J Fluoresc (2012) 22:31–41
DOI 10.1007/s10895-011-0960-x

RAPID COMMUNICATION

Synthesis of Pyrazolopyridine Annulated Heterocycles and Study the Effect of Substituents on Photophysical Properties

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Received: 22 June 2011 / Accepted: 30 August 2011 / Published online: 14 September 2011

Abstract Pyrazolo[3,4-*b*]pyridines having 4-chloro-5-chloroethyl side chain are synthesized by the reaction of 5-aminopyrazole and cyclic β-formylester gave amino-pyrazolodihydrofuranone intermediate, which on cyclization in phosphorous oxychloride exclusively converted in to 4-chloro-5-chloroethyl pyrazolo[3,4-*b*]pyridines **4(a-b)** in major amount. The side chain with acetic acid, thiourea and aromatic amines are used to form angular ring leads to formation of tricyclic Furo[2,3-*d*]pyrazolo[2,3-*b*]pyridines **5(a-b)**, pyrazolo[3,4-*b*]thieno[2,3-*d*]pyridines **6(a-b)** and pyrazolo[3,4-*b*]pyrrolo[2,3-*d*]pyridines **7(a-n)** respectively. The substituents effect at C_4 position on fluorescence properties of pyrazolopyridines has been studied. Moreover the effect of electron donor and halogen substituents on fluorescence properties of pyrazolopyrrolopyridines **7(a-n)** has been investigated along with their fluorescent quantum yield.

Keywords Pyrazolo[3,4-*b*]pyridine · Fluorescence · HOMO-LUMO · Quantum yield

Introduction

The design and synthesis of organic chromophores as non-linear optical (NLO) materials has much attention in recent years and have great potential especially for use in optical communication, information processing, frequency doubling and integrated optics [1–4]. One commonly used strategy to design π-electron chromophores for second order NLO application is to end-cap a suitably conjugated bridge with donor (D) and acceptor (A) substituents. In the 90s several authors pointed out that the strength of electron donor and acceptor substituents must be optimized for the specific π-conjugated system and the loss of aromaticity between the neutral form and the charge separated zwitterionic form of the chromophores is believed to be responsible for the reduced or saturated β values [5–9]. The electron excessive/deficient heterocycles act as an auxiliary donors/acceptors while connected to donating/withdrawing groups, and the increase of donor/acceptors ability leads to substantial increases in β values [10, 11]. Having in mind this idea, several investigators reported on the synthesis and characterization of conjugated heterocyclic system in which the donor moiety was represented by a π-excessive five membered heterocycle (pyrrolo or thiophene) and the acceptor group was a deficient heterocyclic azine ring. These new heterocyclic derivatives exhibited improved solvatochromic, electrochromic, photochromic, fluorescent, and nonlinear optical properties [12–21].

Despite the growing interest in NLO heteroaromatic chromophores, relevant information concerning the relation between molecular structure and effective material properties for these NLO systems is still scarce. Derivatives with various other substituents in position C_4 showed intense fluorescence can be used as fluorescence standard and found application as blue-green organic light-emitting diode. Thus, pyrazolopyridine having different substituents at C_4 position with blue-emission, high brightness, high quantum yield and good thermal stability remain to be developed [22–25].

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Apart from this, the pyrazolo annelated heterocycles have demonstrated wide spectrum of agriculture and pharmacological activity [26, 27]. Pyrazolo[3,4-*b*]pyridine are promising candidates in organic synthesis due to their significant application in medicinal chemistry, such as diagnosis of brain disorder [28], treatment of coronary heart disease [29], viral disease [30] and the pyrazolothienopyridine showed the anti-inflammatory and anti-platelet agents [31].

Our recent report on the effect of C_4 substituent on the fluorescence properties of pyrazolo[3,4-*b*]pyrrolo[2,3-*d*] pyridine [32], dipyrazolo[3,4-*b*:3,4-*d*]pyridines [33] and this reports have attracted us to synthesize this particular family of compounds. Encouraged by this study and hunt for new fluorescent pyrazolo-annelated heterocycles herein we synthesized pyrazolo[3,4-*b*] pyridine **4(a-b)**, dihydro-2H-furo[2,3-*d*]pyrazolo[3,4-*b*]pyridine **5(a-b)**, pyrazolo [3,4-*b*]thieno [2,3-*d*]pyridine **6(a-b)** and pyrazolo[3,4-*b*] pyrrolo[2,3-*d*]pyridines **7(a-n)** and studied the effect of Cl, O, S and N at C_4 position of pyrazolo pyridines ring on fluorescent behavior. Photophysical properties of **7(a-n)** are also studied and compared absorption and fluorescence emission maxima with reference to donor and halogen substituent on D ring (Fig. 2). Moreover, substituents effect on the performance of **7(a-n)** are studied by calculating HOMO, LUMO energies and electron hole gap by using MOPAC-2009 to investigate the fluorescence properties.

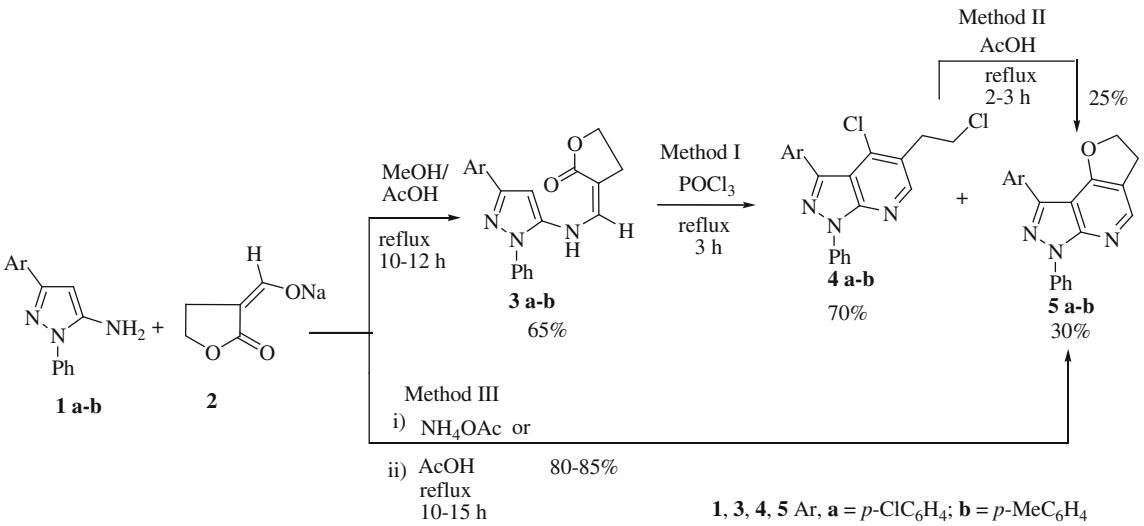
Experimental

Synthesis and Compound Identification

Intermediate pyrazoloaminodihydrofuranones **3**, (Scheme 1) were obtained by condensation of 5-aminopyrazole **1** with sodium salt of α-formyl-γ-butyrolactone **2** in AcOH and MeOH at reflux temperature. The in situ formation of free formyl ester generated by weak acid catalyst undergoes attack of amino group yielding the *Z*-enamine **3**. Compounds **1** and **2** on refluxing in presence of AcOH or NH_4OAc furnished into fused tricyclic dihydrofuropyrazolopyridines **5** in 85% yield. Similar reactions with intermediate **3** in $POCl_3$ at refluxed temperature furnished mixture of compounds **4** and **5** (TLC check), are separated by column chromatography (chloroform-methanol/v:v 9:1) and obtained in 70% and 30% yields respectively. We assighned structure **4** and **5** on the basis of spectral and analytical data.

