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A Fluoride-sensing Receptor Based on 2,2'-Bis(indolyl)methane by Dual-function of Colorimetry and Fluorescence

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Abstract:

A compound based on 2,2'-bis(indolyl)methane containing nitro group was studied as a new anion receptor. It could recognize selectively F^- by an increasing fluorescence signal and a visible color change from colorless to blue. The introduction of nitro group induced the spectral dual-function related to the deprotonation of N–H protons.

Keywords:

Anion recognition, Indolylmethane, deprotonation, Spectroscopy

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1. Introduction

Among the development of a variety of receptors for anions, especially for fluoride ions [1-11], indole-based anion receptors such as biindole, carbazole and indolocarbazole, have received considerable attention in molecular recognition because indole groups, like pyrrole, donate N–H groups as hydrogen bonding donors [12-17]. Indole-based receptors bind more easily with anions by hydrogen-bonding interactions than pyrrole because indole contains more acidic N–H groups [18]. In this field, biindole-based receptors have been reported as one of the feature anion receptors [19-21].

In our previous work, we have taken an interest in the research of biindole-based anion receptors such as 3-linked bis(indolyl)methane/methene [22-23]. We found that phenyl-3,3'-bis(indolyl)methene can show favorable anion recognition properties by UV-vis spectroscopy techniques, whereas, phenyl-3,3'-bis(indolyl)methane had faint even no obvious response to anions (See Fig. S1). Similar results have also been observed by Ito and co-workers [24]. They investigated the anion binding properties of indolylmethanes containing 2- and 3- linked indole groups by ^{1}H NMR titration techniques in $CDCl_3$. Their research results indicated that the position of the N–H binding sites of the indolylmethane is one of the important factors for the anion recognition properties. The stability constants for anion complexes of 3-linked receptors are obviously smaller than that of 2-linked complexes possibly because the position of the two N–H binding sites of 2-linked receptors may be more suitable to match anions.

In view of this facts and as a part of our work on anion recognition of receptors based on 2-linked tri(indolyl)methane we reported last time [25], herein we developed a series of receptors **1**–**4** based on 2,2'-bis(indolyl)methane. Remarkably, receptor **4** containing nitro group could recognize selectively F^- by

an increasing fluorescence signal and clear color change from colorless to blue.

2. Experimental

The synthesis of receptors **1–4** is showed in Scheme 1, as described in the literature [26]. They were prepared from sulfuric-acid-catalyzed reactions of 3-methylindole with appropriate aryl aldehyde.

2.1. General Remarks

Chemicals were purchased from commercial suppliers, and used without further purification. Acetonitrile was chromatogram pure. Melting points were determined on a PHMK 05 microscopic melting-point apparatus (Germany) and are uncorrected. The FTIR spectra were recorded on a Nicolet NEXUS FTIR spectrometer in 4000-400 cm^{-1} region using KBr pellets. MS results were determined on Agilent-1100 LC/MSD Trap instrument. ^{1}H and ^{13}C NMR spectra were recorded at 400 MHz in Inova-400 spectrometer (Varian Company) and were performed with TMS as an internal reference (^{1}H in d_6-DMSO, ^{13}C in $CDCl_3$). The absorbance measurements were performed on a PerkinElmer Lambda 35 UV/VIS Spectrometer. The fluorescence measurements were performed on a PerkinElmer LS 55 Luminescence Spectrometer.

2.2. Synthetic method

Appropriate aryl aldehyde (16 mmol) was added dropwise to a stirred solution of 3-methylindole (4.20 g, 32.0 mmol) in 30 mL of ethanol. Concentrated sulfuric acid (10 drops) was added and the reaction solution stirred at room temperature and in the N_2 atmosphere. The resulting precipitate was isolated by filtration and washed with cold ethanol when the reaction was finished. Recrystallization from hot ethanol afforded compounds **1–4**.

