Synthesis of new fluorescent pyrazolo[4,3-*a*]acridine derivatives having strong antibacterial activities

Leila Rezaei Daghigh, Mehdi Pordel* and Abolghasem Davoodnia

Department of Chemistry, Mashhad Branch, Islamic Azad University, Mashhad, Iran

New 3*H*-pyrazolo[4,3-*a*]acridine derivatives have been prepared by the reaction of 1-alkyl-5-nitro-1*H*-indazole with phenylacetonitrile and 2-(4-bromophenyl)acetonitrile in basic conditions *via* the nucleophilic substitution of hydrogen and concomitant cyclisation. The new compounds exhibited potent antibacterial activities and their antibacterial activities against Gram positive (*Staphylococcus aureus*, methicillin resistant *S. aureus* and *Bacillus subtilis*) and Gram negative bacterial (*Pseudomonas aeruginosa* and *Escherichia coli*) species were determined. The fluorescence properties of these derivatives were also studied.

Keywords: 5-nitro-1*H*-indazole, nucleophilic substitution of hydrogen, pyrazolo[4,3-*a*]acridine, antibacterial agents, fluorescence, emission and absorption spectra

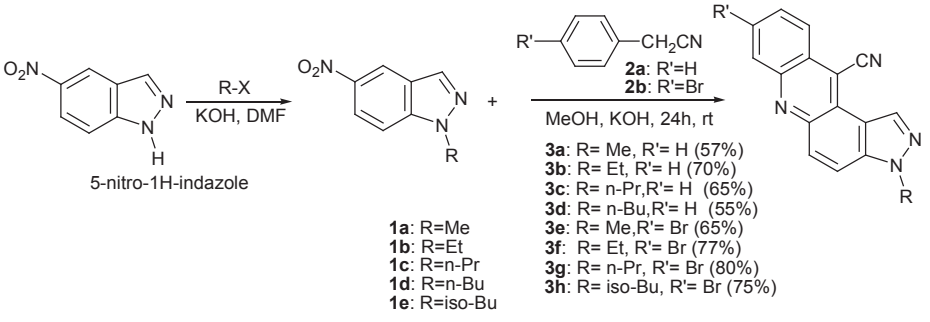
Nitrogen heterocyclic compounds have long interested organic and inorganic researchers because they constitute an important class of natural and non-natural products, many of which exhibit useful biological activities and unique electrical and optical properties.[1–3] Pyrazoles have attracted much attention recently because of their synthetic accessibility and their diverse chemical and biological properties. Some of the most important biological activities of pyrazoles are the effective antirheumatoidal (SC-58635 Celecoxib), antiviral agents (Pyrazomycin), hormone oxytocin agonists (WAY VNA-932) and selective Human C1s inhibitors.[4] In addition, the photophysical properties of pyrazoles have attracted interest in both aqueous and non-aqueous solvents as well as in various microheterogeneous media due to the possibility of charge transfer (CT) emission.[5]

As an important type of tricyclic nitrogen heterocycle, acridine derivatives are one of the oldest classes of photoactive and bioactive compounds that are widely used for the production of dyes and some valuable drugs. In particular, some of them are found to be efficient fluorescent chemosensors for recognition of transition metal ions such as Hg(II)[6] and emitters for luminescence studies,[7] as well as antibacterial,[8,9] antiviral,[10,11] antiprion,[12] and antimalarial[13–17] agents. Some work in these areas continues, but recent research has focused mainly on their utility as anticancer[18,19] and antitumour[20,21] drugs. This is because of the ability of the acridine chromophore to intercalate within the double-stranded DNA structure and inhibit topoisomerase enzymes. A combination of the acridine moiety with the pyrazole nucleus may enhance these properties.

Prompted by this information and in continuation of our research work on the synthesis of fluorescent[22–27] and bioactive[28–31] nitrogen heterocyclic compounds, we aimed to obtain new derivatives of the 3-alkyl-3*H*-pyrazolo[4,3-*a*] acridine-11-carbonitrile, *via* the nucleophilic substitution of hydrogen in 1-alkyl-5-nitro-1*H*-indazoles with phenylacetonitrile and with 2-(4-bromophenyl)acetonitrile in basic solution, and to evaluate their spectroscopic properties and biological activities.