For instance IR of **3b** shows lactone carbonyl stretching at 1,722 cm^{-1}, NH at 3,230 cm^{-1} and (C=C) at 1,640 cm^{-1}. The ^1H NMR of this compound in $CDCl_3$ shows doublet for broad exchangeable with D_2O NH proton at 6.05 δ with *J*=9.3 Hz, 2H showed multiplet at 2.81 *δ*, 2H shows triplet at 4.21 *δ* with *J*=8.4 Hz. All aromatic proton shows expected chemical shifts and splitting pattern which resemble with structure of **3b**. The ^{13}C NMR spectrum of this compound with the structure proposed. The mass spectrum **3b** revealed a molecular ion peak *m*/*z* at 345. The structure of **4** and **5** are established by spectral and analytical data, the compound **4a** shows absences of carbonyl and NH streching frequency in IR, while compound **5a** showed absences of carbonyl and NH streching frequency but shows CH_2-O-C, stretching frquency at 1,280 cm^{-1}. The ^1H NMR of **5a** in $CDCl_3$ clearly showed (O-CH_2) at 4.27 *δ* as a triplet with *J*= 6.6 Hz, and (CH_2-CH_2) at 2.88 *δ* as triplet with *J*=6.6 Hz. Advantage of C_4-Cl and C_3-chloroethyl is also taken to annelated five member tetrahydrofuran rings on pyridine nucleus to yield compounds **5a-b** (Scheme 1).

Reaction of compounds **4(a-b)** with thiourea in acetic acid under reflux condition furnished thienopyrazolopyr-



Scheme 1 Synthesis of 4-chloro-5-(2-chloroethyl)-pyrazolo[3,4-*b*]pyridines **4** and furo[2,3-*d*]pyrazolo[3,4-*b*]pyridine **5** derivatives

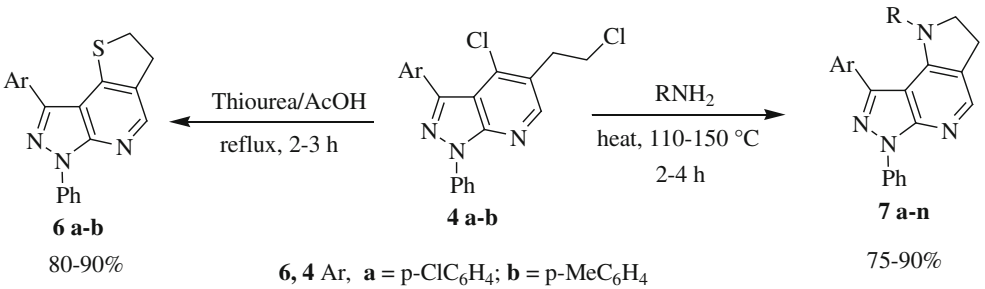
idines **6(a-b)** in good yields. The targeted new fused heterocyclic compound pyrazolo[3,4-*b*]pyrrolo[2,3-*d*]pyridine **7(a-n)** are successfully synthesized in 65–85% yield, from pyrazolo[3,4-*b*]pyridine **4** by neat heat with primary aromatic amines. The compound **7** are characterized by IR, ^{1}H NMR, ^{13}C NMR, Mass and elemental analysis given in experimental part (Scheme 2). Synthesized pyrazolopyridine are further studied for their photophysical properties.

Semi-empirical Study

As a keen interest into the atomic contribution on the frontier orbital, we have analyzed three-dimensional HOMO and LUMO coefficient contribution by the MOPAC-2009 (Version 8.331) [34, 35] and are given in Table 1. From Table 1, we observed that, among **4(a-b)**, **5(a-b)** and **6(a-b)**, **4b**, **5b** and **6b** bears electron donating group through +I effect i.e. methyl group at para-position of aromatic ring, shows low electron hole gap and fluorescent at longer wavelength with high quantum yield as compare to **4a**, **5a** and **6a**. For **7(a-n)**, it observed that, charge is more concentrated on ring D as compared to A, B, C and E (Fig. 1). The donor chromophores i.e. OCH_3 (+R effect) and CH_3 (+I effect) on ring D plays an important role in increasing the electron density and lowering electron hole gap. Among **7(a-n)**, compounds **7b**, **7c**, **7e**, **7f**, **7h**, **7i**, **7j**, **7l** and **7m** shows low GAP values indicates higher overlapping of HOMO or LUMO orbitals which shows red shift in its fluorescence emission and high quantum yields as compare to others (Table 1 and Fig. 2).

Photophysical Properties

UV-visible and fluorescence spectra of compounds **4(a-b)**, **5(a-b)**, **6(a-b)** and **7(a-n)** are taken in DMF as a solvent at same concentration i.e. 1.0×10^{-3} M. The UV−visible and fluorescence spectral data of pyrazolopyridine are summarized in Tables 2 and 3. Fluorescence quantum yield of all synthesized compounds are determined by standard literature procedure using quinine sulfate as an a reference standard [36, 37] and are given Tables 2 and 3. We observed effect of substituents at C_4 position on UV–vis and fluorescence emission. Among Cl, O, S and N substituent at C_4 position, N-substituted pyrazolopyridine shows red shift in its fluorescence emission and higher quantum yields (Φ_f) as compare to Cl, O and S substituents at C_4 position. Thus, C_4-N pyrazolopyridine (**7a-n**) shows greater fluorescence emission as compare to C_4-Cl, C_4-O, C_4-S and it shown by above sequence: C_4-N(λ_f max) > C_4-S (λ_f max) > C_4-O(λ_f max) > C_4-Cl(λ_f max) (Tables 2 and 3). The comparative absorption and emission spectra of compound **4b**, **5b**, **6b** and **7j** are graphically presented in Fig. 2. From Table 2, we observed the moderate shift in absorption maxima for **5(a-b)** and **6(a-b)** but on the other hand fluorescence maxima shift to red from C_4-O to C_4-S (i.e. from **5a-b** to **6a-b**), may be because of oxygen is more electronegative as compare to sulfur. It also observed that **4a-b** shows blue shifted fluorescence maxima as compare to **5 (a-b)** and **6(a-b)**, may be because of Cl at C_4 position shows quenching of fluorescence as a substituents. From Table 3, it observed that substituents on D ring exhibit moderate shift



Scheme 2 Synthesis of pyrazolo[3,4-*b*]thieno[2,3-*d*]pyridine **6** and pyrazole[3,4-*b*] pyrrolo [2,3-*d*]pyridine **7** derivatives

4a, 7	Ar	R	4b, 7	Ar	R
a	*p*-ClC_6H_4	*m*-ClC_6H_4	**h**	*p*-Me-C_6H_4	*m*-ClC_6H_4
b	*p*-ClC_6H_4	*p*-MeC_6H_4	**i**	*p*-Me-C_6H_4	*p*-MeC_6H_4
c	*p*-ClC_6H_4	*p*-$OMeC_6H_4$	**j**	*p*-Me-C_6H_4	*p*-$OMeC_6H_4$
d	*p*-ClC_6H_4	*p*-ClC_6H_4	**k**	*p*-Me-C_6H_4	*p*-ClC_6H_4
e	*p*-ClC_6H_4	C_6H_5	**l**	*p*-Me-C_6H_4	C_6H_5
f	*p*-ClC_6H_4	*m*-MeC_6H_4	**m**	*p*-Me-C_6H_4	*m*-MeC_6H_4
g	*p*-ClC_6H_4	4-Cl 3-FC_6H_4	**n**	*p*-Me-C_6H_4	4-Cl 3-FC_6H_4

Table 1 The molecular electronic properties, (HOMO-LUMO energy, Gap) of Pyrazolo[3,4-*b*] pyridine **4(a-b)**, **5(a-b)**, **6(a-b)** and **7(a-n)**

