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RAPID COMMUNICATION

A Fluorescence Study of New Angular Polycyclic Blue Light-Emitting pyrazolo[3,4-*h*][1,6]naphthyridine and their Interaction with Bovine Serum Albumin (BSA)

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Abstract The blue light-emitting pyrazolo[3,4-*h*][1,6]naphthyridines has been synthesized by *Friedländer* condensation of 4-amino-3-(4-phenyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carbaldehyde (o-aminoaldehyde) **1** with different cyclic ketones and 1,3-diketones. The synthesized angular polycyclic naphthyridine derivatives were studied for Semi-empirical, thermal, UV–vis and fluorescence spectroscopic properties on binding with bovin serum albumin (BSA). These fluorescence properties together with the neutral, hydrophobic nature of these compounds make these fluorophores good fluorescence probe for studying the micropolarity of proteins like BSA and in general the ligand-protein interactions. All of them displays bright absorption at 394 nm & emission in visible region (491 nm). Quantum yields of all synthesized compounds were calculated.

Keywords HOMO-LUMO · Absorption and emission · Quantum yield · DSC · TGA · BSA

Introduction

Organic materials have previously been considered for the fabrication of practical electroluminescent (EL) devices [1]. The primary reason is that a large number of organic materials are known to have extremely high fluorescence quantum efficiencies in the visible spectrum [2, 3] including the blue region, some approaching 100%. In this regard, they are ideally suited for multicolor display applications. For full color application red, green, and blue (RGB) emission are required. An efficient blue emission is of particular interest because other colors can be down converted from the blue emission. There are a number of efficient blue dyes developed in the past several years [4–10] some of which possess reasonable or high glass transition temperature, T_g, a property suggested to be desirable for morphological stability reasons [11–13]. There is increasing interest in the development of efficient fluorescent materials particularly those emitting in the blue spectral region. These materials are potential candidate for use in opto- or optoelectronic devices, such as tuneable lasers and amplifers, optical fibres, switches or modulators with a variety of applications in optical communications, photonics, medicine, optical spectroscopy and information displays, for example, organic electroluminescent devices [14–18]. From literature, it was observed that the photophysical properties of pyrazolonaphthyridines were little explored. Thus, suitable blue emitters with high brightness along with good thermostability still remain to be developed.

The early work on the use of fluorescent labeled antisera in immunology was performed by Coons et al. (1942) and Coons and Kaplan (1950). For a review up to 1954 see Coons (1954). This defined technique permits selective "staining" of antigens either in tissue section or isolated on a glass slide. Recently, considerable attention has been focused on the study of the interaction between small molecules (drugs) and biological macromolecules (e.g. proteins), especially discussing the thermodynamic quality, binding force quality, and mechanism of interactions [19–21]. These studies play crucial role in promoting research on proteins because they

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can provide useful information for study of pharmacological and biological effects of drugs as well as conformational changes of proteins caused by drugs. Serum albumin is one of the most abundant proteins in circulatory system of a wide variety of organisms and one of the most extensively studied proteins at all [22, 23]. Perhaps, its most outstanding property is the ability to bind a variety of ligands. It is well known that many drugs bind to serum albumin and their effectiveness depends on the binding ability [23, 24].

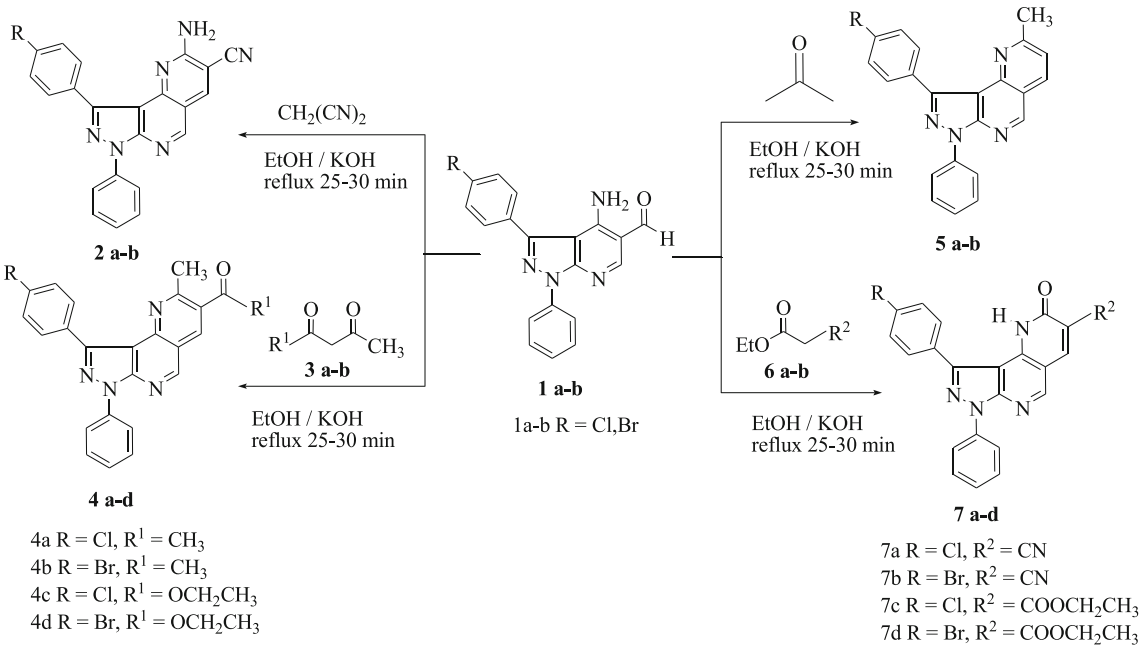
In our earlier communication, we have reported fluorescence properties of pyridine-3-carbonitriles [25], Spiro-Oxazino-Quinoline derivatives [26] pyrazolopyrrolopyrimidine (PPP) [27]. Recently we reported synthesis and effect of specific solute-solvent interaction on fluorescence of pyrazolonaphthyridines using **1** (o-aminoaldehyde) [28]. In this communication we extend work towards the synthesis of new angular polycyclic blue light-emitting pyrazolo[3,4-*h*][1, 6]naphthyridine derivatives with (o-aminoaldehydes) **1** and studied their effect of binding interaction in aqueous buffer and in bovine serum albumin (BSA) on fluorescence properties, (a well-known protein responsible for transport of a variety of ligands [29]) and also thermostabality of some representative pyrazolonaphthyridine derivatives were studied with Semi-empirical calculations.

Results and Discussion

An annulations reaction with heterocyclic aminoaldehyde provides synthetic entry in to heterocyclic systems, fused to a pyridine or pyrimidine nucleus with methylene active compounds by *Friedländer* condensation reactions. The required o-aminoaldehyde **1** was synthesized by multistep reactions employed in our earlier paper [28]. Then, *Friedländer* condensation of o-aminoaldehyde **1** with active methylenes compounds was performed. Thus, a mixture of **1a** or **1b** and α-active methylenes such as malononitrile, acetylacetone **3a**, ethylaceto- acetate **3b**, acetone, ethylcynoacetate **6a**, diethylmalonate **6b**, on refluxing in ethanolic potassium hydroxide furnished pyrazolo[3,4-*h*][1,6]naphthyridines **2**, **4**, **5** and **7** respectively in good yields (Scheme 1). Compounds **2**, **4**, **5** and **7** were characterized by spectral and analytical methods.

The readily availability and wide choice of cyclic ketenes, the ease of operation and the high yields obtained make this heteroannulation sequence a versatile tool for construction of multiple, fused ring structures. The use of cyclic ketones such as derivatives of tetralone or indanone allows rapid buildup of large polycyclic ring assemble with o-aminoaldehydes. Thus, o-aminoaldehyde **1** was condensed with series of cyclic ketones to obtain the angular polycyclic heterocyles. Thus, a mixture of **1a** or **1b** and cyclic ketones such as cyclopentanone **8**, cyclohexanone **10a** or 2/3-methylcyclohexanones **10b-c** on refluxing in ethanolic potassium hydroxide furnished 1-(4-chloro/bromo-phenyl)-3-phenyl-3,7,8,9-tetrahydrocyclopenta[*b*]- pyrazolo [3,4-*h*][1,6]naphthyridine **9a-b**, 1-(4-chloro/bromo-phenyl)-3-phenyl-7,8,9,10-tetra- hydro-3*H*-benzo[*b*]pyrazolo[3,4-*h*][1,6]naphthyridine **11a-b**, and 1-(4-chloro/bromo-phenyl)-9/10-methyl-3-phenyl-7,8,9,10-tetrahydro-3*H*-benzo[*b*]pyrazolo[3,4-*h*][1,6]naphthyridine **11c-f** in 79%–85% yield respectively. It was interesting to observe that when cyclocondensation of ethyl 2-oxocyclohexane carboxylate **12** was performed with **1a** or **1b** resulted in the formation of ethyl-1-(4-chloro/bromo-phenyl)-3-phenyl-7, 8, 9,10-tetrahydro-3*H*-benzo[*b*]pyrazolo[3,4-*h*][1,6]- naphthyridine-10-carboxylate **13a-b** without hydrolyzing ester functionality in **12**. However the reaction of o-aminoaldehyde **1a** or **1b** with dimedone **14a** and 5,5-dimethyl-1,3-dimedone **14b** was unsuccessful in ethanolic KOH, hence this cyclocondensation was achieved by heating the reaction mixture without using any solvent at 140–150 °C, which offered 1-(4-chloro/bromo-phenyl)-3-phenyl-7,8-dihydro-3*H*-benzo[*b*]pyrazolo [3,4-*h*][1,6]naphthyridine −9-(10*H*)one **15a-b** and 1-(4-chloro/bromo-phenyl)-7,7-dimethyl-3-phenyl-7,8-dihydro-3*H*-benzo[*b*]pyrazolo- [3,4-*h*][1,6]naphthyridine-9(10*H*)-one **15c-d**, respectively in 80–82% yield. Condensation of **1** with tetralone **16a**, 6-methoxy-1-tetralone **16b**, indanone **18a**, 5,6-dimethoxy-1-indanone **18b**, and cetralene **20** yield a pentacyclic heterocycle, 1-(4-chloro/bromo-phenyl)-3-phenyl-7,8-dihy- dro-3*H*-naphtho[1,2-*b*] pyrazolo[3,4-*h*][1,6] naphthayridine **17a-b**, 1-(4-chloro/bromo-phenyl)-10-methoxy-3-phenyl-7,8-dihydro-3*H*-naphtho[1,2-*b*]pyrazolo [3,4-*h*][1,6]naphthyridine **17c–d**, 1-(4-chloro/bromo-phenyl)-3-phenyl-3,7-dihydroindeno[1,2-*b*]pyrazolo[3,4-*h*][1,6]naphthyridine **19a-b**, 1-(4-chloro/bromo-phenyl)-9,10-dimethoxy-3-phenyl-3,7-dihydroindeno[1,2-*b*]pyrazolo- [3,4-*h*][1,6]-naphthyridine **19c-d** and 1-(4-chloro/bromo-phenyl)-8-(3,4-dichlorophenyl)-3-phenyl-7,8-dihydro-3*H*-naphtho[1,2-*b*] pyrazolo-[3,4-*h*][1,6]naphthyridine **21a–b**, respectively in excellent yield under similar reaction conditions. The cycloconden- sation of N-substituted piperidones such as N-methyl-piperidone **22a**, N-acetyl-piperidone **22b** and N-BOC-piperidone **22c** with **1** under similar reaction condition smoothly yielded pyrazolo[3,4-*h*][1,6]- naphthyridine derivatives **23a–f** in 80%–85% yield (Scheme 2).

All these compounds were characterized by IR, ^{1}H NMR, mass, elemental analysis and some were characterized by ^{13}C NMR; e.g. the IR spectrum of **23c** shows carbonyl stretching bands at 1715 cm^{-1}. The ^{1}H NMR spectrum shows a singlet at 2.18 δ for –CH_3 protons; it shows two triplets at 3.14 and 3.28 δ for four protons of piperidone ring, a singlet corresponds to -CH_2 protons of piperidone ring were observed at 3.97δ. All aromatic protons showed expected chemical shifts and splitting patterns which resembles with the structure of **23c**. The mass spectrum of **23c** reveled a



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

molecular ion peaks m/z at 498[M^+] and at 500[M + 2] respectively, due to presence of chlorine atom.

