PALLADIUM- AND COPPER-MEDIATED SYNTHESIS OF QUINO, ISOCHROMENO, PYRIMIDO, INDENO AND CYCLOPENTACARBAZOLONE DERIVATIVES

A THESIS SUBMITTED FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

BY

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HYDERABAD-500 046
INDIA

December 2011

STATEMENT

I hereby declare that the matter embodied in this thesis entitled **"PALLADIUM- AND COPPER-MEDIATED SYNTHESIS OF QUINO, ISOCHROMENO, PYRIMIDO, INDENO AND CYCLOPENTACARBAZOLONE DERIVATIVES"** is the result of investigations carried out by me in the School of Chemistry, University of Hyderabad under the supervision of **Dr. R. NAGARAJAN**.

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

Date:

Hyderabad **(D. K. Sreenivas)**

CERTIFICATE

This is to certify that the work described in this thesis entitled **"PALLADIUM- AND COPPER-MEDIATED SYNTHESIS OF QUINO, ISOCHROMENO, PYRIMIDO, INDENO AND CYCLOPENTACARBAZOLONE DERIVATIVES"** has been carried out by **D. K. SREENIVAS** under my supervision and that the same has not been submitted elsewhere for any degree.

Dr. R. NAGARAJAN

(Thesis Supervisor)

Dean
School of Chemistry
University of Hyderabad

LIST OF PUBLICATIONS

1. Highly diastereoselective synthesis of new chromenylaminoanthraquinones through a one-pot, three-component hetero Diels–Alder reaction. Vikram Gaddam, **Devanga K. Sreenivas** and Rajagopal Nagarajan *Tetrahedron Lett*. **2006**, *47*, 9291–9295.

2. Palladium-mediated intramolecular *O*-arylation: A simple route for the synthesis of quino[2,3-*c*] and quino[3,2-*b*]carbazoles. **Devanga K. Sreenivas** and Rajagopal Nagarajan *Tetrahedron* **2010**, *66*, 9650-9654.

3. An efficient route for the synthesis of Isochromenocarbazolones through palladium catalyzed intramolecular *ortho* arylation. **Devanga K. Sreenivas** and Rajagopal Nagarajan *Synthesis* **2011**, 3195-3203.

4. Synthesis of cyclopentacarbazolones *via* palladium-catalyzed annulation of internal alkynes **Devanga K. Sreenivas**, Jatoth Sandhyarani and Rajagopal Nagarajan, (Communicated).

5. Copper-mediated domino synthesis of Pyrimido[4,5-*b*]carbazolones via Ullmann *N*-arylation and aerobic oxidative C-H amidation. **Devanga K. Sreenivas**, Nagarajan Ramkumar and Rajagopal Nagarajan, (Communicated).

6. Highly regioselective synthesis of Indenocarbazolones via palladium-catalyzed intramolecular *ortho* Arylation. **Devanga K. Sreenivas** and Rajagopal Nagarajan, (Communicated).

7. Highly regioselective synthesis of pyridocarbazolones through palladium-mediated intramolecular *ortho* arylation. **Devanga K. Sreenivas**, Nagarajan Ramkumar and Rajagopal Nagarajan, (manuscript under preparation).

Posters and Presentations

1. Participated and gave an oral presentation on "Palladium-Catalyzed Intramolecular Arylation: Synthesis of fused heterocyclic-carbazole derivatives" at 7th "*CHEMFEST 2011*" (In-house symposium), School of Chemistry, University of Hyderabad, Hyderabad.

2. Participated and presented poster on "Palladium-Mediated Intramolecular *O*-Arylation: A Simple Route for the Synthesis of Quino[2,3-*c*] and Quino[3,2-*b*]carbazoles" at 6th "*CHEMFEST 2009*" (In-house symposium), School of Chemistry, University of Hyderabad, Hyderabad.

3. Participated and presented poster on "Highly diastereoselective synthesis of new chromenylaminoanthraquinones through a one-pot, three-component hetero Diels–Alder reaction" at 4th "*CHEMFEST 2007*" (In-house symposium), School of Chemistry, University of Hyderabad, Hyderabad.

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.....DK

Dedicated to

Amma and Nanna…….

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-tion and Aerobic Oxidative C-H Amidation

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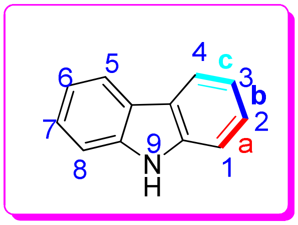
List of Abbreviations

Ac	**Acetyl**
aq.	**Aqueous**
Bn	**Benzyl**
DCM	**Dichloromethane**
DMF	***N,N′*-dimethylformamide**
DMSO	**Dimethyl sulfoxide**
Et	**Ethyl**
Eq.	**Equation**
***i*-Pr**	***iso*-propyl**
LDA	**Lithium diisopropylamide**
***m*-CPBA**	***meta*-chloroperbenzoic acid**
Me	**Methyl**
MOM	**Methoxy methyl ether**
Mp	**Melting point**
Ph	**Phenyl**
Bu	**Butyl**
***p*-TSA**	***para*-Toluenesulfonic acid**
rt	**Room temperature**
TBS	***tert*-butyldimethylsilyl**
***t*-Bu**	***tert*-butyl**
TFA	**Trifluoroacetic acid**
THF	**Tetrahydrofuran**
TMS	**Trimethylsilyl**
TPPT	**Triphenylphosphonium triflate**
DME	**Dimethoxyethane**
Tf	**Triflate**
DBA	**Dibenzilideneacetone**
Phen	**1,2-Phenylenediamine**
Equiv.	**Equivalent**

PE	**Petroleum ether**
DNA	**Deoxyribonucleic acid**
Naph	**Naphthyl**

INTRODUCTION:

Carbazole was first isolated from coal tar in 1872 by Graebe and Glazer.[1] In 1965, Chakraborty *et al*. described the isolation and antibiotic properties of murrayanine from *Murraya koenigii* Spreng.[2] In India, the leaves of this small tree (known as currypatta or curry-leaf tree) are used in the preparation of an Indian food curry. The isolation of murrayanine was the first report of a naturally occurring carbazole alkaloid. Since there has been a strong interest in this area among chemists and biologists due to the intriguing structural features and promising biological activities exhibited by many carbazole alkaloids. The explosive growth of carbazole chemistry is emphasized by a large number of monographs, accounts and reviews.[3-4]

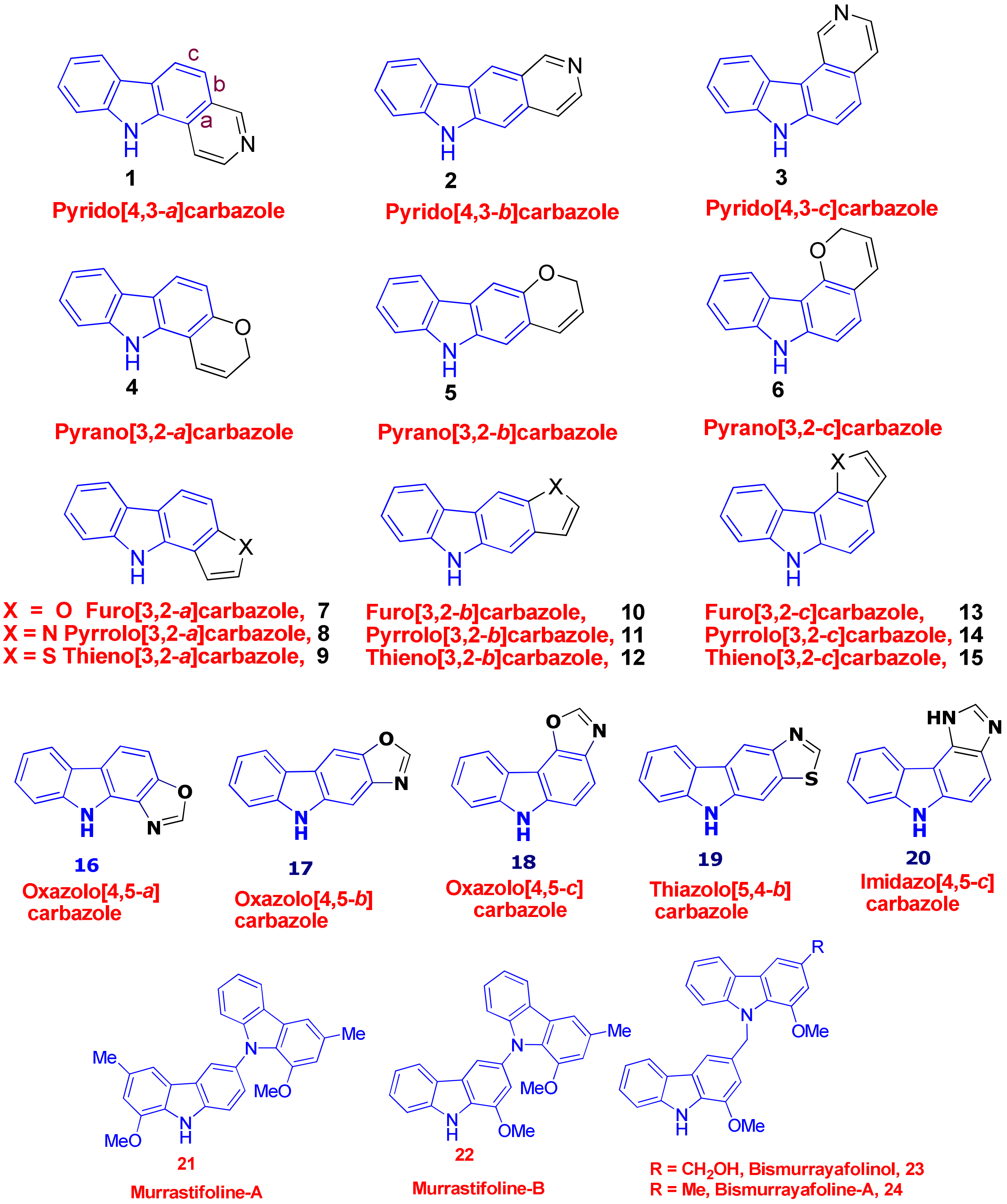


Carbazole
a, b and c Phases

HETEROARYLCARBAZOLES:

Heteroarylcarbazoles are molecules with a heterocyclic moiety fused with carbazole skeleton. The rapidly growing class of heteroaryl-condensed carbazoles began to attract increasing synthetic interest because of their broad spectrum of useful biological activities.[5] To provide an overview on the heteroaryl-annulated carbazole derivatives, these compounds are classified into [*a*]-annulated, [*b*]-annulated, and [*c*]-annulated pyrido-, pyrano-, furo-, pyrrolo-, thieno-, oxazolo-, imidazolocarbazoles *etc*. This classification is solely based on the position at which the heteroaromatic ring is fused to the carbazole nucleus, either at bond a, b, or c. In figure 1 only the structures with a [4,3]-annulated pyridine ring, [3,2]-annulated pyrano- and furan rings and also some of oxazolo, isooxazolo and biscarbazoles are shown, as these are more commonly found in nature. Moreover, the mode of fusion of the annulated heteroaromatic ring itself can vary, which leads to an even broader variety of heterocyclic ring systems.

Figure 1



1 Pyrido[4,3-*a*]carbazole

2 Pyrido[4,3-*b*]carbazole

3 Pyrido[4,3-*c*]carbazole

4 Pyrano[3,2-*a*]carbazole

5 Pyrano[3,2-*b*]carbazole

6 Pyrano[3,2-*c*]carbazole

X = O Furo[3,2-*a*]carbazole, 7
X = N Pyrrolo[3,2-*a*]carbazole, 8
X = S Thieno[3,2-*a*]carbazole, 9

Furo[3,2-*b*]carbazole, 10
Pyrrolo[3,2-*b*]carbazole, 11
Thieno[3,2-*b*]carbazole, 12

Furo[3,2-*c*]carbazole, 13
Pyrrolo[3,2-*c*]carbazole, 14
Thieno[3,2-*c*]carbazole, 15

16 Oxazolo[4,5-*a*] carbazole

17 Oxazolo[4,5-*b*] carbazole

18 Oxazolo[4,5-*c*] carbazole

19 Thiazolo[5,4-*b*] carbazole

20 Imidazo[4,5-*c*] carbazole

21 Murrastifoline-A

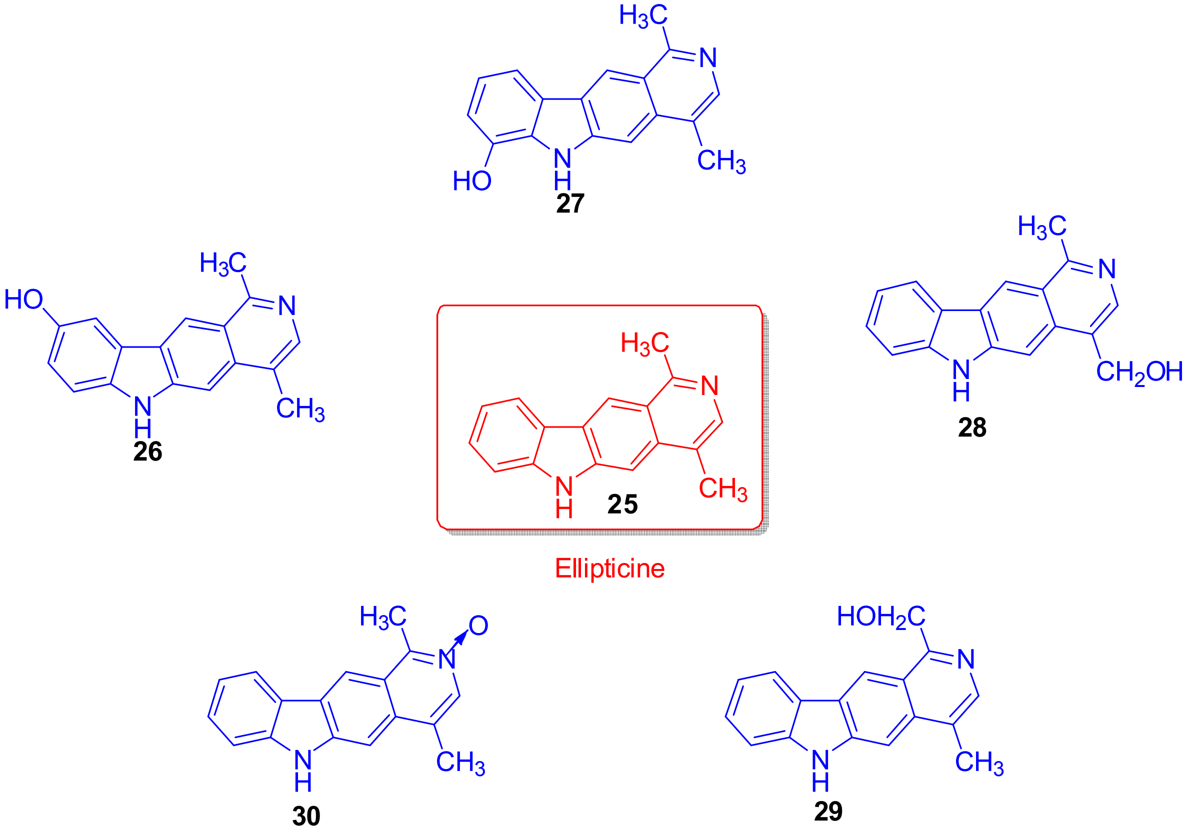
22 Murrastifoline-B

R = CH_2OH, Bismurrayafolinol, 23
R = Me, Bismurrayafoline-A, 24

Pyridocarbazoles:

It is well-established that the pyridocarbazole ring system is an appropriate skeleton to design DNA intercalating drugs.[6] For this reason, there has been a strong synthetic activity in this area. Examples of potential annulation modes are the compounds with pyrido[4,3-*a*]carbazole **1**, the pyrido[4,3-*b*]carbazole **2** and the pyrido[4,3-*c*]carbazole **3** skeleton. Among the different isomeric pyridocarbazole frameworks, the pyrido[4,3-*b*]carbazoles **2** has attracted most of the interest because ellipticine (5,11-dimethyl-6*H*-pyrido[4,3-*b*]carbazole) **28** and its more soluble hydroxyl salts as shown in Figure 2.

Figure 2

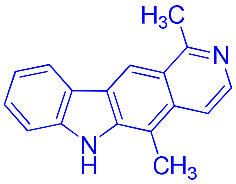


They showed activity against cancer cell lines such as leukemias, melanoma, sarcomas, myelomas, lymphomas, colon adenocarcinoma, lung carcinoma, diverse brain tumors, osteosarcoma, breast cancer and neuroblastomas, which were killed at concentrations ranging from 10^{-10} to 10^{-6} M.[7]

Pyrido[4,3-*b*]carbazole Alkaloids

Ellipticine (5,11-dimethyl-6*H*-pyrido[4,3-*b*]carbazole), an alkaloid isolated from *Apocynaceae* plants (i.e., *Ochrosiaborbonica*, *Excavat iacoccinea*), is one of the simplest naturally occurring alkaloids and has a planar structure. It was first isolated by Goodwin *et al* in 1959 from leaves of the evergreen tree *Ochrosia elliptica*, which grows wild in Oceania.[8] In the same year Woodward *et al*. assigned this plant alkaloid as 5,11-dimethyl-6*H*-pyrido[4,3-*b*]carbazole, confirmed by the first total synthesis.[9] In the following years, ellipticine **28** and its derivatives (Figure 3) were isolated from the various other species of the Genera *Aspidosperma*, *Tabernaemontana*, *Strychnos* and *Peschiera Buchtieni*.[10] In 1967, Australian scientists disclosed the antitumor activity of ellipticine **25** and 9-methoxyellipticine toward various animal tumors.[11] This discovery stimulated a strong interest in the synthesis of ellipticine and its analogues.

Figure 3



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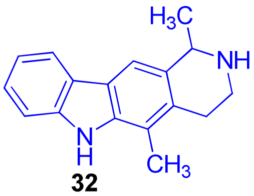
Olivacine



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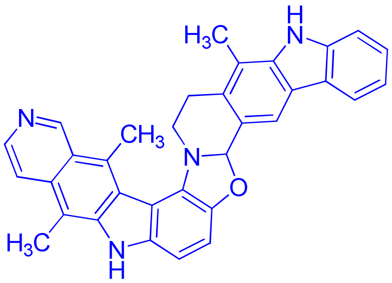
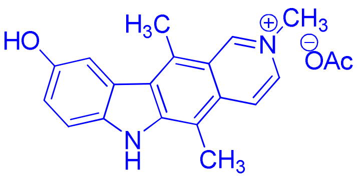
Janetine



33
Sterillidimine

The main reason of the clinical use of ellipticines is their high potencies against several types of cancer (osteolytic breast cancer metastases, kidney cancer, brain tumors and acute myeloblastic leukemia), limited toxic side effects, and their complete lack of hematological toxicity.[12] Nevertheless, mutagenity of these compounds should be evaluated as a potential risk factor for these anticancer agents. Most ellipticines are mutagenic to *Salmonella typhimurium* Ames tester strains, *bacteriophage T4*, *Neurosporacrassa*, and mammalian cells. They are known to induce prophage lambda in *Escherichia coli*.[13]

In the late 1980s, a second generation of ellipticine-derived antitumor agents were developed, including the new clinical candidates elliptinium **34,** datelliptium **35**, retellipticine **36** (BD-84) and pazellipticine (PZE or BD-40).[14,15,16] These findings initiated further extensive activities directed toward the synthesis of pyrido[4,3-*b*]carbazole derivatives for the biological evaluation.



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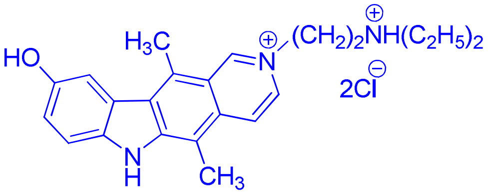
Elliptinium acetate



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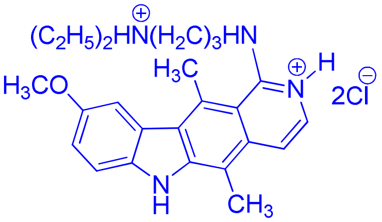
Datelliptium



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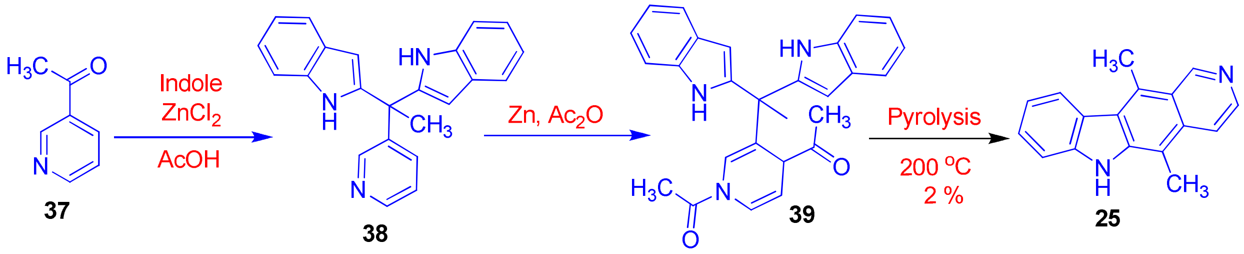
Retellipticine (BD-84)

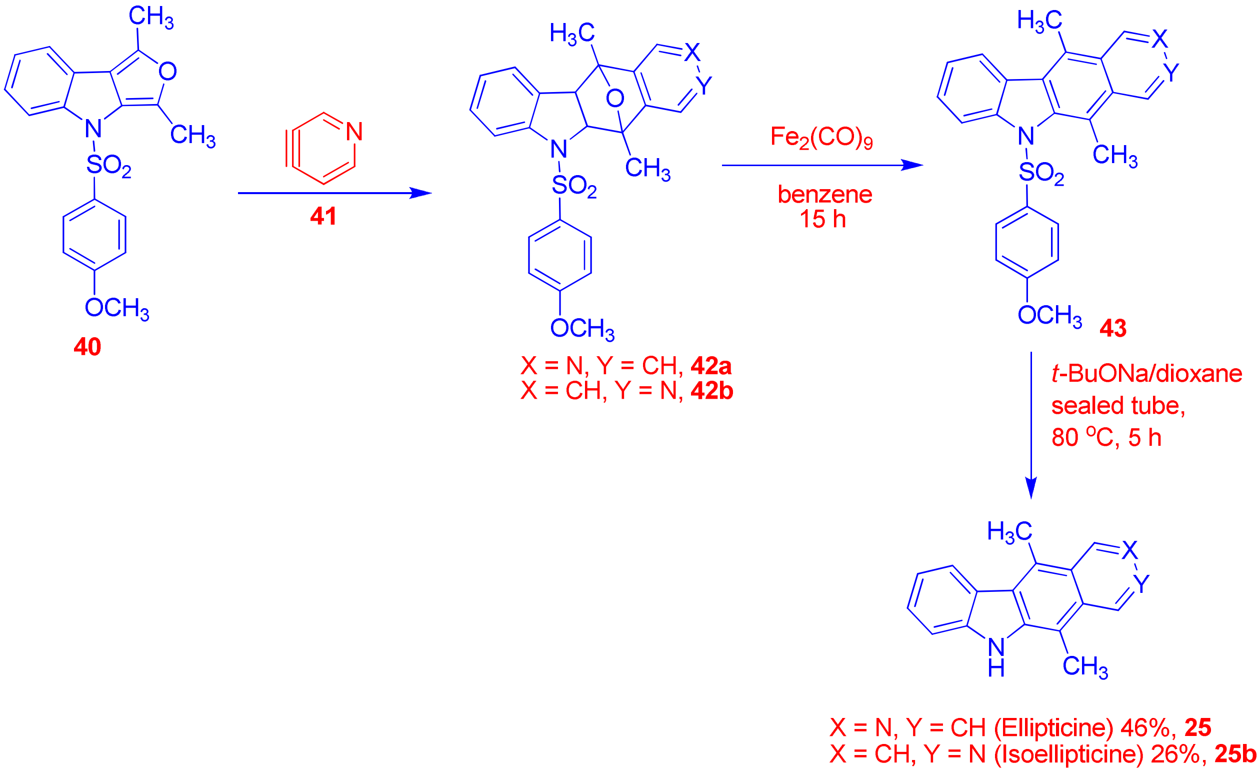
The first total synthesis of ellipticine was reported by R. B. Woodward and co-workers in 1959.[9] The bisindolyl derivative **38** of 3-acetylpyridine **37** upon reductive acetylation followed by pyrolysis at 200 °C provided ellipticine in just 2% yield (Eq. 1).

Eq. 1



Pujol, *et al*. reported the synthesis of ellipticine by treating the diene **40** was successfully converted to the mixture of isomeric Diels-Alder adducts **25** and **25b** by cycloaddition with **41**, 4-pyridyne as the dienophile, obtained from 3-bromopyridine. These adducts were deoxygenated with $Fe_2(CO)_9$ without any further purification obtained **38.** The last step, basic desulfonylation using NaO*t*-Bu in dioxane in a sealed tube, afforded the ellipticine **25** in 46% overall yield and the regioisomer isoellipticine **25b** was obtained in 26% yield (Eq. 2).[17]

Eq. 2



40

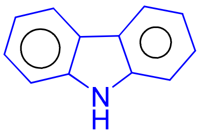
X = N, Y = CH, **42a**
X = CH, Y = N, **42b**

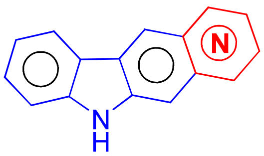
43

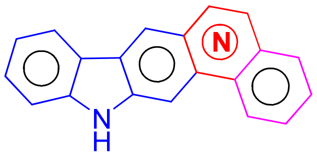
X = N, Y = CH (Ellipticine) 46%, **25**
X = CH, Y = N (Isoellipticine) 26%, **25b**

QUINOCARBAZOLES:

Pyridocarbazole fused with benzene ring called quinocarbazoles. Quinocarbazoles constitute an important class of heterocycles that are known for their potent antitumor, antibacterial, antiinflammatory, psychotropic, and antihistamine properties. Besides, ellipticine has proved to be a popular synthetic target, where a wide variety of synthetic strategies have been reported.


Carbazole

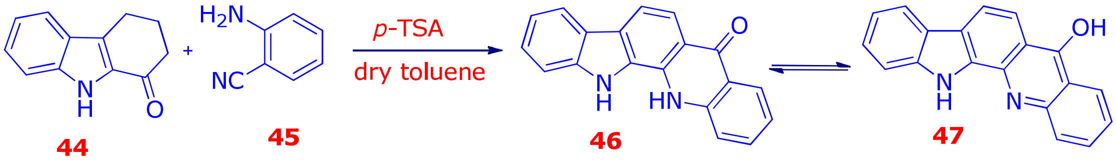

Pyridocarbazole


Quinocarbazole

Also the structurally related heteroaryl annulated carbazoles have received considerable synthetic attention,[18] and these congeners showed a superior pharmacological profile.[19] One of the possible approaches to new ellipticine fused analogs was the modification for the pyridine part (ring D) of the tetracyclic skeleton, which seems to be a sensitive substructure in terms of a modulation of the molecule's antineoplastic proprieties. Thus, the position of the pyridine nitrogen atom has been systematically varied.[20]

As shown in Eq. 3, Rajendra Prasad *et al*. reported the synthesis of quino[2,3-*a*]carbazole **47** by acid-catalysed condensation of 1-oxo-1,2,3,4-tetrahydrocarbazole **44** with *o*-aminobenzonitrile **45**.[21]

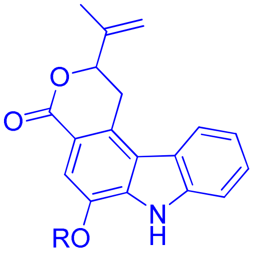
Eq. 3



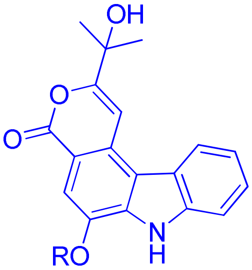
CHROMENOCARBAZOLES:

Another important class of heteroarylcarbazoles is chromenocarbazoles. Prominent structural features of these carbazole alkaloids include 1-oxygenated carbazole framework to which is appended a six-membered lactone at the 3,4-position; as such, the clausamines are given the distinction of being the first alkaloids containing this lactonic carbazole motif to be isolated from nature.[22] Ito and co-workers reported the isolation of clausamines A-C (Figure 4) from the dried branches of *Clausena anisata* in Thailand in 1998. Shortly after, Wu and co-workers identified four other carbazole alkaloids which they named clausevatines D-G, along with known clausamine A, from the root bark of *Clausena excavata*,[23] a wild shrub used in folk medicine for the treatment of snakebites, abdominal pain, and also as a detoxificant. Further study of the extracts of *Clausena excavata* by Itoigawa in 2000 yielded four new carbazoles, clausamines D-G, in addition to previously known alkaloids. In the same account, it was reported that clausamines A-D and F possessed antitumor-promoting properties during short-term *in vitro* assays of TPA-induced EBV-EA activation in Raji cells.[24]

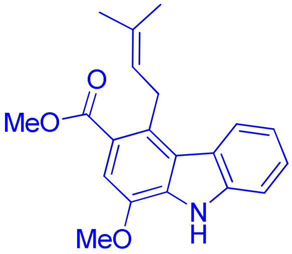
Figure 4



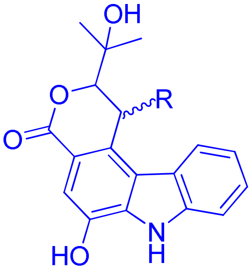
R = H Clausamine A, **48**
R = Me Clausamine B, **49**



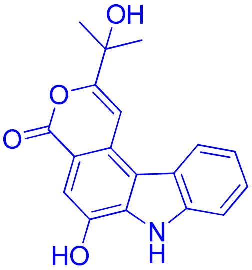
R = H Clausevatine D, **50**
R = Me Clausamine C, **51**



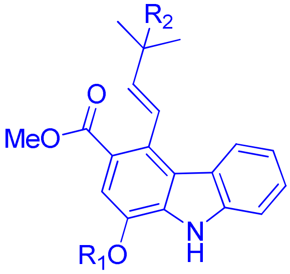
Clausamine D, **52**



R = *cis*-OH Clausevatine E, **53**
R = *trans*-OH Clausevatine F, **54**



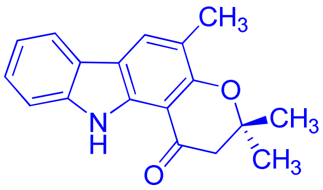
Clausevatine G, **55**



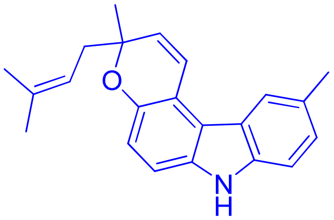
R_1 = Me, R_2 = OH Clausamine E, **56**
R_1 = H, R_2 = OH Clausamine F, **57**
R_1 = Me, R_2 = OOH Clausamine G, **58**

The naturally occurring carbazoles glycomaurrol **65** and glycomaurin **64** (Figure 5) were isolated in 1989 from the stem bark of Glycosmis mauritiana, a small tree growing in the dry zone of Sri Lanka.[25] The following year, eustifolines A-D were isolated from the root bark of *Murraya euchrestifolia* **60**, a shrub growing in the central and southern parts of taiwan.[26] Eustifoline A is in fact the same compound as glycomaurin.

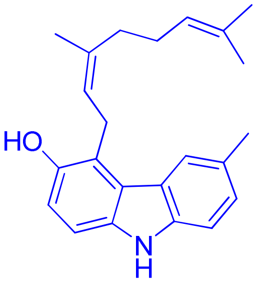
Figure 5



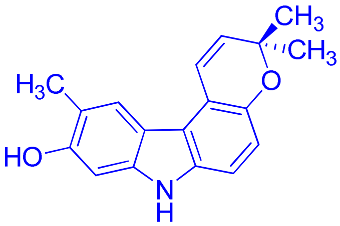
Euchrestifoline, **60**



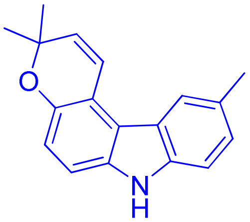
Eustifoline B, **61**



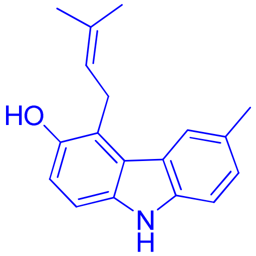
Eustifoline C, **62**



Glycoborinine, **63**



Glycomaurin, **64**

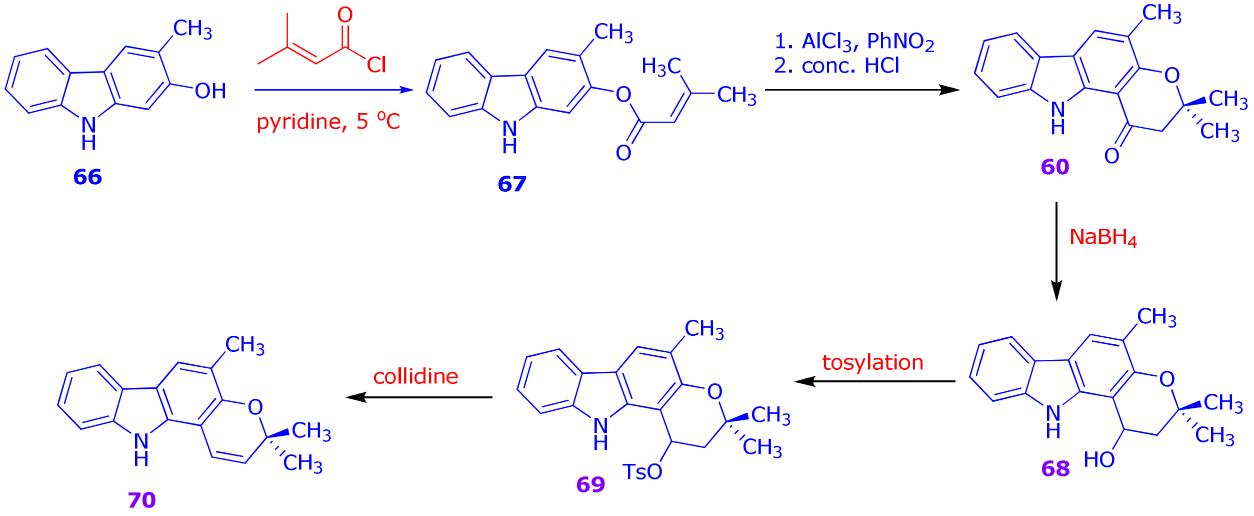


Glycomaurrol, **65**

Until this year, the only synthetic effort toward these compounds has been the semi synthesis of glycomaurin by Wickramasinghe and co-workers in 1989 in their efforts to verify its structure.[27]

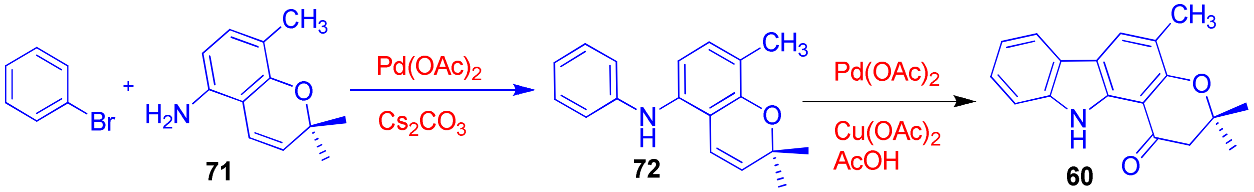
In 1971, Chakraborty and Islam reported the synthesis of girinimbine **70** from 2-hydroxy-3-methylcarbazole[28] **66** by annulation of a 2,2-dimethyl-Δ^3-pyran ring. The acylation of 2-hydroxy-3-methylcarbazole **66** with *β*,*β′*-dimethylacryloyl chloride afforded the acyl derivative **67**. A Fries rearrangement of compound **67** led to the indolochromanone **60**. Twenty-five years later, Wu *et al*. isolated compound **60** from nature and named it euchrestifoline.[29] Finally, the indolochromanone **60** was transformed to girinimbine **70** by the sequence reduction, tosylation and elimination as shown in Eq. 4.[30]

Eq. 4



Knölker and Gruner reported the synthesis **60** by employing a palladium(II)-catalyzed one-pot triple C–H bond activation as key step leading to the Wacker oxidation with concomitant intramolecular oxidative C–C bond formation (Eq. 5).[31] The diarylamine precursor is obtained by a palladium(0)-catalyzed Buchwald–Hartwig coupling of bromobenzene and aminochromene **71**. The aminochromene **71** has been prepared in three steps and 70% overall yield starting from 2-methyl-5-nitrophenol.

Eq. 5

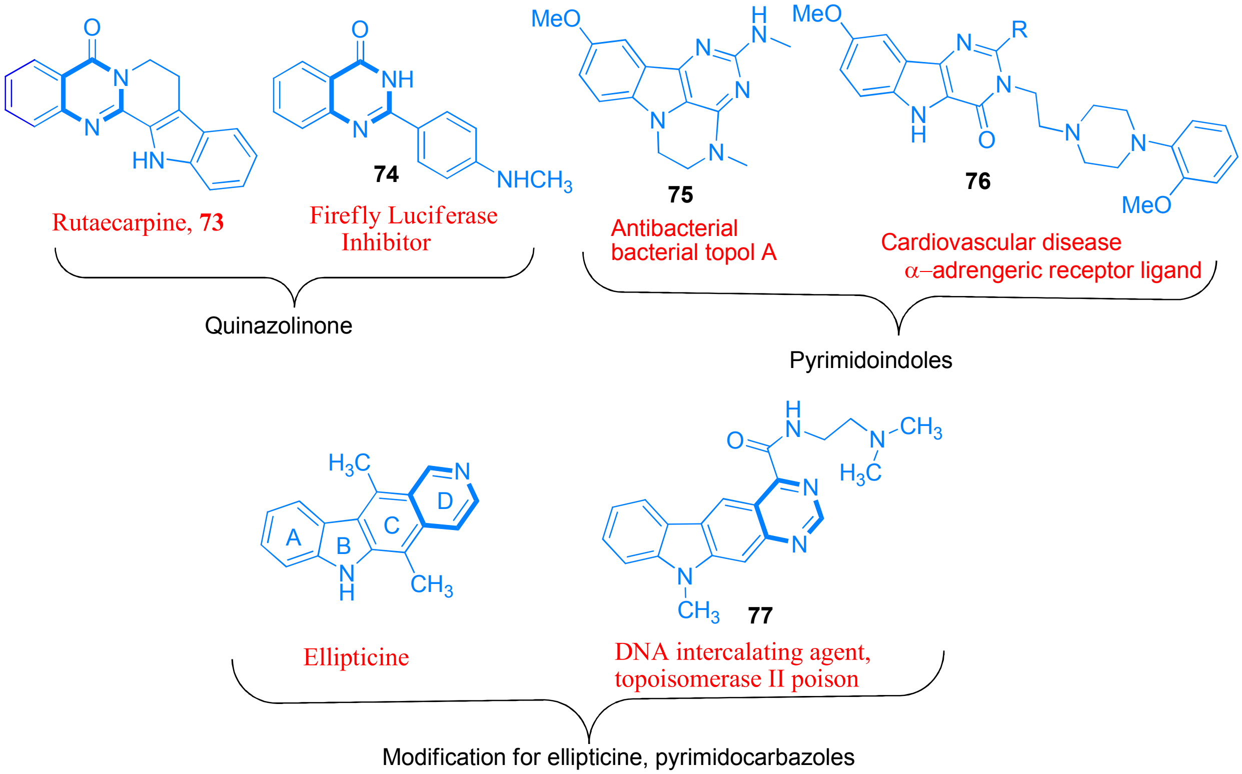


The Diels-Alder reaction between a quinone mono-imine and cyclic diene allows for the construction of substituted carbazoles in a regiospecific manner. This methodology has successfully been employed by M. A. Kerr and T. P. Lebold in a divergent strategy, culminating in the synthesis of eustifolines A-D and glycomaurrol.[32]

PYRIMIDOCARBAZOLES:

Quinazolinone derivatives widely occur in natural products,[33] and they show a wide range of useful biological and pharmacological activities.[34] The quinazolinone derivatives exhibit many central nervous system (CNS) effects, such as analgesic, CNS depressant, and CNS stimulant activities; they also act as psychotropic, hypnotic, cardiotonic, and antihistamine agents[35] and possess cardiovascular activity (including antihypertensive, antiarrhymic, vasodilatory, and lipid-lowering effects) and antiinflammatory activity (including inhibition of cyclooxygenase activity and leukocyte function). They are also potent antibacterial, antifungal, antiviral, antimycobacterial, and antimalarial agents and possess anthelmintic activity.[36] Quinazolinone derivatives are used as inhibitors of various enzymes, and these enzymes include monoamine oxidase, aldose reductase, tumor necrosis factor R, and thymidylate synthase.[36,37] Therefore, they are interesting as structural scaffolds and have been assigned as privileged structures in drug development.[34] So, these structural motifs are fused with indoles and carbazoles to design various types of pharmalogical importance of pyrimido derivatives as shown in Figure 6.

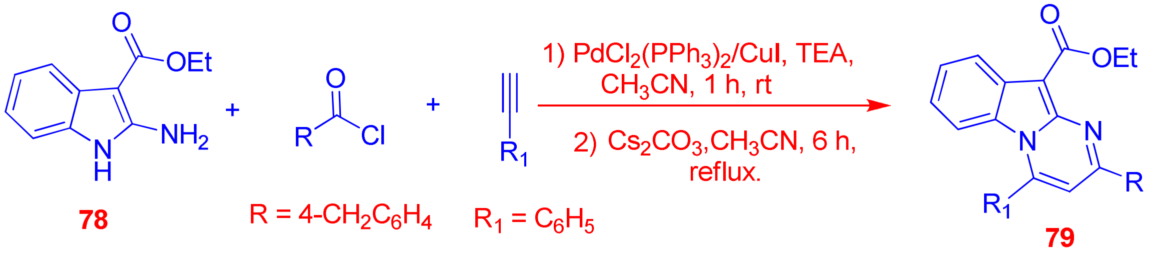
Figure 6



The structurally related heteroarylannulated carbazoles have received considerable synthetic attention, and these congeners showed a superior pharmacological profile. One of the possible approaches to new ellipticine analogs was the modification of the pyridine part (ring D) of the tetracyclic skeleton, which seems to be a sensitive substructure in terms of a modulation of the molecule’s antineoplastic properties. Thus, the position of the pyridine nitrogen atom has been systematically varied.[38] Another strategy consisted in replacement of the pyridine ring by other heterocyclic moieties giving pyridazino-, pyrimidino- ,pyrrolopyrazino-, pyrido-, pyrazolo-, pyrano-, imidazo-, indolo-, furo-, and thieno-carbazoles has been described in literature.

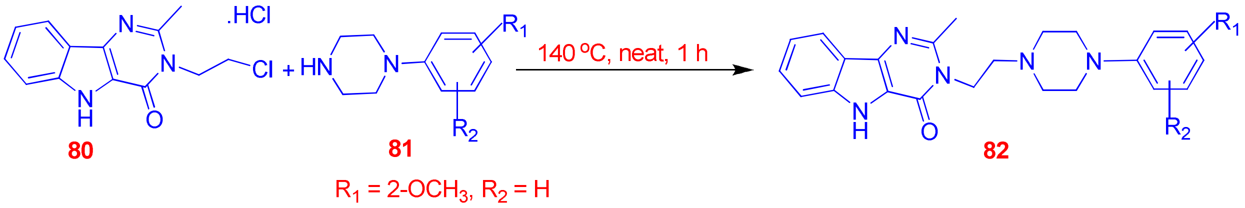
Kundu *et al*. (Eq. 6) synthesized 1-(4-methylphenyl)-3-phenylprop-2-yn-1-one via Sonogashira coupling by treating *p*-tolyl chloride with phenylacetylene in the presence of Pd/C and Et_3N in THF using the literature procedure.[39] The resulting alkynone obtained in 94% isolated yield was then treated with ethyl-2-amino-1*H*-indole-3-carboxylate **78** in the presence of Cs_2CO_3/CH_3CN at 90 °C for 6 h furnished pyrimido[1,2-*a*]indole **79** as a single regioisomer in 78% isolated yield via [3+3] cyclocondensation.[40]

Eq. 6



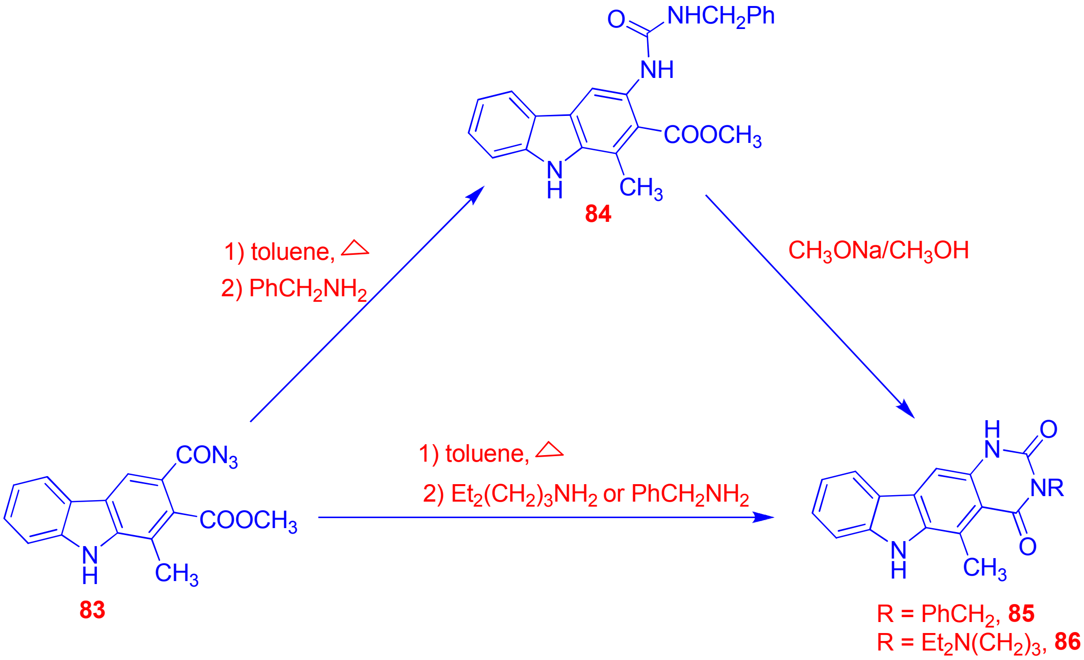
Romeo *et al*. synthesized pyrimidocarbazole derivatives by heating chlorides **80** with the suitable piperazines **81** in neat conditions obtained **82** in good yields in the absence of solvent (Eq. 7).[41]

Eq. 7



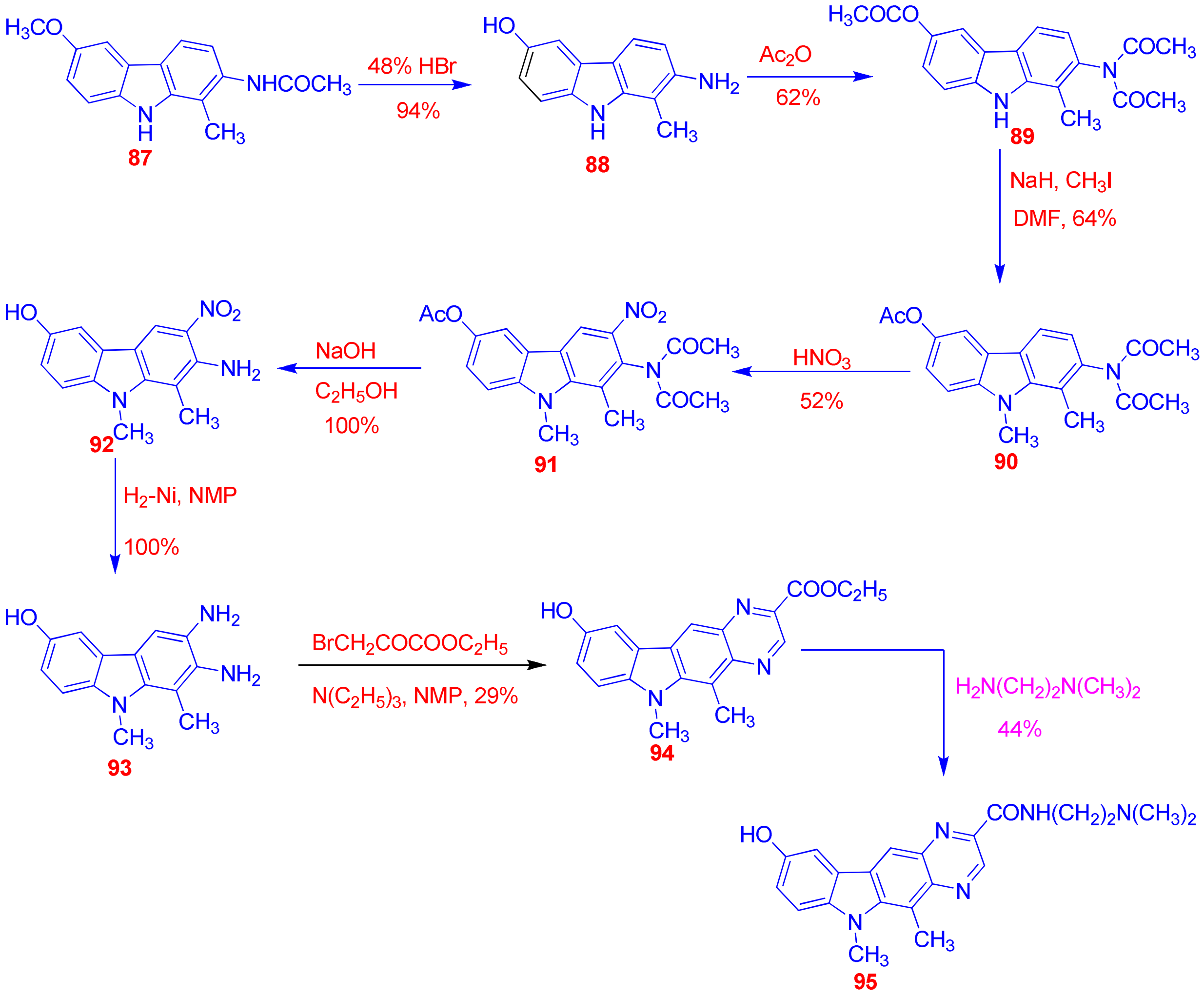
Haider *et al*. prepared the pyrimidocarbazoles by Curtius degradation of the azide **83** in the presence of benzylamine, the unsymmetrically *N*,*N′*-disubstituted urea **84** was obtained in high yield. Refluxing of this compound in methanolic sodium methoxide effected ring closure into the fused pyrimidinedione derivatives **85** almost quantitatively. On the other hand, treatment of the (*in situ* generated) isocyanate with *N*,*N*-diethylpropane-1,3-diamine did not afford the expected urea derivative but, instead, the tetracyclic compound **86** was obtained in 83% yield. Obviously, in this case the basicity of the employed amine component is sufficient to promote spontaneous cyclization, leading to the pyrimidocarbazole **86** (Eq. 8).[42]

Eq. 8



Goldstein *et al*. synthesized the compound **95** started with **87** which in turn prepared from carbazole itself prepared in good yield by a literature described method. Demethylation of the methoxy group as well as deacetylation of the acetamido group of **87** was achieved in good yield by treatment with 48% hydrobromic acid. The amino and hydroxyl functions in compound **88** were then reacetylated with acetic anhydride obtained **89** then *N*-methylated using sodium hydride and iodomethane in DMF. Selective nitration of **90** with nitric acid (fuming 100%) occurred at the *ortho* position to the diacetylamino group to afford **91** in good yield. The acetyl groups were removed in quantitative yield by treatment with sodium hydroxide in ethanol. Nickel mediated catalytic hydrogenation of the aromatic nitro group in compound **92** afforded the diaminocarbazole **93** in good yield. The pyrimido ring was constructed by condensation of diamino compound **93** with ethylbromopyruvate in the presence of triethylamine in NMP to afford **94** in moderate yield. Treatment with amine afford the **95** in moderate yield (Eq. 9).[43]

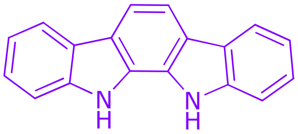
Eq. 9



INDOLOCARBAZOLES:

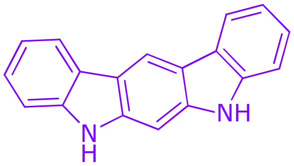
Indolocarbazole family belong the five different isomeric ring systems (Figure 7) namely indolo[2,3-*a*]carbazole **100**, indolo[2,3-*b*]carbazole **101**, indolo[2,3-*c*]carbazole **102**, indolo[3,2-*a*]carbazole **103** and indolo[3,2-*b*]carbazole **104**. Among these, the most interesting structural class is the indolo[2,3-*a*]carbazoles. The indolocarbazole alkaloids are interesting owing to the wide range of biological activites that they possess, including antimicrobial, hypotensive, and cell cytotoxic activities, as well as inhibition of platelet aggregation.[44] The greatest interest in these compounds, however has been due to their potent antitumor activity.

Figure 7



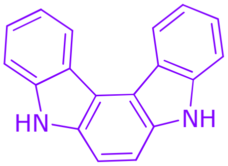
100

Indolo[2,3-*a*]carbazole



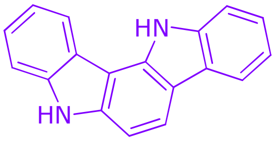
101

Indolo[2,3-*b*]carbazole



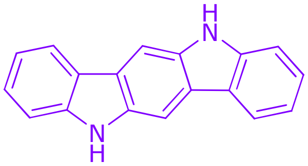
102

Indolo[2,3-*c*]carbazole



103

Indolo[3,2-*a*]carbazole

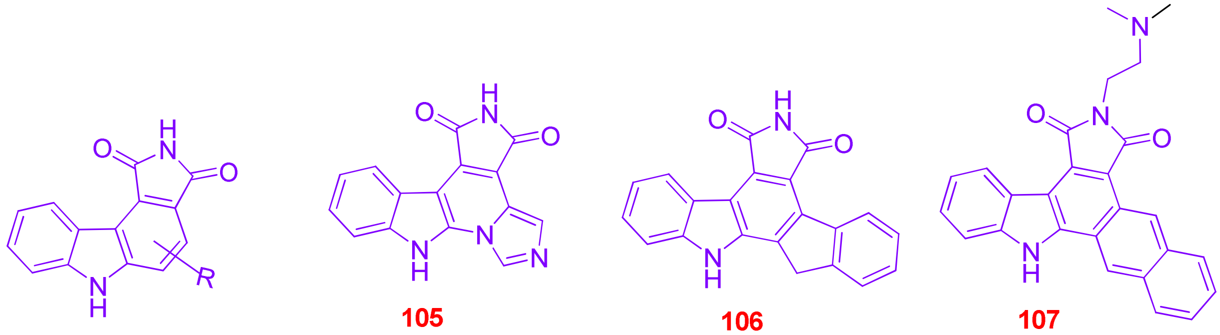


104

Indolo[3,2-*b*]carbazole

Modifications in the indolocarbazole system leads to another class of carbazole alkaloids as indolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole (Figure 8) endowed with potent antitumor, antiviral, and antimicrobial activities. This family has raised considerable attention because of the central role of these molecules in the regulation of cell cycle progression and specific enzyme inhibition.[45] Structure-activity relationships (SAR) in the indolocarbazole series have been extensively studied in the context of topoisomerase I inhibition and tumor cell killing. Compounds bearing a pyrroloindolocarbazole and equipped with one *N*-glycosidic bond, such as the antibiotic rebeccamycin, generally function as DNA topoisomerase I inhibitors. A few analogues, such as NB-506 and J-107088 (also known asedotecarin), have entered clinical trials for cancer treatment.[46] More recently, fluorinated derivatives of such molecules have been reported and their topoisomerase I-dependent anticancer activity looks promising. It is important to mention also that closely related heteroarylcarbazoles (type III) have been described as inhibitors of cyclin D1/CDK4.

Figure 8



R = fused heteroaryl group

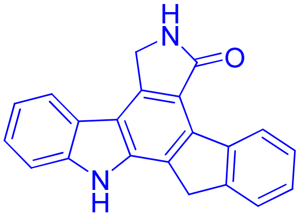
105 Isogranulatimide

106 Indenocarbazole

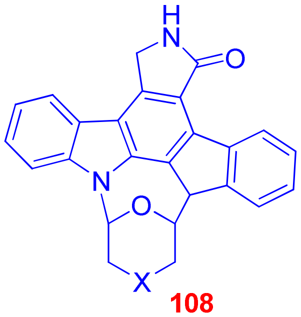
107 Naphthocarbazole

Indenocarbazoles:

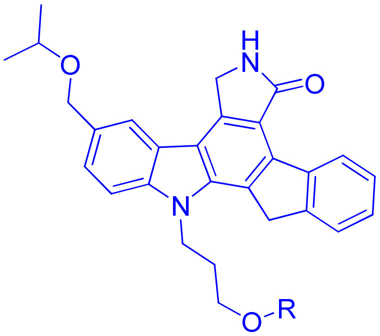
The indenocarbazoles are a new class of heteroarylcarbazole analogs of indolocarbazoles, in which the indole nitrogen is replaced with a carbon. These molecules are not fully explored and were reported by Hudkins group as PKC, VEGFR2 and trkA inhibitors.[47] Gingrich *et al*.[48] have reported an optimized method for the indenocarbazole derivatives (**109** and **110**) CEP-5214 and its prodrug form CEP-7055 as a potent inhibitor of VEGFR3 (Flt-4), VEGFR2 (KDR), VEGFR1 (Flt-1) and Flt-3.



Indenocarbazole

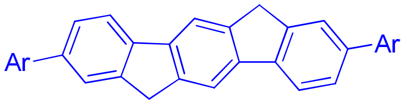


108
fused Indenocarbazole



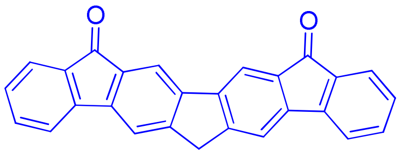
CEP-7055: R = OCH$_2$N(CH$_3$)$_2$,**109**
CEP-5214: R = H, **110**

The importance of fluoren-9-one, found in many biologically active products, has been emphasized in organic chemistry. It consists of essential structural backbone of various pharmaceuticals.[49] Also number of natural products have been found containing fluoren-9-one as the core structure. Examples of such natural products include dengibsin, dengibsinin, dendroflorin, and kinobscurinone showing a range of biological activities.[50] Utility of fluoren-9-one derivatives as photosensitizers in organic photoconductor devices and their electrical and optical properties are also important.[51] In addition to their use in medicinal chemistry, fused heterocycles such as indenofluorene **111**, bisindenofluorenone **112**, and bisindenocarbazoles **113** have attracted increasing attention from the community of material scientists owing to their potential in photophysical and optoelectronic (OLEDs, PLEDs) applications.[52] Strohriegl *et al*. reported liquid crystalline bisindenocarbazole derivatives which exhibit blue fluorescence.[53]



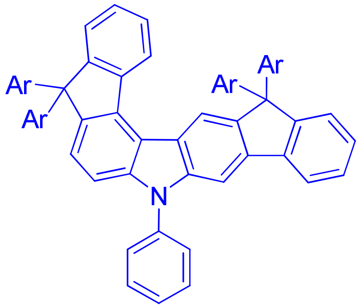
111

Indenofluorene
(OLEDs)



112

Bisindenofluorenone
(Optical and Electrochemical)

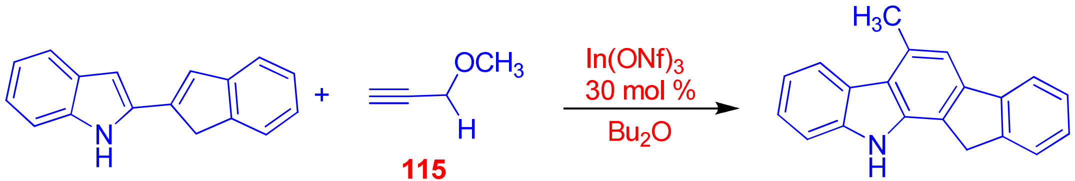


113

Bisindenocarbazole
Ar = 4-CH_3Ph

Tsuchimoto, *et al*.[54] (Eq. 10) reported Lewis acid catalyzed annulation of 2-arylindoles with propargyl ethers in a route that comprises two successive carbon–carbon bond-forming reactions should make for a short-step synthesis of aryl- and heteroaryl-annulated[*a*]carbazoles. Various 2-arylindoles are readily accessible through the Fischer indole synthesis. Treatment of **114** and **115** with 30 mol % of indium nonaflate $In(ONf)_3$, in Bu_2O at 70-80 °C for 72 h gave 6-methyl-11*H*-benzo[*a*]carbazole **116** in 62% yield by a route in which two subsequent inter- and intramolecular carbon–carbon bond-forming reactions took place in one step.

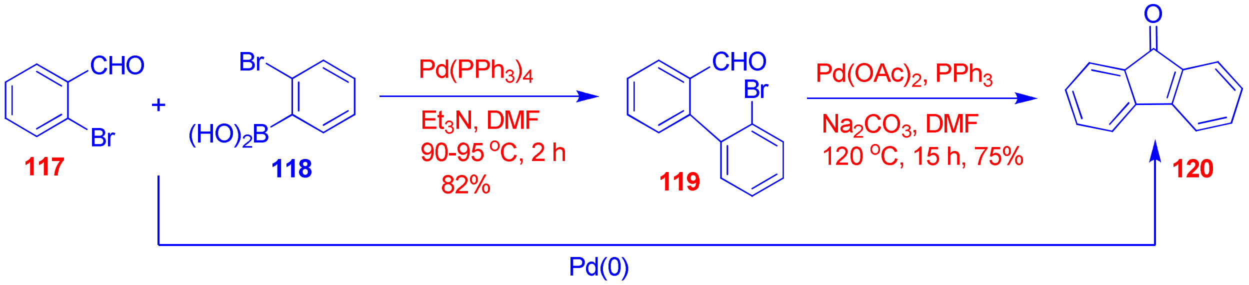
Eq. 10



114 **115** **116**

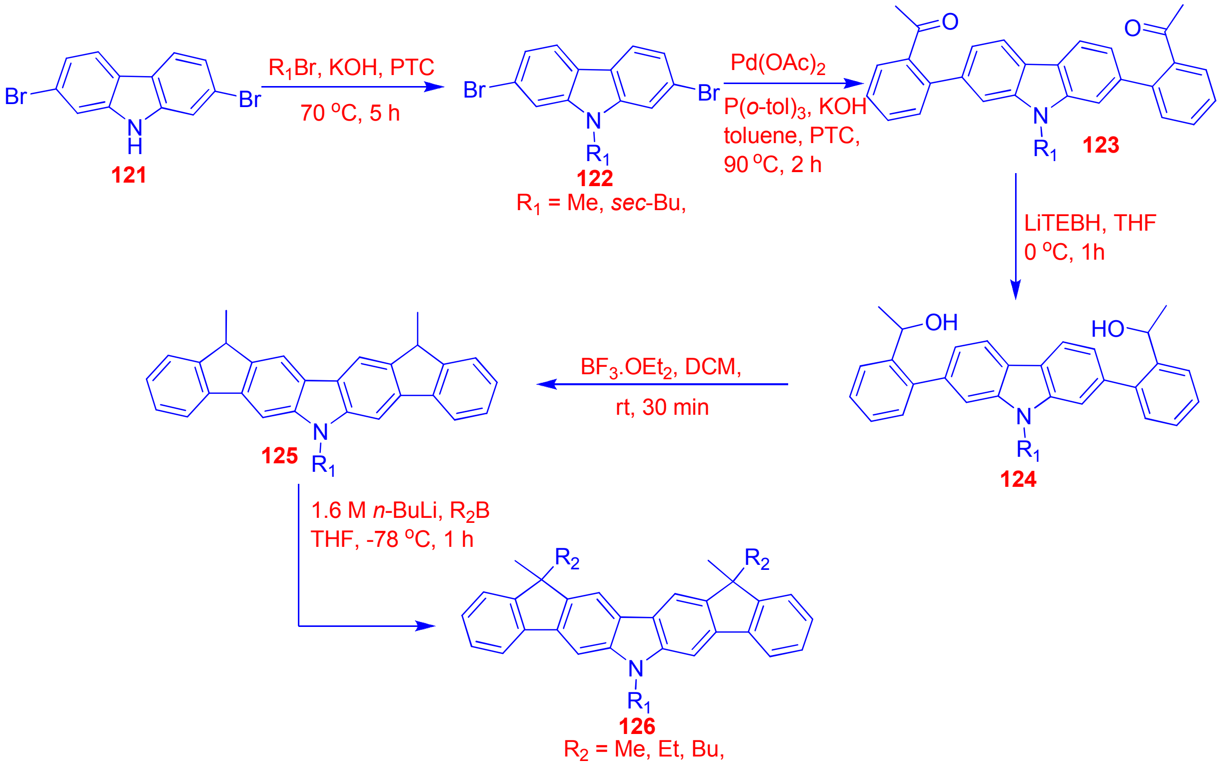
Ray *et al*. reported a simple route for the fluorenone derivatives by Pd-catalyzed synthesis starting from various various 2-bromocarboxaldehydes **117** along with 2-bromophenyl boronic acid **118** with two distinct sequential steps, Suzuki coupling followed by arylpalladium addition to aldehyde, in one-pot (Eq. 11).[55]

Eq. 11



Strohriegl *et al*.[53] (Eq. 12) reported the synthesis of bisindenocarbazole derivatives starting from 2,7-dibromocarbazole **121** protected with methyl or *sec*-butyl group in presence of KOH under phase transfer catalysis to obtain **122**. Under Suzuki coupling with 2-acetylphenylboronic acid with *N*-alkylated 2,7-dibromocarbazoles **122**, and a mixture of $Pd(OAc)_2$ and $P(o\text{-}tol)_3$ was used as catalystobtained **123** in excellent yields. The keto groups were reduced to the corresponding secondary alcohols **124** by reaction with lithium triethylborohydride (super-hydride) in absolute THF. The ring closure reaction of **124** to the bisindenocarbazoles **125** was carried out with boron trifluoride etherate as Lewis-acid catalyst in dichloromethane at room temperature. Ring closure occurs exclusively in the 3- and 6-positions of the carbazole, which are highly activated. In the last step the alkylation had with *n*-BuLi to obtain dialkylated bisindenocarbazole **126** in good yield which are useful in optical and electrical properties.

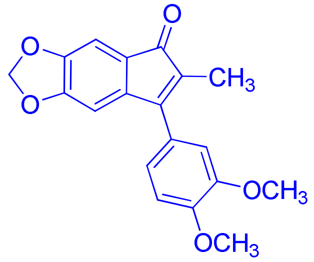
Eq. 12



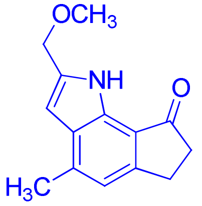
CYCLOPENTACARBAZOLONES:

Annulated as well as substituted indenones[56] are potentially useful building blocks in organic, organometallic, and medicinal chemistry. They possess a broad range of biological activities such as antiproliferative,[57] antitumor,[58] fungicidal[59] and also act as alcoholic fermentation activators[60] and estrogen binding receptors.[61] Benzannulated indenones inhibit cancer growth *in vitro* and extend life span in living organisms.[62] They are also used as important starting materials in the synthesis of kynamycin antibiotics, which show excellent activity against gram positive bacteria.[63] Due to their significant pharmacological importance, the development of facile strategies to obtain such frameworks has become an attractive endeavor in synthetic organic and medicinal chemistry. Some of the indenone based natural products are shown in Figure 9.

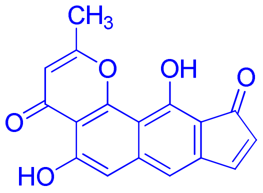
Figure 9



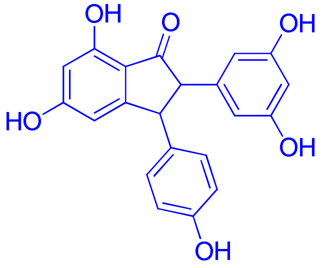
Dilemmaone A, **127**



Virola indenone, **128**



Euplectin, **129**

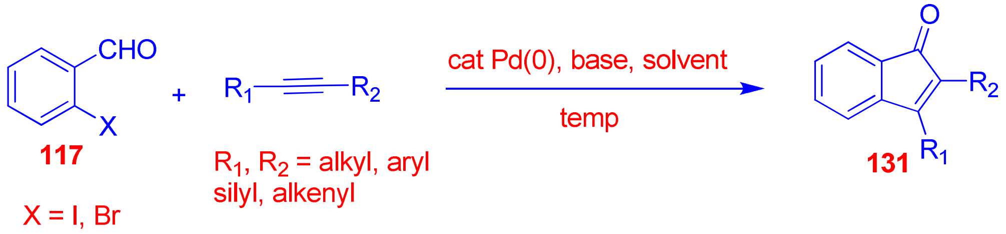


Pauciflorol F, **130**

Cyclopentadienones[64] are members of a diverse class of attractive molecules with demonstrated value and even broader potential in synthesis, biology, materials science, and nanotechnology.[65] Fused and substituted cyclopentadienones[66] are also potentially useful building blocks in organic, organometallic, and medicinal chemistry and also possess a broad range of biological activities such as antiproliferative,[67] antitumor,[68] fungicidal and also act as estrogen binding receptors.[69] Moreover, carbazole motif is prominent structural unit discerned in various natural products and synthetic compounds with vital medicinal values.

Larock has been demonstrated the first palladium-catalyzed annulation methodology[71] can be effectively employed for the synthesis of indoles, benzo-furans, benzopyrans, isocoumarins, pyrones, indenones, and polycyclic aromatic hydrocarbons.

Eq. 13



117

X = I, Br

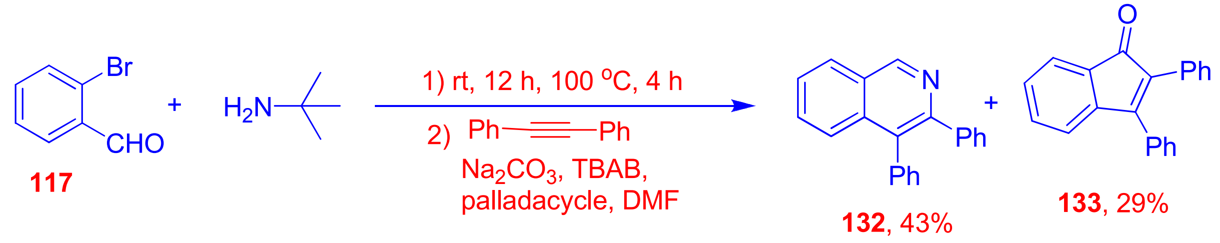
R_1, R_2 = alkyl, aryl silyl, alkenyl

131

Larock have developed a general procedure for the annulation of internal alkynes by *o*-iodo- or *o*-bromobenzaldehyde, **117** and an alkyne undergoing annulation in two different procedures. By using procedure A, 5 mol % $Pd(OAc)_2$, 4 equiv of NaOAc, 1 equiv of *n*-BuNCl, 10 mL of DMF at 100 °C; procedure B, 5 mol % $Pd(OAc)_2$, 4 equiv of Na_2CO_3, 1.0 equiv of *n*-BuNC1, 10 mL of *N*,*N*-dimethylacetamide (DMA) at 100 °C obtained corresponding 2,3-disubstituted indenones **131** in good yields (Eq. 13).

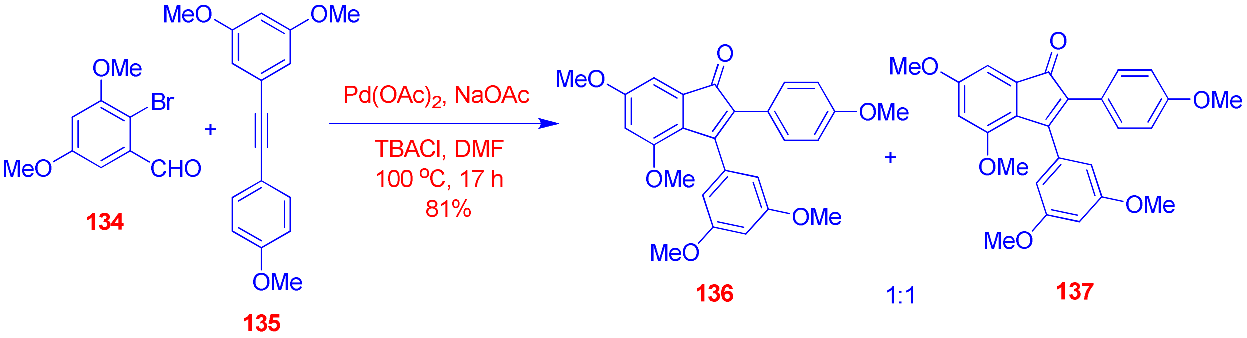
Wu *et al*. reported disubstituted phenyl isoquinoline **132** and 2,3-disubstituted indenone **133** starting from the imination of 2-bromobenzaldehyde **117** with *tert*-butyl amine and subsequent palladacycle-catalyzed iminoannulation of diphenylacetylene were carried out using Na_2CO_3 as the base, TBAB as additive, affording the desired product in a moderate yield of 43% and 2,3-diphenyl-1*H*-inden-1-one 29% as the byproduct (Eq. 14).[72]

Eq. 14



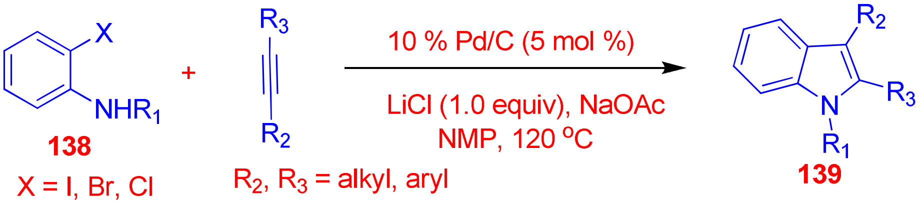
When a mixture of **134** and **135** was subjected to Larock's original annulation conditions, a 1:1 mixture of 2,3-disubstituted indenone regioisomers **136** and **137** was obtained (Eq. 15).[73]

Eq. 15



Sajiki *et al*. (Eq. 16) developed a new synthetic route for the construction of substituted indoles **139** by applying internal alkynes using pd catalysis.[74]

Eq. 16



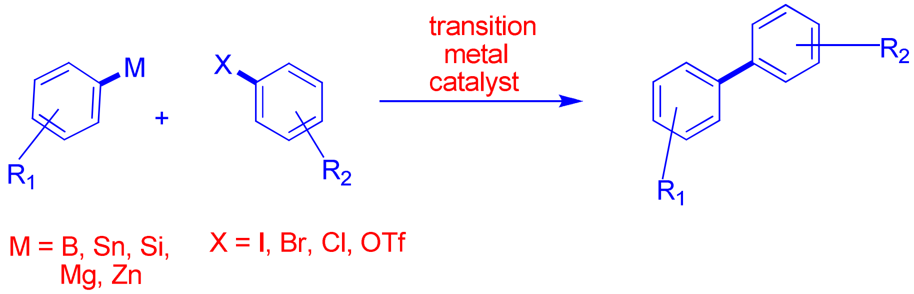
Palladium chemistry:

The use of transition metal-mediated reactions in organic synthesis has become of increasing importance over the past several decades. In particular, a variety of methods have been developed to allow for the formation of a number of types of bonds, including C-C, C-H, C-N, C-O, C-S, and C-P.[75] While a number of transition metals have been employed for these classes of reactions, catalysts based on palladium and copper have recently emerged as capable of performing a number of transformations in high yield, while maintaining low loadings, high functional group tolerance, and mild reaction conditions. Many of these features have been obtained through the proper choice of supporting ligands, bases, additives for the metal catalyst. One area in which palladium catalysis has had a major impact in chemistry has been in the formation of carbon-carbon bonds. Of the several methods that have been developed, C-H activation reactions have emerged as some of the most powerful and widely utilized transformations.

C-H ACTIVATION

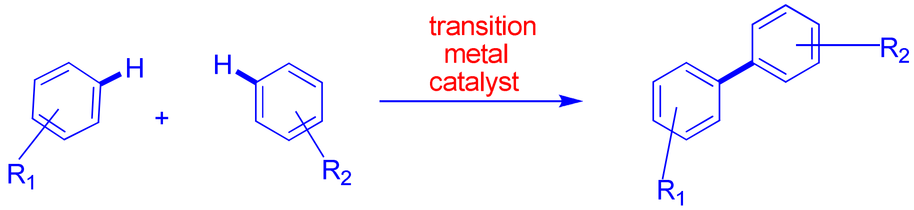
The biaryl structural motif is a predominant feature in many pharmaceutically relevant and biologically active compounds. As a result, for over a century[76] organic chemists have sought to develop new and more efficient aryl-aryl bond-forming methods. Although there exist a variety of routes for the construction of aryl-aryl bonds, arguably the most common method is through the use of transition-metal-mediated reactions.[77] While earlier reports focused on the use of stoichiometric quantities of a transition metal to carry out the desired transformation, modern methods of transition-metal-catalyzed aryl-aryl coupling have focused on the development of high-yielding reactions achieved with excellent selectivity and high functional group tolerance under mild reaction conditions. Typically, these reactions involve either the coupling of an aryl halide or pseudohalide with an organometallic reagent (Eq. 17), or the homocoupling of two aryl halides or two organometallic reagents. Although a number of improvements have developed the former process into an industrially very useful and attractive method for the construction of aryl-aryl bonds, the need still exists for more efficient routes whereby the same outcome is accomplished, but with reduced waste and in fewer steps. In particular, the obligation to use coupling partners that are both activated is wasteful since it necessitates the installation and then subsequent disposal of stoichiometric activating agents. Furthermore, preparation of pre-activated aryl substrates often requires several steps, which in itself can be a time-consuming and economically inefficient process.

Eq. 17



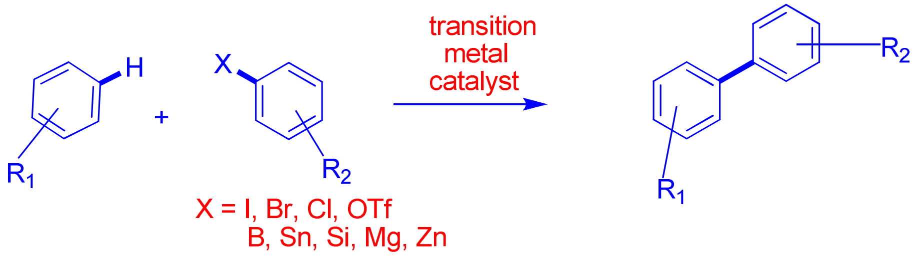
An attractive alternative to this approach is to treat the aryl C-H bond as a functional group, in analogy to a carbon-metal or carbon-halogen bond. The simplest approach would involve the coupling of two aryl C-H bonds to give the corresponding biaryl product (Eq. 18), although this process is unfavorable from a thermodynamic perspective due to the high bond strength of an aryl C-H bond (e.g., the homocoupling of benzene to give biphenyl and hydrogen is thermodynamically disfavored by 13.8 kJ/mol).[78] Furthermore, while such an approach is alluring, the ubiquitous and diverse nature of C-H bonds in complex organic compounds makes a regioselective oxidative coupling of this type a formidable challenge.

Eq. 18



While the coupling of an aryl halide or pseudohalide with an organometallic reagent is commonly referred to as a cross coupling reaction, several terms such **as C-H (bond) activation, C-H (bond) functionalization, cross-dehalogenative coupling, and catalytic direct arylation have been used to describe the corresponding coupling of an aryl halide or pseudohalide with a simple arene** (Eq. 19).[79] Although the former two terms are more prevalent in the literature, we have elected to use the term **direct arylation**, which we define as the direct coupling of a nonactivated aryl C-H bond with an activated arene. This term best describes the overall process illustrated in Scheme 3, while additionally preventing any erroneous implications regarding the mechanistic pathway by which the process occurs.

Eq. 19

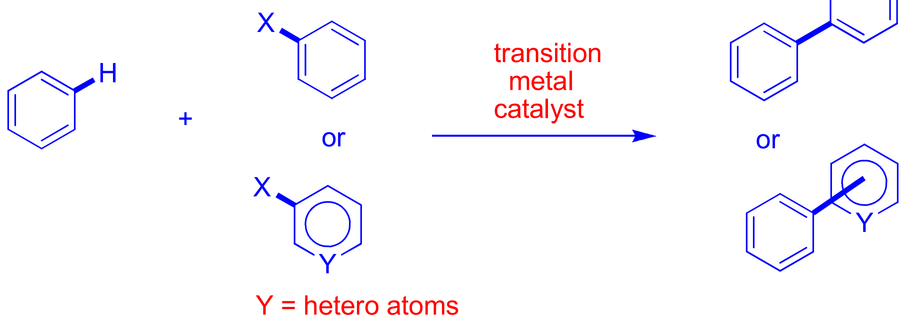


Direct arylation of aryl C−H Bonds

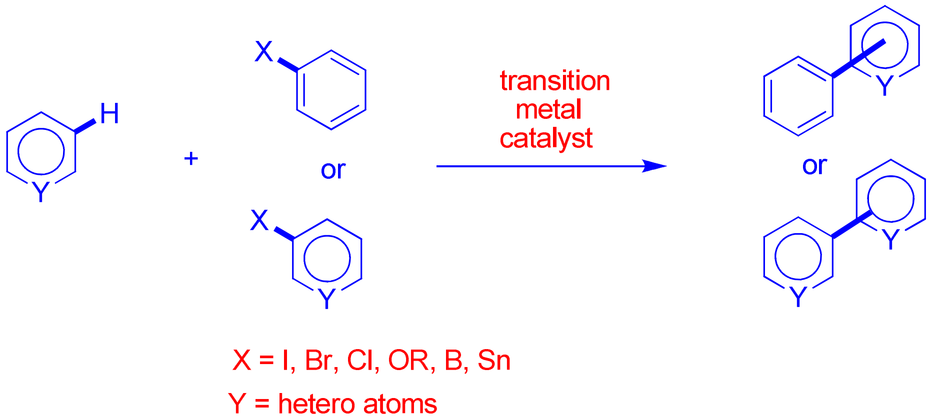
The development and advances in transition-metal-catalyzed aryl-aryl bond formation by direct arylation, as well as direct arylation of aryl and heteroaryl C-H bonds as shown in Eq. 20.

Eq. 20

Direct arylation of aryl C-H bonds



Direct arylation of heteroaryl C-H bonds



Although a variety of transition metals have been used for the formation of aryl-aryl bonds, second-row transition metals in low oxidation states (Rh, Ru, Pd) have emerged as the preferred catalysts in catalytic direct arylation reactions. The ligands used in direct arylation depend on the nature of the aryl halide being used. For more reactive aryl iodides, moderately electron-rich monodentate phosphines such as PPh_3 are typically used. These same phosphines have also been successfully utilized for aryl bromides, although in some systems far superior yields have been obtained using palladium and more sterically bulky and electron-rich trialkylphosphine or Buchwald's biphenylphosphines.[80] Recently, the use of aryl chlorides in a palladium-catalyzed direct arylation reaction has also been reported. However, as in other cross-coupling reactions,[81] the low reactivity of the C-Cl bond to oxidative addition necessitated the use of electron-rich and sterically-hindered trialkylphosphines, Buchwald's biphenylphosphines, or *N*-heterocyclic carbene ligands to achieve synthetically useful yields of the direct arylation product.[82] It should also be noted that ligand-free conditions (Jeffery's conditions) have also been successfully used in palladium-catalyzed direct arylation reactions for a variety of aryl halides.

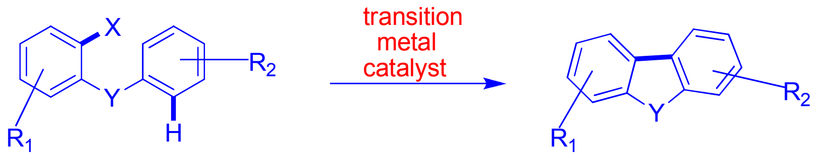
While base is generally required in direct arylation reactions, in most cases the exact role of the base remains unclear. Some recent evidence, however, suggests that in some systems the base may be intimately involved in the formation of the diarylpalladium(II) species (and not simply as a bystander whose role is to regenerate the active catalyst).[83] Typically, inorganic bases such as K_2CO_3, Cs_2CO_3, KOAc, *t*-BuOK, and CsOPiv are used. In particular, cesium carbonate and CsOPiv have proven to be very effective in many cases due to increased solubility in organic solvents. While polar, aprotic solvents such as DMF, DMA, CH_3CN, NMP, and DMSO are commonly used, nonpolar solvents such as toluene and xylene have also been employed successfully. In addition, temperatures >100 °C are typically used, and in most cases heating for several hours to days is necessary.

Intra and Intermolecular Direct Arylation:

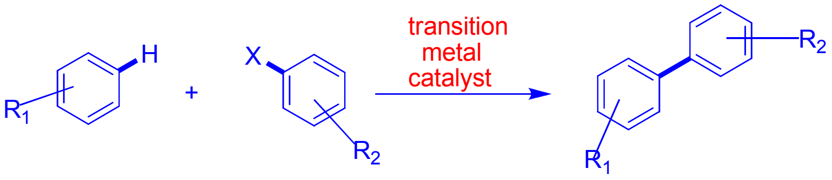
Direct arylation reactions can take place in either an intermolecular or an intramolecular fashion (Eq. 21). While intramolecular direct arylation reactions employ tethers to limit the degree of freedom in a system, thereby controlling the regioselectivity of the reaction (Eq. 21) where as intermolecular direct arylation reactions present a more formidable task since the catalyst has a greater degree of freedom when reacting at the C-H bond. Two factors that influence the regioselectivity of the intermolecular direct arylation are the electronics of the arene being functionalized (the reaction occurs *ortho* or *para* to the electron-donating group via an electrophilic aromatic substitution process), and more commonly the directing group.

Eq. 21

Intramolecular direct arylation

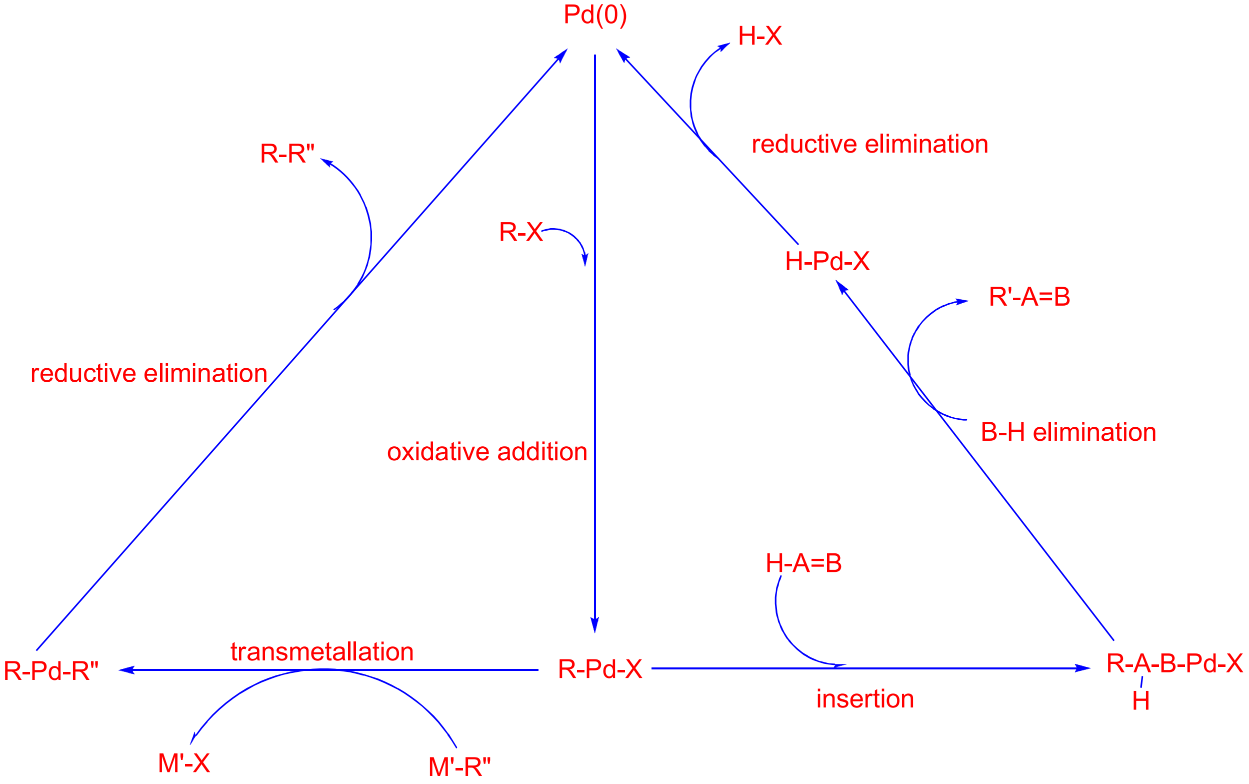


Intermolecular direct arylation



R_1 = electron-donating or electron-withdrawing group

CATALYTIC CYCLE

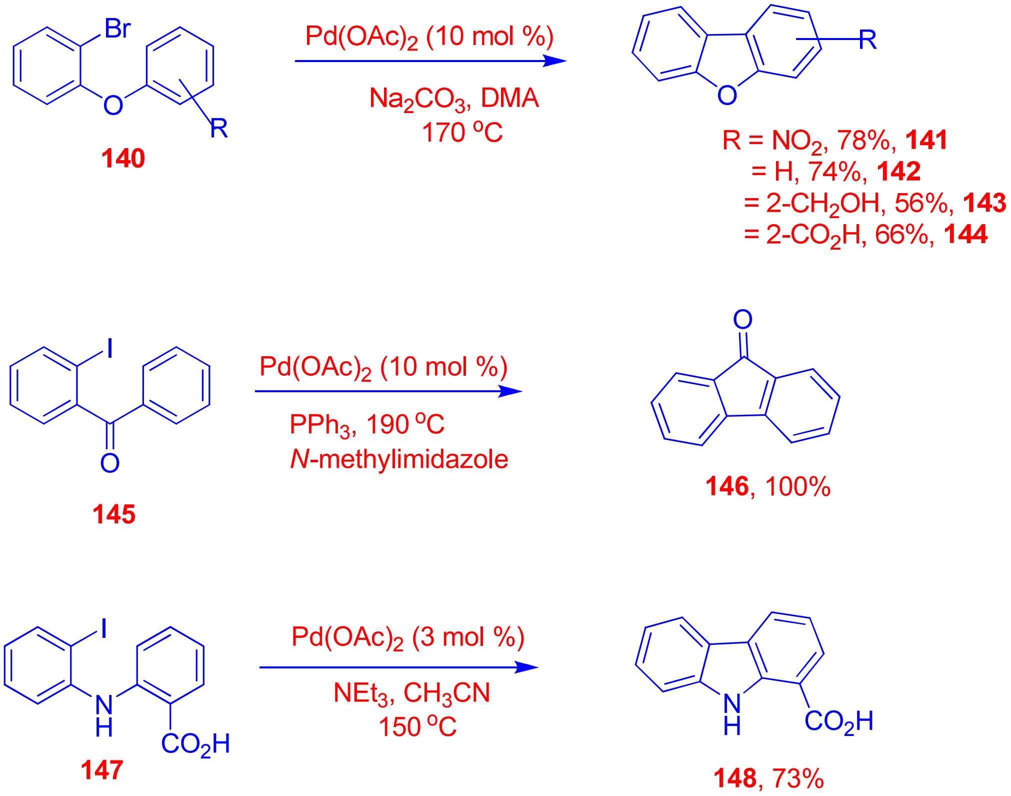


Palladium-catalyzed catalytic cycle

The catalytic reactions which can be carried out with a small amount of Pd complexes is the most useful feature of synthetic reactions involving Pd complexes. In the catalytic reactions, an active catalytic species must be regenerated in the last step of the reactions. Reductive elimination and β-H elimination are two key reactions that regenerate the catalytic species, making the whole reaction catalytic.