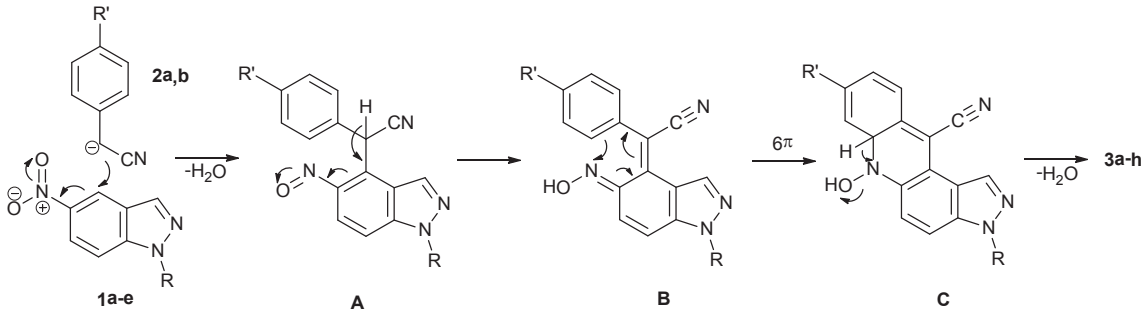
Results and discussion

As depicted in Scheme 1, the synthesis of the new compounds commenced with the preparation of 1-alkyl-5-nitro-1*H*-indazoles **1a–e** from 5-nitro-1*H*-indazole, by treatment with a variety of different alkyl halides in DMF in the presence of KOH, according to a literature method.[32] The reaction of 1-alkyl-5-nitro-1*H*-indazoles with phenylacetonitrile **2a** and with 2-(4-bromophenyl)acetonitrile **2b**, in basic MeOH solution, led to the formation of the new 3-alkyl-3*H*-pyrazolo[4,3-*a*] acridine-11-carbonitriles **3a–h** *via* the nucleophilic substitution of hydrogen.[33] The cyclisation proceeds at room temperature and in good yields (Scheme 1). As we have previously reported,[22–27] these reactions are accomplished by the condensation of nitroarenes with different arylacetonitriles and concomitant cyclisation. The following mechanism is offered for the formation of compounds **3a–h**. The ring closure proceeds *via* an electrocyclic pathway following tautomerism of nitrile **A**, whereby intermediate **B** is converted to **C** followed by elimination of H_2O, to afford **3a–h** (Scheme 2). The simple work-up procedure was performed by filtration of the precipitated product after the mixture was concentrated at reduced pressure.



Scheme 1 Synthesis of new compounds **3a–h.**

* Correspondent. E-mail: mehdipordel58@yahoo.com



Scheme 2 Proposed reaction mechanism for the formation of compounds **3a–h.**

The structure of products **3a–h** was confirmed by NMR and IR spectroscopy in addition to mass spectral and microanalytical data. The spectral details of all these are given in experimental section. For example, in the expanded ^{1}H NMR spectrum of compound **3g**, there is a doublet of doublets at δ 7.85 and two doublet signals at 8.24 and 8.45 ppm attributed to the ring A protons. Two doublet peaks at δ 7.89 and 8.00 are assignable to the two ring C protons and a singlet peak at 9.10 ppm is attributed to the D ring (Fig. 1).

The antibacterial activity of compounds **3a–h** was tested against a panel of strains of Gram positive [*Staphylococcus aureus*, methicillin resistant *S. aureus* (MRSA), clinically isolated *S. aureus* and *Bacillus subtilis* (ATCC 6633)] and Gram negative bacterial [*Pseudomonas aeruginosa* (ATCC 27853) and *Escherichia coli* (ATCC 25922)] species (Table 1) using a broth microdilution method as previously described.[34] Sulfamethoxazole, ampicillin and penicillin G were used as references. The lowest concentration of the antibacterial agent that prevents growth of the test organism, as detected by lack of visual turbidity (matching the negative growth control), is designated the minimum inhibitory concentration (MIC). Experimental details of the tests can be found in our earlier studies.[28–30]

The antimicrobial tests performed on pyrazolo[4,3-*a*]acridine derivatives **3a–h** confirmed that they are super-effective against both Gram-positive and Gram-negative bacteria and some showed greater inhibitory activity against a number of Gram-positive and Gram-negative bacteria than did the well-known antibacterial agents ampicillin and sulfamethoxazole.

Also, the results revealed that compounds **3e–h** in which the R′ substituent is a bromine function displayed greater antibacterial activity than did **3a–d**. Compound **3g** was the most potent of the tested compounds against both Gram-positive and Gram-negative bacteria. We propose that the chain lengths and bromine substituent might change the binding characteristics of ligands to their respective receptors and, thereby, improve the biological activities.

The compounds **3a–h** were characterised by both UV-Vis and fluorescence spectra. The wavelength range of both spectrophotometers used was 200–1000 nm. The fluorescence

