Universität Rostock Traditio et Innovatio

SYNTHESIS OF FUSED HETEROCYCLES BY SEQUENTIAL PALLADIUM CATALYZED CROSS-COUPLING REACTIONS

Dissertation

zur

Erlangung des Doktorgrades

doctor rerum naturalium (Dr. rer. nat.)

der Mathematisch-Naturwissenschaftlichen Fakultät

der Universität Rostock

vorgelegt von

Tran Quang Hung. am 05 February 1980, Hanoi, Vietnam

Rostock, December 2014

urn:nbn:de:gbv:28-diss2015-0222-4

Die vorliegende Arbeit wurde im Institut für Chemie April 2011 bis Dezember 2014 angefertigt.

Erster Gutachter Prof. Dr. Peter Langer

Institut für Chemie

Universität Rostock

Zweiter Gutachter Prof. Dr. Jens Christoffers

Institut für Chemie

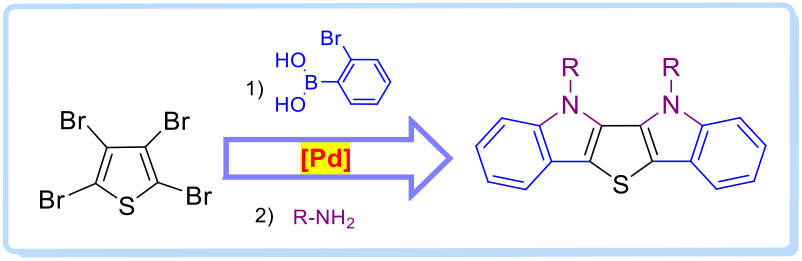
Carl von Ossietzky Universität Oldenburg

Eingereicht am: 01.09.2014

Tag der Verteidigung: 02.12.2014

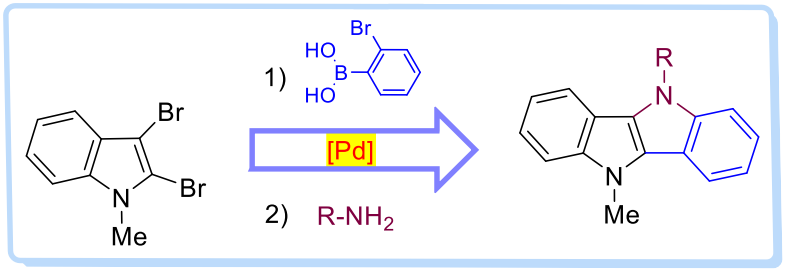
SYNTHESIS OF FUSED HETEROCYCLES BY SEQUENTIAL PALLADIUM CATALYZED CROSS-COUPLING REACTIONS

MAIN CONTENTS

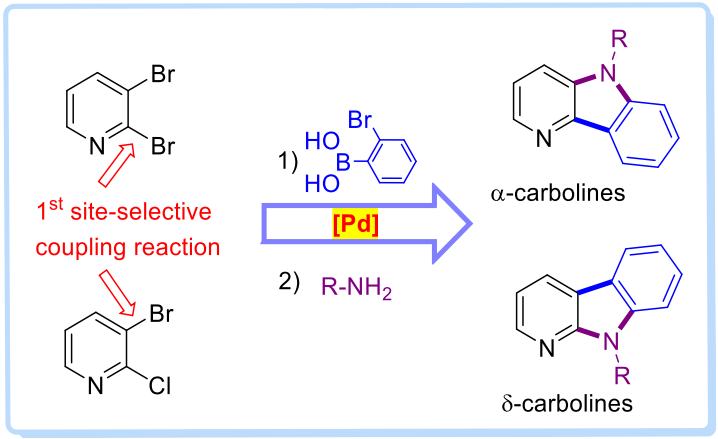


This chapter was published in *Org. Biomol. Chem.* **2012**, *10*, 9041–9044 by Hung, T. Q.; Dang, T. T.; Villinger, A.; Sung, T. Van; Langer, P.

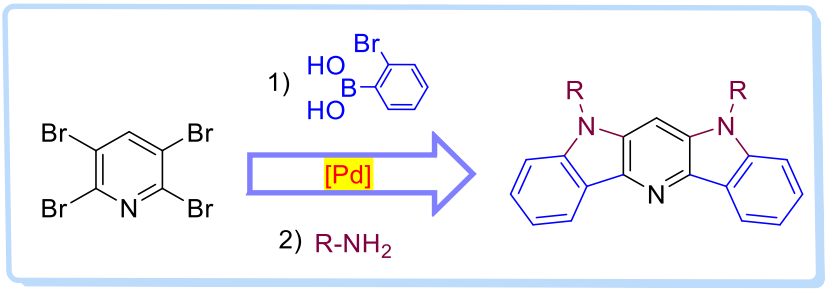
Abstract: *Heteroacenes (thieno[3,2-b:4,5-b']diindoles and benzothieno[3,2-b]indoles) were efficiently synthesized from tetrabromothiophene and 2,3-dibromobenzothiophene in two steps, respectively. In the first step, a site-selective Pd-catalyzed C-C coupling is carried out, followed by a two-fold C-N coupling with aromatic and aliphatic amines.*



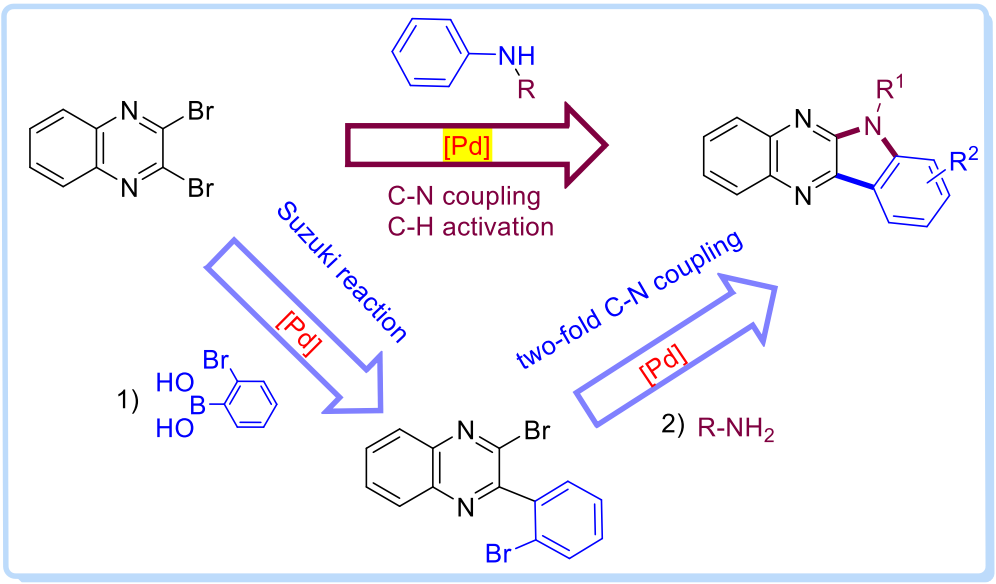
Abstract: *A series of 5,10-dihydroindolo[3,2-b]indoles was successfully prepared by an efficient two-step strategy based on site-selective Pd-catalyzed cross-coupling reaction with N-methyl-2,3-dibromoindole and subsequent cyclization by two-fold Pd-catalyzed C-N coupling with amines. The products show a strong fluorescence.*



Abstract: *Two concise and efficient approaches were developed for the synthesis of α- and δ-carboline derivatives. The success of the synthesis relies on site-selective Suzuki-Miyaura reaction of 1-chloro-2-bromopyridine or 2,3-dibromopyridine with 2-bromophenylboronic acid and subsequent cyclization with amines which proceeds by twofold Pd-catalyzed C-N coupling.*



Abstract: *5,7-Dihydropyrido[3,2-b:5,6-b']diindoles were prepared by a highly efficient two-step synthesis based on site-selective Suzuki coupling reactions of 2,3,5,6-tetrabromopyridine and subsequent Pd-catalyzed cyclization by two-fold C-N coupling with aromatic and aliphatic amines. Except from a patent, the parent molecule, mentioned in a patent without characterization, 5,7-dihydropyrido[3,2-b:5,6-b']diindoles represent a new chemical entity. The electrochemical and photochemical properties of the products were investigated. The products show promising fluorescence properties with good quantum yields and an interesting electrochemical behaviour. The optical and electronical properties were analyzed and explained based on DFT calculations.*

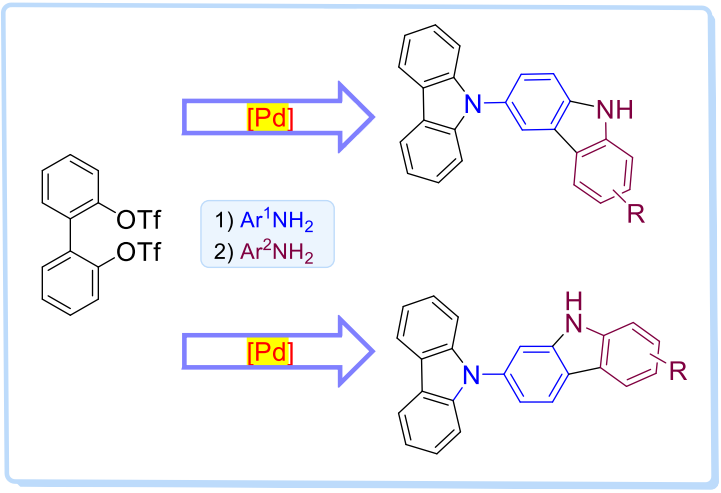


This chapter was published in *Org. Biomol. Chem.* **2014**, *12*, 6151-6166 by Hung, T. Q.; Hoang, D. H.; Thang, N. N.; Dang, T. T.; Ayub, K.; Villinger, A.; Friedrich, A.; Lochbrunner, S.; Flechsig, G. U.; Langer, P.

Abstract: *A series of indolo[2,3-b]quinoxaline derivatives were efficiently synthesized from 2,3-dibromoquinoxaline by two pathways. A one-pot approach, using Pd-catalyzed two-fold C-N coupling and C-H activation reactions, gave indolo[2,3-b]quinoxaline derivatives in good yields, but with limited substrate scope. In addition, a two-step approach to indolo[2,3-b]quinoxalines was developed which is based on Pd-catalyzed Suzuki coupling reactions and subsequent annulation by Pd-catalyzed two-fold C-N coupling with aromatic and aliphatic amines. The electrochemical and photochemical properties of indolo[2,3-b]quinoxaline derivatives were investigated. These studies show that 6-(4-methoxyphenyl)-6H-indolo[2,3-b]quinoxaline showed the highest HOMO energy level and lowest band gap.*

Chapter 6 Page 82

Efficient Synthesis of Biscarbazoles by Palladium-Catalyzed Twofold C-N Coupling and C-H Activation Reactions



This chapter was published in *Org. Biomol. Chem.* **2014**, *12*, 2596-2605 by Hung, T. Q.; Thang, N. N.; Hoang, D. H.; Dang, T. T.; Villinger, A.; Langer, P.

Abstract*: A new and efficient strategy for the synthesis of 3,9'- and 2,9'-biscarbazoles was developed. My strategy relies on the cyclization of 1,1'-biphenyl-2,2'-diyl bis(trifluoromethanesulfonate) with 4- or 3-anisidine, transformation of the methoxy to a triflate group and subsequent oxidative Pd-catalyzed cyclization with various anilines.*

DETAIL CONTENTS

Acknowledgement

First of all I would like to express my sincere appreciation to my academic supervisor, **Professor Peter Langer** for his guidance and valuable support during my thesis. His encouragement and interesting scientific discussions promote significantly the progress of my work.

I also would like to express my deeply grateful to **Dr. Dang Thanh Tuan** for helpful scientific discussions and the possibility to broaden my scientific knowledge.

Special thanks go to **Dr. Peter Ehlers** for valuable comment and assistance during my work and his enthusiasm, meticulousness in correction help me very much.

I am truly thankful to **Professor Stefan Lochbrunner** for his enthusiastic cooperation of my work in the field of photochemistry. Many thanks go to **M.Sc. Aleksej Friedrich**, **Mr. Wolfgang Breitsprecher** for their measurement and conducive discussions.

I would like to express my gratitude to **Dr. Khurshid Ayub** in Dpartment of Chemistry, CIIT Abottabad, Pakistan. His contribution in DFT calculation elucidated the physical properties of the compound series in theory aspect.

Furthermore, I would like to thank **Dr. Gerd-Uwe Flechsig** and his student, **M.Sc. Xiaoqi Ni**, for a successful and straightforward cooporation in the field of electrochemistry.

For a pleasant and friendly environment in the lab as well as several successful collaborations, I am thankful to my lab fellows **Dr. Omer Akrawi**, **Ngo Ngoc Thang**, **Do Huy Hoang**.

Many thanks go to **Sören Hancker**, **Julia Janke** and **Lars Ohlendorf** for the assiduous work and creativity during their bachelor theses.

Lot of gratitude also goes to **Dr. Dirk Michalik**, **Dr. Alexander Villinger**, **Dr. Martin Hein**, **Dr. Holger Feist** for their responbility and reliability in their work and their advice.

None of the research accomplished in this dissertation could have been achieved without the top-notch service available by the technical members of the analytical and technical staff at the Department of Chemistry, University of Rostock and LIKAT (Leibniz-Institut für Katalyse).

Additionally, I would like to thank all of my friends for sharing the moment during my stay in Germany. I am grateful for all funny activities.

Finally, I would like to express the deepest thank to all members of my family for their tremendous support and encouragement during my academic endeavor. My special respect and appreciation goes to my wife, my daughter and my parents who always are on my side.

Tran Quang Hung, Rostock, 10 December 2014

Erklärung

Hiermit erkläre ich, dass ich die vorliegende Arbeit selbstständig angefertigt und ohne fremde Hilfe verfasst habe, keine außer den von mir angegebenen Hilfsmitteln und Quellen dazu verwendet habe und die den benutzten Werken inhaltlich und wörtlich entnommenen Stellen als solche kenntlich gemacht habe.

Rostock, 10 December 2014

Tran Quang Hung

Abstract

The dissertation deals with the synthesis of fused-heterocycle-ring-system which are potential candidates for applications in organic materials and pharmacology. Site-selective Suzuki reactions of polyhalogenated substrates with *o*-bromophenylboronic acid followed by two-fold C-N cross-coupling reactions afforded the final products. The physical properties were investigated and explained based on DFT theoretical calculations. Most compounds exhibit high quantum yields and narrow band gaps.

Moreover, biscarbazoles were synthesized via C-N coupling and C-H bond activation as key steps. A highly efficient strategy is developed requiring only four steps from simple starting materials to afford both 3,9'- and 2,9'-biscarbazoles.

Zusammenfassung

Diese Arbeit behandelt die Synthese von kondensierten, heterozyklischen Ringsystemen, die potentiell für Anwendungen in den Materialwissenschaften sowie der Pharmazie in Frage kommen. Positionsselektive Suzuki Reaktionen an polyhalogenierten Startmaterialien 2-Bromphenyl Boronsäure, gefolgt von einer zweifachen C-N- Kupplungsreaktion lieferte das Zielprodukt. Die physikalischen Eigenschaften wurden untersucht und durch theoretische DFT-Rechnungen unterstützt. Viele Verbindungen besitzen hohe Quantenausbeuten und geringe HOMO-LUMO-Abstände.

Weiterhin wurden Dicarbazole mittels C-N-Kupplung und einer C-H-Aktivierung als Schlüsselreaktion synthetisiert. Eine sehr effiziente Methodik wurde entwickelt, welche in nur 4 Stufen, ausgehend von einfachen Ausgangsverbindungen, zu den gewünschten 3,9'- und 2,9'-Dicarbazolen führt.

1 General introduction

1.1 Pd-Catalyzed Cross-coupling reactions

Since Palladium catalyzed cross-coupling reactions were firstly applied in organic synthesis over last 40 years, they have played important roles in synthesis of pharmaceuticals, natural products and novel materials.[1] Located in the second row of transition metals and belonging to the Ni triad, Pd has the tendency of transferring two electrons to afford complexes in oxidative state 0 and 2^+. Due to the important feature of quite high electronegativity (2.2 according to Pauling scale)[2], the Pd-C bond is relatively stable, non-polar and useful for synthetic processes. Due to the interactive ability of Pd with non-polar π-bonds, heteroatom containing lone pair electrons readily get involved in the oxidative addition, transmetalation and reductive elimination processes, which make Pd become an optimal metal to be used in organic transformations.[3]

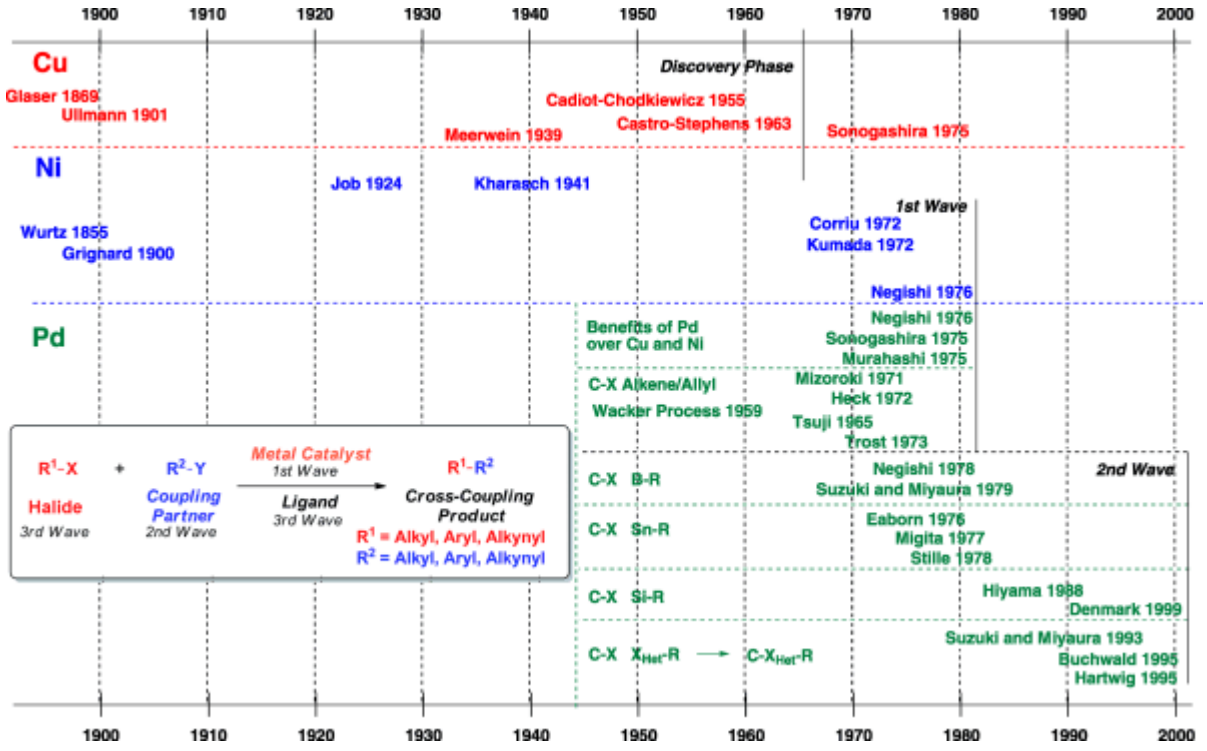


Figure 1.1 Timeline of discovery and development of cross-coupling reaction[3] (This picture was copied from *Angew. Chem. Int. Ed.* 2012, *51*, 5062–5085)

Notably, for their very important contributions, Heck, Suzuki and Negishi were pioneers in the development of palladium catalyzed cross-coupling reactions and received the Nobel Prize in 2010. In addition, many efforts of chemists have been made to investigate the mechanism and broaden the scope of substrates in this field over the last decade. The term of

cross coupling implies reactions between two different partners with the aid of metal catalyst. The general cross coupling reactions are depicted in figure 1.2.

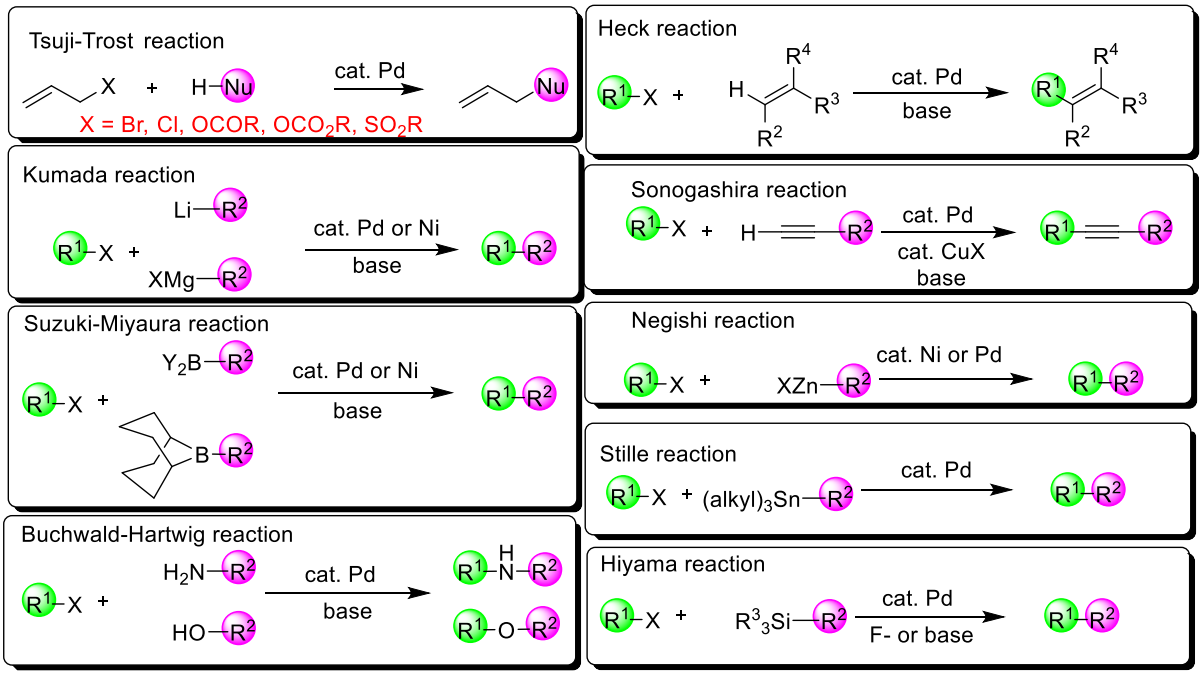


Figure 1.2. Palladium-catalyzed cross coupling reactions in organic synthesis

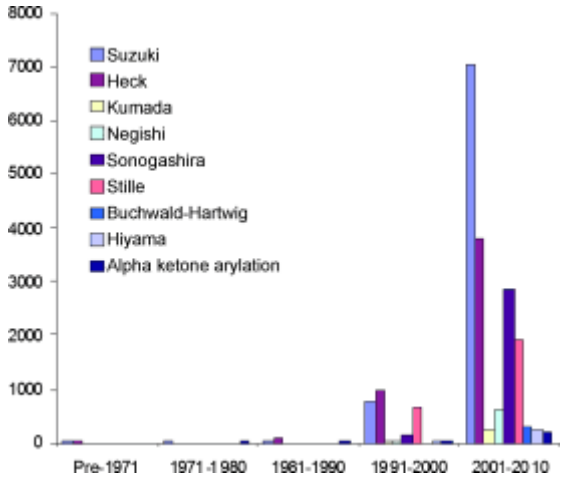


Figure 1.3. The development of cross-coupling reactions in the number of publications and patents[1] (This picture was copied from *Angew. Chem. Int. Ed.* 2012, *51*, 5062–5085)

1.1.1 General mechanism of cross-coupling reactions

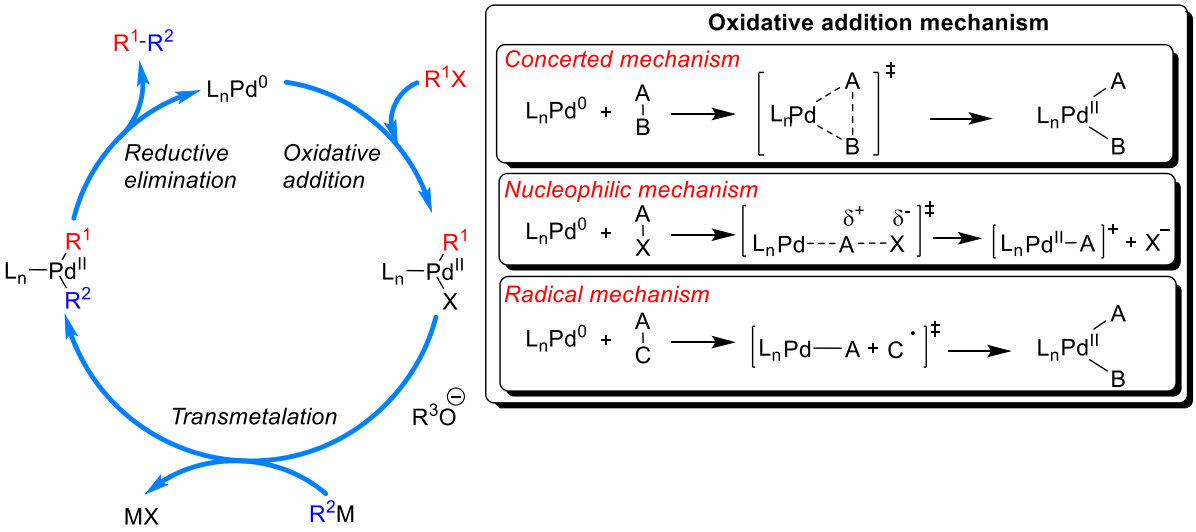


Figure 1.4. General mechanism of cross coupling reactions

A palladium(0) complex containing 18 electrons in the outer shell (stable state) is in situ activated to afford a Pd(0) species with 14 electrons in the outer shell by a dissociation process of ligands. Once the active Pd(0) is formed, the combination with electrophile R-X in the oxidative addition stage affords the complex L_nR-Pd(II)-X. This stage is slow and regarded as rate determinating of the reaction. The oxidative addition followed three general mechanisms including concerted (for non-polar substrate), nucleophile displacement (for polar substrate) and radical (for both polar and non-polar substrate) mechanism. Subsequently, the organic group R^2, derived from on organometallic compound, is transferred to palladium (II) center with no change in the oxidation state, namely the transmetalation stage. The last stage, reductive elimination, affords the corresponding product and regenerates the Pd(0) complex for a new catalytic cycle.

The electrophilic substrates have significant influence on the rate and selectivity of the reaction. The activity of halides in cross-coupling reactions follows the rule: R-I > ROTf ≈ R-Br >> R-Cl >>> R-F (nearly unreactive). The bond dissociation energy of C-I, C-Br, C-Cl is 65±1, 80.4 ± 1.5, 95 ± 1.5 kcal/mol, respectively.[4]

When inactive palladium precursor (Pd (II) salts) such as $Pd(OAc)_2$, $PdCl_2$, Na_2PdCl_4 is employed, reduction of Pd(II) to Pd(0) is required prior to enter the catalytic cycle.[5] The

reduction mechanism is still unclear in some reactions. Some general mechanism involving reduction of the Pd(II) reagent may include tertiary aliphatic amines, phosphines (using as ligand), ethylene reagents,[6] or the action of solvents, such as 1,4-dioxane, THF, DMF, DMSO, toluene, etc. Alternatively, Pd nanoparticles,[7] palladium supported on solid supports could become highly active catalysts in some cases.[8]

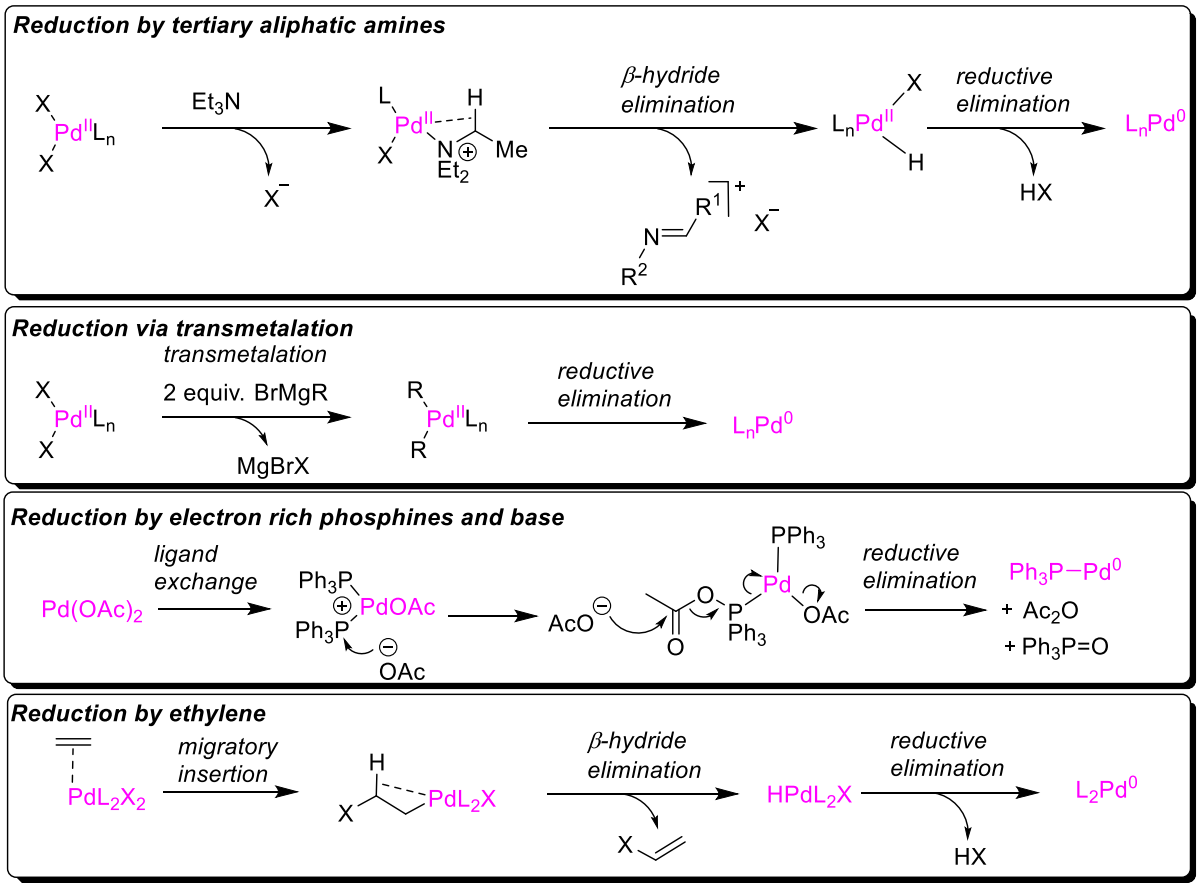


Figure 1.5. Mechanism of reduction from Pd(II) to Pd(0)

The employment of ligands in combination with Pd is believed to stabilize the Pd complex center. Moreover, electron rich phosphine ligands promote the oxidative addition stage. Conversely, stericilly hindered ligands accelerate the reductive elimination stage by their large cone angle effect.[9] Because of competition with β-hydride elimination, faster reductive elimination processes minimize side-products in these reactions. Triphenyl phosphine is known as the most common ligand in cross-coupling reactions.[10] As early as 1979, Dppf was used by Kumada and gave benefit.[11] It is noteworthy that monodentate biaryl phosphine

ligands developed by Buchwald and coworkers showed significant advantages in Pd catalyzed cross-coupling reactions. Until now, a lot of efficient monodentate and bidentate ligands were invented and successfully applied in Pd-catalyzed cross coupling reactions under mild condition.[5b,12] It showed advantages in cross-coupling reactions of inactive aryl chlorides, highly steric substrates and heterocycles. The features of dialkylbiarylphosphine ligands are depicted in figure 1.5. According to theory, the ratio of metal and ligand is expected to be 1:1. But in case of inactive substrates, difficult and slow reactions, an excess amount of ligand is required. Additionally, an additional amount of ligand assists to activate catalyst and stabilizes the Pd metal center to give high turn-over-numbers (TON).[13] Besides, Fu's ligands, including PCy_3, $P(tBu)_3$, also proved beneficial in some reactions. Especially in the case of less active aryl chlorides, these ligands give high yield and show high selectivity.[12f] Notably, Beller *et al.* developed diadamantylalkylphosphanes Cata*CX*ium A which showed highly efficient catalytic activity with very low catalyst loading and resulting in high yield.[8a] In addition to phosphine ligands, *N*-heterocyclic carbenes (NHCs) exhibit a wide range of application in cross coupling reactions under mild condition and allow the usage of water as solvent.[4,14] NHCs, regarding as tertiary phosphine mimics, have improved catalyst performance (depicted in figure 1.5). NHCs in salt form and phosphines share the point of easy handling. However, in the case of NHCs·HX, the use of a base is required to liberate free NHC to the reaction. Comparing to phosphine ligands, NHCs are binding to metal, forming more stable NHC-Metal complexes.

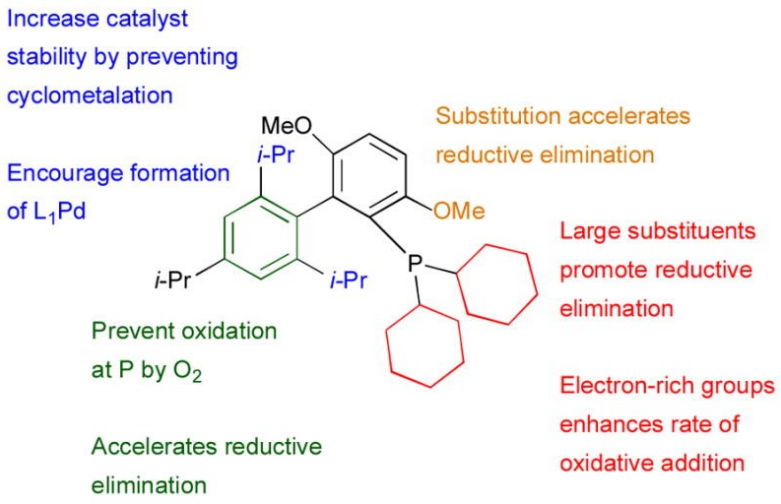
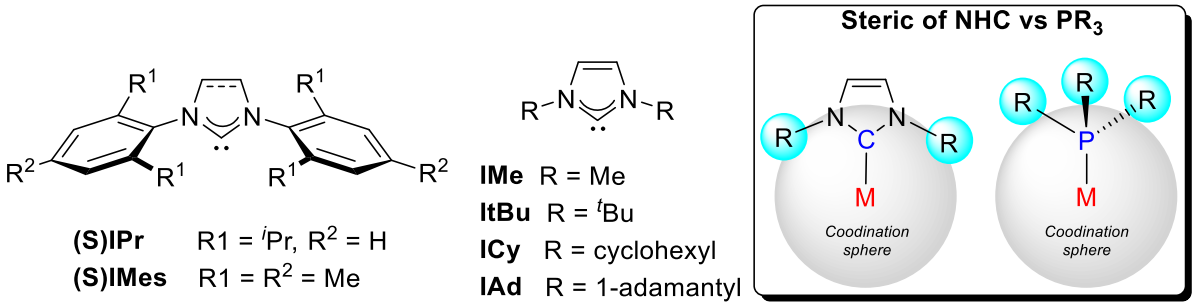


Figure 1.6. Feature of dialkylbiarylphosphane ligands structure.[5b] (This picture was copied from *Chem. Sci.* 2011, *2*, 27–50)



(S) denotes saturated imidazolium backbone

Figure 1.7. Common NHC ligands and feature.

In cross coupling reactions, the solvent plays dual roles. Firstly, the solvent choice bases on high solubility of components in reaction, low solubility of inorganic by-product and effectively allows respective temperature range of reactions. Secondly, it stabilizes intermediates in the catalytic cycle. Both single solvent and mixture of two solvents in homogenous or heterogeneous phase (monophase or biphase) are employed in various reactions.[1e,15] The most common solvents include toluene, 1,4-dioxane, THF, DMF, DMA, DMSO. Water is the ideal solvent, but until now the applications are still limited.[16] Solvents have to be deoxygenated to avoid impact on the catalyst system.

Temperature influences on the rate of the reaction and formation of side products. Ideal conditions can be obtained by optimization of some factors, such as, Pd source, ligand, base, solvent and temperature in order to achieve the highest yield of desired product.

1.1.2 Suzuki-Miyaura Cross-coupling reactions

Beginning with the first report of Miyaura[17] in 1979, palladium-catalyzed cross-coupling reactions between aryl halide and 1-alkenylboranes, Suzuki-Miyaura reactions (SMR), had become extremely popular in the last decade (depicted in figure 1.3).[1b,g,18] Today, the Suzuki-Myaura reaction concept is the cross-coupling reaction of alkenyl, aryl halides (or pseudo-halides) with a variety of organoboron reagents (boranes, boronic acids, boronic esters). Many papers and patents regarding the Suzuki-Myaura reaction were reported to improve site-selectivity, chemo-selectivity, low catalyst loading, expansion of substrates scope and applications of greener process-conditions (green solvent, low catalyst loading, recycling catalyst, low temperature, minimizing site-products).[14c,19]

The boron electronegativity is relative small (2.0 according to Pauling scale)[2] and make the C-B bond rather unpolar and more stable as compared to the bond of other metal-C bonds, such as Mg, Li, Zr, Al, Cu, Si, Sn. Thereby, oganoboranes are nontoxic, air and moisture stable and easy to handle. With such advantages of mild and convenient conditions, tolerance to functional groups and facile removal of toxic inorganic by-products, SMR became the most useful and versatile method in industrial applications.[20]

Initially, alkenylboranes, as starting materials for SMR, were synthesized by reaction of terminal alkynes with catecholborane. The reaction of Grignard or Lithium reagents with boronic ester is also widely employed to construct organoboranes.[21] In 1993, Miyaura and Suzuki reported a novel method to add boron ester to triple bond via Platinum catalysis under convenient condition. Two years later, Miyaura found that the $B_2(pin)_2$ (bis(pinacolato)diboron) reagent undergoes coupling with aryl halide in the present of $[Pd(dppf)Cl_2]$ as catalyst.[22] Nowadays, $B_2(pin)_2$ or HB(pin) are widely employed to form organoboranes.[21a,23]

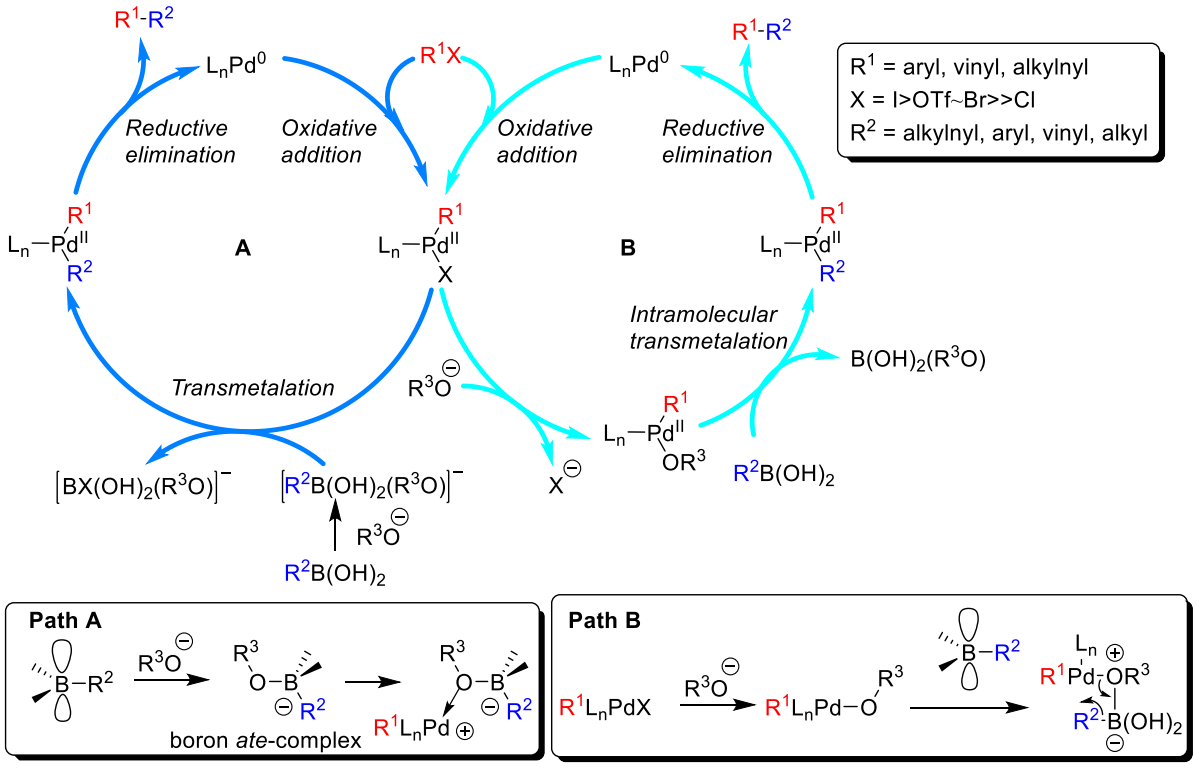


Figure 1.8. General mechanism of Suzuki-Myaura cross-coupling reaction and role of base in SMR[24]

Similar to the mechanism of other cross coupling reactions, the SMR mechanism begins with the oxidative addition step, followed by the transmetalation step and finishes with the

reductive elimination step. Here, the role of the base is of importance. In most organoboron species, the carbon-boron bond is highly covalent. Therefore, the complex does not readily involve a transmetalation. It is noteworthy that the role of the base in SMR activates the organoboron derivative by forming a hypervalent, anionic boron-"ate" complex which represents a better leaving-group and readily undergoes transmetalation. An alternatively proposed mechanism involves the displacement of halide in the $[PdXR^1L_2]$ complex by base to form a $[Pd(OR^2)R^1L_2]$ complex. The most common employed bases in SMR are K_2CO_3, K_3PO_4, Na_2CO_3, NaOH, $NaHCO_3$. In some substrates containing fragile functional groups and large molecular weight, SMR cannot occur without the presence of TlOH.[25]

The most common catalysts used in SMR are $Pd(PPh_3)_4$, $PdCl_2$, $Pd(OAc)_2$, Pd_2dba_3 in combination with various phosphine ligands. The $Pd(PPh_3)_4$ catalyst, known as "Tetrakis", is cheap and easy to handle but exhibits low activity and is unstable under air. Using $Pd(OAc)_2$ in the combination with phosphine ligands could significantly improve selectivity and activity.[12f,24d] Pd nanoparticles, Pd supported on inorganic solid materials or polymers showed many advantages in various cases.[26]

SMR can be performed in various solvents. Solvents influences on the activity and the selectivity of the reaction. Toluene, 1,4-dioxane, benzene, DMF, THF, MeCN are the most common solvents.[1b,18a] A mixture of organic solvent and water was used to improve the yield of coupling product and its high selectivity in SMR.[27] The biphasic media (organic/aqua) affords high solubility of both boron partner and inorganic salt. Additionally, the mixture of organic solvents is an alternative choice to make reaction occur faster. These mixture generally include two organic solvents with very different in polarities such as toluene-EtOH, toluene-MeOH, dioxane-toluene.[28] Recently, PEG,[7a,29] neat water,[16a,30] or ionic liquids[26b] were used instead of classical solvents. The advantages of these solvents are low cost, non-toxic, thermal stability and feasible to recycle.

SMR plays an important role in the synthesis of many natural products, drugs such as Crizotinib (a potent anti-cancer agent),[31] Yuehchukene (bisindole alkaloid isolated from *Murraya paniculata* (L.)),[32] Michellamine B (strong anti-HIV-1, anti-HIV-2 agent),[33] Ribisins A, B and D (bioactive polyoxygenerated benzofuranes),[34] Diazonamide A,[35] Vitamin A[36] (figure 1.8) and many others.

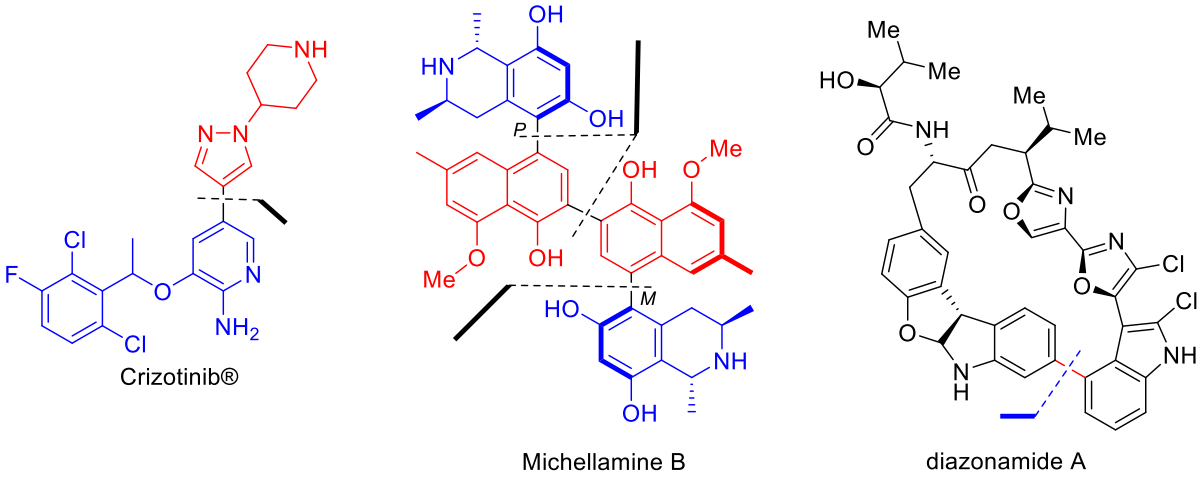


Figure 1.9. SMR as key step in natural product and drug synthesis.

1.1.3 Buchwald-Hartwig amination reactions (BHAR)

Buchwald-Hartwig amination is one of most important reactions in modern organic synthesis, in which C-N bonds formed by Pd-catalyzed cross-coupling of amines with aryl halides. This reaction was independently developed by the group of Stephen L. Buchwald and John F. Hartwig in 1994.[37] The development of the BHAR shows many advantages in the efficient synthesis of aryl amines, replacing the conventional methods (the Goldberg reaction, nucleophilic aromatic substitution, reductive amination, etc.) while significantly expanding substrate scope and functional groups tolerance.

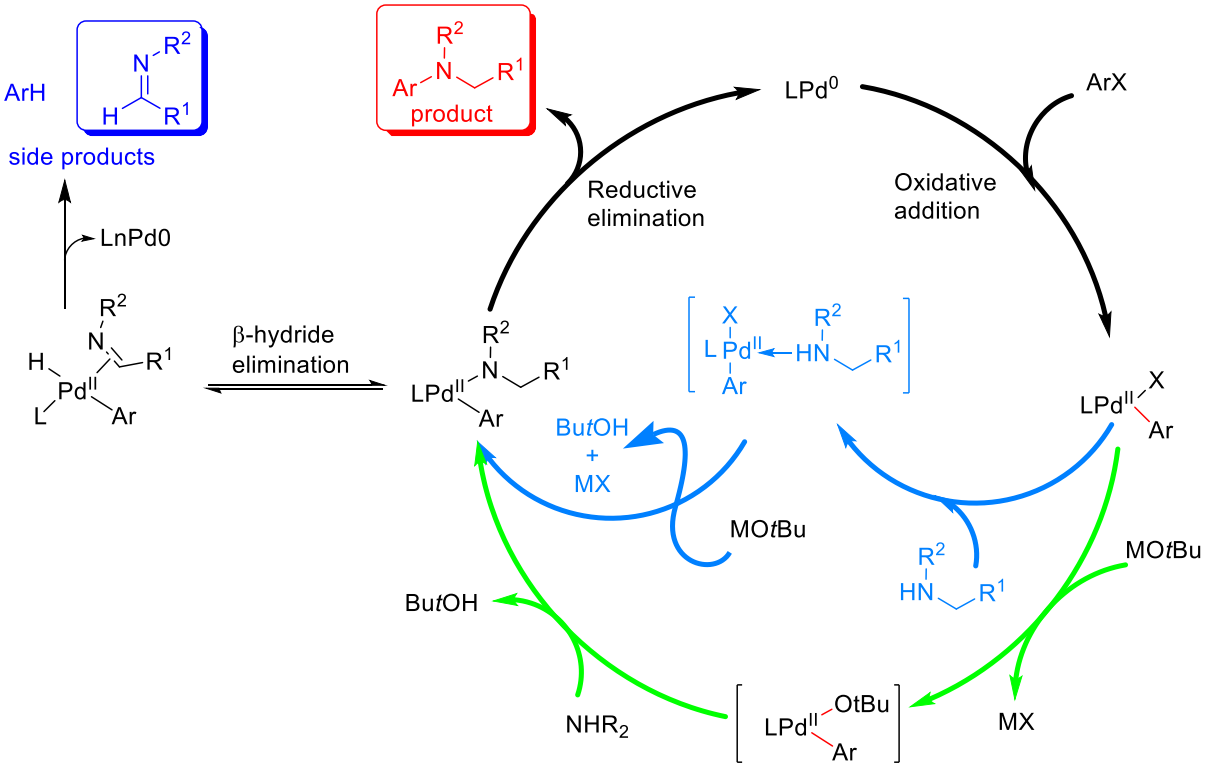


Figure 1.10. Mechanism of Buchwald-Hartwig reaction[5b,12d,38]

Initially, the formation of active catalytic species is required. In the case of monodentate ligands, for example P(*t*Bu)$_3$, the active monophosphine complex Pd[P(*t*Bu)$_3$] is formed (depicted in Figure 1.11).[38] In the case of bidentate ligands, such as BINAP, the active complex form of Pd^{0}L is generated from the Pd^{0}L$_2$ precusor via ligand dissociation.

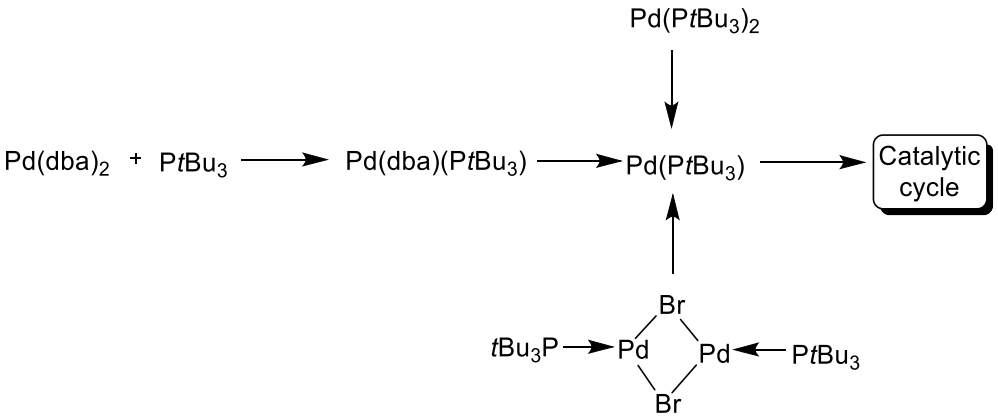


Figure 1.11. Forming of active actalytic species of monodentate

In the first stage, the active catalytic species PdL readily enters the catalytic cycle via oxidative addition with an aryl halide as in all cross-coupling reactions. Then, the amine binds to this Pd(II) species to form an coordination bond. The deprotonation with the aid of base results in the formation of [PdLAr($(NCH_2R_1)R_2$)]. Alternatively, the replacement of halide by base, subsequent with amine binding afford [PdLAr($(NCH_2R_1)R_2$)]. At the end of the catalytic cycle, the reductive elimination step completes the catalytic cycle to regenerate the Pd(0) species. Besides, if amines possess hydrogen atom at the α-position to nitrogen atom, the [PdLAr($(NCH_2R_1)R_2$)] complex can undergo a β-hydride elimination reaction to generate an imine as side-product.

When palladium salts, as $Pd(OAc)_2$ is employed, reduction of Pd(II) to Pd(0) is required. Amines containing α-hydrogen atoms may reduce Pd(II) to Pd(0) to enter catalytic cycle, by a *β*-hydride elimination reaction. Besides, primary amines, primary amides need a reductant such as a phosphine ligand, a tertiary amine (NEt_3). Because of difficulties in the reduction from Pd(II) to Pd(0), the employment of Pd(0) stable complexes can directly coordinate to dialkylbiaryl ligands generating active LPd complex to enter the catalytic cycle.

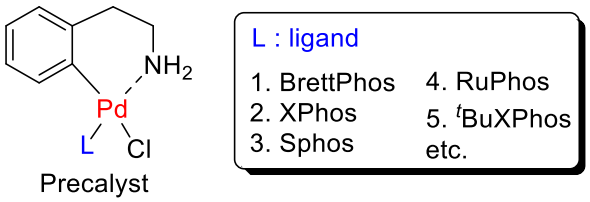


Figure 1.12. Precatalyst of Buchwald-Hartwig amination reaction

For BHAR media, toluene and 1,4-dioxane solvents are commonly used because of their high boiling point and the solubility property of many organic compounds in these solvents. Moreover, ethereal solvents such as THF and Bu_2O are alternative choices.[5b,12b] Some reactions require more polar solvents, such as DMSO, DMF and DMA.[4b,11b,39] The solvent plays the role of dissolving components in reaction, accelerating reaction by poor solubility of inorganic by-products, eliminating side-products. The solvent must be dried and deoxygenated. A mixture of two solvents (polar mixing with unpolar solvent) has also known as good idea for BHAR. [4b,11b]

Strong bases are generally employed in BHAR. The choice of base may influence on reaction rate, functional groups tolerance and side products formation. Because of significant p*K*a changing of nucleophile by binding with Pd, the choice of base is not merely based on p*K*a. [4b]

NaO*t*Bu or KO*t*Bu in toluene are generally employed in BHAR to afford high yields, high reaction rates and low catalyst loadings. Due to the application of relatively strong bases (p*K*a ≈ 17.0), reactions with electrophilic groups, such as ketones and esters, may occur as side reactions. Some weaker bases, such as NaOMe, NaOH, KOH showed benefit in functional groups tolerance. In the case that substrates contain sensitive functional groups, weak inorganic bases such as Cs_2CO_3, K_2CO_3, K_3PO_4 are alternative choices.

BHARs found many applications in the synthesis of natural products, bioactive compounds and drugs. For example, A-366833, a selective neuronal nicotinic receptor agonist was prepared by C-N coupling as the key step.[40] Federsel *et al.* successfully synthesized 5-HT_{1B} receptor antagonist using $Pd(dba)_2$/BINAP.[41] Many important drugs were synthesized using BHAR. Imatinib, a tyrosine kinase inhibitor, is used for treatment of chronic myeloid leukaemia and gastrointestinal stromal tumors and was developed by Norvartis AG in 2003[42] Chida et al. finished the total synthesis of Murrayayoline (a carbazole alkaloid isolated from genus Murraya) using two-fold BHAR as key step.[43] Very recently, Piersanti used intramolecular BHAR for the total synthesis of (-)-epi-Indolactam V.[44]

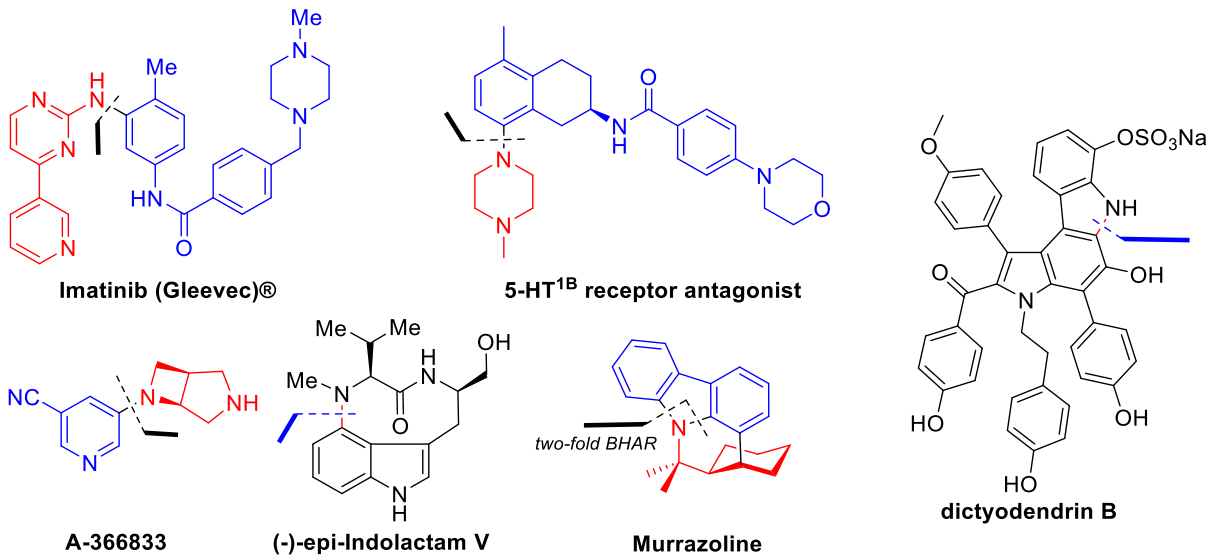


Figure 1.13. Some total synthesis natural products and bioactive compounds used BHAR as key step

1.2 Pd-catalyzed C-H bond activation reactions

Recently, C-H bond activation reactions have been receiving much attention. C-H activation provides many direct routes to form C-C and C-Heteroatom bonds without need of prefunctionalization of starting materials leading to low cost and environmentally friendlier procedures.

1.2.1 C-X/C-H coupling reactions

Over the last decade, C-X/C-H bond activations have been proven to be one of the the most efficient methodologies to functionalize and construct polycyclic (hetero)aromatic compounds.[45]

Even though, the efficiency of C-H activation reactions has been dramatically improved in recent years. The mechanism of C-H bond activation reactions is still unclear to date. They are divided into three general mechanisms: electrophilic substitution, σ-bond metathesis, oxidative addition (Figure 1.14). The catalytic cycle is believed to undergo in three main steps: firstly, Pd(0) coordinates to an aryl halide in a oxidative addition step resulting in the formation of ArPd(II)X complex, followed by C-H bond activation of Ph-H to form PhPd(II)Ar species and subsequently finishing with a reductive elimination step to afford the product and regenerate Pd(0). Recent research showed that caboxylates assist the C-H activation in many cases and are involved in several steps of the catalytic cycle.[46] The mechanism of carboxylate-assisted C-H bond activation is also proposed with assisting by pivalic acid.[47]

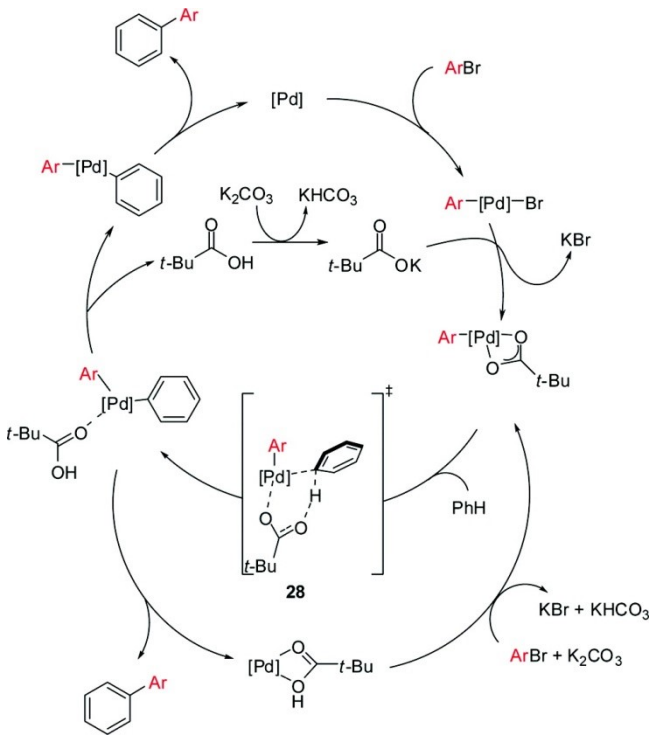


Figure 1.14. Proposed C-H bond activation reaction mechanism (this picture was copied from *Chem. Rev.* 2011, *111*, 1315–1345)[46]

The C-H activations have been applied in the synthesis of natural products and drugs as well as advanced organic materials.[48] One of the most notable examples is the formation of heterocycles including, pyrroles, indoles, carbazoles, quinazolines, etc.[45b,49] One interesting example includes synthesis of Kibdelone, a potent nematocidal, antibiotic and anticancer reagent by intramolecular C-I/C-H annulations by Pd-catalysis.[50] Functionalization of cyclobutane in the total synthesis of Piperarborenine B and D, using C-H activation, is another important example. The reaction could give desired products in high stereo-selectivity.[51]

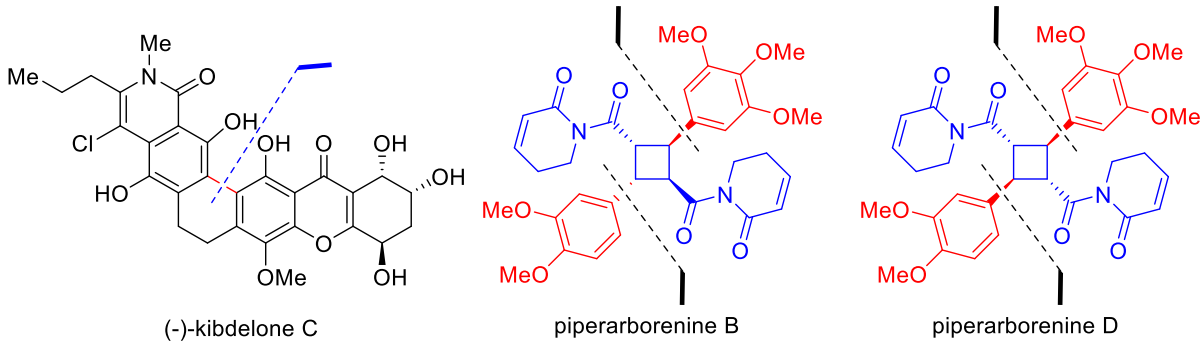


Figure 1.15. Some total synthesis of natural products and bioactive compounds using C-X/C-H coupling reactions as key step

1.2.2 C-H/C-H coupling reactions (Oxidative CH bond activation)

The direct C-C bond formation by oxidative C-H/C-H coupling using non-toxic and inexpensive oxidants is an ideal strategy in the development of green and sustainable processes. One of the most important applications in C-H/C-H coupling reaction is to form the C-C bond with heteroaromatic compounds.[45b]

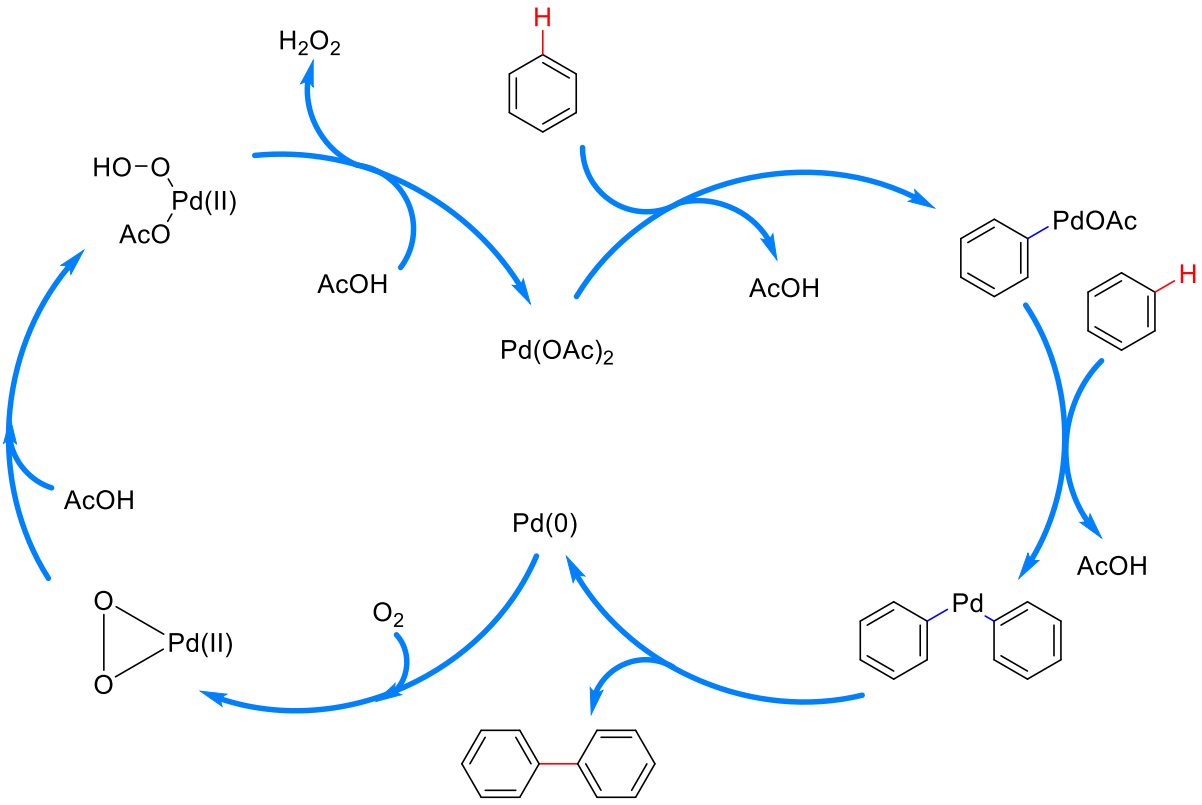


Figure 1.16. Proposed catalytic cycle of oxidative C-H bond activation reaction[52]

The catalytic cycle of C-H/C-H coupling is assumed to proceed in three steps including two C-H activation steps to afford a Pd(II) intermediate species followed by a reductive elimination step to form the product and generate a Pd(0) species (Figure 1.16). With the aid of oxygen or any other oxidants (such as $Cu(OAc)_2$, AgOAc, Ag_2O), this Pd(0) species is reoxidized to Pd(II) and begins a new catalytic cycle.

Many natural carbazoles were synthesized in the employment of $Pd(OAc)_2$ in the combination with $Cu(OAc)_2$ or oxygen as oxidant reagent in acetic acid media.[49,53] It is

noteworthy that pivalic acid, a convenient solvent could accelerate to give higher yields of cyclized products.[46,54] Many natural carbazoles, for examples, Mukonine[54] and Clausine L[52] were successfully synthesized. Dragmacidin D, an important drug for treating Pakinson's and Alzheimer's deseases, was synthesized by C-I/C-H coupling and C-H/C-H coupling.[55]

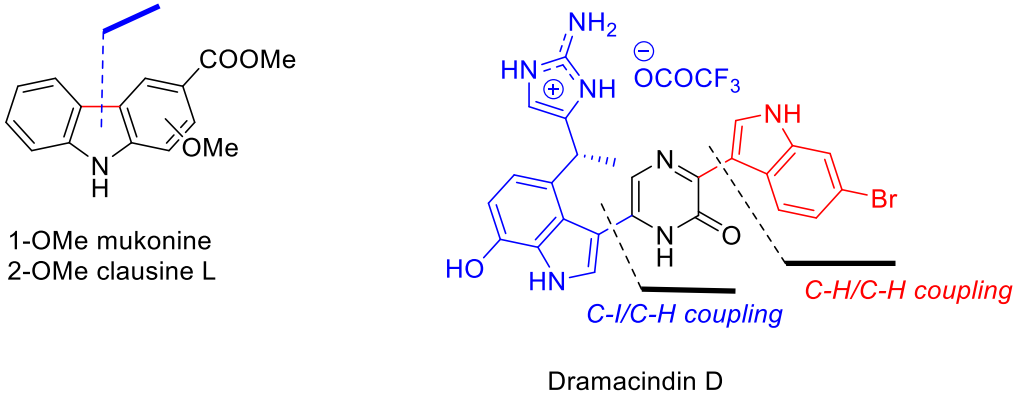


Figure 1.17. Some total synthesis of natural products and drugs used C-X/C-H coupling reactions as key step

In 2009, Watanabe *et al.* proposed some possible oxidative coupling mechanisms in detail by trapping and deuterium experiments (Figure 1.16).[52] The first C-H coupling may undergo by three different mechanisms including electrophilic substitution, σ-bond metathesis or oxidative addition, followed by reductive elimination to afford complex A or B. Afterward, the second C-H coupling may occur by four different possibilities including the three mechanisms mentioned above or carbopalladation followed by β-hydride elimination to give the cyclized product.

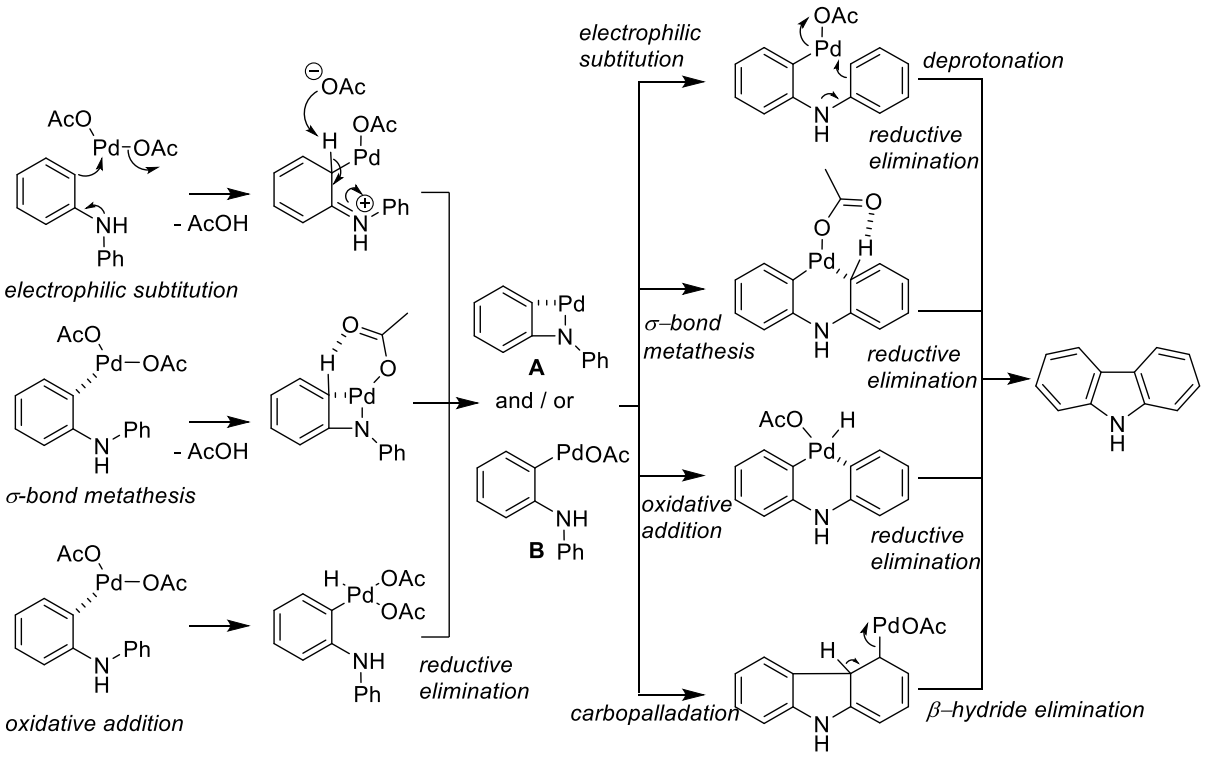


Figure 1.18. Possible mechanism of oxidative C-H bond activation in detail[52]

1.3 Ligands employed in this dissertation

Monodentate and bidentate phosphine ligands were utilized in the combination with palladium precursors such as $Pd(OAc)_2$, $Pd_2(dba)_3$ during the optimizations of Buchwald-Hartwig reactions. In most cases, bidentate ligands with large bite angles, such as BINAP, XantPhos, DPEPhos or Dppf, efficiently influent on Buchwald-Hartwig amination reactions. It can be explained by the rigid five membered ring complex of two phosphines coordinating to Pd and diphosphine backbond influences. The wider backbone results in the larger angle of P-Pd-P and it influents on steric and electronic properties of bidentate ligands. Wide bite angles increase steric bulk and favor or disfavor certain geometries of transition metal complex. For example, square planar complexes stabilize bite angle around 90º. The wider bite angles favor zero-valent complexes and trigonal or tetrahedral geometries. Those ligands accelerate reductive elimination and hence reduce β-hydride elimination which leads to by-products in Buchwald-Hartwig aminations.[38]

The utility of tetrakis(triphenylphosphine)palladium(0) ($Pd(PPh_3)_4$) is successfully demonstrated in Suzuki reaction with heterocyclic substrates such as thiophene, indole, pyridine, quinoxaline. The using of other Pd precursors, such as $Pd(OAc)_2$, $Pd[Cl_2(MeCN)_2]$, $Pd[Cl_2(PPh_3)_2]$, accompanying other phosphine ligands gave lower yield and complex reaction mixtures.

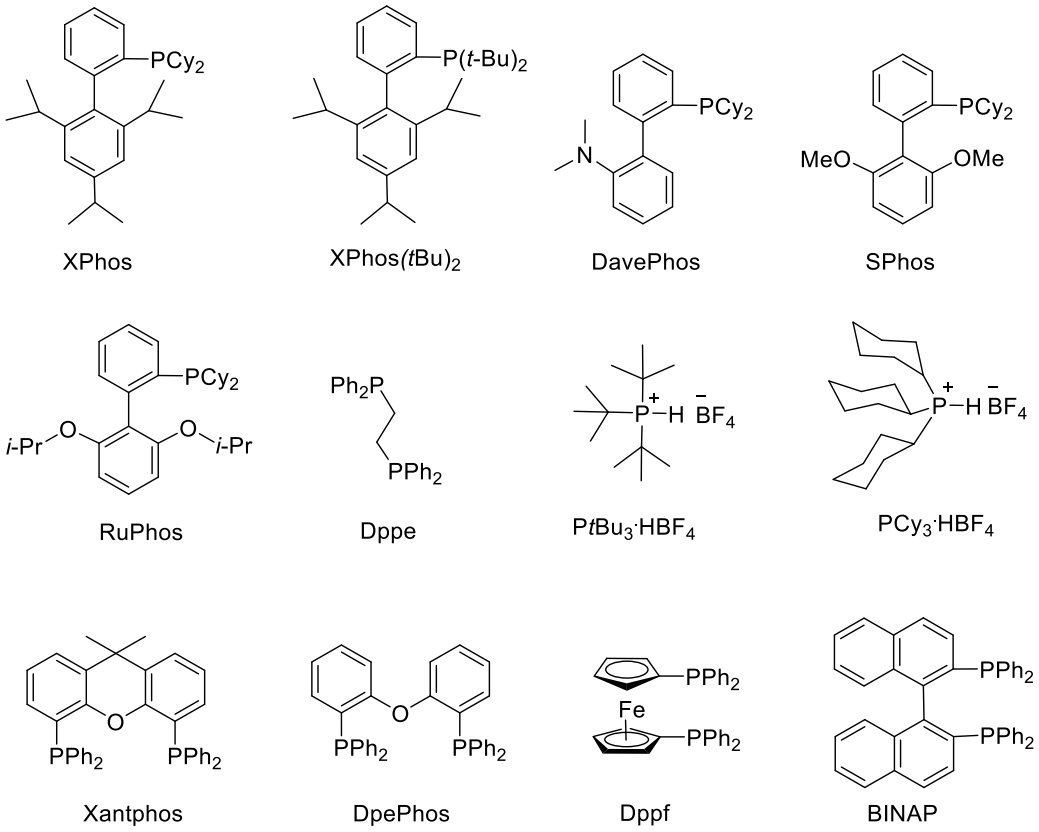
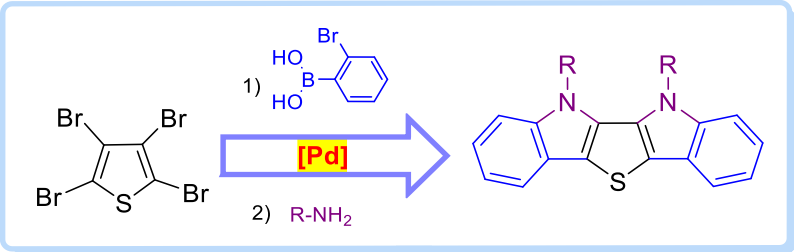


Figure 1.19. Monodentate and bidentate phosphine ligands.

2 Synthesis of thieno[3,2-*b*:4,5-*b'*]diindoles and benzothieno[3,2-*b*]indoles



2.1 Introduction

Thiophene-containing fused acenes have found many applications in organic field-effect transistors (OFETs) as well as organic light-emitting diodes (OLEDs).[56] Especially, great effort has been devoted to study of pentacenes, their heterocyclic derivatives and π-extended ladder-type analogues due to their excellent charge carrier mobility.[57] Some heteroatom-containing pentacenes play an important role in OFETs applications, such as anthradithiophene,[58] tetraceno[2,3-*b*]thiophene,[59] indole[3,2-*b*]carbazole,[60] 5,7,12,14-tetraazapentacene,[61] pentathieoacene,[62] and dibenzo[*d*,*d'*]thieno[3,2-*b*:4,5-*b'*]dithiophene.[63] The first introduction of both sulphur and nitrogen atoms to multi-cycle-structures was developed by Liu and co-workers.[64] 5,6-Disubstituted thieno[3,2-*b*:4,5-*b'*]diindoles **3**, containing one thiophene ring and two pyrrole rings, were synthesized from the corresponding indoles. Later, Liu *et al.* developed the synthesis of dibenzothieno[*b,d*]pyrroles **4** from benzothiophene.[65] The electronic transport increased due to intermolecular sulfur-sulfur interactions between two neighbouring molecules. In 2009, Balaji and Valiyaveettil reported the synthesis of symmetrical and unsymmetrical dibenzothieno-pyrroles **2** and **3**.[66] Their studies showed that intermolecular sulfur-sulfur interactions, π-π stacking and van der Waals interactions play an important role to provide high intermolecular charge mobility. [66] In 2010, with the same method, they synthesized a molecule with seven fused rings affording diindolodithienopyrroles **4.**[66] These compounds exhibited lower HOMO energy level and larger band gap affording environmental stability.

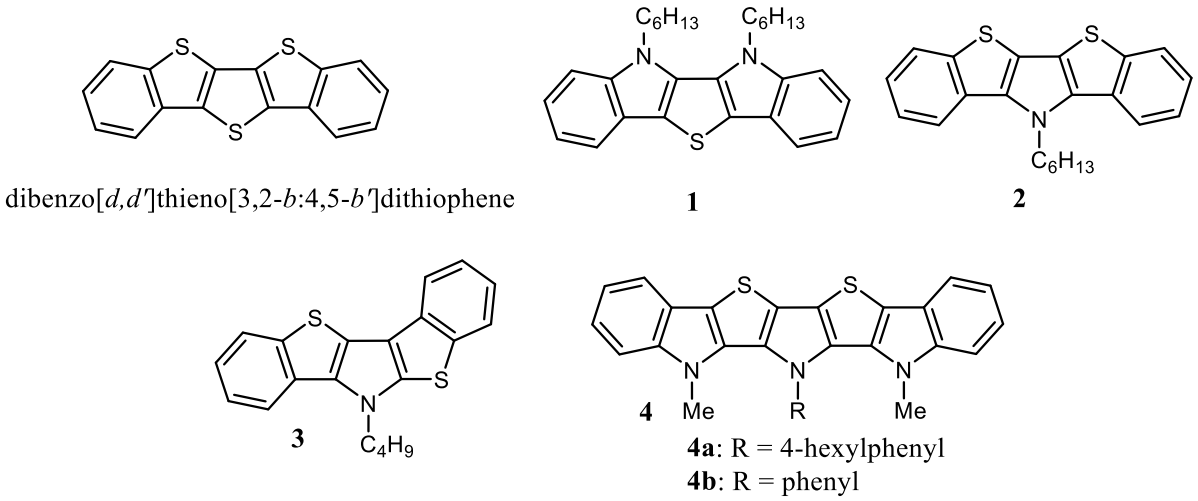


Figure 2.1. Organic semiconductors based on fused pentacenes

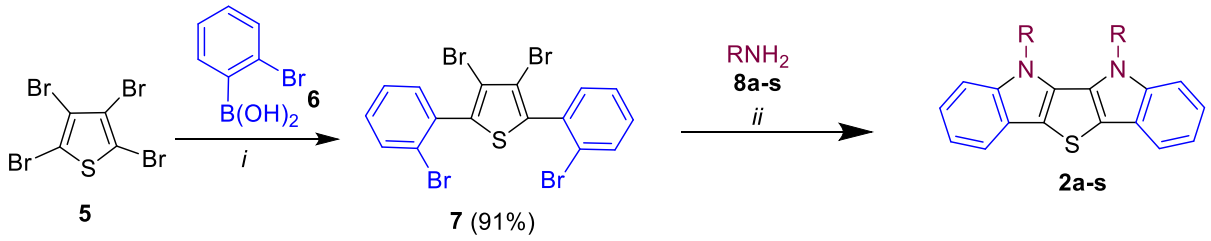
Likewise, tetracenes and their heterocyclic analogues were broadly applied in material chemistry,[56,67] but also in medicinal chemistry. In 2005, Wang *et al.* synthesized a series of estrogen receptor ligands, a benzothieno[3,2-*b*]indole scaffold, which showed a high binding affinity for estrogen receptor subtypes (ERα and ERβ) in comparison with the Raloxifene drug.[68]

Due to the interesting properties of 5,6-disubstituted thieno[3,2-*b*:4,5-*b'*]diindoles and benzothieno-[3,2-*b*]indoles in material and medicinal chemistry, I was interested in developing an independent and efficient strategy for their syntheses. In fact, current synthetic approaches are often complicated and require several steps. Recently, the group of Prof. Langer reported the synthesis of tetrasubstituted thiophenes by site-selective Suzuki-Miyaura reactions of tetrabromo-thiophene.[27,69] During my thesis, I studied a concise and efficient two-step synthesis of thieno[3,2-*b*:4,5-*b'*]diindoles and benzothieno[3,2-*b*]indoles by site-selective Suzuki-Miyaura reactions of tetrabromo-thiophene and 2,3-dibromobenzothiophene, respectively, and subsequent palladium catalyzed twofold C-N coupling[5b,12d,19c,70] with amines.[71]

2.2 Results and Discussion

The site-selective Suzuki-Miyaura reaction of tetrabromothiophene (**5**) with 2.2 equivalents of *o*-bromophenylboronic acid **6**, in the presence of 5 mol% of $Pd[PPh_3]_4$, afforded the

tetrabrominated compound **7** in 91% yield. The Pd-catalyzed two-fold cyclization reactions of **7** with amines **8a-s** gave the desired thieno[3,2-*b*:4,5-*b'*]diindoles **2a-s** (Scheme 2.1).



Scheme 2.1. Synthesis of 5,6-disubstituted thieno[3,2-*b*:4,5-*b'*]diindoles **2a-s**.

Conditions: i, 2.2 equiv. of **6**, 5 mol% of $Pd(PPh_3)_4$ catalyst, Na_2CO_3 (2 M, 10 mL), dioxane 110 °C, 6h. *ii,* 3 equiv. of **8**, 6 equiv. of NaO*t*Bu, 5 mol% of $Pd_2(dba)_3$, ligand (method A: 10 mol% of $P(tBu)_3 \cdot HBF_4$, method B: 5 mol% BINAP).

The cycliczation reaction of **7** with 4-methoxyaniline **8b** was chosen for optimizations using 1,4-dioxane as an internal standard (Table 2.1). The bidentate ligands, such as Dppe and DPEPhos, gave excellent yield of 88% and 93%, respectively (entries 10 and 11). Some bulky monodentate phosphine ligands, e. g. SPhos and $P(tBu)_3$, also exhibited suitable ligands for this reaction (entries 1-6).[15] Up to 98% yield of **2b** was achieved by employment of $P(tBu)_3$ as the ligand in combination with $Pd_2(dba)_3$ as the catalyst (method A). The yield was significant decreased when $Pd(OAc)_2$ instead of $Pd_2(dba)_3$ was used as palladium precursor

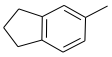
.**Table 2.1.** Optimization for the synthesis of **2b**

Entry	Catalyst	Ligand	Base	Yield (%)[a]
1	$Pd_2(dba)_3$	$P(tBu)_3 \cdot HBF_4$	NaO*t*Bu	98
2	$Pd(OAc)_2$	$P(tBu)_3 \cdot HBF_4$	NaO*t*Bu	58
3	$Pd_2(dba)_3$	$P(tBu)_3 \cdot HBF_4$	KO*t*Bu	63
4	$Pd_2(dba)_3$	$P(Cy)_3 \cdot HBF_4$	NaO*t*Bu	52
5	$Pd_2(dba)_3$	SPhos	NaO*t*Bu	92
6	$Pd_2(dba)_3$	XPhos	NaO*t*Bu	61
7	$Pd_2(dba)_3$	DavePhos	NaO*t*Bu	76
8	$Pd_2(dba)_3$	BINAP	NaO*t*Bu	12
9	$Pd_2(dba)_3$	XantPhos	NaO*t*Bu	52
10	$Pd_2(dba)_3$	DPEPhos	NaO*t*Bu	88
11	$Pd_2(dba)_3$	Dppe	NaO*t*Bu	93
12	$Pd_2(dba)_3$	Dppf	NaO*t*Bu	73

[a] *Yields were calculated by ^{1}H-NMR of the crude product using dioxane as internal standard.*

With optimized conditions in hand, I studied the scope of the cyclization reaction of **7** with different amines. The employment of various anilines afforded the corresponding products **2a-m** in good to excellent yields (Table 2.2). The method A has failed to apply with alkyl amines. Only very low yields of the desired products were obtained. With further optimization, I found that the use of the bidentate ligand BINAP allowed the synthesis of products **2n-s** in acceptable yields (method B). The structures of the products were established by spectroscopic methods. The structures of **2i**, **2k** and **2p** were independently confirmed by X-ray crystal structure analysis.

Table 2.2. Synthesis of 2a-r

2	R	Conditions	Time (hours)	Yield (%)[a]
a	Ph	A	14	83
b	4-(MeO)C_6H_4	A	14	94
c	4-MeC_6H_4	A	14	90
d	3,5-$Me_2C_6H_4$	A	14	89
e	3,5-$(MeO)_2C_6H_3$	A	14	95
f	3,4,5-$(MeO)_3C_6H_2$	A	14	92
g	4-FC_6H_4	A	14	94
h	4-ClC_6H_4	A	14	86
i	4-*t*-BuC_6H_4	A	14	86
j	3-$CF_3C_6H_4$	A	14	88
k	4-$(Et_2N)C_6H_4$	A	14	59
l		A	14	90
m	4-(MeS)C_6H_4	A	14	91
n	*n*-C_3H_7	B	14	46
o	*n*-C_5H_{11}	B	14	45
p	*n*-C_7H_{15}	B	14	44
q	$PhCH_2CH_2$	B	14	62
r	Bn	B	14	53
s	*c*-Pr	B	14	33

[a] *Isolated yields*

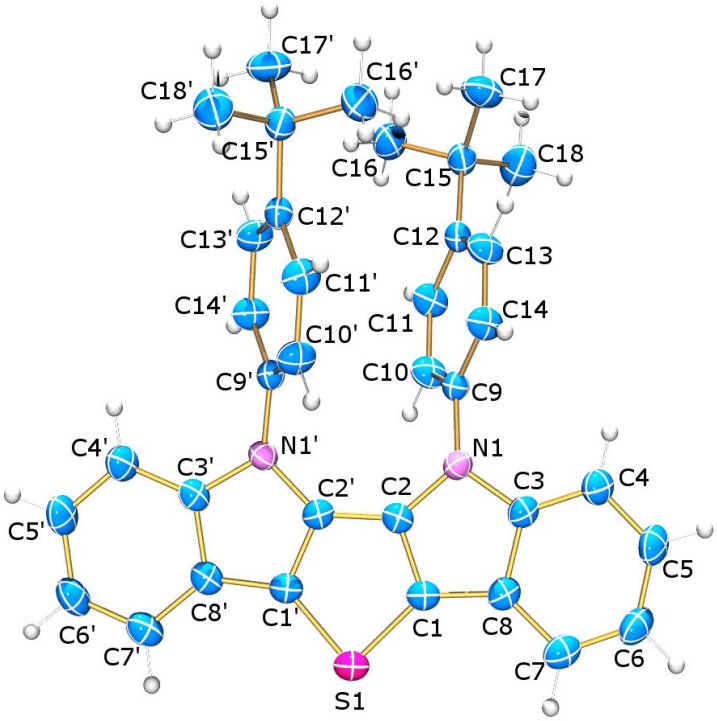


Figure 2.2. Ortep plot of 2i

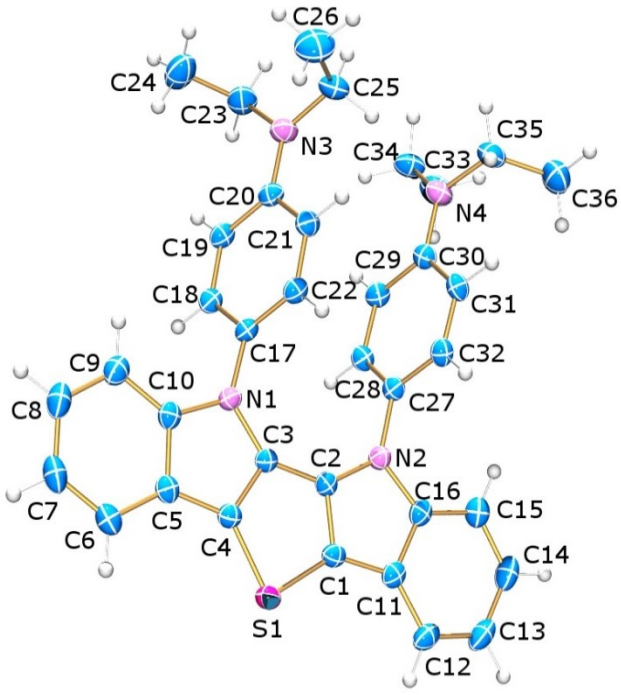


Figure 2.3. Ortep plot of 2k

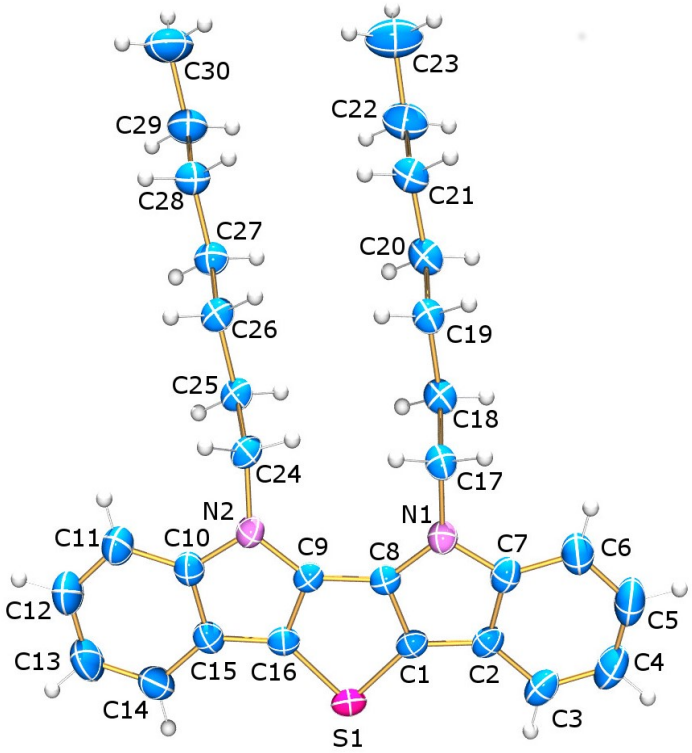
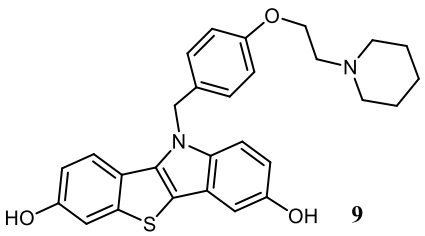


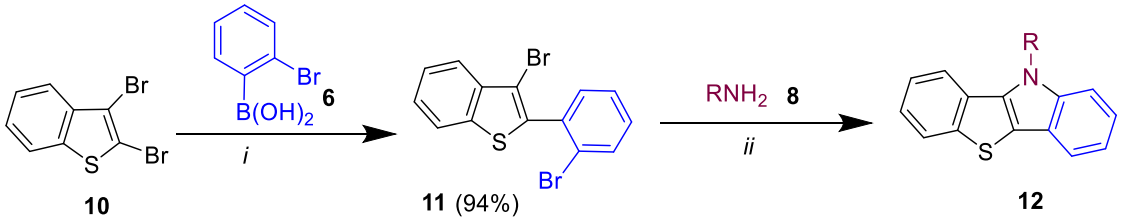
Figure 2.4. Ortep plot of 2p

Besides, benzothieno[3,2-*b*]indole **9** showed a highly binding affinity to ERα (IC_{50} = 2.84 nmol) and made a strong increase of the bone mineral density of ovariectomized mice (Figure 2.3).[68] Therefore, I applied my methodology for the synthesis of benzothieno[3,2-*b*]indoles from 2,3-dibromobenzothiophene **10**. During the preparation of this thesis, the Suzuki reaction of **10** to give **11** was reported for the synthesis of *S,P*-bridged *trans*-stilbenes.[72] The Pd-catalyzed cyclization of **11** with amines has not been reported so far. Products **12a-c** were synthesized in excellent yields using either method A or method B.



