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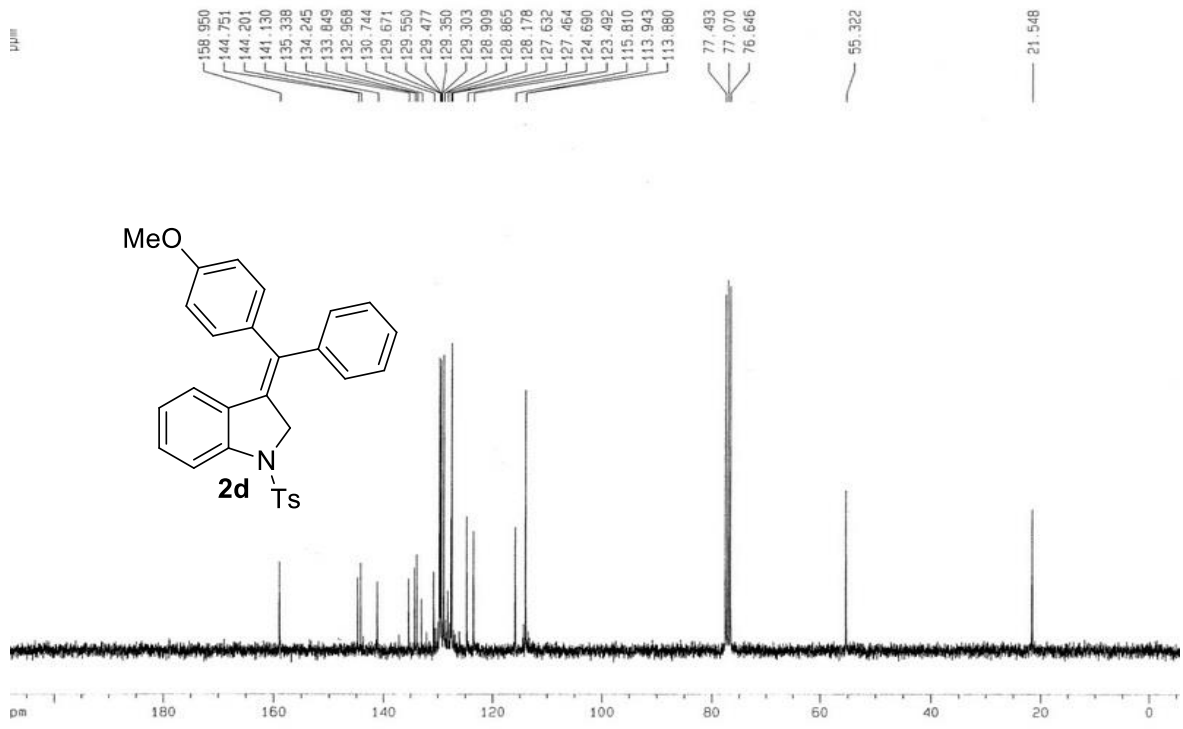

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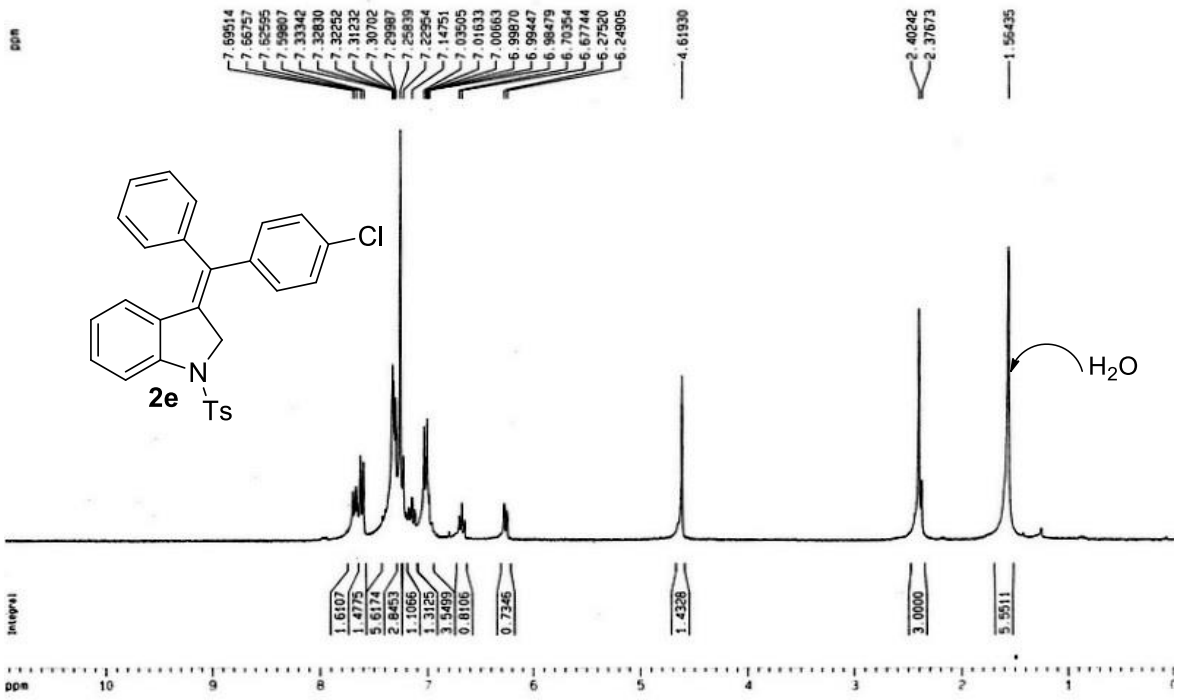

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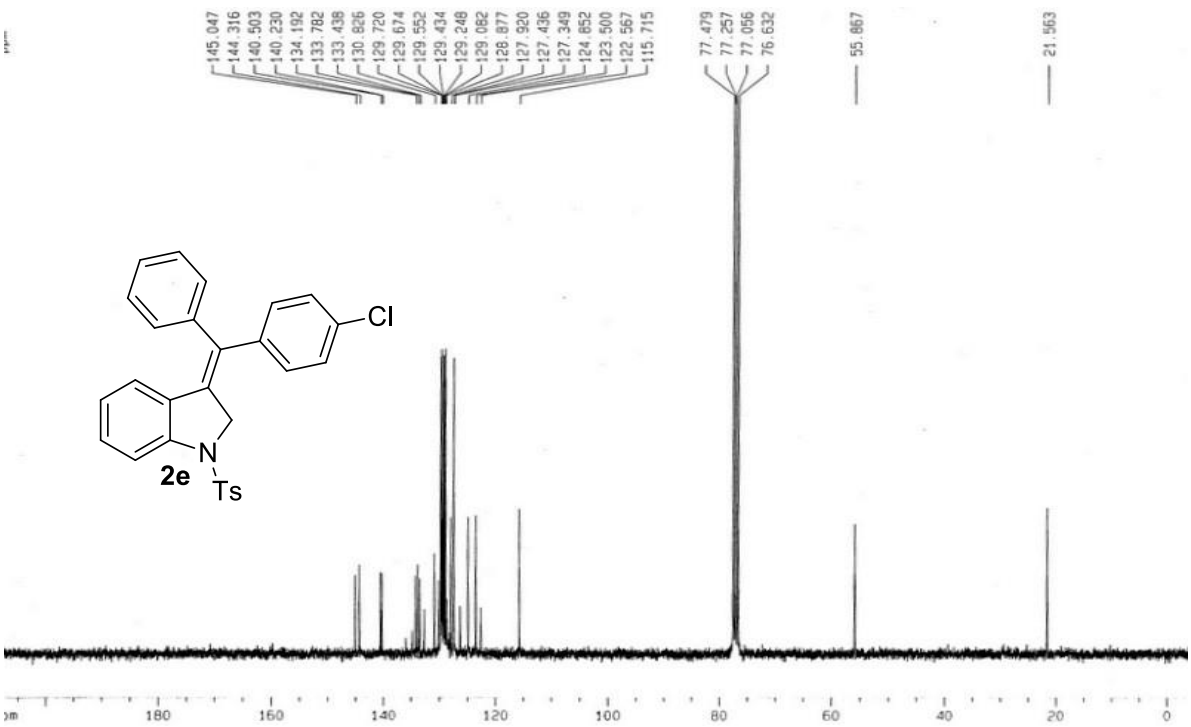

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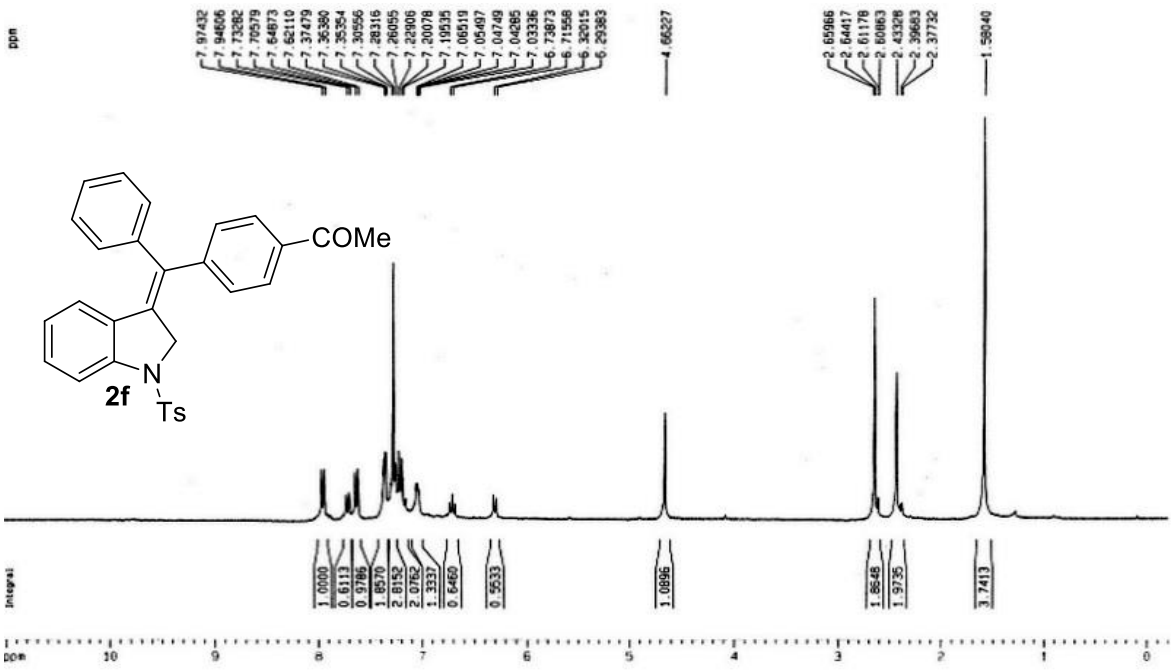

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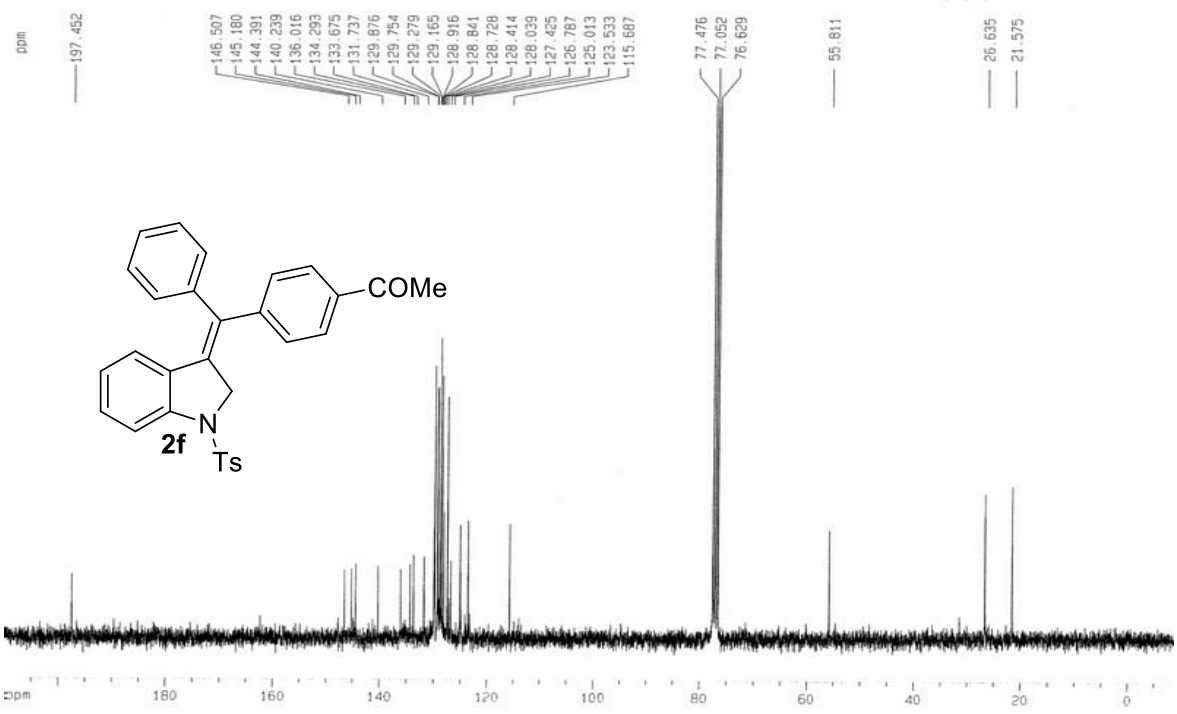

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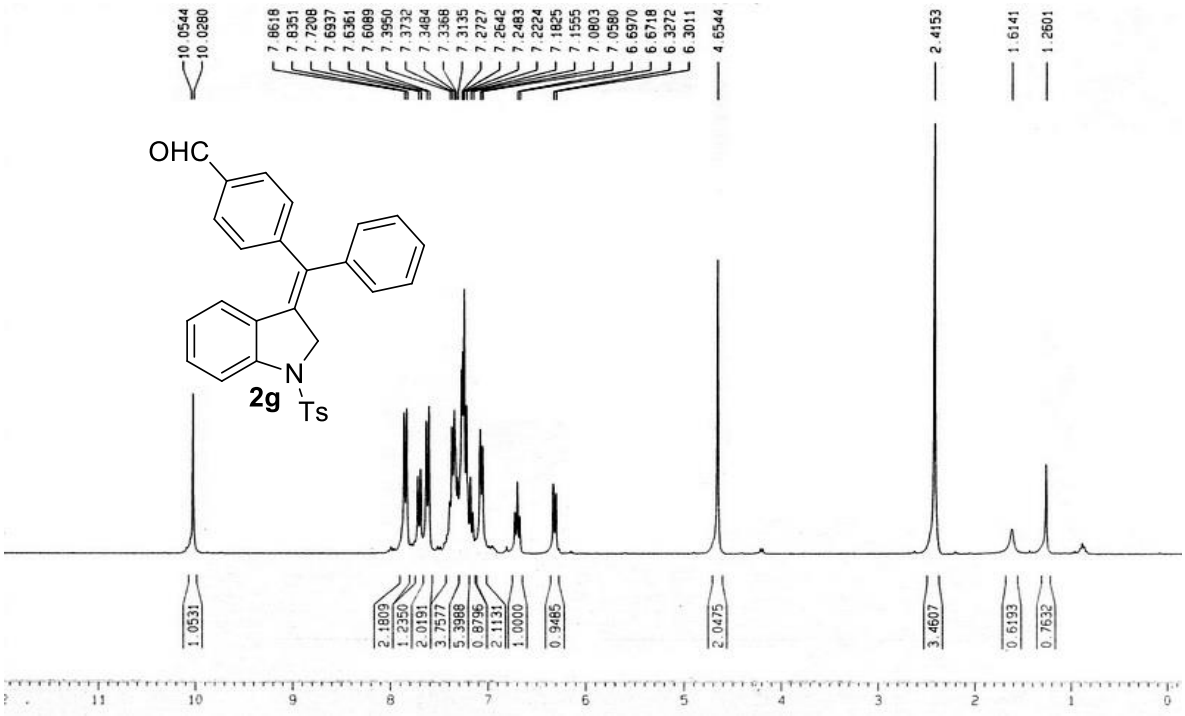

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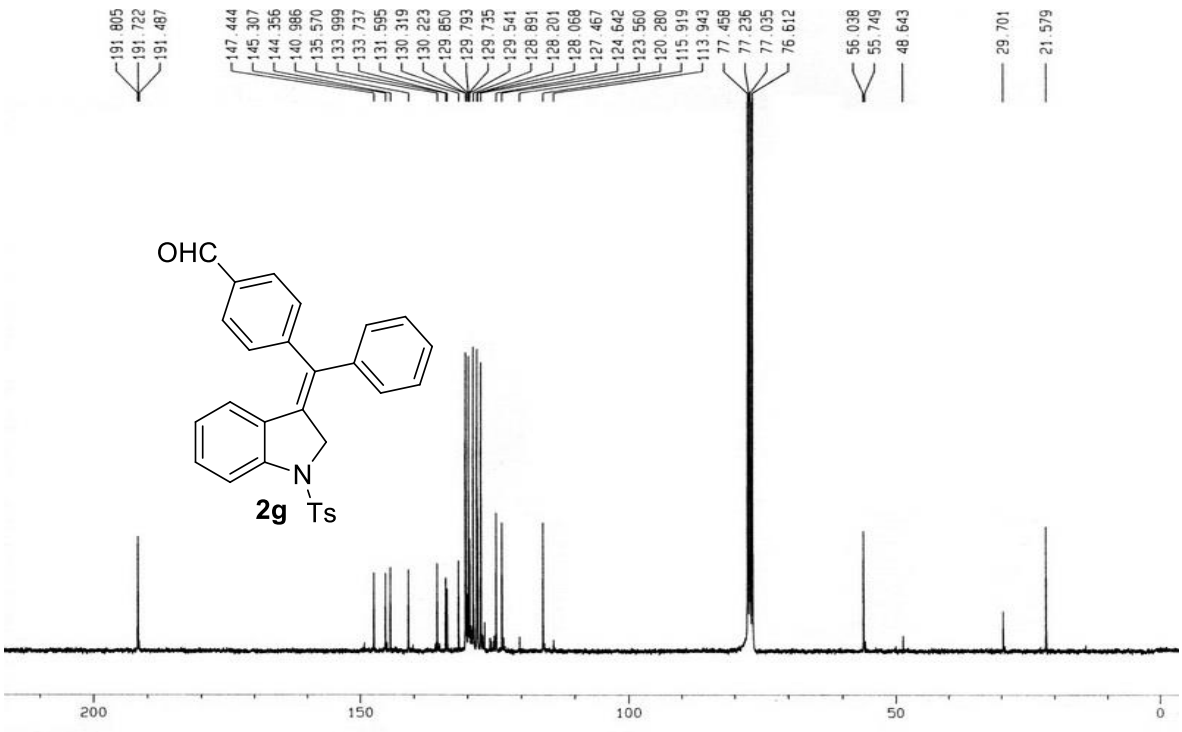

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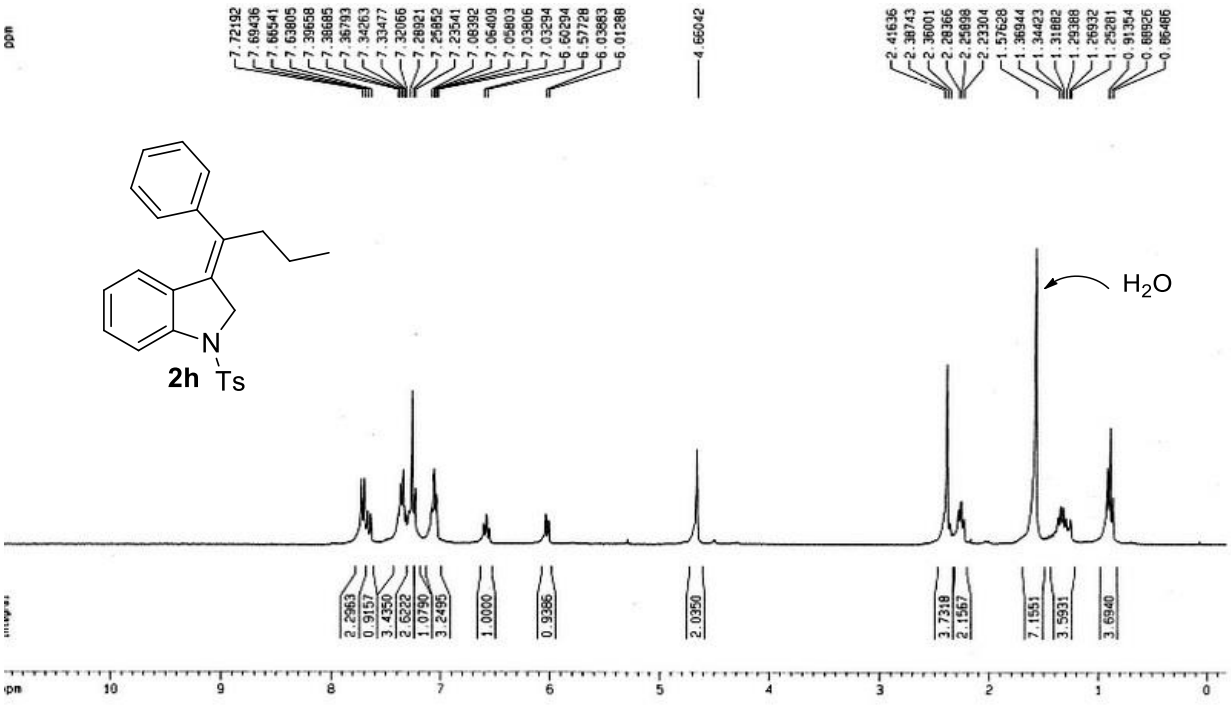
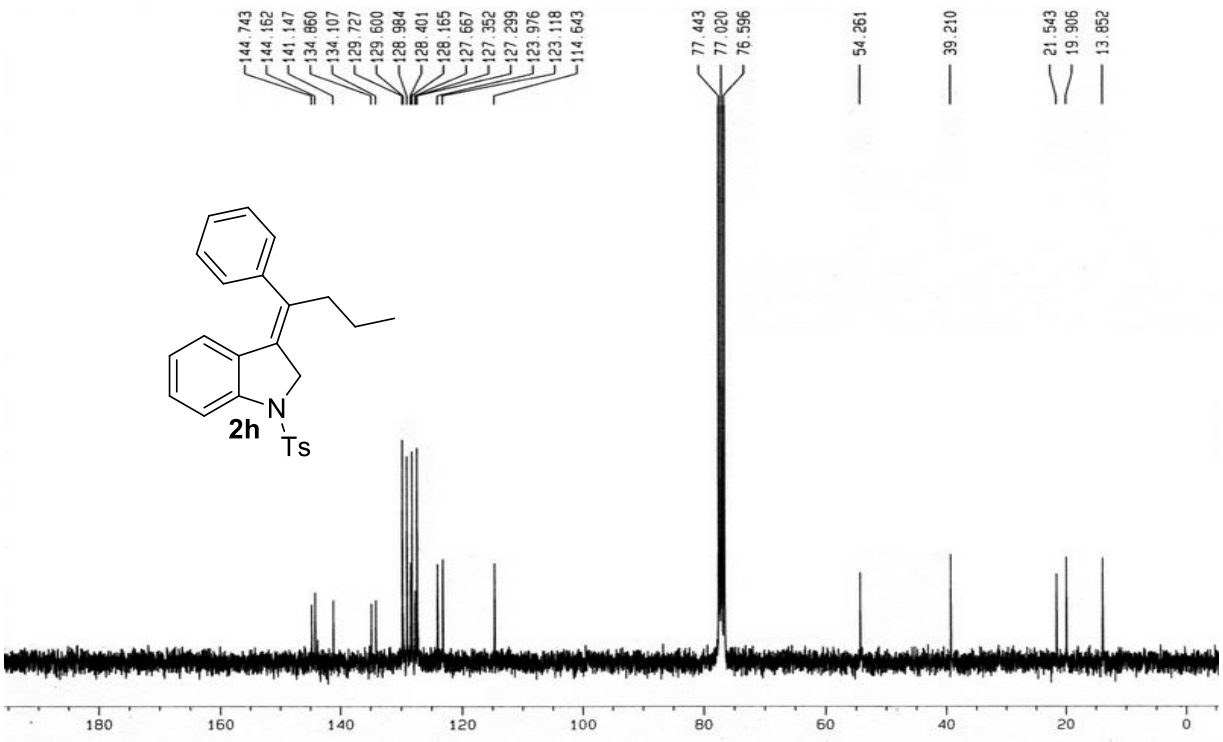
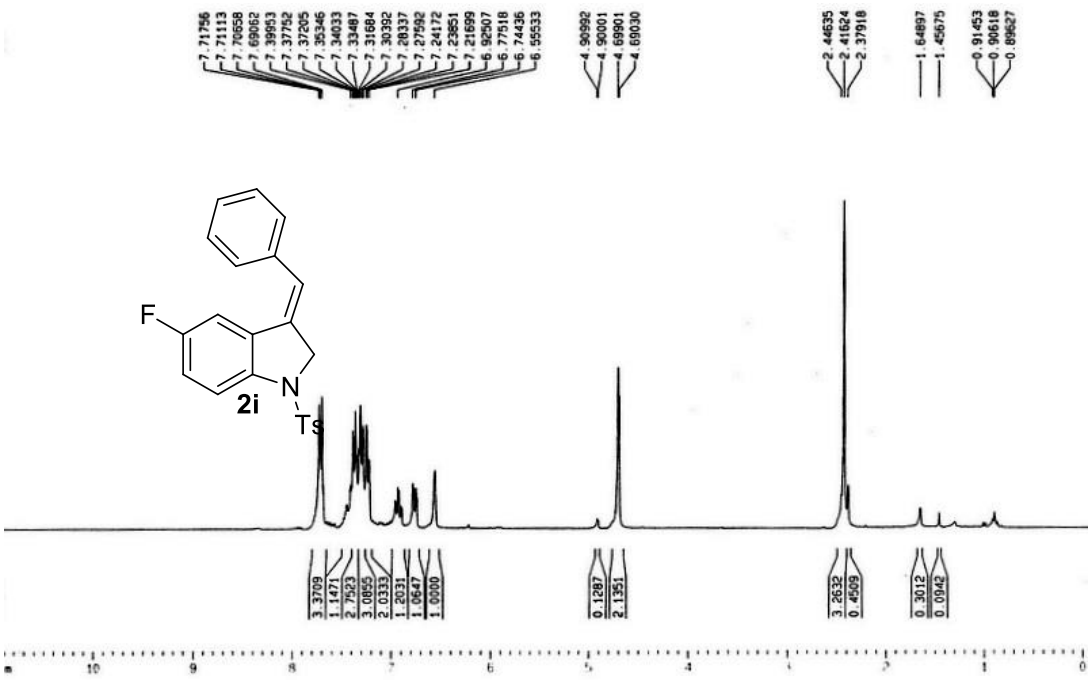


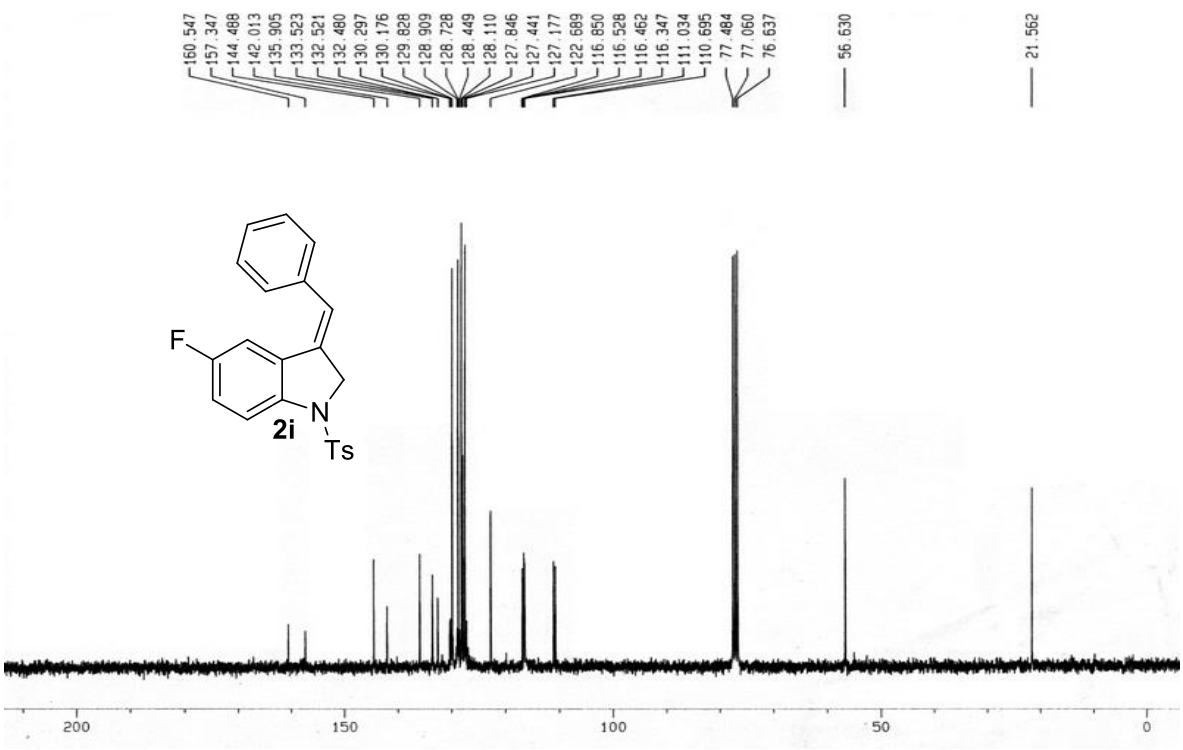
^{13}C NMR of 2h, $CDCl_3$, 75 MHz



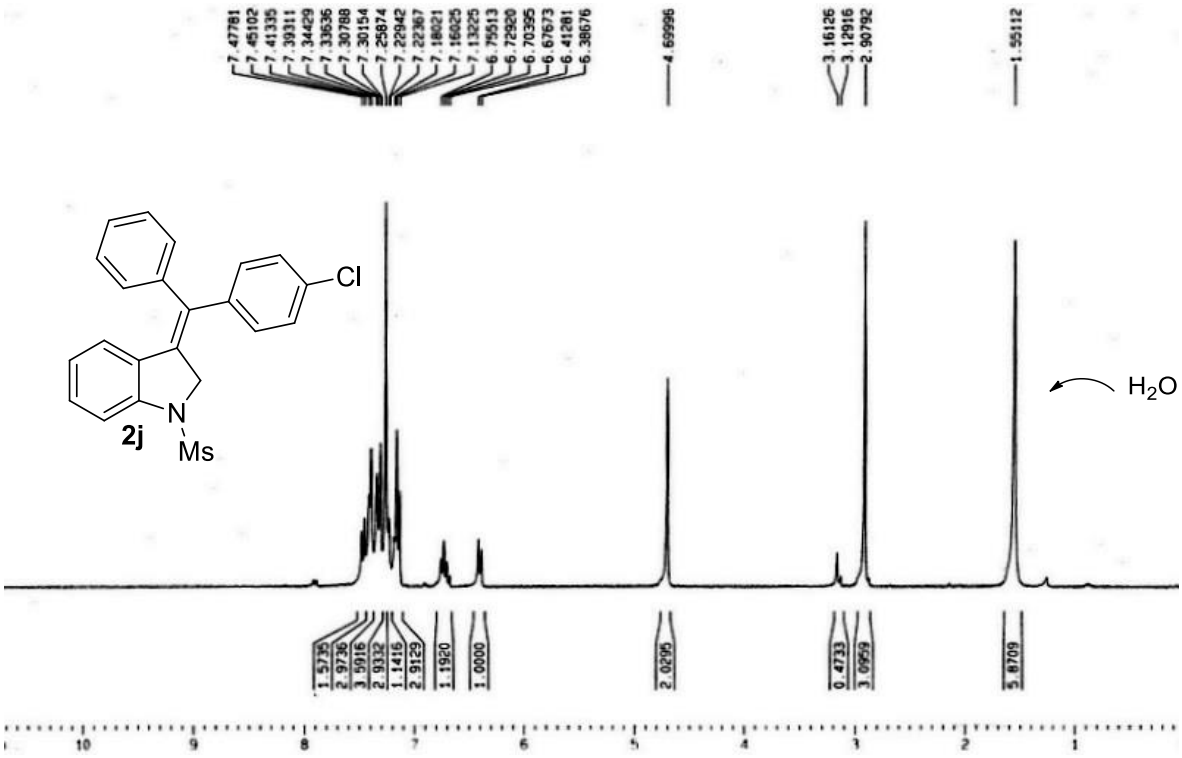
^{1}H NMR of 2i, $CDCl_3$, 300MHz



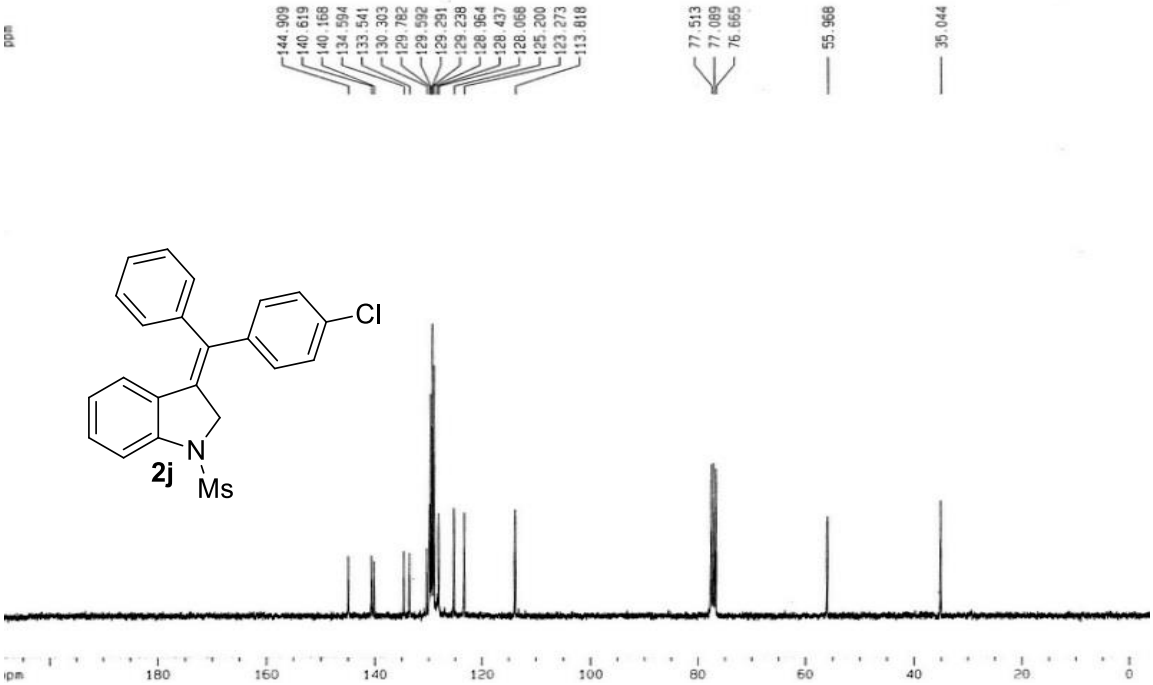
^{13}C NMR of 2i, $CDCl_3$, 75 MHz



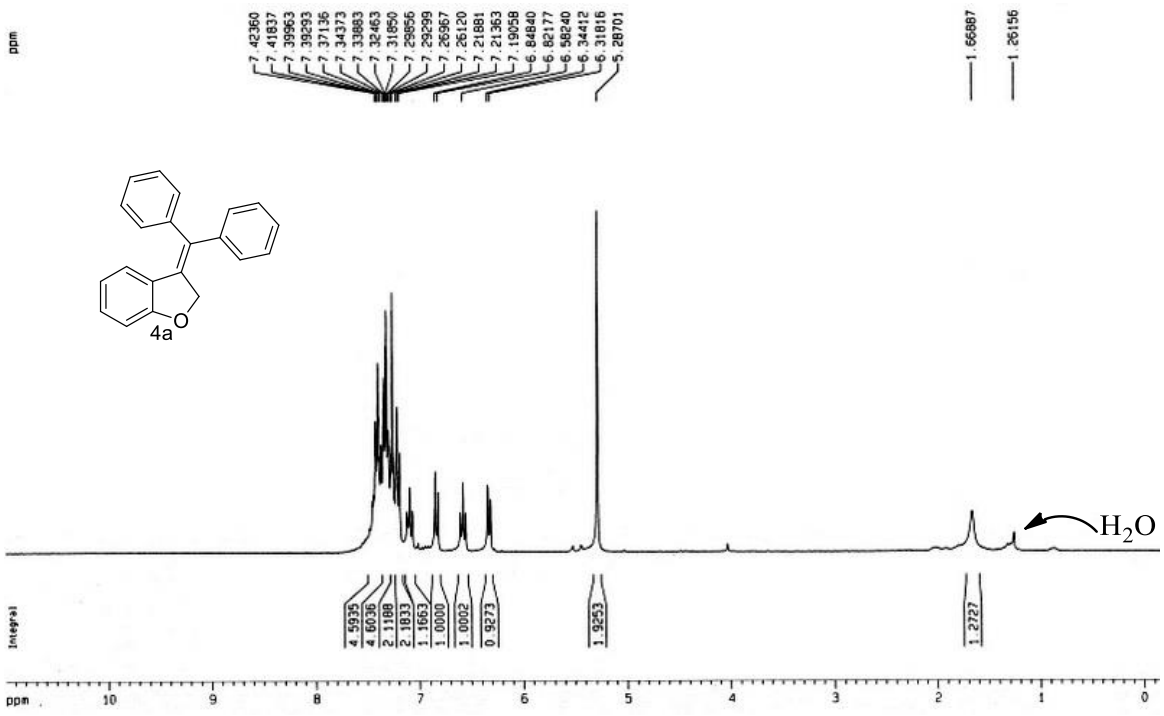
^{1}H NMR of 2j, $CDCl_3$, 300 MHz



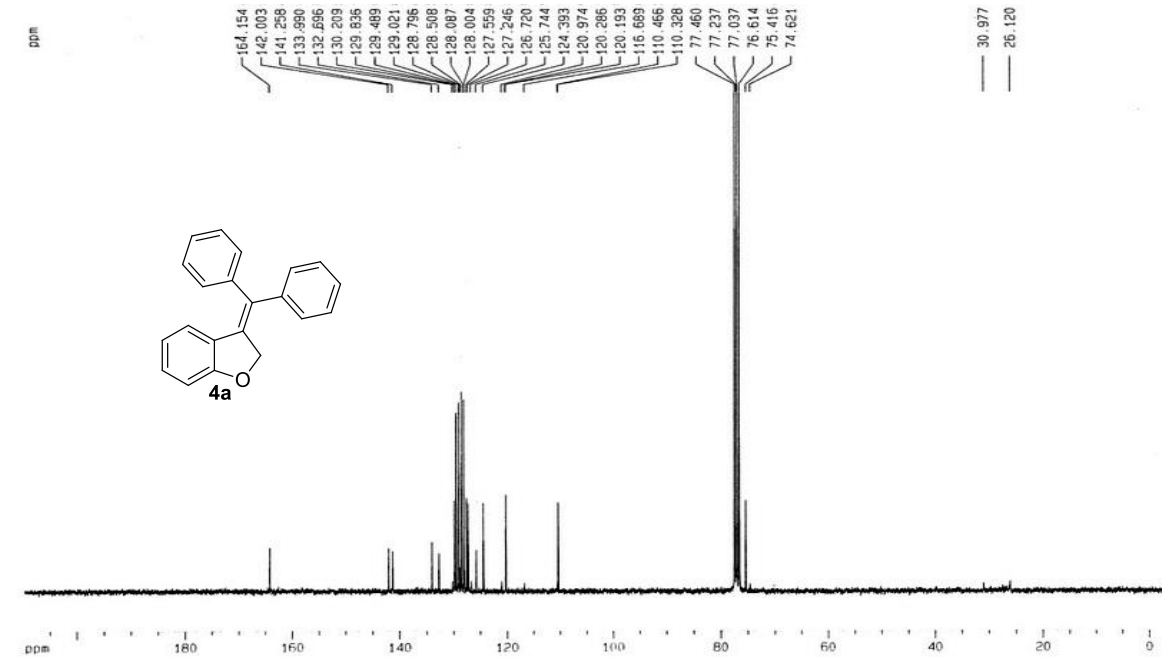
^{13}C NMR of 2j, $CDCl_3$, 75MHz



^{1}H NMR of 4a, $CDCl_3$, 300MHz



^{13}C NMR of 4a, $CDCl_3$, 75 MHz



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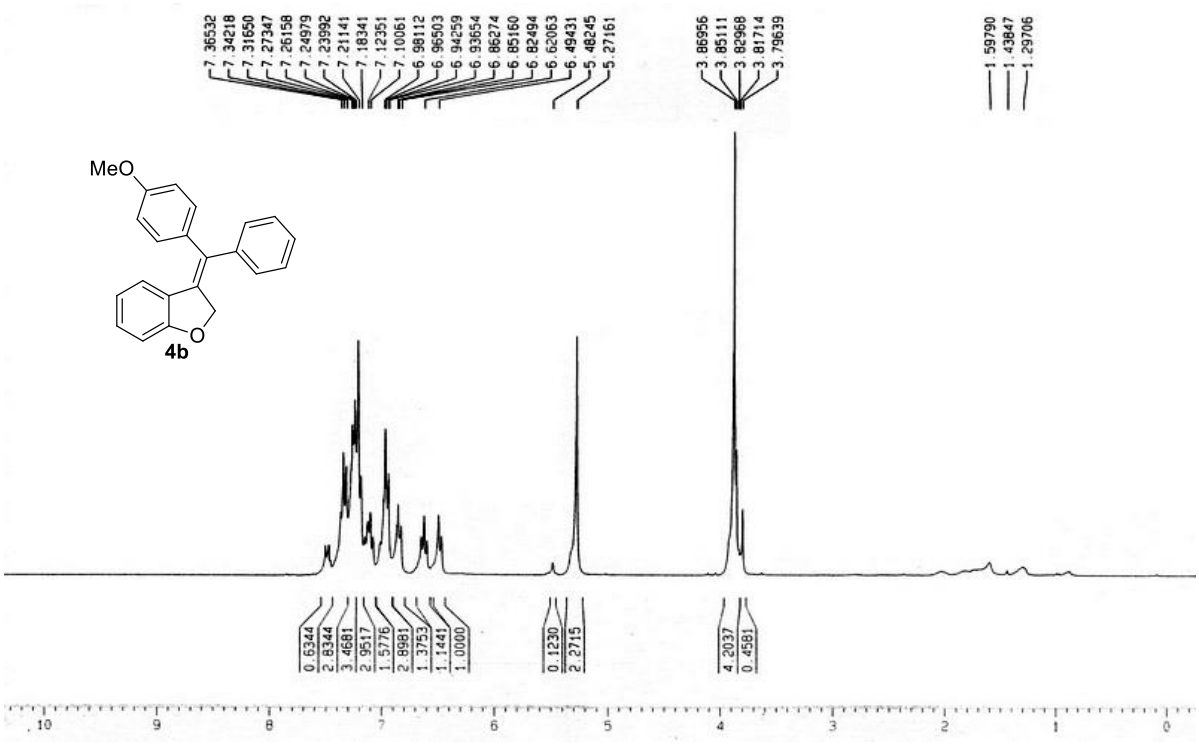
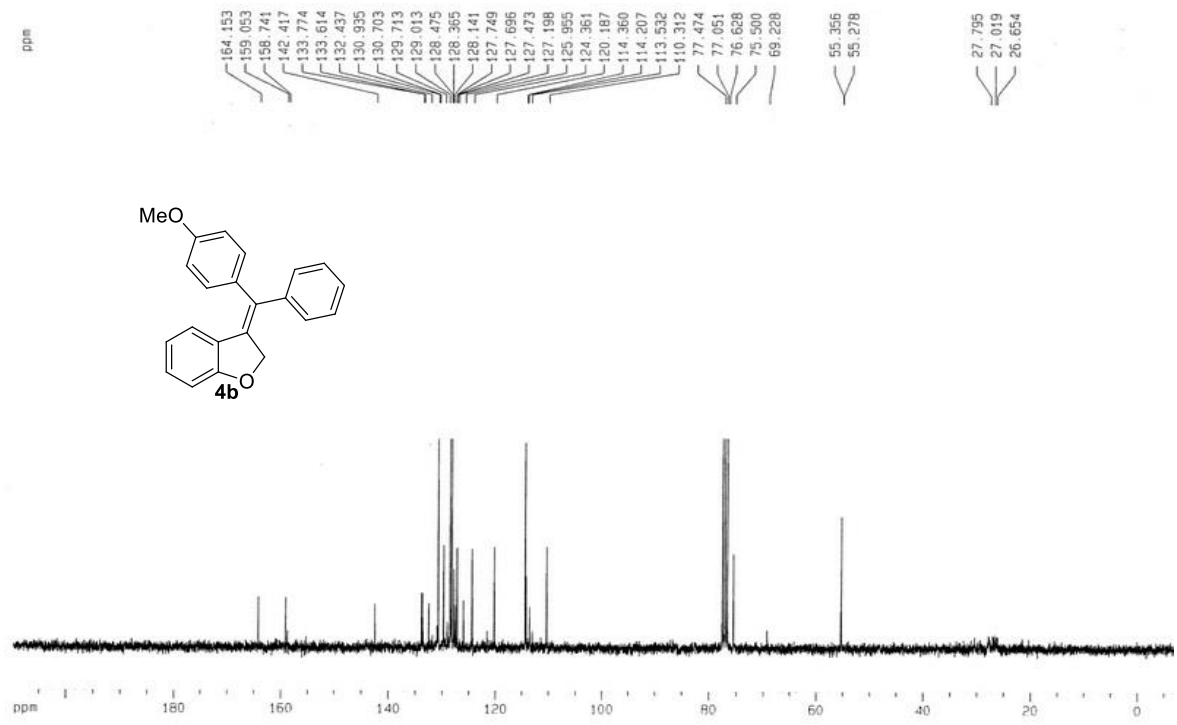
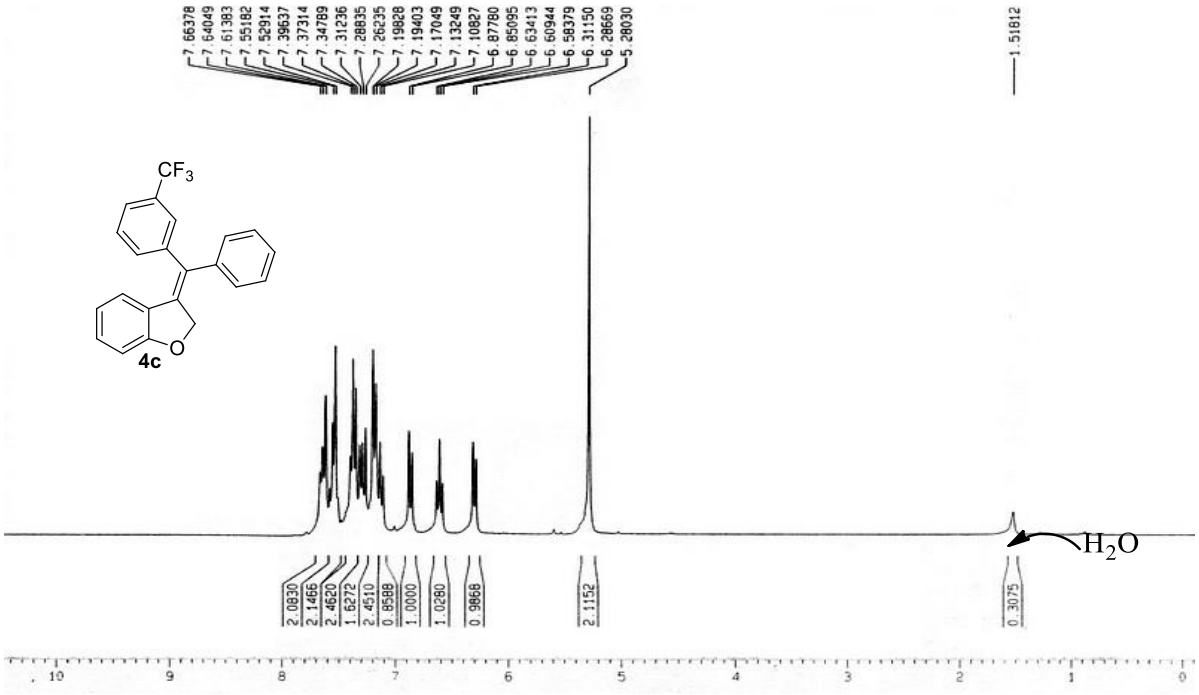


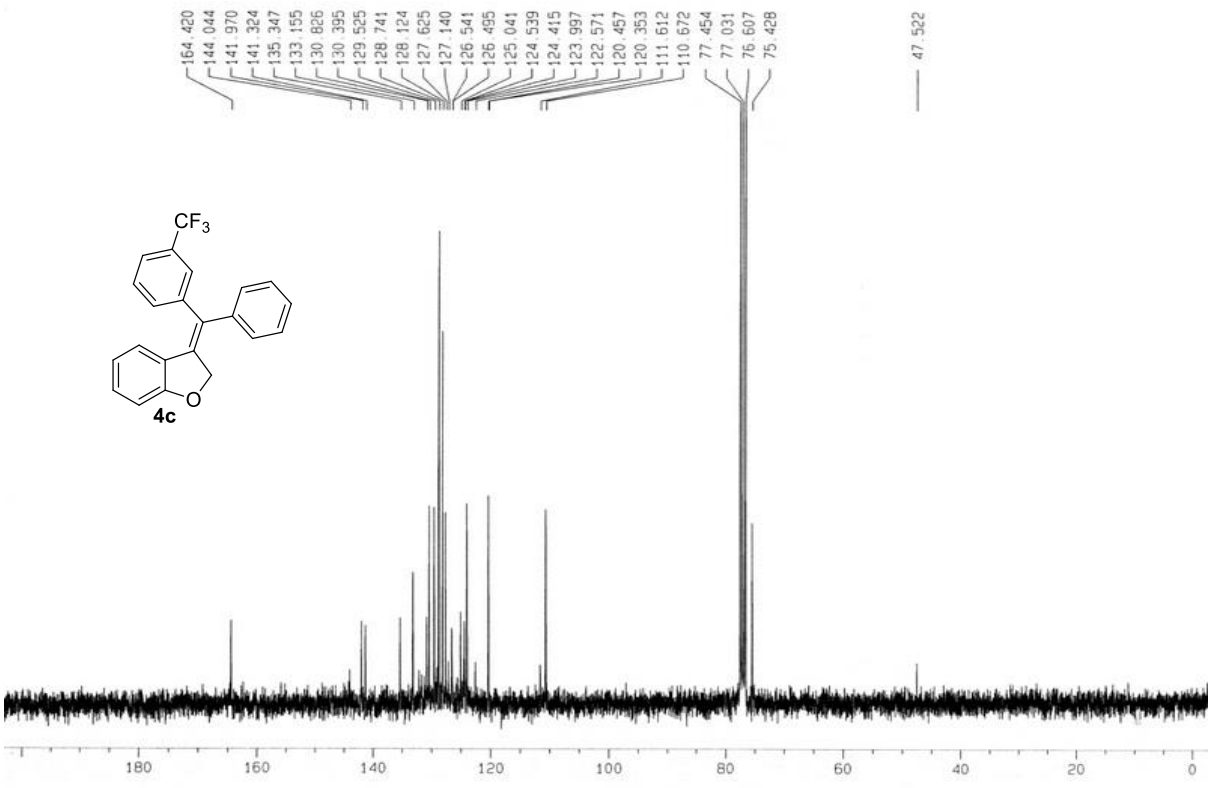
^{13}C NMR of 4b, $CDCl_3$, 75 MHz



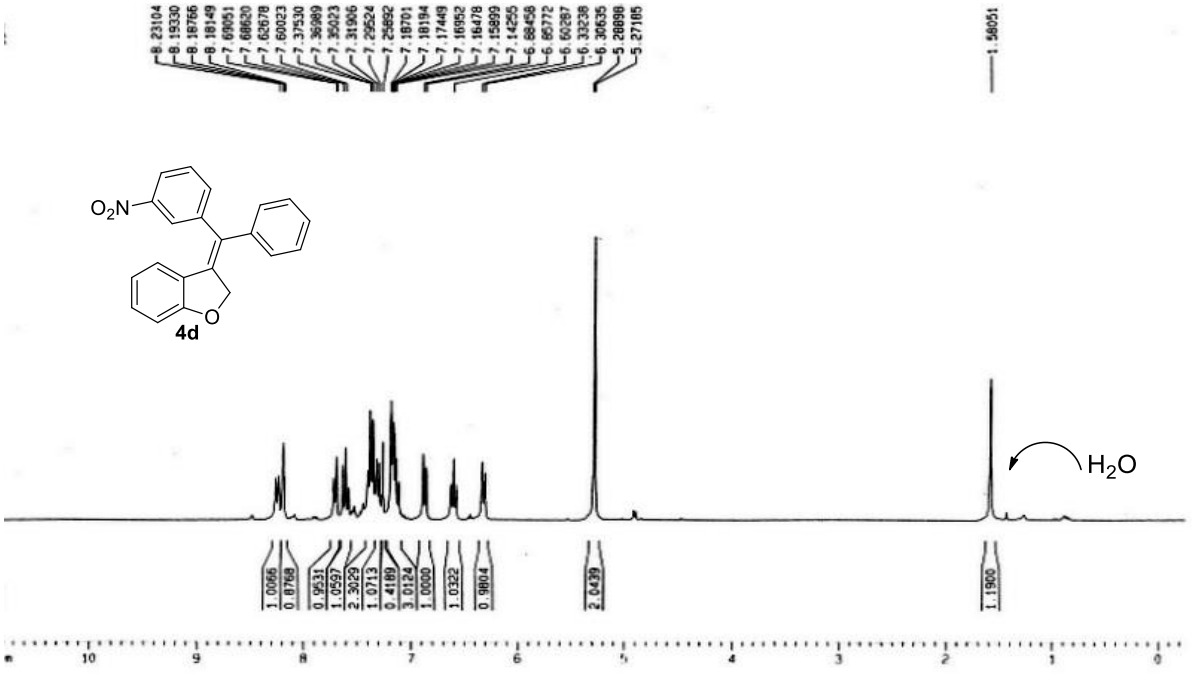
^{1}H NMR of 4c, $CDCl_3$, 300MHz



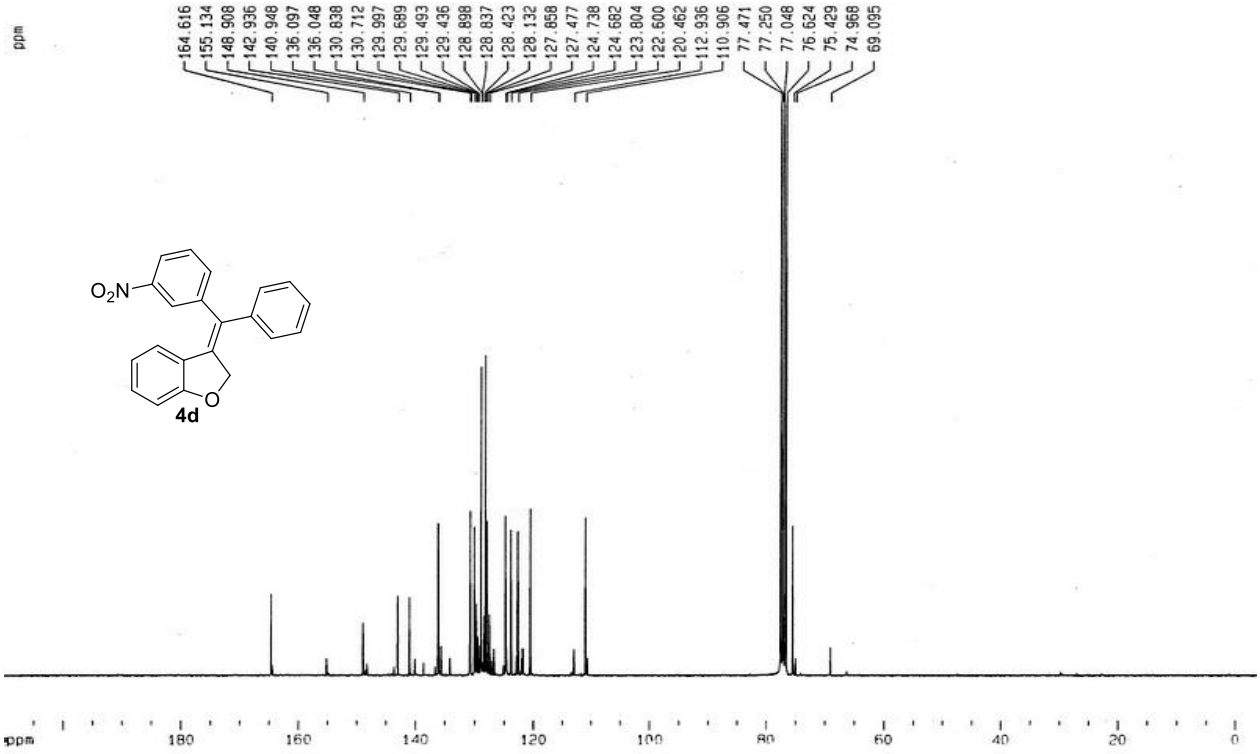
^{13}C NMR of 4c, $CDCl_3$, 75 MHz



^{1}H NMR of 4d, $CDCl_3$, 300MHz



^{13}C NMR of 4d, $CDCl_3$, 75 MHz



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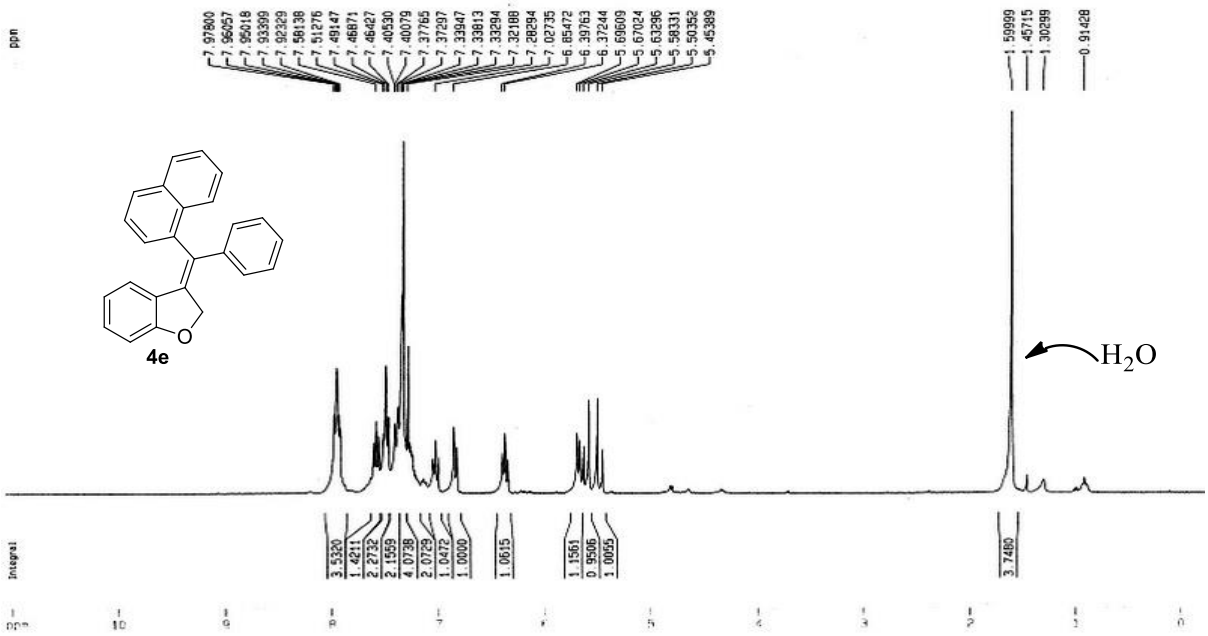

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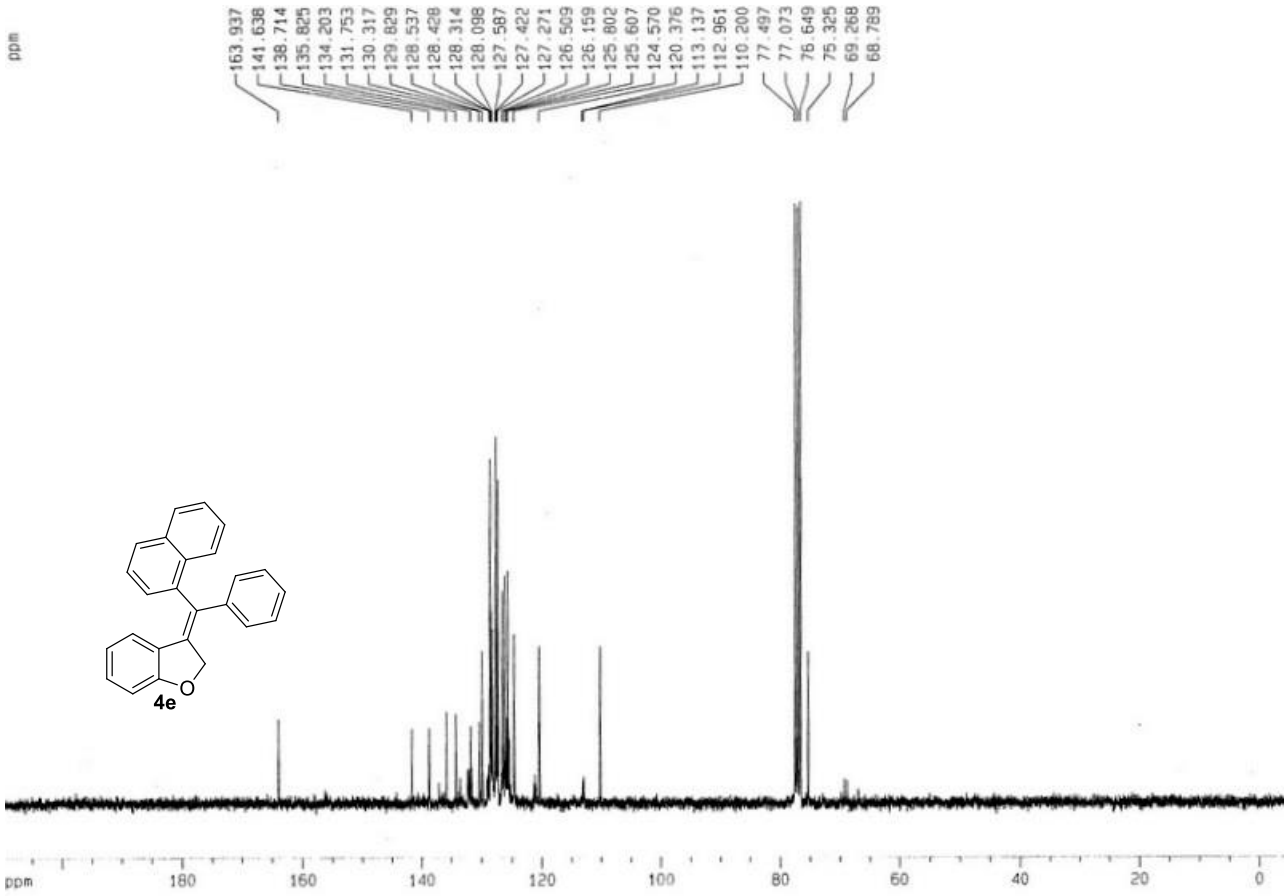
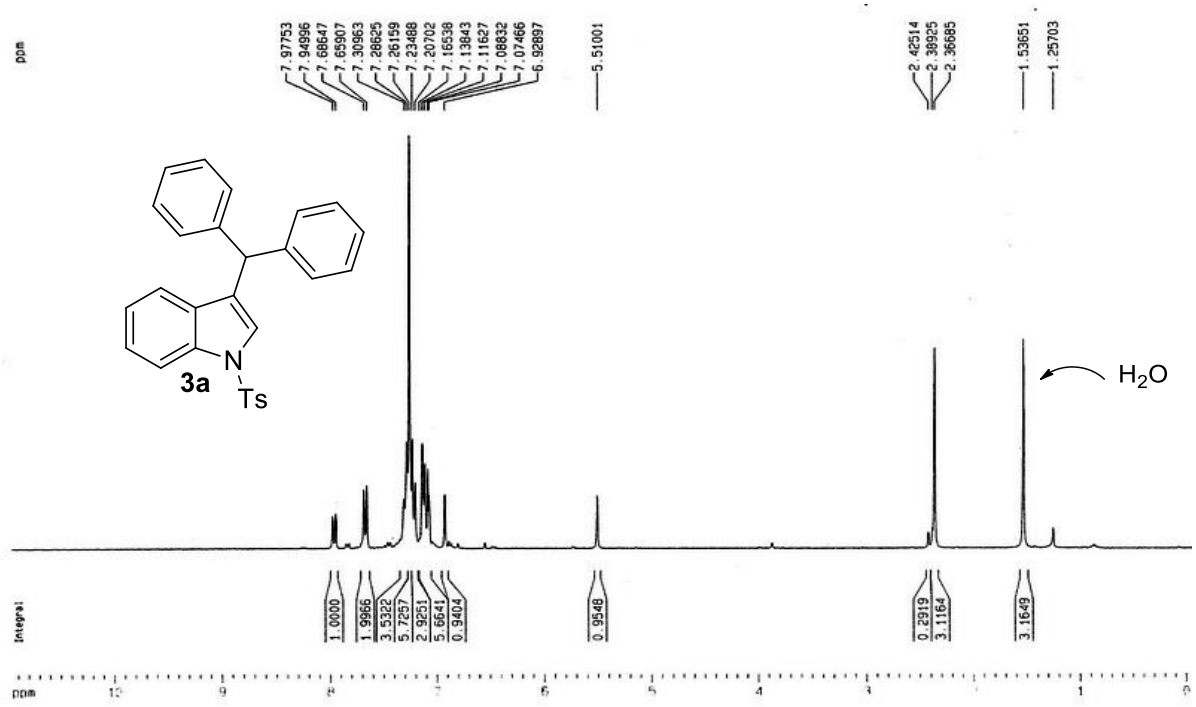
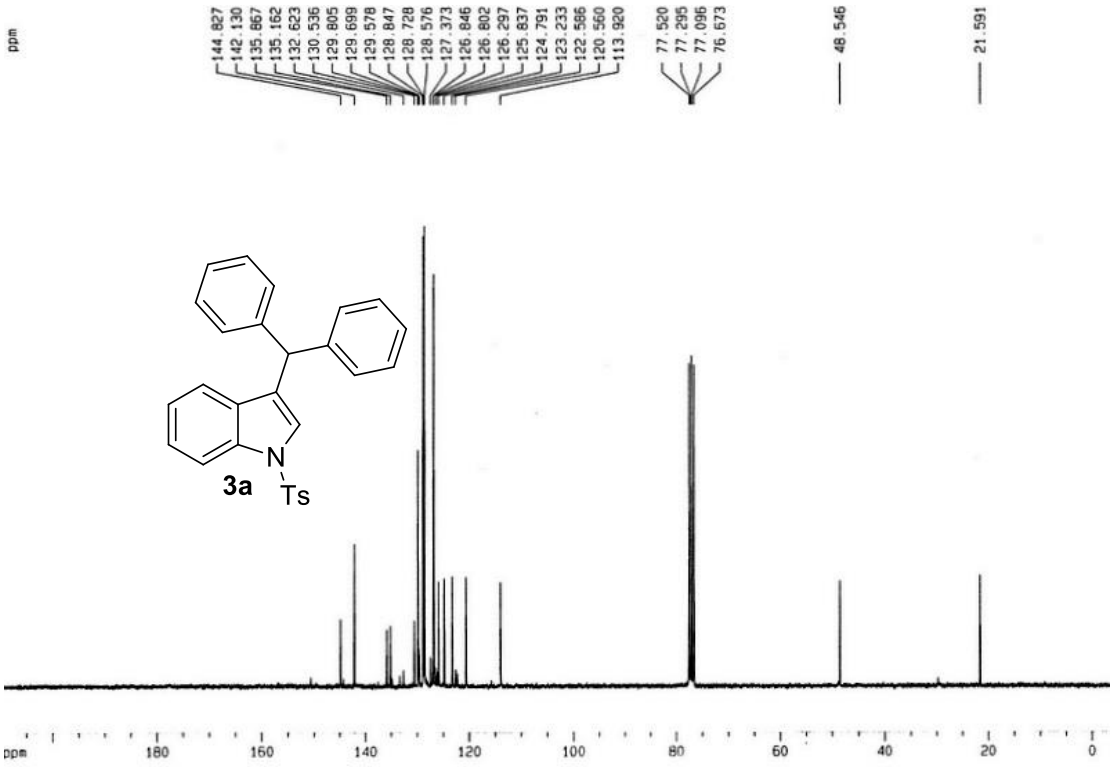