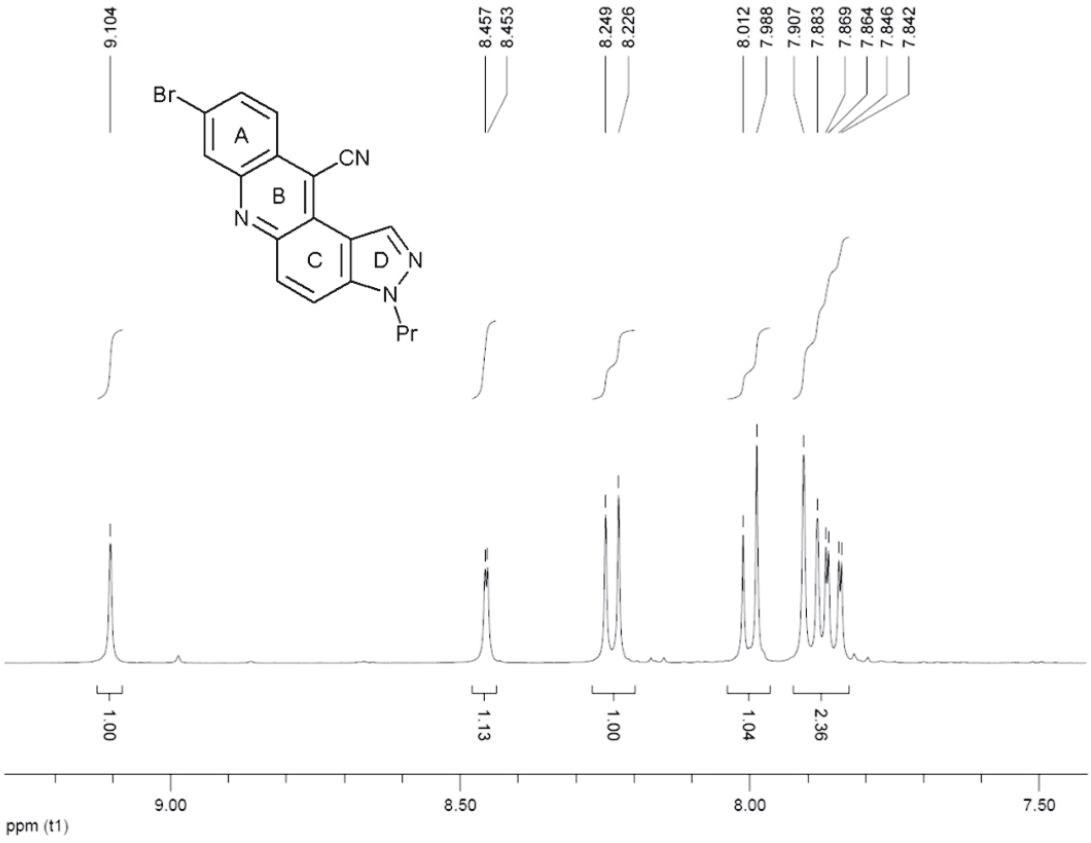


Fig. 1 The expanded ^{1}H NMR spectrum of compound **3g** in the downfield region.

Table 1 Antibacterial activity (MIC, μg mL^{-1}) of references and newly synthesised compounds **3a–h**

Compound	*Staphylococcus aureus* (MRSA)	*Bacillus subtilis* (ATCC 6633)	*Pseudomonas aeruginosa* (ATCC 27853)	*Escherichia coli* (ATCC 25922)
3a	6	10	6	6
3b	3	9	3	3
3c	3	3	3	3
3d	2	4	2	2
3e	2	2	1	1
3f	2	2	1	1
3g	1	0.50	1	1
3h	6	3	3	3
Sulfamethoxazole	16	16	62	16
Ampicillin	62	0.50	125	8
Penicillin G	0.06	8	–	–

absorption and emission spectra of **3a–h** were recorded at concentrations of 1×10^{-5} and 1×10^{-6} mol L^{-1} respectively in dichloromethane (DCM). Figures 2 and 3 show the visible absorption and emission spectra of compounds **3a–h**.

Table 2 shows the wavelengths of maximum absorbance (λ_{abs}/nm), wavelengths of fluorescence excitation (λ_{ex}/nm), wavelengths of fluorescence emission (λ_{flu}/nm) values of extinction coefficient (ε) and fluorescence quantum yield (Φ_F) data. Values of the extinction coefficient (ε) were calculated as the slope of the plot of absorbance *versus* concentration. The fluorescence excitation (λ_{ex}) wavelength at 390 nm (λ_{ex}/nm) was used for all compounds **3a–h**. The fluorescence quantum yields (Φ_F) of compounds **3a–h** were determined *via* comparison methods, using fluorescein as a standard sample in 0.1 M NaOH and MeOH solution.[35] The absorbance and fluorescence spectral properties (Table 2) of compounds **3a–d** as well as **3e–h** are similar to each other, however, the fluorescence intensity of compound **3d**, having a butyl group had the maximal value.

The fluorescence intensity in these compounds can be explained by efficient intramolecular charge transfer (ICT) states from the donor site (endocyclic N) to the acceptor moiety (CN group).[22–27] Scheme 3 shows neutral and charge-separated mesomeric structures of **3a–h.**

The fluorescence absorption and emission spectra of compound **3h** were measured in a variety of solvents such as tetrahydrofuran (THF), dioxane and methanol. As shown in Figs 4 and 5, the fluorescence absorption and emission spectra of **3h** in polar solvents exhibited a bathochromic shift. Increasing solvent polarity stabilises the ICT excited-state molecule relative to the ground-state molecule with the observed redshift of the absorption maximum as the experimentally observed result (Table 3). For example, in Table 3, one can see that in the emission spectrum of **3h**, λ_{flu} shifts from 430 to 458 nm as the solvent is changed from *n*-heptane to methanol.

