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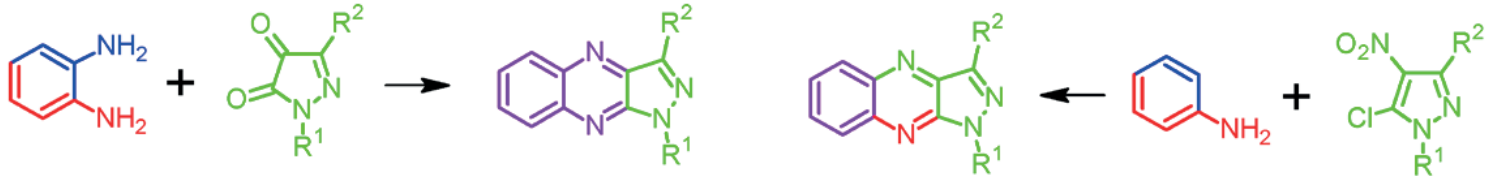
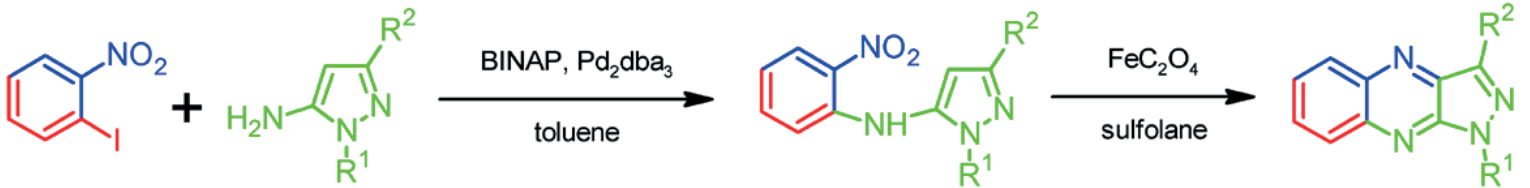
Older methods - not-regioselective, isomers possible



THIS WORK - new method



REGIOSPECIFIC - **ONLY ONE** PRODUCT

A new regiospecific synthesis method of 1*H*-pyrazolo[3,4-*b*]quinoxalines – potential materials for organic optoelectronic devices, and a revision of an oldest scheme

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Abstract

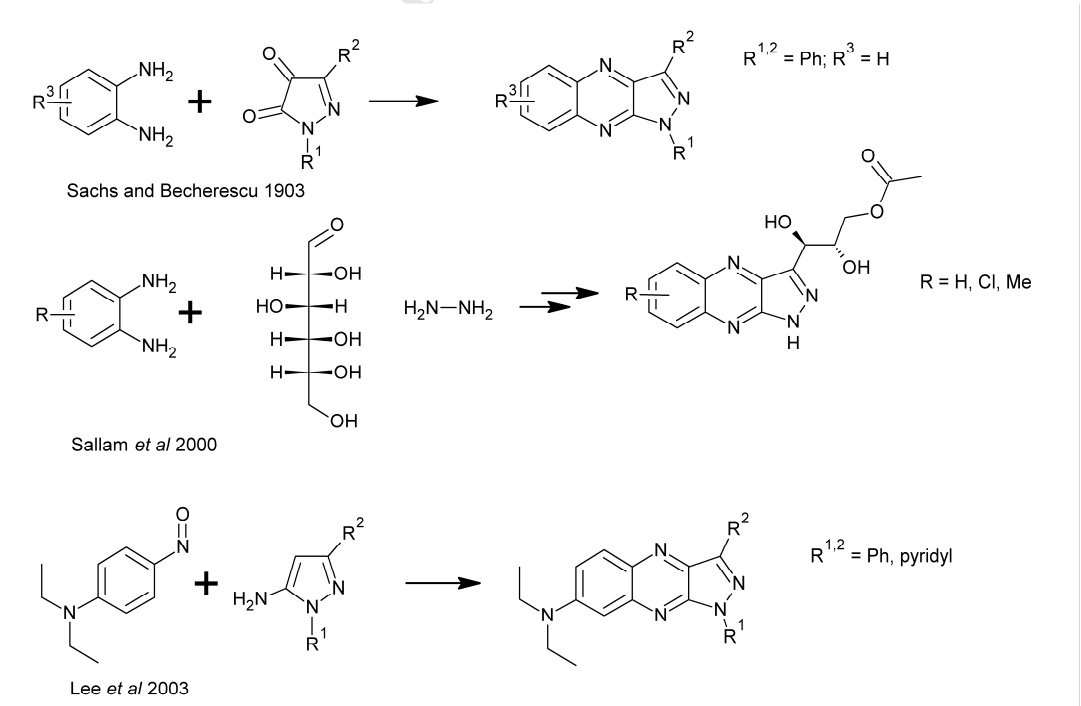
A series of 6-substituted-1,3-diphenyl-1*H*-pyrazolo[3,4-*b*]quinoxalines were prepared using a new synthetic pathway: reductive cyclization of appropriate 5-(*o*-nitrophenyl)-pyrazoles with ferrous oxalate or triphenylphosphine. The main advantage of this procedure is that, contrary to the older protocols of pyrazolo[3,4-*b*]quinoxaline synthesis, this method allows for a substituent to be introduced to the carbocyclic ring without the formation of isomers. The pyrazole ring can also be modified to some extent. Furthermore, we propose a new mechanism for the oldest reported pyrazolo[3,4-*b*]quinoxaline synthesis, based on the condensation between *o*-phenylenediamine and 3,4-pyrazolin-5-diones.

Keywords:

1*H*-pyrazolo[3,4-*b*]quinoxaline,
palladium aminoarylation,
reductive cyclization,
ferrous oxalate,
Cadogan synthesis,
X-ray crystallography

1. Introduction

In 1903 Sachs and Becherescu synthesized the first examples of the 1*H*-pyrazolo[3,4-*b*]quinoxaline (**PQX**) system by heating *o*-phenylenediamine with 2,5-diphenylpyrazole-3,4-dione.[1] Since then, this particular class of compounds, sometimes called flavazoles, has attracted the attention of many scientists. A significant amount of research has been carried out in order to determine their biological properties. For example, it has been discovered that 1*H*-Pyrazolo[3,4-*b*]quinoxalines exhibit antibacterial activity.[2] Additionally, these compounds have been investigated as possible antifungal, antihypertensive, antiproliferative or anti-inflammatory agents.[3] Regardless of their biological activity, the photophysical properties of **PQX** make them quite attractive for practical applications. Many pyrazoloquinoxalines exhibit strong fluorescence in solution, as well as in solid-state.[4] Kucybała *et al.* synthesized a series of pyrazoloquinoxaline dyes and tested them as novel photoinitiators for free radical polymerization.[5] Numerous quinoxaline derivatives are applied in the field of organic electronics, either as electron transporting materials ETM, or emissive materials EM.[6,7] 1*H*-Pyrazolo[3,4-*b*]quinolines substituted with *N*,*N*-dialkylamino groups have been applied as green emitters in multilayer organic light emitting diodes OLED.[8] Quinoxaline-based oligomers and polymers are used in the fabrication of organic photovoltaic devices.[9] We have previously synthesized fluorene/1,3-diphenyl-1*H*-pyrazolo[3,4-*b*]quinoxaline copolymers and applied them in a bulk heterojunction solar cell.[10] The most common synthetic procedures for the production of pyrazolo[3,4-*b*]quinoxalines are depicted on Scheme 1.

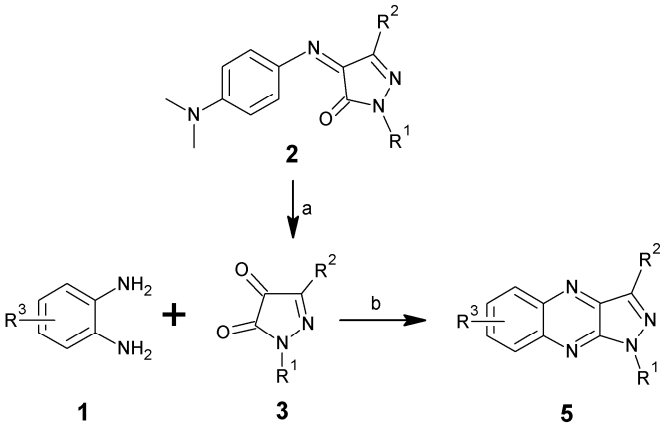


Scheme 1. Some of the synthetic approaches to the 1*H*-pyrazolo[3,4-*b*]quinoxaline system.