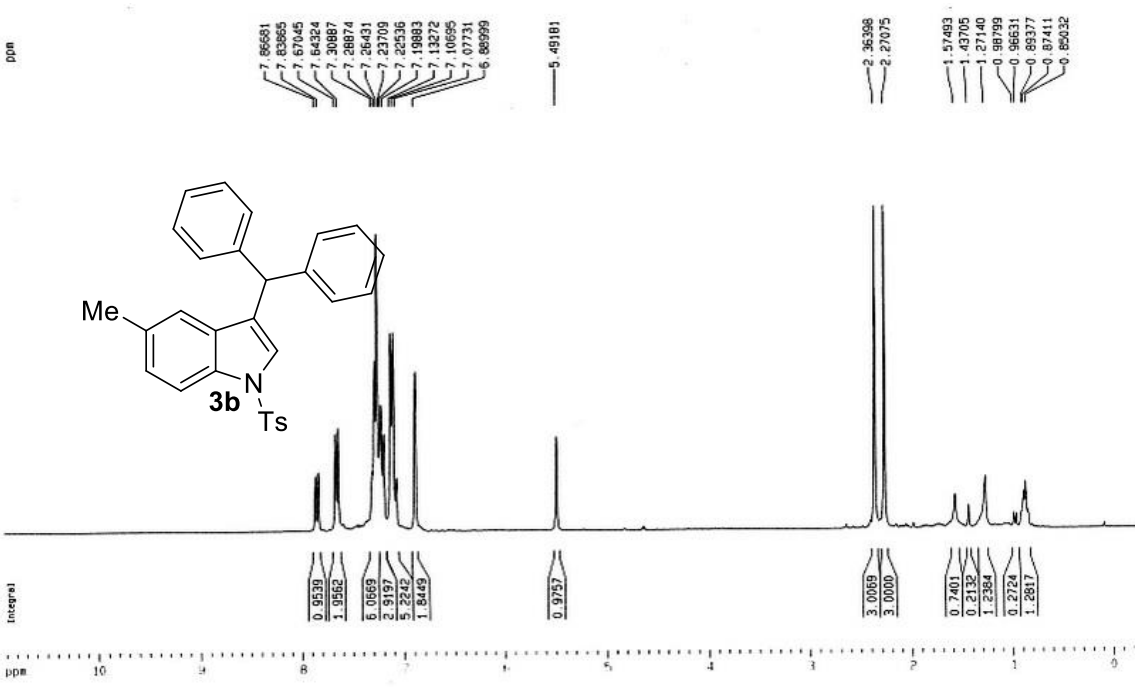
^{1}H NMR of 3a, $CDCl_3$, 300 MHz



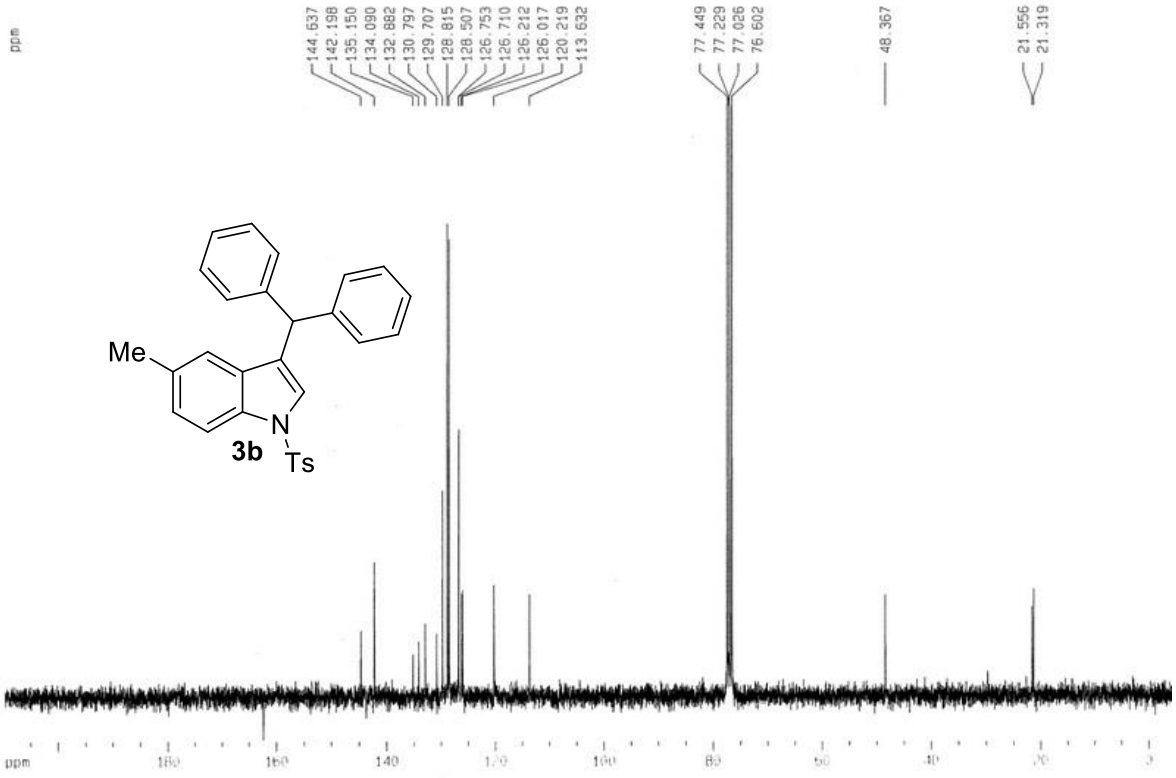
^{13}C NMR of 3a, $CDCl_3$, 75 MHz



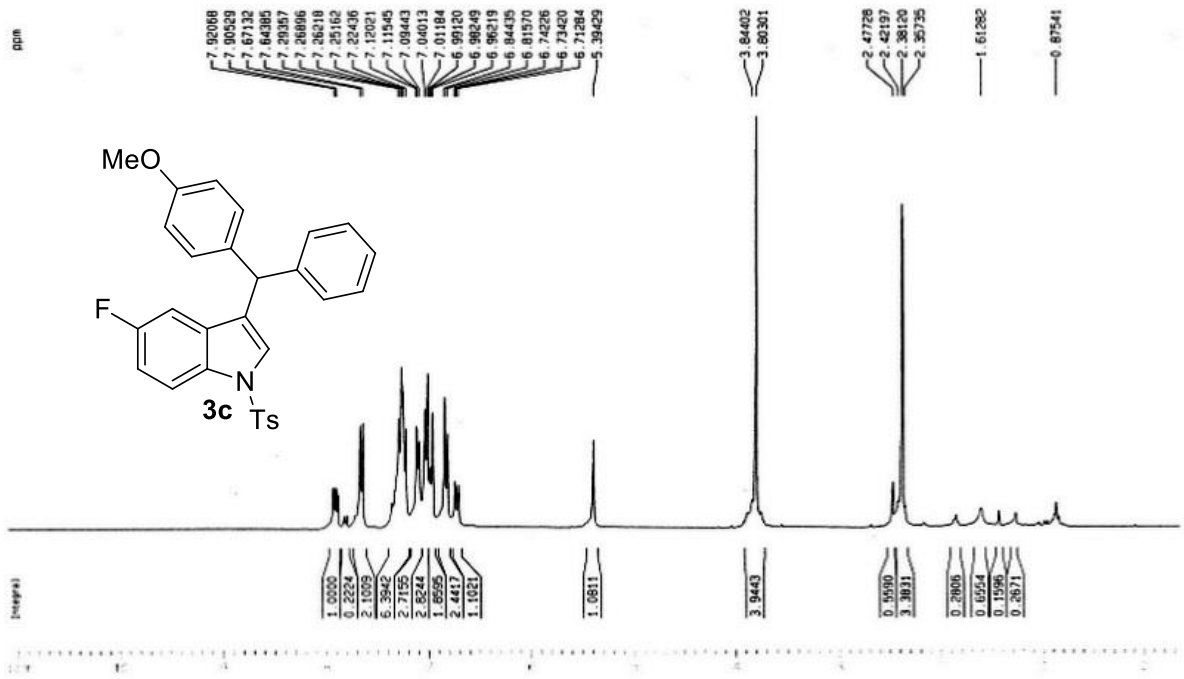
^{1}H NMR of 3b, $CDCl_3$, 300MHz



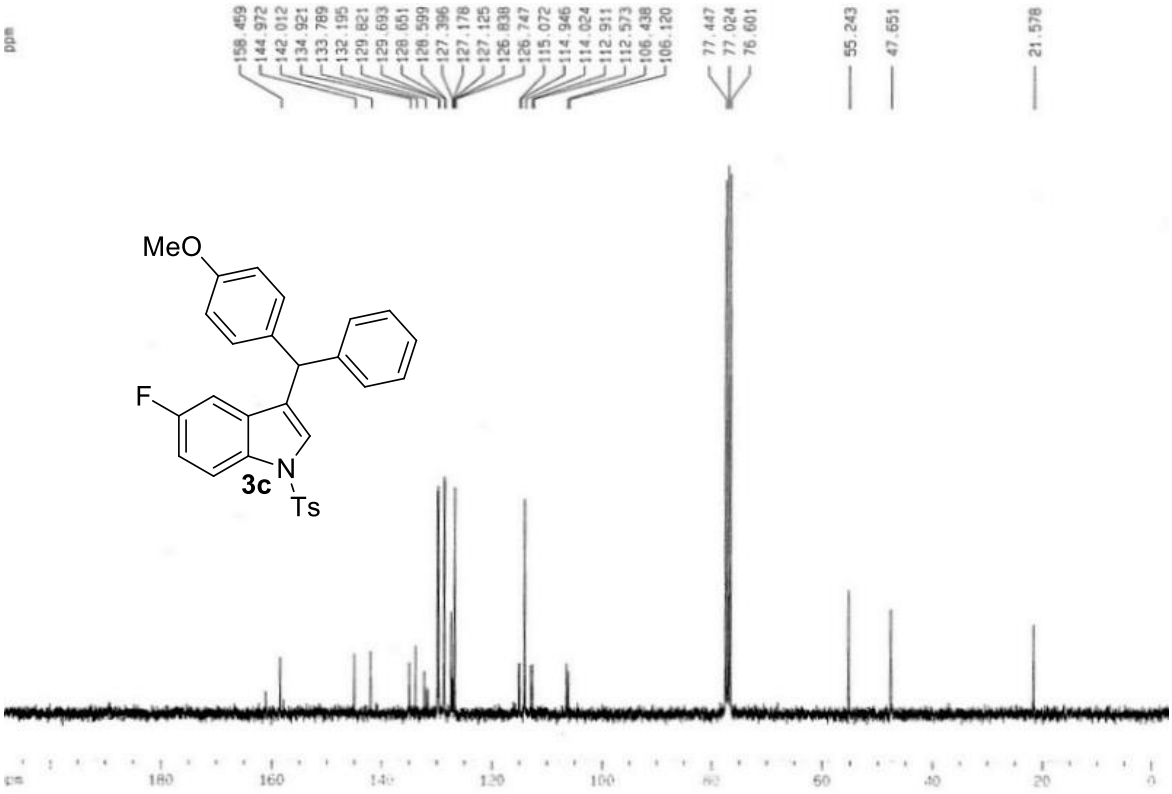
^{13}C NMR of 3b, $CDCl_3$, 75 MHz



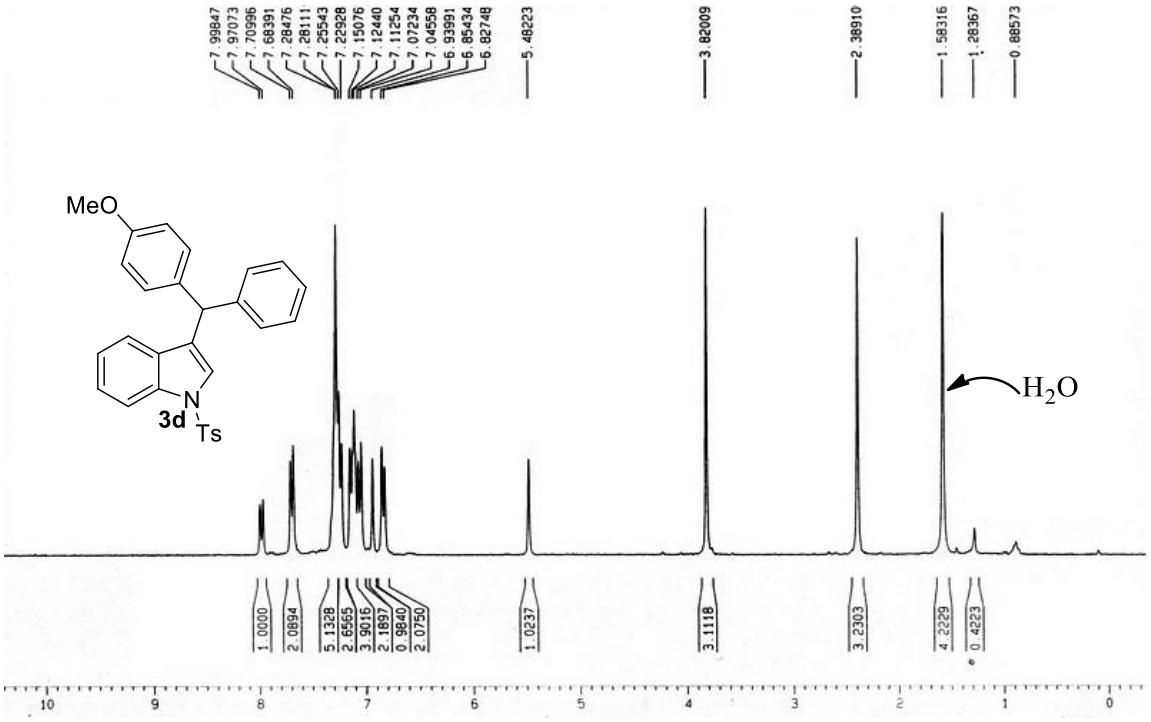
^{1}H NMR of 3c, $CDCl_3$, 300 MHz



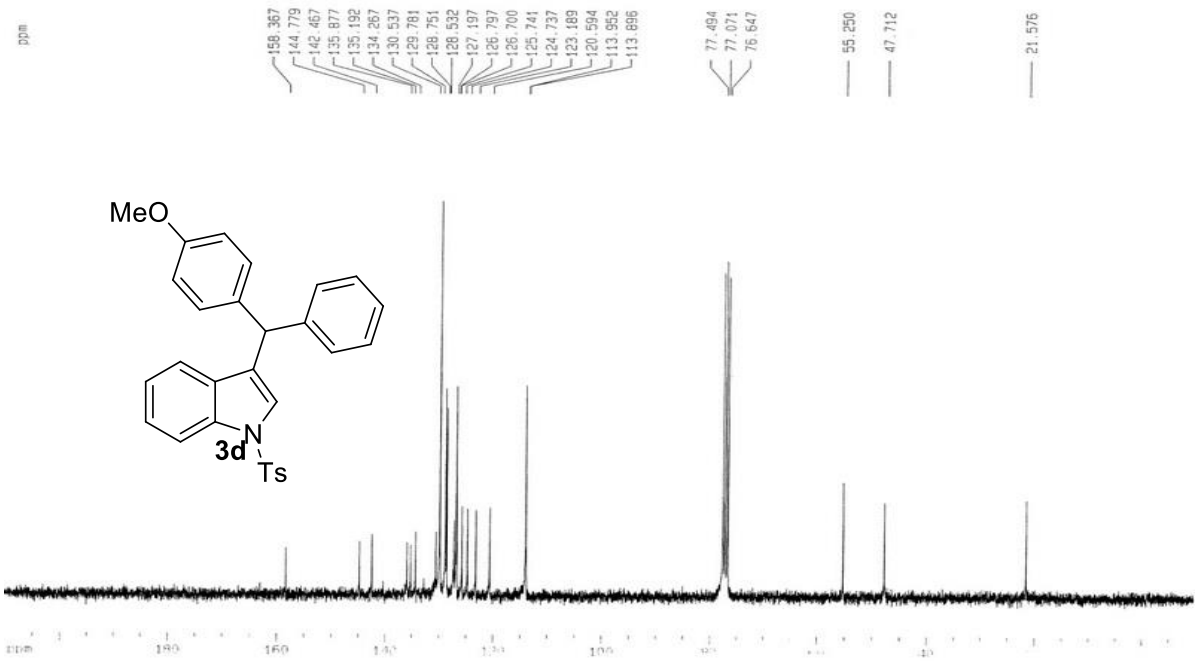
^{13}C NMR of 3c, $CDCl_3$, 75 MHz



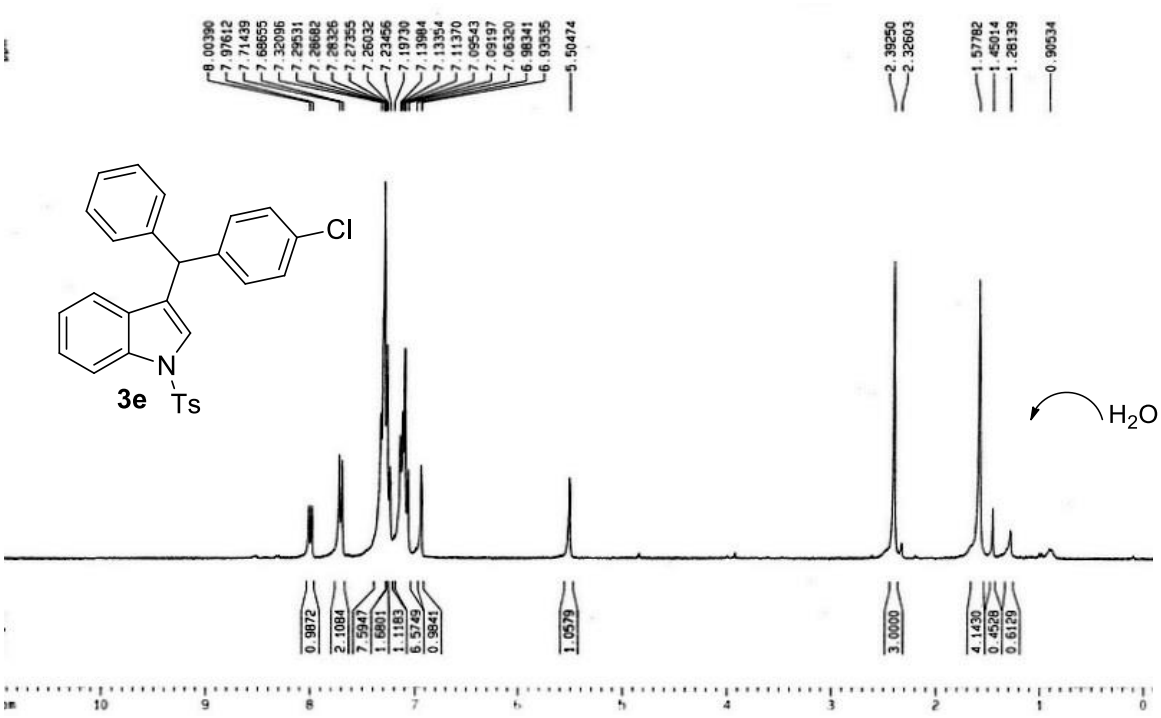
^{1}H NMR of 3d,$CDCl_3$, 300 MHz



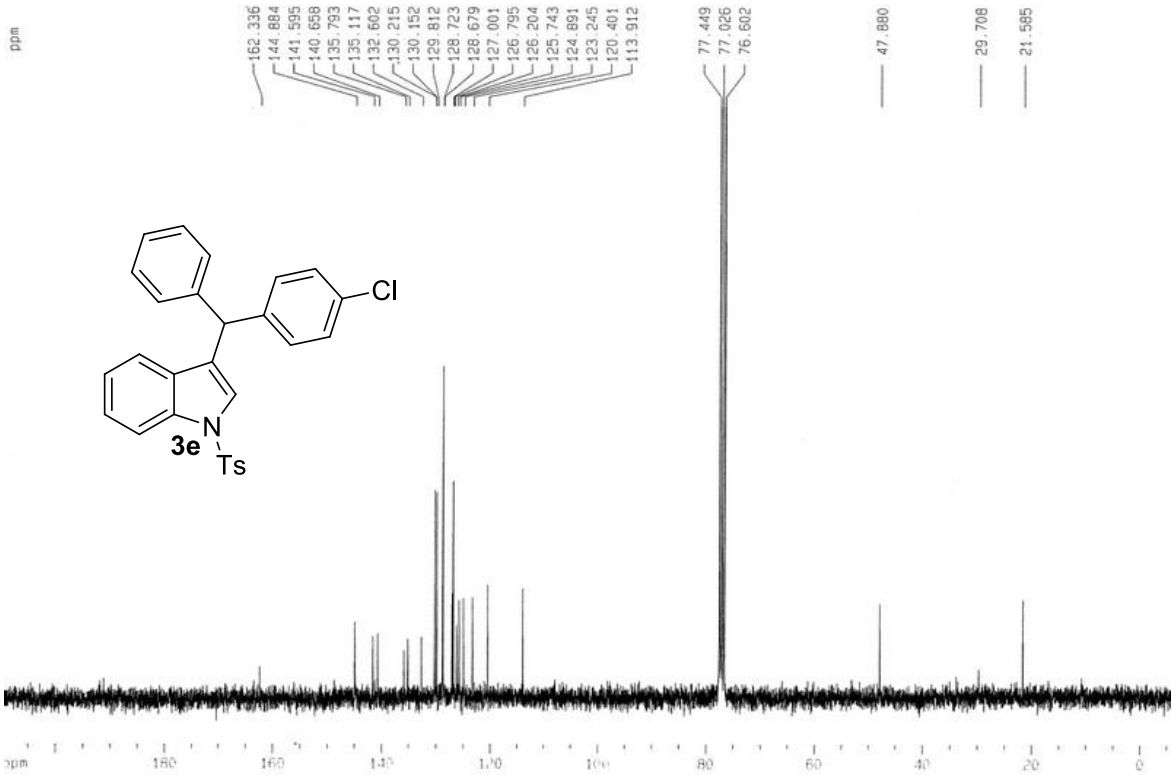
^{13}C NMR of 3d, $CDCl_3$, 75 MHz



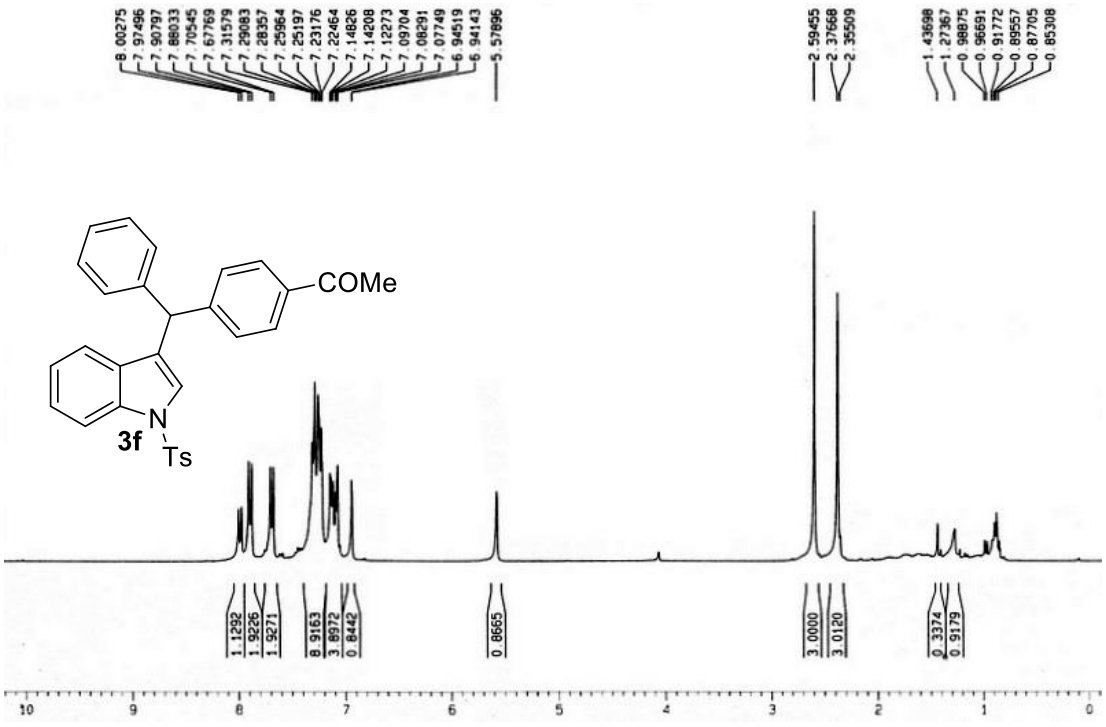
^{1}H NMR of 3e, $CDCl_3$, 300MHz



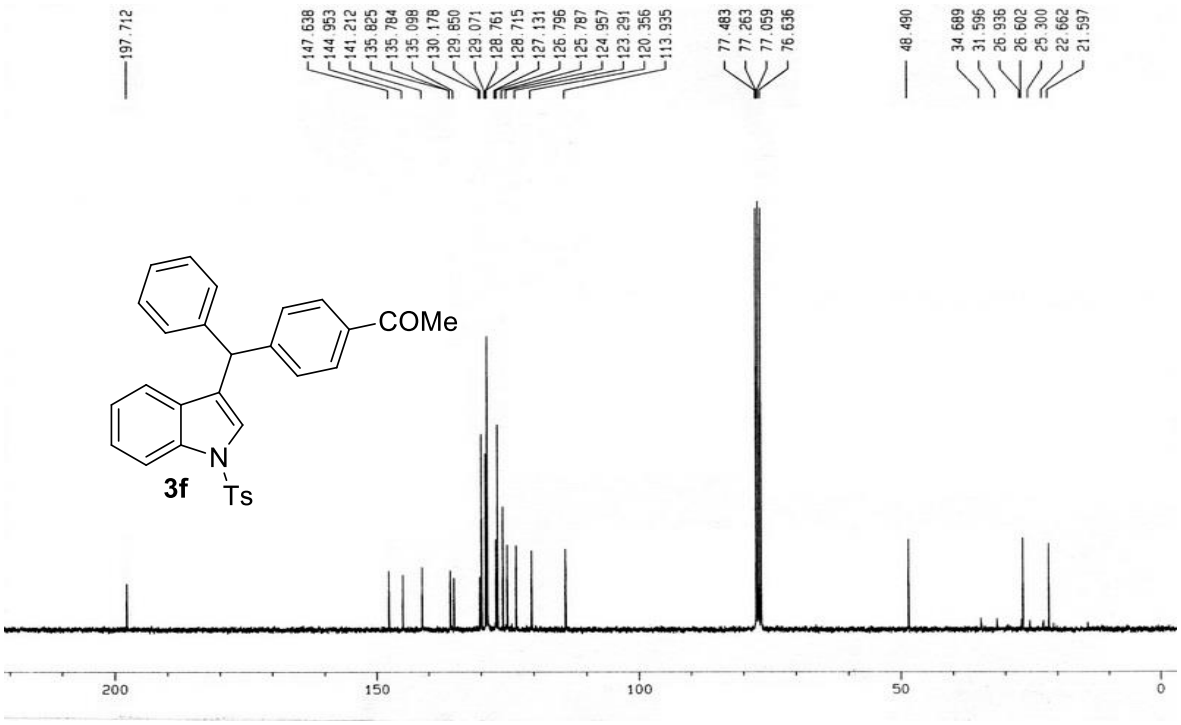
^{13}C NMR of 3e, $CDCl_3$, 75 MHz



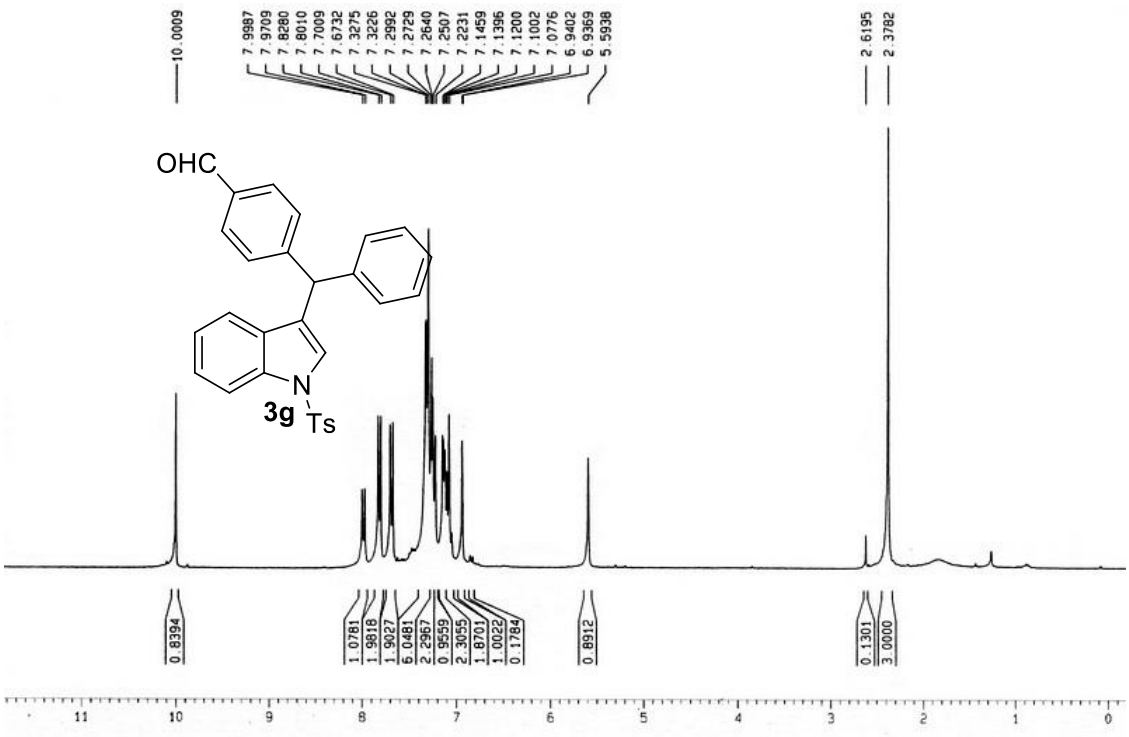
^{1}H NMR of 3f, $CDCl_3$, 300MHz



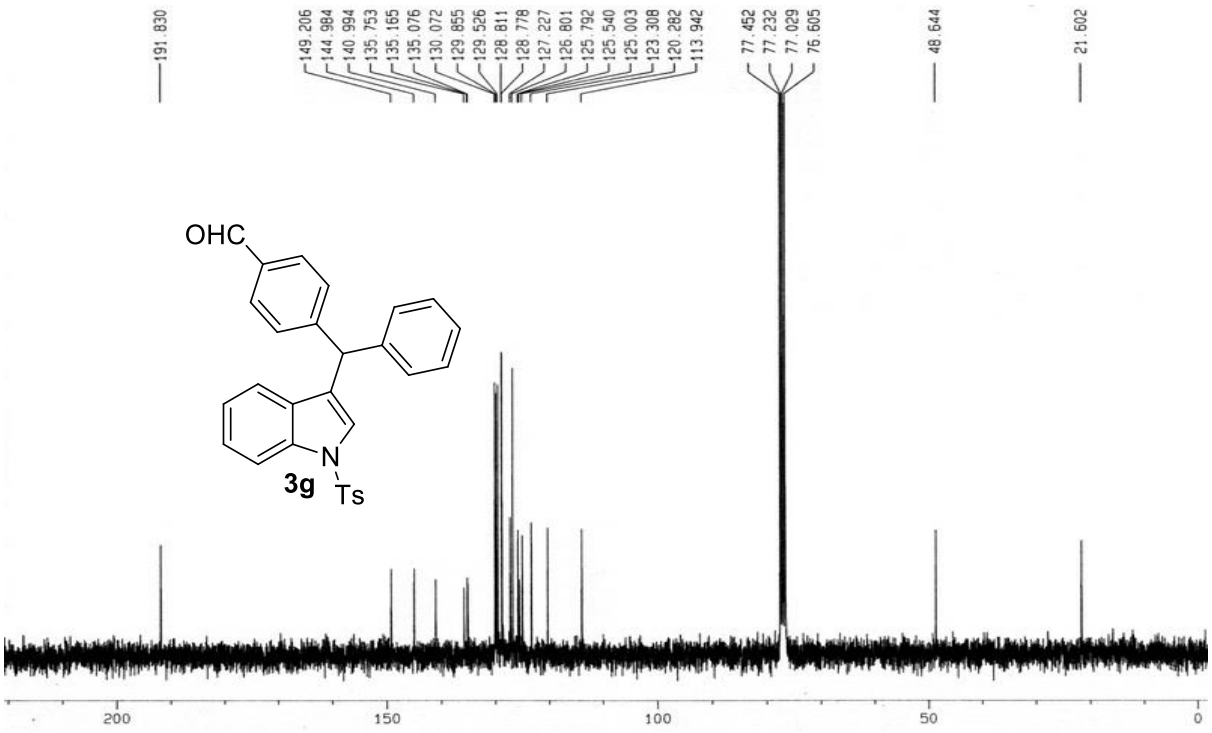
^{13}C NMR of 3f, $CDCl_3$, 75 MHz



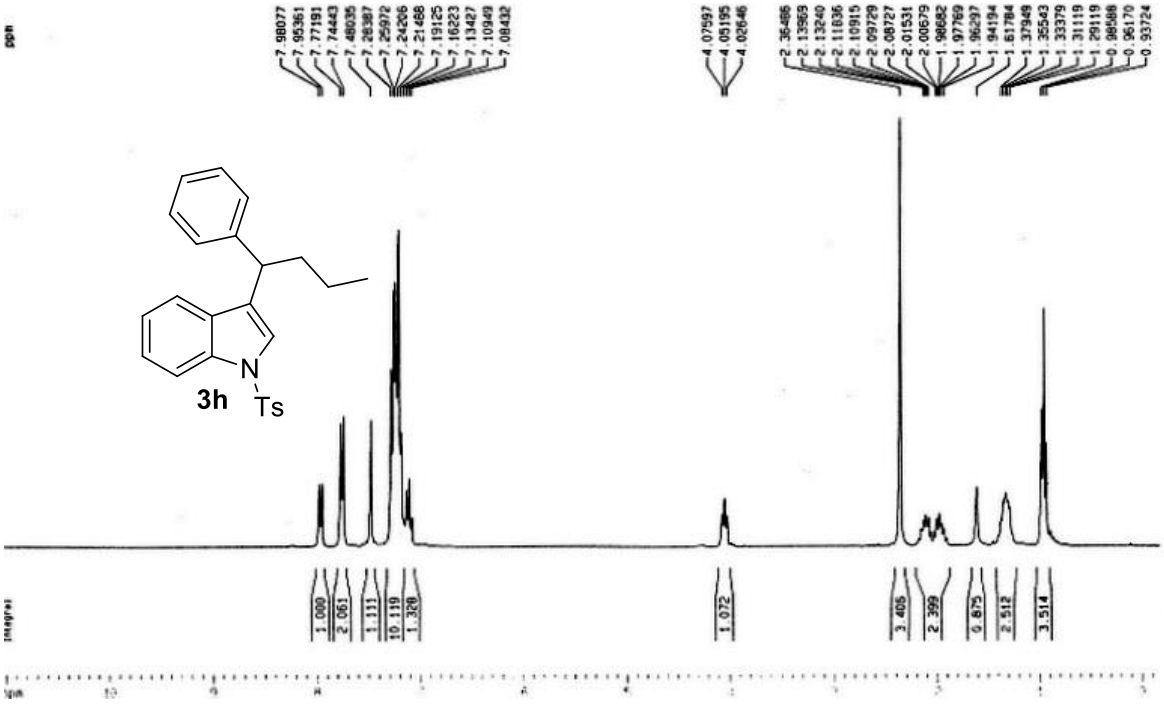
^{1}H NMR of 3g, $CDCl_3$, 300MHz



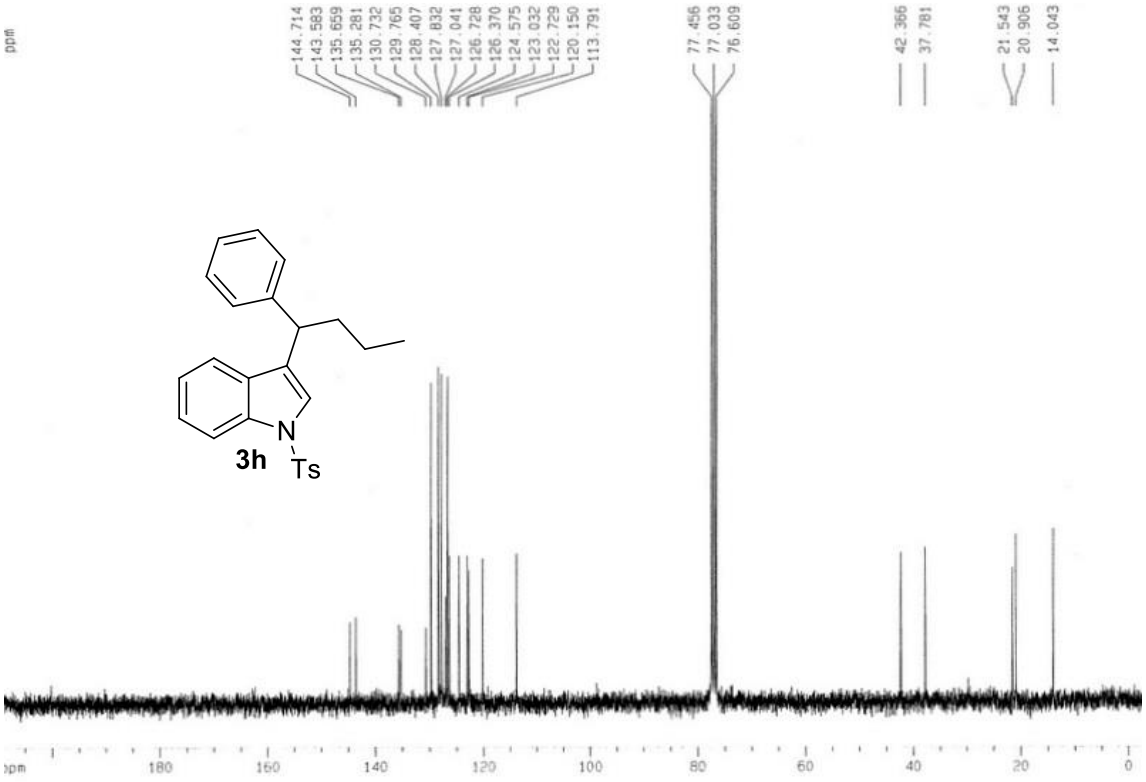
^{13}C NMR of 3g, $CDCl_3$, 75 MHz



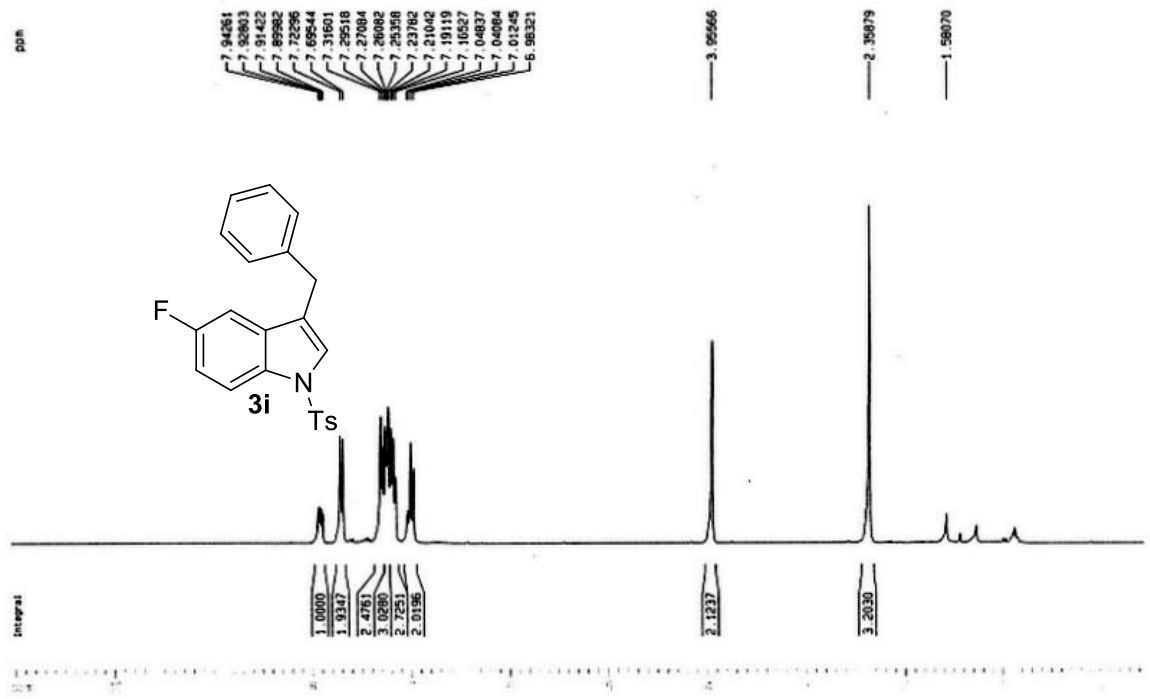
^{1}H NMR of 3h,$CDCl_3$, 300 MHz



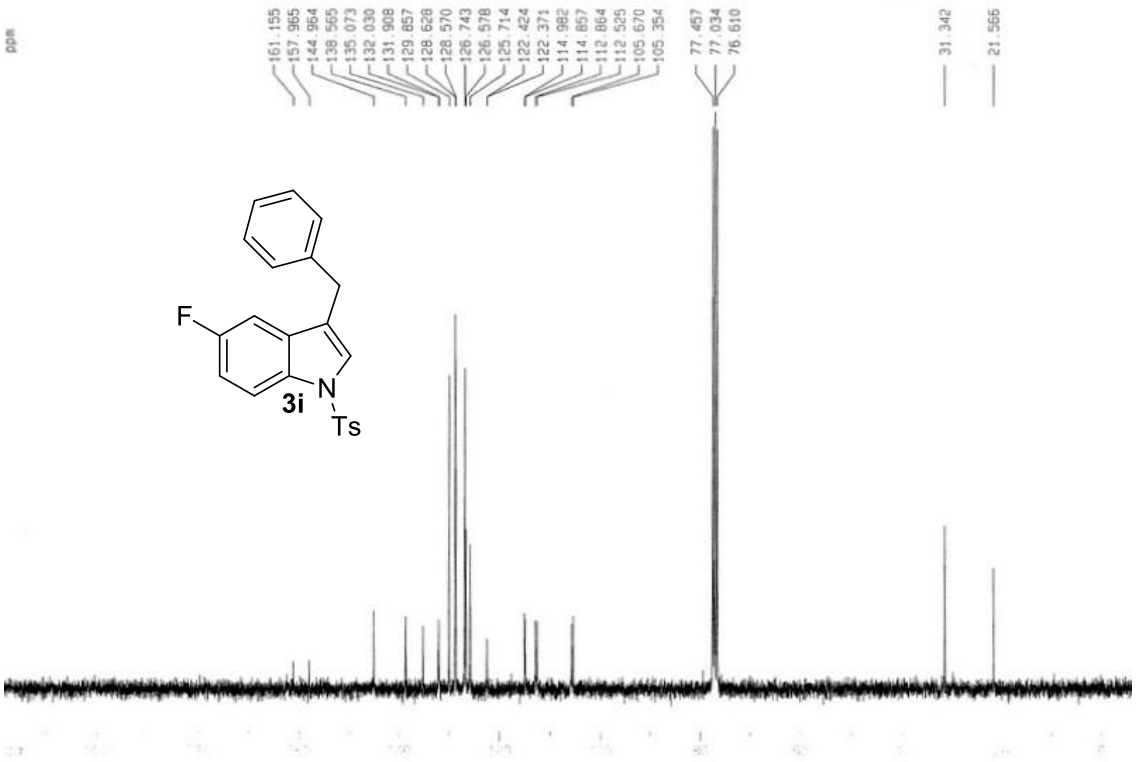
^{13}C NMR of 3h, $CDCl_3$, 75 MHz



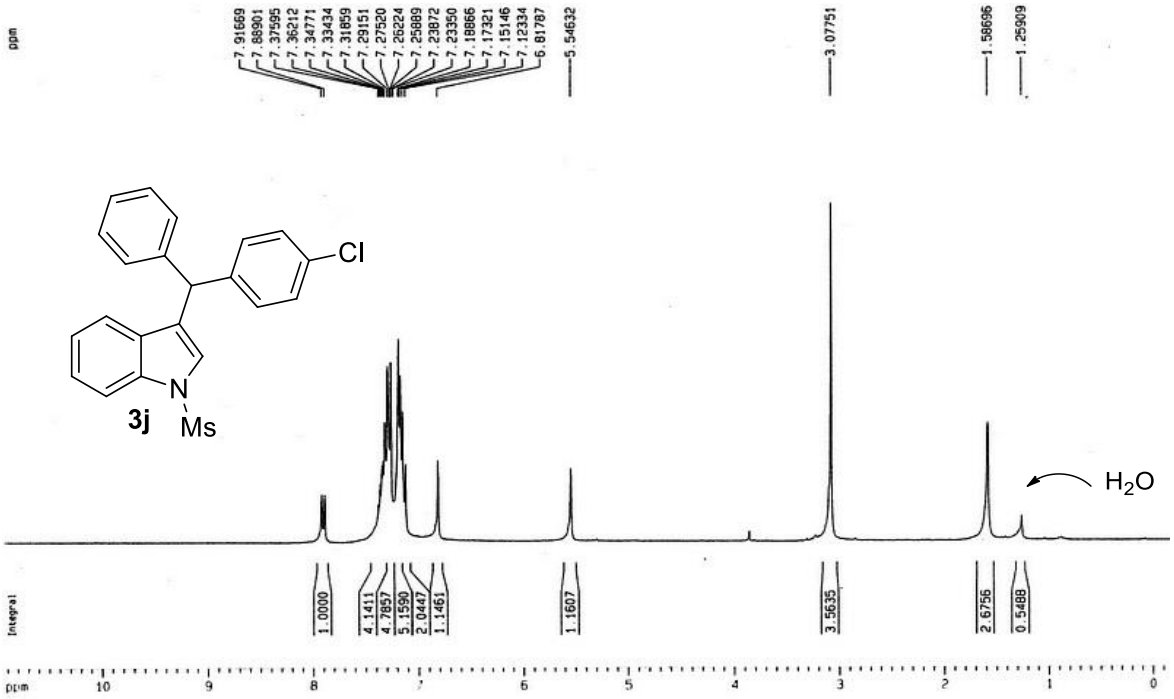
^{1}H NMR of 3i, $CDCl_3$, 300MHz



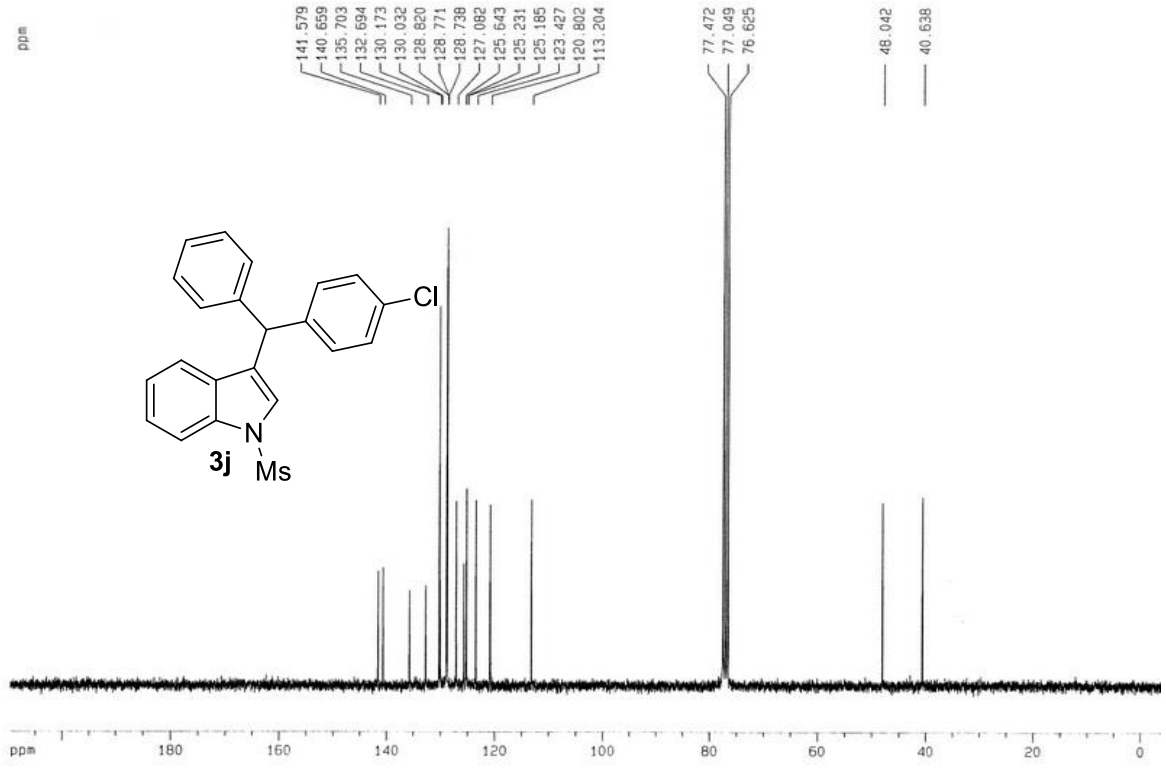
^{13}C NMR of 3i, $CDCl_3$, 75 MHz



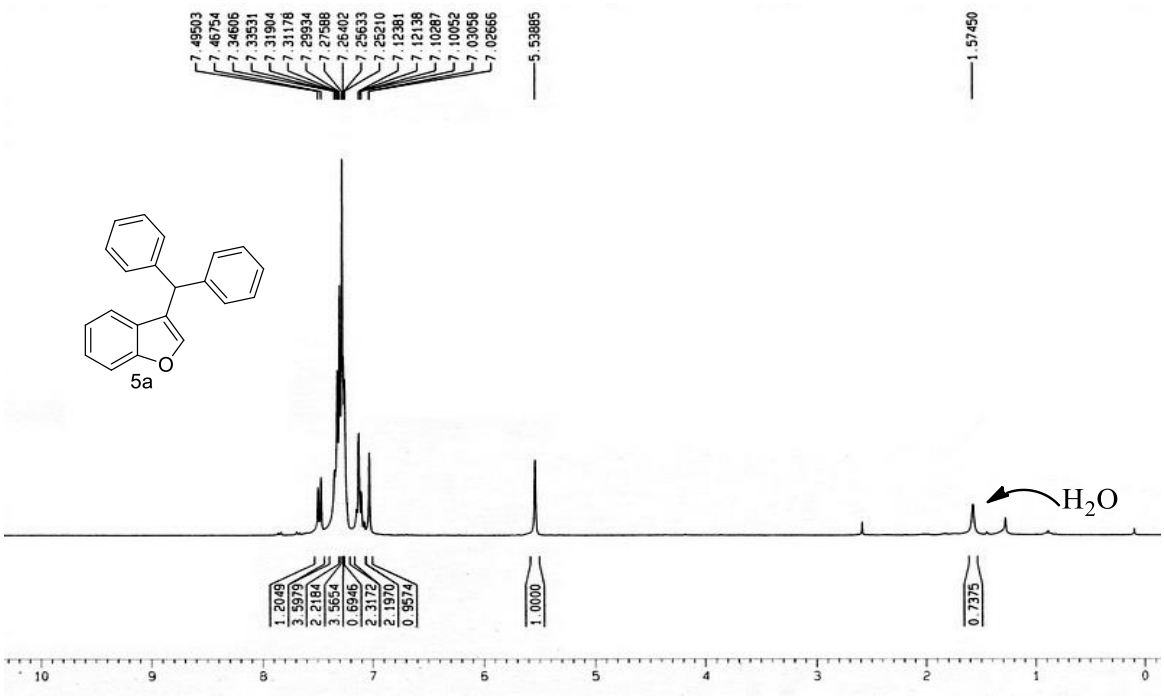
^{1}H NMR of 3j, $CDCl_3$, 300MHz



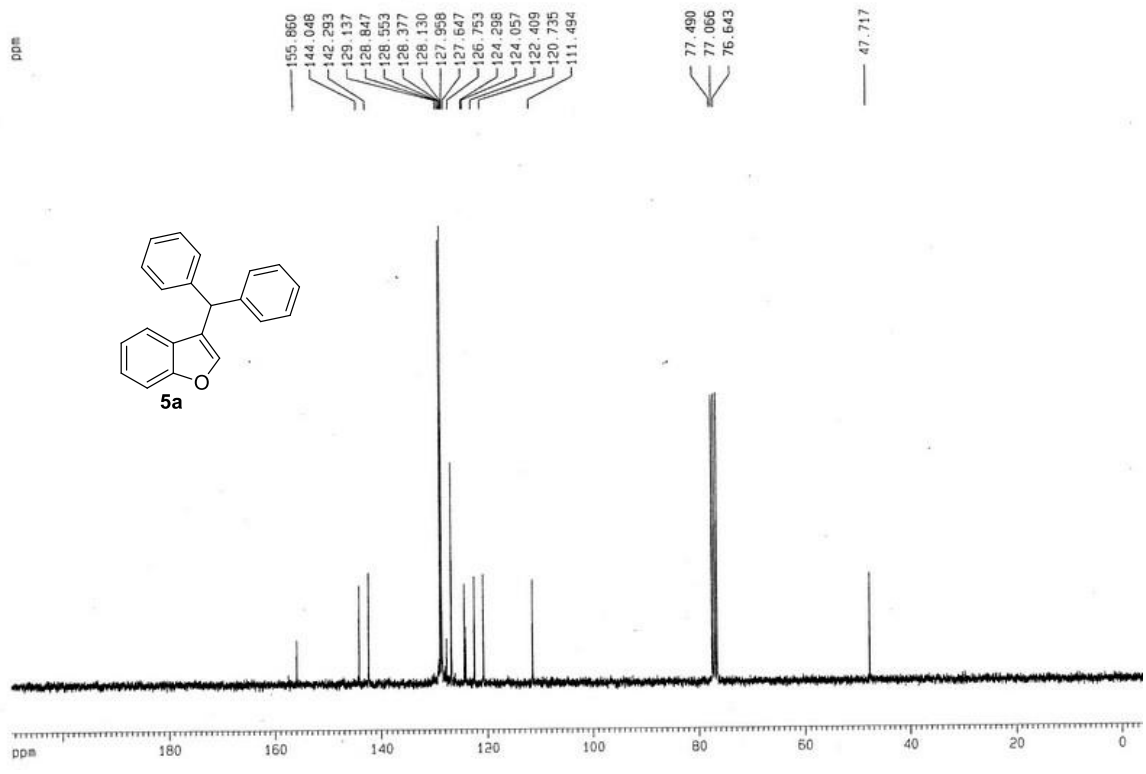
^{13}C NMR of 3j, $CDCl_3$, 75 MHz



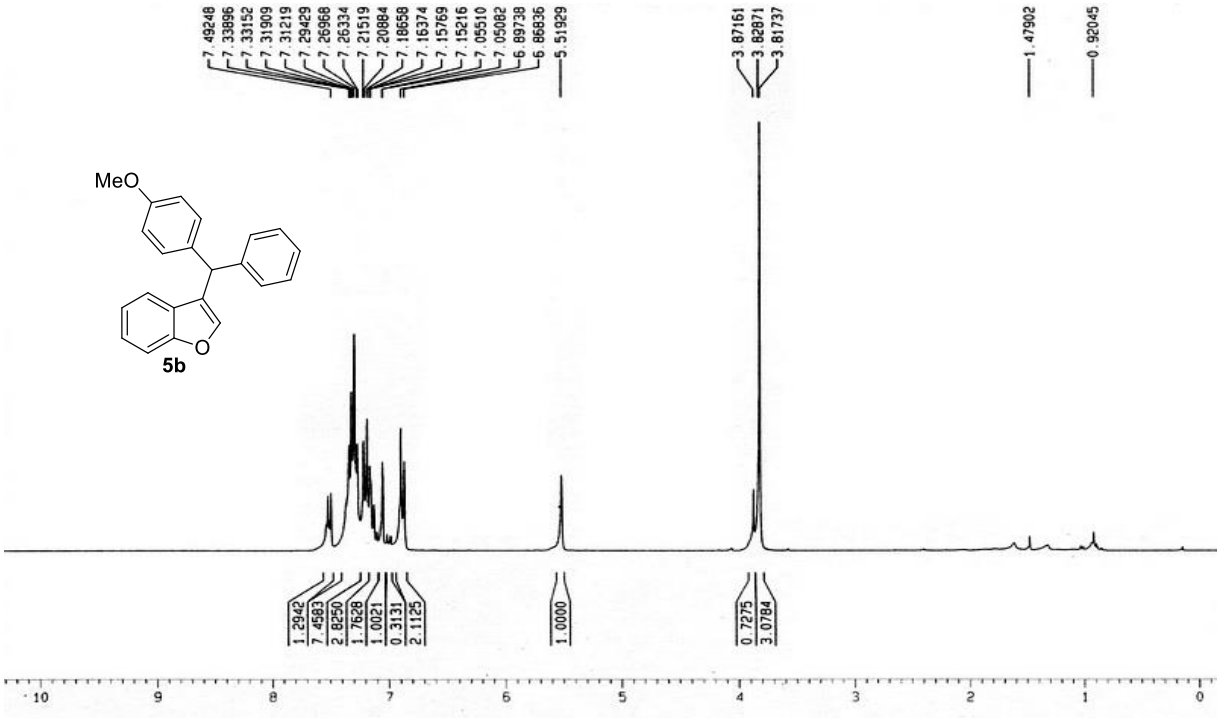
^{1}H NMR of 5a, $CDCl_3$, 300MHz



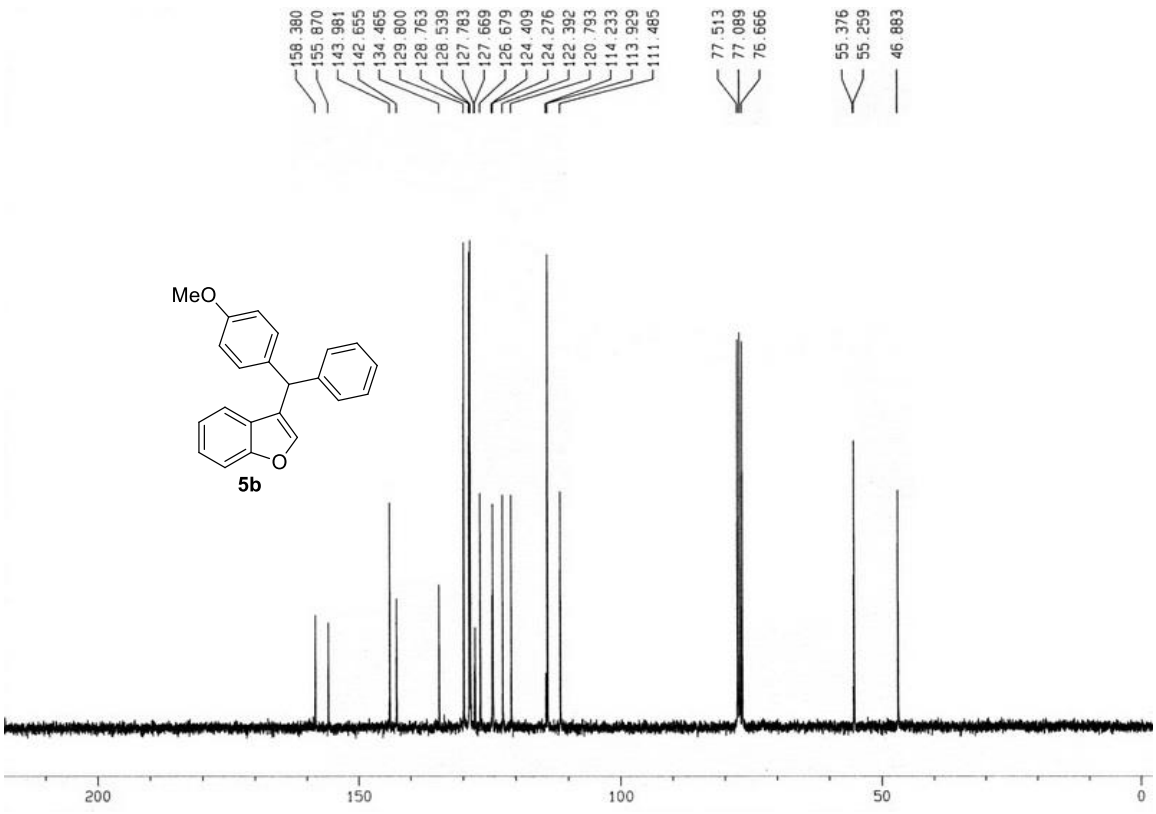
^{13}C NMR of 5a, $CDCl_3$, 75 MHz



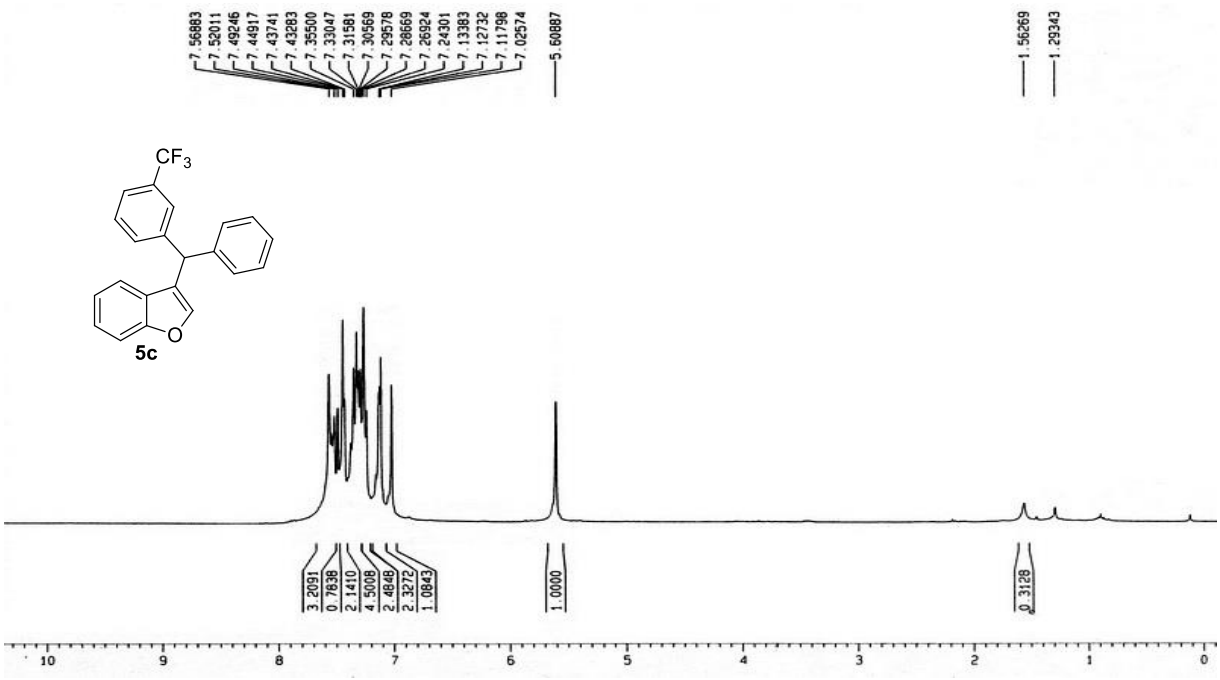
^{1}H NMR of 5b, $CDCl_3$, 300MHz



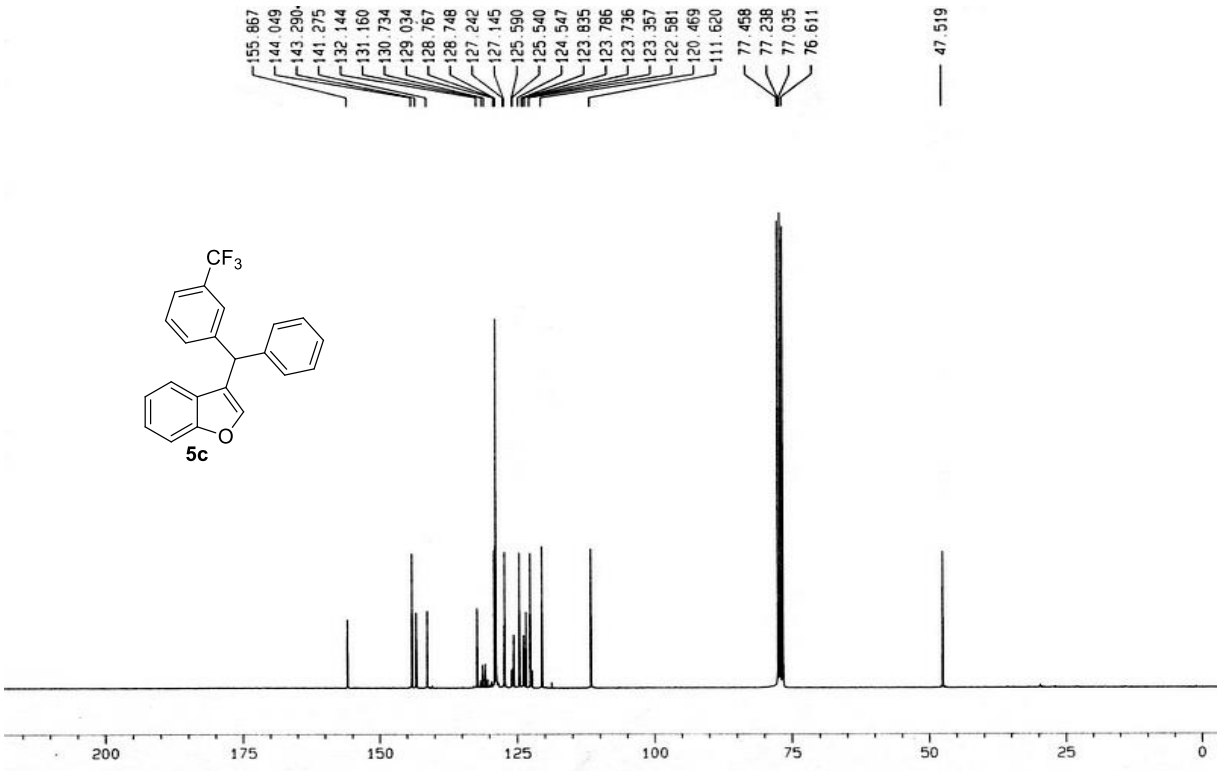
^{13}C NMR of 5b, $CDCl_3$, 75 MHz



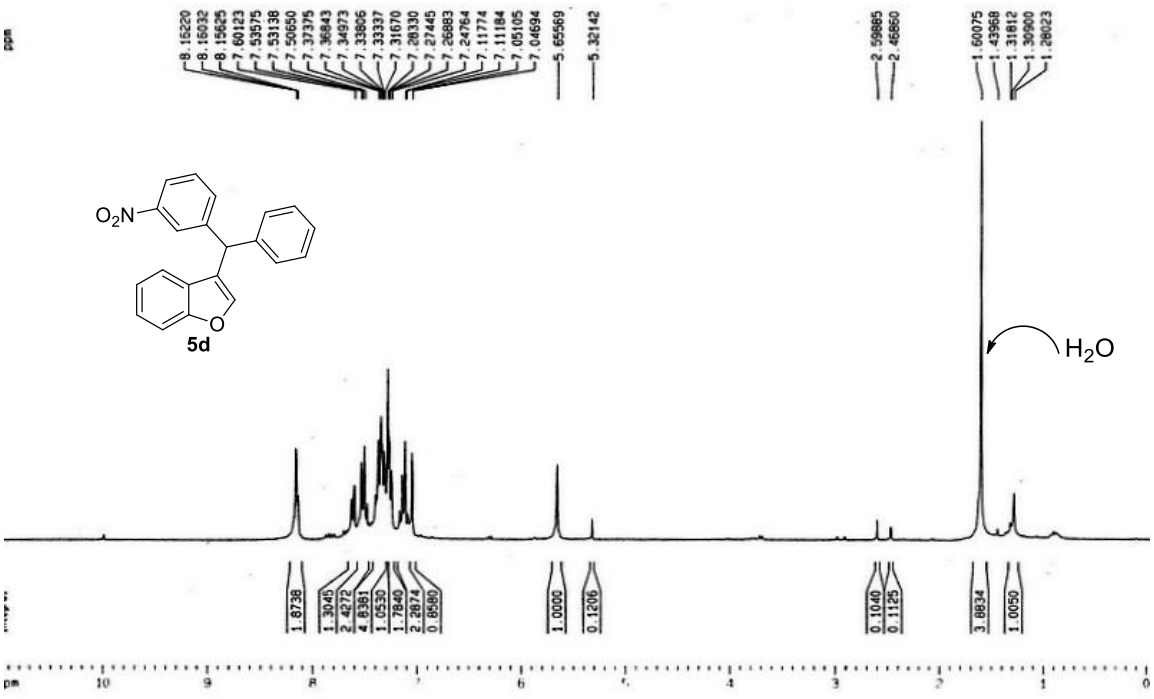
^{1}H NMR of 5c, $CDCl_3$, 300MHz



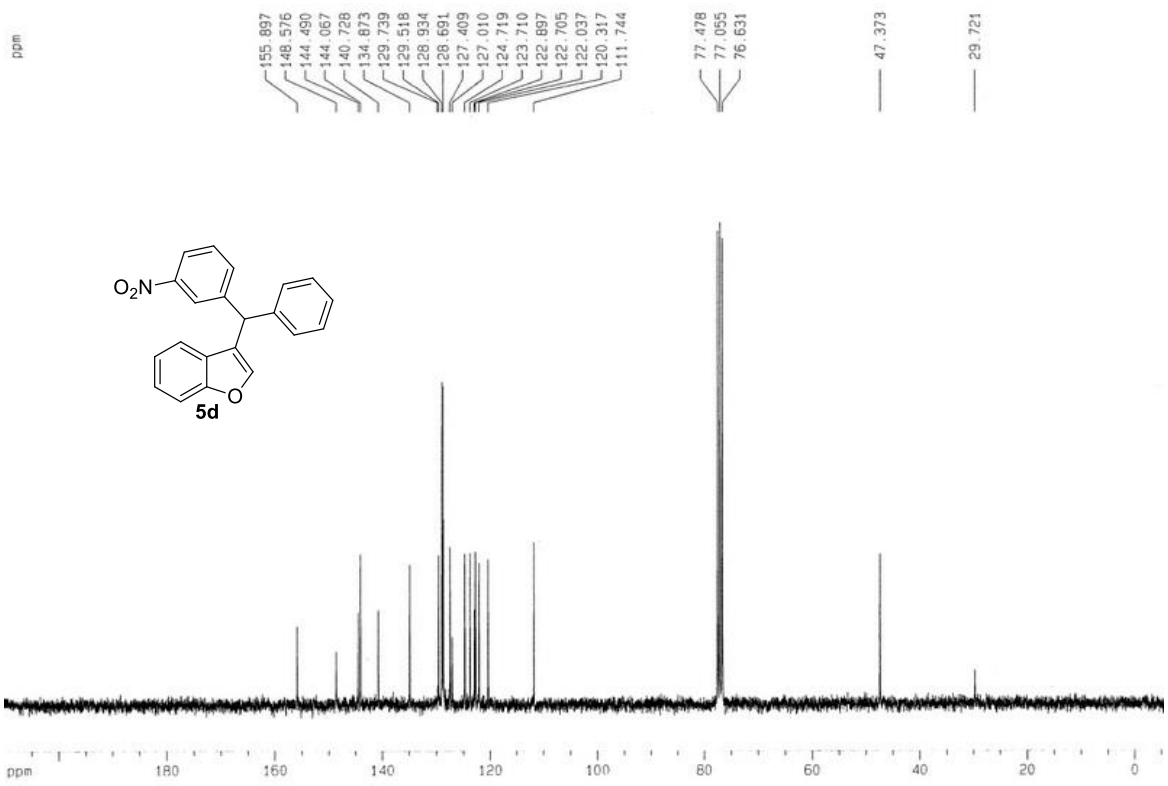
^{13}C NMR of 5c, $CDCl_3$, 75 MHz



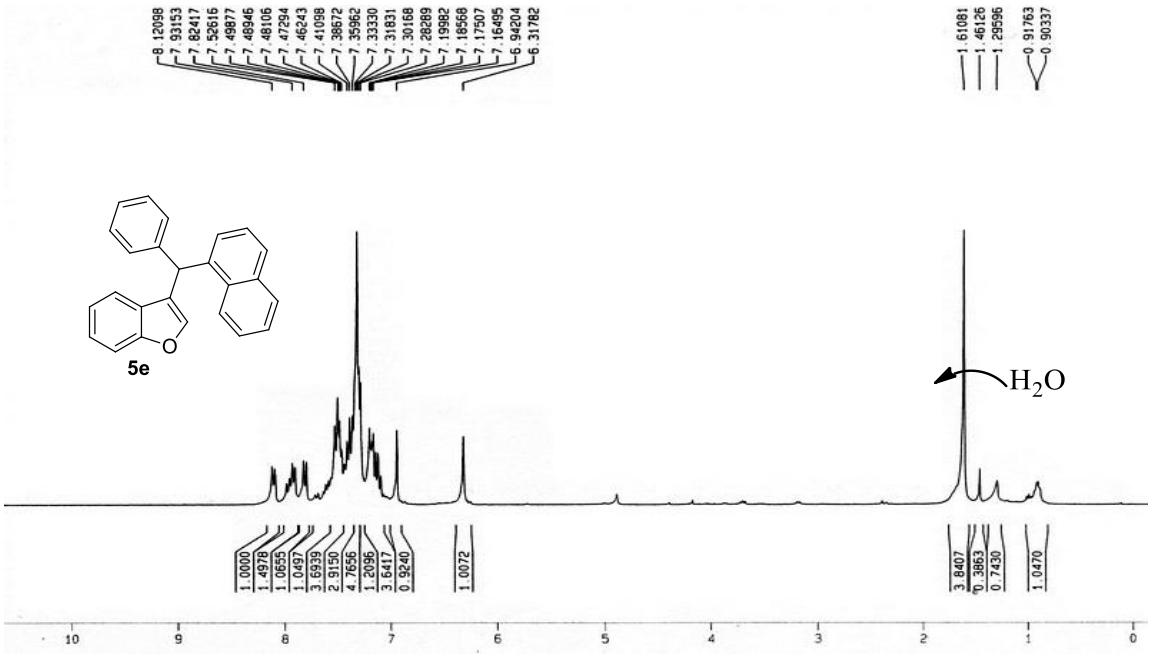
^{1}H NMR of 5d, $CDCl_3$, 300MHz



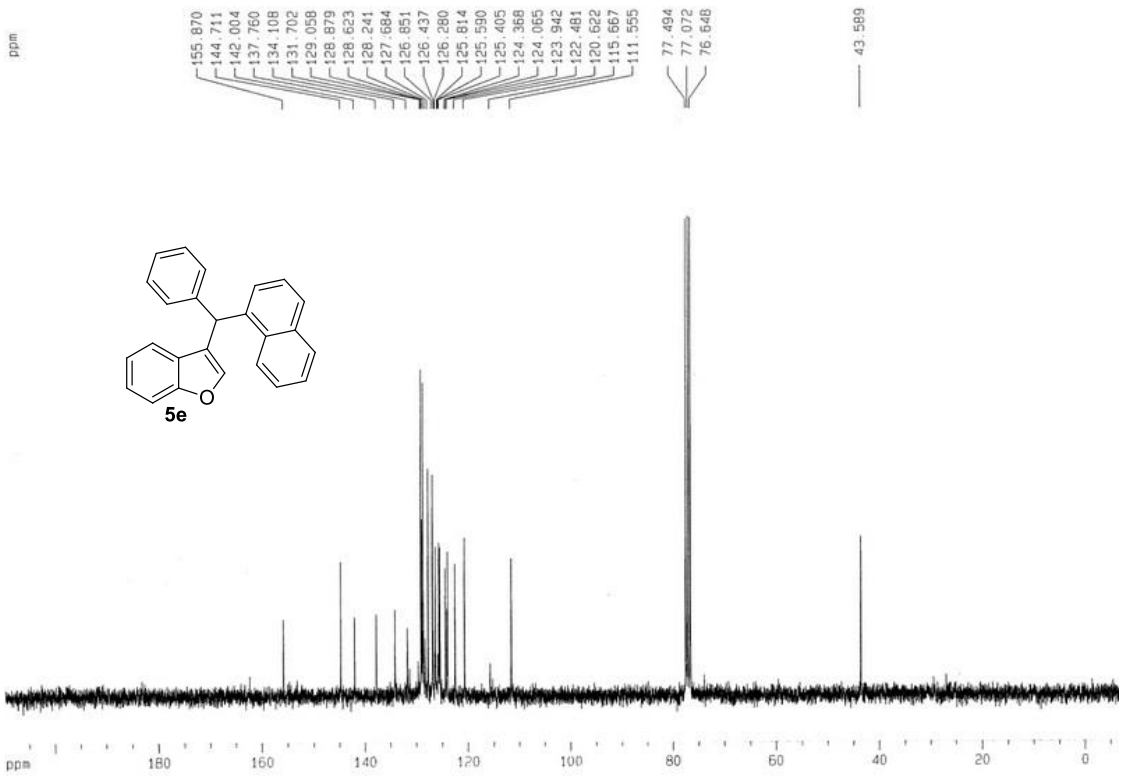
^{13}C NMR of 5d, $CDCl_3$, 75 MHz



^{1}H NMR of 5e, $CDCl_3$, 300MHz



^{13}C NMR of 5e, $CDCl_3$, 75 MHz



Chapter II

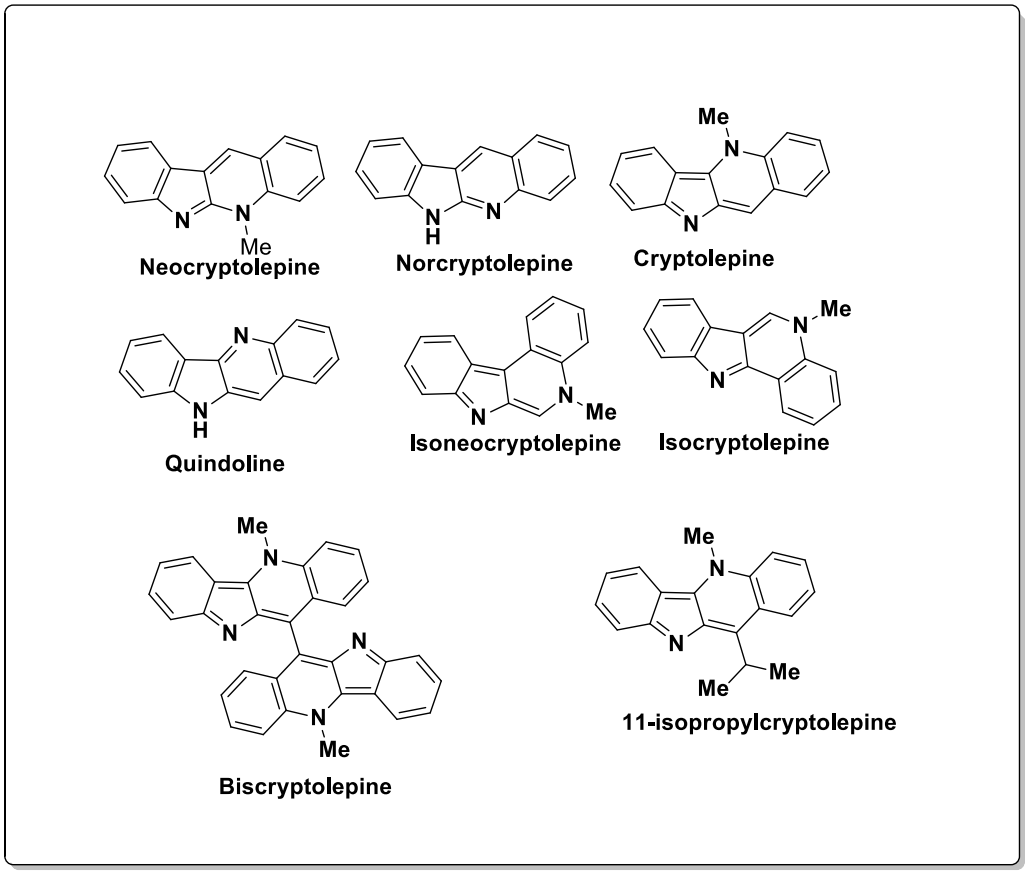
Efficient Two Steps Synthesis of Structurally Diverse Indolo[2,3-b]quinolines Derivatives

Chapter II

II.1. *Introduction:*

Structural motifs with tetracyclic indoloquinolines are privileged structures present in scaffolds of wide variety of natural alkaloids and bioactive compounds (**Fig 1**).[1] In recent past, these motifs drew major attention because of their promising biological activities and potent role in the medicinal chemistry, specially as DNA intercalating and antimalarial properties and many other important pharmacological properties.[2] As an example, 5-methylindolo[2,3-*b*]quinoline (neocryptolepine), is isolated from Cryptolepissanguinolenta is a traditional medicine, generally used to treat malaria in West African region.[3] Likewise, 6*H*-indolo[2,3-*b*]quinoline (Norcryptotackieine) was isolated from the leaves of Justicia betonica,[4] shows major pharmacological properties such as potent antiplasmodial, antiproliferative, and antitumor activities.[5]

Figure 1: Some bioactive heterocycles containing indoloquinoline skeleton.



Additionally, in recent years, indoloquinoline scaffolds were incorporated in the part of drug designing and synthesis of modern era.[6] As a result, because of their valuable roles in research over drug discovery, quite a few synthetic routes have been developed for the construction structures containing indolo[2,3-*b*]quinolone ring since last few years[7].

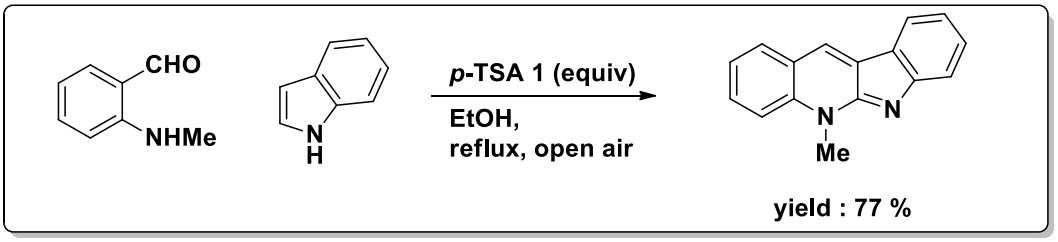
II. 2 . *A brief review on indolo[2,3-b]quinolines :*

It is due to the abundance of indolo[2,3-*b*]quinolines structural motifs in the natural bioactive compounds and severe medicinal importance of the moiety, it has been a part of major interest of the synthetic organic chemists to synthesis these compounds in diverse synthetic pathways.

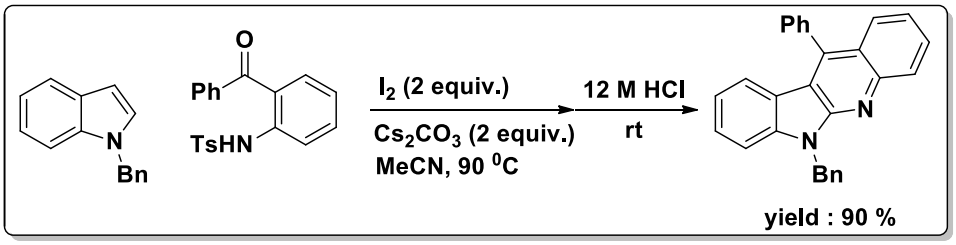
Among these recently developed methods, some of the methods are quite unique in the fabrication of their designs and, at the same time, rationality of their strategies.

Seidel's group were able to develop an easy method to synthesize indolo[2,3-*b*]quinolines by the condensation reation of indoles and 2-aminobenzaldehydes using TFA or *p*-TsOH as additives, under refluxing condition in ethanol. (**Scheme 1**)[8].

Scheme 1: Acid catalysed condensation between indoles and 2-aminobenzaldehydes.



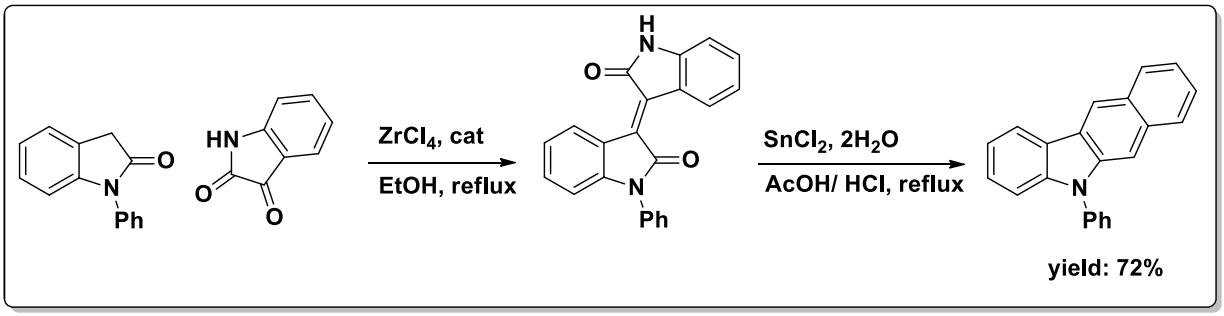
Liang et al. proposed a methodology for synthesis of indolo[2,3-*b*]quinolones throgh electrophilic **Scheme 2:** Substitution reaction of indoles with 1-(2-Tosylaminophenyl)ketones in metal-free condition**.**



substitution as well as amination reaction of indole with 1-(2- tosylaminophen-yl)ketones, in the presence of iodine and Cs_2CO_3. (**Scheme 2**)[9].