We observed blue light-emission of all synthesized compounds with naked eyes under fluorescence wave length (400–600 nm) in DMF; it was a fulfilling experience, for instance, the blue emission by **23a** and **23b** shown in Fig. 1. Hence according to observed results we decided to study photophysical properties of synthesized compounds.

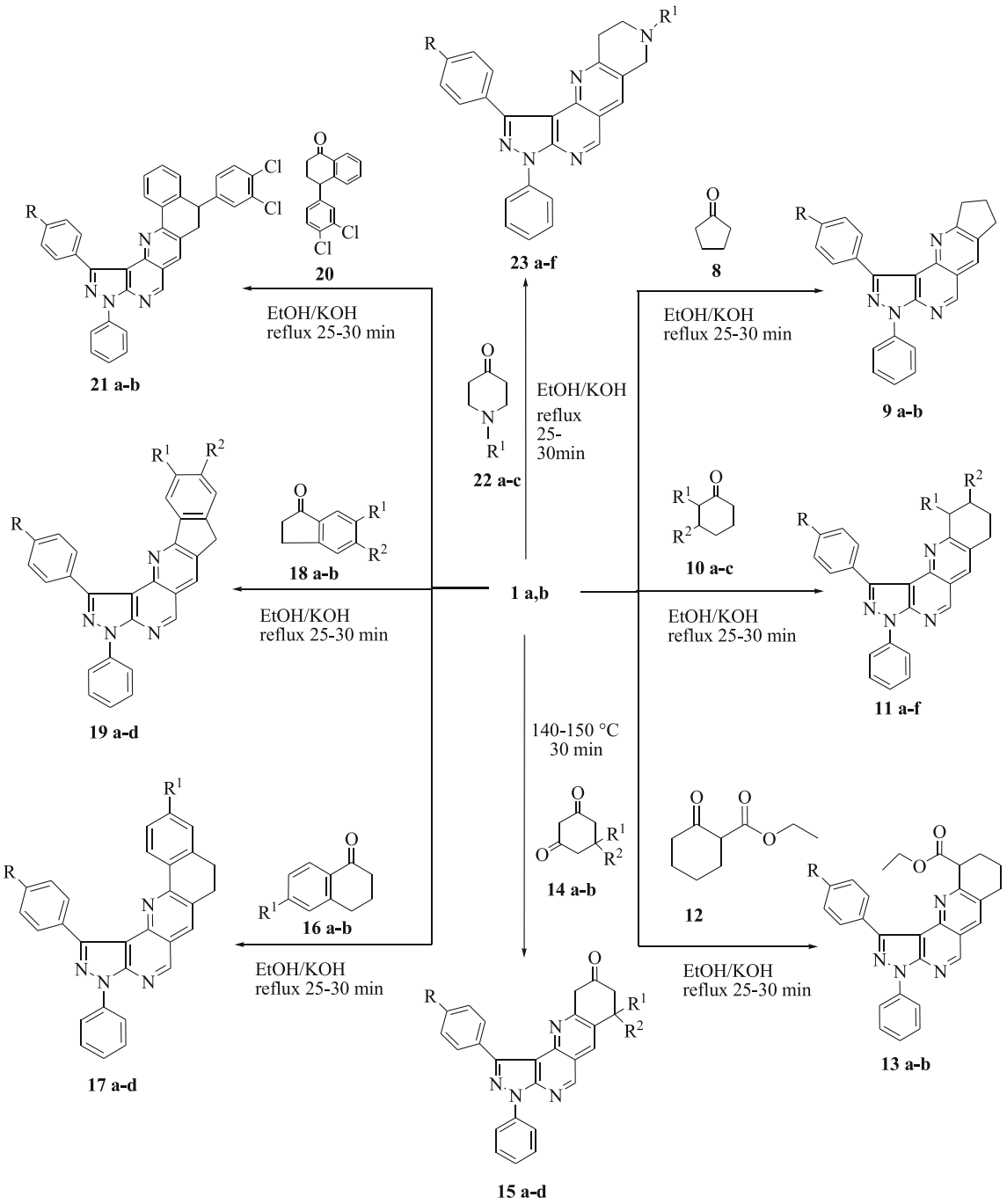
Semi-empirical Study of Pyrazolo[3,4-*h*][1,6] naphthyridines

The HOMO and LUMO of a molecule are usually important characteristics for its chemical reactivity and for biological activity [30–33]. The fluorophores which are useful as Organic Light Emitting Diodes (OLEDs) should fluoresces between 400 and 700 nm and should have an electron hole gap up to 4 eV [34]. Prompted with these report, we perform some computational calculations like HOMO, LUMO energy and electron hole gap (HOMO-LUMO energy separations) of synthesised pyrazolonaphthyridine derivatives using self-consistent field Hartree-Fock(SCF-HF) method within the semi-empirical PM3 approximation [35, 36], as implemented in the MOPAC program [37], and are listed in Table 1. The HOMO energies for all these molecules are rather close to each other, i.e., ranging between −8.435 eV and −8.850 eV, while LUMO energies are ranging between −1.150 eV and −1.439 eV (Table 1). Similarly, the HOMO-LUMO energy separations were found to uniformly distribute from 7.115 to 7.521 eV. From these calculations it is observed that there is more overlappings between HOMOs and LUMOs for compounds **17c–d**, **19c–d** and **21a–b** which show low gap value in the range 7.115–7.211 eV.

Thermal Properties

Organic compounds which used in OLEDs and in opto-electronic applications should be thermally and chemically stable [38]. Thermal analysis of representative compounds **23a, 23b** by TGA and DSC were performed, which shows their thermostability up to 350 °C. In Table 2, losses in weight of these compounds observed during TGA in the different temperature ranges are listed. It observed that, at the temperature range 350–360 °C the loss in weight is 0.92% and 0.44% of **23a** and **23b** respectively which is marginally constant. Where as loss in weight at the 450 °C temperature is 51.50% and 55.56% respectively, which is in good agreement to prove the decomposition temperature of **23a** and **23b** (Fig. 2)

Differential scanning calorimetry experiments of **23b** was performed, which should give information about melting temperatures and decomposition temperatures and in addition about the enthalpy as security hint. From DSC experiment of compound **23b**, it was observed that melting onset temperature of about 258 °C is visible and enthalpy is 85.84 J/g. The decomposition of compound is shown by an exothermic peak starting at 357.5 °C (Fig. 3). From TGA and DSC analysis we conclude that the synthesized pyrazolonaphthyridine derivatives are stable up to 350 °C temperature.



Scheme 2 Synthetic route of pyrazolo[3,4-*h*][1,6]naphthyridines

Spectral Properties

Absorption and Fluorescence Emission Properties of Pyrazolonaphthyridine Derivatives in Organic Solvent DMF

The absorption and fluorescence emission spectral properties of all pyrazolonaphthyridine derivatives were undertaken in polar aprotic solvent such as DMF and spectral data are summarized in Table 3. Typical UV–vis spectra of naphthyridines derivatives are found between **~360** and **~394 nm**, ($\lambda_{ab\ max}$) at room temperature and the concentration of the solute were maintained at 10^{-3} M. Among naphthyridine derivatives **17**c–d, **19c**–d & **21a–b** are significantly red-shifted, having shows absorption maxima ($\lambda_{ab\ max}$) at longer wavelength (388–394 nm). It is also

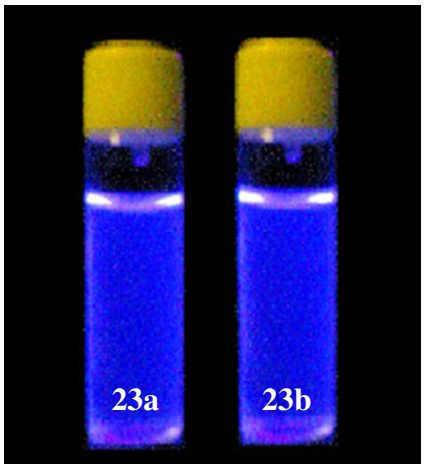


Fig. 1 Blue light emission under fluorescence lamp of compounds **23a** and **23b**

supported by low gap value of HOMO-LUMO energy levels (Table 1). The compounds **17c–d** & **19c** shows absorption in the range **390–394 nm** and are may be good source in blue LEDs.

The fluorescence maximums ($\lambda_{f\ max}$) of these compounds were studied and their quantum yields (ϕ_f) were calculated by standard literature procedures using quinine sulphate as reference standard (ϕ_{ref}=0.57 in 0.1 M H_2SO_4) [39–43] and are listed in Table 3. All these compounds fluoresces between **~434 nm** and **~491 nm** and have quantum yields (ϕ_f) between 0.188 and 0.240. From Table 3, it was observed that naphthyridine derivatives **21b**, **23a**, and **23b** shows higher emission maxima at **482 nm**, **485 nm** and **491 nm** than other derivatives with quantum yields (ϕ_f) **0.220**, **0.221** and **0.240** respectively. The graphical representation of the absorption ($\lambda_{ab\ max}$) and fluorescence ($\lambda_{f\ max}$) spectra of compounds **21b**, **23a** and **23b** is shown in Fig. 4.

Table 1 The molecular electronic properties (HOMO-LUMO energy, GAP) of the pyrazolo-[3,4-*h*][1,6]naphthyridines

Comp.	R	R^1	R^2	HOMO (eV)	LUMO (eV)	GAP (eV)
9a	Cl	–	–	−8.636	−1.168	7.468
9b	Br	–	–	−8.670	−1.179	7.491
11a	Cl	H	H	−8.628	−1.165	7.463
11b	Br	H	H	−8.658	−1.186	7.472
11c	Cl	CH_3	H	−8.651	−1.152	7.499
11d	Br	CH_3	H	−8.684	−1.163	7.521
11e	Cl	H	CH_3	−8.635	−1.150	7.485
11f	Br	H	CH_3	−8.672	−1.164	7.508
13a	Cl	–	–	−8.850	−1.352	7.498
13b	Br	–	–	−8.821	−1.347	7.474
15a	Cl	H	H	−8.626	−1.166	7.462
15b	Br	H	H	−8.628	−1.174	7.454
15c	Cl	CH_3	CH_3	−8.803	−1.355	7.448
15d	Br	CH_3	CH_3	−8.841	−1.365	7.476
17a	Cl	H	H	−8.665	−1.370	7.295
17b	Br	H	H	−8.638	−1.371	7.267
17c	Cl	OCH_3	H	−8.492	−1.309	7.183
17d	Br	OCH_3	H	−8.489	−1.374	7.115
19a	Cl	H	H	−8.648	−1.382	7.266
19b	Br	H	H	−8.695	−1.380	7.315
19c	Cl	OCH_3	OCH_3	−8.435	−1.314	7.121
19d	Br	OCH_3	OCH_3	−8.440	−1.233	7.207
21a	Cl	–	–	−8.647	−1.439	7.208
21b	Br	–	–	−8.644	−1.433	7.211
23a	Cl	CH_3	–	−8.642	−1.398	7.244
23b	Br	CH_3	–	−8.651	−1.412	7.239
23c	Cl	$COCH_3$	–	−8.627	−1.384	7.243
23d	Br	$COCH_3$	–	−8.659	−1.387	7.272
23e	Cl	$COOC(CH_3)_3$	–	−8.617	−1.340	7.277
23f	Br	$COOC(CH_3)_3$	–	−8.649	−1.359	7.290

GAP = E_{LUMO}-E_{HOMO}

Table 2 Thermal analysis of **23a** and **23b**

Sr. no.	Temp.rang °C	loss (wt. mg)		Loss (wt%)	
		23a	**23b**	**23a**	**23b**
1	25–100	4.48	4.66	0.0	0.43
2	100–200	4.47	4.61	0.22	1.07
3	200–300	4.43	4.56	0.89	1.08
4	300–350	4.33	4.50	2.26	1.32
5	350–450	2.1	2.00	51.50	55.56

The Effect of BSA on Fluorescence Emission of Pyrazolonaphthyridine Derivatives in Phosphate Buffer

In order to examine the interaction of pyrazolonaphthyridine with bovine serum albumin (BSA), the fluorescence titration with BSA were thus carried out in phosphate buffer of pH 7.4. The absorption and fluorescent spectral data are collected in Table 4 and $\lambda_{f.\ max.}$ of **21b**, **23a**, **23b** is graphically presented in Fig. 5. A gradual increase in concentration of BSA in the solution of naphthyridines in phosphate buffer results in an enhancement of the fluorescence intensity and ϕ_f for all the compounds. The $\lambda_{f\ max}$ gets blue-shifted upon binding with BSA, in general the fluorescence intensity of compounds increased linearly with increasing BSA concentration. The effect of increasing BSA concentration in the solution of **23b** in phosphate buffer is shown in Fig. 6. Further, the observed $\lambda_{f\ max}$ remains insensitive to the change in BSA concentration. The blue shift in the $\lambda_{f\ max}$ suggests that the polarities of the protein environments in which the pyrazolonaphthyridine are located are less than the polarity of the bulk phase. This shows the binding of the probes to a hydrophobic site of the protein.