The procedure applied by Sachs and Becherescu belongs to the family of quinoxaline derivatives syntheses, and is based on a condensation between 1,2-diaminobenzenes and two-carbonyl-group-carrying molecules, mentioned in the recent reviews by Mamedov and Zhukova.[11] The method is limited only to unsubstituted 1,2-diaminobenzene (R^3 = H) or to symmetrical 4,5- and 3,6-disubstituted examples. Otherwise, 1,2-diaminobenzene and pirazolin-3,4-dione condensation, results in a mixture of isomers.[12] Sometimes their separation involves tedious chromatographic procedures, due to relatively close R_f values. The majority of pyrazoloquinoxaline synthetic procedures described in the literature are based on pyrazole ring formation. One of the most exploited synthetic pathways involves the heating of *o*-phenylenediamine, an excess of phenylhydrazine, and a reducing sugar. As a result, derivatives of 1-phenyl-1*H*-pyrazolo[3,4-*b*]quinoxaline modified in the 3 position of the pyrazole ring are formed.[13] Sardonick and Linker developed an easy synthetic procedure for flavazole preparation starting from 2-acetylquinoxaline oxime and hydrazines.[14] The pyrazol ring can also be formed by dehydrogenation, or dehydrohalogenation of appropriate arylhydrazones prepared from 2-acylquinoxalines.[15,16] Modifications on the carbocyclic ring of the flavazole system are less common. Credner prepared 7-*N*,*N*-diethylamine substituted **PQX** by reacting *N*,*N*-diethyl-*p*-phenylenediamine and 4-methyl-*N*-(5-methyl-2-phenylpyrazol-3-yl)benzenesulfonamide in the presence of potassium persulfate.[4a] Derivatives of the same type were prepared by Wang *et al.*, but in that case *p*-nitroso-*N*,*N*-dialkylamine was used instead of *p*-phenylenediamine.[8a] We have developed a new synthetic method for the synthesis of 6-substituted-1*H*-pyrazolo[3,4-*b*]quinoxalines, starting from substituted *o*-nitroiodobenzene and commercially available 3-aminopyrazoles. Moreover, we have revised the reaction mechanism of **PQX** formation based on the condensation of *o*-phenylenediamine with pyrazolin-3,4-diones.

2. Results and discussion

In previous studies, we used 1*H*-pyrazolo[3,4-*b*]quinolines as effective luminophores in organic light emitting diodes, either as dopants in poly(9-*N*-vinylcarbazole),[17] or as vacuum evaporated films in multilayer devices.[18] Afterwards we applied a structurally similar system of 1*H*-pyrazolo[3,4-*b*]quinoxalines, **PQX**, because of its strong emission both in solution and in solid-state.[19] The 1,3-diphenyl-1*H*-pyrazolo[3,4-*b*]quinoxaline (**5**) luminophore was prepared according to the procedure by Sachs and Becherescu, which involves heating equimolar amounts of *o*-phenylenediamine (**1**) with 2,5-diphenylpyrazole-3,4-dione (**3**) (Scheme 2; **5a** $R^{1,2}$ = Ph, R^3 = H).[1] The same procedure was applied for other methyl/phenyl substituted pyrazoloquinoxalines **5b-d** (Table 1).



Scheme 2. a) H_2SO_4, ethanol/reflux/2 hrs, b) glacial acetic acid/reflux/24 hrs.

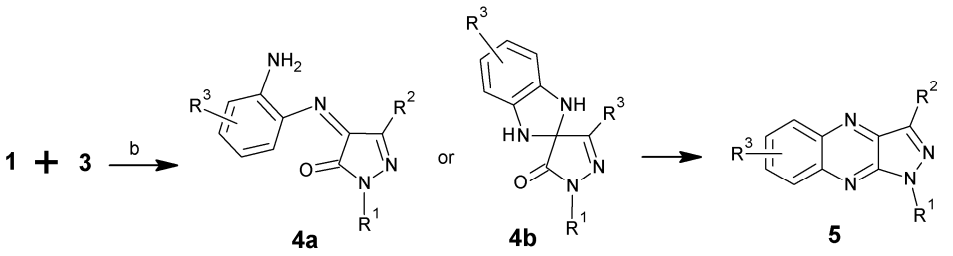
Table 1. The reaction times and yields of unsubstituted 1*H*-pyrazolo[3,4-*b*]quinoxalines

Entry	Product	R^1	R^2	R^3	Time	% Yield
1	**5a**	Ph	Ph	H	24 h	70
2	**5b**	Ph	Me	H	24 h	55
3	**5c**	Me	Ph	H	2-3 h	70
4	**5d**	Me	Me	H	2-3 h	70

Pyrazole-3,4-diones (**3**) were prepared in the reaction of appropriate 2,4-dihydro-3*H*-pyrazol-3-ones with *p*-nitroso-*N*,*N*-dimethylaniline leading to imino compounds (**2**). These imino compounds (**2)** have an interesting feature – in the crystalline state they form black crystals (dark red in transmitted light) with a metallic, usually green, lustre. In our case this feature

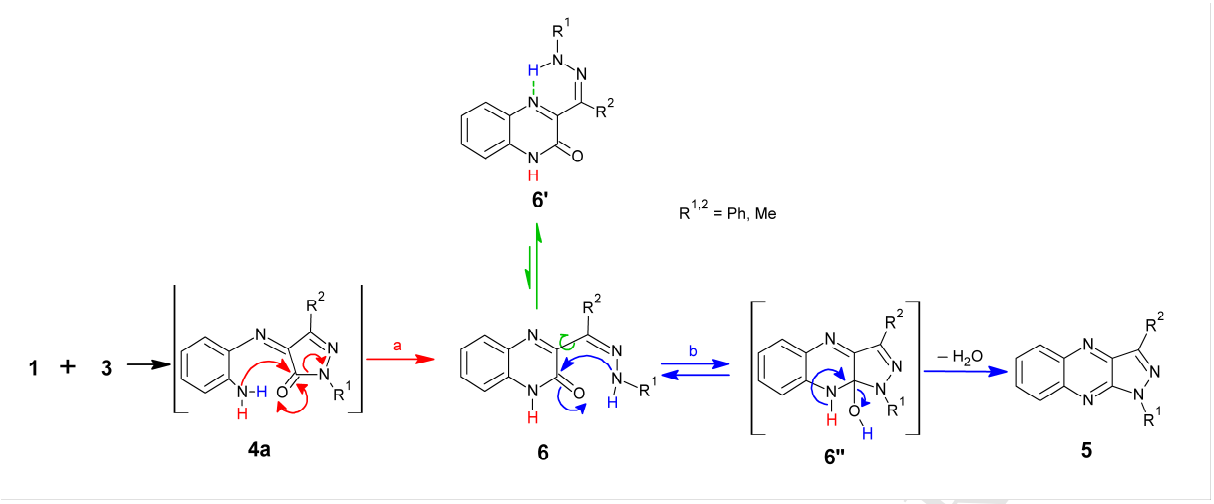
could be explained by analysing the crystal structure determined for (4*Z*)-4-[4-(dimethylamino)phenyl]imino-5-methyl-2-phenyl-pyrazol-3-one (**2b**). Single crystals of **2b** were obtained from an acetone solution by slow evaporation at ambient temperature. The measurement conditions and refinement parameters are summarized in Table S1 (Supplementary Data). The shape of the molecule is presented in Figure S1. The **2b** molecule is almost planar: dihedral angles between the rings do not exceed 10° (cf. Table S2). The conformation is stabilized by intramolecular hydrogen-bond-like interactions of C-H…O and C-H…N types (Table S3 and Figure S1). Additionally, the "single" bonds: N1-C11, N4-C41, and C44-N50 are also significantly shortened (cf. Table S2), which is caused by strong conjugation through the 1-phenyl—pyrazol—4-phenyl—*N*,*N*-dimethyl moieties. These features are responsible for the dark-red colour of the chromophore in the solid-state (observed as black by the naked eye), and red in solution: $\lambda_{\max(CHCl_3)}$ for **2b** is 513 nm (green), which is complementary to red.[20] The molecules of **2b** form dimers in solid-state with π…π and N…π interactions between the pyrazole rings (Table S3). The dimers form layers parallel to (-101) (see Figure S2 in Supplementary Data). The conformation of the molecule of **2b** and the packing in the crystal structure are similar to those found previously for (4*Z*)-4-[4-(diethylamino)phenyl]imino-5-methyl-2-phenyl-pyrazol-3-one.[21] These two characteristics (i.e. the specific conformation of the molecules and their packing scheme) found for **2b** might be responsible for the metallic lustre of the crystals. The effect (metallic lustre of organic crystals) was observed previously, and it was explained to be caused by the specific relative position of molecules in the crystalline state, which form layers consisting of relatively long molecules with conjugated π-systems.[22]

Subsequent hydrolysis of **2** with dilute H_2SO_4 produced **3** (Scheme 2). Sachs and Becherescu noticed that a red precipitate was formed in the first stage of the reaction between **1** and **3**.[1] It was transformed into pyrazoloquinoxaline **5** after prolonged heating in glacial acetic acid at reflux. At that time the structure of the red precipitate was not fully determined. Ohle and Melkonian after studying Becherescu's results, concluded that the intermediate product was 2,5-diphenyl-4-phenyliminopyrazol-3-one **4a** (Scheme 3).[23] Kappe *et al.* also reached the same conclusion.[24] On the other hand, Metwally and co-workers suggested a formation of spiro-compound (**4b**), resulting from the condensation of two of *o*-phenylenediamine amino groups with a carbonyl group at C4 of the pyrazole ring.[25] The proposed structure was based on elemental analyses and ^{1}H NMR (DMSO, 90 MHz) spectra.