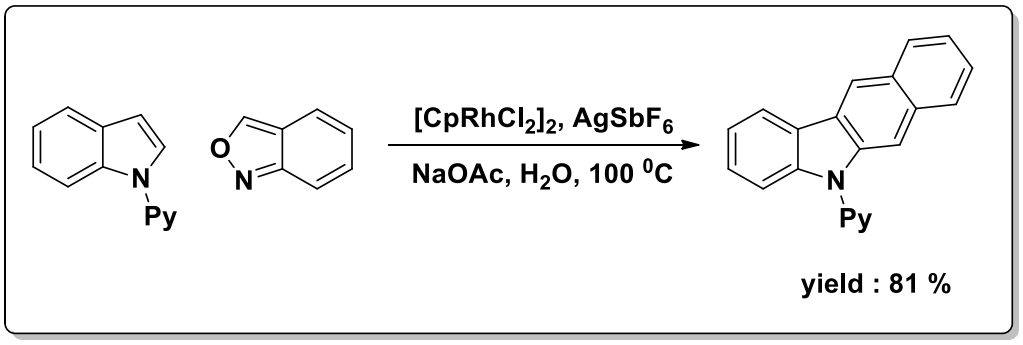
Yin *et al*. reported a method of synthesis of indolo[2,3-*b*]quinolines where isoindigo derivatives are used as substrate and $SnCl_2$ alongwith AcOH/HCl mixture under reflux contion are used to promote moderate to good yields (**Scheme 3)**[10].

Scheme 3: Preparation of 6*H*-Indolo[2,3-*b*]quinolines from Isoindigo derivatives.



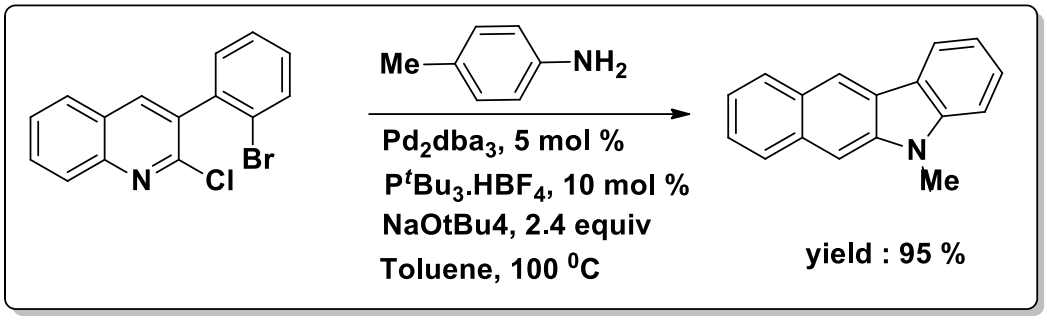
Wang's group described a method of synthesis of indoloquinoline by Rh(III)-catalyzed reation of indoles and isoxazoles and using $AgSbF_5$/NaOAc at 100 °C (**Scheme 4)**[11].

Scheme 4: Preparation of indoloquinoline by Rh(III)-catalyzed reaction of indoles and isoxazoles.



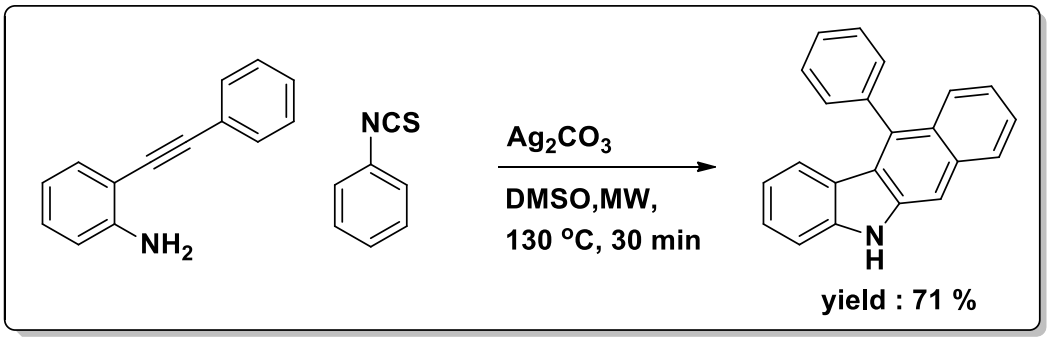
Langer et.al. developed a regioselective synthesis of two series of indolo[2,3-*b*]quinolines, namely 10*H*-indolo[3,2-*b*]quinolines and 6*H*-indolo[2,3-*b*]quinolines. This method proceeds in moderate to high yields through a chemoselective palladium catalyzed Suzuki reaction of 2,3-dihaloquinolines with 2-bromophenylboronic acid, followed by a double Buchwald-Hartwig C-N coupling (**Scheme 5)**[12].

Scheme 5: Synthesis of indolo[2,3-*b*]quinolines by sequential chemoselective Suzuki reaction followed by double C-N coupling.



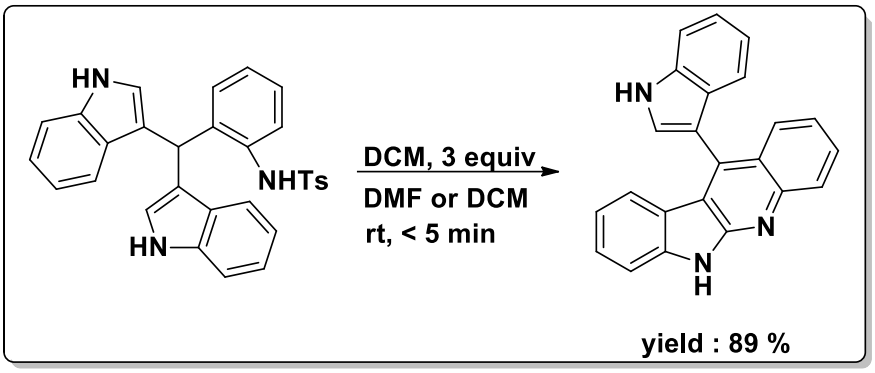
Patel et.al. developed a method of synthesis of indolo[2,3-*b*]quinolines where 2-(phenylethynyl)anilines and aryl isothiocynates reacts to obtain *in situ* generated *o*-alkynyl thioureas which is subjected to microwave assisted cascade cyclization using of Ag_2CO_3 to afford indoloquinolines. This method tolerates a wide range of functional groups thereby the producing a big array of indolo[2,3-*b*]quinolines derivatives in good to moderate yields (**Scheme 6)**[13].

Scheme 6: Production of Indolo[2,3-*b*]quinolines from 2-(Phenylethynyl)anilines and Aryl Isothiocynates under microwave irradiation.



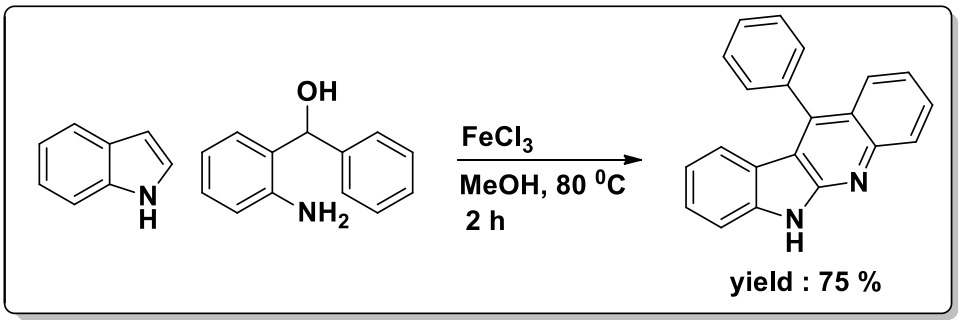
Lankapalli et. al. developed a diverse method where easily accessible 3,3' -diindolylmethanes (DIMs) with ortho-NHTosyl (NHTs) phenyl group were utilized to generate a variety of indolo[2,3-*b*]quinolones under 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ)-mediated oxidative conditions (**Scheme 7)**[14].

Scheme 7: Synthesis of Indolo[2,3-*b*]quinolones by Intramolecular C2−N Bond Formation with assistance of DDQ.



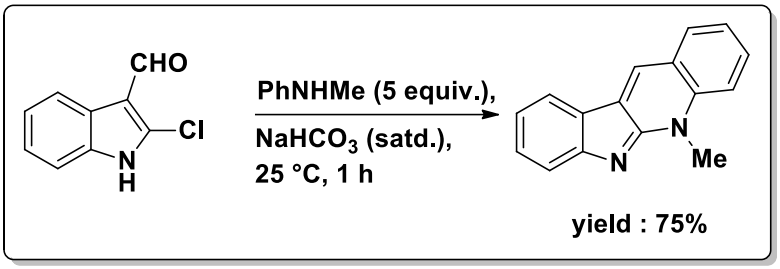
Wan & Wang and co-workers developed a facile method for the preparation of 6*H*-indolo[2,3-*b*]quinolines and other derivatives of neocryptolepine. The reaction method consists of substrates 2-amino-α-phenylbenzenemethanol and differently substituted indoles using easily available ferric trichloride, which promotes the target products with moderate to good yields (**Scheme 8)**[15].

Scheme 8: Synthesis of 6*H*-indolo[2,3-*b*]quinolines through the reaction of 2-amino-α-phenylbenzenemethanol with indoles**.**



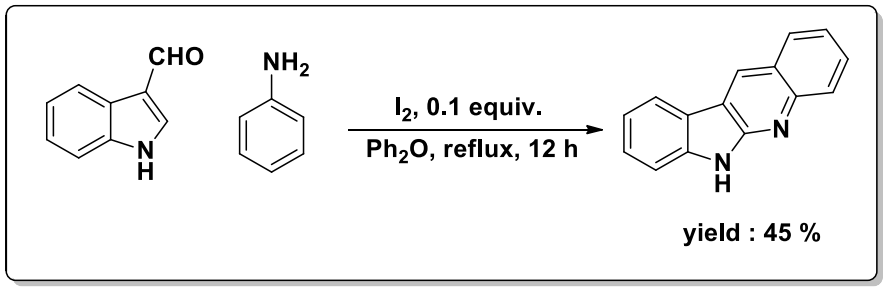
Followed by an earlier report by the group of Stoess, a upfront synthesis of neocryptolepine was reported in 2004 by Engqvist and Bergman. The key step is includes the condensation of 2-chloroindole-3-carbaldehyde with *N*-methylaniline for producing anilinoaldehyde, followed by in situ cyclization which finally furnished the natural product in good yield (**Scheme 9**)[16].

Scheme 9: Synthesis of neocryptolepine through the reaction of 2-chloroindole-3-carbaldehyde with *N*-methylaniline.



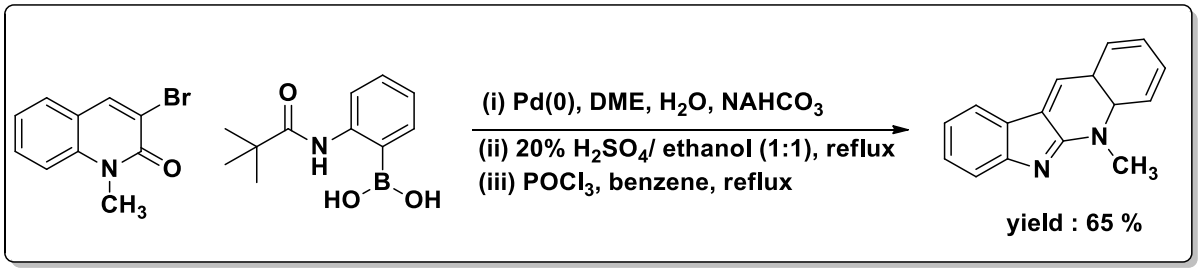
Tilve et.al described a novel one-pot method for synthetis of chain of 6*H*-indolo[2,3-*b*]-quinolines with different substituents on the quinolone ring. The method involves reaction of indole-3-carboxyaldehyde with aryl amines by using catalytic amount of iodine in refluxing diphenyl ether to afford indolo[2,3-*b*]quinolines. This synthetic approach provides a new route for the synthesis of polycyclic structures related to neocryptolepine (**Scheme 10)**[17].

Scheme 10: One-pot synthesis of indoloquinolines Using I_2 as a Catalyst.



Timári's group described a synthesis of neocryptolepine from the multistep reaction of 3-bromo-

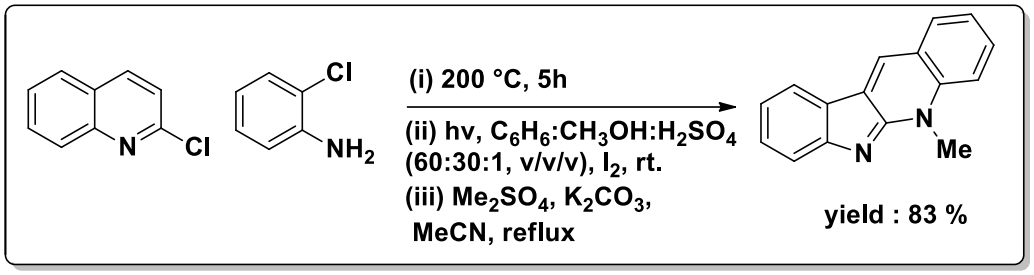
Scheme 11: Multistep synthesis of neocryptolepine from 3-bromo-1*H*-quinolin-2-one.



1*H*-quinolin-2-one with 2-(pivaloylamino)phenylboronic acid through Suzuki reaction thereby refluxing the product with (1:1) H_2SO_4/ ethanol mixture & finally treating of the product with $POCl_3$ for cyclization/ aromatization to lead the final product (**Scheme 11)**[18].

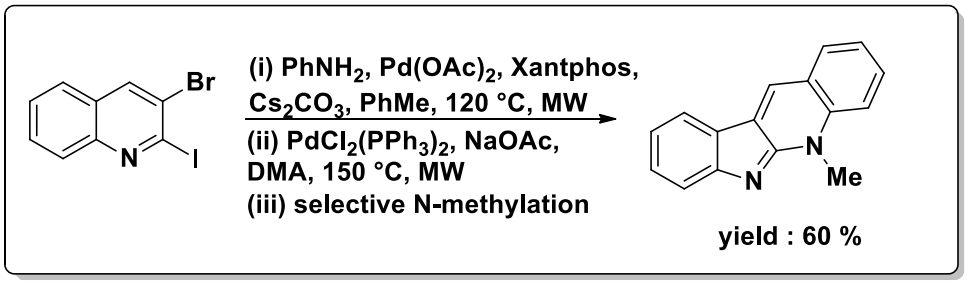
A method total synthesis of neocryptolepine has been reported by Mohan's group, which involve regioselective amination of the starting materials, 2-chloroquinoline with 2-chloroaniline. The key step involves photo-irradiation of intermediate product with ultra–violet light which leads to cyclization/aramatization of the key product. This classical procedure proved to be more effective, despite of the availability of new catalysts for this reaction (**Scheme 12)**[19].

Scheme 12: Multistep synthesis of neocryptolepine through heteroatom directed photoannulation.



Bóganyi and Kámán reported a strategy which describes regioselective Buchwald–Hartwig amination of the quinoline with aniline using Xantphos-$Pd(OAc)_2$ catalysis under microwave assisted conditions which followed by a $PdCl_2(PPh_3)_2$-catalyzed intramolecular Heck-coupling reaction of the intermediate which leads to ring-closed to afford indoloquinoline moiety after double bond rearrangement. Finally, N-methylation of the product produces neocryptolepine (**Scheme 13)**[20].

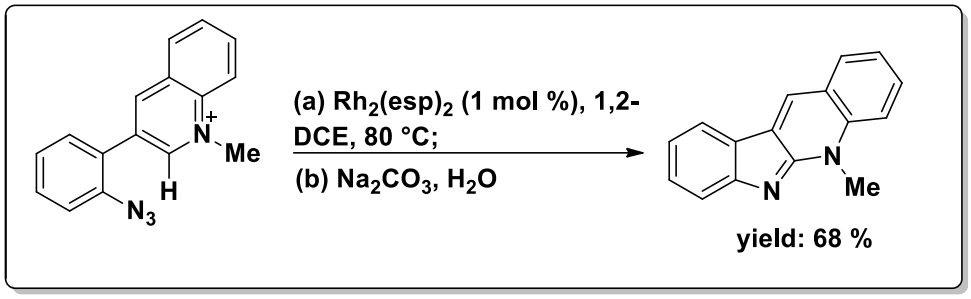
Scheme 13: Multistep synthesis of neocryptolepine through microwave assisted regioselective amination followed by cyclization.



Driver's group reported synthesis of different heterocycles by Rh_2^{II}-catalyst which shows controlled breakdown of aryl and vinyl azides. The research group established that reaction of azide with $[Rh_2(esp)_2]$ in dichloroethane solvent at 80 °C (esp = α,α,α',α'-tetramethyl-1,3-

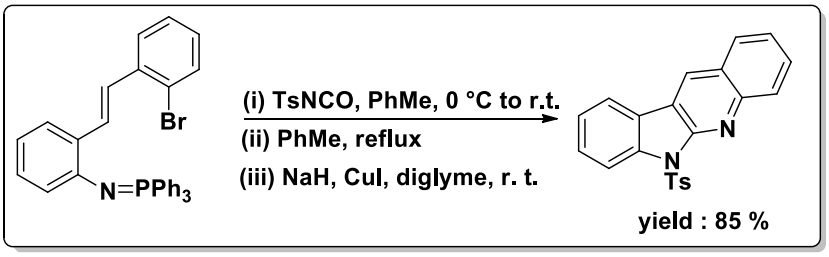
benzenedipropionate) to generate neocryptolepine as only regioisomer in 68% yield which is generated.after alkalification of quinolinium derivative by Na_2CO_3 (**Scheme 14)**[21].

Scheme 14: Rh_2^{II}-catalyzed synthesis of neocryptolepine through controlled decomposition of aryl azides



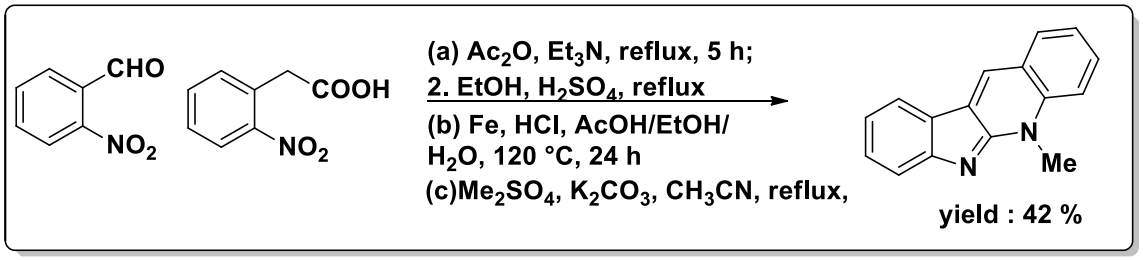
Molina et al. employed aza-Wittig electrocyclic ring-closure strategy for an improved synthesis of neocryptolepine. When iminophosphorane is subjected to aza-Wittig type reaction alongwith tosyl isocyanate generated carbodiimide, which is again heated in refluxing toluene to produce 2-amino-3-arylquinoline derivative. This when treated with NaH, and CuI, gives the complete carbon framework producing indolo[2,3- *b*]quinolone upto 85 % yield. (**Scheme 15)**[22].

Scheme 15: Iminophosphorane-Mediated Synthesis of indoloquinoline framework.



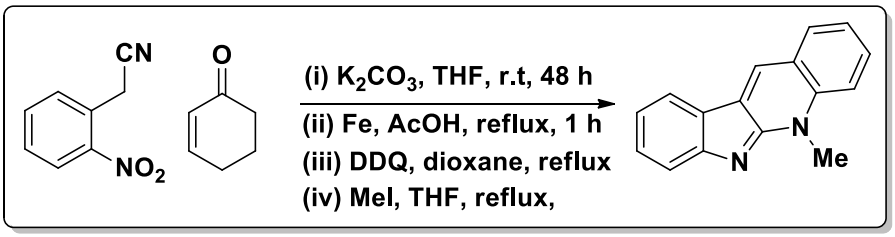
Tilve. et. al. describes an competent total synthesis of neocryptolepine, which comprises of three steps and gave 42 % yield. There are three major steps involved, Perkin reaction followed by tandem double reduction & cyclization and finally regioselective N-methylation (**Scheme 16)**[23].

Scheme 16: Synthesis of neocryptolepine double reductive cyclization.



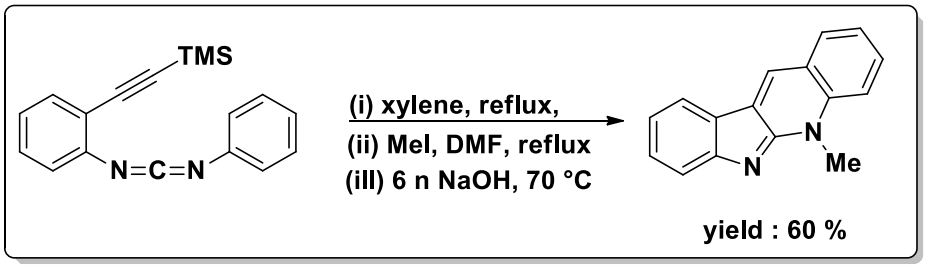
Basavaiah and Mallikarjuna Reddy proposed a synthetic approach to afford pyrido[2,3-*b*]indole derivatives using Baylis–Hillman acetates. The stategy includes monoalkylation of suitably substituted 2-nitroarylacetonitriles by BH-acetates, followed by nitro group reduction and sequential generation of the five- and six-membered closed rings structures, which happens one-pot method. (**Scheme 17)**[24].

Scheme 17: One-pot synthesis of neocryptolepine using Baylis–Hillman acetates.



The group of Pieters, one of the research teams devised a synthetic methodology of the natural product neocryptolepine, which is proven to be beneficial for the production of both benzenoid rings (**Scheme 18)**[25].

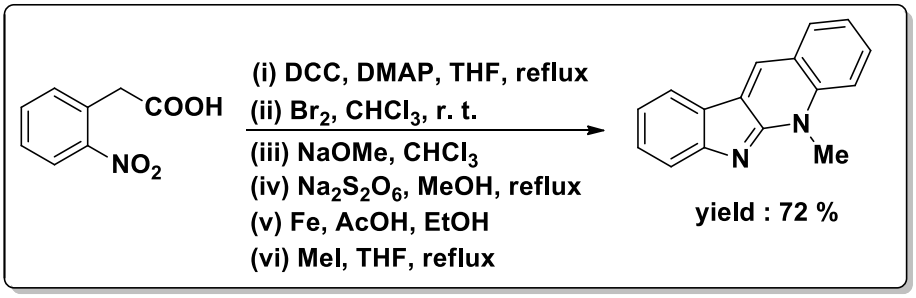
Scheme 18: Biradical Cyclization of Carbodiimides to 11-Trimethylsilyl-6*H*-indolo[2,3-*b*]quinolines



Ho and Jou described a method for total synthesis of neocryptolepine. Ortho-nitrophenylacetic acid and dicyclohexyl carbodiimide were selected as starting materials to avail 1,3-bis(2-nitrophenyl)-

propan-2-one for which bromination furnished bromo ketone, which upon Favorskii rearrangement, which was done by treating with NaOMe, produced methyl ester. The reduction of nitro moieties with iron-powder-mediated in hot AcOH, produced quinindoline, which upon N-methylation finally lead to neocryptolepine (**Scheme 19)**[26].

Scheme 19 : Synthesis of neocryptolepine using Favorskii reaction followed by in situ reduction/ cyclization method.



II. 3. Summary:

A number of organic synthetic and extraction methodologies are reported for the synthesis of the naturally occurring alkaloid neocryptolepine or indolo[2,3-*b*]quinoline moieties, due to their significant applications in drug discovery research and hence becomes the point of interest of the synthetic organic chemists. Among these strategies, few appear to be quite efficient and diverse in nature from the synthetic point of view in the development of their designs and efficacy of their approaches. However most of the approaches are suffering from lack of synthetic diversity, compulsion of using pre functionalized starting materials, low yield of the product, complex reaction assembly, easiness of the method, number of the steps involved, inconvenient general approach, use of expensive and excess of starting materials, use of toxic reagents and commercial viability of the strategies.

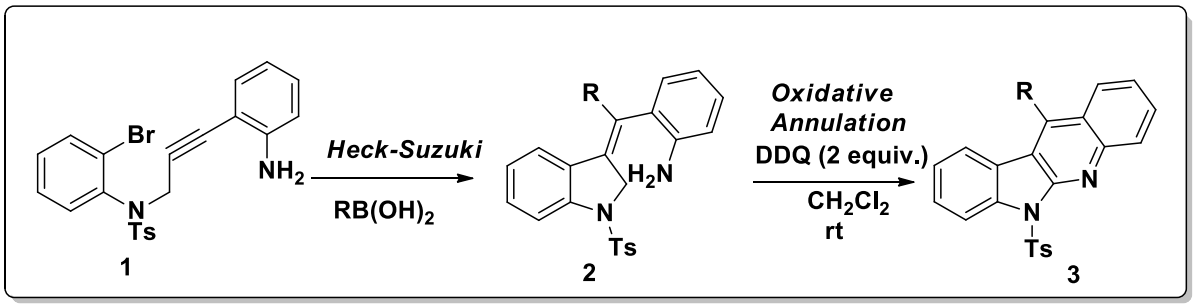
Seeing the potential in medicinal science and vast pharmaceutical uses of indolo[2,3-*b*]quinolines derivatives, the development of concrete, direct, flexible and resourceful synthetic methodologies are still in demand. The construction of pharmaceutically significant molecular frameworks involving novel synthetic approaches that are selective, atom-efficient and environmentally tolerant is the principal requirement to synthetic chemists of the new era.

II. 4. Present work:

Indolo[2,3-*b*]quinoline types compounds are quite significant class of which are ubiquitously present in nature as naturally occurring alkaloids which are proven to be potentially highly beneficial in medicinal chemistry and hence synthesis of these type of organic moieties are important research topic and draw a major point of interest as a synthetic organic chemist. In the course of our contemporary studies towards the synthesis of polycyclic heterocycles and carbocycles through annulations reactions,[27] in very recent times, we have implemented a unique and competent approach which involves the synthesis of polycyclic heterocycles comprising of palladium-catalyzed intramolecular carbopalladation/Suzuki coupling and successive cycloisomerisation under mild conditions.

In prolongation to these investigations[9e, f, g, h], first we synthesized 3-indoline derivative containing *ortho*-amino group on the aryl ring of methylene moiety as a key product by means of intra-molecular palladium-catalyzed domino carbopalladation-Suzuki coupling of the starting materials, 2-halo-*N* propargylanilide derivatives with arylboronic acids. We expected that key compound may undergo oxidative cross dehydrogenative coupling (CDC) with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) between allylic Csp^3-H of indoline ring with free $–NH_2$ group. In a recent past, it has been established that DDQ can act as a resourceful metal free oxidant for CDC type carbon carbon bond formation reactions[28]. Whereas the development of C–N bond through DDQ-mediated cross-dehydrogenative couplings (CDC) are comparatively infrequent until some findings in available in recent past[29].

Scheme 20 : Our strategy for the synthesis of indolo[2,3-*b*]quinoline derivatives**.**



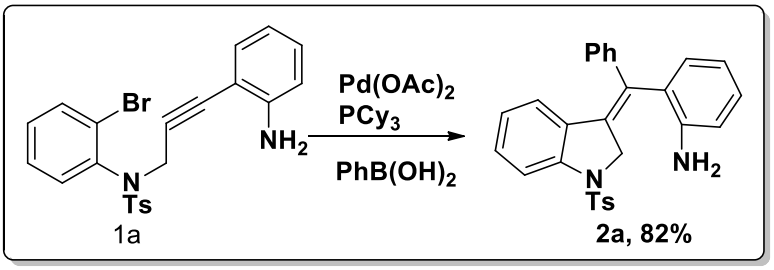
Thus, the current strategy of synthesis of indolo[2,3-*b*]quinolines may claim a very rational, useful, competitive and interesting in the contemporary research of organic chemistry. Hence, as a result

of our ongoing study, in this communication, we have documented a novel, proficient and general strategy for the synthesis of variously substituted indolo[2,3-*b*]quinolines derivatives in a diverse way through two stages domino reaction (**Scheme 20**).

II.5. Result and Discussion:

Our general approach initiated with the synthesis of 3-indoline derivative **2a** by palladium-catalyzed domino Heck-Suzuki coupling of 2-bromo- *N*-propargylanilide **1a** with phenylboronic acid rendering to our recently established method[9e, f]. The reaction of compound **1a** and phenylboronic acid was executed using 5 mol% of $Pd(OAc)_2$, 10 mol% of tricyclohexylphosphine (PCy_3) at 75 °C in the presence of 2.5 M K_2CO_3, to construct the desired 3-substituted indoline derivative **2a** in 82% yield (**Scheme 21**). The reaction proceeds through an intramolecular *syn*-carbopalladation method via a 5-*exo-dig* cyclisation pathway in preference to 6-*endo-dig* method of cyclisation with the alkyne unit to give a σ-alkylpalladium(II) intermediate, and a successive intermolecular Suzuki coupling with phenylboronic acid derivatives produced the anticipated product **2a** in a stereoselective manner. The reason for selecting the pathway of the 5-*exo-dig* cyclisation over 6-*endo-dig* cyclisation process in this reaction may be explained by the theory of lower energy transition state in case of 5-*exo-dig* cyclisation as bulky palladium complex furnishes at the less hindered side of the product, and chain length also contributes a major role for this mode of cyclisation (**Scheme 21).** The reaction was afforded by 0.5 mmol of **1a**, 0.75 mmol of phenylboronic acid, 0.01 mmol of $Pd(OAc)_2$ in 1 mL of aq 2.5 M K_2CO_3 solution, 1 mL of ethanol and 1 mL of toluene at 70-75° C under Ar atmosphere.

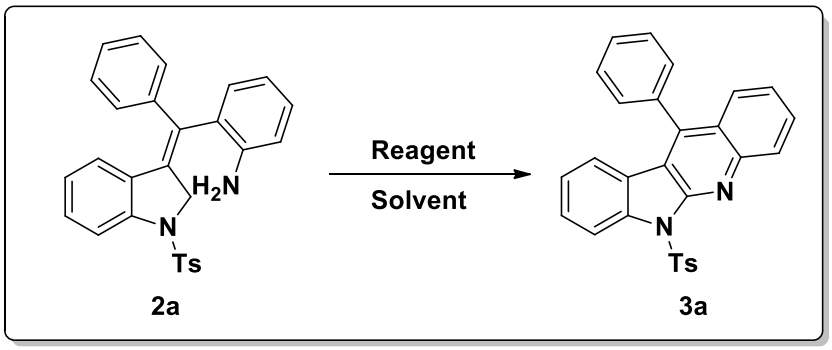
Scheme 21 : Preparation of Substrate 2a by Heck-Suzuki coupling[a]



Once the desired substrate **2a** was prepared, we tried to optimize an appropriate reaction condition for the oxidative crossdehydrogenative coupling (CDC) of allylic Csp^3-H of indoline ring with $–NH_2$ group to complete the synthesis of indolo[2,3-*b*]quinoline **3a** using different oxidizing agents, solvents, and temperature. Bearing in mind the proficiency of DDQ for metal free oxidant in CDC

reactions, first the reaction was carried out the intramolecular oxidative C–H amination of **2a** in the presence of DDQ (1 equiv). In this course of reaction substrate **2a** found to be promptly converted into the mixture of compounds at room temperature. We concluded that because of the inadequate amount of DDQ, a mixture of compounds was formed in addition to some unreacted starting materials. Next we attempted the said reaction with 2 equiv. of DDQ and it was a pleasure to observe that the starting compound **2a** was completely transformed into **3a** at room temperature in quantitative yield within 1 h (**Table 1, entry 1**). Some other solvents like 1,2-dichloroethane and nitromethane also shown good results, but found to produce comparatively lower yields of **3a**, in 90% and 93%, respectively (**Table 1**, **entries 3 and 4**). In continued study, the competency of some other common oxidizing agents, such as TBHP, CAN, PIDA and TEMPO, were verified for this process using **2a** in DCM at room temperature. Consequently it was observed that TBHP, PIDA and TEMPO (**Table 1**, **entries 4, 6 and 7**) are not suitable to work under these very reaction conditions, while CAN may produce 85% yield (**Table 1, entry 5**). Though, the method of cycloammination reaction with DDQ along with the combination of TEMPO (Tetramethyl morphline *N*-Oxide) as a co-oxidant (**Table 1, entry 8**) also perfomed efficiently and furnished the desired product quntitatively. Hence, finally DDQ (2 equiv) in DCM at room temperature was adopted as the standard reaction condition for the additional study. The reaction was afforded by adding **2a** (0.3 mmol), reagents (0.6 mmol), solvent (2 mL).

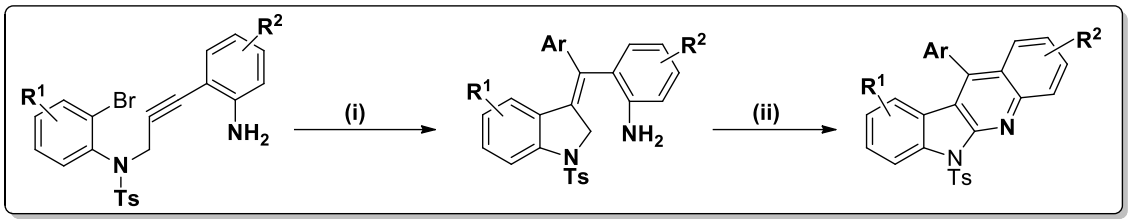
Table 1. Optimization of Reaction Conditions for the Synthesis of 3a.

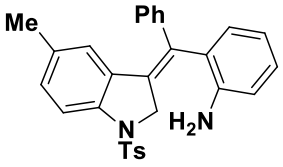
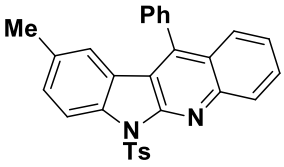
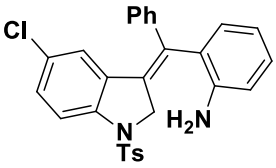
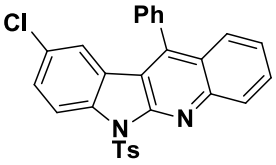
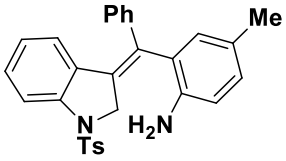
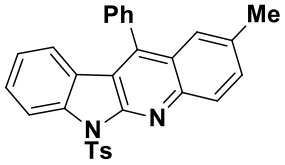
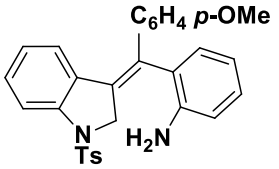
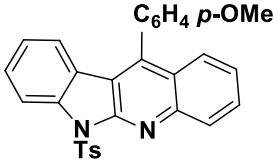
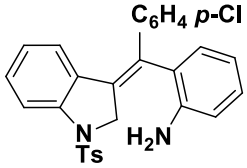
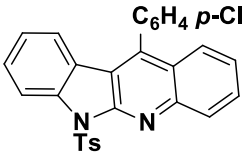


Entry	Reagent	Solvent	T (^{0}C)	Time (h)	Yield (%)
1	DDQ (2 equiv.)	DCM	RT	1	quant
2	DDQ (2 equiv.)	1,2-DCE	RT	1.5	90
3	DDQ (2 equiv.)	CH_3NO_2	RT	1	93
4	CAN (2 equiv.)	DCM	RT	1.5	85
5	TBHP (2 equiv.)	DCM	RT	3	n.r
6	PIDA (2 equiv.)	DCM	RT	3	n.r.
7	TEMPO (2 equiv.)	DCM	RT	3	n.r
8	DDQ + TEMPO (2 +2 equiv.)	DCM	RT	1	quant

We envisioned to synthesize a series of indolo[2,3-*b*]quinolines following the aforesaid two steps reactions, to validate the generality of this strategy. The preparations of the intermediate substrates **2b**–**2f** were carried out by domino Heck-Suzuki coupling in high yields (79% to 90%) (**Table 2**). Substrates containing different groups, such as electron-donating –Me and weakly electron withdrawing –Cl on the 2-bromo-*N*-propargylanilide ring, experienced smooth reaction in excellent yields, 83% and 79%, respectively (**Table 2, entries 2b–2c**). Likewise, phenylboronic acids containing –OMe and –Cl were well accepted under the reaction conditions, (**Scheme 2, entries 2e**–**2f**) and gave the desired products in good yields, 85% and 81%, respectively. Substrate **2d**, in which –Me group is present on the aryl ring of 2-alkynyl aniline moiety, afforded **2d** in 90% yield (Table 2). In the next step, the 3-indoline derivatives **2b**–**2f** were treated with DDQ-mediated oxidative cycloamination process as described for the synthesis of **3a**. To our pleasure, it was observed that the substrates **2b**–**2e** swiftly transformed into the desired products **3b**–**3e** at room temperature in quantitative yield, and the substrate **2f** furnished 92% yield of the desired product **3f** (**Table 2**). Thus, it give the idea that there are no substantial electronic effect of the substituent on the aryl ring on the olefinic motif during the formation of C–N bond.

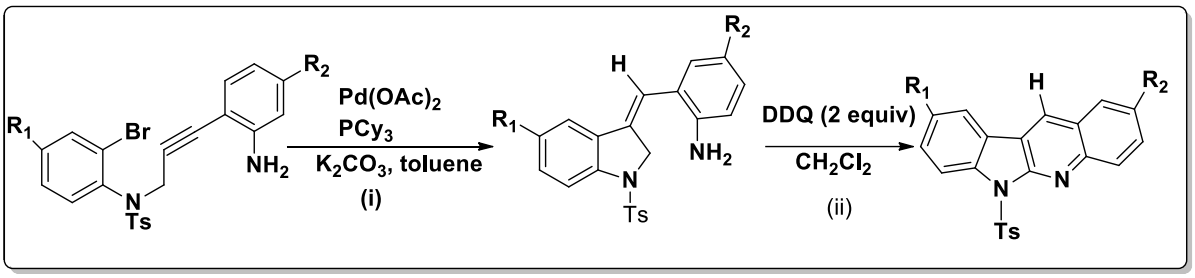
Table 2. Scope of the synthesis of indolo[2,3-*b*]quinolines via Heck-Suzuki and DDQ mediated C-H amination.



Entry	Substrates	3-indolines	Indolo[2,3-*b*]quinolines
1	R^1 = Me, R = H, Ar = Ph	 2b, 3 h, 83 %	 3b, 1 h, quant
2	R^1 = Cl, R = H, Ar = Ph	 2c, 3 h, 79 %	 3c, 1 h, quant
3	R^1 =H, R = Me, Ar = Ph	 2d, 3 h, 90 %	 3d, 1 h, quant
4	R^1 = H, R = H, Ar = C_6H_4 *p*-OMe	 2e, 3 h, 85 %	 3e, 1 h, quant
5	R^1 = H, R = H, Ar = C_6H_4 *p*-Cl	 2f, 3 h, 81 %	 3f, 1 h, 92 %

In the next step, in order to expand the synthetic usefulness of this strategy, we arranged to prepare the substrates **2g** and **2h** by Pd-catalyzed reductive carobopalladation of 2-bromo-N-propergylanilide derivatives using $Pd(OAC)_2/PCy_3$, in the presence of 2.5 M K_2CO_3 in toluene ethanol mixture as described in our previous method. The desired 3-indoline derivatives **2g** and **2h** were acquired in 89% and 88%, respectively. Finally, when these substrates were subjected to 2 equiv of DDQ in DCM at room temperature, these furnished the desired products **3g** and **3h** in 82% and 75% yields, respectively (**Scheme 22**). The reaction was afforded by the reaction conditions, (i) **1a**, **1b** and **1i** (0.5 mmol, 1 equiv.), $Pd(OAc)_2$ (0.1 equiv.), PCy_3 (0.2 equiv.) and 1 mL of aq.K_2CO_3 (2.5 M) solution, 1mL of ethanol and 1 mL of toluene, 70-75 °C, 3h,Argon atm; (ii) **2g- 2i** (0.5 mmol, 1 equiv.), DDQ (1 mmol, 2 equiv.), 2 mL of CH_2Cl_2 , room temperature.

Scheme 22: Substrates Scope for Carbopalladation and Cycloamination**.**

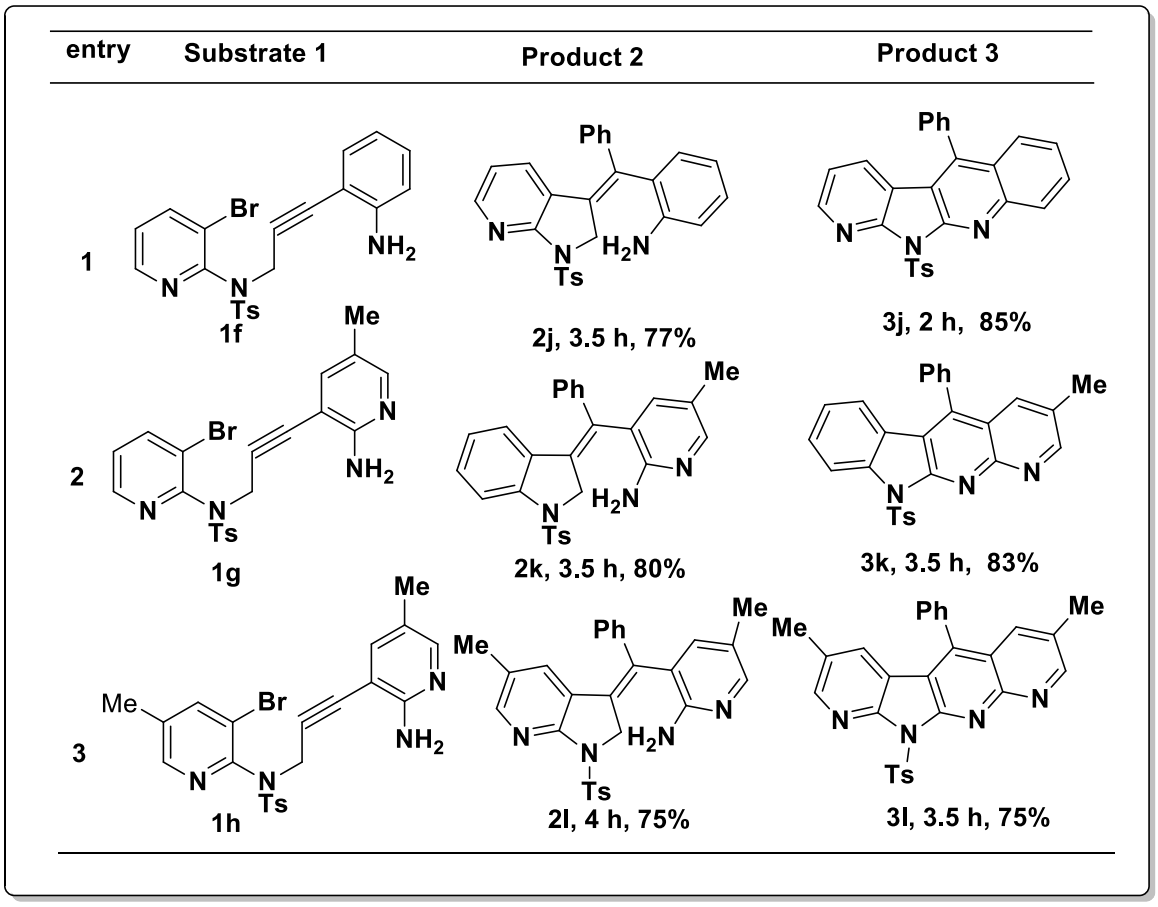


1a, R^1 = H, R^2 = H	**2g, 3 h, 89%**	**3g, 2 h, 82%**
1b, R^1 = Me, R^2 = H	**2h, 3 h, 91%**	**3h, 2 h, 81%**
1e, R^1 = H, R^2 = Cl	**2i, 3 h, 88 %**	**3i, 2.5 h, 75%**

In conclusion, to make this scheme even more general and flexible, we tried to incorporate additional nitrogen atoms into both of the rings at two ends of the tetracyclic system; the results are demonstrated in (**Scheme 23**). Likewise, 3-indoline derivative containing 2-amino pyridine ring for the formation of new (**Scheme 23**, **2j**) pharmaceutically active indolo[2,3-*b*]naphthyridine **3j** in 83% yield. Lastly, we were satisfied to find that *aza*-indoline tethered 2-amino pyridine derivative **2k** afforded the hitherto unknown tetracyclic *aza*-indolo[2,3-*b*]naphthyridine **3k** in 75% yield. In the same context, it is important to keep in mind that, as indolo[2,3-*b*]quinolines acted as DNA-intercalator, the development of the synthesis of these *aza*-heterocyclic ring systems would be highly promising as well as attractive in order to assemble a library of new tetracyclic framework

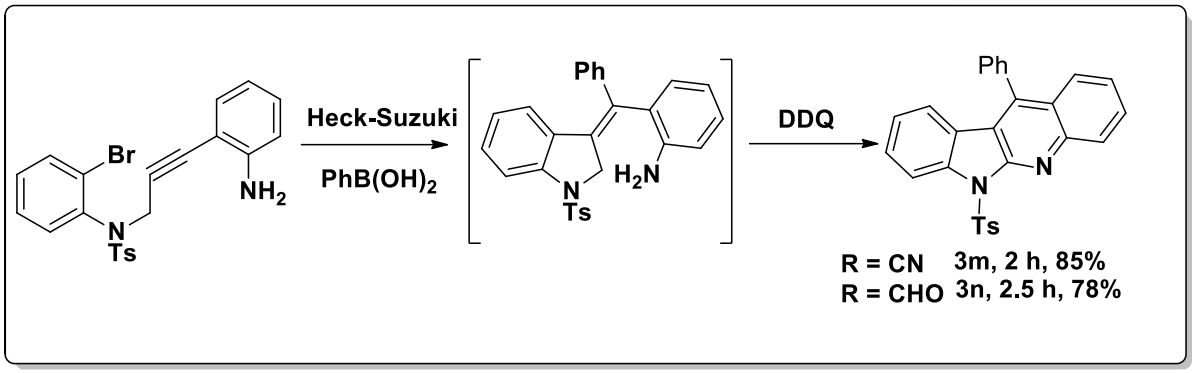
compounds. The reaction was afforded by the reaction condition (i) Compound **1** (0.3 mmol), $PhB(OH)_2$(0.45 mmol), $Pd(OAc)_2$ (0.015 mmol), PCy_3 (0.03 mmol), 2.5 M K_2CO_3 (1 mL), 2 mL 75 °C. (ii) Compound **2** (0.2 mmol), DDQ (0.4 mmol), CH_2Cl_2 (2 mL), rt.

Scheme 23: Synthesis of *aza*-indolo[2,3-*b*]quinolones.



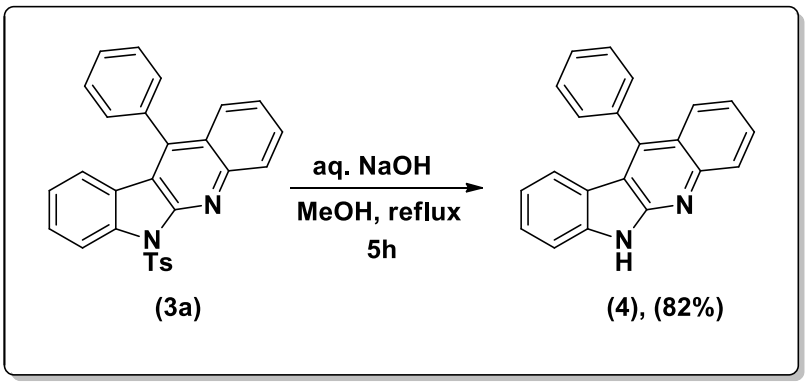
Even though, the Heck Suzuki reaction in the most of the cases produce a unmixed reaction product, but in this case we have observed that the product of Heck-Suzuki coupling reaction of aryllboronic acid bearing strong electron withdrawing groups such as –CHO and –CN, afforded a non-separable mixture. To sidestep the ungainly purification of these compounds, the crude products were treated directly with DDQ, as described in (**Scheme 25)**. To our pleasure, the desired products were also obtained in high yields in the two steps, such as **3l** and **3m**, in 74% and 71%, respectively. . The reaction was afforded by the reaction condition i) **1a** (0.3 mmol), $PhB(OH)_2$ (0.45 mmol), $Pd(OAc)_2$ (0.015mmol), PCy_3 (0.03 mmol), K_2CO_3 (2.5 M, 1mL), 75 ^oC, 3h. Ii) DDQ (0.6 mmol), CH_2Cl_2(2 mL), rt. [b]Two step yields.

Scheme 24: Synthesis of Indoloquinoline without Isolation of Intermediate**.**



Moreover, as the natural products do not contain any protecting groups, hence, detosylation of **3a,** was also attempted in the presence of dil NaOH solution and methanol under reflux. Gratifyingly, the detosylated product **4** was obtained in 82% yield (**Scheme 25**).

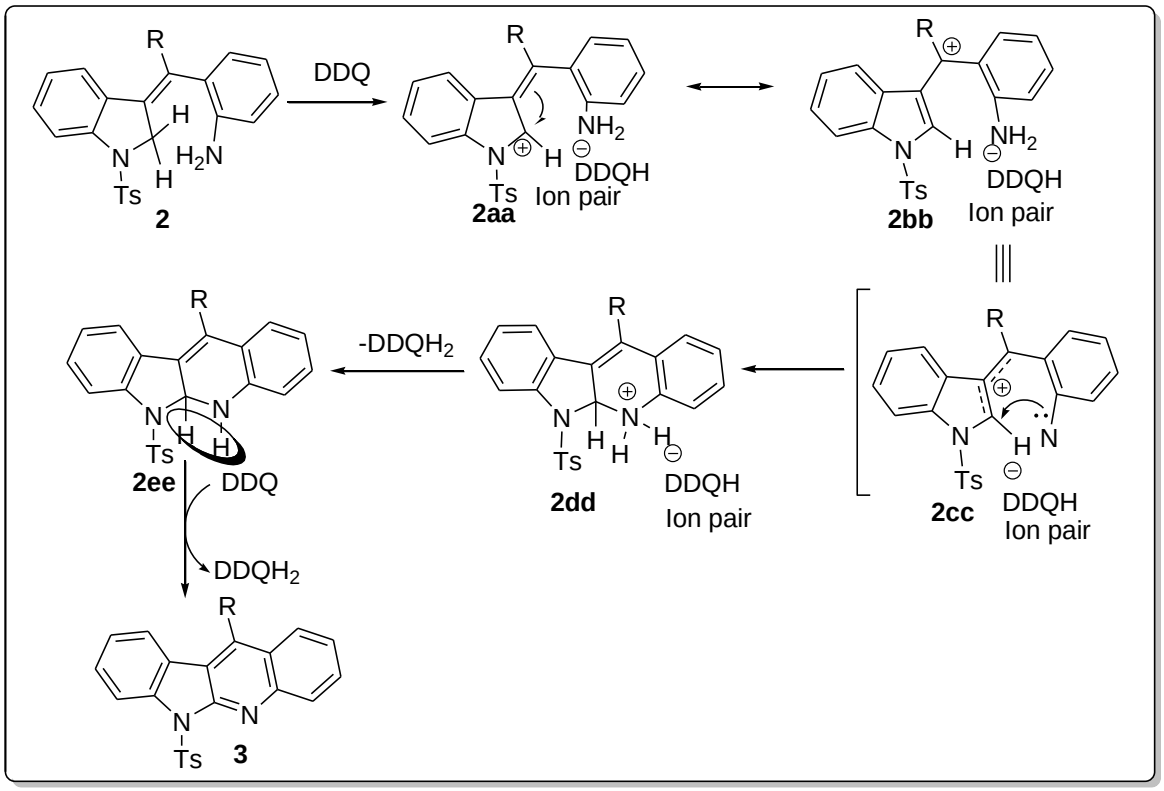
Scheme 25: Detosylation of indolo[2,3-*b*]quinolone 3a**.**



The mechanism of domino Heck-Suzuki/reductive carbopalladtion has been demonstrated already in our earlier reports. Depending upon of our experimental results and considering the previous literature[30], a plausible mechanism for the DDQ mediated oxidative C–H amination is outlined in **Scheme 25**. Various mechanistic pathways have been hypothesised in the literatures for the DDQ mediated oxidation depending on substrates and reaction conditions. The most popular and straight mechanism is initial one step hydride transfer from the substrate to DDQ and as a result carbocation intermediated is formed. Another mechanistic pathways is initial electron transfer

from the substrates to DDQ to generate the radical cation of the substrates. DDQ mediated radical pathway is generally established by the method of inhibition of reaction by a radical scavenger (**Scheme 26**)[31], for which we found that the radical scavanger, TEMPO (2 equiv) had no effect on the DDQ mediated dehydrogenative cycloamination process, when in the present reaction system (**Table 1, entry 8**). Thus, we draw the conclusion that the activation of allylic sp^3 C–H bond might be initiated through an hydride ion transfer mechanism from the substrate **2** to DDQ thereby formation of an allylic carbocation **2aa**/$DDQH^-$ ion pair. The allylic carbocation intermediate **2aa** is stabilized by resonance and furnished a benzylic cation **2bb**. In the next step cycloamination step was carried out by intramolecular nucleophilic attack of -NH_2 group to the allylic cationic centre resulting dihydropyridinium ion intermediate **2dd**. Finally, deprotonation of the substrate **2dd** by $DDQH^-$ furnished dihyropyridine intermediate **2ee** with simultaneous formation of DDQH2. As a conclusive step, hydride transfer from **2ee** to DDQ and subsequent deprotonation leads to the desired indolo[2,3-*b*]quinolone derivative **3**.

Scheme 26: Proposed mechanism for DDQ mediated cycloamination**.**



II. 6. Conclusion:

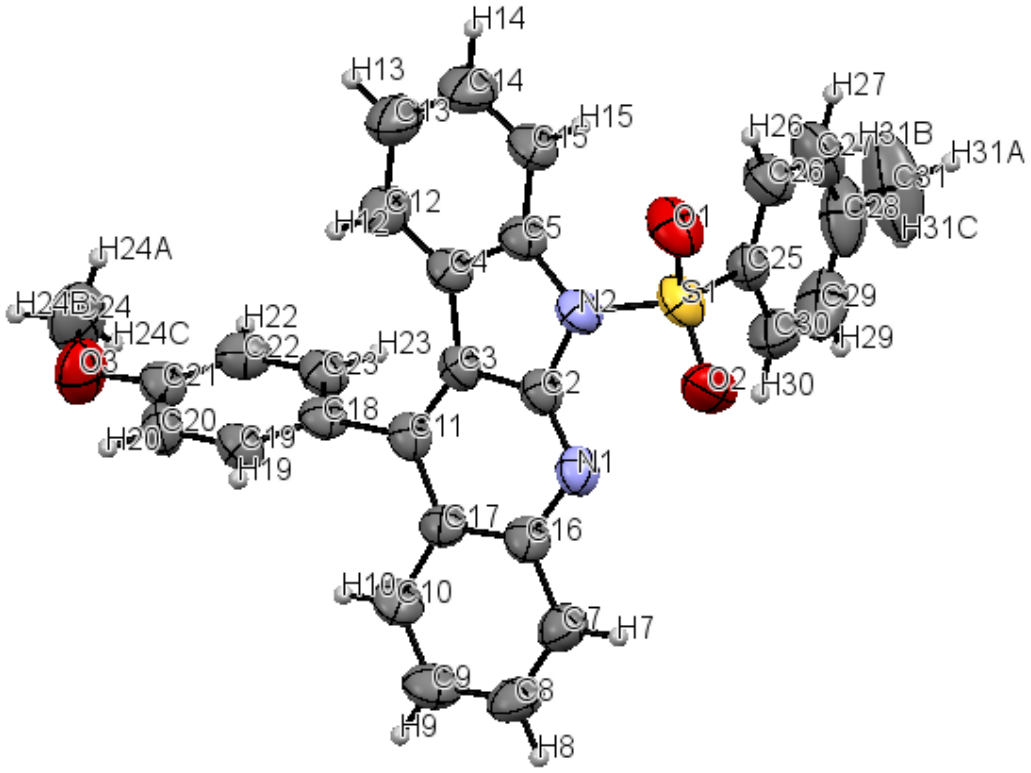
This work represents not only a novel approach to deliver a strategically alternative route, but also accessible method because of easy availability of starting materials and efficiency of the double annulations processes, this method would provide a practical and debatably a model strategy for the rapid access to diversified indolo[2,3-*b*]quinoline derivatives with high atom and step economy. Furthermore, the products afforded in our scheme might easily be converted to natural occurring indolo[2,3-*b*]quinolines such as Norcryptotackieine, by simple detosylation of **3g**. To the best of our knowledge this is the first report of preparation of indolo[2,3-*b*]quinoline derivatives through carbopalladation/cross-coupling and subsequent DDQ mediated allylic Csp^3–H amination reaction from 2-bromo-N-[3-(2-aminophenyl)prop-2-ynyl]-N-tosylanilide. All the structures were characterized by ^1H, ^{13}C NMR and HRMS spectra and one of the structure **3e** confirmed by X-ray diffraction (See supporting information).

In conclusion, we have developed a new and efficient two steps strategies involving Pd-catalyzed carbocyclisation/crosscoupling and subsequent DDQ-mediated intramolecular double oxidative amination reaction to afford medicinally useful indolo[2,3-*b*]quinoline derivatives in an atom efficient manner. This method was proved to be general and exhibits a wide substrate scopes, good functional groups tolerance, and provides excellent yields of the desired products. Importantly, this strategy has also been utilized for the synthesis of tetracyclic *aza*-indolo[2,3-*b*]quinolines, indolo[2,3-*b*]napthyridine and *aza*-inolo[2,3-*b*]napthyridine derivatives for the first time. Further studies toward applications of these short protocol to afford other bioactive scaffolds are currently ongoing in our laboratory the first time.

II. 7. Experimental Section:

General: All NMR spcetral data were recorded by Bruker 300, 400, 500 (300, 400, 500 MHz) spectrometer in $CDCl_3$solutions expressing chemical shifts in parts per million (ppm, δ) and are referenced to $CHCl_3$ (δ = 7.26 ppm) as an internal standard. All coupling constants are absolute values and are expressed in Hz. The description of the signals include: s = singlet, d = doublet, t = triplet, m = multiplet, dd = doublet of doublets and brs = broad singlet. ^{13}C NMR spectra were recorded with a Bruker 300, 400, 500 (75, 100, 125 respictively MHz) spectrometer as solutions in $CDCl_3$ with complete proton decoupling. Chemical shifts are expressed in parts per million (ppm, δ) and are referenced to $CDCl_3$ (δ = 77.0 ppm) as an internal standard. High-Resolution Mass Spectra (HRMS) were performed with a Qtof Micro YA263 spectrometer in dichloromethane solvent. The molecular fragments are quoted as the relation between mass and charge (m/z). IR (infrared spectroscopy) was recorded with an FT-IR spectrometer, the IR spectra were recorded as thin films with KBr. The routine monitoring of reactions was performed with silica gel coated glass slides (Merck, silica gel G for TLC), and pre-coated Al plate, which were analyzed with iodine and uv light respectively. Solvents, reagents and chemicals were purchased from Aldrich, Fluka, Merck, SRL, Spectrochem and Process Chemicals. All reactions involving moisture-sensitive reactants were executed with oven-dried glassware.

Ortep diagram for the crystal structure of the compound 3e (Thermal ellipsoid contour at 50% probability level)

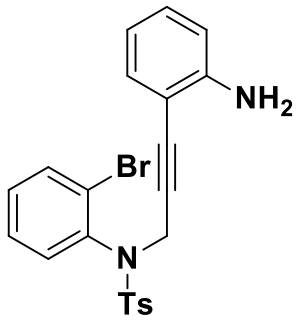


CCDC no. 1848645

Table for crystallographic data and structural refinement parameters for 3e:

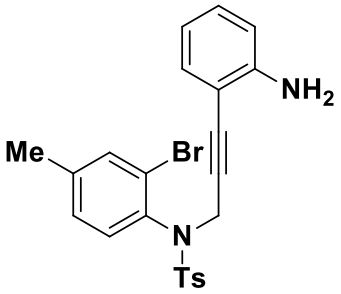
Identification code	matrix_0m
Empirical formula	$C_{29}H_{22}N_2O_3S$
Formula weight	478.55
Temperature/K	296.15
Crystal system	triclinic
Space group	P-1
a/Å	12.875(2)
b/Å	13.030(2)
c/Å	15.195(3)
α/°	76.583(12)
β/°	78.566(12)
γ/°	72.177(12)
Volume/Å^3	2338.3(6)
Z	4
ρ_{calc}g/cm^3	1.359
μ/mm^{-1}	0.174
F(000)	1000.0
Crystal size/mm^3	15 × 10 × 7
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	3.34 to 49.28
Index ranges	$-15 \leq h \leq 15$, $-15 \leq k \leq 15$, $-17 \leq l \leq 17$
Reflections collected	31369
Independent reflections	7820 [R_{int} = 0.2685, R_{sigma} = 0.2299]
Data/restraints/parameters	7820/0/635
Goodness-of-fit on F^2	0.773
Final R indexes [I>=2σ (I)]	R_1 = 0.0691, wR_2 = 0.1304
Final R indexes [all data]	R_1 = 0.1707, wR_2 = 0.1594
Largest diff. peak/hole / e Å^{-3}	0.30/-0.40

Representative experimental procedure for the synthesis of *N*-(3-(2-aminophenyl)prop-2-yn-1-yl)-*N*-(2-bromophenyl)-4-methylbenzenesulfonamide (1a):



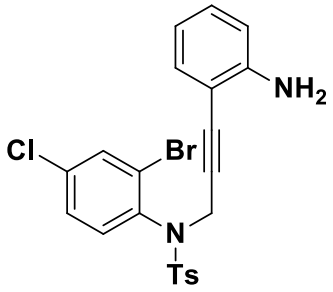
To a solution of *N*-(2-bromophenyl)-4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide (363 mg, 1 mmol) in dimethyl sulfoxide (2 mL) and 2-iodoaniline (241 mg, 1.1mmol), triethylamine (202 mg, 2mmol), CuI (4 mg, 0.02mmol) and $Pd(PPh_3)_4$ (12 mg, 0.01mmol) were added successively. The resulting solution was stirred at room temperature under argon atmosphere for overnight. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with ethyl acetate. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **1a** as a yellow semisolid (341 mg, 0.75mmol, 75%).^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.41 (s, 3H), 3.55 (br s, 2H), 4.41 (d, *J* = 17.4 Hz,1H), 4.94 (d, *J* = 18 Hz, 1H), 6.61–6.64 (m, 2H), 7.02–7.08 (m, 2H), 7.23–7.33 (m, 5H), 7.63 (d, *J* = 1.8 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 2H) ppm. HRMS (ESI) calcd for $C_{22}H_{20}BrN_2O_2S$ $[M+H]^+$ 455.0429; found 455.0429.

***N*-(3-(2-aminophenyl)prop-2-yn-1-yl)-*N*-(2-bromo-4-methylphenyl)-4-methylbenzenesulfonamide (1b):**



To a solution of *N*-(2-bromophenyl)-4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide (377 mg, 1 mmol) in dimethyl sulfoxide (2 mL) and 2-iodoaniline (241 mg, 1.1mmol), triethylamine (202 mg, 2mmol), CuI (4 mg, 0.02 mmol) and $Pd(PPh_3)_4$ (12 mg, 0.01mmol) were added successively. The resulting solution was stirred at room temperature under argon atmosphere for overnight. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with ethyl acetate. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **1b** as a yellow semisolid (360 mg, 0.77 mmol, 77%).^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.32 (s, 3H), 2.42 (s, 3H), 4.39 (d, *J* = 17.7 Hz, 1H), 4.94 (d, *J* = 17.7 Hz, 1H), 6.63 (d, *J* = 8.1 Hz, 2H), 7.04–7.14 (m, 3H), 7.20 (d, *J* = 8.1 Hz, 1H), 7.27–7.35 (m, 2H), 7.47 (s, 1H), 7.76 (d, *J* = 8.1Hz, 2H) ppm. HRMS (ESI) calcd for $C_{23}H_{22}BrN_2O_2S$ $[M+H]^+$ 469.0585; found 469.0586.

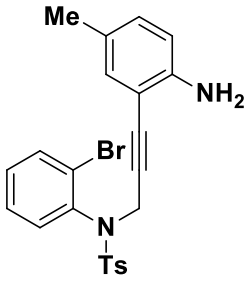
***N*-(3-(2-aminophenyl)prop-2-yn-1-yl)-*N*-(2-bromo-4-chlorophenyl)-4-methylbenzenesulfonamide (1c):**



To a solution of *N*-(2-bromo-4-chlorophenyl)-4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide (397 mg, 1 mmol) in dimethyl sulfoxide (2 mL) and 2-iodoaniline (241 mg, 1.1mmol), triethylamine (202 mg, 2mmol), CuI (4 mg, 0.02 mmol) and $Pd(PPh_3)_4$ (12 mg, 0.01mmol) were added successively. The resulting solution was stirred at room temperature under argon atmosphere for overnight. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with ethyl acetate. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **1c** as a yellow semisolid (395 mg, 0.81 mmol, 81%).^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.41 (s, 3H), 4.12 (s, 2H), 4.38 (d, *J* = 16.2 Hz, 1H), 4.94 (d, *J* = 16.8 Hz, 1H), 6.62 (d, *J* = 8.4 Hz, 2H), 7.02–7.11 (m, 2H), 7.28 (d, *J* = 8.1Hz,

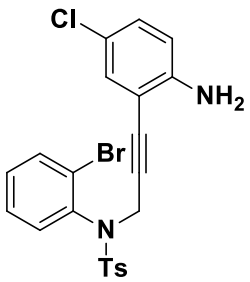
4H), 7.65 (s, 1H), 7.75 (d, *J* = 8.1Hz, 2H) ppm. HRMS (ESI) calcd for $C_{22}H_{18}BrClN_2NaO_2S$ $[M+Na]^+$ 510.9859; found 510.9860.

_N_-(3-(2-amino-5-methylphenyl)prop-2-yn-1-yl)-_N_-(2-bromophenyl)-4-methylbenzenesulfonamide (1d):



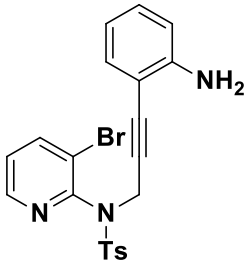
To a solution of *N*-(2-bromophenyl)-4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide (363 mg, 1 mmol) in dimethyl sulfoxide (2 mL) and 2-iodo-4-methylaniline (255 mg, 1.1mmol), triethylamine (202 mg, 2mmol), CuI (4 mg, 0.02 mmol) and $Pd(PPh_3)_4$ (12 mg, 0.01mmol) were added successively. The resulting solution was stirred at room temperature under argon atmosphere for overnight. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with ethyl acetate. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **1d** as a yellow semisolid (370 mg, 0.79 mmol, 79%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.17 (s, 3H), 2.42 (s, 3H), 4.40 (d, *J* = 17.4 Hz, 1H), 4.95 (d, *J* = 18.6 Hz, 1H), 6.54 (d, *J* = 8.1 Hz, 1H), 6.84 (s, 1H), 6.89 (d, *J* = 8.1 Hz, 1H), 7.19–7.34 (m, 5H), 7.64 (d, *J* = 6.3Hz, 1H), 7.76 (d, *J* = 8.1Hz, 2H) ppm. HRMS (ESI) calcd for $C_{23}H_{22}BrN_2O_2S$ $[M+H]^+$ 469.0585; found 469.0586.

_N_-(3-(2-amino-5-chlorophenyl)prop-2-yn-1-yl)-_N_-(2-bromophenyl)-4-methylbenzenesulfonamide (1e):



To a solution of *N*-(2-bromophenyl)-4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide (363 mg, 1 mmol) in dimethyl sulfoxide (2 mL) and 4-chloro-2-iodoaniline (253 mg, 1.1mmol), triethylamine (202 mg, 2mmol), CuI (4 mg, 0.02 mmol) and $Pd(PPh_3)_4$ (12 mg, 0.01mmol) were added successively. The resulting solution was stirred at room temperature under argon atmosphere for overnight. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with ethyl acetate. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **1e** as a yellow semisolid (361 mg, 0.74 mmol, 74%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.43 (s, 3H), 4.37 (d, *J* = 17.1 Hz, 1H), 4.92 (d, *J* = 17.1 Hz, 1H), 6.55 (d, *J* = 8.7 Hz, 1H), 6.95 (s, 1H), 7.02 (d, *J* = 8.4 Hz, 1H), 7.23–7.30 (m, 5H), 7.64 (d, *J* = 7.5Hz, 1H), 7.75 (d, *J* = 8.1 Hz, 2H) ppm. HRMS (ESI) calcd for $C_{22}H_{18}BrClN_2NaO_2S$ $[M+Na]^+$ 510.9859; found 510.9859.

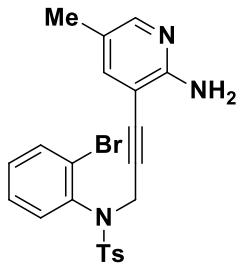
_N_-(3-(2-aminophenyl)prop-2-yn-1-yl)-_N_-(3-bromopyridin-2-yl)-4-methylbenzenesulfonamide (1f):



To a solution of *N*-(3-bromopyridin-2-yl)-4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide(364 mg, 1 mmol) in dimethyl sulfoxide (2 mL) and 2-iodoaniline (241 mg, 1.1mmol), triethylamine (202 mg, 2mmol), CuI (4 mg, 0.02 mmol) and $Pd(PPh_3)_4$ (12 mg, 0.01mmol) were added successively. The resulting solution was stirred at room temperature under argon atmosphere for overnight. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with ethyl acetate. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **1f** as a yellow semisolid (327 mg, 0.72 mmol, 72%).^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.37 (s, 3H), 3.85 (br, s, 2H), 4.60 (s, 2H), 6.56 (d, *J* = 7.2 Hz, 2H), 6.98–7.05 (m, 2H), 7.15–7.19 (m, 1H), 7.27 (d, *J* = 7.5Hz, 2H), 7.79 (d, *J* = 8.1 Hz, 2H), 8.37 (d, *J*

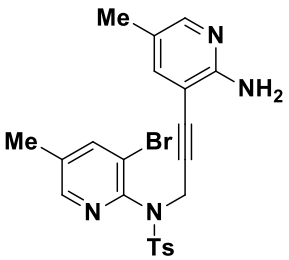
= 8.1 Hz, 1H, 8.36 (d, *J* = 4.2 Hz, 1H) ppm. HRMS (ESI) calcd for $C_{21}H_{18}BrN_3NaO_2S$ $[M+Na]^+$ 478.0201; found 478.0202.

_N_-(3-(2-amino-5-methylpyridin-3-yl)prop-2-yn-1-yl)-_N_-(2-bromophenyl)-4-methylbenzenesulfonamide (1g):



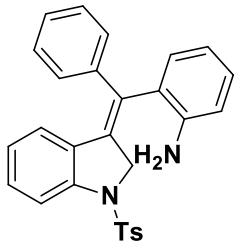
To a solution of *N*-(2-bromophenyl)-4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide(363 mg, 1 mmol) in dimethyl sulfoxide (2 mL) and 3-iodo-5-methylpyridin-2-amine (257 mg, 1.1mmol), triethylamine (202 mg, 2mmol), CuI (4 mg, 0.02 mmol) and $Pd(PPh_3)_4$ (12 mg, 0.01mmol) were added successively. The resulting solution was stirred at room temperature under argon atmosphere for overnight. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with ethyl acetate. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **1g** as a yellow semisolid (342 mg, 0.73 mmol, 73%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.11 (s, 3H), 2.41 (s, 3H), 4.37 (d, *J* = 16.5 Hz, 1H), 4.77 (s, 2H), 4.88 (d, *J* = 17.4 Hz, 1H), 7.13 (s, 1H), 7.19–7.37 (m, 5H), 7.63 (d, *J* = 7.8Hz, 1H), 7.73 (d, *J* = 8.1 Hz, 2H), 7.80 (s, 1H) ppm. HRMS (ESI) calcd for $C_{22}H_{21}BrN_3O_2S$ $[M+H]^+$ 470.0538; found 470.0538.

_N_-(3-(2-amino-5-methylpyridin-3-yl)prop-2-yn-1-yl)-_N_-(3-bromo-5-methylpyridin-2-yl)-4-methylbenzenesulfonamide (1h):



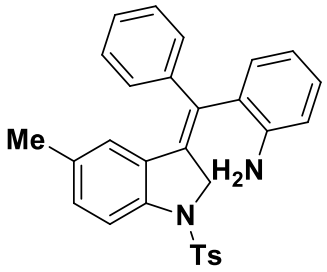
To a solution of *N*-(3-bromo-5-methylpyridin-2-yl)-4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide(378 mg, 1 mmol) in dimethyl sulfoxide (2 mL) and 3-iodo-5-methylpyridin-2-amine (257 mg, 1.1mmol), triethylamine (202 mg, 2mmol), CuI (4 mg, 0.02 mmol) and $Pd(PPh_3)_4$ (12 mg, 0.01mmol) were added successively. The resulting solution was stirred at room temperature under argon atmosphere for overnight. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with ethyl acetate. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **1h** as a yellow semisolid (344 mg, 0.71 mmol, 71%).^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.09 (s, 3H), 2.34 (s, 6H), 4.57 (s, 2H), 4.83 (s, 2H), 7.23 (d, *J* = 8.7 Hz, 1H), 7.46 (d, *J* = 5.1 Hz, 1H), 7.53 (d, *J* = 7.2 Hz, 1H), 7.63–7.64 (m, 2H), 7.77 (d, *J* = 8.1Hz, 2H), 7.87 (s, 1H) ppm. HRMS (ESI) calcd for $C_{22}H_{22}BrN_4O_2S$ $[M+H]^+$ 485.0647; found 485.0648.

(*Z*)-2-(phenyl(1-tosylindolin-3-ylidene)methyl)aniline (2a):



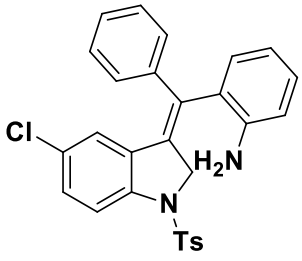
To a solution of **1a** (227 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), phenyl boronic acid (92 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively. The resulting solution was stirred at 70-75°C under argon atmosphere for 3 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with ethyl acetate. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **2a** as a yellow solid (185 mg, 0.41mmol, 82%); m.p. 136-138 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.39 (s, 3H), 3.69 (brs, 2H) , 4.50 (s, 2H), 6.64- 6.73 (m, 4H), 6.88 (d, *J* = 7.2 Hz,1H), 7.08–7.29 (m, 9H), 7.68 (dd, *J* = 8.1, 9 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 55.8, 115.5, 116.0, 118.7, 123.2, 124.3, 127.2, 127.4, 127.8, 128.6, 128.8, 128.9, 129.1, 129.2, 129.5, 129.6, 131.3, 132.0, 133.9, 140.0, 142.7, 144.1, 145.7 ppm. HRMS (ESI) calcd for $C_{28}H_{24}N_2NaO_2S$ $[M+Na]^+$ 475.1456; found 475.1457.

(*Z*)-2-((5-methyl-1-tosylindolin-3-ylidene)(phenyl)methyl)aniline (2b) :



To a solution of **1b** (234 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), phenyl boronic acid (92 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively. The resulting solution was stirred at 75-75°C under argon atmosphere for 3 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with ethyl acetate. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **2b** as a yellow solid (196 mg, 0.42 mmol, 83%); m.p. 142-144 °C.^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.01 (s, 3H), 2.38 (s, 3H), 3.66 (br s, 2H) , 4.45 (s, 2H), 6.41 (s, 1H), 6.71 (t, *J* = 4.5 Hz, 2H), 6.85 (d, *J* = 4.5 Hz, 1H), 6.97 (d, *J* = 4.8 Hz,1H), 7.09 (t, *J* = 4.5 Hz, 1H), 7.15-7.16 (m, 2H), 7.22-7.28 (m, 5H), 7.60 (dd, *J* = 3.9, 4.5 Hz,3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.5, 21.6, 56.2, 115.7, 116.2, 118.9, 125.0, 127.4, 127.6, 127.9, 128.8, 128.9, 129.0, 129.3, 129.4, 129.7, 130.4, 131.2, 132.4, 132.9, 134.0, 140.2, 142.9, 143.8, 144.1 ppm. HRMS (ESI) calcd for $C_{29}H_{27}N_2O_2S$ $[M+H]^+$467.1793; found 467.1794.

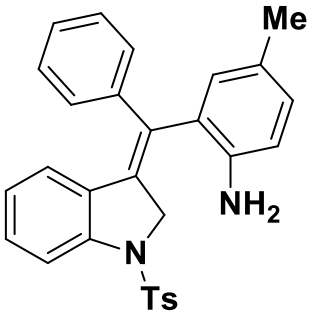
(*Z*)-2-((5-chloro-1-tosylindolin-3-ylidene)(phenyl)methyl)aniline (2c) :



To a solution of **1c** (244 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), phenyl boronic acid (92 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively. The resulting solution was stirred at 75-75°C under argon

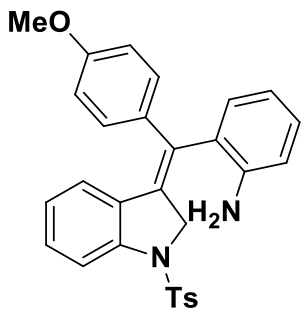
atmosphere for 3 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with EtOAc. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **2c** as a yellow solid (194 mg, 0.40 mmol, 79%); m.p. 154-156 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.41 (s, 3H), 3.67 (brs, 2H) , 4.51 (s, 2H), 6.55 (s, 1H), 6.70-6.73 (m, 2H), 6.86 (d, *J* = 7.5 Hz, 1H), 7.14–7.32 (m, 9H), 7.63 (d, *J* = 8.1 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 56.1, 116.1, 116.4, 118.8, 124.3, 126.8, 127.4, 128.3, 128.4, 128.6, 128.7, 129.0, 129.1, 129.2, 129.7, 130.9, 133.0, 133.5, 139.4, 142.6, 144.3, 144.4 ppm. HRMS (ESI) calcd for $C_{28}H_{24}ClN_2O_2S$ $[M+H]^+$ 487.1247; found 487.1248.