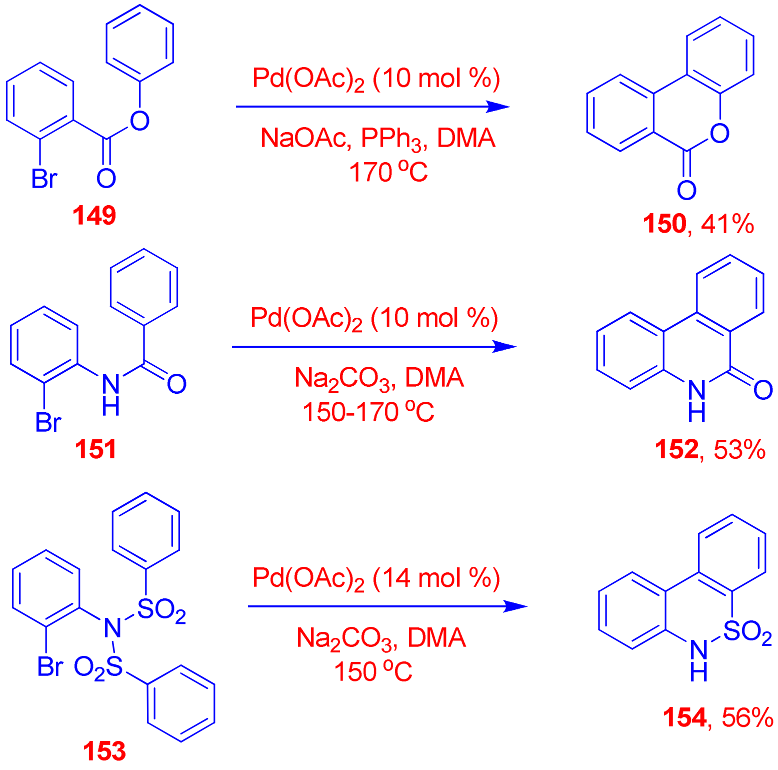
First example of intramolecular direct arylation was reported by Ames in the early 1980s (Eq. 22).[84] In this seminal study, a variety of functionalized dibenzofurans were prepared by treating the corresponding 2-bromophenyl phenylethers **140** in DMA at 170 °C in the presence of Pd(OAc)$_2$ and Na$_2$CO$_3$. Electron-donating and electron-withdrawing substituents were tolerated under the reaction conditions to afford the desired products **141**-**144** in moderate to good yields. In addition, reactions using 2-iodobenzophenone **145** and 2-(iodophenyl)phenylamine **147** were found to yield the corresponding fluorenone **146** nearlyquantitative and carbazole **148** products in high yield.[85]

Eq. 22



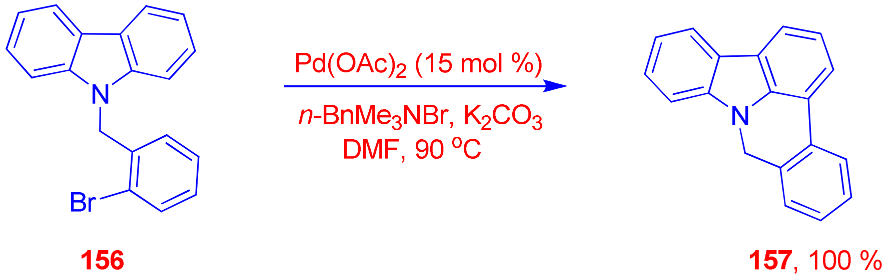
The same methodology was extended to the other cyclic compounds by preparing substrates with varying linkages between the two aryl groups (CH$_2$O, NRCO, SO$_2$NR) (**149**, **151**and **153**) and subjecting these compounds to their palladium-catalyzed direct arylation conditions obtained their corresponding products (**150**, **152**, and **154**) (Eq. 23).[85] In these cases however, preparation of the desired fused six-membered ring products occurred in low yields.

Eq. 23



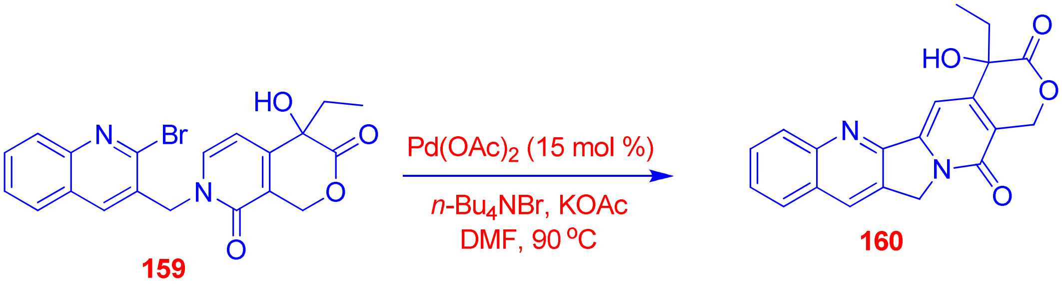
A direct arylation has also been employed for the preparation of a triaza analogue of a "crushed-fullerene" carbazole fragment **157** by employing of the corresponding carbazole **156** proceeded in quantitative yields under the reaction conditions[86] as shown in Eq. 24.

Eq. 24



Comins has reported (Eq. 25) the use of an intramolecular palladium-catalyzed cyclization as the final step in the synthesis of camptothecin **160**.[87] This approach has subsequently been used for the synthesis of the camptothecin analogue GI147211C, and also for the assembly of ring C in the synthesis of several homocamptothecin analogues.[88]

Eq. 25



DOMINO REACTIONS:

The development of efficient syntheses of bioactive compounds such as natural products and analogs, drugs, diagnostics, and agrochemicals in academia and industry is a very important issue of modern chemistry.[89] Thus, multistep syntheses with more than 20 steps have to be avoided since they are neither economically nor ecologically justifiable. Modern syntheses must deal carefully with our resources and our time, must reduce the amount of waste formed, should use catalytic transformations, and, finally, must avoid all toxic reagents and solvents. In addition, synthetic methodology must be designed in a way that allows access to diversified substance libraries in an automatized way. A general way to improve synthetic efficiency and also to give access to a multitude of diversified molecules is the development of domino reactions which allow the formation of complex compounds starting from simple substrates in a single transformation consisting of several steps. We have defined domino reactions as processes of two or more bond-forming reactions under identical conditions, in which the subsequent transformations take place at the functionalities obtained in the former transformations.[90] The quality and importance of a domino reaction can be correlated to the number of bonds generated in such a process and the increase of complexity. They can be performed as single-, two- and multicomponent transformations. Thus, most of the known multicomponent processes, but not all, can be defined as a subgroup of domino reactions.

Transition metal catalyzed coupling transformations are now serving as one of the most useful and powerful tools in organic synthesis. Their application, from laboratory to industrial scale, has permitted to a great number of different subjects.[75] Notably, the latest decade witnessed an unprecedented blossom in the research of transition metal-catalyzed synthesis.[91] Among the massive numbers of reaction styles catalyzed by transition metals, the coupling process forming C–X bonds (X = C, N, O, S) consists of a central issue.[92] In general, Pd, Au, Ag, Rh, Ni, Cu and Fe etc. are the most investigated and employed metal species for these coupling reactions. While different advantages could be specifically ascribed to each of these metals, Cu-catalysis represents a promising direction in C–X coupling reactions for the following reasons:

a) Abundant storage of Cu in the earth and low cost;

b) high catalyst activity in C–X coupling reactions;

c) low toxicity and easy to recycle;

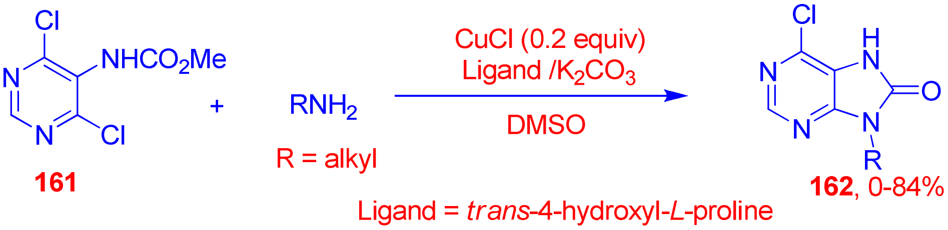
d) excellent tolerance to different reaction protocols as well as functional groups.

Actually, the past decade witnessed sharp increase on the attention to Cu-catalyzed coupling transformations due to the important discovery on organic ligand facilitated copper catalysis, which significantly lowered the demand on reaction conditions and expanded the compatibility of Cu-catalyzed couplings.[93] Accordingly, the research on exploring new application of Cu-catalyzed coupling also gained extensive interest. The synthesis of natural products and biologically interesting molecules are typical examples and have been comprehensively reviewed.[94] An interesting newly emerging direction in the application of Cu-catalysis is that of domino reactions providing heterocyclic products in which the Cu-catalyzed C–X bond formation serves as key transformation. In these reactions, the insertion of Cu to unsaturated C-halo or C–H bonds led to the formation of new C–X (X = C, N, O, S) bonds and initiated the construction of various heterocycles. Considering the boom in Cu-catalyzed synthesis and the importance of C- heteroatom bonds forming reactions, it is not surprising that these reactions rapidly gained numerous attention and have been regarded as one of the major strategies for assembling heterocycles.

Cu-catalyzed C–N coupling reactions between N-nucleophiles and aryl halides are the earliest forms of both Ullmann and Goldberg reactions.[95] These reactions therefore attracted most attention among all Cu-catalyzed coupling transformations.

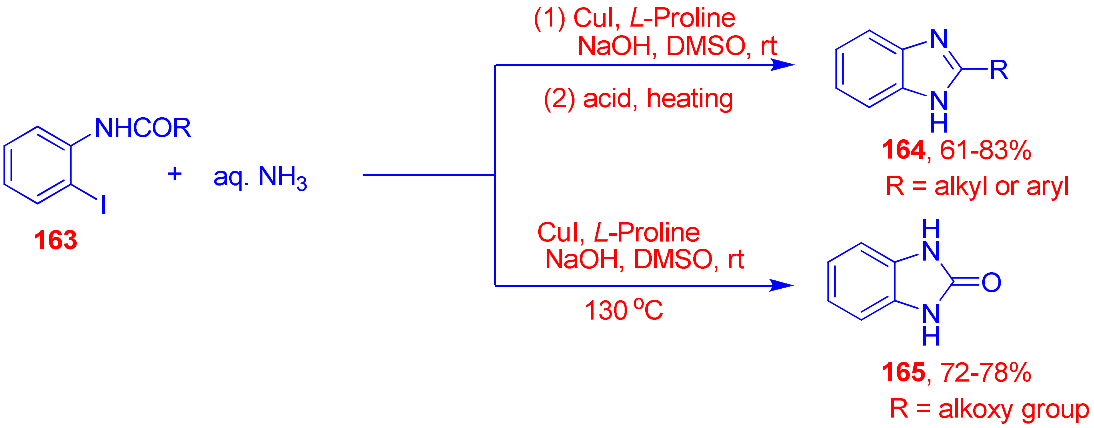
Sun *et al*.[96] developed the tandem synthesis of analogous pyrimidine fused heterocyclic compounds via cascade C–Cl bond amination and an intramolecular carbamate amidation reaction of corresponding substrate **161**, CuCl and *trans*-4-hydroxyl-L-proline were employed as catalyst and ligand, furnished the product **162** in 0-82% yield (Eq. 26).

Eq. 26



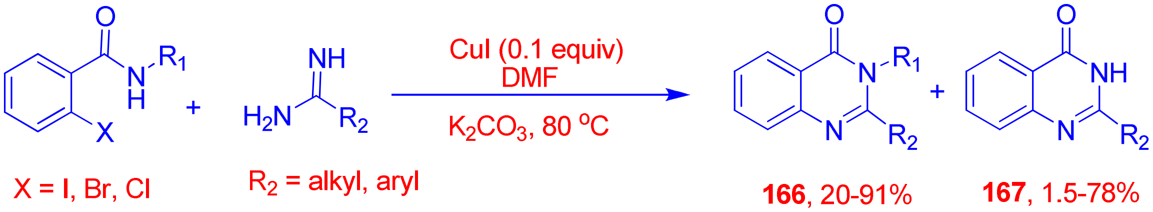
When ammonia was used instead of primary amines, in the above reaction **161** or **163** were able to undergo similar tandem reactions to provide 2-substituted benzimidazoles **164** and 1,3-dihydrobenzimidazol-2-ones **165** (Eq. 27).[97]

Eq. 27



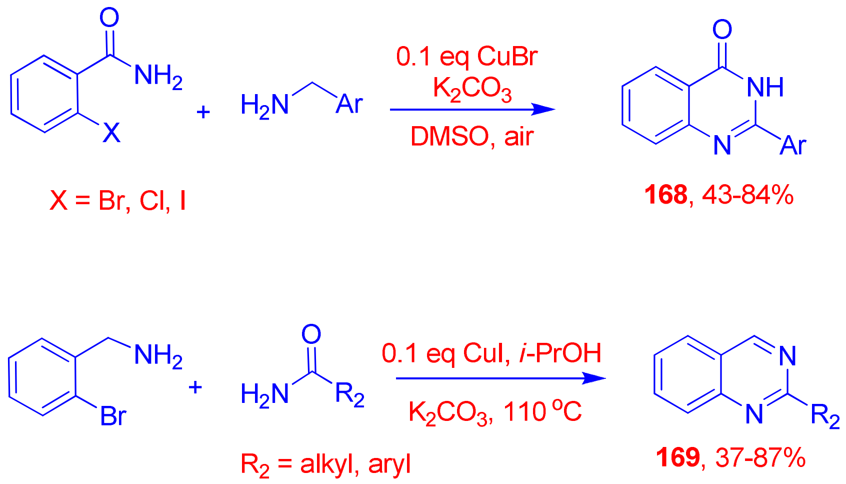
Interestingly, products of type **166** and **167** have also been successfully synthesized by CuI-catalyzed domino reactions of amidines with 2-halobenzamides, could be selectively formed depending on the use of reactants containing different functional groups (Eq. 28).[98]

Eq. 28



And rather recently, the domino C–N coupling–oxidation–cyclization–oxidation reaction between *o*-halo benzamides and arylmethylamine had been devised to directly prepare **168**.[99a] Moreover, products of type **169** were also accessed by new CuI-catalyzed cascade reaction of 2-bromobenzylamines with amides (Eq. 29).[99b]

Eq. 29



168, 43-84%

169, 37-87%

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Palladium-Mediated Intramolecular *O*-Arylation: Synthesis of Quino, Isochromenocarbazolones

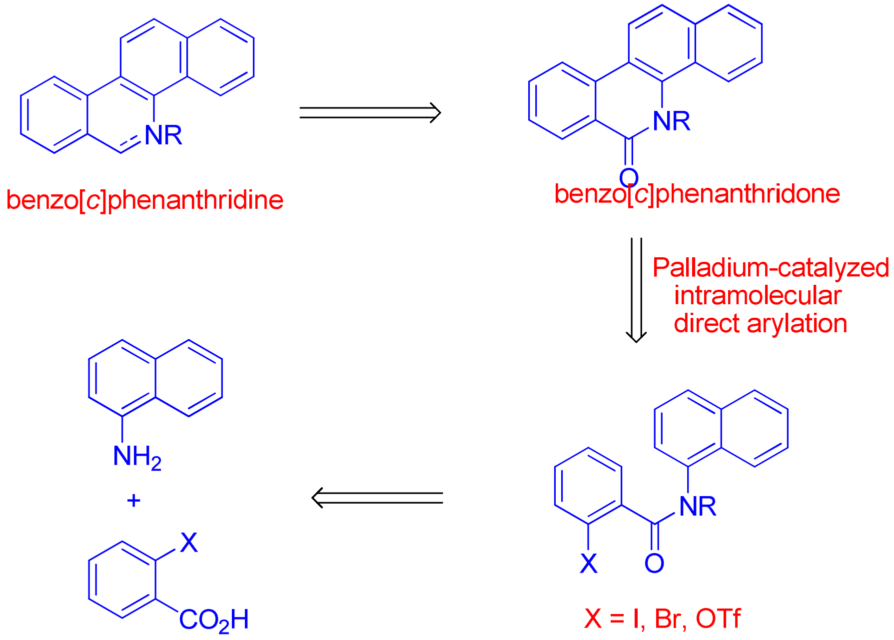
CHAPTER

1

1.1. Introduction

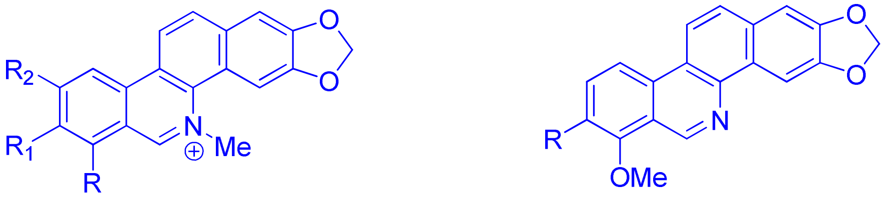
Direct arylation reactions have also been used as an efficient method for generating the biaryl bond in a number of biologically active alkaloids. Harayama and co-workers have reported the synthesis of numerous benzo[*c*]phenanthridine alkaloids using an intramolecular direct arylation reaction as the key step.[100] Their approach involves the coupling of naphthylamine and 2-halobenzoic acid to generate *N*-napthylbenzamide followed by Palladium-catalyzed intramolecular direct arylation furnishes the benzo[*c*]phenanthridone, subsequent convertion of benzo[*c*]phenanthridine can be easily accomplished (Eq. 30).

Eq. 30



Some of the natural products were synthesized by using the the above methodology were represented in Figure 10.

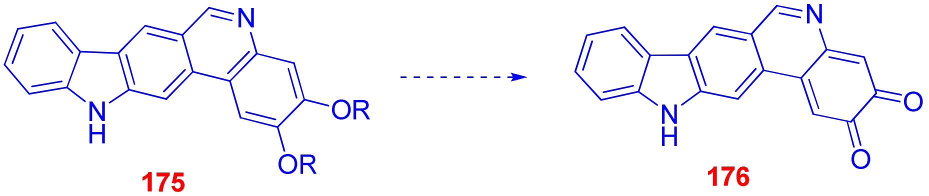
Figure 10



R = R$_1$ = OMe, R$_2$ = H, chelerythrine, **170**
R = H, R$_1$ = R$_2$ = OMe, nitidine, **171**
R = OMe, R$_1$ = OH, R$_2$ = H, fagardine, **172**

R = OMe, norchelerythrine, **173**
R = OH, decarine, **174**

The plant alkaloid ellipticine, 9-methoxyellipticine, 9-hydroxyellipticine and olivacine are potent antitumor agents and elliptinium is used clinically as a drug to treat advanced breast cancer, myeloblastic leukemia and some solid tumors. In recent years many second generation ellipticine-derived antitumor agents like datelliptium and retelliptine have been developed. The molecular basis for their antitumor activity stems from their ability to intercalate between the base pairs in DNA. 9-Hydroxyellipticine exhibits enhanced antitumor activity relative to ellipticine, since the presence of the 9-hydroxyl group could stabilize the intercalating complex by hydrogen bonding with the phosphate groups or base pairs present in the DNA.[101] Further, 9-hydroxyellipticine undergoes oxidation *in vivo* resulting in the formation of electrophilic quinine imines. This type of quinone imines could covalently bind to biomolecules such as proteins and nucleic acids.[102] It was conceived that quinolino carbazole **175** having adjacent methoxy groups at the E ring may undergo similar *in vivo* oxidation to give quinone derivatives **176** which in turn may covalently bind to DNA or proteins.

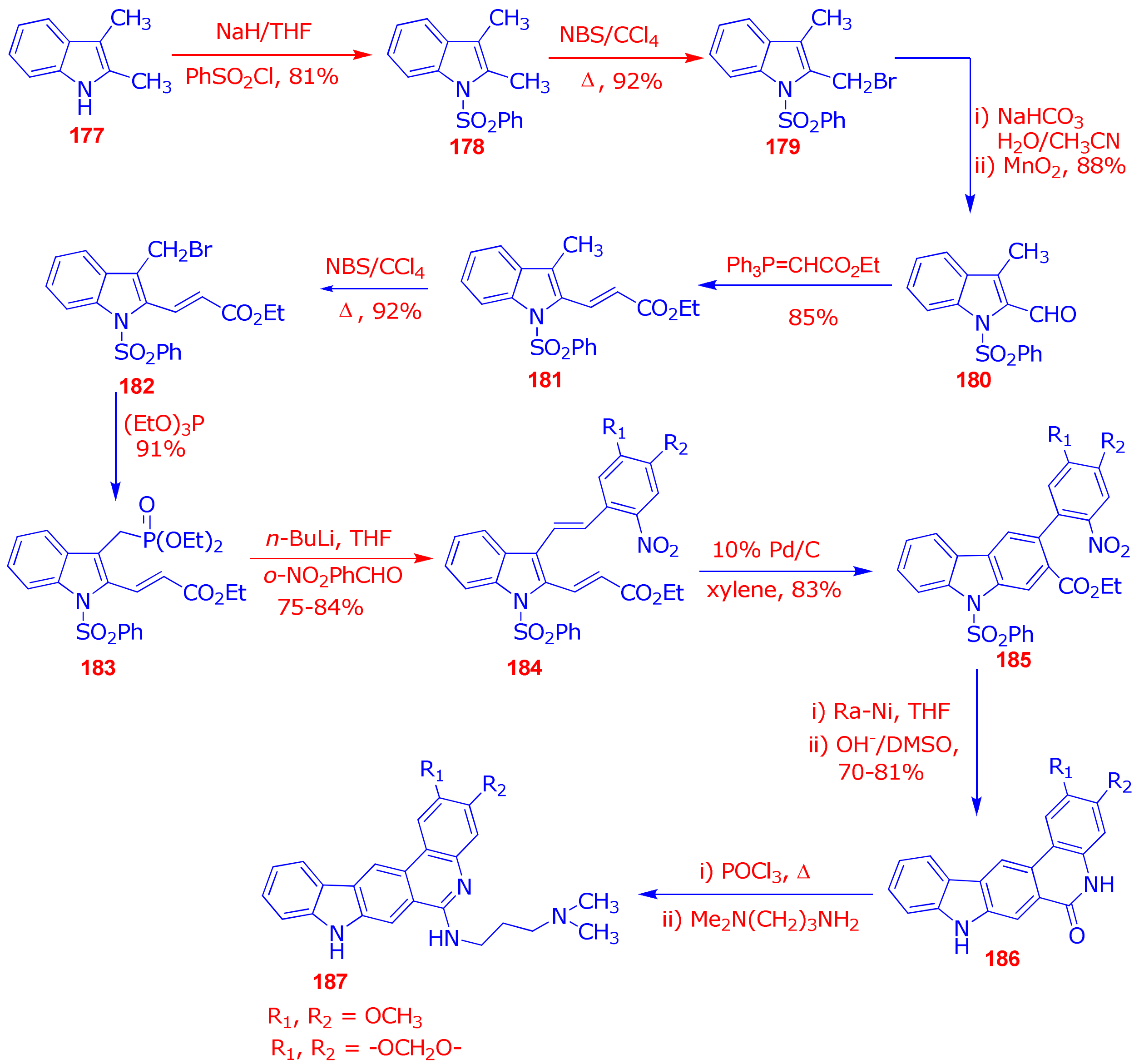


175 **176**

The promising anticancer activity of ellipticine and its analogues prompted chemists to develop simple synthetic routes to access ellipticine nucleus and to synthesize a number of analogues for pharmacological evaluation.[103]

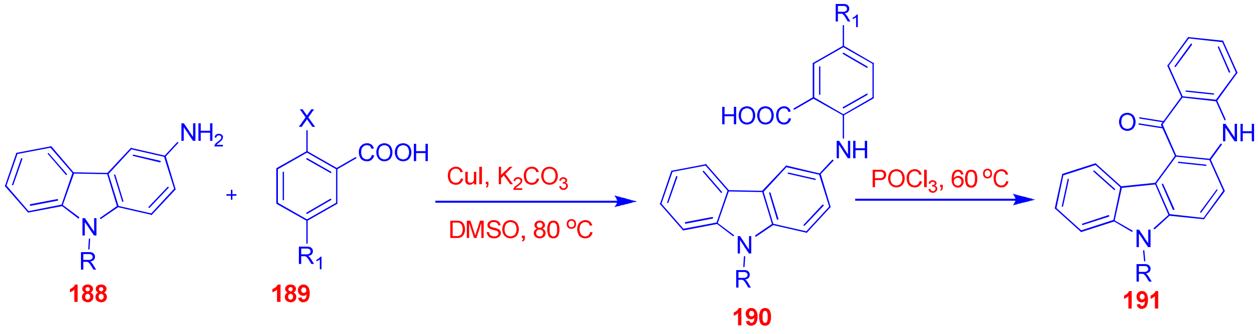
Srinivasan *et al*. reported[104] a new synthetic route (Eq. 31) for the construction of quino[3,4-*b*]carbazole analogues, oxygenated in A, D and E rings as potential DNA binders. 2,3-dimethylindole **177** was phenylsulfonylated by treatment with NaH and phenylsulfonyl chloride in THF to give **178**. Bromination of **178** with 1 equiv. of NBS in boiling CCl_4 gave the monobromo compound **179** in almost quantitative yield. The subsequent solvolysis of **179** using $NaHCO_3$ in CH_3CN followed by oxidation with MnO_2 in boiling 1,2-dichloroethane gave the known 1-(phenylsulfonyl)-3-methylindole-2-carboxaldehyde **180** in 88% yield. The Wittig reaction of **180** with (carbethoxymethylene)triphenylphosphorane in THF gave **181** in 85% yield. The bromination of **181** to give **182** followed by subsequent Arbuzov reaction with triethyl phosphate gave the phosphonate ester **183** which underwent Wittig-Horner reaction with 2-nitrobenzaldehyde in *n*-BuLi/THF condition to give **184**. Boiling a xylene solution of **184** in the presence of 10% Pd/C gave the expected carbazole **185** as a single product. The reductive cyclization of the carbazole **185** with Ra-Ni in boiling THF followed by cleavage of the phenylsulfonyl group gave the expected amide **186**. The quinocarbazole analogue **186** was converted to the corresponding [(dimethylamino)propyl]amino derivative **187** by treatment with $POCl_3$ and [(dimethylamino)propyl]amine.

Eq. 31



Nagarajan *et al*. have reported the synthesis of quinocarbazoles by carried out the condensation of 3-amino-9-ethylcarbazole **188** with various *o*-iodobenzoic acids **189** in presence of CuI (0.1 equiv.) and K_2CO_3 (2.0 equiv.) in DMSO at 80 °C obtained the Ullmann coupled product in good yields. The condensed products underwent cyclization with phosphorous oxychloride at 60 °C furnished the corresponding quinocarbazoles **191** in good yields (Eq. 32).[105]

Eq. 32

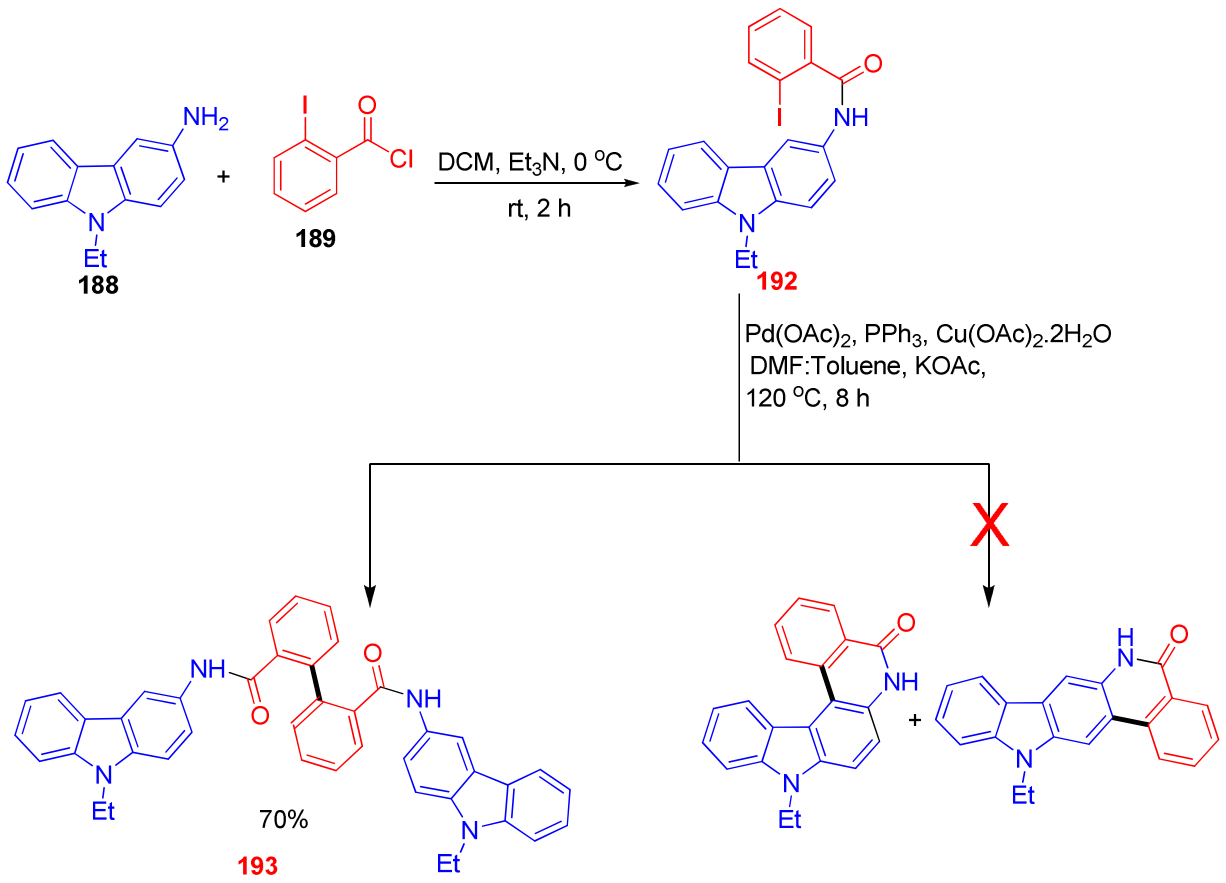


The promising anticancer activity of ellipticine and its analogues prompted chemists to develop simple synthetic routes to access ellipticine nucleus and to synthesize a number of analogues for pharmacological evaluation.

1.2. SYNTHESIS OF QUIONOCARBAZOLONES:

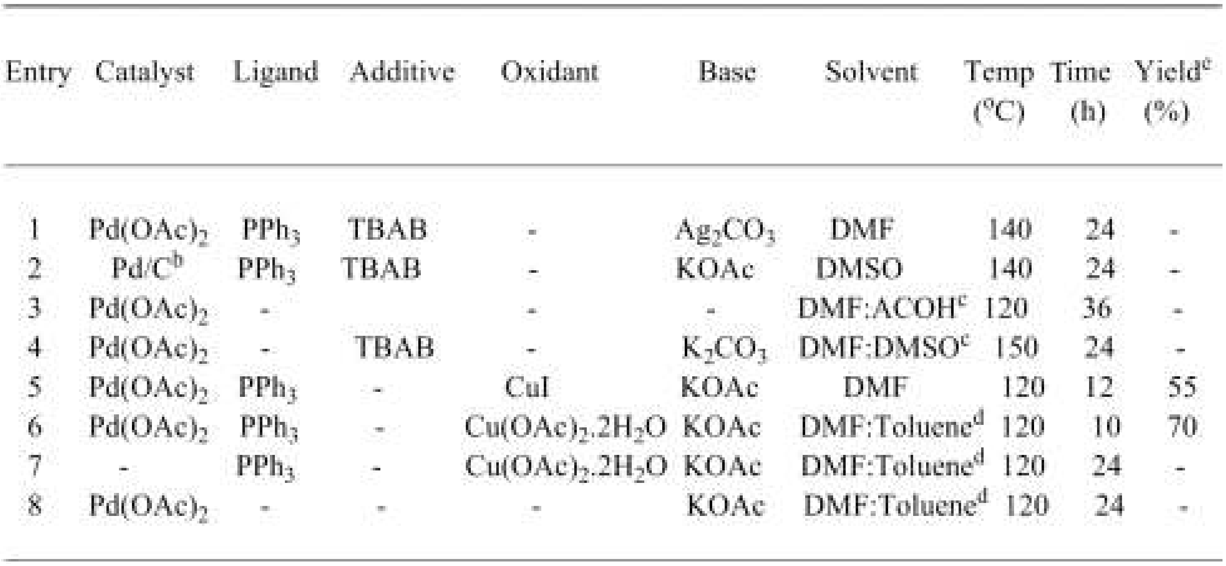
Intramolecular direct arylation of arenes using palladium catalysts is one of the very useful alternative method for the synthesis of various heterocycles such as cabazoles, isoquinolines and indoles.[106] Among these carbazoles[107] and its fused derivatives such as pyrido,[108] pyrrolo[109] and quinocarbazoles[110] have attracted considerable attention from medicinal and synthetic chemists mainly because of the wide range of biological applications (antitumor,[111] anticancer,[112] DNA intercalator[113]) displayed by this class of compounds. As a result, immense interest has grown in the development of various methods for the efficient and rapid synthesis of these molecules. Developing new synthetic methodologies for the synthesis of biologically active indole and carbazole skeleton has been our longstanding quest.[114]

The first attempt of cyclization with *N*-(9-ethyl-9*H*-carbazol-3-yl)-2-iodobenzamide **192** (prepared from 9-ethyl-3-aminocarbazole **188** and 2-iodobenzoyl chloride **189**) using various conditions like changing catalyst, base and solvent gave unsatisfactory results and starting material was recovered in most of the the cases as shown in Scheme 1. When we examined the reaction with oxidants like Cu(OAc)$_2$ and CuI etc. in a mixture of solvents, homo coupled product *N*^{2},*N*$^{2'}$-bis(9-ethyl-9*H*-carbazol-3-yl)biphenyl-2,2′-dicarboxamide **193** was obtained. Various reaction conditions performed are summarized in Table 1.



Scheme 1. Attempted synthesis of quinocarbazoles

Table 1. Biaryl coupling[a] of *N*-(9-ethyl-*H*-carbazole-3-yl)-2-iodobenzamide (192)



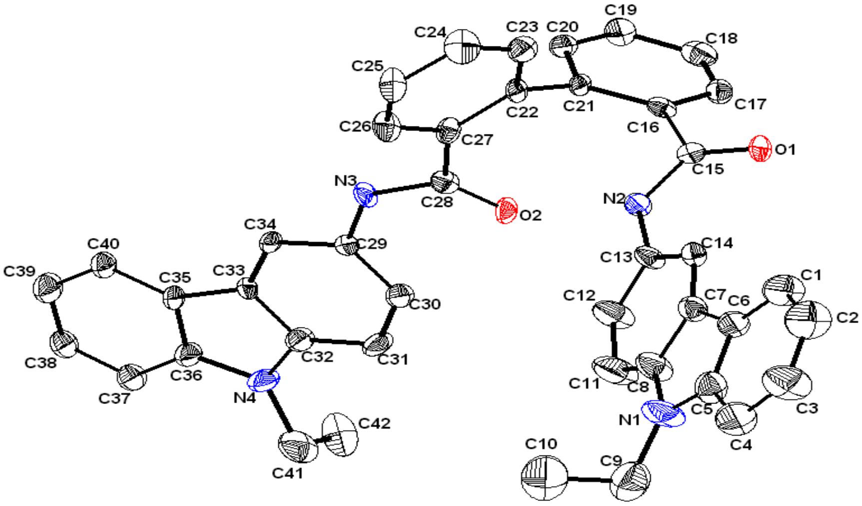
Entry	Catalyst	Ligand	Additive	Oxidant	Base	Solvent	Temp (°C)	Time (h)	Yield[e] (%)
1	$Pd(OAc)_2$	PPh_3	TBAB	-	Ag_2CO_3	DMF	140	24	-
2	Pd/C[b]	PPh_3	TBAB	-	KOAc	DMSO	140	24	-
3	$Pd(OAc)_2$	-		-	-	DMF:ACOH[c]	120	36	-
4	$Pd(OAc)_2$	-	TBAB	-	K_2CO_3	DMF:DMSO[c]	150	24	-
5	$Pd(OAc)_2$	PPh_3	-	CuI	KOAc	DMF	120	12	55
6	$Pd(OAc)_2$	PPh_3	-	$Cu(OAc)_2.2H_2O$	KOAc	DMF:Toluene[d]	120	10	70
7	-	PPh_3	-	$Cu(OAc)_2.2H_2O$	KOAc	DMF:Toluene[d]	120	24	-
8	$Pd(OAc)_2$	-	-	-	KOAc	DMF:Toluene[d]	120	24	-

[a] Unless otherwise stated, all reactions were carried out by using 0.1 equiv. of catalyst, 0.2 equiv. of ligand, 1.5 equiv. of additive/oxidant, 2 equiv. of base. [b] 0.2 equiv. of Pd/C was

used. [c] mixture of solvents were used in the ratio 1:1. [d] (DMF:Toluene) used in the ratio 1:1. [e] isolated yields. (TBAB = Tetrabutylammonium bromide).

The structure of **193** was also confirmed by the single crystal X-ray analysis. The ORTEP diagram is shown in Figure 11.[115]

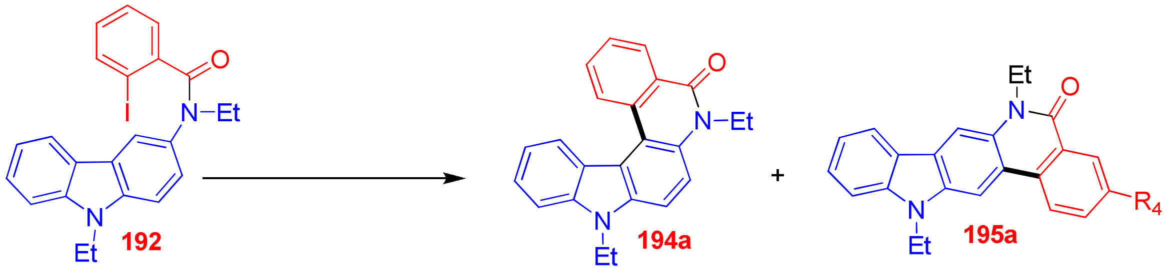
Figure 11 ORTEP diagram of 193



This homo coupling was probably due to the free N-H group of amide that forms the Pd(II) complexes with both *ortho* positions i.e. C2 and C4 of **192** in the presence of a base to undergo the coupling reaction.[116]

To avoid homocoupled product, we performed the reaction using *N*-alkylated amides (Scheme 2). The *N*-ethyl-*N*-(9-ethyl-*H*-carbazol-3-yl)-2-iodobenzamide **192a** successfully underwent cyclization to give the products **194a** and **195a**. The two regioisomeric products **194a** and **195a** are formed due to the availability of two *ortho* C-H positions. Then we made consequential changes to catalyst, ligand, additive, base and solvent to improve the yield and regioselectivity. Various reaction conditions were checked and the details are listed in Table 2.

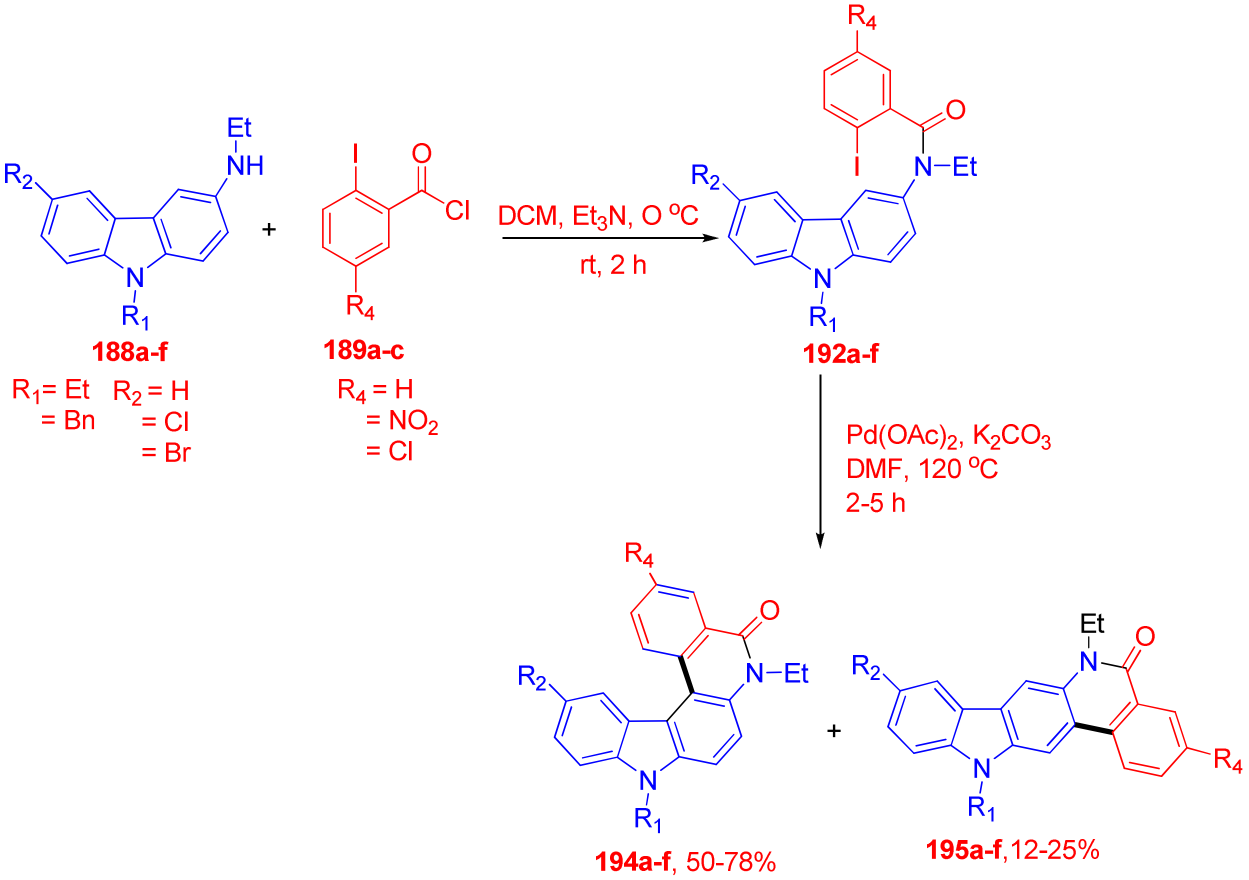
Table 2. Optimization[a] of palladium mediated cyclization of 192 to 194a and 195a



Entry	Catalyst	Ligand	Additive	Base	Solvent	Time (h)	Yield[g] (%)
1	$Pd(OAc)_2$	PPh_3	TBAB	KOAc	Toluene	20	20
2	$Pd(OAc)_2$	PPh_3	TBAB	Et_3N	DMSO	24	45
3	$Pd(OAc)_2$	PPh_3	TBAB	Et_3N	DMF	18	70
4	$Pd(OAc)_2$	PPh_3	TBAB	Ag_2CO_3	DMF	20	55
5	$Pd(OAc)_2$	PPh_3	TBAB	KOAc	DMF	10	80
6	$Pd(OAc)_2$	PPh_3	TBAB	K_2CO_3	DMF	10	80
7	$Pd(OAc)_2$	PPh_3		KOAc	DMF	10	80
8	$Pd(OAc)_2$		TBAB	KOAc	DMF	10	80
9	$Pd(OAc)_2$			KOAc	DMF	10	88
10	$PdCl_2$			K_2CO_3	DMF	3	85
11	-			K_2CO_3	DMF	24	nr
12	**$Pd(OAc)_2$**			**K_2CO_3**	**DMF**	**2**	**88**
13	Pd/C			K_2CO_3	DMF	3	80
14	-			K_2CO_3	$DMF+H_2O$[c]	3	80
15	Pd/C[b]			K_2CO_3	$DMF+H_2O$[c]	3	80
16	Pd/C[b]			K_2CO_3	$DMF+H_2O$[d]	24	20
17	$PdCl_2(PPh_3)_2$			K_2CO_3	DMF	3	85
18	$Pd(OAc)_2$			K_2CO_3	H_2O	20	nr

[a] Unless otherwise stated, all reactions were carried at 120 °C in a seal tube using 1.5 mL solution, using 0.05 equiv. of catalyst, 0.2 equiv. of ligand, 1.5 equiv. of additive, 2.5 equiv. of base. [b] Pd/C used 10 mol%. [c] DMF+H_2O in the ratio 1:0.2 mL. [d] DMF+H_2O in the ratio 1:1. [e] no reaction. [f] high regioselectivity and high yield obtained i.e. (50:38). [g] isolated and combined yield of **194a+195a**. (TBAB = tetrabutylammonium bromide).

We performed the reaction with various catalysts. Among them, $Pd(OAc)_2$ was found to be the best. Even though Pd/C also gave better results, yields were poor when substituents were introduced. When PPh_3, TBAB were used as ligand and additive respectively, longer reaction times were required. When we performed the reaction without ligand and additive, the reaction proceeded well within 2 h in 88% yield and with good regioselectivity (50:38). All the products were well characterized. The effect of the base on the reaction was also investigated. KOAc and K_2CO_3 were more effective than the other bases while DMF is better solvent than DMSO and toluene. No reaction was found to occur at or below 80 °C.



Scheme 2. Synthesis of quinocarbazole derivatives

To examine the versatility of this intramolecular palladium catalyzed *ortho* arylation, a number of quinocarbazole annulated cyclic amide derivatives were synthesized by employing the optimized reaction condition, $Pd(OAc)_2$, K_2CO_3 and DMF. When the products **192a-f** were subjected to cyclization under optimized conditions, they underwent facile cyclization to give isomeric products **194a-f** and **195a-f**. These results are summarized in Scheme 2 and Table 3.

Table 3. Synthesis of quinocarbazole derivatives

Entry	R_1	R_2	R_3	R_4	Amide	Yield (%)	Cyclized Product	Time (h)	Yield[a] (%)
1	Et	H	Et	H	**192a**	79	**194a**:**195a**	2	88 (50:38)
2	Et	H	Et	NO_2	**192b**	82	**194b**:**195b**	2	90 (78:12)
3	Et	H	Et	Cl	**192c**	76	**194c**:**195c**	5	70 (52:18)
4	Bn	H	Et	H	**192d**	75	**194d**:**195d**	3	85 (60:25)
5	Et	Cl	Et	H	**192e**	70	**194e**:**195e**	5	78 (62:16)
6	Et	Br	Et	H	**192f**	68	**194f**:**195f**	5	70 (55:15)

[a] isolated yield and regioisomeric ratio of **194a-f** and **195a-f**.

The two regioisomers were characterized by ^1H NMR. In the ^1H NMR spectrum of **194a,** two doublets were observed at δ 9.01 and δ 8.61 ppm, where as for **195a** two singlets were observed at δ 8.12 and δ 8.29 ppm. Structure of **194a** was further confirmed by the single crystal X-ray analysis.[115] When nitro group is present, the reaction was proceeded with in 2 h with high yield due to its high electron withdrawing nature. ORTEP diagrams of **195b** was shown in Figure 12.[115] The ORTEP diagrams of chloro substituted derivatives **194c** and **195c** were shown in Figure 13.[115]

Figure 12 ORTEP diagram of 194a and 195b

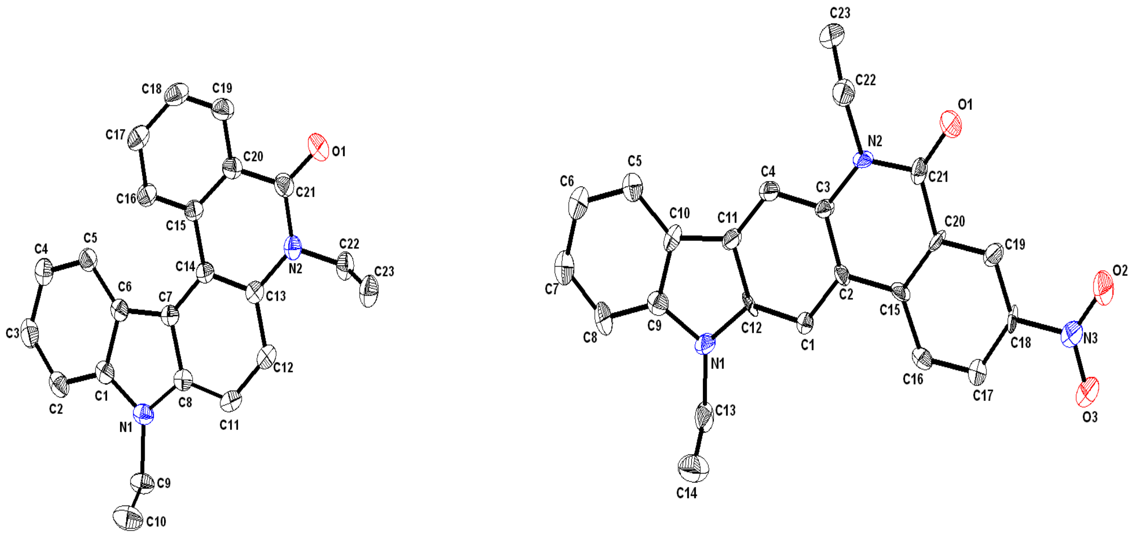
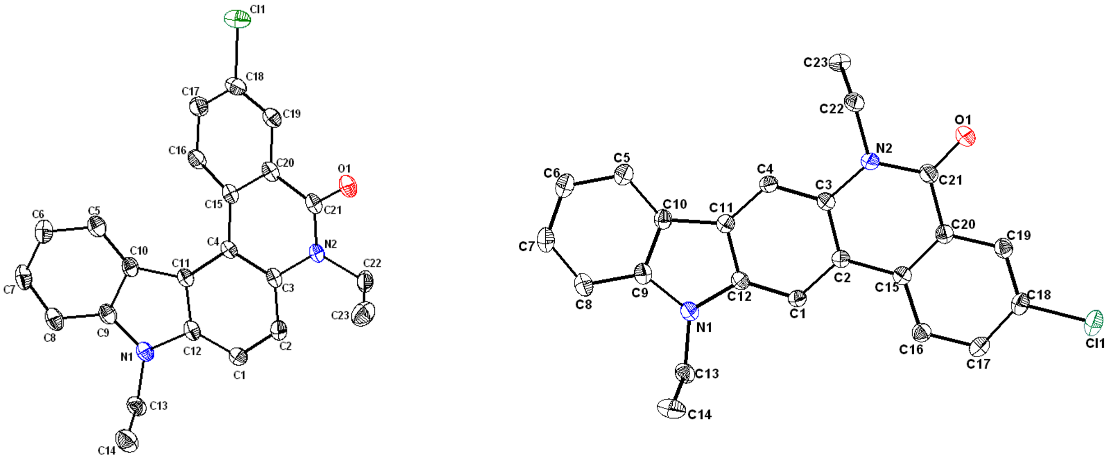
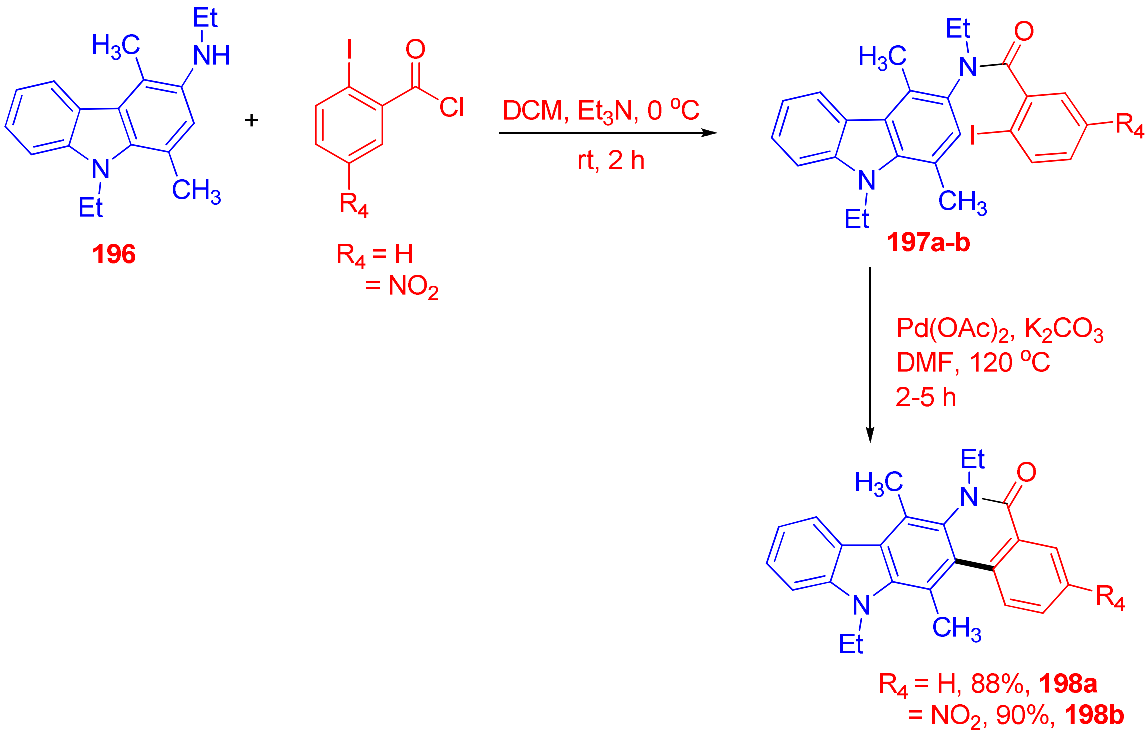


Figure 13 ORTEP diagrams of 194c and 195c



The same methodology is also extended to various substituted 1,4-dimethylcarbazoloiodobenzamides **197a-b** under optimized conditions to give the products **198a-b** in good yields as shown in Scheme 3.

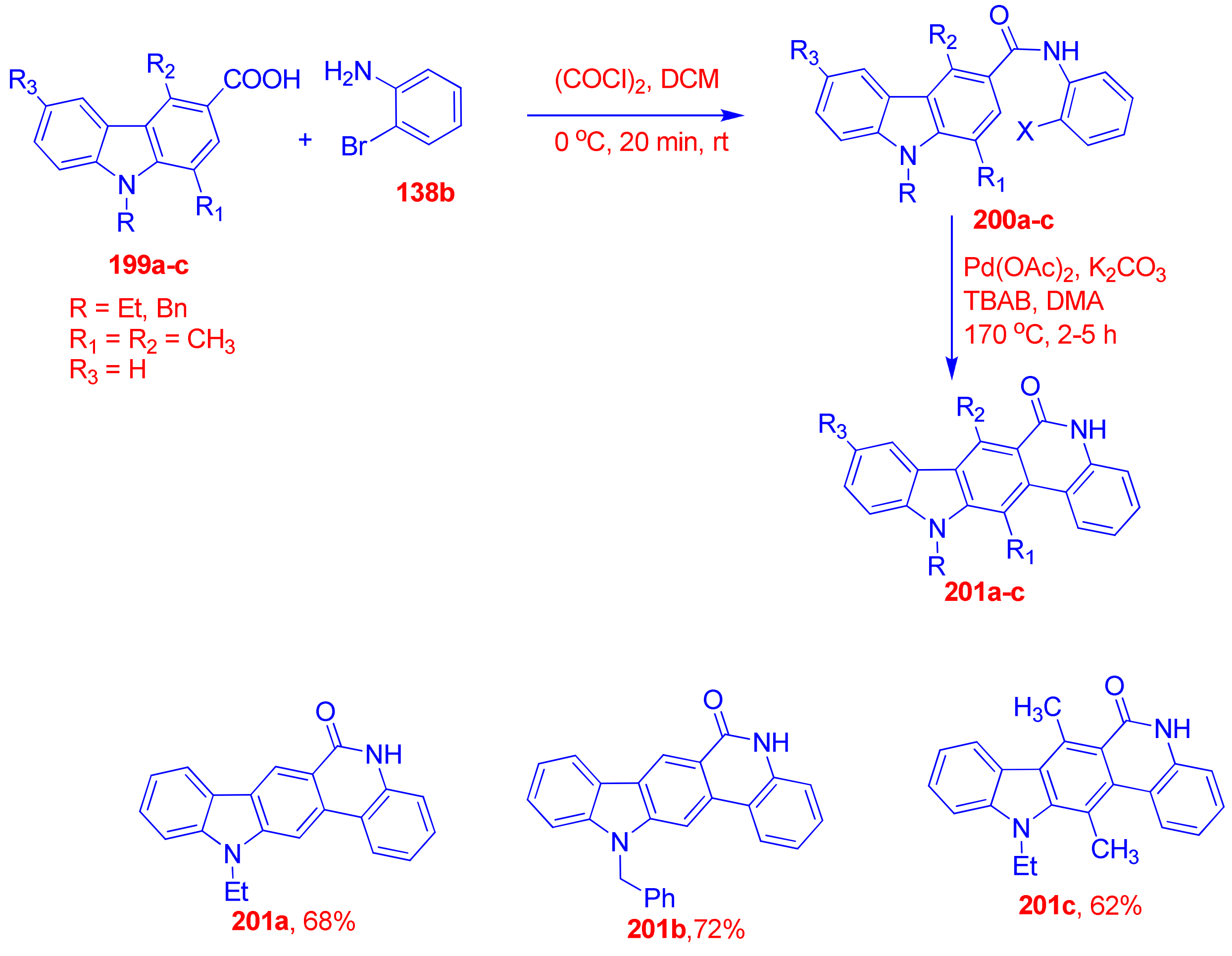


Scheme 3. Synthesis of indolo[2,3-*b*]phenanthridinone derivatives

SYNTHESIS OF QUINO CARBAZOLONE DERIVATIVES:

N-(2-Bromophenyl)-9-ethyl-9*H*-carbazole-3-carboxamide **200a** which was synthesized from 9-ethyl-9*H*-carbazole-3-carbonyl chloride and 2-bromoaniline were used as the prototype substrates for optimizing the reaction conditions. The initial screenings with various solvents like toluene, 1,4-dioxane were unsuccessful, recovering the starting material in all cases. When DMF was used, at 120-140 °C observed the product in poor yields. When increased the temperature to 170 °C obtained **201a** as major isomer. The influence of catalyst, ligand, additive and temperature in the reaction outcome were examined. By examining various catalysts, we found that $Pd(OAc)_2$ was suitable catalyst. The effect of bases on the reaction was studied, different bases such as Et_3N, pyridine were not effective but K_2CO_3 and Na_2CO_3 were most effective. DMA was the best solvent compared to other solvents. TBAB and trifluoroacetic acid were suitable additives. Ligand had no effect on the reaction, without ligand reaction proceeded well within 2 h. No reaction was found to occur at or below 100 °C.

After all these optimization assays, the best optimized conditions were found to involve 10 mol % of $Pd(OAc)_2$ in DMA with K_2CO_3 (3 equiv) as a base and TBAB (1 equiv) as additive at 170 °C. At these optimized conditions, **200a** was converted to give the product 2**01a** in good yield.



Scheme 4. Synthesis of indolo[2,3-*b*]phenanthridinone derivatives

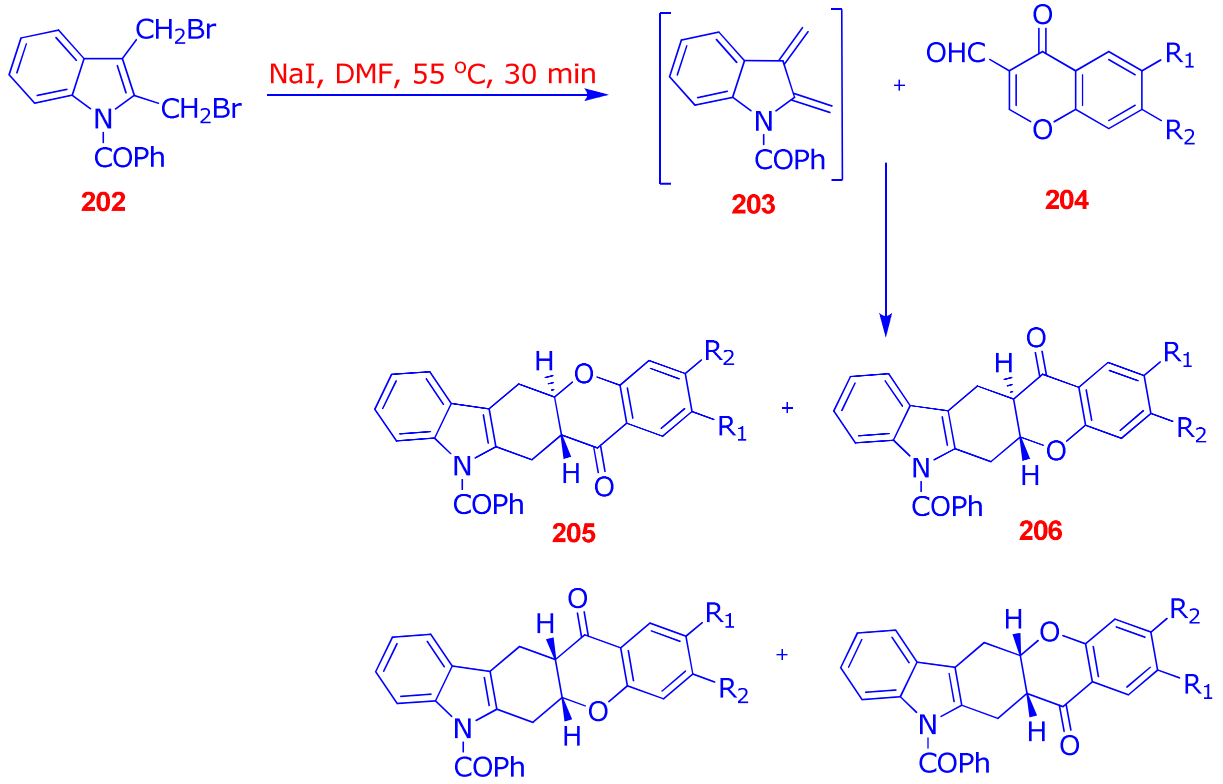
1.3. SYNTHESIS OF ISOCHROMENOCARBAZOLONES:

Carbazole and its fused derivatives such as pyranocarbazoles have attracted great attention from medicinal and synthetic chemists due to their wide range of biological applications. Glycoborinine, euchrestifoline and clausamines are some of the important pyranocarbazole alkaloids[3] as shown in Figure 5. Among these, clausamines A-C and D-E isolated from *Clausena anisata* and *Clausena excavate* respectively, possess various biological activities such as antitumor,[117] antioxidative, and antiinflammatory[118] and also potently inhibit Epstein-Barr virus early antigen (EBV-EA) activation induced by 12-*O*-tetradecanoylphorbol-13-acetate (TPA) in Raji cells.

The syntheses of Euchrestifoline, Eustifoline D and Glycomaurrol were reported by Knölker and co-workers using an elegant cross-coupling strategy to assemble the carbazole core of the targets. Despite the great interest that has risen for the synthesis of pyranocarbazole alkaloids and its derivatives, very little attention has been paid to the synthesis of its isomers and fused with other biologically important molecules.[119]

Stephanidou-Stephanatou *et al*. developed[120] a synthetic route for the synthesis of a new class of indole derivatives, tetrahydrochromeno[2,3-*b*]carbazoles **205-208**. The cycloaddition reactions of chromone-3-carboxaldehydes **204** with indole-*o*-quinodimethane **203** which was synthesized from (2,3-bis(bromomethyl)-1*H*-indol-1-yl)(phenyl)methanone **202** gave a diastereomeric mixture of Diels–Alder cycloadducts in good yields after *insitu* deformylation as shown in Eq. 33.

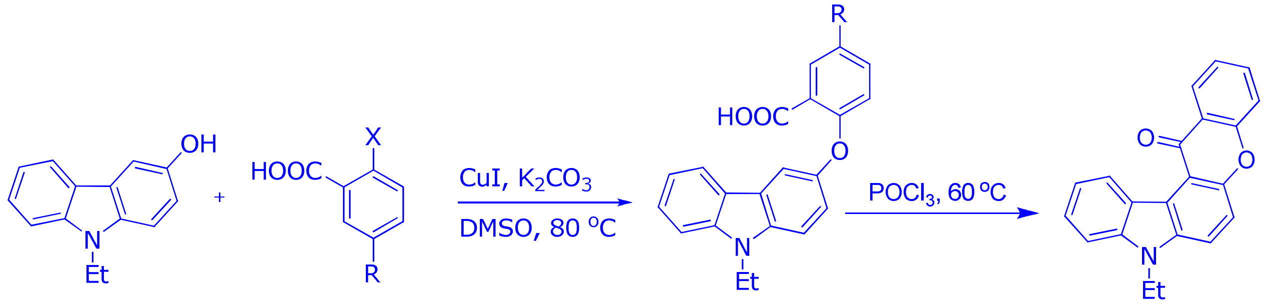
Eq. 33



202 **203** **204** **205** **206** **207** **208**

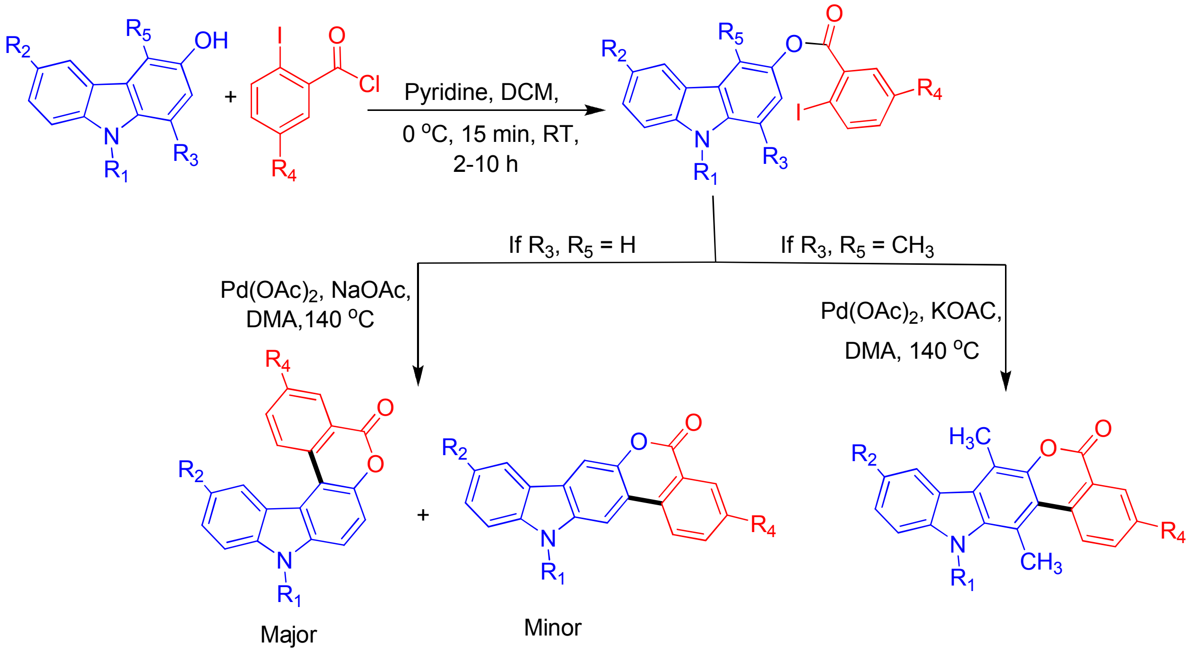
Nagarajan *et al*. have reported the synthesis of chromenocarbazoles. 3-Hydroxy-9-ethylcarbazole **209** condensed with *o*-halobenzoic acids **189** to provide the corresponding products **210** in good yield. The condensed products **210** underwent the cyclization to the corresponding chromenocarbazoles **211** in good yields on treatment with excess of $POCl_3$ (Eq. 34).[105]

Eq. 34



209 **189** **210** **211**

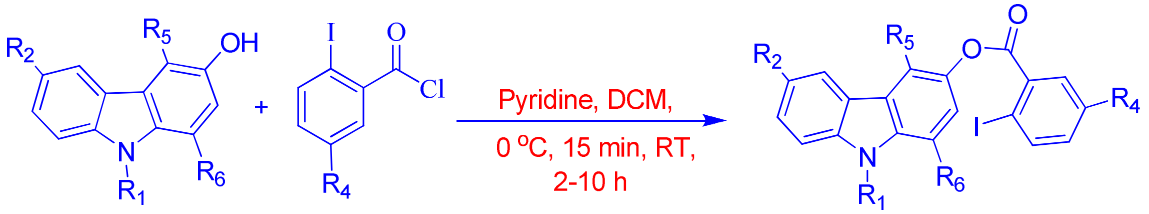
In particular, palladium catalyzed intramolecular direct arylation of C–H bond of a heteroaromatic compound is of considerable interest due to its significant utility in organic synthesis.[10] In the present work, we wish to demonstrate the synthesis of isochromenocarbazolones by intramolecular palladium catalyzed *ortho* arylation starting from various derivatives of carbazolyliodobenzoates and the schematic representation as shown in Scheme 5.



Scheme 5. Plan of synthetic work

9-Ethyl-9*H*-carbazol-3-yl 2-iodobenzoate **213a** which was synthesized from 9-ethyl-3-hydroxycarbazole **212a** and 2-iodobenzoyl chloride **189a** were used as the prototype substrates for optimizing the reaction conditions as shown in Table 4.

Table 4. Synthesis of carbazoloiodobenzoates:

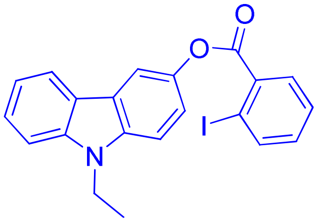


Pyridine, DCM,
0 ^{o}C, 15 min, RT,
2-10 h

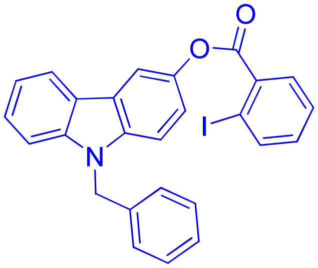
212a-h **189a-c** **213a-h**

R_1 = H, Et, Bn
R_2 = CH_3, H
R_5, R_6 = H, CH_3

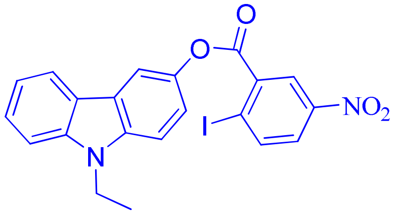
R_4 = H,
= NO_2
= Cl



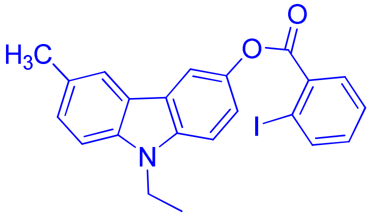
213a, 65%



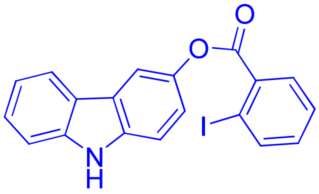
213b, 68%



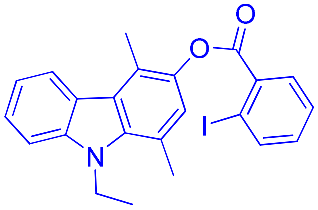
213c, 72%



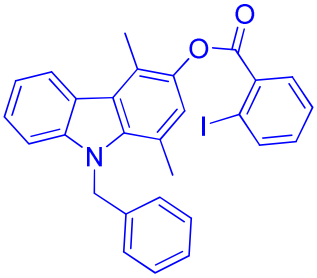
213d, 62%



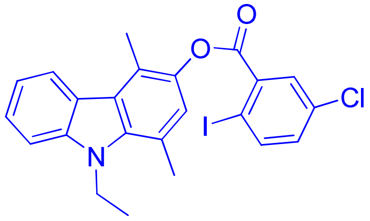
213e, 85%



213f, 70%



213g, 72%



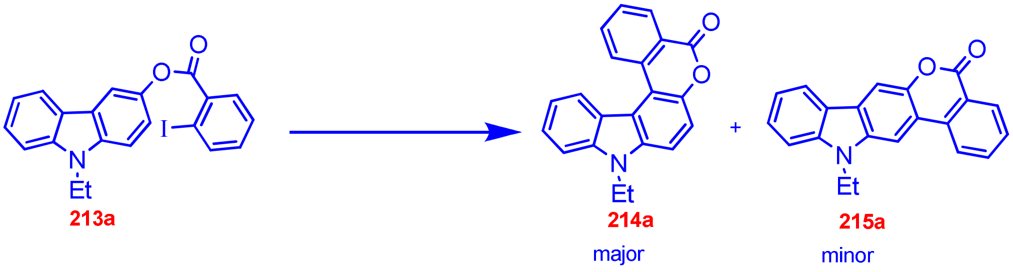
213h, 65%

The initial screenings with various solvents like toluene, 1,4-dioxane, 1,2-dichlorobenzene were unsuccessful, recovering the starting material in all cases. When a mixture of solvents such as DMF:DMA was used, the two regioisomeric products **214a** and **215a** were obtained in poor yields (entry 5, Table 5). The influence of catalyst, ligand, additive and temperature in the reaction outcome were examined as shown in Table 1. By examining various catalysts, we found that $Pd(OAc)_2$ was suitable catalyst. The effect of bases on the reaction was studied, different bases such as Et_3N, DABCO, pyridine and Cs_2CO_3 were not effective but NaOAc and KOAc were most effective. DMA was the best solvent compared to other solvents. Ligand and additives had no effect on the reaction, without ligand and additive the reaction proceeded well within 4 h (entry 16, Table 5). No reaction was found to occur at or below 110 $^{\circ}$C.

After all these optimization assays, the best optimized conditions were found to involve 10 mol % of $Pd(OAc)_2$ in DMA with NaOAc (2.5 equiv) as a base at 140 °C. At these optimized conditions, **213a** was converted to give a mixture of products **214a** and **215a** in 85% yield, which on column chromatographed over silica gel obtained **214a** and **215a** in 55 and 27% yields respectively, within 4 h (entry 16, Table 5). The formation of two isomers **214a** and **215a** is due to the two reactive *ortho* positions of **213a**. **214a** is formed as the major and **215a** as minor product.

The two regioisomers **214a** and **215a** were characterized by their ^{1}H NMR spectra. In the ^{1}H NMR spectrum of **214a**, two doublets were observed at δ 8.94 and δ 8.56 where as for **215a** clearly two singlets at δ 8.04 and δ 7.98 were observed.

Table 5. Optimization reaction conditions



213a

214a major

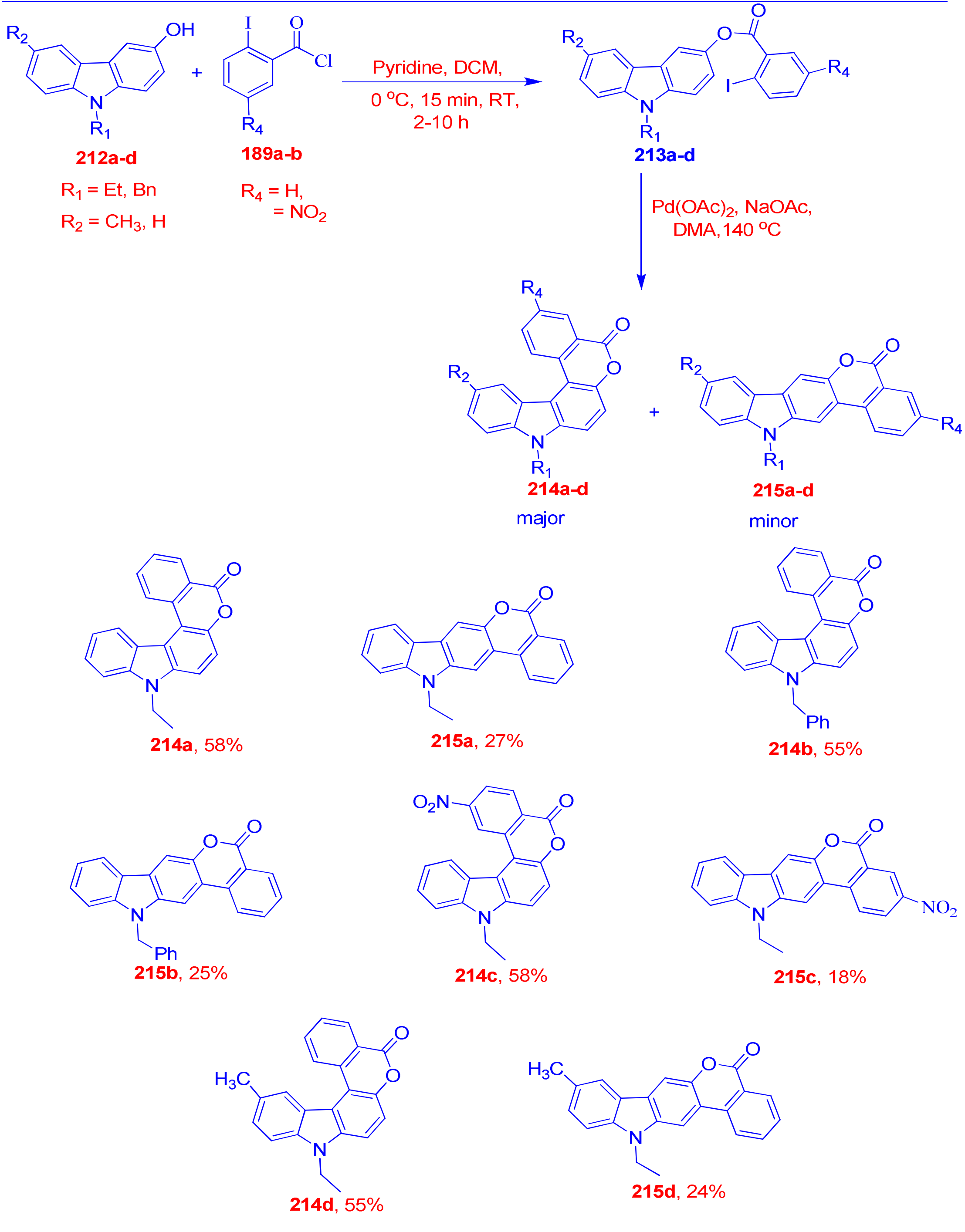
215a minor

Entry	Catalyst	Ligand	Additive	Base	Solvent	Temp (°C)	Time (h)	Yield(%)[g] **(214a+215a)**
1	$Pd(OAc)_2$	PPh_3		K_2CO_3	Toulene	120		nr[h]
2	$Pd(OAc)_2$	PPh_3	TBAB	KOAc	1,4-dioxane	120	24	nr
3	$Pd(OAc)_2$			KOAc	DMF	110	24	nr
4	$Pd(OAc)_2$	PPh_3	TBAB	NaOAc	DMF	140	12	35
5	$Pd(OAc)_2$	PCy_3		NaOAc	DMF:DMA[f]	140	12	55
6	$PdCl_2(PPh_3)_2$			KOH	DMSO	140	16	78
7	CuI[b]		TBAB	K_2CO_3	DMSO	140	16	nr
8	$Pd(OAc)_2$	PPh_3	TBAB	NaOAc	TEG	120	16	53
9	$Pd(OAc)_2$	PPh_3	TBAB	$NaHCO_3$	DMA	130	12	75
10	$Pd(OAc)_2$	PPh_3	TBAB	NaOAc	DMA	130	10	80(52:22)
11	$Pd(OAc)_2$	PCy_3		DABCO	DMA	130	24	nr
12	$Pd(OAc)_2$	PCy_3	SDS[e]	K_2CO_3	DMA	130	10	58
13	$Pd(OAc)_2$		TBAB	NaOAc	DMA	130	10	80(52:22)
14	$Pd(OAc)_2$	PPh_3		NaOAc	DMA	130	10	80(52:22)
15	$Pd(OAc)_2$			NaOAc	DMA	140	8	85(58:27)[i]
16	$Pd(OAc)_2$[c]			NaOAc	DMA	140	4	85(58:27)
17	$PdCl_2(PPh_3)_2$			NaOAc	DMA	130	10	80(58:22)
18	$PdCl_2$			NaOAc	DMA	140	10	60(25:15)
19	Pd/C[d]			NaOAc	DMA	140	16	44
20	$Pd(PPh_3)_4$			KOAc	DMA	140	10	85(58:27)
21	$Pd(OAc)_2$			$NaOAc.3H_2O$	DMA	130	8	68
22	$Pd(OAc)_2/H_2O$ act			KOAc	DMA	140	16	nr
23	$Pd(OAc)_2$			NaOAc	DMA	120		24[j]

[a] Unless otherwise stated, all reactions were carried out in a sealed tube using 2.0 mL solvent, 0.05 equiv of catalyst, 0.2 equiv of ligand, 1.0 equiv of additive, 2.5 equiv of base. [b] CuI used 10 mol %. [c] $Pd(OAc)_2$ used as 10 mol %. d Pd/C used 20 mol %. [e] SDS used 1.5 equiv. [f] DMF:DMA in the ratio 1:1. [g] Combined yield of **214a**+**215a**. [h] no reaction. [i] in parenthesis isolated yields of regioisomers **214a** and **215a** in 58 and 27% respectively. [j] In domestic microwave at temperature 120 °C for 10 minutes.

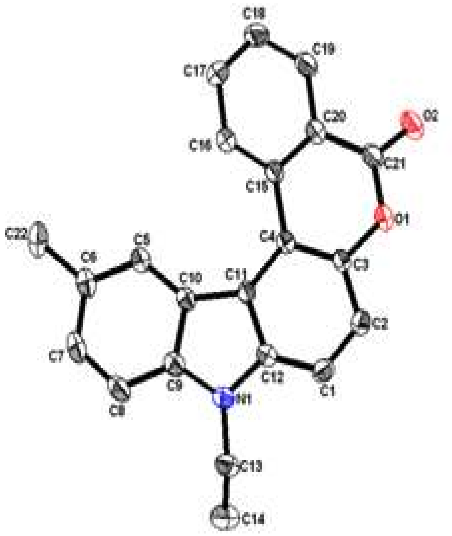
By employing the above optimized conditions, various isochromenocarbazolone derivatives were synthesized. **213a-d** were subjected to cyclization to provide isomeric products **214a-d** and **215a-d** in good yields. These results are summarized in Table 6.

Table 6. Synthesis of isochromenocarbazolone derivatives

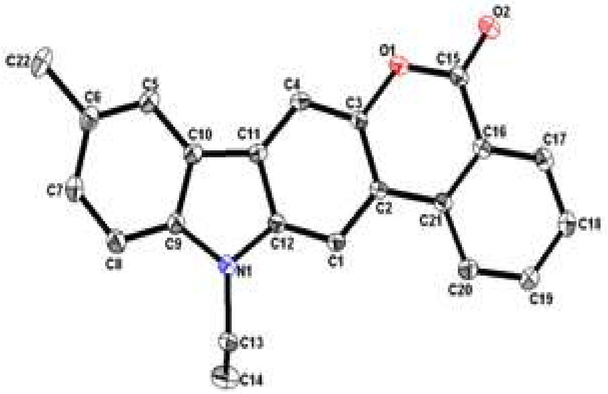


The regioisomers of methyl substituted derivatives **214d** and **215d** were characterized by single crystal X-ray analysis. The ORTEP is shown in Figure 14.[120] The structure of **214b** was also confirmed by the single crystal X-ray analysis. The ORTEP diagram is shown in Figure 14.[120]

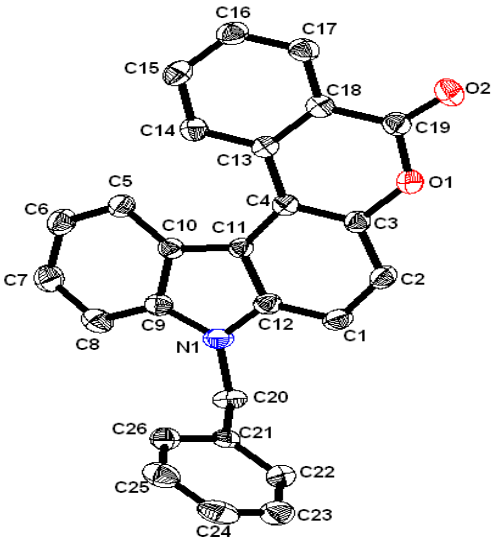
Figure 14. ORTEP diagrams of 214d, 215d and 214b



214d

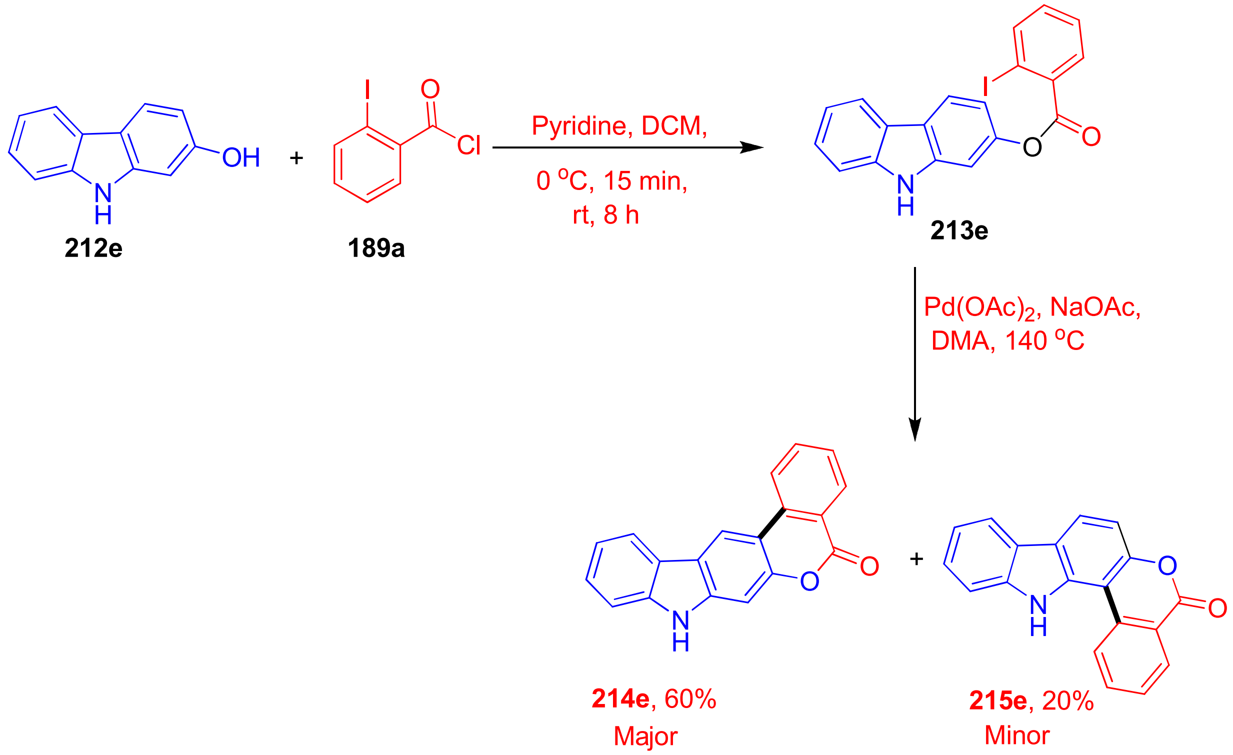


215d



214b

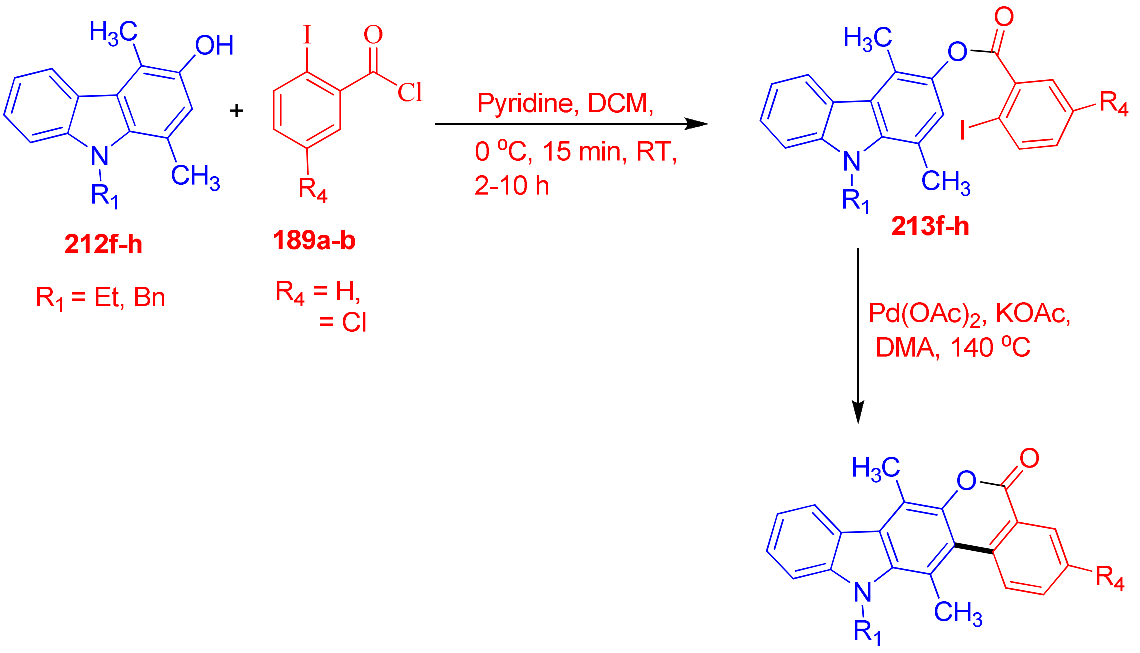
By employing similar conditions, we have synthesized isochromeno[3,4-*b*] and [4,3-*a*]carbazolones from 9*H*-carbazol-2-yl 2-iodobenzoate **213e** to afford a mixture of products **214e** and **215e** in 80% yield, which on chromatographed over basic alumina obtained **214e** and **215e** in 60 and 20% yield respectively, as shown in Scheme 6. The two isomers **214e** and **215e** were distinguished by their ^{1}H NMR spectra. From ^{1}H NMR of **214e**, two singlets were observed at δ 9.20 and δ 7.43, whereas in isomer **215e** two doublets were observed at δ 8.79 and δ 7.91.