9

Figure 2.5. Potent estrogen receptor ligand 9



Scheme 2.2. Synthesis of 5,6-disubstituted thieno[3,2-*b*:4,5-*b'*]diindoles **12a-c**.

Conditions: i, 2.2 equiv. of **2**, 5 mol% of $Pd(PPh_3)_4$ catalyst, Na_2CO_3 (7 mL, 2M), dioxane, 110 °C, 6h. *ii,* 3 equiv. of **8**, 6 equiv. of NaO*t*Bu, 5 mol% of $Pd_2(dba)_3$, ligand (method A: 10 mol% of $P(tBu)_3 \cdot HBF_4$, method B: 5 mol% BINAP).

Table 2.3. Synthesis of tetracenes 12a-c

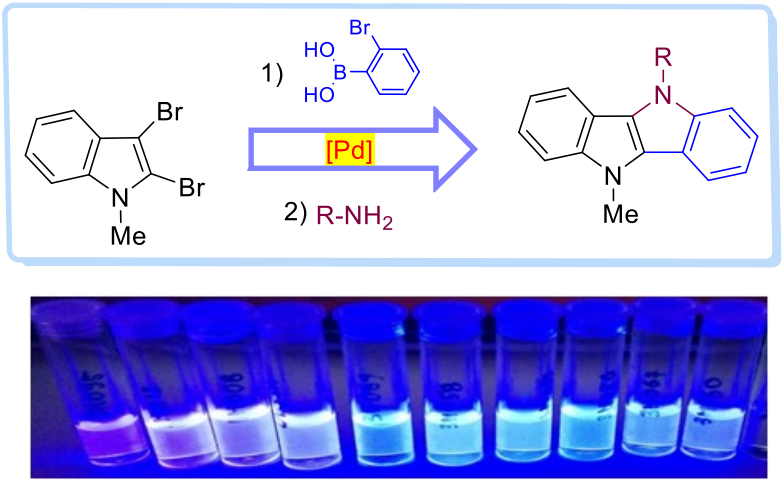
12	R	Conditions	Time (hours)	Yield (%)[a]
a	4-$MeOC_6H_4$	A	8	96
b	*n*-C_7H_{15}	B	8	92
c	Bn	B	8	95

[a] *Isolated yields*

2.3 Conclusions

I described a highly efficient and convenient procedure for the synthesis of substituted thieno[3,2-*b*:4,5-*b'*]diindoles and benzothieno[3,2-*b*]indoles based on a new two-step strategy which involves Pd-catalyzed C-C and C-N coupling reactions. These results are of considerable interest for applications in material sciences and medicinal chemistry.

3 Synthesis and physical properties of 5-methyl-5,10-dihydroindolo[3,2-*b*]indoles



3.1 Introduction

Acenes and heteroacenes are widely known for their applications in organic light-emitting diodes (OLEDs), organic field-effect transistors (OFETs) and organic photovoltaic cells.[56,73] Tetracene, which represents a *p*-type semiconductor, is one of the most studied acenes. This molecule in the form of single crystal devices possesses hole mobilities as high as 1.3 $cm^2V^{-1}s^{-1}$.[74] The introduction of heteroatoms into acenes significantly modifies the electronic properties and crystal packing of the molecules as well as improving the stability of the materials.[73a] Therefore, the preparation of new heterotetracenes are atracting much attention. In 2009, Liu and coworkers reported that tetrathienoacenes (TTAs) could be used in potential OFETs applications, due to their high hole mobilities and on/off current ratio.[75] Recently, Takimiya and co-workers prepared and investigated the synthesis and interesting electronic properties of naphthodithiophenes (NDTs) and other chalcogenotetracenes.[76] The synthesis and physical properties of a series of highly substituted benzothieno[3,2-*b*]benzothiophenes and benzoselenopheno[3,2-*b*]benzoselenophenes were reported by Takimiya's group.[77] Recently, parent 5,10-dihydroindolo[3,2-*b*]indole was found to be a promising candidate for OFET applications.[78] Functionalized 5,10-dihydroindolo[3,2-*b*]indoles are known as

important heterotetracenes which represent core building blocks in OLED polymers and high-spin organic polymers.[79]

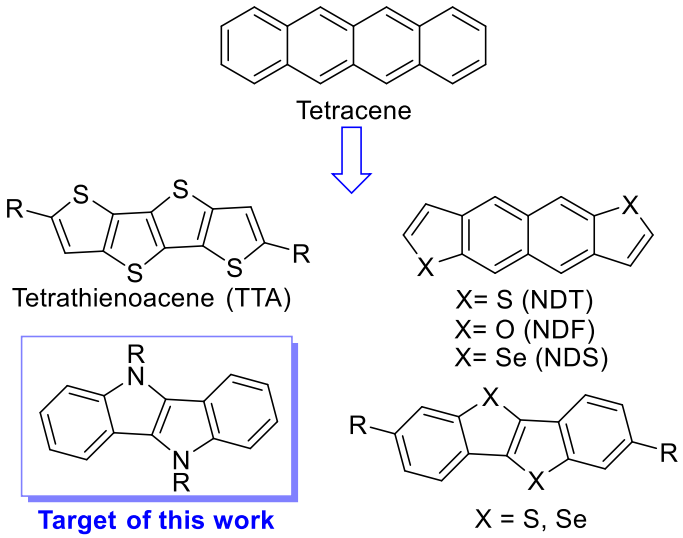


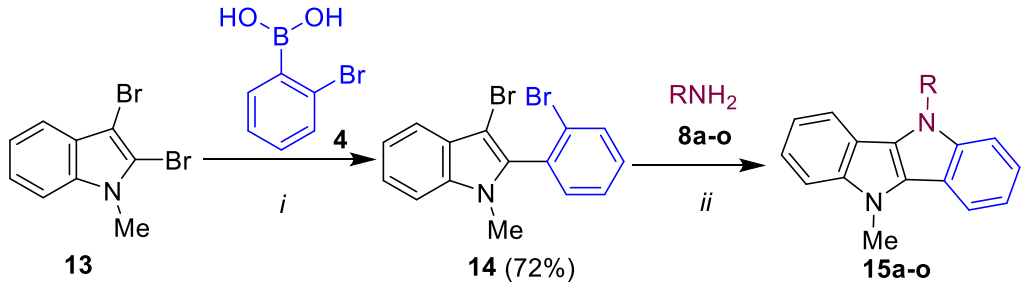
Figure 3.1. Molecular structures of tetracene and heterotetracenes for OFET applications

Several synthetic approaches to 5,10-dihydroindolo[3,2-*b*]indoles have been reported so far. Most of the conventional methods base on a C-N bond formation as the key step.[80] Heller reported the first synthesis of 5,10-dihydroindolo[3,2-*b*]indole by reduction of *o,o'*-dinitrobenzil with zinc in the present of acetic acid.[81] Reduction of 2-(*o*-nitrophenyl)indole with $P(OEt)_3$ was described to give the product in moderate yields.[82] Then, Grinyov *et al.* reported an efficient synthesis of 5,10-dihydroindolo[3,2-*b*]indoles by Fischer condensation of indolones with hydrazine derivatives.[83] Recently, Liu *et al.* reported an interesting method for the preparation of 5,10-dihydroindolo[3,2-*b*]indoles by reduction of 6,12-dichlorodibenzo[*b,f*][1,5]diazocines by using an excess of zinc under acidic conditions.[78] Generally, most of the reported syntheses of highly functionalized 5,10-dihydroindolo[3,2-*b*]indoles are difficult to perform, low yielding or require many synthetic steps. Because of their potential application of material science, I was interested in developing a new and convernient two-step strategy for the synthesis of highly functionalized 5,10-dihydroindolo[3,2-*b*]indoles. My strategy bases on the first site-selective Pd-catalyzed Suzuki-Miyaura reaction of *N*-methyl-2,3-dibromoindole and subsequent cyclization by Pd-catalyzed two-fold C-N coupling with amines. Site-selective Suzuki-Miyaura reactions of *o*-bromophenylboronic acid with several substrates, for examples 2,3-dibromopyridine, 2,3-

dibromothiophene, 2,3,5-tribromothiophene, 2,3-dibromobenzothiophene, 3'-bromo-4'-iodo-2-nitro-1,1'-biphenyl, have been previously reported.[72,84]

3.2 Result and discussion

2,3-Dibromo-*N*-methylindole **13** was prepared from *N*-methylindole in 72% yield by bromination of *N*-methylindole with bromine at -78 ºC.[85] The site-selective Suzuki-Miyaura reaction of 2,3-dibromo-*N*-methylindole **13** with *o*-bromophenylboronic acid **6** using a reported procedure of the group of Prof. Langer,[85] gave 2-aryl-3-bromoindole **14** in 72 % yield.



Scheme 3.1. Synthesis of 5,10-dihydroindolo[3,2-*b*]indoles 5a-o.

Condition: (i) 1.2 equiv. of **6**, 5 mol% of $Pd(PPh_3)_4$ catalyst, 3 equiv. of NaOH, THF, H_2O, 70 ºC, 4h. (ii) 3 equiv. of **8**, 3 equiv. of NaO*t*Bu, 5% mol of $Pd_2(dba)_3$, 10 mol% of XantPhos, toluene, 90 ºC, 6-10h.

For the optimization of this step, I chose the reaction of **14** with *p*-toluidine **8b** (Table 3.1). Some important parameters, which can affect the reaction, including ligand, palladium source, solvent and temperature, were examined. Interestingly, up to 89% yield of **15b** was achieved when XantPhos as ligand, in combination with $Pd_2(dba)_3$, was employed. The yields decreased when $Pd(OAc)_2$ was used as the palladium source and when the solvents were changed. When the temperature was decreased to 90 °C, the yield increased to 91% and the reaction mixture contained a smaller amount of side products.

Table 3.1. Optimizations for the synthesis of 15b

Entry	Catalyst	Ligand	Solvent	Temperature (ºC)	Yield (%)[a]
1	$Pd_2(dba)_3$	BINAP	Tol	100	11
2	$Pd_2(dba)_3$	XantPhos	Tol	100	89
3	$Pd_2(dba)_3$	DPEPhos	Tol	100	-
4	$Pd_2(dba)_3$	Dppe	Tol	100	7
5	$Pd_2(dba)_3$	Dppf	Tol	100	-
6	$Pd_2(dba)_3$	$PCy_3.HBF_4$	Tol	100	-
7	$Pd_2(dba)_3$	$PBu_3.HBF_4$	Tol	100	4
8	$Pd_2(dba)_3$	XPhos	Tol	100	79
9	$Pd_2(dba)_3$	XPhos.*t*Bu_2	Tol	100	-
10	$Pd_2(dba)_3$	SPhos	Tol	100	72
11	$Pd_2(dba)_3$	DavePhos	Tol	100	4
12	$Pd_2(dba)_3$	RuPhos	Tol	100	11
13	$Pd(OAc)_2$	XantPhos	Dioxane	100	57
14	$Pd_2(dba)_3$	XantPhos	DMF	100	20
15	$Pd_2(dba)_3$	XantPhos	Tol	90	91
16	$Pd_2(dba)_3$	XantPhos	Tol	80	82

[a]Yield was calculated by ^{1}H-NMR of the crude product using 4-nitroacetophenone as an internal standard

With the optimized conditions in hand, I studied the scope of the two-fold C-N coupling reaction of **14** with various aniline derivatives. The products **15a-o** were obtained in good to excellent yields with different anilines (Table 3.2). Very good yields were achieved for both aniline derivatiarves bearing electron donating and withdrawing substituents. On the other hand, the cyclization of **3** with aliphatic amines afforded lower yields (products **15j-o**, Table 3.2).

Table 3.2. Synthesis of 15a-t

15	R	Time (h)	Temperature (°C)	Yield (%)[a]
a	Ph	6	90	80
b	4-(*t*-Bu)C_6H_4	6	90	84
c	4-MeC_6H_4	6	90	81
d	4-FC_6H_4	6	90	82
e	3-(CF_3)C_6H_4	6	90	84
f	4-(MeO)C_6H_4	6	90	76
g	4-(MeS)C_6H_4	6	90	83
h	(4-CN)C_6H_4	6	90	82
i	*n*-C_3H_7	10	90	86
j	Allyl	10	90	84
k	Bn	10	90	72
l	4-(MeO)$C_6H_4CH_2$	10	90	79
m	(4-FC_6H_4)CH_2	10	80	64
n	3-(CF_3)$C_6H_4CH_2$	10	80	60
o	$PhCH_2CH_2$	10	90	83

[a]Yield of isolated products

The structures of products **15a-o** were determined by spectroscopic methods. The structure of **15b** was independently confirmed by X-ray crystal structure analysis (Figure 3.2). As expected, the heterocyclic core structure is planar. The aryl group is twisted out of plane.

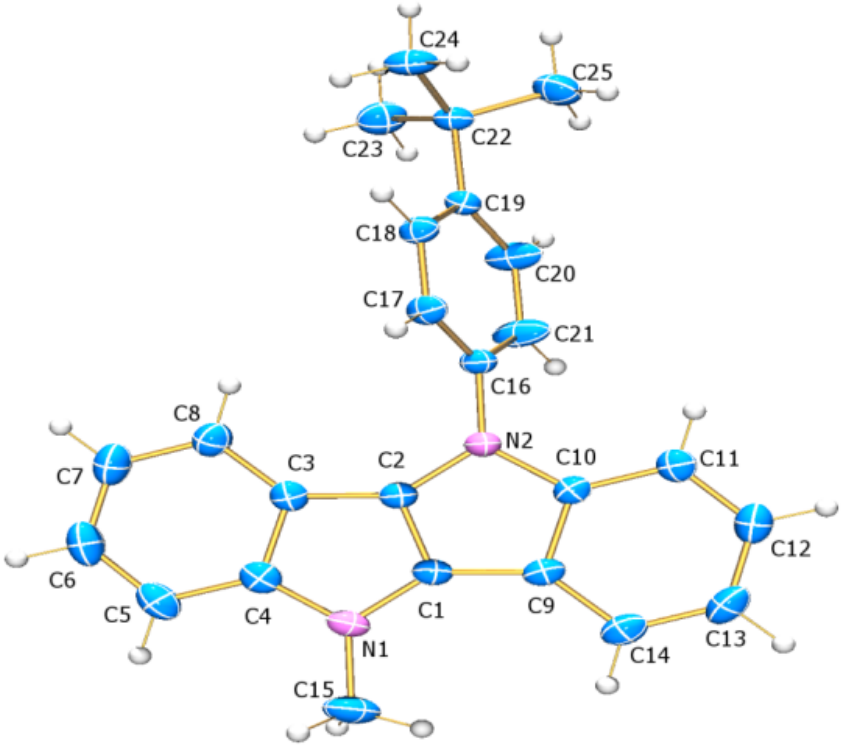


Figure 3.2. Ortep plot of 15b

3.3 Absorption and Fluorescence Properties

Some selected 5,10-dihydroindolo[3,2-*b*]indoles **15** which bear different types of substituents located at the nitrogen atom, were investigated by UV-VIS and fluorescence analysis. The measurements were performed in acetonitrile as shown in Figure 3.3. The corresponding spectral data are summarized in Table 3.3. The UV-VIS absorption spectra of the compounds show three absorption bands around 361, 351, 324, and 261 nm with increasing absorption strength. The spectra of all derivatives **15** are quite similar indicating that the substituent located at the nitrogen atom has only a weak influence. Due to the conjugative effect, the bands of derivative **15i** shift a little to the longer wavelenghs. Derivative **15a**, containing a phenyl group at N-position, exhibits a small blue-shift.

Table 3.3. Spectroscopic data characterizing the absorption and emission properties of **15**

Comp.	λ_{1abs}^{max} [nm]	Logε λ_{1abs}^{max}	λ_{2abs}^{max} [nm]	Logε λ_{2abs}^{max}	λ_{3abs}^{max} [nm]	Logε λ_{3abs}^{max}	λ_{4abs}^{max} [nm]	Logε λ_{4abs}^{max}
15a	361	4.49	349	4.51	324	4.86	260	5.23
15b	363	3.56	351	3.57	324	3.93	260	4.33
15d	362	3.34	351	3.35	324	3.73	261	4.15
15f	363	3.65	352	3.64	324	4.02	261	4.47
15g	363	3.43	351	4.05	323	4.08	259	3.62
15i	365	3.34	354	3.35	325	3.83	263	3.28
15j	363	3.41	351	3.42	325	3.89	262	4.33
15k	363	3.24	351	4.10	323	4.10	259	4.02
15l	362	4.29	351	4.28	325	4.75	262	5.18
15m	363	3.49	351	3.53	325	4.02	262	3.57

The fluorescence spectra were again measured in actonitrile with excitation at 340 nm. The fluorescence quantum yields were determined by comparison to the standard quinine hemisulfate salt monohydrate (in 0.05M H_2SO_4) which exhibits a fluorescence yield of 52%.[86] All emission spectra have their maximum around 400 nm and exhibit a shoulder at around 363 nm. Derivatives **15a** and **15b** containing an aromatic substituent located at the nitrogen atom exhibit the most blue-shifted emission with a maximum at 398 nm, while **15l,** containing a 4-methoxybenzyl group, exhibits a slight red-shift (404 nm). The Stokes shift is similar for all compounds and varies only in the range of 19 nm and 25 nm. It is important to note that the quantum yields of the 5,10-dihydroindolo[3,2-*b*]indoles **15** are quite high. The highest quantum yield (47%) was observed for **15m**.

The band gaps, determined from the crossing of the absorption and fluorescence spectra, vary again only slightly among the studied compounds. Derivative **15a,** containing a phenyl group, has the largest band gap of 3.344 eV, while the smallest band gap of 3.313 eV is observed for **15l** which contains a 4-methoxybenzyl group as the substituent.

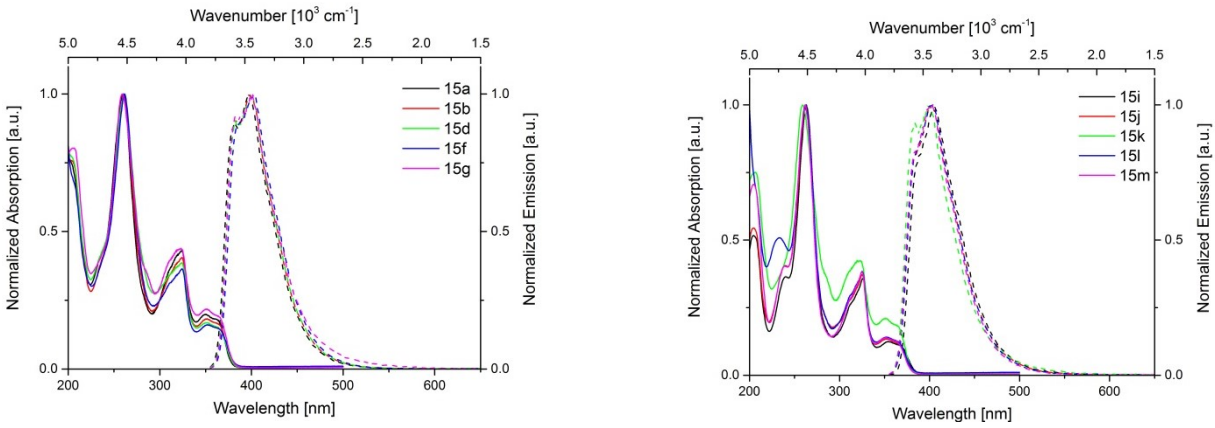


Figure 3.3. Normalized absorption and emission spectra of selected compounds **15** measured in acetonitrile. Emission spectra were recorded with excitation at 340 nm.

Table 3.4. Spectroscopic data characterizing the absorption and emission properties of **15**

Comp.	λ_{1abs}^{max} [nm]	λ_{1em}^{max} [nm]	λ_{2em}^{max} [nm]	Stokes shift [nm]	λ_{00}[a] [nm]	Band gaps[b] (eV)	ϕ_{fluo} Quantum yield
15a	361	382	398	21	370.8	3.344	46%
15b	363	383	398	20	372.6	3.328	46%
15d	362	382	400	20	372.6	3.328	44%
15f	363	387	403	24	374.0	3.315	43%
15g	363	382	399	19	372.8	3.326	30%
15i	365	388	403	23	377.0	3.289	41%
15j	363	385	400	22	374.0	3.315	42%
15k	363	383	399	20	372.6	3.328	31%
15l	362	387	404	25	374.2	3.313	43%
15m	363	386	403	23	373.4	3.320	47%

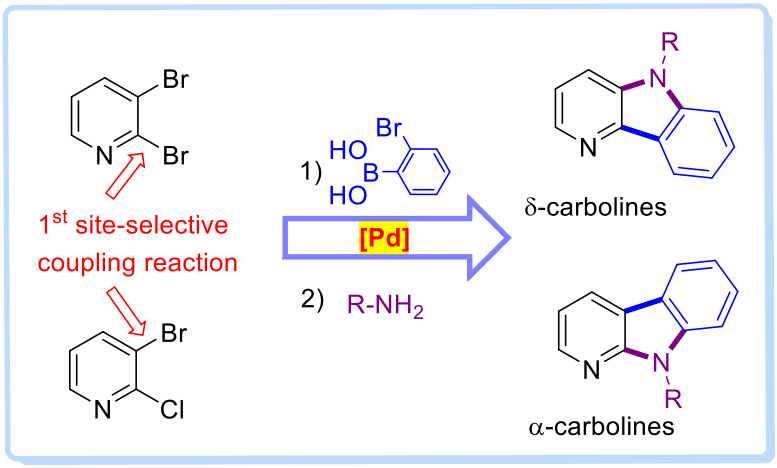
[a] *λ_{00} is determined from the crossing point of the normalized absorption and emission spectra.*[87]

[b] *optical band gaps were calculated from λ_{00}.* [87]

3.4 Conclusions

In conclusion, I reported a concise, practical and efficient strategy to prepare highly functionalized 5,10-dihydroindolo[3,2-*b*]indoles in very good yields. The reactions proceeded with very good site-selectivity in favour of positions 2 and 6. The site-selectivity of the reaction of the 2-bromophenylboronic acid with *N*-methyl-2,3-dibromoindole can be explained by the fact that position 2 is less electron rich than position 3. It has been previously reported that the oxidative addition of Pd(0) catalysed cross-coupling reactions of polyhalogenated substrates proceed by predominant attack at the more electron poor position.[88] Absorption and fluorescence properties of the 5,10-dihydroindolo[3,2-*b*]indoles were studied. Although the substituents have only a small influence on the absorption and fluorescence, very good quantum yields were generally observed.

4 Synthesis of α- and δ-carbolines



4.1 Introduction

Carbolines (pyridoindoles) are widely spread in many natural products and synthetic bioactive molecules.[89] Among the class of carbolines, especially *β*-carbolines and *γ*-carbolines are the most present in nature. A smaller number of *α*-carbolines were also isolated as natural alkaloids. Examples of *α*-carbolines include Grossularine 1 and 2, anticancer compounds isolated from *Dendrodoa grossularia*,[90] and Mescengricin which exhibit an inhibitor of *L*-glutamate excitotoxicity isolated from *Streptomyces griseoflavu*.[91] A few researches reported on *δ*-carbolines, such as Quindoline, Cryptolepine, Cryptoquindoline, Cryptomisrine and Jusbetonin.[92] All of these alkaloids were isolated from *Cryptolepis sanguinolenta* and *Justica bentonica* which have been traditionally used for the treatment of malaria and several infectious diseases in Central and West Africa.[93] Previous researches in medicinal chemistry demonstrated that *α*- and *δ*-carboline derivatives possessed important biological properties, such as antitumor,[94] antimalarial,[95] antimicrobial,[96] antiviral,[97] and anti-inflammatory[98] activities. In the context of drug discovery, Implitapide, a potential drug containing an *α*-carboline moiety, was used for the treatment of atherosclerosis in clinical trials.[99]

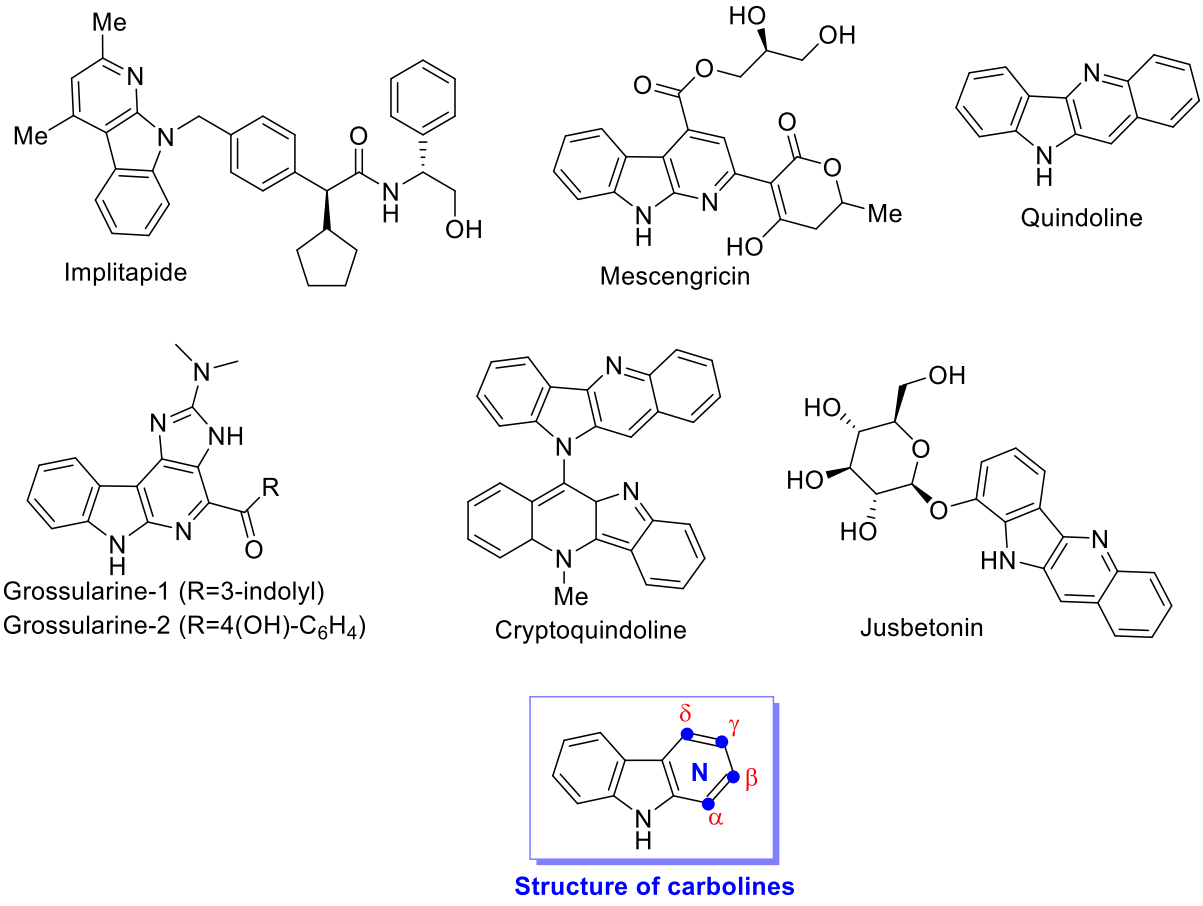


Figure 4.1. Some bioactive compounds containing α- and δ-carboline substructures.

Current research indicates that carbolines not only play an important role in many applications in medicinal chemistry, but also in material sciences. For example, carbolines and their derivatives were commonly employed as electron transport unit in bipolar host materials.[100] The introduction of a carboline unit instead of the carbazole improved the electron carrier mobility.[100] In 2013, **CzBPCb** and **CbBPCb**, which were synthesized by Lee *et al.,* reached above 30% external quantum efficiency in blue phosphorescence organic light emitting diodes.[101] The trimer **TATA** exhibited a 200 times longer life-time than the analogue carrying three carbazole units.[102]

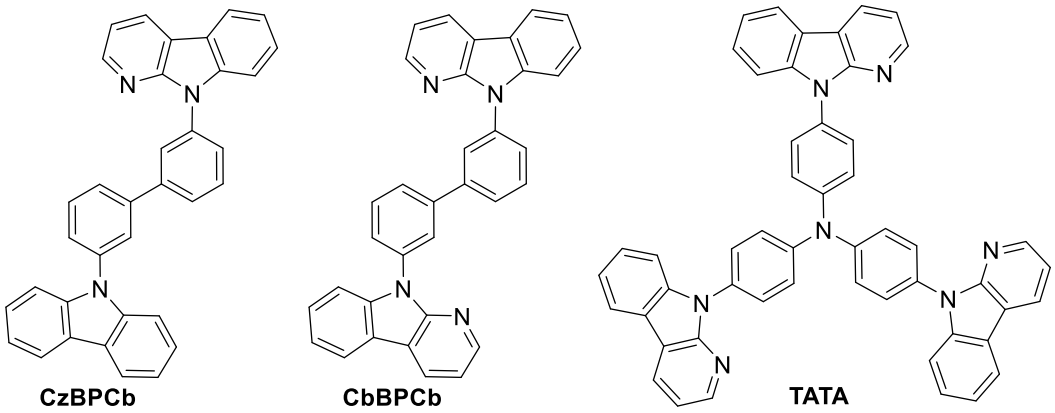


Figure 4.2. Some organic materials contain α-carbolines structure.

Due to the importance of carbolines in both medicinal chemistry and material sciences, the synthesis of carbolines has been attracted much attention in developing new synthetic methodologies. α-Carbolines were synthesized by various classic methods, including intramolecular Diels-Alder reactions,[103] Graebe-Ullmann reactions of triazoles,[104] annulations of azaindoles[105] and multi-component reactions.[106] In 2011, Kumar and Nagarajan prepared α-carbolines via two-step Pd-catalyzed amidation of 3-acetyl-2-chloroindoles followed by a Vilsmeier-Haack reaction.[107] Recently, several syntheses of carbolines in one-pot procedures based on Pd-catalyzed aryl aminations and subsequent intramolecular arylations were reported.[108] In 2013, Moody *et al.* developed a new method for the synthesis of α-carbolines by 6π-electrocyclizations of indole-3-alkenyl oximes.[109] Very recently, Yang *et al.* described a convenient approach to α-carbolines by a one-pot tandem reaction of α,β-unsaturated ketones with 2-nitrophenylacetonitriles in the presence of zinc dust.[110]

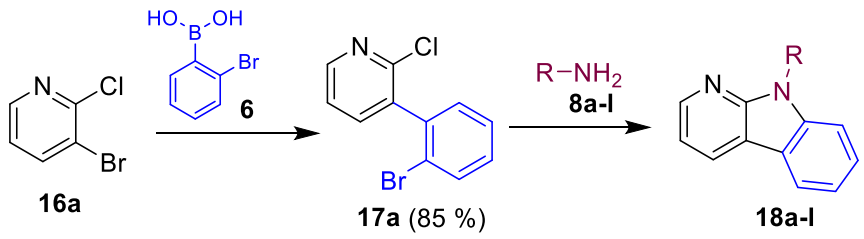
In contrast to α-, β-, and γ-carbolines, only a few procedures for the synthesis of δ-carbolines have been developed so far. In 1997, Yang *et al.* synthesized δ-carboline derivatives from α-(*o*-bromoanilino)alkenenitriles by domino Pd-catalyzed cyclizations.[111] Dupas *et al.* successfully synthesized 3,4-disubtituted δ-carbolines by cyclizations of indole amines with 1,3-dicarbonyl compounds.[112] In the effort to synthesize bioactive analogues of Eudistomin D, Kobayashi and coworkers developed the photocyclizations of *N*-(4-methoxy-3,5-dimethylphenyl)pyridin-3-amine which gave mixtures of regioisomeric β- and δ–carbolines.[113] In 2011, Ablordeppey *et al.* described a short pathway for the formation of δ-

carboline derivatives in moderate yields by another Pd-catalyzed intramolecular arylation of *N*-aryl-3-aminopyridine.[114] Recently, Kundu *et al.* synthesized δ-carbolines in good yields by an efficient one-pot multicomponent reation using *N*-Boc-3-amido indoles, aryl aldehydes and terminal alkynes under microwave conditions.[115] δ-Carbolines could also be prepared by intramolecular reductive ring closure of 3-nitro-2-phenylpyridines using phosphine reagents.[116] In 2012, the group of Detert synthesized δ-carboline in 6 steps starting from 2-chloro-3-nitropyridine.[117] Very recently, Cao *et al.* reported an interesting synthesis of δ-carbolines by a Pd-catalyzed cascade reaction of 2-iodoanilines and *N*-tosyl-enynamines.[118] Although, all four types of carbolines can be prepared by general methods, but these methods still have limitations in the preparation of starting materials and the tolerance of substrates scope. Sakamoto and coworkers firstly reported a very convenient and general method to access all four regioisomeric carbolines in 31-61% yield by Pd-catalyzed intramolecular arylation of *ortho*-bromo-substituted anilinopyridines.[119] Recently, Cuny and coworkers describe a general method for the selective synthesis of α-, β-, γ-, and δ–carbolines in good yields employing photostimulated cyclization of anilinohalopyridines.[120]

In fact, the current synthetic methods are often complicated, low yielding or require many synthetic steps to prepare the starting materials. During my thesis, I studied a new and efficient two-step strategy for the chemoselective synthesis of α- and δ- carbolines from readily available starting materials. My synthesis is based on what are, to the best of my knowledge, the first site-selective Suzuki reactions of *o*-bromophenylboronic acid with 2,3-dihalopyridines (1-chloro-2-bromopyridine or 2,3-dibromopyridine) and subsequent two-fold C-N coupling reactions.

4.2 Results and discussion

The chemoselective Suzuki-Miyaura reaction of commercially available 2-chloro-3-bromopyridine **16a** with 1.2 equivalents of *o*-bromophenylboronic acid **6** in the presence of 5% mol of $Pd(PPh_3)_4$ as catalyst afforded product **17a** in 85% isolated yield. The reaction proceeded chemoselectively at position 3 of bromide atom which is a better leaving group than chloride. The subsequent cyclization of **17a** with different amines **4**, by two-fold Pd-catalyzed C-N coupling, resulted in the formation of the desired α- carbolines **18** (Scheme 4.1).



Scheme 4.1. Synthesis of of α-carbolines.

Conditions: (*i*) 1.2 equiv. of **6**, 5.0 mol% of $Pd(PPh_3)_4$ catalyst, 3 equiv. of NaOH, THF, H_2O, 70 ºC, 4h. (*ii*) 1.5 equiv. of **8**, 3 equiv. of NaO*t*-Bu, 5 mol% of $Pd_2(dba)_3$, ligand (method A: 10% of Dppf, method B: 10% of DPEPhos), toluene, 100 ºC, 7h.

The cyclization of **17a** with *tert*-butylaniline **8c** was chosen for optimizations using 4-nitroacetophenone as an internal standard (Table 4.1). Important factors including palladium source, ligand, solvent and temperature were examined in detail. The screening of different monodentate phosphine ligands, for example, XPhos, XPhos(tBu)$_2$, SPhos, DavePhos, PCy_3, P(tBu)$_3$ gave **18c** in up to 93% yield (Entries 6-11). In order to investigate the effect of bidentate ligands in this cyclization, I carried out some further optimizations using bidentate phosphine ligands, such as XantPhos, DPEPhos and Dppf. Under optimized condition, using Dppf as ligand in combination with Pd_2dba_3 (method A), afforded up to 97% yield. The replacement of $Pd(OAc)_2$ as palladium precursor resulted in a lower yield (85%). During the optimizations, toluene was the most suitable solvent for this cyclization.

Table 4.1. Optimizations for the synthesis of 18c

Entry	Catalyst	Ligand	Solvent	Time (h)	Temperature (ºC)	Yield (%)[a]
1	$Pd_2(dba)_3$	BINAP	Tol	7	100	56
2	$Pd_2(dba)_3$	XantPhos	Tol	7	100	93
3	$Pd_2(dba)_3$	DPEPhos	Tol	7	100	95
4	$Pd_2(dba)_3$	Dppe	Tol	7	100	81
5	$Pd_2(dba)_3$	Dppf	Tol	7	100	97
6	$Pd_2(dba)_3$	$PCy_3 \cdot HBF_4$	Tol	7	100	64
7	$Pd_2(dba)_3$	$P(t\text{-}Bu)_3 \cdot HBF_4$	Tol	7	100	79
8	$Pd_2(dba)_3$	XPhos	Tol	7	100	87
9	$Pd_2(dba)_3$	XPhos·tBu$_2$	Tol	7	100	35
10	$Pd_2(dba)_3$	SPhos	Tol	7	100	93
11	$Pd_2(dba)_3$	DavePhos	Tol	7	100	88
12	$Pd(OAc)_2$	Dppf	Tol	7	100	85[b]
13	$Pd_2(dba)_3$	Dppf	Dioxane	7	100	87
14	$Pd_2(dba)_3$	Dppf	DMF	7	100	53
15	$Pd_2(dba)_3$	Dppf	Tol	7	110	82
16	$Pd_2(dba)_3$	Dppf	Tol	7	80	77

[a] Yield was calculated by ^{1}H-NMR of crude product using 4-nitroacetophenone as an internal standard. [b] 10 mol% of $Pd(OAc)_2$ was used.

With the optimized conditions in hand (method A), I was interested in extending the substrates scope of the cyclization of **17a** with a various amines. The cyclization products **18a-h**, depicted in Table 4.2, were isolated in 83-98% yields. The reaction showed compatibility with a variety of functional groups. All the products were proven by spectroscopic method. The structure of **18d** was independently confirmed by single-crystal X-ray diffraction (Figure 4.3).[121] Unfortunately, the Pd-catalyzed cyclization of **17a** with aliphatic amines using method A resulted in unsatisfactory yields, due to the formation of side products. After some optimization studies, using different conditions, I found that the employment of the DPEPhos as the ligand (method B) allowed improvement the yield. Up to 90% isolated yields of the cyclization products were achieved (products **18i-l**).

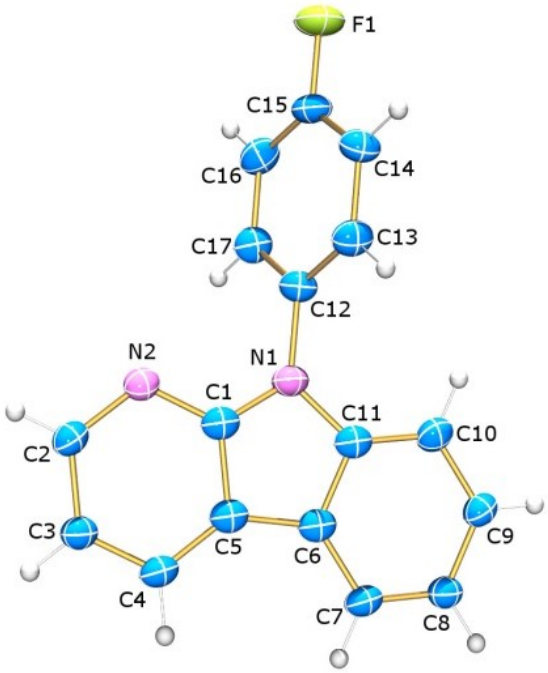


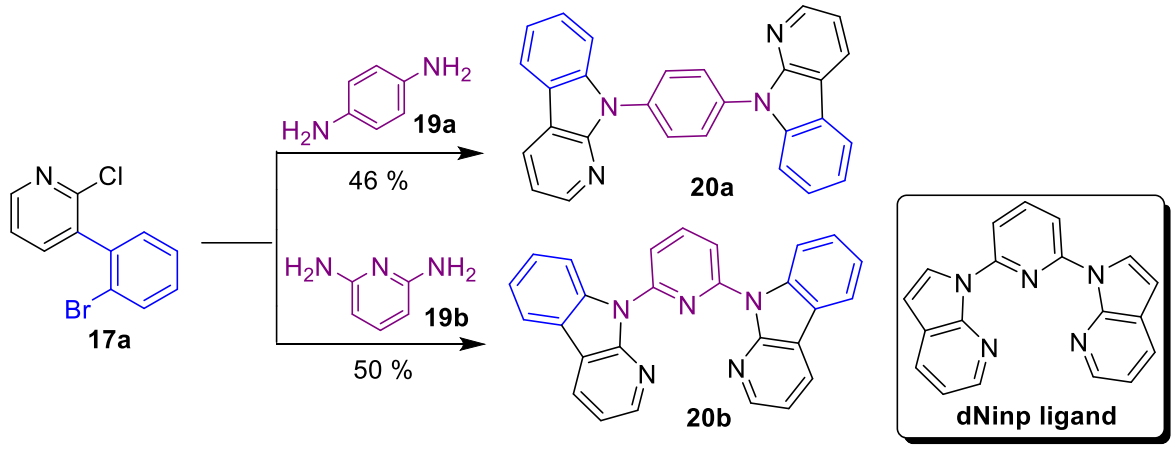
Figure 4.3. Ortep plot of 18d

Table 4.2. Synthesis of α-carbolines 18a-l

18	R	Method [a]	Yield (%)[a]
a	Ph	A	92
b	4-MeC_6H_4	A	95
c	4-(t-Bu)C_6H_4	A	94
d	4-FC_6H_4	A	89
e	3-(CF_3)C_6H_4	A	88
f	4-(MeO)C_6H_4	A	98
g	4-(MeS)C_6H_4	A	92
h	4-(CN)C_6H_4	A	83
i	Bn	B	88
j	(4-FC_6H_4)CH_2	B	87
k	3-(CF_3)$C_6H_4CH_2$	B	90
l	n-C_3H_7	B	91

[a] Isolated yields

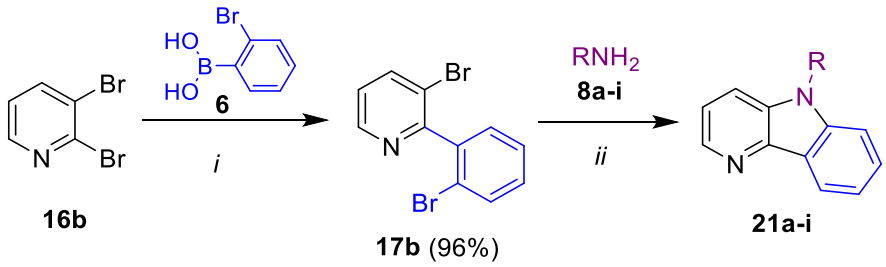
With an optimal procedure in hand, I was interested to extending the synthesis to bis(carbolines). Products **20a** and **20b** were prepared in 46 and 50% yields, respectively, by the Pd-catalyzed cyclization of **17a** with diamines **19a** and **19b**. It is noteworthy that product **20b** represents an analogue of the recently developed dNinp ligand.[33] Thus, my method allows for a convenient access to this type of molecule.



Scheme 4.2. Synthesis of bis(carbolines) 20a,b.

Conditions: 2.2 equiv. of **17a**, 1 equiv. of **19a (19b)**, 6 equiv. of NaO*t*Bu, 5% mol of $Pd_2(dba)_3$, 10% of Dppf, toluene, 110 ºC, 10h.

My next goal was to apply my methodology to the synthesis of δ-carbolines. The Suzuki-Miyaura coupling of *o*-bromophenylboronic acid **6** with 2,3-dibromopyridine **16b** proceeded, following my optimized procedure, with very good regioselectivity at the more electron-deficient 2-position of the pyridine ring and afforded product **17b** in 96% isolated yield. With intermediate **17b** in hand, I prepared a series of δ-carbolines **21a-j,** using either method A or method B, in moderate to excellent yields. The yields were moderate in case of less nucleophilic amines carrying an electron withdrawing substituent located at the aryl group. The structure of **21b** was independently confirmed by X-ray crystal structure analysis (Figure 4.4).[122]



Scheme 4.3. Synthesis of δ-carbolines 21a-i

Conditions: (*i*) 1.2 equiv. of **6**, 5% of $Pd(PPh_3)_4$ catalyst, 3 equiv. of NaOH, THF, H_2O, 70 ºC, 4h. (*ii*) 3 equiv. of **8**, 6 equiv. of NaO*t*Bu, 5% mol of $Pd_2(dba)_3$, ligand (method A: 10 mol% of Dppf, method B: 10 mol% of DPEPhos), toluene, 100 ºC, 7h.

Table 4.3. Synthesis of δ-carbolines **21a-i**

21	R	Conditions	Yield (%)
a	Ph	A	83
b	4-FC_6H_4	A	73
c	3-$(F_3C)C_6H_4$	A	64
d	4-$(MeO)C_6H_4$	A	94
e	3,5-$(MeO)_2C_6H_4$	A	75
f	4-$(NC)C_6H_4$	B	42
g	Bn	B	92
h	4-$(MeO)C_6H_4CH_2$	B	65
i	$PhCH_2CH_2$	B	77

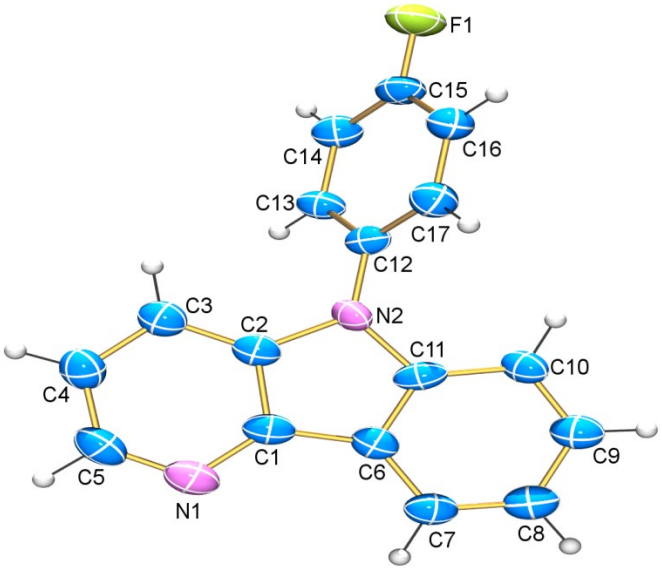
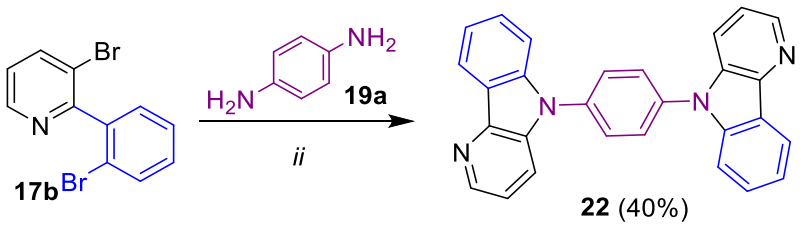


Figure 4.4. Ortep plot of 21b.

The bis(carboline) **22** was synthesized in 40% isolated yield by the cyclization of **17b** with diamine **19a** (Scheme 4.4).



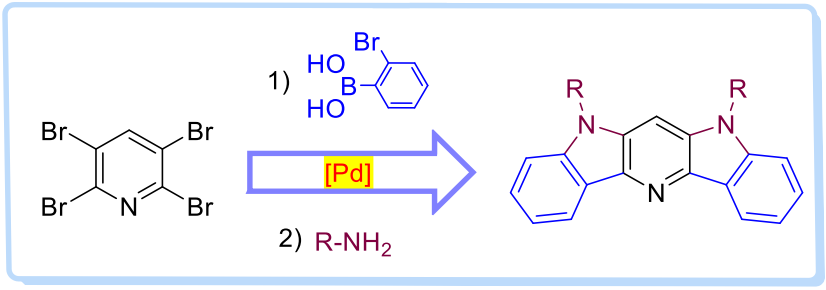
Scheme 4.4. Synthesis of bis(carboline) 22.

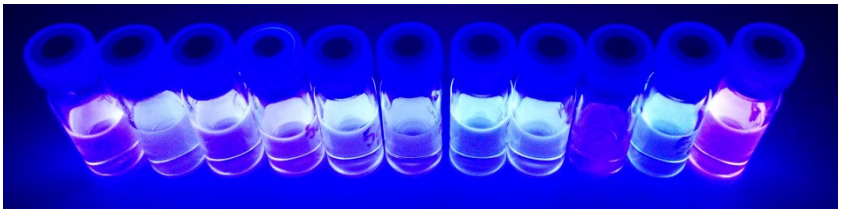
Condition: 2.5 equiv. of **17b**, 1 equiv. of **19a**, 6 equiv. of NaO*t*Bu, 5% mol of $Pd_2(dba)_3$, 10% of Dppf, toluene, 100 ºC, 10h.

4.3 Conclusion

In conclusion, I have successfully developed an efficient two-step synthesis of α- and δ-carbolines from readily available chemicals. The success of syntheses bases on site-selective Suzuki-Miyaura reaction and subsequent two-fold C-N coupling reactions. My results would be interesting for further applications in both medicinal chemistry and materials science.

5 Synthesis and physical properties of 5,7-Dihydropyrido[3,2-*b*:5,6-*b'*]diindoles



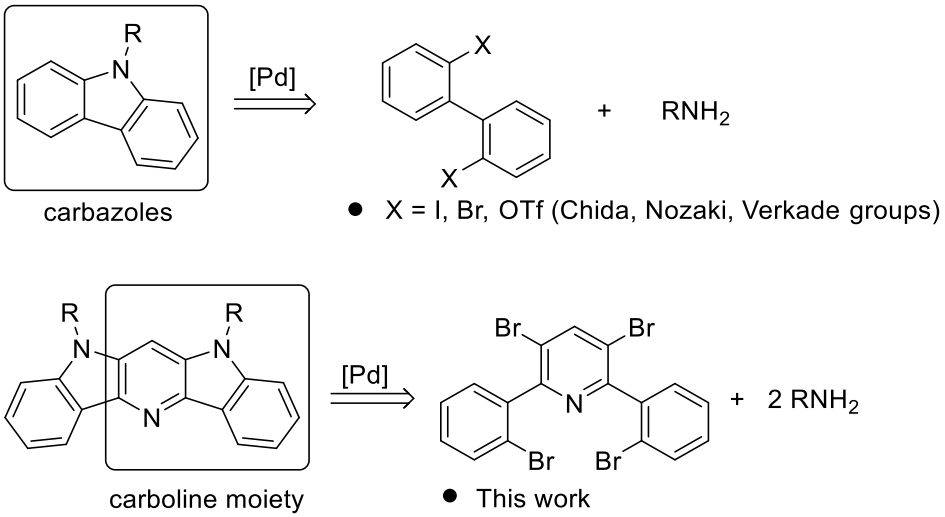


5.1 Introduction

Carbolines (pyridoindoles) and their derivatives are employed as electronic transport units in host materials.[100,102,123] The replacement of the carbazole unit by a carboline improves the electron mobility. The carbazole ring is assumed to accelerate the electron-accepting properties owing to its electron deficient ring system. [100b,c,101-102] The high quantum efficiency was achieved by the combination of the carbazole and carboline unit which improves the triplet energy. The materials containing carboline moieties have been studied for the development of novel bipolar host materials. In 2013, Lee *et al.* prepared bi- and triphenyl derivatives which contain carbazole and carboline moieties (via the nitrogen atom). These compounds exhibit 30% external quantum efficiency and high triplet energy (2.90 eV) in blue phosphorescence organic light emitting diodes.[100b,101] Kwon *et al.* reported the synthesis of the novel compounds, containing three *α*-carbolinyl substituents attached to a triphenylamine moiety, which show a longer life-time than related derivatives containing three carbazole moieties.[102] Recently, Lee *et al.* demonstrated that related *α*- and *β*-carbolines possess a higher quantum efficiency and a higher triplet energy than isomeric *γ*-carbolines.[100d] The quantum efficiency are up to 22.1 %.[100a]

The organic materials containing acenes and heteroacenes have found many applications in organic photovoltaic cells,[73b] light-emitting diodes (OLEDs),[56a] and especially in organic field-effect transitors (OFETs) due to their optical properties.[56b,73a,124] In this context, pentacene and its heterocyclic derivatives atracted much attention in current research, due to their excellent charge mobility. In fact, pentacene-based OFETs exhibit very high charge mobilities in the range of 5-40 $cm^2/(Vs)$.[73a] However, pentacene derivatives are easily oxidized by air,[124] which limits their practical applications. The replacement of heteroatoms in pentacenes results in tuning the electronic properties like solubility, stability and molecular packing.[56b,73a,124] For example, indolocarbazoles,[60] pentathienoacenes,[62] dibenzothienopyrroles,[66a] tetraazapentacenes,[125] *N*-heteropentacenes,[56b,73a,124] and thiophene-benzene annulated pentacenes[56b,63,73a,124] offer excellent OFET properties.

Due to the importance of both *N*-heteropentacenes and carbolines in the field of organic materials, I was interested in developing a novel class of *N*-heteropentacenes (5,7-dihydropyrido[3,2-*b*:5,6-*b'*]diindoles) which combine the core structures of indoles and *δ*-carbolines. My approach to 5,7-dihydropyrido[3,2-*b*:5,6-*b'*]diindoles relies on the Pd-catalyzed two-fold C-N coupling of 3,5-dibromo-2,6-bis(2-bromophenyl)pyridine with 2 equivalents of corresponding amines. Groups of Nozaki, Chida and Verkade published the preparation of carbazoles from 2,2'-dihalobiphenyl derivatives and amines (Scheme 5.1).[126] My work herein based on the first site-selective Suzuki reaction of 2,3,5,6-tetrabromopyridine with *ortho*-(bromophenyl)boronic acid and subsequent cyclization by two-fold palladium catalyzed C-N coupling which is, to the best of my knowledge, not reported so far. The products show excellent fluorescence properties with good quantum yields. The photophysical and electronic properties were studied in detail experimentally and theoretically by DFT calculations.

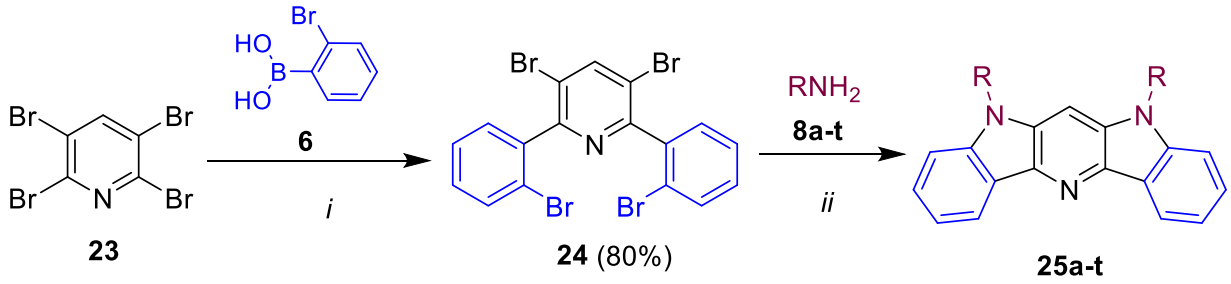


Scheme 5.1. Retrosynthetic analysis of 5,7-dihydropyrido[3,2-*b*:5,6-*b′*]diindoles

The 5,7-dihydropyrido[3,2-b:5,6-*b′*]diindole core structure is rather new. To the best of my knowledge, only the *N*-hydrogen substituted parent molecule, 5,7-dihydropyrido[3,2-b:5,6-*b′*]diindoles, has been reported so far. The compounds were published in a patent in Korean language using a different and more complicated synthetic methodology.[127] However, compound characterization, details of the synthesis and the physical properties were not provided in the patent which is, therefore, of limited utility for the chemical community.

5.2 Result and discussion

2,3,5,6-Tetrabromopyridine (**23**) was synthesized from 2,6-diaminopyridine according to Flower's procedure. [128] The site-selective Suzuki-Miyaura reaction of 2,3,5,6-tetrabromopyridine with 2.2 equivalents of *o*-bromophenylboronic acid **6,** using 5% mol $Pd(PPh_3)_4$ as catalyst, gave adduct **24** in 80% isolated yield. The site-selectivity of the reaction is excellent. The twofold C-N coupling cyclization of **24** with different amines **8a-t** afforded the desired 5,7-dihydropyrido[3,2-*b*:5,6-*b′*]diindoles in good to excellent yields (Scheme 5.2).



Scheme 5.2. Synthesis of 5,7-disubstituted 5,7-dihydropyrido[3,2-b:5,6-*b*′]diindoles **25a-t**.

Conditions: (i) 2.2 equiv. of **6**, 5% of $Pd(PPh_3)_4$, 3 equiv. of NaOH, THF, H_2O, 70 ºC, 4 h. (ii) 3 equiv. of **8**, 6 equiv. of NaO*t*Bu, 5% mol of $Pd_2(dba)_3$, ligand (method A: 10% of Dppf, method B: 10% of DPEPhos), toluene, 100 ºC, 7h.

The conditions of the annulation reaction of **24** with *tert*-butylaniline **8c** were optimized (Table 5.1). The ligand, palladium precursor, solvent and temperature were examined. The monodentate phosphine ligands, such as XPhos, XPhos·tBu$_2$, SPhos, DavePhos, RuPhos, $PCy_3 \cdot HBF_4$, or $P(t\text{Bu})_3 \cdot HBF_4$ afforded **25c** in unsatisfactory yields. The optimization indicated that the employment of bidentate phosphine ligands, such as BINAP, XantPhos, DPEPhos, Dppe, or Dppf, give significantly improved yields. The bidentate ligands with bite angles higher than 90º gave the best yields. For example, when Dppf was employed as the ligand in combination with Pd_2dba_3 (method A), product **25c** was isolated in up to 90% yield. The change to $Pd(OAc)_2$ as the palladium source resulted in lower yields. Toluene was demonstrated to be the best solvent. The success of BINAP, XantPhos, DPEPhos, Dppe or Dppf can be assumed by their rigid structure and their bidentate character[129] and the influence of diphosphane back-bonding.[130] The dissociation of one P-Pd bond (arm-off mechanism) has been previously reported which leads to an acceleration of the reductive elimination with respect to β-hydride emilination. [131]

Table 5.1. Optimization for the synthesis of 25c

Entry	Catalyst	Ligand	Solvent	Time (h)	Temperature (ºC)	Yield (%)
1	$Pd_2(dba)_3$	BINAP	Tol	7	100	73
2	$Pd_2(dba)_3$	XantPhos	Tol	7	100	84
3	$Pd_2(dba)_3$	DPEPhos	Tol	7	100	52
4	$Pd_2(dba)_3$	Dppe	Tol	7	100	40
5	$Pd_2(dba)_3$	Dppf	Tol	7	100	90
6	$Pd_2(dba)_3$	$PCy_3 \cdot HBF_4$	Tol	7	100	13
7	$Pd_2(dba)_3$	$P(tBu)_3 \cdot HBF_4$	Tol	7	100	35
8	$Pd_2(dba)_3$	XPhos	Tol	7	100	31
9	$Pd_2(dba)_3$	$XPhos \cdot tBu_2$	Tol	7	100	37
10	$Pd_2(dba)_3$	SPhos	Tol	7	100	12
11	$Pd_2(dba)_3$	DavePhos	Tol	7	100	45
12	$Pd_2(dba)_3$	RuPhos	Tol	7	100	32
13	$Pd(OAc)_2$	Dppf	Tol	7	100	34
14	$Pd_2(dba)_3$	Dppf	Dioxane	7	100	25
15	$Pd_2(dba)_3$	Dppf	DMF	7	100	0
16	$Pd_2(dba)_3$	Dppf	Tol	7	110	82
17	$Pd_2(dba)_3$	Dppf	Tol	7	80	77

[a]Yield calculated by ^{1}H-NMR of crude product using 1,4-dioxane as an internal standard

With the optimized conditions (method A) in hand, I studied the scope of substrates. The reaction of **24** with different aniline derivatives afforded products **25a-h** in good to excellent yields (Table 5.2). Generally, the electron rich (more nucleophilic) anilines gave higher yields of corresponding products compared to electron poor anilines. An exception was the use of 4-(*N,N*-diethylaminoaniline), presumably due to interaction of the diethylamino group with the catalyst.

Table 5.2. Synthesis of 25a-t

25	R	Method	Yield (%)
a	Ph	A	83
b	4-*t*BuC$_6$H$_4$	A	84
c	3,5-Me$_2$C$_6$H$_4$	A	85
d	4-FC$_6$H$_4$	A	66
e	3-(CF$_3$)C$_6$H$_4$	A	70
f	4-(MeO)C$_6$H$_4$	A	93
g	3,5-(MeO)$_2$C$_6$H$_4$	A	95
h	4-(Et$_2$N)C$_6$H$_4$	A	69
i	*n*-C$_7$H$_{15}$	B	80
j	*n*-C$_3$H$_7$	B	86
k	*n*-C$_{12}$H$_{25}$	B	71
l	Allyl	B	84
m	Bn	B	70
n	4-(MeO)C$_6$H$_4$CH$_2$	B	60
o	(4-FC$_6$H$_4$)CH$_2$	B	53
p	3-(CF$_3$)C$_6$H$_4$CH$_2$	B	52
q	PhCH$_2$CH$_2$	B	75
r	3,4-(MeO)$_2$C$_6$H$_4$CH$_2$CH$_2$	B	56
s	PhCH$_2$CH$_2$CH$_2$	B	68
t	Cyclohexyl	B	55

[a] *compounds **25j-o** were prepared by my colleague Ngo Ngoc Thang.*

Encouraged by the the successful result above, I applied the method A to alkyl amines and only obtained in low yields. Therefore, further optimization for the synthesis of derivative **25l** was carried out (Table 5.3). Among different tested ligands, DPEPhos gave the best yields of alkyl substituted products when it used in combination with Pd$_2$dba$_3$ (method B, Table 5.3). Only bidentate ligands catalyzed these reactions, but no obvious correlation between their bite angle and yields was observed. [131-132] The application of method B allowed the synthesis of desired products **25i-t** in good yields (Table 5.2).

Table 5.3. Optimization for the synthesis of 25l

Entry	Catalyst	Ligand	Solvent	Time (h)	Temperature (ºC)	Yield (%)
1	$Pd_2(dba)_3$	BINAP	Tol	7	100	11
2	$Pd_2(dba)_3$	XantPhos	Tol	7	100	17
3	$Pd_2(dba)_3$	DPEPhos	Tol	7	100	74
4	$Pd_2(dba)_3$	Dppe	Tol	7	100	58
5	$Pd_2(dba)_3$	Dppf	Tol	7	100	41
6	$Pd_2(dba)_3$	$PCy_3 \cdot HBF_4$	Tol	7	100	0
7	$Pd_2(dba)_3$	$PBu_3 \cdot HBF_4$	Tol	7	100	6
8	$Pd_2(dba)_3$	XPhos	Tol	7	100	4
9	$Pd_2(dba)_3$	XPhos·*t*Bu_2	Tol	7	100	7
10	$Pd_2(dba)_3$	SPhos	Tol	7	100	8
11	$Pd_2(dba)_3$	DavePhos	Tol	7	100	7
12	$Pd_2(dba)_3$	RuPhos	Tol	7	100	5

[a]Yield calculated by ^{1}H-NMR of crude product using 1,4-dioxane as an internal standard

The structures of product **25a-t** were determined by spectroscopic methods. The structures of **25g** and **25j** were independently confirmed by X-ray crystal structure analyses (Figures 5.1 and 5.2).[133] Moreover, DFT calculations were performed to compare the geometric parameters of theoretical and experimental structures. The experimental and calculated results indicate that the heterocyclic core structure is planar. Some important calculated bond lengths and bond angles of **25j** (as an example) are compared with those of the crystal structure (Table 5.4). A maximum difference of 0.008Å in bond lengths is observed between theoretical and experimental structures, whereas the difference in bond angles reaches to a maximum of 0.7 degrees. A good correlation between the theoretical and experimental geometric parameters illustrates the validity of the applied computational method.

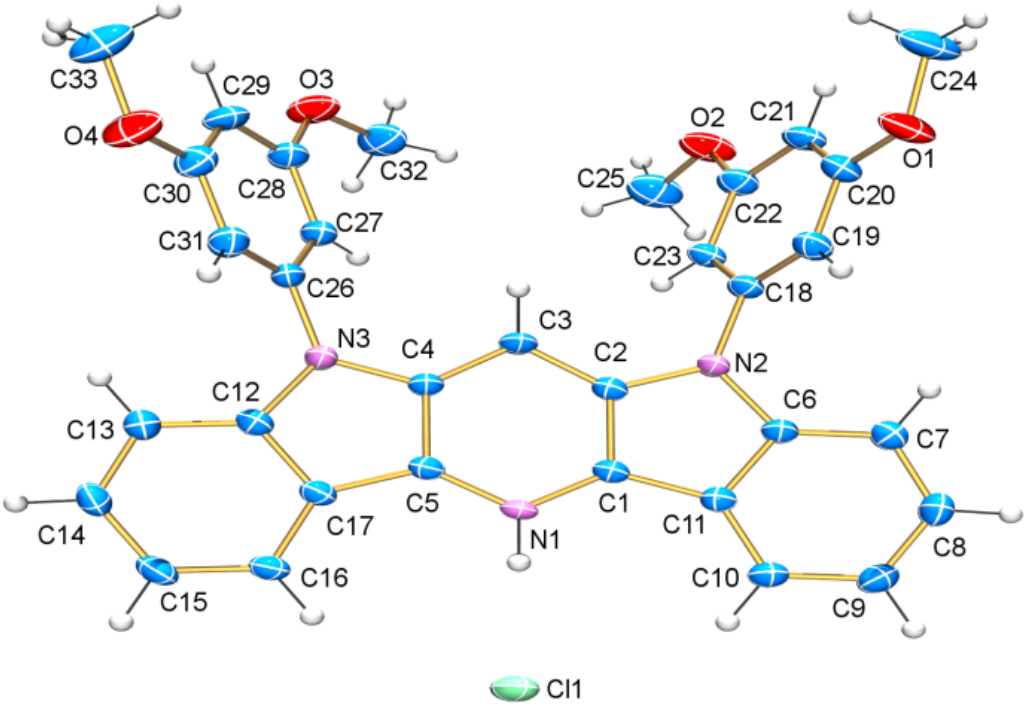


Figure 5.1. Ortep plot of 25g

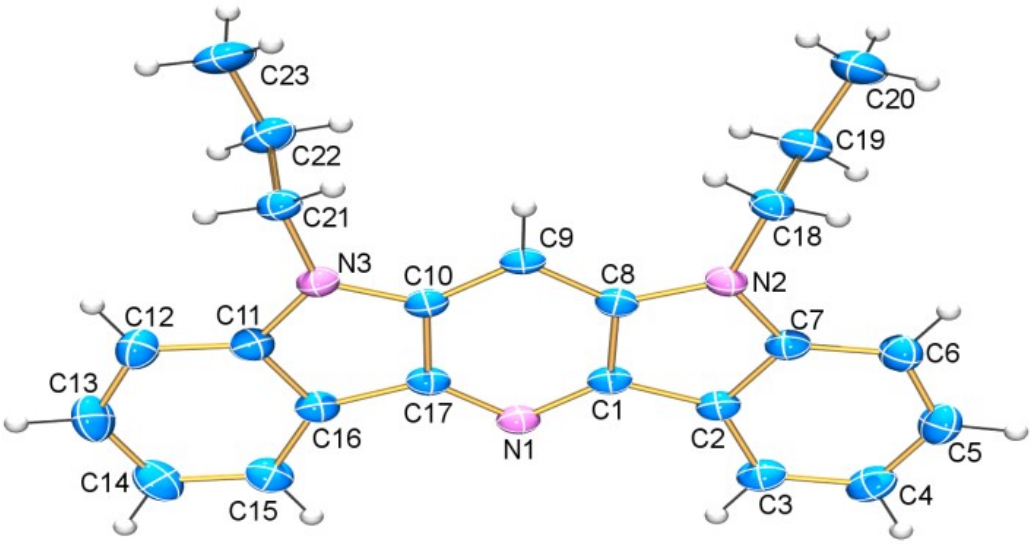


Figure 5.2. Ortep plot of **25j**

Table 5.4. Comparison of bond lengths and bond angles of **25j** based on DFT calculations and X-ray crystal structure analysis

Bond length	Experimental	Theoretical	Bond Angle	Experimental	Theoretical
N1-C1	1.335	1.335	N1-C1-C8	124.7	124.3
C1-C8	1.427	1.433	N1-C1-C2	128.31	129.08
N2-C8	1.387	1.386	N2-C2-C6	128.82	129.37
N1-C17	1.339	1.338	N2-C7-C2	109.55	109.30
N3-C10	1.380	1.386	C9-C8-N2	130.42	130.12
C16-C17	1.444	1.447	C12-C10-N3	108.46	108.85
C9-C10	1.387	1.395	N3-C11-C12	128.56	129.30
N2-C7	1.392	1.397	N3-C11-C16	109.78	109.31

5.3 Electrochemical properties

Electrochemical properties of some *δ*-carbolines with three different concentrations (1 x 10^{-3}; 3 x 10^{-3}; 6 x 10^{-3} mol·L^{-1}) using DMF as solvent were studied including Cyclic Voltammetry (CV) and Differential Pulse Voltammetry (DPV), (Figure 5.3). Tetrabutylammonium hexafluorophosphate ($TBAPF_6$) was used as supporting electrolyte in 0.01 mol·L^{-1} of concentration. All potentials were calibrated with the ferrocene/ferrocenium couple (Fc/Fc^+) as internal standard. Oxidation and reduction energy levels were determined from the better-resolved DPV measurements (Table 5.5). The formal potential of Fc/Fc^+ vs. vacuum was assumed to be -4.8 eV.

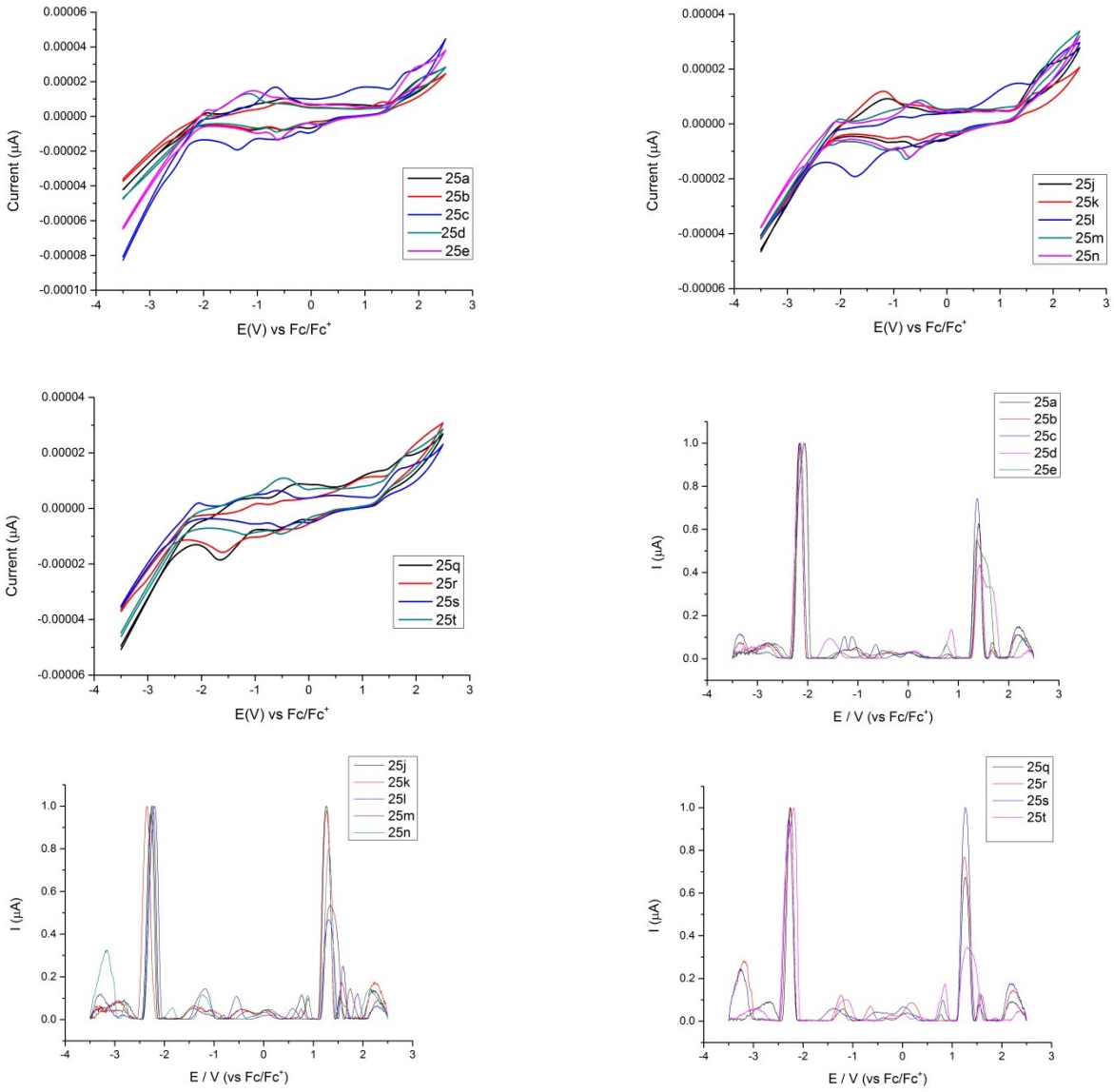


Figure 5.3. Cyclic Voltammograms and Differential Pulse Voltammograms of **25**

Table 5.5. Cyclic Voltammetry and Differential Pulse Voltammetry parameters and calculated energy values of **25**

Comp.	$E_{redox}^{1/2}$ (V vs Fc/Fc+)[a]	$E_{ox}^{1/2}$ (V) (V vs Fc/Fc+)[b]	E_{HOMO} (eV)[c]	E_{LUMO} (eV)[d]	ΔEg (eV)[e]	ΔEgcal. (eV)[f]
25a	-2.167	1.4	-6.250	-2.683	3.567	4.107
25b	-2.171	1.407	-6.207	-2.629	3.578	4.096
25c	-2.143	1.376	-6.176	-2.657	3.519	4.057
25d	-2.056	1.421	-6.221	-2.744	3.477	4.112
25g	-2.07	1.37	-6.170	-2.730	3.440	4.117
25i	-2.268	1.263	-6.063	-2.532	3.531	4.103
25k	-2.35	1.265	-6.065	-2.450	3.615	4.102
25l	-2.197	1.312	-6.112	-2.603	3.509	4.124
25m	-2.003	1.657	-6.457	-2.797	3.660	4.132
25n	-2.256	1.312	-6.112	-2.544	3.568	4.123
25q	-2.254	1.267	-6.067	-2.546	3.521	4.107
25r	-2.264	1.241	-6.041	-2.536	3.505	4.07
25s	-2.299	1.254	-6.054	-2.501	3.553	4.105
25t	-2.191	1.304	-6.104	-2.609	3.495	4.105
CBP			-5.91	-2.51	3.40	

[a] $E_{redox}^{1/2} = E_{redox} + (E_{ampli}/2)$. *Eampli = 0.0501 (V).* E_{redox} *values were determined by DPV in Acetonitrile.*

[b] $E_{ox}^{1/2} = E_{ox} + (E_{ampli}/2)$. E_{ox} *values were determined by DPV in Acetonitrile.V vsFc/Fc*$^{+}$ *in 0.1 M* $TBABF_6$.

[c] *The HOMO levels were estimated from* $E_{HOMO} = -(E_{ox}^{1/2} + 4.8)$ *(eV).*

[d] *The LUMO levels were estimated from* $E_{LUMO} = -(E_{redox}^{1/2} + 4.8)$ *(eV).*

[e] *Electrochemical band gaps ΔEg were estimated from* $\Delta Eg = E_{LUMO} - E_{HOMO}$.

[f] *The band gaps* ΔEg_{cal} *were estimated from computational DFT calculation method.*

Figure 5.3 depicts voltammograms of **25** with reversible and well-defined redox peaks around -2.2 V for the formation and re-oxidation of the reduced forms of **25**. However, corresponding redox-peaks for the oxidized form are hardly visible in the CVs due to the overlapping background current. Therefore, the DPV method was chosen for electrochemical

investigations and revealed the redox signals of the oxidized forms of **25** at ca. +1.3 V. The results indicated that the band gaps were independent from the structure. It suggest that the 5,7-dihydropyrido[3,2-*b*:5,6-*b′*]diindole core plays the key role for the electrochemical properties. Compared to 4,4'-bis(*N*-carbazolyl)-1,1'-biphenyl (**CBP**), which is commonly used in the host material, **25** possess lower HOMO and lower LUMO levels and slightly bigger band gaps. Phenyl substituted derivatives **25a** and **25d** show the lowest HOMO energy levels and band gaps. In contrast, the highest HOMO level and highest LUMO level were found in the case of substrates **25r** and **25s**, presumably cause by thier aliphatic subtituents. The band gaps of phenyl substituted groups located in the *N*-position show smaller band gaps than those of derivatives containing aliphatic substituents. Most likely this fact is attributed to some electronic interaction of the central heterocyclic core with the phenyl substituents. However, it can be anticipated that this interaction is small because of orthogonal twisting of the aryl groups.

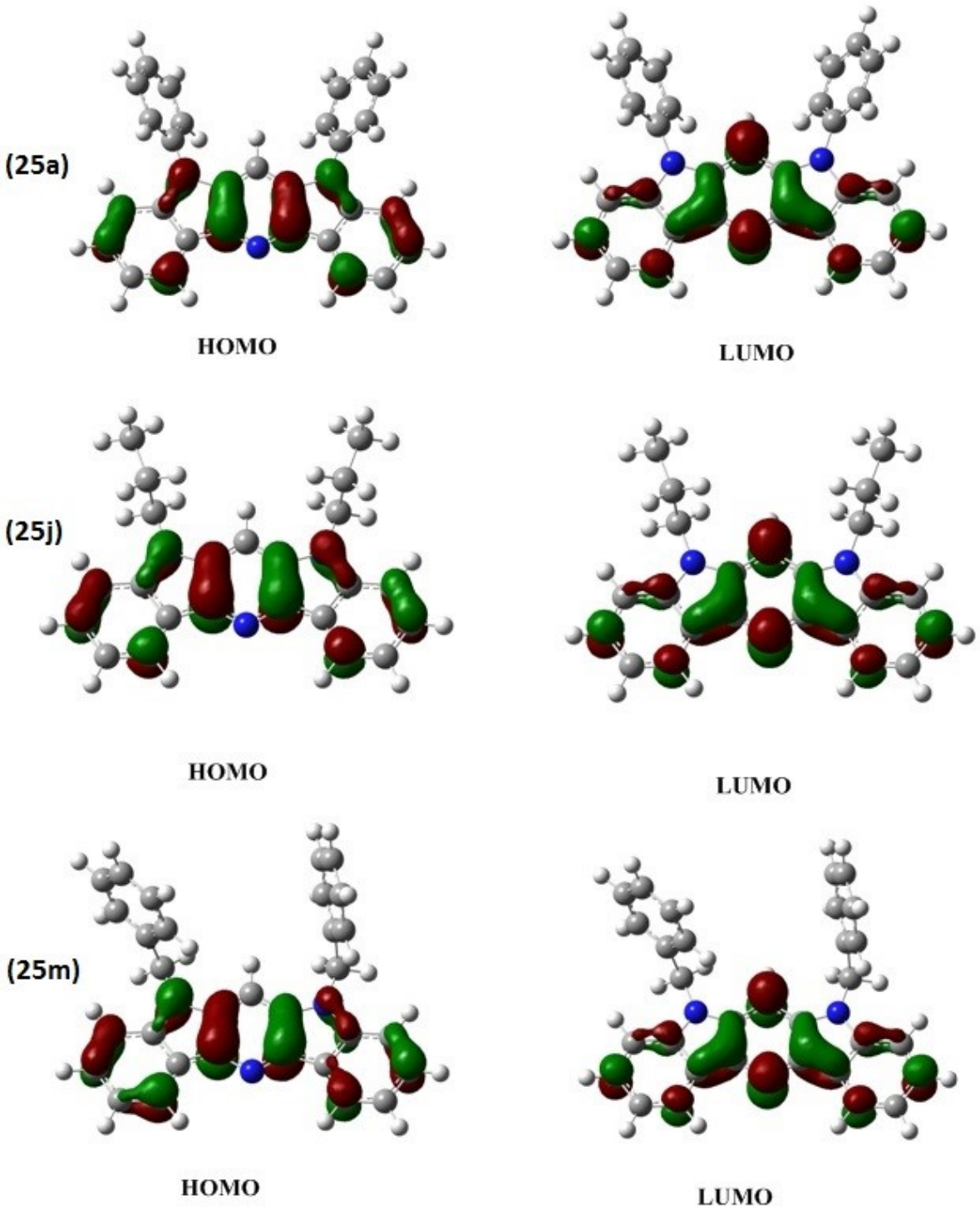


Figure 5.4. Isodensity plot of HOMO and LUMO orbitals of 25a, 25j and 25m

Density functional theory (DFT) calculations have also been caried out for the determination of HOMO-LUMO band gaps.[134] The difference of theoretical and experimental values is given in Table 5.5 (*vide supra*). The calculated band gaps are slightly higher than the experimental values. The comparation between theoretical and experimental band gaps has already been discussed in the literature.[135] The energy of the virtual orbitals (LUMO) is not

properly captured by DFT methods, which leads to over-estimated theoretical band gaps. The results shown in Table 5.5 demontrate that theoretical and experimental band gaps are only slightly influenced by structural modifications. The substituents at nitrogen position can be mainly categorized as aliphatic, benzylic and phenyl moieties. HOMO-LUMO gaps have no significant differences among various substituents which can conclude that HOMOs and LUMOs are not much influenced by the substituents. Towards this end, the HOMO and LUMOs of **25a**, **25j** and **25m** were analyzed and the orbital diagrams are depited in Figure 5.4. As expected, the HOMOs and LUMOs are not extended to the nitrogen substituents and only spread over the pyrido-diindole skeleton. The highest calculated HOMO-LUMO band gap is for **25m** (4.132 eV) which correlate with the highest experimental band gap for the same compound (3.66 eV).

Molecular orbitals and iso density plots of HOMO-2 and LUMO+2 for *N*-phenyl pyrido-diindoles **25a** are shown as a representative example in Figure 5.5. The HOMO-1, and HOMO-2 are almost equal in energy and lie about 0.13 eV lower in energy relative to the HOMO. The HOMO-1 and HOMO-2 are mainly centered on the pyrido-diindole skeleton. LUMO+1 and LUMO+2 orbitals, on the other hand, have iso densities mostly located on the *N*-phenyl substituents. They are located about 0.36 eV and 0.66 eV higher in energy, respectively, than the respective LUMOs.

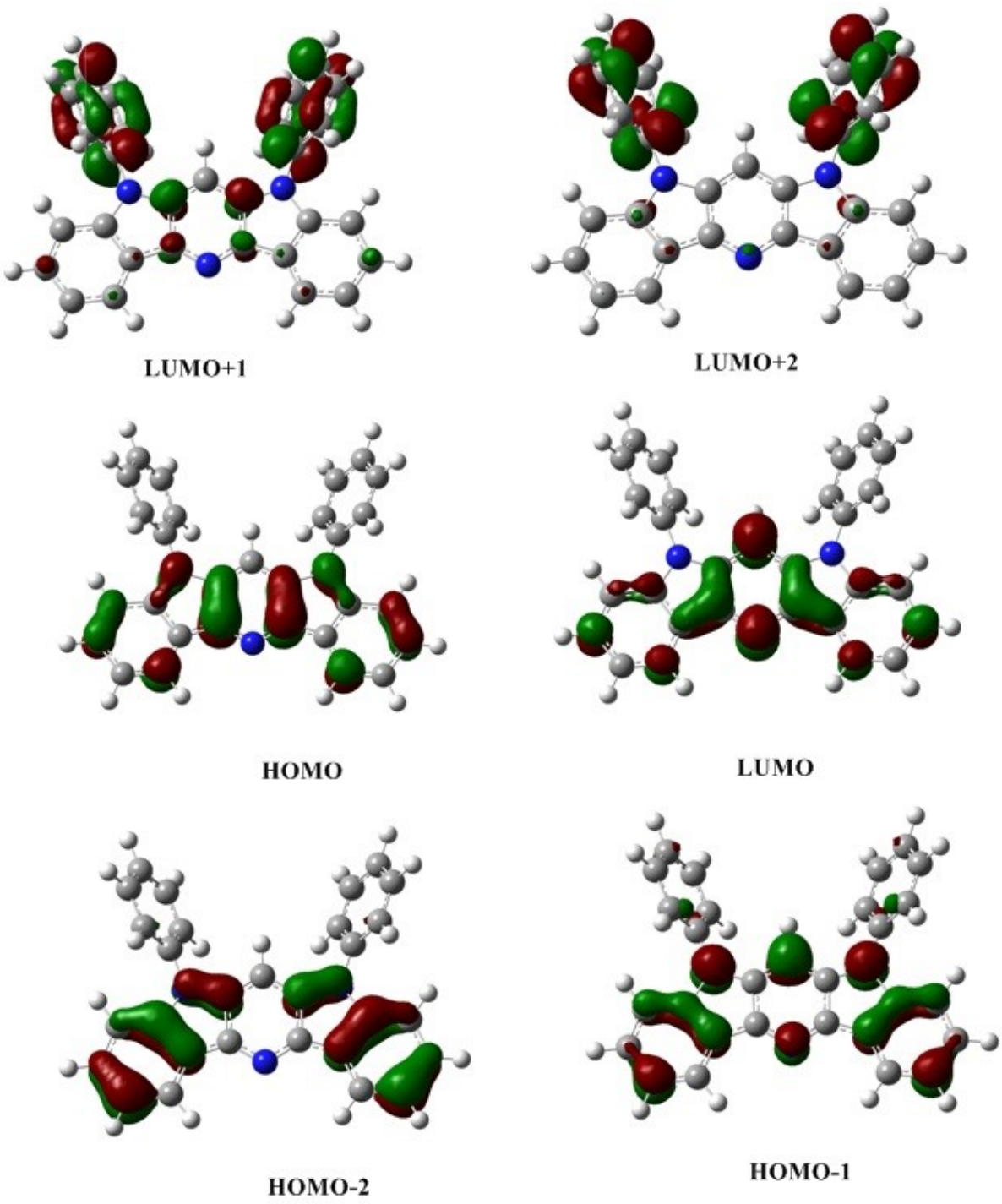


Figure 5.5. Iso density plot of HOMO-2 to LUMO+2 of 25a

5.4 Absorption and Fluorescence Properties

The optical properties were investigated by UV-VIS and fluorescence spectroscopy in acetonitrile and the data is sumarized in Table 5.6. The UV-VIS spectra of various 5,7-

dihydropyrido[3,2-b:5,6-b']diindoles **25** as main chromophores are shown in Figure 5.6. The UV-VIS spectra possess three absorption bands around 290, 310 and 380 nm. No significant influence, caused by the substituent located at the nitrogen atom, was observed. The absorption band of the compounds **25j**, **25k** and **25t,** containing aliphatic subtituents, are slightly red-shifted, presumably due to the positive inductive effect of the alkyl group. For the compounds, containing electron withdrawing groups, for example **25d**, the absorption bands are somewhat shifted to shorter wavelengths.

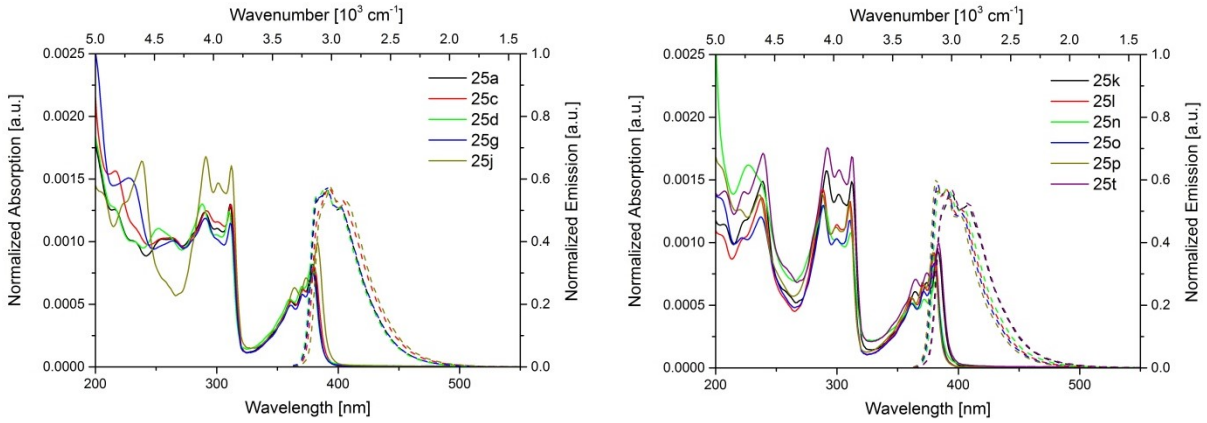


Figure 5.6. Normalized absorption and emission spectra of **25** measured in acetonitrile. Emission spectra were recorded at an excitation of 360 nm.

