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ORIGINAL ARTICLE

5-(1*H*-Indol-3-yl)-pyrazolyl derivatives as colorimetric sensor for anions

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Abstract The synthesis, characterisation and binding and deprotonation studies with anions for four 5-(1*H*-indol-3-yl)-pyrazolyl derivatives (**2**–**5**) have been described. It is worthy to mention that sensor **2** shows a drastic change in absorption spectrum (ca. 335 nm) and colour (colourless to blue) upon addition of F^- in DMSO solution due to the deprotonation of indole –NH proton, as confirmed by ^1H NMR titration. Sensor **4** recognizes F^- and CN^- ions by deprotonation mechanism with visible colour change of the solution in a similar manner to that of **2**. However, in contrary to **2** and **4**, sensor **3** binds with F^-, CN^-, $H_2PO_4^-$, AcO^- and $PhCOO^-$ ions exploiting hydrogen-bonding interaction with the shifting of absorption band to longer wavelength and subsequent colour change of the solution. Compound **5** recognizes F^- without any visual colour change and its binding is studied by ^1H NMR titration to acquire the important information about the nature of binding between F^- and **5**.

Keywords Indolyl-pyrazolyl derivatives · Colorimetric anion sensors · Deprotonation · Hydrogen-bond

Introduction

Development of chemosensors for recognition and sensing of anions is a fast growing and demanding area for chemists due to their profound applications in chemical, biological and environmental processes [1–11]. Neutral anion chemosensors consisting of hydrogen-bonding donors such as amide [12, 13], urea and thiourea [14–20], pyrroles [21–25], indole [26–29] as binding units have been extensively studied by different group of workers. Indole, like pyrrole, contains a hydrogen-bond donor group which is very well exploited in biological systems to bind anions such as sulphate [30] and chloride [31]. Compounds containing indole viz., bisindolylmaleimides and indolocarbazoles show biological activity and work as protein kinase *C* inhibitors [32, 33]. Pyrazole moiety containing ligands bind with a range of inorganic anions, and pyrazole-anion supramolecular interaction can be used to template new metal cluster structures [34].

Gale and co-workers [35] reported isophthalamides and 2,6-dicarboxamidopyridines with pendant indole groups which recognized fluoride ion selectively in DMSO–H_2O solution and crystallographic studies showed a 'twisted' binding mode for fluoride in the solid state. The same group described the synthesis of 1,3-di(1*H*-indol-7-yl)ureas which recognized dihydrogen phosphate ion selectively in polar solvent mixture (DMSO-d_6–25 % water) [26]. Ghosh and co-workers [36] reported two thiourea and urea based indole chemosensors which binds fluoride ion with selective colour change and generation of a new absorption band in near IR region.

Our interest in the domain of colorimetric anion sensing and anion recognition has led us to explore a series of compounds containing both indole and pyrazole moieties. In this paper, we have reported the synthesis, characterization and binding and deprotonation studies with anions of four

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5-(1*H*-indol-3-yl)-pyrazolyl derivatives **2**, **3**, **4** and **5**. These four derivatives were synthesized using simple reaction methodologies and characterized by IR, ESI–Mass and ^{1}H NMR spectroscopy. Interestingly, sensor **2** exhibits a significant and unusual change in absorption spectrum (ca. from 300 to 635 nm) and colour selectively on addition of F^- ion in DMSO due to the deprotonation of indole –NH proton, which is clearly revealed by ^{1}H NMR titration. Sensor **4** shows visible colour change with F^- and CN^- ions in solution exploiting deprotonation mechanism also. In sharp contrast to the deprotonation behaviour of **2** and **4** in presence of anions, sensor **3** exhibits non-selective binding with the anions F^-, CN^-, $H_2PO_4^-$, AcO^- and $PhCOO^-$ by hydrogen-bonding interaction in DMSO with visible binding-induced change in colour of the solutions. The equilibrium constants associated to binding or deprotonation have been evaluated by utilizing the change in absorption spectral data. Recognition of F^- ion by **5**, which exhibits no visual colour change, was investigated by ^{1}H NMR titration and provides significant information about the mode of binding between F^- and **5**. Details of these studies have been presented in this paper.

Experimental

General methodologies

The infrared spectra were recorded on a Perkin-Elmer Spectra GX 2000 spectrometer. The spectra of the solid samples were recorded by dispersing the samples as KBr pellets. ESI–MS measurements were carried out on a Waters QTof-Micro instrument. The ^{1}H NMR spectra were recorded on a Bruker 300, 400 or 500 MHz FT-NMR spectrometer using DMSO-d_6 as the solvent and tetramethylsilane (TMS) as an internal standard. UV–visible spectra were recorded with a Shimadzu UV-2450 spectrophotometer at 298 ± 1 K, using slit width of 2 nm. A matched pair of quartz cuvettes (path length = 1 cm) were employed. All reagents for synthesis were obtained commercially and used without further purification. All anions, in the form of tetrabutylammonium (TBA) salts, were purchased from Aldrich Chemical Co. (USA), stored in a dessicator under vacuum containing self-indicating silica and used for anion titration without any further purification. Acetonitrile (ACN) was stirred with CaH_2 for 5–6 h and then distilled at 82 °C under dry conditions. Dimethyl sulphoxide (DMSO) was dried over CaH_2 and then distilled at 76 °C under reduced pressure (12 mm of Hg) [37]. The binding or deprotonation ability of sensors **2**–**5** with different anions are demonstrated by calculating the necessary equilibrium constants, using the equations described by Connors (also see supplementary material) and other authors [38, 39].

