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Palladium Catalyzed Synthesis and Physical Properties of Indolo[2,3-*b*]quinoxalines

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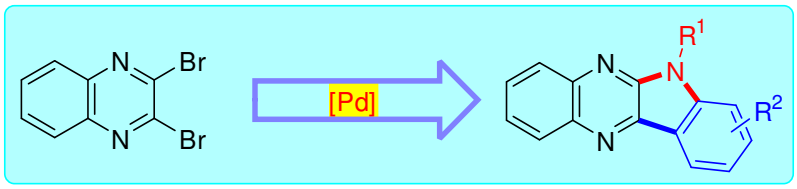
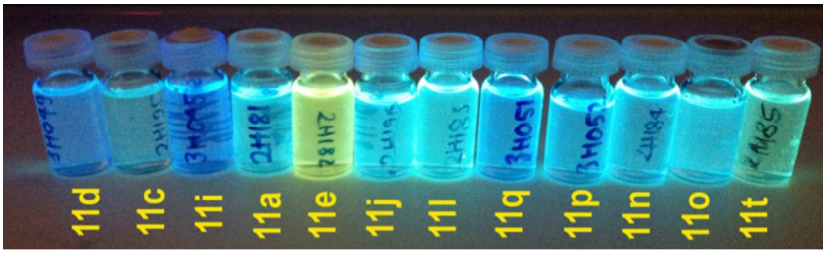




Abstract

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)-6*H*-indolo[2,3-*b*]quinoxaline showed the highest HOMO energy level and lowest band gap.

Introduction

Indolo[2,3-*b*]quinoxalines found many applications in organic light-emitting diodes (OLEDs)[1,2,3] and excitonic solar cells.[4] Their ability to harvest both singlet and triplet energy for emission improved the device efficiency. In 2010, Thomas *et al.* found that indolo[2,3-*b*]quinoxalines **1** lead to red-shift in absorption and emission spectra as well as larger Stokes shifts.[4] The introduction of indolo[2,3-*b*]quinoxaline segments increased the thermal stability and resulted in a higher glass transition temperature. To reduce π-π stacking interaction, which was assumed to decrease luminescence and propensity for crystal forming in the solid state, bulky and nonplanar structural segments were introduced instead of tertiary amine groups.[2] These novel materials displayed good quantum yields in solution and remarkable fluorescence in solid state. Thomas *et al.* also prepared electronic devices containing compound **2b** as electron transporting (ETL) and emitting layers (EML). These devices showed a maximum luminescence of 3910 cd/m^2 and maximum external quantum efficiency of 0.46%. In 2011, Cheng *et al.* prepared the novel host material BIQS **3** for deep-red PhOLEDs.[3] The BIQS material displayed a relatively low LUMO energy that facilitates electron injection resulting in a significantly lower operating voltage requirement and higher current density. This material provided an efficient energy transfer to deep-red emitting layers, due to singlet and triplet energies. Two years later, Cheng *et al.*

prepared three new host materials BIQF, BIQTP, BIQMCz with two indoloquinoline moiety.[1] Using these molecules as hosts in the deep-red devices, these materials exhibited EQE_{max} over 20%. The operational lifetimes were also promoted and were much longer than in the CBP-based devices.

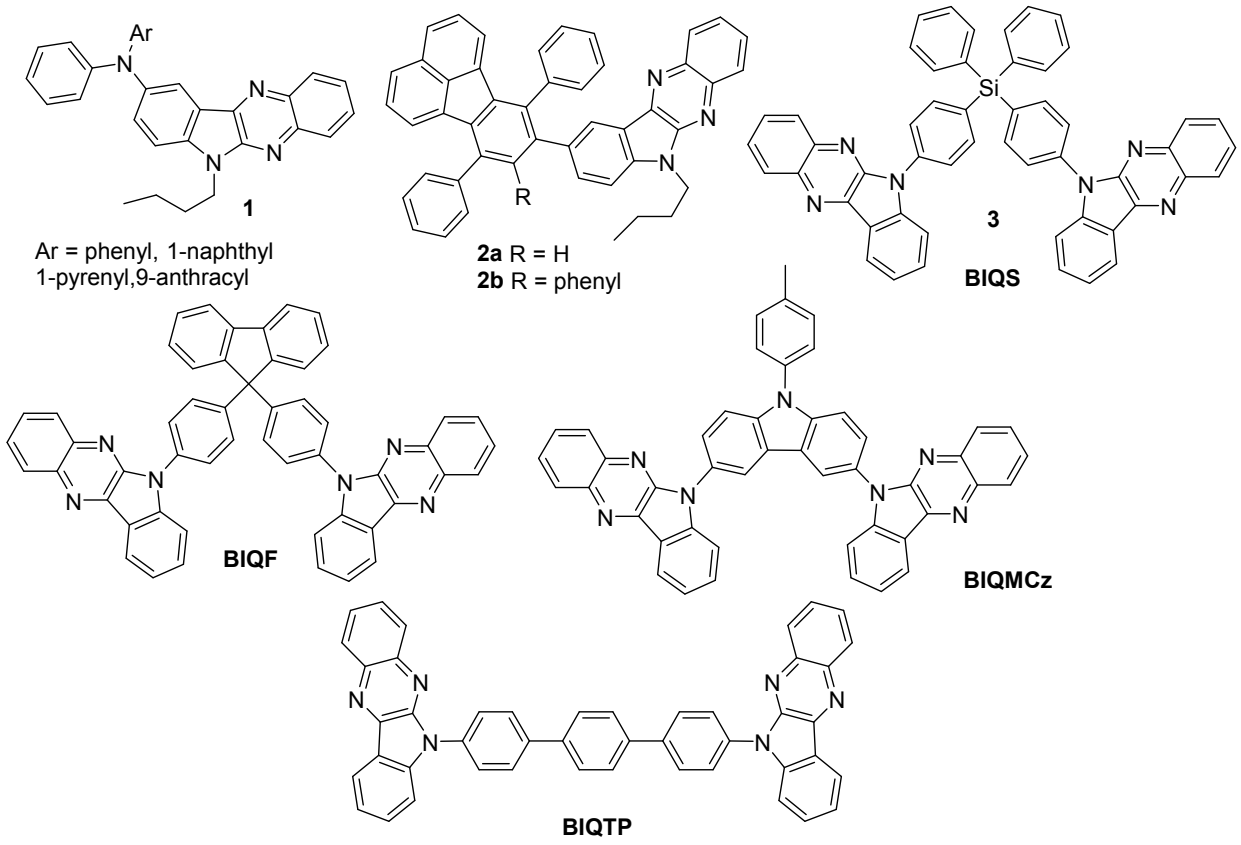


Figure 1. Some materials based on indolo[2,3-*b*]quinoxaline moieties.

Indolo[2,3-*b*]quinoxalines not only possess many important applications in material sciences, but also in medicinal chemistry. Earlier research showed that indolo[2,3-*b*]quinoxaline derivatives exhibit a wide range of interesting biological activities, such as antivirus,[5,6] anticancer,[7,8] antimicrobial,[9] and antibacterial activities.[10] Indolo[2,3-*b*]quinoxalines also represent antivirus agents.[5] A series of indolo[2,3-*b*]quinoxaline derivatives were examined for antiviral activity against Herpes virus. These results showed that B-220 exhibited potent antiviral activity against herpes simplex virus type 1 (HSV-1), varicella-zoster virus (VZV) and cytomegalovirus (CMV)

(Figure 2).[5,6] In 2010, Shibinskaya *et al*. reported the synthesis of 6-(2-aminoethyl)-6*H*-indolo[2,3-*b*]quinoxalines **4** (Figure 2),[11] which act as potent interferon inducers and antiviral agents with low toxicity. One year later these authors modified the structure of **4** to 7*H*-benzo[4,5]indolo[2,3-*b*]quinoxalines **5,**[12] which bind to DNA more strongly (lgK_a = 6.23-6.87) than **4** (lgK_a = 5.57-5.89). The antiviral activity is significantly reduced by the presence of an annulated benzene ring present in compound **5**. In their research related to the antitumor activity of tetracyclic quinoline and quinoxaline derivatives, Deady *et al.* showed that quinoxaline derivatives exhibit a broad range of cytotoxic activities.[8] In 2001, compounds NCA0424 and NCA0465 were reported to possess antitumor activity toward various types of blood cancer (leukemia), fibrosarcoma sand melanomas.[7] Recently, Kanugula *et al.* synthesized 6{(1-aryl-1H-1,2,3-triazol-4-yl)methyl}-6*H*-indolo[2,3-*b*]quinoxaline derivatives **6** and examined these compounds against three human cancer cell lines, namely cervical, prostate and lung using an MTT assay.[13] The results showed 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 enhanced their bioactivity.