(*Z*)-4-methyl-2-(phenyl(1-tosylindolin-3-ylidene)methyl)aniline (2d) :



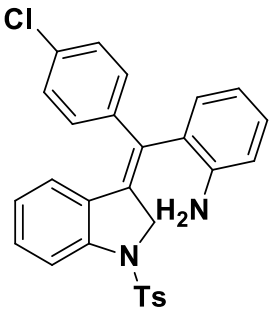
To a solution of **1d** (234 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), phenyl boronic acid (92 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively. The resulting solution was stirred at 75-75°C under argon atmosphere for 3 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with ethyl acetate. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **2d** as a yellow solid (210 mg, 0.45mmol, 90%); m.p. 158-160 °C.^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.12 (s, 3H), 2.32 (s, 3H), 3.48 (s, 2H), 4.42 (s, 2H), 6.55-6.64 (m, 4H), 6.83 (d, *J* = 8.5 Hz, 1H), 7.07-7.24 (m, 8H), 7.60 (dd, *J* = 8, 17.5 Hz, 3H), ppm. ^{13}C NMR ($CDCl_3$, 125 MHz) δ 20.5, 21.7, 85.9, 115.6, 116.3, 123.3, 124.7, 127.5, 127.6, 127.9, 128.0, 128.7, 129.0, 129.3, 129.4, 129.5, 129.7, 131.6, 132.0, 134.0, 140.3, 142.2, 145.8 ppm. HRMS (ESI) calcd for $C_{29}H_{27}N_2O_2S$ $[M+H]^+$ 467.1793 ; found 467.1793.

(*Z*)-2-((4-methoxyphenyl)(1-tosylindolin-3-ylidene)methyl)aniline (2e):



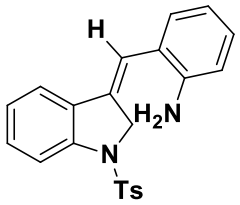
To a solution of **1a** (227 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL),*p*-methoxyphenylboronic acid (114 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively. The resulting solution was stirred at 70-75 °C under argon atmosphere for 3 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with EtOAc. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **2e** as a yellow solid(205 mg, 0.43mmol, 85%); m.p. 200-202 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.39 (s, 3H), 2.94 (brs, 2H) ,3.80 (s, 3H), 4.48 (s, 2H), 6.71- 6.88 (m, 8H), 7.09-7.12 (d, J = 8.4 Hz ,3H), 7.17–7.26 (m, 2H), 7.68 (dd, J = 8.1, 9.3 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 55.2, 55.9, 114.2, 115.5, 116.1, 118.8, 123.2, 124.3, 127.4, 128.9, 129.2, 129.3, 129.4, 129.6, 129.9, 131.1, 131.3, 132.1, 133.8, 142.7, 144.1, 145.6, 159.2 ppm. HRMS (ESI) calcd for $C_{29}H_{27}N_2O_3S$ $[M+H]^+$ 483.1742; found 483.1741.

(*Z*)-2-((4-chlorophenyl)(1-tosylindolin-3-ylidene)methyl)aniline (2f) :



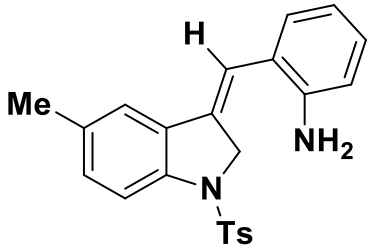
To a solution of **1a** (227 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), *p*-chlorophenylboronic acid (117 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively. The resulting solution was stirred at 70-75 °C under argon atmosphere for 3 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with EtOAc. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **2f** as a yellow solid (195 mg, 0.40 mmol, 81%); m.p. 138-140 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.39 (s, 3H), 4.47 (s, 2H), 6.74- 6.84 (m, 5H), 7.09-7.17 (m, 3H), 7.20–7.28 (m, 5H), 7.68 (dd, *J* = 8.1, 13.5 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 55.8, 115.6, 116.1, 118.8, 123.3, 124.2, 126.8, 127.4, 128.7, 129.1, 129.6, 129.8, 129.9, 130.1, 132.6, 133.6, 133.8, 138.5, 142.6, 144.2, 145.9 ppm. HRMS (ESI) calcd for $C_{28}H_{23}ClN_2NaO_2S$ $[M+Na]^+$ 509.1066; found 509.1065.

(*Z*)-2-((1-tosylindolin-3-ylidene)methyl)aniline (2g) :



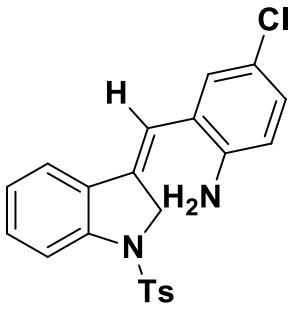
To a solution of **1a** (227 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively. The resulting solution was stirred at 70-75 °C under argon atmosphere for 3 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with ethyl acetate. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **2g** as a yellow solid (166 mg, 0.44 mmol, 89%); m.p. 146-148 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.37 (s, 3H), 4.73 (s, 2H), 6.73-6.81 (m, 3H), 7.05-7.25 (m, 6H), 7.48 (d, *J* = 6 Hz, 1H),7.70-7.72 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 54.2, 113.7, 114.9, 116.3, 118.8, 120.4, 122.1, 123.7, 126.8, 127.2, 127.8, 128.7, 129.8, 130.6, 133.9, 134.1, 143.6, 144.0, 144.3 ppm. HRMS (ESI) calcd for $C_{22}H_{20}N_2NaO_2S$ $[M+Na]^+$ 399.1143; found 399.1143.

(*Z*)-2-((5-methyl-1-tosylindolin-3-ylidene)methyl)aniline (2h):



To a solution of **1b** (234 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively. The resulting solution was stirred at 70-75 °C under argon atmosphere for 3 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with ethyl acetate. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **2h** as a yellow solid (166 mg, 0.45 mmol, 91%); m.p. 150-152 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.37 (s, 6H), 3.82 (br s, 2H), 4.73 (s, 2H), 6.67 (s, 1H), 6.73 (d, *J* = 8 Hz, 1H), 6.81 (t, *J* = 7 Hz, 1H), 6.96 (dt, *J* = 2.5, 6.5 Hz, 1H), 7.03 (d, *J* = 7.5 Hz, 1H), 7.11-7.14 (m, 2H), 7.22-7.27 (m, 2H), 7.64-7.71 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.6, 54.9, 107.1, 115.3, 116.3, 116.7, 119.0, 121.8, 127.4, 128.0, 129.2, 129.9, 132.8, 133.6, 134.0, 140.0, 144.5, 159.1, 161.0 ppm. HRMS (ESI) calcd for $C_{23}H_{23}N_2O_2S$ $[M+H]^+$ 391.1480; found 391.1481.

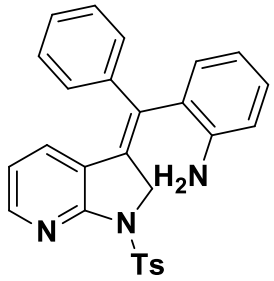
(*Z*)-4-chloro-2-((1-tosylindolin-3-ylidene)methyl)aniline (2i) :



To a solution of **1e** (244 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively. The resulting solution was stirred at 70-75 °C under argon atmosphere for 3 h. After the completion of

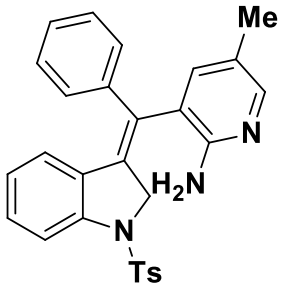
the reaction (monitored by TLC), the crude reaction mixture was extracted with EtOAc. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **2i** as a yellow solid (181 mg, 0.44 mmol, 88%); m.p. 134-136 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.36 (s, 3H), 4.66 (s, 2H), 6.64 (t, *J*= 8.4 Hz, 2H), 6.97-7.05 (m, 3H), 7.22-7.29 (m, 3H), 7.45 (d, *J* = 6.9 Hz, 1H),7.69_7.76 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 53.9, 112.3, 113.4, 114.9, 120.7, 123.7, 124.6, 126.7, 127.2, 127.4, 128.4, 129.9, 130.0, 130.3, 133.9, 136.1, 144.0, 144.4 ppm. HRMS (ESI) calcd for $C_{22}H_{20}ClN_2O_2S$ $[M+H]^+$ 411.0934; found 411.0934.

(*Z*)-2-(phenyl(1-tosyl-1H-pyrrolo[2,3-b]pyridin-3(2H)-ylidene)methyl)aniline (2j) :



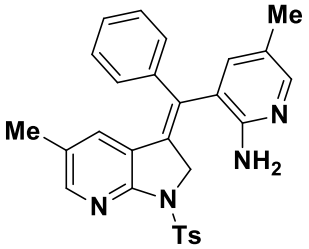
To a solution of **1f** (228 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), phenyl boronic acid (92 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively. The resulting solution was stirred at 75-75°C under argon atmosphere for 3.5 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with ethyl acetate. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **2j** as a yellow solid(174 mg, 0.38mmol, 77%); m.p. 204-206 °C.^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.39 (s, 3H), 3.14 (br s, 2H) , 4.63 (s, 2H), 6.57-6.59 (m, 1H), 6.76 (t, *J* = 7.8 Hz, 2H), 6.89 (d, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 6.9 Hz, 1H), 7.13 (t, *J* = 7.2 Hz, 1H), 7.26-7.33 (m, 7H), 7.98 (d, *J* = 7.8 Hz, 2H), 8.10 (d, *J* = 3.6 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.6, 54.0, 116.3, 117.5, 118.9, 121.9, 126.4, 128.0, 128.2, 128.3, 129.0, 129.1, 129.2, 129.4, 131.7, 134.4, 135.5, 139.7, 142.6, 144.2, 148.3 ppm. HRMS (ESI) calcd for $C_{27}H_{24}N_3O_2S$ $[M+H]^+$ 454.1589 ; found 454.1590.

(*Z*)-5-methyl-3-(phenyl(1-tosylindolin-3-ylidene)methyl)pyridin-2-amine (2k) :



To a solution of **1g** (235 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), phenyl boronic acid (92 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively. The resulting solution was stirred at 75-75 °C under argon atmosphere for 3.5 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with ethyl acetate. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **2k** as a yellow solid (187 mg, 0.40 mmol, 80%); m.p. 166-168 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.17 (s, 3H), 2.39 (s, 3H) , 4.33 (s, 2H), 4.49 (s, 2H), 6.63 (d, *J* = 7.8 Hz, 1H), 6.71 (t, *J* = 7.8 Hz, 1H), 7.00 (s, 1H), 7.17-7.33 (m, 8H), 7.19 (dd, *J* = 8.1, 10.2 Hz, 3H), 7.88 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.3, 21.5, 55.4, 115.5, 121.7, 123.2, 123.4, 124.5, 127.4, 127.7, 128.2, 128.5, 129.1, 129.7, 130.0, 133.1, 133.7, 138.8, 139.2, 144.3, 145.9, 146.5, 152.4 ppm. HRMS(ESI)calcd for $C_{28}H_{26}N_3O_2S$ $[M+H]^+$468.1746 ; found 468.1746.

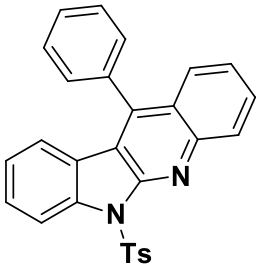
(*Z*)-5-methyl-3-((5-methyl-1-tosyl-1H-pyrrolo[2,3-*b*]pyridin-3(2H)-ylidene)(phenyl)methyl)pyridin-2-amine (2l):



To a solution of **1h** (242 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), phenyl boronic acid (92 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg,

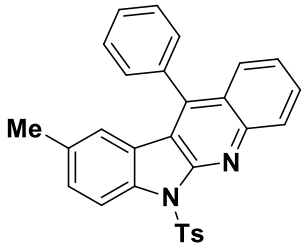
0.025 mmol) were added successively. The resulting solution was stirred at 75-75°C under argon atmosphere for 4 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with ethyl acetate. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **2l** as a yellow solid (181 mg, 0.37 mmol, 75%); m.p. >300 °C.^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.98 (s, 3H), 2.18 (s, 3H) , 2.38 (s, 3H), 4.40 (s, 2H), 4.59 (s, 2H), 6.66 (s, 1H), 7.06 (s, 1H), 7.26 (d, *J* = 8.1 Hz, 3H), 7.35-7.37 (m, 3H), 7.90 (s, 1H), 7.96 (d, *J* = 14.5 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ17.5, 18.0, 21.7, 54.1, 120.6, 121.4, 123.7, 127.0, 128.1, 128.4, 128.7, 129.4, 129.5, 130.0, 132.3, 132.8, 135.4, 138.3, 139.2, 144.3, 148.9, 149.7, 152.6, 156.5 ppm. HRMS (ESI) calcd for $C_{28}H_{27}N_4O_2S$ $[M+H]^+$ 483.1855; found 483.1855.

11-phenyl-6-tosyl-6H-indolo[2,3-*b*]quinolone (3a) :



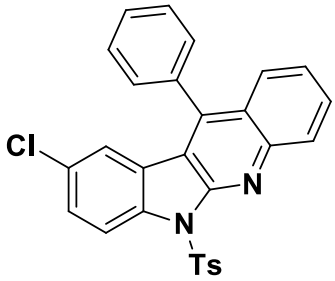
To a solution of **2a** (226 mg, 0.5 mmol) in dichloromethane (3 mL), DDQ (227 mg, 1mmol) were added successively. The resulting solution was stirred at room temperature for 1 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with dichloromethane. The organic extract was washed with sodium bicarbonate solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **3a** as a yellow solid (224 mg, quantitative); m.p. 208-210 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.32 (s, 3H), 6.85 (d, *J* = 7.5 Hz, 1H), 7.08 (t, *J* = 7.5 Hz, 1H),7.22 (d, *J* = 7.8 Hz, 2H), 7.40-7.62 (m, 8H), 7.74 (t, *J* = 7.2 Hz, 1H),8.25 (dd, *J* = 8.1, 12.6 Hz, 3H), 8.51 (d, *J* = 8.4 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.6, 114.6, 116.6, 122.8, 122.9, 123.4, 125.0, 125.3, 126.0, 128.3, 128.7, 128.8, 129.1, 129.3, 135.6, 135.9, 139.6, 142.6, 144.9, 146.2, 150.5 ppm. HRMS (ESI) calcd for $C_{28}H_{21}N_2O_2S$ $[M+H]^+$ 449.1324 ; found 435.1324.

9-methyl-11-phenyl-6-(phenylsulfonyl)-6H-indolo[2,3-*b*]quinolone (3b) :



To a solution of **2b** (233 mg, 0.5 mmol) in dichloromethane (3 mL), DDQ (227 mg, 1mmol) were added successively. The resulting solution was stirred at room temperature for 1 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with dichloromethane. The organic extract was washed with sodium bicarbonate solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **3b** as a light yellow solid (231 mg, quantitative); m.p. 206-208 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.22 (s, 3H), 2.31 (s, 3H),6.60 (s, 1H), 7.20 (d, *J* = 7.8 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 1H),7.40-7.44 (m, 3H), 7.62 (s, 4H), 7.74 (t, *J* = 7.2 Hz, 1H), 8.24 (dd, *J* = 8.4, 22.8 Hz, 3H), 8.37 (d, *J* = 8.4 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.2, 21.6, 114.4, 116.7, 123.0,123.1, 124.9, 125.3, 126.0, 128.2, 128.8, 129.1, 129.3, 129.7, 133.0, 135.6, 135.8, 137.6, 142.5, 144.8, 146.1, 150.7ppm. HRMS (ESI) calcd for $C_{29}H_{23}N_2O_2S$ $[M+H]^+$ 463.1480 ; found 463.1481.

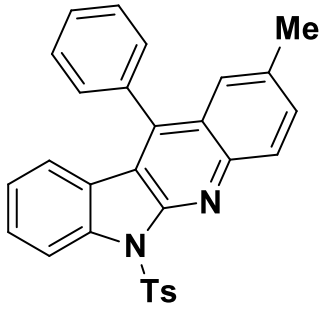
9-chloro-11-phenyl-6-tosyl-6H-indolo[2,3-*b*]quinolone (3c) :



To a solution of **2c** (244 mg, 0.5 mmol) in dichloromethane (3 mL), DDQ (227 mg, 1mmol) were added successively. The resulting solution was stirred at room temperature for 1 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with dichloromethane. The organic extract was washed with sodium bicarbonate solution, dried over

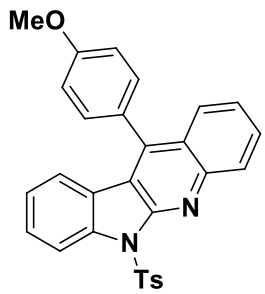
anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **3c** as a yellow solid (237 mg, 0.49 mmol, 98%); m.p. 208-210 °C.^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.33 (s, 3H), 6.76 (s, 1H), 7.24 (t, *J* = 4.8 Hz, 2H),7.37-7.39 (m, 2H), 7.42-7.45 (m, 2H), 7.63-7.65 (m, 4H), 7.76 (t, *J* = 3.9 Hz, 1H),8.19 (d, *J* = 4.8 Hz, 2H),8.27 (d, *J* = 5.1 Hz, 1H), 8.44 (d, *J* = 5.4 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.7, 115.7, 115.9, 122.7, 124.5, 125.4, 126.3, 128.5, 128.7, 129.0, 129.2, 129.3, 129.4, 129.5, 129.8, 135.1, 135.8, 138.0, 143.5, 145.3, 146.7, 150.7 ppm. HRMS (ESI) calcd for $C_{28}H_{19}ClN_2NaO_2S$ $[M+Na]^+$ 505.0753 ; found 505.0753.

2-methyl-11-phenyl-6-tosyl-6H-indolo[2,3-*b*]quinolone (3d):



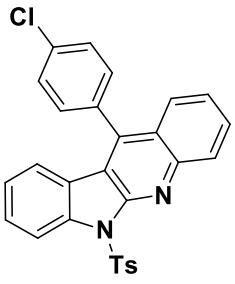
To a solution of **2d** (233 mg, 0.5 mmol) in dichloromethane (3 mL), DDQ (227 mg, 1mmol) were added successively. The resulting solution was stirred at room temperature for 1 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with dichloromethane. The organic extract was washed with sodium bicarbonate solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **3d** as a yellow solid (231 mg, quantitative); m. p. 214-216 °C.^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.31 (s, 3H), 2.43 (s, 3H), 6.79 (d, *J* = 7.8 Hz, 1H), 7.06 (t, *J* = 7.8 Hz, 1H), 7.19-7.26 (m, 2H), 7.36-7.63 (m, 8H),8.17-8.21 (m, 3H), 8.49 (d, *J* = 8.4 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.7, 21.8, 114.8, 116.7, 122.9, 123.2, 123.5, 124.8, 125.4, 128.4, 128.7, 128.9, 129.0, 129.2, 129.3, 129.5, 131.6, 135.0, 135.9, 136.0, 139.7, 142.0, 144.9, 145.0, 150.2 ppm. HRMS (ESI) calcd for $C_{29}H_{23}N_2O_2S$ $[M+H]^+$ 463.1480; found 463.1480.

11-(4-methoxyphenyl)-6-tosyl-6H-indolo[2,3-*b*]quinolone(3e) :



To a solution of **2e** (241 mg, 0.5 mmol) in dichloromethane (3 mL), DDQ (227 mg, 1mmol) were added successively. The resulting solution was stirred at room temperature for 1 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with dichloromethane. The organic extract was washed with sodium bicarbonate solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **3e** as a yellow solid(239 mg, quantitative); m. p. 210-212 °C.^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.31 (s, 3H), 3.96 (s, 3H), 6.97 (d, J = 7.8 Hz, 1H), 7.16 (dq, d, J = 8.4 Hz, J = 13.2, 5H),7.32 (d, J = 8.4 Hz, 2H), 7.39-7.51 (m, 2H), 7.66-7.75 (m, 2H), 8.23 (dd, J = 8.1 Hz, J = 11.4, 3H), 8.50 (d, J = 8.4 Hz, 1H)ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.6, 55.4, 114.6, 116.9, 122.9, 123.1, 123.4, 124.9, 125.7, 126.0, 127.5, 128.3, 128.6, 129.1, 129.3, 130.4, 135.9, 139.5, 142.6, 144.9, 146.2, 150.6, 160.0 ppm. HRMS (ESI) calcd for $C_{29}H_{23}N_2O_3S$ $[M+H]^+$ 479.1429 ; found 479.1430.

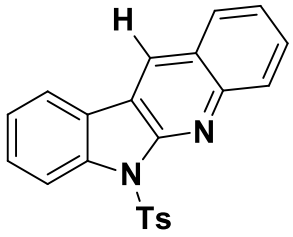
11-(4-chlorophenyl)-6-tosyl-6H-indolo[2,3-*b*]quinolone (3f):



To a solution of **2f** (243 mg, 0.5 mmol) in dichloromethane (3 mL), DDQ (227 mg, 1mmol) were added successively. The resulting solution was stirred at room temperature for 1 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with

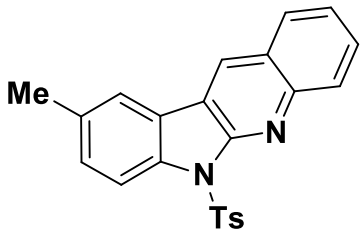
dichloromethane. The organic extract was washed with sodium bicarbonate solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **3f** as a yellow solid (222 mg, 0.46 mmol, 92%); m. p. 222-224 °C.^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.31 (s, 3H), 6.91 (d, *J* = 7.5 Hz, 1H), 7.12 (t, *J* = 7.5 Hz, 1H), 7.22 (d, *J* = 8.1 Hz, 2H), 7.35 (d, *J* = 8.4 Hz, 2H), 7.41-7.57 (m, 3H), 7.61 (d,*J* = 8.1 Hz, 2H),7.75(t, *J* = 7.2 Hz, 1H), 8.25 (dd, *J* = 8.1,13.5 Hz, 3H), 8.52 (d, *J* = 8.4 Hz, 1H)ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ21.7, 114.4, 116.6, 119.2, 125.3, 125.5, 126.1, 126.3, 127.2, 127.6, 128.7, 129.1, 129.2, 129.4, 129.5, 129.6, 129.8, 129.9, 130.7, 135.3, 136.7, 143.8, 145.1, 146.8, 148.0, 149.8, 152.4ppm. HRMS (ESI) calcd for $C_{28}H_{19}ClN_2NaO_2S$ $[M+Na]^+$ 505.0753 ; found 505.0753.

6-tosyl-6H-indolo[2,3-b]quinolone (3g):



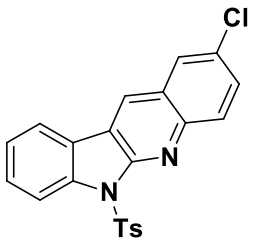
To a solution of **2g** (188 mg, 0.5 mmol) in dichloromethane (3 mL), DDQ (227 mg, 1mmol) were added successively. The resulting solution was stirred at room temperature for 2 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with dichloromethane. The organic extract was washed with sodium bicarbonate solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **3g** as a yellow solid (153 mg, 0.41mmol, 82%); m. p. 226-228 °C.^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.27 (s, 3H), 7.04-7.16 (m, 5H), 7.25-7.35 (m, 3H),7.52 (s, 1H), 7.70 (d,*J* = 8.1 Hz, 2H), 7.89 (d, *J* = 7.8 Hz, 1H), 8.49 (d, *J* = 6.6 Hz, 1H)ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.6, 113.3, 121.7, 122.3, 123.6, 124.1, 124.3, 125.5, 126.8, 127.1, 127.6, 128.6, 130.0, 131.1, 132.2, 134.9, 135.7, 145.5, 151.6, 164.5 ppm. HRMS (ESI) calcd for $C_{22}H_{16}N_2NaO_2S$ $[M+Na]^+$ 395.0830; found 395.0831.

9-methyl-6-tosyl-6H-indolo[2,3-*b*]quinolone (3h) :



To a solution of **2h** (195 mg, 0.5 mmol) in dichloromethane (3 mL), DDQ (227 mg, 1mmol) were added successively. The resulting solution was stirred at room temperature for 2 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with dichloromethane. The organic extract was washed with sodium bicarbonate solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **3h** as a yellow solid (155 mg, 0.40 mmol, 81%); m. p. 234-236 °C.^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.38 (s, 3H), 2.45 (s, 3H), 7.20-7.31 (m, 4H), 7.62 (t, *J* = 7.8 Hz, 1H), 7.78 (d, *J* = 7.8 Hz, 1H), 8.07-8.11 (m, 3H), 8.33 (d, *J* = 15.6 Hz, 2H), 8.56 (d,*J* = 7.8 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 18.6, 21.8, 25.2, 117.8, 121.0, 122.2, 123.0, 125.1, 128.7, 130.0, 131.3, 131.4, 134.0, 134.5, 139.3, 145.8, 146.2, 147.5, 169.0 ppm. HRMS (ESI) calcd for $C_{23}H_{19}N_2O_2S$ $[M+H]^+$ 387.1167; found 387.1166.

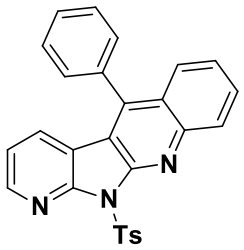
2-chloro-6-(phenylsulfonyl)-6H-indolo[2,3-*b*]quinolone (3i) :



To a solution of **3i** (205 mg, 0.5 mmol) in dichloromethane (3 mL), DDQ (227 mg, 1mmol) were added successively. The resulting solution was stirred at room temperature for 2.5 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with dichloromethane. The organic extract was washed with sodium bicarbonate solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **3i** as a yellow solid (152 mg, 0.37 mmol, 75%); m. p. 266-268 °C.^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.29 (s, 3H), 7.00-7.04 (m,

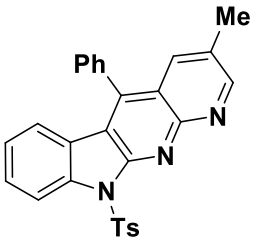
2H), 7.18 (d, *J* = 8.1 Hz, 2H), 7.30-7.37 (m, 3H), 7.50 (s, 1H), 7.71 (d, *J* = 8.1 Hz, 2H),7.91 (d, *J* = 7.8 Hz, 1H), 8.42 (d, *J* = 7.2 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) *δ* 21.7, 113.4, 121.8, 123.4, 123.8, 124.5, 125.8, 127.1, 127.4, 128.0, 128.2, 129.2, 130.2, 130.5, 132.5, 134.8, 135.7, 145.7, 149.8, 163.7 ppm. HRMS (ESI) calcd for $C_{22}H_{15}ClN_2NaO_2S$ $[M+Na]^+$ 429.0440 ; found 429.0439.

5-phenyl-11-tosyl-11H-pyrido[3',2':4,5]pyrrolo[2,3-*b*]quinolone (3j) :



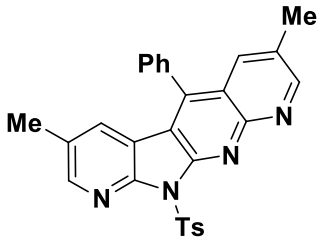
To a solution of **2j** (227 mg, 0.5 mmol) in dichloromethane (3 mL), DDQ (227 mg, 1mmol) were added successively. The resulting solution was stirred at room temperature for 2 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with dichloromethane. The organic extract was washed with sodium bicarbonate solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **3j** as a yellow solid (189 mg, 0.42 mmol, 85%); m. p. 204-206 °C.^{1}H NMR ($CDCl_3$, 300 MHz) *δ* 2.39 (s, 3H), 3.14 (br s, 2H), 4.63 (s, 2H), 6.57-6.59 (m, 1H), 6.76 (t, *J* = 7.8 Hz, 2H), 6.89 (d, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 6.9 Hz, 1H),7.13 (t, *J* = 7.2 Hz, 1H),7.26-7.33 (m, 7H), 7.98 (d, *J* = 7.8 Hz, 2H),8.10 (d, *J* = 3.6 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) *δ* 21.6, 54.0, 116.3, 117.5, 118.9, 121.9, 126.4, 128.0, 128.2, 128.3, 129.0, 129.1, 129.2, 129.4, 131.7, 134.4, 135.5, 139.7, 142.6, 144.2, 148.3 ppm. HRMS (ESI) calcd for $C_{27}H_{20}N_3O_2S$ $[M+H]^+$ 450.1276 ; found 450.1277.

3-methyl-5-phenyl-10-tosyl-10H-indolo[2,3-*b*][1,8]naphthyridine (3k) :



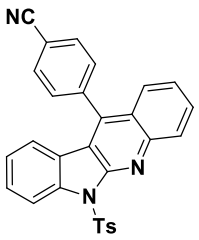
To a solution of **2k** (234 mg, 0.5 mmol) in dichloromethane (3 mL), DDQ (227 mg, 1mmol) were added successively. The resulting solution was stirred at room temperature for 3.5 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with dichloromethane. The organic extract was washed with sodium bicarbonate solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **3k** as a yellow solid (192 mg, 0.41 mmol, 83%); m. p. 236-238 °C.^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.32 (s, 3H), 2.45 (s, 3H), 6.87 (d, *J* = 7.6 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H),7.24-7.26 (m, 2H), 7.38-7.40 (m, 2H),7.51 (t, *J* = 7.6 Hz, 1H), 7.64 (t, *J* = 3.2 Hz, 3H), 7.74 (s, 1H), 8.32 (d, *J* = 8 Hz, 2H), 8.51 (d, *J* = 8.4 Hz, 1H), 8.97 (s, 1H)ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ18.7, 21.7, 114.8, 117.5, 119.7, 122.4, 123.0, 123.6, 128.5, 129.2, 129.3, 129.4, 129.7, 130.3, 134.1, 134.8, 136.0, 140.0, 142.9, 145.2, 152.2, 152.5, 154.9ppm. HRMS (ESI) calcd for $C_{28}H_{22}N_3O_2S$ $[M+H]^+$464.1433 ; found 464.1433.

3,7-dimethyl-5-phenyl-11-tosyl-11H-pyrido[3',2':4,5]pyrrolo[2,3-*b*][1,8]naphthyridine (3l):



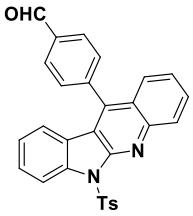
To a solution of **2l** (241 mg, 0.5 mmol) in dichloromethane (3 mL), DDQ (227 mg, 1mmol) were added successively. The resulting solution was stirred at room temperature for 3.5 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with dichloromethane. The organic extract was washed with sodium bicarbonate solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **3l** as a yellow solid (177 mg, 0.37 mmol, 75%); m. p. 236-238 °C.^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.23 (s, 3H), 2.34 (s, 3H),2.47 (s, 3H), 6.92 (s, 1H), 7.29 (s, 2H), 7.39 (s, 2H), 7.67 (s, 3H), 7.77 (s, 1H), 8.42 (s, 3H), 9.01 (s, 1H)ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.4, 18.7, 21.7, 115.6, 119.6, 128.5, 128.7, 129.1, 129.5, 129.6, 131.2, 132.0, 132.1, 132.2, 132.3, 134.0, 134.5, 136.6, 143.9, 145.1, 148.9, 150.9, 151.6, 155.3 ppm. HRMS (ESI) calcd for $C_{28}H_{23}N_4O_2S$ $[M+H]^+$ 479.1542; found 479.1542.

4-(6-tosyl-6H-indolo[2,3-*b*]quinolin-11-yl)benzonitrile (3m) :



To a solution of **1a** (227 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), (4-cyanophenyl)boronic acid (110 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively. The resulting solution was stirred at 75-75°C under argon atmosphere for 3 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with ethyl acetate. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated. To a solution of this crude product in dichloromethane (3 mL), DDQ (227 mg, 1mmol) were added successively. The resulting solution was stirred at room temperature for 2 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with dichloromethane. The organic extract was washed with sodium bicarbonate solution, dried over anhydrous Na_2SO_4 and concentrated The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **3m** as a yellow solid (199 mg, 0.42 mmol, 85%); m. p. 236-238 °C.^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.30 (s, 3H), 7.04-7.13 (m, 4H), 7.18 (d, *J* = 8.4 Hz, 2H), 7.23-7.41 (m, 3H), 7.52 (t, *J* = 8 Hz, 1H), 7.63-7.72 (m, 2H), 7.82 (d,*J* = 6.5 Hz, 2H), 8.21 (d,*J* = 23 Hz, 1H), 8.51 (d,*J* = 7.2 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.6, 113.3, 118.4, 122.2, 123.1, 123.6, 124.1, 125.5, 126.8, 127.1, 127.6, 128.5, 129.8, 130.3, 132.2, 132.7, 134.9, 135.7, 145.5, 151.5, 164.6 ppm. HRMS (ESI) calcd for $C_{29}H_{19}N_3NaO_2S$ $[M+Na]^+$ 496.1096; found 496.1097.

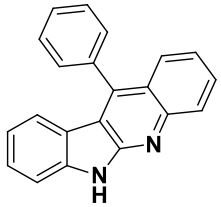
4-(6-tosyl-6H-indolo[2,3-*b*]quinolin-11-yl)benzaldehyde(3n) :



To a solution of **1a** (227 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), (4-formylphenyl)boronic acid(113 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05

mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively. The resulting solution was stirred at 75-75°C under argon atmosphere for 3 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with ethyl acetate. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated. To a solution of this crude product in dichloromethane (3 mL), DDQ (227 mg, 1mmol) were added successively. The resulting solution was stirred at room temperature for 2.5 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with dichloromethane. The organic extract was washed with sodium bicarbonate solution, dried over anhydrous Na_2SO_4 and concentrated The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **3n** as a yellow solid (186 mg, 0.39 mmol, 78%); m. p. 236-238 °C.^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.33 (s, 3H), 6.81 (s, 1H), 7.09 (s, 1H), 7.25 (s, 3H), 7.45-7.62 (m, 5H), 7.77 (s, 1H), 8.17-8.29 (m, 4H), 8.51-8.53 (m, 1H),10.22 (s, 1H)ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.7, 115.0, 116.4, 122.5, 122.7, 123.7, 124.7, 125.5, 128.5, 129.2, 129.4, 129.5, 129.6, 130.0, 130.2, 130.6, 136.0, 136.8, 139.9, 140.8, 142.2, 145.2, 146.3, 150.5, 191.8 ppm. HRMS (ESI) calcd for $C_{29}H_{21}N_2O_3S$ $[M+H]^+$ 477.1273; found 477.1274.

11-phenyl-6H-indolo[2,3-*b*]quinolone (4) :



To a solution of **3a** (224 mg, 0.5 mmol) in methanol (3 mL), NaOH (40 mg, 1mmol), water(2 mL)were added successively. The resulting solution was refluxed in a sealed tube for 5 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with ethyl acetate. The organic extract was washed with water, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **4** as a yellow solid (121 mg, 0.41mmol, 82%).^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.45 (s, 3H), 6.97 (t, J = 7 Hz, 1H), 7.06 (d, J = 8 Hz, 1H), 7.25-7.45 (m, 2H), 7.48 (d, J = 8 Hz, 1H), 7.49-7.56 (m, 2H), 7.62-7.68 (m, 3H), 7.73-7.78 (m, 2H),7.77 (d,J = 8 Hz, 1H), 9.8 (brs, 1H)ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ110.7, 116.6, 120.2, 121.4, 123.2, 123.3, 124.1, 126.7, 127.1, 128.1, 128.7, 129.1, 129.5, 136.5, 141.2, 143.0, 146.6, 153.0 ppm. HRMS (ESI) calcd for $C_{21}H_{15}N_2$ $[M+H]^+$295.1235; found 295.1236.

II.8. References :

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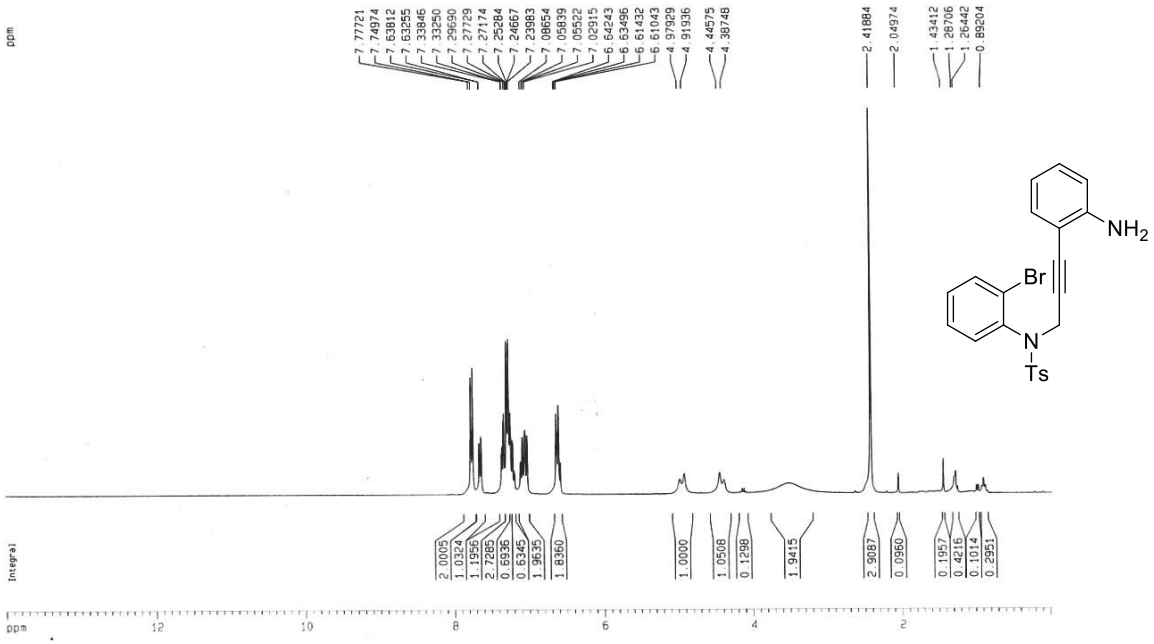
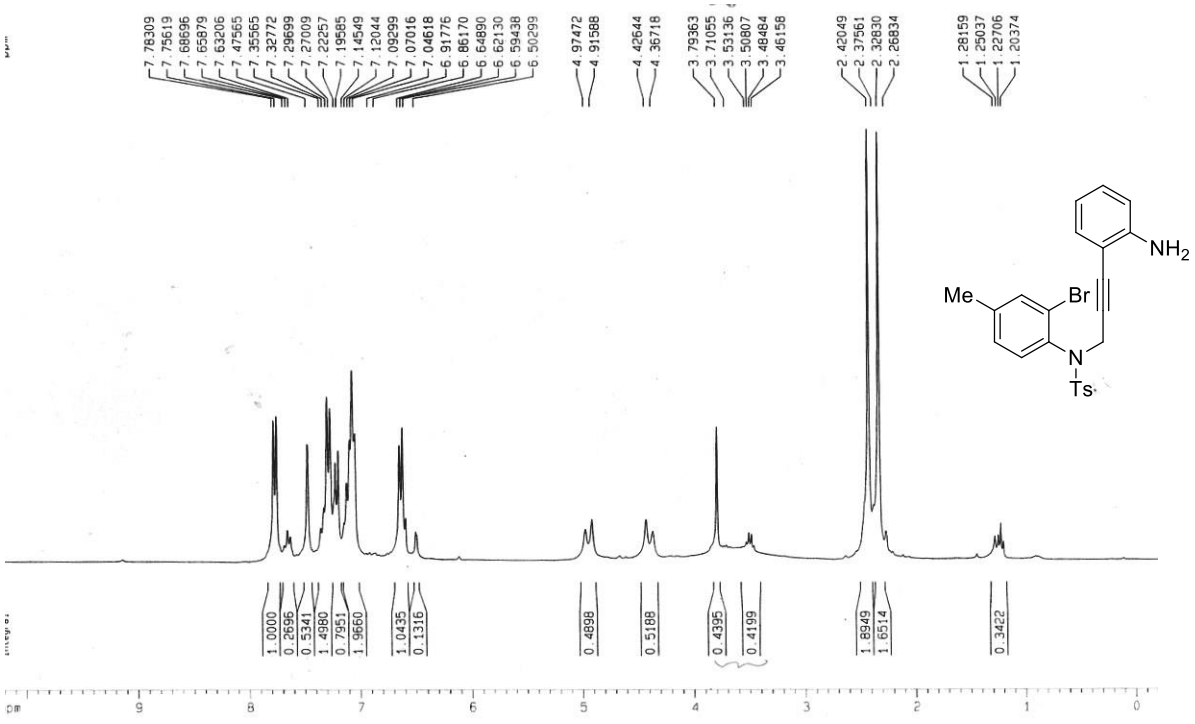
II. 9. Copies of some important ^{1}H and ^{13}C NMR spectra of compounds described in Chapter II