Syntheses

Compound **1** (3-cyanoacetylindole) was synthesized according the literature procedure [40]. Compounds **2**–**5** were synthesized by the following methods which are given below.

5-(1H-Indol-3-yl)-2H-pyrazol-3-ylamine (**2**)

Compound **1** (2 g, 10.8 mmol), hydrazine hydrate (0.633 mL, 21.6 mmol) and *p*-toluene sulphonic acid monohydrate (PTSA·H_2O) (2 g, 10.8 mmol) were placed in a flask containing dry CH_3CN (50 mL) and were refluxed at 82 °C for 8 h under nitrogen atmosphere. After the completion of reaction (monitored on TLC), the reaction mixture was cooled and solvent was evaporated under reduced pressure. The residue was stirred with a mixture of ethyl acetate and hexane for five minutes. The solid was filtered and crystallized from ethanol to obtain **2** as pure colourless solid. Yield: 72 % (1.56 g). IR (KBr Pellet, cm^{-1}): 3410, 3159, 1602. ^{1}H NMR (500 MHz, DMSO-d_6, TMS) δ/ppm: 11.30 (s, 2H), 7.84 (d, 1H, J = 8.0 Hz), 7.65 (d, 1H, J = 2.5 Hz), 7.43 (d, 1H, J = 8.0 Hz), 7.14−7.07 (m, 2H), 5.77 (s, 1H), 2.29 (s, 2H). ESI–MS (*m*/*z*): 199.14 $[M + H]^+$.

2-(2,4-Dinitrophenyl)-5-(1H-indol-3-yl)-2H-pyrazol-3-ylamine (**3**)

Compound **1** (1 g, 5.43 mmol), 2,4-dintrophenyl hydrazine (1.076 g, 5.43 mmol) and PTSA·H_2O (1.032 g, 5.43 mmol) were placed in a flask containing dry CH_3CN (50 mL) and were refluxed at 82 °C for 20 h under nitrogen atmosphere. After the completion of reaction (monitored on TLC), the reaction mixture was cooled, the solid precipitate was separated which was filtered, washed with hexane and dried under vacuum, to afford the compound **3**. Yield: 80 % (1.58 g). IR (KBr Pellet, cm^{-1}): 3408, 3345, 3224, 1599, 1447. ^{1}H NMR (400 MHz, DMSO-d_6, TMS) δ/ppm: 11.31 (s, 1H), 8.81 (d, 1H, J = 2.4 Hz), 8.59 (dd, 1H, J = 9.2 Hz, 2.4 Hz), 8.16 (d, 1H, J = 8.8 Hz), 7.96 (d, 1H, J = 7.6 Hz), 7.47 (d, 1H, J = 8.0 Hz), 7.39 (d, 1H, J = 8.0 Hz), 7.12 (t, 1H, J = 7.2 Hz), 7.04 (t, 1H, J = 7.6 Hz), 5.88 (s, 1H), 2.29 (s, 2H). ESI–MS (*m*/*z*): 365.08 $[M + H]^+$.

5-Amino-3-(1H-indol-3-yl)-1-[(4-nitrophenyl)aminocarbonyl]pyrazole (**4**)

4-Nitrophenylisocyanate (165 mg, 1.01 mmol) was added to a solution of **2** (200 mg, 1.01 mmol) in CH_3CN (25 mL), and the reaction mixture was heated to reflux at 82 °C for 16 h. After the completion of reaction (monitored on TLC), the reaction mixture was evaporated with

rotary vacuum evaporator. The solid was purified by silica gel (100–200 mesh) column chromatography using ethyl acetate: hexane (1:9 v/v) as eluent. Yield: 68 % (250 mg). IR (KBr Pellet, cm^{-1}): 3371, 3075, 1717, 1608, 1541. ^1H NMR (400 MHz, DMSO-d_6, TMS) δ/ppm: 11.44 (s, 1H), 10.29 (s, 1H), 8.37 (d, 1H, J = 8.0 Hz), 8.28 (d, 1H, J = 9.2 Hz), 8.22−8.19 (m, 1H), 8.05 (d, 1H, J = 9.6 Hz), 7.95−7.89 (m, 1H), 7.74−7.60 (m, 1H), 7.42 (d, 1H, J = 7.2 Hz), 7.16−7.12 (m, 1H), 6.71−6.58 (m, 1H), 5.79 (s, 1H), 2.16 (s, 2H). ESI–MS (*m/z*): 363.09 $[M + H]^+$.