Scheme 3. Structures of intermediate products **4a**/**4b** in **PQX** synthesis proposed in the literature

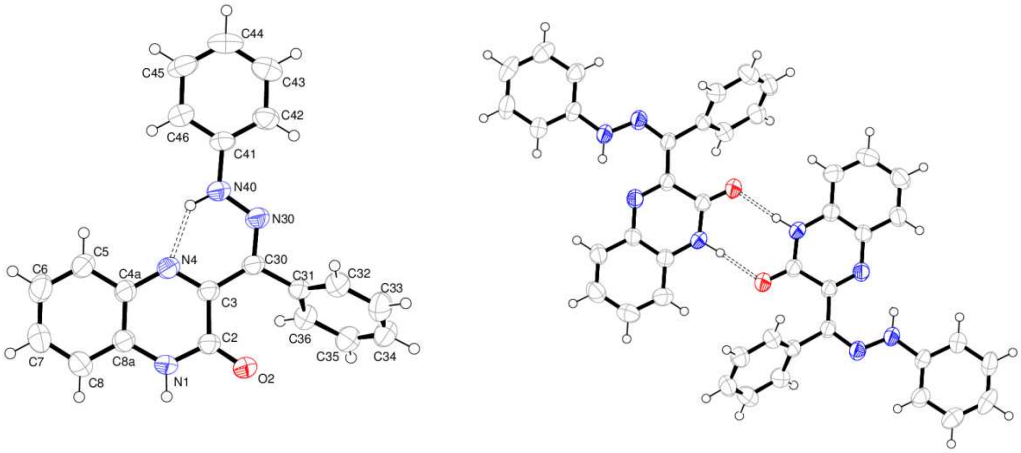
To clarify the uncertainties concerning the exact structure of **4,** we isolated the red crystalline intermediate mentioned earlier.[1,25] After studying the ^{13}C NMR spectra of the supposed spiro system **4b** ($R^{1,2}$ = Ph, R^3 = H) we discovered the presence of 17 signals instead of 14. The presence of the phenyl ring perpendicular to the pyrazole should reduce the amount of ^{13}C NMR signals (in **4a** the phenyl ring has six different carbon atoms, in **4b** there are only three as an effect of the symmetry plane perpendicular to the ring). The same situation occurred when analyzing the intermediate products in the case of 3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]quinoxaline synthesis. An analysis of the ^{1}H NMR spectra again suggested quite different structure of the isolated compounds. In the downfield region of the ^{1}H NMR spectra, two peaks of one-proton singlets at 12.60-12.20 ppm and at 9.80-9.60 ppm, respectively, were observed. This fact excludes both of the previously proposed intermediate structures **4a** and **4b.** It seems that at the beginning of the reaction one amino group of *o*-phenylenediamine (**1**) reacts first with the keto group at C4 of **3**, forming a labile intermediate compound **4a**, which immediately reacts further (Scheme 4)**.** Subsequently an attack on the second carbonyl group in the **4a** molecule, by the second amino group in that molecule (red arrows), leads to an opening of the pyrazole ring, and the formation of phenylhydrazone **6** (Scheme 4; path a, red arrows). From the crystal structure analysis performed for **6a** (see below), it can be concluded, that after the formation of **6**, it rearranges itself to the more stable, but less reactive **6'** conformer (green arrows, hydrogen bond in **6'** marked by green dashed line).



Scheme 4. The proposed mechanism of intermediate **6** and 1*H*-pyrazolo[3,4-*b*]quinoxaline **5** formation.

The heating of phenylhydrazones **6a**,**b** in boiling glacial acetic acid resulted in the formation of pyrazolo[3,4-*b*]quinoxaline **5a**,**b** (Scheme 4, path b, blue arrows). The R^1 substituent plays a crucial role in the formation of **5**. If a phenyl group acts as R^1 substituent, it is able to delocalize a pair of electrons – therefore **6** is more stable (in the form of **6'**) and the reaction time is much longer (up to 24 h), than in the case of alkyl R^1 substituents. An alkyl substituent allows for a shorter reaction time, with the reaction being complete within 2-3 h.

The structure of **6** was conclusively confirmed by the crystal structure analysis performed for 3-[(*Z*)-phenyl(2-phenylhydrazinylidene)methyl]quinoxalin-2(1*H*)-one (**6a**). Single crystals of **6a** were obtained from the DMF solution by slow evaporation at ambient temperature. The measurement conditions and refinement parameters are summarized in Table S1 (Supplementary Data). The shape of the **6a** molecule is presented at Figure 1a, with the intramolecular N-H…N hydrogen bond marked by a dashed line. Figure 1b shows the intermolecular N-H…O hydrogen bonds between two molecules of **6a** in the crystalline state.



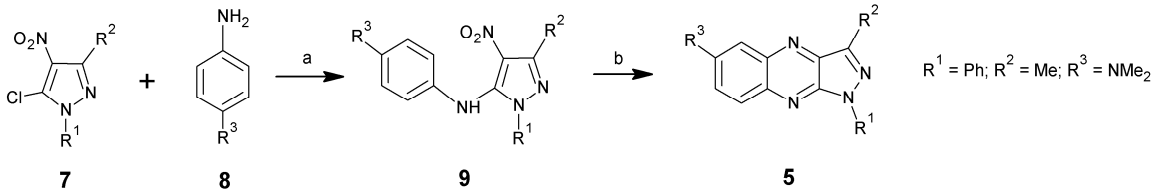
a) b)

Figure 1. a) The shape of molecule for **6a** with the atom numbering scheme. Displacement ellipsoids are drawn at the 50% probability level. The intramolecular N-H…N hydrogen bond is marked by dashed line. b) Two molecules of **6a** with intermolecular N-H…O hydrogen bonds marked by dashed lines.

The energy of these hydrogen bonds was calculated with DFT methodology using the Gaussian09 suite of programs.[26] Counterpoise corrected interaction energy was calculated for the dimer of **6a** at the experimental geometry fitted to neutron X-H distances using M052X/6-311+G(2df,2p) functional/basis set.[27,28] The basis set superposition error (BSSE) corrected energy is equal to -20.94 kcal/mole. For comparison: interaction energy calculated using the same approach for uracil dimer is: -8.47 kcal/mol.[29] QTAIM charge density analysis performed for the dimer of **6a**, evaluated the intra- and intermolecular hydrogen bond energies.[30] It has previously been proven that hydrogen bond energy can be correlated to the pressure employed on the electrons around the critical point: E(HB) = ½ V(rcp).[31] Taking this relation into account, the selected interactions (Table S4 and Figure S3, see Supplementary Data) can be classified as intermediate between closed and shared shell. These energy barriers, stabilizing such conformation of **6a** (Figure 1, and **6'** on Scheme 4), are responsible for the relatively low reactivity of **6a** and **6b.** The reaction of these compounds, leading to 1*H*-pyrazolo[3,4-*b*]quinoxalines **5a** and **5b**, respectively, needs 24 h of heating under reflux in acetic acid solution, until the reaction is finished. The geometrical parameters of **6a** are summarized in Table S5, whereas the data for hydrogen bonds can be found in Table S6 (for both tables see Supplementary Data). Additionally, the comparison of ^{1}H NMR data of the compound **6a** obtained by us, with the product obtained by Mamedov *et al.* (they prepared **6a** from phenylhydrazine and 3-benzoyl-1*H*-quinoxalin-2-one)[32] confirms the proposed structure. Vinot *et al.* also observed an intermediate product of similar structure, while conducting the

reaction between *o*-phenylenediamine and 4-(2-phenylhydrazinylidene)-2*H*-chromene-2,3(4*H*)-dione.[33]

As mentioned earlier, the condensation of substituted *o*-phenylenediamines with 2,5-disubstituted pyrazolin-3,4-diones leads to isomer formation (Scheme 3; for $R^3 \neq H$). In order to avoid isomer formation in the synthesis of 1*H*-pyrazolo[3,4-*b*]quinoxalines, we applied a different synthetic pathway, depicted in Scheme 5 and 6.

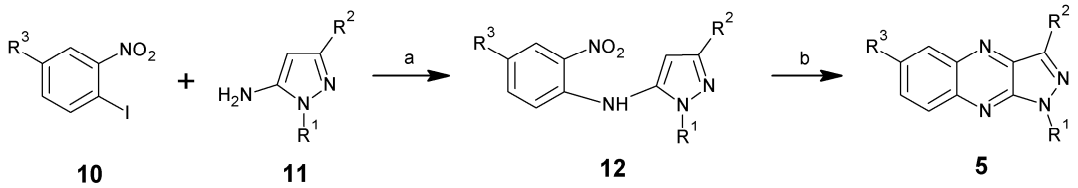


Scheme 5. a) K_2CO_3/DMF or KOH/H_2O/Pd_2dba_3/(*o*-biphenyl)P(*t*-Bu)$_2$; b) $FeC_2O_4 \cdot 2H_2O$ /sulfolane/250 °C/10 min.

