Exploration of Amines for the Synthesis of Substituted Quinolines and Indoles

A Dissertation Submitted to the
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DOCTOR OF PHILOSOPHY

by

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Dedicated to

Dr. A. P. J. Abdul Kalam

11th President of India

(25 July 2002 – 25 July 2007)

and

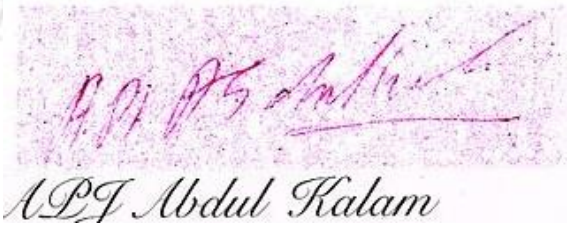
Scientist at

Defence Research and Development Organization,

Indian Space Research Organization,

as well as

Inspiration to the Young Generation



(15 October 1931 – 27 July 2015)

INDIAN INSTITUTE OF TECHNOLOGY, GUWAHATI

Department of Chemistry

STATEMENT

I do hereby declare that the matter embodied in this thesis entitled "*Exploration of Amines for the Synthesis of Substituted Quinolines and Indoles"* is the result of investigations carried out by me under the supervision of Prof. Abu T. Khan in the Department of Chemistry, Indian Institute of Technology Guwahati, India.

In keeping with the general practice of reporting scientific observations, due acknowledgements have been made wherever the work described is based on the findings of other investigators.

IIT Guwahati
April 27, 2018

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Professor of Chemistry

CERTIFICATE

This is to certify that Mr. Radhakrishna Gattu has been working in my research group since July, 2012 as a regular registered Ph. D. student. I am forwarding his thesis entitled "*Exploration of Amines for the Synthesis of Substituted Quinolines and Indoles"* for submission for the Ph. D. (Science) Degree of this Institute. I certify that he has fulfilled all the requirements according to the rules of this Institute regarding the investigations embodied in his thesis and this work has not been submitted elsewhere for a degree.

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This is to certify that Mr. Radhakrishna Gattu has completed his Ph. D. thesis work that he has performed since July, 2012 as a regular registered Ph. D. student in the group of my colleague, Prof. Abu T. Khan. I have been appointed as a Co-Supervisor when Prof. Khan served as the Vice-Chancellor of Aliah University in West Bengal on deputation. I am forwarding his thesis entitled, "*Exploration of Amines for the Synthesis of Substituted Quinolines and Indoles,"* for submission for the Ph. D. (Science) Degree to this institute as a Co-supervisor. I also certify that he has fulfilled all the requirements according to the rules of this Institute regarding the investigations embodied in his thesis and this work has not been submitted elsewhere for a degree.

IIT Guwahati
April 27, 2018

Dr. Bhubaneswar Mandal
(Thesis Co-Supervisor)

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Finally, my Ph. D. endeavor could not have been completed without the endless love, unending support, tolerance and blessings from my family members and relatives. I wish to express my sincere gratitude to my parents. My special thanks to my elder sister Mrs. Vijaya. She is the main soul and inspiration for each and every step that I have achieved in my life.

At last but not least, I thank for this beautiful nature for being there for me in a way no one else can.

Radhakrishna Gattu

CONTENTS OF THE THESIS

GENERAL REMARKS

The present investigations were carried out at the Department of Chemistry, Indian Institute of Technology Guwahati, Guwahati -781 039, Assam during the period from 19th July, 2012 to 27th April, 2018 as a Ph.D. student under the supervision of Prof. Abu T. Khan.

The analytical samples were routinely dried *in vacuo* at 50 ^{o}C. In TLC experiments, silica gel G (SRL) or silica gel GF 254 (SRL) was employed as adsorbent were used. Column chromatography was carried out with silica gel (60-120 mesh, Merck, SRL or Qualigen), for purifications of reaction mixture. After purification, the solvent was usually removed on rotavapor using Büchi R-114V instrument. Melting points were determined on a Büchi melting point apparatus. IR spectra were recorded on Perkin-Elmer 281 IR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on Varian 400 MHz, Bruker 600 MHz and Varian 100 MHz, Bruker 75 and 150 MHz spectrometer TMS as internal reference; chemical shifts (δ scale) are reported in parts per million (ppm). ^{1}H NMR Spectra are reported in the order: multiplicity, no of protons and coupling constant (*J* value) in hertz (Hz); signals were characterized as s (singlet), d (doublet), t (triplet), m (multiplet), brs (broad singlet), dq (doublet of quartet), dt (doublet of triplet) and ddt (doublet of doublet of triplet) at the Department of Chemistry, Indian Institute of Technology, Guwahati and Gauhati University. HRMS spectra were recorded using ESI (TOF) mode and Crystal data were collected with Bruker Smart Apex-II CCD diffractometer using graphite monochromated MoKα radiation (λ = 0.71073 Å) at 296 K.

ABBREVIATIONS

Ac	Acetyl
Ac_2O	Acetic anhydride
AcOH	Acetic acid
APCI	Atmospheric Pressure Chemical Ionization
AUNPS	Gold nanoparticle
BDMS	Bromodimethylsulfonium bromide
Bn	Benzyl
Bu	Butyl
Bz	Benzoyl
BINAP	(2,2'-bis(diphenylphosphino)-1,1'-binaphthyl)
^{t}Bu	*tert*-Butyl
CCDC	Cambridge Crystallographic Data Centre
CSA	Camphorsulfonic Acid
DCE	1,2-Dichloroethene
DCM	Dichloromethane
DHTP	Dihydroxyterphenylphosphine
DMF	*N*,*N*-dimethylformamide
DMSO	Dimethylsulfoxide
ESI (TOF)	Electrospray ionization (Time-of-flight)
Et	Ethyl
EtOH	Ethanol
g	gram
h	hour
HRMS	High-Resolution Mass Spectrometry
IBr	Iodine monobromide
ICl	Iodine monochloride
IR	Infrared
MCR	Multicomponent reaction

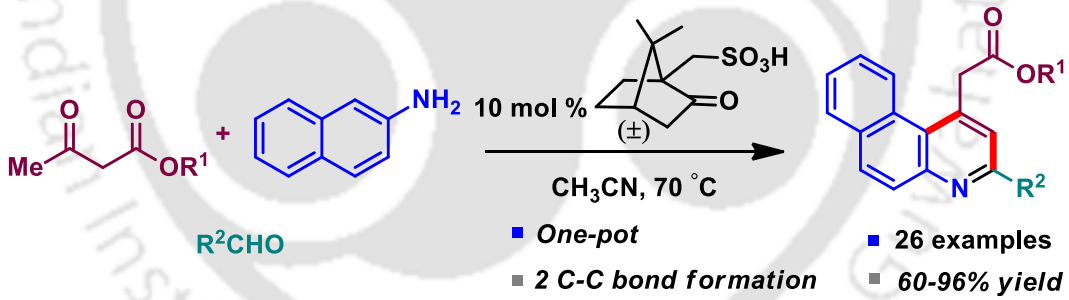
MeOH	Methanol
mp	Melting point
NMR	Nuclear Magnetic Resonance
ORTEP	Oak Ridge Thermal Ellipsoid Program
PEG	Polyethylene glycol
Ph	Phenyl
Pr	Propyl
PPA	Polyphosphoric Acid
ppm	parts per million
p-TSA	*p*-toluenesulfonic acid
rt	room temperature
$TBPA^{+\cdot}$	(*tris*(4-bromophenyl)-aminium hexachloroantimonate)
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography
TMS	Tetramethylsilane
TfOH	Triflic acid
Ts	Tosyl
XRD	X-Ray Diffraction

Abstract

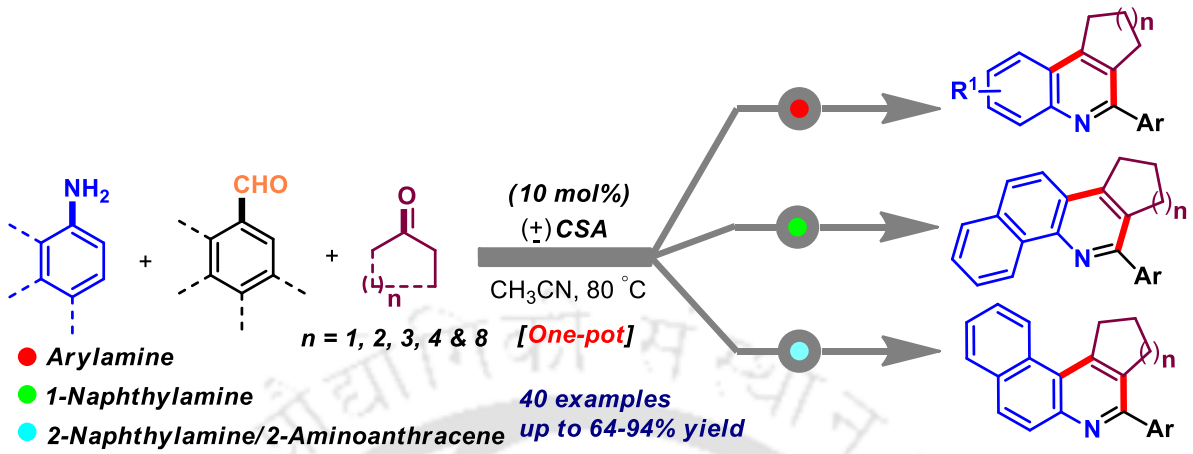
The contents of this thesis entitled ***"Exploration of Amines for the Synthesis of Substituted Quinolines and Indoles"*** have been divided into six chapters based on the results of experimental work performed during the complete course of the research period.

Chapter I of the thesis represents a brief introduction to nitrogen containing heterocyclic compounds with emphasis on substituted quinoline and indole derivatives. In this chapter we have described the literature view of reported methods for substituted quinolines and indoles.

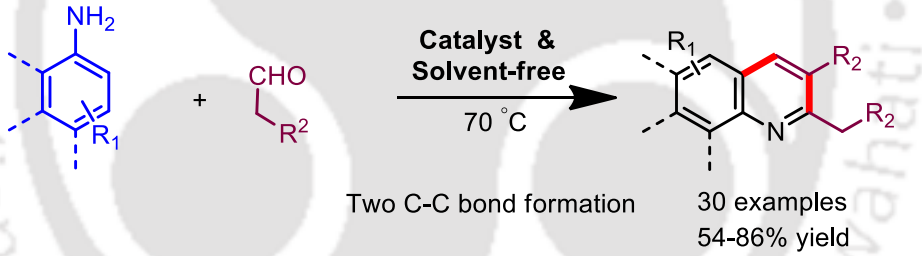
Chapter II describes an efficient method for regioselective synthesis of C1-functionalised 3-arylbenzo[*f*]quinoline has been demonstrated via *γ*-selective aromatization using *β*-ketoester, 2-naphthylamine and aromatic aldehyde by employing 10 mol % camphorsulfonic acid as a catalyst in acetonitrile at 70 °C. In this approach, two C–C bond formations will result in functionalised benzo[*f*]quinoline in a one-pot three-component reaction. In addition, the present protocol has a diverse substrate scope with good yields.



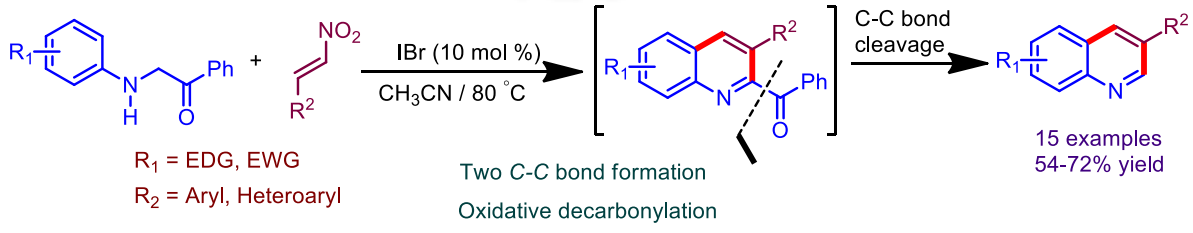
Chapter III illustrates a simple and an efficient one-pot three-component reaction of arylamines, aromatic aldehydes and cyclic ketones was described for the synthesis of various fused quinoline, benzoquinoline, and naphthoquinoline derivatives by using camphorsulfonic acid as a catalyst. The exploitation of pregnenolone steroid for benzoquinolines and terephthalaldehyde for bisbenzoquinolines synthesis was achieved with 68−75% yields.



Chapter IV elucidates the synthesis of 2,3-di-substituted quinoline and benzoquinoline derivatives through one-pot pseudo three-component reaction by employing arylamine (1 mmol) and aliphatic aldehyde (2 mmol) under solvent and catalyst free condition at 70 °C.

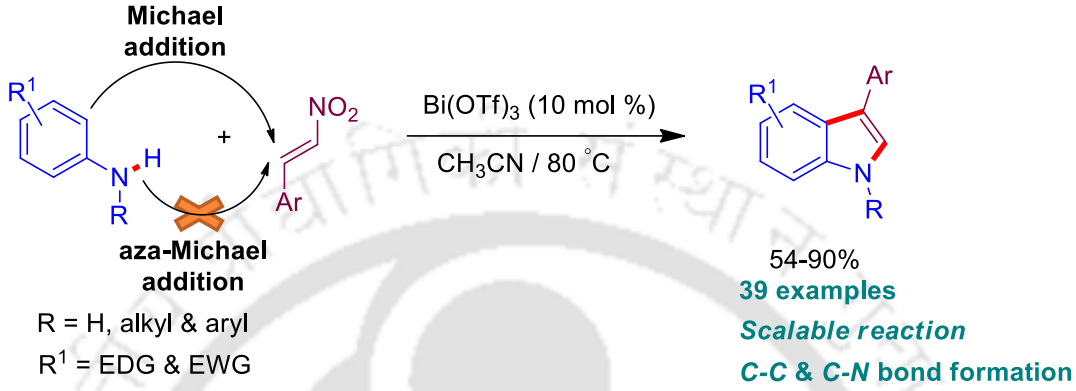


Chapter V demonstrates a novel and an efficient method for the regioselective synthesis of 3-arylquinolines through tandem cyclisation of 1-phenyl-2-(phenylamino)ethanone and *trans-β*-nitrostyrene in acetonitrile solvent at 80 °C by using 20 mol % Iodine monobromide as a catalyst. This protocol involves the two new C-C bond formations and cleavage of one C-C bond through metal-free reaction condition.



Chapter VI explains a simple and an efficient method for the regioselective synthesis of N-alkyl/aryl/H 3-arylindole derivatives from N-substituted anilines and *trans-β*-nitrostyrenes

using 10 mol % of bismuth(III) triflate as a catalyst in acetonitrile at 80 °C. The present protocol profits from the formation of new C-C and C-N bonds, broad substrate scope with moderate to good yields.



Chapter-I

Review on Substituted Quinolines and Indoles

1. Introduction to quinolines

Nitrogen containing heterocyclic compounds are widely distributed in nature mainly as alkaloids and they exhibit immense pharmacological activities.[1-6] Among various nitrogen heterocycles, quinoline, benzoquinoline, isoquinoline, indole derivatives and so on are an interesting class of organic compounds having a large scope to be investigated by the synthetic chemists because of their natural occurrence and having medicinal value.[7] In addition, these scaffolds have several applications in agrochemicals, pharmaceuticals, dyestuffs and functional materials.[8] Interestingly, both natural and synthetic quinoline derivatives are well known for antimalarial drugs.[9] Moreover, many quinoline compounds have antitubercular,[10] anticancer,[11,12] antipsychotics,[13] antimicrobial,[14] anti-HIV[15] activities and also used for the treatment of neurodegenerative diseases.[16] Similarly, functionalized quinolines, fused quinolines and alkyl/aryl substituted quinolines are recognized as one of the forefront of N-heterocyclic compounds and they are found in many alkaloids, bioactive scaffolds and potent marketed drugs as shown in Figure **1**.

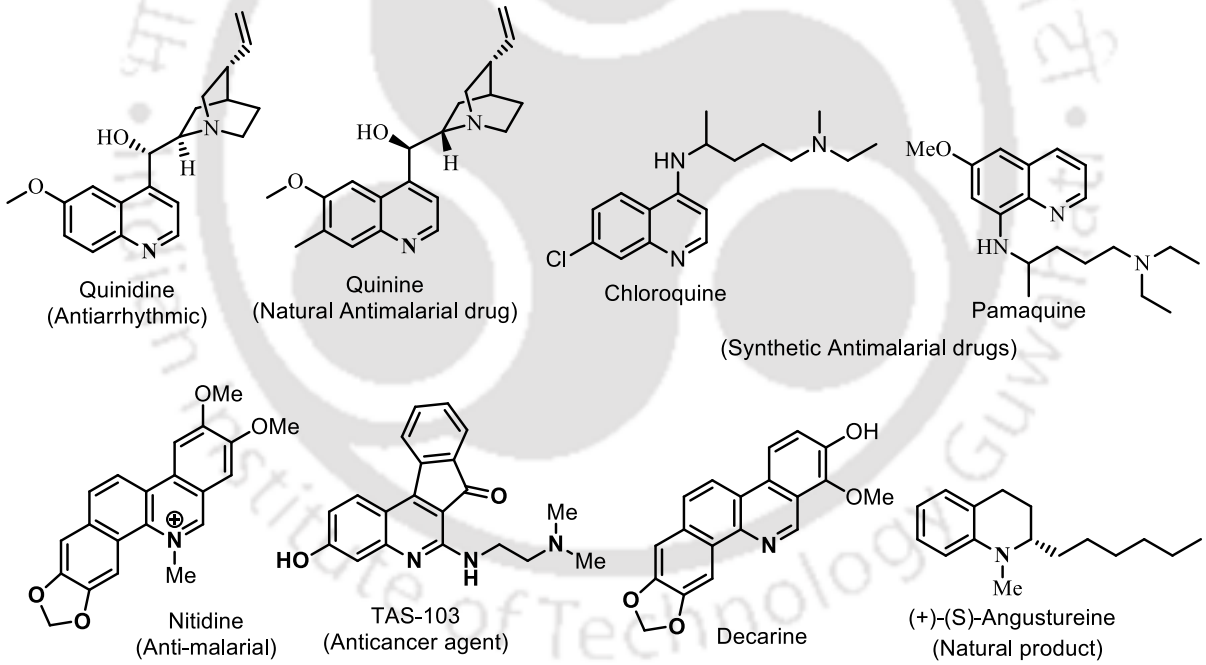


Figure 1. Biologically active Quinoline and Benzoquinoline core units

Remarkably, quinolines act as an effective ligands in cross-coupling reaction[17] and plays a pivotal role in asymmetric synthesis as catalyst.[18,19] In addition, they are also used as ligands for the preparation of OLED complexes[20] and act as chemo-sensors for detection of metal ions.[21,22] Due to potential biological activity and tremendous applications of quinolines, chemists have developed various new synthetic methods for quinolines and derivatives.

1.1 Classical methods of quinoline synthesis from anilines

The classical methods of quinoline synthesis from aniline as readily available starting material include Skraup reaction,[23] Doebner-von Miller,[24] Conrad-Limpach,[25,26] Doebner reaction,[27] Combes reaction[28] and Povarov reaction[29] which occurs through the formation of new C-C and C-N bonds as shown in Figure **2**.

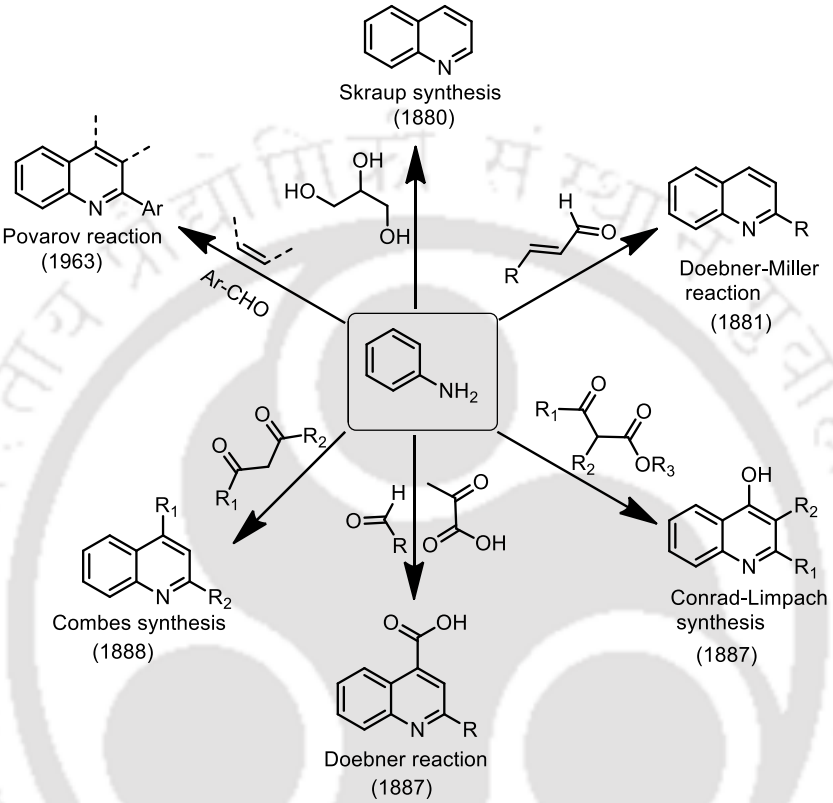
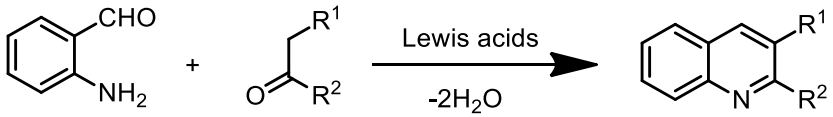


Figure 2. Classical methods of quinoline synthesis from aniline

Besides the methods of quinoline synthesis from simple anilines, there are few other classical methods for quinoline synthesis from substituted anilines such as Friedländer synthesis, Knorr synthesis, and Pfitzinger reaction.

1.2 Friedländer synthesis

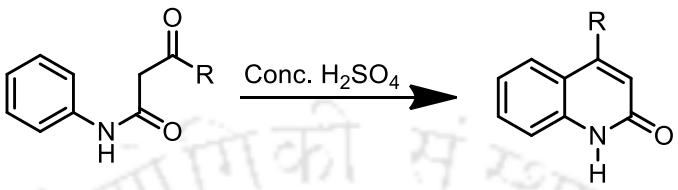
Friedländer[30] first reported in the year 1882 a mild and efficient approach for the synthesis of 2,3-di-substituted quinolines from 2-amino benzaldehyde and ketone through an acid catalysed condensation reaction as depicted in Scheme **1**.



Scheme 1

1.3 Knorr quinoline synthesis

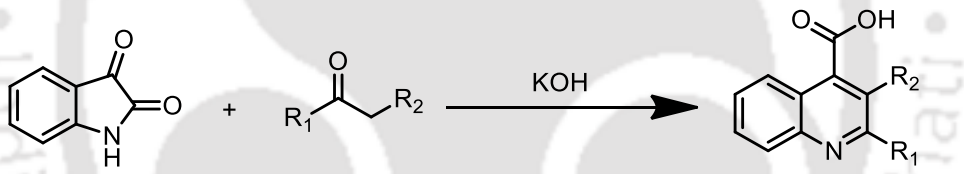
Ludwig Knorr[31] in 1886 developed an efficient protocol for the synthesis of quinolin-2(1H)-one via intramolecular cyclization reaction of *β*-ketoanilide in the presence of Conc. sulfuric acid as shown in Scheme **2**.



Scheme 2

1.4 Pfitzinger reaction

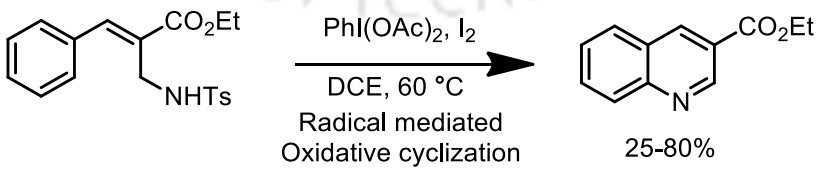
Pfitzinger synthesized quinoline-4-carboxylic acids[32] from isatin and carbonyl compound. The reaction proceeds through the base hydrolysis of isatin to form keto-acid, which subsequently reacts with carbonyl compound to give the final product as represented in Scheme **3**.



Scheme 3

1.5 Recently developed methods for quinoline synthesis

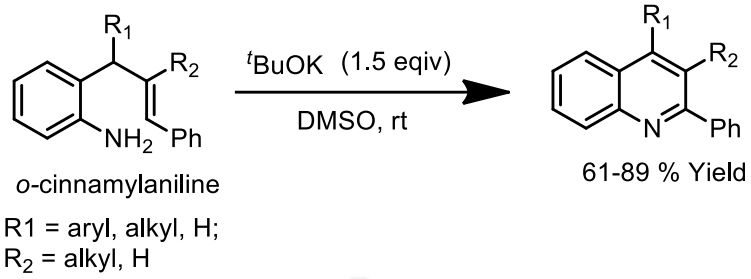
Kim et al. have developed a facile method for the synthesis of ethyl quinoline-3-carboxylate from the Baylis-Hillman acetates[33] in moderate to good yields via radical mediated oxidative cyclization as represented in Scheme **4**.



Scheme 4

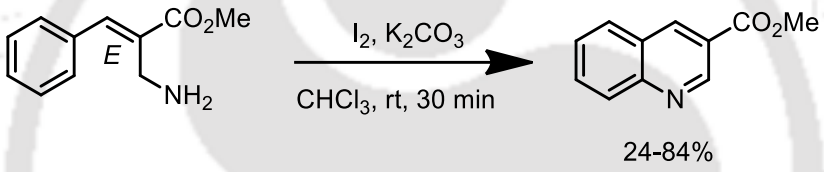
A simple and an efficient method for synthesis of substituted quinolines under metal-free oxidative cycloisomerization[34] of *o*-cinnamylanilines using ^{t}BuOK in DMSO at room

temperature was described by Ghorai and his co-workers as given in Scheme **5**. The reaction occurred *via* intramolecular *exo-trig* oxidative cyclization in a regioselective manner.



Scheme 5

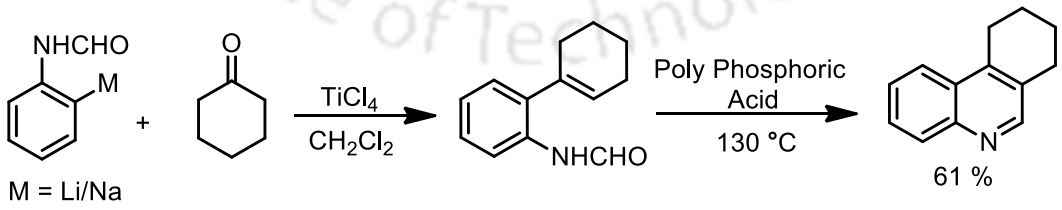
Recently, Batra[35] et al. demonstrated synthesis of quinolines from substituted primary allylamines via intramolecular electrophilic aromatic cyclization by employing molecular iodine and potassium carbonate under mild reaction conditions as depicted in Scheme **6**.



Scheme 6

1.6 Synthesis of fused quinolines

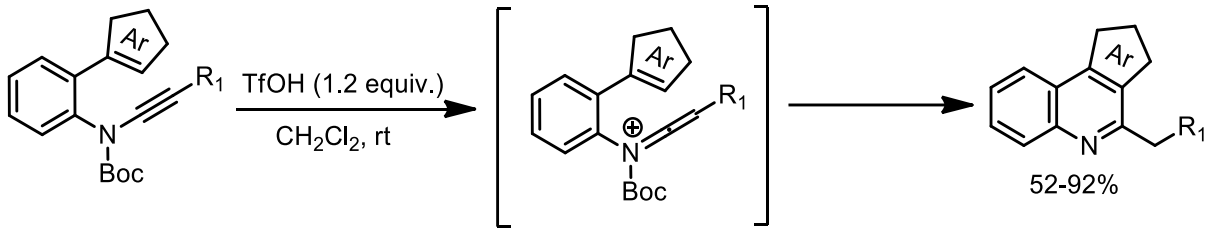
Currian and co-workers accomplished the synthesis of tetrahydrophenanthridine. The reaction of *ortho*-metalated formanilide[36] and cyclic ketone in presence of $TiCl_4$ gave *o*-vinyl anilide which acted intermediate to furnish tetrahydrophenanthridine derivative using poly phosphoric acid (PPA) as shown in Scheme **7**.



Scheme 7

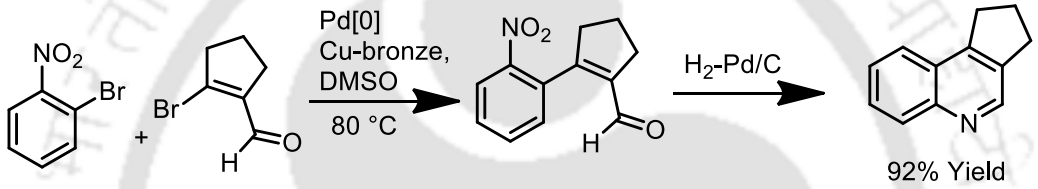
Takasu and coworkers reported Brønsted acid-promoted cyclization of arene-ynamide[37] to afford arene-fused quinolines. In this reaction arene-ynamide converted to a highly reactive

keteniminium intermediate to give arene-fused quinolines in excellent yields as represented in Scheme **8**.



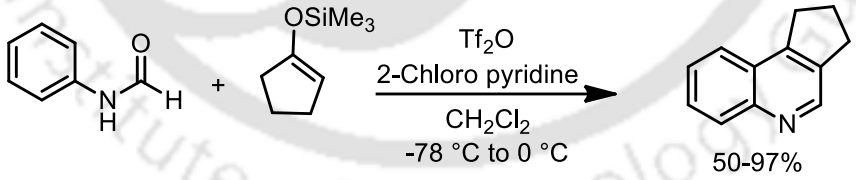
Scheme 8

Banwell and co-workers reported palladium (0) mediated Ullmann cross-coupling reaction of 1-bromo-2-nitrobenzene and its derivatives with *β*-halo-enals[38] to give the corresponding *β*-aryl enal derivatives, which are converted into the corresponding quinolines on reaction with molecular hydrogen in the presence of Pd/C as shown in Scheme **9**.



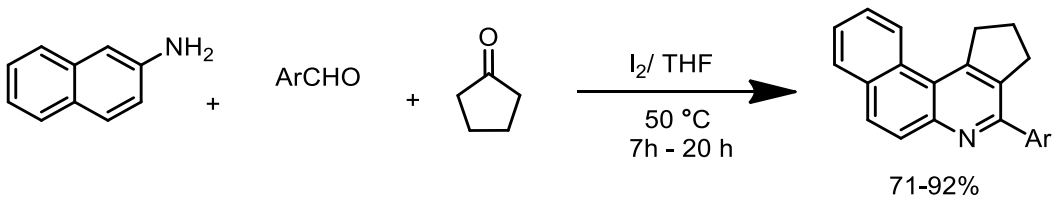
Scheme 9

Movassaghi group developed fused quinoline derivatives from N-aryl amides[39] and trimethylsilyl enol ether. The reaction carried out with trifluoromethanesulfonic anhydride (Tf_2O) in the presence of 2-chloropyridine at low temperature as given in Scheme **10**.



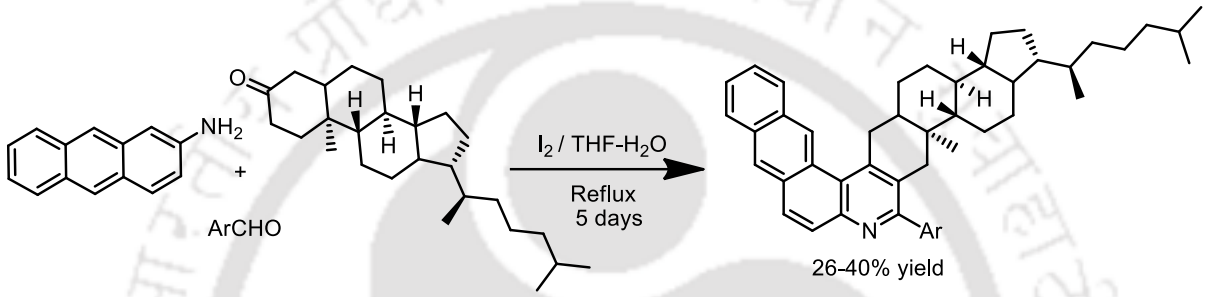
Scheme 10

A simple and an elegant method was developed by Wang[40] and co-workers for the synthesis of benzo[*f*]quinoline derivatives through a three-component reaction of arenecarbaldehyde, 2-naphthylamine, and cyclic ketone using molecular iodine as catalyst as shown in Scheme **11**.



Scheme 11

Stryker and co-workers developed naphthoquinolines[41] from 2-aminoanthracene, aromatic aldehyde, and 5-*α*-cholestan-3-one using in situ generated hydroiodic acid, which is formed from the reaction of iodine with water as shown in Scheme **12**.

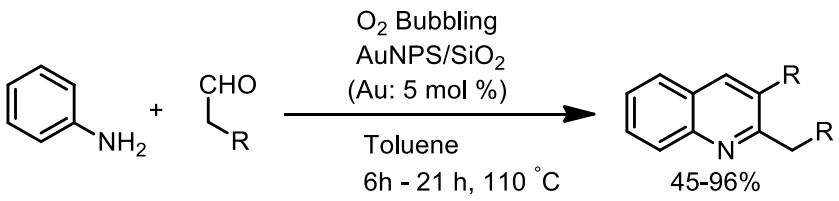


Scheme 12

From the literature reports, it reveals that numerous methods have been found for the synthesis of fused quinoline derivatives. However, some of these methods have demerits such as long reaction time, low temperature reaction condition, preparation of starting material and use of expensive catalysts. Therefore, there is a need to develop a new method which proceeds under mild and less expensive reagents.

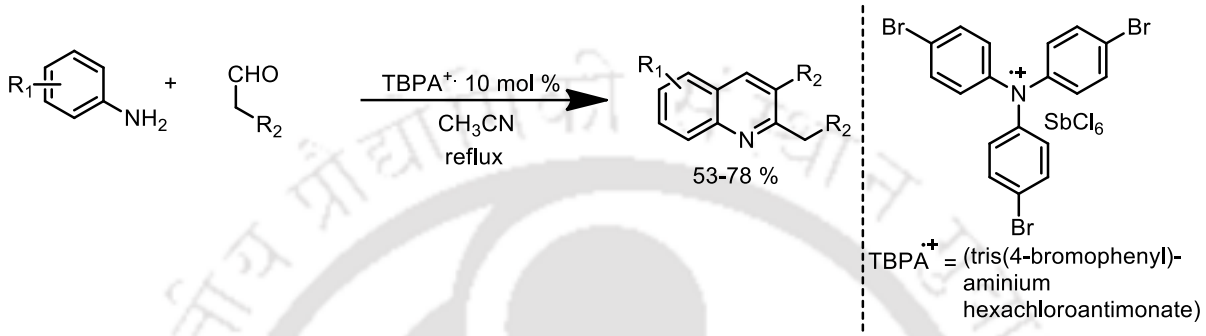
1.7 Synthesis of 2,3-disubstituted quinolines:

Che and his co-workers reported silica-supported gold nanoparticle catalyzed reaction for the synthesis of 2,3-disubstituted quinolines[42] from aniline and aliphatic aldehyde as depicted in Scheme **13**.



Scheme 13

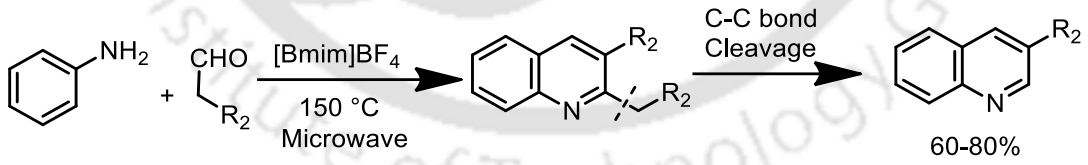
Later on, Wang et al. described the synthesis of 2,3-disubstituted quinolines[43] from anilines and aliphatic aldehydes using 10 mol% $TBPA^{+\cdot}$ (*tris*(4-bromophenyl)-aminium hexachloroantimonate) as shown in Scheme **14**. The mechanism involves tautomerization of of insitu generated imine to enamine, which acts as a dienophile to participate in tandem cyclization, and further elimination of the aniline group initiates the aromatization of tetrahydroquinolines to form 2,3-disubstituted quinolines.



Scheme 14

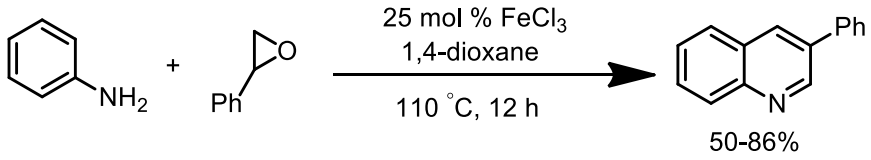
1.8 Synthesis of 3-arylquinolines

Bharate and co-workers reported metal-free[44] synthetic protocol for construction of 3-arylquinolines from anilines and phenylacetaldehydes using ionic liquids as the reaction medium. Mechanistic analysis proved that the reaction occurs through C-C and C-N bond formation to produce 2,3-di-substituted quinoline intermediates, which undergo C-C bond cleavage to give 3-arylquinolines as depicted in Scheme **15**.



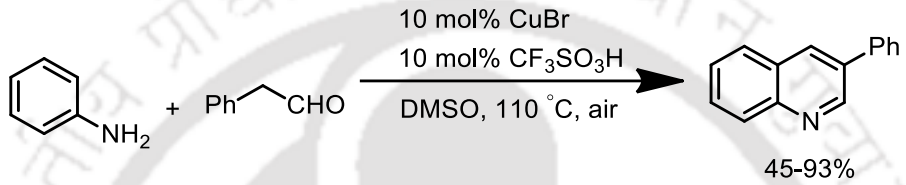
Scheme 15

A novel synthetic protocol for the synthesis of 3-arylquinolines was developed by Zhang[45] and co-workers through C-H activation of anilines with styrene oxides using $FeCl_3$ catalyst as represented in Scheme **16**. The reaction involves the cleavage of C-C bond to form 3-arylindoles.



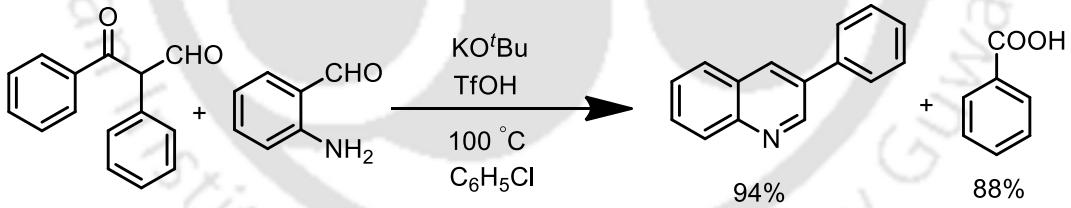
Scheme 16

Huang et al. developed an efficient method for the direct synthesis of 3-arylquinolines from anilines and aldehydes through C-H functionalization.[46] The reaction involves the formation of new C-C/C-N bond formation and C-C bond cleavage by employing 10 mol% CuBr, CF_3SO_3H as catalyst and air as an oxidant as shown in Scheme **17**.



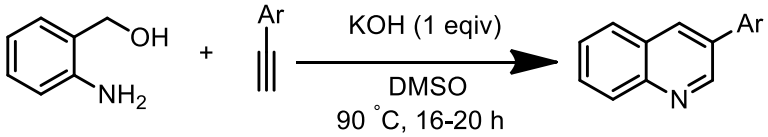
Scheme 17

Tang and co-workers reported Friedlander-type[47] reaction with 3-oxo-2,3-diarylpropionaldehydes and 2-amino-arylaldehydes for the synthesis of 3-arylquinolines as shown in the Scheme **18**. The reaction proceeds in presence of a KO^{t}Bu and CF_3SO_3H (Triflic acid) through enaminone intermediate.



Scheme 18

Diels-Alder is the one of the most important reaction for the construction of various carbocyclic and heterocyclic compounds. Verma[48] et al. have also developed a straight forward regioselective synthesis of 3-arylquinolines via hetero-diels-alder cycloaddition of azadienes with terminal alkynes in presence of base as given in Scheme **19**.



Scheme 19

Despite the benefits of the reported methods for the synthesis of 3-arylquinolines there are disadvantages such as limited substrate scope, non-availability of epoxides,[45] phenylacetaldehyde[46] and 3-oxo-2,3-diarylpropionaldehydes[47] derivatives. Hence, there is a requirement for developing a new protocol for the synthesis of 3-arylquinolines using a readily available and cheaper starting materials.

The synthetic strategies for substituted quinolines are shown in Figure **3**, which involve formation of C-C/C-N/N-C bonds.

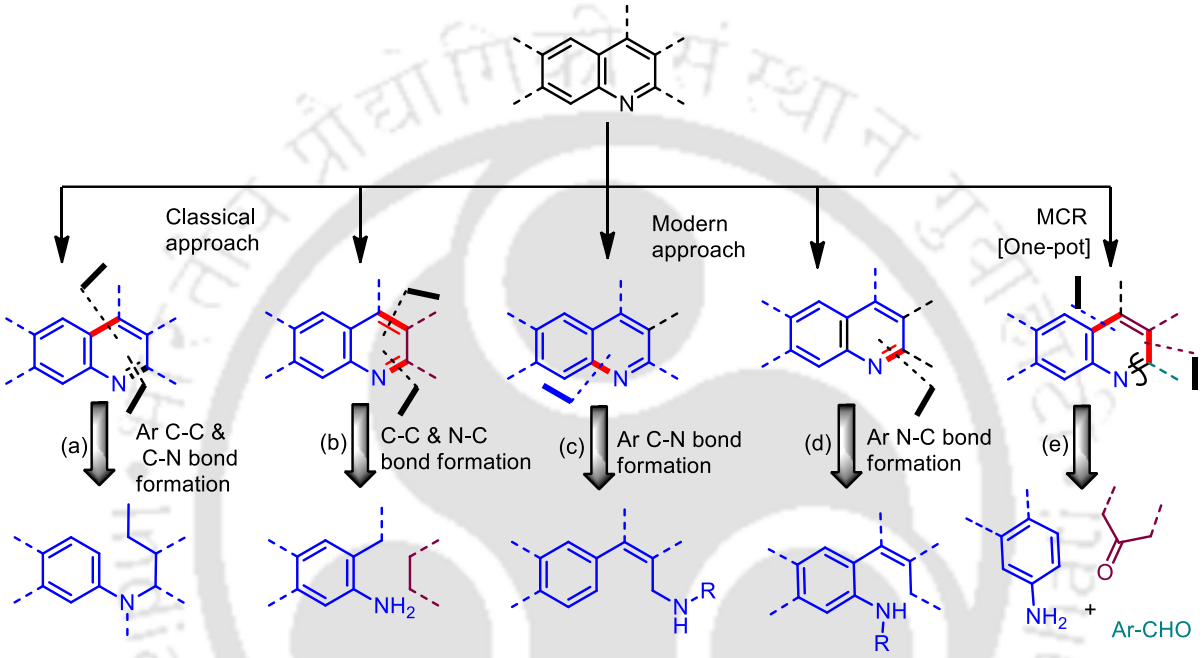


Figure 3. Synthetic approaches for substituted quinolines

2.0 Introduction to Indoles

Indole is an aromatic heterocyclic compound with benzene ring fused to pyrrole. Indole scaffolds have gained a significant attention in the field of organic chemistry due to their extensive scope of applications. Particularly, 3-arylindole exhibit wide range of biological activity[49-53] as shown in Figure **4**. These reasons make the synthesis of 3-arylindoles and their analogues as precious target molecules in a commercial scale. Based on the immense importance, various methods have been developed for the synthesis of 3-arylindoles.

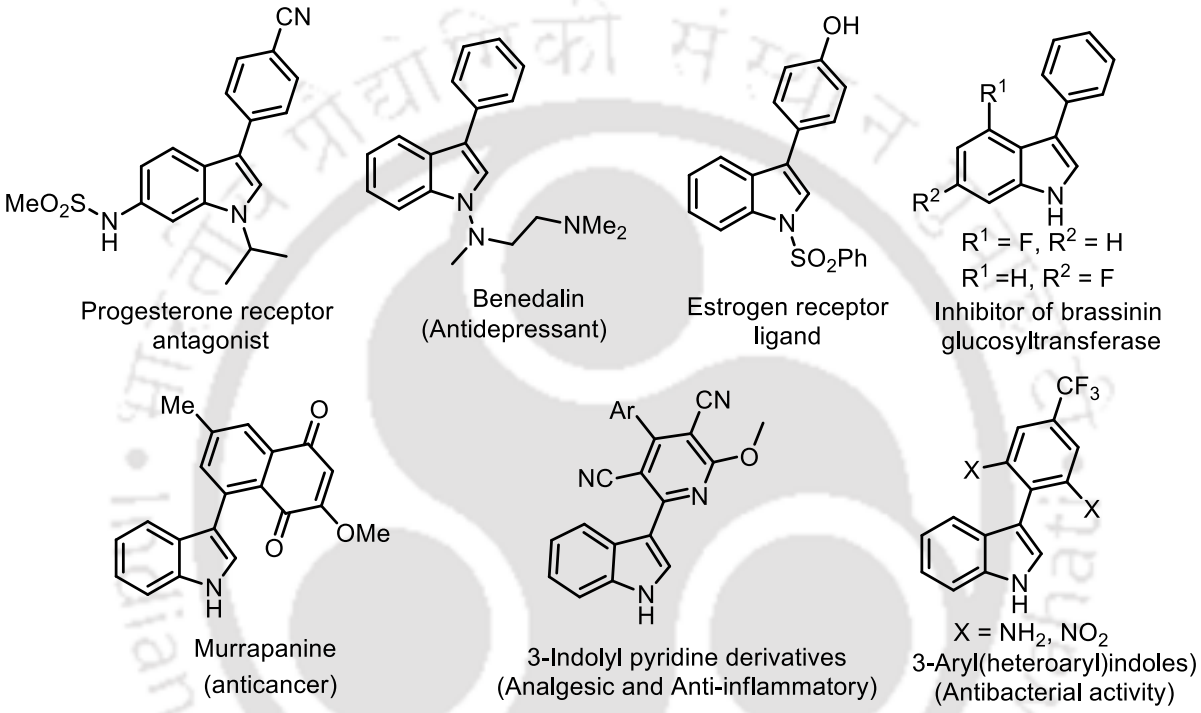
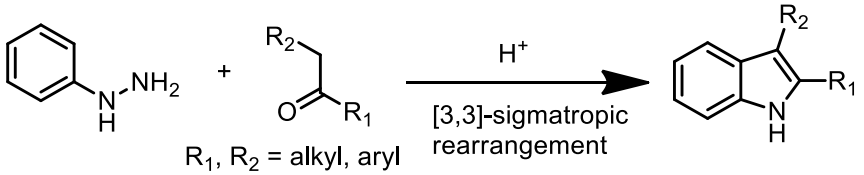


Figure 4. Some of the biologically active 3-arylindoles.

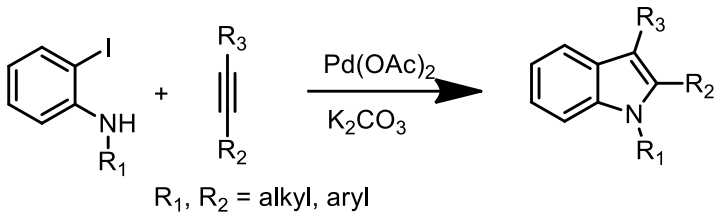
2.1 Classical methods for Indole synthesis:

Fischer indole synthesis is one of the most reliable method developed by Emil Fischer[54,55] in 1883. The reaction was carried out with phenylhydrazine and carbonyl compound by employing acid catalysts such as HCl, H_2SO_4, *p*-toluenesulfonic acid and Lewis acids as represented in Scheme **20**.



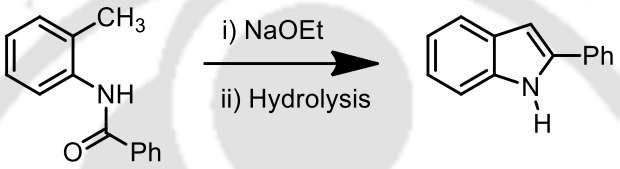
Scheme 20

Larock and co-worker reported synthesis of indole derivatives using palladium catalysed reaction of an *ortho*-iodoanilines[56] and disubstituted alkynes as given in Scheme **21**.



Scheme 21

Walter Madelung in 1912 reported an intramolecular cyclization of N-benzoyl-*o*-toluidine[57] to 2-phenylindole in presence of sodium ethoxide followed by hydrolysis as shown in Scheme **22**.



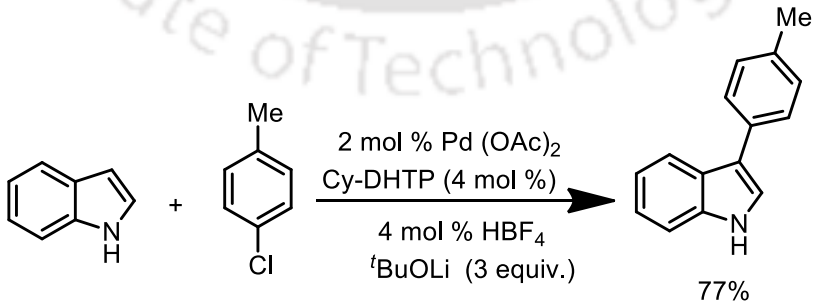
Scheme 22

2.2 Synthesis of 3-Arylindoles:

3-Arylindoles are synthesized by direct C3 arylation of indoles, intramolecular cyclisation and intermolecular cyclisation. The few important methods for the synthesis of 3-arylindoles are discussed here.

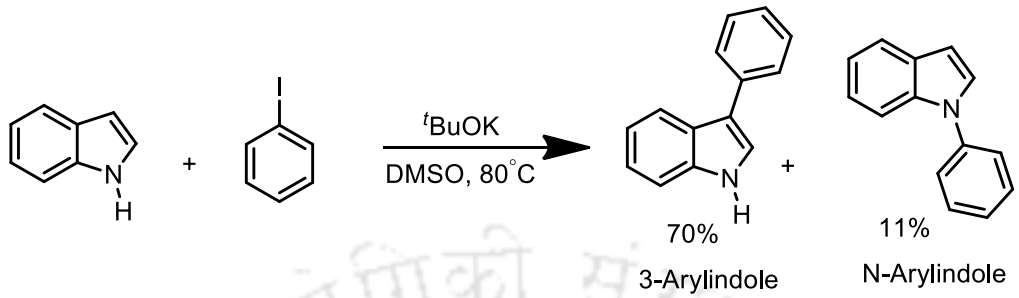
2.2.1 C3 arylation of indoles:

Manabe group developed direct C3-arylation[58] of N-unsubstituted indoles with aryl chlorides using a palladium-dihydroxyterphenylphosphine (DHTP) catalyst as shown in Scheme **23**. The DHTP ligand forms a complex between the lithium salts of the ligand and the indole.



Scheme 23

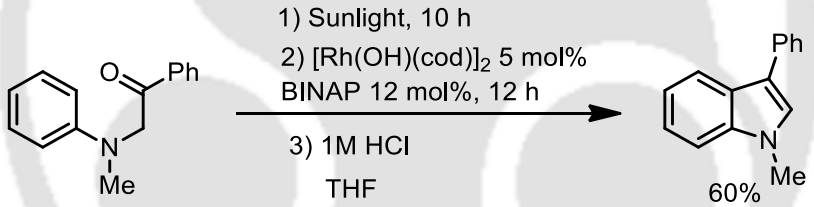
Wu et al accomplished ^{t}BuOK promoted coupling of indoles with aryl halides for regioselective C3-arylation[59] of indoles. However, the N-arylated product is also forming through metal and ligand free coupling reaction as shown in Scheme **24**.



Scheme 24

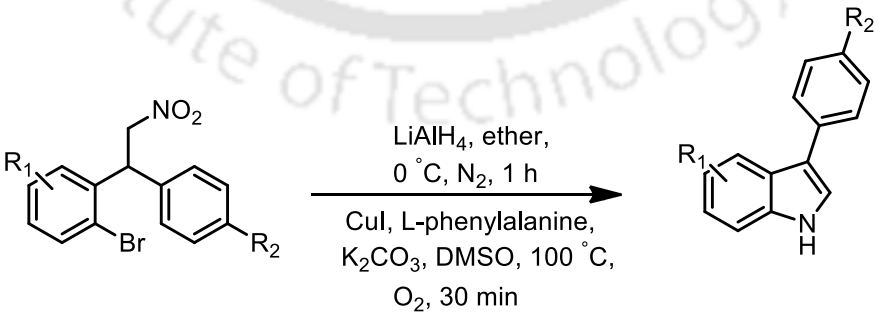
2.2.2 Intramolecular cyclisation

Murakami and co-workers developed 3-arylindoles from N-aryl-N-methylaminoacetophenones through the sequential actions of photocyclization[60] promoted by sunlight and a rhodium catalyst as shown in Scheme **25**.



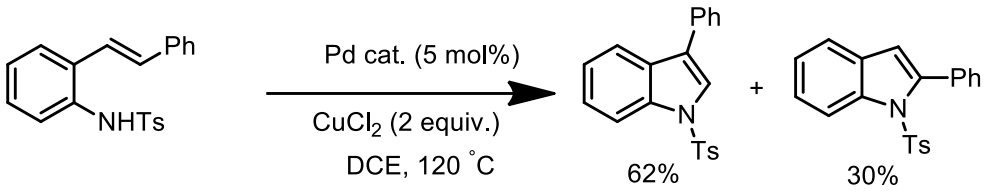
Scheme 25

Yao group reported Cu(I) catalysed intramolecular Ullmann coupling of 2-bromoarylaminoalkanes[61] for the formation of 3-arylindole derivatives as shown in scheme **26**.



Scheme 26

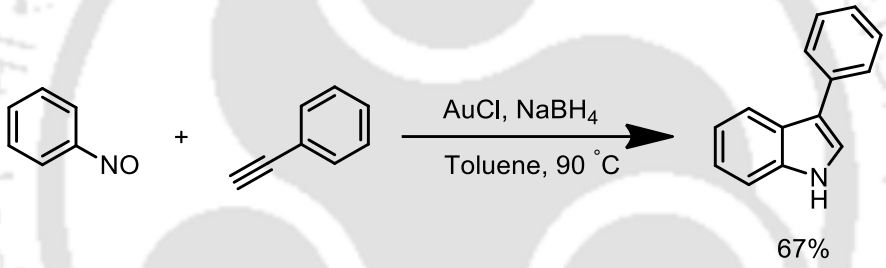
The unusual 1,2-aryl shift[62] in Pd(II)-catalyzed aza-Wacker-type cyclization of 2-alkenylanilines for the formation of 3-arylindoles was developed by Youn group as shown in Scheme **27**.



Scheme 27

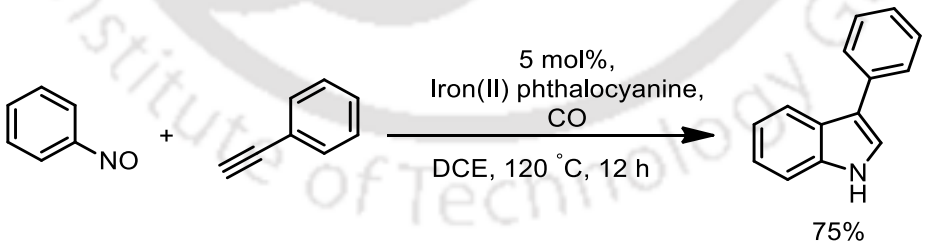
2.2.3 Intermolecular cyclisation

Srivastava group established Au-catalyzed 3-arylindoles from the reaction of nitrosoarenes[63] with phenylacetylenes under reductive conditions using sodium borohydride as given in Scheme **28**.



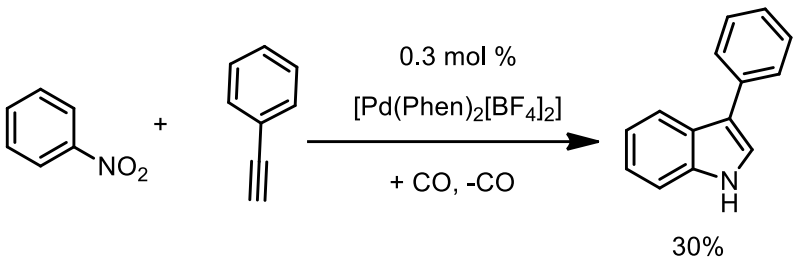
Scheme 28

Wu et al. also developed 3-arylindoles from nitrosoarenes[64] and alkynes using Iron(II) phthalocyanine as the catalyst and CO as the reductant as shown in Scheme **29**.



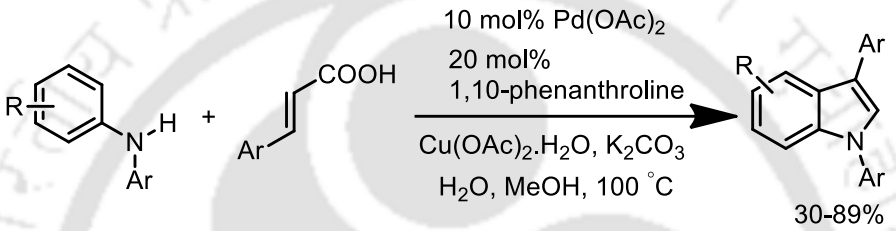
Scheme 29

Ragaini and co-workers reported 3-arylindoles by an *ortho*-C-H functionalization of the nitroarene[65] with arylalkynes and CO in presence of Palladium-phenanthroline complexes as represented in Scheme **30**. In this reaction, initially the nitroarene got to aniline which on cyclisation with phenylacetylene furnished 3-arylindoles.



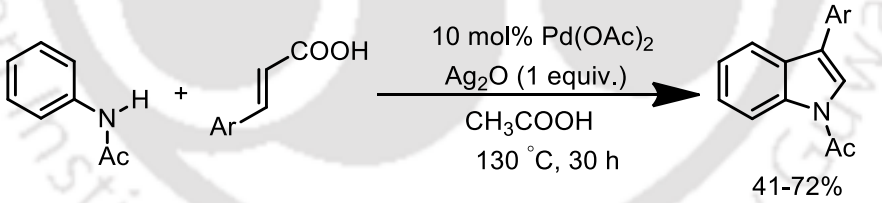
Scheme 30

Maiti group reported a palladium-catalyzed *ortho* C-H activation[66] of di-arylamines with *α, β*-unsaturated acids for the synthesis of 1,3-di-arylindole derivatives through [3+2] annulation under basic conditions as shown in Scheme **31**.



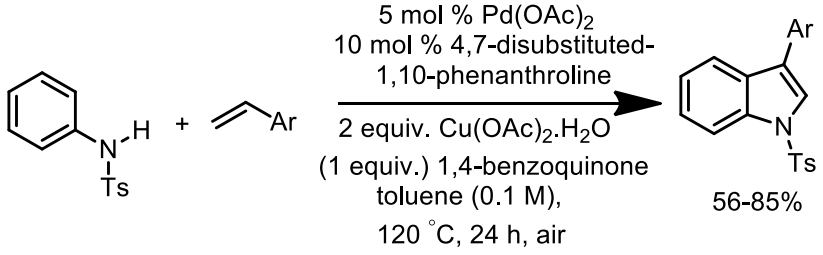
Scheme 31

Similarly, Singh and co-workers reported biologically important N-acylated indoles[67] from N-acetylanilines and cinnamic acids through palladium catalyzed C-H activation and decarboxylation as shown in Scheme **32**.



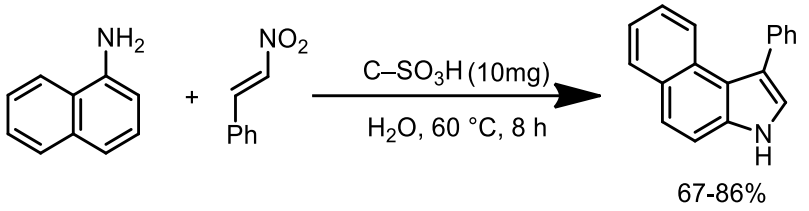
Scheme 32

Palladium catalyzed regioselective synthesis of 3-arylindoles from N-Ts-anilines[68] and styrenes through an oxidative annulation was developed by Jang group as given in Scheme **33**.



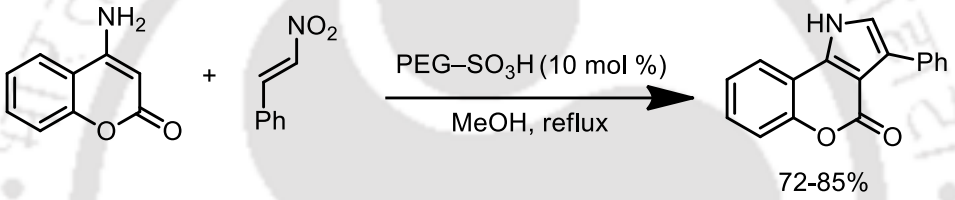
Scheme 33

Qi and co-workers reported a cost-effective and environmentally benign synthesis of benzoindoles[69] from *trans*-*β*-nitrostyrene and naphthylamines under aqueous mediated metal-free reaction conditions in good to excellent yields as represented in the Scheme **34**.



Scheme 34

Similarly, Das[70] et al. developed a simple and convenient synthetic protocol for the synthesis of coumarin fused pyrrole through Michael addition of 4-aminocoumarin to *α*,*β*-unsaturated nitroalkene using PEG-SO_3H polymer supported catalyst as shown in Scheme **35**.

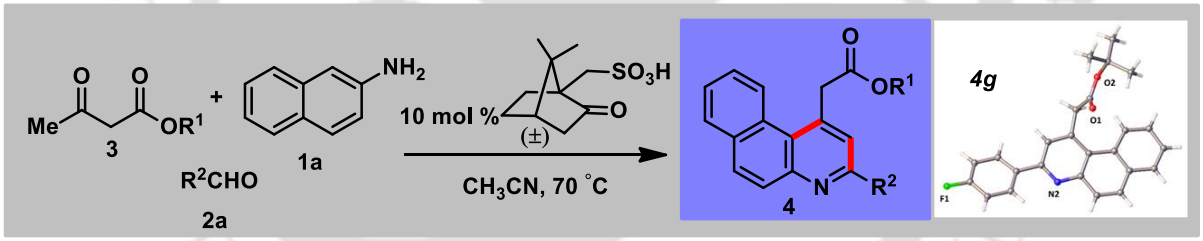


Scheme 35

Apart from several advantages, all of these methods have one or other shortcomings such as the site-selective C3-arylation of indoles and intramolecular cyclisation of substituted anilines leads to 2-arylindoles, requirement of expensive metal catalysts, use of ligands and additives, restricted reaction conditions, failure of the reaction with N-alkyl anilines[66-68] and simple anilines[69] in intermolecular cyclisation. Consequently, there is a further scope to develop a new methodology for the regioselective synthesis of 3-arylindoles and N-alkylated 3-arylindoles using inexpensive reagent.

Chapter II

Regioselective Synthesis of C1-Functionalised 3-Arylbenzo[f]quinoline Through MCR



- One-pot
- 2 C-C bond formation
- 21 examples
- 60-96% yield

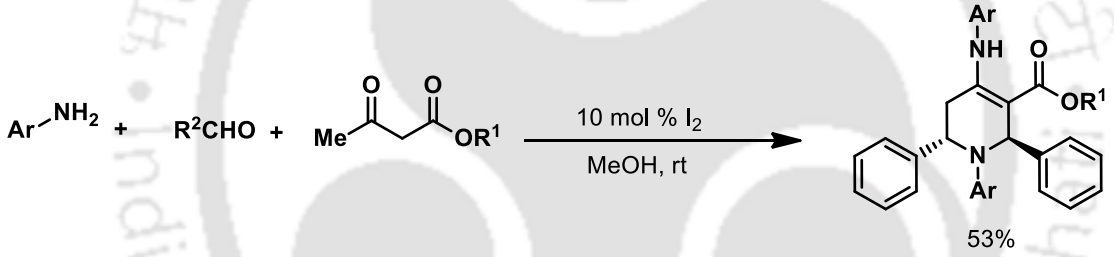
(4g X-ray crystal)

Result & Discussion

Experimental Section

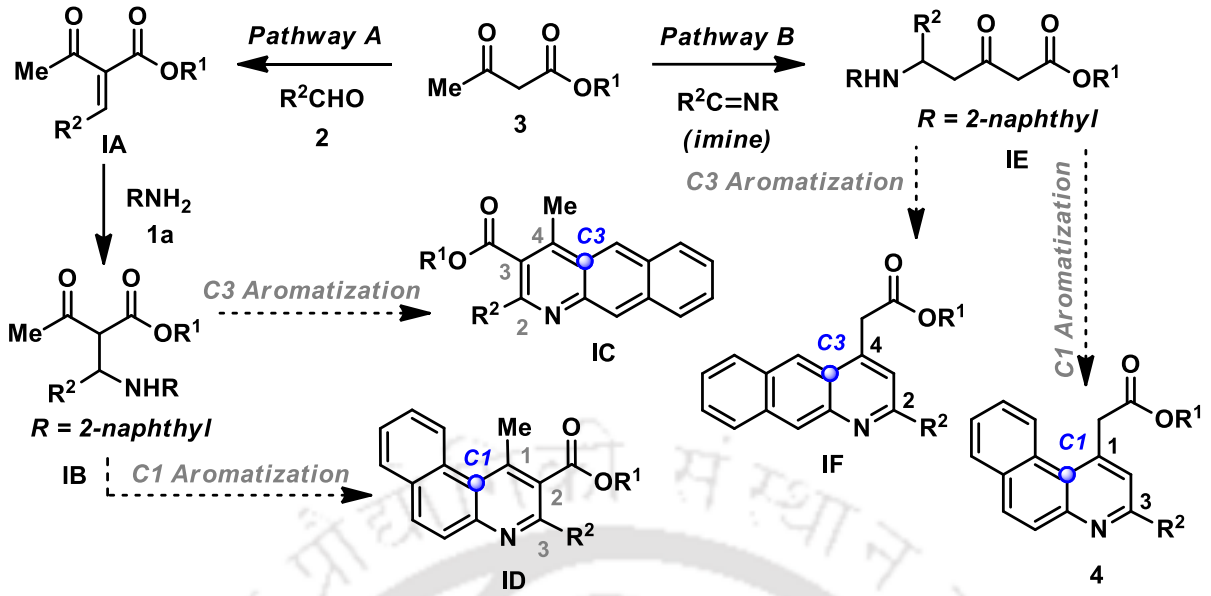
Results and Discussion

In 2008, our research group have developed a simple and convenient one-pot multicomponent reactions (MCR) for the synthesis of highly functionalized piperidines[71] from arylamine, arylaldehydes and *β*-ketoester using 10 mol % bromodimethylsulfonium bromide (BDMS) in acetonitrile at room temperature. This strategy demonstrated five component reaction of 1,3-dicarbonyl compound, arylamine and aromatic aldehyde as shown in Scheme **36**. In the meantime Wang et al. reported the synthesis of benzo[*f*]quinoline[72] derivatives via three-component reaction using a combination of 2-naphthylamine, arylaldehydes and *β*-ketoester using 5 mol % iodine as catalyst in THF solvent under reflux conditions. Interestingly, the same combination of 2-naphthylamine, arylaldehydes and *β*-ketoester provided highly substituted tetrahydropyridines[73] using 10 mol % iodine at room temperature. By these observations, we are very much curious to investigate whether benzo[*f*]quinolines can be achieved from the above mentioned reactants by tuning the reaction condition.

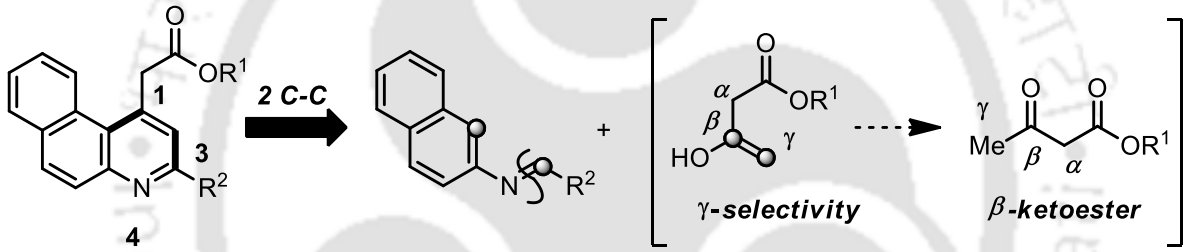


Scheme 36

There are four possibilities for the formation of different kinds of products as shown in the retrosynthetic analysis Scheme **37**. In pathway **A**, *β*-ketoester with aldehyde prefer to attain species **IA** which react with amine *via* Michael addition to form **IB** and it may aromatize either at C3 or C1 position of the naphthylamine to form alkyl 4-methyl-2-arylbenzo[*g*]quinoline-3-carboxylate **IC** and alkyl 1-methyl-3-arylbenzo[*f*]quinoline-2-carboxylate **ID**. On the other hand in pathway **B**, alkyl-5-(naphthalen-2-ylamino)-3-oxo-5-arylpentanoate **IE** prefer to form alkyl 2-(3-arylbenzo[*f*]quinolin-1-yl)acetate **4** and alkyl 2-(2-arylbenzo[*g*]quinolin-4-yl)acetate **IF**. Among the possible reaction site-pathways, the regioselective synthesis of alkyl-2-(3-arylbenzo[*f*]quinolin-1-yl)acetate **4** are highly desirable, which may act as a scaffold in drug discovery unit. Since there were disadvantages in the reported methods such as harsh conditions and long reaction times,[74-75] we were interested to find out an elegant method for the synthesis of functionalised benzo[*f*]quinoline **4**.

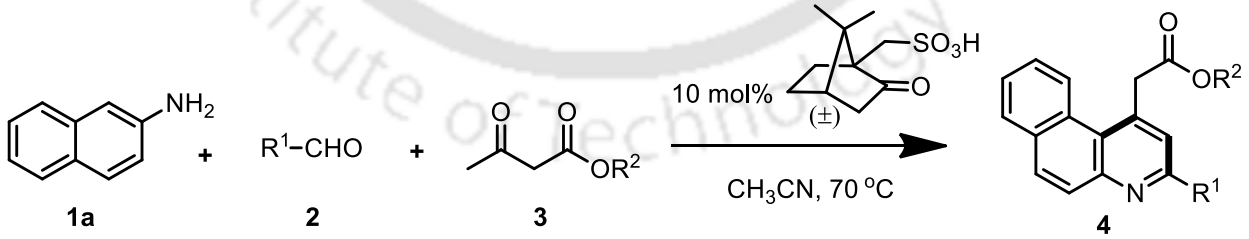


Scheme 37



Scheme 38. Synthetic route and its pre-centre of alkyl 2-(3-arylbenzo[*f*]quinolin-1-yl)acetate

In this chapter, we will discuss 3-arylbenzo[*f*]quinoline using 2-naphthylamine, arylaldehydes and *β*-ketoester by employing 10 mol% camphorsulfonic acid as catalyst in acetonitrile at 70 °C.

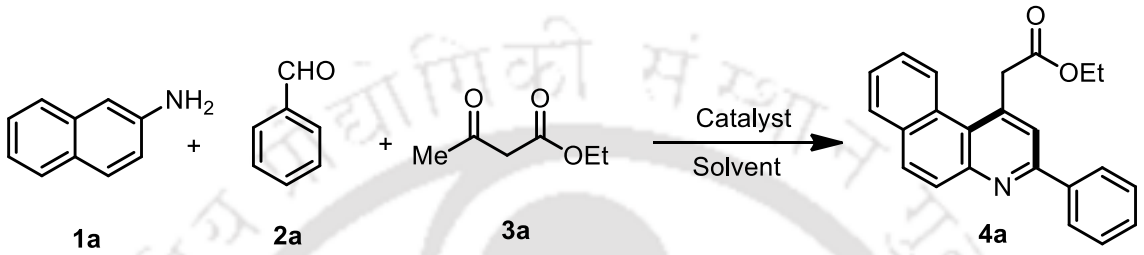


Scheme 39

To optimise the reaction conditions, we have tested a series of reactions with 2-napthylamine **1a**, benzaldehyde **2a** and ethyl acetoacetate **3a** as depicted in Table **1**. It is to be noted that the 10 mol % camphorsulfonic acid catalyst in acetonitrile at 70 °C which gave better yield (Table 1, entry 5). However, different solvents such as DCE,

THF and *n*-BuOH afforded lower yield. (Table 1, entries 8-10). It is also noteworthy that in our present protocol we have not observed any other byproducts such as **IC**, **ID** and **IF** in the reaction medium. The compound **4a** was characterized by ^{1}H and ^{13}C NMR spectra and HRMS. The ^{1}H NMR shows the characteristic peaks 4.49 (s, 2H), 4.25 (q, *J* = 7.2 Hz, 2H), 1.23 (t, *J* = 7.2 Hz, 3H) and 7.87 (s, 1H) indicates the formation of *Ethyl 2-(3-phenylbenzo[f]quinolin-1-yl)acetate* **4a**.

Table 1. Optimization of the reaction conditions[a]



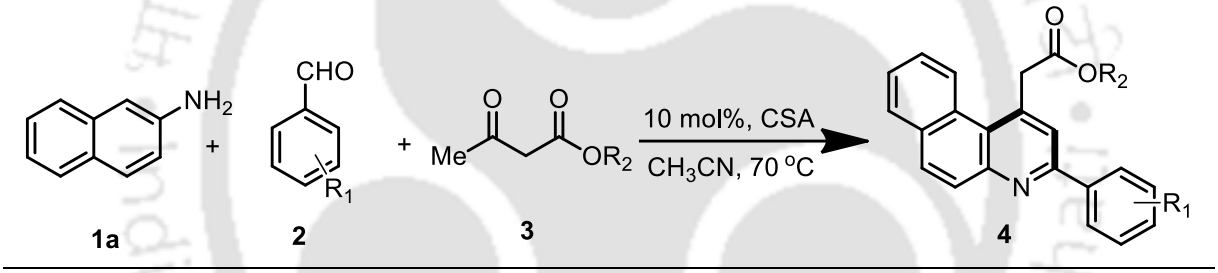
S.No	Catalyst	Mol %	Solvent	Time (h)	Yield (%)[b]
01	AcOH	10	CH_3CN	8.0	55
02	*p*-TSA	10	CH_3CN	12.0	NR
03	Iodine	10	CH_3CN	2.5	60
04	L-Proline	10	CH_3CN	12.0	NR
05	**(±)-CSA**	**10**	**CH_3CN**	**2.0**	**92**
06	(±)-CSA	05	CH_3CN	3.0	80
07	(±)-CSA	15	CH_3CN	2.5	89
08[c]	(±)-CSA	10	DCE	12.0	35
09[c]	(±)-CSA	10	THF	6.0	65
10	(±)-CSA	10	*n*-BuOH	12.0	25

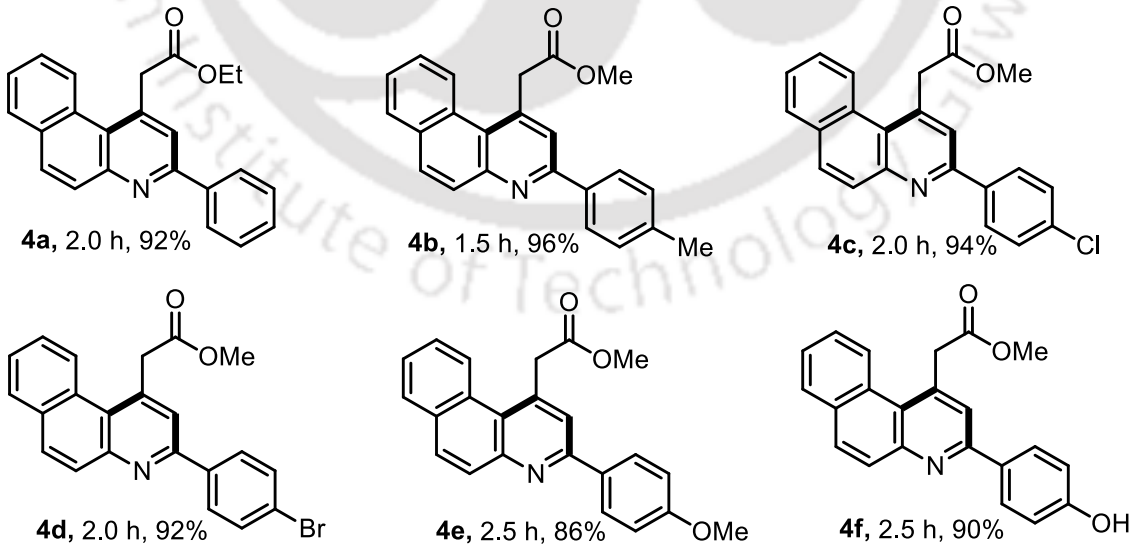
[a]The reactions were performed in 0.5 mmol scale using 2-naphthylamine **1a**, benzaldehyde **2a**, ethyl acetoacetate **3a**. [b]Isolated yield. [c]Reaction temperature at 50 °C. NR = No Reaction.

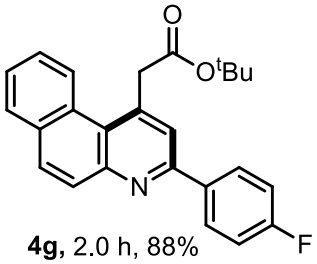
After optimisation, we conducted reactions with 2-naphthylamine **1a**, methyl acetoacetate **3b** and a various *para*-substituted benzaldehyde such as 4-methyl, 4-chloro, 4-bromo, 4-methoxy and 4-hydroxy moiety which afforded the desired product **4b-f** in 86-96% yield. Subsequent reaction of 2-naphthylamine **1a**, *tert*-butyl acetoacetate **3c** with 4-fluorobenzaldehyde/furfural delivered the required product **4g**

and **4h** in 88% and 76% yield. Further, the reaction was examined with 2/3-halobenzaldehyde/2,4-dimethoxy benzaldehyde, 2-naphthylamine and methyl acetoacetate and the resultant product **4i-k** were obtained in 78-88% yield. In addition, 2/3-(allyloxy) benzaldehyde underwent reactions with allyl acetoacetate **3d** and 2-naphthylamine **1a** which gave the corresponding product **4l** and **4m** in 74% and 76% yield respectively. Reactions with different substituted benzaldehyde, ethyl acetoacetate and 2-naphthylamine resulted in **4n-r** in 72-90% yield. Inspired by these results, we performed reactions of allyl acetoacetate **3d**, 2-naphthylamine **1a** and with a variety of *para*-substituted benzaldehyde such as 4-methyl, 4-fluoro and 4-methoxy under the optimized reaction condition which afford the required benzo[*f*]quinolines **4s-u** in 78-86% yield as shown in Table **2**. The crystal structure of compound **4g** was determined through single crystal XRD analysis and ORTEP diagram is shown in Figure **5**.

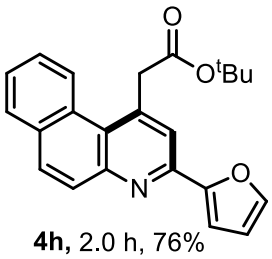
Table 2. Representative examples of alkyl 2-(3-arylbenzo[*f*]quinolin-1-yl)acetate[a,b]



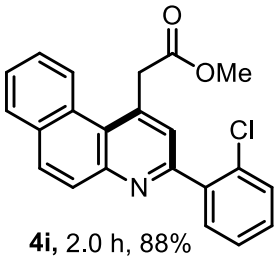




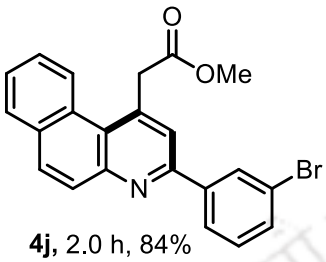
4g, 2.0 h, 88%



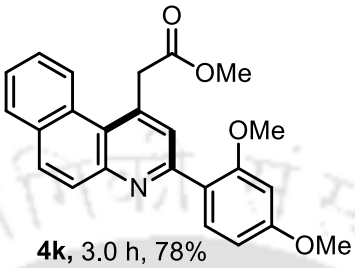
4h, 2.0 h, 76%



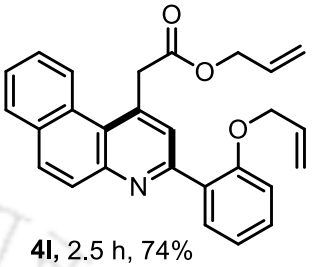
4i, 2.0 h, 88%



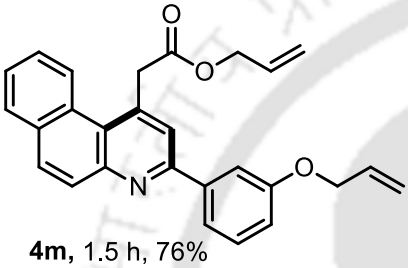
4j, 2.0 h, 84%



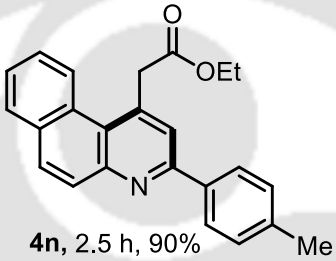
4k, 3.0 h, 78%



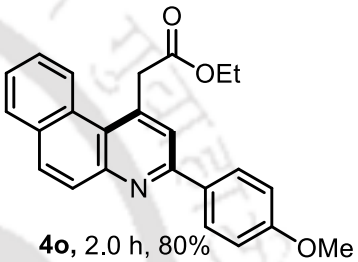
4l, 2.5 h, 74%



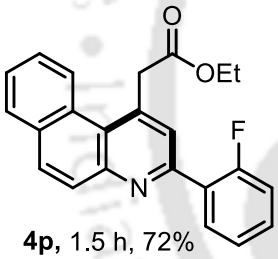
4m, 1.5 h, 76%



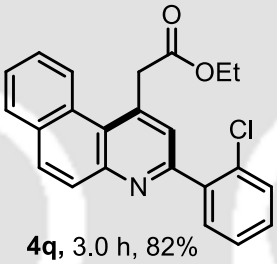
4n, 2.5 h, 90%



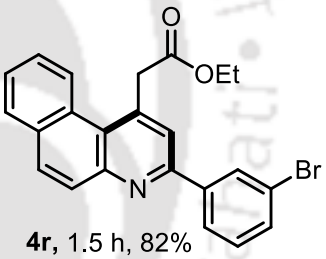
4o, 2.0 h, 80%



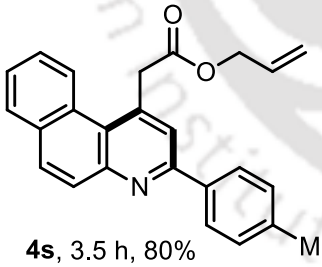
4p, 1.5 h, 72%



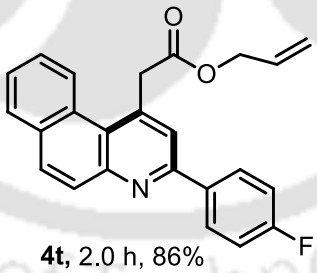
4q, 3.0 h, 82%



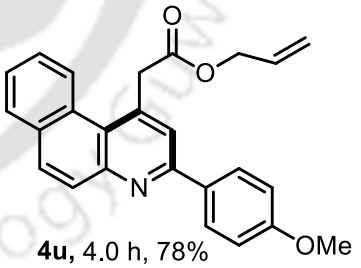
4r, 1.5 h, 82%



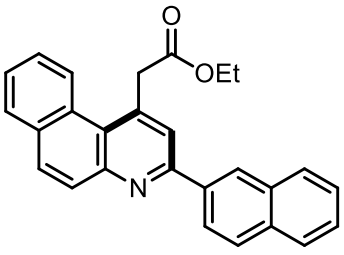
4s, 3.5 h, 80%



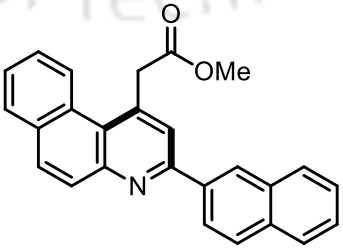
4t, 2.0 h, 86%



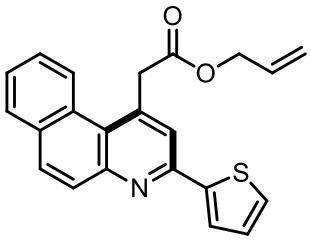
4u, 4.0 h, 78%



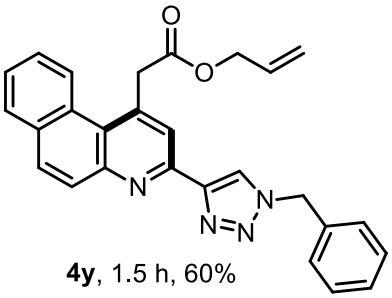
4**v,** 3.5h, 74%



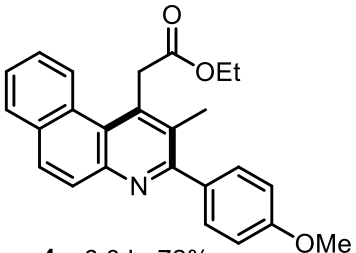
4w, 3.0h, 87%



4x, 3.0h, 76%



4y, 1.5 h, 60%



4z, 6.0 h, 72%

[a]The reactions were performed in 0.5 mmol scale using 2-naphthylamine (**1a**), aromatic aldehyde (**2**), *β*-ketoester (**3**). [b]Isolated yield.

All the synthesized compounds are characterized by ^{1}H and ^{13}C NMR spectra and HRMS. The compound **4g** was also confirmed through single crystal XRD. The ORTEP diagram of compound **4g** shown in Figure **5**. The NMR spectra of compound **4t** and **4w** are shown in Figure **6** and **7** (See Page No. 34 and 35 in Experimental Section).

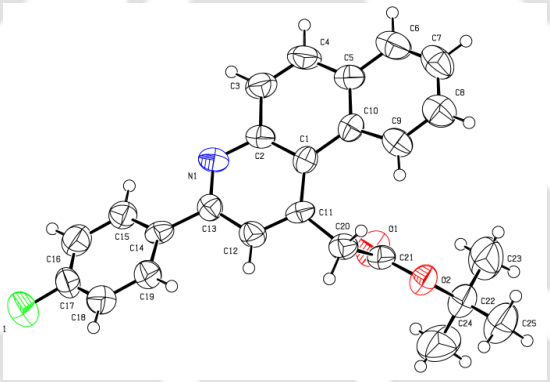
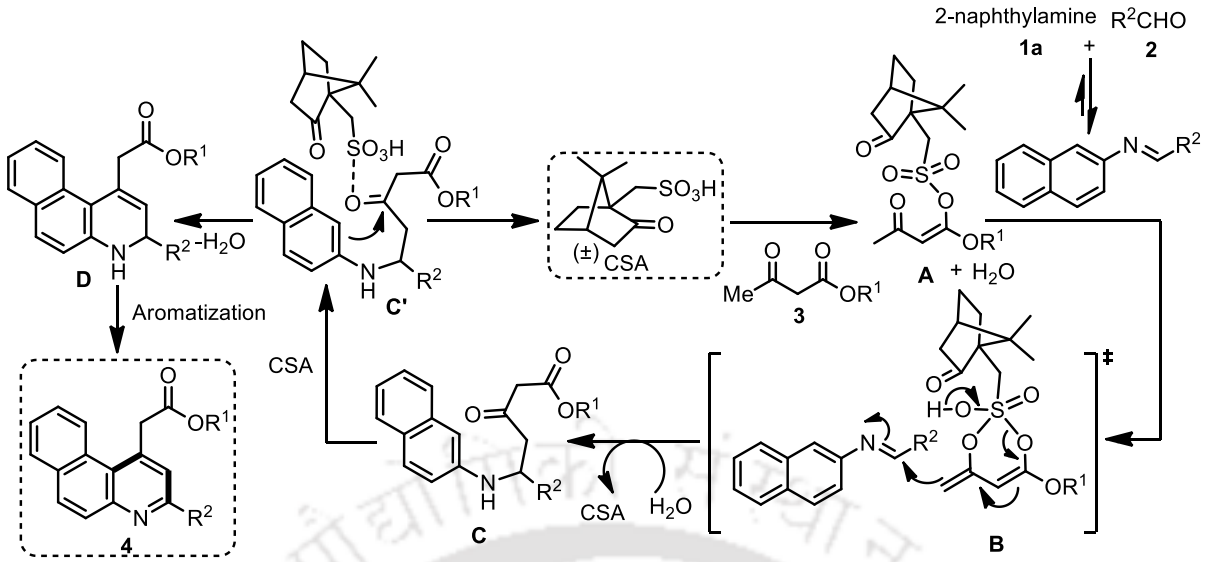


Figure 5. ORTEP diagram of compound of **4g** with 45% ellipsoid probability

A plausible mechanism is described as shown in scheme **40**. Initially, the *β*-ketoester **3** most likely to react with camphorsulfonic acid to form an intermediate **A**, which subsequently undergoes rearrangement and reacts with the generated imine *via* **B** to form a Michael addition product **C** through *γ*-selective of *β*-ketoester. Further, **C** undergoes cyclisation to form dihydroquinoline **D** which undergo aromatization to form the desired product **4** as shown in Scheme **40**.



Scheme 40

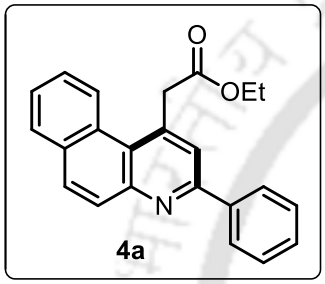
In summary, the regioselective synthesis of alkyl 2-(3-arylbenzo[*f*]quinolin-1-yl)acetate **4** has been achieved using camphorsulfonic acid through *γ*-selectivity of *β*-ketoester. It is a straight forward methodology which provide access to diverse range of substrates. The prominent aspect of this present method was that two new *C-C* bonds were formed in a one-pot fashion under mild reaction conditions. In addition, the protocol enables the synthesis of hetero aromatic and trisubstituted benzo[*f*]quinoline analogues in good yields.

Experimental Section

*General procedure for synthesis of alkyl 2-(3-arylbenzo[f]quinolin-1-yl)acetate (**4**)*

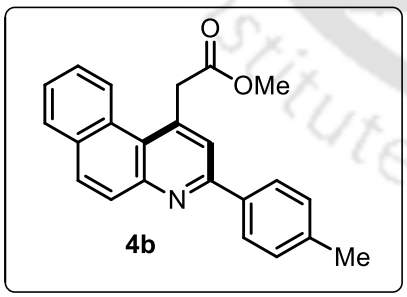
A mixture of 2-naphthylamine **1a** (0.5 mmol) aromatic aldehyde **2** (0.5 mmol) and *β*-ketoester **3** (0.5 mmol) was taken in 5 mL acetonitrile. Camphorsulfonic acid (0.011 g, 0.05 mmol) was added in to it and allow to stir at 70 °C. After completion of the reaction, the solvent was removed under reduced pressure and it was extracted with DCM, washed with water, dried over sodium sulfate and concentrated under reduced pressure. Then, the residue was purified through column chromatography to obtain the pure product **4**.

*Ethyl 2-(3-phenylbenzo[f]quinolin-1-yl)acetate (**4a**)*



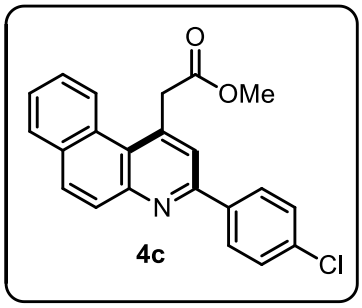
Yield 92% (157 mg), white solid, mp 131-132 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.54 (d, *J* = 8.8 Hz, 1H), 8.22 (d, *J* = 8.8 Hz, 2H), 8.09 (d, *J* = 9.2 Hz, 1H), 7.99- 7.97 (m, 2H), 7.87 (s, 1H), 7.67-7.64 (m, 2H), 7.56 (t, *J* = 7.2 Hz, 2H), 7.49 (t, *J* = 6.8 Hz, 1H), 4.49 (s, 2H), 4.25 (q, *J* = 7.2 Hz, 2H), 1.23 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.8, 155.9, 150.3, 141.1, 139.2, 133.2, 131.5, 130.0, 129.8, 129.5, 129.4, 129.1, 127.6, 127.0, 126.9, 126.8, 124.6, 123.2, 61.7, 44.0, 14.4; **IR (KBr)ν_{max}** 3056, 2980, 2902, 1735, 1584, 1552, 1484, 1455, 1391, 1367, 1322, 1255, 1194, 1156, 1029 cm^{-1}; **HRMS (ESI)** Calcd For $C_{23}H_{20}NO_2$ 342.1489 (M + H^+); Found 342.1489.

*Methyl 2-(3-(p-tolyl)benzo[f]quinolin-1-yl)acetate (**4b**)*



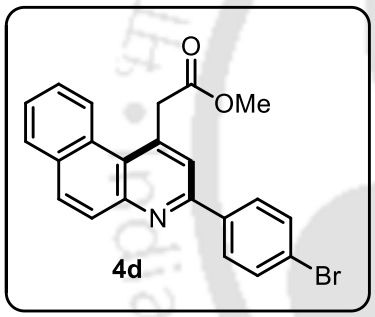
Yield 96% (164 mg), light yellow, mp 168-169 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.49 (d, *J* = 7.6 Hz, 1H), 8.12 (t, *J* = 8.0 Hz, 2H), 8.08 (s, 1H), 7.97-7.93 (m, 2H), 7.83 (s, 1H), 7.68-7.61 (m, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 4.47 (s, 2H), 3.77 (s, 3H), 2.45 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.3, 155.8, 150.2, 140.8, 139.6, 136.2, 133.1, 131.4, 129.9, 129.7, 129.6, 129.4, 128.2, 127.5, 126.8, 126.7, 124.3, 122.9, 52.7, 43.7, 21.5; **IR (KBr)ν_{max}** 3029, 2952, 2922, 2853, 1737, 1579, 1548, 1481, 1452, 1437, 1392, 1353, 1259, 1184, 1132, 1057 cm^{-1}; **HRMS (ESI)** Calcd For $C_{23}H_{20}NO_2$ 342.1489 (M + H^+); Found 342.1505.

*Methyl 2-(3-(4-chlorophenyl)benzo[f]quinolin-1-yl)acetate (**4c**)*



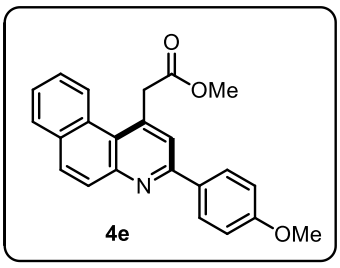
Yield 94% (170 mg), white solid, mp 138-139 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.49 (d, *J* = 7.2 Hz, 1H), 8.17 (d, *J* = 8.8 Hz, 2H), 8.12 (d, *J* = 8.8 Hz, 1H), 8.00-7.96 (m, 2H), 7.83 (s, 1H), 7.69-7.66 (m, 2H), 7.51 (d, *J* = 8.8 Hz, 2H), 4.51 (s, 2H), 3.78 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.1, 154.3, 149.9, 141.4, 137.0, 135.9, 133.2, 131.9, 129.7, 129.5, 129.2, 128.9, 127.2, 127.0, 126.8, 124.7, 122.9, 52.8, 43.7; **IR (KBr)ν_{max}** 3056, 2942, 2924, 2852, 1741, 1585, 1550, 1481, 1435, 1390, 1328, 1257, 1198, 1157, 1091, 1012 cm^{-1}; **HRMS (ESI)** Calcd For $C_{22}H_{17}ClNO_2$ 362.0943 ($M + H^+$); Found 362.0942.

*Methyl 2-(3-(4-bromophenyl)benzo[f]quinolin-1-yl)acetate (**4d**)*



Yield 92% (186 mg), light yellow solid, mp 143-144 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.51 (d, *J* = 9.0 Hz, 1H), 8.11 (d, *J* = 8.4 Hz, 2H), 8.06 (d, *J* = 9.0 Hz, 1H), 7.99- 7.96 (m, 2H), 7.83 (s, 1H), 7.68-7.66 (m, 4H), 4.51 (s, 2H), 3.78 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.2, 154.5, 150.3, 141.1, 137.9, 133.2, 132.2, 131.7, 129.8, 129.6, 129.5, 129.1, 127.1, 126.9, 126.8, 124.7, 124.1, 122.7, 52.8, 43.6; **IR (KBr)ν_{max}** 3051, 2951, 2915, 2854, 1736, 1584, 1549, 1481, 1455, 1434, 1387, 1356, 1328, 1257, 1199, 1159, 1087, 1008 cm^{-1}; **HRMS (ESI)** Calcd For $C_{22}H_{17}BrNO_2$ 406.0437 ($M + H^+$); Found 406.0437.

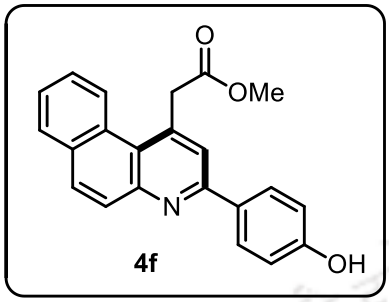
*Methyl 2-(3-(4-methoxyphenyl)benzo[f]quinolin-1-yl)acetate (**4e**)*



Yield 86% (153 mg), light yellow solid, mp 149-150 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.47 (d, *J* = 8.4 Hz, 1H), 8.18 (d, *J* = 8.4 Hz, 2H), 8.09 (d, *J* = 9.0 Hz, 1H), 7.93 (t, *J* = 9.0 Hz, 2H), 7.78 (s, 1H), 7.65-7.56 (m, 2H), 7.04 (d, *J* = 8.4 Hz, 2H), 4.46 (s, 2H), 3.87 (s, 3H), 3.76 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 171.2, 161.1, 155.3, 149.9, 140.9, 132.9, 131.8, 131.5, 131.2, 129.9, 129.4, 128.9, 126.8, 126.7, 126.6, 124.1, 122.7, 114.4, 55.5, 52.7, 43.6; **IR (KBr)ν_{max}** 3068, 2995, 2948, 2937, 2830, 1737, 1604, 1544, 1503, 1434, 1354, 1337, 1252,

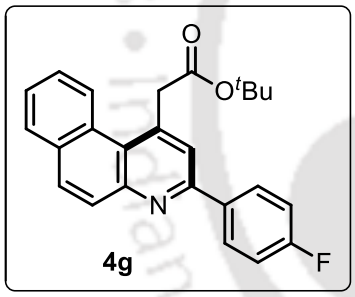
1202, 1183, 1161, 1028 cm^{-1}; **HRMS (ESI)** Calcd For $C_{23}H_{20}NO_3$ 358.1438 (M + H^+); Found 358.1430.

*Methyl 2-(3-(4-hydroxyphenyl)benzo[f]quinolin-1-yl)acetate (**4f**)*



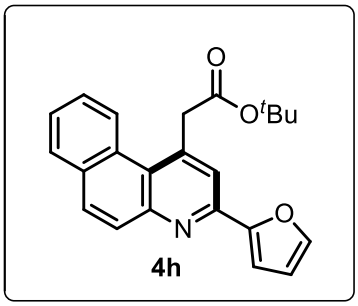
Yield 90% (154 mg), white solid, mp 141-142 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.30 (s, 1H), 8.40 (d, *J* = 6.0 Hz, 1H), 8.02 (d, *J* = 6.6 Hz, 2H), 7.93 (d, *J* = 2.4, 1H), 7.92 (d, *J* = 1.8 Hz, 2H), 7.75 (s, 1H), 7.56-7.53 (m, 2H), 6.91 (d, *J* = 6.0 Hz, 2H), 4.44 (s, 2H), 3.69 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 170.4, 158.5, 154.8, 149.2, 140.1, 132.0, 129.1, 129.0, 128.6, 128.5, 128.1, 128.0, 126.1, 125.9, 125.7, 122.9, 121.8, 121.7, 115.4, 115.3, 51.8, 42.8; **IR (KBr)ν_{max}** 3058, 2995, 2953, 2838, 1738, 1608, 1588, 1549, 1514, 1484, 1451, 1353, 1258, 1171, 1130, 1058 cm^{-1}; **HRMS (ESI)** Calcd For $C_{22}H_{18}NO_3$ 344.1281 (M + H^+); Found 344.1286.

*Tert-butyl 2-(3-(4-fluorophenyl)benzo[f]quinolin-1-yl)acetate (**4g**)*



Yield 88% (170 mg), white solid, mp 140-141 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.58 (d, *J* = 7.8 Hz, 1H), 8.23-8.21 (m, 2H), 8.06 (d, *J* = 8.4 Hz, 1H), 7.98-7.95 (m, 2H), 7.81 (s, 1H), 7.67-7.64 (m, 2H), 7.23-7.20 (m, 2H), 4.41 (s, 2H), 1.44 (s, 9H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 169.5, 165.2, 163.5, 154.1, 133.5, 133.1, 131.2, 131.1, 130.3, 130.1, 129.7, 129.6, 129.3, 128.3, 127.3, 127.2, 127.1, 127.0, 126.6, 124.8, 123.6, 116.3, 116.1, 115.6, 115.5, 82.6, 45.6, 28.2; **IR (KBr)ν_{max}** 3057, 2976, 2927, 2850, 1727, 1602, 1585, 1553, 1532, 1510, 1483, 1455, 1392, 1368, 1329, 1226, 1149, 1073, 1014 cm^{-1}; **HRMS (ESI)** Calcd For $C_{25}H_{23}FNO_2$ 388.1708 (M + H^+); Found 388.1707.

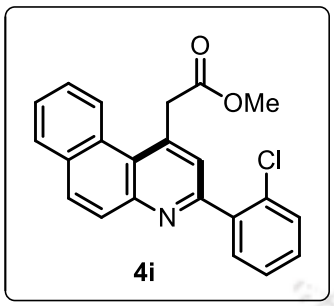
*Tert-butyl 2-(3-(furan-2-yl)benzo[f]quinolin-1-yl)acetate (**4h**)*



Yield 76% (136 mg), brown solid, mp 94-95 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.56 (d, *J* = 8.4 Hz, 1H), 8.04 (d, *J* = 9.2 Hz, 1H), 7.96-7.95 (m, 3H), 7.84 (s, 1H), 7.66-7.64 (m, 2H), 7.27 (d, *J* = 3.2 Hz, 1H), 6.62-6.61 (m, 1H), 4.41 (s, 2H), 1.43 (s, 9H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 169.8, 153.6, 150.2, 147.8, 144.1, 141.7, 133.1, 131.6, 129.4, 129.4, 126.9, 126.8, 126.7, 124.6, 121.6, 112.4, 110.0, 82.2, 45.3, 28.2; **IR (KBr)ν_{max}** 3029, 2974, 2926, 1728,

1601, 1551, 1491, 1454, 1393, 1368, 1325, 1254, 1224, 1072 cm^{-1}; **HRMS (ESI)** Calcd For $C_{23}H_{22}NO_3$ 360.1594 ($M + H^+$); Found 360.1609.

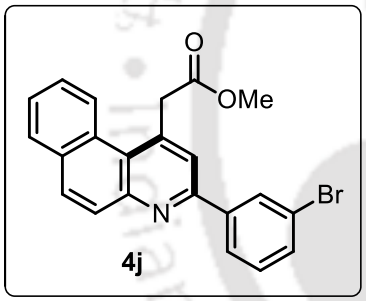
*Methyl 2-(3-(2-chlorophenyl)benzo[f]quinolin-1-yl)acetate (**4i**)*



4i

Yield 88% (159 mg), brown solid, mp 79-80 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.56 (d, *J* = 8.0 Hz, 1H), 8.19 (d, *J* = 8.0 Hz, 1H), 8.00 (t, *J* = 8.4 Hz, 2H), 7.84 (s, 2H), 7.69 (s, 2H), 7.53 (d, *J* = 7.2 Hz, 1H), 7.42 (t, *J* = 8.4 Hz, 2H), 4.52 (s, 2H), 3.77 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.9, 155.0, 149.4, 133.3, 132.7, 132.3, 132.2, 130.4, 129.6, 128.6, 127.5, 127.4, 127.2, 127.1, 126.9, 124.8, 52.8, 43.6; **IR (KBr)ν_{max}** 3059, 2987, 2953, 2850, 1738, 1596, 1580, 1550, 1476, 1435, 1395, 1351, 1330, 1258, 1201, 1160, 1094, 1057 cm^{-1}; **HRMS (ESI)** Calcd For $C_{22}H_{17}ClNO_2$ 362.0943 ($M + H^+$); Found 362.0943.

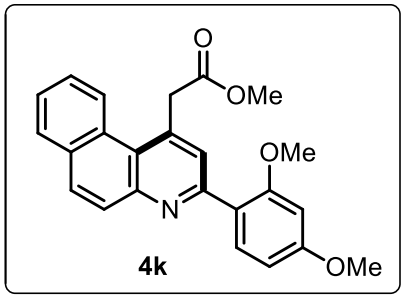
*Methyl 2-(3-(3-bromophenyl)benzo[f]quinolin-1-yl)acetate (**4j**)*



4j

Yield 84% (170 mg), white solid, mp 130-131 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.50 (d, *J* = 12.0 Hz, 1H), 8.40 (s, 1H), 8.12 (d, *J* = 12.0 Hz, 1H), 8.06 (d, *J* = 12.0 Hz, 1H), 7.97 (d, *J* = 12.0 Hz, 2H), 7.81(s, 1H), 7.69-7.65 (m, 2H), 7.59 (d, *J* = 12.0 Hz, 1H), 7.39 (t, *J* = 12.0 Hz, 1H), 4.49 (s, 2H), 3.78 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.4, 154.1, 150.3, 141.1, 141.0, 133.3, 132.4, 131.8, 130.6, 130.5, 129.8, 129.6, 129.5, 127.1, 126.9, 126.8, 126.1, 124.9, 123.3, 122.9, 52.8, 43.7; **IR (KBr)ν_{max}** 3031, 2950, 2916, 2848, 1724, 1605, 1582, 1549, 1488, 1454, 1424, 1383, 1357, 1323, 1306, 1247, 1161, 1053 cm^{-1}; **HRMS (ESI)** Calcd For $C_{22}H_{17}BrNO_2$ 406.0437 ($M + H^+$); Found 406.0435.

*Methyl 2-(3-(2,4-dimethoxyphenyl)benzo[f]quinolin-1-yl)acetate (**4k**)*

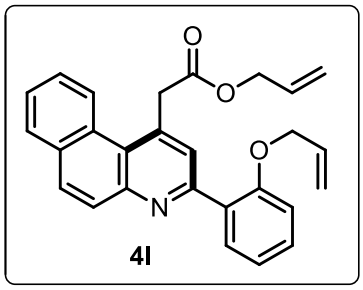


4k

Yield 78% (151 mg), brown solid, mp 111-112 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.52 (d, *J* = 7.6 Hz, 1H), 8.12 (d, *J* = 8.0 Hz, 1H), 8.02-7.94 (m, 4H), 7.64 (s, 2H), 6.69 (d, *J* = 6.8 Hz, 1H), 6.60 (s, 1H), 4.49 (s, 2H), 3.87 (s, 6H), 3.75 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.3, 162.1, 158.8, 154.6, 149.7, 139.8, 133.0, 132.7, 131.2, 129.9, 129.4, 129.2, 127.3, 126.7, 123.9, 105.7, 99.2, 55.9, 55.7, 52.6, 43.7; **IR (KBr)ν_{max}** 3059, 3003, 2950, 2837, 1736, 1608, 1579,

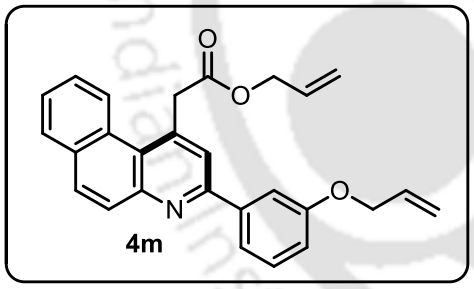
1547, 1505, 1455, 1437, 1300, 1283, 1209, 1160, 1030 cm^{-1}; HRMS (ESI) Calcd For $C_{24}H_{22}NO_4$ 388.1544 ($M + H^+$); Found 388.1542.