1-[5-(1H-Indol-3-yl)-2H-pyrazol-3-yl]-3-phenyl-thiourea (**5**)

Phenylisothiocyanate (136 mg, 1.01 mmol) was added to a solution of **2** (200 mg, 1.01 mmol) in CH_3CN (25 mL), and the reaction mixture was refluxed at 82 °C for 16 h. After the completion of reaction (monitored on TLC), the reaction mixture was evaporated with rotary vacuum evaporator. The solid was purified by silica gel (100–200 mesh) column chromatography using ethyl acetate: hexane (1:9 v/v) as eluent. Yield: 62 % (210 mg). IR (KBr Pellet, cm^{-1}): 3371, 1627, 1218. ^1H NMR (500 MHz, DMSO-d_6, TMS) δ/ppm: 12.78 (s, 1H), 11.90 (s, 1H), 11.55 (s, 1H), 10.76 (s, 1H), 7.81 (d, 1H, J = 2.0 Hz), 7.75 (d, 1H, J = 7.5 Hz), 7.68 (d, 1H, J = 8.0 Hz), 7.49 (d, 1H, J = 8.0 Hz), 7.40 (t, 1H, J = 7.5 Hz), 7.23–7.15 (m, 5H), 6.34 (s, 1H). ESI–MS (*m/z*): 332.38 $[M–H^+]$.

Results and discussions

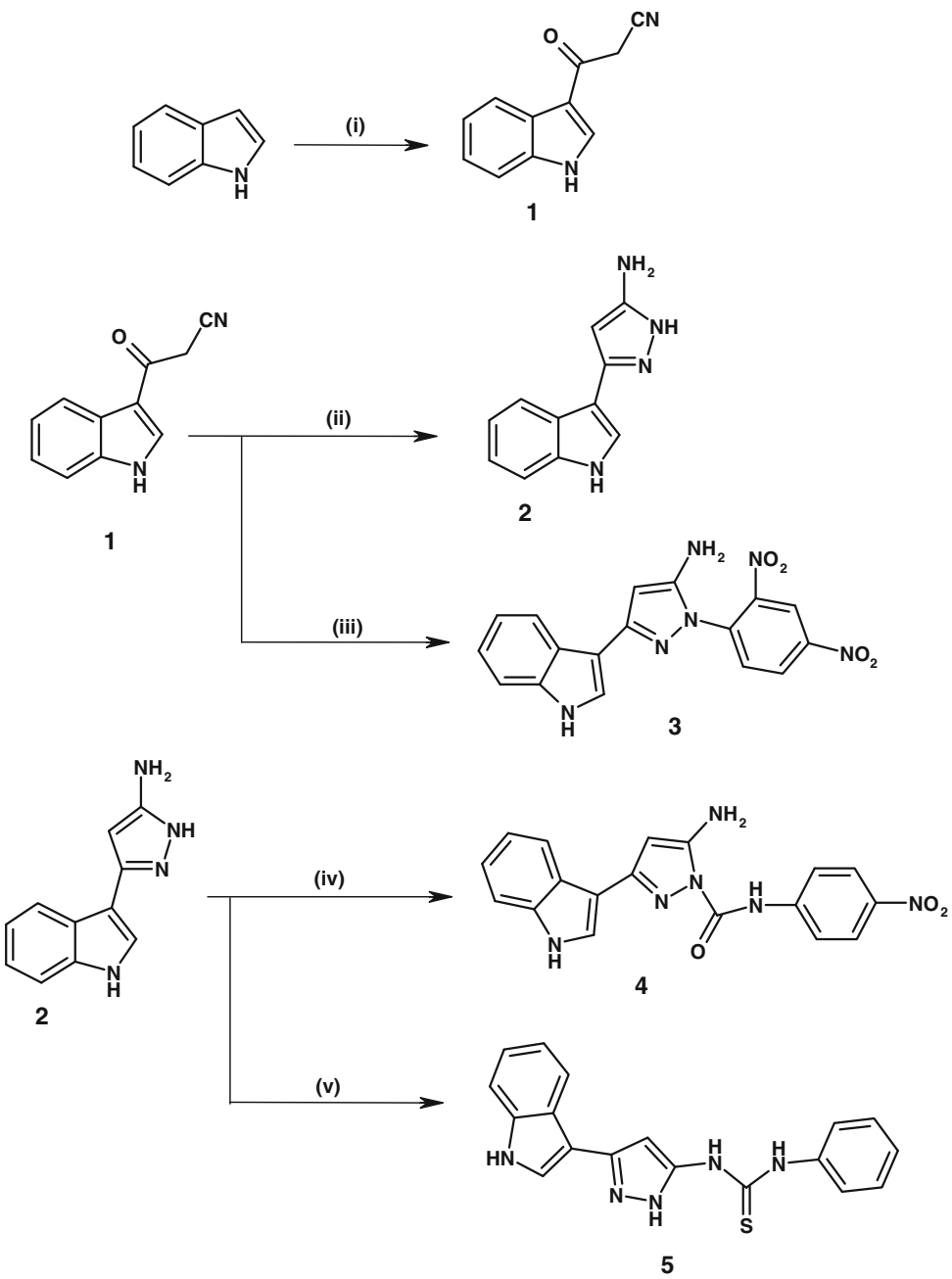
Compound **1** is synthesized by reaction of indole and cyanoacetic acid in acetic anhydride at 85 °C (Scheme 1) [40]. Reaction of **1** with hydrazine hydrate in presence of *p*-toluenesulphonic acid monohydrate ($PTSA{\cdot}H_2O$) catalyst under reflux condition in ethanol generates pyrazol-3-ylamine derivative **2** in a 72 % yield. When 2,4-dinitrophenylhydrazine is reacted with **1** instead of hydrazine hydrate, an *N*-substituted pyrazol-3-ylamine derivative **3** is formed in a 80 % yield. Treatment of **2** with 4-nitrophenylisocyanate in CH_3CN under refluxing condition affords 5-amino-3-(1*H*-indol-3-yl)-pyrazole-1-carboxylic acid (4-nitro-phenyl)-amide (**4**) as the product in 68 % isolated yield. On the other hand, reaction of **2** with phenylisothiocyanate produced 1-[5-(1H-Indol-3-yl)-2H-pyrazol-3-yl]-3-phenyl-thiourea (**5**) under the same reaction conditions in 62 % yield. The different product formation on addition of 4-nitrophenyl-isocyanate and phenylisothiocyanate to **2** may be explained in terms of hardness of the two electrophiles. Harder electrophile 4-nitrophenylisocyanate is attacked by harder heterocyclic N atom of pyrazole ring with the formation of a more polar transition state. Similar regiochemistry was also reported by Halcrow and co-workers [34], when 5-amino-3-(pyrid-2-yl)-1*H*-pyrazole was made to react with different isocyanates and isothiocyanates.