Comp.	Ar	R	HOMO (eV)	LUMO (eV)	GAP (eV)
4a	*p*-ClC_6H_4	–	−8.4515	−1.5793	6.8722
4b	*p*-MeC_6H_4	–	−8.1693	−1.8095	6.3598
5a	*p*-ClC_6H_4	–	−8.3551	−1.8988	6.4563
5b	*p*-MeC_6H_4	–	−8.0999	−2.1570	5.9429
6a	*p*-ClC_6H_4	–	−8.8961	−1.8961	7.0000
6b	*p*-MeC_6H_4	–	−8.1554	−2.1715	5.9839
7a	*p*-ClC_6H_4	*m*-ClC_6H_4	−8.3736	−1.7823	6.5913
7b	*p*-ClC_6H_4	*p*-MeC_6H_4	−8.2599	−1.9540	6.3059
7c	*p*-ClC_6H_4	*p*-$OMeC_6H_4$	−8.2871	−1.9078	6.3778
7d	*p*-ClC_6H_4	*p*-ClC_6H_4	−8.3802	−1.7739	6.6063
7e	*p*-ClC_6H_4	C_6H_5	−8.2792	−1.9236	6.3556
7f	*p*-ClC_6H_4	*m*-MeC_6H_4	−8.2621	−1.9481	6.3140
7g	*p*-ClC_6H_4	4-Cl-3-FC_6H_4	−8.4446	−1.6825	6.7621
7h	*p*-MeC_6H_4	*m*-ClC_6H_4	−6.4010	−1.7954	4.6056
7i	*p*-MeC_6H_4	*p*-MeC_6H_4	−8.0304	−2.2360	5.7944
7j	*p*-MeC_6H_4	*p*-$OMeC_6H_4$	−8.0629	−2.1881	5.8748
7k	*p*-MeC_6H_4	*p*-ClC_6H_4	−8.1603	−2.0496	6.1107
7l	*p*-MeC_6H_4	C_6H_5	−8.0501	−2.2058	5.8443
7m	*p*-MeC_6H_4	*m*-MeC_6H_4	−8.0308	−2.2259	5.8049
7n	*p*-MeC_6H_4	4-Cl-3-FC_6H_4	−8.2310	−1.9581	6.2729

GAP = *E*LUMO-*E*HOMO

on the absorption maximum and on the other hand there is marked influence of substituents on the fluorescence emission behavior of pyrazolopyridnes **7(a-n)**. Compound **7b**, **7c**, **7f**, **7i**, **7j**, **7m** shows fluorescence band appearing at longest wavelength was substantially bathochromically shifted, we ascribed to the increased π-electron density on the D ring arising from the electron donating nature of OCH_3 and CH_3 group. Another interesting feature is that halo-substituted molecule (**7a**, **7b**, **7g**, **7h**, **7k** and **7n**) has less fluorescence emission (λ_f max) and fluorescence quantum yield (Φ_f) than methoxy and methyl substituted compounds. This may be due to the quenching of fluorescence with halogen atoms as the substitution. From Tables 1, 3 and Fig. 2, we reveal that charge is more concentrate on ring D and substituents on ring D plays important role to decide the fluorescence wavelength of **7(a-n)**. It observed that Cl or CH_3 substituent on ring E, much not play a role to decide the absorption maxima and fluorescence emission of **7(a-n)**.

We observed that, on replace CH_3 group by H at C_6 in pyrazolopyrrolopyridines which reported previously [32] resulting increase in absorption, emission and quantum yields. This may be due to disturbance in planarity of pyrazolopyrrolopyridines by replacement of in CH_3 by H.

Conclusion

In summary, fluorescent pyrazolopyridines have been synthesized in good yields, in which C_4 position of pyridine ring is substituted by Cl, S, O and N with different substituent's on phenyl rings. These compounds show considerable absorption (λ_{abs} max) and fluorescence emission (λ_f max). Among Cl (**4a-b**), S (**5a-b**), O **(6a-b)** and N

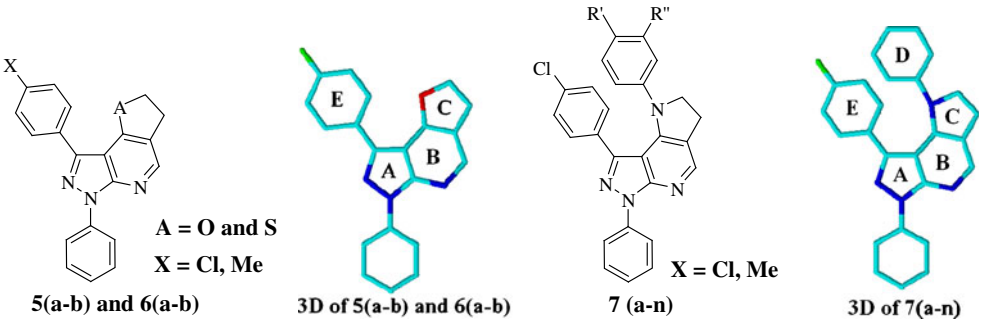


Fig. 1 3D picture of furo[2,3-*d*] pyrazolo[3,4-*b*]pyridine **5(a-b)**, pyrazolo[3,4-*b*]thieno [2,3-*d*] pyridine **6(a-b) and** pyrazolo [3,4-*b*]pyrrolo[2,3-*d*]pyridine **7 (a-n)**

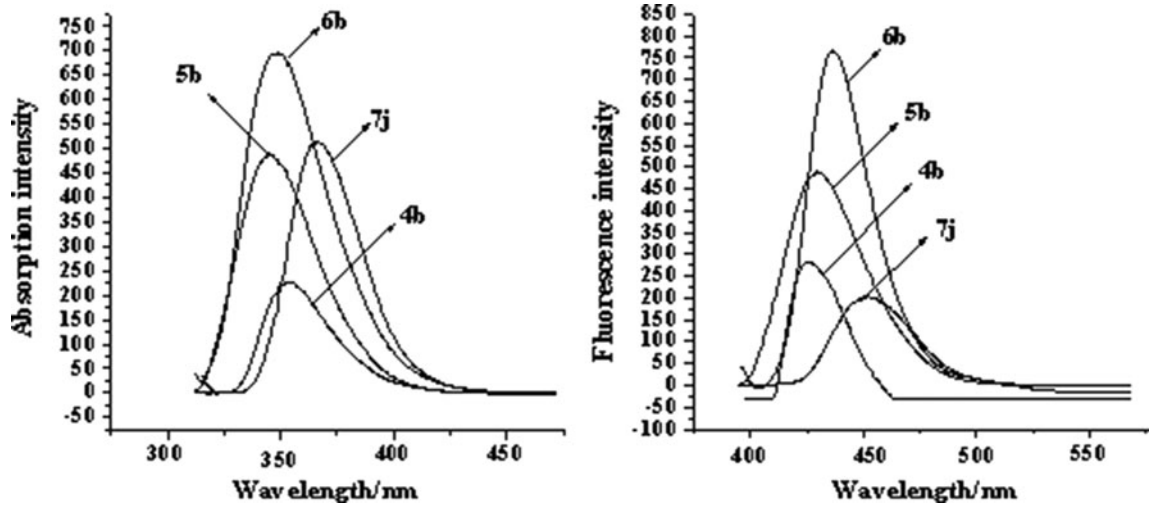


Fig. 2 The comparative absorption (λ_{abs} max) and fluorescence emission (λ_f max) spectra of compounds **4b**, **5b**, **6b** and **7j** respectively

(7a-n) substituents at C_4 position of pyrazolopyridine, C_4-N i.e. **7(a-n)** shows maximum fluorescence emission as compare to others. The fluorescence emission maxima of **7(a-n)** depend upon the nature of substituents on D ring (Table 3). Thus, donor chromophores on ring D such as OCH_3, CH_3 (compound **7b**, **7c**, **7f**, **7i**, **7j** and **7m**) are shows red shifted fluorescence emission (bathochromic shift). From empirical calculations, we reveals that pyrazolopyridines which shows low electron hole gap values (**5b**, **6b**, **7b**, **7c**, **7f**, **7i**, **7j**, **7l** and **7m**) have high fluorescence emission as well as high quantum yields (except **7h** and **7k**). While compound have high electron–hole gap (**4a**, **5a**, **6a**, **7a**, **7d** and **7g**) shows low fluorescence emission and low quantum yields and are in agreement with theoretical observation. Quantum yield of all synthesized compound are calculated. This study has brought out interesting substituents dependent fluorescence properties of pyrazolopyridine can be used as NLO materials. These pyrazolopyridine synthesized compounds are addition to library of heterocyclic compounds.