Phenyl bis(3-methylindole-2-yl)methane (Compound **1**): Yield: 57.1%. White powder. M.p.: 160-162 °C; ε 64750 L/mol^{-1}·cm^{-1} (λ_{max} 224 nm); IR (KBr, cm^{-1}): 3439, 3384, 3022, 2914, 2856, 1596, 1485, 1459, 1331, 1308, 1262, 1206, 1028, 1006, 873, 745; ^{1}H NMR (400 MHz, d_6-DMSO): δ 10.44 (s, 2H, N–*H*), 7.42 (d, *J* = 8 Hz, 2H, Ar-*H*), 7.28 (m, 4H, Ar-*H*), 7.14 (d, *J* = 8 Hz, 2H, Ar-*H*), 7.01 (t, *J* = 8 Hz, 2H, Ar-*H*), 6.96 (t, *J* = 8 Hz, 2H, Ar-*H*), 6.03 (s, 1H, C–*H*), 2.15 (s, 3H, Me-*H*); MS (ESI): 349.5 [M – H]$^-$.

4-Methyloxyphenyl bis(3-methylindole-2-yl)methane (Compound **2**): Yield: 85%. White powder. M.p.: 173-175 °C; ε 98080 L/mol^{-1}·cm^{-1} (λ_{max} 228 nm); IR (KBr, cm^{-1}): 3433, 3413, 3026, 2949, 2914, 2857, 2834, 1608, 1508, 1458, 1333, 1305, 1251, 1178, 1032, 1007, 818, 745; ^{1}H NMR (400 MHz, d_6-DMSO): δ 10.38 (s, 2H, N–*H*), 7.41 (d, *J* = 8 Hz, 2H, Ar-*H*), 7.28 (d, *J* = 8 Hz, 2H, Ar-*H*), 7.04 (m, 4H, Ar-*H*), 6.97 (t, *J* = 14 Hz, 2H, Ar-*H*), 6.92 (t, *J* = 12 Hz, 2H, Ar-*H*), 5.96 (s, 1H, C–*H*), 3.71 (s, 3H, OMe-*H*), 2.13 (s, 3H, Me-*H*); ^{13}C NMR (400 MHz, $CDCl_3$): δ 158.69, 135.14, 133.74, 131.92, 129.54, 129.48, 121.55, 119.39, 118.42, 114.29, 110.80, 108.47, 55.27, 39.99, 8.50; MS (ESI): 379.8 [M + H]$^+$.

4-Chlorophenyl bis(3-methylindole-2-yl)methane (Compound **3**): Yield: 82%. White needle crystal. M.p.: 180-182 °C; ε 68520 L/mol^{-1}·cm^{-1} (λ_{max} 226 nm); IR (KBr, cm^{-1}): 3430, 3379, 3046, 2916, 2856, 1618, 1487, 1460, 1332, 1309, 1246, 1179, 1089, 1012, 924, 858, 804, 745; ^{1}H NMR (400 MHz, d_6-DMSO): δ 10.41 (s, 2H, N–*H*), 7.40 (m, 4H, Ar-*H*), 7.28 (d, *J* = 12 Hz, 2H, Ar-*H*), 7.14 (d, *J* = 12 Hz, 2H, Ar-*H*), 7.01 (t, *J* = 8 Hz, 2H, Ar-*H*), 6.95 (t, *J* = 8 Hz, 2H, Ar-*H*), 6.03 (s, 1H, C–*H*), 2.12 (s, 1H, Me-*H*); ^{13}C NMR (400 MHz, $CDCl_3$): δ 138.52, 135.26, 133.17, 132.75, 129.79, 129.42, 129.15, 121.86, 119.58, 118.54, 110.89, 108.91, 40.21, 8.54; MS (ESI): 383.4 [M – H]$^-$.

4-Nitrophenyl bis(3-methylindole-2-yl)methane (Compound **4**): Yield: 36.6%. Yellow powder. M.p.: 240-242 °C; ε 58488 L/mol^{-1}·cm^{-1} (λ_{max} 222 nm); IR (KBr, cm^{-1}): 3450, 3419, 3287, 3057, 2913, 2857, 1594, 1513, 1458, 1346, 1239, 1183, 1108, 1006, 851, 747; ^{1}H NMR (400 MHz, d_6-DMSO): δ 10.46 (s, 2H, N–*H*), 8.21 (d, *J* = 8 Hz, 2H, Ar-*H*), 7.28 (d, *J* = 8 Hz, 2H, Ar-*H*), 7.42 (m, 4H, Ar-*H*), 7.02 (t, *J* = 6 Hz, 2H, Ar-*H*), 6.96 (t, *J* = 8 Hz, 2H, Ar-*H*), 6.21 (s, 1H, C–*H*), 2.13 (s, 1H, Me-*H*); ^{13}C NMR (400 MHz, $CDCl_3$): δ 147.72, 146.98, 135.48, 131.64, 129.34, 129.24, 124.09, 122.19, 119.74, 118.65, 110.98, 109.40, 40.67, 8.62; MS (ESI): 394.4 [M − H]$^-$.