Sensors **2**-**5** are well characterised by ESI–MS and ^1H NMR spectra. Sensor **2** shows the characteristic signal of indole –NH and pyrazole –NH protons together at δ 11.30, pyrazole –CH proton at δ 5.77 and $–NH_2$ signal at δ 2.29. In the ^1H NMR spectrum of **3**, indole –NH and $–NH_2$ signals appear at δ 11.31 and 2.29, respectively. The $–NH_2$ signal for **4** appears at δ 2.16 which is very close to the position of $–NH_2$ signal in **2** and indicates the formation of **4** with the attack of the heterocyclic (pyrazole) N atom of **2** on 4-nitrophenylisocyanate. The thiourea –NH signals of **5** appear at δ 11.55 and 11.90 in ^1H NMR spectrum of **5**.

The absorption spectra of **2**–**5** are shown in Fig. 1. DMSO solution of sensor **2** is colourless and shows only a shoulder at 295 nm. Presence of two electron-withdrawing-NO_2 groups in the phenyl ring of **3** and subsequently, more electron delocalization might be the reason for occurrence of the band at 415 nm. Sensor **4** and **5** may be considered as derivatives of **2** bearing 4-nitrophenyl and phenyl-thiourea groups in their architectures. New bands at 330 and 280 nm are observed in the absorption spectra of **4** and **5**, respectively in comparison to **2**.

The colour changes observed for the sensors **2**–**4** are illustrated in Fig. 2. Solution of sensor **2** in DMSO is colourless and shows a selective colour change to blue on addition of F^- ion. Solution of **3** in DMSO is yellow which changes to reddish-brown on addition of F^-, CN^-, $H_2PO_4^-$, AcO^-, $PhCOO^-$ whereas, the colourless solution of **4** in CH_3CN converts to yellow upon addition of F^- and CN^-.

Figure 3(A) displays the changes in the UV–Visible spectrum of **2** upon addition of F^- in DMSO solution. The initial spectrum of **2** contains only a shoulder at 295 nm. Upon addition of F^-, new bands are formed in the lower wavelength region (275 and 310 nm) and higher wavelength region (635 nm) with the change of the colourless solution to blue. Such a significant change in absorption spectrum (ca. from 300 to 635 nm) and colour are not usual, in general. It is worth-mentioning that no precise isosbestic point is observed in the absorption spectra of **2** on addition of F^- which is a clear indication of the existence of multiple equilibria in the system, as demonstrated by Connors [38]. Job's plot analysis indicates 1:2 stoichiometry between **2** and F^- ion (supplementary material). Absorption spectral change for **2** upon addition of F^- ion fits well in the equation corresponding to 1:2 stoichiometry and yields two equilibrium constants. The spectral change indicates the involvement of the pyrazole –NH proton in binding with F^- in the first step, followed by deprotonation of indole –NH proton in presence of F^- in the next step. Finally, HF_2^- ion is formed by the reaction between HF and excess F^- ion. This fact is depicted in Scheme 2 and



Scheme 1 Synthesis procedure of compounds **2**–**5**. Reagents and conditions: (i) $CNCH_2COOH$, $(CH_3CO)_2O$, 60–70 °C, 5 min; (ii) $PTSA{\cdot}H_2O$, $N_2H_4{\cdot}H_2O$, CH_3CN, reflux, 8 h; (iii) $PTSA{\cdot}H_2O$, 2,4-dinitrophenylhydrazine, CH_3CN, reflux, 20 h; (iv) 4-nitrophenylisocyanate, CH_3CN, reflux, 16 h; (v) phenylisothiocyanate, CH_3CN, reflux, 16 h

supported by ^1H NMR titration of **2** with F^- ion (vide infra).