Table 2 The photophysical data for electronic absorption (λ_{abs} max) and fluorescence (λ_f max) of Pyrazolo[3,4-*b*]pyridine **4(a-b)**, **5(a-b)** and **6(a-b)** in DMF as the solvent (ca. 10^{-3}) at room temperature

Comp.	Ar	λ_{abs}	λ_f	Φ_f
4a	*p*-ClC_6H_4	335	414	0.177
4b	*p*-Me-C_6H_4	336	424	0.185
5a	*p*-ClC_6H_4	318	414	0.188
5b	*p*-Me-C_6H_4	325	429	0.213
6a	*p*-ClC_6H_4	324	421	0.211
6b	*p*-Me-C_6H_4	327	436	0.234

Instrumentation

Quinine sulphate [for determination of Φ_f] was purchased from Research-Lab Fine Chem Industries, Mumbai (India) respectively. All other chemicals, reagents and solvents [such as acetonitrile, dimethylformamide (DMF), dioxane, ethanol, ethyl acetate, n-hexane, pet-ether methanol and tetrahydrofuran (THF)] used in spectroscopic and other studies were obtained from LOBA Chemie. Pvt. Ltd., Mumbai (India), Spectrochem, Mumbai (India) and E. Merck (India). All AR-grade organic solvents were dried and freshly distilled prior to use. The UV-grade solvents were used for spectral studies. Melting points were

Table 3 The photophysical data for electronic absorption (λ_{abs} max) and fluorescence (λ_f max) of Pyrazolo[3,4-*b*]pyrrolo[2,3-*d*]pyridine **7** in DMF as the solvent (ca. 10^{-3}) at room temperature

Comp.	Ar	R	λ_{abs}	λ_{flu}	Φ_F
7a	*p*-ClC_6H_4	*m*-ClC_6H_4	364.20	416	0.182
7b	*p*-ClC_6H_4	*p*-MeC_6H_4	366.50	437	0.271
7c	*p*-ClC_6H_4	*p*-$OMeC_6H_4$	369.00	452	0.284
7d	*p*-ClC_6H_4	*p*-ClC_6H_4	364.80	423	0.196
7e	*p*-ClC_6H_4	C_6H_5	364.50	419	0.192
7f	*p*-ClC_6H_4	*m*-MeC_6H_4	367.60	431	0.261
7g	*p*-ClC_6H_4	4-Cl,3-FC_6H_4	346.00	408	0.179
7h	*p*-MeC_6H_4	*m*-ClC_6H_4	364.70	413	0.187
7i	*p*-MeC_6H_4	*p*-MeC_6H_4	369.50	444	0.282
7j	*p*-MeC_6H_4	*p*-$OMeC_6H_4$	370.50	461	0.291
7k	*p*-MeC_6H_4	*p*-ClC_6H_4	363.50	418	0.192
7l	*p*-MeC_6H_4	C_6H_5	363.60	429	0.258
7m	*p*-MeC_6H_4	*m*-MeC_6H_4	365.00	430	0.231
7n	*p*-MeC_6H_4	4-Cl,3-FC_6H_4	356.00	412	0.195

determined on a Gallenkamp melting point apparatus, Mod. MFB595 in open capillary tubes and are uncorrected. Fourier transform infrared (FTIR) spectra in KBr disk were measured on a Shimadzu FTIR-408 spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian XL-300 MHz spectrometer using tetramethylsilane (TMS) as internal standard and solvents are deuterio-chloroform ($CDCl_3$) and deuterio-dimethylsulphoxide (DMSO-d_6). Chemical shifts were reported in ppm from internal tetramethylsilane standard and were given in δ-units. High-resolution mass spectra are obtained with a Mat 112 Varian Mat Bremen (70 eV) mass spectrometer. Elemental analyses were performed on a Hosli CH-Analyzer and within ± 0.3 of the theoretical percentage. The absorption spectra were measured using a Shimadzu UV-1601 UV–VIS spectrophotometer. The fluorescence spectra were recorded on a RF-5301 PC spectrofluorophotometer by exciting the samples at their absorption maximum ($\lambda_{abs.\ max.}$). Compounds for UV and fluorescence measurements were dissolved in DMF, UV and fluorescence scan were recorded from 200 to 700 nm. Both samples and standard were excited at the same excitation wavelength and the optical density (OD) of the standard and the sample was adjusted to be nearly equal. For all electronic spectroscopic studies (absorption, fluorescence excitation and emission) 1.0×10^{-3} mol L^{-1} solutions of the compounds were used. All reactions are monitored by thin layer chromatography, carried out on 0.2 mm silica gel 60 F_{254} (Merck) plates using UV light (250 and 400 nm) and Fluorescence light (400 and 600 nm) for detection.

Synthesis

Synthesis of (Z)-3-((3-Aryl)-1-phenyl-1H-pyrazol-5-ylamino)methylene)-dihydrofuran-2-(3H)-one (3a-b)

A mixture of 5-aminopyrazole (0.1 mol) and Na-salt of α-formyl-γ-butyrolactone (13.6 g, 0.1 mol) in 80 mL MeOH and 70 mL AcOH was refluxed in an oil bath for 10–12 h. (TLC check (hexane: ethyl acetate, 1:1 *v/v*). Reaction mixture was cooled to room temperature and poured in ice cold water. The solid separated was isolated by filtration, dried and recrystallized from toluene.

(Z)-3-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-5-ylamino)methylene)-dihydrofuran-2(3H)-one (3a)

Yield: 23.7 g (65%), recrystallized from toluene to afford white crystalline solid; M.p. 190–192 °C. IR (KBr): 3246 (NH), 2,959, 1,718, 1,647, 1,593, 1,564, 1,055, 1,026 cm^{-1}. ^{1}H NMR (300 MHz $CDCl_3$) δ: 2.72 (dt, 2H, CH_2), 4.19 (t, *J*=8.2 Hz, 2H, CH_2), 5.56 (d, *J*=9.1 Hz, 1H, NH), 6.16 (s, 1H, ArH), 7.15 (d, *J*=6.2 Hz, 2H, ArH), 7.40 (m, 1H, ArH), 7.48–7.54 (m, 5H, ArH), 7.58–7.60 (d, *J*=6 Hz, 2H, ArH). ^{13}C NMR (75 MHz $CDCl_3$) δ: 33.5, 43.1, 96.4, 99.2, 121.8, 125.7, 126.7, 128.2, 129.1, 131.9, 135.1, 137.4, 138.7, 144.0, 151.5, 168.9. MS (70 eV) *m/z*: 365 (M+), 367 (M+2). Anal. Calcd for $C_{20}H_{16}ClN_3O_2$ (365.81): C, 65.67; H, 4.41; N, 11.49% Found: C, 65.74; H, 4.33; N, 11.27%.

(Z)-3-((1-phenyl-3-p-tolyl-1H-pyrazol-5-ylamino)methylene)-dihydrofuran-2(3H)-one (3b)

Yield: 24.1 g (70%), recrystallized from toluene to afford white crystalline solid. M.p.178–180 °C. IR (KBr): 3,230, 2,938, 2,723, 1,722, 1,640, 1,578, 1,048 cm^{-1}. ^{1}H NMR (300 MHz $CDCl_3$) δ: 2.41 (s, 3H, CH_3), 2.81 (dt, *J*=2 Hz, CH_2), 4.21 (t, *J*=8.4 Hz, 2H, CH_2), 6.05 (d, *J*=9.3 Hz, 1H, NH), 6.20 (s, 1H, ArH), 7.22 (d, *J*=6 Hz, 2H, ArH), 7.39–7.42 (m, 1H, ArH), 7.44–7.53 (m, 5H, ArH), 7.73 (d, *J*= 6 Hz, 2H, ArH). ^{13}C NMR (75 MHz $CDCl_3$) δ: 20.8, 24.4, 64.8, 94.8, 97.2, 123.5, 125.1, 127.2, 129.2, 129.9, 137.3, 138.0, 138.7, 142.4, 150.4, 172.7. MS (70 eV) *m/z*: 345 (M+). Anal. Calcd for $C_{21}H_{19}N_3O_2$ (345.39): C, 73.03; H, 5.54; N, 12.17% Found: C, 73.22; H, 5.66; N, 12.12%.

