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RAPID COMMUNICATION

Effect of Specific Solute-Solvent Interaction and Electron Donor-Acceptor Substituents of Novel Pyrazolo Naphthyridines on Fluorescence

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Abstract Heterocyclic orthoaminoaldehyde such as 4-amino-3-(4-phenyl)-1-phenyl-1H-Pyrazolo[3,4-b]pyridine-5-carbaldehyde was synthesized by multistep reactions involving reduction of azido derivative 2 with LAH to yield aminoalcohol 3 and oxidation of it with MnO_2 to aminoaldehyde 4.The pyridine ring annulated on to 4 by *Friedländer* condensation using acetophenones in presence of base to obtained pyrazolo[3,4-h][1,6]naphthyridine 5 in excellent yield. Study of photophysical properties of 5 revealed that the absorption and emission of them depends up on the substituents present on benzene ring in newly annulated pyridine ring.

Keywords Chloroester · Pyrazolo[3,4-b]pyridine-5-carbaldehyde · Pyrazolo[3,4-h] [1,6]naphthyridine · HOMO-LUMO · Quantum yields · Absorption and emission

Introduction

Annulation reactions with hetrocyclic aminoaldehydes provides synthectic entry in to hetrocyclic systems fused to a pyridine or pyrimidine nucleus by condensation reactions with reactive methylenes. It was noted from literature [1, 2], that heterocyclic orthoaminoaldehydes are generally accessible from aminocarboxylic acid precursors by a number of different reductive methods. The aldehyde function is thus elaborated in the presence of the amino group, in contrast with the standard method employed in the carbocyclic series wherein the reverse order of introduction is followed. Catalytic reduction of amino-nitriles, conducted in acid medium to hydrolyze the intermediate amino imines, is a valuable synthetic method for heterocyclic aminoaldehyde, since the starting amino-nitriles are readily accessible [3].

In our earlier communication we have introduce the aldehyde functionality by Vilsmeier-Haack formylation of 5-aminopyrazole [4] and resulted orthoaminoaldehyde after hydrolysis was utilized for annulation of various hetrocyclic ring on to 5-aminopyrazole-4-carbaldehydes by *Friedländer* condensation with reactive methylenes. Recently we have reported the synthesis of orthoaminoaldehyde on to quinoline nucleus introduced by azidation of orthochloroquinoline-3-carbaldehyde and subsequent reduction of azido functionality using triphenylphosphine to yield 2-aminoquinoline-3-carbaldehyde, in our laboratry. The *Friedländer* condensation of it with reactive methylenes were performed [5] and resulted naphthyridines were studied for their photophysical analysis.

From literature it was also noted that naphthyridine derivatives were not only use as luminescence materials in molecular recognition because of their rigid planer structure [6–8], but also as new drug leaders [9, 10] and anticancer active screening agents in new drug discovery [11, 12].

These literature reports and our ongoing interest in this area prompted us for the synthesis of new heterocyclic orthoaminoaldehyde. In this communication we are reporting the synthesis of novel orthoaminoaldehyde on pyrazolo [3, 4-b] pyridine nucleus. Then the pyridine nucleus annulated on it by *Friedländer* condensation with acetophenone to obtained naphthyridine derivatives and studied their photophysical properties.

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Result and Discussion

The orthoaminoaldehyde 4 required for this work was synthesized by multistep reactions. Thus, the chloroester 1 synthesized by lit. Method [13], then introduction of aminoaldehyde functionality on 1 was accomplished via the azidation of 1 with sodium azide in DMF to obtain the azido ester 2 [14]. Then, the formyl group was incorporated by oxidation of alcohol 3 with MnO_2 (without protecting amino group), obtained by reduction of 2 with LAH. In this step, expected N-oxide was not formed as revealed by spectral and analytical data. The orthoaminoaldehyde 4 obtained was characterized by IR, ^{1}H NMR, ^{13}C NMR, mass and elemental analysis. For instance, Compound 4a shows broad singlet at 6.65δ in its ^{1}H NMR, corresponds to two protons of -NH_2 and singlet at 9.75δ corresponds to aldehydic proton. All aromatic protons showed expected chemical shifts and splitting patterns which resembles with the structure of 4a. The mass spectrum of 4a revealed a molecular ion peak m/z at 348. The ^{13}C NMR spectrum of this compound is agreement with the structure proposed. In our approach, the yields of intermediates 2, 3 and 4 are excellent. This method is versatile and scalable.

The base catalyzed *Friedländer* condensation with acetophenone can be studied with compound orthoaminoaldehyde 4. Thus compound 4 and acetophenone/substituted acetophenone on condensation in refluxing ethanol using KOH as a base yielded a naphthyridine derivative 5 in 80–90% yields and were characterized by IR, ^{1}H NMR, ^{13}C NMR, mass and elemental analysis. These compounds are further studied for their photophysical properties (Scheme 1).

Semi-Empirical Study

From literature it was noted that pyrazolonaphthyridine derivatives are not explored for their photophysical properties. Hence, we had undertaken semi-empirical calculations such as HOMO-LUMO energy, Heat of formation, Ionization potential, and Electron hole gap (gap value) before determination of their UV and Emission spectra.

We analyzed the three dimensional coefficient contribution by the MOPAC 2009 (Version 8.331) [15, 16] and are given in Table 1. From these we observed that there is more overlapping between the HOMO-LUMO energy for 5h, 5i, 5j, 5k, 5l, 5t, 5u, 5v, 5w and 5x which shows low gap value and high heat of formation hence more stability. (Table 1). The 3D picture of pyrazolnaphthyridine 5 is depicted in Fig. 1. The charge is more concentrated on ring D as compared to ring A, B and C. The donor chromophore on ring D is playing important role in increasing electron density hence increased the stability and reactivity of these molecules. In this compound the practical results obtained are in agreement with the HOMO-LUMO, Heat of formation obtained by semi-empirical PM3/PM6 methods.

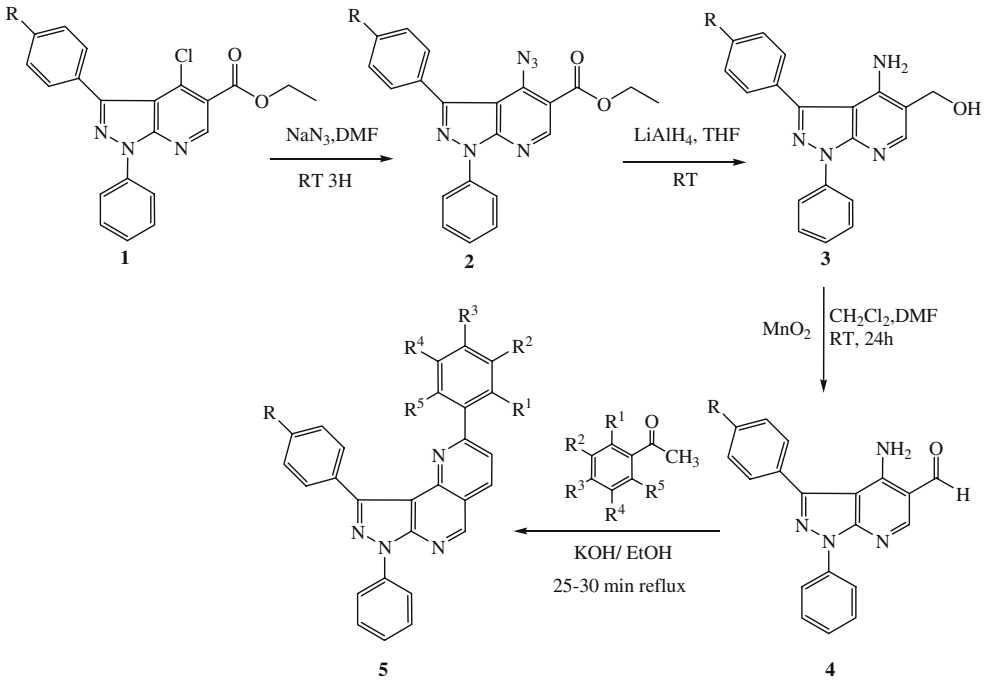
Spectral Properties

Absorption Spectra

The absorption spectra (UV model- Shimadzu UV-1601 UV-VIS spectrophotometer) of the synthesized pyrazolo [3,4-h][1,6]naphthyridine 5a–x (Table 2) were taken in non-polar dichloromethane, polar aprotic acetonitrile and polar protic methanol solvents at room temperature. All absorption band maxima are given in Table 2 and spectra for 5x are shown in all three solvents in Fig. 2. In all pyrazolo [3,4-h][1,6]naphthyridines have chromophore present on the substituted benzene ring i.e. on D ring (Fig 1). The spectral pattern and band maxima clearly indicate that the observed absorption band corresponds to substituents present on D ring. High absorbance values indicate that these transitions are from $\pi \rightarrow \pi^*$ transition of the substituted benzene ring. It was also observed that the absorption band maxima are slightly solvent dependent indicating less polar character of these molecules in the ground state. In protic solvent the band shows a blue shift due to intermolecular hydrogen bond between solvent methanol and the solute with several possible hydrogen bond making centers.

