Effect of substituents on absorption and fluorescence properties of pyrazolo[3,4-*b*]pyrrolo[2,3-*d*]pyridines

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Abstract: A convenient route was successfully developed for the synthesis of novel heterocycles such as pyrazolo[3,4-*b*]pyrrolo[2,3-*d*]pyridines (PPP) from pyrazolo[3,4-*b*]pyridines in good yield. The PPP derivatives synthesized were further studied for their photophysical properties, and it was observed that absorption and emission λ_{max} changed, owing to the substituent effect at 4 positions. These compounds were obtained from highly reactive starting materials, 5-aminopyrazoles and α-acetyl γ-butyrolactone.

Key words: α-acetyl γ-butyrolactone, pyrazolo[3,4-*b*]pyrrolo[2,3-*d*] pyridine, absorption, emission, fluorescence.

Résumé : On a mis au point une voie réactionnelle qui permet de réaliser la synthèse de nouveaux hétérocycles, telles les pyrazolo[3,4-*b*]pyrrolo[2,3-*d*]pyridines (PPP) à partir de pyrazolo[3,4-*b*]pyridines, avec de bons rendements. On a soumis les dérivés PPP synthétisés à des études de leurs propriétés photophysiques et on a observé que les valeurs des λmax de leurs absorptions et de leurs émissions varient sous l'effet d'un changement dans la nature des substituants en position 4. On a obtenu ces composés à partir de produits de départ très réactifs, soit les 5-aminopyrazoles et l'α-acétyl-γ-butyrolactone.

Mots-clés : l'α-acétyl-γ-butyrolactone, pyrazolo[3,4-*b*]pyrrolo[2,3-*d*]pyridine, absorption, émission, fluorescence.

[Traduit par la Rédaction]

Introduction

Photoinduced intramolecular electron transfer plays a key role in the photophysics of electron-donor (D)-electron-acceptor (A) pi/π conjugated systems connected formally by a single bond. The molecular structure of their charge-transfer excited states has been the object of numerous discussions for more than twenty years. One of the best known and also widely accepted proposals for such a system is the so-called TICT (twisted intramolecular charge transfer) state model (1–3). The perpendicular geometry was questioned recently as an inherent precondition to obtain intramolecular charge transfer in such D–A systems (4, 5). For bulky π donor and acceptor systems (e.g., 9-(4-dimethylaminophenyl)-anthracene or 9,9′-bianthryl), the D–A conformation in the fluorescing charge-transfer excited state was postulated to become more coplanar than in the ground state (6). Recently, several donor and (or) acceptor substituted compounds related to carbazoles, acridines, and so forth were synthesized, and their photoinduced charge separation has been intensively studied (7–9). The 4-*N*,*N*-dimethylaminophenyl derivatives of bis-pyrazolo[3,4-*b*;4′,3′-*e*]pyridine (DMA-DMPP) and pyrazolo[3,4-*b*]quinoline (DMA-DPPQ) (Fig. 1) are further representatives of bulky π-electron donor–acceptor compounds and were recently investigated in some detail both experimentally and semi-empirically (10–16). It has been shown that pyrazoloquinoline derivatives are efficient blue emitters with absorption in the near-ultraviolet region and with a fluorescence quantum yield near to unity. Substitution with a dimethylanilino donor group results in strongly solvent-polarity-dependent fluorescence properties (11, 12). Derivatives of 3,5-dimethyl-1,7-diphenyl-bis-pyrazolo-[3,4-*b*;4′,3′-*e*]-pyridine (DMA-DMPP) with different substituents in position 4 are compounds showing intense fluorescence in the blue–green region and are considered for application as fluorescence standards and luminophores in organic light-emitting diodes (17–20). The derivatives with phenyl and 4-methoxyphenyl substituent (H-DMPP and CH_3O-DMPP, respectively) are characterized by a very intense, solvent-independent fluorescence. The nitro derivatives (NO_2-DMPP) show an unexpected photophysical behaviour. Similarly, The pyrazolopyrrolopyridines with different substituents in position 4 are compounds that show intense fluorescence in the blue–green region with a fluorescence quantum yield near to unity (Fig. 2).

Apart from this, the pyrazolo[3,4-*b*]pyridines and pyrazolo[3,4-*b*]pyrrolo[2,3-*d*]pyridine are examples of condensed heterocyclic compounds with notable pharmacological and biological activities, such as hypotensive (21), cytotoxic (22), and antibacterial activity (23), and found to

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Fig. 1. X-diphenylpyrazoloquinolines.

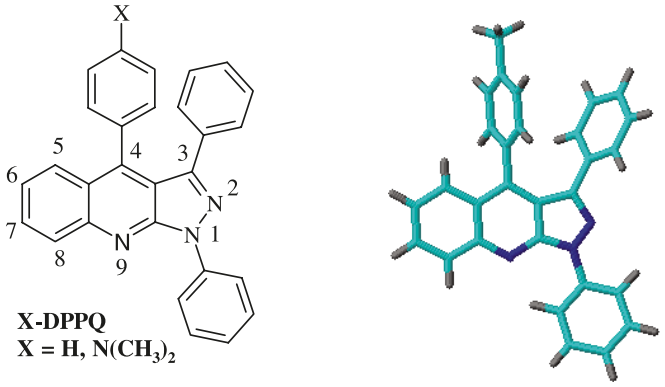
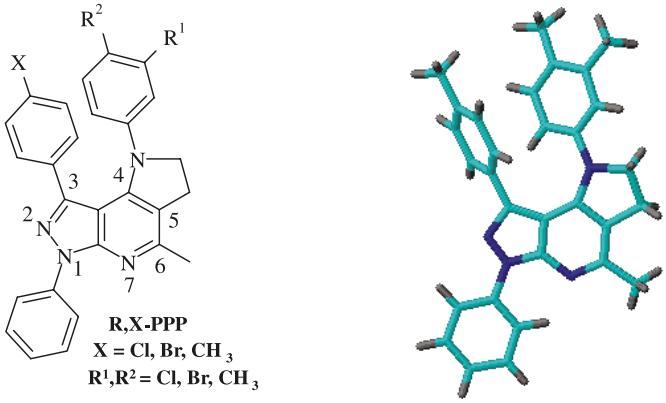