General procedure for the synthesis of 4-Chloro-5-(2-chloroethyl)-3-(aryl)-1-phenyl-1H-pyrazolo [3,4-b]pyridine (4) and 8-(aryl)-6-phenyl-3,6-dihydro-2H-furo [2,3-d]pyrazolo[3,4-b] pyridine (5)

Method-I

Aminopyrazolyldihydrofuranone **3** (0.01 mol) was stirred at room temperature in phosphorus oxychloride (20 mL) until the end of the exothermic reaction, which usually starts about 80–90 °C. The mixture was then refluxed further for 3–4 h. The excess $POCl_3$ was removed under vacuum. The residue obtained was stirred in ice-cold water for 2 h and then the resulting solution was neutralizing by addition of solid sodium carbonate (2–3 g). The solid separated was isolated by filtration and dried. The TLC analysis showed two products. These two solid were separated by column chromatography, using chloroform : methanol, (9:1) as eluent, afforded pyrazolo[3,4-*b*]pyridine **4** in 70% and 3,6-dihydro-2H-furo[2,3-*d*]pyrazolo[3,4-*b*]pyridine **5** in 30% yield respectively.

Method-II

General procedure for the synthesis of and 8-(Aryl)-6-phenyl-3,6-dihydro-2H-furo[2,3-d] pyrazolo[3,4-b] pyridine (5)

4-Chloro-5-(2-chloroethyl)-3-(4-aryl)-1-phenyl-1H-pyrazolo[3,4-*b*]pyridine **4** (0.001 mol) was refluxed in acetic acid (5 mL) for 2–3 h (TLC check hexane: ethyl acetate, 1:1 *v/v*). After completion of the reaction cooled reaction mixture and poured on ice cold, water upon which a solid separated.

Obtained solid was isolated by filtration, dried and recrystallized from ethanol to furnish compound **5** in 25% yield.

Method-III

General procedure for the synthesis of and 8-(Aryl)-6-phenyl-3,6-dihydro-2H-furo[2,3-d] pyrazolo[3,4-b] pyridine (5)

A mixture of 5-aminopyrazole **1** (0.001 mol) and Na-salt of α-formyl-γ-butyrolactone **2** (0.136 g, 0.001 mol) in NH_4OAc (5 g) or AcOH (5 mL) was refluxed for 10–15 h (TLC check hexane: ethyl acetate, 1:1 *v/v*). Reaction mixture was cooled to room temperature and poured in ice cold water. The solid separated was filter dried and recrystallized from ethanol: DMF (9:1), to furnish compound **5** in 80–85% yield.

4-Chloro-5-(2-chloroethyl)-3-(4-chlorophenyl)-1-phenyl-1H-pyrazolo[3,4-b]pyridine (4a)

Yield: 0.241 g (60%), recrystallized from ethanol to afford colorless crystalline solid; M.p. 185–187 °C. IR (KBr): 2,930, 1,601, 1,590, 1,290 cm^{-1}. ^1H NMR (300 MHz $CDCl_3$) δ: 3.37 (t, *J*=6.9 Hz, 2H, CH_2), 3.80 (t, *J*=6.9 Hz, 2H, CH_2), 7.33–7.57 (m, 5H, ArH), 7.71 (d, *J*=8.4 Hz, 2H, ArH), 8.24 (d, *J*=8.4 Hz, 2H, ArH) 8.52 (s, 1H, ArH). ^{13}C NMR (75 MHz $CDCl_3$) δ: 33.4, 43.1, 121.8, 125.7, 126.1, 126.7, 128.2, 128.4, 129.0, 129.1, 130.7, 131.7, 135.0, 137.4, 138.7, 144.0, 151.0, 151.5. MS (70 eV) *m/z*: 403 (M+), 405 (M+2), 407 (M+4), 409 (M+6). Anal. Calcd for $C_{20}H_{14}Cl_3N_3$ (402.7): C, 59.65; H, 3.50; N, 10.43% Found: C, 59.54; H, 3.42; N, 10.48%.

4-Chloro-5-(2-chloroethyl)-1-phenyl-3-p-tolyl-1H-pyrazolo[3,4-b]pyridine (4b)

Yield: 0.248 g (65%), recrystallized from ethanol to afford white crystalline solid; M.p. 140–142 °C. IR (KBr): 2,942, 1,610, 1,599, 1,254 cm^{-1}; ^1H NMR (300 MHz $CDCl_3$) δ: 2.45 (s, 3H, CH_3) 3.63 (t, *J*=5.4 Hz, 2H, CH_2), 3.79 (t, *J*=5.4 Hz, 2H, CH_2), 7.30–7.55 (m, 5H, ArH), 7.60 (d, *J*=6 Hz, 2H, ArH), 8.39 (d, *J*=6 Hz, 2H, ArH) 8.52 (s, 1H, ArH). ^{13}C NMR (75 MHz $CDCl_3$) δ: 20.9, 33.3, 43.1, 121.1, 126.1, 126.5, 126.8, 128.2, 128.8, 129.0, 129.1, 130.7, 131.6, 135.3, 137.4, 140.1, 143.0, 150.9, 151.4. MS (70 eV) *m/z*: 381 (M+), 383 (M+2), 385 (M+4).

Anal. Calcd for $C_{21}H_{17}Cl_2N_3$ (382.29): C, 65.98; H, 4.48; N, 10.99% Found: C, 65.80; H, 4.42; N, 11.08%.

8-(4-Chlorophenyl)-6-phenyl-3,6-dihydro-2H-furo[2,3-d] pyrazolo[3,4-b]pyridine (5a)

Yield: Method-I 0.104 g (30%), Method-II 0.087 g (25%), Method-III 0.277 g (80%) recrystallized from ethanol to afford crystalline cream colored solid; M.p. 189–191 °C. IR (KBr): 2,955, 1,602, 1,593, 1,280 cm^{-1}. ^1H NMR (300 MHz $CDCl_3$) δ: 2.88 (t, *J*=6.6 Hz, 2H, CH_2), 4.27 (t, *J*=6.6 Hz, 2H, CH_2), 7.39–7.57 (m, 5H, ArH), 7.20 (d, *J*=7.5 Hz, 2H, ArH), 7.80 (d, *J*=7.5 Hz, 2H, ArH) 7.89 (s, 1H, ArH). ^{13}C NMR (75 MHz $CDCl_3$) δ: 27.3, 70.8, 110.4, 116.6, 121.0, 125.7, 126.5, 128.2, 128.8, 128.9, 131.5, 134.2, 139.2, 142.8, 150.3, 168.5. MS (70 eV) *m/z*: 347 (M+), 349 (M+2). Anal. Calcd for $C_{20}H_{14}ClN_3O$ (347.8): C, 69.00; H, 4.06; N, 12.08% Found: C, 68.88; H, 4.06; N, 11.98%.