The fluorescence spectra were measured in acetonitrile (excitation at 360 nm) using standard quinine hemisulfate salt monohydrate in 0.05M H_2SO_4 which has a fluorescence yield of 52%.[86] The spectra showed emission bands around 400 nm. The Stokes shifts are in the range of 20 nm. The UV-VIS and fluorescence spectra show a similar pattern, but the quantum yields vary depending on the type of substituents. Derivatives **25i** and **25k** exhibit the largest Stokes shifts, but lowest quantum yield. Compounds **25o** and **25p**, containing fluorine or trifluoromethyl substituents, possess the highest quantum yields 44% and 47%, respectively.

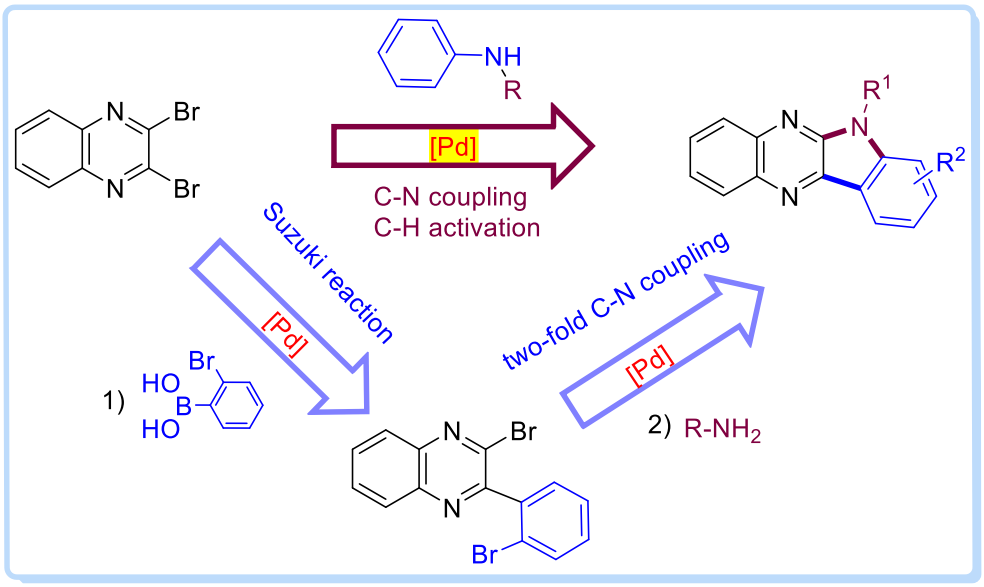
Table 5.6. Absorption and emission spectroscopic data of **25**

25	λ_{1abs}^{max} **[nm]**	**Logε** λ_{1abs}^{max}	λ_{2abs}^{max} **[nm]**	**Logε** λ_{2abs}^{max}	λ_{3abs}^{max} **[nm]**	**Logε** λ_{3abs}^{max}	λ_{em}^{max} **[nm]**	**Stockes shift [nm]**	ϕ_{fluo} **(%)**
a	290	4.557	310	4.569	379	4.381	402	23	42
c	291	4.743	311	4.764	380	4.568	403	23	37
d	288	4.694	310	4.684	378	4.500	402	24	39
g	290	4.712	311	4.700	379	4.519	402	23	39
j	291	4.674	311	4.648	382	4.471	407	25	33
k	291	4.649	312	4.629	382	4.413	407	25	31
l	288	4.649	310	4.633	380	4.488	404	24	35
n	289	4.390	311	4.335	381	4.184	404	23	34
o	288	4.413	310	4.381	379	4.232	402	23	44
p	288	4.753	310	4.716	380	4.575	402	22	47
t	292	4.511	312	4.496	383	4.245	407	24	34

5.5 Conclusion

In conclusion, I successfully synthesized a novel series of *N*-heteropentacenes (5,7-dihydropyrido[3,2-*b*:5,6-*b′*]diindoles) using Pd-catalyzed site-selective Suzuki reaction and two-fold C-N coupling annulations. During the optimization of the reaction condition, the employment of bidentate ligands proved to be important. The electrochemical and optical properties of the products were studied in detail. The results of DFT calculations and the experimental studies demonstrate that *N*-phenyl-substituted derivatives possess smaller band gaps as compared to *N*-alkyl-substituted derivatives. The smallest band gaps were observed for compound **25d**. All studied compounds **25a-t** exhibited high quantum yields **25a-t** (ϕ_{fluo} = 31-47%). The Stokes shifts of **25a-t** are not much dependent on the substituents (variation in the range of only 22-25 nm). Besides the new and interesting synthesis developed, the electronic, optical and electrochemical properties herein might be used as an interesting basis for further applications.

6 Synthesis and physical properties of Indolo[2,3-*b*]quinoxalines



6.1 Introduction

Indolo[2,3-*b*]quinoxalines found many applications in organic light-emitting diodes (OLEDs)[136] and excitonic solar cells.[137] Due to their ability to harvest both singlet and triplet energy for emission, the device efficiency was improved. In 2010, Thomas *et al.* reported that indolo[2,3-*b*]quinoxalines **26** lead to a red-shift in absorption and emission spectra as well as larger Stokes shifts.[137] The thermal stability was increased by introduction of indolo[2,3-*b*]quinoxaline segments which resulted in a higher glass transition temperature. The introduction of bulky and nonplanar structural segments instead of tertiary amine groups reduced π-π stacking interactions, which was assumed to decrease luminescence and propensity for crystal forming in the solid state,.[136b] These novel materials exhibited good quantum yields in solution and remarkable fluorescence in solid state. Thomas *et al.* also fabricate electronic devices with electron transporting (ETL) and emitting layers (EML)

containing compound **27b**. These devices exhibited a maximum luminescence of 3910 cd/m^2 and maximum external quantum efficiency of 0.46%. In 2011, the novel host material BIQS **28** was prepared by Cheng *et al.* for deep-red PhOLEDs.[136c] The BIQS material possess a relatively low LUMO energy that facilitates electron injection allowing a significantly lower voltage operation and higher current density. Due to singlet and triplet energies, this material provided an efficient energy transfer to deep-red emitting layers,. Two years later, three new host materials BIQF, BIQTP, BIQMCz with two indoloquinoline moieties were prepared by Cheng *et al.*[136a] The host layers in deep-red devices containing these materials exhibited EQE_{max} over 20%. The operational lifetimes were also increased and much longer than in the CBP-based devices.

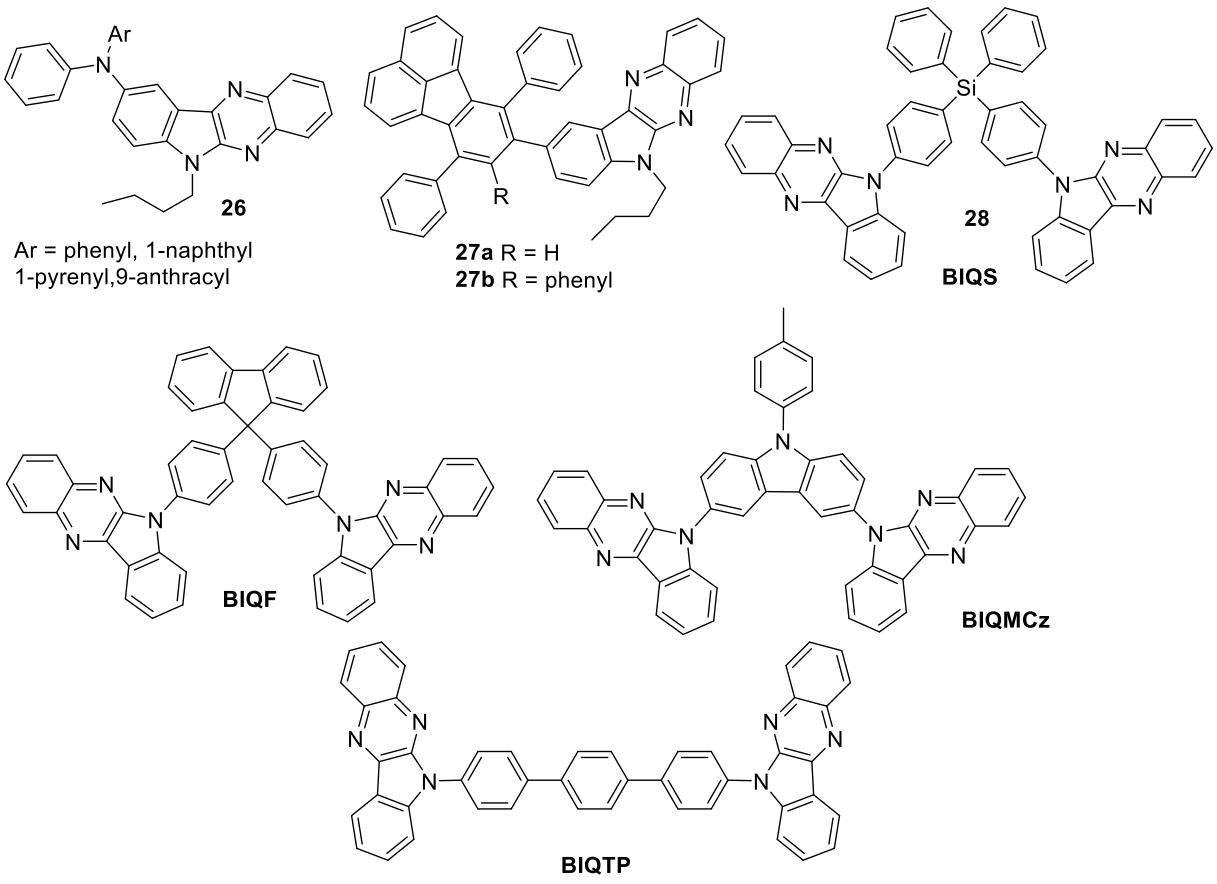


Figure 6.1. Some materials based on indolo[2,3-*b*]quinoxaline moieties.

Indolo[2,3-*b*]quinoxalines not only find many important applications in material sciences, but also in medicinal chemistry. Many reports show that indolo[2,3-*b*]quinoxaline derivatives exhibit a wide range of interesting biological activities, such as antivirus,[138] anticancer,[139]

antimicrobial,[140] and antibacterial activities[141] A series of indolo[2,3-*b*]quinoxaline derivatives were investigated for bioactivity against Herpes virus. These results indicated that B-220 exhibited potent antiviral activity against herpes simplex virus type 1 (HSV-1), varicella-zoster virus (VZV) and cytomegalovirus (CMV) (Figure 6.2).[138] In 2010, 6-(2-aminoethyl)-6*H*-indolo[2,3-*b*]quinoxalines **29** (Figure 6.2) were synthesized by Shibinskaya *et al*. [142] The bioactive test showed that these compounds act as potent interferon inducers and antiviral agents with low toxicity. Furthermore, 7*H*-benzo[4,5]indolo[2,3-*b*]quinoxalines **30,** modificated from the structure of **29,** bind to DNA more strongly (lgK_a = 6.23-6.87) than **29** (lgK_a = 5.57-5.89).[143] The antiviral activity is significantly reduced by the presence of an annulated benzene ring present in compound **30**. In the antitumor research, Deady *et al.* indicated that quinoxaline derivatives exhibited a broad range of cytotoxic activities comparing to tetracyclic quinoline.[139b] In 2001, Hirata *et al.* reported that compounds NCA0424 and NCA0465 possesses antitumor activity toward various types of blood cancer (leukemia), fibrosarcoma sand melanomas.[139a] Recently, indolo[2,3-*b*]quinoxaline derivatives **31** were synthesized and examined against three human cancer cell lines, namely cervical, prostate and lung using an MTT assay by Kanugula *et al*.[144] The results indicate that 9-fluoroindolo[2,3-*b*]quinoxalines, containing CF_3, Cl, H substituents located at the 3-position of the arene attached to the triazole ring, promoted their bioactivity.

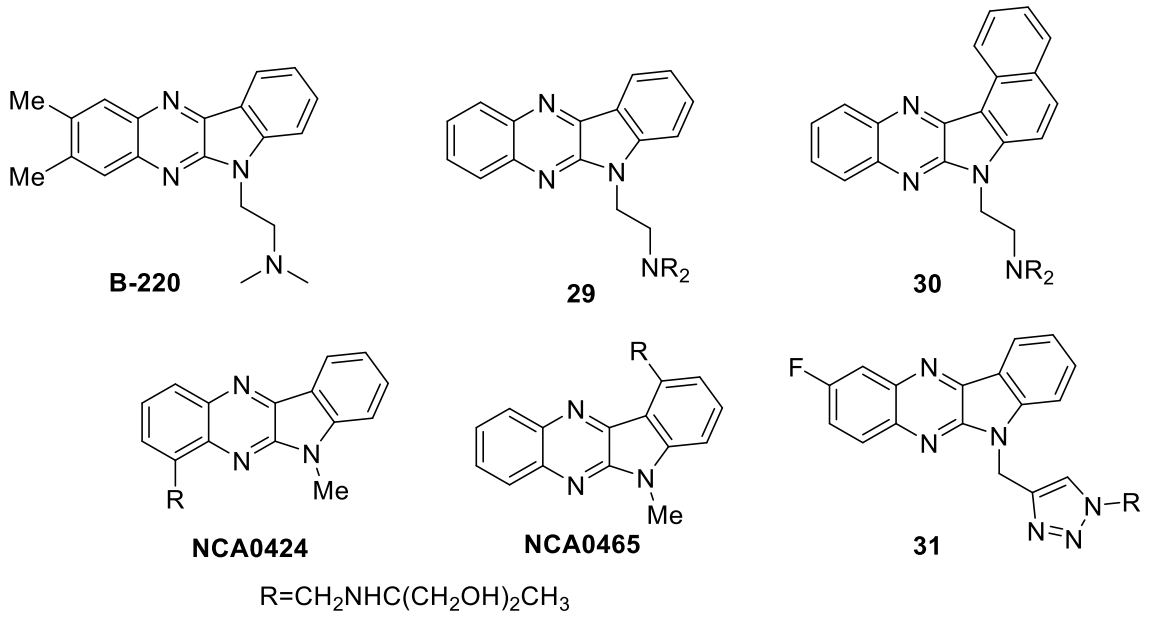
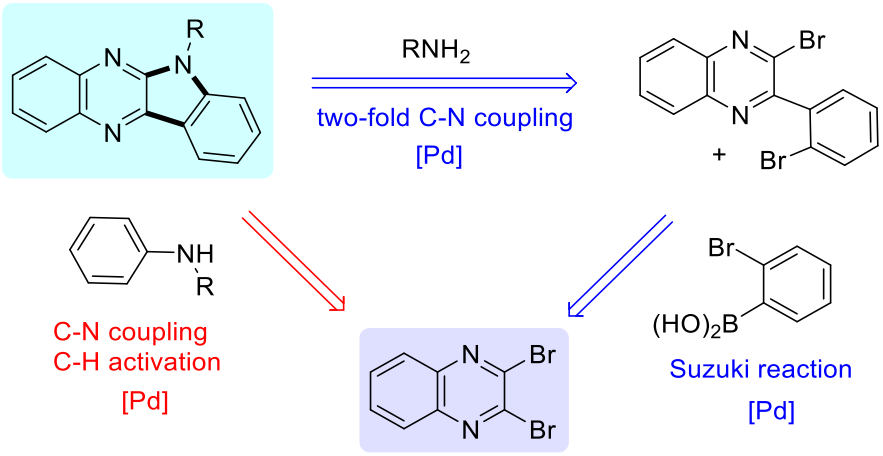


Figure 6.2. Some bioactive compounds containing the indolo[2,3-*b*]quinoxaline moiety

Due to the importance of indolo[2,3-*b*]quinoxalines in both material sciences and medicinal chemistry, I was interested in developing a new and efficient strategy for the synthesis of indolo[2,3-*b*]quinoxalines. Until now, synthetic approaches to these molecules are often complicated, low yielding and require several steps. Most of the reported syntheses of indolo[2,3-*b*]quinoxalines base on the cyclocondensation of isatin with *o*-phenylenediamine derivatives. In 1895, Marchlewski firstly synthesized of indolo[2,3-*b*]quinoxaline by condensation of isatin with *o*-phenylenediamine in the present of AcOH.[145] In 1980, Reisenauer and coworkers described the cyclization of carbodiimide compounds by rearrangement of nitrenes to give indolo[2,3-*b*]quinoxalines in good yields.[146] Indolo[2,3-*b*]quinoxalines could also be synthesized by cyclization of *o*-phenylenediamine with 1-acetyl-2-bromo-3-indolinone.[147] Generally, the synthesis of highly functionalized indolo[2,3-*b*]quinoxalines is still limited, because starting materials are not readily available. During my thesis, I approached to synthesize indolo[2,3-*b*]quinoxalines by a one-pot Pd-catalyzed domino reaction of 1,2-dibromoquinoxaline with secondary aromatic amines. These reactions also gave indolo[2,3-*b*]quinoxaline derivatives in good yields, but with some limitations with regard to the substrates scope. I also want to introduce a second approach by practical and efficient two-step synthesis of indolo[2,3-*b*]quinoxalines based on a Pd-catalyzed Suzuki-Miyaura reaction of 2,3-dibromoquinoxaline and subsequent Pd-catalyzed two-fold C-N coupling annulation with amines.

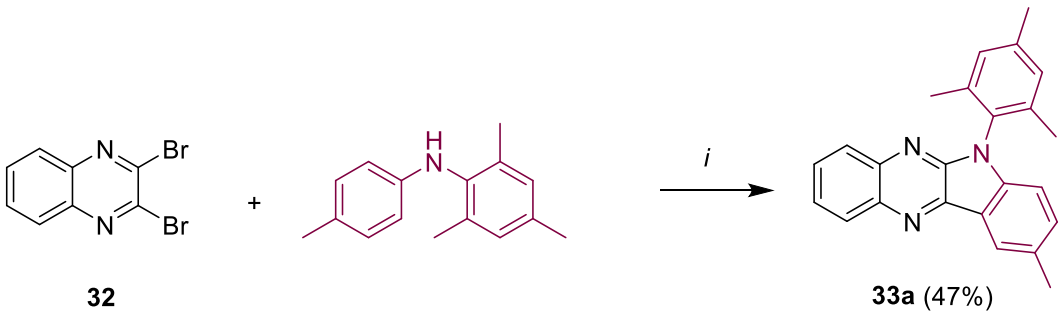
6.2 Results and discussion

I envisaged to synthesize the indolo[2,3-*b*]quinoxaline scaffold relying on two retrosynthetic strategies depicted in Scheme 6.1. My first approach bases on Ackermann's procedure for the one-pot Pd-catalyzed domino synthesis of carbazole derivatives from aryl 1,2-dihalides.[148] This approach directly provides the indolo[2,3-*b*]quinoxaline core structure. The second approach is based on a two-step synthesis using a Pd-catalyzed Suzuki reaction and subsequent two-fold C-N coupling annulation.[149]



Scheme 6.1. Retrosynthetic analysis of the synthesis of indolo[2,3-*b*]quinoxalines

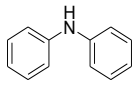
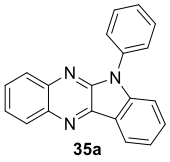
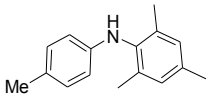
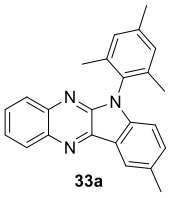
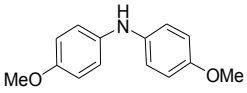
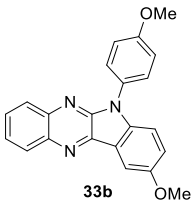
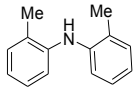
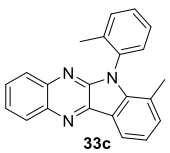
I first started to study the one-pot reaction of 2,3-dibromoquinoxaline (**32**) with secondary aromatic amines using $Pd(OAc)_2/PCy_3 \cdot HBF_4$ as catalyst applying Ackermann's protocol developed for other heterocyclic substrates.[148] I was pleased to find that the reaction of **32**, synthesized in two steps from 1,2-diaminobenzene using Li's procedure,[150] with diphenylamine afforded indolo[2,3-*b*]quinoxalines **35a** in 90% yield (Scheme 6.2). The preparative scope was studied (Table 6.1). The results showed that indolo[2,3-*b*]quinoxalines derived from sterically less bulky amines afforded good yields. The unsymmetrical diarylamine, including **33a,** could be successfully prepared, albeit, in only moderate yield. In contrast, the synthesis of **33e** is unsuccessful. In general, sterically encumbered anilines containing substituents located at the *ortho*-position provided low yields or the reactions completely failed (formation of complex mixtures). The bis(adduct) **33d** instead of the desired cyclization product was formed in case of 2-(methoxy)aniline. In addition, all the reaction of **32** with amines such as *N*-alkylanilines or simple anilines $ArNH_2$ failed. The failure in case of *N*-alkylanilines was already reported by Ackermann for cyclization reactions with other aromatic dihalides.[16] I have tried to vary the conditions to optimize the yields by changing the palladium precursors in combination with various ligands, but I was not able to isolate the products in good yields.

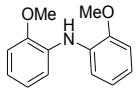
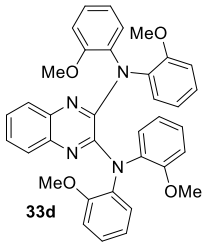
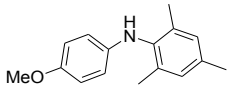
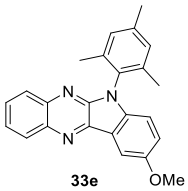
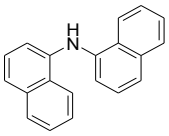
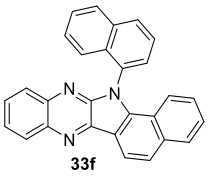


Scheme 6.2. Synthesis of indolo[2,3-*b*]quinoxaline **33a**.

Conditions: (i) 1.5 equiv. of **7**, 1 equiv. of secondary amine, 3 equiv. of NaO*t*Bu, 5% mol of $Pd(OAc)_2$, 10% of $PCy_3 \cdot HBF_4$, toluene, 105 ºC, 18h.

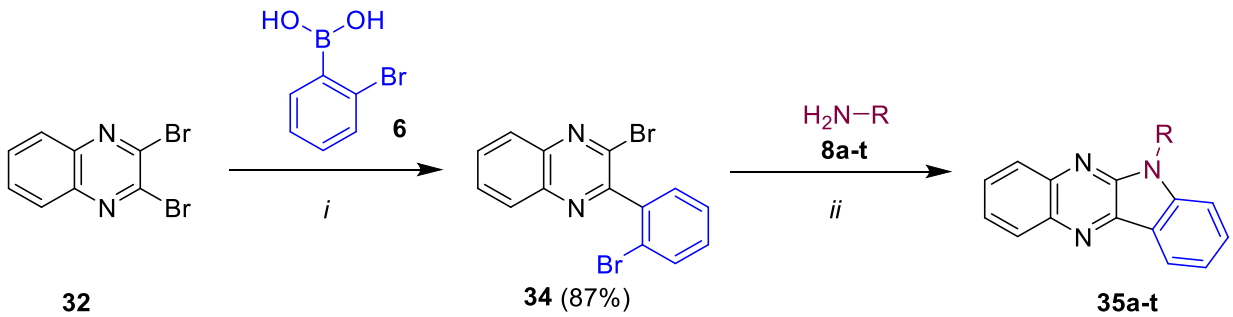
Table 6.1. Synthesis of products **33a-f** and **35a** following the domino C-N/C-H bond activation pathway

Entry	Amine	Product	Yield (%)[a]
1		 **35a**	90
2		 **33a**	47
3		 **33b**	54
4		 **33c**	0[b]

Entry	Amine	Product	Yield (%)[a]
5		 **33d**	30
6		 **33e**	0[b]
7		 **33f**	0[b]

[a] *Isolated yields;* [b] *formation of a complex mixture*

In order to improve the yields and to develop a more efficient procedure for the synthesis of indolo[2,3-*b*]quinoxalines, I studied a second approach relying on a two-step synthesis. In the first step, a Suzuki-Miyaura reaction is performed, followed by a twofold C-N coupling annulation (Scheme 6.3). The Suzuki-Miyaura reaction of **32** with 2-bromophenylboronic acid in the presence of catalytic amounts of $Pd(PPh_3)_4$ gave intermediate **34** in 87% isolated yield. The Pd-catalyzed twofold C-N coupling annulation of **34** with various amines **8a-t** afforded the desired products **35a-t** in good to excellent yields (Table 6.3).



Scheme 6.3. Synthesis of indolo[2,3-*b*]quinoxalines 35a-t.

Conditions: (i) 1.2 equiv. of 2-bromophenylboronic acid **6**, 2.5 % of $Pd(PPh_3)_4$ catalyst, 3 equiv. of NaOH, THF, H_2O, 70 ºC, 4h. (ii) 3 equiv. of **8**, 3 equiv. of NaO*t*Bu, 5% mol of $Pd_2(dba)_3$, ligand (method A: 10 mol% of Dppf, toluene, 100 ºC, 6 h; or method B: 10 mol% of DPEPhos, toluene, 100 ºC, 6h).

My optimizations started with the annulation reaction of adduct **34** with *p*-toluidine **8b** was using 4-nitroacetophenone as an internal standard (Table 6.2). Some important parameters, which can influence the reaction outcome including ligand, Pd precursor, solvent and temperature, were investigated. The results show that bidentate ligands proved to be better ligands than monodentate ligands in this annulation reaction. In fact, up to 92% yield of **35b** was achieved by employment of Dppf as ligand in combination with $Pd_2(dba)_3$ as the Pd source (method A).

Table 6.2. Optimization for the synthesis of 35b

Entry	Pd precursor	Ligand	Solvent	Temperature (ºC)	Yield (%)[a]
1	$Pd_2(dba)_3$	BINAP	Tol	100	67
2	$Pd_2(dba)_3$	XantPhos	Tol	100	84
3	$Pd_2(dba)_3$	DPEPhos	Tol	100	76
4	$Pd_2(dba)_3$	Dppe	Tol	100	62
5	$Pd_2(dba)_3$	Dppf	Tol	100	92
6	$Pd_2(dba)_3$	$PCy_3 \cdot HBF_4$	Tol	100	52
7	$Pd_2(dba)_3$	$PBu_3 \cdot HBF_4$	Tol	100	61
8	$Pd_2(dba)_3$	XPhos	Tol	100	36
9	$Pd_2(dba)_3$	XPhos·*t*Bu_2	Tol	100	40
10	$Pd_2(dba)_3$	SPhos	Tol	100	24
11	$Pd_2(dba)_3$	DavePhos	Tol	100	15
12	$Pd_2(dba)_3$	RuPhos	Tol	100	5
13	$Pd(OAc)_2$	Dppf	Tol	100	52
14	$Pd_2(dba)_3$	Dppf	1,4-Dioxane	100	85
15	$Pd_2(dba)_3$	Dppf	DMF	100	14
16	$Pd_2(dba)_3$	Dppf	Tol	110	83
17	$Pd_2(dba)_3$	Dppf	Tol	80	75

[a] *Yield calculated by ^{1}H-NMR of the crude product using 4-nitroacetophenone as an internal standard*

With the optimized conditions in hand, I studied the scope of the twofold C-N annulation reaction of **34** with various amines. The employment of different anilines afforded the corresponding products **35a-i** in good to excellent yields in 6 hours reaction time only (Table

6.3). The results showed that the annulations gave high yields for substrates bearing both electron-withdrawing and -donating substituents. In contrast, the reactions of **34** with alkyl amines, using my optimized conditions (method A), resulted in the formation of side products which were difficult to separate from the main product. Therefore, further optimization for the synthesis of derivative **35n,** derived from benzyl amine, was carried out. The optimized condition obtained with the employment of DPEPhos as ligand in combination with Pd_2dba_3 (method B), resulted in the formation of product **35n** in up to 96% yield (Table 6.4). The application of these conditions allowed for the synthesis of products **35j-t**, derived from aliphatic amines, in very good yields (Table 6.3).

Table 6.3. Synthesis of 35a-t

35	R	Method	Yield (%)[a]
a	Ph	A	83
b	4-MeC_6H_4	A	86
c	4-FC_6H_4	A	80
d	3-$(CF_3)C_6H_4$	A	90
e	4-$(MeO)C_6H_4$	A	98
f	3,5-$(MeO)_2C_6H_4$	A	95
g	4-$(MeS)C_6H_4$	A	94
h	4-$(Et_2N)C_6H_4$	A	75
i	$(4\text{-NC})C_6H_4$	A	83
j	*n*-C_3H_7	B	96
k	*n*-C_5H_{11}	B	93
l	*n*-C_7H_{15}	B	85
m	Allyl	B	73[b]
n	Bn	B	94
o	4-$(MeO)C_6H_4CH_2$	B	92
p	$(4\text{-}FC_6H_4)CH_2$	B	87
q	3-$(CF_3)C_6H_4CH_2$	B	84
r	$PhCH_2CH_2$	B	89
s	$PhCH_2CH_2CH_2$	B	91
t	Cyclohexyl	B	74

[a]*Isolated yields*

[b]*the product was 6-(prop-1-en-1-yl)-6H-indolo[2,3-b]quinoxaline formed by isomerization of the allylic double bond.*

[c]*compounds **35j-o** were prepared by my colleague Do Huy Hoang.*

Table 6.4. Optimization for the synthesis of 35n

Entry	Pd precursor	Ligand	Solvent	Temperature (ºC)	Yield (%)[a]
1	$Pd_2(dba)_3$	BINAP	Tol	100	51
2	$Pd_2(dba)_3$	XantPhos	Tol	100	63
3	$Pd_2(dba)_3$	DPEPhos	Tol	100	96
4	$Pd_2(dba)_3$	Dppe	Tol	100	14
5	$Pd_2(dba)_3$	Dppf	Tol	100	73
6	$Pd_2(dba)_3$	$PCy_3 \cdot HBF_4$	Tol	100	-
7	$Pd_2(dba)_3$	$PBu_3 \cdot HBF_4$	Tol	100	15
8	$Pd_2(dba)_3$	XPhos	Tol	100	61
9	$Pd_2(dba)_3$	XPhos·*t*Bu_2	Tol	100	59
10	$Pd_2(dba)_3$	SPhos	Tol	100	25
11	$Pd_2(dba)_3$	DavePhos	Tol	100	34
12	$Pd_2(dba)_3$	RuPhos	Tol	100	39

[a] *Yield calculated by* ^{1}*HNMR of the crude product using 4-nitroacetophenone as an internal standard*

The structures of products **35a-t** were proved by spectroscopic methods. The structures of **35e** and **35r** were independently confirmed by X-ray crystal structure analyses (Figure 6.3 and 6.4).[151] The geometric parameters of the X-ray structure for compound **35e** were also compared with those derived from the DFT calculations. The optimized geometry of compound **35e** (from DFT calculations) shows a good correlation with the X-ray structure. The quinoxaline scaffold is planar, whereas the methoxy phenyl ring has a dihedral angle of 52.3 degrees from the quinoxaline plane. A few important calculated bond lengths and bond angles are compared with the experimental values (Table 6.5). The differences between theoretical and experimental bond lengths and bond angles are in the range of 0.015Å and 2.1 degrees, respectively.

Table 6.5. Comparison of experimental bond lengths and bond angles with theoretical values, calculated at B3LYP/6-31G*

Bond Length	Experimental	Theoretical	Bond Angle	Experimental	Theoretical
N3-C15	1.433	1.425	C1-N1-C5	113.1	114.0
N1-C5	1.380	1.370	C2-N2-C10	114.57	115.09
N2-C10	1.373	1.367	C1-N3-C3	108.15	108.09
N2-C2	1.314	1.314	C1-N3-C15	127.67	125.63

Bond Length	Experimental	Theoretical	Bond Angle	Experimental	Theoretical
N1-C1	1.306	1.308	C3-N3-C15	124.18	126.25
N3-C3	1.401	1.407	C18-O1-C21	116.93	118.29
O-C18	1.369	1.363	N1-C1-N3	126.22	126.59
O-C21	1.433	1.419	N1-C1-C2	125.21	124.60
N3-C1	1.379	1.389	N2-C2-C4	130.76	130.98

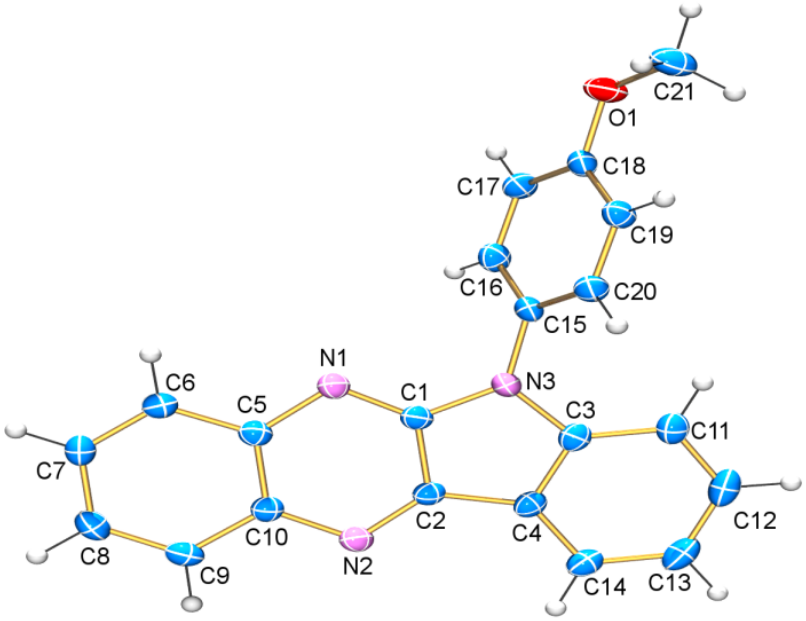


Figure 6.3. Ortep plot of 35e

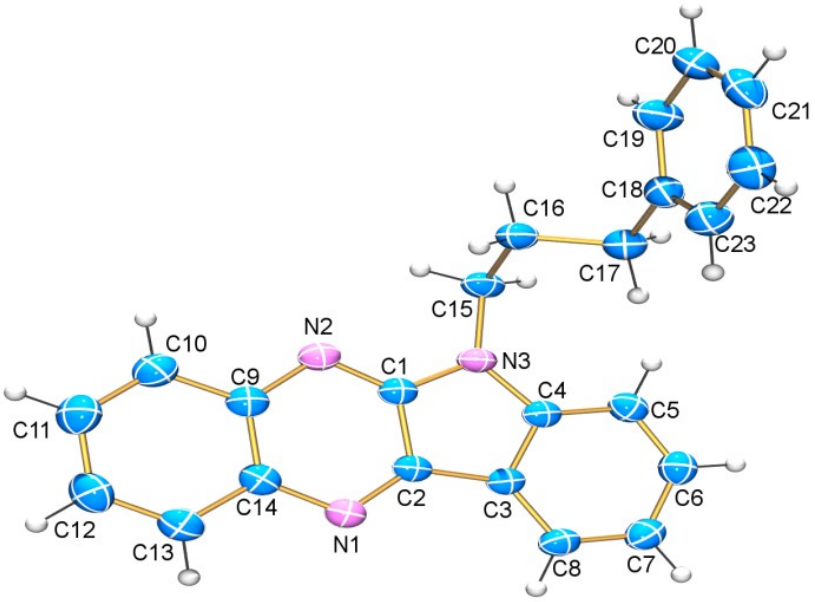
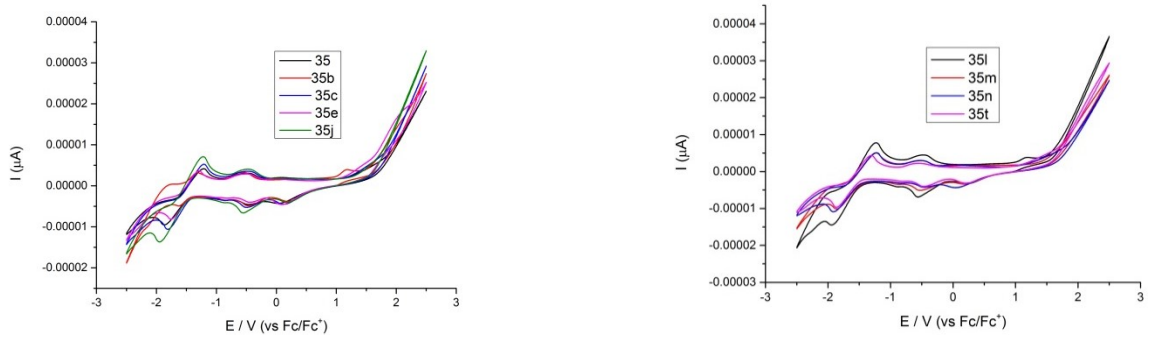


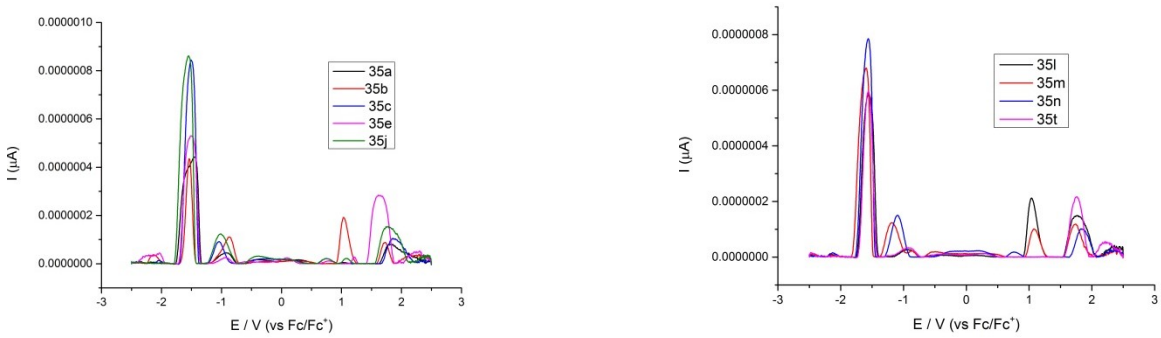
Figure 6.4. Ortep plot of 35r

6.3 Electrochemical properties

Electrochemical properties of some compounds were evaluated by Cyclic Voltammetry (CV) and Differential Pulse Voltammetry (DPV) measurements with three different concentrations (1 x 10^{-3}; 3 x 10^{-3}; 6 x 10^{-3} mol·L^{-1}) in DMF. These solutions also contained 0.01 mol·L^{-1} tetrabutylammonium hexafluorophosphate ($TBAPF_6$) as supporting electrolyte. All potentials were calibrated with the ferrocene/ferrocenium couple (Fc/Fc^+) as internal standard. Oxidation and reduction energy levels were determined from the better-resolved DPV measurement (Table 6.6). The formal potential of Fc/Fc^+ vs. vacuum was assumed to be -4.8 eV.



Cyclic Voltammograms of **35**



Differential Pulse Voltammograms of **35**

Figure 6.5. Electrochemical properties of some quinoxaline derivatives.

Table 6.6. Electrochemical properties of some synthesized quinoxaline derivatives

Comp.	$E_{redox}^{1/2}$ (V vs Fc/Fc$^+$)[a]	$E_{ox}^{1/2}$ (V) (V vs Fc/Fc$^+$)[b]	E_{HOMO} (eV)[c]	E_{LUMO} (eV)[d]	ΔEg (eV)[e]	$\Delta Eg_{cal.}$ (eV)[f]
35a	-1.395	1.872	-6.672	-3.405	3.267	3.707
35b	-1.488	1.779	-6.579	-3.312	3.267	3.670
35c	-1.456	1.910	-6.710	-3.344	3.366	3.704
35e	-1.456	1.666	-6.466	-3.344	3.122	3.605
35j	-1.496	1.819	-6.619	-3.304	3.315	3.637
35l	-1.508	1.813	-6.613	-3.292	3.321	3.750
35m	-1.545	1.787	-6.587	-3.255	3.332	
35n	-1.512	1.874	-6.674	-3.288	3.386	3.784
35t	-1.512	1.813	-6.613	-3.288	3.325	3.744
CBP			-5.91	-2.51	3.40	

[a] $E_{redox}^{1/2} = E_{redox} + (E_{ampli}/2)$. *Eampli = 0.0501 (V). E_{redox} values were determined by DPV in DMF.* [b] $E_{ox}^{1/2} = E_{ox} + (E_{ampli}/2)$. *$E_{ox}$ values were determined by DPV in DMF.V vs Fc/Fc$^+$ in 0.1 M $TBABF_6$.*

[c] *The HOMO levels were estimated from* $E_{HOMO} = -(E_{ox}^{1/2} + 4.8)$ *(eV).* [d] *The LUMO levels were estimated from* $E_{LUMO} = -(E_{redox}^{1/2} + 4.8)$ *(eV).* [e] *Electrochemical band gaps ΔEg were estimated from* $\Delta Eg = E_{LUMO} - E_{HOMO}$.

[d] *The band gaps $\Delta Eg_{cal.}$ were estimated from computational DFT calculation method.*

The voltammograms of compound **35** showed a reversible cycle and well-defined redox peaks around -1.4 V for the formation and re-oxidation of the reduced forms of **35** (Figure 6.5). However, corresponding redox-peaks for the oxidized form are hardly visible in the CVs, due to the overlapping background current. Thus, the DPV method was chosen for the investigation of the electrochemical properties. The experiments showed that the band gaps were independent from the exact substitution pattern. It suggests that the quinoxaline core plays the key role. Quinoxaline derivatives gave lower HOMO and LUMO levels and slightly smaller band gaps compared to 4,4'-bis(*N*-carbazolyl)-1,1'-biphenyl (**CBP**), which is commonly used as host material. Among derivatives bearing a phenyl substituent located at the nitrogen atom, compound **35c,** containing an electron withdrawing group, possesses a HOMO energy level lower than compound **35a**. In contrast, compound **35e,** containing an electron donating group, provided a shift to a higher HOMO level yielding a smaller band gap. Compound **35e,** containing a 4-methoxyphenyl substituent, displayed the smallest band gap and highest HOMO energy level. It is noteworthy that compounds **35c** and **35n,**

containing a 4-fluorophenyl and a benzyl substituent located at the nitrogen atom, respectively, were found to exhibit the lowest HOMO as well as the biggest band gap.

Density functional theory (DFT) calculations have also been carried out for the determination of HOMO-LUMO band gaps.[152] Table 6.6 describe the difference of theoretical and experimental values. The results show the correlation between theoretical and experimental band gaps. The comparation of theoretical and experimental band gaps has already been discussed in the literature.[135] The difference between theoretical and experimental HOMO-LUMO gaps decreases with the increase in the size of the hydrocarbon.[153]

The results shown in Table 6.6 indicate that structural modifications insignificantly affected the band gaps. *N*-alkylindolo[2,3-*b*]quinoxalines possess higher HOMO-LUMO band gaps compared to their *N*-phenyl analogues. The highest HOMO-LUMO band gap was calculated for **35n** (3.78 eV) which correlates with the highest experimental band gap for this compound (3.38 eV). *N*-phenylindolo[2,3-*b*]quinoxalines exhibit lower band gaps, probably due to extended conjugation. The electron delocalization in *N*-phenylindolo[2,3-*b*]quinoxalines reduces the band gaps. Among *N*-phenylindolo[2,3-*b*]quinoxalines, **35a** and **35c** have comparable bands gaps which indicate that the introduction of a fluorine atom has a negligible effect. This might be explained by attribution to the high electronegativity of fluorine which prevents its lone pairs to delocalize over the organic π frame. The introduction of a methyl group at the *para* position of the *N*-phenyl group resulting in a decrease of the band gap by 0.037 eV whereas a methoxy group at the same position also reduce the band gap by 0.1 eV.

Molecular orbitals and iso density plots of HOMO-2 and LUMO+2 for *N*-phenylindolo[2,3-*b*]quinoxalines are shown in Figure 6.6 as a representative example. The HOMO-1 and HOMO-2 are situated at 0.5 and 1.0 eV, respectively. The HOMO-1 and HOMO-2 are mainly centered on the indolo[2,3-*b*]quinoxaline skeleton whereas the HOMO is also extended to the *N*-phenyl substituent. LUMO+1 and LUMO+2 orbitals are at 1.374 eV and 1.548 eV higher in energy, respectively. HOMOs and LUMOs of quinoxalines **35a**, **35l** and **35t** were also analyzed and are depicted in Figure 6.7. The replacement of the phenyl ring of **35a** with an aliphatic heptyl chain in **35l** and an alicyclic fragment (cyclohexyl) in **35t** does not affect the iso densities of the LUMOs, however, a small effect on the HOMO is observed. In **35l** and **35t**, HOMOs are centered on the quinoxaline core whereas in **35a** it has some density on the *N*-phenyl ring as well.

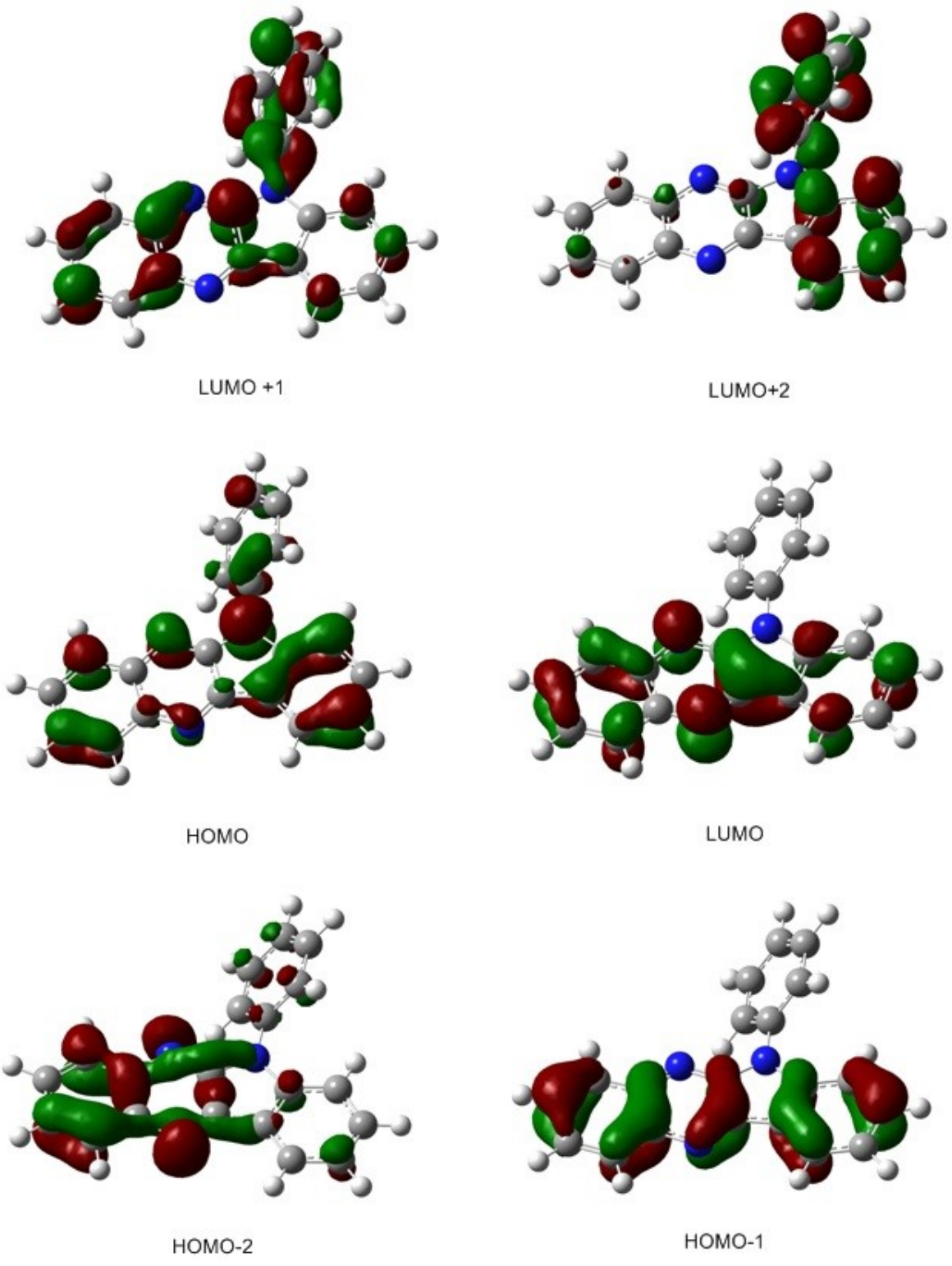


Figure 6.6. HOMO-2 to LUMO+2 molecular orbitals of quinoxaline 35a

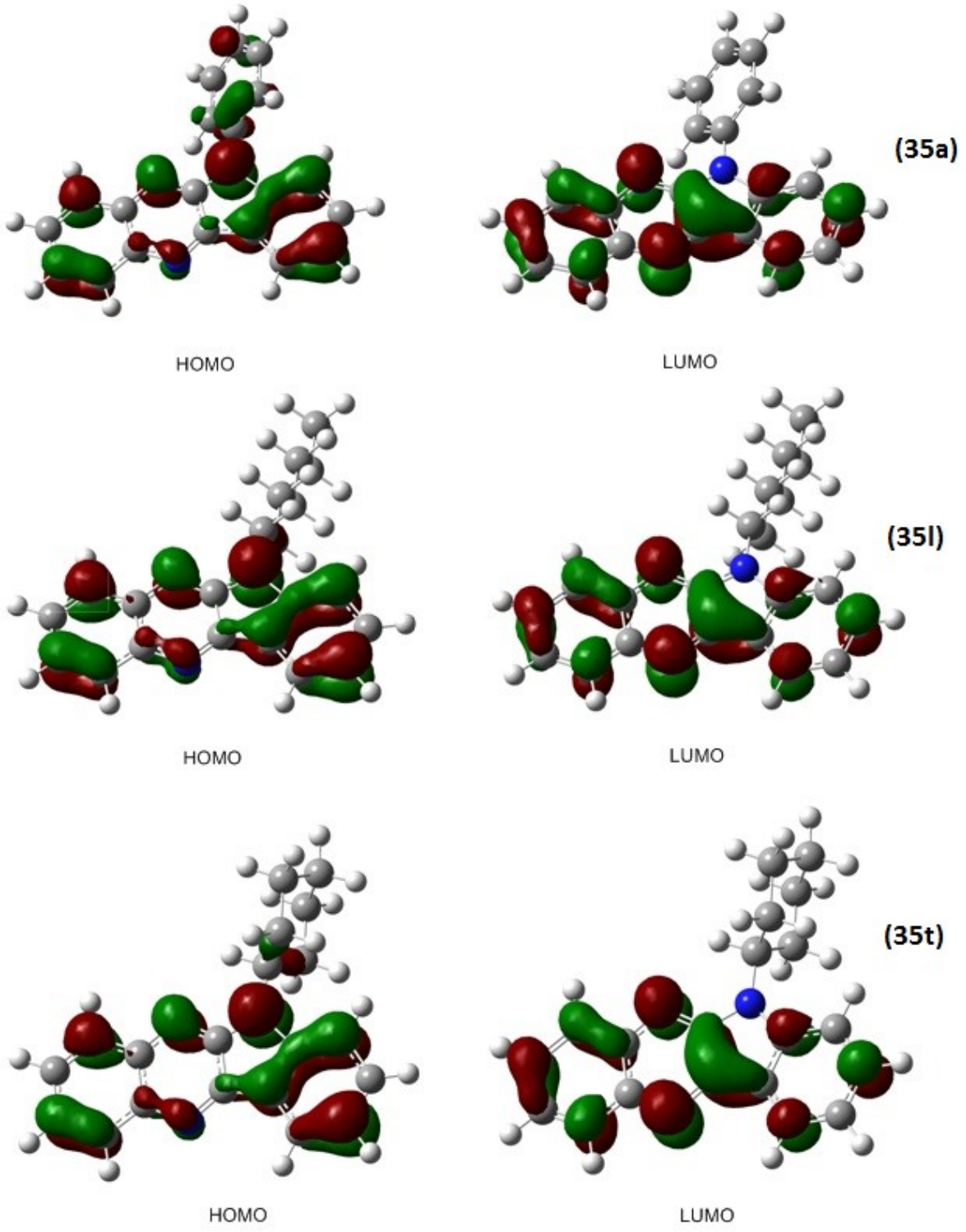


Figure 6.7. HOMO and LUMO of 35a, 35l and 35t calculated at B3LYP/6-31G*

6.4 Absorption and Fluorescence Properties

UV-VIS and fluorescence spectra of some selected indolo[2,3-*b*]quinoxalines **35** were performed in acetonitrile (Figure 6.8) and the corresponding spectral data are summarized in Table 6.7. The UV-VIS absorption spectra of the compounds possess three bands around 400 nm, 350 nm, and 270 nm with increasing absorption strength. The subtituent groups at nitrogen insignificantly affect the absoption spectra due to the similar UV-VIS band in all quinoxalines **35**. The compound **35i** exhibits a band around 270 nm which seems to be splited into two well separated contributions. The absorptions spectra of compounds **35j**, **35l** and **35t**, bearing an aliphatic group located at the nitrogen atom, are slightly shifted to longer wavelength due to the positive inductive effect. In contrast, the absoption bands are blue-shifted in the case of compounds **35d** and **35i**, containing electron withdrawing groups.

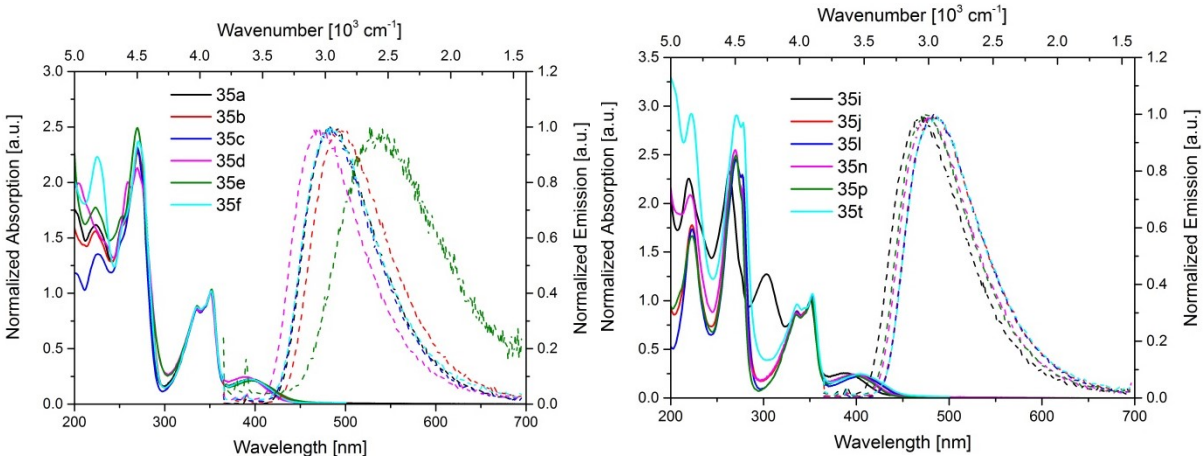


Figure 6.8. Normalized absorption and emission spectra of selected compounds **35** measured in acetonitrile. Emission spectra were recorded with excitation at 350 nm.

The emission spectra were measured using again acetonitrile as solvent and an excitation wavelength of 350 nm. The fluorescence quantum yields were determined by comparison to the standard quinine hemisulfate salt monohydrate in 0.05M H_2SO_4 which has a fluorescence yield of 0.52.[86] The spectra provide emission bands around 480 nm. The bluest emission was observed at 471 nm for the compound **35d,** containing a trifluormethyl group In contrast, the compound **35e,** containing a methoxy group, exhibit the stronglest red-shifted to 538 nm. The Stokes shifts show in medium size and in the range of 80 nm to 90 nm. However, the compound **35e** exhibits a large Stokes shift of 140 nm. The quantum yields of the indolo[2,3-*b*]quinoxalines **35** are in the order of a few percent with the highest yield of 8.6% observed

for **35l**. It is noteworthy that compound **35e** shows also an exceptionally low yield of only 1.1% which seems to correlate with the large red shift of its fluorescence.

The weak dependence of the absorption and fluorescence spectra on the substituent are in line with the small variation of the electrochemical properties and the band gap of the compounds (see above). Only **35e** exhibits a significant higher HOMO level and smaller band gap than the other compounds which correlate to its red shifted fluorescence. The general behavior can be explained by the involved orbitals. As shown in Figure 6.7 HOMO and LUMO, which determine the fluorescence and the first absorption band, are more or less completely restricted to the indolo[2,3-*b*]quinoxaline core and therefore only little affected by the substitution pattern on the nitrogen. Since the energy differences between the HOMO and HOMO-1 and HOMO-2 are smaller than those between the LUMO and LUMO+1 and LUMO+2 the next higher lying electronically excited states should dominantly contain configurations with excitations from HOMO-1 and HOMO-2 to the LUMO. Since the former two orbitals are again restricted to the indolo[2,3-*b*]quinoxaline core (see Fig. 6.6), the corresponding absorption bands around 350 nm and 270 nm are also rather insensitive to the substituent.

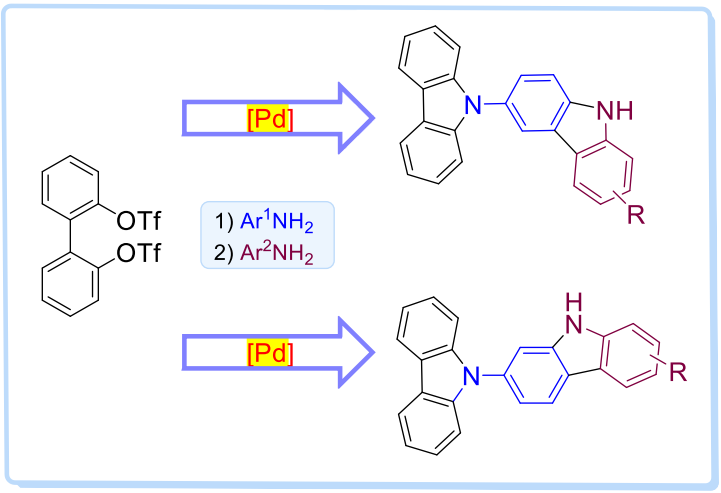
Table 6.7. Spectroscopic data characterizing the absorption and emission properties of **35**

Comp.	λ_{1abs}^{max} [nm]	Lgε λ_{1abs}^{max}	λ_{2abs}^{max} [nm]	Lgε λ_{2abs}^{max}	λ_{3abs}^{max} [nm]	Lgε λ_{3abs}^{max}	λ_{em}^{max} [nm]	Stokes shift [nm]	ϕ_{fluo} Quantum yield
35a	395	3.616	351	4.353	270	4.696	484	89	5.9
35b	396	3.738	351	4.491	269	4.848	490	94	5.2
35c	394	3.809	351	4.547	268	4.903	482	88	5.9
35d	389	3.684	350	4.338	269	4.642	471	82	4.3
35e	398	3.954	351	4.795	269	5.188	538	140	1.1
35f	394	3.387	351	4.078	270	4.451	485	91	4.8
35i	389	3.463	350	4.133	262	4.500	474	85	4.6
35j	403	2.827	352	3.728	269	4.126	484	81	6.7
35l	404	3.952	352	4.939	269	5.334	483	79	8.6
35n	398	4.220	351	4.934	269	5.322	477	79	7.1
35p	396	3.615	351	4.278	269	4.672	475	79	7.4
35t	404	4.144	352	5.005	270	5.402	486	82	7.7

6.5 Conclusion

In conclusion, I developed two strategies for the synthesis of indolo[2,3-*b*]quinoxalines. The one-pot approach, using domino Pd-catalyzed two-fold C-N coupling and C-H activation reactions, afforded indolo[2,3-*b*]quinoxalines in good yields. However, the substrates scope were limited. A two-step approach, relying on a Suzuki coupling reaction followed by an annulation by Pd-catalyzed two-fold C-N coupling, afforded indolo[2,3-*b*]quinoxalines in very good yields. The physical properties of indolo[2,3-*b*]quinoxalines, including electronic, electrochemical and optical properties, were examined experimentally and by DFT calculations. It turned out that the electronic and spectroscopic properties are quite insensitive to the substituents since the relevant orbitals are restricted to the indolo[2,3-*b*]quinoxaline core. The substituent might therefore be used to control and optimize the solubility, the interaction with the environment, and the crystallization behavior in the solid state without changing the electronic properties of the core.

7 Synthesis of biscarbazoles



7.1 Introduction

Carbazoles are presented in a number of alkaloids which possess various biological properties, such as anti-tumor, antibiotic, anti-inflammatory, anti-viral, and anti-malarial activity.[49,154] Due to the interesting biological activities of carbazoles, many efforts for their synthesis have been undertaken.[49,154] The literature on carbazoles synthesis shows a variety of approaches. A representative classic method for the synthesis of carbazoles represent the Fischer-Borsche reaction, which relies on the dehydrogenation of 1,2,3,4-tetrahydrocarbazoles.[155] The Diels-Alder reaction of pyrano[3,4-*b*]indoles with alkynes also give a simple access to carbazole derivatives.[156] In addition, carbazoles are available by metal-free cyclizations, for example, the deoxygenative cyclization of *o*-nitrobiphenyls in the presence of triethyl phosphate[157] and the electrocyclization[158] of 2,3-divinyl indoles. Knölker *et al.* reported an efficient method to construct carbazoles by iron-mediated oxidative cyclizations.[159] In recent years, the synthesis of carbazoles based on palladium-catalyzed cyclizations has attracted much attention and a number of methods have been developed.[49,148,154,160,126b] Nozaki *et al.* described Pd-catalyzed twofold C-N coupling reactions of biphenyls containing leaving groups located at C-2 and C-2′.[126b] A one-pot tandem synthesis of carbazoles, based on Pd-catalyzed cross coupling reactions of iodoanilines with silylated aryl triflates, was reported by Larock and coworker.[161] The group of Prof. Langer have reported the synthesis of carbazoles by domino 'twofold Heck / 6π-electrocyclization' reactions of 2,3-dibromoindoles.[85,162] Carbazoles have also been synthesized by C-H activation reactions. For example, carbazoles are prepared by oxidative

Pd-catalyzed cyclizations of diaryl amines. The synthesis of carbazoles from aniline and 1,2-dihalobenzene derivatives by application of a domino N-H/C-H activation strategy was developed by the group of Ackermann.[148]

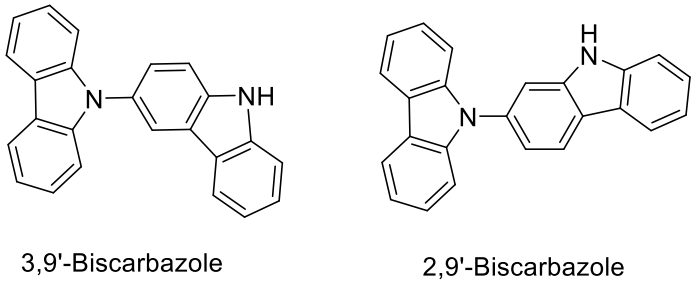


Figure 7.1. Structures of biscarbazoles

Four different core structures of biscarbazoles linked by a carbon and a nitrogen atom are theoretically possible, which includes 3,9'- and 2,9'-biscarbazoles as most important subgroups (Figure 7.1). Biscarbazoles are present in natural products. For example, the 3,9'-biscarbazole alkaloids Murastifoline A and B and the 2,9'-biscarbazole Murastifoline F were isolated from the plant species *Murraya euchrestifolia* and *M. koenigii,* which belong to the *Rutaceae* family (Figure 7.2).[154] 3,9'- and 2,9'-Biscarbazoles have been reported to possess a wide range of pharmacological properties.[49,126c,154,163] In addition, 3,9'-biscarbazoles are also reported as potential molecules in material science, due to their photoemission properties.[164] Biscarbazoles **BCz1** and **BCz2** exhibit high quantum efficiencies along with low voltages and provide maximum brightness values (Figure 7.2).[165] Previously, biscarbazoles preparation was based on methods developed for the synthesis of simple carbazoles.[1] For example, Bringmann *et al.* described the total synthesis of Murastifoline F by oxidative dimerization of the readily available carbazole alkaloid Murrayafoline A.[163a] In 2005, total synthesis of Murrastifoline A was reported by an efficient Pd-catalyzed reaction based on twofold C-N coupling of a 2,2'-dibromobiphenyl derivative with 3-aminocarbazole by the group of Chida.[126c,163b] Very recently, Knölker *et al.* efficiently synthesized Murrastifoline using an Ullmann reaction of the mono-carbazol Murrayafoline A with a 3-bromocarbazole derivative.[163c]

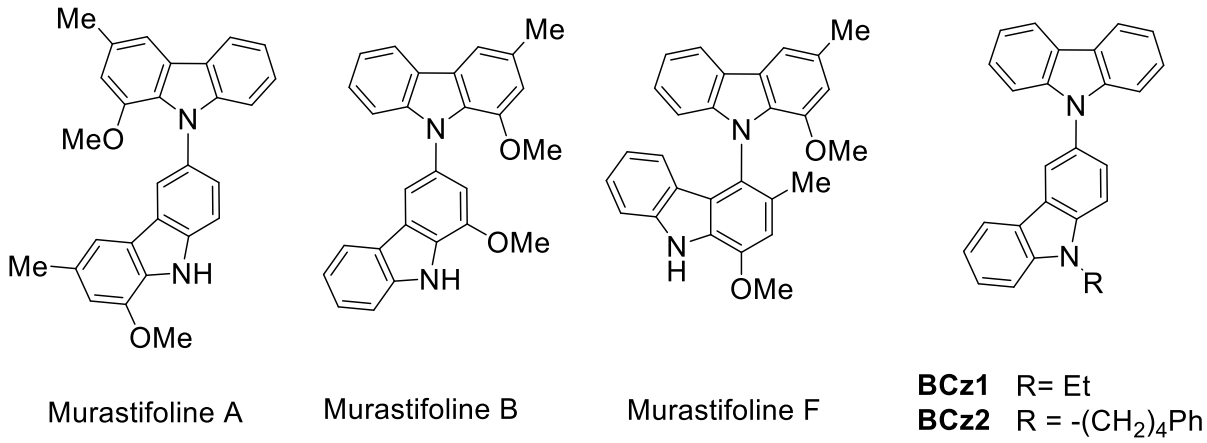
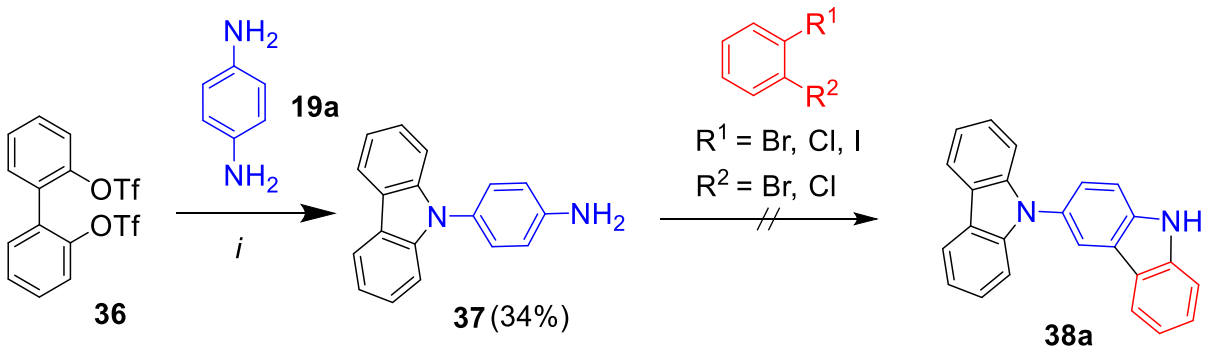


Figure 7.2. Some natural products and materials containing a 3,9'-biscarbazole moiety

Syntheses of 3,9'-biscarbazoles, despite their great usefulness and applicability, are not general. The syntheses are either complicated and require many synthetic steps or access to highly functionalized derivatives is difficult to achieve. In addition, some syntheses are limited by not readily available starting materials. The method of oxidative dimerization is limited to the production of dimers with identical substitution pattern. During my thesis, I developed a new and convenient strategy which can be applied to the synthesis of both 3,9'- and 2,9'-biscarbazoles. My strategy takes advantage of known palladium catalyzed C-N and C-C coupling reactions which were previously applied to the synthesis of simple carbazoles, but not for the synthesis of biscarbazoles.

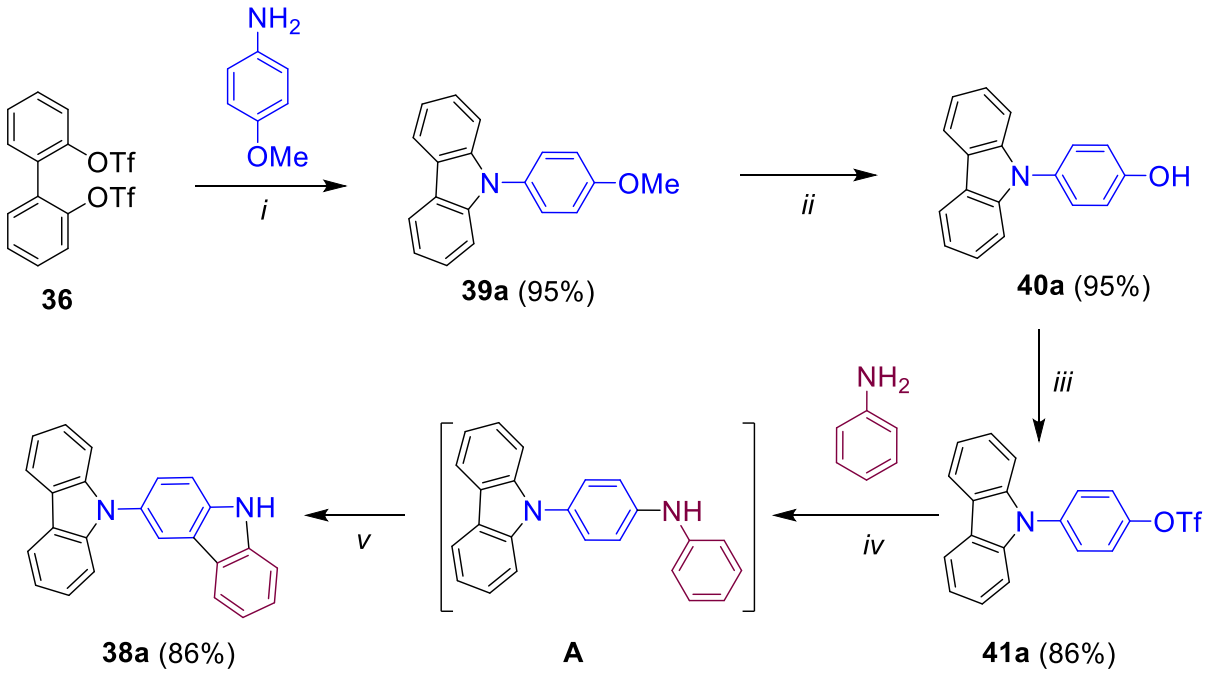
7.2 Results and Discussion

The synthesis of carbazoles by twofold Pd catalyzed C-N coupling of 1,1'-biphenyl-2,2'-diyl bis(trifluoromethanesulfonate) (**36**) with anilines was described by Nozaki *et al.*[70a] At the beginning, I was pleased to apply this methodology to the synthesis of biscarbazoles. The double C-N coupling reaction of **36** with *p*-diaminobenzene afforded carbazole **37**, albeit, in only 34% yield (Scheme 7.1). Unfortunately, all attempts to synthesize biscarbazole **38a** using Ackermann´s method (i.e., the Pd-catalyzed domino C-N/C-C coupling reaction of **37** with various 1,2-dihalobenzene derivatives) failed.



Scheme 7.1. Unsuccessful attempt for the synthesis of 3,9'-biscarbazole **38a**

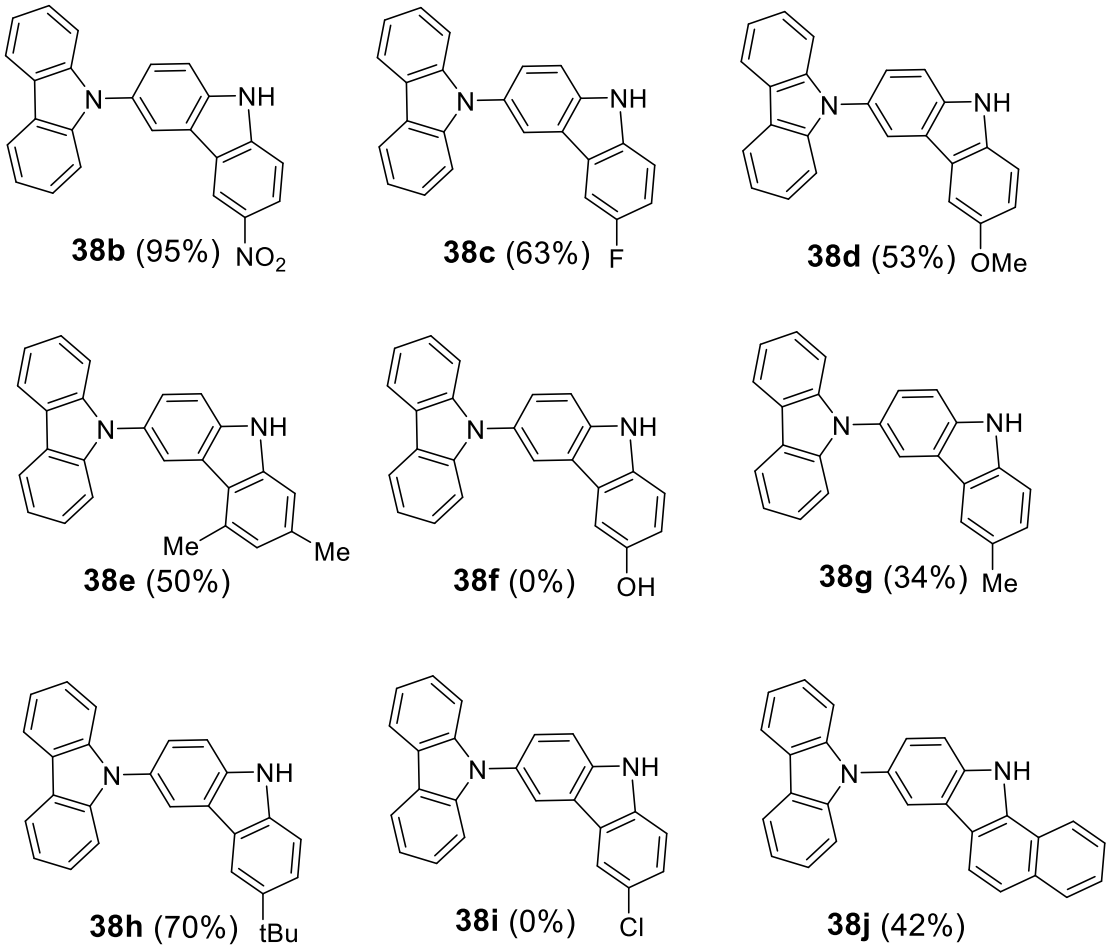
In order to solve this problem, I had to change my strategy. The twofold C-N coupling of bistriflate **36** with anisidine, in the employment of $Pd_2(dba)_3$ and XantPhos as catalyst, afforded carbazole **39a** in 95% yield (Scheme 7.2). Treatment of **39a** with BBr_3 gave demethylated product **40a.** The hydroxyl group in **40a** was converted into a triflate group in high yield by using trifluoromethanesulfonic anhydride. Afterwards, I attempted the synthesis of biscarbazole **38a** by C-N coupling of **41a** with 2-iodo-, 2-bromo and 2-chloro-1-aminobenzene and subsequent cyclization by C-H activation.[160,166] However, all these experiments were unsuccessful. Therefore, I decided to performed a Buchwald-Hartwig amination of **41a** with aniline (C-N coupling). In the presence of $Pd(OAc)_2$ combinating with XPhos, afforded intermediate **A** in a clean transformation. Subsequently, intermediate **A** was successfully transformed to the desired biscarbazole **38a** by Pd-catalyzed oxidative intramolecular C-H activation (using air as the oxidant). The transformation of **41a** to **38a** could be successfully performed in a one-pot reaction which gave 86% yield.[167] The employment of pivalic acid as the solvent proved to be important as employment of acetic acid resulted in a significant decrease of the yield to 61%.[52,168] During the optimization, I studied the employment of several other oxidants, such as $Cu(OAc)_2$ and Ag_2O, but these reactions resulted in complex mixtures. Likewise, the simple uncatalyzed reaction of **A** with molecular oxygen under microwave conditions failed.



Scheme 7.2. Synthesis of 3,9'-biscarbazole 38a.

Conditions: i, 4-anisidine (1.2 equiv.), $Pd_2(dba)_3$ (2.5 mol %), XantPhos (5 mol %), K_3PO_4 (2.8 equiv.), toluene, 100 °C, 5 h; *ii,* 1) BBr_3 (4.0 equiv.), CH_2Cl_2, -78 °C to 20 °C, 2) H_2O, $NaHCO_3$; *iii*, pyridine, Tf_2O, 0 °C; *iv*, aniline (1.1 equiv.), $Pd(OAc)_2$ (5 mol%), XPhos (10 mol %), Cs_2CO_3 (1.5 equiv.), toluene, 110 °C, 6 h; *v,* $Pd(OAc)_2$ (5 mol%), K_2CO_3 (1.0 equiv.), pivalic acid, 110 °C, air, 72 h.

With the optimized conditions in hand, I studied the scope of substrates (Scheme 7.2). The reaction of **41a** with different aniline derivatives afforded 3,9'-biscarbazoles **38a-e** and **38g**, **38h** and **38j** in moderate to high yields. No clear correlation of the yields and the substitution pattern was observed. The employment of 4-hydroxyaniline and of 4-chloroaniline failed in this reaction (formation of complex mixtures). It is assumed that the interaction of the free hydroxyl group with the catalyst might be the reason for the failure. The failure of reaction with 4-chloroaniline is assumed by a competing oxidative addition and coupling reaction of the carbon atom attached to the chlorine atom, although, I cannot provide experimental evidence for this assumption.



Scheme 7.3. Structures of 3,9'-biscarbazoles 38b-j

The structures of products were determined by spectroscopic methods. The structure of **38b** was independently confirmed by X-ray crystal structure analysis (Figure 7.3).[169] The two carbazole moieties are twisted out of plane, due to steric reasons.

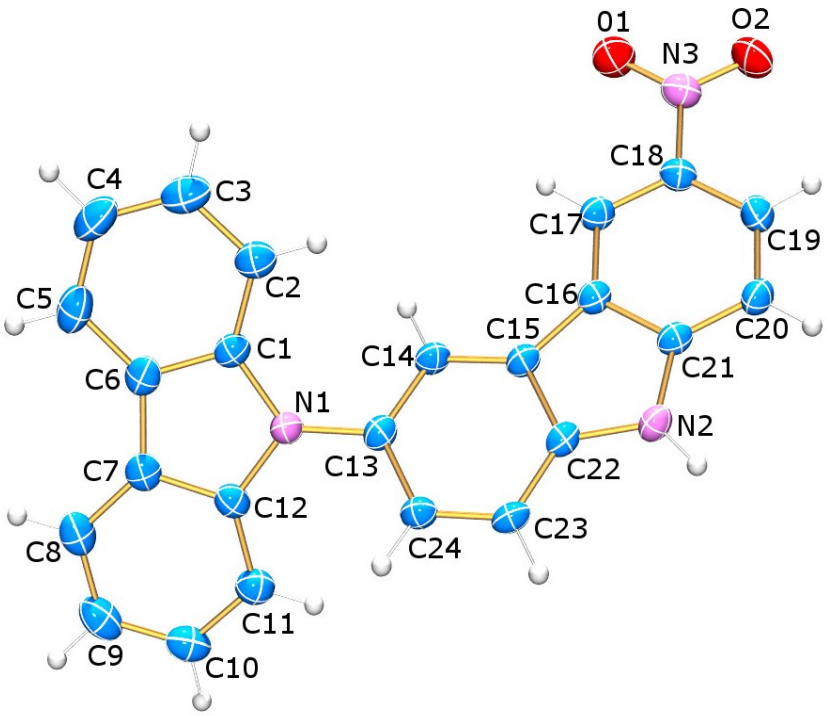
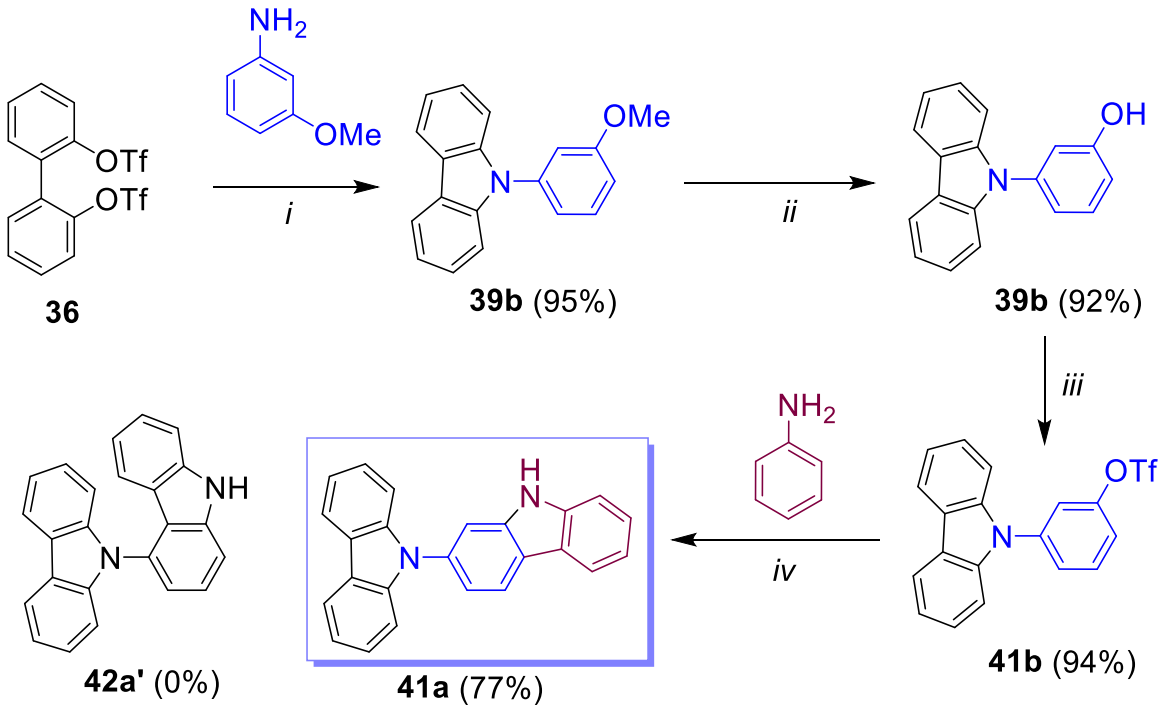


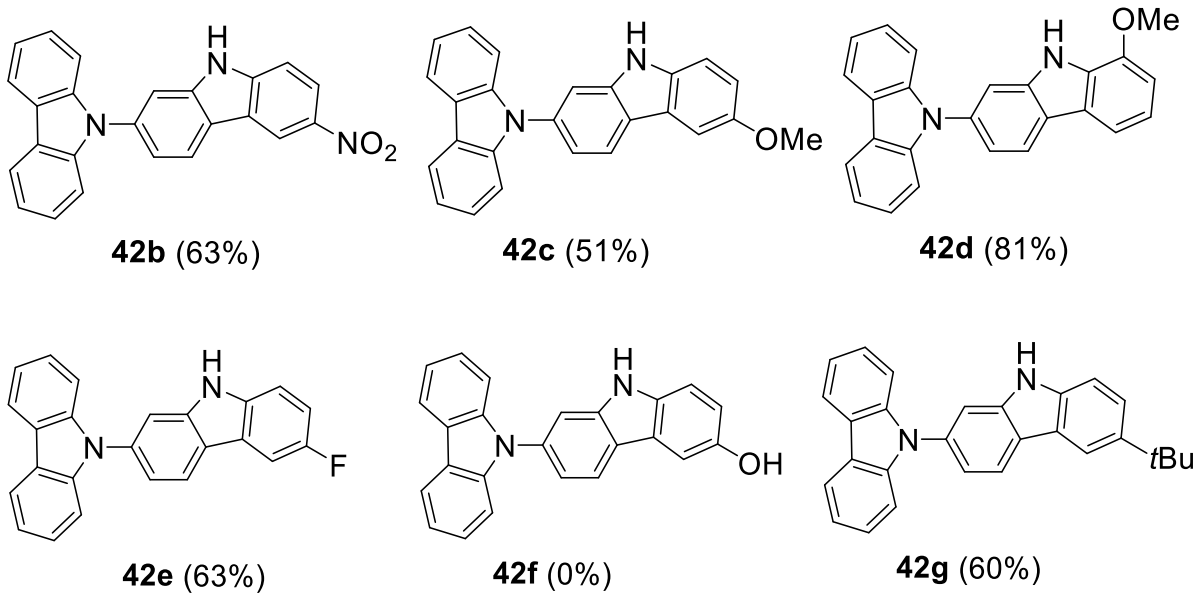
Figure 7.3. Ortep plot of 38b

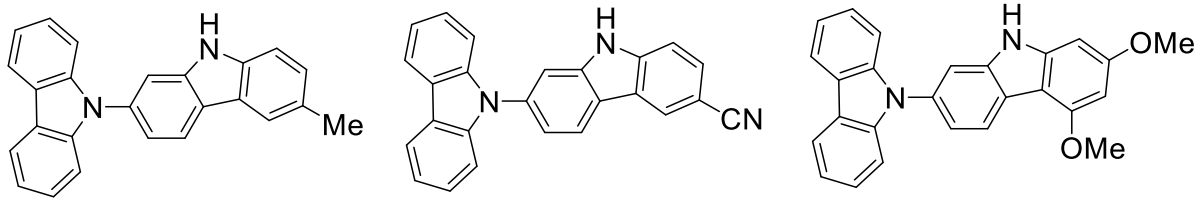
With the successful strategy outlined above for the synthesis of 3,9'-biscarbazoles, I was interested in applying it this methodology to the synthesis of isomeric 2,9'-biscarbazoles. Firstly, carbazole **39b** was obtained in 95% yield by the Pd-catalyzed twofold C-N coupling of **36** with *m*-methoxyaniline (Scheme 7.4). Subsequently, the transformation of methoxy group in **39b** into triflate group in **41b** was produced via two steps in high yield. The reaction of **41b** with aniline by Buchwald-Hartwig amination and subsequent oxidative Pd-catalyzed cyclization afforded 2,9'-biscarbazole **42a** in 77% yield. I was also able to perform the reaction again in a one-pot process. The cyclization proceeded with excellent regioselectivity. Interestingly, regioisomeric product **42a'** was not observed as a side-product (NMR of the crude product). The reaction of **39b** with different anilines gave 2,9'-biscarbazoles **42a-e** and **42g-j** in moderate to good yields (except for **42i**) (Scheme 7.4). No clear correlation of the substitution pattern and the yields of the products were observed. The structures of products were determined by spectroscopic methods. The structure of **42c** was independently confirmed by X-ray crystal structure analysis (Figure 7.4).[170]



Scheme 7.4. Synthesis of 2,9'-biscarbazole **42a**.

Conditions: i, 3-anisidine (1.2 equiv.), $Pd_2(dba)_3$ (2.5 mol %), XantPhos (5 mol %), K_3PO_4 (2.8 equiv.), toluene, 100 °C, 5 h; *ii,* 1) BBr_3 (4.0 equiv.), CH_2Cl_2, -78 ºC to 20 ºC, 2) H_2O, $NaHCO_3$; *iii*, pyridine, Tf_2O, 0 °C; *iv*, aniline (1.1 equiv.), $Pd(OAc)_2$ (5 mol%), XPhos (10 mol %), Cs_2CO_3 (1.5 equiv.), toluene, 110 ºC, 6 h; *v,* $Pd(OAc)_2$ (5 mol%), K_2CO_3 (1.0 equiv.), pivalic acid, 110 ºC, air, 72 h.





42h (51%) **42i** (21%) **42j** (47%)

Scheme 7.5. Structures of 2,9'-biscarbazoles 42b-j

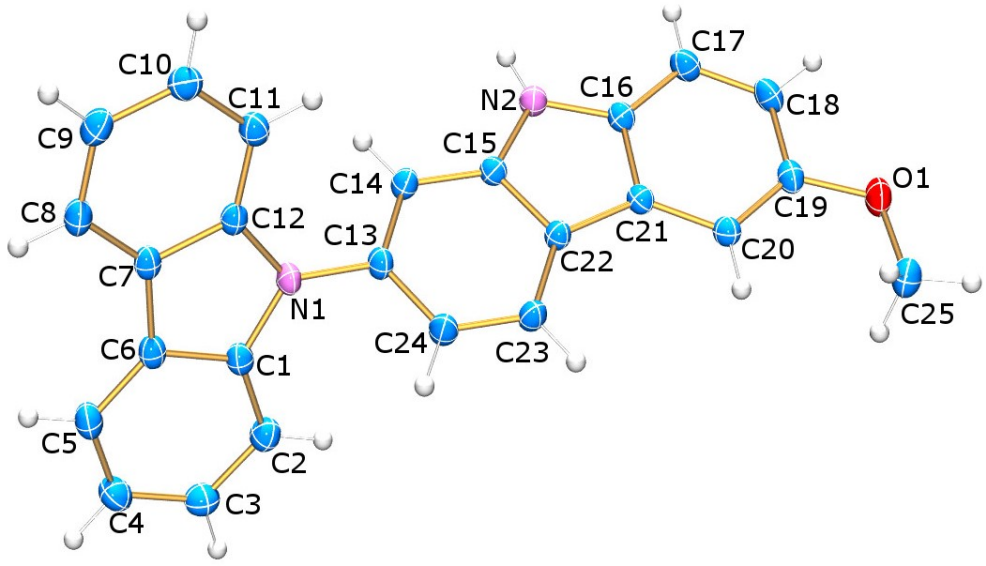


Figure 7.4. Ortep plot of 42c

7.3 Conclusions

In conclusion, I developed a new and efficient strategy for the synthesis of 3,9'- and 2,9'-biscarbazoles. My strategy bases on the cyclization of 1,1'-biphenyl-2,2'-diyl bis(trifluoromethanesulfonate) with 4- or 3-anisidine, transformation of the methoxy to a triflate group and subsequent oxidative Pd-catalyzed cyclization with different anilines. The strategy is highly efficient as it only requires four steps from simple starting materials and it can be applied to the synthesis of both 3,9'- and 2,9'-biscarbazoles.