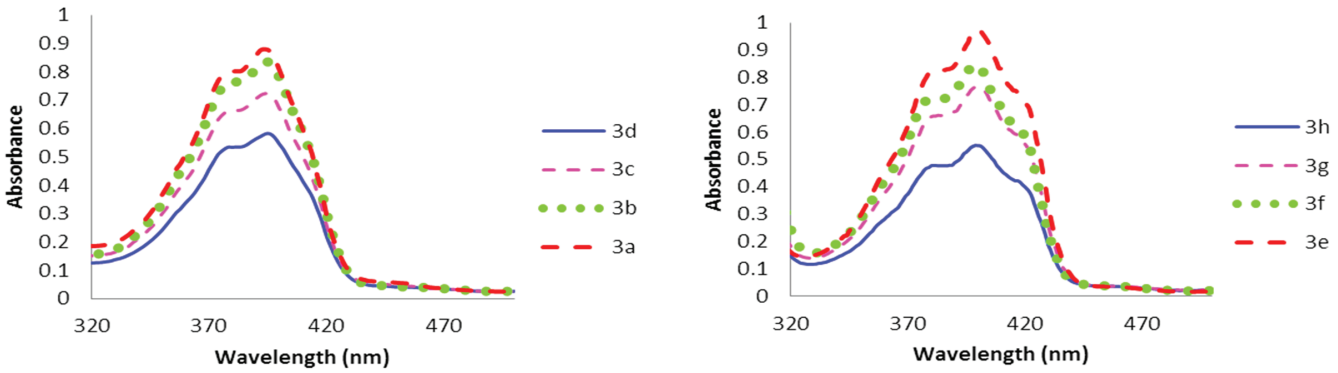


Fig. 2 Visible absorption spectra of compounds **3a–h** in DCM solution (1×10^{-5} mol L^{-1}).

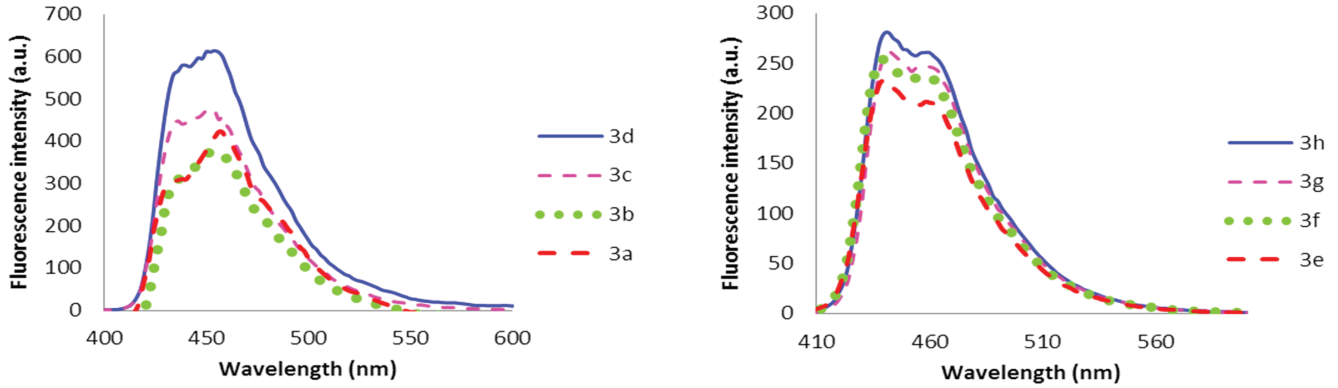


Fig. 3 Emission spectra of compounds **3a–h** in DCM solution (1×10^{-6} mol L^{-1}).

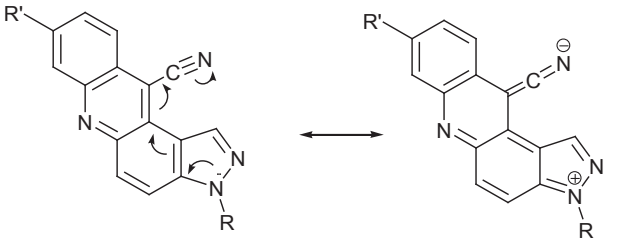
Table 2 Photophysical data for absorption (abs) and fluorescence (flu) of **3a–h**

Dye	3a	3b	3c	3d	3e	3f	3g	3h
λ_{abs}/nm[a]	395	395	395	395	400	398	398	398
$\varepsilon \times 10^{-4}$/(mol L^{-1})$^{-1}$ cm^{-1}[b]	8.7	8.0	7.2	5.5	9.5	8.2	7.3	5.2
λ_{ex}/nm[c]	390	390	390	390	390	390	390	390
λ_{flu}/nm[d]	455	455	455	455	440	440	440	440
Φ_F[e]	0.45	0.47	0.50	0.52	0.36	0.37	0.40	0.42

[a]Wavelengths of maximum absorbance.
[b]Extinction coefficient.
[c]Wavelengths of fluorescence excitation.
[d]Wavelengths of fluorescence emission.
[e]Fluorescence quantum yield.

Table 3 Spectroscopic data for **3h** at 298 K in dependence of the solvent

Solvent	λ_{abs}/nm	λ_{flu}/nm
Acetone	410	456
Dioxane	405	450
Methanol	415	458
n-Heptane	390	430
Toluene	395	440
THF	400	450
DMF	410	456



Scheme 3 Neutral and charge-separated mesomeric structures of **3a–h**.

Experimental

Methanol, *N*,*N*-dimethylformamide (DMF), methyl iodide, ethyl bromide, *n*-propyl bromide, *n*-butyl bromide, isobutyl bromide, phenylacetonitrile and 2-(4-bromophenyl)acetonitrile were purchased from Merck. Potassium hydroxide was purchased from Sigma–Aldrich. All solvents were dried according to standard procedures. Compounds **1a–e** were synthesised as described in the literature.[32] The microorganisms *Bacillus subtilis* ATCC 6633, *Pseudomonas aeruginosa* ATCC 27853 and *Escherichia coli* ATCC 25922 were purchased from the Pasteur Institute of Iran and *S. aureus* methicillin resistant (MRSA) was isolated from different specimens which were referred to the Microbiological Laboratory of Ghaem Hospital of Medical University of Mashhad, Iran and its methicillin resistance was tested according to the NCCLS guidelines.[36]