In the search for new OLED luminophores we synthesized 6-*N*,*N*-dimethyl-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]quinoxaline, in order to investigate its photophysical properties.[4c] The derivative **9** (R^3=NMe_2) was cyclised according to a modified procedure for phenazine synthesis used by Vivian *et al*.[34] They used ferrous oxalate/lead shot mixture as a reducing agent in the synthesis of phenazines from 2-nitrodipenylamines. The exact mechanism of this reaction is not yet fully established. It seems that in the first stage ferrous oxalate decomposes and the resulting products are involved in the deoxygenation of the nitro group. The resulting nitrene attacks a neighbouring aromatic ring and phenazines are formed. Pyrazolo[3,4-b]quinoxaline **5** (R^1 = Ph, R^2 = Me, R^3 = NMe_2) was prepared via the cyclization of **9** using ferrous oxalate in boiling sulfolane. However due to the harsh reaction conditions, the resulting product underwent partial decomposition and the final yield of **5** was relatively low (~27%).

4-Nitro-5-arylaminoderivative (**9**) can be prepared either by heating **7** with aniline **8** in the presence of anhydrous potassium carbonate in DMF, or by a palladium aminoarylation protocol developed by Surry and Buchwald.[35] The reductive cyclization of **9** is limited to only two types of pyrazoloquinoxalines **5**: R^1 = Ph / R^2 = Me and $R^{1,2}$ = Me. It is linked to the synthesis of a starting reagent 5-chloro-4-nitropyrazole (**7**). This compound can be prepared either by nitration of appropriate 5-chloropyrazoles with fuming HNO_3 in acetic anhydride (for R^1 = Ph, R^2 = Me), or with a mixture of fuming H_2SO_4 and HNO_3 ($R^{1,2}$ = Me).[36] Unfortunately, attempts to prepare **7** with $R^{1,2}$ = Ph or R^1 = Me, R^2 = Ph failed. In both cases,

we obtained a mixture of polynitrated compounds. Thus, the pathway according to scheme 5 is limited as far as the modification of pyrazole ring is concerned. This inconvenience can be avoided by applying a slightly different synthetic procedure using aminopyrazoles as starting materials (Scheme 6).



Scheme 6. a) BINAP, Pd_2dba_3 b) $FeC_2O_4 \cdot 2H_2O$/sulfolane or Ph_3P/*o*-chlorobenzene.

Certain aminopyrazoles **11** can be purchased from commercial chemical suppliers, or prepared in a reaction of aryl/alkyl hydrazines with aroyl/acetylacetonitriles. [37] Nitroderivatives **10** were prepared by nitration of *p*-substituted acetanilides, followed by removal of the protecting group, and subsequent Sandmayer iodination.[38] The coupling of **10** and **11** was accomplished via a palladium catalyzed reaction in the presence of *rac*-BINAP.[34] The structure of compound **12** in the solid state was determined for **12a** and **12b** by crystal structure analysis. Single crystals were obtained by slow cooling of hot, saturated toluene solutions. The details of measurement conditions, together with refinement parameters can be found in Table S1 (see Supplementary Data). Additionally, the most important geometrical parameters for the analyzed structures are listed in Supplementary Data in Table S7 and Table S8 contains the geometry of intramolecular N-H…O hydrogen bonds and the most important weak interactions. Figure S4 shows the shape of the molecules **12a** and **12b**. The geometry of both molecules is comparable with that found earlier for a similar compound, methyl 4-[(1-acetyl-3-*tert*-butyl-1*H*-pyrazol-5-yl)amino]-3-nitrobenzoate, with corresponding intramolecular hydrogen bonds also observed for this structure.[39]

Compound **12** was heated with ferrous oxalate dihydrate in boiling sulfolane, yielding pyrazolo[3,4-*b*]quinoxaline **5**. The yields varied between 27-70% (Table 2). An alternative strategy for this reaction is the application of triethylphosphite/triphenylphosphine as a reducing agent. This method was employed in the synthesis of phenazines, indoles, and carbazoles, starting from the appropriate nitro compounds. [40] When we applied triphenylphosphine in the synthesis of unsubstituted pyrazoloquinoxalines from **12** (R^3=H), the yields varied between 7-50% for the final products (Table 2).

Table 2. The reaction conditions for cyclization of **12**

Entry	Product	R^1	R^2	R^3	Reagent	Solvent	Time	% Yield
1	**5a**	Ph	Ph	H	FeC_2O_4	sulfolane	20 min	68
2	**5b**	Ph	Me	H	FeC_2O_4	sulfolane	20 min	50
3	**5c**	Me	Ph	H	FeC_2O_4	sulfolane	20 min	44
4	**5d**	Me	Me	H	FeC_2O_4	sulfolane	20 min	51
5	**5a**	Ph	Ph	H	Ph_3P	DCB[a]	24 h	52
6	**5b**	Ph	Me	H	Ph_3P	DMAc[b]	46 h	16
7	**5c**	Me	Ph	H	Ph_3P	DCB[a]	43 h	8
8	**5d**	Me	Me	H	Ph_3P	DMAc[b]	48 h	7
9	**5e**	Ph	Ph	Cl	FeC_2O_4	sulfolane	20 min	61
10	**5f**	Ph	Ph	Br	FeC_2O_4	sulfolane	20 min	24
11	**5g**	Ph	Ph	F	FeC_2O_4	sulfolane	20 min	15
12	**5h**	Ph	Ph	Me	FeC_2O_4	sulfolane	20 min	43
13	**5i**	Ph	Ph	MeO	FeC_2O_4	sulfolane	20 min	38

[a] 1,2-Dichlorobenzene
[b] *N*,*N*-Dimethylacetamide

The reaction conditions were unoptimized. 6-*N*,*N*-Diphenylamine-1,3-diphenyl-1*H*-pyrazolo[3,4-*b*]quinoxaline (**5j**) ($R^{1,2}$ = Ph, R^3 = *N*,*N*-Ph) was prepared by the palladium-catalysed aminoarylation of **5e** ($R^{1,2}$ = Ph, R^3 = Cl) with diphenylamine. All of the pyrazolo[3,4-*b*]quinoxalines **5a-j** will be tested as potential luminophores for use in OLEDs.

3. Conclusions

We have developed a new regiospecific method for the synthesis of pyrazoloquinoxalines from aminopyrazoles and substituted *o*-iodonitrobenzene derivatives. This method is suitable for the modification of both the carbocyclic ring and the pyrazole. It is anticipated that the application of appropriate *o*-iodonitro derivatives will also allow for a regiospecific synthesis of 8-, 7- and 5-substituted pyrazoloquinoxaline derivatives. Furthermore, we have determined the specific mechanism of the oldest reported 1*H*-pyrazolo[3,4-*b*]quinoxaline synthesis.

4. Experimental

4.1. Materials and methods

All reagents and solvents were purchased from commercial sources (Aldrich and POCh – Polish chemical company) and were used without further purification. Aluminium oxide 90 active neutral 70-230 mesh purchased from Merck, was used for column chromatography. The purity of final compounds was monitored using silica gel GF_{254} precoated thin layer chromatography (TLC) plates (Merck). The compounds were characterized by ^{1}H NMR, ^{13}C NMR, and elemental analyses. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker Avance III 600. Chemical shifts (δ) were reported in ppm, using TMS as internal standard. Melting points were determined on a Mel-Temp II Apparatus (capillary), and they were left uncorrected. Elemental analyses were conducted at Elementar Vario MICRO cube. IR spectra were recorded on a Thermo Nicolet iS5 infrared spectrometer with ATR. Diffraction datasets were collected for single crystals either with an Agilent Technologies SuperNova™ diffractometer, [41] (low-temperature Cryo-Jet device, Atlas CCD detector), using Mo Kα radiation or Cu Kα radiation; or with the Nonius KappaCCD diffractometer using graphite monochromated Mo Kα radiation (data collection: COLLECT, [42] cell refinement: HKL SCALEPACK, [43] data reduction: HKL DENZO and SCALEPACK).[42] The programs used for the crystal structure analyses: SIR92 for solving the structures with direct methods, [44] SHELXL2013 for the refinement of the structures, [45] ORTEP3 for the preparation of molecular graphics, [46] were working under WinGX environment. [47] The supplementary materials were stored at CCDC.[48]

*4.2. General procedure for synthesis of 4-[4-(dimethylamino)phenyl]imino-2,5-disubstituted pyrazol-3-ones (**2**)*

Compounds were prepared using modified literature procedure[1]. A 30% solution (3.0 mL) of Na_2CO_3 was added in portions to a stirred hot (75 °C) solution of 4-nitroso-*N*,*N*-dimethylaniline (3.0 g, 0.02 mol) in ethanol (20 mL). After 5 min, a solution of appropriate pyrazolone (0.02 mol) in ethanol (50 mL) was added dropwise. The reaction mixture was kept at 85 °C for 3 h. After the reaction was complete it was refrigerated overnight at 4 °C and the resulting precipitate was filtered off and recrystallized from toluene.

*4.2.1. (4Z)-4-[4-(dimethylamino)phenyl]imino-2,5-diphenyl-pyrazol-3-one (**2a**)*

Black prisms with green metallic lustre, 5.2 g, 70%, mp. 216-217 °C (toluene) (lit. 218.5 °C[1]); ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ = 8.29-8.26 (m, 4H), 8.09-8.07 (m, 2H), 7.48-7.43 (m, 5H), 7.22 (t, *J* = 7.3 Hz, 1H), 6.74-6.71 (m, 2H), 3.15 (s, 6H, $N(CH_3)_2$); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ = 153.7, 153.4, 148.7, 141.6, 138.7, 136.6, 133.2, 131.1, 129.4, 128.8, 128.4, 128.2, 125.1, 119.1, 111.1, 40.3; IR (ATR): ν = 3059, 1679, 1600, 1492, 1372, 1299, 1147, 1109, 932, 821, 761, 691, 669, 504 cm^{-1}. Anal. Calcd for $C_{23}H_{20}N_4O$: C, 74.98; H, 5.47; N, 15.21. Found: C, 74.81; H, 5.50; N, 15.13.