Figure 3(B) displays the changes in the UV–Visible spectrum of **3** upon addition of F^- in DMSO solution. The initial spectrum of **3** shows a band at 415 nm which, upon addition of F^-, shifts to 435 nm with decrease in absorbance and a shoulder is observed at 535 nm. Well-defined and sharp isosbestic point at 445 nm is observed during the titration of **3** with F^-. The binding isotherm for **3** fits nicely in the equation corresponding to 1:1 stoichiometry, as shown in the inset of Fig. 3b and the single equilibrium constant is extracted employing the above-mentioned equation which corresponds to binding of F^- to indole –NH proton. Similar absorption spectral responses are observed for **3** on titration with CN^-, $H_2PO_4^-$, AcO^-, $PhCOO^-$ ions and binding constants are calculated exploiting the 1:1 stoichiometry equation.

Sensor **4** shows major spectral changes with both F^- and CN^- ions in CH_3CN solution and the spectral changes with F^- ion are shown in Fig. 4. The absorption band at 330 nm is decreased and new band is formed at 430 nm upon gradual addition of F^- to **4**. The absorption spectral changes for sensor **4** also deviate from clear and sharp isosbestic point on due course of titration with F^- like

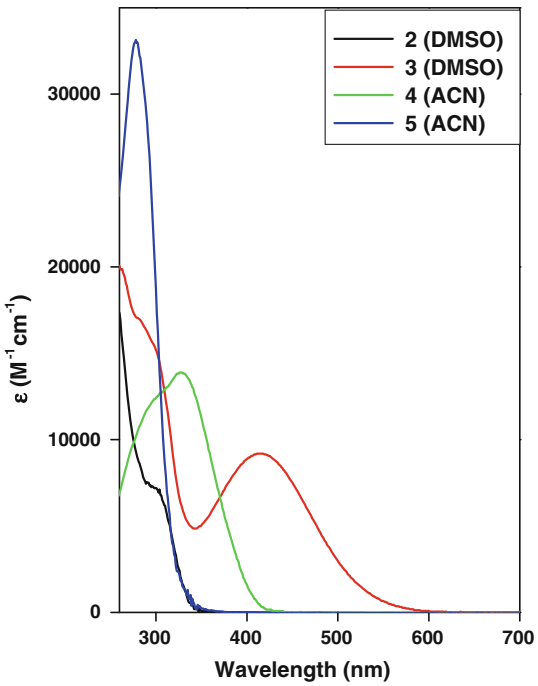


Fig. 1 Absorption spectrum of **2–5**

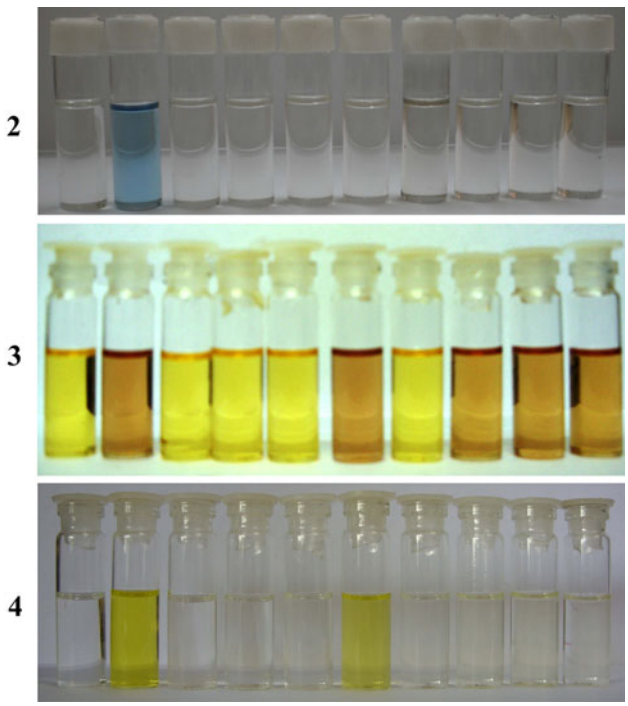


Fig. 2 Colour changes observed for **2** (in DMSO), **3** (in DMSO) and **4** (in ACN) upon addition of different anions as TBA salts. From *left* to *right*: sensor (**2**, **3** or **4**), F^-, Cl^-, Br^-, I^-, CN^-, HSO_4^-, $H_2PO_4^-$, AcO^-, $PhCOO^-$