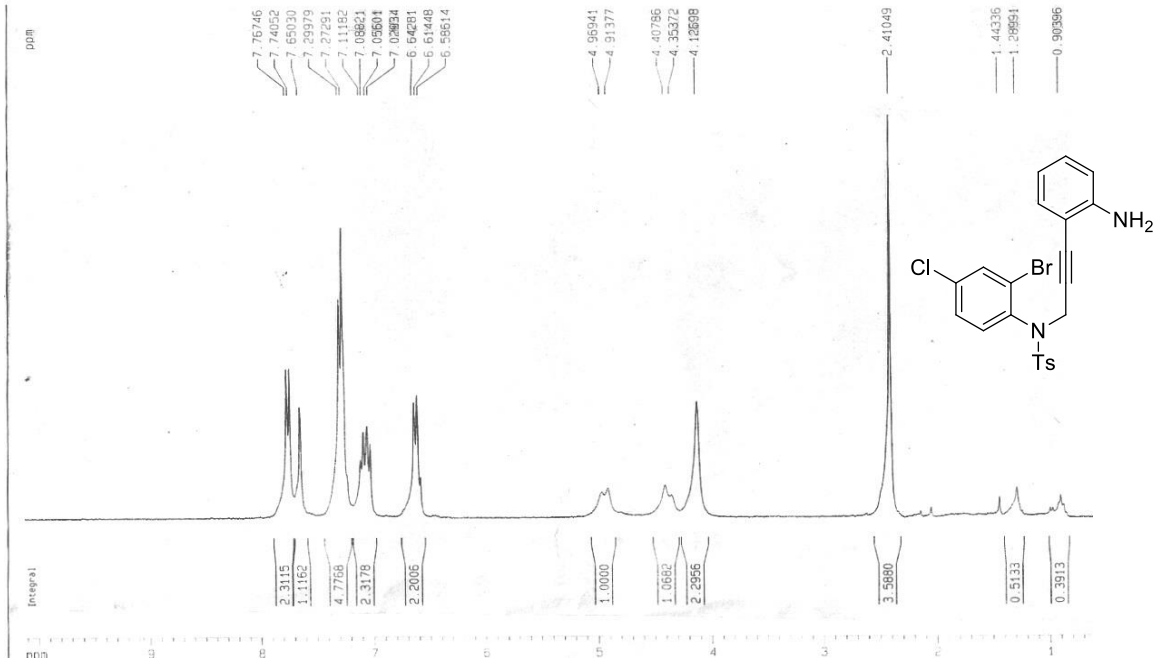
^{1}H NMR spectrum of compound 1a



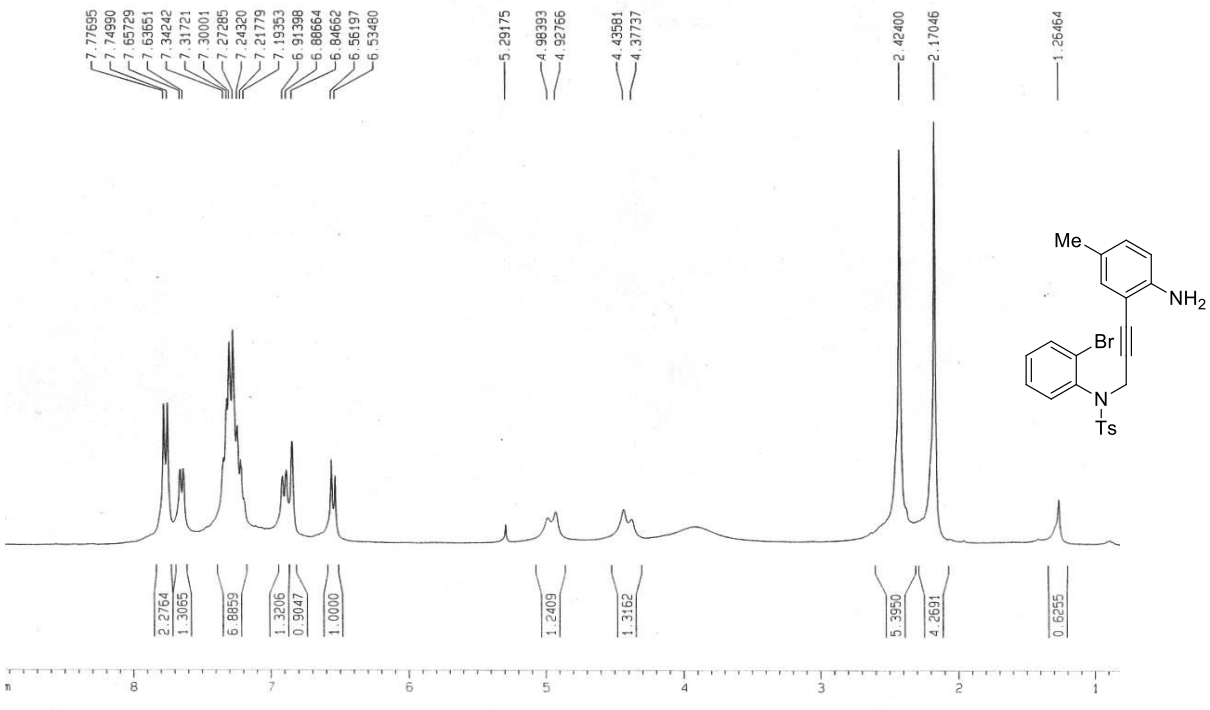
^{1}H NMR spectrum of compound 1b



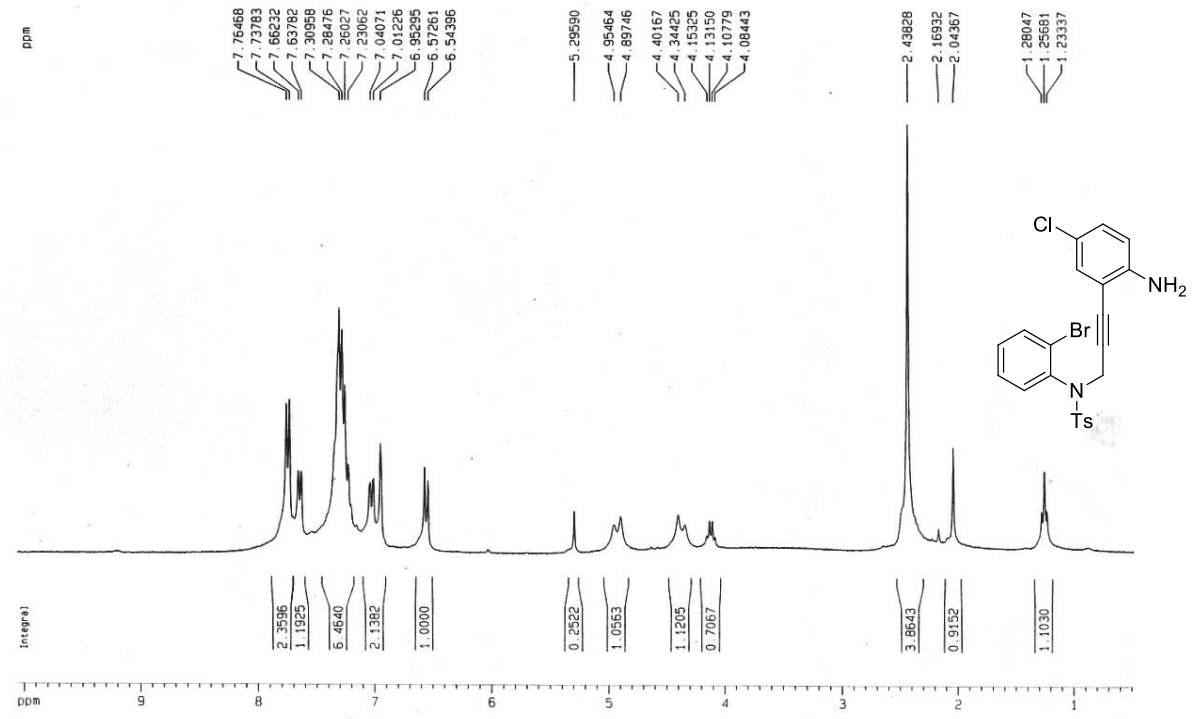
^{1}H NMR spectrum of compound 1c



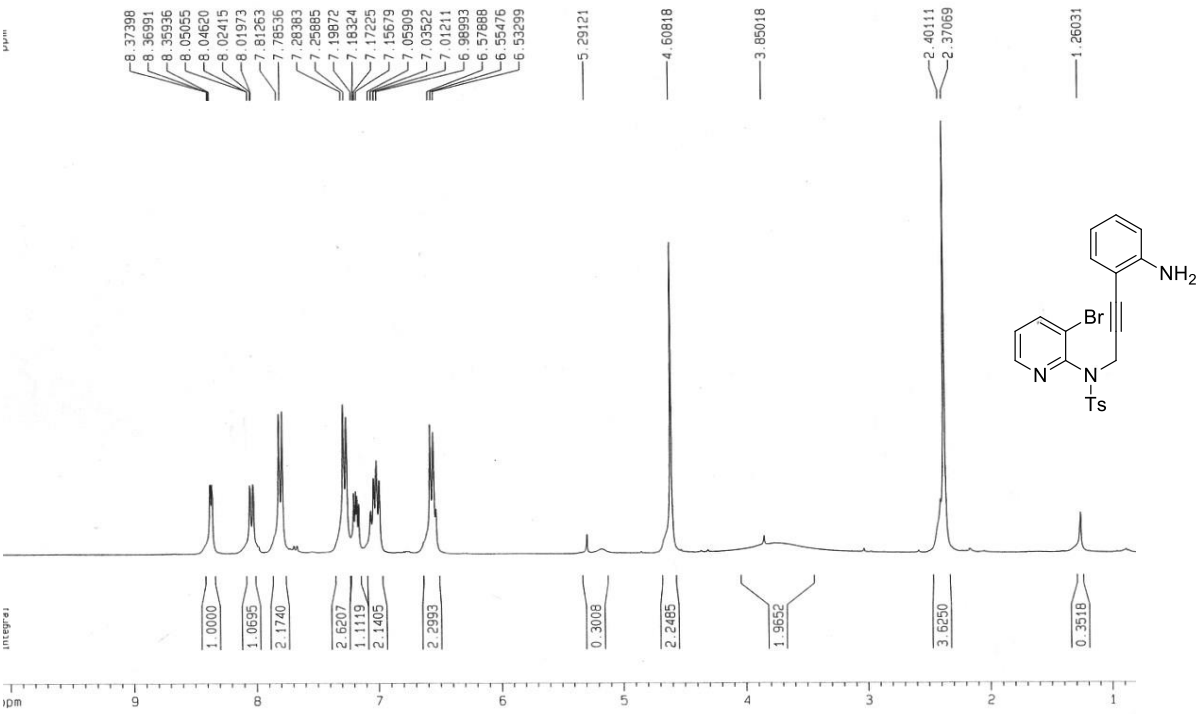
^{1}H NMR spectrum of compound 1d



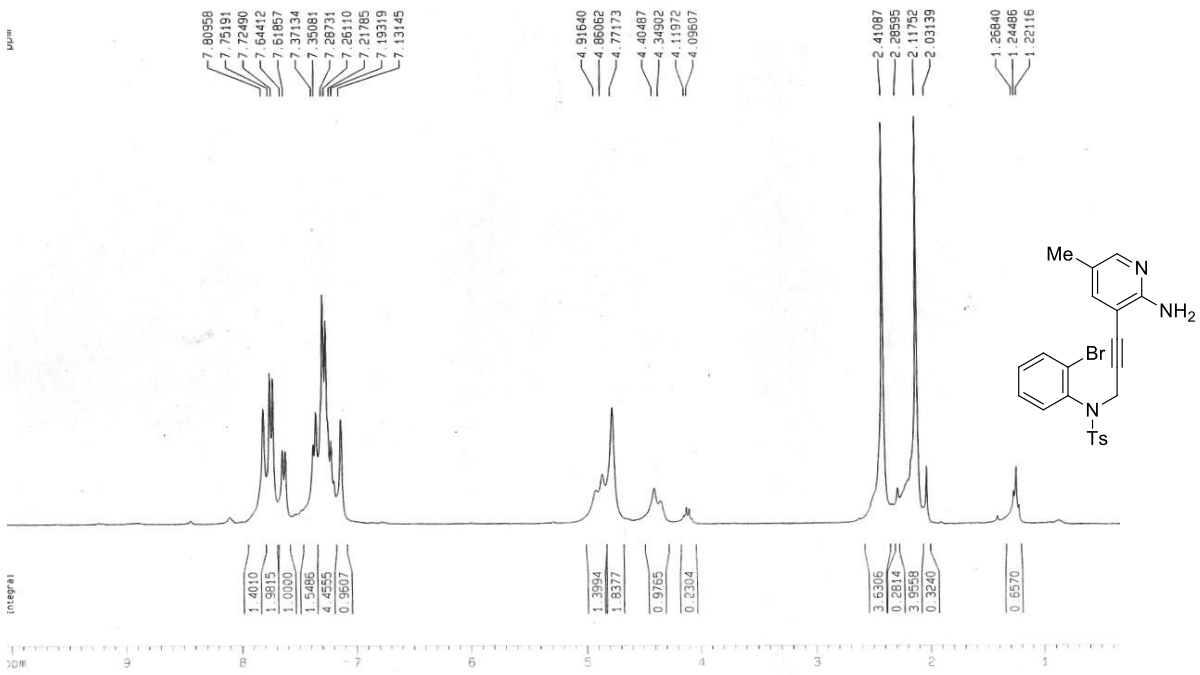
^{1}H NMR spectrum of compound 1e



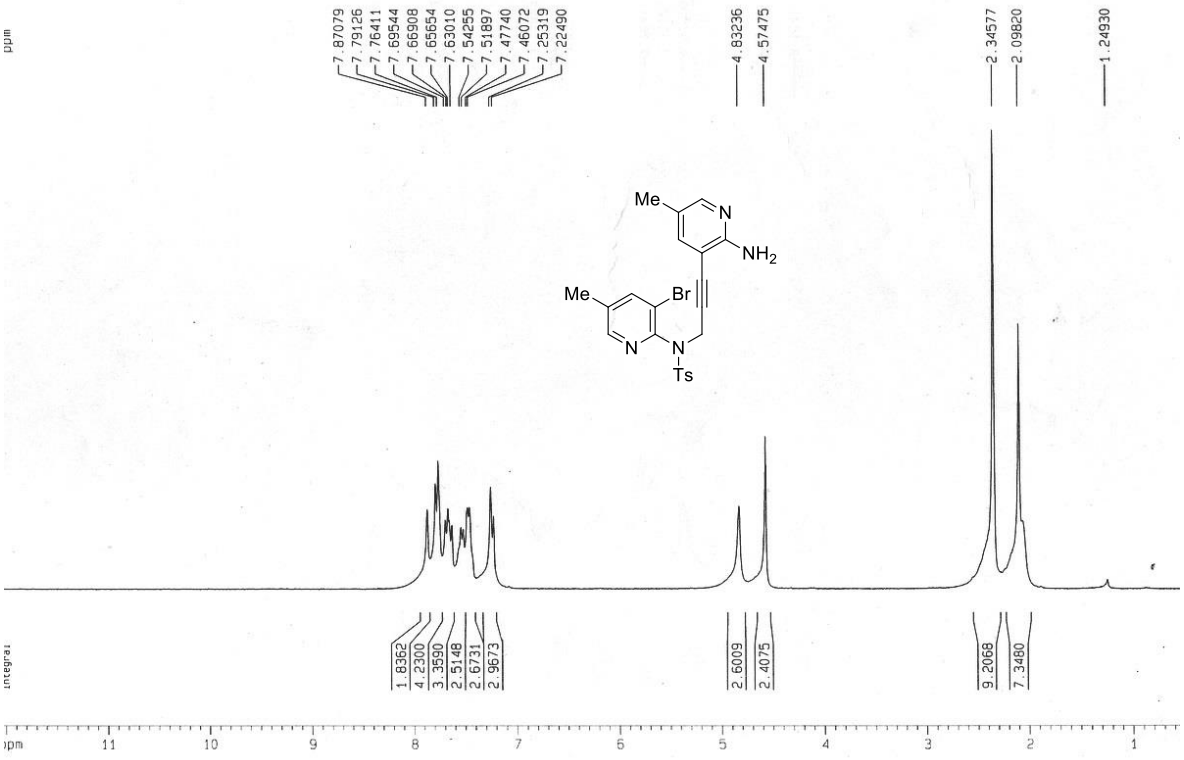
^{1}H NMR spectrum of compound 1f



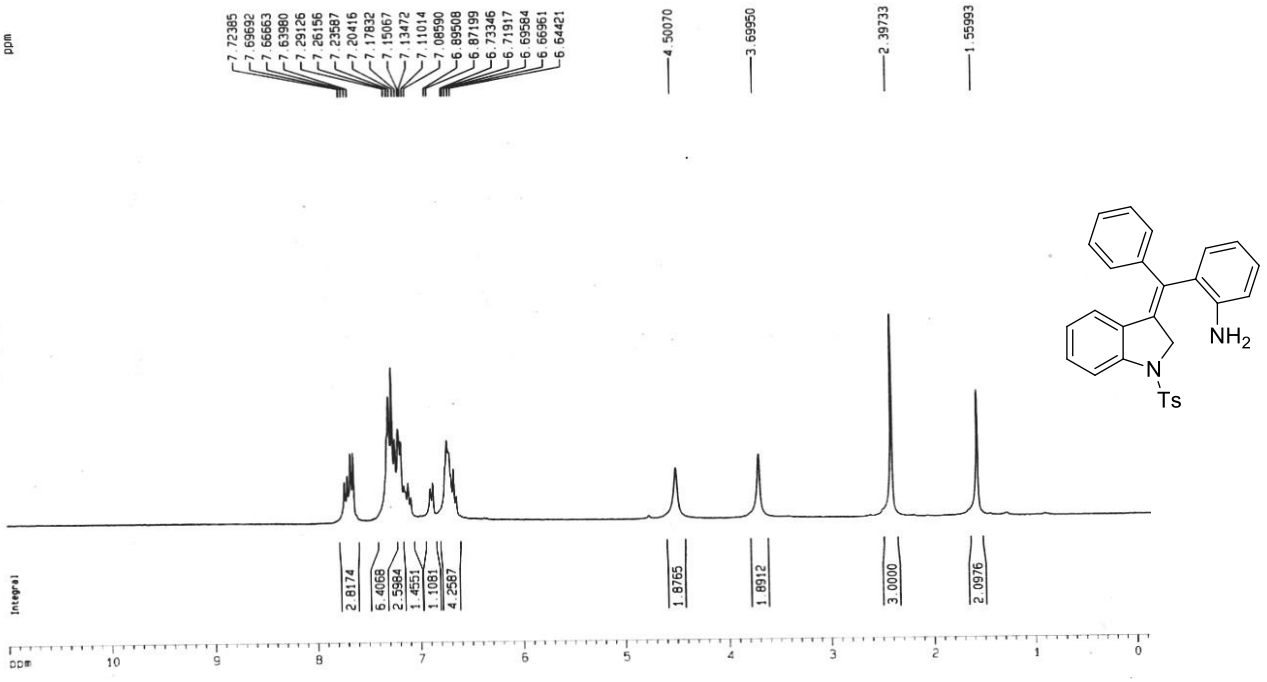
^{1}H NMR spectrum of compound 1g



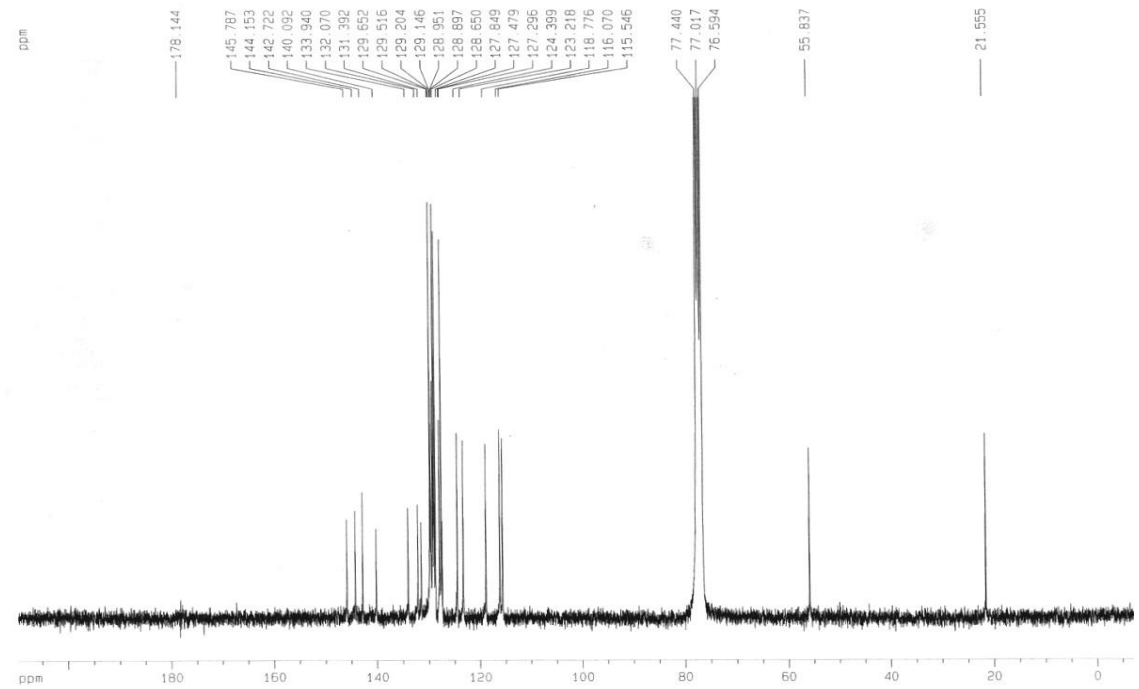
^{1}H NMR spectrum of compound 1h



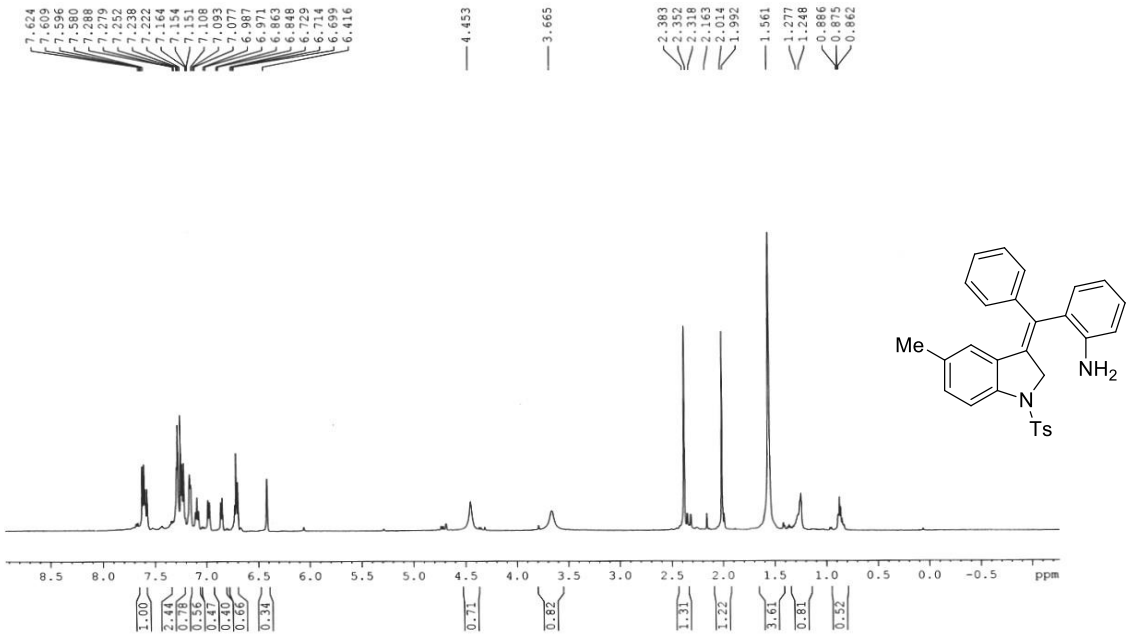
^{1}H NMR spectrum of compound 2a



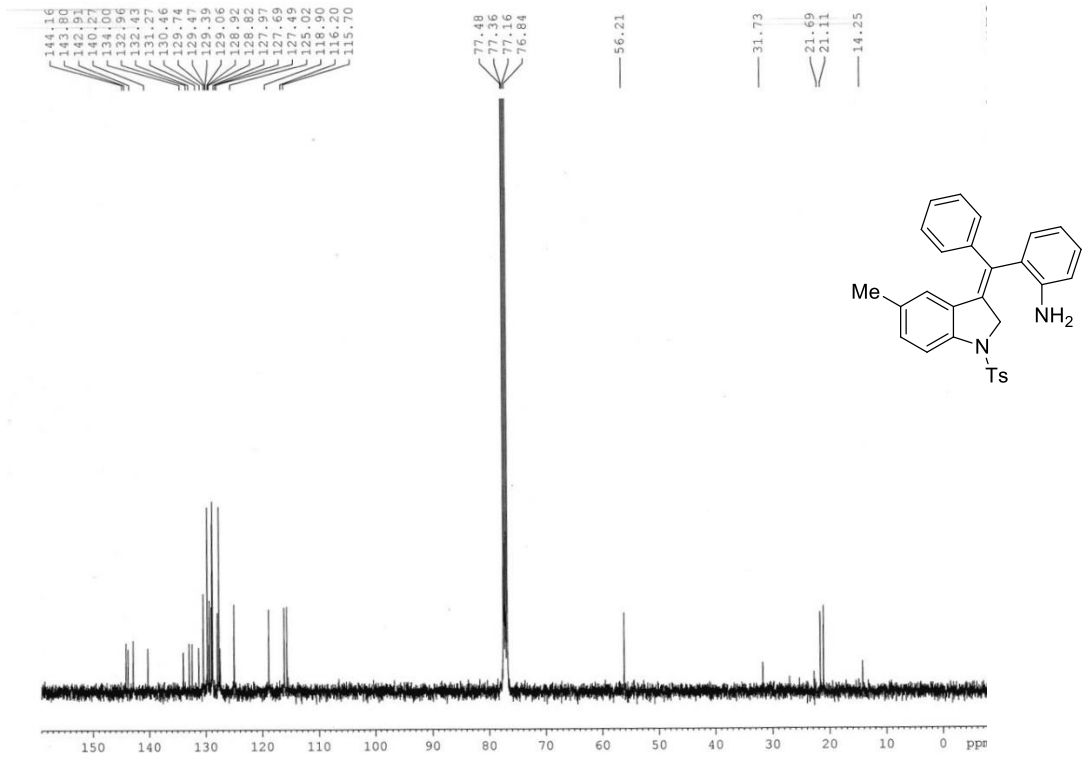
^{13}C NMR spectrum of compound 2a



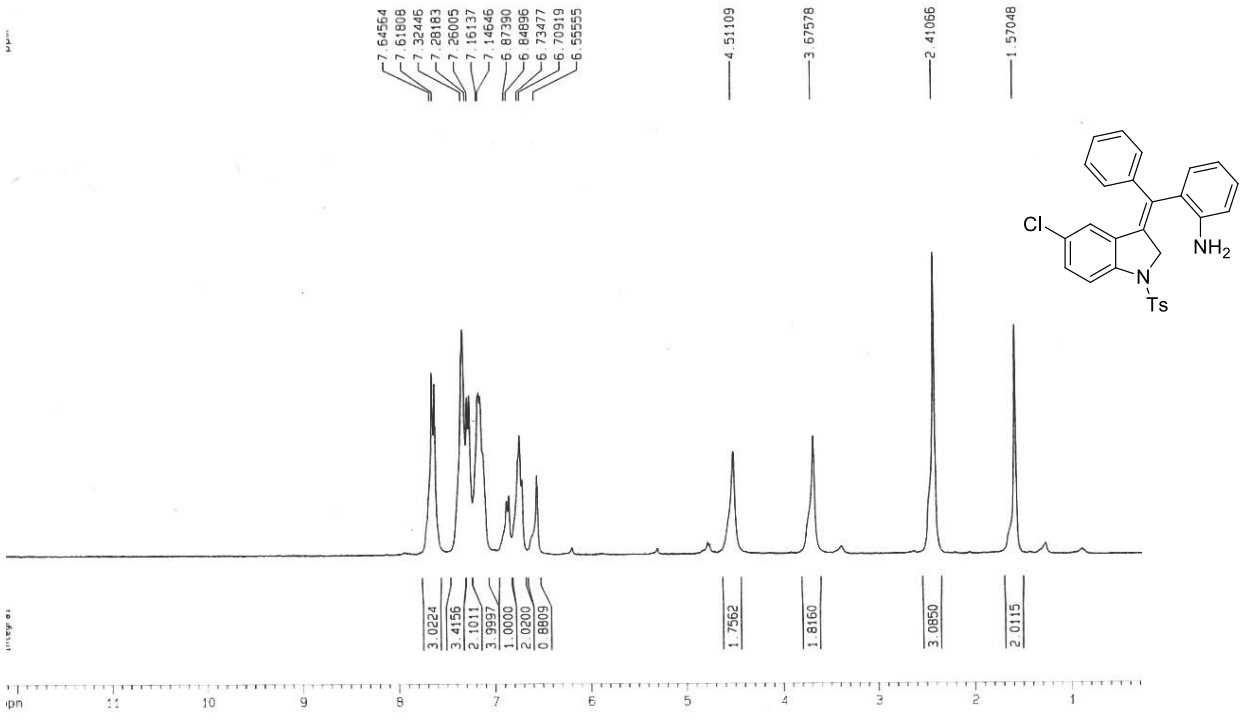
^{1}H NMR spectrum of compound 2b



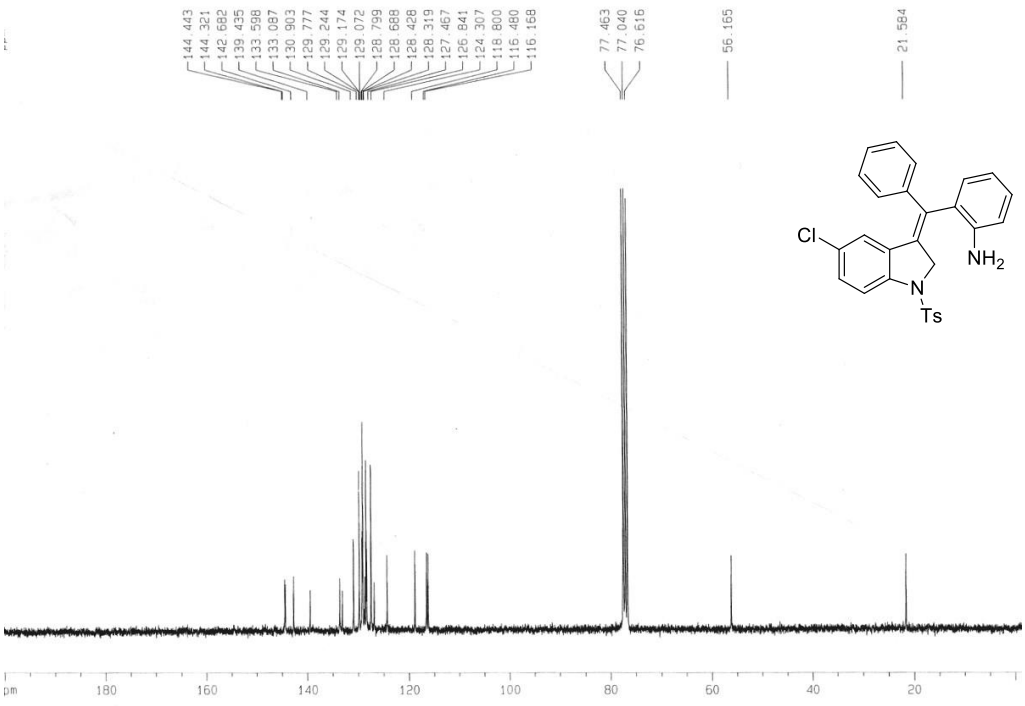
^{13}C NMR spectrum of compound 2b



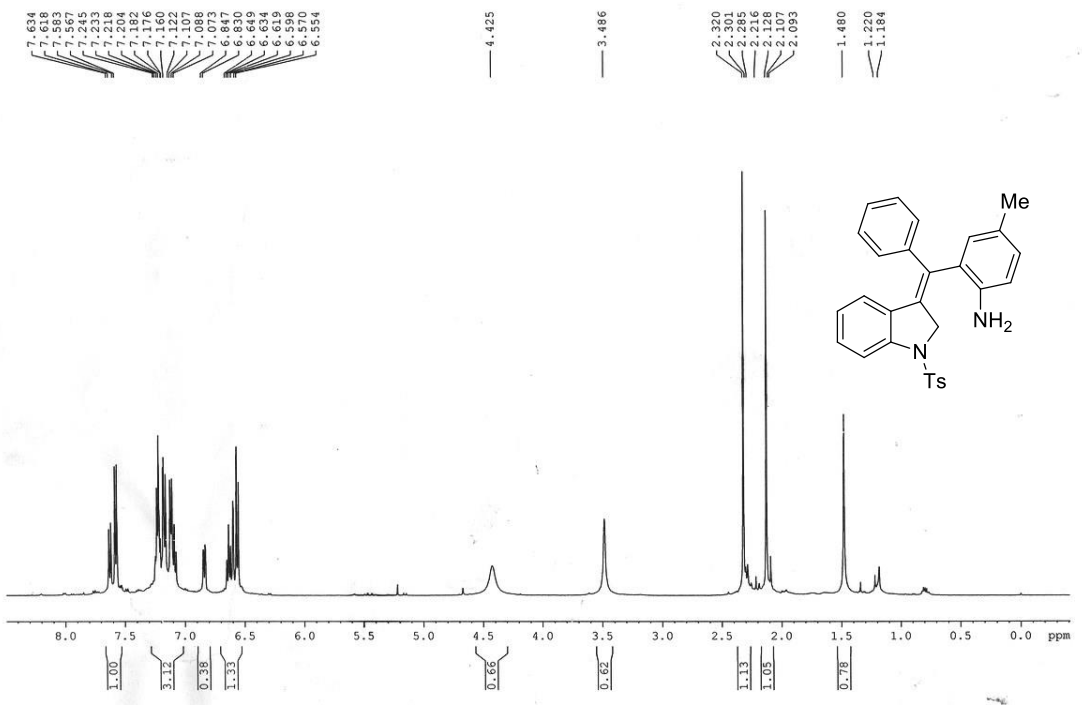
^{1}H NMR spectrum of compound 2c



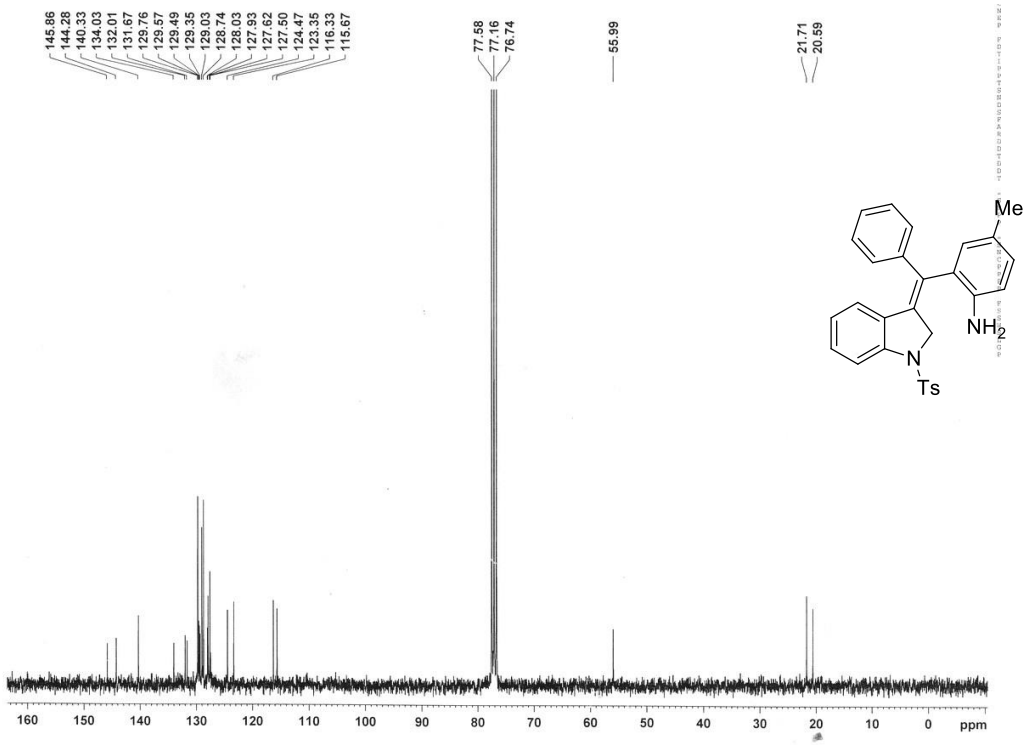
^{13}C NMR spectrum of compound 2c



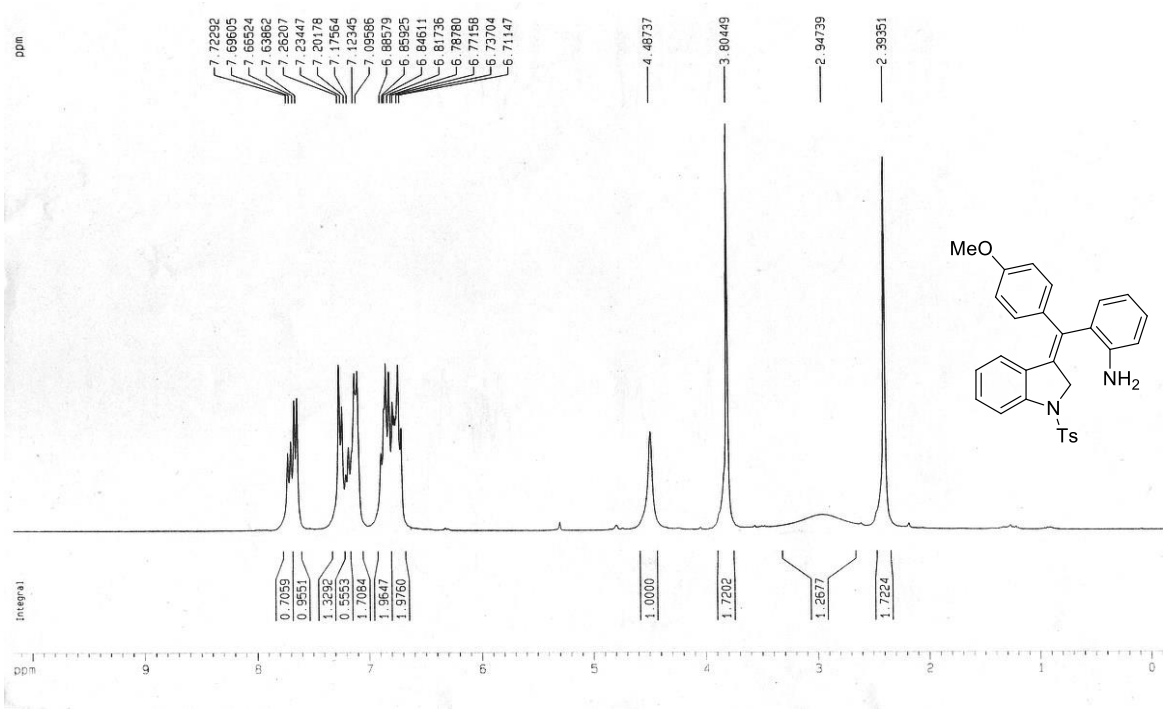
^{1}H NMR spectrum of compound 2d



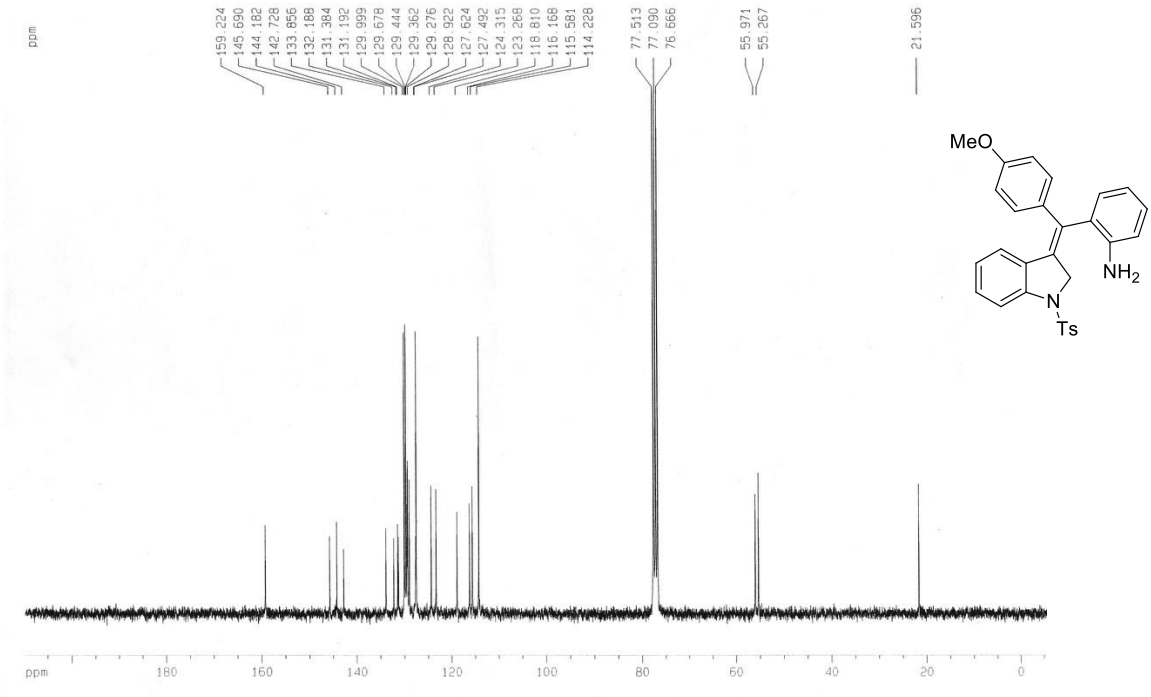
^{13}C NMR spectrum of compound 2d



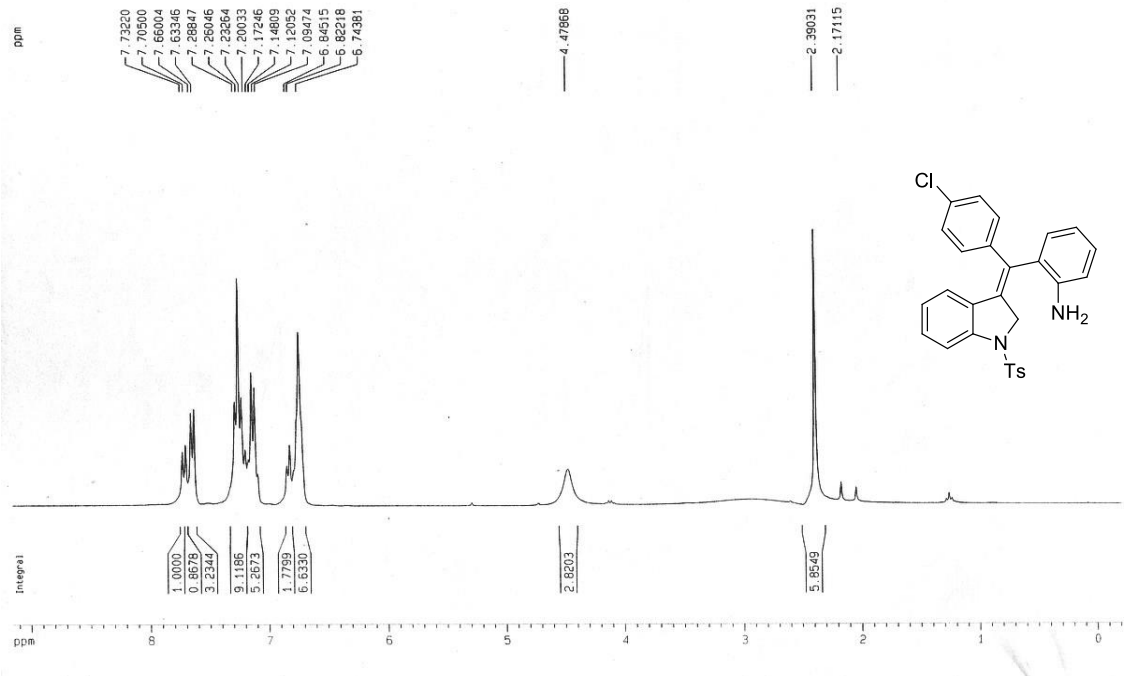
^{1}H NMR spectrum of compound 2e



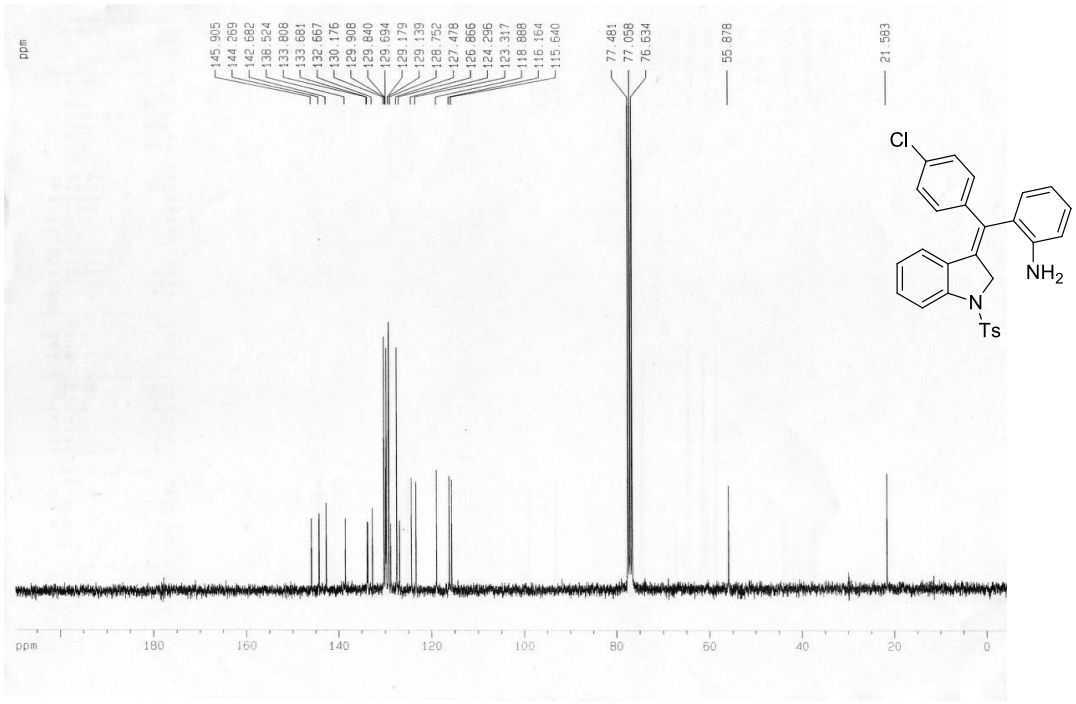
^{13}C NMR spectrum of compound 2e



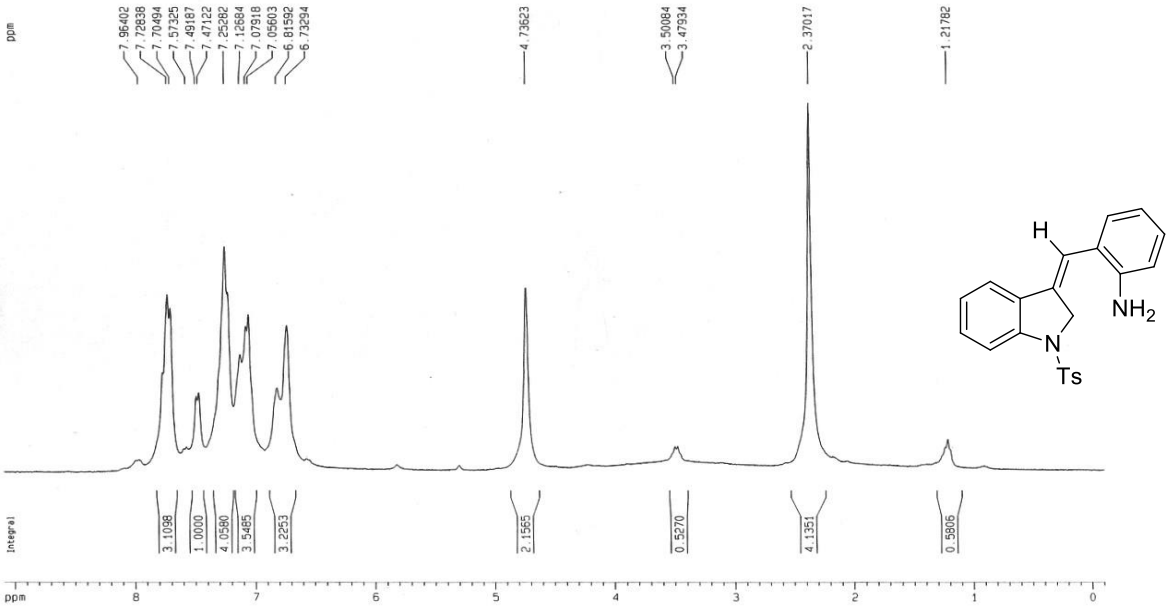
^{1}H NMR spectrum of compound 2f



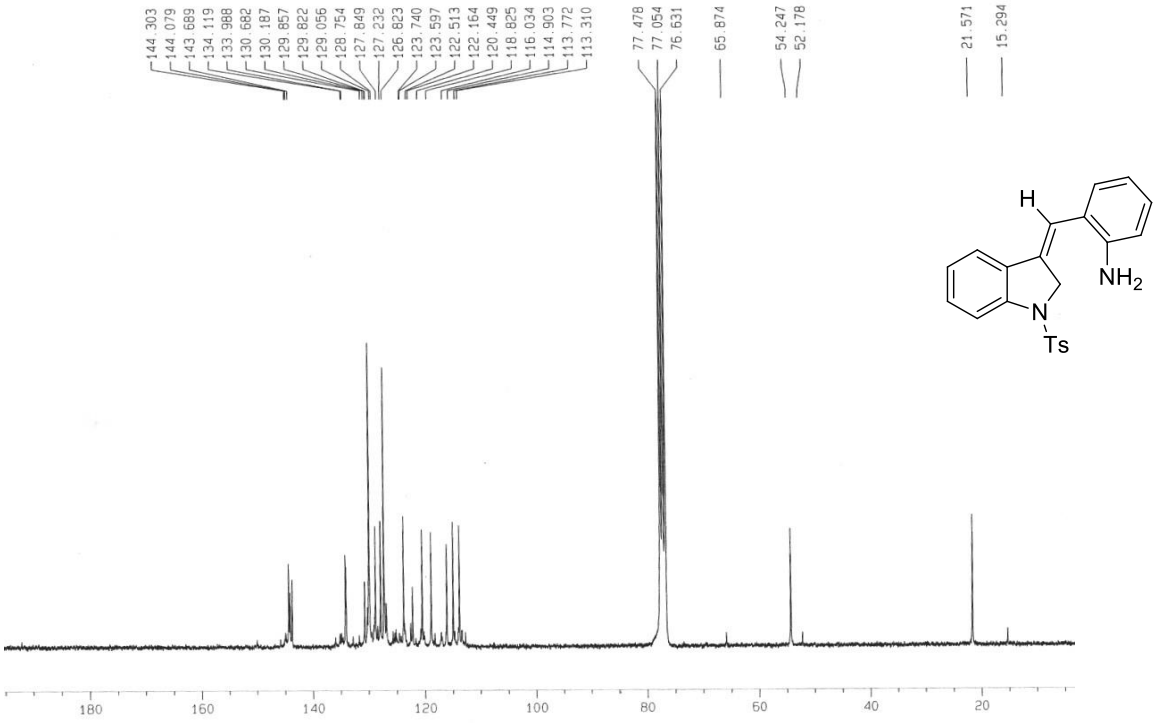
^{13}C NMR spectrum of compound 2f



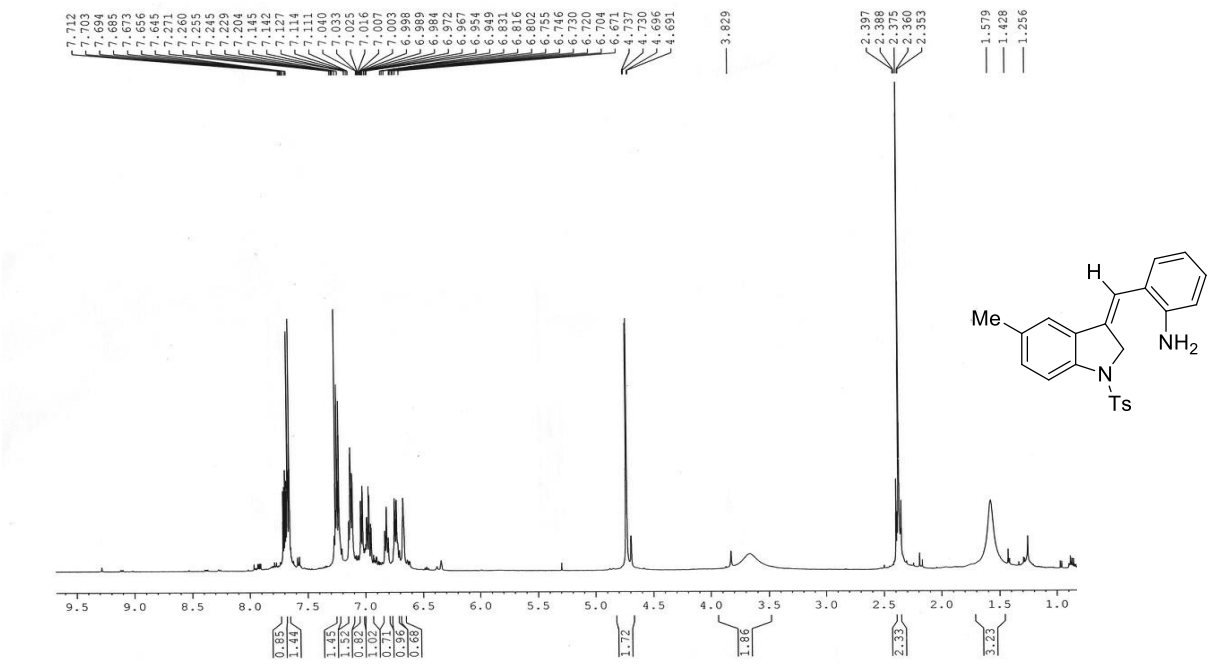
^{1}H NMR spectrum of compound 2g



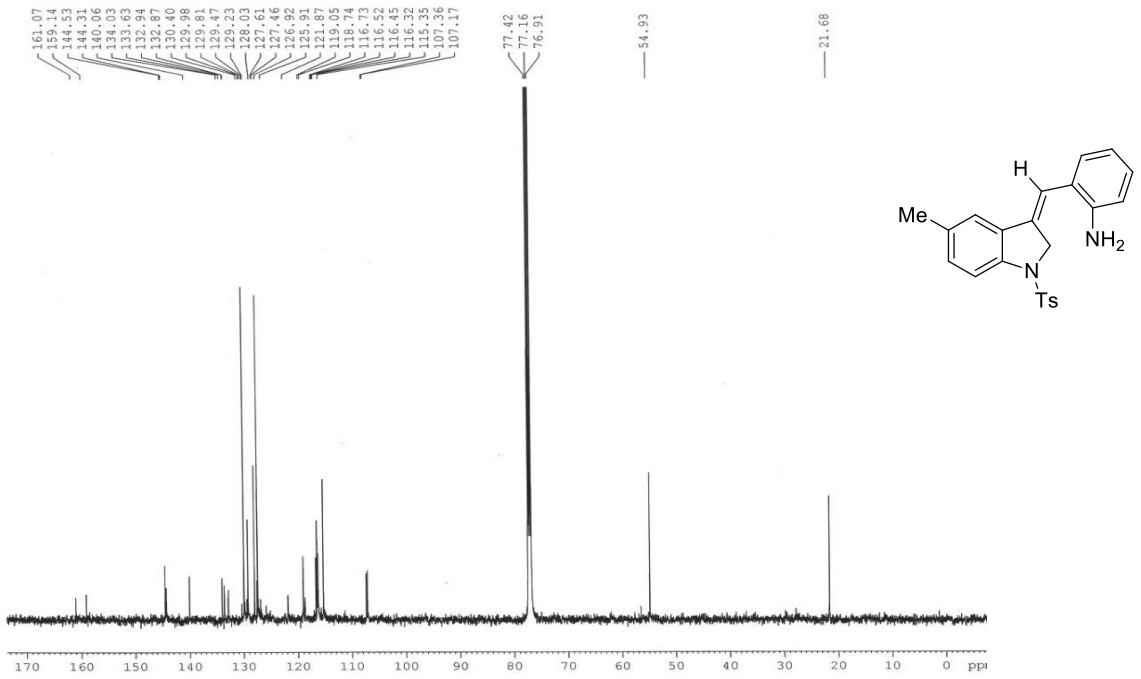
^{13}C NMR spectrum of compound 2g



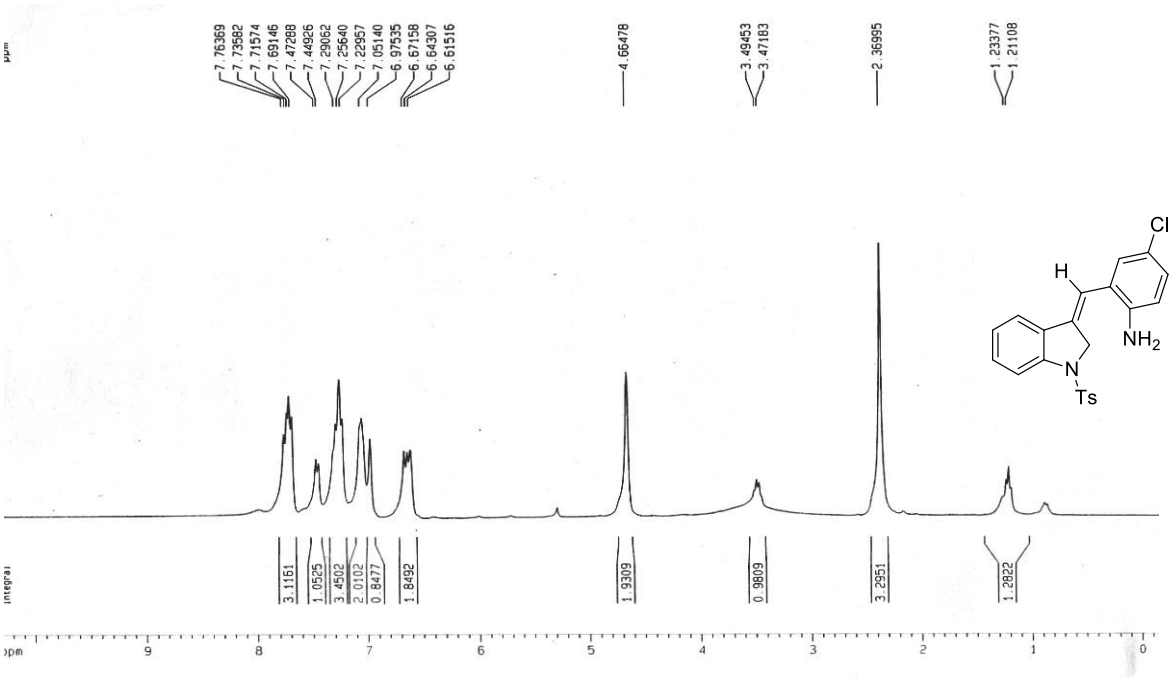
^{1}H NMR spectrum of compound 2h



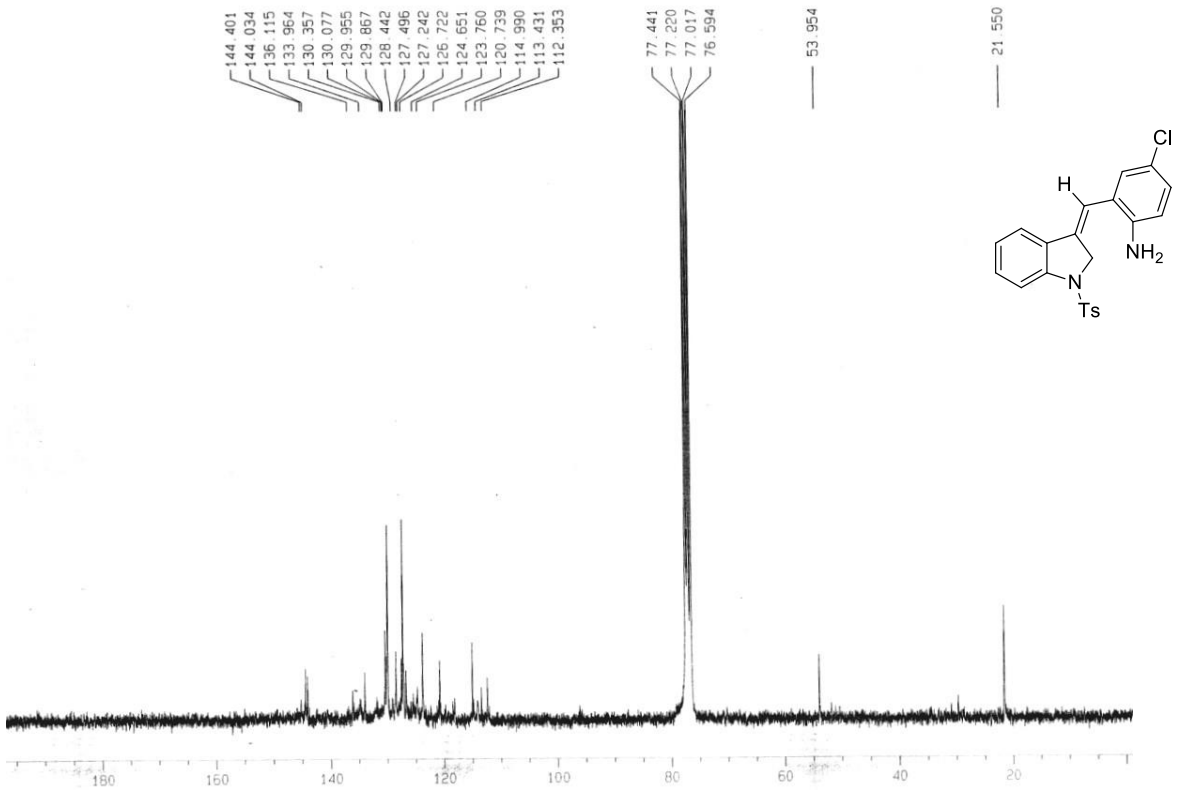
^{13}C NMR spectrum of compound 2h



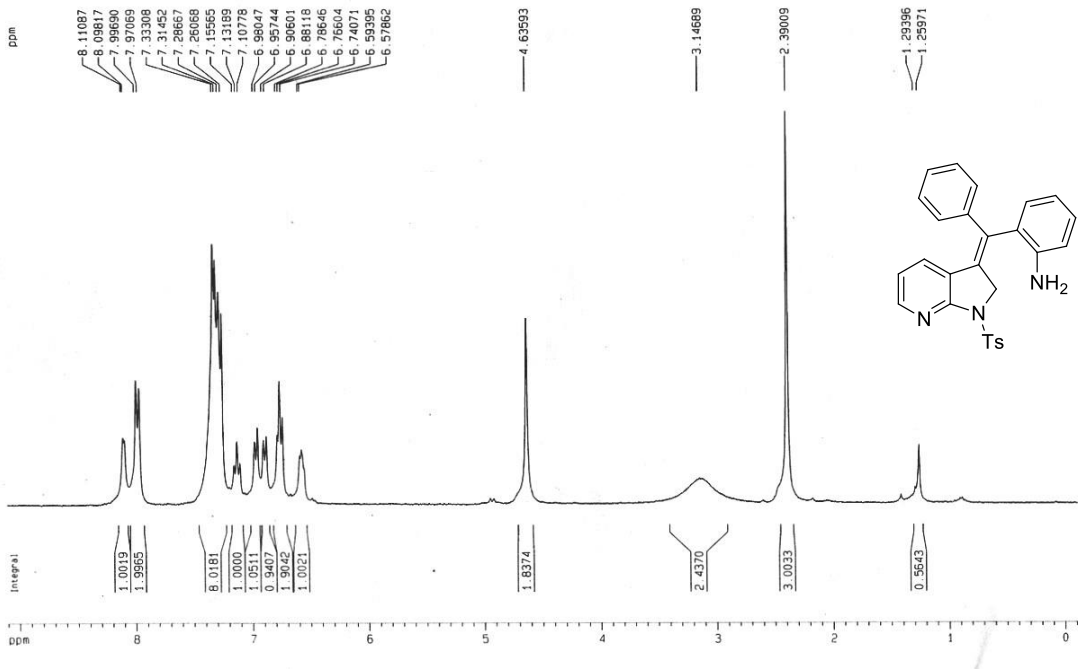
^{1}H NMR spectrum of compound 2i



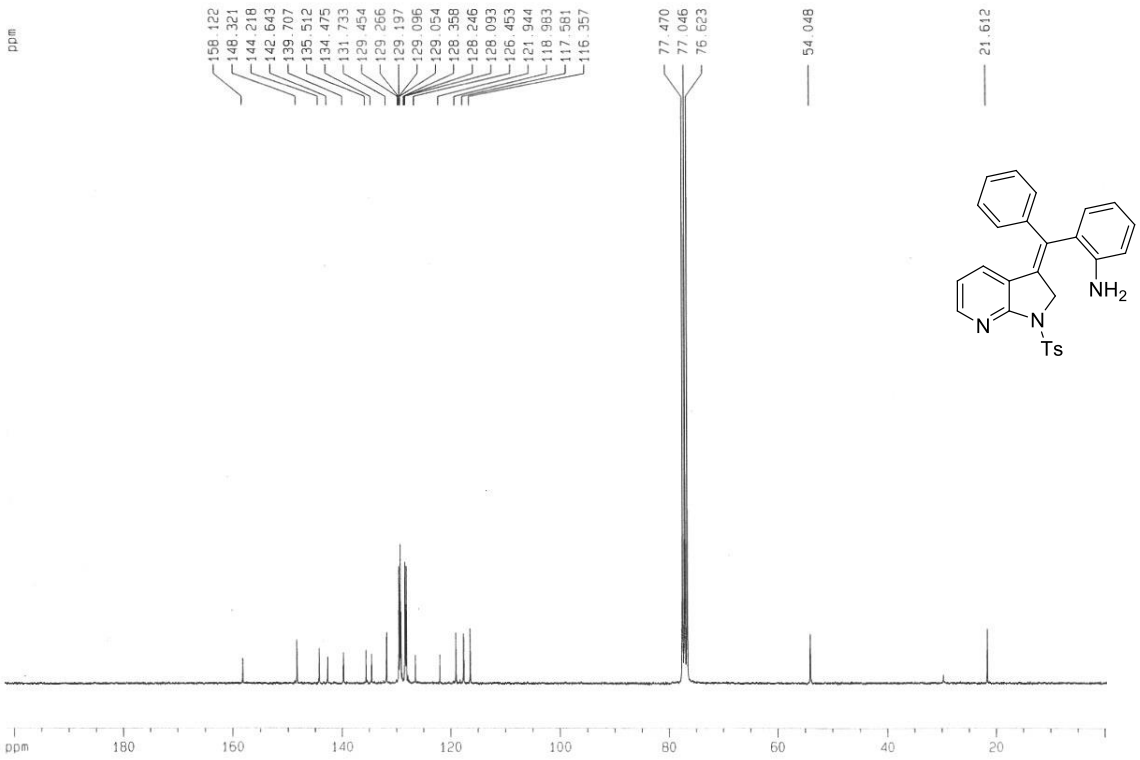
^{13}C NMR spectrum of compound 2i



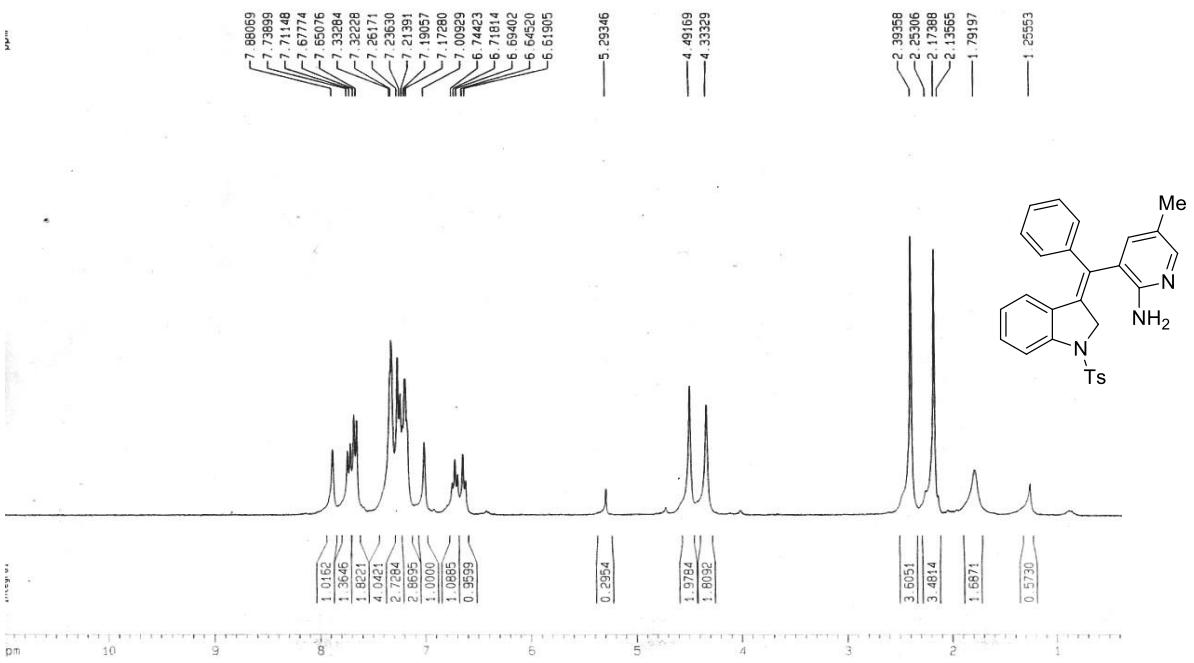
^{1}H NMR spectrum of compound 2j



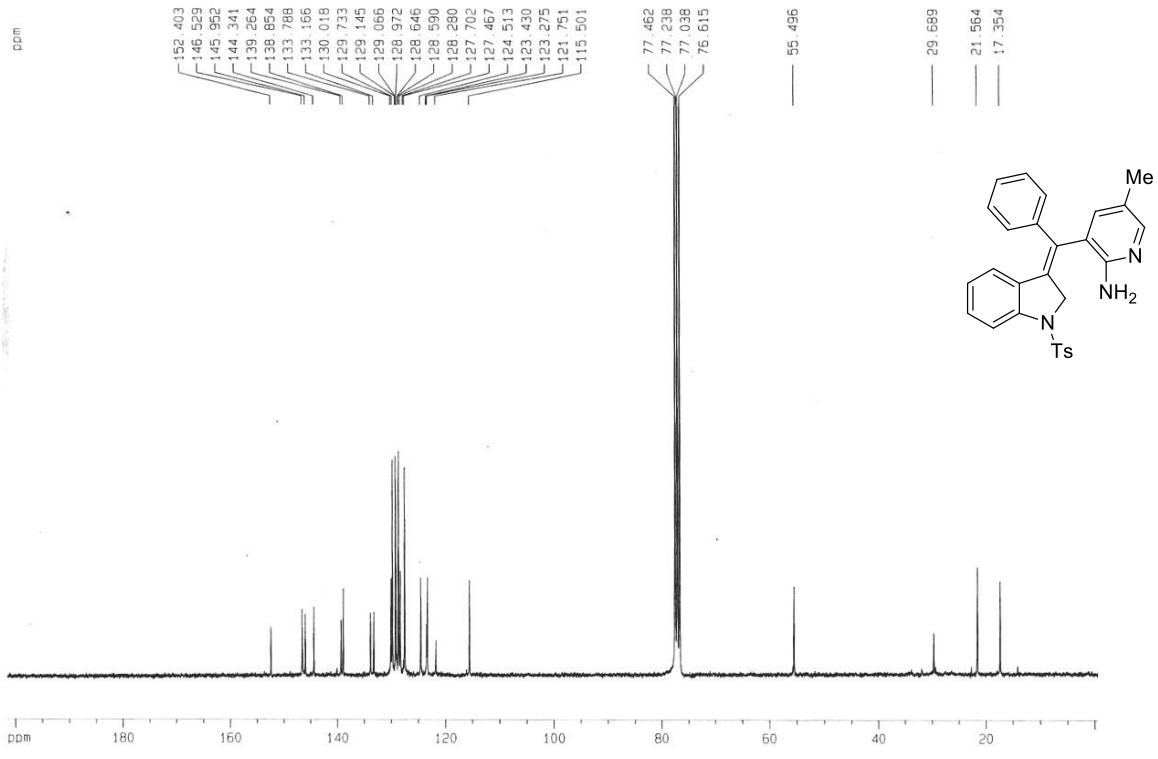
^{13}C NMR spectrum of compound 2j



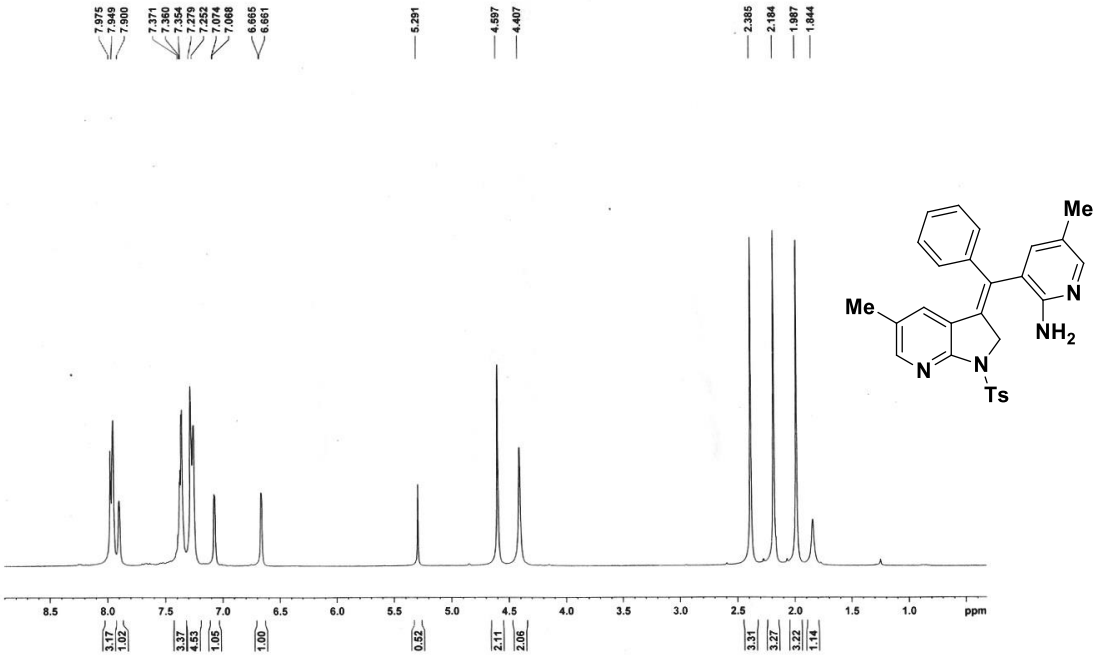
^{1}H NMR spectrum of compound 2k



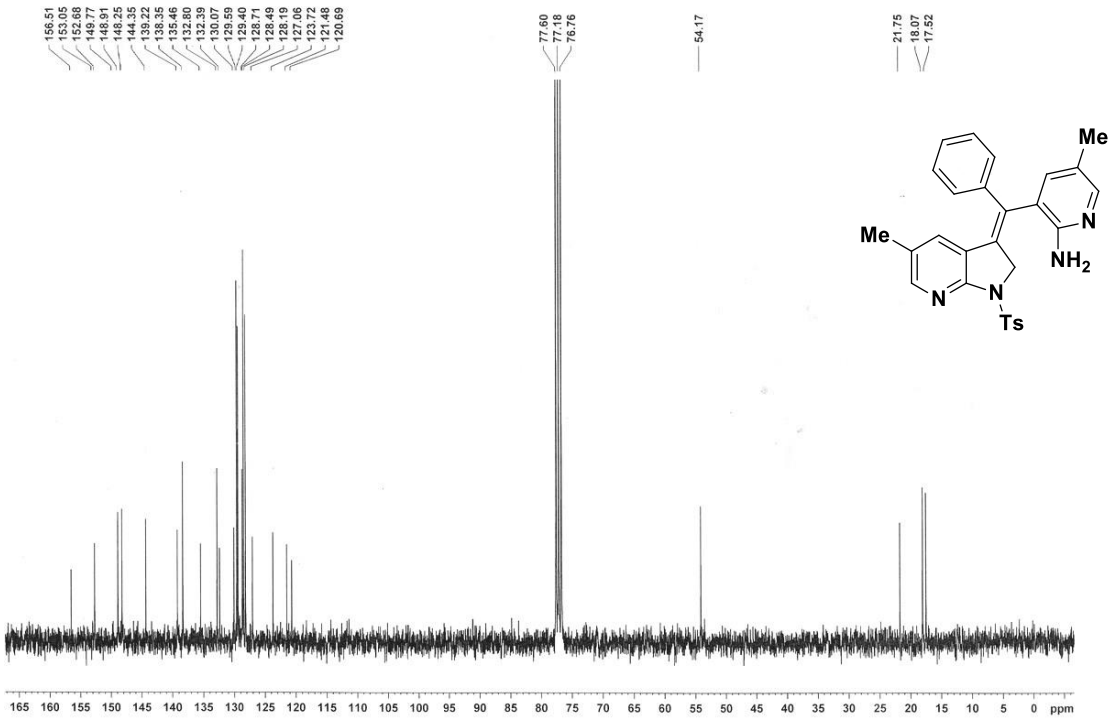
^{13}C NMR spectrum of compound 2k



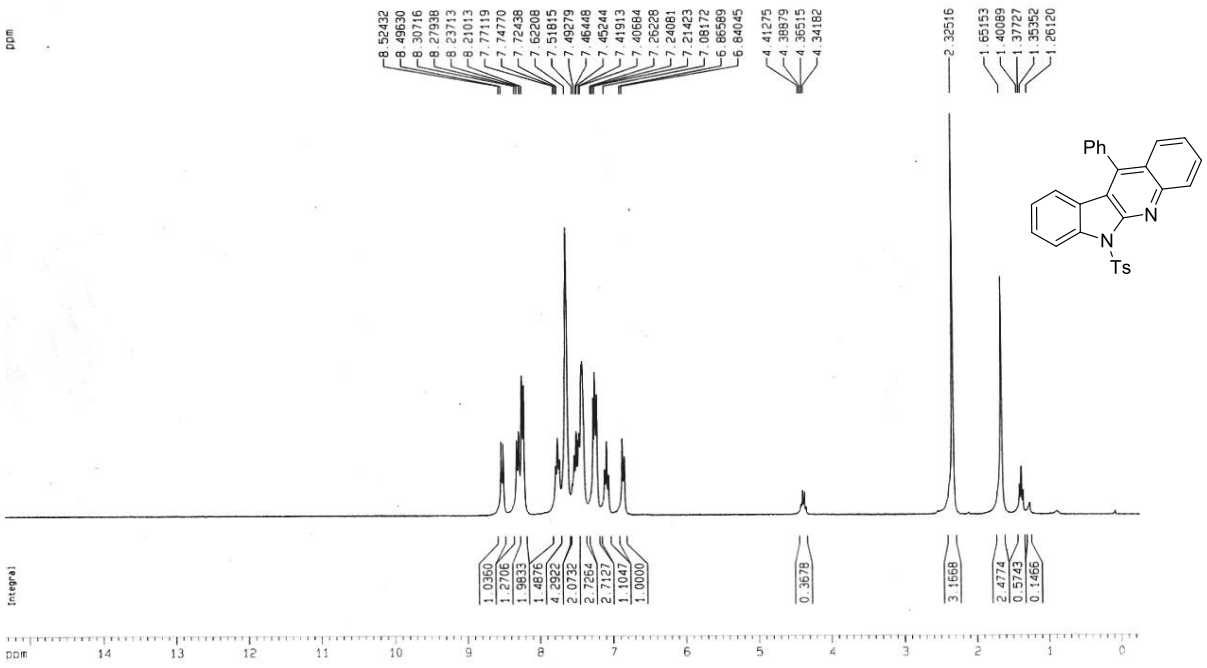
^{1}H NMR spectrum of compound 2l



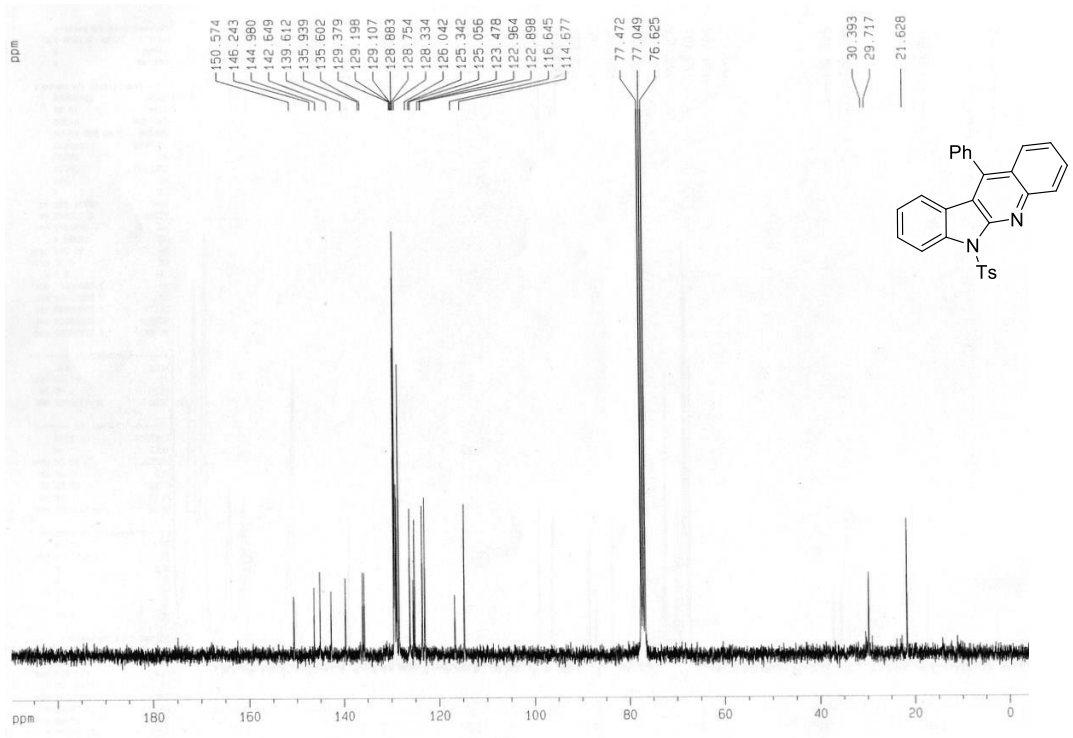
^{13}C NMR spectrum of compound 2l



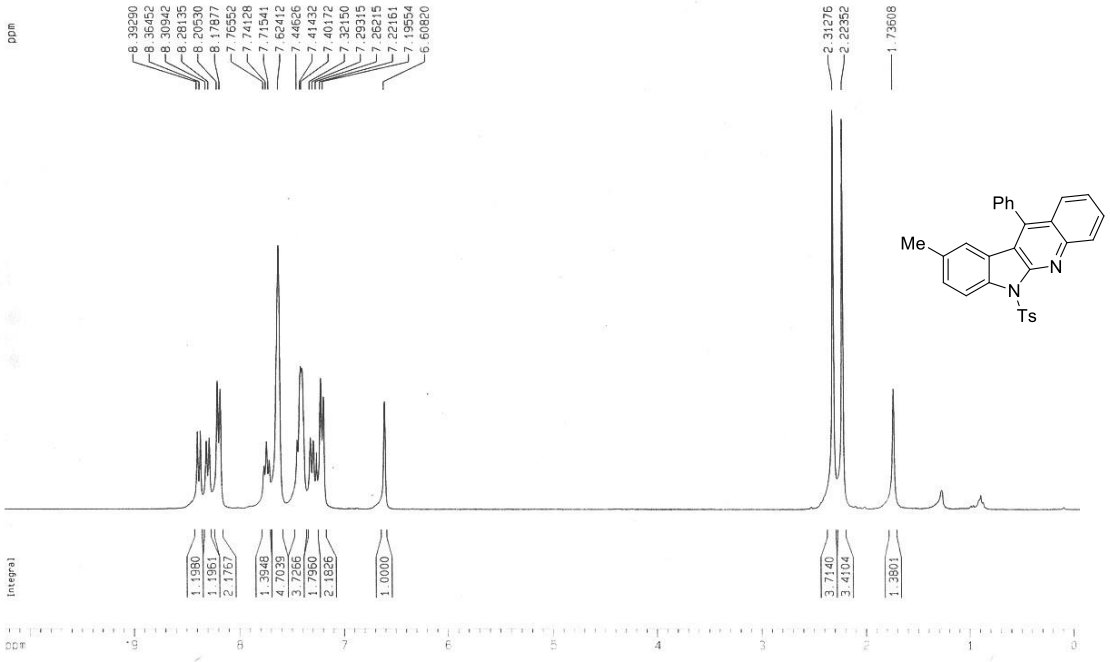
^{1}H NMR spectrum of compound 3a



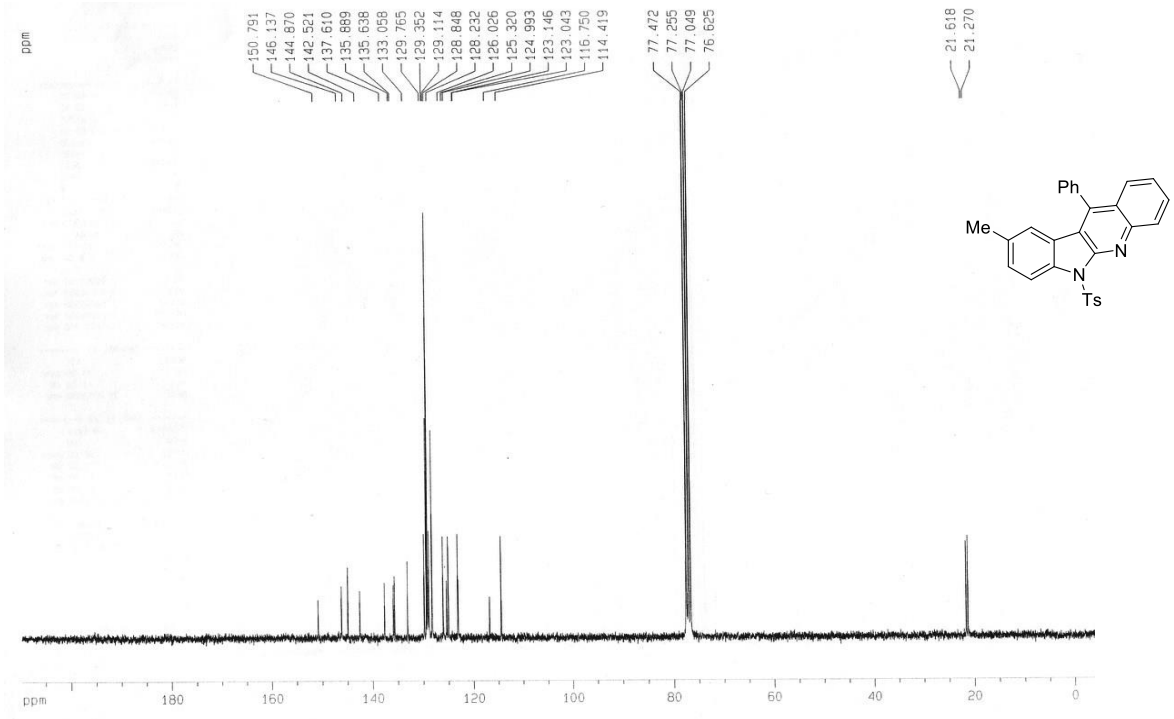
^{13}C NMR spectrum of compound 3a



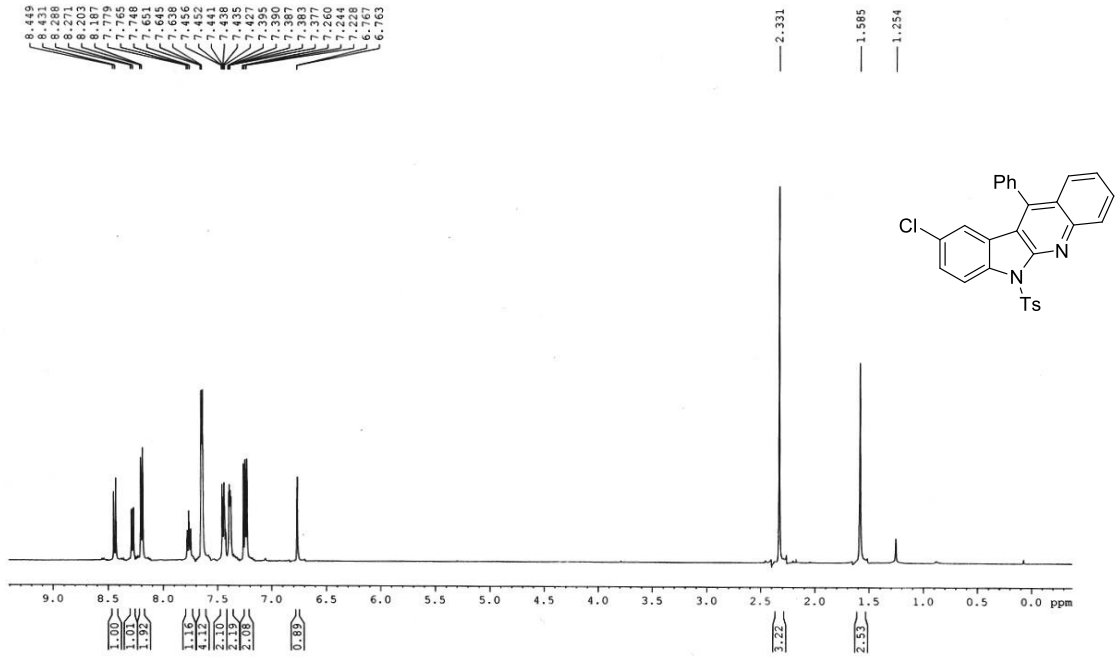
^{1}H NMR spectrum of compound **3b**



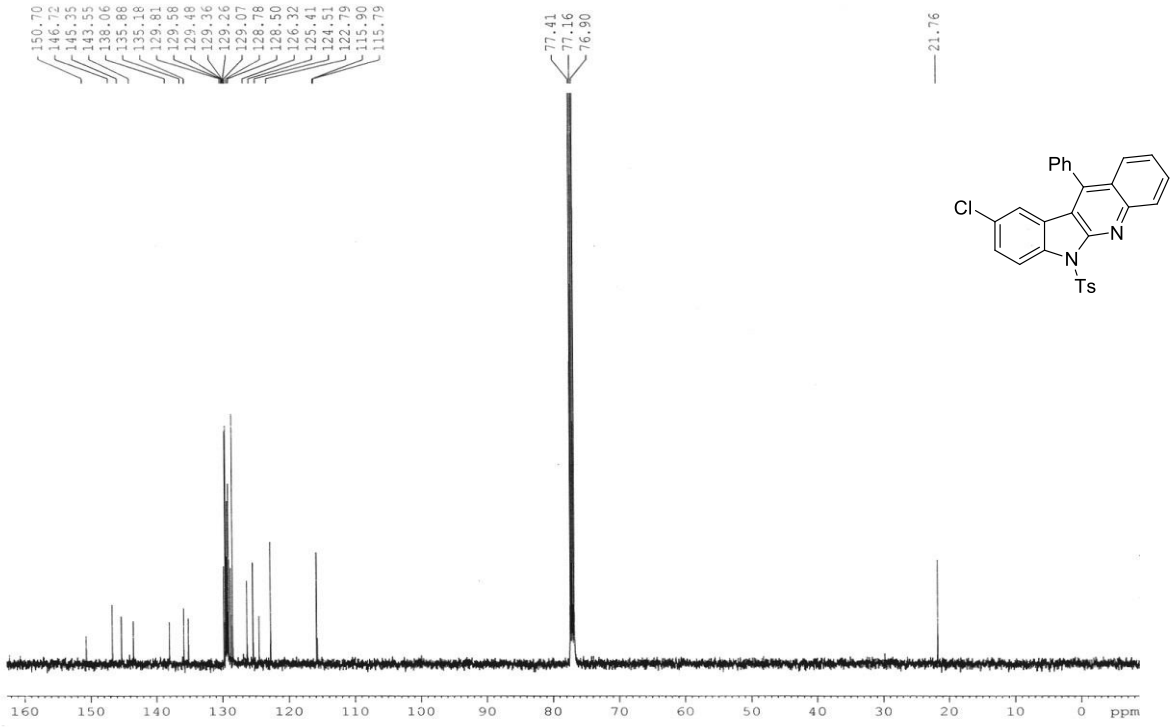
^{13}C NMR spectrum of compound 3b



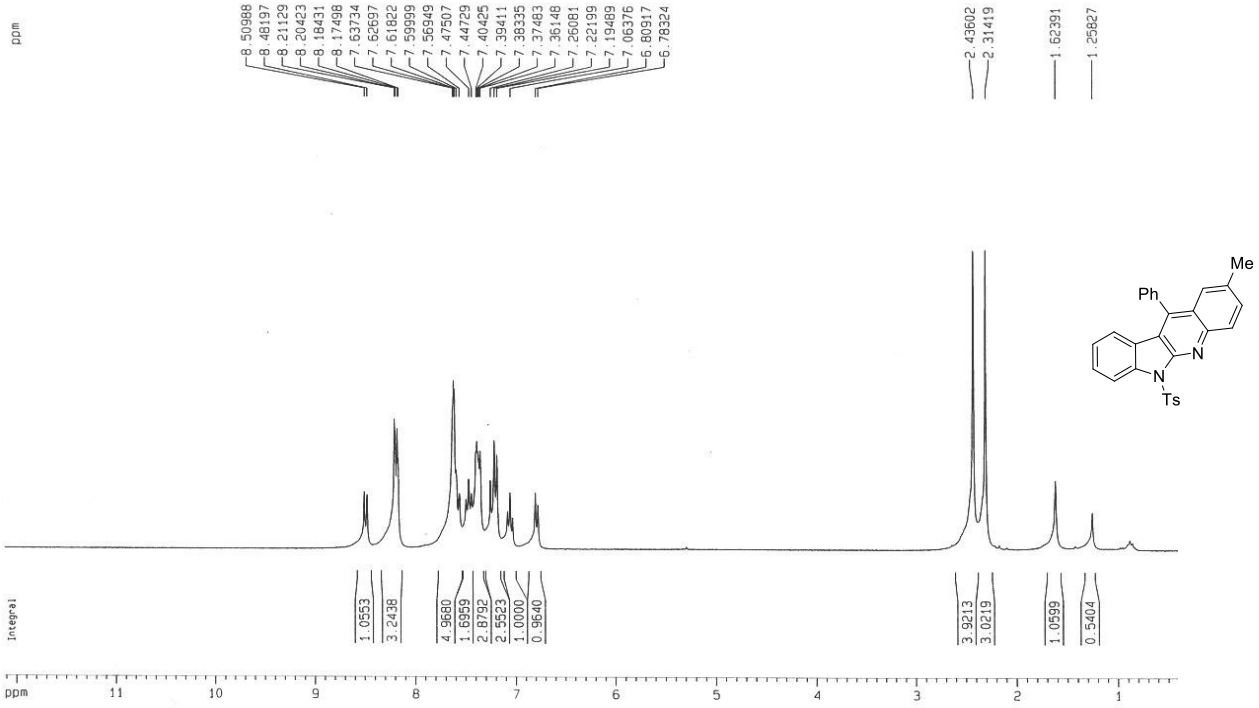
^{1}H NMR spectrum of compound 3c



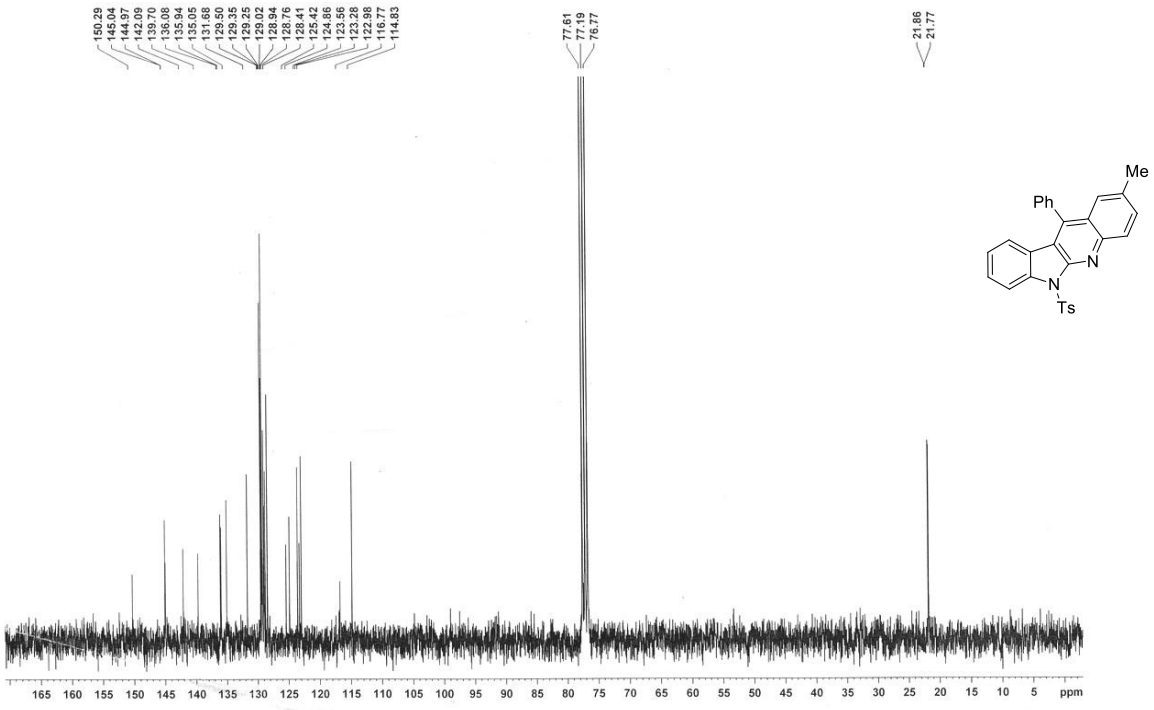
^{13}C NMR spectrum of compound 3c



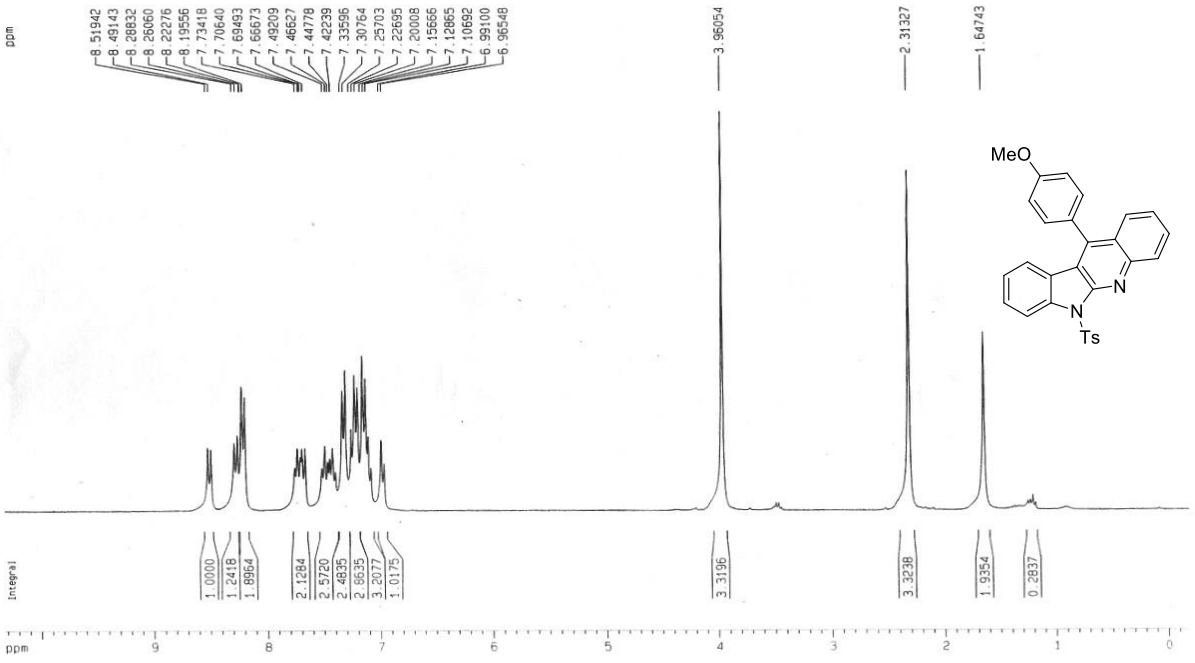
^{1}H NMR spectrum of compound 3d



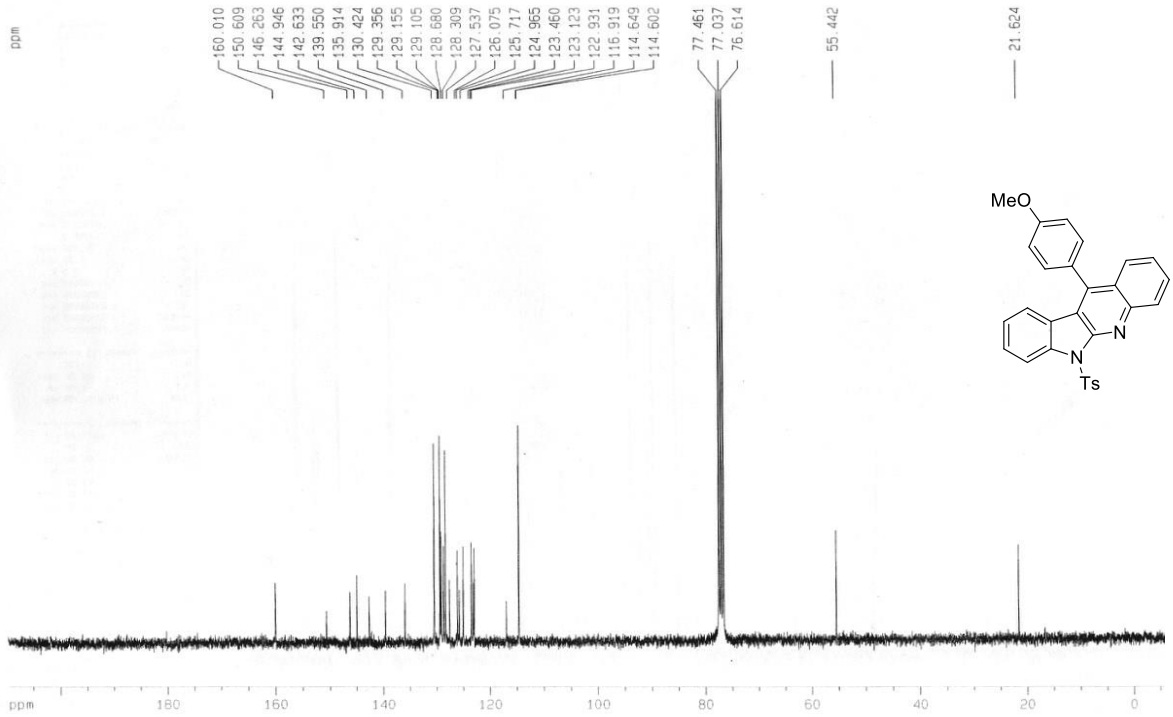
^{13}C NMR spectrum of compound 3d



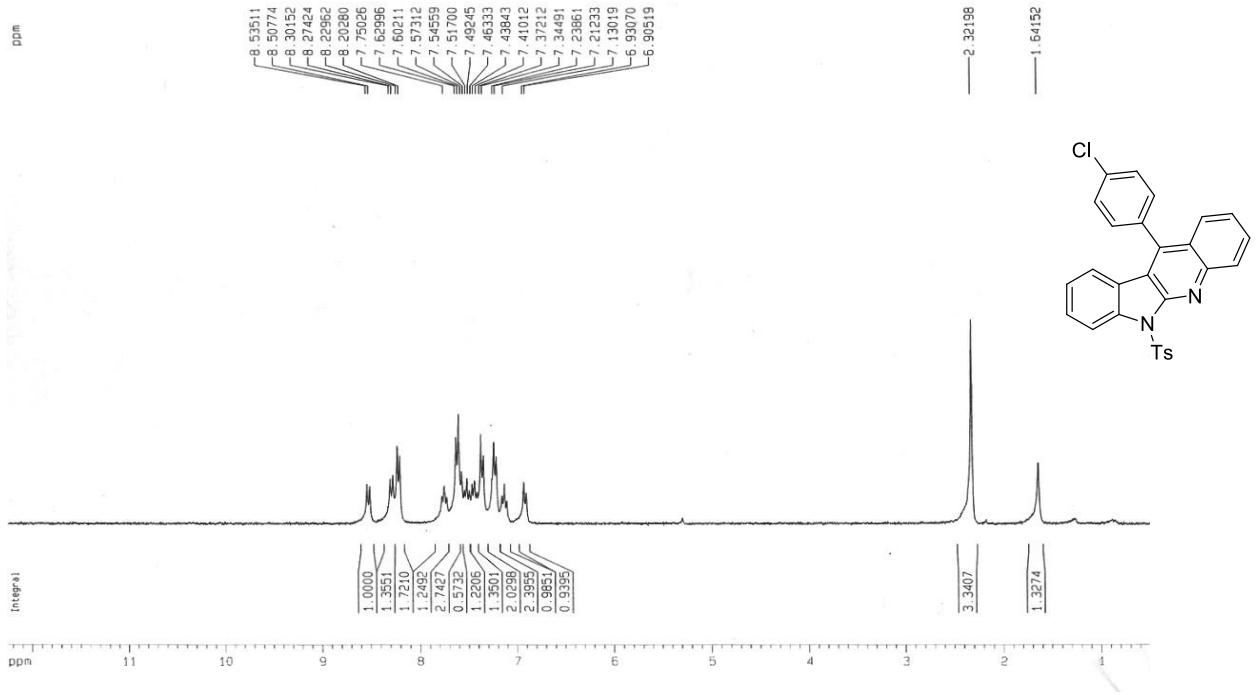
^{1}H NMR spectrum of compound 3e



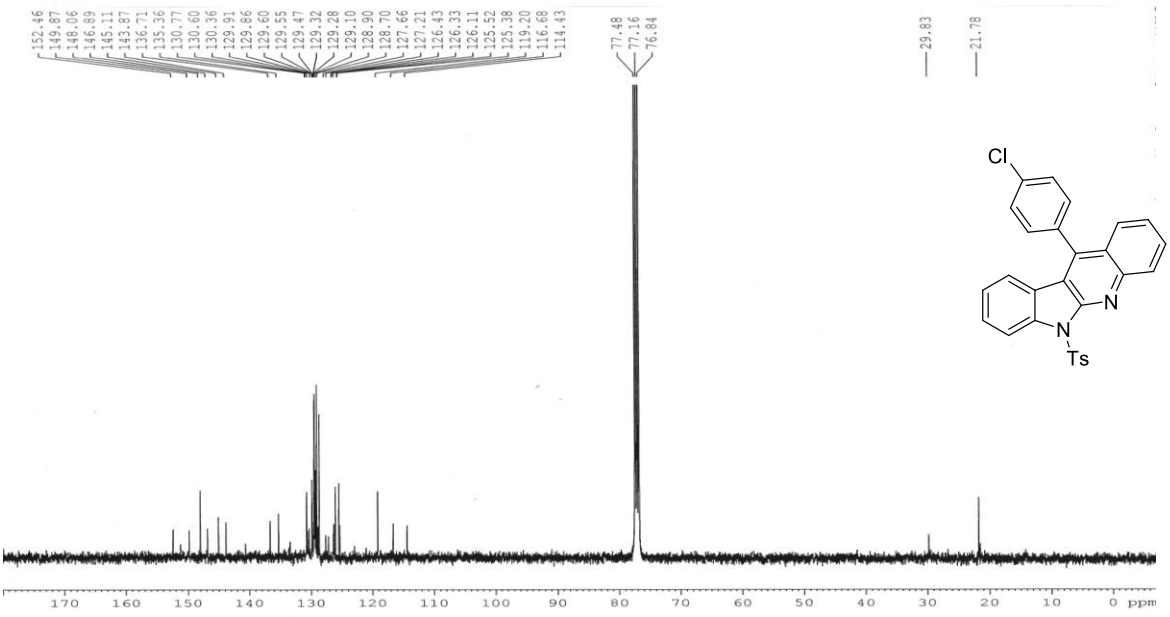
^{13}C NMR spectrum of compound 3e



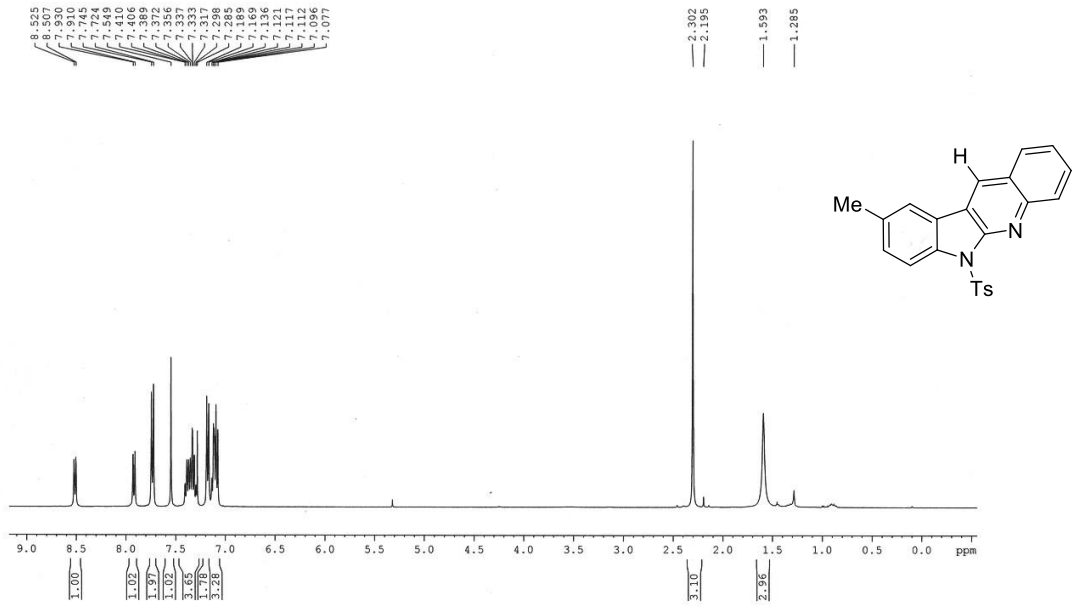
^{1}H NMR spectrum of compound 3f



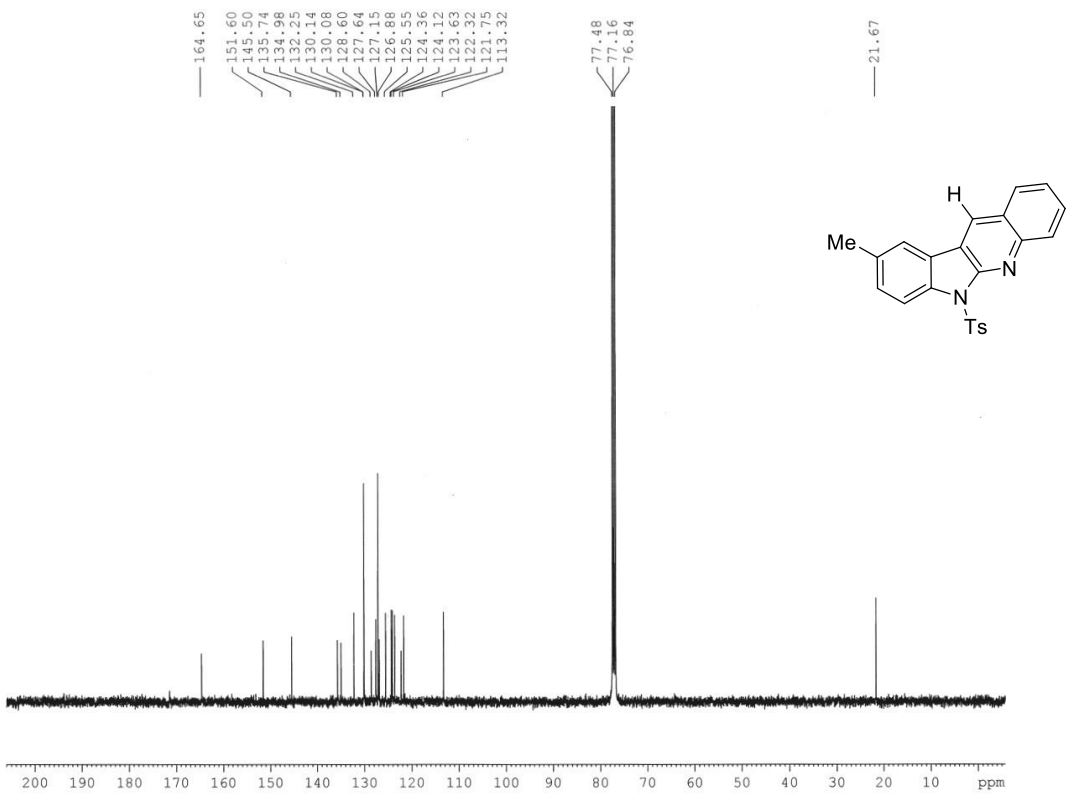
^{13}C NMR spectrum of compound 3f



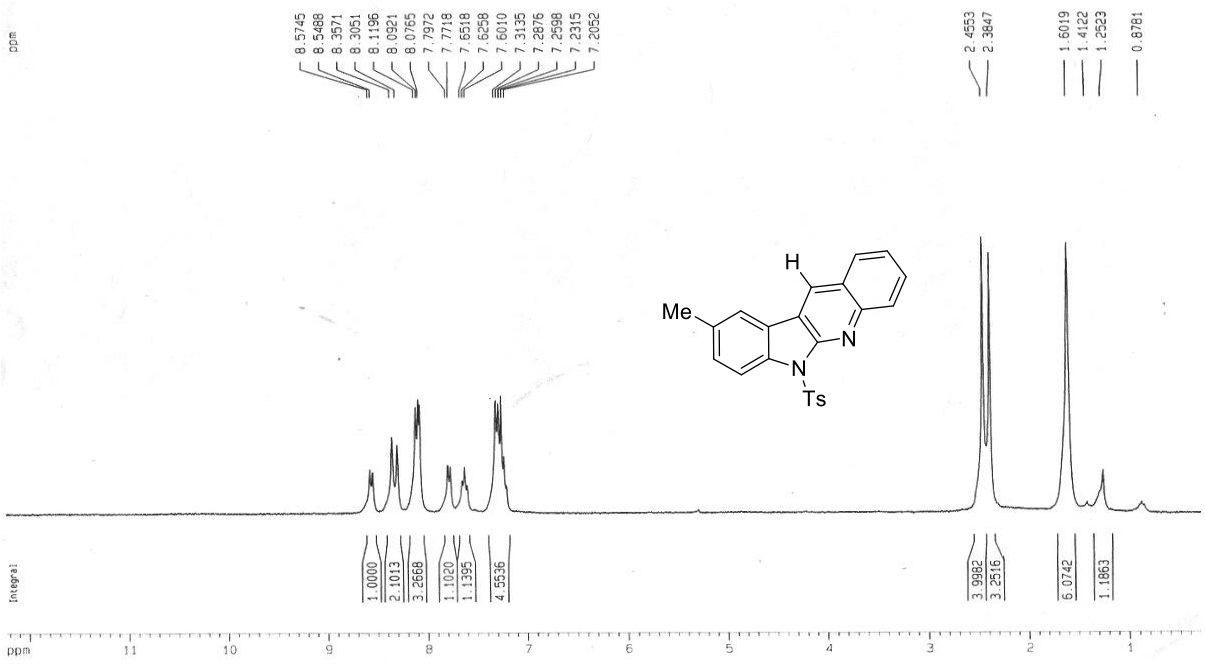
^{1}H NMR spectrum of compound 3g



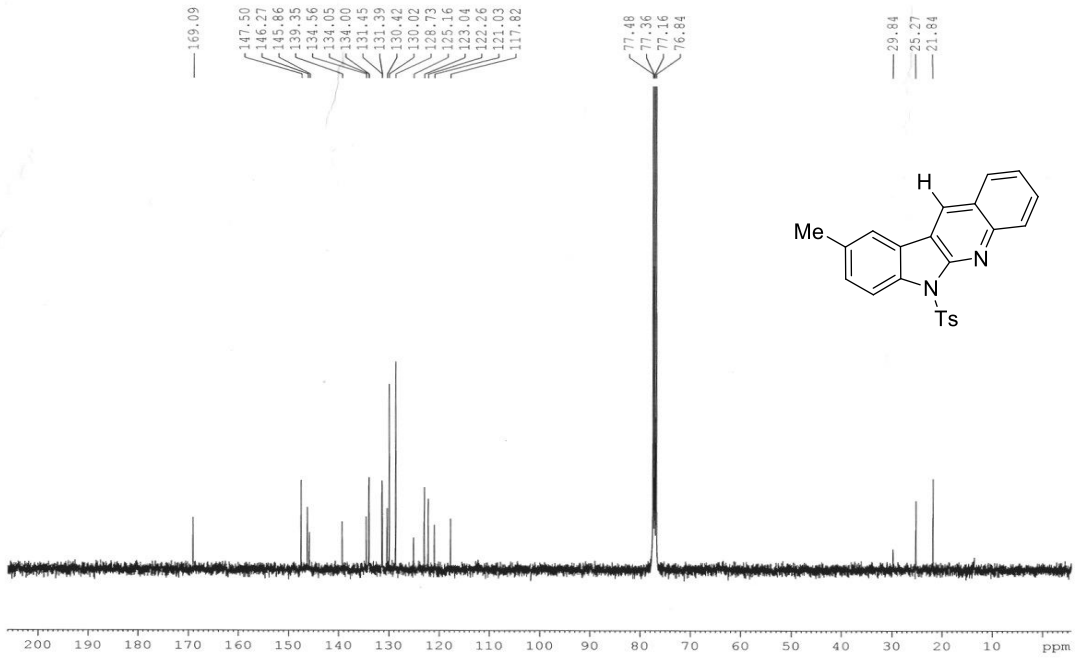
^{13}C NMR spectrum of compound 3g



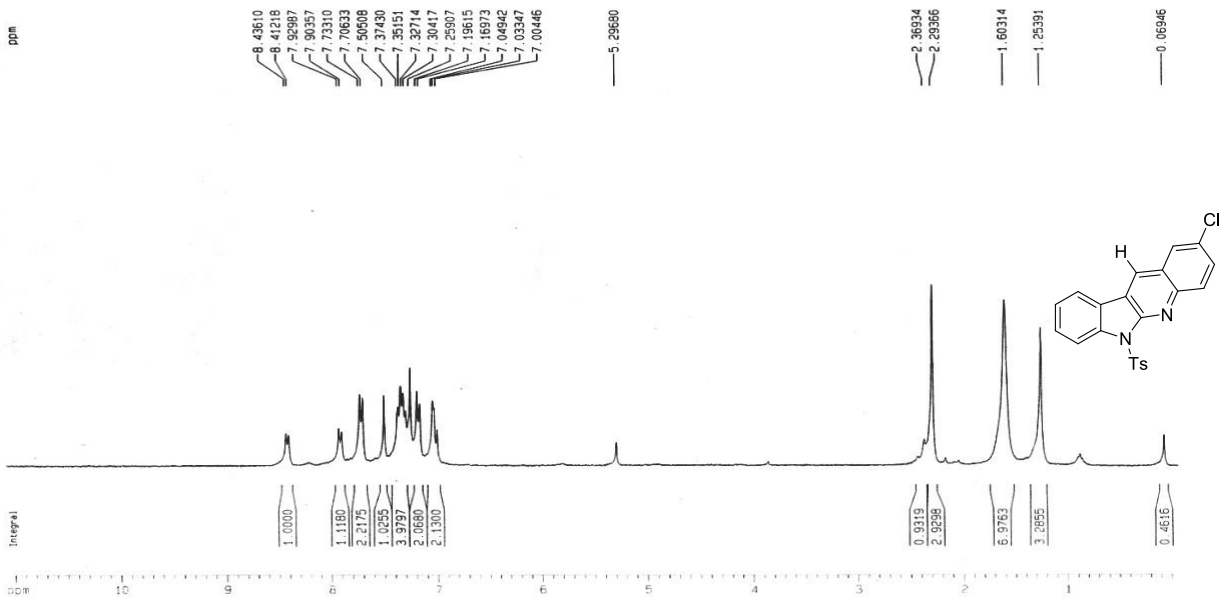
^{1}H NMR spectrum of compound 3h



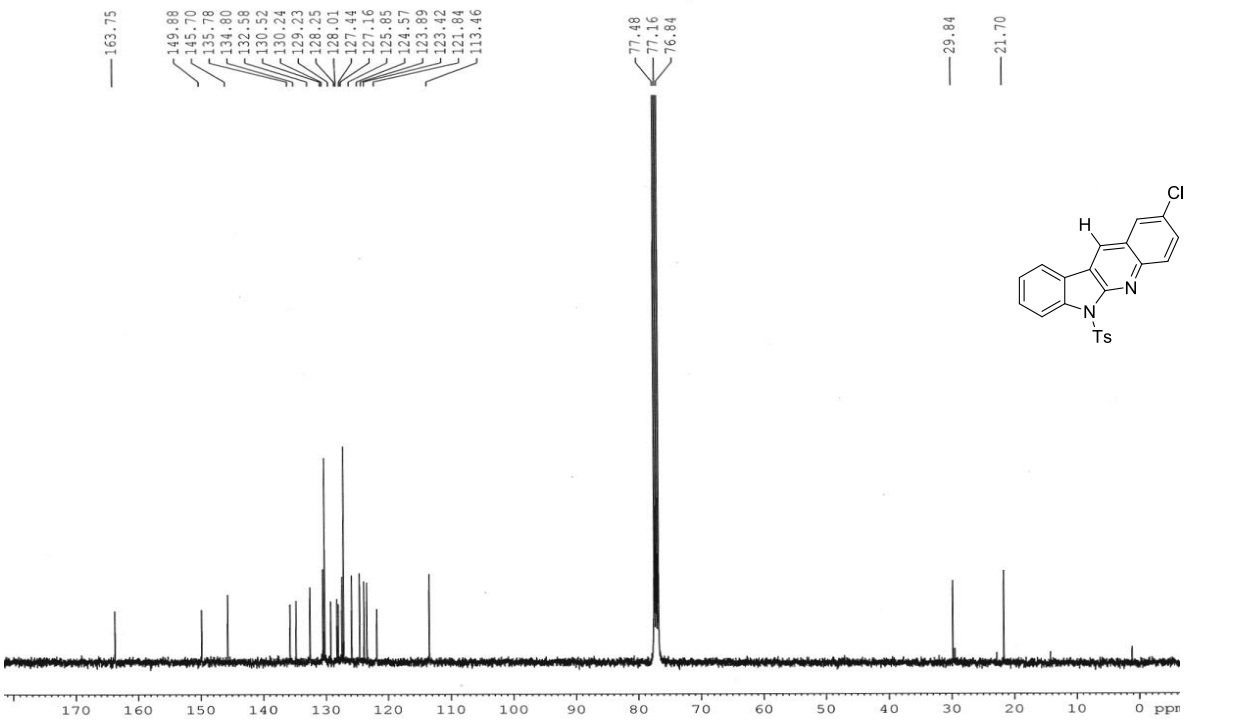
^{13}C NMR spectrum of compound 3h



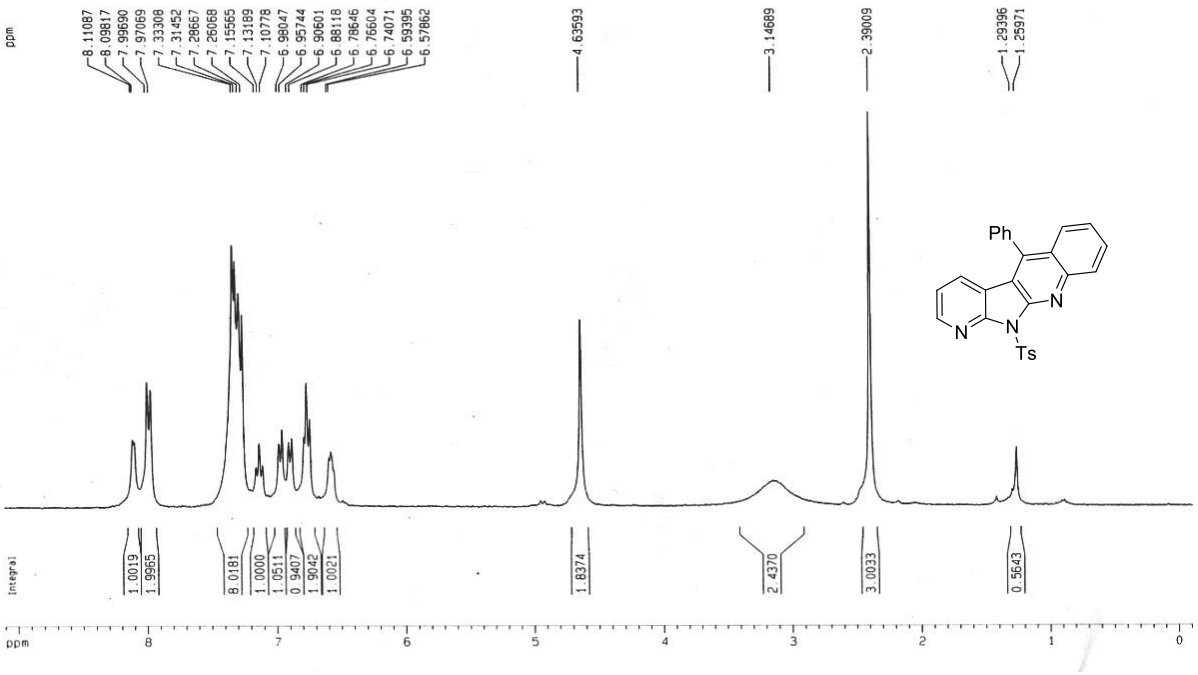
^{1}H NMR spectrum of compound 3i



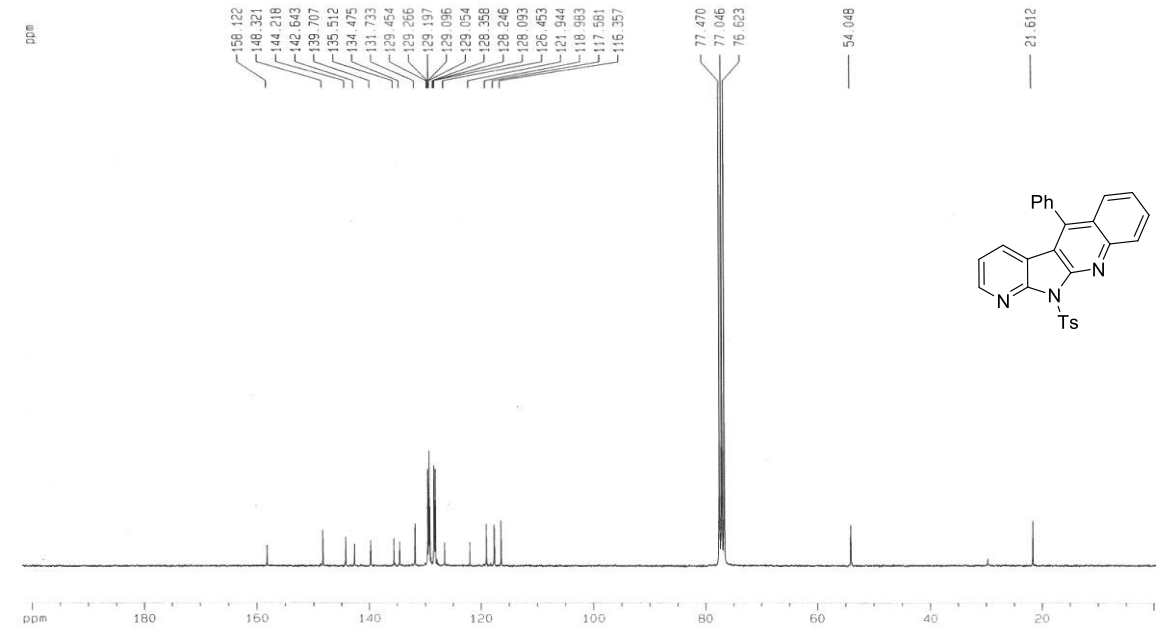
^{13}C NMR spectrum of compound 3i



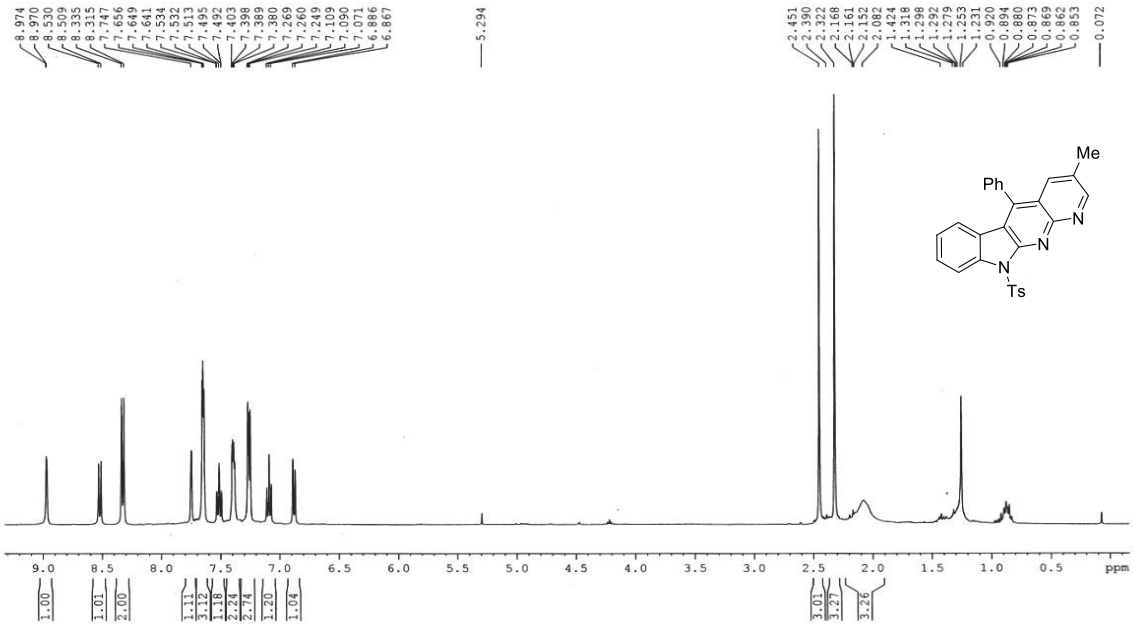
^{1}H NMR spectrum of compound 3j



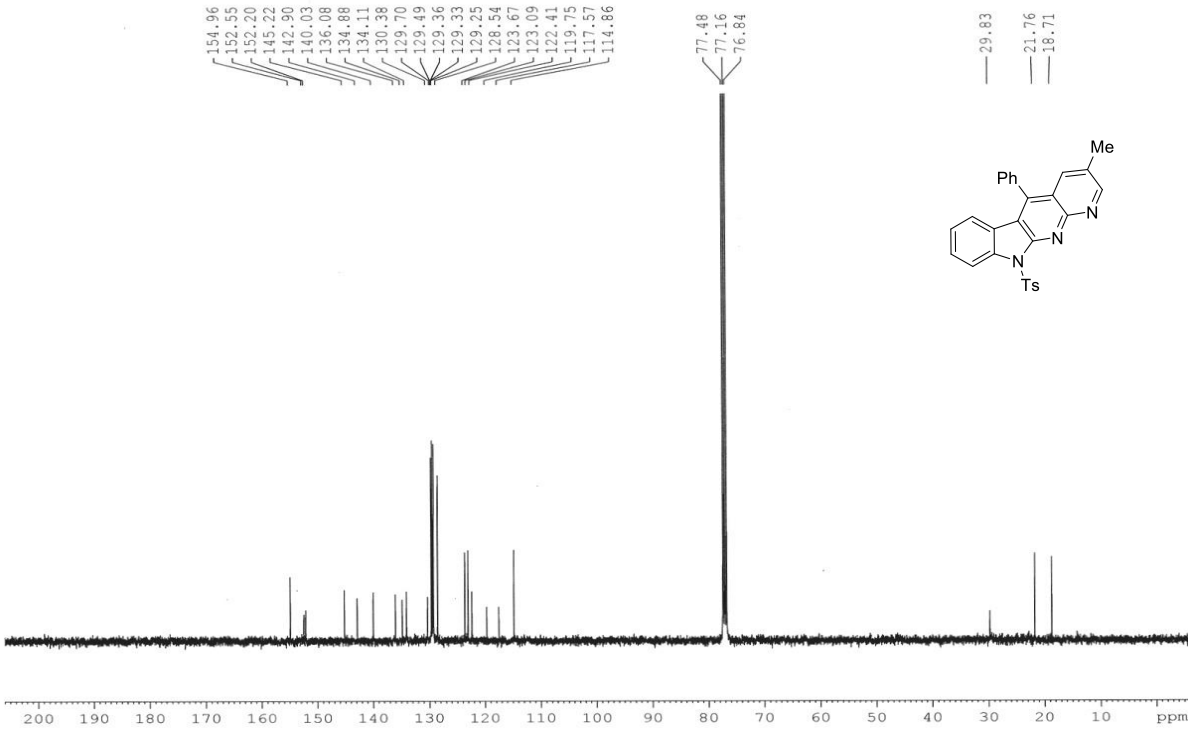
^{13}C NMR spectrum of compound 3j



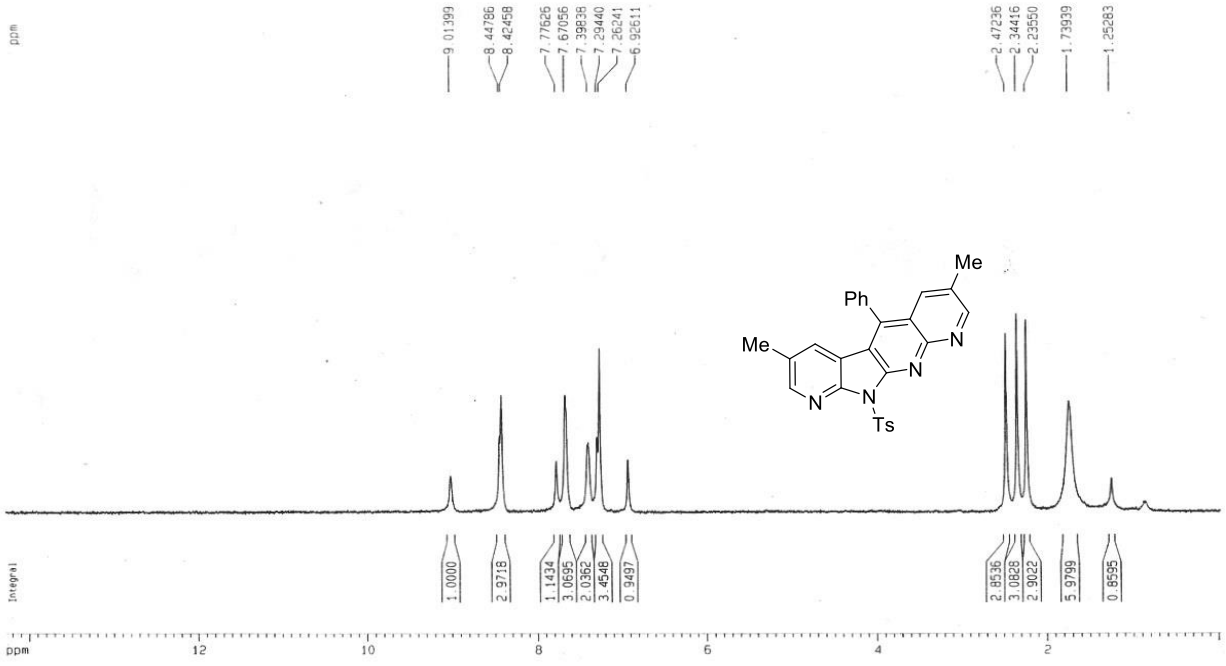
^{1}H NMR spectrum of compound 3k



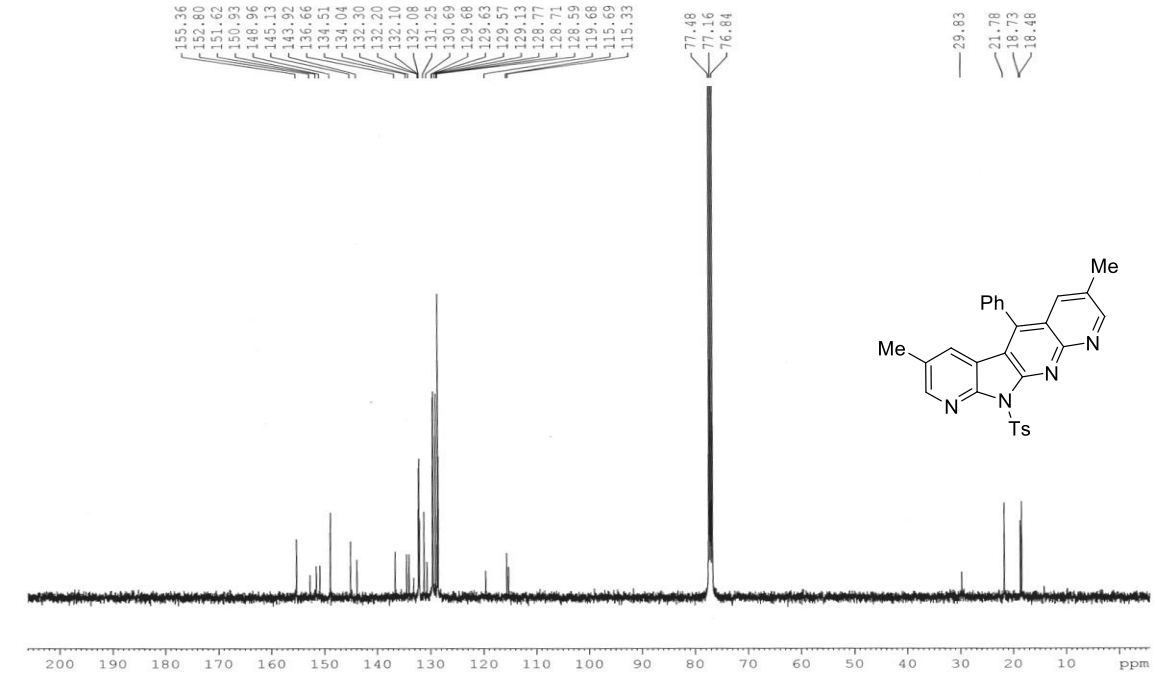
^{13}C NMR spectrum of compound 3k



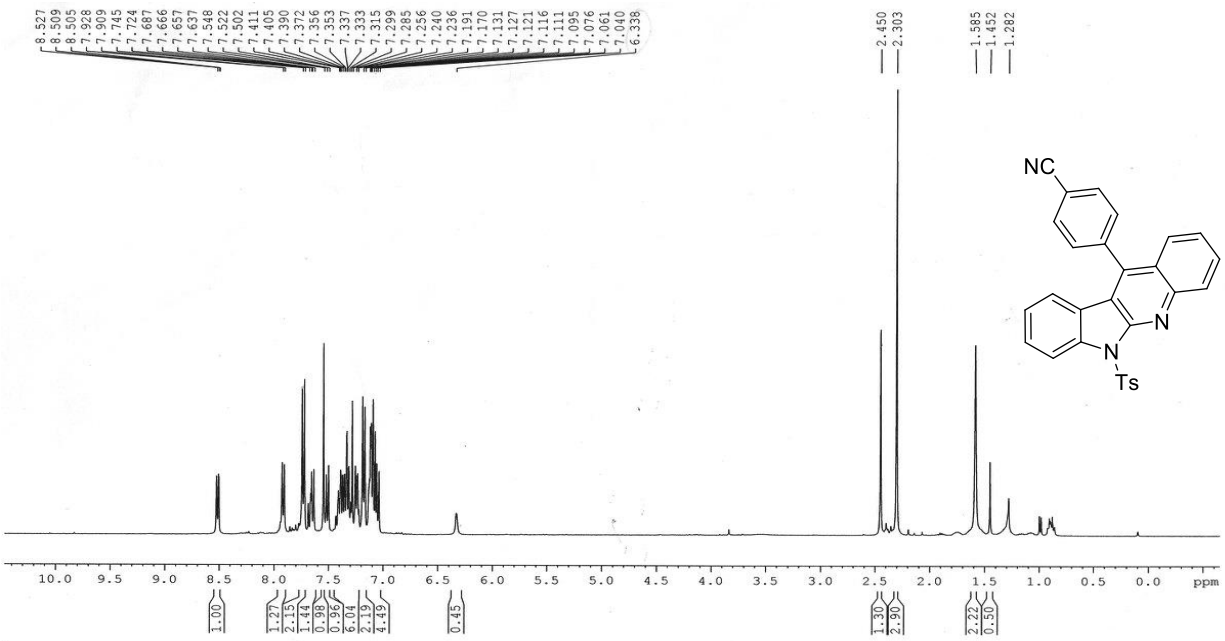
^{1}H NMR spectrum of compound 3l



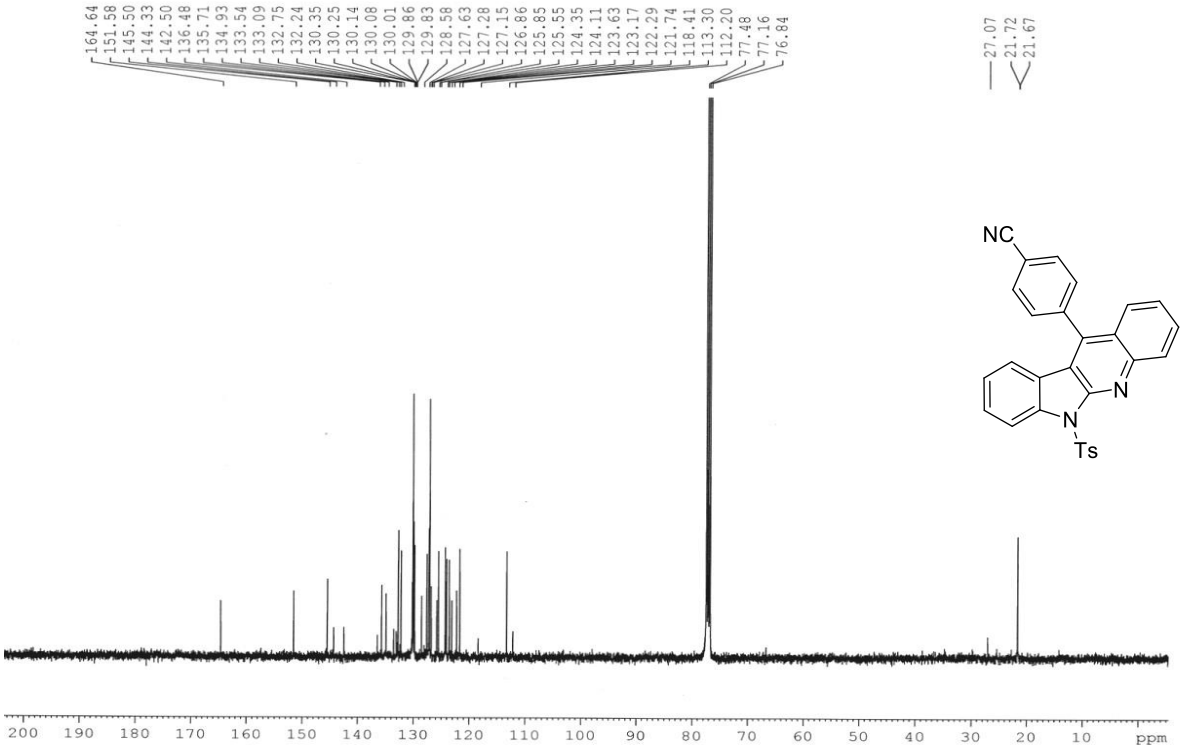
^{13}C NMR spectrum of compound 3l



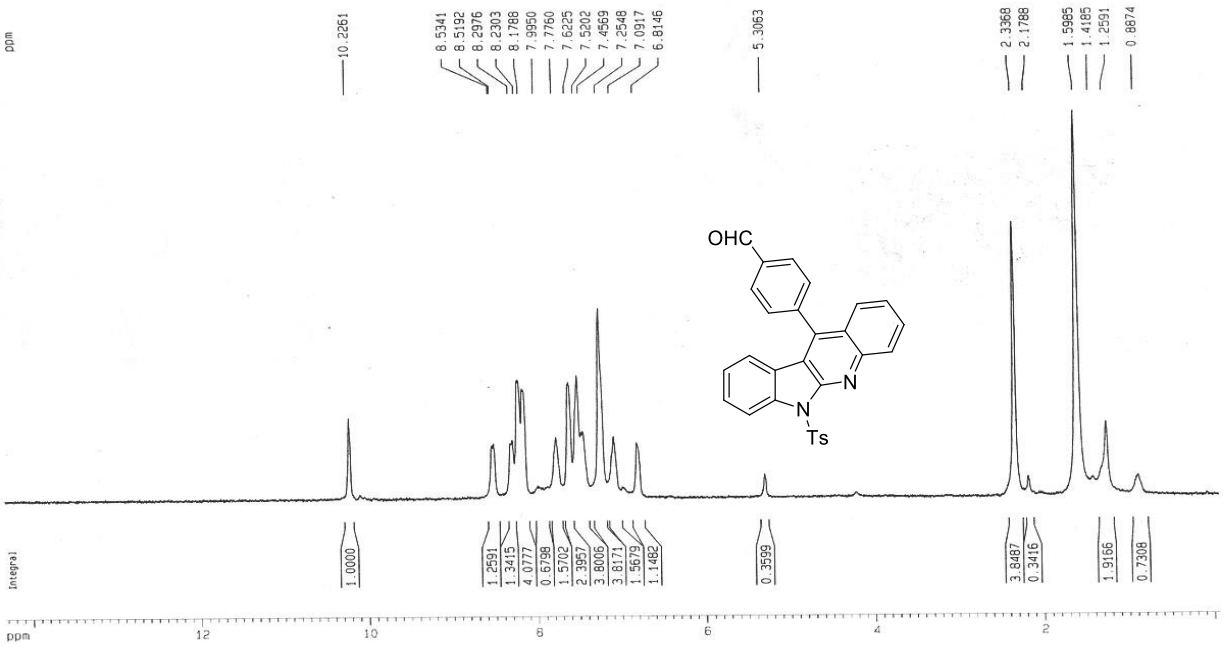
^{1}H NMR spectrum of compound 3m



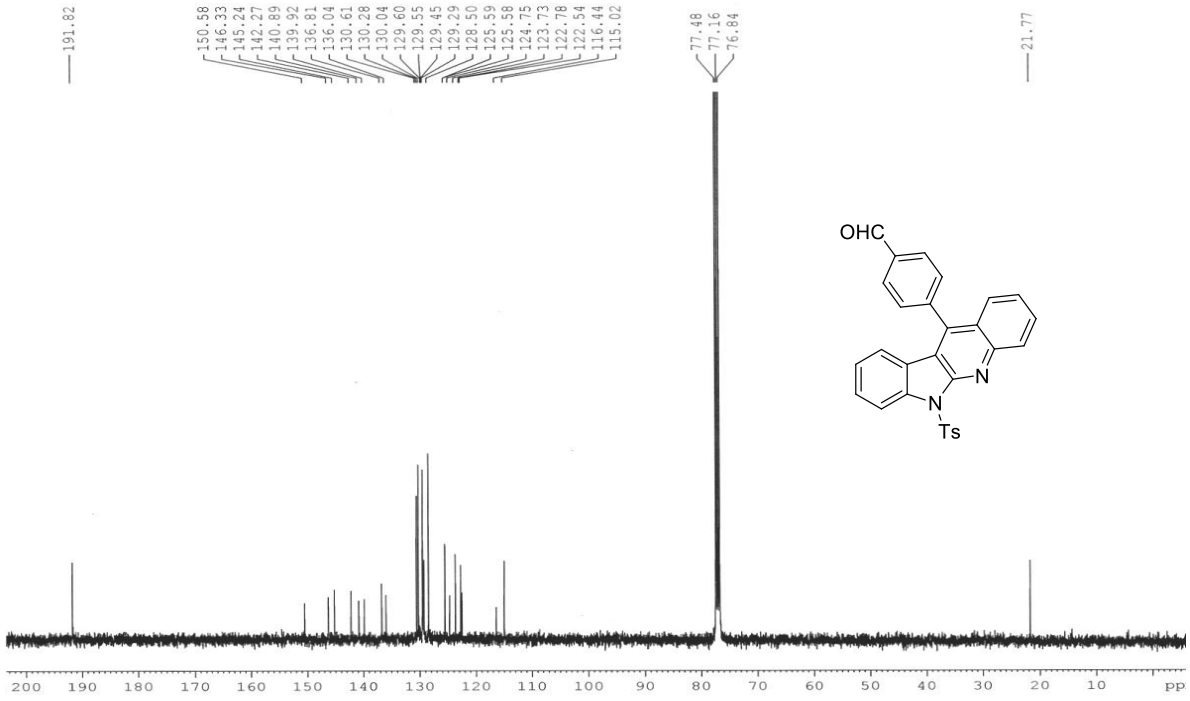
^{13}C NMR spectrum of compound 3m



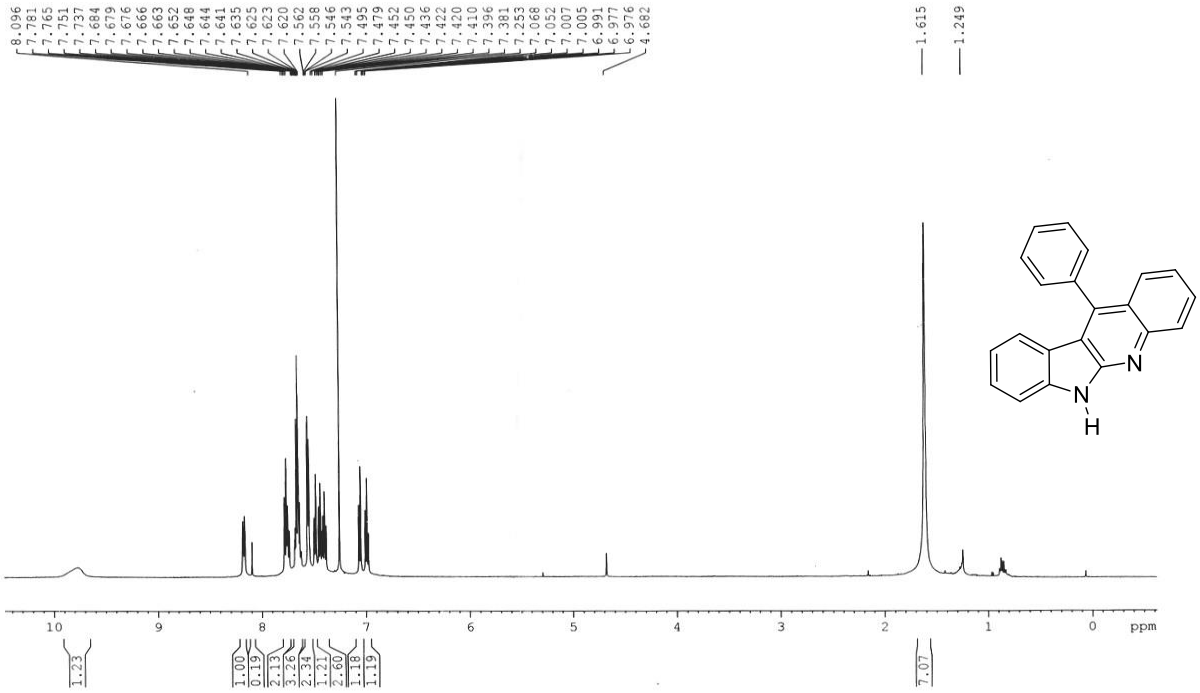
1H NMR spectrum of compound 3n



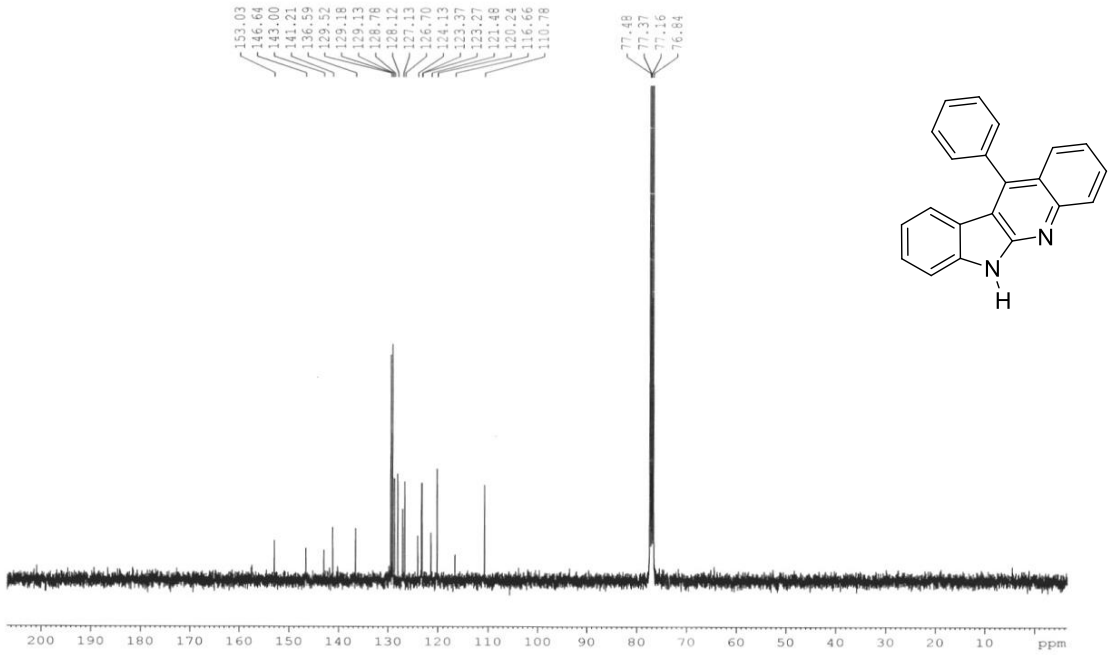
^{13}C NMR spectrum of compound 3n



1H NMR spectrum of compound 4



^{13}C NMR spectrum of compound 4



Chapter III

Synthesis of Indole-3-carbinols (I3C) and their Application to Access unsymmetrical bis(3-indolyl)methanes (BIMs) bearing quaternary sp3 -carbon

Chapter III

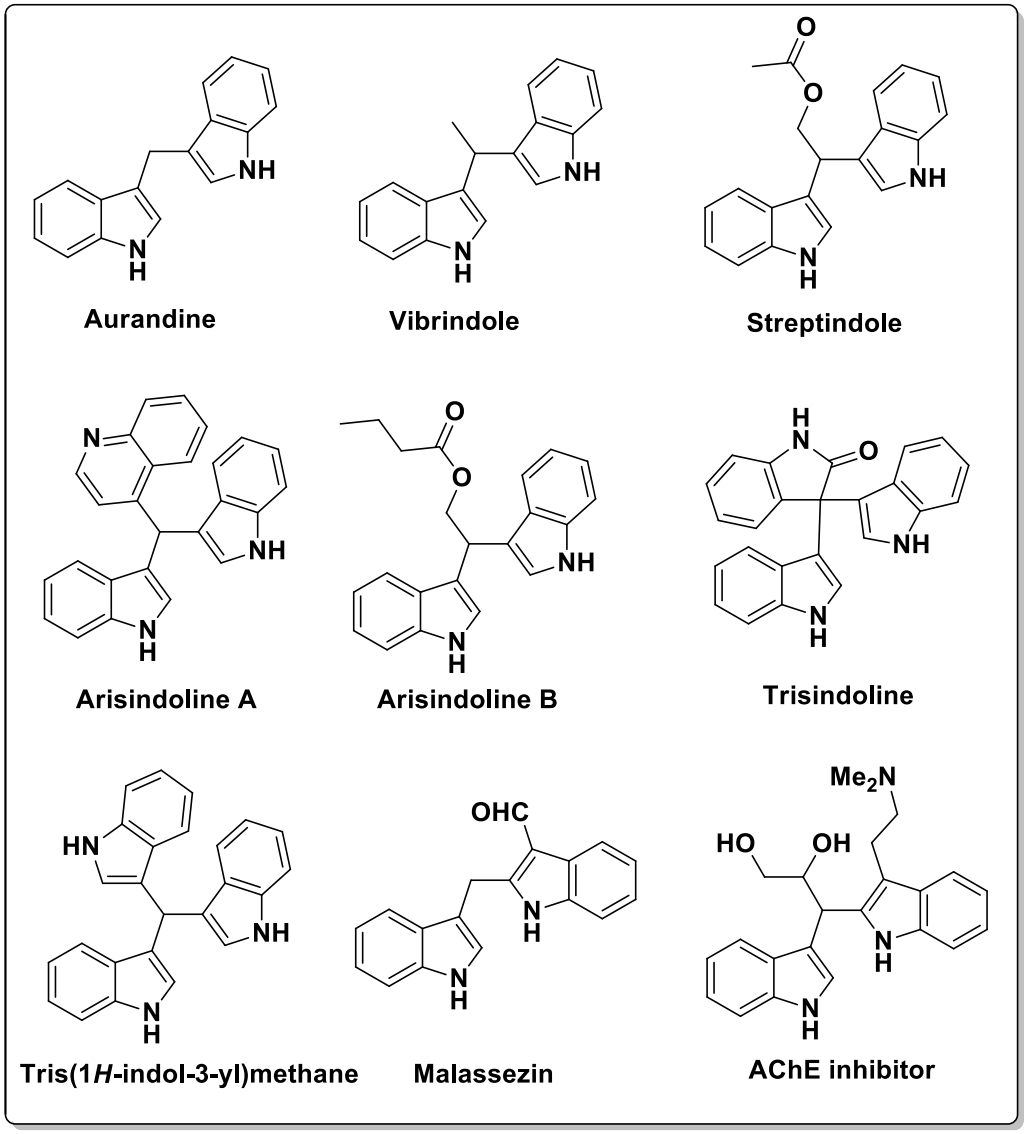
III.1. Introduction:

Functionalized indole[1] moieties has always drawn a special attention of organic synthetic community because of its broad-spectrum occurrence in the class of bio-active frameworks, natural products, pharmaceuticals, material science and agrochemicals [2,3]. As we all know, specially, 3-substituted indoles has occupied a huge portion of this subject due to its broad-spectrum applications and diversified variation in organic chemistry regarding medicines and material science [4,5]. Particularly, indole-3-carbinol which is the core chemical component of the vegetables of *Cruciferae* family, is a significant motif, as it exhibits the potential of binding with DNA and hence shows anti-carcenogenic activity [6]. It has been already proven by many researchers that indole-3-carbinol (I3C) or its analogues can bind to estrogen receptors (EA) and modify the metabolism of estrogen.[7] Indole-3-carbinol shows antiproliferative action in different types of human cancers, like breast, lung, prostate, leukemia, colon, and cervical cancer[8]. Furthermore, these molecules shows potential as synthetic precursors towards the construction of biologically active heterocyclic frameworks [9]. However, a simple and efficient strategy still in high demand to synthesize such value added bioactive molecules. Oxidative conversion of carbon-hydrogen bonds to different functional groups are well warranted opportunities for increasing molecular structural modifications of indole bearing scaffolds from simple to complex with the readily available starting materials[10]. With continuous efforts to develop successful C-C/C-N bond formation strategies for the synthesis of structurally modified C-3-functionalised[11], hybrid[12] indoles, carbazoles[13] and quinolines[14] starting from presubstituted 3-benzylidine indolines, we herein, reported a metal free DDQ-mediated regioselective, atom-economic, very simple and mild synthetic protocol to obtain tertiary indole-3-carbinols using water as green source of hydroxyl oxygen.

On the other hand, bisindolylmethanes (BIMs), another class of bioactive molecules which are generated by the condensation of I3C (the major product of hydrolysis of indole-GLSs) in the acidic pH of the stomach [15]. They exhibits strong inhibitory effects on phenobarbital induced hepatic cyp-mRNA expression [16a] and anti-cancer activity.[16b] Bisindolylmethane derivatives are well-known for excellent bioactivity. Their presence are found in many terrestrial plants and other marine organisms.[17](**Figure 1**). Simple structured compounds such as arundine, which are isolated from plant roots, exhibits anticancer properties. Few other examples like malassezin, a yeast metabolite found to be active against human melanocytes, and a few unsymmetrical bisindolylmethanes with

synthetic origin are known for their AChE inhibitory effect and anticancer activity[18, 19]. Due to their wide application in medicinal chemistry, drug discovery, and agrochemicals, the synthesis and isolation of bis(indolyl)methanes have attracted the attention of several chemists.

Figure 1: Some important bioactive bis(indolyl)methane derivatives.

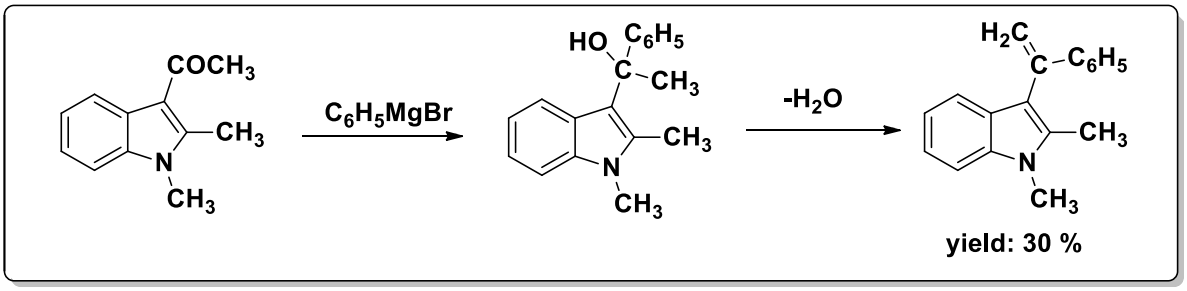


III.2.1. A brief review on Indole-3-carbinols :

Indole-3-carbinols are present naturally in the vegetables of *Cruciferae* family, although the synthesis of this compound is less invaded part in the field of organic synthesis. Till date, a few

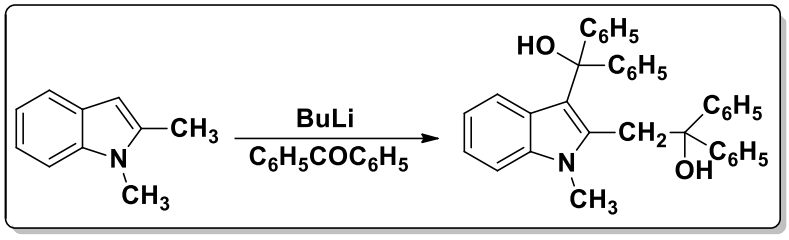
number of methods are reported for the synthesis of Indole-3-carbinols and its derivatives. Considering the pharmacological importance of these compounds, it has become an utmost requirement in the synthetic organic chemistry to synthesize the molecular framework in a simple and diversified manner. Synthesis of Indole-3-carbinol framework, especially tertiary indole-3-carbinols motifs are almost rare. However, very few number of scientific groups have reported the synthetic strategies which afford the targeted framework. Like, conventional strategies of organic synthesis are used for developing substituted and funtionalized indole-3-carbinols, which involves the usage of indole-Grignard reagents having the boundary of restricted substrate choice and delicate reaction conditions. (**Scheme 1a**) [20].

Scheme 1a: Reaction of 3-acylindoles with Grignard reagents to afford Indole-3-carbinols derivatives.



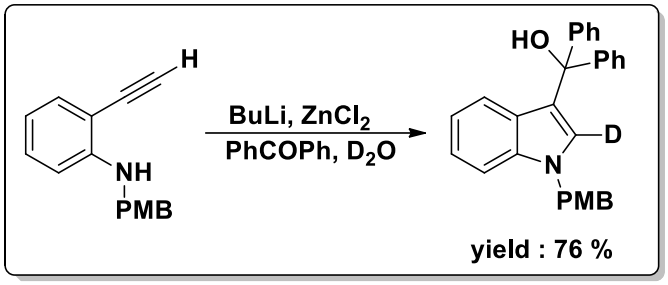
The reaction of 1, 2-dimethylindole with butyl-lithium also leads to Indole-3-carbinols (**Scheme 1b**) [20].

Scheme 1b: Reaction of 1, 2-dimethylindole with butyl-lithium to afford Indole-3-carbinols.



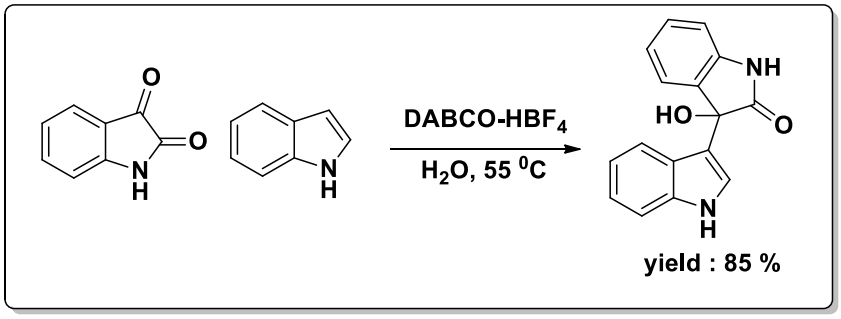
In recent past, Laurean Ilies and group have reported the construction of indole-3-carbinols via transition metal catalysed cyclic metallation of 2-alkynylaniline, capturing external carbonyl electrophiles by means of a harsh reaction condition and expensive metals (**Scheme 2**) [21].

Scheme 2: Synthesis of Indole-3-carbinols regioselective electrophilic trapping.



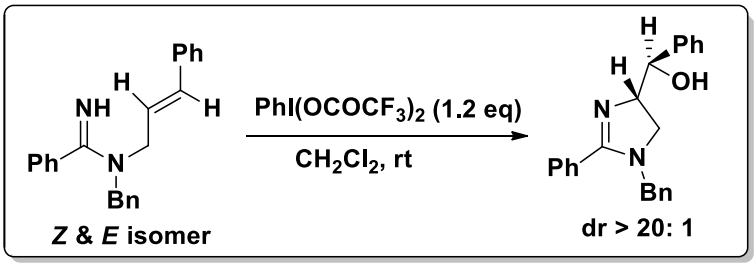
Da-Zhen Xu *et*. *al*. reported a method where the production of 3-indolyl-3-hydroxy oxindoles[22] was availed using Dabco-based ionic liquids catalyst via Friedel–Crafts alkylation method (**Scheme 3**).

Scheme 3: Synthesis of 3-indolyl-3-hydroxy oxindoles via Friedel-Crafts alkylation method.



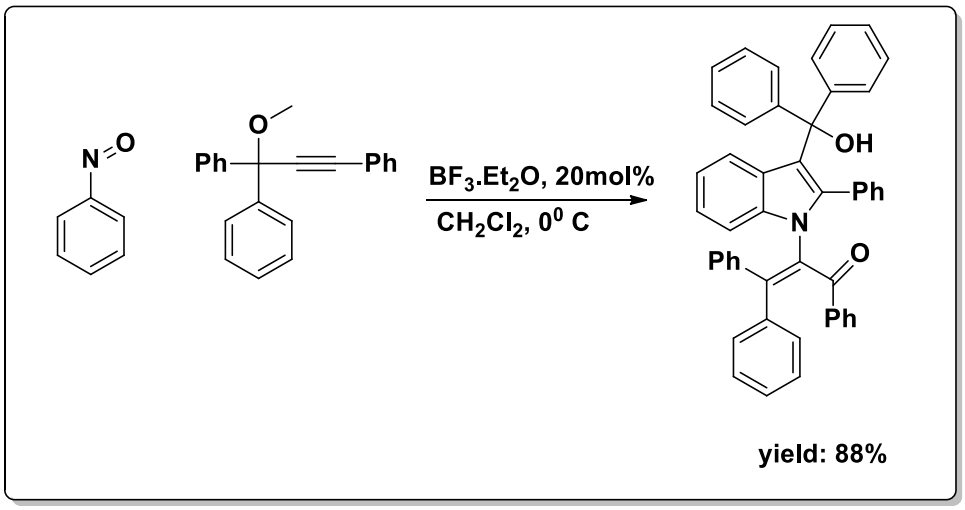
The group of Savitha and Reddy proposed a method of metal free oxidative cyclization for the development of *N*-heterocycles. Tertiary alcohols containing *N*-hetetrocyclic ring may be afforded by this method in a stereoselective manner, choosing suitable precursor molecule as substrate (**Scheme 4**)[23].

Scheme 4: Metal-Free Oxidative cyclizations with Hypervalent Iodine (III) Reagents



So far, a few procedures are existing to produce tertiary indole-3-carbinols. S. Muthusamy *et. al.* had demonstrated a $BF_3.OEt_2$ catalysed method for tertiary indole-3-carbinol *via* tandem reaction of nitrosobenzene and excess propargyl alcohols (**Scheme 5**)[24].

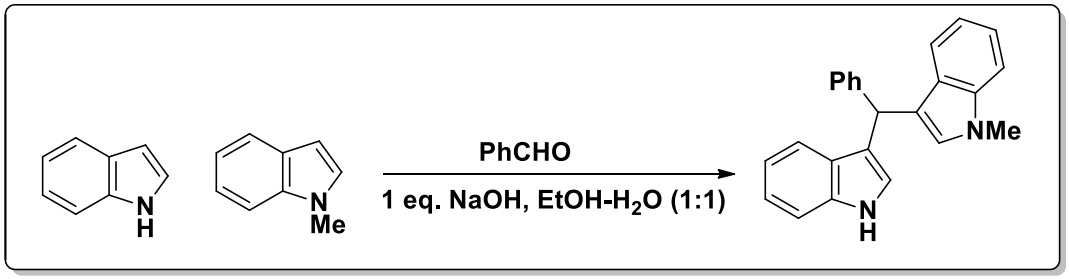