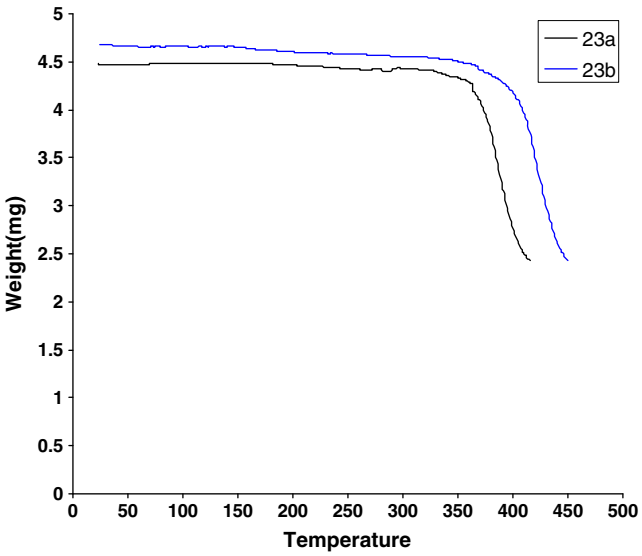


Fig. 2 TGA of compound **23a** and **23b**

Conclusion

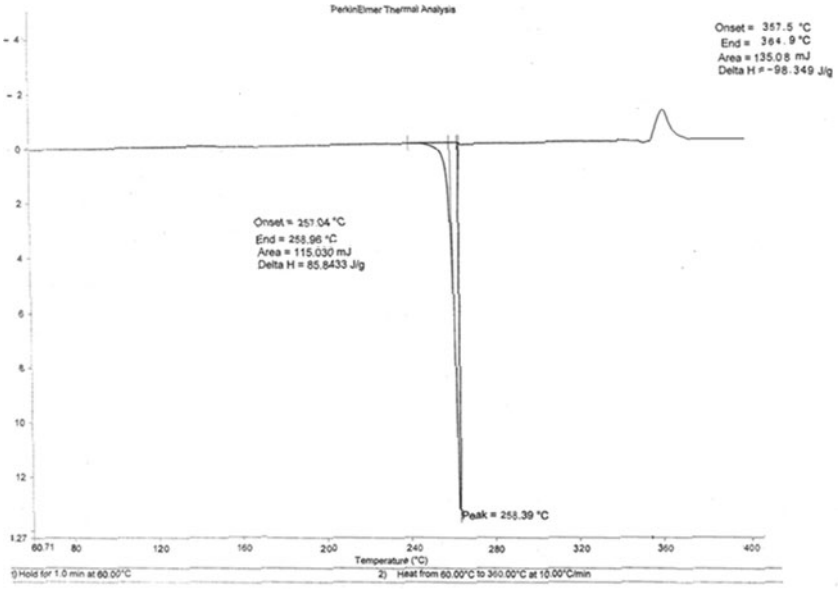
In summary, the heterocyclic o-aminoaldehyde **1** has been utilized for *Friedländer* condensation with active methylenes and cyclicketones to obtained tetracyclic/pentacyclic heterocycles. This heteroannulation has been performed under basic reaction condition. This transformation is scalable and obtained products in high yields. Fluorescence studies of pyrazolonaphthyridine derivatives have been done in organic polar aprotic solvent DMF. All these compounds emits blue light in visible region between 434 and 491 nm with quantum yield (ϕ_F) between 0.188 and 0.240. The interactions of pyrazolonaphthyridines with BSA have been investigated by UV–vis absorption and fluorescence spectroscopy. The $\lambda_{f.\ max.}$ gets blue-shifted upon binding with BSA; however the fluorescence intensity enhancement is linear with the increasing in BSA concentration (**23b**). The pyrazolonaphthyridines are good fluorescence probe, which can be use for studying the protein-ligand interaction and their binding behavior. From TGA and DSC experiment, we conclude that synthesized pyrazolonaphthyridine derivatives are thermally stable up to 350 °C. The efficient blue light emission and thermostability of these compounds may have applications in opto-electronic devices and are addition in the library of new heterocyclic compounds.

Experimental

General

Bovine serum albumin (BSA) and Quinine sulphate was purchased from HiMedi Laboratories Pvt. Ltd. Mumbai (India) and Research-Lab Fin Chem. Industries, Mumbai (India) respectively. All other chemicals, reagents and solvents 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 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 are reported in ppm from internal tetramethylsilane standard and are given in δ-units. High-resolution mass spectra are obtained with a Mat 112 Varian Mat Bremen (70 eV) mass spectrometer. Elemental analyses are

Fig. 3 DSC of compound **23b**



performed on a Hosli CH-Analyzer and are 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 are dissolved in DMF, UV and fluorescence scan are recorded from 200 to 600 nm. The Φ_f relative to quinine sulphate in 1.0×10^{-3} mol L^{-1} H_2SO_4 (Φ_f=0.57) was measured at room temperature by standard literature procedure (32–36). 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. For fluorescence quenching studies, the required amount of BSA solution (in phosphate buffer) and the required amount of pyrazolo[3,4-*h*][1,6]naphthyridines solution in dimethylsulphoxide (DMSO) (1.0×10^{-4} mol L^{-1}) were taken in a 5 ml volumetric flask. Since the pyrazolo[3,4-*h*][1,6]naphthyridines are sparingly soluble in water, their stock solutions were prepared in DMSO, which is used as a solvent for interaction studies of serum albumins [44].

Synthesis

General Procedure for the Synthesis of Compounds **2a–b** A mixture of **1a–b** (0.01 mol) and malononitrile (0.01 mol) was refluxed in ethanol (10 cm^3) in presence of catalytic amount of potassium hydroxide for 25–30 min. After completion of reaction (TLC check), reaction mixture was allowed to cool at room temperature. The separated solid was collected by suction filtration, washed with cold ethanol, dried and recrystallized from Ethanol: DMF (8:2) to yield **2a–b** in 82%–85% yield.

2-Amino-9-(4-chlorophenyl)-7-phyenyl-7H-pyrazolo[3,4-b][1,6]naphthyridine-3-carbonitrile **(2a)** Colorless prisms, yield 0.340 g (85%); mp: 253–254 °C; IR (KBr): 3341, 3268, 2926, 2242, 1628, 1413 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ, 7.28–7.56 (m, 5H, Ar-H), 7.72 (s, 2H, -NH_2), 8.13 (s, 1H, Ar-H), 8.31 (d, 2H, J=8.4 Hz, Ar-H), 8.51 (s,1H, Ar-H), 8.90 (b, 2H, J=8.4 Hz, Ar-H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ, 109.27, 110.39, 116.87, 118.34, 121.24 (2 C's), 125.48, 127.51, 128.39 (2 C's), 129.42 (2 C's), 131.43, 132.23 (2 C's), 134.14, 137.28, 142.31, 143.83, 148.02, 149.37, 158.96 ppm; ms: *m/z* (%) 396 [M^+] (100), 398 [M + 2] (27). *Anal.*Calcd. for $C_{22}H_{13}N_6Cl$ (396.84): C, 66.58; H, 3.29; N, 21.18. Found: C, 66.60; H, 3.32; N, 21.20.

2-Amino-9-(4-bromophenyl)-7-phyenyl-7H-pyrazolo[3,4-b][1,6]naphthyridine-3-carbonitrile **(2b)** Colorless prisms, 0.365 g (82%); mp: 256–257 °C; IR (KBr): 3341, 3268, 2926, 2242, 1628, 1413 cm^{-1}; ^{1}H NHR (300 MHz, DMSO-d_6): δ, 7.28–7.56 (m, 5H, Ar-H), 7.72 (s, 2H, -NH_2), 8.13 (s, 1H, Ar-H), 8.31 (d, 2H, J=8.4 Hz, Ar-H), 8.51 (s, 1H, Ar-H), 8.90 (b, 2H, J=8.4 Hz, Ar-H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ, 109.27, 110.39, 116.87, 118.34, 121.24 (2 C's), 125.48, 127.51, 128.39 (2 C's), 129.42 (2 C's), 131.43, 132.23 (2 C's), 134.14, 137.28, 142.31,

Table 3 The Photophysical data for electronic absorption ($\lambda_{abs.\ max.}$), fluorescence ($\lambda_{f.\ max.}$) and quantum yield (ϕ_F) of pyrazolo[3,4-*h*][1,6] naphthyridines for 0.01 M Conc. at room temp in DMF

Comp.	$\lambda_{Abs.}$ (nm)	$\lambda f._{max}$ (nm)	Quantum yield (ϕ_f)
2a	326	434	0.189
2b	337	451	0.197
4a	353	454	0.198
4b	361	467	0.201
4c	346	465	0.198
4d	354	468	0.202
5a	349	452	0.196
5b	355	461	0.197
7a	370	434	0.188
7b	357	448	0.191
7c	360	442	0.192
7d	358	463	0.198
9a	355	445	0.188
9b	354	449	0.189
11a	357	444	0.194
11b	343	447	0.188
11c	357	447	0.190
11d	354	451	0.188
11e	356	450	0.189
11f	354	451	0.190
13a	355	463	0.193
13b	369	469	0.200
15a	363	452	0.194
15b	356	463	0.201
15c	345	471	0.212
15d	348	469	0.206
17a	376	453	0.190
17b	381	461	0.198
17c	390	457	0.196
17d	394	468	0.208
19a	382	447	0.189
19b	377	464	0.202
19c	393	458	0.212
19d	388	472	0.216
21a	383	473	0.214
21b	369	482	0.220
23a	357	485	0.221
23b	349	491	0.240
23c	355	459	0.196
23d	371	463	0.192
23e	358	455	0.188
23f	366	469	0.198

143.83, 148.02, 149.37, 158.96 ppm; ms: *m*/*z* (%) 441 [M^+] (94) 443 [M + 2] (91). *Anal*.Calcd. for $C_{22}H_{13}N_6Cl$ (396.84): C, 66.58; H, 3.29; N, 21.18. Found: C, 66.60; H, 3.32; N, 21.20.

General Procedure for the Synthesis of Compounds **4a–d** A mixture of **1a–b** (0.01 mol) and acetylacetone **3a**, ethyl-acetoacetate **3b** (0.01 mol) were refluxed in ethanol (10 cm^3) in presence of catalytic amount of potassium hydroxide for 25–30 min. after completion of reaction (TLC check), reaction mixture was allowed to cool at room temperature. The separated solid was collected by suction filtration, washed with cold ethanol, dried and recrystallized from Ethanol: DMF (8:2) to obtain compounds **4a–d** in 79–84% yield.

1-(9-(4-Chlorophenyl)-2-methyl-7-phenyl-7H-pyrazolo[3,4-b][1,6]naphthyridine-3-yl)ethanone **(4a)** White solid, 0.334 g (81%); mp: 247–248 °C; IR (KBr): 2966, 1715, 1618, 1,569 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ, 2.48 (s, 3H, -CH_3), 2.51 (s, 3H, -CH_3), 7.37–7.54 (m, 5H, Ar-H), 8.19 (s, 1H, Ar-H), 8.32 (d, 2H, J=8.6 Hz, Ar-H), 8.54 (s, 1H, Ar-H), 8.83 (d, 2H, J=8.6 Hz, Ar-H) ppm; ms: *m*/*z* (%) 412 [M^+] (98), 414 [M + 2] (29). *Anal*.Calcd. for $C_{24}H_{17}N_4ClO$ (412.88): C, 69.81; H, 4.14; N, 13.57. Found: C, 69.83; H, 4.17; N, 13.58.