Fig. 2. R,X-pyrazolopyrrolopyridines.



be potential purine antagonists (24). Analogous to bis-pyrazolo-[3,4-b;4′,3′-*e*]-pyridines and pyrazolo-[3,4-*b*]-quinolines, the substituent effect of 4 position on the fluorescence of pyrazolo[3,4-*b*]pyrrolo[2,3-*d*]pyridine has attracted us to synthesize this particular family of compounds. As a part of our ongoing interest in this area (25–28), we have reported the synthesis of pyrazolo[3,4-*b*]pyridines, pyrazolo-[3,4-*b*]quinolines, pyrazolonaphthyridines, and pyrazolo-pyridopyrimidines by Friedlander condensation of reactive methylene compounds with 5-aminopyrazole and synthesis of fused pyrimidines. In our recent communications (29, 30), we reported the synthesis and study of fluorescence properties of benzo[*h*]quinolines and dipyrazolo[3,4-*b*:3,4-*d*]pyridines.

In the present article, we report the study of the photophysical properties of newly synthesized pyrazolo[3,4-*b*]pyridines with 4-chloro-5-chloroethyl side chain (31, 32) and pyrazolo[3,4-*b*]pyrrolo[2,3-*d*]pyridines. All these compounds, having large non-coplanar π-electron donor and acceptor subsystems because of sterical hindrance, are suitable objects to check the validity of the photophysical properties of these compounds.

Results and discussion

The syntheses of pyrazolo[3,4-*b*]pyridines **3** were achieved from highly reactive starting materials, 5-aminopyrazoles **1** and α-acetyl-γ-butyrolactone **2**. Compounds **3** were used as precursors for the syntheses of compounds **4**. Thus, the syntheses of pyrazolo[3,4-*b*]pyrrolo[2,3-*d*]pyridines **4** were achieved by the reaction of compounds **3** with primary aliphatic or aromatic amines containing catalytic amount of triethylamine at 120–150 °C to furnish the desired compound **4**. All crude products that were dissolved in methanol and collected by suction filtration, washed with ethanol, and purified by using suitable solvents, afforded the title compounds **4** in about 70%–80% yield. These compounds showed the absorption and fluorescence near ultraviolet region.

The structure of compounds **3** was confirmed by IR, ^{1}H NMR, ^{13}C NMR, mass spectroscopy, and formulae confirm by elemental analysis. For example, the ^{1}H NMR spectrum of **3a** showed a singlet at δ 2.81 for methyl protons, two triplets at δ 3.39 and 3.75 corresponding to $-CH_2$ and $-CH_2Cl$ protons, respectively, and aromatic protons showed expected chemical shifts and splitting patterns. The mass spectrum of **3a** revealed a molecular ion peak *m*/*z* at 416. The ^{13}C NMR spectrum of this compound is in agreement with the structure proposed. Further, this structure was confirmed by NOE experiment; thus, on irradiation of methyl signal at δ 2.81, the compounds showed no NOE enhancement of any aromatic protons. This indicated that the methyl group present at 6 positions and not at 4, which supported the proposed structure **3**. Similarly, the structure of **4** was confirmed by spectroscopic and analytical methods, which is given in the Experimental section. The absorption and fluorescence data listed in Tables 1 and 2 showed that the incorporation of constituent on to the pyrazolo[3,4-*b*]pyridine and pyrazolo[3,4-*b*]pyrrolo[2,3-*d*]pyridine nucleus at 4 position has profound influence on the absorption and emission properties. It was observed that substitution at 4 position showed considerable increase in the emission wavelength, as the π-electron-donating effect of amino group increases (Scheme 1).

It was interesting to note that the pyrazolo[3,4-*b*]pyridines showed the lower absorption and emission maxima than pyrazolo[3,4-*b*]pyrrolo[2,3-*d*]pyridines. In the pyrazolo[3,4-*b*]pyridines **3**, this might be due to a chloro group at 4 position with a weak and small electron-donor unit in para position, and in pyrazolo[3,4-*b*]pyrrolo[2,3-*d*]pyridines **4**, the substituted amino group at 4 position with a strong and bulky electron-donor unit at para position showed higher absorption and emission maxima.

It is clearly indicated that the fluorescence property of organic compounds is the substituent-dependent property, and it is changed with changing the nature of different substituent (e.g., in compounds **3** and **4**, the nature of substituent changed the photophysical properties of these compounds). It is enhanced by substituting the strong π-electron donor group at 4 position. Compounds **3a** and **4a** showed good absorption and emission spectra as shown in Fig. 3.