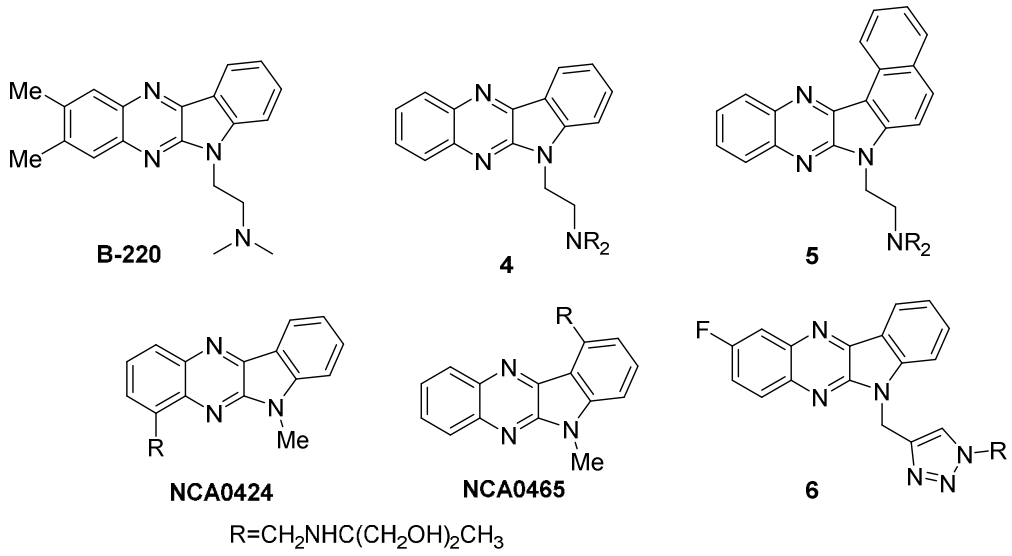
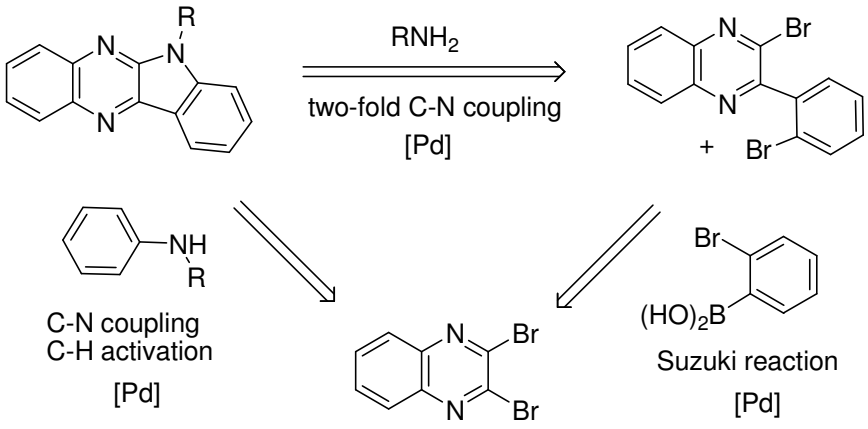


Figure 2. Some bioactive compounds containing the indolo[2,3-*b*]quinoxaline moiety

Due to the importance of indolo[2,3-*b*]quinoxalines in both material sciences and medicinal chemistry, we were 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 known syntheses of indolo[2,3-*b*]quinoxalines rely on the cyclocondensation of isatin with *o*-phenylenediamine derivatives. Marchlewski carried out the first synthesis of parent indolo[2,3-*b*]quinoxaline by condensation of isatin with *o*-phenylenediamine in the presence of AcOH as acidic catalyst. In 1980, Reisenauer and coworkers reported the cyclization of carbodiimide compounds by rearrangement of nitrenes to give indolo[2,3-*b*]quinoxalines in good yields.[14] Indolo[2,3-*b*]quinoxalines could also be prepared by cyclization of *o*-phenylenediamine with 1-acetyl-2-bromo-3-indolinone.[15] In general, the synthesis of highly functionalized indolo[2,3-*b*]quinoxalines is difficult, because starting materials are not readily available. Herein, we wish to report a practical and efficient two-step synthesis of indolo[2,3-*b*]quinoxalines by Pd-catalyzed Suzuki-Miyaura reaction of 2,3-dibromoquinoxaline and subsequent Pd-catalyzed two-fold C-N coupling annulation with amines. In addition, a second approach was developed based on the 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 substrate scope.

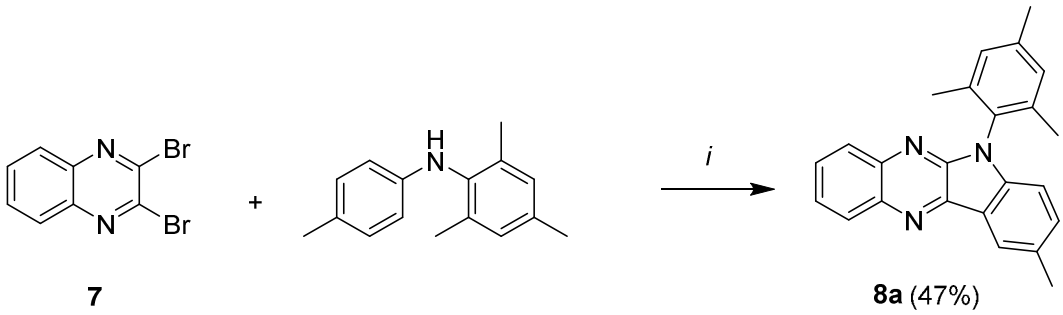
Results and discussion

We envisaged to prepare the indolo[2,3-*b*]quinoxaline scaffold based on two retrosynthetic strategies depicted in Scheme 1. Our first approach relies on Ackermann's procedure for the one-pot Pd-catalyzed domino synthesis of carbazole derivatives from aryl 1,2-dihalides.[16, 17] This approach provides a direct access to 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.[18]



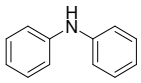
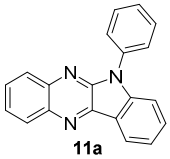
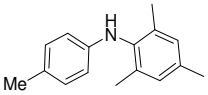
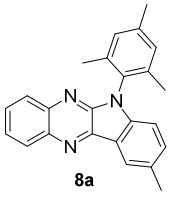
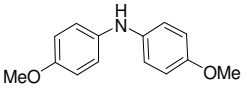
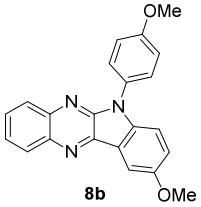
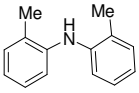
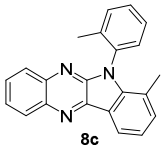
Scheme 1. Retrosynthetic analysis of the synthesis of indolo[2,3-*b*]quinoxalines

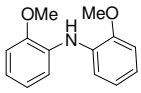
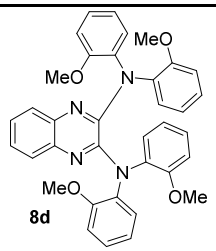
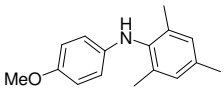
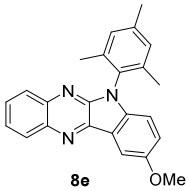
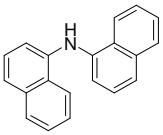
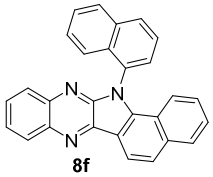
We first started to study the one-pot reaction of 2,3-dibromoquinoxaline (**7**) with secondary aromatic amines in the presence of $Pd(OAc)_2/PCy_3 \cdot HBF_4$ as catalyst applying Ackermann's protocol developed for other heterocyclic substrates.[16,17] We were pleased to find that the reaction of **7**, prepared in two steps from 1,2-diaminobenzene using Li's procedure,[19] with diphenylamine afforded indolo[2,3-*b*]quinoxalines **11a** in 90% yield (Scheme 2). The preparative scope was studied (Table 1). We observed that good yields were obtained for indolo[2,3-*b*]quinoxalines derived from sterically less bulky amines. Product **8a** derived from an unsymmetrical diarylamine could be successfully prepared, albeit, in only moderate yield. In contrast, the synthesis of **8e** failed. The yields generally decreased or the reactions completely failed in case of sterically encumbered anilines containing substituents located at the *ortho*-position (formation of complex mixtures). In case of 2-(methoxy)aniline, the bis(adduct) **8d** instead of the desired cyclization product was isolated. In addition, the employment of *N*-alkylanilines ArN(Alkyl)H or simple anilines $ArNH_2$ as substrates failed. The failure in case of *N*-alkylanilines was already reported before by Ackermann for cyclization reactions with other aromatic dihalides.[16] To optimize the yields we have tried to vary the conditions by changing the palladium catalyst in combination with different ligands, but so far we were not able to isolate the products in good yields.



Scheme 2. Synthesis of indolo[2,3-*b*]quinoxaline **8a**. *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.