1-(9-(4-Bromophenyl)-2-methyl-7-phenyl-7H-pyrazolo[3,4-b][1,6]naphthyridine-3-yl)ethanone **(4b)** White solid, 0.362 g (79%); mp: 250–251 °C; IR (KBr): 2966, 1715, 1618, 1569 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ, 2.48 (s, 3H, -CH_3), 2.51 (s, 3H, -CH_3), 7.37–7.54 (m, 5H, Ar-H), 8.19 (s, 1H, Ar-H), 8.32 (d, 2H, J=8.6 Hz, Ar-H), 8.54 (s, 1H, Ar-H), 8.83 (d, 2H, J=8.6 Hz, Ar-H) ppm; ms: *m*/*z* (%) 457 [M^+] (100), 459 [M + 2] (94). *Anal*.Calcd. for $C_{24}H_{17}N_4BrO$ (457.33): C, 63.02; H, 3.74; N, 12.24. Found: C, 63.04; H, 3.76; N, 12.26.

Ethyl-9-(4-chlorophenyl)-2-methyl-7-phenyl-7H-pyrazolo[3,4-b][1,6]naphthyridine-3-carboxylate **(4c)** White solid, 0.375 g (84%); mp: 258–259 °C; IR (KBr): 2912, 1738, 1604,1522 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ, 1.24 (t, 3H, J=4.2 Hz), 2.25 (s, 3H, -CH_3), 4.19 (q, 2H, J=4.2 Hz), 7.36–7.52 (m, 5H, Ar-H), 8.13 (s, 1H, Ar-H), 8.31 (d, 2H, J=8.4 Hz, Ar-H), 8.56 (s, 1H, Ar-H), 8.89 (d, 2H, J=8.4 Hz, Ar-H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ, 16.23, 21.34, 61.91, 69.03, 108.47, 120.39, 121.44 (2 C's), 125.32, 127.43, 128.97 (2 C's), 129.32 (2 C's), 131.41, 132.33 (2 C's), 133.66, 136.70, 142.16, 146.52, 147.92, 148.61, 150.43, 163.61 ppm; ms: *m*/*z* (%) 442 [M^+] (100), 444 [M + 2] (28). *Anal*.Calcd. for $C_{25}H_{19}N_4ClO_2$ (442.91): C, 67.79; H, 4.31; N, 12.64. Found: C, 67.81; H, 4.30; N, 12.68.

Ethyl-9-(4-bromophenyl)-2-methyl-7-phenyl-7H-pyrazolo[3,4-b][1,6]naphthyridine-3-carboxylate **(4 d)** Colorless prisms, 0.392 g (80%); mp: 257–258 °C; IR (KBr): 2912, 1738, 1604,1522 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ,

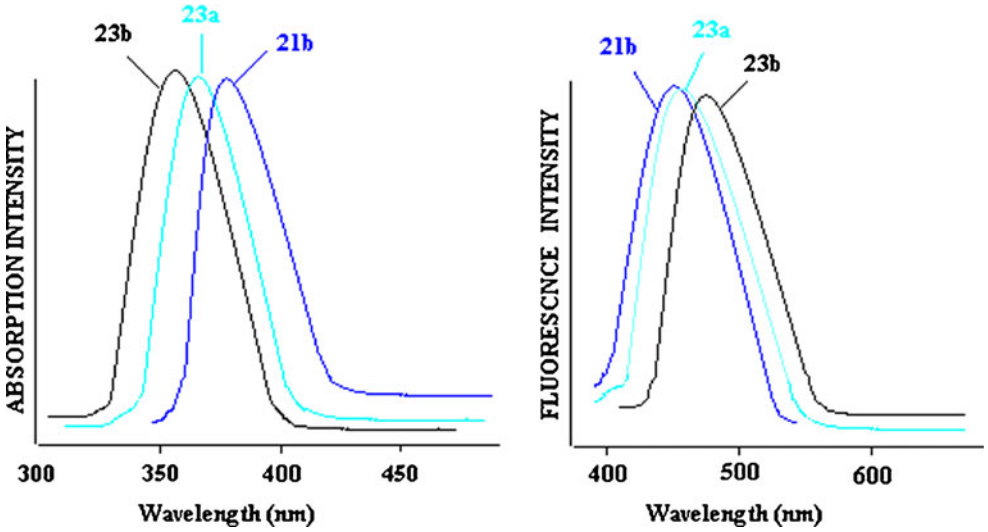


Fig. 4 The absorption ($\lambda_{ab\ max}$) and fluorescence ($\lambda_{f\ max}$) spectra (λ_{ext}=380 nm) of compounds **21b**, **23a** and **23b** respectively

1.24 (t, 3H, J=4.2 Hz), 2.25 (s, 3H, -CH_3), 4.19 (q, 2H, J=4.2 Hz), 7.36–7.52 (m, 5H, Ar-H), 8.13 (s, 1H, Ar-H), 8.31 (d, 2H, J=8.4 Hz, Ar-H), 8.56 (s, 1H, Ar-H), 8.89 (d, 2H, J=8.4 Hz, Ar-H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ, 16.23, 21.34, 61.91, 69.03, 108.47, 120.39, 121.44 (2 C's), 125.32, 127.43, 128.97 (2 C's), 129.32 (2 C's), 131.41, 132.33 (2 C's), 133.66, 136.70, 142.16, 146.52, 147.92, 148.61, 150.43, 163.61 ppm; ms: *m/z* (%) 487 [M^+] (100), 489 [M + 2] (96). *Anal.* Calcd. For $C_{25}H_{19}N_4BrO_2$ (487.36): C, 61.60; H, 3.92; N, 11.49. Found: C, 61.64; H, 3.93; N, 11.52.

General Procedure for the Synthesis of Compounds **5a–b** A mixture of **1a–b** (0.01 mol) and acetone (0.01 mol) in ethanolic potassium hydroxide solution (10 cm^3, 2%) were reflux for 25–30 min (TLC check). The mixture was allowed to cool at room temperature. The separated solid was collected by suction filtration, washed with cold ethanol, dried and recrystallized from Ethanol: DMF (9:1) to furnish compounds **5a–b** in 82% yield.

Table 4 Absorption maximum ($\lambda_{abs.\ max.}$), fluorescence emission maximum ($\lambda_{f.}$ max.) and fluorescence quantum yield (ϕ_F) of pyrazolo [3,4-*h*][1,6]naphthyridine (in phosphate buffer (pH, 7.4) and BSA (5.0×10^{-6} mol L^{-1})

Compound	$\lambda_{abs.\ max.}$ (nm)		$\lambda_{f.\ max.}$ (nm)		ϕ_F (±0.002)	
	Buffer	BSA	Buffer	BSA	Buffer	BSA
4d	318	320	473	417	0.181	0.210
7d	316	319	460	404	0.172	0.204
11f	319	322	442	398	0.169	0.201
13b	327	325	455	418	0.190	0.213
15d	333	329	448	409	0.179	0.209
17d	977	379	454	416	0.188	0.224
19d	369	371	449	424	0.214	0.251
21b	352	355	463	427	0.223	0.267
23a	339	341	467	433	0.242	0.277
23b	322	325	472	440	0.257	0.287

9-(4-chlorophenyl)-2-methyl-7-phenyl-7H-pyrazolo[3,4-b][1,6]naphthyridine **(5a)** Colorless solid, 0.305 g (82%); mp: 177–178 °C; IR (KBr): 2929, 1622, 1508, 1423 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ, 2.82 (s, 3H, CH_3), 7.37 (d, 1H, J=7.4 Hz, Ar-H), 7.35–7.58 (m, 5H, Ar-H), 8.21 (d, 1H, J=7.4 Hz, Ar-H), 8.26 (d, 2H, J=8.4 Hz, Ar-H), 8.54 (d, 2H, J=8.4 Hz, Ar-H), 8.82 (s, 1H, Ar-H) ppm; ms: *m/z* (%) 370 [M^+] (100), 372 [M + 2] (31). *Anal.* Calcd. for $C_{22}H_{15}N_4Cl$ (370.84): C, 71.24; H, 4.07; N, 15.10. Found: C, 71.27; H, 4.09; N, 15.12.

9-(4-Bromophenyl)-2-methyl-7-phenyl-7H-pyrazolo[3,4-b][1,6]naphthyridine **(5b)** Colorless solid, 0.342 g (82%); mp: 180–181 °C; IR (KBr): 2929, 1622, 1508, 1423 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ, 2.82 (s, 3H, CH_3), 7.37 (d, 1H, J=7.4 Hz, Ar-H), 7.35–7.58 (m, 5H, Ar-H), 8.21 (d, 1H, J=7.4 Hz, Ar-H), 8.26 (d, 2H, J=8.4 Hz, Ar-H), 8.54 (d, 2H, J=8.4 Hz, Ar-H), 8.82 (s, 1H, Ar-H) ppm; ms: *m/z* (%) 415 [M^+] (100), 417 [M + 2] (93). *Anal.* Calcd. for $C_{22}H_{15}N_4Br$ (415.30): C, 63.62; H, 3.63; N, 13.48. Found: C, 63.65; H, 3.64; N, 13.49.

General Procedure for the Synthesis of Compounds **7a–d** A mixture of **1a–b** (0.01 mol) and ethylcynoacetate **6a**, diethylmalonate **6b** (0.01 mol) were refluxed in ethanol (10 cm^3) in presence of catalytic amount of potassium hydroxide for 25–30 min. after completion of reaction (TLC check), reaction mixture was allowed to cool at room temperature. The separated solid was collected by suction

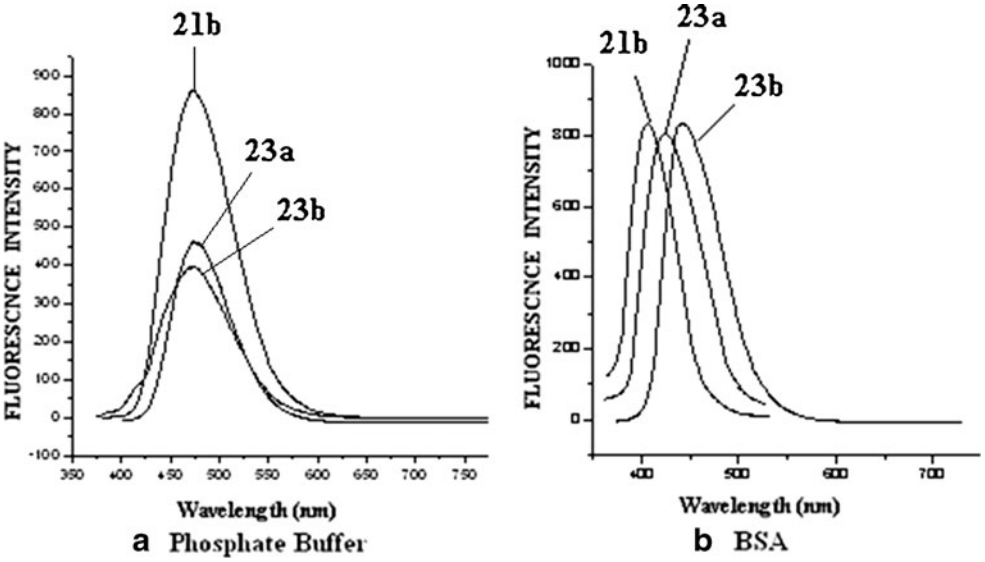


Fig. 5 Comparative fluorescence ($\lambda_{f\ Max.}$) spectra (λ_{ext}=350 nm) of **21b**, **23a**, and **23b**: A] In Phosphate Buffer, B] In BSA

filtration, washed with cold ethanol, dried and recrystallized from Ethanol: DMF (9:1) to obtain compounds **7a–d** in 78%–82% yield.