Photophysical properties

From the results obtained (Tables 1 and 2), it has been found that both pyrazolo[3,4-*b*]pyridines **3** and pyrazolo[3,4-*b*]pyrrolo[2,3-*d*]pyridines **4** show florescence properties. The compounds **4f**, **4g**, **4k**, and **4l** exhibit remarkable fluorescence characters with high relative quantum yields. It is concluded that the attachment of an electron-donating group to phenyl function oriented at the 4 position of pyrazolo[3,4-

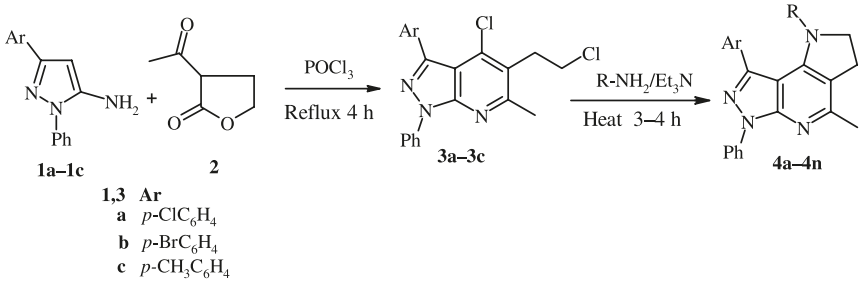
Table 1. The photophysical data for electronic absorption (abs) and fluorescence (flu) of pyrazolo[3,4-***b***]pyridines **3** in $CHCl_3$.

Compound	Ar	λ_{abs} ($CHCl_3$)	λ_{flu} ($CHCl_3$)	Φ_F ($CHCl_3$)
3a	*p*-ClC_6H_4	362.00	394.00	0.120
3b	*p*-BrC_6H_4	366.00	401.00	0.126
3c	*p*-MeC_6H_4	361.00	392.00	0.123

Table 2. The photophysical data for electronic absorption (abs) and fluorescence (flu) of pyrazolo[3,4-***b***]pyrrolo[2,3-***d***]pyridines **4** in $CHCl_3$.

Compd.	Ar	R	λ_{abs} ($CHCl_3$)	λ_{flu} ($CHCl_3$)	Φ_F ($CHCl_3$)
4a	*p*-ClC_6H_4	$C_6H_5CH_2$–	392.00	416.00	0.141
4b	*p*-ClC_6H_4	C_6H_5	393.00	419.00	0.145
4c	*p*-ClC_6H_4	m-ClC_6H_4	392.00	417.00	0.138
4d	*p*-ClC_6H_4	*p*-ClC_6H_4	395.00	421.00	0.136
4e	*p*-ClC_6H_4	*p*-BrC_6H_4	397.00	422.00	0.129
4f	*p*-ClC_6H_4	*o*-MeC_6H_4	399.00	425.00	0.151
4g	*p*-ClC_6H_4	*p*-MeC_6H_4	380.00	429.00	0.146
4h	*p*-BrC_6H_4	m-ClC_6H_4	395.00	420.00	0.119
4i	*p*-BrC_6H_4	*p*-ClC_6H_4	390.00	412.00	0.124
4j	*p*-BrC_6H_4	*p*-BrC_6H_4	373.00	421.00	0.127
4k	*p*-BrC_6H_4	*o*-MeC_6H_4	396.00	425.00	0.148
4l	*p*-BrC_6H_4	*p*-MeC_6H_4	398.00	427.00	0.153
4m	*p*-MeC_6H_4	$C_6H_5CH_2$–	377.00	406.00	0.133
4n	*p*-MeC_6H_4	C_6H_5	396.00	418.00	0.131

Scheme 1. Synthesis of pyrazolopyridines **3** and pyrazolopyrrolopyridines **4**.



4	Ar	R	4	Ar	R
a	*p*-ClC_6H_4	$C_6H_5CH_2$-	**h**	*p*-BrC_6H_4	*m*-ClC_6H_4
b	*p*-ClC_6H_4	C_6H_5	**i**	*p*-BrC_6H_4	*p*-ClC_6H_4
c	*p*-ClC_6H_4	*m*-ClC_6H_4	**j**	*p*-BrC_6H_4	*p*-BrC_6H_4
d	*p*-ClC_6H_4	*p*-ClC_6H_4	**k**	*p*-BrC_6H_4	*o*-MeC_6H_4
e	*p*-ClC_6H_4	*p*-BrC_6H_4	**l**	*p*-BrC_6H_4	*p*-MeC_6H_4
f	*p*-ClC_6H_4	*o*-MeC_6H_4	**m**	*p*-MeC_6H_4	$C_6H_5CH_2$-
g	*p*-ClC_6H_4	*p*-MeC_6H_4	**n**	*p*-MeC_6H_4	C_6H_5

b]pyrrolo[2,3-*d*]pyridine enhances the fluorescence properties and in turn gives high relative quantum yield.