3. Results and discussion

3.1. UV spectral studies

The anion recognition properties of receptors **1**–**4** were firstly investigated by UV-vis absorption spectroscopy techniques. The absorption spectra of receptors **1**–**3** have obvious bathochromic shifts on adding of F^-, AcO^- or $H_2PO_4^-$, but have not the obvious interactions of other anions (See Fig. S2). The association constants for 1:1 stoichiometry complexes between receptors **1**–**3** and anions have been given by non-linear fitting curve [27] (See Table S1). These results indicated 2,2'-bis(indolyl)methane receptors could more easily bind with anions by double hydrogen-binding interactions than 3,3'-bis(indolyl)methane probably because of the suitable position of the two N–H binding sites, which accordant with the previous results studied by Ito and our laboratory.

Interestingly, receptor **4** containing nitro group can even recognize selectively F^- over AcO^-, $H_2PO_4^-$ and other anions by a favorable color change of colorless-to-blue, as shown in Fig. 1, but similar color change had not been observed in receptors **1**–**3** upon addition of F^-. The intense absorption band of

receptor **4** at 283 nm declined with the excessive addition of F^-, while three absorption bands at 320, 410 and 593 nm appeared pertained to the solution color changed from colorless to blue (See Fig. 2). On adding of other anions such as Cl^-, Br^-, I^-, AcO^-, $H_2PO_4^-$, HSO_4^- and ClO_4^-, no noticeable spectra were observed under the same conditions.

Moreover, the interactions of receptor **4** with F^- were studied in detail by UV-vis spectroscopic titration techniques, as shown in Fig. 3. On addition of F^- from 0 to 4 equiv., the bands at 223 nm and 280 nm decreased slightly, and a weak bathochromic shift was observed from 280 to 285 nm. The spectral changes were similar to the results of receptors **1–3** with anions, which was responsible for the formation of the complex between receptor **4** and F^- (See Fig. 3a). With gradually increasing the concentration of F^- from 4 to 580 equiv., the absorption bands at 223 nm and 280 nm decreased drastically and three new bands at 320, 410 and 593 nm evolved (See Fig. 3b). The absorption changes can be ascribed to the N–H deprotonations of receptor **4** with the excessive addition of F^-. However, when nitro group was introduced into the same position of the 3,3'-bis(indolyl)methane framework, similar spectral changes were not observed under the same conditions (See Fig. S3).

In our further studies, the reversible work of receptor **4** had been investigated by the addition of polar solvent. The peaks at 410 and 593 nm decreased gradually and even vanished on addition of polar solvent MeOH (See Fig. S4). The result suggested that polar solvent MeOH can destroy hydrogen bonding interactions or deprotonation of receptor **4** with fluoride ions, and the reversible protonation of receptor **4** can also take place. Similarly, the reversible protonation for other receptors with anions can also be observed under the same conditions.

3.2. Fluorescence spectral studies

The fluorescence emission spectra of the receptor **4** with 100 equiv. of various anions in MeCN were observed in Fig. 4. Surprisingly, receptor **4** exhibited high selective recognition of F^- over other anions with a favorite increase of fluorescence intensity. With gradual adding of F^-, as shown in Fig. 5, a drastic increase of the fluorescence intensity of receptor **4** at 420 nm was observed. The results indicated that the excessive addition of F^- induced the N–H deprotonations and enhanced the conjugation and co-planarity of the molecular structure of receptor **4**. In contrast, the fluorescence intensities of receptors **1–3** decreased obviously on adding of F^- probably because the hydrogen bonding interactions of receptors **1–3** with F^- destroyed the planarity of original structure of the receptors (See Fig. S5).