Absorption and fluorescence spectra were measured on Varian Cary 50-bio UV-Vis spectrophotometer and Varian Cary Eclipse spectrofluorophotometer. UV-Vis and fluorescence scans were recorded from 200 to 1000 nm. Melting points were measured on an Electrothermal type-9100 melting-point apparatus. The IR spectra (as KBr discs) were obtained on a Tensor 27 spectrometer and only noteworthy absorptions are listed. The ^{13}C NMR (100 MHz) and the ^{1}H NMR (400 MHz) were recorded on a Bruker Avance DRX-400 FT spectrometer in $CDCl_3$. Chemical shifts are reported in ppm downfield from TMS as internal standard; coupling constants *J* are given in Hz. The mass spectra were recorded on a Varian Mat, CH-7 instrument at 70 eV. Elemental analysis was performed on a Thermo Finnigan Flash EA microanalyser. All measurements were carried out at room temperature.

Synthesis of compounds (**3a–h**)*; general procedure*

The appropriate 1-alkyl-5-nitro-1*H*-indazoles **1a–e** (10 mmol) and arylacetonitriles **2a–b** (12 mmol) were added with stirring to a solution of KOH (13 g, 238 mmol) in methanol (50 mL). The mixture was stirred at room temperature for 24 h. After concentration at reduced pressure, the precipitate was collected by filtration, washed with water, followed by EtOH, and then air dried to give crude **3a–h**.

*3-Methyl-3*H*-pyrazolo[4,3-*a*]acridine-11-carbonitrile* (**3a**): Shiny yellow needles (EtOH), yield 57%; m.p. 251–253 °C; IR (KBr disk) ν_{max}/cm^{-1} 2223 (CN). ^{1}H NMR ($CDCl_3$): δ 4.30 (3H, s, CH_3), 7.87–7.98 (3H, m, ArH), 8.21 (1H, d, *J*=8.8 Hz, ArH), 8.44 (1H, d, *J*=8.8 Hz, ArH), 8.50 (1H, dd, *J*=8.4, 1.2 Hz, ArH), 9.21 (1H, s, ArH); ^{13}C NMR ($CDCl_3$): δ 38.49, 113.62, 116.80, 117.29, 120.59, 124.16, 127.22, 128.63, 130.28, 135.75, 135.89, 136.51, 136.76, 137.50, 141.94, 147.21 ppm. MS (*m/z*) 258 (M^+). Anal. calcd for $C_{16}H_{10}N_4$ (258.3): C, 74.41; H, 3.90; N, 21.69; found: C, 74.09; H, 3.84; N, 21.43%.

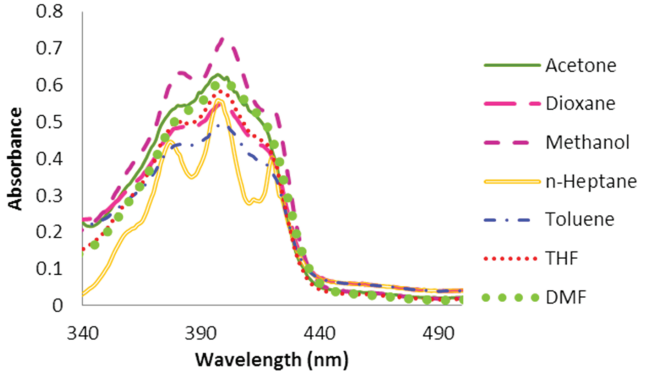


Fig. 4 Visible absorption spectra of compound **3h** in different solvents (1×10^{-5} mol L^{-1}).

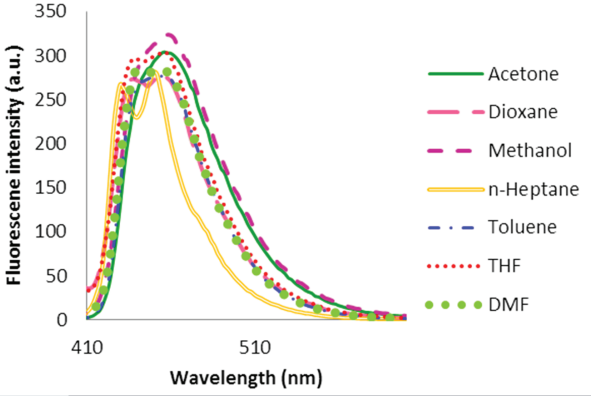


Fig. 5 Emission spectra of compound **3h** in different solvents (1×10^{-6} mol L^{-1}).

*3-Ethyl-3*H-*pyrazolo[4,3-*a*]acridine-11-carbonitrile* (**3b**): Shiny yellow needles (EtOH), yield 70%; m.p. 209–211 °C; IR (KBr disk): ν_{max}/cm^{-1} 2223 (CN). ^{1}H NMR ($CDCl_3$): δ 1.65 (3H, t, *J*=7.6 Hz, CH_2CH_3), 4.62 (2H, q, *J*=7.6 Hz, CH_2CH_3), 7.84–7.94 (3H, m, ArH), 8.13 (1H, d, *J*=9.0 Hz, ArH), 8.39 (1H, d, *J*=9.0 Hz, ArH), 8.45 (1H, dd, *J*=8.0, 1.2 Hz, ArH), 9.18 (1H, s, ArH); ^{13}C NMR ($CDCl_3$): δ 15.50, 44.49, 113.61, 116.40, 117.09, 119.04, 125.76, 127.20, 127.69, 130.10, 134.14, 135.09, 136.61, 136.81, 137.55, 141.83, 147.54; MS (*m/z*) 272 (M^+). Anal. calcd for $C_{17}H_{12}N_4$ (272.3): C, 74.98; H, 4.44; N, 20.57; found: C, 74.62; H, 4.35; N, 20.39%.