Conclusion

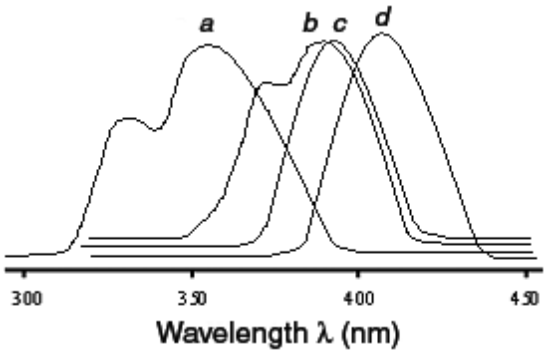
The reactions reported here represent the synthesis of a new class of fluorescent compounds in which the 4 position of pyrazolopyridine ring is substituted by the chlorine or nitrogen atom with different phenyl rings. These compounds showed considerable absorption and emission λ_{max}. Pyrazolo[3,4-*b*]pyrrolo[2,3-*d*]pyridines showed higher fluorescent properties than the pyrazolo[3,4-*b*]pyridines; it might be due to the steric hindrance of bulky phenyl rings and large π-electron donor group at 4 position.

Experimental

General

Melting points were determined on a Gallenkamp melting-point apparatus, Model MFB595, in open capillary tubes

Fig. 3. The comparative (a, b) absorption and (c, d) emission spectra of compounds **3a** and **4a**.



and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Varian XL-300 spectrometer (300 and 75 MHz). Chemical shifts are reported in ppm from internal tetramethylsilane standard and are given in δ units. The solvents for NMR spectra was duterio-chloroform unless otherwise stated. Infrared spectra were taken on a Shimadzu IR-408 (a Shimadzu FTIR instrument) in potassium bromide pellets unless otherwise stated. UV spectra were recorded on a Shimadzu UV-1601 UV–vis Spectrophotometer. Compounds for UV scan were dissolved in methanol. Fluorescence spectra were recorded using RF-5301 PC spectrofluorophotometer. Compounds for fluorescence measurements were dissolved in chloroform. UV and fluorescence scans were recorded from 200 to 600 nm. Elemental analyses were performed on a Hosli CH-Analyzer and the results are within ± 0.4 of the theoretical percentage. HR-MS were obtained with a Mat 112 Varian Mat Bremen (70 eV) mass spectrometer. Solutions were concentrated in a rotary evaporator under reduced pressure. All reactions were monitored by TLC, carried out on 0.2 mm silica gel 60 F 254 (Merck) plates, using UV light (254 and 366 nm) for detection. Common reagent-grade chemicals are either commercially available and were used without further purification or prepared by standard literature procedures.

General procedure for the 4-chloro-5-(2-chloroethyl)-3-(4-aryl)-6-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine (3a–3c)

A mixture of 5-aminopyrazole **1** (0.01 mol) and α-acetyl-γ-butyrolactone **2** (1.282 g, 1.078 mL 0.01 mol) was refluxed in phosphorous oxychloride (20 mL) until the end of the exothermic reaction, which usually starts about 80–90 °C. The mixture was then refluxed for further 4 h. Excess $POCl_3$ was removed under vacuum, and the oily residue solidified upon treatment with ice-water, neutralization with sodium carbonate, and stirring overnight. The separated product was then filtered, dried, and recrystallized to afford compound **3** in good yield.

*4-Chloro-5-(2-chloroethyl)-3-(4-chlorophenyl)-6-methyl-1-phenyl-1*H*-pyrazolo[3,4-b]pyridine (3a)*

Yield: 3.25 g (78%), recrystallized from acetonitrile/ethanol (8:2) to afford colourless prisms; mp 163–164 °C. IR (KBr): 2918m, 1595m, 1500s, 1257m, 1147m, 1093w, 1018w, 906w, 756m, 686w cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.81 (s, 3H, CH_3), 3.39 (t, J = 7.2 Hz, 2H, CH_2), 3.75 (t, J = 7.2 Hz, 2H, CH_2), 7.44–7.54 (m, 5H, Ar–H), 7.69 (d, J = 8.2, Hz, 2H, Ar–H), 8.26 (d, J = 8.2, Hz, 2H, Ar–H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 22.3, 27.5, 55.4, 115.4, 121.2, 124.6, 126.5, 128.2, 129.6, 130.5, 131.1, 134.3, 139.5, 144.8, 154.2, 156.1, 159.2. MS (70 eV) *m*/*z* (%): 422 (20) [M + 6], 420 (60) [M + 4], 418 (92) [M + 2], 416 (90) [M$^+$], 366 (10), 255 (10), 111 (15), 85 (40), 71 (60), 57 (100), 55 (30). Anal. calcd. for $C_{21}H_{16}Cl_3N_3$ (416.73): C, 60.52; H, 3.87; N, 10.08. Found: C, 61.02; H, 3.18; N, 10.18.

*3-(4-Bromophenyl)-4-chloro-5-(2-chloroethyl)-6-methyl-1-phenyl-1*H*-pyrazolo[3,4-b] pyridine (3b)*

Yield: 3.55 g (77%), recrystallized from acetonitrile/ethanol (8:2) to afford colourless needles; mp 175–176 °C. IR (KBr): 2911m, 1591m, 1500s, 1259m, 1149m, 1093w, 1018w, 910w, 762m, 686w cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.82 (s, 3H, CH_3), 3.40 (t, J = 7.2 Hz, 2H, CH_2), 3.70 (t, J = 7.2 Hz, 2H, CH_2), 7.29–7.48 (m, 5H, Ar–H), 7.53 (d, J = 8.2 Hz, 2H, Ar–H), 8.14 (d, J = 8.2 Hz, 2H, Ar–H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.1, 29.8, 53.9, 118.2, 122.3, 125.8, 128.1, 129.2, 130.6, 131.5, 132.1, 134.1, 139.9, 144.8, 155.3, 157.2, 163.2. MS (70 eV) *m*/*z* (%): 466 (20) [M + 6], 464 (60) [M + 4], 462 (92) [M + 2], 460 (90) [M$^+$], 437 (10), 425 (100), 404 (10), 378 (15), 362 (40), 338 (60), 313 (10), 299 (30), 182 (30), 127 (15), 117 (40), 77 (80), 65 (60). Anal. calcd. for $C_{21}H_{16}BrCl_2N_3$ (461.18): C, 54.69; H, 3.50; N, 9.11. Found: C, 54.98; H, 3.78; N, 9.21.