*Allyl 2-(3-(2-(allyloxy)phenyl)benzo[f]quinolin-1-yl)acetate (**4l**)*



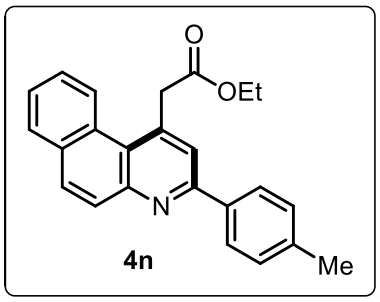
Yield 74% (151 mg), light yellow solid, mp 169-170 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.55 (d, *J* = 8.0 Hz, 1H), 8.17 (s, 1H), 8.07 (s, 1H), 8.04 (d, *J* = 7.6 Hz, 1H), 7.98 (d, *J* = 8.4 Hz, 2H), 7.66-7.64 (m, 2H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.17 (t, *J* = 7.6 Hz, 1H), 7.04 (d, *J* = 8.4 Hz, 1H), 6.09-6.00 (m, 1H), 5.91-5.81 (m, 1H), 5.38 (d, *J* = 17.2 Hz, 1H), 5.26 (d, *J* = 13.6 Hz, 2H), 5.22-5.18 (m 1H), 4.67-4.63 (m, 4H), 4.51 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.5, 156.5, 155.1, 150.1, 139.3, 133.3, 133.1, 131.8, 131.7, 131.0, 130.5, 129.9, 129.7, 129.3, 129.2, 127.8, 126.8, 126.7, 126.6, 124.2, 121.7, 118.9, 117.2, 113.3, 69.5, 66.1, 43.8; **IR (KBr)ν_{max}** 3055, 2969, 2948, 2930, 2835, 1741, 1687, 1624, 1577, 1544, 1480, 1451, 1352, 1316, 1257, 1224, 1182, 1148, 1059 cm^{-1}; **HRMS (ESI)** Calcd For $C_{27}H_{24}NO_3$ 410.1751 ($M + H^+$); Found 410.1755.

*Allyl 2-(3-(3-(allyloxy)phenyl)benzo[f]quinolin-1-yl)acetate (**4m**)*



Yield 76% (155 mg), white solid, mp 81-82 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.53 (d, *J* = 6.0 Hz, 1H), 8.08 (d, *J* = 6.0 Hz, 1H), 7.98-7.95 (m, 2H), 7.86-7.84 (m, 2H), 7.76 (d, *J* = 6.0 Hz, 1H), 7.66-7.63 (m, 2H), 7.44 (t, *J* = 6.0 Hz, 1H), 7.04 (d, *J* = 6.0 Hz, 1H), 6.17-6.10 (m, 1H), 5.92-5.85 (m, 1H), 5.49 (d, *J* = 18.0 Hz, 1H), 5.33 (d, *J* = 6.0 Hz, 1H), 5.28 (d, *J* = 18.0 Hz, 1H), 5.22 (d, *J* = 12.0 Hz, 1H), 4.68 (d, *J* = 6.0 Hz, 4H), 4.52 (s, 2H)); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 170.4, 159.4, 155.6, 150.2, 140.8, 140.5, 133.5, 133.2, 131.8, 131.5, 130.0, 129.9, 129.7, 129.4, 126.9, 126.8, 126.8, 124.7, 123.3, 120.2, 119.1, 117.9, 116.3, 113.7, 69.2, 66.3, 43.8; **IR (KBr)ν_{max}** 3056, 2924, 2896, 1733, 1647, 1583, 1552, 1488, 1455, 1423, 1358, 1319, 1281, 1231, 1195, 1154, 1024, 991 cm^{-1}; **HRMS (ESI)** Calcd For $C_{27}H_{24}NO_3$ 410.1756 ($M + H^+$); Found 410.1754.

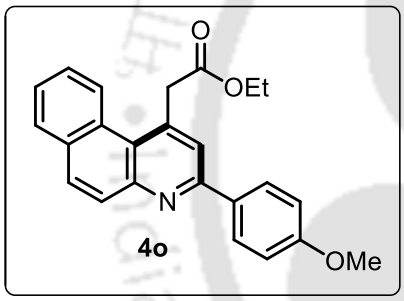
*Ethyl 2-(3-(p-tolyl)benzo[f]quinolin-1-yl)acetate (**4n**)*



4n

Yield 90% (160 mg), brown solid, mp 102-103 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.53 (d, *J* = 8.0 Hz, 1H), 8.13 (d, *J* = 8.4 Hz, 2H), 8.08 (s, 1H), 7.96 (d, *J* = 9.6 Hz, 2H), 7.85 (s, 1H), 7.67-7.63 (m, 2H), 7.34 (d, *J* = 7.6 Hz, 2H), 4.48 (s, 2H), 4.24 (q, *J* = 6.8 Hz, 2H), 2.45 (s, 3H), 1.23 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.8, 155.8, 150.2, 141.1, 139.7, 136.2, 133.1, 131.4, 130.0, 129.8, 129.7, 129.4, 127.5, 126.9, 126.8, 126.7, 124.4, 123.0, 61.7, 43.9, 21.6, 14.4; **IR (KBr)ν_{max}** 3053, 3025, 2980, 2923, 2855, 1734, 1606, 1585, 1550, 1512, 1482, 1455, 1391, 1366, 1322, 1248, 1217, 1184, 1156, 1094, 1054 cm^{-1}; **HRMS (ESI)** Calcd For $C_{24}H_{22}NO_2$ 356.1645 ($M + H^+$); Found 356.1646.

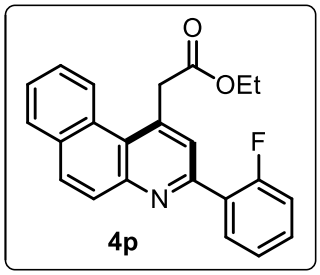
*Ethyl 2-(3-(4-methoxyphenyl)benzo[f]quinolin-1-yl)acetate (**4o**)*



4o

Yield 80% (148 mg), white solid, mp 120-121 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.53 (d, *J* = 6.0 Hz, 1H), 8.19 (d, *J* = 6.0 Hz, 2H), 8.06 (d, *J* = 12.0 Hz, 1H), 7.96 (d, *J* = 6.0 Hz, 1H), 7.95-7.94 (m, 1H), 7.81 (s, 1H), 7.66-7.63 (m, 2H), 7.07 (d, *J* = 6.0 Hz, 2H), 4.48 (s, 2H), 4.24 (q, *J* = 6.0 Hz, 2H), 3.90, (s, 3H), 1.23 (t, *J* = 6.0 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 170.8, 161.0, 155.5, 150.2, 140.9, 133.0, 131.7, 131.3, 130.1, 129.7, 129.4, 128.9, 126.8, 126.7, 126.7, 124.1, 122.6, 114.4, 61.7, 55.6, 44.0, 14.4; **IR (KBr)ν_{max}** 3027, 2957, 2924, 2852, 1732, 1631, 1606, 1583, 1550, 1531, 1512, 1482, 1455, 1392, 1364, 1324, 1248, 1224, 1175, 1145, 1030 cm^{-1}; **HRMS (ESI)** Calcd For $C_{24}H_{22}NO_3$ 372.1594 ($M + H^+$); Found 372.1594.

*Ethyl 2-(3-(2-fluorophenyl)benzo[f]quinolin-1-yl)acetate (**4p**)*

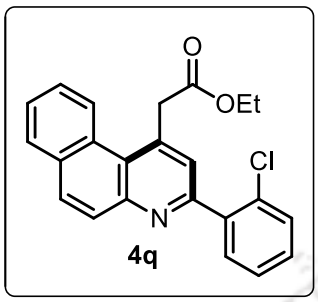


4p

Yield 72% (129 mg), semisolid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.57 (d, *J* = 6.0 Hz, 1H), 8.24-8.21 (m, 1H), 8.08 (d, *J* = 6.0 Hz, 1H), 7.98 (d, *J* = 6.0Hz, 2H), 7.97-7.95 (m, 1H), 7.68-7.66 (m, 2H), 7.43 (t, *J* = 6.0 Hz, 1H), 7.34 (t, *J* = 6.0 Hz, 1H), 7.23-7.20, (m, 1H), 4.50 (s, 2H), 4.24 (q, *J* = 6.0Hz, 2H), 1.23 (t, *J* = 6.0 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 170.7, 161.9, 160.2, 152.2, 150.2, 140.7, 133.3, 131.6, 131.6, 131.5, 131.1, 131.0, 129.9, 129.6, 129.4, 127.1, 127.0,

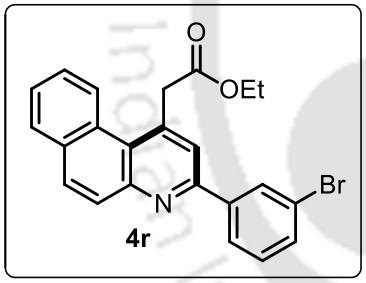
126.8, 124.9, 124.9, 124.7, 116.6, 116.4, 61.7, 44.0, 14.3; **IR (KBr)ν_{max}** 3028, 2956, 2923, 2852, 1733, 1586, 1582, 1550, 1484, 1452, 1371, 1364, 1320, 1249, 1215, 1155, 1080, 1030 cm^{-1}; **HRMS (ESI)** Calcd For $C_{23}H_{19}FNO_2$ 360.1395 ($M + H^+$); Found 360.1396.

*Ethyl 2-(3-(2-chlorophenyl)benzo[f]quinolin-1-yl)acetate (**4q**)*



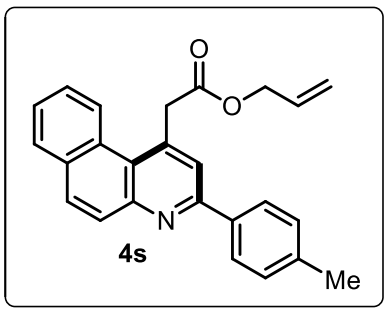
Yield 82% (154 mg), white solid, mp 151-152 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.60 (d, *J* = 8.4 Hz, 1H), 8.12 (d, *J* = 7.2 Hz, 1H), 8.01-7.97 (m, 2H), 7.83-7.81 (m, 2H), 7.70-7.67 (m, 2H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.45-7.31 (m, 1H), 7.43-7.38 (m, 1H), 4.49 (s, 2H), 4.24 (q, *J* = 7.2 Hz, 2H), 1.23 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.4, 155.9, 149.3, 133.2, 132.7, 132.3, 132.1, 130.5, 130.4, 129.7, 129.6, 129.5, 128.6, 127.5, 127.4, 127.3, 127.1, 124.9, 61.8, 43.9, 14.3; **IR (KBr)ν_{max}** 3060, 2982, 2933, 2849, 1734, 1627, 1596, 1578, 1550, 1475, 1442, 1394, 1369, 1350, 1330, 1244, 1210, 1160, 1133, 1094, 1055, 1038 cm^{-1}; **HRMS (ESI)** Calcd For $C_{23}H_{19}ClNO_2$ 376.1099 ($M + H^+$); Found 376.1099.

*Ethyl 2-(3-(3-bromophenyl)benzo[f]quinolin-1-yl)acetate (**4r**)*



Yield 82% (172 mg), white solid, mp 125-126 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.54 (d, *J* = 12.0 Hz, 1H), 8.40 (s, 1H), 8.13 (d, *J* = 6.0 Hz, 1H), 8.07 (d, *J* = 6.0 Hz, 1H), 8.00-7.97, (m, 2H), 7.84 (s, 1H), 7.68-7.66 (m, 2H), 7.60 (d, *J* = 6.0 Hz, 1H), 7.41 (t, *J* = 12.0 Hz, 1H), 4.50 (s, 2H), 4.25 (q, *J* = 6.0 Hz, 2H), 1.25 (t, *J* = 6.0 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 170.7, 154.2, 150.2, 141.4, 141.1, 133.3, 132.5, 131.7, 130.7, 130.6, 129.9, 129.6, 129.4, 126.9, 126.2, 126.1, 124.9, 123.4, 123.1, 123.0, 61.5, 43.9, 13.9; **IR (KBr)ν_{max}** 3025, 2922, 2852, 1733, 1586, 1572, 1550, 1480, 1452, 1442, 1428, 1371, 1322, 1213, 1197, 1158, 1019 cm^{-1}; **HRMS (ESI)** Calcd For $C_{23}H_{19}BrNO_2$ 420.0594 ($M + H^+$); Found 420.0623.

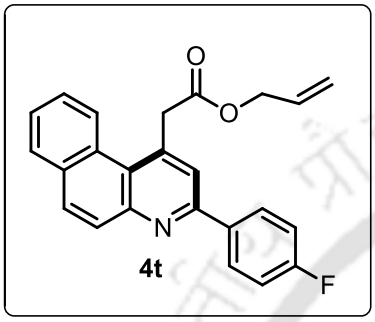
*Allyl 2-(3-(p-tolyl)benzo[f]quinolin-1-yl)acetate (**4s**)*



Yield 80% (147 mg), brown solid, mp 83-84 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.52 (d, *J* = 8.8 Hz, 1H), 8.12 (d, *J* = 8.0 Hz, 2H), 8.08 (d, *J* = 9.2 Hz, 1H), 7.99-7.95 (m, 2H), 7.86 (s, 1H), 7.69-7.63 (m, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 5.92-5.83 (m, 1H), 5.30-5.17 (m, 2H), 4.68 (d, *J* = 5.2 Hz,

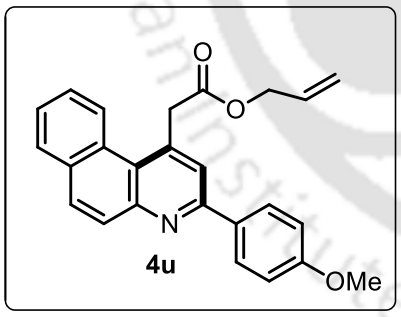
2H), 4.52 (s, 2H), 2.45 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.4, 155.8, 150.2, 140.7, 139.6, 136.2, 133.1, 131.8, 131.4, 130.0, 129.8, 129.4, 128.7, 127.5, 126.8, 124.4, 122.9, 119.0, 66.2, 43.8, 21.5; **IR (KBr)ν_{max}** 3062, 3035, 2923, 2853, 1735, 1653, 1605, 1582, 1548, 1479, 1451, 1352, 1330, 1274, 1216, 1185, 1154, 1130, 1054 cm^{-1}; **HRMS (ESI)** Calcd For $C_{25}H_{22}NO_2$ 368.1645 ($M + H^+$); Found 368.1649.

*Allyl 2-(3-(4-fluorophenyl)benzo[f]quinolin-1-yl)acetate (**4t**)*



Yield 86% (159 mg), white solid, mp 154-155 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.55 – 8.49 (m, 1H), 8.24 – 8.19 (m, 2H), 8.10 (d, *J* = 9.0 Hz, 1H), 7.99 – 7.94 (m, 2H), 7.83 (s, 1H), 7.68 – 7.62 (m, 2H), 7.22 (t, *J* = 8.6 Hz, 2H), 5.94 – 5.83 (m, 1H), 5.32 – 5.27 (m, 1H), 5.23 (dq, *J* = 10.4, 1.2 Hz, 1H), 4.69 (dt, *J* = 5.8, 1.4 Hz, 2H), 4.52 (s, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 170.3, 164.9, 163.2, 154.6, 150.0, 141.2, 134.9, 133.2, 131.8, 131.7, 129.8, 129.6, 129.5, 129.5, 129.3, 127.0, 126.9, 126.8, 124.5, 122.9, 119.2, 116.1, 115.9, 66.3, 43.8; **IR (KBr)ν_{max}** 3059, 2954, 2924, 2848, 1735, 1653, 1601, 1585, 1552, 1508, 1483, 1454, 1390, 1358, 1322, 1228, 1191, 1156, 1014 cm^{-1}; **HRMS (ESI)** Calcd For $C_{24}H_{19}FNO_2$ 372.1395 ($M + H^+$); Found 372.1384.

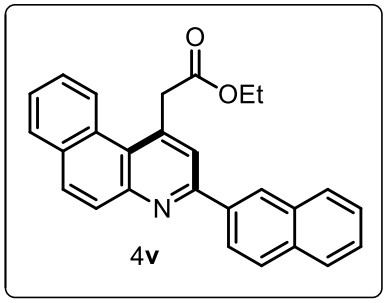
*Allyl 2-(3-(4-methoxyphenyl)benzo[f]quinolin-1-yl)acetate (**4u**)*



Yield 78% (149 mg), pale yellow solid, mp 92-95 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.50 (d, *J* = 6.4 Hz, 1H) 8.18 (d, *J* = 8.0 Hz, 2H), 8.05 (d, *J* = 9.2 Hz, 1H), 7.95 (d, *J* = 7.6 Hz, 2H), 7.81 (s, 1H), 7.62 (d, *J* = 3.2 Hz, 2H), 7.05 (d, *J* = 8.0 Hz, 2H), 5.89-5.85 (m, 1H), 5.31-5.21 (m, 2H), 4.68 (s, 2H), 4.49 (s, 2H), 3.89 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 170.5, 161.0, 155.4, 150.2, 140.6, 133.0, 131.8, 131.6, 131.3, 129.9, 129.6, 129.3, 128.9, 126.7, 126.6, 124.1, 122.6, 119.0, 114.4, 66.1, 55.5, 43.8; **IR (KBr)ν_{max}** 3051, 2959, 2933, 2836, 1735, 1675, 1653, 1606, 1583, 1550, 1530, 1511, 1482, 1455, 4140, 1358, 1323, 1306, 1176, 1155, 1111, 1030 cm^{-1}; **HRMS (ESI)** Calcd For $C_{25}H_{22}NO_3$ 384.1594 ($M + H^+$); Found 384.1612.

*Ethyl 2-(3-(naphthalen-2-yl)benzo[f]quinolin-1-yl)acetate (**4v**)*

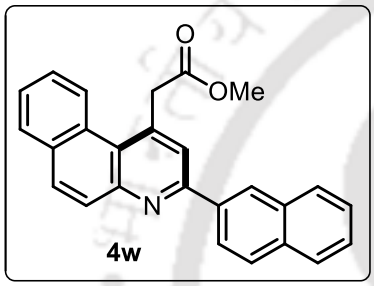
Yield 74% (145 mg), pale yellow solid, mp 76-77 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.69 (s, 1H), 8.56 (d, *J* = 8.8 Hz, 1H), 8.41 (d, *J* = 8.4 Hz, 1H), 8.18 (d, *J* = 8.8 Hz, 1H), 8.03-8.02



4v

(m, 3H), 8.00-7.96 (m, 2H), 7.92-7.89 (m, 1H), 7.69-7.64 (m, 2H), 7.55-7.53 (m, 2H), 4.54 (s, 2H), 4.27 (q, *J* = 7.2 Hz, 2H), 1.25 (t, *J* =7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.8, 155.6, 150.2, 141.4, 136.2, 134.1, 133.7, 133.2, 131.7, 130.0, 129.5, 129.4, 129.1, 128.8, 127.9, 127.3, 127.0, 126.9, 126.9, 126.8, 126.5, 125.1, 124.7, 123.5, 61.7, 44.1, 14.4; **IR (KBr)ν_{max}** 3056, 2978, 2923, 2851, 1734, 1583, 1552, 1509, 1482, 1452, 1389, 1367, 1321, 1256, 1215, 1195, 1156, 1029; cm^{-1}; **HRMS (ESI)** Calcd For $C_{27}H_{22}NO_2$ 392.1645 ($M + H^+$); Found 392.1648.

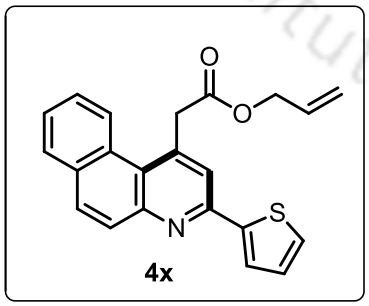
*Methyl 2-(3-(naphthalen-2-yl)benzo[f]quinolin-1-yl)acetate (**4w**)*



4w

Yield 87% (164 mg), white solid, mp 80-81 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.71 – 8.66 (m, 1H), 8.55 – 8.52 (m, 1H), 8.41 (dd, *J* = 8.5, 1.8 Hz, 1H), 8.15 (d, *J* = 8.9 Hz, 1H), 8.03 – 8.00 (m, 3H), 8.00 – 7.99 (m, 1H), 7.97 (dd, *J* = 7.5, 1.9 Hz, 1H), 7.93 – 7.89 (m, 1H), 7.67 (ddd, *J* = 9.7, 7.7, 1.4 Hz, 2H), 7.56 – 7.52 (m, 2H), 4.54 (s, 2H), 3.79 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 171.3, 155.6, 150.3, 141.0, 136.3, 134.1, 133.7, 133.2, 131.6, 129.9, 129.7, 129.5, 129.0, 128.8, 127.9, 127.2, 126.9, 126.9, 126.9, 126.8, 126.6, 125.1, 124.6, 123.4, , 52.8, 43.7; **IR (KBr)ν_{max}** 3057, 2986, 2952, 2848, 1736, 1595, 1549, 1472, 1432, 1391, 1347, 1198, 1158, 1088, 1055 cm^{-1}; **HRMS (ESI)** Calcd For $C_{26}H_{20}NO_2$ 378.1489 ($M + H^+$); Found 378.1486.

*Allyl 2-(3-(thiophen-2-yl)benzo[f]quinolin-1-yl)acetate (**4x**)*

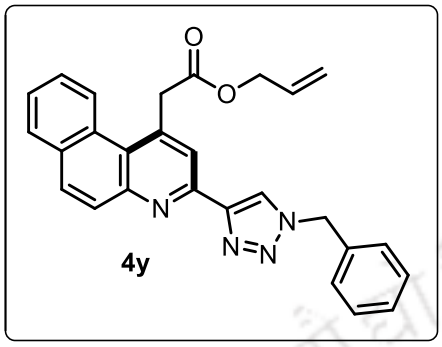


4x

Yield 76% (136 mg), brown solid, mp 114-115 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.48 (d, *J* = 9.6 Hz, 1H), 8.01 (d, *J* = 9.0 Hz, 1H), 7.95-7.93 (m, 2H), 7.78 (s, 1H), 7.76 (d, *J* = 3.4 Hz, 1H), 7.65-7.61 (m, 2H), 7.47 (d, *J* = 5.4 Hz, 1H), 7.18-7.16 (m, 1H), 5.91-5.84 (m, 1H), 5.29-5.26 (m, 1H), 5.22 (d, *J* = 9.6 Hz, 1H), 4.68 (d, *J* = 6.0 Hz, 2H), 4.48 (s, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 170.3, 151.1, 150.2, 144.7, 140.8, 133.1, 131.8, 131.7, 129.9, 129.5, 129.3, 128.6, 128.3, 126.9, 126.8, 126.7, 125.9, 124.9, 121.7, 119.1, 66.2, 43.7; **IR (KBr)ν_{max}** 3071, 2958, 2930, 2857, 1739, 1584, 1552, 1523, 1482, 1455, 1423, 1365, 1326,

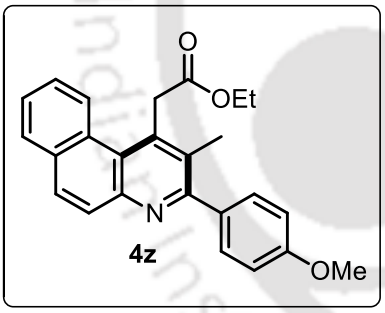
1259, 1155, 1071, 1015 cm^{-1}; **HRMS (ESI)** Calcd For $C_{22}H_{18}NO_2S$ 360.1053 (M + H^+); Found 360.1052.

*Allyl 2-(3-(1-benzyl-1H-1,2,3-triazol-4-yl)benzo[f]quinolin-1-yl)acetate (**4y**)*



Yield 60% (130 mg), brown solid, mp 124-125 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.53 (d, *J* = 8.1 Hz, 1H), 8.45 (s, 1H), 8.02-7.97 (m, 2H), 7.69 (s, 2H), 7.40-7.39 (m, 6H), 7.28 (s, 1H), 5.86-5.83 (m, 1H), 5.65 (s, 2H), 5.26 (d, *J* = 17.4 Hz, 1H), 5.20 (d, *J* = 10.8 Hz, 1H), 4.66 (d, *J* = 5.6 Hz, 2H), 4.57 (s, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 170.3, 150.2, 148.9, 148.7, 141.3, 134.7, 133.2, 131.8, 131.7, 130.1, 129.4, 129.1, 129.0, 128.5, 128.1, 127.0, 126.8, 125.3, 123.4, 123.1, 122.9, 119.1, 66.3, 54.7, 43.9; **IR (KBr)ν_{max}** 3148, 3062, 2924, 2853, 1736, 1647, 1597, 1557, 1497, 1454, 1430, 1362, 1338, 1296, 1232, 1187, 1156, 1092, 1043, 1017 cm^{-1}; **HRMS (ESI)** Calcd For $C_{27}H_{23}N_4O_2$ 435.1821 (M + H^+); Found 435.1813.

*Ethyl 2-(3-(4-methoxyphenyl)-2-methylbenzo[f]quinolin-1-yl)acetate (**4z**)*



Yield 72% (138 mg), white solid, mp 76-77 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.37 (d, *J* = 6.8 Hz, 1H), 7.94 (d, *J* = 8.8 Hz, 2H), 7.88 (d, *J* = 8.8 Hz, 1H), 7.63-7.62 (m, 3H), 7.58 (s, 1H), 7.03 (d, *J* = 8.4 Hz, 2H), 4.42 (s, 2H), 4.38 (q, *J* = 7.6 Hz, 2H), 3.89 (s, 3H), 2.47 (s, 3H), 1.38 (t, *J* = 7.6 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.2, 159.9, 158.9, 147.1, 139.4, 133.9, 133.4, 130.9, 130.4, 129.8, 129.6, 129.2, 129.1, 128.9, 127.2, 126.9, 126.3, 125.0, 122.1, 114.0, 61.7, 55.6, 40.1, 17.7, 14.6; **IR (KBr)ν_{max}** 3055, 2957, 2932, 2836, 1738, 1607, 1577, 1516, 1549, 1510, 1477, 1451, 1427, 1368, 1301, 1178, 1109, 1019 cm^{-1}; **HRMS (ESI)** Calcd For $C_{25}H_{24}NO_3$ 386.1751 (M + H^+); Found 386.1753.

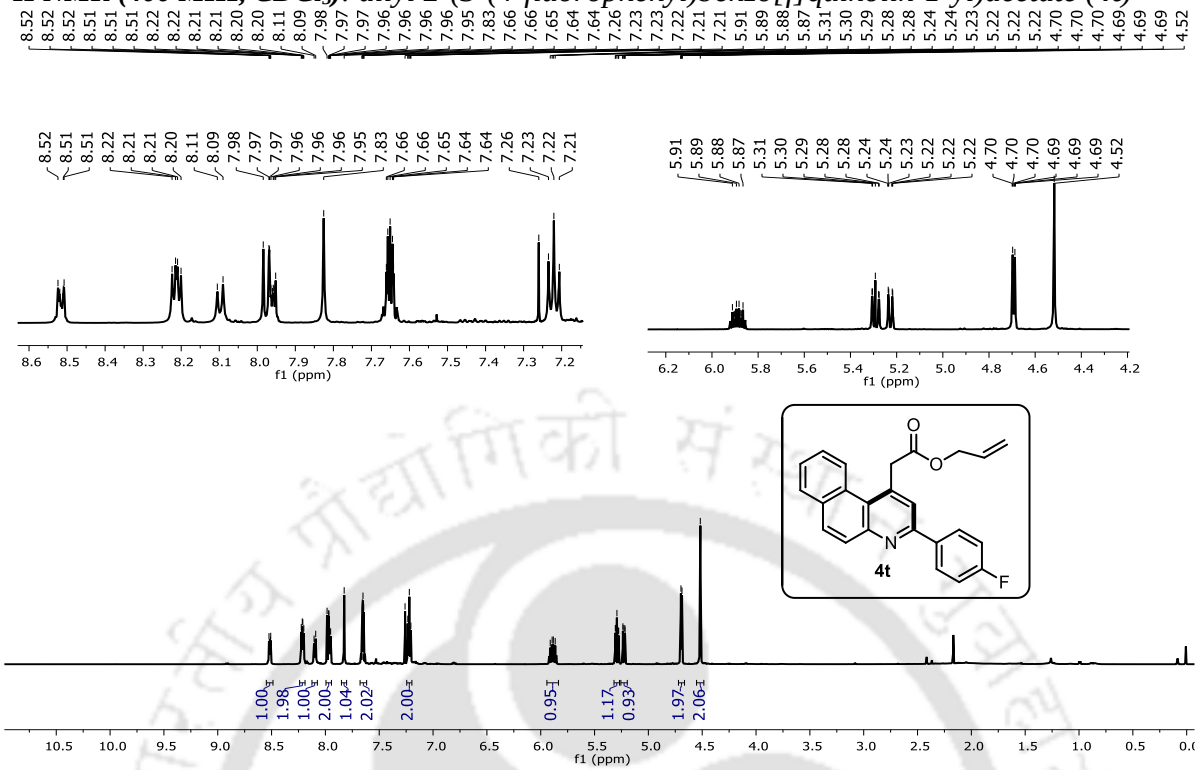
XRD for Compound **4g**

Complete crystallographic data of compound **4g** for the structural analyses has been deposited with the Cambridge Crystallographic Data Centre, CCDC No. are 1434638. Copy of this information may be obtained free of charge from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk or via: www.ccdc.cam.ac.uk).

Table 3. Crystal data and structures refinement for the compound **4g**.

Entry	Identification code	Compound **4g**
01	Empirical formula	C_{25} H_{22} F N O_2
02	Formula weight	387.44
03	Temperature	293(2) K
04	Wavelength	0.71073
05	Radiation type	Mo K\a
06	Radiation source	'fine-focus sealed tube'
07	Crystal system	monoclinic
08	Space group	C2/c
09	Cell length	a 28.746 (3) b 10.589 (9) c 16.238 (15)
10	Cell Angle	α 90.0 β 123.742 (6) δ 90.0
11	Cell Volume	4110.3 (7)
12	Density	1.252
13	Absorption correction	multi-scan
14	Refinement method	Full-matrix least-squares on F2
15	Index ranges	-33<=h<=30, -10<=k<=11, -16<=l<=17
16	Reflection number	12686
17	Theta range	1.70-24.24
18	Cell formula units Z	8
19	CCDC no	1434638

***^{1}H NMR (400 MHz, $CDCl_3$)**: allyl 2-(3-(4-fluorophenyl)benzo[f]quinolin-1-yl)acetate (**4t**)*



***^{13}C NMR (100 MHz, $CDCl_3$)**: Allyl 2-(3-(4-fluorophenyl)benzo[f]quinolin-1-yl)acetate (**4t**)*

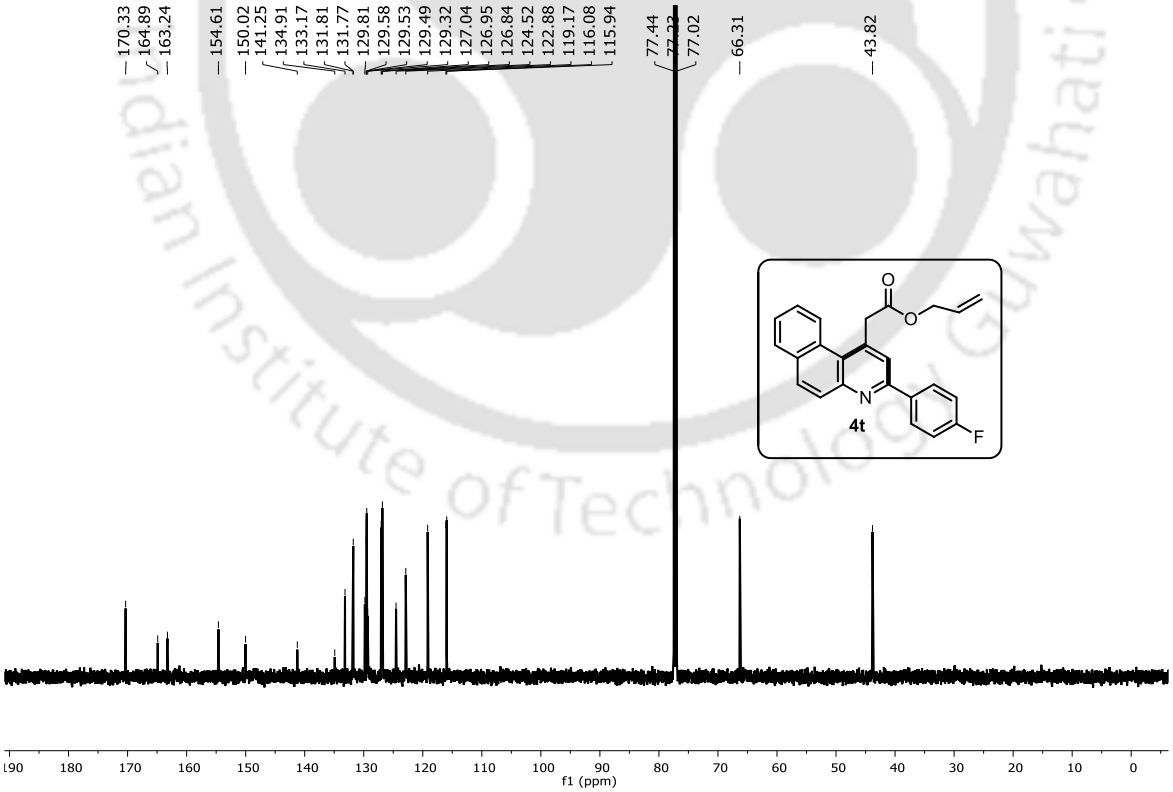
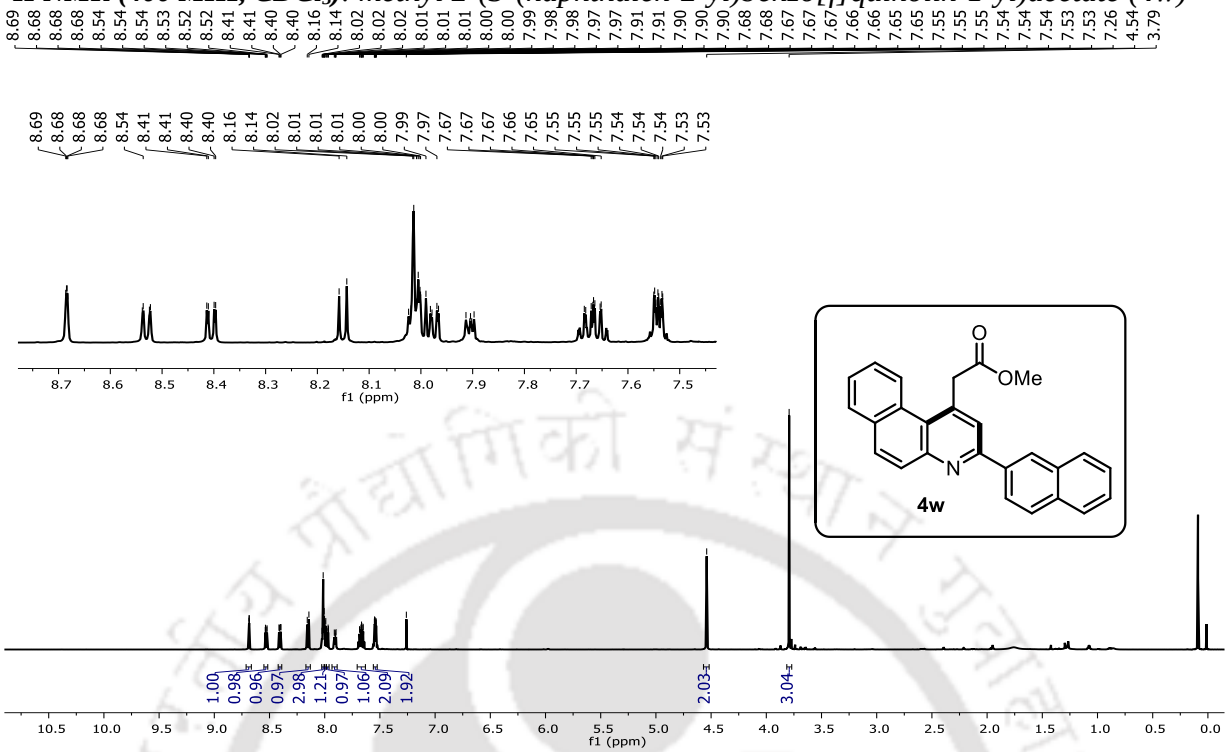


Figure 6

***^{1}H NMR (400 MHz, $CDCl_3$)**: methyl 2-(3-(naphthalen-2-yl)benzo[f]quinolin-1-yl)acetate (**4w**)*



***^{13}C NMR (100 MHz, $CDCl_3$)**: methyl 2-(3-(naphthalen-2-yl)benzo[f]quinolin-1-yl)acetate (**4w**)*

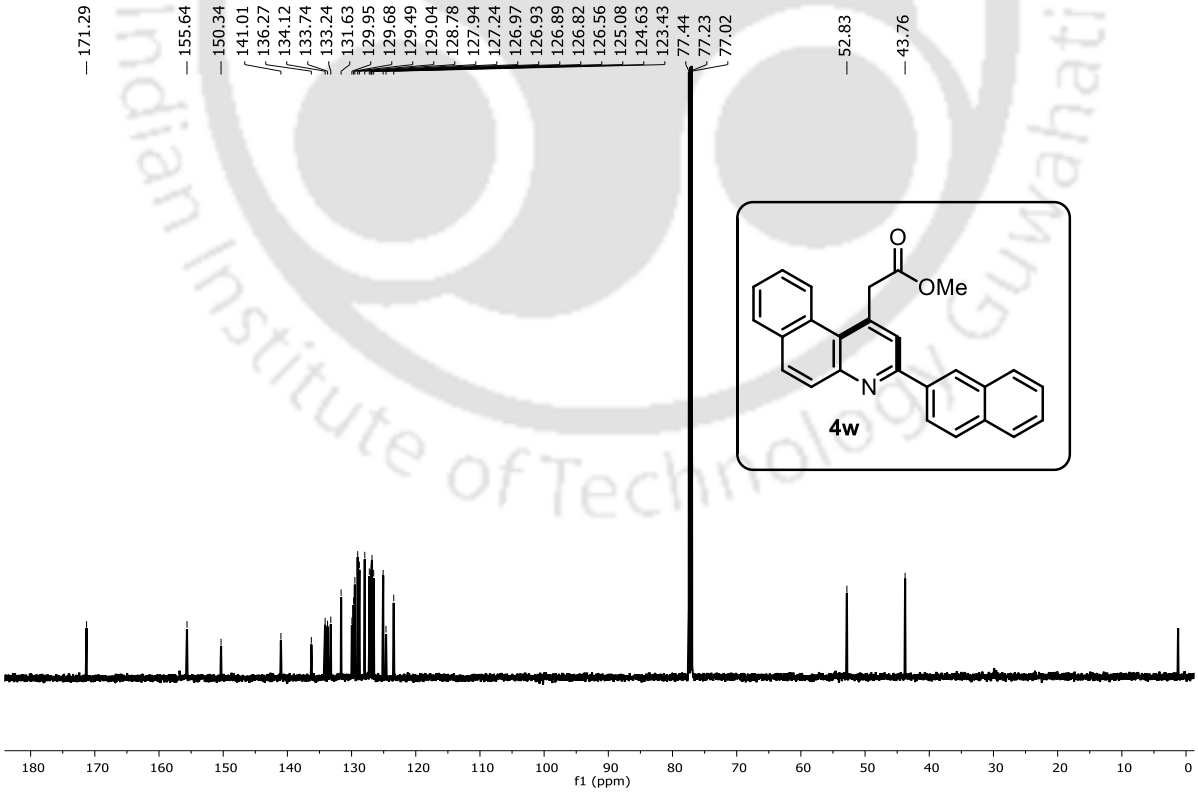
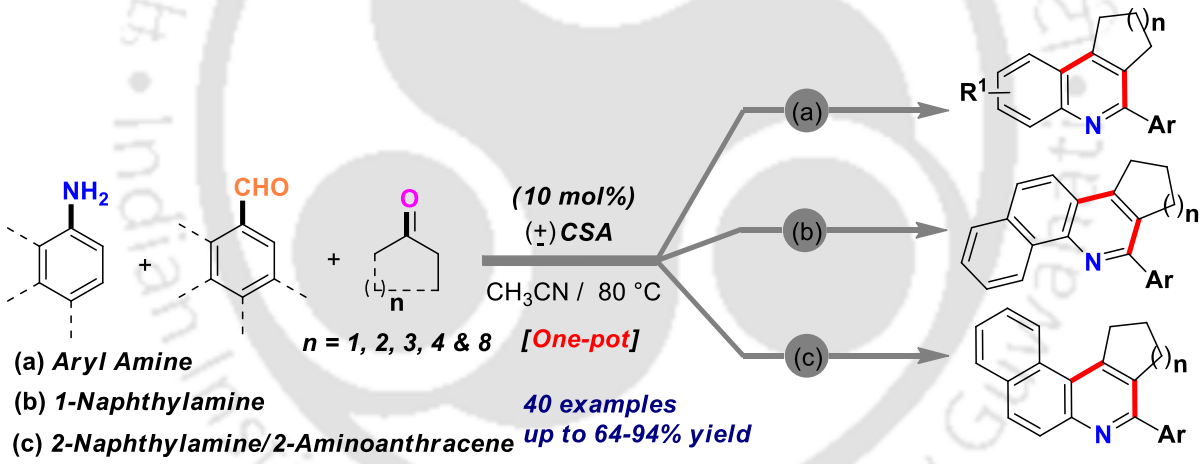


Figure 7

Chapter III

Camphorsulfonic Acid Catalysed One-Pot Three Component Reaction for the Synthesis of Fused Quinoline and Benzoquinoline Derivatives

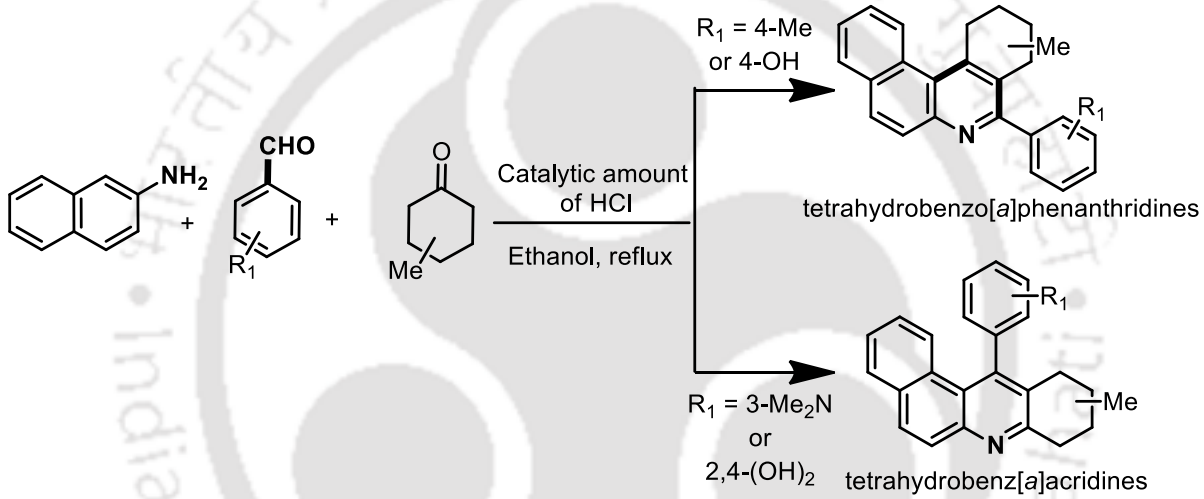


Result & Discussion

Experimental Section

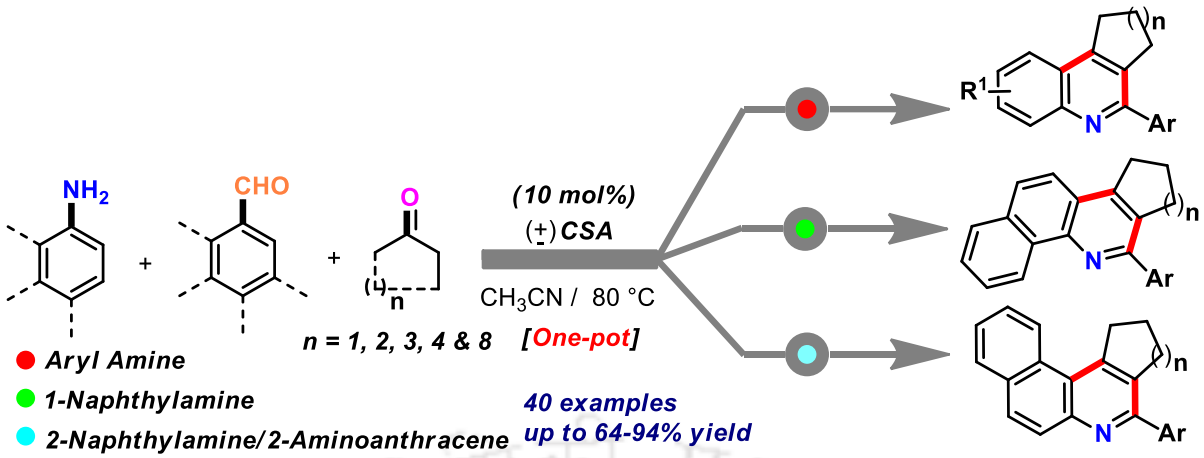
Results and Discussion

In chapter II, we have elaborated a simple and an efficient method for the synthesis of various benzo[*f*]quinolines from 2-naphthylamine, aromatic aldehyde and *β*-ketoester through a three-component reaction by employing camphor sulfonic acid as a catalyst. From the literature it was found that Kozlov and co-workers synthesised tetrahydrobenzo[*a*]phenanthridines derivatives along with tetrahydrobenz[*a*]-acridines[76] from 2-naphthylamine, aromatic aldehyde and cyclohexanone in the presence Conc HCl as shown in Scheme **41**. Recently, Wang et al. successfully achieved the synthesis of exclusively benzo[*f*]quinoline[40] derivatives through MCRs from the same three reactants using catalytic amount of molecular iodine in THF under reflux condition.



Scheme 41

However, both the protocols have some drawbacks such as formation of tetrahydrobenz[*a*]-acridine product and failure to synthesize the quinoline and benzo[*h*]quinoline from aniline, aromatic aldehyde and cyclic ketone as well as from 1-naphthylamine, aromatic aldehyde and cyclic ketone respectively because of low reactivity of the reactants in presence of the catalyst. These observations encouraged us to investigate whether fused quinoline derivative can be achieved using anilines, aromatic aldehyde and cyclic ketones.

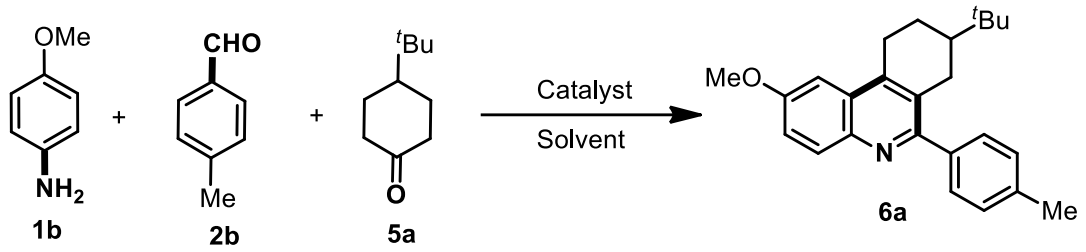


Scheme 42. *Synthesis of Fused Quinoline and Benzoquinoline Derivatives*

In this Chapter, we will discuss a new protocol for one-pot three component reaction of arylamines, aromatic aldehydes and cyclic ketones for the synthesis of various fused quinoline, benzoquinoline and naphthoquinoline derivatives using 10 mol % camphorsulfonic acid as a catalyst as shown in scheme **42**. The exploitation of pregnenolone steroid moiety for benzoquinolines and terephthalaldehyde for bis-benzoquinolines synthesis was achieved with 68-75% yields. We have also described the reactivity of aryl amines and the mechanistic study for the formation of benzoquinoline. The present protocol offers a great potential for atom-economy with good to excellent yields.

We initially, investigated on optimization study for the synthesis of fused quinoline using *p*-anisidine **1b** (1.0 mmol), *p*-tolualdehyde **2b** (1.0 mmol) and 4-(*tert*-butyl)cyclohexanone **5a** (1.0 mmol) as model substrate at 80 °C in acetonitrile and the results are summarized in Table **4**. Primarily, when the reaction was carried out in the absence of catalyst proved futile (Table 4, entry 1). Next, the reaction was tested with various lewis acid catalysts. On screening the reaction with $Yb(OTf)_3$ (Table 4, entry 2) in CH_3CN resulted in isolation of the desired product **6a** in 54% yield. The product **6a** was confirmed through IR, ^1H, ^{13}C NMR and HRMS. The other lewis acids $Cu(OTf)_2$, $Zn(OTf)_2$, $In(OTf)_3$, AgOTf, $Bi(OTf)_3$ and $FeCl_3$ gave unsatisfactory yields (Table 4, entries 3-8). Whereas, by employing iodine as a catalyst resulted in 54% and 48% yields of product **6a** in THF and CH_3CN respectively (Table 4, entries 9 and 10). Then, we observed the protic acid catalysts like AcOH, TfOH and L-Proline the reactions were failed to obtain the desired product (Table 4, entries 11-13) but, *p*-TSA resulted with satisfactory yields (Table 4, entry 14). Further for inferior results, the same set of reaction was executed with 10 mol% CSA and the desired product **6a** was isolated in 78% yield. (Table 4, entry 15).

Table 4. Optimization of Reaction Conditions[a]



Entry	Catalyst	Mol %	Solvent	Time (h)	Yield **6a** (%)[b]
1	No catalyst	-	CH_3CN	24.0	NR
2	$Yb(OTf)_3$	10	CH_3CN	3.0	54
3	$Cu(OTf)_2$	10	CH_3CN	6.0	42
4	$Zn(OTf)_2$	10	CH_3CN	2.5	64
5	$In(OTf)_3$	10	CH_3CN	2.5	60
6	AgOTf	10	CH_3CN	3.0	62
7	$Bi(OTf)_3$	10	CH_3CN	2.5	36
8	$FeCl_3$	10	CH_3CN	12.0	30
9	Iodine	10	THF	4.0	54
10	Iodine	10	CH_3CN	4.0	48
11	AcOH	1 equiv	-	3.0	NR
12	TfOH	10	CH_3CN	24.0	NR
13	L-Proline	10	CH_3CN	24.0	NR
14	*p*-TSA	10	CH_3CN	6.0	68
15	**(±)-CSA**	**10**	**CH_3CN**	**1.5**	**78**
16	(±)-CSA	20	CH_3CN	1.5	78
17	(±)-CSA	05	CH_3CN	2.0	75
18	(±)-CSA	10	EtOH	2.0	72
19	(±)-CSA	10	MeOH	2.0	68
20	(±)-CSA	10	DMSO	24.0	20
21[c]	(±)-CSA	10	DCE	12.0	35
22	(±)-CSA	10	DMF	24.0	NR
23[c]	(±)-CSA	10	THF	12.0	NR
24	(±)-CSA	10	H_2O	12.0	NR
25	(±)-CSA	10	Toluene	8.0	NR

[a]All the reactions were performed using *p*-anisidine (1.0 mmol), *p*-tolualdehyde (1.0 mmol) and 4-(*tert*-butyl)cyclohexanone (1.0 mmol) at 80 °C. [b]Isolated yields. [c]Reaction Performed at 50 °C.

In order to obtain better results, the reaction was also scrutinized with 20 mol% and 5 mol% CSA, but the increment in yield was not observed (Table 4, entries 16 and 17). However, the other solvents such as EtOH, MeOH, DMSO and DCE gave lower yields (Table 4, entries 18-21), whereas DMF, THF, H_2O and toluene failed to give the desired product **6a** (Table 4, entries 22-25). Thus, it was noted that 10 mol% CSA in CH_3CN at 80 °C is the optimized condition for our present protocol in terms of reaction time and yield. The ^1H NMR of compound **6a** shows the characteristic peaks such as 3.95 (s, 3H), 2.42 (s, 3H), and 0.90 (s, 9H) with respect to 4-OMe, 4-Me and tertiary butyl group respectively. The structure of the compound **6a** was also confirmed through single crystal XRD and ORTEP diagram is shown in Figure **8**.

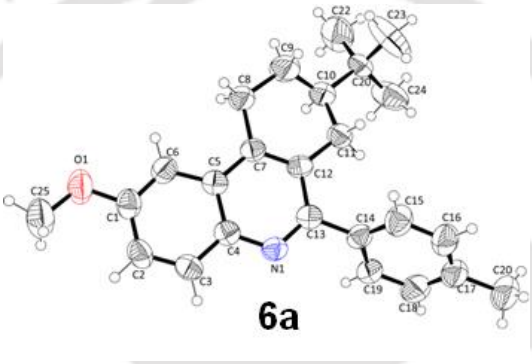
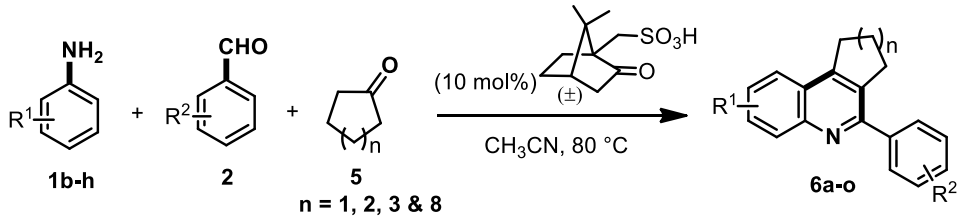
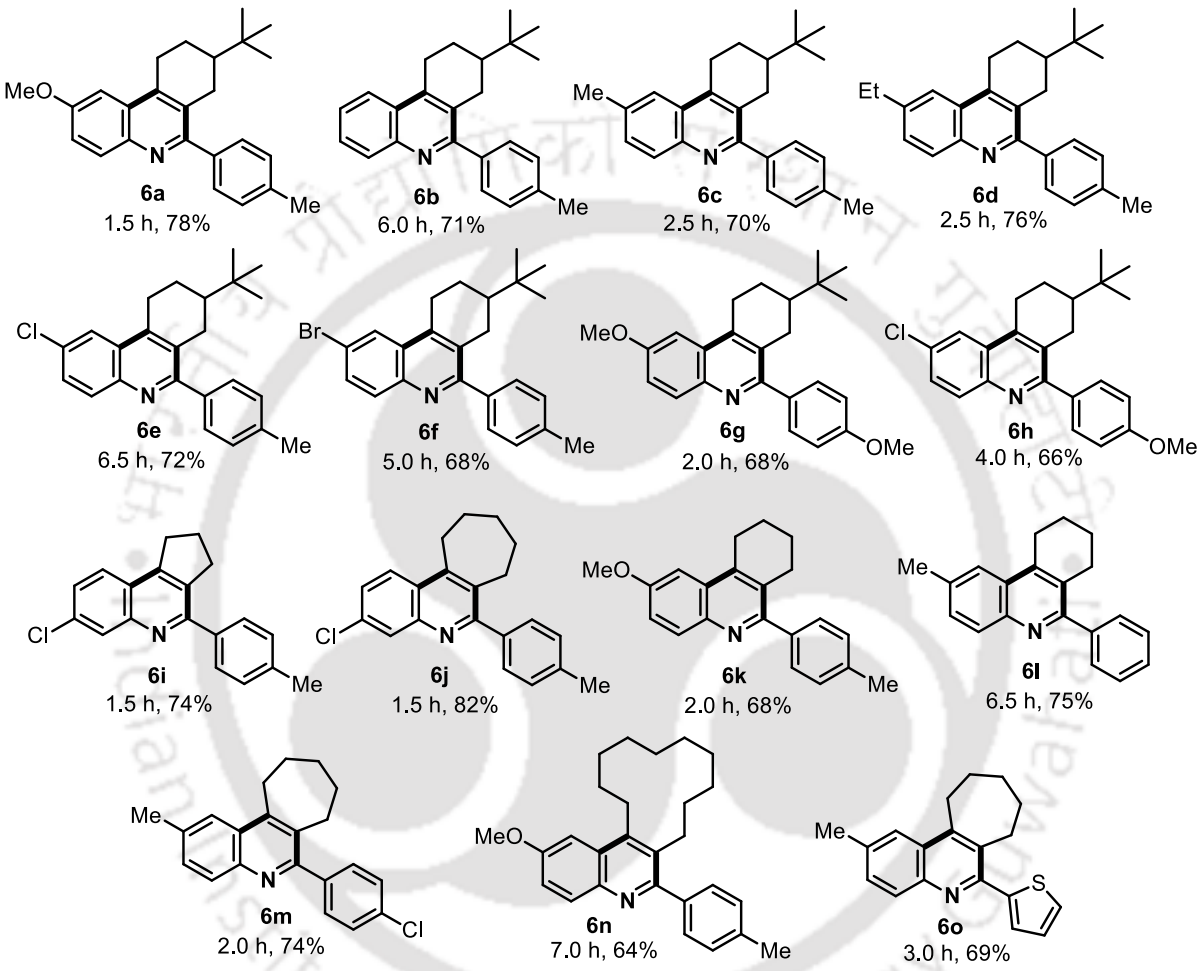


Figure 8. ORTEP Diagram of compound **6a**

With standard optimisation reaction condition, the scope of the reaction was investigated with 4-(*tert*-butyl)cyclohexanone, aromatic aldehydes (4-Me and 4-OMe) and various anilines having *para* substituents on aromatic ring such as -Me, -Et, -Cl, -Br and -OMe which gave the products **6b-h** in 66-78% yield (Table 5). The aniline derivatives such as 4-NO_2, 2-NO_2, 2-I and 2,4-Me failed to produce desired product which might be due to the strong withdrawing nature and steric crowding at *ortho* position. On the other hand, the reaction of *m*-chloroaniline, *p*-tolualdehyde and different cyclic ketones like cyclopentanone and cycloheptanone lead to the isolation of products **6i** and **6j** in 74 and 82% yield. Since the formation of other tautomer was not observed in *meta*-substituted aniline due to steric hindrance on *ortho* postion, it is to be considered as a regiospecfic reaction. Next, the reaction was extended with various other cyclic ketones namely cyclohexanone, cycloheptanone and cyclododecanone all the reactions proceeded smoothly to produce the products **6k-n**. In addition, the heterocyclic aldehyde, thiophene-2-aldehyde on reaction with *p*-toluidine and cycloheptanone to afford the product **6o** in 69% yield.

Table 5. Substrate scope of aniline[a,b]





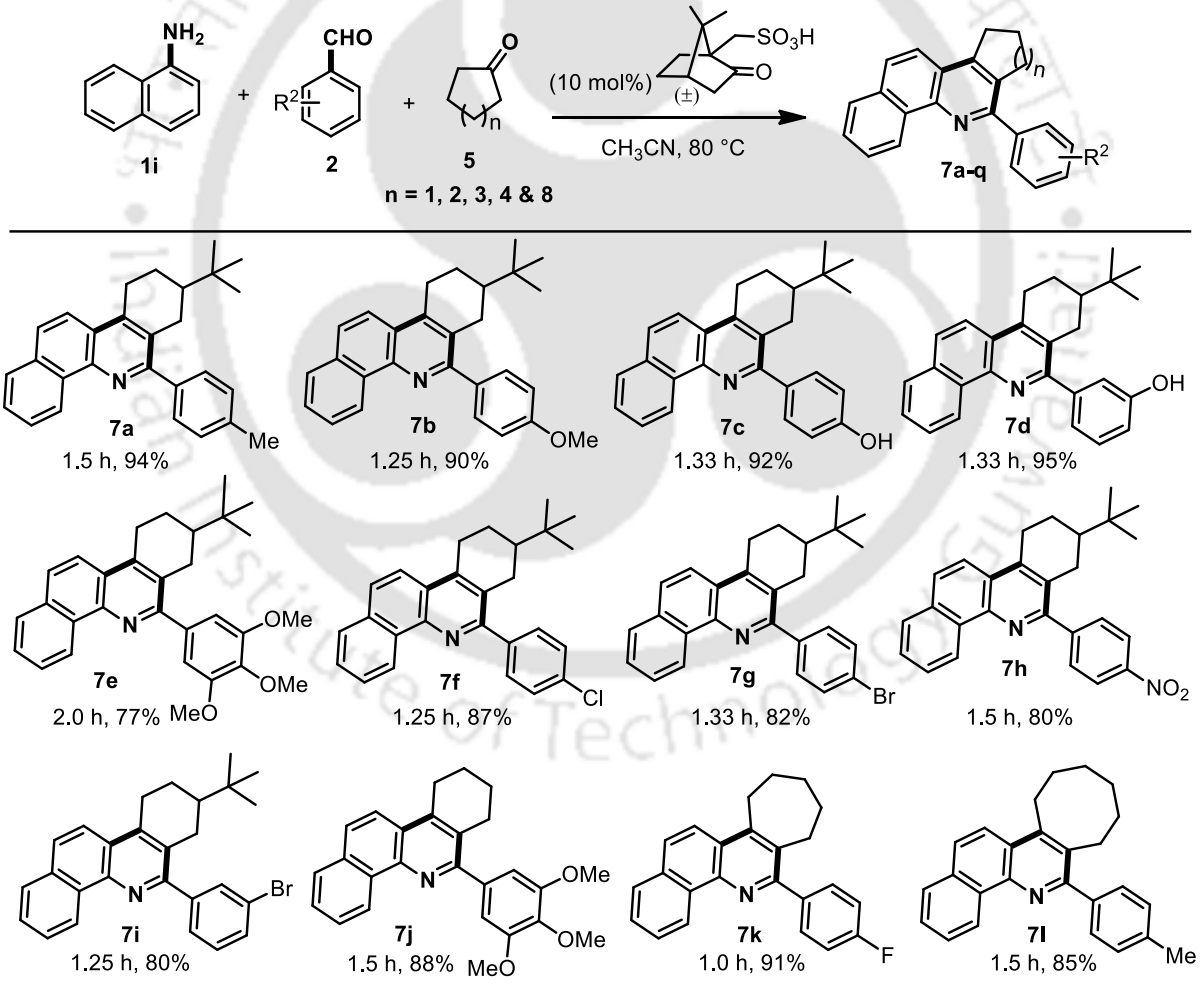
[a]The reactions were carried out using anilines (1.0 mmol), aldehydes (1.0 mmol) and cyclic ketones (1.0 mmol) in CH_3CN. [b]Isolated yields.

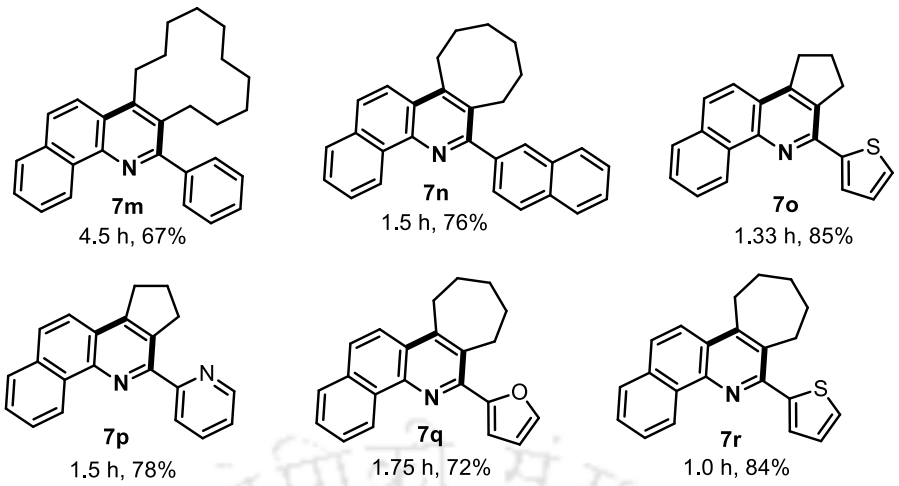
Inspired by the above transformations, we have further explored the generality of the reaction with 1-naphthylamine instead of anilines which produced fused benzo[*h*]quinoline derivatives and the results are summarised in Table 3. When the reaction was carried out with 1-naphthylamine **1i** (1.0 mmol), *p*-tolualdehyde **2b** (1.0 mmol) and 4-(*tert*-butyl)cyclohexanone **5a** (1.0 mmol) under similar reaction condition, the product 7**a** was formed in 94% yield without any column chromatographic separation. Substituted aromatic aldehydes with electron donating and electron withdrawing groups such as 4-OMe, 4-OH, 3-

OH, 3,4,5-OMe, 4-Cl, 4-Br, 4-NO_2 and 3-Br underwent reaction with 4-(*tert*-butyl)cyclohexanone to generate the products **7b-i** in 77-95% yields.

The reaction was also extended with various substituted benzaldehydes and cyclic ketones such as cyclohexanone, cycloheptanone, cyclooctanone and cyclododecanone which lead to the formation of desired products **7j-m** in 67-91% yields. The reaction with 2-naphthaldehyde and cycloheptanone furnished the product **7n** in 76% yield. Heteroaromatic aldehydes, thiophene-2-aldehyde and pyridine-2-carbaldehyde on reaction with cyclopentanone gave the products **7o-p** in 78-85% yields, whereas 2-furfural and thiophene-2-aldehyde on reaction with cycloheptanone deliver the products **7q** and **7r** in 72% and 84% yields respectively. The ORTEP diagram for the compound **7n** was shown in Figure **9**.

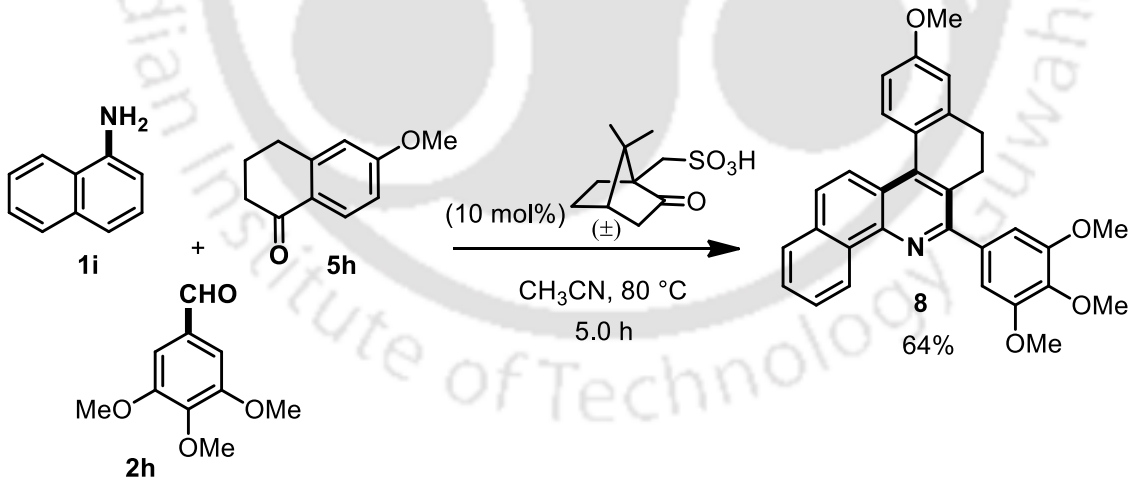
Table 6. Substrate scope of 1-naphthylamine[a,b]





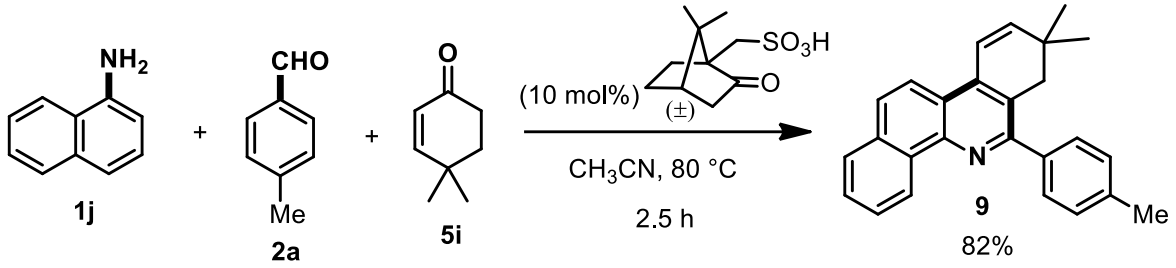
[a]The reactions were carried out using aldehydes (1.0 mmol), cyclic ketones (1.0 mmol) and 1-naphthylamine (1.0 mmol) in CH_3CN. [b]Isolated yields.

In addition, we have applied our present methodology for the synthesis of 3-methoxy-14-(3,4,5-trimethoxyphenyl)-5,6-dihydrodibenzo[*c*,*i*]phenanthridine **8** by employing 1-naphthylamine **1i**, 3,4,5-trimethoxybenzaldehyde **2h** and 6-methoxytetralone **5h** in the presence of 10 mol% CSA under similar reaction conditions as shown in Scheme **43**. The compound **8** structure was also confirmed through single crystal XRD data and ORTEP diagram is shown in Figure **9**. (For crystallographic data See Experimental Section).



Scheme 43

The reactivity of *α*,*β*-unsaturated cyclic ketone was investigated by performing the reaction with 1-naphthylamine **1i**, *p*-tolualdehyde **2a** and 4,4-Dimethyl-2-cyclohexen-1-one **5i** in the presence of 10 mol% CSA at 80 °C to give 8,8-dimethyl-6-(*p*-tolyl)-7,8-dihydrobenzo[*c*]phenanthridine **9** in 82 % yield as shown in Scheme **44**.



Scheme 44

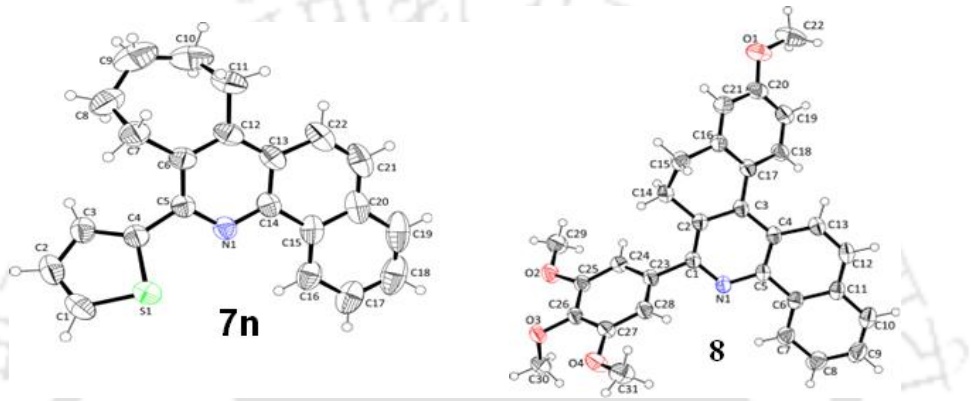
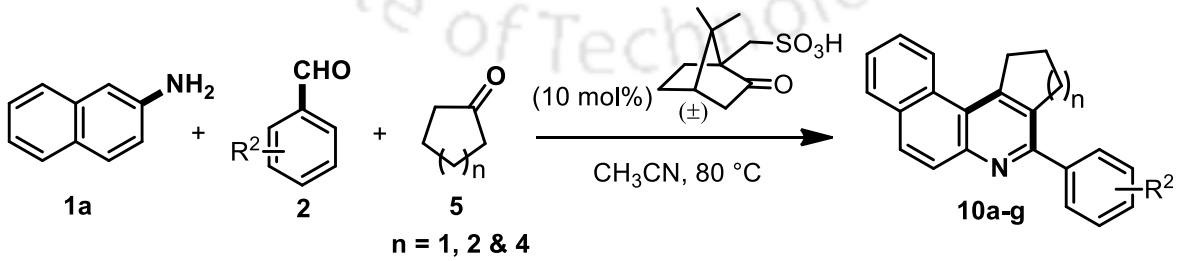
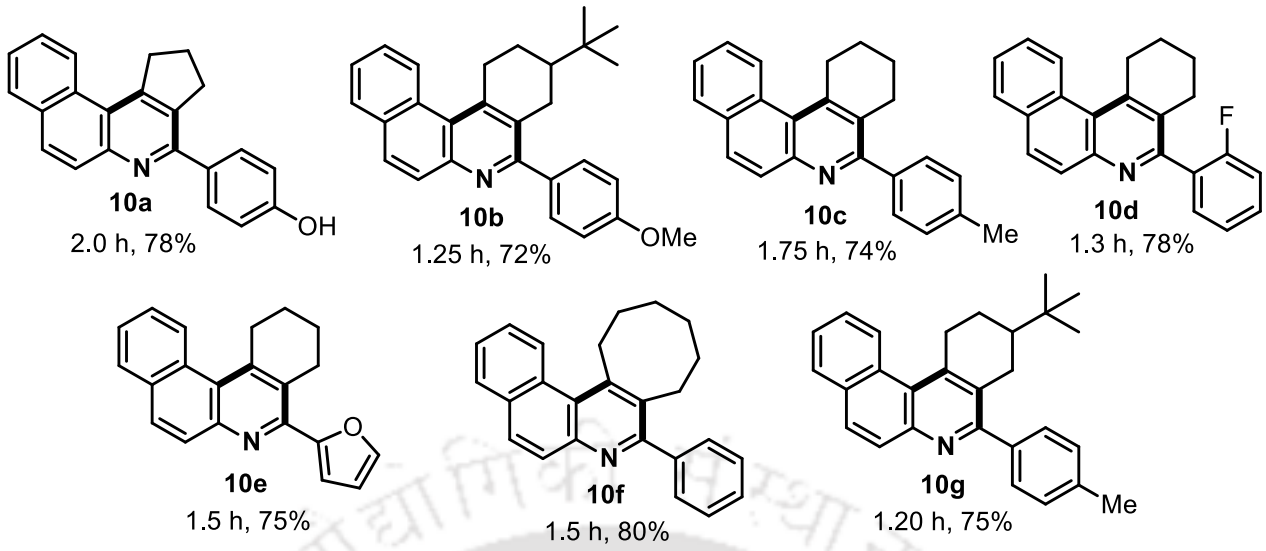


Figure 9. ORTEP Diagram of compound **7n** and **8** with ellipsoid counter 40% probalility

The present protocol was further explored for the synthesis of fused benzoquinoline derivatives using 2-naphthylamine (**1a**), with different substituted aromatic aldehydes (**2**) and cyclic ketones (**5**) in the presence of catalytic amount of CSA under identical reaction conditions to offer the corresponding products **10a-g** with 72-80% yields as depicted in Table **7**. The compound **10e** structure was also confirmed through single crystal XRD data and ORTEP diagram was shown in Figure **10**

Table 7. Substrate scope of 2-naphthylamine[a,b]





[a]The reactions were performed using aldehyde (1.0 mmol), cyclic ketone (1.0 mmol) and 2-naphthylamine (2.0 mmol) in CH_3CN. [b]Isolated yields.

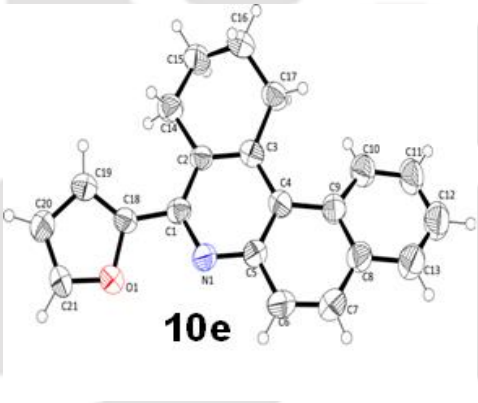
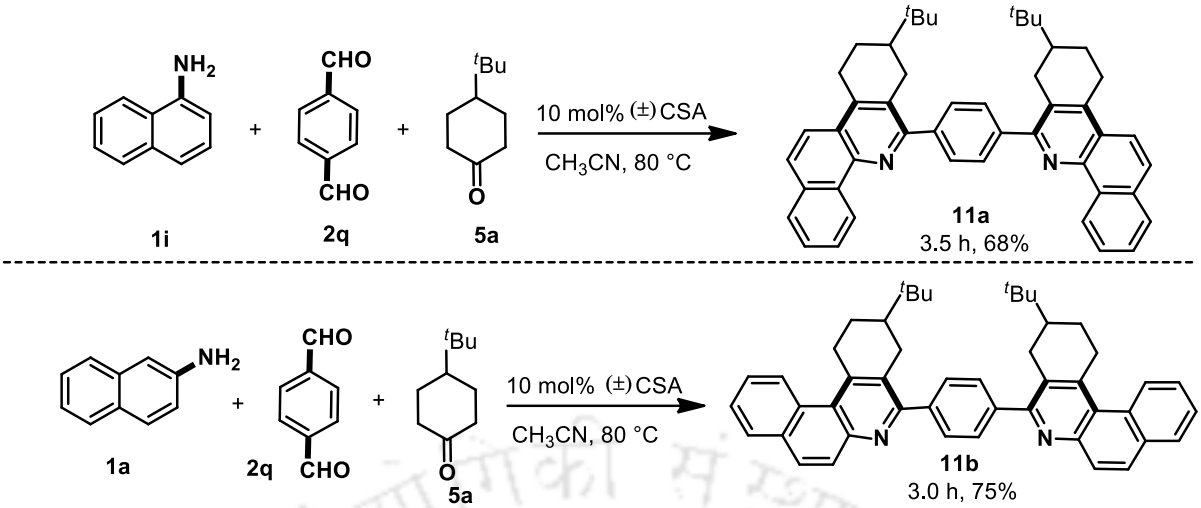


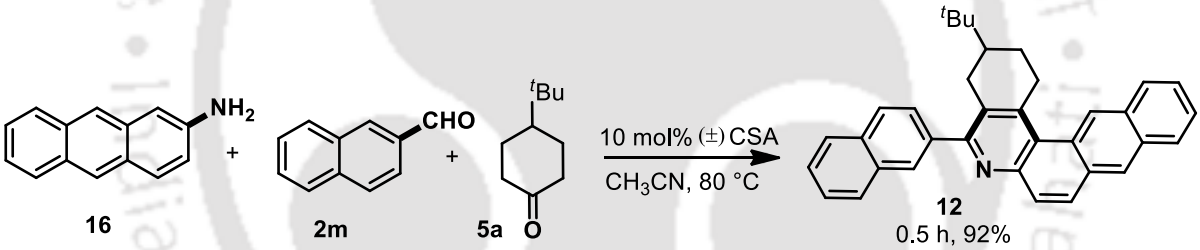
Figure 10. ORTEP Diagram of compound **10e** with ellipsoid counter 45% probalility

Next, our protocol was applied for the synthesis of fused bis-benzoquinoline derivatives by using 1-naphthylamine **1i** /2-naphthylamine **1a** (1.0 mmol), terephthalaldehyde **2q** (0.5 mmol) and 4-(*tert*-butyl)cyclohexanone **5a** (1.0 mmol) in presence of 10 mol% CSA catalyst under similar reaction condition and the results are shown in Scheme **45** along with their reaction time and yields. It was observed that *p*-anisidine failed to give the desired product under identical reaction condition.



Scheme 45

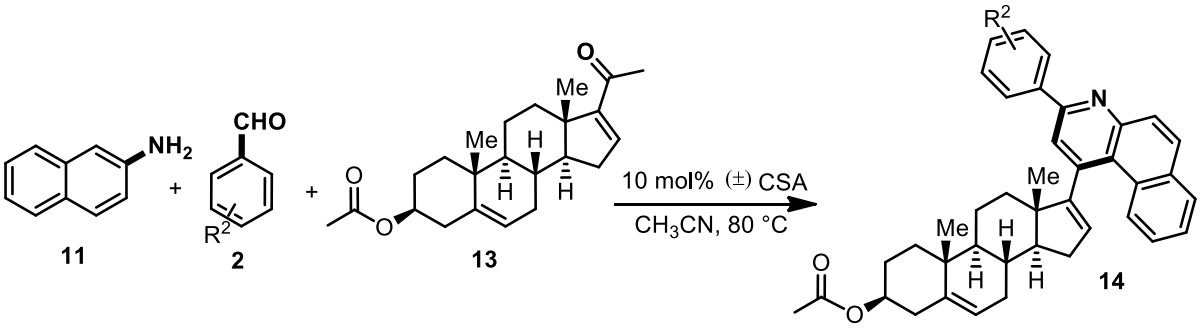
We also find that 2-Aminoanthracene **1k** (1.0 mmol) on reaction with 2-naphthaldehyde **2n** (1.0 mmol) and 4-(*tert*-butyl)cyclohexanone **5a** (1.0 mmol) in presence of 10 mol % CSA at 80 °C gave the product 3-(*tert*-butyl)-5-(naphthalen-2-yl)-1,2,3,4-tetrahydronaphtho[2,3-*a*]phenanthridine **12** as shown in Scheme **46**.

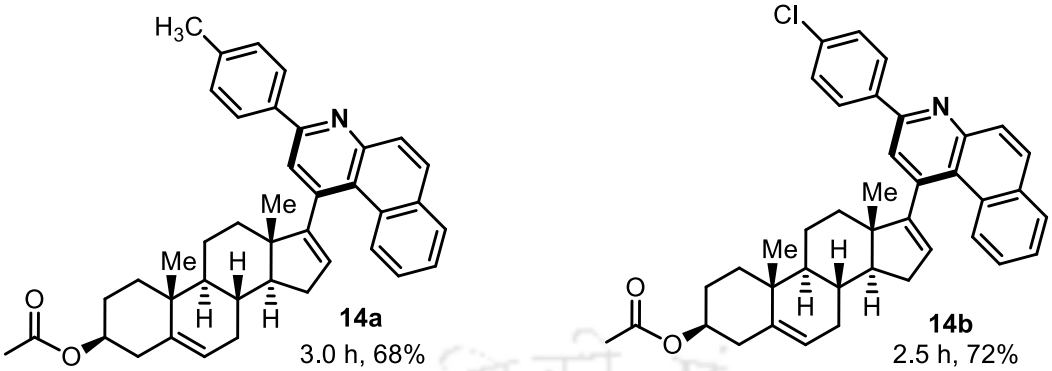


Scheme 46

Next, we synthesized steroid substituted benzo[*f*]quinoline derivatives from 16-dehydro-pregnenolone acetate **13**, 2-naphthylamine **1a** and 4-Me/4-Cl benzaldehydes using 10 mol% CSA under identical reaction condition which offered the desired products **14a-b** in 68 and 72% yields as shown in Table **8**.

Table 8. Reaction of 16-dehydro-pregnenolone acetate with aldehyde and 2-naphthylamine[a,b]





[a]The reactions were performed using aldehyde (1.0 mmol), 16-dehydro-pregnenolone acetate (1.0 mmol) and 2-naphthylamine (1.0 mmol) in CH_3CN. [b]Isolated yields.

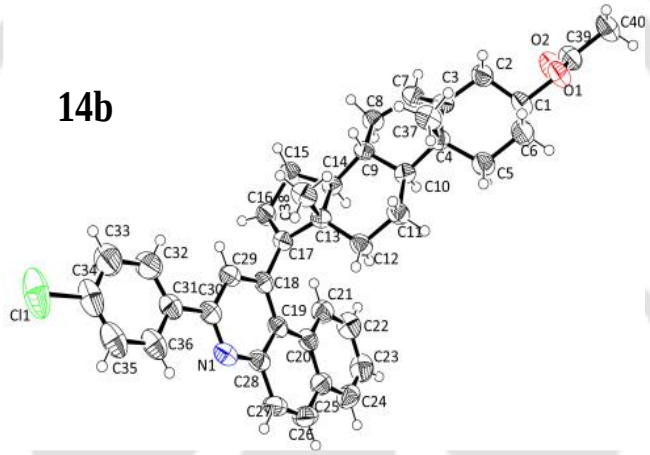
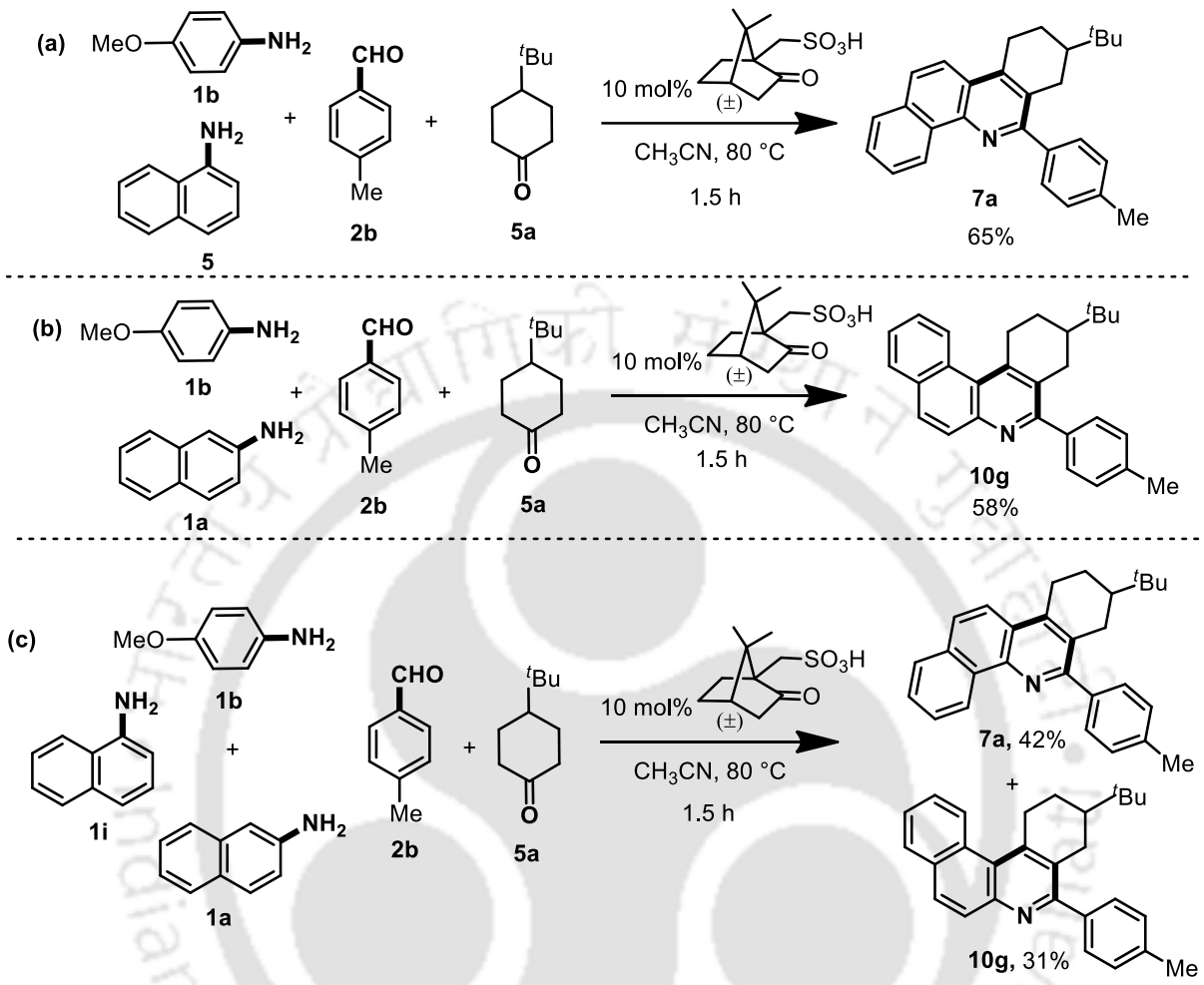


Figure 11. ORTEP Diagram of compound **14b** with ellipsoid counter 45% probalility

All the synthesised products were characterized by IR, ^1H and ^{13}C NMR spectra and HRMS. In addition, the structure of the compound **14b** was confirmed by single-crystal X-ray crystallographic data. The ORTEP diagram for the compound **14b** is shown in Figure **11**.

To understand the reactivity of aryl amines, we carried out three sets of reactions. Initially, *p*-anisidine (1.0 mmol), 1-naphthylamine (1.0 mmol), *p*-tolualdehyde (1.0 mmol), and 4-(*tert*-butyl)cyclohexanone (1.0 mmol) under same reaction condition produced single product **7a**. Next, the reaction of *p*-anisidine (1.0 mmol), 2-naphthylamine (1.0 mmol), *p*-tolualdehyde (1.0 mmol) and 4-(*tert*-butyl)cyclohexanone (1.0 mmol) gave only product **10g**. Finally, a mixture of *p*-anisidine (1.0 mmol), 1-naphthylamine (1.0 mmol), 2-naphthylamine (1.0 mmol), *p*-tolualdehyde (1.0 mmol) and 4-(*tert*-butyl)cyclohexanone (1.0 mmol) afforded products **7a** and **10g**. The product **6a** was not observed, due to poor reactivity of *p*-anisidine

in presence of 1-naphthylamine and 2-naphthylamine and the results are represented in Scheme **47**.



Scheme 47. The reactivity of various arylamines

To study the mechanism, we performed one pot three component reaction using 2-naphthylamine, *p*-tolualdehyde and 4-(*tert*-butyl)cyclohexanone in the presence of 10 mol % CSA at 80 °C in Argon atmosphere as shown in Scheme **48**. As expected, we have observed the formation of emine **15** in 15% yield, which on readily reacted with 4-(*tert*-butyl)cyclohexanone **5a** to give the corresponding products **16** and **10g** in 25% and 45% yield respectively after 0.5 h. In addition, the product **16** was stirred at 80 °C with 2 mL CH_3CN in open atmosphere without any catalyst resulted aromatized product **10g** with 100% conversion in 86% yield in 2 h, whereas at room temperature, reaction time prolonged up to 24 h to produce compound **10g** with 100% conversion of 84% yield. From the literature[40] the intermediate **17** was expected to be formed however we did not we have not observe such dihydroquinoline. All the compounds are isolated and characterised individually by IR, ^1H

and ^{13}C NMR spectra and HRMS. In addition, product **16** was confirmed by single crystal XRD. The ORTEP diagram for the compound **16** was shown in Figure **12**. The ^{1}H and ^{13}C NMR spectra of compounds **16a**, **7a**, **10a**, **11a**, **14a**, **16** are shown in Figure **13**, **14**, **15**, **16**, **17** and **18a** respectively (See Page No 71-77 in experimental section). The HRMS of intermediate compound **16** is represented in Figure **18b** (Page No. 77) in experimental section of this chapter.

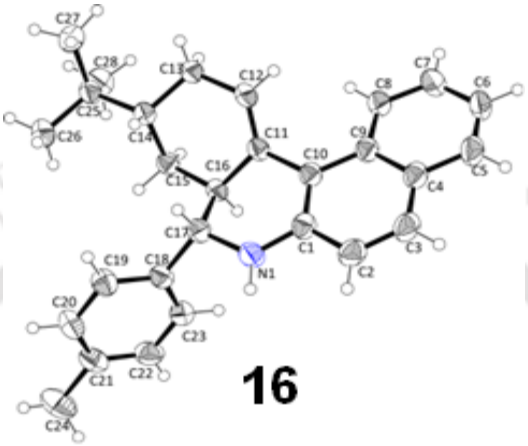
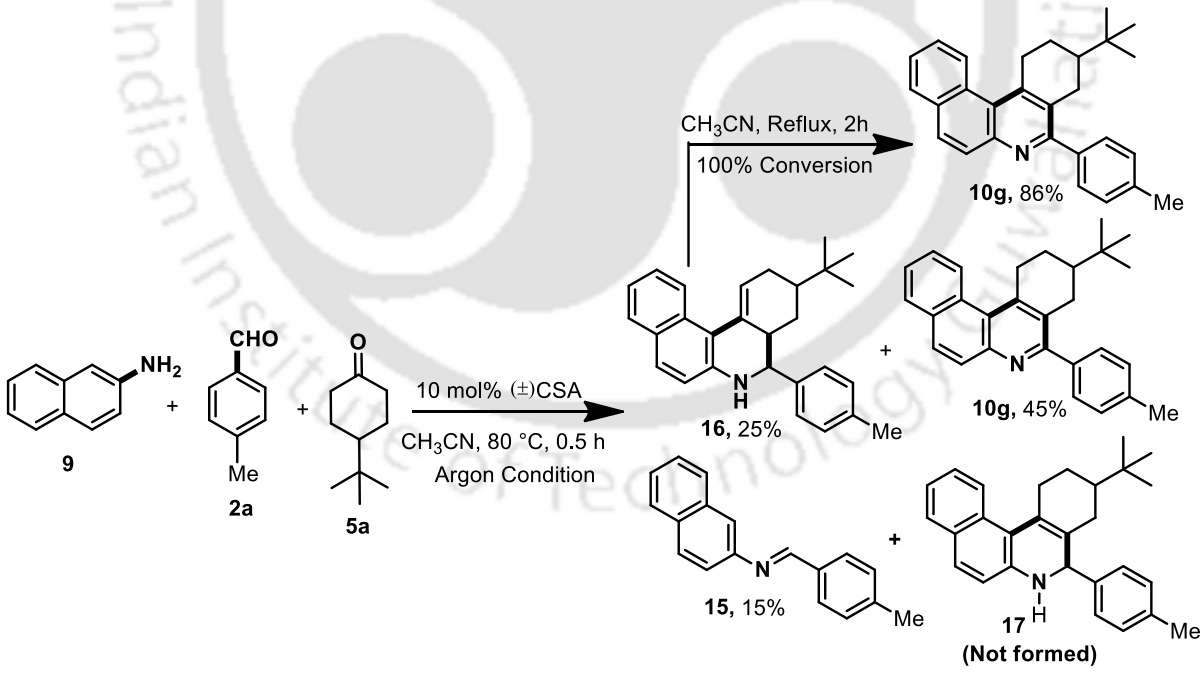


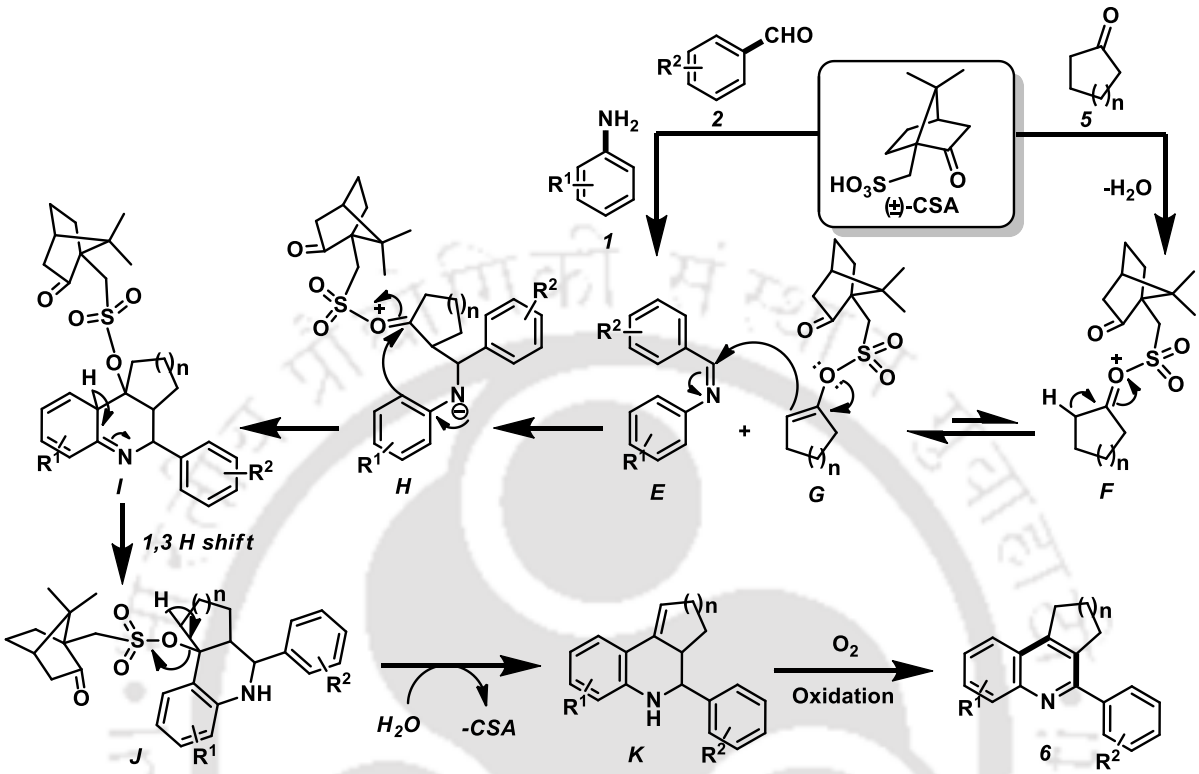
Figure 12. ORTEP Diagram of compound **16** with ellipsoid counter 45% probalility



Scheme 48. Experiment for mechanistic pathway

The plausible mechanism for the formation of fused quinoline is shown in Scheme **49**. Initially, the aryl amine **1** reacts with aldehyde **2** to form the imine **E** and the cyclic ketone **5** in presence of camphorsulphonic acid forms an active species **F** which tautomerize to most

stable enol form **G**. The generated imine **E** further reacted with **G** to form Micheal addition product **H**, which subsequently undergoes an intramolecular cyclization to give dihydroquinoline **K** which undergoes oxidative aromatization to give the desired product **6**.



Scheme 49

In summary, we have developed a simple and an efficient method for the synthesis of fused quinoline and benzoquinoline derivatives from readily available starting materials such as aryl amine, aromatic aldehyde and cyclic ketone through one pot three component reaction using camphorsulphonic acid as a catalyst. The protocol offers several advantages which include commercially available cheap catalyst, less reaction time, mild reaction condition, simple isolation procedure, broad substrate scope and two new *C*-*C* bond formations. Along with this, we have developed the utility of pregnenolone acetate and terephthalaldehyde for the synthesis of steroid substituted benzo[*f*]quinoline and bis-benzo[*f*]quinoline respectively.

Experimental Section

General Procedure for Synthesis of cycloalkyl fused quinolines **6**.

Into a dry 25 mL round bottom flask a mixture of aniline **1** (1.0 mmol), aromatic aldehyde **2** (1.0 mmol) and cyclic ketone **5** (1.0 mmol) was taken in 5 mL acetonitrile. Camphorsulfonic acid (0.023 g, 0.10 mmol) was added into it and stirred at 80 °C. The progress of the reaction was monitored by TLC. After completion of the reaction, the solvent was removed under reduced pressure and the reaction mixture was extracted with DCM (2 x 25 mL). The organic extract was dried over sodium sulphate and concentrated under reduced pressure. Finally, the residue was purified through silica gel (60-120 mesh) column chromatography with petroleum ether/ethyl acetate (9.5 : 0.5, v/v) to obtain the pure product **6**.

General Procedure for the Synthesis of cycloalkyl fused benzoquinolines **7**, **8**, **9 & 10**.

To a mixture 1-naphthylamine (**1i**) (1.0 mmol), aromatic aldehyde **2** (1.0 mmol), cyclic ketone **5**, camphorsulfonic acid (0.023 g, 0.10 mmol) and 5 mL of acetonitrile was added and stirred at 80 °C. After completion of the reaction indicated by TLC, the reaction mixture was allowed to cooled down to room temperature for complete precipitation. Then, the solid precipitate was filtered off through a Büchner funnel, washed with acetonitrile and dried under reduced pressure to obtain the pure products **7**. The similar reaction procedures were followed for the synthesis of products **8**, **9** & **10**.

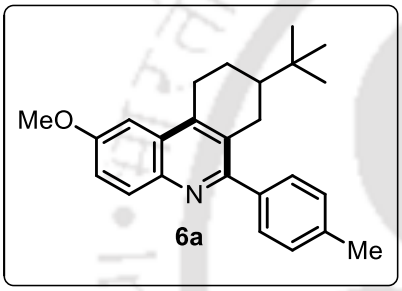
*General procedure for synthesis of cycloalkyl fused bis-benzoquinolines **11***.

To a mixture naphthylamine **1a** (1.0 mmol), terephthalaldehyde **2q** (0.5 mmol) and 4-(tert-butyl)cyclohexanone **5a** (1.0 mmol) in 3 mL acetonitrile camphorsulfonic acid (0.023 g, 0.10 mmol) was added and stirred at 80 °C for 1.0-4.5 h. After completion of the reaction indicated by TLC. The reaction mixture was cooled down to room temperature to obtain the solid product . Then, the pure solid products **11a-b** were obtained after washing with acetonitrile and dried under reduced pressure. The NMR of products were analyzed by dissolving in 2-3 drops of CF_3COOH in $CDCl_3$.

*General procedure for synthesis of steroid substituted benzo[f]quinoline (**14**)*

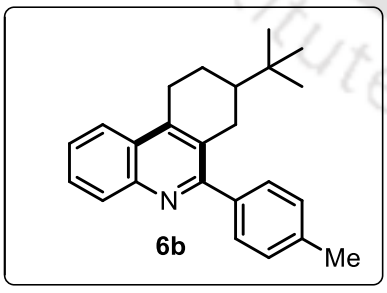
Into a 25 mL round bottom flask, a mixture of 2-naphthylamine **1a** (1 mmol), aromatic aldehyde **2** (1 mmol) and 16-dehydropregnenolone acetate **13** (1 mmol) was taken in 5 mL acetonitrile. Then, camphorsulfonic acid (0.023 g, 0.10 mmol) was added into the above reaction mixture and stirred at 80 °C for 2.5 to 3.0 h until the completion of the starting materials as indicated by TLC. The reaction mixture was cooled to room temperature. The solvent was removed under reduced pressure and reaction mixture was extracted with DCM (2 x 25 mL), dried over sodium sulphate and concentrated under reduced pressure. Then, the crude residue was purified through silica gel (60-120) column chromatography with petroleum ether-ethylacetate (9.5 : 0.5, v/v) to get the pure product **14**.

*8-(tert-butyl)-2-methoxy-6-(p-tolyl)-7,8,9,10-tetrahydrophenanthridine (**6a**)*



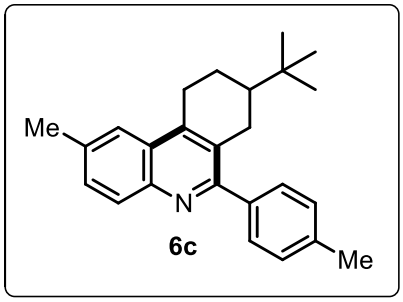
Yield 78% (280 mg), white solid, mp 180-181˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.01 (d, *J* = 8.4 Hz, 1H), 7.42 (d, *J* = 7.8 Hz, 2H), 7.31-7.29 (m, 1H), 7.27-7.26 (m, 2H), 7.18 (m, 1H), 3.95 (s, 3H), 3.76 (dd, *J* = 17.4, 4.8 Hz, 1H), 2.99 (m, 1H), 2.74 (d, *J* = 16.8 Hz, 1H), 2.53 (t, *J* = 12.6 Hz, 1H), 2.42 (s, 3H), 2.20-2.19 (m, 1H), 1.49-1.44 (m, 1H), 1.40-1.36 (m, 1H), 0.90 (s, 9H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 158.7, 157.8, 138.4, 137.7, 131.6, 129.4, 129.1, 128.9, 127.7, 120.3, 101.4, 55.7, 44.7, 32.6, 30.5, 27.6, 27.5, 23.9, 21.5; **IR (KBr)ν_{max}** 3051, 2957, 2867, 1585, 1497, 1068, 1031, 957 cm^{-1}; **HRMS (ESI)** Calcd For $C_{25}H_{30}NO$ 360.2322 ($M + H^+$); Found 360.2323.

*8-(tert-butyl)-6-(p-tolyl)-7,8,9,10-tetrahydrophenanthridine) (**6b**)*



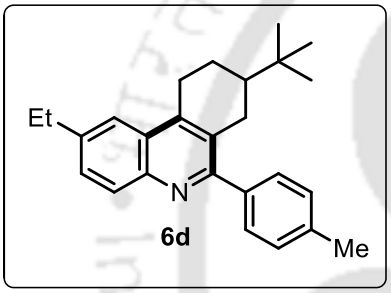
Yield 71% (233 mg), brown solid, mp 145-146˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.20 (s, 1H), 7.98 (d, *J* = 8.4 Hz, 1H), 7.66 (t, *J* = 7.2 Hz, 1H), 7.55 (t, *J* = 7.2 Hz, 1H), 7.45 (d, *J* = 7.8 Hz, 2H), 7.29 (d, *J* = 7.2 Hz, 2H), 3.48 (dd, *J* = 18.0, 4.2 Hz, 1H), 3.07 (m, 1H), 2.76 (d, *J* = 16.2 Hz, 1H), 2.55 (t, *J* = 12.0 Hz, 1H), 2.43 (s, 3H), 2.23-2.20 (m, 1H), 1.51-1.45 (m, 1H), 1.42-1.37 (m, 1H), 0.91 (s, 9H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 159.5, 158.3, 157.7, 141.8, 140.7, 133.9, 131.6, 130.3, 129.4, 127.6, 120.2, 113.8, 101.3, 55.7, 44.8, 32.5, 30.6, 27.6, 27.5, 23.9; **IR (KBr)νmax** 3059, 2984, 2867, 1683, 1585, 1559, 1110, 1040, 1016 cm^{-1}; **HRMS** (APCI) Calcd For $C_{24}H_{28}N$ 330.2216 ($M + H^+$); Found 330.2205.

*8-(tert-butyl)-2-methyl-6-(p-tolyl)-7,8,9,10-tetrahydrophenanthridine (**6c**)*



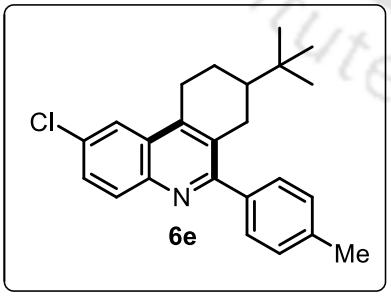
Yield 70% (240 mg), white solid, mp 182-183˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.72 (s, 1H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.45 (d, *J* = 7.8 Hz, 2H), 7.27 (d, *J* = 7.8 Hz, 2H), 3.44 (dd, *J* = 18.0, 4.8 Hz, 1H), 3.02 (m, 1H), 2.74 (d, *J* = 16.2 Hz, 1H), 2.56 (s, 3H), 2.52 (d, *J* = 16.2 Hz, 1H), 2.42 (s, 3H), 2.21-2.18 (m, 1H), 1.47-1.42 (m, 1H), 1.39-1.35 (m, 1H), 0.90 (s, 9H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 159.8, 143.6, 142.2, 138.0, 137.6, 136.2, 130.8, 129.3, 129.1, 128.9, 126.7, 121.8, 44.7, 32.5, 32.4, 30.4, 27.4, 23.8, 22.2, 21.5; **IR (KBr)νmax** 3043, 3016, 2941, 2864, 1646, 1585, 1471, 1102, 1010, 922 cm^{-1}; **HRMS** (APCI) Calcd For $C_{25}H_{30}N$ 344.2373 ($M + H^+$); Found 344.2361.