Emission Spectra

Usually naphthyridine compounds are highly fluorescent after excitation to the locally exited state and some of the naphthyridine derivatives show interesting photo-induced properties. Therefore, we have tried to measure emission and excitation spectra of these molecules in all the three solvents after excitation of the emission band maxima as shown in Fig. 3 (for 5x), the excitation of each molecule at their corresponding absorption band of each substituted naphthyridine shows single emission band (RF-5301 PC Spectrofluorophotometer) in the wavelength range ~370 nm to ~495 nm which was due to emission from their locally excited state. The emission band maxima and the corresponding fluorescence quantum yields are shown in Table 2. In general, in the emission bands are found to be similar in aprotic solvents (dichloromethane and acetonitrile). This indicates that stabilization of the ground and excited state is not modified with polarity of the solvents. On the other hand, in protic solvent (methanol) the emission band shifts to the blue due to intermolecular hydrogen bond interaction between solvent and solute. As



Scheme 1 Synthetic route of Pyrazolo [3, 4-*h*] [1, 6] naphthyridines

5 (a-x)	R	R^1	R^2	R^3	R^4	R^5
a	Cl	H	H	H	H	H
b	Cl	H	H	Cl	H	H
c	Cl	H	H	Br	H	H
d	Cl	H	Cl	Cl	H	H
e	Cl	Br	H	Cl	H	H
f	Cl	H	H	CH_3	H	H
g	Cl	H	H	NO_2	H	H
h	Cl	H	CF_3	H	CF_3	H
i	Cl	H	H	OCH_3	H	H
j	Cl	H	OCH_3	OCH_3	H	H
k	Cl	OCH_3	H	H	OCH_3	H
l	Cl	OCH_3	H	OCH_3	H	OCH_3
m	Br	H	H	H	H	H
n	Br	H	H	Cl	H	H
o	Br	H	H	Br	H	H
p	Br	H	Cl	Cl	H	H
q	Br	Br	H	Cl	H	H
r	Br	H	H	CH_3	H	H
s	Br	H	H	NO_2	H	H
t	Br	H	CF_3	H	CF_3	H
u	Br	H	H	OCH_3	H	H
v	Br	H	OCH_3	OCH_3	H	H
w	Br	OCH_3	H	H	OCH_3	H
x	Br	OCH_3	H	OCH_3	H	OCH_3

Table 1 The molecular electronic properties (HOMO-LUMO energy, GAP) of the Pyrazolo [3,4-h][1,6]naphthyridine 5 (a–x)

Comp.	R	R^1	R^2	R^3	R^4	R^5	Heat of Formation (K Cal.)	Ionization Potential (eV)	HOMO (eV)	LUMO (eV)	GAP (eV)
5a	Cl	H	H	H	H	H	165.11	8.718	−8.719	−1.373	7.346
5b	Cl	H	H	Cl	H	H	155.03	8.819	−8.820	−1.480	7.340
5c	Cl	H	H	Br	H	H	167.08	8.829	−8.829	−1.499	7.330
5d	Cl	H	Cl	Cl	H	H	149.56	8.846	−8.846	−1.607	7.230
5e	Cl	Br	H	Cl	H	H	158.91	8.803	−8.804	−1.463	7.341
5f	Cl	H	H	CH_3	H	H	154.46	8.699	−8.700	−1.295	7.405
5g	Cl	H	H	NO_2	H	H	160.96	8.965	−8.965	−1.885	7.080
5h	Cl	H	CF_3	H	CF_3	H	−159.11	8.978	−8.978	−1.805	7.173
5i	Cl	H	H	OCH_3	H	H	123.25	8.656	−8.657	−1.273	7.384
5j	Cl	H	OCH_3	OCH_3	H	H	88.90	8.500	−8.501	−1.311	7.170
5k	Cl	OCH_3	H	H	OCH_3	H	87.62	8.507	−8.507	−1.230	7.277
5l	Cl	OCH_3	H	OCH_3	H	OCH_3	40.59	8.485	−8.486	−0.968	7.518
5m	Br	H	H	H	H	H	177.05	8.771	−8.772	−1.369	7.403
5n	Br	H	H	Cl	H	H	167.00	8.858	−8.859	−1.490	7.369
5o	Br	H	H	Br	H	H	179.23	8.837	−8.838	−1.528	7.310
5p	Br	H	Cl	Cl	H	H	161.35	8.920	−8.921	−1.597	7.324
5q	Br	Br	H	Cl	H	H	170.90	8.844	−8.845	−1.473	7.372
5r	Br	H	H	CH_3	H	H	166.49	8.735	−8.736	−1.306	7.430
5s	Br	H	H	NO_2	H	H	172.94	9.00	−9.007	−1.893	7.114
5t	Br	H	CF_3	H	CF_3	H	−145.82	8.992	−8.992	−1.786	7.206
5u	Br	H	H	OCH_3	H	H	135.22	8.685	−8.685	−1.283	7.400
5v	Br	H	OCH_3	OCH_3	H	H	100.89	8.501	−8.502	−1.323	7.179
5w	Br	OCH_3	H	H	OCH_3	H	99.59	8.510	−8.510	−1.243	7.267
5x	Br	OCH_3	H	OCH_3	H	OCH_3	52.36	8.512	−8.512	−0.977	7.535

GAP = E_{LUMO}-E_{HOMO}

the absorption band shifts to the blue, the emission band also shifts to the blue and this blue shifted emission is nothing but the local emission from the hydrogen bonded clusters. We have measured fluorescence quantum yield of these compounds by using quinine sulphate as reference standard (φ_{ref}=0.54 in 0.1 M H_2SO_4) [17]. The fluorescence quantum yield of these studied systems is very high in polar aprotic solvent and very poor in hydrogen bonding solvent methanol. Weak intermolecular hydrogen bonding interaction usually triggered non-radiative channels and hence fluorescence quantum yield is very low in methanol solvent [18].

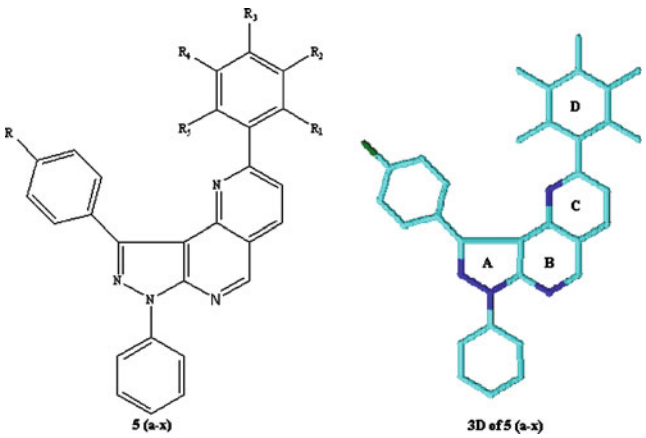


Fig. 1 3D picture of Pyrazolo [3, 4-*h*] [1, 6] naphthyridines

Further it was noted that halo-substituted molecules have less fluorescence quantum yield as compared to methoxy substituted compounds. This may be due to quenching of fluorescence with halogen atoms as the substituent. Pyrazolonaphthyridine 5u, 5v, 5w and 5x having donor chromophores e.g. C_4-OCH_3, C_3 & C_4-di-OCH_3, C_2 & C_5-di-OCH_3, C_2, C_4 & C_6-tri-OCH_3 on phenyl ring sowed absorption and emission maxima at 477 nm, 484 nm, 479 nm and 495 nm and quantum yields (φ_F) 0.248, 0.309, 0.292 and 0.345 respectively. Compound 5s having acceptor chromophore e.g. C_4-NO_2 on phenyl ring showed large decrease in emission maxima at 441 nm and quantum yield (φ_F) 0.185 (Table 2). High quantum yield of these molecules and sensitivity of the emission band on polarity and hydrogen bonding ability of solvent could be useful to be a good fluorescence sensor.