*4-Chloro-5-(2-chloroethyl)-6-methyl-3-(4-methylphenyl)-1-phenyl-1*H*-pyrazolo[3,4-b] pyridine (3c)*

Yield: 2.57 g (65%), recrystallized from acetonitrile/ethanol (8:2) to afford colourless needles; mp 145–146 °C. IR (KBr): 2919m, 1592m, 1500s, 1255m, 1149m, 1093w, 1020w, 915w, 760m, 688w cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.39 (s, 3H, Ar–CH_3), 2.80 (s, 3H, CH_3), 3.38 (t, J = 7.3 Hz, 2H, CH_2), 3.68 (t, J = 7.3 Hz, 2H, CH_2), 7.30–7.56 (m, 5H, Ar–H), 7.60 (d, J = 8.3 Hz, 2H, ArH), 8.18 (d, J = 8.3 Hz, 2H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 18.1, 24.3, 26.8, 41.3, 106.7, 120.2, 126.3, 127.4, 129.4, 129.6 130.1, 138.4, 138.9, 139.7, 140.6, 145.9, 150.5, 155.3. Anal. calcd. for $C_{22}H_{19}Cl_2N_3$ (396.31): C, 66.67; H, 4.83; N, 10.60. Found: C, 66.90; H, 4.38; N, 10.83.

General procedure for the synthesis of 1-phenyl-8-(4-aryl)-4-methyl-6-phenyl-1,2,3,6-tetrahydropyrazolo[3,4-*b*]pyrrolo[2,3-*d*]pyridine (4a–4n)

A mixture of **3** (0.01 mol) and primary aliphatic and aromatic amines (0.04 mol) was heated at 110–120 °C for about 2 h until TLC showed no more starting material. Then, the mixture was cooled at 20 °C. After cooling, methanol (20 ml) was added, and the resulting solid was filtered by suction, washed with methanol, dried, and recrystallized from the proper solvent to afford **4** in good yield.

1-Benzyl-8-(4-chlorophenyl)-4-methyl-6-phenyl-1,2,3,6-tetrahydropyrazolo[3,4-b]pyrrolo [2,3-d]pyridine (4a)

Yield: 4.01 g (89%), recrystallized from ethanol to afford colourless prisms; mp 150–151 °C. IR (KBr): 2909m, 1744m, 1598s, 1500s, 1257m, 1147m, 1093m, 1018m, 906m, 756w, 686m cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ:

2.50 (s, 3H, CH_3), 3.06 (t, J = 7.3 Hz, 2H, CH_2), 3.50 (t, J = 7.3 Hz, 2H, CH_2), 4.14(s, 2H, Ar–CH_2), 6.98–7.06 (m, 5H, Ar–H), 7.24 (d, J = 8.2 Hz, 2H, ArH), 7.43–7.49 (m, 5H, ArH), 8.29 (d, J = 8.2 Hz, 2H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21, 26, 53, 56, 101, 112, 115, 122, 124, 126, 126, 127, 128, 128, 129, 130, 133, 134, 136, 143, 154 156. MS *m*/*z* (%): 452 (90) [M + 2], 450 (100) [M^+], 447 (20), 359 (25), 324 (35), 186 (20), 167 (20), 139 (10), 123 (30), 111 (15), 91 (90), 77 (80), 65 (60). Anal. calcd. for $C_{28}H_{23}ClN_4$ (450.96): C, 74.57; H, 5.14; N, 12.42. Found: C, 74.67; H, 4.88; N, 12.69.

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

Yield: 3.58 g (82%), recrystallized from ethanol/DMF (8:2) to afford light green prisms; mp 212–213 °C. IR (KBr): 2910m, 1738m, 1588s, 1503s, 1251m, 1144m, 1099m, 1017m, 906m, 756w, 686m cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.56 (s, 3H, CH_3), 3.21 (t, J = 7.1 Hz, 2H, CH_2), 4.20 (t, J = 7.1 Hz, 2H, CH_2), 6.74–6.90 (m, 5H, Ar–H), 7.24–7.45 (m, 5H, Ar–H), 7.48 (d, J = 7.5 Hz, 2H, Ar–H), 8.31 (d, J = 7.5 Hz, 2H, Ar–H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 19.3, 22.8, 51.5, 104.6, 113.5, 117.2, 120.2, 124.7, 126.8, 128.9, 129.4, 129.6 131.1, 134.3, 139.7, 145.9, 149.1, 154.3, 156.3. MS *m*/*z* (%): 438 (80) [M + 2], 436 (100) [M^+], 419 (20), 399 (25), 361 (35), 298 (20), 255 (20), 218 (10), 200 (30), 192 (15), 179 (30), 152 (35), 111 (10), 91 (10), 77 (60), 65 (15). Anal. calcd. for $C_{27}H_{21}ClN_4$ (436.93): C, 74.22; H, 4.84; N, 12.82. Found: C, 73.87; H, 5.05; N, 12.68.