8-(4-Methylphenyl)-6-phenyl-3,6-dihydro-2H-furo[2,3-d]pyrazolo[3,4-b]pyridine (5b)

Yield: Method-I 0.098 g (30%), Method-II 0.081 g (25%), Method-III 0.278 g (85%), recrystallized from ethanol to afford cream colored crystalline solid; M.p. 197–199 °C. IR (KBr): 2,955, 1,602, 1,593, 1,280 cm^{-1}; ^1H NMR (300 MHz $CDCl_3$) δ: 2.39 (s, 3H, CH_3) 2.78 (t, *J*=6.9 Hz, 2H, CH_2), 4.32 (t, *J*=6.9 Hz, 2H, CH_2), 7.09–7.46 (m, 5H, ArH), 7.29 (d, *J*=8.1 Hz, 2H, ArH), 7.74 (d, *J*=8.1 Hz, 2H, ArH) 8.01 (s, 1H, ArH). ^{13}C NMR (75 MHz $CDCl_3$) δ: 21.1, 27.3, 70.7, 110.4, 116.7, 120.9, 126.1, 126.5, 128.7, 128.9, 129.0, 131.5, 134.2, 141.4, 143.0, 150.2, 168.7. MS (70 eV) *m/z*: 327 (M+). Anal. Calcd for $C_{21}H_{17}N_3O$ (327.38): C, 77.04; H, 5.23; N, 12.84% Found: C, 77.18; H, 5.16; N, 12.98%.

General procedure for the synthesis of Pyrazolo[3,4-b] thieno[2,3-d]pyridine (6)

A solution of **4** (0.01 mol) in acetic acid (10 mL) and thiourea (2.28 g, 0.01 mol) was refluxed for about 2–3 h (TLC check chloroform/methanol, 9:1). The excess of acetic acid was removed under pressure. The obtained residue was stirred in cold water (15 mL). The resulting precipitated solid was isolated by filtration, washed with water and dried to get analytical pure solid **9** in good yield, This solid product did not need further purification.

8-(4-Chlorophenyl)-6-phenyl-3,6-dihydro-2H-pyrazolo [3,4-b]thieno[2,3-d]pyridine (6a)

Yield: 2.91 g (80%), recrystallized from ethanol to afford white amorphous solid; M.p. 268–270 °C; IR (KBr): 2,921, 1,616, 1,545, 1,210 cm^{-1}. ^1H NMR (300 MHz $CDCl_3$) δ: 3.30 (t, *J*=6.7 Hz, 2H), 3.78 (t, *J*=6.7 Hz, 2H), 7.20–7.54 (m, 5H, ArH), 7.80 (d, *J*=8.5 Hz, 2H, ArH), 8.24 (d, *J*= 8.5 Hz, 2H, ArH), 8.30 (s, 1H, ArH). ^{13}C NMR (75 MHz $CDCl_3$) δ: 29.6, 34.4, 121.6, 126.7, 128.7, 129.0, 130.1, 130.3, 134.9, 139.3, 143.4. MS (70 eV) *m/z*: 363(M+) 365 (M+2); Anal. Calcd for $C_{20}H_{14}ClN_3S$ (363.83): C, 66.02; H, 3.88; N, 11.55% Found: C, 66.18; H, 3.79; N, 11.60%.

8-(4-Methylphenyl)-6-phenyl-3,6-dihydro-2H-pyrazolo [3,4-b]thieno[2,3-d]pyridine (6b)

Yield: 3.10 g (90%), recrystallized from ethanol to afford white amorphous solid; M.p.177–180 °C; IR (KBr): 2,934,

2,730, 1,599, 1,545, 1,234 cm^{-1}; ^1H NMR (300 MHz $CDCl_3$) δ: 2.45 (s, 3H CH_3), 3.34 (t, *J*=6.8 Hz, 2H), 3.86 (t, *J*=6.8 Hz, 2H), 7.29–7.38 (m, 3H, ArH), 7.50–7.57 (m, 2H, ArH), 7.89 (d, *J*=8.3 Hz, 2H, ArH), 8.26 (s, 1H, ArH), 8.30 (d, *J*=8.3 Hz, 2H, ArH). ^{13}C NMR (75 MHz $CDCl_3$) δ: 21.0, 29.6, 34.3, 121.6, 126.7, 128.6, 130.2, 130.3, 131.1, 135.0, 139.4, 143.4. MS (70 eV) *m/z*: 343 (M+). Anal. Calcd for $C_{21}H_{17}N_3S$ (345.44): C, 73.44; H, 4.99; N, 12.23% Found: C, 73.32; H, 4.93; N, 12.29%.

General procedure for the synthesis of 1-Phenyl-8-(4-aryl)-6-phenyl-1,2,3,6-tetrahydro pyrazole[3,4-b]pyrrolo[2,3-d]pyridine (7)

A mixture of **4** (0.01 mol) and primary aliphatic or aromatic amines (0.04 mol) was heated at 110–120 °C for about 2–3 h, until TLC showed no more starting material. Then the mixture was cooled at 20 °C, after cold methanol 5 °C (20 mL) was added. The resulting solid was filtered by suction, washed with methanol, dried and recrystallized from the ethanol:DMF to furnish compound **10** in good yield.

8-(4-Chlorophenyl)-1-(3-chlorophenyl)-6-phenyl-1,2,3,6-tetrahydropyrazole[3,4-b]pyrrolo[2,3-d]pyridine (7a)

Yield: 3.43 g (75%), recrystallized from ethanol: DMF (9:1) to afford colorless crystalline solid, M.p. 176–178 °C. IR (KBr): 2,930, 1,595, 1,588, 1,228 cm^{-1}; ^1H NMR (300 MHz $CDCl_3$) δ: 3.35 (t, *J*=8.7 Hz, 2H), 4.22 (t, *J*= 8.7 Hz, 2H), 6.81 (m, 1H, ArH), 6.85 (m, 3H, ArH), 7.08–7.14 (m, 5H, ArH) 7.52 (t, *J*=7.8 Hz, 2H, ArH), 8.26 (d, *J*= 8.4 Hz, 2H, ArH), 8.30 (s, 1H, ArH). MS (70 eV) *m/z*: 456 (M+), 458 (M+2), 460 (M+4). Anal. Calcd for $C_{26}H_{18}Cl_2N_4$ (457.35): C, 68.28; H, 3.97; N, 12.25% Found: C, 68.14; H, 3.88; N, 12.29%.

8-(4-Chlorophenyl)-6-phenyl-1-p-tolyl-1,2,3,6-tetrahydropyrazole[3,4-b]pyrrolo[2,3-d]pyridine (7b)

Yield: 3.05 g (70%), recrystallized from ethanol: DMF (9:1) to afford off white solid; M.p. 192–194 °C; IR (KBr): 2,950, 2,717, 1,610, 1,202 cm^{-1}; ^1H NMR (300 MHz $CDCl_3$) δ: 2.23 (s, 3H, CH_3), 3.33 (t, *J*=9 Hz, 2H), 4.18 (t, *J*=9 Hz, 2H), 6.50 (d, *J*=8.1 Hz, 2H, ArH), 6.80 (d, *J*= 8.4 Hz, 2H, ArH), 6.92 (d, *J*=8.4 Hz, 2H, ArH), 7.26 (m, 2H, ArH), 7.30 (d, *J*=7.5 Hz, 2H, ArH), 7.51 (t, *J*=7.5 Hz, 2H, ArH), 8.22 (d, *J*=8.1 Hz, 2H), 8.24 (s, 1H, ArH). ^{13}C NMR (75 MHz $CDCl_3$) δ: 21.1, 31.2, 43.6, 120.1, 120.8, 121.9, 126.5, 126.7, 127.5, 128.2, 128.3, 128.7, 129.0, 129.5, 130.1, 132.5, 134.3, 140.3, 143.7, 150.8. MS (70 eV) *m/z*: 434 (M+), 436 (M+2).

Anal. Calcd for $C_{27}H_{21}ClN_4$ (434.36): C, 74.22; H, 4.84; N, 12.82% Found: C, 74.08; H, 4.90; N, 12.96%.