*3-Propyl-3*H-*pyrazolo[4,3-*a*]acridine-11-carbonitrile* (**3c**): Shiny yellow needles (EtOH), yield 65%; m.p. 208–209 °C; IR (KBr disk): ν_{max}/cm^{-1} 2225 (CN). ^{1}H NMR ($CDCl_3$): δ 1.03 (3H, t, *J*=7.2 Hz, $CH_2CH_2CH_3$), 2.11 (2H, m, $CH_2CH_2CH_3$), 4.54 (2H, t, *J*=7.2 Hz, $CH_2CH_2CH_3$), 7.87–7.95 (3H, m, ArH), 8.18 (1H, d, *J*=9.0 Hz, ArH), 8.43 (1H, d, *J*=9.0 Hz, ArH), 8.49 (1H, dd, *J*=8.0, 1.2 Hz, ArH), 9.22 (1H, s, ArH); ^{13}C NMR ($CDCl_3$): δ 11.38, 23.76, 51.20, 110.13, 115.54, 117.10, 117.16, 122.53, 124.53, 125.96, 129.34, 129.61, 129.98, 130.32, 135.06, 137.71, 145.98, 147.41; MS (*m/z*) 286 (M^+). Anal. calcd for $C_{18}H_{14}N_4$ (286.3): C, 75.51; H, 4.93; N, 19.57; found: C, 75.32; H, 4.88; N, 19.82%.

*3-Butyl-3*H-*pyrazolo[4,3-*a*]acridine-11-carbonitrile* (**3d**): Shiny yellow needles (EtOH), yield 55%; m.p. 200–201 °C; IR (KBr disk): ν_{max}/cm^{-1} 2225 (CN). ^{1}H NMR ($CDCl_3$): δ 1.01 (3H, t, *J*=7.2 Hz, $CH_2CH_2CH_2CH_3$), 1.43 (2H, m, $CH_2CH_2CH_2CH_3$), 2.05 (2H, m, $CH_2CH_2CH_2CH_3$), 4.58 (2H, t, *J*=7.2 Hz, $CH_2CH_2CH_2CH_3$), 7.87–7.97 (3H, m, ArH), 8.20 (1H, d, *J*=9.0 Hz, ArH), 8.45 (1H, d, *J*=9.0 Hz, ArH), 8.50 (1H, dd, *J*=8.4, 1.2 Hz, ArH), 9.22 (1H, s, ArH; ^{13}C NMR ($CDCl_3$): δ 13.50, 20.01, 33.50, 42.76, 112.05, 113.97, 115.84, 119.64, 125.25, 127.88, 128.15, 130.33, 136.81, 136.90, 137.01, 137.86, 138.04, 142.60, 146.37; MS (*m/z*) 300 (M^+). Anal. calcd for $C_{19}H_{16}N_4$ (300.4): C, 75.98; H, 5.37; N, 18.65; found: C, 75.65; H, 5.32; N, 18.41%.

*8-Bromo-3-methyl-3*H-*pyrazolo[4,3-*a*]acridine-11-carbonitrile* (**3e**): Shiny yellow needles (EtOH), yield 65%; m.p. 266–268 °C; IR (KBr disk): ν_{max}/cm^{-1} 2219 (CN). ^{1}H NMR ($CDCl_3$): δ 4.27 (3H, s, CH_3), 7.89 (1H, dd, *J*=8.8, 2.0 Hz, ArH), 7.91 (1H, d, *J*=9.2 Hz, ArH), 8.06 (1H, d, *J*=9.2 Hz, ArH), 8.28 (1H, d, *J*=8.8 Hz, ArH), 8.51 (1H, d, *J*=2.0 Hz, ArH), 9.12 (1H, s, ArH); ^{13}C NMR ($CDCl_3$): δ 38.54, 115.49, 115.89, 116.93, 117.34, 124.56, 124.76, 125.12, 129.16, 132.05, 132.19, 135.45, 137.34, 142.60, 146.65, 148.25; MS (*m/z*) 339 (M^++2). Anal. calcd for $C_{16}H_9BrN_4$ (337.2): C, 57.00; H, 2.69; N, 16.62; found: C, 56.65; H, 2.62; N, 16.35%.