APPENDIX

8 Experimental section

8.1 General Remarks

The coupling reactions were carried out in pressure tubes or Schlenck flask under inert atmosphere (Argon 4.6). The back-filled technique was applied to exclude oxygen. The solvents for the reactions were purchased from Merck, Sigma Aldrich, Acros Organics. The solvents for column chromatography and reaction work-up were distilled prior use.

8.2 Methods for Compound Characterization and Analysis

8.2.1 Melting Points

Micro heating table HMK 67/1825 Kuestner (Büchi apparatus); Melting points are uncorrected.

8.2.2 Nuclear Magnetic Reasonance Spectroscopy (NMR)

Bruker: AM 250, (62.9 MHz); Bruker: ARX 300, (75.4 MHz), Bruker: ARX 500, (125 MHz). The chemical shifts are given in parts per million (ppm). Coupling constants are given in Hz.

References for ^{1}H NMR: TMS(δ = 0.00) or residual deuterated solvent ($CDCl_3$ (δ = 7.26), C_6D_6 (δ = 7.16), $(CD_3)_2CO$ (δ = 2.05), $(CD_3)_2SO$ (δ = 2.50)), for ^{13}C NMR TMS(δ = 0.00) or residual deuterated solvent ($CDCl_3$ (δ = 77.16), C_6D_6 (δ = 128.06), $(CD_3)_2CO$ (δ = 29.84; 206.26), $(CD_3)_2SO$ (δ = 39.52)) were taken as internal standard. The splitting pattern were characterized by s: singlet, d: doublet, t: triplet, q: quartet, quin: quintet, sex: sextet, m: multiplet. More complicate coupling peaks are represented by combinations of the respective symbol. For example, dt indicate to doublet of triplet. Distortionless enhancement polarization transfer (DEPT) spectra were taken to determine the types of carbon signals.

8.2.3 Mass Spectroscopy (MS)

AMD MS40, Varian MAT CH 7, MAT 731 (EI, 70 eV), Intecta AMD 402 (EI, 70 eV and CI).

8.2.4 High Resolution Mass Spectroscopy (HRMS)

Finnigan MAT 95 or Varian MAT 311; Bruker FT CIR, AMD 402 (AMD Intectra).

8.2.5 Infrared Spectroscopy (IR)

Bruker IFS 66 (FT IR), Nicolet 205 FT IR; Nicolet Protege 460, Nicolet 360 Smart Orbit (ATR); KBr, KAP, Nujol, and ATR; Peaks were characterized with abbreviation: w = weak, m = medium, s = strong, br = broad

8.2.6 X-ray Crystal Structure Analysis

Bruker X8Apex diffractometer with CCD camera (Mo Kαradiation and graphite monochromator, λ= 0.71073 Å). The structures were solved by direct methods and refined by full-matrix least-squares procedures on F^2 with the SHELXTL software package

8.2.7 UV/Vis spectroscopy

Lambda 5 (Perkin Elmer) and Analytic Jena Specord 50 UV/VIS spectrometer in acetonitril.

8.2.8 Fluorescence spectroscopy

Fluoromax4P-0759D-0311-FM. The samples were dissolved in acetonitrile. The quinine hemisulfate salt monohydrate in 0.05M H_2SO_4 which has a fluorescence yield of 0.52, was used as standard for the fluorescent quantum yield determination.

8.2.9 Electrochemical properties

Cyclic Voltammetry (CV) and Differential Pulse Voltammetry (DPV) measurement were performed by mean of μAutolab III potentiostat (Ecochemie, Utrecht, The Netherlands in three different concentrations (1×10^{-3}; 3×10^{-3}; 6×10^{-3} mol·L^{-1}) in DMF. All potentials were calibrated with the ferrocene/ferrocenium couple (Fc/Fc^+) as internal standard. The formal potential of Fc/Fc^+ vs. vacuum was assumed to be -4.8 eV.

8.3 Chromatographic Methods

8.3.1 Thin Layer Chromatography (TLC)

Merck Silica 60 F254 on aluminum aluminum foil from Macherey-Nagel. Detection under UV light at 254 nm and/or 365 nm of wavelength and visualize by dipping in TLC stains solution including conc. H_2SO_4/vaniline, Cerium-ammonium-molybdate (CAM), ceric sulfate and dragendorff reagent.

8.3.2 Column chromatography

Column chromatography was performed over Merck silica gel (63-200 μm) as nomal column and (40-63 μm) as flash column. All the solvent were distilled prior of use.

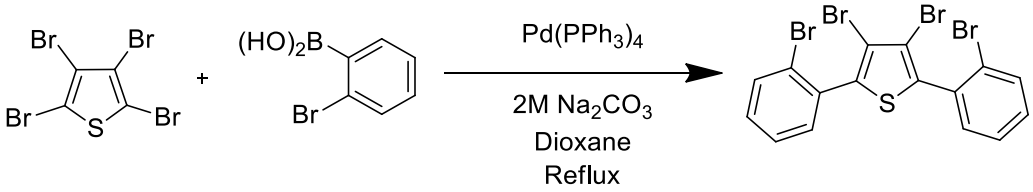
8.4 Computational Methods

DFT calculations were performed with the Gaussian 09Revision C.01.[171] The visualization of the results was performed with GaussView. The geometries of indolo[2,3-*b*]quinoxalines were optimized using the hybrid functional B3LYP method, which consists of Becke's three-parameter[172] (B3) hybrid exchange functional in conjunction with the correlation functional of LeeYang and Parr (LYP)[173] method using 6-31G* basis set.[174] The B3LYP/6-31G* method of DFT has been reliable for the prediction of geometric and electronic properties of neutral[135a] and charged species[175] ranging from simple molecular to polymer structures[176]. Frequency calculations were performed at the same method in order to confirm these structures as true minima (absence of an imaginary frequency). Molecular orbital calculations are also performed at the B3LYP/6-31G* level of theory.

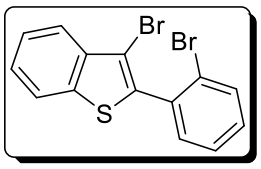
8.5 General Procedures and spectroscopic data

8.5.1 Synthesis of thieno[3,2-b:4,5-b']diindoles and Benzothieno[3,2-b]indoles

General procedure 1 for preparation of *3,4-dibromo-2,5-di-(2-bromophenyl)thiophene* 7.



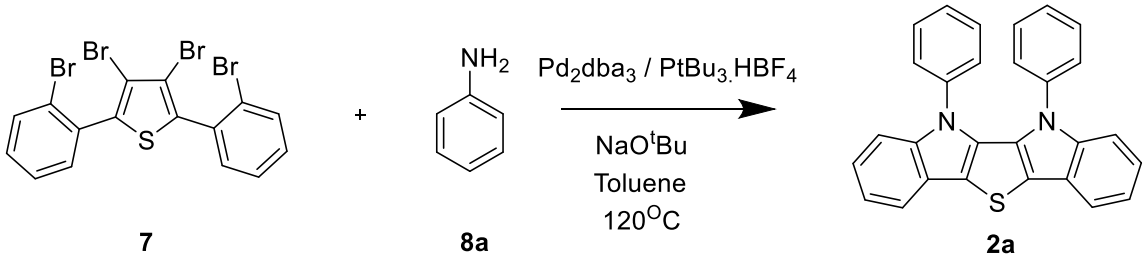
2,3,4,5-Tetrabromothiophene (1.00 g, 2.5 mmol), (2-bromophenyl)boronic acid (1.10 g, 5.5 mmol) and $Pd(PPh_3)_4$ (5 mol%, 144 mg, 125 µmol) were dissolved in 1,4-dioxane (40 mL) under argon atmosphere. Then, a degassed aqueous solution of 2M Na_2CO_3 (10 mL) was added. The reaction mixture was heated under reflux for 6 h. The solvent was removed *in vacuo*. The residue was extracted with dichloromethane and water. The organic layer was dried over $MgSO_4$, filtered, and the solvent was evaporated. The yellow residue was purified by column chromatography (silica gel, heptane) to give **7** as a white solid (1.26 g, 91%); mp 132 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 7.68 – 7.59 (m, 2H), 7.41 – 7.16 (m, 6H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 137.6, 133.6, 133.1, 132.6, 130.8, 127.3, 124.8, 114.2; IR (ATR, cm^{-1}): ν = 602 (m), 627 (m), 648 (s), 673 (m), 708 (m), 731 (s), 739 (vs), 985 (m), 1026 (m), 1055 (m), 1284 (m), 1417 (m), 1431 (m), 1456 (m), 3055 (w); GC-MS (EI, 70 eV): *m/z* (%) = 552 (100), 392 (67), 232 (68), 187 (37), 116 (35); HRMS (EI): calcd. for $C_{16}H_8Br_4S$ ($[M]^+$): 547.70747; found: 547.708302; calcd. for $C_{16}H_8Br_3{}^{81}BrS$ ($[M]^+$): 549.70543; found: 549.705972; calcd. for $C_{16}H_8Br_2{}^{81}Br_2S$ ($[M]^+$): 553.70133; found: 553.701289; calcd. for $C_{16}H_8{}^{81}Br_4S$ ($[M]^+$): 555.69929; found: 555.699282.



3-bromo-2-(2-bromophenyl)benzo[b]thiophene **11** was prepared following general procedure 1**.** 2,3-Dibromobenzo[*b*]thiophene (500 mg, 1.7 mmol), 2-bromophenyl boronic acid (412.6 mg, 2.0 mmol) and (5 mol%) $Pd(PPh_3)_4$ (99 mg, 85 µmol) were dissolved in 1,4-dioxane (30 mL) under argon atmosphere. Then, a degassed aqueous solution of 2M Na_2CO_3 (7 mL) was added. The reaction mixture was heated under reflux for 6 hrs. The solvent was removed *in vacuo*. The residue was extracted with dichloromethane and water. The organic layer was dried over $MgSO_4$, filtered, and the solvent was evaporated. The yellow residue was purified by column chromatography (silica gel, heptane) to give **11** as white solid (592 mg, 94 %); mp 76-78 °C;

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.83 – 7.73 (m, 2H), 7.65 (dd, *J* = 7.9, 0.8 Hz, 1H), 7.46 – 7.21 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 138.4, 137.9, 137.3, 134.1, 133.0, 132.5, 130.6, 127.2, 125.7, 125.2, 124.6, 123.6, 122.3, 108.5; IR (ATR, cm^{-1}): ν = 559 (w), 602 (m), 625 (m), 648 (s), 671 (m), 708 (m), 731 (s), 742 (vs), 856 (m), 872 (m), 943 (m), 984 (m), 1026 (s), 1053 (m), 1119 (w), 1161 (w), 1228 (m), 1261 (m), 1284 (m), 1302 (m), 1417 (m), 1431 (m), 1456 (s), 1560 (w), 1562 (m), 1587 -(w), 1888 (w), 1925 (w), 1957 (w), 3055 (m), 3109 (w); GC-MS (EI, 70 eV): m/z (%) = 368 (87), 208 (100), 163 (25), 104 (23); HRMS (EI): calcd. for $C_{14}H_8Br_2S$ ($[M]^+$): 365.87080; found: 365.87074; calcd. for $C_{14}H_8Br^{81}BrS$ ($[M]^+$): 367.86875; found: 367.86875; calcd. for $C_{14}H_8{}^{81}Br_2S$ ($[M]^+$): 369.86670; found: 369.86651.

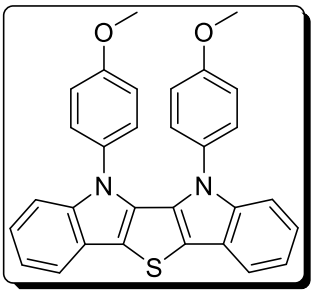
General procedure 2 for double C-N coupling with aniline derivatives, exemplified by: *5,6-diphenyl-5,6-dihydrothieno[3,2-b:4,5-b']diindole* 2a



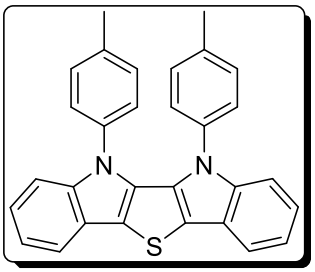
7 **8a** **2a**

Sodium *tert*-butoxide (105 mg, 1.1 mmol) was added to a pressure tube charged with $Pd_2(dba)_3$ (16.7 mg, 0.02 mmol) and ligand P*t*Bu_3·HBF_4 (5.3 mg, 0.2 mmol) under argon atmosphere. Compound **7** (100 mg, 0.18 mmol) and aniline (0.1 mL, 1.1 mmol) were added to the mixture and the tube was backfilled with argon several times. The mixture was stirred at 120 °C in anhydrous toluene (5 mL) for 14 hours. After cooling, the reaction mixture was diluted with dichloromethane (5 mL), filtered through a celite pad, and washed with dichloromethane (20 mL). The filtrate was concentrated *in vacuo*. The product was purified by flash chromatography (silica gel, dichloromethane/heptane = 1:10) to yield **2a** (63 mg, 84%) as white crystals; mp 266 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.76 – 7.67 (m, 2H), 7.22 – 7.03 (m, 10H), 6.99 – 6.92 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 142.3, 138.9, 130.2, 129.0, 127.2, 126.5, 123.3, 123.0, 121.6, 120.7, 118.2, 111.3. IR (ATR, cm^{-1}): ν = 565(m), 615 (m), 660 (s), 677 (s), 690 (vs), 729 (vs), 744 (s), 760 (m), 810 (m), 835 (m), 849 (m), 903 (m), 926 (m), 962 (m), 1003 (m), 1014 (m), 1072 (m), 1115 (m), 1149 (m), 1159 (m), 1215 (m), 1290 (s), 1308 (s), 1323 (s), 1363 (m), 1385 (m), 1450 (s), 1495 (m), 1516 (m), 1593 (m), 1878 (w), 1886 (w), 1915 (w), 1942 (w), 1963 (w), 3034 (w), 3057 (w); GC-

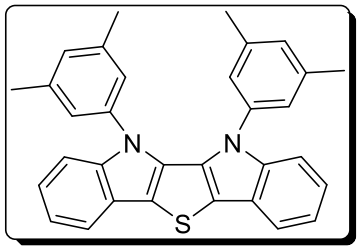
MS (EI, 70 eV): *m/z* (%) = 414 (100), 308 (5), 207 (11); HRMS (EI): calcd. for $C_{28}H_{18}N_2S$ ($[M]^+$): 414.11852; found: 414.118357.



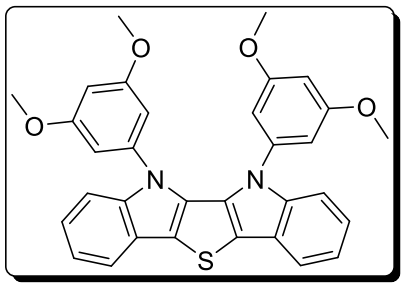
5,6-Bis(4-methoxyphenyl)-5,6-dihydrothieno[3,2-b:4,5-b']diindole **2b** was prepared following general procedure 2 using compound **7** (100 mg, 0.18 mmol) and 4-methoxyaniline (135 mg, 1.1 mmol). The product was purified by flash chromatography (slica gel, ethylacetate/heptane = 1:10) to yield **2b** (81 mg, 94 %) as white crystals; mp 251 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 7.88 – 7.56 (m, 2H), 7.20 – 7.01 (m, 6H), 7.00 – 6.88 (m, 4H), 6.56 – 6.39 (m, 4H), 3.75 (s, 6H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 158.3, 142.6, 131.6, 130.6, 128.3, 122.9, 122.7, 120.7, 120.3, 118.0, 114.2, 111.2, 55.1; IR (ATR, cm^{-1}): ν = 563 (m), 580 (s), 592 (m), 650 (m), 658 (w), 741 (vs), 746 (s), 812 (s), 835 (s), 1014 (m), 1030 (s), 1105 (m), 1169 (m), 1182 (m), 1225 (m), 1250 (vs), 1290 (m), 1300 (m), 1327 (m), 1362 (w), 1406 (w), 1444 (m), 1456 (m), 1510 (s), 1529 (s), 1606 (w), 1873 (vw), 1894 (vw), 1934 (vw), 2839 (w), 2914 (w), 2964 (w), 2995 (w), 3016 (w), 3047 (w); GC-MS (EI, 70 eV): m/z (%) = 474 (100), 458 (8), 237 (6); HRMS (EI): calcd. for $C_{30}H_{22}O_2N_2S$ ($[M]^+$): 474.13965; found: 474.139083.



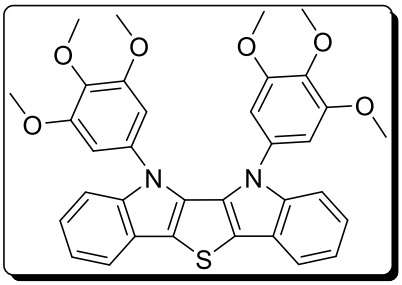
5,6-Di-p-tolyl-5,6-dihydrothieno[3,2-b:4,5-b']diindole **2c** was prepared following general procedure 2 using compound **7** (100 mg, 0.18 mmol) and 4-methylaniline (117 mg, 1.1 mmol). The product was purified by flash chromatography (silica gel, dichloromethane/heptane = 1:10) to yield **2c** (73 mg, 92 %) as white crystals; mp 211-213 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 7.78 – 7.65 (m, 2H), 7.22 – 7.08 (m, 6H), 6.98 – 6.86 (m, 4H), 6.77 (d, *J* = 8.0 Hz, 4H), 2.25 (s, 6H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 142.4, 136.7, 136.3, 130.4, 129.5, 126.6, 123.1, 122.7, 121.1, 120.4, 118.1, 111.3, 21.1; IR (ATR, cm^{-1}): ν = 559 (m), 586 (m), 640 (m), 658 (m), 681 (m), 710 (s), 729 (vs), 806 (s), 831 (m), 964 (m), 1001 (m), 1016 (m), 1107 (m), 1213 (s), 1321 (s), 1389 (s), 1450 (s), 1506 (s), 1514 (s), 1605 (w), 1867 (w), 1878 (w), 1905 (w), 2351 (w), 2727 (w), 2856 (m), 2918 (m), 3030 (m), 3053 (w); GC-MS (EI, 70 eV): m/z (%) = 442 (100), 221 (10); HRMS (EI): calcd. for $C_{30}H_{22}N_2S$ ($[M]^+$): 442.14982; found: 442.149965.



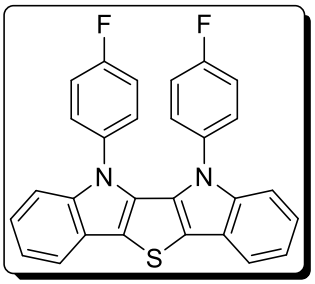
5,6-Bis(3,5-dimethylphenyl)-5,6-dihydrothieno[3,2-b:4,5-b']diindole **2d** was prepared following general procedure 2 using compound **7** (100 mg, 0.18 mmol) and 3,5-dimethylaniline (0.14 mL, 1.1 mmol). The product was purified by flash chromatography (silica gel, dichloromethane/heptane = 1:10) to yield the indole **2d** (77 mg, 91 %) as white crystals; mp 258-260 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.77 – 7.63 (m, 2H), 7.26 (dd, *J* = 6.8, 2.0 Hz, 2H), 7.20 – 7.05 (m, 4H), 6.73 (s, 4H), 6.56 (s, 2H), 2.10 (s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 142.3, 139.0, 138.4, 130.3, 128.5, 123.8, 123.4, 122.8, 121.4, 120.6, 118.2, 111.4, 21.2; IR (ATR, cm^{-1}): ν = 544 (m), 650 (m), 685 (s), 725 (vs), 729 (vs), 744 (s), 827 (m), 839 (s), 1012 (m), 1036 (m), 1115 (m), 1219 (m), 1284 (m), 1298 (m), 1323 (s), 1377 (m), 1392 (m), 1454 (s), 1464 (m), 1525 (m), 1593 (m), 1867 (vw), 1907 (vw), 1934 (vw), 2854 (w), 2912 (w), 2943 (w), 3030 (w), 3049 (w); GC-MS (EI, 70 eV): m/z (%) = 470 (100), 235 (7); HRMS (EI): calcd. for $C_{32}H_{26}N_2S$ ($[M]^+$): 470.18112; found: 470.181420.



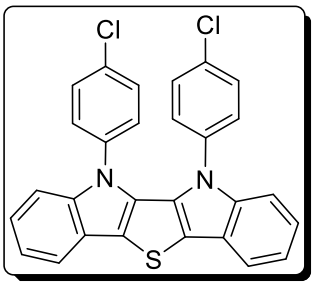
5,6-Bis(3,5-dimethoxyphenyl)-5,6-dihydrothieno[3,2-b:4,5-b']diindole **2e** was prepared following general procedure 2 using compound **7** (100 mg, 0.18 mmol) and 3,5-dimethoxyaniline (167 mg, 1.1 mmol). The product was purified by flash chromatography (silica gel, ethylacetate/heptane = 1:5) to yield **2e** (93 mg, 97 %) as white crystals; mp 232 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.75 – 7.66 (m, 2H), 7.30 (dd, *J* = 7.0, 1.8 Hz, 2H), 7.19 – 7.09 (m, 4H), 6.31 (d, *J* = 2.3 Hz, 4H), 6.09 (t, *J* = 2.3 Hz, 2H), 3.64 (s, 12H); ^{13}C NMR (126 MHz, $CDCl_3$) δ = 160.6, 141.9, 140.8, 130.0, 123.2, 123.0, 121.4, 120.7, 118.2, 111.5, 104.8, 99.8, 55.0; IR (ATR, cm^{-1}): ν = 534 (m), 634 (m), 656 (m), 663 (m), 681 (s), 704 (m), 731 (s), 744 (vs), 814 (m), 825 (s), 849 (m), 877 (m), 928 (m), 970 (m), 987 (w), 1012 (m), 1038 (s), 1063 (s), 1155 (s), 1198 (s), 1203 (s), 1286 (s), 1319 (m), 1358 (m), 1371 (m), 1431 (m), 1452 (s), 1477 (m), 1529 (m), 1593 (s), 1842 (vw), 1859 (vw), 1894 (vw), 1932 (vw), 2897 (w), 2935 (w), 2953 (w), 2993 (w), 3012 (w), 3049 (w); GC-MS (EI, 70 eV): m/z (%) = 534 (100), 267 (4); HRMS (EI): calcd. for $C_{32}H_{26}O_4N_2S$ ($[M]^+$): 534.16078; found: 534.160294.



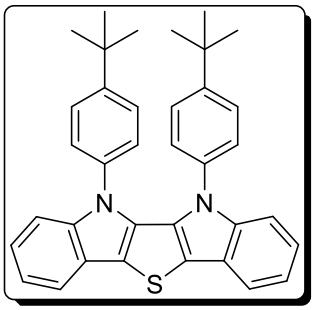
5,6-Bis(3,4,5-trimethoxyphenyl)-5,6-dihydrothieno[3,2-b:4,5-b']diindole **2f** was prepared following general procedure 2 using **7** (100 mg, 0.18 mmol) and 3,4,5-trimethoxyaniline (201 mg, 1.1 mmol). The product was separated via flash chromatography (elutant: 20 % ethylacetate – heptane) to yield **2f** (99 mg, 92 %) as white crystals; mp 214-217 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.72 (dd, *J* = 6.0, 2.6 Hz, 2H), 7.31 (dd, *J* = 6.3, 2.7 Hz, 2H), 7.21-7.15 (m, 4H), 6.37 (s, 4H), 3.76 (s, 6H), 3.68 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ = 152.9, 142.6, 136.6, 134.9, 130.2, 123.4, 123.2, 121.8, 121.0, 118.4, 111.4, 103.8, 60.8, 55.9; IR (ATR, cm^{-1}): ν = 567 (m), 611 (m), 627 (m), 656 (m), 667 (m), 677 (m), 698 (s), 715 (s), 729 (vs), 771 (m), 829 (m), 910 (m), 999 (s), 1080 (m), 1124 (vs), 1225 (s), 1290 (s), 1323 (m), 1371 (m), 1417 (s), 1433 (m), 1454 (s), 1504 (s), 1591 (s), 1842 (vw), 1905 (vw), 2835 (w), 2931 (w), 2951 (w), 2995 (w), 3051 (w); GC-MS (EI, 70 eV): m/z (%) = 594 (100), 297 (15), 69 (16); HRMS (EI): calcd. for $C_{34}H_{30}O_6N_2S$ ($[M]^+$): 594.18191; found: 594.182214.



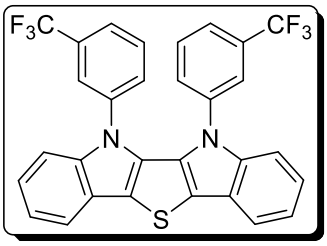
5,6-Bis(4-fluorophenyl)-5,6-dihydrothieno[3,2-b:4,5-b']diindole **2g** was prepared following general procedure 2 using compound **7** (100 mg, 0.18 mmol) and 4-fluoroaniline (0.104 mL, 1.1 mmol). The product was purified by flash chromatography (silica gel, dichloromethane/heptane = 1:10) to yield **2g** (77 mg, 95 %) as white crystals; mp 298-230 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.72 (d, *J* = 6.9 Hz, 2H), 7.18-7.01 (m, 10H), 6.75 (t, *J* = 8.5 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 161.5 (d, *J* = 247.8 Hz), 142.5, 135.0, 130.2, 128.7 (d, *J* = 8.7 Hz), 123.2, 121.7, 120.9, 118.3, 116.0 (d, *J* = 22.8 Hz), 111.1.^{19}F NMR (282 MHz, $CDCl_3$) δ = 114.11; IR (ATR, cm^{-1}): ν = 569 (s), 586 (m), 644 (m), 712 (s), 733 (v), (s), 758 (m), 779 (m), 818 (s), 837 (m), 847 (m), 1001 (m), 1007 (m), 1011 (m), 1092 (m), 1113 (m), 1151 (s), 1209 (s), 1225 (s), 1267 (m), 1300 (m), 1323 (s), 1367 (m), 1392 (m), 1452 (m), 1506 (s), 1533 (m), 1606 (w), 1882 (w), 3064 (w), 3115 (w); GC-MS (EI, 70 eV): m/z (%) = 450 (100), 225 (9), 60 (6); 43 (6); HRMS (EI): calcd. for $C_{28}H_{16}N_2F_2S$ ($[M]^+$): 450.09968; found: 450.09984.



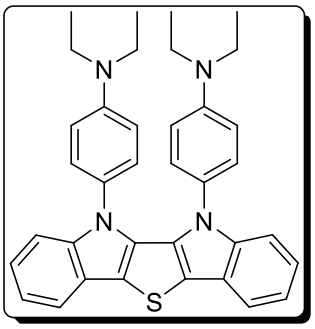
5,6-Bis(4-chlorophenyl)-5,6-dihydrothieno[3,2-b:4,5-b']diindole **2h** was prepared following general procedure 2 using compound **7** (100 mg, 0.18 mmol) and 4-chloroaniline (140 mg, 1.1 mmol). The product was purified by flash chromatography (silica gel, dichloromethane/heptane = 1:10) to yield **2h** (75 mg, 86 %) as white crystals; mp 308 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 7.76 – 7.68 (m, 2H), 7.24 – 7.10 (m, 6H), 7.08 – 6.96 (m, 8H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 142.20, 137.53, 133.48, 129.87, 129.33, 128.00, 123.35, 122.13, 121.11, 118.42, 111.09; IR (ATR, cm^{-1}): ν = 569 (m), 615 (w), 634 (w), 652 (w), 679 (m), 723 (m), 737 (vs), 798 (s), 839 (s), 1014 (m), 1090 (s), 1221 (m), 1269 (m), 1286 (m), 1302 (m), 1323 (s), 1390 (s), 1454 (s), 1493 (s), 1520 (m), 1591 (w), 1890 (vw), 1900 (vw), 2322 (vw), 2351 (vw), 3053 (w), 3091 (w); GC-MS (EI, 70 eV): m/z (%) = 482 (100), 335 (7), 241 (10), 205 (9); HRMS (EI): calcd. for $C_{28}H_{16}N_2Cl_2S$ ($[M]^+$): 482.04058; found: 482.040632; calcd. for $C_{28}H_{16}N_2Cl^{37}ClS$ ($[M]^+$): 484.03763; found: 484.038435; calcd. for $C_{28}H_{16}N_2{}^{37}Cl_2S$ ($[M]^+$): 486.03468; found: 486.034440.



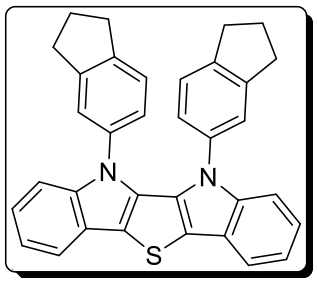
5,6-Bis(4-(tert-butyl)phenyl)-5,6-dihydrothieno[3,2-b:4,5-b']diindole **2i** was prepared following general procedure 2 using compound **7** (100 mg, 0.18 mmol) and 4-(*tert*-butyl)aniline (0.17 mL, 1.1 mmol). The product was purified by flash chromatography (silica gel, dichloromethane/heptane = 1:10) to yield **2i** (83 mg, 87 %) as white crystals; mp 287 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 7.73 – 7.67 (m, 2H), 7.22 – 7.05 (m, 6H), 7.05 – 6.98 (m, 4H), 6.95 – 6.89 (m, 4H), 1.21 (s, 18H).^{13}C NMR (63 MHz, $CDCl_3$) δ = 149.2, 144.0, 136.9, 131.4, 125.7, 125.6, 124.1, 122.9, 122.2, 120.9, 118.3, 111.8, 34.4, 31.3; IR (ATR, cm^{-1}): ν = 544 (s), 557 (m), 573 (m), 584 (m), 625 (w), 640 (w), 658 (w), 688 (m), 708 (m), 733 (vs), 800 (m), 839 (m), 922 (w), 958 (w), 995 (m), 1014 (m), 1109 (m), 1194 (m), 1221 (m), 1265 (m), 1279 (m), 1290 (m), 1313 (s), 1362 (m), 1402 (m), 1450 (m), 1512 (s), 1547 (m), 1574 (w), 1601 (w), 1842 (vw), 1900 (vw), 2864 (w), 2901 (w), 2928 (w), 2958 (m), 3036 (w), 3053 (w); GC-MS (EI, 70 eV): m/z (%) = 526 (100), 494 (13), 454 (15); HRMS (EI): calcd. for $C_{36}H_{34}N_2S$ ($[M]^+$): 526.24372; found: 526.243665.



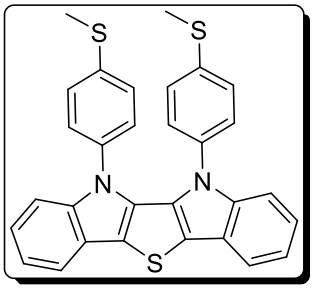
5,6-Bis(3-(trifluoromethyl)phenyl)-5,6-dihydrothieno[3,2-b:4,5-b']diindole **2j** was prepared following general procedure 2 using compound **7** (100 mg, 0.18 mmol) and 3-(trifluoromethyl)aniline (0.14 mL, 1.1 mmol). The product was purified by flash chromatography (silica gel, dichloromethane/heptane = 1:10) to yield **2j** (88 mg, 89 %) as white crystals; mp 203-205 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 7.76 – 7.68 (m, 2H), 7.36 (s, 2H), 7.33 – 7.26 (m, 2H), 7.25 – 7.08 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 142.3, 139.8, 131.5 (q, *J* = 33.0 Hz), 130.1, 129.6, 129.5, 124.0 (q, *J* = 2.0 Hz), 123.7, 123.3 (q, *J* = 272.5 Hz), 123.2 (q, *J* = 1.6 Hz),123.1, 121.6, 118.6, 110.9.^{19}F NMR (282 MHz, $CDCl_3$) δ = 62.73; IR (ATR, cm^{-1}): ν = 563 (m), 619 (m), 658 (s), 675 (s), 700 (v), (s), 735 (v), (s), 798 (s), 843 (w), 899 (m), 1011 (m), 1051 (s), 1068 (s), 1093 (s), 1117 (v), (s), 1165 (s), 1219 (m), 1263 (s), 1302 (s), 1317 (s), 1335 (s), 1392 (m), 1454 (s), 1495 (m), 1525 (w), 1593 (w), 1886 (v), (w), 1929 (v), (w), 3032 (w), 3055 (w); GC-MS (EI, 70 eV): m/z (%) = 550 (100), 275 (14); HRMS (EI): calcd. for $C_{30}H_{16}N_2F_6S$ ([M]$^+$): 550.09329; found: 550.093522.



4,4'-(Thieno[3,2-b:4,5-b']diindole-5,6-diyl)bis(N,N-diethylaniline) **2k** was prepared following general procedure 2 using compound **7** (100 mg, 0.18 mmol) and *N*^{1},*N*^{1}-diethylbenzene-1,4-diamine (0.18 mL, 1.1 mmol). The product was purified by flash chromatography (silica gel, dichloromethane/heptane = 1:2) to yield **2k** (60 mg, 60 %) as white crystals; mp 256 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.68 (dd, *J* = 6.9, 1.6 Hz, 2H), 7.17 – 7.01 (m, 6H), 6.81 (d, *J* = 8.9 Hz, 4H), 6.21 (d, *J* = 8.9 Hz, 4H), 3.22 (q, *J* = 7.0 Hz, 8H), 1.09 (t, *J* = 7.0 Hz, 12H).^{13}C NMR (75 MHz, $CDCl_3$) δ = 146.6, 143.3, 131.3, 127.9, 126.8, 122.9, 122.3, 119.9, 117.8, 111.7, 111.3, 44.3, 12.8; IR (ATR, cm^{-1}): ν = 565 (m), 580 (m), 617 (m), 636 (m), 644 (m), 652 (m), 727 (s), 744 (vs), 787 (s), 798 (s), 822 (m), 1009 (s), 1080 (s), 1159 (m), 1184 (s), 1198 (s), 1267 (s), 1323 (s), 1352 (s), 1375 (s), 1387 (s), 1408 (m), 1450 (s), 1516 (vs), 1608 (m), 1842 (w), 1857 (w), 1888 (w), 1932 (w), 2868 (m), 2891 (m), 2928 (m), 2966 (m), 3024 (w), 3047 (w), 3076 (w); GC-MS (EI, 70 eV): m/z (%) = 556 (100), 512 (8), 97 (11), 83 (11), 57 (19); HRMS (EI): calcd. for $C_{36}H_{36}N_4S$ ([M]$^+$): 556.26552; found: 556.264565.

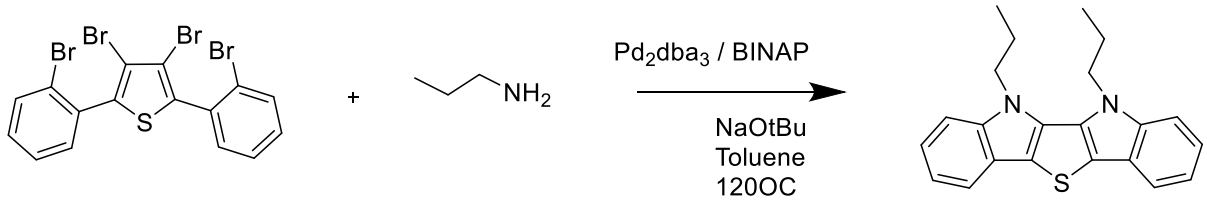


5,6-Bis(2,3-dihydro-1H-inden-5-yl)-5,6-dihydrothieno[3,2-b:4,5-b']diindole **2l** was prepared following general procedure 2 using compound **7** (100 mg, 0.18 mmol) and 2,3-dihydro-1H-inden-5-amine (145 mg, 1.1 mmol). The product was purified by flash chromatography (silica gel, dichloromethane/heptane = 1:10) to yield **2l** (81 mg, 91%) as white crystals; mp 246 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.75 – 7.64 (m, 2H), 7.31 – 7.19 (m, 2H), 7.17 – 7.05 (m, 4H), 7.02 – 6.75 (m, 6H), 2.71 (t, *J* = 7.3 Hz, 4H), 2.58 (s, 4H), 1.94 (p, *J* = 7.5 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 145.0, 142.5, 142.3, 137.3, 130.4, 124.0, 123.9, 123.3, 122.8, 122.4, 121.2, 120.5, 118.1, 111.4, 32.6, 32.5, 25.3; IR (ATR, cm^{-1}): ν = 542 (m), 575 (m), 619 (m), 690 (m), 729 (vs), 781 (m), 820 (m), 918 (m), 1009 (m), 1115 (m), 1155 (m), 1215 (m), 1296 (m), 1321 (s), 1363 (m), 1390 (m), 1435 (m), 1452 (s), 1489 (m), 1520 (m), 1583 (w), 1605 (w), 1867 (w), 1888 (w), 2839 (w), 2929 (w), 3014 (w), 3043 (w); GC-MS (EI, 70 eV): m/z (%) = 494 (100), 464 (20); HRMS (EI): calcd. for $C_{34}H_{26}N_2S$ ($[M]^+$): 494.18112; found: 494.180637.

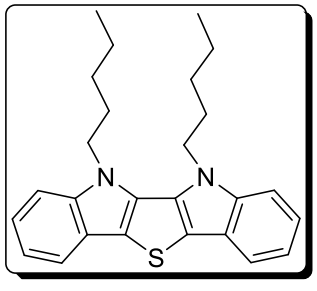


5,6-Bis(4-(methylthio)phenyl)-5,6-dihydrothieno[3,2-b:4,5-b']diindole **2m** was prepared following general procedure 2 using compound **7** (100 mg, 0.18 mmol) and 4-(methylthio)aniline (0.14 mL, 1.1 mmol). The product was purified by flash chromatography (silica gel, ethylacetate/heptane = 1:10) to yield **2m** (82 mg, 90 %) as white crystals; mp 262 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.75 – 7.66 (m, 2H), 7.22 – 7.07 (m, 6H), 7.01 – 6.90 (m, 4H), 6.90 – 6.80 (m, 4H), 2.47 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 142.5, 137.9, 135.7, 130.2, 127.2, 126.3, 123.2, 123.0, 121.5, 120.7, 118.2, 111.3, 15.6; IR (ATR, cm^{-1}): ν = 569 (m), 638 (m), 648 (m), 692 (m), 717 (s), 739 (vs), 795 (s), 835 (m), 918 (w), 958 (m), 1014 (m), 1095 (m), 1151 (w), 1176 (m), 1217 (m), 1292 (m), 1304 (m), 1319 (m), 1392 (s), 1454 (m), 1495 (s), 1531 (m), 1842 (vw), 1878 (vw), 2848 (w), 2918 (w), 2951 (w), 3047 (w); GC-MS (EI, 70 eV): m/z (%) = 506 (100), 458 (11); HRMS (EI): calcd. for $C_{30}H_{22}N_2S_3$ ($[M]^+$): 506.09396; found: 506.09362.

General procedure 3 for double C-N coupling with aniline derivatives, exemplified by: ***5,6-dipropyl-5,6-dihydrothieno[3,2-b:4,5-b']diindole*** **2n**

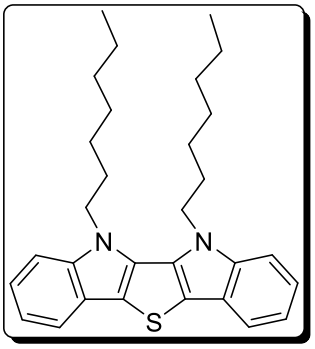


Sodium *tert*-butoxide (105 mg, 1.1 mmol) was added to a pressure tube charged with $Pd_2(dba)_3$ (16.7 mg, 0.02 mmol) and BINAP (5.7 mg, 0.009 mmol) under argon atmosphere. Compound **7** (100 mg, 0.18 mmol) and *n*-propylamine (0.09 mL, 1.1 mmol) were added to this mixture and the tube was backfilled with argon several times. The mixture was heated at 120 °C in anhydrous toluene (5 mL) for 14 hours. After cooling, the reaction mixture was diluted with dichloromethane (5 mL), filtered through a celite pad, and washed with dichloromethane (20 mL). The filtrate was concentrated *in vacuo*. The product was purified by flash chromatography (silica gel, dichloromethane/heptane = 1:10) to yield **2n** (29 mg, 46%) as white crystals; mp 162-164 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.67 (d, *J* = 7.7 Hz, 2H), 7.37 (d, *J* = 8.3 Hz, 2H), 7.30 – 7.03 (m, 4H), 4.49 – 4.31 (t, *J* = 7.7 Hz, 4H), 2.00 – 1.80 (m, 4H), 0.94 (t, *J* = 7.4 Hz, 6H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 141.1, 130.1, 123.0, 122.3, 119.9, 119.6, 118.3, 110.1, 47.9, 23.9, 11.3; IR (ATR, cm^{-1}): ν = 563 (m), 615 (m), 658 (m), 723 (vs), 812 (m), 845 (w), 881 (m), 897 (m), 974 (m), 1012 (m), 1111 (m), 1153 (m), 1292 (m), 1319 (m), 1367 (m), 1381 (m), 1456 (m), 1520 (w), 1867 (vw), 1915 (vw), 2850 (w), 2872 (w), 2924 (m), 2953 (w); GC-MS (EI, 70 eV): *m/z* (%) = 346 (100), 317 (14), 275 (17); HRMS (EI): calcd. for $C_{22}H_{22}N_2S$ ($[M]^+$): 346.14982; found: 346.15023.

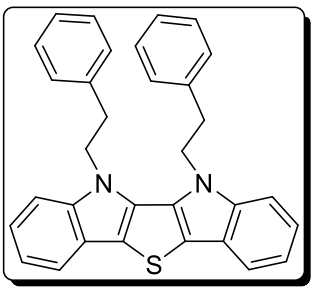


5,6-Dipentyl-5,6-dihydrothieno[3,2-b:4,5-b']diindole **2o** was prepared following general procedure 3 using compound **7** (100 mg, 0.18 mmol) and n-pentylamine (0.13 ml, 1.1 mmol). The product was purified by flash chromatography (silica gel, dichloromethane/heptane = 1:10) to yield **2o** (33 mg, 45 %) as white crystals; mp 105-107 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.71 – 7.61 (m, 2H), 7.36 (d, *J* = 8.3 Hz, 2H), 7.18 (m, 4H), 4.41 (t, *J* = 7.8 Hz, 4H), 1.94 – 1.75 (m, 4H), 1.38 – 1.20 (m, 8H), 0.82 (t, *J* = 7.0 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 141.1, 130.1, 123.0, 122.3, 119.9, 119.6, 118.3, 110.1, 46.4, 30.4, 29.2, 22.5, 13.9; IR (ATR,

cm^{-1}): ν = 565 (w), 586 (w), 609 (m), 617 (m), 654 (m), 690 (m), 731 (vs), 916 (w), 976 (w), 1014 (m), 1111 (m), 1138 (m), 1155 (m), 1173 (m), 1232 (m), 1321 (s), 1362 (m), 1377 (m), 1387 (m), 1456 (s), 1471 (m), 1520 (m), 1606 (w), 1747 (vw), 1790 (vw), 1834 (vw), 1867 (vw), 1907 (vw), 2858 (m), 2866 (m), 2922 (m), 2949 (m), 3026 (vw), 3055 (w), 3078 (vw); GC-MS (EI, 70 eV): m/z (%) = 402 (100), 275 (15); HRMS (EI): calcd. for $C_{26}H_{30}N_2S$ ($[M]^+$): 402.21242; found: 402.21232.

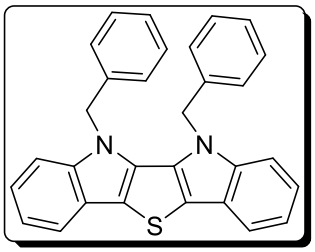


5,6-Diheptyl-5,6-dihydrothieno[3,2-b:4,5-b']diindole **2p** was prepared following general procedure 3 using compound **7** (100 mg, 0.18 mmol) and n-heptylamine (0.16 mL, 1.1 mmol). The product was purified by flash chromatography (silica gel, dichloromethane/heptane = 1:10) to yield **2p** (37 mg, 45 %) as white crystals; mp 127-129 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 7.66 (d, *J* = 7.2 Hz, 2H), 7.35 (d, *J* = 8.2 Hz, 2H), 7.29 – 7.06 (m, 4H), 4.40 (t, *J* = 7.9 Hz, 4H), 1.96 – 1.68 (m, 4H), 1.41 – 1.02 (m, 16H), 0.79 (t, *J* = 6.7 Hz, 6H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 141.1, 130.1, 123.0, 122.3, 119.9, 119.6, 118.3, 110.1, 46.5, 31.6, 30.7, 29.0, 27.0, 22.5, 14.0; IR (ATR, cm^{-1}): ν = 550 (vw), 567 (w), 588 (w), 609 (w), 621 (w), 656 (w), 729 (vs), 756 (m), 808 (w), 837 (w), 916 (w), 970 (w), 1012 (m), 1115 (m), 1157 (m), 1169 (m), 1221 (m), 1321 (s), 1373 (m), 1389 (m), 1458 (s), 1471 (m), 1522 (w), 1608 (w), 1790 (vw), 1830 (vw), 1867 (vw), 1907 (vw), 2852 (m), 2922 (s), 2947 (m), 3030 (vw), 3057 (w), 3074 (vw); GC-MS (EI, 70 eV): m/z (%) = 458 (100), 275 (16); HRMS (ESI): calcd. for $C_{30}H_{39}N_2S$ ($[M + H]^+$): 459.28285; found: 459.28189.

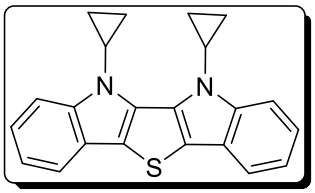


5,6-Diphenethyl-5,6-dihydrothieno[3,2-b:4,5-b']diindole **2q** was prepared following general procedure 3 using compound **7** (100 mg, 0.18 mmol) and 2-phenylethanamine (0.14 mL, 1.1 mmol). The product was purified by flash chromatography (silica gel, dichloromethane/heptane = 1:7) to yield **2q** (53 mg, 62 %) as dark brown crystals; mp 141 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.68 (dd, *J* = 7.3, 1.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.25 – 7.09 (m, 10H), 6.96 (dd, *J* = 6.5, 3.0 Hz, 4H), 4.66 (t, *J* = 8.0 Hz, 4H), 3.07 (t, *J* = 8.0 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 140.9, 137.5, 130.0, 128.7, 128.5, 126.8, 123.2, 122.5, 120.3, 119.8, 118.4, 110.1, 47.7, 36.5; IR (ATR, cm^{-1}): ν = 538 (m), 557 (m), 567 (w), 590 (w), 615 (m), 633 (m), 696 (vs), 731 (vs), 845 (w), 904 (w), 974 (w), 1014 (m), 1026 (m), 1076 (w), 1084 (w), 1159 (m), 1232

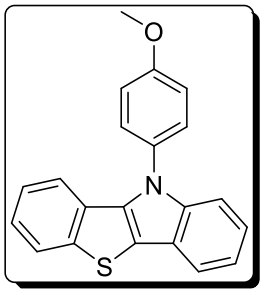
(m), 1284 (m), 1315 (m), 1352 (m), 1387 (m), 1456 (s), 1495 (m), 1516 (w), 1531 (m), 1867 (vw), 1882 (vw), 2854 (w), 2872 (w), 2924 (w), 2966 (w), 3024 (w), 3055 (w); GC-MS (EI, 70 eV): m/z (%) = 470 (100), 379 (24), 346 (10), 287(23), 275 (74), 207 (10); HRMS (EI): calcd. for $C_{32}H_{26}N_2S$ ($[M]^+$): 470.18112; found: 470.180791.



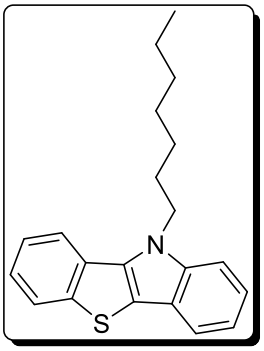
5,6-Dibenzyl-5,6-dihydrothieno[3,2-b:4,5-b']diindole **2r** was prepared following general procedure 3 using compound **7** (100 mg, 0.18 mmol) and 2-benzylamine (0.12 mL, 1.1 mmol). The product was purified by flash chromatography (silica gel, dichloromethane/heptane = 1:7) to yield **2r** (43 mg, 53 %) as dark crystals; mp 227-229 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.75 – 7.67 (m, 2H), 7.26 – 7.08 (m, 12H), 6.93 – 6.81 (m, 4H), 5.27 (s, 4H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 141.4, 137.2, 130.4, 129.0, 127.5, 125.1, 123.0, 122.8, 120.2, 120.0, 118.3, 110.1, 48.7; IR (ATR, cm^{-1}): ν = 557 (s), 592 (m), 609 (m), 652 (s), 690 (vs), 719 (vs), 737 (vs), 758 (m), 843 (m), 904 (m), 926 (m), 964 (m), 1014 (m), 1032 (m), 1072 (m), 1157 (m), 1167 (m), 1188 (m), 1259 (m), 1315 (s), 1321 (s), 1346 (s), 1381 (s), 1450 (s), 1495 (m), 1520 (m), 1605 (w), 1886 (w), 1927 (w), 2848 (w), 2918 (w), 3028 (m), 3063 (w), 3080 (w); GC-MS (EI, 70 eV): m/z (%) = 442 (100), 365 (12), 351 (60), 260 (7), 91 (9); HRMS (EI): calcd. for $C_{30}H_{22}N_2S$ ($[M]^+$): 442.14982; found: 442.14992.



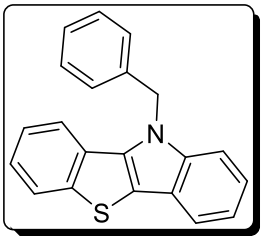
5,6-Dicyclopropyl-5,6-dihydrothieno[3,2-b:4,5-b']diindole **2s** was prepared following general procedure 3 using compound **7** (100 mg, 0.18 mmol) and cyclopropylamine (0.08 mL, 1.1 mmol). The product was purified by flash chromatography (silica gel, dichloromethane/heptane = 1:7) to yield **2s** (20 mg, 33 %) as a yellow solid; mp 222-224 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.67 – 7.53 (m, 4H), 7.28 – 7.08 (m, 4H), 3.86 – 3.75 (m, 2H), 1.29 – 1.12 (m, 8H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 142.2, 130.6, 122.9, 122.3, 119.8, 119.5, 118.2, 112.1, 28.0, 10.1; IR (ATR, cm^{-1}): ν = 546 (m), 571 (m), 646 (m), 696 (m), 735 (vs), 760 (m), 804 (m), 829 (m), 874 (m), 926 (m), 976 (m), 1011 (m), 1024 (s), 1055 (m), 1113 (m), 1151 (m), 1186 (m), 1223 (m), 1259 (m), 1309 (s), 1348 (s), 1394 (s), 1454 (s), 1531 (m), 1537 (m), 1606 (w), 1807 (w), 1849 (w), 1884 (w), 1921 (w), 2850 (m), 2920 (m), 3003 (w), 3022 (w), 3049 (w), 3076 (w); GC-MS (EI, 70 eV): m/z (%) = 342 (100), 313 (11), 299 (17), 268 (8); HRMS (EI): calcd. for $C_{22}H_{18}N_2S$ ($[M]^+$): 342.11852; found: 342.11827.



10-(4-Methoxyphenyl)-10H-benzo[4,5]thieno[3,2-b]indole **12a** was prepared following general procedure 1 using compound **11** (200 mg, 0.54 mmol) and 4-methoxyaniline (401 mg, 3.3 mmol). The product was purified by flash chromatography (silica gel, ethylacetate/heptane = 1:10) to yield **12a** (172 mg, 96 %) as white crystals; mp 158-160 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.77 (m, 2H), 7.40 (d, *J* = 6.8 Hz, 2H), 7.26 – 7.00 (m, 8H), 3.86 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 158.8, 142.5, 142.3, 137.4, 129.9, 128.4, 126.2, 123.7, 123.3, 123.3, 122.6, 121.3, 119.8, 119.6, 118.6, 115.5, 114.2, 110.3, 55.0; IR (ATR, cm^{-1}): ν = 575 (m), 596 (s), 642 (m), 710 (m), 742 (vs), 806 (m), 827 (m), 858 (m), 1018 (s), 1028 (s), 1057 (m), 1103 (m), 1165 (m), 1182 (m), 1213 (s), 1248 (s), 1298 (m), 1346 (s), 1421 (m), 1437 (m), 1450 (s), 1512 (s), 1583 (w), 1591 (w), 1606 (w), 1867 (w), 1894 (w), 2833 (w), 2928 (w), 2955 (w), 3014 (w), 3049 (w); GC-MS (EI, 70 eV): m/z (%) = 329 (100), 314 (17), 286 (13), 165 (7), 142 (6); HRMS (EI): calcd. for $C_{21}H_{15}ONS$ ($[M]^+$): 329.08689; found: 329.08677.



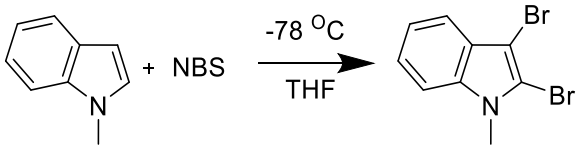
10-Heptyl-10H-benzo[4,5]thieno[3,2-b]indole **12b** was prepared following general procedure 3 using compound **11** (200 mg, 0.54 mmol) and n-heptylamine (0.16 mL, 3.3 mmol). The product was purified by flash chromatography (silica gel, dichloromethane/heptane = 1:10) to yield **12b** (160 mg, 92 %) as a colorless liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.94 – 7.78 (m, 2H), 7.69 (dd, *J* = 7.8, 0.9 Hz, 1H), 7.43 – 7.19 (m, 4H), 7.91-7.82 (m, 1H), 4.46 (t, *J* = 7.5 Hz, 2H), 1.92 – 1.82 (m, 2H), 1.41 – 1.09 (m, 8H), 0.78 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 143.2, 141.4, 137.4, 127.0, 124.6, 124.2, 123.7, 122.8, 121.6, 119.9, 119.4, 119.3, 115.3, 109.9, 45.0, 31.7, 30.5, 29.1, 27.0, 22.6, 14.0; IR (ATR, cm^{-1}): ν = 586 (w), 619 (w), 663 (m), 723 (vs), 731 (vs), 752 (m), 825 (w), 920 (w), 982 (w), 1020 (m), 1072 (m), 1115 (m), 1155 (w), 1171 (m), 1252 (w), 1271 (w), 1323 (m), 1346 (m), 1429 (m), 1454 (m), 1491 (m), 1591 (vw), 1608 (vw), 2852 (m), 2924 (m), 2953 (m), 3026 (vw), 3053 (w); GC-MS (EI, 70 eV): m/z (%) = 321 (100), 236 (94), 222 (14), 165 (7); HRMS (ESI): calcd. for $C_{21}H_{24}NS$ ($[M + H]^+$): 322.1624; found: 322.1623.



10-Benzyl-10H-benzo[4,5]thieno[3,2-b]indole **12c** was prepared following general procedure 3 using compound **11** (200 mg, 0.54 mmol) and benzylamine (0.36 mL, 3.3 mmol). The product was purified by flash chromatography (silica gel, dichloromethane/heptane = 1:7) to yield **12c** (162 mg, 95 %) as white crystals; mp 150-152 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.85 – 7.77 (m, 1H), 7.77 – 7.66 (m, 2H), 7.34 (d, *J* = 8.2 Hz, 1H), 7.28 – 7.10 (m, 7H), 7.08 (dd, *J* = 4.6, 3.5 Hz, 2H), 5.70 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 143.25, 141.89, 137.75, 137.39, 128.98, 127.61, 126.91, 126.08, 124.53, 124.30, 123.91, 123.25, 121.91, 120.00, 119.92, 119.50, 115.88, 110.14, 48.41; IR (ATR, cm^{-1}): ν = 555 (m), 586 (m), 613 (m), 633 (s), 694 (vs), 719 (vs), 731 (vs), 737 (vs), 804 (m), 833 (m), 847 (m), 926 (m), 968 (m), 1018 (m), 1068 (m), 1119 (m), 1153 (m), 1174 (m), 1201 (m), 1257 (m), 1271 (m), 1321 (m), 1348 (s), 1427 (s), 1452 (m), 1495 (m), 1583 (w), 1605 (w), 1888 (w), 1923 (w), 3022 (w), 3053 (w); GC-MS (EI, 70 eV): m/z (%) = 313 (93), 222 (100), 91 (23); HRMS (EI): calcd. for $C_{21}H_{15}NS$ ($[M]^+$): 313.09197; found: 313.09228.

8.5.2 Synthesis of 5-methyl-5,10-dihydroindolo[3,2-b]indole

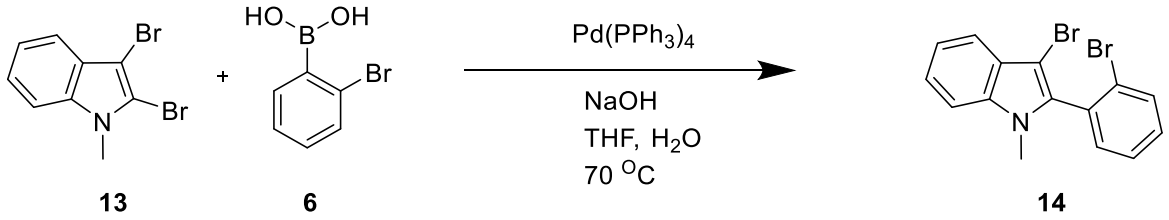
Procedure for prepared of *2,3-dibromo-1-methyl-1H-indole* 13



To solution of 1-methyl-1*H*-indole (1 mL, 8 mmol) in 20 mL THF was added wisely NBS (3.14 g, 17.6 mmol) at -78 ºC. Then the mixture was stirred for 5h at this temperature. The reaction mixture was treated with water (20 mL). The solvent THF was reduced by evaporator *in vacuo* and then extracted with dihloromethane (3 x 20 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$ and then evaporated *in vacuo* affording yellow syrup. The mixture was separated over column chromatography (silica gel, heptane) to yield 2,3-dibromo-1-methyl-1*H*-indole **13** (2 g, 86%) as white solid; m.p. 38-40 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.41 (dt, *J* = 7.6, 1.1 Hz, 1H), 7.15 (dd, *J* = 4.9, 1.2 Hz, 2H), 7.13 – 7.02 (m, 1H), 3.66 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 136.34, 126.96, 122.91, 120.81, 118.86, 114.90, 109.63, 92.68, 32.34; GC/MS (EI,

70eV): m/z (%) = 289 (100), 291 (50), 288 (20), 274 (18), 129 (15), 114 (23), 88 (12); HRMS (EI): calculated for $C_9H_7Br_2N_1$ ([M^+]): 286.89398; found: 286.89391, calculated for $C_9H_7Br_1{}^{81}Br_1N_1$ ([M^+]): 288.89193; found: 288.89183, calculated for $C_9H_7{}^{81}Br_2N_1$ ([M^+]): 290.88988; found: 290.88980.

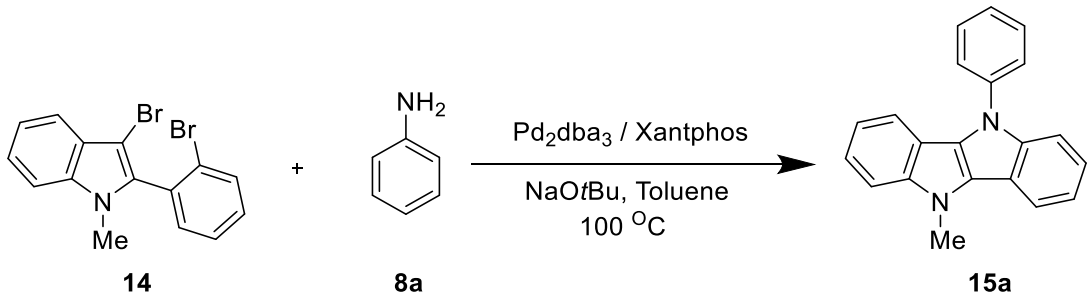
Procedure for prepared of *3-bromo-2-(2-bromophenyl)-1-methyl-1H-indole* 14.



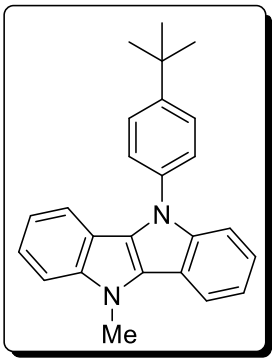
13 6 14

2,3-dibromoindole **13** (1 g, 3.46 mmol), 2-bromophenyl boronic acid **6** (0.83 g, 4.15 mmol), $Pd(PPh_3)_4$ (200 mg, 173 µmol) and sodium hydroxide (415 mg, 10.38 mmol) were added to 500 mL Schlenk flask. The mixture was back-filled several times with Argon. To the mixture 70 mL THF and 10 mL distilled water were added, then, back-filled several times. The reaction was heated at 70 ºC for 4h. The solvent was evaporated *in vacuo*. The residue was extracted with dichloromethane and water. The organic layer was dried over $MgSO_4$, filtered and the solvent was evaporated *in vacuo*. The yellow residue was purified by column chromatography (silica gel, Heptane/ethylacetate/dichloromethane 3:1:1) to yield *3-bromo-2-(2-bromophenyl)-1-methyl-1H-indole* **14** (0.91 g, 72 %) as white solid; m.p. 83-85 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 – 7.66 (m, 1H), 7.59 – 7.52 (m, 1H), 7.44 – 7.12 (m, 6H), 3.50 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 137.12, 136.30, 133.29, 132.95, 132.20, 130.90, 127.43, 126.80, 125.52, 122.95, 120.48, 119.46, 109.71, 90.75, 31.26; IR (ATR, cm^{-1}): ν = 3053 (m), 3018 (w), 2939 (w), 2875 (w), 2833 (w), 1498 (m), 1473 (m), 1460 (s), 1427 (m), 1412 (m), 1356 (m), 1325 (s), 1319 (s), 1230 (s), 1201 (m), 1173 (w), 1153 (s), 1126 (m), 1105 (m), 1084 (m), 1009 (m), 947 (m), 922 (m), 808 (w), 729 (vs), 606 (m), 546 (m); GC-MS (EI, 70 eV): m/z (%) = 365 (100), 204 (82), 176 (22), 102 (26), 88 (13); HRMS (EI): calcd. for $C_{15}H_{11}Br_2N_1$ ([M^+]): 362.92528; found: 362.92484, calculated for $C_{15}H_{11}Br_1{}^{81}Br_1N_1$ ([M^+]): 364.92323; found: 364.92292, calculated for $C_{15}H_{11}{}^{81}Br_2N_1$ ([M^+]): 366.92118; found: 366.92109.

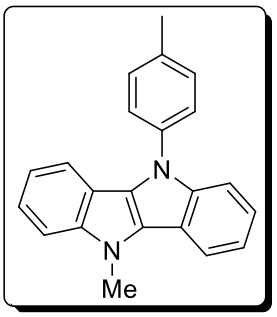
General procedure 4 for double C-N coupling with aniline derivatives, exemplified by: ***5-methyl-10-phenyl-5,10-dihydroindolo[3,2-b]indole*** **15a**



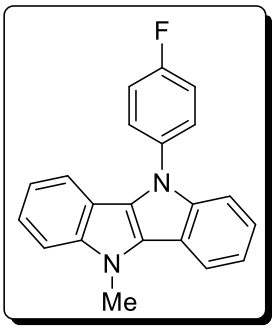
Aniline (75 µL, 0.82 mmol) was added to pressure tube charged with **14** (100 mg, 0.27 mmol), $Pd_2(dba)_3$ (12.5 mg, 14 µmol), ligand Xantphos (15.9 mg, 28 µmol) and sodium *tert*-butoxide (79 mg, 0.82 mmol) under Argon. The mixture was back-filled with Argon several times. The mixture was dissolved in anhydrous toluene (10 mL) and heated to 90 ºC for 6 h. After cooling, the reaction mixture was diluted with dichloromethane (20 mL) and filtered through a celite pad, washing with dichloromethane (40 mL). The filtrate was evaporated *in vacuo*. The product was separated via flash chromatography (silica gel, heptane/dichloromethane 5:1) to yield **15a** (65 mg, 80 %) as a white solid; m.p. 130-131 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.88 – 7.81 (m, 1H), 7.66 – 7.41 (m, 6H), 7.37 – 7.26 (m, 2H), 7.24 – 7.08 (m, 3H), 6.97 (ddd, *J* = 8.0, 7.1, 1.0 Hz, 1H), 4.03 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 141.32, 140.72, 139.16, 129.64, 127.89, 126.44, 125.53, 125.25, 122.56, 121.96, 119.65, 118.46, 118.24, 117.63, 116.05, 114.67, 110.99, 109.57, 31.65; IR (ATR, cm^{-1}): ν = 3047 (w), 2928 (w), 1593 (m), 1576 (m), 1500 (s), 1471 (s), 1460 (s), 1435 (m), 1423 (m), 1398 (s), 1365 (m), 1340 (m), 1323 (m), 1309 (m), 1282 (m), 1267 (w), 1232 (s), 1174 (m), 1151 (m), 1126 (m), 1103 (m), 1076 (m), 1061 (m), 1028 (m), 1014 (m), 987 (w), 966 (w), 949 (m), 918 (w), 910 (m), 883 (w), 831 (w), 823 (m), 779 (w), 729 (vs), 700 (vs), 677 (s), 650 (s), 617 (m), 596 (m), 588 (s), 565 (m), 542 (m); GC-MS (EI, 70 eV): m/z (%) = 296 (100), 281 (45); HRMS (EI): calculated for $C_{21}H_{16}N_2$ ([M^+]): 296.13080; found: 296.13042.



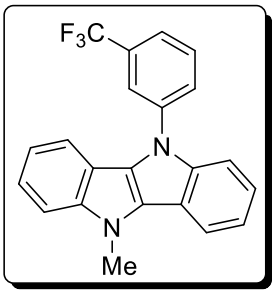
5-(4-(tert-butyl)phenyl)-10-methyl-5,10-dihydroindolo[3,2-b]indole **15b** was prepared following general procedure 4 using compound **14** (100 mg, 0.27 mmol) and 4-(*tert*-butyl)aniline (131 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane 5:1) to yield **15b** (81 mg, 84%) as a white solid; m.p. 210-213 ºC; ^{1}H NMR (250 MHz, C_6D_6) δ = 7.99 – 7.89 (m, 2H), 7.84 – 7.75 (m, 1H), 7.73 – 7.65 (m, 2H), 7.48 – 7.33 (m, 5H), 7.33 – 7.18 (m, 2H), 3.56 (s, 3H), 1.36 (s, 9H); ^{13}C NMR (63 MHz, C_6D_6) δ = 149.25, 141.81, 141.43, 137.08, 127.84, 126.67, 125.43, 122.80, 122.22, 119.85, 118.92, 118.62, 117.99, 116.63, 115.39, 111.46, 109.82, 34.59, 31.46, 30.98; IR (ATR, cm^{-1}): ν = 3057 (w), 2960 (m), 2929 (w), 2901 (w), 2864 (w), 1516 (s), 1495 (m), 1471 (s), 1441 (m), 1423 (m), 1402 (s), 1365 (m), 1329 (m), 1309 (w), 1265 (w), 1234 (s), 1200 (m), 1184 (m), 1161 (w), 1151 (w), 1136 (m), 1111 (m), 1030 (w), 1022 (w), 1012 (m), 955 (w), 922 (w), 833 (m), 823 (m), 775 (w), 729 (vs), 712 (m), 685 (m), 665 (w), 607 (w), 590 (m), 571 (w), 561 (w), 550 (m); GC/MS (EI, 70eV): m/z (%) = 352 (100), 337 (22), 322 (19),155 (20); HRMS (EI): calculated for $C_{25}H_{24}N_2$ ([M^+]): 352.19340; found: 352.19295.



5-methyl-10-(p-tolyl)-5,10-dihydroindolo[3,2-b]indole **15c** was prepared following general procedure 4 using compound **14** (100 mg, 0.27 mmol) and *p*-toluidine (88 mg, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane 5:1) to yield **15c** (69 mg, 81 %) as a white solid; m.p. 140-141 ºC; ^{1}H NMR (300 MHz, Acetone) δ = 7.92 – 7.85 (m, 1H), 7.48 – 7.29 (m, 7H), 7.14 – 7.00 (m, 3H), 6.87 (ddd, *J* = 8.0, 7.1, 1.0 Hz, 1H), 4.02 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (63 MHz, Acetone) δ = 142.29, 141.63, 137.35, 137.20, 131.14, 128.45, 126.07, 125.85, 123.39, 122.75, 120.40, 118.99, 118.78, 118.71, 116.86, 115.37, 111.50, 110.69, 31.81, 21.15; IR (ATR, cm^{-1}): ν = 3057 (w), 3036 (w), 2918 (w), 1514 (s), 1487 (m), 1473 (m), 1454 (m), 1441 (m), 1421 (m), 1402 (m), 1365 (m), 1325 (m), 1304 (w), 1232 (m), 1174 (w), 1153 (m), 1126 (m), 1109 (m), 1063 (w), 1032 (m), 1012 (m), 968 (w), 951 (m), 918 (m), 822 (m), 796 (w), 760 (w), 748 (m), 727 (vs), 683 (m), 665 (w), 640 (w), 615 (w), 590 (m), 563 (m), 542 (w); GC/MS (EI, 70eV): m/z (%) = 310 (100), 295 (40); HRMS (EI): calculated for $C_{22}H_{18}N_2$ ([M^+]): 310.14645; found: 310.14704.

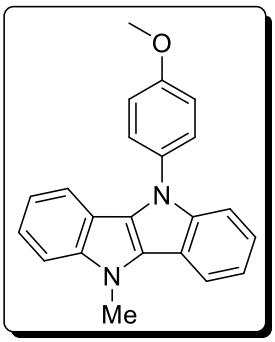


5-(4-fluorophenyl)-10-methyl-5,10-dihydroindolo[3,2-b]indole **15d** was prepared following general procedure 4 using compound **14** (100 mg, 0.27 mmol) and 4-fluoroaniline (78 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptane/ dichloromethane 4:1) to yield **15d** (71 mg, 82 %) as a white solid; m.p. 106-108 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.82 (dd, *J* = 7.2, 1.4 Hz, 1H), 7.57 – 7.46 (m, 2H), 7.48 – 7.28 (m, 3H), 7.23 – 7.08 (m, 5H), 6.96 (ddd, *J* = 8.0, 7.1, 1.0 Hz, 1H), 4.01 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 161.11 (d, *J* = 246.0 Hz), 141.28, 140.91, 135.18 (d, *J* = 3.0 Hz), 127.75, 127.24 (d, *J* = 8.4 Hz), 125.34, 122.62, 122.03, 119.72, 118.32, 118.12, 117.67, 116.53 (d, *J* = 22.8 Hz), 116.00, 114.49, 110.69, 109.64, 31.63; IR (ATR, cm^{-1}): ν = 3055 (w), 2922 (w), 1504 (s), 1471 (s), 1439 (m), 1423 (m), 1398 (s), 1367 (m), 1323 (m), 1281 (w), 1230 (s), 1217 (s), 1153 (m), 1134 (m), 1124 (m), 1095 (m), 1061 (m), 1032 (m), 1016 (m), 949 (m), 918 (m), 872 (m), 841 (m), 827 (s), 808 (s), 785 (m), 760 (m), 725 (vs), 710 (s), 679 (m), 636 (m), 611 (m), 588 (s), 565 (s), 542 (m); GC/MS (EI, 70eV): m/z (%) = 314 (100), 299 (48), 157 (10); HRMS (EI): calculated for $C_{21}H_{15}F_1N_2$ ([M^+]): 314.12138; found: 314.12142.

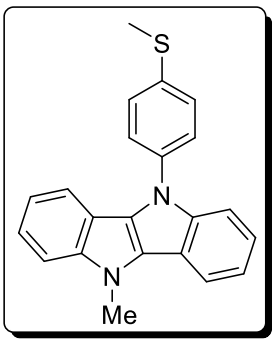


5-methyl-10-(3-(trifluoromethyl)phenyl)-5,10-dihydroindolo[3,2-b]indole **15e** was prepared following general procedure 4 using compound **14** (100 mg, 0.27 mmol) and 3-(trifluoromethyl)aniline (103 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane 4:1) to yield **15e** (84 mg, 84 %) as a white solid; m.p. 86-87 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.90 (s, 1H), 7.88 – 7.74 (m, 2H), 7.64 – 7.46 (m, 3H), 7.35 (dd, *J* = 15.7, 8.2 Hz, 2H), 7.22 – 7.12 (m, 3H), 6.99 (ddd, *J* = 8.0, 7.1, 1.0 Hz, 1H), 4.00 (s, 3H); ^{19}F NMR (282 MHz, $CDCl_3$) δ = -62.54 (s); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 141.29, 140.50, 139.84, 132.26 (q, *J* = 32.7 Hz), 130.29, 128.40 (d, *J* = 0.9 Hz), 128.33, 124.63, 123.03, 122.79 (q, *J* = 3.8 Hz), 122.53 (q, *J* = 272.7 Hz), 122.52 (d, *J* = 272.7 Hz), 122.17, 122.09 (q, *J* = 7.8, 4.1 Hz), 120.33, 118.59, 117.85, 116.55, 114.43, 110.61, 109.75, 31.60; IR (ATR, cm^{-1}): ν = 3061 (w), 2931 (w), 1612 (w), 1595 (m), 1574 (w), 1514 (w), 1495 (s), 1471 (s), 1441 (s), 1421 (m), 1396 (m), 1373 (m), 1335 (s), 1321 (s), 1308 (s), 1286 (s), 1263 (m), 1232 (s), 1176 (s), 1163 (s), 1113 (vs), 1095 (s), 1066 (s), 1034 (m), 1020 (m), 1001 (m), 968 (m), 957 (m), 924 (m), 916 (m), 899 (m), 872 (w), 839 (s), 802 (s), 729 (vs), 706 (vs), 696 (s), 679 (m), 665 (s), 650 (m), 638 (m), 596 (m), 588 (m), 569 (m), 542 (m);

GC/MS (EI, 70eV): m/z (%) = 364 (100), 349 (39); HRMS (EI): calculated for $C_{22}H_{15}F_3N_2$ ([M^+]): 364.11818; found: 364.11786.

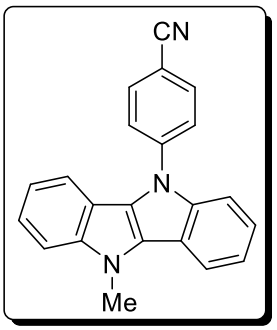


5-(4-methoxyphenyl)-10-methyl-5,10-dihydroindolo[3,2-b]indole **15f** was prepared following general procedure 4 using compound **14** (100 mg, 0.27 mmol) and *p*-anisidine (101 mg, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 5:1) to yield **15f** (68 mg, 76 %) as a white solid; m.p. 114-116 ºC; ^{1}H NMR (300 MHz, Acetone) δ = 7.91 – 7.81 (m, 1H), 7.49 – 7.41 (m, 2H), 7.40 – 7.32 (m, 2H), 7.31 – 7.26 (m, 1H), 7.14 – 7.00 (m, 5H), 6.86 (m, 1H), 4.01 (s, 3H), 3.75 (s, 3H); ^{13}C NMR (75 MHz, Acetone) δ = 159.43, 142.28, 141.93, 132.64, 128.18, 127.70, 126.24, 123.28, 122.73, 120.23, 118.97, 118.65, 116.65, 115.78, 115.36, 111.40, 110.67, 55.95, 31.82; IR (ATR, cm^{-1}): ν = 3057 (m), 2955 (m), 2926 (m), 2912 (m), 2835 (m), 1510 (s), 1473 (s), 1464 (s), 1441 (s), 1421 (m), 1400 (s), 1367 (m), 1331 (m), 1296 (m), 1284 (m), 1234 (s), 1182 (m), 1169 (m), 1161 (m), 1151 (m), 1132 (m), 1124 (m), 1107 (s), 1065 (m), 1030 (s), 1018 (m), 968 (m), 953 (m), 947 (m), 931 (m), 914 (m), 870 (m), 827 (s), 806 (m), 795 (m), 756 (m), 742 (m), 723 (vs), 685 (m), 675 (m), 665 (m), 640 (m), 613 (m), 590 (s), 573 (s), 542 (m); GC/MS (EI, 70eV): m/z (%) = 326 (100), 311 (25), 268 (12); HRMS (EI): calculated for $C_{21}H_{15}N_2O_1$ ([M^+]): 326.14136; found: 326.14118.

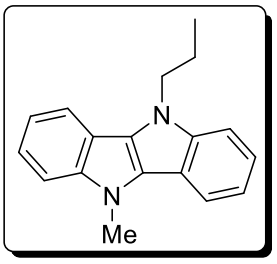


5-methyl-10-(4-(methylthio)phenyl)-5,10-dihydroindolo[3,2-b]indole **15g** was prepared following general procedure 4 using compound **14** (100 mg, 0.27 mmol) and 4-(methylthio)aniline (102 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 5:1) to yield **15g** (78 mg, 83 %) as a white solid; m.p. 107-108 ºC; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 8.04 – 7.95 (m, 1H), 7.75 – 7.58 (m, 4H), 7.58 – 7.46 (m, 3H), 7.43 – 7.24 (m, 3H), 7.15 (t, *J* = 7.5 Hz, 1H), 4.17 (s, 3H), 2.64 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 141.28, 140.71, 136.48, 136.32, 127.79, 125.92, 125.16, 122.57, 121.98, 119.68, 118.37, 118.28, 117.64, 116.03, 114.59, 110.90, 109.59, 31.62, 16.23; IR (ATR, cm^{-1}): ν = 3057 (w), 2916 (m), 1495 (s), 1468 (s), 1439 (s), 1419 (m), 1396 (s), 1365 (m), 1323 (s), 1302 (m), 1284 (m), 1265 (m), 1228 (s), 1180 (m), 1161 (m), 1153 (m), 1132 (m), 1090 (s), 1065 (m), 1030 (m), 1011 (m), 962 (m), 957 (m), 949 (m), 924 (m), 916 (m), 870 (w), 835 (w), 822 (s), 773

(m), 735 (vs), 727 (vs), 700 (s), 687 (s), 679 (s), 634 (m), 602 (m), 588 (s), 569 (m), 544 (m); GC/MS (EI, 70eV): m/z (%) = 342 (100), 327 (35), 171 (8); HRMS (EI): calculated for $C_{22}H_{18}N_2S_1$ ([M^+]): 342.11852; found: 342.11846.

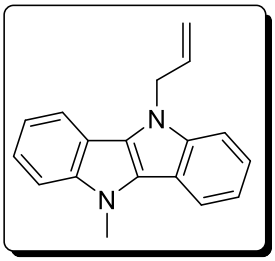


5-methyl-10-(4-cyanophenyl)-5,10-dihydroindolo[3,2-b]indole **15h** was prepared following general procedure 4 using compound **14** (100 mg, 0.27 mmol) and 4-aminobenzonitrile (97 mg, 0.82 mmol). The product was purified by flash chromatography (silica gel, Heptane/ethylacetate 4:1) to yield **15h** (72 mg, 82 %) as a white solid; m.p. 158-160 ºC; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 7.84 – 7.77 (m, 1H), 7.76 – 7.59 (m, 4H), 7.58 – 7.48 (m, 1H), 7.39 – 7.31 (m, 2H), 7.26 – 7.13 (m, 3H), 7.00 (ddd, *J* = 8.0, 7.1, 1.0 Hz, 1H), 3.98 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 143.01, 141.20, 140.10, 133.63, 128.80, 124.97, 123.86, 123.27, 122.27, 120.85, 118.73, 118.66, 118.24, 117.98, 117.01, 114.32, 110.73, 109.85, 108.87, 31.55; IR (ATR, cm^{-1}): ν = 3055 (w), 2929 (w), 2218 (m), 1601 (m), 1508 (s), 1470 (s), 1441 (s), 1423 (m), 1396 (s), 1373 (m), 1346 (m), 1325 (s), 1308 (m), 1279 (w), 1230 (m), 1200 (w), 1174 (m), 1163 (m), 1155 (m), 1134 (m), 1059 (w), 1034 (m), 1024 (m), 949 (w), 872 (w), 843 (m), 831 (m), 741 (s), 729 (vs), 687 (w), 681 (w), 673 (w), 646 (w), 607 (w), 590 (m), 567 (w), 548 (m); GC/MS (EI, 70eV): m/z (%) = 321 (100), 306 (36), 219 (12), 161 (10); HRMS (EI): calculated for $C_{22}H_{15}N_3$ ([M^+]): 321.12605; found: 321.12595.

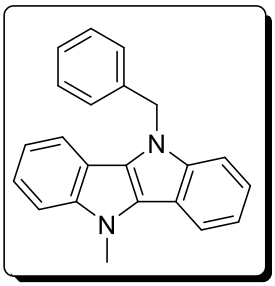


5-methyl-10-propyl-5,10-dihydroindolo[3,2-b]indole **15i** was prepared following general procedure 4 using compound **14** (100 mg, 0.27 mmol) and n-propylamine (68 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane 5:1) to yield **15i** (54 mg, 86 %) as a white solid; m.p. 121-122 ºC; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 7.81 – 7.71 (m, 2H), 7.36 – 7.02 (m, 6H), 4.33 (s, 2H), 3.98 (s, 3H), 1.89 (sex, *J* = 7.3 Hz, 2H), 0.86 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 141.23, 140.63, 126.54, 125.81, 121.61, 118.15, 117.99, 117.66, 117.51, 114.73, 109.78, 109.53, 46.80, 31.59, 23.65, 11.68; IR (ATR, cm^{-1}): ν = 3053 (w), 2960 (w), 2931 (m), 2874 (w), 1497 (m), 1475 (s), 1466 (m), 1439 (m), 1423 (m), 1406 (m), 1381 (m), 1363 (s), 1298 (m), 1267 (m), 1246 (w), 1225 (s), 1188 (m), 1151 (m), 1132 (m), 1119 (m), 1014 (m), 951 (w), 920 (m), 899 (m), 841 (m), 729 (vs), 675 (m), 660 (m), 644 (m), 590 (m), 575 (m), 567 (m), 544 (m); GC/MS (EI, 70eV): m/z (%) =

262 (100), 233 (89), 219 (48); HRMS (EI): calculated for $C_{18}H_{18}N_2$ ([M^+]): 262.14645; found: 262.14588.

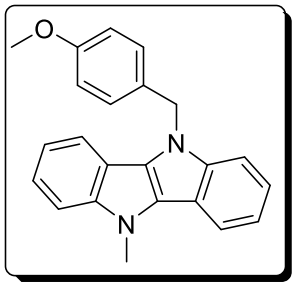


5-methyl-10-allyl-5,10-dihydroindolo[3,2-b]indole **15j** was prepared following general procedure 4 using compound **14** (100 mg, 0.27 mmol) and allylamine (62 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane 5:1) to yield **15j** (60 mg, 84 %) as a white solid; m.p. 125-126 ºC; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 8.08 – 7.65 (m, 2H), 7.62 – 6.95 (m, 6H), 6.17 – 5.90 (m, 1H), 5.20 – 4.95 (m, 4H), 4.03 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 141.15, 140.60, 133.49, 126.68, 125.76, 121.75, 121.67, 118.35, 118.16, 117.79, 117.47, 116.67, 115.03, 114.62, 109.84, 109.47, 47.49, 31.60; IR (ATR, cm^{-1}): ν = 3063 (w), 2920 (m), 2852 (w), 1643 (w), 1497 (m), 1475 (s), 1448 (m), 1433 (m), 1406 (s), 1367 (m), 1352 (m), 1294 (w), 1273 (m), 1246 (m), 1221 (s), 1174 (m), 1149 (m), 1132 (m), 1119 (m), 1061 (w), 1041 (w), 1016 (m), 993 (m), 976 (m), 953 (w), 943 (w), 924 (m), 914 (m), 904 (m), 841 (m), 831 (m), 771 (w), 741 (m), 721 (vs), 663 (m), 598 (m), 584 (s), 565 (m), 544 (m); GC/MS (EI, 70eV): m/z (%) = 260 (47), 219 (100); HRMS (EI): calculated for $C_{18}H_{16}N_2$ ([M^+]): 260.13080; found: 260.13081.

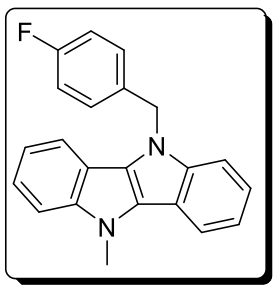


5-methyl-10-benzyl-5,10-dihydroindolo[3,2-b]indole **15k** was prepared following general procedure 4 using compound **14** (100 mg, 0.27 mmol) and benzylamine (90 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane 3:1) to yield **15k** (61 mg, 72 %) as a white solid; m.p. 151-152 ºC; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 7.89 – 7.80 (m, 1H), 7.55 – 7.52 (m, 1H), 7.39 – 7.29 (m, 2H), 7.26 – 7.06 (m, 8H), 7.05 – 6.94 (m, 1H), 5.61 (s, 2H), 4.05 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 141.16, 140.87, 137.99, 128.77 (x 2C), 127.42, 126.53 (x 2C), 121.90, 121.67, 118.49, 118.20, 115.10, 114.67, 109.99, 109.46, 48.82, 31.62; IR (ATR, cm^{-1}): ν = 3055 (w), 3030 (w), 2935 (w), 1603 (w), 1579 (w), 1495 (m), 1475 (s), 1448 (m), 1431 (m), 1406 (m), 1387 (m), 1360 (m), 1346 (m), 1340 (m), 1317 (m), 1300 (m), 1288 (m), 1273 (m), 1246 (m), 1223 (m), 1171 (m), 1149 (w), 1132 (m), 1122 (m), 1099 (w), 1074 (w), 1028 (w), 1014 (m), 978 (m), 849 (w), 766 (w), 731 (vs), 694 (s), 658 (m), 594 (w), 584 (m), 569 (w), 536 (w); GC/MS (EI, 70eV):

m/z (%) = 310 (49), 219 (100); HRMS (EI): calculated for $C_{22}H_{18}N_2$ ([M^+]): 310.14645; found: 310.14720.

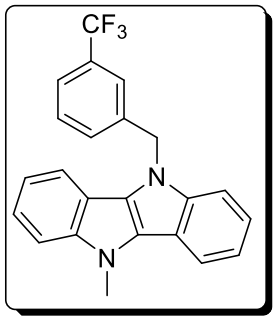


5-methyl-10-(4-methoxybenzyl)-5,10-dihydroindolo[3,2-b]indole **15l** was prepared following general procedure 4 using compound **14** (100 mg, 0.27 mmol) and 4-methoxybenzylamine (107 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 5:1) to yield **15l** (74 mg, 79 %) as a white solid; m.p. 161-162 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.86 – 7.78 (m, 1H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.32 (dd, *J* = 8.3, 4.0 Hz, 2H), 7.25 – 6.95 (m, 6H), 6.74 – 6.62 (m, 2H), 5.49 (s, 2H), 4.00 (s, 3H), 3.60 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 158.98, 141.22, 140.86, 130.15, 128.44, 127.85, 121.91, 121.70, 118.48, 118.26, 117.77, 117.54, 115.14, 114.75, 114.20, 114.07, 110.09, 109.51, 55.26, 48.32, 31.63; IR (ATR, cm^{-1}): ν = 3047 (w), 2928 (w), 1610 (w), 1512 (m), 1497 (m), 1475 (m), 1450 (m), 1437 (m), 1421 (w), 1404 (m), 1363 (m), 1342 (m), 1311 (w), 1300 (w), 1294 (w), 1271 (m), 1252 (m), 1221 (m), 1171 (m), 1149 (m), 1132 (m), 1120 (m), 1109 (m), 1030 (m), 1014 (m), 984 (w), 957 (w), 926 (w), 843 (m), 831 (w), 823 (w), 810 (m), 768 (w), 752 (m), 742 (s), 727 (vs), 665 (w), 656 (w), 642 (m), 629 (w), 592 (m), 577 (w), 565 (w), 534 (m); GC/MS (EI, 70eV): m/z (%) = 340 (53), 219 (100), 121 (32); HRMS (EI): calculated for $C_{23}H_{20}N_2O_1$ ([M^+]): 340.15701; found: 340.15763.

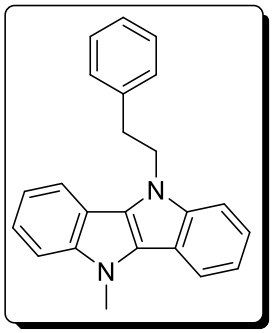


5-methyl-10-(4-fluorobenzyl)-5,10-dihydroindolo[3,2-b]indole **15m** was prepared following general procedure 4 using compound **14** (100 mg, 0.27 mmol) and 4-fluorobenzylamine (94 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane 3:1) to yield **15m** (58 mg, 64 %) as a white solid; m.p. 153-154 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.80 (d, *J* = 7.6 Hz, 1H), 7.46 (d, *J* = 7.9 Hz, 1H), 7.28 (t, *J* = 8.5 Hz, 2H), 7.22 – 6.92 (m, 6H), 6.83 – 6.77 (m, 2H), 5.44 (s, 2H), 3.95 (s, 3H); ^{19}F NMR (282 MHz, $CDCl_3$) δ = -115.08 (s); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.20 (d, *J* = 245.5 Hz), 141.21, 140.81, 133.82 (d, *J* = 3.1 Hz), 128.22 (d, *J* = 8.1 Hz), 126.89, 125.71, 122.06, 121.82, 118.70, 118.36, 117.65, 117.58, 115.72 (d, *J* = 21.6 Hz), 115.25, 114.64, 109.94, 109.62, 48.11, 31.61; IR (ATR, cm^{-1}): ν = 3055 (w), 2926 (w), 1606 (m), 1508 (s), 1497 (m), 1473 (s), 1448 (m), 1433 (m), 1423 (m), 1406 (s), 1360 (m), 1340 (m), 1296 (w), 1288 (m), 1271 (m), 1244 (m), 1221 (s),

1171 (m), 1157 (s), 1132 (m), 1122 (m), 1092 (m), 1049 (w), 1014 (m), 978 (m), 957 (w), 930 (w), 920 (w), 843 (m), 814 (s), 779 (w), 729 (vs), 681 (m), 650 (m), 623 (m), 592 (m), 580 (m), 567 (m), 542 (w); GC/MS (EI, 70eV): m/z (%) = 328 (44), 219 (100), 109 (9); HRMS (EI): calculated for $C_{22}H_{17}N_2F_1$ ([M^+]): 328.13703; found: 328.13740.