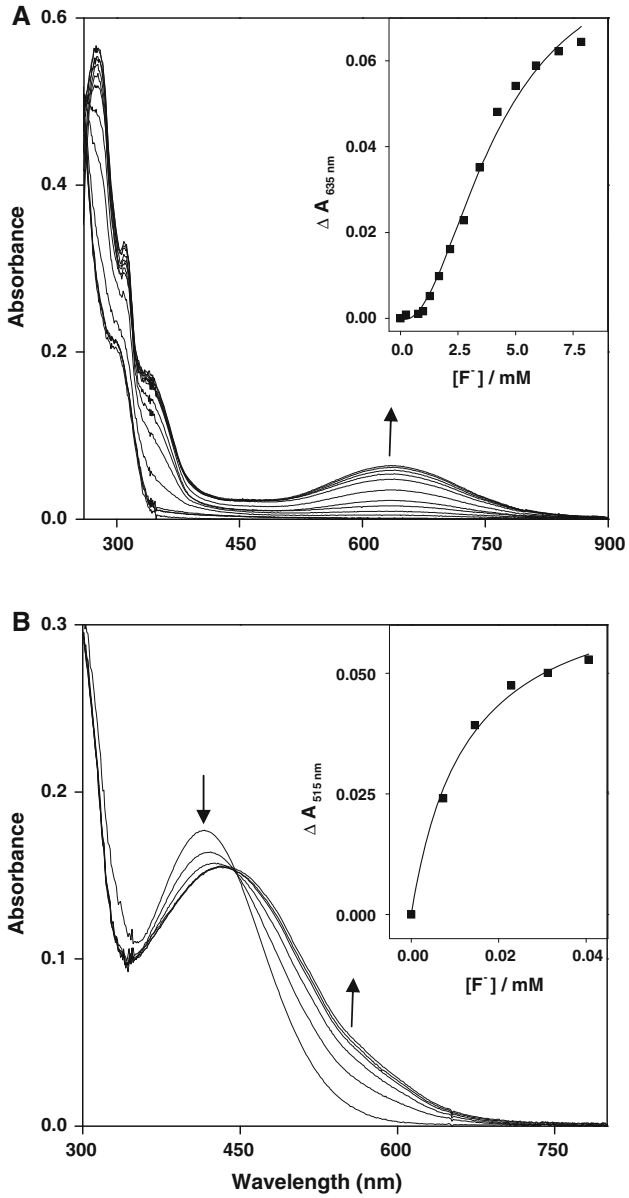
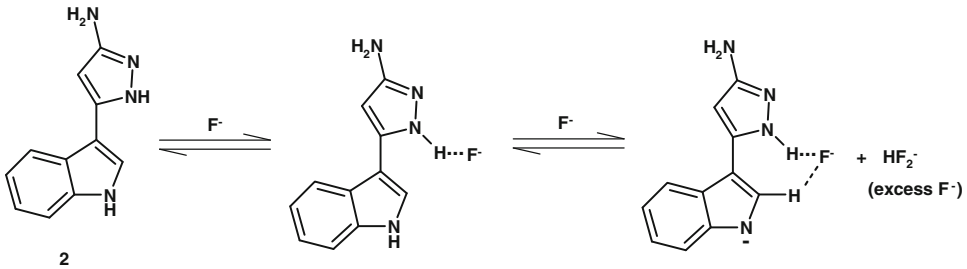


Fig. 3 UV–Visible spectral changes observed for (**A**) **2** and (**B**) **3**, upon addition of F^- ion in DMSO at 298 K. [**2**] = 3.151 × 10^{-5} M, [F^-] = (0 − 7.86) × 10^{-3} M. [**3**] = 2.582 × 10^{-5} M, [F^-] = (0 − 4.062) × 10^{-5} M. *Inset* of (**A**): Fitting of the experimental data (change in absorbance for **2** at 635 nm ($\Delta A_{635\ nm}$) vs. [F^-]) to a 1:2 stoichiometry. *Inset* of (**B**): Fitting of the experimental data (change in absorbance for **3** at 515 nm ($\Delta A_{515\ nm}$) vs. [F^-]) to a 1:1 stoichiometry

sensor **2**. Job's plot analysis indicates 1:2 stoichiometry between **4** and F^- ion (supplementary material). Fitting of absorption spectral data follows 1:2 stoichiometry quite well and two equilibrium constants are extracted. Sensor **4** is involved in binding with F^- employing –CONH proton in the first step and second equilibrium constant accounts for the deprotonation of indole –NH proton by F^- ion. Similar observations are obtained from the absorption spectra of **4** on titration with CN^- ion.

The equilibrium constants for **2**, **3** and **4** with different anions are calculated using the proper equations

Scheme 2 Binding and deprotonation of **2** in presence of F^-



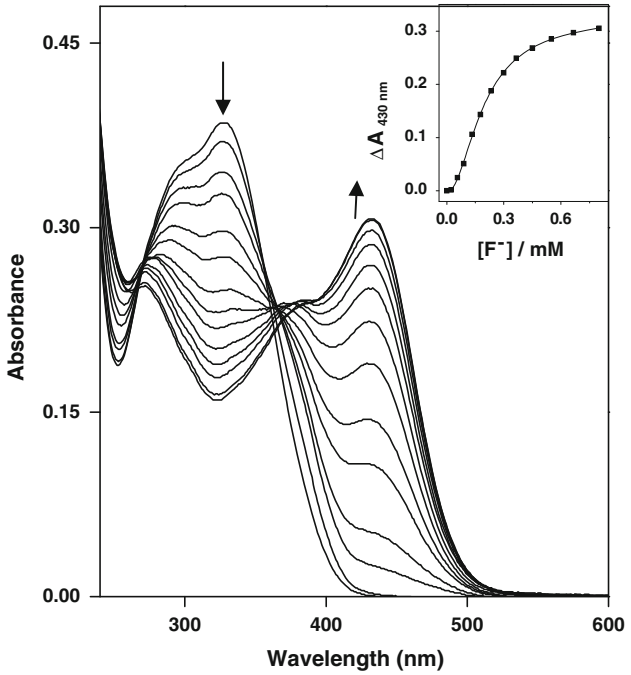


Fig. 4 UV–Visible spectral changes observed for **4**, upon addition of F^- ion in ACN at 298 K. [**4**] = 2.771 × 10^{-5} M, [F^-] = (0 − 8.0) × 10^{-4} M. *Inset*: Fitting of the experimental data (change in absorbance for **4** at 430 nm ($\Delta A_{430\ nm}$) vs. [F^-]) to a 1:2 stoichiometry