*4.2.2. (4Z)-4-[4-(dimethylamino)phenyl]imino-5-methyl-2-phenyl-pyrazol-3-one (**2b**)*

Black prisms with green metallic lustre, 2.4 g, 42%, mp. 190-191 °C (toluene) (187 °C[49]); ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ = 8.29-8.27 (m, 2H), 7.97-7.95 (m, 2H), 7.42-7.39 (m, 2H), 7.17 (t, *J* = 7.4 Hz, 1H), 6.72-6.69 (m, 2H), 3.13 (s, 6H, $N(CH_3)_2$), 2.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ = 153.8, 153.2, 152.0, 142.8, 138.6, 136.4, 133.2, 128.7, 124.8, 118.8, 111.1, 40.3, 12.5; IR (ATR): ν = 3250, 2914, 1666, 1476, 1435, 1369, 1299, 1255, 1169, 1100, 992, 818, 751, 688, 656, 517, 457 cm^{-1}. Anal. Calcd for $C_{18}H_{18}N_4O$: C, 70.57; H, 5.92; N, 18.29. Found: C, 70.44; H, 5.93; N, 18.12.

*4.2.3. (4Z)-4-[4-(dimethylamino)phenyl]imino-2-methyl-5-phenyl-pyrazol-3-one (**2c**)*

Black small needles with green metallic lustre, 1.5 g, mp. 135-136 °C (toluene). ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ = 8.30-8.28 (m, 2H), 8.14-8.12 (m, 2H), 7.44-7.38 (m, 3H), 6.72-6.69 (m, 2H), 3.49 (s, 3H), 3.14 (s, 6H).^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ = 154.9, 153.2, 147.5, 141.8, 136.7, 133.0, 131.2, 129.1, 128.2, 128.1, 111.1, 40.3, 32.2; IR (ATR): ν = 3053, 1654, 1616, 1499, 1473, 1372, 1337, 1166, 1033, 973, 821, 755, 647, 527, 495, 463 cm^{-1}. Anal. Calcd for $C_{18}H_{18}N_4O$: C, 70.57; H, 5.92; N, 18.29. Found: C, 70.45; H, 5.61; N, 18.01.

*4.2.4. (4Z)-4-[4-(dimethylamino)phenyl]imino-2,5-dimethyl-pyrazol-3-one (**2d**)*

Black small prisms with metallic lustre, 2.1 g, 50%, mp. 174-176 °C (toluene) (lit. 172 °C[50]). ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ = 8.28-8.26 (m, 2H), 6.69-6.67 (m, 2H), 3.36 (s, 3H),

3.12 (s, 6H), 2.18 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ = 155.1, 153.0, 150.2, 143.2, 136.4, 132.9, 111.1, 40.2, 31.8, 12.3; IR (ATR): ν = 2908, 2819, 1644, 1609, 1527, 1486, 1432, 1356, 1318, 1248, 1226, 1160, 1046, 1017, 941, 824, 770, 644, 603, 571, 517, 463 cm^{-1}. Anal. Calcd for $C_{13}H_{16}N_4O$: C, 63.91; H, 6.60; N, 22.93. Found: C, 63.96; H, 6.38; N, 22.39.

*4.3. General procedure for 2,5-disubstituted pyrazolin-3,4-dione (**3**)*

The diones **3a**, **3b** and **3d** were prepared according to literature procedures. [1,51,52]

*4.3.1. 2-methyl-5-phenyl-pyrazole-3,4-dione (**3c**)*

Compound **2c** (1.53 g, 5 mmol) was dissolved in ethanol (20 mL), and 10 mL of 10% H_2SO_4 was added. The reaction mixture was heated at 85 °C for 3 h. After cooling, the contents were poured into water (100 mL) and extracted with ethyl acetate (3 × 25 mL). The organic phase was dried over anhydrous $MgSO_4$ and evaporated. The residue was recrystallized from toluene/petrol ether.

Brown powder, 836 mg, 87%, mp. 102-104 °C; ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ = 8.05-8.03 (m, 2H), 7.48-7.44 (m, 3H), 3.49 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ = 185.0, 157.1, 150.6, 139.8, 131.3, 129.1, 126.8, 32.8. IR (ATR): ν = 3240, 2923, 1685, 1087, 1036, 859, 751, 685, 647, 590 cm^{-1}. Anal. Calcd for $C_{10}H_8N_2O_2$: C, 63.82; H, 4.28; N, 14.89. Found: C, 63.76; H, 4.19; N, 14.56.

*4.4. Synthesis of 1,3-disubstituted-1H-pyrazolo[3,4-b]quinoxalines (**5**) from 1,2-phenylenediamine - general procedure*

A mixture of 1,2-diphenylamine **1** (0.34 g, 2 mmol) and corresponding pyrazolin-3,4-dione **3** (2 mmol) in 5 mL glacial acetic acid was stirred and heated at reflux for 24 h in the case of **5a** and **5b**, or 2-3 h for **5c** and **5d**. The reaction was cooled and the resulting precipitate was collected by filtration and washed with ethanol, and recrystallized from the solvent indicated in each case.

*4.4.1. 1,3-Diphenyl-1H-pyrazolo[3,4-b]quinoxaline (**5a**)*

Light orange needles, 456 mg, 70%, mp. 238-239 °C (toluene) (lit. 231 °C[1]); ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ = 8.77 (dd, *J* = 8.3, 1.2 Hz, 2H), 8.57 (dd, *J* = 8.6, 1 Hz, 2H), 8.35 (dd, *J* = 8.5, 0.9 Hz, 1H), 8.22 (dd, *J* = 8.6, 0.8 Hz, 1H), 7.86 (dtd, *J* = 7.5, 1.4, 1.5 Hz, 1H), 7.77 (dtd, *J* = 7.5, 1.3, 1.6 Hz, 1H), 7.62-7.58 (m, 4H), 7.50 (t, *J* = 7.4 Hz, 1H), 7.35 (t, *J* = 7.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$, ppm): δ = 143.4, 143.0, 141.4, 141.3, 139.5, 137.0, 131.2, 131.1, 130.6, 129.4, 129.2, 129.1, 128.8, 128.2, 127.4, 125.8, 120.1; IR (ATR): ν = 3056, 1590, 1562, 1459, 1416, 1353, 1252, 1195, 1125, 983, 751, 688, 669, 641, 599, 492, 422 cm^{-1}.

*4.4.2. 3-Methyl-1-phenyl-1H-pyrazolo[3,4-b]quinoxaline (**5b**)*

Deep yellow needles, 286 mg, 55%, mp. 135-136 °C (toluene) (lit. 133.5-134 °C[25]); ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ = 8.45 (dd, *J* = 8.7, 1.1Hz, 2H), 8.28 (dd, *J* = 8.9, 1.3 Hz, 1H), 8.20 (dd, *J* = 8.6, 0.8 Hz, 1H), 7.84 (dtd, *J* = 7.5, 1.4, 1.5 Hz, 1H), 7.75 (dtd, *J* = 7.5, 1.4, 1.7 Hz, 1H), 7.58-7.55 (m, 2H), 7.31 (t, *J* = 7.4 Hz, 1H), 2.89 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$, ppm): δ = 144.4, 142.6, 141.6, 140.8, 139.4, 137.8, 130.9, 130.2, 129.20, 129.1, 128.0, 125.4, 119.6, 11.8; IR (ATR): ν = 3063, 1597, 1562, 1499, 1429, 1356, 1233, 1192, 1112, 1074, 745, 685, 672, 656, 599, 504, 419 cm^{-1}.

*4.4.3. 1-Methyl-3-phenyl-1H-pyrazolo[3,4-b]quinoxaline (**5c**)*

Light orange crystalline powder, 187 mg, 70%, mp. 165°C (toluene); ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ = 8.64 (dd, *J* = 8.3, 1.2 Hz, 2H), 8.33 (dd, *J* = 8.6, 0.9 Hz, 1H), 8.14 (dd, *J* = 8.6, 0.8 Hz, 1H), 7.82 (dtd, *J* = 7.8, 1.4, 1.5 Hz, 1H), 7.73 (dtd, *J* = 7.8, 1.3, 1.7 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 2H), 7.45 (t, *J* = 7.4 Hz, 1H); 4.29 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$, ppm): δ = 143.3, 141.9, 141.4, 141.3, 135.7, 131.6, 130.9, 130.7, 128.9, 128.8, 128.5, 127.5, 126.9, 34.2; IR (ATR): ν = 3053, 1575, 1486, 1464, 1198, 1122, 1084, 929, 881, 755, 742, 691, 675, 656, 631, 599, 504, 422 cm^{-1}.