9-(4-Chlorophenyl)-2,7-dihydro-2-oxo-7-phenyl-7H-pyrazolo [3,4-b][1,6]naphthyridine-3-carbonitrile **(7a)** Colorless solid, 0.314 g (79%); mp: 261–262 °C; IR (KBr): 3412, 2922, 2212, 1672, 1603, 1406, cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ, 7.38–7.54 (m, 5H, Ar-H), 8.19 (d, 2H, J=8.2 Hz, Ar-H), 8.28 (s, 1H, -NH), 8.64 (d, 2H, J=8.2 Hz, Ar-H), 8.74 (s, 1H, Ar-H), 8.87 (s, 1H, Ar-H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ, 106.32, 108.71, 114.71, 115.24, 118.81, 121.35 (2 C's), 126.44, 128.9 (2 C's), 129.52 (2 C's), 131.26, 132.17 (2 C's), 135.12, 139.93, 147.35, 149.41, 150.90, 152.33, 169.66 ppm; ms: *m/z* (%) 397 [M^+] (100), 399 [M + 2] (33). *Anal*. Calcd. for $C_{22}H_{12}N_5ClO$ (397.83): C, 66.41; H, 3.03; N, 17.59. Found: C, 66.44; H, 3.07; N, 17.61.

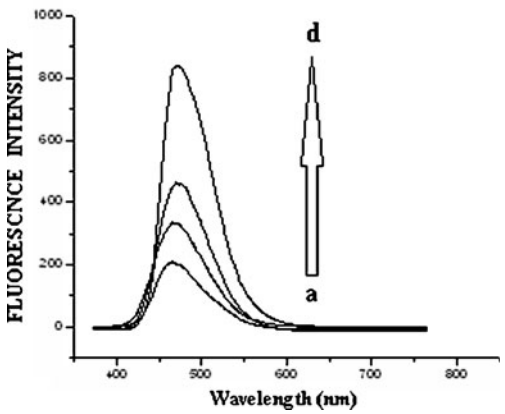


Fig. 6 Fluorescence emission spectra (λ_{ext}=350 nm) of **23b** with increasing BSA Concentration; curves a-d correspond to [BSA] 1.0, 2.0, 3.0, and 4.0 ($\times 10^{-6}$ mol L^{-1}), respectively

9-(4-Bromophenyl)-2,7-dihydro-2-oxo-7-phenyl-7H-pyrazolo[3,4-b][1,6]naphthyridine-3-carbonitrile **(7b)** Colorless solid, 0.347 g (78%); mp: 264–265 °C; IR (KBr): 3412, 2922, 2212, 1672, 1603, 1406 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ, 7.38–7.54 (m, 5H, Ar-H), 8.19 (d, 2H, J=8.2 Hz, Ar-H), 8.28 (s, 1H, -NH), 8.64 (d, 2H, J=8.2 Hz, Ar-H), 8.74 (s, 1H, Ar-H), 8.87 (s, 1H, Ar-H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ, 106.32, 108.71, 114.71, 115.24, 118.81, 121.35 (2 C's), 126.44, 128.91 (2 C's), 129.52 (2 C's), 131.26, 132.17 (2 C's), 135.12, 139.93, 147.35, 149.41, 150.90, 152.33, 169.66 ppm; ms: *m/z* (%) 442 [M^+] (100), 444 [M + 2] (95). *Anal*. Calcd. for $C_{22}H_{12}N_5BrO$ (442.28): C, 59.74; H, 2.72; N, 15.82. Found: C, 59.76; H, 2.75; N, 15.84.

Ethyl-9-(4-chlorophenyl)-2,7-dihydro-2-oxo-7-phenyl-7H-pyrazolo[3,4-b][1,6]naphthyridine-3-carboxylate **(7c)** Colorless solid, 0.367 g (82%); mp: 244–445 °C; IR (KBr): 3369, 3012, 2968, 1741, 1669, 1598, 1420 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ, 1.42 (t, 3H, J=7.2 Hz, CH_3), 4.49 (q, 2H, J=7.2 Hz, CH_2), 7.38–7.52 (m, 5H, Ar-H), 8.28 (s, 1H, NH), 8.31 (d, 2H, J=8.4 Hz, Ar-H), 8.51(s, 1H, Ar-H), 8.84 (s, 1H, Ar-H), 9.01 (d, 2H, J=8.4 Hz, Ar-H) ppm; ms: *m/z* (%) 444 [M^+] (100), 446 [M + 2] (27). *Anal*. calcd. for $C_{24}H_{17}N_4O_3Cl$ (444.88): C, 64.79; H, 3.84; N, 12.58. Found: C, 64.81; H, 3.86; N, 12.61.

Ethyl-9-(4-bromophenyl)-2,7-dihydro-2-oxo-7-phenyl-7H-pyrazolo[3,4-b][1,6]naphthyridine-3-carboxylate **(7d)** Colorless solid, 0.389 g (79%); mp: 243–244 °C; IR (KBr): 3369, 3012, 2968, 1741, 1669, 1598, 1420 cm^{-1}; ^1H NMR

(300 MHz, DMSO-d_6): δ, 1.42 (t, 3H, J=7.2 Hz, CH_3), 4.49 (q, 2H, J=7.2 Hz, CH_2), 7.38–7.52 (m, 5H, Ar-H), 8.28 (s, 1H, NH), 8.31 (d, 2H, J=8.4 Hz, Ar-H), 8.51 (s, 1H, Ar-H), 8.84 (s, 1H, Ar-H), 9.01 (d, 2H, J=8.4 Hz, Ar-H) ppm; ms: *m/z* (%) 489 [M^+] (100), 491 [M + 2] (96). *Anal*. calcd. for $C_{24}H_{17}N_4O_3Br$ (489.33): C, 58.90; H, 3.49; N, 11.44. Found: C, 58.93; H, 3.52; N, 11.47.

General Procedure for the Synthesis of Compounds **9a–b** A mixture of **1a–b** (0.01 mol) and cyclopentanone **8** (0.01 mol) in ethanolic potassium hydroxide solution (10 cm^3, 2%) was refluxed for 25–30 min. after completion of reaction (TLC check), reaction mixture was allowed to cool at room temperature. The separated solid was collected by suction filtration, washed with cold ethanol, dried and recrystallized from Ethanol: DMF (9:1) to obtain compounds **9a–b** in 79–80% yield.

1-(4-Chlorophenyl)-3-phenyl-3,7,8,9-tetrahydrocyclopenta [b]pyrazolo[3,4-h][1,6]naphthyridine **(9a)** Colorless solid, 0.314 g (79%); mp: 188–189 °C; IR (KBr): 2942, 2914, 1621, 1562, 1437 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ, 2.42 (m, 2H, CH_2), 3.08 (t, 2H, J=6.2 Hz, CH_2), 3.19 (t, 2H, J=7.8 Hz, CH_2), 7.33–7.52 (m, 5H, Ar-H), 8.29 (s, 1H, Ar-H), 8.37 (d, 2H, J=8.4 Hz, Ar-H), 8.55 (s, 1H, Ar-H), 9.04 (d, 2H, J=8.4 Hz, Ar-H) ppm; ms: *m/z* (%) 396 [M^+] (100), 398 [M + 2] (29). *Anal.* Calcd. For $C_{24}H_{17}N_4Cl$ (396.88): C, 72.62; H, 4.31; N, 14.11. Found: C, 72.65; H, 4.33; N, 14.14.

1-(4-Bromophenyl)-3-phenyl-3,7,8,9-tetrahydrocyclopenta [b]pyrazolo[3,4-h][1,6]naphthyridine **(9b)** Colorless solid, 0.354 g (80%); mp: 182–183 °C; IR (KBr): 2942, 2914, 1621, 1562, 1437 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ, 2.42 (m, 2H, CH_2), 3.08 (t, 2H, J=6.2 Hz, CH_2), 3.19 (t, 2H, J=7.8 Hz, CH_2), 7.33–7.52 (m, 5H, Ar-H), 8.29 (s, 1H, Ar-H), 8.37(d, 2H, J=8.4 Hz, Ar-H), 8.55 (s, 1H, Ar-H), 9.04 (d, 2H, J=8.4 Hz, Ar-H) ppm; ms: *m/z* (%) 441 [M^+] (100), 443 [M + 2] (96). *Anal.* Calcd. For $C_{24}H_{17}N_4Br$ (441.33): C, 65.31; H, 3.87; N, 12.68. Found: C, 65.35; H, 3.90; N, 12.71.

General Procedure for the Synthesis of Compounds **11a–f** A mixture of **1a–b** (0.01 mol), and cyclohexanone **10a** and 2/3-methylcyclohexanones **10b–c** (0.01 mol) in ethanolic potassium hydroxide solution (10 cm^3, 2%) was refluxed for 25–30 min, after completion of reaction (TLC check), reaction mixture was allowed to cool at room temperature. The separated solid was collected by suction filtration, washed with cold ethanol, dried and recrystallized from Ethanol: DMF (8:2) to obtain compounds **11a–f** in 79%–84% yield.

1-(4-Chlorophenyl)-3-phenyl-7,8,9,10-tetrahydro-3H-benzo [b]pyrazolo[3,4-h][1,6]- naphthyridine **(11a)** Colorless prisms, 0.345 g (84%); mp: 147–148 °C; IR (KBr): 3015, 2942, 1622, 1560, 1442 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ, 1.79 (m, 2H, CH_2), 1.94 (m, 2H, CH_2), 2.59 (t, 2H, J=6.0 Hz, CH_2), 2.94 (t, 2H, CH_2), 7.34–7.52 (m, 5H, Ar-H), 8.17 (s, 1H, Ar-H), 8.35 (d, 2H, J=8.6 Hz, Ar-H), 8.49 (s, 1H, Ar-H), 8.89 (b, 2H, J=8.6 Hz, Ar-H) ppm; ms: *m/z* (%) 410 [M^+] (100), 412 [M + 2] (29). *Anal.* Calcd. For $C_{25}H_{19}N_4Cl$ (410.91): C, 73.07; H, 4.65; N, 13.62. Found: C, 73.10; H, 4.66; N, 13.66.

1-(4-Bromophenyl)-3-phenyl-7,8,9,10-tetrahydro-3H-benzo [b]pyrazolo[3,4-h][1,6]- naphthyridine **(11b)** Colorless prisms, 0.361 g (79%); mp: 145–146 °C; IR (KBr): 3015, 2942, 1622, 1560, 1442 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ, 1.79 (m, 2H, CH_2), 1.94 (m, 2H, CH_2), 2.59 (t, 2H, J=6.0 Hz, CH_2), 2.94 (t, 2H, CH_2), 7.34–7.52 (m, 5H, Ar-H), 8.17 (s, 1H, Ar-H), 8.35 (d, 2H, J=8.6 Hz, Ar-H), 8.49 (s, 1H, Ar-H), 8.89 (b, 2H, J=8.6 Hz, Ar-H) ppm; ms: *m/z* (%) 455 [M^+] (96), 457 [M + 2] (89). *Anal.* Calcd. For $C_{25}H_{19}N_4Br$ (455.36): C, 65.93; H, 4.20; N, 12.29. Found: C, 65.96; H, 4.22; N, 12.33.

1-(4-Chlorophenyl)-10-methyl-3-phenyl-7,8,9,10-tetrahydro-3H-benzo[b]pyrazolo[3,4-h][1,6]- naphthyridine **(11c)** Colorless prisms, 0.344 g (81%); mp: 138–139 °C; IR (KBr): 3015, 2942, 1622, 1560, 1442 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ, 1.32 (d, 3H, J=5.6 Hz, CH_3), 1.81 (m, 1H, CH), 1.87 (m, 1H, CH), 1.92 (m, 1H, CH), 2.07 (m, 1H, CH), 2.54 (m, 1H, CH), 2.61 (m, 1H, CH), 2.84 (m, 1H, CH), 7.37–7.55 (m, 5H, Ar-H), 8.29 (s, 1H, Ar-H), 8.33 (d, 2H, J=8.4 Hz, Ar-H), 8.52 (s, 1H, Ar-H), 9.07 (d, 2H, J= 8.4 Hz, Ar-H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ, 22.07, 24.24, 31.33, 31.96, 32.64, 107.81, 121.11 (2 C's), 123.31, 127.24, 128.91 (2 C's), 129.77 (2 C's), 131.17, 132.01 (2 C's), 133.67, 134.49, 134.94, 139.97, 142.87, 147.97, 149.60, 150.50, 162.32 ppm; ms: *m/z* (%) 424 [M^+] (100), 426 [M + 2] (28). *Anal.* Calcd. For $C_{26}H_{21}N_4Cl$ (424.94): C, 73.48; H, 4.97; N, 13.17. Found: C, 73.51; H, 4.99; N, 13.20.