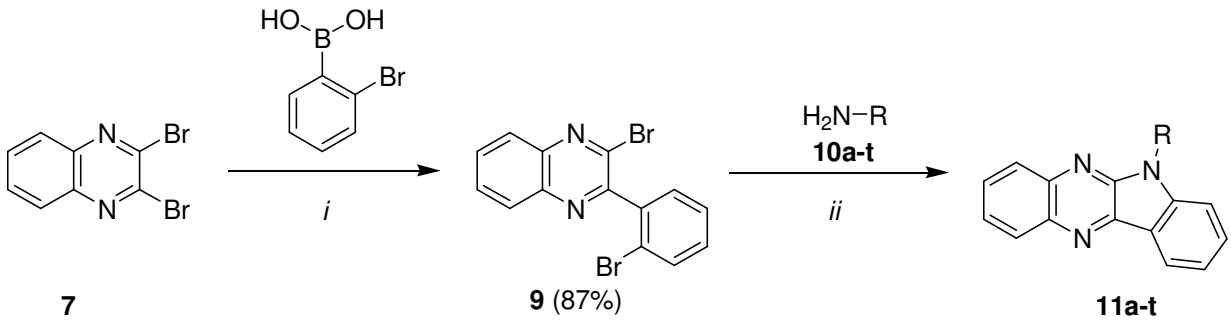
Table 1. Synthesis of products **8a-f** and **11a** following the domino C-N/C-H bond activation pathway

Entry	Amine	Product	Yield (%)[a]
1		 **11a**	90
2		 **8a**	47
3		 **8b**	54
4		 **8c**	0[b]

5		 **8d**	30
6		 **8e**	0 [b]
7		 **8f**	0 [b]

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

In order to optimize the yields and to develop a more efficient procedure for the synthesis of indolo[2,3-*b*]quinoxalines, we studied a second approach based on a two-step synthesis. In the first step, a Suzuki-Miyaura reaction is carried out followed by a twofold C-N coupling annulation (Scheme 3). The Suzuki-Miyaura reaction of **7** with 2-bromophenylboronic acid in the presence of catalytic amounts of $Pd(PPh_3)_4$ afforded intermediate **9** in 87% isolated yield. The Pd-catalyzed twofold C-N coupling annulation of **9** with different amines **10a-t** gave the desired products **11a-t** in good to excellent yields (Table 3).



Scheme 3. Synthesis of indolo[2,3-*b*]quinoxalines **11a-t**. *Conditions*: (i) 1.2 equiv. of 2-bromophenylboronic acid, 2.5 % of $Pd(Ph_3)_4$ catalyst, 3 equiv. of NaOH, THF, H_2O, 70 ºC, 4h. (ii) 3 equiv. of **10**, 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).

The conditions of the annulation reaction of **9** with *p*-toluidine **10b** were optimized (Table 2). The ligand, palladium precursor, solvent and temperature were varied. The results showed that bidentate ligands often gave higher yields than monodentate ligands. In fact, up to 92% yield of **11b** was achieved by employment of dppf as ligand in combination with $Pd_2(dba)_3$ as the Pd source (method A).

Table 2. Optimization for the synthesis of **11b**

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

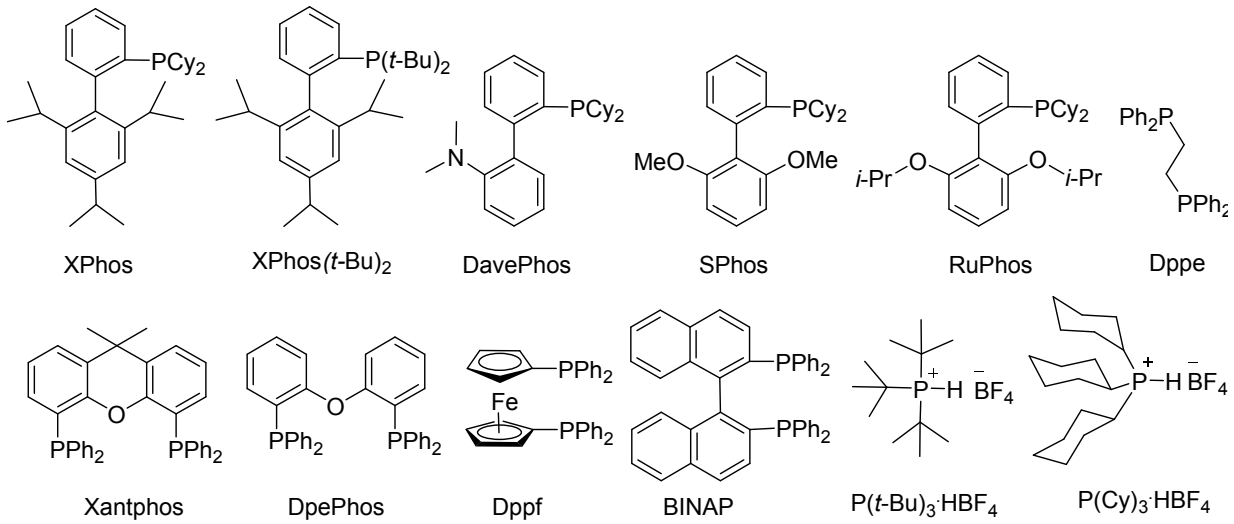


Figure 3. Monodentate and bidentate phosphine ligands.

With the optimized conditions in hand, we explored the scope of the twofold C-N annulation reaction of **9** with different amines. The employment of various secondary aromatic amines afforded the corresponding products **11a-i** in good to excellent yields in only 6 hours reaction time (Table 3). The results showed that the annulations gave high yields for substrates bearing both electron-withdrawing or -donating substituents. In contrast, the reactions of **9** with alkyl amines, using our optimized conditions (method A), resulted in the formation of side products which were difficult to separate from the main product. Therefore, an additional optimization of the reaction conditions was carried out for the synthesis of product **11n** derived from benzyl amine. It was found that employment of DPEPhos as ligand in combination with Pd_2dba_3 (method B) resulted in the formation of product **11n** in up to 96% yield (Table 4). The application of these conditions allowed for the synthesis of products **11j-t**, derived from aliphatic amines, in very good yields (Table 3).

Table 3. Synthesis of **11a-t**

11	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-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-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)-6*H*-indolo[2,3-*b*]quinoxaline formed by isomerization of the allylic double bond.

Table 4. Optimization for the synthesis of **11n**

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·tBu$_2$	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 **11a-t** were established by spectroscopic methods. The structures of **11e** and **11r** were independently confirmed by X-ray crystal structure analyses. The geometric parameters of the X-ray structure for compound **11e** were also compared with those derived from the DFT calculations. The optimized geometry of compound **11e** (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 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 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
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