8-(4-Chlorophenyl)-1-(4-methoxyphenyl)-6-phenyl-1,2,3,6-tetrahydropyrazole[3,4-b]pyrrolo [2,3-d]pyridine (7c)

Yield: 4.07 g (90%), recrystallized from ethanol: DMF (9:1) to afford grey crystalline solid, M.p.199–200 °C. IR (KBr): 2,945, 1,598, 1,350, 1,120 cm^{-1}. ^1H NMR (300 MHz $CDCl_3$) δ: 3.33 (t, *J*=8.7 Hz, 2H), 3.69 (s, 3H, OCH_3) 4.12 (t, *J*=8.7 Hz, 2H), 6.41 (d, *J*=8 Hz, 2H, ArH), 6.73 (d, *J*= 8.3 Hz, 2H, ArH), 6.83 (d, *J*=8.3 Hz, 2H, ArH), 7.06 (m, 3H, ArH), 7.10–7.34 (m, 2H, ArH) 8.20 (d, *J*=8 Hz, 2H, ArH), 8.26 (s, 1H, ArH). MS (70 eV) *m/z*: 452 (M+), 454 (M+2). Anal. Calcd for $C_{27}H_{21}ClN_4O$ (452.93): C, 71.60; H, 4.67; N, 12.37% Found: C, 71.86; H, 4.74; N, 12.42%.

1,8-Bis(4-chlorophenyl)-6-phenyl-1,2,3,6-tetrahydropyrazolo[3,4-b]pyrrolo[2,3-d]pyridine (7d)

Yield: 3.75 g 82%, recrystallized from ethanol:DMF 9:1 to afford grey amorphous solid, M.p. 190–192 °C. IR (KBr): 2,980, 2,940, 1,610, 1,580 cm^{-1}. ^1H NMR (300 MHz $CDCl_3$) δ: 3.36 (t, *J*=8.5 Hz, 2H, ArH), 4.20 (t, *J*=8.5 Hz, 2H, ArH), 6.53 (d, *J*=7.9, 2H, ArH), 7.01 (d, *J*=7.9, 2H, ArH), 7.08–7.47 (m, 5H, ArH), 7.48 (d, *J*=8.3, 2H, ArH), 7.78 (d, *J*=8.3, 2H, ArH), 8.22 (s, 1H, ArH). MS (70 eV) *m/z*: 456 (M+), 458 (M+2), 460 (M+4). Anal. Calcd for $C_{26}H_{18}Cl_2N_4$ (457.35): C, 68.28; H, 3.97; N, 12.25% Found: C, 68.16; H, 4.01; N, 12.34%.

8-(4-Chlorophenyl)-1,6-diphenyl-1,2,3,6-tetrahydropyrazolo[3,4-b]pyrrolo[2,3-d]pyridine (7e)

Yield: 3.29 g (78%), recrystallized from ethanol: DMF (9:1) to afford white amorphous solid; M.p. 207–209 °C. IR (KBr): 2,908, 1,616, 1,598, 1,238 cm^{-1}. ^1H NMR (300 MHz $CDCl_3$) δ: 3.34 (t, *J*=6.9 Hz, 2H), 4.23 (t, *J*= 6.9 Hz, 2H), 6.78–6.84 (m, 2H, ArH), 6.88–6.92 (m, 5H, ArH), 7.32–7.34 (m, 3H, ArH), 7.52 (d, *J*=8.7 Hz, 2H, ArH), 8.25 (d, *J*=8.7 Hz, 2H, ArH), 8.25 (s, 1H, ArH). ^{13}C NMR (75 MHz $CDCl_3$) δ: 31.3, 43.9, 119.8, 120.6, 121.0, 122.2, 126.4, 126.7, 127.1, 128.1, 128.5, 129.1, 129.5, 130.1, 131.1, 138.5, 143.2, 144.4, 151.3. MS (70 eV) *m/z*: 422 (M+), 424 (M+2). Anal. Calcd for $C_{26}H_{19}ClN_4$ (422.91): C, 73.84; H, 4.53; N, 13.25% Found: C, 73.64; H, 4.58; N, 13.18%.

8-(4-Chlorophenyl)-6-phenyl-1-m-tolyl-1,2,3,6-tetrahydropyrazolo[3,4-b]pyrrolo[2,3-d]pyridine (7f)

Yield: 3.71 g (75%), recrystallized from ethanol: DMF (9:1) to afford off white amorphous solid, M.p. 148–150 °C; IR (KBr): 2,930, 2,728, 1,600, 1,588 cm^{-1}; ^1H NMR (300 MHz $CDCl_3$) δ: 2.18 (s, 3H, CH_3), 3.27 (t, *J*=7.2 Hz, 2H), 4.22 (t, *J*=7.2 Hz, 2H), 6.56 (d, *J*=8.2 Hz, 2H, ArH), 6.78 (s, 1H, ArH), 6.95–7.18 (m, 5H, ArH), 7.30–7.38 (m,

3H, ArH), 8.10 (d, *J*=8.2 Hz, 2H, ArH), 8.22 (s, 1H, ArH). MS (70 eV) *m/z*: 436 (M+), 438 (M+2). Anal. Calcd for $C_{27}H_{21}ClN_4$ (436.94): C, 74.22; H, 4.84; N, 12.82% Found: C, 74.35; H, 4.80; N, 12.78%.

1-(3-Chloro-4-fluoro)-8-(4-chlorophenyl)-6-phenyl-1,2,3,6-tetrahydropyrazolo[3,4-b]pyrrolo [2,3-d]pyridine (7g)

Yield: 3.56 g (75%), recrystallized from ethanol: DMF (9:1) to afford orange amorphous solid, M.p. 158–160 °C; IR (KBr): 2,900, 1,616, 1,585, 1,240 cm^{-1}. ^1H NMR (300 MHz $CDCl_3$) δ: 3.20 (t, *J*=8 Hz, 2H), 4.26 (t, *J*=8 Hz, 2H), 6.72 (s, 1H), 6.80–6.82 (m, 2H, ArH), 7.01 (d, *J*=6 Hz, 2H, ArH), 7.26–7.45 (m, 5H, ArH), 7.89 (d, *J*=6 Hz, 2H, ArH), 8.02 (s, 1H, ArH). MS (70 eV) *m/z*: 474 (M+), 476 (M+2), 478 (M+4). Anal. Calcd for $C_{26}H_{17}Cl_2FN_4$ (475.34): C, 65.70; H, 3.60; N, 11.79% Found: C, 65.47; H, 3.72; N, 11.89%.

1-(3-Chlorophenyl)-6-phenyl-8-p-tolyl-1,2,3,6-tetrahydropyrazolo[3,4-b]pyrrolo[2,3-d]pyridine (7h)

Yield; 2.84 g (65%), recrystallized from ethanol: DMF (9:1) to afford grey crystalline solid, M.p. 162–164 °C; IR (KBr): 2,919, 2,726, 1,605, 1,267 cm^{-1}. ^1H NMR (300 MHz $CDCl_3$) δ: 2.22 (s, 3H, CH_3), 3.22 (t, *J*=8.4 Hz, 2H), 4.17 (t, *J*=8.4 Hz, 2H), 6.43–6.72 (m, 3H, ArH), 6.80 (s, 1H, ArH), 6.98–7.33 (m, 5H, ArH), 7.43 (d, *J*=7.7 Hz, 2H, ArH), 8.03 (s, 1H, ArH), 8.33 (d, *J*=7.7 Hz, 2H, ArH). ^{13}C NMR (75 MHz $CDCl_3$) δ: 21.0, 26.0, 56.9, 118.8, 119.8,121.2, 122.6, 123.4, 125.7, 128.0, 128.2, 128.3, 128.5, 128.9, 129.3, 130.8, 133.9, 137.3, 139.7, 144.2, 146.7, 148.5. MS (70 eV) *m/z*: 436 (M+), 438 (M+2). Anal. Calcd for $C_{27}H_{21}ClN_4$ (436.94): C, 74.22; H, 4.84; N, 12.82% Found: C, 74.38; H, 4.80; N, 12.76%.