Scheme 6. Synthesis of isochromeno[4,3-*b*] and [4,3-*a*]carbazolones

Employing similar conditions, we obtained 45% of cyclized product **215f**. To improve the yield, just by changing base from NaOAc to KOAc at 140 °C by using 10 mol % Pd(OAc)$_2$ in DMA, 75% yield of **215f** was obtained. A variety of dimethylisochromeno[4,3-*b*]carbazolone derivatives **215f-h** were prepared in 62-85% yield as shown in Table 7.

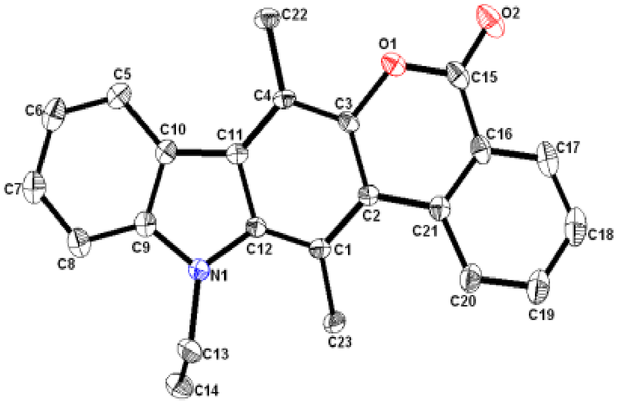
Table 7. Synthesis of dimethylisochromeno[4,3-*b*]carbazolone derivatives



R_1 = Et, R_4 = H, 75%, **215f**
R_1 = Bn, R_4 = H, 82%, **215g**
R_1 = Et, R_4 = Cl, 62%, **215h**

Among these, one of the derivative **215f** was also confirmed by its single crystal X-ray analysis. The ORTEP diagram is shown in Figure 15.[120]

Figure 15. ORTEP diagram of 215f



1.4. Conclusion

In conclusion, we have developed an efficient route for the construction of new classes of quino[2,3-*c*]-, -[3,2-*b*]-, isochromeno[3,4-*b*]-, -[4,3-*a*]-, -[4,3-*b*]-, and -[3,4-*c*]carbazolones and indolo[3,2-*j*]phenanthridinone derivatives via palladium-catalyzed intramolecular *ortho* arylation.

1.5. Experimental Section

Melting Points: The melting point of the products was recorded on a Superfit (India) capillary melting point apparatus and is uncorrected.

IR: Infrared spectra were recorded on a JASCO FT/IR-5300 spectrophotometer. All the spectra were calibrated against polystyrene absorption at 1601 cm^{-1}. Solid samples were recorded as KBr wafers and liquid samples as thin film between NaCl plates or solution spectra in DCM.

NMR Spectra: ^{1}H NMR and ^{13}C NMR spectra were recorded on BRUKER AVANCE-400 spectrometer. ^{1}H NMR (400 MHz) spectra of the some samples were measured in chloroform-*d* (δ = 7.26 ppm) or in DMSO-d_6 (δ = 2.50 ppm) or in the mixture of $CDCl_3$/DMSO-d_6 with TMS (δ = 0 ppm) as an internal standard. ^{13}C NMR (100 MHz) spectra of some samples were measured in chloroform-*d* (δ = 77.10 ppm, with its middle peak of the triplet as an internal standard) or in DMSO-d_6 (δ = 39.70 ppm its middle peak of the septet) or in the mixture of $CDCl_3$/DMSO-d_6.

Mass Spectral Analysis: Shimadzu LCMS 2010A mass spectrometer. All the cases DCM or MeOH were used to dissolve the compounds.

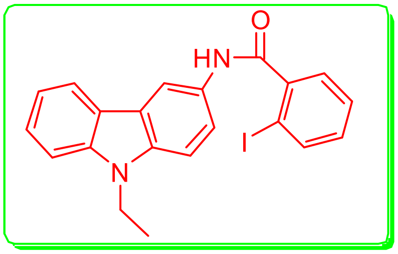
Elemental Analysis: Elemental analyses were performed on a Thermo Finnigan Flash EA 1112-CHN analyzer.

X-ray Crystallography: The X-ray diffraction measurements were carried out at 293 K on a Bruker SMART APEX CCD area detector system equipped with a graphite monochromator and a Mo-Kα fine-focus sealed tube (λ = 0.71073 Å) operated at 1500 W power (50 kV, 30 mA). The detector was placed at a distance of 4.995 cm from the crystal. The frames were integrated with the Bruker SAINT Software package using a narrow-frame algorithm. Data were corrected for absorption effects using the multiscan technique (SADABS). The structure was solved and refined using the Bruker SHELXTL (Version 6.1) software package.

General procedure A

To the compound **188** (0.5 g, 2.1 mmol) in 10 mL DCM was added Et$_3$N (0.42 mL, 4.3 mmol), stirred at room temperature for 15 minutes. Then the reaction mixture was cooled in an ice bath and added freshly prepared **189** (0.7 mL, 2.6 mmol) (prepared from *o*-iodobenzoic acid and thionyl chloride) was added dropwise. After stirring for 15 minutes the reaction mixture brought to room temperature and stirring continued up to 2 h. Water was added to the reaction mixture and extracted with DCM, washed with brine (20 mL) and dried over anhydrous Na$_2$SO$_4$. The solvent was evaporated and the crude material was purified by siligel column chromatography using 25% ethylacetate in hexanes to obtain the pure product **192**.

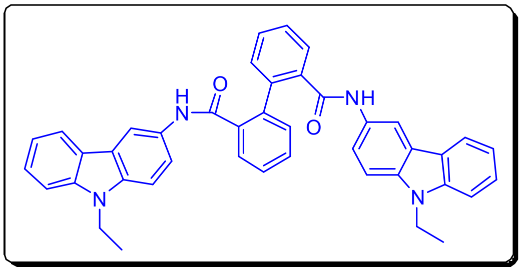
N-(9-Ethyl-9*H*-carbazol-3-yl)-2-iodobenzamide (192):



Yield:	70%
Mp:	189-191 °C
IR (KBr) ν_{max} cm^{-1}:	3248, 3057, 2970, 1645, 1469, 1327, 1012, 800
^{1}H NMR (400 MHz, DMSO-d$_6$):	δ 10.42 (1H, s, NH), 8.55 (1H, s, ArH), 8.07 (1H, d, J = 7.6 Hz), 7.94 (1H, d, J = 8.0 Hz), 7.67 (1H, d, J = 8.4 Hz,) 7.58 (2H, d, J = 8.4 Hz), 7.51 (2H, t, J = 8.4 Hz), 7.44 (1H, t, J = 7.2 Hz), 7.24-7.21 (1H, dd, J_1 = 4.0 Hz, J_2 = 3.6 Hz), 7.18 (1H, t, J = 7.2 Hz), 4.42 (2H, d, J = 7.2 Hz, N-C$\underline{H}_2$CH$_3$), 1.29 (3H, t, 6.8 Hz, N-CH$_2$C$\underline{H}_3$)
^{13}C NMR (100 MHz, DMSO-d$_6$):	δ 167.4, 142.2, 140.4, 139.9, 137.5, 131.3, 129.3, 128.5, 128.3, 125.9, 123.0, 122.7, 120.8, 119.5, 118.8, 113.1, 108.5, 92.7, 37.6, 13.8
LC-MS (m/z):	441 (M+H)$^+$ positive mode
Anal. Calcd. for C$_{21}$H$_{17}$IN$_2$O:	C, 57.29; H, 3.89; N, 6.36%
Found:	C, 57.20; H, 3.81; N, 6.45%

N^{2},*N*$^{2'}$-Bis(9-ethyl-9*H*-carbazole-3-yl)biphenyl-2,2′-dicarboxamide (193):

Compound **193** was prepared from **192** and the product was obtained through silica gel column chromatography with 50% ethylacetate in hexanes, as brown colored solid.



Yield: 70%

Mp: 134 °C

IR (KBr) ν_{max} cm^{-1}: 3427, 3271, 3057, 2978, 2924, 1722, 1635,1491, 1329,1232, 744

^{1}H NMR (400 MHz, CDCl$_3$): δ 9.01 (1H, s, NH), 8.23 (1H, s), 8.04 (1H, d, *J* = 8.0 Hz), 7.80 (1H, dd, J_1 = 2.0, J_2 = 2.8 Hz), 7.78 (1H, d, *J* = 2.8 Hz), 7.36-7.48 (5H, m), 7.32-7.29 (1H, m), 7.19 (1H, t, *J* = 7.2 Hz), 4.34 (2H, q, *J* = 7.6 Hz, N-C$\underline{H}_2$CH$_3$), 1.37 (3H, t, *J* = 7.2 Hz, N-CH$_2$C$\underline{H}_3$)

^{13}C NMR (100 MHz,DMSO-d$_6$): δ 169.6, 143.4, 140.3, 138.8, 138.5, 133.2, 129.9, 128.7, 127.7, 126.7, 126.3, 122.4, 122.1, 120.7, 120.5, 119.4, 109.7, 109.5, 94.6, 44.67, 37.4, 14.1, 13.1

LC-MS (m/z): 627 (M+H)$^+$ positive mode. LC-MS: *m/z* = 625 (M-H)$^-$ negative mode.

Anal. Calcd. for $C_{42}H_{34}N_4O_2$: C, 80.49; H, 5.87; N, 8.94%

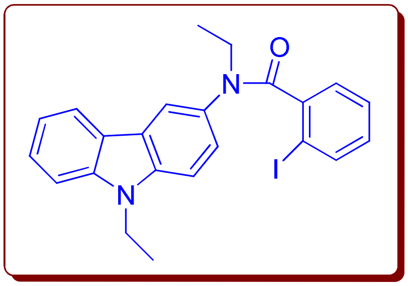
Found: C, 80.65, H, 5.56; N, 8.81%

General procedure B

To the compound **188a** (0.5 g, 2.1 mmol) in 10 mL DCM was added Et$_3$N (0.42 mL, 4.3 mmol), stirred at room temperature for 15 minutes. Then the reaction mixture was cooled in an ice bath and added freshly prepared **189a** (0.7 mL, 2.6 mmol) (prepared from *o*-

iodobenzoic acid and thionyl chloride) was added dropwise. After stirring for 15 minutes the reaction mixture brought to room temperature and stirring continued up to 2 h. Water was added to the reaction mixture and extracted with DCM, washed with brine (20 mL) and dried over anhydrous Na_2SO_4. The solvent was evaporated and the crude material was purified by column chromatography using 25% ethylacetate in hexanes to obtain the pure product **192a**. Similarly compounds **192b-f** and **197a-b** were obtained by the same procedure.

N-(9-Ethyl-9*H*-carbazol-3-yl)-2-iodobenzamide (192a):



Yield: 79%

Mp: 139 °C

IR (KBr) ν_{max} cm^{-1}: 3047, 2976, 2928, 2866, 1633, 1485, 1116, 1008, 808, 744

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (1H, d, *J* = 7.6 Hz), 7.9 (1H, s), 7.5 (1H, d, *J* = 8.0 Hz), 7.47 (1H, t, *J* = 8.0 Hz), 7.36 (1H, d, *J* = 8.0 Hz), 7.31 (1H, d, *J* = 8.4 Hz), 7.25 (1H, d, *J* = 7.6 Hz), 7.19 (1H, d, *J* = 8.4 Hz), 7.07 (1H, d, *J* = 6.0 Hz), 6.99 (1H, t, *J* = 6.0 Hz), 6.69 (1H, t, *J* = 7.2 Hz), 4.26 (2H, q, *J* = 7.2 Hz), 4.09 (2H, q, *J* = 7.2 Hz, N-C$\underline{H}_2$CH$_3$), 1.47 (3H, t, *J* = 6.8 Hz, N-CH$_2$C$\underline{H}_3$), 1.39 (3H, t, *J* = 7.2 Hz, N-CH$_2$C$\underline{H}_3$)

^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 143.0, 140.3, 139.2, 139.0, 138.6, 133.1, 129.2, 128.2, 127.2, 126.2, 125.9, 120.5, 120.1, 119.6, 119.1, 109.1, 108.7, 108.5, 93.9, 44.9, 37.6, 13.8, 12.9

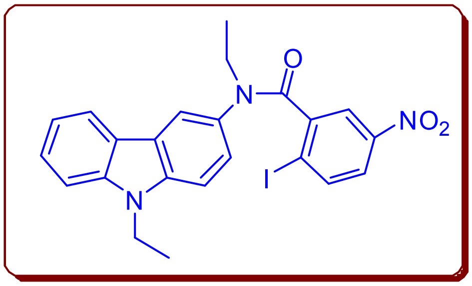
LC-MS (m/z): 469 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{23}H_{21}IN_2O$: C, 58.99; H, 4.52; N, 5.98%

Found: C, 58.89; H, 4.56; N, 5.89%

N-Ethyl-*N*-(9-ethyl-9*H*-carbazol-3-yl)-2-iodo-5-nitrobenzamide (192b):

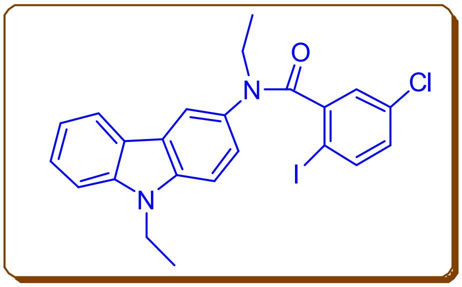
The compound **192b** was prepared from **188b** and **189b** according to general procedure B. 0.88 g of red solid was obtained through silica gel column chromatography using 30% ethylacetate in hexanes.



Yield:	82%
Mp:	216 °C
IR (KBr) ν_{max} cm^{-1}:	3088, 3043, 2982, 2935, 1663, 1523, 1467, 1346, 1224, 1116, 1018, 754, 642
^{1}H NMR (400 MHz, CDCl$_3$):	δ 8.05 (1H, d, *J* = 7.6 Hz), 7.99 (1H, s), 7.47 (2H, d, *J* = 6.8 Hz), 7.37 (1H, d, *J* = 8.0 Hz), 7.27 (3H, q, *J* = 9.6 Hz), 7.09 (1H, s), 6.68 (1H, d, *J* = 8.0 Hz), 4.29 (2H, q, *J* = 7.2 Hz, N-C$\underline{H}_2$CH$_3$), 4.06 (2H, s), 1.38 (3H, t, *J* = 7.2 Hz, N-CH$_2$C$\underline{H}_3$), 1.14 (3H, t, *J* = 7.2 Hz, N-CH$_2$C$\underline{H}_3$)
^{13}C NMR (100 MHz, CDCl$_3$):	δ 168.9, 144.5, 140.4, 138.8, 133.7, 132.5, 129.5, 128.2, 125.7, 123.0, 122.3, 120.5, 120.1, 119.5, 119.2, 108.2, 108.7, 90.9, 45.0, 37.7, 13.8, 12.8
LC-MS (m/z):	514 (M+H)$^+$, positive mode
Anal. Calcd. for $C_{23}H_{20}IN_3O_3$:	C, 53.81; H, 3.93; N, 8.19 %
Found:	C, 53.85; H, 3.98; N, 8.25 %

5-Chloro-*N*-ethyl-*N*-(9-ethyl-9*H*-carbazol-3-yl)-2-iodobenzamide (192c):

The compound **192c** was prepared from **188c** and **189c** according to general procedure B. 0.80 g of white gummy solid was obtained through silica gel column chromatography using 25% ethylacetate in hexanes.



Yield: 76%

Mp: 71 °C

IR (KBr) ν_{max} cm^{-1}: 3057, 2974, 1637, 1491, 1464, 1410, 1226, 1014, 748, 644

^{1}H NMR (400 MHz, DMSO-d_6): δ 8.05 (1H, d, J = 7.6 Hz), 7.99 (1H, s), 7.47 (2H, d, J = 6.8 Hz), 7.37 (1H, d, J = 8.0 Hz), 7.27 (3H, q, J = 9.6 Hz), 7.09 (1H, s), 6.68 (1H, d, J = 8.0 Hz), 4.29 (2H, q, J = 7.2 Hz, N-C$\underline{H}_2$CH$_3$), 4.06 (2H, s), 1.38 (3H, t, J = 7.2 Hz, N-CH$_2$C$\underline{H}_3$), 1.14 (3H, t, J = 7.2 Hz, N-CH$_2$C$\underline{H}_3$)

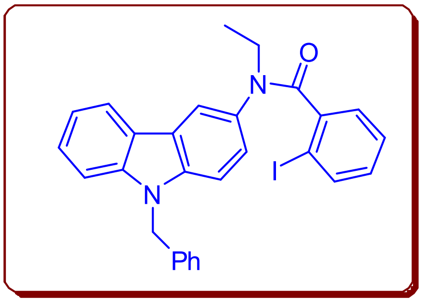
^{13}C NMR (100 MHz, DMSO-d_6): δ 168.1, 145.3, 140.5, 140.4, 138.7, 132.9, 132.8, 129.8, 128.5, 126.7, 126.3, 122.4, 122.1, 120.6, 119.5, 109.8, 109.6, 92.6, 44.6, 37.5, 14.1, 13.1

LC-MS (m/z): 503 (M+H)$^+$, 504 (M+1)

Anal. Calcd. for C$_{23}$H$_{20}$ClIN$_2$O: C, 54.94; H, 4.01; N, 5.57%

Found: C, 54.85; H, 4.08; N, 5.67%

N-(9-Benzyl-9*H*-carbazol-3-yl)-*N*-ethyl-2-iodobenzamide (192d):



The compound **192d** was obtained from **188d** and **189** according to general procedure B. 0.66 g of white solid was obtained through silica gel column chromatography in 25% ethylacetate in hexanes.

Yield: 75%

Mp: 62 °C

IR (KBr) ν_{max} cm^{-1}: 3045, 2935, 1637, 1466, 1205, 1016, 802, 742

^{1}H NMR (400 MHz, DMSO-d_6): δ 8.07 (1H, d, J = 7.6 Hz), 8.00 (1H, s), 7.43 (2H, d, J = 8.0 Hz), 7.33 (1H, d, J = 8.0 Hz), 7.24 (6H, q, J = 4.4

Hz), 7.21 (1H, s), 7.20 (1H, d, *J* = 6.0 Hz), 7.08 (2H, d, *J* = 7.2 Hz), 6.84-6.81 (1H, dd, J_1 = 2.0 Hz, J_2 = 2.0 Hz), 5.43 (2H, s, N-C$\underline{H}_2$-Ph), 4.06 (2H, s), 1.13 (3H, t, *J* = 6.8 Hz, N-$CH_2C\underline{H}_3$)

^{13}C NMR (100 MHz, DMSO-d_6): δ 168.7, 144.7, 141.1, 140.3, 139.5, 136.6, 133.0, 132.3, 131.1, 128.8, 127.6, 126.5, 125.9, 123.2, 122.5, 121.6, 120.5, 119.7, 109.2, 91.8, 46.7, 44.9, 12.9

LC-MS (m/z): 531 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{28}H_{23}IN_2O$: C, 63.40; H, 4.37; N, 5.28%

Found: C, 63.31; H, 4.45; N, 5.35%

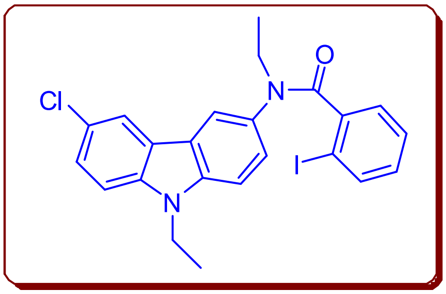
N-(6-Chloro-9-ethyl-9*H*-carbazol-3-yl)-*N*-ethyl-2-iodobenzamide (192e):

The compound **192e** was obtained from **188e** and **189** according to general procedure B. 0.64 g of white solid was obtained through silica gel column chromatography in 25% ethylacetate in hexanes.

Yield: 70%

Mp: 134 °C

IR (KBr) ν_{max} cm^{-1}: 3049, 2967, 2923, 1635, 1404, 1311, 1012, 808



^{1}H NMR (400 MHz, CDCl$_3$): δ 7.98 (1H, d, *J* = 2.0 Hz), 7.92 (1H, s), 7.60 (1H, d, *J* = 8.0 Hz), 7.41-7.38 (1H, dd, J_1 = 2.0 Hz, J_2 = 1.6 Hz), 7.33-7,31 (1H, dd, J_1 = 2.0 Hz, J_2 = 1.6 Hz), 7.27-7.25 (1H, dd, J_1 = 2.8 Hz, J_2 = 2.8 Hz), 7.19 (1H, d, *J* = 8.8 Hz), 7.07 (1H, d, *J* = 6.0 Hz), 7.01 (1H, t, *J* = 6.8 Hz), 6.7 (1H, t, *J* = 5.6 Hz), 4.25 (2H, t, *J* = 7.2 Hz, N-$C\underline{H}_2CH_3$), 4.14 (2H, d, *J* = 7.2 Hz), 1.43 (6H, t, *J* = 7.2 Hz)

^{13}C NMR (100 MHz, $CDCl_3$): δ 165.8, 145.3, 140.6, 138.6, 132.9, 132.8, 129.8, 128.6, 126.7, 122.4, 120.6, 119.6, 109.8, 92.6, 44.6, 37.5, 14.1, 13.0

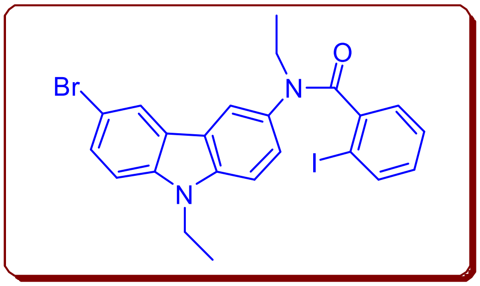
LC-MS (m/z): 503(M), 504 (M+1) positive mode

Anal. Calcd. for $C_{23}H_{20}ClIN_2O$: C, 54.94; H, 4.01; N, 5.57%

Found: C, 55.12; H, 4.10; N, 5.65%

N-(6-Bromo-9-ethyl-9*H*-carbazol-3-yl)-*N*-ethyl-2-iodobenzamide (192f):

The compound **192f** was obtained from **188f** and **189** according to general procedure B. 0.58 g of white solid was obtained through silica gel column chromatography in 25% ethylacetate in hexanes.



Yield: 68%

Mp: 129 °C

IR (KBr) ν_{max} cm^{-1}: 3445, 3057, 2970, 1645, 1575, 1294, 1014, 798

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (1H, s), 7.91 (1H, s), 7.60 (1H, d, *J* = 8.0 Hz), 7.53 (1H, *J* = 7.2 Hz), 7.32 (1H, d, *J* = 8.4), 7.25 (1H, d, *J* = 8.4 Hz), 7.20 (1H, d, *J* = 6.4 Hz), 7.07-7.00 (2H, m), 6.72 (1H, t, *J* = 7.2 Hz), 4.26 (2H, q, *J* = 6.8 Hz, N-C$\underline{H}_2$CH$_3$), 4.06 (2H, s), 1.44 (6H, t, *J* = 8.0 Hz)

^{13}C NMR (100 MHz, $CDCl_3$): δ 170.8, 142.9, 139.0, 138.9, 138.7, 133.4, 129.3, 128.2, 127.2, 126.7, 126.2, 124.6, 123.4, 122.0, 120.2, 119.8, 109.6, 108.8, 93.8, 44.9, 37.8, 13.8, 12.8

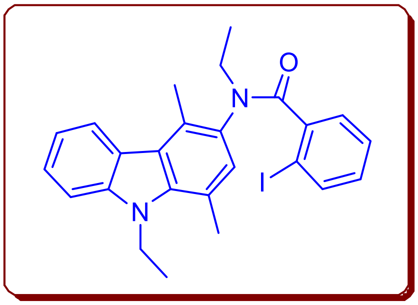
LC-MS (m/z): 547 $(M+H)^+$, 549 (M+2) positive mode

Anal. Calcd. for $C_{23}H_{20}BrIN_2O$: C, 50.48; H, 3.68; N, 5.12%

Found: C, 50.35; H, 3.72; N, 5.21%

N-Ethyl-*N*-(9-ethyl-1,4-dimethyl-9*H*-carbazol-3-yl)-2-iodobenzamide (197a):

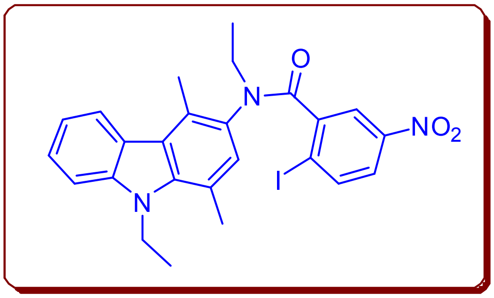
The compound **197a** was obtained from **196** and **189a** according to general procedure B. 0.73 g of yellow solid was obtained through silica gel column chromatography in 22% ethylacetate in hexanes.



Yield:	79%
Mp:	154 °C
IR (KBr) ν_{max} cm^{-1}:	2976, 2916, 2870, 1637, 1329, 1010, 746
^{1}H NMR (400 MHz, CDCl$_3$):	δ 8.18 (1H, d, *J* = 8.0 Hz), 7.66 (1H, d, *J* = 8.0 Hz), 7.48 (2H, t, *J* = 8.0 Hz), 7.40 (1H, d, *J* = 8.0 Hz), 7.27 (1H, t, *J* = 4.0 Hz), 6.96-6.94 (2H, m), 6.73 (1H, d, *J* = 8.0 Hz), 4.49 (4H, q, *J* = 4.0 Hz), 2.28 (3H, s), 2.68 (3H, s), 1.37 (3H, t, *J* = 8.0 Hz), 1.30 (3H, t, *J* = 8.0 Hz)
^{13}C NMR (100 MHz, CDCl$_3$):	δ 170.6, 142.7, 140.9, 139.1, 138.0, 137.8, 131.8, 130.0, 129.3, 127.8, 126.5, 125.3, 123.7, 122.7, 122.6, 119.2, 117.4, 108.6, 94.0, 44.5, 39.2, 19.6, 16.2, 15.5, 12.5
LC-MS (m/z):	497 $(M+H)^+$ positive mode.
Anal. Calcd. for $C_{25}H_{25}IN_2O$:	C, 60.49; H, 5.08; N, 5.64%
Found:	C, 60.35; H, 5.15; N, 5.71%

N-Ethyl-*N*-(9-ethyl-1,4-dimethyl-9*H*-carbazol-3-yl)-2-iodo-5-nitrobenzamide (197b):

The compound **197b** was obtained from **196** and **189b** according to general procedure B. 0.83 g of red solid was obtained through silica gel column chromatography in 25% ethylacetate in hexanes.



Yield:	82%
Mp:	98 °C
IR (KBr) ν_{max} cm^{-1}:	2962, 2924, 2868, 1645, 1346, 1020, 734
^{1}H NMR (400 MHz, CDCl$_3$):	δ 8.14 (1H, d, J = 8.0 Hz), 7.88 (1H,s), 7.83-7.81 (1H, dd, J_1 = 2 Hz, J_2 = 1.6 Hz), 7.51 (1H, d, J = 6.0 Hz), 7.46 (1H, J = 6.8 Hz), 7.38 (1H, d, J = 8.0 Hz), 7.24 (1H, d, J = 3.6 Hz), 7.07 (1H, s), 5.05 (2H, s), 4.49 (2H, d, J = 4.4 Hz), 2.81 (3H, s, C$\underline{H}_3$), 2.61 (3H, s, C$\underline{H}_3$), 1.38 (3H, t, J = 6.8 Hz, N-CH$_2$C$\underline{H}_3$), 0.85 (3H, t, J = 8.0 Hz, N-CH$_2$C$\underline{H}_3$)
^{13}C NMR (100 MHz, CDCl$_3$):	δ 168.6, 146.7, 144.3, 140.8, 140.5, 137.9, 133.1, 130.6, 129.8, 129.0, 128.0, 125.5, 123.5, 122.8, 121.8, 119.4, 117.4, 108.6, 102.1, 57.2, 39.2, 21.1, 19.5, 16.4, 15.6
LC-MS (m/z):	542 (M+H)$^+$ positive mode
Anal. Calcd. for $C_{25}H_{24}IN_3O_3$:	C, 55.46; H, 4.47; N, 7.76%
Found:	C, 55.35; H, 4.51; N, 7.81%

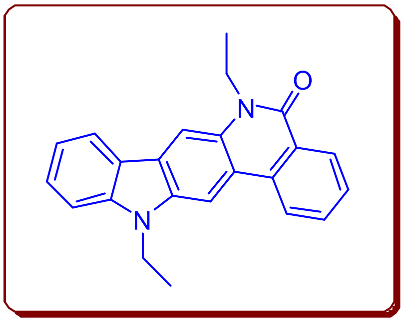
General procedure C

A mixture of compound **192a** (0.15 g, 0.3 mmol), anhydrous K_2CO_3 (0.096 g, 7.5 mmol) and Pd(OAc)$_2$ (0.004 mg, 5 mol %) in DMF was taken in a sealed tube and heated at 120 °C for 2 h with continuous stirring. After completion of the reaction as monitored by

TLC, the reaction mixture was cooled and water was added (10 mL). A solid precipitate was formed, extracted with $CHCl_3$ or DCM (3 x 20 mL) and washed with water (3 x 20 mL) followed by brine (20 mL) and dried over Na_2SO_4. Evaporation of solvent and the crude material was purified by column chromatography over silica-gel (100-200 mesh), using 15% ethylacetate in hexanes as an eluent up on seperation to give mixture of the products **194a** and **195a**. Similarly compounds **194b-f**, **195b-f** and **198a-b** were obtained in the same manner.

7,12-Diethyl-7*H*-indolo[2,3-*c*]phenanthridin-13(12*H*)-one (194a):

The compound **194a** was obtained from **192a** according to general procedure C. 0.047 g of yellow solid was obtained through silica gel column chromatography in 13% ethylacetate in hexanes.



Yield: 50%

Mp: 176 °C

IR (KBr) ν_{max} cm^{-1}: 3051, 2972, 1637, 1483, 1419, 1332, 1302, 1224, 1180, 1072, 798

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.01 (1H, d, *J* = 8.0 Hz), 8.61 (1H, d, *J* = 2.8 Hz), 8.38 (1H, d, *J* = 4.0 Hz), 7.78 (1H, t, *J* = 8.0 Hz), 7.66 (1H, d, *J* = 8.0 Hz), 7.63 (1H, s), 7.58 (1H, d, *J* = 8.0 Hz), 7.51 (2H, d, *J* = 4.0 Hz), 7.19 (1H, m), 4.58 (2H, q, *J* = 8.0 Hz, N-C$\underline{H}_2$CH$_3$), 4.49 (2H, q, *J* = 8.0 Hz, N-C$\underline{H}_2$CH$_3$), 1.32-1.50 (6H, m)

^{13}C NMR (100 MHz, $CDCl_3$): δ 160.8, 141.6, 136.1, 134, 132.1, 130.6, 129, 127.5, 126.9, 125.4, 124.8, 122.3, 121.5, 120.8, 118.9, 118.6, 108.7, 105.7, 101.8, 38, 37.6, 13.8, 12.7

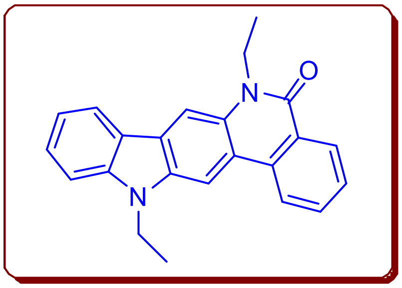
LC-MS (m/z): 341 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{23}H_{20}N_2O$: C, 81.15; H, 5.92; N, 8.23%

Found: C, 81.36, H, 5.85; N, 8.32%

6,12-Diethyl-6,12-dihydro-5*H*-indolo[2,3-*b*]phenanthridin-5-one (195a):

The compound **195a** was obtained from **192a** according to general procedure C. 0.036 g of yellow solid was obtained through silica gel column chromatography in 13% ethylacetate in hexanes.



Yield: 38%

Mp: 172 °C

IR (KBr) ν_{max} cm^{-1}: 3021, 2974, 2926, 1651, 1440, 1323, 846, 771, 740, 696

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.64 (1H, d, *J* = 8.0 Hz), 8.48 (1H, d, *J* = 7.6 Hz), 8.29 (1H, s, Ar*H*), 8.22 (1H, d, *J* = 7.6 Hz), 8.12 (1H, s, Ar*H*), 7.82 (1H, t, *J* = 7.2 Hz), 7.63 (1H, d, *J* = 7.2 Hz), 7.56 (1H, d, *J* = 7.6 Hz), 7.47 (1H, d, *J* = 8.4 Hz), 7.16 (1H, d, *J* = 7.6 Hz), 4.65 (2H, q, *J* = 6.8 Hz, N-CH_2CH$_3$), 4.49 (2H, q, *J* = 7.6 Hz, N-CH_2CH$_3$), 1.52 (6H, m)

^{13}C NMR (100 MHz, CDCl$_3$): δ 160.9, 140.5, 136.8, 133.3, 131.6, 130.5, 128.2, 127.8, 126.7, 126.3, 123.4, 122.6, 118.1, 118.0, 116.1, 113.2, 110.4, 109.0, 38.3, 37.6, 13.8, 13.2.

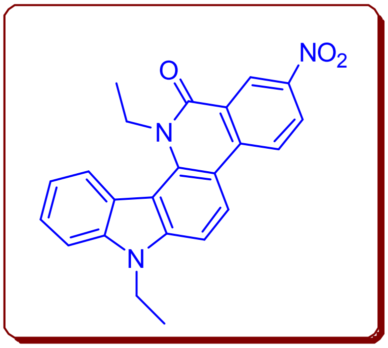
LC-MS (m/z): 341 (M+H)$^+$ positive mode

Anal. Calcd. for $C_{23}H_{20}N_2O$: C, 81.15; H, 5.92; N, 8.23%

Found: C, 81.10, H, 5.98; N, 8.28%

7,12-Diethyl-2-nitro-7*H*-indolo[2,3-*c*]phenanthridin-13(12*H*)-one (194b):

The compound **194b** was obtained from **192b** according to general procedure C. 0.07 g of red solid was obtained through silica gel column chromatography in 15% ethylacetate in hexanes.



Yield: 78%

Mp: 224 °C

IR (KBr) ν_{max} cm^{-1}: 3070, 2970, 1647, 1512, 1481, 1332, 1172, 1089, 858, 798, 744

^{1}H NMR (400 MHz, CDCl$_3$): δ 9.38 (1H, s), 9.06 (1H, d, J = 8.0 Hz), 8.46 (1H, d, J = 8.4 Hz), 8.41 (1H, d, J = 7.6 Hz), 7.73 (1H, d, J = 8.8 Hz), 7.55 (3H, d, J = 12.4 Hz), 7.19 (1H, s), 4.52 (4H, q, J = 8.4 Hz), 1.49 (6H, t, J = 6.8 Hz)

^{13}C NMR (100 MHz, CDCl$_3$): δ 159.6, 146.3, 140.7, 138.0, 136.7, 132.9, 127.7, 126.6, 126.3, 124.4, 124.3, 123.0, 121.9, 118.5, 118.2, 114.3, 113.2, 112.9, 109.5, 38.7, 37.7, 13.9, 13.0

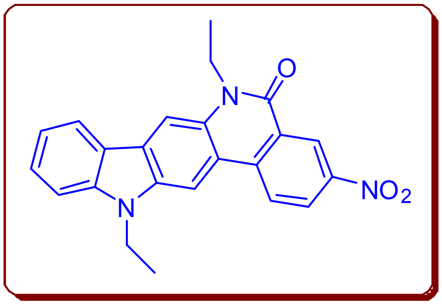
LC-MS (m/z): 386 (M+H)$^+$ positive mode

Anal. Calcd. for $C_{23}H_{19}N_3O_3$: C, 71.69; H, 4.97; N, 10.90 %

Found: C, 71.55; H, 4.88; N, 11.12%

6,12-Diethyl-3-nitro-6,12-dihydro-5*H*-indolo[2,3-*b*]phenanthridin-5-one (195b):

The compound **195b** was obtained from **192b** according to general procedure C. 0.012 g of red solid was obtained through silica gel column chromatography in 15% ethylacetate in hexanes.



Yield: 12%

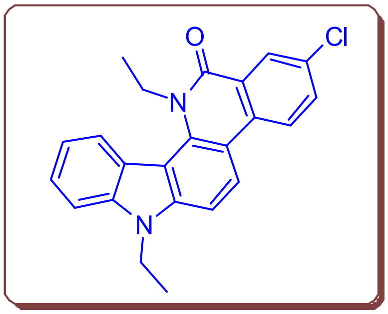
Mp: 210 °C

IR (KBr) ν_{max} cm^{-1}: 3057, 2968, 2926, 1647, 1512, 1477, 1329, 1170, 1087, 744, 696

^{1}H NMR (400 MHz, CDCl$_3$):	δ 9.46 (1H, s, Ar*H*), 8.57 (2H, s), 1.26 (1H, s, Ar*H*), 8.23 (1H, d, *J* = 7.6 Hz), 8.13 (1H, s, Ar*H*), 7.75 (1H, t, *J* = 7.6 Hz), 7.48 (1H, d, *J* = 8.0 Hz), 7.32 (1H, d, *J* = 7.6 Hz), 4.63 (2H, q, *J* = 7.2 Hz, N-C*H*$_2$CH$_3$), 4.52 (2H, q, *J* = 7.2 Hz, N-C*H*$_2$CH$_3$), 1.45 (6H, t, *J* = 15.6 Hz)
^{13}C NMR (100 MHz, CDCl$_3$):	δ 158.3, 145.0, 139.5, 136.9, 135.6, 131.8, 126.7, 125.5, 125.0, 123.3, 122.9, 121.7, 120.6, 117.4, 116.9, 112.9, 112.4, 108.5, 37.5, 36.6, 12.9, 12.0
LC-MS (m/z):	386 (M+H)$^+$ positive mode
Anal. Calcd. for $C_{23}H_{19}N_3O_3$:	C, 71.69; H, 4.97; N, 10.90 %
Found:	C, 71.65; H, 4.91; N, 10.88 %

2-Chloro-7,12-diethyl-7*H*-indolo[2,3-*c*]phenanthridin-13(12*H*)-one (195c):

The compound **195c** was obtained from **192c** according to general procedure C. 0.04 g of yellow solid was obtained through silica gel column chromatography in 13% ethylacetate in hexanes.



Yield:	52%
Mp:	198 °C
IR (KBr) ν_{max} cm^{-1}:	3042, 2972, 1649, 1491, 1462, 1331, 1130,1086, 819, 706
^{1}H NMR (400 MHz, CDCl$_3$):	δ 8.93 (1H, d, *J* = 6.0 Hz), 8.59 (1H, s, ArH), 8.52 (1H, d, *J* = 8.0 Hz), 7.72 (1H, d, *J* = 6.8 Hz), 7.65 (1H, d, *J* = 8.8 Hz), 7.57 (1H, d, *J* = 9.2 Hz), 7.53 (2H, s), 7.21-7.17 (1H, m), 4.56 (2H, q, *J* = 7.2 Hz, N-C*H*$_2$CH$_3$), 4.54 (2H, q, *J* = 7.2 Hz, N-C*H*$_2$CH$_3$), 1.47 (6H, t, *J* = 7.2 Hz)
^{13}C NMR (100 MHz, CDCl$_3$):	δ 159.9, 140.6, 136.9, 133.7, 131.8, 131.5, 130.9, 128.3, 127.8, 120.6, 126.2, 123.2, 122.4, 118.2, 117.9, 115.3, 113.3, 110.8, 109.1, 38.5, 38.7, 13.8, 13.1

LC-MS (m/z): 375 $(M+H)^+$, 376 (M+1)

Anal. Calcd. for $C_{23}H_{19}ClN_2O$: C, 73.69; H, 5.11; N, 7.47%

Found: C, 73.61; H, 5.15; N, 7.39%

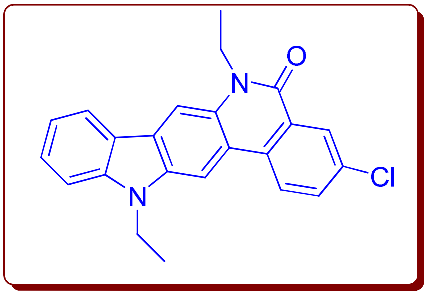
3-Chloro-6,12-diethyl-6,12-dihydro-5*H*-indolo[2,3-*b*]phenanthridin-5-one(195c):

The compound **195c** was obtained from **192c** according to general procedure C. 0.014 g of yellow solid was obtained through silica gel column chromatography in 13% ethylacetate in hexanes.

Yield: 18%

Mp: 239 °C

IR (KBr) v_{max} cm^{-1}: 3057, 2972, 1649, 1599, 1331, 1228, 1086, 819, 706



^{1}H NMR (400 MHz, CDCl$_3$): δ 8.61 (1H, d, *J* = 3.2 Hz), 8.40 (1H, d, *J* = 8.8 Hz), 8.24 (1H, s), 8.22 (1H, s), 8.12 (1H, s), 7.71-7.44 (1H, dd, J_1 = 2, J_2 = 2.4 Hz), 7.58 (1H, t, *J* = 7.2 Hz), 7.48 (1H, d, *J* = 8.4 Hz), 7.29 (1H, d, *J* = 11.2 Hz), 4.66 (2H, q, *J* = 7.2 Hz, N-C$\underline{H}_2$CH$_3$), 4.51 (2H, q, *J* = 7.2 Hz, N-C$\underline{H}_2$CH$_3$), 1.46 (6H, t, *J* = 7.2 Hz)

^{13}C NMR (100 MHz, CDCl$_3$): δ 158.9, 140.4, 140.1, 138.8, 133.7, 132.5, 129.5, 128.2, 126.3, 125.7, 123.0, 122.3, 120.5, 120.1, 119.5, 119.2, 108.8, 38.5, 37.0, 13.8, 12.8

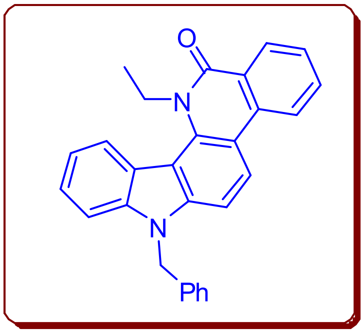
LC-MS (m/z): 375 $(M+H)^+$, 376 (M+1)

Anal. Calcd. for $C_{23}H_{19}ClN_2O$: C, 73.69; H, 5.11; N, 7.47%

Found: C, 73.61; H, 5.14; N, 7.41%

7-Benzyl-12-ethyl-7*H*-indolo[2,3-*c*]phenanthridin-13(12*H*)-one (194d):

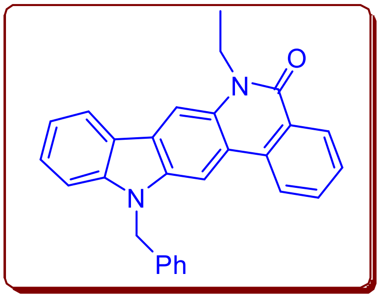
The compound **194d** was obtained from **192d** according to general procedure C. 0.05 g of yellow solid was obtained through silica gel column chromatography in 13% ethylacetate in hexanes.



Yield:	60%
Mp:	56 °C
IR (KBr) ν_{max} cm^{-1}:	3091, 2964, 2928, 2856, 1641, 1467, 1332, 1261, 1082, 1026, 798
^{1}H NMR (400 MHz, CDCl$_3$):	δ 9.05 (1H, d, *J* = 8.0 Hz), 8.64 (2H, t, *J* = 8.0 Hz), 7.80 (1H , t, *J* = 8.0 Hz), 7.68 (1H, d, *J* = 8.0 Hz), 7.55 (2H, q, *J* = 12.0 Hz), 7.48 (2H, s), 7.29 (4H, t, *J* = 8.0 Hz), 7.17 (2H, d, *J* = 7.6 Hz), 5.63 (2H, s, N-C$\underline{H}_2$-Ph), 4.5 (2H, d, *J* = 6.8 Hz), 1.46 (3H, t, *J* = 7.2 Hz, N-CH$_2$C$\underline{H}_3$)
^{13}C NMR (100 MHz, CDCl$_3$):	δ 161.0, 141.3, 137.5, 136.8, 133.3, 131.9, 130.6, 128.9, 128.4, 128.2, 127.9, 127.6, 126.7, 126.3, 126.2, 123.5, 122.7, 118.4, 118.3, 116.1, 113.5, 110.9, 109.4, 46.6, 38.3, 13.1
LC-MS (m/z):	403 (M+H)$^+$ positive mode
Anal. Calcd. for $C_{28}H_{22}N_2O$:	C, 83.56; H, 5.51; N, 6.96%
Found:	C, 83.41; H, 5.59; N, 6.85%

12-Benzyl-6-ethyl-6,12-dihydro-5*H*-indolo[2,3-*b*]phenanthridin-5-one (195d):

The compound **195d** was obtained from **192d** according to general procedure C. 0.024 g of yellow solid was obtained through silica gel column chromatography in 13% ethylacetate in hexanes.



Yield: 25%

Mp: 58 °C

IR (KBr) ν_{max} cm^{-1}: 2996, 2922, 1631, 1593, 1473, 1356, 1149, 815, 748, 638, 576

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.56 (1H, d, *J* = 8.0 Hz), 8.29-8.23 (2H, dd, J_1 = 8.0 Hz, J_2 = 8.0 Hz), 8.21 (1H, s), 8.13 (1H, s), 7.74 (1H, t, *J* = 8.0 Hz), 7.59 (2H, t, *J* = 4.0 Hz), 7.51 (1H, t, *J* = 8.0 Hz), 7.41 (3H, t, *J* = 8.0 Hz), 7.07 (3H, t, *J* = 8.0 Hz), 5.64 (2H, s, N-C$\underline{H_2}$Ph), 4.65 (2H, q, *J* = 4.0 Hz), 1.41 (3H, t, *J* = 12.0 Hz, N-CH$_2$C$\underline{H_3}$)

^{13}C NMR (100 MHz, CDCl$_3$): δ 161.0, 141.3, 137.5, 136.8, 133.3, 132.1, 131.9, 130.6, 128.3, 127.9, 127.2, 126.7, 123.4, 122.7, 121.6, 120.8, 118.4, 118.2, 116.1, 113.5, 110.9, 109.4, 109.1, 105.7, 102.4, 46.6, 38.3, 13.1

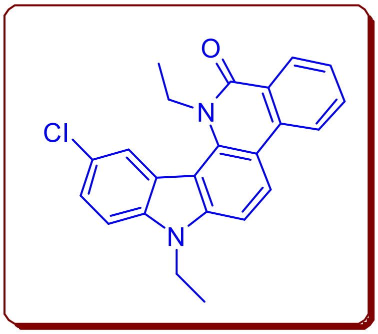
LC-MS (m/z): 403 (M+H)$^+$ positive mode.

Anal. Calcd. for $C_{28}H_{22}N_2O$: C, 83.56; H, 5.51; N, 6.96%

Found: C, 83.45; H, 5.60; N, 7.12%

10-Chloro-7,12-diethyl-7*H*-indolo[2,3-*c*]phenanthridin-13(12*H*)-one (194e):

The compound **194e** was obtained from **192e** according to general procedure C. 0.05 g of yellow solid was obtained through silica gel column chromatography in 13% ethylacetate in hexanes.



Yield: 62%

Mp: 178 °C

IR (KBr) ν_{max} cm^{-1}: 3051, 2972, 1637, 1483, 1332, 1224, 1180, 1072, 798

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.89 (1H, d, J = 8.4 Hz), 8.63 (1H, d, J = 7.6 Hz), 8.59 (1H, s), 7.81 (1H, t, J = 7.6 Hz), 7.66 (1H, t, J = 7.2 Hz), 7.60 (2H, s), 7.48-7.41 (2H, dd, J_1 = 8.8 Hz, J_2 = 8.8 Hz), 4.57 (2H, q, J = 6.8 Hz, N-C$\underline{H}_2$CH$_3$), 4.46 (2H, q, J = 6.8 Hz, N-C$\underline{H}_2$CH$_3$), 1.49 (6H, t, J = 3.6 Hz)

^{13}C NMR (100 MHz, CDCl$_3$): δ 170.1, 142.9, 139, 138.9, 133.4, 129.3, 128.2, 127.2, 126.7, 126.2, 124.6, 123.4, 122, 120.2, 119.8, 108.8, 93.8, 44.9, 37.8, 13.8, 12.8

LC-MS (m/z): 375 (M+H)$^+$, 376 (M+1) positive mode.

Anal. Calcd. for $C_{23}H_{19}ClN_2O$: C, 73.69; H, 5.11; N, 7.47%

Found: C, 73.61; H, 5.14; N, 7.41%

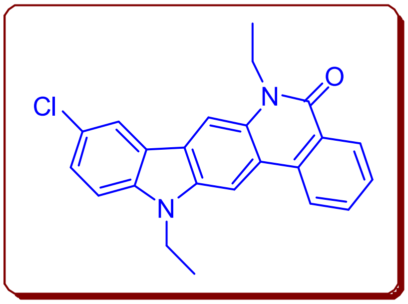
9-Chloro-6,12-diethyl-6,12-dihydro-5*H*-indolo[2,3-*b*]phenanthridin-5-one (195e):

The compound **195e** was obtained from **192e** according to general procedure C. 0.013 g of yellow solid was obtained through silica gel column chromatography in 13% ethylacetate in hexanes.

Yield: 16%

Mp: 142 °C

IR (KBr) ν_{max} cm^{-1}: 3057, 2974, 1637, 1491, 1464, 1410, 1226, 1014, 748, 644



^{1}H NMR (400 MHz, CDCl$_3$): δ 8.62 (1H, d, J = 6.8 Hz), 8.44 (1H, d, J = 8.0 Hz), 8.27 (1H, s), 8.17 (1H, d, J = 1.6 Hz), 8.05 (1H, s), 7.81 (1H, t, J = 6.8 Hz), 7.63 (1H, d, J = 7.6 Hz), 7.51-7.41 (1H, dd, J_1 = 8.4 Hz, J_2 = 6.0 Hz), 7.37 (1H, d, J = 8.8 Hz), 4.64 (2H, q, J = 7.2 Hz, N-C$\underline{H}_2$CH$_3$), 4.48 (2H, q, J = 7.2 Hz, N-C$\underline{H}_2$CH$_3$), 1.48 (6H, t, J = 6.8 Hz)

^{13}C NMR (100 MHz, CDCl$_3$): δ 160.8, 141.6, 136.1, 134.0, 132.1, 130.6, 129.0, 127.5, 126.9, 125.4, 124.8, 122.3, 121.5, 120.8, 118.9, 118.6, 108.7, 38.0, 37.6, 13.8, 12.7

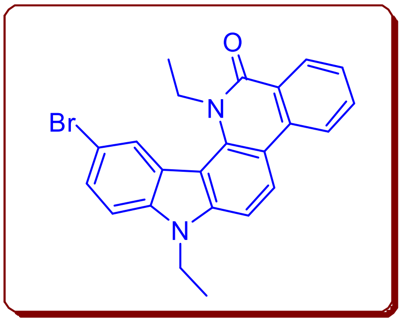
LC-MS (m/z): 375 (M+H)$^+$, 376 (M+1)

Anal. Calcd. for $C_{23}H_{19}ClN_2O$: C, 73.69; H, 5.11; N, 7.47%

Found: C, 73.61; H, 5.14; N, 7.41%

10-Bromo-7,12-diethyl-7*H*-indolo[2,3-*c*]phenanthridin-13(12*H*)-one (194f):

The compound **194f** was obtained from **192f** according to general procedure C. 0.04 g of yellow solid was obtained through silica gel column chromatography in 14% ethylacetate in hexanes.



Yield: 55%

Mp: 197 °C

IR (KBr) ν_{max} cm^{-1}: 3070, 2970, 1612, 1491, 1468, 1410, 1236, 1014, 798, 644

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.90 (1H, d, *J* = 8.0 Hz), 8.75 (1H, s), 8.63 (1H, d, *J* = 7.6 Hz), 7.83 (1H, t, *J* = 6.8 Hz), 7.68 (1H, t, *J* = 8.4 Hz), 7.58 (3H, d, *J* = 12.8 Hz), 7.38 (1H, d, *J* = 8.8 Hz), 4.59 (2H, q, *J* = 6.4 Hz, N-C$\underline{H_2}$CH$_3$), 4.46 (2H, q, *J* = 6.8 Hz, N-C$\underline{H_2}$CH$_3$), 1.48 (6H, t, *J* = 3.2 Hz)

^{13}C NMR (100 MHz, CDCl$_3$): δ 161.1, 140.5, 136.8, 133.0, 131.6, 130.0, 128.2, 127.8, 126.7, 126.0, 123.4, 122.6, 120.1, 119.1, 118.1, 116.1, 113.3, 110.4, 109.0, 38.3, 37.6, 13.8, 13.2

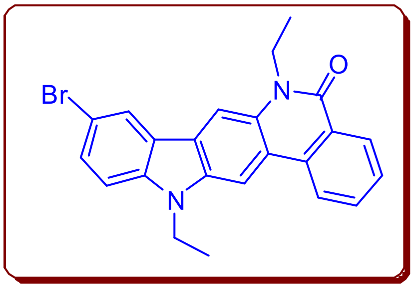
LC-MS (m/z): 419 (M+H)$^+$, 421 (M+2) positive mode

Anal. Calcd. for $C_{23}H_{19}BrN_2O$: C, 65.88; H, 4.57; N, 6.68%

Found: C, 65.92; H, 4.53; N, 6.56%

9-Bromo-6,12-diethyl-6,12-dihydro-5*H*-indolo[2,3-*b*]phenanthridin-5-one (195f):

The compound **195f** was obtained from **192f** according to general procedure C. 0.012 g of yellow solid was obtained through silica gel column chromatography in 14% ethylacetate in hexanes.



Yield: 15%

Mp: 192 $^{\circ}$C

IR (KBr) ν_{max} cm^{-1}: 3047, 2880, 1645, 1478, 1336, 1257, 984, 724

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.62 (1H, d, J = 8.0 Hz), 8.45 (1H, d, J = 8.4 Hz), 8.32 (1H, s), 8.27 (1H, s), 8.05 (1H, s), 7.81 (1H, t, J = 7.2 Hz), 7.63 (2H, d, J = 4.0 Hz), 7.33 (1H, d, J = 9.6 Hz), 4.64 (2H, q, J = 7.6 Hz, N-C$\underline{H}_2$CH$_3$), 4.48 (2H, q, J = 7.2 Hz, N-C$\underline{H}_2$CH$_3$), 1.49 (6H, t, J = 7.2 Hz)

^{13}C NMR (100 MHz, CDCl$_3$): δ 159.7, 146.4, 140.7, 138.1, 136.8, 133.0, 127.9, 126.7, 126.5, 124.4, 123.1, 122.0, 118.3, 114.4, 113.3, 112.9, 109.5, 38.7, 37.8, 13.9, 13.0

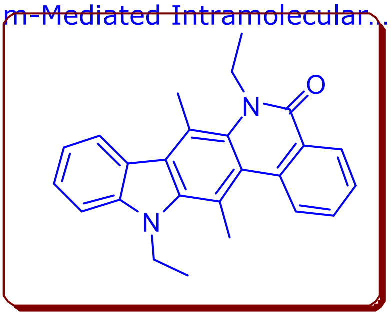
LC-MS (m/z): 419 (M+H)$^+$, 421 (M+2) positive mode

Anal. Calcd. for $C_{23}H_{19}BrN_2O$: C, 65.88; H, 4.57; N, 6.68%

Found: C, 65.79; H, 4.55; N, 6.75%

6,12-Diethyl-7,13-dimethyl-6,12-dihydro-5*H*-indolo[2,3-*b*]phenanthridin-5-one (198a):

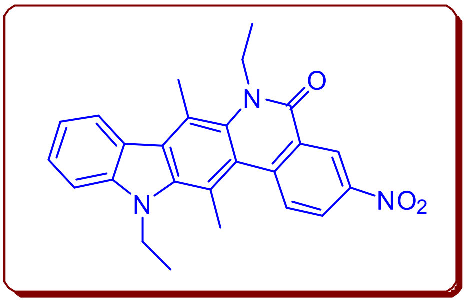
The compound **198a** was obtained from **197a** according to general procedure C. 0.08 g of yellow solid was obtained through silica gel column chromatography in 15% ethylacetate in hexanes.



Yield:	79%
Mp:	197-198 °C
IR (KBr) ν$_{max}$ cm^{-1}:	3051, 2974, 2930, 2872, 1643, 1502, 1332, 1151, 1010, 746
^{1}H NMR (400 MHz, CDCl$_3$):	δ 8.54 (1H, d, *J* = 8.0 Hz), 8.26 (1H, d, *J* = 8.0 Hz), 8.17 (1H, d, *J* = 8.0 Hz), 7.7 (1H, t, *J* = 8.0 Hz), 7.57-7.50 (3H, m), 7.30 (1H, t, *J* = 4.0 Hz), 4.62 (2H, q, *J* = 8.0 Hz, N-C$\underline{H}_2$CH$_3$), 4.42 (2H, q, *J* = 4.0 Hz, N-C$\underline{H}_2$CH$_3$), 3.16 (3H, s, C$\underline{H}_3$), 3.00 (3H, s, C$\underline{H}_3$), 1.48 (3H, t, *J* = 8.0 Hz, *N*-CH$_2$C$\underline{H}_3$), 1.20 (3H, t, *J* = 8.0 Hz, *N*-CH$_2$C$\underline{H}_3$)
^{13}C NMR (100 MHz, CDCl$_3$):	δ 160.7, 143.2, 142.8, 140.9, 139.1, 137.8,132.1, 130.1, 129.9, 127.7, 126.5, 125.4, 123.7, 122.8, 122.6, 119.2, 118.0, 117.4, 108.6, 55.0, 51.5, 21.5, 21.1, 16.3, 15.5
LC-MS (m/z):	369 (M+H)$^+$ positive mode
Anal. Calcd. for $C_{25}H_{24}N_2O$:	C, 81.49; H, 6.57; N, 7.70%
Found:	C, 81.32; H, 6.50; N, 7.76%

6,12-Diethyl-3-nitro-6,12-dihydro-5*H*-indolo[2,3-*b*]phenanthridin-5-one (11b):

The compound **198b** was obtained from **197b** according to general procedure C. 0.09 g of yellow solid was obtained through silica gel column chromatography in 15% ethylacetate in hexanes.



Yield:	82%
Mp:	68 °C
IR (KBr) ν$_{max}$ cm^{-1}:	3059, 2961, 2926, 2868, 1647, 1521,

1344, 1022, 742

^{1}H NMR (400 MHz, CDCl$_3$): δ 9.35 (1H, s), 8.49 (1H, d, *J* = 6.4 Hz), 8.27 (2H, t, *J* = 8.0 Hz), 7.56 (2H, t, *J* = 6.4 Hz), 7.30 (1H, d, *J* = 7.2 Hz), 4.86 (2H, s), 4.62 (2H, s), 3.17 (3H, s, $C\underline{H}_3$), 3.01 (3H, s, $C\underline{H}_3$), 1.51 (3H, t, *J* = 6.4 Hz, $N\text{-}CH_2C\underline{H}_3$), 1.23 (3H, t, *J* = 7.0 Hz, $N\text{-}CH_2C\underline{H}_3$)

^{13}C NMR (100 MHz, CDCl$_3$): δ 163.3, 145.7, 143.9, 140.0, 129.5, 129.1, 128.3, 126.9, 124.6, 124.4, 124.3, 123.8, 121.0, 120.1, 119.8, 115.9, 109.6, 58.2, 41.1, 20.8, 19.7, 13.9, 13.8

LC-MS (m/z): 414 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{25}H_{23}N_3O_3$: C, 72.62; H, 5.61; N, 10.16%

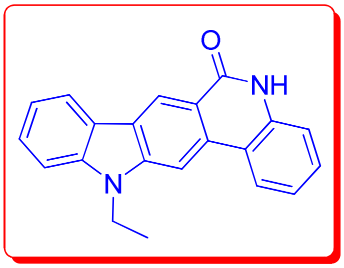
Found: C, 72.55; H, 5.71; N, 10.25%

General procedure D

A mixture of compound **200a** (0.10 g, 0.25 mmol), anhydrous K_2CO_3 (0.102 g, 7.5 mmol), TBAB (0.08 g, 0.25 mmol) and $Pd(OAc)_2$ (0.008 mg, 10 mol %) in DMA (2 mL) was taken in a Schlenk tube and heated at 170 °C for 2 h with continuous stirring. After completion of the reaction as monitored by TLC, the reaction mixture was cooled and poured into water (10 mL). A solid precipitate was formed, extracted with ethylacetate (3 x 20 mL) and washed with water (3 x 20 mL) followed by brine (20 mL) and dried over Na_2SO_4. Evaporation of solvent and the crude material was purified by column chromatography over silica-gel (100-200 mesh), using 12% ethylacetate in hexanes as an eluent to give the products **201a**.

12-Ethyl-5*H*-indolo[3,2-*j*]phenanthridin-6(12*H*)-one (201a):

The title compound **201a** was obtained from **200a** according to the general procedure D. The white solid was obtained through silica-gel column chromatography using 14% ethylacetate in hexanes.



Yield: 68%

IR (KBr) ν_{max} cm^{-1}: 2976, 1680, 1601, 1442, 1302, 798, 765

^{1}H NMR (400 MHz, DMSO-d_6): δ 11.4 (s, 1H), 9.12 (s, 1H), 8.67 (d, 1H, J = 8.0 Hz), 8.64 (s, 1H) 8.35 (d, 1H, J = 8.0 Hz), 7.77 (d, 1H, J = 12.0 Hz), 7.56 (t, 1H, J = 8.0 Hz), 7.46 (t, 1H, J = 10.4 Hz), 7.35 (d, 1H, J = 8.0 Hz), 7.31-7.26 (m, 2H), 4.64 (q, 2H, J = 8.0 Hz), 1.38 (t, 3H, J = 8.0 Hz)

^{13}C NMR (100 MHz, CDCl$_3$): δ 168.4, 144.3, 141.6, 137.1, 135.6, 134.5, 130.7, 128.3, 127.2, 125.0, 122.1, 121.6, 121.2, 121.0, 119.2, 116.0, 108.7, 108.4, 100.7, 37.7, 12.7

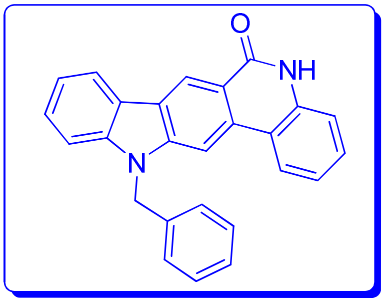
LC-MS (m/z): 313 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{21}H_{16}N_2O$: C, 80.75; H, 5.6; N, 8.97

Found: C, 80.65; H, 5.55; N, 8.90

12-Benzyl-5*H*-indolo[3,2-*j*]phenanthridin-6(12*H*)-one (201b):

The title compound **201b** was obtained from **200b** according to the general procedure D. The white solid was obtained through silica-gel column chromatography using 14% ethylacetate in hexanes.



Yield: 72%

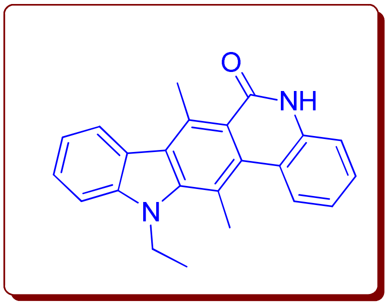
IR (KBr) ν_{max} cm^{-1}: 2949, 1683, 1602, 1530, 1456, 1392, 1278, 1142, 1084, 789

^{1}H NMR (400 MHz, DMSO-d_6): δ 11.3 (s, 1H), 8.9 (s, 1H), 8.64 (d, 1H, J = 8.0 Hz), 8.52 (s, 1H), 8.41 (d, 1H, J = 4.0 Hz), 8.14 (t, 2H, J = 12.0 Hz), 7.97 (t, 1H, J = 8.0 Hz), 7.56-7.48 (m, 1H), 7.37 (d, 1H, J = 8.0 Hz), 7.34 (d, 4H, J = 4.0 Hz), 7.17 (d, 2H, J = 4.0 Hz), 5.59 (s, 2H)

^{13}C NMR (100 MHz, DMSO-d_6):	δ 166.6, 144.6, 142.4, 137.9, 136.6, 135.5, 134.6, 130.7, 128.9, 128.4, 127.7, 127.5, 126.2, 125.1, 122.2, 121.6, 121.2, 120.9, 119.7, 116.3, 109.1, 108.5, 101.3, 46.7
LC-MS (m/z):	375 $(M+H)^+$ positive mode
Anal. Calcd. for $C_{26}H_{17}NO_2$:	C, 83.40; H, 4.85; N, 7.48%
Found:	C, 83.35; H, 4.82; N, 7.45%

12-Ethyl-7,13-dimethyl-5*H*-indolo[3,2-*j*]phenanthridin-6(12*H*)-one (201c):

The title compound **201c** was obtained from **200c** according to the general procedure D. The white solid was obtained through silica-gel column chromatography using 14% ethylacetate in hexanes.

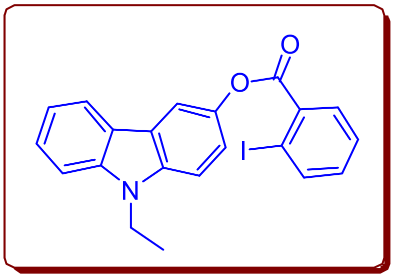


Yield:	62%
IR (KBr) ν_{max} cm^{-1}:	2964, 2930, 2872, 1683, 1502, 1332, 1151, 1010, 746
^{1}H NMR (400 MHz, CDCl$_3$):	δ 8.28 (d, 1H, *J* = 8.0 Hz), 7.72 (d, 1H, *J* = 4.0 Hz), 7.52-7.47 (m, 2H), 7.38 (d, 2H, *J* = 8.0 Hz), 7.30 (d, 1H, *J* = 8.0 Hz), 7.17 (d, 1H, *J* = 8.0 Hz), 4.64 (q, 2H, *J* = 8.0 Hz, N-C$\underline{H}_2$CH$_3$), 3.02 (s, 3H, C$\underline{H}_3$), 2.84 (s, 3H, C$\underline{H}_3$), 1.44 (t, 3H, *J* = 8.0 Hz, *N*-CH$_2$C$\underline{H}_3$)
^{13}C NMR (100 MHz, CDCl$_3$):	δ 166.7, 143.2, 142.8, 140.9, 139.1, 137.8,132.1, 130.1, 129.9, 127.7, 126.5, 125.4, 123.7, 122.8, 122.6, 119.2, 118.0, 117.4, 108.6, 39.3, 20.1, 17.6, 15.5
LC-MS (m/z):	340 $(M+H)^+$ positive mode
Anal. Calcd. for $C_{25}H_{24}N_2O$:	C, 81.15; H, 5.92; N, 8.23%
Found:	C, 81.10; H, 5.90; N, 8.20%

General procedure E

To the compound **212a** (0.5 g, 2.1 mmol) in 10 mL DCM, pyridine (0.42 mL, 4.3 mmol) was added, stirred at room temperature for 15 minutes. Then the reaction mixture was cooled in an ice bath and added freshly prepared **189a** (0.7 mL, 2.6 mmol) (prepared from *o*-iodobenzoic acid and thionyl chloride) in dropwise manner. After stirring for 15 minutes the reaction mixture was brought to room temperature and stirring continued up to 6 h. The solvent was evaporated and adsorbed on basic alumina using 12% ethylacetate in hexanes as eluent to obtain pure product **213a**. Similarly compounds **213a-e** and **213f-h** were obtained by the following procedure.

9-Ethyl-9*H*-carbazol-3-yl 2-iodobenzoate (213a):



Yield: 65%

Mp: 89 °C

IR (KBr) ν_{max} cm^{-1}: 3059, 2930, 1732, 1689, 1577, 1462, 1244, 1080, 1037, 891, 744

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.16-8.11 (m, 3H), 8.02 (1H, s), 7.55-7.51 (m, 2H), 7.45 (q, 2H, J = 4.0 Hz), 7.41-7.38 (dd, 1H, J_1 = 2.0 Hz, J_2 = 2.0 Hz), 7.29-7.24 (m, 2H), 4.40 (q, 2H, J = 7.2 Hz, N-C$\underline{H}_2$CH$_3$), 1.47 (t, 3H, J = 7.2 Hz, N-CH$_2$C$\underline{H}_3$)

^{13}C NMR (100 MHz, CDCl$_3$): δ 165.8, 143.5, 141.6, 140.6, 137.8, 134.7, 133.8, 128.1, 126.1, 123.3, 122.6, 120.7, 119.2, 118.9, 113.0, 108.8, 108.7, 94.6, 37.7, 13.8

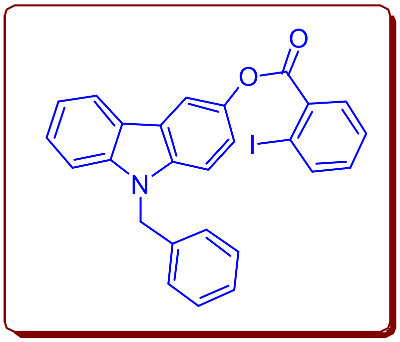
LC-MS (m/z): 441 (M+H)$^+$, positive mode

Anal. Calcd. for $C_{21}H_{16}INO_2$: C, 57.16; H, 3.65; N, 3.17%

Found: C, 57.28; H, 3.71; N, 3.22%

9-Benzyl-9*H*-carbazol-3-yl 2-iodobenzoate (213b):

The product **213b** was prepared from **212b** and **189a** according through the general procedure E. The white product obtained was purified on basic alumina using 12% ethylacetate in hexanes.



Yield: 68%

Mp: 48 °C

IR (KBr) ν_{max} cm^{-1}: 3418, 3061, 1734, 1693, 1583, 1466, 1242, 1014, 891, 794, 680

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.09-8.04 (m, 3H), 8.02-8.00 (2H, m), 7.51-7.47 (2H, ddd, J_1 = 0.8 Hz, J_2 = 0.4 Hz, J_3 = 0.8 Hz), 7.43 (t, 3H, J = 6.0 Hz), 7.37-7.35 (m, 2H), 7.24 (s, 1H), 7.20-7.17 (1H, ddd, J_1 = 1.2 Hz, J_2 = 1.2 Hz, J_3 = 1.2 Hz), 7.13 (d, 2H, J = 5.6 Hz), 5.51 (s, 2H)

^{13}C NMR (100 MHz, CDCl$_3$): δ 165.8, 141.9, 141.6, 141.3, 138.5, 136.9, 133.5, 133.1, 132.0, 131.5, 128.9, 128.0, 126.4, 126.3, 123.4, 122.7, 120.7, 118.8, 119.4, 119.3, 113.0, 109.3, 109.1, 94.7, 46.7

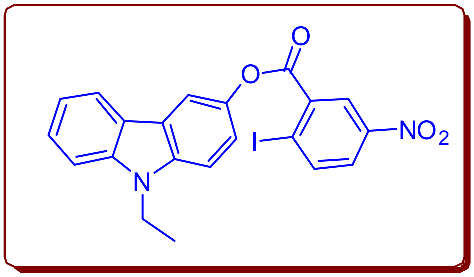
LC-MS (m/z): 504 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{26}H_{18}INO_2$: C, 62.04; H, 3.60; N, 2.78%

Found: C, 62.15; H, 3.72; N, 2.71%

9-Ethyl-9*H*-carbazol-3-yl 2-iodo-5-nitrobenzoate (213c):

The product **213c** was prepared from **212a** and **189c** according through the general procedure E. The red product obtained was purified on basic alumina using 12% ethylacetate in hexanes.



Yield: 78%

Mp: 98 ^{o}C

IR (KBr) ν_{max} cm^{-1}: 3057, 2970, 1745, 1569, 1317, 1016, 829

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.91 (s, 1H), 8.28 (d, 1H, *J* = 8.8 Hz), 8.09-8.0 (m, 3H), 7.52 (d, 1H, *J* = 7.6 Hz), 7.49-7.43 (m, 2H), 7.36 (d, 1H, *J* = 8.8 Hz), 7.24 (d, 1H, *J* = 7.2 Hz), 4.4 (q, 2H, *J* = 7.2 Hz, $NC\underline{H}_2CH_3$), 1.46 (t, 3H, *J* = 6.8 Hz, $NCH_2C\underline{H}_3$)

^{13}C NMR (100 MHz, $CDCl_3$): δ 164.0, 143.1, 143.0, 140.6, 138.0, 135.9, 126.7, 126.3, 125.9, 123.3, 122.5, 120.7, 119.0, 118.8, 112.8, 108.9, 103.1, 37.7, 13.8

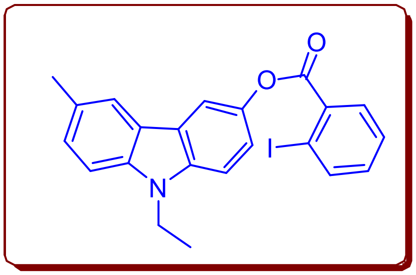
LC-MS (m/z): 487 $(M+H)^+$ positive mode.

Anal. Calcd. for $C_{21}H_{15}IN_2O_4$: C, 51.87; H, 3.11; N, 5.76%

Found: C, 51.73; H, 3.18; N, 5.71%

9-Ethyl-6-methyl-9*H*-carbazol-3-yl 2-iodobenzoate (213d):

The product **213d** was prepared from **212d** and **189a** according through the general procedure E. The white product obtained was purified on basic alumina using 12% ethylacetate in hexanes.



Yield: 62%

Mp: 74 ^{o}C

IR (KBr) ν_{max} cm^{-1}: 2962, 1738, 1577, 1458, 1344, 1302, 1182, 1141, 1068, 891, 640, 607

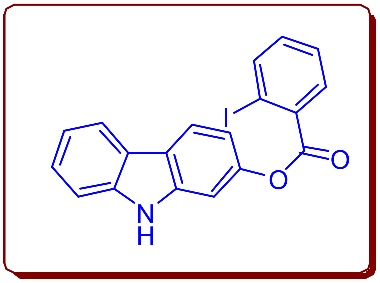
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15-8.11 (m, 2H), 7.93 (d, 1H, *J* = 2.4 Hz), 7.90 (s, 1H), 7.55-7.51 (ddd, 1H, J_1 = 1.2 Hz, J_2 = 0.8 Hz, J_3 = 1.2 Hz), 7.44 (s, 1H), 7.41 (s, 1H), 7.38 (d, 2H, *J* = 2.4 Hz), 7.28-7.24 (ddd, 1H, J_1 = 1.6 hz, J_2 = 1.6 Hz, J_3 =

1.6 Hz), 4.37 (q, 2H, *J* = 7.2 Hz, NC<u>H</u>$_2$CH$_3$), 2.57 (s, 3H, C<u>H</u>$_3$), 1.45 (t, 3H, *J* = 7.2 Hz, NCH$_2$C<u>H</u>$_3$)

^{13}C NMR (100 MHz, CDCl$_3$):	δ 165.9, 143.3, 141.6, 138.9, 138.0, 134.7, 133.0, 131.5, 128.2, 128.0, 127.5, 123.0, 122.7, 120.6, 119.0, 112.9, 108.7, 108.4, 94.6, 37.7, 21.4, 13.8
LC-MS (m/z):	456 (M+H)$^+$ positive mode
Anal. Calcd. for $C_{22}H_{18}INO_2$:	C, 58.04; H, 3.98; N, 3.08%
Found:	C, 58.12; H, 3.91; N, 3.15%

9*H*-Carbazol-2-yl 2-iodobenzoate (213e):

The product **209e** was prepared from **212e** and **189a** according through the general procedure E. The white product obtained was purified on basic alumina using 25% ethylacetate in hexanes.

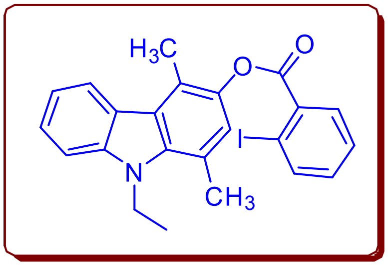


Yield:	85%
Mp:	179 °C
IR (KBr) ν_{max} cm^{-1}:	3396, 1728, 1601, 1458, 1325, 1251, 1138, 1012, 802, 742
^{1}H NMR (400 MHz, DMSO-*d*$_6$):	δ 11.41 (s, 1H), 8.18 (d, 1H, *J* = 8.4 Hz), 8.11 (t, 2H, *J* = 9.2 Hz), 8.01 (d, 1H, *J* = 8.0 Hz), 7.61 (t, 1H, *J* = 6.8 Hz), 7.50 (d, 1H, *J* = 8.0 Hz), 7.42 (s, 1H), 7.36 (d, 2H, *J* = 6.8 Hz), 7.18 (t, 1H, *J* = 7.2 Hz), 7.09 (d, 1H, *J* = 6.8 Hz)
^{13}C NMR (100 MHz, DMSO-*d*$_6$):	δ 166.0, 149.0, 141.2, 140.8, 135.5, 133.9, 131.4, 128.9, 126.0, 122.4, 121.2, 121.0, 120.6, 119.4, 113.0, 111.5, 104.5, 95.2
LC-MS (m/z):	414 (M+H)$^+$ positive mode
Anal. Calcd. for $C_{19}H_{12}INO_2$:	C, 55.23; H, 2.93; N, 3.39%

Found: C, 55.42; H, 2.86; N, 3.31%

9-Ethyl-1,4-dimethyl-9*H*-carbazol-3-yl 2-iodobenzoate (213f):

The product **213f** was prepared from **212f** and **189a** according the general procedure E. The white product obtained was purified on basic alumina using 12% ethylacetate in hexanes.



Yield: 70%

Mp: 108 °C

IR (KBr) ν_{max} cm^{-1}: 2964, 2924, 1745, 1601, 1456, 1280, 1176, 1101, 869, 748

^{1}H NMR (400 MHz, CDCl$_3$): *δ* 8.23 (d, 1H, *J* = 8.0 Hz), 8.18-8.16 (dd, 1H, J_1 = 1.6 Hz, J_2 = 1.2 Hz), 8.11 (d, 1H, *J* = 8.0 Hz), 7.54-7.44 (m, 3H), 7.24 (t, 2H, *J* = 6.4 Hz), 7.07 (s, 1H), 4.64 (q, 2H, *J* = 8.0 Hz, $NC\underline{H_2}CH_3$), 2.83 (s, 3H), 2.74 (s, 3H), 1.43 (t, 3H, *J* = 16.0 Hz, $NCH_2C\underline{H_3}$)

^{13}C NMR (100 MHz, CDCl$_3$): *δ* 165.7, 141.7, 141.3, 141.2, 136.7, 134.4, 133.1, 131.5, 128.1, 125.2, 123.9, 122.9, 122.7, 122.4, 118.9, 118.1, 108.1, 94.7, 39.3, 20.1, 15.5, 13.6

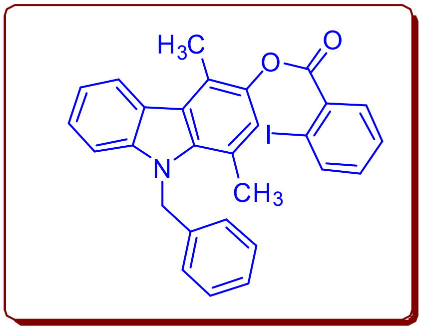
LC-MS (m/z): 470 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{23}H_{20}INO_2$: C, 58.86; H, 4.30; N, 2.98%

Found: C, 58.75; H, 4.36; N, 2.91%

9-Benzyl-1,4-dimethyl-9*H*-carbazol-3-yl 2-iodobenzoate (213g):

The product **213g** was prepared from **212g** and **189a** according through the general procedure E. The white product obtained was purified on basic alumina using 12% ethylacetate in hexanes.



Yield: 72%

Mp: 122-124 °C

IR (KBr) ν_{max} cm^{-1}: 2922, 1739, 1682, 1579, 1508, 1396, 1165, 1014, 885, 796

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.29–8.17 (m, 1H), 8.15–8.09 (m, 2H), 7.52 (q, 1H, J = 8.0 Hz), 7.32 (s, 1H), 7.30–7.22 (m, 5H), 7.10 (d, 1H, J = 8.0 Hz), 7.04 (d, 1H, J = 8.0 Hz), 6.95 (d, 1H, J = 8.0 Hz), 5.80 (s, 2H), 2.80 (s, 3H), 2.64 (s, 3H)

^{13}C NMR (100 MHz, CDCl$_3$): δ 165.8, 143.9, 141.6, 140.0, 139.3, 138.5, 134.6, 133.1, 131.5, 129.4, 128.9, 128.1, 127.3, 125.5, 124.0, 122.6, 122.4, 121.9, 121.2, 119.4, 118.8, 117.8, 115.0, 109.1, 94.6, 48.3

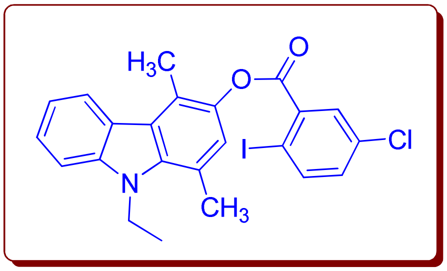
LC-MS (m/z): 530 (M-H)$^-$ négative mode.

Anal. Calcd. for $C_{28}H_{22}INO_2$: C, 63.29; H, 4.17; N, 2.64%

Found: C, 63.15; H, 4.22; N, 2.58%

9-Ethyl-1,4-dimethyl-9*H*-carbazol-3-yl 5-chloro-2-iodobenzoate (213h):

The product **213h** was prepared from **212f** and **189c** according through the general procedure E. The white product obtained was purified on basic alumina using 12% ethylacetate in hexanes.



Yield: 65%

Mp: 84 °C

IR (KBr) ν_{max} cm^{-1}: 2994, 1736, 1608, 1504, 1180, 1010, 804, 615

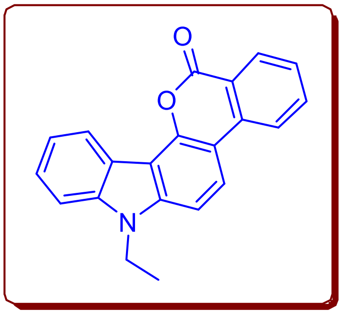
^{1}H NMR (400 MHz, CDCl$_3$):	δ 8.21 (d, 1H, *J* = 8.0 Hz), 8.12 (d, 1H, *J* = 2.8 Hz), 8.0 (d, 1H, *J* = 8.0 Hz),7.50-7.43 (m, 2H), 7.24-7.21 (m, 2H), 7.03 (s, 1H), 4.60 (q, 2H, *J* = 7.2 Hz, $NC\underline{H}_2CH_3$), 2.81 (s, 3H), 2.72 (s, 3H), 1.42 (t, 3H, *J* = 8.0 Hz, $NCH_2C\underline{H}_3$)
^{13}C NMR (100 MHz, CDCl$_3$):	δ 164.5, 142.8, 141.1, 136.8, 135.8, 134.7, 133.2, 131.4, 128.3, 125.3, 123.9, 122.9, 122.5, 122.2, 121.9, 119.0, 118.2, 108.6, 91.9, 39.3, 20.1, 15.5, 13.7
LC-MS (m/z):	504 (M+1), 506 (M+2) positive mode
Anal. Calcd. for $C_{23}H_{19}ClINO_2$:	C, 54.84; H, 3.80; N, 2.78%
Found:	C, 54.75; H, 3.86; N, 2.71%

General procedure F

A mixture of compound **213a** (0.15 g, 0.34 mmol), anhydrous KOAc (0.08 g, 0.85 mmol), and Pd(OAc)$_2$ (0.007 mg, 10 mol %) in DMA (3.0 mL) was taken in a sealed tube and heated at 140 °C for 4 h with continuous stirring. After completion of the reaction as monitored by TLC, the reaction mixture was cooled and poured into cold water (10 mL). A solid precipitate was formed, extracted with CHCl$_3$ (3 x 20 mL), and washed with water (3 x 20 mL) followed by brine (20 mL) and dried over Na$_2$SO$_4$. Evaporation of solvent and the crude material was purified by column chromatography over silica-gel (100-200 mesh), using 14% EtOAc in hexanes as eluent to give mixture of the products **214a** and **215a**. Similarly compounds **214b-e**, **215b-e**, and **215f-h** were obtained in the same procedure. Compounds **214e** and **215e** were chromatographed on basic alumina using 35% EtOAc in hexanes as eluent. For **215f–h**, anhyd. KOAc (2.5 equiv) was used as base.

7-Ethylisochromeno[4,3-*c*]carbazol-13(7*H*)-one (214a):

The title compound **214a** was obtained from **213a** according to general procedure F. The white solid was obtained through silica-gel column chromatography using 14% ethylacetate in hexanes.



Yield: 58%

Mp: 189-191 °C

IR (KBr) ν_{max} cm^{-1}: 3057, 2962, 1714, 1595, 1485, 1261, 1086, 800, 694

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.94 (d, 1H, J = 8.4 Hz), 8.56 (d, 1H, J = 8.4 Hz), 8.49-8.47 (dd, 1H, J_1 = 1.2, J_2 = 1.2 Hz), 7.91-7.87 (ddd, 1H, J_1 = 1.2 Hz, J_2 = 1.2 Hz, J_3 = 1.2 Hz), 7.67-7.63 (ddd, 1H, J_1 = 4.0Hz, J_2 = 4.0 Hz, J_3 = 4.0 Hz), 7.57-7.48 (m, 4H), 7.24-7.20 (ddd, 1H, J_1 = 4.0 Hz, J_2 = 4.0 Hz, J_3 = 4.0 Hz), 4.46 (q, 2H, J = 8.0 Hz, $NC\underline{H}_2CH_3$), 1.48 (t, 3H, J = 8.0 Hz, $NCH_2C\underline{H}_3$)

^{13}C NMR (100 MHz, CDCl$_3$): δ 161.8, 146.4, 140.7, 137.7, 135.2, 133.5, 130.2, 128.6, 126.3, 126.2, 123.2, 122.0, 118.3, 117.1, 115.5, 114.2, 111.0, 109.2, 37.7, 13.8

LC-MS (m/z): 314 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{21}H_{15}NO_2$: C, 80.49; H, 4.82; N, 4.47

Found: C, 80.32; H, 4.75; N, 4.41

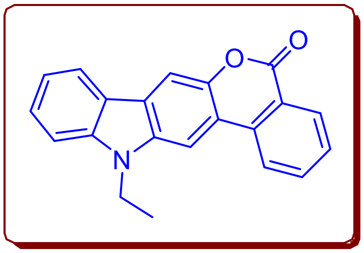
12-Ethylisochromeno[4,3-*b*]carbazol-5(12*H*)-one (215a):

The title compound **215a** was obtained from **213a** according to general procedure F. The white solid was obtained through silica-gel column chromatography using 14% ethylacetate in hexanes.