Table 2 The photophysical data for electronic absorption (UV $\lambda_{Max.}$), fluorescence (Em $\lambda_{Max.}$) and quantum yield (ϕ_F) of Pyrazolo[3,4-h][1,6]naphthyridine 5 (a-x) for 0.1 M Conc. at room temp

Comp.	Solvents	λAbs. (nm)	λEm. (nm)	Quantum Yield (ϕ_f)
5a	CH_2Cl_2	370	457	0.264
	CH_3CN	364	456	0.259
	CH_3OH	368	452	0.258
5b	CH_2Cl_2	371	466	0.278
	CH_3CN	369	464	0.272
	CH_3OH	366	459	0.270
5c	CH_2Cl_2	373	472	0.281
	CH_3CN	368	470	0.277
	CH_3OH	364	467	0.278
5d	CH_2Cl_2	375	470	0.280
	CH_3CN	371	468	0.279
	CH_3OH	372	465	0.278
5e	CH_2Cl_2	379	471	0.271
	CH_3CN	375	469	0.268
	CH_3OH	369	465	0.269
5f	CH_2Cl_2	370	474	0.273
	CH_3CN	367	471	0.271
	CH_3OH	366	464	0.266
5g	CH_2Cl_2	385	438	0.179
	CH_3CN	377	435	0.176
	CH_3OH	379	429	0.174
5h	CH_2Cl_2	377	488	0.330
	CH_3CN	371	484	0.327
	CH_3OH	372	481	0.328
5i	CH_2Cl_2	373	467	0.277
	CH_3CN	370	466	0.275
	CH_3OH	370	463	0.273
5j	CH_2Cl_2	379	477	0.295
	CH_3CN	374	473	0.288
	CH_3OH	374	461	0.281
5k	CH_2Cl_2	378	473	0.281
	CH_3CN	370	469	0.279
	CH_3OH	373	460	0.271
5l	CH_2Cl_2	379	490	0.339
	CH_3CN	377	487	0.324
	CH_3OH	377	455	0.298
5m	CH_2Cl_2	368	460	0.272
	CH_3CN	363	459	0.270
	CH_3OH	365	455	0.271
5n	CH_2Cl_2	369	469	0.281
	CH_3CN	367	467	0.278
	CH_3OH	365	461	0.274
5o	CH_2Cl_2	371	475	0.281
	CH_3CN	365	472	0.277
	CH_3OH	363	466	0.275
5p	CH_2Cl_2	374	475	0.282
	CH_3CN	370	471	0.279
	CH_3OH	373	469	0.277
5q	CH_2Cl_2	377	474	0.286
	CH_3CN	375	471	0.281
	CH_3OH	375	469	0.279
5r	CH_2Cl_2	368	479	0.289
	CH_3CN	365	476	0.285
	CH_3OH	367	471	0.284
5s	CH_2Cl_2	371	441	0.185
	CH_3CN	368	437	0.181
	CH_3OH	369	433	0.179
5t	CH_2Cl_2	374	491	0.326
	CH_3CN	370	489	0.325
	CH_3OH	369	485	0.322
5u	CH_2Cl_2	376	477	0.284
	CH_3CN	371	475	0.283
	CH_3OH	371	470	0.280
5v	CH_2Cl_2	372	484	0.309
	CH_3CN	368	481	0.307
	CH_3OH	369	472	0.298
5w	CH_2Cl_2	375	479	0.292
	CH_3CN	371	477	0.289
	CH_3OH	369	466	0.277
5x	CH_2Cl_2	376	495	0.345
	CH_3CN	371	487	0.338
	CH_3OH	373	458	0.284

Conclusion

In this communication novel Pyrazolo[3,4-h][1,6]naphthyridine derivatives has been synthesized by *Friedländer* condensation using hitherto not described hetrocyclic orthoaminoaldehyde 4 and acetophenones. These intresting Pyrazolo[3,4-h][1,6]naphthyridine 5 are studied for their photophysical properties in protic and aprotic solvents. It was observed that quantum yield of compounds is solvent dependent and greatly influenced by the nature of substituent present in the benzene ring on newly annulated pyridine ring. The donor substituent (OCH_3) increases the fluorescence and acceptor substituent (NO_2) decreases fluorescence as well as quantum yields. The empirical calculations of compounds 5 are in agreement with the observed values of emissions. For instance naphthyridine derivatives 5l and 5x having low LUMO energy values showed red shift and high quantum yields (φ_F =0.339 and 0.345) as compared to other derivatives of 5. Thermal analysis of compounds 5a–x by differential scanning calorimetry (DSC) shows that they are thermally stable up to 350°C. The efficient blue light emission and physical and chemical stability makes Pyrazolonaphthyridine a promising family of materials which may

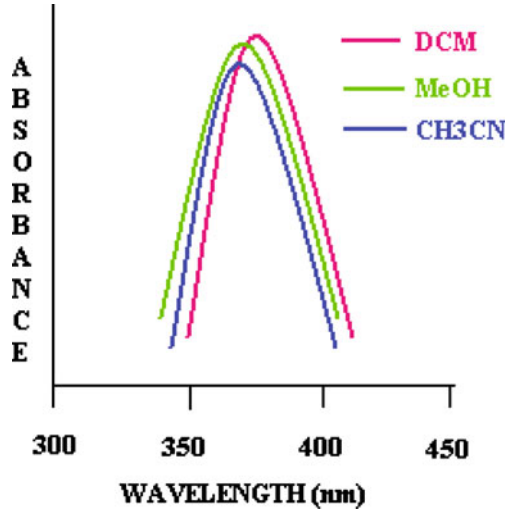


Fig. 2 Absorption Spectra of compound 5x

be useful in opto-electronic applications and are addition in the library of new heterocyclic compounds.

Experimental

General

Melting points were determined on a Gallenkamp melting point apparatus, Mod. MFB595 in open capillary tubes and are uncorrected. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra were measured on a Varian XL-300 spectrometer using tetramethylsilane as the internal standard. IR spectra were recorded using a Shimadzu IR-408, a Shimadzu FTIR instrument with potassium bromide discs. Mass spectrum was recorded on Shimadzu GC-MS QP mass spectrometer with an ionization potential of 70 eV. Elemental analysis were obtained on a Hosli CH-Analyzer and are within ±0.3 of the theoretical percentage.

All reactions were monitored by thin layer chromatography on 0.2 mm silica gel F-254 (Merck) plates using UV light (254 and 366 nm) for detection. Common reagents-grade chemicals were either commercially available and were used without further purification or prepared by standard literature procedures.

4-Amino-3-(4-phenyl)-1-phenyl-1H-pyrazolo[3,4-b] pyridine-5-yl)-methanol(3a–b)

A solution of 1 (4.18 g, 0.01 mol) in tetrahydrofuran (15 mL) was added slowly into the dispersed lithium-aluminium hydride (2.17gm, 4 mol) in tetrahydrofuran (20 mL) at 0°C, after addition the reaction mass was allowed to come at 25°C and stirred it for 4 h. The reaction mass was quenched with saturated sodium sulfate solution (20 mL) at 0°C and extracted in ethyl acetate (2×20 mL). The combined organic layer was washed with water (2× 15 mL), then dried over anhydrous sodium sulfate, filtered and the solvent was evaporated under reduced pressure, the crude solid was taken in ethanol, filtered and dried under high vacuum to provide 3 as a colorless solid,

4-Amino-3-(4-Cl-phenyl)-1-phenyl-1H-pyrazolo[3,4-b] pyridine-5-yl)-methanol (3a)

Yield: 3.22 g (77%); mp 188–189°C; IR (KBr): 3479 (s), 3369 (m), 3302 (m), 2964 (m), 1611 (s), 1505 (s) cm^{-1}; ^{1}H NMR (DMSO-d_6): 4.53 (d, 2H, J=5.7 Hz, CH_2), 5.04 (t, 1H, J = 5.7 Hz, OH, D_2O exchangeable), 6.29 (bs, 2H, NH_2, D_2O exchangeable), 7.19 (t, 1H, J=7.4 Hz, Ar-H), 7.45 (t, 2H, J = 7.4 Hz, Ar-H), 7.61(d, 2H, J = 7.5 Hz Ar-H), 8.01 (s, 1H, Ar-H), 8.26 (d, 2H, J = 7.4 Hz, Ar-H), 8.30 (d, 2H, J = 7.5 Hz Ar-H); ^{13}C NMR (DMSO-d_6): δ 59.9, 107.6, 115.3, 119.6 (2 C's), 126.6, 127.7 (2 C's), 128.6 (2 C's), 129.4 (2 C's), 130.8, 132.1, 134.2, 144.3, 148.4, 152.7, 152.4; MS (70 eV) m/z (%) : 350 [M^{+}] (100), 352 [M+2] (28); *Anal.* Calcd. for $C_{19}H_{14}N_4OCl$ (349.75): C, 65.14; H, 4.00; N, 16.00. Found: C, 65.12; H, 4.02; N, 15.98.