1-(3-Chlorophenyl)-8-(4-chlorophenyl)-4-methyl-6-phenyl-1,2,3,6-tetrahydropyrazolo[3,4-b]pyrrolo[2,3-d]pyridine (4c)

Yield: 3.67 g (78%), recrystallized from ethanol/DMF (6:4) to afford light green prisms; mp 217–218 °C. IR (KBr): 2918m, 1743m, 1595s, 1500s, 1257m, 1147m, 1093m, 1018m, 906m, 756w, 686m cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.57 (s, 3H, CH_3), 3.26 (t, J = 7.2 Hz, 2H, CH_2), 4.86 (t, J = 7.2 Hz, 2H, CH_2), 6.23–7.51 (m, 9H Ar–H), 8.20 (d, J = 7.8 Hz, 2H, Ar–H), 8.34 (d, J = 7.8 Hz, 2H, Ar–H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 19.4, 22.5, 53.2, 106.2, 113.6, 114.1, 116.1, 121.3, 122.8, 123.5, 128.2, 129.1, 130.5, 131.6, 133.3, 134.1, 135.4, 140.7, 144.9, 148.3, 151.2, 154.6, 158.6. Anal. calcd. for $C_{27}H_{20}Cl_2N_4$ (471.38): C, 68.80; H, 4.28; N, 11.89. Found: C, 69.09; H, 4.60; N 12.10.

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

Yield: 3.39 g (72%), recrystallized from ethanol/DMF (6:4) to afford light yellow prisms; mp 235–237 °C. IR (KBr): 2918m, 1743m, 1595s, 1500s, 1257m, 1147m, 1093m, 1018m, 906m, 756w, 686m cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.57 (s, 3H, CH_3), 3.26 (t, J = 7.2 Hz, 2H, CH_2), 4.86 (t, J = 7.2 Hz, 2H, CH_2), 6.23–7.51 (m, 9H, Ar–H), 8.20 (d, J = 7.8 Hz, 2H, Ar–H), 8.34 (d, J = 7.8 Hz, 2H, Ar–H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 18.4, 21.6, 52.5, 108.6, 115.3, 119.2, 121.2, 124.7, 126.3, 128.8, 129.1, 129.9, 132.3, 135.4, 138.2, 144.4, 147.5, 149.1, 154.3, 155.3. Anal. calcd. for $C_{27}H_{20}Cl_2N_4$ (471.38): C, 68.80; H, 4.28; N, 11.89. Found: C, 68.67; H, 4.10; N, 12.02.

1-(4-Bromophenyl)-8-(4-chlorophenyl)-4-methyl-6-phenyl-1,2,3,6-tetrahydropyrazolo[3,4-b]pyrrolo[2,3-d]pyridine (4e)

Yield: 4.07 g (79%), recrystallized from ethanol/DMF (6:4) to afford yellow prisms; mp 231–232 °C. IR (KBr): 2918m, 1743m, 1595s, 1500s, 1257m, 1147, 1093m, 1018m, 906m, 756w, 686m cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.58 (s, 3H CH_3), 3.28 (t, J = 7.1 Hz, 2H, CH_2), 4.87 (t, J = 7.1 Hz, 2H, CH_2), 6.22–7.55 (m, 9H, Ar–H), 8.20 (d, J = 7.8 Hz, 2H, Ar–H), 8.33 (d, J = 7.8 Hz, 2H, Ar–H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.9, 23.2, 52.5, 103.2, 111.5, 115.7, 120.2, 124.7, 126.3, 128.9, 129.4, 131.2, 132.5, 134.3, 139.7, 138.2, 145.9, 148.4, 149.1, 154.3, 156.2. Anal. calcd. for $C_{27}H_{20}BrClN_4$ (515.83): C, 62.87; H, 3.91; N, 10.86. Found: C, 62.63; H, 4.16; N, 11.09.

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

Yield: 3.96 g (88%), recrystallized from ethanol/DMF (8:2) to afford light green prisms; mp 220–222 °C. IR (KBr): 2918m, 1743m, 1595s, 1500s, 1257m, 1147, 1093m, 1018m, 906m, 756w, 686m cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.30 (s, 3H, Ar–CH_3), 2.61 (s, 3H, CH_3), 3.25 (t, J = 7.2 Hz, 2H, CH_2), 4.22 (t, J = 7.2 Hz, 2H, CH_2), 7.24–7.45 (m, 9H, Ar–H), 7.45 (d, J = 8.2 Hz, 2H, Ar–H), 8.35 (d, J = 8.2 Hz, 2H, Ar–H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 15.8, 18.6, 21.3, 51.8, 105.6, 113.3, 117.1, 120.2, 124.7, 126.2, 126.3, 126.6, 128.9, 129.4, 129.9, 131.2, 134.3, 139.7, 145.9, 149.1, 154.9, 157.4. Anal. calcd. for $C_{28}H_{23}ClN_4$ (450.96): C, 74.57; H, 5.14; N, 12.42. Found: C, 74.78; H, 4.96; N, 12.18.