Yield: 27%

Mp: 122 °C

IR (KBr) ν_{max} cm^{-1}: 3491, 2916, 1720, 1601, 1442, 1302, 798, 765



^{1}H NMR (400 MHz, CDCl$_3$): δ 8.46-8.44 (dd, 1H, J_1 = 0.8 Hz, J_2 = 1.2 Hz), 8.30 (d, 1H, J = 8.0 Hz), 8.12 (d, 1H, J = 8.0 Hz), 8.04 (s, 1H), 7.98 (s, 1H), 7.88-7.44 (ddd, 1H, J_1 = 1.6 Hz, J_2 = 0.8 Hz, J_3 = 1.2 Hz), 7.60-7.51 (m, 2H), 7.43 (d, 1H, J =

8.0 Hz), 7.28-7.24 (m, 1H), 4.46 (q, 2H, *J* = 8.0 Hz, $N\mathrm{C}\underline{\mathrm{H}}_2\mathrm{CH}_3$), 1.50 (t, 3H, *J* = 8.0 Hz, $N\mathrm{CH}_2\mathrm{C}\underline{\mathrm{H}}_3$)

^{13}C NMR (100 MHz, $CDCl_3$): δ 161.7, 145.3, 141.6, 137.1, 135.6, 134.5, 130.7, 128.3, 127.2, 125.0, 122.1, 121.6, 121.2, 121.0, 119.2, 116.0, 108.7, 108.4, 100.7, 37.7, 12.7

LC-MS (m/z): 314 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{21}H_{15}NO_2$: C, 80.49; H, 4.82; N, 4.47

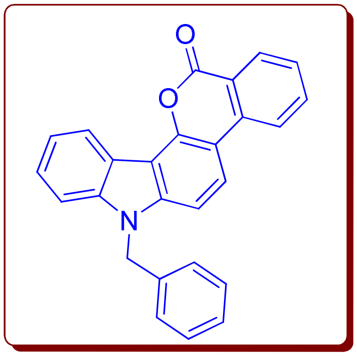
Found: C, 80.35; H, 4.91; N, 4.42

7-Benzylisochromeno[4,3-*c*]carbazol-13(7*H*)-one(214b):

The title compound **214b** was obtained from **213b** according to general procedure F. The white solid was obtained through silica-gel column chromatography using 14% ethylacetate in hexanes. Compound was recrystallized from (50% MeOH–MeCN).

Yield: 50%

Mp: 136 °C



IR (KBr) ν_{max} cm^{-1}: 2924, 1714, 1602, 1446, 1302, 1176, 1084, 800, 692

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.99 (d, 1H, *J* = 8.0 Hz), 8.64-8.61 (dd, 1H, J_1 = 4.0 Hz, J_2 = 4.0 Hz), 8.52-8.50 (dd, 1H, J_1 = 1.2 Hz, J_2 = 1.2 Hz), 7.95-791 (ddd, 1H, J_1 = 1.2 Hz, J_2 = 1.2 Hz, J_3 = 1.6 Hz), 7.70-7.66 (ddd, 1H, J_1 = 0.8 Hz, J_2 = 1.2 Hz, J_3 = 1.2 Hz), 7.53-7.45 (m, 4H), 7.33-7.25 (m, 4H), 7.15 (d, 2H, *J* = 8.0 Hz), 5.63 (s, 2H)

^{13}C NMR (100 MHz, $CDCl_3$): δ 161.7, 146.6, 141.5, 138.4, 136.5, 135.1, 133.6, 130.2, 128.9, 128.7, 126.5, 126.2, 123.2, 122.0, 118.8, 117.3, 115.8, 114.3, 111.5, 109.7, 46.6

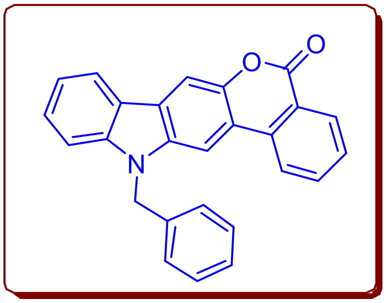
LC-MS (m/z): 376 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{26}H_{17}NO_2$: C, 83.18; H, 4.56; N, 3.73%

Found: C, 83.65; H, 4.72; N, 3.81%

12-Benzylisochromeno[4,3-*b*]carbazol-5(12*H*)-one (215b):

The title compound **215b** was obtained from **213b** according to the general procedure F. The white solid was obtained through silica-gel column chromatography using 14% ethylacetate in hexanes.



Yield: 25%

Mp: 112 °C

IR (KBr) ν_{max} cm^{-1}: 2949, 1710, 1602, 1530, 1456, 1392, 1278, 1142, 1084, 789

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (d, 1H, *J* = 4.0 Hz), 8.14 (t, 2H, *J* = 12.0 Hz), 8.05 (s, 1H), 7.90 (s, 1H), 7.97 (t, 1H, 8.0 Hz), 7.56-7.48 (m, 2H), 7.37 (d, 1H, *J* = 8.0 Hz), 7.34 (d, 4H, *J* = 4.0 Hz), 7.17 (d, 2H, *J* = 4.0 Hz), 5.59 (s, 2H)

^{13}C NMR (100 MHz, $CDCl_3$): δ 161.6, 145.6, 142.4, 137.9, 136.6, 135.5, 134.6, 130.7, 128.9, 128.4, 127.7, 127.5, 126.2, 125.1, 122.2, 121.6, 121.2, 120.9, 119.7, 116.3, 109.1, 108.5, 101.3, 46.7

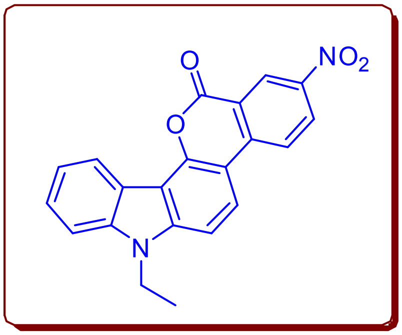
LC-MS (m/z): 376 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{26}H_{17}NO_2$: C, 83.18; H, 4.56; N, 3.73%

Found: C, 83.84; H, 4.72; N, 3.81%

7-Ethyl-2-nitroisochromeno[4,3-*c*]carbazol-13(7*H*)-one (214c):

The title compound **214c** was obtained from **213c** according to the general procedure F. The red solid was obtained through silica-gel column chromatography using 18% ethylacetate in hexanes.



Yield: 58%

Mp: 182 °C

IR (KBr) ν_{max} cm^{-1}: 2922, 2852, 1714, 1614, 1469, 1332, 1114, 1020, 866, 690

^{1}H NMR (400 MHz, CDCl$_3$): δ 9.28 (s, 1H), 9.09 (d, 1H, J = 8.0 Hz), 8.69-8.66 (dd, 1H, J_1 = 4.0 Hz, J_2 = 4.0 Hz), 8.45 (d, 1H, J = 8.0 Hz), 7.71 (d, 1H, J = 12.0 Hz), 7.60-7.53 (m, 3H), 7.30-7.26 (dd, 1H, J_1 = 4.0 Hz, J_2 = 2.0 Hz), 4.52 (q, 2H, J = 8.0 Hz), 1.52 (t, 3H, 4.0 Hz)

^{13}C NMR (100 MHz, CDCl$_3$): δ 159.8, 147.3, 146.7, 140.9, 140.1, 137.6, 127.5, 127.1, 126.9, 125.7, 122.8, 122.2, 121.3, 118.9, 117.1, 115.5, 113.5, 112.4, 109.7, 37.8, 13.9

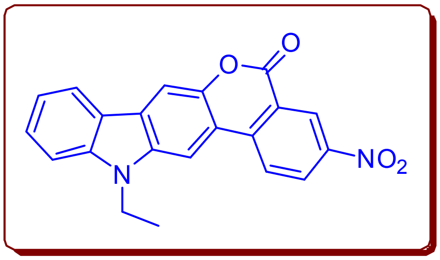
LC-MS (m/z): 359 (M+H)$^+$ positive mode

Anal. Calcd. for $C_{21}H_{14}N_2O_4$: C, 70.39; H, 3.94; N, 7.82%

Found: C, 70.28; H, 4.02; N, 7.75%

12-Ethyl-3-nitroisochromeno[4,3-*b*]carbazol-5(12*H*)-one (215c):

The title compound **215c** was obtained from **213c** according to the general procedure F. The red solid was obtained through silica-gel column chromatography using 18% ethylacetate in hexanes.



Yield: 18%

Mp: 216 °C

IR (KBr) ν_{max} cm^{-1}: 3057, 2916, 1714, 1595, 1485, 1329, 1086,744

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.06 (d, 1H, J = 8.8 Hz), 8.96 (s, 1H), 8.84 (t, 1H, J = 8.0 Hz), 8.48 (d, 1H, J = 8.0 Hz), 8.13-8.07 (dd, 1H, J_1 = 0.8 Hz, J_2 = 0.4 Hz), 7.85 (d, 1H, J = 8.0 Hz), 7.67

(s, 1H), 7.64 (s, 1H), 7.31 (t, 1H, *J* = 8.0 Hz), 4.62 (q, 2H, *J* = 24.0 Hz), 1.41 (t, 3H, *J* = 8.0 Hz)

^{13}C NMR (100 MHz,DMSO-d_6): δ 160.0, 147.8, 143.5, 143.0, 140.6, 138.0, 137.0, 127.4, 126.7, 125.3, 122.8, 122.2, 121.1, 119.8, 119.3, 113.5, 110.1, 109.9, 108.5, 37.6, 14.1

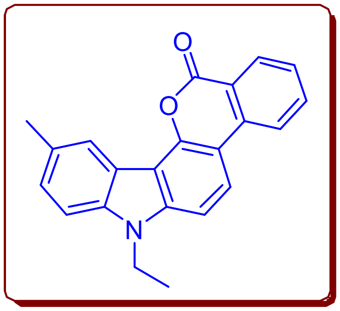
LC-MS (m/z): 359 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{21}H_{14}N_2O_4$: C, 70.39; H, 3.94; N, 7.82%

Found: C, 70.31; H, 3.98; N, 7.76%

7-Ethyl-10-methylisochromeno[4,3-*c*]carbazol-13(7*H*)-one (214d):

The title compound **214d** was obtained from **213d** according to the general procedure F. The white solid was obtained through silica-gel column chromatography using 14% ethylacetate in hexanes. Compound is recrystallized from 10% ethylacetate in hexanes.



Yield: 55%

Mp: 140 °C

IR (KBr) ν_{max} cm^{-1}: 2922, 2852, 1712, 1605, 1514, 1461, 1322, 1014, 1020, 766, 690

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.94 (d, 1H, *J* = 8.0 Hz), 8.48 (d, 1H, *J* = 8.0 Hz), 8.35 (s, 1H), 7.89 (t, 1H, *J* = 8.0 Hz), 7.63 (t, 1H, *J* = 8.0 Hz), 7.54-7.35 (m, 3H), 7.20-7.10 (dd, 1H, J_1 = 4.0 Hz, J_2 = 4.0 Hz), 4.46 (q, 2H, *J* = 8.0 Hz, N-C$\underline{H}_2$CH$_3$), 2.54 (s, 3H), 1.46 (t, 3H, *J* = 8.0 Hz, N-CH$_2$C$\underline{H}_3$)

^{13}C NMR (100 MHz, CDCl$_3$): δ 161.9, 146.2, 139.1, 137.9, 135.3, 133.4, 130.1, 128.5, 127.7, 126.2, 123.1, 122.1, 121.9, 116.8, 115.3, 114.1, 111.0, 108.9, 37.7, 21.7, 13.8

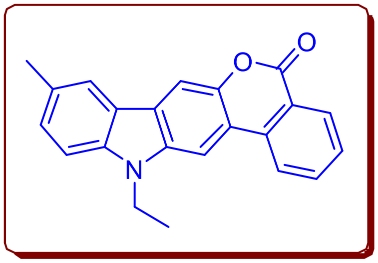
LC-MS (m/z): 328 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{22}H_{17}NO_2$: C, 80.71; H, 5.23; N, 4.28%

Found: C, 80.65; H, 5.18; N, 4.36%

12-Ethyl-9-methylisochromeno[4,3-*b*]carbazol-5(12*H*)-one (215d):

The title compound **215d** was obtained from **213d** according to the general procedure F. The white solid was obtained through silica-gel column chromatography using 14% ethylacetate in hexanes. Compound is recrystallized from 10% EtOAc in hexanes.



Yield: 24%

Mp: 122 ˚C

IR (KBr) ν_{max} cm^{-1}: 3057, 2962, 1714, 1595, 1485, 1261, 1086, 800, 694

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.42 (d, 1H, *J* = 8.0 Hz), 8.25 (d, 1H, *J* = 8.0 Hz), 7.96 (s, 1H), 7.90 (s, 1H), 7.88 (s, 1H), 7.84 (t, 1H, *J* = 8.0 Hz), 7.55 (t, 1H, *J* = 8.0 Hz), 7.35 (d, 1H, *J* = 8.0 Hz), 7.29 (t, 1H, *J* = 8.0 Hz), 4.41 (q, 2H, *J* = 8.0 Hz, N-C$\underline{H_2}$CH$_3$), 2.54 (s, 3H), 1.47 (t, 3H, *J* = 8.0 Hz)

^{13}C NMR (100 MHz, CDCl$_3$): δ 161.7, 145.1, 139.6, 134.5, 133.3, 130.6, 128.6, 128.5, 127.7, 126.2, 123.1, 122.8, 121.5, 121.0, 115.2, 110.9, 108.9, 108.2, 100.6, 37.5, 21.2, 13.9

LC-MS (m/z): 328 (M+H)$^+$ positive mode

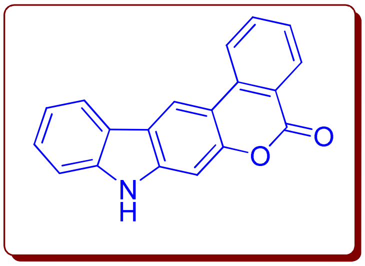
Anal. Calcd. for $C_{22}H_{17}NO_2$: C, 80.71; H, 5.23; N, 4.28%

Found: C, 80.62; H, 5.32; N, 4.21%

Isochromeno[3,4-*b*]carbazol-5(8*H*)-one (214e):

The title compound **214e** was obtained from **213e** according to the general procedure F. The white solid was obtained through basic alumina using 35% ethylacetate in hexanes.

Yield: 60%



Mp: 232 °C

IR (KBr) ν_{max} cm^{-1}: 3418, 1770, 1608, 1460, 1412, 1373, 1201, 1014, 750, 678

^{1}H NMR (400 MHz, DMSO-d_6): δ 11.55 (s, 1H, N<u>H</u>), 9.20 (s, 1H), 8.59 (d, 1H, *J* = 6.8 Hz), 8.25 (t, 2H, *J* = 10.4 Hz), 7.96 (t, 1H, *J* = 5.2 Hz), 7.59 (t, 1H, *J* = 6.8 Hz), 7.51 (d, 1H, *J* = 8.0 Hz), 7.43 (s, 1H), 7.30-7.13 (m, 2H)

^{13}C NMR (100 MHz, DMSO-d_6): δ 160.8, 141.8, 141.2, 140.0, 135.9, 134.2, 131.1, 129.7, 128.8, 125.1, 123.0, 121.2, 120.8, 120.1, 119.3, 112.5, 109.5, 108.7

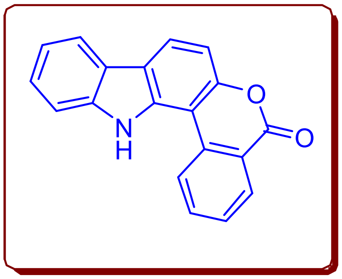
LC-MS (m/z): 284 (M-H) negative mode

Anal. Calcd. for $C_{19}H_{11}NO_2$: C, 79.99; H, 3.89; N, 4.91%

Found: C, 79.86; H, 3.94; N, 4.85%

Isochromeno[4,3-*a*]carbazol-5(13*H*)-one (215e):

The title compound **215e** was obtained from **213e** according to the general procedure F. The white solid was obtained through basic alumina using 35% ethylacetate in hexanes.



Yield: 20%

Mp: 182 °C

IR (KBr) ν_{max} cm^{-1}: 3424, 2920, 1762, 1638, 1501, 1492, 1358, 1019, 823, 725

^{1}H NMR (400 MHz, DMSO-d_6): δ 11.7 (s, 1H), 8.79 (d, 1H, *J* = 8.0 Hz), 8.41-8.39 (dd, 1H, J_1 = 1.2 Hz, J_2 = 1.2 Hz), 8.19 (d, 1H, *J* = 7.6 Hz), 8.10 (t, 1H, *J* = 6.8 Hz), 7.91 (d, 1H, *J* = 8.0 Hz), 7.84 (d, 1H, *J* = 8.4 Hz), 7.75 (d,1H, *J* = 16.0 Hz), 7.25-7.21 (m, 1H), 7.08-7.04 (ddd, 1H, J_1 = 0.8 Hz, J_2 = 0.8 Hz, J_3 = 1.2 Hz), 6.81 (d, 1H, *J* = 2.0 Hz)

^{13}C NMR (100 MHz, DMSO-d_6): δ 156.8, 150.5, 141.2, 140.0, 135.9, 133.3, 130.6, 129.0, 126.0, 124.1, 123.4, 122.3, 121.1, 120.5, 118.7, 112.5, 110.8, 103.8, 96.7

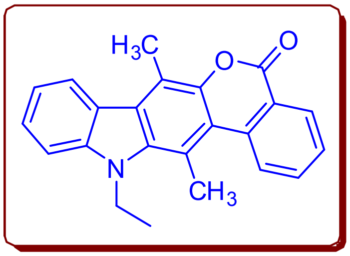
LC-MS (m/z): 286 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{19}H_{11}NO_2$: C, 79.99; H, 3.89; N, 4.91%

Found: C, 79.85; H, 3.84; N, 5.07%

12-Ethyl-7,13-dimethylisochromeno[4,3-*b*]carbazol-5(12*H*)-one (215f):

The title compound **215f** was obtained from **213f** according to the general procedure F. The white solid was obtained through silica-gel column chromatography using 14% ethylacetate in hexanes. Yellow solid Compound is recrystallized from 14% ethylacetate in hexanes.



Yield: 75%

Mp: 159 °C

IR (KBr) ν_{max} cm^{-1}: 2978, 2916, 1712, 1599, 1562, 1448, 1269, 1101, 744, 692.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.49 (d, 1H, *J* = 8.0 Hz), 8.29 (d, 1H, *J* = 8.0 Hz), 8.22 (d, 1H, *J* = 8.0 Hz), 7.81 (t, 1H, *J* = 8.0 Hz), 7.59-7.48 (m, 3H), 7.29 (d, 1H, *J* = 4.0 Hz), 4.60 (q, 2H, *J* = 8.0 Hz, N-C$\underline{H}_2$CH$_3$), 3.15 (s, 3H), 3.0 (s, 3H), 1.46 (t, 3H, *J* = 8.0 Hz, N-CH$_2$C$\underline{H}_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ 161.9, 143.9, 138.9, 136.4, 134.4, 133.2, 130.3, 127.7, 127.4, 126.5, 124.2, 124.1, 123.4, 122.3, 119.6, 117.9, 117.1, 114.7, 109.5, 41.1, 20.7, 14.9, 12.7.

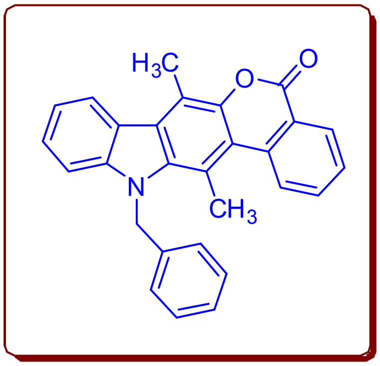
LC-MS (m/z): 342 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{23}H_{19}NO_2$: C, 80.92; H, 5.61; N, 4.10%

Found: C, 80.85; H, 5.68; N, 4.21%

12-Benzyl-7,13-dimethylisochromeno[4,3-*b*]carbazol-5(12*H*)-one (215g):

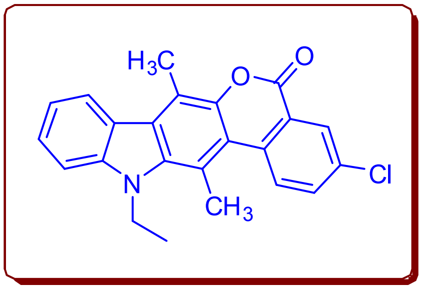
The title compound **215g** was obtained from **213g** according to the general procedure F. The white solid was obtained through silica-gel column chromatography using 15% ethylacetate in hexanes.



Yield:	82%
Mp:	177 °C
IR (KBr) v_{max} cm^{-1}:	3018, 2918, 1724, 1602, 1564, 1494, 1460, 1311, 1242, 1155, 1126, 1026, 987, 746.
^{1}H NMR (400 MHz, CDCl$_3$):	δ 8.47-8.45 (dd, 1H, J_1 = 0.8 Hz, J_2 = 1.2 Hz), 8.32 (d, 1H, J = 6.0 Hz), 8.1 (d, 1H, J = 6.0 Hz), 7.78-7.43 (m, 1H), 7.54 (t, 1H, J = 5.6 Hz), 7.47 (t, 1H, J = 5.6 Hz), 7.35 (q, 2H, J = 6.8 Hz), 7.29 (t, 3H, J = 5.2 Hz), 7.21 (d, 2H, J = 5.6 Hz), 5.71 (s, 2H), 3.02 (s, 3H), 2.97 (s, 3H).
^{13}C NMR (100 MHz, CDCl$_3$):	δ 161.8, 144.6, 144.1, 139.6, 138.3, 136.4, 133.2, 130.3, 128.9, 127.6, 127.5, 127.3, 126.8, 125.7, 125.4, 124.1, 123.8, 123.3, 122.3, 120.0, 118.1, 117.3, 114.9, 110.5, 109.7, 50.3, 20.7, 12.8.
LC-MS (m/z):	402 (M-H) negative mode
Anal. Calcd. for $C_{28}H_{21}NO_2$:	C, 83.35; H, 5.25; N, 3.47%
Found:	C, 83.28; H, 5.18; N, 3.41%

3-Chloro-12-ethyl-7,13-dimethylisochromeno[4,3-*b*]carbazol-5(12*H*)-one (215h):

The title compound **215h** was obtained from **213h** according to the general procedure F. The yellow solid was obtained through silica-gel column chromatography using 14% ethylacetate in hexanes.



Yield: 62%

Mp: 224-226 °C

IR (KBr) ν_{max} cm^{-1}: 3012, 1708, 1622, 1589, 1464, 1332, 1260, 1089, 742

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.46 (s, 1H), 8.29 (d, 1H, J = 8.0 Hz), 8.17 (d, 1H, J = 8.0 Hz), 7.77-7.74 (dd, 1H, J_1 = 2.4 Hz, J_2 = 4.0 Hz), 7.57-7.48 (m, 2H), 7.29 (t, 1H, J = 8.0 Hz), 4.59 (q, 2H, J = 4.0 Hz, N-C$\underline{H_2}$CH$_3$), 3.13 (s, 3H), 3.0 (s, 3H), 1.46 (t, 3H, J = 4.0 Hz, NCH$_2$C$\underline{H_3}$)

^{13}C NMR (100 MHz, CDCl$_3$): δ 160.0, 143.9, 142.3, 142.2, 137.9, 136.8, 135.8, 134.3, 132.5, 129.4, 126.4, 125.0, 124.0, 123.8, 123.2, 120.1, 119.3, 109.7, 40.4, 21.1, 16.6, 14.7

LC-MS (m/z): 376 (M+H)$^+$, 378 (M+2) positive mode

Anal. Calcd. for $C_{23}H_{18}ClNO_2$: C, 73.50; H, 4.83; N, 3.70%

Found: C, 73.25; H, 4.51; N, 3.69%

Table 8. Crystal data and structure refinement for 193.

Empirical formula	: $C_{42}H_{32}N_4O_2$	
Formula weight	: 624.72	
Temperature	: 298(2) K	
Wavelength	: 0.71073 Å	
Crystal system	: Triclinic	
Space group	: P-1	
Unit cell dimensions	: a = 9.0391(19) Å	α = 77.39(2)°.
	: b = 11.043(3) Å	β = 87.34(2)°.
	: c = 17.740(5) Å	γ = 88.207(18)°.
Volume	: 1725.7(7) Å^{3}	
Z	: 2	
Density (calculated)	: 1.202 Mg/m^{3}	
Absorption coefficient	: 0.075 mm^{-1}	
F(000)	: 656	
Crystal size	: 0.24 x 0.18 x 0.14 mm^{3}	
Theta range for data collection	: 3.20 to 18.84°.	
Index ranges	: -8<=h<=8, -10<=k<=10, -16<=l<=16	
Reflections collected	: 5846	
Independent reflections	: 2612 [R(int) = 0.0847]	
Completeness to theta = 18.84°	: 96.6 %	
Absorption correction	: Semi-empirical from equivalents	
Max. and min. transmission	: 0.9896 and 0.9822	
Refinement method	: Full-matrix least-squares on F^{2}	
Data / restraints / parameters	: 2612 / 0 / 435	
Goodness-of-fit on F^{2}	: 1.002	
Final R indices [I>2sigma(I)]	: R1 = 0.0701, wR2 = 0.1911	
R indices (all data)	: R1 = 0.1061, wR2 = 0.2087	
Largest diff. peak and hole	: 0.230 and -0.227 e.Å^{-3}	

Table 9. Crystal data and structure refinement for 194a.

Empirical formula : $C_{23}H_{20}N_2O$
Formula weight : 340.41
Temperature : 298(2) K
Wavelength : 0.71073 Å
Crystal system : Monoclinic
Space group : P2(1)/n
Unit cell dimensions : a = 9.1260(18) Å α = 90°.
: b = 8.2593(16) Å β = 96.462(3)°.
: c = 22.851(5) Å γ = 90°.
Volume : 1711.4(6) Å^3
Z : 4
Density (calculated) : 1.321 Mg/m^3
Absorption coefficient : 0.081 mm^{-1}
F(000) : 720
Crystal size : 0.54 x 0.40 x 0.12 mm^3
Theta range for data collection : 1.79 to 24.96°.
Index ranges : -10<=h<=10, -9<=k<=9, -27<=l<=27
Reflections collected : 15752
Independent reflections : 2999 [R(int) = 0.0302]
Completeness to theta = 24.96° : 100.0 %
Absorption correction : Empirical
Max. and min. transmission : 0.9903 and 0.9573
Refinement method : Full-matrix least-squares on F^2
Data / restraints / parameters : 2999 / 0 / 237
Goodness-of-fit on F^2 : 1.101
Final R indices [I>2sigma(I)] : R1 = 0.0445, wR2 = 0.1124
R indices (all data) : R1 = 0.0487, wR2 = 0.1155
Largest diff. peak and hole : 0.161 and -0.233 e.Å^{-3}

Table 10. Crystal data and structure refinement for 195b.

Empirical formula	: $C_{23}H_{19}N_3O_3$	
Formula weight	: 385.41	
Temperature	: 298(2) K	
Wavelength	: 0.71073 Å	
Crystal system	: Monoclinic	
Space group	: C2/c	
Unit cell dimensions	: a = 25.978(15) Å	α = 90°.
	: b = 11.634(2) Å	β = 121.89(8)°.
	: c = 13.874(8) Å	γ = 90°.
Volume	: 3560(3) $Å^3$	
Z	: 8	
Density (calculated)	: 1.438 Mg/m^3	
Absorption coefficient	: 0.097 mm^{-1}	
F(000)	: 1616	
Crystal size	: 0.32 x 0.14 x 0.08 mm^3	
Theta range for data collection	: 3.28 to 17.99°.	
Index ranges	: -22<=h<=21, -10<=k<=8, -11<=l<=12	
Reflections collected	: 2633	
Independent reflections	: 1148 [R(int) = 0.0514]	
Completeness to theta = 17.99°	: 93.6 %	
Absorption correction	: Semi-empirical from equivalents	
Max. and min. transmission	: 0.9923 and 0.9696	
Refinement method	: Full-matrix least-squares on F^2	
Data / restraints / parameters	: 1148 / 0 / 264	
Goodness-of-fit on F^2	: 1.056	
Final R indices [I>2sigma(I)]	: R1 = 0.0425, wR2 = 0.1048	
R indices (all data)	: R1 = 0.0513, wR2 = 0.1092	
Largest diff. peak and hole	: 0.161 and -0.230 $e.Å^{-3}$	

Table 11. Crystal data and structure refinement for 194c.

Empirical formula	: $C_{23}H_{19}ClN_2O$	
Formula weight	: 374.85	
Temperature	: 298(2) K	
Wavelength	: 0.71073 Å	
Crystal system	: Monoclinic	
Space group	: P2(1)	
Unit cell dimensions	: a = 5.0196(7) Å	α = 90°.
	: b = 17.051(2) Å	β = 90.965(2)°.
	: c = 10.5546(15) Å	γ = 90°.
Volume	: 903.2(2) $Å^3$	
Z	: 2	
Density (calculated)	: 1.378 Mg/m^3	
Absorption coefficient	: 0.227 mm^{-1}	
F(000)	: 392	
Crystal size	: 0.22 x 0.18 x 0.16 mm^3	
Theta range for data collection	: 1.93 to 26.00°.	
Index ranges	: -6<=h<=6, -20<=k<=21, -13<=l<=12	
Reflections collected	: 9176	
Independent reflections	: 3525 [R(int) = 0.0286]	
Completeness to theta = 26.00°	: 99.4 %	
Absorption correction	: Empirical	
Max. and min. transmission	: 0.9646 and 0.9517	
Refinement method	: Full-matrix least-squares on F^2	
Data / restraints / parameters	: 3525 / 1 / 246	
Goodness-of-fit on F^2	: 1.086	
Final R indices [I>2sigma(I)]	: R1 = 0.0438, wR2 = 0.1047	
R indices (all data)	: R1 = 0.0463, wR2 = 0.1060	
Absolute structure parameter	: 0.08(6)	
Largest diff. peak and hole	: 0.253 and -0.183 e.$Å^{-3}$	

Table 12. Crystal data and structure refinement for 195c.

Identification code	: global	
Empirical formula	: $C_{23}H_{19}ClN_2O$	
Formula weight	: 374.85	
Temperature	: 298(2) K	
Wavelength	: 0.71073 Å	
Crystal system	: Monoclinic	
Space group	: C2/c	
Unit cell dimensions	: a = 25.965(2) Å	α = 90°.
	: b = 11.4538(10) Å	β = 121.6480(10)°.
	: c = 13.9605(13) Å	γ = 90°.
Volume	: 3534.4(5) Å^3	
Z	: 8	
Density (calculated)	: 1.409 Mg/m^3	
Absorption coefficient	: 0.232 mm^{-1}	
F(000)	: 1568	
Crystal size	: 0.24 x 0.22 x 0.16 mm^3	
Theta range for data collection	: 1.84 to 25.99°.	
Index ranges	: -31<=h<=32, -14<=k<=14, -17<=l<=17	
Reflections collected	: 17896	
Independent reflections	: 3470 [R(int) = 0.0319]	
Completeness to theta = 25.99°	: 99.7 %	
Absorption correction	: Empirical	
Max. and min. transmission	: 0.9638 and 0.9464	
Refinement method	: Full-matrix least-squares on F^2	
Data / restraints / parameters	: 3470 / 0 / 246	
Goodness-of-fit on F^2	: 1.103	
Final R indices [I>2sigma(I)]	: R1 = 0.0529, wR2 = 0.1272	
R indices (all data)	: R1 = 0.0632, wR2 = 0.1335	
Largest diff. peak and hole	: 0.222 and -0.250 e.Å^{-3}	

Table 13. Crystal data and structure refinement for 214b.

Empirical formula	$C_{26}H_{15}NO_2$	
Formula weight	373.39	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 8.2147(7) Å	α = 88.285(6)°.
	b = 9.9766(7) Å	β = 87.066(7)°.
	c = 12.2199(11) Å	γ = 67.350(7)°.
Volume	922.97(13) Å^3	
Z	2	
Density (calculated)	1.344 Mg/m^3	
Absorption coefficient	0.085 mm^{-1}	
F(000)	388	
Crystal size	0.42 x 0.26 x 0.12 mm^3	
Theta range for data collection	2.76 to 24.71°.	
Index ranges	-9<=h<=9, -9<=k<=11, -12<=l<=14	
Reflections collected	5808	
Independent reflections	3139 [R(int) = 0.0224]	
Completeness to theta = 24.71°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9899 and 0.9651	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3139 / 0 / 262	
Goodness-of-fit on F^2	1.030	
Final R indices [I>2sigma(I)]	R1 = 0.0552, wR2 = 0.1440	
R indices (all data)	R1 = 0.0781, wR2 = 0.1637	
Largest diff. peak and hole	0.537 and -0.242 e.Å^{-3}	

Table 14. Crystal data and structure refinement for 214d.

Empirical formula	: $C_{22}H_{17}NO_2$	
Formula weight	: 327.37	
Temperature	: 298(2) K	
Wavelength	: 0.71073 Å	
Crystal system	: Orthorhombic	
Space group	: P n a 21	
Unit cell dimensions	: a = 7.5580(5) Å	α = 90°.
	: b = 19.9905(8) Å	β = 90°.
	: c = 10.6520(6) Å	γ = 90°.
Volume	: 1609.39(15) Å^3	
Z	: 4	
Density (calculated)	: 1.351 Mg/m^3	
Absorption coefficient	: 0.087 mm^{-1}	
F(000)	: 688	
Crystal size	: 0.22 x 0.20 x 0.16 mm^3	
Theta range for data collection	: 2.88 to 26.37°.	
Index ranges	: -9<=h<=6, -23<=k<=24, -11<=l<=13	
Reflections collected	: 4424	
Independent reflections	: 2577 [R(int) = 0.0238]	
Completeness to theta = 26.37°	: 99.9 %	
Absorption correction	: Semi-empirical from equivalents	
Max. and min. transmission	: 0.9863 and 0.9812	
Refinement method	: Full-matrix least-squares on F^2	
Data / restraints / parameters	: 2577 / 1 / 228	
Goodness-of-fit on F^2	: 1.033	
Final R indices [I>2sigma(I)]	: R1 = 0.0435, wR2 = 0.0845	
R indices (all data)	: R1 = 0.0587, wR2 = 0.0931	
Absolute structure parameter	: 0.8(15)	
Largest diff. peak and hole	: 0.159 and -0.219 e.Å^{-3}	

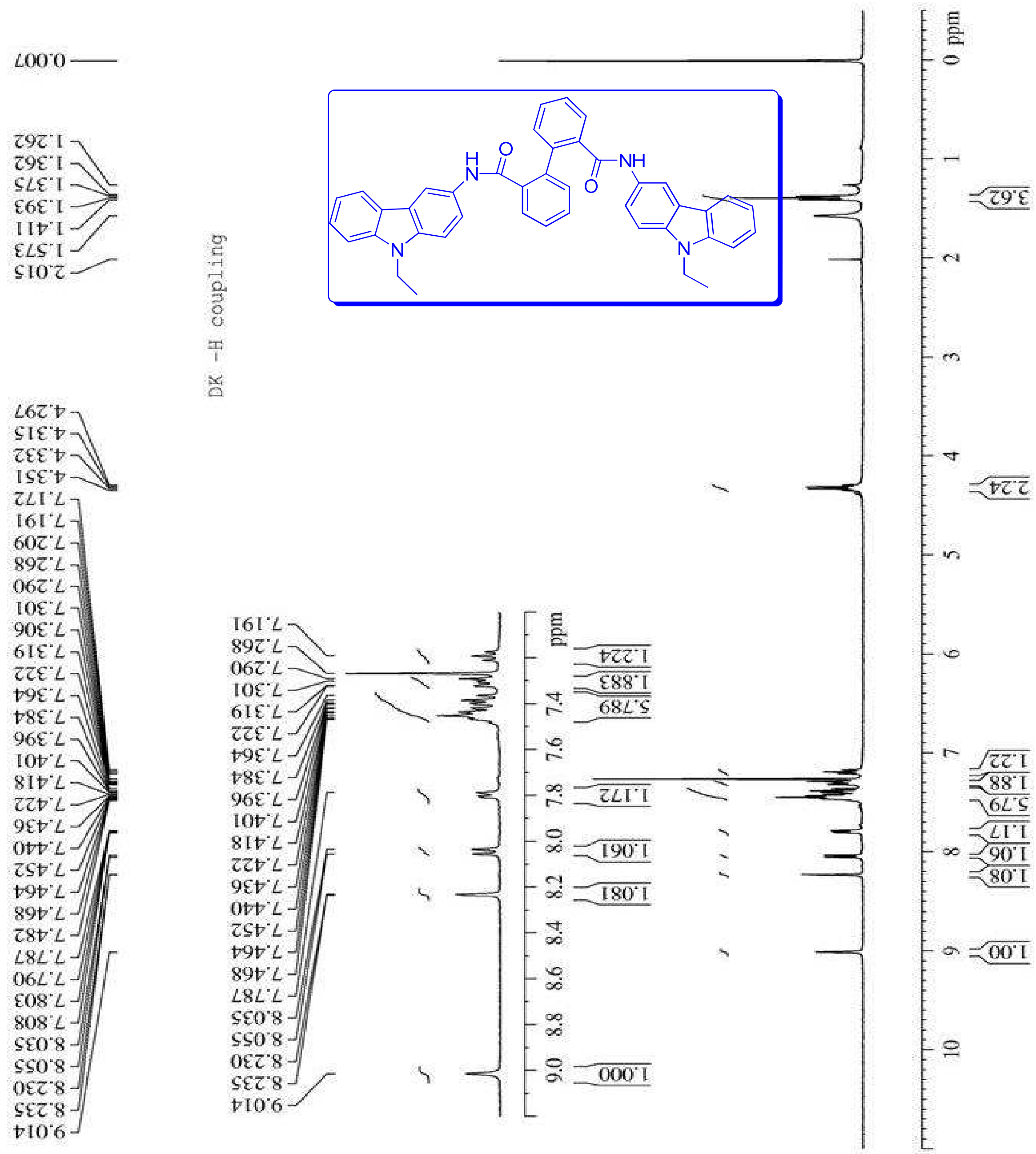
Table 15. Crystal data and structure refinement for 215d.

Empirical formula	: $C_{22}H_{17}NO_2$	
Formula weight	: 327.37	
Temperature	: 298(2) K	
Wavelength	: 0.71073 Å	
Crystal system	: Monoclinic	
Space group	: P 21/c	
Unit cell dimensions	: a = 8.5988(6) Å	α = 90°.
	: b = 15.5481(14) Å	β = 122.242(6)°.
	: c = 14.6529(12) Å	γ = 90°.
Volume	: 1656.9(2) $Å^3$	
Z	: 4	
Density (calculated)	: 1.312 Mg/m^3	
Absorption coefficient	: 0.084 mm^{-1}	
F(000)	: 688	
Crystal size	: 0.46 x 0.18 x 0.16 mm^3	
Theta range for data collection	: 2.97 to 24.71°.	
Index ranges	: -10<=h<=10, -16<=k<=18, -17<=l<=17	
Reflections collected	: 6291	
Independent reflections	: 2830 [R(int) = 0.0311]	
Completeness to theta = 24.71°	: 99.8 %	
Absorption correction	: Semi-empirical from equivalents	
Max. and min. transmission	: 0.9867 and 0.9624	
Refinement method	: Full-matrix least-squares on F^2	
Data / restraints / parameters	: 2830 / 0 / 228	
Goodness-of-fit on F^2	: 0.978	
Final R indices [I>2sigma(I)]	: R1 = 0.0528, wR2 = 0.1051	
R indices (all data)	: R1 = 0.0965, wR2 = 0.1304	
Largest diff. peak and hole	: 0.147 and -0.215 e.$Å^{-3}$	

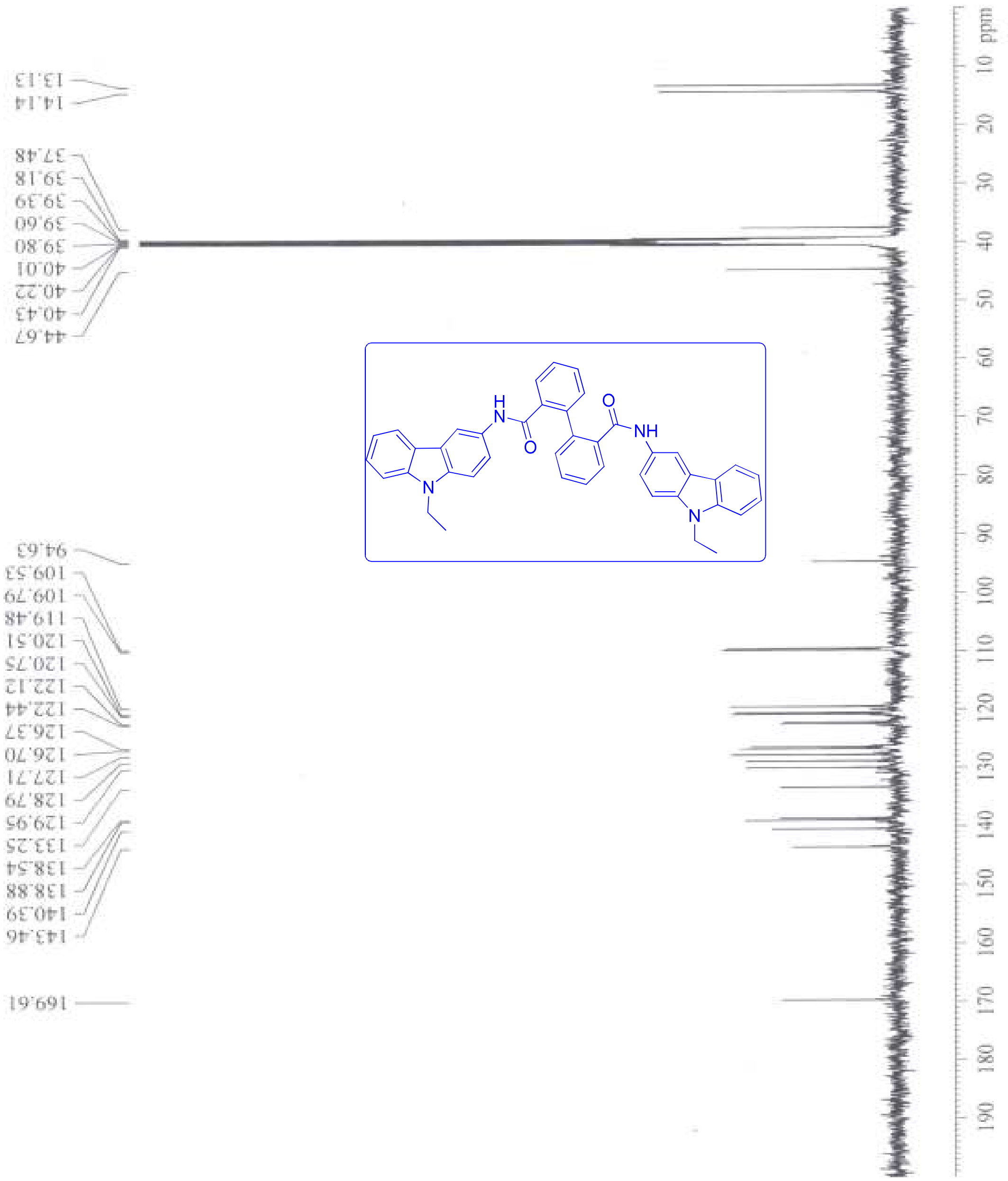
Table 16. Crystal data and structure refinement for 215f.

Empirical formula	: $C_{23}H_{19}NO_2$	
Formula weight	: 341.39	
Temperature	: 298(2) K	
Wavelength	: 0.71073 Å	
Crystal system	: Triclinic	
Space group	: P -1	
Unit cell dimensions	: a = 7.5037(6) Å	α = 100.156(10)°.
	: b = 9.1436(12) Å	β = 101.632(8)°.
	: c = 12.7349(13) Å	γ = 92.456(9)°.
Volume	: 839.61(15) $Å^3$	
Z	: 2	
Density (calculated)	: 1.350 Mg/m^3	
Absorption coefficient	: 0.086 mm^{-1}	
F(000)	: 360	
Crystal size	: 0.44 x 0.22 x 0.12 mm^3	
Theta range for data collection	: 2.78 to 24.71°.	
Index ranges	: -8<=h<=8, -8<=k<=10, -14<=l<=14	
Reflections collected	: 5172	
Independent reflections	: 2853 [R(int) = 0.0197]	
Completeness to theta = 24.71°	: 99.9 %	
Absorption correction	: Semi-empirical from equivalents	
Max. and min. transmission	: 0.9898 and 0.9631	
Refinement method	: Full-matrix least-squares on F^2	
Data / restraints / parameters	: 2853 / 0 / 238	
Goodness-of-fit on F^2	: 0.859	
Final R indices [I>2sigma(I)]	: R1 = 0.0716, wR2 = 0.2458	
R indices (all data)	: R1 = 0.0928, wR2 = 0.2696	
Largest diff. peak and hole	: 0.213 and -0.231 e.$Å^{-3}$	

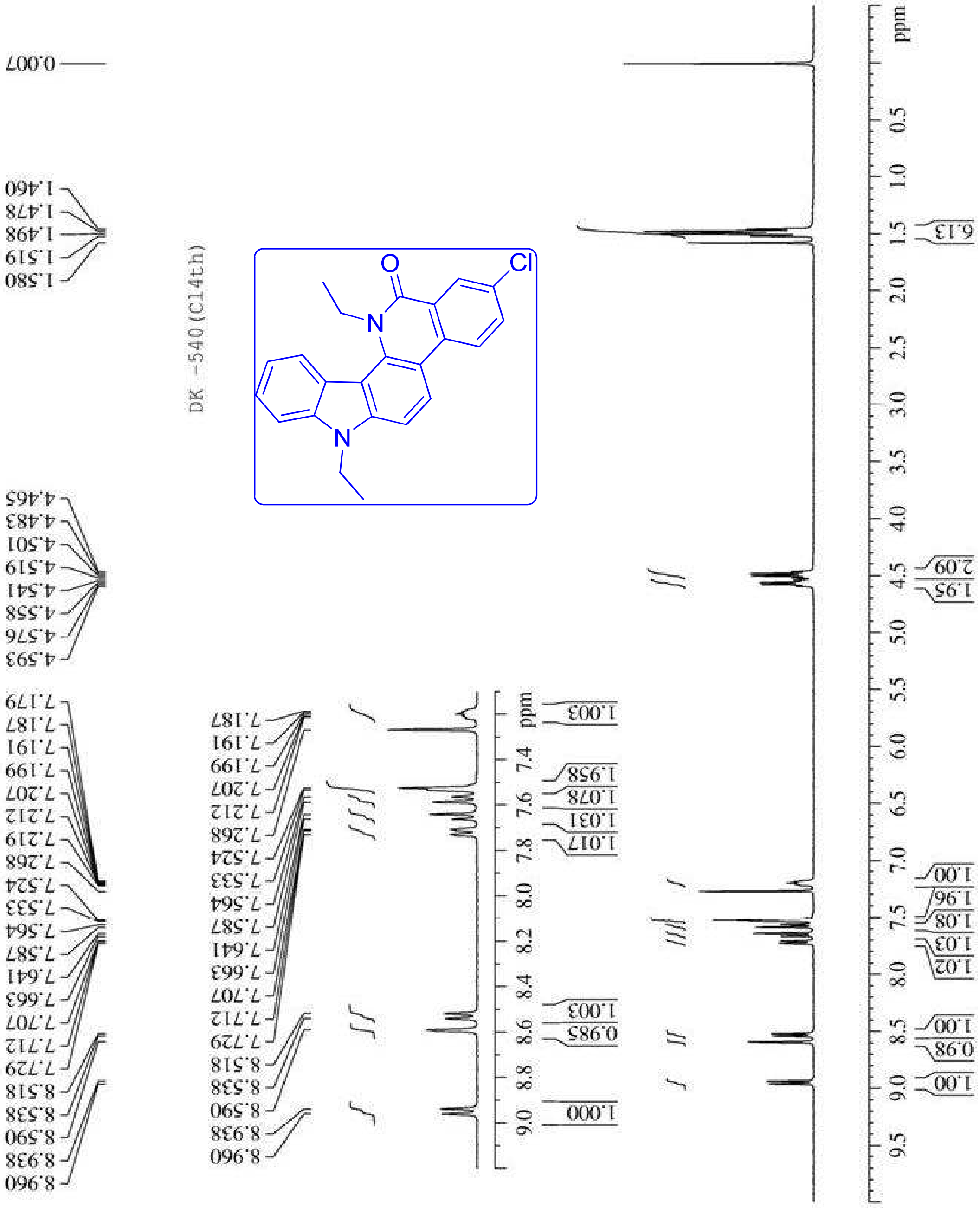
Spectrum 1. ^{1}H NMR of 193



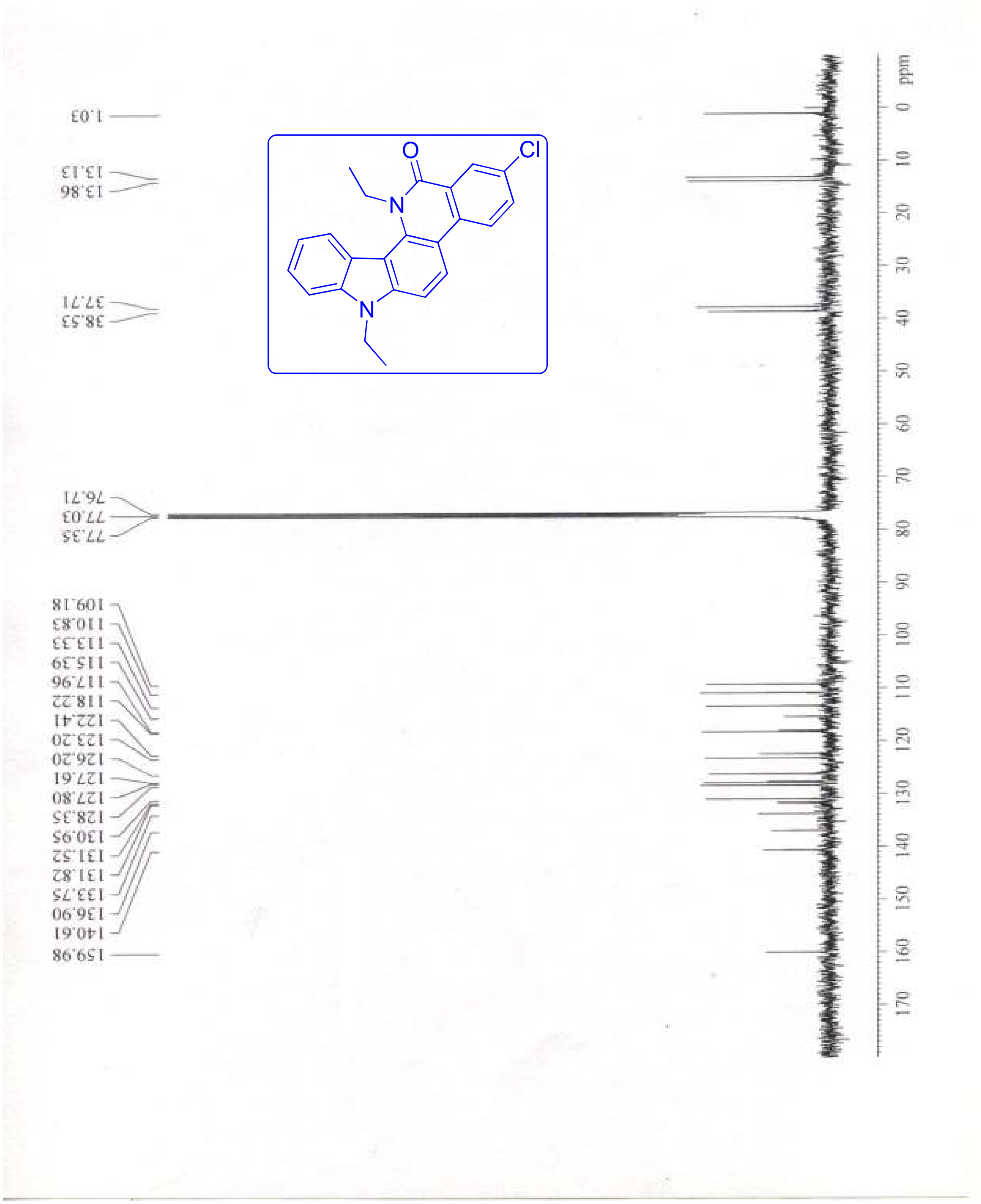
Spectrum 2. ^{13}C NMR of 193



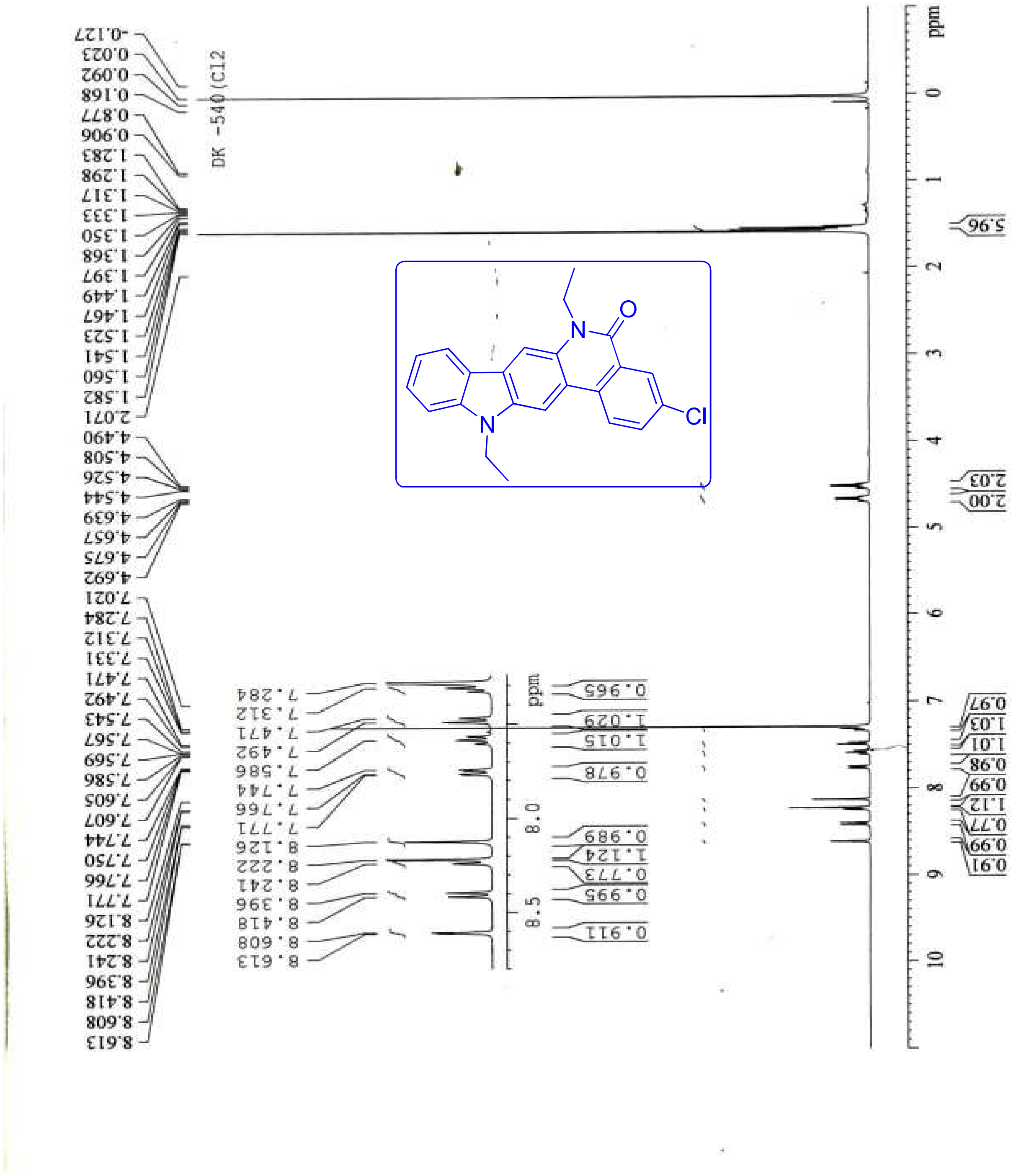
Spectrum 3. ^{1}H NMR of 194e



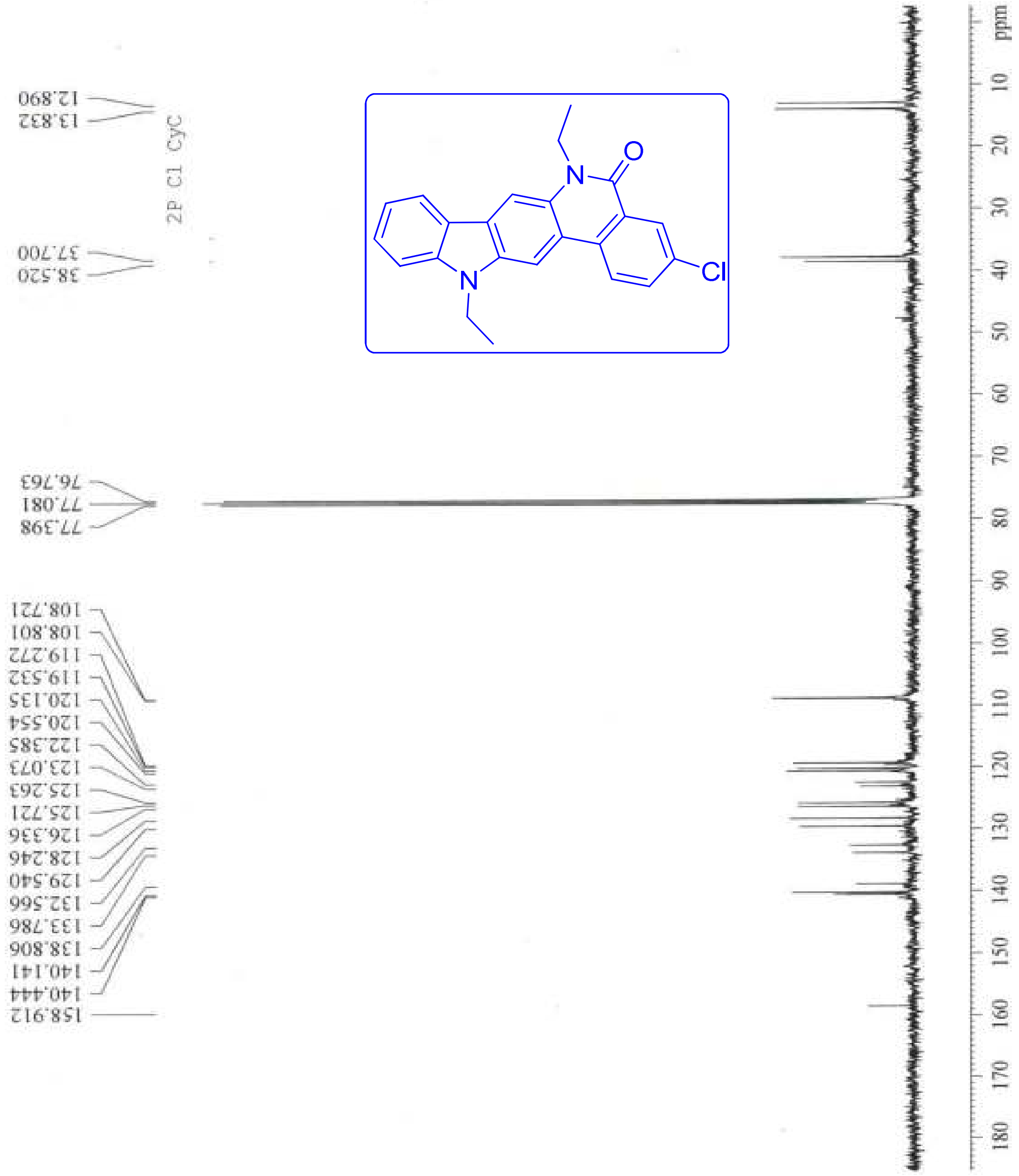
Spectrum 4. ^{13}C NMR of 194e



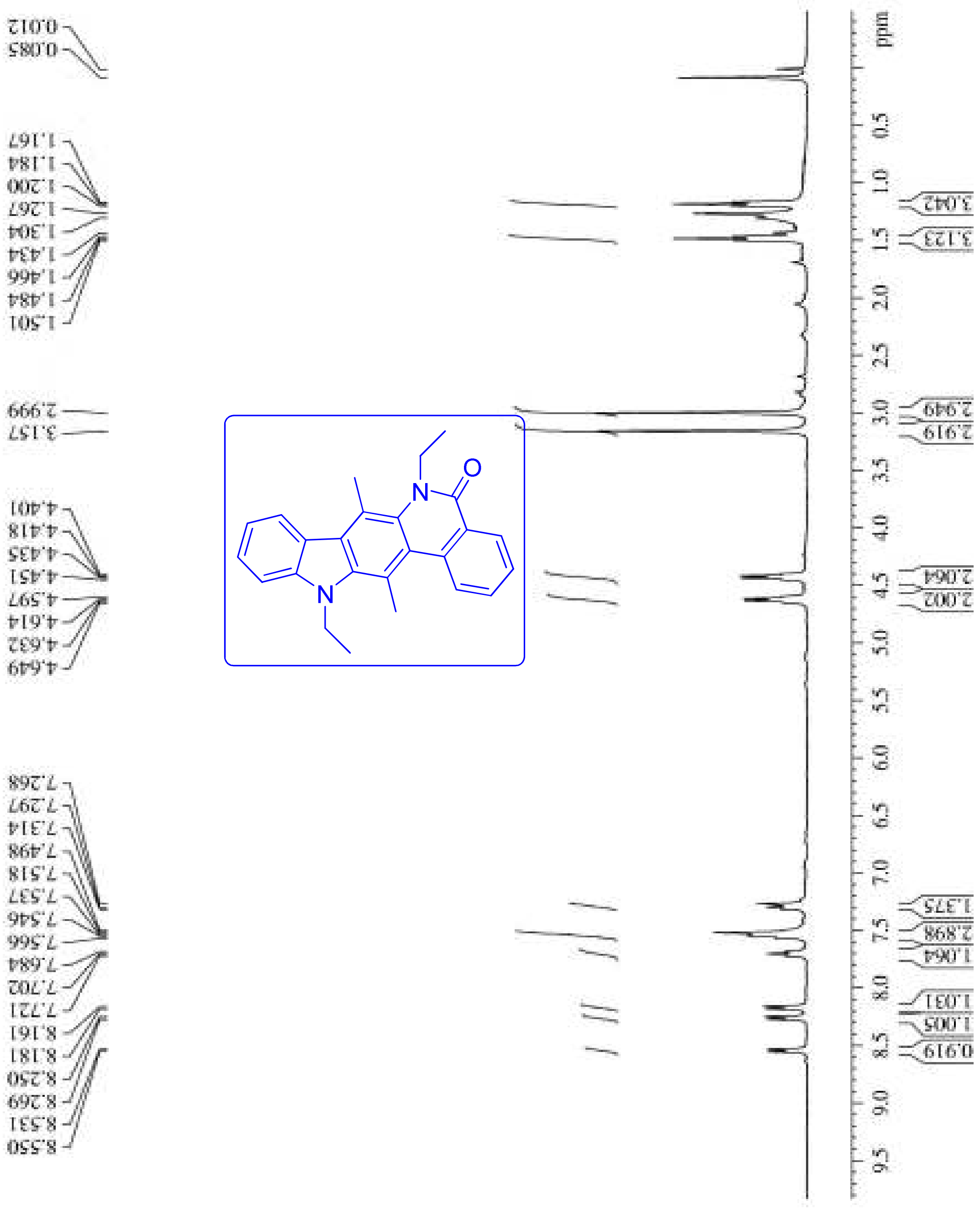
Spectrum 5. ^{1}H NMR of 195e



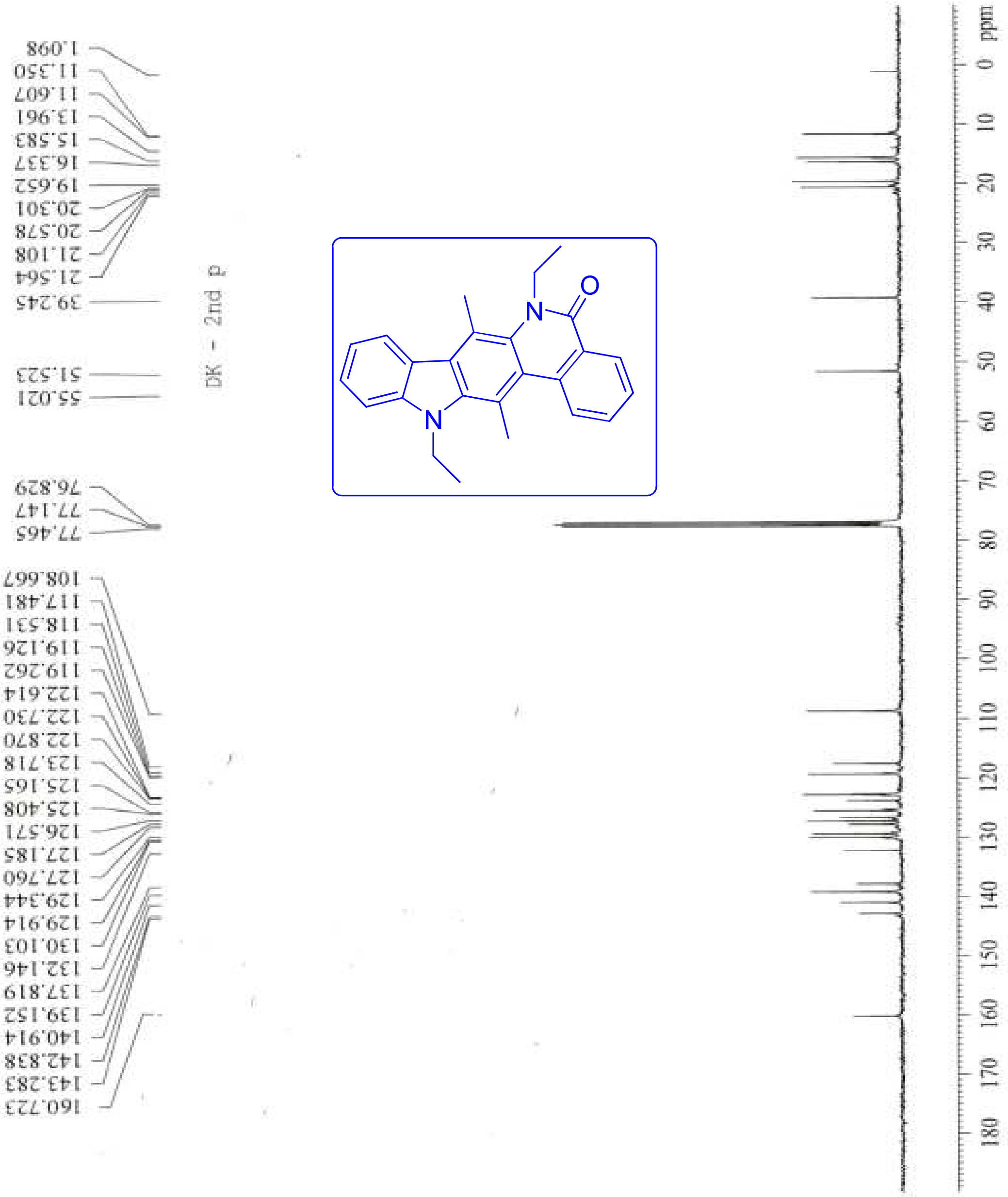
Spectrum 6. ^{13}C NMR of 195e



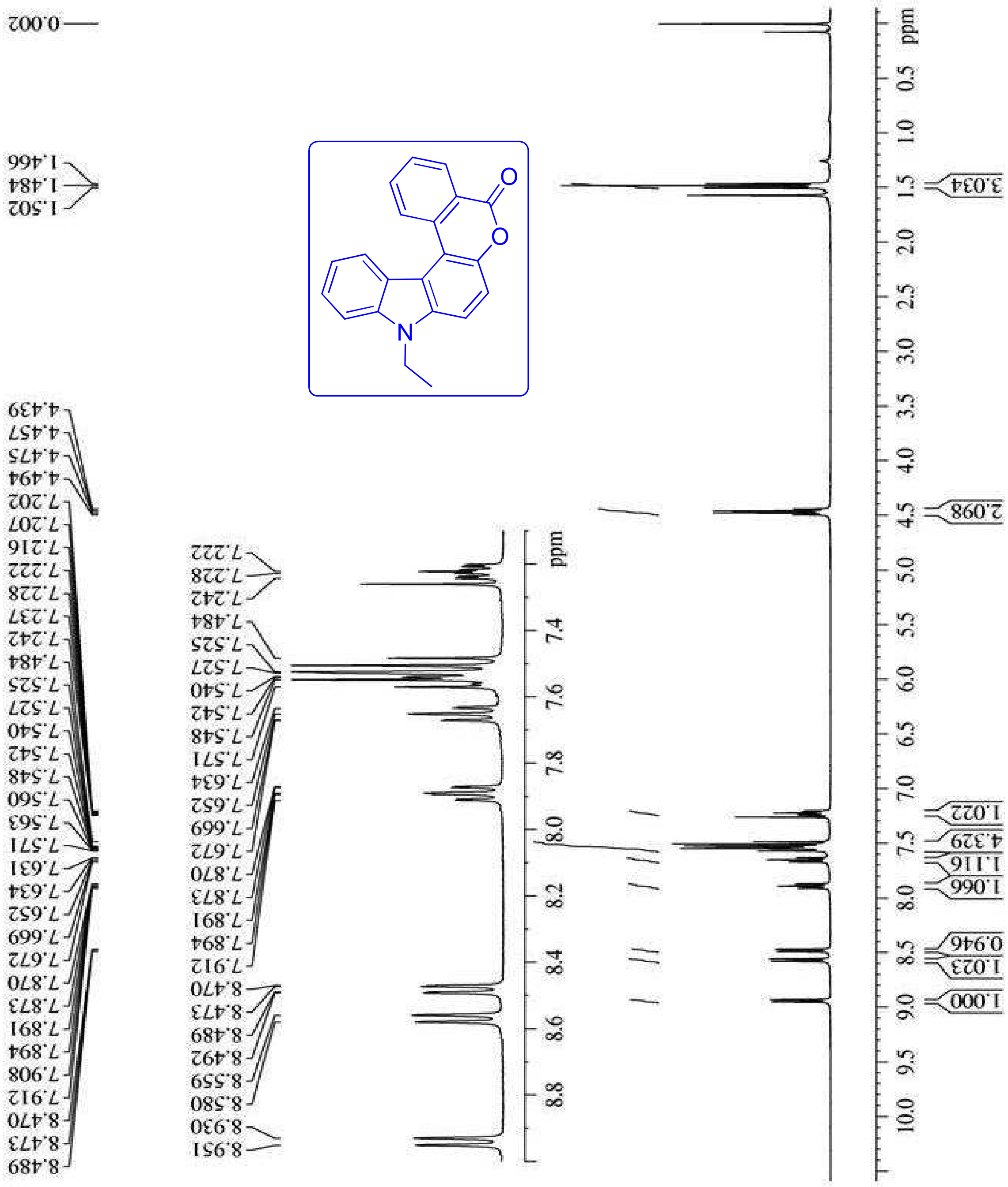
Spectrum 7. ^{1}H NMR of 198a



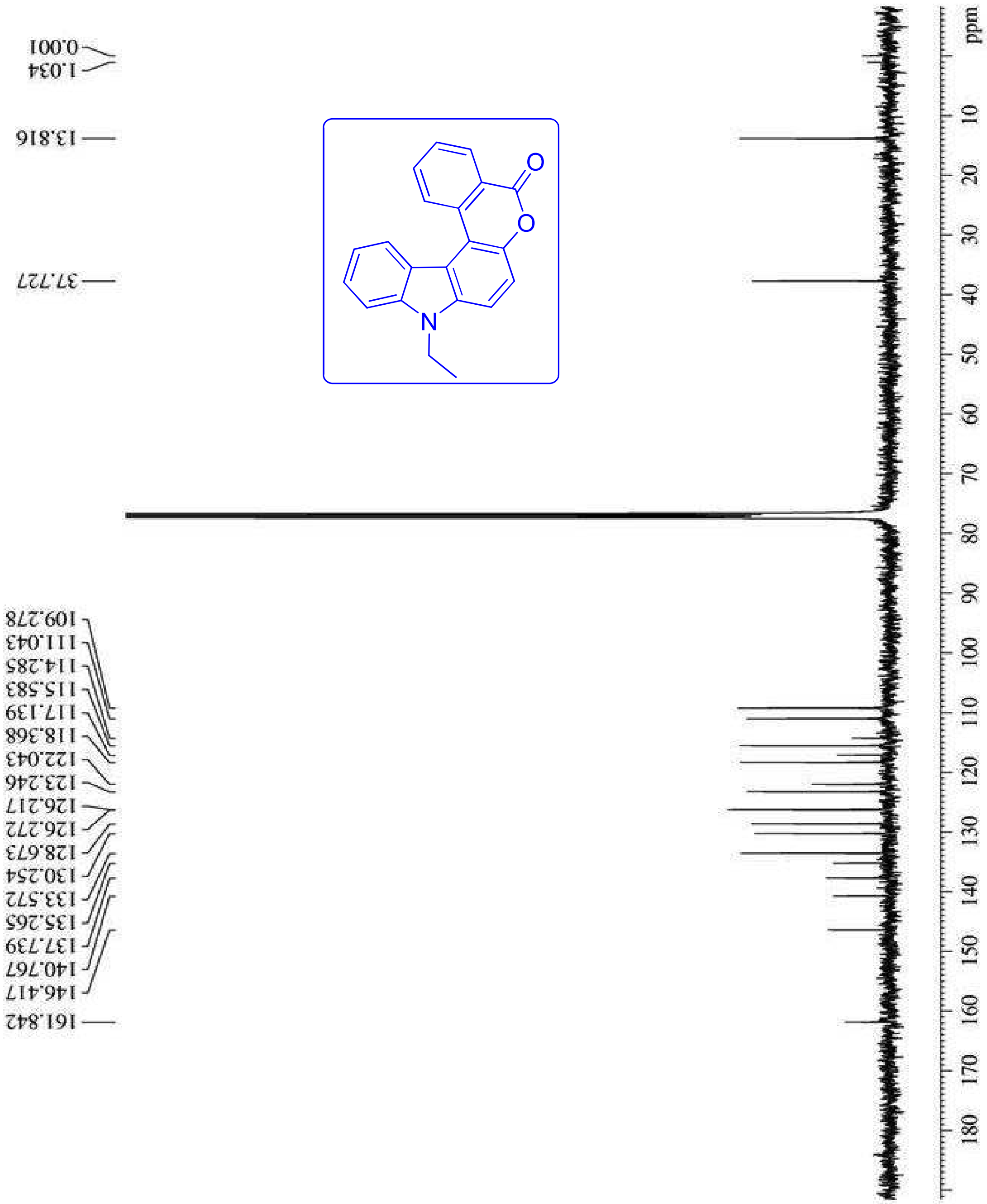
Spectrum 8. ^{13}C NMR of 198a



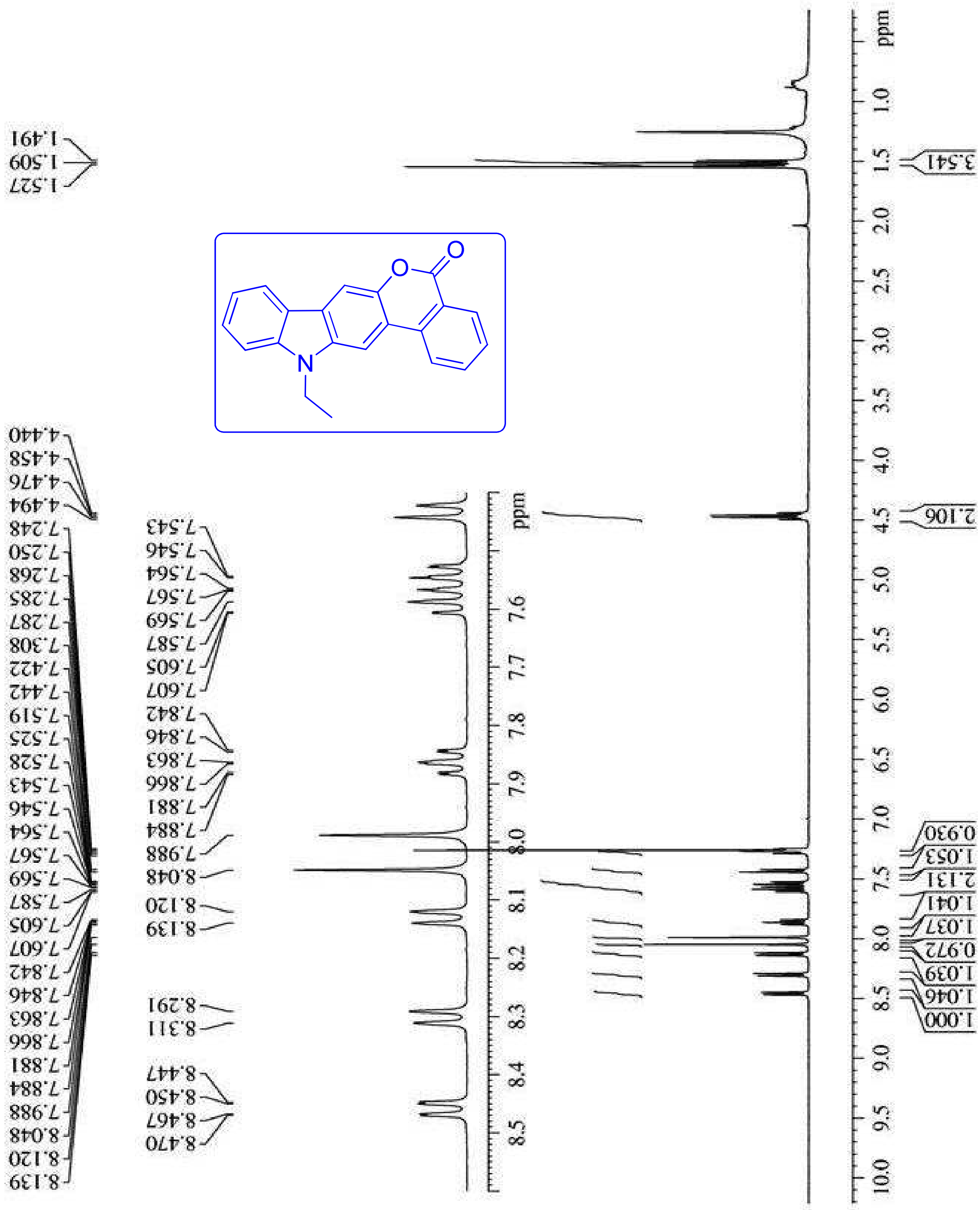
Spectrum 9. ^{1}H NMR of 214a



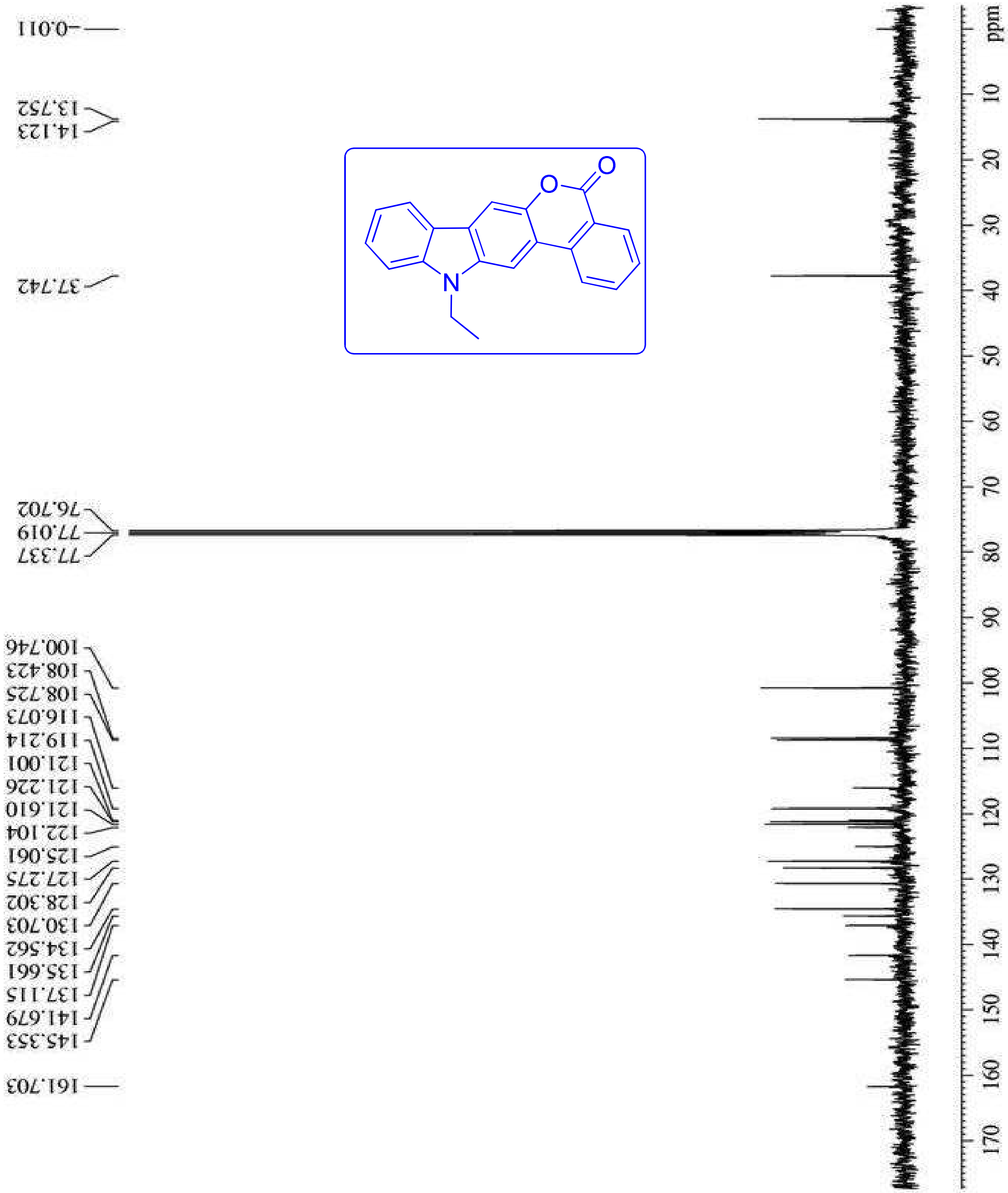
Spectrum 10. ^{13}C NMR of 214a



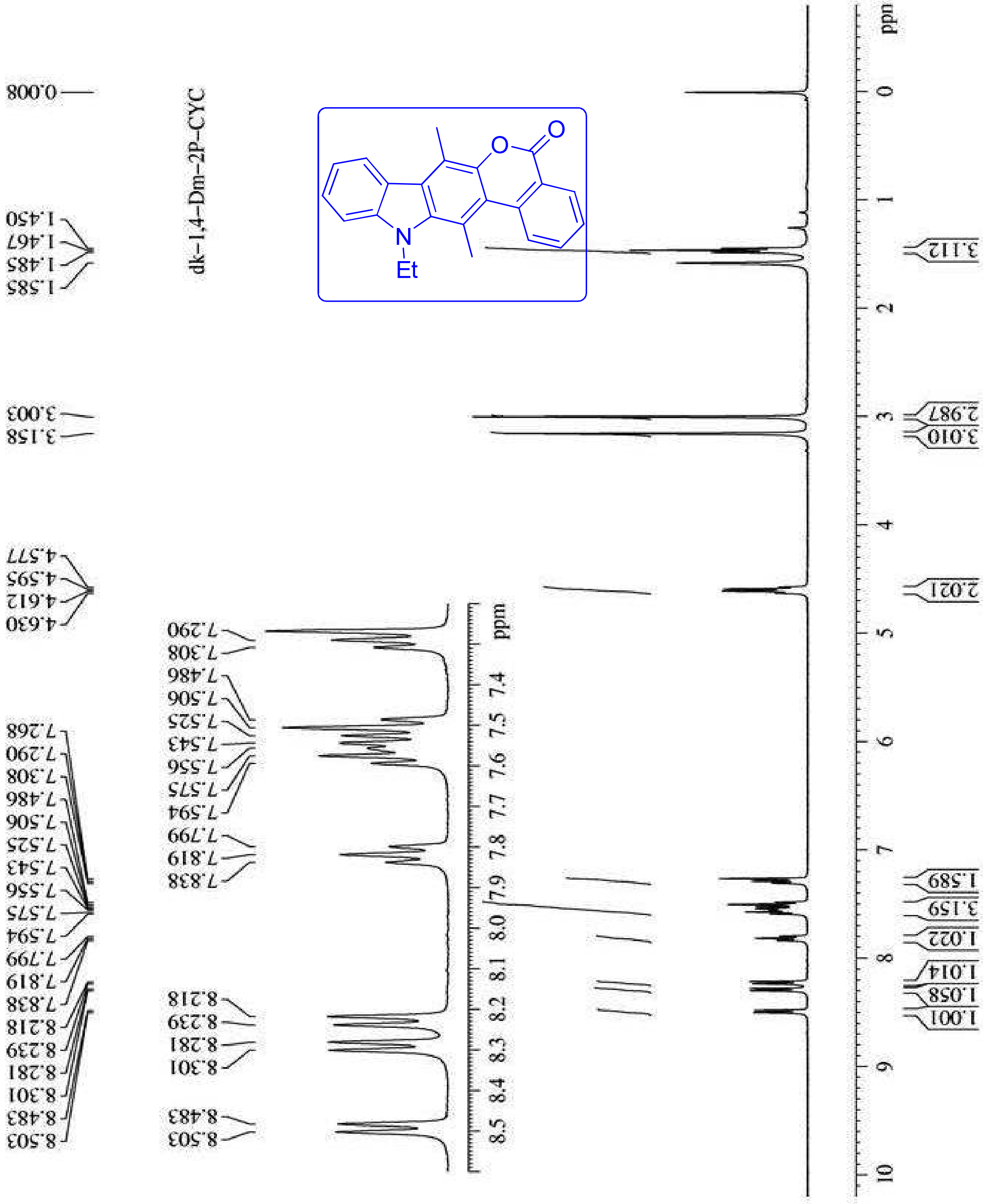
Spectrum 11. ^{1}H NMR of 215a



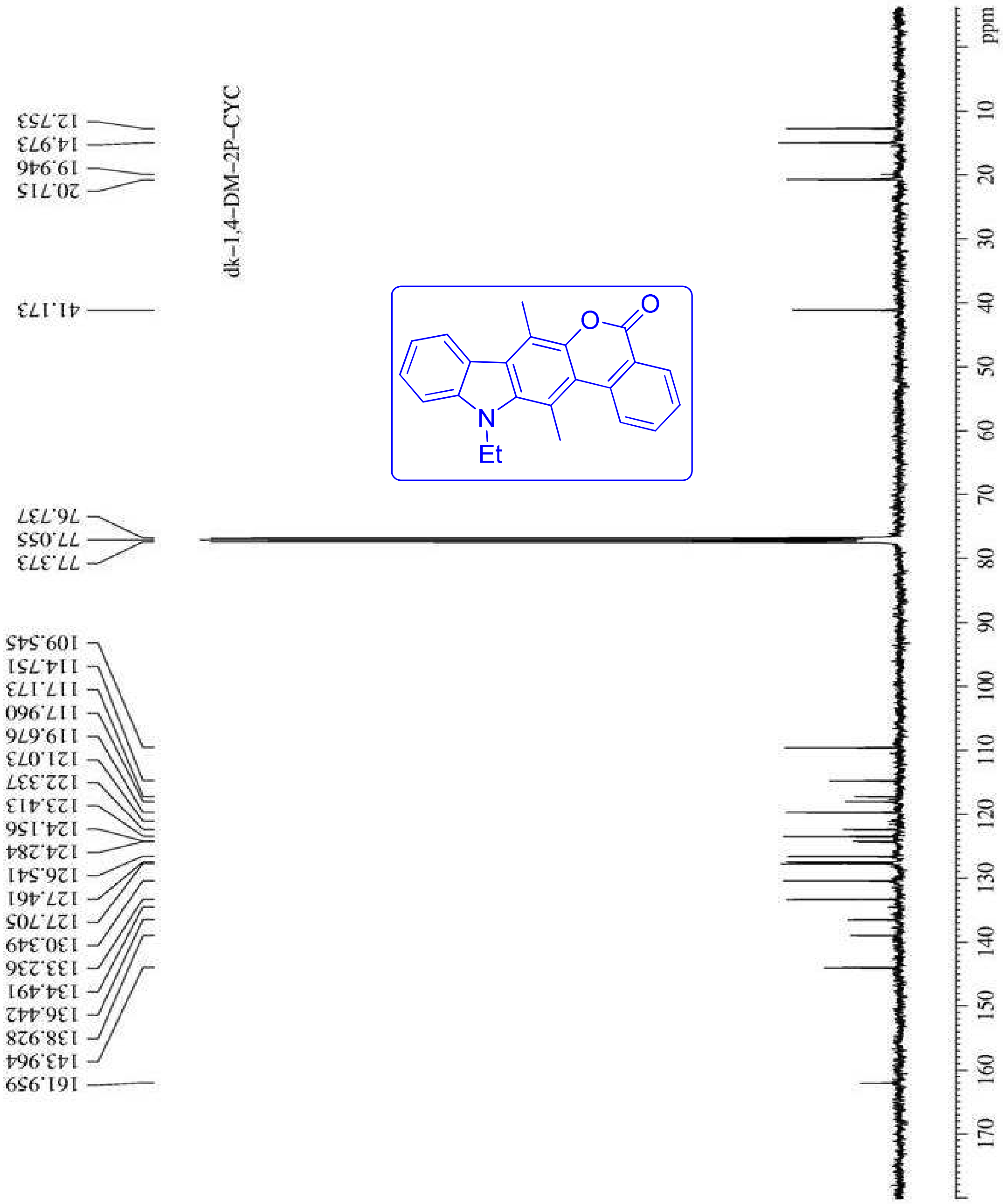
Spectrum 12. ^{13}C NMR of 215a



Spectrum 13. ^1H NMR of 215c



Spectrum 14. ^{13}C NMR of 215c



1.6. References:

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115. The CCDC deposition number of **193** is 772615; Formula: $C_{42}H_{32}N_4O_2$. Unit cell parameters: a = 9.0391(19), b = 11.043 (3), c = 17.740 (5), α = 77.39 (2), β = 87.34 (2), γ = 88.207 (18), space group P-1. The CCDC deposition number of **194a** is 772616; Formula: $C_{23}H_{20}N_2O_1$. Unit cell parameters: a = 9.1260 (18), b = 8.2593 (16), c = 22.851 (5), b = 96.462 (3), space group P21/n. The CCDC deposition number of **195b** is 772619; Formula: $C_{23}H_{19}N_3O_3$. Unit cell parameters: a = 25.978 (15), b = 11.634 (2), c = 13.874 (8), b = 121.89 (8), space group C2/c. The CCDC deposition number of **194c** is 772617; Formula: $C_{23}H_{19}Cl_1N_2O$. Unit cell parameters: a = 5.0196 (7), b = 17.051 (2), c = 10.5546 (15), b = 90.965 (2), space group P21. The CCDC deposition number of **195c** is 772618; Formula: $C_{23}H_{19}Cl_1N_2O$. Unit cell parameters: a = 5.965 (2), b = 1.4538 (10), c = 13.9605 (13), b = 121.6480 (10), space group C2/c.
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120. Terzidis, M.; Tsoleridis, C. A.; Stephanidou-Stephanatou, J. *Tetrahedron Lett*. **2005**, *46,* 7239.
121. The CCDC deposition number for compound **211b** is 823151. Formula: $C_{26}H_{15}NO_2$. Unit cell parameters: a = 8.2147(7), b = 9.9766(7), c = 12.2199(11), α = 88.285(6), β = 87.066(7), γ = 67.350(7), space group P-1. The CCDC deposition number for compound **211d** is 824502. Formula: $C_{22}H_{17}NO_2$. Unit cell parameters: a = 7.5580(5), b = 19.9905(8), c = 10.6520(6), space group Pna21. The CCDC deposition number for

compound **212d** is 823152. Formula: $C_{22}H_{17}NO_2$. Unit cell parameters: a = 8.5988(6), b = 15.5481(14), c = 14.6529(12), β = 122.242(6), space group P21/c. The CCDC deposition number for compound **212f** is 824503. Formula: $C_{23}H_{19}NO_2$. Unit cell parameters: a = 7.5027(6), b = 9.1436(12), c = 12.7349(13), α = 100.156(0), β = 101.632(8), γ = 92.456(9), space group P-1.