*8-Bromo-3-ethyl-3*H-*pyrazolo[4,3-*a*]acridine-11-carbonitrile* (**3f**): Shiny yellow needles (EtOH), yield 77%; m.p. 233–235 °C; IR (KBr disk): ν_{max}/cm^{-1} 2219 (CN). ^{1}H NMR ($CDCl_3$): δ 1.66 (3H, t, *J*=7.2 Hz, CH_2CH_3), 4.61 (2H, q, *J*=7.2 Hz, CH_2CH_3), 7.87 (1H, dd, *J*=8.8, 2.0 Hz, ArH), 7.91 (1H, d, *J*=9.2 Hz, ArH), 8.02 (1H, d, *J*=9.2 Hz, ArH), 8.26 (1H, d, *J*=8.8 Hz, ArH), 8.48 (1H, d, *J*=2.0 Hz, ArH), 9.11 (1H, s, ArH); ^{13}C NMR ($CDCl_3$): δ 15.54, 44.61, 115.61, 115.70, 116.77, 117.60, 124.28, 124.49, 125.77, 129.50, 132.36, 132.77, 135.12, 137.21, 142.40, 146.21, 148.11; MS (*m/z*) 353 (M^++2). Anal. calcd for $C_{17}H_{11}BrN_4$ (351.2): C, 58.14; H, 3.16; N, 15.95; found: C, 57.83; H, 3.11; N, 16.23%.

*8-Bromo-3-propyl-3*H-*pyrazolo[4,3-*a*]acridine-11-carbonitrile* (**3g**): Shiny yellow needles (EtOH), yield 80%; m.p. 228–229 °C; IR (KBr disk): ν_{max}/cm^{-1} 2223 (CN). ^{1}H NMR ($CDCl_3$): δ 1.01 (3H, t, *J*=7.2 Hz, $CH_2CH_2CH_3$), 2.08 (2H, m, $CH_2CH_2CH_3$), 4.51 (2H, t, *J*=7.2 Hz, $CH_2CH_2CH_3$), 7.85 (1H, dd, *J*=9.0, 1.6 Hz, ArH), 7.89 (1H, d, *J*=9.6 Hz, ArH), 8.00 (1H, d, *J*=9.6 Hz, ArH), 8.24 (1H, d, *J*=9.0 Hz, ArH), 8.45 (1H, d, *J*=1.6 Hz, ArH), 9.10 (1H, s, ArH); ^{13}C NMR ($CDCl_3$): δ 11.43, 23.59, 51.71, 115.54, 115.84, 116.34, 118.04, 123.94, 124.38, 126.11, 129.70, 132.37, 133.07, 134.89, 137.07, 142.38, 146.16, 148.04; MS (*m/z*) 367 (M^++2). Anal. calcd for $C_{18}H_{13}BrN_4$ (365.2): C, 59.19; H, 3.59; N, 15.34; found: C, 58.79; H, 3.52; N, 15.04%.

*8-Bromo-3-isobutyl-3*H-*pyrazolo[4,3-*a*]acridine-11-carbonitrile* (**3h**): Shiny yellow needles (EtOH), yield 75%; m.p. 192–194 °C; IR (KBr disk): ν_{max}/ cm^{-1} 2222 (CN). ^{1}H NMR ($CDCl_3$): δ 1.01 [6H, d, *J*=6.8 Hz, $CHCH_2(CH_3)_2$], 2.44–2.53 [1H, m, $CHCH_2(CH_3)_2$], 4.33 [2H, d, *J*=6.8 Hz, $CHCH_2(CH_3)_2$], 7.85 (1H, dd, *J*=8.8, 1.6 Hz, ArH), 7.88 (1H, d, *J*=9.6 Hz, ArH), 7.99 (1H, d, *J*=9.6 Hz, ArH), 8.23 (1H, d, *J*=8.8 Hz, ArH), 8.44 (1H, d, *J*=1.6 Hz, ArH), 9.11 (1H, s, ArH); ^{13}C NMR ($CDCl_3$): δ 13.63, 19.87, 33.55, 43.10, 115.61, 115.73, 116.30, 118.02, 123.87, 124.12, 126.20, 130.21, 132.54, 133.19, 134.71, 136.96, 142.19, 146.14, 147.98; MS (*m/z*) 381 (M^++2). Anal. calcd for $C_{19}H_{15}BrN_4$ (379.3): C, 60.17; H, 3.99; N, 14.77; found: C, 59.77; H, 3.93; N, 14.49%.

Conclusions

We have successfully designed, synthesised and characterised new derivatives of pyrazolo[4,3-*a*]acridine by the reaction of 1-alkyl-5-nitro-1*H*-indazoles with different arylacetonitriles in basic media. The results clearly show that these compounds have fluorescent properties in addition to strong antibacterial activities and provide an excellent opportunity for the study of physiological functions of bacteria at single-cell level.[37] Because of the promising antibacterial activity of our new derivatives, we are undertaking further synthetic and biological studies on similar substrates to expand this field of knowledge and establish sound conclusions.