6-Phenyl-1,8-bis-p-tolyl-1,2,3,6-tetrahydropyrazolo [3,4-b]pyrrolo[2,3-d]pyridine (7i)

Yield: 3.33 g (80%), recrystallized from ethanol: DMF (9:1) to afford yellow solid, M.p. 206–208 °C. IR (KBr): 3,065, 2,918, 2,864, 1,593, 1,494 cm^{-1}. ^1H NMR (300 MHz $CDCl_3$) δ: 2.35 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 3.27 (t, *J*=8.3 Hz, 2H), 4.20 (t, *J*=8.3, 2H), 6.49 (d, *J*=7.3 Hz, 2H, ArH), 6.89–7.04 (m, 4H, ArH), 7.29 (t, *J*=6.9 Hz, 2H, ArH), 7.37–7.40 (m, 3H, ArH), 8.14 (d, *J*=8.7 Hz, 2H, ArH), 8.20 (s, 1H, ArH). MS (70 eV) *m/z*: 416 (M+), Anal. Calcd for $C_{28}H_{24}ClN_4$ (416.52): C, 80.74; H, 5.81; N, 13.45% Found: C, 80.60; H, 5.77; N, 13.53%.

1-(4-Methoxyphenyl)-6-phenyl-8-p-tolyl-1,2,3,6-tetrahydropyrazolo[3,4-b]pyrrolo[2,3-d] pyridine (7j)

Yield: 3.67 g (85%), recrystallized from ethanol: DMF (9:1) to afford grey solid, M.p. 224–226 °C; IR (KBr): 2,937, 2,720, 1,589, 1,357, 1,267 cm^{-1}. ^1H NMR (300 MHz $CDCl_3$) δ: 2.34 (s, 3H, CH_3), 3.18 (t, *J*=8.1 Hz, 2H), 3.74 (s, 3H, OCH_3), 4.13 (t, *J*=8.1 Hz, 2H), 6.77 (d, *J*=8.6 Hz, 2H, ArH), 6.84 (d, *J*=6.9 Hz, 2H, ArH), 6.89–6.92 (m, 4H, ArH), 7.10–7.34 (m, 3H, ArH), 8.01 (s, 1H, ArH), 8.10 (d, *J*=6.9 Hz, 2H, ArH). MS (70 eV) *m/z*: 432 (M+). Anal. Calcd for $C_{28}H_{24}ON_4$ (432.52): C, 77.75; H, 5.59; N, 12.95% Found: C, 77.62 H, 5.55; N, 12.99%.

1-(4-Chlorophenyl)-6-phenyl-8-p-tolyl-1,2,3,6-tetrahydropyrazolo[3,4-b]pyrrolo[2,3-d]pyridine (7k)

Yield: 3.05 g (73%), recrystallized from ethanol: DMF (9:1) to afford off white amorphous solid, M.p. 167–169 °C; IR (KBr): 2,920, 2,736, 1,596, 1,580 cm^{-1}. ^1H NMR (300 MHz $CDCl_3$) δ: 2.32 (s, 3H, CH_3), 3.33 (t, *J*=8.7 Hz, 2H), 4.19 (t, *J*=8.7 Hz, 2H), 6.79 (d, *J*=7 Hz, 2H, ArH), 6.98–7.02 (m, 3H, ArH), 7.12–7.34 (m, 4H, ArH), 7.54 (d, *J*=6.9 Hz, 2H, ArH), 8.20 (d, *J*=6.9 Hz, 2H, ArH), 8.28 (s, 1H, ArH). ^{13}C NMR (75 MHz $CDCl_3$) δ: 20.8, 32.4, 43.6, 120.7, 121.2, 122.1, 126.0, 126.5, 128.1, 128.5, 128.8, 129.1, 130.1, 138.3, 144.6, 151.9. MS (70 eV) *m/z*: 436 (M+), 438 (M+2). Anal. Calcd for $C_{27}H_{21}ClN_4$ (436.94): C, 74.22; H, 4.84; N, 12.82% Found: C, 74.06; H, 4.90; N, 12.80%.

1,6-Diphenyl-8-p-tolyl-1,2,3,6-tetrahydropyrazolo[3,4-b] pyrrolo[2,3-d]pyridine (7l)

Yield: 3.17 g (79%), recrystallized from ethanol: DMF (9:1) to afford off white crystalline solid, M.p. 175–177 °C. IR (KBr): 2,920, 2,736, 1,596, 1,580 cm^{-1}. ^1H NMR (300 MHz $CDCl_3$) δ: 2.34 (s, 3H CH_3), 3.28 (t, *J*=8.0 Hz, 2H), 4.22 (t, *J*=8.0 Hz, 2H), 6.60–6.64 (m, 3H, ArH), 6.70 (d, *J*=7.8 Hz, 2H, ArH), 7.05–7.27 (m, 5H, ArH), 7.30–7.38 (m, 2H, ArH), 8.08 (s, 1H, ArH), 8.12 (d, *J*=7.1 Hz, 2H, ArH). MS (70 eV) *m/z*: 402 (M+). Anal. Calcd for $C_{27}H_{22}N_4$ (402.49): C, 80.57; H, 5.51; N, 13.92% Found: C, 80.46; H, 5.56; N, 13.82%.

6-Phenyl-1-m-tolyl-8-p-tolyl-1,2,3,6-tetrahydropyrazolo [3,4-b]pyrrolo[2,3-d]pyridine (7m)

Yield: 2.83 g (68%), recrystallized from ethanol: DMF (9:1) to afford off white solid, M.p. 179–181 °C. IR (KBr): 2,916, 2,727, 1,600, 1,589 cm^{-1}. ^1H NMR (300 MHz $CDCl_3$) δ: 2.30 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 3.34 (t, *J*=8.4 Hz, 2H), 4.22 (t, *J*=8.4 Hz, 2H), 6.49–6.54 (m, 1H, ArH), 6.69 (s, 1H, ArH), 6.89 (d, *J*=7.8 Hz, 2H, ArH), 6.91–6.98 (m, 2H, ArH), 7.08–732 (m, 5H, ArH), 8.04 (d, *J*=7.8 Hz, 2H, ArH), 8.11 (s,1H, ArH). MS (70 eV) *m/z*: 416 (M+). Anal. Calcd for $C_{28}H_{24}N_4$ (416.52): C, 80.74; H, 5.81; N, 13.45% Found: C, 80.61; H, 5.75; N, 13.53%.

1-(4-Chloro-3-fluorophenyl)-6-phenyl-8-p-tolyl-1,2,3,6-tetrahydropyrazolo[3,4-b]pyrrolo[2,3-d] pyridine (7n)

Yield: 3.41 g (75%), recrystallized from ethanol: DMF (9:1) to afford colorless solid, M.p. 160–162 °C. IR (KBr):

2,949, 2,716, 1,608, 1,588 cm^{-1}. ^1H NMR (300 MHz $CDCl_3$) δ: 2.32 (s, 3H, CH_3), 3.28 (t, J=8.8 Hz, 2H), 4.17 (t, J=8.8 Hz, 2H), 6.62 (s, 1H, ArH), 6.78 (d, J=7.2 Hz, 1H, ArH), 6.83 (d, J=7.2 Hz, 1H, ArH), 7.02 (d, J=6.9 Hz, 2H, ArH), 7.08–7.34 (m, 5H, ArH), 8.02 (s, 1H, ArH), 8.12 (d, J=6.9 Hz, 2H, ArH). MS (70 eV) m/z: 454 (M+), 456 (M+2); Anal. Calcd for $C_{27}H_{20}ClFN_4$ (454.93): C, 80.74; H, 5.81; N, 13.45% Found: C, 80.89; H, 5.74; N, 13.38%.

Acknowledgements The authors thank to CSIR New Delhi and BCUD University of Pune, India for financial support to this research project. Authors also thanks to Department of Chemistry University of Pune, IIT-Powai Mumbai and Principal KTHM College Nashik, for spectral and analytical facilities.

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