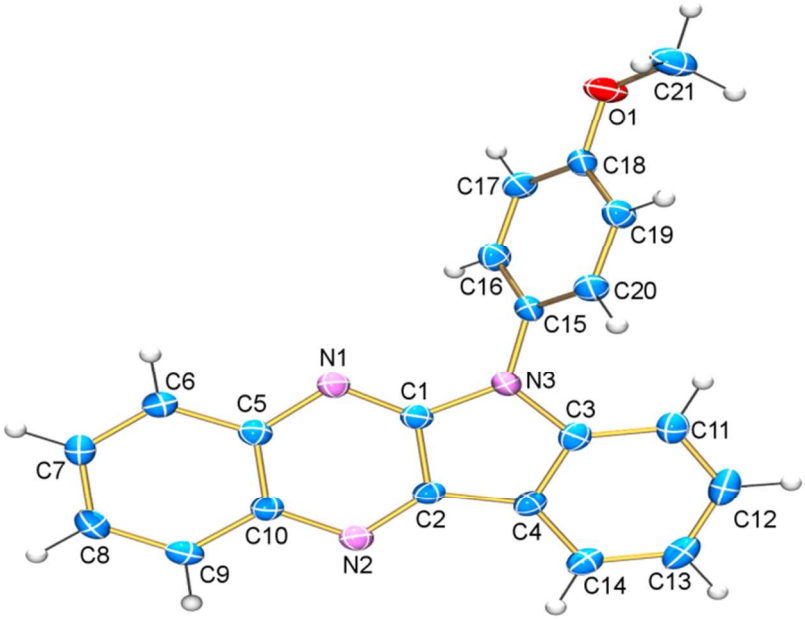


Figure 3. Ortep plot of **11e**

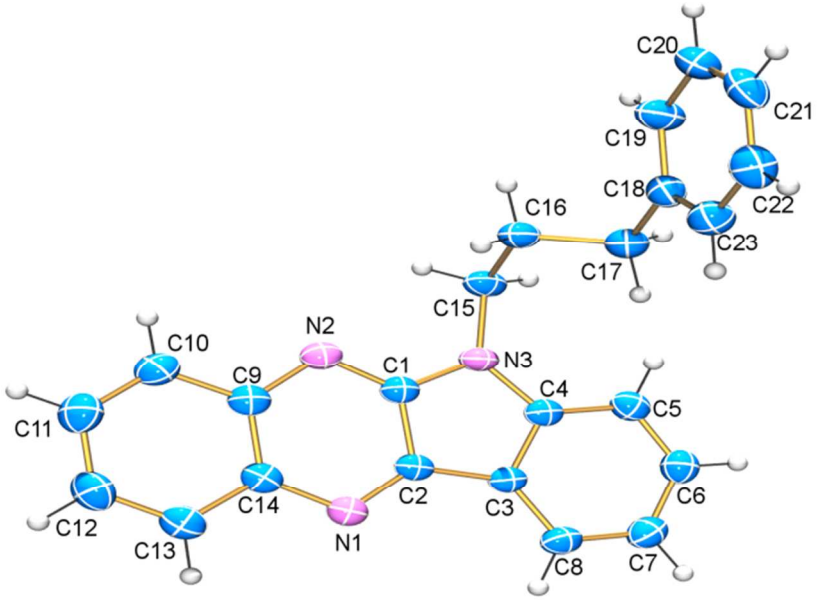
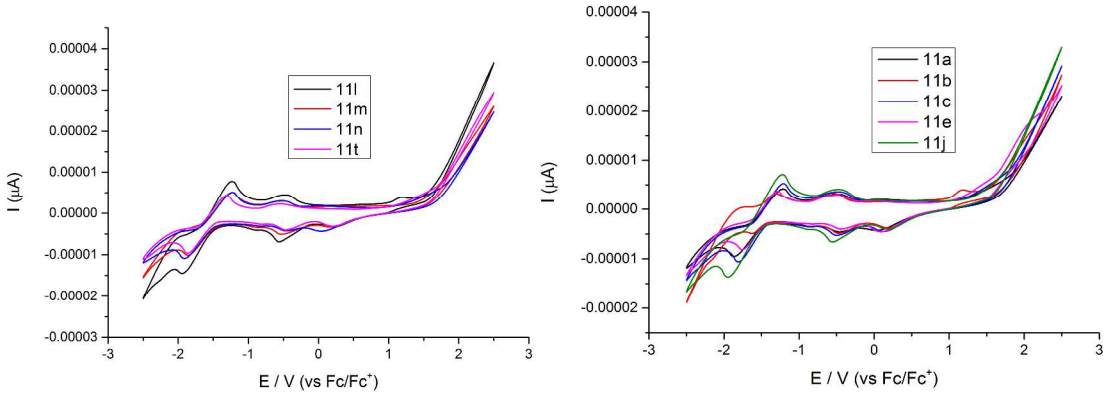


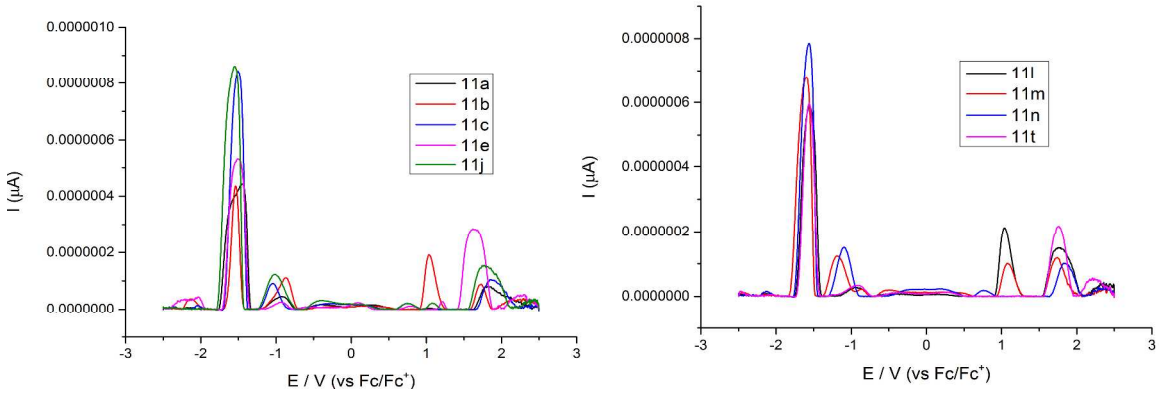
Figure 4. Ortep plot of **11r**

Electrochemical properties

Electrochemical properties of some compounds were examined 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 by means of a μAutolab III potentiostat (Ecochemie, Utrecht, The Netherlands). A 0.01 mol·L^{-1} solution of tetrabutylammonium hexafluorophosphate ($TBAPF_6$) was used as the 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 DPV measurement (Table 6). The formal potential of Fc/Fc^+ vs. vacuum was assumed to be -4.8 eV.



Cyclic Voltammograms of **11**



Differential Pulse Voltammograms of **11**

Figure 5. Electrochemical properties of some quinoxaline derivatives.

Table 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	ΔEg$_{cal.}$ (eV)^f
11a	-1.395	1.872	-6.672	-3.405	3.267	3.707
11b	-1.488	1.779	-6.579	-3.312	3.267	3.670
11c	-1.456	1.910	-6.710	-3.344	3.366	3.704

11e	-1.456	1.666	-6.466	-3.344	3.122	3.605
11j	-1.496	1.819	-6.619	-3.304	3.315	3.637
11l	-1.508	1.813	-6.613	-3.292	3.321	3.750
11m	-1.545	1.787	-6.587	-3.255	3.332	
11n	-1.512	1.874	-6.674	-3.288	3.386	3.784
11t	-1.512	1.813	-6.613	-3.288	3.325	3.744
CBP			-5.91	-2.51	3.40	

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

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

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

The CV diagram of compound **11a** showed a reversible and well-defined redox peak (Figure 5). However, an oxidation peak was not present, due to low electrochemical activity of quinoxaline in the CV experiment. Thus, the DPV method was chosen for investigation of the electrochemical properties. The experiments showed that the band gaps were independent from the exact substitution pattern. It is assumed that the quinoxaline core play the key role. Compared to 4,4'-bis(*N*-carbazolyl)-1,1'-biphenyl (CBP), which is commonly used as host material, quinoxaline derivatives gave lower HOMO and LUMO levels and slightly smaller band gaps. Among derivatives containing a phenyl substituent located at the nitrogen atom, compound **11c** containing an electron withdrawing group had a HOMO energy level lower than compound **11a**. In contrast, compound **11e,** containing an electron donating group, resulted in a shift to a higher HOMO level yielding a smaller band gap. The smallest band gap and highest HOMO energy level was displayed by **11e** containing a 4-methoxyphenyl substituent. It is noteworthy that compounds **11c** and **11n,** 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 performed for the determination of HOMO-LUMO band gaps. A comparison of theoretical and experimental values is given in Table 6. Although the absolute values of theoretical and experimental band gaps are different however, the trend is very similar. A linear relationship is observed between the theoretical and experimental band gaps. The difference between theoretical and experimental band gaps has already been discussed in the literature by us[20] and others[21]. The difference between theoretical and experimental HOMO-LUMO gaps decreases with increase in the size of the hydrocarbon.[22]

The results shown in Table 6 indicate that both theoretical and experimental band gaps are not much affected by structural modifications. *N*-aliphatic or *N*-benzylindolo[2,3-*b*]quinoxalineshave higher HOMO-LUMO band gaps as compared to their *N*-phenyl analogues. The highest HOMO-LUMO band gap was calculated for **11n** (3.78 eV) which is consistent with the highest experimental band gap for this compound (3.38 eV). The lower band gap for *N*-phenylindolo[2,3-*b*]quinoxalines is probably due to extended conjugation which provides enhanced delocalization, and therefore the band gap decreases. Among *N*-phenylindolo[2,3-*b*]quinoxalines, **11a** and **11c** have comparable bands gaps which indicate that introduction of a fluorine atom has a negligible effect. This may be attributed to the high electronegativity of fluorine which prevents its lone pairs to delocalize over the organic π frame. Introduction of a methyl group at the *para* position of the *N*-phenyl group decreases the band gap by 0.037 eV whereas a methoxy group at the same position decreases 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*]quinoxalinesareare shown in Figure 6 as a representative example. The HOMO-1 and HOMO-2 lie at 0.5 and 1.0 eV, respectively,lower in energy relative to HOMO. 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 situated 1.374 eV and 1.548 eV higher in energy, respectively, than LUMO. HOMO and LUMO of quinoxalines **11a**, **11l** and **11t** were also analyzed and are shown in Figure 7. Replacement of the phenyl ring of **11a** with an aliphatic heptyl chain in **11l** and an alicyclic fragment (cyclohexyl) in **11t** does not affect the iso densities of the LUMOs, however, a small effect on the HOMO is observed. In

11l and **11t**, HOMOs are centered on the quinoxaline core whereas in **11a** it has some density on the *N*-phenyl ring as well.