Copper-Mediated Domino Synthesis of Pyrimido[4,5-*b*]carbazolones via Ullmann *N*-Arylation and Aerobic Oxidative C-H Amidation

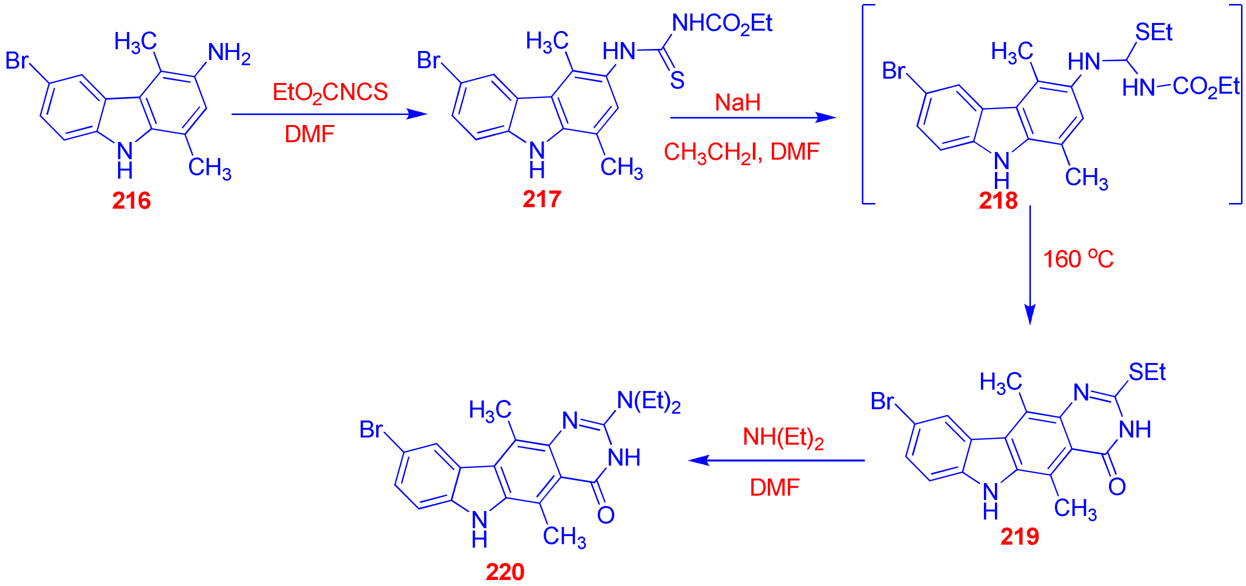
CHAPTER 2

2.1 Introduction:

Carbazoles are interesting structural scaffolds of a vast number of biologically active natural and unnatural compounds that are known for their potent biological activities (e.g., cytotoxic, anti-tumor, anti-biotic, anti-viral and anti-oxidative activities).[122-125] Carbazole and its derivatives are also widely used as organic materials due to their photophysical properties.[123] The syntheses and functionalization of carbazoles has been the main object of research over the years and makes them privileged structures in drug design and development. Considering the importance of its role in drug design, it is more valuable to synthesize new carbazole derivatives containing fused pyrimidine ring.[124] A variety of fused *N*-heterocycles exhibit a number of useful biological and pharmacological activities.[125] The structurally related heteroaryl-annulated carbazole, Ellipticine (5,11-dimethyl-6*H*-pyrido[4,3-*b*]carbazole) and its derivatives are known for their high potencies as anti-cancer, antiHIV and DNA intercalating activities where a variety of well-established synthetic methods have been reported.[126] One of the possible approaches to new ellipticine analogues was the modification of pyridine moiety (ring D) of the tetracyclic skeleton replaced by other heterocycles producing benzo-, pyrrolo-, pyrazino-, pyrano-, imidazo-, indolo-, furo-, and thieno-carbazoles have been described in the literature.[128]

To prepare the pyrimidocarbazole **220**, (Eq. 35)[129] starting from 3-amino-6-bromo-1,4-dimethylcarbazole **216** was reacted with ethoxycarbonylisothiocyanate in DMF to give the corresponding thiourea **217**, which was treated with NaH and ethyliodide to give the ethylisothiourea **218.** Heating the reaction mixture at reflux temperature led to ring closure of the ethoxycarbonyl-*S*-ethylisothiourea group onto C2 of the carbazole ring giving the 9-bromo-2-ethylthio-5,11-dimethyl-6*H*-pyrimido-carbazol-4(3*H*)-one **219**. Treatment of **219** with diethylamine resulted in a nucleophilic displacement of the 2-ethylthio substituent by a diethylamino group giving rise to **220**.

Eq. 35



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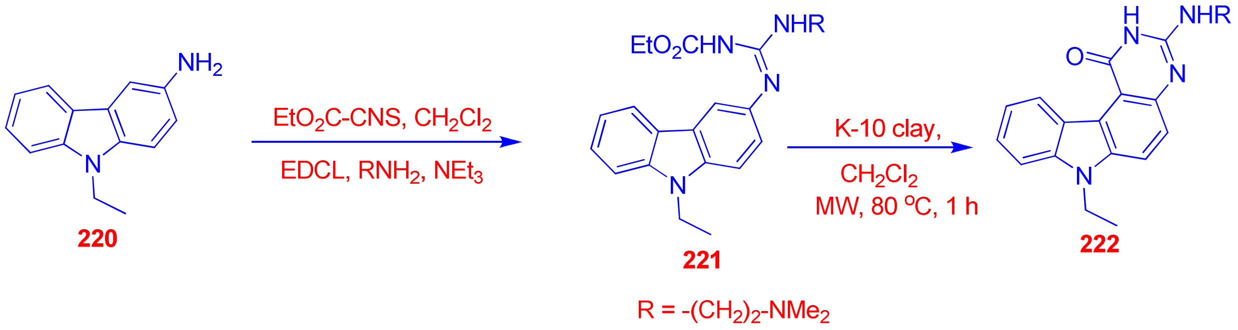
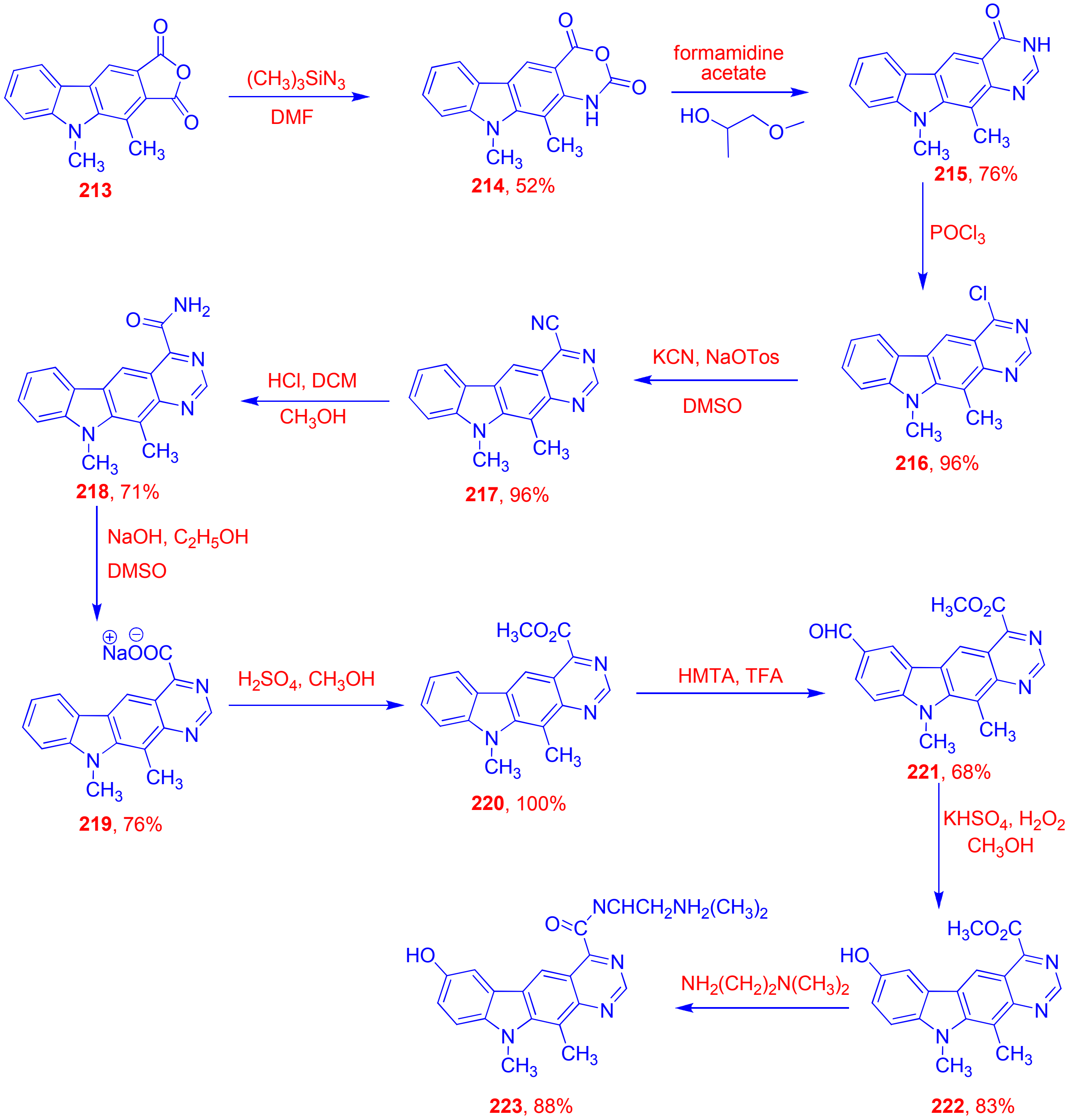
Following the importance of pyrimidocarbazoles derivatives **222**, (Eq. 36)[130] starting from 3-amino-*N*-ethylcarbazole **220** treated with chlorotrimethylsilane or trichloromethylsilane obtained the protected amines **221**. Then **221** was heated in dichloroethane in the presence of clay at 80 °C obtained the corresponding tetracyclic pyrimido[4,5-*c*]carbazole **222** in good yield.

Eq. 36



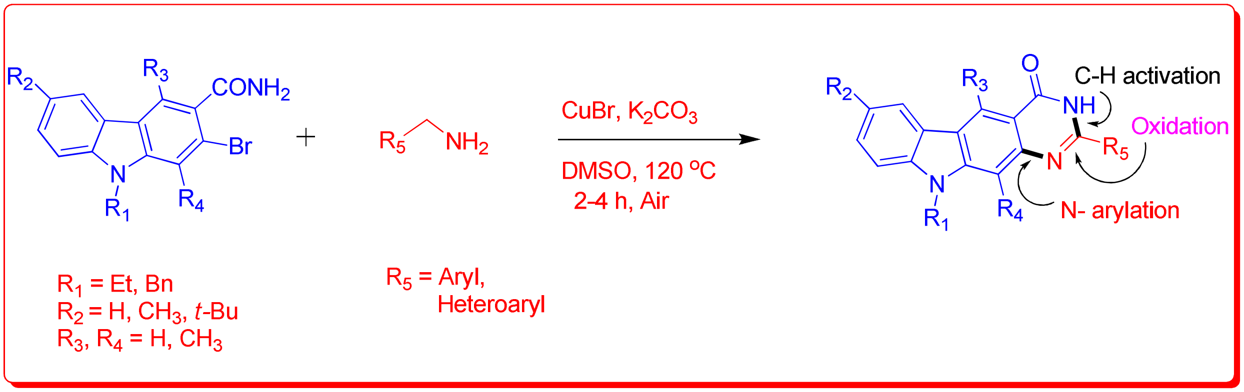
Preparation of compound **223** started with the known tetracyclic anhydride **213** with trimethylsilylazide in DMF afforded in good yield tetracycle **214**, which could be transformed into pyrimidocarbazole **215** in presence of formamidine acetate and 1-methoxy-2-propanol. The cyano substituted pyrimidocarbazole **217** could be easily obtained by a two-step procedure involving quantitative reaction of **215** with phosphorous oxychloride affording the chloro derivative **216** followed by chlorine displacement using potassium cyanide and a catalytic amount of sodium tosylate in DMSO. Transformation of the nitrile **216** into the corresponding amide **217** was achieved by treatment with an excess of hydrogen chloride in a mixture of dichloromethane and methanol. The amide **218** was quantitatively transformed into carboxylic acid sodium salt **219** using sodium hydroxide in a mixture of ethanol and DMSO. The corresponding ester **220**, obtained in methanol in the presence of sulfuric acid, was formylated with hexamethylenetetramine in TFA to give aldehyde **221** whose oxidation in methanol using hydrogen peroxide gave phenolic compound **222** in moderate yield. The introduction of the amide chain was performed in good yield by reaction with *N*,*N*-dimethylethylenediamine to give **223** (Eq. 37).[131]

Eq. 37



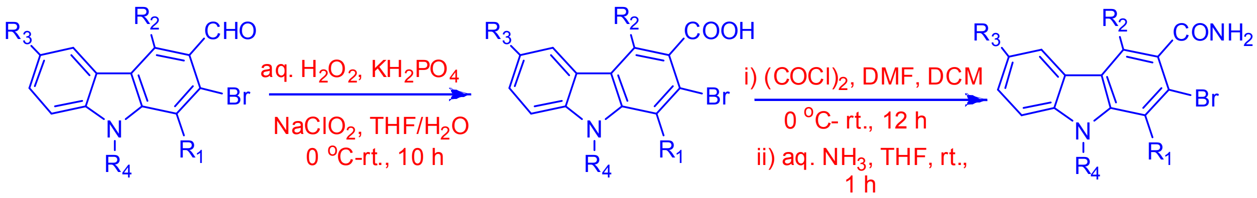
2.2 Synthesis of Pyrimidocarbazolones:

A great deal of studies have been directed toward the use of copper salts in the synthesis and functionalization of heterocycles.[132] Recent progress in modern copper-mediated Ullmann coupling reactions has led to emergence of numerous methods to condense aryl halides with amines.[133] Oxidative insertion reactions into saturated C-H bonds to form amines or amine derivatives using copper salts are attractive synthetic methodologies and these reactions also offer opportunities to understand the fundamental mechanism of C-H activation.[134] The domino reaction has thus emerged as a powerful tool for constructing complex molecules from readily available building blocks in which a series of chemical reactions can be controlled in a particular step.[135] Hence, copper-catalyzed domino reactions are very useful for constructing various *N*-heterocycles.[136] We herein report a facile synthesis of new pyrimido[4,5-*b*]carbazolone derivatives through cascade Ullmann *N*-arylation and aerobic oxidative C-H amidation reactions catalyzed by CuBr under air and ligand–free conditions. The schematic representation of our work is outlined in Scheme 7.



Scheme 7. Schematic representation of our work

A new route to pyrimidine ring formation, starting from substituted 2-bromo-9*H*-carbazole-3-carboxamides **226a-e** which can be readily prepared from the corresponding aldehydes **224a-e** (Scheme 8).[137]



224a-e
$R_1 = R_2 =$ H, Me
$R_3 =$ H, Me, *t*-Bu
$R_4 =$ Et, *n*-Bu, Bn

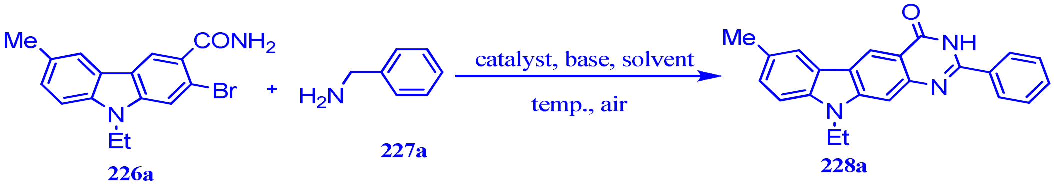
225a-e

226a-e

Scheme 8. Synthesis of 226a-e.

Initially, 2-bromo-9-ethyl-6-methyl-9*H*-carbazole-3-carboxamide **226a** and benzylamine **227a** were used as the model substrates to optimize reaction conditions including catalysts, bases, solvents, and reaction temperatures under air (1 atm). As shown in Table 17, five copper salts (0.01 mmol) were tested with 4.0 equiv. of K_2CO_3 relative to amount of **226a** as a base and DMSO as the solvent at 120 °C (entries 1, 3-5 and 7), and CuBr provided the better yield (entry 8). Other bases, Na_2CO_3, Cs_2CO_3, K_3PO_4, DABCO and *t*-BuOK (entries 7 and 9-12), were screened, and K_2CO_3 showed the best activity (compare entries 8, 7 and 9-12). The effect of solvents was also examined; and DMSO was the optimal solvent (compare entries 8 and 13-15). We attempted different reaction temperatures (entries 16-18), and 120 °C was the best choice.

Table 17. Optimization of the reaction conditions.[a]

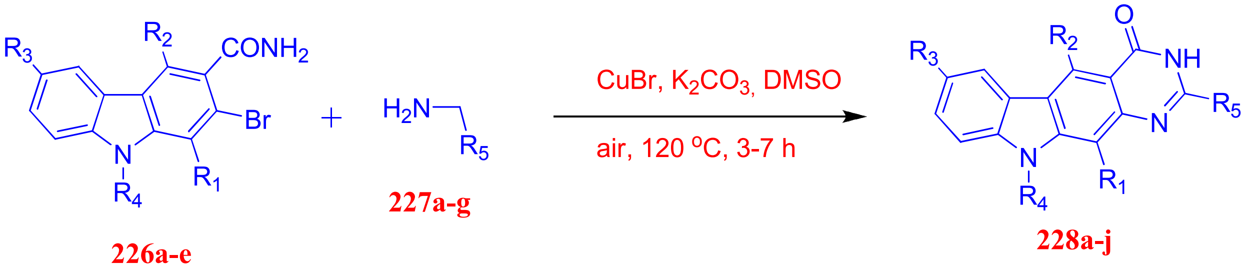


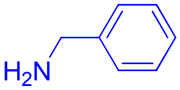
entry	catalyst	base	solvent	temp (°C) /time (h)	yield (%)[b]
1	CuCl	K_2CO_3	DMSO	120/3	0
2	CuO	K_2CO_3	DMSO	120/3	trace
3	CuO	AcONa	DMSO	120/3	0
4	$Cu(OAc)_2$	K_2CO_3	DMSO	120/3	20
5	CuI	K_2CO_3	DMSO	120/3	63
6	CuI	Cs_2CO_3	DMSO	120/6	71
7	CuBr	Na_2CO_3	DMSO	120/13	67
8	**CuBr**	**K_2CO_3**	**DMSO**	**120/3**	**78**
9	CuBr	Cs_2CO_3	DMSO	120/3	73
10	CuBr	K_3PO_4	DMSO	120/3	33
11	CuBr	DABCO	DMSO	120/8	22
12	CuBr	*t*-BuOK	DMSO	120/3	54
13	CuBr	K_2CO_3	toluene	120/3	18
14	CuBr	K_2CO_3	ethylene glycol	120/3	27
15	CuBr	K_2CO_3	NMP	120/3	trace
16	CuBr	K_2CO_3	DMSO	70/2	0
17	CuBr	K_2CO_3	DMSO	90/6	47
18	CuBr	K_2CO_3	DMSO	110/5	66
19	CuBr	K_2CO_3	DMSO	120/24	13[c]
20	CuBr	K_2CO_3	DMSO	120/3	54[d]

[a] Reaction conditions: 2-bromo-9-ethyl-6-methyl-9*H*-carbazole-3-carboxamide **226a** (0.2 mmol), benzylamine **227a** (0.24 mmol), catalyst (0.01 mmol), base (0.6 mmol), solvent (3.0 mL) under air. [b] Isolated yield. Under [c] nitrogen and [d] oxygen balloons.

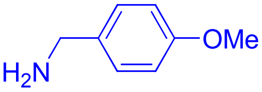
The scope of copper-catalyzed domino reactions of substituted 2-bromo-9*H*-carbazole-3-carboxamides with (aryl)methanamines was investigated under the optimized conditions using 10 mol % of CuBr as the catalyst, 4.0 equiv. of K_2CO_3 as the base, and DMSO as the solvent. As shown in Table 18, most of the substrates examined provided good yields at 120-130 °C. In general, no significant difference of reactivity was observed for the examined substituted 2-bromo-9*H*-carbazole-3-carboxamides and (aryl)methanamines with varied electronic properties, including electron-rich, electron-poor, and neutral substrates. The copper-mediated domino synthesis of pyrimido[4,5-*b*]carbazolones could tolerate various functional groups including ether (entry 2 of Table 18), C-Cl and C-F bonds (entries 4 and 5 of Table 9) and heterocyclic ring containing oxygen and sulphur (entries 6 and 9-10 of Table 18) in the (aryl)methanamines.

Table 18. Synthesis of pyrimido[4,5-*b*]carbazolone derivatives.[a]

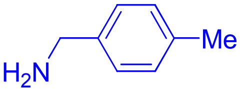




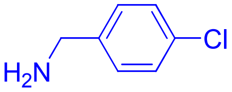
227a



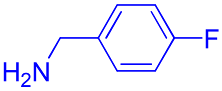
227b



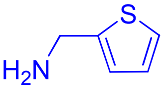
227c



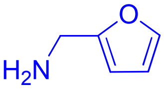
227d



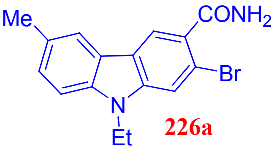
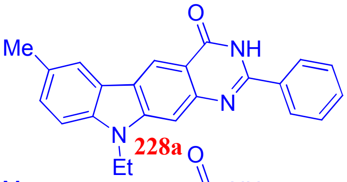
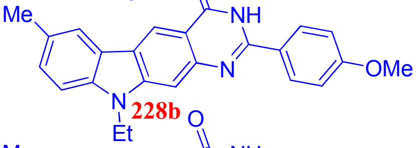
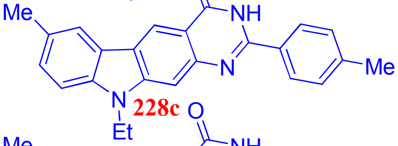
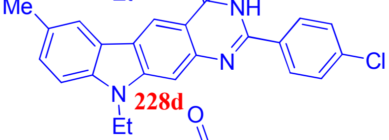
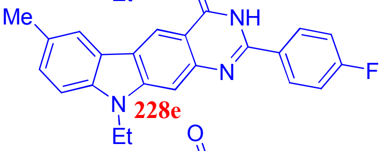
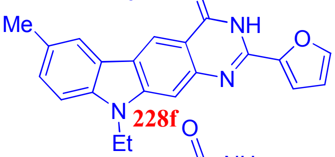
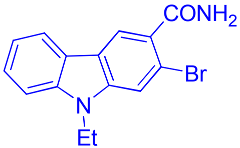
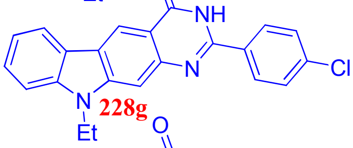
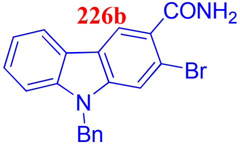
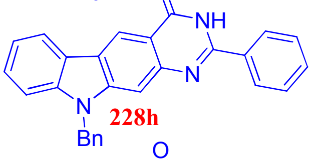
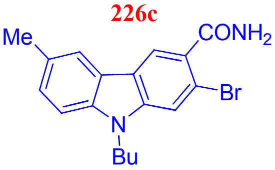
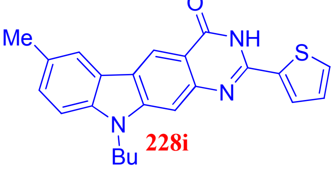
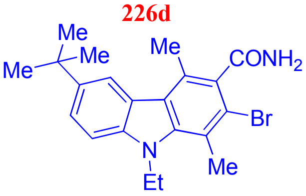
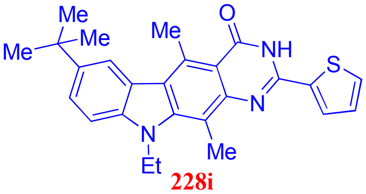
227e



227f

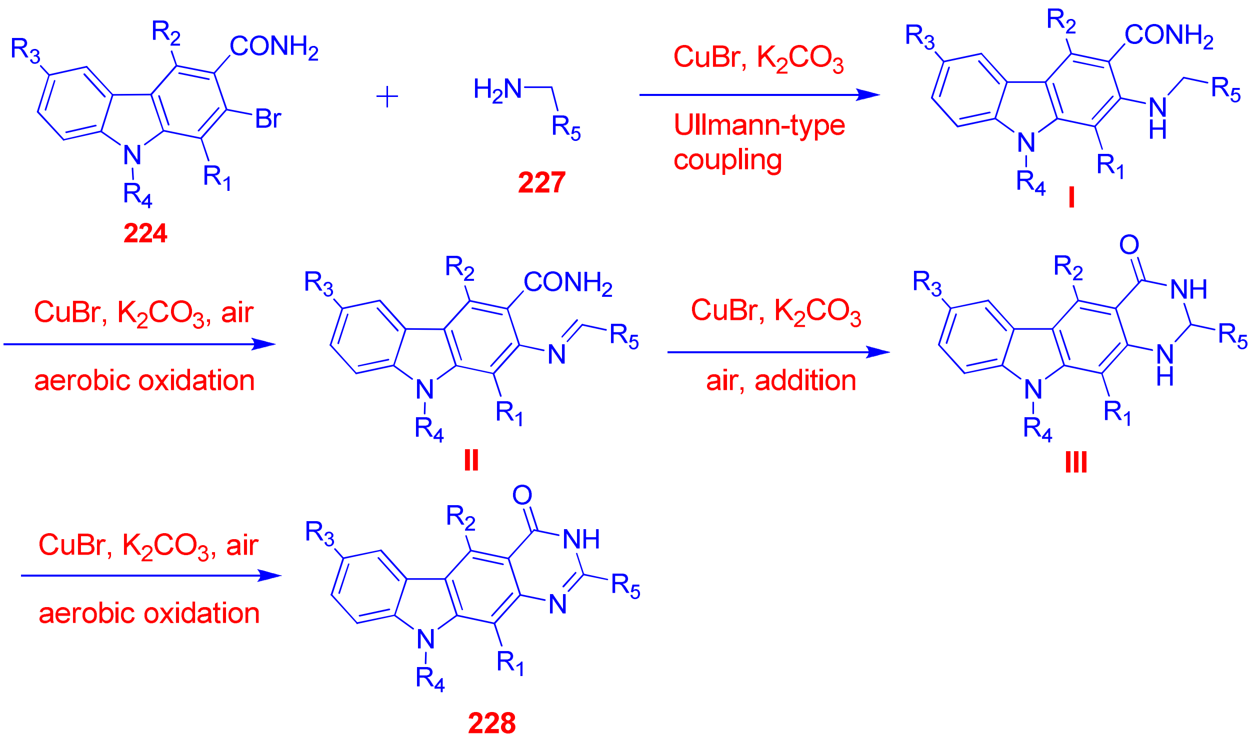


227g

entry	substrate	temp (°C) / time (h)	product	yield (%)[b]
1	 **226a**	120 /3	 **228a**	78
2	**226a**	120 /3	 **228b**	77
3	**226a**	120 /3	 **228c**	72
4	**226a**	120 /4	 **228d**	74
5	**226a**	120 /4	 **228e**	69
6	**226a**	120 /6	 **228f**	57
7	 **226b**	120 /5	 **228g**	71
8	 **226c**	120 /3.5	 **228h**	73
9	 **226d**	120 /3	 **228i**	75
10	 **226e**	120 /6.5	 **228i**	51

[a]Reaction conditions: **226a-e** (0.2 mmol), **227a-g** (0.24 mmol), CuBr (0.01 mmol), K_2CO_3 (0.8 mmol) and DMSO (3.0 mL) under air. [b]Isolated yield.

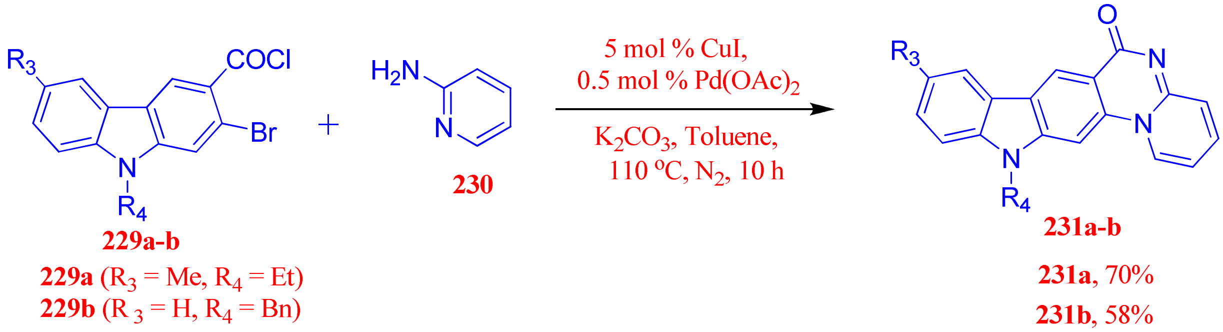
A possible mechanism for synthesis of pyrimido[4,5-*b*]carbazolone derivatives is proposed in Scheme 9 according to the results above. Copper-catalyzed Ullmann-type coupling of substituted 2-bromo-9*H*-carbazole-3-carboxamides with (aryl)methanamine provides a *N*-arylation product (**I**). Surprisingly, no ligand or additive was required in the reaction system, and the result showed an *ortho*-substituent effect of the amide group in **224** during *N*-arylation. Copper catalyzed aerobic oxidation of **I** affords intermediate **II** containing a C=N bond, and intramolecular nucleophilic addition of the amide to the C=N bond in **II** gives **III**. Finally, further aerobic oxidation of **III** provides the target compound **228**.



Scheme 9. Possible mechanism

2.3 Synthesis of fused pyrimidocabazolones:

We have also synthesized fused pyrimido[4,5-*b*]carbazolones from subsititutted 2-bromo-9*H*-carbazole-3-carbonyl chlorides **229a-b** and pyridin-2-amine **230** using CuI as a catalyst (Scheme 10). We herein used $Pd(OAc)_2$ as a co-catalyst to form *insitu* amide from the corresponding acid chlorides and amine followed by intramolecular Ullmann-type *N*-arylation led to the desired products **231a-b** due to *ortho*-subsituent effect of pyridine group.[12]



Scheme 10. Synthesis of fused pyrimido[4,5-*b*]carbazolone derivatives

2.4 Conclusion

In conclusion, we have synthesized a series of pyrimido[4,5-*b*]carbazolone derivatives using cascade Ullmann *N*-arylation and aerobic oxidative C-H amidation reactions that allow the assembly of readily accessible building blocks into diverse (heteroaryl-annulated) pyrimido[4,5-*b*]carbazolones with the aid of CuBr as a catalyst without any additives or ligands. An attractive feature of this synthetic approach is not only to provide a new approach for constructing pyrimido[*b*]carbazoles but also offers an efficient method for preparation of synthetically and medicinally important hetero-arylated carbazoles. Furthermore, some of the resulting pyrimido[4,5-*b*]carbazolone derivatives exhibit intense fluorescence.

2.5 Experimental Section:

General procedure G:

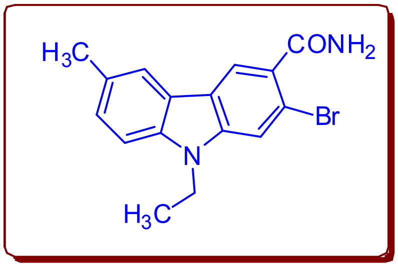
Preparation of starting materials (226a-e):

A mixture of 2-bromo-9-ethyl-6-methyl-9*H*-carbazole-3-carbaldehyde (1 g, 3.16 mmol), tetrahydrofuran, 20 mL, were combined in a 50 mL round bottom flask with magnetic stirring bar. The mixture was cooled to 0 °C, followed by addition of 35% H_2O_2 (5.23 mL, 52.3 mmol), KH_2PO_4 (0.45 g, 3.31 mmol) and $NaClO_2$ (0.56 g, 6.19 mmol) in water 10 mL was added dropwise. The reaction mixture was returned to room temperature and stirred for overnight. Monitored the reaction by TLC with 30% ethylacetate in hexanes showed complete conversion to new spot with lower R*f*. Acidify with dil.HCl and filter the solid. Recrystallized from warm ethyl acetate to yield white solid (0.98 g, 93%).

The mixture of 2-bromo-9-ethyl-6-methyl-9*H*-carbazole-3-carboxylic acid (1 g, 4.6 mmol), oxalyl chloride (2 mL) in 20 mL of dichloromethane and 2-3 drops of DMF was added at 0 °C and stirred for overnight at room temperature. Oxalyl chloride was removed by co-evaporation with toluene (10 mL) with rotary evaporation. The concentrated crude product was dissolved in THF (20 mL). Ammonium hydroxide (5 mL, conc.) was added drop wise to the mixture and stirred for 1 h at room temperature. The precipitate was filtered and recrystallized from ethyl acetate/hexane (5:5) to afford the pure product **226a** as white solid (0.76 g, 77%). The remaining starting materials **226b-e** was also prepared using above described procedures.

NOTE: For the starting materials **226a-e**, ^{1}H NMR signals for amide protons (CO$\underline{NH_2}$) are not observed and for the compounds **228a-f** and **228i**, the methyl (-CH$_3$) protons merged with DMSO-d_6 at δ 2.50 ppm.

2-Bromo-9-ethyl-6-methyl-9*H*-carbazole-3-carboxamide (226a):



Yield: 77%

Mp: 201-203 °C

IR (KBr) ν_{max} cm^{-1}: 3362, 2976, 1645, 1392, 1230, 1145, 682

^{1}H NMR (400 MHz, DMSO-d_6): δ 8.63 (s, 1H), 8.01 (s, 1H), 7.92 (s, 1H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.30 (d, *J* = 8 4 Hz, 1H), 4.39 (q, *J* = 6.8 Hz, 2H), 2.44 (s, 3H), 1.25 (t, *J* = 6.8 Hz, 3H)

^{13}C NMR (100 MHz, DMSO-d_6): δ 167.9, 141.9, 139.1, 129.4, 128.5, 124.2, 122.5, 122.3, 121.3, 121.1, 118.9, 114.6, 109.9, 37.7, 21.4, 14.1

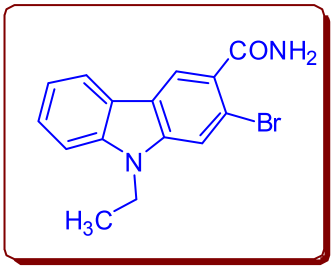
LC-MS (m/z): 332 [M], 334 [M+2] positive mode

Anal. Calcd. for $C_{16}H_{15}BrN_2O$: C, 58.02; H, 4.56; N, 8.46%

Found: C, 58.12; H, 4.61; N, 8.56%

2-Bromo-9-ethyl-9*H*-carbazole-3-carboxamide (226b):

The title compound **3b** was obtained as white solid from silica-gel column chromatography using 50% ethylacetate in hexanes according to general procedure G.



Yield: 85%

Mp: 141-143 °C

IR (KBr) ν_{max} cm^{-1}: 3439, 2254, 1668, 1471, 1383, 1234, 1026, 821

^{1}H NMR (400 MHz, DMSO-d_6): δ 8.47 (s, 1H), 8.29 (d, *J* = 7.6 Hz, 2H), 8.24 (d, *J* = 8.0 Hz, 2H), 7.85 (s, 1H), 4.51 (q, *J* = 6.4 Hz, 2H), 1.33 (t, *J* = 6.8 Hz, 3H)

^{13}C NMR (100 MHz, DMSO-d_6): δ 162.8, 144.7, 140.4, 132.2, 129.2, 129.1, 128.9, 124.7, 123.9, 121.4, 119.8, 114.2, 111.3, 31.7, 13.8

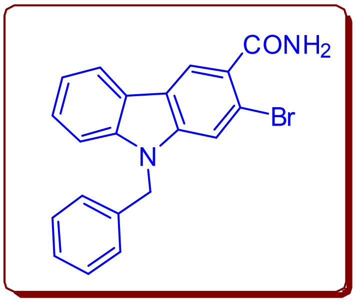
LC-MS (m/z): 317 [M], 319 [M+2] positive mode

Anal. Calcd. for $C_{15}H_{13}BrN_2O$: C, 56.80; H, 4.13; N, 8.83%

Found: C, 56.75; H, 4.18; N, 8.91%

9-Benzyl-2-bromo-9*H*-carbazole-3-carboxamide (226c):

The title compound **3c** was obtained as white solid from silica-gel column chromatography using 50% ethylacetate in hexanes according to general procedure G.

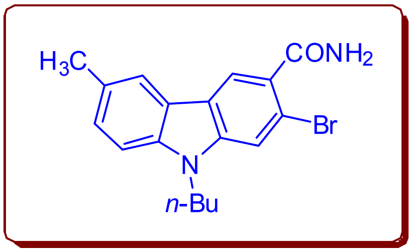


Yield: 85%

Mp:	141-143 °C
IR (KBr) ν_{max} cm^{-1}:	3356, 1649, 1398, 1261, 1199, 1014, 696
^{1}H NMR (400 MHz, DMSO-d_6):	δ 8.41-8.40 (m, 1H), 8.38 (s, 1H), 8.26 (d, *J* = 6.0 Hz, 1H), 8.00 (s, 1H), 7.96 (s, 1H), 7.67-7.64 (m, 2H), 7.53-7.47 (m, 2H), 7.29-7.22 (m, 1H), 7.13-7.10 (m, 1H), 5.72 (s, 2H)
^{13}C NMR (100 MHz, DMSO-d_6):	δ 170.2, 141.2, 137.8, 130.5, 129.1, 127.8, 127.1, 127.04, 127.02, 122.2, 121.5, 121.2, 121.0, 120.3, 116.5, 113.9, 110.5, 46.1
LC-MS (m/z):	379 [M], 381 [M+2] positive mode
Anal. Calcd. for $C_{20}H_{15}BrN_2O$:	C, 63.34; H, 3.99; N, 7.39%
Found:	C, 63.25; H, 3.91; N, 7.45%

2-Bromo-9-butyl-6-methyl-9*H*-carbazole-3-carboxamide (226d):

The title compound **3d** was obtained as white solid from silica-gel column chromatography using 50% ethylacetate in hexanes according to general procedure G.



Yield:	83%
Mp:	197-198 °C
IR (KBr) ν_{max} cm^{-1}:	3377, 3177, 2957, 2864, 1645, 1481, 1211, 1105, 829
^{1}H NMR (400 MHz, DMSO-d_6):	δ 8.19 (s, 1H), 7.98 (s, 1H), 7.86 (s, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 4.35 (t, *J* = 7.2 Hz, 2H), 2.45 (s, 3H), 1.71-1.64 (m, 2H), 1.26-1.17 (m, 2H), 0.83 (t, *J* = 7.2 Hz, 3H)

^{13}C NMR (100 MHz, DMSO-d_6): δ 170.4, 141.2, 139.4, 129.6, 128.8, 128.3, 122.1, 120.9, 116.2, 113.6, 110.0, 42.6, 31.0, 21.4, 20.1, 14.1

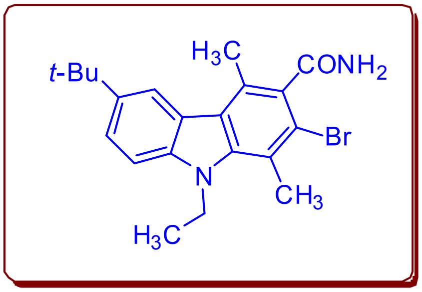
LC-MS (m/z): 359 [M], 361 [M+2]

Anal. Calcd. for $C_{18}H_{19}BrN_2O$: C, 60.18; H, 5.33; N, 7.80%

Found: C, 60.25; H, 5.39; N, 7.75%

6-*t*-Butyl-2-bromo-9-ethyl-1,4-dimethyl-9*H*-carbazole-3-carboxamide (227e):

The title compound **3e** was obtained as white solid from silica-gel column chromatography using 50% ethylacetate in hexanes according to general procedure G.



Yield: 74%

Mp: 109-110 °C

IR (KBr) ν_{max} cm^{-1}: 3437, 2961, 1649, 1454, 1365, 1236, 1168, 800

^{1}H NMR (400 MHz, DMSO-d_6): δ 8.21 (s, 1H), 7.62-7.60 (m, 1H), 7.40 (d, *J* = 8.8 Hz, 1H), 4.56 (q, *J* = 6.8 Hz, 2H), 2.94 (s, 3H), 2.91 (s, 3H), 1.47-1.44 (m, 12H)

^{13}C NMR (100 MHz, DMSO-d_6): δ 174.0, 142.8, 139.8, 128.6, 127.8, 123.9, 123.1, 121.8, 119.0, 117.9, 108.6, 40.1, 34.7, 31.7, 19.1, 18.5, 15.5

LC-MS (m/z): 400 [M], 402 [M+2] positive mode

Anal. Calcd. for $C_{21}H_{25}BrN_2O$: C, 62.85; H, 6.28; N, 6.98%

Found: C, 62.75; H, 6.32; N, 6.88%

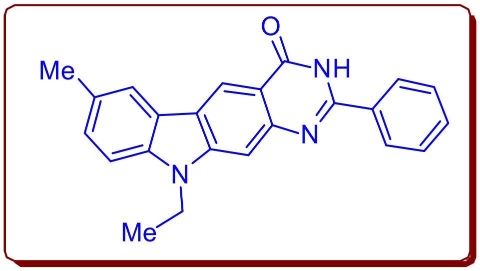
General procedure H

General procedure for synthesis of pyrimido[5,4-b]carbazolone derivatives (228a-j):

A 25 mL flask equipped with a magnetic stirring bar was charged with substituted 2-bromo-carbazole-3-carboxamide (0.2 mmol), (aryl)methanamine (0.24 mmol), K_2CO_3 (0.8 mmol) and CuBr (0.01 mmol) in DMSO (3 mL). The mixture was allowed to stir under air (1 atm) at 120 ~ 130 °C for 3 ~ 7 h. After completion of the reaction, the resulting solution was cooled to room temperature, poured into water and extracted with ethyl acetate. The solvent of extract was removed with the aid of a rotary evaporator. The residue was purified by column chromatography on silica gel using ethyl acetate/hexanes as eluent to provide the desired product **228a-j**.

10-Ethyl-7-methyl-2-phenyl-3*H*-pyrimido[4,5-*b*]carbazol-4(10*H*)-one (228a):

The compound **228a** was obtained from **226a** and **227a** as pale yellow solid by column chromatography on silica-gel using 70% ethylacetate in hexanes according to general procedure H.



Yield: 78%

Mp: >300 °C

IR (KBr) ν_{max} cm^{-1}: 3391, 2253, 2125, 1651, 1377, 1145, 1026, 763

^{1}H NMR (400 MHz, DMSO-d_6): δ 12.30 (s, 1H), 8.93 (s, 1H), 8.26-8.24 (m, 2H), 8.15 (s, 1H), 7.83 (s, 1H), 7.58-7.55 (m, 4H), 7.38 (d, *J* = 8.4 Hz, 1H), 4.50 (q, *J* = 7.2 Hz, 2H), 1.34 (t, *J* = 6.8 Hz, 3H)

^{13}C NMR (100 MHz, DMSO-d_6): δ 163.2, 151.2, 147.2, 144.6, 140.2, 133.5, 131.5, 129.2, 129.0, 128.8, 128.0, 122.9, 122.7, 121.5, 118.6, 113.6, 109.5, 105.3, 37.7, 21.4, 13.8

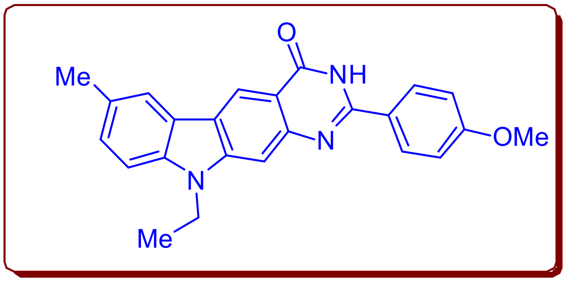
LC-MS (m/z): 354 $[M+H]^+$ positive mode

Anal. Calcd. for $C_{23}H_{19}N_3O$: C, 78.16; H, 5.42; N, 11.89%

Found: C, 78.35; H, 5.48; N, 11.79%

10-Ethyl-2-(4-methoxyphenyl)-7-methyl-3*H*-pyrimido[4,5-*b*]carbazol-4(10*H*)-one (**228b**):

The compound **228b** was obtained from **226a** and **227b** as yellow solid by column chromatography on silica-gel using 70% ethylacetate in hexanes according to general procedure H.



Yield: 77%

Mp: 198-199 °C

IR (KBr) v_{max} cm^{-1}: 3441, 2253, 2125, 1651, 1377, 1145, 1026, 763

^{1}H NMR (400 MHz, DMSO-d_6): δ 12.19 (s, 1H), 8.90 (s, 1H), 8.24 (d, J = 9.2 Hz, 1H), 8.13 (s, 1H), 7.78 (s, 1H). 7.55 (d, J = 8.4 Hz, 1H), 7.37-7.35 (m, 1H), 7.16 (d, J = 8.8 Hz, 1H), 7.11 (d, J = 8.8 Hz, 1H), 6.86 (d, J = 8.8 Hz, 1H), 4.49 (q, J = 6.8 Hz, 2H), 3.86 (s, 3H), 1.34 (t, J = 7.2 Hz, 3H)

^{13}C NMR (100 MHz, DMSO-d_6): δ 163.3, 158.4, 150.8, 147.4, 144.6, 140.1, 133.2, 129.7, 129.2, 128.7, 125.6, 122.6, 121.4, 118.5, 114.4, 113.4, 109.5, 105.0, 55.9, 21.4, 13.8

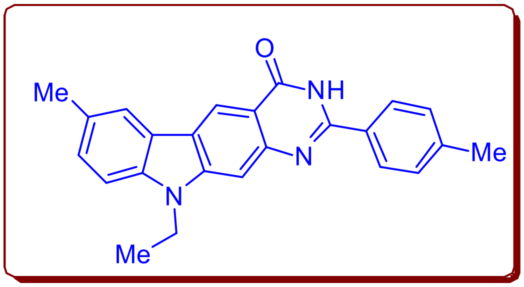
LC-MS (m/z): 384 $[M+H]^+$ positive mode

Anal. Calcd. for $C_{24}H_{21}N_3O_2$: C, 75.18; H, 5.52; N, 10.96%

Found: C, 75.26; H, 5.48; N, 11.07%

10-Ethyl-7-methyl-2-p-tolyl-3*H*-pyrimido[4,5-*b*]carbazol-4(10*H*)-one (228c):

The compound **228c** was obtained from **226a** and **227c** as pale yellow solid by column chromatography on silica-gel using 70% ethylacetate in hexanes according to general procedure H.



Yield: 72%

Mp: 276-277 °C

IR (KBr) ν_{max} cm^{-1}: 3450, 2254, 2125, 1668, 1485, 1304, 1217, 1028, 760

^{1}H NMR (400 MHz, DMSO-*d*$_6$): *δ* 12.22 (s, 1H), 8.91 (s, 1H), 8.15 (d, *J* = 8.4 Hz, 1H), 8.12 (s, 1H), 7.79 (s, 1H), 7.54 (d, *J* = 8.4 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 4H), 4.49 (q, *J* = 7.2 Hz, 2H), 2.40 (s, 3H), 1.34 (t, *J* = 7.2 Hz, 3H)

^{13}C NMR (100 MHz, DMSO-*d*$_6$): *δ* 163.3, 151.2, 147.3, 144.6, 141.5, 140.2, 130.7, 129.6, 129.2, 128.7, 127.9, 122.8, 122.7, 121.4, 118.5, 113.5, 109.5, 105.2, 37.7, 21.5, 21.4, 13.8

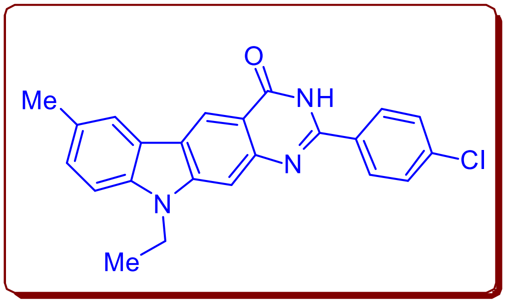
LC-MS (m/z): 368 [M+H]$^+$ positive mode

Anal. Calcd. for $C_{24}H_{21}N_3O$: C, 78.45; H, 5.76; N, 11.44%

Found: C, 78.32; H, 5.71; N, 11.56%

2-(4-Chlorophenyl)-10-ethyl-7-methyl-3*H*-pyrimido[4,5-*b*]carbazol-4(10*H*)-one (228d):

The compound **228d** was obtained from **226a** and **227d** as pale yellow solid by column chromatography on silica-gel using 70% ethylacetate in hexanes according to general procedure H.



Yield: 74%

Mp: 284-285 °C

IR (KBr) v_{max} cm^{-1}: 3381, 2968, 2922, 1637, 1593, 1483, 1342, 1234, 1089, 794

^{1}H NMR (400 MHz, DMSO-d_6): δ 12.38 (s, 1H), 8.93 (s, 1H), 8.25 (d, *J* = 8.4 Hz, 2H), 8.15 (s, 1H), 7.83 (s, 1H), 7.65 (d, *J* = 8.8 Hz, 2H), 7.56 (d, *J* = 8.4 Hz, 1H), 7.39-7.37 (m, 1H), 4.50 (q, *J* = 7.2 Hz, 2H), 1.34 (t, *J* = 7.2 Hz, 3H)

^{13}C NMR (100 MHz, DMSO-d_6): δ 163.2, 150.3, 147.0, 144.5, 140.2, 136.4, 132.3, 129.9, 129.3, 129.1, 128.9, 123.0, 122.6, 121.5, 118.6, 113.6, 109.6, 105.4, 37.7, 21.4, 13.8

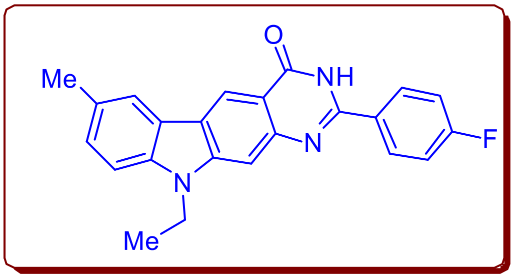
LC-MS (m/z): 387 [M], 388 [M+1] positive mode

Anal. Calcd. for $C_{23}H_{18}ClN_3O$: C, 71.22; H, 4.68; N, 10.83%

Found: C, 71.35; H, 4.62; N, 10.76%

10-Ethyl-2-(4-fluorophenyl)-7-methyl-3*H*-pyrimido[4,5-*b*]carbazol-4(10*H*)-one (228e):

The compound **228e** was obtained from **226a** and **227e** as pale yellow solid by column chromatography on silica-gel using 70% ethylacetate in hexanes according to general procedure H.



Yield: 69%

Mp: 291-292 °C

IR (KBr) v_{max} cm^{-1}: 3414, 2962, 2856, 2258, 1649, 1481, 1304, 1240, 1024, 825

^{1}H NMR (400 MHz, DMSO-d_6): δ 12.33 (s, 1H), 8.91 (s, 1H), 8.31-8.28 (m, 1H), 8.13 (s, 1H), 7.80 (s, 1H), 7.55 (d, *J* = 8.4 Hz, 1H), 7.43-

7.36 (m, 4H), 4.49 (q, *J* = 6.8 Hz, 2H), 1.34 (t, *J* = 6.8 Hz, 3H)

^{13}C NMR (100 MHz, DMSO-d_6): δ 163.2, 150.3, 147.1, 144.6, 140.2, 130.6, 130.5, 130.0, 129.3, 128.8, 123.0, 122.7, 121.4, 118.5, 116.1, 115.9, 113.5, 109.8, 109.5, 105.3, 37.7, 21.4, 13.8

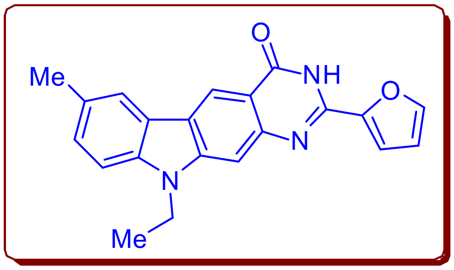
LC-MS (m/z): 372 $[M+H]^+$ positive mode

Anal. Calcd. for $C_{23}H_{18}FN_3O$: C, 74.38; H, 4.88; N, 11.31%

Found: C, 74.21; H, 4.82; N, 11.25%

10-Ethyl-2-(furan-2-yl)-7-methyl-3*H*-pyrimido[4,5-*b*]carbazol-4(10*H*)-one (228f):

The compound **228f** was obtained from **226a** and **227g** as yellow solid by column chromatography on silica-gel using 70% ethylacetate in hexanes according to general procedure H.



Yield: 57%

Mp: 248-250 °C

IR (KBr) ν_{max} cm^{-1}: 3462, 2254, 2127, 1653, 1026, 823

^{1}H NMR (400 MHz, DMSO-d_6): δ 12.25 (s, 1H), 8.89 (s, 1H), 8.12 (s, 1H), 7.99 (s, 1H), 7.79 (s, 1H), 7.61 (m, 1H), 7.54 (d, *J* = 8.8 Hz, 1H), 7.36 (d, *J* = 8.8 Hz, 1H), 6.76-6.75 (m, 1H), 4.48 (q, *J* = 6.8 Hz, 2H), 1.32 (t, *J* = 6.8 Hz, 3H)

^{13}C NMR (100 MHz, DMSO-d_6): δ 162.6, 147.0, 146.9, 146.7, 144.5, 143.2, 140.1, 129.2, 129.8, 122.8, 122.7, 121.4, 118.7, 114.2, 113.7, 112.9, 109.5, 105.2, 37.7, 21.4, 13.8

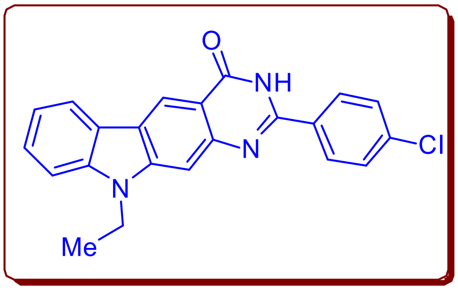
LC-MS (m/z): 344 $[M+H]^+$ positive mode

Anal. Calcd. for $C_{21}H_{17}N_3O_2$: C, 73.45; H, 4.99; N, 12.24%

Found: C, 74.21; H, 4.82; N, 11.25%

2-(4-Chlorophenyl)-10-ethyl-3*H*-pyrimido[4,5-*b*]carbazol-4(10*H*)-one (228g):

The compound **228g** was obtained from **226b** and **227d** as pale yellow solid by column chromatography on silica-gel using 70% ethylacetate in hexanes according to general procedure H.



Yield: 71%

Mp: 286-288 °C

IR (KBr) ν_{max} cm^{-1}: 3427, 2254, 2129, 1668, 1026, 999, 825

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 12.40 (s, 1H), 9.04 (s, 1H), 8.47 (s, 1H), 8.29 (d, *J* = 7.6 Hz, 1H), 8.24 (d, *J* = 8.0 Hz, 2H), 7.85 (s, 1H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.54(d, *J* = 8.4 Hz, 2H), 4.51 (q, *J* = 6.4 Hz, 2H), 1.34 (t, *J* = 6.0 Hz, 3H)

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 162.8, 147.5, 144.7, 140.4, 132.2, 130.0, 129.9, 129.2, 129.1, 128.9, 124.7, 123.9, 121.4, 119.8, 114.2, 111.3, 105.8, 31.7, 13.8

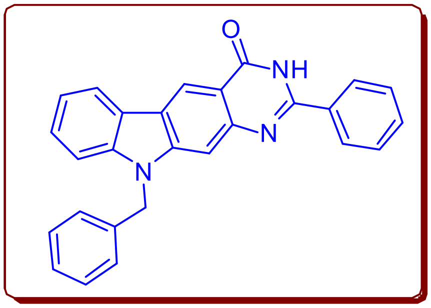
LC-MS (m/z): 373 $[M]^+$, 374 [M+1] positive mode

Anal. Calcd. for $C_{22}H_{16}ClN_3O$: C, 70.68; H, 4.31; N, 11.24%

Found: C, 70.59; H, 4.36; N, 11.28%

10-Benzyl-2-phenyl-3*H*-pyrimido[4,5-*b*]carbazol-4(10*H*)-one (228h):

The compound **228h** was obtained from **226c** and **227a** as pale yellow solid by column chromatography on silica-gel using 70% ethylacetate in hexanes according to general procedure H.



Yield: 73%

Mp: >300 ˚C

IR (KBr) ν_{max} cm^{-1}: 3499, 2253, 2127, 1651, 1028, 823, 756

^{1}H NMR (400 MHz, DMSO-d_6): δ 12.37 (s, 1H), 9.04 (s, 1H), 8.41 (d, *J* = 7.6 Hz, 2H), 8.23-8.20 (m, 1H), 7.88 (s, 1H), 7.71 (d, *J* = 8 Hz, 1H), 7.58-7.54 (m, 4H), 7.31-7.23 (m, 6H), 5.79 (s, 2H)

^{13}C NMR (100 MHz, DMSO-d_6): δ 163.2, 151.5, 147.4, 145.0, 142.6, 137.8, 133.4, 131.6, 129.1, 129.0, 128.0, 127.8, 127.7, 127.2, 123.1, 122.6, 121.7, 120.6, 118.9, 114.2, 110.2, 106.0, 46.3

LC-MS (m/z): 402 $[M+H]^+$ positive mode

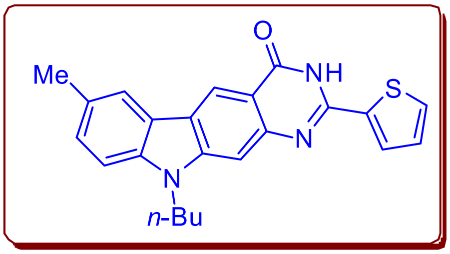
Anal. Calcd. for $C_{27}H_{19}N_3O$: C, 80.78; H, 4.77; N, 10.47%

Found: C, 80.65; H, 4.85; N, 10.36%

10-Butyl-7-methyl-2-(thiophen-2-yl)-3*H*-pyrimido[4,5-*b*]carbazol-4(10*H*)-one (228i):

The compound **228i** was obtained from **226d** and **227f** as pale yellow solid by column chromatography on silica-gel using 70% ethylacetate in hexanes according to general procedure H.

Yield: 75%



Mp: 268-270 ˚C

IR (KBr) ν_{max} cm^{-1}: 3437, 2934, 2150, 1666, 1496, 1439, 1390, 1255, 1101, 661

^{1}H NMR (400 MHz, DMSO-d_6): δ 12.41 (s, 1H), 8.87 (s, 1H), 8.21 (s, 1H), 8.01 (s, 1H), 7.84 (d, J = 5.2 Hz, 1H), 7.70 (s, 1H), 7.51 (d, J = 8.4 Hz, 1H), 7.34 (d, J = 7.6 Hz, 1H), 7.23 (s, 1H), 4.43 (t, J = 6.8 Hz, 2H), 1.76-1.73 (m, 2H), 1.34-1.28 (m, 2H), 0.87 (t, J = 7.2 Hz, 3H)

^{13}C NMR (100 MHz, DMSO-d_6): δ 162.8, 147.0, 146.9, 145.0, 140.6, 138.3, 132.1, 129.3, 129.2, 128.9, 128.7, 122.6, 122.5, 121.3, 118.7, 113.4, 109.7, 105.0, 42.8, 30.9, 21.4, 20.2, 14.2

LC-MS (m/z): 388 $[M+H]^+$ positive mode

Anal. Calcd. for $C_{23}H_{21}N_3SO$: C, 71.29; H, 5.46; N, 10.84%

Found: C, 71.35; H, 5.41; N, 10.96%

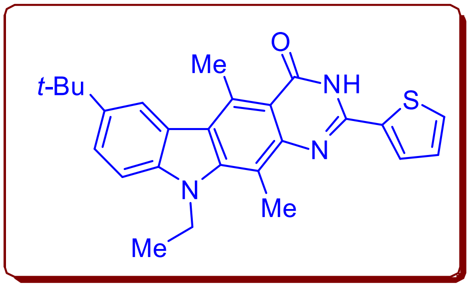
7-*t*-Butyl-10-ethyl-5,11-dimethyl-2-(thiophen-2-yl)-3*H*-pyrimido[4,5-*b*]carbazol-4(10*H*)-one (228j):

The compound **228j** was obtained from **226e** and **227f** as pale yellow solid by column chromatography on silica-gel using 70% ethylacetate in hexanes according to general procedure H.

Yield: 51%

Mp: 173-174 ˚C

IR (KBr) ν_{max} cm^{-1}: 3429, 2254, 2129, 1660, 1028, 825



^{1}H NMR (400 MHz, DMSO-d_6): δ 12.20 (s, 1H), 8.28 (s, 1H), 8.21-8.20 (m, 1H), 7.83-7.82 (m, 1H), 7.62-7.61 (m, 2H), 7.24-7.22

(m, 1H), 4.70 (q, *J* = 6.4 Hz, 2H), 3.45 (s, 3H), 3.08 (s, 3H), 1.43 (s, 12H)

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 164.3, 146.0, 145.2, 142.8, 140.9, 138.7, 134.4, 131.8, 128.99, 128.91, 124.5, 23.3, 122.6, 119.7, 114.9, 113.0, 112.2, 109.3, 34.8, 32.2, 18.5, 15.7, 14.4

LC-MS (m/z): 428 (M-H) negative mode

Anal. Calcd. for $C_{26}H_{27}N_3OS$: C, 72.69; H, 6.34; N, 9.78%

Found: C, 72.56; H, 6.31; N, 9.65%

General procedure I

General procedure for synthesis of compounds (231a-b).

A schlenk tube was charged with a magnetic pellet, evacuated and back-filled with nitrogen. Substituted 2-bromo-9*H*-carbazole-3-carbonyl chloride **229a-b** (0.28 mmol), pyridin-2-amine **230** (0.28 mmol), K_2CO_3 (0.85 mmol), and toluene (2.0 mL) were added. After a 10 min stirring at room temperature under nitrogen atmosphere, charge $Pd(OAc)_2$ (0.5 mol %) and CuI (5 mol %) The mixture was stirred at 110 °C for 10 h under nitrogen atmosphere. After completion of the reaction work up, the residue was recrystallized from ethyl acetate/hexane (5:5) to afford the desired product.

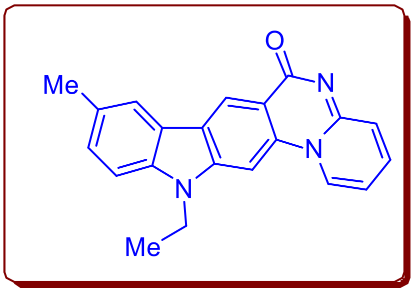
12-Ethyl-9-methyl pyrido[2',1':2,3]pyrimido[4,5-*b*]carbazol-6(12*H*)-one (231a):

The compound **231a** was obtained from **229a** and **230** as pale yellow solid by column chromatography on silica-gel using 50% ethylacetate in hexanes according to general procedure I.

Yield: 70%

Mp: 269-270 °C

IR (KBr) ν$_{max}$ cm^{-1}: 3096, 3018, 2966, 1672, 1527, 1423,

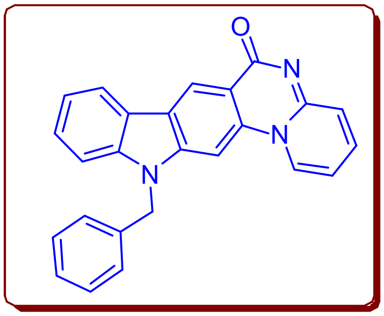


1304, 1234, 1124, 829

^{1}H NMR (400 MHz, CDCl$_3$):	δ 9.15 (s, 1H), 8.93-8.91 (m, 1H), 8.02 (s, 1H), 7.61 (s, 1H), 7.48-7.47 (m, 2H), 7.38-7.30 (m, 2H), 6.82-6.81 (m, 1H), 4.39 (q, *J* = 7.6 Hz, 2H), 2.57 (s, 3H), 1.49 (t, *J* = 7.2 Hz, 3H)
^{13}C NMR (100 MHz, CDCl$_3$):	δ 159.5, 147.0, 146.6, 145.6, 140.3, 133.6, 129.6, 128.4, 126.8, 125.7, 123.6, 123.0, 121.2, 119.6, 111.3, 109.3, 108.2, 102.0, 38.0, 21.3, 13.3
LC-MS (m/z):	328 $(M+H)^+$ positive mode
Anal. Calcd. for $C_{21}H_{17}N_3O$:	C, 77.04; H, 5.23; N, 12.84%
Found:	C, 77.15; H, 5.19; N, 12.75%

12-Benzylpyrido[2',1':2,3]pyrimido[4,5-*b*]carbazol-6(12*H*)-one (231b):

The compound **231b** was obtained from **229b** and **230** as pale yellow solid by column chromatography on silica-gel using 50% ethylacetate in hexanes according to general procedure H.



Yield:	58%
Mp:	283-284 °C
IR (KBr) ν_{max} cm^{-1}:	2924, 1635, 1531, 1431, 1253, 1084, 1018, 802
^{1}H NMR (400 MHz, CDCl$_3$):	δ 8.41-8.40 (m, 1H), 8.38 (s, 1H), 8.26 (d, *J* = 6.0 Hz, 1H), 8.00 (s, 1H), 7.96 (s, 1H), 7.67-7.64 (m, 4H), 7.53-7.47 (m, 4H), 7.29-7.22 (m, 1H), 7.13-7.10 (m, 1H), 5.72 (s, 2H)

^{13}C NMR (100 MHz, CDCl$_3$): δ 170.4, 148.4, 141.1, 138.6, 136.2, 129.9, 127.7, 126.9, 126.6, 126.2, 122.4, 122.3, 120.7, 120.6, 120.1, 119.7, 119.4, 115.8, 114.1, 112.8, 112.3, 109.3, 108.8, 46.7

LC-MS (m/z): 376 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{25}H_{17}N_3O$: C, 79.98; H, 4.56; N, 11.19%

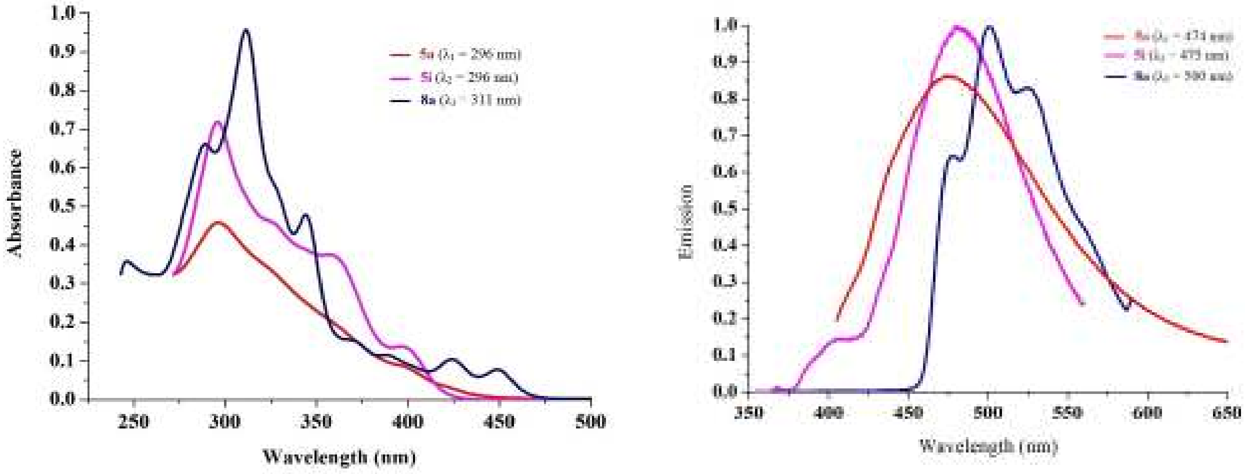
Found: C, 79.83; H, 4.61; N, 11.09%

Photo-physical properties of the compounds 228a, 228i and 231a:

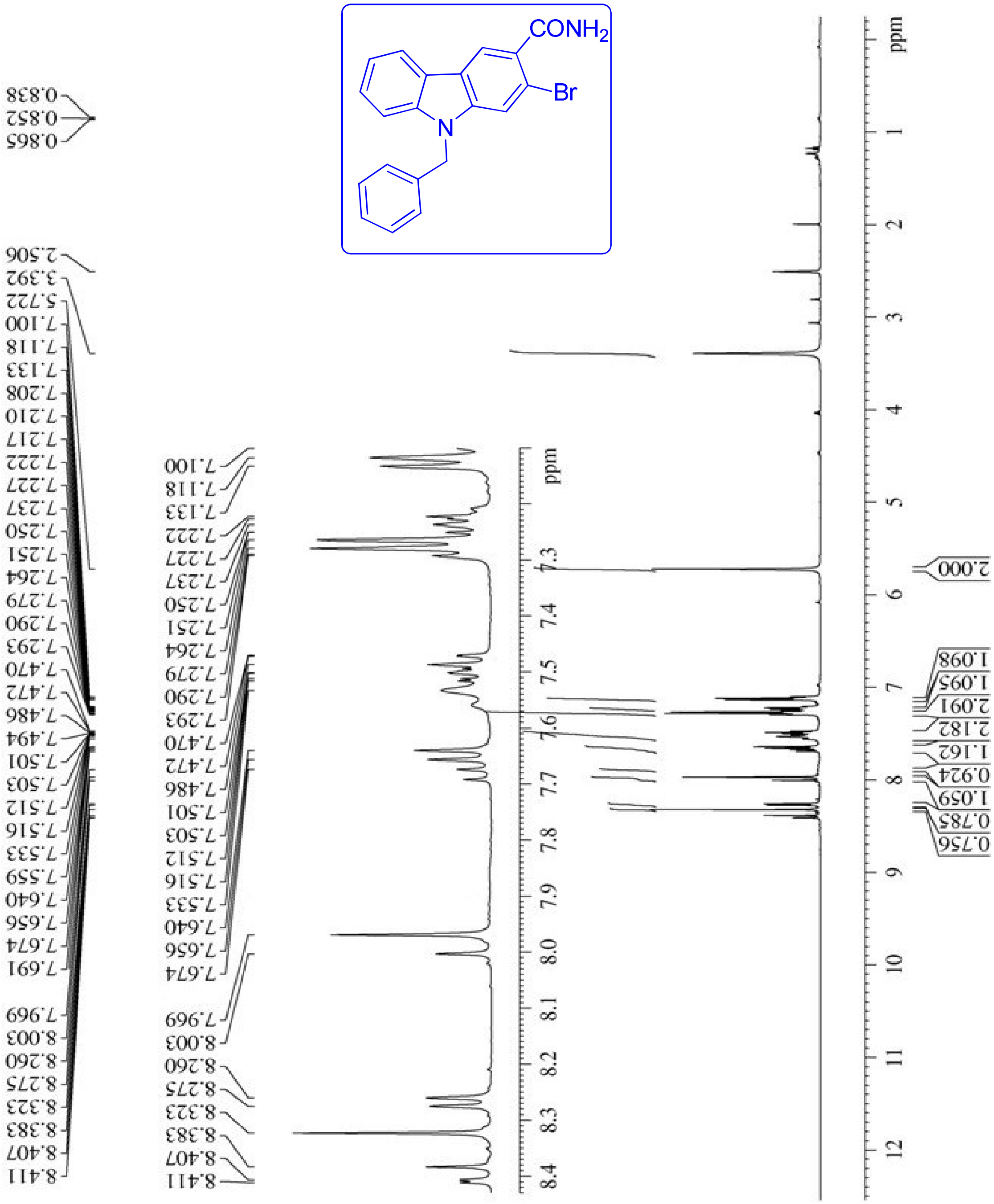
Figure 17 Compounds **228a**, **228i** in DMSO and **231a** in Chloroform (from left to right).


Visible region
UV region

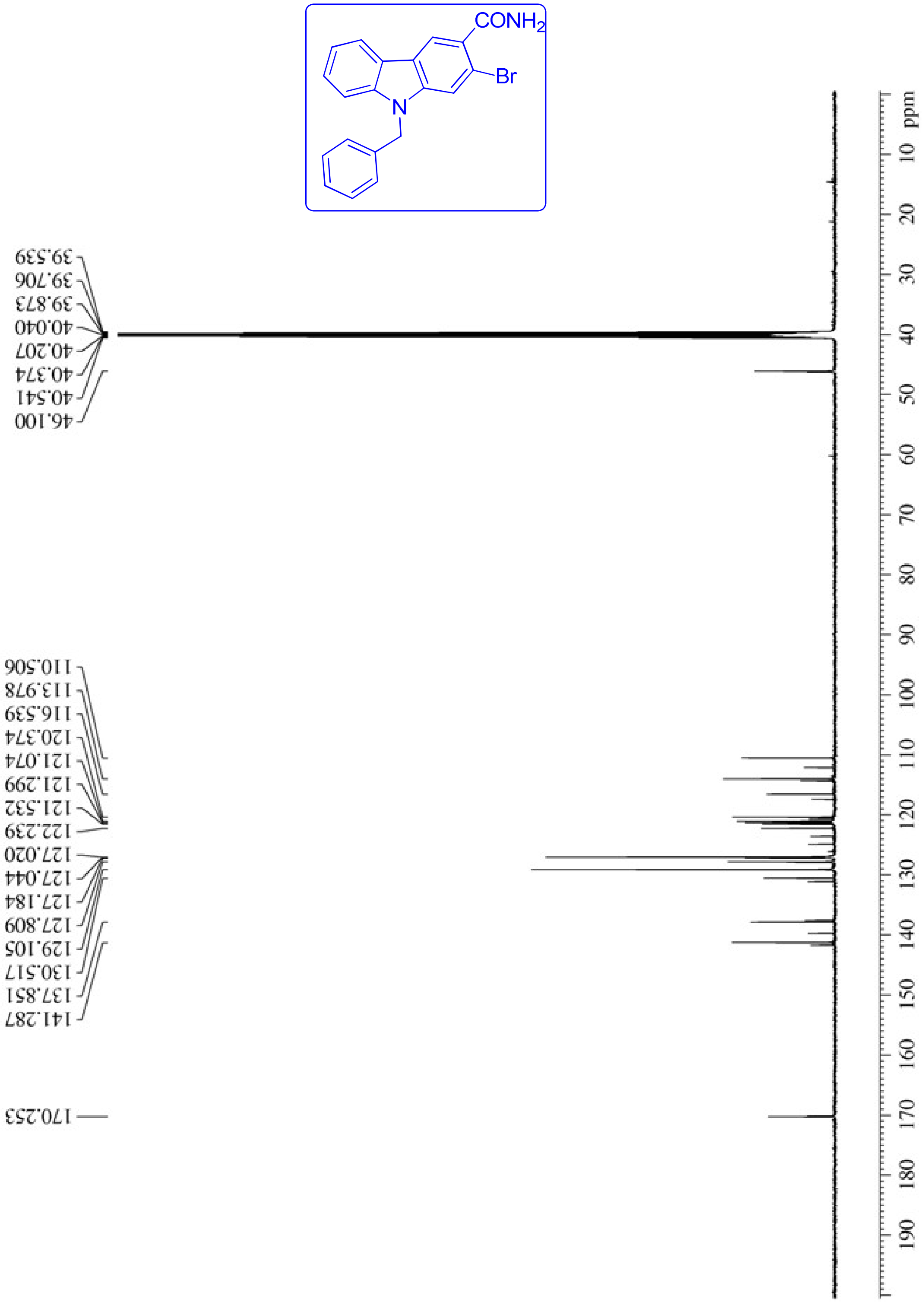
Figure 18 Absorption and Emission spectra of **228a**, **228i** recorded in DMSO and **231a** in Chloroform.