(supplementary material) and shown in Table 1. The interaction between sensor **2** and F^- ion is selective in nature where binding of pyrazole –NH proton with F^- occurs first, followed by the deprotonation of indole –NH proton by F^-. Similar deprotonation of indole –NH proton was also reported by Shao and co-workers [41]. Sensor **3** binds with five anions viz., F^-, CN^-, $H_2PO_4^-$, AcO^-, $PhCOO^-$ and the binding constants for all the five anions are almost in the same order. Absorption spectral behaviours of sensor **4** are similar in nature to that of **2**, involving the binding of –CONH proton with F^- and then, the deprotonation of indole –NH proton by F^-.

The sensor **2** exhibits selective colour change with fluoride ion with a drastic change of around 335 nm in absorption spectral band. ^{1}H NMR titration of **2** was carried out with TBAF in DMSO-d_6 to analyse this large absorption spectral change and displayed in Fig. 5. Salient features of the ^{1}H NMR titration are the following: (a) the singlet at 11.30 ppm, corresponding to –NH proton of indole and pyrazole, is broadened on gradual addition of F^- and vanished from spectral window, (b) new broad signal at 16.05 ppm is formed on gradual addition of F^-, (c) the position of $–NH_2$ proton signal remains almost unchanged. The broad signal at 16.05 ppm corresponds to HF_2^- ion proton which is generated due to deprotonation of indole –NH proton in presence of excess F^- during the titration [36, 41, 42]. Absence of binding-induced broadening of the $–NH_2$ proton signal and its unchanged position during the course of titration are direct proof for its insignificant binding with F^- (supplementary material).

A meticulous inspection of the change in the chemical shift of the aromatic protons on addition of F^- ion in Fig. 5 provides us unambiguous information about the origin of the –NH proton undergoing deprotonation during the titration i.e., whether it is indole –NH proton or pyrazole –NH proton. Doublets at 7.84 and 7.65 ppm, corresponding to indole –CH proton at 4-position and 2-position respectively, shift in opposite directions during the titration: the former shifts towards lower δ values, whereas the latter one transforms into singlet and moves towards higher δ values. Finally, they merge and appear at 7.70–7.72 ppm. The deprotonatiom of indole –NH proton of **2** by F^- increases the shielding at the –CH proton at 4-position which results in the shifting of doublet signal at 7.84 ppm to lower δ values (7.70–7.72 ppm). The doublet at 7.65 transforms into a singlet and shifts towards higher δ values on gradual addition of F^-. The F^- bound to the pyrazole –NH proton is in close vicinity to the –CH proton of indole at 2-position (Scheme 2) and, most probably, the former is creating a hydrogen-bond with the latter, leading to the down-field shift of the singlet signal of the latter. The other doublet at 7.43 ppm, corresponding to indole –CH proton at 7-position, is shielded and shifted to 7.40 ppm. The multiplet at 7.07–7.14 ppm is associated to 5- and 6-position –CH protons of indole which is also shielded by deprotonation of indole to appear at 6.88–6.95 ppm. The sole pyrazole –CH proton is shielded on gradual addition of F^- ion and appears at 5.63 ppm. However, the $–NH_2$ protons singlet signal (2.29 ppm) is unaffected during the titration. Relative larger shifting of the –CH protons of the indole ring

Table 1 Binding constant or deprotonation constant of **2**, **3** and **4** with different anions[a] determined by absorption titration data at 25 °C[b]

Anion	**2**[c]	**3**[c]	**4**[d]
F^-	$K_1 = 50\ M^{-1}$, $K_2 = 1.3 \times 10^3$	$7.9 \times 10^4\ M^{-1}$	$K_1 = 900\ M^{-1}$, $K_2 = 3.2 \times 10^4$
Cl^-	ND[e]	ND	ND
Br^-	ND	ND	ND
I^-	ND	ND	ND
CN^-	ND	$2.3 \times 10^4\ M^{-1}$	$K_1 = 2.0 \times 10^3\ M^{-1}$, $K_2 = 1.1 \times 10^4$
$H_2PO_4^-$	ND	$8.6 \times 10^3\ M^{-1}$	ND
HSO_4^-	ND	ND	ND
AcO^-	ND	$4.2 \times 10^4\ M^{-1}$	ND
$PhCOO^-$	ND	$4.8 \times 10^4\ M^{-1}$	ND

[a] Counter cation was tetrabutylammonium ion. [b]All errors are ±10 %

[c] In DMSO

[d] In CH_3CN

[e] Not determined, change in UV–Visible spectra was not enough to calculate binding constant. K_1 and K_2 denotes the binding constant and deprotonation constant, respectively for both the sensors **2** and **4** (see text and also Scheme 2)