1-(4-Bromophenyl)-10-methyl-3-phenyl-7,8,9,10-tetrahydro-3H-benzo[b]pyrazolo[3,4-h][1,6]- naphthyridine **(11 d)** Colorless solid, 0.377 g (80%); mp: 142–143 °C; IR (KBr): 3015, 2942, 1622, 1560, 1442 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ, 1.32 (d, 3H, J=5.6 Hz, CH_3), 1.81 (m, 1H, CH), 1.87 (m, 1H, CH), 1.92 (m, 1H, CH), 2.07 (m, 1H, CH), 2.54 (m, 1H, CH), 2.61(m, 1H, CH), 2.84 (m, 1H, CH), 7.37–7.55 (m, 5H, Ar-H), 8.29 (s, 1H, Ar-H), 8.33 (d, 2H, J=8.4 Hz, Ar-H), 8.52 (s, 1H, Ar-H), 9.07 (d, 2H, J= 8.4 Hz, Ar-H) ppm; ^{13}C NMR(75 MHz, $CDCl_3$): δ, 22.07, 24.24, 31.33, 31.96, 32.64, 107.81, 121.11 (2Cs), 123.31, 127.24, 128.91 (2Cs), 129.77 (2Cs), 131.17, 132.01 (2Cs), 133.67, 134.49, 134.94, 139.97, 142.87, 147.97, 149.60,

150.50, 162.32 ppm; ms: *m/z* (%) 469 [M^+] (96), 471 [M + 2] (92). *Anal.* Calcd. For $C_{26}H_{21}N_4Br$(469.39): C, 66.52; H, 4.50; N, 11.93. Found: C, 66.54; H, 4.56; N, 11.96.

1-(4-Chlorophenyl)-9-methyl-3-phenyl-7,8,9,10-tetrahydro-3H-benzo[b]pyrazolo[3,4-h][1,6]- naphthyridine **(11e)** Colorless solid, 0.347 g (81%); mp: 146–147 °C; IR (KBr): 3015, 2942, 1622, 1560, 1442 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ, 1.17 (d, 3H, J=6.2 Hz, CH_3), 1.56 (m, 1H, CH), 1.72 (m, 1H, CH), 2.12 (m, 1H, CH), 2.58 (m, 1H, CH), 2.67 (m, 1H, CH), 2.88 (m, 1H, CH), 2.94 (m, 1H, CH), 7.34–7.51 (m, 5H, Ar-H), 8.25 (s, 1H, Ar-H), 8.37 (d, 2H, J=8.4 Hz, Ar-H), 8.56 (s, 1H, Ar-H), 9.02 (d, 2H, J=8.4 Hz, Ar-H) ppm; ms: *m/z* (%) 424 [M^+] (100), 426 [M + 2] (29). *Anal.* Calcd. For $C_{26}H_{21}N_4Cl$ (424.94): C, 73.48; H, 4.97; N, 13.17. Found: C, 73.51; H, 4.99; N, 13.20.

1-(4-Bromophenyl)-9-methyl-3-phenyl-7,8,9,10-tetrahydro-3H-benzo[b]pyrazolo[3,4-h][1,6]- naphthyridine **(11f)** Colorless prisms, 0.372 g (79%); mp: 150–151 °C; IR (KBr): 3015, 2942, 1622, 1560, 1442 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ, 1.17 (d, 3H, J=6.2 Hz, CH_3), 1.56 (m, 1H, CH), 1.72 (m, 1H, CH), 2.12 (m, 1H, CH), 2.58 (m, 1H, CH), 2.67 (m, 1H, CH), 2.88 (m, 1H, CH), 2.94 (m, 1H, CH), 7.34–7.51 (m, 5H, Ar-H), 8.25 (s, 1H, Ar-H), 8.37 (d, 2H, J=8.4 Hz, Ar-H), 8.56 (s, 1H, Ar-H), 9.02 (d, 2H, J=8.4 Hz, Ar-H) ppm; ms: *m/z* (%) 469 [M^+] (98), 471 [M + 2] (83). *Anal*. Calcd. For $C_{26}H_{21}N_4Br$ (469.39): C, 66.52; H, 4.50; N, 11.93. Found: C, 66.54; H, 4.56; N, 11.96.

General Procedure for the synthesis of compounds **13a–b** A mixture of **1a–b** (0.01 mol) and ethyl 2-oxocyclohexane carboxylate **12** (0.01 mol) was refluxed in ethanol (10 cm^3) in presence of catalytic amount of potassium hydroxide for 25–30 min (TLC check). The mixture was then allowed to cool at room temperature and the separated solid was collected by suction filtration, washed with ethanol and dried, to obtain **13a–b** in 82%–83% yield.

Ethyl-1-(4-chlorophenyl)-3-phenyl-7,8,9,10-tetrahydro-3H-benzo[b]pyrazolo[3,4-h][1,6]- naphthyridine-10-carboxylate **(13a)** White solid, 0.396 g (82%); mp: 161–162 °C; IR (KBr): 3035, 2912, 1741, 1612, 1522, 1032 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ, 1.84 (t, 3H, J=6.1 Hz, CH_2), 1.90 (m, 1H, CH), 2.09 (m, 1H, CH), 2.84 (m, 1H, CH), 2.96 (m, 1H, CH), 3.14 (m, 1H, CH), 3.21 (m, 1H, CH), 3.41 (t, 1H, J=6.3 & 4.1 Hz, Ar-H), 4.21 (q, 2H, J=6.1 Hz, CH_2), 7.33–7.51 (m, 5H, Ar-H), 8.34 (d, 2H, J=8.4 Hz, Ar-H), 8.53 (s, 1H, Ar-H), 8.86 (s, 1H, Ar-H), 9.05 (d, 2H, J=8.4 Hz, Ar-H) ppm; ms: *m/z* (%) 482 [M^+] (100), 484 [M + 2] (29). *Anal.* Calcd. For $C_{28}H_{23}N_4O_2Cl$ (482.97): C, 69.62; H, 4.79; N, 11.59. Found: C, 69.64; H, 4.84; N, 11.63.

Ethyl-1-(4-bromophenyl)-3-phenyl-7,8,9,10-tetrahydro-3H-benzo[b]pyrazolo[3,4-h][1,6]- naphthyridine-10-carboxylate **(13b)** white solid, 0.441 g (83%); mp: 166–167 °C; IR (KBr): 3035, 2912, 1741, 1612, 1522, 1032 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ, 1.84 (t, 3H, J=6.1 Hz, CH_2), 1.90 (m, 1H, CH), 2.09(m, 1H, CH), 2.84 (m, 1H, CH), 2.96 (m, 1H, CH), 3.14 (m, 1H, CH), 3.21 (m, 1H, CH), 3.41 (t, 1H, J=6.3 & 4.1 Hz, Ar-H), 4.21 (q, 2H, J=6.1 Hz, CH_2), 7.33–7.51 (m, 5H, Ar-H), 8.34 (d, 2H, J=8.4 Hz, Ar-H), 8.53 (s, 1H, Ar-H), 8.86 (s, 1H, Ar-H), 9.05 (d, 2H, J=8.4 Hz, Ar-H) ppm; ms: *m/z* (%) 527 [M^+] (100), 529 [M + 2] (94). *Anal*. Calcd. For $C_{28}H_{23}N_4O_2Br$ (527.43): C, 63.75; H, 4.39; N, 10.61. Found: C, 63.77; H, 4.42; N, 10.63.

General Procedure for the synthesis of compounds **15a–d** A mixture of **1** (0.01 mol) and dimedone **14a**, 5,5-dimethyl-1,3-dimedone **14b** (0.01 mol) was heated at 140–150 °C for 30–35 min. the solid obtained on cooling was stirred in methanol (10 cm^3) for 15 min. the solid obtain was collected by filtration and washed with cold ethanol (5 cm^3), dried to obtain **15a–d** in 80%–82% yield.

1-(4-Chlorophenyl)-3-phenyl-7,8-dihydro-3H-benzo[b]pyrazolo[3,4-h][1,6]naphthyridine-9(10H)-one **(15a)** Colorless prisms, 0.341 g (80%); mp: 224–225 °C; IR (KBr): 3004, 2958, 1704, 1602, 1445 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ, 2.64 (t, 2H, J=5.4 Hz, CH_2), 2.82 (t, 2H, J=5.4 Hz, CH_2), 3.44 (s, 2H, CH_2), 7.33–7.51 (m, 5H, Ar-H), 8.21 (s, 1H, Ar-H), 8.36 (d, 2H, J=8.6 Hz, Ar-H), 8.52 (s, 1H, Ar-H), 8.89 (d, 2H, J=8.6 Hz, Ar-H) ppm; ms: *m/z* (%) 424 [M^+] (100), 426 [M + 2] (32). *Anal.* Calcd. For $C_{25}H_{17}N_4OCl$ (424.89): C, 70.67; H, 4.02; N, 13.18. Found: C, 70.69; H, 4.06; N, 13.23.

1-(4-Bromophenyl)-3-phenyl-7,8-dihydro-3H-benzo[b]pyrazolo[3,4-h][1,6]naphthyridine-9(10H)-one **(15b)** Colorless prisms, 0.380 g (81%); mp: 229–230 °C; IR (KBr): 3004, 2958, 1704, 1602, 1445 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ, 2.64 (t, 2H, J=5.4 Hz, CH_2), 2.82 (t, 2H, J=5.4 Hz, CH_2), 3.44 (s, 2H, CH_2), 7.33–7.51 (m, 5H, Ar-H), 8.21 (s, 1H, Ar-H), 8.36 (d, 2H, J=8.6 Hz, Ar-H), 8.52 (s, 1H, Ar-H), 8.89 (d, 2H, J=8.6 Hz, Ar-H) ppm; ms: *m/z* (%) 469 [M^+] (100), 471 [M + 2] (93). *Anal.* Calcd. For $C_{25}H_{17}N_4OBr$ (469.34): C, 63.97; H, 3.65; N, 11.93. Found: C, 63.99; H, 3.67; N, 11.96.

1-(4-Chlorophenyl)-7,7-dimethyl-3-phenyl-7,8-dihydro-3H-benzo[b]pyrazolo[3,4-h][1,6]- naphthyridine-9(10H)-one **(15c)** Colorless prisms, 0.371 g (82%); mp: 242–243 °C;

IR (KBr): 3004, 2958, 1704, 1602, 1445 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ, 1.14 (s, 6H, $(CH_3)_2$), 3.12 (s, 2H, CH_2), 3.74 (s, 2H, CH_2), 7.35–7.52 (m, 5H, Ar-H), 8.27 (s, 1H, Ar-H), 8.39 (d, 2H, J=8.6 Hz, Ar-H), 8.54 (s, 1H, Ar-H), 9.01 (d, 2H, J=8.6 Hz, Ar-H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ, 29.93, 29.93, 39.43, 46.36, 58.44, 109.31, 121.21 (2 C's), 122.71, 127.30, 129.11 (2 C's), 129.75 (2 C's), 131.44, 132.21 (2 C's), 133.37, 135.54, 138.07, 140.63, 141.90, 147.65, 148.37, 150.75, 158.28, 210.03 ppm; ms: *m/z* (%) 452 [M^+] (100), 454 [M + 2] (28). *Anal.* Calcd. For $C_{27}H_{21}N_4OCl$ (452.95): C, 71.59; H, 4.66; N, 12.36. Found: C, 71.63; H, 4.68; N, 12.39.

1-(4-Bromophenyl)-7,7-dimethyl-3-phenyl-7,8-dihydro-3H-benzo[b]pyrazolo[3,4-h][1,6]- naphthyridine-9(10H)-one **(15 d)** Colorless solid, 0.405 g (81%); mp: 248–249 °C; IR (KBr): 3004, 2958, 1704, 1602, 1445 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ, 1.14 (s, 6H, $(CH_3)_2$), 3.12 (s, 2H, CH_2), 3.74 (s, 2H, CH_2), 7.35–7.52 (m, 5H, Ar-H), 8.27 (s, 1H, Ar-H), 8.39 (d, 2H, J=8.6 Hz, Ar-H), 8.54 (s, 1H, Ar-H), 9.01 (d, 2H, J=8.6 Hz,Ar-H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ, 29.93, 29.93, 39.43, 46.36, 58.44, 109.31, 121.21 (2 C's), 122.71, 127.30, 129.11 (2 C's), 129.75 (2 C's), 131.44, 132.21 (2 C's), 133.37, 135.54, 138.07, 140.63, 141.90, 147.65, 148.37, 150.75, 158.28, 210.03 ppm; ms: *m/z* (%) 497 [M^+] (100), 499 [M + 2] (90). *Anal.* Calcd. For $C_{27}H_{21}N_4OBr$ (497.40): C, 65.19; H, 4.25; N, 11.25. Found: C, 65.21; H, 4.28; N, 11.28.