Scheme 5: Synthesis of $BF_3{\cdot}Et_2O$ Catalyzed substituted indole-3-carbinols from nitrosobenzenes and propargylic alcohols.



III.2.2. A brief review on bis-Indolylmethanes (BIMs):

Synthesis of the unsymmetrical indoles may be afforded under basic condition which give access of the reaction of 1-unsubstituted indoles with N-alkylindoles alongwith arylaldehydes (**Scheme 6**)[25].

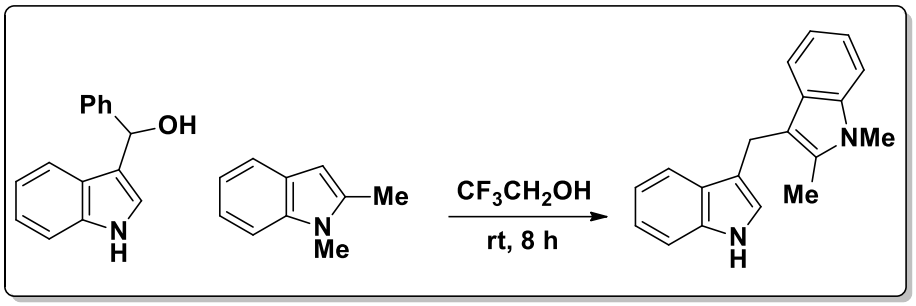
Scheme 6: Synthesis of unsymmetrical bisindolylmethanes from three omponent coupling.



Unsymmetrical bisindolylmethanes may be produced by the dehydration of 3-indolylmethanols through their ionic intermediate which happens under acidic conditions. It has been established

that, polar solvents like water and 2,2,2-trifluoroethanol (TFE) are capable of promoting SN^1-type pathway.[26, 27]

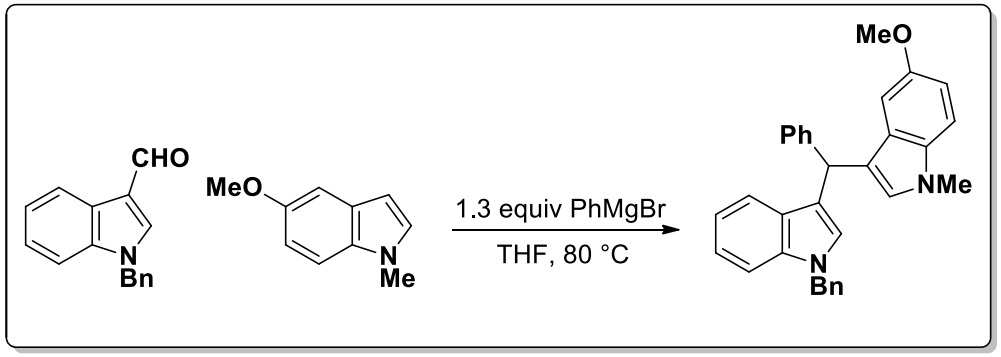
Scheme 7: Synthesis of unsymmetrical bis-Indolylmethanes via dehydration of alcohols



on the substrate aryl(indolyl)methanols which leads to bis-Indolylmethanes (**Scheme 7).** Using water as the solvent needs very heating whereas TFE is capable of producing the same product at room temperature and shorter time.

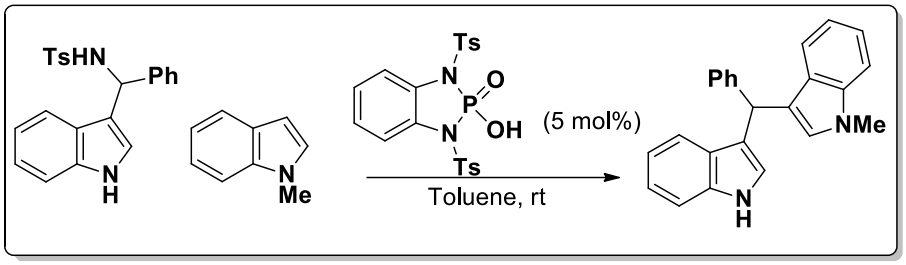
A method was developped for the synthesis of bis-Indolylmethanes derivatives via coupling reactions of 3-formylindoles with phenylmagnesium bromide and a substitued indole (**Scheme 8**)[28]. The nucleophilic adduct of the Grignard reagent to the aldehyde leads to formation of magnesium alkoxide which upon heating eliminates MgBrOH and thereby generating corresponding iminium ion which finally reacts with indoles leading to bis-Indolylmethanes.

Scheme 8: Synthesis of bisindolylmethanes via formation of a magnesium alkoxide intermediate.



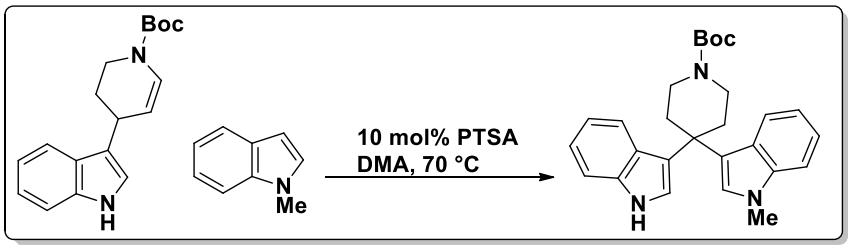
N-Tosyl-3-indolylmethanamines are easily converted into bisindolylmethanes where the tosyl groups behaves as a leaving group, using a phosphate catalyst at room temperature (**Scheme 9**).[29]

Scheme 9: Preparation of bisindolylmethanes using indolylmethanamines as substrates.



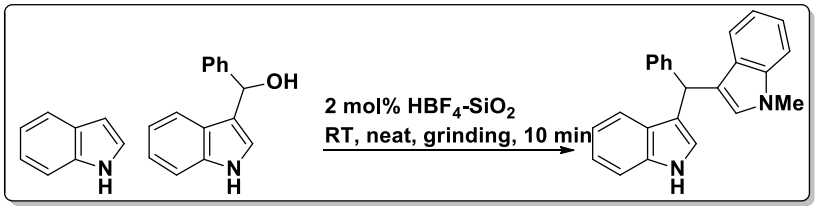
3-vinylindoles produces benzylic-type carbocationic motifs upon protonation which can be attacked by indoles which generates unsymmetrical bisindolylmethanes. *p*-toluenesulfonic acid acts as a catalyst and facilitates the method and utilization of substituted vinylindole gives synthetically more useful bisindolylmethanes (**Scheme 10**).[30] The following group of product exhibits cytotoxic activity against MCF-7 breast cancer.

Scheme 10: Preparation of unsymmetrical bisindolylmethanes from 3-Vinylindoles.



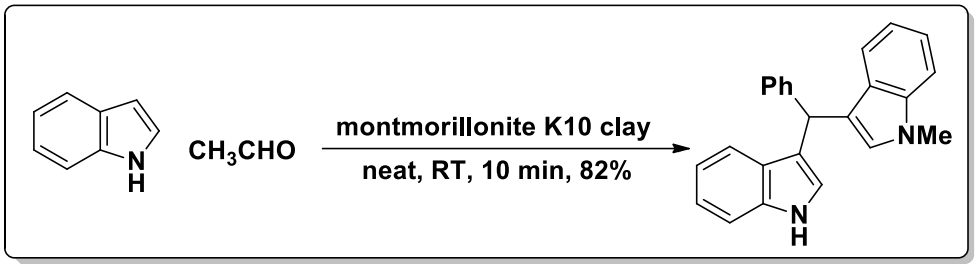
Bandgar et al. reported a method for the synthesis of bis(indolyl)methanes through electrophilic substitution reaction of (1*H*-indol-3-yl)(phenyl)methanol with indoles under solvent free conditions by means of fluoroboric acid adsorbed silica gel (HBF_4-SiO_2) as a catalyst, by grinding the mass at room temperature (**Scheme 11**).[31]

Scheme 11: Synthesis of bis(indolyl)methanes from indolylmethanol using fluoroboric acid adsorbed silica gel catalyst



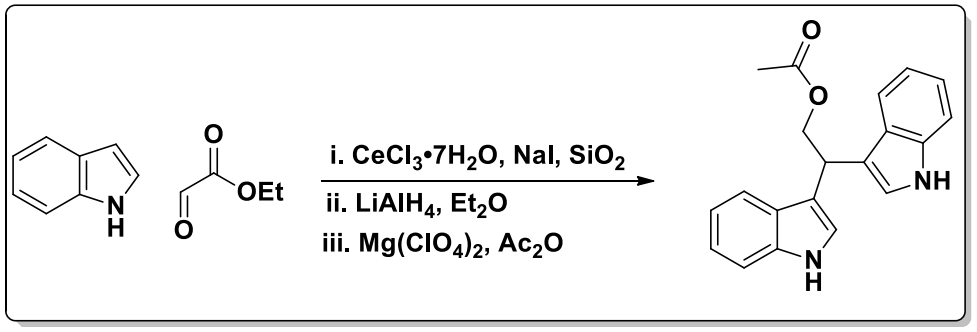
Chakrabarty and his group proposed a pathway to synthesize Vibrindole A, a naturally occurring compound from bacterial metabolism, from the reactions of indole and acetaldehyde (2:1 ratio) by means of montmorillonite K10 clay as catalyst under solvent-free conditions (**Scheme 12**).[32]

Scheme 12: Synthesis of Vibrindole A using montmorillonite K10 clay as catalyst.



Bartoli et al. reported a method for the development of bis(indolyl)methanes under solvent-free conditions in excellent yield using cerium(III) chloride heptahydrate–sodium iodide–silica gel as a promoter for the addition step in solvent free condition (**Scheme 13**).[33] Indole reacts with ethyl glyoxylate in the presence of cerium(III) chloride heptahydrate–sodium iodide–silica gel to produce ethyl bis(1*H*-indol-3-yl)acetate which upon reduction, produces corresponding alcohol, which at last undergoes acetylation by means of magnesium perchlorate to generate streptindole.

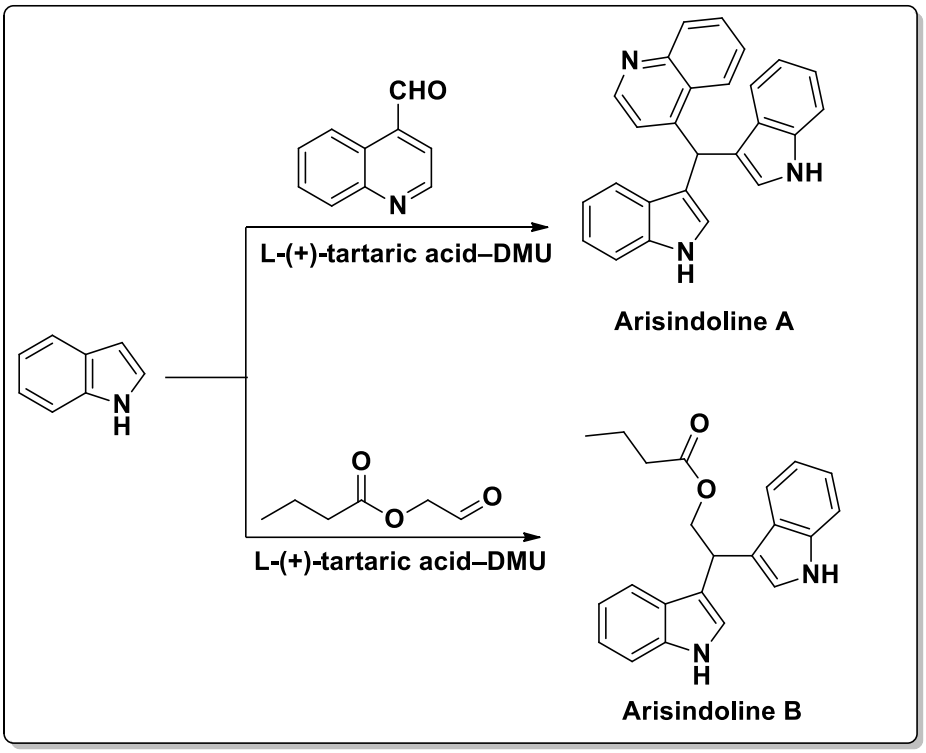
Scheme 13: Synthesis of Streptindole in a solvent free condition



Jella and Nagarajan had proposed the methodology synthesis of arsindoline A and arsindoline B, and their analogues, using low melting mixture which were used for the coupling of indoles and aldehydes. Low-melting mixtures. L-(+)-Tartaric acid–dimethylurea (DMU) was the most suitable and efficient medium giving highest yield which has been treated with indole and aldehyde (2:1) to

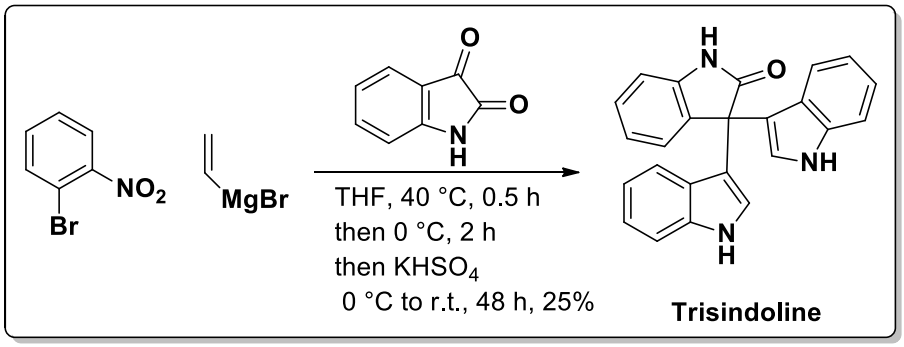
give the arsindoline skeleton.[34] (**Scheme 14**) Arsindoline A was generated from quinoline-4-carbaldehyde, while, arsindoline B was generated from 2- oxoethyl butanoate applying this process.

Scheme 14: Synthesis of arsindoline using L-(+)-Tartaric acid–dimethylurea



Abe et al. described a strategy for the synthesis of trisindoline with O-nitrobromobenzene and vinyl magnesium bromide followed by addition of isatin. During the quenching step of isatin led to the formation of trisindole[35] (**Scheme 15**).

Scheme 15: Synthesis of trisindole using isatin as a substrate



III. 3. Summary:

A few attempts have been taken by different researcher groups for the synthesis of 3-indolylmethanols and extraction of the similar compounds specially indole-3-carbinol since these moieties are quite established in showing bioactivity and promising medicinal properties. Among these approaches, very few appear to be efficient and general from the synthetic point of view. However most of the methodologies are suffering from lack of synthetic diversity and crisis of using pre functionalized starting materials, insufficient yields, limited sources, promptness of the method, number of the steps, use of costly and toxic reagents and commercial and environmental viability of the strategies. Especially synthesis of the diversely functionalized tertiary 3-indolylmethanols are rare.

Besides, the formation of the product bis(indolyl)methanes, which are coupling derivatives of 3-indolylmethanols which may also considered to be analogous of the metabolic product of the substrate 3-indolylmethanols are also bears the high biological importance in nature. The presence of the bis(indolyl)methanes compounds with diversified structures in different living bodies alongwith its huge applications makes it more noteworthy to replicate the formation of these compounds under synthetic conditions. However, the reported synthetic strategies, of these framework are harsh in nature, suffer from lacks of diversity due to limited choice of the pre-functionalized substrates. Specially the synthesis of quaternary chiral carbon centres bearing bis(indolyl)methanes products with high synthetic diversity are rare till date.

Seeing the pharmacological importance of both the products discussed earlier, the development of easy, direct, cheap and flexible and greener synthetic methodologies are still in awaited.

III. 4. Present work:

Synthesis of functionalized indoles are always draw major attention synthetic organic chremists due to its broad-spectrum occurrence in the pool of of biologically active molecules, natural products, pharmaceuticals, material science and agrochemicals. In the continued study, as described in the other chapters (Chapter I), our cuurent approach for the synthesis of indole-3-carbinols, involes same steps for the generation of 3-methyleneindoline derivatives. These compounds are subjected to regioselective dehydrogenation at the allylic sp^3-carbon N-sulfonylated indoline scaffold bearing an exocyclic double bonds using non metal oxidant. This treatment results isomerization/ aromatization of substituted C-3 benzylidine indolines which impose an electrophilic character over

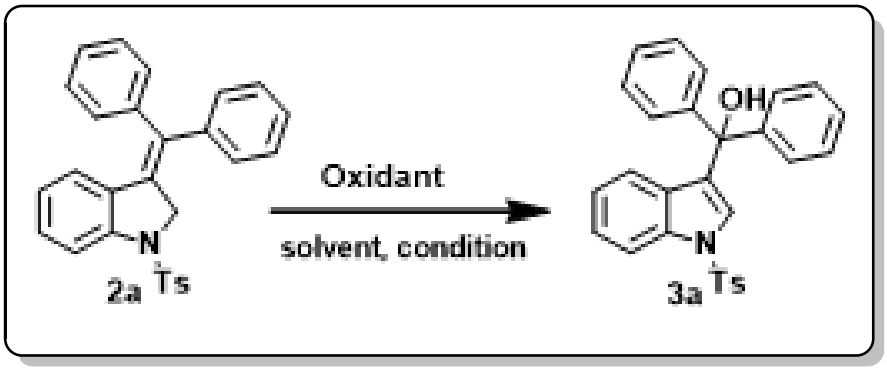
the benzylic carbon and consequently the benzylic carbon was oxyfunctionalized with high selectivity. In this method, DDQ was used as dehydrogenating agent and water as hydroxyl source to produce tertiary indole-3-carbinols in a quantitative yield. In the next part, the synthetic viability of such indole based *tert*- carbinols were again described through serving as excellent methylene surrogates to put in highly significant unsymmetrical *bis*-indolylmethanes containing all carbon quaternary center. Therefore, we sought to use the tertiary indole-3-carbinols (I3C) as a methylene source for a straightforward synthesis of BIMs containing a quaternary sp^3 carbon centre in presence of $FeCl_3$ catalyst.

III.5. Result and Discussion:

Our pre-demonstrated tandem cyclopalladation/heck-suzuki coupling strategies were utilized to get readily access of the precursor substituted C-3 benzylidine indolines **2**. After harvesting a series of substrates **2**, we then set out for the investigation to optimize the reaction conditions to afford indole-3-carbinols **3** by applying various metal free organic oxidants, solvents and temperature. The results are summarized in **Table-1**.

Our investigation was initiated focusing on the oxidation of C(sp^3)-H bond because these simple handling and easily accessible *N*-sulfonylated indoline moieties (**2**) with exocyclic double bonds are excellent latent sulphonamides with isomerizable hydrogens at the C-2 position[36] . We postulated that in reactions, that could proceed through oxidatively generated cation at the allylic C-2 carbon through dehydrogenation and subsequent isomerisation/ aromatization could regioselectively lead to the formation of indole-3-carbinols by trapping water from the medium. Therefore, an organic

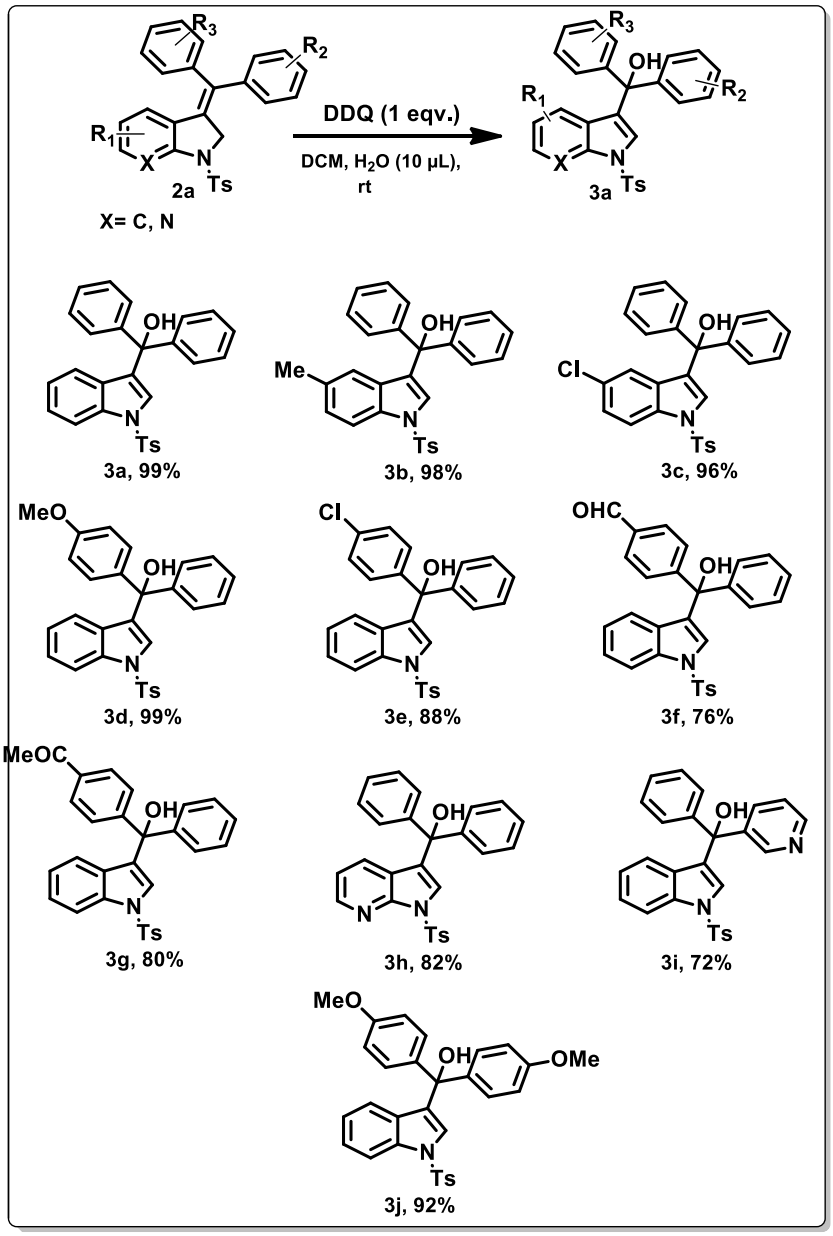
Table 1: Optimization of the reaction conditions.[a]



Entry	Oxidant	Hydroxyl source	Solvent	Temp (ºC)	Time (h)	Yield[b] (%)
1	DDQ	H_2O	THF	rt	22	89
2	DDQ	H_2O	THF	60	19	91
3	**DDQ**	**H_2O**	**DCM**	**rt**	**3**	**99**
4	DDQ	H_2O	DCM	60	3	98
5	DDQ	H_2O	DCE	rt	3	76
6	DDQ	H_2O	MeCN	rt	3	46
7	DDQ	H_2O	CH_3NO_2	rt	3	59
8	DDQ	H_2O	toluene	rt	3	trace
9	DDQ	H_2O	MeOH	rt	3	nr[c]
10	DDQ	O_2	DCM(dry)+ M.S. 4Å	rt	3	trace[d]
11	DDQ + TEMPO	H_2O	DCM	rt	3	99
12	TEMPO	H_2O	DCM	rt	3	nd[e]
13	$K_2S_2O_8$	H_2O	DCM	rt	3	nr
14	CAN	H_2O	DCM	rt	3	nr
15	PIDA	H_2O	DCM	rt	3	30
16.	TBN	H_2O	DCM	rt	3	nd
17.	PBQ	H_2O	DCM	rt	3	nr

[a]Reaction conditions: **2a** (1.0 equiv), oxidant (1.0 equiv.), H_2O (10 µL), solvent (2 mL). [b]Isolated pure yield. [c]no reaction. [d]dry DCM with molecular sieve (4Å). [e]not desired reaction. DDQ:2,3-Dichloro-5,6-dicyano-1,4-benzoquinone. TEMPO: (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl. CAN: Ceric ammonium nitrate. PIDA: phenyliodine(III) diacetate. TBN: tert-Butyl nitrite. PBQ: 1,4-Benzoquinone

Table 2: Scope of the substrates[a,b]



[a]Reaction conditions: **2** (0.22 mmol), DDQ (0.22 mmol), H_2O (10 µL), DCM (1.5 mL), room temperature. [b]Isolated yields

dehydrogenating agent DDQ was introduced to install such electrophilic feature into **2** and green nucleophile water was chosen as green source of hydroxyl functionality.