4-Amino-3-(4-Br-phenyl)-1-phenyl-1H-pyrazolo[3,4-b] pyridine-5-yl)-methanol (3b)

Yield: 3.22 g (77%); mp 185–186°C; IR (KBr): 3479 (s), 3369 (m), 3302 (m), 2964 (m), 1611 (s), 1505 (s) cm^{-1}; ^{1}H NMR (DMSO-d_6): 4.53 (d, 2H, J=5.7 Hz, CH_2), 5.04 (t, 1H, J = 5.7 Hz, OH, D_2O exchangeable), 6.29 (bs, 2H, NH_2, D_2O exchangeable), 7.19 (t, 1H, J=7.4 Hz, Ar-H), 7.45 (t, 2H, J = 7.4 Hz, Ar-H), 8.01 (s, 1H, Ar-H), 7.61 (d, 2H, J = 7.4 Hz Ar-H), 8.26 (d, 2H, J = 7.4 Hz, Ar-H) 8.30 (d, 2H, J = 7.4 Hz Ar-H); ^{13}C NMR (DMSO-d_6): δ 59.9, 107.6, 115.3, 119.6 (2 C's), 126.6, 127.7 (2 C's), 128.6 (2 C's), 129.4 (2 C's), 130.8, 132.1, 134.2, 144.3, 148.4, 152.7, 152.4; MS

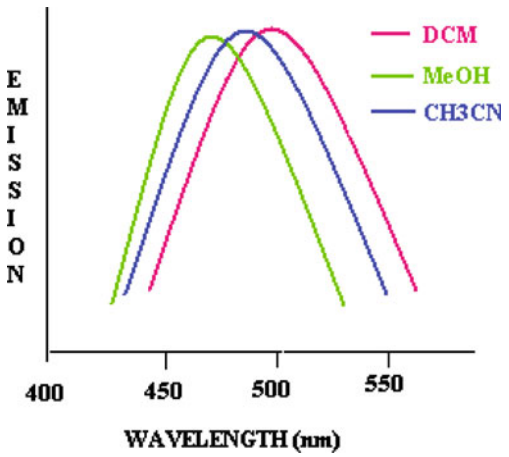


Fig. 3 Emission Spectra of compound 5x

(70 eV) m/z (%) : 393 [M^+] (89), 395 [M+2] (95). *Anal*. Calcd. for $C_{19}H_{14}N_4OBr$ (394.20) : C, 58.01; H, 3.56; N, 14.24. Found: C, 58.05; H, 3.59; N, 14.27.

4-Amino-3-(4-phenyl)-1-phenyl-1H-pyrazolo[3,4-b] pyridine-5-carbaldehyde(4a–b)

Manganese(IV)dioxide (2.58 g, 3 mol) was added into the solution of 3 (3.50 g, 0.01 mol) in dichloromethane (20 mL) at 25°C for 24 h. After completion of reaction (TLC check). The reaction mass was filtered through celite and evaporated dichloromethane under reduced pressure, the crude solid was washed with methanol,filtered, dried under high vacuum and recrystallized from Ethanol: DMF (8:2) to gives 4 as a pale yellow solid.

4-Amino-3-(4-Cl-phenyl)-1-phenyl-1H-pyrazolo[3,4-b] pyridine-5-carbaldehyde (4a)

Yield: 3.28 g (93%); recrystalized from Ethanol:DMF (8:2) (v: v) to afford yellow solid mp 181–182°C; IR (KBr): 3487 (m), 3335 (m), 2922 (s), 2775 (s), 1658 (s), 1618 (s), 1502 (s) cm^{-1}; ^1H NMR (DMSO-d_6) δ: 6.65 (bs, 2H, NH_2), 7.29 (t, 1H, J= 7.6 Hz, Ar-H), 7.49 (t, 2H, J = 7.6 Hz, Ar-H), 7.78 (d, 2H, J=8.4 Hz, Ar-H), 8.08 (d, 2H, J=7.6 Hz, Ar-H) 8.20 (d, 2H, J = 7.4 Hz Ar-H), 8.43 (s, 1H, Ar-H), 9.75 (s, 1H, -CHO). ^{13}C NMR (DMSO-d_6): δ 17.64, 106.26, 112.67, 123.73 (2 C's), 128.68 (2 C's), 131.71, 141.48, 146.83, 153.98, 155.24, 161.26, 195.56; MS (70 eV) m/z (%) : 348 [M^+] (100), 350 [M+2] (33); *Anal*. Calcd. for $C_{19}H_{12}N_4OCl$ (347.74): C, 65.51; H, 3.44; N, 16.09. Found: C, 65.52; H, 3.46; N, 16.11.

4-Amino-3-(4-Br-phenyl)-1-phenyl-1H-pyrazolo[3,4-b] pyridine-5-carbaldehyde (4b)

Yield: 3.28 g (93%); recrystalized from Ethanol:DMF (8:2) (v:v) to afford yellow solid mp 184–185°C; IR (KBr): 3487 (m), 3335 (m), 2922 (s), 2775 (s), 1658 (s), 1618 (s), 1502 (s) cm^{-1}; ^1H NMR (DMSO-d_6) δ: 6.65 (bs, 2H, NH_2), 7.29 (t, 1H, J=7.6 Hz, Ar-H), 7.49 (t, 2H, J = 7.6 Hz, Ar-H), 7.78 (d, 2H, J=8.4 Hz, Ar-H), 8.08 (d, 2H, J=7.6 Hz, Ar-H), 8.20 (d, 2H, J =7.4 Hz Ar-H), 8.43 (s, 1H, Ar-H), 9.75 (s, 1H, CHO). ^{13}C NMR (DMSO-d_6): δ 17.64, 106.26, 112.67, 123.73 (2 C's), 128.68 (2 C's), 131.71, 141.48, 146.83, 153.98, 155.24, 161.26, 195.56; MS (70 eV) m/z (%): 391 [M^+] (86), 393 [M+ 2] (96); *Anal*. Calcd. for $C_{19}H_{12}N_4OBr$ (392.19): C, 58.31; H, 3.06; N, 14.32. Found: C, 58.33; H, 3.05; N, 14.30.

General Procedure for the synthesis of compounds (5a–x)

A mixture of 4 (0.001 mol), substituted acetophenones (0.001 mol) and ethanolic potassium hydroxide solution (5 mL, 2%) was heated under reflux for 25–30 min. The mixture was cooled to room temperature and the obtained solid was collected by suction filtration and washed with ethanol to furnish compound 5 in 80–90% yield and recrystallized from ethanol.

9-(4-Chloro-phenyl)-2,7-diphenly-7H-pyrazolo[3,4-h][1,6] naphthyridine (5a)

This compound was obtained as a pale brown solid, 0.388 g (89%); mp 212–213°C; IR (KBr): 2925 m, 1610 s, 1510 s cm^{-1}; ^1H NMR ($CDCl_3$): 7.35 (t, 1H, J=7.8 Hz, Ar-H), 7.51–7.62 (m, 5H, Ar-H), 8.01 (d, 1H, J=8.4 Hz, Ar-H), 8.25 (d, 2H, J=7.8 Hz, Ar-H), 8.35 (d, 2H, J=8.2 Hz, Ar-H), 8.42 (d, 1H, J = 8.4 Hz, Ar-H), 8.45(d, 2H, J = 8.6 Hz, Ar-H),8.64(d, 2H, J = 8.6 Hz, Ar-H), 9.08 (s, 1H, Ar-H); MS (70 eV) m/z (%): 432 [M^+] (100), 433 [M+1] (28); *Anal*. calcd. for $C_{27}H_{17}N_4Cl$ (432.87): C, 75.00; H, 3.93; N, 12.96. Found: C, 75.02; H, 3.91; N, 12.95.