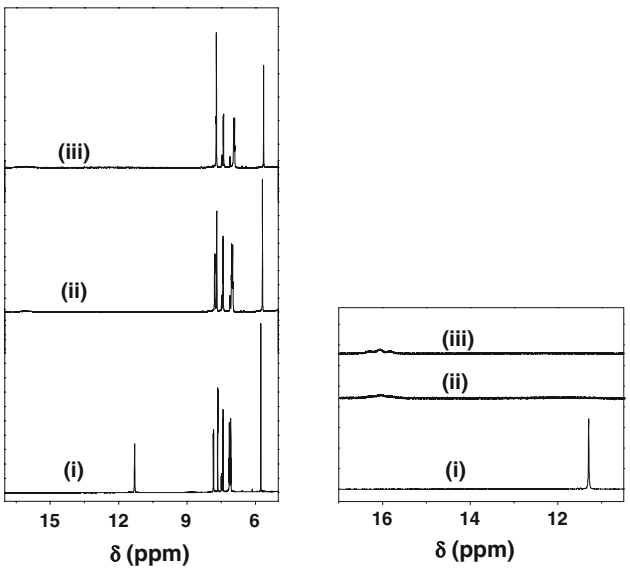


Fig. 5 *Left*: ^1H NMR titration of **2** with TBAF in $(CD_3)_2SO$; [**2**] = 5.555×10^{-2} M; [**2**]:[F^-] in these traces are (i) 1:0, (ii) 1:1.1, (iii) 1:2.6. *Right*: Expansion of the same traces for the region 10.5–17 ppm

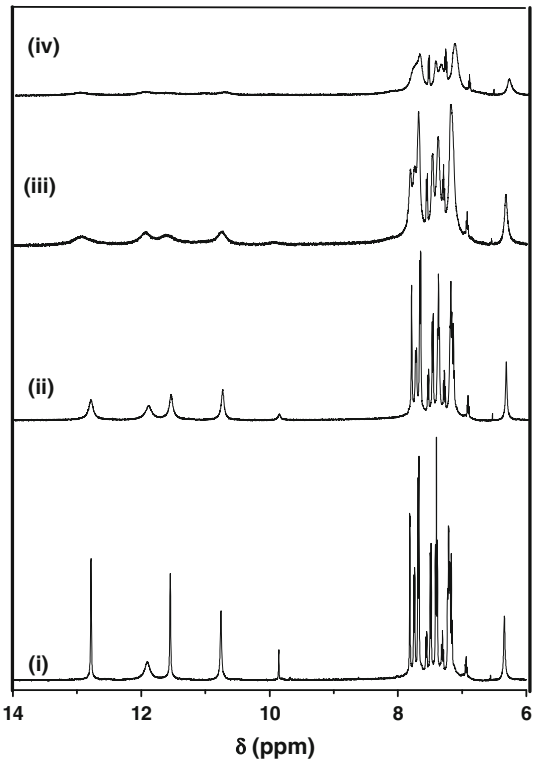


Fig. 6 ^1H NMR titration of **5** with TBAF in $(CD_3)_2SO$; [**5**] = 3.243×10^{-2} M; [**5**]:[F^-] in these traces are (i) 1:0, (ii) 1:0.1, (iii) 1:0.5, (iv) 1:1

and unchanged position of the $–NH_2$ protons singlet signal unambiguously indicate towards the deprotonation of indole –NH proton in course of titration and, not the pyrazole –NH proton. The negative change of deprotonated **2** is delocalized over the molecule due to conjugation which may be responsible for the formation of the new absorption band at a higher wavelength at 635 nm.

Compound **5** did not show any change of colour in presence of anions. ^1H NMR titration of **5** was carried out with TBAF in DMSO-d_6 and the spectral changes are displayed in Fig. 6. Gradual broadening of the –NH proton signals corresponding to indole, pyrazole and thiourea are observed due to the binding with F^-. However, appearance of HF_2^- proton signal at ~16.0 ppm is not observed during the titration which indicates hydrogen-bonding interaction between –NH protons and F^-, but not for deprotonation of –NH protons [36, 41, 42]. There is no appreciable change in the chemical shift of aromatic protons, indicating the existence of almost same conformation

of the F^- bound **5** in comparison to its free state. The aromatic rings (indole, pyrazole and phenyl rings) are connected with each other by single bonds and hence, they might be remaining in the 'isolated' conditions in F^- bound **5**, leading to less effective conjugation which is responsible for the generation of no visible colour for the **5** $-F^-$ complex.

Conclusions

We have synthesized and characterised four 5-(1*H*-indol-3-yl)-pyrazolyl derivatives **2–5**. Sensor **2** displays large red-shift of around 335 nm of the absorption band upon addition of F^- ion selectively due to deprotonation of indole –NH proton, as demonstrated by ^{1}H NMR titration. Sensor **4** exhibits visible colour change with both F^- and CN^- ions in solution by deprotonation also. Sensor **3** displays non-selective hydrogen-bonding interaction with F^-, CN^-, $H_2PO_4^-$, AcO^- and $PhCOO^-$ in DMSO with visible binding-induced change in colour of the solutions. The binding constants or deprotonation constants of the sensors have been determined by utilizing the change in UV–visible spectra. The recognition event of F^- by compound **5** is investigated by ^{1}H NMR titration, as compound **5** does not show any colour change with anions. We are currently investigating the sensing behaviour of other similar structurally-related sensors having water-soluble functional groups.

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