8-(4-Chlorophenyl)-1-(4-methylphenyl)-4-methyl-6-phenyl-1,2,3,6-tetrahydropyrazolo[3,4-b]pyrrolo[2,3-d]pyridine (4g)

Yield: 3.74 g (83%), recrystallized from ethanol/DMF (8:2) to afford light green prisms; mp 229–230 °C. IR (KBr): 2918m, 1743m, 1595s, 1500s, 1257m, 1147, 1093m, 1018m, 906m, 756w, 686m cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.30 (s, 3H, Ar–CH_3), 2.60 (s, 3H, CH_3), 3.25 (t, J = 7.2 Hz, 2H, CH_2), 4.22 (t, J = 7.2 Hz, 2H, CH_2), 7.24–7.45 (m, 9H, Ar–H), 7.45 (d, J = 8.2 Hz, 2H, Ar–H), 8.35 (d, J = 8.2 Hz, 2H, Ar–H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 18.6, 21.5, 24.3, 51.5, 103.6, 113.4, 120.2, 124.7, 126.3, 126.8, 128.9, 129.4, 129.9, 131.2, 134.9, 139.2, 145.9, 146.4, 149.9, 154.9, 157.4. Anal. calcd. for $C_{28}H_{23}ClN_4$ (450.96): C, 74.57; H, 5.14; N, 12.42. Found: C, 74.69; H, 5.32; N 12.61.

8-(4-Bromophenyl)-1-(3-chlorophenyl)-4-methyl-6-phenyl-1,2,3,6-tetrahydropyrazolo[3,4-b]pyrrolo[2,3-d]pyridine (4h)

Yield: 3.92 g (76%), recrystallized from ethanol/DMF (6:4) to afford light brown prisms; mp 226–227 °C. IR (KBr): 2918m, 1743m, 1595s, 1500s, 1257m, 1147, 1093m, 1018m, 906m, 756w, 686m cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.59 (s, 3H CH_3), 3.28 (t, J = 7.2 Hz, 2H, CH_2), 4.87 (t, J = 7.2 Hz, 2H, CH_2), 6.22–7.55 (m, 9H, Ar–H), 8.20 (d, J = 8.2 Hz, 2H, ArH), 8.33 (d, J = 8.2 Hz, 2H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 18.7, 21.3, 51.5, 104.6, 111.2, 113.8, 117.3, 120.8, 123.1, 124.9, 126.2, 129.1, 129.5, 131.6, 132.2, 132.1, 135.4, 139.7, 145.9, 149.3, 150.2, 154.6, 157.6. Anal. calcd. for $C_{27}H_{20}BrClN_4$

(515.83): C, 62.87; H, 3.91; N, 10.86. Found: C, 63.09; H, 4.06; N 10.66.

8-(4-Bromophenyl)-1-(4-chlorophenyl)-4-methyl-6-phenyl-1,2,3,6-tetrahydropyrazolo[3,4-b]pyrrolo[2,3-d]pyridine (4i)

Yield: 3.81 g (74%), recrystallized from ethanol/DMF (6:4) to afford light green prisms; mp 240–241 °C. IR (KBr): 2918m, 1743m, 1595s, 1500s, 1257m, 1147, 1093m, 1018m, 906m, 756w, 686m cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.58 (s, 3H, CH_3), 3.28 (t, J = 7.2 Hz, 2H, CH_2), 4.87 (t, J = 7.2 Hz, 2H, CH_2), 6.22–7.55 (m, 9H, Ar–H), 8.20 (d, J = 7.8 Hz, 2H, Ar–H), 8.33 (d, J = 7.8 Hz, 2H, Ar–H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.4, 23.6, 53.5, 107.6, 116.3, 119.2, 123.2, 124.7, 126.3, 127.8, 129.8, 130.9, 131.3, 135.4, 140.2, 145.4, 148.5, 150.1, 154.3, 159.3. Anal. calcd. for $C_{27}H_{20}BrClN_4$ (515.83): C, 62.87; H, 3.91; N, 10.86. Found: C, 63.13; H, 4.21; N 10.61.

1,8-Bis(4-bromophenyl)-4-methyl-6-phenyl-1,2,3,6-tetrahydropyrazolo[3,4-b]pyrrolo[2,3-d]pyridine (4j)

Yield: 4.31 g (77%), recrystallized from ethanol/DMF (6:4) to afford light green prisms; mp 243–244 °C. IR (KBr): 2918m, 1743m, 1595s, 1500s, 1257m, 1147, 1093m, 1018m, 906m, 756w, 686m cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.58 (s, 3H, CH_3), 3.28 (t, J = 7.2 Hz, 2H, CH_2), 4.87 (t, J = 7.2 Hz, 2H, CH_2), 6.22–7.55 (m, 9H, Ar–H), 8.20 (d, J = 7.8 Hz, 2H, Ar–H), 8.33 (d, J = 7.8 Hz, 2H, Ar–H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 19.9, 24.2, 50.5, 107.2, 114.5, 118.7, 121.2, 125.7, 127.3, 128.1, 129.6, 130.1, 131.0, 134.6, 139.0, 138.2, 143.9, 147.4, 148.1, 151.3, 160.2. Anal. calcd. for $C_{27}H_{20}Br_2N_4$ (560.28): C, 57.88; H, 3.60; N, 10.00. Found: C, 57.63; H, 3.21; N, 10.27.