*8-(tert-butyl)-2-ethyl-6-(p-tolyl)-7,8,9,10-tetrahydrophenanthridine (**6d**)*



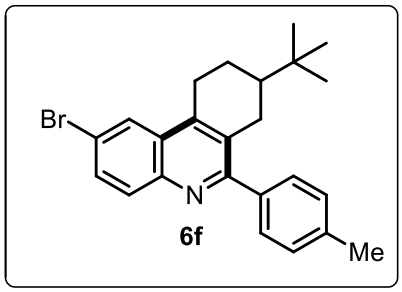
Yield 76% (271 mg), white solid, mp 135-136˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.08 (d, *J* = 7.8 Hz, 1H), 7.73 (s, 1H), 7.53-7.51 (m, 1H), 7.44 (d, *J* = 7.8 Hz, 2H), 7.27 (d, *J* = 7.8 Hz, 2H), 3.45 (dd, *J* = 17.4, 4.8 Hz, 1H), 3.07-3.03 (m, 1H), 2.85 (m, 2H), 2.75 (d, *J* = 16.8 Hz, 1H), 2.54 (t, *J* = 12.0 Hz, 1H), 2.42 (s, 3H), 2.19 (m, 1H), 1.49-1.44 (m, 1H), 1.44-1.39 (m, 1H), 1.35 (t, *J* = 7.8 Hz, 3H), 0.91 (s, 9H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 160.0, 144.1, 142.4, 142.1, 138.1, 137.9, 129.7, 129.6, 129.1, 129.0, 128.9, 126.8, 120.5, 44.7, 32.6, 32.5, 30.4, 29.5, 27.4, 23.8, 21.5, 15.9; **IR (KBr)νmax** 3048, 3024, 2964, 2867, 1612, 1585, 1112, 1058, 1016, 932 cm^{-1}; **HRMS** (ESI) Calcd For $C_{26}H_{32}N$ 358.2530 ($M + H^+$); Found 358.2540.

*8-(tert-butyl)-2-chloro-6-(p-tolyl)-7,8,9,10-tetrahydrophenanthridine (**6e**)*



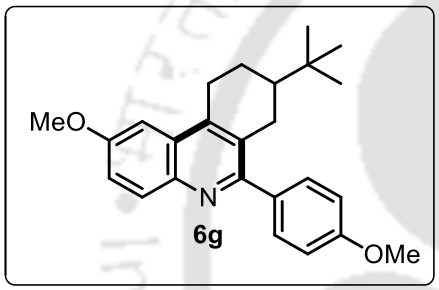
Yield 72% (261 mg), white solid, mp 230-231˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.01 (d, *J* = 9.0 Hz, 1H), 7.92 (d, *J* = 1.8 Hz, 1H), 7.56 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.42 (d, *J* = 7.8 Hz, 2H), 7.27 (d, *J* = 7.8 Hz, 2H), 3.37 (dd, *J* = 18.0, 5.4 Hz, 1H), 3.02-2.96 (m, 1H), 2.74 (d, *J* = 16.8 Hz, 1H), 2.54 (t, *J* = 16.8 Hz, 1H), 2.42 (s, 3H), 2.21- 2.18 (m, 1H), 1.47-1.42 (m, 1H), 1.39-1.35 (m, 1H), 0.90 (s, 9H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 161.4, 144.2, 141.4, 138.2, 138.0, 132.0, 131.7, 130.7, 130.2, 129.2, 128.8, 127.6, 121.9, 44.6, 32.5, 30.5, 27.4, 27.3, 23.7, 21.5; **IR (KBr)νmax** 3042, 2948, 2922, 2863, 1586, 1062, 1011, 942 cm^{-1}; **HRMS** (ESI) Calcd For $C_{24}H_{27}ClN$ 364.1827 ($M + H^+$); Found 364.1835.

*2-bromo-8-(tert-butyl)-6-(p-tolyl)-7,8,9,10-tetrahydrophenanthridine (**6f**)*



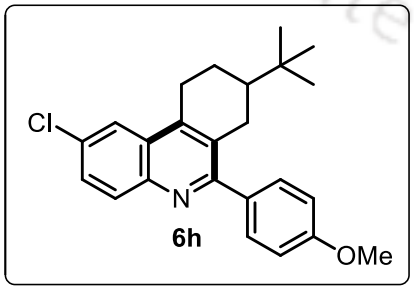
Yield 68% (276 mg), white solid, mp 237-238˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.25 (s, 1H), 8.14 (s, 1H), 7.74 (d, *J* = 8.4 Hz, 1H), 7.46 (d, *J* = 7.8 Hz, 2H), 7.30 (d, *J* = 7.2 Hz, 2H), 3.41 (dd, *J* = 18.0, 4.2 Hz, 1H), 3.03 (m, 1H), 2.75 (d, *J* = 16.8 Hz, 1H), 2.56 (t, *J* = 12.6 Hz, 1H), 2.43 (s, 3H), 2.23-2.20 (m, 1H), 1.51-1.44 (m, 1H), 1.38 (t, *J* = 10.2 Hz, 1H), 0.90 (s, 9H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 161.0, 143.5, 142.4, 138.6, 136.8, 132.2, 131.2, 130.4, 129.2, 128.9, 128.1, 125.3, 120.7, 44.5, 32.5, 30.4, 27.5, 27.4, 23.6, 21.6; **IR (KBr)νmax** 3043, 2947, 2896, 2864, 1584, 1182, 1072, 1016, 976 cm^{-1}; **HRMS** (ESI) Calcd For $C_{24}H_{27}BrN$ 408.1322 ($M + H^+$); Found 408.1336.

*8-(tert-butyl)-2-methoxy-6-(4-methoxyphenyl)-7,8,9,10-tetrahydrophenanthridine (**6g**)*



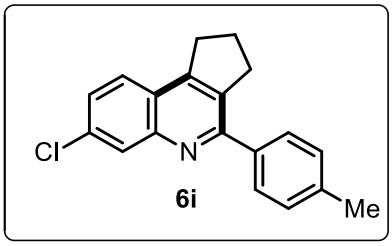
Yield 68% (255 mg), brown solid, mp 145-146˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.00 (d, *J* = 9.2 Hz, 1H), 7.49 (d, *J* = 8.8 Hz, 2H), 7.29 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.17 (d, *J* = 2.4 Hz, 1H), 6.92 (d, *J* = 6.0 Hz, 2H), 3.95 (s, 3H), 3.87 (s, 3H), 3.35 (dd, *J* = 17.6, 5.2 Hz, 1H), 3.03-2.94 (m, 1H), 2.75 (d, *J* = 16.8 Hz, 1H), 2.50 (t, *J* = 11.6 Hz, 1H), 2.22-2.04 (m, 1H), 1.51-1.39 (m, 1H), 1.38-1.34 (m, 1H), 0.91 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 159.5, 158.3, 157.7, 141.8, 140.7, 133.9, 131.6, 130.3, 129.4, 127.6, 120.2, 113.8, 101.3, 55.7, 55.5, 44.8, 32.5, 30.6, 27.6, 27.5, 23.9; **IR (KBr)νmax** 3042, 2955, 2867, 2828, 1620, 1581, 1174, 1106, 1034, 958 cm^{-1}; **HRMS** (APCI) Calcd For $C_{25}H_{30}NO_2$ 376.2271 ($M + H^+$); Found 376.2256.

*8-(tert-butyl)-2-chloro-6-(4-methoxyphenyl)-7,8,9,10-tetrahydrophenanthridine (**6h**)*



Yield 66% (250 mg), white solid, mp 202-203˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.16 (s, 1H), 7.94 (s, 1H), 7.58 (d, *J* = 9.0 Hz,1H), 7.52 (d, *J* = 9.0 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 2H), 3.88 (s, 3H), 3.41-3.37(m, 1H), 3.04-2.98 (m, 1H), 2.76 (d, *J* = 16.8 Hz, 1H), 2.56 (t, *J* = 12.0 Hz, 1H), 2.23-2.19 (m, 1H), 1.51-1.44 (m, 1H), 1.39-1.35 (m, 1H), 0.90 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 160.4, 160.2, 143.1, 142.7, 135.4, 132.4, 130.9, 130.6, 130.5, 129.7, 127.6, 122.0, 114.0, 55.9, 44.6, 32.6, 30.6, 27.5, 27.4, 23.6; **IR (KBr)νmax** 3005, 2952, 2917, 2864, 1608, 1573, 1558, 1149, 1082, 1035, 950 cm^{-1}; **HRMS** (ESI) Calcd For $C_{24}H_{27}ClNO$ 380.1776 ($M + H^+$); Found 380.1778.

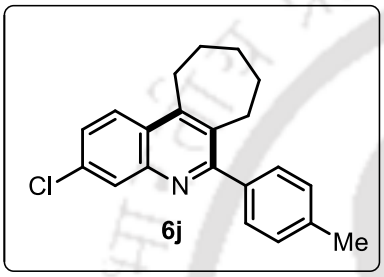
*7-chloro-4-(p-tolyl)-2,3-dihydro-1H-cyclopenta[c]quinoline (**6i**)*



6i

Yield 74% (216 mg), white solid, mp 127-128˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.16 (d, *J* = 2.0 Hz, 1H), 7.74 (d, *J* = 8.4 Hz, 2H), 7.68 (d, *J* = 8.8 Hz, 1H), 7.41 (dd, *J* = 6.8, 2.0 Hz, 1H), 7.30 (d, *J* = 8.4 Hz, 2H), 3.23 (m, 4H), 2.45 (s, 3H), 2.24 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 157.1, 151.4,147.9, 138.9, 137.5, 135.4, 134.3, 129.2, 128.9, 128.8, 126.9, 125.6, 123.7, 33.9, 31.4, 25.1, 21.5; **IR (KBr)νmax** 3025, 2970, 2919, 2849, 1605, 1575, 1559, 1070, 1042, 969 cm^{-1}; **HRMS** (ESI) Calcd For $C_{19}H_{17}ClN$ 294.1044 ($M + H^+$); Found 294.1050.

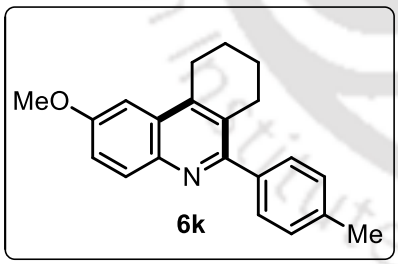
*3-chloro-6-(p-tolyl)-8,9,10,11-tetrahydro-7H-cyclohepta[c]quinoline (**6j**)*



6j

Yield 82% (263 mg), white solid, mp 146-147˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.08 (d, *J* = 2.4 Hz, 1H), 7.97 (d, *J* = 9.2 Hz, 1H), 7.41-7.38 (m, 3H), 7.26 (d, *J* = 8.4 Hz, 2H), 3.24 (t, *J* = 4.8 Hz, 2H), 2.95 (t, *J* = 5.6 Hz, 2H), 2.41 (s, 3H), 1.89 (t, *J* = 6.0 Hz, 2H), 1.73 (t, *J* = 4.8 Hz, 2H), 1.62 (t, *J* = 5.2 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 161.0, 149.6, 146.9, 138.7, 137.9, 134.7, 134.1, 129.1, 129.0, 128.9, 126.9, 124.7, 124.6, 31.9, 30.8, 28.3, 27.0, 26.1, 21.4; **IR (KBr)νmax** 3048, 2978, 2919, 2852, 1637, 1576, 1489, 1069, 1019, 964 cm^{-1}; **HRMS** (ESI) Calcd For $C_{21}H_{21}ClN$ 322.1357 ($M + H^+$); Found 322.1359.

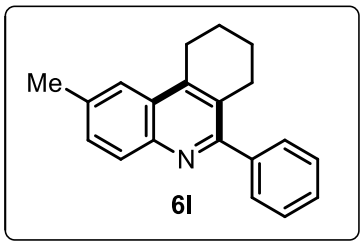
*2-methoxy-6-(p-tolyl)-7,8,9,10-tetrahydrophenanthridine (**6k**)*



6k

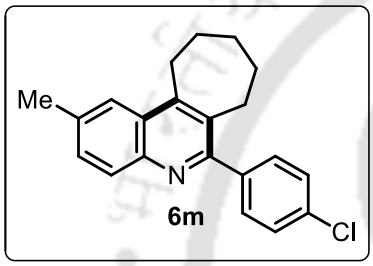
Yield 68% (206 mg), brown solid, mp 135-136˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.00 (d, *J* = 9.0 Hz, 1H), 7.41 (d, *J* = 7.8 Hz, 2H), 7.31-7.30 (m, 1H), 7.30-7.29 (m, 1H), 7.26 (d, *J* = 6.0 Hz, 1H), 7.19 (s, 1H), 3.96 (s, 3H), 3.13 (t, *J* = 6.0 Hz, 2H), 2.73 (t, *J* = 6.0 Hz, 2H), 2.42 (s, 3H), 1.98 (t, *J* = 5.4 Hz, 2H), 1.77 (t, *J* = 5.4 Hz, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 158.5, 157.8, 141.8, 140.8, 138.5, 137.8, 131.7, 129.1, 128.9, 127.9, 120.3, 101.2, 55.7, 29.0, 26.1, 22.9, 22.5, 21.5; **IR (KBr)νmax** 3041, 2933, 2859, 1668, 1655, 1220, 1093, 946 cm^{-1}; **HRMS** (ESI) Calcd For $C_{21}H_{22}NO$ 304.1696 ($M + H^+$); Found 304.1703.

*2-methyl-6-phenyl-7,8,9,10-tetrahydrophenanthridine (**6l**)*



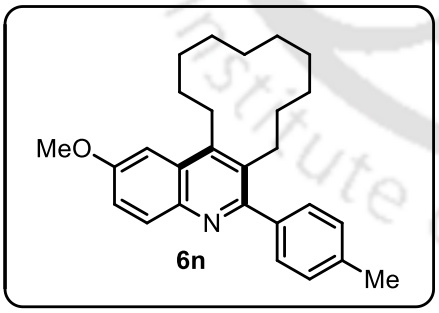
Yield 75% (204 mg), yellow liquid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.00 (d, *J* = 8.4 Hz, 1H), 7.74 (s, 1H), 7.53 (d, *J* = 7.2 Hz, 2H), 7.49-7.45 (m, 3H), 7.41 (t, *J* = 7.2 Hz, 1H), 3.18 (t, *J* = 5.4 Hz, 2H), 2.72 (t, *J* = 5.4 Hz, 2H), 2.57 (s, 3H), 1.97 (t, *J* = 4.8 Hz, 2H), 1.79-1.77 (m, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 160.0, 144.4, 141.5, 141.5, 136.1, 130.6, 129.9, 128.9, 128.5, 128.4, 128.1, 127.1, 121.7, 28.9, 25.9, 22.9, 22.5, 22.2; **IR (KBr)νmax** 3055, 3025, 2932, 2859, 1733, 1621, 1582, 1095, 1029, 1001, 988 cm^{-1}; **HRMS** (APCI) Calcd For $C_{20}H_{20}N$ 274.1590 ($M + H^+$); Found 274.1573.

*6-(4-chlorophenyl)-2-methyl-8,9,10,11-tetrahydro-7H-cyclohepta[c]quinoline (**6m**)*



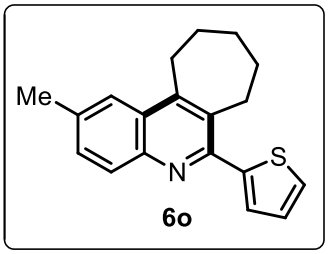
Yield 74% (237 mg), white solid, mp 192-193˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.00 (d, *J* = 8.4 Hz, 1H), 7.87 (s, 1H), 7.49 (d, *J* = 9.0 Hz, 1H), 7.46-7.43 (m, 4H), 3.29 (t, *J* = 4.8 Hz, 2H), 2.92 (t, *J* = 5.4 Hz, 2H), 2.57 (s, 3H), 1.93-1.90 (m, 2H), 1.77 (m, 2H), 1.63 (t, *J* = 4.8 Hz, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 157.7, 149.0, 145.1, 140.5, 136.1, 134.1, 133.9, 130.9, 130.6, 130.1, 128.5, 126.3, 122.1, 32.1, 30.8, 28.1, 27.1, 26.2, 22.2; **IR (KBr)νmax** 3061, 2991, 2972, 2921, 2851, 1682, 1105, 1090, 1012, 965 cm^{-1}; **HRMS** (ESI) Calcd For $C_{21}H_{21}ClN$ 322.1357 ($M + H^+$); Found 322.1371.

*2-methoxy-6-(p-tolyl)-7,8,9,10,11,12,13,14,15,16-decahydrocyclododeca[c]quinoline (**6n**)*



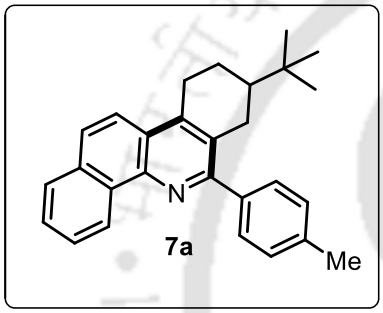
Yield 64% (247 mg), brown solid, mp 149-150 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.98 (d, *J* = 9.0 Hz, 1H), 7.35 (d, *J* = 8.4 Hz, 2H), 7.30-7.28(m, 2H), 7.24 (d, *J* = 7.8 Hz, 2H), 3.96 (s, 3H), 3.16 (t, *J* = 7.8 Hz, 2H), 2.81 (t, *J* = 7.8 Hz, 2H), 2.41 (s, 3H), 1.89-1.88 (m, 2H), 1.67-1.64 (m, 4H), 1.53-1.52 (m, 2H), 1.52-1.45 (m, 6H), 1.25-1.24 (m, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 159.4, 157.6, 145.0, 142.2, 139.6, 137.4, 132.4, 131.7, 128.9, 128.6, 128.1, 120.1, 102.9, 55.7, 28.9, 28.6, 28.5, 28.4, 28.0, 27.6, 27.4, 26.9, 22.8, 21.5; **IR (KBr)νmax** 3058, 2924, 2851, 1621, 1571, 1034, 968 cm^{-1}; **HRMS** (ESI) Calcd For $C_{27}H_{34}NO$ 388.2635 ($M + H^+$); Found 388.2654.

*2-methyl-6-(thiophen-2-yl)-8,9,10,11-tetrahydro-7H-cyclohepta[c]quinoline (**6o**)*



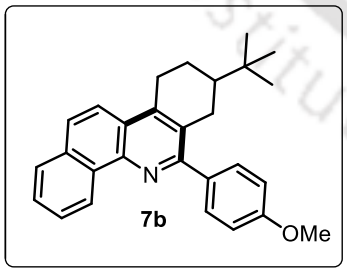
Yield 69% (202 mg), white solid, mp 130-131˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.98 (d, *J* = 8.4 Hz, 1H), 7.82 (s, 1H), 7.47 (d, *J* = 9.0 Hz, 1H), 7.43 (d, *J* = 4.8 Hz, 1H), 7.26 (s, 1H), 7.12 (t, *J* = 7.8 Hz, 1H), 3.30 (t, *J* = 4.8 Hz, 2H), 3.18 (t, *J* = 5.4 Hz, 2H), 2.55 (s, 3H), 1.95-1.94 (m, 2H), 1.78-1.77 (m, 2H), 1.73-1.72 (m, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 151.9, 149.2, 145.3, 144.5, 136.2, 134.4, 130.9, 130.1, 127.6, 127.2, 126.9, 126.2, 122.1, 32.1, 30.7, 28.1, 27.0, 26.4, 22.3; **IR (KBr)νmax** 3070, 2995, 2917, 2852, 1637, 1568, 1056, 1019 cm^{-1}; **HRMS** (APCI) Calcd For $C_{19}H_{20}NS$ 294.1311(M + H^+); Found 294.1325.

*8-(tert-butyl)-6-(p-tolyl)-7,8,9,10-tetrahydrobenzo[c]phenanthridine (**7a**)*



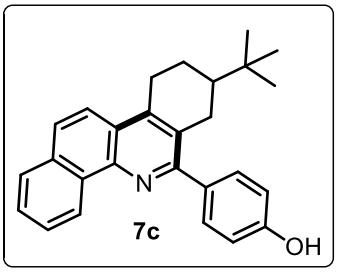
Yield 94% (356 mg), white solid, mp 211-212˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.37 (d, *J* = 6.6 Hz, 1H), 7.91-7.87 (m, 2H), 7.81 (d, *J* = 9.0 Hz, 1H), 7.64-7.62 (m, 4H), 7.32 (d, *J* = 7.8 Hz, 2H), 3.56-3.50 (m, 1H), 3.15-3.11 (m, 1H), 2.91-2.88 (m, 1H), 2.69 (t, *J* = 12.0 Hz, 1H), 2.47 (s, 3H), 2.25-2.22 (m, 1H), 1.57-1.49 (m, 1H), 1.43-1.39 (m, 1H), 0.94 (s, 9H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 158.7, 143.4, 142.3, 138.9, 137.9, 133.2, 132.3, 129.7, 129.6, 128.9, 127.6, 127.2, 126.8, 125.2, 124.1, 120.9, 44.7, 32.6, 30.6, 27.8, 27.5, 24.1, 21.6; **IR (KBr)νmax** 3045, 3022, 2955, 2867, 2837, 1573, 1099, 1019 cm^{-1}; **HRMS** (ESI) Calcd For $C_{28}H_{30}N$ 380.2373 (M + H^+); Found 380.2376.

*8-(tert-butyl)-6-(4-methoxyphenyl)-7,8,9,10-tetrahydrobenzo[c]phenanthridine (**7b**)*



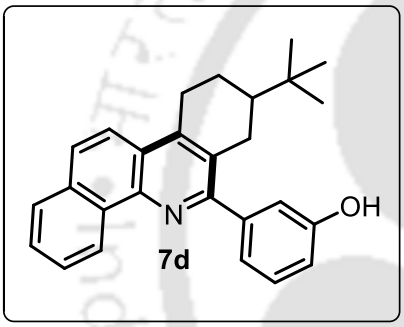
Yield 90% (355 mg), brown solid, mp 270-271˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.34 (d, *J* = 7.6 Hz, 1H), 7.86 (d, *J* = 9.2 Hz, 2H), 7.77 (d, *J* = 9.2 Hz, 1H), 7.69 (d, *J* = 8.8 Hz, 2H), 7.64 (t, *J* = 6.4 Hz, 2H), 7.04 (d, *J* = 8.8 Hz, 2H), 3.89 (s, 3H), 3.51-3.46 (m, 1H), 3.12-3.03 (m, 1H), 2.87 (d, *J* = 16.0 Hz, 1H), 2.68 (t, *J* = 12.0 Hz, 1H), 2.21-2.19 (m, 1H), 1.53-1.43 (m, 1H), 1.36 (t, *J* = 10.0 Hz, 1H), 0.93 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 159.7, 158.2, 143.3, 142.4, 134.1, 133.1, 132.1, 131.0, 129.6, 127.7, 127.6, 127.1, 126.8, 125.1, 123.9, 120.8, 113.6, 58.5, 44.7, 32.5, 30.7, 27.8, 27.5, 23.9; **IR (KBr)νmax** 3051, 2956, 2897, 1608, 1506, 1174, 1073, 1012 cm^{-1}; **HRMS** (ESI) Calcd For $C_{28}H_{30}NO$ 396.2322 (M + H^+); Found 396.2322.

*4-(8-(tert-butyl)-7,8,9,10-tetrahydrobenzo[c]phenanthridin-6-yl)phenol (**7c**)*



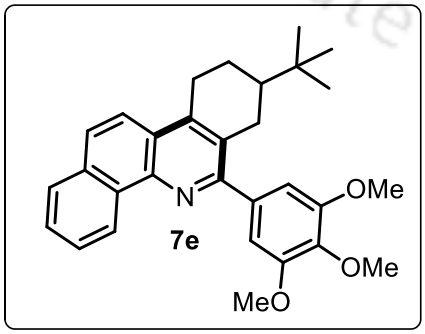
Yield 92% (350 mg), white solid, mp 256-257˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.35-9.33 (m, 1H), 7.91-7.87 (m, 2H), 7.81 (d, *J* = 9.6 Hz, 1H), 7.66-7.63 (m, 4H), 6.96 (d, *J* = 8.8 Hz, 2H), 3.56-3.49 (m, 1H), 3.16-3.06 (m, 1H), 2.87 (d, *J* = 16.4 Hz, 1H), 2.69 (t, *J* = 12.4 Hz, 1H), 2.54-2.18 (m, 1H), 1.57-1.47 (m, 1H), 1.41-1.38 (m, 1H), 0.94 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 158.3, 157.3, 142.8, 142.2, 132.9, 132.3, 131.7, 130.8, 129.5, 127.4, 127.3, 126.7, 126.5, 124.7, 123.6, 120.7, 115.1, 44.5, 32.3, 30.5, 27.6, 27.2, 23.8; **IR (KBr)νmax** 3473, 3049, 2962, 2915, 2858, 1636, 1518, 1100, 1022 cm^{-1}; **HRMS** (ESI) Calcd For $C_{27}H_{28}NO$ 382.2166 ($M + H^+$); Found 382.2166.

*3-(8-(tert-butyl)-7,8,9,10-tetrahydrobenzo[c]phenanthridin-6-yl)phenol (**7d**)*



Yield 95% (362 mg), white solid, mp 220-221˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.32 (d, *J* = 7.8 Hz, 1H), 7.86 (d, *J* = 7.2 Hz, 1H), 7.83 (d, *J* = 9.0 Hz, 1H), 7.78 (d, *J* = 9.0 Hz, 1H), 7.65-7.61 (m, 2H), 7.29-7.27 (m, 1H), 7.13-7.12 (m, 2H), 6.86-6.84 (m, 1H), 3.46-3.42 (m, 1H), 3.07-3.01 (m, 1H), 2.78 (d, *J* = 6.2 Hz, 1H), 2.54 (t, *J* = 12.6 Hz, 1H), 2.18-2.15 (m, 1H), 1.45-1.38 (m, 1H), 1.35-1.31 (m, 1H), 0.89 (s, 9H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 158.4, 156.0, 143.5, 142.6, 141.9, 133.2, 131.4, 130.1, 129.4, 127.9, 127.8, 127.6, 127.1, 125.0, 124.4, 121.6, 120.7, 116.9, 115.8, 44.5, 32.5, 30.2, 27.9, 27.4, 23.8; **IR (KBr)νmax** 3446, 3051, 2956, 2861, 1636, 1121, 996 cm^{-1}; **HRMS** (ESI) Calcd For $C_{27}H_{28}NO$ 382.2166 ($M + H^+$); Found 382.2161.

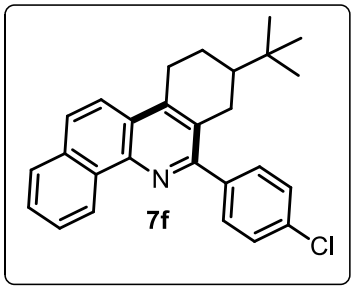
*8-(tert-butyl)-6-(3,4,5-trimethoxyphenyl)-7,8,9,10-tetrahydrobenzo[c]phenanthridine (**7e**)*



Yield 77% (350 mg), white solid, mp 196-197˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.41,(s, 1H), 7.90 (t, *J* = 3.6 Hz, 2H), 7.83, (d, *J* = 9.6 Hz, 1H), 7.71-7.64, (m, 2H), 6.95, (s, 2H), 3.96, (s, 3H), 3.94, (s, 6H), 3.54-3.51, (m, 1H), 3.15-3.09, (m, 1H), 2.93, (d, *J* = 16.2 Hz, 1H), 2.67, (t, *J* = 12.6 Hz, 1H), 2.24, (t, *J* = 4.2 Hz, 1H), 1.55-1.48,(m, 1H), 1.42 (t, *J* = 10.2 Hz, 1H), 0.95, (s, 9H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 158.1, 153.1, 142.8, 141.4, 138.4, 136.5, 133.3, 131.6, 129.7, 127.9, 127.8, 127.7, 127.1, 125.3, 124.3, 120.7, 107.2, 61.2, 56.5, 44.7, 32.6, 30.6, 27.9, 27.5, 23.9;

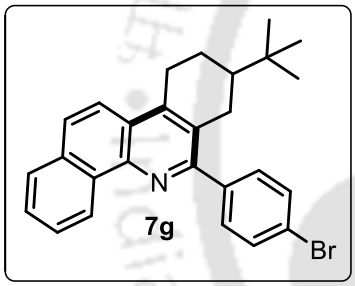
IR (KBr)νmax 3042, 2997, 2956, 2886, 1637, 1585, 1127, 1006 cm^{-1}; **HRMS** (ESI) Calcd For $C_{30}H_{34}NO_3$ 456.2533 ($M + H^+$); Found 456.2527.

*8-(tert-butyl)-6-(4-chlorophenyl)-7,8,9,10-tetrahydrobenzo[c]phenanthridine (**7f**):* Yield 87%



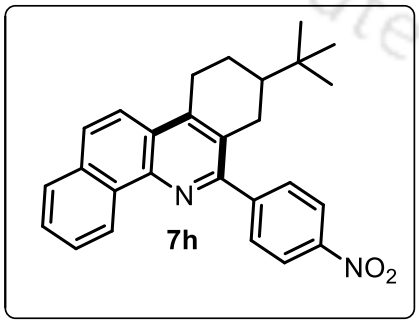
(347 mg), white solid, mp 217-218 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.40, (s, 1H), 7.90-7.89, (m, 2H), 7.85,(s, 1H), 7.67-7.66, (m, 4H), 7.51-7.50, (m, 2H), 3.53, (d, *J* = 17.2 Hz, 1H), 3.12-3.11, (m, 1H), 2.82, (d, *J* = 16.0 Hz, 1H), 2.65, (t, *J* = 12.8 Hz, 1H), 2.24-2.23, (m, 1H), 1.51, (d, *J* = 12.0 Hz, 1H),1.41,(d, *J* = 11.0 Hz, 1H), 0.94, (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 157.1, 143.3, 143.0, 139.6, 134.4, 133.2, 131.7, 131.1, 129.6, 128.5, 127.9, 127.7, 127.1, 125.1, 124.4, 1207, 44.6, 32.6, 30.5, 27.8, 27.5, 23.9;.**IR (KBr)νmax** 3022, 2958, 2873, 2840, 1652, 1573, 1123, 1090, 1014 cm^{-1}; **HRMS** (ESI) Calcd For $C_{27}H_{27}ClN$ 400.1827 ($M + H^+$); Found 400.1825.

*6-(4-bromophenyl)-8-(tert-butyl)-7,8,9,10-tetrahydrobenzo[c]phenanthridine (**7g**):*



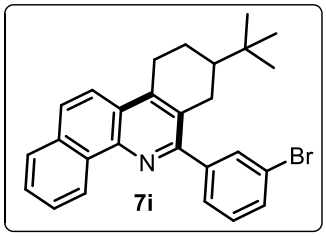
Yield 82% (363 mg), white solid, mp 215-216 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.45 (s, 1H), 7.89(s, 2H), 7.87, (s, 1H), 7.68-7.66 (m, 4H), 7.61(s, 2H), 3.54 (d, *J* = 17.2 Hz, 1H), 3.14 (s, 1H), 2.82 (d, *J* = 16.0 Hz, 1H), 2.64 (t, *J* = 12.8 Hz, 1H), 2.23 (s, 1H), 1.51 (d, *J* = 11.6 Hz, 1H), 1.41 (d, *J* = 11.2 Hz, 1H), 0.94, (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 157.0, 143.7, 142.8, 139.6, 133.3, 131.5, 131.4, 129.7, 128.1, 127.9, 127.8, 127.2, 125.2, 124.5, 122.8, 120.6, 44.5, 32.5, 30.4, 27.9, 27.4, 23.9; **IR (KBr)νmax** 2953, 2869, 2840, 1573, 1122, 1099, 1073, 1010 cm^{-1}; **HRMS** (ESI) Calcd For $C_{27}H_{27}BrN$ 444.1322 ($M + H^+$); Found 444.1323.

*8-(tert-butyl)-6-(4-nitrophenyl)-7,8,9,10-tetrahydrobenzo[c]phenanthridine(**7h**)*



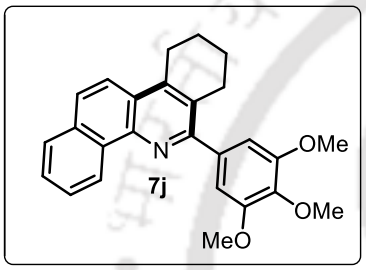
Yield 80% (328 mg), yellow solid, mp > 350 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.27 (d, *J* = 8.8 Hz, 1H), 8.39 (d, *J* = 8.8 Hz, 2H), 7.93-7.89 (m, 4H), 7.86 (d, *J* = 9.2 Hz, 1H), 7.68 (t, *J* = 3.6 Hz, 2H), 3.56 (dd, *J* = 17.6, 5.2Hz, 1H), 3.18-3.09 (m, 1H), 2.79 (d, *J* = 15.2 Hz, 1H), 2.69 (t, *J* = 12.0 Hz, 1H), 2.26 (dd, *J* = 12.4, 5.6Hz, 1H), 1.57-1.49 (m, 1H), 1.44-1.39 (m, 1H), 0.93 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 156.1, 148.2, 147.7, 143.6, 143.2, 133.3, 132.1,130.7, 129.3, 128.2, 128.0, 127.8, 127.2, 124.9, 124.7, 123.5, 120.7, 44.6, 32.6, 30.4, 27.8, 27.4, 23.9; **IR (KBr)νmax** 3069, 2957, 2926, 2896, 2864, 1639, 1599, 1108, 1014 cm^{-1}; **HRMS** (APCI) Calcd For $C_{27}H_{27}N_2O_2$ 411.2067 ($M + H^+$); Found 411.2064.

*6-(3-bromophenyl)-8-(tert-butyl)-7,8,9,10-tetrahydrobenzo[c]phenanthridine (**7i**)*



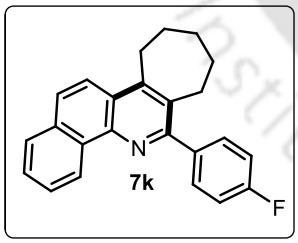
Yield 80% (354 mg), white solid, mp 185-186 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.32 (d, *J* = 8.0 Hz, 1H), 7.96 (s, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.76 (s, 2H), 7.68-7.61 (m, 4H), 7.38 (t, *J* = 8.0 Hz, 1H), 3.35-3.30 (m, 1H), 2.98-2.92 (m, 1H), 2.80 (d, *J* = 16.0 Hz, 1H), 2.62-2.55 (m, 1H), 2.12 (d, *J* = 12.0 Hz, 1H), 1.37-1.30 (m, 1H), 0.94 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 156.7, 143.6, 143.3, 142.6, 133.1,132.8, 132.0, 131.0, 129.5, 129.2, 128.1, 127.7, 127.6, 127.4, 126.9, 124.9, 124.2, 122.4, 120.7, 44.3, 32.4, 30.3, 27.5, 27.4, 23.7; **IR (KBr)νmax** 3067, 3053, 2960, 2886, 1556, 1549, 1129, 1064, 1022, 997 cm^{-1}; **HRMS** (ESI) Calcd For $C_{27}H_{27}BrN$ 444.1321 ($M + H^+$); Found 444.1330.

*6-(3,4,5-trimethoxyphenyl)-7,8,9,10-tetrahydrobenzo[c]phenanthridine (**7j**)*



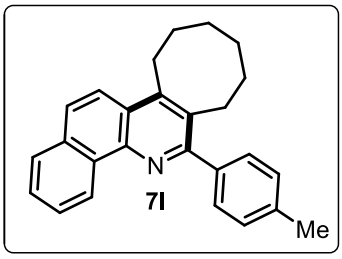
Yield 88% (351 mg), brown solid, mp 138-139 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.37 (d, *J* = 7.2 Hz, 1H), 7.90 (t, *J* = 9.0 Hz, 2H), 7.83 (d, *J* = 9.6 Hz, 1H), 7.69-7.64 (m, 2H), 6.91 (s, 2H), 3.95 (s, 3H), 3.94 (s, 6H), 3.28 (t, *J* = 6.0 Hz, 2H), 2.89 (t, *J* = 6.0 Hz, 2H), 2.04-2.00 (m, 2H), 1.84-1.80 (m, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 158.2, 153.2, 143.2, 143.0, 138.3, 136.6, 133.3, 131.7, 129.3, 127.9, 127.7, 127.6, 127.0, 125.3, 124.6, 120.6, 107.1, 61.2, 56.5, 29.1, 26.5, 22.9, 22.6; **IR (KBr)νmax** 3051, 2996, 2936, 2860, 2834, 1622, 1584, 1170, 1126, 1006 cm^{-1}; **HRMS** (ESI) Calcd For $C_{26}H_{26}NO_3$ 400.1907 ($M + H^+$); Found 400.1927.

*6-(4-fluorophenyl)-8,9,10,11-tetrahydro-7H-benzo[h]cyclohepta[c]quinoline (**7k**)*



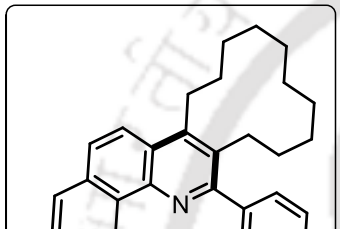
Yield 91% (310 mg), white solid, mp 159-160 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.35 (d, *J* = 5.4 Hz, 1H), 8.04 (d, *J* = 9.6 Hz, 1H), 7.88-7.87 (m, 1H), 7.81 (d, *J* = 9.0 Hz, 1H), 768-7.64 (m, 4H), 7.21 (t, *J* = 8.4 Hz, 2H), 3.38 (t, *J* = 5.4 Hz, 2H), 3.08-3.06 (m, 2H), 1.97-1.93 (m, 2H), 1.84-1.81 (m, 2H), 1.73-1.69(m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 164.1, 161.6, 156.4, 150.0, 144.3, 138.2, 134.8, 133.2, 132.2, 131.7, 131.6, 128.0, 127.5, 127.4, 126.9, 125.2, 123.7, 121.2, 115.3, 115.1, 32.1, 30.9, 28.7, 27.5, 26.5; **IR (KBr)νmax** 3046, 2981, 2936, 2910, 2875, 1635, 1538, 1052, 1014 cm^{-1}; **HRMS** (ESI) Calcd For $C_{24}H_{21}FN$ 342.1653 ($M + H^+$); Found 342.1659.

*6-(p-tolyl)-7,8,9,10,11,12-hexahydrobenzo[h]cycloocta[c]quinoline (**7l**)* Yield 85% (298 mg), white solid, mp 151-152 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.32-9.31 (m, 1H), 7.98 (d, *J* = 9.0 Hz, 1H), 7.88-7.86 (m, 1H), 7.80 (d, *J* = 9.0 Hz, 1H), 7.63-7.62 (m, 2H), 7.50 (d, *J* = 7.8 Hz, 2H), 7.31 (d, *J* = 7.8 Hz, 2H), 3.37-3.36 (m, 2H), 3.02 (t, *J* = 5.4 Hz, 2H), 2.46 (s, 3H), 1.94-1.93 (m, 2H), 1.64-1.63 (m, 2H), 1.46-1.45 (m, 2H), 1.39-1.38 (m, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 158.8, 146.6, 144.2, 139.9, 137.5, 133.1, 132.4, 129.3, 128.8, 127.7, 127.5, 127.2, 126.8, 125.2, 123.8, 121.7, 32.1, 30.4, 28.8, 26.9, 26.8, 26.2, 21.5; **IR (KBr)νmax** 3054, 2925, 2846, 1634, 1570, 1117, 1068, 1027 cm^{-1}; **HRMS** (APCI) Calcd For $C_{26}H_{26}N$ 352.2060 ($M + H^+$); Found 352.2074.



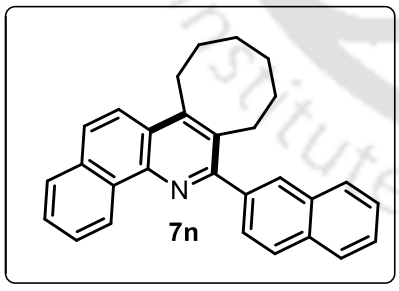
*6-phenyl-7,8,9,10,11,12,13,14,15,16-decahydrobenzo[h]cyclododeca[c]quinoline (**7m**)*

Yield 67% (263 mg), white solid, mp 166-167 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.31 (s, 1H), 7.96, (d, *J* = 9.2 Hz, 1H), 7.87 (s, 1H), 7.80 (d, *J* = 9.2 Hz, 1H), 7.63 (s, 4H), 7.50-7.45 (m, 3H), 3.25 (t, *J* = 6.8 Hz, 2H), 2.93 (t, *J* = 7.2 Hz, 2H), 1.92-1.91 (m, 2H), 1.67-1.66 (m, 4H), 1.58-1.48 (m, 8H), 1.35-1.34 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 159.5, 146.7, 143.0, 133.1, 132.6, 132.4, 129.2, 128.2, 127.8, 127.5, 127.2, 126.8, 125.2, 124.8, 122.1, 29.1, 28.9, 28.6, 28.5, 28.4, 27.7, 27.4, 27.0, 22.8; **IR (KBr)νmax** 3058, 2925, 2845, 1570, 1118, 1072, 1025 cm^{-1}; **HRMS** (ESI) Calcd For $C_{29}H_{32}N$ 394.2530 ($M + H^+$); Found 394.2530.

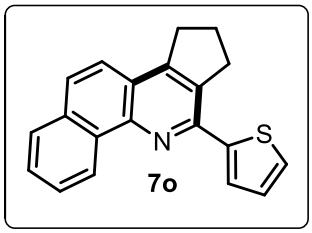


*6-(naphthalen-2-yl)-7,8,9,10,11,12-hexahydrobenzo[h]cycloocta[c]quinoline (**7n**)*

Yield 76% (294 mg), white solid, mp 166-167 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.36 (s, 1H), 8.09 (s, 1H), 8.02 (d, *J* = 9.6 Hz, 1H), 7.98 (d, *J* = 8.4 Hz, 1H), 7.94 (d, *J* = 3.0 Hz, 2H), 7.89 (t, *J* = 3.0 Hz, 1H), 7.84 (d, *J* = 9.0 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.65 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.55 (dd, *J* = 5.4, 2.4 Hz, 2H), 3.41 (t, *J* = 5.4 Hz, 2H), 3.06 (t, *J* = 6.0 Hz, 2H), 1.97 (t, *J* = 5.4 Hz, 2H), 1.64-1.63 (m, 2H), 1.47-1.46 (m, 2H), 1.43-1.42 (m, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 158.3, 147.5, 143.8, 139.6, 133.4, 133.2, 133.1, 133.0, 131.9, 128.7, 128.6, 128.0, 127.9, 127.8, 127.7, 127.6, 127.0, 126.4, 126.3, 125.3, 124.0, 121.6, 32.0, 30.5, 28.9, 27.1, 26.7, 26.3; **IR (KBr)νmax** 3042, 2929, 2854, 1608, 1549, 1082, 1036, 1012, 956 cm^{-1}; **HRMS** (APCI) Calcd For $C_{29}H_{26}N$ 388.2060 ($M + H^+$); Found 388.2045.

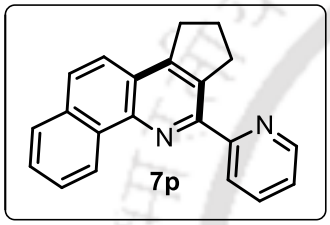


*6-(thiophen-2-yl)-8,9-dihydro-7H-benzo[h]cyclopenta[c]quinoline (**7o**)*



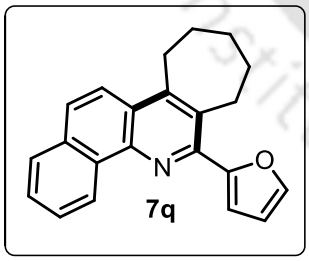
Yield 85% (255 mg), white solid, mp 166-167 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.40 (d, *J* = 8.4 Hz, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.74 (t, *J* = 6.8 Hz, 1H), 7.69-7.67 (m, 2H), 7.63-7.62 (m, 1H), 7.61-7.56 (m, 1H), 7.51 (d, *J* = 18.8 Hz, 1H), 7.17 (t, *J* = 4.4 Hz, 1H), 3.29 (t, *J* = 7.6 Hz, 2H), 3.23 (t, *J* = 7.6 Hz, 2H), 2.31-2.24 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 152.1, 147.5, 147.1, 144.6, 133.6, 133.5, 131.8, 128.2, 128.1, 127.9, 127.8, 127.1, 127.0, 126.7, 125.2, 122.6, 122.2, 33.8, 31.2, 24.5; **IR (KBr)νmax** 3053, 2954, 2915, 2847, 1577, 1119, 1055, 1024 cm^{-1}; **HRMS** (ESI) Calcd For $C_{20}H_{16}NS$ 302.0998 ($M + H^+$); Found 302.1012.

*6-(pyridin-2-yl)-8,9-dihydro-7H-benzo[h]cyclopenta[c]quinoline (**7p**)*



Yield 78% (230 mg), brown solid, mp 128-129 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.45 (d, *J* = 8.4 Hz, 1H), 8.74 (d, *J* = 4.2 Hz, 1H), 8.67 (d, *J* = 7.8 Hz, 1H), 7.90 (d, *J* = 7.2 Hz, 2H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.75-7.71 (m, 2H), 7.67 (t, *J* = 7.2 Hz, 1H), 7.33 (t, *J* = 6.0 Hz, 1H), 3.68 (t, *J* = 7.2 Hz, 2H), 3.35 (t, *J* = 7.8 Hz, 2H), 2.33-2.28 (m, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 153.1, 147.3, 144.8, 139.1, 137.2, 133.6, 132.1, 128.7, 128.1, 128.0, 127.4, 125.5, 124.6, 124.2, 123.7, 122.2, 34.2, 31.3, 25.1; **IR (KBr)νmax** 3052, 2921, 2850, 1574, 1192, 1097, 1022, 987 cm^{-1}; **HRMS** (APCI) Calcd For $C_{21}H_{17}N_2$ 297.1386 ($M + H^+$); Found 297.1376.

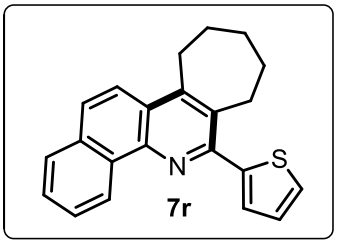
*6-(furan-2-yl)-8,9,10,11-tetrahydro-7H-benzo[h]cyclohepta[c]quinoline (**7q**)*



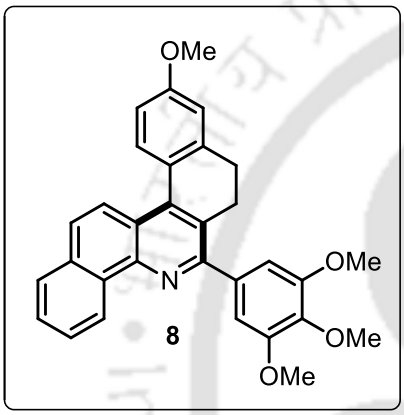
Yield 72% (225 mg), brown solid, mp 83-84 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.37 (d, *J* = 7.6 Hz, 1H), 7.99 (d, *J* = 8.8 Hz, 1H), 7.86 (d, *J* = 7.2 Hz, 1H), 7.77 (d, *J* = 9.2 Hz, 1H), 7.70 (d, *J* = 6.8 Hz, 1H), 7.68-7.65 (m, 2H), 7.08 (d, *J* = 3.2 Hz, 1H), 6.62-6.61 (m, 1H), 3.78 (t, *J* = 5.6 Hz, 2H), 3.31 (t, *J* = 5.2 Hz, 2H), 1.94 (d, *J* = 5.6 Hz, 2H), 1.79 (d, *J* = 3.2 Hz, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 155.5, 150.4, 146.8, 144.6, 143.1, 134.6, 133.2, 132.2, 128.0, 127.5, 127.4, 127.0, 125.2, 123.7, 121.2, 111.6, 111.5, 31.9, 29.9, 28.3, 27.0, 26.6; **IR (KBr)νmax** 3049, 2921, 2853, 1621, 1571, 1163, 1126, 1076, 1009 cm^{-1}; **HRMS** (ESI) Calcd For $C_{22}H_{20}NO$ 314.1540 ($M + H^+$); Found 314.1547.

*6-(thiophen-2-yl)-8,9,10,11-tetrahydro-7H-benzo[h]cyclohepta[c]quinoline (**7r**)* Yield 84% (276 mg), brown solid, mp 142-143 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.39 (d, *J* = 8.0 Hz,

1H), 7.96 (d, *J* = 9.2 Hz, 1H), 7.86 (d, *J* = 7.6 Hz, 1H), 7.76 (d, *J* = 9.2 Hz, 1H), 7.71 (t, *J* = 10.0 Hz, 1H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.51 (d, *J* = 5.2 Hz, 1H), 7.40 (d, *J* = 2.8 Hz, 1H), 7.18 (t, *J* = 3.6 Hz, 1H), 3.55, (t, *J* = 5.2 Hz, 2H), 3.31 (t, *J* = 5.2 Hz, 2H), 1.97 (d, *J* = 4.8 Hz, 2H), 1.80, (s, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 150.5, 150.1, 145.7, 144.2, 134.4, 133.2, 131.9, 128.1, 127.6, 127.6,127.5, 127.4, 127.4, 127.0, 125.3, 123.4, 121.1, 31.9, 30.4, 28.5, 27.0, 26.6; **IR (KBr)νmax** 3062, 2966, 2923, 2853, 1683, 1652, 1101, 1079, 1027 cm^{-1}; **HRMS** (ESI) Calcd For $C_{22}H_{20}NS$ 330.1311 ($M + H^+$); Found 330.1311.

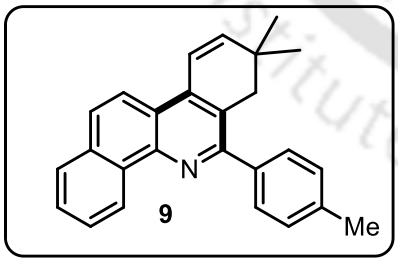


*10-methoxy-6-(3,4,5-trimethoxyphenyl)-7,8-dihydrodibenzo[c,k]phenanthridine (**8**)*



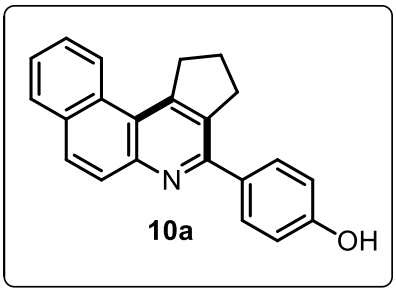
Yield 64% (305 mg), brown solid, mp 208-209 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.41 (d, *J* = 6.8 Hz, 1H), 8.33 (d, *J* = 8.8 Hz, 1H), 7.91 (t, *J* = 8.0 Hz, 2H), 7.80 (d, *J* = 9.6 Hz, 1H), 7.23-7.66 (m, 2H), 7.02 (s, 2H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.97 (s, 1H), 3.96 (s, 3H), 3.94 (s, 6H), 3.92 (s, 3H), 3.03 (t, *J* = 6.4 Hz, 2H), 2.77 (t, *J* = 7.2 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 160.1, 156.4, 153.2, 145.9, 142.5, 141.6, 138.5, 136.8, 133.2, 132.2, 131.3, 129.2, 128.1, 127.5, 127.2, 126.9, 125.6, 125.2, 123.5, 121.5, 113.6, 111.8, 107.3, 61.2, 56.5, 55.6, 30.2, 27.8; **IR (KBr)νmax** 3062, 2935, 2834, 1607, 1584, 1123, 1064, 1034, 1005 cm^{-1}; **HRMS** (ESI) Calcd For $C_{31}H_{28}NO_4$ 478.2013 ($M + H^+$); Found 478.2014.

*8,8-dimethyl-6-(p-tolyl)-7,8-dihydrobenzo[c]phenanthridine (**9**)*



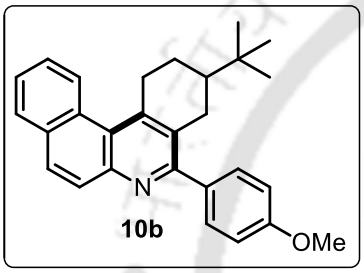
Yield 82% (286 mg), brown solid, mp 174-175 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.37 (d, *J* = 8.0 Hz, 1H), 8.01 (d, *J* = 12.0 Hz, 1H), 7.89-7.87 (m, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.68-7.63 (m, 3H), 7.36 (d, *J* =12.0 Hz, 2H), 7.25 (d, *J* = 12.0 Hz, 1H), 6.25 (d, *J* = 8.0 Hz, 1H), 4.45 (s, 1H), 2.96 (s, 2H), 2.48 (s, 3H), 1.07 (s, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 157.0, 145.1, 144.7, 138.2, 137.8, 136.6, 133.0, 131.9, 129.6, 128.8, 127.7, 127.4, 127.1, 126.7,124.9, 124.8, 120.5, 120.2, 120.1, 39.9, 32.0, 29.7, 27.2, 21.4; **IR (KBr)νmax** 3029, 2956, 2918, 2895, 2857, 1627, 1583, 1564, 1115, 1024, 1000 cm^{-1}; **HRMS** (ESI) Calcd For $C_{26}H_{24}N$ 350.1903 ($M + H^+$); Found 350.1908.

*4-(2,3-dihydro-1H-benzo[f]cyclopenta[c]quinolin-4-yl)phenol (**10a**)*



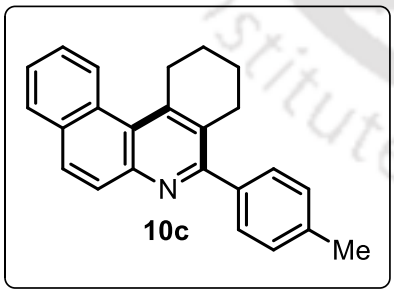
Yield 78% (242 mg), white solid, mp 308-309 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.42 (s, 1H), 8.56 (d, *J* = 8.4 Hz, 1H), 7.91-7.83 (m, 3H), 7.72 (d, *J* = 7.8 Hz, 2H), 7.59-7.55 (m, 2H), 6.89 (d, *J* = 8.4 Hz, 2H), 3.65-3.62 (m, 2H), 3.18-3.16 (m, 2H), 2.17-2.15 (m, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 156.9, 152.6, 149.5, 146.0, 134.9, 130.9, 129.6, 129.1, 128.9, 128.6, 127.6, 127.3, 125.3, 125.2, 125.1, 121.0, 114.0, 35.8, 31.8, 24.6; **IR (KBr)νmax** 3446, 1636, 1607, 1548, 1145, 1104, 1018 cm^{-1}; **HRMS** (ESI) Calcd For $C_{22}H_{18}NO$ 312.1383 ($M + H^+$); Found 312.1382.

*3-(tert-butyl)-5-(4-methoxyphenyl)-1,2,3,4-tetrahydrobenzo[a]phenanthridine (**10b**)*



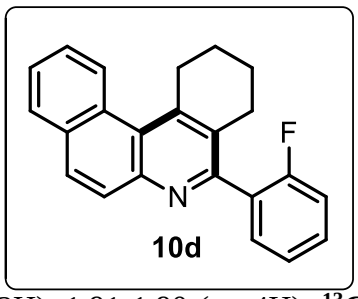
Yield 72% (284 mg), brown solid, mp 206-207 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.76 (d, *J* = 8.4 Hz, 1H), 7.98 (d, *J* = 8.4 Hz, 1H), 7.95-7.94 (m, 1H), 7.88 (d, *J* = 9.0 Hz, 1H), 7.64-7.61 (m, 2H), 7.52 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 8.4 Hz, 2H), 3.89 (s, 3H), 3.70 (d, *J* = 16.2 Hz, 1H), 3.63-3.61 (m, 1H), 3.01 (dd, *J* = 16.8, 5.4 Hz, 1H), 2.56 (dd, *J* = 16.8, 11.4 Hz, 1H), 2.16 (dd, *J* = 12.6, 2.4 Hz, 1H), 1.64-1.63 (m, 1H), 1.26-1.22 (m, 1H), 0.90 (s, 9H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 159.6, 159.2, 146.6, 145.2, 133.9, 133.5, 130.4, 130.3, 130.1, 130.0, 129.4, 129.1, 128.5, 126.3, 125.7, 124.6, 113.9, 55.5, 44.3, 34.6, 32.7, 30.4, 27.2, 24.9; **IR (KBr)νmax** 3016, 2948, 2858, 1635, 1609, 1109, 1033, 834 cm^{-1}; **HRMS** (ESI) Calcd For $C_{28}H_{30}NO$ 396.2322 ($M + H^+$); Found 396.2341.

*5-(p-tolyl)-1,2,3,4-tetrahydrobenzo[a]phenanthridine (**10c**)*



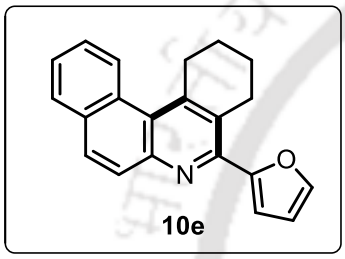
Yield 74% (239 mg), white solid, mp 146-147 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.77 (d, *J* = 9.0 Hz, 1H), 8.04 (d, *J* = 8.4 Hz, 1H), 7.96-7.95 (m, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.66-7.61 (m, 2H), 7.44 (d, *J* = 7.8 Hz, 2H), 7.30 (d, *J* = 7.8 Hz, 2H), 3.62 (t, *J* = 6.0 Hz, 2H), 2.89 (t, *J* = 6.6 Hz, 2H), 2.44 (s, 3H), 1.92-1.83 (m, 4H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 159.1, 146.3, 145.7, 138.0, 133.6, 130.4, 130.3, 129.3, 129.2, 129.1, 128.9, 128.6, 126.4, 125.8, 124.9, 33.5, 28.7, 23.3, 22.4, 21.5; **IR (KBr)νmax** 3049, 3027, 2936, 2860, 1613, 1559, 1118, 1020 cm^{-1}; **HRMS** (ESI) Calcd For $C_{24}H_{22}N$ 324.1747 ($M + H^+$); Found 324.1746.

*5-(2-fluorophenyl)-1,2,3,4-tetrahydrobenzo[a]phenanthridine (**10d**)*



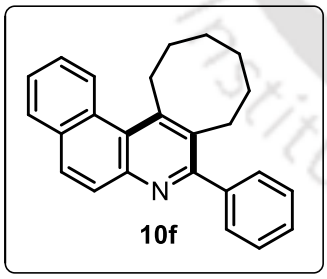
Yield 78% (255 mg), brown solid, mp 108-109 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.78-8.76 (m, 1H), 8.01 (d, *J* = 9.0 Hz, 1H), 7.96-7.94 (m, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.65-7.61 (m, 2H), 7.49-7.47 (m, 1H), 7.46-7.42 (m, 1H), 7.30 (t, *J* = 6.6 Hz, 1H), 7.21-6.98 (m, 1H), 3.62 (t, *J* = 5.4 Hz, 2H), 2.90-2.69 (m, 2H), 1.91-1.90 (m, 4H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 160.7, 159.1, 154.5, 146.7, 145.5, 133.6, 131.2, 131.1, 130.5, 130.3, 130.2, 129.1, 129.0, 128.6, 126.6, 125.8, 125.5, 124.8, 116.0, 115.9, 33.5, 27.4, 23.4, 22.2; **IR (KBr)νmax** 3055, 2935, 2861, 1616, 1579, 1122, 1092, 1030, 1006 cm^{-1}; **HRMS** (ESI) Calcd For $C_{23}H_{19}FN$ 328.1496 ($M + H^+$); Found 328.1496.

*5-(furan-2-yl)-1,2,3,4-tetrahydrobenzo[a]phenanthridine (**10e**)*



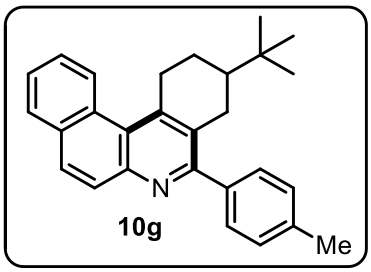
Yield 75% (224 mg), brown solid, mp 116-118 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.74-8.72 (m, 1H), 8.00-7.98 (d, *J* = 8.0 Hz, 1H), 7.94-7.92 (m, 1H), 7.89-7.87 (d, *J* = 9.2 Hz, 1H), 7.68-7.67 (m, 1H), 7.62-7.59 (m, 2H), 7.06 (d, *J* = 3.6 Hz, 1H), 6.60-6.59 (m, 1H), 3.58 (t, *J* = 6.0 Hz, 2H), 3.22 (t, *J* = 6.8 Hz, 2H), 2.03-1.99 (m, 2H), 1.86-1.84 (m, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 153.8, 147.9, 146.9, 145.8, 143.5, 133.7, 130.4, 130.3, 129.4, 129.1, 128.7, 128.6, 126.4, 125.8, 124.9, 112.7, 111.6, 33.9, 27.9, 23.2, 22.5; **IR (KBr)νmax** 3054, 2962, 2905, 1944, 1605, 1543, 1096 cm^{-1}; **HRMS** (APCI) Calcd For $C_{21}H_{18}NO$ 300.1383 ($M + H^+$); Found 300.1391.

*8-phenyl-9,10,11,12,13,14-hexahydrobenzo[f]cycloocta[c]quinoline (**10f**)*



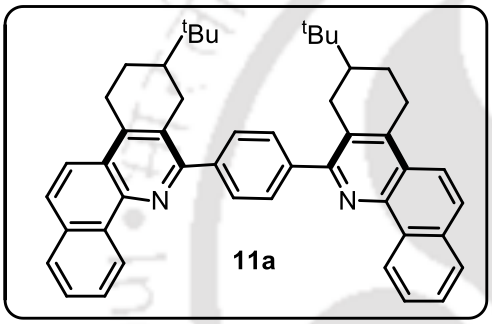
Yield 80% (269 mg), brown solid, mp 128-129 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.83 (d, *J* = 8.4 Hz, 1H), 8.05 (s, 1H), 7.95 (d, *J* = 7.8 Hz, 1H), 7.91 (d, *J* = 9.0 Hz, 1H), 7.69-7.63 (m, 2H), 7.51-7.49 (t, *J* = 7.8 Hz, 4H), 7.47-7.43 (m, 1H), 3.62 (s, 2H), 2.97 (t, *J* = 6.0 Hz, 2H), 2.26 (t, *J* = 4.8 Hz, 2H), 1.72-1.71 (m, 2H), 1.70-1.64 (m, 2H), 1.54-1.53 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 159.6, 148.8, 147.2, 142.1, 133.6, 133.2, 130.7, 130.3, 129.5, 129.4, 128.8, 127.9, 127.8, 126.4, 126.3, 124.8, 31.2, 31.1, 30.8, 28.5, 27.4, 26.0; **IR (KBr)νmax** 3055, 2925, 2852, 1737, 1605, 1548, 1118, 1072, 1029, 1009 cm^{-1}; **HRMS** (ESI) Calcd For $C_{25}H_{24}N$ 338.1903 ($M + H^+$); Found 338.1903.

*3-(tert-butyl)-5-(p-tolyl)-1,2,3,4-tetrahydrobenzo[a]phenanthridine (**10g**)*



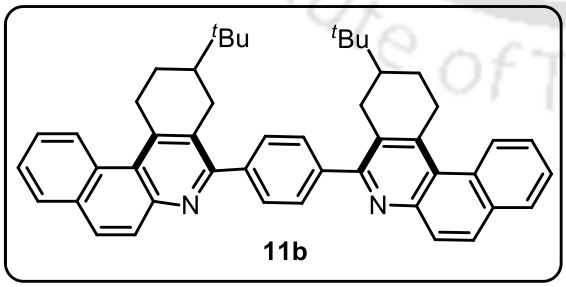
Yield 75% (284 mg), white solid, mp 255-256 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.76 (d, *J* = 6.0 Hz, 1H), 7.99 (d, *J* = 12.0 Hz, 1H), 7.95 (d, *J* = 6.0 Hz, 1H), 7.89 (d, *J* = 6.0 Hz. 1H), 7.62-7.61 (t, *J* = 6.0 Hz, 2H), 7.46 (d, *J* = 12.0 Hz, 2H), 7.31 (d, *J* = 6.0 Hz, 2H), 3.71 (d, *J* = 18.0 Hz, 1H), 3.63 (d, *J* = 6.0 Hz, 1H), 3.0 (dd, *J* = 6.0, 12.0 Hz, 1H), 2.56 (t, *J* = 12.0 Hz, 1H), 2.45 (s, 3H), 2.17 (d, *J* = 12.0 Hz, 1H), 1.64 (s, 1H), 1.26-1.22 (m, 1H), 0.90 (s, 9H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 159.6, 146.6, 145.2, 138.5, 137.8, 133.5, 130.4, 130.1, 129.4, 129.2, 129.1, 128.9, 128.5, 126.3, 125.7, 124.7, 44.3, 34.6, 32.7, 30.3, 27.2, 24.9, 21.5; **IR (KBr)νmax** 3016, 2931, 2868, 1619, 1554, 1180, 1121, 1016 cm^{-1}; **HRMS** (ESI) Calcd For $C_{28}H_{30}N$ 380.2373 ($M + H^+$); Found 380.2387.

*1,4-bis(8-(tert-butyl)-7,8,9,10-tetrahydrobenzo[c]phenanthridin-6-yl)benzene (**11a**)*



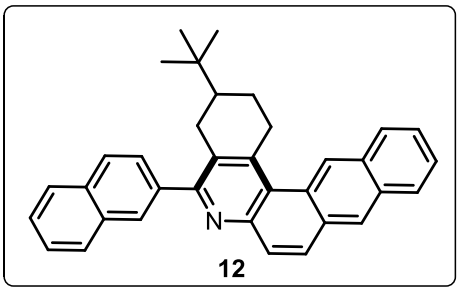
Yield 68% (443 mg), pale yellow solid, mp > 350 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.00 (t, *J* = 12.0 Hz, 2H), 8.25 (d, *J* = 6.0 Hz, 2H), 8.17 (s, 4H), 7.98 (d, *J* = 6.0 Hz, 2H), 7.94 (s, 2H), 7.90 (s, 4H), 3.90 (d, *J* = 18.0 Hz, 2H), 3.47 (d, *J* = 12.0 Hz, 2H), 2.88 (d, *J* = 18.0 Hz, 2H), 2.67 (d, *J* = 12.0 Hz, 2H), 2.42 (s, 2H), 1.62 (d, *J* = 12.0 Hz, 4H), 0.93 (s, 9H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 161.7, 161.5, 161.2, 160.9, 158.2, 151.1, 135.2, 134.8, 134.2, 133.1, 132.8, 132.3, 130.2, 130.1, 129.9, 127.3, 122.8, 122.3, 119.4, 117.7, 115.8, 113.9, 111.9, 43.5, 32.5, 29.6, 29.5, 26.9, 22.9; **IR (KBr)νmax** 3082, 2996, 2956, 2867, 1581, 1081, 1019, 999 cm^{-1}; **HRMS** (ESI) Calcd For $C_{48}H_{49}N_2$ 653.3890 ($M + H^+$); Found 653.3887.

*1,4-bis(3-(tert-butyl)-1,2,3,4-tetrahydrobenzo[a]phenanthridin-5-yl)benzene (**11b**)*



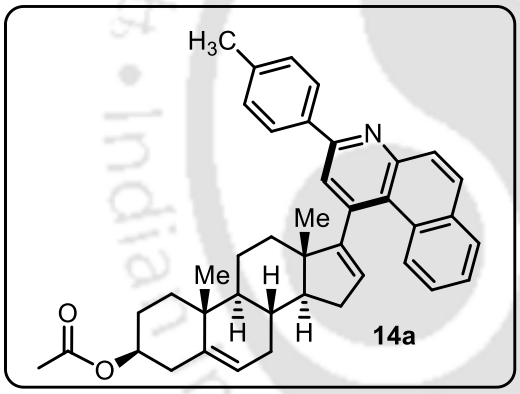
Yield 75% (489 mg), pale yellow solid, mp > 350 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.93 (d, *J* = 8.0 Hz, 2H), 8.37-8.34 (m, 2H), 8.20-8.17 (m, 2H), 7.99-7.92 (m, 6H), 7.89-7.86 (m, 4H), 4.05-3.90 (m, 4H), 3.05-2.99 (m, 2H), 2.77-2.68 (m, 2H), 2.38 (d, *J* = 18.0 Hz, 2H), 1.79 (s, 2H), 1.48-1.38(m, 2H), 0.91 (s, 9H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 161.6, 161.2, 160.8, 160.4, 160.1, 149.3, 138.4, 138.3, 134.1, 133.5, 133.4, 130.9, 130.1, 129.9, 129.7, 128.7, 128.2, 127.4, 119.2, 117.5, 116.3, 113.5, 110.6, 43.3, 36.1, 32.6, 29.7, 26.7, 23.9; **IR (KBr)νmax** 3136, 3080, 2968, 2874, 1683, 1555, 1057, 1021, 998 cm^{-1}; **HRMS** (APCI) Calcd For $C_{48}H_{49}N_2$ 653.3890 ($M + H^+$); Found 653.3897.

*3-(tert-butyl)-5-(naphthalen-2-yl)-1,2,3,4-tetrahydronaphtho[2,3-b]phenanthridine (**12**)* Yield



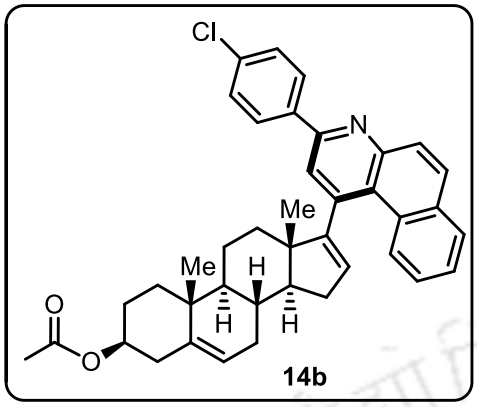
92% (428 mg), brown solid, mp 285-286 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.24 (s, 1H), 8.43 (s, 1H), 8.15-8.14 (m, 1H), 8.07-8.04 (m, 2H), 7.98-7.96 (m, 2H), 7.94-7.92 (m, 2H), 7.89 (d, *J* = 8.4 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.60 (t, *J* = 4.2 Hz, 2H), 7.54 (t, *J* = 4.2 Hz, 2H), 3.84-3.80 (m, 2H), 3.08 (dd, *J* = 16.8, 5.4Hz, 1H), 2.62 (dd, *J* = 16.8, 11.4 Hz, 1H), 2.24 (d, *J* = 12.0 Hz, 1H), 1.69 (t, *J* = 12.0 Hz, 2H), 0.85 (s, 9H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 158.9, 147.3, 145.9, 138.8, 133.7, 133.2, 131.9, 131.5, 131.4, 130.9, 130.3, 128.9, 128.7, 128.6, 128.5, 128.4, 128.1, 127.9, 127.7, 127.1, 127.0, 126.6, 126.4, 126.3, 126.1, 125.0, 44.4, 34.7, 32.8, 30.3, 27.2, 25.1; **IR (KBr)νmax** 3064, 2926, 2847, 1639, 1558, 1105, 1017, 885 cm^{-1}; **HRMS** (ESI) Calcd For $C_{35}H_{32}N$ 466.2530 ($M + H^+$); Found 466.2532.

*(3S,8R,9S,10R,13S,14S)-10,13-dimethyl-17-(3-(p-tolyl)benzo[f]quinolin-1-yl)-2,3,4,7,8,9,10,11,12,13,14,15-dodecahydro-1H-cyclopenta[a]phenanthren-3-yl acetate (**14a**)*



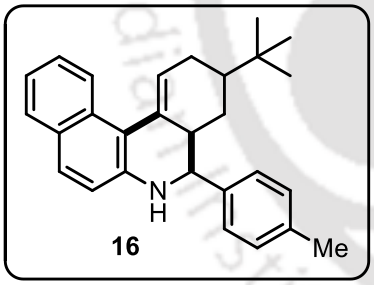
Yield 68% (395 mg), white solid, mp 216-217 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.46 (d, *J* = 6.0 Hz, 1H), 8.11 (d, *J* = 6.0 Hz, 2H), 8.07 (d, *J* = 6.0 Hz, 1H), 7.95 (d, *J* = 12.0 Hz, 1H), 7.90 (d, *J* = 6.0 Hz, 1H), 7.59 (d, *J* = 6.0 Hz, 1H), 7.55 (s, 2H), 7.35(d, *J* = 6.0 Hz, 2H), 6.03 (s, 1H), 5.45 (s, 1H), 4.59 (s, 1H), 2.62 (d, *J* = 12.0 Hz, 1H), 2.44 (s, 3H), 2.37-2.25 (m, 3H), 2.16 (s, 1H), 2.03 (s, 3H), 1.97 (s, 1H), 1.80 (s, 3H), 1.71 (d, *J* = 12.0 Hz, 1H), 1.54 (t, *J* = 12.0 Hz, 1H), 1.37 (s, 1H), 1.27 (d, *J* = 18.0 Hz, 2H), 1.06 (t, *J* = 12.0 Hz, 3H), 0.99 (s, 3H), 0.92 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 170.8, 157.7, 155.5, 149.3, 144.9, 140.3, 139.5, 136.7, 132.6, 131.2, 131.1, 129.7, 129.5, 128.6, 128.4, 128.1, 127.5, 126.9, 125.7, 123.8, 122.4, 122.2, 57.5, 51.7, 50.4, 38.3, 37.0, 33.2, 32.8, 32.0, 31.3, 27.9, 21.6, 21.5, 20.8, 19.4, 17.2; **IR (KBr)νmax** 3157, 2967, 2722, 1647, 1567, 1167, 1102, 1019, 952 cm^{-1}; **HRMS** (ESI) Calcd For $C_{41}H_{44}NO_2$ 582.3367 ($M + H^+$); Found 582.3371.

*(3S,8R,9S,10R,13S,14S)-17-(3-(4-chlorophenyl)benzo[f]quinolin-1-yl)-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15-dodecahydro-1H-cyclopenta[a]phenanthren-3-yl acetate (**14b**)*



Yield 72% (432 mg), white solid, mp 229-230 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.47 (d, *J* = 12.0 Hz, 1H), 8.17 (d, *J* = 6.0 Hz, 2H), 8.05 (d, *J* = 6.0 Hz, 1H), 7.96 (d, *J* = 12.0 Hz, 1H), 7.90, (d, *J* = 6.0 Hz, 1H), 7.61 (d, *J* = 6.0 Hz, 1H), 7.57 (d, *J* = 6.0 Hz, 1H), 7.54 (s, 1H), 7.51 (d, *J* = 6.0 Hz, 2H), 6.00 (s, 1H), 5.45 (s, 1H), 4.60 (s, 1H), 2.63 (d, *J* = 12.0 Hz, 1H), 2.37 (d, *J* = 6.0 Hz, 1H), 2.33-2.25 (m, 2H), 2.18 (d, *J* = 18.0 Hz, 1H), 2.03 (s, 3H), 1.99 (s, 1H), 1.85-1.81 (m, 3H), 1.71-1.69 (d, *J* = 18.0 Hz, 2H), 1.56-1.50 (m, 1H), 1.38-1.37 (m, 1H), 1.28 (s, 2H), 1.09-1.02 (m, 2H), 0.99 (s, 3H), 0.92 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 170.7, 157.5, 154.2, 149.4, 145.2, 140.3, 137.9, 135.6, 132.7, 131.4, 131.1, 129.3, 129.2, 128.8, 128.7, 128.4, 128.3, 127.1, 125.9, 124.1, 122.4, 121.9, 74.0, 57.5, 51.5, 50.4, 38.3, 36.9, 33.2, 32.8, 31.9, 31.3, 27.9, 21.6, 20.7, 19.4, 17.2; **IR (KBr)νmax** 3047, 3028, 2926, 1689, 1653, 1589, 1030, 964 cm^{-1}; **HRMS** (ESI) Calcd For $C_{40}H_{41}ClNO_2$ 602.2820 (M + H^+); Found 602.2823.

*(4aR,5S)-3-(tert-butyl)-5-(p-tolyl)-2,3,4,4a,5,6-hexahydrobenzo[a]phenanthridine (**16**)*



Yield 25% (93.5 mg), brown solid, mp 120-121 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.08 (d, *J* = 8.0 Hz, 1H), 7.55 (d, *J* = 4.0 Hz, 1H), 7.37-7.34 (m, 1H), 7.25-7.21 (m, 3H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.02 (t, *J* = 8.0 Hz, 1H), 6.89-6.86 (m, 1H), 6.24 (s, 1H), 6.15 (d, *J* = 4.0 Hz, 1H), 4.47 (d, *J* = 12.0 Hz, 1H), 2.49-2.47 (d, *J* = 8.0 Hz, 1H), 2.31 (s, 3H), 2.23 (s, 1H), 2.16-2.08 (m, 1H), 1.45 (d, *J* = 12.0 Hz, 2H), 1.35 (dd, *J* = 12.0, 4.0 Hz, 2H), 0.81 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 141.0, 140.6, 137.9, 132.8, 130.9, 129.4, 128.6, 128.1, 127.9, 126.3, 125.3, 123.7, 121.4, 116.8, 114.3, 110.1, 62.8, 39.4, 38.4, 32.4, 27.7, 27.4, 25.1, 21.4; **IR (KBr)ν_{max}** 3042, 2957, 2925, 2856, 1619, 1569, 1152, 1082, 1020, 968 cm^{-1}; **HRMS** (APCI) Calcd For $C_{28}H_{32}N$ 382.2529 (M + H^+); Found 382.2526.

Single crystal data for the Compounds.

Complete crystallographic data of compounds for the structural analyses have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. Copies of this information may be obtained free of charge from the Director, Cambridge Crystallographic Data Centre, 12

Union Road, Cambridge CB2 1EZ, UK, (fax: +44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk or via: www.ccdc.cam.ac.uk).

Table 9. Crystal Data and Structure Refinement for Compound **6a** and **7n**

Entry	Identification code	Compound 6a	Compound 7n
01	Empirical formula	C_{25} H_{29} N O	C_{22} H_{19} N S
02	Formula weight	359.49	329.44
03	Temperature	296(2) K	296(2) K
04	Wavelength	0.71073	0.71073
05	Radiation type	MoK\a	MoK\a
06	Radiation source	'fine-focus sealed tube'	'fine-focus sealed tube'
07	Crystal system	triclinic	monoclinic
08	Space group	P-1	P21/n
09	Cell length	a 6.2831(7) b 12.7652(14) c 13.3011(14)	a 10.3709(13) b 16.766(2) c 10.7394(13)
10	Cell Angle	α 83.604 (8) β 84.300 (9) δ 89.560 (9)	α 90.00 β 114.581(6) δ 90.00
11	Cell Volume	1054.9(2)	1698.1(4)
12	Density	1.132	1.289
13	Completeness to theta	25.24° / 89.5%	25.04° / 99.9%
14	Absorption correction	multi-scan	multi-scan
15	Refinement method	Full-matrix least-squares on F2	Full-matrix least-squares on F2
16	Index ranges	-7<=h<=7, -15<=k<=15, -15<=l<=15	-12<=h<=12, -19<=k<=19, -12<=l<=12
17	Reflection number	3416	3000
18	Theta range	1.78-25.24	1.89-25.04
19	Cell formula units Z	2	4
20	CCDC no	1448168	1448169

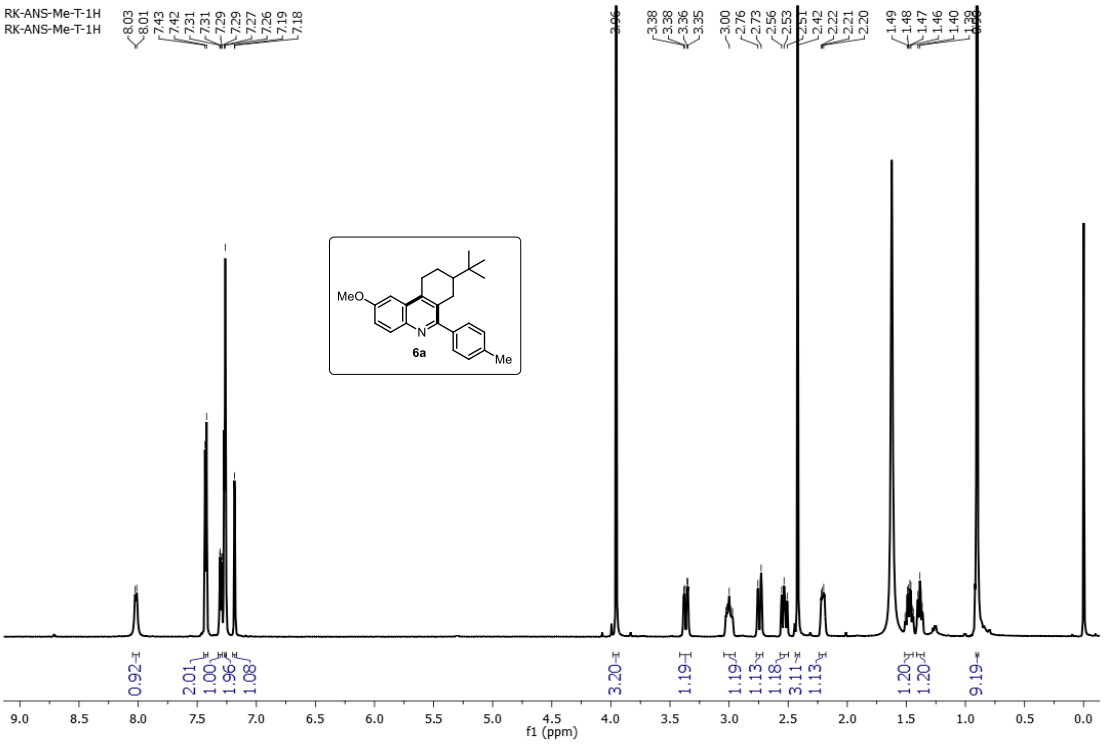
Table 10. Crystal Data and Structure Refinement for Compound **8 and 10e**

Entry	Identification code	Compound 8	Compound 10e
01	Empirical formula	C_{31} H_{27} N O_4	C_{21} H_{17} N O
02	Formula weight	477.54	299.36
03	Temperature	293(2) K	293(2) K
04	Wavelength	0.71073	0.71073
05	Radiation type	MoK\a	MoK\a
06	Radiation source	'fine-focus sealed tube'	'fine-focus sealed tube'
07	Crystal system	monoclinic	triclinic
08	Space group	P21/n	P-1
09	Cell length	a 8.4733(10) b 8.8139(10) c 32.111(3)	a 9.1124(9) b 9.1345(10) c 10.9267(12)
10	Cell Angle	α 90.00 β 92.043(11) δ 90.00	α 113.534(7) β 97.413(7) δ 108.934(7)
11	Cell Volume	2396.6(5)	752.86(14)
12	Density	1.322	1.321
13	Completeness to theta	28.80° / 88.2%	25.24° / 98.0%
14	Absorption correction	multi-scan	multi-scan
15	Refinement method	Full-matrix least-squares on F2	Full-matrix least-squares on F2
16	Index ranges	-7<=h<=11, -9<=k<=11, -43<=l<=42	-10<=h<=10, -10<=k<=10, -13<=l<=13
17	Reflection number	5522	2659
18	Theta range	2.99-28.80	1.73-25.24
19	Cell formula units Z	4	2
20	CCDC no	1448171	1448180

Table 11. Crystal Data and Structure Refinement for Compound **14b and 16**

Entry	Identification code	Compound 14b	Compound 16
01	Empirical formula	$C_{40}H_{40}ClNO_2$	$C_{28}H_{31}N$
02	Formula weight	602.18	381.54
03	Temperature	296(2) K	293(2) K
04	Wavelength	0.71073	0.71073
05	Radiation type	MoK\a	Mo K\a
06	Radiation source	'fine-focus sealed tube'	'fine-focus sealed tube'
07	Crystal system	monoclinic	triclinic
08	Space group	P21	P-1
09	Cell length	a 7.3419(7) b 15.3072(12) c 14.5765(14)	a 10.2452(8) b 10.4468(8) c 10.9779(9)
10	Cell Angle	α 90.00 β 90.22(10) δ 90.00	α 77.834(7) β 86.634(7) δ 71.187(7)
11	Cell Volume	1638.2(2)	1087.15(15)
12	Density	1.232	1.169
13	Completeness to theta	36.98° / 98.0%	28.94° / 98.3%
14	Absorption correction	multi-scan	multi-scan
15	Refinement method	Full-matrix least-squares on F2	Full-matrix least-squares on F2
16	Index ranges	-9<=h<=9, -20<=k<=20, -19<=l<=19	-13<=h<=13, -14<=k<=14, -14<=l<=14
17	Reflection number	8410	5636
18	Theta range	2.98-36.98	2.98-28.94
19	Cell formula units Z	2	2
20	CCDC no	1500291	1500292

***^{1}H NMR (600 MHz, $CDCl_3$)**: 8-(tert-butyl)-2-methoxy-6-(p-tolyl)-7,8,9,10-tetrahydrophenanthridine) (6a)*



***^{13}C NMR (150 MHz, $CDCl_3$)**: 8-(tert-butyl)-2-methoxy-6-(p-tolyl)-7,8,9,10-tetrahydrophenanthridine (6a)*

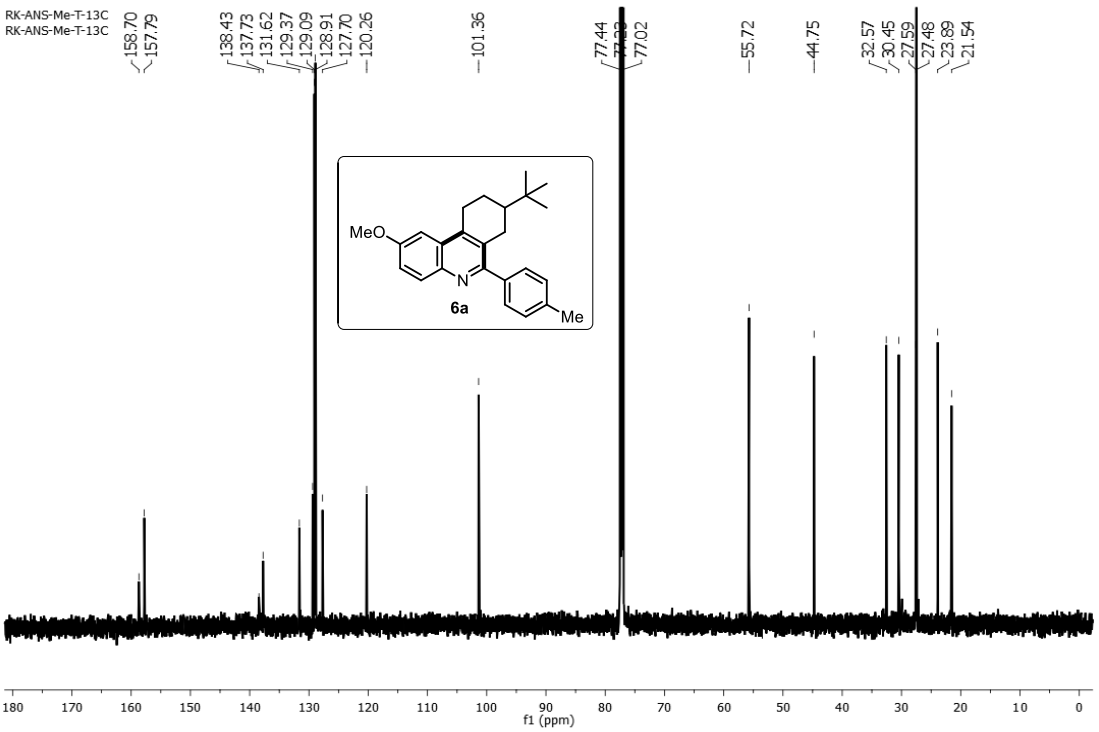
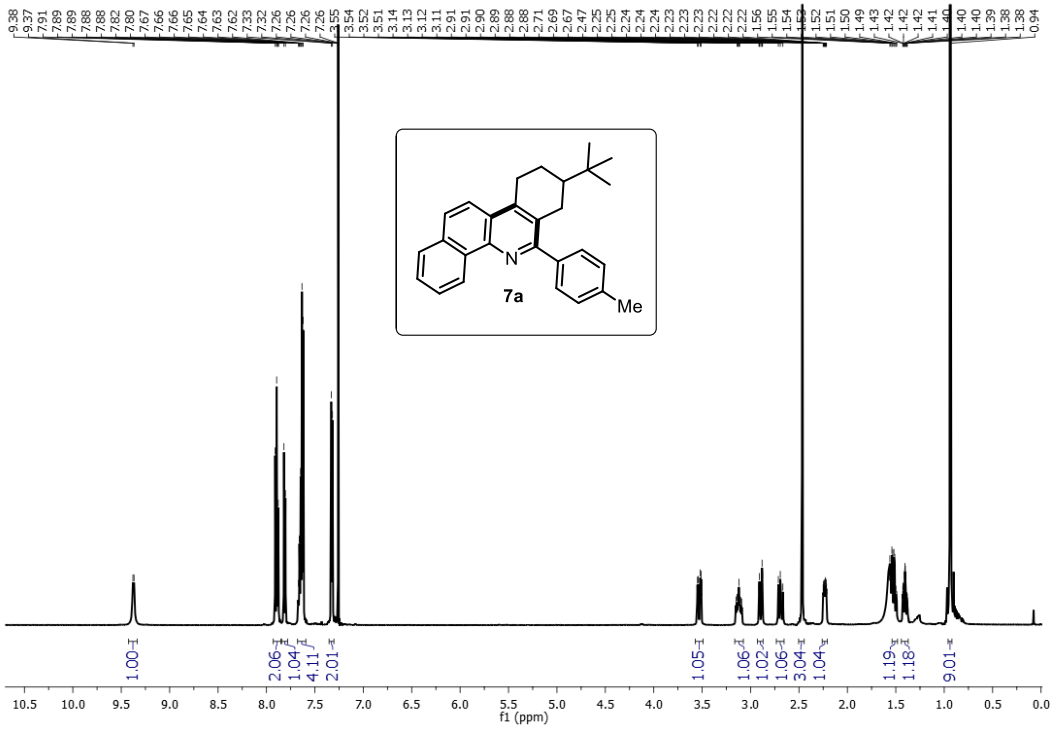


Figure 13

^{1}H NMR (600 MHz, $CDCl_3$): **8**-*(tert-butyl)-6-(p-tolyl)-7,8,9,10-tetrahydrobenzo[c]phenanthridine (**7a**)*



^{13}C NMR (150 MHz, $CDCl_3$): *8-(tert-butyl)-6-(p-tolyl)-7,8,9,10-tetrahydrobenzo[c]phenanthridine (**7a**)*

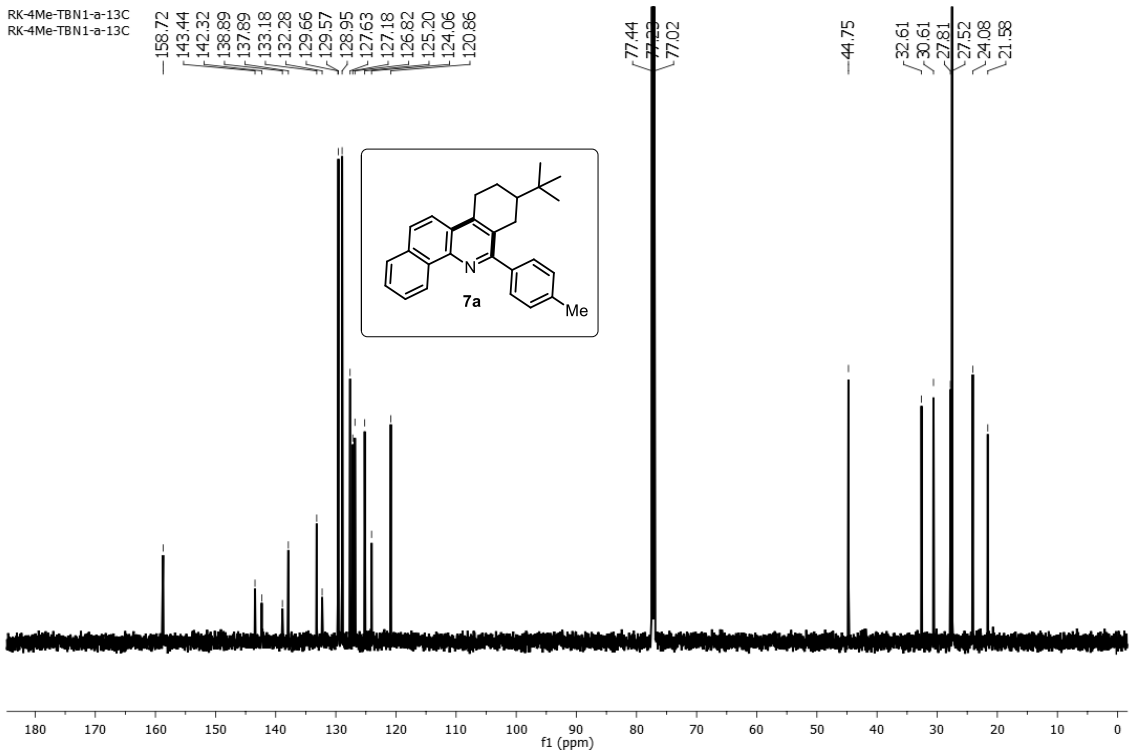
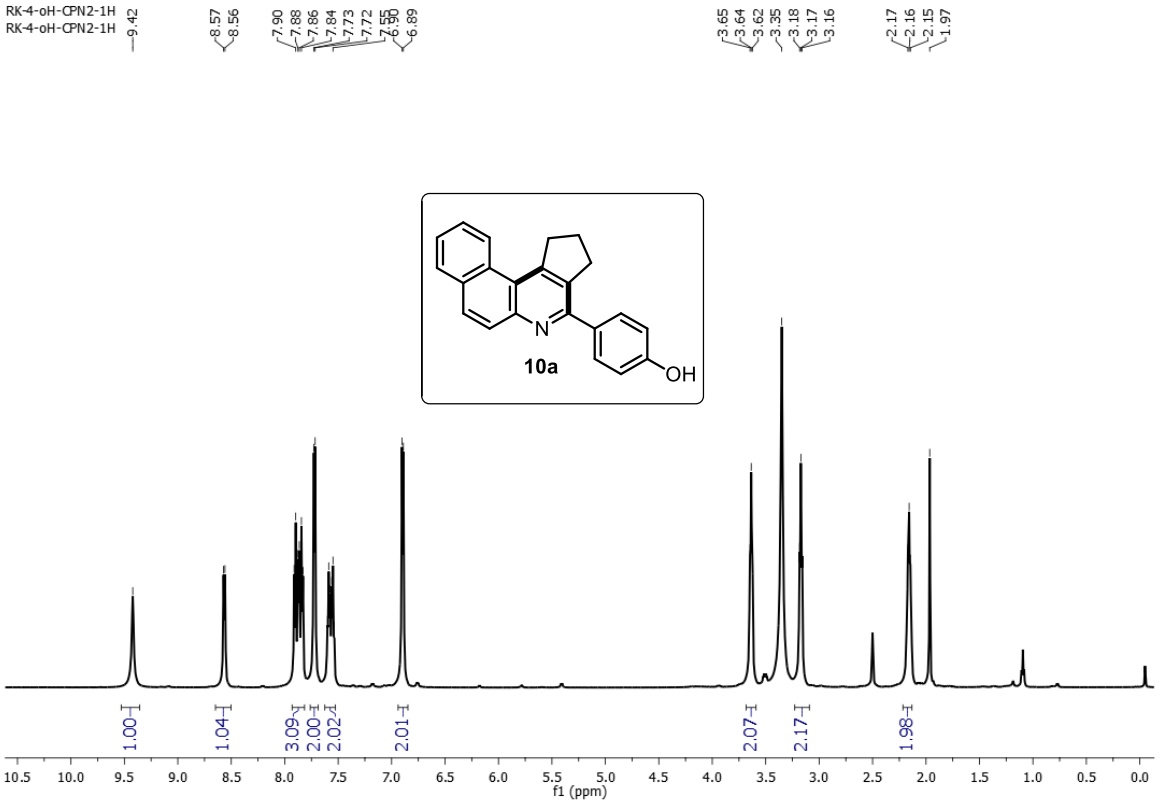


Figure 14

***^{1}H NMR (600 MHz, $CDCl_3$)**: 4-(2,3-dihydro-1H-benzo[f]cyclopenta[c]quinolin-4-yl)phenol (**10a**)*



***^{13}C NMR (150 MHz, $CDCl_3$)**: 4-(2,3-dihydro-1H-benzo[f]cyclopenta[c]quinolin-4-yl)phenol (**10a**)*

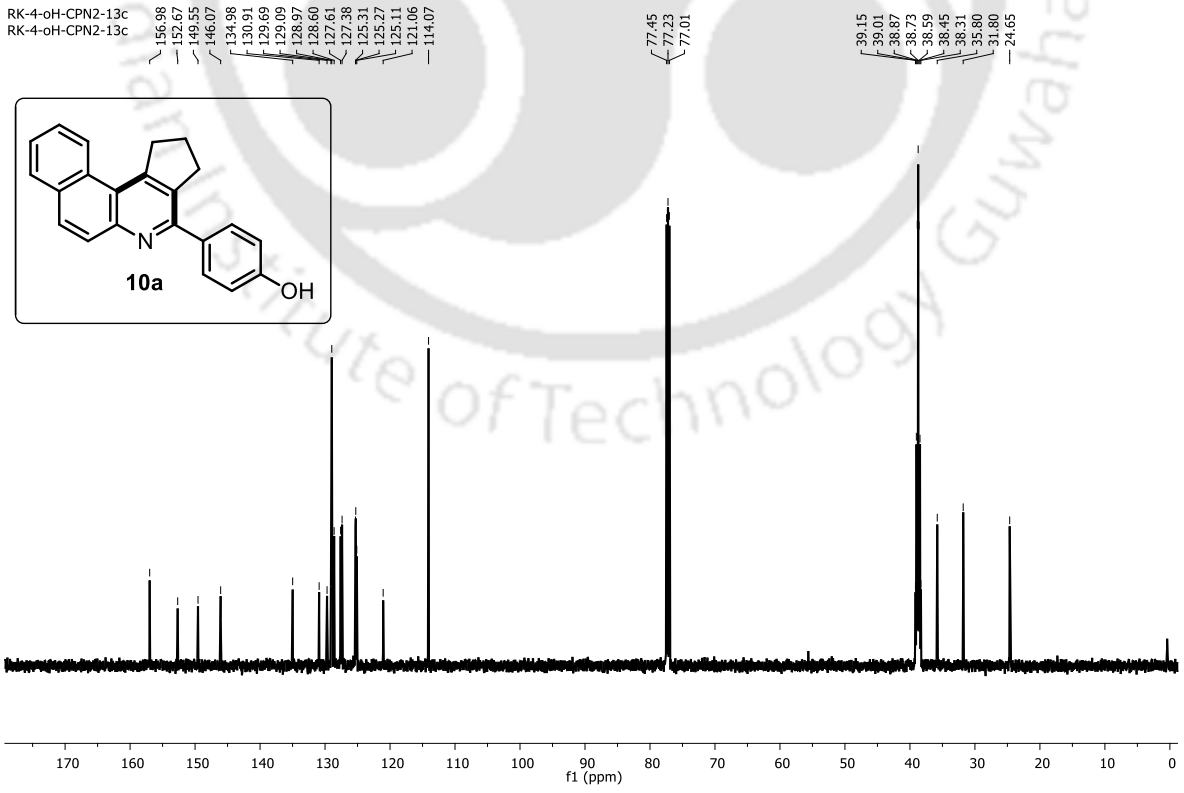
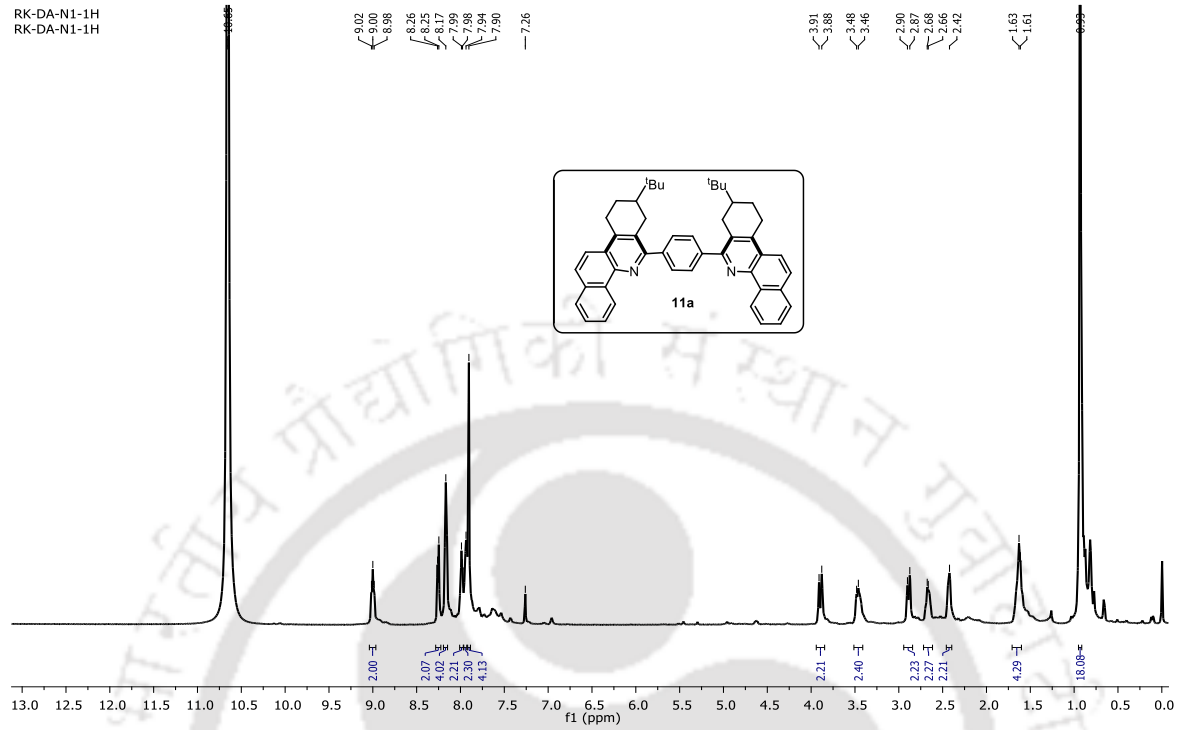


Figure 15

***^{1}H NMR (600 MHz, $CDCl_3$)**: 1,4-bis(8-(tert-butyl)-7,8,9,10-tetrahydrobenzo[c]phenanthridin-6-yl)benzene (**11a**)*



***^{13}C NMR (150 MHz, $CDCl_3$)**: 1,4-bis(8-(tert-butyl)-7,8,9,10-tetrahydrobenzo[c]phenanthridin-6-yl)benzene (**11a**)*

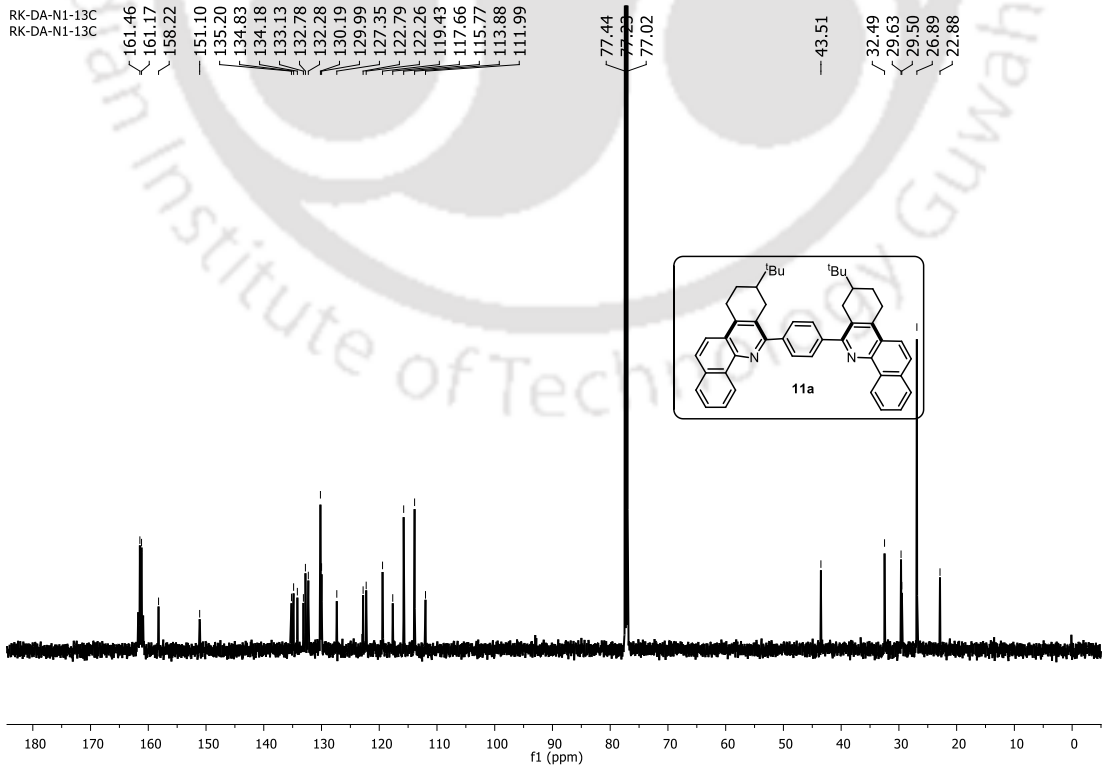
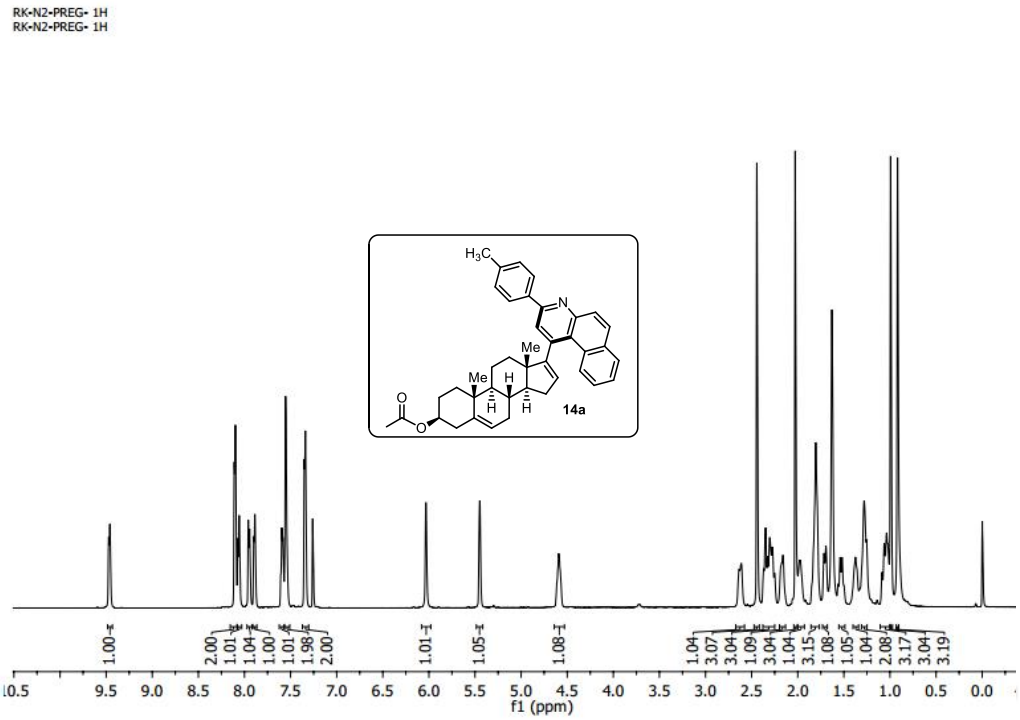


Figure 16

***^{1}H NMR (600 MHz, $CDCl_3$)**: (3S,8R,9S,10R,13S,14S)-10,13-dimethyl-17-(3-(p-tolyl)benzo[f]quinolin-1-yl)-2,3,4,7,8,9,10,11,12,13,14,15-dodecahydro-1H-cyclopenta[a]phenanthren-3-yl acetate (**14a**)*



***^{13}C NMR (150 MHz, $CDCl_3$)**: (3S,8R,9S,10R,13S,14S)-10,13-dimethyl-17-(3-(p-tolyl)benzo[f]quinolin-1-yl)-2,3,4,7,8,9,10,11,12,13,14,15-dodecahydro-1H cyclopenta[a]phenanthren-3-yl acetate (**14a**)*

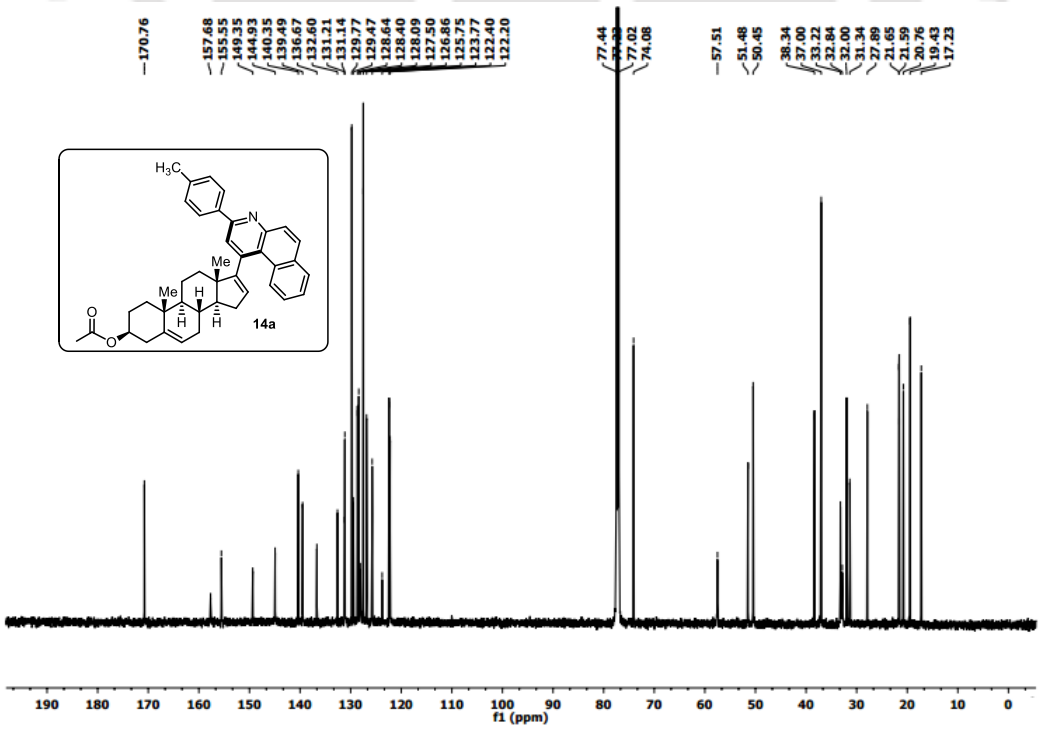
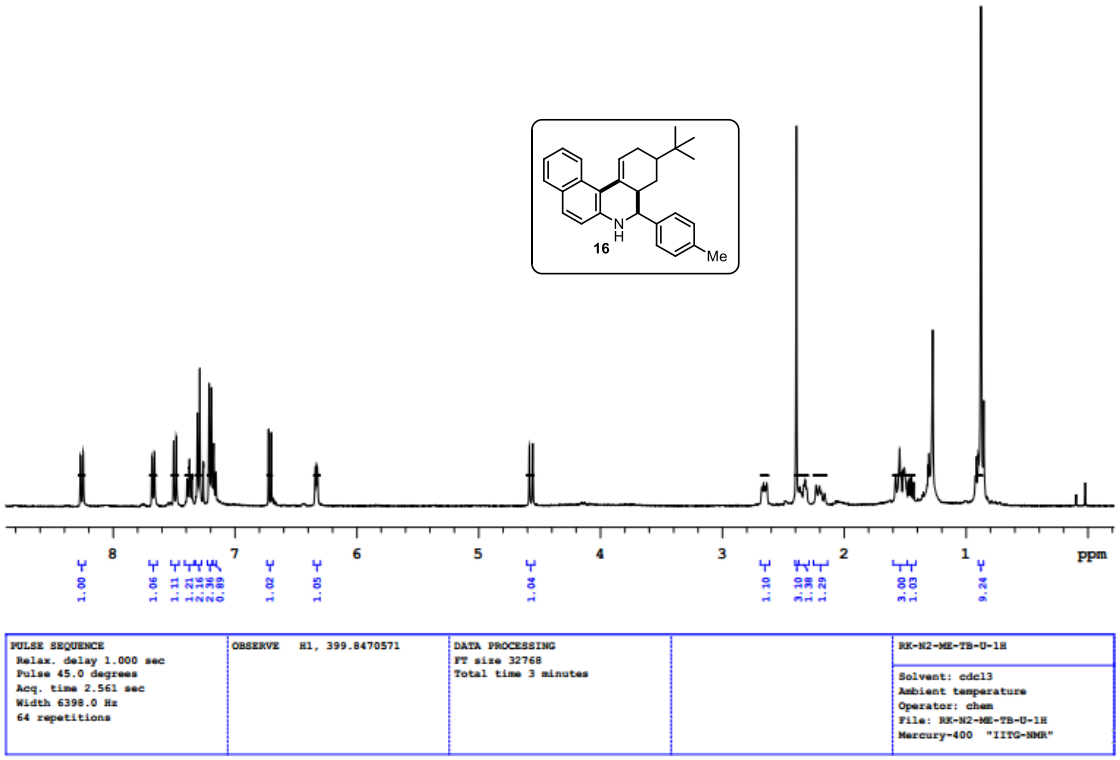


Figure 17

^{1}H NMR (400 MHz, $CDCl_3$): *(4aR,5S)-3-(tert-butyl)-5-(p-tolyl)-2,3,4,4a,5,6 hexahydrobenzo[a]phenanthridine (**16**)*



^{13}C NMR (100 MHz, $CDCl_3$): *(4aR,5S)-3-(tert-butyl)-5-(p-tolyl)-2,3,4,4a,5,6-hexahydrobenzo[a]phenanthridine (**16**)*

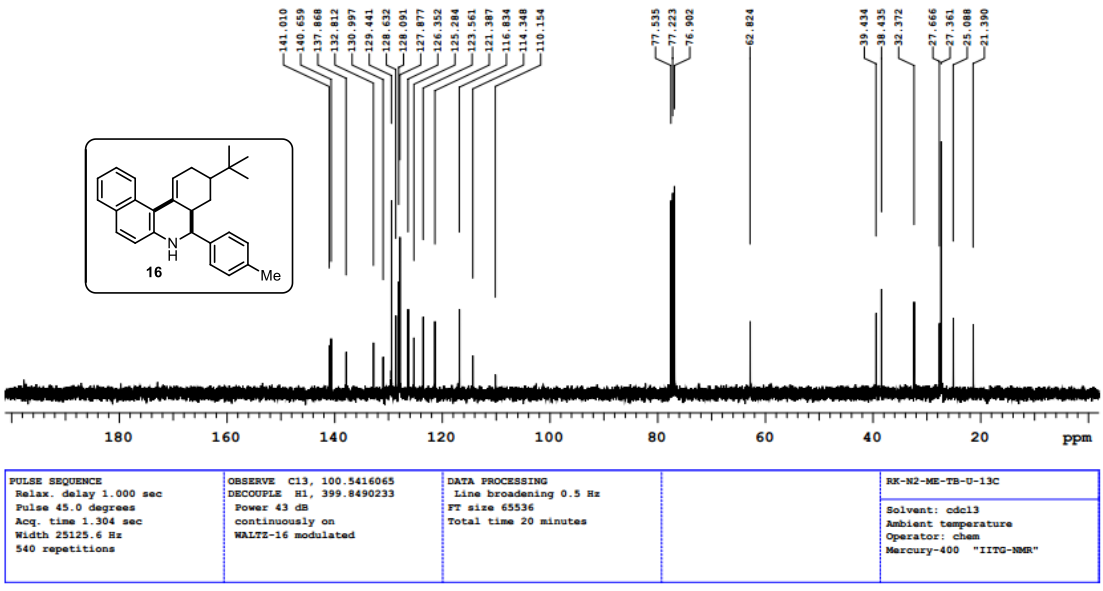


Figure 18a

***HRMS** (ESI): (4aR,5S)-3-(tert-butyl)-5-(p-tolyl)-2,3,4,4a,5,6-hexahydrobenzo[a]phenanthridine (**16**)*

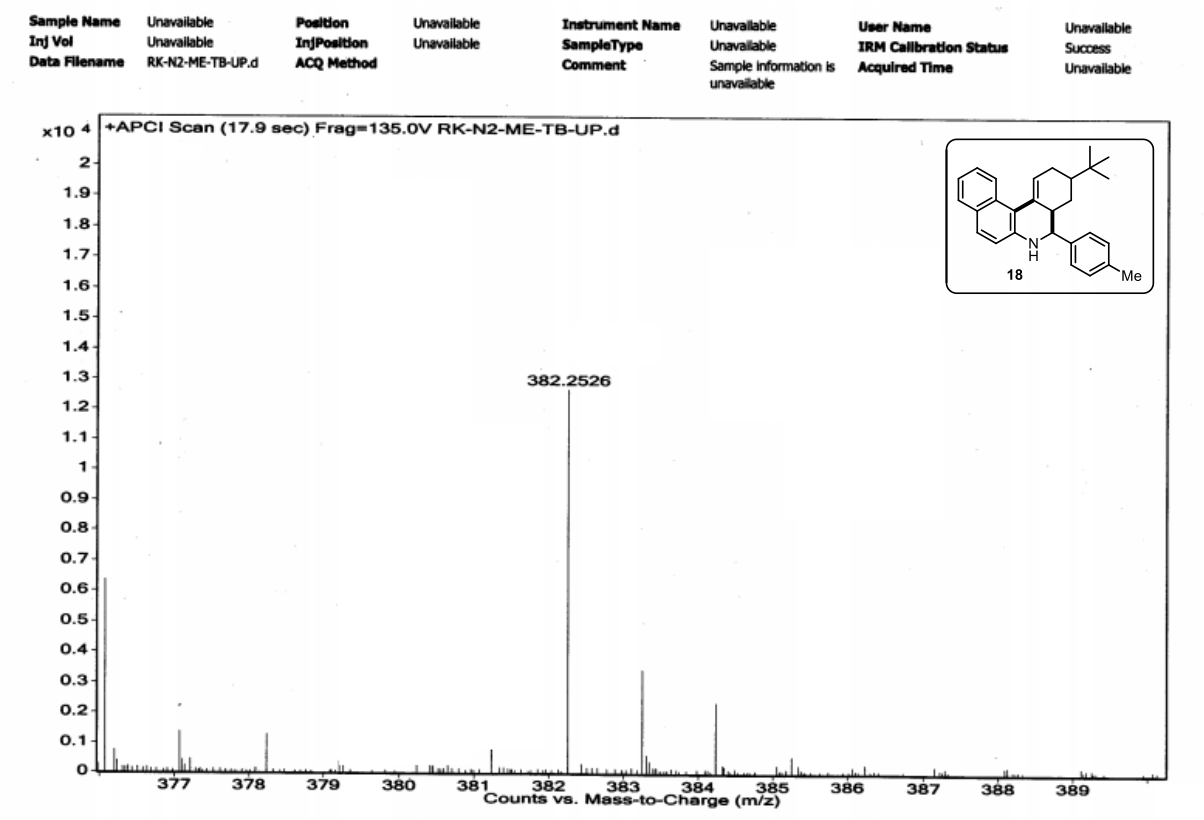
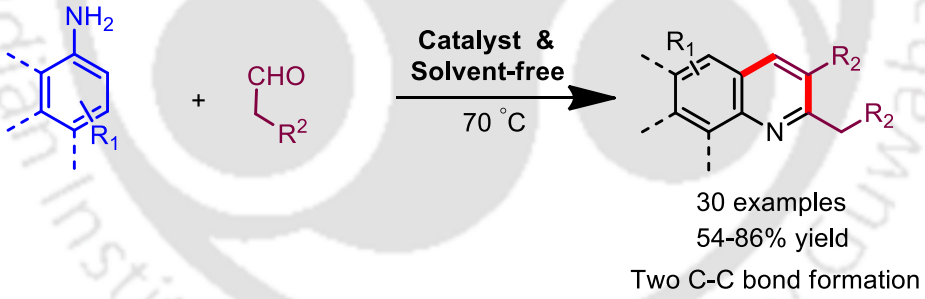


Figure 18b

Chapter IV

Synthesis of 2,3-Di-Substituted Quinoline and Benzoquinolines Through Imino Diels–Alder/ Intramolecular Reaction under Catalyst and Solvent Free



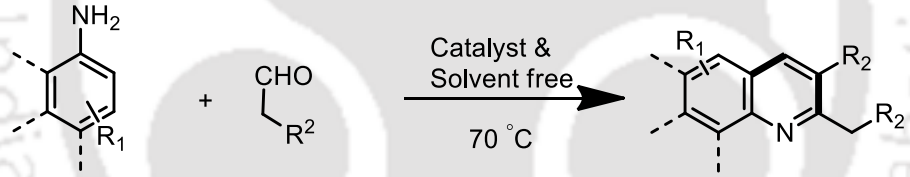
30 examples
54-86% yield
Two C-C bond formation

Result & Discussion

Experimental Section

Results and Discussion

In the previous chapters II and III, various benzoquinoline[77] and quinoline[78] derivatives have been synthesized by employing aromatic aldehyde as one of the reactant. It is noteworthy to mention that when aromatic aldehyde was replaced with aliphatic aldehyde in the reaction with 2-naphthylamine and *β*-ketoester in presence of 10 mol % of camphorsulfonic acid in acetonitrile at 70 °C, it resulted in the formation of 2,3 di-alkyl benzoquinolines. However, the combination of aliphatic aldehyde, aniline and cyclic ketone also resulted in the formation of 2,3-disubstituted quinolines. From the above two reactions, it was observed that neither *β*-keto ester nor cyclic ketone was involved in the reaction in presence of aliphatic aldehyde. These results encouraged us to further explore the reaction of one pot pseudo three component reaction of aniline (1 mmol) and aliphatic aldehyde (2 mmol) for the synthesis of 2,3-di-alkyl quinolines. From the literature reports, it was found that synthesis of 2,3-di-alkyl quinolines was carried out by employing aliphatic aldehyde and anilines using various catalysts. We were interested to study whether catalyst and solvent free reaction condition at 70 °C are favorable for the synthesis of 2,3-di-alkyl quinolines derivatives as shown in the Scheme **50**.