*4.4.4. 1,3-Dimethyl-1H-pyrazolo[3,4-b]quinoxaline (**5d**)*

Yellow flat needles, 277 mg, 70%, mp. 140-141 °C (toluene/petrol ether 60-90) (lit. 137-138 °C [16]); ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ = 8.27 (dd, *J* = 8.6, 0.9 Hz, 1H), 8.14 (dd, *J* = 8.6, 0.8 Hz, 1H); 7.81 (dtd, *J* = 7.5, 1.4, 1.6 Hz, 1H), 7.71 (dtd, *J* = 7.5, 1.3, 1.7 Hz, 1H), 4.19 (s, 3H), 2.81 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$, ppm): δ = 143.1, 142.2, 141.8, 140.7, 136.4, 130.7, 130.3, 128.5, 127.3, 33.8, 11.7; IR (ATR): ν = 2977, 1581, 1518, 1486, 1400, 1378, 1347, 1309, 1179, 1122, 960, 764, 653, 628, 599, 425 cm^{-1}.

*4.5. Synthesis of 3-acyl-1H-quinoxalin-2-one hydrazones (**6**) - general procedure*

A mixture of 1,2-diaminobenzene **1** (108 mg, 1 mmol) and corresponding pyrazolin-3,4-dione **3** (1 mmol) in 5 mL glacial acetic acid was heated at reflux for 30 min. After cooling, the resulting precipitate was filtered off.

*4.5.1. 3-Benzoyl-1H-quinoxalin-2-one phenylhydrazone (**6a**)*

Red needles, 260 mg, 76%, mp. 255-256 °C (Lit. 240-241 °C[1]); ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ = 12.61 (br. s, 1H), 9.86 (s, 1H), 7.84 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.62 (t, *J* = 7.75 Hz, 1H), 7.51-7.50 (m, 2H), 7.41 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.36-7.31 (m, 3H), 7.23-7.20 (m, 3H), 7.17-7.15 (m, 2H), 6.77 (t, *J* = 7.2 Hz, 1H); ^{13}C NMR (150MHz, $CDCl_3$, ppm): δ = 155.9, 154.3, 145.7, 138.0, 137.7, 133.4, 133.0, 131.6, 129.6, 129.5, 128.9, 128.1, 125.7, 123.7, 119.9, 116.1, 113.1; IR (ATR): ν = 3173, 2967, 2884, 2817, 1663, 1592, 1513, 1489, 1427, 1248, 1224, 1130, 1092, 777, 756, 738, 688, 571, 535 cm^{-1}.

*4.5.2. 3-Acetyl-1H-quinoxalin-2-one phenylhydrazone (**6b**)*

Red crystalline powder, 123 mg, 44%, mp. 234-235 °C. (Lit. 223 °C[25]); ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ = 12.21 (br.s, 1H), 9.65 (s, 1H), 7.72 (d, *J* = 7.9 Hz, 1H), 7.46 (t, *J* = 7.4 Hz, 1H), 7.32-7.20 (m, 6H), 6.80 (t, *J* = 7.2 Hz, 1H), 2.28 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$, ppm): δ = 154.1, 153.9, 145.8, 139.9, 132.5, 132.1, 130.3, 129.3, 128.8, 123.5, 120.4, 115.3, 114.0, 13.7; IR (ATR): ν = 3173, 2976, 2881, 2831, 1666, 1592, 1510, 1218, 1165, 1130, 1080, 1065, 909, 741, 686, 585, 541 cm^{-1}.

*4.6. Synthesis of 5-(4-R-2-nitrophenyl)-amino-1,3-disubstituted pyrazoles (**12**) (R = H, Cl, Br, F, CH_3, OCH_3) – general procedure*

The appropriate 4-substituted-1-iodo-2-nitrobenzene **10** (1 mmol), appropriate 1,3-disubstituted-5-aminopyrazole **11** (1.3 mmol), and anhydrous potassium carbonate (248 mg, 1.8 mmol) were heated in the presence of *rac*-BINAP (23 mg, 0.036 mmol, 3.7 mol%), Pd_2dba_3 (23 mg, 0.024 mmol, 2.5 mol%), and 18-crown-6 (10 mg, 0.038 mmol) in toluene (8 mL, purged with argon) at 100 °C. The reaction was carried out under argon for 24 h. After cooling the reaction mixture was filtered and purified using column chromatography on aluminium oxide with toluene, or a toluene-ethyl acetate mixture (10:1) as an eluent. The product was recrystallized from toluene.

*4.6.1. (2,5-diphenyl-2H-pyrazol-3-yl)-(2-nitrophenyl)-amine (**12a**)*

Red long plates, 345 mg, 97%, mp. 130-131 °C; ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ = 9.42 (s, 1H), 8.2 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.9 (d, *J* = 7.1 Hz, 2H), 7.59 (dd, *J* = 8.6, 1.2 Hz, 2H), 7.47-7.34 (m, 5H), 7.37-7.34 (m, 2H), 7.22 (dd, *J* = 8.5, 1.0 Hz, 1H), 6.87 (dtd, *J* = 7.8, 1.2, 1.3 Hz, 1H), 6.7 (s 1H); ^{13}C NMR (150 MHz, $CDCl_3$, ppm): δ = 151.7, 141.6, 138.1, 138.0, 136.2, 132.8, 129.4, 128.7, 128.4, 128.3, 128.1, 126.53, 125.56, 124.0, 119.0, 116.3, 98.8; IR (ATR): ν = 3246, 3056, 1609, 1587, 1555, 1506, 1494, 1341, 1270, 1238, 1140, 1071, 954, 777, 737, 691, 616, 515, 470 cm^{-1}. Anal. Calcd for $C_{21}H_{16}N_4O_2$: C, 70.77; H, 4.53; N, 15.72. Found: C, 71.28; H, 4.61; N, 15.25.

*4.6.2. (5-methyl-2-phenyl-2H-pyrazol-3-yl)-(2-nitrophenyl)-amine (**12b**)*

Orange plates, 250 mg, 85%, mp. 108 °C; ^{1}H NMR (600 MHz, $CDCl_3$, ppm): 9.36 (s, 1H); 8.18 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.49 (dd, *J* = 8.7, 1.2 Hz, 2H), 7.45-7.39 (m, 3H), 7.31 (t, *J* = 7.4 Hz, 1H), 7.16 (dd, *J* = 8.6, 1.0 Hz, 1H), 6.85 (dtd, *J* = 7.8, 1.2, 1.3 Hz, 1H), 6.18 (s, 1H), 2.38 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$, ppm): δ = 149.5, 141.7, 138.1, 137.2, 136.1, 133.5, 129.3, 127.7, 126.5, 123.8, 118.7, 116.2, 101.2, 14.2; IR (ATR): ν = 3323, 3072, 1606, 1578, 1559, 1498, 1435, 1337, 1270, 1138, 1022, 767, 739, 698, 686, 636, 485 cm^{-1}. Anal. Calcd for $C_{16}H_{14}N_4O_2$: C, 65.30; H, 4.79; N, 19.04. Found: C, 65.32; H, 4.81; N, 18.81.

*4.6.3. (2-methyl-5-phenyl-2H-pyrazol-3-yl)-(2-nitrophenyl)-amine (**12c**)*

Orange prisms, 265 mg, 90%, mp. 114 °C; ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ = 9.15 (s, 1H), 8.25 (dd, *J* = 8.8, 1.5 Hz, 1H), 7.79 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.47-7.40 (m, 3H), 7.34-7.31 (m, 1H), 6.91-6.88 (m, 2H), 6.51 (s, 1H), 3.80 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$, ppm): δ = 150.6, 142.6, 137.8, 136.4, 133.4, 133.1, 128.7, 127.9, 126.6, 125.3, 118.8, 115.9, 98.9, 35.3; IR (ATR): ν = 3320, 3063, 1616, 1575, 1551, 1492, 1333, 1259, 1142, 1039, 953, 759, 741, 683, 665, 538, 518, 500 cm^{-1}. Anal. Calcd for $C_{16}H_{14}N_4O_2$: C, 65.30; H, 4.79; N, 19.04. Found: C, 65.29; H, 4.81; N, 19.02.

*4.6.4. (2,5-dimethyl-2H-pyrazol-3-yl)-(2-nitrophenyl)-amine (**12d**)*

Yellow flat needels, 208 mg, 90% yield, mp. 126-127 °C; ^{1}H NMR (600 MHz,$CDCl_3$, ppm): δ = 9.08 (s, 1H), 8.23 (d, *J* = 8.5 Hz, 1H), 7.44 (t, *J* = 7.9 Hz, 1H), 6.87 (t, *J* = 7.7 Hz, 1H), 6.83 (d, *J* = 8.5 Hz, 1H), 5.97 (s, 1H), 3.67 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$, ppm): δ = 148.0, 142.7, 137.0, 136.3, 133.3, 126.5, 118.5, 115.9, 101.1, 34.8, 14.1; IR (ATR): ν = 3332, 3098, 1610, 1551, 1507, 1489, 1336, 1262, 1212, 1139, 783, 749, 677, 668, 647, 541, 503 cm^{-1}. Anal. Calcd for $C_{11}H_{12}N_4O_2$: C, 56.89; H, 5.21; N, 24.12. Found: C, 56.75; H, 5.22; N, 24.05.