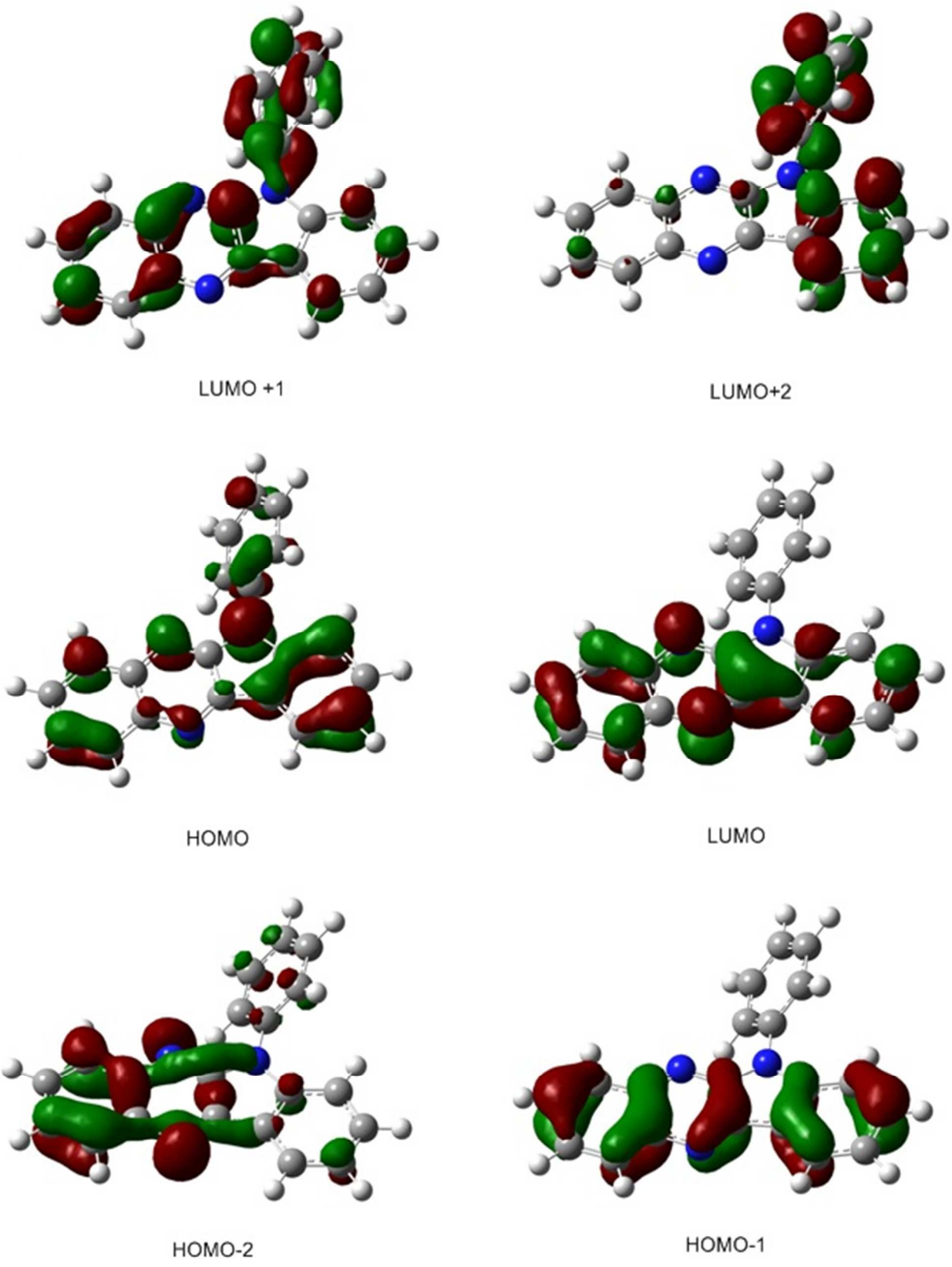


Figure 6. HOMO-2 to LUMO+2 molecular orbitals of quinoxaline **11a**

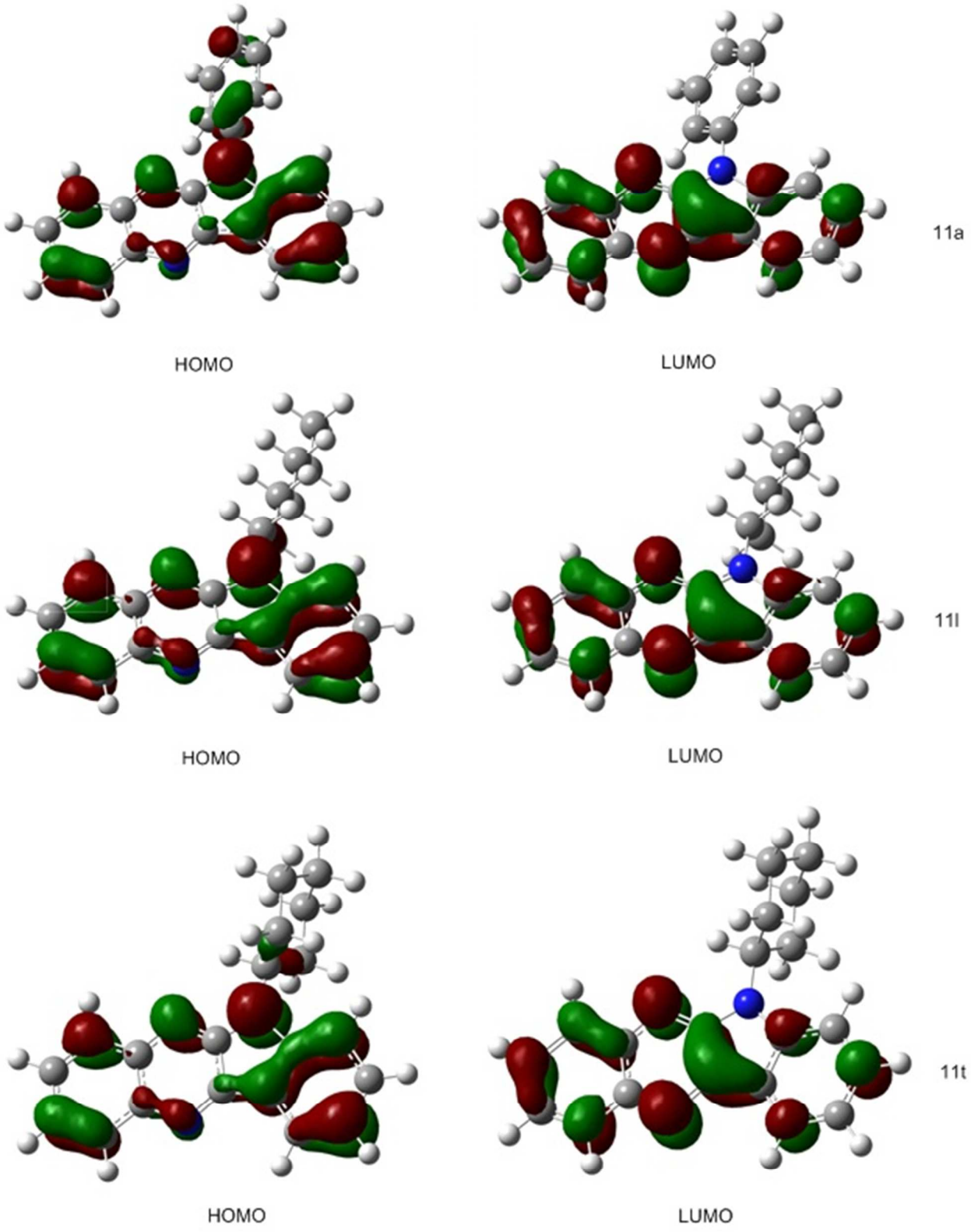


Figure 7. HOMO and LUMO of **11a, 11l** and **11t** calculated at B3LYP/6-31G*

Absorption and Fluorescence Properties

UV-VIS and fluorescence spectra of some selected indolo[2,3-*b*]quinoxalines **11** dissolved in acetonitrile are shown in Figure 8 and the corresponding spectral data are summarized in Table 7. The UV-VIS absorption spectra of the compounds exhibit below 230 nm three bands around 400 nm, 350 nm, and 270 nm with increasing absorption strength. The spectra of all derivatives **11** are quite similar suggesting that the substituent located at the nitrogen atom has only a weak influence. In the case of compound **11i** the band around 270 nm seems to be split into two well separated contributions. The absorptions of compounds **11j**, **11l**, **11t**, bearing an aliphatic group located at the nitrogen atom, are slightly red-shifted due to the positive inductive effect. For compounds **11d** and **11i**, containing electron withdrawing groups, a shift to shorter wavelenghths is observed.