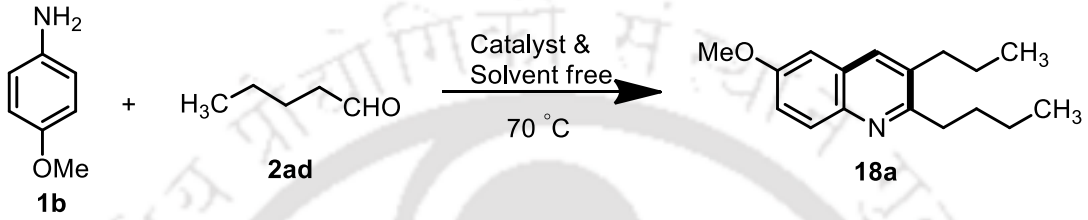


Scheme 50

In order to the optimize reaction condition for the synthesis of 2,3-di-substituted quinolines, we chose *p*-anisidine **1b** (1.0 mmol) and pentanal **2ad** (1.0 mmol) as model substrates and the results are summarized in Table **12**. Initially, when the reaction was carried out in the absence of catalyst in acetonitrile at room temperature, no desired product was obtained (Table 12, entry 1). When the same set of reaction was carried out at 70 °C (Table 12, entry 2), it resulted in the formation of desired product **18a** in 74% yield. The structure of compound **18a** was analysed by using IR, ^{1}H, ^{13}C NMR and HRMS data. The presence of peaks in NMR spectra representative of four aromatic protons, one methoxy group at 3.88 (s, 3H) and alkyl groups at 2.97 – 2.91 (m, 2H), 2.77 – 2.71 (m, 2H), 1.78 – 1.68 (m, 4H), 1.51 – 1.45 (m, 2H), 1.03 (t, J = 7.3 Hz, 3H), 0.97 (t, J = 7.3 Hz, 3H) indicate the formation of compound **18a**. Further, the compound was confirmed through HRMS data ($M + H^{+}$) 258.1855.

Next, the reaction was performed in absence of solvent at 70 °C which resulted in increased yield of 78% (Table 12, entry 3). Further, there was no improvement in the yield when the reaction was screened with various acid catalysts like Acetic acid, HCl and Camphor sulphonic acid (Table 12, entry 4-6). From these observations, it was found that solvent and catalyst free condition was found to be best reaction condition in terms of reaction time and yield.

Table 12. Optimization of Reaction Conditions[a,b,c,d]

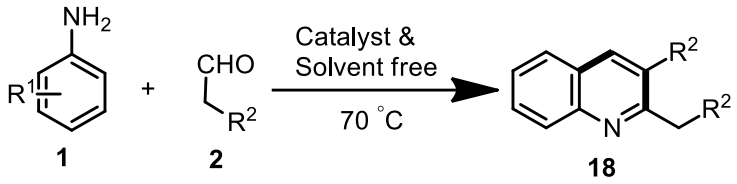


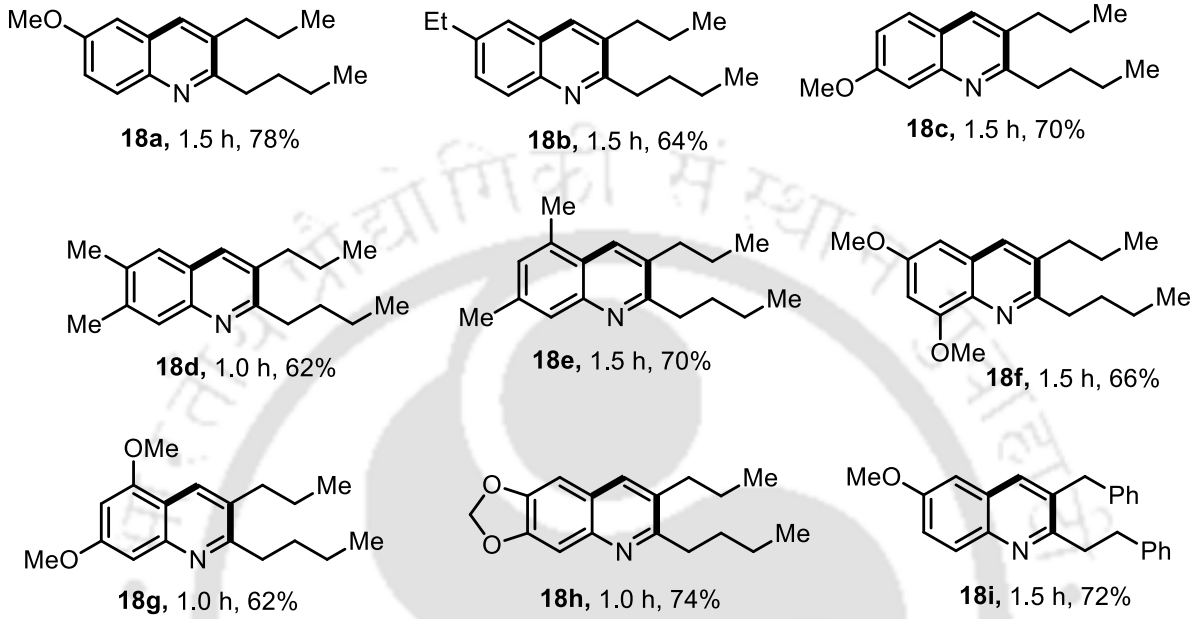
S.No	Catalyst	Mol %	Solvent	Time (h)	Yield (%)[b]
1[c]	No catalyst	-	CH_3CN	24	NR
2	No catalyst	-	CH_3CN	16	74
3	No catalyst	-	-	12	78
4	CH_3COOH	1 equiv.	CH_3CN	12	15
5	HCl	10	CH_3CN	16	trace
6	(±)-CSA	10	CH_3CN	12	66

[a]The reactions were performed using (1a) 2-naphthylamine (1 mmol), (2ad) Pentanal (2 mmol). [b]Isolated yield. [c]Reaction performed at room temperature. NR = No reaction.

With the standard optimisation reaction condition, the scope of the reaction was investigated with various anilines (**1**) and pentanal (**2ad**) which furnished the products **18a-18i** in 66-78% yield as represented in Table **13**. Anilines with electron donating groups worked well, whereas, anilines with electron withdrawing groups such as 4-F, 4-Cl and 4-Br failed to produce desired products. The compound **18i** was identified by XRD analysis and the ORTEP diagram of **18i** is represented in Figure **19**.

Table 13. Scope of Anilines[a,b]





[a]All the reactions were carried out using various anilines (1 mmol) and aliphatic aldehyde (2 mmol) under solvent and catalyst free condition at 70 °C. [b]Isolated yield.

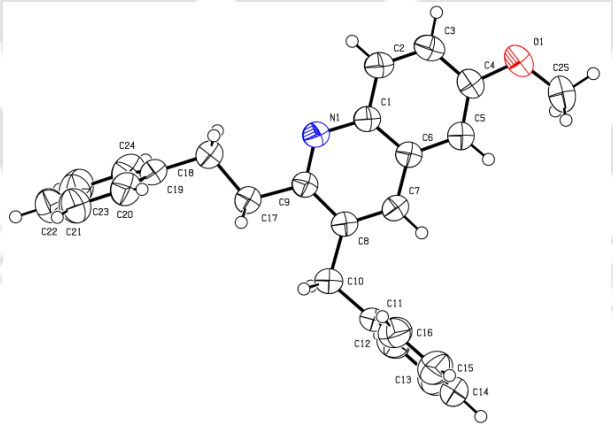
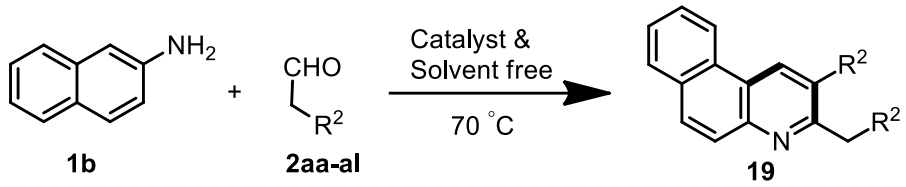


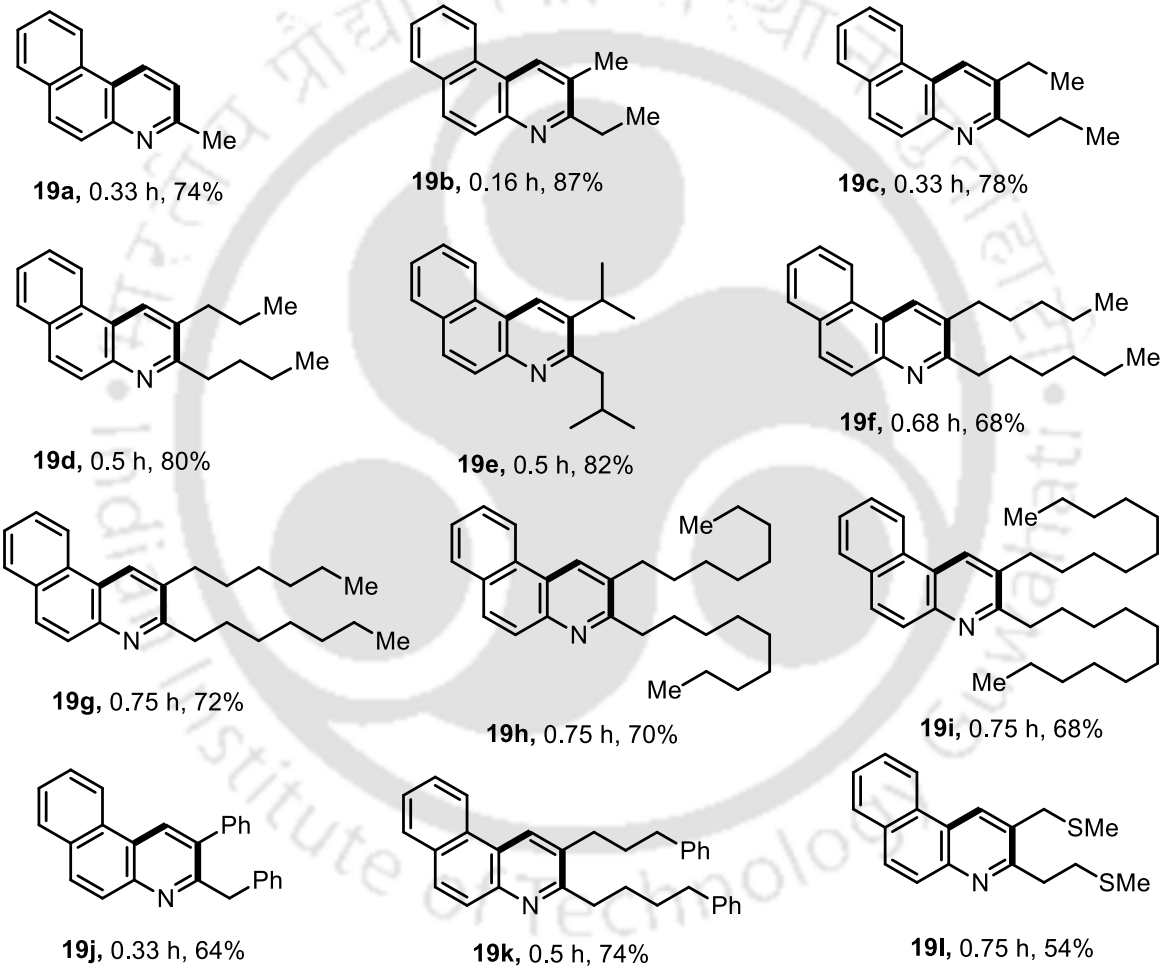
Figure 19. ORTEP Diagram of compound **18i** with ellipsoid counter 40% probalility

The present protocol was explored for the synthesis of 2,3-disubstituted benzo[*f*]quinoline derivatives using 2-naphthylamine **1a** with different aliphatic aldehydes **2** under similar reaction conditions to offer the corresponding products **19a-k** with 60-87% yields as depicted in Table **14**. The reaction proceeded well with 3-(methylthio)propanal to form 3-(2-(methylthio)ethyl)-2-((methylthio)methyl)benzo[*f*]quinoline **19l**. The crystal structure of

compound **19f** was determined through single crystal XRD analysis and ORTEP diagram is shown in Figure **20**.

Table 14. Reaction of 2-naphthylamine with various aldehydes[a,b]





[a]All the reactions were carried out using 2-naphthylamine (1 mmol) and various aliphatic aldehyde (2 mmol) at 70 °C. [b]Isolated yield.

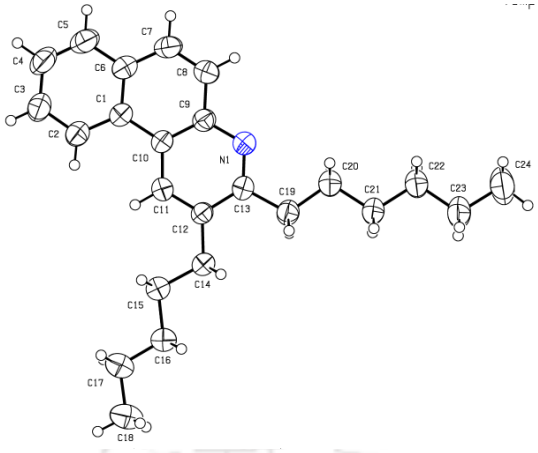
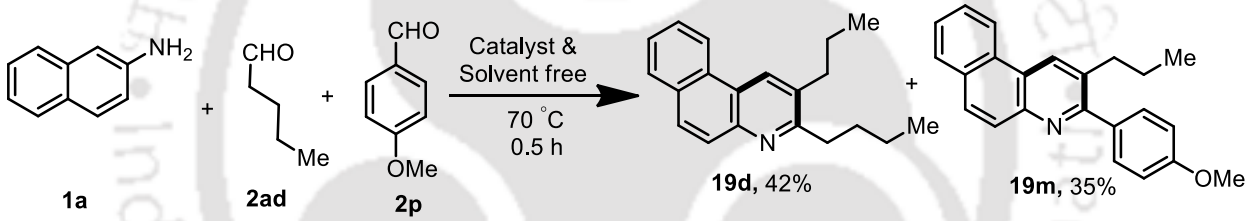


Figure 20. ORTEP Diagram of compound **19f** with ellipsoid counter 40% probalility

Next, the protocol was studied using 2-naphthylamine with a mixture of two varieties of aldehyde such as pentanal and 4-OMe benzaldehyde which resulted in the formation of two types of products as shown in the Scheme **51**. The structure of compound **19m** was also determined through single XRD analysis and ORTEP diagram is depicted in Figure **21**.



Scheme 51

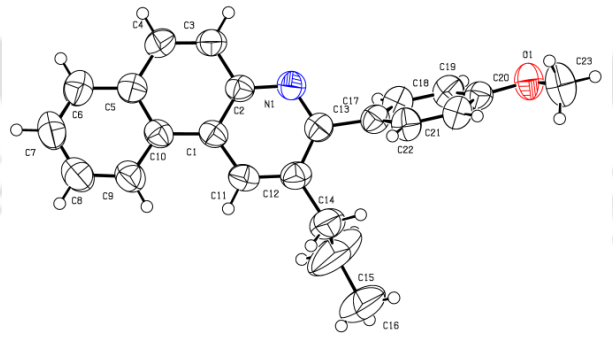
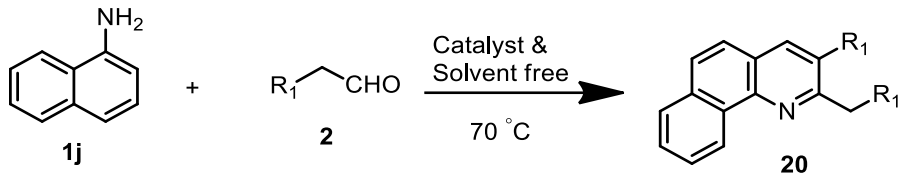
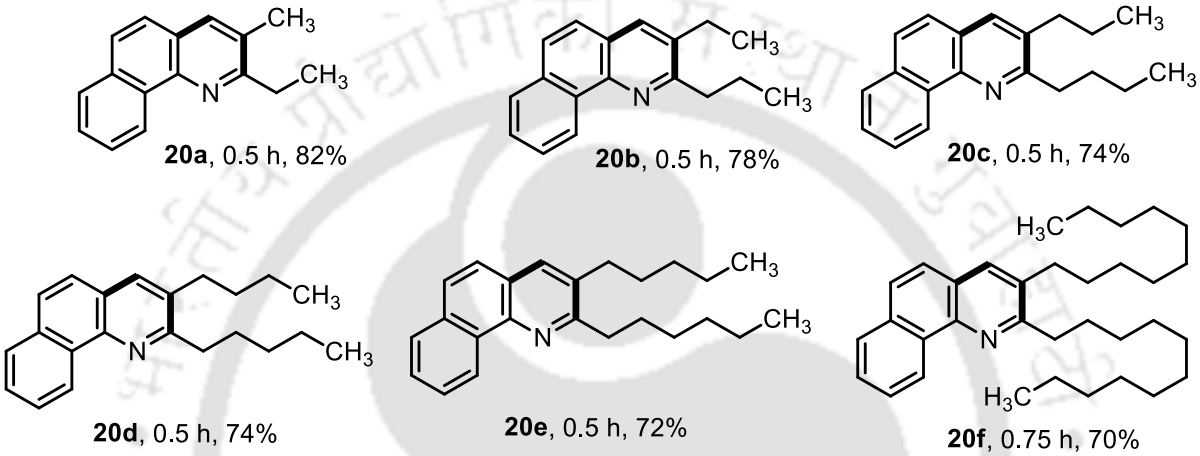


Figure 21. ORTEP Diagram of compound **19m** with ellipsoid counter 40% probalility

We have further explored the generality of the reaction with 1-naphthylamine **1j** (1 mmol) with various aliphatic aldehydes **2** (2 mmol) which resulted in the formation of 2,3-disubstituted benzo[*h*]quinoline **20** derivatives with 70 - 82% yield as shown in Table **14**.

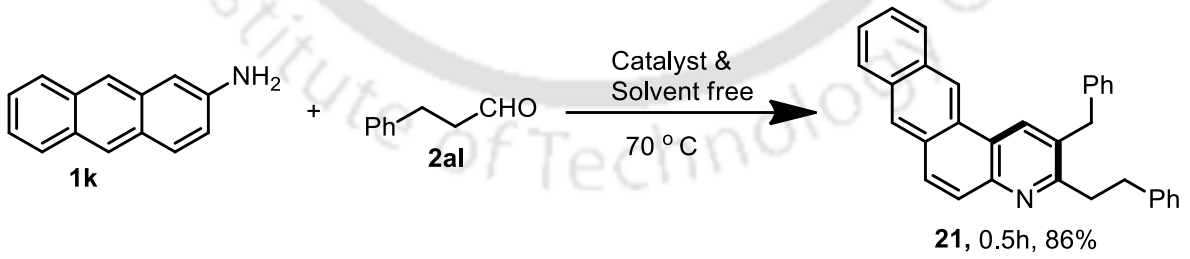
Table 14. Reaction of 1-naphthylamine with various aldehydes[a,b]





[a]All the reactions were carried out using 1-naphthylamine (1 mmol) and various aliphatic aldehyde (2 mmol) at 70 °C. [b]Isolated yield.

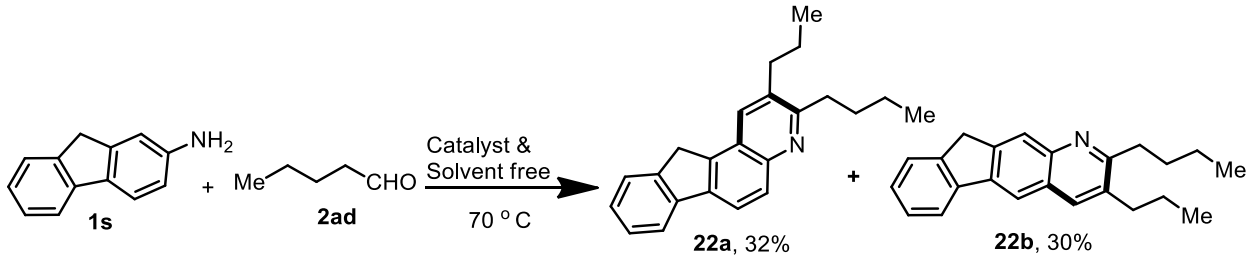
Similarly, when we performed reaction using 2-aminoanthracene and 3-phenylpropanal gave 2,3-di-alkylnapthoquinoline **21** was formed under optimized reaction conditions as shown in the Scheme **52**.



Scheme 52

Finally, 2-aminofluorene **1s** (1.0 mmol) on reaction with pentanal **2ad** (2.0 mmol) under reflux condition in catalyst and solvent free condition offered the C1 and C3 aromatisation products **22a** and **22b** as shown in Scheme **53**. Both the structures were identified by ^{1}H NMR, ^{13}C NMR, IR spectra and HRMS. The structure of the compounds 3-butyl-2-propyl-

11H-indeno[2,1-*f*]quinoline **22a** was also identified using single crystal XRD. The ORTEP diagram of compound **22a** is shown in Figure **22**.



Scheme 53

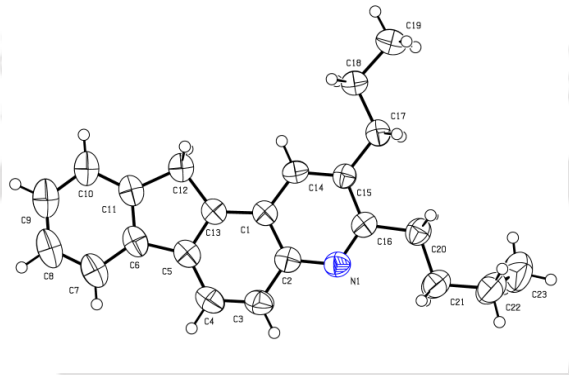
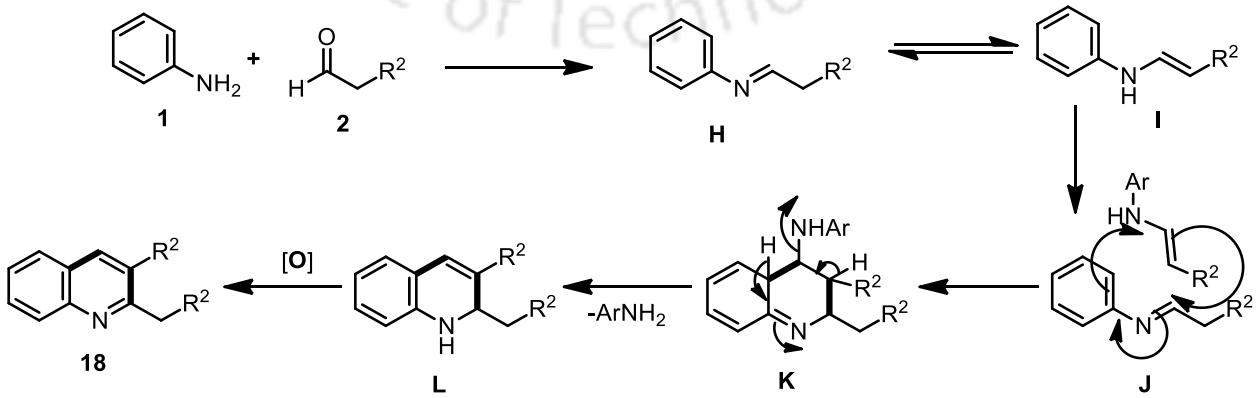


Figure 22. ORTEP Diagram of compound **22a** with ellipsoid counter 45% probalility

The ^{1}H and ^{13}C NMR spectra of compounds **18b**, **19c** and **20c** are shown in Figure **23**, **24** and **25** respectively. (See Page No. 101-103 in Experimental Section).

The Plausible mechanism for formation of 2,3-disubstituted quinolines may be explained by the following mechanistic pathway as shown in Scheme **54**. Initially, aniline **1** reacts with aliphatic aldehyde **2** to form imine **H** which tautomerises to form enamine **I**. Both imine **H** and enamine **I** react to form tetrahydroquinoline **K** which on aromatisation through elimination of aniline gives the desired 2,3-di-substituted quinoline **18**.



Scheme 54

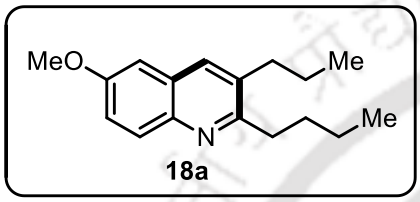
In summary, we have developed catalyst and solvent free reaction protocol for tandem cyclization between substituted anilines/naphthylamines and aldehydes for the synthesis of 2,3-di-substituted quinoline/benzoquinoline derivatives in good yields. It is worth to highlight in this reaction, the in-situ generated imine from aliphatic aldehyde and 2-naphthylamine tautomerizes to enamine, which acted as a dienophile to participate in the tandem cyclization with the *in-situ* generated imine from 2-naphthylamine and 4-methoxy benzaldehyde in one pot reaction which resulted in the formation of product **19m**. This protocol avoids harsh conditions and solvent free which facilitates green reaction.

Experimental Section

General Procedure for Synthesis of 2,3- di-substituted quinolines **18**.

A mixture of arylamine **1** (1.0 mmol) and aliphatic aldehyde **2** (2.0 mmol) was added to a dry 25 mL round bottom flask and stirred at 70 °C. The progress of the reaction was monitored by TLC. After completion of the reaction the reaction mixture was purified through silica gel (60-120 mesh) column chromatography with petroleum ether/ethyl acetate (9.5 : 0.5, v/v) to obtain the pure product **18**.

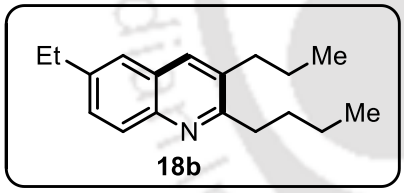
*2-butyl-6-methoxy-3-propylquinoline (**18a**)*



18a

Yield 78% (201 mg), yellow liquid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.92 (dt, *J* = 9.2, 0.6 Hz, 1H), 7.76 – 7.73 (m, 1H), 7.28 – 7.24 (m, 1H), 6.98 (d, *J* = 2.8 Hz, 1H), 3.88 (s, 3H), 2.97 – 2.91 (m, 2H), 2.77 – 2.71 (m, 2H), 1.78 – 1.68 (m, 4H), 1.51 – 1.45 (m, 2H), 1.03 (t, *J* = 7.3 Hz, 3H), 0.97 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 159.8, 157.3, 142.5, 134.3, 134.2, 129.8, 128.2, 121.1, 104.7, 55.5, 35.4, 34.5, 32.2, 23.7, 23.2, 14.2, 14.2; **IR (KBr)ν_{max}** 3052, 2964, 2932, 2872, 1636, 1564, 1451, 1372, 1076, 922 cm^{-1}; **HRMS** (ESI) Calcd For $C_{17}H_{24}NO$ 258.1852 ($M + H^+$); Found 258.1855.

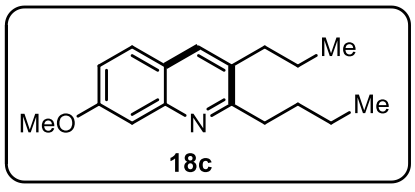
*2-butyl-6-ethyl-3-propylquinoline (**18b**)*



18b

Yield 64% (163 mg), light brown liquid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.93 (d, *J* = 8.5 Hz, 1H), 7.78 (s, 1H), 7.51 – 7.45 (m, 2H), 2.99 – 2.93 (m, 2H), 2.80 (d, *J* = 7.7 Hz, 2H), 2.75 (t, *J* = 7.9 Hz, 2H), 1.78 – 1.70 (m, 4H), 1.49 (q, *J* = 7.5 Hz, 2H), 1.32 (t, *J* = 7.6 Hz, 3H), 1.04 (t, *J* = 7.4 Hz, 3H), 0.98 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 161.5, 145.4, 141.6, 134.7, 133.9, 129.7, 128.4, 127.4, 124.6, 35.7, 34.6, 32.2, 28.9, 23.8, 23.2, 15.6, 14.2, 14.2; **IR (KBr)ν_{max}** 3057, 2961, 2930, 2869, 1630, 1562, 1492, 1457, 1377, 1081, 919 cm^{-1}; **HRMS** (ESI) Calcd For $C_{18}H_{26}N$ 256.2060 ($M + H^+$); Found 256.2062.

*2-butyl-7-methoxy-3-propylquinoline (**18c**)*

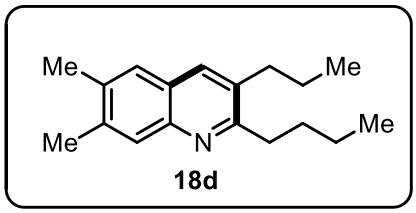


18c

Yield 70% (180 mg), yellow liquid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.77 (s, 1H), 7.59 (d, *J* = 8.9 Hz, 1H), 7.36 (d, *J* = 2.5 Hz, 1H), 7.10 (dd, *J* = 8.9, 2.5 Hz, 1H), 3.93 (s, 3H), 2.98 – 2.92 (m, 2H), 2.76 – 2.69 (m, 2H), 1.80 – 1.66 (m, 4H), 1.52 – 1.46 (m, 2H), 1.03 (t, *J* = 7.3 Hz, 3H), 0.98 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 162.6, 160.2, 148.1, 135.1, 131.7, 128.1, 122.5, 118.9, 106.7, 55.7, 35.9, 34.5,

32.3, 23.9, 23.3, 14.3, 14.3; **IR (KBr)ν_{max}** 3052, 2958, 2928, 2872, 1634, 1568, 1494, 1447, 1372, 1078, 921 cm^{-1}; **HRMS** (ESI) Calcd For $C_{17}H_{24}NO$ 258.1852 ($M + H^+$); Found 258.1860.

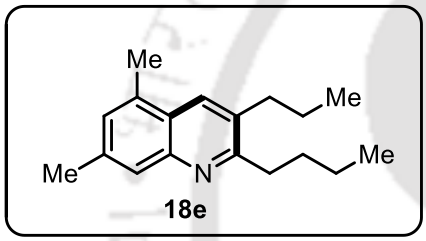
*2-butyl-6,7-dimethyl-3-propylquinoline (**18d**)*



18d

Yield 62% (158 mg), light yellow liquid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.78 (s, 1H), 7.71 (s, 1H), 7.43 (s, 1H), 2.97 – 2.91 (m, 2H), 2.74 – 2.71 (m, 2H), 2.43 (d, *J* = 1.0 Hz, 3H), 2.40 (d, *J* = 1.1 Hz, 3H), 1.75 (d, *J* = 7.7 Hz, 2H), 1.73 – 1.67 (m, 2H), 1.51 – 1.45 (m, 2H), 1.03 (t, *J* = 7.3 Hz, 3H), 0.98 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 161.4, 145.8, 138.5, 135.4, 134.2, 133.0, 128.0, 126.3, 125.9, , 35.7, 34.6, 32.2, 23.8, 23.3, 20.5, 20.1, 14.3; **IR (KBr)ν_{max}** 3064, 2962, 2928, 2867, 1562, 1496, 1457, 1081, 914 cm^{-1}; **HRMS** (ESI) Calcd For $C_{18}H_{26}N$ 256.2060 ($M + H^+$); Found 256.2070.

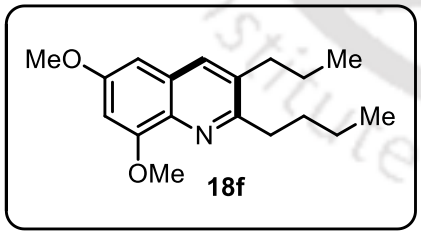
*2-butyl-5,7-dimethyl-3-propylquinoline (**18e**)*



18e

Yield 70% (179 mg), light yellow liquid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.95 (s, 1H), 7.70 (s, 1H), 7.13 (s, 1H), 3.02 – 2.94 (m, 2H), 2.82 – 2.74 (m, 2H), 2.62 (s, 3H), 2.49 (s, 3H), 1.81 – 1.68 (m, 4H), 1.54 – 1.45 (m, 3H), 1.06 (t, *J* = 7.3 Hz, 3H), 0.99 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 161.7, 146.9, 138.3, 133.4, 132.7, 131.8, 128.6, 125.6, 113.3, 35.5, 34.9, 32.2, 24.2, 23.2, 21.9, 18.7, 14.3, 14.2; **IR (KBr)ν_{max}** 3057, 2958, 2922, 2854, 1560, 1492, 1454, 1074, 924 cm^{-1};**HRMS** (ESI) Calcd For $C_{18}H_{26}NO_2$ 256.2060 ($M + H^+$); Found 256.2068.

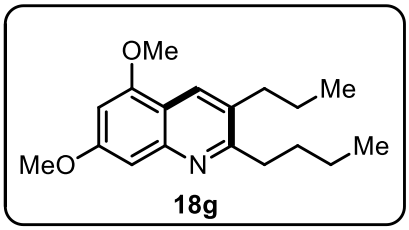
*2-butyl-6,8-dimethoxy-3-propylquinoline (**18f**)*



18f

Yield 66% (190 mg), light yellow liquid, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.31 (d, *J* = 7.8 Hz, 2H), 3.01 – 2.93 (m, 2H), 2.77 (s, 3H), 2.73 (d, *J* = 8.0 Hz, 2H), 2.47 (s, 3H), 1.90 – 1.84 (m, 2H), 1.73 – 1.68 (m, 2H), 1.53 – 1.46 (m, 2H), 1.04 (t, *J* = 6.1 Hz, 3H), 1.02 – 0.98 (m, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 158.9, 157.7, 156.1, 135.2, 135.0, 134.3, 129.0, 100.4, 96.6, 56.4, 55.6, 35.9, 34.6, 32.4, 23.9, 23.4, 14.3, 14.3; **IR (KBr)ν_{max}** 3066, 2954, 2924, 2866, 1560, 1496, 1448, 1072, 912 cm^{-1}; **HRMS** (ESI) Calcd For $C_{18}H_{26}NO_2$ 288.1958 ($M + H^+$); Found 288.1966.

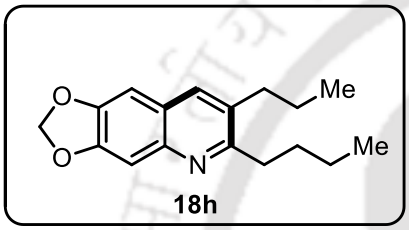
*2-butyl-5,7-dimethoxy-3-propylquinoline (**18g**)*



18g

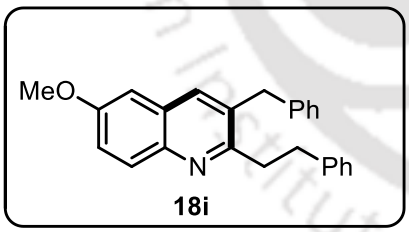
Yield 62% (187 mg, light yellow liquid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.12 (s, 1H), 6.96 (d, *J* = 2.1 Hz, 1H), 6.43 (d, *J* = 2.2 Hz, 1H), 3.94 (s, 3H), 3.91 (d, *J* = 1.5 Hz, 3H), 2.95 – 2.90 (m, 2H), 2.72 (dd, *J* = 8.7, 6.9 Hz, 2H), 1.76 – 1.68 (m, 4H), 1.51 – 1.45 (m, 2H), 1.02 (t, *J* = 7.3 Hz, 3H), 0.96 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 162.9, 160.6, 155.7, 148.6, 130.8, 130.2, 115.6, 99.1, 97.4, 55.9, 55.7, 34.6, 32.4, 24.2, 23.3, 14.3, 14.3; **IR (KBr)ν_{max}** 3046, 2944, 2926, 2870, 1632, 1564, 1484, 1444, 1368, 1072, 916 cm^{-1}; **HRMS** (ESI) Calcd For $C_{18}H_{26}NO_2$ 288.1958 ($M + H^+$); Found 288.1966.

7*-benzyl-6-phenethyl-[1,3]dioxolo[4,5-g]quinoline (**18h**)* Yield 74% (272 mg), brown color liquid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.59 (s, 1H), 7.30 (s, 1H), 6.89 (t, *J* = 1.6 Hz, 1H), 5.97 (q, *J* = 1.6 Hz, 2H), 2.90 – 2.83 (m, 2H), 2.64 (t, *J* = 7.8 Hz, 2H), 1.75 – 1.67 (m, 2H), 1.67 – 1.59 (m, 2H), 1.44 (q, *J* = 7.4 Hz, 2H), 0.99 (dd, *J* = 7.4, 1.2 Hz, 3H), 0.94 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 162.9, 160.6, 155.7, 148.6, 130.8, 130.2, 115.6, 99.1, 97.4, 55.9, 55.7, 34.6, 32.4, 24.2, 23.3, 14.3, 14.3; **IR (KBr)ν_{max}** 3048, 2952, 2932, 2868, 1630, 1562, 1478, 1442, 1362, 912 cm^{-1}; **HRMS** (ESI) Calcd For $C_{18}H_{26}NO_2$ 272.1645 ($M + H^+$); Found 272.1658.



18h

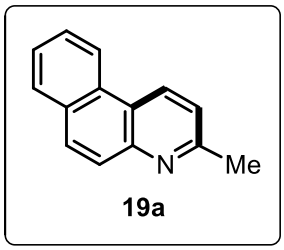
3-benzyl-6-methoxy-2-phenethylquinoline (***18i***)



18i

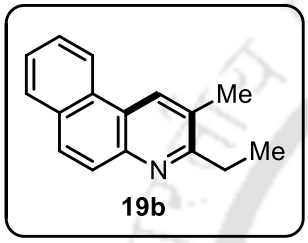
Yield 72% (254 mg), white solid, mp 180-181˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.98 (d, *J* = 9.1 Hz, 1H), 7.65 (s, 1H), 7.32 (d, *J* = 8.4 Hz, 3H), 7.26 (d, *J* = 7.0 Hz, 3H), 7.20 (d, *J* = 7.6 Hz, 1H), 7.16 (d, *J* = 7.5 Hz, 2H), 7.12 (d, *J* = 7.5 Hz, 2H), 6.98 (d, *J* = 2.8 Hz, 1H), 4.05 (s, 2H), 3.90 (s, 3H), 3.19 (t, *J* = 8.3 Hz, 2H), 3.07 – 3.02 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 158.7, 157.6, 142.2, 139.6, 135.6, 132.6, 130.1, 129.2, 128.9, 128.8, 126.7, 126.1, 121.7, 104.9, 55.7, 38.9, 37.7, 35.7; **IR (KBr)ν_{max}** 3054, 2956, 2872, 1582, 1468, 1069, 1028, 964 cm^{-1}; **HRMS** (ESI) Calcd For $C_{25}H_{24}NO$ 354.1852 ($M + H^+$); Found 354.1860.

*3-methylbenzo[f]quinoline (**19a**)*



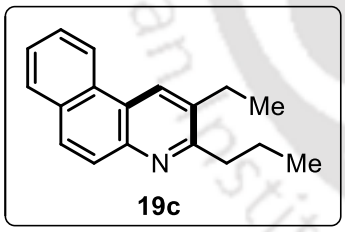
Yield 74% (143 mg), colorless liquid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.83 (d, *J* = 8.4 Hz, 1H), 8.57 (d, *J* = 8.2 Hz, 1H), 7.96 (d, *J* = 1.6 Hz, 2H), 7.92 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.68 (ddd, *J* = 8.3, 7.0, 1.5 Hz, 1H), 7.65 – 7.59 (m, 1H), 7.43 (d, *J* = 8.5 Hz, 1H), 2.79 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 158.6, 147.8, 131.6, 131.3, 131.0, 129.8, 128.8, 127.9, 127.2, 127.0, 123.5, 122.6, 122.1, 25.1; **IR (KBr)ν_{max}** 3058, 2923, 2853, 1928, 1672, 1599, 1528, 1488, 1411, 1374, 1243, 1033, 999, 868 cm^{-1}; **HRMS** (ESI) Calcd For $C_{14}H_{12}N$ 194.0964 ($M + H^+$); Found 194.0964.

*3-ethyl-2-methylbenzo[f]quinoline (**19b**)*



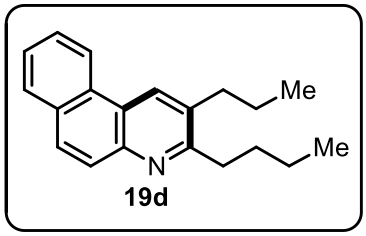
Yield 87% (192 mg), colorless liquid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.65 (s, 1H), 8.61 – 8.56 (m, 1H), 7.97 (d, *J* = 9.0 Hz, 1H), 7.94 – 7.88 (m, 2H), 7.66 (ddd, *J* = 8.3, 7.0, 1.4 Hz, 1H), 7.61 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 3.05 (q, *J* = 7.6 Hz, 2H), 2.59 (d, *J* = 0.9 Hz, 3H), 1.41 (t, *J* = 7.6 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 162.5, 146.2, 131.7, 131.7, 129.9, 129.6, 129.6, 128.8, 127.8, 126.9, 126.9, 124.0, 122.6, 29.4, 19.6, 13.2; **IR (KBr)ν_{max}** 3056, 2968, 2930, 2872, 1483, 1454, 1403, 1260, 1216, 1031 cm^{-1}; **HRMS** (ESI) Calcd For $C_{16}H_{16}N$ 222.1277 ($M + H^+$); Found 222.1277.

*2-ethyl-3-propylbenzo[f]quinoline (**19c**)*



Yield 78% (195 mg), colorless liquid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.58 (d, *J* = 8.1 Hz, 1H), 8.02 (d, *J* = 9.1 Hz, 1H), 7.89 (dd, *J* = 8.6, 4.8 Hz, 2H), 7.69 – 7.62 (m, 1H), 7.59 (td, *J* = 7.4, 6.9, 1.2 Hz, 1H), 3.07 – 2.99 (m, 2H), 2.91 (q, *J* = 7.5 Hz, 2H), 1.87 (h, *J* = 7.4 Hz, 2H), 1.39 (t, *J* = 7.5 Hz, 3H), 1.09 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 160.8, 145.4, 135.6, 131.6, 130.4, 130.3, 129.5, 128.8, 127.1, 127.0, 126.9, 124.1, 122.5, 37.3, 25.7, 23.4, 15.1, 14.6; **IR (KBr)ν_{max}** 3056, 2963, 2930, 2871, 1602, 1513, 1480, 1450, 1407, 1378, 1326, 865 cm^{-1}; **HRMS (ESI)** Calcd For $C_{18}H_{20}N$ 250.1590 ($M + H^+$); Found 250.1591.

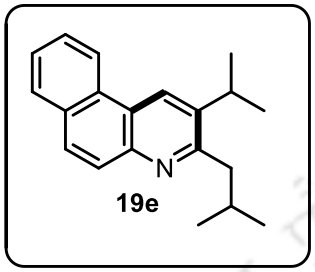
*3-butyl-2-propylbenzo[f]quinoline (**19d**)*



Yield 80% (222 mg), colorless liquid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.63 (d, *J* = 3.0 Hz, 1H), 8.59 (dd, *J* = 8.4, 2.8 Hz, 1H), 7.96 (dd, *J* = 9.1, 3.0 Hz, 1H), 7.89 (dd, *J* = 9.0, 2.9 Hz, 2H), 7.68 – 7.61 (m, 1H), 7.59 (dt, *J* = 9.5, 4.6 Hz, 1H), 3.09 – 2.97 (m, 2H), 2.91 – 2.78 (m, 2H), 1.90 – 1.70 (m, 4H), 1.52

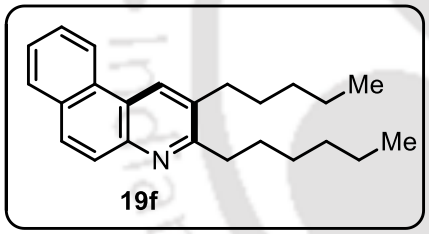
(qd, *J* = 7.5, 2.9 Hz, 2H), 1.08 (td, *J* = 7.3, 2.9 Hz, 3H), 1.01 (dt, *J* = 10.6, 5.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 161.5, 146.2, 134.0, 131.6, 130.6, 129.8, 129.7, 128.8, 127.9, 126.8, 126.8, 123.8, 122.6, 35.5, 35.1, 32.3, 24.3, 23.3, 14.3, 14.3; **IR (KBr)ν_{max}** 3048, 2996, 2925, 2871, 1749, 1732, 1583, 1558, 1408, 1269, 1380, 1269, 1252, 1080, 1018 cm^{-1}; **HRMS** (ESI) Calcd For $C_{20}H_{24}N$ 278.1903 ($M + H^+$); Found 278.1913.

*3-isobutyl-2-isopropylbenzo[f]quinoline (**19e**)*



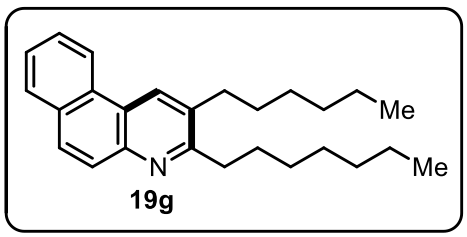
Yield 82% (227 mg), colorless liquid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.78 (s, 1H), 8.64 (d, *J* = 8.2 Hz, 1H), 8.02 – 7.94 (m, 1H), 7.90 (d, *J* = 8.6 Hz, 2H), 7.73 – 7.63 (m, 1H), 7.63 – 7.55 (m, 1H), 3.43 (p, *J* = 6.9 Hz, 1H), 2.99 (d, *J* = 7.3 Hz, 2H), 2.32 (dt, *J* = 13.6, 6.8 Hz, 1H), 1.42 (d, *J* = 6.8 Hz, 6H), 1.03 (d, *J* = 6.6 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 159.9, 145.9, 140.7, 131.6, 129.8, 129.8, 128.8, 128.0, 126.9, 126.8, 126.8, 123.9, 122.5, 44.0, 29.7, 29.2, 24.2, 22.8; **IR (KBr)ν_{max}** 3056, 2960, 2868, 1606, 1461, 1409, 1364, 1335, 1242, 1106, 1057, 907 cm^{-1}; **HRMS** (ESI) Calcd For $C_{20}H_{24}N$ 278.1903 ($M + H^+$); Found 278.1905.

*3-hexyl-2-pentylbenzo[f]quinoline (**19f**)*



Yield 68% (227 mg), colorless solid, mp 68-70 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.63 (s, 1H), 8.59 (d, *J* = 8.2 Hz, 1H), 7.97 (d, *J* = 9.1 Hz, 1H), 7.93 – 7.84 (m, 2H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.58 (t, *J* = 7.4 Hz, 1H), 3.09 – 2.95 (m, 2H), 2.85 (t, *J* = 8.0 Hz, 2H), 1.84 (t, *J* = 7.9 Hz, 2H), 1.74 (t, *J* = 7.7 Hz, 2H), 1.50 (t, *J* = 7.5 Hz, 2H), 1.44 (dp, *J* = 7.9, 4.8, 4.4 Hz, 4H), 1.37 (q, *J* = 4.1 Hz, 4H), 0.96 (t, *J* = 6.8 Hz, 3H), 0.91 (d, *J* = 6.5 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 161.4, 146.1, 134.3, 131.6, 130.6, 129.8, 129.68, 128.7, 127.8, 126.8, 126.7, 123.9, 122.5, 35.7, 32.9, 32.0, 31.9, 30.8, 30.1, 29.8, 22.8, 22.7, 14.3, 14.2; **IR (KBr)ν_{max}** 3056, 2925, 2855, 1607, 1448, 1406, 1379, 1304, 1031, 897 cm^{-1}; **HRMS** (ESI) Calcd For $C_{24}H_{32}N$ 334.2529 ($M + H^+$); Found 334.2538.

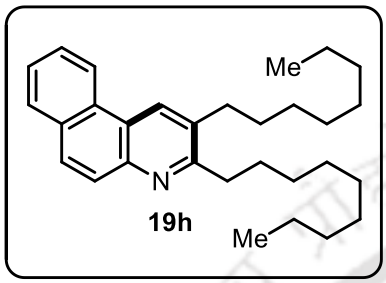
*3-heptyl-2-hexylbenzo[f]quinoline (**19g**)*



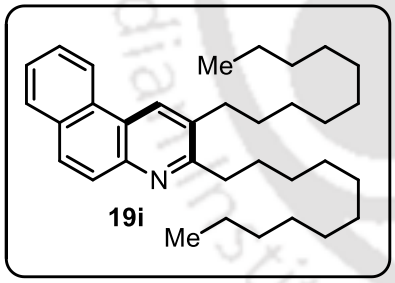
Yield 72% (260 mg), colorless liquid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.64 (s, 1H), 8.60 (d, *J* = 8.2 Hz, 1H), 7.96 – 7.92 (m, 1H), 7.91 (s, 1H), 7.90 – 7.88 (m, 1H), 7.70 – 7.63 (m, 1H), 7.63 – 7.57 (m, 1H), 5.81 (dddt, *J* = 16.9, 9.6, 6.7, 3.3 Hz, 2H), 5.06 – 4.96 (m, 2H), 4.93 (ddt, *J* = 8.5, 3.5, 1.9 Hz, 2H), 3.05 – 2.97 (m, 2H), 2.91 – 2.83 (m, 2H), 2.05 (h, *J* = 6.7 Hz,

4H), 1.86 – 1.78 (m, 2H), 1.78 – 1.69 (m, 2H), 1.52 – 1.44 (m, 4H), 1.41 – 1.36 (m, 6H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 161.5, 146.2, 139.4, 139.3, 134.3, 131.6, 130.6, 129.8, 129.7, 128.8, 127.9, 126.9, 126.8, 123.9, 122.6, 114.4, 114.3, 35.8, 34.0, 33.9, 33.0, 31.2, 30.2, 29.8, 29.7, 29.6, 29.6, 29.3, 29.3, 29.1; **IR (KBr)ν_{max}** 3048, 2962, 2858, 1582, 1495, 1062, 1030, 958 cm^{-1}; **HRMS** (ESI) Calcd For $C_{26}H_{36}N$ 362.2842 ($M + H^+$); Found 362.2846.

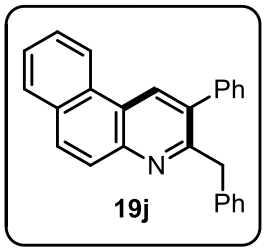
*3-nonyl-2-octylbenzo[f]quinoline (**19h**)* Yield 70% (292 mg), colorless liquid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.65 (s, 1H), 8.60 (d, *J* = 8.2 Hz, 1H), 7.94 (t, *J* = 9.9 Hz, 1H), 7.91 (s, 1H), 7.90 – 7.88 (m, 1H), 7.66 (ddd, *J* = 8.3, 7.0, 1.5 Hz, 1H), 7.60 (td, *J* = 7.5, 7.0, 1.3 Hz, 1H), 3.06 – 2.97 (m, 2H), 2.92 – 2.82 (m, 2H), 1.86 – 1.78 (m, 2H), 1.74 (td, *J* = 7.1, 6.4, 3.5 Hz, 2H), 1.47 (tdd, *J* = 7.1, 4.6, 2.5 Hz, 4H), 1.42 – 1.34 (m, 4H), 1.29 (dqd, *J* = 10.8, 6.5, 2.4 Hz, 14H), 0.89 (td, *J* = 6.8, 4.9 Hz, 6H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 164.4, 146.0, 136.5, 131.6, 130.7, 129.9, 129.6, 128.8, 127.7, 126.9, 126.8, 123.9, 122.5, 35.7, 32.9, 33.1, 32.1, 31.2, 30.2, 30.1, 29.9, 29.7, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 22.8, 14.3; **IR (KBr)ν_{max}** 3052, 2955, 2926, 2851, 1740, 1717, 1689, 1559, 1532, 1408, 1284, 1098, 1070, 1020, 1001 cm^{-1}; **HRMS** (ESI) Calcd For $C_{30}H_{44}N$ 418.3468 ($M + H^+$); Found 418.3478.



*2-decyl-3-undecylbenzo[f]quinoline (**19i**)* Yield 68% (322 mg), colorless liquid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.66 (s, 1H), 8.61 (d, *J* = 8.1 Hz, 1H), 7.97 (d, *J* = 9.1 Hz, 1H), 7.93 – 7.89 (m, 2H), 7.67 (ddd, *J* = 8.3, 6.9, 1.5 Hz, 1H), 7.64 – 7.58 (m, 1H), 3.07 – 2.98 (m, 2H), 2.90 – 2.85 (m, 2H), 1.87 – 1.78 (m, 3H), 1.74 (dq, *J* = 15.5, 8.0, 6.6 Hz, 3H), 1.47 (ddd, *J* = 14.1, 6.9, 4.2 Hz, 4H), 1.38 (q, *J* = 7.3, 6.7 Hz, 4H), 1.28 (dd, *J* = 12.0, 5.4 Hz, 20H), 0.88 (td, *J* = 6.9, 1.6 Hz, 6H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 161.3, 155.6, 139.5, 134.5, 131.7, 131.2, 130.3, 129.6, 128.9, 127.0, 124.1, 122.6, 114.3, 32.9, 32.1, 32.1, 31.2, 30.3, 30.2, 29.9, 29.9, 29.9, 29.8, 29.8, 29.7, 29.6, 29.6, 22.9, 14.3; **IR (KBr)ν_{max}** 3050, 2995, 2921, 2887, 1740, 1716, 1558, 1506, 1411, 1286, 1189, 1060, 1000 cm^{-1}; **HRMS** (ESI) Calcd For $C_{34}H_{52}N$ 474.4094 ($M + H^+$); Found 474.4093.

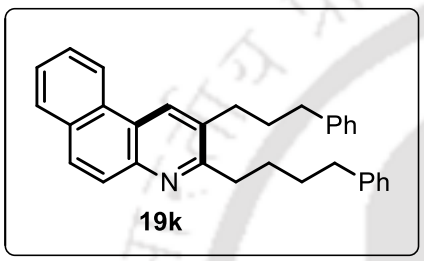


*3-benzyl-2-phenylbenzo[f]quinoline (**19j**)* Yield 64% (221 mg), colorless liquid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.78 (s, 1H), 8.57 (d, *J* = 7.4 Hz, 1H), 8.11 (d, *J* = 9.1 Hz, 1H), 8.02 (d, *J* = 9.0 Hz, 1H), 7.96 (d, *J* = 7.4 Hz, 1H), 7.69 – 7.63 (m, 2H), 7.44 (dt, *J* = 3.7, 1.7 Hz, 3H), 7.32 – 7.29 (m, 2H), 7.14 (p, *J* = 6.4, 5.9 Hz, 3H), 7.01 (d, *J* = 7.2 Hz, 2H), 4.41 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 158.3, 140.0, 139.7, 136.2, 132.7, 131.9, 131.2, 129.7, 129.1, 128.9, 128.5, 128.3, 127.9, 127.4, 127.3, 126.1, 124.0, 122.8, 42.4.; **IR (KBr)ν_{max}** 3058, 3027, 2923, 2852, 1677, 1602, 1492, 1455, 1401, 1031, 974 cm^{-1}; **HRMS** (ESI) Calcd For $C_{26}H_{20}N$ 346.1590 ($M + H^+$); Found 346.1591.



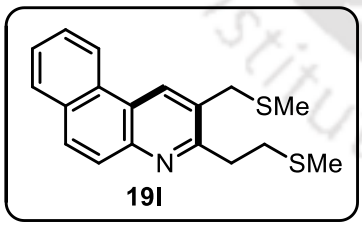
19j

*3-(4-phenylbutyl)-2-(3-phenylpropyl)benzo[f]quinoline (**19k**)* Yield 74% (318 mg), colorless liquid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.61 (s, 1H), 8.56 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.90 (t, *J* = 7.8 Hz, 3H), 7.62 (ddd, *J* = 15.4, 7.9, 1.2 Hz, 2H), 7.34 – 7.29 (m, 2H), 7.28 – 7.24 (m, 2H), 7.25 – 7.20 (m, 3H), 7.18 (dd, *J* = 7.4, 1.3 Hz, 3H), 3.00 – 2.93 (m, 2H), 2.89 – 2.83 (m, 2H), 2.77 (t, *J* = 7.5 Hz, 2H), 2.66 (t, *J* = 7.5 Hz, 2H), 2.06 (ddd, *J* = 8.3, 6.3, 1.5 Hz, 2H), 1.87 – 1.79 (m, 2H), 1.76 (tdd, *J* = 8.6, 5.6, 2.9 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 161.1, 146.2, 142.7, 141.9, 133.7, 131.6, 130.7, 129.9, 129.6, 128.8, 128.7, 128.6, 128.6, 128.4, 127.8, 126.9, 126.9, 126.2, 125.8, 123.9, 122.6, 36.06, 35.9, 35.6, 32.6, 32.3, 31.8, 29.7; **IR (KBr)ν_{max}** 3083, 3060, 3025, 2948, 2850, 1944, 1603, 1495, 1408, 1079, 1030, 907 cm^{-1}; **HRMS** (ESI) Calcd For $C_{32}H_{32}N$ 430.2529 ($M + H^+$); Found 430.2529.



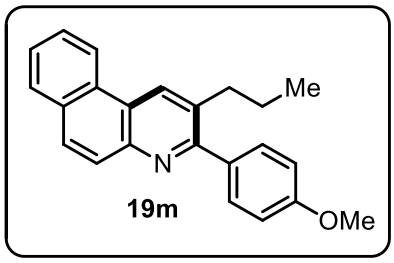
19k

*3-(2-(methylthio)ethyl)-2-((methylthio)methyl)benzo[f]quinoline (**19l**)* Yield 54% (169 mg), colorless liquid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.74 (s, 1H), 8.60 (d, *J* = 8.1 Hz, 1H), 7.96 (s, 2H), 7.95 – 7.90 (m, 1H), 7.73 – 7.60 (m, 2H), 3.99 (s, 2H), 3.42 (t, *J* = 7.7 Hz, 2H), 2.80 – 2.72 (m, 2H), 2.11 (q, *J* = 11.2 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 159.0, 153.9, 146.8, 141.2, 131.9, 131.8, 131.0, 129.5, 128.9, 127.3, 127.3, 123.8, 122.7, 43.4, 36.2, 26.6, 15.6.; **IR (KBr)ν_{max}** 3059, 2956, 2921, 2853, 1740, 1605, 1586, 1559, 1532, 1483, 1406, 1286, 1189, 1081, 1055 cm^{-1}; **HRMS** (ESI) Calcd For $C_{18}H_{20}NS_2$ 314.1032 ($M + H^+$); Found 314.1037.



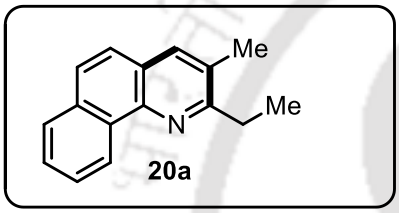
19l

*3-(4-methoxyphenyl)-2-propylbenzo[f]quinoline (**19m**)* Yield 35% (114 mg), colorless liquid,



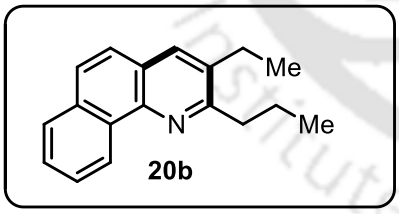
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (dt, *J* = 9.2, 0.6 Hz, 1H), 7.76 – 7.73 (m, 1H), 7.26 (dd, *J* = 9.2, 2.8 Hz, 1H), 6.98 (d, *J* = 2.8 Hz, 1H), 3.88 (s, 3H), 2.97 – 2.91 (m, 2H), 2.76 – 2.70 (m, 2H), 1.78 – 1.67 (m, 4H), 1.51 – 1.45 (m, 2H), 1.03 (t, *J* = 7.3 Hz, 3H), 0.97 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 159.7, 157.3, 142.5, 134.3, 134.2, 129.8, 128.2, 121.0, 104.7, 55.5, 35.4, 34.5, 32.2, 23.7, 23.2, 14.2, 14.2; **IR (KBr)ν_{max}** 3060, 2999, 2959, 2924, 2870, 1740, 1605, 1520, 1477,1405, 1379, 1288, 1250, 1175, 1105, 1082, 1026, 1009 cm^{-1}; **HRMS** (ESI) Calcd For $C_{23}H_{22}NO$ 328.1696 ($M + H^+$); Found 328.1697.

*2-ethyl-3-methylbenzo[h]quinoline (**20a**)*



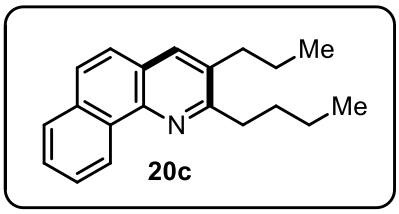
Yield 82% (182 mg), browncolor liquid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.41 (ddt, *J* = 8.1, 1.4, 0.7 Hz, 1H), 7.92 – 7.88 (m, 1H), 7.82 (d, *J* = 1.0 Hz, 1H), 7.75 (t, *J* = 3.5 Hz, 1H), 7.73 (t, *J* = 3.4 Hz, 1H), 7.67 (ddd, *J* = 7.8, 7.0, 1.4 Hz, 1H), 7.61 (d, *J* = 8.8 Hz, 1H), 3.08 (q, *J* = 7.4 Hz, 2H), 2.50 (s, 3H), 1.55 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 161.2, 144.2, 135.89, 133.4, 131.8, 129.9, 127.8, 127.5, 126.7, 126.7, 125.0, 124.9, 124.4, 29.3, 19.1, 12.5.; **IR (KBr)ν_{max}** 3054, 2948, 2864, 1578, 1490, 1056, 1034, 948 cm^{-1}; **HRMS** (ESI) Calcd For $C_{16}H_{16}N$ 222.1277 ($M + H^+$); Found 222.1282.

*3-ethyl-2-propylbenzo[h]quinoline (**20b**)*



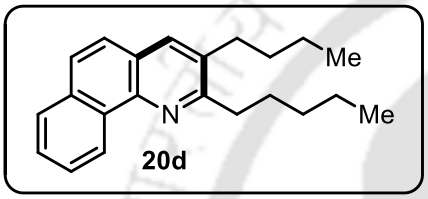
Yield 78% (195 mg), brown color liquid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.35 (ddq, *J* = 8.1, 1.4, 0.7 Hz, 1H), 7.90 – 7.86 (m, 2H), 7.73 (d, *J* = 8.7 Hz, 1H), 7.71 – 7.66 (m, 1H), 7.65 (s, 1H), 7.63 (d, *J* = 1.7 Hz, 1H), 3.07 – 3.02 (m, 2H), 2.87 (qd, *J* = 7.6, 0.7 Hz, 2H), 2.04 (dddd, *J* = 8.9, 7.5, 6.4, 1.1 Hz, 2H), 1.37 (t, *J* = 7.5 Hz, 3H), 1.13 (td, *J* = 7.4, 1.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 160.1, 144.1, 135.9, 134.1, 133.5, 131.8, 127.8, 127.5, 126.8, 126.7, 125.3, 124.9, 124.5, 37.5, 25.4, 22.3, 14.7, 14.6; **IR (KBr)ν_{max}** 3054, 2962, 2864, 1546, 1486, 1088, 1031, 948 cm^{-1}; **HRMS** (ESI) Calcd For $C_{18}H_{20}N$ 250.1590 ($M + H^+$); Found 250.1586.

*2-butyl-3-propylbenzo[h]quinoline (**20c**)*



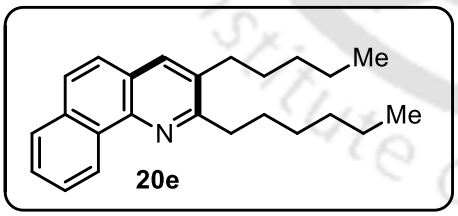
Yield 74% (205 mg), brown color liquid, mp 180-181˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.38 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.89 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.85 (s, 1H), 7.73 (dd, *J* = 8.1, 5.9 Hz, 2H), 7.69 – 7.65 (m, 1H), 7.63 (d, *J* = 8.9 Hz, 1H), 3.12 – 3.06 (m, 2H), 2.85 – 2.79 (m, 2H), 2.00 (dd, *J* = 8.8, 6.4 Hz, 2H), 1.81 – 1.74 (m, 2H), 1.58 (q, *J* = 7.5 Hz, 2H), 1.11 – 1.05 (m, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 160.3, 144.2, 135.1, 134.4, 133.5, 131.8, 127.8, 127.5, 126.8, 126.7, 125.2, 124.8, 124.5, 35.3, 34.6, 31.4, 23.8, 23.1, 14.4, 14.3; **IR (KBr)ν_{max}** 3058, 2928, 2854, 1614, 1454, 1416, 1382, 1314, 1042, 892 cm^{-1}; **HRMS** (ESI) Calcd For $C_{20}H_{24}N$ 278.1903 ($M + H^+$); Found 278.1915.

*3-butyl-2-pentylbenzo[h]quinoline (**20d**)*



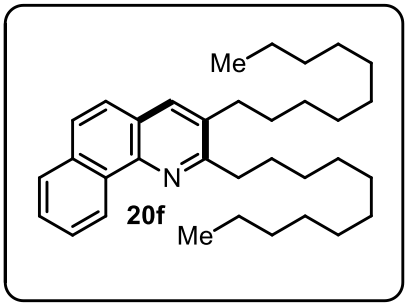
Yield 74% (226 mg), brown color liquid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.35 – 9.30 (m, 1H), 7.90 – 7.85 (m, 2H), 7.73 – 7.70 (m, 1H), 7.70 – 7.65 (m, 1H), 7.64 – 7.62 (m, 1H), 7.61 (d, *J* = 3.8 Hz, 1H), 3.09 – 3.01 (m, 2H), 2.85 – 2.79 (m, 2H), 2.02 – 1.92 (m, 2H), 1.73 – 1.66 (m, 2H), 1.53 – 1.43 (m, 6H), 0.99 (t, *J* = 7.4 Hz, 3H), 0.97 – 0.92 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 160.4, 135.1, 134.7, 133.4, 131.7, 127.8, 127.8, 127.5, 126.8, 126.7, 126.6, 125.2, 125.2, 124.8, 124.4, 124.4, 110.2, 35.5, 32.9, 32.3, 32.2, 29.9, 28.9, 22.9, 22.9, 14.4, 14.2; **IR (KBr)ν_{max}** 3048, 2932, 2858, 1610, 1444, 1412, 1364, 1314, 1028, 892 cm^{-1}; **HRMS** (ESI) Calcd For $C_{22}H_{28}N$ 306.2216 ($M + H^+$); Found 306.2218.

*2-hexyl-3-pentylbenzo[h]quinoline (**20e**)*



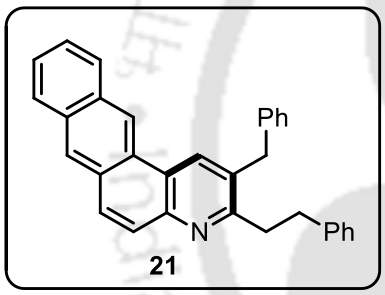
Yield 72% (240 mg), liquid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.51 – 9.44 (m, 1H), 7.93 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.85 (s, 1H), 7.82 – 7.77 (m, 1H), 7.76 (d, *J* = 7.8 Hz, 1H), 7.70 (ddd, *J* = 8.2, 6.9, 1.4 Hz, 1H), 7.64 (d, *J* = 8.8 Hz, 1H), 3.16 – 3.09 (m, 2H), 2.86 – 2.80 (m, 2H), 2.13 – 2.04 (m, 2H), 1.81 – 1.71 (m, 2H), 1.66 – 1.58 (m, 2H), 1.56 – 1.42 (m, 8H), 1.04 (tdd, *J* = 7.1, 4.7, 2.1 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 160.2, 144.1, 134.9, 134.6, 133.4, 131.8, 127.7, 127.5, 126.7, 126.6, 125.2, 124.8, 124.5, 35.5, 32.4, 32.2, 32.0, 30.3, 29.7, 29.1, 22.9, 22.8, 14.4, 14.3; **IR (KBr)ν_{max}** 3046, 2932, 2854, 1608, 1446, 1372, 1308, 1034, 894 cm^{-1}; **HRMS** (ESI) Calcd For $C_{24}H_{32}N$ 334.2529 ($M + H^+$); Found 334.1534.

*3-decyl-2-undecylbenzo[h]quinoline (**20f**)*

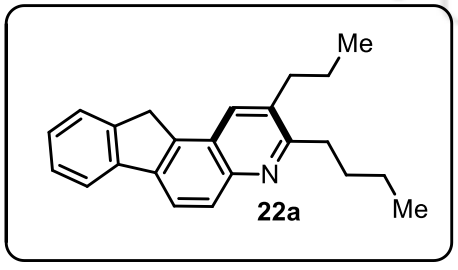


Yield 70% (331 mg), colorless liquid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.45 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.91 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.84 (s, 1H), 7.79 – 7.76 (m, 1H), 7.75 (d, *J* = 4.8 Hz, 1H), 7.71 – 7.67 (m, 1H), 7.63 (d, *J* = 8.8 Hz, 1H), 3.18 – 3.06 (m, 2H), 2.89 – 2.76 (m, 2H), 2.07 (q, *J* = 7.7 Hz, 2H), 1.78 – 1.72 (m, 2H), 1.59 (q, *J* = 7.4, 6.9 Hz, 2H), 1.50 (ddt, *J* = 10.4, 7.2, 3.4 Hz, 6H), 1.38 (d, *J* = 7.8 Hz, 22H), 1.01 – 0.97 (m, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 160.2, 144.2, 134.9, 134.6, 133.4, 131.8, 127.7, 127.5, 126.7, 126.6, 125.2, 124.8, 124.5, 35.5, 32.5, 32.2, 32.2, 30.7, 30.1, 30.1, 30.0, 29.9, 29.9, 29.9, 29.9, 29.8, 29.8, 29.8, 29.6, 29.6, 29.6, 29.2, 22.9, 22.9, 14.4; **IR (KBr)ν_{max}** 3052, 2934, 2882, 1572, 1418, 1358, 1262, 1084, 1008 cm^{-1}; **HRMS** (ESI) Calcd For $C_{34}H_{52}N$ 474.4094 ($M + H^+$); Found 278.1915.

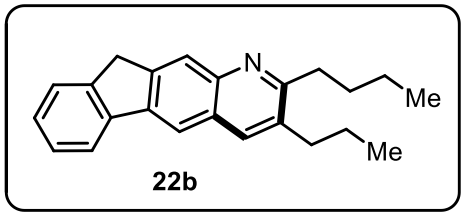
*2-benzyl-3-phenethylnaphtho[2,3-f]quinoline (**21**)* Yield 86% (363 mg), light yellow semisolid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.55 (s, 1H), 8.45 – 8.38 (m, 1H), 7.99 (s, 1H), 7.94 – 7.84 (m, 2H), 7.58 (td, *J* = 6.3, 5.9, 2.6 Hz, 2H), 7.25 (t, *J* = 7.4 Hz, 2H), 7.22 – 7.16 (m, 5H), 7.13 (d, *J* = 7.0 Hz, 1H), 7.07 (dd, *J* = 12.5, 7.5 Hz, 4H), 4.09 (s, 2H), 3.21 (d, *J* = 8.3 Hz, 2H), 3.02 (dd, *J* = 9.9, 6.3 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 160.5, 146.6, 142.1, 139.6, 132.5, 132.0, 131.7, 130.3, 129.6, 128.9, 128.8, 128.8, 128.7, 128.7, 128.5, 127.8, 127.0, 126.7, 126.1, 123.9, 122.6, 39.1, 37.6, 35.6; **IR (KBr)ν_{max}** 3025, 2923, 2880, 1739, 1557, 1412, 1394, 1268, 1219, 1097, 1018 cm^{-1}; **HRMS** (ESI) Calcd For $C_{32}H_{26}N$ 424.2060 ($M + H^+$); Found 424.2048.



*3-butyl-2-propyl-11H-indeno[2,1-f]quinoline (**22a**)* Yield 32% (101 mg), white solid, mp 109-110 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.04 (s, 2H), 8.00 (s, 1H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.62 (d, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 1H), 7.32 (t, *J* = 7.4 Hz, 1H), 4.14 (s, 2H), 3.04 – 2.94 (m, 2H), 2.81 (t, *J* = 7.9 Hz, 2H), 1.78 (dt, *J* = 14.8, 7.6 Hz, 4H), 1.51 (q, *J* = 7.5 Hz, 2H), 1.09 (t, *J* = 7.3 Hz, 3H), 1.00 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 161.8, 146.5, 143.5, 142.5, 139.2, 138.8, 134.5, 131.4, 128.5, 127.1, 126.5, 125.1, 124.9, 121.2, 119.9, 35.9, 35.5, 32.1, 24.0, 23.3, 14.4, 14.3; **IR (KBr)ν_{max}** 3054, 2928, 2848, 1614, 1442, 1368, 1310, 1028, 908 cm^{-1}; **HRMS** (ESI) Calcd For $C_{23}H_{26}N$ 316.2060 ($M + H^+$); Found 316.2067.



*2-benzyl-3-phenethylnaphtho[2,3-f]quinoline (**22b**)* Yield 30% (94 mg), white solid, mp 94-95˚C, **^{1}H NMR** (100 MHz, $CDCl_3$): δ 8.14 – 8.11 (m, 1H), 8.05 (s, 1H), 7.92 (s, 1H), 7.91 – 7.88 (m, 1H), 7.57 (dt, *J* = 7.4, 1.0 Hz, 1H), 7.44 – 7.39 (m, 1H), 7.36 (dd, *J* = 7.4, 1.3 Hz, 1H), 4.10 (s, 2H), 3.03 – 2.96 (m, 2H), 2.81 – 2.75 (m, 2H), 1.86 – 1.69 (m, 5H), 1.51 (dt, *J* = 13.7, 6.9 Hz, 3H), 1.07 (t, *J* = 7.3 Hz, 3H), 1.00 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 161.7, 146.5, 144.3, 144.0, 141.0, 140.3, 135.3, 133.5, 127.8, 127.2, 126.8, 125.5, 124.2, 120.7, 116.7, 36.8, 35.8, 34.6, 32.1, 23.8, 23.3, 14.3, 14.3; **IR (KBr)ν_{max}** 3052, 2928, 2854, 1612, 1442, 1410, 1362, 1308, 1034, 914 cm^{-1}; **HRMS** (ESI) For $C_{23}H_{26}N$ 316.2060 ($M + H^+$); Found 316.2064.



22b

Single crystal data for the Compounds.

Complete crystallographic data of compounds for the structural analyses has been deposited with the Cambridge Crystallographic Data Centre, CCDC No. Copies of this information may be obtained free of charge from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk or via: www.ccdc.cam.ac.uk).

Table 15. Crystal Data and Structure Refinement for Compound **18i**

Entry	Identification code	Compound 18i
01	Empirical formula	$C_{25}H_{24}NO$
02	Formula weight	354.45
03	Temperature	566(2)
04	Wavelength	0.71073
05	Radiation type	MoK\a
06	Radiation source	'fine-focus sealed tube'
07	Crystal system	triclinic
08	Space group	P-1
09	Cell length	a 9.3942(13) b 9.9931(15) c 12.7427(11)
10	Cell Angle	α 67.992(11) β 77.742(10) δ 63.490(14)
11	Cell Volume	991.0(3)
12	Density	1.188
13	Completeness to theta	85.7%
14	Absorption correction	multi-scan
15	Refinement method	Full-matrix least-squares on F2
16	Index ranges	$-11 \leq h \leq 11$, $-13 \leq k \leq 12$, $-16 \leq l \leq 16$
17	Reflection number	4440
18	Theta range	6.76 to 57.63°
19	Cell formula units Z	2
20	CCDC no	1835013

Table 16. Crystal Data and Structure Refinement for Compound **19f**

Entry	Identification code	Compound **19f**
01	Empirical formula	$C_{24}H_{31}N_1$
02	Formula weight	333.42
03	Temperature	569(2)
04	Wavelength	0.71073
05	Radiation type	Mo K\a
06	Radiation source	'fine-focus sealed tube'
07	Crystal system	triclinic
08	Space group	P-1
09	Cell length	a 7.8746(4) b 11.6169(5) c 12.7516(9)
10	Cell Angle	α 108.275(4) β 96.901(4) δ 108.339(3)
11	Cell Volume	1019.95(10)
12	Density	1.109
13	Absorption correction	multi-scan
14	Refinement method	Full-matrix least-squares on F2
15	Index ranges	$-8 \leq h \leq 8, -12 \leq k \leq 12, -13 \leq l \leq 13$
16	Reflections collected	10837
17	Theta range	3.468 to 43.968°
18	Cell formula units Z	3
19	CCDC no	1835014

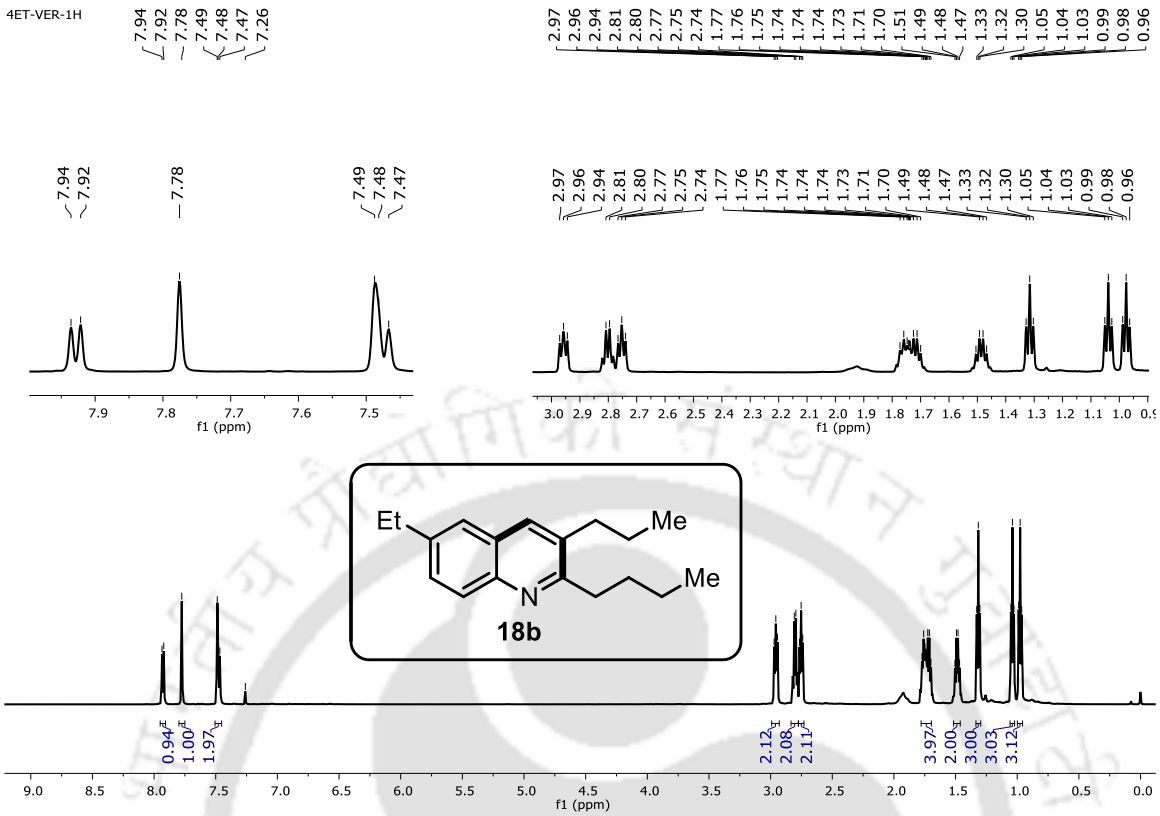
Table 17. Crystal Data and Structure Refinement for Compound **19m**

Entry	Identification code	Compound 19m
01	Empirical formula	$C_{23}H_{21}NO$
02	Formula weight	327.41
03	Temperature	566(2)
04	Wavelength	0.71073
05	Radiation type	MoK\a
06	Radiation source	'fine-focus sealed tube'
07	Crystal system	monoclinic
08	Space group	$P2_1/c$
09	Cell length	a 5.8056(4) b 20.1517(17) c 15.8042(10)
10	Cell Angle	α 90 β 91.245(7) δ 90
11	Cell Volume	1848.5(2)
12	Density	1.176
13	Completeness to theta	99.9%
14	Absorption correction	multi-scan
15	Refinement method	Full-matrix least-squares on F2
16	Index ranges	$-6 \leq h \leq 4$, $-24 \leq k \leq 22$, $-18 \leq l \leq 18$
17	Reflection number	3256
18	Theta range	6.554 to 50.094°
19	Cell formula units Z	4
20	CCDC no	1835008

Table 18. Crystal Data and Structure Refinement for Compound **22a**

Entry	Identification code	Compound 22a
01	Empirical formula	$C_{22}H_{25}N_2$
02	Formula weight	317.44
03	Temperature	566(2)
04	Wavelength	0.71073
05	Radiation type	MoK\a
06	Radiation source	'fine-focus sealed tube'
07	Crystal system	monoclinic
08	Space group	$P2_1/c$
09	Cell length	a 11.8010(14) b 7.4153(9) c 21.283(2)
10	Cell Angle	α 90 β 104.980(11) δ 90
11	Cell Volume	1799.1(4)
12	Density	1.172
13	Completeness to theta	99.9%
14	Absorption correction	multi-scan
15	Refinement method	Full-matrix least-squares on F2
16	Index ranges	$-14 \leq h \leq 9$, $-8 \leq k \leq 7$, $-23 \leq l \leq 25$
17	Reflection number	3173
18	Theta range	5.84 to 50.098°
19	Cell formula units Z	4
20	CCDC no	1835010

^{1}H NMR (600 MHz, $CDCl_3$): *2-butyl-6-ethyl-3-propylquinoline* ***(18b)***



^{13}C NMR (150 MHz, $CDCl_3$): *2-butyl-6-ethyl-3-propylquinoline* ***(18b)***

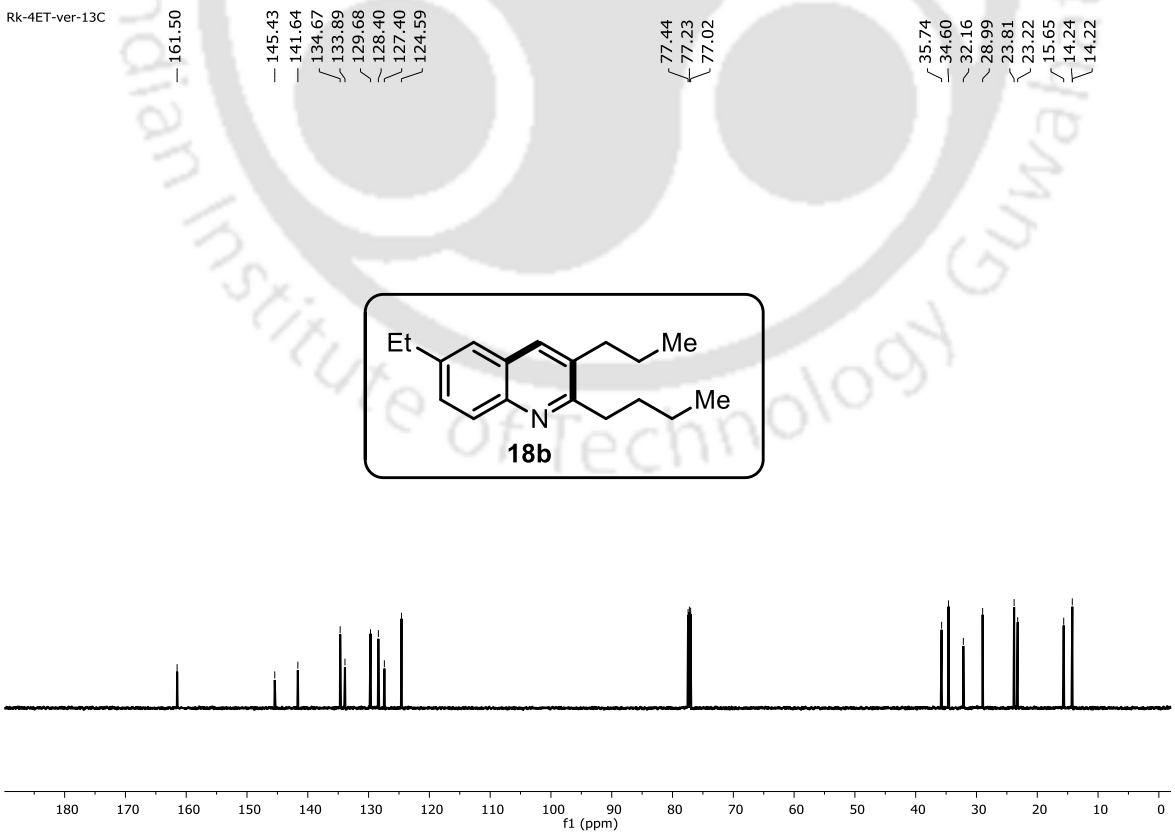
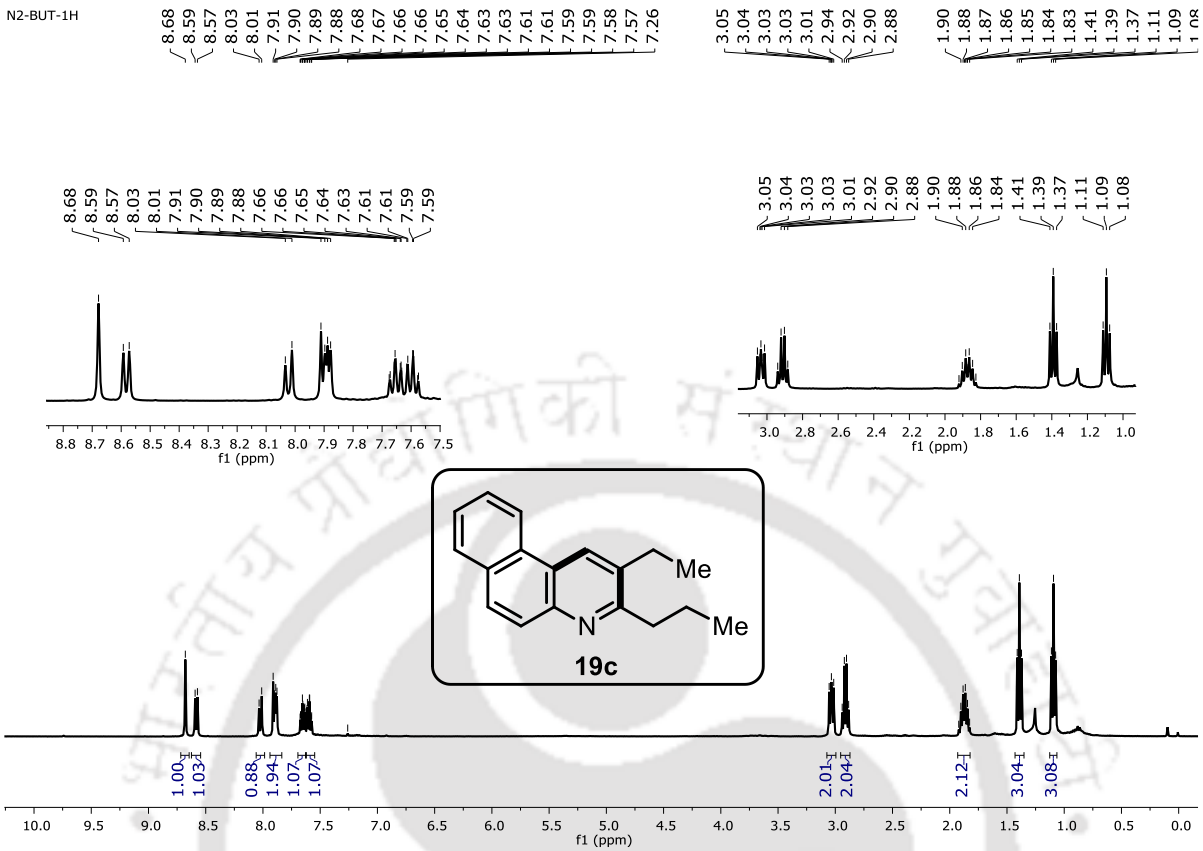


Figure 23

***^{1}H NMR (600 MHz, $CDCl_3$)**: 2-ethyl-3-propylbenzo[f]quinoline (**19c**)*



***^{13}C NMR (150 MHz, $CDCl_3$)**: 2-ethyl-3-propylbenzo[f]quinoline (**19c**)*

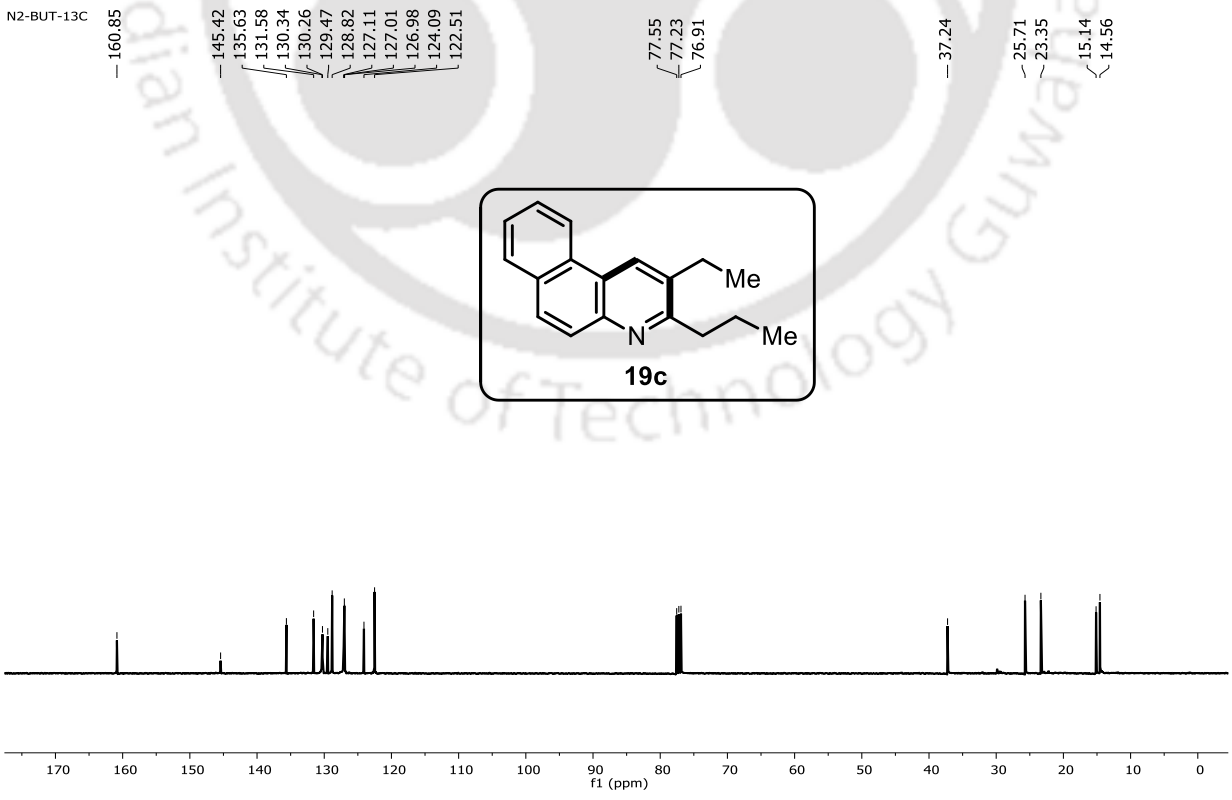
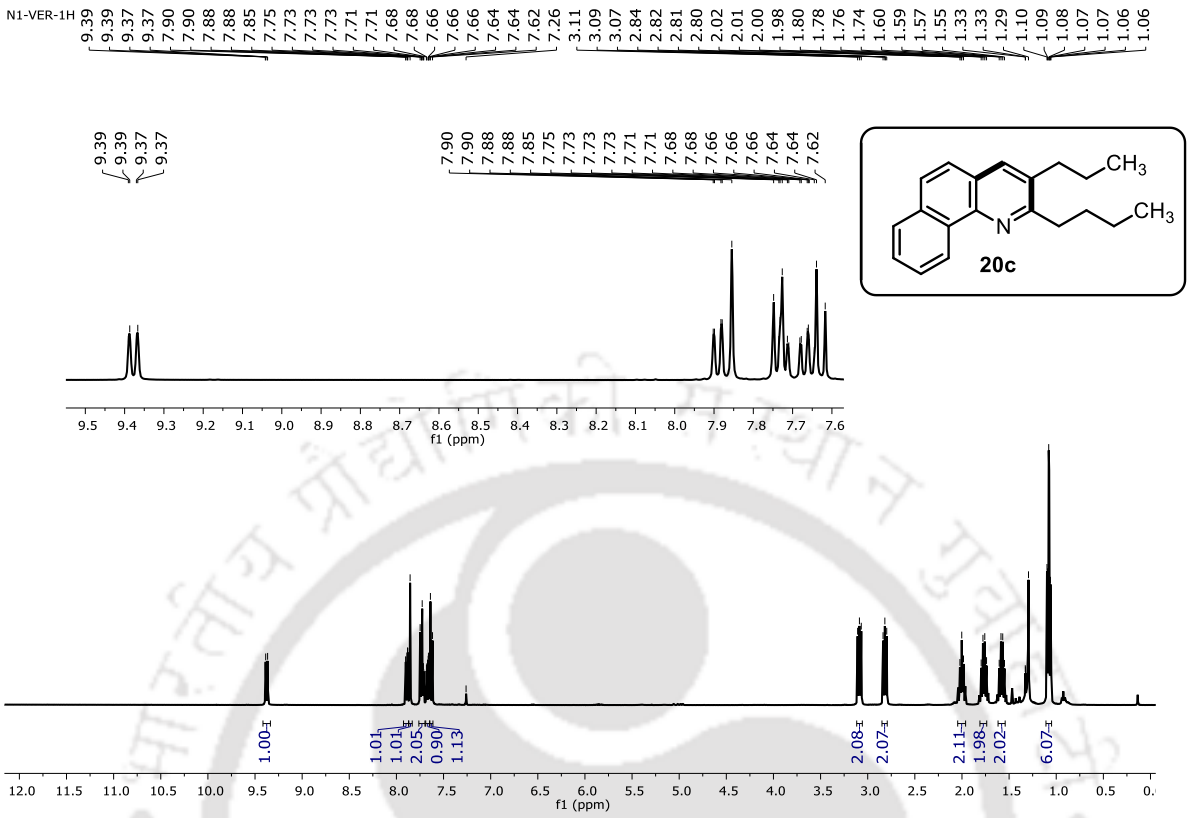


Figure 24

***^{1}H NMR (600 MHz, $CDCl_3$)**: 2-ethyl-3-propylbenzo[f]quinoline (**20c**)*



***^{13}C NMR (600 MHz, $CDCl_3$)**: 2-ethyl-3-propylbenzo[f]quinoline (**20c**)*

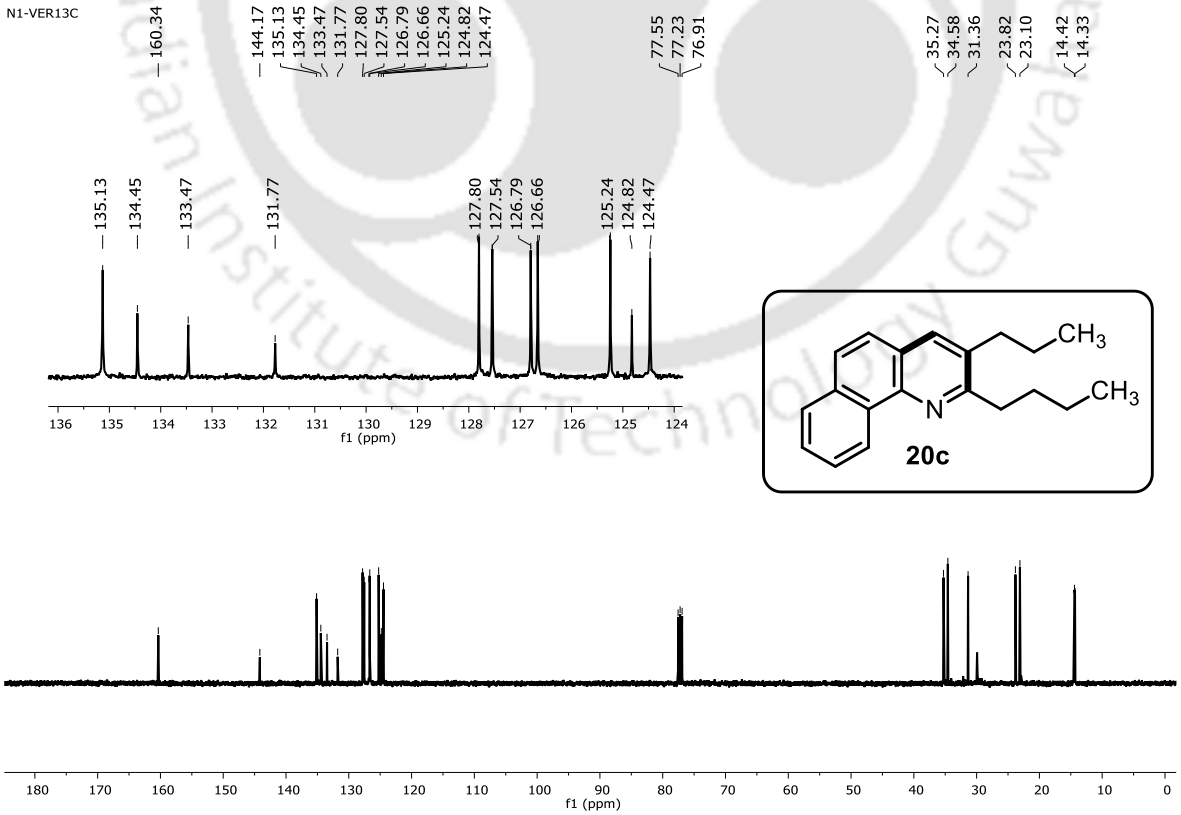
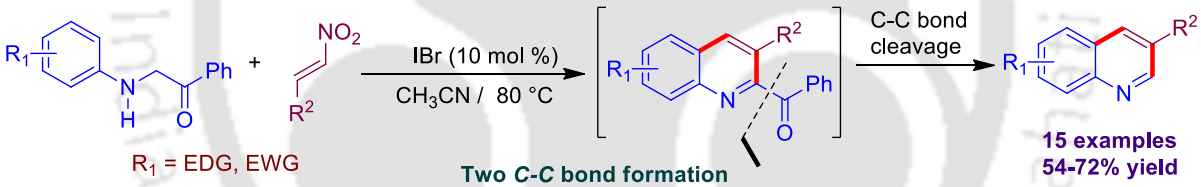


Figure 25

Chapter V

Regioselective Synthesis of 3-arylquinolines Through Tandem Cyclisation of 1-phenyl-2-(phenylamino) ethanone and *trans-β*-Nitrostyrenes



R_1 = EDG, EWG
R_2 = Aryl, Heteroaryl

Two *C-C* bond formation
Oxidative decarbonylation
Broad substrate scope

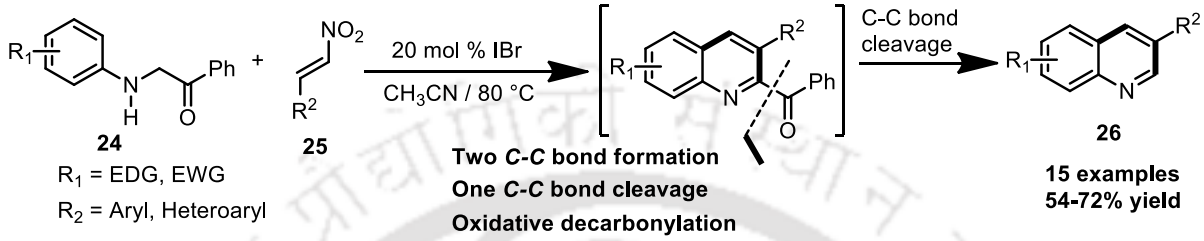
15 examples
54-72% yield

Result & Discussion

Experimental Section

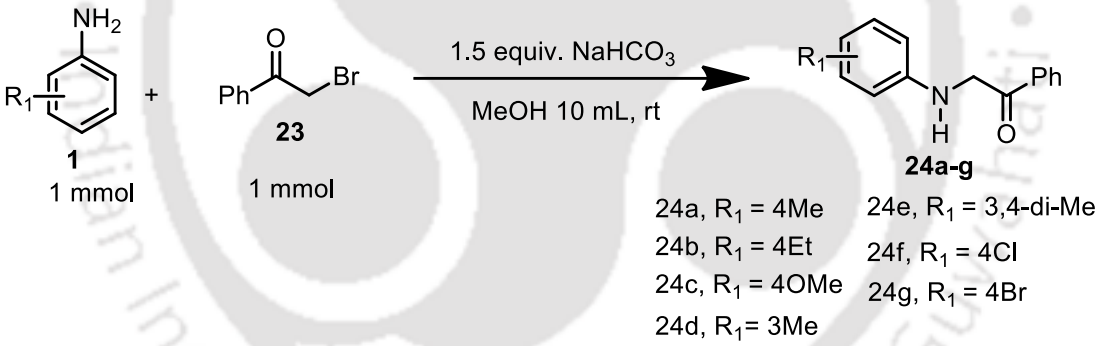
Results and Discussion

In this chapter, we demonstrated a novel and efficient method for the regioselective synthesis of 3-arylquinolines through tandem cyclisation of 1-phenyl-2-(phenylamino)ethanone and *trans*-*β*-nitrostyrene in acetonitrile solvent at 80 °C by using 20 mol % Iodine monobromide as a catalyst as shown in Scheme **55**. This protocol involves the formation of two new C-C bonds and cleavage of one C-C bond through metal-free reaction condition.