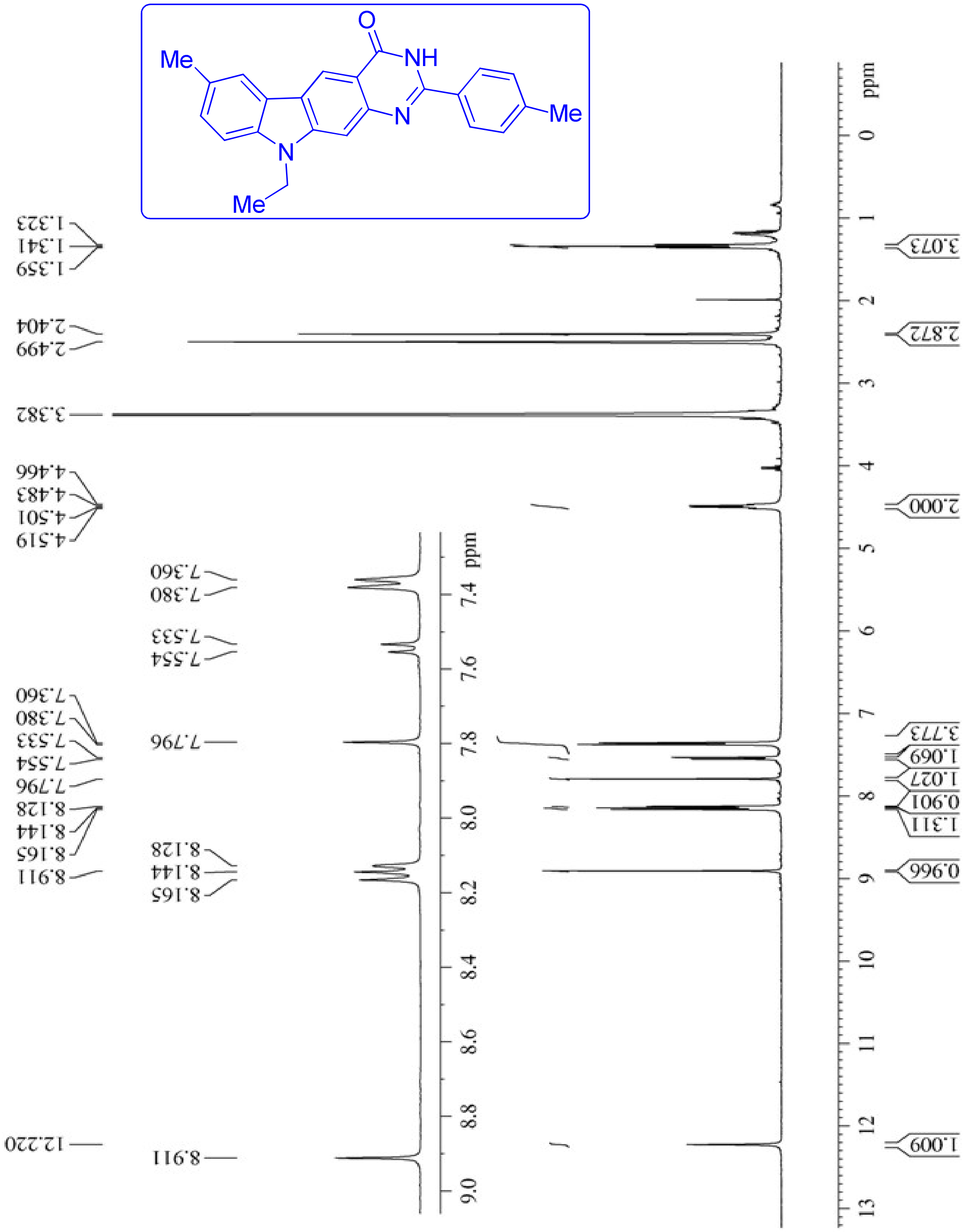
Spectrum 15. ^{1}H NMR of 226c



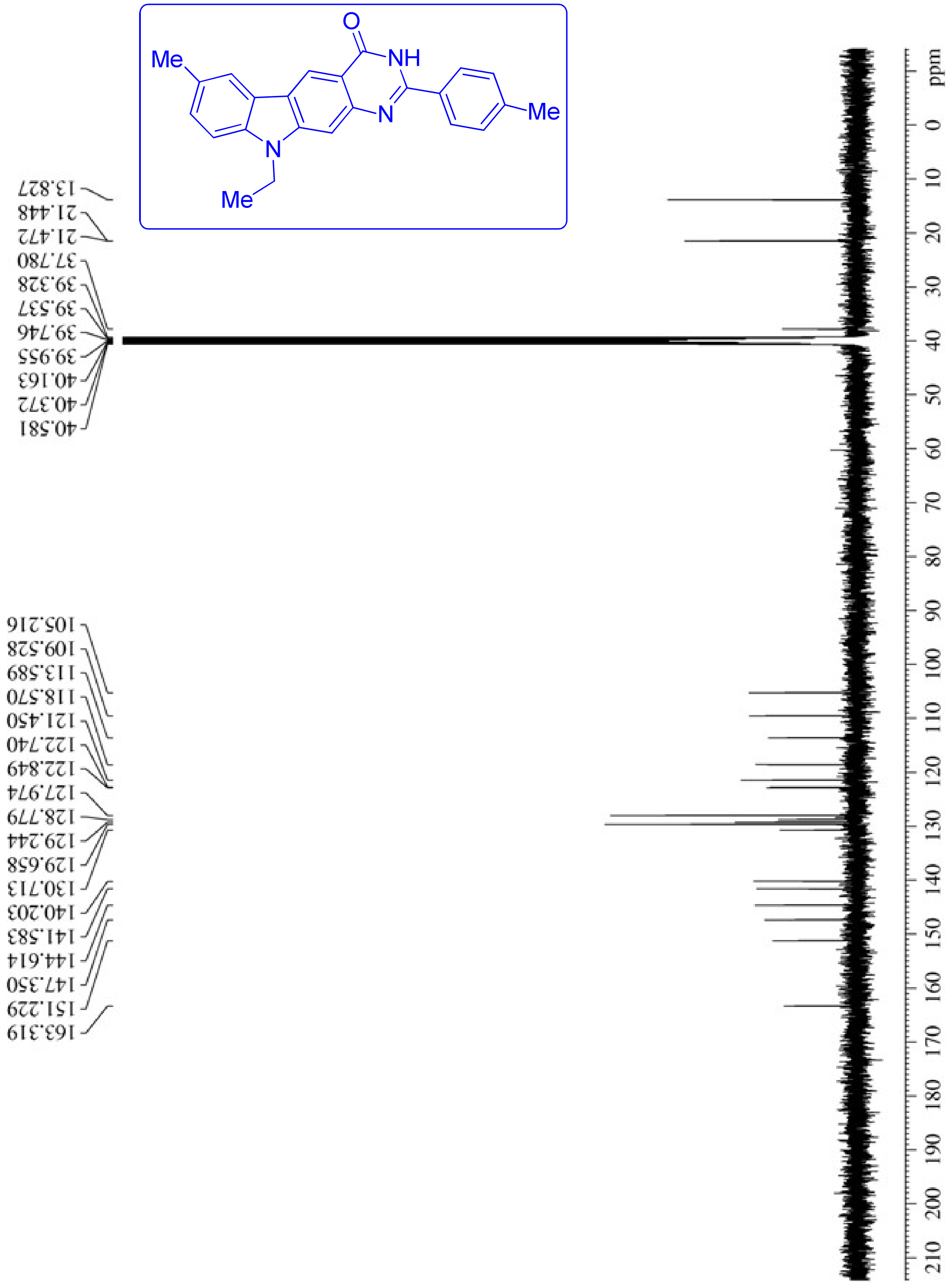
Spectrum 16. ^{13}C NMR of 226c



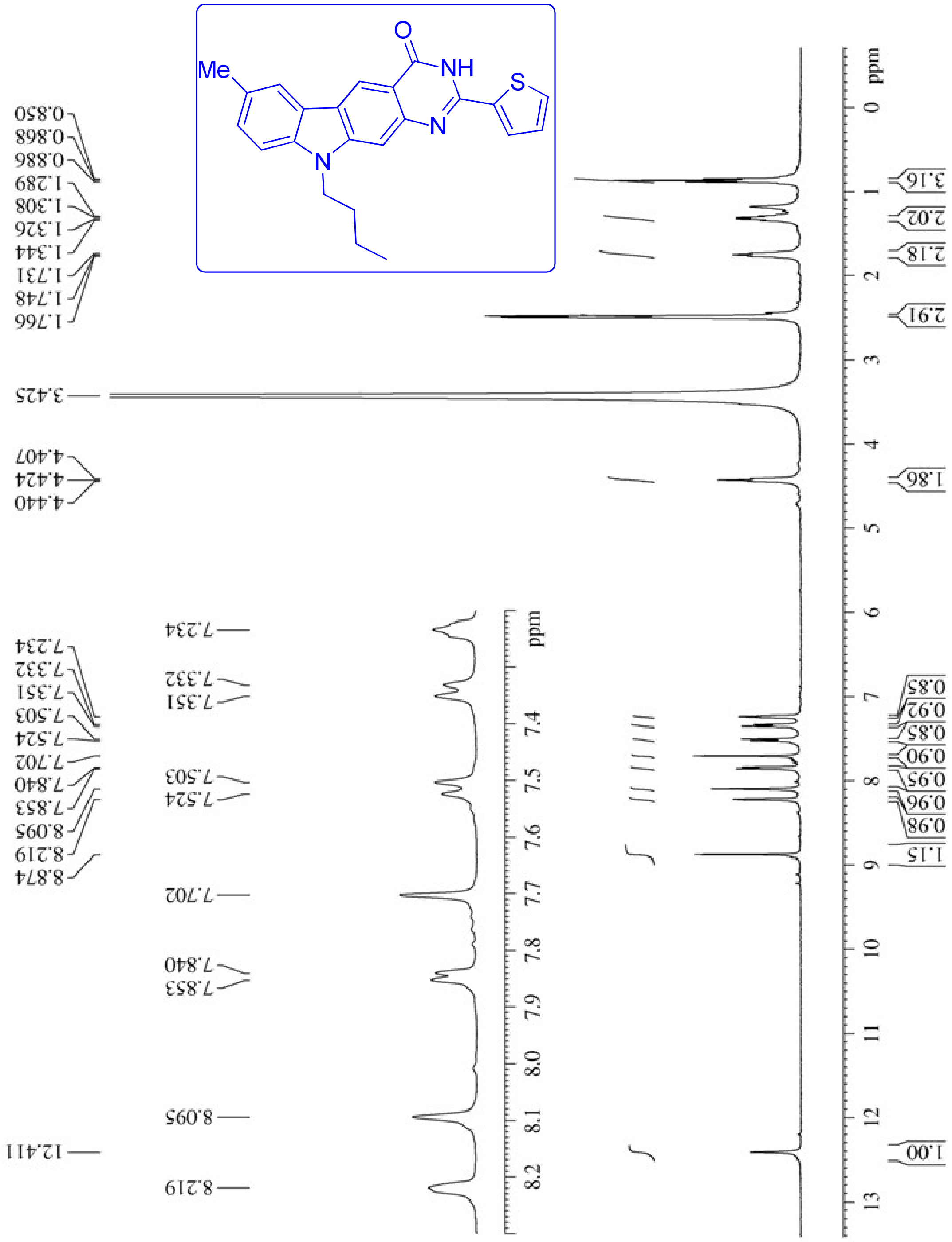
Spectrum 17. ^{1}H NMR of228c



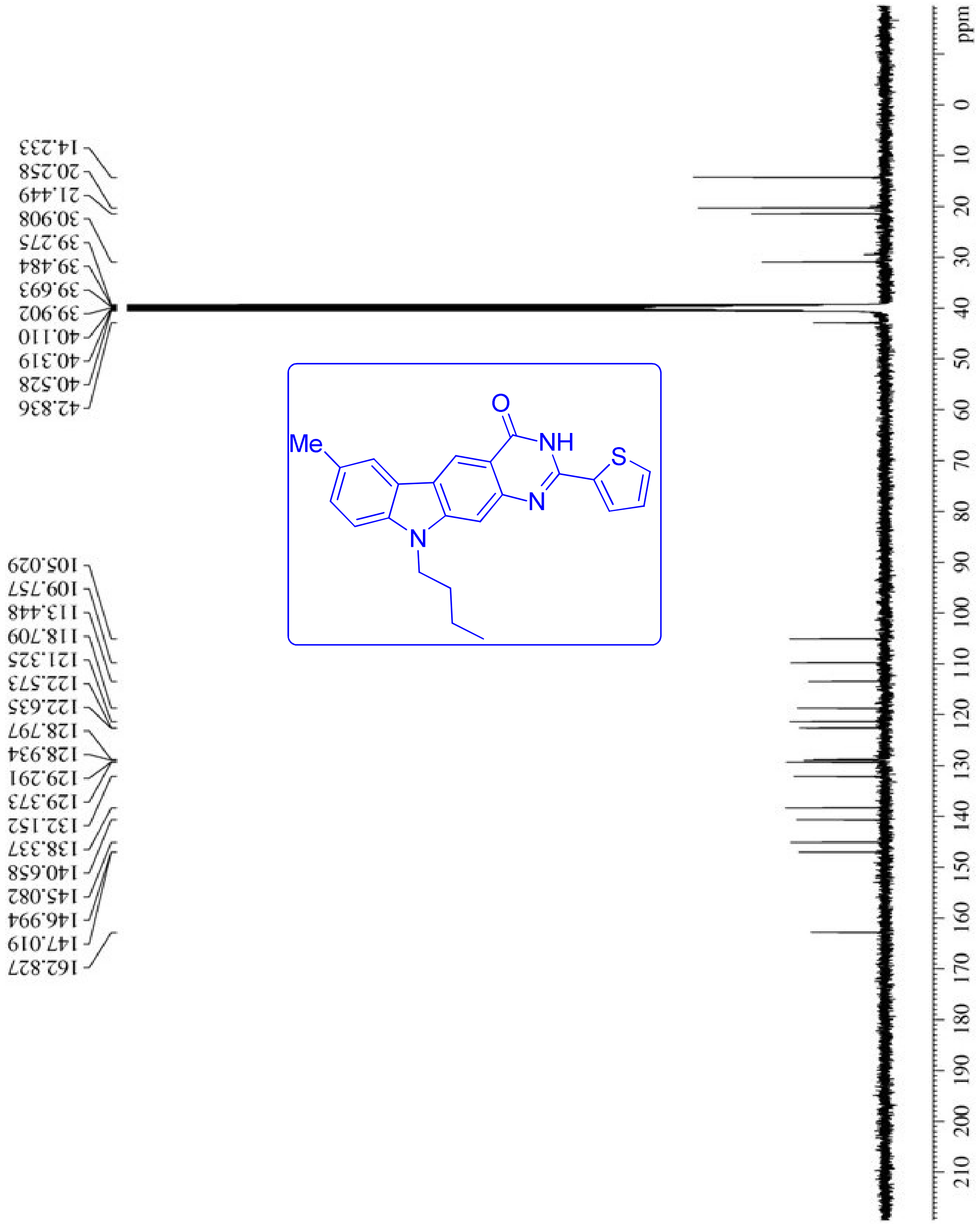
Spectrum 18. ^{13}C NMR of 228c



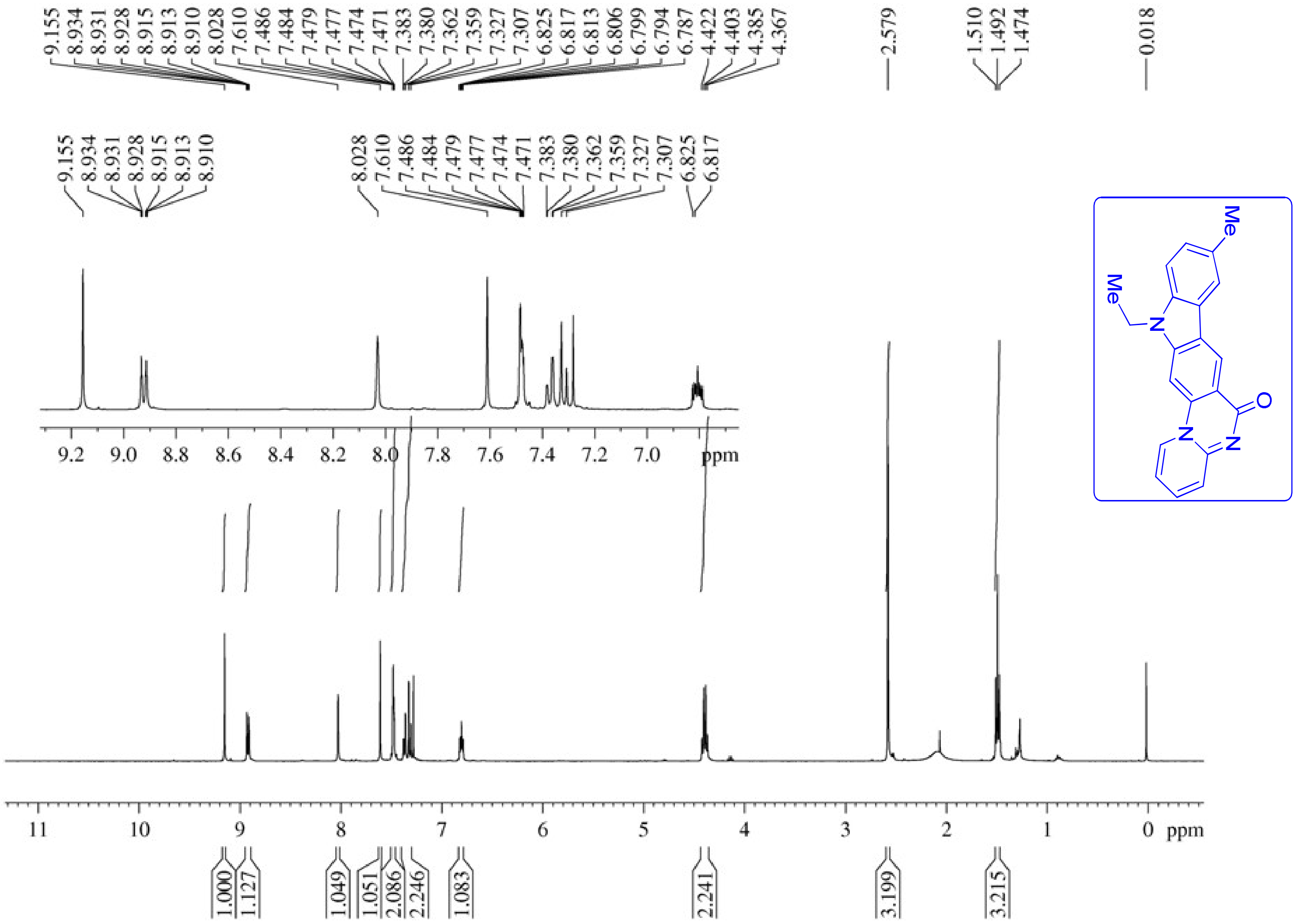
Spectrum 19. ^{1}H NMR of 228i



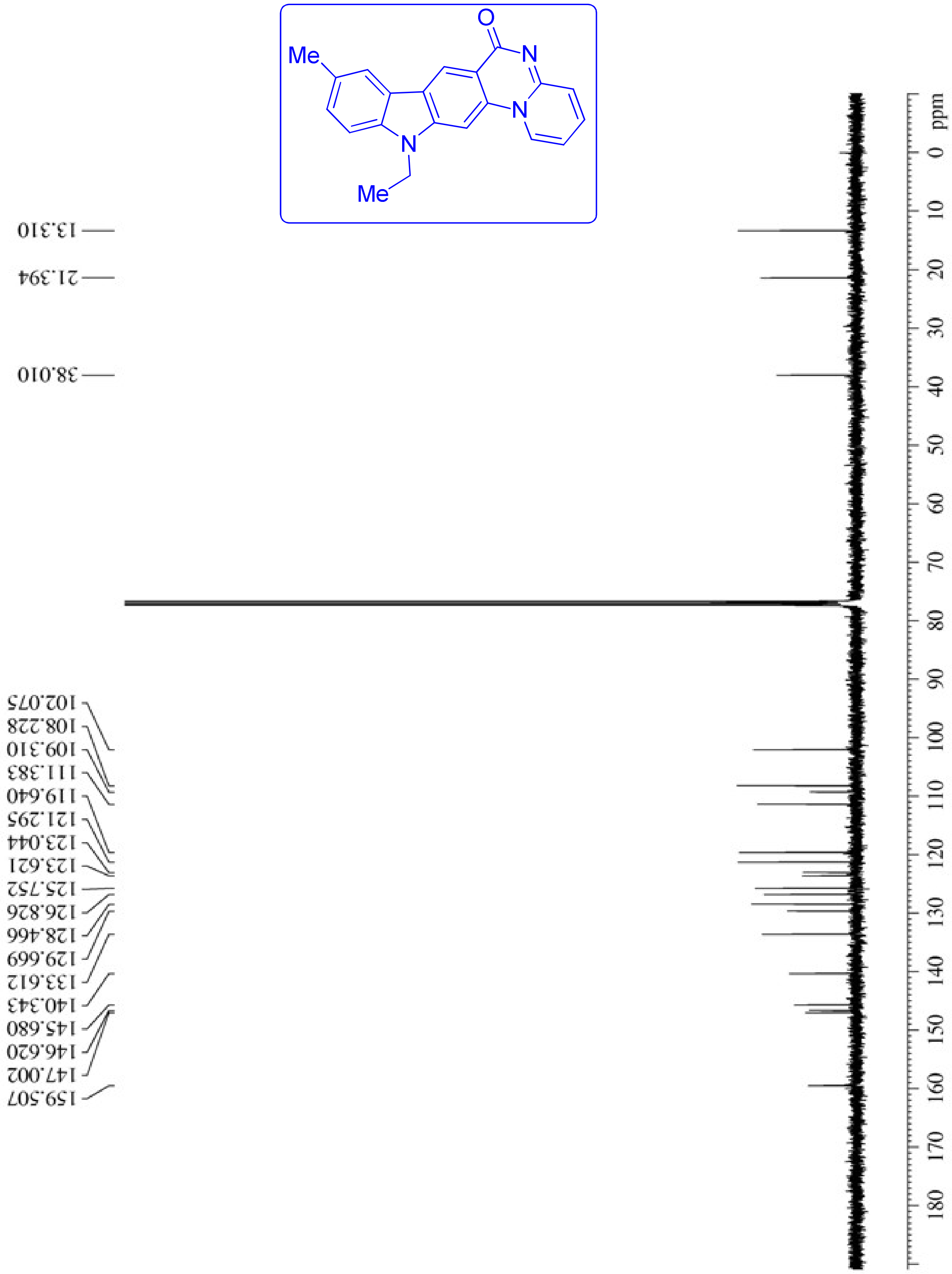
Spectrum 20. ^{13}C NMR of 228i



Spectrum 21. ^{1}H NMR of 231a



Spectrum 22. ^{13}C NMR of 231a



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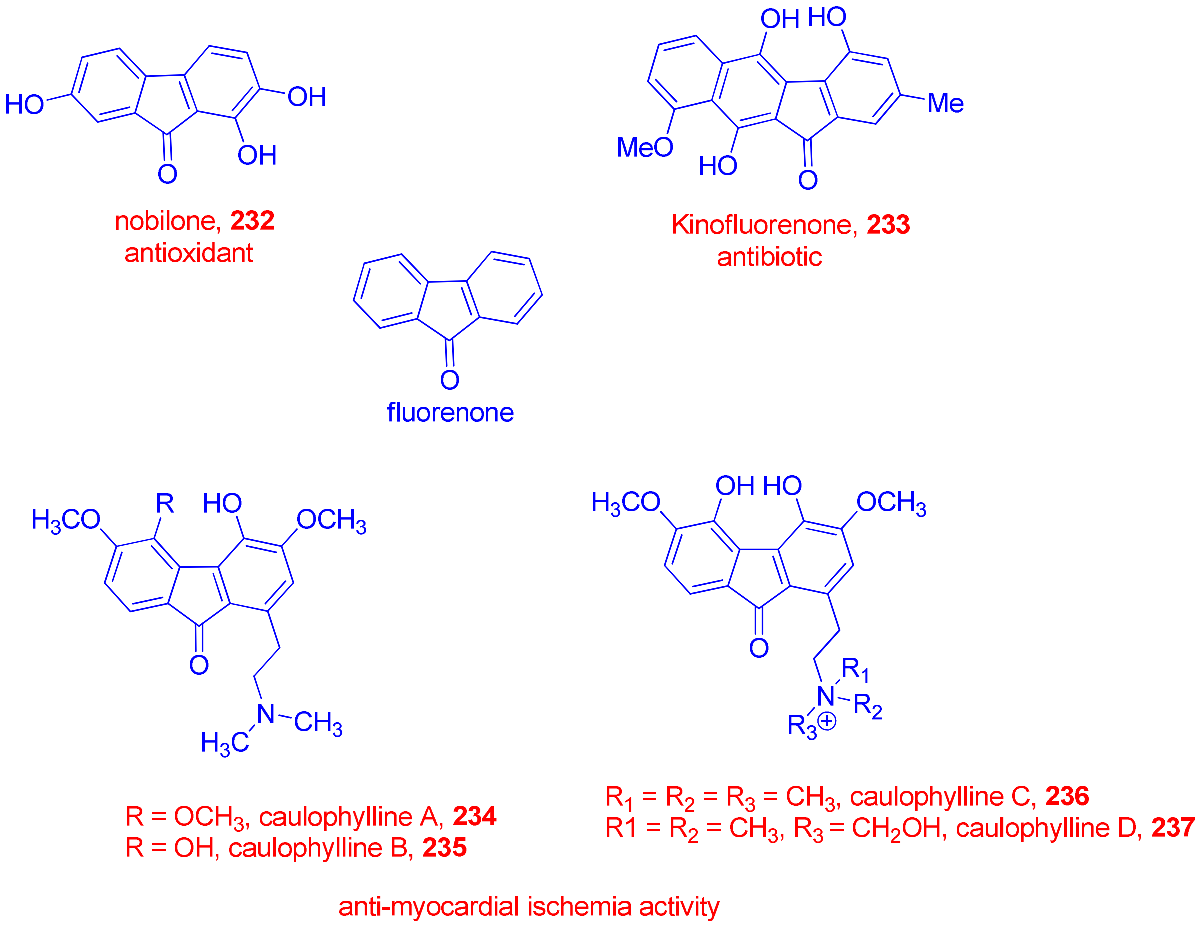
Highly Regioselective Synthesis of Indenocarbazolones via Palladium-Catalyzed Intramolecular *ortho*-Arylation

CHAPTER 3

3.1. Introduction:

Fluorenone has been found in many natural products such as dengibsin, dengibsinin, dendroflorin, kinofluorenone, kinobscurinone and caulophyline A-D showing a range of biological activities[138] as shown in Figure 16.

Figure 16



nobilone, **232**
antioxidant

Kinofluorenone, **233**
antibiotic

fluorenone

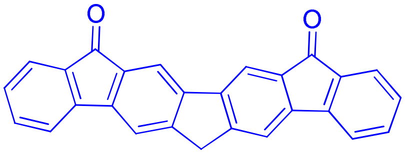
R = OCH_3, caulophylline A, **234**
R = OH, caulophylline B, **235**

$R_1 = R_2 = R_3 = CH_3$, caulophylline C, **236**
R1 = $R_2 = CH_3$, $R_3 = CH_2OH$, caulophylline D, **237**

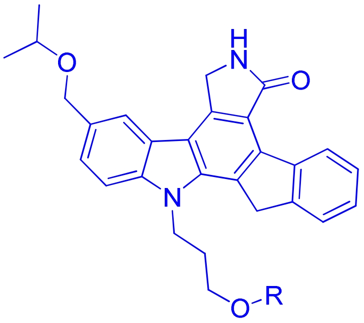
anti-myocardial ischemia activity

Moreover, carbazole and its fused derivatives have attracted great attention from medicinal and synthetic chemists due to their wide range of biological applications. In addition to their use in medicinal chemistry,[139-140] fused heterocycles (Figure 17) such as heteroarylcarbazoles have attracted increasing attention from the community of material scientists owing to their potential in photophysical and optoelectronic (OLEDs, PLEDs) applications.[141-146]

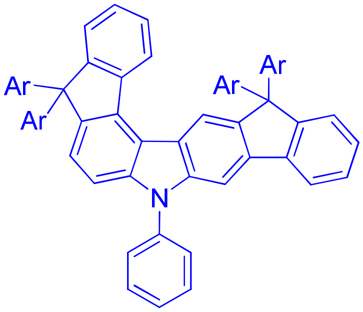
Figure 17



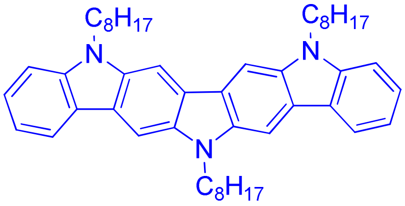
Bisindenofluorene
(Optical and Electrochemical)
111



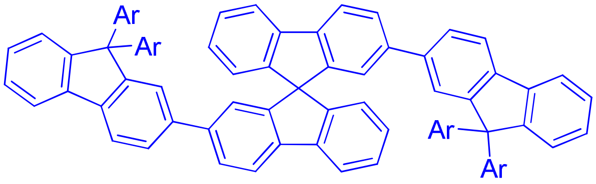
CEP-7055 R = COCH$_2$N(CH$_3$)$_2$
CEP-5214 R = H
112



Bisindenocarbazole
Ar = 4-CH$_3$Ph
113



238
semiconducting material

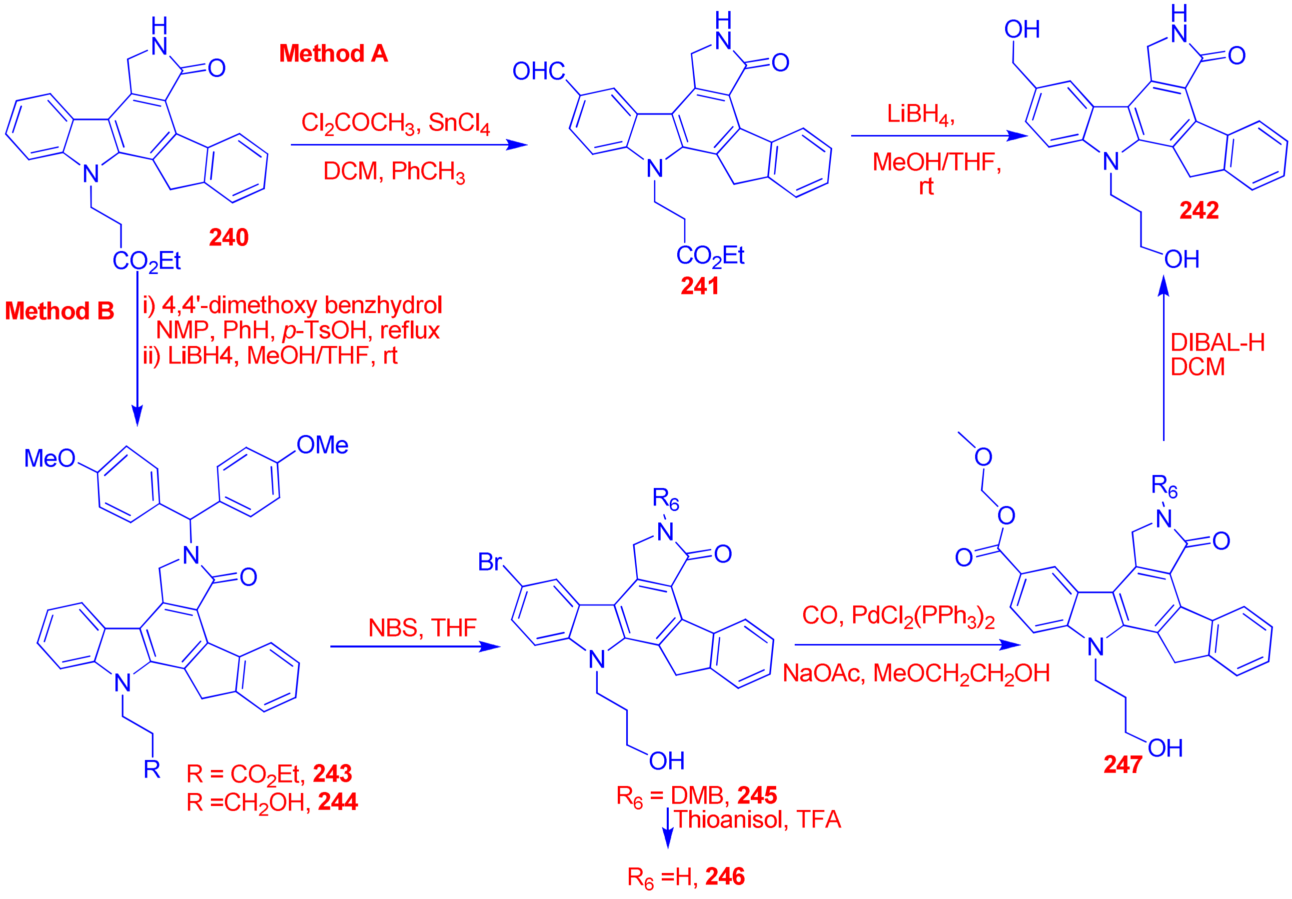


239
OLEDs

Hudkins *et al*. reported[147] a series of potent vascular endothelial growth factor R2 (VEGF-R2) tyrosine kinase inhibitors from a new indenopyrrolocarbazole. Angiogenesis, the generation and growth of new blood vessels from the endothelium of an existing vascular network, is an essential event in a variety of physiological and pathological processes.[148-150] Vascular endothelial growth factor (VEGF) is a key mediator of angiogenesis. Due to importance of these type of molecules he reported starting from indenopyrrolocarbazole, **240** in method A, formylation of **240** with *R*,*R*-dichloromethyl methyl ether and tin(IV) chloride produced aldehyde **241** in 79% yield, which was reduced to **242** using lithium borohydride in a THF/methanol solution (96% yield).In another way i.e method B they elevated the preparation of **242** as protection of ester **240** with 4,4′-dimethoxybenzhydrol **243** & **244** (NMP/benzene, *p*-TsOH), LiBH$_4$ reduction to propanol **245**, using bromination with NBS in THF. Removal of the DMB group to **246** (TFA, anisole, methylene chloride).

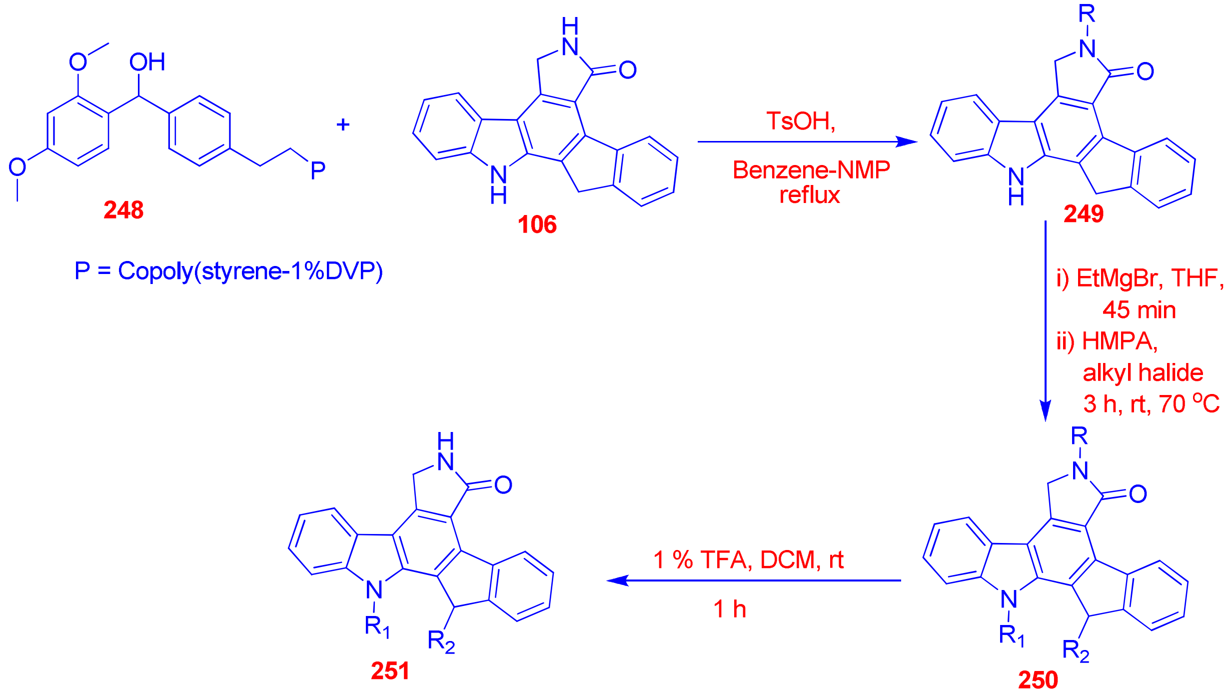
Then treated with, carbon monoxide, and $PdCl_2(PPh_3)_2$ catalyst in methoxyethanol at 155 °C in a sealed tube produced the DMB protected methoxyethoxy ester **247** in 85% yield followed by diisobutylaluminum hydride reduction of the ester gave diol **242** as shown in Eq. 38.

Eq. 38



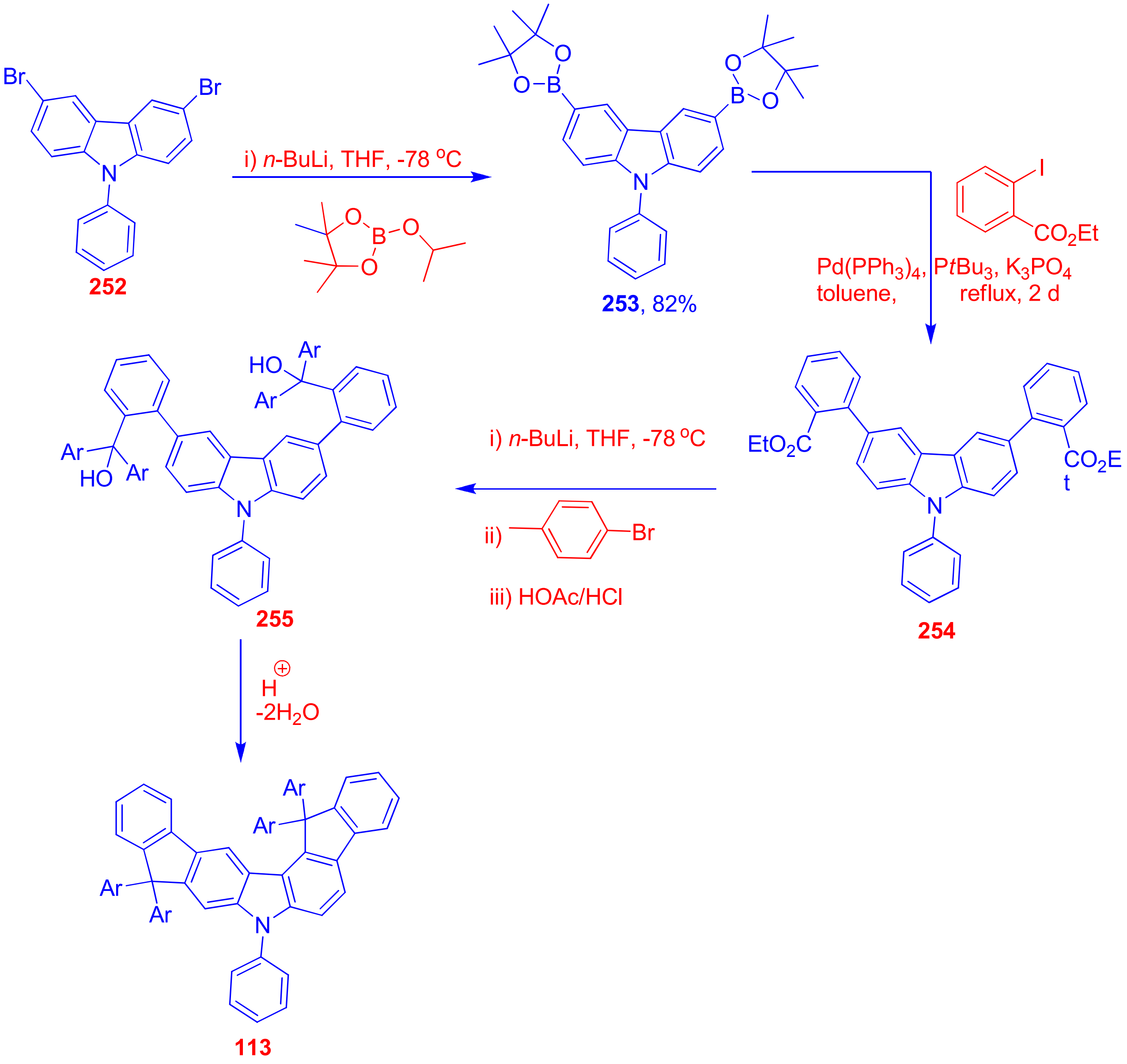
With the emergence of natural product based combinatorial synthesis in recent years, Tripathy *et al*. (eq. 39)[151] envisioned that parallel synthesis could be a viable approach to generate potent and specific kinase inhibitors strating from indenocarbazole with Rink **248** acid resin in a mixture of solvents with *p*-TsOH obtained **249** treated with ethylmagnesiumbromide and then alkylation HMPA gives **250**. On treatment with 1% TFA in dichloromethane gives the final compound **251**.

Eq. 39



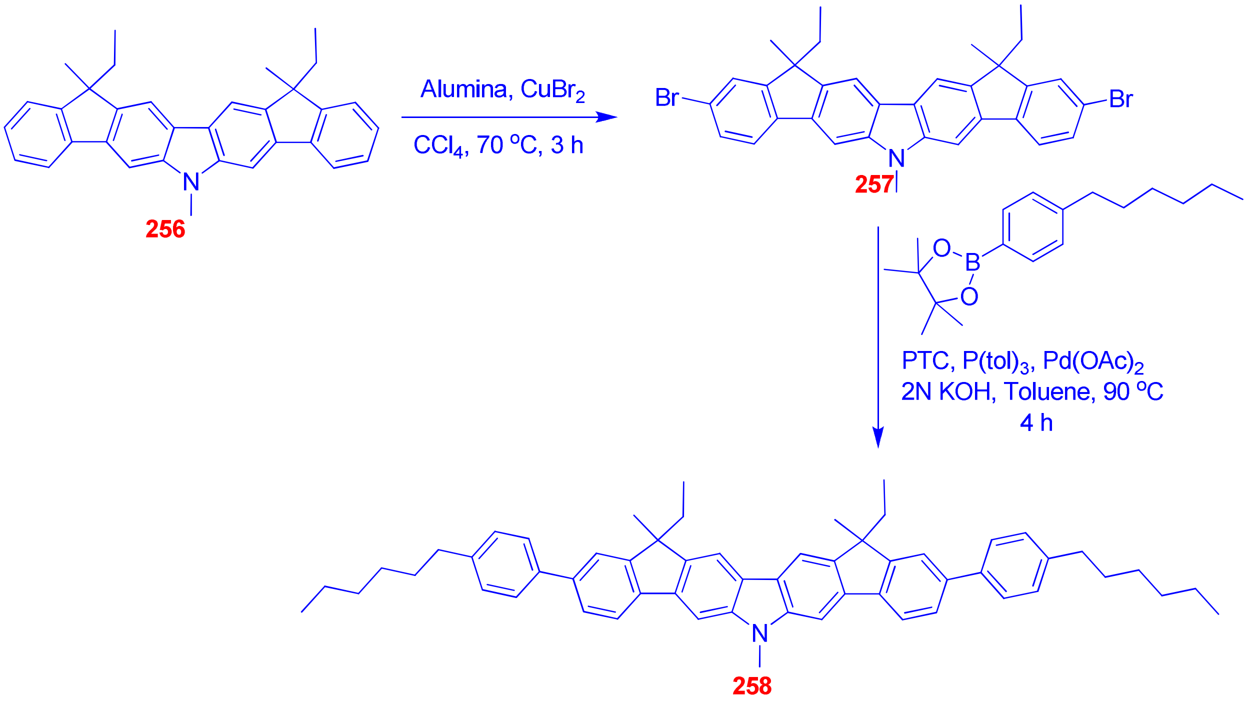
Recently, interesting carbazole-based coplanar molecules were reported that featured phenylene substituents at the C2 and C7 positions of their carbazole units. Carbazole-based conjugated oligomers and polymers are often used as hole-transporting materials, as well as host materials,[152] in organic light-emitting devices (OLEDs). Much research effort has been exerted toward the realization of carbazole derivatives for optoelectronic applications. With these applications Wong *et al*. reported[153] the synthesis of bisindenocarbazoles starting from 3,6-dibromo-9-phenylcarbazole **252** with *n*-BuLi at -78 °C, followed by quenching of the dilithiated intermediate with 2-isopropoxy-4,4,5,5-tetramethyl-[1,3,2]-dioxaborolane, to obtain the bis(pinacol boronate) **253** in 82% yield. Suzuki coupling of the diboronate **253** with ethyl 2-iodobenzoate afforded the diester **254** in excellent yield (92%). Subsequent double addition of aryl lithium onto the ester groups of **254**, followed by acid-mediated intramolecular annulation, gave the novel coplanar carbazole-cored chromophore **113** having two bridging carbon atoms attached to the C4 and C7 positions, respectively, of the central carbazole moiety as shown in Eq. 40.

Eq. 40



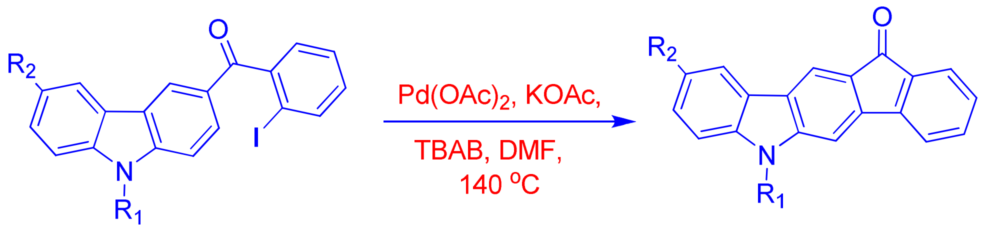
Strohrieg *et al*. bisindenocarbazoles, which are a new class of fused aromatic heterocycles with different alkyl side chains shows the various thermal properties can be tailored ranging from crystalline materials to molecular glasses. Preparation of these compounds starting from **256** alumina-supported copper(II) bromide in carbon tetrachloride obtained **257** on treatment with with *n*-BuLi and 2-iso-propoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in dry THF under palladium catalyzed Suzuki crosscoupling reaction furnished the final product **258** as shown in eq. 41.[154] These derivatives which also exhibit blue fluorescence.

Eq. 41



3.2. Synthesis of Indenocarbazolone derivatives:

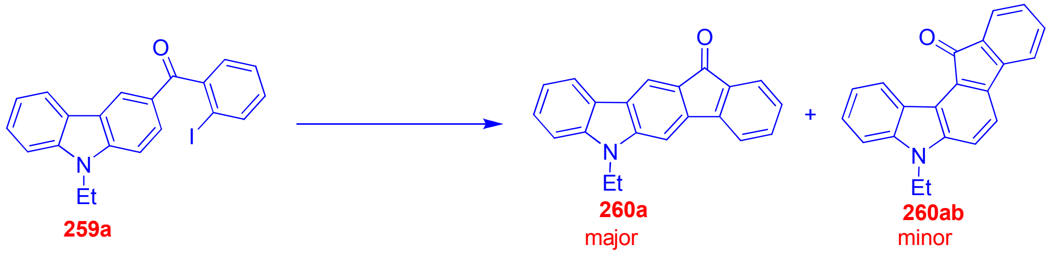
Considering pharmalogical as well as photophysical properties, as we have seen in the above literature reports, a careful analysis of literature disclosed that no reports were available for the synthesis of the indenocarbazolones. Therefore, we explored the synthetic methodology for the synthesis of indenocarbazolones. Herein, we wish to report the synthesis of indenocarbazolone derivatives starting with various carbazolyliodophenylmethanone derivatives through palladium catalyzed *ortho*-arylation as shown in Scheme 11.



Scheme 11. Schematic representation of our work

(9-Ethyl-9*H*-carbazol-3-yl)(2-iodophenyl)methanone which was synthesized from *N*-ethylcarbazole and 2-iodobenzoyl chloride by Friedel-Crafts acylation was used as model substrate for optimizing the reaction conditions. The influence of catalyst, ligand, additive, solvent, and temperature in the reaction outcome were examined as shown in Table 19. Initially we performed the reaction with $Pd(OAc)_2$ as catalyst, and PPh_3, TBAB, KOAc in toluene were unsuccessful. (entry 1, Table 19). By changing different solvents with different bases using various catalysts such as $Pd(OAc)_2$, $Pd(PPh_3)_4$, $Pd(PPh_3)_2Cl_2$ and $PdCl_2$ two regioisomers **260a** as major and **260ab** as minor were obtained (entry 3-7, Table 19). Of the various solvents which were tested for the reaction, DMF was found to be the most effective. Furthermore, different bases such as KOAc, Ag_2CO_3, and K_2CO_3 were tested in the reaction; it was found that KOAc was superior to the other bases. Ligand had no effect on the reaction, without ligand the reaction proceeded well within 3 h (entry 9, Table 19). Different additives such as TBAB, LiCl, SDS, and TBAI were tested in the reaction; 1.0 equiv of TBAB was suitable for the reaction (entry 9, Table 19). Amongst the various catalysts that were tested $Pd(OAc)_2$ produced the best yields. No reaction occurred below 110 $^{\circ}$C. After careful screening, the best reaction condition was found to involve 5 mol % of $Pd(OAc)_2$, 1.0 equiv. of TBAB, and 2.0 equiv. of KOAc in DMF at 140 $^{\circ}$C furnishing **260a** in good yield with high regioselectivity (entry 9, Table 19).

Table 19. Optimization conditions for the conversion 259a to 260a and 260ab[a]

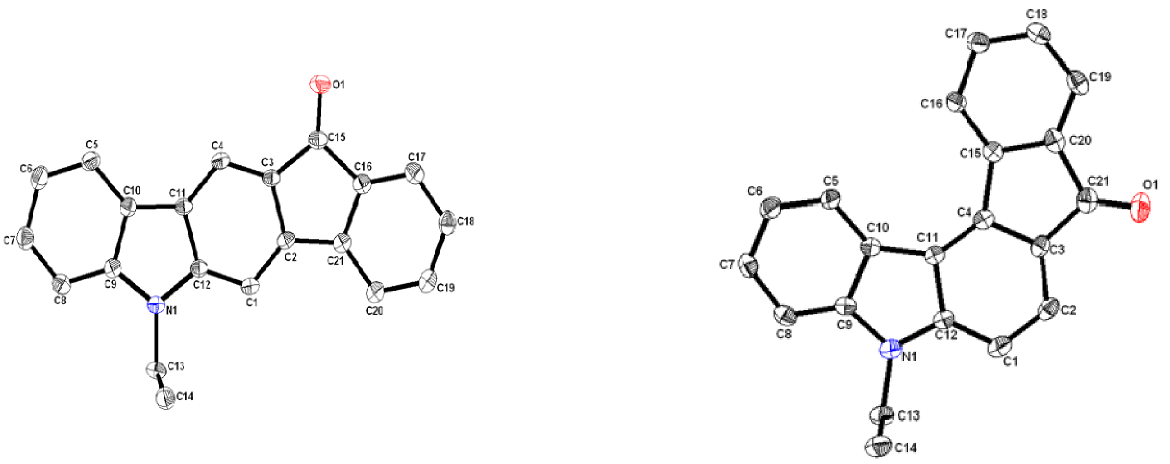


Entry	Catalyst	Ligand	Additive	Base	Solvent	Temp (°C)	Time (h)	Yield(%)[d]	
								259a:	**260ab**
1	$Pd(OAc)_2$	PPh_3	TBAB	KOAc	Toluene	140	12	nr[c]	
2	$Pd(OAc)_2$	PPh_3	TBAI	K_2CO_3	DMA	130	8	25	03
3	$Pd(OAc)_2$	PPh_3	TBAB	K_2CO_3	DMSO	130	12	20	03
4	$Pd(OAc)_2$	PPh_3	TBAB	Ag_2CO_3	DMF	140	24	nr[c]	
5	$Pd(PPh_3)_4$	PCy_3	TBAB	KOAc	DMF	110	12	15	04
6	$Pd(PPh_3)_2Cl_2$	PCy_3	TBAB	KOAc	DMF	120	12	15	05
7	$PdCl_2$	PCy_3	TBAB	KOAc	DMF	120	18	15	05
8	$Pd(OAc)_2$	-	TBAB	KOAc	DMF	120	8	62	03
9	**$Pd(OAc)_2$**	**-**	**TBAB**	**KOAc**	**DMF**	**140**	**3**	**68**	**00**
10	-	PPh_3	TBAB	KOAc	DMF	140	24	nr[c]	
11	$Pd(OAc)_2$	-	-	KOAc	DMF	140	12	60	05
12	$Pd(OAc)_2$	-	TBAB	KOAc	NMP	130	5	55	08
13	$Pd(OAc)_2$	-	LiCl	KOAc	DMF	140	4	50	10
14	Pd/C[b]	-	TBAB	KOAc	TEG	150	24	nr[c]	
15	$Pd(OAc)_2$	-	TBAB	K_2CO_3	DMF	130	6	58	08
16	$Pd(OAc)_2$	-	SDS	K_2CO_3	DMF	140	5	50	08

[a] Unless otherwise stated all reactions are carried out using 5 mol % catalyst, 15 mol % ligand, 1.0 equiv additive, 2.0 equiv of base [b] Pd/C used 10 mol %. [c] No reaction. [d] isolated yield.

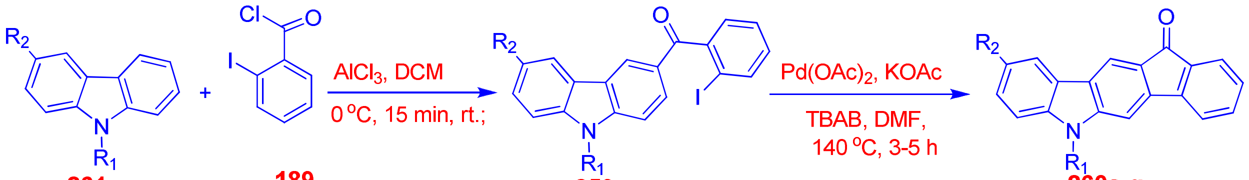
The two regioisomers **260a** and **260ab** were characterized by their ^{1}H NMR spectra. In the ^{1}H NMR spectrum of **260a**, two singlets were observed at δ 8.39 and δ 7.42 where as for **260ab** clearly two doublets at δ 8.81 and δ 8.71 were observed. The two regioisomers were further confirmed by the single crystal X-ray analysis. The ORTEP diagrams are shown in Figure 18.[155]

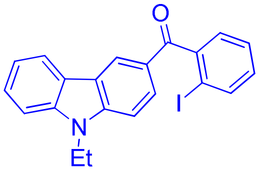
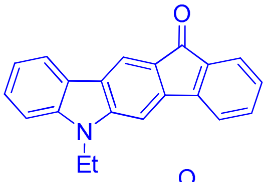
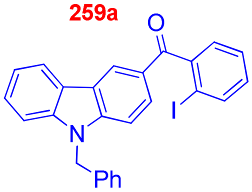
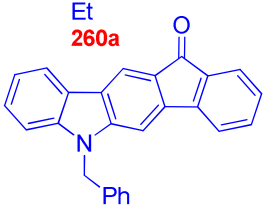
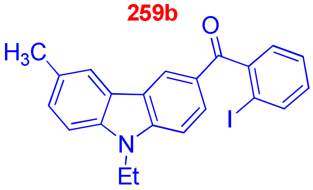
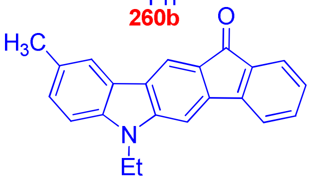
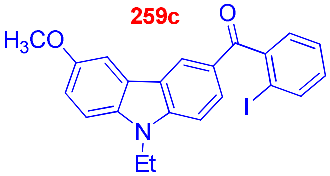
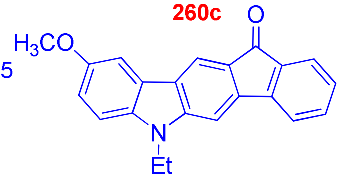
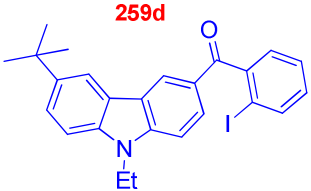
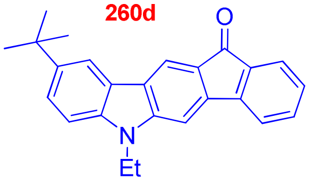
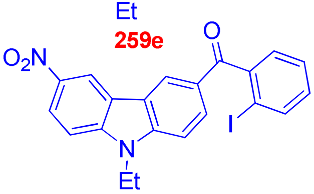
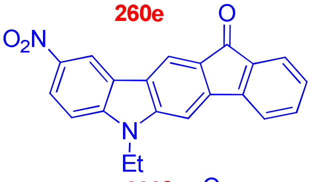
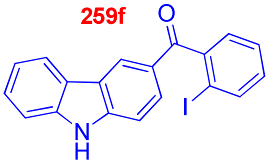
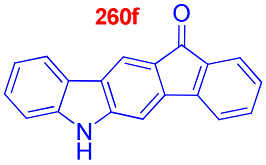
Figure 18 ORTEP diagrams of 260a and 260ab



By utilizing the above optimized condition various indenocarbazolone derivatives were synthesized by subjecting **259a-g** to provide the cyclized products **260a-g** in good yields as shown in table 20.

Table 20. Synthesis of indenocarbazolone derivatives

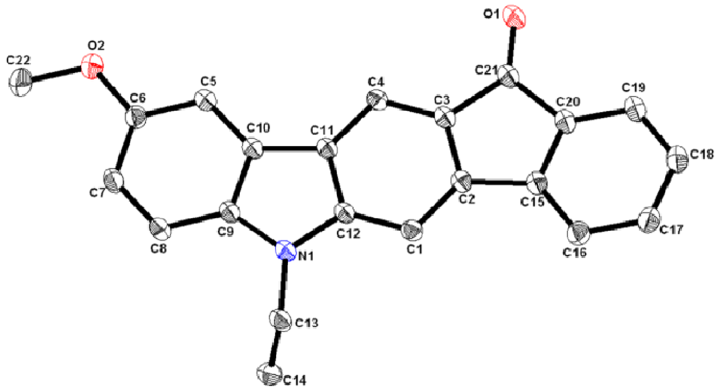


Entry	Substrate	Yield (%)[b]	Product	Time (h)	Yield (%)[b]
1	 **259a**	80	 **260a**	3	68
2	 **259b**	86	 **260b**	3	72
3	 **259c**	82	 **260c**	4	68
4	 **259d**	85	 **260d**	4	68
5	 **259e**	82	 **260e**	4	70
6	 **259f**	72	 **260f**	5	72
7	 **259g**	94	 **260g**	6	55

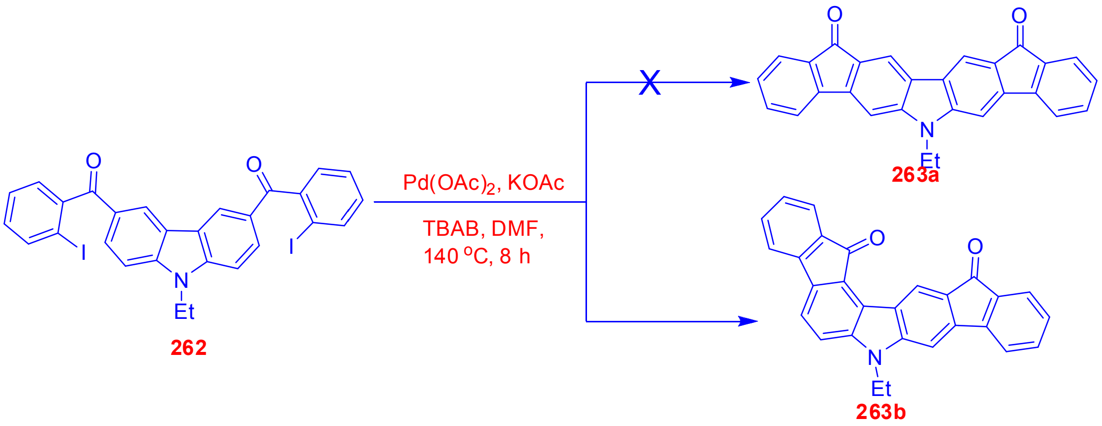
[a]Reaction conditions: **259a-g** (0.02 mmol), TBAB (0.02 mmol), KOAc (0.04 mmol), Pd(OAc)$_2$ (5 mol %) in DMF 3.0 mL; [b]isolated yield.

The methoxy derivative **260d** was also confirmed by the single crystal X-ray analysis. The ORTEP diagram is shown in Figure 19.[155]

Figure 19 ORTEP diagram of **260d**



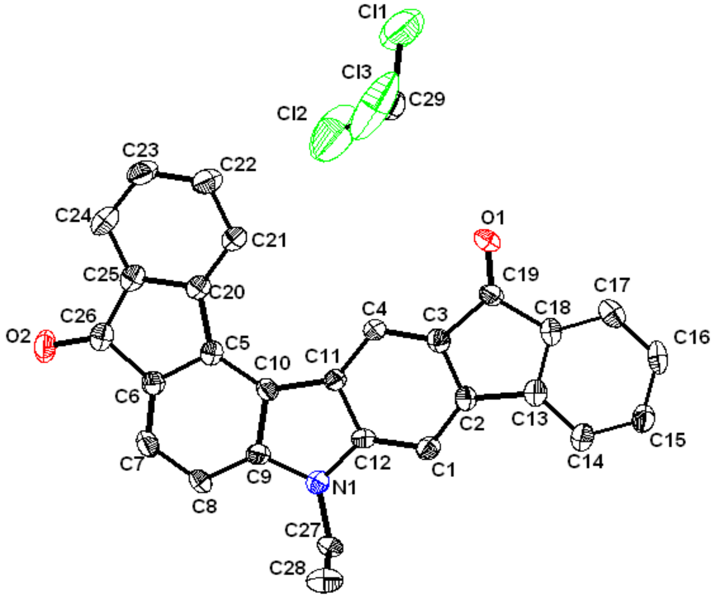
When **262a** was subjected to the above optimized condition, **263a** was expected to be the major product. But from the ^{1}H NMR spectra only two singlet's were observed at δ 8.59 and δ 7.37 which confirmed that **263b** was the product as shown in Scheme 12.



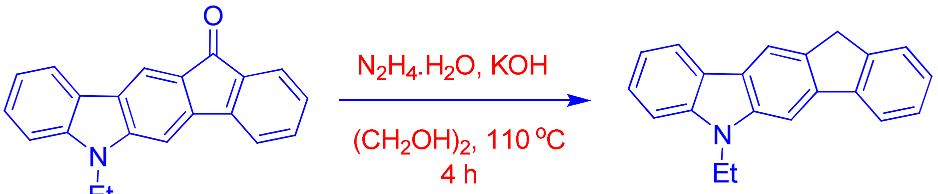
Scheme 12. Synthesis of diindenocarbazolone derivatives

Further, **263b** was confirmed by single crystal X ray analysis. The ORTEP diagram is shown in Figure 20.[155]

Figure 20 ORTEP diagram of 263b



The indenocarbazoles are a new class of heteroarylcarbazole analogs of indolocarbazoles, in which the indole nitrogen is replaced with a carbon. These molecules are not fully explored and were reported by Hudkins group as PKC, VEGFR2 and trkA inhibitors.[156] Underiner *et al*. and Singh *et al*. have prepared indenocarbazole analogs of the STP ring system, which show activity against trkA and VEGF-R2 (KDR) but weak activity against PKC and PDGFR.[157] Tripathy *et al*.[151] have also prepared indenocarbazoles via parallel synthesis. Gingrich *et al*.[140-141] have reported an optimized method for the indenocarbazole derivatives CEP-5214 and its prodrug form CEP-7055 as a potent inhibitor of VEGFR3 (Flt-4), VEGFR2 (KDR), VEGFR1 (Flt-1) and Flt-3.



259a

264
52%

Scheme 13. Synthesis of indenocarbazole derivatives

The reduction of the indenocarbazolone **259a** with hydrazine hydrate, KOH in ethylene glycol furnished the indenocarbazole 5-ethyl-5,11-dihydroindeno[1,2-*b*]carbazole **264a** in 52% yield (Scheme 13). These molecules can further be used in photochemical applications.

We also studied spectral properties of the compounds **260a-f** and **263b**. The electronic absorption spectrum of the compound **260a** shows absorption at 395 nm in the visible region in CH_2Cl_2 and the corresponding emission band was observed at 571 nm as shown in Figure 22(a).

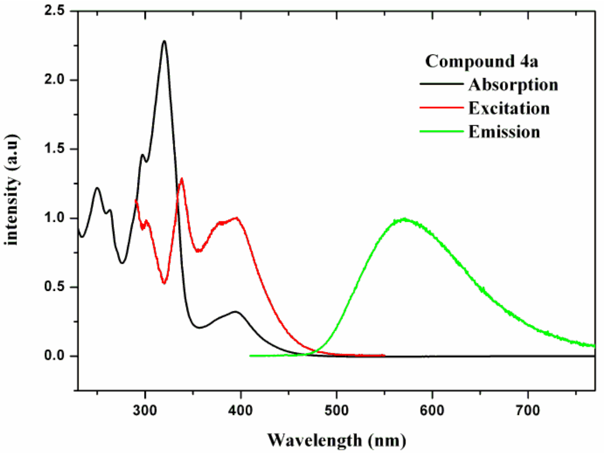


Figure 22 (a) Electronic spectra of compound **260a**, [4x10^{-5} M, absorption spectra, black line; excitation spectra (λ_{em} = 571 nm), red line; and emission spectra (λ_{ex} = 395 nm), green line; (excitation and emission spectra are normalized to 1)].

The emission spectrum of compound **260a** is dependent on polarity of the solvents. The emission band maximum shifts to low energy region with increasing the polarity of the solvents as shown in Figure 22(b). It varies from 517–573 nm from hexane to DMF.[15] Benzyl substituted compound **260b** shows slight changes in the absorption and emission wavelengths compared to the ethyl substituted compound **260a**. If donating groups such as methyl, methoxy, and *t*-butyl are present at 2nd position (**260c**, **260d**, and **260e**) there is slight increase in the absorption and emission wavelengths compared to **260a**.

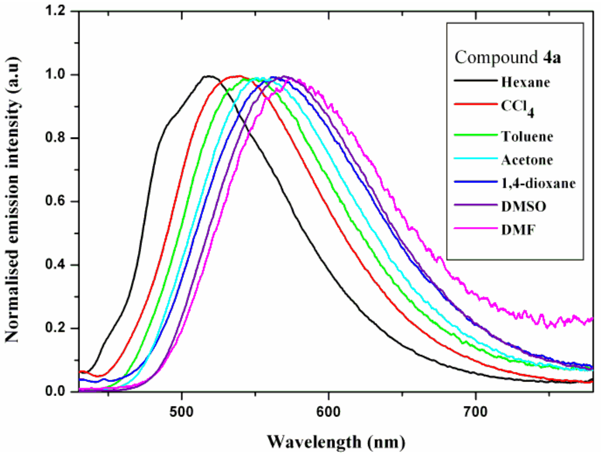


Figure 22 (b) Emission spectra of compound **260a** in different solvents when excited at 395 nm.

On the other hand, if an electron withdrawing group such as $-NO_2$ group is present at 2nd position a decrease in the absorption wavelength at 360nm and emission wavelength at 547 nm respectively is observed as shown in Table 13.

Table 21. Electronic properties of the compounds **260a-f** and **263b** (concentration of the samples being ~3 x 10^{-5} M, MA_{max} and E_{max} = absorption and emission maxima, respectively, ε = molar extension coefficient and Φ_F = fluorescence quantum yield).

Comp	A_{max} (nm)	(ε) L.mol^{-1}.cm^{-1}	E_{max} (nm)	(Φ_F)
260a	395	7445	571	0.034
260b	392	8021	568	0.040
260c	400	8249	582	0.029
260d	400	8920	581	0.037
260e	400	10707	583	0.024
260f	360	13947	547	0.082
263b	394	8720	562	0.045

3.3. Conclusion:

In conclusion, we developed a new class of indenocarbazolones with high regioselectivity in good yield by palladium catalyzed intramolecular *ortho*-arylation. Further studies on biological and photochemical properties of corresponding compounds are under progress in our laboratory.

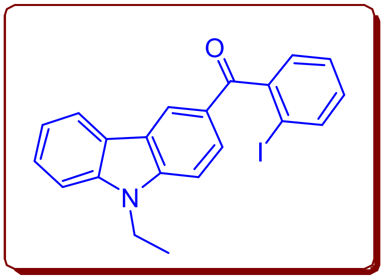
3.4. EXPERIMENTAL SECTION:

General procedure I

To a solution of 9-ethylcarbazole **261a** (1.0 g, 0.55 mmol) in CH_2Cl_2 (20 mL), anhydrous $AlCl_3$ (0.73 g, 0.55 mmol) was added quickly, and the mixture was stirred at room temperature under nitrogen atmosphere for 15 minutes. The reaction mixture was cooled in an ice bath and add freshly prepared *o*-iodobenzoyl chloride **189** (2.2 mL, 0.83 mmol) drop wise for 15 minutes. Then brought to room temperature stirred for 8 h. Then cold water (50 mL) was added to the mixture and extracted with CH_2Cl_2 (3 x 20 mL). The mixture was dried over anhydrous sodium sulphate evaporated, and the residue was purified by column chromatography using a mixture of ethyl acetate and hexanes (3:7) as eluent to obtain **259a** in 80% yield. The same procedure was applied for all the compounds **259b-g**.

(9-Ethyl-9*H*-carbazol-3-yl)(2-iodophenyl)methanone (259a):

The product **259a** was obtained as white solid from **261a** and **189** from column chromatography using a mixture of 30% ethyl acetate and hexanes as described in procedure I.



Yield: 80%

Mp: 118-120 °C

IR (KBr) ν_{max} cm^{-1}: 2968, 1653, 1589, 1350, 1010, 719

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.58 (s, 1H), 8.09 (d, 1H, J = 8.0 Hz), 8.0-7.96 (m, 2H), 7.54-7.38 (m, 5H) 7.31-7.27 (m, 1H), 7.23-7.19 (ddd, 1H, J_1 = 1.6 Hz, J_2

= 7.6 Hz, J_3 = 15.2 Hz), 4.39 (q, 2H, J = 7.2 Hz), 1.46 (t, 3H, J = 7.2 Hz)

^{13}C NMR (100 MHz, $CDCl_3$): δ 196.9, 145.5, 143.1, 140.7, 139.5, 130.7, 128.6, 128.3, 127.8, 126.8, 126.6, 124.3, 123.2, 123.0, 120.8, 120.2, 109.1, 108.3, 92.6, 37.9, 13.8

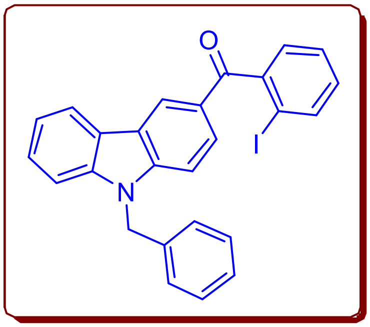
LC-MS (m/z): 426 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{21}H_{16}INO$: C, 59.31; H, 3.79; N, 3.29

Found: C, 59.25; H, 3.68; N, 3.35%

(9-Benzyl-9*H*-carbazol-3-yl)(2-iodophenyl)methanone (259b):

The product **259b** was obtained as light brown solid from **261b** and **189** from column chromatography using a mixture of 25% ethyl acetate and hexanes as described in procedure I.



Yield: 86%

Mp: 86-88 °C

IR (KBr) ν_{max} cm^{-1}: 2924, 1651, 1460, 1321, 808, 725, 626

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.61 (s, 1H), 8.12 (d, 1H, J = 7.6 Hz), 8.08-8.01 (m, 2H), 7.98-7.93 (m, 2H) 7.46 (t, 2H, J = 7.6 Hz), 7.41-7.38 (m, 3H), 7.30 (d, 1H, J = 7.6 Hz), 7.21 (d, 2H, J = 8.0 Hz), 7.15 (d, 2H, J = 6.0 Hz), 5.54 (s, 2H)

^{13}C NMR (100 MHz, $CDCl_3$): δ 196.8, 144.9, 144.6, 141.8, 139.6, 135.4, 133.4, 131.9, 131.0, 129.7, 129.1, 128.5, 128.3, 128.1, 127.9, 126.4, 124.4, 123.4, 109.5, 92.4, 47.2

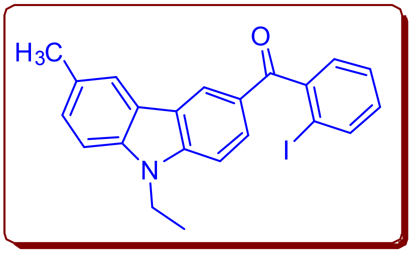
LC-MS (m/z): 488 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{26}H_{18}INO$: C, 64.08; H, 3.72; N, 2.87%

Found: C, 64.21; H, 3.65; N, 2.92%

(9-Ethyl-6-methyl-9*H*-carbazol-3-yl)(2-iodophenyl)methanone (259c):

The product **259c** was obtained as white solid from **261c** and **189** from column chromatography using a mixture of 25% ethyl acetate and hexanes as described in procedure I.



Yield: 82%

Mp: 60-61 °C

IR (KBr) ν_{max} cm^{-1}: 2945, 1642, 1472, 1024, 1016, 756

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.50 (s, 1H), 7.99-7.95 (m, 3H), 7.87 (s, 1H), 7.48 (t, 1H, *J* = 6.4 Hz), 7.46-7.37 (m, 2H), 7.33 (d, 1H, *J* = 1.2 Hz), 7.23-7.19 (ddd, 1H, J_1 = 1.6 Hz, J_2 = 8.0 Hz, J_3 = 15.6 Hz), 4.36 (q, 2H, *J* = 7.2 Hz), 2.52 (s, 3H), 1.44 (t, 3H, *J* = 7.2 Hz)

^{13}C NMR (100 MHz, CDCl$_3$): δ 196.9, 145.6, 143.3, 141.9, 139.5, 138.9, 133.4, 131.9, 130.6, 129.7, 128.3, 127.8, 126.6, 124.5, 122.7, 120.8, 108.7, 108.3, 92.6, 37.9, 21.3, 13.8

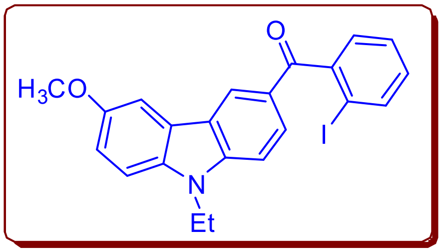
LC-MS (m/z): 440 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{22}H_{18}INO$: C, 60.15; H, 4.13; N, 3.19%

Found: C, 60.21; H, 4.18; N, 3.25%

9-Ethyl-6-methoxy-9*H*-carbazol-3-yl)(2-iodophenyl)methanone (259d):

The product **259d** was obtained white light brown solid from **261d** and **189** from column chromatography using a mixture of 25% ethyl acetate and hexanes as described in procedure I.



Yield: 85%

Mp: 63-64 °C

IR (KBr) ν_{max} cm^{-1}: 2924, 1649, 1485, 1309, 1124, 1016, 964, 736

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.55 (s, 1H), 7.99-7.95 (ddd, 2H, J_1 = 0.8 Hz, J_2 = 6.0 Hz, J_3 = 14.8 Hz), 7.58 (d, 1H, J = 2.4 Hz), 7.52-7.49 (ddd, 1H, J_1 = 0.8 Hz, J_2 = 7.2 Hz, J_3 = 14.8 Hz), 7.42-7.35 (m, 3H), 7.25-7.21 (ddd, 1H, J_1 = 1.6 Hz, J_2 = 7.6 Hz, J_3 = 15.2 Hz), 7.18-7.15 (dd, 1H, J_1 = 2.4 Hz, J_2 = 8.8 Hz), 4.37 (q, 2H, J = 7.2 Hz), 3.93 (s, 3H), 1.46 (t, 3H, J = 7.6 Hz)

^{13}C NMR (100 MHz, CDCl$_3$): δ 196.9, 154.5, 145.5, 143.5, 139.5, 135.5, 130.6, 128.5, 128.3, 127.8, 126.3, 124.4, 123.7, 122.7, 115.9, 109.8, 108.4, 103.6, 92.6, 56.1, 38.0, 13.9

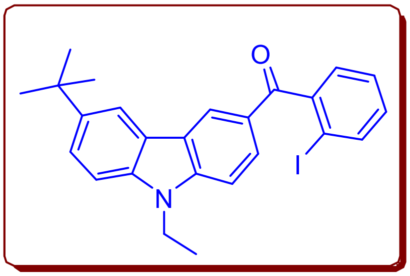
LC-MS (m/z): 456 (M+H)$^+$ positive mode

Anal. Calcd. for $C_{22}H_{18}INO_2$: C, 58.04; H, 3.98; N, 3.08%

Found: C, 58.15; H, 3.91; N, 3.12%

(6-*t*-Butyl-9-ethyl-9*H*-carbazol-3-yl)(2-iodophenyl)methanone (259e):

The product **259e** was obtained as white solid from **261e** and **189** from column chromatography using a mixture of 25% ethyl acetate and hexanes as described in procedure I.



Yield: 82%

Mp: 101-103 °C

IR (KBr) ν_{max} cm^{-1}: 2957, 1647, 1585, 1332, 1240, 1014, 756

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.61 (s, 1H), 8.11 (s, 1H), 7.98 (d, 1H, J = 7.6), 7.92 (d, 1H, J = 8.8 Hz), 7.60 (d, 1H, J = 8.4 Hz), 7.50 (t, 1H, J = 7.2 Hz), 7.40 (t, 3H, J = 8.0 Hz), 7.22 (t, 1H, J = 7.6 Hz), 4.38 (q, 2H, J = 7.2 Hz), 1.46 (t, 3H, J = 7.2 Hz), 1.44 (s, 9H)

^{13}C NMR (100 MHz, CDCl$_3$): δ 197.0, 145.6, 143.5, 143.4, 139.5, 138.9, 130.7, 128.6, 128.3, 127.8, 126.6, 124.6, 124.0, 123.2, 122.9, 117.1, 108.6, 108.1, 92.6, 37.9, 34.8, 31.9, 13.9

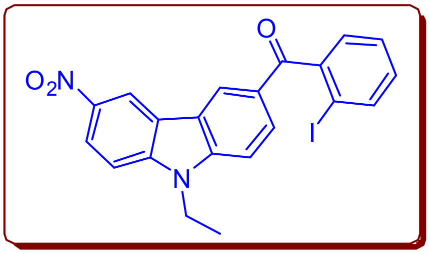
LC-MS (m/z): 482 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{25}H_{24}INO$: C, 62.38; H, 5.03; N, 2.91%

Found: C, 62.21; H, 5.06; N, 3.12%

(9-Ethyl-6-nitro-9*H*-carbazol-3-yl)(2-iodophenyl)methanone (259f):

The product **259f** was obtained as green solid from **261f** and **189** from column chromatography using a mixture of 45% ethyl acetate and hexanes as described in procedure I.



Yield: 82%

Mp: 143-145 °C

IR (KBr) ν_{max} cm^{-1}: 2976, 1655, 1591, 1446, 1307, 1242, 1016, 817, 634

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.97 (s, 1H), 8.48 (s, 1H), 8.44-8.41 (dd, 1H, J_1 = 2.0 Hz, J_2 = 9.2 Hz), 8.19 (d, 1H, J = 8.4 Hz), 7.99 (d, 1H, J = 8.4 Hz), 7.56-7.48 (m, 3H), 7.39 (d, 1H, J = 7.6 Hz), 7.29-7.25 (m, 1H), 4.47 (q, 2H, J = 7.6 Hz), 1.52 (t, 3H, J = 7.2 Hz)

^{13}C NMR (100 MHz, CDCl$_3$): δ 192.6, 144.8, 144.3, 143.8, 141.4, 139.7, 131.1, 129.5, 128.6, 128.3, 128.0, 125.0, 122.9, 122.7, 122.3, 117.6, 109.6, 108.8, 92.3, 38.6, 13.9

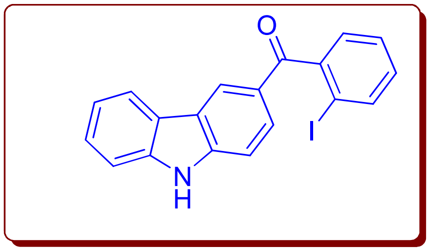
LC-MS (m/z): 471 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{21}H_{15}IN_2O_3$: C, 53.64; H, 3.22; N, 5.96%

Found: C, 53.75; H, 3.19; N, 5.81%

(9*H*-Carbazol-3-yl)(2-iodophenyl)methanone (259g):

The product **259g** was obtained as white solid from **261g** and **189** from column chromatography using a mixture of 45% ethyl acetate and hexanes as described in procedure I.



Yield: 94%

Mp: 150-152 °C

IR (KBr) ν_{max} cm^{-1}: 3263, 1620, 1483, 1446, 1334, 1280, 727

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.74 (s, 1H, N<u>H</u>), 8.56 (s, 1H), 8.06 (d, 1H, *J* = 8.0 Hz), 7.98-7.94 (m, 2H), 7.51-7.39 (m, 5H), 7.31-7.27 (m, 1H), 7.24-7.20 (m, 1H)

^{13}C NMR (100 MHz, CDCl$_3$): δ197.3, 145.3, 143.0, 140.1, 139.6, 130.8, 128.7, 128.3, 127.8, 127.4, 126.8, 124.3, 123.4, 123.3, 120.7, 120.5, 112.2, 110.6, 92.5

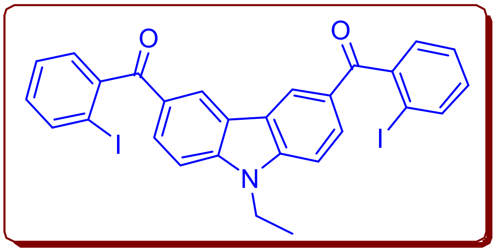
LC-MS (m/z): 398 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{19}H_{12}INO$: C, 57.45; H, 3.05; N, 3.53%

Found: C, 57.36; H, 3.12; N, 3.48%

(9-Ethyl-9*H*-carbazole-3,6-diyl)bis((2-iodophenyl)methanone) (262):

The product **262** was obtained as pale yellow solid from **261a** and **189** from column chromatography using a mixture of 35% ethyl acetate and hexanes as described in procedure I.



Yield: 94%

Mp: 178-180 °C

IR (KBr) ν_{max} cm^{-1}: 2926, 1711, 1602, 1435, 1113, 761

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55 (s, 2H), 8.02-7.96 (m, 4H), 7.52-7.46 (m, 4H), 7.37 (d, 2H, *J* = 6.4 Hz), 7.26-7.22 (m, 2H), 4.44 (q, 2H, *J* = 7.2 Hz), 1.51 (t, 3H, *J* = 7.2 Hz)

^{13}C NMR (100 MHz, $CDCl_3$): δ 196.8, 145.0, 143.9, 139.6, 131.0, 129.4, 128.2, 128.1, 127.9, 124.5, 123.3, 109.0, 92.4, 38.3, 13.9

LC-MS (m/z): 656 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{28}H_{19}I_2NO_2$: C, 51.32; H, 2.92; N, 2.14%

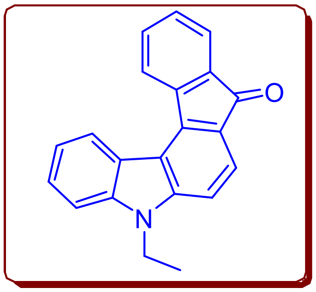
Found: C, 51.45; H, 2.88; N, 2.16%

GENERAL PROCEDURE J:

A mixture of compound **259a** (0.10 g, 0.02 mmol), anhydrous KOAc (0.04 g, 0.04 mmol), TBAB (0.06 g, 0.02 mmol) and $Pd(OAc)_2$ (0.003 g, 5 mol %) in DMA (3.0 mL) was taken in a Schlenk tube and heated at 140 °C for 3 h with continuous stirring. After completion of the reaction as monitored by TLC, the reaction mixture was cooled and poured into cold water (10 mL). A solid precipitate was formed, extracted with $CHCl_3$ (3 x 20 mL), and washed with water (3 x 20 mL) followed by brine (20 mL) and dried over Na_2SO_4. Evaporation of solvent and the crude material was purified by column chromatography over silica-gel (100-200 mesh), using 12% ethylacetate in hexanes as eluent to give products **260a** in 68% yield. Compounds **260a-g** and **263b** were obtained using same procedure.

5-Ethylindeno[2,1-*c*]carbazol-8(5*H*)-one (260ab):

The yellow compound **260ab** obtained from **259a** as described in procedure J with the elution of 13% ethylacetate in hexanes.



Yield: 5%

Mp: 205-207 °C

IR (KBr) ν_{max} cm^{-1}: 2936, 1679, 1478, 1024, 819, 742

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.81 (d, 1H, *J* = 8.0 Hz), 8.71 (d, 1H, *J* = 8.0 Hz), 8.11 (d, 1H, *J* = 7.6 Hz), 7.92 (d, 1H, *J* = 7.6 Hz), 7.67 (t, 1H, *J* = 8.0 Hz), 7.56-7.52 (m, 2H), 7.39-7.30 (m, 2H), 7.25-7.21 (m, 1H), 4.97 (q, 2H, *J* = 7.6 Hz), 1.50 (t, 3H, *J* = 7.6 Hz)

^{13}C NMR (100 MHz, CDCl$_3$): δ 193.5, 145.5, 144.6, 141.4, 136.1, 134.0, 128.9, 126.8, 126.2, 123.9, 123.1, 121.9, 120.4, 120.1, 119.8, 117.9, 109.1, 107.7, 37.9, 13.5

LC-MS (m/z): 298 (M+H)$^+$ positive mode

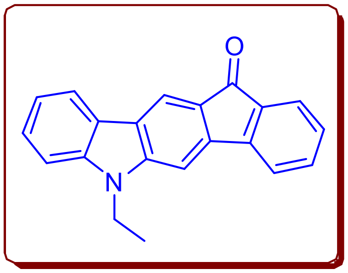
Anal. Calcd. for $C_{21}H_{15}NO$: C, 84.82; H, 5.08; N, 4.71%

Found: C, 84.76; H, 5.12; N, 4.67%

5-Ethylindeno[1,2-*b*]carbazol-11(5*H*)-one (260a):

The yellow compound **260a** obtained from **259a** as described in procedure J with the elution of 13% ethylacetate in hexanes.

Yield: 68%



Mp: 181-182 °C

IR (KBr) ν_{max} cm^{-1}: 2986, 1697, 1570, 1446, 1331, 1111, 931, 742

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.39 (s, 1H), 8.05 (d, 1H, *J* = 7.6 Hz), 7.66 (d, 1H, *J* = 7.2 Hz), 7.59 (d, 1H, *J* = 7.2 Hz), 7.50-7.46 (ddd, 2H, J_1 = 1.2 Hz, J_2 = 7.6 Hz, J_3 = 15.2 Hz), 7.42 (s, 1H), 7.33-7.27 (m, 3H), 4.41 (q, 2H, *J* = 7.2 Hz), 1.51 (t, 3H, *J* = 7.2 Hz)

^{13}C NMR (100 MHz, CDCl$_3$): δ 193.2, 144.6, 144.1, 142.6, 140.7, 136.3, 134.1, 128.8, 126.4, 126.2, 123.8, 123.1, 120.6, 120.5, 119.9, 118.0, 109.1, 100.7, 37.9, 14.0

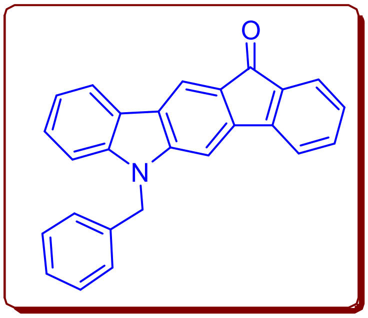
LC-MS (m/z): 298 (M+H)$^+$ positive mode

Anal. Calcd. for $C_{21}H_{15}NO$: C, 84.82; H, 5.08; N, 4.71%

Found:	C, 84.65; H, 5.12; N, 4.68%

5-Benzylindeno[1,2-*b*]carbazol-11(5*H*)-one (260b):

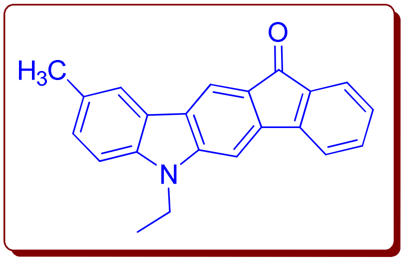
The yellow compound **260b** obtained from **259b** as described in procedure J with the elution of 14% ethylacetate in hexanes.



Yield:	72%
Mp:	148-150 °C
IR (KBr) ν_{max} cm^{-1}:	2924, 1739, 1687, 1454, 1329, 692
^{1}H NMR (400 MHz, CDCl$_3$):	δ 8.32 (s, 1H), 7.84 (s, 1H), 7.61 (d, 1H, *J* = 7.2 Hz), 7.47-7.38 (m, 2H), 7.32-7.22 (m, 8H), 7.13 (d, 2H, *J* = 6.4 Hz), 5.48 (s, 2H)
^{13}C NMR (100 MHz, CDCl$_3$):	δ 193.0, 145.1, 144.5, 142.6, 141.5, 140.0, 136.2, 134.1, 133.9, 129.0, 128.8, 128.5, 127.8, 127.6, 126.7, 126.2, 126.1, 124.0, 123.8, 123.1, 120.4, 119.9, 118.0, 109.6, 101.1, 46.8
LC-MS (m/z):	360 (M+H)$^+$ positive mode
Anal. Calcd. for $C_{26}H_{17}NO$:	C, 86.88; H, 4.77; N, 3.90%
Found:	C, 86.71; H, 4.71; N, 3.83%

5-Ethyl-2-methylindeno[1,2-*b*]carbazol-11(5*H*)-one (260c):

The yellow compound **260c** obtained from **259c** as described in procedure J with the elution of 14% ethylacetate in hexanes.

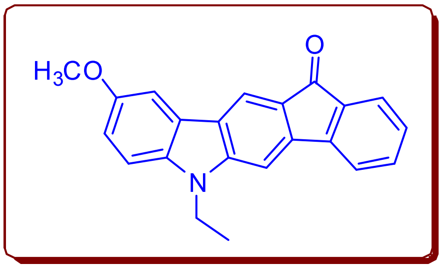


Yield:	68%
Mp:	139-140 °C
IR (KBr) ν_{max} cm^{-1}:	2922, 1697, 1458, 1020, 484
^{1}H NMR (400 MHz, CDCl$_3$):	δ 8.31 (s, 1H), 7.80 (s,

	1H), 7.62 (d, 1H, J = 7.2 Hz), 7.54 (d, 1H, J = 7.2 Hz), 7.44 (t, 1H, J = 7.6 Hz), 7.35 (s, 1H), 7.25-7.18 (m, 3H), 4.34 (q, 2H, J = 7.2 Hz), 2.51 (s, 3H), 1.46 (t, 3H, J = 7.2 Hz)
^{13}C NMR (100 MHz, $CDCl_3$):	δ 193.1, 144.6, 144.2, 142.3, 138.9, 136.4, 134.0, 129.9, 128.7, 127.6, 126.1, 123.9, 122.9, 121.8, 120.4, 119.8, 117.9, 108.8, 100.6, 37.8, 21.4, 14.0
LC-MS (m/z):	312 $(M+H)^+$ positive mode
Anal. Calcd. for $C_{22}H_{17}NO$:	C, 84.86; H, 5.50; N, 4.71%
Found:	C, 84.75; H, 5.58; N, 4.50%

5-Ethyl-2-methoxyindeno[1,2-*b*]carbazol-11(5*H*)-one (260d):

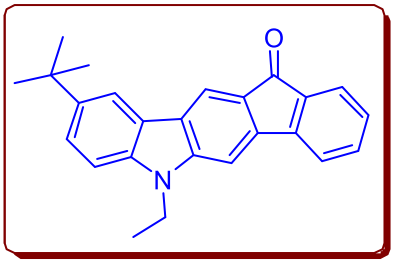
The yellow compound **260d** obtained from **259d** as described in procedure J with the elution of 14% ethylacetate in hexanes.



Yield:	68%
Mp:	139-140 °C
IR (KBr) ν_{max} cm^{-1}:	2924, 1689, 1454, 1304, 1165, 1020, 841
^{1}H NMR (400 MHz, $CDCl_3$):	δ 8.28 (s, 1H), 7.61 (d, 1H, J = 7.2 Hz), 7.52 (d, 1H, J = 7.6 Hz), 7.46 (s, 1H), 7.42 (d, 1H, J = 7.2 Hz), 7.30 (s, 1H), 7.27-7.22 (m, 2H), 7.08-7.06 (dd, 1H, J_1 = 8.8 Hz, J_2 = 8.8 Hz), 4.30 (q, 2H, J = 7.2 Hz), 3.91 (s, 3H, $OC\underline{H}_3$), 1.45 (t, 3H, J = 7.2 Hz)
^{13}C NMR (100 MHz, $CDCl_3$):	δ 193.0, 154.6, 144.6, 144.3, 142.2, 136.6, 135.5, 134.0, 128.7, 125.9, 124.3, 123.7, 122.8, 119.8, 118.0, 115.5, 109.9, 103.0, 100.7, 55.9, 37.9, 14.0
LC-MS (m/z):	328 $(M+H)^+$ positive mode
Anal. Calcd. for $C_{22}H_{17}NO_2$:	C, 80.71; H, 5.23; N, 4.28%
Found:	C, 80.59; H, 5.18; N, 4.35%

2-*t*-Butyl-5-ethylindeno[1,2-*b*]carbazol-11(5*H*)-one (260e):

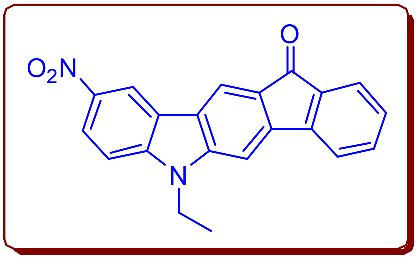
The yellow compound **260e** obtained from **259e** as described in procedure J with the elution of 14% ethylacetate in hexanes.



Yield:	70%
Mp:	186-187 °C
IR (KBr) ν_{max} cm^{-1}:	2951, 1695, 1462, 1302, 968, 756
^{1}H NMR (400 MHz, CDCl$_3$):	δ 8.39 (s, 1H), 8.06 (s, 1H), 7.63 (d, 1H, *J* = 7.2 Hz), 7.55 (t, 2H, *J* = 7.2 Hz), 7.45 (t, 1H, *J* = 7.6 Hz), 7.38 (s, 1H), 7.33 (d, 1H, *J* = 8.4 Hz), 7.24 (d, 1H, *J* = 7.6 Hz), 4.36 (q, 2H, *J* = 7.2 Hz), 1.47 (t, 3H, *J* = 7.6 Hz), 1.44 (s, 9H)
^{13}C NMR (100 MHz, CDCl$_3$):	δ 193.1, 144.7, 144.4, 143.6, 142.3, 138.8, 136.4, 134.0, 128.7, 126.2, 124.3, 123.7, 123.5, 123.3, 119.8, 117.9, 116.6, 108.7, 100.7, 37.9, 34.7, 31.8, 14.0
LC-MS (m/z):	354 (M+H)$^+$ positive mode
Anal. Calcd. for $C_{25}H_{23}NO$:	C, 84.95; H, 6.56; N, 3.96%
Found:	C, 84.85; H, 6.62; N, 3.91%

5-Ethyl-2-nitroindeno[1,2-*b*]carbazol-11(5*H*)-one (260f):

The yellow compound **260f** obtained from **259f** as described in procedure J with the elution of 20% ethylacetate in hexanes.



Yield:	72%
Mp:	232-234 °C
IR (KBr) ν_{max} cm^{-1}:	2986, 1701, 1572, 1460, 1327, 1141, 1093, 748, 696

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.39 (s, 1H), 8.86 (s, 1H), 8.45 (d, 1H, *J* = 9.2 Hz), 8.33 (s, 1H), 8.14 (d, 1H, *J* = 8.0 Hz), 7.88 (d, 1H, *J* = 8.4 Hz), 7.66 (d, 1H, *J* = 7.6 Hz), 7.47 (d, 1H, *J* = 9.2 Hz), 7.32 (d, 1H, *J* = 8.4 Hz), 4.44 (q, 2H, *J* = 5.2 Hz), 1.53 (t, 3H, *J* = 5.6 Hz)

^{13}C NMR (100 MHz, CDCl$_3$): δ 192.9, 146.3, 144.4, 143.4, 141.7, 141.1, 135.4, 134.6, 129.5, 128.1, 124.1, 123.7, 123.1, 122.5, 121.4, 120.2, 118.4, 108.8, 108.6, 38.5, 13.5

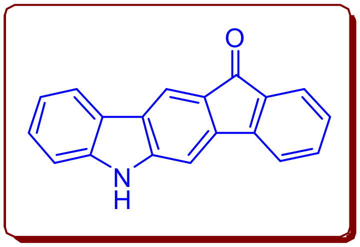
LC-MS (m/z): 343 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{21}H_{14}N_2O_3$: C, 73.68; H, 4.12; N, 8.26%

Found: C, 73.55; H, 4.18; N, 8.26%

Indeno[1,2-*b*]carbazol-11(5*H*)-one (260g):

The white compound **260g** obtained from **259g** as described in procedure J with the elution of 35% ethylacetate in hexanes.



Yield: 55%

Mp: 280 °C

IR (KBr) ν_{max} cm^{-1}: 2926, 1699, 1452, 1280, 1124, 742

^{1}H NMR (400 MHz, DMSO-d_6): δ 11.88 (s, 1H, N<u>H</u>), 8.41 (s, 1H), 8.18 (d, 1H, *J* = 8.0 Hz), 7.84 (d, 1H, *J* = 7.6 Hz), 7.76 (s, 1H), 7.58-7.49 (m, 3H), 7.41-7.37 (m, 1H), 7.34-7.30 (m, 1H), 7.19 (t, 1H, *J* = 8.0 Hz)

^{13}C NMR (100 MHz, DMSO-d_6): δ 192.6, 144.7, 144.6, 142.1, 140.9, 135.9, 135.2, 129.5, 126.7, 125.9, 123.8, 123.7, 123.0, 121.3, 121.0, 120.5, 118.4, 112.1, 104.5

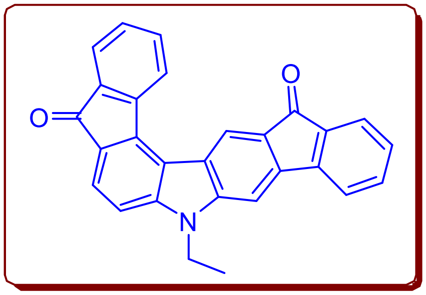
LC-MS (m/z): 270 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{19}H_{11}NO$: C, 84.74; H, 4.12; N, 5.20%

Found: C, 84.63; H, 4.08; N, 5.31%

8-Ethyl-5*H*-diindeno[1,2-*b*:1',2'-*g*]carbazole-5,14(8*H*)-dione (263b):

The orange solid compound **263b** obtained from **262** as described in procedure J with the elution of 35% ethylacetate in hexanes.



Yield: 58%

Mp: 128-130 °C

IR (KBr) ν_{max} cm^{-1}: 2922, 1732, 1645, 1483, 1290, 1126, 922, 756

^{1}H NMR (400 MHz, DMSO-d_6): δ 8.59 (s, 1H), 8.11 (d, 1H, *J* = 7.6 Hz), 7.75 (d, 1H, *J* = 8.0 Hz), 7.69-7.64 (m, 3H), 7.55 (d, 1H, *J* = 7.2 Hz), 7.50-7.46 (ddd, 1H, J_1 = 0.8 Hz, J_2 = 7.2 Hz, J_3 = 14.8 Hz), 7.37 (s, 1H), 7.35-7.30 (m, 2H), 7.20 (d, 1H, *J* = 8.0 Hz), 4.37 (q, 2H, *J* = 7.2 Hz), 1.51 (t, 3H, *J* = 7.2 Hz)

^{13}C NMR (100 MHz, CDCl$_3$): δ 193.3, 192.8, 144.2, 144.0, 139.6, 136.0, 134.3, 132.5, 131.9, 129.8, 129.6, 128.7, 128.3, 127.9, 127.3, 126.8, 124.5, 123.9, 123.3, 123.2, 122.7, 120.0, 117.9, 108.9, 108.4, 38.8, 14.2

LC-MS (m/z): 400 $(M+H)^+$ positive mode

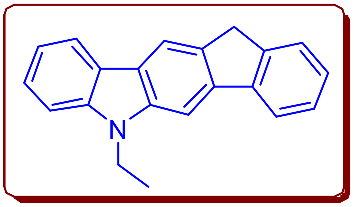
Anal. Calcd. for $C_{28}H_{17}NO_2$: C, 84.19; H, 4.29; N, 3.51%

Found: C, 84.35; H, 4.22; N, 3.61%

General Procedure K:

A mixture of **260a** (0.1 g, 0.034 mmol), hydrazine monohydrate (0.051 g, 0.1 mmol), KOH (0.027 g, 0.068 mmol) in 5 mL of diethylenen glycol was stirred at 100 °C for 4 h. The resulting mixture was cooled to room temperature, poured in cold water, extracted with ethyl acetate and dried over sodium sulphate. The solvent was removed under reduced pressure, and the residue was purified by column chromatography using a mixture of ethyl acetate and hexanes (1:9) as eluent to obtain the product **264** in 52% yield.