Our continuous efforts met the first glimpses of success on exposing **2a** to 1 eq. of DDQ in THF in presence of 10 µL H_2O resulted in the formation of diphenyl indole-3-carbinol **3a** at room temperature under ambient atmosphere with 89% yields, but the reaction took 22 hrs to complete (**Table 1, Entry 1**). Even rising the temperature could not give any remarkable change (**Table 1, Entry 2**). Next switching to various polar aprotic and non-polar solvents like MeCN, $MeNO_2$, 1,4-dioxane, 1,2-dicholobenzene and toluene could not offer any considerable improvement in yields and the time-scale (**Table 1, Entry 4-8**) . Protic polar solvent like methanol fails to undergo such conversions (**Table 1, Entry 9**). Surprisingly, on exposing the reaction in 1,1-dichloromethane (DCM), diphenylindole-3-carbinols **3a** was obtained in almost quantitative yield (99%) just after 3hrs (**Table 1, Entry 3**). 20% and 64% yields was observed when the reaction allowed to continue for 0.5 h and 2 h respectively. It is worth mentioning, the aerial oxygen does not have any effect on the reaction (**Table 1, Entry 10**), but solvent used for the reaction plays an important role to reduce the conversion time.

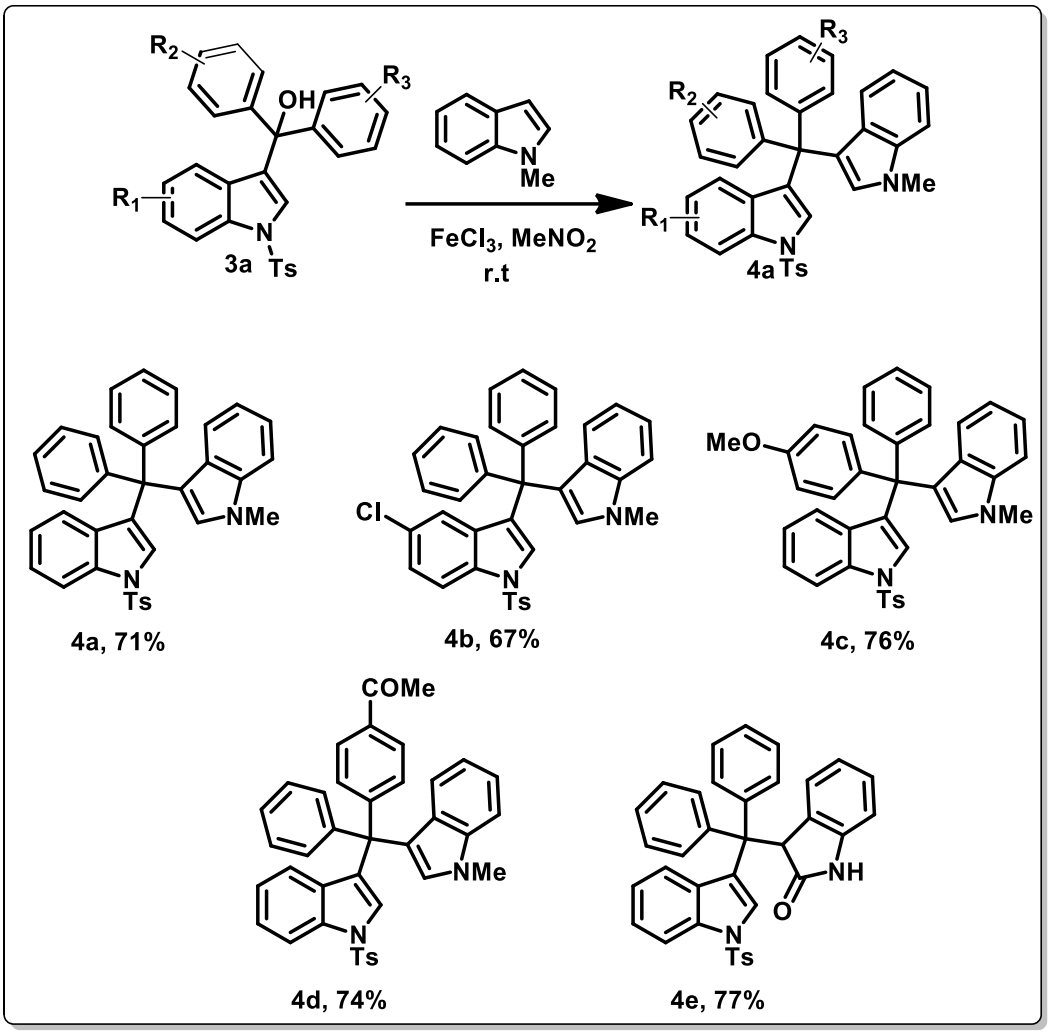
Further screening of different organic oxidants like TEMPO, $K_2S_2O_8$, CAN, PIDA, TBN and PBQ (**Table 1, Entry 12-17**), only PIDA could oxidize 2a to obtain 3a with 30 % of yield (**Table 1, Entry 15**) and the rest were not able to do so. Therefore, DDQ (1.0 equiv) in aquatic (10 µL H_2O DCM) at room temperature was established as the most suitable condition for the regioselective oxyfunctionalization of C-3 benzylidine indoline derivatives.

Next, we applied the standard conditions to variety of substrates to check scope of the method and it was observed that various functionalities were well-tolerated giving moderate to excellent yields. After that, the scope of this dehydrogenativeoxyfunctionalization protocol was probed and the results are summarized in Table 2. Regarding the precursors **2**, we found that functionalized products **3** with both electron donating (**3b**, **98%**) and electron withdrawing (**3c**, **96%**) groups gave

almost quantitative yields. However, in presence of electron withdrawing substituents at the benzylidine sides (**3e** to **3g**) dropped the yields of the products (**76%** to **82%**) while electron-donating group (**3d** and **3j**) at that side gave quantitative yields (**99%**). To our delight, 7-azaindole-donating group (**3d** and **3j**) at that side gave quantitative yields (**99%**). To our delight, 7-azaindole-3-carbinols (**3h**) were synthesized by this protocol with an excellent yield (**80%**). Carbinol with heterocyclic benzylidine substituent (**3i**) gave **72%** yield. All the structures of the products were

characterized by ^{1}H, ^{13}C NMR and HRMS spectra and one of the structures, **3h** was confirmed by X-ray diffraction (See SI).

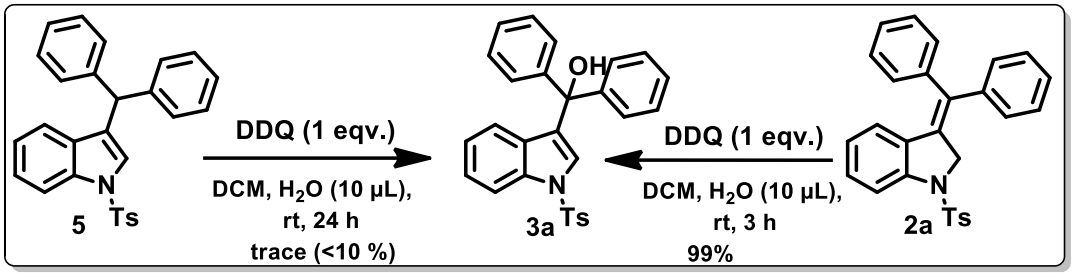
Table 3: Scope of the 3, 3'-bis(indolyl)methanes [a]

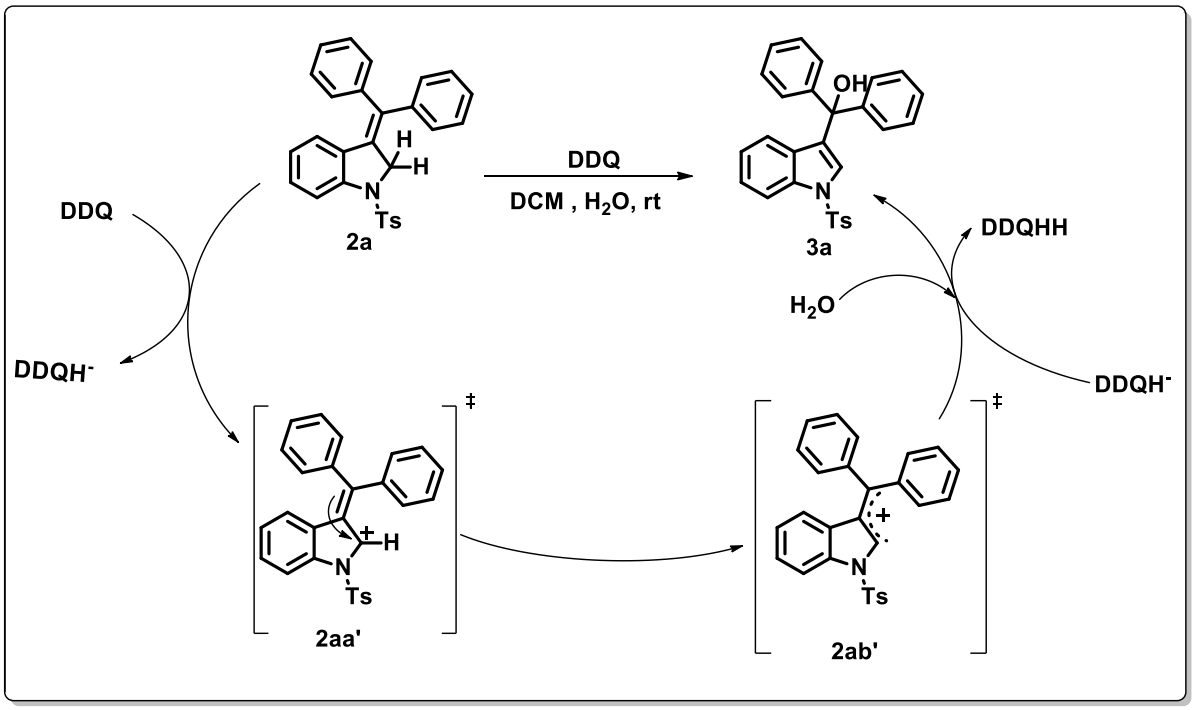


In addition, to explore the synthetic value of the products formed through our developed method, further intermolecular nucleophilic substitution reactions were set up using these indole based carbinols as methylene surrogate to indole nucleophiles for accessing unsymmetrical bis-indolylmethanes (BIMs) bearing quaternary sp^3- carbon centres. For this a straightforward Friedel-Craft reactions were performed in presence of environmentally friendly and inexpensive $FeCl_3$ catalyst in nitromethane solvent at room temperature (Table 3). The alkylated products (**3a** to **3e**) formed with very good yields (**67%** to **77%**).

It is noteworthy to mention that, taking the isomerized product **5** of **2a** prepared according to our earlier report [36], we performed oxyfunctionalization reaction according to our present protocol (Scheme 1). It was observed that there was just a trace (<10 %) of **2a** in the reaction mixture, most of the substrate was intact even after 24 hours of reaction. That means triaryl carbocation generation was not smooth for DDQ rather carbocation generation at alpha sp^3 carbon of allylic sulphonamide moiety in **2a** was more facile. Therefore, subsequent aromatization drove the reaction to tertiary indolylmethanol through the regioselective formation of carbocation at C-3 position of indole.

Scheme 16: Comparative study.





For better understanding the mechanistic path, the reaction was performed in presence of TEMPO (mentioned in **Table 1, Entry 11**). However, the yield of the carbinol formed was not suppressed (quantitative yield).

Based on the previous literature precedents [37] the plausible mechanism of this reaction was depicted in scheme 2. In presence of DDQ, dehydrogenation occurs to form carbocation selectively at the C-2 position (**2aa'**) which is an isomerizable allylic carbocation (**2ab'**). Through isomerization stable indole ring was formed and consequently water in the medium was trapped to form **3a.**

III. 6. Conclusion:

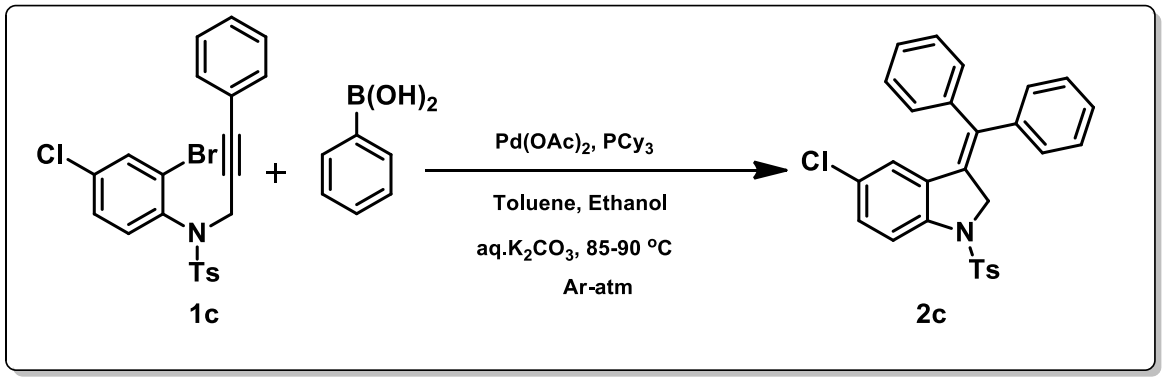
In summary, we have developed a new, metal free, atom-efficient and highly regioselctive oxyfunctionalization strategy to afford tertiary indole-3-carbinols. Previously we reported using those previously mentioned 3-benzylidine precursors as nucleophile. However, in this manuscript, these were used as an electrophilic probe for the synthesis of tertiary C-3 alcohols of indoles, which on extension offered value added unsymmetrical bisindoles with all carbon quaternary centres through straightforward $FeCl_3$ catalysed Friedel- Craft reactions.

III. 7. Experimental Section:

General: All NMR spcetral data were recorded by Bruker 300, 400, 500 (300, 400, 500 MHz) spectrometer in $CDCl_3$solutions expressing chemical shifts in parts per million (ppm, δ) and are referenced to $CHCl_3$ (δ = 7.26 ppm) as an internal standard. All coupling constants are absolute values and are expressed in Hz. The description of the signals include: s = singlet, d = doublet, t = triplet, m = multiplet, dd = doublet of doublets and brs = broad singlet. ^{13}C NMR spectra were recorded with a Bruker 300, 400, 500 (75, 100, 125 respictively MHz) spectrometer as solutions in $CDCl_3$ with complete proton decoupling. Chemical shifts are expressed in parts per million (ppm, δ) and are referenced to $CDCl_3$ (δ = 77.0 ppm) as an internal standard. High-Resolution Mass Spectra (HRMS) were performed with a Qtof Micro YA263 spectrometer in dichloromethane solvent. The molecular fragments are quoted as the relation between mass and charge (*m*/*z*). IR (infrared spectroscopy) was recorded with an FT-IR spectrometer, the IR spectra were recorded as thin films with KBr. The routine monitoring of reactions was performed with silica gel coated glass slides

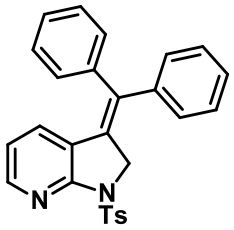
(Merck, silica gel G for TLC), and pre-coated Al plate, which were analyzed with iodine and uv light respectively. Solvents, reagents and chemicals were purchased from Aldrich, Fluka, Merck, SRL, Spectrochem and Process Chemicals. All reactions involving moisture-sensitive reactants were executed with oven-dried glassware.

Representative experimental procedure for the synthesis of 5-chloro-3-(diphenylmethylene)-1-tosylindoline (2c) :



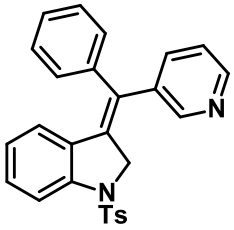
To a solution of *N*-(2-bromo-4-chlorophenyl)-4-methyl-*N*-(3-phenylprop-2-yn-1-yl)benzenesulfonamide **1c** (237 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), phenyl boronic acid (92 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively. The resulting solution was stirred at 85-90 °C under argon atmosphere for 3 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with EtOAc. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated. The product was subjected to column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **2c** as a yellow solid (167 mg, 0.36 mmol, 71%), m.p. 186 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.41 (s, 3H), 4.66 (s, 2H), 6.13 (s, 1H), 6.98-7.00 (m, 2H), 7.08 (d, *J*=8.1 Hz, 3H), 7.25-7.35 (m, 8H), 7.57-7.61 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) : δ 21.6, 59.2, 116.6, 124.7, 127.4, 127.9, 128.0, 128.6, 128.9, 129.0, 129.1, 129.8, 132.1, 133.5, 137.1, 140.2, 141.3, 143.4, 144.5 ppm. HRMS: cacld for $C_{28}H_{22}ClNNaO_2S$ $[M+Na]^+$ 494.0957; found 494.0959.

3-(diphenylmethylene)-1-tosyl-2,3-dihydro-1*H*-pyrrolo[2,3-*b*]pyridine (2h) :



To a solution of *N*-(3-bromopyridin-2-yl)-4-methyl-*N*-(3-phenylprop-2-yn-1-yl)benzenesulfonamide (220 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), phenyl boronic acid (92 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively and treated as described for the synthesis of **2c** for 3.5 h to afford **2h** as a white solid (149 mg, 0.34 mmol, 68%), m.p. 159 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.12 (s, 3H), 4.81 (s, 2H), 6.41 (d, *J*=7.8 Hz, 1H), 6.52 (dd, *J*=2.7, 4.8 Hz, 1H), 7.16-7.19 (m, 3H), 7.25-7.38 (m, 9H), 8.02 (dd, *J*=4.8, 8.1 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) : δ 21.6, 54.0, 117.7, 122.9, 126.9, 127.9, 128.0, 128.2, 128.3, 128.7, 128.8, 129.3, 129.4, 132.1, 135.3, 138.1, 140.6, 140.8, 144.2, 147.8, 157.5 ppm. HRMS: cacld for $C_{27}H_{23}N_2O_2S$ $[M+H]^+$ 439.1480; found 439.1486.

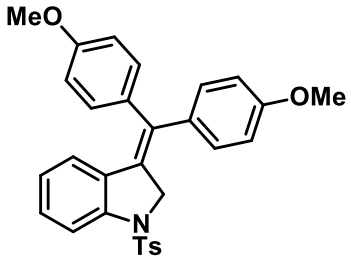
(*Z*)-3-(phenyl(pyridin-3-yl)methylene)-1-tosylindoline (2i) :



To a solution of *N*-(2-bromophenyl)-4-methyl-*N*-(3-(pyridin-3-yl)prop-2-yn-1-yl)benzenesulfonamide (220 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), phenyl boronic acid (92 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively and treated as described for the synthesis of **2c** for 3.5 h to afford **2i** as a white solid (145 mg, 0.33 mmol, 66%), m.p. 166 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.39 (s, 3H), 4.62 (s, 2H), 6.30 (d, *J*=7.8 Hz, 1H), 6.68 (t, *J*=7.8 Hz, 1H), 7.05 (t, *J*=3.6 Hz, 2H), 7.16 (t, *J*=8.1 Hz, 1H), 7.23-7.41 (m, 7H), 7.62 (d, *J*=8.1 Hz, 2H), 7.70 (d, *J*=8.1 Hz, 1H), 8.42 (s, 1H), 8.51

(d, *J*=3.3 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) : δ 21.5, 55.6, 115.5, 123.4, 123.6, 124.9, 127.4, 128.1, 129.2, 129.5, 129.8, 131.5, 132.1, 133.5, 135.7, 137.7, 139.9, 144.4, 145.2, 148.4, 148.9 ppm. HRMS: cacld for $C_{27}H_{23}N_2O_2S$ $[M+H]^+$ 439.1480; found 439.1479.

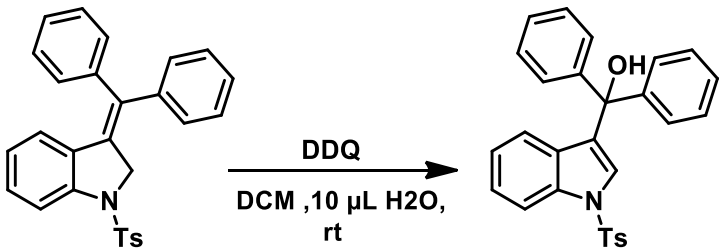
3-(bis(4-methoxyphenyl)methylene)-1-tosylindoline (2j) :



To a solution of *N*-(2-bromophenyl)-*N*-(3-(4-methoxyphenyl)prop-2-yn-1-yl)-4-methylbenzenesulfonamide (235 mg, 0.5 mmol) in toluene (2 mL) and ethanol (2 mL), (4-methoxyphenyl)boronic acid (114 mg, 0.75 mmol), aq. K_2CO_3 solution (2.5 M, 2 mL), PCy_3 (14 mg, 0.05 mmol) and $Pd(OAc)_2$ (6 mg, 0.025 mmol) were added successively and treated as described for the synthesis of **2c** for 2 h to afford **2j** as a white solid (194 mg, 0.39 mmol, 78%), m.p. 187 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.39 (s, 3H), 3.81 (s, 3H), 3.83 (s, 3H), 4.66 (s, 2H), 6.36 (d, *J*=7.6 Hz, 1H), 6.70 (t, *J*=7.6 Hz, 1H), 6.81-6.90 (m, 6H), 6.99 (d, *J*=8.4 Hz, 2H), 7.11 (t, *J*=8.0 Hz, 1H), 7.23 (t, *J*=8.0 Hz, 2H), 7.60 (d, *J*=8.0 Hz, 2H), 7.66 (d, *J*=8.0 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 21.6, 55.3, 55.4, 56.4, 114.0, 114.3, 116.0, 123.6, 124.7, 127.6, 128.8, 129.1, 129.7, 130.7, 131.1, 133.5, 134.0, 134.7, 135.2, 144.2, 144.8, 159.0, 159.2 ppm. HRMS: cacld for $C_{30}H_{28}NO_4S$ $[M+H]^+$ 498.1739; found 498.1737.

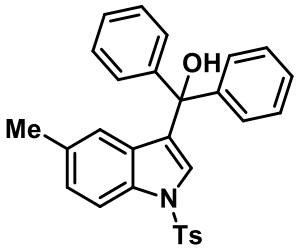
Compounds **2a**, **2b**, **2d**, **2e**, **2f**, **2g** were reported earlier and synthesised by the above similar procedure.

diphenyl(1-tosyl-1H-indol-3-yl)methanol (3a):



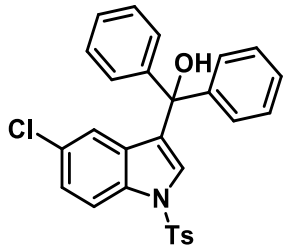
To a solution of **2a** (96 mg, 0.22 mmol) in aquatic (10 µL H_2O) DCM (2 mL) was added DDQ (2,3-Dichloro-5,6-dicyano-1,4-benzoquinone) (50 mg, 0.22 mmol). The reaction mixture was stirred at room temperature for 3 h. After the completion of the reaction (monitored by TLC), the crude reaction mixture was extracted with dichloromethane. The organic extract was washed with sodium bicarbonate solution, dried over anhydrous Na_2SO_4 and concentrated. The product was purified by column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 95:5 (v/v) to afford the product **3a** as a white solid (99 mg, 0.22 mmol, 99%, quantitative), m.p. 151 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) : δ 2.40 (s, 3H), 6.90 (t, *J*=7.5 Hz, 1H), 7.21 (t, *J*=7.5 Hz, 1H), 7.27-7.29 (m, 3H), 7.33-7.39 (m, 4H), 7.44-7.46 (m, 2H), 7.49-7.56 (m, 4H), 7.83 (d, *J*=8.5 Hz, 2H), 7.89 (d, *J*=8.0 Hz, 1H), 8.36 (d, *J*=7.5 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 21.7, 75.2, 116.5, 121.3, 121.5, 124.3, 126.1, 126.4, 127.2, 128.4, 128.6, 129.0, 129.1, 129.3, 129.8, 129.9, 132.8, 133.5, 137.4, 141.9, 142.5, 144.8, 148.0, 150.6 ppm. HRMS: cacld for $C_{28}H_{24}NO_3S$ $[M+H]^+$ 454.1477; found 454.1478.

(5-methyl-1-tosyl-1H-indol-3-yl)diphenylmethanol (3b) :



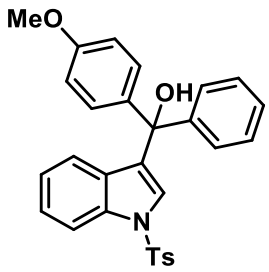
Compound **2b** (100 mg, 0.22 mmol) in aquatic DCM was treated with DDQ (50 mg, 0.22 mmol) as described for the synthesis of **3a** for 3 h to afford **3b** as a white solid (101 mg, 0.21 mmol, 98%), m.p. 148 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) : δ 2.24 (s, 3H), 2.36 (s, 3H), 6.92 (s, 1H), 7.04 (s, 1H), 7.09 (d, *J*=9 Hz, 1H), 7.21-7.30 (m, 12H), 7.67 (d, *J*=8.4 Hz, 2H), 7.85 (d, *J*=8.4 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) : δ 21.3, 21.5, 78.5, 113.5, 122.2, 126.3, 127.1, 127.6, 128.1, 129.0, 129.3, 129.8, 133.0, 134.3, 135.0, 144.9, 145.2, 162.3 ppm. HRMS: cacld for $C_{29}H_{26}NO_3S$ $[M+Na]^+$ 468.1633; found 468.1634.

(5-chloro-1-tosyl-1H-indol-3-yl)diphenylmethanol (3c) :



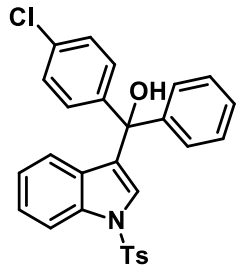
Compound **2c** (104 mg, 0.22 mmol) in aquatic DCM was treated with DDQ (50 mg, 0.22 mmol) as described for the synthesis of **3a** for 3 h to afford **3c** as a white solid (103 mg, 0.21 mmol, 96%), m.p. 167 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.38 (s, 3H), 7.00 (s, 1H), 7.20-7.34 (m, 14H), 7.66 (d, *J*=8.4 Hz, 2H), 7.88 (d, *J*=8.8 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 21.7, 78.6, 114.9, 122.3, 125.3, 126.9, 127.2, 127.4, 127.9, 128.4, 128.9, 129.4, 130.1, 130.6, 134.5, 135.0, 145.0, 145.4 ppm. HRMS: cacld for $C_{28}H_{22}ClNNaO_3S$ $[M+Na]^+$ 510.0907; found 510.0905.

(4-methoxyphenyl)(phenyl)(1-tosyl-1H-indol-3-yl)methanol (3d) :



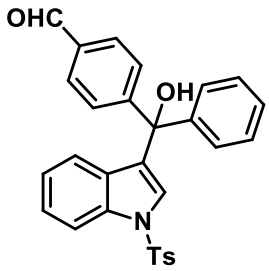
Compound **2d** (103 mg, 0.22 mmol) in aquatic DCM was treated with DDQ (50 mg, 0.22 mmol) as described for the synthesis of **3a** for 3 h to afford **3d** as a white solid (106 mg, 99%, quantitative), m.p. 171 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.36 (s, 3H), 3.80 (s, 3H), 6.81-6.84 (m, 2H), 7.02-7.09 (m, 2H), 7.19 (s, 1H), 7.22-7.46 (m, 10H), 7.70 (d, *J*=8.4 Hz, 2H), 7.96 (d, *J*=8.4 Hz, 1H)ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.6, 55.2, 78.1, 113.4, 113.7, 122.5, 123.2, 124.7, 126.0, 126.8, 127.0, 127.5, 128.1, 128.4, 128.7, 129.1, 129.5, 135.0, 136.0, 137.4, 145.0, 145.3, 158.9 ppm. HRMS: cacld for $C_{29}H_{26}NO_4S$ $[M+H]^+$ 484.1583; found 484.1588.

(4-chlorophenyl)(phenyl)(1-tosyl-1H-indol-3-yl)methanol (3e) :



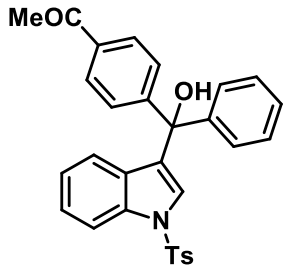
Compound **2e** (104 mg, 0.22 mmol) in aquatic DCM was treated with DDQ (50 mg, 0.22 mmol) as described for the synthesis of **3a** for 3 h to afford **3e** as a white solid (94 mg, 0.20 mmol, 88%), m.p. 165 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.37 (s, 3H), 7.00 (s, 1H), 7.08 (d, *J*=7.2 Hz, 1H), 7.18-7.42 (m, 12H), 7.67 (dd, *J*=8.4 Hz, 10.8 Hz, 3H), 7.96 (d, *J*=8.4 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.6, 78.0, 113.8, 122.3, 123.3, 124.9, 126.0, 126.8, 126.9, 127.3, 127.8, 128.3, 128.6, 129.6, 129.9, 132.6, 133.4, 135.0, 135.9, 143.6, 144.7, 145.1 ppm. HRMS: cacld for $C_{28}H_{22}ClNO_3S$ $[M+H]^+$ 487.1009; found 487.1006.

4-(hydroxy(phenyl)(1-tosyl-1H-indol-3-yl)methyl)benzaldehyde (3f) :



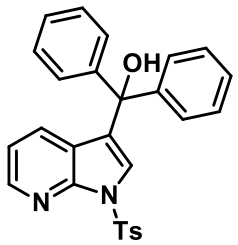
Compound **2f** (102 mg, 0.22 mmol) in aquatic DCM was treated with DDQ (50 mg, 0.22 mmol) as described for the synthesis of **3a** for 3.5 h to afford **3f** as a white solid (81 mg, 0.17 mmol, 76%), m.p. 159 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.37 (s, 3H), 7.02-7.11 (m, 2H), 7.18 (d, *J*=7.5 Hz, 1H), 7.23-7.32 (m, 8H), 7.53 (d, *J*=8.1 Hz, 2H), 7.70 (d, *J*=8.1 Hz, 2H), 7.80 (d, *J*=8.1 Hz, 2H), 7.97 (d, *J*=8.1 Hz, 1H), 9.96 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.6, 78.2, 113.8, 122.2, 123.4, 125.0, 126.1, 126.8, 126.9, 127.7, 128.0, 128.2, 128.4, 128.7, 129.5, 129.9, 134.9, 135.4, 135.9, 144.3, 145.2, 151.6, 191.9 ppm. HRMS: cacld for $C_{29}H_{24}NO_4S$ $[M+H]^+$ 482.1426; found 482.1429.

1-(4-(hydroxy(phenyl)(1-tosyl-1H-indol-3-yl)methyl)phenyl)ethanone (3g) :



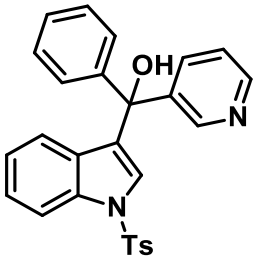
Compound **2g** (105 mg, 0.22 mmol) in aquatic DCM was treated with DDQ (50 mg, 0.22 mmol) as described for the synthesis of **3a** for 3.5 h to afford **3g** as a white solid (89 mg, 0.18 mmol, 80%), m.p. 171 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.37 (s, 3H), 2.58(s, 3H), 7.01 (s, 1H), 7.06 (t, *J*=7.8 Hz, 2H), 7.17 (d, *J*=8.1 Hz, 1H), 7.23-7.31 (m, 6H), 7.45 (d, *J*=8.4 Hz, 3H), 7.70 (d, *J*=8.1 Hz, 2H), 7.88 (d, *J*=8.4 Hz, 2H), 7.96 (d, *J*=8.4 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ 21.7, 26.7, 78.4, 114.0, 122.4, 123.5, 125.1, 126.3, 127.0, 127.1, 127.5, 128.1, 128.3, 128.5, 128.6, 128.9, 130.1, 135.3, 136.2, 136.5, 144.7, 145.3, 150.2, 197.7 ppm. HRMS: cacld for $C_{30}H_{26}NO_4S$ $[M+H]^+$ 496.1583; found 496.1589.

diphenyl(1-tosyl-1H-pyrrolo[2,3-b]pyridin-3-yl)methanol (3h) :



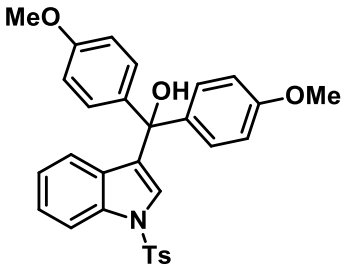
Compound **2h** (96 mg, 0.22 mmol) in aquatic DCM was treated with DDQ (50 mg, 0.22 mmol) as described for the synthesis of **3a** for 4 h to afford **3h** as a white solid (82 mg, 0.18 mmol, 82%), m.p. 173 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.39 (s, 3H), 7.00-7.04 (m, 1H), 7.22 (s, 1H), 7.26 (s, 1H), 7.30-7.33 (m, 11H), 7.54 (d, *J*=6.3 Hz, 1H), 8.04 (d, *J*=8.4 Hz, 2H), 8.38 (d, *J*=6.0 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.8, 78.7, 118.9, 121.8, 125.5, 125.6, 127.1, 127.9, 128.3, 128.4, 129.8, 131.0, 135.5, 144.9, 145.9, 145.2, 145.3 ppm. HRMS: cacld for $C_{27}H_{23}N_2O_3S$ $[M+H]^+$ 455.1429; found 455.1421.

phenyl(pyridin-3-yl)(1-tosyl-1H-indol-3-yl)methanol (3i) :



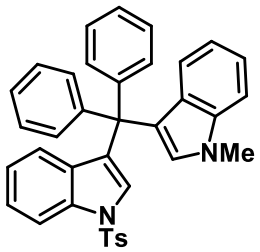
Compound **2i** (96 mg, 0.22 mmol) in aquatic DCM was treated with DDQ (50 mg, 0.22 mmol) as described for the synthesis of **3a** for 3.5 h to afford **3i** as a white solid (77 mg, 0.17 mmol, 72%), m.p. 163 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.28 (s, 3H), 6.93 (s, 1H), 6.98 (t, *J*=7.5 Hz, 2H), 7.09-7.27 (m, 9H), 7.57-7.59 (m, 1H), 7.62 (d, *J*=8.5 Hz, 2H), 7.89 (d, *J*=8.5 Hz, 1H), 8.38 (s, 1H), 8.49 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.7, 77.4, 113.9, 122.3, 123.1, 123.5, 125.1, 126.1, 126.9, 127.0, 128.1, 128.4, 128.5, 128.7, 130.1, 135.1, 136.1, 141.0, 144.4, 145.3, 148.4, 148.5 ppm. HRMS: cacld for $C_{27}H_{23}N_2O_3S$ $[M+H]^+$ 455.1429; found 455.1427.

bis(4-methoxyphenyl)(1-tosyl-1H-indol-3-yl)methanol (3j) :



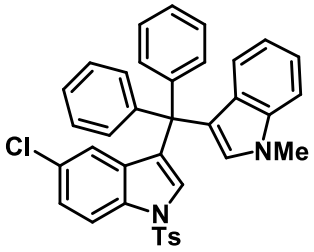
Compound **2j** (109 mg, 0.22 mmol) in aquatic DCM was treated with DDQ (50 mg, 0.22 mmol) as described for the synthesis of **3a** for 3 h to afford **3j** as a white solid (104 mg, 0.20 mmol, 92%), m.p. 181 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.35 (s, 3H), 3.78 (s, 6H), 6.80 (d, *J*=8.8 Hz, 4H), 6.99 (s, 1H), 7.05 (t, *J*=8.0 Hz, 1H), 7.16-7.23 (m, 8H), 7.68 (d, *J*=8.4 Hz, 2H), 7.94 (d, *J*=8.0 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ 21.7, 55.3, 78.0, 113.5, 113.8, 122.6, 123.3, 124.8, 126.0, 126.9, 128.5, 129.3, 129.9, 130.0, 135.2, 136.1, 137.7, 145.1, 158.9 ppm. HRMS: cacld for $C_{30}H_{28}NO_5S$ $[M+H]^+$ 514.1688; found 514.1692.

3-(diphenyl(1-tosyl-1H-indol-3-yl)methyl)-1-methyl-1H-indole (4a) :



To a solution of **3a** (82 mg, 0.18 mmol) in dry nitromethane (2 mL) was added *N*-methylindole (24 mg, 0.18 mmol) and anhydrous $FeCl_3$ (3 mg, 0.018 mmol). The reaction mixture was stirred at room temperature under an argon atmosphere for overnight. After the completion of the reaction (monitored by TLC), the solvent was evaporated and the product was purified by column chromatography (silica gel, 60-120 mesh), eluting with pet ether/EtOAc 97:3 (v/v) to afford the product **4a** as a white solid (72 mg, 0.13 mmol, 71%), m.p. 192 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.33 (s, 3H), 3.59 (s, 3H), 6.12 (s, 1H), 6.34 (d, *J*=7.8 Hz, 1H), 6.49 (s, 1H), 6.77 (t, *J*=8.7 Hz, 4H), 6.96-7.32 (m, 15H), 7.44 (d, *J*=7.8 Hz, 1H), 7.59 (d, *J*=7.8 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.7, 32.8, 55.2, 109.3, 113.1, 113.9, 118.8, 120.9, 121.4, 122.2, 122.9, 123.4, 124.2, 126.4, 126.9, 127.8, 129.4, 129.8, 130.0, 130.6, 131.0, 131.4, 135.4, 136.2, 137.1, 137.8, 144.7, 145.2, 158.0 ppm. HRMS: cacld for $C_{37}H_{31}N_2O_2S$ $[M+H]^+$ 567.2106; found 567.2109.

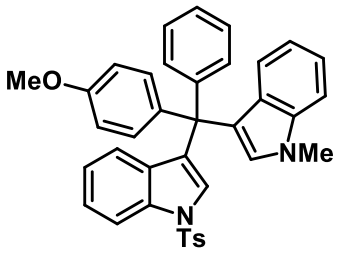
5-chloro-3-((1-methyl-1H-indol-3-yl)diphenylmethyl)-1-tosyl-1H-indole (4b) :



Compound **3c** (88 mg, 0.18 mmol) was treated with *N*-methylindole (24 mg, 0.18 mmol) and anhydrous $FeCl_3$ (3 mg, 0.018 mmol) under argon atmosphere at room temperature as described for the synthesis of **4a** for overnight to afford **4b** as an white solid (72 mg, 0.12 mmol, 67%), m.p.

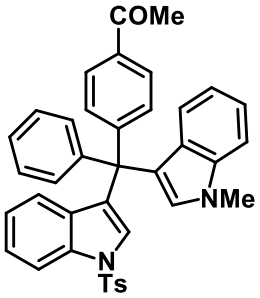
183 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.35 (s, 3H), 3.62 (s, 3H), 6.13 (s, 1H), 6.20 (s, 1H), 6.51 (s, 1H), 6.76 (d, *J*=7.6 Hz, 2H), 7.03-7.13 (m, 6H), 7.16-7.31 (m, 10H), 7.50 (d, *J*=8.4 Hz, 2H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.8, 32.7, 64.6, 109.2, 119.7, 120.4, 121.8, 124.7, 127.4, 127.5, 128.0, 128.1, 128.2, 128.8, 129.0, 129.4, 129.7, 143.8 ppm. HRMS: cacld for $C_{37}H_{30}ClN_2O_2S$ $[M+H]^+$ 601.1717; found 601.1714.

3-((4-methoxyphenyl)(1-methyl-1H-indol-3-yl)(phenyl)methyl)-1-tosyl-1H-indole (4c) :



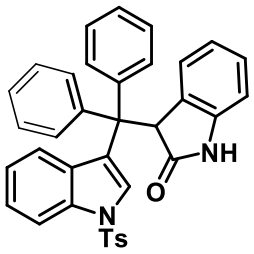
Compound **3d** (87 mg, 0.18 mmol) was treated with *N*-methylindole (24 mg, 0.18 mmol) and anhydrous $FeCl_3$ (3 mg, 0.018 mmol) under argon atmosphere at room temperature as described for the synthesis of **4a** for overnight to afford **4c** as an off white solid (82 mg, 0.14 mmol, 76%), m.p. 198 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.39 (s, 3H), 3.68 (s, 3H), 3.77 (s, 3H), 6.59 (s, 1H), 6.60-6.75 (m, 5H), 6.86 (t, *J*=7.2 Hz, 1H), 7.10-7.26 (m, 13H), 7.66 (d, *J*=8.1 Hz, 2H), 7.97 (d, *J*=8.1 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.5, 32.6, 64.3, 78.6, 109.1, 114.3, 118.3, 119.6, 120.5, 121.7, 124.2, 124.7, 126.0, 127.2, 127.4, 127.6, 128.0, 128.3, 128.8, 128.9, 129.2, 131.9, 135.3, 135.7, 137.2, 137.4, 141.3, 141.8, 143.5, 144.0 ppm. HRMS: cacld for $C_{38}H_{33}N_2O_3S$ $[M+H]^+$ 597.2212; found 597.2214.

1-(4-((1-methyl-1H-indol-3-yl)(phenyl)(1-tosyl-1H-indol-3-yl)methyl)phenyl)ethanone (4d) :



Compound **3g** (89 mg, 0.18 mmol) was treated with *N*-methylindole (24 mg, 0.18 mmol) and anhydrous $FeCl_3$ (3 mg, 0.018 mmol) under argon atmosphere at room temperature as described for the synthesis of **4a** for overnight to afford **4d** as an white solid (81 mg, 0.13 mmol, 74%), as a mixture of non-separable isomers (*E*:*Z*=1:1), m.p. 147 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.35 (s, 6H), 2.57 (s, 3H), 2.62 (s, 3H), 3.62 (s, 6H), 6.14 (d, *J*=12 Hz, 2H), 6.40 (t, *J*=9.6 Hz, 2H), 6.49 (s, 1H), 6.54 (s, 1H), 6.74 (d, *J*=7.6 Hz, 2H), 6.81 (t, *J*=7.6 Hz, 3H), 6.88 (d, *J*=8.0 Hz, 3H), 7.03 (d, *J*=8.0 Hz, 7H), 7.12 (t, *J*=7.6 Hz, 3H), 7.18-7.23 (m, 9H), 7.28-7.34 (m, 5H), 7.39 (d, *J*=8.0 Hz, 1H), 7.48 (d, *J*=7.6 Hz, 1H), 7.61-7.64 (m, 2H), 7.70 (d, *J*=8.0 Hz, 2H), 7.87 (d, *J*=8.4 Hz, 2H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.5, 26.7, 32.6, 32.7, 64.0, 64.3, 109.1, 109.2, 113.8, 113.9, 118.2, 119.6, 119.7, 120.3, 121.3, 121.7, 124.3, 124.6, 124.9, 125.9, 127.3, 127.5, 128.0, 128.1, 128.2, 128.3, 128.4, 128.5, 128.8, 128.9, 129.1, 129.2, 129.6, 129.7, 131.1, 131.4, 135.5, 135.6, 135.7, 136.0, 136.2, 136.3, 136.6, 137.2, 140.5, 141.2, 143.5, 143.6, 144.2, 146.4, 146.6, 197.5 ppm. HRMS: cacld for $C_{39}H_{33}N_2O_3S$ $[M+H]^+$ 609.2212; found 609.2212.

3-(diphenyl(1-tosyl-1H-indol-3-yl)methyl)indolin-2-one (4e) :

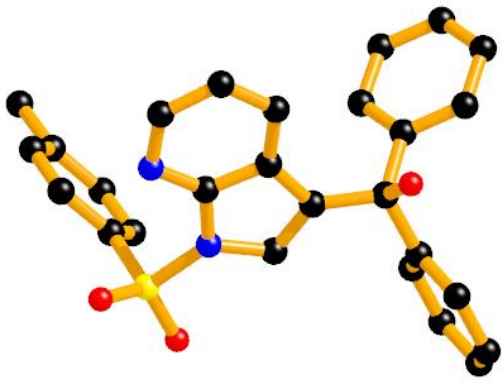


Compound **3a** (82 mg, 0.18 mmol) was treated with oxindole (24 mg, 0.18 mmol) and anhydrous $FeCl_3$ (3 mg, 0.018 mmol) under argon atmosphere at room temperature as described for the synthesis of **4a** for overnight to afford **4e** as an yellow solid (88 mg, 0.15 mmol, 77%), m.p. 162 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.40 (s, 3H), 2.61 (d, *J*=22.8 Hz, 1H), 3.19 (d, *J*=21.9 Hz, 1H), 6.36 (d, *J*=7.5 Hz, 1H), 6.69-6.77 (m, 4H), 6.99 (t, *J*=7.5 Hz, 2H), 7.09-7.17 (m, 6H), 7.21-7.29 (m, 7H), 7.89 (t, *J*=9.0 Hz, 3H), ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.6, 34.7, 69.7, 110.8, 114.7, 122.3, 123.4, 124.1, 124.4, 124.6, 127.0, 127.4, 127.9, 128.5, 129.2, 129.8, 129.9, 133.6, 139.8, 140.7, 141.0, 141.3, 143.6, 144.5, 173.0 ppm. HRMS: cacld for $C_{36}H_{29}N_2O_3S$ $[M+H]^+$ 569.1899; found 569.1898.

Crystallographic data of 3h:

	3h
Formula	$C_{27}H_{22}N_2O_4S$
M_r	470.53
Crystal system	Triclinic
Space group	P -1
a / Å	8.6868(10)
b / Å	11.8781(14)
c / Å	13.2771(15)
α /°	104.028(3)
β /°	95.447(3)
γ /°	108.651(3)
V /Å^3	1237.0(2)
Z	2
D_{calcd} /mg m^{-3}	1.263
μ /mm^{-1}	0.166
θ /°	1.890 – 24.999
T /K	273

Fig. 1: Crystal structure of **3h**



III. 8. References:

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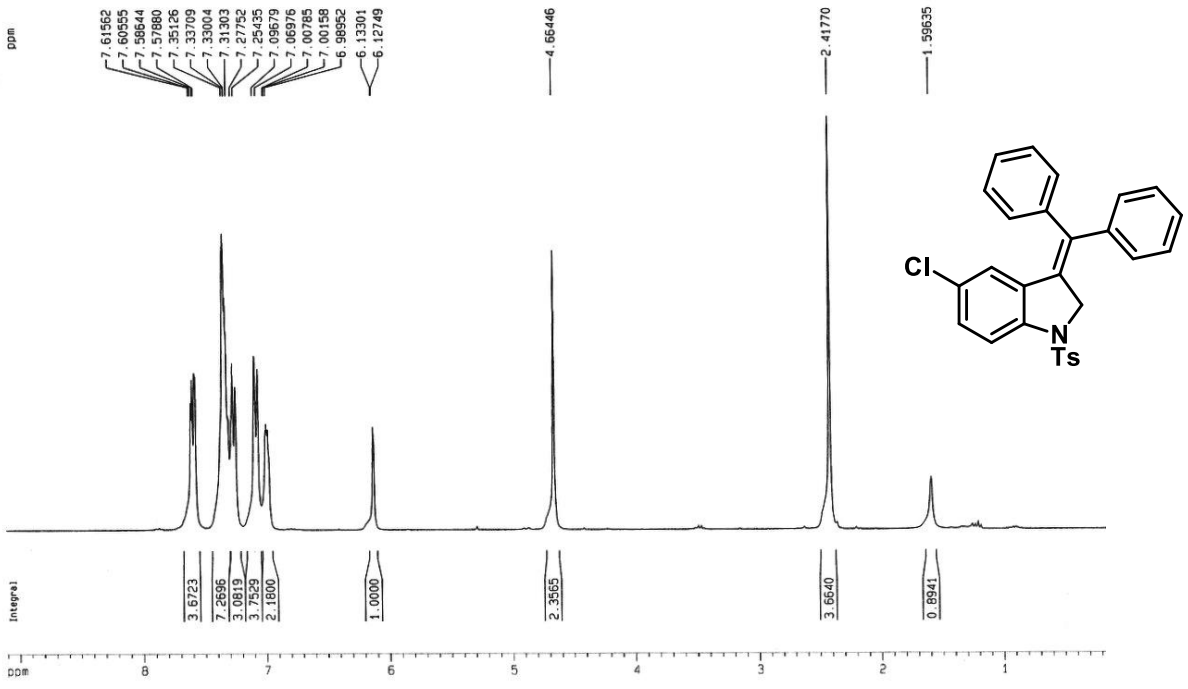
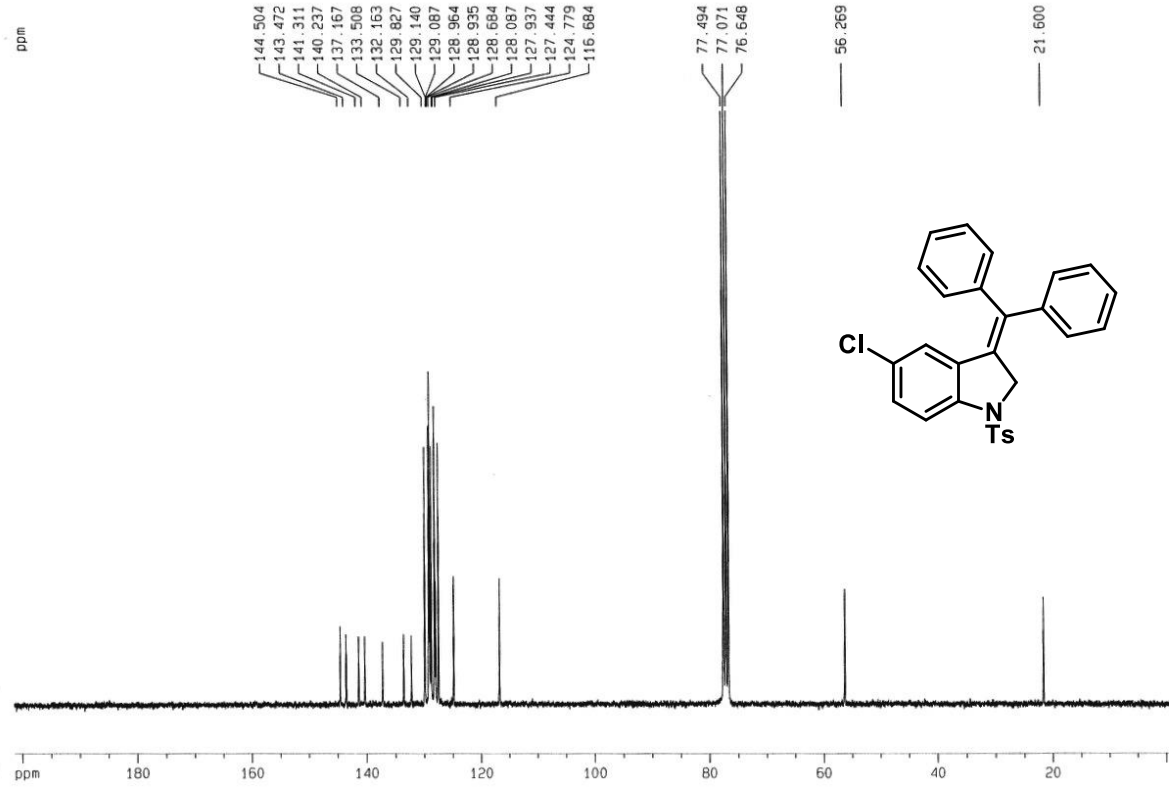
III.10. Copies of some important ^{1}H and ^{13}C NMR spectra of compounds described in Chapter III