5-methyl-10-(3-(trifluoromethyl)benzyl)-5,10-dihydroindolo[3,2-b]indole **15n** was prepared following general procedure 4 using compound **14** (100 mg, 0.27 mmol) and 3-(trifluoromethyl)benzylamine (118 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane 3:1) to yield **15n** (62 mg, 60 %) as a white solid; m.p. 153-154 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.90 – 7.84 (m, 1H), 7.56 – 7.45 (m, 2H), 7.45 – 7.09 (m, 8H), 7.01 (ddd, *J* = 8.0, 7.1, 1.0 Hz, 1H), 5.63 (s, 2H), 4.05 (s, 3H); ^{19}F NMR (282 MHz, $CDCl_3$) δ = -62.55 (s); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 141.18, 140.83, 139.12, 131.12 (d, *J* = 32.3 Hz), 129.81, 129.47, 126.96, 125.65, 124.44 (q, *J* = 3.8 Hz), 123.99 (q, *J* = 274.3 Hz), 123.28 (q, *J* = 3.8 Hz), 122.17, 121.85, 118.87, 118.39, 117.67, 117.35, 115.36, 114.51, 109.80, 109.63, 48.46, 31.64; IR (ATR, cm^{-1}): ν = 3055 (w), 2926 (w), 1579 (w), 1497 (m), 1473 (m), 1446 (m), 1433 (m), 1406 (m), 1363 (w), 1346 (w), 1327 (s), 1288 (m), 1271 (m), 1246 (m), 1221 (m), 1186 (m), 1161 (s), 1153 (s), 1117 (vs), 1092 (s), 1072 (s), 1049 (m), 1014 (m), 1003 (m), 989 (m), 980 (m), 957 (w), 947 (w), 920 (m), 893 (m), 872 (w), 841 (m), 827 (m), 793 (s), 737 (s), 727 (vs), 700 (s), 677 (m), 665 (m), 648 (m), 613 (m), 602 (m), 586 (m), 567 (m), 552 (m), 540 (m); GC/MS (EI, 70eV): m/z (%) = 378 (52), 219 (100), 159 (8); HRMS (EI): calculated for $C_{23}H_{17}N_2F_3$ ([M^+]): 378.13383; found: 378.13375.

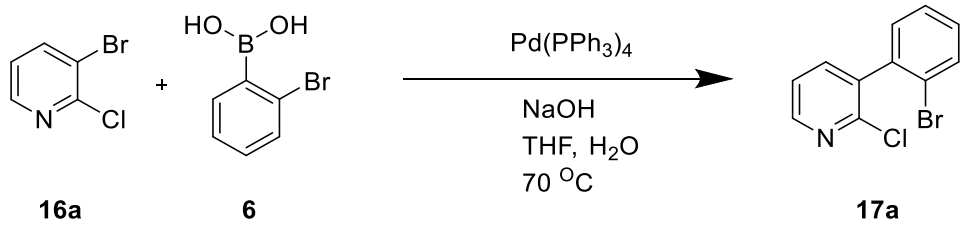


5-methyl-10-phenethyl-5,10-dihydroindolo[3,2-b]indole **15o** was prepared following general procedure 4 using compound **14** (100 mg, 0.27 mmol) and phenethylamine (104 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane 4:1) to yield **15o** (74 mg, 83 %) as a white solid; m.p. 138-139 ºC; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 7.98 – 7.88 (m, 2H), 7.62 – 6.96 (m, 11H), 4.83 – 4.59 (m, 2H), 4.15 (s, 3H), 3.34 – 3.15 (m, 2H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 141.22, 140.46, 138.76, 128.87, 128.71, 126.78, 126.66, 125.39, 121.74, 121.69, 118.32, 118.23, 117.53, 117.46, 114.94, 114.73,

109.65, 109.59, 47.13, 36.74, 31.63; IR (ATR, cm^{-1}): ν = 3026 (w), 2929 (m), 1495 (m), 1477 (s), 1450 (m), 1439 (m), 1423 (m), 1406 (s), 1362 (m), 1348 (s), 1281 (m), 1228 (s), 1203 (m), 1167 (m), 1155 (m), 1132 (m), 1122 (m), 1082 (w), 1016 (m), 999 (m), 850 (w), 829 (w), 742 (s), 727 (vs), 694 (vs), 646 (m), 596 (m), 580 (m), 569 (w), 532 (m); GC-MS (EI, 70 eV): m/z (%) = 324 (54), 233 (100), 218 (42); HRMS (ESI): calcd. for $C_{23}H_{20}N_2$ ($[M]^+$): 324.16265; found: 324.16235.

8.5.3 Synthesis of α-,δ-Carbolines

Procedure for preparation of *3-(2-bromophenyl)-2-chloropyridine* 17a.

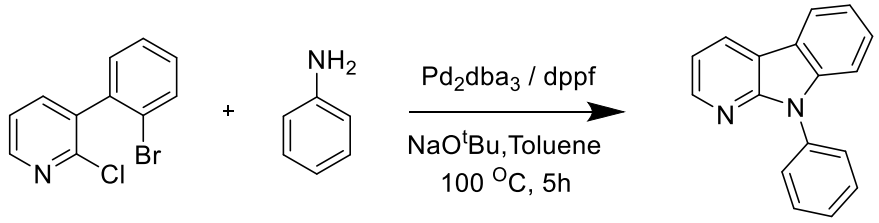


16a **6** **17a**

3-bromo-2-chloropyridine **16a** (1 g, 5.2 mmol), 2-bromophenyl boronic acid **2** (1.25 g, 6.2 mmol), $Pd(PPh_3)_4$ (300 mg, 260 µmol) and sodium hydroxide (624 mg, 15.6 mmol) were added to 500 mL Schlenk flask. The mixture was back-filled several times with Argon. To the mixture 70 mL THF and 10 mL distilled water were added, then, back-filled with argon several times. The reaction was heated at 70 ºC for 4h. The solvent was evaporated *in vacuo*. The residue was extracted with dichloromethane and water. The organic layer was dried over $MgSO_4$, filtered and the solvent was evaporated *in vacuo*. The yellow residue was purified by column chromatography (silica gel, Heptane/ethylacetate 4:1) to yield 3-(2-bromophenyl)-2-chloropyridine **17a** (1.19 g, 85 %) as colorless syrup; ^1H NMR (300 MHz, $CDCl_3$) δ = 8.38 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.66 – 7.59 (m, 1H), 7.54 (dd, *J* = 7.5, 2.0 Hz, 1H), 7.33 (td, *J* = 7.6, 1.3 Hz, 1H), 7.29 – 7.13 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 150.36, 149.18, 139.84, 138.41, 136.39, 132.88, 130.95, 130.07, 127.42, 123.40, 122.16; IR (ATR, cm^{-1}): ν = 3051 (w), 1576 (m), 1558 (m), 1479 (w), 1441 (m), 1427 (m), 1390 (vs), 1300 (w), 1255 (w), 1242 (w), 1207 (m), 1122 (m), 1103 (s), 1063 (s), 1053 (m), 1026 (m), 997 (s), 945 (w), 802 (m), 781 (m), 748 (vs), 723 (s), 694 (s), 654 (s), 615 (m), 569 (m), 553 (m); GC-MS (EI, 70 eV): m/z (%) = 269 (59), 188 (100), 153 (58), 126(29); HRMS (EI): calcd. for $C_{11}H_7N_1Br_1Cl_1$

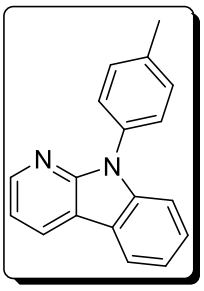
([M]$^+$): 266.94449; found: 266.94495; calcd. for $C_{11}H_7N_1{}^{81}Br_1Cl_1$ ([M]$^+$): 268.94244; found: 268.94288; calcd. for $C_{11}H_7N_1Br_1{}^{37}Cl_1$ ([M]$^+$): 270.93949; found: 270.94012.

General procedure 5 for double C-N coupling with aniline derivatives, exemplified by: ***9-phenyl-9H-pyrido[2,3-b]indole*** **18a**

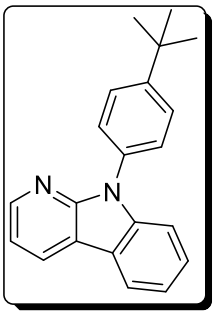


17a **8a** **18a**

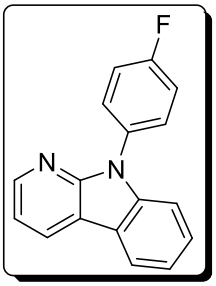
Aniline (52 µL, 0.56 mmol) was added to pressure tube charged with **17a** (100 mg, 0.37 mmol), $Pd_2(dba)_3$ (17 mg, 19 µmol), ligand Dppf (21 mg, 37 µmol) and sodium *tert*-butoxide (107 mg, 1.12 mmol) under Argon. The mixture was back-filled with Argon several times. The mixture was dissolved in anhydrous Toluene (10 mL) and heated at 110 ºC for 7 h. After cooling, the reaction mixture was diluted with dichloromethane (20 mL) and filtered through a celite pad, washing with dichloromethane (40 mL). The filtrate was reduced *in vacuo*. The product was separated via flash chromatography (silica gel, heptane/ethylacetate 3:1) to yield 9-phenyl-9*H*-pyrido[2,3-*b*]indole **18a** (84 mg, 92%) as a white solid; m.p. 110-111 ºC; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 8.42 (dd, *J* = 4.9, 1.6 Hz, 1H), 8.31 (dd, *J* = 7.7, 1.6 Hz, 1H), 8.05 (dt, *J* = 7.7, 0.9 Hz, 1H), 7.63 – 7.48 (m, 4H), 7.47 – 7.33 (m, 3H), 7.33 – 7.22 (m, 1H), 7.20 – 7.10 (m, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 151.93, 146.47, 140.11, 136.26, 129.65, 128.28, 127.64, 127.38, 126.93, 120.91, 120.81, 120.71, 116.36, 116.04, 110.41; IR (ATR, cm^{-1}): ν = 3037 (m), 1591 (s), 1568 (m), 1504 (s), 1473 (s), 1452 (s), 1414 (vs), 1377 (m), 1354 (m), 1335 (s), 1309 (m), 1290 (s), 1228 (s), 1176 (m), 1167 (m), 1115 (s), 1074 (m), 1051 (m), 1026 (m), 997 (m), 970 (m), 958 (m), 951 (m), 937 (m), 766 (s), 756 (s), 748 (s), 735 (vs), 715 (m), 692 (vs), 636 (s), 617 (s), 579 (s), 569 (m); GC-MS (EI, 70 eV): m/z (%) = 243 (100), 122 (17); HRMS (ESI): calcd. for $C_{17}H_{12}N_2$ ([M + H]$^+$): 245.10732; found: 245.10756.



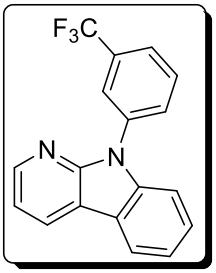
9-(p-tolyl)-9H-pyrido[2,3-b]indole **18b** was prepared following general procedure 5 using **17a** (100 mg, 0.37 mmol) and 4-toluidine (60 mg, 0.56 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 3:1) to yield **18b** (91 mg, 95 %) as a white solid; m.p. 102-103 ºC; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 8.40 (dd, *J* = 4.9, 1.6 Hz, 1H), 8.29 (dd, *J* = 7.7, 1.6 Hz, 1H), 8.04 (d, *J* = 7.7 Hz, 1H), 7.48 – 7.29 (m, 6H), 7.28 – 7.19 (m, 1H), 7.18 – 7.09 (m, 1H), 2.39 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 152.10, 146.50, 140.28, 137.60, 133.56, 130.30, 128.21, 127.25, 126.85, 120.87, 120.71, 120.54, 116.24, 115.87, 110.39, 21.26; IR (ATR, cm^{-1}): ν = 3039 (w), 2920 (w), 1589 (m), 1568 (m), 1514 (s), 1475 (m), 1456 (s), 1412 (vs), 1377 (m), 1354 (m), 1336 (s), 1311 (m), 1290 (s), 1228 (s), 1219 (s), 1200 (m), 1182 (m), 1169 (m), 1155 (w), 1120 (m), 1109 (m), 1051 (w), 1038 (w), 1018 (m), 997 (m), 966 (w), 951 (w), 941 (w), 924 (m), 841 (w), 812 (s), 798 (m), 771 (vs), 744 (s), 735 (vs), 714 (s), 702 (s), 646 (m), 633 (s), 617 (m), 577 (s), 571 (s); GC-MS (EI, 70 eV): m/z (%) = 258 (100), 242 (17), 128 (9); HRMS (ESI): calcd. for $C_{18}H_{14}N_2$ ($[M + H]^+$): 259.12297; found: 259.12331.



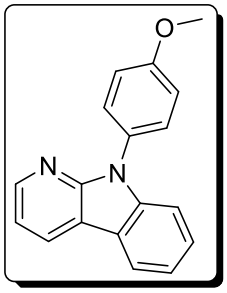
9-(4-(tert-butyl)phenyl)-9H-pyrido[2,3-b]indole **18c** was prepared following general procedure 5 using **17a** (100 mg, 0.37 mmol) and 4-*tert*-butylaniline (83 mg, 0.56 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 3:1) to yield **18c** (105 mg, 94 %) as a white solid; m.p. 147-148 ºC; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 8.41 (dd, *J* = 4.9, 1.6 Hz, 1H), 8.29 (dd, *J* = 7.7, 1.6 Hz, 1H), 8.06 – 7.99 (m, 1H), 7.58 – 7.32 (m, 6H), 7.23 (ddd, *J* = 8.1, 6.7, 1.6 Hz, 1H), 7.19 – 7.08 (m, 1H), 1.32 (s, 9H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 152.01, 150.43, 146.50, 140.26, 133.51, 128.22, 126.84, 126.77, 126.63, 120.84, 120.72, 120.56, 116.31, 115.87, 110.55, 34.76, 31.42; IR (ATR, cm^{-1}): ν = 2960 (m), 2902 (w), 2868 (w), 1587 (m), 1568 (m), 1520 (s), 1475 (m), 1454 (s), 1414 (vs), 1360 (m), 1335 (s), 1288 (s), 1269 (m), 1228 (s), 1186 (m), 1169 (m), 1153 (w), 1119 (m), 1097 (w), 1018 (m), 997 (m), 930 (m), 833 (m), 825 (m), 800 (w), 769 (vs), 748 (s), 739 (vs), 687 (m), 638 (s), 617 (m), 580 (m), 569 (m), 552 (s); GC-MS (EI, 70 eV): m/z (%) = 300 (45), 285 (100), 128 (13); HRMS (EI): calcd. for $C_{21}H_{20}N_2$ ($[M]^+$): 300.16210; found: 300.16183.



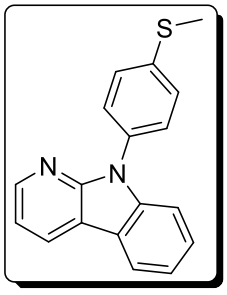
9-(4-fluorophenyl)-9H-pyrido[2,3-b]indole **18d** was prepared following general procedure 5 using **17a** (100 mg, 0.37 mmol) and 4-fluoroaniline (53 µL, 0.56 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 3:1) to yield **18d** (87 mg, 89 %) as a white solid; m.p. 156-157 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.38 (dd, *J* = 4.9, 1.6 Hz, 1H), 8.27 (dt, *J* = 5.0, 2.5 Hz, 1H), 8.02 (d, *J* = 7.8 Hz, 1H), 7.55 – 7.46 (m, 2H), 7.42 – 7.29 (m, 2H), 7.28 – 7.10 (m, 4H) ; ^{19}F NMR (282 MHz, $CDCl_3$) δ = -112.83 (s); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 161.79 (d, *J* = 247.2 Hz), 152.02, 146.54, 140.17, 132.23 (d, *J* = 3.1 Hz), 129.23 (d, *J* = 8.6 Hz), 128.39, 127.08, 121.04, 120.89, 120.83, 116.66 (d, *J* = 22.8 Hz), 116.35, 116.22, 110.19; IR (ATR, cm^{-1}): ν = 3061 (w), 1589 (m), 1570 (m), 1510 (s), 1475 (s), 1456 (s), 1416 (s), 1356 (m), 1336 (s), 1294 (s), 1228 (s), 1213 (s), 1173 (s), 1151 (s), 1119 (s), 1092 (s), 1053 (m), 1020 (m), 1012 (m), 997 (m), 964 (m), 953 (m), 941 (m), 931 (m), 924 (m), 899 (w), 870 (w), 856 (w), 833 (s), 816 (s), 798 (m), 769 (vs), 762 (s), 746 (s), 737 (vs), 715 (s), 704 (s), 665 (m), 644 (m), 629 (m), 617 (m), 579 (s), 569 (s); GC-MS (EI, 70 eV): m/z (%) = 261 (100), 131 (9); HRMS (ESI): calcd. for $C_{17}H_{11}F_1N_2$ ($[M + H]^+$): 263.0979; found: 263.09813.



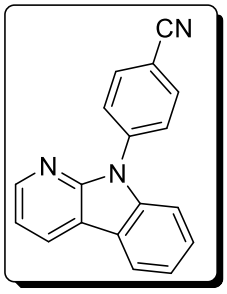
9-(3-(trifluoromethyl)phenyl)-9H-pyrido[2,3-b]indole **18e** was prepared following general procedure 5 using **17a** (100 mg, 0.37 mmol) and 4-fluoroaniline (53 µL, 0.56 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 3:1) to yield **18e** (87 mg, 89 %) as a white solid; m.p. 71-72 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.38 (dd, *J* = 4.9, 1.6 Hz, 1H), 8.28 (dd, *J* = 7.7, 1.6 Hz, 1H), 8.02 (dt, *J* = 7.8, 0.9 Hz, 1H), 7.87 (s, 1H), 7.84 – 7.76 (m, 1H), 7.68 – 7.59 (m, 2H), 7.41 – 7.35 (m, 2H), 7.26 (ddd, *J* = 8.2, 5.4, 2.9 Hz, 1H), 7.20 – 7.13 (m, 1H) ; ^{19}F NMR (282 MHz, $CDCl_3$) δ = -62.70 (s); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 151.71, 146.56, 139.59, 136.99, 132.14 (q, *J* = 32.8 Hz), 130.73 (d, *J* = 1.0 Hz), 130.25, 128.49, 127.28, 124.47 – 123.68 (m, 2xC), 123.83 (q, *J* = 272.6 Hz), 121.31, 121.17, 121.14, 116.66, 116.57, 110.10; IR (ATR, cm^{-1}): ν = 3051 (w), 1612 (w), 1591 (m), 1574 (m), 1497 (m), 1477 (m), 1458 (s), 1410 (s), 1358 (m), 1338 (m), 1321 (s), 1306 (s), 1290 (s), 1275 (s), 1228 (s), 1178 (m), 1167 (s), 1155 (s), 1119 (vs), 1103 (s), 1093 (s), 1068 (s), 1020 (m), 999 (m), 972 (s), 937 (m), 931 (m), 914 (m), 889 (m), 852 (m), 810 (s), 796 (s), 771 (s), 760 (m), 744 (s), 737 (vs), 715 (m), 694 (vs), 661 (s), 642 (s), 619 (s), 582 (m), 565 (m), 528 (s); GC-MS (EI, 70 eV): m/z (%) = 311 (100), 243 (11); HRMS (ESI): calcd. for $C_{18}H_{11}F_3N_2$ ($[M + H]^+$): 313.09471; found: 313.09460.



9-(4-methoxyphenyl)-9H-pyrido[2,3-b]indole **18f** was prepared following general procedure 5 using **17a** (100 mg, 0.37 mmol) and *p*-anisidine (69 mg, 0.56 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 2:1) to yield **18f** (100 mg, 98 %) as a white solid; m.p. 137-138 ºC; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 8.40 (dd, *J* = 4.9, 1.6 Hz, 1H), 8.30 (dd, *J* = 7.7, 1.6 Hz, 1H), 8.04 (d, *J* = 7.7 Hz, 1H), 7.51 – 7.41 (m, 2H), 7.40 – 7.30 (m, 2H), 7.29 – 7.19 (m, 1H), 7.18 – 7.09 (m, 1H), 7.09 – 7.01 (m, 2H), 3.82 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 159.00, 152.24, 146.51, 140.55, 128.90, 128.73, 128.22, 126.86, 120.86, 120.60, 120.49, 116.17, 115.81, 115.00, 110.30, 55.58; IR (ATR, cm^{-1}): ν = 3057 (w), 2960 (w), 2935 (w), 2908 (w), 2835 (w), 1589 (m), 1570 (m), 1512 (s), 1477 (m), 1456 (s), 1441 (m), 1416 (s), 1358 (m), 1336 (m), 1298 (m), 1288 (s), 1230 (vs), 1190 (m), 1174 (s), 1149 (m), 1117 (s), 1103 (s), 1053 (w), 1028 (s), 999 (m), 962 (m), 951 (m), 939 (m), 930 (m), 918 (m), 847 (w), 827 (s), 814 (m), 798 (m), 769 (vs), 744 (s), 735 (vs), 721 (s), 702 (m), 646 (s), 631 (s), 617 (m), 586 (s), 579 (s), 571 (m), 530 (vs); GC-MS (EI, 70 eV): m/z (%) = 274 (100), 259 (55), 231 (25), 168 (10), 115 (9); HRMS (EI): calcd. for $C_{18}H_{14}O_1N_2$ ($[M]^+$): 274.11006; found: 274.10996.

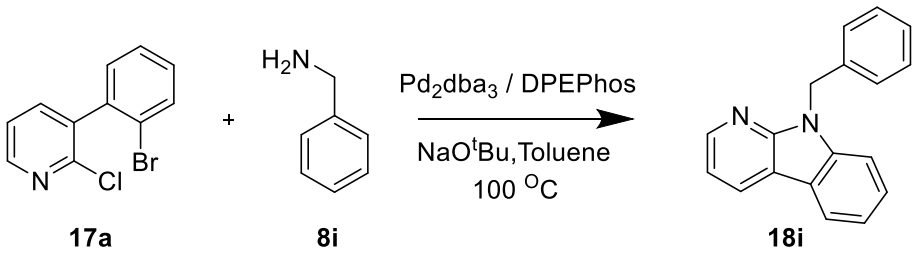


9-(4-(methylthio)phenyl)-9H-pyrido[2,3-b]indole **18g** was prepared following general procedure 5 using **17a** (100 mg, 0.37 mmol) and 4-(methylthio)aniline (69 µL, 0.56 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 2:1) to yield **18g** (99 mg, 92 %) as a white solid; m.p. 136-137 ºC; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 8.40 (dd, *J* = 4.9, 1.6 Hz, 1H), 8.30 (dd, *J* = 7.7, 1.6 Hz, 1H), 8.04 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.52 – 7.36 (m, 6H), 7.31 – 7.21 (m, 1H), 7.15 (dd, *J* = 7.6, 4.8 Hz, 1H), 2.48 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 150.92, 145.46, 139.03, 137.06, 132.25, 127.27, 126.70 (x2C), 125.94, 119.92, 119.78, 119.73, 115.32, 115.05, 109.30, 15.00; IR (ATR, cm^{-1}): ν = 3039 (w), 2960 (m), 2920 (m), 1626 (w), 1589 (m), 1568 (m), 1500 (s), 1475 (m), 1452 (m), 1437 (m), 1414 (s), 1356 (m), 1335 (m), 1309 (m), 1300 (m), 1290 (s), 1259 (m), 1228 (s), 1182 (m), 1169 (m), 1151 (m), 1117 (m), 1103 (m), 1090 (s), 1049 (m), 1014 (s), 997 (s), 980 (m), 970 (m), 953 (m), 933 (m), 924 (m), 858 (m), 814 (s), 798 (s), 769 (vs), 735 (vs), 714 (s), 679 (m), 642 (s), 629 (s), 617 (m), 580 (m), 569 (m); GC-MS (EI, 70 eV): m/z (%) = 290 (100), 275 (50), 243 (24); HRMS (EI): calcd. for $C_{18}H_{14}N_2S_1$ ($[M]^+$): 290.08722; found: 290.08702.



9-(4-cyanophenyl)-9H-pyrido[2,3-b]indole **18h** was prepared following general procedure 5 using **17a** (100 mg, 0.37 mmol) and 4-aminobenzonitrile (66 mg, 0.56 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 1.5:1) to yield **18h** (83 mg, 83 %) as a white solid; m.p. 179-180 ºC; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 8.38 (dd, *J* = 4.9, 1.6 Hz, 1H), 8.29 (dd, *J* = 7.7, 1.6 Hz, 1H), 8.03 (d, *J* = 7.7 Hz, 1H), 7.48 – 7.16 (m, 8H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 151.32, 146.45, 140.52, 138.85, 133.45, 128.58, 127.37, 127.28, 121.74, 121.45, 121.28, 118.52, 117.11, 116.85, 110.41, 110.23; IR (ATR, cm^{-1}): ν = 3057 (w), 2227 (m), 1603 (m), 1591 (m), 1574 (m), 1512 (m), 1487 (w), 1475 (w), 1450 (m), 1410 (s), 1356 (m), 1336 (m), 1311 (w), 1286 (m), 1228 (m), 1217 (m), 1184 (w), 1169 (m), 1155 (w), 1119 (m), 1103 (w), 1057 (w), 1020 (w), 1001 (w), 960 (w), 953 (w), 945 (w), 928 (w), 856 (m), 833 (m), 823 (m), 800 (w), 789 (w), 773 (m), 766 (s), 744 (m), 735 (vs), 694 (m), 656 (w), 631 (m), 619 (w), 577 (m), 569 (m), 550 (s), 532 (m); GC-MS (EI, 70 eV): m/z (%) = 268 (100), 134 (7); HRMS (EI): calcd. for $C_{18}H_{10}N_3$ ([M]$^+$): 268.08692; found: 268.08700.

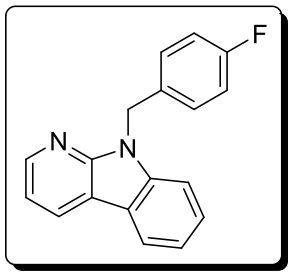
General procedure 6 for double C-N coupling with chain amine derivatives, exemplified by: ***5-benzyl-5H-pyrido[3,2-b]indole*** **18i**



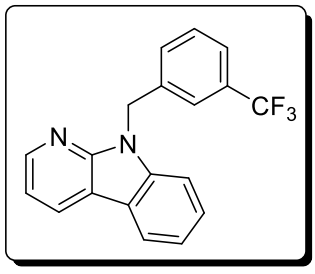
17a **8i** **18i**

To pressure tube charged with **17a** (100 mg, 0.37 mmol), $Pd_2(dba)_3$ (17 mg, 19 µmol), ligand DPEPhos (21 mg, 37 µmol) and sodium *tert*-butoxide (107 mg, 0.12 mmol) under Argon. The mixture was back-filled with argon several times. The mixture was dissolved in anhydrous toluene (10 mL). Benzylamine (61 µL, 0.56 mmol) was added to the mixture and heated at 100 ºC for 7 h. After cooling, the reaction mixture was diluted with dichloromethane (20 mL) and filtered through a celite pad, washing with dichloromethane (40 mL). The filtrate was reduced *in vacuo*. The product was separated via flash chromatography (silica gel, heptane/ethylacetate 3:1) to yield **18i** (85 mg, 88 %) as a white solid; m.p. 98-99 ºC; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 8.41 (dd, *J* = 4.9, 1.6 Hz, 1H), 8.20 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.99 – 7.92 (m, 1H), 7.36 – 7.20 (m, 2H), 7.19 – 7.01 (m, 7H), 5.58

(s, 2H) ; ^{13}C NMR (63 MHz, $CDCl_3$) δ = 150.65, 145.10, 138.49, 136.25, 127.55, 127.08, 126.26, 125.88, 125.68, 119.92, 119.56, 118.93, 114.79, 114.24, 108.80, 43.87; IR (ATR, cm^{-1}): ν = 3028 (w), 2960 (w), 2918 (w), 1626 (w), 1589 (m), 1568 (m), 1483 (s), 1466 (s), 1452 (m), 1431 (s), 1412 (s), 1356 (m), 1348 (m), 1333 (m), 1315 (w), 1292 (m), 1259 (s), 1211 (s), 1194 (m), 1155 (m), 1128 (m), 1119 (m), 1092 (m), 1078 (m), 1065 (m), 1053 (m), 1030 (s), 1020 (s), 995 (s), 970 (m), 947 (m), 928 (w), 906 (w), 870 (w), 850 (m), 839 (m), 800 (s), 791 (s), 773 (vs), 748 (s), 729 (vs), 694 (s), 652 (s), 619 (m), 606 (m), 582 (m), 569 (m), 555 (s), 528 (s); GC-MS (EI, 70 eV): m/z (%) = 257 (100), 181 (34), 91 (45); HRMS (ESI): calcd. for $C_{18}H_{14}N_2$ ($[M + H]^+$): 259.12297; found: 259.12298.

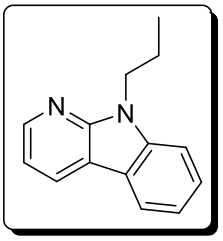


5-(4-fluorobenzyl)-5H-pyrido[3,2-b]indole **18j** was prepared following general procedure 6 using **17a** (100 mg, 0.37 mmol) and 4-fluorobenzylamine (61 µL, 0.56 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 3:1) to yield **18j** (90 mg, 87 %) as a white solid; m.p. 103-104 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.43 (dd, *J* = 4.9, 1.6 Hz, 1H), 8.25 (dd, *J* = 7.7, 1.6 Hz, 1H), 8.02 – 7.96 (m, 1H), 7.36 (ddd, *J* = 8.3, 7.2, 1.2 Hz, 1H), 7.28 – 7.07 (m, 5H), 6.89 – 6.79 (m, 2H), 5.57 (s, 2H) ; ^{19}F NMR (282 MHz, $CDCl_3$) δ = -115.23 (s); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 161.07 (d, *J* = 245.4 Hz), 150.56, 145.15, 138.33, 132.02 (d, *J* = 3.2 Hz), 127.62 (d, *J* = 8.1 Hz), 127.20, 125.77, 120.05, 119.63, 119.09, 114.85, 114.47 (d, *J* = 21.6 Hz), 114.39, 108.65, 43.24; IR (ATR, cm^{-1}): ν = 3053 (w), 3034 (w), 2935 (w), 1624 (w), 1587 (m), 1572 (m), 1508 (s), 1481 (m), 1464 (s), 1439 (m), 1416 (s), 1383 (w), 1354 (m), 1335 (m), 1294 (m), 1252 (m), 1217 (s), 1207 (s), 1163 (m), 1128 (m), 1119 (m), 1101 (m), 1061 (m), 1049 (m), 1030 (w), 1020 (m), 1001 (w), 987 (m), 966 (w), 928 (w), 862 (m), 849 (m), 823 (m), 800 (m), 791 (m), 777 (vs), 762 (s), 746 (s), 735 (vs), 704 (m), 665 (w), 638 (m), 629 (s), 619 (m), 609 (m), 580 (m), 565 (m); GC-MS (EI, 70 eV): m/z (%) = 276 (100), 181 (30), 109 (73); HRMS (ESI): calcd. for $C_{18}H_{13}F_1N_2$ ($[M + H]^+$): 277.11355; found: 277.11394.



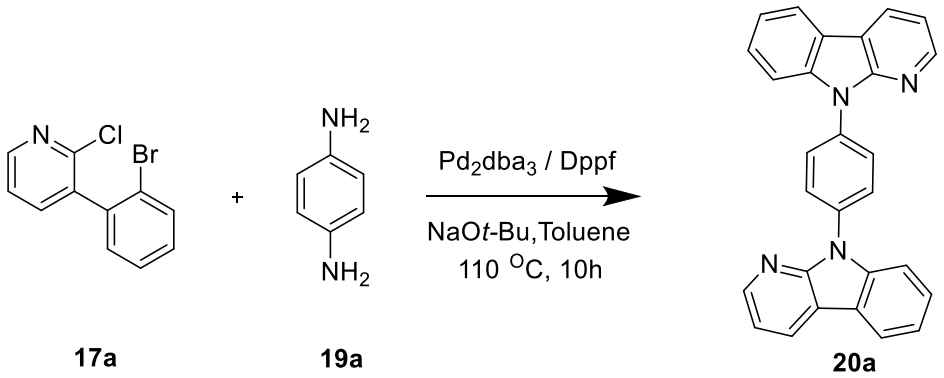
5-(3-(trifluoromethyl)benzyl)-5H-pyrido[3,2-b]indole **18k** was prepared following general procedure 6 using **17a** (100 mg, 0.37 mmol) and 3-(trifluoromethyl)benzylamine (80 µL, 0.56 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 3:1) to yield **18k** (109 mg, 90 %) as a white solid; m.p. 81-82 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.39 (dd, *J*

= 4.9, 1.6 Hz, 1H), 8.21 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.96 (d, *J* = 7.8 Hz, 1H), 7.49 (s, 1H), 7.39 – 7.30 (m, 2H), 7.21 – 7.17 (m, 4H), 7.12 – 7.03 (m, 1H), 5.60 (s, 2H); ^{19}F NMR (282 MHz, $CDCl_3$) δ = -62.51 (s); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 151.65, 146.29, 139.36, 138.47, 131.04 (q, *J* = 32.3 Hz), 130.30, 129.26, 128.36, 126.99, 124.38 (q, *J* = 3.8 Hz), 124.06 (q, *J* = 272.4 Hz), 123.89 (q, *J* = 3.8 Hz), 121.23, 120.81, 120.37, 115.99, 115.68, 109.55, 44.61; IR (ATR, cm^{-1}): ν = 3053 (w), 1628 (w), 1591 (m), 1572 (m), 1483 (m), 1466 (m), 1450 (w), 1433 (m), 1416 (s), 1325 (vs), 1296 (m), 1281 (m), 1261 (m), 1217 (m), 1205 (m), 1186 (m), 1157 (s), 1117 (vs), 1097 (s), 1072 (vs), 1022 (m), 1011 (m), 993 (m), 966 (m), 937 (m), 922 (m), 903 (m), 868 (m), 852 (m), 800 (s), 791 (s), 771 (s), 744 (s), 735 (s), 702 (vs), 671 (m), 646 (s), 619 (m), 600 (m), 575 (m), 559 (m); GC-MS (EI, 70 eV): m/z (%) = 326 (100), 181 (62), 159 (20), 140 (13), 109 (13); HRMS (ESI): calcd. for $C_{19}H_{13}F_3N_2$ ($[M + H]^+$): 327.11036; found: 327.11066.



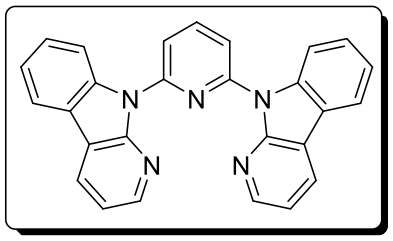
5-propyl-5H-pyrido[3,2-b]indole **18l** was prepared following general procedure 6 using **17a** (100 mg, 0.37 mmol) and n-propylamine (46 µL, 0.56 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 3:1) to yield **18l** (71 mg, 91 %) as a white liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.38 (dd, *J* = 4.9, 1.6 Hz, 1H), 8.16 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.97 – 7.89 (m, 1H), 7.43 – 7.29 (m, 2H), 7.14 (ddd, *J* = 8.0, 6.9, 1.4 Hz, 1H), 7.01 (dd, *J* = 7.6, 4.9 Hz, 1H), 4.37 – 4.26 (m, 2H), 1.90 – 1.73 (m, 2H), 0.86 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 151.61, 145.94, 139.71, 128.03, 126.61, 121.03, 120.44, 119.62, 115.83, 114.86, 109.38, 43.16, 22.32, 11.65; IR (ATR, cm^{-1}): ν = 3049 (w), 2962 (m), 2929 (m), 2874 (w), 1626 (w), 1589 (m), 1570 (m), 1481 (s), 1466 (s), 1443 (m), 1414 (vs), 1381 (m), 1371 (m), 1360 (m), 1342 (s), 1333 (s), 1313 (w), 1290 (s), 1255 (m), 1219 (s), 1157 (m), 1138 (m), 1128 (m), 1119 (s), 1090 (w), 1068 (m), 1049 (w), 1018 (w), 997 (m), 960 (w), 926 (w), 893 (w), 845 (w), 800 (w), 771 (vs), 748 (s), 733 (vs), 712 (m), 633 (m), 619 (m), 580 (m), 561 (m); GC-MS (EI, 70 eV): m/z (%) = 210 (32), 181 (100), 168 (82), 140 (12), 127 (14); HRMS (EI): calcd. for $C_{14}H_{14}N_2$ ($[M]^+$): 210.11515; found: 210.11500.

General procedure 7 for double C-N coupling with diamine derivatives, exemplified by: ***1,4-bis(9H-pyrido[2,3-b]indol-9-yl)benzene*** **7a**



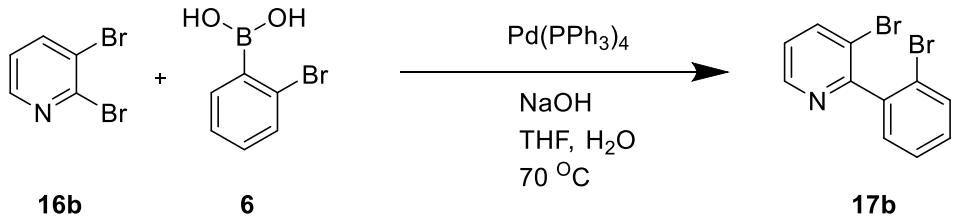
17a **19a** **20a**

To pressure tube was charged with **17a** (200 mg, 0.75 mmol), 1,4-diaminobenzen (37 mg, 0.34 mmol), $Pd_2(dba)_3$ (15 mg, 17 µmol), ligand Dppf (19 mg, 34 µmol) and sodium *tert*-butoxide (195 mg, 2.0 mmol) under Argon. The mixture was back-filled with Argon several times. The mixture was dissolved in anhydrous Toluene (10 mL) and heated at 110 ºC for 10 h. After cooling, the reaction mixture was diluted with dichloromethane (20 mL) and filtered through a celite pad, washing with dichloromethane (40 mL). The filtrate was reduced *in vacuo*. The product was separated via flash chromatography (silica gel, heptane/dichloromethane/ethylacetate 1:1:1) to yield 1,4-bis(9*H*-pyrido[2,3-*b*]indol-9-yl)benzene **20a** (64 mg, 46 %) as a white solid; m.p. 307-308 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.46 (dd, *J* = 4.8, 1.4 Hz, 2H), 8.34 (dt, *J* = 9.4, 4.7 Hz, 2H), 8.09 (d, *J* = 7.7 Hz, 2H), 7.87 (s, 4H), 7.62 (d, *J* = 8.2 Hz, 2H), 7.50 – 7.37 (m, 2H), 7.30 (t, *J* = 7.5 Hz, 2H), 7.25 – 7.16 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 151.90 (x2C), 146.48 (x2C), 139.94 (x2C), 135.34 (x2C), 128.42 (x2C), 128.32 (x4C), 127.14 (x2C), 121.02 (x4C), 116.61 (x2C), 116.37 (x2C), 110.73 (x2C); IR (ATR, cm^{-1}): ν = 3045 (m), 2922 (m), 1591 (m), 1572 (m), 1518 (s), 1481 (m), 1450 (s), 1406 (s), 1356 (m), 1338 (s), 1317 (m), 1290 (s), 1228 (s), 1173 (m), 1128 (m), 1120 (m), 1111 (m), 1051 (m), 1018 (m), 999 (m), 928 (m), 918 (m), 827 (m), 762 (s), 742 (s), 727 (vs), 700 (s), 642 (s), 619 (m), 579 (m), 567 (m), 534 (s); GC-MS (EI, 70 eV): m/z (%) = 410 (100), 242 (24), 205 (23), 191 (12); HRMS (EI): calcd. for $C_{28}H_{18}N_4$ ($[M]^+$): 410.15260; found: 410.15147.



9-(6-(9H-indeno[2,1-b]pyridin-9-yl)pyridin-2-yl)-9H-pyrido[2,3-b]indole **20b** was prepared following general procedure 7 using **17a** (200 mg, 0.75 mmol) and 2,6-diaminopyridine (37 mg, 0.34 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane/ethylacetate 1:1:1) to yield **20b** (70 mg, 50 %) as a white solid; m.p. 236-237 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.51 (dd, *J* = 4.8, 1.5 Hz, 2H), 8.43 – 8.29 (m, 4H), 8.29 – 8.21 (m, 2H), 8.13 (dd, *J* = 8.8, 7.1 Hz, 1H), 8.00 (t, *J* = 9.9 Hz, 2H), 7.38 – 7.14 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 151.36, 149.76, 146.01, 140.02, 139.02, 128.26, 127.54, 121.79, 121.57, 120.37, 117.76, 117.15, 116.61, 114.34; IR (ATR, cm^{-1}): ν = 3047 (w), 2922 (w), 1599 (m), 1591 (s), 1570 (m), 1485 (w), 1450 (vs), 1414 (m), 1400 (vs), 1362 (m), 1340 (m), 1331 (s), 1286 (s), 1242 (m), 1223 (m), 1209 (m), 1180 (s), 1165 (m), 1155 (m), 1120 (m), 1105 (m), 1095 (m), 1057 (m), 1039 (m), 1026 (m), 999 (m), 985 (w), 974 (w), 968 (w), 957 (w), 943 (m), 933 (m), 922 (m), 849 (w), 796 (m), 764 (vs), 744 (s), 727 (vs), 700 (m), 683 (m), 658 (m), 634 (m), 619 (m), 611 (m), 579 (m), 567 (w), 559 (m); GC-MS (EI, 70 eV): m/z (%) = 410 (100), 244 (28), 206 (89); HRMS (EI): calcd. for $C_{27}H_{16}N_5$ ([M]$^+$): 410.14002; found: 410.13958.

Procedure for preparation of *3-bromo-2-(2-bromophenyl)pyridine* 17b.

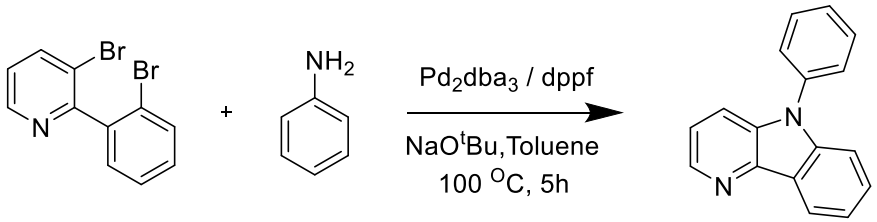


16b **6** **17b**

2,3-dibromopyridine **1b** (1 g, 4.2 mmol), 2-bromophenyl boronic acid **2** (1.0 g, 5.1 mmol), $Pd(PPh_3)_4$ (244 mg, 211 μmol) and sodium hydroxide (507 mg, 12.7 mmol) were added to 500 mL Schlenk flask. The mixture was back-filled several times with Argon. To the mixture 70 mL THF and 10 mL distilled water were added, then, back-filled with argon several times. The reaction was heated at 70 ºC for 4h. The solvent was evaporated *in vacuo*. The residue was extracted with dichloromethane and water. The organic layer was dried over $MgSO_4$, filtered and the solvent was evaporated *in vacuo*. The yellow residue was purified by column chromatography (silica gel, Heptane/dichloromethane/ethylacetate 4:1:1) to yield 3-bromo-2-(2-bromophenyl)pyridine **17b** (1.27 g, 96 %) as colorless syrup; ^{1}H NMR (300 MHz,

$CDCl_3$) δ = 8.57 (dd, *J* = 4.7, 1.5 Hz, 1H), 7.93 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.63 – 7.58 (m, 1H), 7.39 – 7.32 (m, 1H), 7.29 – 7.13 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 147.84, 140.99, 140.46, 132.69, 130.23, 130.08, 127.34, 124.13, 122.46, 121.35; IR (ATR, cm^{-1}): ν = 3053 (w), 2920 (w), 2850 (w), 1593 (m), 1568 (m), 1549 (m), 1479 (m), 1437 (m), 1412 (s), 1298 (w), 1269 (w), 1252 (m), 1230 (w), 1211 (w), 1201 (w), 1159 (w), 1124 (m), 1093 (m), 1055 (m), 1024 (s), 1011 (vs), 943 (m), 793 (s), 777 (m), 748 (vs), 723 (s), 694 (m), 681 (s), 650 (m), 615 (s), 561 (m); GC-MS (EI, 70 eV): m/z (%) = 313 (37), 234 (99), 233 (100), 153 (82), 126 (28), 99 (10), 75 (14), 63 (10), 50 (12); HRMS (EI): calcd. for $C_{11}H_7N_1Br_2$ ($[M]^+$): 310.89398; found: 310.89479; calcd. for $C_{11}H_7N_1Br_1{}^{81}Br_1$ ($[M]^+$): 312.89193; found: 312.89233; calcd. for $C_{11}H_7N_1{}^{81}Br_2$ ($[M]^+$): 314.88988; found: 314.89073.

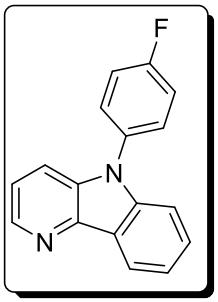
General procedure 8 for double C-N coupling with aniline derivatives, exemplified by: ***5-phenyl-5H-pyrido[3,2-b]indole*** **21a**



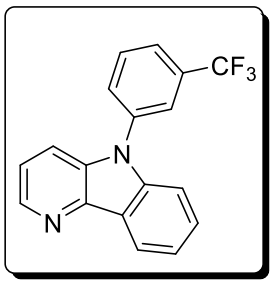
17b **8a** **21a**

Aniline (44 µL, 479 µmol) was added to pressure tube charged with **17b** (100 mg, 0.32 mmol), $Pd_2(dba)_3$ (15 mg, 16 µmol), ligand Dppf (18 mg, 32 µmol) and sodium *tert*-butoxide (92 mg, 0.96 mmol) under Argon. The mixture was back-filled with Argon several times. The mixture was dissolved in anhydrous Toluene (10 mL) and heated at 100 ºC for 4 h. After cooling, the reaction mixture was diluted with dichloromethane (20 mL) and filtered through a celite pad, washing with dichloromethane (40 mL). The filtrate was reduced *in vacuo*. The product was separated via flash chromatography (silica gel, heptane/dichloromethane/ethylacetate 10:1:1) to yield 5-phenyl-5*H*-pyrido[3,2-*b*]indole **21a** (65 mg, 83%) as a white solid; m.p. 99-101 ºC; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 8.50 (dd, *J* = 4.7, 1.3 Hz, 1H), 8.40 – 8.30 (m, 1H), 7.60 – 7.12 (m, 11H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 142.54, 142.26, 141.54, 136.84, 134.31, 130.04, 127.95, 127.80, 126.79, 122.45, 120.87, 120.83, 120.18, 116.72, 110.04; IR (ATR, cm^{-1}): ν = 3053 (m), 1622 (m), 1593 (s), 1574 (m), 1502 (s), 1481 (s), 1452 (s), 1412 (vs), 1371 (m), 1340 (m), 1315 (m), 1304 (s), 1282 (m),

1234 (m), 1209 (s), 1178 (m), 1167 (m), 1147 (m), 1119 (m), 1107 (m), 1072 (m), 1026 (m), 1011 (m), 931 (m), 906 (m), 787 (m), 777 (s), 762 (s), 744 (vs), 727 (vs), 698 (vs), 665 (m), 642 (m), 633 (s), 615 (s), 582 (m), 567 (m), 534 (m); GC-MS (EI, 70 eV): m/z (%) = 244 (100), 216 (4), 189 (3), 167 (3), 152 (3), 140 (4), 122 (9), 88 (3), 77 (4), 63 (3), 51 (5), 39 (4); HRMS (EI): calcd. for $C_{17}H_{12}N_2$ ($[M]^+$): 244.09950; found: 244.09922.

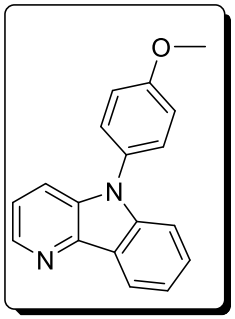


5-(4-fluorophenyl)-5H-pyrido[3,2-b]indole **21b** was prepared following general procedure 8 using **17b** (100 mg, 0.32 mmol) and 4-fluoroaniline (45 µL, 0.48 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane/ethylacetate 8:1:1) to yield **21b** (61 mg, 73 %) as a white solid; m.p. 115-117 ºC; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 8.49 (dd, *J* = 4.7, 1.3 Hz, 1H), 8.39 – 8.29 (m, 1H), 7.53 – 7.32 (m, 4H), 7.31 – 7.11 (m, 3H), 6.78 – 6.65 (m, 1H), 6.48 (ddd, *J* = 6.7, 5.2, 2.9 Hz, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ = -112.83 (s); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 161.79 (d, *J* = 248.2 Hz), 142.62, 141.69, 134.45, 132.77, 128.73 (d, *J* = 8.6 Hz), 128.06, 122.38, 120.94, 120.27, 117.24, 116.88, 116.50, 115.61 (d, *J* = 22.4 Hz), 109.80; IR (ATR, cm^{-1}): ν = 3055 (m), 3037 (m), 1620 (m), 1587 (m), 1506 (vs), 1477 (s), 1452 (s), 1412 (s), 1354 (m), 1342 (m), 1311 (s), 1294 (m), 1281 (m), 1215 (s), 1207 (s), 1169 (s), 1151 (s), 1119 (m), 1105 (m), 1093 (s), 1049 (m), 1034 (m), 1028 (m), 1011 (m), 937 (m), 912 (s), 845 (s), 833 (s), 816 (s), 781 (s), 764 (m), 742 (vs), 727 (vs), 715 (s), 700 (s), 646 (m), 627 (m), 617 (s), 575 (s), 534 (s); GC-MS (EI, 70 eV): m/z (%) = 262 (100), 261 (29), 131 (10); HRMS (EI): calcd. for $C_{17}H_{11}F_1N_2$ ($[M]^+$): 262.09008; found: 262.08948.

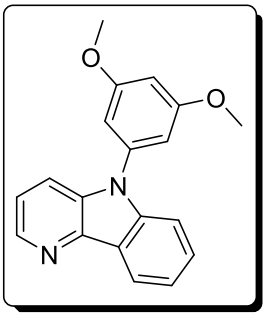


5-(3-(trifluoromethyl)phenyl)-5H-pyrido[3,2-b]indole **21c** was prepared following general procedure 8 using **17b** (100 mg, 0.32 mmol) and 3-(trifluoromethyl)aniline (60 µL, 0.48 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane/ethylacetate 8:1:1) to yield **21c** (64 mg, 64 %) as a white solid; m.p. 144-146 ºC; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 8.54 (dd, *J* = 4.7, 1.3 Hz, 1H), 8.47 – 8.29 (m, 1H), 7.84 – 7.53 (m, 5H), 7.52 – 7.14 (m, 4H); ^{19}F NMR (282 MHz, $CDCl_3$) δ = -62.70 (s); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 143.08, 142.52, 141.17, 137.65, 133.96, 132.76 (q, *J* = 33.2 Hz), 130.80, 130.03, 128.26, 124.44 (q, *J* = 3.6 Hz), 123.61 (q, *J* = 3.6 Hz), 122.75, 121.41, 121.09, 120.39, 116.43, 109.66; IR (ATR, cm^{-1}): ν = 3055 (w), 3041 (w), 1622 (m), 1606 (w), 1595 (m), 1579 (w), 1498 (m), 1481 (m),

1456 (s), 1412 (s), 1362 (m), 1356 (m), 1333 (m), 1309 (s), 1292 (m), 1275 (m), 1232 (m), 1217 (m), 1207 (m), 1182 (s), 1163 (s), 1155 (s), 1117 (vs), 1095 (s), 1074 (s), 1028 (m), 1014 (m), 1001 (m), 966 (m), 945 (m), 935 (m), 928 (m), 918 (m), 906 (m), 854 (w), 810 (m), 802 (s), 791 (m), 781 (s), 760 (w), 744 (vs), 727 (s), 715 (s), 706 (vs), 673 (m), 663 (s), 638 (m), 621 (m), 607 (m), 582 (w), 563 (w), 536 (m); GC-MS (EI, 70 eV): m/z (%) = 312 (100), 242 (8); HRMS (EI): calcd. for $C_{18}H_{11}F_3N_2$ ($[M]^+$): 312.08688; found: 312.08662.

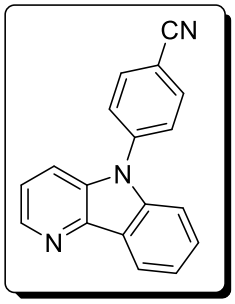


5-(4-methoxyphenyl)-5H-pyrido[3,2-b]indole **21d** was prepared following general procedure 8 using **17b** (100 mg, 0.32 mmol) and *p*-anisidine (59 mg, 0.48 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane/ethylacetate 5:1:1) to yield **21d** (88 mg, 94 %) as a white solid; m.p. 128-130 ºC; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 8.53 (dd, *J* = 4.7, 1.3 Hz, 1H), 8.43 – 8.30 (m, 1H), 7.55 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.50 – 7.21 (m, 6H), 7.11 – 6.99 (m, 2H), 3.85 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 159.13, 142.22, 142.06, 134.81, 129.36, 128.30, 127.90, 122.13, 120.85, 120.59, 120.12, 116.68, 115.22, 109.97, 55.62; IR (ATR, cm^{-1}): ν = 2955 (w), 2929 (w), 2837 (w), 1620 (m), 1510 (vs), 1479 (m), 1454 (s), 1441 (m), 1414 (s), 1385 (w), 1342 (m), 1313 (s), 1300 (m), 1286 (m), 1242 (s), 1209 (s), 1176 (s), 1149 (m), 1120 (m), 1107 (s), 1066 (m), 1028 (s), 1012 (m), 937 (m), 912 (m), 860 (w), 829 (s), 812 (m), 791 (s), 748 (vs), 729 (vs), 700 (s), 667 (m), 646 (m), 629 (m), 617 (s), 584 (s), 536 (s); GC-MS (EI, 70 eV): m/z (%) = 274 (100), 259 (55), 231 (13), 230 (15), 229 (14), 115 (9); HRMS (EI): calcd. for $C_{18}H_{14}O_1N_2$ ($[M]^+$): 274.11006; found: 274.11009.



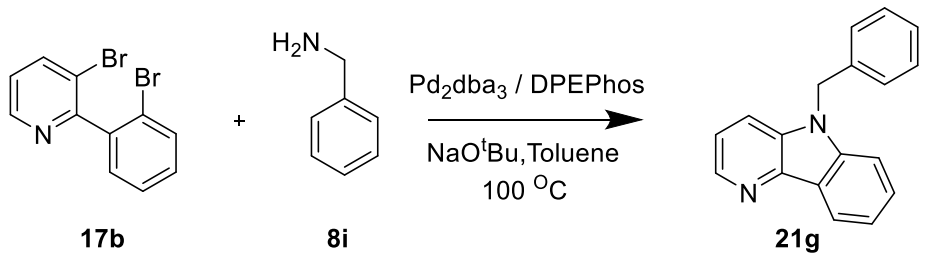
55-(3,5-dimethoxyphenyl)-5H-pyrido[3,2-b]indole **21e** was prepared following general procedure 8 using **17b** (100 mg, 0.32 mmol) and 3,5-dimethoxyaniline (73 mg, 0.48 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane/ethylacetate 3:1:1) to yield **21d** (88 mg, 94 %) as a white solid; m.p. 150-152 ºC; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 8.58 – 8.41 (m, 1H), 8.33 (dd, *J* = 7.7, 0.7 Hz, 1H), 7.64 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.53 – 7.12 (m, 4H), 6.57 (d, *J* = 2.2 Hz, 2H), 6.45 (t, *J* = 2.2 Hz, 1H), 3.71 (s, *J* = 9.9 Hz, 6H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 161.82, 142.55, 142.26, 141.37, 138.46, 134.17, 127.95, 122.48, 120.82, 120.20, 116.99, 110.33, 104.96, 99.76, 93.72, 55.59; IR (ATR, cm^{-1}): ν = 3051 (m), 3007 (m), 2970 (m), 2945 (m), 2916 (m), 2841 (m), 1620 (m), 1605 (s), 1583 (s), 1495 (m),

1475 (m), 1452 (s), 1425 (s), 1416 (s), 1367 (m), 1342 (m), 1331 (m), 1313 (s), 1296 (s), 1282 (s), 1252 (m), 1223 (m), 1194 (s), 1147 (vs), 1057 (s), 1009 (s), 991 (m), 928 (m), 906 (m), 868 (m), 852 (m), 833 (s), 823 (s), 783 (s), 773 (s), 741 (s), 723 (vs), 696 (s), 690 (s), 675 (s), 660 (s), 621 (s), 607 (s), 573 (s), 557 (m), 532 (m); GC-MS (EI, 70 eV): m/z (%) = 304 (100), 261 (8), 245 (10), 218 (7); HRMS (EI): calcd. for $C_{19}H_{16}O_2N_2$ ($[M]^+$): 304.12063; found: 304.12015.



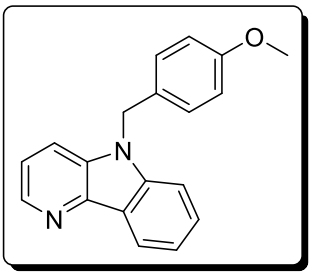
5-(4-cyanophenyl)-5H-pyrido[3,2-b]indole **21f** was prepared following general procedure 8 using **17b** (100 mg, 0.32 mmol) and 4-aminobenzonitrile (56 mg, 0.48 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane/ethylacetate 4:1:1) to yield **21f** (36 mg, 42 %) as a white solid; m.p. 162-164 ºC; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 8.57 (dd, *J* = 4.7, 1.3 Hz, 1H), 8.41 – 8.33 (m, 1H), 7.90 – 7.81 (m, 2H), 7.71 – 7.60 (m, 3H), 7.52 – 7.23 (m, 4H), ^{13}C NMR (63 MHz, $CDCl_3$) δ = 143.51, 142.86, 141.21, 140.63, 134.10, 133.45, 128.42, 126.86, 123.12, 121.88, 121.23, 120.49, 118.10, 116.59, 111.02, 109.77; IR (ATR, cm^{-1}): ν = 3051 (w), 3007 (w), 2226 (m), 1616 (w), 1601 (s), 1587 (m), 1558 (w), 1506 (s), 1489 (w), 1479 (m), 1454 (m), 1412 (s), 1373 (w), 1354 (m), 1340 (m), 1315 (s), 1290 (m), 1246 (w), 1234 (m), 1221 (m), 1207 (s), 1182 (m), 1169 (m), 1153 (m), 1136 (m), 1128 (m), 1117 (m), 1107 (m), 1053 (w), 1028 (w), 1014 (m), 978 (w), 968 (w), 953 (w), 935 (w), 916 (m), 885 (w), 841 (s), 783 (s), 748 (vs), 731 (vs), 723 (s), 667 (m), 656 (m), 631 (m), 619 (s), 582 (w), 567 (m), 552 (s), 528 (m); GC-MS (EI, 70 eV): m/z (%) = 269 (100), 270 (25), 75 (7), 39 (7); HRMS (EI): calcd. for $C_{18}H_{11}N_3$ ($[M]^+$): 269.09475; found: 269.09432.

General procedure 9 for double C-N coupling with chain amine derivatives, exemplified by: ***5-benzyl-5H-pyrido[3,2-b]indole*** **21g**



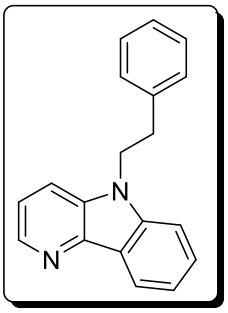
To pressure tube charged with **17b** (100 mg, 0.32 mmol), $Pd_2(dba)_3$ (15 mg, 16 µmol), ligand DPEPhos (17 mg, 32 µmol) and sodium *tert*-butoxide (92 mg, 0.96 mmol) under Argon. The

mixture was back-filled with argon several times. The mixture was dissolved in anhydrous toluene (10 mL). Benzylamine **4i** (52 µL, 0.48 mmol) was added to the mixture and heated at 100 ºC for 7 h. After cooling, the reaction mixture was diluted with dichloromethane (20 mL) and filtered through a celite pad, washing with dichloromethane (40 mL). The filtrate was reduced *in vacuo*. The product was separated via flash chromatography (silica gel, heptane/dichloromethane/ethylacetate 5:1:1) to yield **21g** (76 mg, 92 %) as a white solid; m.p. 137-139 ºC; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 8.43 (dd, *J* = 4.7, 1.2 Hz, 1H), 8.32 (d, *J* = 7.7 Hz, 1H), 7.45 – 7.30 (m, 2H), 7.28 – 7.01 (m, 6H), 6.93 (dd, *J* = 6.7, 2.6 Hz, 2H), 5.26 (s, 2H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 140.82, 140.75, 140.27, 135.40, 132.91, 127.78, 126.80, 126.62, 125.25, 121.08, 119.82, 119.07, 118.93, 114.75, 108.14, 45.35; IR (ATR, cm^{-1}): ν = 3051 (w), 3028 (w), 2926 (w), 1622 (m), 1603 (w), 1589 (m), 1576 (w), 1558 (w), 1495 (m), 1483 (m), 1458 (s), 1450 (s), 1414 (s), 1373 (m), 1356 (w), 1335 (s), 1319 (s), 1281 (w), 1263 (w), 1242 (m), 1211 (m), 1194 (s), 1178 (m), 1149 (m), 1132 (m), 1117 (m), 1080 (m), 1057 (w), 1047 (w), 1028 (m), 1012 (m), 999 (w), 972 (w), 962 (w), 937 (w), 912 (w), 845 (m), 802 (w), 789 (m), 781 (s), 742 (vs), 731 (vs), 721 (vs), 694 (s), 644 (m), 621 (m), 600 (m), 584 (m), 567 (m), 557 (m), 536 (m); GC-MS (EI, 70 eV): m/z (%) = 258 (88), 181 (5), 167 (8), 91 (100), 39 (9); HRMS (EI): calcd. for $C_{18}H_{14}N_2$ ($[M]^+$): 258.11515; found: 258.11534.



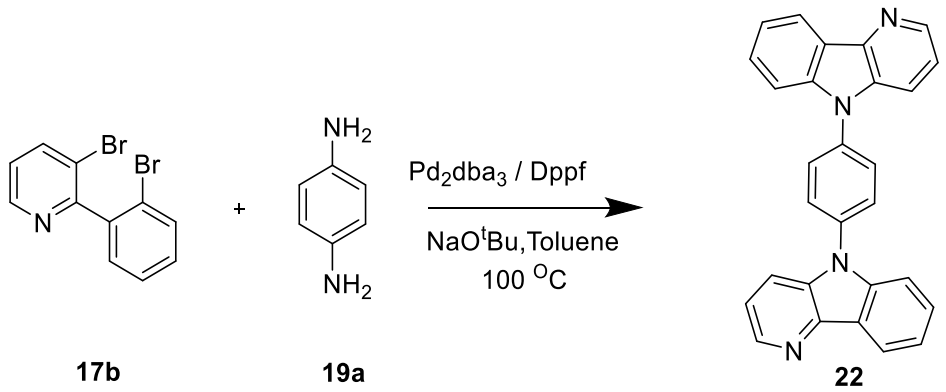
5-(4-methoxybenzyl)-5H-pyrido[3,2-b]indole **21h** was prepared following general procedure 9 using compound **17b** (100 mg, 0.32 mmol) and 4-methoxybenzylamine (63 µL, 0.48 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane/ethylacetate 3:1:1) to yield **21h** (60 mg, 65 %) as a white solid; m.p. 124-126 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.42 (dd, *J* = 4.7, 1.3 Hz, 1H), 8.36 – 8.28 (m, 1H), 7.48 – 7.31 (m, 2H), 7.30 – 7.07 (m, 3H), 6.88 (t, *J* = 5.8 Hz, 2H), 6.68 – 6.58 (m, 2H), 5.22 (s, 2H), 3.57 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 159.15, 141.92, 141.77, 141.37, 134.01, 128.51, 127.90, 127.71, 122.17, 120.94, 120.12, 120.02, 115.94, 114.27, 109.30, 55.24, 46.00; IR (ATR, cm^{-1}): ν = 2931 (w), 2835 (w), 1624 (m), 1610 (m), 1583 (m), 1512 (s), 1485 (s), 1460 (s), 1443 (m), 1412 (s), 1377 (m), 1354 (w), 1323 (s), 1308 (s), 1246 (vs), 1211 (m), 1203 (m), 1194 (s), 1178 (s), 1155 (m), 1134 (m), 1113 (s), 1059 (w), 1034 (s), 1009 (m), 984 (m), 962 (m), 939 (w), 864 (w), 845 (s), 837 (m), 820 (m), 791 (s), 775 (s), 746 (vs), 727 (vs), 708 (s), 665 (m), 640 (m), 625 (s), 600 (s), 582 (m), 565 (m), 540 (s); GC-MS (EI, 70 eV): m/z (%) = 288 (29), 242 (3), 167 (8), 140 (5),

121 (100), 91 (7), 78 (10), 77 (9); HRMS (EI): calcd. for $C_{19}H_{16}N_2O_1$ ($[M]^+$): 288.12571; found: 288.12541.



5-phenethyl-5H-pyrido[3,2-b]indole **21i** was prepared following general procedure 9 using compound **17b** (100 mg, 0.32 mmol) and 2-phenylethylamine (60 µL, 0.48 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane/ethylacetate 5:1:1) to yield **21j** (67 mg, 77 %) as a white solid; m.p. 61-63 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.38 (dd, *J* = 4.7, 1.3 Hz, 1H), 8.29 (d, *J* = 7.7 Hz, 1H), 7.38 (ddd, *J* = 8.2, 7.1, 1.2 Hz, 1H), 7.28 – 7.13 (m, 3H), 7.13 – 6.96 (m, 4H), 6.96 – 6.82 (m, 2H), 4.30 (t, *J* = 7.2 Hz, 2H), 2.93 (t, *J* = 7.2 Hz, 2H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 141.61, 141.46, 140.80, 138.37, 133.73, 128.73, 128.66, 127.66, 126.76, 122.05, 120.91, 119.88, 119.75, 115.45, 108.91, 44.82, 35.27; IR (ATR, cm^{-1}): ν = 3051 (w), 3041 (w), 3026 (w), 3001 (w), 2964 (w), 2939 (w), 2922 (w), 1622 (m), 1603 (w), 1587 (m), 1562 (w), 1483 (s), 1462 (s), 1452 (s), 1414 (vs), 1377 (m), 1360 (m), 1342 (s), 1319 (s), 1248 (w), 1223 (s), 1200 (m), 1186 (s), 1151 (m), 1132 (m), 1122 (m), 1080 (m), 1065 (w), 1049 (w), 1028 (m), 1009 (m), 974 (w), 962 (w), 939 (w), 926 (w), 881 (w), 856 (w), 839 (w), 791 (m), 777 (m), 764 (w), 742 (vs), 727 (vs), 696 (vs), 642 (w), 623 (m), 613 (m), 606 (m), 590 (m), 582 (w), 565 (w), 548 (m), 540 (m); GC-MS (EI, 70 eV): m/z (%) = 272 (23), 181 (100), 154 (5), 127 (12), 91 (5), 78 (5); HRMS (EI): calcd. for $C_{19}H_{16}N_2$ ($[M]^+$): 272.13080; found: 272.13063.

Synthesis of *1,4-bis(5H-pyrido[3,2-b]indol-5-yl)benzene* 22



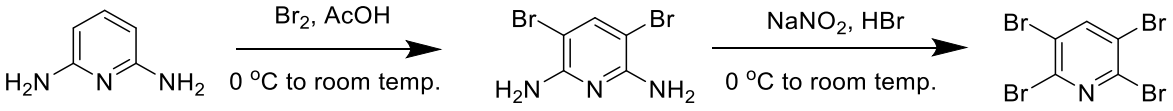
17b **19a** **22**

A pressure tube was charged with **17b** (200 mg, 0.64 mmol), 1,4-diaminobenzene (34 mg, 0.32 mmol), $Pd_2(dba)_3$ (12 mg, 13 µmol), ligand Dppf (14 mg, 26 µmol) and sodium *tert*-

butoxide (147 mg, 1.53 mmol) under Argon. The mixture was back-filled with Argon several times. The mixture was dissolved in anhydrous toluene (10 mL) and heated at 100 ºC for 10 h. After cooling, the reaction mixture was diluted with dichloromethane (20 mL) and filtered through a celite pad, washing with dichloromethane (40 mL). The filtrate was reduced *in vacuo*. The product was separated via flash chromatography (silica gel, heptane/dichloromethane/ethylacetate 1:1:1) to yield 1,4-bis(5*H*-pyrido[3,2-*b*]indol-5-yl)benzene **22** (52 mg, 40 %) as a white solid; m.p. 277-279 ºC; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 8.76 – 8.33 (m, 4H), 7.96 – 7.06 (m, 14H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 142.02, 141.51, 140.20, 137.74, 132.99, 127.24, 124.84, 121.75, 120.36, 120.12, 119.37, 115.61, 108.83; IR (ATR, cm^{-1}): ν = 3053 (w), 1620 (w), 1595 (m), 1585 (m), 1576 (m), 1497 (s), 1475 (m), 1450 (s), 1408 (s), 1373 (w), 1362 (w), 1340 (m), 1315 (s), 1306 (s), 1288 (m), 1263 (m), 1238 (w), 1215 (m), 1203 (s), 1178 (m), 1155 (m), 1120 (m), 1111 (m), 1101 (m), 1090 (m), 1049 (m), 1026 (m), 1012 (m), 968 (w), 922 (m), 903 (w), 877 (w), 850 (w), 810 (m), 800 (m), 779 (s), 742 (vs), 727 (vs), 700 (s), 671 (m), 648 (m), 631 (m), 619 (s), 584 (m), 567 (m), 536 (m); GC-MS (EI, 70 eV): m/z (%) = 410 (100), 242 (28), 205 (11); HRMS (ESI): calcd. for $C_{28}H_{18}N_4$ ($[M + H]^+$): 411.16042; found: 411.15977.

8.5.4 Synthesis and Properties of 5,7-Dihydropyrido[3,2-b:5,6-b']diindoles

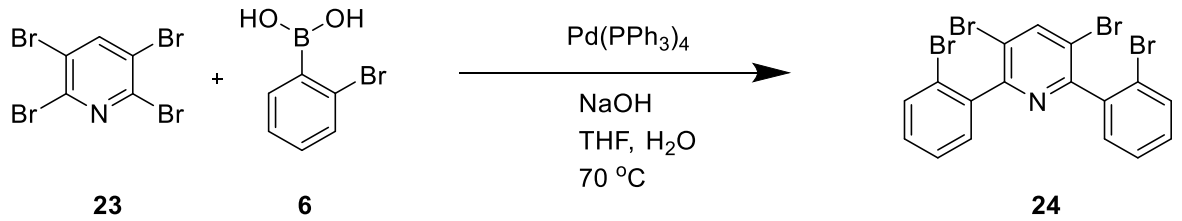
Procedure for preparation of *2,3,5,6-tetrabromopyridine*



To solution of pyridine-2,6-diamine (10.9 g, 100 mmol) in 200 mL glacial acetic acid was dropwised added 11.4 mL bromine (220 mmol)at 0 ºC. Then the temperature was raised to room temperature and the mixture was stirred for 5h. The reaction mixture was treated with aqueous Na_2SO_3 solution to remove residues of bromine. The mixture was neutralized with NaOH to pH 8-9. The brown solid (22 g, 83%) was obtained after filtering, washing with water and drying *in vacuo*.

To solution of 3,5-dibromopyridine-2,6-diamine (10 g, 37.5 mmol) in 30 mL 48 % HBr was dropwised added saturate aqueous $NaNO_2$ (20.7 g, 300 mmol) solution at -3 ˚C. Afterwards, the reaction mixture was stirred at the same temperature for 2h, then, the temperature was raised to room temperature and kept for additional 2h. The solution was neutralized to pH 8-9 by NaOH then extracted with ethylacetate. The organic layer was collected, dried over $MgSO_4$, filtered and evaporated *in vacuo*. The mixture was separated over column chromatography (silica gel, heptane/dichloromethane 5:1) to yield 2,3,5,6-tetrabromopyridine **23** (3 g, 20%) as white crystals, m.p. 172-174 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.99 (s, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 145.32 (s), 140.60 (s), 123.01 (s); IR (ATR, cm^{-1}): ν = 3084 (m), 3036 (m), 1529 (m), 1502 (s), 1362 (vs), 1352 (vs), 1288 (s), 1277 (s), 1238 (m), 1213 (m), 1149 (vs), 1136 (s), 1016 (vs), 945 (m), 931 (m), 897 (vs), 833 (m), 806 (m), 798 (m), 781 (m), 704 (s), 656 (s), 648 (s); GC-MS (EI, 70 eV): m/z (%) = 395 (100), 314 (42), 235 (26), 154 (13), 75 (42); HRMS (EI): calcd. for $C_5H_1N_1Br_3{}^{81}Br_1$ ($[M]^+$): 392.6815; found: 392.68185; calcd. for $C_5H_1N_1Br_2{}^{81}Br_2$ ($[M]^+$): 394.67961; found: 394.67983; calcd. for $C_5H_1N_1Br_1{}^{81}Br_3$ ($[M]^+$): 396.67756; found: 396.67761.

General procedure for preparation of *3,5-dibromo-2,6-bis(2-bromophenyl)pyridine* 24.

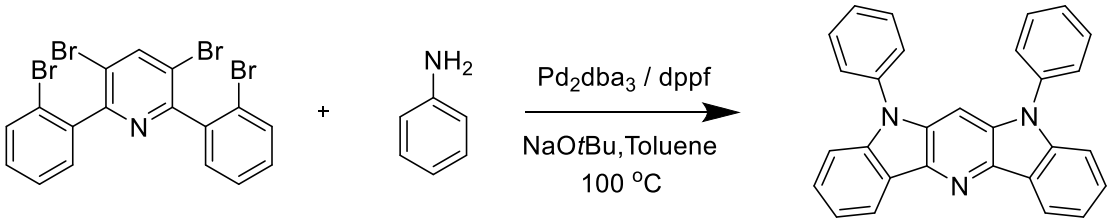


23 **6** **24**

2,3,5,6-tetrabromopyridine **23** (1 g, 2.5 mmol), 2-bromophenyl boronic acid **6** (1.1 g, 5.5 mmol), $Pd(PPh_3)_4$ (73 mg, 63 µmol) and sodium hydroxide (608 mg, 15.2 mmol) were added to 500 mL Schlenk flask. The mixture was back-filled several times with Argon. To the mixture 70 mL THF and 10 mL distilled water were added, then, back-filled several times with argon. The reaction was heated at 70 ºC for 4h. The solvent was evaporated *in vacuo*. The residue was extracted with dichloromethane and water. The organic layer was dried over $MgSO_4$, filtered and the solvent was evaporated *in vacuo*. The yellow residue was purified by column chromatography (silica gel, Heptane/ethylacetate 10:1) to yield *3,5-dibromo-2,6-bis(2-bromophenyl)pyridine* **24** (1.1 g, 80 %) as white solid; m.p. 174-175 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.24 (s, 1H), 7.58 (d, *J* = 8.0 Hz, 2H), 7.37 – 7.25 (m, 4H), 7.20 (dd, *J* = 8.4, 7.3 Hz, 2H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 156.75, 143.78, 139.78, 132.75, 130.33

(x2C), 127.37, 122.50, 120.43; IR (ATR, cm^{-1}): ν = 2922 (m), 2850 (m), 1562 (m), 1529 (m), 1477 (m), 1470 (m), 1441 (m), 1427 (m), 1406 (s), 1348 (m), 1329 (m), 1284 (m), 1275 (w), 1265 (m), 1240 (m), 1194 (m), 1117 (m), 1041 (s), 1024 (s), 1005 (s), 984 (m), 951 (m), 889 (s), 870 (m), 850 (m), 756 (vs), 725 (s), 692 (s), 683 (s), 660 (m), 646 (m), 631 (s), 596 (m), 532 (m); GC-MS (EI, 70 eV): m/z (%) = 547 (21), 468 (73), 227 (100), 193 (10), 113 (13), 75 (11); HRMS (EI): calcd. for $C_{17}H_9N_1Br_4$ ($[M]^+$): 542.74630; found: 542.74628; calcd. for $C_{17}H_9N_1Br_3{}^{81}Br_1$ ($[M]^+$): 544.74425; found: 544.74445; calcd. for $C_{17}H_9N_1Br_2{}^{81}Br_2$ ($[M]^+$): 546.74221; found: 546.74277; calcd. for $C_{17}H_9N_1Br_1{}^{81}Br_3$ ($[M]^+$): 548.74016; found: 548.74086; calcd. for $C_{17}H_9N_1{}^{81}Br_4$ ($[M]^+$): 550.73811; found: 550.73897.

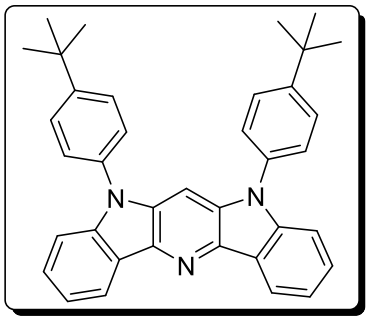
General procedure 10 for double C-N coupling with aniline derivatives, exemplified by: *5,7-diphenyl-5,7-dihydropyrido[3,2-b:5,6-b']diindole* 25a



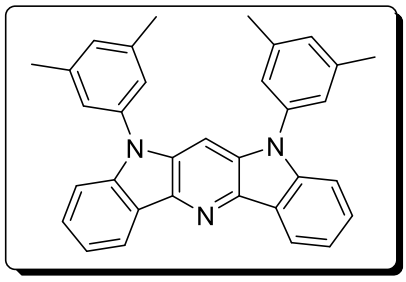
24 **8a** **25a**

Aniline (0.1 mL, 1.09 mmol) was added to a pressure tube charged with **24** (100 mg, 0.18 mmol), $Pd_2(dba)_3$ (8 mg, 9 µmol), ligand Dppf (10 mg, 18 µmol) and sodium *tert*-butoxide (105 mg, 1.09 mmol) under Argon. The mixture was back-filled with Argon several times. The mixture was dissolved in anhydrous toluene (10 mL) and heated at 100 ºC for 7 h. After cooling, the reaction mixture was diluted with dichloromethane (20 mL) and filtered through a celite pad, washing with dichloromethane (40 mL). The filtrate was reduced *in vacuo*. The product was separated via flash chromatography (silica gel, heptane/dichloromethane/ethylacetate 10:1:1) to yield **25a** (62 mg, 83%) as a white solide; m.p. 298-300 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.69 (d, *J* = 7.2 Hz, 2H), 7.63 – 7.55 (m, 9H), 7.50 – 7.38 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 142.35, 137.85, 137.31, 134.32, 130.26, 127.86, 127.09, 126.71, 122.55, 121.08, 120.78, 109.80, 96.93; IR (ATR, cm^{-1}): ν = 3036 (m), 2926 (w), 2852 (w), 1591 (s), 1497 (s), 1479 (m), 1454 (s), 1435 (m), 1404 (s), 1387 (s), 1313 (m), 1242 (s), 1205 (m), 1188 (s), 1178 (s), 1155 (m), 1144 (m), 1103 (m), 1074 (m), 1039 (m), 1028 (m), 1011 (m), 939 (m), 924 (m), 847 (m), 829 (m), 760 (m), 739 (s), 729 (s), 692 (vs), 667 (m), 638 (s), 623 (m), 615 (s), 582 (s), 567 (m), 536 (s); GC-MS (EI, 70 eV): m/z (%) = 409 (100), 332 (8), 204 (14); HRMS (ESI): calcd. for $C_{29}H_{20}N_3$ ([M +

H]$^+$): 410.16517; found: 41016512; calcd. for $C_{29}H_{20}N_3Na$ ([M + Na]$^+$): 432.14712; found: 432.14744.

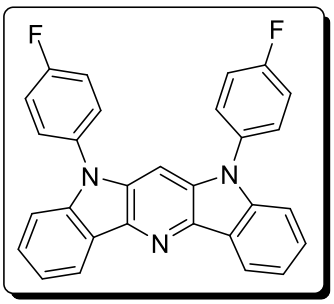


5,7-Bis(4-(tert-butyl)phenyl)-5,7-dihydropyrido[3,2-b:5,6-b']diindole **25b** was prepared following general procedure 10 using compound **24** (100 mg, 0.18 mmol) and 4-(*tert*-butyl)aniline (118 mg, 1.09 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane/ethylacetate 8:1:1) to yield **25b** (80 mg, 84%) as a white solide; m.p. 317-319 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.64 (d, *J* = 7.5 Hz, 2H), 7.68 – 7.59 (m, 5H), 7.56 – 7.35 (m, 10H), 1.42 (s, 18H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 150.65, 142.37, 138.00, 134.61, 134.27, 126.96, 126.72, 126.46, 122.68, 120.65, 120.37, 109.76, 96.77, 34.80, 31.39; IR (ATR, cm^{-1}): ν = 2958 (m), 2902 (w), 2866 (w), 1591 (m), 1518 (m), 1479 (w), 1456 (s), 1408 (m), 1392 (m), 1363 (m), 1350 (w), 1325 (w), 1309 (m), 1290 (w), 1261 (m), 1242 (s), 1207 (m), 1188 (m), 1169 (m), 1153 (m), 1147 (m), 1105 (m), 1036 (m), 1011 (m), 951 (w), 937 (w), 928 (w), 893 (w), 850 (m), 841 (m), 822 (m), 800 (m), 785 (m), 741 (vs), 729 (vs), 706 (m), 660 (m), 640 (m), 625 (m), 592 (w), 561 (s); GC-MS (EI, 70 eV): m/z (%) = 521 (100), 491 (9), 253 (15), 217 (93), 172 (21); HRMS (EI): calcd. for $C_{37}H_{35}N_3$ ([M]$^+$): 521.28255; found: 521.28186.

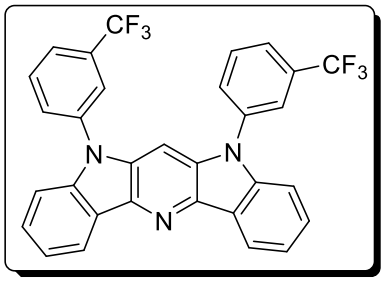


5,7-Bis(3,5-dimethylphenyl)-5,7-dihydropyrido[3,2-b:5,6-b']diindole **25c** was prepared following general procedure 10 using compound **24** (100 mg, 0.18 mmol) and 3,5-dimethylaniline (175 µL, 1.09 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane/ethylacetate 8:1:1) to yield **25c** (72 mg, 85%) as a white solide; m.p. 306-308 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.53 (d, *J* = 7.6 Hz, 2H), 7.48 (s, 1H), 7.41 – 7.26 (m, 6H), 7.11 (s, 4H), 7.00 (s, 2H), 2.32 (s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 142.23, 139.85, 138.03, 137.20, 134.29, 129.32, 126.73, 124.49, 122.76, 120.70, 120.38, 109.80, 96.90, 21.37; IR (ATR, cm^{-1}): ν = 3045 (w), 2914 (m), 2854 (w), 1589 (s), 1470 (s), 1456 (s), 1435 (m), 1417 (m), 1404 (s), 1387 (m), 1373 (m), 1311 (m), 1298 (m), 1242 (s), 1190 (s), 1153 (m), 1138 (m), 1105 (m), 1011 (m), 916 (m), 864 (m), 843 (s), 785 (m), 741 (vs), 725 (vs), 708 (s), 698 (s), 631 (m), 588 (m), 575 (m), 557 (m); GC-MS (EI, 70 eV): m/z

(%) = 465 (100), 233 (12), 79 (7); HRMS (EI): calcd. for $C_{33}H_{27}N_3$ ($[M]^+$): 465.21995; found: 465.21908.

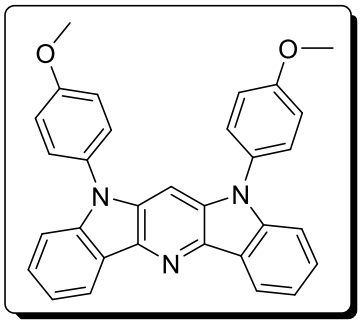


5,7-Bis(4-fluorophenyl)-5,7-dihydropyrido[3,2-b:5,6-b']diindole **25d** was prepared following general procedure 10 using compound **24** (100 mg, 0.18 mmol) and 4-fluoroaniline (104 µL, 1.09 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane/ethylacetate 8:1:1) to yield **25d** (54 mg, 66 %) as a white solide; m.p. 338-340 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.53 (d, *J* = 7.3 Hz, 2H), 7.48 – 7.28 (m, 9H), 7.27 – 7.17 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.03 (d, *J* = 248.1 Hz), 142.62 , 138.39 , 134.62 , 133.36 (d, *J* = 3.1 Hz), 129.20 (d, *J* = 8.6 Hz), 127.24 , 122.94 , 121.00 , 120.96 , 117.44 (d, *J* = 22.8 Hz), 109.69 , 96.18; IR (ATR, cm^{-1}): ν = 3053 (w), 2918 (w), 2848 (w), 1591 (m), 1506 (vs), 1481 (m), 1456 (s), 1406 (s), 1390 (m), 1311 (s), 1244 (s), 1221 (s), 1192 (s), 1173 (s), 1155 (s), 1113 (m), 1101 (s), 1041 (m), 1011 (m), 935 (m), 889 (m), 835 (s), 812 (s), 800 (m), 744 (vs), 723 (vs), 700 (m), 671 (m), 661 (m), 640 (m), 619 (m), 573 (s), 565 (s), 536 (s); GC-MS (EI, 70 eV): m/z (%) = 445 (100), 222 (10), 95 (8); HRMS (EI): calcd. for $C_{29}H_{17}N_3F_2$ ($[M]^+$): 445.13851; found: 445.13827.

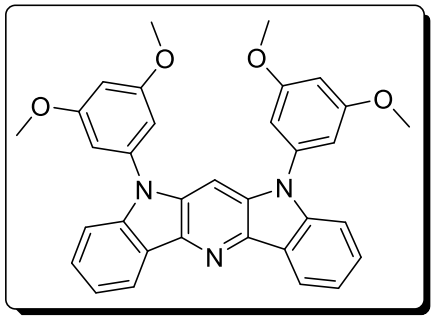


5,7-Bis(3-(trifluoromethyl)phenyl)-5,7-dihydropyrido[3,2-b:5,6-b']diindole **25e** was prepared following general procedure 10 using compound **24** (100 mg, 0.18 mmol) and 3-(trifluoromethyl)aniline (137 µL, 1.09 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane/ethylacetate 8:1:1) to yield **25e** (70 mg, 70 %) as a white solide; m.p. 268-269 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.49 (d, *J* = 7.7 Hz, 2H), 7.81 (s, 2H), 7.71 – 7.63 (m, 6H), 7.47 – 7.26 (m, 7H); ^{19}F NMR (282 MHz, $CDCl_3$) δ = -62.78; ^{13}C NMR (63 MHz, $CDCl_3$) δ = 141.71, 138.69, 137.91, 133.61, 132.80 (q, *J* = 33.2 Hz), 130.85, 129.97, 127.30, 124.35 (q, *J* = 3.6 Hz), 123.65 (q, *J* = 3.9 Hz), 123.53 (q, *J* = 272.7 Hz), 123.01, 121.25, 120.92, 109.38, 96.01; IR (ATR, cm^{-1}): ν = 3061 (w), 2928 (w), 2854 (w), 1591 (m), 1495 (m), 1485 (m), 1460 (s), 1404 (s), 1387 (m), 1354 (m), 1344 (m), 1323 (s), 1309 (s), 1279 (m), 1271 (m), 1244 (s), 1182 (s), 1173 (s), 1155 (s), 1115 (vs), 1097 (s), 1070 (s), 1041 (m), 1012 (m), 1003 (m), 962 (m), 931 (w), 918 (m), 904 (m), 854 (m), 849 (m), 800 (s), 746 (s), 727 (s), 708 (vs), 700 (vs), 669 (m), 661 (s), 646 (m),

609 (w), 582 (m), 538 (m); GC-MS (EI, 70 eV): m/z (%) = 545 (100), 273 (22); HRMS (EI): calcd. for $C_{31}H_{17}N_3$ ($[M]^+$): 545.13212; found: 545.13199.

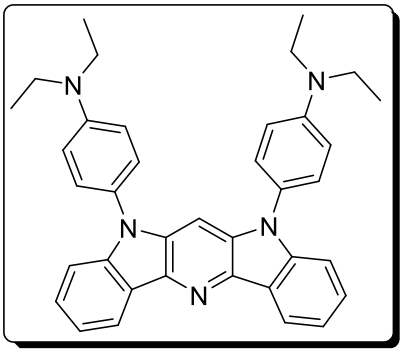


5,7-Bis(4-methoxyphenyl)-5,7-dihydropyrido[3,2-b:5,6-b']diindole **25f** was prepared following general procedure 10 using compound **24** (100 mg, 0.18 mmol) and p-anisidine (135 mg, 1.09 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane/ethylacetate 5:1:1) to yield **25f** (80 mg, 93 %) as a white solide; m.p. 300-302 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.67 – 8.58 (m, 2H), 7.49 – 7.30 (m, 11H), 7.14 – 7.04 (m, 4H), 3.90 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 159.19, 142.89, 138.11, 134.99, 130.05, 128.70, 126.91, 122.84, 120.81, 120.47, 115.51, 109.78, 96.35, 55.80; IR (ATR, cm^{-1}): ν = 3047 (m), 2951 (m), 2924 (m), 2835 (m), 1614 (w), 1589 (m), 1510 (s), 1477 (m), 1456 (s), 1441 (s), 1408 (s), 1392 (m), 1315 (m), 1298 (m), 1279 (m), 1242 (vs), 1211 (m), 1190 (s), 1180 (s), 1144 (s), 1113 (m), 1103 (s), 1032 (s), 1007 (m), 953 (m), 928 (m), 887 (m), 835 (s), 825 (s), 810 (m), 793 (m), 742 (vs), 733 (s), 727 (s), 671 (m), 660 (m), 642 (m), 619 (m), 584 (s), 575 (s), 542 (s); GC-MS (EI, 70 eV): m/z (%) = 469 (100), 291 (27), 43 (57); HRMS (EI): calcd. for $C_{31}H_{23}O_2N_3$ ($[M]^+$): 469.17848; found: 469.17813.