3.3. ^{1}H NMR spectral studies

To further investigate the interactions between receptor **4** and F^-, ^{1}H NMR titration experiments of receptor **4** and F^- were carried out in d_6-DMSO. (See Fig. 6) The addition of 0.2 equiv. of F^- caused the drastic decreases of the signals of N–H protons of receptor **4** at 10.49 ppm and large downfield shifts to 12.72 ppm take place, and the signals almost vanished upon addition of 1 equiv. of F^-, and a new proton peak regarded as the $[HF_2]^-$ peak was appeared at 16.1 ppm upon addition of 4 equiv. of F^-, which was consistent with the other groups reported [28–29]. It suggested that the excessive addition of fluoride ions induced the deprotonation of receptor **4**.

In addition, the interactions of receptors **1-3** with fluoride ions have also been evaluated by the ^{1}H NMR titration. The results indicated that the N–H protons of receptor **1** bind with fluoride ions by double hydrogen bonding interactions (See Fig. S6). The signals of N–H protons of receptor **1** almost vanished

upon addition of 1 equiv. of F^- or even excessive F^-, whereas the similar proton peak of $[HF_2]^-$ was not observed at 16.1 ppm. Similarly, the variations of the signals for receptor **2** and **3** with fluoride ions can also be observed in the same conditions. The results suggested that receptors **1-3** bound with anions by double hydrogen bonding interactions instead of deprotonation.

4. Conclusion

In summary, we have developed a series of 2,2'-bis(indolyl)methane **1–4** as anion receptors. The anion recognition properties of receptors **1–4** are superior to that of 3,3'-bis(indolyl)methane possibly because of the suitable position of the two N–H binding sites of 2-linked receptors. It is notable that receptor **4**, as a new anion receptor, exhibited an excellent selectivity of F^- by a dual-function of a colorless-to-blue color change and increasing fluorescence signals in MeCN. The introduction of nitro group into 2,2'-bis(indolyl)methane framework caused a deshielding effect in the whole molecule of receptor and activated the N–H protons. The excessive addition of F^- resulted in the N–H deprotonations and probably enhanced the conjugation and co-planarity of molecular structure of receptor **4**, which displayed the excellent spectral changes. To our best knowledge, this is the first report of anion recognition employing 2-linked bis(indoly)methane by the naked-eye detection and increasing fluorescence signals. Then more detailed studies of the mechanism between receptor **4** and anions are under investigation.

Acknowledgements

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Scheme and Figures caption:

Scheme 1. Synthesis of receptors **1**–**4**

Fig. 1. (a) Color changes of receptor **4** (6×10^{-5} M, MeCN) upon addition of 200 equiv. of various anions; (b) Color comparison of receptors **1**–**4** upon addition of F^- under the same conditions

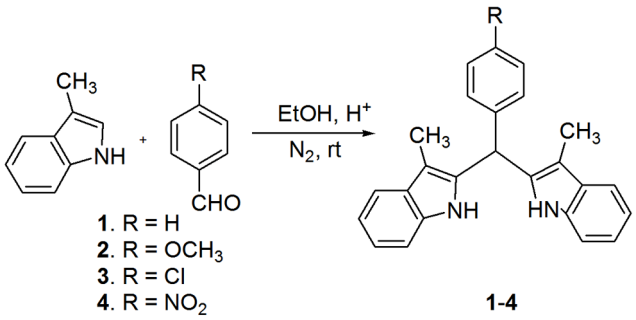
Fig. 2. Absorption spectra of receptor **4** (5×10^{-5} M, MeCN) in the presence of 200 equiv. of various anions

Fig. 3. Changes in the UV-vis absorption spectra of receptor **4** in MeCN (1×10^{-5} M) after addition of F^- from (a) 0 to 4 equiv.; (b) 4 to 580 equiv.

Fig. 4. Fluorescence emission spectra (a) and the column graph (b) of receptor **4** (1×10^{-5} M) upon addition of 100 equiv. of various anions in MeCN (λ_{ex} = 300 nm)

Fig. 5. Changes in the fluorescence spectra of receptor **4** (1×10^{-5} M) with gradual increasing of the concentration of F^- in MeCN (λ_{ex} = 300 nm)

Fig. 6. The ^{1}H NMR titrations of receptor **4** and tetrabutylammonium fluoride in DMSO-d_6



Scheme 1. Synthesis of receptors **1–4**

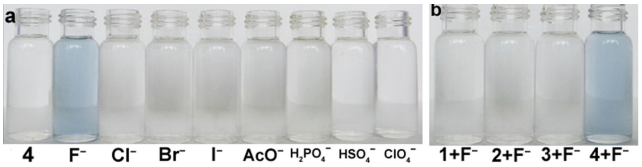


Fig. 1. (a) Color changes of receptor **4** (6×10^{-5} M, MeCN) upon addition of 200 equiv. of various anions;