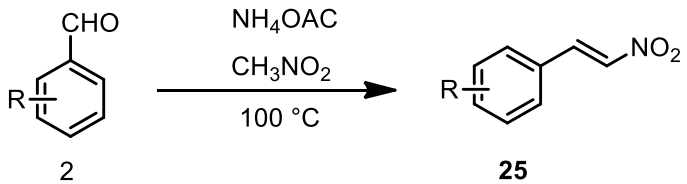
Scheme 55

Various substituted 1-phenyl-2-(phenylamino)ethanones **24a-24g** were prepared from various arylamines **1** and 2-Bromoacetophenone **25** from the literature methods[79] as shown in scheme **56**.



Scheme 56

Various *trans*-*β*-nitrostyrenes **25** were prepared from aldehyde, nitromethane and ammonium acetate at 90 °C from the literature method[80] as shown in Scheme **57.**



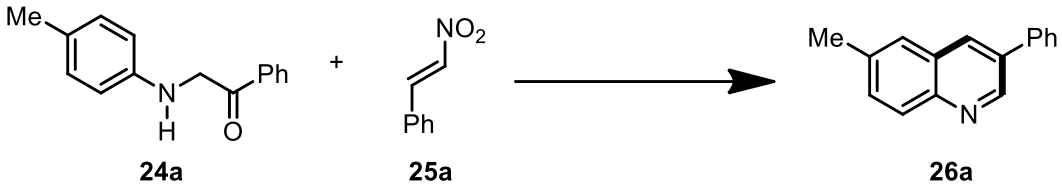
Scheme 57

To find the optimisation reaction condition, we had chosen 1-phenyl-2-(*p*-tolylamino)ethanone **24a** and (*E*)-(2-nitrovinyl)benzene **25a** as the model substrates. (Table

19). Initially, when the reaction was carried out without catalyst, the reaction failed to produce any product (Table 19, entry 1). However, the same set of reaction when examined with 10 mol % of $Bi(OTf)_3$ in CH_3CN under reflux condition, it resulted in the formation of 6-methyl-3-phenylquinoline **26a** in 58% yield (Table 19, entry 2). The structure of **26a** was confirmed through IR, ^1H NMR, ^{13}C NMR spectra and HRMS.

The ^1H NMR shows ten aromatic protons and one singlet at δ 2.57 for methyl group. In addition, no carbonyl carbon signal was present in the ^{13}C spectrum and IR spectrum, which clearly indicates the elimination of benzoyl group. From these data, we have concluded that the product **26a** is 3-arylquinoline derivative. On screening the identical set of reactions with other metal triflates like $Yb(OTf)_3$, $Sc(OTf)_3$, AgOTf and $Cu(OTf)_2$, it was found that the reaction with $Yb(OTf)_3$ and $Sc(OTf)_3$ provided 42% and 24% yields respectively whereas, AgOTf and $Cu(OTf)_2$ were unproductive (Table 19, entries 3-6). In addition to metal triflates, the same set of reactions were also examined with $CuBr_2$, $Cu(OAc)_2$, $FeCl_3$ and $InCl_3$. These reactions did not offer any desired product (Table 19, entries 7-10). Next, the reaction was tested with camphor sulphonic acid, molecular iodine and ICl which were proved to be futile (Table 19, entries 11-13). Whereas, the same reaction in presence of IBr afforded the desired product in 62% yield (Table 19, entry 14). In order to improve the yield, the reaction was carried out with 20 mol % of IBr. It was observed that the reaction time was reduced from 14 h to 10 h and the yield was increased from 62% to 72% (Table 19, entry 15). However, no further increment in the yield was observed by increasing the amount of catalyst to 50 mol % (Table 19, entry 16). Then, the same reaction was examined with 20 mol % of IBr in CH_3CN at room temperature which was unsuccessful (Table 19, entry 17). In addition, various solvents such as MeOH, DMSO, THF and DCE were also screened for the similar reaction in the presence of 20 mol % of IBr. It was found that most of these solvents lead to either poor or negligible yield for the desired product (Table 19, entries 18-21). By summing up, 20 mol % of IBr in acetonitrile at 80 °C was the optimized reaction condition to obtain 6-methyl-3-phenylquinoline **26a**.

Table 19. Optimization of Reaction Conditions[a,b,c,d]



24a **25a** **26a**

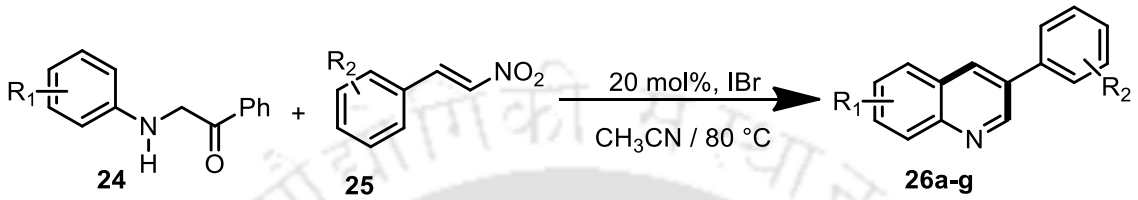
Entry	Catalyst	Mol %	Solvent	Time (h)	Yield 26a (%)[b]
1	No catalyst	-	CH_3CN	24	NR
2	$Bi(OTf)_3$	10	CH_3CN	16	58
3	$Yb(OTf)_3$	10	CH_3CN	24	42
4	$Sc(OTf)_3$	10	CH_3CN	24	24
5	AgOTf	10	CH_3CN	24	NR
6	$Cu(OTf)_2$	10	CH_3CN	24	NR
7	$CuBr_2$	10	CH_3CN	24	NR
8	$Cu(OAc)_2$	10	CH_3CN	24	NR
9	$FeCl_3$	10	CH_3CN	24	NR
10	$InCl_3$	10	CH_3CN	24	NR
11	CSA	10	CH_3CN	24	Traces
12	Iodine	10	CH_3CN	24	NR
13	ICl	10	CH_3CN	24	Trace
14	IBr	10	CH_3CN	14	62
15	**IBr**	**20**	**CH_3CN**	**10**	**72**
16	IBr	50	CH_3CN	08	66
17[c]	IBr	20	CH_3CN	12	NR
18	IBr	20	MeOH	24	NR
19	IBr	20	DMSO	24	NR
20[d]	IBr	20	THF	24	NR
21[d]	IBr	20	DCE	14	40

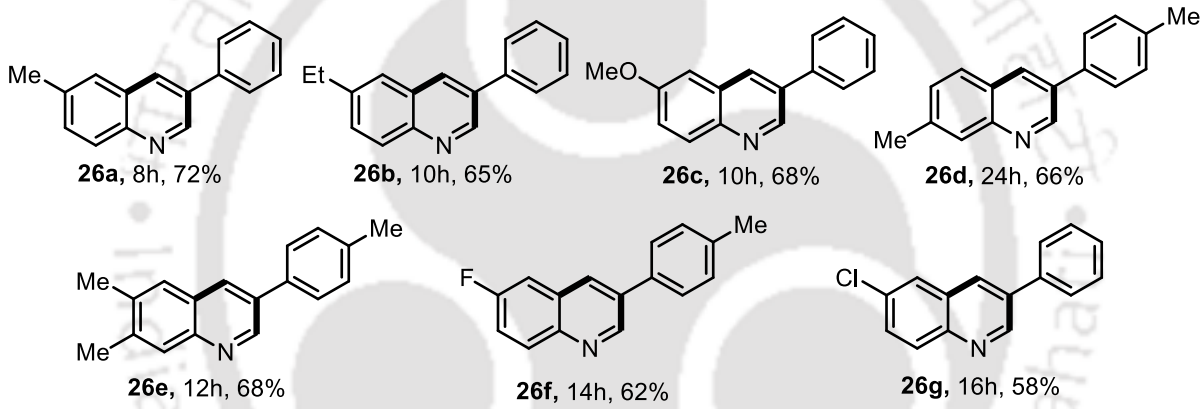
[a]All the reactions were performed using 1-phenyl-2-(*p*-tolylamino)ethanone **24a** (1.0 mmol), and *(E)*-(2-nitrovinyl)benzene **25a** (1.0 mmol) at 80 °C. [b]Isolated yield. [c]Reaction performed at room temperature. [d]Reaction performed at 50 °C. NR = No desired product.

With the optimised condition, the substrate scope for the present protocol was studied with various substituents on the arene ring of the aniline moiety of **24** with *trans-β*-nitrostyrenes **25a** and **25b** as shown in Table **20**. It was found that 1-phenyl-2-(phenylamino)ethanone with

having the electron donating groups 4-Me, 4-Et, 4-OMe, 3-Me, 3,4-Me and electron withdrawing groups like 4-F, 4-Cl worked well leading to the desired products **26a-g** in 58-72% yields. The reaction with electron withdrawing groups such as 4-Br and 4-NO_2 substituents on aniline was unsuccessful to afford desired products.

Table 20: Substrate scope of various substituted anilines with *trans-β*-nitrostyrenes[a,b]

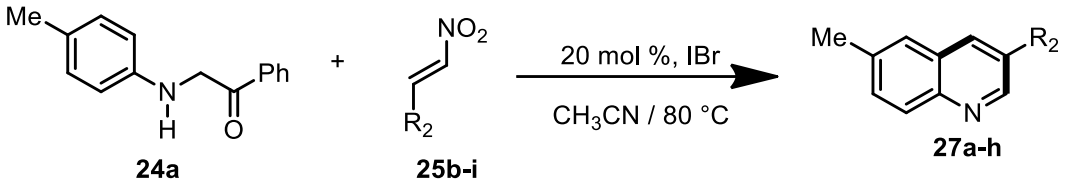


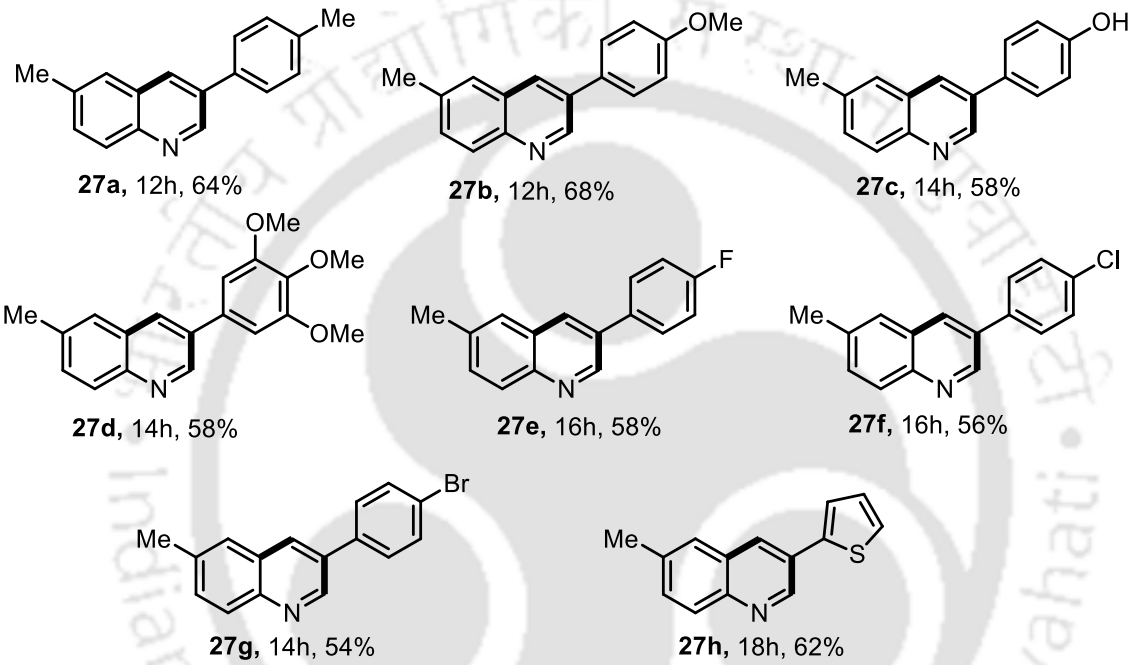


[a]The reactions were carried out using substituted anilines **24** (1 mmol), *trans-β*-nitrostyrenes **25** (1mmol), CH_3CN (1 mL) and IBr (10 mol %) at 80 °C. [b]Isolated yield.

The scope of this protocol was further extended with 1-phenyl-2-(*p*-tolylamino)ethanone (**24a**) and various substituted *trans-β*-nitrostyrenes **25b-i** under optimized reaction condition and the desired products **27a-h** were obtained in good yields as shown in Table **21**. Both electron donating and electron withdrawing group(s) on the aromatic ring of *trans-β*-nitrostyrenes were well tolerated for this reaction. In addition, it was found that the (*E*)-2-(2-nitrovinyl)thiophene **25i** also worked well under the same protocol, whereas strong electron withdrawing groups such as 4-NO_2 substituent on the phenyl ring of *trans-β*-nitrostyrenes **25j** failed to give desired product.

Table 21: Reaction of 1-phenyl-2-(*p*-tolylamino)ethanone with various *trans-β*-nitrostyrenes[a,b]





[a]The reactions were carried out using 1-phenyl-2-(*p*-tolylamino)ethanone **24a** (1 mmol), *trans-β*-nitrostyrenes **25b-i** (1 mmol), CH_3CN (2 mL) and IBr (20 mol %) at 80 °C. [b]Isolated yield.

All the synthesized compounds **26-27** were characterized by IR, ^{1}H NMR, ^{13}C NMR spectra and HRMS. In addition, the structure of compound **27g** was confirmed through single X-ray crystallographic data. ORTEP Diagram of compound **27g** with 40% ellipsoid probability (CCDC no. 1835007) is shown in Figure **26**. The ^{1}H and ^{13}C NMR spectra of compound **26b**, **27a** and **27h** are shown in Figure **27**, **28** and **29** respectively (See Page No 117-119 in experimental section).

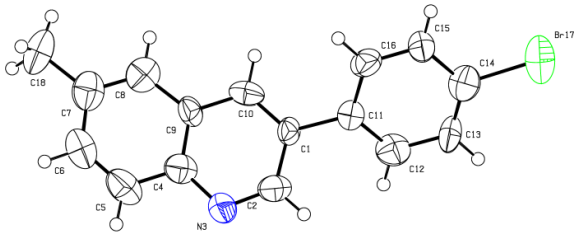
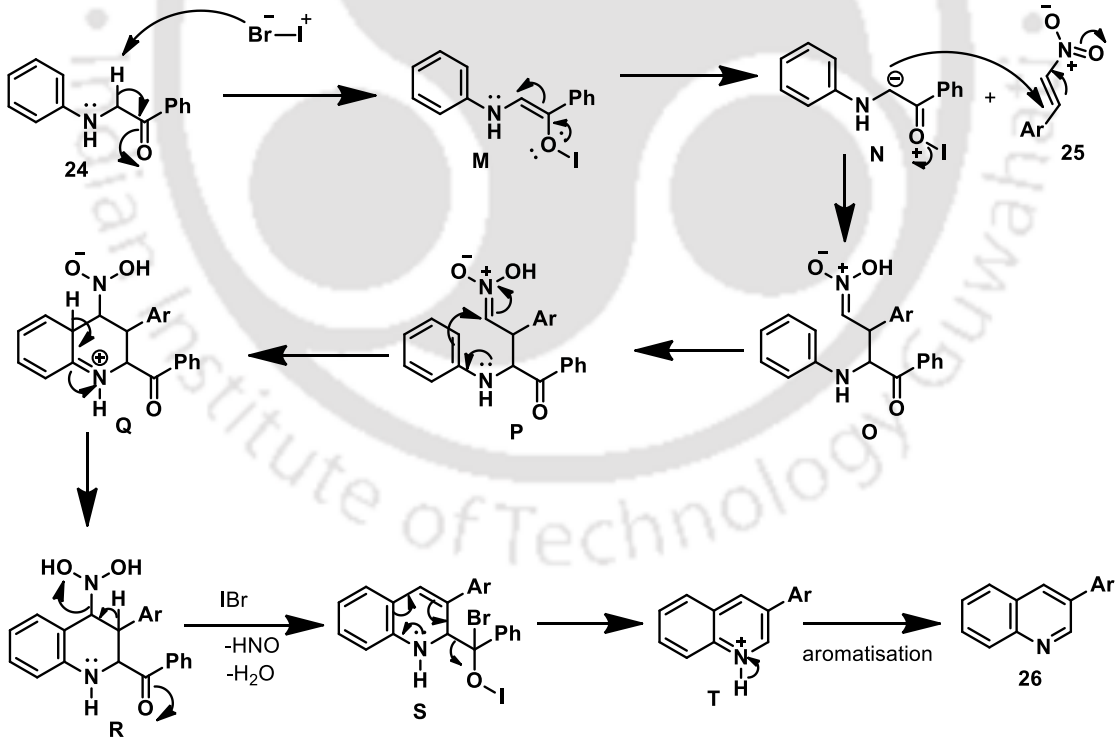


Figure 26

The plausible mechanism for the formation of 3-arylquinolines is shown in the Scheme **58**. Initially, 1-phenyl-2-(*p*-tolylamino)ethanone **24** transforms to enol form **M** and transforms to **N** which reacts with *trans*-*β*-nitrostyrene **25** to form an intermediate **O** through formation of new C-C bond. The intermediate **O** undergoes *ortho* cyclisation with arene ring of aniline to form tetrahydroquinoline **R**. The intermediate **R** undergoes aromatisation to form dihydroquinoline **S** which is involved in aromatisation through elimination of aldehyde group to form stable 3-arylquinoline **26**.



Scheme 58

In summary, we have developed a novel method for the regioselective synthesis of 3-arylquinolines via tandem cyclisation of 1-phenyl-2-(*p*-tolylamino)ethanone and *trans*-*β*-nitrostyrenes by employing 20 mol % iodine monobromide as catalyst. Some of the

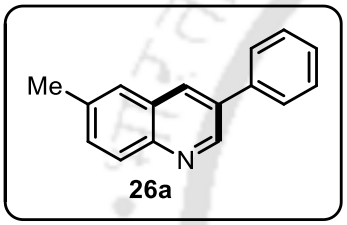
advantages of the present method are formation of two new C-C bonds and cleavage of one C-C bond with large substrate scope in good yields. In addition, the protocol is useful for the synthesis of 3-heteroaryl quinolines.

Experimental Section

General Procedure for Synthesis of 3-arylquinolines **26** & **27**.

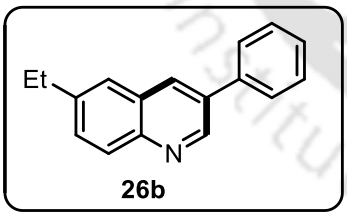
In a dry 25 mL round bottom flask a mixture N-substituted aniline **24** (1.0 mmol), *trans-β*-nitrostyrene **25** (1.0 mmol), IBr (20 mol %) and 5 mL acetonitrile was added and stirred at 80 °C. The progress of the reaction was monitored by TLC. After completion of the reaction the solvent was removed under reduced pressure and it was extracted with DCM (2 x 25 mL) and sodium thiosulfate solution. The organic extract was dried over sodium sulphate and concentrated under reduced pressure. Finally, the residue was purified through silica gel (60-120 mesh) column chromatography with petroleum ether/ethyl acetate (9.5 : 0.5, v/v) to obtain the pure products.

*6-methyl-3-phenylquinoline (**26a**)*



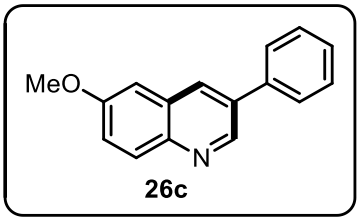
Yield 72% (158 mg), white solid mp 61-62 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.11 (d, *J* = 2.2 Hz, 1H), 8.22 (d, *J* = 2.2 Hz, 1H), 8.03 (d, *J* = 8.6 Hz, 1H), 7.73 – 7.69 (m, 2H), 7.67 – 7.62 (m, 1H), 7.57 – 7.51 (m, 4H), 7.44 (t, *J* = 7.4 Hz, 2H), 2.57 (s, 3H); ^{13}C **NMR** (150 MHz, $CDCl_3$): δ 149.2, 146.2, 138.3, 137.1, 134.0, 132.9, 131.9, 129.4, 129.1, 128.2, 127.6, 127.0, 21.9; **IR (KBr)ν_{max}** 3054, 2927, 2824, 1644, 1514, 1324, 1236, 1214, 1042, 922 cm^{-1}; **HRMS** (ESI) Calcd For $C_{16}H_{14}N$ 220.1121 (M + H^+); Found 220.1141.

*6-ethyl-3-phenylquinoline (**26b**)*



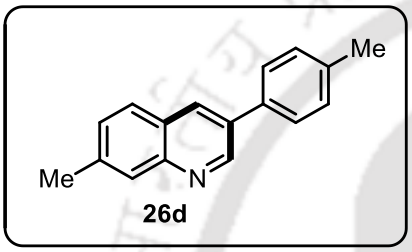
Yield 65% (152 mg), colorless liquid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.12 (d, *J* = 2.3 Hz, 1H), 8.25 (d, *J* = 2.3 Hz, 1H), 8.06 (d, *J* = 8.6 Hz, 1H), 7.73 – 7.70 (m, 2H), 7.66 (d, *J* = 1.9 Hz, 1H), 7.60 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.54 – 7.51 (m, 2H), 7.45 – 7.43 (m, 1H), 2.90 – 2.83 (m, 2H), 1.36 (t, *J* = 7.6 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 149.2, 146.24, 143.4, 138.2, 134.0, 133.1, 130.9, 129.36, 129.1, 128.3, 128.2, 127.6, 125.7, 29.1, 15.6; **IR (KBr)ν_{max}** 2928, 2974, 1624, 1424, 1084, 822 cm^{-1}; **HRMS** (ESI) Calcd For $C_{17}H_{16}N$ 234.1277 (M + H^+); Found 234.1266.

*6-methoxy-3-phenylquinoline (**26c**)*



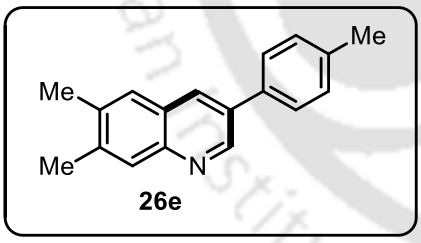
Yield 68% (160 mg), white solid, mp 118-119 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.03 (d, J = 2.2 Hz, 1H), 8.22 (d, *J* = 2.2 Hz, 1H), 8.05 (d, *J* = 9.1 Hz, 1H), 7.74 – 7.68 (m, 2H), 7.53 (t, *J* = 7.7 Hz, 2H), 7.45 – 7.42 (m, 1H), 7.38 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.14 (d, *J* = 2.8 Hz, 1H), 3.96 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 158.4, 147.4, 143.4, 138.2, 134.4, 132.6, 130.5, 129.4, 128.3, 127.6, 122.6, 105.5, 55.80; **IR (KBr)ν_{max}** 2928, 2964, 1632, 1414, 1264, 1084, 822 cm^{-1}; **HRMS** (ESI) Calcd For $C_{16}H_{14}NO$ 236.1070 ($M + H^+$); Found 236.1092.

*7-methyl-3-(p-tolyl)quinoline (**26d**)*



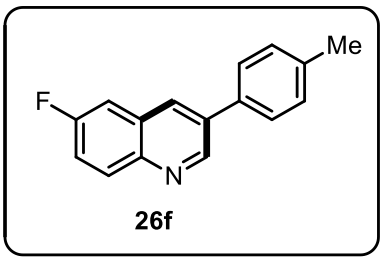
Yield 66% (154 mg), colorless liquid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.15 (s, 1H), 8.26 (d, *J* = 2.2 Hz, 1H), 7.92 (s, 1H), 7.79 (d, *J* = 8.3 Hz, 1H), 7.65 – 7.60 (m, 2H), 7.43 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.37 – 7.32 (m, 2H), 2.61 (s, 3H), 2.46 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 150.1, 147.6, 139.8, 138.1, 135.3, 132.8, 130.1, 130.1, 129.4, 128.3, 127.8, 127.6, 127.4, 22.2, 21.4; **IR (KBr)ν_{max}** 2921, 2978, 1628, 1411, 1092, 817 cm^{-1}; HRMS (ESI) Calcd For $C_{17}H_{16}N$ 234.1277 ($M + H^+$); Found 234.1289.

*6,7-dimethyl-3-(p-tolyl)quinoline (**26e**)*



Yield 68% (168 mg), yellow liquid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.07 (d, *J* = 2.2 Hz, 1H), 8.17 (d, *J* = 2.3 Hz, 1H), 7.88 (s, 1H), 7.61 (d, *J* = 1.7 Hz, 2H), 7.59 (s, 1H), 7.32 (d, *J* = 7.9 Hz, 2H), 2.49 (s, 3H), 2.46 (s, 3H), 2.43 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 149.1, 146.4, 139.8, 138.0, 137.1, 135.5, 133.2, 132.2, 130.0, 128.5, 127.6, 127.4, 127.3, 126.9, 21.4, 20.7, 20.3; **IR (KBr)ν_{max}** 2928, 2974, 1624, 1414, 1084, 832 cm^{-1}; **HRMS** (ESI) Calcd For $C_{18}H_{18}N$ 248.1434 ($M + H^+$); Found 248.1436.

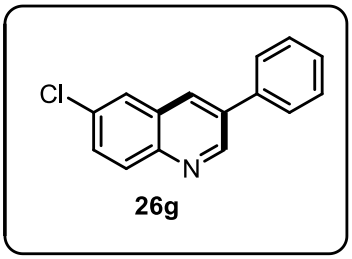
*6-fluoro-3-(p-tolyl)quinoline (**26f**)*



Yield 62% (147 mg), light yellow color liquid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.15 (d, *J* = 2.2 Hz, 1H), 8.25 (d, *J* = 2.2 Hz, 1H), 8.17 – 8.12 (m, 1H), 7.65 – 7.62 (m, 2H), 7.51 (dd, *J* = 8.6, 2.3 Hz, 2H), 7.37 (d, *J* = 7.8 Hz, 2H), 2.46 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 161.8, 160.1, 149.4, 144.4, 138.6, 134.7, 134.7, 132.5, 132.4, 131.8, 131.8, 130.2, 127.5,

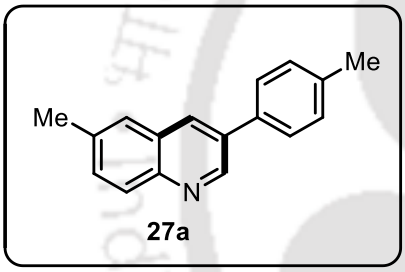
119.8, 119.6, 111.1, 110.9, 21.4; **IR (KBr)ν_{max}** 3062, 2928, 2846, 1654, 1348, 1228, 1098, 1024, 924, 828 cm^{-1}; **HRMS** (ESI) Calcd For $C_{16}H_{13}FN$ 238.1027 ($M + H^+$); Found 238.1018.

*6-chloro-3-phenylquinoline (**26g**)*



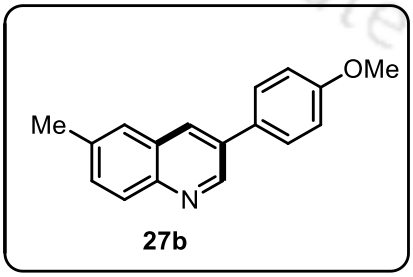
Yield 58% (139 mg), light brown colour solid, mp 110 – 111 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.17 (d, *J* = 2.3 Hz, 1H), 8.22 (d, *J* = 2.2 Hz, 1H), 8.09 (d, *J* = 8.9 Hz, 1H), 7.87 (d, *J* = 2.3 Hz, 1H), 7.73 – 7.69 (m, 2H), 7.66 (dd, *J* = 9.0, 2.3 Hz, 1H), 7.54 (dd, *J* = 8.3, 6.7 Hz, 2H), 7.48 – 7.44 (m, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 150.3, 145.8, 137.6, 134.9, 133.0, 132.5, 130.9, 130.6, 129.5, 128.9, 128.7, 127.7, 126.8; **IR (KBr)ν_{max}** 3054, 2928, 2852, 1648, 1608, 1512, 1328, 1232, 1098, 1034, 926, 828 cm^{-1}; **HRMS** (ESI) Calcd For $C_{15}H_{11}ClN$ 240.0575 ($M + H^+$); Found 240.0597.

*6-methyl-3-(p-tolyl)quinoline (**27a**)*



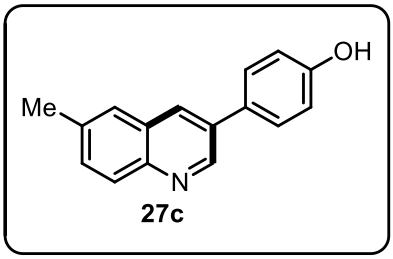
Yield 64% (149 mg), colourless liquid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.10 (d, *J* = 2.3 Hz, 1H), 8.22 – 8.17 (m, 1H), 8.03 (d, *J* = 8.5 Hz, 1H), 7.64 – 7.62 (m, 1H), 7.62 – 7.59 (m, 2H), 7.54 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.35 – 7.31 (m, 2H), 2.56 (d, *J* = 1.0 Hz, 3H), 2.44 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 149.1, 145.8, 138.2, 137.1, 135.2, 133.9, 132.6, 131.8, 130.1, 128.8, 128.3, 127.4, 126.9, 21.9, 21.4; **IR (KBr)ν_{max}** 2928, 2972, 1632, 1421, 1084, 1024, 814 cm^{-1}; **HRMS** (ESI) Calcd For $C_{17}H_{16}N$ 234.1277 ($M + H^+$); Found 234.1299.

*3-(4-methoxyphenyl)-6-methylquinoline (**27b**)*



Yield 68% (170 mg), colourless liquid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.09 (s, 1H), 8.17 (d, *J* = 2.3 Hz, 1H), 8.02 (d, *J* = 8.5 Hz, 1H), 7.66 (s, 1H), 7.62 (s, 1H), 7.53 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.06 (d, *J* = 8.7 Hz, 2H), 3.88 (s, 3H), 2.56 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 159.9, 149.0, 145.6, 137.1, 133.7, 133.2, 132.2, 131.7, 130.6, 128.8, 128.7, 126.9, 114.8, 55.6, 21.9; **IR (KBr)ν_{max}** 2922, 2851, 1716, 1607, 1514, 1251, 1028, 830 cm^{-1}; **HRMS** (ESI) Calcd For $C_{17}H_{16}NO$ 250.1226 ($M + H^+$); Found 250.1248.

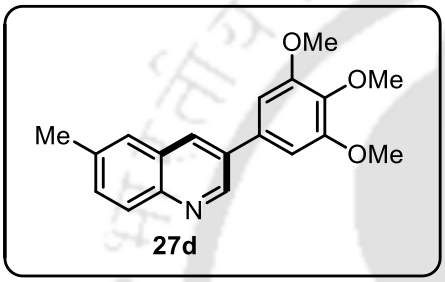
*4-(6-methylquinolin-3-yl)phenol (**27c**)*



27c

Yield 58% (136 mg), light yellow liquid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.07 (d, *J* = 2.3 Hz, 1H), 8.16 (d, *J* = 2.3 Hz, 1H), 8.01 (d, *J* = 8.6 Hz, 1H), 7.62 (s, 1H), 7.62 – 7.58 (m, 2H), 7.53 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.00 (d, *J* = 8.6 Hz, 2H), 2.56 (s, 3H); **^{13}C NMR** (400 MHz, $CDCl_3$): δ 147.9, 146.1, 141.2, 137.4, 131.9, 131.1, 129.1, 128.6, 128.2, 127.8, 126.9, 126.2, 124.5, 21.9; **IR (KBr)ν_{max}** 2928, 2856, 1724, 1614, 1512, 1254, 1038, 1016, 824 cm^{-1}; **HRMS** (ESI) Calcd For $C_{16}H_{14}NO$ 236.1070 ($M + H^+$); Found 236.1091.

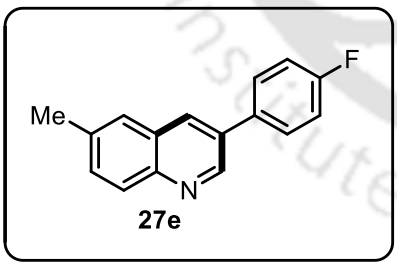
*6-methyl-3-(3,4,5-trimethoxyphenyl)quinoline (**27d**)*



27d

Yield 58% (179 mg), yellow colour liquid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 9.07 (d, *J* = 2.1 Hz, 1H), 8.18 (d, *J* = 2.2 Hz, 1H), 8.04 (d, *J* = 8.6 Hz, 1H), 7.66 (s, 1H), 7.56 (dd, *J* = 8.6, 1.9 Hz, 1H), 6.88 (s, 2H), 3.97 (s, 6H), 3.92 (s, 3H), 2.57 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 154.0, 149.1, 146.1, 138.5, 137.2, 134.2, 134.1, 132.7, 131.9, 129.0, 128.2, 126.9, 104.9, 61.2, 56.5, 21.9; **IR (KBr)ν_{max}** 2926, 2854, 1720, 1612, 1521, 1248, 1022, 824 cm^{-1}; **HRMS** (ESI) Calcd For $C_{19}H_{20}NO_3$ 310.1438 ($M + H^+$); Found 310.1452.

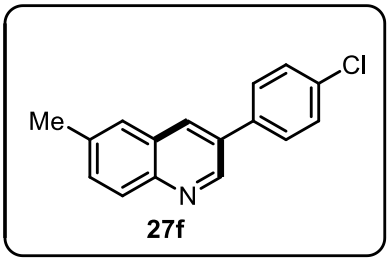
*3-(4-fluorophenyl)-6-methylquinoline (**27e**)*



27e

Yield 58% (138 mg), light yellow liquid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.05 (d, *J* = 2.3 Hz, 1H), 8.19 (d, *J* = 2.3 Hz, 1H), 8.02 (d, *J* = 8.6 Hz, 1H), 7.65 – 7.60 (m, 3H), 7.56 (dd, *J* = 8.5, 1.9 Hz, 1H), 7.51 – 7.47 (m, 2H), 2.57 (s, 3H); **^{13}C NMR** (600 MHz, $CDCl_3$): δ 163.9, 162.3, 148.9, 146.1, 137.3, 133.1, 132.7, 132.1, 129.3, 129.3, 129.0, 128.2, 126.9, 116.4, 116.3, 21.9; **IR (KBr)ν_{max}** 3061, 2924, 2855, 1653, 1600, 1509, 1344, 1231, 1099, 1037, 917, 831 cm^{-1}; **HRMS** (ESI) Calcd For $C_{16}H_{13}FN$ 238.1027 ($M + H^+$); Found 238.1053.

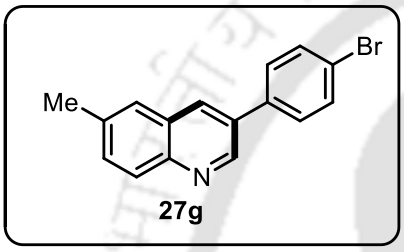
*3-(4-chlorophenyl)-6-methylquinoline (**27f**)*



27f

Yield 56% (142 mg), brown colour solid, mp 150-151 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.05 (d, *J* = 2.3 Hz, 1H), 8.19 (d, *J* = 2.3 Hz, 1H), 8.02 (d, *J* = 8.6 Hz, 1H), 7.65 – 7.60 (m, 3H), 7.56 (dd, *J* = 8.5, 1.9 Hz, 1H), 7.51 – 7.47 (m, 2H), 2.57 (s, 3H); **^{13}C NMR** (600 MHz, $CDCl_3$): δ 148.7, 146.2, 137.4, 136.7, 134.5, 132.9, 132.8, 132.2, 129.6, 128.9, 128.8, 128.2, 127.0, 21.8; **IR (KBr)ν_{max}** 3024, 2922, 2852, 1607, 1513, 1456, 1347, 1252, 1178, 1090, 1026, 829 cm^{-1}; **HRMS** (ESI) Calcd For $C_{16}H_{13}ClN$ 254.0731 ($M + H^+$); Found 254.0749

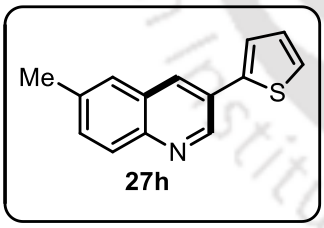
*3-(4-bromophenyl)-6-methylquinoline (**27g**)*



27g

Yield 54% (160 mg), white solid, mp 180-181 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.06 (d, *J* = 2.3 Hz, 1H), 8.19 (dd, *J* = 2.3, 0.8 Hz, 1H), 8.03 (d, *J* = 8.6 Hz, 1H), 7.67 – 7.64 (m, 1H), 7.64 (d, *J* = 2.0 Hz, 2H), 7.58 – 7.57 (m, 2H), 7.56 (d, *J* = 1.9 Hz, 1H), 2.56 (s, 3H); **^{13}C NMR** (600 MHz, $CDCl_3$): δ 148.6, 146.1, 137.4, 137.1, 132.9, 132.5, 132.3, 129.1, 128.9, 128.2, 127.0, 122.7, 21.9; **IR (KBr)ν_{max}** 2921, 2854, 1651, 1484, 1078, 825 cm^{-1}; **HRMS** (ESI) Calcd For $C_{16}H_{13}BrN$ 298.0226 ($M + H^+$); Found 298.0245 and 300.0236.

*6-methyl-3-(thiophen-2-yl)quinoline (**27h**)*



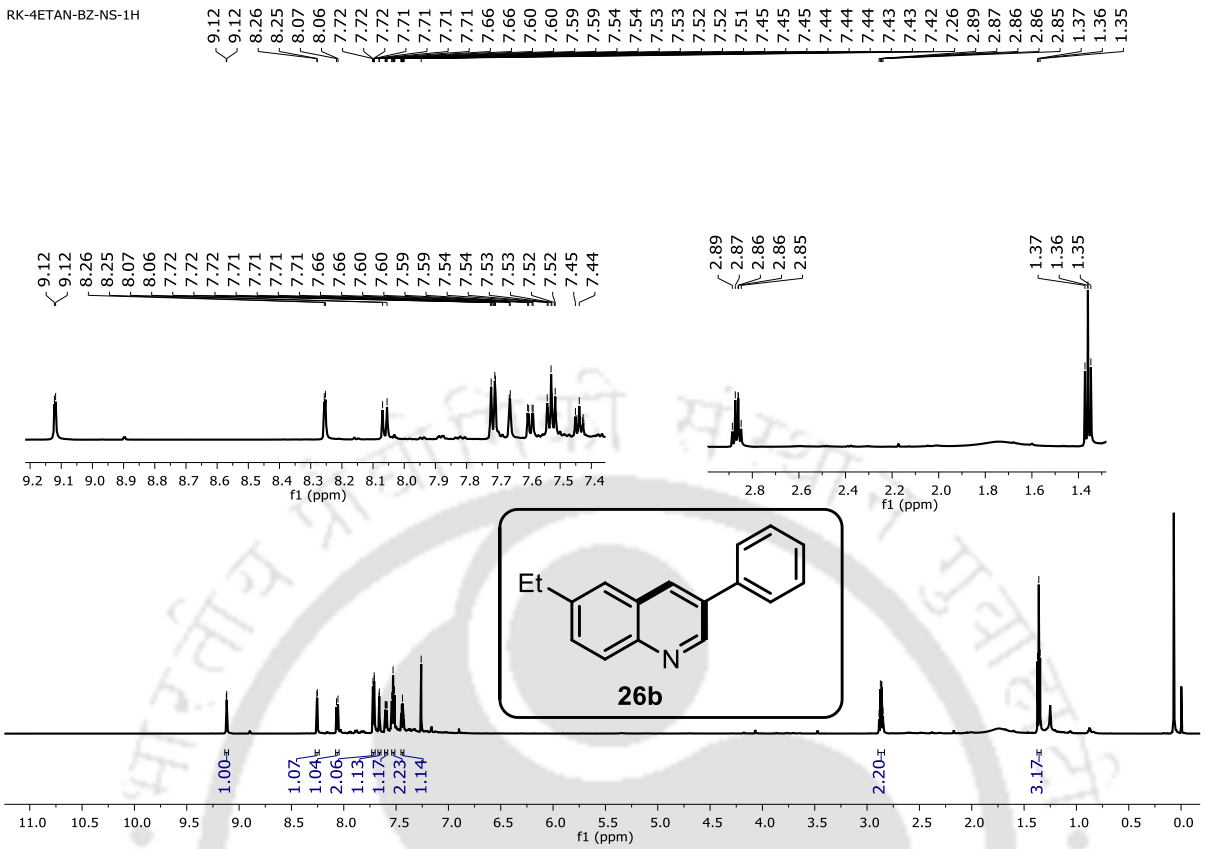
27h

Yield 62% (140 mg), colourless liquid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.13 (d, *J* = 2.3 Hz, 1H), 8.19 (d, *J* = 2.3 Hz, 1H), 7.99 (d, *J* = 8.6 Hz, 1H), 7.60 (d, *J* = 1.7 Hz, 1H), 7.52 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.49 (dd, *J* = 3.6, 1.1 Hz, 1H), 7.39 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.17 (dd, *J* = 5.1, 3.6 Hz, 1H), 2.55 (s, 3H); **^{13}C NMR** (400 MHz, $CDCl_3$): δ 13C NMR (101 MHz, CDCl3) δ 147.9, 146.1, 141.2, 137.4, 131.9, 131.1, 129.1, 128.6, 128.2, 127.8, 126.8, 126.2, 124.5, 21.8; **IR (KBr)ν_{max}** 2928, 2862, 1654, 1478, 1072, 828 cm^{-1}; **HRMS** (ESI) Calcd For $C_{14}H_{12}NS$ 226.0685 ($M + H^+$); Found 226.0709.

Table 11. Crystal Data and Structure Refinement for Compound **27g**

Entry	Identification code	Compound 27g
01	Empirical formula	$C_{16}H_{12}BrN$
02	Formula weight	298.18
03	Temperature	296(2) K
04	Wavelength	0.71073
05	Radiation type	MoK\a
06	Radiation source	'fine-focus sealed tube'
07	Crystal system	monoclinic
08	Space group	Pbcn
09	Cell length	a 13.856(2) b 6.4827(11) c 28.807(3)
10	Cell Angle	α 90 β 90 δ 90
11	Cell Volume	2587.5(6)
12	Density	1.531
13	Completeness to theta	36.98° / 99.7%
14	Absorption correction	multi-scan
15	Refinement method	Full-matrix least-squares on F2
16	Index ranges	$-15 \leq h \leq 16$, $-7 \leq k \leq 7$, $-34 \leq l \leq 32$
17	Reflection number	2283
18	Theta range	5.88 to 50.1°
19	Cell formula units Z	8
20	CCDC no	1835007

***^{1}H NMR (600 MHz, $CDCl_3$)**: 6-ethyl-3-phenylquinoline (**26b**)*



***^{13}C NMR (150 MHz, $CDCl_3$)**: 6-ethyl-3-phenylquinoline (**26b**)*

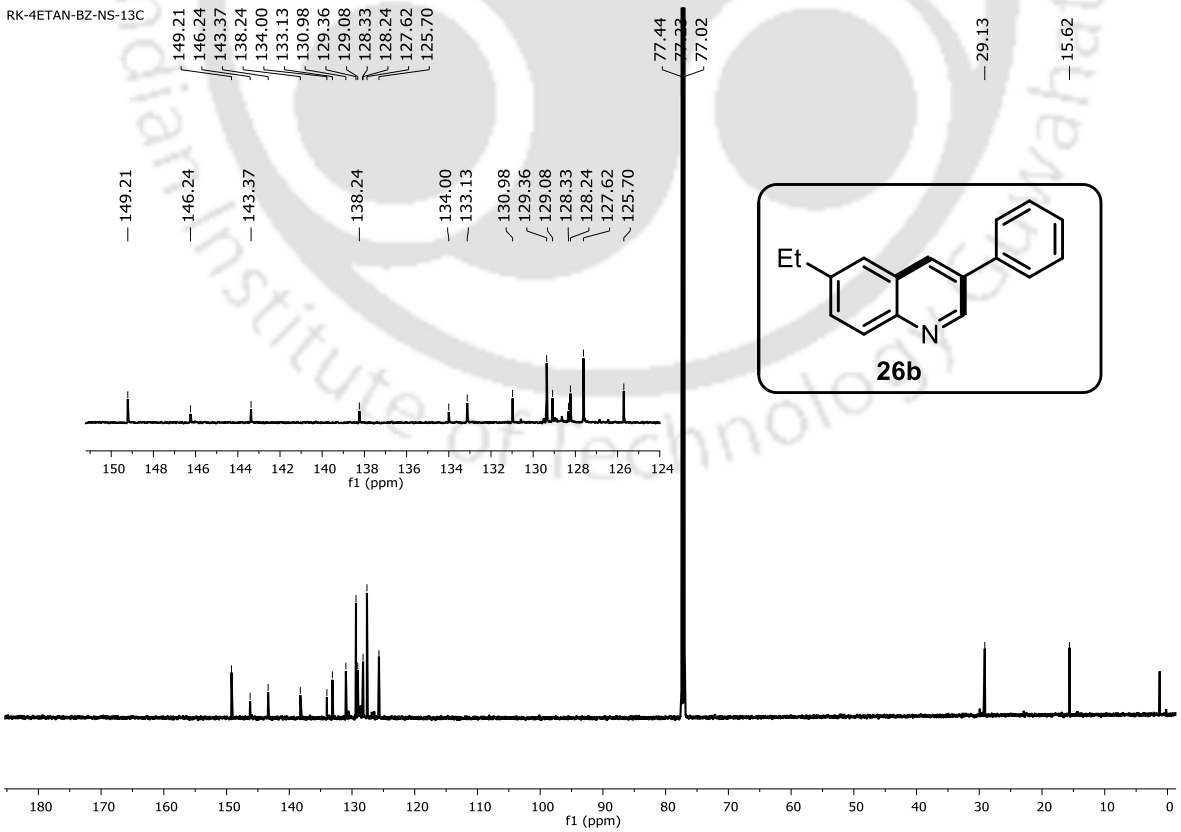
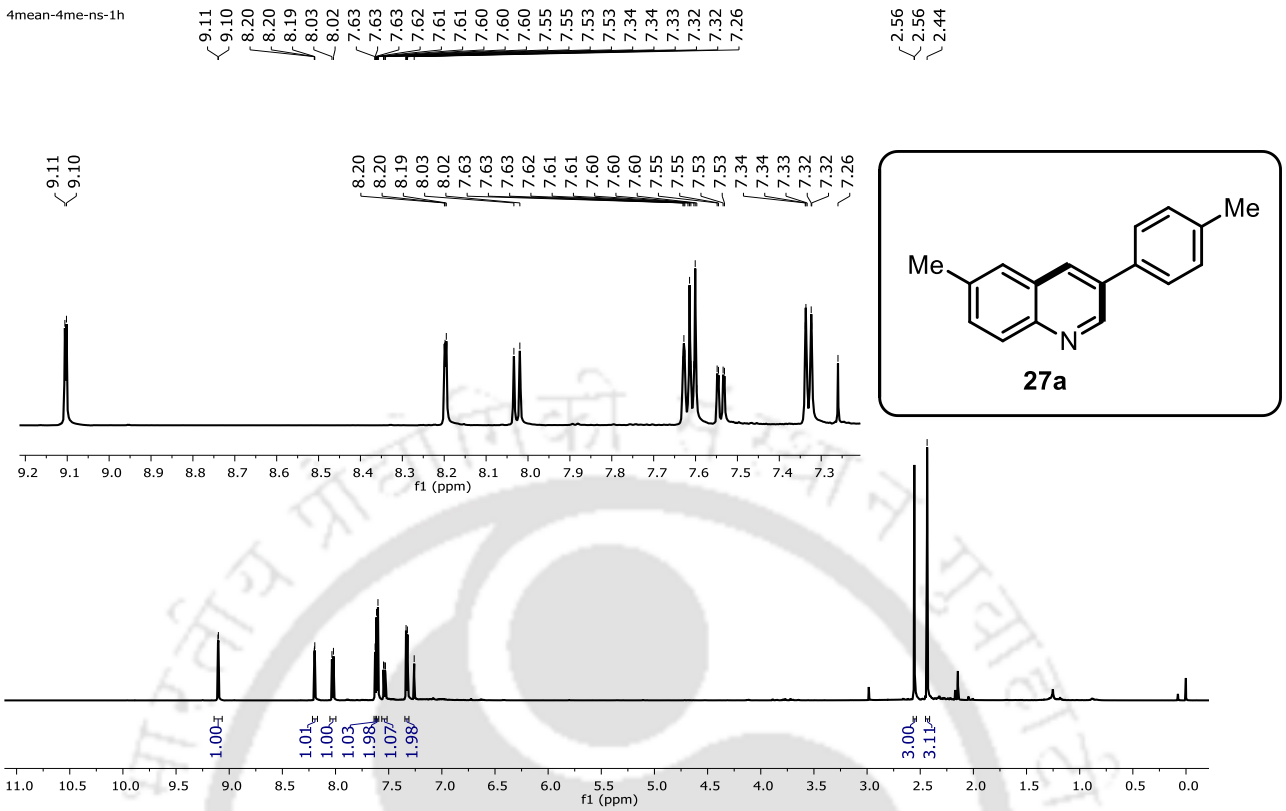


Figure 27

^{1}H NMR (600 MHz, $CDCl_3$): *6-methyl-3-(p-tolyl)quinolone* ***(27a)***



^{13}C NMR (150 MHz, $CDCl_3$): *6-methyl-3-(p-tolyl)quinoline* ***(27a)***

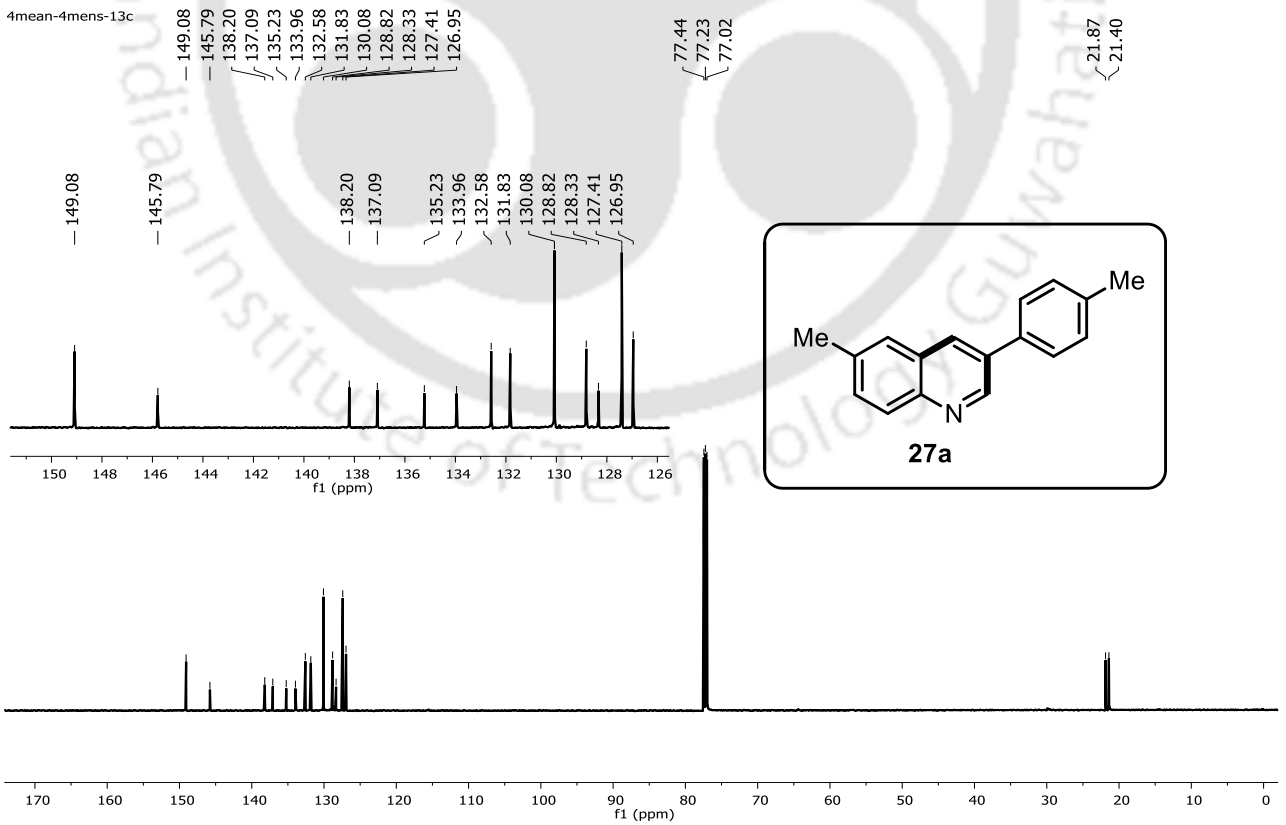
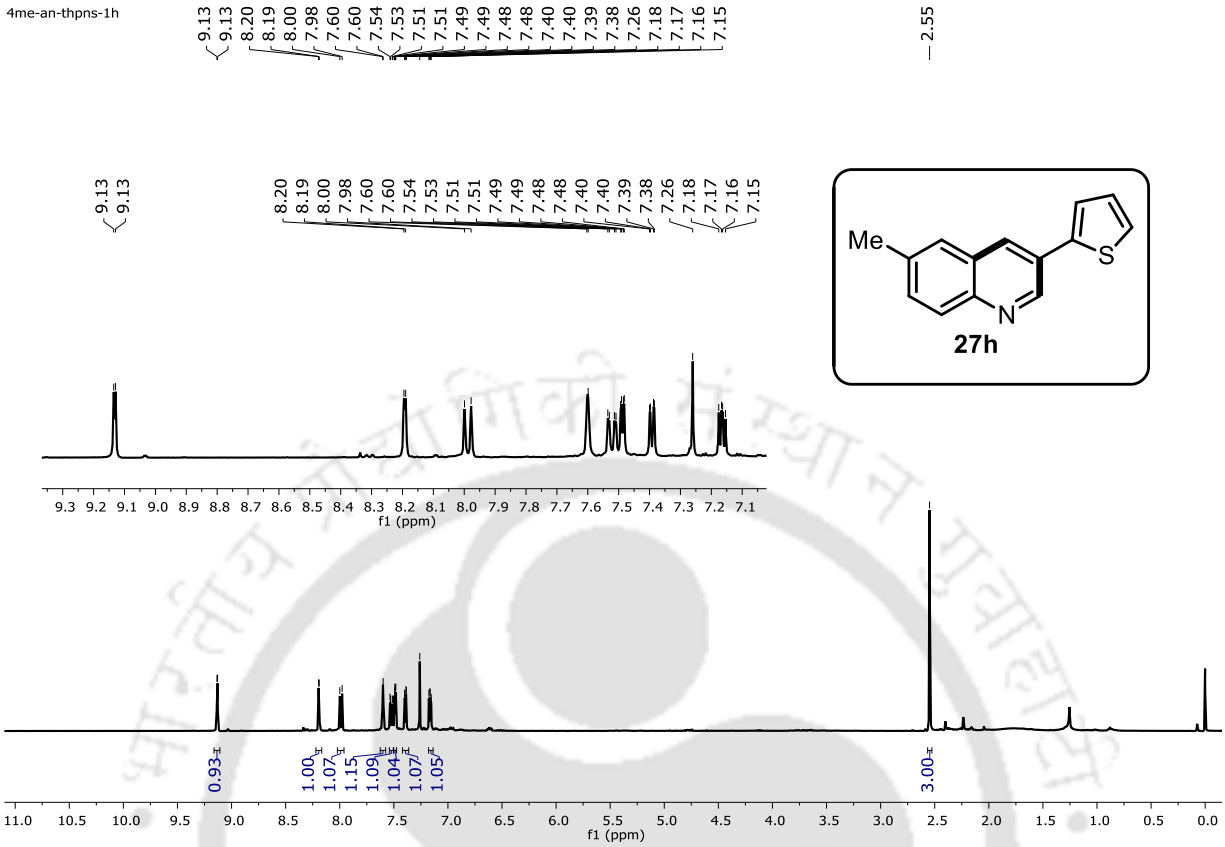


Figure 28

^{1}H NMR (600 MHz, $CDCl_3$): *6-methyl-3-(thiophen-2-yl)quinoline* ***(27h)***



^{13}C NMR (150 MHz, $CDCl_3$): *6-methyl-3-(thiophen-2-yl)quinoline* ***(27h)***

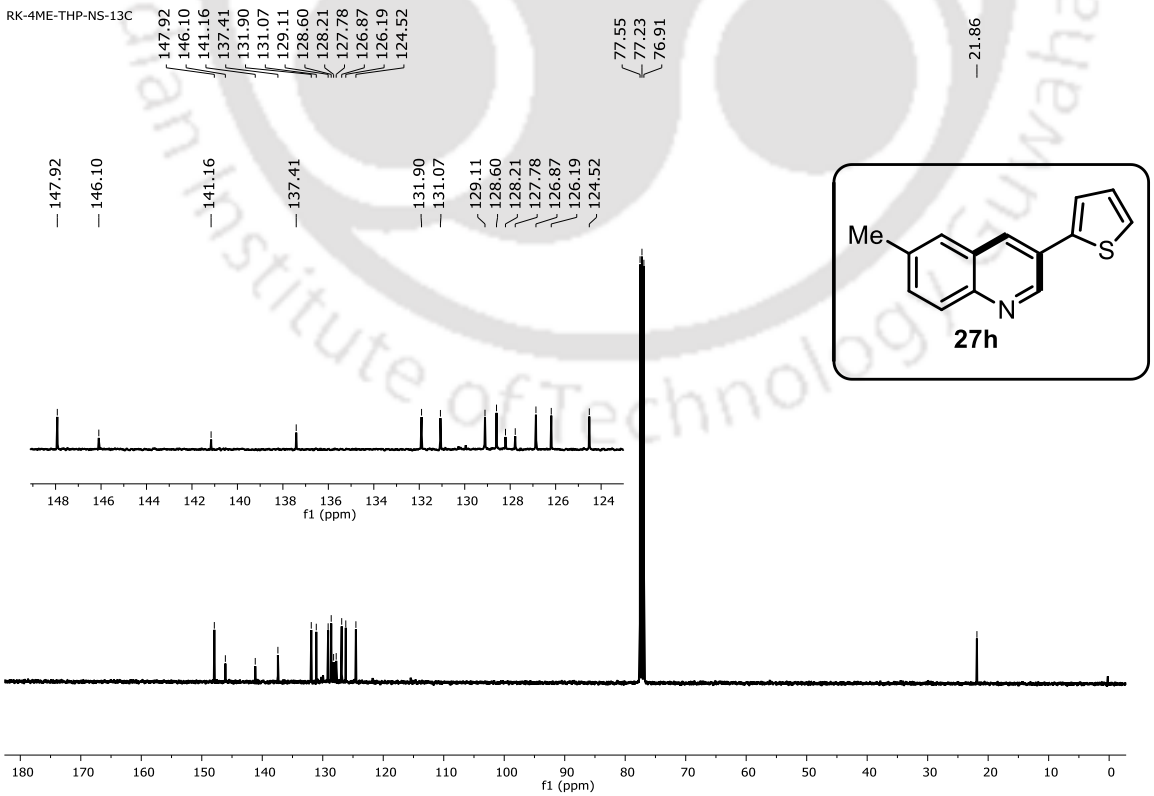
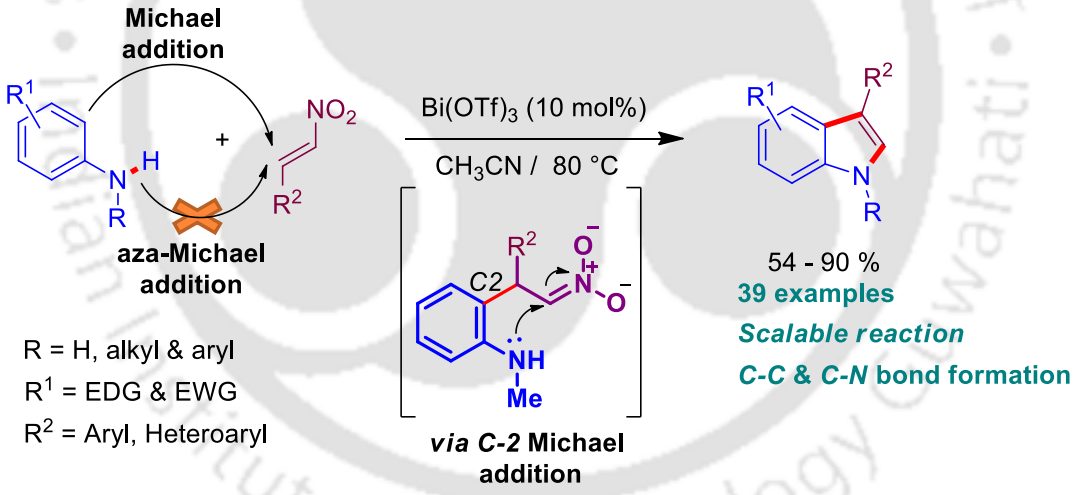


Figure 29

Chapter VI

$Bi(OTf)_3$ Catalyzed Regioselective Syntheses of 3-Arylindoles from Arylamine and *trans*-β-Nitrostyrene

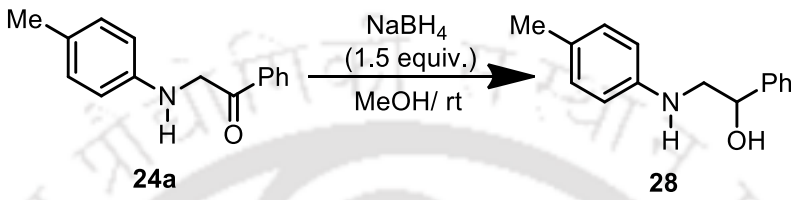


Result & Discussion

Experimental Section

Results and Discussion

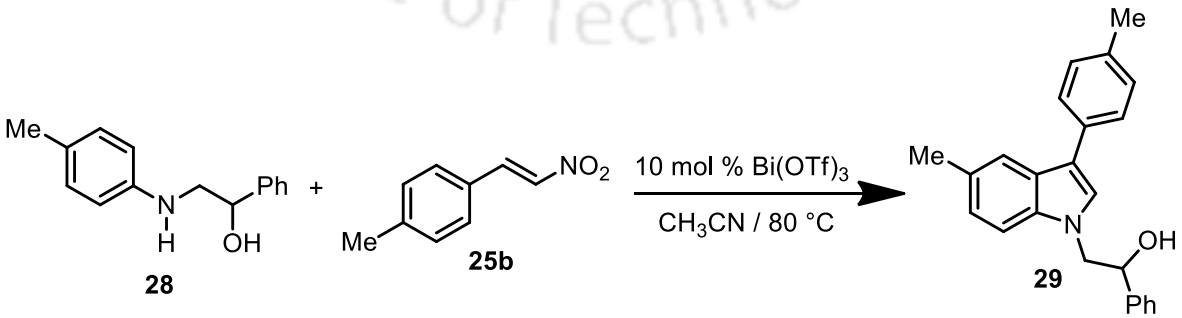
In the previous chapter, we have described the regioselective synthesis of 3-arylquinolines from 1-phenyl-2-(phenylamino)ethanone **24a** and *trans-β*-nitrostyrene **25** by using 20 mol % iodine monobromide as catalyst. To study the effect of functional group for the formation of 3-arylquinolines, the carbonyl functional group of 1-phenyl-2-(phenylamino)ethanone **24a** was reduced to 1-phenyl-2-(*p*-tolylamino)ethanol **28** using $NaBH_4$ as shown in Scheme **59**.



24a **28**

Scheme 59

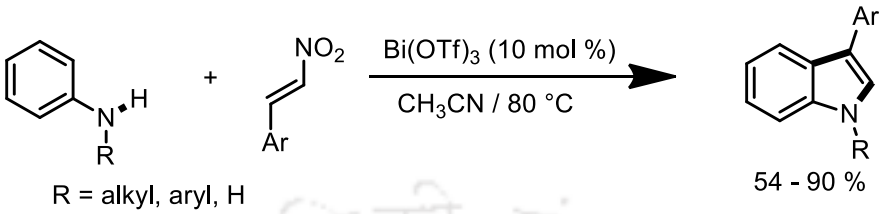
When the reaction was carried out using 1-phenyl-2-(*p*-tolylamino)ethanol **28** and (*E*)-1-methyl-4-(2-nitrovinyl)benzene **25b** in presence of 20 mol % of iodine monobromide as catalyst in acetonitrile at 80 °C, the anticipated product 3-arylquinoline was not formed. Interestingly, when the same reaction was examined with 10 mol % $Bi(OTf)_3$ catalyst and it provided N-substituted 3-arylindole **29** as shown in scheme **60**. The compound 2-(5-methyl-3-(*p*-tolyl)-1H-indol-1-yl)-1-phenylethanol **29** was identified through ^1H and ^{13}C NMR, IR Spectra and HRMS. No strong absorption peaks appeared at 1350 cm^{-1} and 1550 cm^{-1} corresponding to the NO_2 group in the IR spectrum which indicated the elimination of -NO_2 group during the reaction. The ^1H showed the presence of 13 aromatic protons, 5.04 (dd, J = 8.3, 3.7 Hz, 1H), 4.29 – 4.20 (m, 2H) and two methyl peaks at 2.41 (s, 3H) and 2.33 (s, 3H) corresponding to methyl groups of **28** and **25b** which indicated the formation of product **29**.



28 **25b** **29**

Scheme 60

From the above observation, we were further interested in the synthesis of 3-arylindole derivatives from various N-alkylanilines and *trans-β*-nitrostyrenes. In this chapter, we have discussed the regioselective synthesis of 3-arylindoles from N-alkyl anilines and *trans-β*-nitrostyrene by using 10 mol % $Bi(OTf)_3$ catalyst as shown in Scheme **61**.

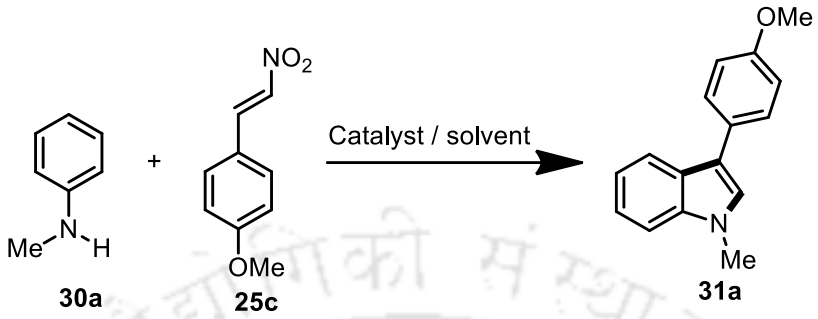


Scheme 61

To find out the optimum reaction conditions, *N*-methylaniline **30** (1.0 mmol) and (*E*)-1-methoxy-4-(2-nitrovinyl)benzene **23ac** (1.0 mmol) were selected as the model substrates (Table 23). When the reaction was performed without catalyst in acetonitrile at 80 °C, the reaction did not proceed well, and starting materials were recovered (Table 23, entry 1). Next, the same set of reaction was carried out with 20 mol % of IBr as a catalyst in CH_3CN solvent at 80 °C and it was also unsuccessful for getting expected product (Table 23, entry 2). Further, the reaction was examined with 5 mol % $Bi(OTf)_3$ as catalyst in CH_3CN solvent at 80 °C which resulted a yellow semi-solid product **31a** after chromatographic separation in 52% yield (Table 23, entry 3). In the ^{1}HNMR spectrum, it showed two singlets at δ 3.86 and 3.89 corresponding to *N*-Me and -OMe groups present in the molecule. There was no absorption peak at 1350 cm^{-1} and 1550 cm^{-1} which indicated elimination of NO_2 group leading to the formation of 3-(4-methoxyphenyl)-1-methyl-1H-indole **31a**. In addition, the compound **31a** was also confirmed by HRMS. It was observed that the reaction proceeded faster and offered better yield when the catalyst was increased from 5 mol % to 10 mol % (Table 23, entry 4). However, further increase of catalyst to 15 mol % led to an insignificant change in the reaction time as well as the yield (Table 23, entry 5). In order to determine the efficacy of various metal triflates as a catalyst for the synthesis of 3-arylindole derivatives, the same set of reaction was performed with 10 mol % of $Yb(OTf)_3$, $Sc(OTf)_3$, AgOTf and $Cu(OTf)_2$. It was found that while $Yb(OTf)_3$ and $Sc(OTf)_3$ gave lower yields and other metal triflates were unsuccessful (Table 23, entries 6-9). In addition to the metal triflates, the similar reaction was also screened with $Cu(OAc)_2$ and $FeCl_3$ however, these catalysts for this particular reaction were found to be ineffective (Table 23, entries 10-11). The reaction failed to afford desired product when it was performed at room temperature (Table 23, entry 12).

Next, various polar solvents were also scrutinized and these solvents gave either poor or no yield of the expected product (Table 23, entries 13-19).

Table **23**. Optimization of Reaction Conditions[a,b,c,d]



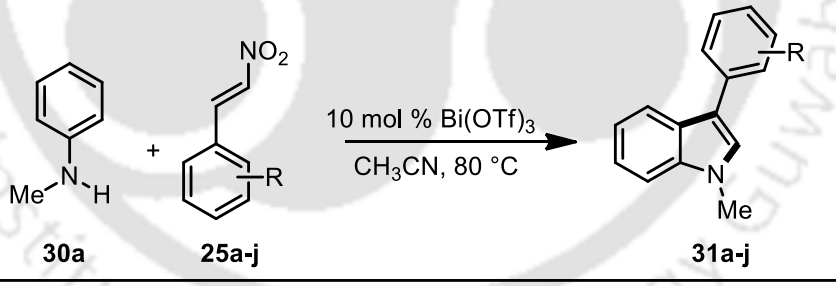
Entry	Catalyst	Mol %	Solvent	Time (h)	Yield **3** (%)[b]
1	No catalyst	-	CH_3CN	24	NR
2	IBr	20	CH_3CN	24	NR
3	$Bi(OTf)_3$	05	CH_3CN	20	52
4	**$Bi(OTf)_3$**	**10**	**CH_3CN**	**16**	**74**
5	$Bi(OTf)_3$	15	CH_3CN	16	74
6	$Yb(OTf)_3$	10	CH_3CN	18	68
7	$Sc(OTf)_3$	10	CH_3CN	24	46
8	AgOTf	10	CH_3CN	24	Trace
9	$Cu(OTf)_2$	10	CH_3CN	24	Trace
10	$Cu(OAc)_2$	10	CH_3CN	24	NR
11	$FeCl_3$	10	CH_3CN	24	NR
12[c]	$Bi(OTf)_3$	10	CH_3CN	24	NR
13	$Bi(OTf)_3$	10	DMSO	24	NR
14	$Bi(OTf)_3$	10	DMF	24	NR
15[d]	$Bi(OTf)_3$	10	DCE	24	62
16[d]	$Bi(OTf)_3$	10	DCM	24	25
17	$Bi(OTf)_3$	10	Toluene	24	48
18	$Bi(OTf)_3$	10	H_2O	24	56
19[d]	$Bi(OTf)_3$	10	THF	24	28

[a]All the reactions were performed using *N*-methylaniline **30** (1.0 mmol), *(E)*-1-methoxy-4-(2-nitrovinyl)benzene **25c** (1.0 mmol) at 80 °C. [b]Isolated yield. [c]Reaction performed at room temperature. [d]Reaction performed at 50 °C.

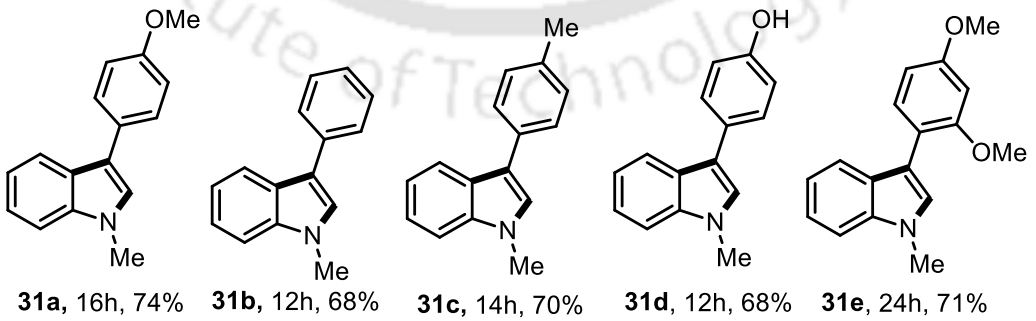
The acetonitrile solvent was found to be better in terms of reaction time and yield. By summing up, 10 mol % of $Bi(OTf)_3$ in acetonitrile at 80 °C was the best optimized condition for attaining 3-arylindole derivatives from *N*-methylaniline and (*E*)-1-methoxy-4-(2-nitrovinyl)benzene.

With the optimized conditions in hand, the scope of the protocol was investigated for the reaction of *N*-methylaniline **30a** with a series of various substituted *trans-β-n*itrostyrenes **25c**, as represented in Table **24**. The reaction was feasible for various *trans-β*-nitrostyrenes with electron-donating groups like 4-Me, 4-OH, 2,4-OMe, 3,4,5-OMe as well as electron-withdrawing groups such as 4-F, 4-Cl giving the products **31a-h** in moderate to good yields. The best yield (85%) was obtained in the case of (*E*)-2-(2-nitrovinyl)naphthalene **31i**. In addition, it was found that the *(E)-2-(2-nitrovinyl)thiophene* worked well under the same protocol. The strong electron-withdrawing groups such as 4-Br, 4-NO_2 on phenyl ring of *trans-β*-nitrostyrene failed to give corresponding 3-arylindoles. The (*E*)-(2-nitroprop-1-en-1-yl)benzene also failed to give 1,2-dimethyl-3-phenyl-1H-indole which may be due to steric crowding between methyl groups of *N*-methylaniline and (*E*)-(2-nitroprop-1-en-1-yl)benzene.

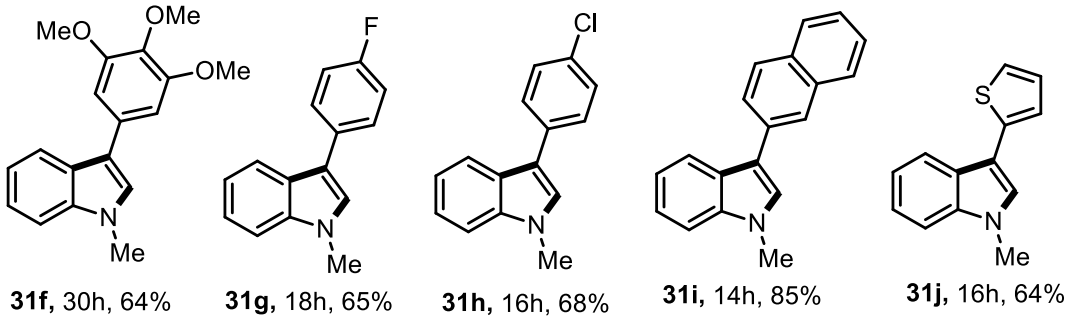
Table 24: Reaction of *N*-methylaniline with various *trans-β-nitrostyrenes*[a,b]



30a **25a-j** **31a-j**



31a, 16h, 74% **31b,** 12h, 68% **31c,** 14h, 70% **31d**, 12h, 68% **31e**, 24h, 71%

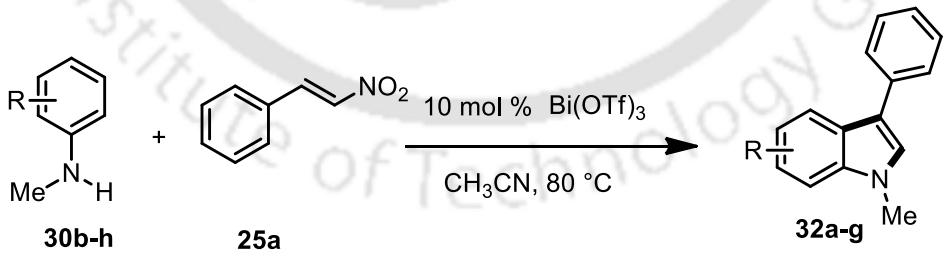


31f, 30h, 64% **31g,** 18h, 65% **31h,** 16h, 68% **31i,** 14h, 85% **31j,** 16h, 64%

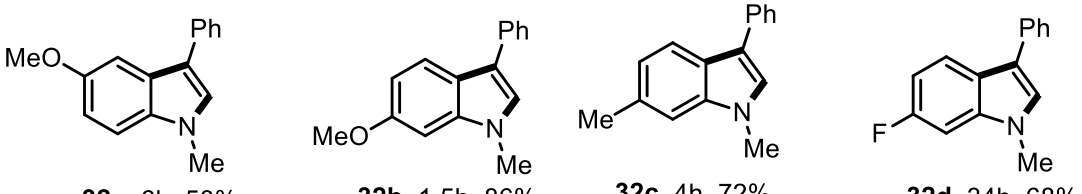
[a]The reactions were carried out using *N*-methylaniline **30a** (1 mmol), *trans*-*β*-nitrostyrenes **25a-j** (1 mmol), CH_3CN (2 mL) and $Bi(OTf)_3$ (10 mol %) at 80 °C. [b]Isolated yield.

To study the generality of the present protocol, the reactions were performed with various substituted *N*-methylaniline **30b-30h** with (*E*)-(2-nitrovinyl)benzene **25a** as shown in Table **25**. It was found that *N*-methylanilines with the electron-donating groups 4-OMe, 3-OMe, 3-Me and 3,5-di-Me or electron-withdrawing group like 3-F, 3-Cl worked well giving the products **32a-f** in 58-86% yield. We find that delight the reaction underwent smoothly with *N*-methyl-2-aminofluorene affording the product **32g** in 62% yield. The reason for the better yield in case of **32b** is +M (mesomeric) effect of the 3-OMe group and +I (inductive) effect of N-methyl group which increase the nucleophilicity in a synergistic manner at the C6 position of 3-methoxy-N-methylaniline to enhance 1,4-addition with *trans*-*β*-nitrostyrenes. The reaction with electron withdrawing groups such as 4-F, 4-Cl, and 4-Br substituted *N*-methylanilines (**30i-k**) failed which might be due to less electron density on the aromatic ring and hence reluctance to form *C*-*C* bond through 1,4-addition with *trans*-*β*-nitrostyrene.

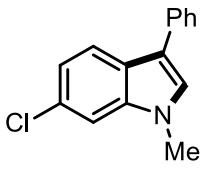
Table 25: Substrate scope of various *N*-methylaniline with (*E*)-(2-nitrovinyl)benzene[a,b]



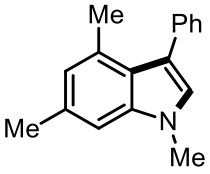
30b-h **25a** **32a-g**



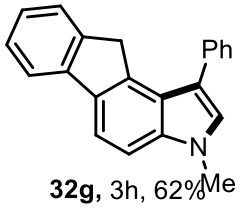
32a, 6h, 58% **32b,** 1.5h, 86% **32c,** 4h, 72% **32d,** 34h, 68%



32e, 36h, 58%



32f, 4h, 72%

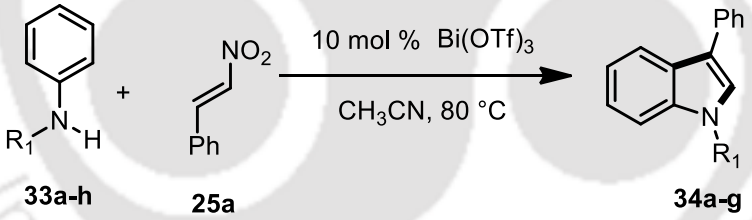


32g, 3h, 62%

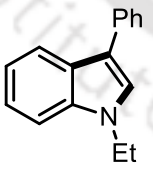
[a]The reactions were carried out using *N*-arylamines **30b-h** (1 mmol), (*E*)-(2-nitrovinyl)benzene **25a** (1 mmol), CH_3CN (1 mL) and $Bi(OTf)_3$ (10 mol %) at 80 °C. [b]Isolated yield.

Next, the present procedure was further extended for the synthesis of 1-substituted-3-phenyl-1*H*-indole derivatives **33** using various *N*-substituted anilines **33a-h** with *trans-β*-nitrostyrenes under the optimized reaction condition to offer the corresponding products **34a-h** with 62-78% yields, as depicted in Table **26**. The N-substituted anilines with electron donating groups such as N-ethyl, N-butyl, N-ethyl-2-ol, N-cyclohexyl, N-phenyl, N-benzyl groups worked well for this protocol. However, the electron withdrawing groups such N-tosylaniline **33i** and N-benzoylanilines **33j** on reaction with *trans-β*-nitrostyrene failed to obtain desired product due to less electron density at *ortho* position of aniline to form 1,4 addition with *trans-β*-nitrostyrene.

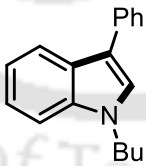
Table 26: Reaction of various *N*-substituted anilines with *trans-β*-nitrostyrene[a,b]



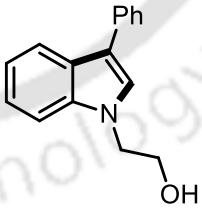
33a-h **25a** **34a-g**



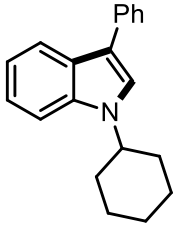
34a, 5h, 68%



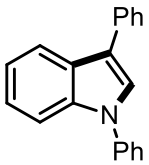
34b, 16h, 72%



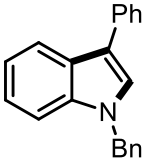
34c, 12h, 68%



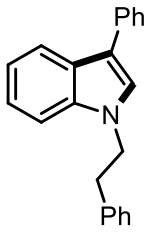
34d, 24h, 62%



34e, 16h, 66%



34f, 20h, 78%

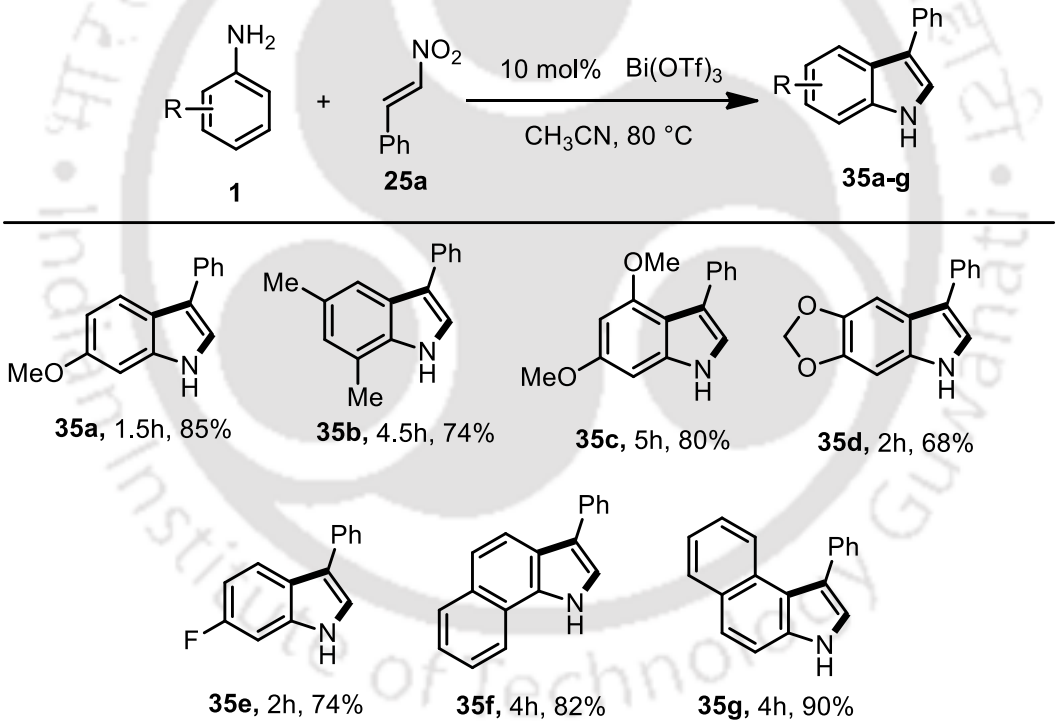


34g, 32h, 64%

[a]The reactions were carried out using *N*-substituted anilines **33a-h** (1 mmol), *trans-β*-nitrostyrenes **25a** (1 mmol), CH_3CN (1 mL) and $Bi(OTf)_3$ (10 mol %) at 80 °C. [b]Isolated yield.

Under the similar reaction conditions, a variety of anilines were converted to the corresponding 3-phenyl-1*H*-indole **35a-g** with 68-90% yield. The anilines with electron-donating groups such as 3-OMe, 2,4-Me, 3,5-OMe and 3,4-Methylenedioxy were well tolerated. 3-Fluoroaniline on reaction with *trans-β*-nitrostyrene gave the product **35e** which is an inhibitor of brassinin glucosyltransferase.[81] Similarly, the reaction worked well with 1-naphthyl- and 2-naphthylamines as illustrated in Table **27**. However, the reaction completely failed to offer the desired product with 4-F/4-Cl/4-Br aniline. Thus, it may be concluded that when the electron-withdrawing groups were present at the *para* position of aniline, the reaction was unsuccessful due to less electron density on the π-electrons of the aryl ring to participate in 1,4-addition with the *trans-β*-nitrostyrene to form the corresponding 3-arylindole derivative.

Table **27**: Reaction of various arylamines with *trans-β*-nitrostyrene[a,b]

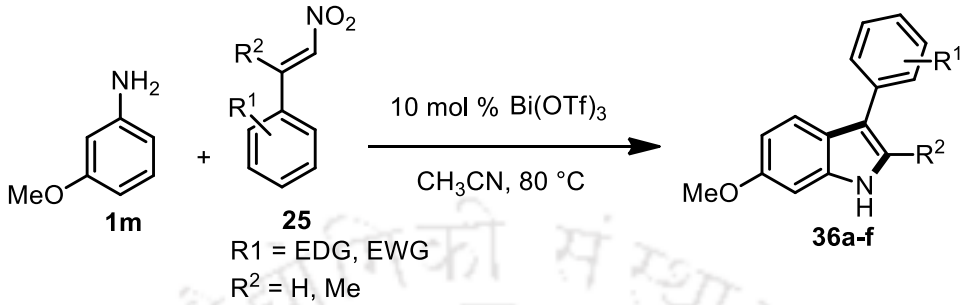


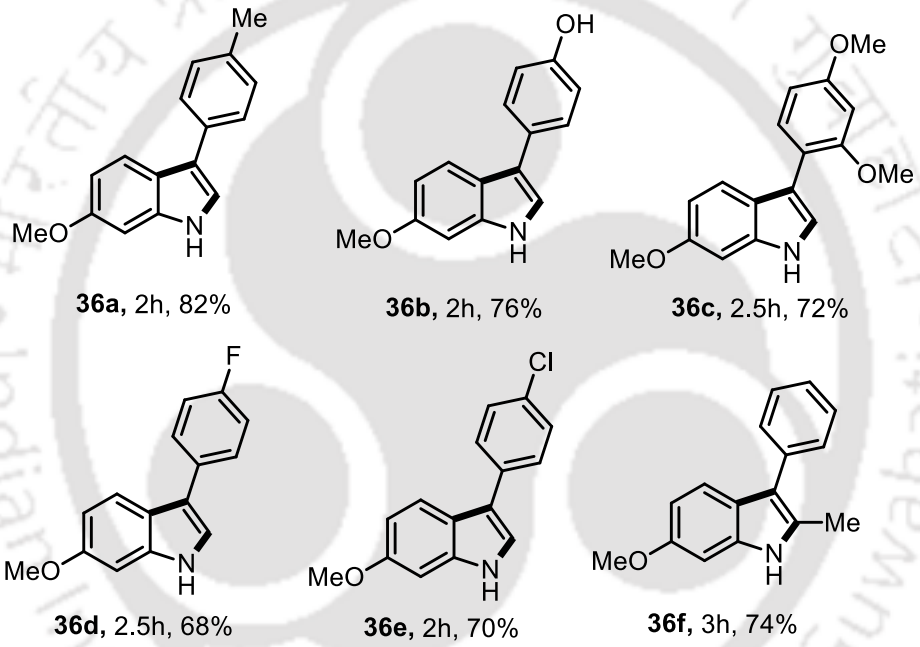
[a]The reactions were carried out using various arylamines **1** (1 mmol), (*E*)-(2-nitrovinyl)benzene **25a** (1 mmol), CH_3CN (2 mL) and $Bi(OTf)_3$ (10 mol %) at 80 °C. [b]Isolated yield.

Further, the reaction condition was applied for the reaction of *m*-anisidine **1m** with various *trans-β*-nitrostyrenes **25** having electron-donating as well as electron-withdrawing group present on the phenyl ring of *trans-β*-nitrostyrene which resulted in the formation of desired products **36a-e**. (*E*)-(2-nitroprop-1-en-1-yl)benzene on reaction with *m*-anisidine gave 6-methoxy-2-methyl-3-phenyl-1H-indole **36f**. The yield obtained in these reactions was quite

good as shown in Table **28**. We did not observed the formation of other isomer product when the reaction was performed with *meta* substituted anilines and *trans-β*-nitrostyrenes.

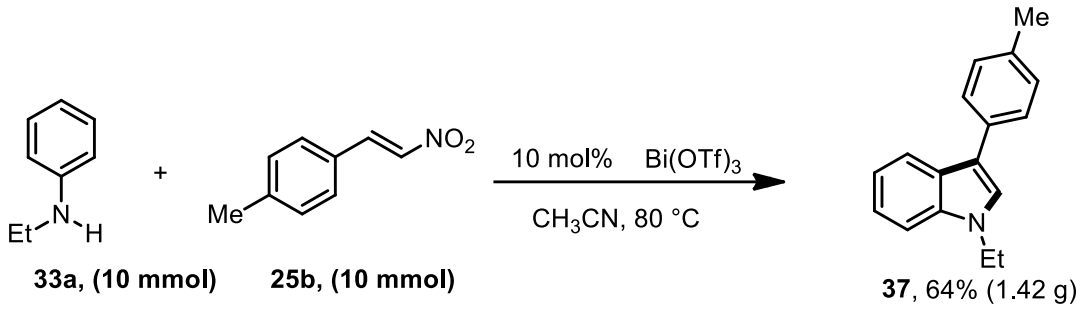
Table 28: Reaction of *m*-anisidine with various *trans-β*-nitrostyrene[a,b]





[a]The reactions were carried out using *m*-anisidine **1m** (1 mmol), various *trans-β*-nitrostyrenes **25** (1 mmol), CH_3CN (2 mL), $Bi(OTf)_3$ (10 mol %) at 80 °C. [b]Isolated yield.

Finally, the scale up procedure was investigated using *N*-ethylaniline **33a** (10 mmol) and (*E*)-1-methyl-4-(2-nitrovinyl)benzene **25b** (10 mmol) which resulted in the formation of the product **37** in 64% yield as in shown **62**.



Scheme 62

All the synthesized compounds **26-29** were characterized by ^{1}H NMR, ^{13}C NMR, IR spectra and HRMS. In addition, the structure of compound **27h** was confirmed by single X-ray crystallographic data (See Experimental Section). ORTEP Diagram of compound **27h** with 40% ellipsoid probability (CCDC no. 1576147) is shown in Figure **30**. The ^{1}HNMR and ^{13}C NMR spectra of compound **31a**, **34a** and **35a** is shown in Figure **31**, **32** and **33** respectively (See Page No. 143-145 in Experimental Section). The intermediate compound **Z** was confirmed through ^{1}HNMR, ^{13}C NMR and HRMS is represented in Figure **34a** and **34b** (See Page No. 146 & 147 in Experimental Section).

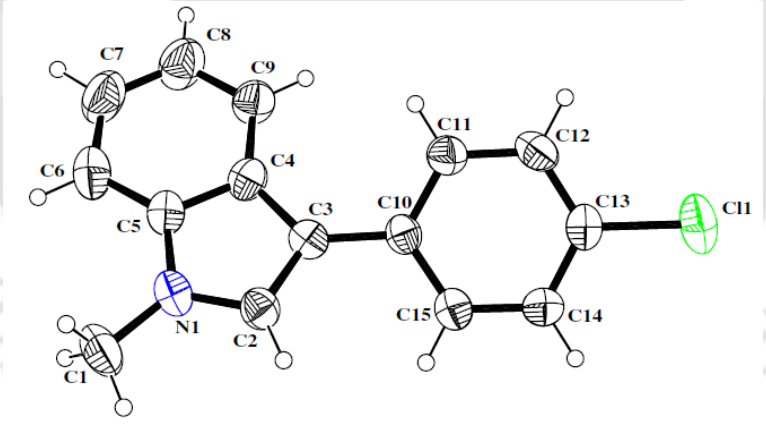
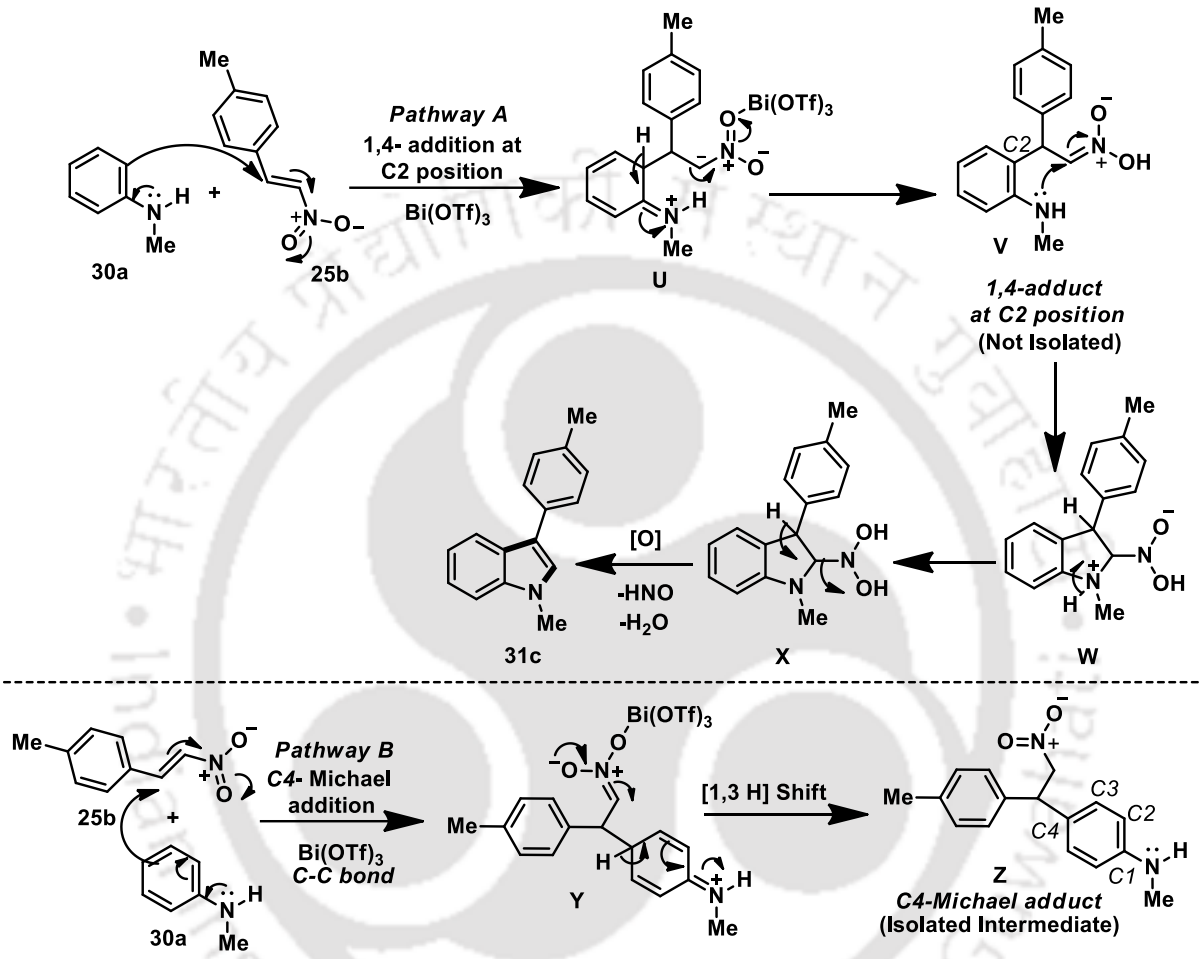


Figure 30

In general, the aniline derivatives undergo aza-Michael addition[82] to *trans-β*-nitrostyrene to form aza-Michael adduct (N-C bond). It was observed that the presence of alkyl group on nitrogen atom of aniline or electron donating group on arene ring of anilines favoured 1,4 addition (C-C bond) rather than aza-michael addition.

The proposed mechanism for the formation of N-methyl 3-arylindoles from N-methylaniline **30a** and (*E*)-1-methyl-4-(2-nitrovinyl)benzene **25b** in presence of $Bi(OTf)_3$ catalyst is shown in the scheme **63**. Initially, N-methylaniline undergoes 1,4-addition at the C2 position as well as at the C4 position with (*E*)-1-methyl-4-(2-nitrovinyl)benzene to furnish 1,4-adduct **V** and

Z through pathway A and pathway B respectively. The 1,4-adduct **V** subsequently undergoes concomitant cyclisation to form **W**, followed by aromatization to afford the desired product **31c.** We find that intermediate **Z** formed through pathway B was not involved in cyclisation and obtained in 12% yield.



Scheme 63

In summary, the +I (Inductive) and +M (Mesomeric) effect of an alkyl and alkoxy groups present on aromatic ring of aniline or nitrogen atom of aniline increases the nucleophilicity at the *ortho* position of aniline which ultimately prefers 1,4-addition to *trans-β*-nitrostyrenes instead of aza-Michael addition. Consequently, 3-arylindoles/N-substituted 3-arylindoles[83] can be accomplished easily in good yield with wide substrate scope using inexpensive $Bi(OTf)_3$ as a catalyst. Our protocol is also applicable for the synthesis of biologically active compound **35e** which acts as an inhibitor of Brassinin glucosyltransferase.

Experimental Section

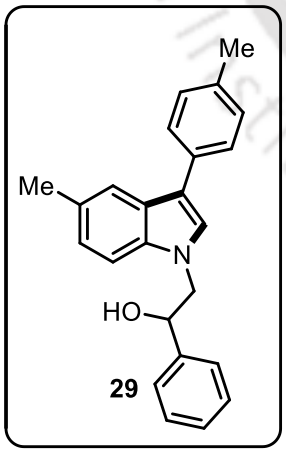
*General Procedure for Synthesis of N-alkyl/aryl 3-arylindoles **29**, **31**, **32** & **34**.*

In a dry 10 mL round bottom flask a mixture *N*-alkyl aniline **30** (1.0 mmol), *trans-β*-nitrostyrene **25** (1.0 mmol) was taken in 2 mL acetonitrile followed by the addition of bismuth(III) trifluoromethanesulfonate (0.065 g, 0.10 mmol) and the reaction mixture was stirred at 80 °C in an oil bath. The progress of the reaction was monitored by TLC. After completion of the reaction, the solvent was removed by a rotatory evaporator and the reaction mixture was extracted with ethyl acetate (2 x 25 mL). The organic extract was dried over sodium sulfate and concentrated under reduced pressure. Finally, the crude residue was purified through silica gel (60-120 mesh) column chromatography with petroleum ether/ethyl acetate (9.8 : 0.2, v/v) to obtain the pure product **29, 31, 32 & 34**.