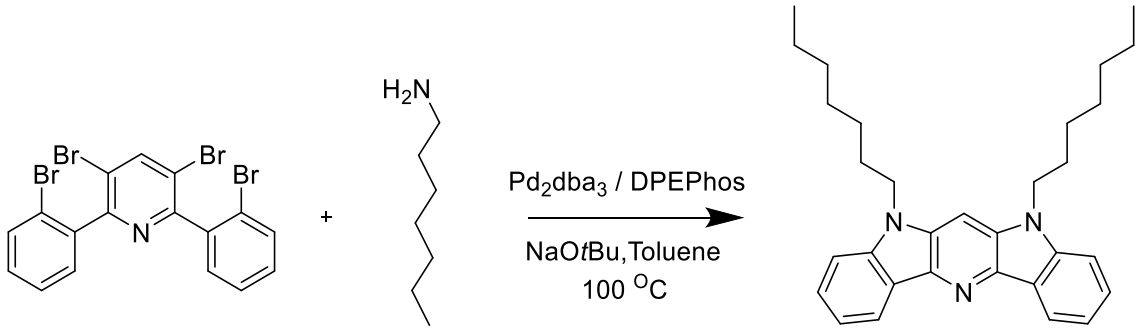
5,7-Bis(3,5-dimethoxyphenyl)-5,7-dihydropyrido[3,2-b:5,6-b']diindole **25g** was prepared following general procedure 10 using compound **24** (100 mg, 0.18 mmol) and 3,5-dimethoxyaniline (168 mg, 1.09 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane/ethylacetate 4:1:1) to yield **25f** (92 mg, 95 %) as a white solide; m.p. 230-231 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.66 (d, *J* = 6.6 Hz, 2H), 7.74 (s, 1H), 7.46 (dd, *J* = 26.3, 6.9 Hz, 6H), 6.75 (d, *J* = 1.9 Hz, 4H), 6.57 (s, 2H), 3.84 (s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 161.94, 142.13, 134.11, 127.38, 121.43, 120.89, 110.03, 105.08, 100.05, 55.67; IR (ATR, cm^{-1}): ν = 3066 (w), 2999 (w), 2935 (w), 2841 (w), 1740 (w), 1595 (vs), 1477 (s), 1462 (s), 1446 (m), 1423 (m), 1404 (m), 1346 (m), 1311 (m), 1300 (m), 1292 (s), 1234 (s), 1201 (vs), 1190 (s), 1151 (vs), 1142 (s), 1065 (s), 1055 (m), 827 (s), 741 (s), 733 (s), 708 (m), 690 (s), 579 (w); GC-MS (EI, 70 eV): m/z (%) =

529 (100), 471 (10), 207 (6); HRMS (EI): calcd. for $C_{33}H_{27}O_4N_3$ ($[M]^+$): 529.19961; found: 529.19898.



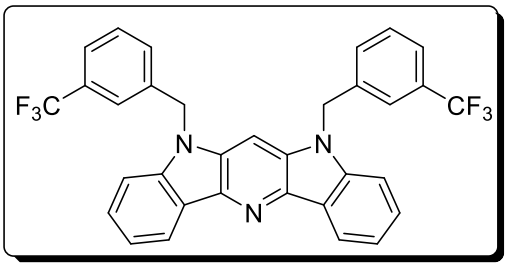
5,7-Bis(4-(N,N-diethylamino)phenyl)-5,7-dihydropyrido[3,2-b:5,6-b']diindole **25h** was prepared following general procedure 10 using compound **24** (100 mg, 0.18 mmol) and N^1,N^1-diethylbenzene-1,4-diamine (182 µL, 1.09 mmol). The product was purified by flash chromatography (silica gel, Heptane/dichloromethane/ethylacetate 5:1:1) to yield **25h** (70 mg, 69 %) as a brown solid; m.p. 222-223 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.58 – 8.49 (m, 2H), 7.38 – 7.23 (m, 11H), 6.72 (d, *J* = 9.0 Hz, 4H), 3.35 (q, *J* = 7.0 Hz, 8H), 1.15 (t, *J* = 7.1 Hz, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 147.30, 143.08, 137.58, 135.22, 128.41, 126.38, 124.72, 122.48, 120.44, 119.79, 112.29, 109.75, 96.57, 44.50, 12.67; IR (ATR, cm^{-1}): ν = 3043 (w), 2968 (m), 2929 (m), 2897 (w), 2864 (w), 1732 (w), 1606 (m), 1591 (m), 1520 (vs), 1477 (m), 1460 (s), 1448 (m), 1394 (m), 1373 (m), 1354 (s), 1323 (m), 1309 (s), 1269 (s), 1240 (s), 1192 (s), 1149 (s), 1140 (s), 1119 (m), 1109 (m), 1097 (m), 1074 (m), 1047 (m), 1032 (m), 1007 (m), 930 (m), 922 (m), 885 (m), 841 (m), 823 (m), 812 (s), 793 (m), 785 (m), 750 (vs), 742 (s), 731 (vs), 725 (s), 696 (m), 656 (m), 640 (m), 621 (m), 561 (s), 536 (s); GC-MS (EI, 70 eV): m/z (%) = 551 (100), 507 (15), 463 (13), 268 (7), 69 (20), 44 (59); HRMS (ESI): calcd. for $C_{37}H_{37}N_5$ ($[M + H]^+$): 552.31217; found: 552.31208; calcd. for $C_{37}H_{37}N_5Na$ ($[M + Na]^+$): 574.29412; found: 574.2944.

General procedure 11 for double C-N coupling with alkyl amine derivatives, exemplified by: *5,7-diheptyl-5,7-dihydropyrido[3,2-b:5,6-b']diindole* 25i

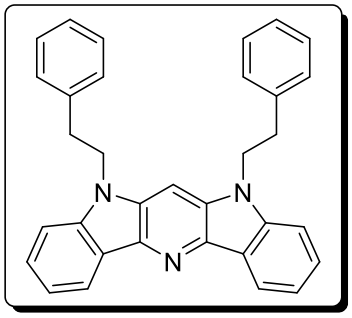


24 **8i** **25i**

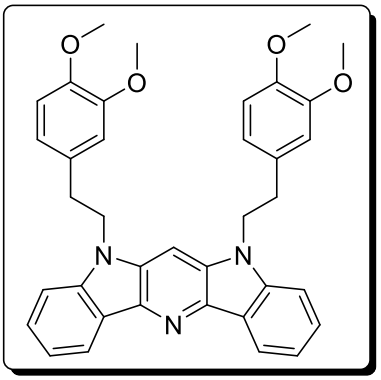
To pressure tube charged with **24** (100 mg, 0.18 mmol), $Pd_2(dba)_3$ (8 mg, 9 µmol), ligand DPEPhos (10 mg, 18 µmol) and sodium *tert*-butoxide (105 mg, 1.09 mmol) under Argon. The mixture was back-filled with Argon several times. The mixture was dissolved in anhydrous toluene (10 mL). *n*-Heptylamine (0.2 mL, 1.09 mmol) was added to the mixture and heated at 100 ºC for 7 h. After cooling, the reaction mixture was diluted with dichloromethane (20 mL) and filtered through a celite pad, washing with dichloromethane (40 mL). The filtrate was reduced *in vacuo*. The product was separated via flash chromatography (silica gel, heptane/dichloromethane/ethylacetate 5:1:1) to yield **25i** (66 mg, 80%) as a white solid; m.p. 162-164 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.58 (d, *J* = 7.4 Hz, 2H), 7.59 – 7.46 (m, 2H), 7.39 – 7.28 (m, 5H), 4.16 (t, *J* = 7.1 Hz, 4H), 1.97 – 1.78 (m, 4H), 1.41 – 1.19 (m, 16H), 0.86 (t, *J* = 6.8 Hz, 6H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 141.49, 136.62, 133.73, 126.41, 122.32, 120.76, 119.38, 108.60, 94.25, 43.08, 31.82, 29.19, 28.85, 27.43, 22.69, 14.15; IR (ATR, cm^{-1}): ν = 3061 (w), 3020 (w), 2953 (w), 2933 (w), 2877 (w), 2852 (w), 1595 (s), 1466 (s), 1454 (m), 1441 (m), 1410 (m), 1390 (m), 1352 (s), 1319 (s), 1257 (s), 1227 (m), 1203 (m), 1171 (s), 1124 (m), 1111 (m), 1080 (m), 1068 (m), 1012 (m), 827 (m), 742 (vs), 729 (vs), 698 (vs), 687 (s), 648 (m), 594 (m), 579 (m), 563 (m), 544 (s); GC-MS (EI, 70 eV): m/z (%) = 453 (100), 368 (40), 282 (12), 269 (25); HRMS (EI): calcd. for $C_{31}H_{39}N_3$ ($[M]^+$): 453.31385; found: 453.31353.



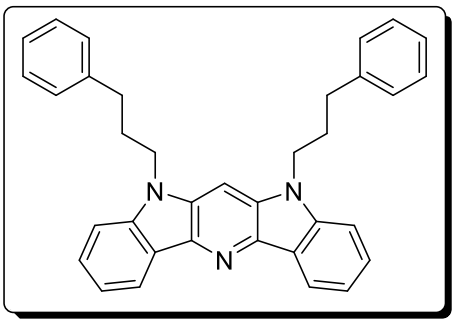
5,7-Bis(3-(trifluoromethyl)benzyl)-5,7-dihydropyrido[3,2-b:5,6-b']diindole **25p** was prepared following general procedure 11 using compound **24** (100 mg, 0.18 mmol) and 3-(trifluoromethyl)benzylamine (157 µL, 1.09 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane/ethylacetate 5:1:1) to yield **25p** (54 mg, 52 %) as a white solid; m.p. 229-231 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.53 (d, *J* = 7.6 Hz, 2H), 7.52 – 7.28 (m, 9H), 7.18 (m, *J* = 6.9 Hz, 3H), 6.96 (d, *J* = 8.7 Hz, 3H), 5.24 (s, 4H); ^{19}F NMR (282 MHz, $CDCl_3$) δ = -62.70 (s); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 141.50 (s), 137.49 (s), 133.54 (s), 131.24 (q, *J* = 32.5 Hz), 129.46 (s), 129.42 (s), 126.95 (s), 124.55 (q, *J* = 3.4 Hz), 123.81 (q, *J* = 272.5 Hz), 123.12 (q, *J* = 3.7 Hz), 122.63 (s), 120.81 (s), 120.28 (s), 108.59 (s), 94.52 (s), 46.11 (s); IR (ATR, cm^{-1}): ν = 3047 (w), 2926 (w), 1595 (m), 1466 (m), 1443 (m), 1410 (m), 1327 (vs), 1315 (vs), 1254 (s), 1223 (m), 1182 (s), 1167 (s), 1111 (vs), 1097 (vs), 1070 (vs), 1007 (m), 968 (m), 949 (m), 937 (m), 930 (m), 916 (m), 881 (m), 862 (m), 823 (m), 804 (m), 789 (s), 744 (vs), 733 (s), 714 (m), 696 (vs), 661 (s), 634 (m), 615 (m), 602 (m), 582 (m), 565 (s); GC-MS (EI, 70 eV): m/z (%) = 573 (100), 414 (42), 255 (30), 159 (10); HRMS (EI): calcd. for $C_{33}H_{21}N_3F_6$ ($[M]^+$): 573.16342; found: 573.16519.



5,7-Diphenethyl-5,7-dihydropyrido[3,2-b:5,6-b']diindole **25q** was prepared following general procedure 11 using compound **24** (100 mg, 0.18 mmol) and phenylethylamine (138 µL, 1.09 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane/ethylacetate 5:1:1) to yield **25q** (64 mg, 75 %) as a white solid; m.p. 124-126 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.47 (d, *J* = 7.6 Hz, 2H), 7.38 (m, 2H), 7.30 – 6.79 (m, 15H), 4.19 (t, *J* = 6.9 Hz, 4H), 2.93 (t, *J* = 6.9 Hz, 4H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 141.00, 138.83, 136.22, 133.46, 128.87, 128.59, 126.68, 126.43, 122.10, 120.70, 119.50, 108.35, 94.50, 44.77, 34.96; IR (ATR, cm^{-1}): ν = 2951 (m), 2928 (m), 2874 (m), 2856 (m), 2845 (m), 1591 (s), 1481 (m), 1470 (s), 1464 (s), 1412 (m), 1387 (m), 1371 (m), 1354 (m), 1319 (s), 1250 (s), 1230 (s), 1215 (m), 1201 (m), 1186 (m), 1174 (m), 1144 (s), 1124 (m), 1113 (s), 1070 (m), 1024 (w), 1011 (m), 903 (m), 847 (m), 744 (s), 725 (vs), 706 (s), 696 (m), 673 (m), 596 (m), 577 (m), 565 (m); GC-MS (EI, 70 eV): m/z (%) = 465 (35), 374 (100), 282 (42); HRMS (EI): calcd. for $C_{33}H_{27}N_3$ ($[M]^+$): 465.21995; found: 465.21945.

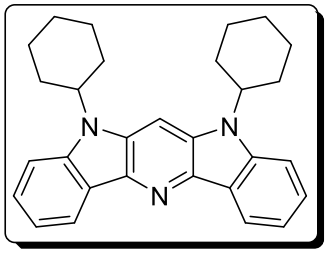


5,7-Bis(3,4-dimethoxyphenethyl)-5,7-dihydropyrido[3,2-b:5,6-b']diindole **25r** was prepared following general procedure 11 using compound **24** (100 mg, 0.18 mmol) and 3,4-dimethoxyphenylethylamine (185 µL, 1.09 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane/ethylacetate 3:1:1) to yield **25r** (60 mg, 56 %) as a white solid; m.p. 164-165 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.45 (s, 2H), 7.42 – 7.34 (m, 2H), 7.28 – 7.16 (m, 4H), 6.72 – 6.50 (m, 5H), 6.19 (s, 2H), 4.29 (d, *J* = 6.4 Hz, 4H), 3.60 (s, 6H), 3.39 (s, 6H), 2.92 (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 148.94, 147.90, 141.20, 133.51, 131.47, 126.39, 122.31, 120.71, 120.56, 119.55, 112.48, 111.26, 108.52, 94.37, 55.78, 55.67, 45.07, 34.52; IR (ATR, cm^{-1}): ν = 2955 (w), 2937 (w), 2916 (w), 2833 (w), 1597 (m), 1516 (s), 1464 (m), 1454 (m), 1441 (w), 1435 (w), 1414 (m), 1387 (w), 1354 (m), 1327 (m), 1317 (m), 1261 (vs), 1236 (s), 1228 (s), 1211 (m), 1198 (m), 1190 (m), 1157 (s), 1136 (s), 1122 (m), 1041 (w), 1030 (m), 1018 (s), 860 (m), 808 (m), 764 (m), 742 (vs), 727 (vs), 683 (m), 644 (m), 557 (m); GC-MS (EI, 70 eV): m/z (%) = 585 (45), 434 (100), 284 (27); HRMS (ESI): calcd. for $C_{37}H_{35}N_3O_4$ ($[M + H]^+$): 586.26276; found: 586.2700.



5,7-Bis(3-phenylpropyl)-5,7-dihydropyrido[3,2-b:5,6-b']diindole **25s** was prepared following general procedure 11 using compound **24** (100 mg, 0.18 mmol) and 3-phenylpropylamine (156 µL, 1.09 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane/ethylacetate 5:1:1) to yield **25s** (61 mg, 68 %) as a white solid; m.p. 194-196 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.46 (d, *J* = 7.6 Hz, 2H), 7.39 (ddd, *J* = 8.3, 7.3, 1.2 Hz, 2H), 7.28 – 6.97 (m, 15H), 4.05 (t, *J* = 7.3 Hz, 4H), 2.58 (t, *J* = 7.5 Hz, 4H), 2.19 – 1.99 (m, 4H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 141.30, 140.90, 136.80, 133.47, 128.54, 128.39, 126.34, 126.22, 122.38, 120.61, 119.41, 108.45, 93.98, 42.10, 33.11, 29.72; IR (ATR, cm^{-1}): ν = 3024 (w), 2924 (w), 1593 (s), 1497 (m), 1464 (s), 1452 (s), 1435 (m), 1408 (m), 1387 (m), 1356 (m), 1315 (s), 1250 (s), 1227 (m), 1207 (m), 1194 (m), 1174 (m), 1163 (m), 1149 (m), 1124 (m), 1111 (m), 1088 (m), 1070 (m), 1028 (m), 1016 (m), 1009 (m), 928 (w), 831 (m), 768 (m), 742 (vs), 729 (vs), 694 (vs), 615 (m), 584 (m), 575 (m), 557 (m); GC-MS (EI, 70 eV): m/z (%) = 493 (100), 388 (48), 269

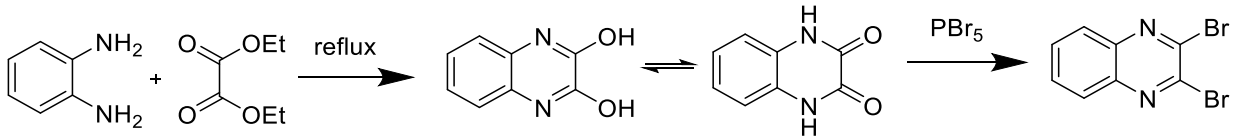
(18), 69 (23), 44 (38); HRMS (ESI): calcd. for $C_{35}H_{31}N_3$ ([M + H]$^+$): 494.25907; found: 494.25922; calcd. for $C_{35}H_{31}N_3Na$ ([M + Na]$^+$): 516.24102; found: 516.2405.



5,7-Dicyclohexyl-5,7-dihydropyrido[3,2-b:5,6-b']diindole **25t** was prepared following general procedure 11 using compound **24** (100 mg, 0.18 mmol) and cyclohexylamine (127 µL, 1.09 mmol). The product was purified by flash chromatography (silica gel, heptane/dichloromethane/ethylacetate 5 :1:1) to yield **25t** (42 mg, 55 %) as a white solid; m.p. 277-279 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.50 (d, *J* = 7.7 Hz, 2H), 7.58 (s, 1H), 7.47 – 7.36 (m, 4H), 7.23 (ddd, *J* = 7.9, 6.0, 2.1 Hz, 2H), 5.19 – 5.03 (m, 2H), 2.42 – 1.63 (m, 20H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 140.81, 137.05, 132.62, 126.12, 122.85, 120.83, 119.21, 109.65, 96.35, 55.93, 28.96, 25.48; IR (ATR, cm^{-1}): ν = 2928 (m), 2854 (m), 1591 (m), 1485 (m), 1454 (m), 1416 (m), 1404 (m), 1377 (m), 1344 (m), 1327 (m), 1304 (m), 1250 (m), 1225 (s), 1188 (s), 1155 (m), 1142 (m), 1126 (m), 1117 (m), 1072 (m), 1057 (m), 1028 (m), 1012 (m), 968 (m), 893 (m), 837 (m), 742 (s), 729 (vs), 700 (m), 658 (m), 594 (m), 577 (s), 532 (m); GC-MS (EI, 70 eV): m/z (%) = 421 (100), 256 (31), 55 (22); HRMS (EI): calcd. for $C_{29}H_{31}N_3$ ([M]$^+$): 421.25125; found: 421.25089.

8.5.5 Synthesis and Physical Properties of Indolo[2,3-b]quinoxalines

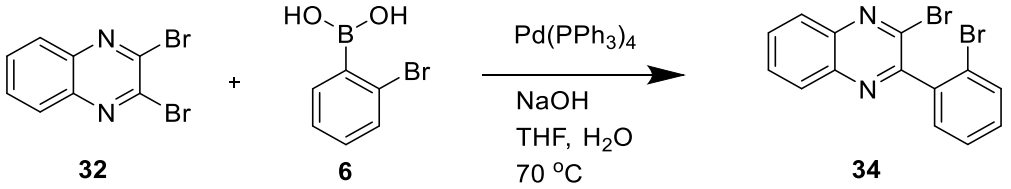
Synthesis of 2,3-dibromoquinoxaline



2,3-Dibromoquinoxaline was synthesized in 94% of overall yield using Li's procedure by reflux of 1,2-phenylenediamine with diethyl oxalate, to give 1,4-dihydroquinoxaline-2,3-dione, and subsequent reaction with PBr_5.[150] M.p. 179-180 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.08 – 8.01 (m, 2H), 7.86 – 7.78 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 141.42, 140.97, 131.49, 128.57; IR (ATR, cm^{-1}): ν =3097 (m), 3034 (m), 1564 (m), 1549 (s), 1514 (s), 1479 (m), 1254 (s), 1169 (s), 1126 (m), 1107 (s), 1072 (m), 1059 (m), 957 (vs), 901 (m), 883 (m), 868 (s), 769 (vs), 692 (m), 677 (m), 621 (m), 582 (s); GC-MS (EI, 70 eV): m/z (%) = 288

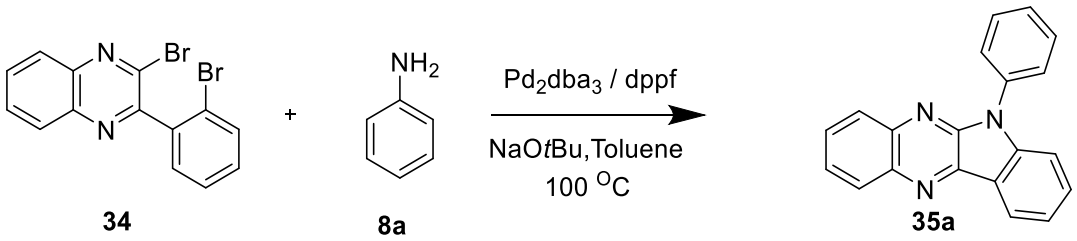
(96), 209 (95), 128 (61), 102 (100), 75 (98), 50 (59); HRMS (EI): calcd. for $C_8H_4N_2Br_2$ ($[M]^+$): 285.87357; found: 285.87325; calcd. for $C_8H_4N_2Br_1{}^{81}Br_1$ ($[M]^+$): 287.87153; found: 287.87137; calcd. for $C_8H_4N_2{}^{81}Br_2$ ($[M]^+$): 289.86948; found: 289.86935.

General procedure for the preparation of 2-bromo-3-(2-bromophenyl)quinoxaline 34.

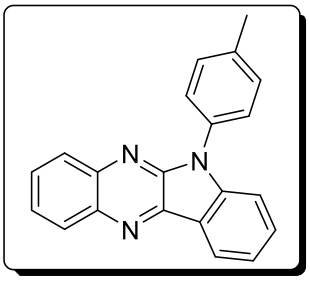


2,3-Dibromoquinoxaline **32** (1 g, 3.5 mmol), 2-bromophenyl boronic acid (837 mg, 4.2 mmol), $Pd(PPh_3)_4$ (100 mg, 87 µmol) and sodium hydroxide (417 mg, 10.4 mmol) were added to a 500 mL Schlenk flask. The mixture was back-filled several times with Argon. To the mixture 70 mL THF and 10 mL distilled water were added, then, back-filled several times. The reaction was heated at 70 ºC for 4h. The solvent was evaporated *in vacuo*. The residue was extracted with dichloromethane and water. The organic layer was dried over $MgSO_4$, filtered and the solvent was evaporated *in vacuo*. The yellow residue was purified by column chromatography (silica gel, Heptane/ethylacetate 10:1) to yield 2-bromo-3-(2-bromophenyl)quinoxaline **34** (1.1 g, 87 %) as white solid. M.p. 127-129 ºC; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 8.20 – 8.07 (m, 2H), 7.90 – 7.79 (m, 2H), 7.73 (dd, *J* = 7.9, 0.8 Hz, 1H), 7.55 – 7.35 (m, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 154.95, 142.47, 140.67, 140.11, 139.38, 132.99, 131.46, 131.01, 130.84, 130.49, 129.58, 128.57, 127.76, 122.83; IR (ATR, cm^{-1}): ν =3059 (w), 1610 (w), 1556 (m), 1535 (w), 1477 (m), 1433 (m), 1385 (w), 1333 (m), 1290 (m), 1273 (w), 1252 (m), 1236 (w), 1213 (w), 1167 (w), 1147 (m), 1132 (m), 1084, 1041, 1024 (m), 999 (w), 970, 955 (m), 943 (m), 885 (m), 870 (w), 862 (w), 752 (vs), 727, 715, 710, 690 (m), 652 (m), 638 (m), 613 (m), 588, 571 (m), 557 (m); GC-MS (EI, 70 eV): m/z (%) = 364 (32), 285 (100), 102 (48), 75 (28), 50 (14); HRMS (EI): calcd. for $C_{14}H_8N_2Br_2$ ($[M]^+$): 361.90488; found: 361.90467;calcd. for $C_{14}H_8N_2Br_1{}^{81}Br_1$ ($[M]^+$): 363.90283; found: 363.90277; calcd. for $C_{14}H_8N_2{}^{81}Br_2$ ($[M]^+$):365.90078; found: 365.90082.

General procedure 12 for double C-N coupling with aniline derivatives,exemplified by the synthesis of6-phenyl-6*H*-indolo[2,3-*b*]quinoxaline(35a)

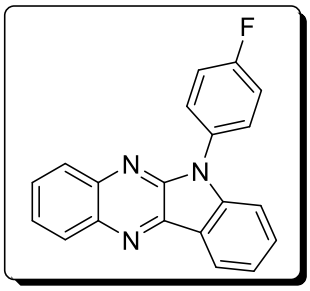


Aniline **8a** (75 µL, 0.82 mmol) was added to a pressure tube charged with **34** (100 mg, 0.28 mmol), $Pd_2(dba)_3$ (12 mg, 14 µmol), ligand Dppf (15mg, 27 µmol) and sodium *tert*-butoxide (79 mg, 0.82 mmol) under Argon. The mixture was back-filled with Argon several times. The mixture was dissolved in anhydrous Toluene (10 mL) and heated at 100 ºC for 7 h. After cooling, the reaction mixture was diluted with dichloromethane (20mL) and filtered through a celite pad, washing with dichloromethane (40 mL). The filtrate was reduced *in vacuo*. The product was separated via flashchromatography (silica gel, heptane/ethylacetate 5:1) to yield 6-phenyl-6*H*-indolo[2,3-*b*]quinoxaline **35a** (67 mg, 83%) as a yellow solid; m.p. 238-239 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.56 (d, *J* = 7.7 Hz, 1H), 8.40 – 8.29 (m, 1H), 8.14 – 8.06 (m, 1H), 7.84 – 7.59 (m, 7H), 7.59 – 7.38 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 146.00, 144.90, 140.72, 140.08, 139.69, 135.50, 131.25, 129.92, 129.24, 128.99, 128.38, 128.13, 127.27, 126.71, 122.94, 122.02, 119.83, 110.75; IR (ATR, cm^{-1}): ν =3053 (m), 1608 (m), 1597 (m), 1581 (m), 1500, 1483 (m), 1470 (m), 1458, 1402, 1390, 1354 (m), 1336 (m), 1317 (m), 1304 (m), 1252 (m), 1227 (m), 1205, 1174 (m), 1147 (m), 1132 (m), 1126 (m), 1099 (m), 1072 (m), 1041 (m), 1024 (m), 1014 (m), 1007 (m), 955 (m), 924 (m), 779 (m), 766 (m), 748 (vs), 719 (m), 694, 687, 648, 590, 567 (m); GC-MS (EI, 70 eV): m/z (%) = 295 (100), 147 (9), 90 (6), 77 (6); HRMS (ESI): calcd. for $C_{20}H_{14}N_3$ ($[M + H]^+$): 296.11822; found: 296.11835.

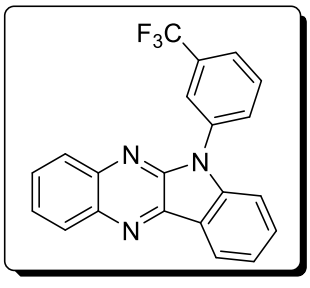


6-(p-Tolyl)-6H-indolo[2,3-b]quinoxaline **35b** was prepared following general procedure 12 using compound **34** (100 mg, 0.28 mmol) and toluidine (88 mg, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 5:1) to yield **35b** (73 mg, 86%) as a yellow solid; m.p. 216-217 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.50 – 8.43 (m, 1H), 8.29 – 8.22 (m, 1H), 8.05 – 7.99 (m, 1H), 7.68 – 7.57 (m, 2H), 7.57 – 7.49 (m, 3H), 7.45 – 7.31 (m, 4H),

2.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 146.01, 144.99, 140.66, 140.06, 139.62, 138.04, 132.68, 131.06, 130.45, 129.17, 128.79, 128.27, 127.02, 126.46, 122.72, 121.73, 119.68, 110.62, 21.35; IR (ATR, cm^{-1}): ν =3057 (w), 3034 (w), 2918 (w), 1606 (m), 1585 (m), 1514, 1485 (m), 1470 (m), 1460, 1404, 1354 (m), 1335 (m), 1317, 1304 (m), 1255 (m), 1227 (m), 1221 (m), 1205, 1182 (m), 1169 (m), 1130 (m), 1122 (m), 1099 (m), 1043 (m), 1016 (m), 955 (m), 924 (m), 816 (m), 764, 750 (vs), 721 (m), 710 (m), 673 (w), 633 (m), 602, 579, 567 (m), 559 (m); GC-MS (EI, 70 eV): m/z (%) = 309 (100), 293 (8), 154 (7), 90 (5); HRMS (EI): calcd. for $C_{21}H_{15}N_3$ ([M]$^+$): 309.12605; found: 309.12523.

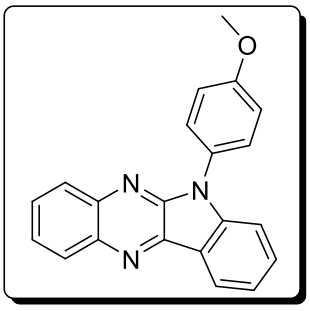


6-(4-Fluorophenyl)-6H-indolo[2,3-b]quinoxaline **35c** was prepared following general procedure 12 using compound **34** (100 mg, 0.28 mmol) and 4-fluoroaniline (78 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 5:1) to yield **35c** (69 mg, 80 %) as a yellow solid; m.p. 219-220 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.55 (d, *J* = 7.8 Hz, 1H), 8.37 – 8.30 (m, 1H), 8.12 – 8.04 (m, 1H), 7.78 – 7.61 (m, 5H), 7.50 – 7.41 (m, 2H), 7.41 – 7.30 (m, 2H); ^{19}F NMR (282 MHz, $CDCl_3$) δ = -113.01; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.08 (d, *J* = 247.9 Hz), 146.07, 144.90, 140.70, 140.01 (d, *J* = 18.0 Hz), 131.43 (d, *J* = 3.2 Hz), 131.32, 129.38, 129.18 (d, *J* = 8.4 Hz), 129.12, 128.32, 126.81, 122.98, 122.15, 119.92, 116.99 (d, *J* = 22.9 Hz), 110.52; IR (ATR, cm^{-1}): ν =3057 (m), 1608 (m), 1579 (m), 1574 (m), 1514, 1485, 1471 (m), 1460, 1402, 1356 (m), 1335 (m), 1313, 1292 (m), 1259 (m), 1223, 1203, 1171 (m), 1151 (m), 1130 (m), 1122, 1099, 1043 (m), 1012 (m), 1007 (m), 949 (m), 924 (m), 872 (m), 831, 812 (m), 800 (m), 764, 748 (vs), 723 (m), 710, 673 (m), 638 (m), 629 (m), 602, 579, 567 (m), 557 (m), 548 (m); GC-MS (EI, 70 eV): m/z (%) = 313 (100), 156 (12), 75 (7); HRMS (EI): calcd. for $C_{20}H_{12}N_3F_1$ ([M]$^+$): 313.10098; found: 313.10007.

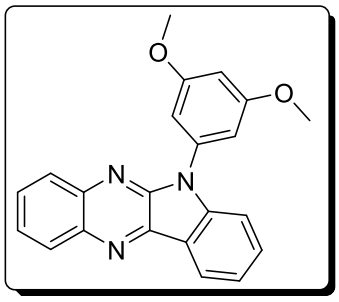


6-(3-(Trifluoromethyl)phenyl)-6H-indolo[2,3-b]quinoxaline **35d** was prepared following general procedure 12 using compound **34** (100 mg, 0.28 mmol) and 3-(trifluoromethyl)aniline (103 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 5:1) to yield **35d** (90 mg, 90 %) as a yellow solid; m.p. 201-202 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.46 (ddd, *J* = 7.7, 1.2, 0.7 Hz, 1H), 8.29 – 8.19 (m, 1H), 8.03 – 7.95 (m, 2H), 7.92 (ddd, *J* =

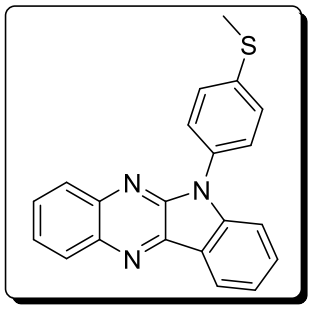
3.7, 3.0, 1.9 Hz, 1H), 7.76 – 7.53 (m, 5H), 7.48 – 7.33 (m, 2H); ^{19}F NMR (282 MHz, $CDCl_3$) δ = -62.58; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 145.55, 144.00, 140.39, 140.07, 136.11, 132.31 (q, *J* = 33.0 Hz), 131.25, 130.40, 130.32, 130.31, 129.33, 129.11, 128.23, 126.90, 124.49 (q, *J* = 3.7 Hz), 123.85 (q, *J* = 3.9 Hz), 122.92, 123.74 (q, *J* = 272.5 Hz),122.41, 120.16, 110.31; IR (ATR, cm^{-1}): ν =3051 (w), 3028 (w), 1608 (w), 1597 (w), 1579 (w), 1574 (w), 1495 (m), 1464 (m), 1446 (m), 1406, 1356 (m), 1329, 1308 (m), 1279 (w), 1250 (m), 1230 (m), 1205 (m), 1167, 1134 (m), 1126 (m), 1113, 1105, 1095, 1068, 1045 (m), 1011 (m), 987 (w), 976 (w), 958 (m), 943 (m), 924 (w), 904 (m), 874 (w), 860 (w), 854 (w), 802 (m), 795 (m), 768 (m), 748 (vs), 719 (m), 700, 671, 656 (m), 631 (w), 615 (w), 588 (m), 567 (w), 546 (w); GC-MS (EI, 70 eV): m/z (%) = 363 (100), 294 (9); HRMS (ESI): calcd. for $C_{21}H_{12}F_3N_3$ ([M + H]$^+$): 364.10561; found: 364.10566; calcd. for $C_{37}H_{37}N_5Na$ ([M + Na]$^+$): 574.29412; found: 574.2944.



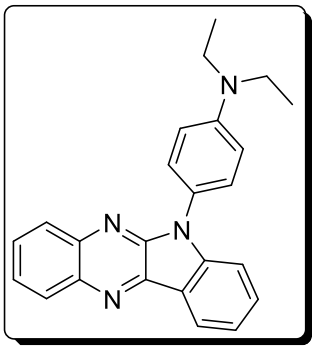
6-(4-Methoxyphenyl)-6H-indolo[2,3-b]quinoxaline **35e** was prepared following general procedure 12 using compound **34** (100 mg, 0.28 mmol) and p-anisidine (101 mg, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 3:1) to yield **35e** (88 mg, 98 %) as a yellow solid; m.p. 226-228 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.57 (d, *J* = 7.6 Hz, 1H), 8.35 (d, *J* = 8.9 Hz, 1H), 8.15 – 8.05 (m, 1H), 7.80 – 7.55 (m, 5H), 7.44 (m, 2H), 7.21 – 7.13 (m, 2H), 3.94 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 159.42, 145.47, 140.85, 139.42, 131.35, 129.13, 129.00, 128.72, 128.38, 128.02, 126.67, 123.02, 121.87, 119.53, 115.27, 113.39, 110.68, 55.77; IR (ATR, cm^{-1}): ν =3076 (w), 3053 (m), 3022 (m), 2956 (m), 2933 (m), 2912 (m), 2839 (m), 1606 (m), 1585 (m), 1578 (m), 1512, 1506, 1487 (m), 1464, 1446, 1406, 1356 (m), 1336 (m), 1313 (m), 1296, 1244, 1230, 1205, 1178, 1167, 1136, 1128, 1103, 1041 (m), 1026, 1009 (m), 968 (m), 955 (m), 939 (m), 924 (m), 870 (m), 852 (m), 829, 820, 804 (m), 795 (m), 768, 748 (vs), 723, 715, 669 (m), 642 (m), 629 (m), 602, 579, 569, 550; GC-MS (EI, 70 eV): m/z (%) = 325 (100), 310 (39), 282 (18), 141 (8); HRMS (ESI): calcd. for $C_{21}H_{15}N_3O$ ([M + H]$^+$): 326.12879; found: 326.12858.



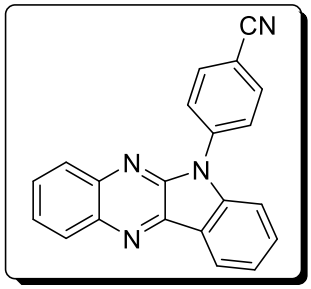
6-(3,5-Dimethoxyphenyl)-6H-indolo[2,3-b]quinoxaline **35f** was prepared following general procedure 12 using compound **34** (100 mg, 0.28 mmol) and 3,5-dimethoxyaniline (126 mg, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 2:1) to yield **35f** (93 mg, 95 %) as a yellow solid; m.p. 188-189 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.45 (d, *J* = 7.6 Hz, 1H), 8.28 – 8.20 (m, 1H), 8.07 – 8.00 (m, 1H), 7.71 – 7.47 (m, 4H), 7.35 (ddd, *J* = 8.1, 6.9, 1.3 Hz, 1H), 6.81 (d, *J* = 2.3 Hz, 2H), 6.54 (m, 1H), 3.79 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 161.59, 145.81, 144.67, 140.60, 140.16, 139.77, 136.91, 131.08, 129.25, 128.83, 128.35, 126.55, 122.66, 121.86, 119.84, 110.92, 105.51, 100.33, 55.66; IR (ATR, cm^{-1}): ν =2993 (w), 2956 (w), 2926 (w), 1606 (m), 1591 (m), 1508 (w), 1491 (m), 1458, 1427 (m), 1404 (m), 1363 (w), 1325 (m), 1298 (m), 1257 (m), 1242 (m), 1207 (m), 1194, 1153, 1134 (m), 1124 (m), 1107 (m), 1066 (m), 1051 (m), 1039 (m), 1014 (m), 1003 (m), 993 (m), 953 (m), 933 (m), 912 (m), 877 (m), 860 (m), 847, 818 (m), 791 (m), 768, 735 (vs), 721, 688, 667 (m), 640 (m), 631 (m), 617 (m), 607 (m), 600 (m), 584, 577 (m), 565 (m), 534 (m); GC-MS (EI, 70 eV): m/z (%) =355 (100), 325 (13), 268 (12); HRMS (EI): calcd. for $C_{22}H_{17}O_2N_3$ ($[M]^+$): 355.13153; found: 355.13066.



6-(4-(Methylthio)phenyl)-6H-indolo[2,3-b]quinoxaline **35g** was prepared following general procedure 12 using compound **34** (100 mg, 0.28 mmol) and 4-(methylthio)aniline (103 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 3:1) to yield **35g** (88 mg, 94 %) as a white solid; m.p. 249-250ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.47 (d, *J* = 7.4 Hz, 1H), 8.28 – 8.20 (m, 1H), 8.06 – 7.98 (m, 1H), 7.72 – 7.53 (m, 5H), 7.51 – 7.30 (m, 4H), 2.53 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 145.88, 144.73, 140.58, 140.17, 139.82, 138.69, 132.30, 131.09, 129.28, 128.89, 128.23, 127.62, 127.52, 126.56, 122.73, 121.91, 119.85, 110.56, 15.92; IR (ATR, cm^{-1}): ν =2955 (m), 2920, 2850 (m), 1608 (m), 1579 (m), 1498, 1483 (m), 1460, 1431 (m), 1402, 1352 (m), 1335 (m), 1311, 1296 (m), 1252 (m), 1230 (m), 1203, 1184 (m), 1132 (m), 1124 (m), 1115 (m), 1103, 1090, 1041 (m), 1012 (m), 1003 (m), 984 (m), 970 (m), 955 (m), 937 (m), 922 (m), 904 (w), 870 (m), 854 (w), 833 (m), 816, 768 (vs), 748 (vs), 719, 702, 661 (m), 634 (m), 625 (m), 590, 567, 548 (m); GC-MS (EI, 70 eV): m/z (%) = 341 (100), 326 (36), 294 (20), 102 (6); HRMS (ESI): calcd. for $C_{24}H_{22}N_4$ ($[M + H]^+$): 342.09467; found: 342.10916.



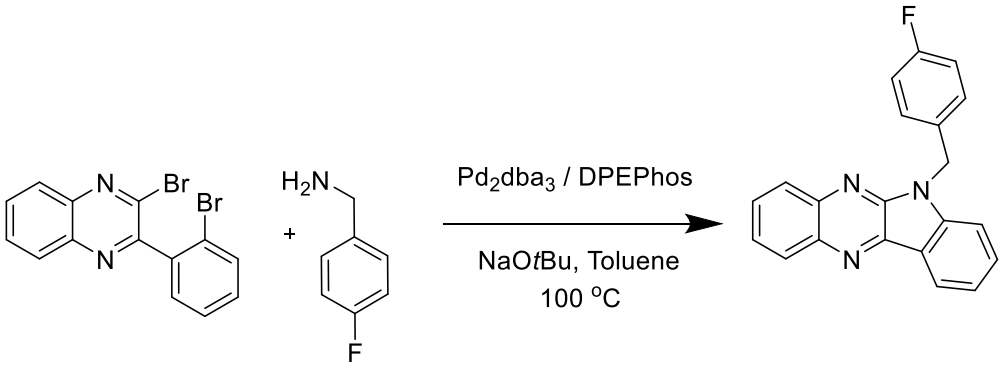
5,7-Bis(4-(N,N-diethylamino)phenyl)-6H-indolo[2,3-b]quinoxaline **35h** was prepared following general procedure 12 using compound **34** (100 mg, 0.28 mmol) and N^1,N^1-diethylbenzene-1,4-diamine (137 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, Heptane/ethylacetate 3:1) to yield **35h** (76 mg, 75 %) as a yellow solid; m.p. 228-229 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.50 – 8.39 (m, 1H), 8.26 – 8.19 (m, 1H), 8.05 – 8.00 (m, 1H), 7.70 – 7.50 (m, 3H), 7.45 – 7.27 (m, 4H), 6.84 – 6.73 (m, 2H), 3.37 (q, *J* = 7.1 Hz, 4H), 1.17 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 147.61, 146.39, 145.80, 140.82, 140.23, 139.58, 130.90, 129.22, 128.57, 128.39, 128.29, 126.09, 122.55, 122.47, 121.29, 119.45, 112.09, 110.74, 44.55, 12.69; IR (ATR, cm^{-1}): ν =2970 (w), 2926 (w), 2866 (w), 1626 (w), 1608 (m), 1578 (w), 1522, 1489 (m), 1462 (m), 1446 (m), 1429 (w), 1404 (m), 1371 (m), 1352 (m), 1333 (m), 1315 (m), 1279 (m), 1259 (m), 1228 (m), 1203, 1194, 1169 (m), 1157 (m), 1149 (m), 1134 (m), 1122 (m), 1101 (m), 1080 (m), 1041 (m), 1014 (m), 1003 (m), 978 (m), 953 (m), 924 (m), 864 (m), 849 (m), 814, 798, 758, 735 (vs), 723, 712, 667 (m), 640 (m), 631 (m), 596, 575, 563 (m), 548 (m), 532 (m); GC-MS (EI, 70 eV): m/z (%) = 366 (67), 351 (100), 322 (28), 294 (14), 243 (35), 194 (13), 165 (22); HRMS (ESI): calcd. for $C_{24}H_{22}N_4$ ($[M + H]^+$): 367.18780; found: 367.19184.



5,7-Bis(4-cyanophenyl)-6H-indolo[2,3-b]quinoxaline **35i** was prepared following general procedure 12 using compound **34** (100 mg, 0.28 mmol) and 4-aminobenzonitrile (97 mg, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 3:1) to yield **35i** (73 mg, 83 %) as a yellow solid; m.p. 272-273 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.47 (d, *J* = 7.7 Hz, 1H), 8.28 – 8.21 (m, 1H), 8.03 – 7.97 (m, 1H), 7.96 – 7.85 (m, 4H), 7.74 – 7.51 (m, 4H), 7.46 – 7.38 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 145.27, 143.33, 140.25, 140.17, 140.11, 139.68, 133.65, 131.31, 129.34, 129.32, 128.20, 127.20, 127.02, 123.06, 122.85, 120.49, 118.40, 110.91, 110.52; IR (ATR, cm^{-1}): ν =2922 (m), 2852 (m), 2227 (m), 1601 (s), 1583 (m), 1506 (s), 1485 (m), 1456 (s), 1400 (s), 1354 (m), 1319 (s), 1304 (m), 1257 (m), 1238 (m), 1228 (m), 1219 (m), 1198 (s), 1169 (m), 1151 (m), 1136 (m), 1124 (s), 1103 (s), 1043 (m), 1014 (m), 955 (m), 949 (m), 922 (m), 837 (s), 823 (m), 769 (m), 758 (s), 746 (vs), 725 (m), 715 (m), 698 (m), 669 (m), 631 (m), 598 (s), 571 (m), 555 (s), 538 (s);

GC-MS (EI, 70 eV): m/z (%) = 320 (100), 160 (9), 102 (7); HRMS (EI): calcd. for $C_{21}H_{12}N_4$ ($[M]^+$): 320.10565; found: 320.10491.

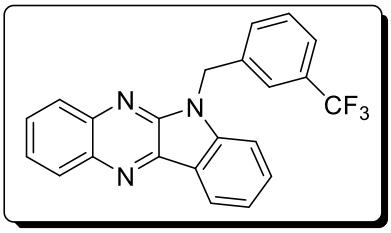
General procedure 13 for double C-N coupling with alkyl amine derivatives, exemplified by *6-(4-fluorobenzyl)-6H-indolo[2,3-b]quinoxaline* 35p



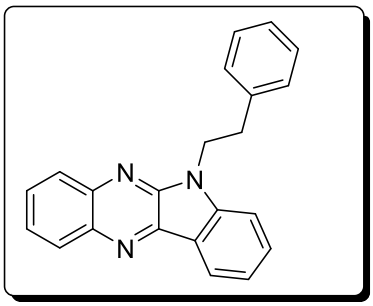
34 **8p** **35p**

To a pressure tube charged with **34** (100 mg, 0.28 mmol), $Pd_2(dba)_3$ (13 mg, 14 µmol), ligand DPEPhos (15 mg, 27 µmol) and sodium *tert*-butoxide (79 mg, 0.82 mmol) under Argon. The mixture was back-filled with Argon several times. The mixture was dissolved in anhydrous toluene (10 mL). *p*-fluorobenzylamine (94 µL, 0.82 mmol) was added to the mixture and heated at 100 ºC for 7 h. After cooling, the reaction mixture was diluted with dichloromethane (20 mL) and filtered through a celite pad, washing with dichloromethane (40 mL). The filtrate was reduced *in vacuo*. The product was purified by flash chromatography (silica gel, heptane/ ethylacetate 4:1) to yield **35p** (78 mg, 87 %) as a yellow solid; m.p. 176-177 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.40 (d, *J* = 7.7 Hz, 1H), 8.24 (dd, *J* = 8.3, 1.5 Hz, 1H), 8.05 (dd, *J* = 8.4, 1.3 Hz, 1H), 7.72 – 7.48 (m, 3H), 7.31 – 7.17 (m, 4H), 6.94 – 6.83 (m, 2H), 5.57 (s, 2H); ^{19}F NMR (282 MHz, $CDCl_3$) δ = -114.59;^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.30 (d, *J* = 246.1 Hz), 145.70, 144.08, 140.63, 140.01, 139.59, 132.30 (d, *J* = 3.2 Hz), 131.05, 129.39, 129.00 (d, *J* = 8.2 Hz), 128.92, 127.88, 126.23, 122.82, 121.29, 119.74, 115.74 (d, *J* = 21.6 Hz), 109.97, 44.36; IR (ATR, cm^{-1}): ν =3057 (w), 3045 (w), 1632 (w), 1610 (m), 1581 (m), 1508 (s), 1489 (m), 1468 (s), 1443 (w), 1435 (w), 1406 (s), 1363 (m), 1344 (m), 1325 (m), 1309 (w), 1300 (w), 1267 (w), 1240 (m), 1230 (w), 1217 (s), 1200 (s), 1171 (w), 1157 (m), 1140 (w), 1126 (w), 1117 (m), 1097 (m), 1066 (w), 1039 (w), 1016 (w), 1007 (w), 984 (w), 955 (w), 939 (w), 858 (m), 850 (m), 825 (m), 768 (m), 762 (s), 746 (vs), 729 (m), 721 (m), 712 (m), 690 (m), 640 (m), 631 (w), 617 (m), 592 (m), 571

(m), 557 (w), 534 (w); GC-MS (EI, 70 eV): m/z (%) = 327 (100), 232 (11), 218 (8), 109 (79), 90 (14); HRMS (EI): calcd. for $C_{21}H_{14}N_3F_1$ ($[M]^+$): 327.11663; found: 327.11625.

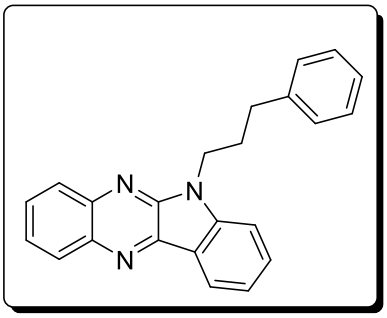


6-(3-(Trifluoromethyl)benzyl)-6H-indolo[2,3-b]quinoxaline **35q** was prepared following general procedure 13 using compound **34** (100 mg, 0.28 mmol) and trifluoromethylbenzylamine (118 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 4:1) to yield **35q** (87 mg, 84 %) as a yellow solid; m.p. 161-162 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.44 – 8.38 (m, 1H), 8.28 – 8.21 (m, 1H), 8.07 – 8.01 (m, 1H), 7.72 – 7.40 (m, 5H), 7.40 – 7.19 (m, 4H), 5.65 (s, 2H);^{19}F NMR (282 MHz, $CDCl_3$) δ = -114.59; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 145.69, 143.97, 140.60, 139.99, 139.71, 137.63, 131.22 (q, *J* = 32.4 Hz), 131.15, 130.48, 129.43, 129.00, 127.89, 126.35, 124.68 (q, *J* = 3.7 Hz), 124.12 (q, *J* = 3.8 Hz), 123.93 (q, *J* = 272.4 Hz), 122.89, 121.48, 119.84, 109.79, 44.67; IR (ATR, cm^{-1}): ν =3064 (w), 1612 (m), 1587 (m), 1489 (m), 1468 (s), 1452 (w), 1435 (w), 1410 (s), 1358 (w), 1338 (s), 1325 (s), 1275 (m), 1267 (w), 1244 (m), 1196 (s), 1163 (m), 1151 (s), 1111 (s), 1099 (vs), 1074 (s), 1043 (m), 1009 (m), 989 (m), 978 (w), 951 (w), 941 (w), 933 (w), 914 (m), 891 (w), 864 (w), 852 (w), 804 (m), 766 (m), 746 (vs), 729 (m), 721 (m), 704 (s), 698 (s), 675 (w), 661 (m), 648 (m), 629 (m), 607 (m), 600 (m), 592 (m), 575 (m), 552 (m), 534 (w); GC-MS (EI, 70 eV): m/z (%) = 377 (100), 232 (25), 218 (11), 159 (27), 90 (19); HRMS (EI): calcd. for $C_{22}H_{14}N_3F_3$ ($[M]^+$): 377.11343; found: 377.11287.

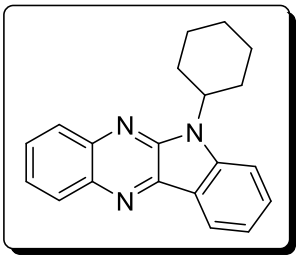


6-Phenethyl-6H-indolo[2,3-b]quinoxaline **35r** was prepared following general procedure 13 using compound **34** (100 mg, 0.28 mmol)and phenylethylamine (104 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 5:1) to yield **35r** (79 mg, 89 %) as a yellow solid; m.p. 155-156 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.39 (d, *J* = 7.7 Hz, 1H), 8.23 (dd, *J* = 8.2, 1.3 Hz, 1H), 8.07 (dd, *J* = 8.4, 1.1 Hz, 1H), 7.74 – 7.49 (m, 3H), 7.35 – 7.04 (m, 7H), 4.69 – 4.56 (m, 2H), 3.22 – 3.09 (m, 2H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 145.46, 144.32, 140.63, 140.05, 139.31, 138.46, 130.86, 129.31, 128.86, 128.69, 128.58, 127.86, 126.65, 125.97, 122.71, 120.80, 119.42, 109.35, 43.11, 34.74; IR (ATR, cm^{-1}): ν =3055 (w), 2933 (w), 1610 (m), 1581 (m), 1487 (m), 1466 (s), 1439 (m), 1410 (s), 1394 (m), 1360 (m), 1344 (m), 1321 (m), 1286 (w), 1259 (w), 1244 (m), 1205 (m), 1184

(m), 1176 (m), 1151 (m), 1138 (m), 1117 (s), 1066 (m), 1039 (m), 1032 (m), 1014 (m), 999 (m), 982 (w), 947 (w), 930 (w), 868 (w), 766 (s), 756 (s), 742 (vs), 725 (m), 704 (s), 692 (s), 640 (m), 619 (w), 594 (s), 571 (m), 559 (m), 532 (m); GC-MS (EI, 70 eV): m/z (%) = 323 (16), 232 (100), 219 (61), 129 (10), 102 (10), 91 (9); HRMS (EI): calcd. for $C_{22}H_{17}N_3$ ($[M]^+$): 323.14170; found: 323.14153.



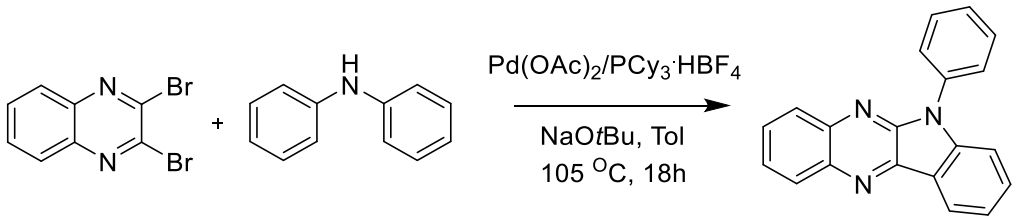
6-(3-Phenylpropyl)-6H-indolo[2,3-b]quinoxaline **35s** was prepared following general procedure 13 using compound **34** (100 mg, 0.28 mmol) and phenylpropylamine (117 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 5:1) to yield **35s** (84 mg, 91 %) as a yellow solid; m.p. 180-181 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.40 (d, *J* = 7.2 Hz, 1H), 8.23 (dd, *J* = 8.2, 1.3 Hz, 1H), 8.07 (dd, *J* = 8.4, 1.1 Hz, 1H), 7.81 – 7.47 (m, 3H), 7.45 – 7.00 (m, 7H), 4.46 (t, *J* = 7.2 Hz, 2H), 2.84 – 2.57 (m, 2H), 2.24 (dt, *J* = 14.7, 7.5 Hz, 2H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 145.68, 144.33, 141.01, 140.61, 140.01, 139.25, 130.92, 129.31, 128.72, 128.39, 128.35, 127.79, 126.06, 125.94, 122.77, 120.82, 119.51, 109.44, 41.01, 33.21, 29.73; IR (ATR, cm^{-1}): ν =3055 (w), 2955 (w), 2931 (w), 2837 (w), 1610 (m), 1581 (m), 1514 (s), 1489 (m), 1466 (s), 1439 (m), 1423 (w), 1408 (s), 1398 (m), 1365 (m), 1344 (m), 1327 (m), 1304 (m), 1271 (m), 1246 (s), 1196 (s), 1184 (s), 1157 (w), 1142 (m), 1115 (s), 1066 (m), 1032 (s), 1005 (m), 984 (w), 953 (w), 933 (w), 858 (w), 835 (m), 820 (m), 802 (w), 762 (s), 742 (vs), 721 (m), 714 (m), 685 (s), 650 (m), 633 (m), 615 (m), 590 (s), 571 (m), 557 (w), 540 (m); GC-MS (EI, 70 eV): m/z (%) = 337 (35), 233 (100); HRMS (ESI): calcd. for ($[M + H]^+$): 338.16517; found: 338.16549; calcd. for $C_{23}H_{19}N_3Na$ ($[M + Na]^+$): 360.14712; found: 360.14751.



6-Cyclohexyl-6H-indolo[2,3-b]quinoxaline **35t** was prepared following general procedure 13 using compound **34** (100 mg, 0.28 mmol) and cyclohexylamine (90 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 5:1) to yield **35t** (61 mg, 74 %) as a yellow solid; m.p. 215-216 ºC; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 8.52 (d, *J* = 7.7 Hz, 1H), 8.30 (dd, *J* = 8.2, 1.2 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.81 – 7.57 (m, 4H), 7.36 (ddd, *J* = 8.0, 4.8, 3.4 Hz, 1H), 4.97 (m, 1H), 2.59 (tt, *J* = 12.4, 6.1 Hz, 2H), 2.23 – 0.59 (m, 8H); ^{13}C NMR (63 MHz, $CDCl_3$) δ =

145.68, 144.03, 140.60, 140.05, 139.06, 130.76, 129.29, 128.70, 128.05, 126.02, 122.96, 120.53, 119.96, 111.27, 54.09, 30.38, 26.40, 25.71; IR (ATR, cm^{-1}): ν =2931 (m), 2854 (m), 1608 (w), 1579 (m), 1574 (m), 1485 (m), 1460 (m), 1435 (w), 1404 (s), 1383 (m), 1346 (m), 1327 (m), 1321 (m), 1298 (m), 1263 (w), 1252 (w), 1234 (m), 1205 (s), 1124 (m), 1117 (s), 1090 (w), 1066 (m), 1043 (m), 1009 (m), 980 (w), 945 (m), 889 (m), 862 (w), 850 (w), 804 (w), 764 (m), 746 (vs), 717 (m), 696 (w), 638 (m), 592 (s), 569 (m), 540 (w); GC-MS (EI, 70 eV): m/z (%) = 301 (20), 219 (100); HRMS (EI): calcd. for $C_{20}H_{19}N_3$ ($[M]^+$): 301.15735; found: 301.15679.

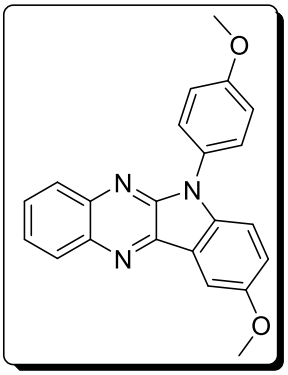
General procedure 14 for C-N coupling/C-H bond activation, exemplified by: *6-phenyl-6H-indolo[2,3-b]quinoxaline* 35a



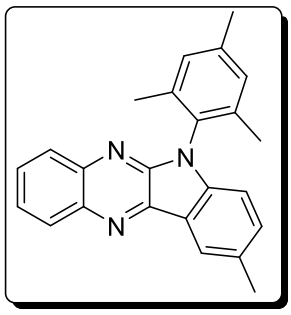
32 **35a**

To a pressure tube charged with 2,3-dibromoquinoxaline **32** (100 mg, 0.35 mmol), $Pd(OAc)_2$ (3 mg, 14 µmol), ligand $PCy_3 \cdot HBF_4$ (11 mg, 29 µmol) and sodium *tert*-butoxide (83 mg, 0.87mmol) under Argon. The mixture was back-filled with Argon several times. The mixture was dissolved in anhydrous toluene (10 mL). Diphenylamine (49 mg, 0.29mmol) was added to the mixture and heated at 105 ºC for 18 h. After cooling, the reaction mixture was diluted with dichloromethane (20 mL) and filtered through a celite pad, washing with dichloromethane (40 mL). The filtrate was reduced *in vacuo*. The product was separated via flash chromatography (silica gel, heptane/ethylacetate 5:1) to yield **35a** (77 mg, 90%) as a yellow solid; m.p. 230-231ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.49 – 8.41 (m, 1H), 8.27 – 8.20 (m, 1H), 8.03 – 7.97 (m, 1H), 7.70 – 7.51 (m, 7H), 7.48 – 7.39 (m, 2H), 7.39 – 7.31 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 145.86, 144.74, 140.60, 140.18, 139.82, 135.43, 131.03, 129.80, 129.27, 128.83, 128.26, 127.99, 127.16, 126.51, 122.70, 121.86, 119.86, 110.62; IR (ATR, cm^{-1}): ν =3054 (w), 1608 (w), 1597 (w), 1581 (m), 1571 (w), 1501 (m), 1483 (m), 1470 (m), 1458 (m), 1451 (m), 1403 (s), 1390 (m), 1354 (w), 1336 (w), 1318 (m), 1303 (m), 1252 (m), 1226 (m), 1219 (m), 1205 (s), 1174 (m), 1166 (m), 1133 (m), 1126 (m), 1100 (m), 1073 (w), 1042 (w), 1025 (w), 1015 (w), 1007 (w), 954 (w), 949 (w), 780 (m), 766 (m), 758 (m), 748 (vs), 719 (w), 694 (s), 687 (s), 649 (m), 590 (s), 485 (m), 451 (s), 428 (w);

GC-MS (EI, 70 eV): m/z (%) = 295 (100), 147 (10); HRMS (EI): calcd. for $C_{20}H_{13}N_3$ ($[M]^+$):295.11040; found: 295.10963.



6-Mesityl-9-methyl-6H-indolo[2,3-b]quinoxaline **33a** was prepared following general procedure 14 using compound **32** (100 mg, 0.35 mmol) and 2,4,6-trimethyl-*N*-(p-tolyl)aniline (65 mg, 0.29 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 5:1) to yield **33a** (48 mg, 47 %) as a yellow solid; m.p.175-176 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.31 – 8.20 (m, 2H), 8.03 – 7.94 (m, 1H), 7.65 – 7.53 (m, 2H), 7.36 – 7.30 (m, 1H), 7.02 (s, 2H), 6.81 (d, *J* = 8.3 Hz, 1H), 2.48 (s, 3H), 2.33 (s, 3H), 1.82 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 145.80, 142.90, 141.03, 139.92, 139.52, 139.07, 137.45, 132.42, 131.04, 130.35, 129.65, 129.30, 128.58, 128.23, 126.08, 122.74, 119.66, 110.07, 21.30, 21.29, 17.88; IR (ATR, cm^{-1}): ν =3019 (w), 2944 (w), 2913 (w), 2855 (w), 1609 (w), 1587 (w), 1577 (w), 1483 (s), 1471 (m), 1454 (m), 1441 (m), 1394 (m), 1386 (m), 1377 (m), 1361 (w), 1349 (m), 1326 (w), 1316 (m), 1303 (m), 1289 (m), 1251 (m), 1237 (m), 1206 (m), 1197 (m), 1179 (m), 1143 (w), 1130 (m), 1124 (m), 1112 (m), 1044 (m), 1032 (w), 1015 (w), 960 (w), 949 (w), 912 (m), 884 (m), 863 (w), 852 (m), 815 (w), 806 (s), 773 (w), 755 (vs), 749 (s), 728 (m), 719 (m), 678 (w), 670 (w), 656 (w), 642 (w), 630 (m), 603 (w), 596 (m), 586 (m), 571 (m), 565 (m), 549 (w), 540 (w), 522 (w), 516 (w), 512 (w), 508 (w), 498 (w), 485 (m), 472 (w), 449 (vs), 428 (m), 422 (m), 409 (w), 400 (w), 396 (w), 393 (w), 389 (w), 380 (w); GC-MS (EI, 70 eV): m/z (%) = 351 (100), 336 (20), 320 (7), 160 (11), 119 (7); HRMS (EI): calcd. for $C_{24}H_{21}N_3$ ($[M]^+$): 351.17300; found: 351.17195.

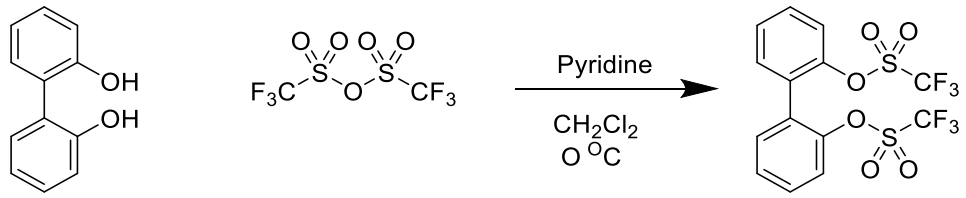


9-Methoxy-6-(4-methoxyphenyl)-6H-indolo[2,3-b]quinoxaline **33b** was prepared following general procedure 14 using compound **32** (100 mg, 0.35 mmol) and bis(4-methoxyphenyl)amine (66 mg, 0.29 mmol). The product was purified by flash chromatography (silica gel, heptane/ethylacetate 1:1) to yield **33b** (56 mg, 54 %) as a yellow solid; m.p.163-164 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.26 – 8.20 (m, 1H), 8.03 – 7.98 (m, 1H), 7.93 (d, *J* = 2.5 Hz, 1H), 7.62 (m, 2H), 7.56 – 7.49 (m, 2H), 7.30 (d, *J* = 8.9 Hz, 1H), 7.17 (dd, *J* = 8.6, 2.9 Hz, 1H), 7.11 – 7.04 (m, 2H), 3.91 (s, 3H), 3.85 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 159.05, 155.31, 146.25, 140.69, 139.95, 139.84, 139.43, 129.13, 128.70, 128.36, 128.20, 128.16, 126.24, 120.47, 119.88, 115.04, 111.51,

104.45, 56.12, 55.59; IR (ATR, cm^{-1}): ν =3054 (w), 3017 (w), 2993 (w), 2837 (m), 1614 (w), 1572 (w), 1512 (s), 1487 (vs), 1473 (s), 1466 (s), 1458 (s), 1454 (s), 1438 (s), 1420 (m), 1395 (s), 1388 (s), 1293 (s), 1247 (s), 1197 (vs), 1185 (s), 1174 (vs), 1164 (s), 1138 (m), 1126 (s), 1107 (m), 1040 (s), 1031 (s), 1024 (s), 954 (m), 925 (m), 888 (m), 827 (vs), 809 (s), 802 (m), 793 (s), 764 (s), 756 (vs), 751 (s), 719 (m), 712 (m), 652 (m), 635 (m), 631 (m), 624 (m), 603 (s), 590 (s), 561 (m), 555 (m), 549 (m), 525 (m), 518 (m), 489 (m), 455 (s), 435 (m), 419 (m); GC-MS (EI, 70 eV): m/z (%) = 355 (100), 340 (76), 269 (12), 178 (7); HRMS (EI): calcd. for $C_{22}H_{17}O_2N_3$ ($[M]^+$): 355.13153; found: 355.13112.

8.5.6 Synthesis of biscarbazoles

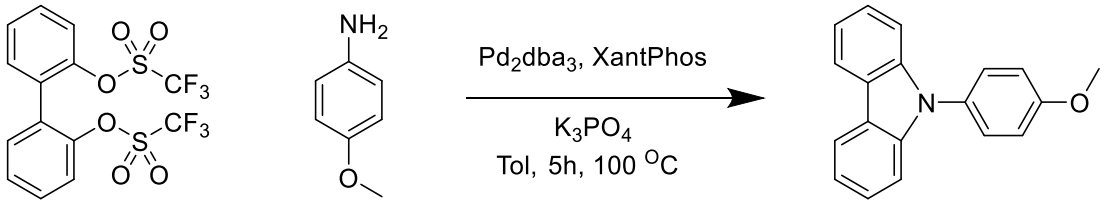
General procedure for the preparation of *2,2'-biphenylene ditriflate* 36.



To a solution of 2,2'-dihydroxyl biphenyl (4.3 g, 23 mmol) in DCM was added pyridine (7.0 mL) under Argon atmosphere. Then, Tf_2O (13.0 g, 46 mmol) was slowly added at O ºC. The reaction was stirred at the same temperature for 3 h until the reaction completed. The reaction mixture was diluted by DCM and subsequently washed with 1M HCl, 1M $NaHCO_3$ and brine. The organic layer was dried over $MgSO_4$, filtered and the solvent was evaporated *in vacuo*. The colorless residue was purified by column chromatography (silica gel, ethylacetate/heptane = 1:10) to yield *1,1'-biphenyl]-2,2'-diyl bis(trifluoromethanesulfonate)* **36** (9.3 g, 90.3 %, white solid)**;** mp 35-36 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.48 – 7.26 (m, 8H); ^{19}F NMR (282 MHz, $CDCl_3$) δ = -74.38 (s); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 147.01, 132.75, 130.90, 129.55, 128.68, 118.50 (q, *J* = 320.1 Hz), 121.81; IR (ATR, cm^{-1}): ν = 1504 (w), 1473 (m), 1452 (w), 1439 (w), 1414 (vs), 1400 (s), 1277 (w), 1244 (s), 1201 (vs), 1165 (m), 1149 (s), 1132 (vs), 1111 (s), 1084 (s), 1045 (m), 1012 (w), 991 (w), 955 (w), 935 (w), 893 (s), 872 (vs), 779 (s), 769 (vs), 760 (s), 735 (m), 725 (s), 667 (w), 646 (w), 619 (s), 588

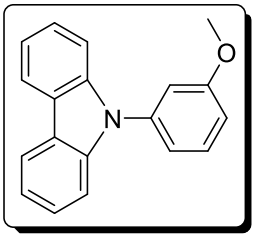
(s), 571 (vs); GC-MS (EI, 70 eV): m/z (%) = 450 (64), 317 (6), 184 (100), 168 (90), 156 (25), 139 (20), 128 (37), 102 (19), 69 (30); HRMS (EI): calcd. for $C_{14}H_8O_6F_6S_2$ ($[M]^+$): 449.96610; found: 449.96583.

General procedure 15 for the preparation of *N-(4-methoxyphenyl)carbazole* 39a.

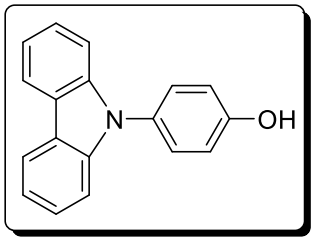


36 **39a**

To 50 mL pressure tube was added successively *2,2'-biphenylylene ditriflate* **36**(460 mg, 1.021 mmol), *p-anisidine* (151 mg, 1.226 mmol), Pd_2dba_3 (23 mg, 0.026 mmol), XantPhos (59 mg, 0.102 mmol), K_3PO_4 (650 mg, 3.062 mmol) and backfilled with argon 3 times. Then, the mixture was dissolved in 20 mL of toluene, subsequently, backfilled with argon 3 times. The reaction mixture was carried out at 100 ºC under argon atmosphere for 5 hours and controlled by TLC. The reaction was cooled down to ambient temperature then the solvent was removed by evaporating *in vacuo*. The crude product was extracted with EtOAc and water several times. The collected organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated under *in vacuo*. The residue was purified by silica gel column chromatography (silica gel, ethylacetate/heptane = 1:10) to give *N-(4-methoxyphenyl)carbazole* **39a** (265 mg, 95 %) as white solid; mp 156-157 ºC; ^{1}H NMR (300 MHz, CDCl3) δ = 8.19 – 8.10 (m, 2H), 7.48 – 7.24 (m, 9H), 7.12 (d, *J* = 9.0 Hz, 2H), 3.92 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 159.02, 141.53, 130.47, 128.73, 125.98, 123.25, 120.39, 119.78, 115.21, 109.83, 55.75; IR (ATR, cm^{-1}): ν = 1591 (w), 1510 (s), 1479 (m), 1450 (s), 1336 (m), 1317 (m), 1246 (s), 1240 (s), 1228 (s), 1178 (s), 1147 (m), 1120 (m), 1107 (m), 1028 (s), 997 (m), 908 (m), 852 (w), 829 (s), 810 (m), 798 (m), 748 (vs), 725 (s), 698 (m), 642 (m), 621 (s), 611 (m), 584 (s), 569 (s), 532 (s); GC-MS (EI, 70 eV): m/z (%) = 273 (100), 258 (47), 230 (12), 228 (30); HRMS (EI): calcd. for $C_{19}H_{15}ON$ ($[M]^+$): 273.11482; found: 273.11474.



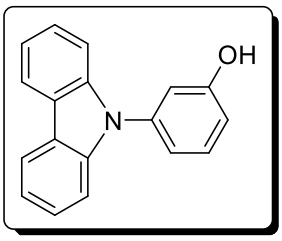
N-(4-methoxyphenyl)carbazole **39b** was prepared following procedure 15 using *2,2'-biphenylylene ditriflate* **36** (460 mg, 1.021 mmol), m-*anisidine* (138 µL, 1.226 mmol). The crude product was separated via flash chromatography (silica gel, ethylacetate/heptane = 1:10) to yield **39b** (265 mg, 95 %) as colorless syrup; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.05 (dd, *J* = 7.7, 0.6 Hz, 2H), 7.46 – 7.27 (m, 5H), 7.25 – 7.12 (m, 2H), 7.12 – 6.97 (m, 2H), 6.91 (dd, *J* = 8.3, 2.5 Hz, 1H), 3.76 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 160.94, 140.95, 138.96, 130.66, 126.07, 123.49, 120.41, 120.04, 119.44, 113.38, 112.80, 110.04, 55.63; IR (ATR, cm^{-1}): ν = 3051 (w), 2955 (w), 2933 (w), 2833 (w), 1927 (w), 1890 (w), 1861 (vw), 1593 (s), 1576 (m), 1495 (s), 1477 (s), 1450 (s), 1362 (m), 1335 (m), 1311 (s), 1281 (s), 1250 (s), 1227 (s), 1184 (m), 1153 (s), 1119 (m), 1099 (m), 1088 (m), 1078 (m), 1039 (s), 1003 (m), 995 (m), 984 (m), 970 (m), 918 (m), 872 (m), 845 (m), 833 (m), 825 (m), 779 (m), 744 (vs), 721 (vs), 692 (vs), 652 (m), 636 (m), 615 (m), 588 (m), 559 (m); GC-MS (EI, 70 eV): m/z (%) = 273 (100), 258 (7), 241 (5), 228 (19); HRMS (EI): calcd. for $C_{19}H_{15}ON$ ($[M]^+$): 273.11484; found: 273.11482.



General procedure 16 for the preparation of *N-(4-hydroxyphenyl)carbazole* 40a.

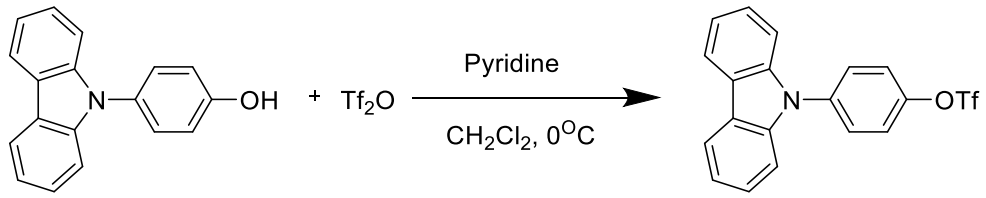
To a solution of **39a** (265 mg, 0.970 mmol) in DCM at -78 ºC was dropped slowly BBr_3 (367 µl, 3.880 mmol). The temperature was raised to ambient temperature. The reaction was controlled by TLC until the starting material completely disappeared. The reaction mixture was poured to ice aqua solution of $NaHCO_3$. The aqueous layer was extracted with DCM three times. The organic residue was dried over $MgSO_4$, filtered, and the solvent was evaporated *in vacuo*. The crude product was purified over flash silica gel column chromatography (silica gel, ethylacetate/heptane = 1:10) to give **40a** (239 mg, 95 %); mp 106-107 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.18 – 8.11 (m, 2H), 7.44 – 7.36 (m, 4H), 7.35 – 7.23 (m, 4H), 7.05 (d, *J* = 8.8 Hz, 2H). ^{13}C NMR (63 MHz, $CDCl_3$) δ = 155.00, 141.50, 130.72, 128.99, 126.00, 123.28, 120.40, 119.82, 116.72, 109.81; IR (ATR, cm^{-1}): ν = 3196 (m), 3043 (w), 1622 (w), 1593 (m), 1512 (s), 1479 (m), 1450 (s), 1363 (m), 1335 (m), 1315 (m), 1248 (m), 1228 (s), 1219 (s), 1178 (s), 1165 (m), 1147 (m), 1099 (m), 1028 (w), 1014 (m), 1003 (w), 910 (m), 833 (s), 820 (m), 746 (vs), 723 (vs), 665 (m), 623 (s), 611 (m), 584 (s), 567 (m), 532 (m); GC-MS (EI, 70 eV): m/z (%) = 259 (100),

241 (6), 228 (10); HRMS (ESI): calcd. for $C_{18}H_{14}ON$ ($[M + H]^+$): 260.10699; found: 260.10686; calcd. for $C_{18}H_{13}ONNa$ ($[M + Na]^+$): 282.08894; found: 282.08872.



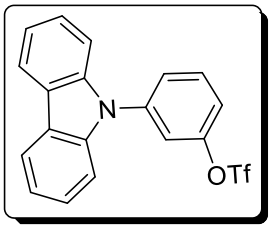
N-(4-hydroxyphenyl)carbazole **40b** was prepared following procedure 16 with carbazole 39b (265 mg, 0.970 mmol) to give **40b** (231 mg, 92 %) as colorless syrup; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 8.09 – 8.03 (m, 2H), 7.41 – 7.31 (m, 5H), 7.25 – 7.16 (m, 2H), 7.07 (ddd, *J* = 7.9, 1.9, 0.9 Hz, 1H), 6.96 (m, 1H), 6.84 (ddd, *J* = 8.2, 2.5, 0.9 Hz, 1H), 4.86 (s, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 156.67, 140.71, 138.99, 130.79, 125.93, 123.37, 120.26, 119.96, 119.48, 114.48, 114.06, 109.88; IR (ATR, cm^{-1}): ν = 3537 (w), 3271 (m), 3047 (w), 1599 (s), 1576 (m), 1498 (s), 1485 (m), 1471 (m), 1450 (s), 1367 (m), 1346 (m), 1335 (m), 1321 (m), 1304 (m), 1261 (m), 1252 (m), 1230 (s), 1209 (m), 1178 (m), 1165 (m), 1151 (s), 1124 (m), 991 (m), 920 (m), 872 (m), 849 (m), 781 (m), 748 (vs), 742 (vs), 719 (vs), 696 (vs), 667 (m), 636 (m), 615 (m), 584 (m), 573 (m), 557 (m); GC-MS (EI, 70 eV): m/z (%) = 259(100), 241 (4), 228 (8), 204 (4); HRMS (EI): calcd. for $C_{18}H_{13}ON$ ($[M]^+$): 259.09917; found: 259.09925.

General procedure 17 for the preparation of *N-(4- trifluoromethanesulfonate)carbazole* 41a .



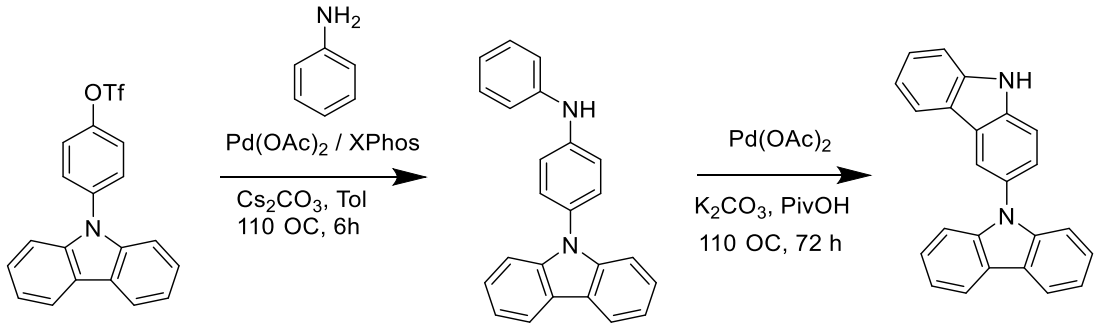
To a solution of *N-(4-hydroxyphenyl)carbazole* **40a** (239 mg, 0.921 mmol) in DCM was added pyridine (298 µL, 3.690 mmol) under Argon atmosphere. Then, Tf_2O (234 µL, 1.383 mmol) was dropwise added at 0 °C. The reaction was carried at same temperature in 3 h until starting material disappeared (controlled by TLC). The reaction mixture was diluted with DCM and subsequently washed with 1M HCl, 1M $NaHCO_3$ and brine. The organic layer was dried over $MgSO_4$, filtered and the solvent was evaporated *in vacuo*. The colorless residue was purified by column chromatography over silica gel (silica gel, ethylacetate/heptane = 1:10) to yield *-(4- trifluoromethanesulfonate)carbazole* **41a** (310 mg, 86 %) as white solid; mp 112 - 114 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.18 – 8.12 (m, 2H), 7.72 – 7.65 (m, 2H),

7.57 – 7.50 (m, 2H), 7.48 – 7.36 (m, 4H), 7.36 – 7.29 (m, 2H); ^{19}F NMR (282 MHz, $CDCl_3$) δ = -72.65 (s); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 147.99, 140.64, 138.12, 128.89, 126.40, 123.82, 123.19, 120.72, 120.65, 109.59; IR (ATR, cm^{-1}): ν = 3063 (w), 2924 (w), 1593 (w), 1504 (s), 1477 (m), 1452 (s), 1421 (s), 1412 (s), 1365 (w), 1335 (m), 1315 (m), 1248 (m), 1228 (s), 1215 (vs), 1167 (m), 1134 (vs), 1101 (m), 1026 (w), 1016 (m), 1001 (w), 916 (m), 887 (vs), 841 (s), 820 (m), 787 (m), 764 (w), 752 (vs), 725 (s), 696 (s), 644 (m), 619 (s), 611 (vs), 602 (vs), 573 (s), 565 (m), 530 (s); GC-MS (EI, 70 eV): m/z (%) = 391 (51), 259 (20), 258 (100), 230 (15), 228 (28), 69 (9); HRMS (EI): calcd. for $C_{19}H_{12}O_3NF_3S$ ($[M]^+$): 391.04845; found: 391.04852.

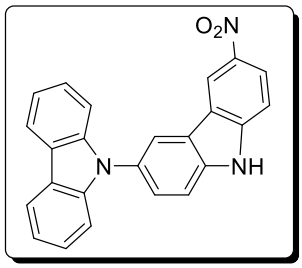


N-(3- trifluoromethanesulfonate)carbazole **41b** was prepared following procedure 17 with carbazole **40b** (231 mg, 0.891 mmol) to give **41b** (328 mg, 94 %) as white solid; mp 76-78 ºC, ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.97 (m, 2H), 7.50 (dd, *J* = 6.4, 4.6 Hz, 2H), 7.38 (t, *J* = 2.0 Hz, 1H), 7.29 – 7.24 (m, 4H), 7.16 (m, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ = -72.63 (s). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 150.33, 140.40, 139.83, 131.53, 126.90, 126.51, 123.92, 120.90, 120.67, 120.32, 120.14, 109.56; IR (ATR, cm^{-1}): ν = 3072 (w), 3047 (w), 3024 (w), 1605 (m), 1585 (w), 1574 (w), 1495 (s), 1483 (s), 1454 (s), 1417 (vs), 1404 (m), 1365 (m), 1335 (m), 1315 (m), 1250 (m), 1230 (m), 1209 (vs), 1184 (s), 1163 (m), 1136 (s), 1119 (s), 1095 (s), 1084 (m), 1028 (m), 1003 (w), 984 (s), 964 (w), 924 (m), 904 (m), 877 (s), 847 (m), 798 (s), 771 (m), 764 (m), 750 (vs), 741 (s), 725 (s), 692 (s), 660 (m), 636 (m), 623 (m), 606 (s), 567 (s), 536 (m); GC-MS (EI, 70 eV): m/z (%) = 391 (100), 258 (57), 230 (58), 228 (42), 202 (12), 69 (13); HRMS (EI): calcd. for $C_{19}H_{12}O_3NF_3S$ ($[M]^+$): 391.04845; found: 391.04816.

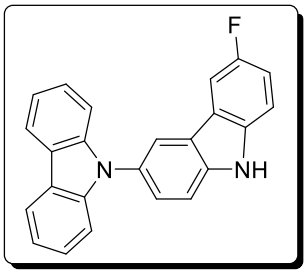
General procedure 18 for C-N coupling and C-H activation reaction, exemplified by *9H-3,9'-bicarbazole* (38a)



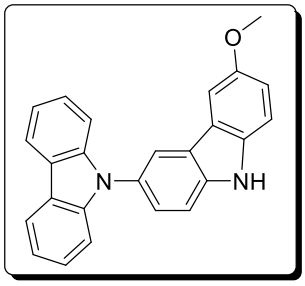
Cesium carbonate (125 mg, 0.383 mmol) was added to a pressure tube charged with $Pd(OAc)_2$ (3 mg, 0.013 ammol) and ligand XPhos (12 mg, 0.026 mmol) under argon atmosphere. *N-(4- trifluoromethanesulfonate)carbazole* **41a** (100 mg, 0.256 mmol) and aniline (26 µL, 0.281 mmol) were added to the mixture and the tube was backfilled with argon several times. The mixture was stirred at 110 °C in anhydrous toluene (5 mL) for 6 hours. After cooling, the reaction mixture was diluted with dichloromethane (10 mL), filtered through a celite pad, and washed with dichloromethane (20 mL). The filtrate was concentrated *in vacuo*. Pivalic acid was added to the mixture of filtrate charged with $Pd(OAc)_2$ (3 mg, 0.013 mmol) and potassium carbonate (35 mg, 0.256 mmol). The mixture was stirred at 110 °C under air atmosphere for 72 hours, controlled by TLC. The solution was then cooled to room temperature, diluted with DCM and washed with a saturated aqueous solution of sodium carbonate, dried over Magnesium sulfate, filtered and evaporated in *vacuo*. The product was purified by flash chromatography (silica gel, ethylacetate/heptane = 1:10) to yield **38a** (73 mg, 86%) as white solid; mp 211-212 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 8.07 (m, 3H), 7.90 (d, *J* = 7.8 Hz, 1H), 7.46 – 7.07 (m, 11H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 142.06, 140.30, 138.71, 129.56, 126.71, 125.99, 125.58, 124.50, 123.21, 123.14, 120.72, 120.40, 120.05, 119.71, 111.73, 111.05, 109.99; IR (ATR, cm^{-1}): ν = 3394 (m), 3076 (w), 3051 (m), 3020 (w), 2926 (w), 1595 (m), 1574 (m), 1495 (m), 1485 (m), 1475 (s), 1462 (s), 1448 (s), 1346 (m), 1333 (m), 1311 (s), 1273 (m), 1230 (s), 1203 (m), 1163 (m), 1149 (m), 1126 (m), 1117 (m), 1097 (m), 1024 (m), 1011 (m), 1003 (m), 957 (m), 926 (m), 918 (m), 845 (m), 820 (s), 742 (vs), 733 (s), 719 (vs), 660 (m), 650 (s), 631 (m), 615 (m), 580 (m), 571 (s); GC-MS (EI, 70 eV): m/z (%) = 332 (100), 166 (14), 139 (4); HRMS (EI): calcd. for $C_{24}H_{16}N_2$ ($[M]^+$): 332.13080; found: 332.13072.



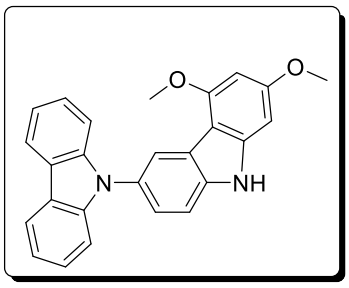
6-nitro-9H-3,9'-bicarbazole **38b** was prepared following general procedure 18 using compound **41a** (100 mg, 0.256 mmol) and *p*-nitroaniline (39 mg, 0.281 mmol). The product was purified by flash chromatography (silica gel, ethylacetate/heptane = 1:3) to yield **38b** (96 mg, 95 %) as red solid; mp 306-308 °C; ^{1}H NMR (300 MHz, DMSO) δ = 12.35 (s, 1H), 9.32 (d, *J* = 2.2 Hz, 1H), 8.72 (d, *J* = 1.8 Hz, 1H), 8.39 – 8.22 (m, 3H), 7.87 (d, *J* = 8.5 Hz, 1H), 7.79 – 7.65 (m, 2H), 7.37 (m, 6H); ^{13}C NMR (75 MHz, DMSO) δ = 144.00, 140.97, 140.13, 140.10, 129.42, 126.29, 126.14, 123.68, 122.49, 122.09, 121.71, 120.43, 120.34, 119.76, 118.33, 113.27, 111.50, 109.70; IR (ATR, cm^{-1}): ν = 3307 (m), 2955 (w), 2922 (w), 2850 (w), 1608 (m), 1585 (m), 1495 (s), 1475 (s), 1448 (s), 1315 (s), 1308 (s), 1288 (s), 1228 (s), 1200 (s), 1163 (s), 1147 (m), 1128 (s), 1103 (m), 1078 (s), 1030 (m), 1016 (m), 889 (m), 852 (m), 823 (s), 816 (s), 748 (vs), 741 (s), 731 (s), 721 (vs), 683 (s), 654 (s), 640 (s), 625 (s), 613 (s), 590 (s), 567 (s), 557 (s), 528 (s); GC-MS (EI, 70 eV): m/z (%) = 377 (2), 329 (51), 314 (16), 114 (14), 73 (33), 60 (45), 44 (100); HRMS (ESI): calcd. for $C_{24}H_{16}O_2N_3$ ([M + H]$^+$): 378.1237; found: 378.12327; calcd. for $C_{24}H_{15}O_2N_3Na$ ([M + Na]$^+$): 400.10565; found: 400.10522.



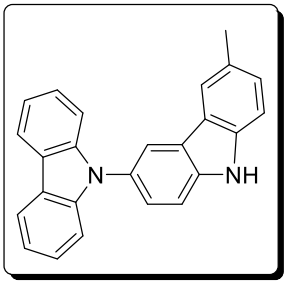
6-fluoro-9H-3,9'-bicarbazole **38c** was prepared following general procedure 18 using compound **41a** (100 mg, 0.256 mmol) and *p*-fluoroaniline (27 µL, 0.281 mmol). The product was purified by flash chromatography (silica gel, ethylacetate/heptane = 1:10) to yield **38c** (90 mg, 63 %) as red solid; mp 238-240 °C; ^{1}H NMR (300 MHz, DMSO) δ = 11.62 (s, 1H), 8.41 (d, *J* = 2.0 Hz, 1H), 8.26 (d, *J* = 7.6 Hz, 2H), 8.06 (dd, *J* = 9.4, 2.6 Hz, 1H), 7.76 (d, *J* = 8.6 Hz, 1H), 7.57 (m, 2H), 7.42 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 2H), 7.37 – 7.22 (m, 5H). ^{13}C NMR (75 MHz, DMSO) δ = 156.47 (d, *J* = 232.6 Hz), 141.23, 139.92, 136.95, 127.70, 126.08, 125.30, 123.19 (d, *J* = 4.2 Hz), 122.69 (d, *J* = 10.1 Hz), 122.35, 120.40, 119.71, 119.59, 113.95 (d, *J* = 25.6 Hz), 112.51, 112.18 (d, *J* = 9.1 Hz), 109.64, 106.35 (d, *J* = 23.9 Hz); IR (ATR, cm^{-1}): ν = 3394 (m), 3053 (w), 2953 (w), 2920 (w), 2850 (w), 1587 (m), 1574 (m), 1495 (s), 1466 (s), 1448 (s), 1315 (m), 1284 (m), 1244 (m), 1228 (s), 1171 (m), 1151 (s), 1140 (m), 1124 (m), 1115 (m), 850 (m), 812 (s), 752 (vs), 744 (s), 721 (s), 656 (s), 646 (s), 615 (m), 596 (m), 575 (s), 565 (s), 544 (s), 532 (m); GC-MS (EI, 70 eV): m/z (%) = 350 (100), 174 (15); HRMS (ESI): calcd. for $C_{24}H_{16}FN_2$ ([M + H]$^+$): 351.1292; found: 351.12844; calcd. for $C_{24}H_{15}OFN_2Na$ ([M + Na]$^+$): 373.11115; found: 373.11065.