(b) Color comparison of receptors **1**–**4** upon addition of F^- under the same conditions

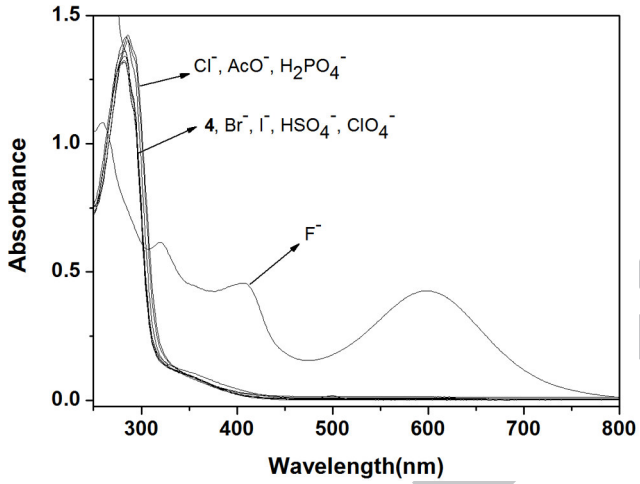


Fig. 2. Absorption spectra of receptor **4** (5×10^{-5} M, MeCN) in the presence of 200 equiv. of various anions

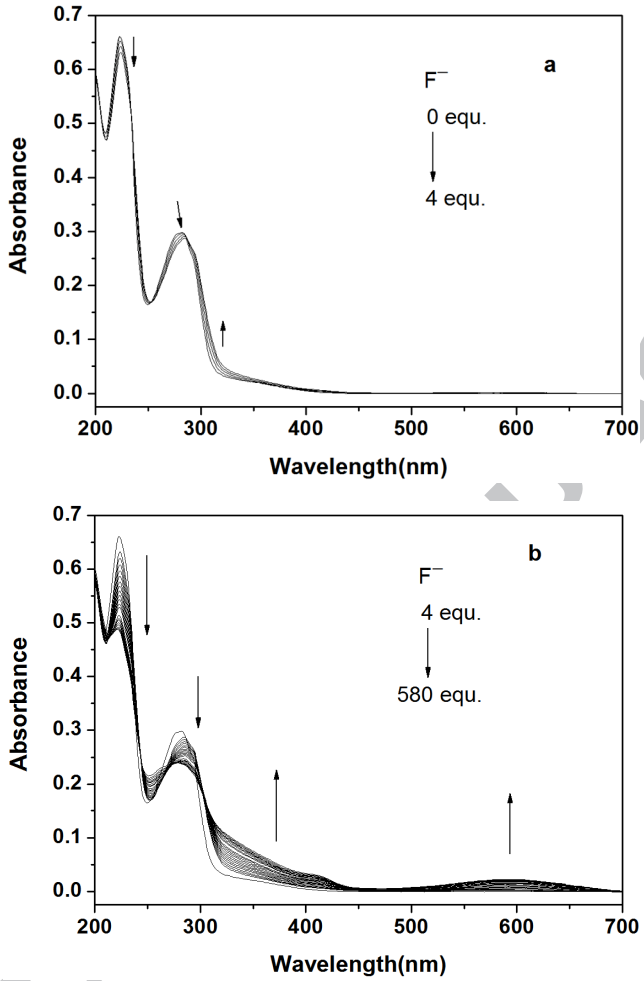


Fig. 3. Changes in the UV-vis absorption spectra of receptor **4** in MeCN (1×10^{-5} M) after addition of F^- from (a) 0 to 4 equiv.; (b) 4 to 580 equiv.