General Procedure for the synthesis of compounds **17a–d** A mixture of **1** (0.01 mol) and derivatives of tetralone **16a**, 6-methoxy-1-tetralone **16b** (0.01 mol) in ethanolic potassium hydroxide solution (10 cm^3, 2%) was refluxed for 25–30 min. after completion of reaction (TLC check), reaction mixture was allowed to cool at room temperature. The separated solid was collected by suction filtration, washed with ethanol, dried and recrystallized from Ethanol: DMF (8:2) to furnish compounds **17a–d** in 78%–82% yield.

1-(4-Chlorophenyl)-3-phenyl-7,8-dihydro-3H-naphtho[1,2-b]pyrazolo[3,4-h][1,6]naphthyridine **(17a)** Colorless prisms, 0.358 g (78%); mp: 264–265 °C; IR (KBr): 3012, 2948, 1619, 1477 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ, 2.94 (t, 2H, J=6.2 Hz, CH_2), 3.01 (t, 2H, J=5.6 Hz, CH_2), 7.14–7.31 (m, 4H, Ar-H), 7.38–7.53 (m, 5H, Ar-H), 8.26 (s, 1H, Ar-H), 8.35 (d, 2H, J=8.6 Hz, Ar-H), 8.53 (s, 1H, Ar-H). 8.97 (d, J=8.6 Hz, 2H, Ar-H) ppm; ms: *m/z* (%) 458 [M^+] (100), 460 [M + 2] (29). *Anal.* Calcd. For $C_{29}H_{19}N_4Cl$ (458.95): C, 75.88; H, 4.16; N, 12.20. Found: C, 75.91; H, 4.18; N, 12.23.

1-(4-Bromophenyl)-3-phenyl-7,8-dihydro-3H-naphtho[1,2-b]pyrazolo[3,4-h][1,6]naphthyridine **(17b)** Colorless prisms, 0.404 g (80%); mp: 268–269 °C; IR (KBr): 3012, 2948, 1619, 1477 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ, 2.94 (t, 2H, J=6.2 Hz, CH_2), 3.01 (t, 2H, J=5.6 Hz, CH_2), 7.14–7.31 (m, 4H, Ar-H), 7.38–7.53 (m, 5H, Ar-H), 8.26 (s, 1H, Ar-H), 8.35 (d, 2H, J=8.6 Hz, Ar-H), 8.53 (s, 1H, Ar-H). 8.97 (d, J=8.6 Hz, 2H, Ar-H) ppm; ms: *m/z* (%) 503 [M^+] (100), 505 [M + 2] (96). *Anal.* Calcd. For $C_{29}H_{19}N_4Br$ (503.41): C, 69.18; H, 3.79; N, 11.12. Found: C, 69.21; H, 3.83; N, 11.16.

1-(4-Chlorophenyl)-10-Methoxy-3-phenyl-7,8-dihydro-3H-naphtho[1,2-b]pyrazolo[3,4-h][1,6]- naphthyridine **(17c)** Colorless prisms, 0.401 g (82%); mp: 256–257 °C; IR (KBr): 2994, 2942, 1602, 1567, 1033 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ, 2.94 (t, 2H, J=5.4 Hz, CH_2), 3.04 (t, 2H, J=5.4 Hz, CH_2), 3.86 (s, 3H, $-OCH_3$), 6.84 (dd, 1H, J=8.4 & 2.7 Hz, Ar-H), 7.06 (d, 1H, J=8.4 Hz, Ar-H), 7.18 (d, 1H, J=2.7 Hz, Ar-H), 7.39–7.52 (m, 5H, Ar-H), 8.31 (s, 1H, Ar-H), 8.39 (d, 2H, J=8.2 Hz, Ar-H), 8.56 (s, 1H, Ar-H), 8.89(d, 2H, J=8.2 Hz, Ar-H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ, 31.34, 32.28, 57.42, 107.78, 113.43, 114.61, 120.02, 121.33 (2 C's), 125.36, 127.19, 128.50, 128.94 (2 C's), 129.62 (2 C's), 131.29, 132.33 (2 C's), 133.12, 134.90, 135.46, 138.67, 141.70, 143.12, 147.46, 149.06, 150.17, 158.44, 159.30 ppm; ms: *m/z* (%) 488 [M^+] (100), 490 [M + 2] (29). *Anal.* Calcd. For $C_{30}H_{21}N_4OCl$ (488.98): C, 73.68; H, 4.33; N, 11.45. Found: C, 73.71; H, 4.37; N, 11.48.

1-(4-Bromophenyl)-10-methoxy-3-phenyl-7,8-dihydro-3H-naphtho[1,2-b]pyrazolo[3,4-h][1,6]- naphthyridine **(17d)** White solid, 0.437 g (81%); mp: 263–264 °C; IR (KBr): 2994, 2942, 1602, 1567, 1033 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ, 2.94 (t, 2H, J=5.4 Hz, CH_2), 3.04 (t, 2H, J=5.4 Hz, CH_2), 3.86 (s, 3H, $-OCH_3$), 6.84 (dd, 1H, J=8.4 & 2.7 Hz, Ar-H), 7.06 (d, 1H, J=8.4 Hz, Ar-H), 7.18 (d, 1H, J=2.7 Hz, Ar-H), 7.39–7.52 (m, 5H, Ar-H), 8.31 (s, 1H, Ar-H), 8.39 (d, 2H, J=8.2 Hz, Ar-H), 8.56 (s, 1H, Ar-H), 8.89(d, 2H, J=8.2 Hz, Ar-H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ, 31.34, 32.28, 57.42, 107.78, 113.43, 114.61, 120.02, 121.33(2 C's), 125.36, 127.19, 128.50, 128.94(2 C's), 129.62(2 C's), 131.29, 132.33(2 C's), 133.12, 134.90, 135.46, 138.67, 141.70, 143.12, 147.46, 149.06, 150.17, 158.44, 159.30 ppm; ms: *m/z* (%) 533 [M^+] (100), 535 [M + 2] (95). *Anal.* Calcd. For $C_{30}H_{21}N_4OBr$ (533.43): C, 67.54; H, 3.96; N, 10.49. Found: C, 67.59; H, 3.99; N, 10.53.

General Procedure for the synthesis of compounds **19a–d** A mixture of **1a–b** (0.01 mol) and indanone **18a**, 5, 6-dimethoxy-1-indanone **18b** (0.01 mol) in ethanolic potassium hydroxide solution (10 cm^3, 2%) was refluxed for 25–30 min. after completion of reaction (TLC check), reaction mixture was allowed to cool at room temperature. The

separated solid was collected by suction filtration, washed with cold ethanol, dried and recrystallized from Ethanol: DMF (8:2) to obtain **19a–d** in 81%–85% yield.

1-(4-Chlorophenyl)-3-phenyl-3,7-dihydroindeno[1,2-b] pyrazolo[3,4-h][1,6]naphthyridine **(19a)** Colorless solid, 0.360 g (81%); mp: 233–234 °C; IR (KBr): 3041, 2968, 1609, 1410 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ, 4.08 (s, 2H, CH_2), 7.31–7.43 (m, 5H, Ar-H), 7.47–7.53 (m, 4H, Ar-H), 8.35 (s, 1H, Ar-H), 8.42 (d, 2H, J=8.4 Hz, Ar-H), 8.58 (s, 1H, Ar-H), 9.03 (d, 2H, J=8.4 Hz, Ar-H) ppm; ms: *m/z* (%) 444 [M^+] (100), 446 [M + 2] (29). *Anal.* Calcd. For $C_{28}H_{17}N_4Cl$ (444.93): C, 75.58; H, 3.84; N, 12.58. Found: C, 75.61; H, 3.87; N, 12.61.

1-(4-Bromophenyl)-3-phenyl-3,7-dihydroindeno[1,2-b] pyrazolo[3,4-h][1,6]naphthyridine **(19b)** Colorless solid, 0.410 g (83%); mp: 243–244 °C; IR (KBr): 3041, 2968, 1609, 1410 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ, 4.08 (s, 2H, CH_2), 7.31–7.43 (m, 5H, Ar-H), 7.47–7.53 (m, 4H, Ar-H), 8.35 (s, 1H, Ar-H), 8.42 (d, 2H, J=8.4 Hz, Ar-H), 8.58 (s, 1H, Ar-H), 9.03 (d, 2H, J=8.4 Hz, Ar-H) ppm; ms: *m/z* (%) 489 [M^+] (100), 491 [M + 2] (97). *Anal.* Calcd. For $C_{28}H_{17}N_4Br$ (489.38): C, 68.71; H, 3.49; N, 11.44. Found: C, 68.74; H, 3.52; N, 11.47.

1-(4-Chlorophenyl)-9,10-dimethoxy-3-phenyl-3,7-dihydroindeno[1,2-b]pyrazolo[3,4-h][1,6]- naphthyridine **(19c)** Colorless prisms, 0.431 g (85%); mp: 251–252 °C; IR (KBr): 3012, 2984, 1618, 1558, 1029 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ, 3.89 (s, 3H, -OCH_3), 4.04 (s, 3H, -OCH_3), 3.94 (s, 2H, CH_2), 6.91 (s, 1H, Ar-H), 7.09 (s, 1H, Ar-H), 7.32–7.51 (m, 5H, Ar-H), 8.41 (s, 1H, Ar-H), 8.47 (d, 2H, J=8.4 Hz, Ar-H), 8.56 (s, 1H, Ar-H), 9.01 (d, 2H, J=8.4 Hz, Ar-H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ, 38.91, 56.41, 57.34, 107.45, 113.36, 115.67, 120.71, 121.42 (2 C's), 127.46, 128.90 (2 C's), 129.75 (2 C's), 130.51, 131.76 (2 C's), 132.43, 133.13, 134.82, 135.24, 136.36, 140.70, 143.52, 146.71, 148.09, 149.79, 150.40, 152.44, 159.47 ppm; ms: *m/z* (%) 504 [M^+] (100), 506 [M + 2] (29). *Anal.* Calcd. For $C_{30}H_{21}N_4O_2Cl$ (504.98): C, 71.35; H, 4.18; N, 11.08. Found: C, 71.37; H, 4.21; N, 11.12.

1-(4-Bromophenyl)-9,10-dimethoxy-3-phenyl-3,7-dihydroindeno[1,2-b]pyrazolo[3,4-h][1,6]- naphthyridine **(19d)** Colorless prisms, 0.464 g (84%); mp: 247–248 °C; IR (KBr): 3012, 2984, 1618, 1558, 1029 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ, 3.89 (s, 3H, -OCH_3), 4.04 (s, 3H, -OCH_3), 3.94 (s, 2H, CH_2), 6.91 (s, 1H, Ar-H), 7.09 (s, 1H, Ar-H), 7.32–7.51 (m, 5H, Ar-H), 8.41 (s, 1H, Ar-H), 8.47 (d, 2H, J=8.4 Hz, Ar-H), 8.56 (s, 1H, Ar-H), 9.01 (d, 2H, J=8.4 Hz, Ar-H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ, 38.91, 56.41, 57.34, 107.45, 113.36, 115.67, 120.71, 121.42 (2 C's), 127.46, 128.90 (2 C's), 129.75 (2 C's), 130.51, 131.76 (2 C's), 132.43, 133.13, 134.82, 135.24, 136.36, 140.70, 143.52, 146.71, 148.09, 149.79, 150.40, 152.44, 159.47 ppm; ms: *m/z* (%) 549 [M^+] (100), 551 [M + 2] (95). *Anal.* Calcd. For $C_{30}H_{21}N_4O_2Br$ (549.43): C, 65.57; H, 3.48; N, 10.19. Found: C, 65.60; H, 3.51; N, 10.23.