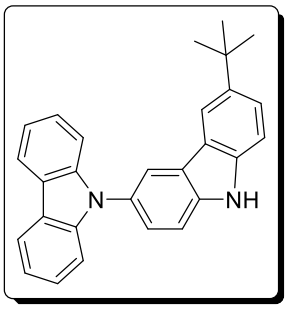
6-methoxy-9H-3,9'-bicarbazole **38d** was prepared following general procedure 18 using compound **41a** (100 mg, 0.256 mmol) and *p*-anisidine (35 mg, 0.281 mmol). The product was purified by flash chromatography (silica gel, ethylacetate/heptane = 1:5) to yield **38d** (93 mg, 53 %) as white solid; mp 256-257 °C; ^{1}H NMR (300 MHz, DMSO) δ = 11.46 (s, 1H), 8.36 (d, *J* = 1.9 Hz, 1H), 8.26 (d, *J* = 7.7 Hz, 2H), 7.80 (d, *J* = 2.4 Hz, 1H), 7.71 (d, *J* = 8.5 Hz, 1H), 7.54 – 7.39 (m, 4H), 7.35 – 7.24 (m, 4H), 7.08 (dd, *J* = 8.8, 2.5 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR (75 MHz, DMSO) δ = 153.17, 141.32, 139.54, 135.31, 127.23, 126.06, 124.45, 123.48, 122.64, 122.33, 120.40, 119.52, 119.29, 115.66, 112.20, 111.95, 109.68, 103.39, 55.56; IR (ATR, cm^{-1}): ν = 3417 (m), 3045 (w), 2928 (w), 2829 (m), 1622 (m), 1589 (s), 1581 (s), 1574 (s), 1497 (s), 1470 (m), 1464 (m), 1450 (s), 1435 (m), 1360 (s), 1335 (m), 1313 (m), 1294 (s), 1232 (s), 1201 (s), 1173 (m), 1151 (m), 1140 (m), 1032 (m), 808 (m), 773 (s), 752 (vs), 727 (s), 656 (m), 648 (m), 617 (m), 607 (m), 569 (s), 528 (m); GC-MS (EI, 70 eV): m/z (%) = 362 (100), 347 (26), 319 (16), 290 (5), 174 (14); HRMS (ESI): calcd. for $C_{25}H_{17}N_2O$ ([M - H]$^-$): 361.13464; found: 361.13557.



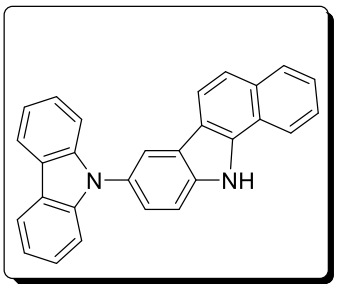
5,7-dimethoxy-9H-3,9'-bicarbazole **38e** was prepared following general procedure 18 using compound **41a** (100 mg, 0.256 mmol) and 3,5-dimethoxyaniline (43 mg, 0.281 mmol). The product was purified by flash chromatography (silica gel, ethylacetate/heptane = 1:4) to yield **38e** (100 mg, 50 %) as white solid; mp 125-127 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.32 (d, *J* = 2.0 Hz, 1H), 8.26 – 8.15 (m, 2H), 8.09 (s, 1H), 7.50 (dd, *J* = 8.4, 0.4 Hz, 1H), 7.46 – 7.34 (m, 5H), 7.34 – 7.25 (m, 3H), 6.56 (d, *J* = 1.9 Hz, 1H), 6.34 (d, *J* = 1.9 Hz, 1H), 3.94 (s, 3H), 3.91 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 160.97, 156.90, 142.35, 142.24, 137.96, 129.65, 125.89, 124.09, 123.44, 123.09, 121.42, 120.30, 119.49, 110.65, 110.20, 106.90, 91.59, 87.00, 55.85, 55.52; IR (ATR, cm^{-1}): ν = 3400 (w), 2918 (w), 2839 (w), 1633 (m), 1622 (m), 1614 (m), 1591 (m), 1495 (s), 1464 (s), 1450 (s), 1435 (m), 1335 (m), 1329 (m), 1315 (m), 1290 (s), 1230 (s), 1209 (s), 1196 (s), 1149 (s), 1120 (s), 1099 (m), 1049 (m), 918 (m), 806 (s), 750 (vs), 723 (s), 656 (s), 642 (m), 557 (m); GC-MS (EI, 70 eV): m/z (%) = 392 (100), 334 (22), 196 (12), 167 (7), 140 (22); HRMS (ESI): calcd. for $C_{26}H_{21}N_2O_2$ ([M + H]$^+$): 393.15975; found: 393.1595; calcd. for $C_{26}H_{20}N_2O_2Na$ ([M + Na]$^+$): 415.1417; found: 415.14155.



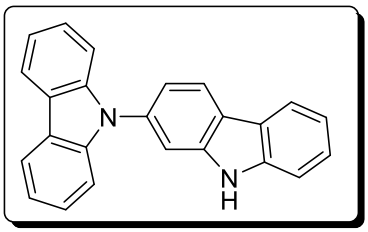
6-methyl-9H-3,9'-bicarbazole **38g** was prepared following general procedure 18 using compound **41a** (100 mg, 0.256 mmol) and *p*-toluidine (30 mg, 0.281 mmol). The product was purified by flash chromatography (silica gel, ethylacetate/heptane = 1:10) to yield **38g** (89 mg, 34 %) as white solid; mp 231-232 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.15 – 8.07 (m, 3H), 7.76 (d, *J* = 0.7 Hz, 1H), 7.46 (m, 2H), 7.39 – 7.14 (m, 9H), 2.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 142.08, 139.05, 138.57, 129.45, 129.38, 128.09, 125.96, 125.39, 124.38, 123.36, 123.21, 120.59, 120.38, 119.67, 119.60, 111.69, 110.73, 110.01, 21.56; IR (ATR, cm^{-1}): ν = 3410 (m), 3057 (w), 2916 (w), 2852 (w), 2831 (w), 1593 (m), 1583 (m), 1574 (m), 1497 (s), 1479 (m), 1464 (s), 1452 (s), 1358 (m), 1338 (m), 1317 (m), 1296 (m), 1277 (m), 1242 (m), 1230 (s), 1153 (m), 820 (s), 806 (m), 748 (vs), 723 (vs), 658 (m), 646 (m), 575 (s), 540 (m), 528 (m); GC-MS (EI, 70 eV): m/z (%) = 346 (100), 173 (9); HRMS (ESI): calcd. for $C_{25}H_{19}N_2$ ($[M + H]^+$): 347.15428; found: 347.15337; calcd. for $C_{25}H_{18}N_2Na$ ($[M + Na]^+$): 369.13622; found: 369.13578.



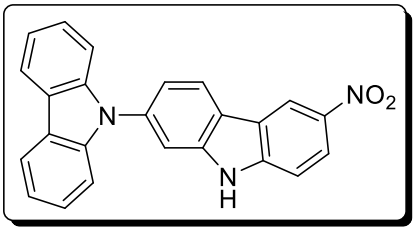
6-(tert-butyl)-9H-3,9'-bicarbazole **38h** was prepared following general procedure 18 using compound **41a** (100 mg, 0.256 mmol) and 4-(*tert*-butyl)aniline (45 μL, 0.281 mmol). The product was purified by flash chromatography (silica gel, ethylacetate/heptane = 1:10) to yield **38h** (99 mg, 70 %) as white solid; mp 183-185 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 8.28 – 7.87 (m, 4H), 7.60 – 7.05 (m, 10H), 1.34 (s, 9H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 143.20, 142.16, 139.18, 138.43, 129.36, 125.94, 125.36, 124.80, 123.20, 122.90, 120.39, 119.65, 116.72, 111.67, 110.57, 110.02, 34.86, 32.06; IR (ATR, cm^{-1}): ν = 3408 (m), 3045 (w), 2953 (m), 2862 (w), 1622 (m), 1614 (m), 1595 (m), 1574 (m), 1495 (s), 1470 (s), 1450 (s), 1362 (m), 1335 (m), 1315 (m), 1294 (m), 1281 (m), 1242 (m), 1230 (s), 1201 (m), 1163 (m), 1138 (m), 1117 (m), 808 (s), 746 (vs), 723 (vs), 661 (m), 648 (m), 627 (vs), 577 (m), 546 (m), 536 (m); GC-MS (EI, 70 eV): m/z (%) = 388 (100), 373 (63), 332 (10), 207 (9), 187 (13), 173 (24); HRMS (ESI): calcd. for $C_{28}H_{25}N_2$ ($[M + H]^+$): 389.20123; found: 389.20074.



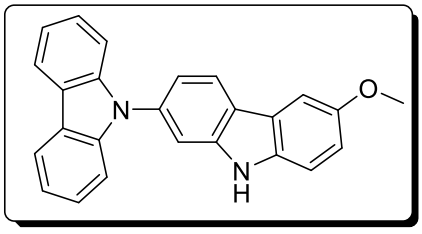
8-(9H-carbazol-9-yl)-11H-benzo[a]carbazole **38j** was prepared following general procedure 18 using compound **41a** (100 mg, 0.256 mmol) and naphthalene-2-amine (40 mg, 0.281 mmol). The product was purified by flash chromatography (silica gel, ethylacetate/heptane = 1:10) to yield **38j** (98 mg, 42 %) as white solid; mp 220-222 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.90 (s, 1H), 8.18 (d, *J* = 1.9 Hz, 1H), 8.13 – 8.10 (m, 3H), 8.00 (d, *J* = 8.6 Hz, 1H), 7.96 (d, *J* = 7.5 Hz, 1H), 7.69 (d, *J* = 8.5 Hz, 1H), 7.61 (d, *J* = 8.7 Hz, 1H), 7.58 – 7.46 (m, 3H), 7.36 – 7.30 (m, 4H), 7.25 – 7.19 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 141.95, 137.57, 135.86, 132.74, 130.05, 129.21, 125.86, 125.68, 125.21, 124.52, 123.13, 121.15, 120.80, 120.55, 120.28, 119.60, 119.24, 119.12, 118.30, 112.11, 109.90; IR (ATR, cm^{-1}): ν = 3417 (w), 3045 (w), 2918 (w), 2848 (w), 1593 (m), 1514 (m), 1495 (s), 1477 (m), 1464 (m), 1450 (s), 1417 (m), 1385 (m), 1358 (m), 1335 (m), 1313 (m), 1304 (m), 1281 (m), 1230 (s), 1205 (m), 1169 (m), 1157 (m), 1146 (m), 1117 (m), 1105 (m), 806 (s), 748 (vs), 723 (s), 687 (m), 650 (m), 604 (m), 565 (m), 550 (m); GC-MS (EI, 70 eV): m/z (%) = 382 (100), 216 (6), 190 (25); HRMS (ESI): calcd. for $C_{28}H_{19}N_2$ ($[M + H]^+$): 383.15428; found: 383.15362; calcd. for $C_{28}H_{18}N_2Na$ ($[M + Na]^+$): 405.13622; found: 405.13638.



9H-2,9'-bicarbazole **42a** was prepared following general procedure 18 using compound **41b** (100 mg, 0.256 mmol) and aniline (26 µL, 0.281 mmol). The product was purified by flash chromatography (silica gel, ethylacetate/heptane = 1:10) to yield **42a** (65 mg, 77 %) as white solid; mp 298-300 °C; ^{1}H NMR (300 MHz, Acetone) δ = 10.61 (s, 1H), 8.40 (d, *J* = 8.2 Hz, 1H), 8.29 – 8.20 (m, 3H), 7.78 – 7.72 (m, 1H), 7.61 (m, 1H), 7.50 – 7.38 (m, 6H), 7.33 – 7.23 (m, 3H); ^{13}C NMR (63 MHz, Acetone) δ = 142.28, 141.82, 141.72, 135.91, 126.95, 126.89, 124.14, 123.66, 123.52, 122.23, 121.18, 121.11, 120.72, 120.28, 118.82, 112.02, 110.76, 110.47; IR (ATR, cm^{-1}): ν = 3414 (m), 3053 (w), 2926 (w), 1603 (m), 1489 (m), 1460 (m), 1450 (s), 1441 (s), 1362 (m), 1336 (m), 1321 (m), 1230 (s), 1201 (m), 1157 (m), 1095 (m), 999 (m), 978 (m), 937 (m), 918 (m), 849 (m), 818 (m), 752 (s), 742 (s), 723 (vs), 663 (s), 631 (m), 615 (m), 565 (s); GC-MS (EI, 70 eV): m/z (%) = 332 (100), 166 (16); HRMS (EI): calcd. for $C_{24}H_{16}N_2$ ($[M]^+$): 332.13080; found: 332.13106.

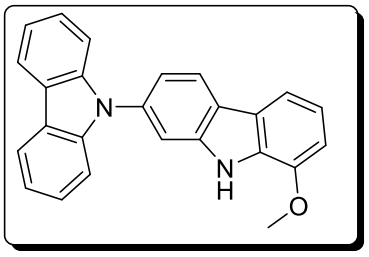


6-nitro-9H-2,9'-bicarbazole **42b** was prepared following general procedure 18 using compound **41b** (100 mg, 0.256 mmol) and *p*-nitroaniline (39 mg, 0.281 mmol). The product was purified by flash chromatography (silica gel, ethylacetate/heptane = 1:3) to yield **42b** (61 mg, 63 %) as red solid; mp 310-312 °C; ^{1}H NMR (300 MHz, Acetone) δ 10.42 (s, 1H), 8.36 (d, *J* = 8.3 Hz, 1H), 8.27 – 8.20 (m, 2H), 7.80 (d, *J* = 2.5 Hz, 1H), 7.71 (d, *J* = 1.5 Hz, 1H), 7.56 – 7.25 (m, 8H), 7.12 (dd, *J* = 8.8, 2.5 Hz, 1H), 3.93 (s, 3H); ^{13}C NMR (63 MHz, DMSO) δ = 144.02, 141.82, 140.47, 140.28, 135.81, 126.29, 122.92, 122.76, 121.97, 121.82, 121.56, 120.54, 120.10, 119.04, 117.68, 111.45, 110.14, 109.76; IR (ATR, cm^{-1}): ν = 3348 (m), 3059 (w), 2916 (w), 1610 (s), 1593 (m), 1583 (m), 1506 (s), 1477 (s), 1464 (m), 1450 (s), 1365 (m), 1331 (s), 1319 (s), 1309 (s), 1279 (s), 1248 (s), 1228 (s), 1196 (m), 1159 (s), 1124 (s), 1099 (s), 1084 (s), 1028 (m), 1014 (m), 1003 (m), 982 (m), 916 (m), 893 (m), 866 (m), 849 (m), 841 (m), 823 (s), 748 (vs), 725 (vs), 692 (s), 663 (s), 636 (m), 627 (m), 615 (m), 584 (s), 573 (s), 565 (s), 528 (m); GC-MS (EI, 70 eV): m/z (%) = 377 (100), 331 (34), 281 (4), 189 (8), 173 (26); HRMS (ESI): calcd. for $C_{24}H_{15}O_2N_3Na$ ([M + Na]$^{+}$): 400.10565; found: 400.10564.

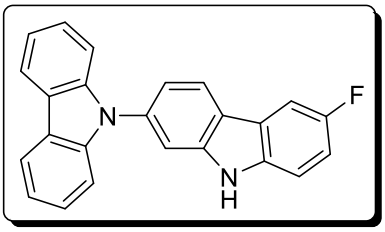


6-methoxy-9H-2,9'-bicarbazole **42c** was prepared following general procedure 18 using compound **41b** (100 mg, 0.256 mmol) and p-anisidine (35 mg, 0.281 mmol). The product was purified by flash chromatography (silica gel, ethylacetate/heptane = 1:5) to yield **42c** (47 mg, 51 %) as white solid; mp 225-227 °C; ^{1}H NMR (300 MHz, Acetone) δ = 10.42 (s, 1H), 8.36 (d, *J* = 8.3 Hz, 1H), 8.27 – 8.20 (m, 2H), 7.80 (d, *J* = 2.5 Hz, 1H), 7.71 (d, *J* = 1.5 Hz, 1H), 7.56 – 7.25 (m, 9H), 7.12 (dd, *J* = 8.8, 2.5 Hz, 1H), 3.93 (s, 3H); ^{13}C NMR (63 MHz, Acetone) δ = 155.14, 142.32, 142.25, 136.59, 135.74, 126.86, 124.11, 123.56, 122.28, 121.10, 120.69, 118.31, 116.35, 112.71, 110.76, 110.48, 103.79, 56.15; IR (ATR, cm^{-1}): ν = 3415 (m), 3053 (w), 2993 (w), 1608 (m), 1589 (m), 1489 (s), 1471 (m), 1462 (m), 1448 (s), 1427 (s), 1335 (m), 1319 (m), 1308 (m), 1288 (s), 1252 (m), 1225 (s), 1217 (s), 1201 (s), 1169 (s), 1159 (s), 1126 (m), 1115 (m), 1095 (m), 1030 (s), 1012 (m), 1003 (m), 980 (m), 914 (m), 906 (m), 895 (m), 860 (m), 850 (m), 837 (s), 822 (m), 804 (vs), 775 (m), 754 (vs), 744 (vs), 725 (vs), 708 (s), 663 (s), 652 (m), 615 (m), 606 (s), 588 (m), 565 (m), 553 (m), 528 (s); GC-MS (EI, 70 eV): m/z (%) = 362 (100), 347 (21), 330

(14), 290 (6), 207 (6), 159 (68), 145 (29), 133 (15); HRMS (EI): calcd. for $C_{25}H_{18}N_2O$ ($[M]^+$): 362.14136; found: 362.14150.

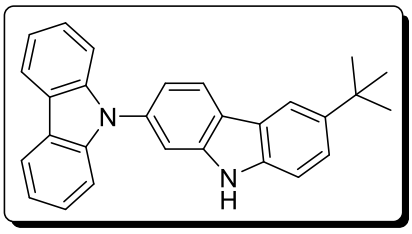


8-methoxy-9H-2,9'-bicarbazole **42d** was prepared following general procedure 18 using compound **41b** (100 mg, 0.256 mmol) and o-anisidine (32 µL, 0.281 mmol). The product was purified by flash chromatography (silica gel, ethylacetate/heptane = 1:5) to yield **42d** (75 mg, 81 %) as white solid; mp 269-270 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.40 (s, 1H), 8.24 (d, *J* = 8.3 Hz, 1H), 8.20 – 8.15 (m, 2H), 7.75 (d, *J* = 7.9 Hz, 1H), 7.62 (d, *J* = 1.4 Hz, 1H), 7.51 – 7.37 (m, 5H), 7.34 – 7.20 (m, 4H), 7.01 – 6.94 (m, 1H), 4.05 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 145.75, 141.38, 139.72, 135.26, 130.49, 125.88, 123.92, 123.26, 123.04, 121.61, 120.37, 120.25, 119.76, 118.83, 112.86, 109.93, 109.70, 106.29, 55.58; IR (ATR, cm^{-1}): ν = 3412 (m), 3055 (w), 2931 (w), 2839 (w), 1614 (w), 1579 (m), 1504 (m), 1450 (s), 1433 (s), 1381 (m), 1365 (m), 1335 (m), 1323 (m), 1313 (m), 1306 (m), 1269 (m), 1259 (m), 1240 (m), 1230 (s), 1188 (w), 1155 (m), 1093 (m), 1063 (w), 1016 (s), 980 (w), 931 (w), 918 (m), 893 (w), 868 (w), 847 (m), 823 (m), 781 (m), 746 (vs), 723 (s), 685 (m), 665 (m), 617 (m), 577 (m), 563 (m), 555 (m), 536 (m); GC-MS (EI, 70 eV): m/z (%) = 362 (100), 347 (7), 319 (27), 181 (7), 159 (10); HRMS (ESI): calcd. for $C_{25}H_{19}N_2O$ ($[M + H]^+$): 363.14919; found: 363.14883; calcd. for $C_{25}H_{18}N_2O$ Na ($[M + Na]^+$): 385.13113; found: 385.13157.

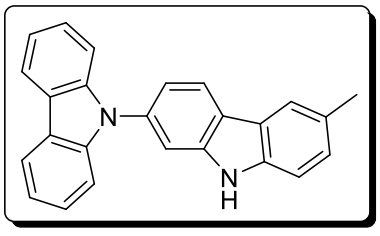


6-fluoro-9H-2,9'-bicarbazole **42e** was prepared following general procedure 18 using compound **41b** (100 mg, 0.256 mmol) and 4-fluoroaniline (27 µL, 0.281 mmol). The product was purified by flash chromatography (silica gel, ethylacetate/heptane = 1:10) to yield **42e** (56 mg, 63 %) as white solid; mp 274-276 °C; ^{1}H NMR (300 MHz, DMSO) δ = 11.52 (s, 1H), 8.40 (d, *J* = 8.3 Hz, 1H), 8.27 (d, *J* = 7.7 Hz, 2H), 8.08 (dd, *J* = 9.4, 2.6 Hz, 1H), 7.70 (d, *J* = 1.5 Hz, 1H), 7.57 (dd, *J* = 8.9, 4.4 Hz, 1H), 7.49 – 7.24 (m, 8H); ^{19}F NMR (282 MHz, DMSO) δ = -124.46 (s); ^{13}C NMR (63 MHz, DMSO) δ = 156.61 (d, *J* = 232.4 Hz), 141.35, 140.55, 136.91, 134.71, 126.17, 122.61, 122.53 (d, *J* = 10.4 Hz), 122.09, 121.55 (d, *J* = 4.2 Hz), 120.47, 119.89, 117.28, 113.61 (d, *J* = 25.1 Hz), 112.08 (d, *J* = 9.3 Hz), 109.72, 109.40, 105.98 (d, *J* = 23.8 Hz); IR (ATR, cm^{-1}): ν = 3412 (m), 3051 (w), 2918 (w), 1610 (m), 1593 (m), 1585

(m), 1487 (m), 1464 (m), 1450 (s), 1362 (m), 1336 (m), 1317 (m), 1282 (m), 1271 (m), 1248 (m), 1230 (s), 1169 (s), 1157 (s), 1122 (m), 1111 (m), 1095 (m), 1053 (m), 1024 (m), 1014 (m), 999 (m), 978 (m), 935 (m), 912 (m), 860 (m), 849 (m), 816 (s), 800 (m), 779 (m), 750 (vs), 723 (vs), 710 (s), 663 (s), 654 (m), 638 (m), 615 (m), 594 (s), 575 (m), 563 (s), 540 (m), 528 (m); GC-MS (EI, 70 eV): m/z (%) = 350 (100), 175 (11), 157 (6); HRMS (EI): calcd. for $C_{24}H_{15}FN_2$ ($[M]^+$): 350.12138; found: 350.12096.

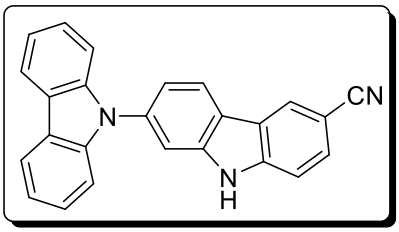


6-(tert-butyl)-9H-2,9'-bicarbazole **42g** was prepared following general procedure 18 using compound **41b** (100 mg, 0.256 mmol) and 4-(*tert*-butyl)aniline (45 µL, 0.281 mmol). The product was purified by flash chromatography (silica gel, ethylacetate/heptane = 1:10) to yield **7g** (60 mg, 60 %) as white solid; mp 238-239 °C; ^{1}H NMR (300 MHz, DMSO) δ = 11.36 (s, 1H), 8.42 (d, *J* = 8.2 Hz, 1H), 8.29 (d, *J* = 7.7 Hz, 1H), 8.24 (d, *J* = 1.5 Hz, 1H); 7.67 (d, *J* = 1.6 Hz, 1H), 7.62 – 7.40 (m, 6H), 7.38 – 7.26 (m, *J* = 11.4, 6.7, 2.9 Hz, 3H), 1.45 (s, 9H); ^{13}C NMR (75 MHz, DMSO) δ = 141.59, 140.71, 140.67, 138.62, 133.89, 126.18, 123.85, 122.62, 122.17, 121.84, 121.42, 120.50, 119.86, 117.00, 116.33, 110.65, 109.74, 109.07, 34.45, 31.87; IR (ATR, cm^{-1}): ν = 3400 (m), 3080 (w), 3051 (w), 3020 (w), 2956 (m), 2899 (w), 2866 (w), 1608 (m), 1500 (m), 1477 (m), 1462 (m), 1450 (s), 1429 (m), 1381 (w), 1363 (m), 1331 (m), 1313 (m), 1294 (m), 1279 (w), 1255 (m), 1246 (m), 1232 (s), 1207 (w), 1155 (m), 1140 (m), 1117 (w), 980 (w), 928 (w), 918 (w), 889 (w), 839 (m), 812 (s), 746 (vs), 723 (s), 702 (w), 665 (s), 634 (s), 615 (m), 565 (m); GC-MS (EI, 70 eV): m/z (%) = 388 (100), 373 (79), 332 (13), 207 (12), 187 (16), 172 (32), 41 (10); HRMS (EI): calcd. for $C_{28}H_{24}N_2$ ($[M]^+$): 388.19340; found: 388.19264.

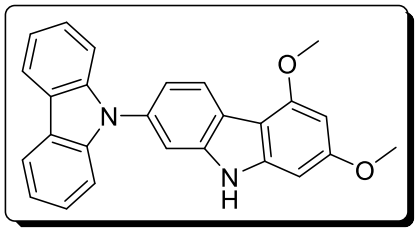


6-methyl-9H-2,9'-bicarbazole **42h** was prepared following general procedure 18 using compound **41b** (100 mg, 0.256 mmol) and *p*-toluidine (31 mg, 0.281 mmol). The product was purified by flash chromatography (silica gel, ethylacetate/heptane = 1:10) to yield **42h** (45 mg, 51 %) as white solid; mp 287-289 °C; ^{1}H NMR (250 MHz, DMSO) δ = 11.36 (s, 1H), 8.29 (dd, *J* = 14.4, 8.0 Hz, 3H), 8.01 (s, 1H), 7.64 (d, *J* = 1.6 Hz, 1H), 7.45 (dd, *J* = 8.4, 3.6 Hz, 5H), 7.40 – 7.20 (m, 5H), 2.49 (s, 3H); ^{13}C NMR (63 MHz, DMSO) δ = 140.70, 140.64, 138.77, 134.06, 127.79, 127.38, 126.23, 122.65, 122.27, 121.75, 121.44, 120.53, 120.17, 119.91,

117.11, 110.95, 109.81, 109.15, 21.18; IR (ATR, cm^{-1}): ν = 3417 (m), 3047 (w), 2916 (w), 2850 (w), 1608 (m), 1595 (m), 1504 (m), 1489 (m), 1477 (m), 1450 (s), 1377 (m), 1362 (m), 1335 (m), 1315 (m), 1304 (m), 1294 (m), 1277 (m), 1244 (m), 1230 (s), 1174 (m), 1155 (m), 1146 (m), 1134 (m), 1120 (m), 1095 (m), 1039 (m), 1024 (m), 980 (m), 935 (m), 916 (m), 876 (m), 860 (m), 847 (m), 818 (m), 804 (s), 750 (vs), 723 (vs), 663 (s), 654 (m), 638 (m), 615 (m), 584 (s), 563 (s), 532 (m); GC-MS (EI, 70 eV): m/z (%) = 346 (100), 330 (9), 173 (9); HRMS (EI): calcd. for $C_{25}H_{18}N_2$ ($[M]^+$): 346.14645; found: 346.14639.



9H-[2,9'-bicarbazole]-6-carbonitrile **42i** was prepared following general procedure 18 using compound **41b** (100 mg, 0.256 mmol) and 4-aminobenzonitrile (33 mg, 0.281 mmol). The product was purified by flash chromatography (silica gel, ethylacetate/heptane = 1:5) to yield **42i** (19 mg, 21 %) as white solid; mp 297-299 °C; ^{1}H NMR (300 MHz, DMSO) δ = 12.06 (s, 1H), 8.83 (d, *J* = 1.1 Hz, 1H), 8.52 (d, *J* = 8.3 Hz, 1H), 8.27 (d, *J* = 7.7 Hz, 2H), 7.85 – 7.77 (m, 2H), 7.77 – 7.69 (m, 1H), 7.55 – 7.38 (m, 5H), 7.38 – 7.25 (m, 2H); ^{13}C NMR (75 MHz, DMSO) δ = 142.47, 141.05, 140.52, 135.54, 128.98, 126.29, 125.91, 122.74, 122.49, 122.37, 121.00, 120.56, 120.48, 120.08, 118.74, 112.35, 109.86, 109.77, 100.84; IR (ATR, cm^{-1}): ν = 3284 (w), 3059 (w), 2918 (w), 2848 (w), 2229 (m), 1603 (s), 1477 (s), 1450 (s), 1435 (m), 1396 (m), 1365 (m), 1335 (s), 1319 (m), 1308 (m), 1288 (m), 1254 (s), 1228 (s), 1200 (m), 1155 (m), 1146 (m), 1132 (m), 1120 (m), 1097 (m), 1016 (m), 1003 (m), 914 (m), 899 (m), 885 (m), 847 (m), 816 (s), 810 (s), 748 (vs), 723 (s), 663 (m), 629 (s), 615 (s), 592 (m), 575 (m), 563 (m), 544 (m), 528 (m); GC-MS (EI, 70 eV): m/z (%) = 357 (100), 281 (9), 253 (8), 207 (29), 191 (15), 178 (48), 164 (15), 97 (10); HRMS (EI): calcd. for $C_{25}H_{15}N_3$ ($[M]^+$): 357.12605; found: 357.12555.



5,7-dimethoxy-9H-2,9'-bicarbazole **42j** was prepared following general procedure 18 using compound **41b** (100 mg, 0.256 mmol) and 3,5-dimethoxyaniline (43 mg, 0.281 mmol). The product was purified by flash chromatography (silica gel, ethylacetate/heptane = 1:4) to yield **42j** (47 mg, 47 %) as white solid; mp 282-284 °C; ^{1}H NMR (300 MHz, DMSO) δ = 10.51 (s, 1H), 7.42 – 7.35 (m, 3H), 6.73 (d, *J* = 1.6 Hz, 1H), 6.66 – 6.51 (m, 4H), 6.48 – 6.37 (m, 3H), 5.82 (d, *J* =

1.8 Hz, 1H), 5.55 (d, *J* = 1.8 Hz, 1H), 3.18 (s, 3H), 3.02 (s, 3H); ^{13}C NMR (63 MHz, DMSO) δ = 160.12, 156.02, 142.54, 140.72, 139.47, 132.01, 126.09, 122.48, 121.97, 121.46, 120.42, 119.72, 117.48, 109.68, 108.47, 105.32, 90.99, 87.21, 55.48, 55.42; IR (ATR, cm^{-1}): ν = 3398 (s), 3003 (w), 2968 (w), 2933 (m), 2918 (m), 2839 (m), 1628 (m), 1606 (s), 1585 (s), 1574 (m), 1514 (m), 1502 (m), 1477 (m), 1446 (s), 1427 (s), 1360 (m), 1333 (m), 1315 (s), 1306 (s), 1279 (s), 1234 (s), 1223 (m), 1205 (s), 1198 (s), 1147 (s), 1124 (s), 1117 (s), 1095 (m), 1049 (s), 1020 (m), 1011 (m), 997 (m), 991 (m), 980 (m), 947 (m), 933 (m), 920 (m), 874 (m), 850 (m), 820 (m), 804 (vs), 789 (m), 756 (vs), 744 (s), 727 (vs), 690 (m), 665 (s), 644 (m), 633 (m), 615 (m), 598 (m), 582 (m), 569 (m), 550 (m); GC-MS (EI, 70 eV): m/z (%) = 392 (100), 377 (17), 349 (6), 334 (22), 196 (10); HRMS (ESI): calcd. for $C_{26}H_{21}N_2O_2$ ($[M + H]^+$): 393.15975; found: 393.15893; calcd. for $C_{26}H_{21}N_2O_2Na$ ($[M + Na]^+$): 415.1417; found: 415.14089.

8.6 CRYSTALLOGRAPHY REPORTS

8.6.1 Crystal data and structure refinement for compound 2p

Identification code	**av_ht1h088**	
Empirical formula	$C_{30}H_{38}N_2S$	
Formula weight	458.68	
Temperature	173 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1/c$	
Space group (Hall)	-P 2ybc	
Unit cell dimensions	a = 26.9277 (11) Å	α = 90.00º
	b = 8.3141 (4) Å	β = 104.439 (2)°
	c = 24.3306 (10) Å	γ = 90.00º
Volume	5275.1 (4) Å^3	
Z	8	
Density (calculated)	1.155 Mg m^{-3}	
Absorption coefficient (mm^{-1})	0.14 mm^{-1}	
F(000)	1984	
Crystal size	0.80 × 0.12 × 0.02 mm	
Θrange for data collection	5.3–55.3°	
Index ranges	h = -36→36, k = -11→11, l = -33→33	
Reflections collected	70216	
Independent reflections	14038, R_{int} = 0.094	
Absorption correction	multi-scan	
Max. and min. transmission	T_{min} = 0.895, T_{max} = 0.997	
Refinement method	Full-matrix least-squares on F2	
Data/ restraints / parameters	14038/0/599	
Goodness-of-fit on F2	0.98	

Final R indices [I>2σ(I)]	$R[F^2 > 2\sigma(F^2)] = 0.054$, $wR(F^2) = 0.102$
R indices (all data)	$R[F^2 > 2\sigma(F^2)] = 0.127$, $wR(F^2) = 0.120$
Largest diff. peak and hole	0.26 e Å^{-3} and -0.32 e Å^{-3}

8.6.2 Crystal data and structure refinement for compound 2i

Identification code	**av_ht1h145**	
Empirical formula	$C_{36}H_{34}N_2S \cdot C_6H_{12}$	
Formula weight	610.87	
Temperature	173 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	*C*2/*c*	
Space group (Hall)	-C 2yc	
Unit cell dimensions	*a* = 10.4817 (8) Å	α = 90.00º
	b = 24.3518 (19) Å	β = 98.238(5)º
	c = 13.6216 (11) Å	γ = 90.00º
Volume	3441.0 (5) Å^3	
Z	4	
Density (calculated)	1.179 Mg m^{-3}	
Absorption coefficient (mm^{-1})	0.13 mm^{-1}	
F(000)	1312	
Crystal size	0.34 × 0.20 × 0.05 mm	
Θrange for data collection	4.5–43.8°	
Index ranges	*h* = -13→13, *k* = -31→27, *l* = -15→17	
Reflections collected	12582	
Independent reflections	3744	
Absorption correction	multi-scan	
Max. and min. transmission	T_{min} = 0.959, T_{max} = 0.994	

Refinement method	Full-matrix least-squares on F2
Data/ restraints / parameters	3744/15/227
Goodness-of-fit on F2	1.01
Final R indices [I>2σ(I)]	$R[F^2 > 2\sigma(F^2)] = 0.057$, $wR(F^2) = 0.120$
R indices (all data)	$R[F^2 > 2\sigma(F^2)] = 0.120$, $wR(F^2) = 0.129$
Largest diff. peak and hole	0.36 e Å^{-3} and -0.27 e Å^{-3}

8.6.3 Crystal data and structure refinement for compound 2k

Identification code	**ch_ht1h142**	
Empirical formula	$C_{36}H_{36}N_4S$	
Formula weight	556.75	
Temperature	173 K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	$P\bar{1}$	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 16.4194 (6) Å	α = 84.990 (2)°
	b = 16.7949 (6) Å	β = 82.485 (2)°
	c = 21.7769 (7) Å	γ = 88.123 (2)°
Volume	5929.5 (4) Å^3	
Z	8	
Density (calculated)	1.247 Mg m^{-3}	
Absorption coefficient (mm^{-1})	0.14 mm^{-1}	
F(000)	2368	
Crystal size	0.23 × 0.18 × 0.12 mm	
Θrange for data collection	4.7–51.2°	
Index ranges	h = -21→22, k = -22→22, l = -29→26	
Reflections collected	141031	

Independent reflections	31470
Absorption correction	multi-scan
Max. and min. transmission	T_{min} = 0.968, T_{max} = 0.983
Refinement method	Full-matrix least-squares on F2
Data/ restraints / parameters	31470/0/1520
Goodness-of-fit on F2	1.01
Final R indices [I>2σ(I)]	$R[F^2 > 2\sigma(F^2)]$ = 0.050, $wR(F^2)$ = 0.050
R indices (all data)	$R[F^2 > 2\sigma(F^2)]$ = 0.098, $wR(F^2)$ = 0.119
Largest diff. peak and hole	0.25 e Å^{-3} and -0.35 e Å^{-3}

8.6.4 Crystal data and structure refinement for compound 15b

Identification code	**is_1h003**	
Empirical formula	$C_{25}H_{24}N_2$	
Formula weight	352.46	
Temperature (K)	173 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1/c$	
Space group (Hall)	-P 2ybc	
Unit cell dimensions	a = 9.8957 (3) Å	α = 90.00º
	b = 23.4982 (7) Å	β = 103.811 (2)°
	c = 8.5844 (3) Å	γ = 90.00º
Volume	1938.43 (11) Å^3	
Z	4	
Density (calculated)	1.208 Mg m^{-3}	
Absorption coefficient (mm^{-1})	0.07 mm^{-1}	
F(000)	752	
Crystal size	0.38 × 0.16 × 0.14 mm	

Θrange for data collection	5.5–60.0°
Index ranges	h = -13→13, k = -32→32, l = -12→12
Reflections collected	27546
Independent reflections	5629
Absorption correction	multi-scan
Max. and min. transmission	T_{min} = 0.974, T_{max} = 0.990
Refinement method	Full-matrix least-squares on F2
Data/ restraints / parameters	5629/80/294
Goodness-of-fit on F2	1.03
Final R indices [I>2σ(I)]	$R[F^2 > 2\sigma(F^2)]$ = 0.051, $wR(F^2)$ = 0.051
R indices (all data)	$R[F^2 > 2\sigma(F^2)]$ = 0.097, $wR(F^2)$ = 0.133
Largest diff. peak and hole	0.24 e Å^{-3} and -0.26 e Å^{-3}

8.6.5 Crystal data and structure refinement for compound 18d

Identification code	**av_ht3h114**	
Empirical formula	$C_{17}H_{11}FN_2$	
Formula weight	262.28	
Temperature	173 K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	$P\bar{1}$	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 6.2637 (4) Å	α = 78.235 (4)°
	b = 9.6026 (6) Å	β = 81.016 (4)°
	c = 11.1057 (8) Å	γ = 74.565 (4)°
Volume	626.68 (7) Å^3	
Z	2	
Density (calculated)	1.390 Mg m^{-3}	

Absorption coefficient (mm^{-1})	0.09 mm^{-1}
F(000)	272
Crystal size	0.16 × 0.13 × 0.09 mm
Θrange for data collection	2.2–24.4°
Index ranges	h = -8→8, k = -12→12, l = 0→14
Reflections collected	2973
Independent reflections	2973
Absorption correction	multi-scan
Max. and min. transmission	T_{min} = 0.672, T_{max} = 0.746
Refinement method	Full-matrix least-squares on F2
Data/ restraints / parameters	2973 /30/159
Goodness-of-fit on F^2	1.03
Final R indices [I>2σ(I)]	$R[F^2 > 2\sigma(F^2)]$ = 0.060, $wR(F^2)$ = 0.118
R indices (all data)	$R[F^2 > 2\sigma(F^2)]$ = 0.111, $wR(F^2)$ = 0.139
Largest diff. peak and hole	0.25 e $Å^{-3}$ and -0.21 e $Å^{-3}$

8.6.6 Crystal data and structure refinement for compound 21b

Identification code	**is_jj2h210**	
Empirical formula	$C_{17}H_{11}FN_2$	
Formula weight	262.28	
Temperature	173 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	*C*2/*c*	
Space group (Hall)	-C 2yc	
Unit cell dimensions	a = 13.9224 (7) Å	α = 90.00º
	b = 11.0347 (5) Å	β = 94.077 (2)°
	c = 16.4227 (9) Å	γ = 90.00º

Volume	2516.6 (2) Å^3
Z	8
Density (calculated)	1.384 Mg m^{-3}
Absorption coefficient (mm^{-1})	0.09 mm^{-1}
F(000)	1088
Crystal size	0.66 × 0.23 × 0.19 mm
Θrange for data collection	4.7–60.5°
Index ranges	h = -18→17, k = -14→15, l = -17→21
Reflections collected	15409
Independent reflections	3322, R_{int} = 0.033
Absorption correction	multi-scan
Max. and min. transmission	T_{min} = 0.941, T_{max} = 0.983
Refinement method	Full-matrix least-squares on F2
Data/ restraints / parameters	3322/0/218
Goodness-of-fit on F^2	1.04
Final R indices [I>2σ(I)]	$R[F^2 > 2\sigma(F^2)]$ = 0.043, $wR(F^2)$ = 0.101
R indices (all data)	$R[F^2 > 2\sigma(F^2)]$ = 0.077, $wR(F^2)$ = 0.116
Largest diff. peak and hole	0.15 e Å^{-3} and -0.20 e Å^{-3}

8.6.7 Crystal data and structure refinement for compound 25g

Identification code	**is_ht2h121p**
Empirical formula	$C_{33}H_{28}ClN_3O_4 \cdot 1.5(CHCl_3)$
Formula weight	745.09
Temperature	173 K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group (H.-M.)	$P\bar{1}$
Space group (Hall)	-P 1

Unit cell dimensions	a = 12.1069 (2) Å	α = 67.635 (1)°
	b = 12.5752 (2) Å	β = 64.074 (1)°
	c = 13.7247 (3) Å	γ = 81.170 (1)°
Volume	1737.68 (6) Å^3	
Z	2	
Density (calculated)	1.424 Mg m^{-3}	
Absorption coefficient (mm^{-1})	0.50 mm^{-1}	
F(000)	766	
Crystal size	0.22 × 0.17 × 0.15 mm	
Θrange for data collection	6.0–51.1°	
Index ranges	h = -17→15, k = -17→17, l = -19→19	
Reflections collected	48893	
Independent reflections	10557, R_{int} = 0.045	
Absorption correction	multi-scan	
Max. and min. transmission	T_{min} = 0.898, T_{max} = 0.929	
Refinement method	Full-matrix least-squares on F2	
Data/ restraints / parameters	10557/0/374	
Goodness-of-fit on F^2	0.93	
Final R indices [I>2σ(I)]	$R[F^2 > 2\sigma(F^2)]$ = 0.055, $wR(F^2)$ = 0.124	
R indices (all data)	$R[F^2 > 2\sigma(F^2)]$ = 0.104, $wR(F^2)$ = 0.138	
Largest diff. peak and hole	0.30 e Å^{-3}and -0.29 e Å^{-3}	

8.6.8 Crystal data and structure refinement for compound 25j

Identification code	**is_ht2h167**
Empirical formula	$C_{23}H_{23}N_3 \cdot 0.043(CHCl_3) \cdot 0.458(C_6H_{12})$
Formula weight	385.00
Temperature	173 K
Wavelength	0.71073 Å

Crystal system	Triclinic	
Space group (H.-M.)	$P\bar{1}$	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 9.7236 (2) Å	α = 92.999 (1)°
	b = 12.5815 (2) Å	β = 99.527 (1)°
	c = 17.7524 (3) Å	γ = 96.347 (1)°
Volume	2123.17 (7) Å^3	
Z	4	
Density (calculated)	1.204 Mg m^{-3}	
Absorption coefficient (mm^{-1})	0.09 mm^{-1}	
F(000)	826	
Crystal size	0.22 × 0.19 × 0.08 mm	
Θrange for data collection	5.1–60.5°	
Index ranges	h = -12→12, k = -16→16, l = -23→23	
Reflections collected	57048	
Independent reflections	10170, R_{int} = 0.037	
Absorption correction	multi-scan	
Max. and min. transmission	T_{min} = 0.981, T_{max} = 0.993	
Refinement method	Full-matrix least-squares on F2	
Data/ restraints / parameters	10170/3/560	
Goodness-of-fit on F^2	1.01	
Final R indices [I>2σ(I)]	$R[F^2 > 2\sigma(F^2)]$ = 0.056, $wR(F^2)$ = 0.127	
R indices (all data)	$R[F^2 > 2\sigma(F^2)]$ = 0.097, $wR(F^2)$ = 0.151	
Largest diff. peak and hole	0.48 e Å^{-3} and -0.43 e Å^{-3}	

8.6.9 Crystal data and structure refinement for compound 35e

Identification code	**is_ht2h182**
Empirical formula	$C_{21}H_{15}N_3O$

Formula weight	325.36	
Temperature	173 K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	$P\bar{1}$	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 5.9259 (3) Å	α = 79.323 (3)°
	b = 11.0893 (6) Å	β = 78.333 (3)°
	c = 12.3340 (6) Å	γ = 86.450 (3)°
Volume	779.78 (7) Å^3	
Z	2	
Density (calculated)	1.386 Mg m^{-3}	
Absorption coefficient (mm^{-1})	0.09 mm^{-1}	
F(000)	340	
Crystal size	0.43 × 0.07 × 0.03 mm	
Θ range for data collection	6.9–45.1°	
Index ranges	h = -7→8, k = -15→15, l = -16→16	
Reflections collected	18870	
Independent reflections	4102, R_{int} = 0.070	
Absorption correction	multi-scan	
Max. and min. transmission	T_{min} = 0.963, T_{max} = 0.997	
Refinement method	Full-matrix least-squares on F2	
Data/ restraints / parameters	4102/0/228	
Goodness-of-fit on F^2	1.01	
Final R indices [I>2σ(I)]	$R[F^2 > 2\sigma(F^2)]$ = 0.058, $wR(F^2)$ = 0.101	
R indices (all data)	$R[F^2 > 2\sigma(F^2)]$ = 0.144, $wR(F^2)$ = 0.132	
Largest diff. peak and hole	0.28 e Å^{-3} and -0.23 e Å^{-3}	

8.6.10 Crystal data and structure refinement for compound 35r

Identification code	**is_ht3h053**	
Empirical formula	$C_{23}H_{19}N_3$	
Formula weight	337.41	
Temperature	173 K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	$P\bar{1}$	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 7.3149 (3) Å	α = 72.116 (2)°
	b = 15.0792 (8) Å	β = 88.582 (2)°
	c = 16.8977 (8) Å	γ = 77.750 (2)°
Volume	V = 1731.78 (14) Å^3	
Z	4	
Density (calculated)	1.294 Mg m^{-3}	
Absorption coefficient (mm^{-1})	0.08 mm^{-1}	
F(000)	712	
Crystal size	0.99 × 0.23 × 0.05 mm	
Θ range for data collection	4.4–50.2°	
Index ranges	h = -10→10, k = -20→20, l = -23→23	
Reflections collected	44254	
Independent reflections	9574, R_{int} = 0.043	
Absorption correction	multi-scan	
Max. and min. transmission	T_{min} = 0.927, T_{max} = 0.996	
Refinement method	Full-matrix least-squares on F2	
Data/ restraints / parameters	9574/18/482	
Goodness-of-fit on F^2	1.02	
Final R indices [I>2σ(I)]	$R[F^2 > 2\sigma(F^2)]$ = 0.053, $wR(F^2)$ = 0.117	
R indices (all data)	$R[F^2 > 2\sigma(F^2)]$ = 0.110, $wR(F^2)$ = 0.145	

Largest diff. peak and hole	0.37 e Å^{-3} and -0.26 e Å^{-3}

8.6.11 Crystal data and structure refinement for compound 38b

Identification code	**is_dh1h017**	
Empirical formula	$C_{24}H_{15}N_3O_2$	
Formula weight	377.39	
Temperature	173 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1/c$	
Space group (Hall)	-P 2ybc	
Unit cell dimensions	a = 12.7311 (10) Å	α = 90.00º
	b = 15.7373 (13) Å	β = 104.025 (2)°
	c = 9.2462 (7) Å	γ = 90.00º
Volume	1797.3 (2) Å^3	
Z	4	
Density (calculated)	1.395 Mg m^{-3}	
Absorption coefficient (mm^{-1})	0.09 mm^{-1}	
F(000)	784	
Crystal size	0.53 × 0.09 × 0.03 mm	
Θ range for data collection	5.2–53.3°	
Index ranges	h = -16→17, k = -21→21, l = -10→12	
Reflections collected	19875	
Independent reflections	5202, R_{int} = 0.058	
Absorption correction	multi-scan	
Max. and min. transmission	T_{min} = 0.953, T_{max} = 0.997	
Refinement method	Full-matrix least-squares on F2	
Data/ restraints / parameters	5202/0/266	

Goodness-of-fit on F^2	1.01
Final R indices [I>2σ(I)]	$R[F^2 > 2\sigma(F^2)] = 0.055$, $wR(F^2) = 0.095$
R indices (all data)	$R[F^2 > 2\sigma(F^2)] = 0.130$, $wR(F^2) = 0.122$
Largest diff. peak and hole	0.21 e Å^{-3} and -0.25 e Å^{-3}

8.6.12 Crystal data and structure refinement for compound 42c

Identification code	**is_t12**	
Empirical formula	$C_{25}H_{18}N_2O$	
Formula weight	362.41	
Temperature	173 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1/c$	
Space group (Hall)	-P 2ybc	
Unit cell dimensions	a = 12.6024 (5) Å	α = 90.00º
	b = 7.6803 (2) Å	β = 102.443 (2)°
	c = 19.0480 (7) Å	γ = 90.00º
Volume	1800.35 (11) Å^3	
Z	4	
Density (calculated)	1.337 Mg m^{-3}	
Absorption coefficient (mm^{-1})	0.08 mm^{-1}	
F(000)	760	
Crystal size	0.24 × 0.21 × 0.20 mm	
Θ range for data collection	4.9–62.9°	
Index ranges	h = -17→19, k = -9→11, l = -25→28	
Reflections collected	25408	
Independent reflections	6521	
Absorption correction	multi-scan	

Max. and min. transmission	T_{min} = 0.981, T_{max} = 0.984
Refinement method	Full-matrix least-squares on F2
Data/ restraints / parameters	6521/0/258
Goodness-of-fit on F^2	1.03
Final R indices [I>2σ(I)]	$R[F^2 > 2\sigma(F^2)]$ = 0.051, $wR(F^2)$ = 0.116
R indices (all data)	$R[F^2 > 2\sigma(F^2)]$ = 0.085, $wR(F^2)$ = 0.135
Largest diff. peak and hole	0.34 e Å^{-3} and -0.30 e Å^{-3}

8.7 Calculations

B3LYP/6-31G* optimized geometries. The cartesian coordinates are given in Å.

Compound 25a

C	-1.126407	-1.767076	-0.042458	**H**	1.916335	1.964987	-1.790622
C	-1.170014	-0.337161	-0.041114	**C**	3.849912	4.069411	0.065808
C	-0.000046	0.420361	-0.027618	**H**	4.918466	3.501185	1.851519
C	1.169955	-0.337165	-0.040918	**H**	2.679072	4.3279	-1.727224
C	1.126313	-1.767073	-0.042269	**H**	4.195843	5.098944	0.087135
H	-0.000038	1.503976	-0.001474	**C**	-4.711415	-1.172356	-0.01231
N	-0.000057	-2.48438	-0.040317	**C**	-3.079173	-3.500412	-0.029725
N	-2.504063	0.070485	-0.016178	**C**	-4.467278	-3.60396	-0.025048
N	2.504026	0.07046	-0.015648	**C**	-5.270104	-2.450125	-0.020251
C	-2.958994	1.416375	0.011063	**H**	-5.339614	-0.287781	-0.018493
C	-2.557971	2.313822	-0.986968	**H**	-2.446068	-4.382541	-0.043144
C	-3.807778	1.851371	1.037091	**H**	-4.93702	-4.58346	-0.029493
C	-2.995984	3.637433	-0.950014	**H**	-6.352086	-2.551733	-0.025641
H	-1.91783	1.965043	-1.791477	**C**	4.711347	-1.172567	-0.01184
C	-4.257111	3.171451	1.055369	**C**	5.269966	-2.450354	-0.020017
H	-4.100473	1.155746	1.817295	**C**	4.467061	-3.604137	-0.024926
C	-3.849589	4.069509	0.066818	**C**	3.078974	-3.500491	-0.029537
H	-2.680246	4.328076	-1.727205	**H**	5.339594	-0.288034	-0.017928
H	-4.916708	3.501192	1.853377	**H**	6.351939	-2.552038	-0.025501
H	-4.195421	5.099067	0.088529	**H**	4.936719	-4.583677	-0.029589
C	2.959044	1.416312	0.011044	**H**	2.445844	-4.382603	-0.043002
C	3.808749	1.851357	1.036316	**C**	-2.497844	-2.228837	-0.022272
C	2.557217	2.313731	-0.986699	**C**	-3.31832	-1.075067	-0.004205
C	4.258204	3.171394	1.054082	**C**	3.318248	-1.075162	-0.00368
H	4.102033	1.155801	1.816351	**C**	2.497704	-2.228886	-0.021897
C	2.995385	3.637302	-0.950226				

Compound 25b

C	-1.12618200	-3.16257800	-0.03348800	**C**	5.27107200	-3.84157600	0.00164600
C	-1.16974800	-1.73265300	-0.05653400	**C**	4.46925500	-4.99609900	0.01645600
C	0.00007200	-0.97489600	-0.05719700	**C**	3.08098300	-4.89395700	0.00918700
C	1.16997200	-1.73252800	-0.05680300	**H**	5.33797500	-1.67911300	-0.03429100
C	1.12655100	-3.16245700	-0.03374400	**H**	6.35318500	-3.94235700	-0.00110000
H	0.00000800	0.10903400	-0.05198200	**H**	4.93989800	-5.97512800	0.02950600
N	0.00022500	-3.87986400	-0.01957300	**H**	2.44883500	-5.77690500	0.01109800
N	-2.50331500	-1.32428700	-0.03903800	**C**	-2.49783000	-3.62335000	-0.00540500

N	2.50351400	-1.32403200	-0.03964400	**C**	-3.31755400	-2.46861500	-0.00739400
C	-2.95754200	0.02208500	-0.03226900	**C**	3.31786400	-2.46828800	-0.00813800
C	-2.56942300	0.90810800	-1.03995200	**C**	2.49824900	-3.62309800	-0.00596700
C	-3.79819500	0.48374900	0.98834800	**C**	-4.36150900	4.16749800	0.03378500
C	-3.00646200	2.23383000	-1.01990100	**C**	4.36098900	4.16798200	0.03467000
H	-1.93466100	0.55546900	-1.84735300	**C**	-3.84208800	5.00684200	-1.14879200
C	-4.24114700	1.80265500	0.98441100	**H**	-2.74784000	5.06857700	-1.15639100
H	-4.09224700	-0.19175100	1.78581900	**H**	-4.16969900	4.60116900	-2.11278600
C	-3.85517600	2.71474300	-0.01370400	**H**	-4.22896900	6.02915100	-1.07309400
H	-2.68165400	2.88972900	-1.81971900	**C**	-3.88442300	4.83538900	1.34568100
H	-4.89296100	2.12790000	1.79020000	**H**	-4.24429800	5.87013500	1.39892300
C	2.95759200	0.02238200	-0.03251800	**H**	-4.25612900	4.30821600	2.23054300
C	3.79860200	0.48375100	0.98794100	**H**	-2.79005600	4.85263100	1.40215900
C	2.56895800	0.90877000	-1.03968600	**C**	-5.90837400	4.17725800	-0.01134700
C	4.24137600	1.80271700	0.98435800	**H**	-6.28289200	5.20739000	0.02612000
H	4.09307300	-0.19201900	1.78502800	**H**	-6.27733400	3.71415700	-0.93351400
C	3.00581700	2.23454700	-1.01926400	**H**	-6.34531300	3.63409000	0.83317300
H	1.93394100	0.55638200	-1.84699600	**C**	3.88462100	4.83514400	1.34719900
C	3.85487000	2.71516900	-0.01321500	**H**	4.25703400	4.30763700	2.23156500
H	4.89348200	2.12770600	1.79001300	**H**	4.24429100	5.86994800	1.40070200
H	2.68060100	2.89072700	-1.81868700	**H**	2.79028700	4.85210800	1.40441200
C	-4.71078200	-2.56489000	-0.01224900	**C**	5.90782400	4.17806500	-0.01145400
C	-3.08045300	-4.89425900	0.00990800	**H**	6.27628000	3.71541100	-0.93404600
C	-4.46871500	-4.99652000	0.01751300	**H**	6.28216500	5.20825500	0.02619100
C	-5.27063700	-3.84206700	0.00288800	**H**	6.34541300	3.63463800	0.83256200
H	-5.33773300	-1.67960500	-0.03303900	**C**	3.84065100	5.00780200	-1.14716100
H	-2.44823200	-5.77715500	0.01168300	**H**	4.16752400	4.60251300	-2.11156500
H	-4.93926800	-5.97559000	0.03069000	**H**	2.74639600	5.06952700	-1.15389300
H	-6.35274200	-3.94294500	0.00041300	**H**	4.22757900	6.03008500	-1.07134800
C	4.71110100	-2.56444800	-0.01334300				

Compound 25c

C	-1.12631400	-2.31520400	-0.09049500	**H**	-6.35254800	-3.09719400	-0.08960100
C	-1.16997500	-0.88538500	-0.06449700	**C**	4.71107900	-1.71895700	-0.05203600
C	0.00002800	-0.12845800	-0.03849400	**C**	5.27066200	-2.99593700	-0.08280600
C	1.17005800	-0.88533300	-0.06464600	**C**	4.46859900	-4.15012700	-0.10744000
C	1.12647100	-2.31515600	-0.09065400	**C**	3.08040000	-4.04725200	-0.10935300
H	0.00001700	0.95445500	0.00424900	**H**	5.33788300	-0.83347100	-0.04219200
N	0.00009300	-3.03260900	-0.10098500	**H**	6.35276300	-3.09680700	-0.09046000
N	-2.50348200	-0.47763000	-0.03301300	**H**	4.93893300	-5.12915700	-0.12933900
N	2.50354500	-0.47751000	-0.03342700	**H**	2.44783400	-4.92945700	-0.13768000
C	-2.95727700	0.86929700	0.01649300	**C**	-2.49791900	-2.77657200	-0.07896300
C	-2.55585700	1.77755700	-0.96794900	**C**	-3.31772500	-1.62239400	-0.04116300

C	-3.80082100	1.28503000	1.05270000	**C**	3.31784500	-1.62221900	-0.04165200
C	-2.98191500	3.10953200	-0.91889300	**C**	2.49810400	-2.77644800	-0.07935200
H	-1.91899400	1.43564100	-1.77897600	**H**	4.17797900	4.53513900	0.15956600
C	-4.25877500	2.60504500	1.10587100	**H**	-4.17837000	4.53494200	0.15833800
H	-4.08833400	0.57339900	1.82129100	**C**	5.20079900	3.04818500	2.20197500
C	-3.83482200	3.50300800	0.11816000	**H**	6.24850900	2.92350500	1.89737400
C	2.95725500	0.86944300	0.01651200	**H**	5.05831300	4.10537100	2.44947800
C	3.80052400	1.28497300	1.05301500	**H**	5.05648000	2.46292600	3.11603000
C	2.55599200	1.77789800	-0.96781300	**C**	2.51788500	4.10182100	-1.96020500
C	4.25833800	2.60502300	1.10663000	**H**	2.42832300	3.63479100	-2.94700100
H	4.08793200	0.57315500	1.82147500	**H**	1.53166200	4.51313800	-1.70538800
C	2.98192000	3.10989900	-0.91832800	**H**	3.21018700	4.94547500	-2.04639000
H	1.91933700	1.43611100	-1.77905800	**C**	-2.51770200	4.10123800	-1.96089700
C	3.83453300	3.50318600	0.11904200	**H**	-3.21016200	4.94470900	-2.04761300
C	-4.71095300	-1.71923500	-0.05139000	**H**	-1.53167400	4.51286100	-1.70581900
C	-3.08012600	-4.04741800	-0.10886400	**H**	-2.42764200	3.63392300	-2.94751200
C	-4.46831700	-4.15039300	-0.10677400	**C**	-5.20152500	3.04842200	2.20088100
C	-5.27045200	-2.99625500	-0.08207300	**H**	-5.05820900	4.10532900	2.44911900
H	-5.33783000	-0.83380300	-0.04150500	**H**	-6.24915400	2.92493400	1.89552000
H	-2.44749500	-4.92957300	-0.13726500	**H**	-5.05833900	2.46247800	3.11467000
H	-4.93858700	-5.12945500	-0.12859300				

Compound 25d

C	-1.126454	-2.139354	-0.040529	**C**	3.842045	3.671628	0.044935
C	-1.169574	-0.709292	-0.046332	**H**	4.845848	3.183584	1.877286
C	-0.000003	0.04879	-0.038409	**H**	2.770109	3.949823	-1.792429
C	1.169562	-0.7093	-0.046301	**C**	-4.711221	-1.541264	-0.012331
C	1.126432	-2.139361	-0.0405	**C**	-3.081273	-3.871463	-0.015769
H	-0.000001	1.132887	-0.019334	**C**	-4.469579	-3.973008	-0.008256
N	-0.000013	-2.856486	-0.035187	**C**	-5.271421	-2.818462	-0.009852
N	-2.503238	-0.301662	-0.026575	**H**	-5.33835	-0.655741	-0.022644
N	2.50323	-0.30168	-0.026497	**H**	-2.449601	-4.754657	-0.022956
C	-2.958245	1.043986	-0.00315	**H**	-4.940444	-4.951921	-0.004829
C	-2.602264	1.926072	-1.031982	**H**	-6.353448	-2.919137	-0.011909
C	-3.764103	1.496923	1.050035	**C**	4.711203	-1.541303	-0.012206
C	-3.034941	3.250845	-1.006033	**C**	5.271391	-2.818506	-0.009702
H	-1.994853	1.566518	-1.856536	**C**	4.469539	-3.973045	-0.008114
C	-4.219561	2.813814	1.07236	**C**	3.081234	-3.871486	-0.015662
H	-4.025757	0.814992	1.852681	**H**	5.338342	-0.655787	-0.022511
C	-3.842001	3.671659	0.045105	**H**	6.353417	-2.91919	-0.011731
H	-2.770114	3.949936	-1.792274	**H**	4.940395	-4.951962	-0.004666
H	-4.845759	3.183534	1.87746	**H**	2.449552	-4.754674	-0.02286
C	2.95825	1.043965	-0.003158	**C**	-2.498298	-2.600566	-0.018439

C	3.764144	1.496946	1.04998	**C**	-3.318235	-1.446501	-0.008649
C	2.602252	1.926002	-1.032026	**C**	3.318218	-1.446526	-0.00856
C	4.219622	2.813831	1.072223	**C**	2.498272	-2.600584	-0.018363
H	4.025808	0.815055	1.852657	**F**	-4.271704	4.949344	0.068682
C	3.034948	3.25077	-1.006158	**F**	4.271769	4.949308	0.068431
H	1.994813	1.566416	-1.856545				

Compound 25g

C	-1.12665200	2.74813700	0.07960200	**H**	-6.35111300	3.53510200	-0.01263300
C	-1.17047500	1.31766400	0.04874000	**C**	4.70949300	2.15698900	-0.02211000
C	-0.00017500	0.55964500	0.02566900	**C**	5.26809900	3.43446300	0.00156400
C	1.16991300	1.31801300	0.04812900	**C**	4.46541000	4.58780900	0.04803900
C	1.12572100	2.74847300	0.07905400	**C**	3.07759900	4.48401200	0.07630300
H	-0.00000700	-0.52366900	-0.02042000	**H**	5.33507900	1.27123300	-0.05620300
N	-0.00057000	3.46538800	0.09530700	**H**	6.34995300	3.53672000	-0.01593600
N	-2.50442400	0.91413800	0.00303000	**H**	4.93526900	5.56722600	0.06310200
N	2.50391700	0.91485200	0.00167300	**H**	2.44499900	5.36572500	0.11692100
C	-2.96998900	-0.42917300	-0.06725100	**C**	-2.49712400	3.21183100	0.05505900
C	-2.67653800	-1.31117100	0.98702500	**C**	-3.31742800	2.05940400	0.00020000
C	-3.71557900	-0.83897000	-1.16572200	**C**	3.31663300	2.06030300	-0.00139700
C	-3.15064900	-2.62178200	0.91328900	**C**	2.49606000	3.21252900	0.05387200
H	-2.11803400	-0.94727600	1.83956300	**O**	-4.91475100	-2.47396100	-2.32877600
C	-4.19108700	-2.16042700	-1.21834400	**O**	-2.94763500	-3.56880700	1.87460800
H	-3.92681000	-0.16208900	-1.98518300	**O**	4.91290900	-2.47445600	-2.32971600
C	-3.90820200	-3.05428800	-0.18752000	**O**	2.95111200	-3.56615900	1.87701200
H	-4.25675500	-4.07917400	-0.19315100	**C**	-5.40701800	-3.79921400	-2.46062300
C	2.96989400	-0.42838200	-0.06785800	**H**	-5.93932900	-3.82571300	-3.41294300
C	3.71438900	-0.83888000	-1.16679800	**H**	-4.58969800	-4.53173400	-2.47976800
C	2.67800200	-1.30949000	0.98758600	**H**	-6.10095700	-4.05335700	-1.64886700
C	4.19037800	-2.16019700	-1.21874900	**C**	-2.25474600	-3.19178300	3.05323300
H	3.92443800	-0.16262700	-1.98708300	**H**	-1.22769300	-2.87136200	2.83180700
C	3.15261400	-2.61996000	0.91455700	**H**	-2.77493400	-2.38552700	3.58646600
H	2.12022600	-0.94504200	1.84036700	**H**	-2.22642800	-4.08356900	3.68192900
C	3.90906800	-3.05318200	-0.18673000	**C**	2.25978500	-3.18819800	3.05626000
H	4.25806800	-4.07791900	-0.19177900	**H**	2.78038300	-2.38113600	3.58786500
C	-4.71032600	2.15577100	-0.01972300	**H**	1.23226000	-2.86846400	2.83602600
C	-3.07894100	4.48317800	0.07783500	**H**	2.23279700	-4.07932700	3.68594500
C	-4.46679100	4.58665100	0.05031600	**C**	5.40556200	-3.79962800	-2.46097800
C	-5.26922400	3.43311200	0.00426600	**H**	4.58852000	-4.53249800	-2.47849500
H	-5.33573600	1.26988000	-0.05345100	**H**	5.93673900	-3.82676000	-3.41391300
H	-2.44651600	5.36503000	0.11815000	**H**	6.10058100	-4.05276600	-1.64983200
H	-4.93687700	5.56595500	0.06565000				

Compound 25i

C	-2.92593300	-1.45014800	-0.05428800	**H**	2.98980000	-2.52437800	1.36470800
C	-1.62241500	-1.33192100	0.53007200	**C**	3.75373300	-3.46308100	-0.42862800
C	-1.07342000	-0.08127100	0.81531200	**H**	3.77709900	-2.54370400	-1.03210700
C	-1.90233200	0.99538300	0.49823800	**H**	3.45837200	-4.26904000	-1.11618700
C	-3.19440000	0.78636400	-0.08571300	**C**	5.15979200	-3.74863300	0.11429400
H	-0.08326700	0.04412200	1.24189300	**H**	5.45858100	-2.93789700	0.79564100
N	-3.70951400	-0.41392200	-0.36246600	**H**	5.13601800	-4.66378900	0.72468400
N	-1.10178300	-2.60244300	0.72543400	**C**	6.21959800	-3.90149600	-0.98440400
N	-1.69691800	2.35744000	0.65705300	**H**	6.23929200	-2.98908000	-1.59736300
C	-1.93838500	-4.93455700	0.23314600	**H**	5.92338700	-4.71524000	-1.66143300
C	-4.25364000	-3.59633800	-0.73249000	**C**	7.62327400	-4.17860800	-0.43656000
C	-4.17173600	-4.98652500	-0.75645800	**H**	8.35544900	-4.28065300	-1.24559700
C	-3.02540700	-5.64393100	-0.27826700	**H**	7.96138000	-3.36562800	0.21786200
H	-1.05749300	-5.45739000	0.59404700	**H**	7.64451200	-5.10510300	0.15040600
H	-5.13306900	-3.07616600	-1.10041400	**C**	-0.48692600	2.97412900	1.17283800
H	-4.99917100	-5.57065400	-1.14925900	**H**	-0.07836300	2.31737500	1.95067700
H	-2.98001700	-6.72938800	-0.30834600	**H**	-0.77079400	3.90582100	1.67547200
C	-3.05821300	4.41213400	0.10187300	**C**	0.57687300	3.25041100	0.09905600
C	-4.27988300	4.83018100	-0.42645400	**H**	0.82389400	2.30760500	-0.40711600
C	-5.23684000	3.90781300	-0.88289400	**H**	0.14688600	3.90907600	-0.66679600
C	-4.98822900	2.53886900	-0.81986300	**C**	1.84840000	3.88065600	0.68068900
H	-2.32659600	5.13836100	0.44388600	**H**	2.26043600	3.22073800	1.45906300
H	-4.49168300	5.89442400	-0.48738100	**H**	1.59162000	4.82279200	1.18768100
H	-6.17716500	4.26897600	-1.28970900	**C**	2.92864400	4.15231300	-0.37449600
H	-5.71850900	1.81568700	-1.17067900	**H**	3.18048400	3.21085600	-0.88471500
C	-3.17633000	-2.86537500	-0.22449700	**H**	2.51956400	4.81687200	-1.14944200
C	-2.02656900	-3.54034700	0.25880900	**C**	4.20628500	4.77290000	0.20489900
C	-2.81490600	3.03785900	0.16740000	**H**	4.61306200	4.10897500	0.98244400
C	-3.77089900	2.09737000	-0.29434000	**H**	3.95532700	5.71599700	0.71315200
C	0.22953900	-2.90608200	1.22185300	**C**	5.28960300	5.04001700	-0.84803700
H	0.50802700	-2.12604500	1.94026700	**H**	5.53911900	4.09817900	-1.35719200
H	0.17341000	-3.84179600	1.79050500	**H**	4.88435200	5.70571500	-1.62326200
C	1.29116600	-3.01745000	0.11640700	**C**	6.56338200	5.65563500	-0.26007200
H	0.98718300	-3.80238700	-0.58833500	**H**	7.01033700	4.99630600	0.49423100
H	1.30919900	-2.07965400	-0.45473000	**H**	7.31721400	5.83341100	-1.03543100
C	2.68969600	-3.32138000	0.66779400	**H**	6.35204300	6.61653200	0.22522100

Compound 25k

C	-5.75656600	-1.12627100	-0.26575000	**H**	-3.16614900	3.92744800	1.78058000
C	-4.52191100	-1.17223500	0.46075900	**C**	-1.76291100	3.08819800	0.34683000
C	-3.86641700	-0.00019200	0.83994200	**H**	-1.55878300	2.10560800	-0.09927900

C	-4.52185300	1.17201300	0.46116800	**H**	-2.04706400	3.75034800	-0.48157700
C	-5.75650400	1.12633300	-0.26538700	**C**	-0.50233700	3.62367000	1.03663500
H	-2.92306200	-0.00032700	1.37684600	**H**	-0.25151700	2.98194700	1.89490100
N	-6.37487600	0.00011000	-0.62845400	**H**	-0.71115900	4.61968200	1.45474000
N	-4.17550400	-2.49811500	0.67275300	**C**	0.71082200	3.71083100	0.10115500
N	-4.17539100	2.49780600	0.67358200	**H**	0.93544600	2.70884700	-0.29324500
C	-5.21178700	-4.70704600	0.01532200	**H**	0.45228600	4.32848100	-0.77142800
C	-7.23614700	-3.08864300	-1.15288700	**C**	1.96334200	4.28515400	0.77533800
C	-7.31093600	-4.47802900	-1.21398000	**H**	2.20886200	3.68192500	1.66223600
C	-6.30779500	-5.27411800	-0.63545200	**H**	1.74240300	5.29611700	1.14875400
H	-4.44242100	-5.33724400	0.45163900	**C**	3.18506900	4.34250100	-0.15092200
H	-8.00334000	-2.46186900	-1.59779400	**H**	3.41534600	3.32826900	-0.50975600
H	-8.15000200	-4.95345000	-1.71407500	**H**	2.93462300	4.93040000	-1.04647100
H	-6.38265800	-6.35663200	-0.69661600	**C**	4.43146900	4.94030700	0.51429300
C	-5.21159000	4.70699500	0.01687700	**H**	4.67451500	4.36132000	1.41782800
C	-6.30760500	5.27432300	-0.63366400	**H**	4.20401600	5.95957500	0.86040200
C	-7.31080600	4.47846300	-1.21240700	**C**	5.65836700	4.97990800	-0.40603100
C	-7.23607400	3.08905400	-1.15176600	**H**	5.41284800	5.55067900	-1.31399500
H	-4.44218700	5.33702100	0.45337600	**H**	5.89066200	3.95905400	-0.74429500
H	-6.38242700	6.35685900	-0.69447400	**C**	6.90153600	5.58987900	0.25421200
H	-8.14986800	4.95408600	-1.71231500	**H**	6.67082400	6.61322900	0.58600500
H	-8.00329900	2.46244800	-1.59685200	**H**	7.14331300	5.02361300	1.16611800
C	-6.14672900	-2.49898700	-0.50598600	**C**	8.13098600	5.62044800	-0.66275700
C	-5.14286200	-3.31294400	0.07814000	**H**	8.36435400	4.59674100	-0.99202100
C	-5.14271600	3.31287100	0.07922800	**H**	7.88947900	6.18400700	-1.57647400
C	-6.14663900	2.49914800	-0.50511900	**C**	9.37350000	6.23436900	-0.00507600
C	-2.95428400	-2.96154800	1.30884900	**H**	9.14154700	7.25809400	0.32187300
H	-2.71252500	-2.26898500	2.12443300	**H**	9.61490400	5.67196800	0.90827500
H	-3.16652000	-3.92819600	1.77942900	**C**	10.59669300	6.25847100	-0.92736800
C	-1.76293500	-3.08833900	0.34641000	**H**	10.87400000	5.24558500	-1.24469100
H	-2.04681600	-3.75024600	-0.48228900	**H**	10.39891400	6.84504800	-1.83306700
H	-1.55874100	-2.10560200	-0.09934500	**C**	5.65850900	-4.97980900	-0.40535500
C	-0.50250000	-3.62394700	1.03637600	**H**	5.41306500	-5.55080100	-1.31320000
H	-0.71140900	-4.62005100	1.45422200	**H**	5.89078600	-3.95902500	-0.74384300
H	-0.25187500	-2.98240500	1.89483200	**C**	6.90166000	-5.58957600	0.25510500
C	0.71085500	-3.71090800	0.10113600	**H**	6.67094800	-6.61282400	0.58721200
H	0.93546100	-2.70887400	-0.29314500	**H**	7.14341700	-5.02302400	1.16684000
H	0.45255500	-4.32851800	-0.77154500	**C**	8.13112700	-5.62044300	-0.66183700
C	1.96330300	-4.28515800	0.77551800	**H**	7.88960500	-6.18425600	-1.57539500
H	2.20868000	-3.68188600	1.66242400	**H**	8.36453100	-4.59683900	-0.99139400
H	1.74234700	-5.29611600	1.14893900	**C**	9.37360800	-6.23421500	-0.00396600
C	3.18515700	-4.34249300	-0.15057900	**H**	9.14161500	-7.25782500	0.32331700
H	3.41536200	-3.32828700	-0.50953400	**H**	9.61504100	-5.67152800	0.90920100
H	2.93488800	-4.93055400	-1.04607000	**C**	10.59679900	-6.25867600	-0.92625500
C	4.43154500	-4.94005300	0.51487700	**H**	11.46664500	-6.70063100	-0.42688300
H	4.67448800	-4.36082700	1.41828500	**H**	10.39898100	-6.84552600	-1.83176900

H	4.20413300	-5.95925200	0.86122000	**H**	10.87416300	-5.24590500	-1.24389700
C	-2.95400500	2.96100300	1.30954500	**H**	11.46656400	6.70053400	-0.42813500
H	-2.71201400	2.26810200	2.12476700				

Compound 25l

C	-1.12669200	-1.03403100	-0.05520000	**H**	4.95219300	-3.77769700	0.49975900
C	-1.17266600	0.37023600	-0.33854900	**H**	2.46064800	-3.59725500	0.45631200
C	-0.00005600	1.11322600	-0.47899600	**C**	-2.49910900	-1.48380600	0.03941100
C	1.17258600	0.37027100	-0.33869200	**C**	-3.31470300	-0.34651400	-0.18467400
C	1.12667500	-1.03400200	-0.05532400	**C**	3.31465200	-0.34646700	-0.18511200
H	-0.00008200	2.18172600	-0.67052100	**C**	2.49911400	-1.48376700	0.03908500
N	0.00001100	-1.73581000	0.08676900	**C**	-2.97692000	2.11297000	-0.69060900
N	-2.50040400	0.76416000	-0.42619500	**H**	-2.17200200	2.64349200	-1.21415900
N	2.50030900	0.76418000	-0.42665700	**H**	-3.82059900	2.05944300	-1.38894400
C	-4.70844000	-0.43212500	-0.15701900	**C**	2.97688900	2.11314000	-0.68986400
C	-3.08756400	-2.72715000	0.28653000	**H**	2.17193800	2.64426000	-1.21278100
C	-4.47694500	-2.81980400	0.30894300	**H**	3.82042300	2.06023100	-1.38844400
C	-5.27404100	-1.68311300	0.09024100	**C**	3.37822100	2.86418500	0.55756900
H	-5.33483900	0.44153700	-0.30549500	**H**	2.64098600	2.87177900	1.36003500
H	-2.46052900	-3.59729200	0.45662100	**C**	-3.37795500	2.86498800	0.55631400
H	-4.95206100	-3.77782400	0.50032100	**H**	-2.64020200	2.87392400	1.35828400
H	-6.35646600	-1.77622100	0.11867100	**C**	-4.54228900	3.49440800	0.70845500
C	4.70840200	-0.43201700	-0.15758600	**H**	-5.29955600	3.49444400	-0.07361600
C	5.27406400	-1.68298000	0.08964500	**H**	-4.78477400	4.03802200	1.61715500
C	4.47702000	-2.81969700	0.30842700	**C**	4.54219400	3.49433900	0.70952600
C	3.08763700	-2.72709500	0.28614500	**H**	4.78486400	4.03728500	1.61857600
H	5.33475000	0.44166700	-0.30613400	**H**	5.29894500	3.49565600	-0.07304300
H	6.35649300	-1.77606200	0.11799500				

Compound 25m

C	1.64451800	-1.85031700	-0.01490900	**C**	-2.83087500	0.42130200	-1.42405800
C	1.50419000	-0.55241500	-0.60131700	**H**	-2.06872900	0.95270100	-2.00613200
C	0.24923000	-0.03167500	-0.91583400	**H**	-3.56169000	0.04765000	-2.15229400
C	-0.81319700	-0.88786900	-0.62478200	**C**	3.02541700	1.29200100	-1.38195200
C	-0.58405900	-2.17585800	-0.03709900	**H**	2.45577800	1.35321500	-2.31853000
H	0.11550600	0.96432900	-1.32507600	**H**	4.08256300	1.30301300	-1.66907700
N	0.62177200	-2.65985000	0.27041100	**C**	-3.51788400	1.38129500	-0.46186300
N	2.76378500	0.00604500	-0.76303500	**C**	-4.66854100	2.06404800	-0.87263200
N	-2.17954200	-0.71572000	-0.80145100	**C**	-3.00228700	1.62895200	0.81527400
C	5.11013600	-0.77754500	-0.22862500	**C**	-5.29050700	2.98447100	-0.02778300

C	3.80711400	-3.12211500	0.71252000	**H**	-5.08364100	1.87266200	-1.86052200
C	5.19405500	-3.00827400	0.76530500	**C**	-3.62560900	2.54519300	1.66295000
C	5.83373400	-1.84725600	0.29931600	**H**	-2.11629300	1.09684300	1.14995100
H	5.62239600	0.11557000	-0.57454000	**C**	-4.76984600	3.22707000	1.24412200
H	3.29925200	-4.01241300	1.07128500	**H**	-6.18557500	3.50373000	-0.36016200
H	5.78899000	-3.82110500	1.17197200	**H**	-3.21686200	2.72457000	2.65380700
H	6.91675200	-1.77510700	0.35267400	**H**	-5.25542800	3.93839800	1.90673500
C	-4.20679700	-2.13582600	-0.31032800	**C**	2.70542200	2.50010600	-0.51167400
C	-4.60367100	-3.37249700	0.19867200	**C**	2.20459200	3.66667500	-1.10029500
C	-3.66673100	-4.30692000	0.67257800	**C**	2.93881300	2.48331200	0.86848100
C	-2.30392400	-4.02106200	0.64824600	**C**	1.94782000	4.80094400	-0.32805800
H	-4.94071700	-1.41408400	-0.65509400	**H**	2.01356400	3.68902800	-2.17166400
H	-5.66282100	-3.61343700	0.23322600	**C**	2.67873900	3.61442700	1.64236600
H	-4.01236900	-5.25937000	1.06445600	**H**	3.31783800	1.57973300	1.33790100
H	-1.57062500	-4.73386400	1.01358100	**C**	2.18425700	4.77701000	1.04687100
C	3.06210200	-2.06358700	0.18582500	**H**	1.55594700	5.69824400	-0.79968200
C	3.71932500	-0.89812100	-0.28547800	**H**	2.86153400	3.58669300	2.71331900
C	-2.83851700	-1.85785700	-0.33770900	**H**	1.98024200	5.65643600	1.65163900
C	-1.88330700	-2.78874000	0.14032900				

Compound 25n

C	2.37178200	-2.04797100	0.14949000	**H**	2.66759600	0.85714600	-2.62419200
C	2.01403200	-0.91141500	-0.64320600	**H**	4.23717600	1.23128500	-1.94256200
C	0.70143300	-0.70978900	-1.06898300	**C**	-3.32603900	-0.07606600	-0.91748900
C	-0.18869400	-1.70753100	-0.66982600	**C**	-4.62693700	0.14609500	-1.36856200
C	0.25490300	-2.81723800	0.12361400	**C**	-2.91161700	0.57057800	0.25730800
H	0.40087700	0.16260200	-1.63981800	**C**	-5.50559400	0.99369400	-0.68593700
N	1.51258700	-2.99427500	0.53580100	**H**	-4.97426600	-0.34860300	-2.27372300
N	3.14707900	-0.14216300	-0.86365400	**C**	-3.77107300	1.41074000	0.95043800
N	-1.54958700	-1.84513500	-0.90673300	**H**	-1.90705000	0.40502400	0.63687000
C	5.56691200	-0.34270700	-0.15100500	**C**	-5.07603600	1.63126400	0.48209500
C	4.69628600	-2.72638100	1.12975300	**H**	-6.51020000	1.13763400	-1.06668900
C	6.02867200	-2.32695900	1.19841000	**H**	-3.45718200	1.90972700	1.86193200
C	6.45434000	-1.14782300	0.56375900	**C**	2.59209900	2.29720300	-1.02499300
H	5.91332500	0.57037100	-0.62638000	**C**	1.92307400	3.25058300	-1.80593300
H	4.35287500	-3.63415500	1.61695200	**C**	2.72800000	2.54240200	0.34246900
H	6.74681300	-2.92870400	1.74820800	**C**	1.41439000	4.41434300	-1.24282400
H	7.49744000	-0.85044200	0.63150400	**H**	1.79819700	3.08065700	-2.87378700
C	-3.28242500	-3.55755400	-0.24945600	**C**	2.21801700	3.70426500	0.92690500
C	-3.45699500	-4.75782800	0.43948700	**H**	3.23295900	1.81401700	0.97106100
C	-2.38391600	-5.39893100	1.08227200	**C**	1.55935300	4.64997600	0.13187500
C	-1.10532200	-4.84784600	1.04981800	**H**	0.89277300	5.15218400	-1.84437800
H	-4.12211800	-3.06078300	-0.72498100	**H**	2.33802800	3.85726100	1.99332700

H	-4.44797900	-5.20193700	0.48294600	**O**	1.02344500	5.81724500	0.59320100
H	-2.55728600	-6.33163800	1.61168800	**O**	-5.84002700	2.47478600	1.23587800
H	-0.26867800	-5.33266800	1.54412100	**C**	1.13450200	6.10612700	1.97795600
C	3.78990700	-1.93628600	0.41754800	**H**	2.18400500	6.17984900	2.29243600
C	4.23194800	-0.74934400	-0.22194900	**H**	0.64667500	7.07186700	2.12199700
C	-1.99672700	-3.01287100	-0.28341500	**H**	0.62735900	5.34919900	2.59073700
C	-0.90660800	-3.64678000	0.36316000	**C**	-7.17070300	2.72989500	0.81677000
C	-2.37833200	-0.96174500	-1.71064100	**H**	-7.58993500	3.41833900	1.55280800
H	-1.69856000	-0.35115600	-2.31579600	**H**	-7.19911100	3.19949000	-0.17562200
H	-2.95282800	-1.57156700	-2.41967600	**H**	-7.77151600	1.81086300	0.79724600
C	3.18781600	1.05905200	-1.67836800				

Compound 25q

C	1.12655600	1.85764800	-0.09112100	**C**	2.94581200	-2.14427600	-1.25387200
C	1.17258000	0.67000300	-0.89056800	**H**	1.94825100	-2.33077200	-0.83877300
C	-0.00006900	0.04105800	-1.31266800	**C**	-2.93565600	-0.76766300	-1.96065200
C	-1.17275700	0.66995600	-0.89060400	**H**	-2.27177500	-0.81694800	-2.83334000
C	-1.12680300	1.85760900	-0.09116500	**H**	-3.93558500	-0.53301100	-2.33730300
H	-0.00004400	-0.86099200	-1.91624500	**C**	-2.94569700	-2.14441900	-1.25390100
N	-0.00014200	2.45204300	0.30941600	**H**	-1.94807600	-2.33085900	-0.83892300
N	2.49851200	0.33786300	-1.12771100	**H**	-3.11357800	-2.90386100	-2.02901100
N	-2.49866700	0.33778000	-1.12781500	**H**	3.11363200	-2.90369900	-2.02901400
C	4.70882200	1.37355900	-0.45835300	**C**	-3.99286200	-2.27751300	-0.17035600
C	3.08451300	3.30787500	0.84718700	**C**	-5.29944200	-2.67460300	-0.48905400
C	4.47282000	3.40258500	0.88385200	**C**	-3.69211700	-1.98328400	1.16574500
C	5.27124500	2.44329700	0.23741300	**C**	-6.28121000	-2.76774800	0.49783500
H	5.34140600	0.62708200	-0.92796400	**H**	-5.54790000	-2.92095400	-1.51989800
H	2.45435100	4.03965800	1.34395100	**C**	-4.67119100	-2.07489500	2.15596500
H	4.94598800	4.22122700	1.41881300	**H**	-2.68335600	-1.67721400	1.43178400
H	6.35357900	2.52940100	0.28447600	**C**	-5.96920200	-2.46624400	1.82499000
C	-4.70904000	1.37342300	-0.45855800	**H**	-7.28716700	-3.08184800	0.23146200
C	-5.27152100	2.44314700	0.23718200	**H**	-4.41846800	-1.84000000	3.18644900
C	-4.47315100	3.40245100	0.88366400	**H**	-6.73146700	-2.54020700	2.59591800
C	-3.08484100	3.30777200	0.84706200	**C**	3.99311500	-2.27734000	-0.17045800
H	-5.34159200	0.62695300	-0.92822500	**C**	5.29966800	-2.67439400	-0.48931000
H	-6.35385900	2.52922800	0.28418300	**C**	3.69252500	-1.98311500	1.16568000
H	-4.94636400	4.22108100	1.41860400	**C**	6.28155700	-2.76751500	0.49746200
H	-2.45471500	4.03957100	1.34385000	**H**	5.54801500	-2.92074100	-1.52018100
C	2.49917500	2.24566900	0.15196200	**C**	4.67171900	-2.07470000	2.15578200
C	3.31526600	1.28661400	-0.49945900	**H**	2.68379000	-1.67706000	1.43183600
C	-3.31548100	1.28650100	-0.49959400	**C**	5.96970100	-2.46602000	1.82465400
C	-2.49944700	2.24558100	0.15186300	**H**	7.28749000	-3.08158500	0.23096300
C	2.93560500	-0.76750500	-1.96058900	**H**	4.41911500	-1.83981100	3.18629700