2,9-Bis(4-chloro-phenyl)-7-diphenyl-7H-pyrazolo[3,4-h] [1,6]naphthyridine(5b)

This compound was obtained as a yellow solid, 0.404 g (86%); mp 235–236°C; IR (KBr): 2924 m, 1610 s, 1500 s cm^{-1}; ^1H NMR (DMSO-d_6): 7.29–7.37 (m, 5H, Ar-H), 7.56 (d, 2H, J=8.4 Hz, Ar-H), 7.98 (d, 2H, J = 8.4 Hz, Ar-H), 8.03 (d, 1H, J = 8.7 Hz, Ar-H), 8.28 (d, 2H, J = 8.6 Hz, Ar-H) 8.49 (d, 2H, J = 8.6 Hz, Ar-H), 8.72 (d, 1H, J = 8.7 Hz, Ar-H), 9.14 (s,1H, Ar-H); MS (70 eV) m/z (%): 467 [M^+] (100), 469 [M+2] (62), 471 [M+4] (14); *Anal*. Calcd. for $C_{27}H_{16}N_4Cl_2$ (467.45): C, 69.37; H, 3.42; N, 11.99. Found: C, 69.39; H, 3.46; N, 11.98.

2-(4-Bromophenyl)-9-(4-chloro-phenyl)-7-phenyl-7H-pyrazolo[3,4-h][1,6] naphthyridine(5c)

This compound was obtained as a yellow solid, 0.440 g (86%); mp 247–248°C; IR (KBr): 2923 m, 1608 s, 1501 s cm^{-1}; ^1H NMR (DMSO-d_6): δ 7.25–7.32 (m, 3H, Ar-H), 7.46 (t, 4H, J=8.4 Hz, Ar-H), 7.74 (d, 2H, J = 8.7 Hz, Ar-H), 8.02 (d, 1H, J = 8.7 Hz, Ar-H), 8.28 (d, 2H, J = 8.6 Hz, Ar-H) 8.49 (d, 2H, J = 8.6 Hz, Ar-H), 8.82 (d, 1H, J = 8.7 Hz, Ar-H), 9.16 (s, 1H, Ar-H); MS (70 eV) m/z (%): 510 [M^+] (72), 512 [M+2] (88), 514 [M+4] (34); *Anal*. Calcd. For $C_{27}H_{16}N_4ClBr$ (511.90): C, 63.52; H, 3.13; N, 10.98. Found: C, 63.55; H, 3.12; N, 10.97.

9-(4-Chloro-phenyl)-2-(3,4-dichloro-phenyl)-7-phenyl-7H-pyrazolo[3,4-h][1,6] naphthyridne (5d)

This compound was obtained as a colorless solid, 0.435 g (87%); mp 252–253°C; IR (KBr): 2930 m, 1614 s, 1508 s cm^{-1}; ^1H NMR (DMSO-d_6): δ 7.28 (d, 1H, J=8.4 Hz,

Ar-H), 7.47 (t, 1H, J=7.5 Hz, Ar-H), 7.59 (d, 2H, J = 7.5 Hz, Ar-H), 7.63 (t, 2H, J = 7.5 Hz, Ar-H), 7.99 (dd, 1H, J= 8.4 Hz & *J*=2.3 Hz Ar-H), 8.21 (d, 1H, J=8.6 Hz, Ar-H),), 8.52 (d, 1H, J=2.3 Hz, Ar-H), 8.64 (d, 2H, J=8.7 Hz, Ar-H), 8.71 (d, 1H, J = 8.6 Hz, Ar-H), 8.80 (d, 2H, J = 8.7 Hz, Ar-H), 9.03 (s, 1H, Ar-H); MS (70 eV) m/z (%): 500 [M^+] (96), 502 [M+2] (97), 504 [M+4] (31), 506 [M+6] (7); *Anal*. Calcd. for $C_{27}H_{15}N_4Cl_3$ (501.90): C, 64.67; H, 2.99; N, 11.17. Found: C, 64.69; H, 2.96; N, 11.18

2-(2-Bromo-4-chloro-phenyl)-9-(4-chloro-phenyl)-7-phenyl-7H-pyrazolo[3,4-h][1,6] naphthyridine (5e)

This compound was obtained as a brown solid, 0.455 g (83%); mp 249–250°C; IR (KBr): 2930 m, 1605 s, 1507 s cm^{-1}; ^1H NMR (DMSO-d_6): δ 7.25(dd, 1H, J=8.4 & 2.6 Hz, Ar-H), 7.44 (t, 1H, J=7.5 Hz, Ar-H), 7.52 (d, 2H, J = 7.5 Hz, Ar-H), 7.58 (t, 2H, J = 7.5 Hz, Ar-H), 7.78 (d, 1H, J=2.6 Hz Ar-H), 8.20(d, 1H, J=8.4 Hr, Ar-H), 8.26 (d, 1H, J = 8.6 Hz, Ar-H), 8.67 (d, 2H, J = 8.7 Hz, Ar-H), 8.73 (d, 1H, J = 8.6 Hz, Ar-H), 8.82 (d, 2H, J = 8.7 Hz, Ar-H), 9.04 (s, 1H, Ar-H); MS (70 eV) m/z (%): 545 [M^+] (96), 502 [M+2] (97), 504 [M+4] (31), 506 [M+6] (7); *Anal*. Calcd. for $C_{27}H_{15}N_4Cl_2Br$ (546.35): C, 59.49; H, 2.75; N, 10.27. Found: C, 59.54; H, 2.71; N, 10.29.

9-(4-Chloro-phenyl)-7-phenyl-2-p-tolyl-7H-pyrazolo[3,4-h][1,6]naphthyridine (5f)

This compound was obtained as a pale yellow solid, 0.395 g (88%); mp 243–244°C; IR (KBr): 2919 m, 1612 s, 1512 scm^{-1}; ^1H NMR ($CDCl_3$): δ 3.12 (s, 3H, CH_3), 7.30 (t, 1H, J=8.1 Hz, Ar-H), 7.34 (d, 2H, J = 8.4 Hz, Ar-H), 7.51 (t, 2H, J = 8.1 Hz, Ar-H), 8.02 (d, 1H, J = 8.4 Hz, Ar-H), 8.26–8.30 (m, 4H, Ar-H), 8.31(d, 2H, J = 8.6 Hz, Ar-H), 8.42 (d, 1H, J = 8.4 Hz, Ar-H), 8.66 (d, 2H, J = 8.6 Hz,Ar-H), 9.08 (s, 1H, Ar-H); MS (70 eV) m/z (%): 446 [M^+] (100), 448 [M+2] (29); *Anal*. Calcd. For $C_{28}H_{19}N_4Cl$ (446.88): C, 75.33; H, 4.26; N, 12.55. Found: C, 75.35; H, 4.24; N, 12.57.

9-(4-Chloro-phenyl)-2-(,4-nitro-phenyl)-7-phenyl-7H-pyrazolo[3,4-h][1,6] naphthyridne (5g)

This compound was obtained as a dark yellow solid, 0.427 g (89%); mp 250–251°C; IR (KBr): 2919 s, 1596 s, 1514 scm^{-1}; ^1H NMR ($CDCl_3$): δ,7.21(d, 2H, J=8.7 Hz, Ar-H), 7.30 (t, 1H, J = 8.1 Hz, Ar-H), 7.34 (d, 2H, J = 8.4 Hz, Ar-H), 7.51 (t, 2H, J = 8.1 Hz, Ar-H), 8.02 (d, 1H, J = 8.4 Hz, Ar-H), 8.31(d, 2H, J = 8.6 Hz, Ar-H), 8.42 (d, 1H, J = 8.4 Hz, Ar-H),8.52 (d, 2H, J = 8.7 Hz, Ar-H), 8.66 (d, 2H, J = 8.6 Hz,Ar-H), 9.08 (s, 1H, Ar-H). MS (70 eV) m/z (%): 477 [M^+] (100), 479 [M+2] (28); *Anal*. Calcd. For $C_{27}H_{16}ClN_5O_2$ (477.99): C, 67.92; H, 3.35; N, 14.67. Found: C, 67.89; H, 3.37; N, 14.69.