General Procedure for the synthesis of compounds **21a–b** A mixture of **1a–b** (0.01 mol) and cetralene **20** (0.01 mol) in ethanolic potassium hydroxide solution (10 cm^3, 2%) was refluxed for 25–30 min. after completion of reaction (TLC check), reaction mixture was allowed to cool at room temperature. The separated solid was collected by suction filtration, washed with cold ethanol, dried and recrystallized from Ethanol: DMF (9:1) to obtain compounds **21a–b** in 83% yield.

1-(4-Chlorophenyl)-8-(3,4-dichlorophenyl)-3-phenyl-7,8-dihydro-3H-naphtho[1,2-b]pyrazolo- [3,4-h][1,6] naphthyridine **(21a)** Colorless prisms, 0.503 g (83%); mp: 273–274 °C; IR (KBr): 2995, 2912, 1620, 1412 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ, 2.99 (t, 1H, CH), 3.30 (t, 1H, CH), 3.98 (t, 1H, CH), 7.27–7.34 (m, 4H, Ar-H), 7.37–7.49 (m, 5H, Ar-H), 7.52 (d, 1H, J=3.2 Hz, Ar-H), 7.66 (dd, 1H, J=3.2 & 8.4 Hz, Ar-H), 8.08 (d, 1H, J=8.4 Hz, Ar-H), 8.38 (s, 1H, Ar-H), 8.44 (d, 2H, J=8.6 Hz, Ar-H), 8.49 (s, 1H, Ar-H), 8.91(d, 2H, J=8.4 Hz, Ar-H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ, 42.80, 47.45, 107.57, 120.43, 121.49 (2 C's), 126.37, 126.97, 127.34, 127.89, 128.10, 128.94 (2 C's), 129.41, 129.91 (2 C's), 130.04, 130.82, 130.97, 131.40, 132.07 (2 C's), 132.63, 132.90, 133.84, 134.79, 135.39, 140.70, 141.17, 142.63, 143.52, 146.89, 148.44, 149.88, 159.60 ppm; ms: *m/z* (%) 602 [M^+] (98), 604 [M + 2] (99), 606 [M + 4] (34), 608 [M + 6] (6). *Anal.* Calcd. For $C_{35}H_{21}N_4Cl_3$ (603.94): C, 69.60; H, 3.49; N, 9.27. Found: C, 69.64; H, 3.52; N, 9.31.

1-(4-Bromophenyl)-8-(3,4-dichlorophenyl)-3-phenyl-7,8-dihydro-3H-naphtho[1,2-b]pyrazolo- [3,4-h][1,6] naphthyridine **(21b)** Colorless prisms, 0.540 g (83%); mp: 278–279 °C; IR (KBr): 2995, 2912, 1620, 1412 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ, 2.99 (t, 1H, CH), 3.30 (t, 1H, CH), 3.98 (t, 1H, CH), 7.27–7.34 (m, 4H, Ar-H), 7.37–7.49 (m, 5H, Ar-H), 7.52 (d, 1H, J=3.2 Hz, Ar-H), 7.66 (dd, 1H, J=3.2 & 8.4 Hz, Ar-H), 8.08 (d, 1H, J=8.4 Hz, Ar-H), 8.38 (s, 1H, Ar-H), 8.44 (d, 2H, J=8.6 Hz, Ar-H), 8.49 (s, 1H, Ar-H), 8.91(d, 2H, J=8.4 Hz, Ar-H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ, 42.80, 47.45, 107.57, 120.43, 121.49 (2 C's), 126.37, 126.97, 127.34, 127.89, 128.10, 128.94 (2 C's), 129.41, 129.91 (2 C's), 130.04, 130.82, 130.97, 131.40, 132.07 (2 C's), 132.63, 132.90, 133.84, 134.79, 135.39, 140.70, 141.17, 142.63, 143.52, 146.89, 148.44, 149.88, 159.60 ppm; ms: *m/z* (%) 648 [M^+] (60), 650 [M + 2]

(98), 652 [M + 4] (54), 654 [M + 6] (12). *Anal.* Calcd. For $C_{35}H_{21}N_4Cl_2Br$ (648.39): C, 68.83; H, 3.25; N, 8.63. Found: C, 68.86; H, 3.27; N, 8.66.

General Procedure for the synthesis of compounds **23a–f** A mixture of **1a–b** (0.01 mol) and N-substituted piperidones **22a–c (**0.01 mol) in ethanolic potassium hydroxide solution (10 cm^3, 2%) was refluxed for 25–30 min. after completion of reaction (TLC check), reaction mixture was allowed to cool at room temperature. The separated solid was collected by suction filtration, washed with cold ethanol, dried and recrystallized from Ethanol: DMF (9:1) to obtain compounds **23a–f** in 81%–84% yield.

1-(4-Chlorophenyl)-8-methyl-3-phenyl-7,8,9,10-tetrahydro-3H-2,3,4,8,11-pentaaz-cyclopenta [a]anthracene **(23a)** Colorless prisms, 0.348 g (81%); mp: 260–261 °C; IR (KBr): 3012, 2944, 1627, 1577, 1480 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ, 2.73 (s, 3H, CH_2), 2.89 (t, 2H, J=5.9 Hz, CH_2), 3.04 (t, 2H, J=5.9 Hz, CH_2), 3.84 (s, 2H, CH_2), 7.33–7.51 (m, 5H, Ar-H), 8.36 (s, 1H, Ar-H), 8.47 (d, 2H, J=8.4 Hz, Ar-H), 8.53 (s, 1H, Ar-H), 9.03 (d, 2H, J=8.4 Hz, Ar-H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ, 35.81, 47.09, 56.67, 63.90, 108.31, 119.46, 121.51 (2 C's), 127.40, 128.69 (2 C's), 129.23, 129.94 (2 C's), 131.74, 132.14 (2 C's), 133.80, 136.32, 141.48, 143.61, 147.86, 149.51, 151.33, 159.08 ppm; ms: *m/z* (%) 425 [M^+] (100), 427 [M + 2] (31). *Anal.* Calcd. For $C_{25}H_{20}N_5Cl$ (425.92): C, 70.49; H, 4.72; N, 16.43. Found: C, 70.53; H, 4.75; N, 16.45.

1-(4-Bromophenyl)-8-methyl-3-phenyl-7,8,9,10-tetrahydro-3H-2,3,4,8,11-pentaaz-cyclopenta [a]anthracene **(23b)** Colorless prisms, 0.391 g (83%); mp: 257–258 °C; IR (KBr): 3012, 2944, 1627, 1577, 1480 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ, 2.73 (s, 3H, CH_2), 2.89 (t, 2H, J=5.9 Hz, CH_2), 3.04 (t, 2H, J=5.9 Hz, CH_2), 3.84 (s, 2H, CH_2), 7.33–7.51 (m, 5H, Ar-H), 8.36 (s, 1H, Ar-H), 8.47 (d, 2H, J=8.4 Hz, Ar-H), 8.53 (s, 1H, Ar-H), 9.03 (d, 2H, J=8.4 Hz, Ar-H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ, 35.81, 47.09, 56.67, 63.90, 108.31, 119.46, 121.51 (2 C's), 127.40, 128.69 (2 C's), 129.23, 129.94 (2 C's), 131.74, 132.14 (2 C's), 133.80, 136.32, 141.48, 143.61, 147.86, 149.51, 151.33, 159.08 ppm; ms: *m/z* (%) 470 [M^+] (100), 472 [M + 2] (96). *Anal.* Calcd. For $C_{25}H_{20}N_5Br$ (470.38): C, 63.83; H, 4.28; N, 14.87. Found: C, 63.85; H, 4.31; N, 14.90.

1-[1-(4-Chlorophenyl)-3-phenyl-3,7,9,10-tetrahydro-2,3,4,8,11-pentaazcyclopenta[a]- anthracene-8-yl]ethanone **(23c)** White solid, 0.373 g (82%); mp: 238–239 °C; IR (KBr): 3019, 2956, 1715, 1607, 1484 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ, 2.18 (s, 3H, CH_3), 3.14 (t, 2H, J=6.3 Hz, CH_2), 3.28 (t, 2H, J=6.3 Hz, CH_2), 3.97 (s, 2H, CH_2), 7.34–7.53 (m, 5H, Ar-H), 8.34 (s, 1H, Ar-H), 8.45 (d, 2H, J=8.6 Hz, Ar-H), 8.54 (s, 1H, Ar-H), 9.01 (d, 2H, J=8.6 Hz, Ar-H) ppm; ms: *m/z* (%) 453 [M^+] (100), 455 [M + 2] (29). *Anal.* Calcd. For $C_{26}H_{20}N_5OCl$ (453.94): C, 68.79; H, 4.43; N, 15.42. Found: C, 68.83; H, 4.46; N, 15.45.

1-[1-(4-Bromophenyl)-3-phenyl-3,7,9,10-tetrahydro-2,3,4,8,11-pentaazcyclopenta[a]- anthracene-8-yl]ethanone **(23d)** White solid, 0.418 g (83%); mp: 252–253 °C; IR (KBr): 3019, 2956, 1715, 1607, 1484 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ, 2.18 (s, 3H, CH_3), 3.14 (t, 2H, J=6.3 Hz, CH_2), 3.28 (t, 2H, J=6.3 Hz, CH_2), 3.97(s, 2H, CH_2), 7.34–7.53 (m, 5H, Ar-H), 8.34 (s, 1H, Ar-H), 8.45 (d, 2H, J=8.6 Hz, Ar-H), 8.54 (s, 1H, Ar-H), 9.01 (d, 2H, J=8.6 Hz, Ar-H) ppm; ms: *m/z* (%) 498 [M^+] (98), 500 [M + 2] (92). *Anal.* Calcd. For $C_{26}H_{20}N_5OBr$ (498.39): C, 62.65; H, 4.03; N, 14.04. Found: C, 62.68; H, 4.06; N, 14.09.

1-(4-Chlorophenyl)-3-phenyl-3,7,9,10-tetrahydro-2,3,4,8,11-pentaaz-cyclopenta-[a]anthracene-8-carboxylic acid tert-butyl ester **(23e)** Colorless prisms, 0.433 g (84%); mp: 230–231 °C; IR (KBr): 2998, 2912, 1738, 1620, 1412, 1033 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ, 1.93 (s, 9H, CH_3), 3.18 (t, 2H, J=5.9 Hz, CH_2), 3.28 (t, 2H, J=5.9 Hz, CH_2), 4.11 (s, 2H, CH_2), 7.32–7.51 (m, 5H, Ar-H), 8.37 (s, 1H, Ar-H), 8.46 (d, 2H, J=8.6 Hz, Ar-H), 8.51 (s, 1H, Ar-H), 8.98 (d, 2H, J=8.6 Hz, Ar-H) ppm; ms: *m/z* (%) 511 [M^+] (100), 513 [M + 2] (28). *Anal*. Calcd. For $C_{29}H_{26}N_5O_2Cl$ (512.02): C, 68.02; H, 5.11; N, 13.67. Found: C, 68.06; H, 5.14; N, 13.70.

1-(4-Bromophenyl)-3-phenyl-3,7,9,10-tetrahydro-2,3,4,8,11-pentaaz-cyclopenta[a]-anthracene-8-carboxylicacid tert-butyl ester **(23f)** Colorless prisms, 0.457 g (82%); mp: 242–243 °C; IR (KBr): 2998, 2912, 1738, 1620, 1412, 1033 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ, 1.93 (s, 9H, CH_3), 3.18 (t, 2H, J=5.9 Hz, CH_2), 3.28 (t, 2H, J=5.9 Hz, CH_2), 4.11 (s, 2H, CH_2), 7.32–7.51 (m, 5H, Ar-H), 8.37 (s, 1H, Ar-H), 8.46(d, 2H, J=8.6 Hz, Ar-H), 8.51 (s, 1H, Ar-H), 8.98 (d, 2H, J=8.6 Hz, Ar-H) ppm; ms: *m/z* (%) 556 [M^+] (100), 558 [M + 2] (96). *Anal.* Calcd. For $C_{29}H_{26}N_5O_2Br$ (556.47): C, 62.59; H, 4.70; N, 12.58. Found: C, 62.63; H, 4.74; N, 12.61.

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