The fluorescence 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 quinin hemisulfate salt monohydrate in 0.05M H_2SO_4 which has a fluorescence yield of 0.52 [Meech, S. R.; Phillips, D. Journal of Photochemistry 1983, **23**, 193-217.]. The spectra feature emission bands around 480 nm. Compound **11d** containing a trifluormethyl group shows the bluest emission with a maximum at 471 nm while **11e** containing a methoxy group exhibits an emission band at 538 nm which is strongly red shifted compared to all other compounds. The Stokes shift is of medium size and in the range of 80 nm to 90 nm. It is similar for all compounds except for **11e** which exhibits a large Stokes shift of 140 nm. The quantum yields of the indolo[2,3-*b*]quinoxalines **11** are in the order of a few percent with the highest yield of 8.6% observed for **11l**. It is noteworthy that compound **11e** shows also an exceptionally low yield of only 1.1% which seems to correlate with the large red shift of its fluorescence.

The week sensitivity of the absorption and fluorescence spectra on the substituent are inline with the small variation of the electrochemical properties and the band gap of the compounds (see above). Only **11e** exhibits a significant higher HOMO level and smaller band gap than the other compounds which fits to its red shifted fluorescence. The general behavior can be rationalized by the involved orbitals. As shown in Figure 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 substitution. 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) the corresponding absorption bands around 350 nm and 270 nm are also rather insensitive to the substituent.

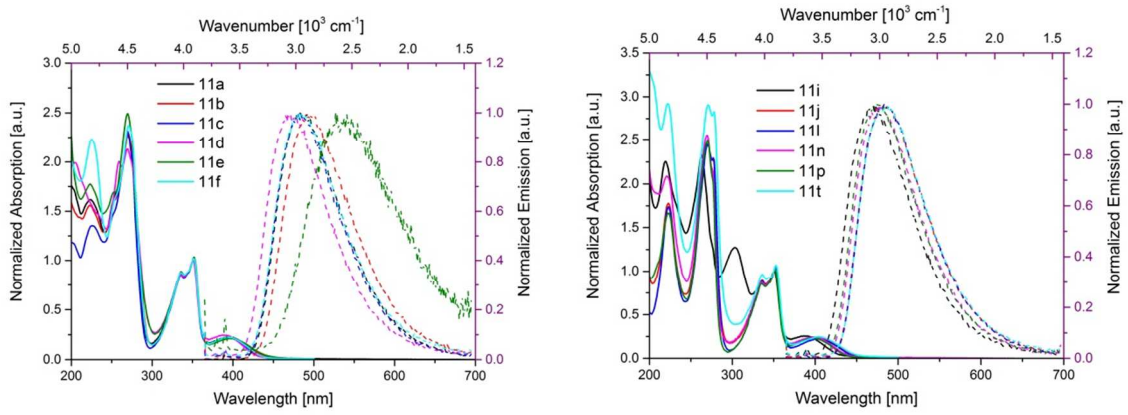


Figure 8. Normalized absorption and emission spectra of selected compounds **11** measured in acetonitrile. Emission spectra were recorded with excitation at 350 nm.

Table 7. Spectroscopic data characterizing the absorption and emission properties of **11**

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 [%]
11a	395	3.616	351	4.353	270	4.696	484	89	5.9
11b	396	3.738	351	4.491	269	4.848	490	94	5.2
11c	394	3.809	351	4.547	268	4.903	482	88	5.9
11d	389	3.684	350	4.338	269	4.642	471	82	4.3
11e	398	3.954	351	4.795	269	5.188	538	140	1.1
11f	394	3.387	351	4.078	270	4.451	485	91	4.8
11i	389	3.463	350	4.133	262	4.500	474	85	4.6

11j	403	2.827	352	3.728	269	4.126	484	81	6.7
11l	404	3.952	352	4.939	269	5.334	483	79	8.6
11n	398	4.220	351	4.934	269	5.322	477	79	7.1
11p	396	3.615	351	4.278	269	4.672	475	79	7.4
11t	404	4.144	352	5.005	270	5.402	486	82	7.7

Computational Methods

DFT calculations were performed with the Gaussian 09Revision C.01.[23] 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[24] (B3) hybrid exchange functional in conjunction with the correlation functional of LeeYang and Parr (LYP)[25] method using 6-31G* basis set.[26] The B3LYP/6-31G* method of DFT has been reliable for the prediction of geometric and electronic properties of neutral[20] and charged species[27] ranging from simple molecular to polymer structures.[28] 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.

Conclusion

In conclusion, we reported two strategies for the preparation indolo[2,3-*b*]quinoxalines. The one-pot approach, using Pd-catalyzed two-fold C-N coupling and C-H activation reactions, gave indolo[2,3-*b*]quinoxalines in good yields, but the substrate scope was limited. A two-step approach, based on 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 studied experimentally and by DFT calculations. It turns out that the electronic and spectroscopic properties are quite insensitive to the substituent 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.

Experimental Section

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.[19] 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 (9). 2,3-Dibromoquinoxaline **7** (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 **9** (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 A for double C-N coupling with aniline derivatives,exemplified by the synthesis of6-phenyl-6*H*-indolo[2,3-*b*]quinoxaline (11a). Aniline **10a** (75 µL, 0.82 mmol) was added to a pressure tube charged with **9** (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, heptanes/ethylacetate 5:1) to yield 6-phenyl-6*H*-indolo[2,3-*b*]quinoxaline **11a** (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 **(11b)** was prepared following general procedure A using compound **9** (100 mg, 0.28 mmol) and toluidine (88 mg, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptanes/ethylacetate 5:1) to yield **11b** (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 **(11c)** was prepared following general procedure A using compound **9** (100 mg, 0.28 mmol) and 4-fluoroaniline (78 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptanes/ethylacetate 5:1) to yield **11c** (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 **(11d)** was prepared following general procedure A using compound **9** (100 mg, 0.28 mmol) and 3-(trifluoromethyl)aniline (103 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptanes/ethylacetate 5:1) to yield **11d** (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 **(11e)** was prepared following general procedure A using compound **9** (100 mg, 0.28 mmol) and p-anisidine (101 mg, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptanes/ethylacetate 3:1) to yield **11e** (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 (t, *J* = 8.3 Hz, 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 **(11f)** was prepared following general procedure A using compound **9** (100 mg, 0.28 mmol) and 3,5-dimethoxyaniline (126 mg, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptanes/ethylacetate 2:1) to yield **11f** (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 (t, *J* = 2.3 Hz, 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 **(11g)** was prepared following general procedure A using compound **9** (100 mg, 0.28 mmol) and 4-(methylthio)aniline (103 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptanes/ethylacetate 3:1) to yield **11g** (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 $C_{24}H_{22}N_4$ ($[M + H]^+$): 367.19172; found: 367.19173.

5,7-Bis(4-(N,N-diethylamino)phenyl)-6H-indolo[2,3-b]quinoxaline **(11h)** was prepared following general procedure A using compound **9**(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 **11h** (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 **(11i)** was prepared following general procedure A using compound **9** (100 mg, 0.28 mmol) and 4-aminobenzonitrile (97 mg, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptanes/ethylacetate 3:1) to yield **11i** (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 B for double C-N coupling with chain amine derivatives, exemplified by *6-propyl-6H-indolo[2,3-b]quinoxaline* (11j). To a pressure tube charged with **9** (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). n-propylamine (68 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 separated via flash chromatography (silica gel, heptanes/ethylacetate 5:1) to yield **11j** (69 mg, 80%) as a yellow solid; m.p. 99-100 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (d, *J* = 7.7 Hz, 1H), 8.31 (dd, *J* = 8.3, 1.3 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.1 Hz, 1H), 7.82 – 7.60 (m, 3H), 7.48 (d, *J* = 8.2 Hz, 1H), 7.44 – 7.33 (m, 1H), 4.58 – 4.37 (m, 2H), 2.13 – 1.90 (m, 2H), 1.03 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 145.88, 144.70, 140.80, 140.09, 139.28, 131.08, 129.41, 128.84, 127.94, 126.05, 122.94, 120.90, 119.54, 109.68, 43.21, 21.96, 11.75; IR (ATR, cm^{-1}): ν =3057 (w), 2970 (m), 2951 (m), 2929 (w), 2870 (m), 1610 (m), 1581 (m), 1574 (m), 1487 (s), 1464 (s), 1435 (m), 1406 (s), 1394 (m), 1369 (m), 1358 (s), 1348 (s), 1321 (s), 1294 (m), 1265 (w), 1257 (m), 1242 (m), 1232 (m), 1203 (s), 1182 (m), 1155 (m), 1113 (s), 1070 (m), 1034 (w), 1014 (m), 1003 (m), 951 (w), 939 (m), 893 (m), 883 (w), 870 (m), 850 (m), 768 (m), 746 (vs), 727 (s), 698 (s), 642 (m), 617 (m), 586 (s), 569 (m), 534 (m);GC-MS (EI, 70 eV): m/z (%) = 261 (46), 232 (73), 219 (100), 102 (11), 90 (10), 77 (7); HRMS (ESI): calcd. for $C_{17}H_{16}N_3$ ($[M + H]^+$): 262.13387; found: 262.13391.