9-(4-Chloro-phenyl)-2-(3,4-diCF$_3$-phenyl)-7-phenyl-7H-pyrazolo[3,4-h][1,6] naphthyridne (5h)

This compound was obtained as a yellow needle, 0.495 g (87%); mp 236–237°C; IR (KBr): 2930 m, 1604 s, 1505 s cm^{-1}; ^1H NMR ($CDCl_3$): δ7.43(t, 1H, J=8.5 Hz, Ar-H),7.54(t, 2H, J = 8.5 Hz, Ar-H), 7.61(d, 2H, J = 8.5 HZ, Ar-H), 8.08(s, 1H, Ar-H), 8.11(d, 1H, J = 8.7 Hz, Ar-H), 8.37(d, 2H, J = 8.4 Hz, Ar-H), 8.41(d, 2H, J = 8.4 Hz, Ar-H), 8.56(d, 1H, J = 8.7 Hz, Ar-H), 8.62(s, 2H, Ar-H), 9.11 (s, 1H, Ar-H) MS (70 eV) m/z (%): 568 [M^+] (100), 570 [M+2] (27) *Anal*. Calcd. For $C_{29}H_{15}N_4F_6Cl$ (568.83): C, 61.26; H, 2.64; N, 9.85. Found: C, 61.28; H, 2.63; N, 9.86.

9-(4-Chloro-phenyl)-2-(4-methoxy-phenyl)-7-phenyl-7H-pyrazolo[3,4-h][1,6] naphthyridine(5i)

This compound was obtained as a silver needle, 0.410 g (88%); mp 239–240°C; IR (KBr): 3022 m, 2919 s, 1596 s, 1501 s, 1070 mcm^{-1}; ^1H NMR ($CDCl_3$): δ 3.93(s, 3H, OCH_3), 7.19(d, 2H, J=8.7 Hz,Ar-H), 7.42(t, 1H, J=7.6 Hz, Ar-H), 7.56(t, 2H, J = 7.6, Ar-H), 7.61(d, 2H, J = 7.6 Hz, Ar-H), 7.99(d, 1H, J=8.4 Hz, Ar-H), 8.28(d, 2H, J = 8.7 Hz, Ar-H), 8.38(d, 2H, J = 8.6 Hz, Ar-H), 8.40(d, 1H, J = 8.4 Hz, Ar-H), 8.63(d, 2H, J = 8.6 Hz, Ar-H), 9.07 (s,1H, Ar-H), ^{13}C NMR ($CDCl_3$): δ 58.45, 115.24, 116.78, 120.17 (2 C's), 124.38, 125.85, 126.17 (2 C's), 127.27 (2 C's), 128.90 (2 C's), 129.14 (2 C's), 132.23 (2 C's), 133.99, 134.26, 135.20, 137.57, 138.96, 142.95, 145.64, 146.23, 148.52, 150.66, 158.97 MS (70 eV) m/z (%): 462 [M^+] (100), 464 [M+4] (31) *Anal*. Calcd. For $C_{28}H_{19}N_4ClO$ (462.87):C, 72.72; H, 4.11; N, 12.12. Found: C, 72.74; H, 4.10; N, 12.14

9-(4-Chloro-phenyl)-2-(3,4-dimethoxy-phenyl)-7-phenyl-7H-pyrazolo[3,4-h][1,6] naphthyridine(5j)

This compound was obtained as a silver needle, 0.424 g (86%); mp 242–243°C; IR (KBr): 3017 m, 2930 m, 1595 s, 1509 s, 1078 mcm^{-1}; ^1H NMR ($CDCl_3$): δ 3.89 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 7.05 (d, 1H, J=8.4 Hz, Ar-H), 7.45 (t, 1H, J=7.8 Hz, Ar-H), 7.56 (d, 2H, J = 7.8 Hz, Ar-H), 7.62 (t, 2H, J = 7.8 Hz, Ar-H), 7.76 (dd, 1H, J=8.4 Hz & J=2.1 Hz Ar-H), 8.01(d, 1H, J=8.7 Hz, Ar-H), 8.11 (d, 1H, J=2.1 Hz, Ar-H), 8.21 (d, 2H, J=8.6 Hz, Ar-H), 8.27 (d, 1H, J = 8.7 Hz, Ar-H), 8.39 (d, 2H, J = 8.6 Hz, Ar-H), 9.01 (s, 1H, Ar-H); MS (70 eV) m/z (%): 492 [M^+] (100), 494 [M+2] (28); *Anal*. Calcd. For $C_{29}H_{21}N_4O_2Cl$ (492.89): C, 70.73; H, 4.26; N, 11.38. Found: C, 70.75; H, 4.24; N, 11.37.

9-(4-Chloro-phenyl)-2-(2,5-dimethoxy-phenyl)-7-phenyl-7H-pyrazolo[3,4-h][1,6] naphthyridine.(5k)

This compound was obtained as a silver solid, 0.430 g (87%); mp 243–244°C; IR (KBr): 3004 m, 2941 m, 1602 s, 1501 s, 1078 mcm^{-1}; ^1H NMR ($CDCl_3$): δ 3.81 (s, 3H, OCH_3), 4.01 (s, 3H, OCH_3), 6.76 (d, 2H, J=8.4 Hz, Ar-H), 6.89(dd, 1H, J = 8.2 & J=2.3 Hz, Ar-H), 7.27(d, 1H, J=8.2 Hz, Ar-H), 7.34 (d, 2H, J=7.8 Hz, Ar-H), 7.42 (t, 1H, J=8.4 Hz, Ar-H), 7.52 (t, 2H, J=7.8 Hz, Ar-H), 7.54(d, 1H, J=2.3 Hz, Az-H), 7.64 (d, 1H, J=8.4 Hz, Ar-H), 8.34 (d, 2H, J=7.8 Hz, Ar-H), 8.62 (d, 1H, J=8.4 Hz, Ar-H), 9.08 (s, 1H, Ar-H); MS (70 eV) m/z (%):492 [M^+] (100), 494 [M+2] (28); *Anal*. Calcd. for $C_{29}H_{21}N_4O_2Cl$ (492.89): C, 70.73; H, 4.26; N, 11.38. Found: C, 70.75; H, 4.24; N, 11.37.

9-(4-Chloro-phenyl)-2-(2,4,6-trimethoxy-phenyl)-7-phenyl-7H-pyrazolo[3,4-h][1,6] naphthyridine(5l)

This compound was obtained as a silver needle, 0.464 g (88%); mp 247–248°C; IR (KBr): 3004 m, 2941 m, 1602 s, 1501 s, 1075 mcm^{-1}; ^1H NMR ($CDCl_3$): δ 3.78 (s, 6H, 2× OCH_3), 3.89 (s, 3H, OCH_3), 6.31 (s, 2H, Ar-H), 7.35 (t, 1H, J=7.5 Hz, Ar-H), 7.51–7.57 (m, 3H, Ar-H), 8.23 (d, 2H, J = 7.5 Hz, Ar-H), 8.31 (d, 1H, J=8.4 Hz, Ar-H), 8.36(d, 2H, J = 8.6 Hz, Ar-H), 8.53(d, 2H, J = 8.6 Hz, Ar-H) 9.06 (s, 1H, Ar-H); ^{13}C NMR ($CDCl_3$): δ 55.42, 55.90 (2C's), 91.45 (2C's), 117.77, 118.10, 121.17 (2C's), 123.5 (2C's), 124.53, 126.01, 127.5, 128.3 (2C's), 129.09 (2C's), 130.89, 136.05, 138.19, 139.05, 141.2, 143.67, 144.2, 146.29, 149.58, 150.23, 151.62 (2 C's), 155.27. MS (70 eV) m/z (%): 522 [M^+] (100), 524 [M+2] (29), *Anal*. Calcd. for $C_{30}H_{23}N_4O_3Cl$ (522.88): C, 68.96; H, 4.40; N, 10.72. Found: C, 68.94; H, 4.41; N, 10.74.