*4.6.5. (2,5-diphenyl-2H-pyrazo-3-yl)-(4-chloro-2-nitrophenyl)-amine (**12e**)*

Dark red crystalline powder, 289 mg, 74%, mp. 98-99 °C; ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ = 9.34 (s, 1H), 8.19 (d, *J* = 2.5 Hz, 1H), 7.89 (d, *J* = 7.1 Hz, 2H), 7.56 (d, *J* = 7.4 Hz, 2H), 7.46-7.43 (m, 4H), 7.39-7.35 (m, 3H), 7.15 (d, *J* = 9.1 Hz, 1H), 6.69 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$, ppm): *δ*= 151.8, 140.3, 138.0, 137.5, 136.3, 132.6, 129.5, 128.7, 128.4, 128.2, 125.8, 125.6, 123.9, 123.8, 117.6, 99.22, 99.21; IR (ATR): ν = 3322, 3058, 1598, 1563, 1495, 1334, 1257, 1124, 1065, 950, 897, 754, 736, 674, 644, 485 cm^{-1}. Anal. Calcd for $C_{21}H_{15}ClN_4O_2$: C, 64.54; H, 3.87; N, 14.34. Found: C, 64.25; H, 3.52; N, 14.05.

*4.6.6. (2,5-diphenyl-2H-pyrazo-3-yl)-(4-bromo-2-nitrophenyl)-amine (**12f**)*

Dark red oil, quantitative yield; ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ = 9.35 (s, 1H), 8.34 (d, *J* = 2.3 Hz, 1H), 7.87 (d, *J* = 7.2 Hz, 2H), 7.56 (d, *J* = 7.6 Hz, 2H), 7.46-7.43 (m, 4H), 7.39-7.35 (m, 3H), 7.09 (d, *J* = 9.1 Hz, 1H), 6.69 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$, ppm): δ = 151.78, 140.7, 138.0 137.4, 136.5, 132.6, 129.5, 128.7, 128.4, 128.2, 125.59, 125.57, 124.1, 123.9, 117.9, 99.27, 99.26; IR (ATR): ν = 3329, 2917, 2846, 1739, 1607, 1495, 1454, 1330, 1251, 1145, 1071, 1012, 945, 756, 683, 485 cm^{-1}. Anal. Calcd for $C_{21}H_{15}BrN_4O_2$: C, 57.95; H, 3.47; N, 12.87. Found: C, 57.75; H, 3.22; N, 12.75.

*4.6.7. (2,5-diphenyl-2H-pyrazo-3-yl)-(4-fluoro-2-nitrophenyl)-amine (**12g**)*

Dark red crystalline powder, 299 mg, 80%, mp. 89 °C; ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ = 9.27 (s, 1H), 7.92-7.88 (m, 3H), 7.57 (d, *J* = 7.7 Hz, 2H), 7.46-7.43 (m, 4H), 7.37-7.35 (m, 2H), 7.24-7.18 (m, 2H), 6.68 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$, ppm): δ = 154.4 (d, $J_{C\text{-}F}$ = 242.8 Hz), 151.8, 138.4, 138.1, 138.0, 132.9 (d, $J_{C\text{-}F}$ = 8.2 Hz), 132.7, 129.5, 128.7, 128.4, 128.2, 125.6, 124.6 (d, $J_{C\text{-}F}$ = 23.5 Hz), 124.0, 117.8 (d, $J_{C\text{-}F}$ = 7.2 Hz), 112.1 (d, $J_{C\text{-}F}$ = 26.7 Hz), 98.8; IR (ATR): ν = 3319, 3063, 1578, 1556, 1511, 1495, 1410, 1274, 1230, 1125, 1059, 941, 751, 675, 533, 489 cm^{-1}. Anal. Calcd for $C_{21}H_{15}FN_4O_2$: C, 67.37; H, 4.04; N, 14.97. Found: C, 67.75; H, 4.22; N, 14.85.

*4.6.8. (2,5-diphenyl-2H-pyrazo-3-yl)-(4-methyl-2-nitrophenyl)-amine (**12h**)*

Yellow crystalline powder, 277 mg, 75%, mp. 109-110 °C; ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ = 9.31 (s, 1H), 8.00 (s, 1H), 7.89 (d, *J* = 7.6 Hz, 2H), 7.59 (d, *J* = 7.8 Hz, 2H), 7.46-7.42 (m, 4H), 7.37-7.34 (m, 2H), 7.28 (d, *J* = 8.3 Hz, 1H), 7.15 (d, *J* = 8.6 Hz, 1H), 6.67 (s, 1H), 2.31 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$, ppm): δ = 151.6, 139.4, 138.5, 138.2, 137.5, 132.8, 129.4, 128.9, 128.7, 128.3, 128.0, 125.9, 125.6, 124.0, 116.3, 98.43, 98.41, 20.1; IR (ATR): ν = 3360, 3060, 1628, 1565, 1518, 1496, 1337, 1268, 1217, 1150, 799, 767, 685, 644, 476, 435 cm^{-1}. Anal. Calcd for $C_{22}H_{18}N_4O_2$: C, 71.34; H, 4.90; N, 15.13. Found: C, 71.55; H, 4.72; N, 15.05.

*4.6.9. (2,5-diphenyl-2H-pyrazo-3-yl)-(4-methoxy-2-nitrophenyl)-amine (**12i**)*

Dark red crystalline powder, 247 mg, 64%, mp. 79-80 °C; ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ = 9.27 (s, 1H), 7.89 (d, *J* = 7.1 Hz, 2H), 7.64 (d, *J* = 3.0 Hz, 1H), 7.60-7.59 (m, 2H), 7.46-7.42 (m, 4H), 7.37-7.34 (m, 2H), 7.11 (d, *J* = 9.3 Hz, 1H), 7.13 (dd, *J* = 9.3, 3.0 Hz, 1H), 6.65 (s, 1H), 3.82 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$, ppm): δ = 152.1, 151.6, 138.7, 138.2, 136.2, 133.3, 132.8; 129.4, 128.7, 128.3, 128.0m 126.1, 125.6, 124.0, 117.9, 107.4, 98.0, 55.9; IR (ATR): ν = 3281, 3056, 1584, 1553, 1515, 1451, 1315, 1280, 1214, 1125, 1059, 1030, 761, 694, 666, 653, 542, 451 cm^{-1}. Anal. Calcd for $C_{22}H_{18}N_4O_3$: C, 68.38; H, 4.70; N, 14.50. Found: C, 68.00; H, 4.52; N, 14.35.

*4.7. Reductive cyclization of **12** with ferrous oxalate – general procedure: method A*

Equimolar amounts of (2,5-disubstituted-2*H*-pyrazol-3-ylo)-(4-substituted-2-nitrophenyl)-amine **12a-i** (1 mmol), and iron(II) oxalate dihydrate (179 mg, 1 mmol) in sulfolane (5 mL) were heated at 250 °C for 20 min. After cooling, the reaction mixture was added to a saturated sodium chloride solution (20 mL) and stirred for 30 min. The precipitate was filtered off and dried. After drying, the compounds were purified by column chromatography on aluminium oxide 90 with chloroform as an eluent. The product was crystallized from toluene.

*4.8. Reductive cyclization of **12** with triphenylphosphine – general procedure: method B*

(2,5-disubstituted-2*H*-pyrazo-3-yl)-(2-nitrophenyl)-amine **12a-d** (0.5 mmol) and triphenylphosphine (459 mg, 1.75 mmol) in dimethylacetamide or 1,2-dichlorobenzene (4 mL) were heated at reflux for 24 – 48 h. After cooling the reaction mixture was purified by column chromatography on aluminium oxide with toluene as an eluent.

*4.7.1. and 4.8.1. 1,3-Diphenyl-1H-pyrazolo[3,4-b]quinoxaline (**5a**)*

Light orange needles, method A: 218 mg, 68%, method B: 83.7 mg, 52%; ^{1}H/^{13}C NMR, m.p. and R_f (toluene/SiO_2) corresponds to the data recorded for **5a** in section 4.4.1.

*4.7.2. and 4.8.2. 3-Methyl-1-phenyl-1H-pyrazolo[3,4-b]quinoxaline (**5b**)*

Deep yellow needles, method A: 130 mg, 50%, method B: 20.8 mg, 16%; $^{1}H/^{13}C$ NMR, m.p. and R_f (toluene/SiO_2) corresponds to the data recorded for **5b** in section 4.4.2.

*4.7.3. and 4.8.3. 1-Methyl-3-phenyl-1H-pyrazolo[3,4-b]quinoxaline (**5c**)*

Light orange crystalline powder, method A: 114 mg, 44%, method B: 9.7 mg, 7.5%; $^{1}H/^{13}C$ NMR, m.p. and R_f (toluene/SiO_2) corresponds to the data recorded for **5c** in section 4.4.3.

*4.7.4. and 4.8.4. 1,3-Dimethyl-1H-pyrazolo[3,4-b]quinoxaline (**5d**)*

Yellow flat needles, method A: 101 mg, 51%, method B: 6.9 mg, 7%; $^{1}H/^{13}C$ NMR, m.p. and R_f (toluene/SiO_2) corresponds to the data recorded for **5d** in section 4.4.4.