8-(4-Bromophenyl)-1-(2-methylphenyl)-4-methyl-6-phenyl-1,2,3,6-tetrahydropyrazolo[3,4-b]pyrrolo[2,3-d]pyridine (4k)

Yield: 4.35 g (88%), recrystallized from ethanol/DMF (8:2) to afford light green prisms; mp 230–232 °C. IR (KBr): 2918m, 1743m, 1595s, 1500s, 1257m, 1147, 1093m, 1018m, 906m, 756w, 686m cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.32 (s, 3H, Ar–CH_3), 2.61 (s, 3H, CH_3), 3.23 (t, J = 7.2 Hz, 2H, CH_2), 4.24 (t, J = 7.2 Hz, 2H, CH_2), 7.25–7.46 (m, 9H, ArH), 7.46 (d, J = 8.1 Hz, 2H, Ar–H), 8.36 (d, J = 8.1 Hz, 2H, Ar–H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.8, 19.3, 25.3, 53.8, 109.6, 111.3, 118.1, 121.2, 123.7, 125.2, 126.3, 126.6, 128.9, 129.3, 129.3, 131.0, 134.1, 139.2, 145.1, 149.3, 154.9, 157.9. Anal. calcd. for $C_{28}H_{23}BrN_4$ (495.41): C, 67.88; H, 4.68; N, 11.31. Found: C, 67.63; H, 4.51; N, 11.49.

8-(4-Bromophenyl)-1-(4-methylphenyl)-4-methyl-6-phenyl-1,2,3,6-tetrahydropyrazolo[3,4-b]pyrrolo[2,3-d]pyridine (4l)

Yield: 3.61 g (73%), recrystallized from ethanol/DMF (8:2) to afford light green prisms; mp 235–236 °C. IR (KBr): 2918m, 1743m, 1595s, 1500s, 1257m, 1147, 1093m, 1018m, 906m, 756w, 686m cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.34 (s, 3H, Ar–CH_3), 2.63 (s, 3H, CH_3), 3.23 (t, J = 7.2 Hz, 2H, CH_2), 4.24 (t, J = 7.2 Hz, 2H, CH_2), 7.25–7.46 (m, 9H, Ar–H), 7.46 (d, J = 8.2 Hz, 2H, Ar–H), 8.36 (d, J = 8.2 Hz, 2H, Ar–H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.6, 23.2, 24.3, 52.5, 105.6, 112.4, 116.2, 121.7, 125.3, 126.8, 127.9, 129.4, 129.9, 131.2, 134.9, 140.2, 142.9, 146.4, 147.9, 151.9, 156.2. Anal. calcd. for $C_{28}H_{23}BrN_4$ (495.41): C, 67.88; H, 4.68; N, 11.31. Found: C, 68.06; H, 4.98; N 11.52.

1-Benzyl-4-methyl-8-(4-methylphenyl)-6-phenyl-1,2,3,6-tetrahydropyrazolo[3,4-b]pyrrolo[2,3-d]pyridine (4m)

Yield: 3.48 g (81%), recrystallized from ethanol to afford colourless prisms; mp 166–67 °C. IR (KBr): 2918m, 1743m, 1595s, 1500s, 1257m, 1147, 1093m, 1018m, 906m, 756w, 686m cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.39 (s, 3H, Ar–CH_3), 2.80 (s, 3H, CH_3), 3.38 (t, J = 7.1 Hz, 2H, CH_2), 3.68 (t, J = 7.1 Hz, 2H, CH_2), 4.14(s, 2H, Ar–CH_2), 6.98–7.06 (m, 5H, Ar–H), 7.24 (d, J = 8.2 Hz, 2H, Ar–H), 7.43–7.49 (m, 5H, Ar–H), 8.29 (d, J = 8.2 Hz, 2H, Ar–H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.6, 21.7, 24.3, 53.4, 104.9, 120.2, 124.7, 126.3, 127.1, 127.4, 128.6, 128.0, 129.4, 129.6, 130.1, 136.5, 138.4, 139.7, 145.9, 149.9, 154.9, 158.8. Anal. calcd. for $C_{29}H_{26}N_4$ (430.54): C, 80.90; H, 6.09; N, 13.01. Found: C, 80.66; H, 6.41; N 13.32.

1,6-Diphenyl-4-methyl-8-(4-methylphenyl)-1,2,3,6-tetrahydropyrazolo[3,4-b]pyrrolo[2,3-d]pyridine (4n)

Yield: 3.49 g (84%), recrystallized from ethanol/DMF (8:2) to afford colourless prisms; mp 208–209 °C. IR (KBr): 2918m, 1743m, 1595s, 1500s, 1257m, 1147, 1093m, 1018m, 906m, 756w, 686m cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.40 (s, 3H, $ArCH_3$), 2.82 (s, 3H, CH_3), 3.21 (t, J = 7.1 Hz, 2H, CH_2), 4.20 (t, J = 7.1 Hz, 2H, CH_2), 6.74–6.90 (m, 5H, Ar–H), 7.24–7.45 (m, 5H, Ar–H), 7.48 (d, J = 7.5 Hz, 2H, Ar–H), 8.31 (d, J = 7.5 Hz, 2H, Ar–H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 18.6, 21.3, 24.3, 51.5, 103.6, 113.5, 117.2, 120.2, 124.7, 126.3, 127.4, 129.6, 130.1, 138.4, 139.7, 145.9, 149.9, 154.9, 157.3. Anal. calcd. for $C_{28}H_{24}N_4$ (416.51): C, 80.74; H, 5.81; N, 13.45. Found: C, 80.54; H, 5.98; N 13.52.

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