*General Procedure for Synthesis of 3-arylindoles **35** & **36**.*

To a mixture of arylamine **1** (1.0 mmol), *trans-β*-nitrostyrene **25** (1.0 mmol), and Bismuth(III) trifluoromethanesulfonate (0.065 g, 0.10 mmol), 2 mL acetonitrile was added and stirred at 80 °C in an oil bath. The completion of the reaction was monitored by TLC. The solvent was removed under reduced pressure and extracted with ethyl acetate (2 x 25 mL). The organic layer was dried over sodium sulfate and concentrated under reduced pressure. Finally, the crude residue was purified through silica gel (60-120 mesh) column chromatography with petroleum ether/ethyl acetate (9.5 : 0.5, v/v) to obtain the pure product **35** & **36**.

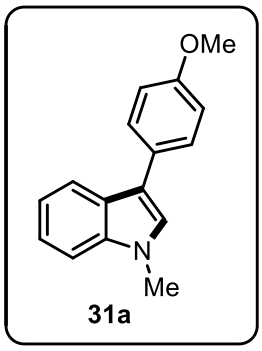
*2-(5-methyl-3-(p-tolyl)-1H-indol-1-yl)-1-phenylethanol (**29**)*



29

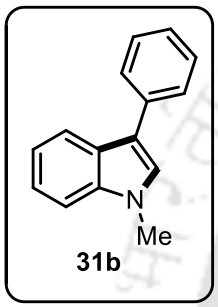
Yield 62% (211 mg), white solid, mp 80-81˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.64 (s, 1H), 7.45 (d, *J* = 8.0 Hz, 2H), 7.36 – 7.30 (m, 4H), 7.29 – 7.27 (m, 1H), 7.26 (d, *J* = 8.4 Hz, 1H), 7.18 (d, *J* = 8.1 Hz, 2H), 7.12 (s, 1H), 7.05 – 7.02 (m, 1H), 5.04 (dd, *J* = 8.3, 3.7 Hz, 1H), 4.29 – 4.20 (m, 2H), 2.41 (s, 3H), 2.33 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 141.2, 135.6, 135.5, 132.8, 129.6, 128.9, 128.5, 127.5, 126.9, 126.3, 126.1, 123.9, 119.9, 116.9, 109.6, 73.8, 54.6, 21.8, 21.4; **IR (KBr)ν_{max}** 3054, 2982, 2852, 1655, 1114, 1018, 998 cm^{-1}; **HRMS** (ESI) Calcd For $C_{24}H_{24}NO$ 342.1852 ($M + H^+$); Found 342.1865.

*3-(4-methoxyphenyl)-1-methyl-1H-indole (**31a**)*



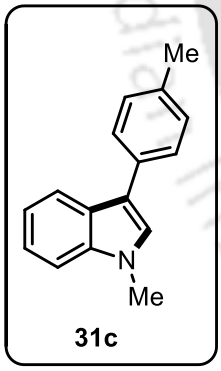
Yield 74% (176 mg), light yellow solid, mp 95-96 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): 1H NMR (600 MHz, CDCl3): δ 7.89 (d, *J* = 8.0 Hz, 1H), 7.59 – 7.55 (m, 2H), 7.36 (d, *J* = 8.2 Hz, 1H), 7.28 (dd, *J* = 7.1, 0.9 Hz, 1H), 7.19 – 7.16 (m, 1H), 7.16 (s, 1H), 7.01 – 6.98 (m, 2H), 3.86 (s, 3H), 3.84 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 158.1, 137.6, 128.7, 128.4, 126.5, 126.1, 122.1, 120.0, 119.9, 116.6, 114.5, 109.6, 55.6, 33.0; **IR (KBr)ν_{max}** 3055, 2923, 2852, 1601, 1488, 1372, 1132, 1034, 861 cm^{-1}; **HRMS** (ESI) Calcd For $C_{16}H_{16}NO$ 238.1226 ($M + H^+$); Found 238.1229.

*1-methyl-3-phenyl-1H-indole (**31b**)*



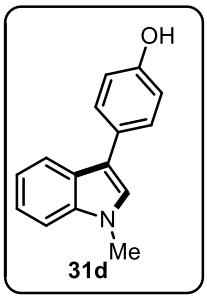
Yield 68% (141 mg), light yellow solid, mp 64-65 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.96 (d, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 7.8 Hz, 2H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.38 (d, *J* = 8.2 Hz, 1H), 7.32 – 7.27 (m, 2H), 7.25 (s, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 3.85 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 137.8, 135.9, 128.9, 127.5, 126.7, 125.9, 122.2, 120.1, 120.1, 117.0, 109.7, 32.9; **IR (KBr)ν_{max}** 3049, 2929, 1718, 1603, 1550, 1483, 1262, 1016, 939 cm^{-1}; **HRMS** (ESI) Calcd For $C_{15}H_{14}N$ 208.1121 ($M + H^+$); Found 208.1126

*1-methyl-3-(p-tolyl)-1H-indole (**31c**)*



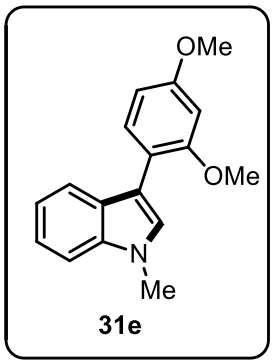
Yield 70% (155 mg), light yellow solid, mp 63-64 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.83 (d, *J* = 8.0 Hz, 1H), 7.46 (d, *J* = 7.9 Hz, 2H), 7.27 (d, *J* = 8.2 Hz, 1H), 7.19 (d, *J* = 7.1 Hz, 1H), 7.16 (d, *J* = 6.4 Hz, 2H), 7.11 (s, 1H), 7.08 (dd, *J* = 7.9, 7.1 Hz, 1H), 3.74 (s, 3H), 2.30 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 137.6, 135.5, 132.9, 129.7, 127.5, 126.5, 126.4, 122.1, 120.2, 119.9, 116.9, 109.7, 33.1, 21.4; **IR (KBr)ν_{max}** 3051, 2928, 2856, 1614, 1485, 1365, 1038, 857 cm^{-1}; **HRMS** (ESI) Calcd For $C_{16}H_{16}NO$ 222.1277 ($M + H^+$); Found 222.1278.

*4-(1-methyl-1H-indol-3-yl)phenol (**31d**)*



Yield 68% (152 mg), colorless semi-solid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.90 (d, *J* = 8.0 Hz, 1H), 7.56 – 7.52 (m, 2H), 7.38 (d, *J* = 8.2 Hz, 1H), 7.30 (dd, *J* = 7.0, 1.0 Hz, 1H), 7.20 (m, 1H), 7.18 (s, 1H), 6.96 – 6.92 (m, 2H), 3.86 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 154.0, 137.5, 128.9, 128.6, 126.4, 126.1, 122.1, 120.0, 119.8, 116.6, 115.9, 109.7, 33.0; **IR (KBr)ν_{max}** 3491, 2923, 2853, 1550, 1468, 1375, 1187, 1017, 924 cm^{-1}; **HRMS** (ESI) Calcd For $C_{15}H_{14}NO$ 224.1070 ($M + H^+$); Found 224.1078.

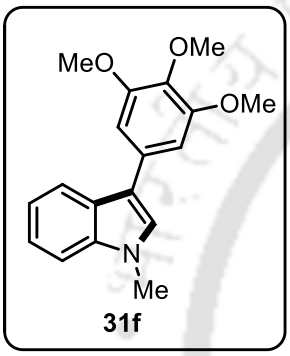
*3-(2,4-dimethoxyphenyl)-1-methyl-1H-indole (**31e**)*



31e

Yield 71% (189 mg), light yellow semi-solid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.73 (d, *J* = 8.0 Hz, 1H), 7.50 (d, *J* = 8.2 Hz, 1H), 7.34 (d, *J* = 8.2 Hz, 1H), 7.29 (s, 1H), 7.26 – 7.22 (m, 1H), 7.15 – 7.11 (m, 1H), 6.61 (t, *J* = 2.6 Hz, 1H), 6.61 – 6.58 (m, 1H), 3.87 (s, 3H), 3.84 (s, 3H), 3.84 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 159.4, 157.8, 137.0, 131.0, 128.4, 127.4, 121.7, 120.7, 119.5, 117.3, 111.7, 109.5, 104.5, 99.3, 55.7, 33.0; **IR (KBr)ν_{max}** 3049, 2936, 2843, 1669, 1604, 1475, 1183, 1008, 928 cm^{-1}; **HRMS** (ESI) Calcd For $C_{17}H_{18}NO_2$ 268.1332 ($M + H^+$); Found 268.1332.

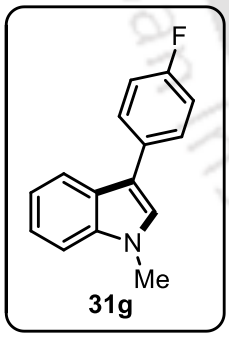
*1-methyl-3-(3,4,5-trimethoxyphenyl)-1H-indole (**31f**)*



31f

Yield 64% (190 mg), colorless semi-solid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.92 (d, *J* = 8.1 Hz, 1H), 7.38 (d, *J* = 8.5 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.22 (s, 1H), 7.20 (s, 1H), 6.86 (s, 2H), 3.94 (s, 6H), 3.91 (s, 3H), 3.86 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 153.7, 137.6, 136.6, 131.6, 126.6, 126.3, 122.3, 120.2, 119.9, 117.1, 109.8, 104.8, 61.2, 56.4, 33.1; **IR (KBr)ν_{max}** 3050, 2934, 2843, 1672, 1567, 1463, 1125, 1055, 925 cm^{-1}; **HRMS** (ESI) Calcd For $C_{18}H_{20}NO_3$ 298.1438 ($M + H^+$); Found 298.1438.

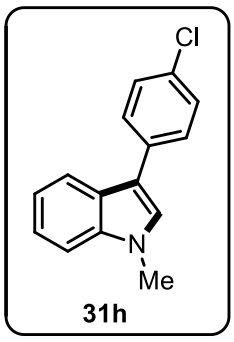
*3-(4-fluorophenyl)-1-methyl-1H-indole (**31g**)*



31g

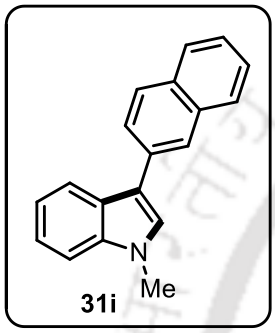
Yield 65% (146 mg), white solid, mp 72-73 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.0 Hz, 1H), 7.49 (dd, *J* = 8.3, 5.5 Hz, 2H), 7.26 (d, *J* = 8.2 Hz, 1H), 7.19 (t, *J* = 7.5 Hz, 1H), 7.10 (t, *J* = 7.5 Hz, 1H), 7.06 (s, 1H), 7.03 (t, *J* = 8.6 Hz, 2H), 3.71 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 163.1, 159.8, 137.5, 131.8, 131.8, 128.9, 128.8, 126.5, 126.2, 122.2, 120.1, 119.8, 115.9, 115.6, 109.8, 33.0; **IR (KBr)ν_{max}** 3048, 2924, 2852, 1568, 1397, 1071, 924 cm^{-1}; **HRMS** (ESI) Calcd For $C_{15}H_{13}FN$ 226.1027 ($M + H^+$); Found 226.1028.

*3-(4-chlorophenyl)-1-methyl-1H-indole (**31h**)*



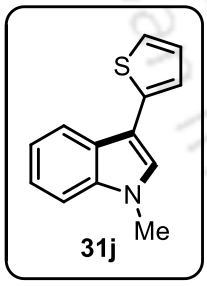
Yield 68% (163 mg), light brown solid, mp 95-96 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.89 (d, *J* = 8.0 Hz, 1H), 7.58 (d, *J* = 8.4 Hz, 2H), 7.42 – 7.38 (m, 2H), 7.37 (s, 1H), 7.30 (t, *J* = 7.7 Hz, 1H), 7.23 (s, 1H), 7.19 (d, *J* = 7.5 Hz, 1H), 3.85 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 137.7, 134.4, 131.5, 129.4, 129.1, 128.6, 126.8, 126.1, 122.4, 120.3, 119.9, 115.8, 109.8, 33.2; **IR (KBr)ν_{max}** 3049, 2922, 2852, 1568, 1398, 1289, 996, 972 cm^{-1}; **HRMS** (ESI) Calcd For $C_{15}H_{13}ClN$ 242.0731 ($M + H^+$); Found 242.0741.

*1-methyl-3-(naphthalen-2-yl)-1H-indole (**31i**)*



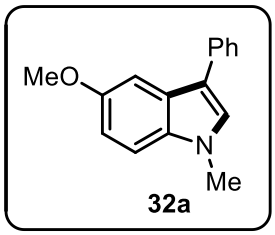
Yield 85% (219 mg), colorless semi-solid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.14 (s, 1H), 8.09 (d, *J* = 8.0 Hz, 1H), 7.92 (d, *J* = 8.5 Hz, 1H), 7.89 (dd, *J* = 16.5, 8.1 Hz, 2H), 7.83 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.53 – 7.49 (m, 1H), 7.46 (td, *J* = 7.5, 6.9, 1.2 Hz, 1H), 7.43 (d, *J* = 8.2 Hz, 1H), 7.39 (s, 1H), 7.36 – 7.32 (m, 1H), 7.27 – 7.25 (m, 1H), 3.91 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 137.8, 134.2, 133.4, 132.1, 128.4, 127.9, 127.9, 127.2, 126.6, 126.5, 126.3, 125.3, 125.1, 122.3, 120.2, 120.2, 116.8, 109.8, 33.1; **IR (KBr)ν_{max}** 3051, 2957, 2853, 1629, 1478, 1240, 1016, 857 cm^{-1}; **HRMS** (ESI) Calcd For $C_{19}H_{16}N$ 258.1277 ($M + H^+$); Found 258.1275.

*1-methyl-3-(thiophen-2-yl)-1H-indole (**31j**)*



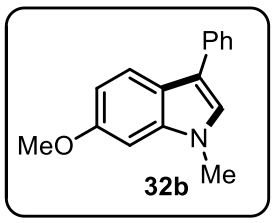
Yield 64% (129 mg), light green liquid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.98 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.36 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.30 (d, *J* = 1.9 Hz, 2H), 7.26 – 7.25 (m, 1H), 7.23 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.22 – 7.20 (m, 1H), 7.13 – 7.10 (m, 1H), 3.83 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 137.8, 137.2, 127.5, 126.5, 125.8, 122.2, 122.1, 122.0, 120.1, 120.0, 110.3, 109.5, 32.8; **IR (KBr)ν_{max}** 3054, 2922, 2851, 1566, 1370, 1188, 1016, 924 cm^{-1}; **HRMS** (ESI) Calcd For $C_{13}H_{12}NS$ 214.0685 ($M + H^+$); Found 214.0691.

*5-methoxy-1-methyl-3-phenyl-1H-indole (**32a**)*



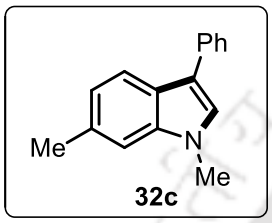
Yield 58% (138 mg), light yellow semi-solid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.68 – 7.63 (m, 2H), 7.49 – 7.43 (m, 2H), 7.41 (d, *J* = 2.5 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.27 (d, *J* = 2.3 Hz, 1H), 7.22 (s, 1H), 6.97 (dd, *J* = 8.9, 2.4 Hz, 1H), 3.89 (s, 3H), 3.84 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 154.8, 136.0, 133.1, 129.0, 127.4, 127.4, 126.6, 125.8, 116.5, 112.4, 110.5, 101.9, 56.3, 33.3; **IR (KBr)ν_{max}** 3052, 2924, 2853, 1608, 1466, 1177, 996 cm^{-1}; **HRMS** (ESI) Calcd For $C_{16}H_{16}NO$ 238.1226 ($M + H^+$); Found 238.1236.

*6-methoxy-1-methyl-3-phenyl-1H-indole (**32b**)*



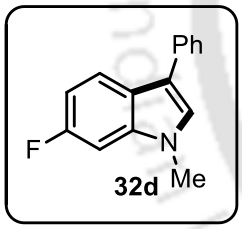
Yield 86% (203 mg), yellow semi-solid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.83 (d, *J* = 8.7 Hz, 1H), 7.65 (dd, *J* = 8.2, 1.3 Hz, 2H), 7.46 – 7.42 (m, 2H), 7.29 – 7.26 (m, 1H), 7.14 (s, 1H), 6.88 (dd, *J* = 8.7, 2.3 Hz, 1H), 6.82 (d, *J* = 2.3 Hz, 1H), 3.92 (s, 3H), 3.79 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 156.7, 138.4, 135.9, 128.9, 127.3, 125.8, 125.5, 120.9, 120.7, 116.9, 109.9, 93.2, 55.9, 33.1; **IR (KBr)ν_{max}** 3049, 2928, 2859, 1611, 1558, 1067, 1021, 987 cm^{-1}; **HRMS** (ESI) Calcd For $C_{16}H_{16}NO$ 238.1226 ($M + H^+$); Found 238.1229.

*1,6-dimethyl-3-phenyl-1H-indole (**32c**)*



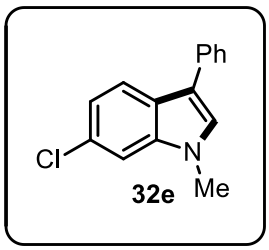
Yield 72% (159 mg), yellow semi-solid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.84 (d, *J* = 8.1 Hz, 1H), 7.72 – 7.62 (m, 2H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.30 – 7.25 (m, 1H), 7.17 (d, *J* = 3.4 Hz, 2H), 7.04 (d, *J* = 8.2 Hz, 1H), 3.81 (s, 3H), 2.54 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 138.0, 136.0, 132.0, 128.9, 127.3, 126.1, 125.7, 124.1, 121.8, 119.8, 116.6, 109.7, 32.9, 22.1; **IR (KBr)ν_{max}** 3058, 2921, 2858, 2252, 1602, 1552, 1383, 1028, 967 cm^{-1}; **HRMS** (ESI) Calcd For $C_{16}H_{16}N$ 222.1277 ($M + H^+$); Found 222.1279.

*6-fluoro-1-methyl-3-phenyl-1H-indole (**32d**)*



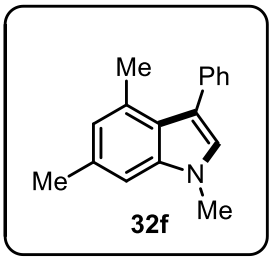
Yield 68% (153 mg), brown semi-solid, **^{1}H NMR** (600 MHz, $CDCl_3$ δ 7.84 (dd, *J* = 8.8, 5.3 Hz, 1H), 7.64 – 7.60 (m, 2H), 7.46 – 7.41 (m, 2H), 7.31 – 7.26 (m, 1H), 7.21 (s, 1H), 7.03 (dd, *J* = 9.7, 2.3 Hz, 1H), 6.95 (ddd, *J* = 9.4, 8.7, 2.3 Hz, 1H), 3.79 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 160.9, 159.4, 137.8, 137.7, 135.4, 129.0, 127.5, 126.9, 126.9, 126.2, 122.9, 121.0, 120.9, 117.2, 108.8, 108.7, 96.2, 95.9, 33.2; **IR (KBr)ν_{max}** 3046, 2924, 2852, 1608, 1560, 1016, 996 cm^{-1}; **HRMS** (ESI) Calcd For $C_{15}H_{13}FN$ 226.1027 ($M + H^+$); Found 226.1015.

*6-chloro-1-methyl-3-phenyl-1H-indole (**32e**)*



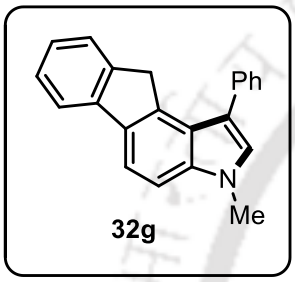
Yield 58% (139 mg), colorless semi-solid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.84 (d, *J* = 8.5 Hz, 1H), 7.65 – 7.59 (m, 2H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.36 (d, *J* = 1.9 Hz, 1H), 7.29 (t, *J* = 7.4 Hz, 1H), 7.22 (s, 1H), 7.16 (dd, *J* = 8.5, 1.9 Hz, 1H), 3.81 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 139.0, 135.2, 129.0, 128.2, 127.5, 127.3, 126.2, 124.9, 121.1, 120.7, 117.2, 109.8, 33.2; **IR (KBr)ν_{max}** 3054, 2928, 2859, 1645, 1491, 1184, 1069, 956 cm^{-1}; **HRMS** (ESI) Calcd For $C_{15}H_{13}ClN$ 242.0731 ($M + H^+$); Found 242.0740.

*1,4,6-trimethyl-3-phenyl-1H-indole (**32f**)*



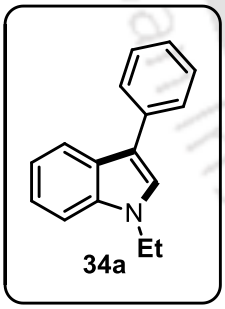
Yield 72% (169 mg), light yellow semi-solid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.56 – 7.49 (m, 2H), 7.45 (tdd, *J* = 7.7, 2.1, 1.2 Hz, 2H), 7.42 – 7.35 (m, 1H), 7.09 (s, 1H), 6.97 (d, *J* = 1.4 Hz, 1H), 6.83 (s, 1H), 3.82 (d, *J* = 1.2 Hz, 3H), 2.56 (d, *J* = 2.2 Hz, 3H), 2.36 (d, *J* = 2.5 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 137.6, 137.3, 131.8, 131.1, 130.7, 127.7, 127.3, 126.3, 123.7, 123.2, 118.2, 107.2, 32.8, 21.8, 20.9; **IR (KBr)ν_{max}** 3058, 2921, 2858, 2252, 1602, 1552, 1085, 967 cm^{-1}; **HRMS** (ESI) Calcd For $C_{17}H_{18}N$ 236.1434 ($M + H^+$); Found 236.1438.

*3-methyl-1-phenyl-3,10-dihydroindeno[2,1-e]indole (**32g**)*



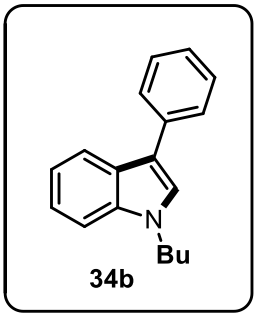
Yield 62% (182 mg), white solid, mp 202–203 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.30 (s, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 2H), 7.54 - 7.48 (m, 4H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.32 (t, *J* = 8.0 Hz, 1H), 7.28-7.23 (m, 2H), 4.04 (s, 2H), 3.87 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 143.1, 142.7, 138.5, 137.9, 135.8, 134.9, 128.8, 127.4, 126.6, 125.7, 125.6, 124.8, 125.1, 119.3, 116.9, 110.5, 105.9, 36.7, 33.10; **IR (KBr)ν_{max}** 3057, 2956, 2869, 1642, 1548, 1368, 1062, 962 cm^{-1}; **HRMS** (ESI) Calcd For $C_{22}H_{18}N$ 296.1434 ($M + H^+$); Found 296.1426.

*11-ethyl-3-phenyl-1H-indole (**34a**)*



Yield 68% (150 mg), yellow semi-solid, mp 77-78 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.98 (d, *J* = 8.0 Hz, 1H), 7.72 – 7.66 (m, 2H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.41 (d, *J* = 8.2 Hz, 1H), 7.32 (s, 1H), 7.28 (dd, *J* = 11.5, 4.5 Hz, 2H), 7.21 (dd, *J* = 11.0, 4.0 Hz, 1H), 4.24 (q, *J* = 7.3 Hz, 2H), 1.53 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 136.6, 135.9, 128.9, 127.5, 126.4, 125.8, 125.0, 122.0, 120.2, 120.0, 116.9, 109.8, 41.22, 15.68; **IR (KBr)ν_{max}** 3051, 2957, 2867, 1619, 1466, 1365, 1068, 957 cm^{-1}; **HRMS** (ESI) Calcd For $C_{16}H_{16}N$ 222.1277 ($M + H^+$); Found 222.1267.

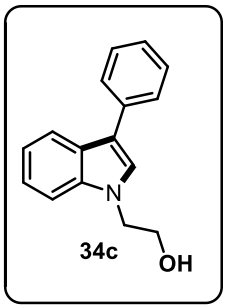
*1-butyl-3-phenyl-1H-indole (**34b**)*



Yield 72% (179 mg), yellow semi-solid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.96 (d, *J* = 8.0 Hz, 1H), 7.68 (dt, *J* = 8.1, 1.3 Hz, 2H), 7.45 (td, *J* = 7.8, 1.4 Hz, 2H), 7.40 (d, *J* = 8.1 Hz, 1H), 7.29 (s, 1H), 7.29 – 7.24 (m, 2H), 7.22 – 7.16 (m, 1H), 4.17 (t, *J* = 7.1 Hz, 2H), 1.97 – 1.82 (m, 2H), 1.40 (q, *J* = 7.5 Hz, 2H), 0.97 (td, *J* = 7.3, 1.2 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 136.9, 135.9, 128.9, 127.5, 126.4, 125.8, 121.9, 120.2,

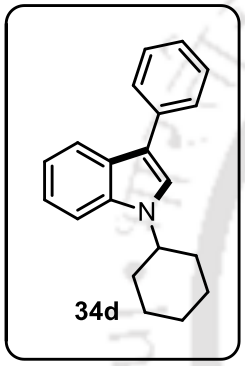
119.9, 116.7, 109.9, 46.4, 32.5, 20.4, 13.9; **IR (KBr)ν_{max}** 3054, 2962, 2857, 1602, 1289, 996 cm^{-1}; **HRMS** (ESI) Calcd For $C_{18}H_{20}N$ 250.1590 ($M + H^+$); Found 250.1589.

*2-(3-phenyl-1H-indol-1-yl)ethanol (**34c**)*



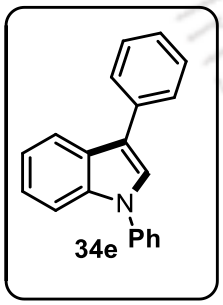
Yield 68% (161 mg), colorless semi-solid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.96 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.69 – 7.64 (m, 2H), 7.46 – 7.43 (m, 2H), 7.43 – 7.41 (m, 1H), 7.36 (s, 1H), 7.28 (m, 2H), 7.20 (m, 1H), 4.34 (t, *J* = 5.3 Hz, 2H), 4.02 (t, *J* = 5.3 Hz, 2H**); ^{13}C NMR** (75 MHz, $CDCl_3$): δ 136.9, 135.5, 128.9, 127.4, 126.4, 126.3, 125.9, 122.2, 120.3, 120.2, 117.1, 109.9, 61.8, 48.8; **IR (KBr)ν_{max}** 3021, 2920, 2836, 1708, 1632, 1355, 1111, 996 cm^{-1}; **HRMS** (ESI) Calcd For $C_{16}H_{16}NO$ 238.1226 ($M + H^+$); Found 238.1245.

*1-cyclohexyl-3-phenyl-1H-indole (**34d**)*



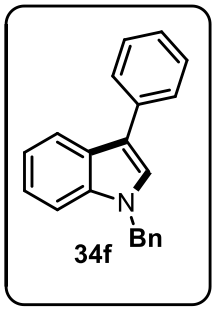
Yield 62% (170 mg), colorless semisolid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.81 (d, *J* = 7.9 Hz, 1H), 7.53 (dd, *J* = 8.0, 1.4 Hz, 2H), 7.33 – 7.26 (m, 3H), 7.26 (s, 1H), 7.14 – 7.09 (m, 2H), 7.06 – 7.00 (m, 1H), 4.19 – 4.06 (m, 1H), 2.06 (d, *J* = 12.5 Hz, 2H), 1.90 – 1.76 (m, 2H), 1.62 (dt, *J* = 12.6, 8.9 Hz, 2H), 1.41 (d, *J* = 3.4 Hz, 2H), 1.24 – 1.13 (m, 2H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 136.5, 136.1, 128.9, 127.5, 126.3, 125.8, 122.2, 121.8, 120.2, 120.0, 116.9, 109.9, 53.3, 33.79, 26.2, 25.8; **IR (KBr)ν_{max}** 3042, 2938, 2842, 1638, 1384, 1298, 1016, 978 cm^{-1}; **HRMS** (ESI) Calcd For $C_{20}H_{22}N$ 276.1747 ($M + H^+$); Found 276.1751.

*1,3-diphenyl-1H-indole (**34e**)*



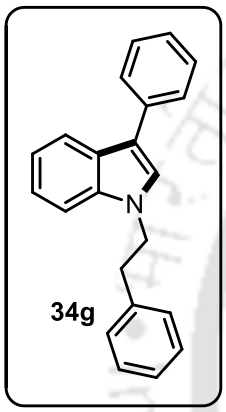
Yield 66% (177 mg), white solid, mp 103-104 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): 8.01 (dd, *J* = 6.9, 1.9 Hz, 1H), 7.77 – 7.71 (m, 2H), 7.65 – 7.61 (m, 1H), 7.57 (d, *J* = 1.8 Hz, 3H), 7.54 (d, *J* = 11.0 Hz, 2H), 7.49 (t, *J* = 7.7 Hz, 2H), 7.40 (tt, *J* = 6.2, 2.2 Hz, 1H), 7.36 – 7.31 (m, 1H), 7.31 – 7.25 (m, 2H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 139.7, 136.8, 135.3, 129.9, 129.0, 127.8, 127.3, 126.9, 126.4, 125.7, 124.7, 123.0, 121.1, 120.3, 119.3, 111.0; **IR (KBr)ν_{max}** 3056, 2921, 2851, 1598, 1018, 999 cm^{-1}; **HRMS** (ESI) Calcd For $C_{20}H_{16}N$ 270.1277 ($M + H^+$); Found 270.1278.

*1-benzyl-3-phenyl-1H-indole (**34f**)*



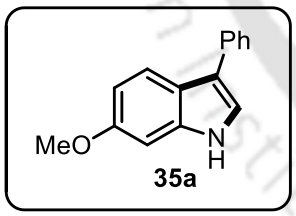
Yield 78% (221 mg), white solid, mp 105 – 106 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.02 (dd, *J* = 7.1, 1.7 Hz, 1H), 7.74 – 7.68 (m, 2H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.39 – 7.29 (m, 6H), 7.29 – 7.26 (m, 1H), 7.24 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.22 – 7.17 (m, 2H), 5.37 (s, 2H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 137.4, 137.3, 135.7, 129.0, 128.9, 127.9, 127.6, 127.1, 126.6, 126.1, 126.0, 122.3, 120.3, 120.2, 117.5, 110.2, 50.3; **IR (KBr)ν_{max}** 3059, 2922, 2853, 1601, 1546, 1259, 1181, 1000, 970 cm^{-1}; **HRMS** (ESI) Calcd For $C_{21}H_{18}NS$ 284.1434 (M + H^+); Found 284.1434.

*1-phenethyl-3-phenyl-1H-indole (**34g**)*



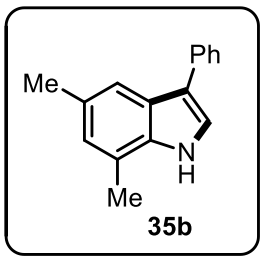
Yield 64% (190 mg), colorless semi-solid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.98 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.65 – 7.61 (m, 2H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.42 (dd, *J* = 8.2, 0.9 Hz, 1H), 7.34 – 7.29 (m, 3H), 7.28 (d, *J* = 7.8 Hz, 2H), 7.22 (m, 1H), 7.17 – 7.13 (m, 2H), 7.12 (s, 1H), 4.43 – 4.40 (m, 2H), 3.18 (t, *J* = 7.5 Hz, 2H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 138.6, 136.7, 135.8, 129.0, 128.9, 128.9, 127.5, 126.9, 126.5, 125.9, 122.1, 120.3, 120.1, 116.9, 109.8, 48.4, 36.9; **IR (KBr)ν_{max}** 3054, 2982, 2852, 1655, 1545, 1018, 998 cm^{-1}; **HRMS** (ESI) Calcd For $C_{22}H_{20}NS$ 298.1590 (M + H^+); Found 298.1595.

*6-methoxy-3-phenyl-1H-indole (**35a**)*



Yield 85% (187 mg), brown color semi-solid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.17 – 8.07 (m, 1H), 7.84 (d, *J* = 8.7 Hz, 1H), 7.73 – 7.64 (m, 2H), 7.51 – 7.42 (m, 2H), 7.33 – 7.30 (m, 1H), 7.29 (d, *J* = 2.3 Hz, 1H), 6.93 (d, *J* = 2.3 Hz, 1H), 6.90 (dd, *J* = 8.7, 2.3 Hz, 1H), 3.90 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 156.8, 137.7, 135.8, 128.9, 127.5, 126.1, 120.7, 120.7, 120.3, 118.5, 110.5, 94.9, 55.9; **IR (KBr)ν_{max}** 3056, 2850, 1568, 1532, 1018, 997 cm^{-1}; **HRMS** (ESI) Calcd For $C_{15}H_{14}NO$ 224.1070 (M + H^+); Found 224.1072.

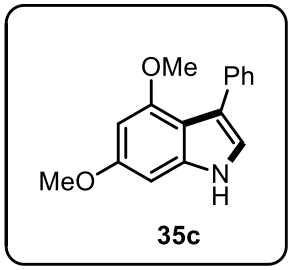
*5,7-dimethyl-3-phenyl-1H-indole (**35b**)*



Yield 74% (163 mg), yellow color semi-solid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.08 (s, 1H), 7.71 – 7.66 (m, 2H), 7.60 (s, 1H), 7.46 (td, *J* = 7.7, 1.6 Hz, 2H), 7.33 (t, *J* = 2.2 Hz, 1H), 7.32 – 7.28 (m, 1H), 6.92 (s, 1H), 2.50 (s, 3H), 2.47 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 136.1, 134.7, 130.0, 128.9, 127.7, 126.0, 125.6, 124.8, 121.9, 120.4, 118.4,

117.2, 21.7, 16.7; **IR (KBr)ν_{max}** 3046, 2847, 1609, 1188, 1020, 996 cm^{-1}; **HRMS** (ESI) Calcd For $C_{16}H_{16}N$ 222.1277 ($M + H^+$); Found 222.1273.

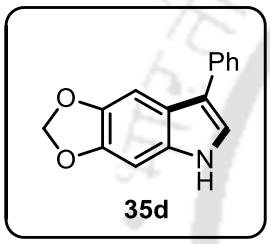
4,6-dimethoxy-3-phenyl-1H-indole (***35c***)



35c

Yield 80% (202 mg), colorless solid mp 56-57 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.66 – 7.59 (m, 2H), 7.37 (t, *J* = 7.7 Hz, 2H), 7.28 – 7.25 (m, 1H), 7.01 (dd, *J* = 2.4, 0.8 Hz, 1H), 6.50 (dd, *J* = 2.0, 0.9 Hz, 1H), 6.27 (d, *J* = 2.0 Hz, 1H), 3.85 (s, 3H), 3.80 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 157.8, 155.1, 138.5, 136.2, 129.7, 127.8, 125.8, 120.6, 119.2, 110.5, 92.4, 86.9, 55.8, 55.3; IR (KBr)ν_{max} 3048, 2959, 2840, 1706, 1625, 1047, 995 cm^{-1}; **HRMS** (ESI) Calcd For $C_{16}H_{16}NO_2$ 254.1176 ($M + H^+$); Found 254.1188.

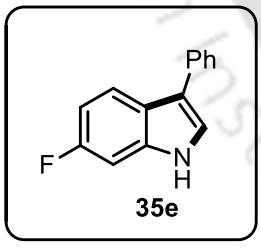
7-phenyl-5H-[1,3]dioxolo[4,5-f]indole (***35d***)



35d

Yield 68% (161 mg), brown color solid, mp < 320˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.11 (s, 1H), 7.65 – 7.58 (m, 2H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.33 (d, *J* = 0.7 Hz, 1H), 7.32 – 7.27 (m, 1H), 7.22 (d, *J* = 2.5 Hz, 1H), 6.87 (d, *J* = 0.6 Hz, 1H), 5.97 (s, 2H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 145.3, 143.7, 135.7, 131.7, 128.9, 127.4, 126.1, 120.6, 119.8, 118.7, 100.9, 98.6, 92.3; **IR (KBr)ν_{max}** 3052, 2958, 2857, 1628, 1028, 978 cm^{-1}; **HRMS** (ESI) Calcd For $C_{15}H_{12}NO_2$ 238.0863 ($M + H^+$); Found 238.0850.

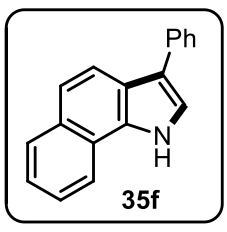
6-fluoro-3-phenyl-1H-indole (***35e***)



35e

Yield 74% (200 mg), colorless solid, mp 45-46˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.24 (s, 1H), 7.85 (dd, *J* = 8.8, 5.3 Hz, 1H), 7.69 – 7.62 (m, 2H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.36 – 7.34 (m, 1H), 7.31 (d, *J* = 7.3 Hz, 1H), 7.11 (dd, *J* = 9.5, 2.3 Hz, 1H), 7.01 – 6.93 (m, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 161.1, 159.5, 136.8, 136.7, 135.3, 129.0, 127.7, 126.4, 122.6, 122.1, 122.1, 120.9, 120.8, 118.7, 109.3, 109.2, 97.9, 97.7; **IR (KBr)ν_{max}** 3046, 2916, 2848, 1642, 1254, 1068, 992 cm^{-1}; **HRMS** (ESI) Calcd For $C_{14}H_{11}FN$ 212.0870 ($M + H^+$); Found 212.0878.

3-phenyl-1H-benzo[g]indole (***35f***)

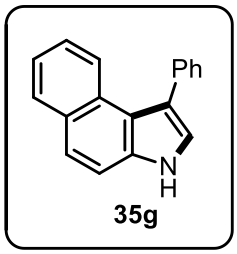


35f

Yield 82% (200 mg), colorless solid, mp 234-235˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.92 (s, 1H), 8.05 – 8.01 (m, 1H), 8.01 – 7.94 (m, 2H), 7.77 – 7.70 (m, 2H), 7.60 (d, *J* = 8.7 Hz, 1H), 7.55 (m, 1H), 7.53 – 7.46 (m, 3H), 7.40 (d, *J* = 2.6 Hz, 1H), 7.38 – 7.32 (m, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 135.7, 131.5, 130.7, 129.0, 129.1, 127.9, 126.4, 125.8, 124.4, 121.9,

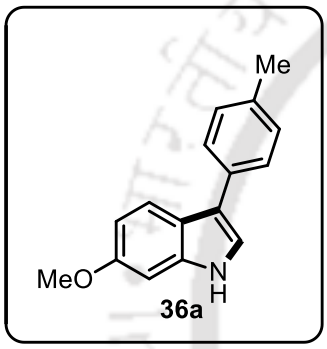
121.8, 121.5, 120.5, 120.1, 119.9, 119.6; **IR (KBr)ν_{max}** 3049, 2919, 2851, 1648, 1553, 1072, 1018, 998 cm^{-1}; **HRMS** (ESI) Calcd For $C_{18}H_{14}N$ 244.1121 ($M + H^+$); Found 244.1112.

*1-phenyl-3H-benzo[e]indole (**35g**)*



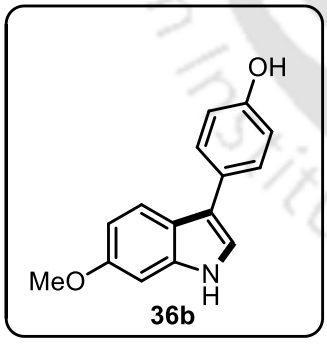
Yield 90% (219 mg), brown color oily liquid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.43 (s, 1H), 8.18 (m, 1H), 7.95 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.70 – 7.66 (m, 3H), 7.55 – 7.51 (m, 3H), 7.49 – 7.46 (m, 1H), 7.43 – 7.39 (m, 1H), 7.39 – 7.34 (m, 1H), 7.15 (d, *J* = 2.5 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 137.3, 132.9, 130.3, 129.9, 128.9, 128.8, 128.5, 126.9, 125.6, 123.9, 123.5, 123.4, 121.7, 121.3, 119.6, 113.1**; IR (KBr)ν_{max}** 3052, 2916, 2848, 1652, 1448, 1180, 992 cm^{-1}; **HRMS** (ESI) Calcd For $C_{18}H_{14}N$ 244.1121 ($M + H^+$); Found 244.1125.

*6-methoxy-3-(p-tolyl)-1H-indole (**36a**)*



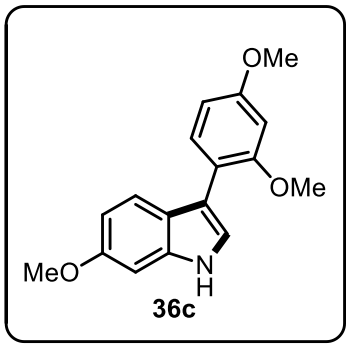
Yield 82% (195 mg), brown semisolid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.07 (s, 1H), 7.79 (d, *J* = 8.7 Hz, 1H), 7.57 – 7.54 (m, 2H), 7.25 (d, *J* = 7.6 Hz, 2H), 7.23 (d, *J* = 2.4 Hz, 1H), 6.91 (d, *J* = 2.2 Hz, 1H), 6.86 (dd, *J* = 8.7, 2.3 Hz, 1H), 3.87 (s, 3H), 2.40 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 156.8, 137.6, 135.7, 132.8, 129.6, 127.4, 120.7, 120.4, 120.3, 118.4, 110.3, 94.9, 55.9, 21.4; **IR (KBr)ν_{max}** 3056, 2850, 1568, 1532, 1187, 1018, 997 cm^{-1}; **HRMS** (ESI) Calcd For $C_{16}H_{16}NO$ 238.1226 ($M + H^+$); Found 238.1241.

*4-(6-methoxy-1H-indol-3-yl)phenol (**36b**)*



Yield 76% (182 mg), brown semi-solid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.06 (s, 1H), 7.74 (d, *J* = 8.7 Hz, 1H), 7.54 – 7.50 (m, 2H), 7.18 (d, *J* = 2.4 Hz, 1H), 6.91 (dd, *J* = 8.2, 2.0 Hz, 3H), 6.85 (dd, *J* = 8.7, 2.3 Hz, 1H), 3.87 (s, 3H).; **^{13}C NMR** (150 MHz, $CDCl_3$): δ 155.1, 154.6, 136.9, 127.1, 126.3, 119.4, 119.2, 119.1, 115.9, 114.9, 108.7, 94.1, 54.7; **IR (KBr)ν_{max}** 3262, 2928, 2856, 1614, 1187, 1019, 998; cm^{-1}; **HRMS** (ESI) Calcd For $C_{15}H_{14}NO_2$ 240.1019 ($M + H^+$); Found 240.1020.

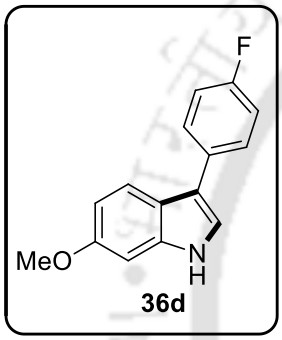
*3-(2,4-dimethoxyphenyl)-6-methoxy-1H-indole (**36c**)*



36c

Yield 72% (203 mg), brown semi-solid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.61 (d, *J* = 8.7 Hz, 1H), 7.51 (d, *J* = 8.2 Hz, 1H), 7.32 (d, *J* = 2.4 Hz, 1H), 6.91 (d, *J* = 2.3 Hz, 1H), 6.83 (dd, *J* = 8.7, 2.3 Hz, 1H), 6.63 (d, *J* = 2.4 Hz, 1H), 6.62 (dd, *J* = 8.2, 2.5 Hz, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.85 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 159.5, 157.9, 156.6, 136.9, 130.9, 122.4, 121.4, 121.3, 117.3, 113.6, 109.9, 104.5, 99.3, 94.8, 55.9, 55.7, 55.7; **IR (KBr)ν_{max}** 3054, 2938, 2848, 2827, 1604, 1214, 1036, 978 cm^{-1}; **HRMS** (ESI) Calcd For $C_{17}H_{18}NO_3$ 284.1281 ($M + H^+$); Found 284.1298.

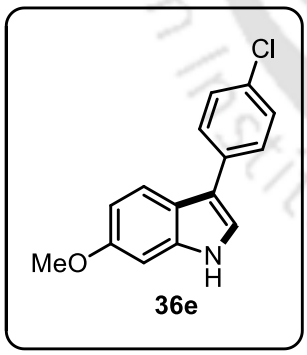
*3-(4-fluorophenyl)-6-methoxy-1H-indole (**36d**)*



36d

Yield 68% (165 mg), brown liquid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.11 (s, 1H), 7.73 (dt, *J* = 8.7, 0.7 Hz, 1H), 7.63 – 7.56 (m, 2H), 7.21 (d, *J* = 2.4 Hz, 1H), 7.17 – 7.09 (m, 2H), 6.92 (d, *J* = 2.3 Hz, 1H), 6.87 (dd, *J* = 8.7, 2.3 Hz, 1H), 3.87 (s, 3H).; **^{13}C NMR** (150 MHz, $CDCl_3$): δ 162.4, 160.8, 156.9, 137.6, 131.8, 131.8, 128.9, 128.9, 120.4, 120.4, 120.3, 117.6, 115.8, 115.7, 110.6, 94.9, 55.9; **IR (KBr)ν_{max}** 3052, 2957, 2868, 1652, 1269, 1048, 972 cm^{-1}; **HRMS** (ESI) Calcd For $C_{15}H_{13}NO$ 242.0976 ($M + H^+$); Found 242.0978.

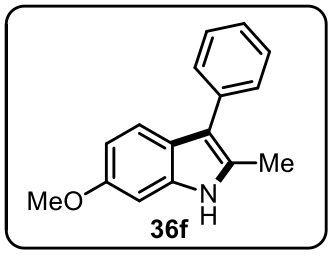
*3-(4-chlorophenyl)-6-methoxy-1H-indole (**36e**)*



36e

Yield 70% (181 mg), brown oil, **^{1}H NMR** (600 MHz, DMSO-*d6*): δ 11.23 (s, 1H), 7.71 (d, *J* = 8.7 Hz, 1H), 7.70 – 7.65 (m, 2H), 7.59 (d, *J* = 2.5 Hz, 1H), 7.46 – 7.41 (m, 2H), 6.95 (d, *J* = 2.3 Hz, 1H), 6.75 (dd, *J* = 8.7, 2.4 Hz, 1H), 3.78 (s, 3H); **^{13}C NMR** (75 MHz, DMSO-*d6*): δ 155.8, 137.9, 134.9, 129.5, 128.8, 127.8, 122.6, 119.7, 119.1, 114.5, 110.1, 94.9, 55.3; **IR (KBr)ν_{max}** 3050, 2994, 2935, 2833, 1647, 1091, 968 cm^{-1}; **HRMS** (ESI) Calcd For $C_{15}H_{13}ClNO$ 258.0680 ($M + H^+$); Found 258.0673.

*6-methoxy-2-methyl-3-phenyl-1H-indole (**36f**)*

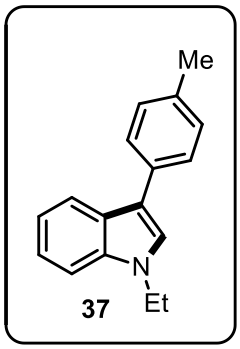


36f

Yield 74% (175 mg), light yellow solid mp 152-153, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.84 (s, 1H), 7.53 (d, *J* = 8.6 Hz, 1H), 7.52 – 7.48 (m, 2H), 7.45 (dd, *J* = 8.6, 6.9 Hz, 2H), 7.32 – 7.27 (m, 1H), 6.85 (d, *J* = 2.3 Hz, 1H), 6.78 (dd, *J* = 8.7, 2.3 Hz, 1H), 3.86 (s, 3H), 2.48 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 156.3, 136.1, 135.7,

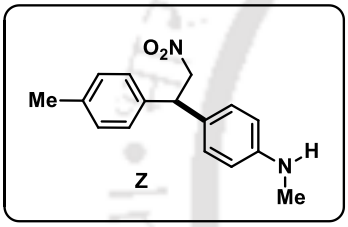
130.2, 129.5, 128.7, 125.9, 122.4, 119.6, 114.4, 109.5, 94.6, 55.9, 12.7; **IR (KBr)ν_{max}** 3052, 2990, 2931, 2838, 1642, 1039, 964 cm^{-1}; **HRMS** (ESI) Calcd For $C_{16}H_{16}NO$ 238.1226 (M + H^+); Found 238.1211.

*1-ethyl-3-(p-tolyl)-1H-indole (**37**)*



Yield 64% (150 mg), Yellow semi-solid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.94 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.59 – 7.55 (m, 2H), 7.40 (d, *J* = 8.2 Hz, 1H), 7.28 (s, 1H), 7.27 – 7.25 (m, 3H), 7.18 (td, *J* = 7.5, 7.1, 1.1 Hz, 1H), 4.22 (q, *J* = 7.3 Hz, 2H), 2.41 (s, 3H), 1.52 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 136.6, 135.4, 132.9, 129.6, 127.4, 126.5, 124.7, 121.9, 120.3, 119.9, 116.9, 109.7, 41.2, 21.4, 15.7; **IR (KBr)ν_{max}** 3048, 2923, 2853, 1613, 1099, 967 cm^{-1}; **HRMS** (ESI) Calcd For $C_{17}H_{18}N$ 236.1434 (M + H^+); Found 236.1451.

*N-methyl-4-(2-nitro-1-(p-tolyl)ethyl)aniline (**Z**)*



Yield 12% (32 mg),light yellow semi-solid, **^{1}H NMR** (600 MHz, DMSO-*d6*): δ 7.25 – 7.21 (m, 2H), 7.09 (d, *J* = 7.8 Hz, 2H), 7.08 – 7.06 (m, 2H), 6.47 – 6.43 (m, 2H), 5.58 (s, 1H), 5.20 (qd, *J* = 13.2, 8.4 Hz, 2H), 4.60 (t, *J* = 8.3 Hz, 1H), 2.61 (s, 3H), 2.23 (s, 3H); **^{13}C NMR** (150 MHz, DMSO-d6): δ 148.9, 138.14, 135.8, 129.1, 128.1, 127.4, 126.9, 111.7, 78.9, 47.6, 29.7, 20.6; **IR (KBr)νmax** 3421, 2926, 2839, 1613, 1551, 1517, 1377, 1251, 1182,1031 cm-1; **HRMS** (ESI) Calcd For $C_{16}H_{19}N_2O_2$ 271.1441 (M + H+); Found 271.1449.

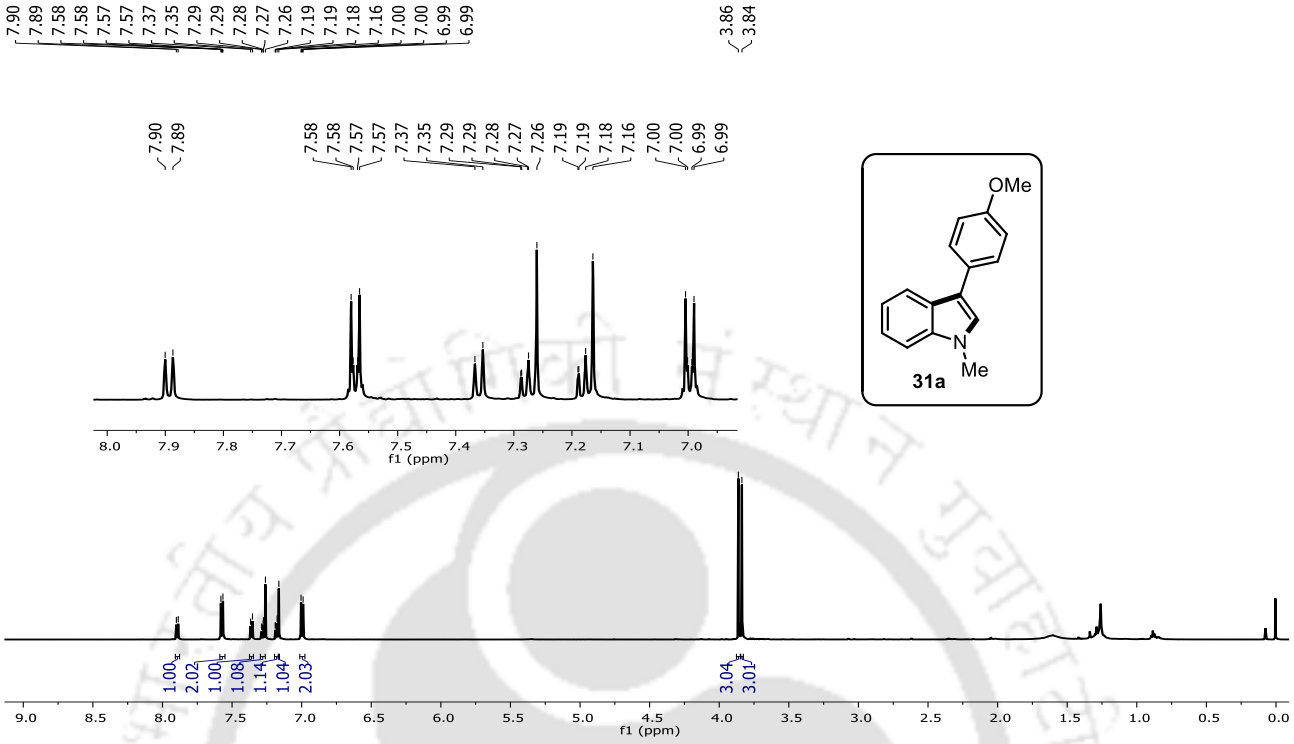
XRD for Compounds **31h**

Complete crystallographic data of compound **31h** for the structural analyses have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. is 1576147. Copies of this information may be obtained free of charge from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk or via: www.ccdc.cam.ac.uk).

Table 29. Crystal Data and Structure Refinement for Compound **31h**

Entry	Identification code	Compound 31h
01	Empirical formula	$C_{15}H_{12}ClN$
02	Formula weight	241.71
03	Temperature	296(2) K
04	Wavelength	0.71073
05	Radiation type	MoK\a
06	Radiation source	'fine-focus sealed tube'
07	Crystal system	Triclinic
08	Space group	P-1
09	Cell length	a 9.4630(12) b 9.9221(11) c 13.5665(16)
10	Cell Angle	α 102.387(10) β 94.259(10) δ 98.976(10)
11	Cell Volume	1221.2(3)
12	Density	1.315
13	Completeness to theta	25.00° / 99.80%
14	Absorption correction	multi-scan
15	Refinement method	Full-matrix least-squares on F2
16	Index ranges	$-11 \leq h \leq 11$, $-11 \leq k \leq 11$, $-14 \leq l \leq 16$
17	Reflection number	4285
18	Theta range	3.09-25.00
19	Cell formula units Z	4
20	CCDC no	1576147

***^{1}H NMR (600 MHz, $CDCl_3$)**: 3-(4-methoxyphenyl)-1-methyl-1H-indole (**31a**)*



***^{13}C NMR (150 MHz, $CDCl_3$)**: 3-(4-methoxyphenyl)-1-methyl-1H-indole (**31a**)*

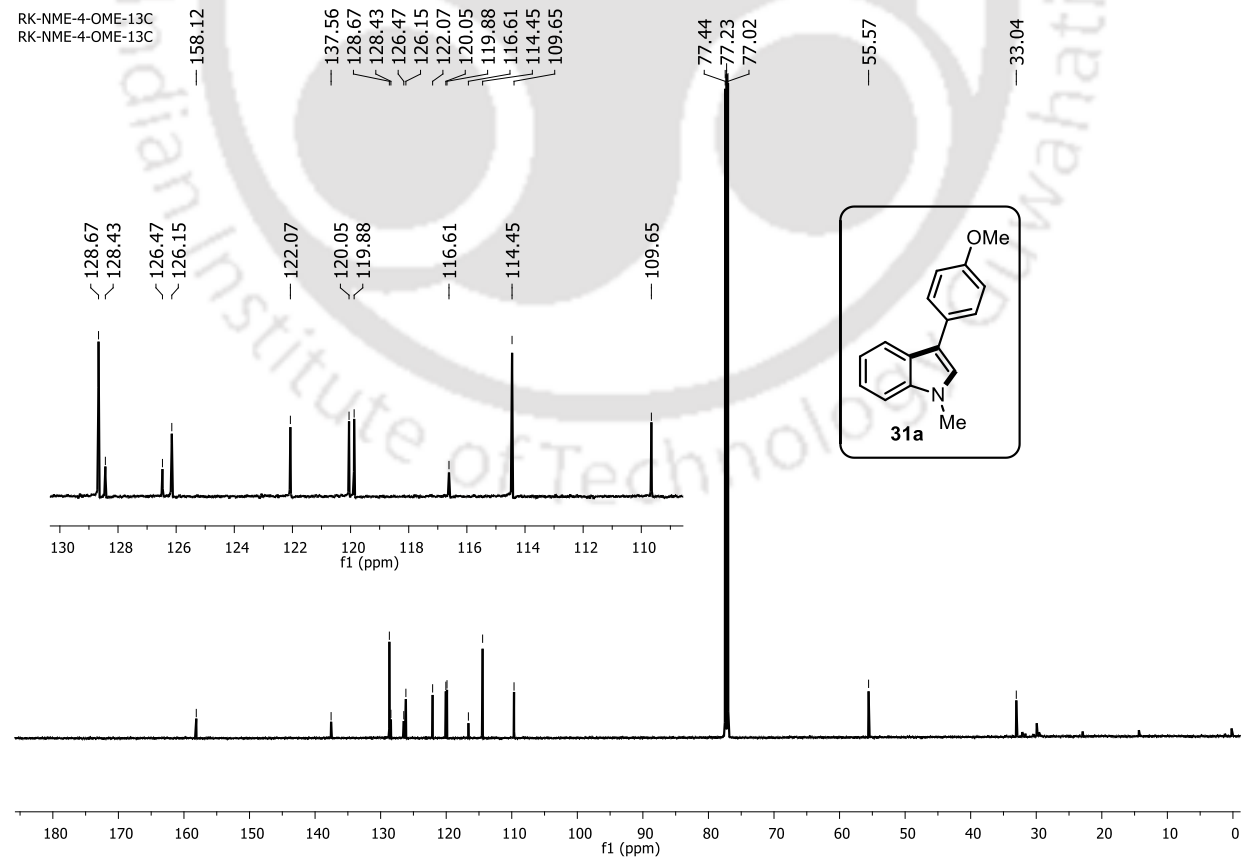
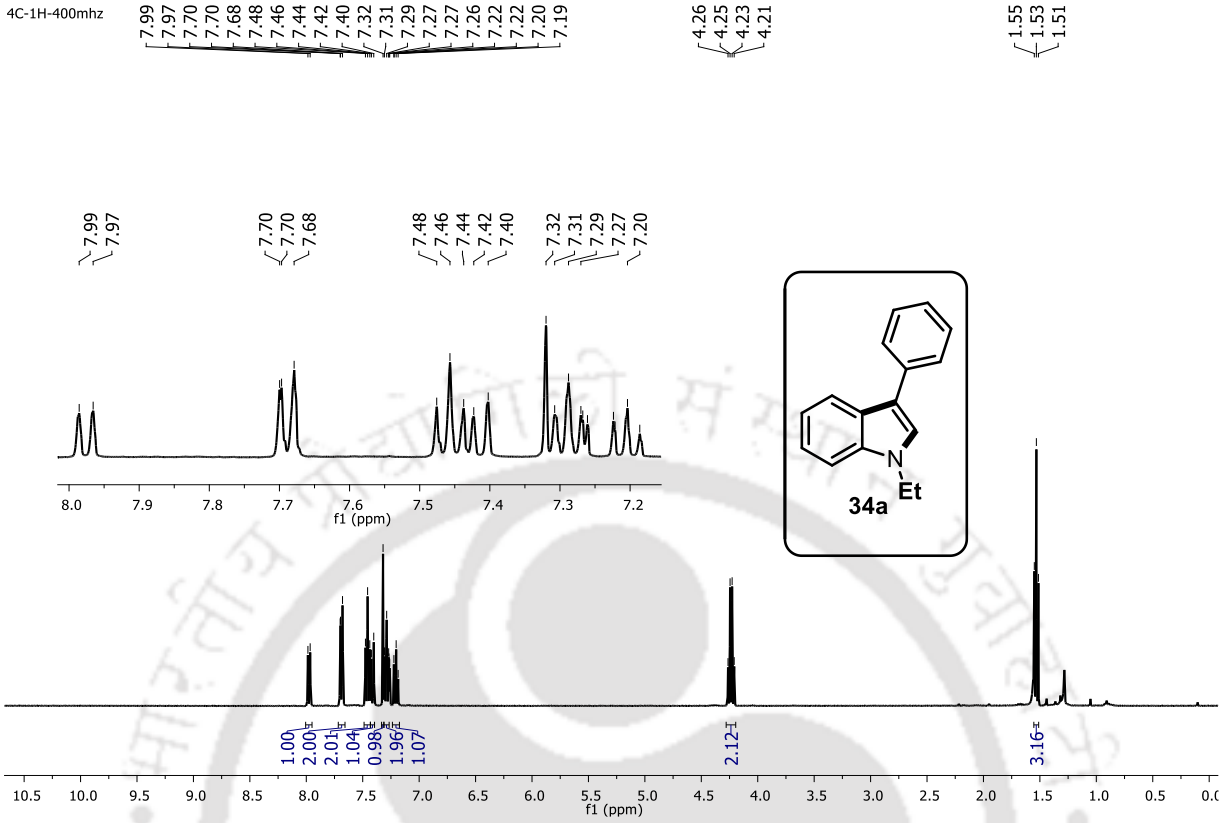


Figure 31

***^{1}H NMR (600 MHz, $CDCl_3$)**: 11-ethyl-3-phenyl-1H-indole (**34a**)*



***^{13}C NMR (150 MHz, $CDCl_3$)**: 11-ethyl-3-phenyl-1H-indole (**34a**)*

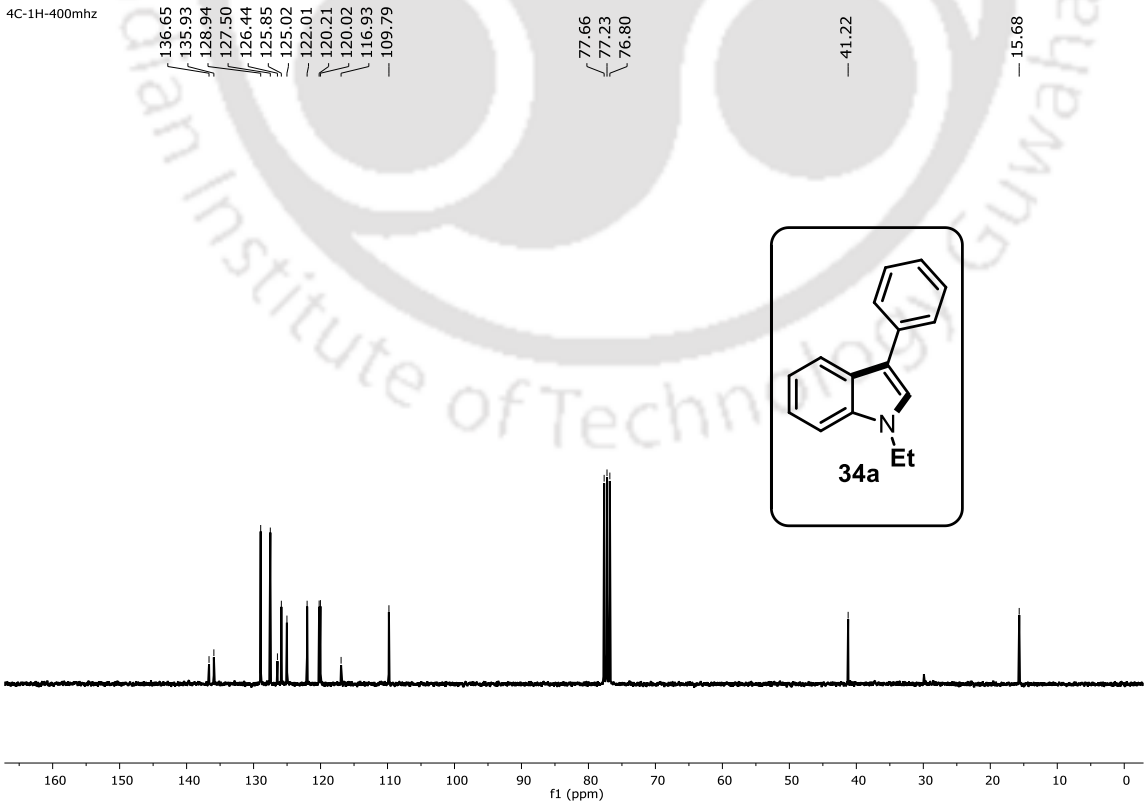
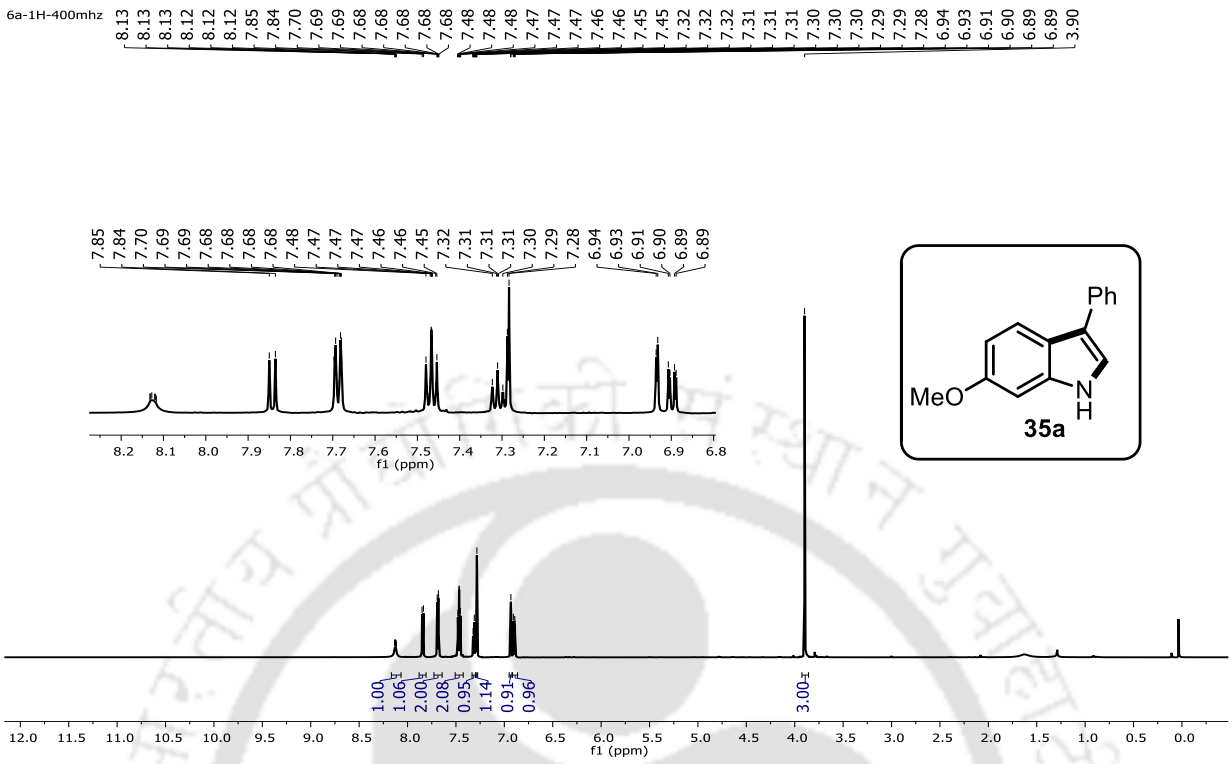


Figure 32

***^{1}H NMR (600 MHz, $CDCl_3$)**: 6-methoxy-3-phenyl-1H-indole (**35a**)*



***^{13}C NMR (150 MHz, $CDCl_3$)**: 6-methoxy-3-phenyl-1H-indole (**35a**)*

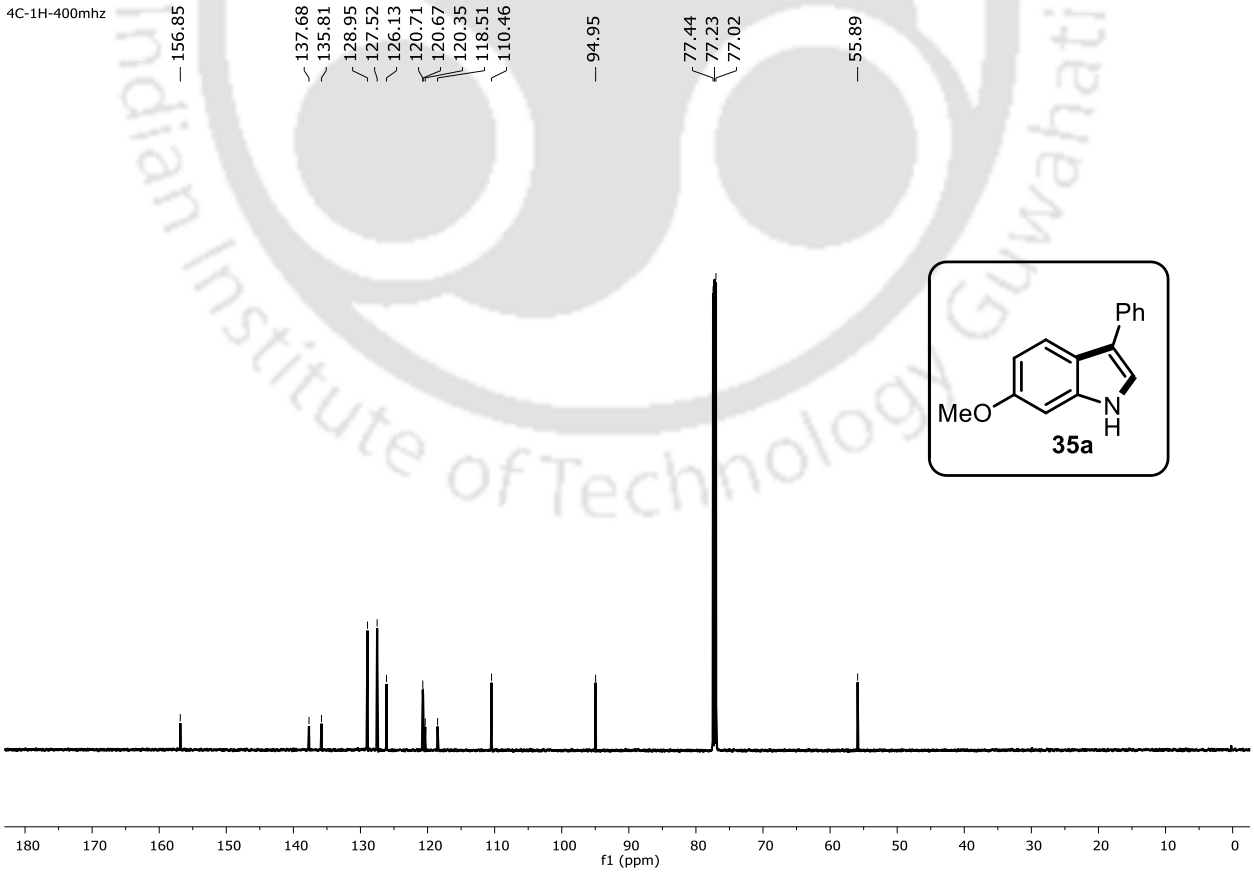
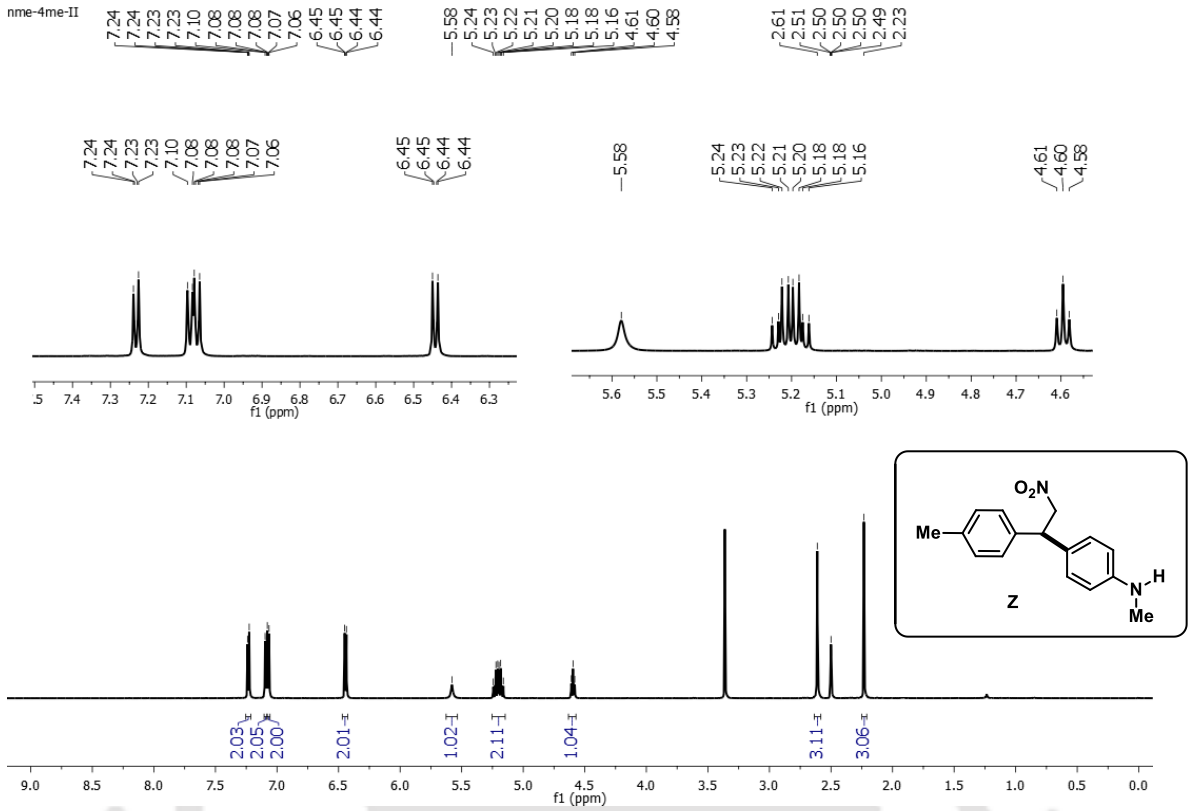


Figure 33

***^{1}H NMR (600 MHz, $CDCl_3$)**: N-methyl-4-(2-nitro-1-(p-tolyl)ethyl)aniline (**Z**)*



***^{13}C NMR (150 MHz, $CDCl_3$)**: N-methyl-4-(2-nitro-1-(p-tolyl)ethyl)aniline (**Z**)*

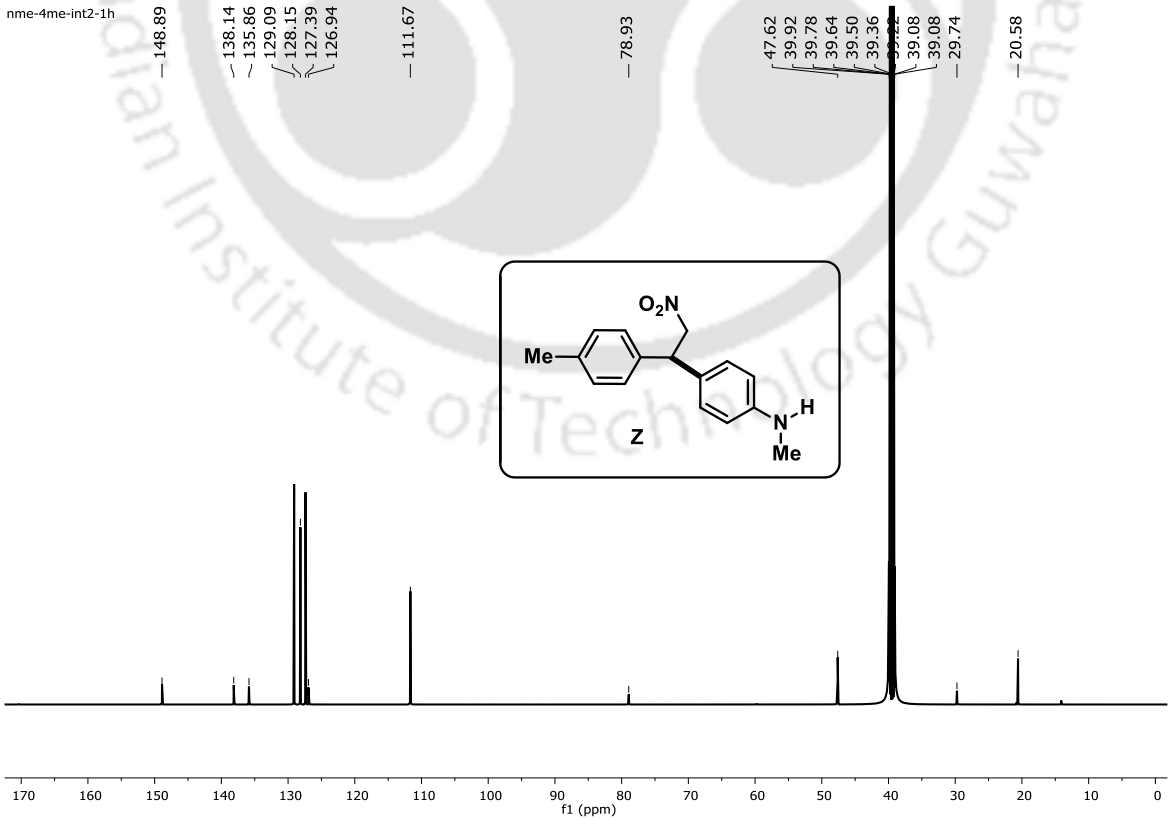


Figure 34a

***HRMS**: N-methyl-4-(2-nitro-1-(p-tolyl)ethyl)aniline (**Z**)*

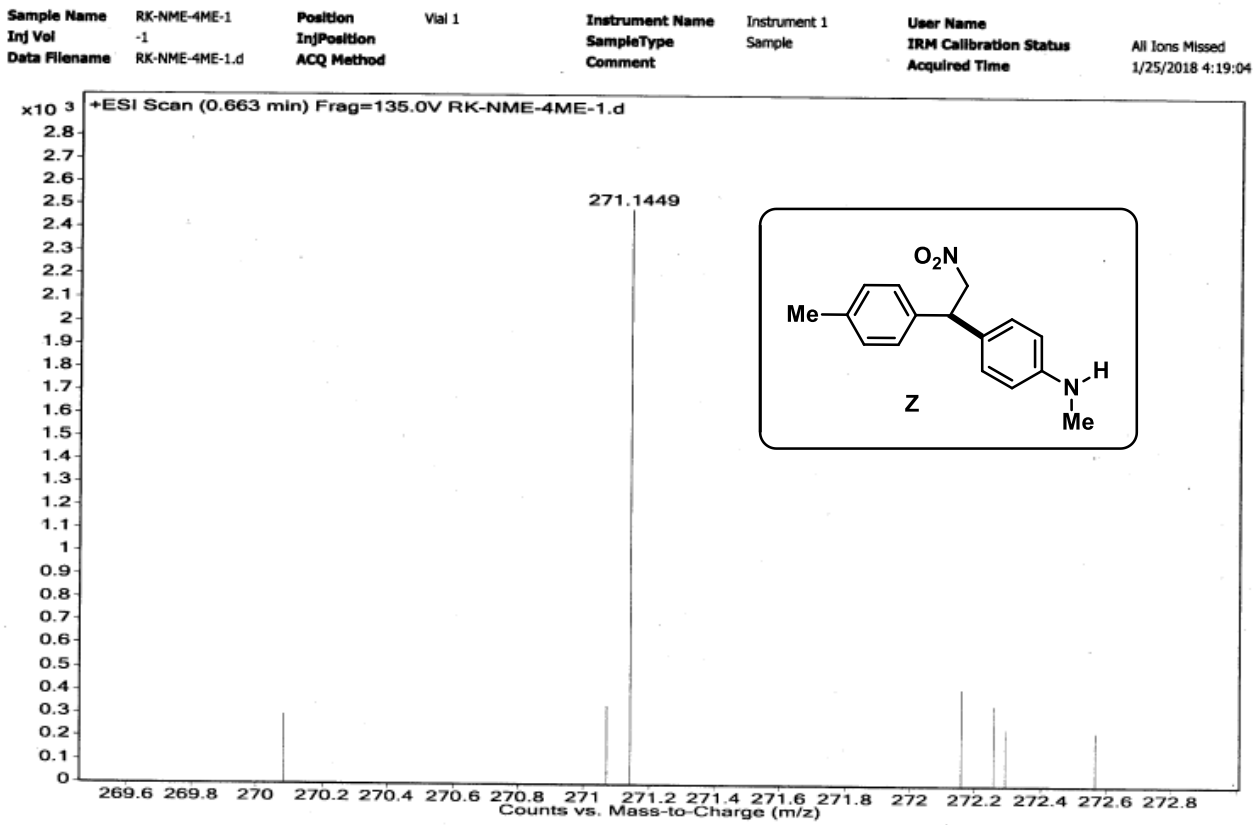


Figure 34b

CONCLUSION AND FUTURE PERSPECTIVES

During the tenure of my PhD, I have focused my research work mainly on the utility arylamines for the synthesis of substituted quinolines and indole derivatives. The summarized results are shown schematically in Figure **35**.

Thesis Overview

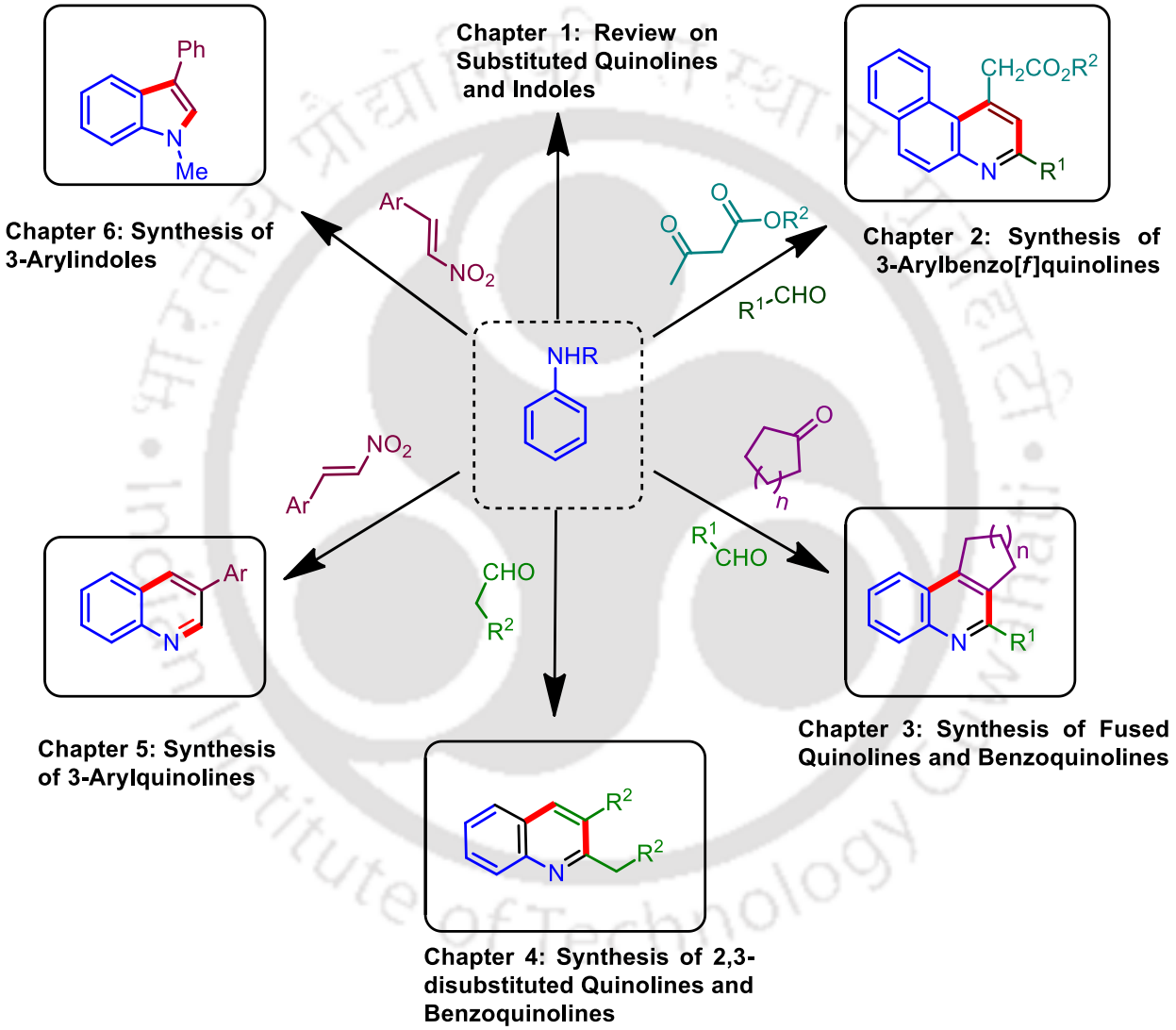
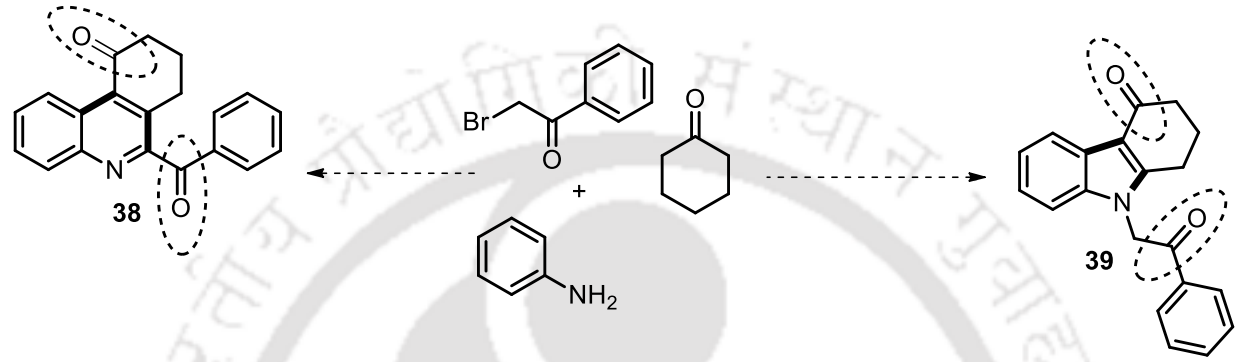


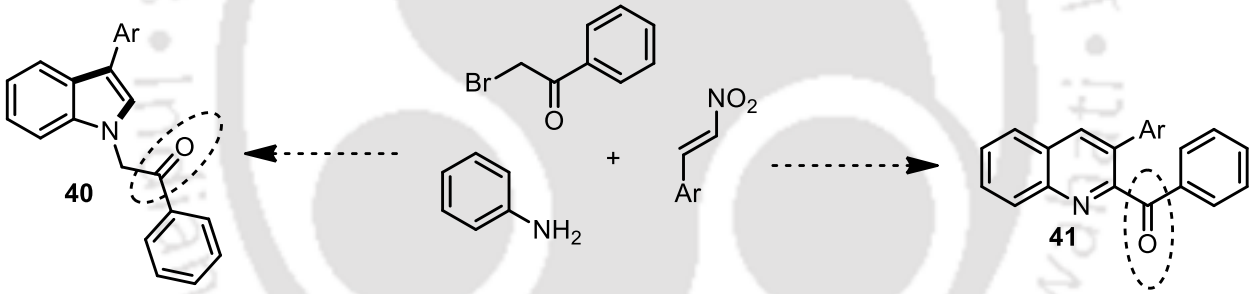
Figure 35

Future Perspectives:

Based on our previous experimental results, we are further interested to explore arylamines for the synthesis of biological active functionalized quinolines and indoles as shown in scheme **64** and **65**. We are also interested to study the biological activity of synthesized compounds.



Scheme 64



Scheme 65

4/27/2018

References

Chapter I -VI

Radhakrishna Gattu
IIT GUWAHATI

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LIST OF PUBLICATIONS AND COMMUNICATIONS

1. 'One-Pot Three-component Regioselective Synthesis of C1-Functionalised 3-Arylbenzo[*f*]quinoline' **Radhakrishna Gattu**, R. Sidick Basha, Prasanta Ray Bagdi and Abu T. Khan, *RSC Adv.*, **2016**, *6*, 11675.
2. 'Camphorsulfonic Acid Catalyzed One-Pot Three-Component Reaction for the Synthesis of Fused Quinoline and Benzoquinoline Derivatives' **Radhakrishna Gattu**, Prasanta Ray Bagdi, R. Sidick Basha, and Abu T. Khan, *J. Org. Chem.* **2017**, *82*, 12416.
3. 'Electronic Effect of Substituents on Anilines Favors 1,4-Addition to *trans-β*-nitrostyrenes: Access to N-Substituted 3-Arylindoles and 3-Arylindoles' **Radhakrishna Gattu,** Suchandra Bhattacharjee, Karuna Mahato and Abu T. Khan, *Org. Biomol. Chem*. **2018**, DOI: 10.1039/C8OB00736E.
4. 'An Oxidative Cross-Coupling Reaction of 4-Hydroxydithiocoumarin and Amines/Thiols Using a Combination of I_2 and TBHP: Access to Lead Molecules for Biomedical Applications' Karuna Mahato, Neha Arora, Prasanta Ray Bagdi, **Radhakrishna Gattu**, Siddhartha Sankar Ghosh and Abu T. Khan, *Chem. Commun*. **2018**, *54*, 1513.
5. 'Triethylamine-Mediated One-Pot Synthesis of Benzo[*f*]Chromene Derivatives' Suchandra Bhattacharjee, **Radhakrishna Gattu** and Abu T. Khan, *Chemistryselect*. **2018**, DOI: 10.1002/slct.201800372.
6. 'Catalyst and Solvent Free Imino Diels−Alder/Intramolecular Reaction for the Synthesis of 2,3-Di-Substituted Quinoline and Benzoquinolines' **Radhakrishna Gattu** and Abu T. Khan (Communicated).
7. 'Regioselective Synthesis of 3-Arylquinolines Through Tandem Cyclisation of 1-phenyl-2-(phenylamino)ethanone and *trans-β*-nitrostyrenes' **Radhakrishna Gattu** and Abu T. Khan (Communicated).

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One-pot three-component regioselective synthesis of C1-functionalised 3-arylbenzo[*f*]quinoline†

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An efficient method for regioselective synthesis of C1-functionalised 3-arylbenzo[*f*]quinoline has been demonstrated *via* γ-selective aromatization using β-ketoester, 2-naphthylamine and aromatic aldehyde by employing 10 mol% camphorsulfonic acid as the catalyst in acetonitrile at 70 °C. In this approach, two *C*–*C* bond formations will result in functionalised benzo[*f*]quinoline in a one-pot three-component reaction. In addition, the present protocol has a diverse substrate scope with good yields. Furthermore, the protocol was directly utilised for the synthesis of alkyl 2-(3-(naphthalen-2-yl)benzo[*f*]quinolin-1-yl) acetate, allyl 2-(3-(heteroaromatic)benzo[*f*]quinolin-1-yl)acetate and functionalised 1,2,3-trisubstituted benzo[*f*]quinoline.

Introduction

C4-functionalized quinolines are recognized to be at the forefront of heterocycles[1a] and are found in many alkaloid natural products, bioactive scaffolds and potent marketed drugs (Fig. 1).[1b–e] Around the active quinoline skeleton,[2,1e] the integral core unit of benzoquinoline features as an eminent biological probe in pharmaceuticals, including selective 5-HT_3 receptor ligands,[3] CFTR activators,[4] D_3 dopamine agonists,[5] vesicular glutamate transporter inhibitors,[6] α_1-receptor agonists[7] and *in vitro* human type 1 & 2 steroid 5α-reductase inhibitors,[8] and shows dopaminergic activity in nerve assays.[9] Certainly, few of them are found to possess antibacterial,[10] antimicrobial,[11] antipsychotic,[12] and antimalarial[13] activities. This emerging wide array of applications demands the development of a facile synthetic method for the future bioactive scaffold of functionalised benzoquinoline. The design and synthesis of functionalised benzoquinoline using β-ketoester **1**, 2-naphthylamine **2** and an aldehyde **3** favours the possible reaction pathways shown in Scheme 1.

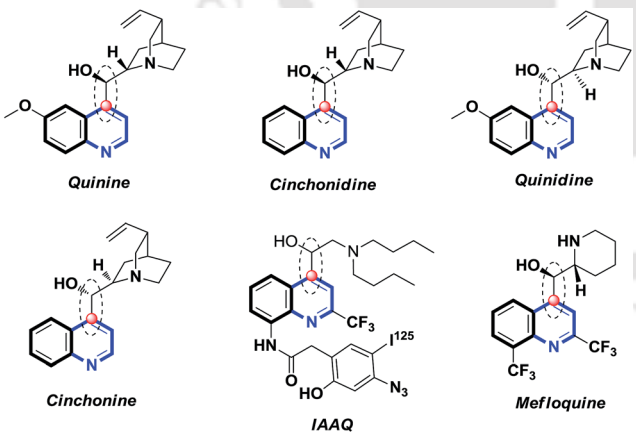
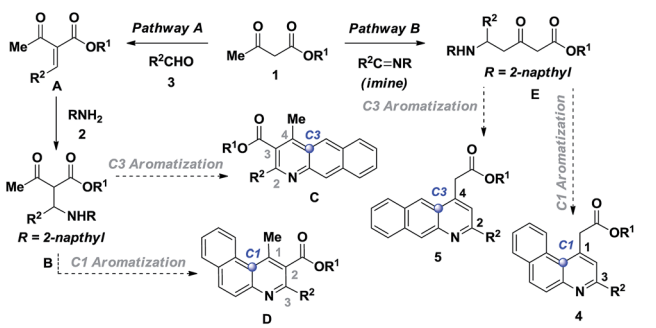


Fig. 1 Biologically active molecules containing the C4-functionalized quinoline skeleton.

In pathway A, the reaction of β-ketoester with aldehyde results in species **A** which reacts with amine *via* Michael addition to give **B** and it may aromatize either at the C3 or C1 position of the naphthylamine to form alkyl 4-methyl-2-arylbenzo[*g*]quinoline-3-carboxylate **C** and alkyl 1-methyl-3-arylbenzo[*f*]quinoline-2-carboxylate **D**. On the other hand, in pathway **B**, alkyl-5-(naphthalen-2-ylamino)-3-oxo-5-arylpentanoate **E** prefers to form alkyl 2-(3-arylbenzo[*f*] quinolin-1-yl)-



Scheme 1 Possible reaction pathways.

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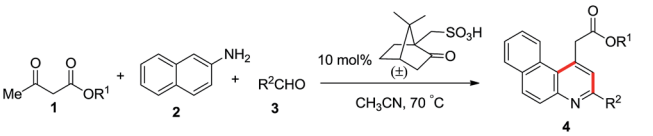
† Electronic supplementary information (ESI) available: XRD of **4g** and copies of ^{1}H & ^{13}C NMR. CCDC 1434638. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c5ra23413a

acetate **4** and alkyl 2-(2-arylbenzo[*g*]quinolin-4-yl)acetate **5**. Among the possible reaction pathways, the regioselective synthesis of alkyl 2-(3-arylbenzo[*f*]quinolin-1-yl)acetate **4** is highly desirable, as it may act as a scaffold in drug discovery. Since the reported methods in the literature[14] are limited, we were interested in finding an elegant method for the synthesis of functionalised benzo[*f*]quinoline **4**. The schematic route leading to the synthesis of alkyl 2-(3-arylbenzo[*f*]quinolin-1-yl) acetate **4** is shown in Scheme 2.

The γ-selectivity in a synthetic precursor plays a vital key role in the transformation to obtain complex heterocycles[15] in pharmaceuticals.[16] In particular, the γ-selectivity of β-ketoester[17a,b] through multicomponent reactions[17c–f] remains a challenging puzzle to synthetic chemists. Multicomponent reactions are often considered as providing growth in molecular diversity[18] to assemble complex molecules having a diverse range of biomedical applications.[19] The existing demand in these reactions is to achieve significant biomolecular scaffolds which are widely accessed through intermolecular *C–C* bond formation.[20] We envisaged that functionalised benzo[*f*]quinoline may be accessible through progressive MCR intermolecular *C–C* bond formations.

The convenient, cheap and readily available camphorsulfonic acid has well-defined versatile applications in organic tranformations[21] and it is used extensively in cyclisation reactions,[22] alkylation of anilines,[23] asymmetric reactions[24] and natural product synthesis.[22,25] We believed that catalytic camphorsulfonic acid might be suitable for the required γ-selectivity in the regioselective synthesis of functionalised benzo[*f*] quinoline.

Overall, herein we wish to report the efficient synthesis of C1-functionalised 3-arylbenzo[*f*]quinoline from β-ketoester, 2-naphthylamine and aromatic aldehyde using 10 mol% camphorsulfonic acid as the catalyst in acetonitrile at 70 °C, as shown in Scheme 3.



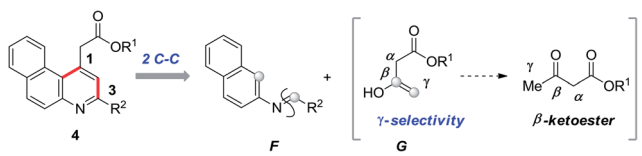
Scheme 3 Synthesis of alkyl 2-(3-arylbenzo[*f*]quinolin-1-yl)acetate.

Results and discussion

In an attempt to optimise the reaction conditions, we tested a series of reactions with ethyl acetoacetate **1a**, 2-napthylamine **2** and benzaldehyde **3a** as depicted in Table 1. It is to be noted that the 10 mol% camphorsulfonic acid catalyst in acetonitrile at 70 °C gave best yield (Table 1, entry 5). However, different solvents such as DCE, THF and *n*-BuOH afford lower yield (Table 1, entries 8–10). It is also noteworthy that in our present protocol we have not observed any other byproducts such as **C**, **D** and **5** in the reaction medium. After optimisation, we conducted reactions with 2-naphthylamine (**2**), methyl acetoacetate (**1b**) and a diverse range of *para*-substituted benzaldehydes such as those containing 4-methyl (**3b**), 4-chloro (**3c**), 4-bromo (**3d**), 4-methoxy (**3e**) and 4-hydroxy (**3f**) moieties, which afforded the desired products **4b–f** in 86–96% yield. Subsequent reaction with *tert*-butyl acetoacetate (**1c**) and 4-fluorobenzaldehyde (**3g**)/furfural (**3h**) delivered the required products **4g** and **4h** in 88% and 76% yield.

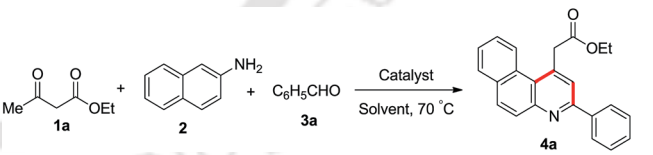
Further, the reaction was examined with 2/3-halobenzaldehyde (**3i**/**3j**)/2,4-dimethoxy benzaldehyde (**3k**), 2-naphthylamine and methyl acetoacetate (**1b**) and the resultant products **4i–k** were obtained in 78–88% yield. In addition, 2/3-(allyloxy)benzaldehyde (**3l**/**3m**) underwent reaction with allyl acetoacetate (**1d**) and 2-naphthylamine, which gave the corresponding products **4l** and **4m** in 74% and 76% yield, respectively. Reactions with different substituted benzaldehydes, ethyl acetoacetate (**1a**) and 2-naphthylamine resulted in **4n–r** in 72–90% yield.

Inspired by these results, we performed reactions of allyl acetoacetate (**1d**), 2-naphthylamine and a variety of *para*-substituted benzaldehydes such as 4-methyl (**3b**), 4-fluoro (**3g**) and 4-methoxy (**3e**) under the optimized reaction conditions, which afforded the required benzo[*f*]quinolines **4s–u** in 78–86% yield as shown in Table 2. The crystal structure of **4g** was



Scheme 2 Synthetic route of alkyl 2-(3-arylbenzo[*f*]quinolin-1-yl) acetate.

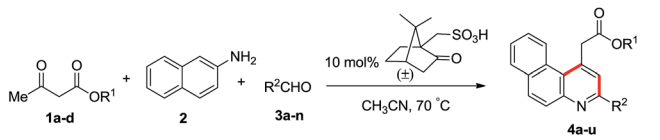
Table 1 Optimization of the reaction conditions[a]

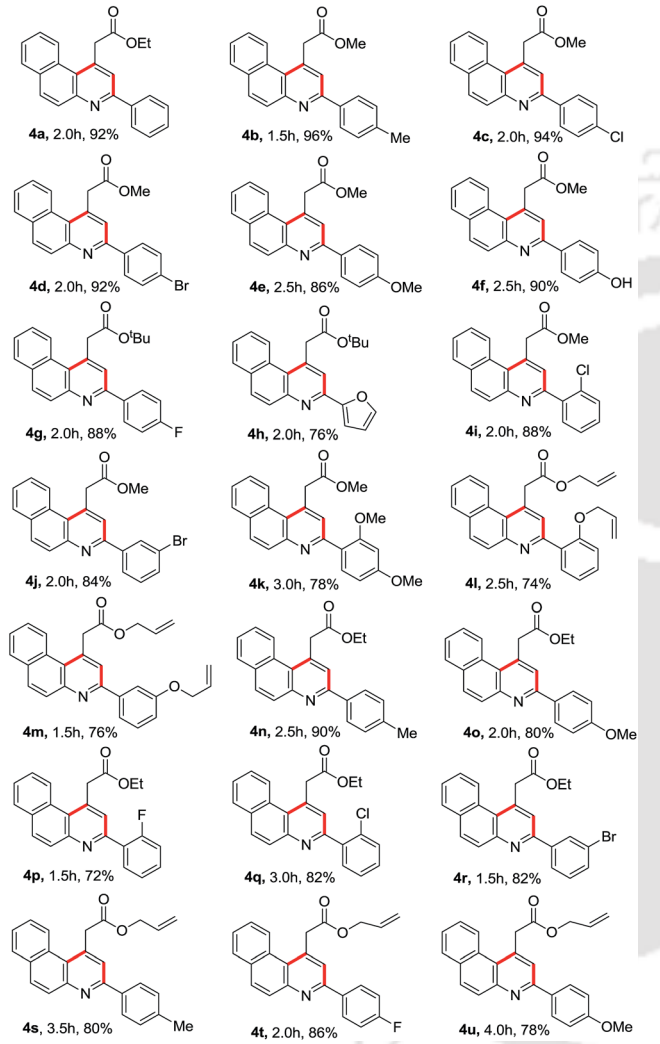


Entry	Catalyst (mol%)	Solvent	Time (h)	Yield[b] (%)
1	AcOH (10)	CH_3CN	8.0	55
2	*p*-TSA (10)	CH_3CN	12	NR
3	Iodine (10)	CH_3CN	2.5	60
4	L-Proline (10)	CH_3CN	12	NR
5	(±)-CSA (10)	CH_3CN	2.0	92
6	(±)-CSA (05)	CH_3CN	3.0	80
7	(±)-CSA (15)	CH_3CN	2.5	89
8	(±)-CSA (10)	DCE	12	35
9	(±)-CSA (10)	THF[c]	6.0	65
10	(±)-CSA (10)	*n*-BuOH	12	25

[a] All the reactions were carried out using ethyl acetoacetate (**1a**, 0.5 equiv.), 2-naphthylamine (**2**, 0.5 equiv.) and benzaldehyde (**3a**, 0.5 equiv.). [b] Isolated yield. [c] Reaction temperature at 55 °C. NR = no reaction.

Table 2 Synthesis of alkyl 2-(3-arylbenzo[*f*]quinolin-1-yl)acetate using (±)-camphorsulfonic acid as the catalyst[ab]





[a] All the reactions were carried out using β-ketoester (0.5 equiv.), 2-naphthylamine (0.5 equiv.) and aromatic aldehyde (0.5 equiv.). [b] Isolated yield.

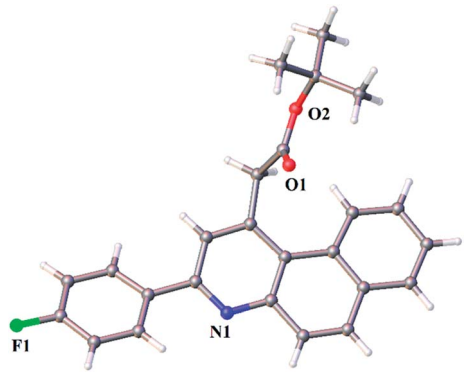
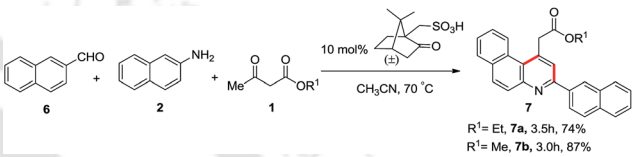
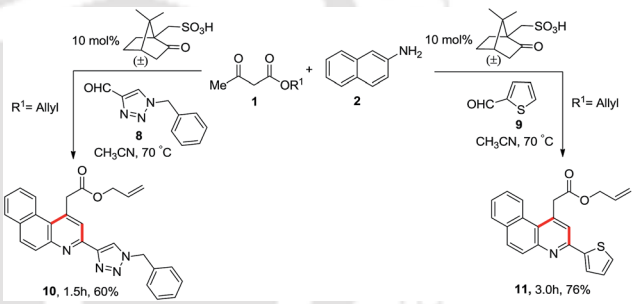


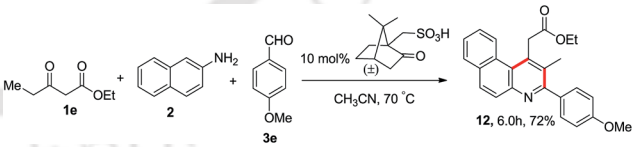
Fig. 2 X-ray crystal structure of **4g**.



Scheme 4 Synthesis of alkyl 2-(3-(naphthalen-2-yl)benzo[*f*] quinolin-1-yl)acetate.



Scheme 5 Synthesis of allyl 2-(3-(heteroaromatic)benzo[*f*]quinolin-1-yl)acetate.



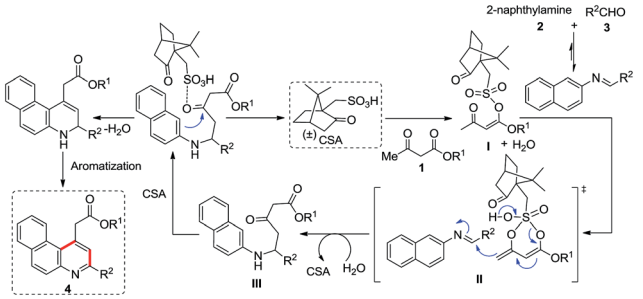
Scheme 6 Synthesis of 1,2,3-trisubstituted benzo[*f*]quinoline.

determined through single crystal XRD analysis, which is shown in Fig. 2.

We have also performed the reaction of a fused aromatic aldehyde, 2-napthaldehyde (**6**), with 2-napthylamine (**2**) and different β-ketoesters in the presence of 10 mol% camphorsulfonic acid as the catalyst in acetonitrile at 70 °C. The desired product alkyl 2-(3-(naphthalen-2-yl)benzo[*f*]quinolin-1-yl)acetate **7** was obtained in good yield as shown in Scheme 4.

The protocol in hand was further investigated with heteroaromatic aldehydes, such as 1-benzyl-1,2,3-triazole-4-carbaldehyde (**8**)/2-thiophenecarboxaldehyde (**9**), 2-napthylamine (**2**) and allyl acetoacetate (**1d**) using a catalytic amount of camphorsulfonic acid and the expected product allyl 2-(3-(heteroaromatic)benzo[*f*]quinolin-1-yl)acetate **10** and **11** were obtained in 60% and 76% yield as shown in Scheme 5.