6-Pentyl-6H-indolo[2,3-b]quinoxaline **(11k)** was prepared following general procedure B using compound **9** (100 mg, 0.28mmol) and n-pentylamine (96 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptanes/ethylacetate 5:1) to yield **11k** (74 mg, 93 %) as a yellow solid; m.p. 90-91 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.40 (d, *J* = 7.6 Hz, 1H), 8.22 (dd, *J* = 8.3, 1.3 Hz, 1H), 8.06 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.73 – 7.53 (m, 3H), 7.39 (d, *J* = 8.2 Hz, 1H), 7.35 – 7.25 (m, 1H), 4.45 – 4.34 (m, 2H), 1.94 – 1.77 (m, 2H), 1.33 (m, 4H), 0.81 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 145.65, 144.46, 140.66, 140.03, 139.23, 130.87, 129.31, 128.63, 127.82, 125.83, 122.72, 120.69, 119.47, 109.48, 41.44, 29.16, 28.15, 22.39, 13.94; IR (ATR, cm^{-1}): ν =2964 (w), 2953 (w), 2931 (w), 2870 (w), 1608 (m), 1579 (m), 1491 (m), 1466 (s), 1441 (w), 1406 (s), 1379 (m), 1358 (m), 1323 (m), 1304 (m), 1246 (s), 1234 (m), 1200 (s), 1163 (m), 1153 (m), 1130 (m), 1115 (s), 1070 (m), 1051 (w), 1036 (w), 1014 (m), 1003 (m), 976 (w), 945 (w), 928 (m), 897 (w), 872 (w), 860 (w), 850 (m), 837 (w), 764 (s), 752 (s), 742 (vs), 729 (s), 717 (s), 692 (s), 665 (m), 640 (m), 629 (w), 613 (m), 606 (m), 586 (s), 571 (s), 555 (m), 534 (m); GC-MS (EI, 70 eV): m/z (%) = 289 (52), 260 (6), 246 (11), 2332 (80), 219 (100), 129 (11), 90 (10), 77 (9); HRMS (EI): calcd. for $C_{19}H_{19}N_3$ ($[M]^+$): 289.15735; found: 289.15720.

6-Heptyl-6H-indolo[2,3-b]quinoxaline **(11k)** was prepared following general procedure B using compound **9** (100 mg, 0.28mmol) and n-heptylamine (122 µL, 0.82mmol). The product was purified by flash chromatography (silica gel, heptanes/ethylacetate 5:1) to yield **11j** (74 mg, 85 %) as a yellow solid; m.p. 66-68 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (d, *J* = 7.7 Hz, 1H), 8.32 (dd, *J* = 8.3, 1.3 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.81 – 7.64 (m, 3H), 7.47 (d, *J* = 8.2 Hz, 1H), 7.42 – 7.32 (m, 1H), 4.58 – 4.40 (m, 2H), 2.03 – 1.85 (m, 2H), 1.51 – 1.16 (m, 8H), 0.86 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.81, 144.67, 140.78, 139.89, 139.05, 131.16, 129.26, 128.86, 127.95, 126.10, 123.05, 120.92, 119.43, 109.67, 41.63, 31.85, 29.11, 28.60, 27.16, 22.73, 14.18; IR (ATR, cm^{-1}): ν =2951 (m), 2922 (m), 2870 (m), 2850 (m), 1606 (m), 1581 (m), 1487 (s), 1464 (s), 1435 (m), 1408 (s), 1394 (m), 1369 (s), 1358 (s), 1346 (m), 1321 (s), 1304 (m), 1250 (m), 1240 (m), 1232 (m), 1203 (m), 1188 (m), 1176 (m), 1161 (m), 1149 (m), 1113 (s), 1070 (m), 1014 (m), 999 (m), 945 (m), 764 (s), 748 (vs), 721 (s), 698 (s), 642

(m), 615 (m), 586 (s), 569 (m), 534 (m); GC-MS (EI, 70 eV): m/z (%) = 317 (41), 233 (100), 219 (96), 102 (6); HRMS (ESI): calcd. for $C_{21}H_{24}N_3$ ($[M + H]^+$): 318.19647; found: 318.19666.

6-(Prop-1-en-1-yl)-6H-indolo[2,3-b]quinoxaline **(11m)** was prepared following general procedure B using compound **9** (100 mg, 0.28mmol) and allylamine (62 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptanes/ethylacetate 5:1) to yield **11m** (52 mg, 73 %) as a yellow solid; m.p. 142-143 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (d, *J* = 7.6 Hz, 1H), 8.32 (dd, *J* = 8.2, 1.4 Hz, 1H), 8.17 (dt, *J* = 12.4, 6.4 Hz, 1H), 7.83 – 7.63 (m, 3H), 7.42 (ddd, *J* = 10.8, 9.2, 8.0 Hz, 2H), 6.92 – 6.79 (m, 1H), 6.27 – 6.07 (m, 1H), 1.76 (dd, *J* = 7.0, 1.8 Hz, 3H);^{13}C NMR (63 MHz, $CDCl_3$) δ 144.21, 140.60, 140.21, 139.48, 131.09, 129.27, 128.90, 128.23, 128.10, 126.42, 122.66, 121.60, 121.15, 119.85, 110.89, 14.18;IR (ATR, cm^{-1}): ν =3055 (m), 3045 (m), 2978 (m), 2931 (m), 2912 (m), 2852 (m), 1662 (m), 1628 (m), 1606 (m), 1581 (m), 1574 (m), 1485 (s), 1462 (s), 1435 (m), 1427 (m), 1408 (vs), 1392 (s), 1358 (m), 1348 (m), 1335 (m), 1315 (s), 1265 (m), 1254 (s), 1234 (m), 1225 (m), 1209 (s), 1201 (s), 1178 (m), 1149 (m), 1138 (m), 1117 (s), 1093 (s), 1059 (m), 1034 (m), 1024 (m), 1016 (m), 1003 (m), 974 (m), 951 (m), 918 (m), 766 (s), 758 (s), 746 (vs), 735 (vs), 714 (s), 640 (m), 627 (s), 596 (s), 569 (m), 557 (m), 536 (s);GC-MS (EI, 70 eV): m/z (%) = 259 (100, 244 (29), 232 (22), 219 (42); HRMS (ESI): calcd. for $C_{17}H_{14}N_3$ ($[M + H]^+$): 260.11822; found: 260.11817.

6-Benzyl-6H-indolo[2,3-b]quinoxaline **(11n)** was prepared following general procedure B using compound **9** (100 mg, 0.28 mmol) and benzylamine (90 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptanes/ethylacetate 4:1) to yield **11n** (80 mg, 94 %) as a yellow solid; m.p. 181-182 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.42 (d, *J* = 7.5 Hz, 1H), 8.25 (dd, *J* = 8.2, 1.3 Hz, 1H), 8.06 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.65 (dtd, *J* = 16.6, 6.9, 1.5 Hz, 2H), 7.57 – 7.47 (m, 1H), 7.36 – 7.08 (m, 7H), 5.63 (s, 2H);^{13}C NMR (75 MHz, $CDCl_3$) δ 145.96, 144.44, 140.81, 140.01, 139.50, 136.62, 131.21, 129.38, 128.99, 128.94, 128.04, 127.82, 127.34, 126.32, 122.95, 121.32, 119.72, 110.29, 45.16; IR (ATR, cm^{-1}): ν =3059 (m), 3026 (w), 1610 (m), 1581 (m), 1574 (m), 1485 (s), 1466 (s), 1452 (m), 1433 (m), 1406 (s), 1394 (s), 1358 (m), 1346 (s), 1321 (s), 1306 (m), 1269 (m), 1259 (m), 1234 (m), 1196 (s), 1151 (m), 1134 (m), 1126 (m), 1113 (s), 1078 (m), 1066 (m), 1034 (m), 1026 (m), 1016 (m), 1007 (m), 985 (m), 918

(m), 895 (m), 854 (m), 766 (s), 746 (vs), 725 (s), 700 (vs), 685 (s), 650 (m), 615 (m), 592 (s), 575 (s), 555 (m), 534 (m); GC-MS (EI, 70 eV): m/z (%) = 309 (100), 266 (7), 251 (7), 232 (14), 207 (7), 91 (43), 84 (17), 66 (15), 49 (8); HRMS (ESI): calcd. for $C_{21}H_{16}N_3$ ([M + H]$^+$): 310.13387; found: 310.13398; calcd. for $C_{21}H_{16}N_3Na$ ([M + Na]$^+$): 332.11582; found: 332.11606.