5-Ethyl-5,11-dihydroindeno[1,2-*b*]carbazole (264):



Yield:	52%
Mp:	38-140 °C
IR (KBr) ν_{max} cm^{-1}:	2957, 1446, 1319, 842, 717
^{1}H NMR (400 MHz, CDCl$_3$):	δ 8.23 (s, 1H), 8.11 (d, 1H, J = 8.0 Hz), 7.92 (d, 1H, J = 7.6 Hz), 7.78 (s, 1H), 7.58 (d, 1H, J = 7.6 Hz), 7.48-7.40 (m, 3H), 7.34-7.30 (ddd, 1H, J_1 = 0.8 Hz, J_2 = 7.6 Hz, J_3 = 14.8 Hz), 7.25-7.21 (m, 1H), 4.46 (q, 2H, J = 7.2 Hz), 4.64 (s, 2H), 1.50 (t, 3H, J = 7.2 Hz)
^{13}C NMR (100 MHz, CDCl$_3$):	δ 144.2, 142.2, 140.5, 140.1, 139.8, 134.3, 126.7, 126.5, 125.3, 125.1, 122.9, 122.7, 120.1, 119.6, 118.6, 116.4, 108.3, 99.4, 37.6, 36.3, 13.8
LC-MS (m/z):	284 (M+H)$^+$ positive mode
Anal. Calcd. for $C_{21}H_{17}N$:	C, 89.01; H, 6.05; N, 4.94%
Found:	C, 88.91; H, 6.12; N, 4.85%

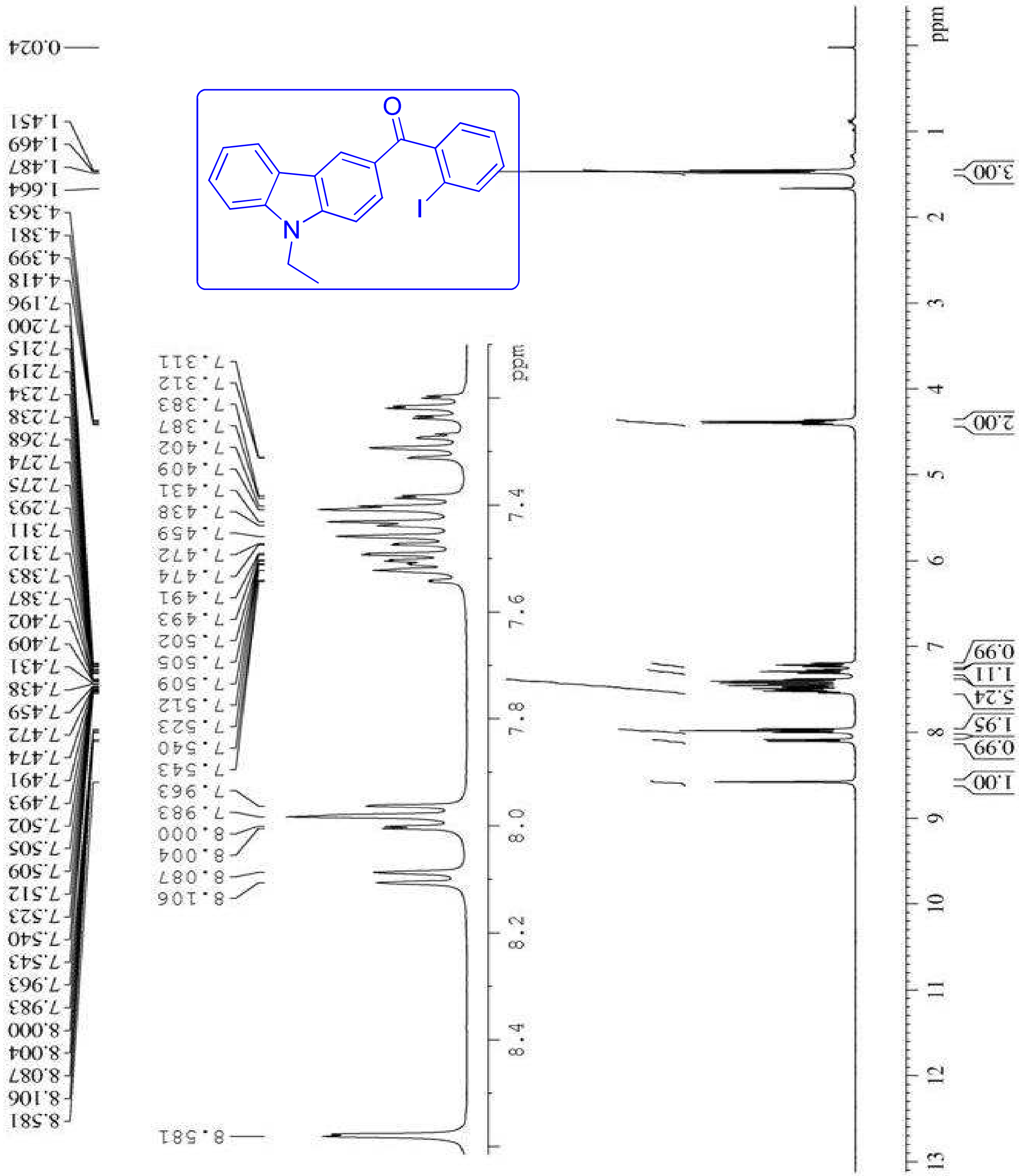
Table 22. Crystal data and structure refinement for 260a.

Empirical formula	: $C_{26}H_{15}NO_2$	
Formula weight	: 373.39	
Temperature	: 298(2) K	
Wavelength	: 0.71073 Å	
Crystal system	: Triclinic	
Space group	: P-1	
Unit cell dimensions	: a = 8.2147(7) Å	α = 88.285(6)°.
	: b = 9.9766(7) Å	β = 87.066(7)°.
	: c = 12.2199(11) Å	γ = 67.350(7)°.
Volume	: 922.97(13) $Å^3$	
Z	: 2	
Density (calculated)	: 1.344 Mg/m^3	
Absorption coefficient	: 0.085 mm^{-1}	
F(000)	: 388	
Crystal size	: 0.42 x 0.26 x 0.12 mm^3	
Theta range for data collection	: 2.76 to 24.71°.	
Index ranges	: -9<=h<=9, -9<=k<=11, -12<=l<=14	
Reflections collected	: 5808	
Independent reflections	: 3139 [R(int) = 0.0224]	
Completeness to theta = 24.71°	: 99.9 %	
Absorption correction	: Semi-empirical from equivalents	
Max. and min. transmission	: 0.9899 and 0.9651	
Refinement method	: Full-matrix least-squares on F^2	
Data / restraints / parameters	: 3139 / 0 / 262	
Goodness-of-fit on F^2	: 1.030	
Final R indices [I>2sigma(I)]	: R1 = 0.0552, wR2 = 0.1440	
R indices (all data)	: R1 = 0.0781, wR2 = 0.1637	
Largest diff. peak and hole	: 0.537 and -0.242 $e.Å^{-3}$	

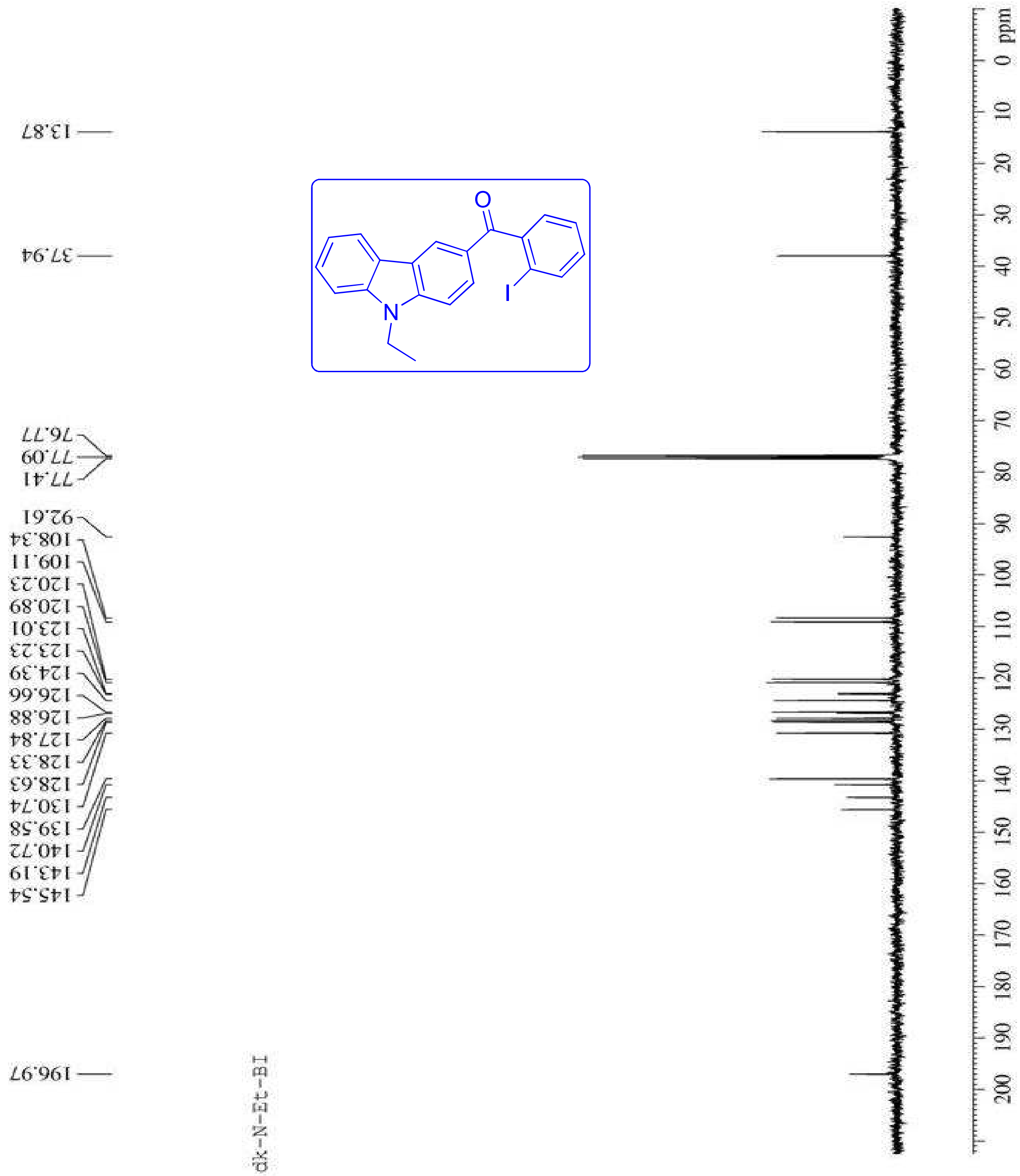
Table 23. Crystal data and structure refinement for 260ab.

Empirical formula : $C_{21}H_{15}NO$
Formula weight : 297.34
Temperature : 298(2) K
Wavelength : 0.71073 Å
Crystal system : Orthorhombic
Space group : P n a 21
Unit cell dimensions : a = 15.9003(8) Å α = 90°.
: b = 5.4237(3) Å β = 90°.
: c = 17.1149(8) Å γ = 90°.
Volume : 1475.96(13) Å^3
Z : 4
Density (calculated) : 1.338 Mg/m^3
Absorption coefficient : 0.082 mm^{-1}
F(000) : 624
Crystal size : 0.34 x 0.24 x 0.12 mm^3
Theta range for data collection : 3.50 to 26.37°.
Index ranges : -10<=h<=19, -6<=k<=4, -21<=l<=21
Reflections collected : 4180
Independent reflections : 2291 [R(int) = 0.0238]
Completeness to theta = 26.37° : 99.8 %
Absorption correction : Semi-empirical from equivalents
Max. and min. transmission : 0.9902 and 0.9726
Refinement method : Full-matrix least-squares on F^2
Data / restraints / parameters : 2291 / 1 / 209
Goodness-of-fit on F^2 : 0.990
Final R indices [I>2sigma(I)] : R1 = 0.0418, wR2 = 0.0862
R indices (all data) : R1 = 0.0587, wR2 = 0.0964
Absolute structure parameter : -1(2)
Largest diff. peak and hole : 0.100 and -0.133 e.Å^{-3}

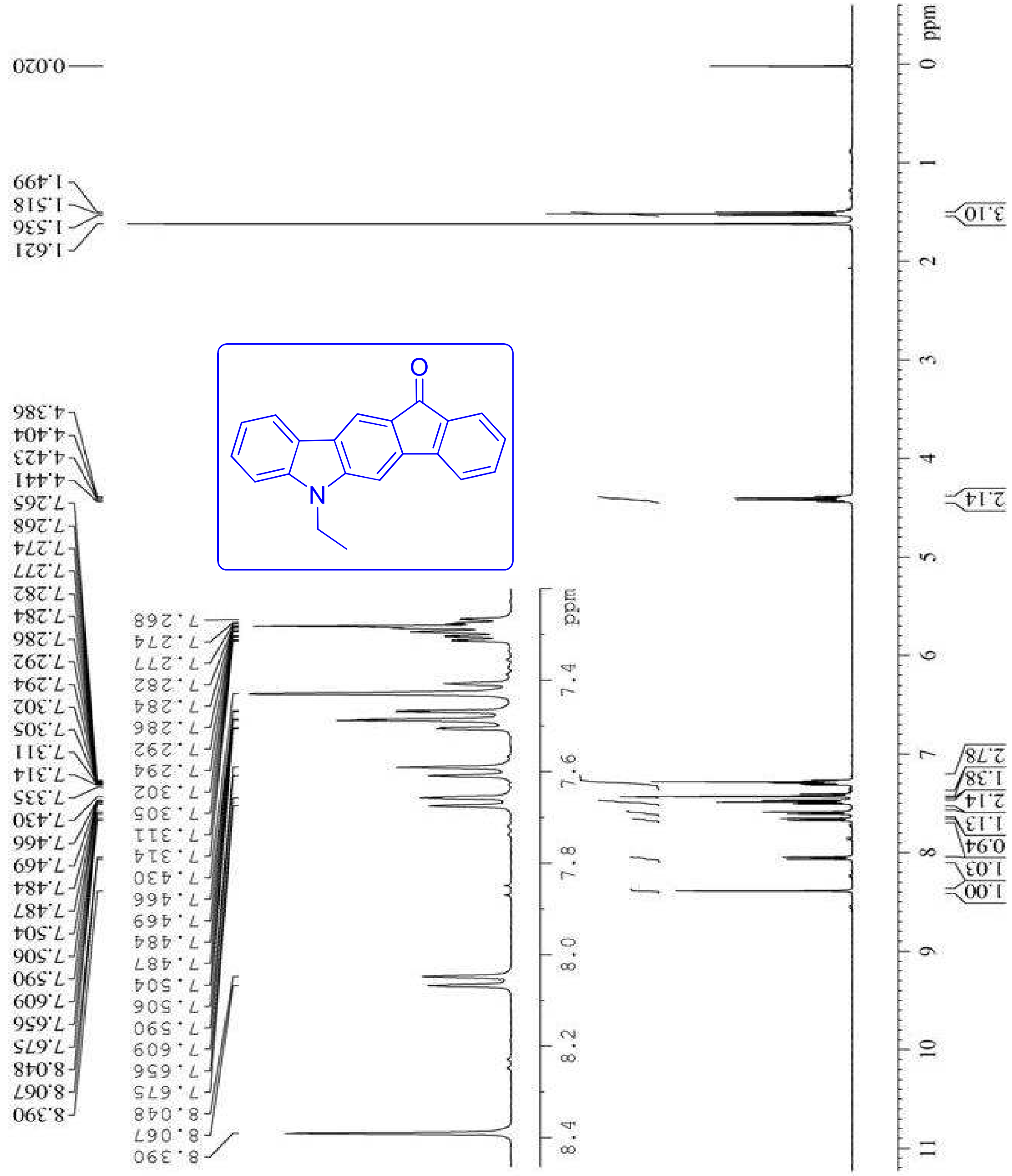
Spectrum 23. ^{1}H NMR of 259a



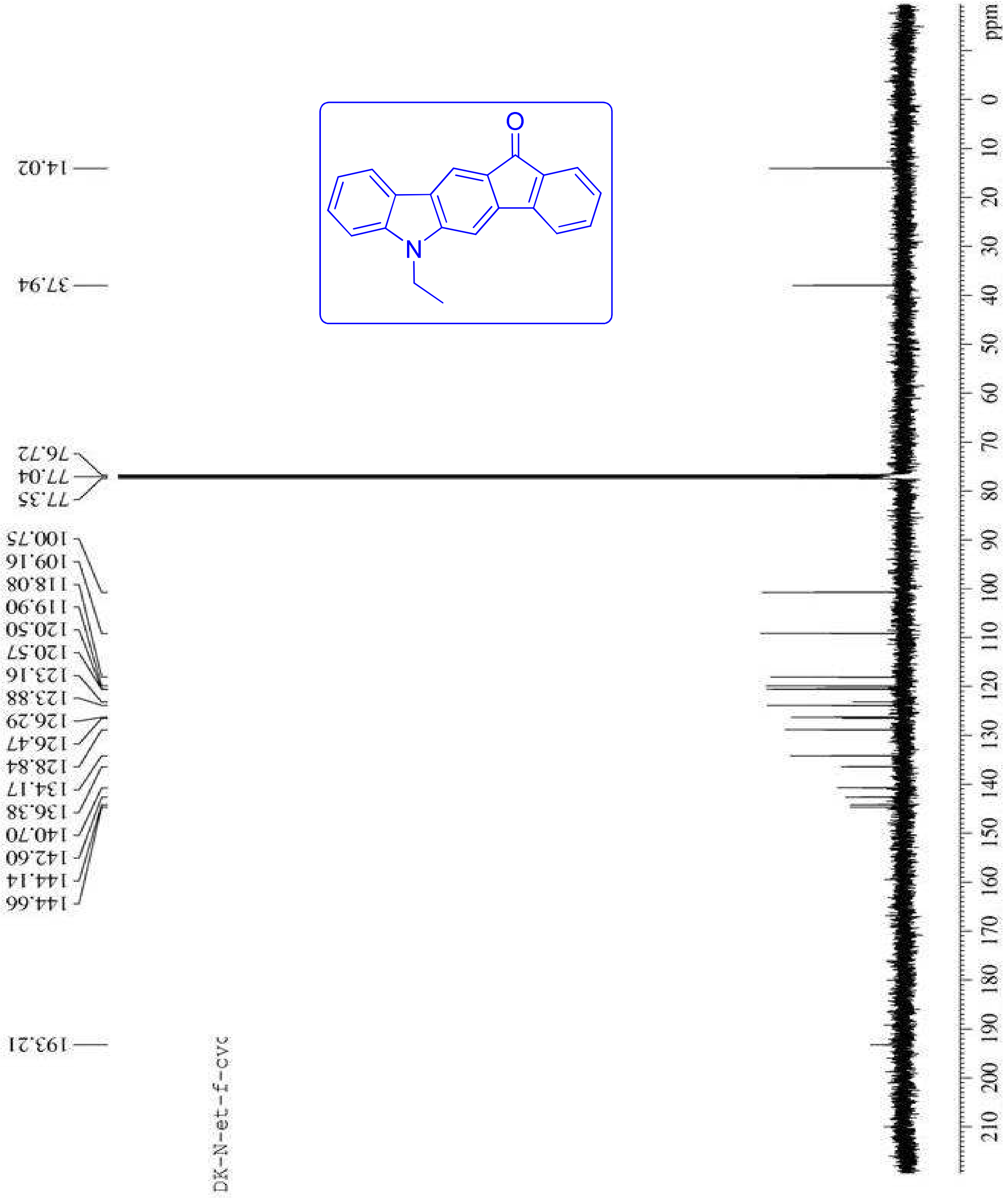
Spectrum 24. ^{13}C NMR of 259a



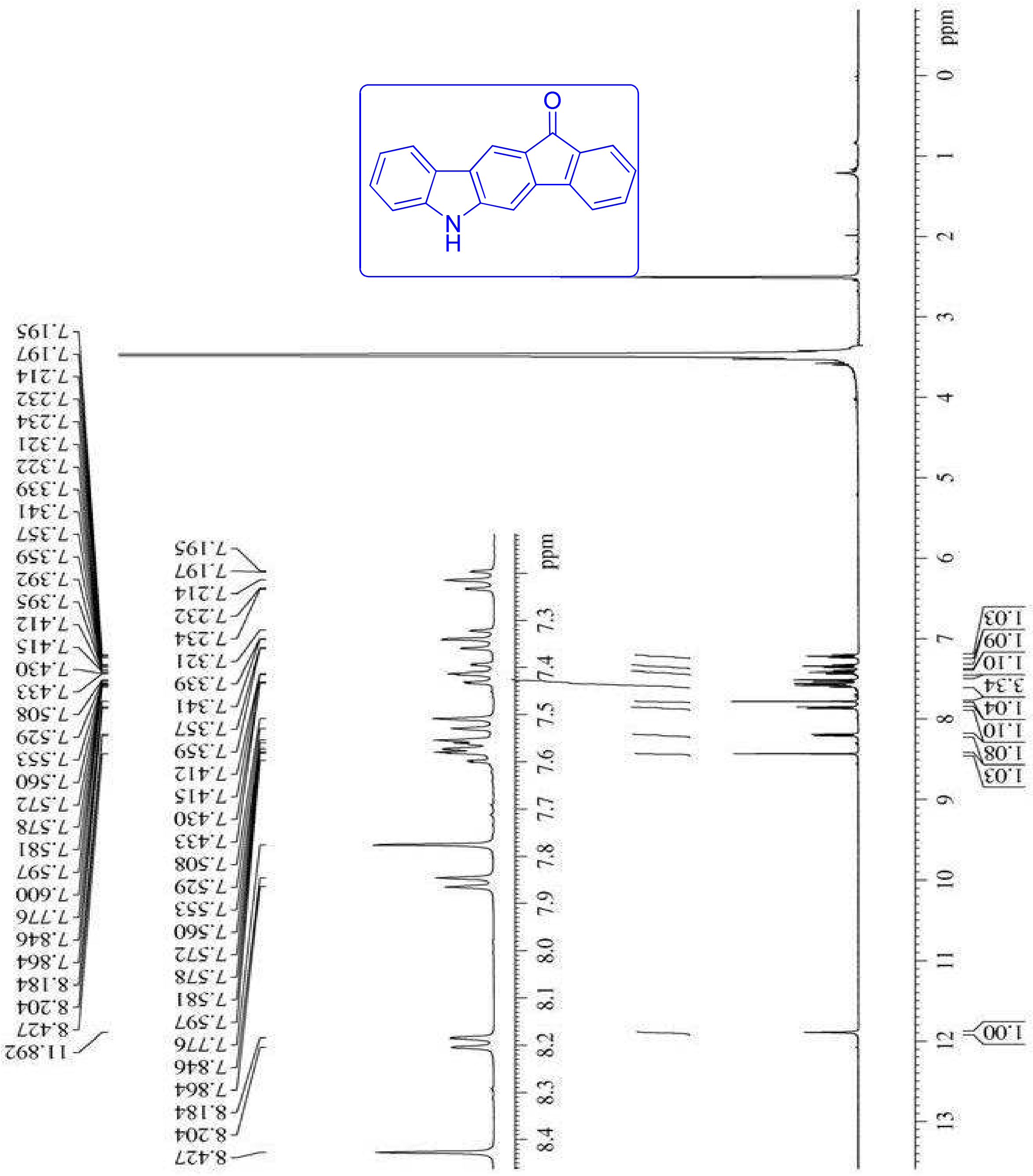
Spectrum 25. ^{1}H NMR of 260a



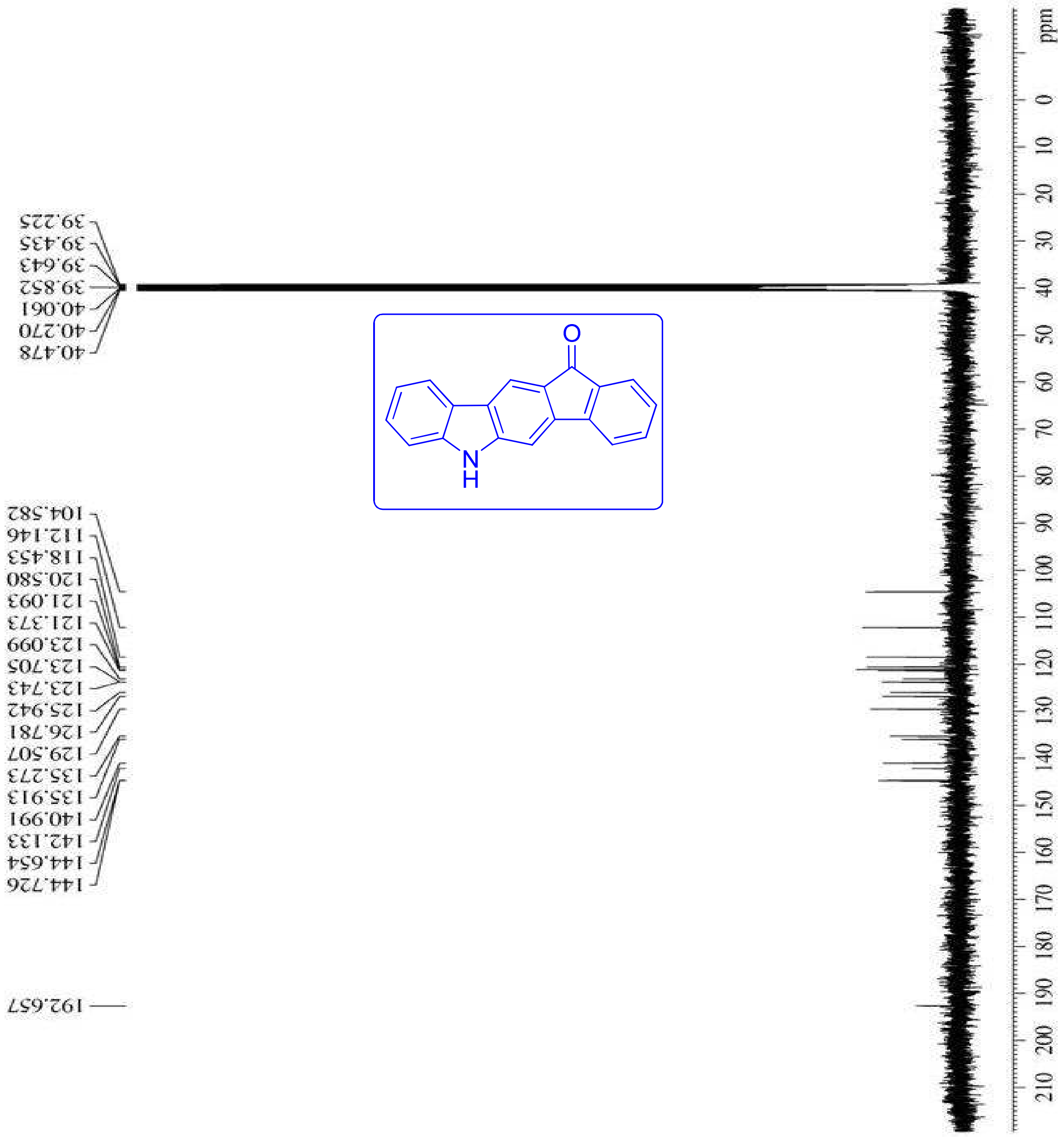
Spectrum 26. ^{13}C NMR of 260a



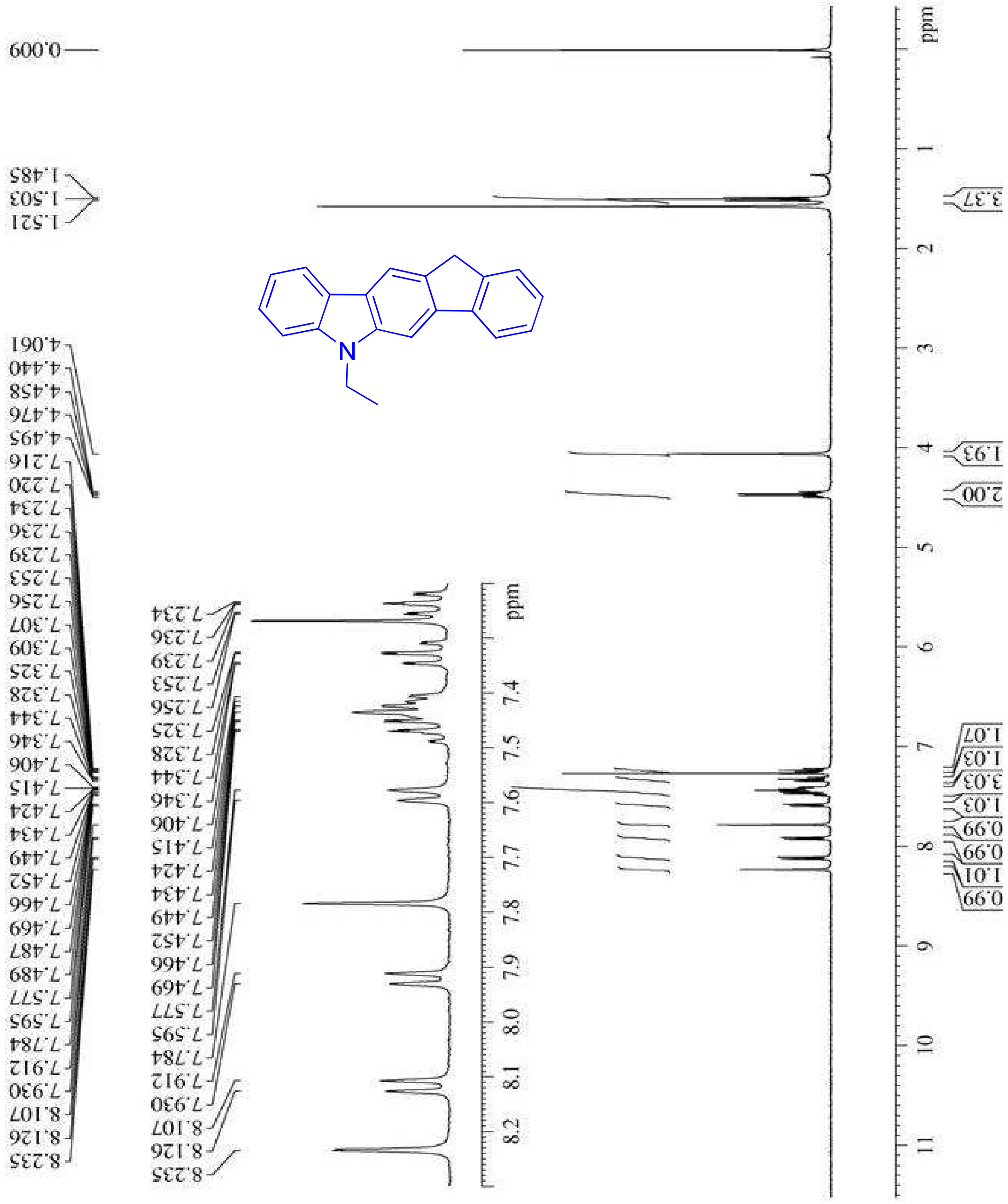
Spectrum 27. ^{1}H NMR of 260g



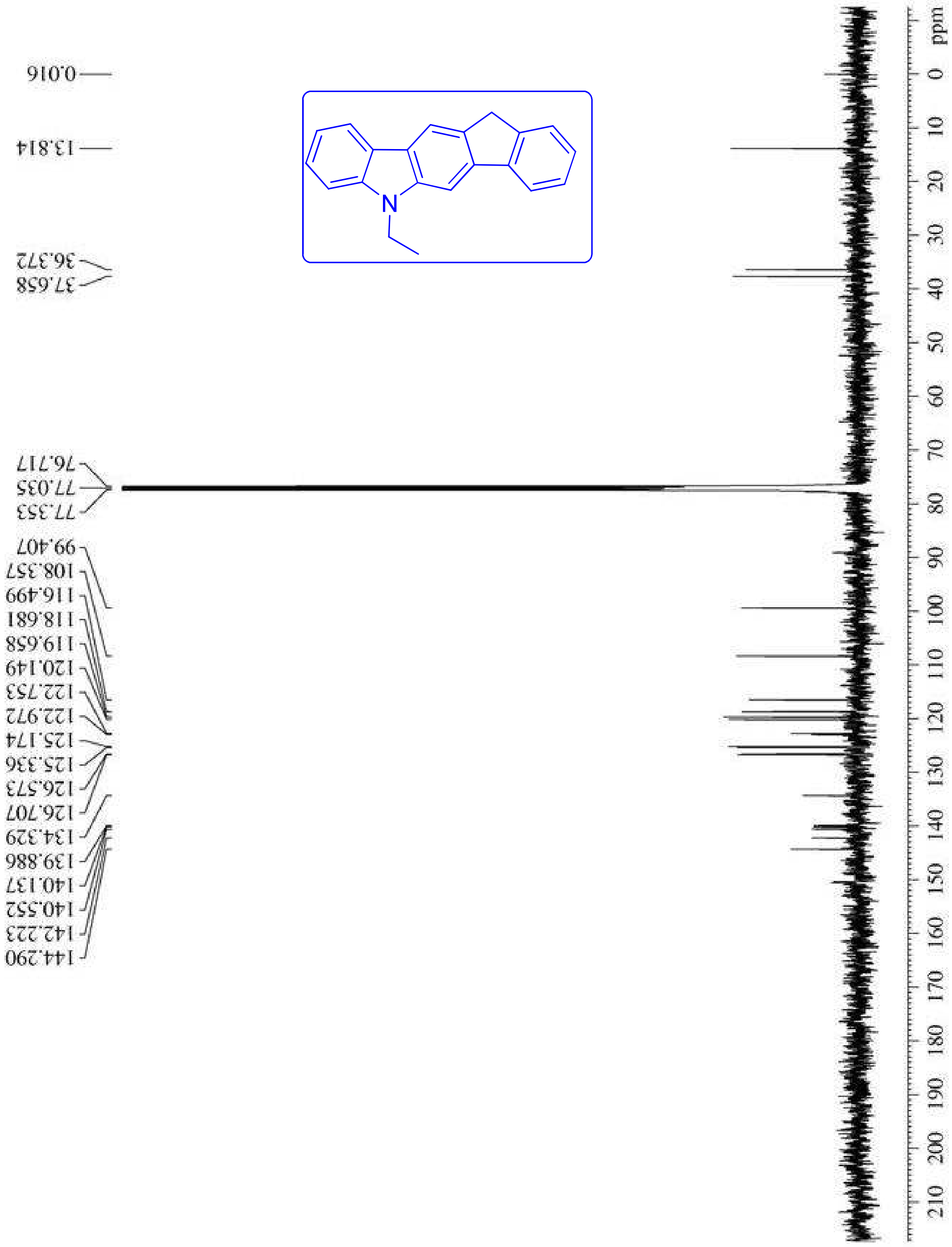
Spectrum 28. ^{13}C NMR of 260g



Spectrum 29. ^{1}H NMR of 264



Spectrum 30. ^{13}C NMR of 264



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139. The CCDC deposition number of compound **260a** is 854724. Formula: $C_{21}H_{15}N_1O_1$. Unit cell parameters: a = 18.8910(15), b = 14.7317(11), c = 5.3252(3), space group P21212. The CCDC deposition number of compound **260ab** is 854725. Formula: $C_{21}H_{15}N_1O_1$. Unit cell parameters: a = 15.9003(8), b = 5.4237(3), c = 17.1149(8), space group Pna21. The CCDC deposition number of compound **260d** is 854726. Formula: $C_{22}H_{17}N_1O_2$. Unit cell parameters: a = 8.3015(8), b = 9.1172(9), c = 10.6868(10), α = 83.461(2), β = 79.759(2), γ = 81.777(2), space group P-1. The CCDC deposition number of compound **263b** is 854727. Formula: $C_{29}H_{18}Cl_3N_1O_2$. Unit cell parameters: a = 9.0516(13), b = 10.4572(20), c = 13.2939(17), α = 100.684(14), β = 101.200(12), γ = 101.784(15), space group P-1.

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Synthesis of Cyclopentacarbazolones via Palladium-Catalyzed Annulation of Internal Alkynes

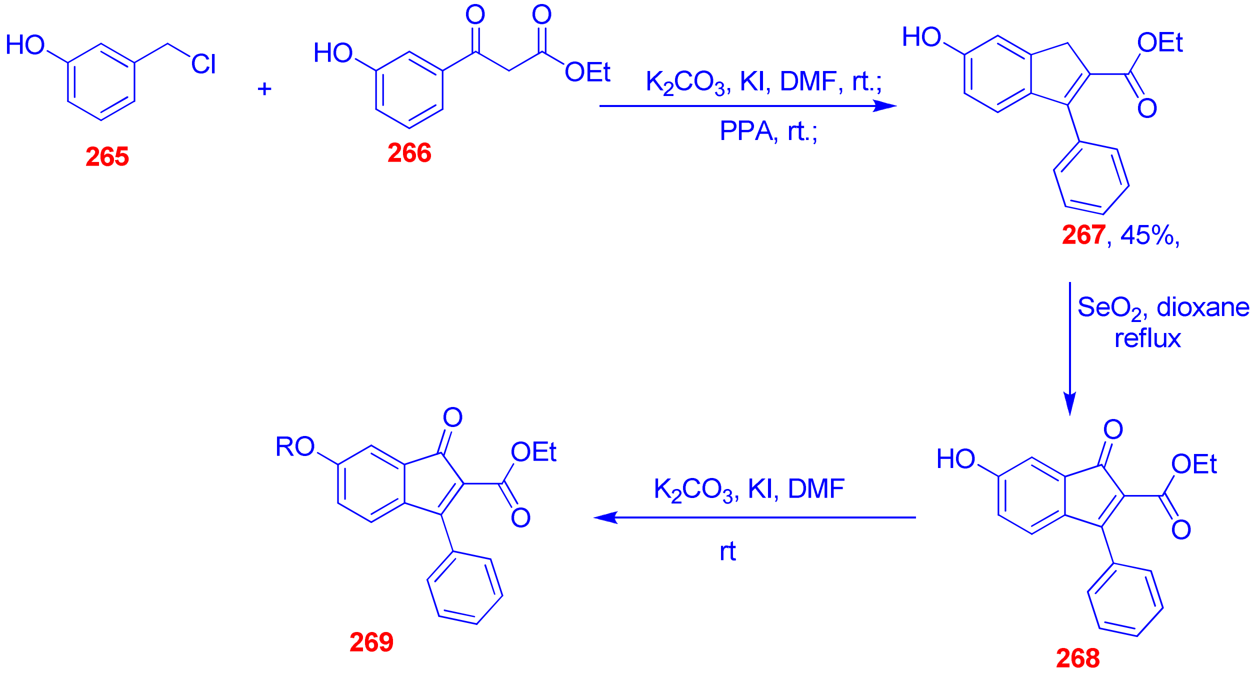
CHAPTER 4

4.1. Introduction:

Cyclopentadienones[64,158] are members of a diverse class of attractive molecules with demonstrated value and even broader potential in synthesis, biology, material science, and nanotechnology.[65,159] Fused and substituted cyclopentadienones[66,160] are also potentially useful building blocks in organic, organometallic, and medicinal chemistry and also possess a broad range of biological activities such as antiproliferative, antitumor, fungicidal and also act as estrogen binding receptors. This initiated the development of many synthetic methods for the fused cyclopentadienones.

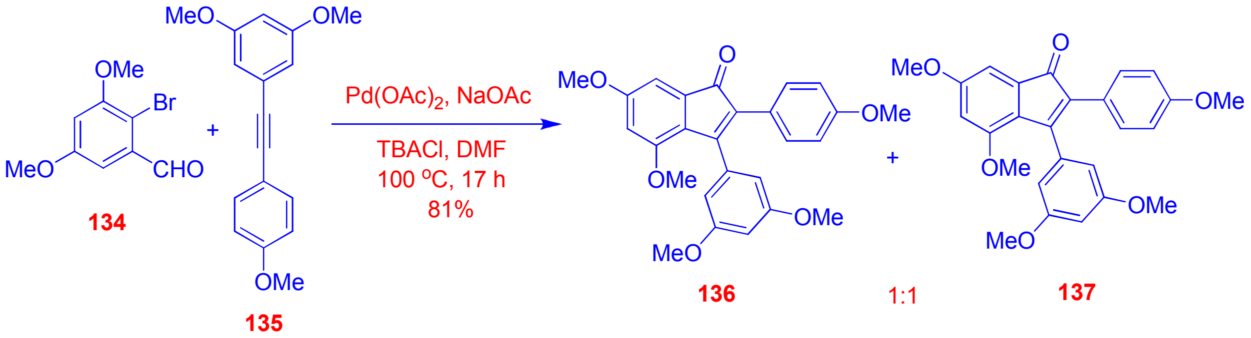
Type 2 diabetes mellitus,[161] also known as non-insulin-dependent diabetes mellitus. In the course of the search for PPARç agonists through HTS (high throughput screening) using the chemical library found that the substituted cyclopentadienone skeleton was discovered as a hit toward PPARç agonists. Kim and Cheon *et al*.[162] reported (eq. 42) the 3-hydoxybenzyl chloride **265** was coupled with ethyl benzoylacetate **266** to produce the coupling product, followed by cyclization using polyphosphoric acid to afford the corresponding indene **267**. Further, **267** was oxidized by SeO_2 to produce the indenone **268**, which was alkylated with RBr to afford the final substituted indenone derivatives **269**.

Eq. 42



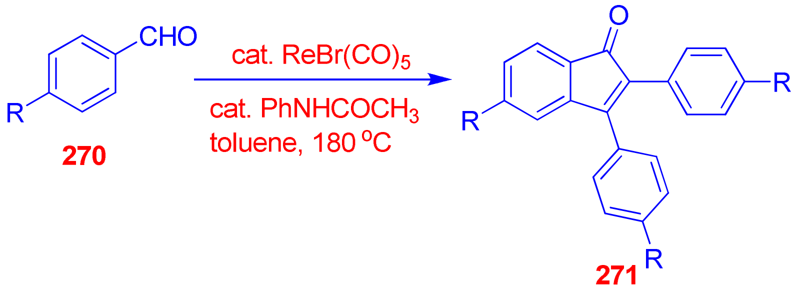
Polyphenolic natural products[162] such as resveratrol and its derivatives have emerged as important synthetic targets due to their diverse architectures and their potential medicinal utility. Sarpong *et al*. reported[74] with a mixture of **134** and **135** was subjected to Larock's original annulations conditions,[71,163] a 1:1 mixture of indenone regioisomers **136** and **137** was obtained, which could be easily seperable by column chromatography.

Eq. 43



Takai and Kuninobu *et al*. reported[165] the transformation via C-H bond activation methods to construct cyclic skeletons, and the skeletons have been constructed by intramolecular cyclization[166] and annulation reactions. Treatment of benzaldehyde **270** with catalytic amounts of a rhenium complex, $ReBr(CO)_5$, and *N*-phenylacetamide in toluene gave indenone derivative **271** in 98% yield (Eq. 44).

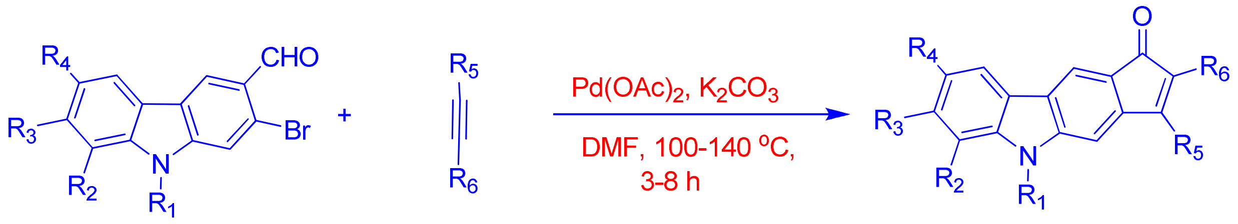
Eq. 44



4.2. Synthesis of Cyclopentacarbazolones:

Moreover, carbazole motif is prominent structural unit discerned in various natural products and synthetic compounds with vital medicinal values. Due to their significant pharmacological importance, the development of facile strategies to obtain such frameworks has become an attractive endeavor in synthetic organic and medicinal chemistry. Therefore, the synthesis of carbazole fused derivatives has become an important research field and several methods have been developed.

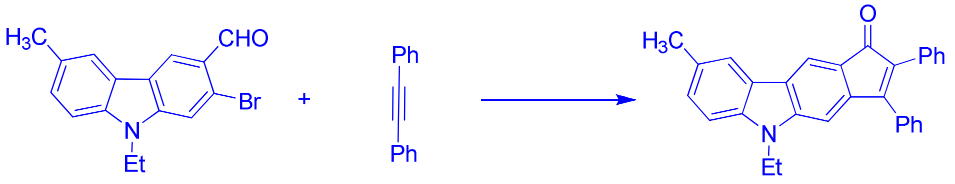
In recent years, several methodologies have been reported for the synthesis of cyclopentadienone fused with heterocyclic based natural products.[167] Palladium catalyzed Larock annulation of internal alkynes by substituted *ortho* halobenzaldehyde have been demonstrated to be a versatile methodology to construct a wide range of complicated hetero- and carbocycles.[168] To the best of our knowledge no reports were available on the synthesis of carbazole fused with substituted cyclopentadienone. Considering the biological as well as material importance of carbazole and cyclopentadienone nuclei in various natural products and drugs, herein we wish to report a simple, an efficient protocol for the synthesis of various 2,3-disubstituted cyclopentacarbazolones by the reaction of 2-bromo-3-formylcarbazole with internal alkynes in the presence of palladium catalyst under ligand-free condition as shown in Scheme 14.



Scheme 14. Schematic representation of our present work.

2-Bromo-9-ethyl-6-methyl-9*H*-carbazole-3-carbaldehyde and diphenylacetylene were used as model substrates for optimizing the reaction conditions. The influence of catalyst, ligand, additive, base, solvent, and temperature in the reaction outcome were examined as shown in Table 24. In the initial screenings, DMF was found to be an efficient media in which various solvents were tested for the reaction. Furthermore, different bases such as Cs_2CO_3, Na_2CO_3, DABCO, KOAc, and K_2CO_3 were tested in the reaction; it was found that K_2CO_3 was superior to the other bases. Ligand and additives had no effect on the reaction, without ligand and additive the reaction proceeded well within 3 h (entry 14, Table 24). No reaction occurred at or below 90 °C. By changing the catalyst loading below 5 mol %, the reaction took more time to reach completion whereas when the catalyst loading was increased (7.5-10 mol %), the reaction reached completion within 3 h with increased yield of the product. Based on above findings, we concluded that the optimal condition for this reaction found to involve 1.0 equiv of **272a**, 1.0 equiv of **273a** and 2.5 equiv of K_2CO_3 in DMF with 7.5 mol % of $Pd(OAc)_2$ at 140 °C. By using the optimized condition the product **274a** was obtained in good yield (74%) within 3 h.

Table 24. The screening of reaction conditions[a]



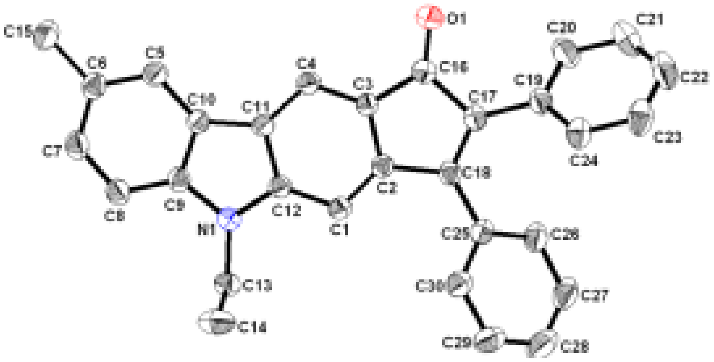
272a **273a** **274a**

entry	catalyst	ligand	additive	base	solvent	temp (^oC)	time (h)	yield[e] (%)
1	Pd/C[b]			Et_3N	DMF	120	24	nr[c]
2	$Pd(PPh_3)_2Cl_2$		TBAB	Cs_2CO_3	Toulene	120	24	22
3	$Pd(OAc)_2$			DABCO	DMF	130	28	30
4	$Pd(PPh_3)_4$			Ag_2CO_3	DMF	140	24	nr
5	$Pd(OAc)_2$	PPh_3	TBAB	K_2CO_3	DMF	120	8	62
6	$Pd(OAc)_2$	PPh_3		K_2CO_3	DMF	120	8	65
7	$Pd(OAc)_2$		TBAB	K_2CO_3	DMF	140	8	65
8	$Pd(OAc)_2$	PCy_3	LiCl	K_2CO_3	DMF	140	10	70
9	$Pd(OAc)_2$	dppe	SDS	K_2CO_3	DMF	140	6	64
10	$Pd(OAc)_2$		SDS	KOAc	DMA	140	8	64
11	$Pd(OAc)_2$		LiCl	Cs_2CO_3	DMSO	140	10	70
12	$Pd(OAc)_2$		TBAB	KOAc	ODCB	130	18	42
13	$Pd(OAc)_2$			K_2CO_3	DMF	140	8	70
14	**$Pd(OAc)_2$[d]**			**K_2CO_3**	**DMF**	**140**	**3**	**74**
15				K_2CO_3	DMF	140	24	nr
16	$Pd(OAc)_2$			KOAc	TEG	140	15	38
17	$PdCl_2$			$NaHCO_3$	DMF	140	15	48

[a] unless otherwise stated, all the reactions were carried at in a Schlenk tube by employing 0.05 equiv of catalyst, 0.2 equiv of ligand, 1.0 equiv of additive and 2.0 equiv of base. [b] 10 mol % of Pd/C was used. [c] nr = no reaction. [d] 7.5 mol% of $Pd(OAc)_2$ was used. [e] isolated yields. (TBAB = tetrabutyl ammonium bromide, SDS = sodium lauryl sulphate), ODCB = 1,2-dichlorobenzene, TEG = tetraethylene glycol).

The product **274a** was confirmed by spectral data and single crystal X-ray analysis. The ORTEP diagram is shown in Figure 22.[169]

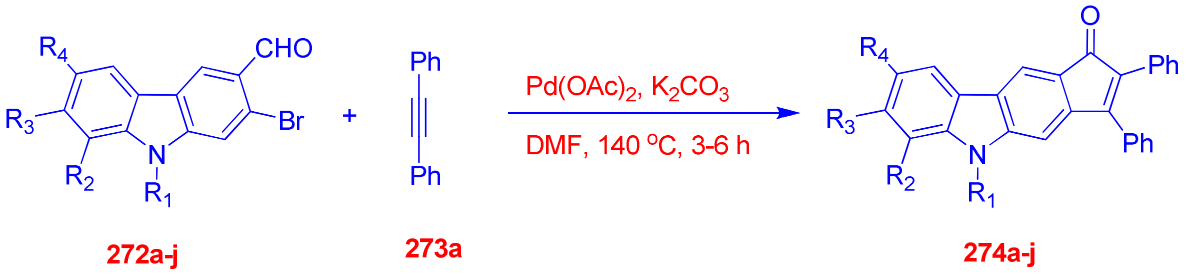
Figure 22 ORTEP diagram of 274a



With the optimized condition in hand, various derivatives **272a-j** were treated with diphenylacetylene **273a**, the reaction proceeded well to afford the corresponding products **274a-j** in moderate to good yields as shown in Table 25. After synthesis of 2,3-diphenylcyclopentacarbazolone derivatives **274a-j**, we noticed that if any electron-withdrawing group present at 5th position gave good yields such as **274j** in 82%, **274d** in 78% as shown in Table 14. In the case of higher alkyl chain substitution present at 5th position such as **274b**, **274c**, **274g**, and **274i** gave moderate yields.

To check the versatility of this annulation, various types of internal alkynes such as symmetrically and unsymmetrically substituted alkyl-aryl alkynes were tested. Symmetrical alkyl acetylenes **273b-c** afforded the products **274k-n** in moderate yields as shown in Table 26. In the case of symmetrically substituted arylalkynes, the products **274o** and **274p** were obtained in good yields.

Table 25. Synthesis of 2,3-diphenylcyclopentacarbazolones



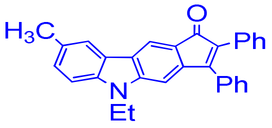
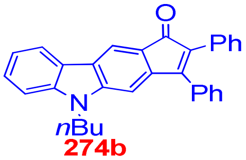
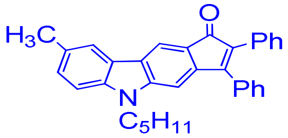
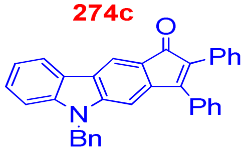
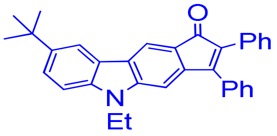
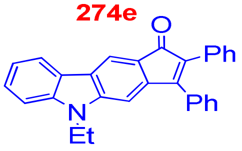
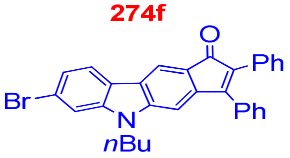
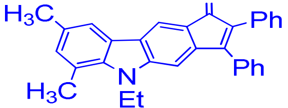
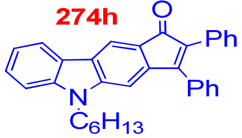
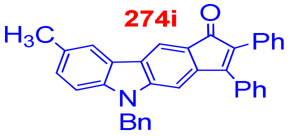
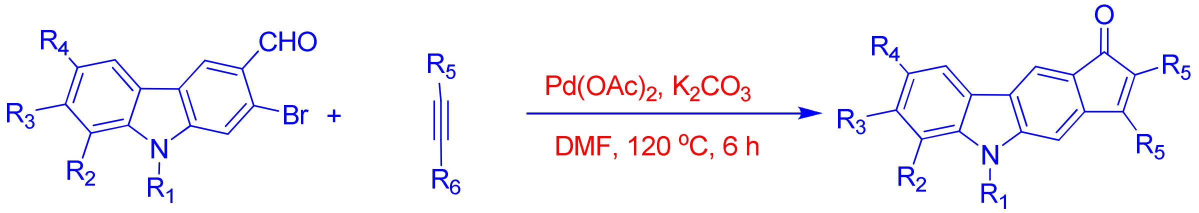
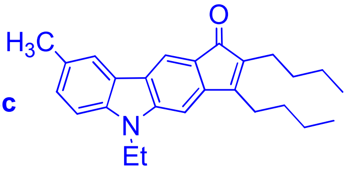
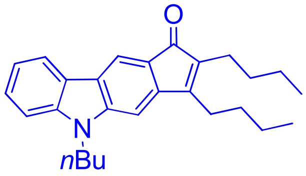
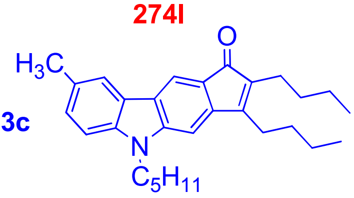
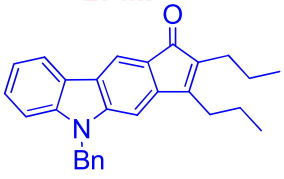
s.no	R_1	R_2	R_3	R_4	time (h)	Product	Yield (%)
1	Et	H	H	CH_3	3	 **274a**	74
2	*n*-Bu	H	H	H	5	 **274b**	65
3	*n*-pentyl	H	H	CH_3	5	 **274c**	63
4	Bn	H	H	H	4	 **274d**	78
5	Et	H	H	*t*Bu	4	 **274e**	76
6	Et	H	H	H	4	 **274f**	68
7	*n*-Bu	H	Br	H	6	 **274g**	56
8	Et	CH_3	H	CH_3	3	 **274h**	80
9	*n*-hexyl	H	H	H	4	 **274i**	65
10	Bn	H	H	CH_3	4	 **274j**	82

Table 26. Synthesis of 2,3-dialkylcyclopentacarbazolones



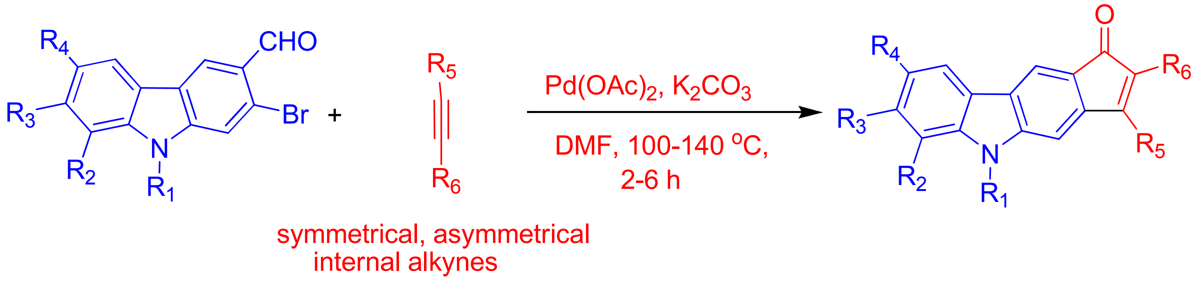
272a-d **273b-c** **274k-n**

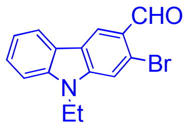
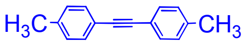
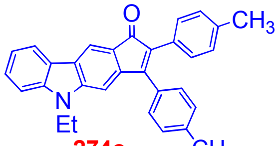
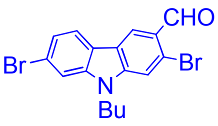
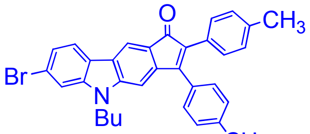
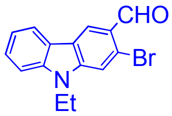
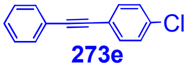
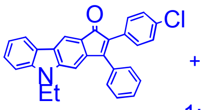
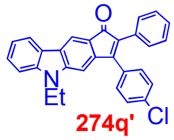
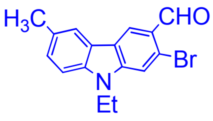
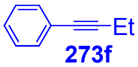
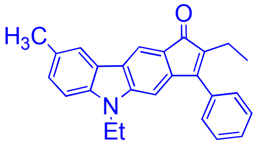
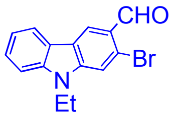
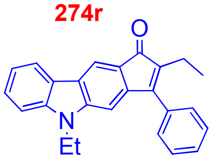
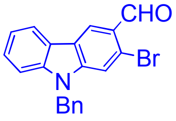
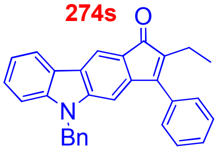
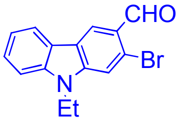
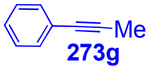
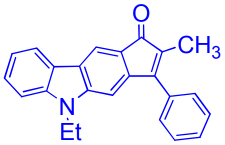
R_5, R_6 = *n*-Pr,
= *n*-Bu

entry	R_1	R_2	R_3	R_4	alkyne[a]	Product	Yield (%)[b]
1	Et	H	H	CH_3	**273c**	 **274k**	60
2	*n*-Bu	H	H	H	**273c**	 **274l**	54
3	*n*-pentyl	H	H	CH_3	**273c**	 **274m**	50
4	Bn	H	H	H	**273b**	 **274n**	64

[a] 2.5 equiv of alkyne used. [b] isolated yield.

Table 27. Synthesis of various 2,3-disubstitutedcyclopentacarbazolones

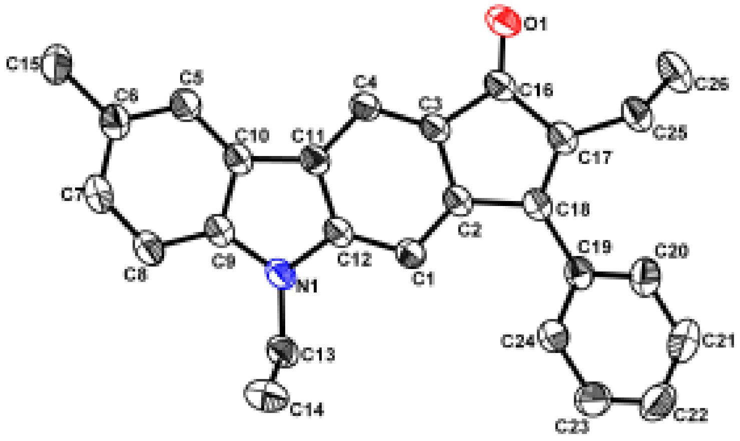


entry	aldehyde	alkyne[a]	time (h)	temp (°C)	product	yield (%)[b]
1		 **273d**	3	140	 **274o**	80
2		**273d**	5	140	 **274p**	58
3		 **273e**	6	140	 **274q** +  **274q'** 1:1	55
4		 **273f**	6	100	 **274r**	60
5		**273f**	6	100	 **274s**	54
6		**273f**	5	120	 **274t**	62
7		 **273g**	7	100	 **274u**	55

[a] **273f-g**, 2.5 equiv of alkyne used. [b] isolated yield.

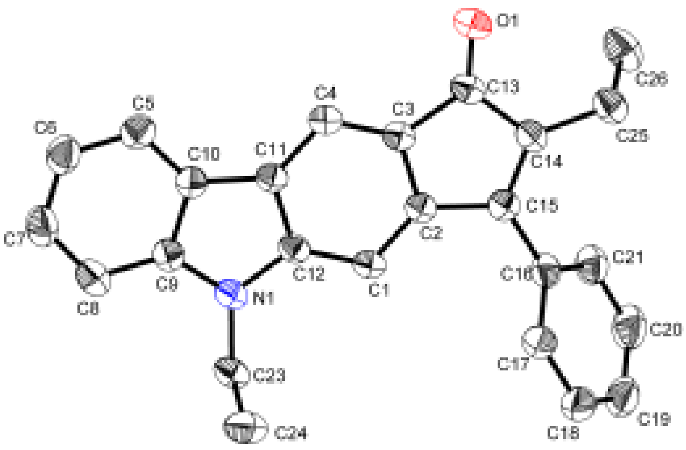
When we used the unsymmetrical arylalkyne chlorodiphenylacetylene **273e**, two regioisomers **274q** and **274q'** were obtained in the ratio 1:1 as shown in Table 27. Treatment of aryl alkyl substituent's such as 1-phenylbutyne **273f**, we obtained only one regioisomer **274r** in 60% yield. From the 2DNOESY, in the product **274r** we confirmed that the ethyl group is adjacent to the carbonyl functional group. The product **274r** was also confirmed by single crystal X-ray analysis. The ORTEP diagram is as shown in Figure 23.[169]

Figure 23 ORTEP diagram of 274r

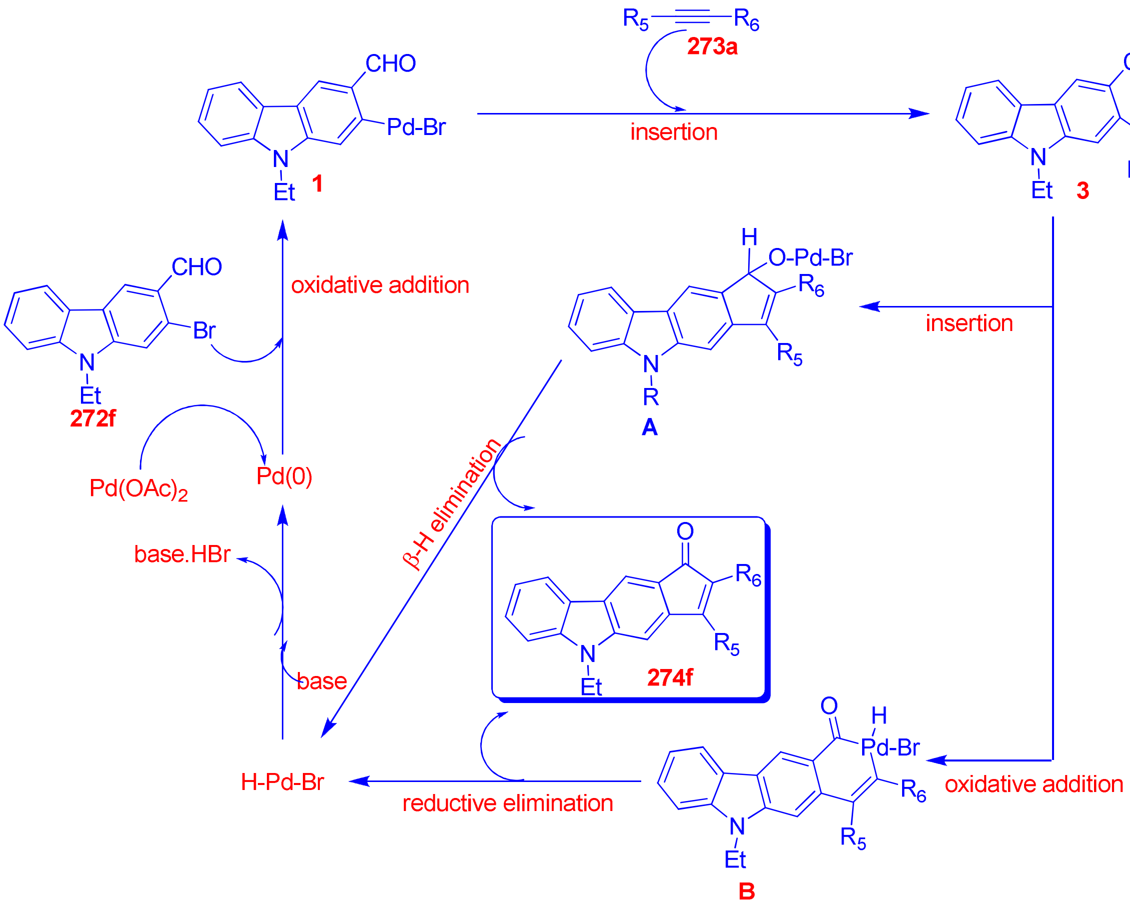


In the same manner we obtained the products **274s**, **274t**, and **274u** as shown in Table 27. The product **274s** was also confirmed by single crystal X-ray analysis and the ORTEP diagram is shown in Figure 24.[169]

Figure 24 ORTEP diagram of 274s



The possible mechanism of annulation is illustrated in Scheme 15. (i) reduction of $Pd(OAc)_2$ to Pd(0) (ii) oxidative addition of aryl halide to Pd(0) (iii) aryl palladium coordination to the alkyne and then insertion of alkyne to form a vinyl palladium intermediate (iv) asecond oxidative insertion into the aldehyde C-H bond to form a palladium(IV) intermediate (v) elimination of HBr by K_2CO_3 (vi) regeneration of Pd(0) by reductive elimination to form 2,3-disubstitutedcyclopentacarbazolone.



Scheme 15. Possible mechanism for annulation reaction

4.3. Conclusion:

In conclusion, an efficient synthesis of 2,3-disubstituted cyclopentacarbazolones has been developed by using palladium catalyzed annulation of internal alkynes with various 2-bromo-3-formylcarbazoles. The reaction proceeds well under relatively mild conditions with shorter reaction times. For unsymmetrical (alkyl, aryl substituted) alkynes, the one-pot annulation approach affords selectively single regioisomer.

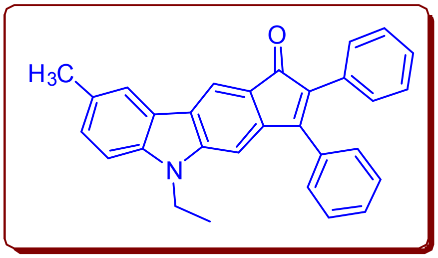
4.4. Experimental Section

General procedure L:

A schlenk tube was charged with **272a** (0.10 g, 0.315 mmol), diphenylacetylene **273a** (0.056 g, 0.315 mmol) in DMF and then K_2CO_3 (0.10 g, 0.78 mmol), $Pd(OAc)_2$ (5.0 mg, 0.023 mmol) were added and heated on oil-bath till the completion of reaction as indicated by TLC. The reaction mixture was cooled to room temperature and then poured in water, extracted with ethylacetate (3 × 10 mL), and washed with water (3 × 10 mL) followed by brine (20 mL) and dried over anhyd. Na_2SO_4. The solvent was evaporated under reduced pressure and the crude product was purified by column chromatography over silicagel (100-200 mesh), using 7% ethylacetate in hexanes as an eluent to obtained the corresponding product **274a** in 74% yield. The same procedure was applied for all the compound preparations.

5-ethyl-8-methyl-2,3-diphenylcyclopenta[*b*]carbazol-1(5*H*)-one (274a):

The orange color solid product **274a** was obtained from **272a** and **273a** followed by general procedure L and was purified by column chromotography using 7% ethylacetate in hexanes.



Yield:	74%
Mp:	170 °C
IR (KBr) ν_{max} cm^{-1}:	2922, 1682, 1589, 1481, 1327, 1244, 788, 509
^{1}H NMR (500 MHz, $CDCl_3$):	δ 8.24 (s,1H), 7.82 (s, 1H), 7.44 (d, 5H, *J* = 3.5 Hz), 7.30-7.23 (m, 7H), 6.97 (s, 1H), 4.26 (q, 2H, *J* = 7.5 Hz), 2.52 (s, 3H), 1.37 (t, 3H, *J* = 7.0 Hz)
^{13}C NMR (125 MHz, $CDCl_3$):	δ 195.3, 154.6, 143.7, 142.9, 138.5, 134.6, 133.4, 131.2, 130.0, 129.9, 128.9, 127.9, 127.4, 127.2, 124.2, 122.9, 121.5, 120.2, 117.1, 108.9, 103.3, 37.8, 21.4, 14.0

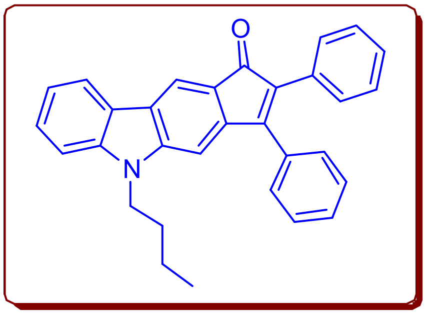
LC-MS (m/z): 414 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{30}H_{23}NO$: C, 87.14; H, 5.61; N, 3.39%

Found: C, 87.21; H, 5.58; N, 3.32%

5-Butyl-2,3-diphenylcyclopenta[*b*]carbazol-1(5*H*)-one (274b):

The orange color solid product **274b** was obtained from **272b** and **273a** followed by general procedure L and was purified by column chromotography using 7% ethylacetate in hexanes.



Yield: 65%

Mp: 120-121 °C

IR (KBr) ν_{max} cm^{-1}: 2926, 1691, 1585, 1365, 727

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.28 (s, 1H), 8.03 (d, 1H, *J* = 10.0 Hz), 7.46-7.37 (m, 7H), 7.31-7.23 (m, 6H), 7.01 (s, 1H), 4.23 (t, 2H, *J* = 6.5 Hz), 1.83-1.77 (m, 2H), 1.38-1.32 (m, 2H), 0.92 (t, 3H, *J* = 7.5 Hz)

^{13}C NMR (125 MHz, $CDCl_3$): δ 195.3, 154.6, 143.8, 143.3, 140.7, 134.6, 133.3, 130.0, 129.0, 128.8, 128.6, 127.9, 127.5, 125.7, 124.0, 123.1, 121.6, 120.4, 120.3, 117.0, 109.5, 103.6, 42.9, 31.2, 20.3, 13.7

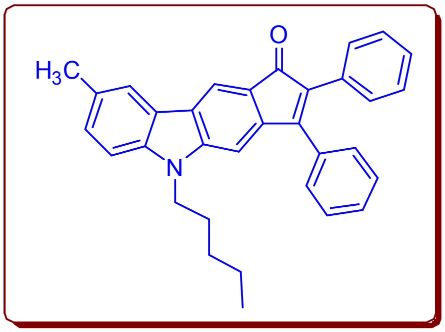
LC-MS (m/z): 426 (M-H) negative mode

Anal. Calcd. for $C_{31}H_{25}NO$: C, 87.09; H, 5.89; N, 3.28%

Found: C, 87.22; H, 5.81; N, 3.19%

8-Methyl-5-pentyl-2,3-diphenylcyclopenta[*b*]carbazol-1(5*H*)-one (274c):

The red color solid product **274c** was obtained from **272c** and **273a** followed by general procedure L and was purified by column chromotography using 7% ethylacetate in hexanes.



Yield: 63%

Mp: 168 °C

IR (KBr) ν_{max} cm^{-1}: 2957, 1693, 1481, 1304, 1122, 794

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.24 (s, 1H), 7.82 (s, 1H), 7.45-7.43 (m, 5H), 7.31-7.22 (m, 7H), 6.98 (s, 1H), 4.19 (t, 2H, *J* = 7.2 Hz), 2.52 (s, 3H), 1.84-1.77 (m, 2H), 1.33-1.27 (m, 4H), 0.85 (t, 3H, *J* = 6.8 Hz)

^{13}C NMR (100 MHz, CDCl$_3$): δ 195.4, 154.6, 143.6, 139.0, 134.5, 133.3, 131.2, 130.0, 128.8, 128.6, 127.9, 127.1, 124.1, 122.9, 121.3, 120.1, 117.1, 109.2, 103.6, 43.2, 29.2, 28.8, 22.3, 21.4, 13.9

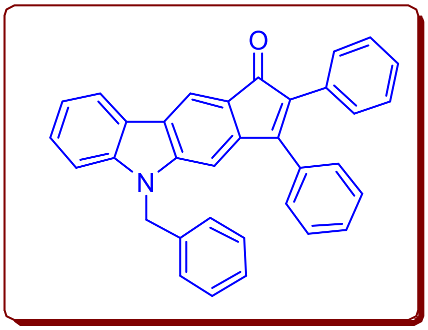
LC-MS (m/z): 456 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{33}H_{29}NO$: C, 87.00; H, 6.42; N, 3.07%

Found: C, 86.75; H, 6.35; N, 3.15%

5-Benzyl-2,3-diphenylcyclopenta[*b*]carbazol-1(5*H*)-one (274d):

Red solid The orange color solid product **274d** was obtained from **272d** and **273a** followed by general procedure L and was purified by column chromotography using 8% ethylacetate in hexanes.



Yield: 78%

Mp: 192 °C

IR (KBr) ν_{max} cm^{-1}: 1691, 1589, 1385, 1263, 1163, 1030, 787

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.30 (s, 1H), 8.05 (d, 1H, *J* = 7.5 Hz), 7.39 (d, 4H, *J* = 5.0 Hz), 7.32 (d, 3H, *J* = 3.5 Hz), 7.27-7.22 (m, 9H), 7.08 (d, 2H, *J* = 6.0 Hz), 6.99 (s, 1H), 5.44 (s, 2H)

^{13}C NMR (125 MHz, CDCl$_3$): δ 195.3, 154.6, 144.0, 143.5, 140.9, 136.3, 134.5, 133.1, 131.1, 130.0, 129.0, 128.9, 128.8, 127.9, 127.7, 126.4, 126.0, 124.1, 123.6, 121.9, 120.8, 120.3, 117.0, 109.7, 103.9, 46.9

LC-MS (m/z): 462 (M+H)$^+$ positive mode

Anal. Calcd. for $C_{34}H_{23}NO$: C, 88.48; H, 5.02; N, 3.07%

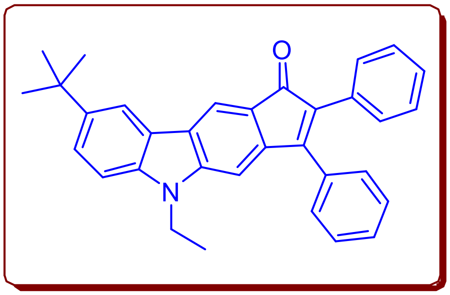
Found: C, 88.32; H, 4.96; N, 3.12%

8-*tert*-Butyl-5-ethyl-2,3-diphenylcyclopenta[*b*]carbazol-1(5*H*)-one (274e):

The red solid product **274e** was obtained from **272e** and **273a** followed by general procedure L and was purified by column chromotography using 6% ethylacetate in hexanes.

Yield: 76%

Mp: 185-187 °C



IR (KBr) ν_{max} cm^{-1}: 2957, 1693, 1591, 1477, 1302, 1059, 1026, 744

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.31 (s, 1H), 8.05 (s, 1H), 7.53-7.22 (m, 6H), 7.33-7.22 (m, 6H), 6.99 (s, 1H), 4.27 (q, 2H, *J* = 7.0 Hz), 1.56 (s, 9H), 1.39 (t, 3H, *J* = 7.5 Hz)

^{13}C NMR (125 MHz, CDCl$_3$): δ 195.4, 154.6, 143.6, 143.1, 138.4, 134.5, 133.4, 131.2, 130.0, 128.9, 128.8, 128.6, 127.9, 127.4, 123.9, 123.8, 123.0, 121.9, 117.1, 116.4, 108.8, 103.3, 37.9, 31.8, 14.1

LC-MS (m/z): 456 (M+H)$^+$ positive mode

Anal. Calcd. for $C_{33}H_{29}NO$: C, 87.00; H, 6.42; N, 3.07%

Found: C, 86.91; H, 6.38; N, 3.15%

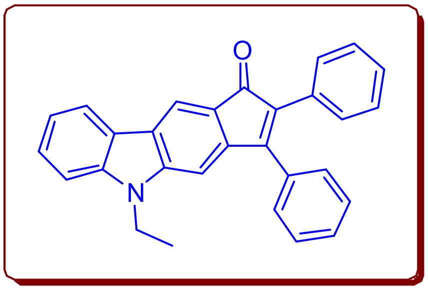
5-Ethyl-2,3-diphenylcyclopenta[*b*]carbazol-1(5*H*)-one (274f):

The orange color solid product **274f** was obtained from **272f** and **273a** followed by general procedure L and was purified by column chromatography using 6% ethylacetate in hexanes.

Yield: 68%

Mp: 220 ˚C

IR (KBr) v_{max} cm^{-1}: 2974, 2930, 1684, 1587, 1469, 1325, 1168, 841, 750, 694, 513



^{1}H NMR (500 MHz, $CDCl_3$): δ 8.31 (s, 1H), 8.07 (d, 1H, *J* = 8.0 Hz), 7.51-7.45 (m, 6H), 7.41 (d, 1H, *J* = 8.0 Hz), 7.34-7.27 (m, 6H), 7.04 (s, 1H), 4.33 (q, 2H, *J* = 7.5 Hz), 1.43 (t, 3H, *J* = 7.5 Hz)

^{13}C NMR (125 MHz, $CDCl_3$): δ 195.3, 154.6, 143.9, 142.8, 140.2, 134.6, 133.3, 131.2, 130.0, 129.0, 128.9, 128.6, 127.9, 127.5, 125.7, 124.1, 123.2, 121.7, 120.4, 117.1, 109.2, 103.3, 37.8, 14.0

LC-MS (m/z): 400 (M+H)$^+$ positive mode

Anal. Calcd. for $C_{29}H_{21}NO$: C, 87.19; H, 5.30; N, 3.51%

Found: C, 87.09; H, 5.36; N, 3.48%

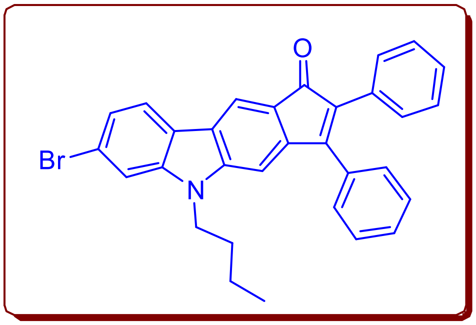
7-Bromo-5-butyl-2,3-diphenylcyclopenta[*b*]carbazol-1(5*H*)-one (274g):

The red color solid product **274g** was obtained from **272g** and **273a** followed by general procedure L and was purified by column chromatography using 7% ethylacetate in hexanes.

Yield: 56%

Mp: 180 ˚C

IR (KBr) v_{max} cm^{-1}: 2961, 2858, 1684, 1585, 1481, 1386,



1244, 1116, 1055, 896, 794, 698

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.22 (s, 1H), 7.87 (d, 1H, J = 8.0 Hz), 7.52 (s, 1H), 7.47-7.42 (m, 5H), 7.37-7.35 (dd, 1H, J_1 = 1.5 Hz, J_2 = 1.5 Hz), 7.30-7.23 (m, 5H), 7.01 (s, 1H), 4.19 (t, 2H, J = 7.5 Hz), 1.82-1.76 (m, 2H), 1.38-1.32 (m, 2H), 0.93 (t, 3H, J = 7.5 Hz)

^{13}C NMR (125 MHz, CDCl$_3$): δ 195.1, 154.5, 144.2, 143.5, 141.4, 134.7, 133.1, 133.0, 129.9, 129.1, 128.9, 128.5, 128.0, 127.6, 123.7, 123.6, 122.8, 121.4, 121.2, 119.3, 116.8, 112.6, 103.7, 43.1, 31.1, 20.3, 13.7

LC-MS (m/z): 507 (M+H)$^{+}$, 509 (M+2) positive mode

Anal. Calcd. for $C_{31}H_{24}BrNO$: C, 73.52; H, 4.78; N, 2.77%

Found: C, 73.45; H, 4.86; N, 2.71%

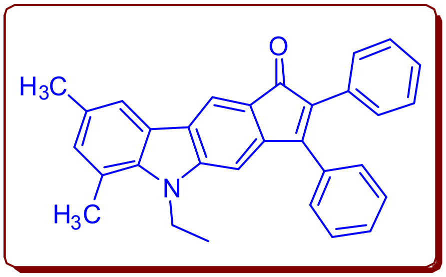
5-Ethyl-6,8-dimethyl-2,3-diphenylcyclopenta[*b*]carbazol-1(5*H*)-one (274h):

The red color solid product **274h** was obtained from **272h** and **273a** followed by general procedure L and was purified by column chromatography using 7% ethylacetate in hexanes.

Yield: 80%

Mp: 187 °C

IR (KBr) ν$_{max}$ cm^{-1}: 2914, 1685, 1593, 1469, 1313, 1232, 846, 744, 582, 511



^{1}H NMR (500 MHz, CDCl$_3$): δ 8.19 (s, 1H), 7.65 (s, 1H), 7.47-7.41 (m, 5H), 7.29-7.20 (m, 5H), 6.97 (s, 1H), 6.93 (s, 1H), 4.43 (q, 2H, J = 7.0 Hz), 2.71 (s, 3H), 2.45 (s, 3H), 1.35 (t, 3H, J = 7.5 Hz)

^{13}C NMR (125 MHz, CDCl$_3$): δ 195.3, 154.7, 143.6, 143.5, 137.2, 134.5, 133.4, 131.3, 130.7, 130.0, 128.9, 128.8, 127.9, 127.4, 125.2, 123.1, 121.8, 120.3, 118.0, 116.8, 103.4, 39.6, 21.0, 19.7, 15.8

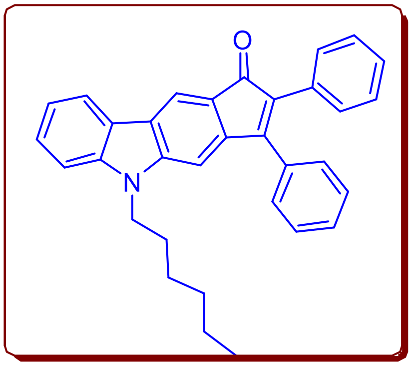
LC-MS (m/z): 428 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{31}H_{25}NO$: C, 87.09; H, 5.89; N, 3.28%

Found: C, 87.22; H, 5.81; N, 3.36%

5-Hexyl-2,3-diphenylcyclopenta[*b*]carbazol-1(5*H*)-one (274i):

The redcolor solid product **274i** was obtained from **272i** and **273a** followed by general procedure L and was purified by column chromotography using 7% ethylacetate in hexanes.



Yield: 65%

Mp: 130 °C

IR (KBr) ν_{max} cm^{-1}: 2924, 1687, 1589, 1468, 1251, 1161, 790

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.27 (s, 1H), 8.02 (d, 1H, *J* = 8.0 Hz), 7.45-7.41 (m, 6H), 7.37 (d, 1H, *J* = 8.0 Hz), 7.30 (d, 2H, *J* = 6.5 Hz), 7.26 (d, 2H, *J* = 8.0 Hz), 7.23 (d, 2H, *J* = 8.5 Hz), 7.00 (s, 1H), 4.21 (t, 2H, *J* = 7.5 Hz), 1.84-1.78 (m, 2H), 1.33-1.25 (m, 6H), 0.84 (t, 3H, *J* = 7.0 Hz)

^{13}C NMR (125 MHz, $CDCl_3$): δ 195.3, 154.6, 143.8, 143.3, 140.7, 134.6, 133.3, 131.2, 130.0, 129.0, 128.8, 127.9, 125.7, 124.0, 123.1, 121.6, 120.4, 117.0, 109.5, 103.6, 43.2, 31.4, 29.0, 26.7, 22.4, 13.9

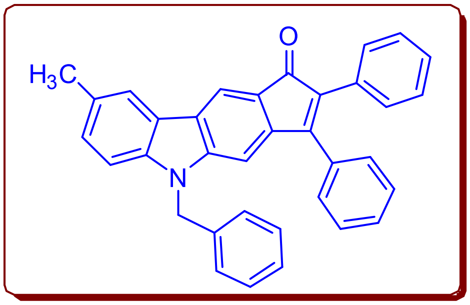
LC-MS (m/z): 456 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{33}H_{29}NO$: C, 87.00; H, 6.42; N, 3.07%

Found: C, 87.19; H, 6.37; N, 3.15%

5-Benzyl-8-methyl-2,3-diphenylcyclopenta[b]carbazol-1(5H)-one (274j):

The orange color solid product **274j** was obtained from **272j** and **273a** followed by general procedure L and was purified by column chromotography using 7% ethylacetate in hexanes.



Yield: 82%

Mp: 156-157 °C

IR (KBr) v_{max} cm^{-1}: 2922, 1685, 1481, 1302, 1149, 1026, 696

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.28 (s, 1H), 7.85 (s, 1H), 7.40-7.38 (m, 3H), 7.33-7.31 (m, 2H), 7.28-7.24 (m, 7H), 7.23 (d, 1H, J = 2.0 Hz), 7.20 (d, 2H, J = 0.8 Hz), 7.08-7.06 (dd, 2H, J_1 = 2.0 Hz, J_2 = 1.2 Hz), 6.97 (s, 1H), 5.42 (s, 2H), 2.52 (s, 3H)

^{13}C NMR (100 MHz, CDCl$_3$): δ 195.3, 154.5, 143.8, 143.7, 139.2, 136.4, 134.5, 131.2, 130.3, 129.9, 128.8, 128.7, 128.5, 127.9, 127.7, 127.5, 127.4, 126.4, 124.3, 123.4, 121.7, 120.2, 117.0, 109.4, 103.9, 46.9, 21.4

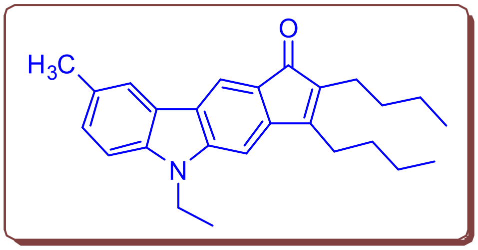
LC-MS (m/z): 476 (M+H)$^+$ positive mode

Anal. Calcd. for $C_{35}H_{25}NO$: C, 88.39; H, 5.30; N, 2.95%

Found: C, 88.25; H, 5.36; N, 2.87%

2,3-Dibutyl-5-ethyl-8-methylcyclopenta[*b*]carbazol-1(5*H*)-one (274k):

The viscous orange liquid product **274k** was obtained from **272a** and **273b** followed by general procedure L and was purified by column chromotography using 7% ethylacetate in hexanes.



Yield: 60%

IR (KBr) v_{max} cm^{-1}: 2926, 1693, 1599, 1483, 1304, 1022, 794

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.06 (s, 1H), 7.79 (s, 1H), 7.32 (d, 1H, *J* = 2.8 Hz), 7.28 (d, 1H, *J* = 2.0 Hz), 6.95 (s, 1H), 4.36 (q, 2H, *J* = 5.6), 2.26 (t, 2H, *J* = 6.4), 2.53 (s, 3H), 2.31 (t, 2H, *J* = 6.0 Hz), 1.72-1.67 (m, 4H), 1.55-1.49 (m, 4H), 1.46 (t, 6H, *J* = 5.6 Hz), 1.03 (t, 3H, *J* = 6.0 Hz)

^{13}C NMR (100 MHz, CDCl$_3$): δ 197.5, 156.4, 144.4, 143.0, 138.2, 137.1, 129.6, 126.6, 123.4, 120.8, 120.0, 115.7, 108.7, 103.6, 100.8, 37.8, 31.5, 30.6, 25.8, 23.0, 22.9, 22.8, 21.3, 14.1, 14.0, 13.9

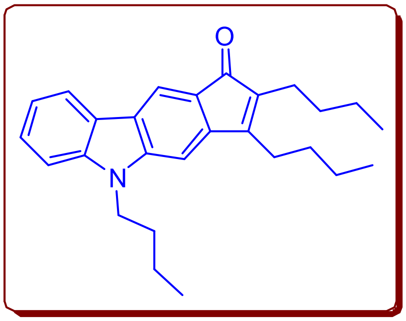
LC-MS (m/z): 374 (M+H)$^+$ positive mode

Anal. Calcd. for $C_{26}H_{31}NO$: C, 83.60; H, 8.37; N, 3.75%

Found: C, 83.45; H, 8.31; N, 3.82%

2,3,5-Tributylcyclopenta[*b*]carbazol-1(5*H*)-one (274l):

The viscous orange liquid product **274l** was obtained from **272b** and **273b** followed by general procedure L and was purified by column chromotography using 6% ethylacetate in hexanes.