Furthermore, we have synthesized a functionalised 1,2,3-trisubstituted benzo[*f*]quinoline from ethyl 3-oxopentanoate (**1e**), 2-napthylamine (**2**) and 4-methoxybenzaldehyde (**3e**) using 10 mol% camphorsulfonic acid in acetonitrile at 70 °C, which



Scheme 7 Proposed mechanism for the formation of alkyl 2-(3-arylbenzo[*f*]quinolin-1-yl)acetate.

afforded the resultant product **12** in 72% yield as shown in Scheme 6.

A plausible mechanism is described as follows: the β-ketoester **1** is most likely to react with camphorsulfonic acid to form an intermediate **I**, which subsequently undergoes rearrangement and reacts with the generated imine to form a Michael-type addition product from γ-selective reaction of β-ketoester with imine *via* **II**[17a] to attain **III**. Further, **III** favors aromatization to form the desired product **4** as shown in Scheme 7. It is to be highlighted here that we have observed the HRMS of the intermediate **III** of **4p** after 10 min under reflux conditions, which indirectly supports the proposed mechanism (see ESI†).

Conclusions

In summary, the regioselective synthesis of alkyl 2-(3-arylbenzo[*f*]quinolin-1-yl)acetate has been achieved using camphorsulfonic acid through the γ-selective reaction of β-ketoester. It is a straight forward methodology which provides flexible access to a diverse range of substrates. The prominent aspect of this present method was that two new *C*–*C* bonds were formed in a one-pot fashion under mild reaction conditions. In addition, the protocol enables the synthesis of naphthalen-2-yl, heteroaromatic and trisubstituted benzo[*f*]quinoline analogues in good yields.

General procedure

Synthesis of alkyl 2-(3-arylbenzo[*f*]quinolin-1-yl)acetate (4)

A mixture of β-ketoester (**1**, 0.5 mmol), 2-naphthylamine (**2**, 0.5 mmol) and aromatic aldehyde (**3**, 0.5 mmol) was taken in 5 ml acetonitrile. Camphorsulfonic acid (0.011 g, 0.05 mmol) was added and the mixture allowed to stir at 70 °C. After completion of the reaction, the solvent was removed under reduced pressure and the mixture was extracted with DCM, washed with water, dried over sodium sulphate and concentrated under reduced pressure. Then, the residue was purified through column chromatography to obtain the pure product **4**. Similarly, compounds **7** and **10–12** were synthesized by following the above reaction procedure.

Ethyl 2-(3-phenylbenzo[*f*]quinolin-1-yl)acetate (4a). Yield 92%, white solid, mp 131–132 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.54 (d, J = 8.8 Hz, 1H), 8.22 (d, J = 8.8 Hz, 2H), 8.09 (d, J = 9.2 Hz, 1H), 7.99–7.97 (m, 2H), 7.87 (s, 1H), 7.67–7.64 (m, 2H), 7.56 (t, J = 7.2 Hz, 2H), 7.49 (t, J = 6.8 Hz, 1H), 4.49 (s, 2H), 4.25 (q, J = 7.2 Hz, 2H), 1.23 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.8, 155.9, 150.3, 141.1, 139.2, 133.2, 131.5, 130.0, 129.8, 129.5, 129.4, 129.1, 127.6, 127.0, 126.9, 126.8, 124.6, 123.2, 61.7, 44.0, 14.4; IR (KBr) ν_{max} 3056, 2980, 2902, 1735, 1584, 1552, 1484, 1455, 1391, 1367, 1322, 1255, 1194, 1156, 1029 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{20}NO_2$ 342.1489 (M + H$^+$); found 342.1489.

Methyl 2-(3-(*p*-tolyl)benzo[*f*]quinolin-1-yl)acetate (4b).[14a] Yield 96%, light yellow solid, mp 168–169 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.49 (d, J = 7.6 Hz, 1H), 8.12 (t, J = 8.0 Hz, 2H), 8.08 (s, 1H), 7.97–7.93 (m, 2H), 7.83 (s, 1H), 7.68–7.61 (m, 2H), 7.35 (d, J = 8.0 Hz, 2H), 4.47 (s, 2H), 3.77 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.3, 155.8, 150.2, 140.8, 139.6, 136.2, 133.1, 131.4, 129.9, 129.7, 129.6, 129.4, 128.2, 127.5, 126.8, 126.7, 124.3, 122.9, 52.7, 43.7, 21.5; IR (KBr) ν_{max} 3029, 2952, 2922, 2853, 1737, 1579, 1548, 1481, 1452, 1437, 1392, 1353, 1259, 1184, 1132, 1057 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{20}NO_2$ 342.1489 (M + H$^+$); found 342.1505.

Methyl 2-(3-(4-chlorophenyl)benzo[*f*]quinolin-1-yl)acetate (4c).[14a] Yield 94%, white solid, mp 138–139 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.49 (d, J = 7.2 Hz, 1H), 8.17 (d, J = 8.8 Hz, 2H), 8.12 (d, J = 8.8 Hz, 1H), 8.00–7.96 (m, 2H), 7.83 (s, 1H), 7.69–7.66 (m, 2H), 7.51 (d, J = 8.8 Hz, 2H), 4.51 (s, 2H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.1, 154.3, 149.9, 141.4, 137.0, 135.9, 133.2, 131.9, 129.7, 129.5, 129.2, 128.9, 127.2, 127.0, 126.8, 124.7, 122.9, 52.8, 43.7; IR (KBr) ν_{max} 3056, 2942, 2924, 2852, 1741, 1585, 1550, 1481, 1435, 1390, 1328, 1257, 1198, 1157, 1091, 1012 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{17}ClNO_2$ 362.0943 (M + H$^+$); found 362.0942.

Methyl 2-(3-(4-bromophenyl)benzo[*f*]quinolin-1-yl)acetate (4d).[14a] Yield 92%, light yellow solid, mp 143–144 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.51 (d, J = 9.0 Hz, 1H), 8.11 (d, J = 8.4 Hz, 2H), 8.06 (d, J = 9.0 Hz, 1H), 7.99–7.96 (m, 2H), 7.83 (s, 1H), 7.68–7.66 (m, 4H), 4.51 (s, 2H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2, 154.5, 150.3, 141.1, 137.9, 133.2, 132.2, 131.7, 129.8, 129.6, 129.5, 129.1, 127.1, 126.9, 126.8, 124.7, 124.1, 122.7, 52.8, 43.6; IR (KBr)ν_{max} 3051, 2951, 2915, 2854, 1736, 1584, 1549, 1481, 1455, 1434, 1387, 1356, 1328, 1257, 1199, 1159, 1087, 1008 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{17}BrNO_2$ 406.0437 (M + H$^+$); found 406.0437.

Methyl 2-(3-(4-methoxyphenyl)benzo[*f*]quinolin-1-yl)acetate (4e). Yield 86%, light yellow solid, mp 149–150 °C, ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.47 (d, J = 8.4 Hz, 1H), 8.18 (d, J = 8.4 Hz, 2H), 8.09 (d, J = 9.0 Hz, 1H), 7.93 (t, J = 9.0 Hz, 2H), 7.78 (s, 1H), 7.65–7.56 (m, 2H), 7.04 (d, J = 8.4 Hz, 2H), 4.46 (s, 2H), 3.87 (s, 3H), 3.76 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.2, 161.1, 155.3, 149.9, 140.9, 132.9, 131.8, 131.5, 131.2, 129.9, 129.4, 128.9, 126.8, 126.7, 126.6, 124.1, 122.7, 114.4, 55.5, 52.7, 43.6; IR (KBr) ν_{max} 3068, 2995, 2948, 2937, 2830, 1737, 1604, 1544, 1503, 1434, 1354, 1337, 1252, 1202, 1183, 1161, 1028 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{20}NO_3$ 358.1438 (M + H$^+$); found 358.1430.

Methyl 2-(3-(4-hydroxyphenyl)benzo[*f*]quinolin-1-yl)acetate (4f). Yield 90%, white solid, mp 141–142 °C, ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.30 (s, 1H), 8.40 (d, J = 6.0 Hz, 1H), 8.02 (d, J =

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6.6 Hz, 2H), 7.93 (d, J = 2.4, 1H), 7.92 (d, J = 1.8 Hz, 2H), 7.75 (s, 1H), 7.56–7.53 (m, 2H), 6.91 (d, J = 6.0 Hz, 2H), 4.44 (s, 2H), 3.69 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.4, 158.5, 154.8, 149.2, 140.1, 132.0, 129.1, 129.0, 128.6, 128.5, 128.1, 128.0, 126.1, 125.9, 125.7, 122.9, 121.8, 121.7, 115.4, 115.3, 51.8, 42.8; IR (KBr) ν_{max} 3058, 2995, 2953, 2838, 1738, 1608, 1588, 1549, 1514, 1484, 1451, 1353, 1258, 1171, 1130, 1058 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{18}NO_3$ 344.1281 (M + H$^+$); found 344.1286.

***tert*-Butyl 2-(3-(4-fluorophenyl)benzo[*f*]quinolin-1-yl)acetate (4g).** Yield 88%, white solid, mp 140–141 °C, ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.58 (d, J = 7.8 Hz, 1H), 8.23–8.21 (m, 2H), 8.06 (d, J = 8.4 Hz, 1H), 7.98–7.95 (m, 2H), 7.81 (s, 1H), 7.67–7.64 (m, 2H), 7.23–7.20 (m, 2H), 4.41 (s, 2H), 1.44 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 169.5, 165.2, 163.5, 154.1, 133.5, 133.1, 131.2, 131.1, 130.3, 130.1, 129.7, 129.6, 129.3, 128.3, 127.3, 127.2, 127.1, 127.0, 126.6, 124.8, 123.6, 116.3, 116.1, 115.6, 115.5, 82.6, 45.6, 28.2; IR (KBr)ν_{max} 3057, 2976, 2927, 2850, 1727, 1602, 1585, 1553, 1532, 1510, 1483, 1455, 1392, 1368, 1329, 1226, 1149, 1073, 1014 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{23}FNO_2$ 388.1708 (M + H$^+$); found 388.1707.

***tert*-Butyl 2-(3-(furan-2-yl)benzo[*f*]quinolin-1-yl)acetate (4h).** Yield 76%, brown solid, mp 94–95 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.56 (d, J = 8.4 Hz, 1H), 8.04 (d, J = 9.2 Hz, 1H), 7.96–7.95 (m, 3H), 7.84 (s, 1H), 7.66–7.64 (m, 2H), 7.27 (d, J = 3.2 Hz, 1H), 6.62–6.61 (m, 1H), 4.41 (s, 2H), 1.43 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 169.8, 153.6, 150.2, 147.8, 144.1, 141.7, 133.1, 131.6, 129.4, 129.4, 126.9, 126.8, 126.7, 124.6, 121.6, 112.4, 110.0, 82.2, 45.3, 28.2; IR (KBr) ν_{max} 3029, 2974, 2926, 1728, 1601, 1551, 1491, 1454, 1393, 1368, 1325, 1254, 1224, 1072 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{22}NO_3$ 360.1594 (M + H$^+$); found 360.1609.

Methyl 2-(3-(2-chlorophenyl)benzo[*f*]quinolin-1-yl)acetate (4i). Yield 88%, brown solid, mp 79–80 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.56 (d, J = 8.0 Hz, 1H), 8.19 (d, J = 8.0 Hz, 1H), 8.00 (t, J = 8.4 Hz, 2H), 7.84 (s, 2H), 7.69 (s, 2H), 7.53 (d, J = 7.2 Hz, 1H), 7.42 (t, J = 8.4 Hz, 2H), 4.52 (s, 2H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.9, 155.0, 149.4, 133.3, 132.7, 132.3, 132.2, 130.4, 129.6, 128.6, 127.5, 127.4, 127.2, 127.1, 126.9, 124.8, 52.8, 43.6; IR (KBr) ν_{max} 3059, 2987, 2953, 2850, 1738, 1596, 1580, 1550, 1476, 1435, 1395, 1351, 1330, 1258, 1201, 1160, 1094, 1057 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{17}ClNO_2$ 362.0943 (M + H$^+$); found 362.0943.

Methyl 2-(3-(3-bromophenyl)benzo[*f*]quinolin-1-yl)acetate (4j). Yield 84%, white solid, mp 130–131 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.50 (d, J = 12.0 Hz, 1H), 8.40 (s, 1H), 8.12 (d, J = 12.0 Hz, 1H), 8.06 (d, J = 12.0 Hz, 1H), 7.97 (d, J = 12.0 Hz, 2H), 7.81 (s, 1H), 7.69–7.65 (m, 2H), 7.59 (d, J = 12.0 Hz, 1H), 7.39 (t, J = 12.0 Hz, 1H), 4.49 (s, 2H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 154.1, 150.3, 141.1, 141.0, 133.3, 132.4, 131.8, 130.6, 130.5, 129.8, 129.6, 129.5, 127.1, 126.9, 126.8, 126.1, 124.9, 123.3, 122.9, 52.8, 43.7; IR (KBr) ν_{max} 3031, 2950, 2916, 2848, 1724, 1605, 1582, 1549, 1488, 1454, 1424, 1383, 1357, 1323, 1306, 1247, 1161, 1053 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{17}BrNO_2$ 406.0437 (M + H$^+$); found 406.0435.

Methyl 2-(3-(2,4-dimethoxyphenyl)benzo[*f*]quinolin-1-yl) acetate (4k). Yield 78%, brown solid, mp 111–112 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.52 (d, J = 7.6 Hz, 1H), 8.12 (d, J = 8.0 Hz, 1H), 8.02–7.94 (m, 4H), 7.64 (s, 2H), 6.69 (d, J = 6.8 Hz, 1H), 6.60 (s, 1H), 4.49 (s, 2H), 3.87 (s, 6H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.3, 162.1, 158.8, 154.6, 149.7, 139.8, 133.0, 132.7, 131.2, 129.9, 129.4, 129.2, 127.3, 126.7, 123.9, 105.7, 99.2, 55.9, 55.7, 52.6, 43.7; IR (KBr) ν_{max} 3059, 3003, 2950, 2837, 1736, 1608, 1579, 1547, 1505, 1455, 1437, 1300, 1283, 1209, 1160, 1030 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{22}NO_4$ 388.1544 (M + H$^+$); found 388.1542.

Allyl 2-(3-(2-(allyloxy)phenyl)benzo[*f*]quinolin-1-yl)acetate (4l). Yield 74%, light yellow solid, mp 169–170 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55 (d, J = 8.0 Hz, 1H), 8.17 (s, 1H), 8.07 (s, 1H), 8.04 (d, J = 7.6 Hz, 1H), 7.98 (d, J = 8.4 Hz, 2H), 7.66–7.64 (m, 2H), 7.42 (t, J = 7.6 Hz, 1H), 7.17 (t, J = 7.6 Hz, 1H), 7.04 (d, J = 8.4 Hz, 1H), 6.09–6.00 (m, 1H), 5.91–5.81 (m, 1H), 5.38 (d, J = 17.2 Hz, 1H), 5.26 (d, J = 13.6 Hz, 2H), 5.22–5.18 (m 1H), 4.67–4.63 (m, 4H), 4.51 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.5, 156.5, 155.1, 150.1, 139.3, 133.3, 133.1, 131.8, 131.7, 131.0, 130.5, 129.9, 129.7, 129.3, 129.2, 127.8, 126.8, 126.7, 126.6, 124.2, 121.7, 118.9, 117.2, 113.3, 69.5, 66.1, 43.8; IR (KBr) ν_{max} 3055, 2969, 2948, 2930, 2835, 1741, 1687, 1624, 1577, 1544, 1480, 1451, 1352, 1316, 1257, 1224, 1182, 1148, 1059 cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{24}NO_3$ 410.1751 (M + H$^+$); found 410.1755.

Allyl 2-(3-(3-(allyloxy)phenyl)benzo[*f*]quinolin-1-yl)acetate (4m). Yield 76%, white solid, mp 81–82 °C, ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.53 (d, J = 6.0 Hz, 1H), 8.08 (d, J = 6.0 Hz, 1H), 7.98–7.95 (m, 2H), 7.86–7.84 (m, 2H), 7.76 (d, J = 6.0 Hz, 1H), 7.66–7.63 (m, 2H), 7.44 (t, J = 6.0 Hz, 1H), 7.04 (d, J = 6.0 Hz, 1H), 6.17–6.10 (m, 1H), 5.92–5.85 (m, 1H), 5.49 (d, J = 18.0 Hz, 1H), 5.33 (d, J = 6.0 Hz, 1H), 5.28 (d, J = 18.0 Hz, 1H), 5.22 (d, J = 12.0 Hz, 1H), 4.68 (d, J = 6.0 Hz, 4H), 4.52 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.4, 159.4, 155.6, 150.2, 140.8, 140.5, 133.5, 133.2, 131.8, 131.5, 130.0, 129.9, 129.7, 129.4, 126.9, 126.8, 126.8, 124.7, 123.3, 120.2, 119.1, 117.9, 116.3, 113.7, 69.2, 66.3, 43.8; IR (KBr) ν_{max} 3056, 2924, 2896, 1733, 1647, 1583, 1552, 1488, 1455, 1423, 1358, 1319, 1281, 1231, 1195, 1154, 1024, 991 cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{24}NO_3$ 410.1756 (M + H$^+$); found 410.1754.

Ethyl 2-(3-(*p*-tolyl)benzo[*f*]quinolin-1-yl)acetate (4n). Yield 90%, brown solid, mp 102–103 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.53 (d, J = 8.0 Hz, 1H), 8.13 (d, J = 8.4 Hz, 2H), 8.08 (s, 1H), 7.96 (d, J = 9.6 Hz, 2H), 7.85 (s, 1H), 7.67–7.63 (m, 2H), 7.34 (d, J = 7.6 Hz, 2H), 4.48 (s, 2H), 4.24 (q, J = 6.8 Hz, 2H), 2.45 (s, 3H), 1.23 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.8, 155.8, 150.2, 141.1, 139.7, 136.2, 133.1, 131.4, 130.0, 129.8, 129.7, 129.4, 127.5, 126.9, 126.8, 126.7, 124.4, 123.0, 61.7, 43.9, 21.6, 14.4; IR (KBr) ν_{max} 3053, 3025, 2980, 2923, 2855, 1734, 1606, 1585, 1550, 1512, 1482, 1455, 1391, 1366, 1322, 1248, 1217, 1184, 1156, 1094, 1054 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{22}NO_2$ 356.1645 (M + H$^+$); found 356.1646.

Ethyl 2-(3-(4-methoxyphenyl)benzo[*f*]quinolin-1-yl)acetate (4o). Yield 80%, white solid, mp 120–121 °C, ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.53 (d, J = 6.0 Hz, 1H), 8.19 (d, J = 6.0 Hz, 2H), 8.06 (d, J = 12.0 Hz, 1H), 7.96 (d, J = 6.0 Hz, 1H), 7.95–7.94 (m, 1H), 7.81 (s, 1H), 7.66–7.63 (m, 2H), 7.07 (d, J = 6.0 Hz, 2H), 4.48 (s, 2H), 4.24 (q, J = 6.0 Hz, 2H), 3.90, (s, 3H), 1.23 (t, J = 6.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.8, 161.0, 155.5, 150.2,

140.9, 133.0, 131.7, 131.3, 130.1, 129.7, 129.4, 128.9, 126.8, 126.7, 126.7, 124.1, 122.6, 114.4, 61.7, 55.6, 44.0, 14.4; IR (KBr) ν_{max} 3027, 2957, 2924, 2852, 1732, 1631, 1606, 1583, 1550, 1531, 1512, 1482, 1455, 1392, 1364, 1324, 1248, 1224, 1175, 1145, 1030 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{22}NO_3$ 372.1594 (M + H^+); found 372.1594.

Ethyl 2-(3-(2-fluorophenyl)benzo[*f*]quinolin-1-yl)acetate (4p). Yield 72%, semi-solid, ^1H NMR (600 MHz, $CDCl_3$): δ 8.57 (d, J = 6.0 Hz, 1H), 8.24–8.21 (m, 1H), 8.08 (d, J = 6.0 Hz, 1H), 7.98 (d, J = 6.0 Hz, 2H), 7.97–7.95 (m, 1H), 7.68–7.66 (m, 2H), 7.43 (t, J = 6.0 Hz, 1H), 7.34 (t, J = 6.0 Hz, 1H), 7.23–7.20, (m, 1H), 4.50 (s, 2H), 4.24 (q, J = 6.0 Hz, 2H), 1.23 (t, J = 6.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.7, 161.9, 160.2, 152.2, 150.2, 140.7, 133.3, 131.6, 131.6, 131.5, 131.1, 131.0, 129.9, 129.6, 129.4, 127.1, 127.0, 126.8, 124.9, 124.9, 124.7, 116.6, 116.4, 61.7, 44.0, 14.3; IR (KBr) ν_{max} 3028, 2956, 2923, 2852, 1733, 1586, 1582, 1550, 1484, 1452, 1371, 1364, 1320, 1249, 1215, 1155, 1080, 1030 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{19}FNO_2$ 360.1395 (M + H^+); found 360.1396.

Ethyl 2-(3-(2-chlorophenyl)benzo[*f*]quinolin-1-yl)acetate (4q). Yield 82%, white solid, mp 151–152 °C, ^1H NMR (600 MHz, $CDCl_3$): δ 8.60 (d, J = 8.4 Hz, 1H), 8.12 (d, J = 7.2 Hz, 1H), 8.01–7.97 (m, 2H), 7.83–7.81 (m, 2H), 7.70–7.67 (m, 2H), 7.53 (d, J = 7.8 Hz, 1H), 7.45–7.31 (m, 1H), 7.43–7.38 (m, 1H), 4.49 (s, 2H), 4.24 (q, J = 7.2 Hz, 2H), 1.23 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4, 155.9, 149.3, 133.2, 132.7, 132.3, 132.1, 130.5, 130.4, 129.7, 129.6, 129.5, 128.6, 127.5, 127.4, 127.3, 127.1, 124.9, 61.8, 43.9, 14.3; IR (KBr) ν_{max} 3060, 2982, 2933, 2849, 1734, 1627, 1596, 1578, 1550, 1475, 1442, 1394, 1369, 1350, 1330, 1244, 1210, 1160, 1133, 1094, 1055, 1038 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{19}ClNO_2$ 376.1099 (M + H^+); found 376.1099.

Ethyl 2-(3-(3-bromophenyl)benzo[*f*]quinolin-1-yl)acetate (4r). Yield 82%, white solid, mp 125–126 °C, ^1H NMR (600 MHz, $CDCl_3$): δ 8.54 (d, J = 12.0 Hz, 1H), 8.40 (s, 1H), 8.13 (d, J = 6.0 Hz, 1H), 8.07 (d, J = 6.0 Hz, 1H), 8.00–7.97, (m, 2H), 7.84 (s, 1H), 7.68–7.66 (m, 2H), 7.60 (d, J = 6.0 Hz, 1H), 7.41 (t, J = 12.0 Hz, 1H), 4.50 (s, 2H), 4.25 (q, J = 6.0 Hz, 2H), 1.25 (t, J = 6.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.7, 154.2, 150.2, 141.4, 141.1, 133.3, 132.5, 131.7, 130.7, 130.6, 129.9, 129.6, 129.4, 126.9, 126.2, 126.1, 124.9, 123.4, 123.1, 123.0, 61.5, 43.9, 13.9; IR (KBr) ν_{max} 3025, 2922, 2852, 1733, 1586, 1572, 1550, 1480, 1452, 1442, 1428, 1371, 1322, 1213, 1197, 1158, 1019 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{19}BrNO_2$ 420.0594 (M + H^+); found 420.0623.

Allyl 2-(3-(*p*-tolyl)benzo[*f*]quinolin-1-yl)acetate (4s). Yield 80%, brown solid, mp 83–84 °C, ^1H NMR (400 MHz, $CDCl_3$): δ 8.52 (d, J = 8.8 Hz, 1H), 8.12 (d, J = 8.0 Hz, 2H), 8.08 (d, J = 9.2 Hz, 1H), 7.99–7.95 (m, 2H), 7.86 (s, 1H), 7.69–7.63 (m, 2H), 7.35 (d, J = 8.0 Hz, 2H), 5.92–5.83 (m, 1H), 5.30–5.17 (m, 2H), 4.68 (d, J = 5.2 Hz, 2H), 4.52 (s, 2H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4, 155.8, 150.2, 140.7, 139.6, 136.2, 133.1, 131.8, 131.4, 130.0, 129.8, 129.4, 128.7, 127.5, 126.8, 124.4, 122.9, 119.0, 66.2, 43.8, 21.5; IR (KBr) ν_{max} 3062, 3035, 2923, 2853, 1735, 1653, 1605, 1582, 1548, 1479, 1451, 1352, 1330, 1274, 1216, 1185, 1154, 1130, 1054 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{22}NO_2$ 368.1645 (M + H^+); found 368.1649.

Allyl 2-(3-(4-fluorophenyl)benzo[*f*]quinolin-1-yl)acetate (4t). Yield 86%, white solid, mp 154–155 °C, ^1H NMR (600 MHz, $CDCl_3$): δ 8.52–8.51 (m, 1H), 8.22–8.20 (m, 2H), 8.09 (d, J = 8.4 Hz, 1H), 7.98–7.95 (m, 2H), 7.83 (s, 1H), 7.67–7.63 (m, 2H), 7.22 (t, J = 8.4 Hz, 2H), 5.92–5.85 (m, 1H), 5.29 (t, J = 8.4 Hz, 1H), 5.23 (d, J = 11.4 Hz, 1H), 4.69 (d, J = 6.0 Hz, 2H), 4.52 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.3, 164.9, 163.3, 154.6, 150.0, 141.2, 133.2, 131.8, 131.7, 129.8, 129.6, 129.5, 129.5, 129.3, 127.0, 126.9, 126.8, 124.5, 122.9, 119.2, 116.1, 115.9, 66.3, 43.8; IR (KBr) ν_{max} 3059, 2954, 2924, 2848, 1735, 1653, 1601, 1585, 1552, 1508, 1483, 1454, 1390, 1358, 1322, 1228, 1191, 1156, 1014 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{19}FNO_2$ 372.1395 (M + H^+); found 372.1384.

Allyl 2-(3-(4-methoxyphenyl)benzo[*f*]quinolin-1-yl)acetate (4u). Yield 78%, pale yellow solid, mp 92–95 °C, ^1H NMR (400 MHz, $CDCl_3$): δ 8.50 (d, J = 6.4 Hz, 1H) 8.18 (d, J = 8.0 Hz, 2H), 8.05 (d, J = 9.2 Hz, 1H), 7.95 (d, J = 7.6 Hz, 2H), 7.81 (s, 1H), 7.62 (d, J = 3.2 Hz, 2H), 7.05 (d, J = 8.0 Hz, 2H), 5.89–5.85 (m, 1H), 5.31–5.21 (m, 2H), 4.68 (s, 2H), 4.49 (s, 2H), 3.89 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.5, 161.0, 155.4, 150.2, 140.6, 133.0, 131.8, 131.6, 131.3, 129.9, 129.6, 129.3, 128.9, 126.7, 126.6, 124.1, 122.6, 119.0, 114.4, 66.1, 55.5, 43.8; IR (KBr) ν_{max} 3051, 2959, 2933, 2836, 1735, 1675, 1653, 1606, 1583, 1550, 1530, 1511, 1482, 1455, 4140, 1358, 1323, 1306, 1176, 1155, 1111, 1030 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{22}NO_3$ 384.1594 (M + H^+); found 384.1612.

Ethyl 2-(3-(naphthalen-2-yl)benzo[*f*]quinolin-1-yl)acetate (7a). Yield 74%, pale yellow solid, mp 76–77 °C, ^1H NMR (400 MHz, $CDCl_3$): δ 8.69 (s, 1H), 8.56 (d, J = 8.8 Hz, 1H), 8.41 (d, J = 8.4 Hz, 1H), 8.18 (d, J = 8.8 Hz, 1H), 8.03–8.02 (m, 3H), 8.00–7.96 (m, 2H), 7.92–7.89 (m, 1H), 7.69–7.64 (m, 2H), 7.55–7.53 (m, 2H), 4.54 (s, 2H), 4.27 (q, J = 7.2 Hz, 2H), 1.25 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.8, 155.6, 150.2, 141.4, 136.2, 134.1, 133.7, 133.2, 131.7, 130.0, 129.5, 129.4, 129.1, 128.8, 127.9, 127.3, 127.0, 126.9, 126.9, 126.8, 126.5, 125.1, 124.7, 123.5, 61.7, 44.1, 14.4; IR (KBr) ν_{max} 3056, 2978, 2923, 2851, 1734, 1583, 1552, 1509, 1482, 1452, 1389, 1367, 1321, 1256, 1215, 1195, 1156, 1029; cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{22}NO_2$ 392.1645 (M + H^+); found 392.1648.

Methyl 2-(3-(naphthalen-2-yl)benzo[*f*]quinolin-1-yl)acetate (7b). Yield 87%, white solid, mp 80–81 °C, ^1H NMR (600 MHz, $CDCl_3$): δ 8.68 (s, 1H), 8.52 (d, J = 6.0 Hz, 1H), 8.41–8.39 (m, 1H), 8.14 (d, J = 6.0 Hz, 1H), 8.02–8.01 (m, 4H), 7.99–7.96 (m, 1H), 7.90 (t, J = 6 Hz, 1H), 7.68–7.65 (m, 2H), 7.55–7.53 (m, 2H), 4.54 (s, 2H), 3.79 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.3, 155.6, 150.3, 141.0, 136.3, 134.1, 133.7, 133.2, 131.6, 129.9, 129.6, 129.4, 129.0, 128.8, 127.9, 127.2, 127.0, 126.9, 126.8, 126.8, 126.6, 125.1, 124.6, 123.4, 52.8, 43.7; IR (KBr) ν_{max} 3057, 2986, 2952, 2848, 1736, 1595, 1549, 1472, 1432, 1391, 1347, 1198, 1158, 1088, 1055 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{20}NO_2$ 378.1489 (M + H^+); found 378.1486.

Allyl 2-(3-(1-benzyl-1*H*-1,2,3-triazol-4-yl)benzo[*f*]quinolin-1-yl)acetate (10). Yield 60%, brown solid, mp 124–125 °C, ^1H NMR (600 MHz, $CDCl_3$): δ 8.53 (d, J = 8.1 Hz, 1H), 8.45 (s, 1H), 8.02–7.97 (m, 2H), 7.69 (s, 2H), 7.40–7.39 (m, 6H), 7.28 (s, 1H), 5.86–5.83 (m, 1H), 5.65 (s, 2H), 5.26 (d, J = 17.4 Hz, 1H), 5.20 (d,

J = 10.8 Hz, 1H), 4.66 (d, J = 5.6 Hz, 2H), 4.57 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.3, 150.2, 148.9, 148.7, 141.3, 134.7, 133.2, 131.8, 131.7, 130.1, 129.4, 129.1, 129.0, 128.5, 128.1, 127.0, 126.8, 125.3, 123.4, 123.1, 122.9, 119.1, 66.3, 54.7, 43.9; IR (KBr) ν_{max} 3148, 3062, 2924, 2853, 1736, 1647, 1597, 1557, 1497, 1454, 1430, 1362, 1338, 1296, 1232, 1187, 1156, 1092, 1043, 1017 cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{23}N_4O_2$ 435.1821 (M + H$^+$); found 435.1813.

Allyl 2-(3-(thiophen-2-yl)benzo[*f*]quinolin-1-yl)acetate (11). Yield 76%, brown solid, mp 114–115 °C, ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.48 (d, J = 9.6 Hz, 1H), 8.01 (d, J = 9.0 Hz, 1H), 7.95–7.93 (m, 2H), 7.78 (s, 1H), 7.76 (d, J = 3.4 Hz, 1H), 7.65–7.61 (m, 2H), 7.47 (d, J = 5.4 Hz, 1H), 7.18–7.16 (m, 1H), 5.91–5.84 (m, 1H), 5.29–5.26 (m, 1H), 5.22 (d, J = 9.6 Hz, 1H), 4.68 (d, J = 6.0 Hz, 2H), 4.48 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.3, 151.1, 150.2, 144.7, 140.8, 133.1, 131.8, 131.7, 129.9, 129.5, 129.3, 128.6, 128.3, 126.9, 126.8, 126.7, 125.9, 124.9, 121.7, 119.1, 66.2, 43.7; IR (KBr) ν_{max} 3071, 2958, 2930, 2857, 1739, 1584, 1552, 1523, 1482, 1455, 1423, 1365, 1326, 1259, 1155, 1071, 1015 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{18}NO_2S$ 360.1053 (M + H$^+$); found 360.1052.

Ethyl 2-(3-(4-methoxyphenyl)-2-methylbenzo[*f*]quinolin-1-yl) acetate (12). Yield 72%, white solid, mp 76–77 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (d, J = 6.8 Hz, 1H), 7.94 (d, J = 8.8 Hz, 2H), 7.88 (d, J = 8.8 Hz, 1H), 7.63–7.62 (m, 3H), 7.58 (s, 1H), 7.03 (d, J = 8.4 Hz, 2H), 4.42 (s, 2H), 4.38 (q, J = 7.6 Hz, 2H), 3.89 (s, 3H), 2.47 (s, 3H), 1.38 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2, 159.9, 158.9, 147.1, 139.4, 133.9, 133.4, 130.9, 130.4, 129.8, 129.6, 129.2, 129.1, 128.9, 127.2, 126.9, 126.3, 125.0, 122.1, 114.0, 61.7, 55.6, 40.1, 17.7, 14.6; IR (KBr)ν_{max} 3055, 2957, 2932, 2836, 1738, 1607, 1577, 1516, 1549, 1510, 1477, 1451, 1427, 1368, 1301, 1178, 1109, 1019 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{24}NO_3$ 386.1751 (M + H$^+$); found 386.1753.

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Camphorsulfonic Acid Catalyzed One-Pot Three-Component Reaction for the Synthesis of Fused Quinoline and Benzoquinoline Derivatives

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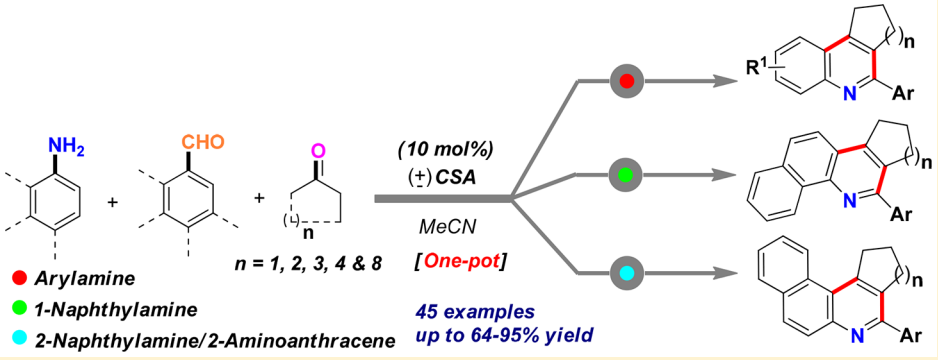
Supporting Information



ABSTRACT: A simple and an efficient one-pot three-component reaction of arylamines, aromatic aldehydes, and cyclic ketones was described for the synthesis of various fused quinoline, benzoquinoline, and naphthoquinoline derivatives by using camphorsulfonic acid as a catalyst. The exploitation of pregnenolone steroid for benzoquinolines and terephthalaldehyde for bis-benzoquinolines synthesis was achieved with 68−75% yields. The reactivity of arylamines and the mechanistic study for the formation of benzoquinoline was described precisely. The present protocol offers a great potential for atom-economy under mild conditions.

INTRODUCTION

N-Heterocyclics are an important class of compounds in biological, medicinal, and material chemistry. Of these, quinoline, benzoquinoline derivatives are an interesting class of heterocyclic compounds having a large scope to be investigated by the synthetic chemists because of their natural occurrence and having medicinal value.[1−3] These scaffolds are found to be having several applications in agrochemicals, pharmaceuticals, dyestuffs, and functional materials.[4] They have a wide range of biological activities including antitubercular,[5a] anticancer,[5b,c] antipsychotic,[5d] antimicrobial,[6a] anti-HIV,[6b] and for the treatment of neurodegenerative diseases.[7] Marinoquinolines are a class of fused quinolines isolated from the marine bacteria having antibacterial and antifungal activities. Fused quinolines and benzoquinolines core units are found in various alkaloids[8a] and commercial drugs[8b] as shown in Figure 1.

Quinolines act as effective ligands in cross-coupling reactions[9a] and they also play a crucial role in asymmetric synthesis as a catalyst.[9b,c] In addition, they are also used as ligands for preparation of OLED complexes[10a] and with conjugated polymers acting as chemosensors of metal ions.[10b,c]

Due to their potential biological activity and tremendous applications, chemists have developed various classical methods for the synthesis of quinolines such as the Combes reaction,[11] Skraup reaction,[12] Doebner−von Miller,[13] Conrad−Limpach,[14]

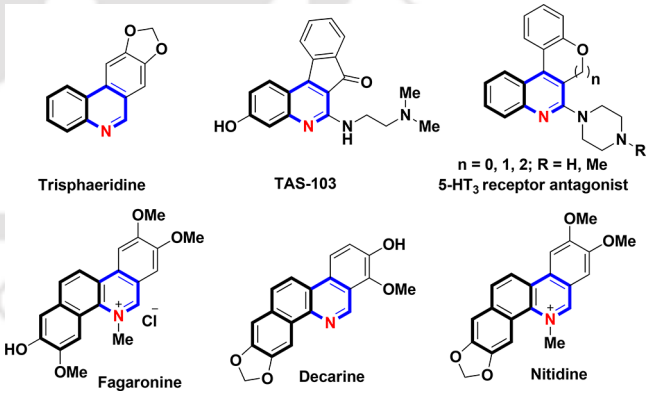


Figure 1. Biologically active quinoline and benzoquinoline core units.

and Knorr synthesis[15] which involve the formation of a new C−C bond as shown in (Figure 2, 1a), whereas, in Pfitzinger[16] and Friedlander[17] reactions, new C−C and C−N bonds were formed as shown in (Figure 2, 1b). In a traditional approach, there are new strategies that have emerged for the synthesis of quinolines through intramolecular cyclization that involve

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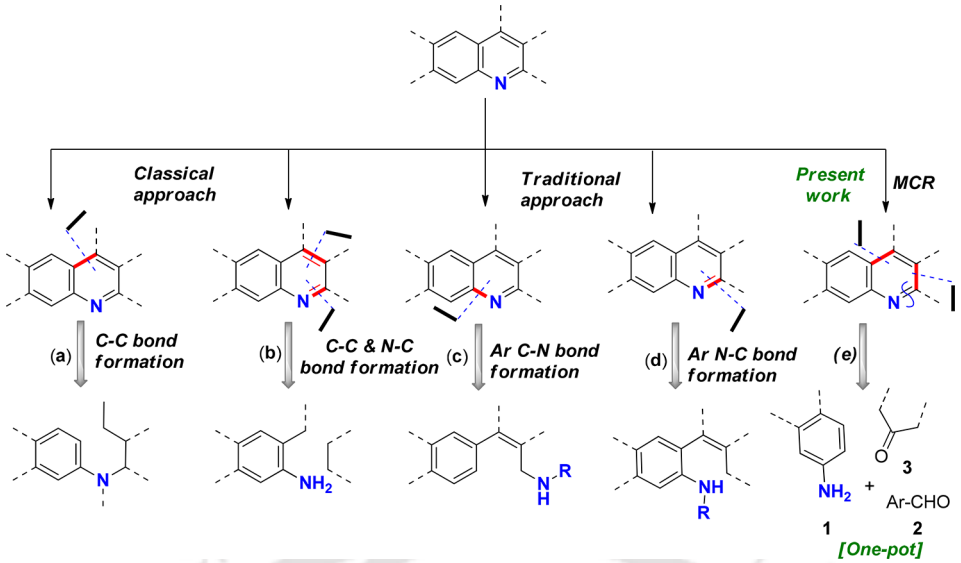
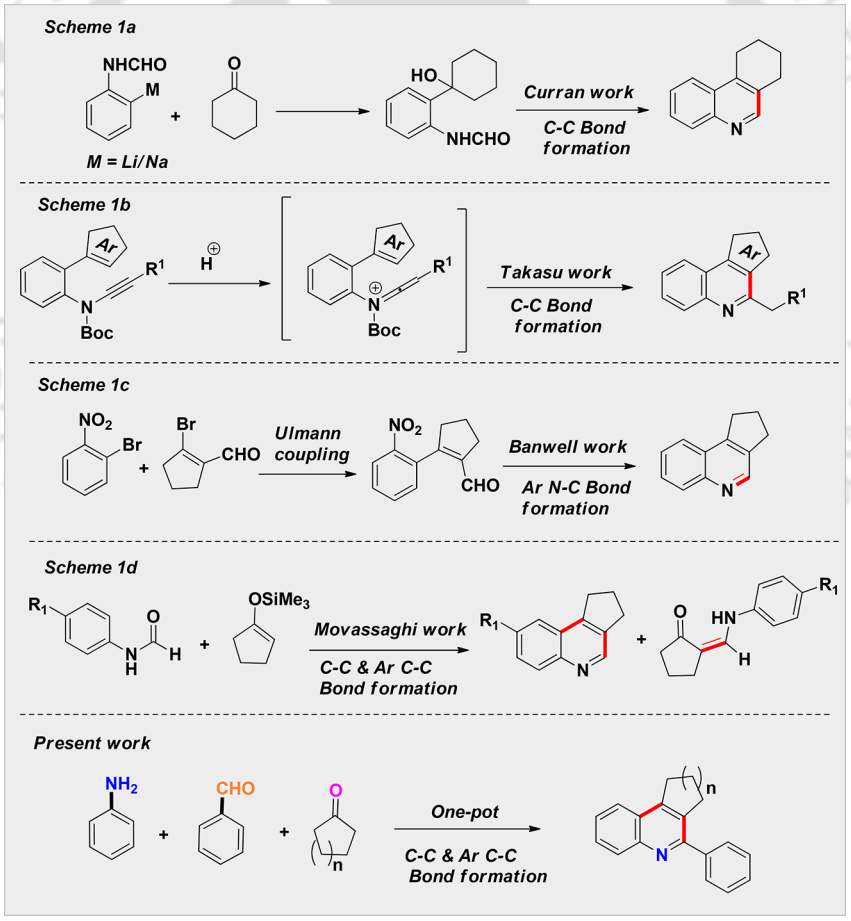


Figure 2. Various approaches of substituted quinoline synthesis with the present work.

Scheme 1. Main Strategies of Fused Quinoline Synthesis with the Present Work



formation of a new *C*−*N* bond[18] (Figure 2, 1c), *N*−*C* bond[19] (Figure 2, 1d), and new *C*−*C* bond[20a] through cross-dehydrogenative coupling,[20b−d] dual oxidative coupling,[20e] and oxidative tandem reactions.[20f] The formation of a new *C*−*C* or *C*−*N*/*N*−*C* bond is an interesting and challenging one for the synthesis of heterocyclic compounds. Herein, we have focused on the synthesis of fused quinoline derivatives through the MCR strategy.

Earlier, Currian et al. developed fused quinoline through formation of a new C−C bond by involving cyclization of in situ generated *o*-vinyl anilides (Scheme 1a).[21a] Takasu et al. also explored quinoline through *C*−*C* bond formation from arene-ynamide cyclization via a highly reactive keteniminium

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intermediate (Scheme 1b).[21b] Banwell and co-workers have developed a fused quinoline involving a new *N*−*C* bond through reductive cyclization of *β*-nitroaryl-enal (Scheme 1c).[21c] The Movassaghi group synthesized fused quinoline by condensation of amide with trimethylsilyl enol ether (Scheme 1d).[21d] Wang[22a] et al. synthesized benzo[*f*]quinoline derivatives using MCRs having a drawback; they were unable to synthesize the quinoline and benzo[*h*]quinoline from aniline and 1-naphthylamine because of low reactivity of the substrate in the presence of iodine catalyst. Apart from these, Kozlov[22b] obtained a 1,2,3,4-tetrahydrobenzo[*a*]phenanthridine derivative along with byproduct benzo[*a*]acridines through reaction of aldehyde with initially formed enamine from 2-naphthylamine and cyclohexanone. More recently, Stryker[22c] and co-workers developed the synthesis of benzo/naphthoquinoline containing steroidal biomarkers[22d,e] through condensation reaction.

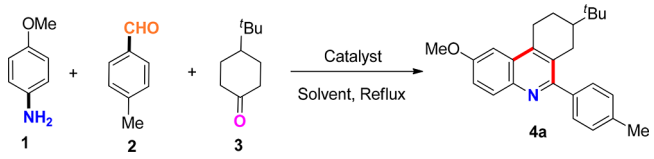
Many of these reported methods suffer from drawbacks such as multistep[23a,b] process, difficulty in isolation procedures, harsh reaction[23c] conditions, unsatisfactory yields, prolonged reaction time, complex starting materials, and also less substrate scope. In this context, the development of new procedures for the synthesis of quinoline derivatives with structural diversity involving readily available starting materials is a challenging effort to the modern synthetic organic chemists. Thus, we have focused on the development of a simple and an efficient method for the synthesis of fused quinoline and benzoquinoline derivatives through intermolecular cyclization of arylamines, aromatic aldehydes, and cyclic ketones in the presence 10 mol % CSA as shown in Scheme 1.

In general, quinolines preferentially undergo electrophilic substitution[24a] at the carbocyclic ring rather than the heterocyclic ring because the sp^2-hybridized nitrogen atom decreases the reactivity by interacting with electrophiles. Nucleophilic substitution occurs in the presence of a strong nucleophile; hence, it is prerequisite to synthesize substitution on a heterocyclic ring rather than a carbocyclic ring. We have focused on synthesizing substituted quinolines by employing a protic acid, camphorsulfonic acid, which is a strong sulfur containing protic acid[24b−e] having broad scope in asymmetric synthesis, cyclization reactions, and monoalkylation of anilines, which promoted us to employ this catalyst for the synthesis of fused quinoline and benzoquinoline derivatives.

RESULTS AND DISCUSSION

We initially, investigated on optimization study for the synthesis of fused quinoline using *p*-anisidine **1** (1.0 mmol), *p*-tolualdehyde **2** (1.0 mmol), and 4-(*tert*-butyl)cyclohexanone **3** (1.0 mmol) as model substrate under reflux condition, and the results are summarized in Table 1. Primarily, carrying out the reaction in the absence of catalyst proved futile (Table 1, entry 1). Next, the reaction was tested with various Lewis acid catalysts. Screening the reaction with $Yb(OTf)_3$ (Table 1, entry 2) in CH_3CN resulted in isolation of the desired product **4a** in 54% yield. The product **4a** was confirmed through IR, ^1H, ^{13}C NMR, and HRMS. The other Lewis acids $Cu(OTf)_2$, $Zn(OTf)_2$, $In(OTf)_3$, AgOTf, $Bi(OTf)_3$, and $FeCl_3$ gave unsatisfactory yields (Table 1, entries 3−8), whereas employing iodine as a catalyst resulted in 54% and 48% yields of product **4a** in THF and CH_3CN, respectively (Table 1, entries 9 and 10). Then, we observed with the protic acid catalysts like AcOH, TfOH, and L-proline that the reactions failed to obtain the desired product (Table 1, entries 11−13), but PTSA resulted with a satisfactory yield (Table 1, entry 14). Further for

Table 1. Optimization of Reaction Conditions[a]



entry	catalyst	mol %	solvent	time (h)	yield **4a** (%)[b]
1	no catalyst		CH_3CN	24.0	NR
2	$Yb(OTf)_3$	10	CH_3CN	3.0	54
3	$Cu(OTf)_2$	10	CH_3CN	6.0	42
4	$Zn(OTf)_2$	10	CH_3CN	2.5	64
5	$In(OTf)_3$	10	CH_3CN	2.5	60
6	AgOTf	10	CH_3CN	3.0	62
7	$Bi(OTf)_3$	10	CH_3CN	2.5	36
8	$FeCl_3$	10	CH_3CN	12.0	30
9	iodine	10	THF	4.0	54
10	iodine	10	CH_3CN	4.0	48
11	AcOH	1 equiv		3.0	NR
12	TfOH	10	CH_3CN	24.0	NR
13	L-proline	10	CH_3CN	24.0	NR
14	*P*-TSA	10	CH_3CN	6.0	68
15	**(±)-CSA**	**10**	**CH_3CN**	**1.5**	**78**
16	(±)-CSA	20	CH_3CN	1.5	78
17	(±)-CSA	05	CH_3CN	2.0	75
18	(±)-CSA	10	EtOH	2.0	72
19	(±)-CSA	10	MeOH	2.0	68
20	(±)-CSA	10	DMSO	24.0	20
21	(±)-CSA	10	DCE	12.0	35
22	(±)-CSA	10	DMF	24.0	NR
23	(±)-CSA	10	THF	12.0	NR
24	(±)-CSA	10	H_2O	12.0	NR
25	(±)-CSA	10	toluene	8.0	NR

[a]All the reactions were performed using *p*-anisidine (1.0 mmol), *p*-tolualdehyde (1.0 mmol), and 4-(*tert*-butyl)cyclohexanone (1.0 mmol). [b]Isolated yields.

inferior results, the same set of reaction was executed with 10 mol % CSA and the desired product **4a** was isolated in 78% yield (Table 1, entry 15).

In order to obtain better results, the reaction was also scrutinized with 20 mol % and 5 mol % CSA, but the increment in yield was not observed (Table 1, entries 16 and 17). However, the other solvents such as EtOH, MeOH, DMSO, and DCE gave lower yields (Table 1, entries 18−21), whereas DMF, THF, H_2O, and toluene failed to give the desired product **4a** (Table 1, entries 22−25). Thus, it was noted that 10 mol % CSA in CH_3CN under reflux condition are optimized conditions for our present protocol in terms of reaction time and yield.

With the standard optimization reaction conditions, the scope of the reaction was investigated with 4-(*tert*-butyl)-cyclohexanone, aromatic aldehydes (4-Me and 4-OMe), and various anilines having *para* substituents on the aromatic ring such as −Me, −Et, −Cl, −Br, and −OMe which gave the products **4b−h** in 66−76% yield (Table 2). The aniline derivatives such as 4-NO_2, 2-NO_2, 2-I, and 2,4-Me failed to produce the desired product which might be due to the strong withdrawing nature and steric crowding at the ortho position.

On the other hand, the reaction of *m*-chloroaniline, *p*-tolualdehyde, and different cyclic ketones like cyclopentanone and cycloheptanone led to the isolation of products **4i−j** in 74−82% yield. Since the formation of other tautomer was not

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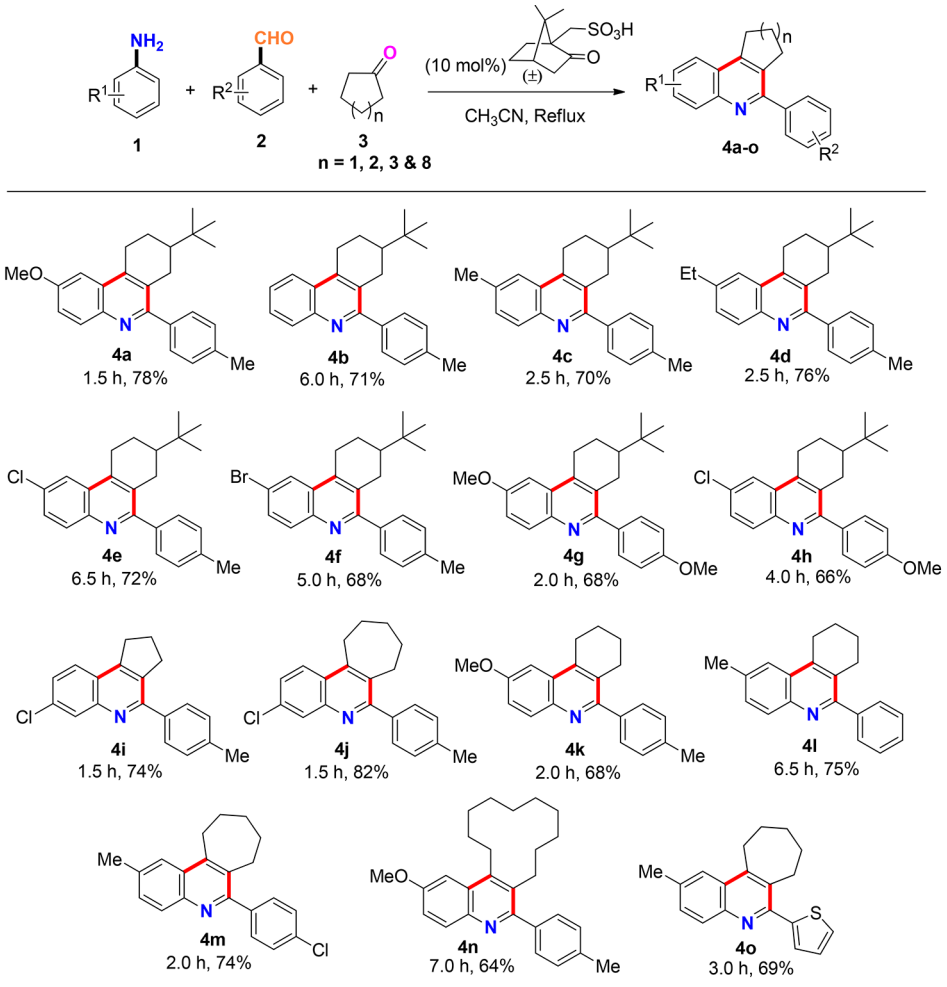
Table 2. Substrate Scope of Aniline[a,b]



[a]The reactions were carried out using anilines (1.0 mmol), aldehydes (1.0 mmol), and cyclic ketones (1.0 mmol) in CH_3CN. [b]Isolated yields.

observed in *meta*-substituted aniline due to steric hindrance on the ortho position, it is to be considered as a regiospecfic reaction. Next, the reaction was extended with various other cyclic ketones, namely, cyclohexanone, cycloheptanone, and cyclododecanone; all the reactions proceeded smoothly to produce the products **4k−n**. In addition, the heterocyclic aldehyde, thiophene-2-aldehyde, on reaction with *p*-toluidine and cycloheptanone afforded the product **4o** in 69% yield.

All the products were characterized by recording IR, ^{1}H, and ^{13}C NMR spectra and HRMS. The structure of the compound **4a** was further confirmed by single-crystal X-ray crystallographic data (see the Supporting Information).

Inspired by the above transformations, we have further explored the generality of the reaction with 1-naphthylamine **5** instead of anilines, which produced fused benzo[*h*]quinoline derivatives, and the results are summarized in Table 3. When the reaction was carried out with 1-naphthylamine **5** (1.0 mmol), *p*-tolualdehyde **2** (1.0 mmol), and 4-(*tert*-butyl)-cyclohexanone **3** (1.0 mmol) under similar reaction conditions, the product **6a** was obtained in 94% yield without any column chromatographic separation. Substituted aromatic aldehydes with electron-donating and electron-withdrawing groups such as 4-OMe, 4-OH, 3-OH, 3,4,5-OMe, 4-Cl, 4-Br, 4-NO_2, and 3-Br underwent reaction with 4-(*tert*-butyl)cyclohexanone to generate the products **6b−i** in 77−95% yields.

The reaction was also extended with various substituted benzaldehydes and cyclic ketones such as cyclohexanone, cycloheptanone, cyclooctanone, and cyclododecanone, which led to the formation of desired products **6j−m** in 67−91% yields. The reaction with 2-naphthaldehyde and cycloheptanone furnished the product **6n** in 76% yield, whereas heteroaromatic aldehydes, thiophene-2-aldehyde and pyridine-2-carbaldehyde, on reaction with cyclopentanone gave the products **6o** and **6p** in 85% and 78% yields, while 2-furfural and thiophene-2-aldehyde on reaction with cycloheptanone delivered the products **6q** and **6r** in 72% and 84% yields, respectively.

In addition, we have applied our present methodology for the synthesis of 3-methoxy-14-(3,4,5-trimethoxyphenyl)-5,6-dihydrodibenzo[*c*,*i*]phenanthridine (**8**) by employing 1-naphthylamine (**5**), 3,4,5-trimethoxybenzaldehyde (**2h**), and 6-methoxytetralone (**7**) in the presence of 10 mol % CSA under similar reaction conditions as shown in Scheme 2.

The reactivity of another *α*,*β*-unsaturated cyclic ketone was investigated by performing the reaction with 1-naphthylamine **5**, *p*-tolualdehyde **2a**, and 4,4-dimethyl-2-cyclohexen-1-one **9** in the presence of 10 mol % CSA under reflux condition to give 8,8-dimethyl-6-(*p*-tolyl)-7,8-dihydrobenzo[*c*]phenanthridine **10** in 82% yield as shown in Scheme 3.

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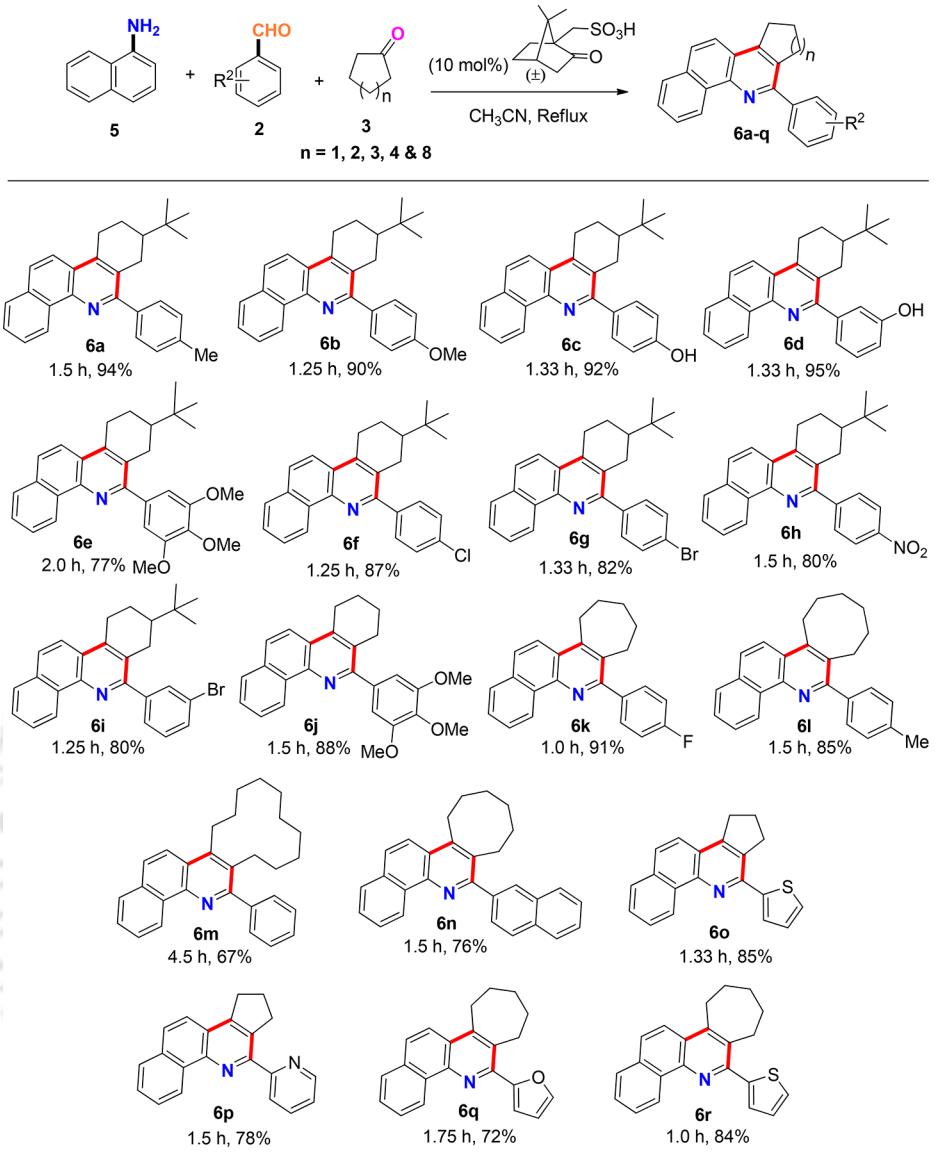
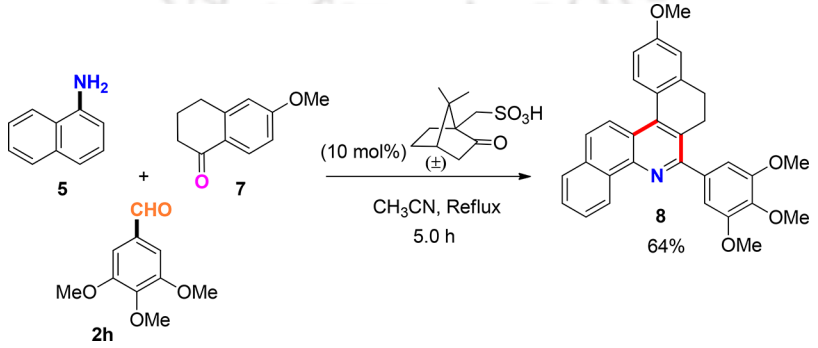
Table 3. Substrate Scope of 1-Naphthylamine[a,b]



[a]The reactions were carried out using aldehydes (1.0 mmol), cyclic ketones (1.0 mmol), and 1-naphthylamine (1.0 mmol) in CH_3CN. [b]Isolated yields.

Scheme 2. Reaction of 1-Naphthylamine with 3,4,5-Trimethoxybenzaldehyde and 6-Methoxytetralone



The present protocol was further explored for the synthesis of fused benzoquinoline derivatives using 2-naphthylamine (**11**), with different substituted aromatic aldehydes (**2**) and cyclic ketones (**3**) in the presence of a catalytic amount of CSA under identical reaction conditions to offer the corresponding products **12a**–**g** with 72–80% yields as depicted in Table 4.

Next, we put our forward effort for the synthesis of steroid substituted benzo[*f*]quinoline derivatives from 16-dehydro-

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Scheme 3. Reaction of 1-Naphthylamine, *p*-Tolualdehyde, and 4,4-Dimethylcyclohexenone

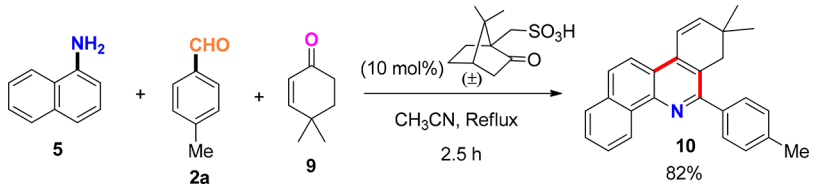
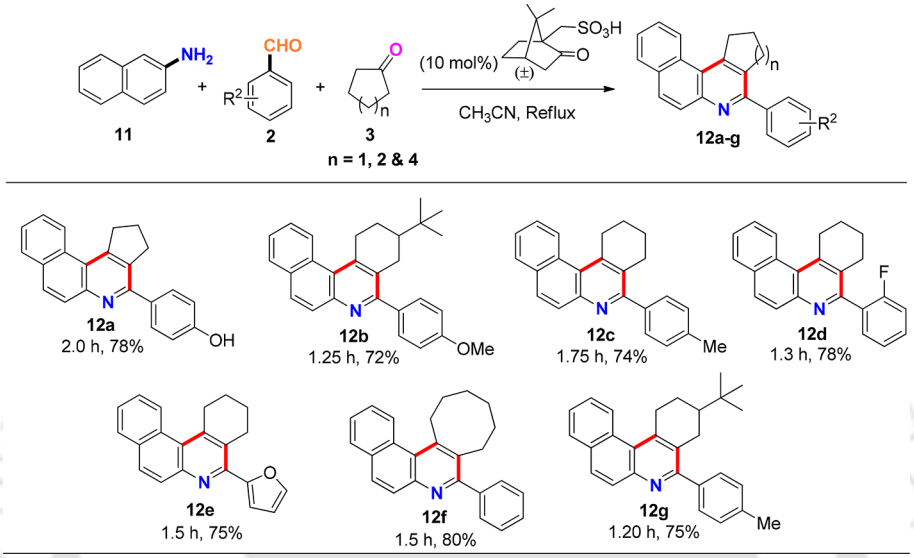
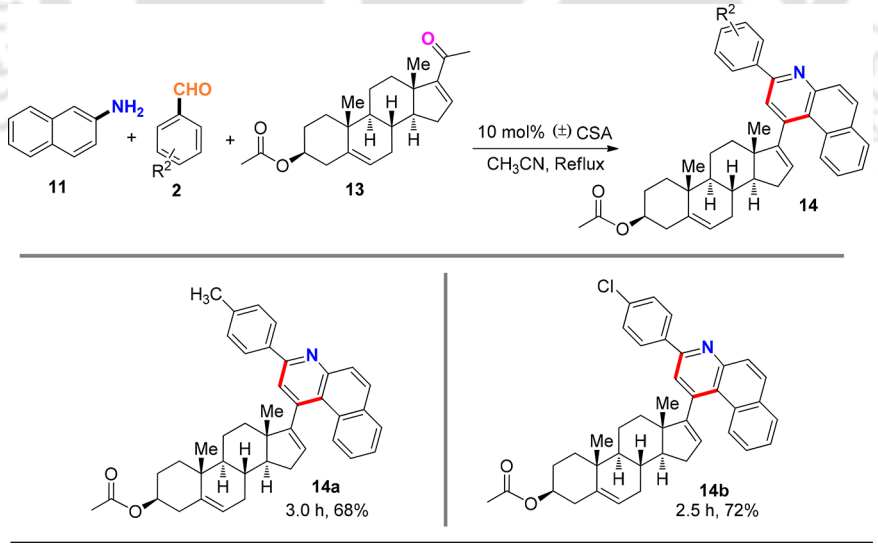


Table 4. Substrate Scope of 2-Naphthylamine[a,b]



[a]The reactions were performed using aldehydes (1.0 mmol), cyclic ketones (1.0 mmol), and 2-naphthylamine (1.0 mmol) in CH_3CN. [b]Isolated yields.

Table 5. Reaction of 16-Dehydro-pregnenolone Acetate with Aldehyde and 2-Naphthylamine[a,b]



[a]The reactions were performed using aldehyde (1.0 mmol), 16-dehydro-pregnenolone acetate (1.0 mmol), and 2-naphthylamine (1.0 mmol) in CH_3CN. [b]Isolated yields.

pregnenolone acetate (**13**), 2-naphthylamine (**11**), and 4-Me/4-Cl benzaldehydes using 10 mol % CSA under identical reaction conditions, which offered the desired products **14a** and **14b** in 68% and 72% yields as shown in Table 5.

Next, our protocol was well applied for the synthesis of fused bis-benzoquinoline derivatives by using 1-naphthylamine/2-naphthylamine (1.0 mmol), terephthalaldehyde (0.5 mmol), and 4-(*tert*-butyl)cyclohexanone (1.0 mmol) in the presence of 10 mol % CSA catalyst under similar reaction conditions, and the successful results are shown in Scheme 4 along with their reaction time and yields. Unfortunately, *p*-anisidine failed to give the desired product under identical reaction conditions.

Finally, 2-aminoanthracene **16** (1.0 mmol) on reaction with 2-naphthaldehyde **2m** (1.0 mmol) and 4-(*tert*-butyl)cyclohex-

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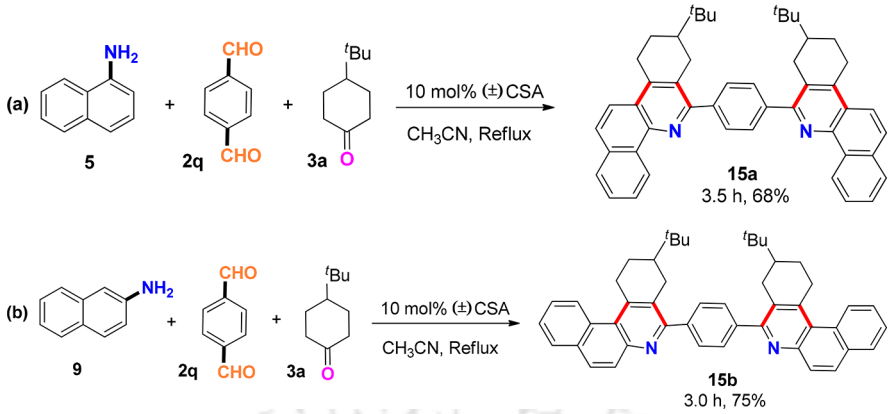
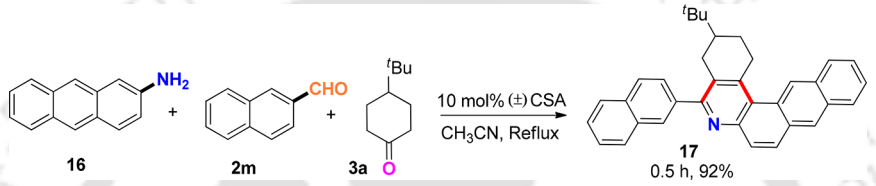
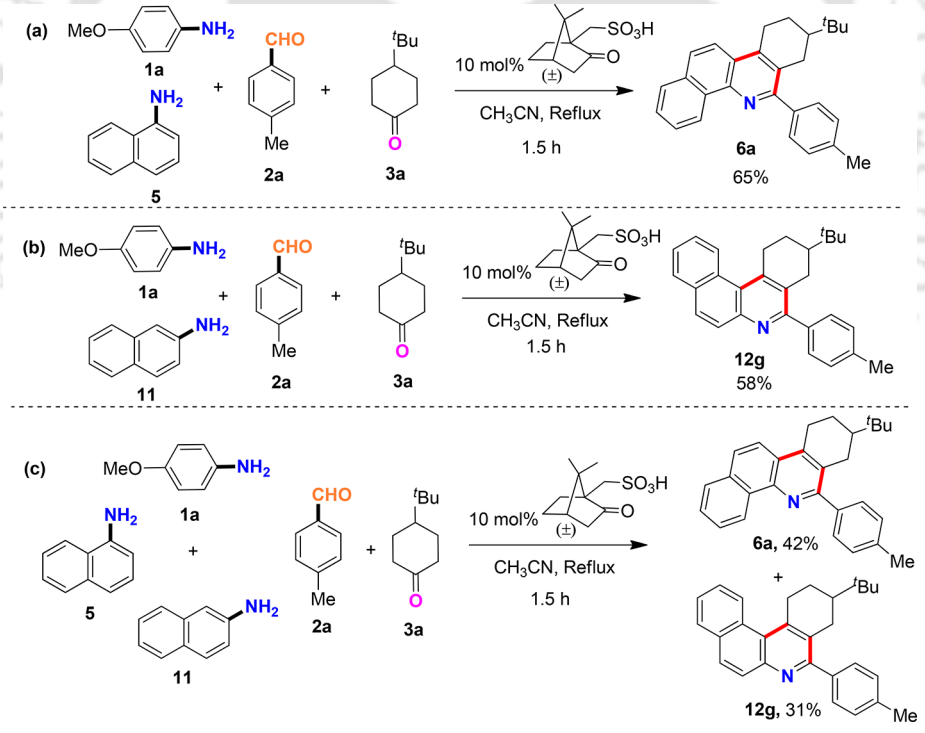
Scheme 4. Reaction Scope of Terephthalaldehyde



Scheme 5. Reaction Scope of 2-Aminoanthracene



Scheme 6. The Reactivity of Arylamines



anone **3a** (1.0 mmol) in the presence of 10 mol % CSA under reflux condition gave the product 3-(*tert*-butyl)-5-(naphthalen-2-yl)-1,2,3,4-tetrahydronaphtho[2,3-*a*]phenanthridine **17** as shown in Scheme 5. All the synthesized products were characterized by IR, ^{1}H, and ^{13}C NMR spectra and HRMS. In addition, the structure of the compounds **6r**, **8**, **12e**, and **14b** were further confirmed by single-crystal X-ray crystallographic data (see the Supporting Information).

To understand the reactivity of arylamines, we carried out three sets of reactions. Initially, *p*-anisidine (1.0 mmol), 1-naphthylamine (1.0 mmol), *p*-tolualdehyde (1.0 mmol), and 4-(*tert*-butyl)cyclohexanone (1.0 mmol) under the same reaction conditions produced single product **6a**. Next, the reaction of *p*-anisidine (1.0 mmol), 2-naphthylamine (1.0 mmol), *p*-tolualdehyde (1.0 mmol), and 4-(*tert*-butyl)cyclohexanone (1.0 mmol) gave only product **12g**.

Finally, a mixture of *p*-anisidine (1.0 mmol), 1-naphthylamine (1.0 mmol), 2-naphthylamine (1.0 mmol), *p*-tolualdehyde (1.0 mmol), and 4-(*tert*-butyl)cyclohexanone (1.0 mmol) afforded products **6a** and **12g**. The product **4a** was not

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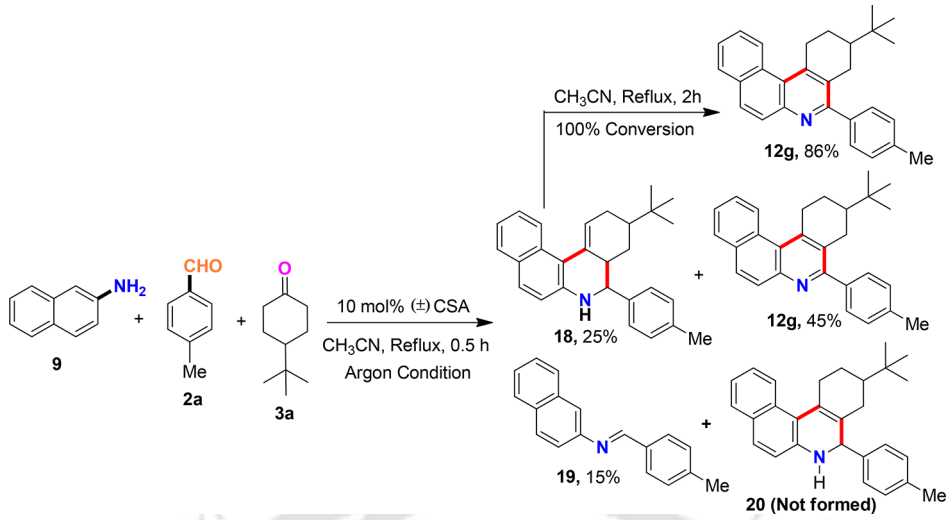
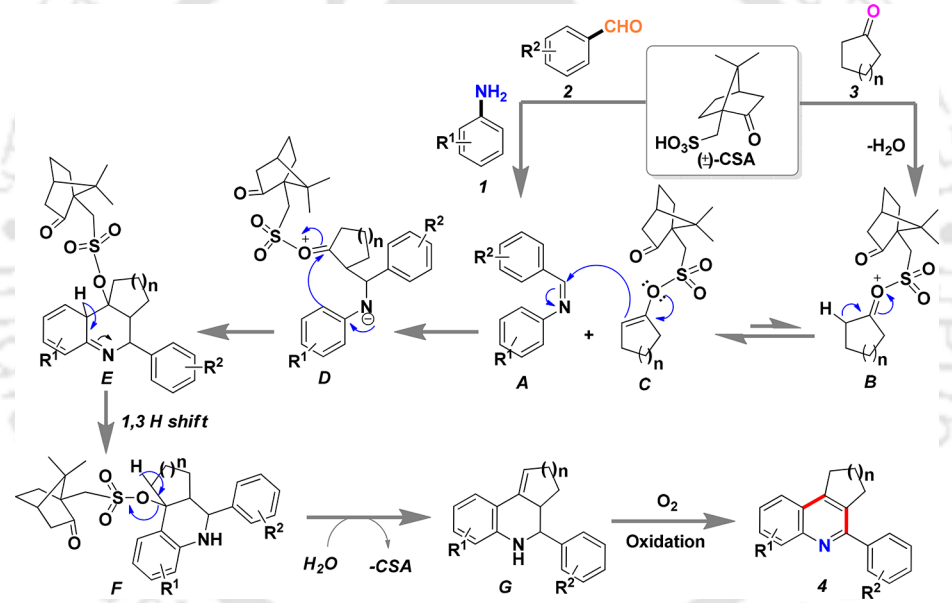
Scheme 7. Experiment for Mechanistic Pathway



Scheme 8. Proposed Reaction Mechanism Pathway



observed, due to poor reactivity of *p*-anisidine in the presence of 1-naphthylamine and 2-naphthylamine, and the results are represented in Scheme 6.

To study the mechanism, we performed a one-pot three-component reaction using 2-naphthylamine, *p*-tolualdehyde, and 4-(*tert*-butyl)cyclohexanone in the presence of 10 mol % CSA under reflux condition in an argon atmosphere as shown in Scheme 7. As expected, we have observed the formation of **19** in 15% yield, which readily reacted with 4-(*tert*-butyl)-cyclohexanone **3a** to give the corresponding products **18** and **12g** in 25% and 45% yield, respectively, after 0.5 h. In addition, the product **18** was further refluxed with 2 mL of CH_3CN in an open atmosphere without any catalyst, which resulted in aromatized product **12g** with 100% conversion in 86% yield in 2 h, whereas, at room temperature and the reaction time prolonged up to 24 h, compound **12g** was produced with 100% conversion of 84% yield.

From the literature,[22a] the intermediate **20** is expected to be formed, but we have not observed such dihydroquinoline. All the compounds are isolated and characterized individually by IR, ^1H, and ^{13}C NMR spectra and HRMS. In addition, product **18** was confirmed by single-crystal XRD (see the Supporting Information).

The plausible mechanism for the formation of fused quinoline is described as shown in Scheme 8. Initially, the arylamine **1** reacts with aldehyde **2** to form the imine **A** and the cyclic ketone **3** to form an active species **B**, which tautomerized to the most stable enol form **C** in the presence of camphorsulfonic acid. The generated imine **A** further reacted with **C** to form Michael-type addition product **D**, which subsequently undergoes an intramolecular cyclization to give dihydroquinoline **G**, which undergoes oxidative aromatization to give the desired product **4**.

CONCLUSION

In summary, we have developed a simple and an efficient method for the synthesis of fused quinoline and benzoquinoline derivatives from readily available starting materials arylamine, aromatic aldehyde, and cyclic ketone through a one-pot three-

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component reaction using camphorsulfonic acid as a catalyst. The protocol offers several advantages which include commercially available cheap catalyst, less reaction time, mild reaction conditions, simple isolation procedure, a wide range of substrate scope, and eco-friendly with high atom economy in one pot with two new *C*−*C* bond formations. Along with these, we have developed the utility of pregnenolone acetate and terephthalaldehyde for the synthesis of steroid substituted benzo[*f*]quinoline and bis-benzo[*f*]quinoline, respectively. To the best of our knowledge, these quinoline and benzoquinoline derivatives were reported for the first time in the literature using camphorsulfonic acid as a catalyst.

EXPERIMENTAL SECTION

General Information and Methods. Melting points were determined on a melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on 400 and 600 MHz and 100 and 150 MHz NMR spectrometers. TMS was used as internal reference; chemical shifts (δ scale) are reported in parts per million (ppm). ^{1}H NMR spectra are reported in the order: multiplicity, coupling constant (J value) in hertz (Hz), and no. of protons; signals were characterized as s (singlet), d (doublet), t (triplet), m (multiplet), and bs (broad). IR spectra were recorded on an IR spectrophotometer. HRMS spectra were recorded using ESI and APCI (TOF) mode. The crystal structures were determined using a single crystal XRD diffractometer.

General Procedure for Synthesis of Cycloalkyl Fused Quinolines 4. Into a dry 25 mL round-bottom flask, a mixture aniline **1** (1.0 mmol), aromatic aldehyde **2** (1.0 mmol), and cyclic ketone **3** was taken in 5 mL of acetonitrile. Camphorsulfonic acid (0.023 g, 0.10 mmol) was added into it and stirring under reflux condition. The progress of the reaction was monitored by TLC; after completion of the reaction, the solvent was removed under reduced pressure and it was extracted with DCM (2 × 25 mL). The organic extract was dried over sodium sulfate and concentrated under reduced pressure. Finally, the residue was purified through silica gel (60−120 mesh) column chromatography with petroleum ether/ethyl acetate (9.5:0.5, v/v) to obtain the pure product **4**.

General Procedure for Synthesis of Cycloalkyl Fused Benzoquinolines 6, 8, 10, and 12. To a mixture 1-naphthylamine (1.0 mmol), aromatic aldehyde **2** (1.0 mmol), and cyclic ketone **3**, camphorsulfonic acid (0.023 g, 0.10 mmol) in 5 mL of acetonitrile was added and allowed to stir at reflux condition. After completion of the reaction, indicated by TLC, the reaction mixture was allowed to cool at room temperature for complete precipitation. Then, the solid precipitate was filtered off through a Büchner funnel, washed with acetonitrile, and dried under reduced pressure to obtain the pure products **6**. The similar reaction procedures were followed for the synthesis of products **8**, **10**, and **12**.

General Procedure for Synthesis of Steroid Substituted Benzo[*f*]quinoline 14. Into a 25 mL round-bottom flask, a mixture of aromatic aldehyde **2**, 2-naphthylamine (**11**), and 16-dehydropregnenolone acetate (**13**) were taken in 5 mL of acetonitrile. Then, camphorsulfonic acid (0.023 g, 0.10 mmol) was added into the above reaction mixture and refluxed for 2.5−3.0 h until the completion of the starting materials, indicated by TLC. The reaction mixture was allowed to cool at room temperature. The solvent was removed under reduced pressure and extracted with DCM (2 × 25 mL), dried over sodium sulfate, and concentrated under reduced pressure. Then, the crude residue was purified through silica gel (60−120) column chromatography with petroleum ether−ethyl acetate (9.5:0.5, v/v) to get the pure product **14**.

General Procedure for Synthesis of Cycloalkyl Fused Bis-benzoquinolines 15 and 3-(*tert*-Butyl)-5-(naphthalen-2-yl)-1,2,3,4-tetrahydronaphtho[2,3-*a*]phenanthridine 17. To a mixture of naphthylamine (1.0 mmol), terephthalaldehyde **2q** (0.5 mmol), and 4-(*tert*-butyl)cyclohexanone **3a** (1.0 mmol) in 3 mL of acetonitrile, camphorsulfonic acid (0.023 g, 0.10 mmol) was added and allowed to stir at reflux for 1.0−4.5 h. After completion of the reaction, indicated by TLC, the reaction mixture was allowed to cool at room temperature to obtain the solid product. Then, the pure solid products **15a−b** were obtained after washing with acetonitrile and dried under reduced pressure. The NMR of products was analyzed by disolving in 2−3 drops of CF_3COOH in $CDCl_3$. The similar reaction procedure was followed for the synthesis of 3-(*tert*-butyl)-5-(naphthalen-2-yl)-1,2,3,4-tetrahydronaphtho[2,3-*a*]phenanthridine **17**.

*8-(tert-Butyl)-2-methoxy-6-(p-tolyl)-7,8,9,10-tetrahydrophenanthridine (**4a**).* Yield 78% (280 mg), white solid, mp 180−181 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.01 (d, J = 8.4 Hz, 1H), 7.42 (d, J = 7.8 Hz, 2H), 7.31−7.29(m, 1H), 7.27−7.26 (m, 2H), 7.18 (m, 1H), 3.95 (s, 3H), 3.76 (dd, J = 17.4, 4.8 Hz, 1H), 2.99 (m, 1H), 2.74 (d, J = 16.8 Hz, 1H), 2.53 (t, J = 12.6 Hz, 1H), 2.42 (s, 3H), 2.20−2.19 (m, 1H), 1.49−1.44 (m, 1H), 1.40−1.36 (m, 1H), 0.90 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 158.7, 157.8, 138.4, 137.7, 131.6, 129.4, 129.1, 128.9, 127.7, 120.3, 101.4, 55.7, 44.7, 32.6, 30.5, 27.6, 27.5, 23.9, 21.5; IR (KBr)ν_{max}: 3051, 2957, 2867, 1585, 1497, 1068, 1031, 957 cm^{-1}; HRMS (ESI) Calcd for $C_{25}H_{30}NO$ 360.2322 (M + H$^+$); Found 360.2323.

*8-(tert-Butyl)-6-(p-tolyl)-7,8,9,10-tetrahydrophenanthridine (**4b**).* Yield 71% (233 mg), brown solid, mp 145−146 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.20 (s, 1H), 7.98 (d, J = 8.4 Hz, 1H), 7.66 (t, J = 7.2 Hz, 1H), 7.55 (t, J = 7.2 Hz, 1H), 7.45 (d, J = 7.8 Hz, 2H), 7.29 (d, J = 7.2 Hz, 2H), 3.48 (dd, J = 18.0, 4.2 Hz, 1H), 3.07 (m, 1H), 2.76 (d, J = 16.2 Hz, 1H), 2.55 (t, J = 12.0 Hz, 1H), 2.43 (s, 3H), 2.23−2.20 (m, 1H), 1.51−1.45 (m, 1H), 1.42−1.37 (m, 1H), 0.91 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 159.5, 158.3, 157.7, 141.8, 140.7, 133.9, 131.6, 130.3, 129.4, 127.6, 120.2, 113.8, 101.3, 55.7, 44.8, 32.5, 30.6, 27.6, 27.5, 23.9; IR (KBr)ν_{max}: 3059, 3029, 2984, 2867, 1683, 1585, 1559, 1110, 1040, 1016 cm^{-1}; HRMS (APCI) Calcd for $C_{24}H_{28}N$ 330.2216 (M + H$^+$); Found 330.2205.

*8-(tert-Butyl)-2-methyl-6-(p-tolyl)-7,8,9,10-tetrahydrophenanthridine (**4c**).* Yield 70% (240 mg), white solid, mp 182−183 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.72 (s, 1H), 7.48 (d, J = 8.4 Hz, 1H), 7.45 (d, J = 7.8 Hz, 2H), 7.27 (d, J = 7.8 Hz, 2H), 3.44 (dd, J = 18.0, 4.8 Hz, 1H), 3.02 (m, 1H), 2.74 (d, J = 16.2 Hz, 1H), 2.56 (s, 3H), 2.52 (d, J = 16.2 Hz, 1H), 2.42 (s, 3H), 2.21−2.18 (m, 1H), 1.47−1.42 (m, 1H), 1.39−1.35 (m, 1H), 0.90 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 159.8, 143.6, 142.2, 138.0, 137.6, 136.2, 130.8, 129.3, 129.1, 128.9, 126.7, 121.8, 44.7, 32.5, 32.4, 30.4, 27.4, 23.8, 22.2, 21.5; IR (KBr)ν_{max}: 3043, 3016, 2941, 2864, 1646, 1585, 1471, 1102, 1010, 922 cm^{-1}; HRMS (APCI) Calcd for $C_{25}H_{30}N$ 344.2373 (M + H$^+$); Found 344.2361.

*8-(tert-Butyl)-2-ethyl-6-(p-tolyl)-7,8,9,10-tetrahydrophenanthridine (**4d**).* Yield 76% (271 mg), white solid, mp 135−136 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.08 (d, J = 7.8 Hz, 1H), 7.73 (s, 1H), 7.53−7.51 (m, 1H), 7.44 (d, J = 7.8 Hz, 2H), 7.27 (d, J = 7.8 Hz, 2H), 3.45 (dd, J = 17.4, 4.8 Hz, 1H), 3.07−3.03 (m, 1H), 2.85 (m, 2H), 2.75 (d, J = 16.8 Hz, 1H), 2.54 (t, J = 12.0 Hz, 1H), 2.42 (s, 3H), 2.19 (m, 1H), 1.49−1.44 (m, 1H), 1.44−1.39 (m, 1H), 1.35 (t, J = 7.8 Hz, 3H), 0.91 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 160.0, 144.1, 142.4, 142.1, 138.1, 137.9, 129.7, 129.6, 129.1, 129.0, 128.9, 126.8, 120.5, 44.7, 32.6, 32.5, 30.4, 29.5, 27.4, 23.8, 21.5, 15.9; IR (KBr)ν_{max}: 3048, 3024, 2964, 2867, 1612, 1585, 1112, 1058, 1016, 932 cm^{-1}; HRMS (ESI) Calcd for $C_{26}H_{32}N$ 358.2530 (M + H$^+$); Found 358.2540.

*8-(tert-Butyl)-2-chloro-6-(p-tolyl)-7,8,9,10-tetrahydrophenanthridine (**4e**).* Yield 72% (261 mg), white solid, mp 230−231 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.01 (d, J = 9.0 Hz, 1H), 7.92 (d, J = 1.8 Hz, 1H), 7.56 (dd, J = 9.0, 2.4 Hz, 1H), 7.42 (d, J = 7.8 Hz, 2H), 7.27 (d, J = 7.8 Hz, 2H), 3.37 (dd, J = 18.0, 5.4 Hz, 1H), 3.02−2.96 (m, 1H), 2.74 (d, J = 16.8 Hz, 1H), 2.54 (t, J = 16.8 Hz, 1H), 2.42 (s, 3H), 2.21−2.18 (m, 1H), 1.47−1.42 (m, 1H), 1.39−1.35 (m, 1H), 0.90 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 161.4, 144.2, 141.4, 138.2, 138.0, 132.0, 131.7, 130.7, 130.2, 129.2, 128.8, 127.6, 121.9, 44.6, 32.5, 30.5, 27.4, 27.3, 23.7, 21.5; IR (KBr)ν_{max}: 3042, 2948, 2922, 2863, 1586, 1062, 1011, 942 cm^{-1}; HRMS (ESI) Calcd for $C_{24}H_{27}ClN$ 364.1827 (M + H$^+$); Found 364.1835.

*2-Bromo-8-(tert-butyl)-6-(p-tolyl)-7,8,9,10-tetrahydrophenanthridine (**4f**).* Yield 68% (276 mg), white solid, mp 237−238 °C; ^{1}H NMR

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(600 MHz, $CDCl_3$): δ 8.25 (s, 1H), 8.14 (s, 1H), 7.74 (d, J = 8.4 Hz, 1H), 7.46 (d, J = 7.8 Hz, 2H), 7.30 (d, J = 7.2 Hz, 2H), 3.41 (dd, J = 18.0, 4.2 Hz, 1H), 3.03 (m, 1H), 2.75 (d, J = 16.8 Hz, 1H), 2.56 (t, J = 12.6 Hz, 1H), 2.43 (s, 3H), 2.23−2.20 (m, 1H), 1.51−1.44 (m, 1H), 1.38 (t, J = 10.2 Hz, 1H), 0.90 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 161.0, 143.5, 142.4, 138.6, 136.8, 132.2, 131.2, 130.4, 129.2, 128.9, 128.1, 125.3, 120.7, 44.5, 32.5, 30.4, 27.5, 27.4, 23.6, 21.6; IR (KBr)ν_{max}: 3043, 2947, 2896, 2864, 1584, 1182, 1072, 1016, 976 cm^{-1}; HRMS (ESI) Calcd for $C_{24}H_{27}BrN$ 408.1322 (M + H$^+$); Found 408.1336.

*8-(tert-Butyl)-2-methoxy-6-(4-methoxyphenyl)-7,8,9,10-tetrahydrophenanthridine (**4g**).* Yield 68% (255 mg), brown solid, mp 145−146 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, J = 9.2 Hz, 1H), 7.49 (d, J = 8.8 Hz, 2H), 7.29 (dd, J = 9.2, 2.8 Hz, 1H), 7.17 (d, J = 2.4 Hz, 1H), 6.92 (d, J = 6.0 Hz, 2H), 3.95 (s, 3H), 3.87 (s, 3H), 3.35 (dd, J = 17.6, 5.2 Hz, 1H), 3.03−2.94 (m, 1H), 2.75 (d, J = 16.8 Hz, 1H), 2.50 (t, J = 11.6 Hz, 1H), 2.22−2.04 (m, 1H), 1.51−1.39 (m, 1H), 1.38−1.34 (m, 1H), 0.91 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.5, 158.3, 157.7, 141.8, 140.7, 133.9, 131.6, 130.3, 129.4, 127.6, 120.2, 113.8, 101.3, 55.7, 55.5, 44.8, 32.5, 30.6, 27.6, 27.5, 23.9; IR (KBr)ν_{max}: 3042, 2955, 2867, 2828, 1620, 1581, 1174, 1106, 1034, 958 cm^{-1}; HRMS (APCI) Calcd for $C_{25}H_{30}NO_2$ 376.2271 (M + H$^+$); Found 376.2256.

*8-(tert-Butyl)-2-chloro-6-(4-methoxyphenyl)-7,8,9,10-tetrahydrophenanthridine (**4h**).* Yield 66% (250 mg), white solid, mp 202−203 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.16 (s, 1H), 7.94 (s, 1H), 7.58 (d, J = 9.0 Hz, 1H), 7.52 (d, J = 9.0 Hz, 2H), 7.01 (d, J = 8.4 Hz, 2H), 3.88 (s, 3H), 3.41−3.37(m, 1H), 3.04−2.98 (m, 1H), 2.76 (d, J = 16.8 Hz, 1H), 2.56 (t, J = 12.0 Hz, 1H), 2.23−2.19 (m, 1H), 1.51−1.44 (m, 1H), 1.39−1.35 (m, 1H), 0.90 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.4, 160.2, 143.1, 142.7, 135.4, 132.4, 130.9, 130.6, 130.5, 129.7, 127.6, 122.0, 114.0, 55.9, 44.6, 32.6, 30.6, 27.5, 27.4, 23.6; IR (KBr)ν_{max}: 3005, 2952, 2917, 2864, 1608, 1573, 1558, 1149, 1082, 1035, 950 cm^{-1}; HRMS (ESI) Calcd for $C_{24}H_{27}ClNO$ 380.1776 (M + H$^+$); Found 380.1778.

*7-Chloro-4-(p-tolyl)-2,3-dihydro-1H-cyclopenta[c]quinoline (**4i**).* Yield 74% (216 mg), white solid, mp 127−128 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (d, J = 2.0 Hz, 1H), 7.74 (d, J = 8.4 Hz, 2H), 7.68 (d, J = 8.8 Hz, 1H), 7.41 (dd, J = 6.8, 2.0 Hz, 1H), 7.30 (d, J = 8.4 Hz, 2H), 3.23 (m, 4H), 2.45 (s, 3H), 2.24 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.1, 151.4,147.9, 138.9, 137.5, 135.4, 134.3, 129.2, 128.9, 128.8, 126.9, 125.6, 123.7, 33.9, 31.4, 25.1, 21.5; IR (KBr)ν_{max}: 3025, 2970, 2919, 2849, 1605, 1575, 1559, 1070, 1042, 969 cm^{-1}; HRMS (ESI) Calcd for $C_{19}H_{17}ClN$ 294.1044 (M + H$^+$); Found 294.1050.

*3-Chloro-6-(p-tolyl)-8,9,10,11-tetrahydro-7H-cyclohepta[c]quinoline (**4j**).* Yield 82% (263 mg), white solid, mp 146−147 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, J = 2.4 Hz, 1H), 7.97 (d, J = 9.2 Hz, 1H), 7.41−7.38 (m, 3H), 7.26 (d, J = 8.4 Hz, 2H), 3.24 (t, J = 4.8 Hz, 2H), 2.95 (t, J = 5.6 Hz, 2H), 2.41 (s, 3H), 1.89 (t, J = 6.0 Hz, 2H), 1.73 (t, J = 4.8 Hz, 2H), 1.62 (t, J = 5.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.0, 149.6, 146.9, 138.7, 137.9, 134.7, 134.1, 129.1, 129.0, 128.9, 126.9, 124.7, 124.6, 31.9, 30.8, 28.3, 27.0, 26.1, 21.4; IR (KBr)ν_{max}: 3048, 2978, 2919, 2852, 1637, 1576, 1489, 1069, 1019, 964 cm^{-1}; HRMS (ESI) Calcd for $C_{21}H_{21}ClN$ 322.1357 (M + H$^+$); Found 322.1359.

*2-Methoxy-6-(p-tolyl)-7,8,9,10-tetrahydrophenanthridine (**4k**).* Yield 68% (206 mg), brown solid, mp 135−136 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.00 (d, J = 9.0 Hz, 1H), 7.41 (d, J = 7.8 Hz, 2H), 7.31−7.30 (m, 1H), 7.30−7.29 (m, 1H), 7.26 (d, J = 6.0 Hz, 1H), 7.19 (s, 1H), 3.96 (s, 3H), 3.13 (t, J = 6.0 Hz, 2H), 2.73 (t, J = 6.0 Hz, 2H), 2.42 (s, 3H), 1.98 (t, J = 5.4 Hz, 2H), 1.77 (t, J = 5.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 158.5, 157.8, 141.8, 140.8, 138.5, 137.8, 131.7, 129.1, 128.9, 127.9, 120.3, 101.2, 55.7, 29.0, 26.1, 22.9, 22.5, 21.5; IR (KBr)ν_{max}: 3041, 2933, 2859, 1668, 1655, 1220, 1093, 946 cm^{-1}; HRMS (ESI) Calcd for $C_{21}H_{22}NO$ 304.1696 (M + H$^+$); Found 304.1703.

*2-Methyl-6-phenyl-7,8,9,10-tetrahydrophenanthridine (**4l**).* Yield 75% (204 mg), yellow liquid; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.00 (d, J = 8.4 Hz, 1H), 7.74 (s, 1H), 7.53 (d, J = 7.2 Hz, 2H), 7.49−7.45 (m, 3H), 7.41 (t, J = 7.2 Hz, 1H), 3.18 (t, J = 5.4 Hz, 2H), 2.72 (t, J = 5.4 Hz, 2H), 2.57 (s, 3H), 1.97 (t, J = 4.8 Hz, 2H), 1.79−1.77 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 160.0, 144.4, 141.5, 141.5, 136.1, 130.6, 129.9, 128.9, 128.5, 128.4, 128.1, 127.1, 121.7, 28.9, 25.9, 22.9, 22.5, 22.2; IR (KBr)ν_{max}: 3055, 3025, 2932, 2859, 1733, 1621, 1582, 1095, 1029, 1001, 988 cm^{-1}; HRMS (APCI) Calcd for $C_{20}H_{20}N$ 274.1590 (M + H$^+$); Found 274.1573.

*6-(4-Chlorophenyl)-2-methyl-8,9,10,11-tetrahydro-7H-cyclohepta[c]quinoline (**4m**).* Yield 74% (237 mg), white solid, mp 192−193 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.00 (d, J = 8.4 Hz, 1H), 7.87 (s, 1H), 7.49 (d, J = 9.0 Hz, 1H), 7.46−7.43 (m, 4H), 3.29 (t, J = 4.8 Hz, 2H), 2.92 (t, J = 5.4 Hz, 2H), 2.57 (s, 3H), 1.93−1.90 (m, 2H), 1.77 (m, 2H), 1.63 (t, J = 4.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 157.7, 149.0, 145.1, 140.5, 136.1, 134.1, 133.9, 130.9, 130.6, 130.1, 128.5, 126.3, 122.1, 32.1, 30.8, 28.1, 27.1, 26.2, 22.2; IR (KBr)ν_{max}: 3061, 2991, 2972, 2921, 2851, 1682, 1105, 1090, 1012, 965 cm^{-1}; HRMS (ESI) Calcd for $C_{21}H_{21}ClN$ 322.1357 (M + H$^+$); Found 322.1371.

*2-Methoxy-6-(p-tolyl)-7,8,9,10,11,12,13,14,15,16-decahydrocyclododeca[c]quinoline (**4n**).* Yield 64% (247 mg), brown solid, mp 149−150 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.98 (d, J = 9.0 Hz, 1H), 7.35 (d, J = 8.4 Hz, 2H), 7.30−7.28 (m, 2H), 7.24 (d, J = 7.8 Hz, 2H), 3.96 (s, 3H), 3.16 (t, J = 7.8 Hz, 2H), 2.81 (t, J = 7.8 Hz, 2H), 2.41 (s, 3H), 1.89−1.88 (m, 2H), 1.67−1.64 (m, 4H), 1.53−1.52 (m, 2H), 1.52−1.45 (m, 6H), 1.25−1.24 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 159.4, 157.6, 145.0, 142.2, 139.6, 137.4, 132.4, 131.7, 128.9, 128.6, 128.1, 120.1, 102.9, 55.7, 28.9, 28.6, 28.5, 28.4, 28.0, 27.6, 27.4, 26.9, 22.8, 21.5; IR (KBr)ν_{max}: 3058, 2924, 2851, 1621, 1571, 1034, 968 cm^{-1}; HRMS (ESI) Calcd for $C_{27}H_{34}NO$ 388.2635 (M + H$^+$); Found 388.2654.

*2-Methyl-6-(thiophen-2-yl)-8,9,10,11-tetrahydro-7H-cyclohepta-[c]quinoline (**4o**).* Yield 69% (202 mg), white solid, mp 130−131 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.98 (d, J = 8.4 Hz, 1H), 7.82 (s, 1H), 7.47 (d, J = 9.0 Hz, 1H), 7.43 (d, J = 4.8 Hz, 1H), 7.26 (s, 1H), 7.12 (t, J = 7.8 Hz, 1H), 3.30 (t, J = 4.8 Hz, 2H), 3.18 (t, J = 5.4 Hz, 2H), 2.55 (s, 3H), 1.95−1.94 (m, 2H), 1.78−1.77 (m, 2H), 1.73−1.72 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 151.9, 149.2, 145.3, 144.5, 136.2, 134.4, 130.9, 130.1, 127.6, 127.2, 126.9, 126.2, 122.1, 32.1, 30.7, 28.1, 27.0, 26.4, 22.3; IR (KBr)ν_{max}: 3070, 2995, 2917, 2852, 1637, 1568, 1056, 1019 cm^{-1}; HRMS (APCI) Calcd for $C_{19}H_{20}NS$ 294.1311(M + H$^+$); Found 294.1325.

*8-(tert-Butyl)-6-(p-tolyl)-7,8,9,10-tetrahydrobenzo[c]phenanthridine (**6a**).* Yield 94% (356 mg), white solid, mp 211−212 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.37 (d, J = 6.6 Hz, 1H), 7.91−7.87 (m, 2H), 7.81 (d, J = 9.0 Hz, 1H), 7.64−7.62 (m, 4H), 7.32 (d, J = 7.8 Hz, 2H), 3.56−3.50 (m, 1H), 3.15−3.11 (m, 1H), 2.91−2.88 (m, 1H), 2.69 (t, J = 12.0 Hz, 1H), 2.47 (s, 3H), 2.25−2.22 (m, 1H), 1.57−1.49 (m, 1H), 1.43−1.39 (m, 1H), 0.94 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 158.7, 143.4, 142.3, 138.9, 137.9, 133.2, 132.3, 129.7, 129.6, 128.9, 127.6, 127.2, 126.8, 125.2, 124.1, 120.9, 44.7, 32.6, 30.6, 27.8, 27.5, 24.1, 21.6; IR (KBr)ν_{max}: 3045, 3022, 2955, 2867, 2837, 1573, 1099, 1019 cm^{-1}; HRMS (ESI) Calcd For $C_{28}H_{30}N$ 380.2373 (M + H$^+$); Found 380.2376.

*8-(tert-Butyl)-6-(4-methoxyphenyl)-7,8,9,10-tetrahydrobenzo[c]-phenanthridine (**6b**).* Yield 90% (355 mg), brown solid, mp 270−271 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.34 (d, J = 7.6 Hz, 1H), 7.86 (d, J = 9.2 Hz, 2H), 7.77 (d, J = 9.2 Hz, 1H), 7.69 (d, J = 8.8 Hz, 2H), 7.64 (t, J = 6.4 Hz, 2H), 7.04 (d, J = 8.8 Hz, 2H), 3.89 (s, 3H), 3.51−3.46 (m, 1H), 3.12−3.03 (m, 1H), 2.87 (d, J = 16.0 Hz, 1H), 2.68 (t, J = 12.0 Hz, 1H), 2.21−2.19 (m, 1H), 1.53−1.43 (m, 1H), 1.36 (t, J = 10.0 Hz, 1H), 0.93 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.7, 158.2, 143.3, 142.4, 134.1, 133.1, 132.1, 131.0, 129.6, 127.7, 127.6, 127.1, 126.8, 125.1, 123.9, 120.8, 113.6, 58.5, 44.7, 32.5, 30.7, 27.8, 27.5, 23.9; IR (KBr)ν_{max}: 3051, 2956, 2897, 1608, 1506, 1174, 1073, 1012 cm^{-1}; HRMS (ESI) Calcd for $C_{28}H_{30}NO$ 396.2322 (M + H$^+$); Found 396.2322.

*4-(8-(tert-Butyl)-7,8,9,10-tetrahydrobenzo[c]phenanthridin-6-yl)-phenol (**6c**).* Yield 92% (350 mg), white solid, mp 256−257 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.35−9.33 (m, 1H), 7.91−7.87 (m, 2H), 7.81 (d, J = 9.6 Hz, 1H), 7.66−7.63 (m, 4H), 6.96 (d, J = 8.8 Hz, 2H),

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3.56−3.49 (m, 1H), 3.16−3.06 (m, 1H), 2.87 (d, J = 16.4 Hz, 1H), 2.69 (t, J = 12.4 Hz, 1H), 2.54−2.18 (m, 1H), 1.57−1.47 (m, 1H), 1.41−1.38 (m, 1H), 0.94 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.3, 157.3, 142.8, 142.2, 132.9, 132.3, 131.7, 130.8, 129.5, 127.4, 127.3, 126.7, 126.5, 124.7, 123.6, 120.7, 115.1, 44.5, 32.3, 30.5, 27.6, 27.2, 23.8; IR (KBr)ν_{max}: 3473, 3049, 2962, 2915, 2858, 1636, 1518, 1100, 1022 cm^{-1}; HRMS (ESI) Calcd for $C_{27}H_{28}NO$ 382.2166 (M + H$^+$); Found 382.2166.

*3-(8-(tert-Butyl)-7,8,9,10-tetrahydrobenzo[c]phenanthridin-6-yl)-phenol (**6d**).* Yield 95% (362 mg), white solid, mp 220−221 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.32 (d, J = 7.8 Hz, 1H), 7.86 (d, J = 7.2 Hz, 1H), 7.83 (d, J = 9.0 Hz, 1H), 7.78 (d, J = 9.0 Hz, 1H), 7.65−7.61 (m, 2H), 7.29−7.27 (m, 1H), 7.13−7.12 (m, 2H), 6.86−6.84 (m, 1H), 3.46−3.42 (m, 1H), 3.07−3.01 (m, 1H), 2.78 (d, J = 6.2 Hz, 1H), 2.54 (t, J = 12.6 Hz, 1H), 2.18−2.15 (m, 1H), 1.45−1.38 (m, 1H), 1.35−1.31 (m, 1H), 0.89 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 158.4, 156.0, 143.5, 142.6, 141.9, 133.2, 131.4, 130.1, 129.4, 127.9, 127.8, 127.6, 127.1, 125.0, 124.4, 121.6, 120.7, 116.9, 115.8, 44.5, 32.5, 30.2, 27.9, 27.4, 23.8; IR (KBr)ν_{max}: 3446, 3051, 2956, 2861, 1636, 1121, 996 cm^{-1}; HRMS (ESI) Calcd for $C_{27}H_{28}NO$ 382.2166 (M + H$^+$); Found 382.2161.