6-(4-Methoxybenzyl)-6H-indolo[2,3-b]quinoxaline **(11o)** was prepared following general procedure B using compound **9** (100 mg, 0.28 mmol) and 4-methoxybenzylamine (108 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptanes/ethylacetate 2:1) to yield **11o** (86 mg, 92 %) as a yellow solid; m.p.129-130 ºC;^{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 =2929 (w), 1612 (w), 1583 (m), 1489 (m), 1470 (m), 1443 (w), 1410 (m), 1369 (m), 1360 (m), 1350 (m), 1325 (m), 1308 (w), 1282 (w), 1267 (w), 1244 (w), 1232 (w), 1207 (m), 1174 (m), 1161 (w), 1140 (w), 1128 (w), 1115 (m), 1088 (w), 1076 (w), 1070 (w), 1039 (w), 1032 (w), 1016 (w), 1005 (w), 987 (w), 976 (w), 951 (w), 935 (w), 928 (w), 758 (m), 737 (vs), 721 (m), 702 (s), 679 (m), 636 (w), 629 (w), 606 (m), 594 (m), 577 (m), 565 (m), 546 (w), 532 (m); GC-MS (EI, 70 eV): m/z (%) = 339 (37), 121 (100), 90 (12); HRMS (ESI): calcd. for $C_{22}H_{17}N_3O_1$ ([M + H]$^+$): 340.14444; found: 340.14427.

6-(4-Fluorobenzyl)-6H-indolo[2,3-b]quinoxaline **(11p)** was prepared following general procedure B using compound **9** (100 mg, 0.28 mmol)and 4-fluorobenzylamine (94 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptanes/ ethylacetate 4:1) to yield **11p** (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), 7.26 (ddd, *J* = 7.5, 6.8, 1.3 Hz, 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 **(11q)** was prepared following general procedure B using compound **9** (100 mg, 0.28 mmol) and trifluoromethylbenzylamine (118 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptanes/ethylacetate 4:1) to yield **11q** (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 **(11r)** was prepared following general procedure B using compound **9** (100 mg, 0.28 mmol)and phenylethylamine (104 µL, 0.82 mmol). The

product was purified by flash chromatography (silica gel, heptanes/ethylacetate 5:1) to yield **11r** (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 **(11s)** was prepared following general procedure B using compound **9** (100 mg, 0.28 mmol) and phenylpropylamine (117 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptanes/ethylacetate 5:1) to yield **11s** (84 mg, 91 %) as a yellow solid; m.p. 180-181 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.41 (d, *J* = 7.7 Hz, 1H), 8.25 (dd, *J* = 8.3, 1.3 Hz, 1H), 8.08 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.77 – 7.49 (m, 3H), 7.36 – 7.19 (m, 4H), 6.78 – 6.71 (m, 2H), 5.58 (s, 2H), 3.67 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 159.11, 145.77, 144.26, 140.67, 140.05, 139.47, 130.95, 129.33, 128.77, 128.62, 128.59, 127.88, 126.06, 122.69, 121.06, 119.66, 114.15, 110.14, 55.22, 44.49; 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 **(11t)** was prepared following general procedure B using compound **9** (100 mg, 0.28 mmol) and cyclohexylamine (90 µL, 0.82 mmol). The product was purified by flash chromatography (silica gel, heptanes/ethylacetate 5:1) to yield **11t** (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 (ddd, *J* = 12.4, 8.8, 3.8 Hz, 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 C for C-N coupling/C-H bond activation. Synthesis of *6-phenyl-6H-indolo[2,3-b]quinoxaline* (11a). To a pressure tube charged with 2,3-dibromoquinoxaline **7** (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, heptanes/ethylacetate 5:1) to yield **11a** (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 **(8a)** was prepared following general procedure C using compound **7** (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, heptanes/ethylacetate 5:1) to yield **8a** (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 **(8b)** was prepared following general procedure C using compound **7** (100 mg, 0.35 mmol) and bis(4-methoxyphenyl)amine (66 mg, 0.29 mmol). The product was purified by flash chromatography (silica gel, heptanes/ethylacetate 1:1) to yield **8b** (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, 2H), 8.03 – 7.98 (m, 2H), 7.93 (d, *J* = 2.5 Hz, 2H), 7.62 (tt, *J* = 6.8, 5.1 Hz, 4H), 7.56 – 7.49 (m, 4H), 7.30 (d, *J* = 8.9 Hz, 2H), 7.17 (dd, *J* = 8.6, 2.9 Hz, 3H), 7.11 – 7.04 (m, 4H), 3.91 (s, 6H), 3.85 (s, 6H); ^{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.

References

1. T.-H. Su, C.-H. Fan, Y.-H. Ou-Yang, L.-C. Hsu, and C.-H. Cheng, *J. Mater. Chem. C*, 2013, **1**, 5084–5092.

2. P. Tyagi, a Venkateswararao, and K. R. J. Thomas, *J. Org. Chem.*, 2011, **76**, 4571–81.

3. C.-H. Fan, P. Sun, T.-H. Su, and C.-H. Cheng, *Adv. Mater.*, 2011, **23**, 2981–5.

4. K. R. J. Thomas and P. Tyagi, *J. Org. Chem.*, 2010, **75**, 8100–8011.

5. J. Harmenberg, B. Wahren, J. A. N. Bergman, S. Akerfeldt, and L. Lundblad, *Antimicrob. Agents Chemother.*, 1988, **32**, 1720–1724.

6. J. Harmenberg, A. Gr, T. Malmfors, J. Bergman, B. Wahren, and S. Cox, *Antiviral Res.*, 1991, **15**, 193–204.

7. K. Hirata, J. Araya, S. Nakaike, K. Kitamura, and T. Ishida, *Chem. Pharm. Bull. (Tokyo).*, 2001, **49**, 44–8.

8. L. W. Deady, a J. Kaye, G. J. Finlay, B. C. Baguley, and W. a Denny, *J. Med. Chem.*, 1997, **40**, 2040–6.

9. K. Manna and Y. K. Agrawal, *Bioorg. Med. Chem. Lett.*, 2009, **19**, 2688–92.

10. N. R. Pai and D. A. Pusalkar, *J. Chem. Pharm. Res.*, 2010, **2**, 485–493.

11. M. O. Shibinskaya, S. a Lyakhov, A. V Mazepa, S. a Andronati, A. V Turov, N. M. Zholobak, and N. Y. Spivak, *Eur. J. Med. Chem.*, 2010, **45**, 1237–43.

12. M. O. Shibinskaya, A. S. Karpenko, S. a Lyakhov, S. a Andronati, N. M. Zholobak, N. Y. Spivak, N. a Samochina, L. M. Shafran, M. J. Zubritsky, and V. F. Galat, *Eur. J. Med. Chem.*, 2011, **46**, 794–8.

13. S. Avula, J. R. Komsani, S. Koppireddi, R. Yadla, A. K. Kanugula, and S. Kotamraju, *Med. Chem. Res.*, 2012, **22**, 3712–3718.

14. V. C. Wentrup, C. Thetaz, E. Tagliaferri, H. J. Lindner, B. Kitschke, and H.-W. Winter, *Angew. Chemie*, 1980, **4**, 556–557.

15. F.-A. Alphonse, S. Routier, G. Coudert, and J.-Y. Mérour, *Heterocycles*, 2001, **55**, 925–940.

16. L. Ackermann, A. Althammer, and P. Mayer, *Synthesis (Stuttg).*, 2009, **2009**, 3493–3503.

17. L. Ackermann and A. Althammer, *Angew. Chem. Int. Ed. Engl.*, 2007, **46**, 1627–9.

18. T. Q. Hung, T. T. Dang, A. Villinger, T. Van Sung, and P. Langer, *Org. Biomol. Chem.*, 2012, **10**, 9041–4.

19. J. J. Li, K. G. Carson, B. K. Trivedi, W. S. Yue, Q. Ye, R. a Glynn, S. R. Miller, D. T. Connor, B. D. Roth, J. R. Luly, J. E. Low, D. J. Heilig, W. Yang, S. Qin, and S. Hunt, *Bioorg. Med. Chem.*, 2003, **11**, 3777–3790.

20. I. Javed, A. Khurshid, M. N. Arshad, and Y. Wang, *New J. Chem.*, 2014, **38**, 752–761.

21. T. Tao, Y.-X. Peng, W. Huang, and X.-Z. You, *J. Org. Chem.*, 2013, **78**, 2472–81.

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

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

24. A. D. Becke, *J. Chem. Phys.*, 1993, **98**, 5648–5652.

25. C. Lee, W. Yang, and R. G. Parr, *Phys. Rev. B*, 1988, **37**, 785–789.

26. P. C. Hariharan and J. A. Pople, *Theor. Chim. Acta*, 1973, **28**, 213–222.

27. V. O. Iaroshenko, D. Ostrovskyi, K. Ayub, A. Spannenberg, and P. Langer, *Adv. Synth. Catal.*, 2013, **355**, 576–588.

28. H. Ullah, A.-H. A. Shah, K. Ayub, and S. Bilal, *J. Phys. Chem. C*, 2013, **117**, 4069–4078.