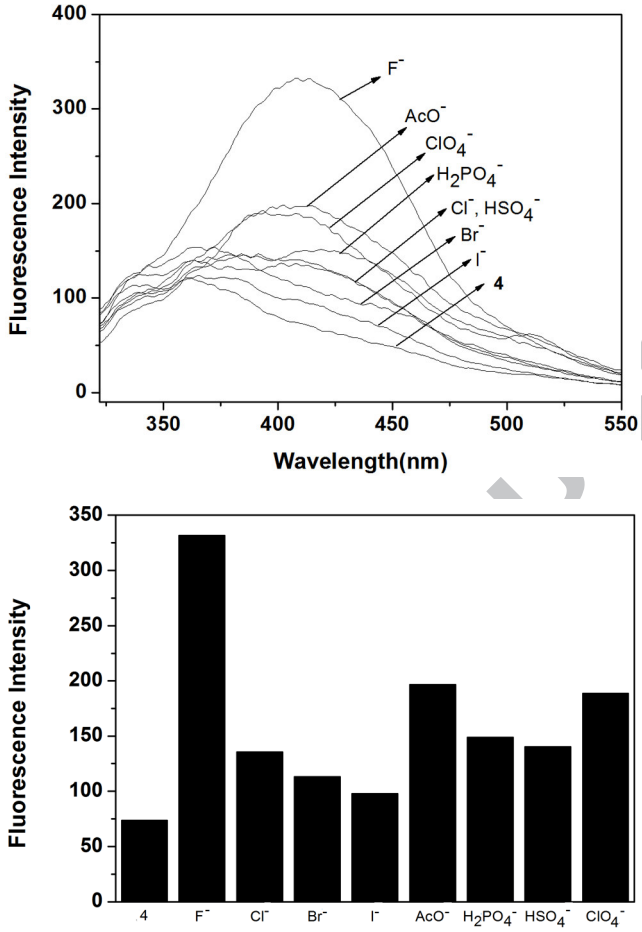


Fig. 4. Fluorescence emission spectra (a) and the column graph (b) of receptor **4** (1×10^{-5} M) upon addition of 100 equiv. of various anions in MeCN (λ_{ex} = 300 nm)

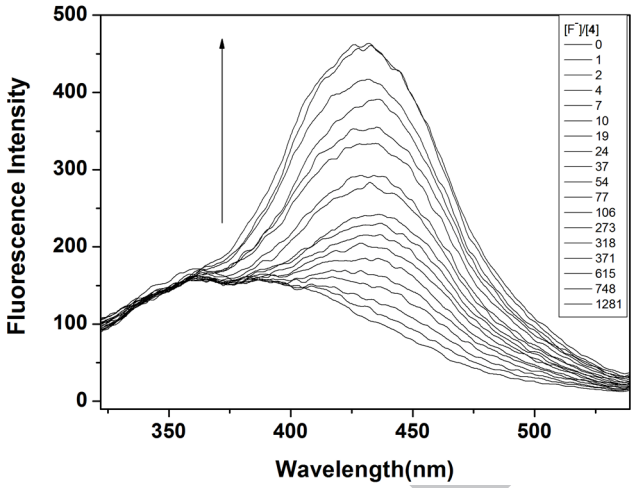


Fig. 5. Changes in the fluorescence spectra of receptor **4** (1×10^{-5} M) with gradual increasing of the concentration of F^- in MeCN (λ_{ex} = 300 nm)

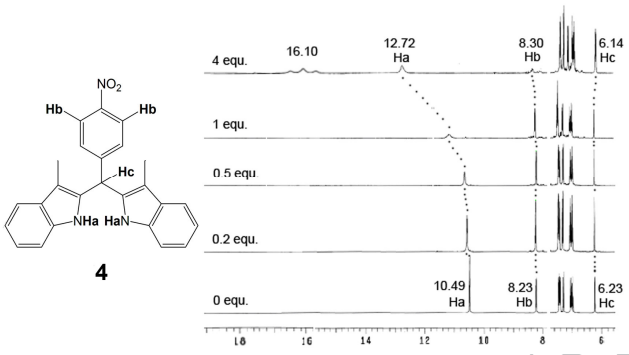


Fig. 6. The ^{1}H NMR titrations of receptor **4** and tetrabutylammonium fluoride in DMSO-d_6

Graphical Abstract:

Receptor **4** based on 2,2'-bis(indolyl)methane containing nitro group can recognize selectively F^- over AcO^-, $H_2PO_4^-$ and other anions by a favorable color change of colorless-to-blue.

Highlights:

- We reported a series of receptors based on 2,2'-bis(indolyl)methane.
- The receptor containing nitro group was studied as a perfect receptor.
- This receptor could recognize selectively F^- by a spectral dual-function.
- The spectral dual-function was related to the deprotonation of N–H protons.