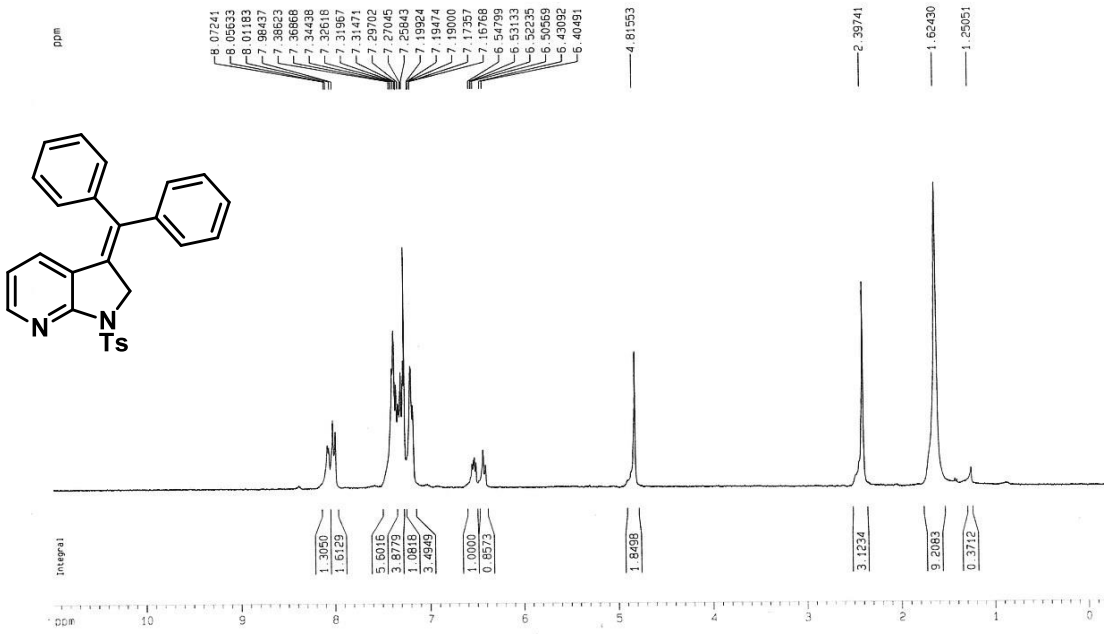
^{1}H NMR of 2c, $CDCl_3$, 300 MHz



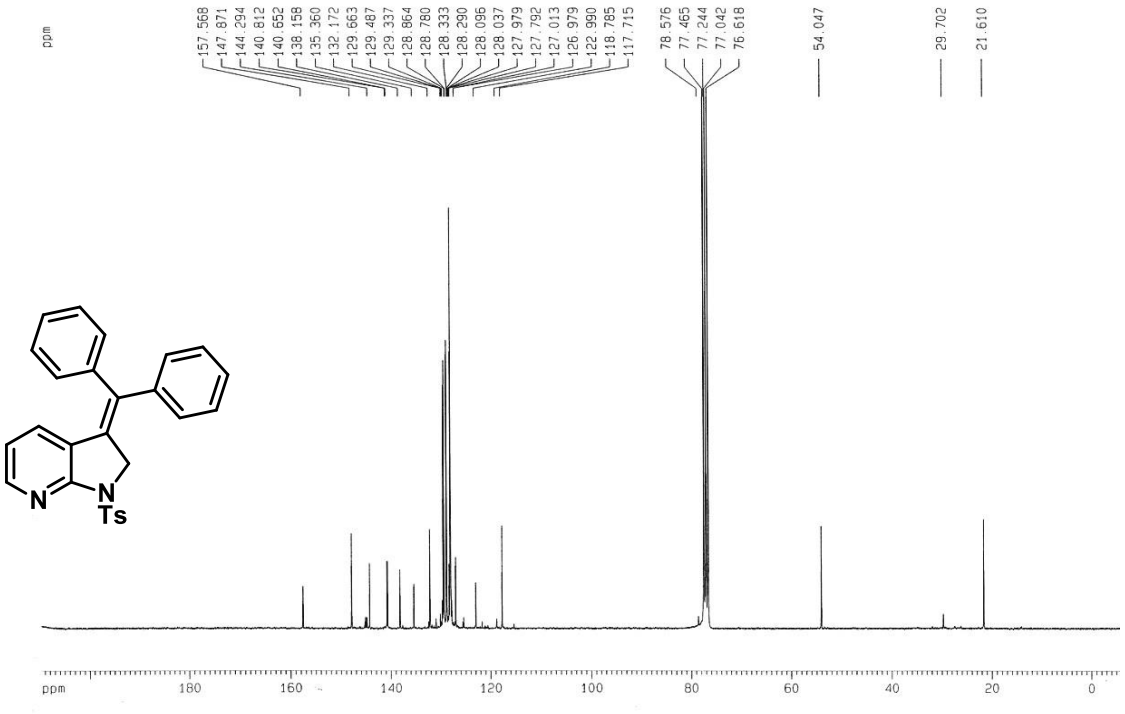
^{13}C NMR of 2c, $CDCl_3$, 75 MHz



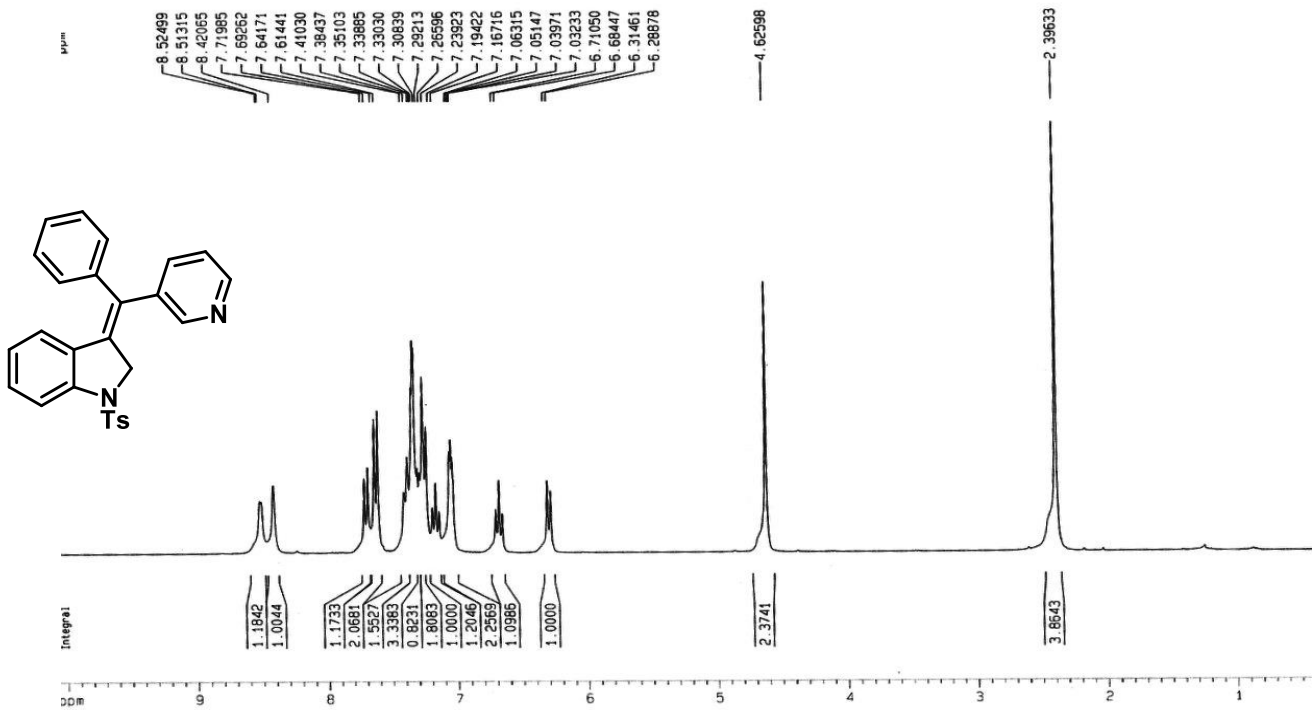
^{1}H NMR of 2h, $CDCl_3$, 300 MHz



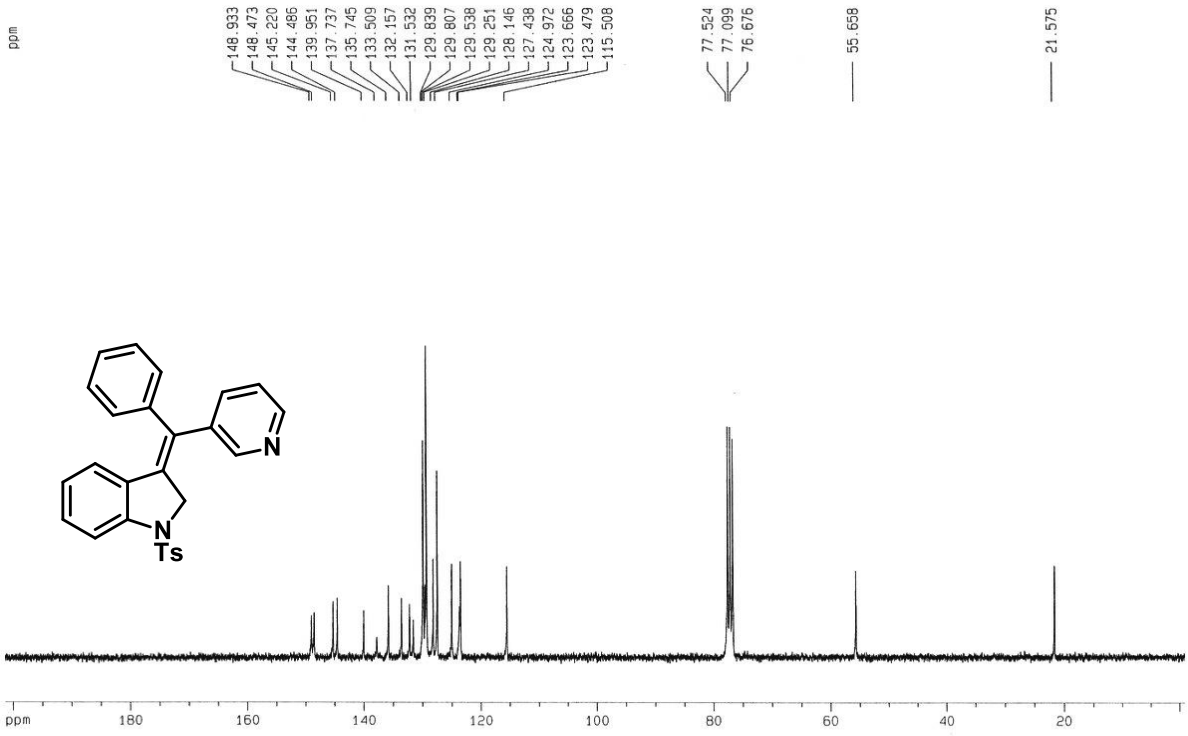
^{13}C NMR of 2h, $CDCl_3$, 75 MHz



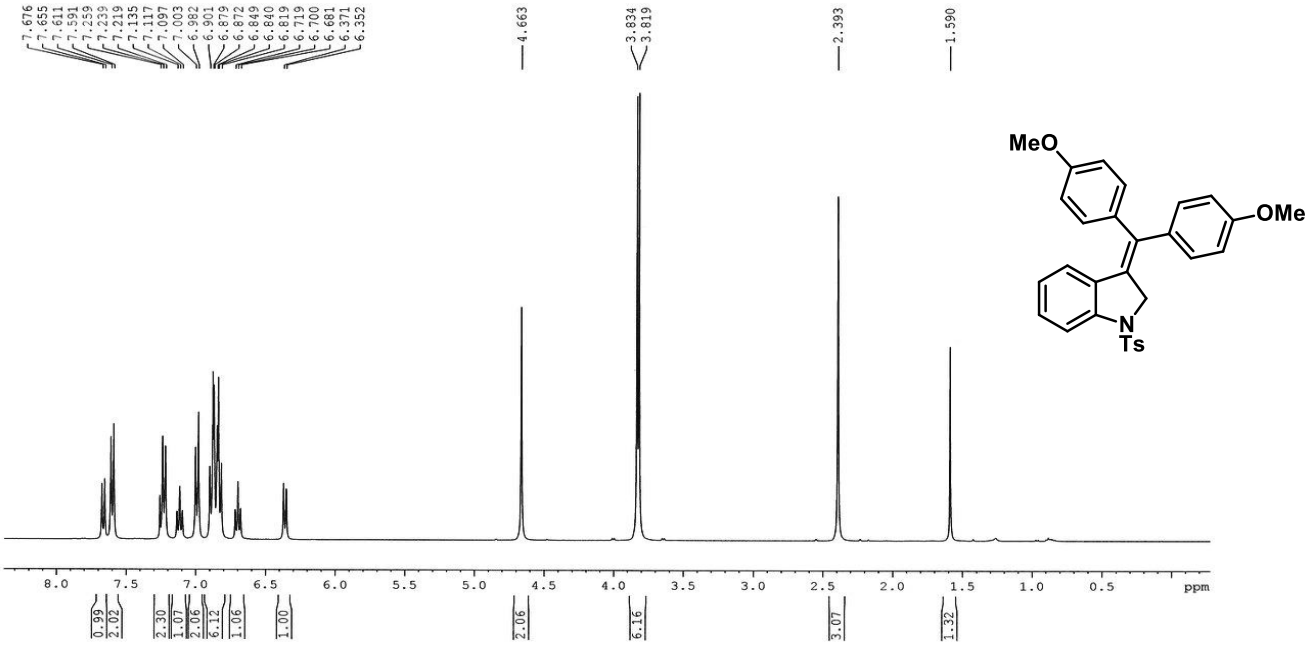
^{1}H NMR of 2i, $CDCl_3$, 300 MHz



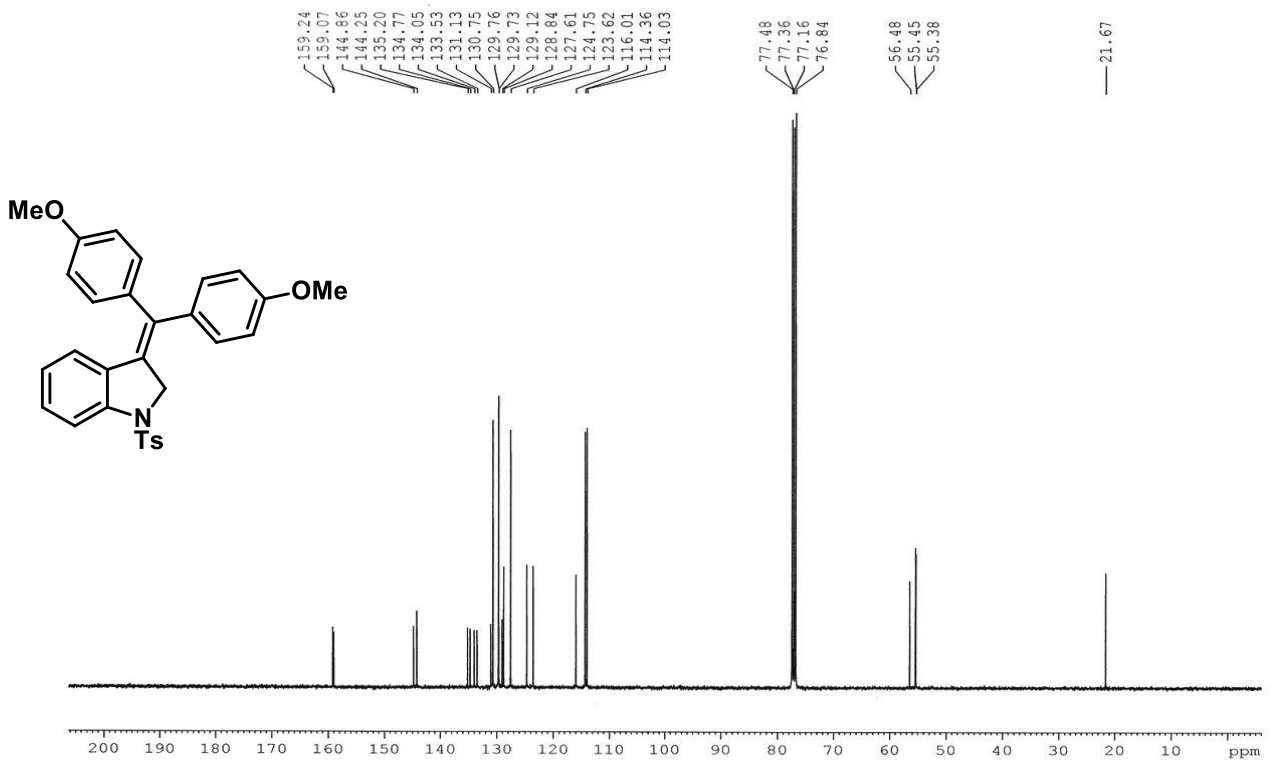
^{13}C NMR of 2i, $CDCl_3$, 75 MHz



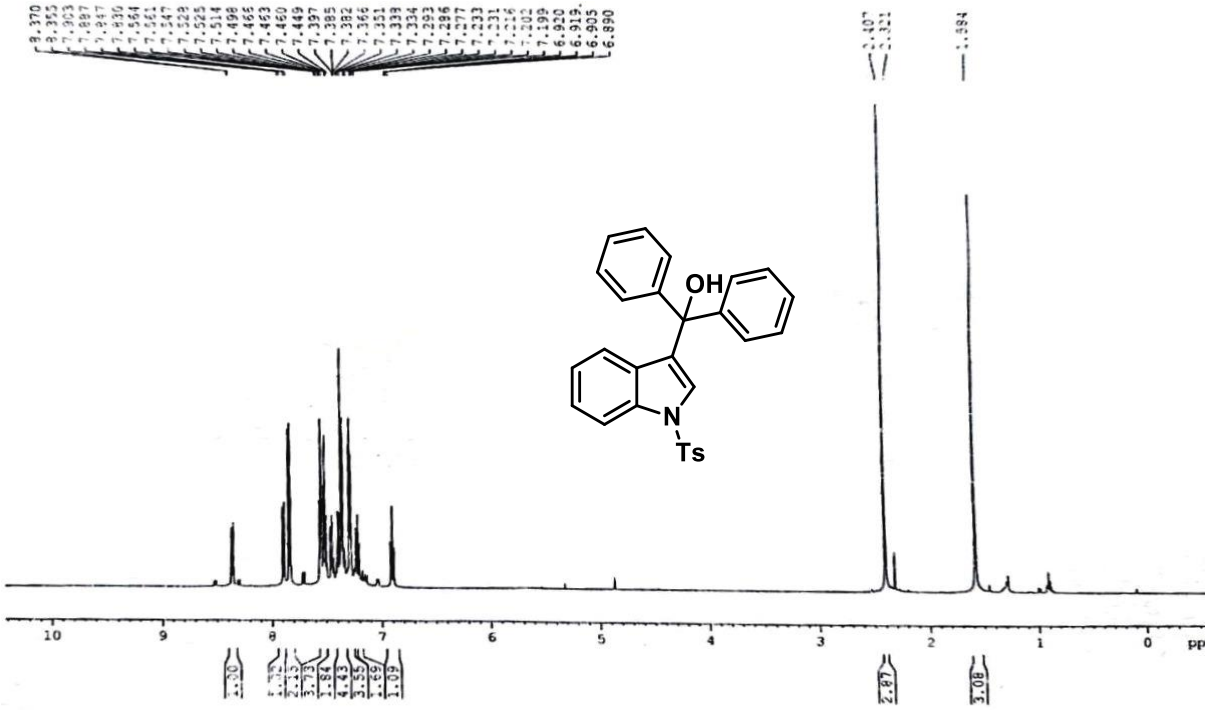
^{1}H NMR of 2j, $CDCl_3$, 400 MHz



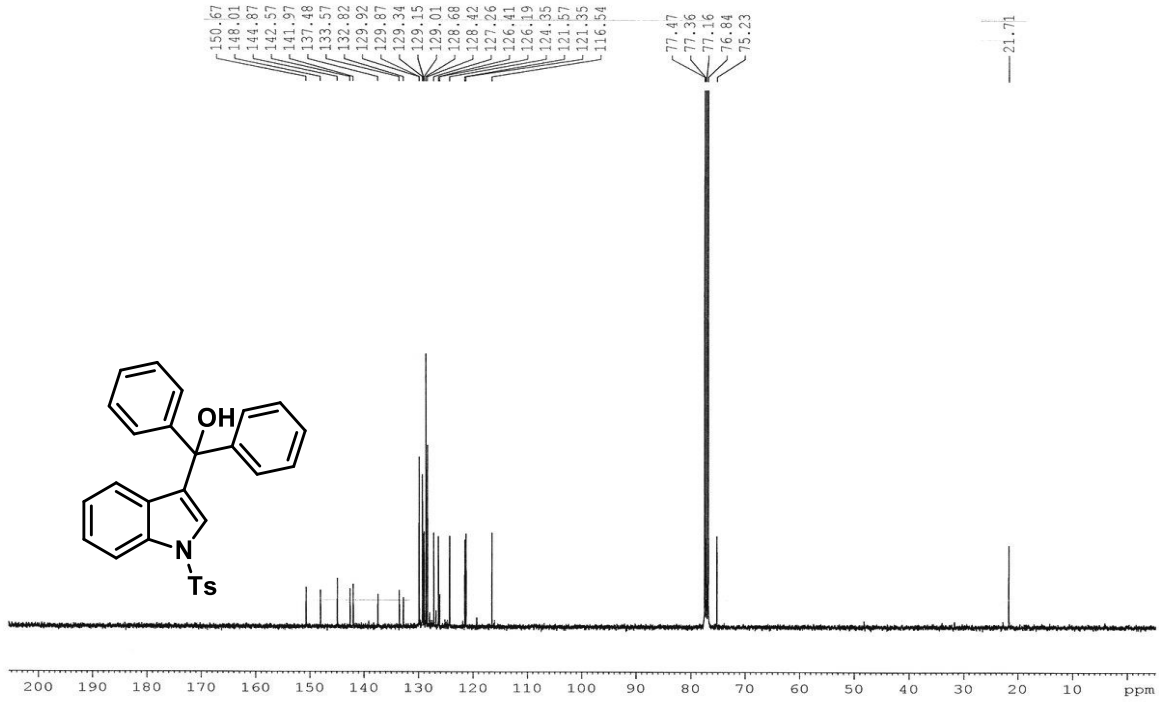
^{13}C NMR of 2j, $CDCl_3$, 100 MHz



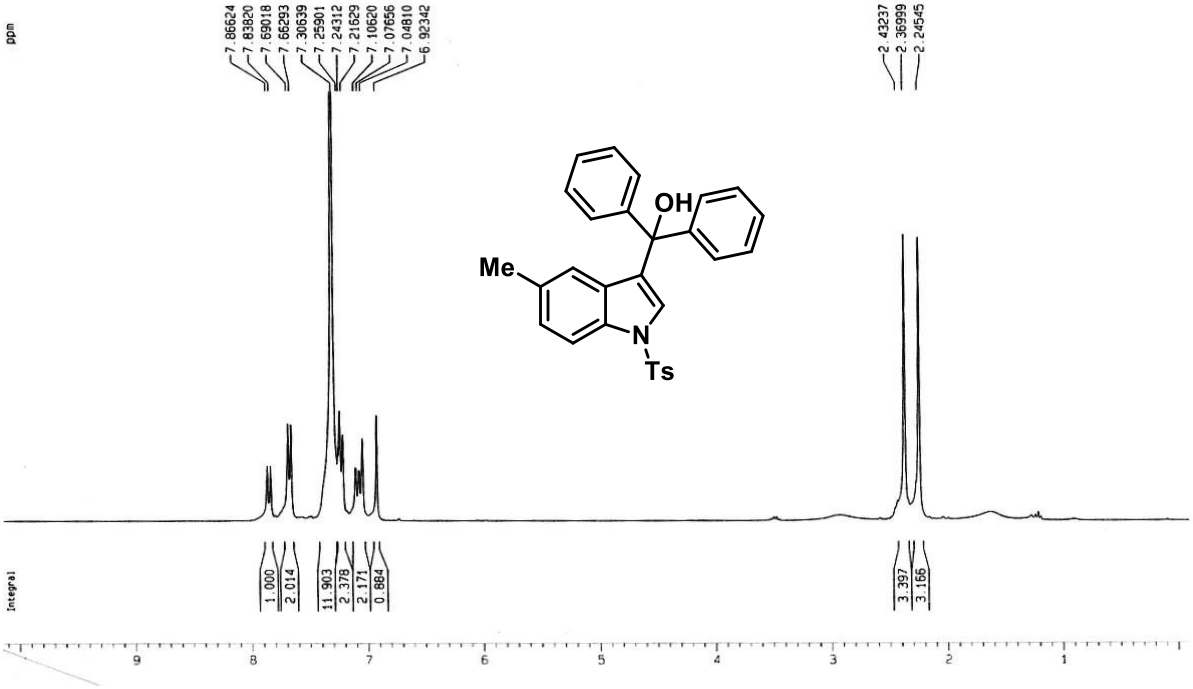
^{1}H NMR of 3a, $CDCl_3$, 500 MHz



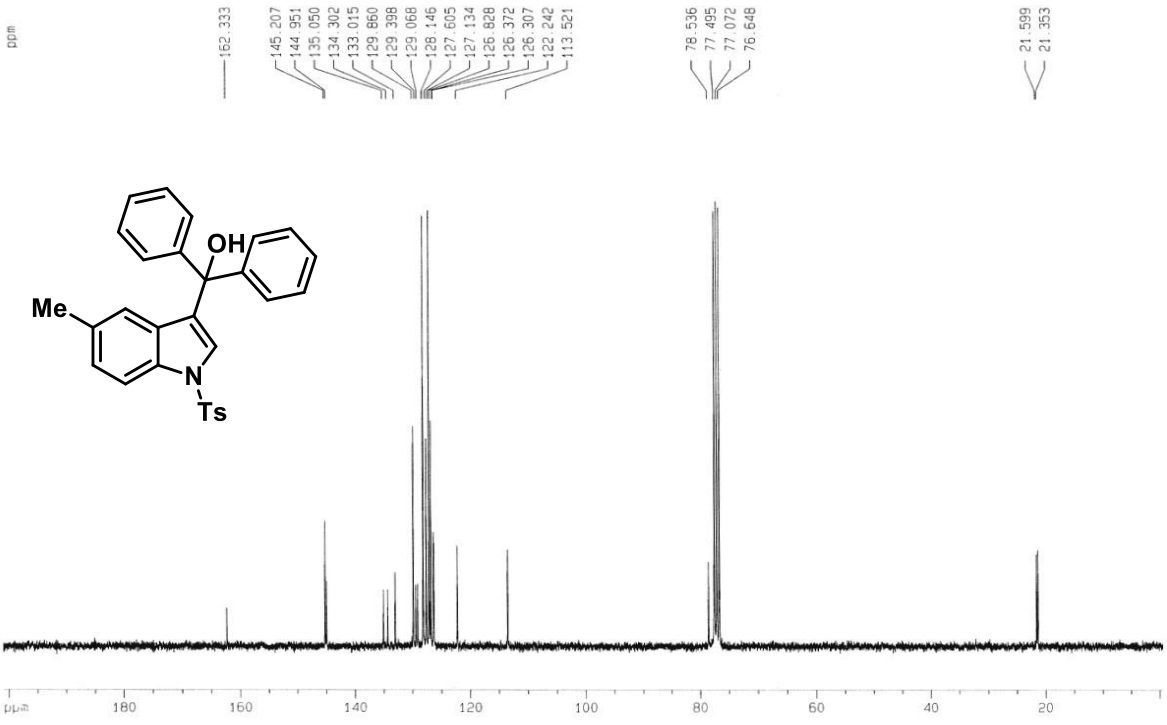
^{13}C NMR of 3a, $CDCl_3$, 100 MHz



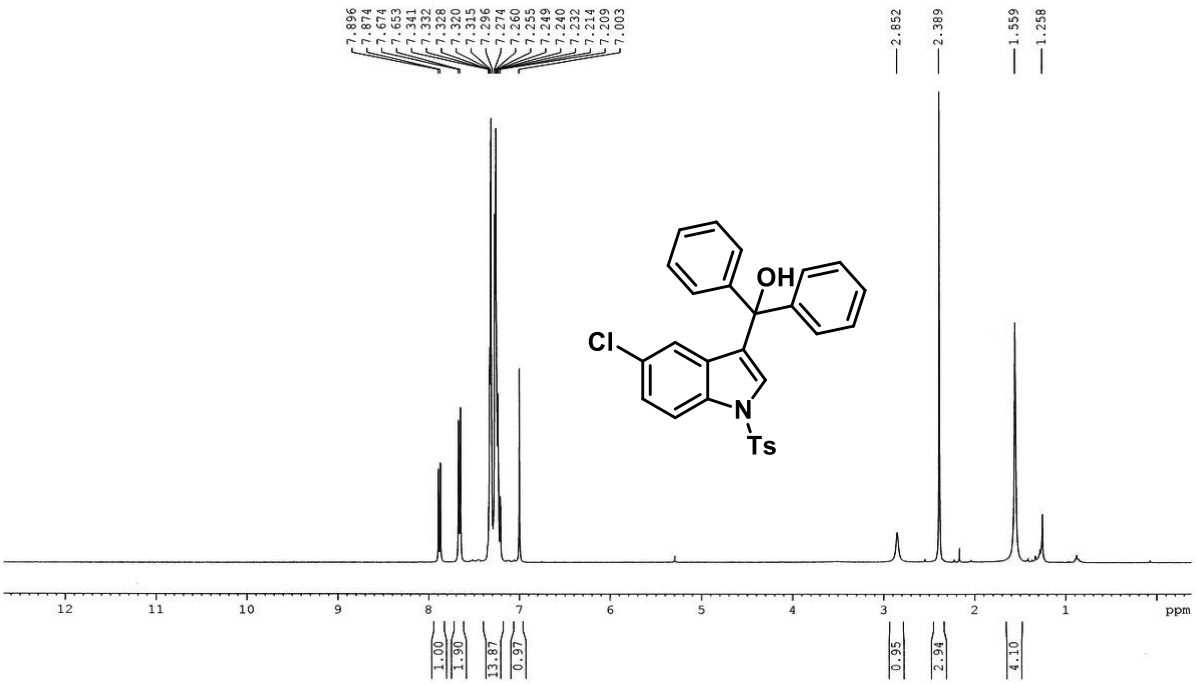
^{1}H NMR of 3b, $CDCl_3$, 300 MHz



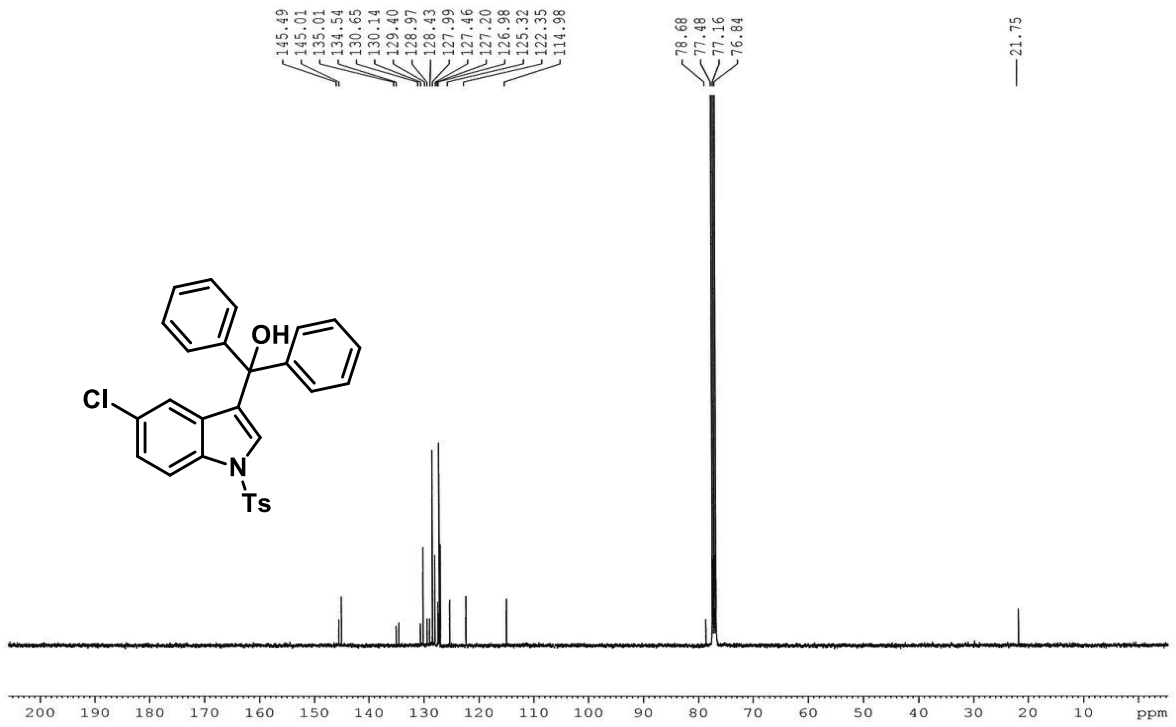
^{13}C NMR of 3b, $CDCl_3$, 75 MHz



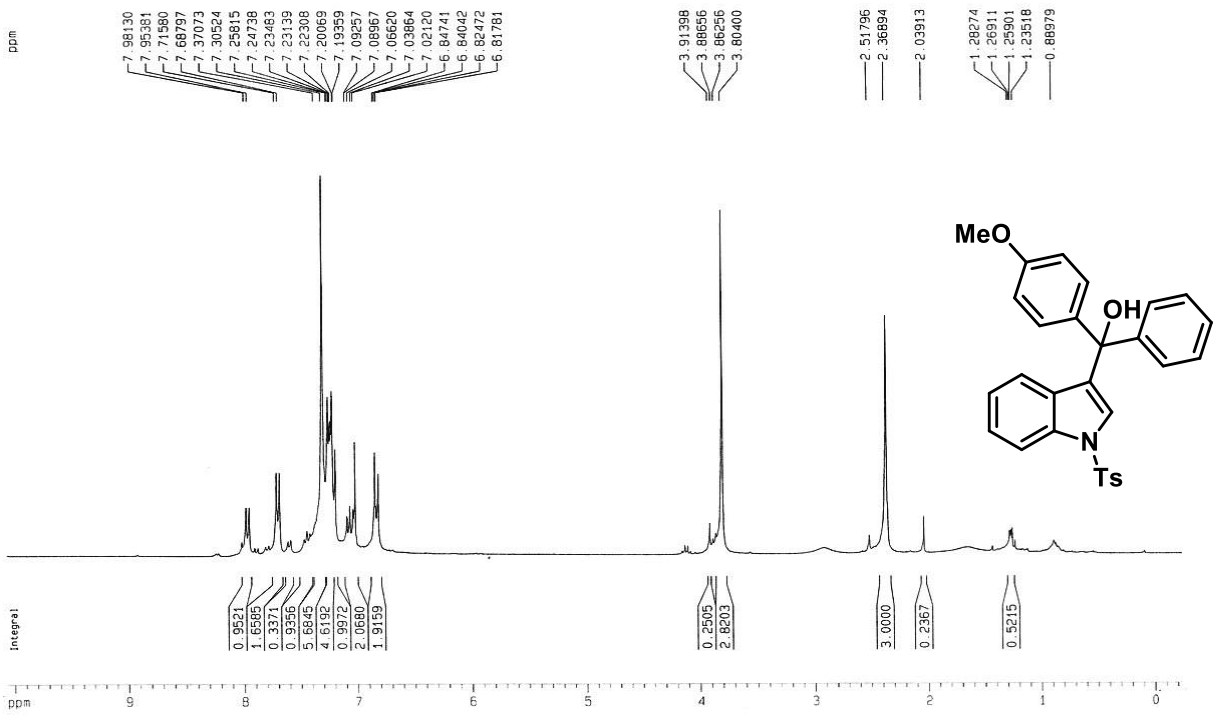
^{1}H NMR of 3c, $CDCl_3$, 400 MHz



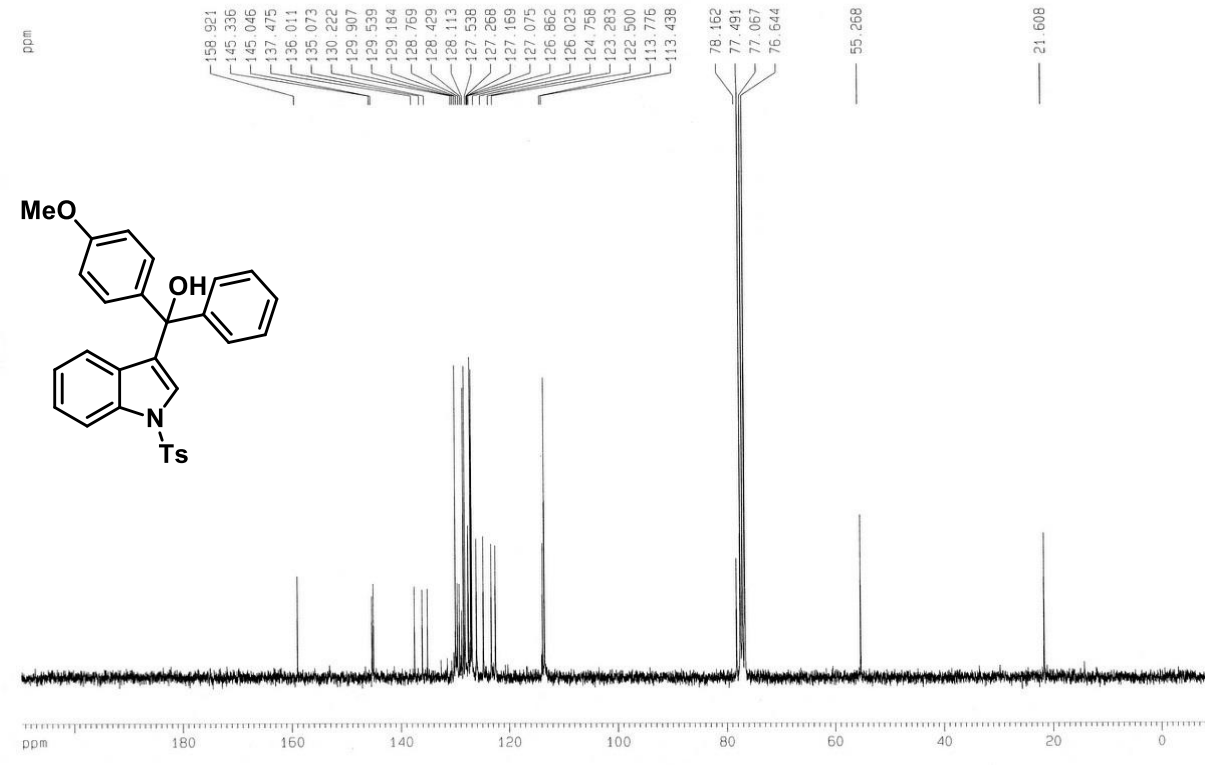
^{13}C NMR of 3c, $CDCl_3$, 100 MHz



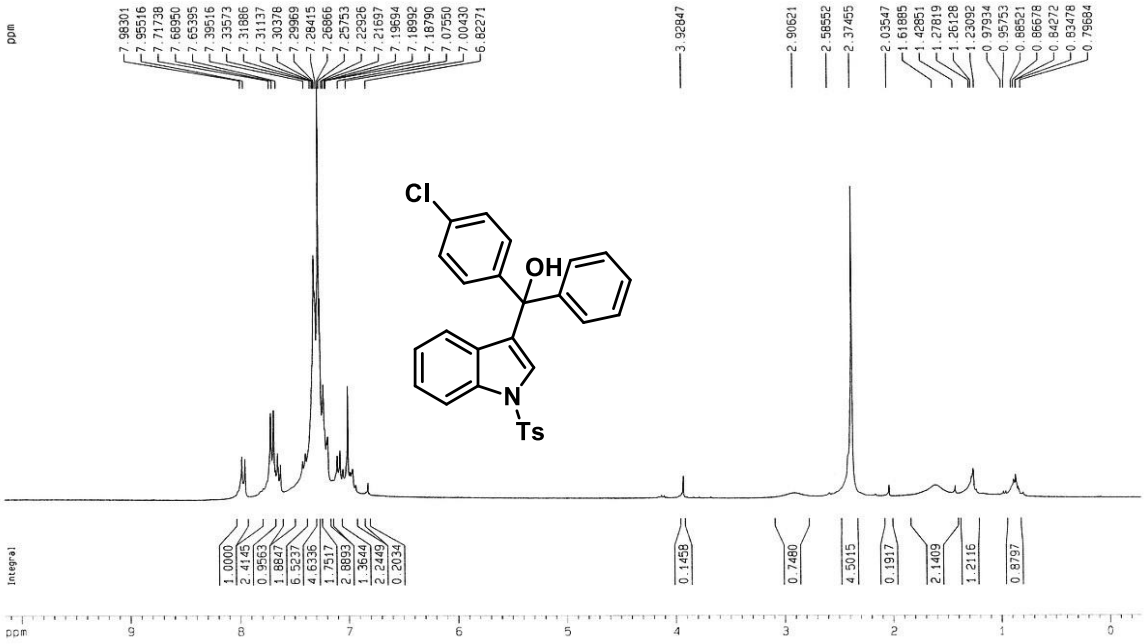
^{1}H NMR of 3d, $CDCl_3$, 300 MHz



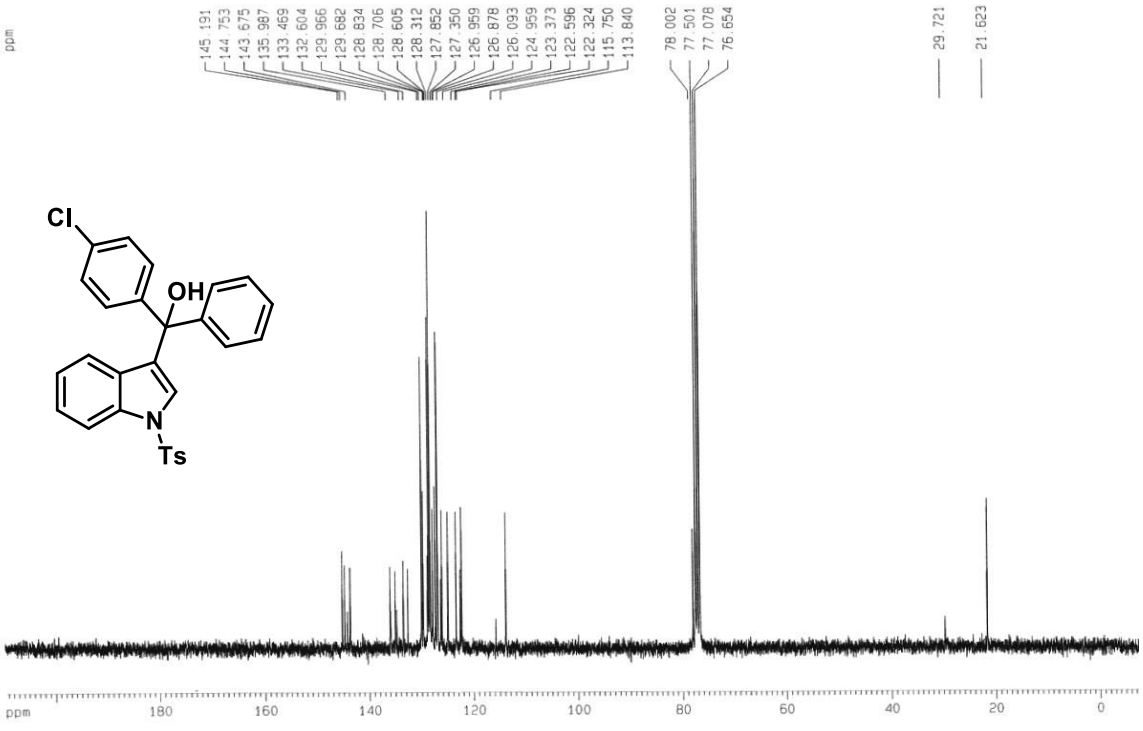
^{13}C NMR of 3d, $CDCl_3$, 75 MHz



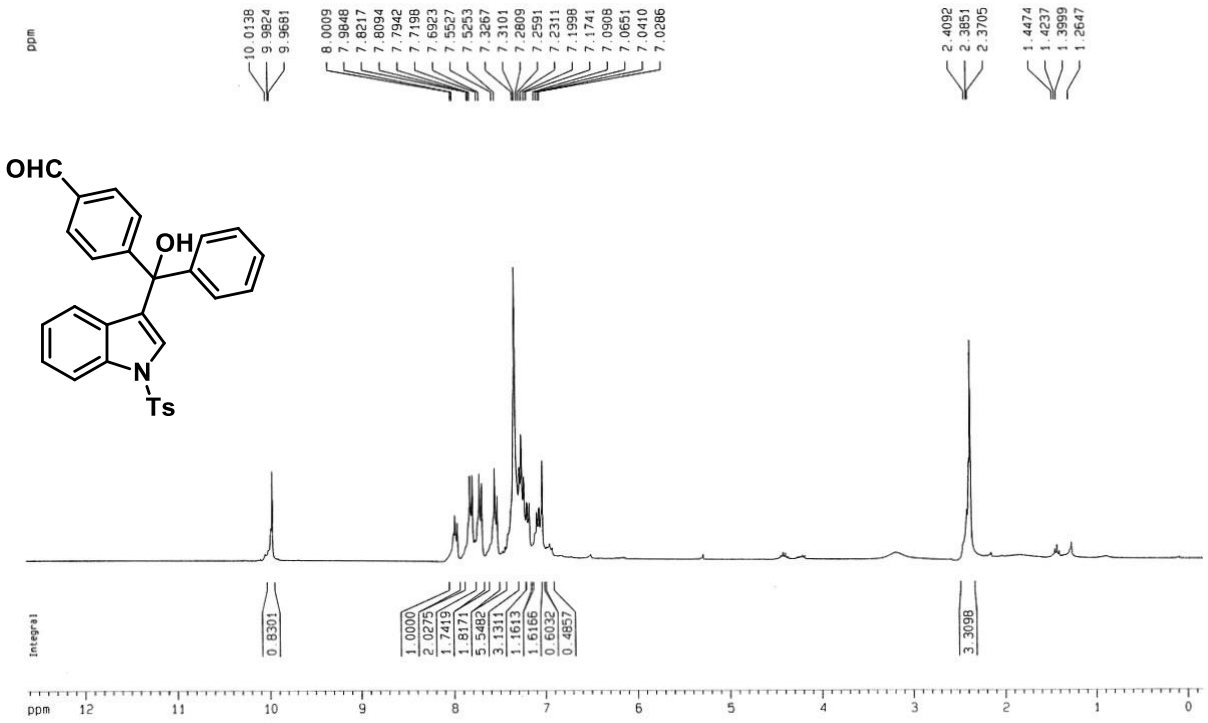
^{1}H NMR of 3e, $CDCl_3$, 300 MHz



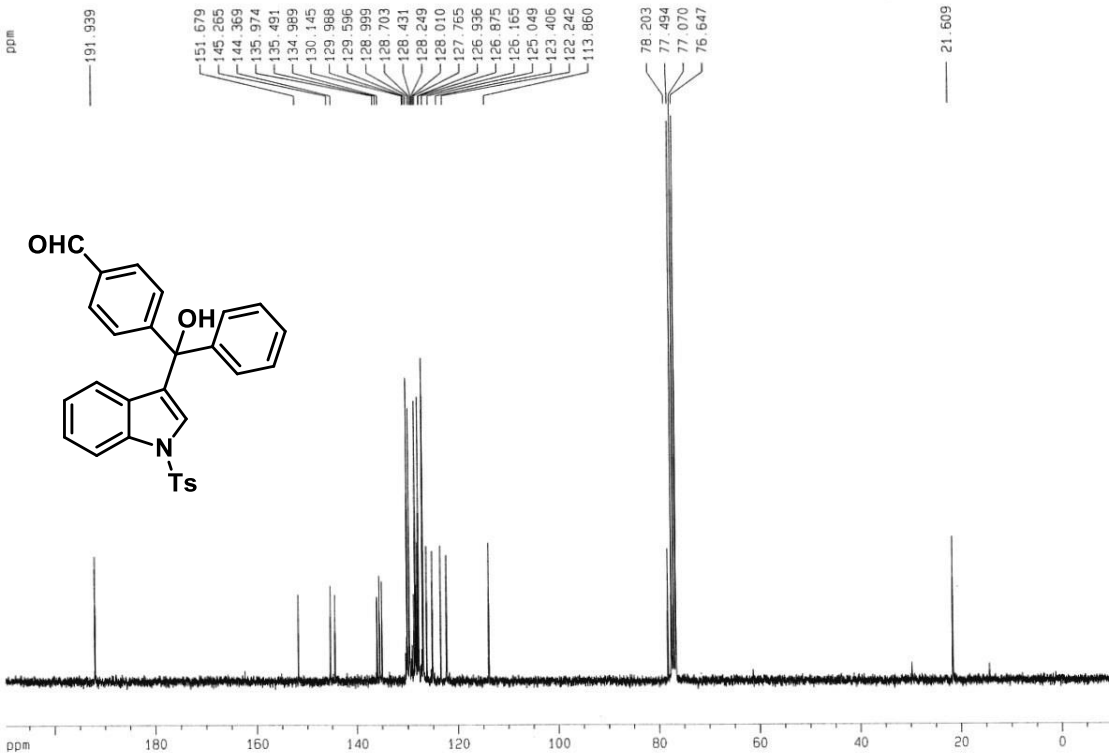
^{13}C NMR of 3e, $CDCl_3$, 75 MHz



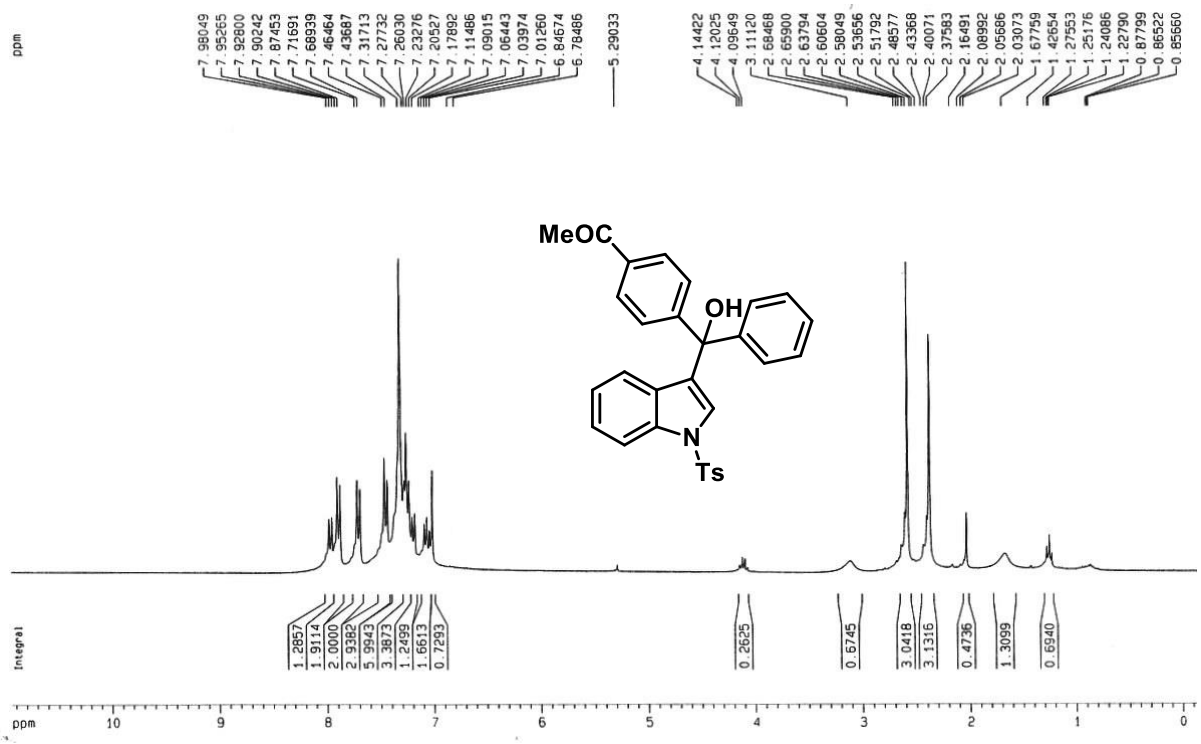
^{1}H NMR of 3f, $CDCl_3$, 300 MHz



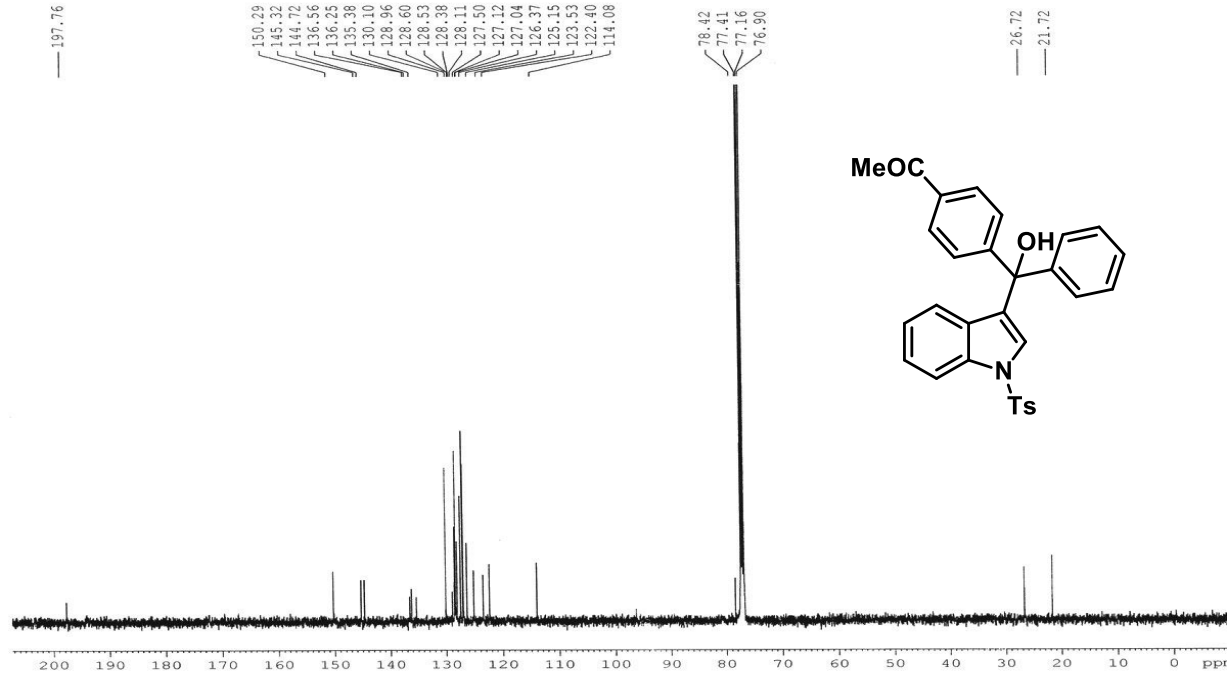
^{13}C NMR of 3f, $CDCl_3$, 75 MHz



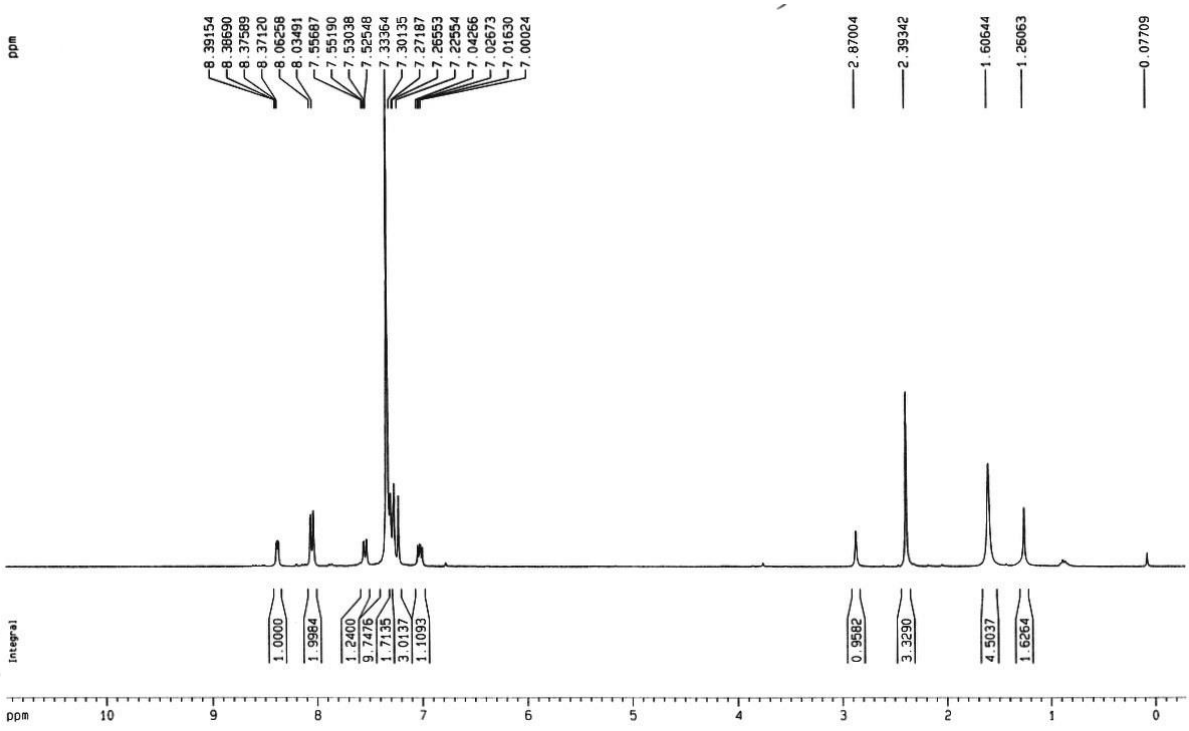
^{1}H NMR of 3g, $CDCl_3$, 300 MHz



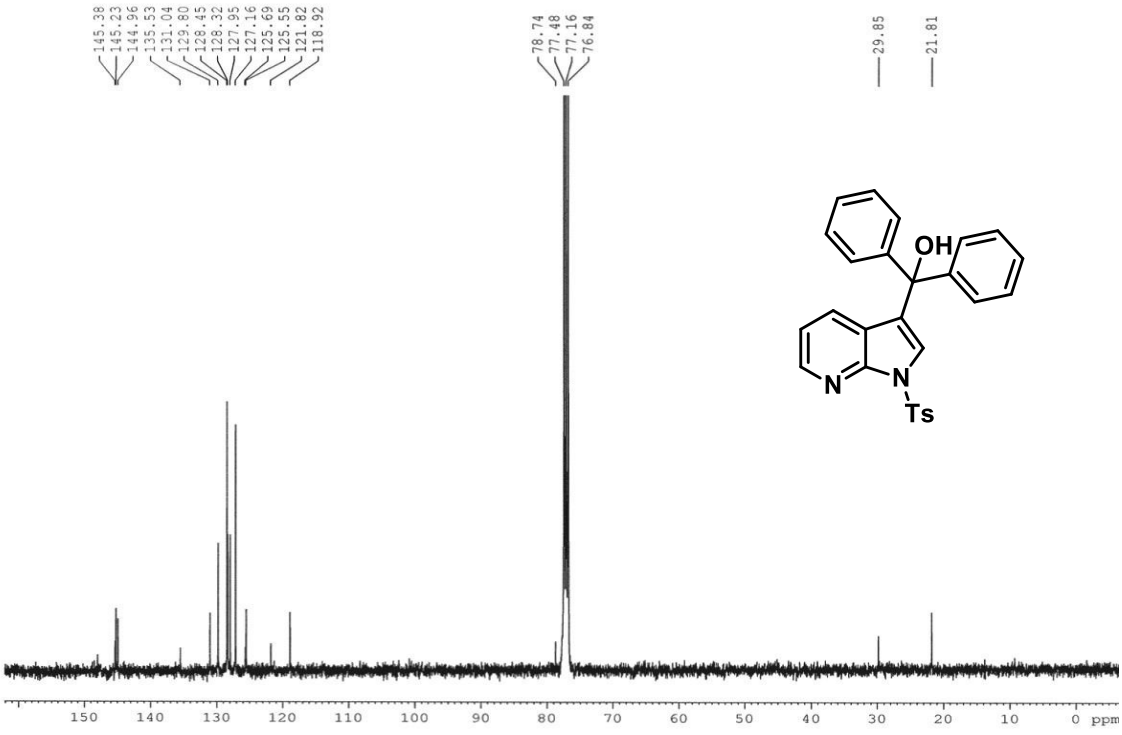
^{13}C NMR of 3g, $CDCl_3$, 125 MHz



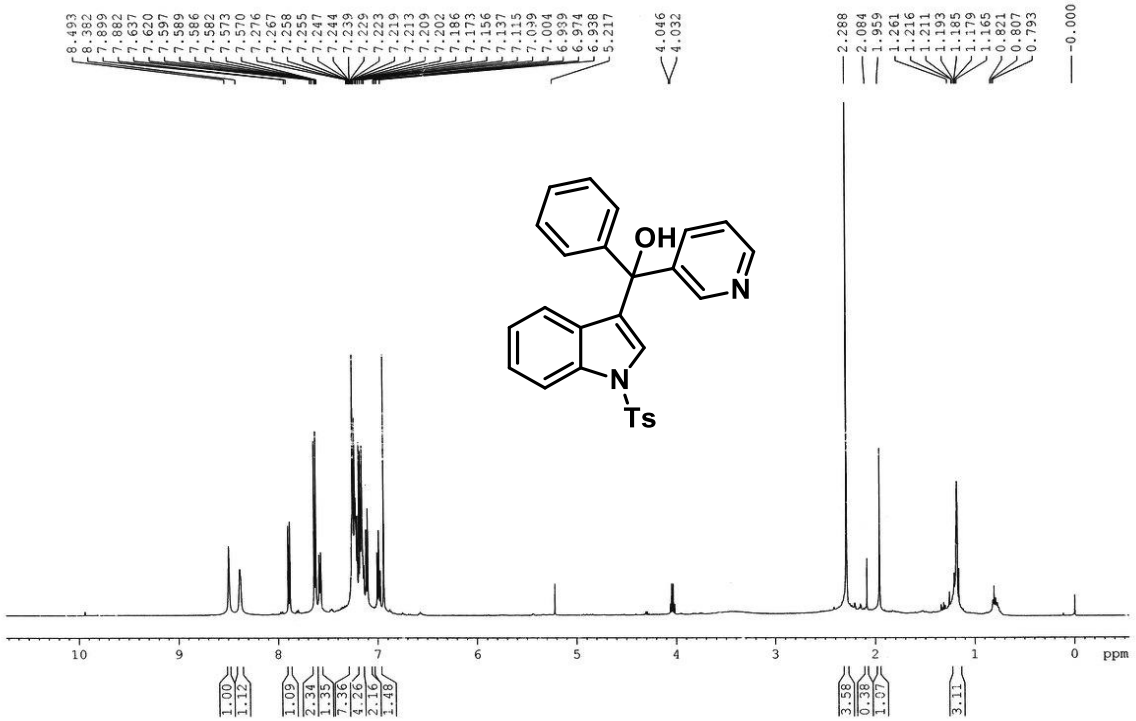
^{1}H NMR of 3h, $CDCl_3$, 300 MHz



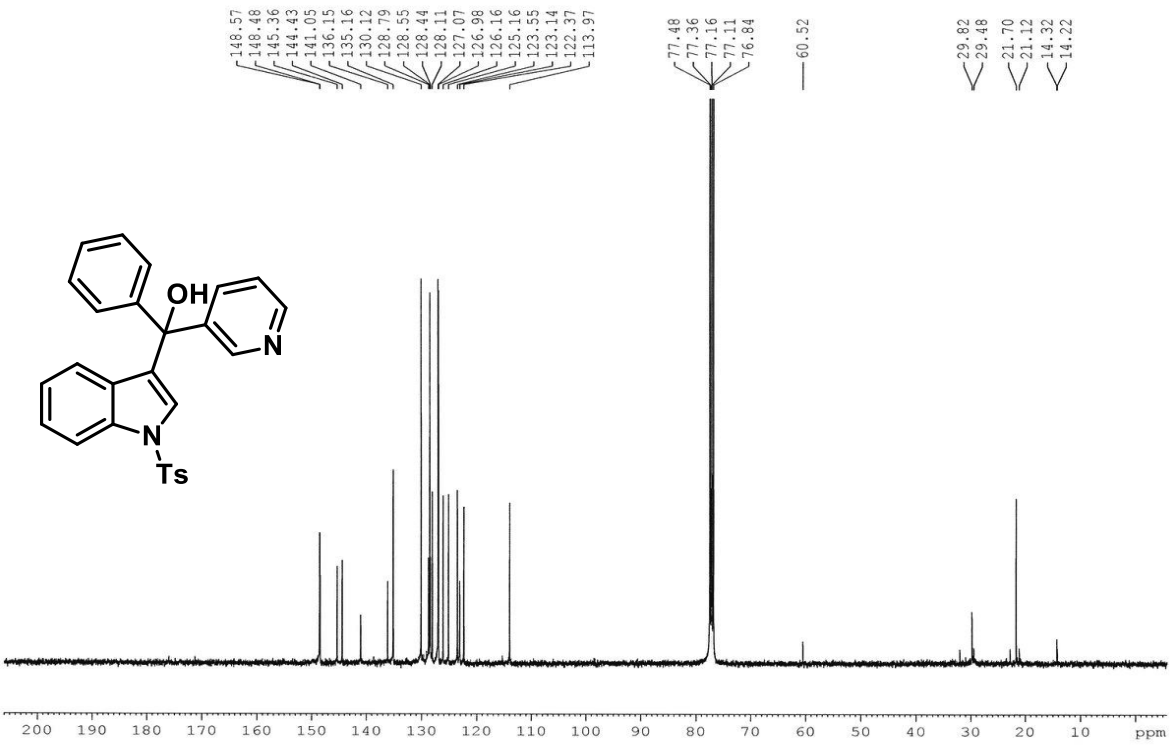
^{13}C NMR of 3h, $CDCl_3$, 100 MHz



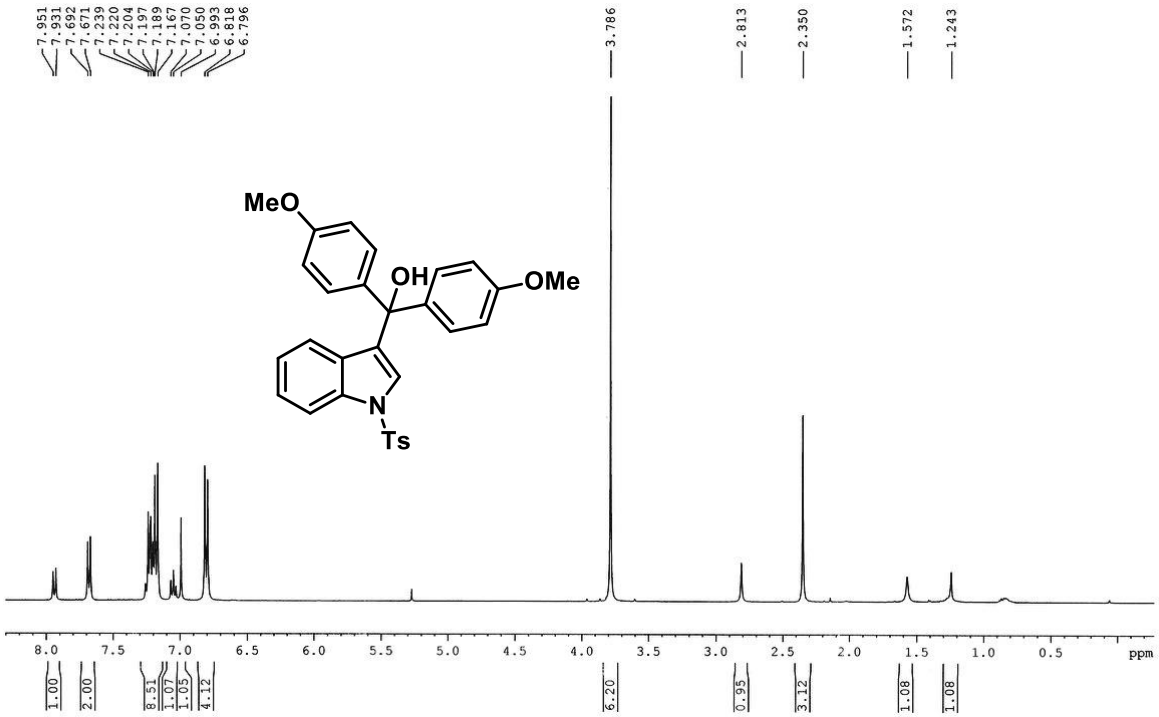
^{1}H NMR of 3i, $CDCl_3$, 500 MHz



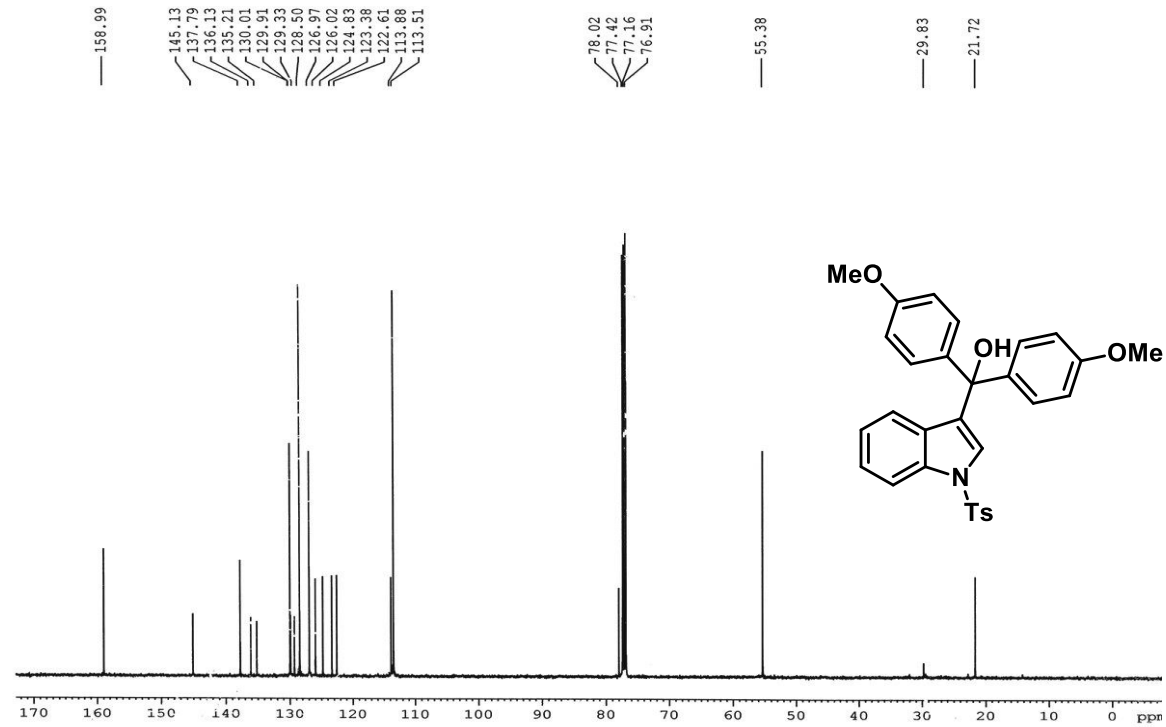
^{13}C NMR of 3i, $CDCl_3$, 100 MHz



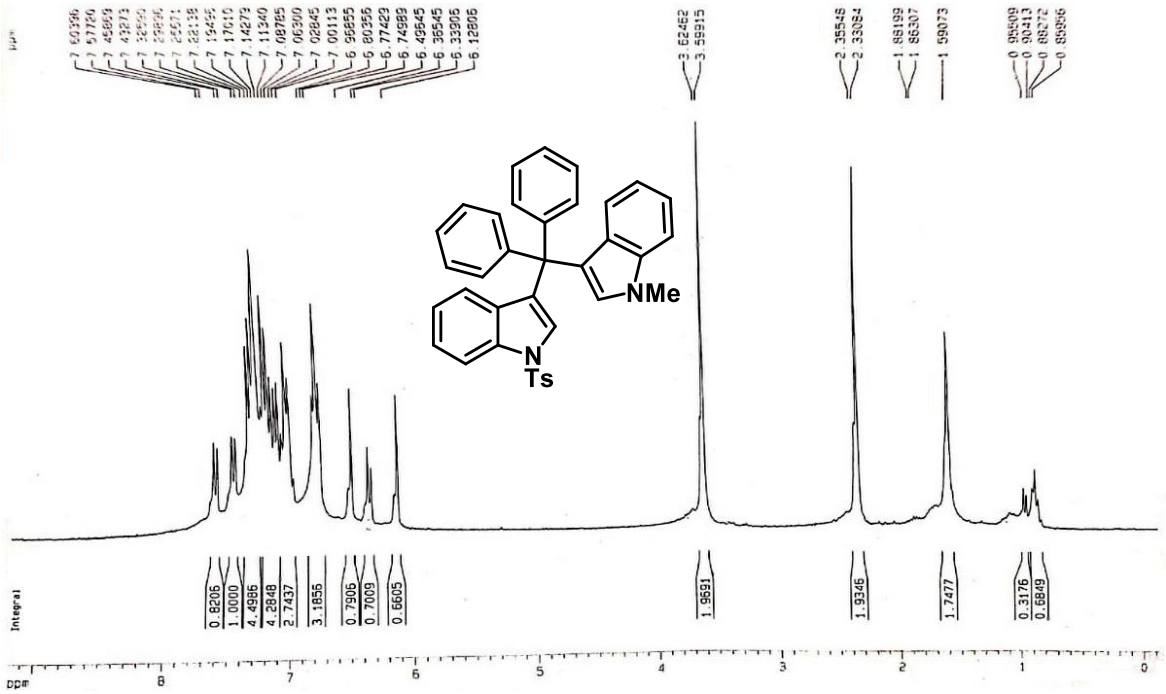
^{1}H NMR of 3j, $CDCl_3$, 400 MHz



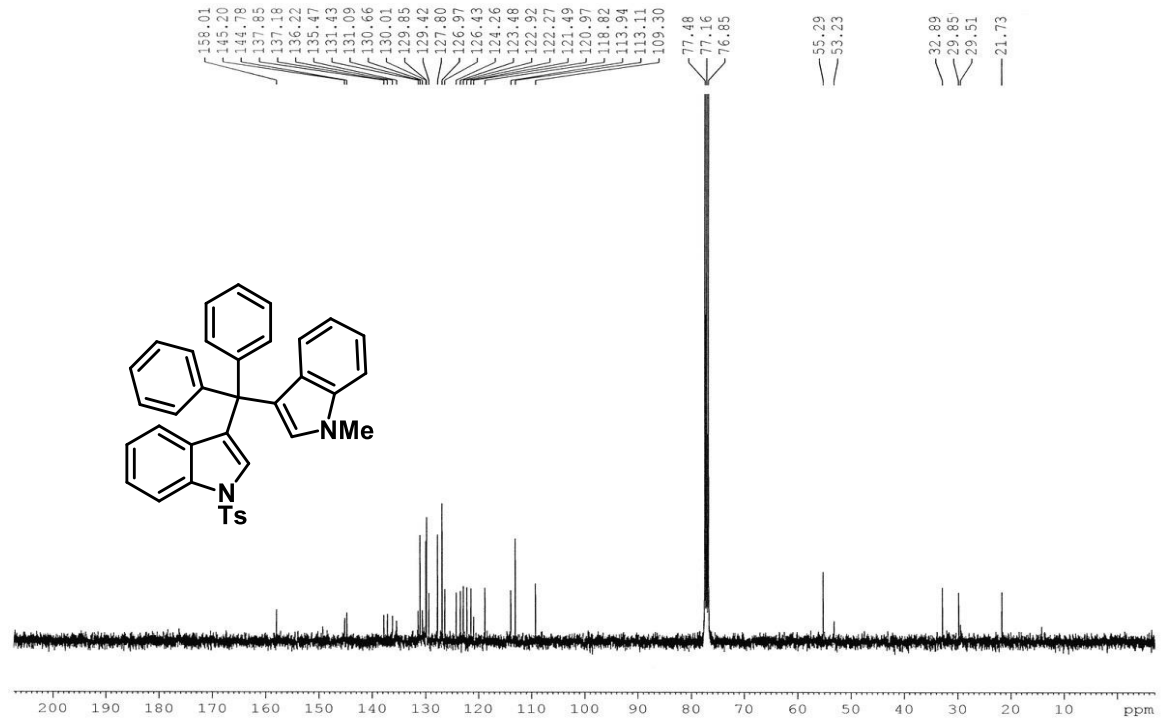
^{13}C NMR of 3j, $CDCl_3$, 125 MHz



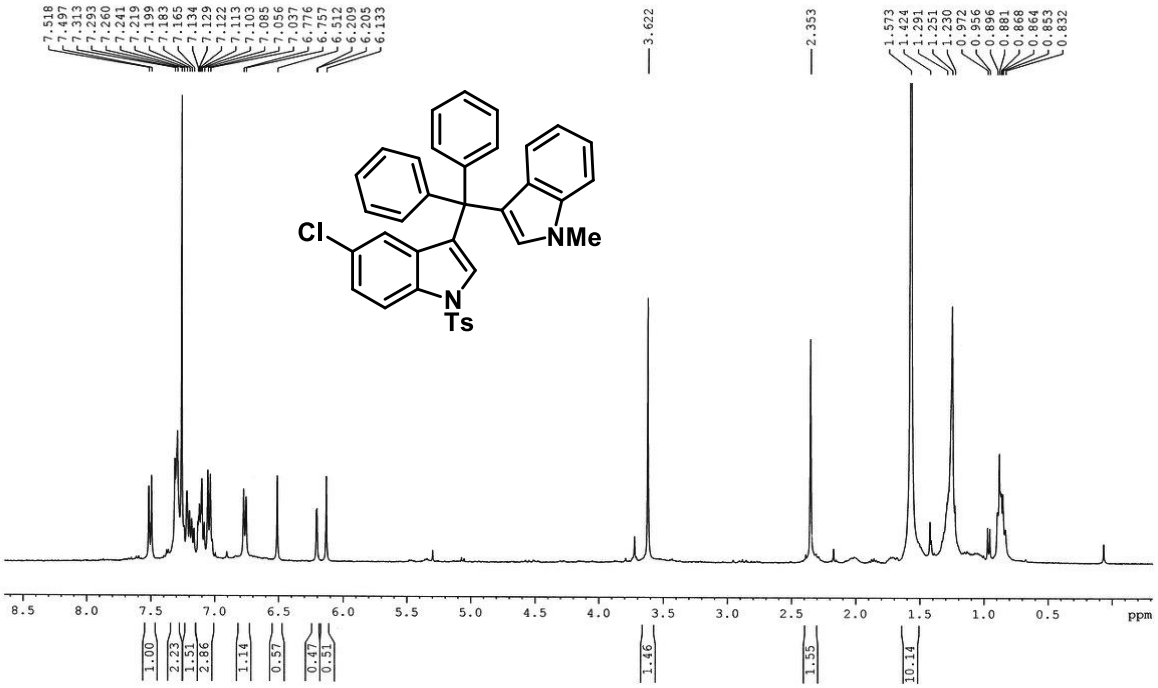
^{1}H NMR of 4a, $CDCl_3$, 300 MHz



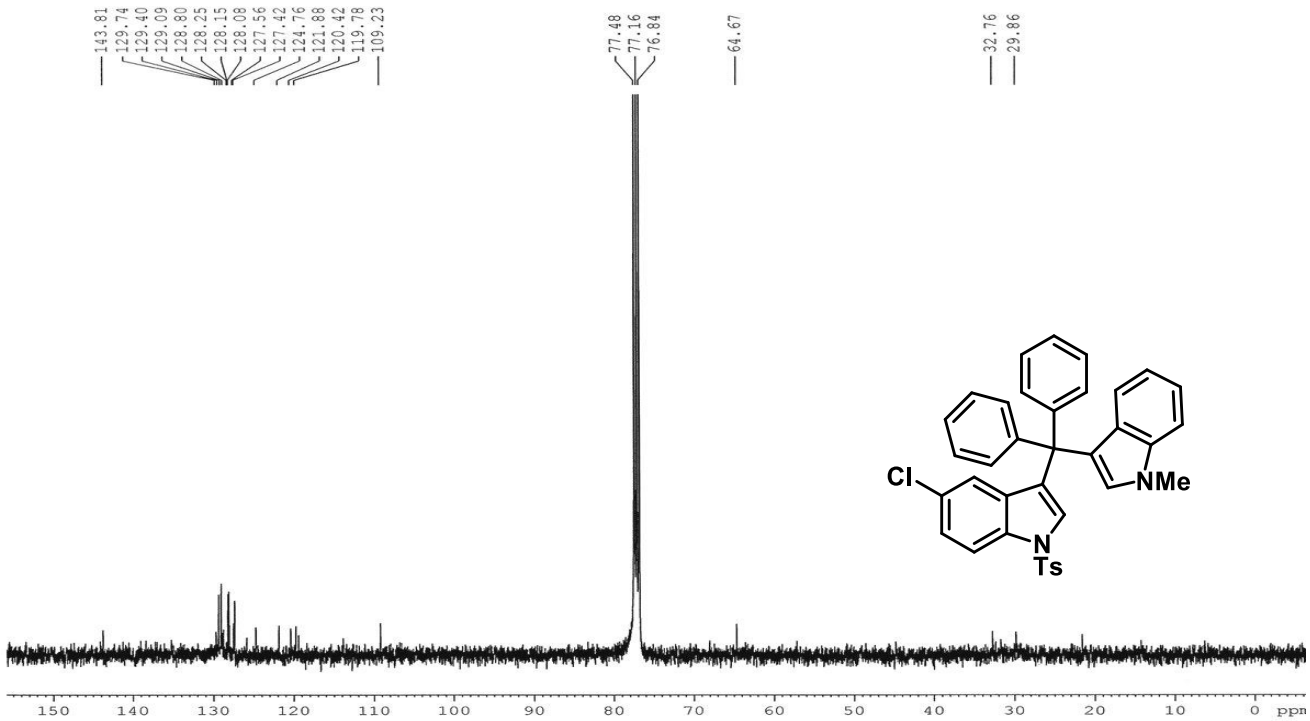
^{13}C NMR of 4a, $CDCl_3$, 100 MHz



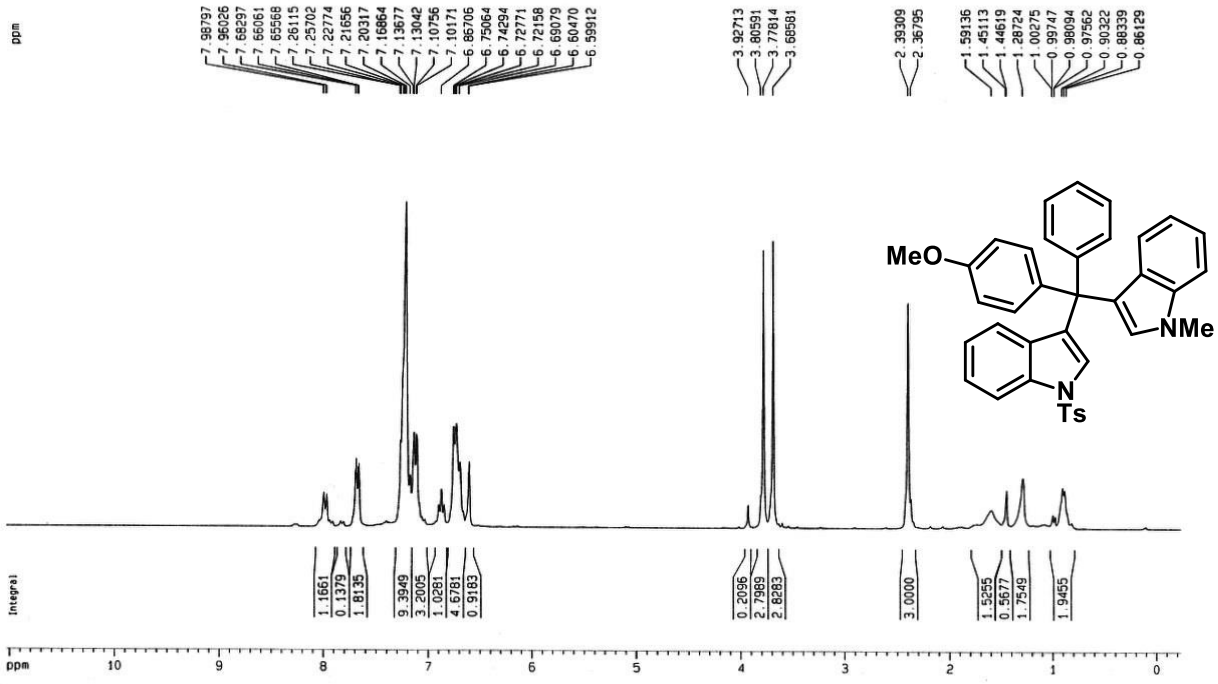
^{1}H NMR of 4b, $CDCl_3$, 400 MHz



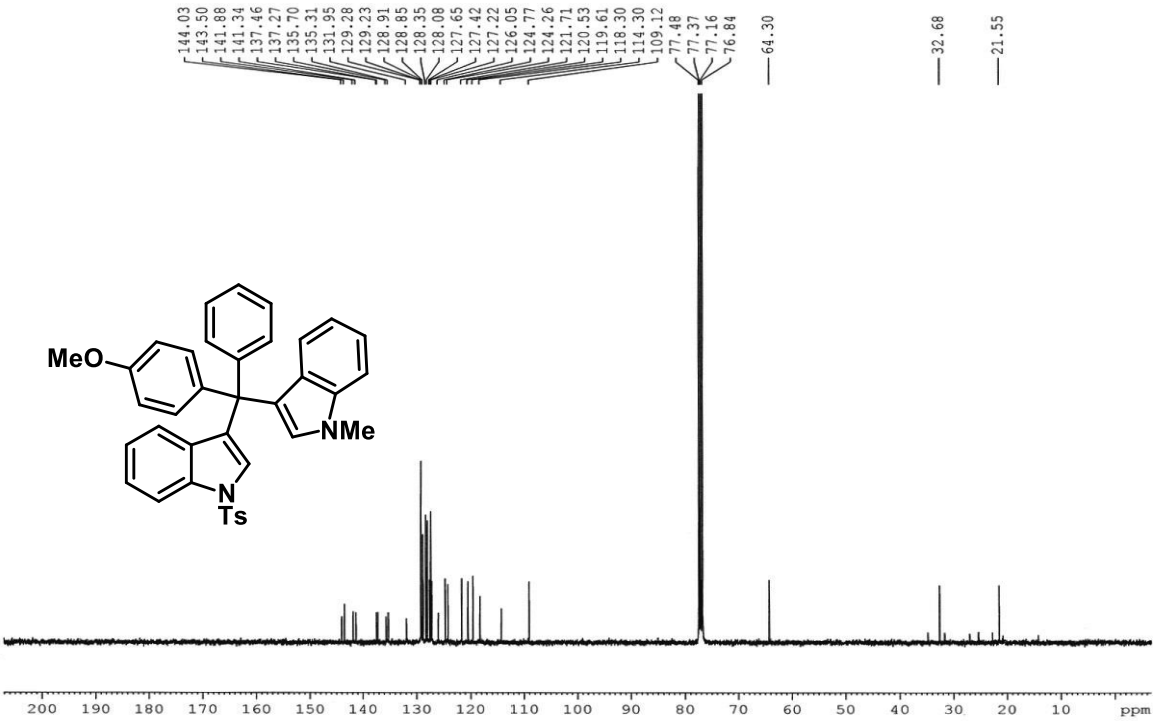
^{13}C NMR of 4b, $CDCl_3$, 100 MHz



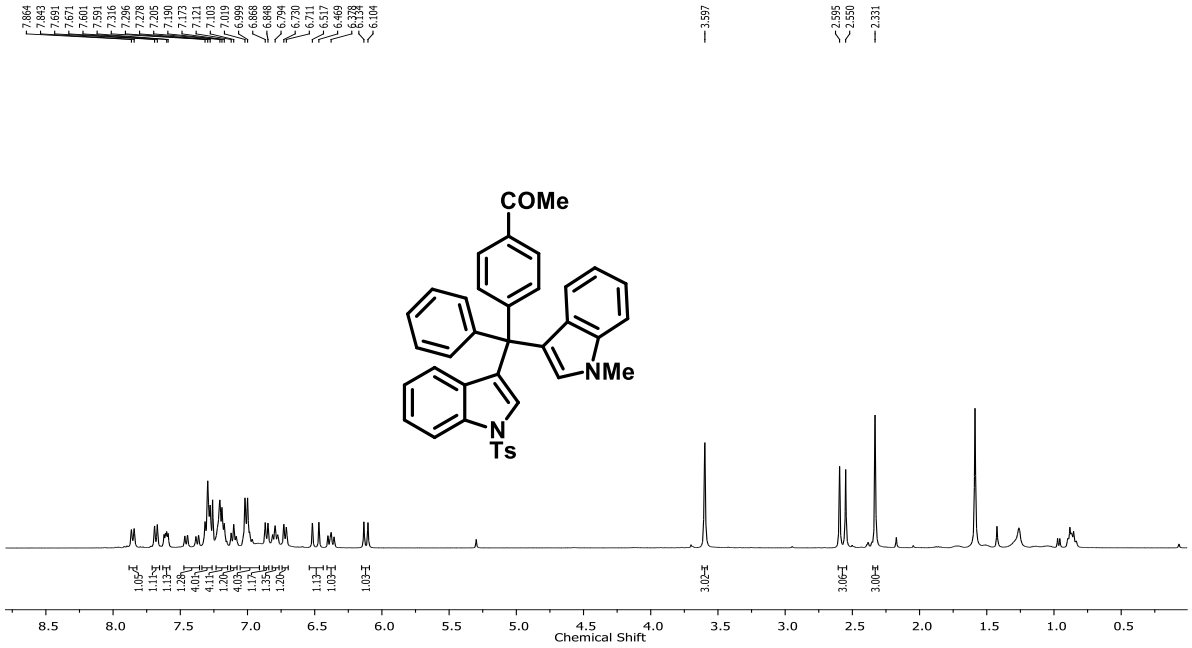
^{1}H NMR of 4c, $CDCl_3$, 300 MHz



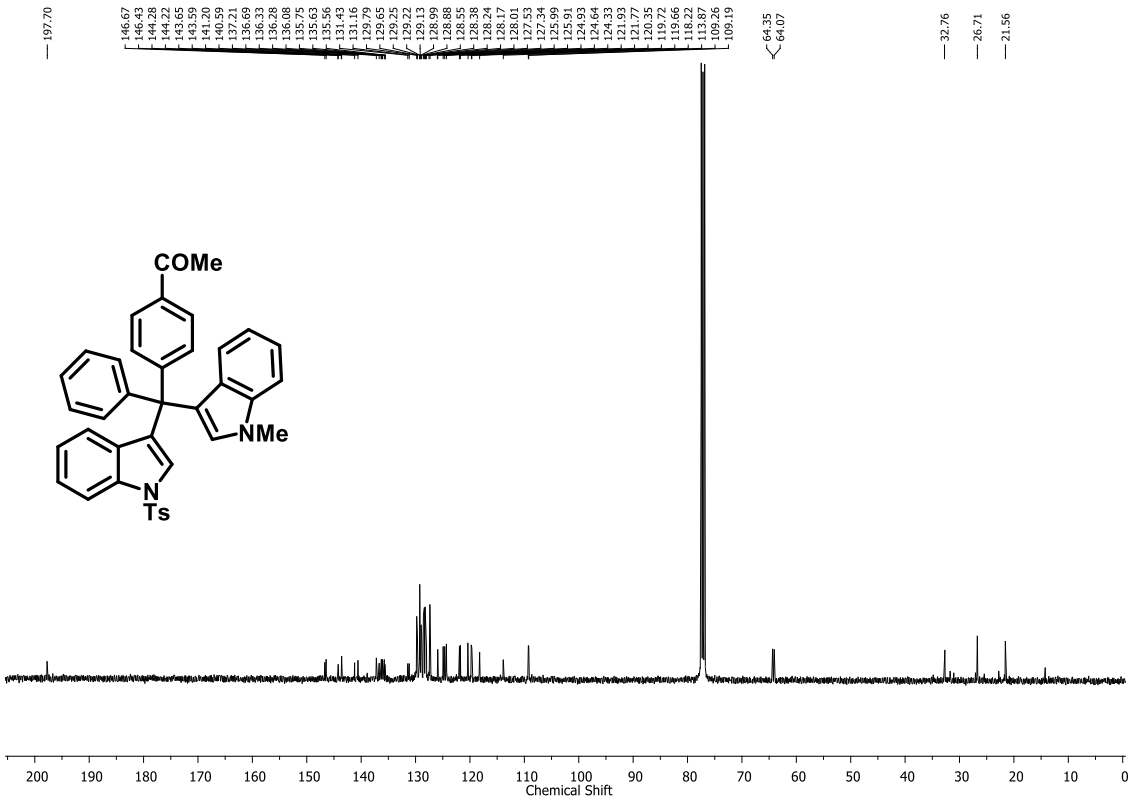
^{13}C NMR of 4c, $CDCl_3$, 100 MHz



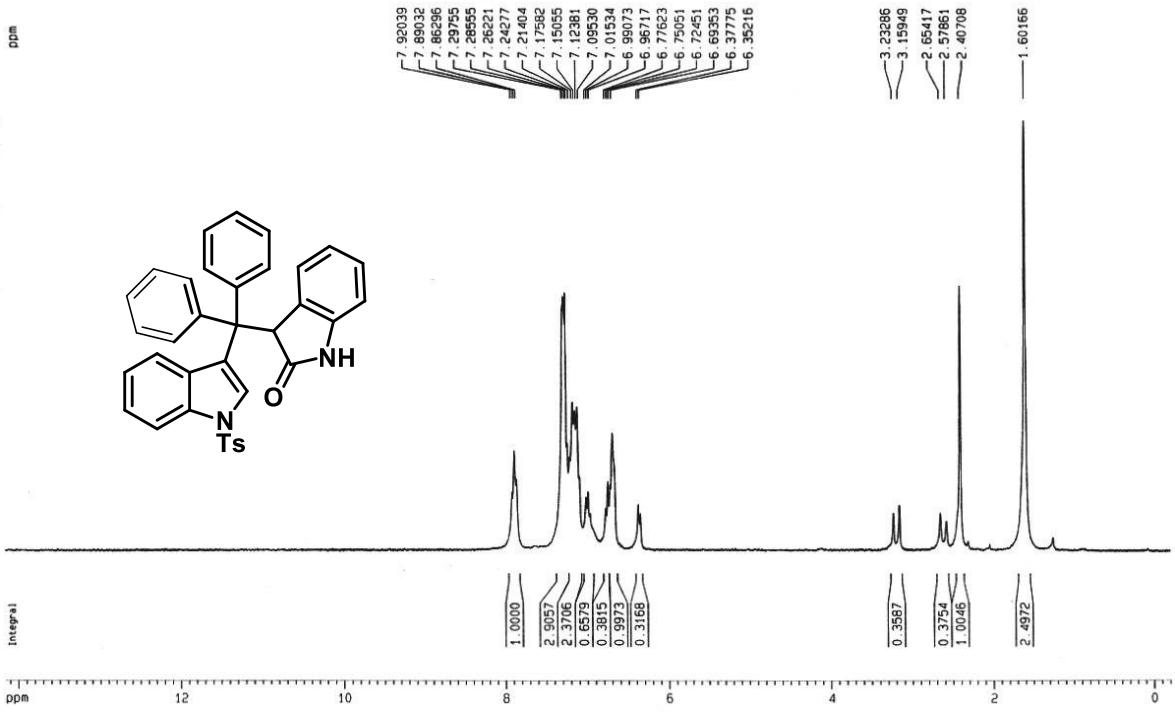
^{1}H NMR of 4d, $CDCl_3$, 400 MHz



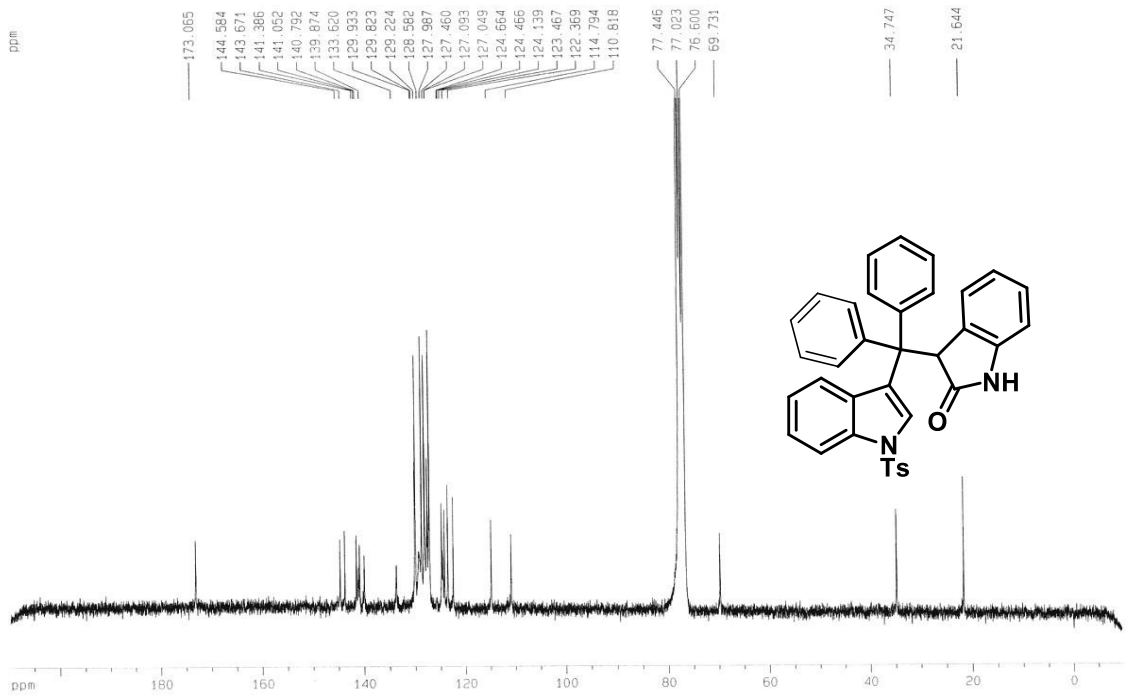
^{13}C NMR of 4d, $CDCl_3$, 100 MHz



^{1}H NMR of 4e, $CDCl_3$, 300 MHz



^{13}C NMR of 4e, $CDCl_3$, 75 MHz



APPENDIX

Appendix

List of publications

1. **$Fe(OTf)_3$-Catalyzed Aromatization of Substituted 3-Methyleneindoline and Benzofuran Derivatives: A Selective Route to C-3-Alkylated Indoles and Benzofurans.**

Sandip Kundal, Swapnadeep Jalal, Kartick Paul, Umasish Jana* (*Eur. J. Org. Chem.* **2015**, 5513–5517).

2**. Synthesis of Fused Dibenzofuran Derivatives via Palladium-Catalyzed Domino C–C Bond Formation and Iron-Catalyzed Cycloisomerization/Aromatization.**

Kartick Paul, Swapnadeep Jalal, **Sandip Kundal**, and Umasish Jana*

(*J. Org. Chem.* **2016**, *81*, 1164−1174).

3**. Iron-Catalyzed Intramolecular Alkyne–Carbonyl Metathesis: A New Cyclization Strategy for the Synthesis of Benzocarbazole and Azepino[1,2-*a*]indole Derivatives.**

Kartick Paul, Swapnadeep Jalal**, Sandip Kundal,** Baitan Chakraborty, Umasish Jana*

(*Synthesis* **2017**; *49*(18): 4205-4212).

4**. Metal-Catalyzed Domino Synthesis of Benzophenanthridines and 6 *H*-Naphtho[2,3- c]-chromenes.**

Baitan Chakraborty, Swapnadeep Jalal**,** Kartick Paul, **Sandip Kundal**, Umasish Jana*.

(*J. Org. Chem.* **2018**, *83*, 15, 8139–8149).

5. **Efficient Two Steps Synthesis of Structurally Diverse Indolo[2,3- *b*]quinolines Derivatives**

Sandip Kundal, Baitan Chakraborty, Kartick Paul, Umasish Jana*

(*Org. Biomol. Chem.*, **2019**, *17*, 2321-2325).

6. **$DDQ/FeCl_3$-mediated tandem oxidative carbon–carbon bond formation for the Synthesis of indole–fluorene hybrid molecules**

Abhishek Kar, Baitan Chakraborty, **Sandip Kundal**, Gopal Rana and Umasish Jana*.

(*Org. Biomol. Chem*., **2021**, *19*, 906–910).

7. **Synthesis of Indole-3-carbinols (I3C) and their Application to Access unsymmetrical bis(3-indolyl)methanes (BIMs) bearing quaternary sp^3 -carbon**

Sandip Kundal, Gopal Rana, Abhishek Kar, Umasish Jana*

(Communicated and **Under Revision** *Org. Biomol. Chem.*, **manuscript id: OB-COM-2022-000502**).