*4.7.5. 6-chloro-1,3-diphenyl-1H-pyrazolo[3,4-b]quinoxaline (**5e**)*

Orange crystalline mass, method A: 217 mg, 61%, mp. 220 °C; ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ = 8.70 (d *J* = 7.7 Hz, 2H), 8.50 (d, *J* = 7.7 Hz, 2H), 8.31 (d, *J* = 2.2 Hz, 1H), 8.11 (d, *J* = 9.1 Hz, 1H), 7.75 (dd, *J* = 9.1, 2.3 Hz, 1H), 7.59-7.55 (m, 4H), 7.48 (t, *J* = 7.4 Hz, 1H), 7.34 (t, *J* = 7.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$, ppm): δ = 143.2, 142.8, 141.2, 139.6, 139.2, 137.4, 133.9, 132.2, 130.9, 130.2, 129.5, 129.2, 129.1, 128.8, 127.3, 125.9, 120.0; IR (ATR): ν = 3063, 1594, 1496, 1486, 1420, 1391, 1340, 1252, 1163, 1125, 1062, 831, 748, 739, 685, 666, 647, 495, 419 cm^{-1}. Anal. Calcd for $C_{21}H_{13}ClN_4$: C, 70.69; H, 3.67; N, 15.70. Found: C, 70.96; H, 3.72; N, 15.35.

*4.7.6. 6-bromo-1,3-diphenyl-1H-pyrazolo[3,4-b]quinoxaline (**5f**)*

Orange crystalline powder, method A: 94 mg, 24%, mp. 206-207 °C; ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ = 8.70 (d, *J* = 7.7 Hz, 2H), 8.51 (d, *J* = 2.2 Hz, 1H), 8.50 (d, *J* = 8.1 Hz, 2H), 8.05 (d, *J* = 9.1 Hz, 1H), 7.88 (dd, *J* = 9.1, 2.2 Hz, 1H), 7.59-7.56 (m, 4H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.34 (t, *J* = 7.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$, ppm): δ = 143.3, 142.8, 141.6, 139.9, 139.2, 137.3, 134.6, 132.5, 130.9, 130.2, 129.6, 129.2, 128.8, 127.3, 125.9, 122.0,

120.0; IR (ATR): ν = 3063, 1594, 1496, 1480, 1420, 1340, 1252, 1166, 1119, 989, 929, 821, 748, 745, 688, 669, 644, 489, 422 cm^{-1}. Anal. Calcd for $C_{21}H_{13}BrN_4$: C, 62.86; H, 3.27; N, 13.96. Found: C, 62.99; H, 3.43; N, 13.68.

*4.7.7. 6-fluoro-1,3-diphenyl-1H-pyrazolo[3,4-b]quinoxaline (**5g**)*

Orange needles, method A: 51 mg, 15%, mp. 235 °C; ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ = 8.72 (d, *J* = 7.2 Hz, 2H), 8.52 (d, *J* = 7.7 Hz, 2H), 8.20 (dd, *J* = 9.3, 5.7 Hz, 1H), 7.94 (dd, *J* = 9.3, 2.7 Hz, 1H), 7.67-7.63 (m, 1H), 7.60-7.57 (m, 4H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.34 (t, *J* = 7,4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$, ppm): δ = 161.6 (d, J_{C-F} = 251.4 Hz), 142.9, 142.8 (d, J_{C-F} = 2.2 Hz), 141.6 (d, J_{C-F} = 13.2 Hz), 139.3, 138.4, 137.3, 131.0, 130.9 (d, J_{C-F} = 9.8 Hz), 129.5, 129.2, 128.8, 127.3, 125.9, 122.3 (d, J_{C-F} = 27.3 Hz), 120.0, 113.1 (d, J_{C-F} = 21.5 Hz); IR (ATR): ν = 3066, 1625, 1590, 1496, 1404, 1340, 1201, 1122, 1103, 979, 824, 748, 729, 682, 669, 653, 647, 606, 536, 489, 428 cm^{-1}. Anal. Calcd for $C_{21}H_{13}FN_4$: C, 74.11; H, 3.85; N, 16.46. Found: C, 74.49; H, 3.99; N, 16.06.

*4.7.8. 6-methyl-1,3-diphenyl-1H-pyrazolo[3,4-b]quinoxaline (**5h**)*

Yellow crystalline mass, method A: 144 mg, 43%, mp. 229-230 °C; ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ = 8.75 (d, *J* = 7.1 Hz, 2H), 8.55 (dd, *J* = 8.6, 1.0 Hz, 2H), 8.06 (d, *J* = 8.9 Hz, 2H), 7.65 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.60-7.57 (m, 4H), 7.48 (t, *J* = 7.4 Hz, 1H), 7.33 (t, *J* = 7,4 Hz, 1H), 2.61 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$, ppm): δ = 143.1, 142.9, 141.5, 139.7, 139.5, 138.6, 136.7, 133.8, 131.3, 129.3, 129.2, 129.0, 128.7, 128.5, 127.3, 125.6, 120.0, 21.7; IR (ATR): ν = 3060, 1597, 1489, 1407, 1344, 1255, 1188, 1128, 983, 818, 751, 694, 666, 641, 495, 419 cm^{-1}. Anal. Calcd. for $C_{22}H_{16}N_4$: C, 78.55; H, 4.79; N, 16.66. Found: C, 78.71; H, 4.89; N, 16.25.

*4.7.9. 6-methoxy-1,3-diphenyl-1H-pyrazolo[3,4-b]quinoxaline (**5i**)*

Yellow crystalline powder, method A: 133 mg, 38%, mp. 203-204 °C; ^{1}H NMR ($CDCl_3$, 600 MHz, ppm): δ = 8.73 (dd, *J* = 8.3, 1.2 Hz, 2H), 8.53 (dd, *J* = 8.6, 1.0 Hz, 2H), 8.04 (d, *J* = 9.3 Hz, 1H), 7.59-7.57 (m, 4H), 7.52 (d, *J* = 2.7 Hz, 1H), 7.50-7.46 (m, 2H), 7.33 (t, *J* = 7.4 Hz,

1H), 4.00 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$, ppm): δ = 159.6, 142.9, 142.6, 142.5, 139.6, 137.6, 136.3, 131.5, 129.8, 129.2, 129.1, 128.7, 127.3, 125.8, 125.6, 120.0, 106.5, 55.8; IR (ATR): ν = 3060, 1625, 1600, 1492, 1404, 1356, 1217, 1119, 1024, 983, 827, 767, 748, 736, 694, 688, 669, 653, 609, 530, 495, 425 cm^{-1}. Anal. Calcd. for $C_{22}H_{16}N_4O$: C, 74.98; H, 4.58; N, 15.90. Found: C, 74.81; H, 4.92; N, 15.66.

*4.9. 6-N,N-diphenylamino-1,3-diphenyl-1H-pyrazolo[3,4-b]quinoxaline (**5j**)*

6-chloro-1,3-diphenyl-1*H*-pyrazolo[3,4-*b*]quinoxaline **5e** (114 mg, 0.32 mmol), diphenylamine (65 mg, 0.38 mmol), sodium *tert*-butoxide (44 mg, 0.45 mmol), Pd_2dba_3 (2.92 mg, 0.0032 mmol, 1mol%), (*o*-biphenyl)P(*t*-Bu)$_2$ (1.9 mg, 0.0064 mmol, 2 mol%), and toluene (2 mL) were added to a Schlenk flask, and the mixture was then purged with argon. The reaction was carried out under argon at 80 °C for 20 h. After cooling, the reaction mixture was filtered and purified using column chromatography on aluminium oxide with toluene or mixture toluene: ether (3:1) as an eluent. The product was crystallized from toluene.

Red crystalline powder, 81 mg, 52%, mp. 209-210 °C; ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ = 8.68 (d, *J* = 7.1 Hz, 2H), 8.54 (d, *J* = 7.7 Hz, 2H), 8.01 (d, *J* = 9.3 Hz, 1H); 7.73 (d, *J* = 2.5 Hz, 1H), 7.67 (dd, *J* = 9.3, 2.5 Hz, 1H), 7.59-7.57 (m, 2H), 7.55-7.53 (m, 2H), 7.44 (t, *J* = 7.4 Hz, 1H), 7.37-7.31 (m, 5H), 7.24 (d, *J* = 7.5 Hz, 4H), 7.17 (t, *J* = 7.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$, ppm): δ = 147.9, 146.9, 143.0, 142.8, 142.6, 139.6, 138.3, 136.7, 131.4, 129.7, 129.20, 129.18, 129.11, 129.06, 128.7, 127.3, 125.58; 125.55; 124.4, 120.0, 117.8; IR (ATR): ν = 3060, 1600, 1483, 1404, 1255, 1122, 989, 821, 745, 736, 685, 672, 656, 647, 492, 416 cm^{-1}. Anal. Calcd. for $C_{33}H_{23}N_5$: C, 80.96; H, 4.74; N, 14.31. Found: C, 80.85; H, 4.85; N, 13.99.

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Appendix A. Supplementary data

Supplementary data related this article can be found at

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