Yield: 54%

IR (KBr) ν_{max} cm^{-1}: 2957, 1693, 1467, 1331, 1209, 1016, 742

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.04 (s, 1H), 7.96 (d, 1H, *J* = 7.5 Hz), 7.39-7.33 (m, 2H), 7.23-7.19 (m, 1H), 6.93 (s, 1H), 4.26 (t, 2H, *J* = 7.0 Hz), 2.58 (t, 2H, *J* = 8.0 Hz), 2.28 (t, 2H, *J* = 7.5 Hz), 1.86-1.80 (m, 2H), 1.70-1.62 (m, 2H), 1.52-1.47 (m, 4H), 1.41-1.37 (m, 4H), 1.00 (t, 3H, *J* = 7.0 Hz), 0.94 (t, 6H, *J* = 7.5 Hz)

^{13}C NMR (125 MHz, CDCl$_3$): δ 197.5, 156.4, 144.5, 143.4, 140.3, 137.2, 125.2, 124.7, 124.1, 123.6, 121.0, 120.6, 120.1, 115.6, 109.3, 101.2, 31.5, 30.6, 25.8, 23.1, 23.0, 22.9, 20.4, 14.0, 13.9, 13.8

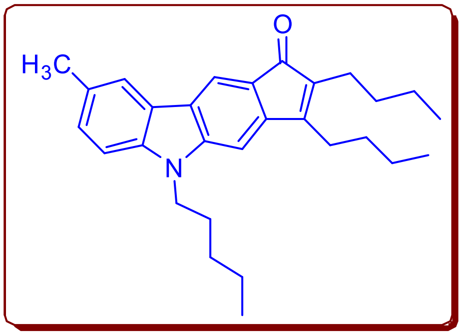
LC-MS (m/z): 388 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{27}H_{33}NO$: C, 83.68; H, 8.58; N, 3.61%

Found: C, 83.55; H, 8.51; N, 3.68%

2,3-Dibutyl-8-methyl-5-pentylcyclopenta[*b*]carbazol-1(5*H*)-one (274m):

The viscous orange liquid product **274m** was obtained from **272c** and **273b** followed by general procedure L and was purified by column chromotography using 6% ethylacetate in hexanes.



Yield: 50%

IR (KBr) ν_{max} cm^{-1}: 2957, 1693, 1601, 1466, 1259, 1022, 794

^1H NMR (400 MHz, $CDCl_3$): δ 8.02 (s, 1H), 7.76 (s, 1H), 7.40 (d, 1H, *J* = 2.0 Hz), 7.24 (d, 1H, *J* = 0.8 Hz), 6.91 (s, 1H), 4.25 (t, 2H, *J* = 7.2 Hz), 2.58 (t, 2H, *J* = 8.0 Hz), 2.50 (s, 3H), 2.28 (t, 2H, *J* = 7.6 Hz), 1.87-1.83 (m, 2H), 1.67-1.62 (m, 2H), 1.52-1.45 (m, 6H), 1.36-1.32 (m, 4H), 0.99 (t, 3H, *J* = 7.6 Hz), 0.93 (t, 6H, *J* = 7.2 Hz)

^{13}C NMR (100 MHz, $CDCl_3$): δ 197.9, 156.4, 144.3, 143.5, 138.7, 137.1, 135.3, 133.2, 128.8, 127.7, 126.6, 119.9, 115.6, 108.9, 101.1, 43.2, 31.5, 30.6, 28.9, 25.8, 23.1, 23.0, 22.9, 22.7, 22.4, 21.4, 14.0, 13.9, 13.8

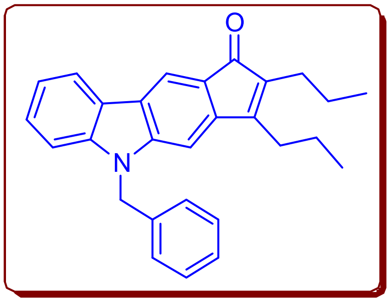
LC-MS (m/z): 416 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{29}H_{37}NO$: C, 83.81; H, 8.97; N, 3.37%

Found: C, 83.95; H, 8.91; N, 3.45%

5-Benzyl-2,3-dipropylcyclopenta[*b*]carbazol-1(5*H*)-one (274n):

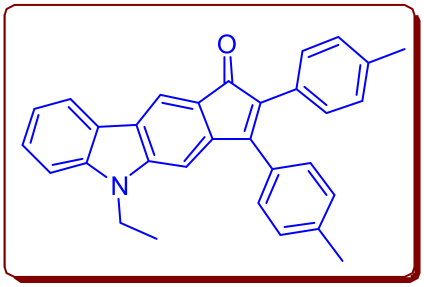
The viscous orange liquid product **274n** was obtained from **272d** and **273c** followed by general procedure L and was purified by column chromatography using 6% ethylacetate in hexanes.



Yield:	64%
Mp:	72 $^{\circ}$C
IR (KBr) ν_{max} cm^{-1}:	2926, 1693, 1467, 1390, 1331
^{1}H NMR (500 MHz, CDCl$_3$):	δ 8.09 (s,1H), 8.00 (d, 1H, *J* = 8.0 Hz), 7.35 (t, 1H, *J* = 7.5 Hz), 7.30-7.22 (m, 5H), 7.12 (d, 2H, *J* = 7.0 Hz), 6.9 (s, 1H), 5.40 (s, 2H), 2.49 (t, 2H, *J* = 10.0 Hz), 2.25 (t, 2H, *J* = 10.0 Hz), 1.64-1.58 (m, 2H), 1.54-1.50 (m, 2H), 1.00 (t, 3H, *J* = 7.5 Hz), 0.95 (t, 3H, *J* = 7.5 Hz)
^{13}C NMR (125 MHz, CDCl$_3$):	δ 197.5, 156.5, 144.7, 143.6, 140.6, 137.2, 136.5, 128.9, 127.7, 126.3, 125.5, 124.2, 120.9, 120.5, 120.0, 115.6, 109.5, 101.5, 46.8, 29.6, 25.2, 22.6, 21.7, 14.4, 14.2
LC-MS (m/z):	394 (M+H)$^+$ positive mode
Anal. Calcd. for $C_{28}H_{27}NO$:	C, 85.46; H, 6.92; N, 3.56%
Found:	C, 85.32; H, 7.06; N, 3.45%

5-Ethyl-2,3-di-*p*-tolylcyclopenta[*b*]carbazol-1(5*H*)-one (274o):

The red color solid product **274o** was obtained from **272f** and **273d** followed by general procedure L and was purified by column chromatography using 6% ethylacetate in hexanes



Yield:	80%
Mp:	195 $^{\circ}$C
IR (KBr) ν_{max} cm^{-1}:	2924, 2852, 1682, 1589, 1467, 1392,

1242, 1168, 1105, 817, 736

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.29 (s, 1H), 8.06 (d, 1H, *J* = 8.0 Hz), 7.46 (t, 1H, *J* = 7.5 Hz), 7.38 (q, 3H, *J* = 8.0 Hz), 7.29 (t, 3H, *J* = 7.5 Hz), 7.24 (d, 2H, *J* = 8.0 Hz), 7.11 (d, 2H, *J* = 7.5 Hz), 7.05 (s, 1H), 4.33 (q, 2H, *J* = 7.5 Hz), 2.47 (s, 3H), 2.35 (s, 3H), 1.43 (t, 3H, *J* = 7.5 Hz)

^{13}C NMR (125 MHz, CDCl$_3$): δ 195.6, 154.1, 144.2, 142.8, 140.1, 138.9, 137.2, 134.3, 130.5, 129.8, 129.5, 128.7, 128.5, 128.4, 125.6, 124.1, 123.4, 121.6, 120.4, 120.3, 116.9, 109.2, 103.2, 37.8, 21.5, 14.0

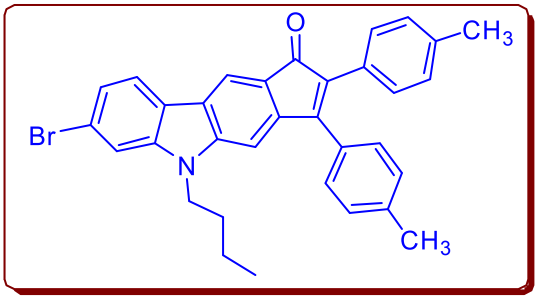
LC-MS (m/z): 428 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{31}H_{25}NO$: C, 87.09; H, 5.89; N, 3.28%

Found: C, 87.12; H, 6.36; N, 3.12%

7-Bromo-5-butyl-2,3-dip-tolylcyclopenta[*b*]carbazol-1(5*H*)-one (274p):

The red color solid product **274p** was obtained from **272g** and **273d** followed by general procedure L and was purified by column chromotography using 6% ethylacetate in hexanes



Yield: 58%

Mp: 167-169 ˚C

IR (KBr) ν_{max} cm^{-1}: 2924, 1693, 1595, 1464, 1388, 1016, 819

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.23 (s, 1H), 7.88 (d, 1H, *J* = 8.5 Hz), 7.54 (s, 1H), 7.37 (t, 3H, *J* = 7.5 Hz), 7.28 (d, 3H, *J* = 4.0 Hz), 7.23 (d, 1H, *J* = 8.0 Hz), 7.11 (d, 2H, *J* = 8.0 Hz), 7.05 (s, 1H), 4.21 (t, 2H, *J* = 7.0 Hz), 2.47 (s, 3H), 2.35 (s, 3H), 1.87-1.89 (m, 2H), 1.39-1.33 (m, 2H), 0.96 (t, 3H, *J* = 6.0 Hz)

^{13}C NMR (100 MHz, $CDCl_3$): δ 195.4, 154.0, 144.4, 143.5, 141.4, 139.1, 137.4, 134.4, 130.2, 129.8, 129.5, 128.7, 128.5, 125.6, 123.5, 121.3, 119.2, 116.6, 112.5, 103.5, 43.1, 31.1, 21.4, 21.3, 20.3, 13.7

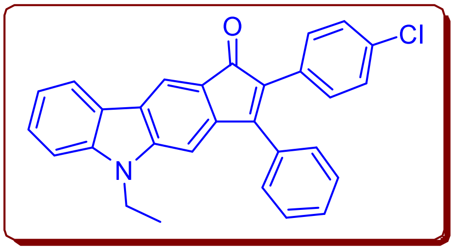
LC-MS (m/z): 535 $(M+H)^+$, 537 (M+2) positive mode

Anal. Calcd. for $C_{33}H_{28}BrNO$: C, 74.16; H, 5.28; N, 2.62%

Found: C, 74.31; H, 5.32; N, 2.58%

2-(4-Chlorophenyl)-5-ethyl-3-phenylcyclopenta[*b*]carbazol-1(5*H*)-one (274q):

The red color solid product **274q** was obtained from **272f** and **273e** followed by general procedure L and was purified by column chromotography using 6% ethylacetate in hexanes



Yield: 50%

Mp: 206-208 °C

IR (KBr) ν_{max} cm^{-1}: 2908, 1676, 1450, 1014

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (s, 1H), 8.06 (d, 1H, *J* = 8.0 Hz), 7.52-7.48 (m, 3H), 7.45 (d, 3H, *J* = 8.0 Hz), 7.41 (d, 1H, *J* = 8.0 Hz), 7.31-7.24 (m, 5H), 7.02 (s, 1H), 4.33 (q, 2H, *J* = 8.0 Hz), 1.42 (t, 3H, *J* = 8.0 Hz)

^{13}C NMR (100 MHz, $CDCl_3$): δ 195.6, 155.3, 143.6, 140.2, 133.5, 133.0, 131.2, 129.6, 129.0, 128.5, 128.2, 125.9, 124.0, 123.0, 121.9, 120.5, 117.3, 109.3, 103.5, 39.7, 14.1

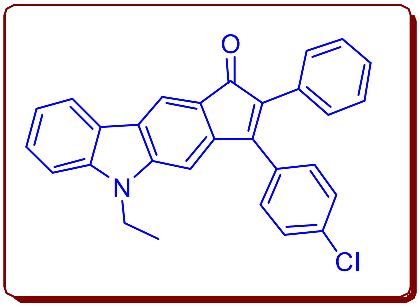
LC-MS (m/z): 433 $(M+H)^+$, 434 (M+1) positive mode

Anal. Calcd. for $C_{29}H_{20}ClNO$: C, 80.27; H, 4.65; N, 3.23%

Found: C, 80.36; H, 4.98; N, 3.07%

3-(4-Chlorophenyl)-5-ethyl-2-phenylcyclopenta[*b*]carbazol-1(5*H*)-one (274q′):

The red colored solid product **274q′** was obtained from **272f** and **273e** followed by general procedure L and was purified by column chromatography using 6% ethylacetate in hexanes



Yield: 50%

Mp: 216-218 °C

IR (KBr) ν_{max} cm^{-1}: 2922, 1682, 1464, 1323, 1086, 750

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.31 (s, 1H), 8.06 (d, 1H, *J* = 7.6 Hz), 7.48-7.45 (m, 3H), 7.42-7.49 (m, 3H), 7.30-7.26 (m, 6H), 6.98 (s, 1H), 4.34 (q, 2H, *J* = 7.32 Hz), 1.43 (t, 3H, *J* = 7.2 Hz)

^{13}C NMR (100 MHz, CDCl$_3$): δ 195.1, 153.2, 143.5, 142.8, 140.2, 134.9, 131.7, 130.8, 129.9, 129.3, 128.1, 127.7, 125.9, 124.0, 122.9, 121.8, 120.5, 120.4, 117.3, 109.3, 103.1, 37.9, 14.1

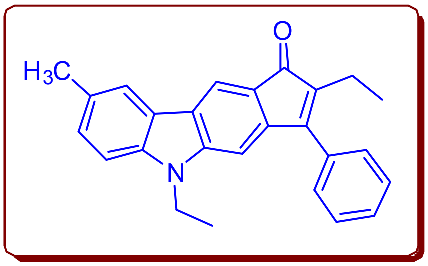
LC-MS (m/z): 433 (M+H)$^+$, 434 (M+1) positive mode

Anal. Calcd. for $C_{29}H_{20}ClNO$: C, 80.27; H, 4.65; N, 3.23%

Found: C, 80.52; H, 4.85; N, 3.18%

2,5-Diethyl-8-methyl-3-phenylcyclopenta[*b*]carbazol-1(5*H*)-one (274r):

The orange colored solid product **274r** was obtained from **272a** and **273f** followed by general procedure L and was purified by column chromatography using 6% ethylacetate in hexanes



Yield: 60%

Mp: 106-108 °C

IR (KBr) ν_{max} cm^{-1}: 2966, 2920, 1689, 1597, 1375, 1238, 1022, 704

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (s, 1H), 7.82 (s, 1H), 7.68-7.50 (m, 5H), 7.27 (dd, 2H, J_1 = 2.0 Hz, J_2 = 1.2 Hz), 6.89 (s, 1H), 4.26 (q, 2H, J = 7.2 Hz), 2.54 (s, 3H), 2.40 (q, 2H, J = 7.2 Hz), 1.38 (t, 3H, J = 7.2 Hz), 1.16 (t, 3H, J = 7.2 Hz)

^{13}C NMR (100 MHz, $CDCl_3$): δ 197.1, 153.8, 144.4, 142.8, 139.1, 138.3, 133.3, 129.8, 128.8, 127.9, 126.0, 123.1, 120.7, 120.0, 116.6, 108.9, 102.7, 37.8, 21.4, 16.9, 14.1, 14.0

LC-MS (m/z): 367 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{26}H_{23}NO$: C, 85.45; H, 6.34; N, 3.83%

Found: C, 85.32; H, 6.41; N, 3.79%

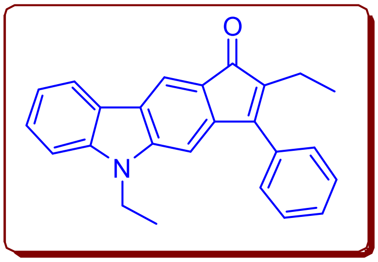
2,5-Diethyl-3-phenylcyclopenta[*b*]carbazol-1(5*H*)-one (274s):

The orange color solid product **274s** was obtained from **272f** and **273f** followed by general procedure L and was purified by column chromotography using 6% ethylacetate in hexanes. Compound is recrystallized from $CDCl_3$.

Yield: 54%

Mp: 178-180 °C

IR (KBr) ν_{max} cm^{-1}: 2976, 1687, 1593, 1392, 1331, 1016, 785



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20 (s, 1H), 8.03 (d, 1H, J = 8.0 Hz), 7.62-7.52 (m, 5H), 7.46-7.38 (m, 2H), 7.29-7.25 (m, 1H), 6.91 (s, 1H), 4.30 (q, 2H, J = 7.2 Hz), 2.40 (q, 2H), 1.40 (t, 3H, J = 7.2 Hz), 1.16 (t, 3H, J = 7.2 Hz)

^{13}C NMR (100 MHz, $CDCl_3$): δ 197.1, 153.9, 144.6, 142.7, 140.0, 139.2, 133.3, 128.8, 127.9, 125.4, 124.1, 123.4, 121.0, 120.3, 120.2, 116.6, 109.1, 102.7, 37.8, 16.9, 14.1

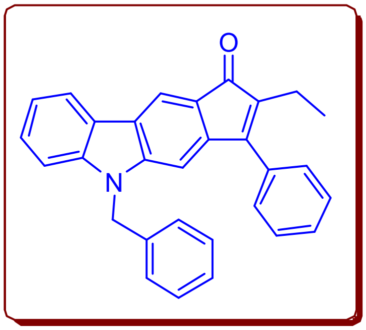
LC-MS (m/z): 351 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{25}H_{21}NO$: C, 85.44; H, 6.02; N, 3.99%

Found: C, 85.36; H, 6.08; N, 3.86%

5-Benzyl-2-ethyl-3-phenylcyclopenta[*b*]carbazol-1(5*H*)-one (274t):

The orange color solid product **274t** was obtained from **272d** and **273f** followed by general procedure L and was purified by column chromatography using 6% ethylacetate in hexanes.



Yield: 62%

Mp: 98-99 °C

IR (KBr) ν_{max} cm^{-1}: 2956, 1690, 1392, 1326, 795

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23 (s, 1H), 8.06 (d, 1H, J = 7.6 Hz), 7.55-7.48 (m, 3H), 7.45-7.43 (m, 2H), 7.39-7.37 (dd, 1H, J_1 = 1.2 Hz, J_2 = 1.0 Hz), 7.34-7.27 (m, 5H), 7.10-7.08 (dd, 2H, J_1 = 2.8 Hz, J_2 = 1.6 Hz), 6.91 (s, 1H), 5.45 (s, 2H), 2.39 (q, 2H, J = 7.6 Hz), 1.15 (t, 3H, J = 7.6 Hz)

^{13}C NMR (100 MHz, $CDCl_3$): δ 197.1, 153.8, 144.7, 143.5, 140.6, 139.1, 136.3, 133.1, 128.9, 128.8, 127.9, 127.7, 126.4, 125.7, 124.1, 123.8, 121.2, 120.6, 120.1, 116.5, 109.7, 103.3, 46.7, 16.9, 14.0

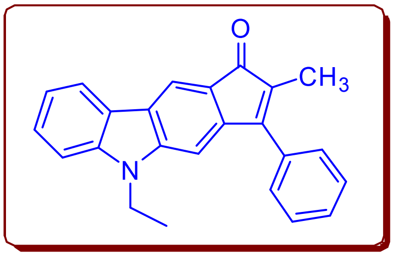
LC-MS (m/z): 414 $(M+H)^+$ positive mode

Anal. Calcd. for $C_{30}H_{23}NO$: C, 85.43; H, 5.68; N, 4.15%

Found: C, 85.32; H, 5.62; N, 4.21%

5-Ethyl-2-methyl-3-phenyl-2,3-dihydrocyclopenta[*b*]carbazol-1(5*H*)-one (274u):

The orange color solid product **274u** was obtained from **272f** and **273g** followed by general procedure L and was purified by column chromatography using 6% ethylacetate in hexanes



Yield:	55%
Mp:	189-190 °C
IR (KBr) ν_{max} cm^{-1}:	1687, 1469, 1339, 785
^{1}H NMR (400 MHz, CDCl$_3$):	δ 8.21 (s, 1H), 8.02 (d, 1H, *J* = 7.6 Hz), 7.62-7.50 (m, 5H), 7.44-7.38 (m, 2H), 7.28 (t, 1H, *J* = 8.0 Hz), 6.97 (s, 1H), 4.31 (q, 2H, *J* = 7.2 Hz), 1.97 (s, 3H), 1.41 (t, 3H, *J* = 7.2 Hz)
^{13}C NMR (100 MHz, CDCl$_3$):	δ 197.2, 153.9, 144.5, 142.7, 140.0, 133.6, 133.2, 128.9, 128.8, 128.1, 125.4, 124.1, 123.4, 120.9, 120.3, 120.2, 116.7, 109.1, 102.6, 37.8, 14.1, 8.89
LC-MS (m/z):	338 $(M+H)^+$ positive mode
Anal. Calcd. for $C_{24}H_{19}NO$:	C, 85.43; H, 5.68; N, 4.15%
Found:	C, 85.32; H, 5.62; N, 4.21%

Table 28. Crystal data and structure refinement for 274a

Empirical formula	: $C_{30}H_{23}NO$	
Formula weight	: 413.49	
Temperature	: 298(2) K	
Wavelength	: 0.71073 Å	
Crystal system	: Triclinic	
Space group	: P-1	
Unit cell dimensions	: a = 9.0690(13) Å	α = 85.794(15)°
	: b = 10.359(2) Å	β = 72.369(13)°
	: c = 13.357(2) Å	γ = 70.831(16)°
Volume	: 1129.2(3) Å^3	
Z	: 2	
Density (calculated)	: 1.216 Mg/m^3	
Absorption coefficient	: 0.073 mm^{-1}	
F(000)	: 436	
Crystal size	: 0.28 x 0.22 x 0.16 mm^3	
Theta range for data collection	: 3.20 to 24.71°.	
Index ranges	: -10<=h<=8, -12<=k<=12, -15<=l<=15	
Reflections collected	: 6949	
Independent reflections	: 3843 [R(int) = 0.0194]	
Completeness to theta = 24.71°	: 99.8 %	
Absorption correction	: Semi-empirical from equivalents	
Max. and min. transmission	: 0.9884 and 0.9799	
Refinement method	: Full-matrix least-squares on F^2	
Data / restraints / parameters	: 3843 / 0 / 291	
Goodness-of-fit on F^2	: 1.027	
Final R indices [I>2sigma(I)]	: R1 = 0.0502, wR2 = 0.1161	
R indices (all data)	: R1 = 0.0857, wR2 = 0.1389	
Largest diff. peak and hole	: 0.149 and -0.136 e.Å^{-3}	

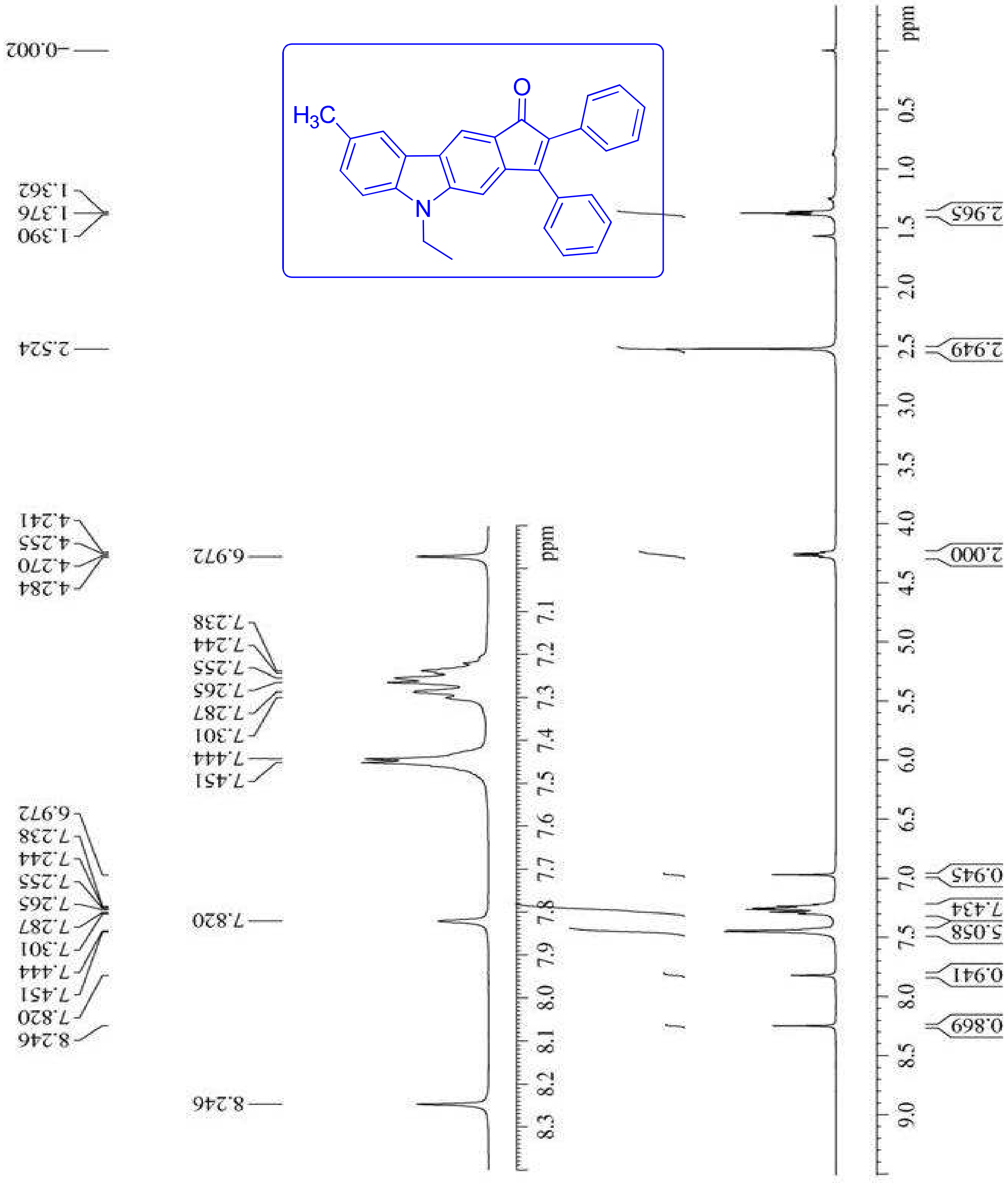
Table 29. Crystal data and structure refinement for 274r

Empirical formula	$C_{26}H_{23}NO$	
Formula weight	365.45	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 8.3997(16) Å	α = 76.514(3)°
	b = 10.227(2) Å	β = 78.141(3)°
	c = 12.402(2) Å	γ = 75.769(3)°
Volume	991.7(3) $Å^3$	
Z	2	
Density (calculated)	1.224 Mg/m^3	
Absorption coefficient	0.074 mm^{-1}	
F(000)	388	
Crystal size	0.48 x 0.22 x 0.10 mm^3	
Theta range for data collection	1.71 to 26.48°.	
Index ranges	-10<=h<=10, -12<=k<=12, -15<=l<=15	
Reflections collected	10749	
Independent reflections	4064 [R(int) = 0.0376]	
Completeness to theta = 26.48°	98.9 %	
Absorption correction	Empirical	
Max. and min. transmission	0.9927 and 0.9655	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4064 / 0 / 256	
Goodness-of-fit on F^2	1.024	
Final R indices [I>2sigma(I)]	R1 = 0.0546, wR2 = 0.1291	
R indices (all data)	R1 = 0.0819, wR2 = 0.1444	
Largest diff. peak and hole	0.165 and -0.208 e.$Å^{-3}$	

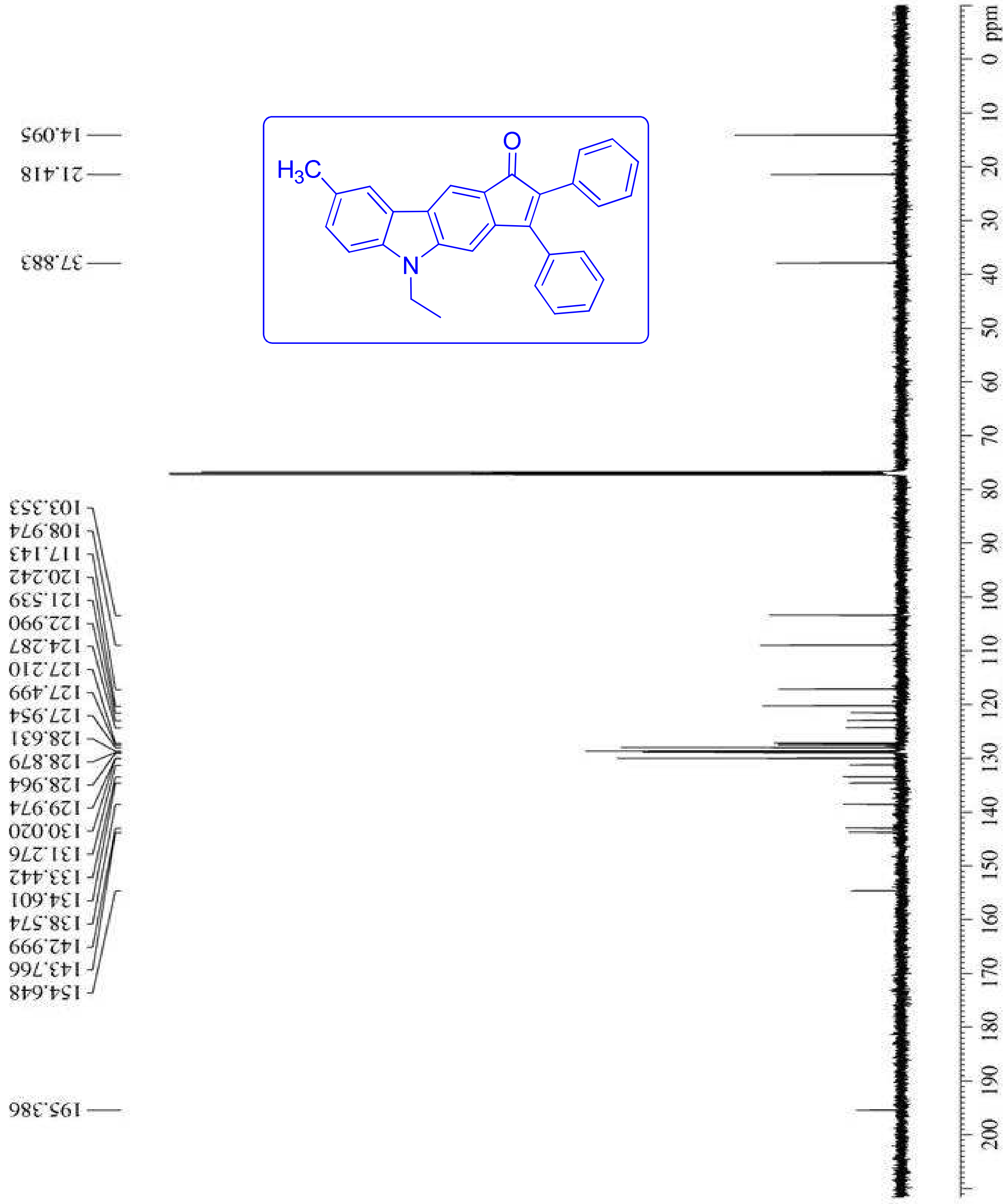
Table 30. Crystal data and structure refinement for 274s

Empirical formula	$C_{25}H_{21}NO$	
Formula weight	351.43	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 7.9184(6) Å	α = 76.338(6)°
	b = 10.4371(7) Å	β = 83.212(7)°
	c = 12.1136(10) Å	γ = 77.905(6)°
Volume	948.72(12) Å^3	
Z	2	
Density (calculated)	1.230 Mg/m^3	
Absorption coefficient	0.074 mm^{-1}	
F(000)	372	
Crystal size	0.24 x 0.18 x 0.12 mm^3	
Theta range for data collection	2.96 to 25.00°.	
Index ranges	-9<=h<=9, -12<=k<=10, -13<=l<=14	
Reflections collected	5809	
Independent reflections	3352 [R(int) = 0.0174]	
Completeness to theta = 25.00°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9911 and 0.9824	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3352 / 0 / 247	
Goodness-of-fit on F^2	1.046	
Final R indices [I>2sigma(I)]	R1 = 0.0462, wR2 = 0.1086	
R indices (all data)	R1 = 0.0761, wR2 = 0.1245	
Extinction coefficient	0.007(2)	
Largest diff. peak and hole	0.140 and -0.127 e.Å^{-3}	

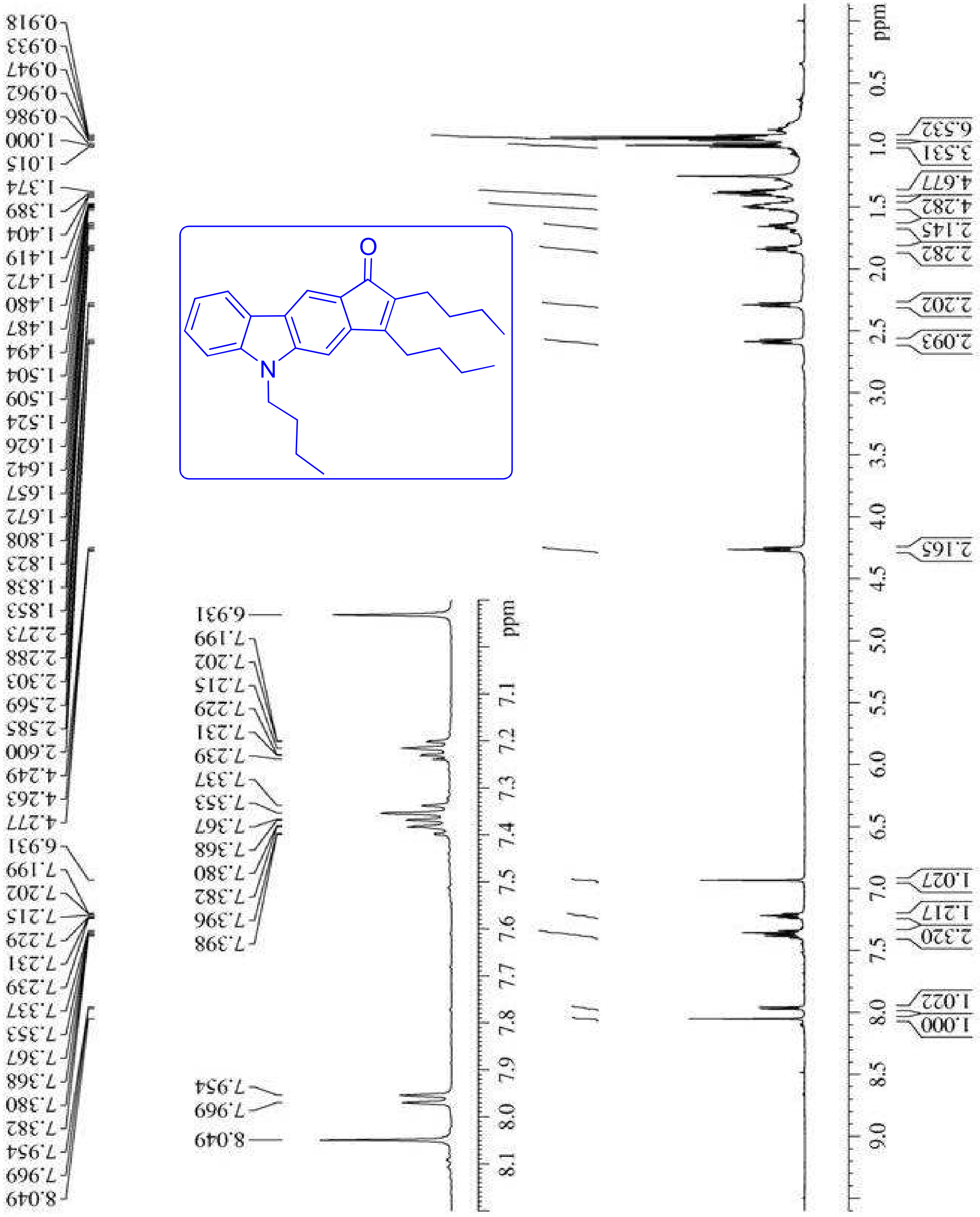
Spectrum 31. ^{1}H NMR of 274a



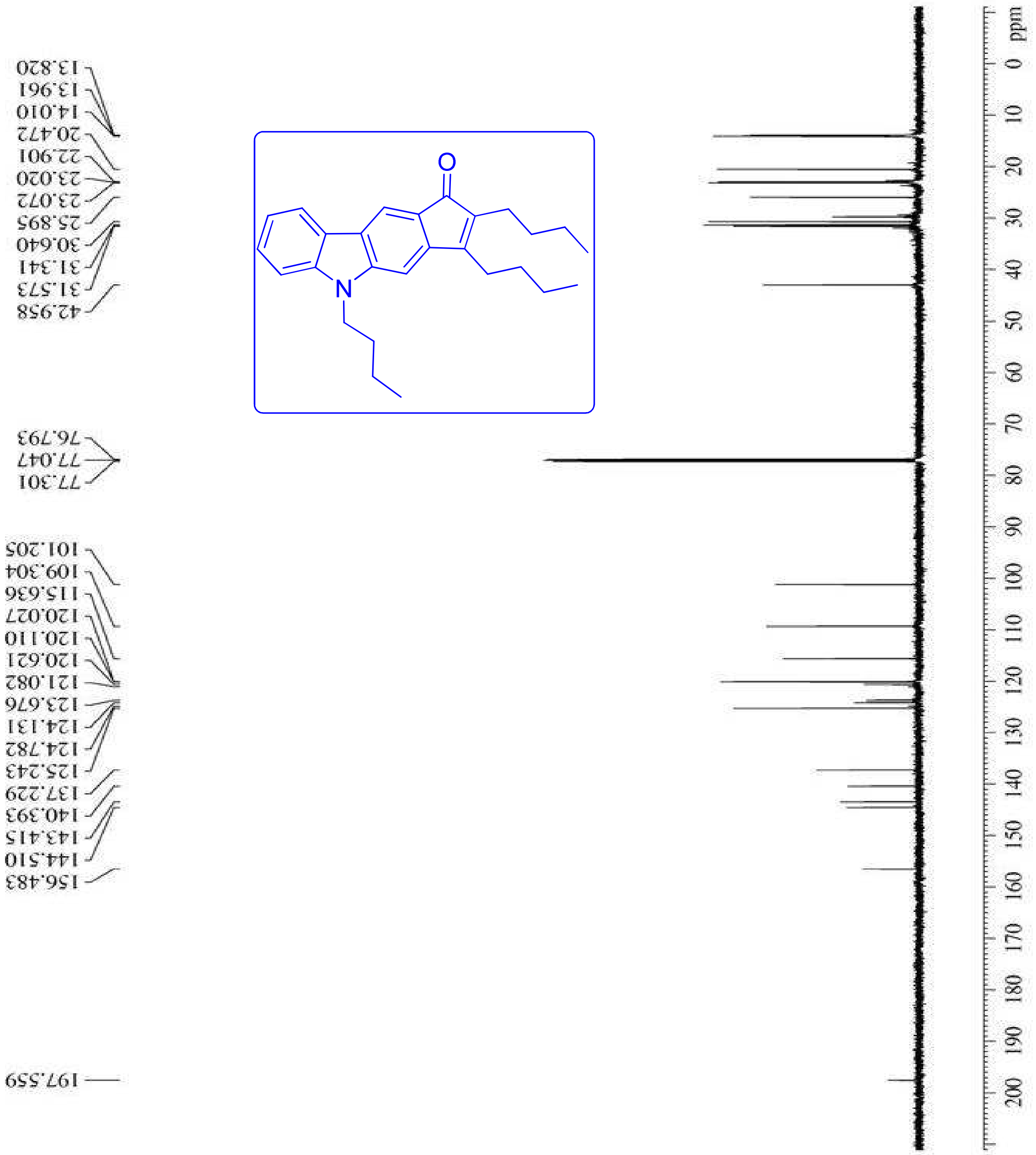
Spectrum 32. ^{13}C NMR of 274a



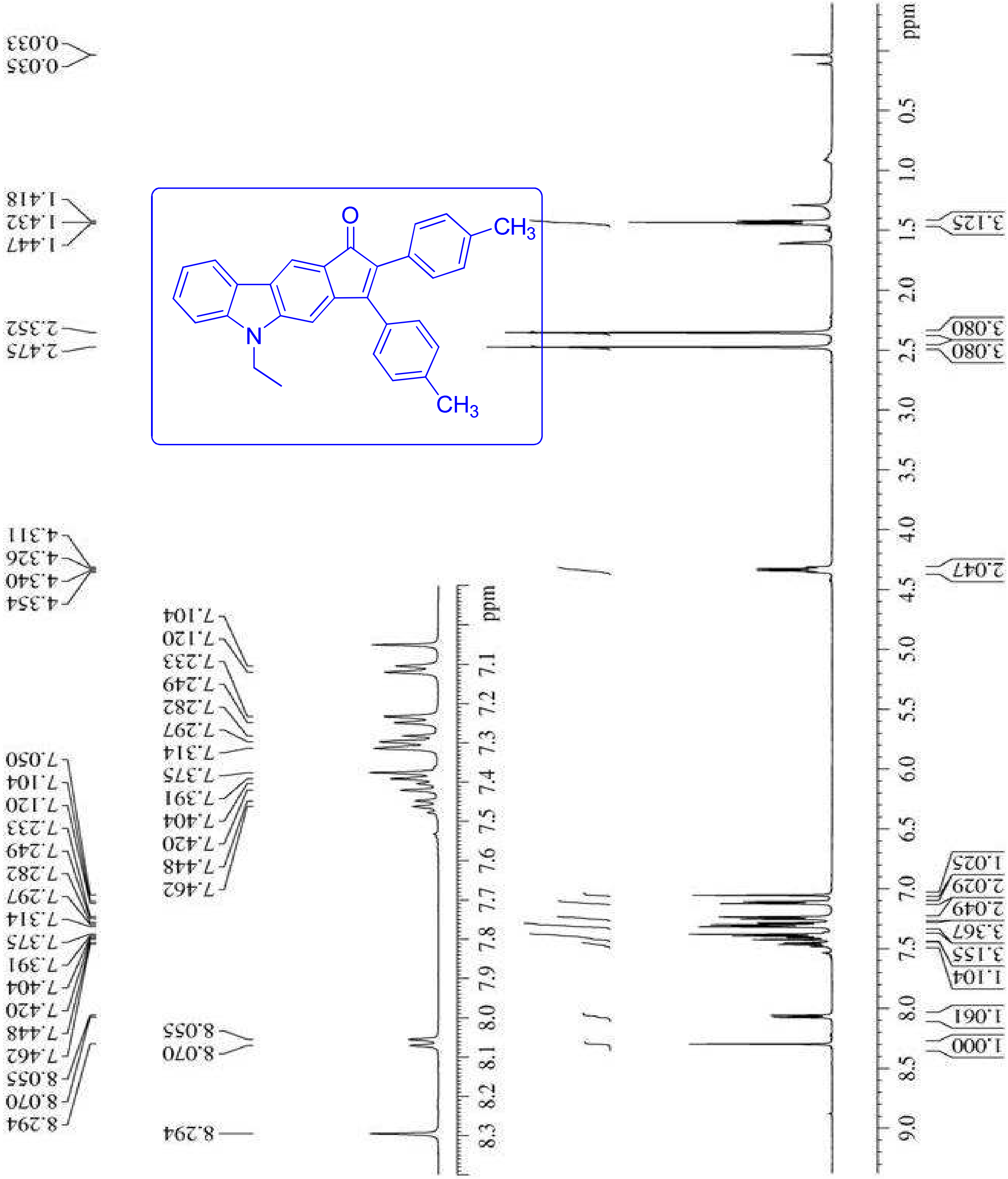
Spectrum 33. ^{1}H NMR of 274i



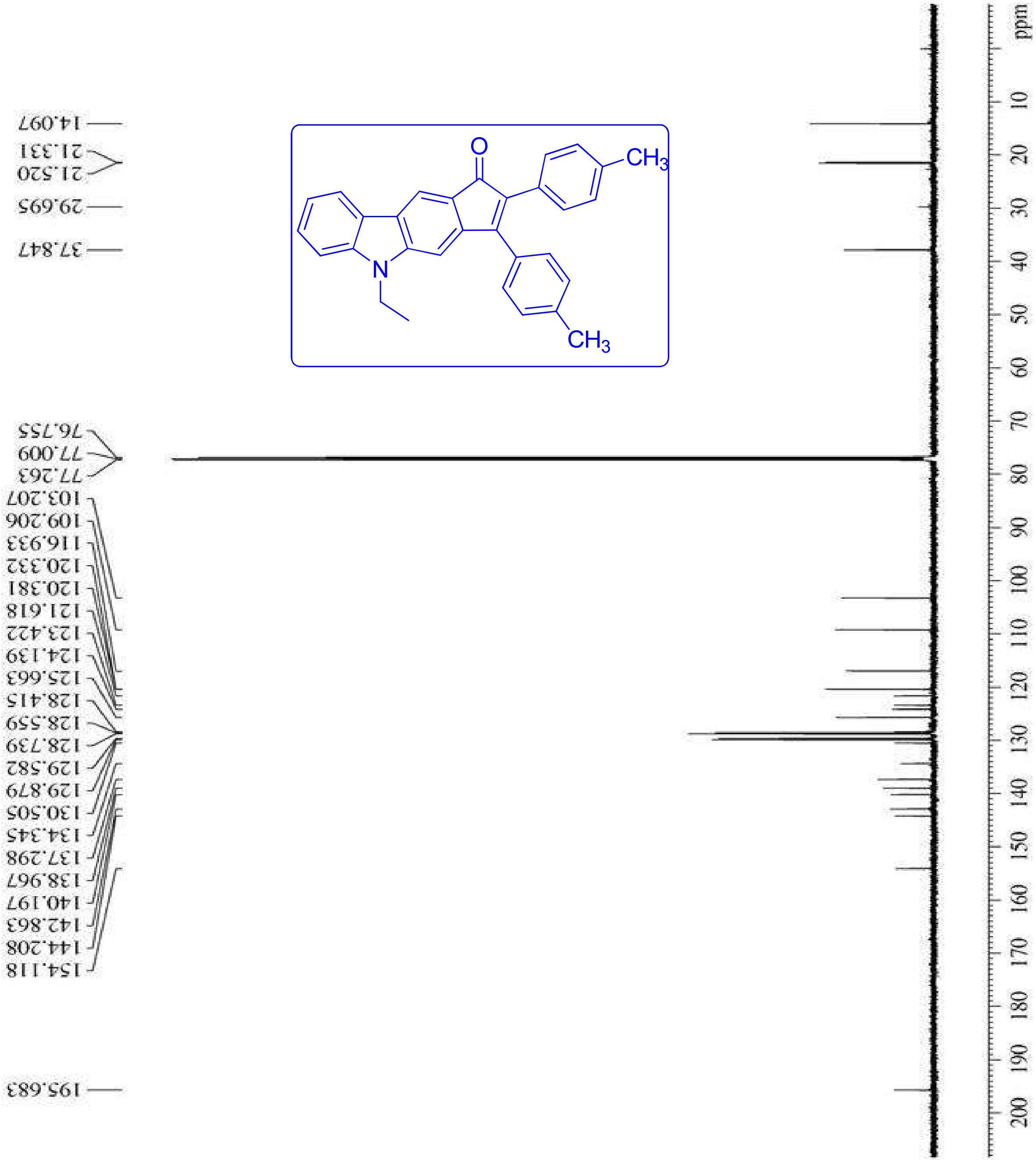
Spectrum 34. ^{13}C NMR of 274i



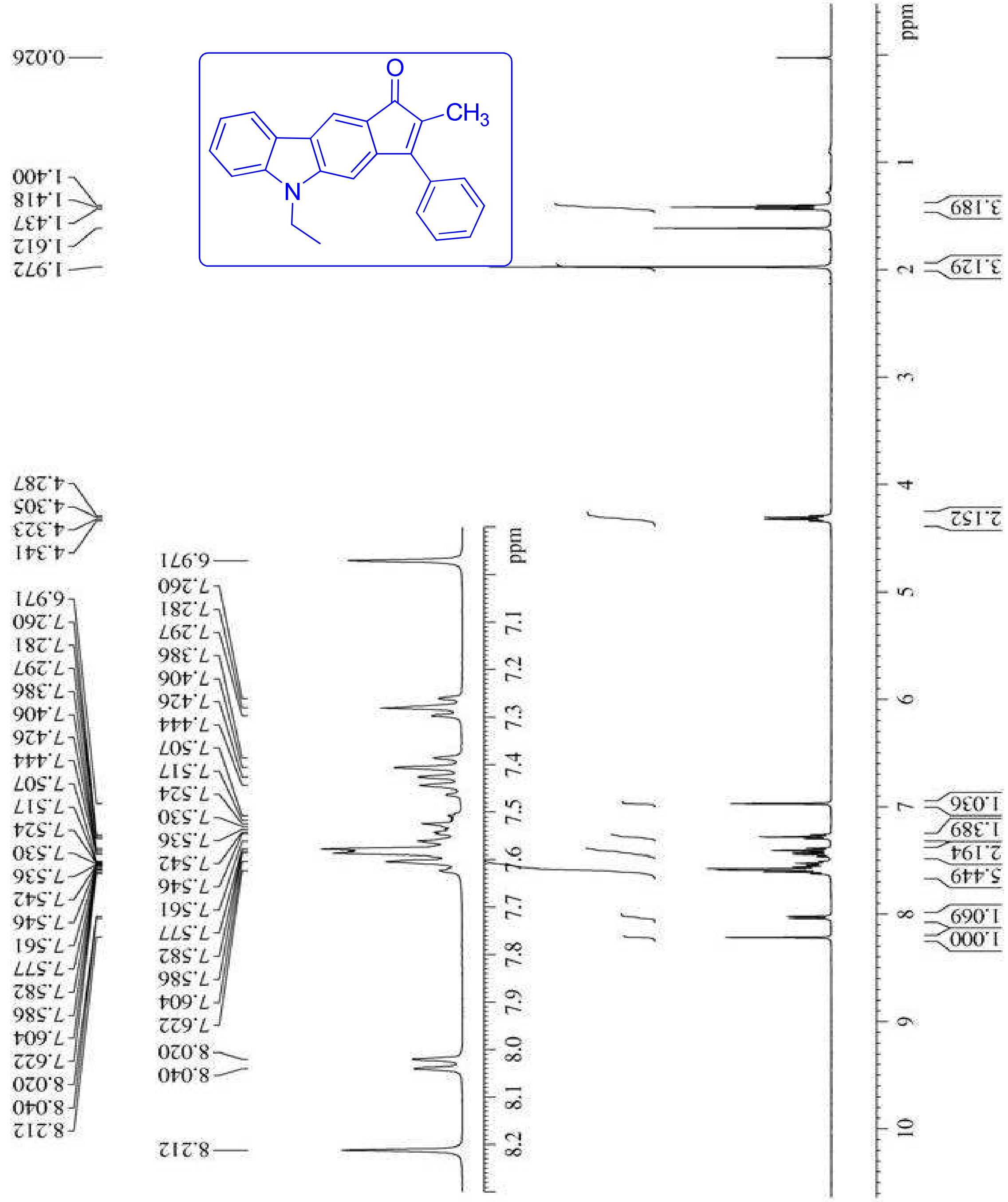
Spectrum 35. ^{1}H NMR of 274o



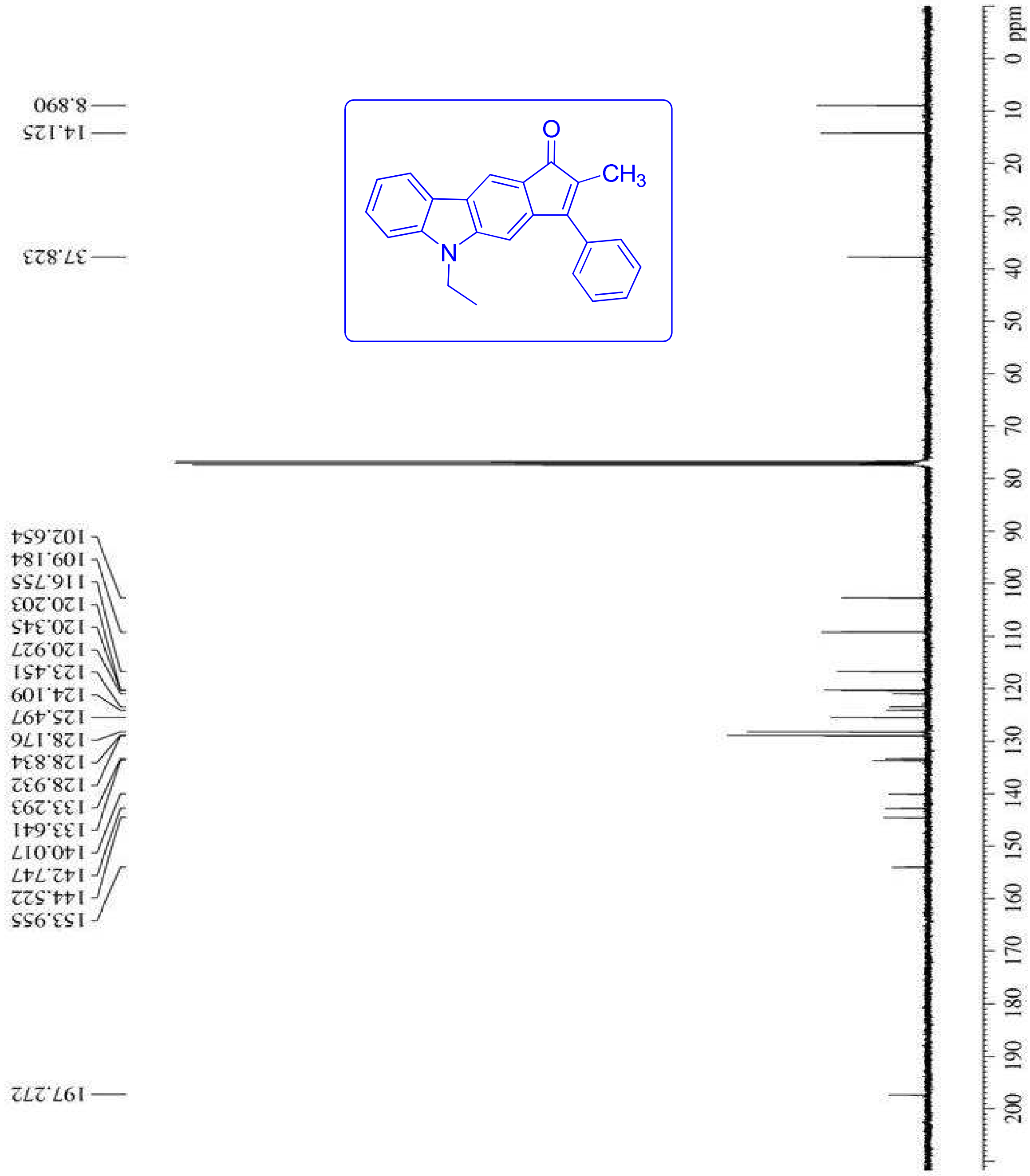
Spectrum 36. ^{13}C NMR of 270o



Spectrum 37. ^{1}H NMR of 274u



Spectrum 38. ^{13}C NMR of 259a



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133. The CCDC deposition number of compound **274a** is 840023. Formula: $C_{30}H_{23}N_1O_1$. Unit cell parameters: a = 9.0690(13), b = 10.359(2), c = 13.357(2), α = 85.794(15), β = 72.369(13), γ = 70.831(16), space group P-1. The CCDC deposition number of compound **274r** is 840025. Formula: $C_{26}H_{23}N_1O_1$. Unit cell parameters: a = 8.3997(16), b = 10.227(2), c = 12.402(2), α = 76.514(3), β = 78.141(3), γ = 75.769(3), space group P-1. The CCDC deposition number of compound **274s** is 840024. Formula: $C_{25}H_{21}N_1O_1$. Unit cell parameters: a = 7.9184(6), b = 10.4371(7), c = 12.1136(10), α = 76.338(6), β = 83.212(7), γ = 77.905(6), space group P-1.

Conclusions:

We have made significant progress and achieved considerable success in our objectives on the synthesis of various heteroarylcarbazoles, which are known to be biologically active.

- We have synthesized biologically important compounds quinocarbazolones (**194a-f**, **195a-f**, **198a-b**, **201a-c**) which are analogues to anticancer drug ellipticine via palladium-catalyzed intramolecular ortho arylation. We have also prepared isochromenocarbazolones (**214a-e**, **215a-h**) which are analogues to naturally occurring Clausamine alkaloids obtained by the same methodoly.

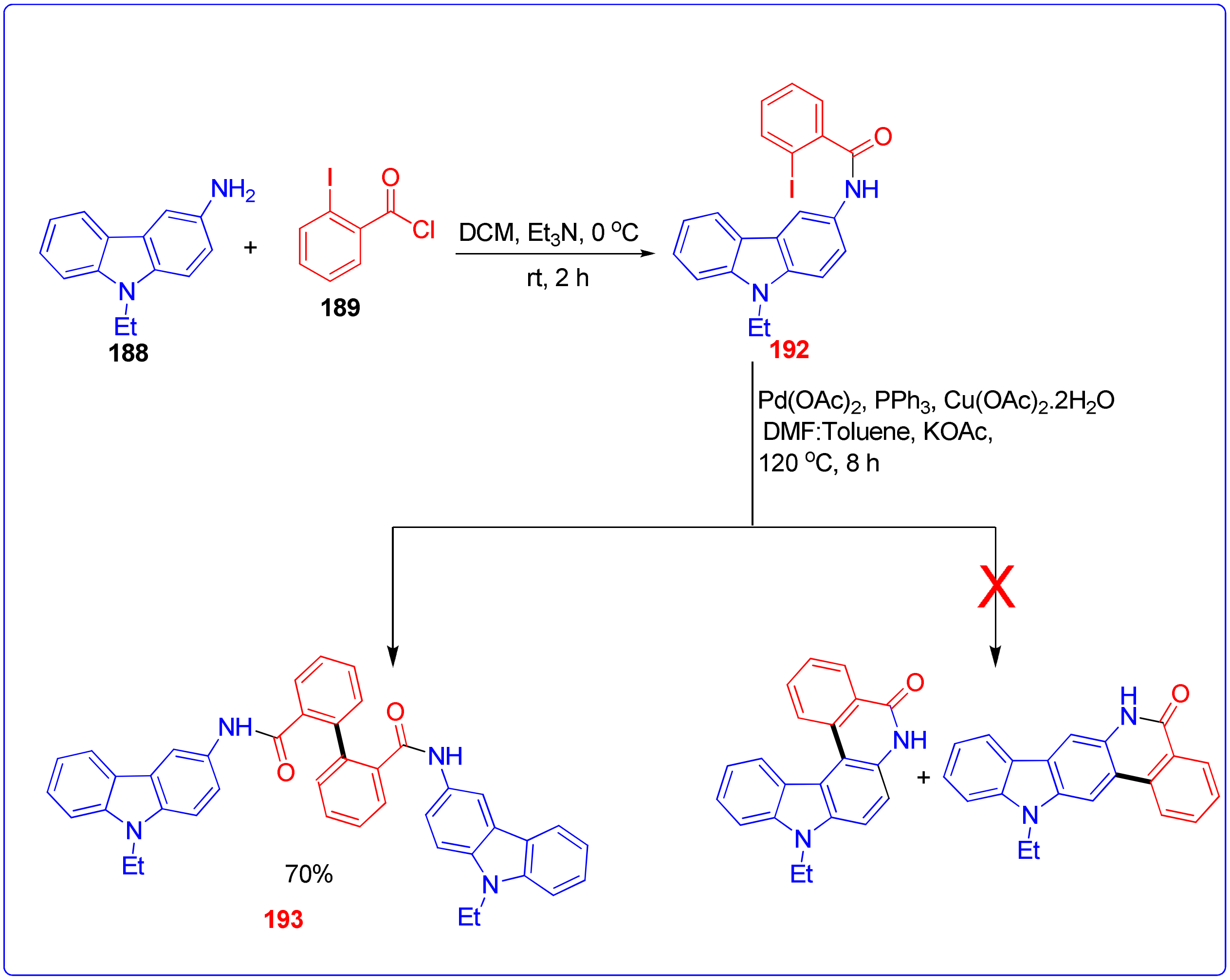
- We have synthesized a series of pyrimido[4,5-*b*]carbazolone derivatives (**228a-j**, **231a-b**) using cascade Ullmann *N*-arylation and aerobic oxidative C-H amidation reactions that allow the assembly of readily accessible building blocks into diverse (heteroaryl-annulated) pyrimido[4,5-*b*]carbazolones with the aid of CuBr as a catalyst without any additives or ligands. An attractive feature of this synthetic approach is not only to provide a new approach for constructing pyrimido[*b*]carbazoles but also offers an efficient method for preparation of synthetically and medicinally important hetero-arylated carbazoles. Furthermore, some of the resulting pyrimido[4,5-*b*]carbazolone derivatives exhibit intense fluorescence.

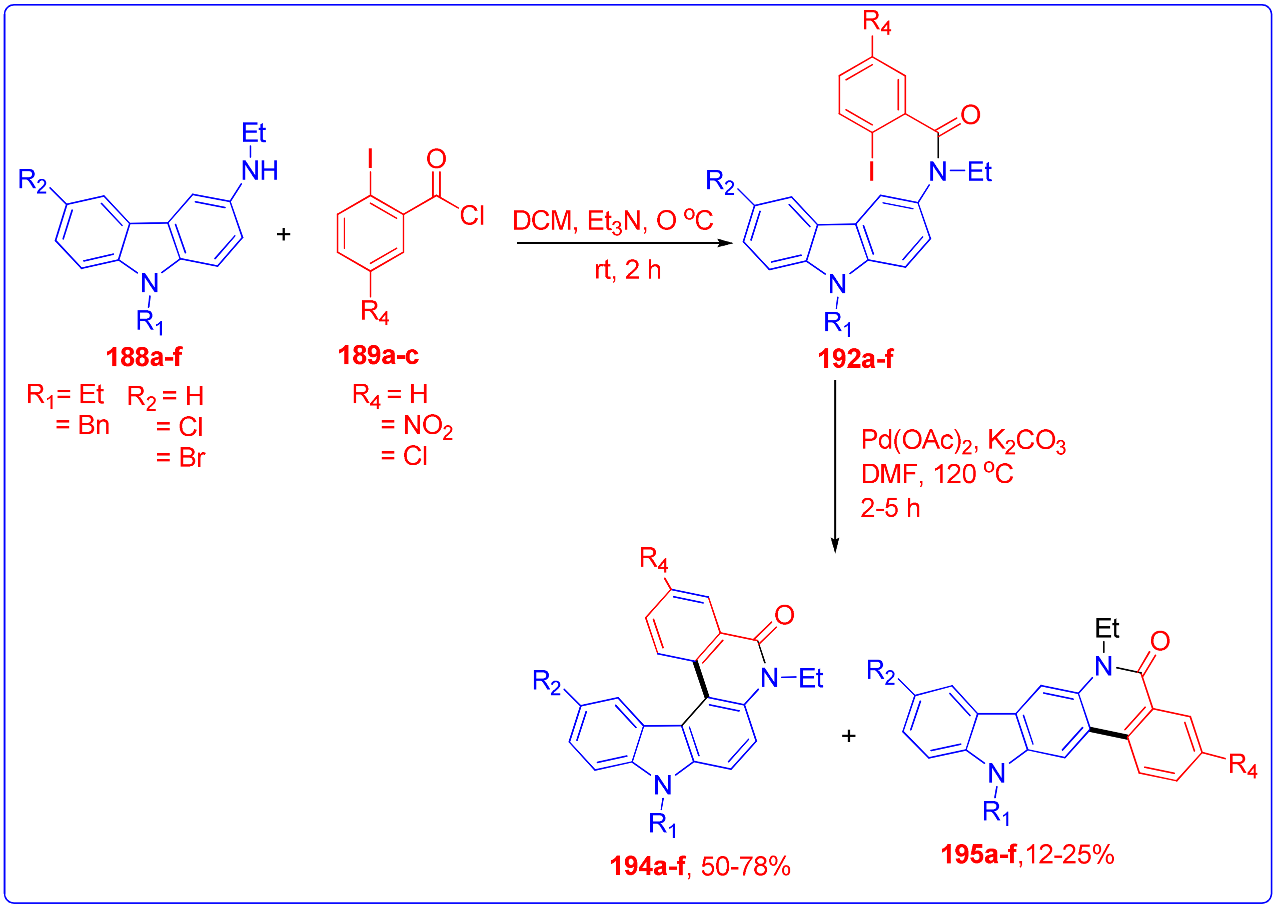
- We developed a new class of indenocarbazolones (**260a-j**, **263b**, **264**) with high regioselectivity in good yield by palladium catalyzed intramolecular *ortho* arylation. Further these molecules may have significant biological properties. These type of compounds can also be used as the potential candidates for the OLEDs and in solar cells.

- We have also synthesized 2,3-disubstituted cyclopentacarbazolones (**274a-u**) by using palladium catalyzed annulation of internal alkynes. This type of molecules useful as precursor molecules in application oriented as iin OLEDs or in solar cells.

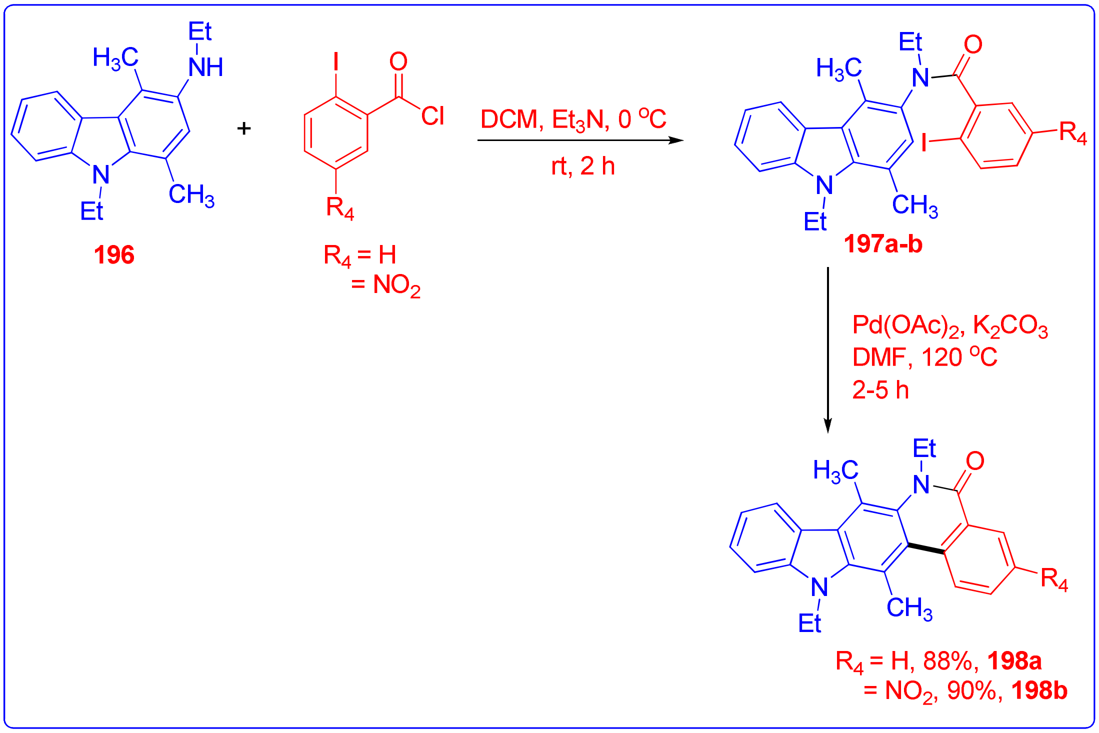
Graphical Abstracts

CHAPTER 1. Palladium-Mediated Intramolecular *Ortho*-Arylation: Synthesis of Quino, Isochromenocarbazolones

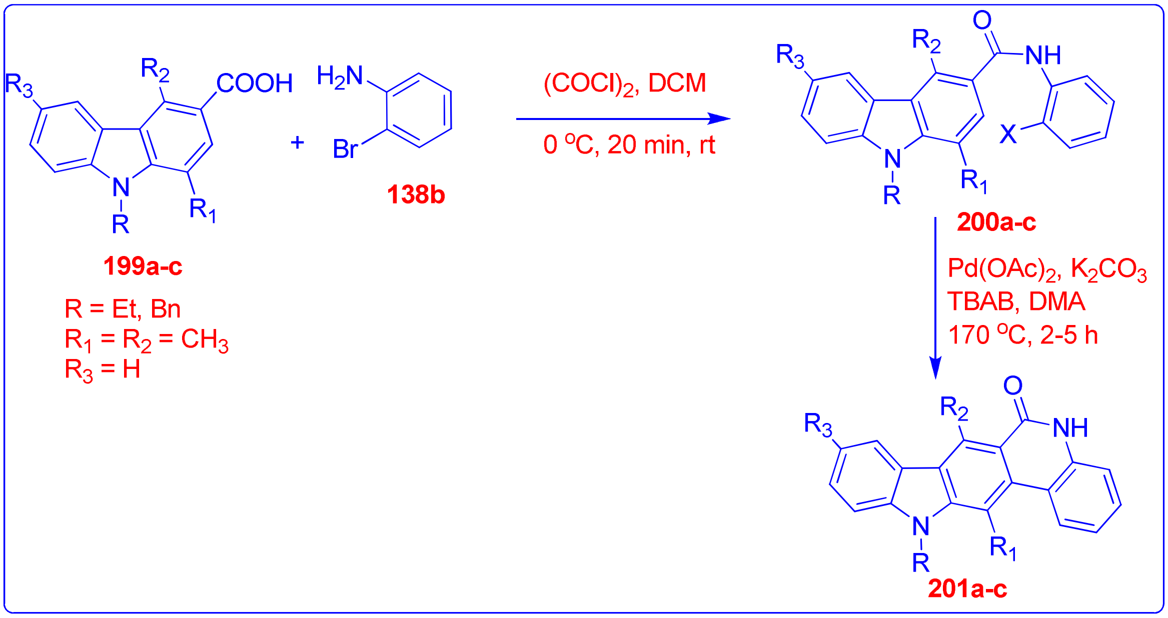




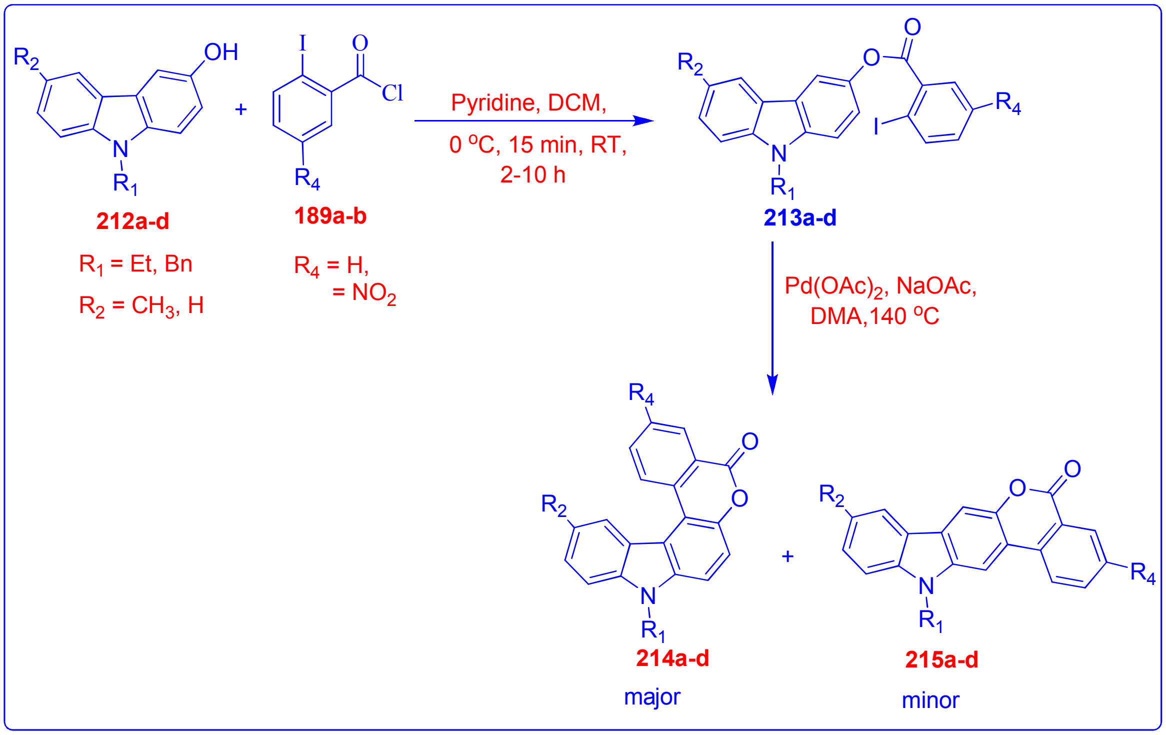
188a-f
R₁= Et R₂ = H
= Bn = Cl
= Br
189a-c
R₄ = H
= NO₂
= Cl
DCM, Et₃N, O °C
rt, 2 h
192a-f
Pd(OAc)₂, K₂CO₃
DMF, 120 °C
2-5 h
194a-f, 50-78%
195a-f,12-25%

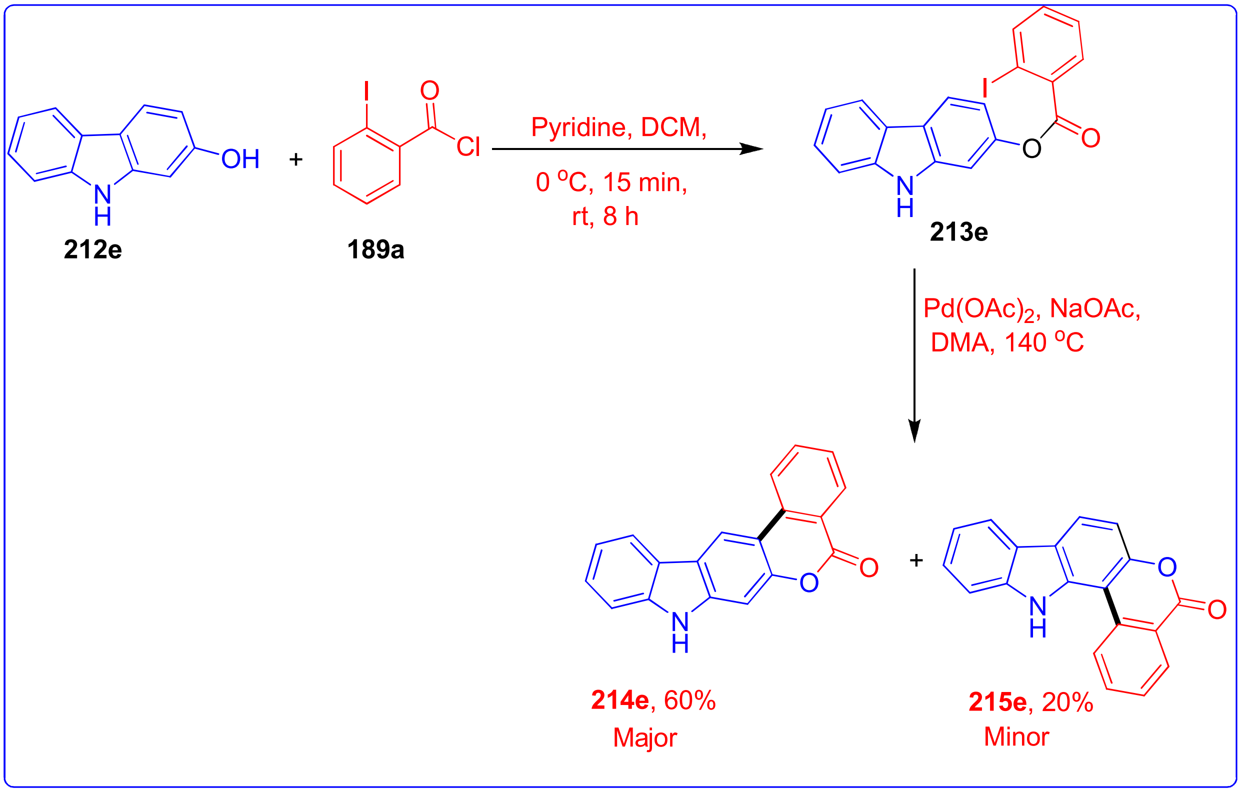


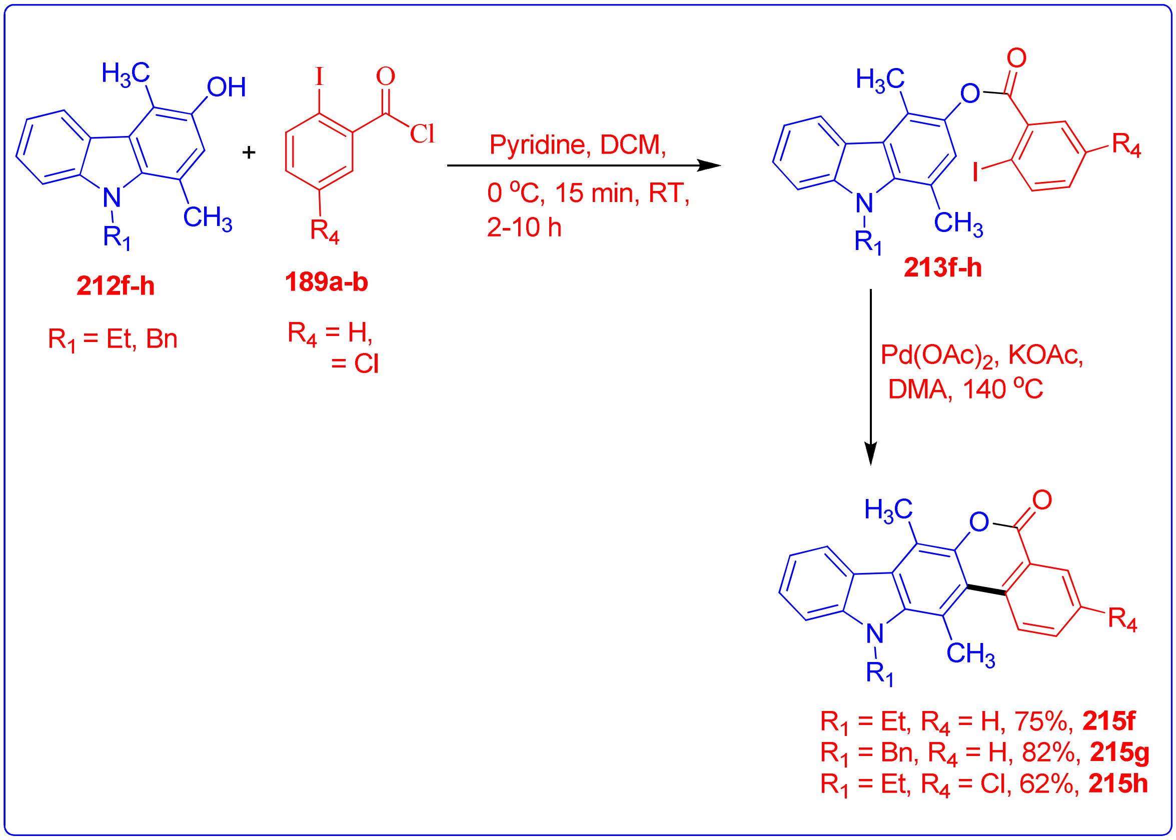
Et
NH
H3C
CH3
N
Et
196
I
O
Cl
R4
R4 = H
= NO2
DCM, Et3N, 0 °C
rt, 2 h
197a-b
Pd(OAc)2, K2CO3
DMF, 120 °C
2-5 h
R4 = H, 88%, 198a
= NO2, 90%, 198b



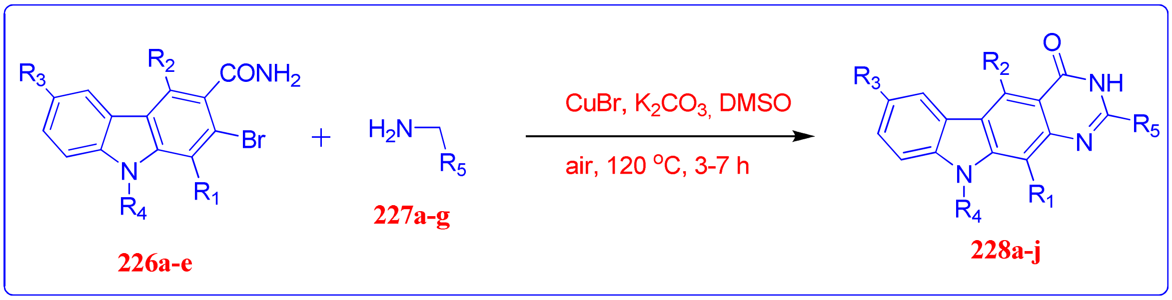
R3
R2
COOH
N
R
R1
199a-c
R = Et, Bn
R1 = R2 = CH3
R3 = H
H2N
Br
138b
(COCl)2, DCM
0 °C, 20 min, rt
O
NH
X
200a-c
Pd(OAc)2, K2CO3
TBAB, DMA
170 °C, 2-5 h
201a-c


R2
OH
N
R1
212a-d
R1 = Et, Bn
R2 = CH3, H
+
I
O
Cl
R4
189a-b
R4 = H,
= NO2
Pyridine, DCM,
0 oC, 15 min, RT,
2-10 h
R2
O
O
I
R4
N
R1
213a-d
Pd(OAc)2, NaOAc,
DMA,140 oC
R4
O
O
R2
N
R1
214a-d
major
+
R2
O
O
N
R1
R4
215a-d
minor

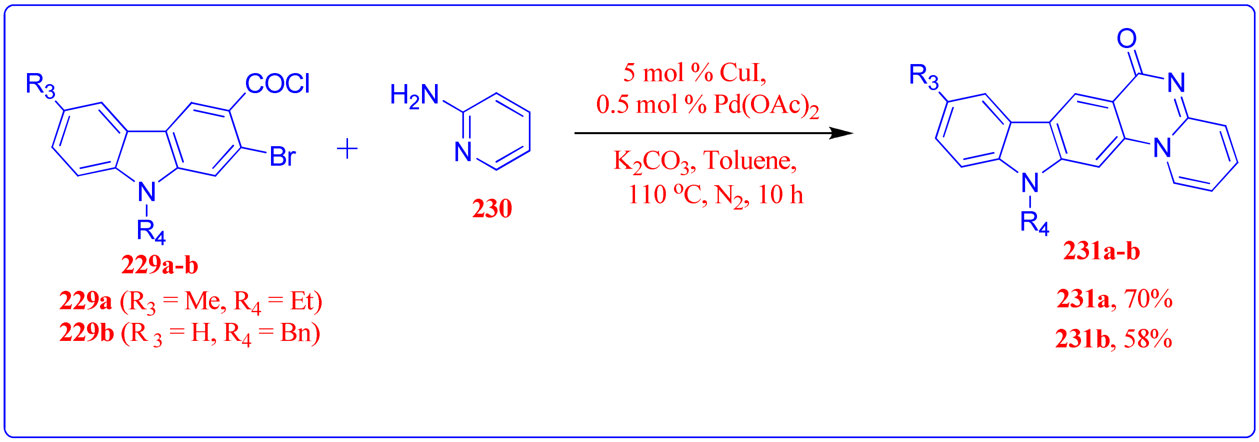

OH
212e
I
O
Cl
189a
Pyridine, DCM,
0 °C, 15 min,
rt, 8 h
I
O
O
N
H
213e
Pd(OAc)2, NaOAc,
DMA, 140 °C
N
H
O
O
214e, 60%
Major
N
H
O
O
215e, 20%
Minor


212f-h
R1 = Et, Bn
189a-b
R4 = H,
= Cl
Pyridine, DCM,
0 °C, 15 min, RT,
2-10 h
213f-h
Pd(OAc)2, KOAc,
DMA, 140 °C
R1 = Et, R4 = H, 75%, 215f
R1 = Bn, R4 = H, 82%, 215g
R1 = Et, R4 = Cl, 62%, 215h

CHAPTER 2. Copper-Mediated Domino Synthesis of Pyrimido[4,5-*b*]carbazolones via Ullmann *N*-Arylation and Aerobic Oxidative C-H Amidation



226a-e **227a-g** **228a-j**



229a-b

229a (R_3 = Me, R_4 = Et)

229b (R_3 = H, R_4 = Bn)

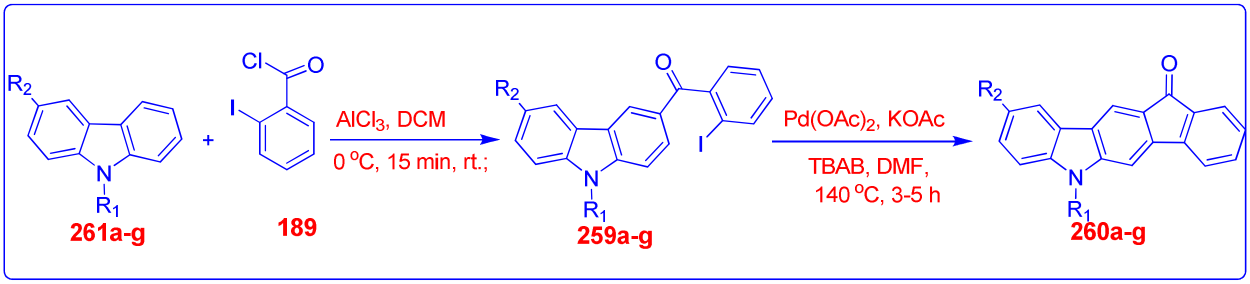
230

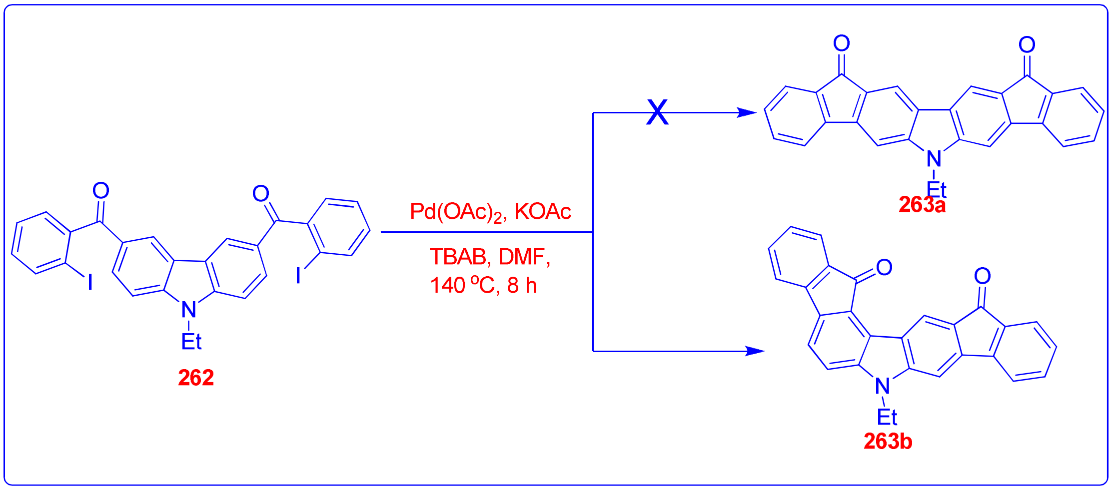
231a-b

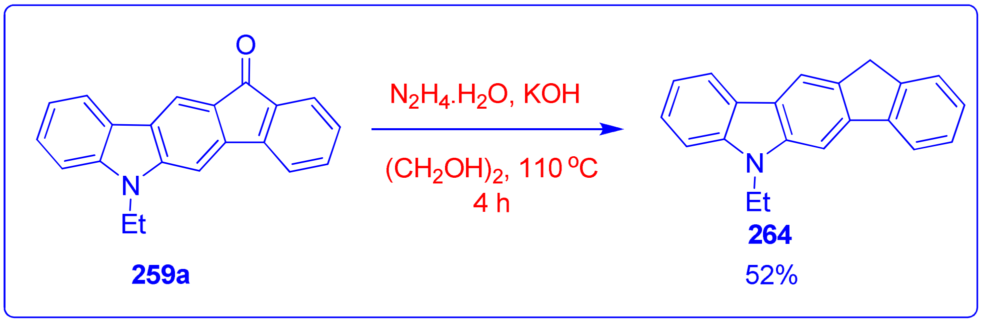
231a, 70%

231b, 58%

CHAPTER 3. Highly Regioselective Synthesis of Indenocarbazolones via Palladium-Catalyzed Intramolecular *ortho*-Arylation







Chapter 4. Synthesis of Cyclopentacarbazolones via Palladium-Catalyzed Annulation of Internal Alkynes