9-(4-Bromo-phenyl)-2,7-diphenly-7H-pyrazolo[3,4-h][1,6] naphthyridine(5m)

This compound was obtained as a pale yellow solid, 0.416 g (87%); mp 226–227°C; IR (KBr): 2925 m, 1591 s, 1500 scm^{-1}; ^1H NMR ($CDCl_3$): 7.35 (t, 1H, J= 7.8 Hz, Ar-H), 7.51–7.62 (m, 5H, Ar-H), 8.01 (d, 1H, J= 8.4 Hz, Ar-H), 8.25 (d, 2H, J=7.8 Hz, Ar-H), 8.35 (d, 2H, J=8.2 Hz, Ar-H), 8.42 (d, 1H, J = 8.4 Hz, Ar-H),8.45(d, 2H, J = 8.6 Hz, Ar-H),8.64(d, 2H, J = 8.6 Hz, Ar-H), 9.08 (s, 1H, Ar-H); MS (70 eV) m/z (%): 476 [M^+] (96), 433 [M+ 2] (88); *Anal*. calcd. for $C_{27}H_{17}N_4Br$ (477.32): C, 68.06.; H, 3.57; N, 11.76. Found: C, 68.09; H, 3.58; N, 11.72.

9-(4-Bromophenyl)-2-(4-chlorophenyl)-7-phenyl-7H-pyrazolo[3,4-h][1,6]naphthyridine (5n)

This compound was obtained as a yellow solid, 0.454 g (89%); mp 243–244°C; IR (KBr): 2924 s, 1610 s, 1500 s cm^{-1}; ^1H NMR (DMSO-d_6): 7.29–7.37 (m, 5H, Ar-H), 7.56 (d, 2H, J=8.4 Hz, Ar-H), 7.98 (d, 2H, J = 8.4 Hz, Ar-H), 8.03 (d, 1H, J = 8.7 Hz, Ar-H), 8.28 (d, 2H, J = 8.6 Hz, Ar-H) 8.49 (d, 2H, J = 8.6 Hz, Ar-H), 8.72 (d, 1H, J = 8.7 Hz, Ar-H), 9.14 (s,1H, Ar-H); MS (70 eV) m/z (%): 510 [M^+] (68), 469 [M+2] (94), 471 [M+4] (31); *Anal*. Calcd. for $C_{27}H_{16}N_4ClBr$ (511.77): C, 63.52; H, 3.13; N, 10.98. Found: C, 63.55; H, 3.14; N, 10.96.

2,9-Bis(4-bromophenyl)-7-phenyl-7H-pyrazolo[3,4-h][1,6] naphthyridine(5o)

This compound was obtained as a pale brown solid, 0.478 g (86%); mp 249–250°C; IR (KBr): 2923 m, 1608 s, 1501 scm^{-1}; ^1H NMR (DMSO-d_6): δ 7.25–7.32 (m, 3H, Ar-H), 7.46 (t, 4H, J=8.4 Hz, Ar-H), 7.74 (d, 2H, J = 8.7 Hz, Ar-H), 8.02 (d, 1H, J = 8.7 Hz, Ar-H), 8.28 (d, 2H, J = 8.6 Hz, Ar-H) 8.49 (d, 2H, J = 8.6 Hz, Ar-H), 8.82 (d, 1H, J = 8.7 Hz, Ar-H), 9.16 (s, 1H, Ar-H); MS (70 eV) m/z (%): 554 [M^+] (48), 556 [M+2] (96), 558 [M+4] (46); *Anal*. Calcd. For $C_{27}H_{16}N_4Br_2$ (556.22): C, 58.48.; H, 2.88; N, 10.10. Found: C, 58.51; H, 2.87; N, 10.12

9-(4-Bromo-phenyl)-2-(3,4-dichloro-phenyl)-7-phenyl-7H-pyrazolo[3,4-h][1,6] naphthyridne(5p)

This compound was obtained as a colorless solid, 0.474 g (86%); mp 263–264°C; IR (KBr): 2930 m, 1612 s, 1508 s cm^{-1}; ^1H NMR (DMSO-d6): δ 7.28 (d, 1H, J=8.4 Hz, Ar-H), 7.47 (t, 1H, J=7.5 Hz, Ar-H), 7.59 (d, 2H, J = 7.5 Hz, Ar-H), 7.63 (t, 2H, J = 7.5 Hz, Ar-H), 7.99 (dd, 1H, J= 8.4 Hz & *J*=2.3 Hz Ar-H), 8.21 (d, 1H, J=8.6 Hz, Ar-H),), 8.52 (d, 1H, J=2.3 Hz, Ar-H), 8.64 (d, 2H, J=8.7 Hz, Ar-H), 8.71 (d, 1H, J = 8.6 Hz, Ar-H), 8.80 (d, 2H, J = 8.7 Hz, Ar-H), 9.03 (s, 1H, Ar-H); MS (70 eV) m/z (%): 545 [M^+] (71), 547 [M+2] (98), 549 [M+4] (64), 551 [M+6] (11); *Anal*. Calcd. for $C_{27}H_{15}N_4Cl_2Br$ (546.32): C, 59.44; H, 2.75; N, 10.27. Found: C, 59.47; H, 2.78; N, 10.25.

2-(2-Bromo-4-chloro-phenyl)-9-(4-Bromo-phenyl)-7-phenyl-7H-pyrazolo[3,4-h][1,6] naphthyridine (5q)

This compound was obtained as a yellow solid, 0.521 g (88%); mp 269–270°C; IR (KBr): 2930 m, 1595 s, 1503 s cm^{-1}; ^1H NMR (DMSO-d6): δ 7.25(dd, 1H, J=8.4 & 2.6 Hz, Ar-H), 7.44 (t, 1H, J=7.5 Hz, Ar-H), 7.52 (d, 2H, J = 7.5 Hz, Ar-H), 7.58 (t, 2H, J = 7.5 Hz, Ar-H), 7.78 (d, 1H, J=2.6 Hz Ar-H), 8.20(d, 1H, J=8.4 Hr, Ar-H), 8.26 (d, 1H, J = 8.6 Hz, Ar-H), 8.67 (d, 2H, J = 8.7 Hz, Ar-H), 8.73 (d, 1H, J = 8.6 Hz, Ar-H), 8.82 (d, 2H, J = 8.7 Hz, Ar-H), 9.04 (s, 1H, Ar-H); MS (70 eV) m/z (%): 588 [M^+]

(48), 590 [M+2] (100), 592 [M+4] (74), 594 [M+6] (19); *Anal*. Calcd. for $C_{27}H_{15}N_4ClBr_2$ (590.67): C,55.10; H, 2.55; N, 9.52. Found: C, 55.14; H, 2.56; N, 9.54.

9-(4-Bromo-phenyl)-7-phenyl-2-p-tolyl-7H-pyrazolo[3,4-h][1,6]naphthyridine (5r)

This compound was obtained as a brown needle, 0.420 g (85%); mp 254–255°C; IR (KBr): 2919 m, 1596 s, 1510 s cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.12 (s, 3H, CH_3), 7.30 (t, 1H, J=8.1 Hz, Ar-H), 7.34 (d, 2H, J = 8.4 Hz, Ar-H), 7.51 (t, 2H, J = 8.1 Hz, Ar-H), 8.02 (d, 1H, J = 8.4 Hz, Ar-H), 8.26–8.30 (m, 4H, Ar-H), 8.31(d, 2H, J = 8.6 Hz, Ar-H), 8.42 (d, 1H, J = 8.4 Hz, Ar-H), 8.66 (d, 2H, J = 8.6 Hz,Ar-H), 9.08 (s, 1H, Ar-H); ^{13}C NMR ($CDCl_3$): δ 19.64, 115.24, 116.78, 120.17 (2 C's), 123.55 (2 C's), 124.38, 125.85, 126.32, 127.27 (2C's), 128.90 (2C's), 129.14 (2C's), 131.22 (2C's), 133.99, 135.20, 137.57, 138.96, 142.95, 144.10, 145.64, 148.52, 150.66, 158.97 MS (70 eV) m/z (%): 490 [M^+] (95), 492 [M+2] (87); *Anal*. Calcd. For $C_{28}H_{19}N_4Br$ (491.33): C, 68.57; H, 3.87; N, 11.42. Found: C, 68.59; H, 3.86; N, 11.44.