H	2.27170800	-0.81683600	-2.83326100	**H**	6.73205800	-2.53996500	2.59549200
H	3.93549800	-0.53272600	-2.33726200				

Compound 25r

C	1.12677700	3.84682800	-0.09603000	**H**	2.19666000	-0.10037200	1.25498600
C	1.17240000	2.43771400	-0.35349600	**C**	-3.66335000	-1.49013700	0.50792500
C	0.00032100	1.69180000	-0.48200400	**C**	-2.79031100	-2.56931600	0.41317600
C	-1.17159200	2.43794700	-0.35343300	**C**	-5.04224700	-1.72857300	0.35054900
C	-1.12567000	3.84706100	-0.09595800	**C**	-3.26795800	-3.86393500	0.16699500
H	0.00021900	0.62172300	-0.66369800	**H**	-1.72113800	-2.41534600	0.53946300
N	0.00062700	4.55233600	0.03262000	**C**	-5.53424400	-3.00739700	0.10512600
N	2.49871200	2.04047500	-0.44140500	**H**	-5.73172600	-0.89486400	0.43504100
N	-2.49800300	2.04098300	-0.44122800	**C**	-4.63097900	-4.09793300	0.00959000
C	4.70751500	3.24192700	-0.19480100	**H**	-2.56429300	-4.68622400	0.10587900
C	3.08959800	5.54292100	0.21730700	**C**	3.66290500	-1.49086100	0.50851500
C	4.47916200	5.63537500	0.23964200	**C**	2.78966100	-2.56996800	0.41496700
C	5.27509300	4.49538600	0.03558800	**C**	5.04166200	-1.72957100	0.35025500
H	5.33670700	2.36980100	-0.34702600	**C**	3.26696100	-3.86478600	0.16912300
H	2.46314800	6.41592900	0.37454300	**H**	1.72060200	-2.41578600	0.54195500
H	4.95492800	6.59568400	0.41728900	**C**	5.53331100	-3.00857800	0.10512600
H	6.35769700	4.58828000	0.05905100	**H**	5.73131700	-0.89591800	0.43383900
C	-4.70653700	3.24285400	-0.19443600	**C**	4.62982900	-4.09904800	0.01082000
C	-5.27386100	4.49640600	0.03603300	**H**	2.56312400	-4.68700300	0.10898400
C	-4.47769600	5.63623800	0.24005800	**O**	5.19870600	-5.31463500	-0.22660400
C	-3.08815300	5.54351900	0.21761100	**O**	6.84891800	-3.32538700	-0.05317300
H	-5.33588200	2.37083500	-0.34663800	**O**	-6.85000600	-3.32395700	-0.05232400
H	-6.35644500	4.58951800	0.05958000	**O**	-5.20020100	-5.31332400	-0.22803300
H	-4.95325500	6.59663700	0.41777300	**C**	4.34348000	-6.44050400	-0.31645700
H	-2.46154600	6.41642100	0.37481700	**H**	3.62795000	-6.34136700	-1.14418300
C	2.49966000	4.29690700	-0.01108100	**H**	4.99524400	-7.29569200	-0.50449000
C	3.31329800	3.15430700	-0.21952500	**H**	3.79040400	-6.60470900	0.61841100
C	-3.31233000	3.15496300	-0.21926800	**C**	7.80257200	-2.28137000	0.03955100
C	-2.49845400	4.29741000	-0.01086400	**H**	7.78433900	-1.80243300	1.02787200
C	2.96436700	0.67631500	-0.61060000	**H**	8.77514500	-2.75211300	-0.11498400
H	2.24801600	0.14227400	-1.24409800	**H**	7.64335100	-1.51684200	-0.73311500
H	3.90809100	0.70187600	-1.16552500	**C**	-7.80346700	-2.27988900	0.04188800
C	3.15539100	-0.08242000	0.72345600	**H**	-7.64485000	-1.51491100	-0.73045300
H	3.85219700	0.48822800	1.34935100	**H**	-8.77622400	-2.75043600	-0.11207100
C	-2.96392400	0.67695300	-0.61069800	**H**	-7.78429500	-1.80156400	1.03048500
H	-2.24759000	0.14283500	-1.24414000	**C**	-4.34523000	-6.43929500	-0.31903300
H	-3.90754500	0.70281000	-1.16579900	**H**	-4.99728000	-7.29429600	-0.50693100
C	-3.15544500	-0.08189600	0.72320500	**H**	-3.63033100	-6.33992500	-1.14727700
H	-3.85221600	0.48887600	1.34902500	**H**	-3.79145600	-6.60400600	0.61533200

H	-2.19684900	-0.10017800	1.25496500

Compound 25s

C	1.17175700	3.07450800	0.15053700	**C**	3.65682400	-2.15246300	-1.32992200
C	1.19877000	1.85759700	-0.60614600	**H**	4.57779900	-1.91924700	-1.88125700
C	0.01663100	1.22602200	-0.99432100	**H**	2.90358600	-2.42024500	-2.08358800
C	-1.14539700	1.88798700	-0.59648600	**C**	-2.96593300	0.38878900	-1.50770300
C	-1.08061900	3.10290600	0.16112500	**H**	-2.24591000	0.13317100	-2.29445400
H	0.00188700	0.29540600	-1.55289500	**H**	-3.89708900	0.65948500	-2.01970100
N	0.05502500	3.69686200	0.53494800	**C**	-3.20027600	-0.81749500	-0.58489600
N	2.51987000	1.50376400	-0.83769600	**H**	-2.25762600	-1.09117500	-0.09474900
N	-2.47705500	1.56856500	-0.81703400	**H**	-3.89295600	-0.52888900	0.21511500
C	4.74440100	2.50656400	-0.18294800	**C**	-3.76415900	-2.03145600	-1.34875100
C	3.15632800	4.51461300	1.05351500	**H**	-3.06655600	-2.31123800	-2.14975500
C	4.54695000	4.57672100	1.09963000	**H**	-4.70068300	-1.73798600	-1.84273700
C	5.32810700	3.58209700	0.48712700	**C**	-4.01511700	-3.22710800	-0.45375600
H	5.36250300	1.74326200	-0.64649300	**C**	-3.05321200	-4.23532800	-0.31040900
H	2.54128000	5.27599400	1.52397800	**C**	-5.20589100	-3.33528200	0.27767800
H	5.03507700	5.39944500	1.61437100	**C**	-3.27124200	-5.31999400	0.54050700
H	6.41179500	3.64735800	0.53677300	**H**	-2.12543600	-4.17237500	-0.87577700
C	-4.66936200	2.62675900	-0.14090000	**C**	-5.42889900	-4.41690100	1.12983400
C	-5.21959600	3.71517600	0.53666500	**H**	-5.96790100	-2.56523800	0.17464800
C	-4.40789400	4.68796900	1.14442900	**C**	-4.46069500	-5.41396500	1.26441500
C	-3.01975000	4.59060100	1.08562600	**H**	-2.51357000	-6.09378800	0.63409600
H	-5.31092100	1.88038200	-0.60006700	**H**	-6.36078000	-4.48344400	1.68532000
H	-6.30079500	3.80781200	0.59613000	**H**	-4.63390500	-6.25917700	1.92502600
H	-4.87024100	5.52155700	1.66544700	**C**	3.89993300	-3.33201300	-0.41174100
H	-2.38139600	5.33498100	1.55222100	**C**	2.85901000	-4.20877900	-0.07809500
C	2.55028800	3.44594000	0.38750800	**C**	5.16270300	-3.55333600	0.15373300
C	3.34924500	2.45020200	-0.22946100	**C**	3.07083400	-5.27395700	0.79785600
C	-3.27655000	2.53492300	-0.19999300	**H**	1.87287100	-4.05689100	-0.51272600
C	-2.44700400	3.50861300	0.41172500	**C**	5.38023500	-4.61715600	1.03018700
C	2.96959300	0.30109100	-1.51550100	**H**	5.98516600	-2.88703300	-0.09886000
H	2.22937600	0.04936700	-2.28443300	**C**	4.33347200	-5.48120400	1.35600900
H	3.89767400	0.53922700	-2.04882200	**H**	2.25067200	-5.94442000	1.04144300
C	3.18895500	-0.89355000	-0.57404600	**H**	6.36842300	-4.77308100	1.45514000
H	3.93018400	-0.62212600	0.18743700	**H**	4.50117800	-6.31194900	2.03611600
H	2.25678200	-1.10805300	-0.03665600				

Compound 25t

C	-1.12593300	-1.84458200	0.00010200	**H**	-2.02076000	1.98263600	-0.00011300
C	-1.17648900	-0.41419600	-0.00016800	**C**	-4.09567500	3.26541900	-1.26770000
C	0.00002900	0.33757100	-0.00048900	**H**	-4.62378700	1.16779600	-1.36259000
C	1.17656700	-0.41417800	-0.00042200	**H**	-3.09898500	1.53895200	-2.15470000
C	1.12604700	-1.84455800	-0.00010100	**C**	-4.09596500	3.26537000	1.26708700
H	0.00001800	1.42223900	-0.00073700	**H**	-4.62407600	1.16772500	1.36178500
N	0.00006200	-2.56123900	0.00011700	**H**	-3.09944400	1.53888100	2.15423800
N	-2.50756600	-0.00707400	-0.00016500	**C**	-4.87858800	3.64079300	-0.00038900
N	2.50765200	-0.00702600	-0.00083300	**H**	-4.67929800	3.50559600	-2.16486900
C	-4.71323000	-1.27978300	0.00029600	**H**	-3.18129000	3.87532700	-1.32003400
C	-3.05900400	-3.58564100	0.00055100	**H**	-4.67979900	3.50550200	2.16413200
C	-4.44486400	-3.70957500	0.00068400	**H**	-3.18160200	3.87528900	1.31965700
C	-5.25736200	-2.56408000	0.00056200	**H**	-5.10867300	4.71350600	-0.00039600
H	-5.36939900	-0.41752300	0.00019100	**H**	-5.84380300	3.11334100	-0.00051000
H	-2.41209500	-4.45793200	0.00065300	**C**	2.94367700	1.39224000	-0.00005500
H	-4.90311100	-4.69450800	0.00089900	**C**	3.71525800	1.77521100	1.27907100
H	-6.33859500	-2.67476500	0.00067300	**C**	3.71550000	1.77640600	-1.27869300
C	4.71334600	-1.27972500	-0.00078500	**H**	2.02064900	1.98264300	0.00010300
C	5.25747400	-2.56401300	-0.00059300	**C**	4.09552800	3.26489900	1.26829900
C	4.44497400	-3.70951800	-0.00026300	**H**	4.62373600	1.16724100	1.36218100
C	3.05911800	-3.58557300	-0.00008500	**H**	3.09891900	1.53797200	2.15447900
H	5.36951800	-0.41745900	-0.00099800	**C**	4.09570800	3.26612500	-1.26647900
H	6.33870800	-2.67468700	-0.00068500	**H**	4.62407800	1.16861200	-1.36217700
H	4.90320400	-4.69446000	-0.00013900	**H**	3.09937400	1.53990800	-2.15444100
H	2.41221200	-4.45786700	0.00019400	**C**	4.87835600	3.64100100	0.00114800
C	-2.49386400	-2.30753600	0.00029600	**H**	4.67920300	3.50459900	2.16556100
C	-3.31851800	-1.15215000	0.00015600	**H**	3.18114500	3.87477600	1.32103000
C	3.31864000	-1.15208400	-0.00061300	**H**	4.67944300	3.50682400	-2.16343500
C	2.49398100	-2.30747000	-0.00025500	**H**	3.18125500	3.87595400	-1.31865700
C	-2.94374500	1.39216000	-0.00021400	**H**	5.10828600	4.71374300	0.00169400
C	-3.71531900	1.77574100	-1.27917700	**H**	5.84365100	3.11368900	0.00096300
C	-3.71559900	1.77569500	1.27859600				

Compound 35a

C	0.88403490	1.26867119	0.00043202	**C**	-2.75897757	3.33247501	-0.16858799
C	0.34410298	-0.07263597	-0.02039398	**H**	-3.57076845	1.32785178	-0.19592400
N	2.17607697	1.50438132	0.03903002	**H**	0.55190061	4.17466637	-0.02922298
N	-1.04508013	0.00383091	-0.05028798	**H**	-1.71737766	5.22356825	-0.13747299
C	-1.93694110	-1.10595426	-0.01490698	**H**	-3.73877369	3.79837495	-0.23048500
C	-2.98019217	-1.13530835	0.91847509	**C**	3.29726439	-2.04852785	0.06018002
C	-1.76445798	-2.17148432	-0.90565605	**C**	4.66093448	-1.85624170	0.10054903

C	-3.85917814	-2.21788252	0.94342309	**C**	5.20640739	-0.54817655	0.12028003
H	-3.09007626	-0.32058730	1.62721315	**C**	4.37777623	0.55124345	0.09968003
C	-2.63791595	-3.25685248	-0.86065105	**H**	2.85927945	-3.04194496	0.04566002
H	-0.94687992	-2.14801024	-1.61662610	**H**	5.32767558	-2.71415171	0.11789003
C	-3.69081403	-3.28206958	0.05621102	**H**	6.28440645	-0.41688245	0.15211003
H	-4.66814820	-2.23313459	1.66862615	**H**	4.76755617	1.56458456	0.11428303
H	-2.49754287	-4.08311954	-1.55206010	**C**	-0.24370627	2.17380115	-0.03140898
H	-4.37259501	-4.12745171	0.08198803	**C**	-1.40721429	1.36540598	-0.06554699
C	-2.67702744	1.93952191	-0.14485499	**C**	2.96900614	0.39027131	0.05854102
C	-0.34720441	3.56645425	-0.05516298	**C**	2.41605822	-0.93860584	0.03823502
C	-1.61284755	4.14281317	-0.11931699	**N**	1.06567414	-1.16325099	-0.00346998

Compound 35b

C	1.50609500	1.11363200	0.00145000	**H**	0.15580000	5.65183700	-0.12054800
C	0.60090600	-0.01411600	-0.02273000	**H**	-2.19061700	4.87042100	-0.21756600
N	2.81101100	0.96508500	0.04216800	**C**	2.85522400	-2.76044800	0.05941600
N	-0.70601100	0.46054000	-0.05518200	**C**	4.21600700	-2.97163500	0.10259700
C	-1.88047400	-0.34514200	-0.02783500	**C**	5.11687000	-1.87766800	0.12507900
C	-2.88538600	-0.09402100	0.91171500	**C**	4.64209000	-0.58539800	0.10447200
C	-2.03317600	-1.39824900	-0.93605900	**H**	2.14816600	-3.58431800	0.04261300
C	-4.03754400	-0.87896300	0.92550600	**H**	4.60548400	-3.98596800	0.11997000
H	-2.76026200	0.70643100	1.63430000	**H**	6.18666800	-2.06402000	0.15915000
C	-3.18174500	-2.18417500	-0.89762300	**H**	5.30879000	0.27151700	0.12138200
H	-1.25199300	-1.59976100	-1.66004200	**C**	0.68804600	2.30617100	-0.02879900
C	-4.20601900	-1.93999000	0.02772000	**C**	-0.65933400	1.86787600	-0.06656900
H	-4.81319600	-0.66796200	1.65798600	**C**	3.24715300	-0.33109700	0.06075900
H	-3.28739700	-3.00020900	-1.60883200	**C**	2.33303200	-1.44290800	0.03739200
C	-1.70982200	2.78391200	-0.14187900	**N**	0.97551500	-1.26713000	-0.00684300
C	0.99016200	3.66977300	-0.04636400	**C**	-5.43761500	-2.81377800	0.07212100
C	-0.05562900	4.58673400	-0.10733000	**H**	-5.25843800	-3.72349700	0.66065400
C	-1.38678400	4.14145200	-0.15917400	**H**	-6.28402500	-2.29129700	0.52971100
H	-2.74184200	2.45534400	-0.19388600	**H**	-5.73940000	-3.13297600	-0.93146400
H	2.02630900	3.99322900	-0.01762000				

Compound 35c

C	1.45443800	1.14565500	0.00025800	**H**	-2.83142400	2.36387200	-0.20266100
C	0.58370100	-0.00800600	-0.02691100	**H**	1.88982900	4.03940700	-0.01360000
N	2.76297300	1.03483500	0.04348600	**H**	-0.02837800	5.64260300	-0.11725900
N	-0.73718500	0.42839900	-0.06236400	**H**	-2.35058600	4.79337900	-0.22000400
C	-1.88537100	-0.41185900	-0.03074200	**C**	2.91583900	-2.68814300	0.05620900

C	-2.88935800	-0.19330900	0.92069000	**C**	4.28213000	-2.85924100	0.10298000
C	-2.00579200	-1.46917600	-0.94084900	**C**	5.15043800	-1.73934700	0.12931300
C	-4.01907300	-1.00929000	0.95106100	**C**	4.63831600	-0.46143800	0.10892900
H	-2.78023000	0.60800600	1.64426700	**H**	2.23347000	-3.53249600	0.03664900
C	-3.12255700	-2.30072700	-0.90286600	**H**	4.70113500	-3.86168400	0.12030500
H	-1.22003800	-1.64401400	-1.66622300	**H**	6.22508200	-1.89443900	0.16613200
C	-4.11552200	-2.05307600	0.03843500	**H**	5.27968000	0.41449100	0.12871400
H	-4.80927200	-0.85546300	1.67824600	**C**	0.60162100	2.31396100	-0.03043900
H	-3.23422700	-3.12824000	-1.59539700	**C**	-0.73232000	1.83708800	-0.07196200
C	-1.80916800	2.72152700	-0.14730700	**C**	3.23667600	-0.24808100	0.06176900
C	0.86370400	3.68580400	-0.04502500	**C**	2.35574500	-1.38642700	0.03456200
C	-0.20854800	4.57179700	-0.10629400	**N**	0.99358000	-1.24954700	-0.01291500
C	-1.52594900	4.08814400	-0.16138700	**F**	-5.20270300	-2.85070600	0.06898200

Compound 35e

C	-1.94433515	0.98383808	-0.02813700	**H**	-1.18283809	5.65874845	0.05586200
C	-0.90287907	-0.01850100	0.03164900	**H**	1.24037609	5.18249739	0.21706102
N	-3.21817625	0.66844905	-0.09454701	**C**	-2.78486521	-3.03214823	-0.05557000
N	0.33034403	0.61967705	0.08954101	**C**	-4.10625331	-3.41634326	-0.12285201
C	1.59975212	-0.02763200	0.11410101	**C**	-5.13886339	-2.44715618	-0.18070801
C	2.57871020	0.30385802	-0.82320906	**C**	-4.83357237	-1.10456209	-0.17105601
C	1.87351815	-1.01021707	1.07645208	**H**	-1.97891215	-3.75841128	-0.01139300
C	3.83099429	-0.31489002	-0.79696506	**H**	-4.36253134	-4.47235734	-0.13215601
H	2.36254618	1.04495508	-1.58656512	**H**	-6.17505647	-2.76955821	-0.23330302
C	3.10782624	-1.64240413	1.09556808	**H**	-5.60371142	-0.34034403	-0.21478302
H	1.11103009	-1.28005910	1.79828814	**C**	-1.28634610	2.27168917	0.00399600
C	4.09928231	-1.29583710	0.16445401	**C**	0.10446901	2.00872516	0.08068501
H	4.57396035	-0.03486800	-1.53466412	**C**	-3.48393926	-0.67320405	-0.10274001
H	3.33298426	-2.40779218	1.83128314	**C**	-2.43582119	-1.65830612	-0.04326100
C	1.02914608	3.05086923	0.16370901	**N**	-1.11331809	-1.30969810	0.02690400
C	-1.75835613	3.58630227	-0.00704500	**O**	5.27945540	-1.96943815	0.27979202
C	-0.83831406	4.62888735	0.06389500	**C**	6.31737848	-1.67036613	-0.64027705
C	0.53699904	4.35659233	0.15244001	**H**	7.15424754	-2.31543118	-0.36699503
H	2.09286516	2.85495922	0.24207002	**H**	6.01555446	-1.88655514	-1.67359613
H	-2.82593422	3.77588629	-0.06539600	**H**	6.63063951	-0.62032004	-0.56809604

Compound 35j

C	0.23248100	-1.07219400	0.01091800	**H**	5.88253400	-0.95383400	0.31711400
C	0.10158500	0.34902900	-0.23358700	**H**	3.86211700	-2.41312100	0.44254600
N	1.40163900	-1.64840000	0.17413600	**C**	-1.11106200	-1.61186300	0.02298400

N	-1.23631900	0.65923700	-0.37214500	**C**	-1.98070100	-0.51368800	-0.21052400
C	-3.36441300	-0.69000800	-0.26175900	**C**	2.47836100	-0.80698300	0.09634300
C	-1.62970000	-2.89535300	0.20468100	**C**	2.33067700	0.60512100	-0.14593200
C	-3.01032600	-3.07477500	0.15299800	**N**	1.10259600	1.18956100	-0.31187300
C	-3.86122500	-1.98162100	-0.07817900	**C**	-1.75788400	2.00156200	-0.58720400
H	-4.03774000	0.14341900	-0.43609800	**H**	-0.95992100	2.57334000	-1.07009300
H	-0.95789900	-3.72982900	0.38226800	**H**	-2.59340700	1.93591800	-1.29490700
H	-3.43428300	-4.06476800	0.29250000	**C**	-2.19976900	2.70068900	0.70658200
H	-4.93557200	-2.14122700	-0.11405600	**H**	-1.33888300	2.75588100	1.38367700
C	3.49298000	1.41339400	-0.21233700	**H**	-2.95800600	2.08751300	1.21021200
C	4.74269500	0.85659700	-0.04851300	**C**	-2.75125500	4.10433300	0.43941500
C	4.88921400	-0.53252500	0.18999100	**H**	-1.99796100	4.74358300	-0.03656400
C	3.78021100	-1.34569500	0.26090300	**H**	-3.62600000	4.07215900	-0.22198900
H	3.35998700	2.47538300	-0.39573100	**H**	-3.05805500	4.58998200	1.37170500
H	5.62646400	1.48670500	-0.10209700				

Compound 35l

C	2.46051500	0.72348300	-0.14027000	**N**	1.36519100	-1.33366000	0.59817700
C	1.35602100	-0.03862600	0.40407500	**C**	-0.98769700	0.40639000	1.19347600
N	3.59430800	0.15916900	-0.48906900	**H**	-0.82584700	-0.53085700	1.73361800
N	0.31192300	0.82017300	0.68210700	**H**	-1.32380200	1.15492900	1.92135800
C	-0.02624500	3.30512500	0.41561200	**C**	-2.04047200	0.20822000	0.09349800
C	2.62954300	3.29005000	-0.60275000	**H**	-1.66921400	-0.54604800	-0.61205200
C	1.91016700	4.47950500	-0.50903900	**H**	-2.15401900	1.14101400	-0.47515700
C	0.59942100	4.48012600	-0.00463700	**C**	-3.39878200	-0.22766300	0.65709500
H	-1.04129200	3.32380100	0.79983600	**H**	-3.27434700	-1.16108600	1.22532600
H	3.64394700	3.27260700	-0.98991700	**H**	-3.75533200	0.52278000	1.37866400
H	2.36297200	5.41370600	-0.82770400	**C**	-4.46419200	-0.43254300	-0.42780700
H	0.05404600	5.41789300	0.05978000	**H**	-4.10406400	-1.17808900	-1.15172100
C	2.67403000	-3.33992900	0.40910700	**H**	-4.59062200	0.50267200	-0.99300700
C	3.84365000	-3.97887200	0.05926600	**C**	-5.82350600	-0.87867700	0.12582900
C	4.93447400	-3.24846500	-0.47419700	**H**	-5.69719200	-1.81550000	0.68875400
C	4.83841800	-1.88603200	-0.64955600	**H**	-6.18332400	-0.13486900	0.85253200
H	1.82724400	-3.88192800	0.81940300	**C**	-6.88897500	-1.08102600	-0.95928100
H	3.93321200	-5.05365500	0.19268500	**H**	-6.52833300	-1.82278100	-1.68603300
H	5.84867100	-3.76941000	-0.74476000	**H**	-7.01665100	-0.14417600	-1.52002900
H	5.65770800	-1.30064700	-1.05598700	**C**	-8.24274800	-1.53022000	-0.39995800
C	2.02331900	2.10295200	-0.18719900	**H**	-8.64608600	-0.79138600	0.30359500
C	0.69743300	2.11521800	0.32146300	**H**	-8.98085900	-1.66678300	-1.19849200
C	3.65000700	-1.19521200	-0.29952100	**H**	-8.15324800	-2.48247600	0.13731700
C	2.54169900	-1.93871700	0.24203800				

Compound 35m

C	0.25237600	-0.96411700	0.01394600	**H**	5.68033500	1.52467400	-0.06185300
C	0.14018000	0.46427400	-0.19292100	**H**	5.90497600	-0.92793000	0.30027000
N	1.41461100	-1.55925200	0.15770700	**H**	3.86580500	-2.36280000	0.40014000
N	-1.19545800	0.79625600	-0.31221500	**C**	-1.09780700	-1.48695700	0.01130400
C	-3.34056300	-0.53109300	-0.24925600	**C**	-1.95538500	-0.37336800	-0.18914700
C	-1.63045900	-2.77003500	0.15222500	**C**	2.50239800	-0.73074900	0.09708500
C	-3.01257700	-2.93214800	0.09027200	**C**	2.37331200	0.68835600	-0.11189000
C	-3.85082900	-1.82278100	-0.10792300	**N**	1.15186100	1.29175200	-0.25869500
H	-4.00112800	0.31811700	-0.38446400	**C**	-1.69263500	2.14445300	-0.55964200
H	-0.96824900	-3.61699500	0.30483400	**H**	-0.80499100	2.74052500	-0.79913500
H	-3.44772000	-3.92139200	0.19715900	**H**	-2.34169100	2.13676800	-1.44434100
H	-4.92680700	-1.96947600	-0.14980200	**C**	-2.41799700	2.73953100	0.62138300
C	3.54564800	1.48260200	-0.16520300	**C**	-3.62307800	3.30426000	0.55236600
C	4.78837300	0.90541300	-0.01916000	**H**	-1.87963500	2.70497400	1.56800600
C	4.91694100	-0.49057700	0.18699100	**H**	-4.18028700	3.35128300	-0.38170300
C	3.79744300	-1.29046600	0.24368400	**H**	-4.09607500	3.75114400	1.42214200
H	3.42632700	2.55022500	-0.32352500				

Compound 35n

C	1.31366500	-1.17197100	0.08738200	**C**	0.25065800	-2.15438200	0.12640200
C	0.73540900	0.03743800	-0.46025200	**C**	-0.90513400	-1.50974700	-0.38685100
N	2.57699400	-1.24357800	0.43987400	**C**	3.29906800	-0.09635200	0.24966300
N	-0.59923600	-0.18875200	-0.73487000	**C**	2.70886700	1.09786700	-0.29757900
C	-2.12129700	-2.18484400	-0.49444500	**N**	1.38779600	1.15464200	-0.65751100
C	0.18981900	-3.48832500	0.53489100	**C**	-1.49356200	0.77663900	-1.35970600
C	-1.02163300	-4.16731600	0.42604500	**H**	-0.85111300	1.60296700	-1.68109400
C	-2.15857700	-3.51816400	-0.08260000	**H**	-1.92812200	0.32681800	-2.26111900
H	-3.01179300	-1.69136900	-0.86883700	**C**	-2.59998600	1.28647600	-0.45127100
H	1.07775500	-3.97572100	0.92623100	**C**	-2.30979900	1.76554600	0.83277900
H	-1.09110700	-5.20524500	0.73793000	**C**	-3.92320800	1.31927100	-0.90290400
H	-3.09540800	-4.06407200	-0.15502900	**C**	-3.32548400	2.26347400	1.64726600
C	3.51981500	2.24745200	-0.46679300	**H**	-1.28436800	1.74731100	1.19248600
C	4.85154500	2.22163300	-0.11347800	**C**	-4.94207400	1.82201600	-0.09026900
C	5.43368100	1.04744900	0.42506700	**H**	-4.15963500	0.95122000	-1.89944600
C	4.67279500	-0.08652700	0.60260800	**C**	-4.64510700	2.29372100	1.18800700
H	3.05547400	3.13738900	-0.88093500	**H**	-3.08706300	2.63077300	2.64191800
H	5.46364600	3.10937500	-0.24815200	**H**	-5.96554200	1.83902200	-0.45543400
H	6.48531300	1.04582700	0.69777700	**H**	-5.43565000	2.68172900	1.82463300
H	5.09196400	-1.00034200	1.01285700				

Compound 35t

C	1.18318800	1.20567400	-0.00008000	**C**	-1.10012100	1.45236600	-0.00020300
C	0.54437000	-0.09156600	-0.00014500	**C**	3.19790300	0.17560400	0.00000300
N	2.48965900	1.34607500	0.00000200	**C**	2.54867800	-1.10987600	-0.00011900
N	-0.82888700	0.07503200	-0.00032100	**N**	1.18500100	-1.23427800	-0.00019100
C	-2.32469000	2.12789000	-0.00026500	**C**	-1.76471800	-1.05680300	-0.00021000
C	0.11605400	3.58011500	0.00028700	**C**	-2.62268300	-1.11498800	1.27785300
C	-1.10444400	4.24942000	0.00022000	**C**	-2.62327200	-1.11488300	-1.27785100
C	-2.30586000	3.52337900	-0.00004600	**H**	-1.10788200	-1.93367900	-0.00042800
H	-3.26930700	1.59746300	-0.00044500	**C**	-3.52967500	-2.35658700	1.26817500
H	1.05823000	4.12009400	0.00043700	**H**	-3.24225200	-0.21258800	1.35831800
H	-1.13070100	5.33503000	0.00036300	**H**	-1.96383800	-1.12442100	2.15424300
H	-3.25188000	4.05833200	-0.00009200	**C**	-3.53009600	-2.35662600	-1.26780000
C	3.34800000	-2.28047000	-0.00011800	**H**	-3.24307400	-0.21260600	-1.35792400
C	4.72273400	-2.18866200	-0.00001000	**H**	-1.96489000	-1.12411900	-2.15459000
C	5.36267800	-0.92417300	0.00010200	**C**	-4.39513400	-2.41605500	0.00033400
C	4.61536100	0.23230700	0.00011800	**H**	-4.16179200	-2.36069500	2.16468600
H	2.83929200	-3.23983300	-0.00019900	**H**	-2.90580700	-3.26062000	1.32247100
H	5.32491500	-3.09329500	-0.00001200	**H**	-4.16249400	-2.36091100	-2.16410900
H	6.44784200	-0.87149200	0.00018100	**H**	-2.90611900	-3.26057800	-1.32219200
H	5.07824200	1.21458100	0.00020800	**H**	-5.00472300	-3.32827400	0.00045300
C	0.11914300	2.18392500	0.00005000	**H**	-5.09867200	-1.57012700	0.00042300

List of Abbreviations

$^{\circ}C$	Degrees Celsius
^{13}C	Carbon 13
^{19}F	Fluorine 19
^{1}H	Hydrogen, proton
9-BBN	9-Borabicyclo[3.3.1]nonane
Å	Angstrom, 10-8m
Ac	Acetyl
AcO	Acetate
Ar	Aryl
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
Bn	Benzyl
Boc	N-*tert*-butoxycarbonyl
Buchwald-Hartwig amination reactions	BHAR
Calcd.	Calculated
CAM	Cerium-ammonium-molybdate
Cata*CX*ium A	Di(1-adamantyl)-n-butylphosphine
CI	Chemical Ionization
cm^{-1}	Wavenumber
CMV	Cytomegalovirus
COSY	Homonuclear Correlation Spectroscopy
CV	Cyclic Voltametry
Cy	Cyclohexane
DavePhos	2-Dicyclohexylphosphino-2′-(N,N-dimethylamino)biphenyl
dba	Dibenzylideneacetone
DEPT	Distortion-less Enhancement by Polarization Transfer
DFT	Density functional theory
DMAc	Dimethylacetamide
DMF	N,N-Dimethylformamide

DPEPhos	Oxydi-2,1-phenylene)bis(diphenylphosphine
Dppe	1,2-Bis(diphenylphosphino)ethane
Dppf	1,1'- Bis(diphenylphosphanyl)ferrocene
DPV	Differential Pulse Voltammetry
EI	Electron Impact
EI-MS	Electron impact- mass spectrometry
Equiv.	Equivalent
ESI	Electrospray ionization
Et_3N	Triethylamine
GC	Gas Chromatography
h	Hour
HMBC	Heteronuclear multiple-bond correlation spectroscopy
HOMO	Highest occupied molecular orbital
HSQC	Heteronuclear single quantum coherence spectroscopy
HSV-1	Simplex virus type 1
Hz	Hertz (S^{-1})
IR	Infrared Spectroscopy
J	Coupling constant
L	Ligand
LCD	Liquid crystal display
LUMO	Lowest unoccupied molecular orbital
m/z	Mass-to-charge ratio
MeCN	Acetonitrile
mp	Melting Point
MS	Mass spectrometry
NHC	N-heterocyclic carbene
NMR	Nuclear magnetic resonance
NOESY	Nuclear Overhauser Effect Spectroscopy
Nu	Nucleophile

ORTEP	Oak Ridge Thermal Ellipsoid Plot
OTf	Triflate (trifluoromethanesulfonate)
$PCy_3 \cdot HBF_4$	Tricyclohexylphosphine tetrafluoroborate
PEG	Polyethylene glycol
Ph	Phenyl
PPh3	Triphenylphosphine
ppm	Parts per Million
$P\mathit{t}Bu_3 \cdot HBF_4$	Tri-*tert*-butylphosphonium tetrafluoroborate
rt	Room temperature
Ru-Phos	2-Dicyclohexylphosphino-2′,6′-diisopropoxybiphenyl
SPhos	2-Dicyclohexylphosphino-2',6'-dimethoxybiphenyl
Suzuki-Miyaura reactions	SMR
TBAPF6	Tetrabutylammonium hexafluorophosphate
Tf_2O	Trifluoromethanesulfonic anhydride
TFA	Trifluoroacetic Acid
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography
TMS	Trimethylsilane
UV/Vis	Ultraviolet and visible absorption spectroscopy
VZV	Varicella-zoster virus
XantPhos	4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene
XPhos	2-Dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl
XPhos($\mathit{t}Bu_2$)	2-Di-*tert*-butylphosphino-2′,4′,6′-triisopropylbiphenyl
λ	Wavelength
ϕ	Fluorescence quantum yield

List of Figures

List of Tables

List of Schemes

`

References and notes

(1) (a) Knappke, C. E.; von Wangelin, A. J. *Chem. Soc. Rev.* **2011**, *40*, 4948-4962; (b) Rossi, R.; Bellina, F.; Carpita, A. *Synthesis* **2004**, *2004*, 2419-2440; (c) Ohno, H. *Asian J. Org. Chem.* **2013**, *2*, 18-28; (d) Beletskaya, I. P.; Averin, A. D.; Bessmertnykh, A. G.; Denat, F.; Guilard, R. *Russ. J. Org. Chem.* **2010**, *46*, 947-967; (e) Torborg, C.; Beller, M. *Adv. Synth. Catal.* **2009**, *351*, 3027-3043; (f) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem. Int. Ed.* **2005**, *44*, 4442-4489; (g) Heravi, M. M.; Hashemi, E. *Tetrahedron* **2012**, *68*, 9145-9178; (h) Heravi, M. M.; Hashemi, E. *Monatsh. Chem.* **2012**, *143*, 861-880; (i) Heravi, M. M.; Hashemi, E.; Nazari, N. *Mol. Divers.* **2014**, *18*, 441-472.

(2) Allred, A. L. *J. Inorg. Nucl. Chem.* **1961**, *17*, 215-221.

(3) Johansson Seechurn, C. C.; Kitching, M. O.; Colacot, T. J.; Snieckus, V. *Angew. Chem. Int. Ed.* **2012**, *51*, 5062-5085.

(4) Fortman, G. C.; Nolan, S. P. *Chem. Soc. Rev.* **2011**, *40*, 5151-5169.

(5) (a) Amatore, C.; Jutand, A.; Mbarki, M. A. *Organometallics* **1992**, *11*, 3009-3013; (b) Surry, D. S.; Buchwald, S. L. *Chem. Sci.* **2011**, *2*, 27-50.

(6) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009-3066.

(7) (a) Colacino, E.; Martinez, J.; Lamaty, F.; Patrikeeva, L. S.; Khemchyan, L. L.; Ananikov, V. P.; Beletskaya, I. P. *Coord. Chem. Rev.* **2012**, *256*, 2893-2920; (b) Balanta, A.; Godard, C.; Claver, C. *Chem. Soc. Rev.* **2011**, *40*, 4973-4985.

(8) (a) Zapf, A.; Ehrentraut, A.; Beller, M. *Angew. Chem. Int. Ed.* **2000**, *39*, 4153-4155; (b) Kollhofer, A.; Pullmann, T.; Plenio, H. *Angew. Chem. Int. Ed.* **2003**, *42*, 1056-1058.

(9) (a) Dierkes, P.; van Leeuwen, P. W. N. M. *J. Chem. Soc., Dalton Trans.* **1999**, 1519-1530; (b) Tolman, C. A. *Chem. Rev.* **1977**, *77*, 313-348; (c) Birkholz, M. N.; Freixa, Z.; van Leeuwen, P. W. *Chem. Soc. Rev.* **2009**, *38*, 1099-1118; (d) Freixa, Z.; van Leeuwen, P. W. N. M. *Dalton Trans.* **2003**, 1890-1901.

(10) Okeefe, D. F.; Dannock, M. C.; Marcuccio, S. M. *Tetrahedron Lett.* **1992**, *33*, 6679-6680.

(11) Hayashi, T.; Konishi, M.; Kumada, M. *Tetrahedron Lett.* **1979**, 1871-1874.

(12) (a) Altman, R. A.; Buchwald, S. L. *Nature protocols* **2007**, *2*, 3115-3121; (b) Altman, R. A.; Fors, B. P.; Buchwald, S. L. *Nature protocols* **2007**, *2*, 2881-2887; (c) Barder, T. E.; Walker, S. D.; Martinelli, J. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 4685-4696; (d) Surry, D. S.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2008**, *47*, 6338-6361; (e) Yang, Y.; Buchwald, S. L. *J. Am. Chem. Soc.* **2013**, *135*, 10642-10645; (f) Fu, G. C. *Acc. Chem. Res.* **2008**, *41*, 1555-1564.

(13) (a) Fors, B. P.; Davis, N. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2009**, *131*, 5766-5768; (b) Biscoe, M. R.; Fors, B. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **2008**, *130*, 6686-6687.

(14) (a) Valente, C.; Calimsiz, S.; Hoi, K. H.; Mallik, D.; Sayah, M.; Organ, M. G. *Angew. Chem. Int. Ed.* **2012**, *51*, 3314-3332; (b) Kantchev, E. A.; O'Brien, C. J.; Organ, M. G. *Angew. Chem. Int. Ed.* **2007**, *46*, 2768-2813; (c) Blangetti, M.; Rosso, H.; Prandi, C.; Deagostino, A.; Venturello, P. *Molecules* **2013**, *18*, 1188-1213.

(15) Lennox, A. J. J.; Lloyd-Jones, G. C. *Angew. Chem. Int. Ed.* **2013**, *52*, 7362-7370.

(16) (a) Polshettiwar, V.; Decottignies, A.; Len, C.; Fihri, A. *ChemSusChem* **2010**, *3*, 502-522; (b) Rohlich, C.; Wirth, A. S.; Kohler, K. *Chemistry* **2012**, *18*, 15485-15494.

(17) (a) Miyaura, N.; Suzuki, A. *J. Chem. Soc., Chem. Commun.* **1979**, 866-867; (b) Miyaura, N.; Yamada, K.; Suzuki, A. *Tetrahedron Lett.* **1979**, *20*, 3437-3440.

(18) (a) Rossi, R.; Bellina, F.; Lessi, M. *Adv. Synth. Catal.* **2012**, *354*, 1181-1255; (b) Gujral, S. S.; Khatri, S.; Riyal, P.; Gahlot, V. *Indo Glob. J. Pharm. Sci.* **2012**, *2*, 351-367.

(19) (a) Noel, T.; Buchwald, S. L. *Chem. Soc. Rev.* **2011**, *40*, 5010-5029; (b) Batail, N.; Genelot, M.; Dufaud, V.; Joucla, L.; Djakovitch, L. *Catal. Today* **2011**, *173*, 2-14; (c) Magano, J.; Dunetz, J. R. *Chem. Rev.* **2011**, *111*, 2177-2250; (d) Kim, A.; Park, J. C.; Kim, M.; Heo, E.; Song, H.; Park, K. H. *J. Nanosci. Nanotechno.* **2014**, *14*, 1872-1883; (e) Slagt, V. F.; de Vries, A. H. M.; de Vries, J. G.; Kellogg, R. M. *Org. Process Res. Dev.* **2010**, *14*, 30-47.

(20) Suzuki, A. *Angew. Chem. Int. Ed.* **2011**, *50*, 6722-6737.

(21) (a) Mkhalid, I. A. I.; Barnard, J. H.; Marder, T. B.; Murphy, J. M.; Hartwig, J. F. *Chem. Rev.* **2010**, *110*, 890-931; (b) Leermann, T.; Leroux, F. R.; Colobert, F. *Org. Lett.* **2011**, *13*, 4479-4481.

(22) Ishiyama, T.; Murata, M.; Miyaura, N. *J. Org. Chem.* **1995**, *60*, 7508-7510.

(23) (a) Hartwig, J. F. *Acc. Chem. Res.* **2012**, *45*, 864-873; (b) Hartwig, J. F. *Chem. Soc. Rev.* **2011**, *40*, 1992-2002; (c) Billingsley, K. L.; Barder, T. E.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2007**, *46*, 5359-5363; (d) Takagi, J.; Sato, K.; Hartwig, J. F.; Ishiyama, T.; Miyaura, N. *Tetrahedron Lett.* **2002**, *43*, 5649-5651.

(24) (a) Crabtree, R. H. *The Organometallic Chemistry of the Transition Metals (4ed)*; John Wiley & Sons: New Jersey, 2005; (b) Meijere, A. d.; Diederich, F. *Metal-Catalyzed Cross-Coupling Reactions*; WILEY-VCH, 1998; (c) Kochi, J. K. *Organometallic Mechanism and Catalysis*; Academic Press: New York, 1978; (d) Martin, R.; Buchwald, S. L. *Acc. Chem. Res.* **2008**, *41*, 1461-1473; (e) Matos, K.; Soderquist, J. A. *J. Org. Chem.* **1998**, *63*, 461-470.

(25) Uenishi, J.; Beau, J. M.; Armstrong, R. W.; Kishi, Y. *J. Am. Chem. Soc.* **1987**, *109*, 4756-4758.

(26) (a) Molnar, A. *Chem. Rev.* **2011**, *111*, 2251-2320; (b) Phan, N. T. S.; Van Der Sluys, M.; Jones, C. W. *Adv. Synth. Catal.* **2006**, *348*, 609-679.

(27) Tùng, Đ. n. T.; Tuân, Đ. n. T.; Rasool, N.; Villinger, A.; Reinke, H.; Fischer, C.; Langer, P. *Adv. Synth. Catal.* **2009**, *351*, 1595-1609.

(28) Rossi, R.; Bellina, F.; Lessia, M. *Adv. Synth. Catal.* **2012**, *354*, 1181-1255.

(29) Zhou, Q.; Wei, S.; Han, W. *J. Org. Chem.* **2014**, *79*, 1454-1460.

(30) Decottignies, A.; Fihri, A.; Azemar, G.; Djedaini-Pilard, F.; Len, C. *Catal. Commun.* **2013**, *32*, 101-107.

(31) de Koning, P. D.; McAndrew, D.; Moore, R.; Moses, I. B.; Boyles, D. C.; Kissick, K.; Stanchina, C. L.; Cuthbertson, T.; Kamatani, A.; Rahman, L.; Rodriguez, R.; Urbina, A.; Sandoval, A.; Rose, P. R. *Org. Process Res. Dev.* **2011**, *15*, 1018-1026.

(32) Ishikura, M.; Imaizumi, K.; Katagiri, N. *Heterocycles* **2000**, *53*, 553-556.

(33) Xu, G.; Fu, W.; Liu, G.; Senanayake, C. H.; Tang, W. *J. Am. Chem. Soc.* **2014**, *136*, 570-573.

(34) (a) Lan, P.; Banwell, M. G.; Ward, J. S.; Willis, A. C. *Org. Lett.* **2014**, *16*, 228-231; (b) Lan, P.; Banwell, M. G.; Willis, A. C. *J. Org. Chem.* **2014**, *79*, 2829-2842.

(35) Nicolaou, K. C.; Bheema Rao, P.; Hao, J.; Reddy, M. V.; Rassias, G.; Huang, X.; Chen, D. Y.; Snyder, S. A. *Angew. Chem. Int. Ed.* **2003**, *42*, 1753-1758.

(36) Torrado, A.; Iglesias, B.; López, S.; de Lera, A. R. *Tetrahedron* **1995**, *51*, 2435-2454.

(37) (a) Guram, A. S.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 7901-7902; (b) Paul, F.; Patt, J.; Hartwig, J. F. *J. Am. Chem. Soc.* **1994**, *116*, 5969-5970.

(38) Abaev, V. T.; Serdyuk, O. V. *Russ. Chem. Rev.* **2008**, *77*, 177-192.

(39) Bariwal, J.; Van der Eycken, E. *Chem. Soc. Rev.* **2013**, *42*, 9283-9303.

(40) Ji, J.; Bunnelle, W. H.; Li, T.; Pace, J. M.; Schrimpf, M. R.; Sippy, K. B.; Anderson, D. J.; Meyer, M. D. *Pure Appl. Chem.* **2005**, *77*, 2041–2045.

(41) Federsel, H.-J.; Hedberg, M.; Tian, W. *Org. Process Res. Dev.* **2008**, *12*, 512-521.

(42) (a) Olivier, L.; Daniel, K.; Stephan, A.; Hans, B. M.; Mark, M.; Beat, S.; Gottfried, S. *WO-Patent 03066613* **2003**; (b) Hopkin, M. D.; Baxendale, I. R.; Ley, S. V. *Org. Biomol. Chem.* **2013**, *11*, 1822-1839.

(43) Ueno, A.; Kitawaki, T.; Chida, N. *Org. Lett.* **2008**, *10*, 1999-2002.

(44) Mari, M.; Bartoccini, F.; Piersanti, G. *J. Org. Chem.* **2013**, *78*, 7727-7734.

(45) (a) Rossi, R.; Bellina, F.; Lessi, M.; Manzini, C. *Adv. Synth. Catal.* **2014**, *356*, 17-117; (b) Mei, T. S.; Kou, L.; Ma, S.; Engle, K. M.; Yu, J. Q. *Synthesis* **2012**, *44*, 1778-1791.

(46) Ackermann, L. *Chem. Rev.* **2011**, *111*, 1315-1345.

(47) (a) Gorelsky, S. I.; Lapointe, D.; Fagnou, K. *J. Org. Chem.* **2012**, *77*, 658-668; (b) Gorelsky, S. I.; Lapointe, D.; Fagnou, K. *J. Am. Chem. Soc.* **2008**, *130*, 10848-10849; (c) Sun, H. Y.; Gorelsky, S. I.; Stuart, D. R.; Campeau, L. C.; Fagnou, K. *J. Org. Chem.* **2010**, *75*, 8180-8189.

(48) (a) Yamaguchi, J.; Yamaguchi, A. D.; Itami, K. *Angew. Chem. Int. Ed.* **2012**, *51*, 8960-9009; (b) Chen, D. Y.; Youn, S. W. *Chemistry* **2012**, *18*, 9452-9474; (c) Schipper, D. J.; Fagnou, K. *Chem. Mater.* **2011**, *23*, 1594-1600.

(49) Schmidt, A. W.; Reddy, K. R.; Knolker, H. J. *Chem. Rev.* **2012**, *112*, 3193-3328.

(50) Butler, J. R.; Wang, C.; Bian, J.; Ready, J. M. *J. Am. Chem. Soc.* **2011**, *133*, 9956-9959.

(51) Gutekunst, W. R.; Baran, P. S. *J. Am. Chem. Soc.* **2011**, *133*, 19076-19079.

(52) Watanabe, T.; Oishi, S.; Fujii, N.; Ohno, H. *J. Org. Chem.* **2009**, *74*, 4720-4726.

(53) Knölker, H.-J. *Chem. Lett.* **2009**, *38*, 8-13.

(54) Liegault, B.; Lee, D.; Huestis, M. P.; Stuart, D. R.; Fagnou, K. *J. Org. Chem.* **2008**, *73*, 5022-5028.

(55) Mandal, D.; Yamaguchi, A. D.; Yamaguchi, J.; Itami, K. *J. Am. Chem. Soc.* **2011**, *133*, 19660-19663.

(56) (a) Anthony, J. E. *Chem. Rev.* **2006**, *106*, 5028-5048; (b) Wu, W.; Liu, Y.; Zhu, D. *Chem. Soc. Rev.* **2010**, *39*, 1489-1502.

(57) (a) Klauk, H.; Halik, M.; Zschieschang, U.; Schmid, G.; Radlik, W.; Weber, W. *J. Appl. Phys.* **2002**, *92*, 5259-5263; (b) Kelley, T. W.; Boardman, L. D.; Dunbar, T. D.; Muyres, D. V.; Pellerite, M. J.; Smith, T. Y. P. *J. Phys. Chem. B* **2003**, *107*, 5877-5881; (c) Lin, Y. Y.; Gundlach, D. J.; Nelson, S. F.; Jackson, T. N. *IEEE Electron Device Lett.* **1997**, *18*, 606-608; (d) Wang, C. S.; Nishida, J.; Bryce, M. R.; Yamashita, Y. *Bull. Chem. Soc. Jpn.* **2012**, *85*, 136-143.

(58) (a) Payne, M. M.; Parkin, S. R.; Anthony, J. E.; Kuo, C. C.; Jackson, T. N. *J. Am. Chem. Soc.* **2005**, *127*, 4986-4987; (b) Laquindanum, J. G.; Katz, H. E.; Lovinger, A. J. *J. Am. Chem. Soc.* **1998**, *120*, 664-672.

(59) (a) Valiyev, F.; Hu, W. S.; Chen, H. Y.; Kuo, M. Y.; Chao, I.; Tao, Y. T. *Chem. Mater.* **2007**, *19*, 3018-3026; (b) Tang, M. L.; Okamoto, T.; Bao, Z. N. *J. Am. Chem. Soc.* **2006**, *128*, 16002-16003.

(60) (a) Li, Y. N.; Wu, Y. L.; Gardner, S.; Ong, B. S. *Adv. Mater.* **2005**, *17*, 849-853; (b) Wu, Y. L.; Li, Y. N.; Gardner, S.; Ong, B. S. *J. Am. Chem. Soc.* **2005**, *127*, 614-618; (c) Wakim, S.; Bouchard, J.; Simard, M.; Drolet, N.; Tao, Y.; Leclerc, M. *Chem. Mater.* **2004**, *16*, 4386-4388.

(61) Ma, Y. Q.; Sun, Y. M.; Liu, Y. Q.; Gao, J. H.; Chen, S. Y.; Sun, X. B.; Qiu, W. F.; Yu, G.; Cui, G. L.; Hu, W. P.; Zhu, D. B. *J. Mater. Chem.* **2005**, *15*, 4894-4898.

(62) Xiao, K.; Liu, Y. Q.; Qi, T.; Zhang, W.; Wang, F.; Gao, J. H.; Qiu, W. F.; Ma, Y. Q.; Cui, G. L.; Chen, S. Y.; Zhan, X. W.; Yu, G.; Qin, J. G.; Hu, W. P.; Zhu, D. B. *J. Am. Chem. Soc.* **2005**, *127*, 13281-13286.

(63) Gao, J. H.; Li, R. J.; Li, L. Q.; Meng, Q.; Jiang, H.; Li, H. X.; Hu, W. P. *Adv. Mater.* **2007**, *19*, 3008-3011.

(64) Qi, T.; Qiu, W. F.; Liu, Y. Q.; Zhang, H. J.; Gao, X. K.; Liu, Y.; Lu, K.; Du, C. Y.; Yu, G.; Zhu, D. B. *J. Org. Chem.* **2008**, *73*, 4638-4643.

(65) Qi, T.; Guo, Y.; Liu, Y.; Xi, H.; Zhang, H.; Gao, X.; Liu, Y.; Lu, K.; Du, C.; Yu, G.; Zhu, D. *Chem. Commun.* **2008**, 6227-6229.

(66) (a) Balaji, G.; Valiyaveettil, S. *Org. Lett.* **2009**, *11*, 3358-3361; (b) Balaji, G.; Phua, D. I.; Shim, W. L.; Valiyaveettil, S. *Org. Lett.* **2010**, *12*, 232-235.

(67) (a) Takahashi, T.; Takenobu, T.; Takeya, J.; Iwasa, Y. *Adv. Funct. Mater.* **2007**, *17*, 1623-1628; (b) Operamolla, A.; Farinola, G. M. *Eur. J. Org. Chem.* **2011**, *2011*, 423-450.

(68) Ji, Q.; Gao, J.; Wang, J.; Yang, C.; Hui, X.; Yan, X.; Wu, X.; Xie, Y.; Wang, M. W. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 2891-2893.

(69) Dang, T. T.; Rasool, N.; Dang, T. T.; Reinke, H.; Langer, P. *Tetrahedron Lett.* **2007**, *48*, 845-847.

(70) (a) Nozaki, K.; Takahashi, K.; Nakano, K.; Hiyama, T.; Tang, H. Z.; Fujiki, M.; Yamaguchi, S.; Tamao, K. *Angew. Chem. Int. Ed. Engl.* **2003**, *42*, 2051-2053; (b) Koeckelberghs, G.; De Cremer, L.; Vanormelingen, W.; Dehaen, W.; Verbiest, T.; Persoons, A.; Samyn, C. *Tetrahedron* **2005**, *61*, 687-691.

(71) Mitsudo, K.; Shimohara, S.; Mizoguchi, J.; Mandai, H.; Suga, S. *Org. Lett.* **2012**, *14*, 2702-2705.

(72) Weymiens, W.; Zaal, M.; Slootweg, J. C.; Ehlers, A. W.; Lammertsma, K. *Inorg. Chem.* **2011**, *50*, 8516-8523.

(73) (a) Mei, J. G.; Diao, Y.; Appleton, A. L.; Fang, L.; Bao, Z. N. *J. Am. Chem. Soc.* **2013**, *135*, 6724-6746; (b) Lin, Y. Z.; Li, Y. F.; Zhan, X. W. *Chem. Soc. Rev.* **2012**, *41*, 4245-4272; (c) Jiang, W.; Li, Y.; Wang, Z. H. *Chem. Soc. Rev.* **2013**, *42*, 6113-6127.

(74) Goldmann, C.; Haas, S.; Krellner, C.; Pernstich, K. P.; Gundlach, D. J.; Batlogg, B. *J. Appl. Phys.* **2004**, *96*, 2080-2086.

(75) Liu, Y.; Wang, Y.; Wu, W. P.; Liu, Y. Q.; Xi, H. X.; Wang, L. M.; Qiu, W. F.; Lu, K.; Du, C. Y.; Yu, G. *Adv. Funct. Mater.* **2009**, *19*, 772-778.

(76) (a) Nakano, M.; Niimi, K.; Miyazaki, E.; Osaka, I.; Takimiya, K. *J. Org. Chem.* **2012**, *77*, 8099-8111; (b) Nakano, M.; Shinamura, S.; Houchin, Y.; Osaka, I.; Miyazaki, E.; Takimiya, K. *Chem. Commun.* **2012**, *48*, 5671-5673.

(77) Takimiya, K.; Shinamura, S.; Osaka, I.; Miyazaki, E. *Adv. Mater.* **2011**, *23*, 4347-4370.

(78) Qiu, L.; Yu, C.; Zhao, N.; Chen, W.; Guo, Y.; Wan, X.; Yang, R.; Liu, Y. *Chem. Commun.* **2012**, *48*, 12225-12227.

(79) (a) Murray, M. M.; Kaszynski, P.; Kaisaki, D. A.; Chang, W. H.; Dougherty, D. A. *J. Am. Chem. Soc.* **1994**, *116*, 8152-8161; (b) Jin, Y.; Kim, K.; Song, S.; Kim, J.; Kim, J.; Park, S. H.; Lee, K.; Suh, H. *Bull. Korean Chem. Soc.* **2006**, *27*, 1043-1047.

(80) (a) Kaszynski, P.; Dougherty, D. A. *J. Org. Chem.* **1993**, *58*, 5209-5220; (b) Samsoniya, S. A.; Trapaidze, M. V. *Russ. Chem. Rev.* **2007**, *76*, 348-361.

(81) Heller, G. *Ber. Dtsch. Chem. Ges.* **1917**, *50*, 1202-1203.

(82) (a) Ruggli, P. *Ber. Dtsch. Chem. Ges.* **1917**, *50*, 883-893; (b) Ruggli, P.; Zaeslin, H. *Helv. Chim. Acta* **1935**, *18*, 845-852; (c) Jackson, A. H.; Johnston, D. N.; Shannon, P. V. R. *J. Chem. Soc., Chem. Commun.* **1975**, 911-912.

(83) (a) Grinyov, A. N.; Ryabova, S. Y. *Khim Geterotsikl+* **1982**, 199-200; (b) Grinyov, A. N.; Ryabova, S. Y. *Khim Geterotsikl+* **1982**, 201-205.

(84) (a) Durben, S.; Baumgartner, T. *Inorg. Chem.* **2011**, *50*, 6823-6836; (b) Chen, D.-M.; Qin, Q.; Sun, Z.-B.; Peng, Q.; Zhao, C.-H. *Chem. Commun.* **2014**, *50*, 782-784; (c) Min, J.; Wang, P.; Srinivasan, S.; Nwachukwu, J. C.; Guo, P.; Huang, M.; Carlson, K. E.; Katzenellenbogen, J. A.; Nettles, K. W.; Zhou, H.-B. *J. Med. Chem.* **2013**, *56*, 3346-3366.

(85) Hussain, M.; Tung, D. T.; Langer, P. *Synlett* **2009**, 1822-1826.

(86) Meech, S. R.; Phillips, D. *J. Photochem.* **1983**, *23*, 193-217.

(87) (a) Galande, C.; Mohite, A. D.; Naumov, A. V.; Gao, W.; Ci, L.; Ajayan, A.; Gao, H.; Srivastava, A.; Weisman, R. B.; Ajayan, P. M. *Sci Rep* **2011**, *1*, 85; (b) Asiri, A. M.; Khan, S. A.; Al-Amoudi, M. S.; Alamry, K. A. *Bull. Korean Chem. Soc.* **2012**, *33*, 1900-1906.

(88) (a) Schroter, S.; Stock, C.; Bach, T. *Tetrahedron* **2005**, *61*, 2245-2267; (b) Bach, T.; Kruger, L. *Eur. J. Org. Chem.* **1999**, 2045-2057; (c) Stock, C.; Hofer, F.; Bach, T. *Synlett* **2005**, 511-513.

(89) (a) Cao, R. H.; Peng, W. L.; Wang, Z. H.; Xu, A. L. *Curr Med Chem* **2007**, *14*, 479-500; (b) Alekseyev, R. S.; Kurkin, A. V.; Yurovskaya, M. A. *Chem. Heterocycl. Compd.* **2009**, *45*, 889-925; (c) Kumar, E. V. K. S.; Etukala, J. R.; Ablordeppey, S. Y. *Mini-Rev. Med. Chem.* **2008**, *8*, 538-554.

(90) (a) Choshi, T.; Yamada, S.; Sugino, E.; Kuwada, T.; Hibino, S. *Synlett* **1995**, 147-148; (b) Choshi, T.; Yamada, S.; Sugino, E.; Kuwada, T.; Hibino, S. *J. Org. Chem.* **1995**,

60, 5899-5904; (c) Achab, S.; Guyot, M.; Potier, P. *Tetrahedron Lett.* **1995**, *36*, 2615-2618; (d) Miyake, F. Y.; Yakushijin, K.; Horne, D. A. *Angew. Chem. Int. Ed.* **2005**, *44*, 3280-3282.

(91) Kim, J. S.; ShinYa, K.; Furihata, K.; Hayakawa, Y.; Seto, H. *Tetrahedron Lett.* **1997**, *38*, 3431-3434.

(92) (a) Subbaraju, G. V.; Kavitha, J.; Rajasekhar, D.; Jimenez, J. I. *J. Nat. Prod.* **2004**, *67*, 461-462; (b) Paulo, A.; Gomes, E. T.; Steele, J.; Warhurst, D. C.; Houghton, P. J. *Planta Med.* **2000**, *66*, 30-34; (c) Sharaf, M. H. M.; Schiff, P. L.; Tackie, A. N.; Phoebe, C. H.; Johnson, R. L.; Minick, D.; Andrews, C. W.; Crouch, R. C.; Martin, G. E. *J. Heterocycl. Chem.* **1996**, *33*, 789-797; (d) Yang, S. W.; Abdel-Kader, M.; Malone, S.; Werkhoven, M. C.; Wisse, J. H.; Bursuker, I.; Neddermann, K.; Fairchild, C.; Raventos-Suarez, C.; Menendez, A. T.; Lane, K.; Kingston, D. G. *J. Nat. Prod.* **1999**, *62*, 976-983.

(93) (a) Arzel, E.; Rocca, P.; Grellier, P.; Labaeid, M.; Frappier, F.; Gueritte, F.; Gaspard, C.; Marsais, F.; Godard, A.; Queguiner, G. *J. Med. Chem.* **2001**, *44*, 949-960; (b) Wright, C. W.; Addae-Kyereme, J.; Breen, A. G.; Brown, J. E.; Cox, M. F.; Croft, S. L.; Gokcek, Y.; Kendrick, H.; Phillips, R. M.; Pollet, P. L. *J. Med. Chem.* **2001**, *44*, 3187-3194; (c) Caprio, V.; Guyen, B.; Opoku-Boahen, Y.; Mann, J.; Gowan, S. M.; Kelland, L. M.; Read, M. A.; Neidle, S. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 2063-2066; (d) Cimanga, K.; Li, Y.; de Bruyne, T.; Apers, S.; Cos, P.; Bakana, P.; Kambu, K.; Tona, L.; Pieters, L.; Vanden Berghe, D.; Vlietinck, A. J. *Pharm. Pharmacol. Commun.* **2000**, *6*, 321-325.

(94) (a) Seville, S.; Phillips, R. M.; Shnyder, S. D.; Wright, C. W. *Bioorg. Med. Chem.* **2007**, *15*, 6353-6360; (b) Riechert-Krause, F.; Eick, A.; Grunert, R.; Bednarski, P. J.; Weisz, K. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 2380-2383; (c) Li, B.; Yue, Z. Z.; Feng, J. M.; He, Q.; Miao, Z. H.; Yang, C. H. *Eur. J. Med. Chem.* **2013**, *66*, 531-539; (d) Rajanarendar, E.; Govardhan Reddy, K.; Ramakrishna, S.; Nagi Reddy, M.; Shireesha, B.; Durgaiah, G.; Reddy, Y. N. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 6677-6680; (e) Yin, R. J.; Zhang, M.; Hao, C.; Wang, W.; Qiu, P. J.; Wan, S. B.; Zhang, L. J.; Jiang, T. *Chem. Commun.* **2013**, *49*, 8516-8518; (f) Boddupally, P. V.; Hahn, S.; Beman, C.; De, B.; Brooks, T. A.; Gokhale, V.; Hurley, L. H. *J. Med. Chem.* **2012**, *55*, 6076-6086; (g) Beauchard, A.; Jaunet, A.; Murillo, L.; Baldeyrou, B.; Lansiaux, A.; Cherouvrier, J. R.; Domon, L.; Picot, L.; Bailly, C.; Besson, T.; Thiery, V. *Eur. J. Med. Chem.* **2009**, *44*, 3858-3865.

(95) (a) Rocha e Silva, L. F.; Montoia, A.; Amorim, R. C.; Melo, M. R.; Henrique, M. C.; Nunomura, S. M.; Costa, M. R.; Andrade Neto, V. F.; Costa, D. S.; Dantas, G.; Lavrado, J.; Moreira, R.; Paulo, A.; Pinto, A. C.; Tadei, W. P.; Zacardi, R. S.; Eberlin, M. N.; Pohlit, A. M. *Phytomedicine* **2012**, *20*, 71-76; (b) Van Baelen, G.; Hostyn, S.; Dhooghe, L.; Tapolcsanyi, P.; Matyus, P.; Lemiere, G.; Dommisse, R.; Kaiser, M.; Brun, R.; Cos, P.; Maes, L.; Hajos, G.; Riedl, Z.; Nagy, I.; Maes, B. U.; Pieters, L. *Bioorg. Med. Chem.* **2009**, *17*, 7209-7217.

(96) Queiroz, M. J.; Ferreira, I. C.; De Gaetano, Y.; Kirsch, G.; Calhelha, R. C.; Estevinho, L. M. *Bioorg. Med. Chem.* **2006**, *14*, 6827-6831.

(97) (a) Sako, K.; Aoyama, H.; Sato, S.; Hashimoto, Y.; Baba, M. *Bioorg. Med. Chem.* **2008**, *16*, 3780-3790; (b) Peczynskaczoch, W.; Pognan, F.; Kaczmarek, L.; Boratynski, J. *J. Med. Chem.* **1994**, *37*, 3503-3510.

(98) (a) Okamoto, T. A., T.; Izumi, T.; Inaba; S.; Yamamoto, H. *Japanese Patent* **1972**, No. 722019; (b) Winters, J. D. M., N. *West German patent* **1975**, No. 2442513.

(99) (a) Shiomi, M.; Ito, T. *Eur. J. Pharmacol.* **2001**, *431*, 127-131; (b) Ueshima, K.; Akihisa-Umeno, H.; Nagayoshi, A.; Takakura, S.; Matsuo, M.; Mutoh, S. *Biol. Pharm. Bull.* **2005**, *28*, 247-252.

(100) (a) Lee, C. W.; Im, Y.; Seo, J.-A.; Lee, J. Y. *Org. Electron.* **2013**, *14*, 2687-2691; (b) Lee, C. W.; Im, Y.; Seo, J. A.; Lee, J. Y. *Chem. Commun.* **2013**, *49*, 9860-9862; (c) Kim, S. J.; Kim, Y. J.; Son, Y. H.; Hur, J. A.; Um, H. A.; Shin, J.; Lee, T. W.; Cho, M. J.; Kim, J. K.; Joo, S.; Yang, J. H.; Chae, G. S.; Choi, K.; Kwon, J. H.; Choi, D. H. *Chem. Commun.* **2013**, *49*, 6788-6790; (d) Im, Y.; Lee, J. Y. *Chem. Commun.* **2013**, *49*, 5948-5950.

(101) Lee, C. W.; Lee, J. Y. *Adv. Mater.* **2013**, *25*, 5450-5454.

(102) Son, Y. H.; Kim, Y. J.; Park, M. J.; Oh, H.-Y.; Park, J. S.; Yang, J. H.; Suh, M. C.; Kwon, J. H. *J. Mater. Chem. C* **2013**, *1*, 5008-5014.

(103) (a) Tahri, A.; Buysens, K. J.; Van der Eycken, E. V.; Vandenberghe, D. M.; Hoornaert, G. J. *Tetrahedron* **1998**, *54*, 13211-13226; (b) Molina, P.; Alajarin, M.; Vidal, A.; Sanchezandrada, P. *J. Org. Chem.* **1992**, *57*, 929-939.

(104) (a) Vera-Luque, P.; Alajarin, R.; Alvarez-Builla, J.; Vaquero, J. J. *Org. Lett.* **2006**, *8*, 415-418; (b) Schneider, C.; Gueyrard, D.; Popowycz, F.; Benoit, J.; Goekjian, P. G. *Synlett* **2007**, 2237-2241.

(105) (a) Okuda, S.; Robison, M. M. *J. Am. Chem. Soc.* **1959**, *81*, 740-743; (b) Portela-Cubillo, F.; Surgenor, B. A.; Aitken, R. A.; Walton, J. C. *J. Org. Chem.* **2008**, *73*, 8124-8127.

(106) (a) Ghahremanzadeh, R.; Ahadi, S.; Bazgir, A. *Tetrahedron Lett.* **2009**, *50*, 7379-7381; (b) Gupta, S.; Kumar, B.; Kundu, B. *J. Org. Chem.* **2011**, *76*, 10154-10162; (c) Sharma, S. K.; Gupta, S.; Saifuddin, M.; Mandadapu, A. K.; Agarwal, P. K.; Gauniyal, H. M.; Kundu, B. *Tetrahedron Lett.* **2011**, *52*, 65-68.

(107) Kumar, A. S.; Rao, P. V. A.; Nagarajan, R. *Org. Biomol. Chem.* **2012**, *10*, 5084-5093.

(108) (a) Hostyn, S.; Van Baelen, G.; Lemière, G. L. F.; Maes, B. U. W. *Adv. Synth. Catal.* **2008**, *350*, 2653-2660; (b) Laha, J. K.; Petrou, P.; Cuny, G. D. *J. Org. Chem.* **2009**, *74*, 3152-3155.

(109) Markey, S. J.; Lewis, W.; Moody, C. J. *Org. Lett.* **2013**, *15*, 6306-6308.

(110) Zhang, X.; He, Q.; Xiang, H.; Song, S.; Miao, Z.; Yang, C. *Org. Biomol. Chem.* **2014**, *12*, 355-361.

(111) Yang, C.-C.; Tai, H.-M.; Sun, P.-J. *J. Chem. Soc., Perkin Trans. 1* **1997**, 2843-2850.

(112) Papamicael, C.; Queguiner, G.; Bourguignon, J.; Dupas, G. *Tetrahedron* **2001**, *57*, 5385-5391.

(113) Ishiyama, H.; Ohshita, K.; Abe, T.; Nakata, H.; Kobayashi, J. *Bioorg. Med. Chem.* **2008**, *16*, 3825-3830.

(114) Mazu, T. K.; Etukala, J. R.; Jacob, M. R.; Khan, S. I.; Walker, L. A.; Ablordeppey, S. Y. *Eur. J. Med. Chem.* **2011**, *46*, 2378-2385.

(115) Sharma, S. K.; Mandadapu, A. K.; Saifuddin, M.; Gupta, S.; Agarwal, P. K.; Mandwal, A. K.; Gauniyal, H. M.; Kundu, B. *Tetrahedron Lett.* **2010**, *51*, 6022-6024.

(116) Peng, H. X.; Chen, X. X.; Chen, Y. H.; He, Q.; Xie, Y. Y.; Yang, C. H. *Tetrahedron* **2011**, *67*, 5725-5731.

(117) Letessier, J.; Detert, H. *Synthesis* **2012**, *44*, 290-296.

(118) Cao, J.; Xu, Y. P.; Kong, L.; Cui, Y. M.; Hu, Z. Q.; Wang, G. H.; Deng, Y.; Lai, G. Q. *Org. Lett.* **2012**, *14*, 38-41.

(119) Iwaki, T.; Yasuhara, A.; Sakamoto, T. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1505-1510.

(120) Laha, J. K.; Barolo, S. M.; Rossi, R. A.; Cuny, G. D. *J. Org. Chem.* **2011**, *76*, 6421-6425.

(121) CCDC-1009792 contains all crystallographic details of this publication and is available free of charge at www.ccdc.cam.ac.uk/conts/retrieving.htmlor can be ordered from the following address: Cambridge Crystallographic Data Centre, 12 Union Road, GBCambridge CB21EZ; Fax: (+44)1223-336-033; or deposit@ccdc.cam.ac.uk.

(122) CCDC-1009793 contains all crystallographic details of this publication and is available free of charge at www.ccdc.cam.ac.uk/conts/retrieving.htmlor can be ordered from the following address: Cambridge Crystallographic Data Centre, 12 Union Road, GBCambridge CB21EZ; Fax: (+44)1223-336-033; or deposit@ccdc.cam.ac.uk.

(123) Jiang, W.; Tang, J.; Yang, W.; Ban, X.; Huang, B.; Dai, Y.; Sun, Y.; Duan, L.; Qiao, J.; Wang, L.; Qiu, Y. *Tetrahedron* **2012**, *68*, 5800-5805.

(124) Miao, Q. *Synlett* **2012**, 326-336.

(125) Liang, Z. X.; Tang, Q.; Mao, R. X.; Liu, D. Q.; Xu, J. B.; Miao, Q. *Adv. Mater.* **2011**, *23*, 5514-5518.

(126) (a) Kuwahara, A.; Nakano, K.; Nozaki, K. *J. Org. Chem.* **2005**, *70*, 413-419; (b) Nozaki, K.; Takahashi, K.; Nakano, K.; Hiyama, T.; Tang, H. Z.; Fujiki, M.; Yamaguchi, S.; Tamao, K. *Angew. Chem. Int. Ed.* **2003**, *42*, 2051-2053; (c) Kitawaki, T.; Hayashi, Y.; Ueno, A.; Chida, N. *Tetrahedron* **2006**, *62*, 6792-6801; (d) Zhou, Y. B.; Verkade, J. G. *Adv. Synth. Catal.* **2010**, *352*, 616-620; (e) Nguyen, H. H.; Kurth, M. J. *Org. Lett.* **2013**, *15*, 362-365.

(127) Hyung, K. T. M., K. S.; Beak, Y. M.; Kim, H. M.; Park, H. C.; Shin, J. Y., *PCT Int. Appl.* **2013**, WO 2013133575 A2013133571 2020130912.

(128) Chen, T. K.; Flowers, W. T. *J. Chem. Soc., Chem. Commun.* **1980**, 1139-1140.

(129) Thorn, D. L.; Hoffmann, R. *J. Am. Chem. Soc.* **1978**, *100*, 2079-2090.

(130) Casey, C. P.; Whiteker, G. T. *Isr. J. Chem.* **1990**, *30*, 299-304.

(131) Hamann, B. C.; Hartwig, J. F. *J. Am. Chem. Soc.* **1998**, *120*, 3694-3703.

(132) (a) Jean, L.; Rouden, J.; Maddaluno, J.; Lasne, M. C. *J. Org. Chem.* **2004**, *69*, 8893-8902; (b) Margolis, B. J.; Long, K. A.; Laird, D. L. T.; Ruble, J. C.; Pulley, S. R. *J. Org. Chem.* **2007**, *72*, 2232-2235.

(133) CCDC-998861-998862 contains all crystallographic details of this publication and is available free of charge at www.ccdc.cam.ac.uk/conts/retrieving.htmlor can be ordered from the following address: Cambridge Crystallographic Data Centre, 12 Union Road, GBCambridge CB21EZ; Fax: (+44)1223-336-033; or deposit@ccdc.cam.ac.uk.

(134) DFT calculations were carried out in cooperation with Dr. Khurshid Ayub; Department of Chemistry, COMSATS Institute of Information Technology, Abbottabad, Pakistan.

(135) (a) Javed, I.; Khurshid, A.; Arshad, M. N.; Wang, Y. *New J. Chem.* **2014**, *38*, 752-761; (b) Tao, T.; Peng, Y. X.; Huang, W.; You, X. Z. *J. Org. Chem.* **2013**, *78*, 2472-2481.

(136) (a) Su, T. H.; Fan, C. H.; Ou-Yang, Y. H.; Hsu, L. C.; Cheng, C. H. *J. Mater. Chem. C* **2013**, *1*, 5084-5092; (b) Tyagi, P.; Venkateswararao, A.; Thomas, K. R. *J. Org. Chem.* **2011**, *76*, 4571-4581; (c) Fan, C. H.; Sun, P.; Su, T. H.; Cheng, C. H. *Adv. Mater.* **2011**, *23*, 2981-2985.

(137) Thomas, K. R.; Tyagi, P. *J. Org. Chem.* **2010**, *75*, 8100-8111.

(138) (a) Harmenberg, J.; Wahren, B.; Bergman, J.; Akerfeldt, S.; Lundblad, L. *Antimicrob. Agents Chemother.* **1988**, *32*, 1720-1724; (b) Harmenberg, J.; Akesson-Johansson, A.; Graslund, A.; Malmfors, T.; Bergman, J.; Wahren, B.; Akerfeldt, S.; Lundblad, L.; Cox, S. *Antiviral Res.* **1991**, *15*, 193-204.

(139) (a) Hirata, K.; Araya, J.; Nakaike, S.; Kitamura, K.; Ishida, T. *Chem. Pharm. Bull.* **2001**, *49*, 44-48; (b) Deady, L. W.; Kaye, A. J.; Finlay, G. J.; Baguley, B. C.; Denny, W. A. *J. Med. Chem.* **1997**, *40*, 2040-2046.

(140) Manna, K.; Agrawal, Y. K. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 2688-2692.

(141) Pai, N. R.; Pusalkar, D. A. *J. Chem. Pharm. Res.* **2010**, *2*, 485-493.

(142) Shibinskaya, M. O.; Lyakhov, S. A.; Mazepa, A. V.; Andronati, S. A.; Turov, A. V.; Zholobak, N. M.; Spivak, N. Y. *Eur. J. Med. Chem.* **2010**, *45*, 1237-1243.

(143) Shibinskaya, M. O.; Karpenko, A. S.; Lyakhov, S. A.; Andronati, S. A.; Zholobak, N. M.; Spivak, N. Y.; Samochina, N. A.; Shafran, L. M.; Zubritsky, M. J.; Galat, V. F. *Eur. J. Med. Chem.* **2011**, *46*, 794-798.

(144) Avula, S.; Komsani, J. R.; Koppireddi, S.; Yadla, R.; Kanugula, A. K.; Kotamraju, S. *Med. Chem. Res.* **2012**, *22*, 3712-3718.

(145) Schunck, E.; Marchlewski, L. *Ber. Dtsch. Chem. Ges.* **1895**, *28*, 2525-2531.

(146) Wentrup, V. C.; Thetaz, C.; Tagliaferri, E.; Lindner, H. J.; Kitschke, B.; Winter, H.-W. *Angew. Chem.* **1980**, *4*, 556-557.

(147) Pratima Nikalje, A.; Alphonse, F.-A.; Routier, S.; Coudert, G.; Mérour, J.-Y. *Heterocycles* **2001**, *55*, 925-940.

(148) (a) Ackermann, L.; Althammer, A.; Mayer, P. *Synthesis* **2009**, *2009*, 3493-3503; (b) Ackermann, L.; Althammer, A. *Angew. Chem. Int. Ed.* **2007**, *46*, 1627-1629.

(149) Hung, T. Q.; Dang, T. T.; Villinger, A.; Sung, T. V.; Langer, P. *Org. Biomol. Chem.* **2012**, *10*, 9041-9044.

(150) Li, J. J.; Carson, K. G.; Trivedi, B. K.; Yue, W. S.; Ye, Q.; Glynn, R. A.; Miller, S. R.; Connor, D. T.; Roth, B. D.; Luly, J. R.; Low, J. E.; Heilig, D. J.; Yang, W.; Qin, S.; Hunt, S. *Biorg. Med. Chem.* **2003**, *11*, 3777-3790.

(151) CCDC 997724 - 997725 contains all crystallographic details of this publication and is available free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or can be ordered from the followingaddress: Cambridge Crystallographic Data Centre, 12 Union Road, GB-Cambridge CB21EZ; Fax: +44 1223 336 033; or deposit@ccdc.cam.ac.uk.

(152) DFT calculations were carried out in cooperation with Dr. Khurshid Ayub; Department of Chemistry, COMSATS Institute of Information Technology, Abbottabad, Pakistan.

(153) Naghavi, S. S.; Gruhn, T.; Alijani, V.; Fecher, G. H.; Felser, C.; Medjanik, K.; Kutnyakhov, D.; Nepijko, S. A.; Schönhense, G.; Rieger, R.; Baumgarten, M.; Müllen, K. *J. Mol. Spectrosc.* **2011**, *265*, 95-101.

(154) Tasler, S.; Bringmann, G. *Chemical record* **2002**, *2*, 113-126.

(155) (a) Fischer, E.; Hess, O. *Ber. Dtsch. Chem. Ges.* **1884**, *17*, 559-568; (b) Fischer, E.; Jourdan, F. *Ber. Dtsch. Chem. Ges.* **1883**, *16*, 2241-2245; (c) Borsche, W. *Liebigs Ann. Chem.* **1908**, *359*, 49-80.

(156) Moody, C. J. *Synlett* **1994**, 681-688.

(157) Sanz, R.; Escribano, J.; Pedrosa, M. R.; Aguado, R.; Arnaiz, F. J. *Adv. Synth. Catal.* **2007**, *349*, 713-718.

(158) Kano, S.; Sugino, E.; Shibuya, S.; Hibino, S. *J. Org. Chem.* **1981**, *46*, 3856-3859.

(159) (a) Knolker, H. J. *Synlett* **1992**, 371-387; (b) Knölker, H.-J. In *Nat. Prod. Synth. II*; Mulzer, J., Ed.; Springer Berlin Heidelberg, 2005; Vol. 244.

(160) Bedford, R. B.; Betham, M. *J. Org. Chem.* **2006**, *71*, 9403-9410.

(161) (a) Liu, Z. J.; Larock, R. C. *Org. Lett.* **2004**, *6*, 3739-3741; (b) Liu, Z. J.; Larock, R. C. *Tetrahedron* **2007**, *63*, 347-355.

(162) Hussain, M.; Toguem, S. M. T.; Ahmad, R.; Tung, D. T.; Knepper, I.; Villinger, A.; Langer, P. *Tetrahedron* **2011**, *67*, 5304-5318.

(163) (a) Bringmann, G.; Tasler, S.; Endress, H.; Kraus, J.; Messer, K.; Wohlfarth, M.; Lobin, W. *J. Am. Chem. Soc.* **2001**, *123*, 2703-2711; (b) Kitawaki, T.; Hayashi, Y.; Chida, N. *Heterocycles* **2005**, *65*, 1561-1567; (c) Borger, C.; Kataeva, O.; Knolker, H. J. *Org. Biomol. Chem.* **2012**, *10*, 7269-7273.

(164) Simokaitiene, J.; Stanislovaityte, E.; Grazulevicius, J. V.; Jankauskas, V. *Mol. Cryst. Liq. Cryst.* **2011**, *536*, 200/[432]-207/[439].

(165) Tsai, M. H.; Hong, Y. H.; Chang, C. H.; Su, H. C.; Wu, C. C.; Matoliukstyte, A.; Simokaitiene, J.; Grigalevicius, S.; Grazulevicius, J. V.; Hsu, C. P. *Adv. Mater.* **2007**, *19*, 862-866.

(166) Oishi, S.; Watanabe, T.; Sawada, J.; Asai, A.; Ohno, H.; Fujii, N. *J. Med. Chem.* **2010**, *53*, 5054-5058.

(167) Liegault, B.; Lee, D.; Huestis, M. P.; Stuart, D. R.; Fagnou, K. *J. Org. Chem.* **2008**, *73*, 5022-5028.

(168) Watanabe, T.; Ueda, S.; Inuki, S.; Oishi, S.; Fujii, N.; Ohno, H. *Chem Commun (Camb)* **2007**, 4516-4518.

(169) CCDC 957610 contains all crystallographic details of this publication and is available free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or can be ordered from the followingaddress: Cambridge Crystallographic Data Centre, 12 Union Road, GB-Cambridge CB21EZ; Fax: +44 1223 336 033; or deposit@ccdc.cam.ac.uk.

(170) CCDC- 957611 contains all crystallographic details of this publication and is available free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or can be ordered from the following address: Cambridge Crystallographic Data Centre, 12 Union Road, GBCambridge CB21EZ; Fax: (+44)1223-336-033; or deposit@ccdc.cam.ac.uk.

(171) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A. *Wallingford CT* **2009**.

(172) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648-5652.

(173) Lee, C. T.; Yang, W. T.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785-789.

(174) Hariharan, P. C.; Pople, J. A. *Theor. Chim. Acta.* **1973**, *28*, 213-222.

(175) Iaroshenko, V. O.; Ostrovskyi, D.; Ayub, K.; Spannenberg, A.; Langer, P. *Adv. Synth. Catal.* **2013**, *355*, 576-588.

(176) Ullah, H.; Shah, A. U. A.; Ayub, K.; Bilal, S. *J. Phys. Chem. C* **2013**, *117*, 4069-4078.

Curriculum Vitae

TRAN QUANG HUNG

M.Sc. in Organic and Bioorganic Chemistry.

Nationality:	Vietnamese.
Date and Place of Birth:	Feb 05, 1980 in Hanoi, Vietnam.
Marital Status:	Married, one child.
Adress:	Erich-Schlesinger str.19, Haus 01, Nr 1.07.03.2, 18059 Rostock, Germany.
E-mail:	*hungtq@gmail.com*

FIELDS OF INTEREST

Developing New Methodologies in Organic Synthesis.

Isolation and identification of Natural Products.

EDUCATION

2011 – now PhD in Organic synthesis (Rostock University)
Supervisor: Prof. Dr. rer. nat. Peter Langer
Subject: Synthesis of fused heterocycles by sequential palladium catalyzed cross-coupling reactions

2002 - 2005 Master in Natural Products Chemistry (Chemistry Department, Hanoi National University, Vietnam).
Supervisor: Dr. Manh Cuong Nguyen.
Subject: "Study on compositions and bioactivities of *Glycosmis Stenocarpa* (Drake) Tan. (Rutaceae)" (Excellent Degree).

1997 - 2001 Bachelor of Sciences (Chemistry Department, Hanoi National University, Vietnam).
Supervisor: Prof. Dr. Van Ngoc Huong.
Subject: "Isolation and identification of some bioactive compounds from *Cocculus trilobus*" (Good Degree).

SCHOLARSHIPS, AWARDS and CERTIFICATES

2010 Vietnamese Ministry of Education and Training scholarship

2006 Certificate of "NMR – Training Course" supported by DAAD

2003 & 2006 Certificate of "L'école franco-vietnamienne"

2002 - 2005 M.Sc. Degree in Organic Chemistry, (Note: Excellent Degree)

1997 - 2001 Bachelor Fellowship granted by University Agency of La Francophonie (AUF)

WORKING EXPERIENCES

2011-now **Prof. Prof. h.c. Dr. rer. nat. Dr. h.c. mult. Peter Langer**
Universität Rostock, Institut für Chemie, Abteilung für Organische Chemie
Albert-Einstein-Straße 3a, 18059 Rostock, Germany.
Subject: Synthesis of fused heterocycles by sequential palladium catalyzed cross-coupling reactions

2010-2011: **Prof. Dr. rer. nat. A. Stephen K. Hashmi**
Ruprecht-Karls-Universität Heidelberg, Organisch-Chemisches Institut
Im Neuenheimer Feld 270, D-69120 Heidelberg, Germany
Subject: Theoretical investigations of Gold-catalyzed reactions

2006-2010: **Laboratory of Organic Synthesis.**
Institute of Chemistry, VAST, Hanoi, Vietnam.
Supervisor: Prof. Dr. Tran Van Sung.
Subject: Research on synthesis of Acyclovir as an antiherpes-virus drug, synthesis some synthon and bioactive compounds.

2004 - 2006: **Devices and Material Lab., Organic EL Group.**
LG Electronics Institute of Technology, Seoul, South Korea.
Supervisor: Dr. Hyoung-Yun Oh.
Subject: Using Pd-catalyzed cross-coupling reactions for the Synthesis of Advanced Materials for OLEDs (Organic Light Emitting Devices).

2001 - 2004: **Laboratory of Bioactive Compounds Research.**
Institute of Chemistry, VAST, Hanoi, Vietnam.
Supervisors: Prof. Dr. Pham Hoang Ngoc and Dr. Nguyen Manh Cuong.
Subject: Phytochemistry study of *Croton tonkinensis* Gagnep. (Euphorbiaceae) and *Alocasia Macrorrhiza* (L.) Schott.(Araceae) and *Glycosmis Stenocarpa* (Drake) Tan. (Rutaceae).

SKILLS AND COMPETENCES

Chemistry Skilled in all major techniques of multi-step organic synthesis: chromatography methods, distillation, recrystallization, and characterization of compounds.
Practical experience of handling air-sensitive compounds, metal complexes and low temperature reactions.
Practical knowledge of analytical techniques: NMR, IR, UV, Fluorescence, Cyclic Voltametry, MS.
Practical knowledge of chemistry softwares: SciFinder, Beilstein, ChemDraw, Chemwin, MestReNoval, Bruker TOPSPIN, Chemsket, PbulCIF, Ortep, Endnote, Mendeley, Origin, Spekwin.

Language Vietnamese (mother tongue), English (fluently), German (read, written, speak), French (read, written).

Hobbies Reading and travelling.

List of Publication

1. **Hung, T. Q.**; Thang, N. N.; Hoang, D. H.; Dang, T. T.; Ayub, K.; Villinger, A.; Lochbrunner, S.; Flechsig, G.-U.; Langer, P., Synthesis and Properties of 5,7-Dihydropyrido[3,2-*b*:5,6-*b′*]diindoles *Eur. J. Org. Chem.* **2014**, accepted.
2. **Hung, T. Q.**; Hancker, S.; Villinger, A.; Lochbrunner, S.; Dang, T.; Friedrich, A.; Breitsprecher, W.; Langer, P., Novel Synthesis of 5-methyl-5,10-dihydroindolo[3,2-*b*]indoles by Pd-catalyzed C-C and two-fold C-N coupling reactions, *Org. Biomol. Chem.* **2014**, in print, **DOI:** 10.1039/C4OB01723D.
3. **Hung, T. Q.**; Dang, T. T.; Janke, J.; Villinger, A.; Langer, P., Efficient Approaches to *α-,δ*-Carbolines via Sequential Pd-Catalyzed Site-selective C-C and Two-fold C-N Coupling Reactions, *Org. Biomol. Chem.* **2014**, in print, **DOI:** 10.1039/C4OB02226B.
4. **Hung, T. Q.**; Hoang, D. H.; Thang, N. N.; Dang, T. T.; Ayub, K.; Villinger, A.; Friedrich, A.; Lochbrunner, S.; Flechsig, G.-U.; Langer, P., Palladium catalyzed synthesis and physical properties of indolo[2,3-*b*]quinoxalines. *Org. Biomol. Chem.* **2014**, *12*, 6151-6166.
5. **Hung, T. Q.**; Thang, N. N.; Hoang do, H.; Dang, T. T.; Villinger, A.; Langer, P., Efficient synthesis of biscarbazoles by palladium-catalyzed twofold C-N coupling and C-H activation reactions. *Org. Biomol. Chem.* **2014,** *12* (16), 2596-2605.
6. Klatt, G.; Xu, R.; Pernpointner, M.; Molinari, L.; **Hung, T. Q.**; Rominger, F.; Hashmi, A. S.; Koppel, H., Are *beta*-H eliminations or alkene insertions feasible elementary steps in catalytic cycles involving gold(I) alkyl species or gold(I) hydrides? *Chem. Eur. J.* **2013,** *19* (12), 3954-3961.
7. **Hung, T. Q.**; Dang, T. T.; Villinger, A.; Sung, T. V.; Langer, P., Efficient synthesis of thieno[3,2-*b*:4,5-*b′*]diindoles and benzothieno[3,2-*b*]indoles by Pd-catalyzed site-selective C-C and C-N coupling reactions. *Org. Biomol. Chem.* **2012,** *10* (45), 9041-9044.
8. **Hung, T. Q.**; Thuong, N. T.; Sung, T. V., New synthesis of acyclovir as an antiherpes-virus drug. *Vietnamese J. Chem.* **2009,** *2*, 167-182.
9. Cuong, N. M.; **Hung, T. Q.**; Chien, N. Q.; Arnold, N.; Wessjohann, L., Antifungal compounds from the Vietnamese plant *Bousingonia mekongenes*. *Adv. Nat. Sci. (Vietnam)* **2005,** *6*, 33-37.

10. Cuong, N. M.; **Hung, T. Q.**; Van Sung, T.; Taylor, W. C., A new dimeric carbazole alkaloid from *Glycosmis stenocarpa* roots. *Chem. Pharm. Bull.* **2004,** *52* (10), 1175-1178.
11. Minh, P. T. H.; Ngoc, P. H.; **Hung, T. Q.**; Kinh, C. D., Some tetrahydroprotoberberins from *Croton tonkinensis* Gagnep., growing in Vietnam. *J. Anal. Chem. Bio. (Vietnam)* **2003,** *12*, 134-137.
12. Tien, N. Q.; Ngoc, P. H.; Kinh, C. D.; **Hung, T. Q.**, A new glucoside isolated from *Alocasia Macrorrhiza* (L.) Schott. growing in Vietnam. *Vietnamese J. Chem.* **2002,** *40*, 127-131.