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References

1 F. Bellina, S. Cauteruccio and R. Rossi, *Tetrahedron,* 2007, **63**, 4571.
2 Z.J. Hu, J.X. Yang, Y.P. Tian, H.P. Zhou, X.T. Tao, G.B. Xu *et al*., *J. Mol. Struct.,* 2007, **839**, 50.
3 Y.Z. Cui, Q. Fang, Z.L. Huang, G. Xue, W.T. Yu and H. Lei, *Opt. Mater.*, 2005, **27**, 1571.
4 A.R. Katritzky, A.V. Vakulenko, R.A. Gedu and J.W. Rogers, *Arkivoc*, 2007, **i**, 8555.
5 Z.R. Grabowski and K. Rotkiewicz, *Chem. Rev.*, 2003, **103**, 3899.
6 F. Karagöz, O. Güney, M. Kandaz and A.T. Bilgiçli, *J. Lumin.*, 2012, **132**, 2736.
7 A.P.G. Ferreira, R. Frederice, K.P.F. Janssen and M.H. Gehlen, *J. Lumin.*, 2011, **131**, 888.
8 O. Tabarrini, V. Cecchetti, A. Fravolini, G. Nocentini, A. Barzi, S. Sabatini, H. Miao and C. Sissi, *J. Heterocycl. Chem.*, 1999, **42**, 2136.
9 W.A. Denny, *Curr. Med. Chem.*, 2002, **9**, 1655.
10 J.R. Goodell, A.A. Madhok, H. Hiasa and D.M. Ferguson, *Bioorg. Med. Chem.,* 2006, **14**, 5467.
11 O. Tabarrini, G. Manfroni, A. Fravolini, V. Cecchetti, S. Sabatini, E. De Clercq, J. Rozenski, B. Canard, H. Dutartre, J. Paeshuyse and J. Neyts, *J. Med. Chem.,* 2006, **49**, 2621.
12 M. Kukowska-Kaszuba and K. Dzierzbicka, *Curr. Med. Chem.,* 2007, **14**, 3079.
13 R.W. Winter, J.X. Kelly, M.J. Smilkstein, R. Dodean, D. Hinrichs and M.K. Riscoe, *Exp. Parasitol.*, 2008, **118**, 487.
14 A.A. Joshi and C.L. Viswanathan, *Anti-Infect. Agents. Med. Chem.*, 2006, **5**, 105.
15 J.P. Dheyongera, W.J. Geldenhuys, T.G. Dekker, M.G. Matsabisa and C.J. Van Der Schyf, *Bioorg. Med. Chem.*, 2005, **13**, 1653.
16 S.J. Kesten, M.J. Degnan, J. Hung, D.J. Mc Namara, D.F. Ortwine, S.E. Uhlendorf and L.M. Werbel, *J. Med. Chem.*, 1992, **35**, 3429.
17 W. Raether, B. Enders, J. Hofmann, U. Schwannecke, H. Seidenath, H. Hanel and M. Uphoff, *Parasitol. Res.*, 1989, **75**, 619.
18 P. Belmont, J. Bosson, T. Godet and M. Tiano, *Anti-Cancer Agents Med. Chem.*, 2007, **7**, 139.
19 A. Kamal, O. Srinivas, P. Ramulu, G. Ramesh and P.P. Kumar, *Bioorg. Med. Chem. Lett.*, 2004, **14**, 4107.
20 M. Demeunynck, *Expert. Opin. Ther. Pat.*, 2004, **14**, 55.
21 I.G.C. Robertson, B.D. Palmer, M. Officer, D.J. Siegers, J.W. Paxton and G.J. Shaw, *Biochem. Pharmacol.*, 1991, **42**, 1879.

22 M. Rahimizadeh, M. Pordel, M. Bakavoli and H. Eshghi, *Dyes Pigm.*, 2010, **86**, 266.
23 R. Sahraei, M. Pordel, H. Behmadi and B. Razavi, *J. Lumin*., 2013, 1**36**, 334.
24 V. Pakjoo, M. Roshani, M. Pordel and T. Hoseini, *Arkivoc*, 2012, **9**, 195.
25 M. Pordel, *J. Chem.* Res., 2012, **36**, 595.
26 M. Rahimizadeh, M. Pordel, M. Ranaei and M. Bakavoli, *J. Heterocycl. Chem*., 2012, **49**, 208.
27 T. Hoseini-Hesar, M. Pordel, M. Roshani and A. Shams, *J. Chem. Res.,* 2013, **37**, 438.
28 M. Rahimizadeh, M. Pordel, M. Bakavoli, Sh. Rezaeian and A. Sadeghian, *World. J. Microbiol. Biotechnol.,* 2010, **26**, 317.
29 H. Sadeghian, A. Sadeghian, M. Pordel, M. Rahimizadeh, P. Jahandari, A. Orafaie and M. Bakavoli, *Med. Chem. Res*., 2010, **19**, 103.
30 A. Sadeghian, M. Pordel, H. Safdari, M.A. Fahmidekar and H. Sadeghian, *Med. Chem. Res*., 2012, **21**, 3897.
31 M. Rahimizadeh, M. Pordel, M. Bakavoli, Z. Bakhtiarpoor and A. Orafaie, *Monatsh. Chem*., 2009, **140**, 633.
32 L. Bouissane, S.E. Kazzouli, J.M. Leger, C. Jarry, E.M. Rakib, M. Khouili and G. Guillaumet, *Tetrahedron*, 2005, **61**, 8218.
33 R.B. Davis and L.C. Pizzini, *J. Org. Chem*., 1960, **25**, 1884.
34 F. Sztaricskai, G. Pintér, E. Röth, P. Herczegh, S. Kardos, F. Rozgonyi and Z. Boda, *J. Antibiot.*, 2007, **60**, 529.
35 J.Q. Umberger and V.K. Lamer, *J. Am. Chem. Soc*., 1945, **67**, 1099.
36 S.M. Finegold, L. Garrod, in *Bailey and Scott's diagnostic microbiology*, 8th edn. C.V. Mosby Co., Toronto, 1995, pp. 171.
37 F. Joux and P. Lebaron, *Microbes Infect*., 2000, **2**, 1523.