9-(4-Bromo-phenyl)-2-(4-nitro-phenyl)-7-phenyl-7H-pyrazolo[3,4-h][1,6]naphthyridne (5s)

This compound was obtained as a dark brown solid, 0.460 g (88%); mp 274–275°C; IR (KBr): 2919 m, 1596 s, 1551 m, 1511 s, 1357 mcm^{-1}; ^1H NMR ($CDCl_3$): δ,7.21(d, 2H, J=8.7 Hz, Ar-H), 7.30 (t, 1H, J = 8.1 Hz, Ar-H), 7.34 (d, 2H, J = 8.4 Hz, Ar-H), 7.51 (t, 2H, J = 8.1 Hz, Ar-H), 8.02 (d, 1H, J = 8.4 Hz, Ar-H), 8.31(d, 2H, J = 8.6 Hz, Ar-H), 8.42(d, 1H, J = 8.4 Hz, Ar-H),8.52 (d, 2H, J = 8.7 Hz, Ar-H), 8.66 (d, 2H, J = 8.6 Hz, Ar-H), 9.08(s, 1H, Ar-H). MS (70 eV) m/z (%): 521 [M^+] (93), 523 [M+2] (89); *Anal*. Calcd. For $C_{27}H_{16}N_5BrO_2$ (522.31): C, 62.18; H, 3.07; N, 13.43. Found: C, 62.21; H, 3.11; N, 13.41.

9-(4-Bromo-phenyl)-2-(3,4-diCF_3-phenyl)-7-phenyl-7H-pyrazolo[3,4-h][1,6] naphthyridine (5t)

This compound was obtained as a brown needles, 0.540 g (88%); mp 248–249°C; IR (KBr): 2930 m, 1595 s, 1505 s cm^{-1}; ^1H NMR ($CDCl_3$): δ7.43(t, 1H, J=8.5 Hz, Ar-H),7.54(t, 2H, J = 8.5 Hz, Ar-H), 7.61(d, 2H, J = 8.5 HZ, Ar-H), 8.08(s, 1H, Ar-H), 8.11(d, 1H, J = 8.7 Hz, Ar-H), 8.37(d, 2H, J = 8.4 Hz, Ar-H), 8.41(d, 2H, J = 8.4 Hz, Ar-H), 8.56(d, 1H, J = 8.7 Hz, Ar-H), 8.62(s, 2H, Ar-H), 9.11 (s, 1H, Ar-H) MS (70 eV) m/z (%): 612 [M^+] (96), 614 [M+2] (90) *Anal*. Calcd. For $C_{29}H_{15}N_4F_6Br$ (613.28): C, 56.86; H, 2.45; N, 9.15. Found: C, 58.88; H, 2.47; N, 9.14.

9-(4-Bromo-phenyl)-2-(4-methoxy-phenyl)-7-phenyl-7H-pyrazolo[3,4-h][1,6] naphthyridine (5u)

This compound was obtained as a silver needle, 0.425 g (83%); mp 271–272°C; IR (KBr): 3022 m, 2919 m, 1610 s, 1501 s, 1070 mcm^{-1}; ^1H NMR ($CDCl_3$): δ 3.93(s, 3H, OCH_3), 7.19(d, 2H, J=8.7 Hz,Ar-H), 7.42(t, 1H, J= 7.6 Hz, Ar-H), 7.56(t, 2H, J = 7.6, Ar-H), 7.61(d, 2H, J = 7.6 Hz, Ar-H), 7.99(d, 1H, J=8.4 Hz, Ar-H), 8.28(d, 2H, J = 8.7 Hz, Ar-H), 8.38(d, 2H, J = 8.6 Hz, Ar-H), 8.40(d, 1H, J = 8.4 Hz, Ar-H), 8.63(d, 2H, J = 8.6 Hz, Ar-H), 9.07 (s,1H, Ar-H). MS (70 eV) m/z (%): 506 [M^+] (100), 508 [M+2] (92) *Anal*. Calcd. For $C_{28}H_{19}N_4BrO$ (507.32): C, 66.40; H, 3.75; N, 11.06. Found: C, 66.43; H, 3.77; N, 11.04.

9-(4-Bromo-phenyl)-2-(3,4-dimethoxy-phenyl)-7-phenyl-7H-pyrazolo[3,4-h][1,6] naphthyridine(5v)

This compound was obtained as a silver solid, 0.469 g (87%); mp 277–278°C; IR (KBr): 3017 m, 2930 m, 1598 s, 1509 s, 1078 mcm^{-1}; ^1H NMR ($CDCl_3$): δ 3.89 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 7.05 (d, 1H, J=8.4 Hz, Ar-H), 7.45 (t, 1H, J=7.8 Hz, Ar-H), 7.56 (d, 2H, J = 7.8 Hz, Ar-H), 7.62 (t, 2H, J = 7.8 Hz, Ar-H), 7.76 (dd, 1H, J=8.4 Hz & J=2.1 Hz Ar-H), 8.01(d, 1H, J=8.7 Hz, Ar-H), 8.11 (d, 1H, J=2.1 Hz, Ar-H), 8.21 (d, 2H, J=8.6 Hz, Ar-H), 8.27 (d, 1H, J = 8.7 Hz, Ar-H), 8.39 (d, 2H, J = 8.6 Hz, Ar-H), 9.01 (s, 1H, Ar-H); ^{13}C NMR ($CDCl_3$): δ 58.45, 59.32, 115.24, 116.78, 123.05, 124.38, 125.85, 126.17 (2 C's), 127.27 (2 C's), 129.14 (2 C's), 131.22, 132.23 (2 C's), 133.99, 134.26, 132.04, 135.20, 137.57, 138.96, 142.95, 145.64, 146.23, 147.23, 148.52, 150.66, 158.97. MS (70 eV) m/z (%): 536[M^+] (98), 538 [M+2] (90); *Anal*. Calcd. For $C_{29}H_{21}N_4O_2Br$ (537.32): C, 64.92; H, 3.91; N, 10.44. Found: C, 64.89; H, 3.94; N, 10.47.

9-(4-Bromo-phenyl)-2-(2,5-dimethoxy-phenyl)-7-phenyl-7H-pyrazolo[3,4-h][1,6] naphthyridine (5w)

This compound was obtained as a silver needle, 0.476 g (88%); mp 275–276°C; IR (KBr): 3004 m, 2941 m, 1602 s, 1501 s, 1078 mcm^{-1}; ^1H NMR ($CDCl_3$): δ 3.81 (s, 3H, OCH_3), 4.01(s, 3H, OCH_3), 6.76 (d, 2H, J=8.4 Hz, Ar-H), 6.89(dd, 1H, J = 8.2 & J=2.3 Hz, Ar-H), 7.27(d, 1H, J= 8.2 Hz, Ar-H), 7.34 (d, 2H, J=7.8 Hz, Ar-H), 7.42 (t, 1H, J=8.4 Hz, Ar-H), 7.52 (t, 2H, J=7.8 Hz, Ar-H), 7.54(d, 1H, J=2.3 Hz, Az-H), 7.64 (d, 1H, J=8.4 Hz, Ar-H), 8.34 (d, 2H, J=7.8 Hz, Ar-H), 8.62 (d, 1H, J=8.4 Hz, Ar-H), 9.08 (s, 1H, Ar-H); MS (70 eV) m/z (%): 536 [M^+] (97), 538 [M+2] (90); *Anal*. Calcd. for $C_{29}H_{21}N_4O_2Br$ (537.32): C, 64.92; H, 3.91; N, 10.44. Found: C, 64.89; H, 3.94; N, 10.47.

9-(4-Bromo-phenyl)-2-(2,4,6-trimethoxy-phenyl)-7-phenyl-7H-pyrazolo[3,4-h][1,6] naphthyridine(5x)

This compound was obtained as a silver solid, 0.495 g (87%); mp 281–282°C; IR (KBr): 3004 m, 2941 m, 1602 s, 1501 s, 1075 mcm^{-1}; ^1H NMR ($CDCl_3$): δ 3.78 (s, 6H, 2 x OCH_3), 3.89 (s, 3H, OCH_3), 6.31 (s, 2H, Ar-H), 7.35 (t, 1H, J=7.5 Hz, Ar-H), 7.51–7.57 (m, 3H, Ar-H), 8.23 (d, 2H, J = 7.5 Hz, Ar-H), 8.31 (d, 1H, J=8.4 Hz, Ar-H), 8.36(d, 2H, J = 8.6 Hz, Ar-H), 8.53(d, 2H, J = 8.6 Hz, Ar-H) 9.06 (s, 1H, Ar-H); MS (70 eV) m/z (%): 566 [M^+] (100), 568 [M+2] (89), *Anal*. Calcd. for $C_{30}H_{23}N_4O_3Br$ (567.30): C, 63.60; H, 4.06; N, 9.89. Found: C, 63.63; H, 4.02; N, 9.92.

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