*8-(tert-Butyl)-6-(3,4,5-trimethoxyphenyl)-7,8,9,10-tetrahydrobenzo[c]phenanthridine (**6e**).* Yield 77% (350 mg), white solid, mp 196−197 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.41,(s, 1H), 7.90 (t, J = 3.6 Hz, 2H), 7.83, (d, J = 9.6 Hz, 1H), 7.71−7.64, (m, 2H), 6.95, (s, 2H), 3.96, (s, 3H), 3.94, (s, 6H), 3.54−3.51, (m, 1H), 3.15−3.09, (m, 1H), 2.93, (d, J = 16.2 Hz, 1H), 2.67, (t, J = 12.6 Hz, 1H), 2.24, (t, J = 4.2 Hz, 1H), 1.55−1.48,(m, 1H), 1.42 (t, J = 10.2 Hz, 1H), 0.95, (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 158.1, 153.1, 142.8, 141.4, 138.4, 136.5, 133.3, 131.6, 129.7, 127.9, 127.8, 127.7, 127.1, 125.3, 124.3, 120.7, 107.2, 61.2, 56.5, 44.7, 32.6, 30.6, 27.9, 27.5, 23.9; IR (KBr)ν_{max}: 3042, 2997, 2956, 2886, 1637, 1585, 1127, 1006 cm^{-1}; HRMS (ESI) Calcd for $C_{30}H_{34}NO_3$ 456.2533 (M + H$^+$); Found 456.2527.

*8-(tert-Butyl)-6-(4-chlorophenyl)-7,8,9,10-tetrahydrobenzo[c]-phenanthridine (**6f**).* Yield 87% (347 mg), white solid, mp 217−218 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.40, (s, 1H), 7.90−7.89, (m, 2H), 7.85,(s, 1H), 7.67−7.66, (m, 4H), 7.51−7.50, (m, 2H), 3.53, (d, J = 17.2 Hz, 1H), 3.12−3.11, (m, 1H), 2.82, (d, J = 16.0 Hz, 1H), 2.65, (t, J = 12.8 Hz, 1H), 2.24−2.23, (m, 1H), 1.51, (d, J = 12.0 Hz, 1H),1.41,(d, J = 11.0 Hz, 1H), 0.94, (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.1, 143.3, 143.0, 139.6, 134.4, 133.2, 131.7, 131.1, 129.6, 128.5, 127.9, 127.7, 127.1, 125.1, 124.4, 120.7, 44.6, 32.6, 30.5, 27.8, 27.5, 23.9; IR (KBr)ν_{max}: 3022, 2958, 2873, 2840, 1652, 1573, 1123, 1090, 1014 cm^{-1}; HRMS (ESI) Calcd for $C_{27}H_{27}ClN$ 400.1827 (M + H$^+$); Found 400.1825.

*6-(4-Bromophenyl)-8-(tert-butyl)-7,8,9,10-tetrahydrobenzo[c]-phenanthridine (**6g**).* Yield 82% (363 mg), white solid, mp 215−216 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.45 (s, 1H), 7.89(s, 2H), 7.87, (s, 1H), 7.68−7.66 (m, 4H), 7.61(s, 2H), 3.54 (d, J = 17.2 Hz, 1H), 3.14 (s, 1H), 2.82 (d, J = 16.0 Hz, 1H), 2.64 (t, J = 12.8 Hz, 1H), 2.23 (s, 1H), 1.51 (d, J = 11.6 Hz, 1H), 1.41 (d, J = 11.2 Hz, 1H), 0.94, (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.0, 143.7, 142.8, 139.6, 133.3, 131.5, 131.4, 129.7, 128.1, 127.9, 127.8, 127.2, 125.2, 124.5, 122.8, 120.6, 44.5, 32.5, 30.4, 27.9, 27.4, 23.9; IR (KBr)ν_{max}: 2953, 2869, 2840, 1573, 1122, 1099, 1073, 1010 cm^{-1}; HRMS (ESI) Calcd for $C_{27}H_{27}BrN$ 444.1322 (M + H$^+$); Found 444.1323.

*8-(tert-Butyl)-6-(4-nitrophenyl)-7,8,9,10-tetrahydrobenzo[c]-phenanthridine (**6h**).* Yield 80% (328 mg), yellow solid, mp > 350 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.27 (d, J = 8.8 Hz, 1H), 8.39 (d, J = 8.8 Hz, 2H), 7.93−7.89 (m, 4H), 7.86 (d, J = 9.2 Hz, 1H), 7.68 (t, J = 3.6 Hz, 2H), 3.56 (dd, J = 17.6, 5.2 Hz, 1H), 3.18−3.09 (m, 1H), 2.79 (d, J = 15.2 Hz, 1H), 2.69 (t, J = 12.0 Hz, 1H), 2.26 (dd, J = 12.4, 5.6 Hz, 1H), 1.57−1.49 (m, 1H), 1.44−1.39 (m, 1H), 0.93 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.1, 148.2, 147.7, 143.6, 143.2, 133.3, 132.1,130.7, 129.3, 128.2, 128.0, 127.8, 127.2, 124.9, 124.7, 123.5, 120.7, 44.6, 32.6, 30.4, 27.8, 27.4, 23.9; IR (KBr)ν_{max}: 3069, 2957, 2926, 2896, 2864, 1639, 1599, 1108, 1014 cm^{-1}; HRMS (APCI) Calcd for $C_{27}H_{27}N_2O_2$ 411.2067 (M + H$^+$); Found 411.2064.

*6-(3-Bromophenyl)-8-(tert-butyl)-7,8,9,10-tetrahydrobenzo[c]-phenanthridine (**6i**).* Yield 80% (354 mg), white solid, mp 185−186 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.32 (d, J = 8.0 Hz, 1H), 7.96 (s, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.76 (s, 2H), 7.68−7.61 (m, 4H), 7.38 (t, J = 8.0 Hz, 1H), 3.35−3.30 (m, 1H), 2.98−2.92 (m, 1H), 2.80 (d, J = 16.0 Hz, 1H), 2.62−2.55 (m, 1H), 2.12 (d, J = 12.0 Hz, 1H), 1.37−1.30 (m, 2H), 0.94 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.7, 143.6, 143.3, 142.6, 133.1, 132.8, 132.0, 131.0, 129.5, 129.2, 128.1, 127.7, 127.6, 127.4, 126.9, 124.9, 124.2, 122.4, 120.7, 44.3, 32.4, 30.3, 27.5, 27.4, 23.7; IR (KBr)ν_{max}: 3067, 3053, 2960, 2886, 1556, 1549, 1129, 1064, 1022, 997 cm^{-1}; HRMS (ESI) Calcd for $C_{27}H_{27}BrN$ 444.1321 (M + H$^+$); Found 444.1330.

*6-(3,4,5-Trimethoxyphenyl)-7,8,9,10-tetrahydrobenzo[c]phenanthridine (**6j**).* Yield 88% (351 mg), brown solid, mp 138−139 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.37 (d, J = 7.2 Hz, 1H), 7.90 (t, J = 9.0 Hz, 2H), 7.83 (d, J = 9.6 Hz, 1H), 7.69−7.64 (m, 2H), 6.91 (s, 2H), 3.95 (s, 3H), 3.94 (s, 6H), 3.28 (t, J = 6.0 Hz, 2H), 2.89 (t, J = 6.0 Hz, 2H), 2.04−2.00 (m, 2H), 1.84−1.80 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 158.2, 153.2, 143.2, 143.0, 138.3, 136.6, 133.3, 131.7, 129.3, 127.9, 127.7, 127.6, 127.0, 125.3, 124.6, 120.6, 107.1, 61.2, 56.5, 29.1, 26.5, 22.9, 22.6; IR (KBr)ν_{max}: 3051, 2996, 2936, 2860, 2834, 1622, 1584, 1170, 1126, 1006 cm^{-1}; HRMS (ESI) Calcd for $C_{26}H_{26}NO_3$ 400.1907 (M + H$^+$); Found 400.1927.

*6-(4-Fluorophenyl)-8,9,10,11-tetrahydro-7H-benzo[h]cyclohepta-[c]quinoline (**6k**).* Yield 91% (310 mg), white solid, mp 159−160 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.35 (d, J = 5.4 Hz, 1H), 8.04 (d, J = 9.6 Hz, 1H), 7.88−7.87 (m, 1H), 7.81 (d, J = 9.0 Hz, 1H), 768−7.64 (m, 4H), 7.21 (t, J = 8.4 Hz, 2H), 3.38 (t, J = 5.4 Hz, 2H), 3.08−3.06 (m, 2H), 1.97−1.93 (m, 2H), 1.84−1.81 (m, 2H), 1.73−1.69 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.1, 161.6, 156.4, 150.0, 144.3, 138.2, 134.8, 133.2, 132.2, 131.7, 131.6, 128.0, 127.5, 127.4, 126.9, 125.2, 123.7, 121.2, 115.3, 115.1, 32.1, 30.9, 28.7, 27.5, 26.5; IR (KBr)ν_{max}: 3046, 2981, 2936, 2910, 2875, 1635, 1538, 1052, 1014 cm^{-1}; HRMS (ESI) Calcd for $C_{24}H_{21}FN$ 342.1653 (M + H$^+$); Found 342.1659.

*6-(p-Tolyl)-7,8,9,10,11,12-hexahydrobenzo[h]cycloocta[c]quinoline (**6l**).* Yield 85% (298 mg), white solid, mp 151−152 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.32−9.31 (m, 1H), 7.98 (d, J = 9.0 Hz, 1H), 7.88−7.86 (m, 1H), 7.80 (d, J = 9.0 Hz, 1H), 7.63−7.62 (m, 2H), 7.50 (d, J = 7.8 Hz, 2H), 7.31 (d, J = 7.8 Hz, 2H), 3.37−3.36 (m, 2H), 3.02 (t, J = 5.4 Hz, 2H), 2.46 (s, 3H), 1.94−1.93 (m, 2H), 1.64−1.63 (m, 2H), 1.46−1.45 (m, 2H), 1.39−1.38 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 158.8, 146.6, 144.2, 139.9, 137.5, 133.1, 132.4, 129.3, 128.8, 127.7, 127.5, 127.2, 126.8, 125.2, 123.8, 121.7, 32.1, 30.4, 28.8, 26.9, 26.8, 26.2, 21.5; IR (KBr)ν_{max}: 3054, 2925, 2846, 1634, 1570, 1117, 1068, 1027 cm^{-1}; HRMS (APCI) Calcd for $C_{26}H_{26}N$ 352.2060 (M + H$^+$); Found 352.2074.

*6-Phenyl-7,8,9,10,11,12,13,14,15,16-decahydrobenzo[h]cyclododeca[c]quinoline (**6m**).* Yield 67% (263 mg), white solid, mp 166−167 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.31 (s, 1H), 7.96, (d, J = 9.2 Hz, 1H), 7.87 (s, 1H), 7.80 (d, J = 9.2 Hz, 1H), 7.63 (s, 4H), 7.50−7.45 (m, 3H), 3.25 (t, J = 6.8 Hz, 2H), 2.93 (t, J = 7.2 Hz, 2H), 1.92−1.91 (m, 2H), 1.67−1.66 (m, 4H), 1.58−1.48 (m, 8H), 1.35−1.34 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.5, 146.7, 143.0, 133.1, 132.6, 132.4, 129.2, 128.2, 127.8, 127.5, 127.2, 126.8, 125.2, 124.8, 122.1, 29.1, 28.9, 28.6, 28.5, 28.4, 27.7, 27.4, 27.0, 22.8; IR (KBr)ν_{max}: 3058, 2925, 2845, 1570, 1118, 1072, 1025 cm^{-1}; HRMS (ESI) Calcd for $C_{29}H_{32}N$ 394.2530 (M + H$^+$); Found 394.2530.

*6-(Naphthalen-2-yl)-7,8,9,10,11,12-hexahydrobenzo[h]cycloocta[c]quinoline (**6n**).* Yield 76% (294 mg), white solid, mp 166−167 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.36 (s, 1H), 8.09 (s, 1H), 8.02 (d, J = 9.6 Hz, 1H), 7.98 (d, J = 8.4 Hz, 1H), 7.94 (d, J = 3.0 Hz, 2H), 7.89 (t, J = 3.0 Hz, 1H), 7.84 (d, J = 9.0 Hz, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.65 (dd, J = 5.4, 3.0 Hz, 2H), 7.55 (dd, J = 5.4, 2.4 Hz, 2H), 3.41 (t, J = 5.4 Hz, 2H), 3.06 (t, J = 6.0 Hz, 2H), 1.97 (t, J = 5.4 Hz, 2H), 1.64−1.63 (m, 2H), 1.47−1.46 (m, 2H), 1.43−1.42 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 158.3, 147.5, 143.8, 139.6, 133.4, 133.2, 133.1, 133.0, 131.9, 128.7, 128.6, 128.0, 127.9, 127.8, 127.7, 127.6, 127.0, 126.4, 126.3, 125.3, 124.0, 121.6, 32.0, 30.5, 28.9, 27.1, 26.7, 26.3; IR (KBr)ν_{max}: 3042, 2929, 2854, 1608, 1549, 1082, 1036, 1012, 956 cm^{-1}; HRMS (APCI) Calcd for $C_{29}H_{26}N$ 388.2060 (M + H$^+$); Found 388.2045.

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*6-(Thiophen-2-yl)-8,9-dihydro-7H-benzo[h]cyclopenta[c]quinoline (**6o**).* Yield 85% (255 mg), white solid, mp 166−167 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.40 (d, J = 8.4 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.74 (t, J = 6.8 Hz, 1H), 7.69−7.67 (m, 2H), 7.63−7.62 (m, 1H), 7.61−7.56 (m, 1H), 7.51 (d, J = 18.8 Hz, 1H), 7.17 (t, J = 4.4 Hz, 1H), 3.29 (t, J = 7.6 Hz, 2H), 3.23 (t, J = 7.6 Hz, 2H), 2.31−2.24 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.1, 147.5, 147.1, 144.6, 133.6, 133.5, 131.8, 128.2, 128.1, 127.9, 127.8, 127.1, 127.0, 126.7, 125.2, 122.6, 122.2, 33.8, 31.2, 24.5; IR (KBr)ν_{max}: 3053, 2954, 2915, 2847, 1577, 1119, 1055, 1024 cm^{-1}; HRMS (ESI) Calcd for $C_{20}H_{16}NS$ 302.0998 (M + H$^+$); Found 302.1012.

*6-(Pyridin-2-yl)-8,9-dihydro-7H-benzo[h]cyclopenta[c]quinoline (**6p**).* Yield 78% (230 mg), brown solid, mp 128−129 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.45 (d, J = 8.4 Hz, 1H), 8.74 (d, J = 4.2 Hz, 1H), 8.67 (d, J = 7.8 Hz, 1H), 7.90 (d, J = 7.2 Hz, 2H), 7.81 (d, J = 8.4 Hz, 1H), 7.75−7.71 (m, 2H), 7.67 (t, J = 7.2 Hz, 1H), 7.33 (t, J = 6.0 Hz, 1H), 3.68 (t, J = 7.2 Hz, 2H), 3.35 (t, J = 7.8 Hz, 2H), 2.33−2.28 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 153.1, 147.3, 144.8, 139.1, 137.2, 133.6, 132.1, 128.7, 128.1, 128.0, 127.4, 125.5, 124.6, 124.2, 123.7, 122.2, 34.2, 31.3, 25.1; IR (KBr)ν_{max}: 3052, 2921, 2850, 1574, 1192, 1097, 1022, 987 cm^{-1}; HRMS (APCI) Calcd for $C_{21}H_{17}N_2$ 297.1386 (M + H$^+$); Found 297.1376.

*6-(Furan-2-yl)-8,9,10,11-tetrahydro-7H-benzo[h]cyclohepta[c]quinoline (**6q**).* Yield 72% (225 mg), brown solid, mp 83−84 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.37 (d, J = 7.6 Hz, 1H), 7.99 (d, J = 8.8 Hz, 1H), 7.86 (d, J = 7.2 Hz, 1H), 7.77 (d, J = 9.2 Hz, 1H), 7.70 (d, J = 6.8 Hz, 1H), 7.68−7.65 (m, 2H), 7.08 (d, J = 3.2 Hz, 1H), 6.62−6.61 (m, 1H), 3.78 (t, J = 5.6 Hz, 2H), 3.31 (t, J = 5.2 Hz, 2H), 1.94 (d, J = 5.6 Hz, 2H), 1.79 (d, J = 3.2 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.5, 150.4, 146.8, 144.6, 143.1, 134.6, 133.2, 132.2, 128.0, 127.5, 127.4, 127.0, 125.2, 123.7, 121.2, 111.6, 111.5, 31.9, 29.9, 28.3, 27.0, 26.6; IR (KBr)ν_{max}: 3049, 2921, 2853, 1621, 1571, 1163, 1126, 1076, 1009 cm^{-1}; HRMS (ESI) Calcd for $C_{22}H_{20}NO$ 314.1540 (M + H$^+$); Found 314.1547.

*6-(Thiophen-2-yl)-8,9,10,11-tetrahydro-7H-benzo[h]cyclohepta-[c]quinoline (**6r**).* Yield 84% (276 mg), brown solid, mp 142−143 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.39 (d, J = 8.0 Hz, 1H), 7.96 (d, J = 9.2 Hz, 1H), 7.86 (d, J = 7.6 Hz, 1H), 7.76 (d, J = 9.2 Hz, 1H), 7.71 (t, J = 10.0 Hz, 1H), 7.66 (t, J = 7.6 Hz, 1H), 7.51 (d, J = 5.2 Hz, 1H), 7.40 (d, J = 2.8 Hz, 1H), 7.18 (t, J = 3.6 Hz, 1H), 3.55, (t, J = 5.2 Hz, 2H), 3.31 (t, J = 5.2 Hz, 2H), 1.97 (d, J = 4.8 Hz, 2H), 1.80, (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.5, 150.1, 145.7, 144.2, 134.4, 133.2, 131.9, 128.1, 127.6, 127.6,127.5, 127.4, 127.4, 127.0, 125.3, 123.4, 121.1, 31.9, 30.4, 28.5, 27.0, 26.6; IR (KBr)ν_{max}: 3062, 2966, 2923, 2853, 1683, 1652, 1101, 1079, 1027 cm^{-1}; HRMS (ESI) Calcd for $C_{22}H_{20}NS$ 330.1311 (M + H$^+$); Found 330.1311.

*10-Methoxy-6-(3,4,5-trimethoxyphenyl)-7,8-dihydrodibenzo[c,k]-phenanthridine (**8**).* Yield 64% (305 mg), brown solid, mp 208−209 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.41 (d, J = 6.8 Hz, 1H), 8.33 (d, J = 8.8 Hz, 1H), 7.91 (t, J = 8.0 Hz, 2H), 7.80 (d, J = 9.6 Hz, 1H), 7.23−7.66 (m, 2H), 7.02 (s, 2H), 6.99 (d, J = 8.4 Hz, 1H), 6.97 (s, 1H), 3.96 (s, 3H), 3.94 (s, 6H), 3.92 (s, 3H), 3.03 (t, J = 6.4 Hz, 2H), 2.77 (t, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.1, 156.4, 153.2, 145.9, 142.5, 141.6, 138.5, 136.8, 133.2, 132.2, 131.3, 129.2, 128.1, 127.5, 127.2, 126.9, 125.6, 125.2, 123.5, 121.5, 113.6, 111.8, 107.3, 61.2, 56.5, 55.6, 30.2, 27.8; IR (KBr)ν_{max}: 3062, 2935, 2834, 1607, 1584, 1123, 1064, 1034, 1005 cm^{-1}; HRMS (ESI) Calcd for $C_{31}H_{28}NO_4$ 478.2013 (M + H$^+$); Found 478.2014.

*8,8-Dimethyl-6-(p-tolyl)-7,8-dihydrobenzo[c]phenanthridine (**10**).* Yield 82% (286 mg), brown solid, mp 174−175 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.37 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 12.0 Hz, 1H), 7.89−7.87 (m, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.68−7.63 (m, 3H), 7.36 (d, J = 12.0 Hz, 2H), 7.25 (d, J = 12.0 Hz, 1H), 6.25 (d, J = 8.0 Hz, 1H), 4.45 (s, 1H), 2.96 (s, 2H), 2.48 (s, 3H), 1.07 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.0, 145.1, 144.7, 138.2, 137.8, 136.6, 133.0, 131.9, 129.6, 128.8, 127.7, 127.4, 127.1, 126.7, 124.9, 124.8, 120.5, 120.2, 120.1, 39.9, 32.0, 29.7, 27.2, 21.4; IR (KBr)ν_{max}: 3029, 2956, 2918, 2895, 2857, 1627, 1583, 1564, 1115, 1024, 1000 cm^{-1}; HRMS (ESI) Calcd for $C_{26}H_{24}N$ 350.1903 (M + H$^+$); Found 350.1908.

*4-(2,3-Dihydro-1H-benzo[f]cyclopenta[c]quinolin-4-yl)phenol (**12a**).* Yield 78% (242 mg), white solid, mp 308−309 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.42 (s, 1H), 8.56 (d, J = 8.4 Hz, 1H), 7.91−7.83 (m, 3H), 7.72 (d, J = 7.8 Hz, 2H), 7.59−7.55 (m, 2H), 6.89 (d, J = 8.4 Hz, 2H), 3.65−3.62 (m, 2H), 3.18−3.16 (m, 2H), 2.17−2.15 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 156.9, 152.6, 149.5, 146.0, 134.9, 130.9, 129.6, 129.1, 128.9, 128.6, 127.6, 127.3, 125.3, 125.2, 125.1, 121.0, 114.0, 35.8, 31.8, 24.6; IR (KBr)ν_{max}: 3446, 1636, 1607, 1548, 1145, 1104, 1018 cm^{-1}; HRMS (ESI) Calcd for $C_{22}H_{18}NO$ 312.1383 (M + H$^+$); Found 312.1382.

*3-(tert-Butyl)-5-(4-methoxyphenyl)-1,2,3,4-tetrahydrobenzo[a]-phenanthridine (**12b**).* Yield 72% (284 mg), brown solid, mp 206−207 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.76 (d, J = 8.4 Hz, 1H), 7.98 (d, J = 8.4 Hz, 1H), 7.95−7.94 (m, 1H), 7.88 (d, J = 9.0 Hz, 1H), 7.64−7.61 (m, 2H), 7.52 (d, J = 8.4 Hz, 2H), 7.03 (d, J = 8.4 Hz, 2H), 3.89 (s, 3H), 3.70 (d, J = 16.2 Hz, 1H), 3.63−3.61 (m, 1H), 3.01 (dd, J = 16.8, 5.4 Hz, 1H), 2.56 (dd, J = 16.8, 11.4 Hz, 1H), 2.16 (dd, J = 12.6, 2.4 Hz, 1H), 1.64−1.63 (m, 1H), 1.26−1.22 (m, 1H), 0.90 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 159.6, 159.2, 146.6, 145.2, 133.9, 133.5, 130.4, 130.3, 130.1, 130.0, 129.4, 129.1, 128.5, 126.3, 125.7, 124.6, 113.9, 55.5, 44.3, 34.6, 32.7, 30.4, 27.2, 24.9; IR (KBr)ν_{max}: 3016, 2948, 2858, 1635, 1609, 1109, 1033, 834 cm^{-1}; HRMS (ESI) Calcd for $C_{28}H_{30}NO$ 396.2322 (M + H$^+$); Found 396.2341.

*5-(p-Tolyl)-1,2,3,4-tetrahydrobenzo[a]phenanthridine (**12c**).* Yield 74% (239 mg), white solid, mp 146−147 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.77 (d, J = 9.0 Hz, 1H), 8.04 (d, J = 8.4 Hz, 1H), 7.96−7.95 (m, 1H), 7.90 (d, J = 8.4 Hz, 1H), 7.66−7.61 (m, 2H), 7.44 (d, J = 7.8 Hz, 2H), 7.30 (d, J = 7.8 Hz, 2H), 3.62 (t, J = 6.0 Hz, 2H), 2.89 (t, J = 6.6 Hz, 2H), 2.44 (s, 3H), 1.92−1.83 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 159.1, 146.3, 145.7, 138.0, 133.6, 130.4, 130.3, 129.3, 129.2, 129.1, 128.9, 128.6, 126.4, 125.8, 124.9, 33.5, 28.7, 23.3, 22.4, 21.5; IR (KBr)ν_{max}: 3049, 3027, 2936, 2860, 1613, 1559, 1118, 1020 cm^{-1}; HRMS (ESI) Calcd for $C_{24}H_{22}N$ 324.1747 (M + H$^+$); Found 324.1746.

*5-(2-Fluorophenyl)-1,2,3,4-tetrahydrobenzo[a]phenanthridine (**12d**).* Yield 78% (255 mg), brown solid, mp 108−109 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.78−8.76 (m, 1H), 8.01 (d, J = 9.0 Hz, 1H), 7.96−7.94 (m, 1H), 7.90 (d, J = 8.4 Hz, 1H), 7.65−7.61 (m, 2H), 7.49−7.47 (m, 1H), 7.46−7.42 (m, 1H), 7.30 (t, J = 6.6 Hz, 1H), 7.21−6.98 (m, 1H), 3.62 (t, J = 5.4 Hz, 2H), 2.90−2.69 (m, 2H), 1.91−1.90 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 160.7, 159.1, 154.5, 146.7, 145.5, 133.6, 131.2, 131.1, 130.5, 130.3, 130.2, 129.1, 129.0, 128.6, 126.6, 125.8, 125.5, 124.8, 116.0, 115.9, 33.5, 27.4, 23.4, 22.2; IR (KBr)ν_{max}: 3055, 2935, 2861, 1616, 1579, 1122, 1092, 1030, 1006 cm^{-1}; HRMS (ESI) Calcd for $C_{23}H_{19}FN$ 328.1496 (M + H$^+$); Found 328.1496.

*5-(Furan-2-yl)-1,2,3,4-tetrahydrobenzo[a]phenanthridine (**12e**).* Yield 75% (224 mg), brown solid, mp 116−118 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.74−8.72 (m, 1H), 8.00−7.98 (d, J = 8.0 Hz, 1H), 7.94−7.92 (m, 1H), 7.89−7.87 (d, J = 9.2 Hz, 1H), 7.68−7.67 (m, 1H), 7.62−7.59 (m, 2H), 7.06 (d, J = 3.6 Hz, 1H), 6.60−6.59 (m, 1H), 3.58 (t, J = 6.0 Hz, 2H), 3.22 (t, J = 6.8 Hz, 2H), 2.03−1.99 (m, 2H), 1.86−1.84 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 153.8, 147.9, 146.9, 145.8, 143.5, 133.7, 130.4, 130.3, 129.4, 129.1, 128.7, 128.6, 126.4, 125.8, 124.9, 112.7, 111.6, 33.9, 27.9, 23.2, 22.5; IR (KBr)ν_{max}: 3054, 2962, 2905, 1944, 1605, 1543, 1096 cm^{-1}; HRMS (APCI) Calcd for $C_{21}H_{18}NO$ 300.1383 (M + H$^+$); Found 300.1391.

*8-Phenyl-9,10,11,12,13,14-hexahydrobenzo[f]cycloocta[c]quinoline (**12f**).* Yield 80% (269 mg), brown solid, mp 128−129 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.83 (d, J = 8.4 Hz, 1H), 8.05 (s, 1H), 7.95 (d, J = 7.8 Hz, 1H), 7.91 (d, J = 9.0 Hz, 1H), 7.69−7.63 (m, 2H), 7.51−7.49 (t, J = 7.8 Hz, 4H), 7.47−7.43 (m, 1H), 3.62 (s, 2H), 2.97 (t, J = 6.0 Hz, 2H), 2.26 (t, J = 4.8 Hz, 2H), 1.72−1.71 (m, 2H), 1.70−1.64 (m, 2H), 1.54−1.53 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.6, 148.8, 147.2, 142.1, 133.6, 133.2, 130.7, 130.3, 129.5, 129.4, 128.8, 127.9, 127.8, 126.4, 126.3, 124.8, 31.2, 31.1, 30.8, 28.5, 27.4, 26.0; IR (KBr)ν_{max}: 3055, 2925, 2852, 1737, 1605, 1548, 1118, 1072, 1029, 1009 cm^{-1}; HRMS (ESI) Calcd for $C_{25}H_{24}N$ 338.1903 (M + H$^+$); Found 338.1903.

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*3-(tert-Butyl)-5-(p-tolyl)-1,2,3,4-tetrahydrobenzo[a]phenanthridine (**12g**).* Yield 75% (284 mg), white solid, mp 255−256 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.76 (d, J = 6.0 Hz, 1H), 7.99 (d, J = 12.0 Hz, 1H), 7.95 (d, J = 6.0 Hz, 1H), 7.89 (d, J = 6.0 Hz. 1H), 7.62−7.61 (t, J = 6.0 Hz, 2H), 7.46 (d, J = 12.0 Hz, 2H), 7.31 (d, J = 6.0 Hz, 2H), 3.71 (d, J = 18.0 Hz, 1H), 3.63 (d, J = 6.0 Hz, 1H), 3.0 (dd, J = 6.0, 12.0 Hz, 1H), 2.56 (t, J = 12.0 Hz, 1H), 2.45 (s, 3H), 2.17 (d, J = 12.0 Hz, 1H), 1.64 (s, 1H), 1.26−1.22 (m, 1H), 0.90 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 159.6, 146.6, 145.2, 138.5, 137.8, 133.5, 130.4, 130.1, 129.4, 129.2, 129.1, 128.9, 128.5, 126.3, 125.7, 124.7, 44.3, 34.6, 32.7, 30.3, 27.2, 24.9, 21.5; IR (KBr)ν_{max}: 3016, 2931, 2868, 1619, 1554, 1180, 1121, 1016 cm^{-1}; HRMS (ESI) Calcd for $C_{28}H_{30}N$ 380.2373 (M + H$^+$); Found 380.2387.

*(3S,8R,9S,10R,13S,14S)-10,13-Dimethyl-17-(3-(p-tolyl)benzo[f]quinolin-1-yl)-2,3,4,7,8,9,10,11,12,13,14,15-dodecahydro-1H-cyclopenta[a]phenanthren-3-yl Acetate (**14a**).* Yield 68% (395 mg), white solid, mp 216−217 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.46 (d, J = 6.0 Hz, 1H), 8.11 (d, J = 6.0 Hz, 2H), 8.07 (d, J = 6.0 Hz, 1H), 7.95 (d, J = 12.0 Hz, 1H), 7.90 (d, J = 6.0 Hz, 1H), 7.59 (d, J = 6.0 Hz, 1H), 7.55 (s, 2H), 7.35(d, J = 6.0 Hz, 2H), 6.03 (s, 1H), 5.45 (s, 1H), 4.59 (s, 1H), 2.62 (d, J = 12.0 Hz, 1H), 2.44 (s, 3H), 2.37−2.25 (m, 3H), 2.16 (s, 1H), 2.03 (s, 3H), 1.97 (s, 1H), 1.80 (s, 3H), 1.71 (d, J = 12.0 Hz, 1H), 1.54 (t, J = 12.0 Hz, 1H), 1.37 (s, 1H), 1.27 (d, J = 18.0 Hz, 2H), 1.06 (t, J = 12.0 Hz, 3H), 0.99 (s, 3H), 0.92 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.8, 157.7, 155.5, 149.3, 144.9, 140.3, 139.5, 136.7, 132.6, 131.2, 131.1, 129.7, 129.5, 128.6, 128.4, 128.1, 127.5, 126.9, 125.7, 123.8, 122.4, 122.2, 57.5, 51.7, 50.4, 38.3, 37.0, 33.2, 32.8, 32.0, 31.3, 27.9, 21.6, 21.5, 20.8, 19.4, 17.2; IR (KBr)ν_{max}: 3157, 2967, 2722, 1647, 1567, 1167, 1102, 1019, 952 cm^{-1}; HRMS (ESI) Calcd for $C_{41}H_{44}NO_2$ 582.3367 (M + H$^+$); Found 582.3371.

*(3S,8R,9S,10R,13S,14S)-17-(3-(4-Chlorophenyl)benzo[f]quinolin-1-yl)-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15-dodecahydro-1H-cyclopenta[a]phenanthren-3-yl Acetate (**14b**).* Yield 72% (432 mg), white solid, mp 229−230 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.47 (d, J = 12.0 Hz, 1H), 8.17 (d, J = 6.0 Hz, 2H), 8.05 (d, J = 6.0 Hz, 1H), 7.96 (d, J = 12.0 Hz, 1H), 7.90, (d, J = 6.0 Hz, 1H), 7.61 (d, J = 6.0 Hz, 1H), 7.57 (d, J = 6.0 Hz, 1H), 7.54 (s, 1H), 7.51 (d, J = 6.0 Hz, 2H), 6.00 (s, 1H), 5.45 (s, 1H), 4.60 (s, 1H), 2.63 (d, J = 12.0 Hz, 1H), 2.37 (d, J = 6.0 Hz, 1H), 2.33−2.25 (m, 2H), 2.18 (d, J = 18.0 Hz, 1H), 2.03 (s, 3H), 1.99 (s, 1H), 1.85−1.81 (m, 3H), 1.71−1.69 (d, J = 18.0 Hz, 2H), 1.56−1.50 (m, 1H), 1.38−1.37 (m, 1H), 1.28 (s, 2H), 1.09−1.02 (m, 2H), 0.99 (s, 3H), 0.92 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.7, 157.5, 154.2, 149.4, 145.2, 140.3, 137.9, 135.6, 132.7, 131.4, 131.1, 129.3, 129.2, 128.8, 128.7, 128.4, 128.3, 127.1, 125.9, 124.1, 122.4, 121.9, 74.0, 57.5, 51.5, 50.4, 38.3, 36.9, 33.2, 32.8, 31.9, 31.3, 27.9, 21.6, 20.7, 19.4, 17.2; IR (KBr)ν_{max}: 3047, 3028, 2926, 1689, 1653, 1589, 1030, 964 cm^{-1}; HRMS (ESI) Calcd for $C_{40}H_{41}ClNO_2$ 602.2820 (M + H$^+$); Found 602.2823.

*1,4-Bis(8-(tert-butyl)-7,8,9,10-tetrahydrobenzo[c]phenanthridin-6-yl)benzene (**15a**).* Yield 68% (443 mg), pale yellow solid, mp > 350 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.00 (t, J = 12.0 Hz, 2H), 8.25 (d, J = 6.0 Hz, 2H), 8.17 (s, 4H), 7.98 (d, J = 6.0 Hz, 2H), 7.94 (s, 2H), 7.90 (s, 4H), 3.90 (d, J = 18.0 Hz, 2H), 3.47 (d, J = 12.0 Hz, 2H), 2.88 (d, J = 18.0 Hz, 2H), 2.67 (d, J = 12.0 Hz, 2H), 2.42 (s, 2H), 1.62 (d, J = 12.0 Hz, 4H), 0.93 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 161.7, 161.5, 161.2, 160.9, 158.2, 151.1, 135.2, 134.8, 134.2, 133.1, 132.8, 132.3, 130.2, 130.1, 129.9, 127.3, 122.8, 122.3, 119.4, 117.7, 115.8, 113.9, 111.9, 43.5, 32.5, 29.6, 29.5, 26.9, 22.9; IR (KBr)ν_{max}: 3082, 2996, 2956, 2867, 1581, 1551, 1081, 1019, 999 cm^{-1}; HRMS (ESI) Calcd for $C_{48}H_{49}N_2$ 653.3890 (M + H$^+$); Found 653.3887.

*1,4-Bis(3-(tert-butyl)-1,2,3,4-tetrahydrobenzo[a]phenanthridin-5-yl)benzene (**15b**).* Yield 75% (489 mg), pale yellow solid, mp > 350 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.93 (d, J = 8.0 Hz, 2H), 8.37−8.34 (m, 2H), 8.20−8.17 (m, 2H), 7.99−7.92 (m, 6H), 7.89−7.86 (m, 4H), 4.05−3.90 (m, 4H), 3.05−2.99 (m, 2H), 2.77−2.68 (m, 2H), 2.38 (d, J = 18.0 Hz, 2H), 1.79 (s, 2H), 1.48−1.38(m, 2H), 0.91 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 161.6, 161.2, 160.8, 160.4, 160.1, 149.3, 138.4, 138.3, 134.1, 133.5, 133.4, 130.9, 130.1, 129.9, 129.7, 128.7, 128.2, 127.4, 119.2, 117.5, 116.3, 113.5, 110.6, 43.3, 36.1, 32.6, 29.7, 26.7, 23.9; IR (KBr)ν_{max}: 3136, 3080, 2968, 2874, 1683, 1555, 1057, 1021, 998 cm^{-1}; HRMS (APCI) Calcd for $C_{48}H_{49}N_2$ 653.3890 (M + H$^+$); Found 653.3897.

*3-(tert-Butyl)-5-(naphthalen-2-yl)-1,2,3,4-tetrahydronaphtho-[2,3-b]phenanthridine (**17**).* Yield 92% (428 mg), brown solid, mp 285−286 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.24 (s, 1H), 8.43 (s, 1H), 8.15−8.14 (m, 1H), 8.07−8.04 (m, 2H), 7.98−7.96 (m, 2H), 7.94−7.92 (m, 2H), 7.89 (d, J = 8.4 Hz, 1H), 7.69 (d, J = 8.4 Hz, 1H), 7.60 (t, J = 4.2 Hz, 2H), 7.54 (t, J = 4.2 Hz, 2H), 3.84−3.80 (m, 2H), 3.08 (dd, J = 16.8, 5.4 Hz, 1H), 2.62 (dd, J = 16.8, 11.4 Hz, 1H), 2.24 (d, J = 12.0 Hz, 1H), 1.69 (t, J = 12.0 Hz, 2H), 0.85 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 158.9, 147.3, 145.9, 138.8, 133.7, 133.2, 131.9, 131.5, 131.4, 130.9, 130.3, 128.9, 128.7, 128.6, 128.5, 128.4, 128.1, 127.9, 127.7, 127.1, 127.0, 126.6, 126.4, 126.3, 126.1, 125.0, 44.4, 34.7, 32.8, 30.3, 27.2, 25.1; IR (KBr)ν_{max}: 3064, 2926, 2847, 1639, 1558, 1105, 1017, 885 cm^{-1}; HRMS (ESI) Calcd for $C_{35}H_{32}N$ 466.2530 (M + H$^+$); Found 466.2532.

*(4aR,5S)-3-(tert-Butyl)-5-(p-tolyl)-2,3,4,4a,5,6-hexahydrobenzo-[a]phenanthridine (**18**).* Yield 25% (93.5 mg), brown solid, mp 120−121 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, J = 8.0 Hz, 1H), 7.55 (d, J = 4.0 Hz, 1H), 7.37−7.34 (m, 1H), 7.25−7.21 (m, 3H), 7.15 (d, J = 8.0 Hz, 2H), 7.02 (t, J = 8.0 Hz, 1H), 6.89−6.86 (m, 1H), 6.24 (s, 1H), 6.15 (d, J = 4.0 Hz, 1H), 4.47 (d, J = 12.0 Hz, 1H), 2.49−2.47 (d, J = 8.0 Hz, 1H), 2.31 (s, 3H), 2.23 (s, 1H), 2.16−2.08 (m, 1H), 1.45 (d, J = 12.0 Hz, 2H), 1.35 (dd, J = 12.0, 4.0 Hz, 2H), 0.81 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.0, 140.6, 137.9, 132.8, 130.9, 129.4, 128.6, 128.1, 127.9, 126.3, 125.3, 123.7, 121.4, 116.8, 114.3, 110.1, 62.8, 39.4, 38.4, 32.4, 27.7, 27.4, 25.1, 21.4; IR (KBr)ν_{max}: 3042, 2957, 2925, 2856, 1619, 1569, 1152, 1082, 1020, 968 cm^{-1}; HRMS (APCI) Calcd for $C_{28}H_{32}N$ 382.2529 (M + H$^+$); Found 382.2526.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b02159.

^{1}H, ^{13}C NMR, HRMS spectra and X-ray crystallography data of all compounds (PDF)

X-ray crystallography data of **4a**, **6r**, **8**, **12e**, **14b**, and **18** (CIF)

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Notes

The authors declare no competing financial interest.

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■ DEDICATION

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PAPER

Electronic effect of substituents on anilines favors 1,4-addition to *trans*-β-nitrostyrenes: access to *N*-substituted 3-arylindoles and 3-arylindoles†‡

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A simple and an efficient method for the regioselective synthesis of *N*-alkyl/aryl/H 3-arylindole derivatives from *N*-substituted anilines and *trans*-β-nitrostyrenes has been described using 10 mol% of bismuth(III) triflate as a catalyst in acetonitrile at 80 °C. The present protocol profits from the formation of new C–C and C–N bonds, broad substrate scope and moderate to good yields.

Introduction

Indole scaffolds are widely distributed in nature as alkaloids[1a,b] and terpenoids,[1c,d] and they exhibit a broad range of biological activities. Moreover, indoles and their derivatives are found to have widespread applications in pharmaceuticals,[2] agrochemicals,[3] functionalized materials,[4] and dyes[5] and as flavour enhancers. In addition, many non-natural indole derivatives particularly 3-arylindole derivatives show interesting biological activities,[6] and some of them are depicted in Fig. 1.

Since the biological importance of 3-arylindoles has been well established, a concise and flexible method for the synthesis of 3-arylindoles is highly desirable. In the literature, a few reported methods are available to construct the 3-arylindoles. Some of the important procedures include direct metal-catalysed C3-arylation[7] of indoles and intramolecular cyclisation reactions such as aza-Wacker-type cyclization of 2-alkenylanilines,[8a–d] Ullmann coupling of 2-bromoarylaminoalkanes,[8e] palladium-catalysed cylisation of enaminoesters,[8f] heteroannulation of α-aminoacetophenones,[9a,b] and amination of an aromatic C–H bond.[9c] The intermolecular cyclisation involves the reaction of nitrosoarenes,[10] arylhydroxylamines[11] and nitroarenes[12] with alkynes as well as 2-iodoanilines[13] with triethyl(phenylethynyl)silane. Since there is a competition for the formation of 2-arylindole and 3-arylindole regioisomers, it is a highly challenging task for chemists to synthesize exclusively 3-arylindoles. Recently, the synthesis of 3-arylindoles has been reported through intermolecular C–C and C–N bond formation from the reactions of *N*-substituted arylamines[14] and cinnamic acids/alkenes which are shown in Scheme 1.

Despite having great advantages, these reported methods have some shortcomings such as the need for costly catalysts, use of ligands and additives, limited substrate scope, restricted reaction conditions and failure of the reactions with simple anilines/*N*-alkylanilines. Zhang and co-workers reported the metal-free synthesis of 3-arylbenzoindoles from *trans*-β-nitrostyrenes and naphthylamines. However, they also failed to obtain 3-arylindoles from anilines.[15a] Consequently, there is a large scope to develop a new methodology for the regioselective synthesis of *N*-alkylated 3-arylindoles[15b] and 3-arylindoles with high reactivity of *N*-alkylanilines and aniline derivatives, respectively.

The importance and usefulness of *trans*-β-nitrostyrenes[16a–d] are well reviewed for the construction of five- and six-mem-

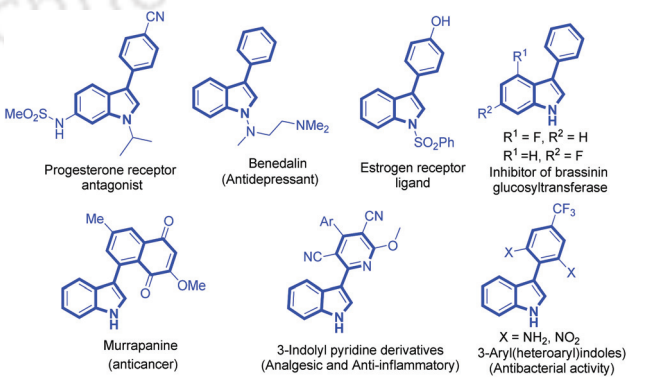

Fig. 1 Some of the biologically active 3-arylindoles.

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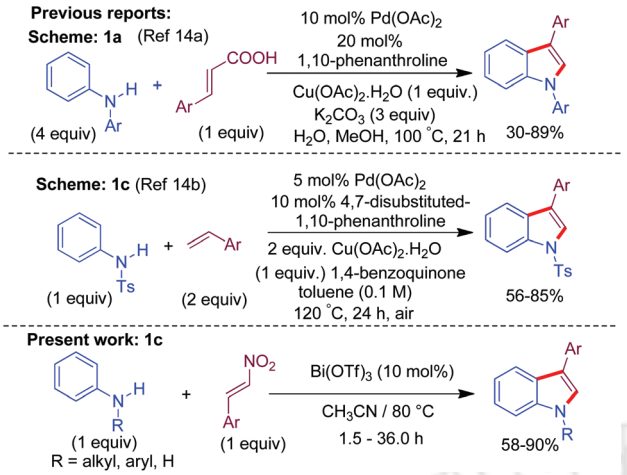
†This work is dedicated to my mentor Professor Dr R. R. Schmidt, Retired Professor, Department of Chemistry, University of Konstanz, Germany, on the occasion of his forthcoming 84th birthday.

‡Electronic supplementary information (ESI) available. CCDC 1576147 for compound **3h**. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c8ob00736e



Scheme 1 The synthetic strategies for 3-arylindoles from *N*-substituted anilines and alkenes.

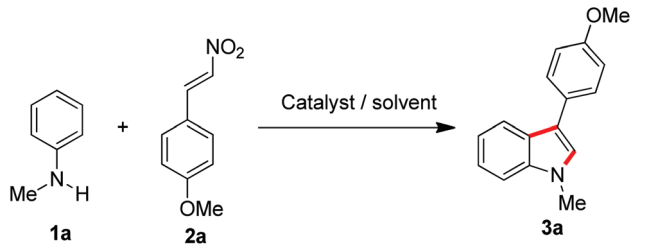
bered heterocycles.[16e,f] Thus, we envisaged that this prized moiety can be further explored for the synthesis of 3-arylindoles. Bismuth(III) triflate is found to be a non-toxic and easy handling reagent.[17] This is also proven as a versatile and efficient Lewis-acid catalyst for various organic transformations.[18] Thus the remarkable properties of bismuth(III) triflate led us to believe that it can be used as a catalyst to facilitate the synthesis of indole derivatives. Herein, we report $Bi(OTf)_3$-catalysed highly regioselective synthesis of 3-arylindole from readily available substituted arylamines and *trans*-β-nitrostyrenes (Scheme 1c).

Results and discussion

N-Methylaniline **1a** (1.0 mmol) and (*E*)-1-methoxy-4-(2-nitrovinyl)benzene **2a** (1.0 mmol) were selected as the model substrates to find out the optimum reaction conditions from a series of reactions. Initially, the ideal reaction was examined using 5 mol% of $Bi(OTf)_3$ as a catalyst in CH_3CN solvent at 80 °C and the results are summarized in Table 1, entry 1. After chromatographic purification, yellow semi-solid product **3a** was isolated in 52% yield. No strong absorption peaks appeared at 1350 cm^{-1} and 1550 cm^{-1} corresponding to the NO_2 group in the IR spectrum, which clearly indicated that the $-NO_2$ group was eliminated during the reaction. In the ^1H NMR spectrum, **3a** showed two singlet peaks at δ 3.86 and 3.89 ppm due to the presence of N–Me and –OMe groups, respectively. In addition, compound **3a** was also confirmed by HRMS.

To determine the optimal conditions, the same reaction was scrutinized in the absence of the catalyst and the result was futile (Table 1, entry 2). It was observed that the reaction proceeded much faster and offered a better yield, when the $Bi(OTf)_3$ catalyst loading was increased from 5 mol% to 10 mol% (Table 1, entry 3). Furthermore, on increasing the catalyst loading to 15 mol% no significant change was observed in the reaction time and yield (Table 1, entry 4). In order to ascertain

Table 1 Optimization of reaction conditions[a,b,c,d]



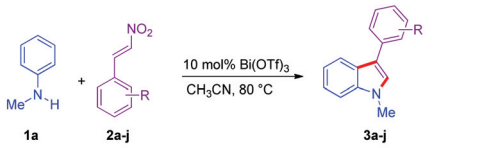
Entry	Catalyst	Mol%	Solvent	Time	Yield 3[b] (%)
1	$Bi(Otf)_3$	05	CH_3CN	20 h	52
2	No catalyst	—	CH_3CN	24 h	NR
3	**$Bi(OTf)_3$**	**10**	**CH_3CN**	**16 h**	**74**
4	$Bi(OTf)_3$	15	CH_3CN	16 h	74
5	$Yb(OTf)_3$	10	CH_3CN	18 h	68
6	$Sc(OTf)_3$	10	CH_3CN	24 h	46
7	AgOTf	10	CH_3CN	24 h	Trace
8	$Cu(OTf)_2$	10	CH_3CN	24 h	Trace
9	$Cu(OAc)_2$	10	CH_3CN	24 h	NR
10	$FeCl_3$	10	CH_3CN	24 h	NR
11	$Bi(OTf)_3$	10	CH_3CN[c]	24 h	NR
12	$Bi(OTf)_3$	10	DMSO	24 h	NR
13	$Bi(OTf)_3$	10	DMF	24 h	NR
14	$Bi(OTf)_3$	10	DCE[d]	24 h	62
15	$Bi(OTf)_3$	10	DCM[d]	24 h	25
16	$Bi(OTf)_3$	10	Toluene	24 h	48
17	$Bi(OTf)_3$	10	H_2O	24 h	56
18	$Bi(OTf)_3$	10	THF[d]	24 h	28

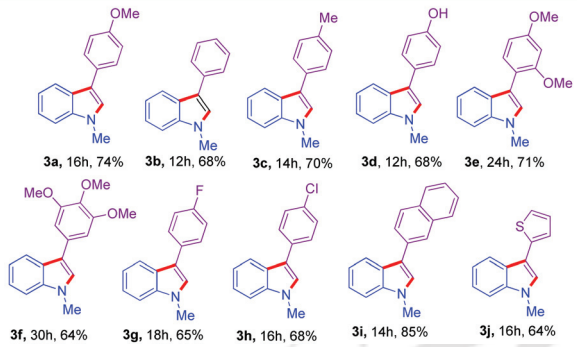
[a] All the reactions were performed using *N*-methylaniline **1a** (1.0 mmol) and (*E*)-1-methoxy-4-(2-nitrovinyl)benzene **2a** (1.0 mmol) at 80 °C. [b] Isolated yield. [c] Reaction performed at room temperature. [d] Reaction performed at 50 °C. NR (no desired product).

the efficacy of various metal triflates, as a catalyst for the synthesis of 3-arylindole derivatives, an identical reaction was performed with 10 mol% of $Yb(OTf)_3$, $Sc(OTf)_3$, AgOTf and $Cu(OTf)_2$. It was found that while $Yb(OTf)_3$ and $Sc(OTf)_3$ provided lower yields, other metal triflates were unproductive (Table 1, entries 5–8). In addition to the metal triflates, the same reaction was also explored with $Cu(OAc)_2$ and $FeCl_3$, but unfortunately, these catalysts for this particular reaction were found to be ineffective (Table 1, entries 9 and 10). The reaction was unsuccessful when it was performed at room temperature (Table 1, entry 11). Next, various polar solvents were also screened for a similar reaction in the presence of 10 mol% of $Bi(OTf)_3$, and it was found that most of these solvents gave either poor or no yield of the expected product (Table 1, entries 12–18). The best solvent was found to be acetonitrile. Thus it was concluded that 10 mol% of $Bi(OTf)_3$ in acetonitrile at 80 °C provided the best optimized reaction conditions to obtain 3-arylindole derivatives from *N*-methylaniline and (*E*)-1-methoxy-4-(2-nitrovinyl)benzene.

With the optimized conditions in hand, the scope of the protocol was investigated for the reaction of *N*-methylaniline **1a** with a series of various substituted *trans*-β-nitrostyrenes **2a–j** as represented in Table 2. The reaction was feasible for various *trans*-β-nitrostyrenes with electron-donating groups like 4-Me, 4-OH, 2,4-OMe, and 3,4,5-OMe as well as electron-

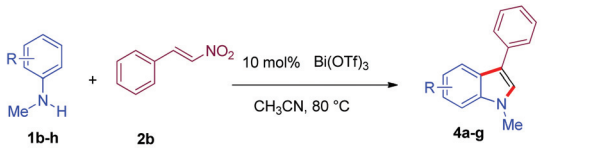
Table 2 Reaction of *N*-methylaniline with various *trans*-β-nitrostyrenes[a,b]

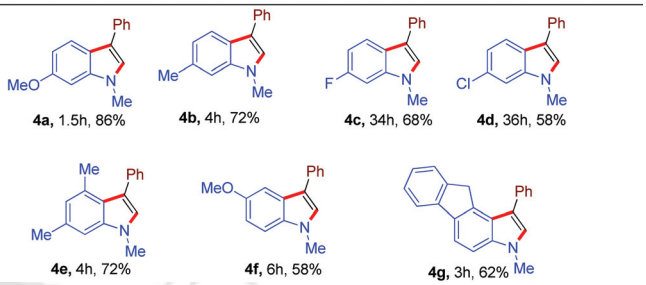




[a] The reactions were carried out using *N*-methylaniline **1a** (1 mmol), *trans*-β-nitrostyrenes **2a–j** (1 mmol), CH_3CN (2 mL) and $Bi(OTf)_3$ (10 mol%) at 80 °C. [b] Isolated yield.

Table 3 Substrate scope of various *N*-methylanilines with (*E*)-(2-nitrovinyl)benzene[a,b]





[a] The reactions were carried out using *N*-arylamines **1b–h** (1 mmol), (*E*)-(2-nitrovinyl)benzene **2b** (1 mmol), CH_3CN (1 mL) and $Bi(OTf)_3$ (10 mol%) at 80 °C. [b] Isolated yield.

withdrawing groups such as 4-F and 4-Cl giving the products **3a–h** in moderate to good yields. The best yield (85%) was obtained in the case of (*E*)-2-(2-nitrovinyl)naphthalene **3i**. In addition, it was found that (*E*)-2-(2-nitrovinyl)thiophene worked well under the same protocol, whereas (*E*)-2-(2-nitrovinyl)furan failed to give the desired product.

The strong electron-withdrawing groups such as 4-Br and 4-NO_2 on the phenyl ring of *trans*-β-nitrostyrene failed to give corresponding 3-arylindoles. (*E*)-(2-Nitroprop-1-en-1-yl) benzene failed to give 1,2-dimethyl-3-phenyl-1*H*-indole which may be due to steric crowding between the methyl groups of *N*-methylaniline and (*E*)-(2-nitroprop-1-en-1-yl)benzene.

To study the generality of the present protocol, the reactions were performed with various substituted *N*-methylanilines **1b–h** and (*E*)-(2-nitrovinyl)benzene **2b** as shown in Table 3. It was found that *N*-methylanilines having the electron-donating groups such as 3-OMe, 3-Me, 3,5-di-Me, and 4-OMe and the electron-withdrawing groups like 3-F and 3-Cl worked well giving the products **4a–f** in 58–86% yields. *m*-Anisidine imparts higher electron density on the π-electrons of the aryl ring to involve in the Michael addition to form the 3-arylindole product as compared to the *p*-anisidine group which was reflected in the sharp decrease of the yield from 86% to 58% in the case of **4a** and **4f**. To our delight the reaction proceeded smoothly with *N*-methyl-2-aminofluorene affording the product **4g** in 62% yield. The reason for the better yield in the case of **4b** may be due to the +M (mesomeric) effect of the 3-OMe group and the +I (inductive) effect of the *N*-methyl group which increase the nucleophilicity in a synergistic manner at the C6 position of 3-methoxy-*N*-methylaniline to enhance 1,4-addition. The reaction with electron-withdrawing group, such as 4-F, 4-Cl, and 4-Br, substituted *N*-methylanilines (**1i–k**) failed which might be due to low electron density on the aromatic ring and hence reluctance to form the C–C bond through 1,4-addition with *trans*-β-nitrostyrene.

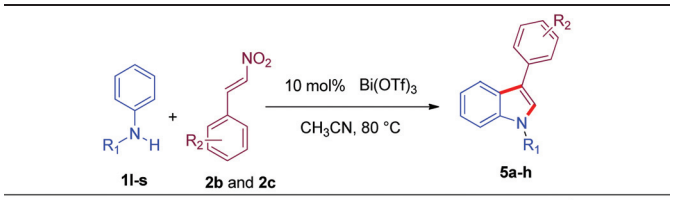
Next, the present procedure was further extended for the synthesis of 1-substituted-3-phenyl-1*H*-indole derivatives using various *N*-substituted anilines and *trans*-β-nitrostyrenes under the optimized reaction conditions to offer the corresponding products **5a–h** with 62–78% yields as depicted in Table 4. The electron-withdrawing groups such as *N*-tosyl and *N*-benzoyl anilines on reacting with *trans*-β-nitrostyrene failed to give the desired product due to low electron density at the *ortho* position of aniline to undergo 1,4-addition with *trans*-β-nitrostyrene.

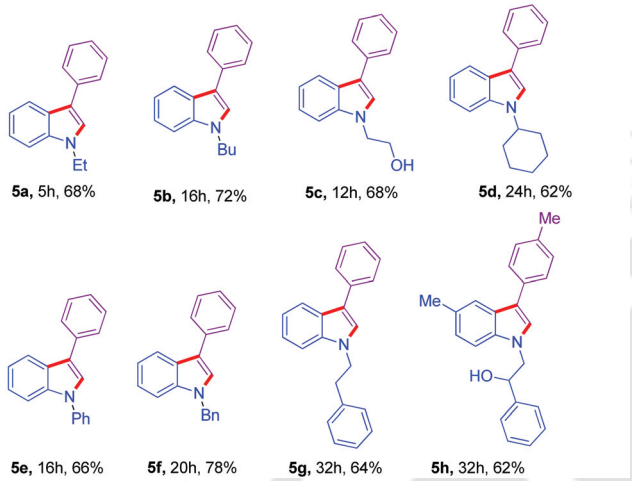
Under similar reaction conditions, a variety of anilines were converted to the corresponding 3-phenyl-1*H*-indoles **6a–g** with 68–90% yields. The anilines having electron-donating groups such as 3-OMe, 2,4-Me, 3,5-OMe and 3,4-(methylenedioxy) were well tolerated. 3-Fluoroaniline on reacting with *trans*-β-nitrostyrene gave the product **6e**. Similarly, the reaction worked well with 1-naphthylamine and 2-naphthylamines, and the successful results are illustrated in Table 5.

But the reaction completely failed to offer the desired product with 4-F/4-Cl/4-Br aniline. Thus, it may be concluded that when electron-withdrawing groups are present at the *para* position of aniline, the reaction is unsuccessful due to low electron density on the π-electrons of the aryl ring to participate in 1,4-addition with *trans*-β-nitrostyrene to form the corresponding 3-arylindole derivative. The synthesized compound **6e** is an inhibitor of brassinin glucosyltransferase[19] as shown in Fig. 1.

Furthermore, the reaction conditions were fruitfully applied for the reaction of *m*-anisidine **1aa** with various *trans*-β-nitrostyrenes **2** having electron-donating groups as well as electron-withdrawing groups on the phenyl ring of *trans*-β-nitrostyrene, whereas (*E*)-(2-nitroprop-1-en-1-yl)benzene on reacting with *m*-anisidine gave 6-methoxy-2-methyl-3-phenyl-

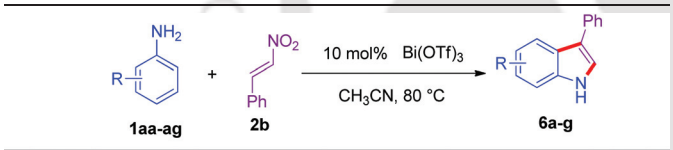
Table 4 Reaction of various *N*-substituted anilines with *trans*-β-nitrostyrene[a,b]

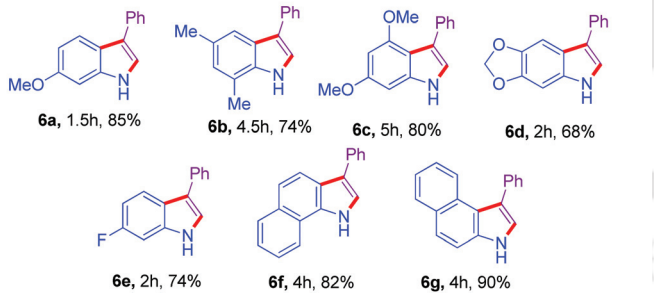




[a] The reactions were carried out using *N*-substituted anilines **1l–s** (1 mmol), *trans*-β-nitrostyrenes **2b** and **2c** (1 mmol), CH_3CN (1 mL) and $Bi(OTf)_3$ (10 mol%) at 80 °C. [b] Isolated yield.

Table 5 Reaction of various arylamines with *trans*-β-nitrostyrene[a,b]



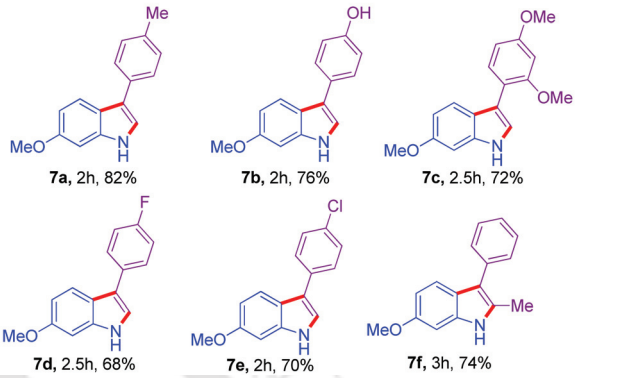


[a] The reactions were carried out using various arylamines **1aa–ag** (1 mmol), (*E*)-(2-nitrovinyl)benzene **2b** (1 mmol), CH_3CN (2 mL) and $Bi(OTf)_3$ (10 mol%) at 80 °C. [b] Isolated yield.

1*H*-indole **7f** as shown in Table 6. The yield obtained in these reactions was quite good. We did not observe the formation of other isomer products when the reaction was performed with *meta*-substituted anilines and *trans*-β-nitrostyrenes.

Finally, the scale-up procedure was investigated using *N*-ethylaniline **1l** (10 mmol) and (*E*)-1-methyl-4-(2-nitrovinyl) benzene **2c** (10 mmol) which resulted in the formation of the product **5i** in 64% yield as shown in Scheme 2.

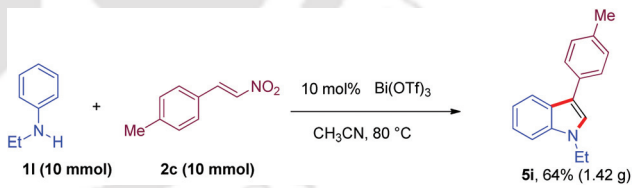
Table 6 Reaction of *m*-anisidine with various *trans*-β-nitrostyrenes[a,b]



[a] The reactions were carried out using *m*-anisidine **1aa** (1 mmol), various *trans*-β-nitrostyrenes **2** (1 mmol), CH_3CN (2 mL), and $Bi(OTf)_3$ (10 mol%) at 80 °C. [b] Isolated yield.

All the synthesized compounds **3–7** were characterized using IR, ^1H NMR, ^{13}C NMR spectra and HRMS. In addition, the structure of compound **3h** was confirmed through the single X-ray crystallographic data (Fig. 2).

In general, the aniline derivatives undergo aza-Michael addition[20] to *trans*-β-nitrostyrene to form (N–C bond) an aza-



Scheme 2 Gram-scale synthesis.

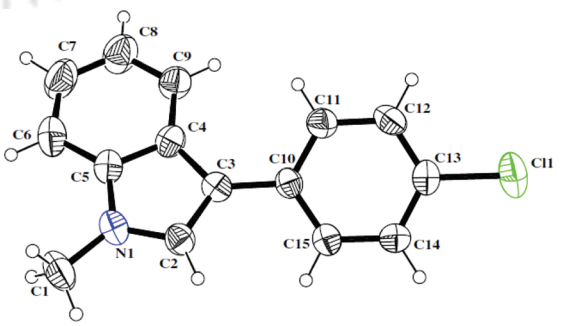
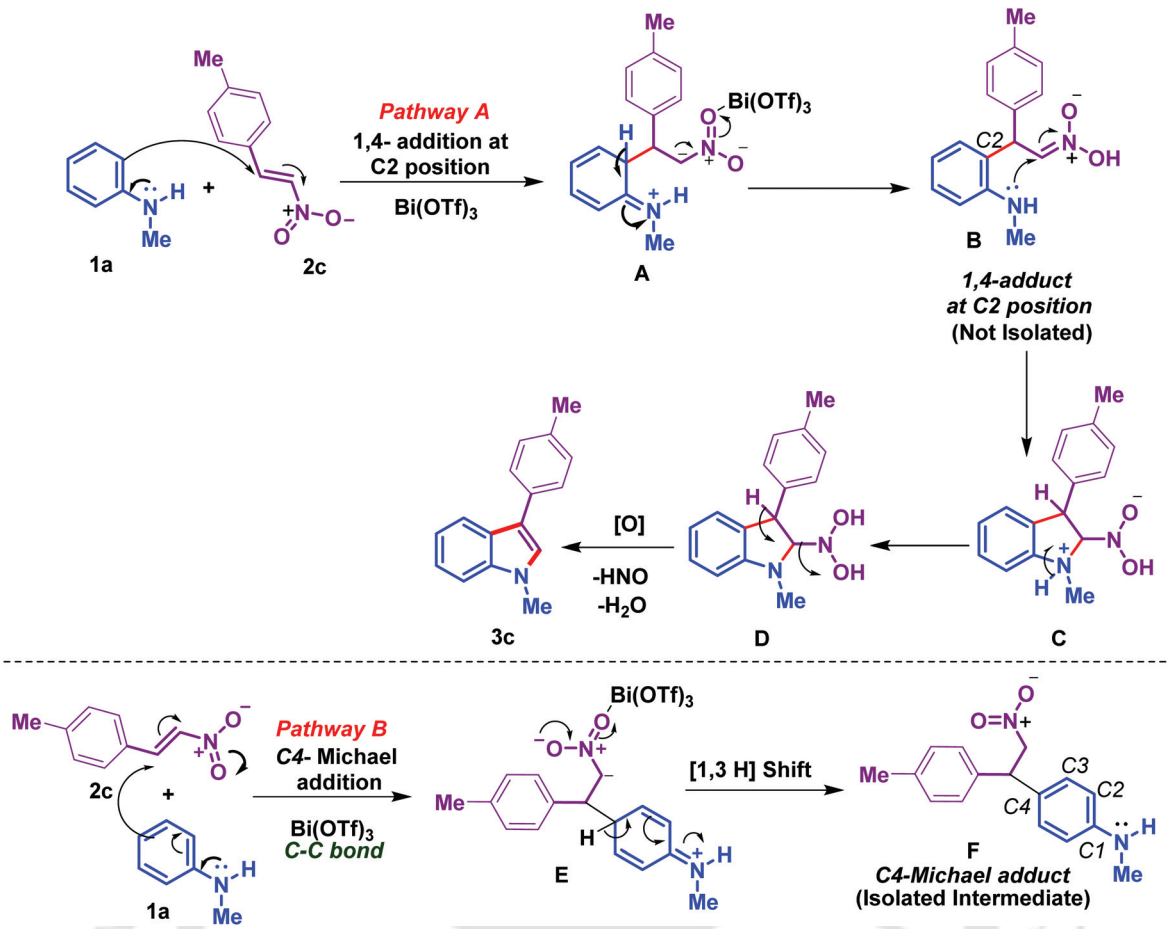


Fig. 2 ORTEP diagram of compound **3h** with 40% ellipsoid probability (CCDC no. 1576147‡).



Scheme 3 Proposed mechanism for the synthesis of 3-arylindole derivatives.

Michael adduct. It was observed that the presence of the alkyl group on the nitrogen atom of aniline or the electron-donating group on the arene ring of anilines favours 1,4 addition (C–C bond) rather than aza-Michael addition.

The proposed mechanism for the formation of *N*-methyl 3-arylindoles from *N*-methylaniline **1a** and (*E*)-1-methyl-4-(2-nitrovinyl)benzene **2c** in the presence of the $Bi(OTf)_3$ catalyst in acetonitrile at 80 °C is shown in Scheme 3. Initially, *N*-methylaniline undergoes 1,4-addition at the C2 position as well as at the C4 position with (*E*)-1-methyl-4-(2-nitrovinyl) benzene to furnish 1,4-adduct **B** and **F** through pathway A and pathway B, respectively. The 1,4-adduct **B** subsequently undergoes concomitant cyclisation to form **C**, followed by aromatization to afford the desired product **3c**, whereas, through pathway B intermediate **F** does not involve in cyclisation and was isolated in 12% yield.

Conclusions

In summary, the +I (inductive) and +M (mesomeric) effects of the alkyl and alkoxy groups which are present on the aromatic ring of aniline or the nitrogen atom of aniline increases the nucleophilicity at the *ortho* position of aniline which ultimately prefers 1,4-addition to *trans*-β-nitrostyrenes instead of aza-Michael addition. Consequently, 3-arylindoles/*N*-substituted 3-arylindoles can be accomplished easily in good yields with a wide substrate scope using inexpensive $Bi(OTf)_3$ as a catalyst. Our protocol is also applicable for the synthesis of biologically active compound **6e** which acts as an inhibitor of Brassinin glucosyltransferase. To the best of our knowledge, this is the first report of $Bi(OTf)_3$ catalyzed synthesis of 3-arylindole derivatives from arylamines and *trans*-β-nitrostyrenes.

Experimental

General information and methods

Melting points were determined on melting point apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on 400, 600, 75, 100 and 150 MHz NMR spectrometers. With TMS as an internal reference, chemical shifts (δ scale) are reported in parts per million (ppm). ^1H NMR spectra are reported in the order: multiplicity, coupling constant (J value) in hertz (Hz) and no. of protons; signals were characterized as s (singlet), d (doublet), t (triplet), m (multiplet) and bs (broad).

TH-1951_126122011

IR spectra were recorded on an IR spectrophotometer. HRMS spectra were recorded using a TOF mass analyser. The X-ray crystal structure was determined using a single XRD diffractometer.

General procedure for the synthesis of *N*-alkyl/aryl 3-arylindoles 3, 4 and 5

Into a dry 10 mL round bottomed flask a mixture of *N*-alkyl aniline **1a** (1.0 mmol) and *trans*-β-nitrostyrene **2** (1.0 mmol) was taken in 2 mL acetonitrile followed by the addition of bismuth(III) triflate (0.065 g, 0.10 mmol) and the reaction mixture was stirred at 80 °C in an oil bath. The progress of the reaction was monitored by TLC. After the completion of the reaction, the solvent was removed on a rotatory evaporator and treated with an aqueous layer to dissolve the salts and the organic compound was extracted with ethyl acetate (2 × 25 mL). The organic extract was dried over sodium sulfate and concentrated under reduced pressure. Finally, the crude residue was purified through silica gel (60–120 mesh) column chromatography with petroleum ether/ethyl acetate (9.8 : 0.2, v/v) to obtain the pure products **3**, **4** and **5**.

General procedure for the synthesis of 3-arylindoles 6 and 7

To a mixture of aryl amine **1aa** (1.0 mmol), *trans*-β-nitrostyrene **2** (1.0 mmol), and bismuth(III) triflate (0.065 g, 0.10 mmol), 2 mL acetonitrile was added and allowed to stir at 80 °C. The completion of the reaction was monitored by TLC. The solvent was removed under reduced pressure, the residue was treated with an aqueous layer to dissolve the salts and the compound was extracted with ethyl acetate (2 × 25 mL). The organic layer was dried over sodium sulfate and concentrated under reduced pressure. Finally, the crude reaction mixture was purified through silica gel (60–120 mesh) column chromatography with petroleum ether/ethyl acetate (9.5 : 0.5, v/v) to obtain the pure products **6** and **7**.

The synthesised compounds **3d**, **3e**, **4a–4e**, **4g**, **5d**, **5g**, **5h**, **7b** and **7c** are new compounds and are not reported in the literature.

3-(4-Methoxyphenyl)-1-methyl-1*H*-indole (3a).[9a] Yield 74% (176 mg), light yellow solid, mp 95–96 °C, ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.89 (d, J = 8.0 Hz, 1H), 7.59–7.55 (m, 2H), 7.36 (d, J = 8.2 Hz, 1H), 7.28 (dd, J = 7.1, 0.9 Hz, 1H), 7.19–7.16 (m, 1H), 7.16 (s, 1H), 7.01–6.98 (m, 2H), 3.86 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 158.1, 137.6, 128.7, 128.4, 126.5, 126.1, 122.1, 120.0, 119.9, 116.6, 114.5, 109.6, 55.6, 33.0; IR (KBr) ν_{max} 3055, 2923, 2852, 1601, 1488, 1372, 1132, 1034, 861 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{16}NO$ 238.1226 (M + H$^+$); found 238.1229.

1-Methyl-3-phenyl-1*H*-indole (3b).[9a] Yield 68% (141 mg), light yellow solid, mp 64–65 °C, ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.96 (d, J = 8.0 Hz, 1H), 7.67 (d, J = 7.8 Hz, 2H), 7.45 (t, J = 7.7 Hz, 2H), 7.38 (d, J = 8.2 Hz, 1H), 7.32–7.27 (m, 2H), 7.25 (s, 1H), 7.20 (t, J = 7.5 Hz, 1H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.8, 135.9, 128.9, 127.5, 126.7, 125.9, 122.2, 120.1, 120.1, 117.0, 109.7, 32.9; IR (KBr) ν_{max} 3049, 2929, 1718, 1603, 1550, 1483, 1262, 1016, 939 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{14}N$ 208.1121 (M + H$^+$); found 208.1126.

1-Methyl-3-(*p*-tolyl)-1*H*-indole (3c).[9a] Yield 70% (155 mg), light yellow solid, mp 63–64 °C, ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.83 (d, J = 8.0 Hz, 1H), 7.46 (d, J = 7.9 Hz, 2H), 7.27 (d, J = 8.2 Hz, 1H), 7.19 (d, J = 7.1 Hz, 1H), 7.16 (d, J = 6.4 Hz, 2H), 7.11 (s, 1H), 7.08 (dd, J = 7.9, 7.1 Hz, 1H), 3.74 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 137.6, 135.5, 132.9, 129.7, 127.5, 126.5, 126.4, 122.1, 120.2, 119.9, 116.9, 109.7, 33.1, 21.4; IR (KBr) ν_{max} 3051, 2928, 2856, 1614, 1485, 1365, 1038, 857 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{16}NO$ 222.1277 (M + H$^+$); found 222.1278.

4-(1-Methyl-1*H*-indol-3-yl)phenol (3d). Yield 68% (152 mg), colourless semi-solid, ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.90 (d, J = 8.0 Hz, 1H), 7.56–7.52 (m, 2H), 7.38 (d, J = 8.2 Hz, 1H), 7.30 (dd, J = 7.0, 1.0 Hz, 1H), 7.20 (m, 1H), 7.18 (s, 1H), 6.96–6.92 (m, 2H), 3.86 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 154.0, 137.5, 128.9, 128.6, 126.4, 126.1, 122.1, 120.0, 119.8, 116.6, 115.9, 109.7, 33.0; IR (KBr) ν_{max} 3491, 2923, 2853, 1550, 1468, 1375, 1187, 1017, 924 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{14}NO$ 224.1070 (M + H$^+$); found 224.1078.

3-(2,4-Dimethoxyphenyl)-1-methyl-1*H*-indole (3e). Yield 71% (189 mg), light yellow semi-solid, ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.73 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 8.2 Hz, 1H), 7.34 (d, J = 8.2 Hz, 1H), 7.29 (s, 1H), 7.26–7.22 (m, 1H), 7.15–7.11 (m, 1H), 6.61 (t, J = 2.6 Hz, 1H), 6.61–6.58 (m, 1H), 3.87 (s, 3H), 3.84 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.4, 157.8, 137.0, 131.0, 128.4, 127.4, 121.7, 120.7, 119.5, 117.3, 111.7, 109.5, 104.5, 99.3, 55.7, 33.0; IR (KBr) ν_{max} 3049, 2936, 2843, 1669, 1604, 1475, 1183, 1008, 928 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{18}NO_2$ 268.1332 (M + H$^+$); found 268.1332.

1-Methyl-3-(3,4,5-trimethoxyphenyl)-1*H*-indole (3f).[21c] Yield 64% (190 mg), colourless semi-solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, J = 8.1 Hz, 1H), 7.38 (d, J = 8.5 Hz, 1H), 7.30 (t, J = 7.6 Hz, 1H), 7.22 (s, 1H), 7.20 (s, 1H), 6.86 (s, 2H), 3.94 (s, 6H), 3.91 (s, 3H), 3.86 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 153.7, 137.6, 136.6, 131.6, 126.6, 126.3, 122.3, 120.2, 119.9, 117.1, 109.8, 104.8, 61.2, 56.4, 33.1; IR (KBr) ν_{max} 3050, 2934, 2843, 1672, 1567, 1463, 1125, 1055, 925 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{20}NO_3$ 298.1438 (M + H$^+$); found 298.1438.

3-(4-Fluorophenyl)-1-methyl-1*H*-indole (3g).[21b] Yield 65% (146 mg), white solid, mp 72–73 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, J = 8.0 Hz, 1H), 7.49 (dd, J = 8.3, 5.5 Hz, 2H), 7.26 (d, J = 8.2 Hz, 1H), 7.19 (t, J = 7.5 Hz, 1H), 7.10 (t, J = 7.5 Hz, 1H), 7.06 (s, 1H), 7.03 (t, J = 8.6 Hz, 2H), 3.71 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.1, 159.8, 137.5, 131.8, 131.8, 128.9, 128.8, 126.5, 126.2, 122.2, 120.1, 119.8, 115.9, 115.6, 109.8, 33.0; IR (KBr) ν_{max} 3048, 2924, 2852, 1568, 1397, 1071, 924 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{13}FN$ 226.1027 (M + H$^+$); found 226.1028.

3-(4-Chlorophenyl)-1-methyl-1*H*-indole (3h).[9a] Yield 68% (163 mg), light brown solid, mp 95–96 °C, ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.81 (d, J = 8.0 Hz, 1H, H-4), 7.51 (d, J = 8.4 Hz, 2H, H-3′ & H-5′), 7.32 (d, J = 8.4 Hz, 2H, H-2′ & H-6′), 7.30 (d, J = 8.4 Hz, 1H, H-7), 7.22 (t, J = 7.6 Hz, 1H, H-6), 7.16 (s, 1H, H-2), 7.13 (t, J = 7.5 Hz, 1H, H-5); ^{13}C NMR (150 MHz, $CDCl_3$):

δ 137.6 (C9), 134.3 (C4′), 131.4 (C1′), 129.1 (C2′ & C6′), 128.6 (C3′ & C5′), 126.8 (C2), 126.1 (C8), 122.3 (C6), 120.3 (C5), 119.8 (C4), 115.7 (C3), 109.8 (C7), 33.2 (CH_3); IR (KBr) ν_{max} 3049, 2922, 2852, 1568, 1398, 1289, 996, 972 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{13}ClN$ 242.0731 ($M + H^+$); found 242.0741.

1-Methyl-3-(naphthalen-2-yl)-1*H*-indole (3i).[9a] Yield 85% (219 mg), colourless semi-solid, ^1H NMR (600 MHz, $CDCl_3$): δ 8.14 (s, 1H), 8.09 (d, J = 8.0 Hz, 1H), 7.92 (d, J = 8.5 Hz, 1H), 7.89 (dd, J = 16.5, 8.1 Hz, 2H), 7.83 (dd, J = 8.4, 1.7 Hz, 1H), 7.53–7.49 (m, 1H), 7.46 (td, J = 7.5, 6.9, 1.2 Hz, 1H), 7.43 (d, J = 8.2 Hz, 1H), 7.39 (s, 1H), 7.36–7.32 (m, 1H), 7.27–7.25 (m, 1H), 3.91 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 137.8, 134.2, 133.4, 132.1, 128.4, 127.9, 127.9, 127.2, 126.6, 126.5, 126.3, 125.3, 125.1, 122.3, 120.2, 120.2, 116.8, 109.8, 33.1; IR (KBr) ν_{max} 3051, 2957, 2853, 1629, 1478, 1240, 1016, 857 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{16}N$ 258.1277 ($M + H^+$); found 258.1275.

1-Methyl-3-(thiophen-2-yl)-1*H*-indole (3j).[21a] Yield 64% (129 mg), light green liquid, ^1H NMR (600 MHz, $CDCl_3$): δ 7.98 (dd, J = 7.9, 1.0 Hz, 1H), 7.36 (dd, J = 8.2, 1.0 Hz, 1H), 7.30 (d, J = 1.9 Hz, 2H), 7.26–7.25 (m, 1H), 7.23 (dd, J = 7.8, 1.1 Hz, 1H), 7.22–7.20 (m, 1H), 7.13–7.10 (m, 1H), 3.83 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.8, 137.2, 127.5, 126.5, 125.8, 122.2, 122.1, 122.0, 120.1, 120.0, 110.3, 109.5, 32.8; IR (KBr) ν_{max} 3054, 2922, 2851, 1566, 1370, 1188, 1016, 924 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{12}NS$ 214.0685 ($M + H^+$); found 214.0691.

6-Methoxy-1-methyl-3-phenyl-1*H*-indole (4a). Yield 86% (203 mg), yellow semi-solid, ^1H NMR (600 MHz, $CDCl_3$): δ 7.83 (d, J = 8.7 Hz, 1H), 7.65 (dd, J = 8.2, 1.3 Hz, 2H), 7.46–7.42 (m, 2H), 7.29–7.26 (m, 1H), 7.14 (s, 1H), 6.88 (dd, J = 8.7, 2.3 Hz, 1H), 6.82 (d, J = 2.3 Hz, 1H), 3.92 (s, 3H), 3.79 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 156.7, 138.4, 135.9, 128.9, 127.3, 125.8, 125.5, 120.9, 120.7, 116.9, 109.9, 93.2, 55.9, 33.1; IR (KBr) ν_{max} 3049, 2928, 2859, 1611, 1558, 1067, 1021, 987 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{16}NO$ 238.1226 ($M + H^+$); found 238.1229.

1,6-Dimethyl-3-phenyl-1*H*-indole (4b). Yield 72% (159 mg), yellow semi-solid, ^1H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, J = 8.1 Hz, 1H), 7.72–7.62 (m, 2H), 7.44 (t, J = 7.8 Hz, 2H), 7.30–7.25 (m, 1H), 7.17 (d, J = 3.4 Hz, 2H), 7.04 (d, J = 8.2 Hz, 1H), 3.81 (s, 3H), 2.54 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.0, 136.0, 132.0, 128.9, 127.3, 126.1, 125.7, 124.1, 121.8, 119.8, 116.6, 109.7, 32.9, 22.1; IR (KBr) ν_{max} 3058, 2921, 2858, 2252, 1602, 1552, 1383, 1028, 967 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{16}N$ 222.1277 ($M + H^+$); found 222.1279.

6-Fluoro-1-methyl-3-phenyl-1*H*-indole (4c). Yield 68% (153 mg), brown semi-solid, ^1H NMR (600 MHz, $CDCl_3$) δ 7.84 (dd, J = 8.8, 5.3 Hz, 1H), 7.64–7.60 (m, 2H), 7.46–7.41 (m, 2H), 7.31–7.26 (m, 1H), 7.21 (s, 1H), 7.03 (dd, J = 9.7, 2.3 Hz, 1H), 6.95 (ddd, J = 9.4, 8.7, 2.3 Hz, 1H), 3.79 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 160.9, 159.4, 137.8, 137.7, 135.4, 129.0, 127.5, 126.9, 126.9, 126.2, 122.9, 121.0, 120.9, 117.2, 108.8, 108.7, 96.2, 95.9, 33.2; IR (KBr) ν_{max} 3046, 2924, 2852, 1608, 1560, 1016, 996 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{13}FN$ 226.1027 ($M + H^+$); found 226.1015.

6-Chloro-1-methyl-3-phenyl-1*H*-indole (4d). Yield 58% (139 mg), colourless semi-solid, ^1H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, J = 8.5 Hz, 1H), 7.65–7.59 (m, 2H), 7.45 (t, J = 7.7 Hz, 2H), 7.36 (d, J = 1.9 Hz, 1H), 7.29 (t, J = 7.4 Hz, 1H), 7.22 (s, 1H), 7.16 (dd, J = 8.5, 1.9 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.0, 135.2, 129.0, 128.2, 127.5, 127.3, 126.2, 124.9, 121.1, 120.7, 117.2, 109.8, 33.2; IR (KBr) ν_{max} 3054, 2928, 2859, 1645, 1491, 1184, 1069, 956 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{13}ClN$ 242.0731 ($M + H^+$); found 242.0740.

1,4,6-Trimethyl-3-phenyl-1*H*-indole (4e). Yield 72% (169 mg), light yellow semi-solid, ^1H NMR (400 MHz, $CDCl_3$): δ 7.56–7.49 (m, 2H), 7.45 (tdd, J = 7.7, 2.1, 1.2 Hz, 2H), 7.42–7.35 (m, 1H), 7.09 (s, 1H), 6.97 (d, J = 1.4 Hz, 1H), 6.83 (s, 1H), 3.82 (d, J = 1.2 Hz, 3H), 2.56 (d, J = 2.2 Hz, 3H), 2.36 (d, J = 2.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.6, 137.3, 131.8, 131.1, 130.7, 127.7, 127.3, 126.3, 123.7, 123.2, 118.2, 107.2, 32.8, 21.8, 20.9; IR (KBr) ν_{max} 3058, 2921, 2858, 2252, 1602, 1552, 1085, 967 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{18}N$ 236.1434 ($M + H^+$); found 236.1438.

5-Methoxy-1-methyl-3-phenyl-1*H*-indole (4f).[21d] Yield 58% (138 mg), light yellow semi-solid, ^1H NMR (600 MHz, $CDCl_3$): δ 7.68–7.63 (m, 2H), 7.49–7.43 (m, 2H), 7.41 (d, J = 2.5 Hz, 1H), 7.29 (d, J = 8.0 Hz, 1H), 7.27 (d, J = 2.3 Hz, 1H), 7.22 (s, 1H), 6.97 (dd, J = 8.9, 2.4 Hz, 1H), 3.89 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 154.8, 136.0, 133.1, 129.0, 127.4, 127.4, 126.6, 125.8, 116.5, 112.4, 110.5, 101.9, 56.3, 33.3; IR (KBr) ν_{max} 3052, 2924, 2853, 1608, 1466, 1177, 996 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{16}NO$ 238.1226 ($M + H^+$); found 238.1236.

3-Methyl-1-phenyl-3,10-dihydroindeno[2,1-*e*]indole (4g). Yield 62% (182 mg), white solid, mp 202–203 °C, ^1H NMR (400 MHz, $CDCl_3$): δ 8.30 (s, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.74 (d, J = 8.0 Hz, 2H), 7.54–7.48 (m, 4H), 7.39 (t, J = 8.0 Hz, 1H), 7.32 (t, J = 8.0 Hz, 1H), 7.28–7.23 (m, 2H), 4.04 (s, 2H), 3.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.1, 142.7, 138.5, 137.9, 135.8, 134.9, 128.8, 127.4, 126.6, 125.7, 125.6, 124.8, 125.1, 119.3, 116.9, 110.5, 105.9, 36.7, 33.10; IR (KBr) ν_{max} 3057, 2956, 2869, 1642, 1548, 1368, 1062, 962 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{18}N$ 296.1434 ($M + H^+$); found 296.1426.

11-Ethyl-3-phenyl-1*H*-indole (5a).[21e] Yield 68% (150 mg), yellow semi-solid, mp 77–78 °C, ^1H NMR (600 MHz, $CDCl_3$): δ 7.98 (d, J = 8.0 Hz, 1H), 7.72–7.66 (m, 2H), 7.46 (t, J = 7.7 Hz, 2H), 7.41 (d, J = 8.2 Hz, 1H), 7.32 (s, 1H), 7.28 (dd, J = 11.5, 4.5 Hz, 2H), 7.21 (dd, J = 11.0, 4.0 Hz, 1H), 4.24 (q, J = 7.3 Hz, 2H), 1.53 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 136.6, 135.9, 128.9, 127.5, 126.4, 125.8, 125.0, 122.0, 120.2, 120.0, 116.9, 109.8, 41.22, 15.68; IR (KBr) ν_{max} 3051, 2957, 2867, 1619, 1466, 1365, 1068, 957 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{16}N$ 222.1277 ($M + H^+$); found 222.1267.

1-Butyl-3-phenyl-1*H*-indole (5b).[21f] Yield 72% (179 mg), yellow semi-solid, ^1H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 8.0 Hz, 1H), 7.68 (dt, J = 8.1, 1.3 Hz, 2H), 7.45 (td, J = 7.8, 1.4 Hz, 2H), 7.40 (d, J = 8.1 Hz, 1H), 7.29 (s, 1H), 7.29–7.24 (m, 2H), 7.22–7.16 (m, 1H), 4.17 (t, J = 7.1 Hz, 2H), 1.97–1.82 (m, 2H), 1.40 (q, J = 7.5 Hz, 2H), 0.97 (td, J = 7.3, 1.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 136.9, 135.9, 128.9, 127.5, 126.4, 125.8, 121.9, 120.2, 119.9, 116.7, 109.9, 46.4, 32.5, 20.4, 13.9;

IR (KBr) ν_{max} 3054, 2962, 2857, 1602, 1289, 996 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{20}N$ 250.1590 ($M + H^+$); found 250.1589.

2-(3-Phenyl-1*H*-indol-1-yl)ethanol (5c). Yield 68% (161 mg), colourless semi-solid, ^1H NMR (600 MHz, $CDCl_3$): δ 7.96 (dt, J = 8.0, 1.0 Hz, 1H), 7.69–7.64 (m, 2H), 7.46–7.43 (m, 2H), 7.43–7.41 (m, 1H), 7.36 (s, 1H), 7.28 (m, 2H), 7.20 (m, 1H), 4.34 (t, J = 5.3 Hz, 2H), 4.02 (t, J = 5.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 136.9, 135.5, 128.9, 127.4, 126.4, 126.3, 125.9, 122.2, 120.3, 120.2, 117.1, 109.9, 61.8, 48.8; IR (KBr) ν_{max} 3021, 2920, 2836, 1708, 1632, 1355, 1111, 996 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{16}NO$ 238.1226 ($M + H^+$); found 238.1245.

1-Cyclohexyl-3-phenyl-1*H*-indole (5d). Yield 62% (170 mg), colourless semi-solid, ^1H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, J = 7.9 Hz, 1H), 7.53 (dd, J = 8.0, 1.4 Hz, 2H), 7.33–7.26 (m, 3H), 7.26 (s, 1H), 7.14–7.09 (m, 2H), 7.06–7.00 (m, 1H), 4.19–4.06 (m, 1H), 2.06 (d, J = 12.5 Hz, 2H), 1.90–1.76 (m, 2H), 1.62 (dt, J = 12.6, 8.9 Hz, 2H), 1.41 (d, J = 3.4 Hz, 2H), 1.24–1.13 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 136.5, 136.1, 128.9, 127.5, 126.3, 125.8, 122.2, 121.8, 120.2, 120.0, 116.9, 109.9, 53.3, 33.79, 26.2, 25.8; IR (KBr) ν_{max} 3042, 2938, 2842, 1638, 1384, 1298, 1016, 978 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{22}N$ 276.1747 ($M + H^+$); found 276.1751.

1,3-Diphenyl-1*H*-indole (5e).[8c] Yield 66% (177 mg), white solid, mp 103–104 °C, ^1H NMR (400 MHz, $CDCl_3$): 8.01 (dd, J = 6.9, 1.9 Hz, 1H), 7.77–7.71 (m, 2H), 7.65–7.61 (m, 1H), 7.57 (d, J = 1.8 Hz, 3H), 7.54 (d, J = 11.0 Hz, 2H), 7.49 (t, J = 7.7 Hz, 2H), 7.40 (tt, J = 6.2, 2.2 Hz, 1H), 7.36–7.31 (m, 1H), 7.31–7.25 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.7, 136.8, 135.3, 129.9, 129.0, 127.8, 127.3, 126.9, 126.4, 125.7, 124.7, 123.0, 121.1, 120.3, 119.3, 111.0; IR (KBr) ν_{max} 3056, 2921, 2851, 1598, 1018, 999 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{16}N$ 270.1277 ($M + H^+$); found 270.1278.

1-Benzyl-3-phenyl-1*H*-indole (5f).[21e] Yield 78% (221 mg), white solid, mp 105–106 °C, ^1H NMR (400 MHz, $CDCl_3$): δ 8.02 (dd, J = 7.1, 1.7 Hz, 1H), 7.74–7.68 (m, 2H), 7.47 (t, J = 7.6 Hz, 2H), 7.39–7.29 (m, 6H), 7.29–7.26 (m, 1H), 7.24 (dd, J = 7.6, 1.6 Hz, 1H), 7.22–7.17 (m, 2H), 5.37 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.4, 137.3, 135.7, 129.0, 128.9, 127.9, 127.6, 127.1, 126.6, 126.1, 126.0, 122.3, 120.3, 120.2, 117.5, 110.2, 50.3; IR (KBr) ν_{max} 3059, 2922, 2853, 1601, 1546, 1259, 1181, 1000, 970 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{18}NS$ 284.1434 ($M + H^+$); found 284.1434.

1-Phenethyl-3-phenyl-1*H*-indole (5g). Yield 64% (190 mg), colourless semi-solid, ^1H NMR (600 MHz, $CDCl_3$): δ 7.98 (dt, J = 8.0, 1.0 Hz, 1H), 7.65–7.61 (m, 2H), 7.45 (t, J = 7.7 Hz, 2H), 7.42 (dd, J = 8.2, 0.9 Hz, 1H), 7.34–7.29 (m, 3H), 7.28 (d, J = 7.8 Hz, 2H), 7.22 (m, 1H), 7.17–7.13 (m, 2H), 7.12 (s, 1H), 4.43–4.40 (m, 2H), 3.18 (t, J = 7.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.6, 136.7, 135.8, 129.0, 128.9, 128.9, 127.5, 126.9, 126.5, 125.9, 122.1, 120.3, 120.1, 116.9, 109.8, 48.4, 36.9; IR (KBr) ν_{max} 3054, 2982, 2852, 1655, 1545, 1018, 998 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{20}NS$ 298.1590 ($M + H^+$); found 298.1595.

2-(5-Methyl-3-(*p*-tolyl)-1*H*-indol-1-yl)-1-phenylethanol (5h). Yield 62% (211 mg), white solid, mp 80–81 °C, ^1H NMR (600 MHz, $CDCl_3$): δ 7.64 (s, 1H), 7.45 (d, J = 8.0 Hz, 2H), 7.36–7.30 (m, 4H), 7.29–7.27 (m, 1H), 7.26 (d, J = 8.4 Hz, 1H), 7.18 (d, J = 8.1 Hz, 2H), 7.12 (s, 1H), 7.05–7.02 (m, 1H), 5.04 (dd, J = 8.3, 3.7 Hz, 1H), 4.29–4.20 (m, 2H), 2.41 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 141.2, 135.6, 135.5, 132.8, 129.6, 128.9, 128.5, 127.5, 126.9, 126.3, 126.1, 123.9, 119.9, 116.9, 109.6, 73.8, 54.6, 21.8, 21.4; IR (KBr) ν_{max} 3054, 2982, 2852, 1655, 1114, 1018, 998 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{24}NO$ 342.1852 ($M + H^+$); found 342.1865.

6-Methoxy-3-phenyl-1*H*-indole (6a).[21g] Yield 85% (187 mg), brown colour semi-solid, ^1H NMR (600 MHz, $CDCl_3$): δ 8.17–8.07 (m, 1H), 7.84 (d, J = 8.7 Hz, 1H), 7.73–7.64 (m, 2H), 7.51–7.42 (m, 2H), 7.33–7.30 (m, 1H), 7.29 (d, J = 2.3 Hz, 1H), 6.93 (d, J = 2.3 Hz, 1H), 6.90 (dd, J = 8.7, 2.3 Hz, 1H), 3.90 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 156.8, 137.7, 135.8, 128.9, 127.5, 126.1, 120.7, 120.7, 120.3, 118.5, 110.5, 94.9, 55.9; IR (KBr) ν_{max} 3056, 2850, 1568, 1532, 1018, 997 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{14}NO$ 224.1070 ($M + H^+$); found 224.1072.

5,7-Dimethyl-3-phenyl-1*H*-indole (6b).[21h] Yield 74% (163 mg), yellow colour semi-solid, ^1H NMR (600 MHz, $CDCl_3$): δ 8.08 (s, 1H), 7.71–7.66 (m, 2H), 7.60 (s, 1H), 7.46 (td, J = 7.7, 1.6 Hz, 2H), 7.33 (t, J = 2.2 Hz, 1H), 7.32–7.28 (m, 1H), 6.92 (s, 1H), 2.50 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 136.1, 134.7, 130.0, 128.9, 127.7, 126.0, 125.6, 124.8, 121.9, 120.4, 118.4, 117.2, 21.7, 16.7; IR (KBr) ν_{max} 3046, 2847, 1609, 1188, 1020, 996 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{16}N$ 222.1277 ($M + H^+$); found 222.1273.

4,6-Dimethoxy-3-phenyl-1*H*-indole (6c).[9b] Yield 80% (202 mg), colourless solid, mp 56–57 °C, ^1H NMR (600 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.66–7.59 (m, 2H), 7.37 (t, J = 7.7 Hz, 2H), 7.28–7.25 (m, 1H), 7.01 (dd, J = 2.4, 0.8 Hz, 1H), 6.50 (dd, J = 2.0, 0.9 Hz, 1H), 6.27 (d, J = 2.0 Hz, 1H), 3.85 (s, 3H), 3.80 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.8, 155.1, 138.5, 136.2, 129.7, 127.8, 125.8, 120.6, 119.2, 110.5, 92.4, 86.9, 55.8, 55.3; IR (KBr) ν_{max} 3048, 2959, 2840, 1706, 1625, 1047, 995 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{16}NO_2$ 254.1176 ($M + H^+$); found 254.1188.

7-Phenyl-5*H*-[1,3]dioxolo[4,5-*f*]indole (6d). Yield 68% (161 mg), brown colour solid, mp < 320 °C, ^1H NMR (400 MHz, $CDCl_3$): δ 8.11 (s, 1H), 7.65–7.58 (m, 2H), 7.45 (t, J = 7.7 Hz, 2H), 7.33 (d, J = 0.7 Hz, 1H), 7.32–7.27 (m, 1H), 7.22 (d, J = 2.5 Hz, 1H), 6.87 (d, J = 0.6 Hz, 1H), 5.97 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.3, 143.7, 135.7, 131.7, 128.9, 127.4, 126.1, 120.6, 119.8, 118.7, 100.9, 98.6, 92.3; IR (KBr) ν_{max} 3052, 2958, 2857, 1628, 1028, 978 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{12}NO_2$ 238.0863 ($M + H^+$); found 238.0850.

6-Fluoro-3-phenyl-1*H*-indole (6e).[8e] Yield 74% (200 mg), colourless solid, mp 45–46 °C, ^1H NMR (400 MHz, $CDCl_3$): δ 8.24 (s, 1H), 7.85 (dd, J = 8.8, 5.3 Hz, 1H), 7.69–7.62 (m, 2H), 7.47 (t, J = 7.6 Hz, 2H), 7.36–7.34 (m, 1H), 7.31 (d, J = 7.3 Hz, 1H), 7.11 (dd, J = 9.5, 2.3 Hz, 1H), 7.01–6.93 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 161.1, 159.5, 136.8, 136.7, 135.3, 129.0, 127.7, 126.4, 122.6, 122.1, 122.1, 120.9, 120.8, 118.7, 109.3, 109.2, 97.9, 97.7; IR (KBr) ν_{max} 3046, 2916, 2848, 1642, 1254, 1068, 992 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{11}FN$ 212.0870 ($M + H^+$); found 212.0878.

3-Phenyl-1*H*-benzo[*g*]indole (6f).[15a] Yield 82% (200 mg), colourless solid, mp 234–235 °C, ^1H NMR (400 MHz, $CDCl_3$):

δ 8.92 (s, 1H), 8.05–8.01 (m, 1H), 8.01–7.94 (m, 2H), 7.77–7.70 (m, 2H), 7.60 (d, J = 8.7 Hz, 1H), 7.55 (m, 1H), 7.53–7.46 (m, 3H), 7.40 (d, J = 2.6 Hz, 1H), 7.38–7.32 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 135.7, 131.5, 130.7, 129.0, 129.1, 127.9, 126.4, 125.8, 124.4, 121.9, 121.8, 121.5, 120.5, 120.1, 119.9, 119.6; IR (KBr) ν_{max} 3049, 2919, 2851, 1648, 1553, 1072, 1018, 998 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{14}N$ 244.1121 (M + H$^+$); found 244.1112.

1-Phenyl-3*H*-benzo[*e*]indole (6g).[15a] Yield 90% (219 mg), brown colour oily liquid, ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.43 (s, 1H), 8.18 (m, 1H), 7.95 (dd, J = 7.9, 1.6 Hz, 1H), 7.70–7.66 (m, 3H), 7.55–7.51 (m, 3H), 7.49–7.46 (m, 1H), 7.43–7.39 (m, 1H), 7.39–7.34 (m, 1H), 7.15 (d, J = 2.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.3, 132.9, 130.3, 129.9, 128.9, 128.8, 128.5, 126.9, 125.6, 123.9, 123.5, 123.4, 121.7, 121.3, 119.6, 113.1; IR (KBr) ν_{max} 3052, 2916, 2848, 1652, 1448, 1180, 992 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{14}N$ 244.1121 (M + H$^+$); found 244.1125.

6-Methoxy-3-(*p*-tolyl)-1*H*-indole (7a).[8e] Yield 82% (195 mg), brown semi-solid, ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.07 (s, 1H), 7.79 (d, J = 8.7 Hz, 1H), 7.57–7.54 (m, 2H), 7.25 (d, J = 7.6 Hz, 2H), 7.23 (d, J = 2.4 Hz, 1H), 6.91 (d, J = 2.2 Hz, 1H), 6.86 (dd, J = 8.7, 2.3 Hz, 1H), 3.87 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 156.8, 137.6, 135.7, 132.8, 129.6, 127.4, 120.7, 120.4, 120.3, 118.4, 110.3, 94.9, 55.9, 21.4; IR (KBr) ν_{max} 3056, 2850, 1568, 1532, 1187, 1018, 997 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{16}NO$ 238.1226 (M + H$^+$); found 238.1241.

4-(6-Methoxy-1*H*-indol-3-yl)phenol (7b). Yield 76% (182 mg), brown semi-solid, ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.06 (s, 1H), 7.74 (d, J = 8.7 Hz, 1H), 7.54–7.50 (m, 2H), 7.18 (d, J = 2.4 Hz, 1H), 6.91 (dd, J = 8.2, 2.0 Hz, 3H), 6.85 (dd, J = 8.7, 2.3 Hz, 1H), 3.87 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 155.1, 154.6, 136.9, 127.1, 126.3, 119.4, 119.2, 119.1, 115.9, 114.9, 108.7, 94.1, 54.7; IR (KBr) ν_{max} 3262, 2928, 2856, 1614, 1187, 1019, 998 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{14}NO_2$ 240.1019 (M + H$^+$); found 240.1020.

3-(2,4-Dimethoxyphenyl)-6-methoxy-1*H*-indole (7c). Yield 72% (203 mg), brown semi-solid, ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.61 (d, J = 8.7 Hz, 1H), 7.51 (d, J = 8.2 Hz, 1H), 7.32 (d, J = 2.4 Hz, 1H), 6.91 (d, J = 2.3 Hz, 1H), 6.83 (dd, J = 8.7, 2.3 Hz, 1H), 6.63 (d, J = 2.4 Hz, 1H), 6.62 (dd, J = 8.2, 2.5 Hz, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.85 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 159.5, 157.9, 156.6, 136.9, 130.9, 122.4, 121.4, 121.3, 117.3, 113.6, 109.9, 104.5, 99.3, 94.8, 55.9, 55.7, 55.7; IR (KBr) ν_{max} 3054, 2938, 2848, 2827, 1604, 1214, 1036, 978 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{18}NO_3$ 284.1281 (M + H$^+$); found 284.1298.

3-(4-Fluorophenyl)-6-methoxy-1*H*-indole (7d).[21c] Yield 68% (165 mg), brown liquid, ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.11 (s, 1H), 7.73 (dt, J = 8.7, 0.7 Hz, 1H), 7.63–7.56 (m, 2H), 7.21 (d, J = 2.4 Hz, 1H), 7.17–7.09 (m, 2H), 6.92 (d, J = 2.3 Hz, 1H), 6.87 (dd, J = 8.7, 2.3 Hz, 1H), 3.87 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 162.4, 160.8, 156.9, 137.6, 131.8, 131.8, 128.9, 128.9, 120.4, 120.4, 120.3, 117.6, 115.8, 115.7, 110.6, 94.9, 55.9; IR (KBr) ν_{max} 3052, 2957, 2868, 1652, 1269, 1048, 972 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{13}NO$ 242.0976 (M + H$^+$); found 242.0978.

3-(4-Chlorophenyl)-6-methoxy-1*H*-indole (7e).[8e] Yield 70% (181 mg), brown oily liquid, ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.23 (s, 1H), 7.71 (d, J = 8.7 Hz, 1H), 7.70–7.65 (m, 2H), 7.59 (d, J = 2.5 Hz, 1H), 7.46–7.41 (m, 2H), 6.95 (d, J = 2.3 Hz, 1H), 6.75 (dd, J = 8.7, 2.4 Hz, 1H), 3.78 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 155.8, 137.9, 134.9, 129.5, 128.8, 127.8, 122.6, 119.7, 119.1, 114.5, 110.1, 94.9, 55.3; IR (KBr) ν_{max} 3050, 2994, 2935, 2833, 1647, 1091, 968 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{13}ClNO$ 258.0680 (M + H$^+$); found 258.0673.

6-Methoxy-2-methyl-3-phenyl-1*H*-indole (7f).[21i] Yield 74% (175 mg), light yellow solid, mp 152–153, ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.84 (s, 1H), 7.53 (d, J = 8.6 Hz, 1H), 7.52–7.48 (m, 2H), 7.45 (dd, J = 8.6, 6.9 Hz, 2H), 7.32–7.27 (m, 1H), 6.85 (d, J = 2.3 Hz, 1H), 6.78 (dd, J = 8.7, 2.3 Hz, 1H), 3.86 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 156.3, 136.1, 135.7, 130.2, 129.5, 128.7, 125.9, 122.4, 119.6, 114.4, 109.5, 94.6, 55.9, 12.7; IR (KBr) ν_{max} 3052, 2990, 2931, 2838, 1642, 1039, 964 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{16}NO$ 238.1226 (M + H$^+$); found 238.1211.

1-Ethyl-3-(*p*-tolyl)-1*H*-indole (5i). Yield 64% (150 mg), yellow semi-solid, ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.94 (dd, J = 8.1, 1.0 Hz, 1H), 7.59–7.55 (m, 2H), 7.40 (d, J = 8.2 Hz, 1H), 7.28 (s, 1H), 7.27–7.25 (m, 3H), 7.18 (td, J = 7.5, 7.1, 1.1 Hz, 1H), 4.22 (q, J = 7.3 Hz, 2H), 2.41 (s, 3H), 1.52 (t, J = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 136.6, 135.4, 132.9, 129.6, 127.4, 126.5, 124.7, 121.9, 120.3, 119.9, 116.9, 109.7, 41.2, 21.4, 15.7; IR (KBr) ν_{max} 3048, 2923, 2853, 1613, 1099, 967 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{18}N$ 236.1434 (M + H$^+$); found 236.1451.

***N*-Methyl-4-(2-nitro-1-(*p*-tolyl)ethyl)aniline (F).** Yield 12% (32 mg), light yellow semi-solid, ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.25–7.21 (m, 2H), 7.09 (d, J = 7.8 Hz, 2H), 7.08–7.06 (m, 2H), 6.47–6.43 (m, 2H), 5.58 (s, 1H), 5.20 (qd, J = 13.2, 8.4 Hz, 2H), 4.60 (t, J = 8.3 Hz, 1H), 2.61 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 148.9, 138.14, 135.8, 129.1, 128.1, 127.4, 126.9, 111.7, 78.9, 47.6, 29.7, 20.6; IR (KBr) ν_{max} 3421, 2926, 2839, 1613, 1551, 1517, 1377, 1251, 1182, 1031 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{19}N_2O_2$ 271.1441 (M + H$^+$); found 271.1449.

Conflicts of interest

There are no conflicts to declare.

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