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Artigo

ANION-BINDING AND SENSING PROPERTIES OF NOVEL RECEPTORS BASED ON N-(INDOL-3-YLGLYOXYLYL)BENZYLAMINE

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Indole-based receptors such as biindole, carbazole, and indolocarbazole are regarded as some of the most favorable anion receptors in molecular recognition. This is because indole groups possess N–H groups as hydrogen-bonding donors. The introduction of amide groups in the indole framework can induce strong binding properties and good water solubility. In this study, we designed and synthesized a series of *N*-(indol-3-ylglyoxylyl)benzylamine derivatives as novel and simple anion receptors. The receptors derived by aryl and aliphatic amines can selectively recognize F^- based on a color change from colorless-to-yellow in DMSO. The receptors derived by hydrazine hydrate can recognize F^-, AcO^-, and $H_2PO_4^-$ by similar color changes in DMSO and can even enable the selective recognition of F^- in a DMSO–H_2O binary solution by the naked eye. Spectrographic data indicate that complexes are formed between receptors and anions through multiple hydrogen-bonding interactions in dual solutions.

Keywords: anion recognition; indoly benzylamine; hydrogen bonds; spectroscopy.

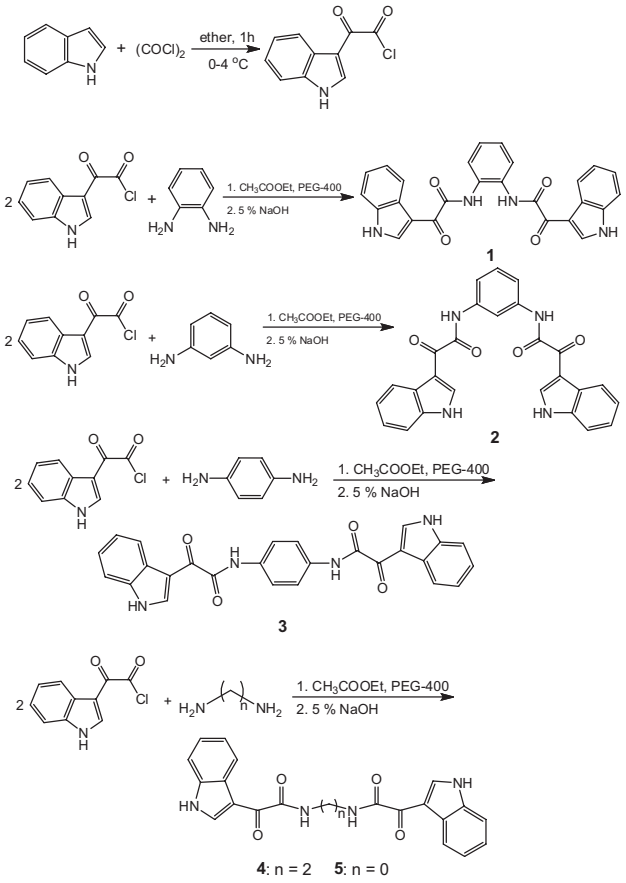
INTRODUCTION

Among the various receptors developed for anions,[1-4] indole--based compounds such as biindole, carbazole and indolocarbazole, are regarded as some of the most favourable anion receptors in molecular recognition, because indole groups possess N–H groups as hydrogen bonding donors.[5-8] Indole-based receptors bind more easily with anions via hydrogen-bonding interactions than pyrrole because the N–H group of indole is more acidic. In this field, biindole-based receptors have been reported as one of the featured anion receptors.[9] Moreover, receptors based on amides have received considerable attention,[10-12] because amide groups have good water solubility and can supply strong hydrogen-bonding interactions with anions. The introduction of amide groups in the indole framework can induce strong binding properties, and even result in the formation of multiple hydrogen-bonding interactions with anions in water-containing media.[13]

Considering these facts and as a part of our work on anion recognition of indole-based receptors,[14-18] we herein report a series of receptors 1–5 based on *N*-(indol-3-ylglyoxylyl)benzylamine. Remarkably, receptors 1–4 are derivatives of aryl and aliphatic amines and can selectively recognize F^- based on a colour change from colourless to yellow. Receptor 5, which was derived using hydrazine hydrate, can recognize F^-, AcO^- and $H_2PO_4^-$ by similar colour changes and can even selectively recognize F^- in water-containing media.

EXPERIMENTAL

Intermediate indolylglyoxylyl chloride was prepared from the reaction of indole with Oxalylchloride. Receptors 1–5 were prepared from the reaction of indolylglyoxylyl chloride with appropriate bisamines in the presence of polyethylene glycol-400 (PEG-400) as a phase-transfer catalyst. The synthesis process of receptors 1–5 is illustrated in Scheme 1.



Scheme 1. *Synthesis of receptors 1–5*

General Remarks

Chemicals were purchased from commercial suppliers, and used without further purification. DMSO was chromatogram pure. Melting points were determined on a PHMK 05 microscopic melting-point

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apparatus (Germany) and are uncorrected. The FTIR spectra were recorded on a Nicolet NEXUS FTIR spectrometer in the 4000–400 cm^{-1} region using KBr pellets. MS results were determined on Agilent-1100 LC/MSD trap instrument. ^1H and ^{13}C NMR spectra were recorded using an Inova-400 spectrometer (Varian Company) and were performed with TMS as an internal reference (in DMSO-d_6). The absorbance measurements were performed on a PerkinElmer Lambda 35 UV/VIS Spectrometer.

Synthetic method

General procedure for the synthesis of intermediate indolylglyoxylyl chloride

Oxalylchloride (5 mmol) was slowly added under cooling to a stirred solution of indole (5 mmol) in 25 mL of anhydrous diethyl ether. The reaction mixture was stirred for 30 min. The resulting yellow precipitate was filtered, washed with anhydrous diethyl ether and dried to give intermediate indolylglyoxylyl chloride in 90% yield. The product was used immediately in the next step without further purification, because of its instability.

General procedure for the synthesis of receptors 1-5

Indolylglyoxylyl chloride (5 mmol), the appropriate bisamine (2.5 mmol), PEG-400 (3% with respect to bisamine) and 30 mL of ethyl acetate were added to a dried round-bottom flask containing a magnetic stirrer bar and were stirred at room temperature for 10 min, followed by the addition of 5% sodium hydroxide solution (10 mL). The mixture was stirred at room temperature for 1 h, the precipitate was filtered, washed with water to remove inorganic salts, dried and crystallized from DMF–H_2O to afford receptors 1–5. The detailed characterization data for receptors 1–5 are presented in the Supplementary Material.

RESULTS AND DISCUSSION

UV-Vis spectral studies

The anion recognition properties of receptors 1–5 were first investigated using UV-Vis absorption spectroscopy. Receptors 1–4 can selectively recognize F^- over AcO^-, $H_2PO_4^-$ and other anions via an obvious bathochromic shift and a favourable colour change of colourless-to-yellow. For example, receptor 1 exhibits high recognition selectivity towards F^-, but lack obvious interactions with other anions, as shown in Figure 1. In each case, the counter cation was tetrabutylammonium.

Titration experiments on receptor 1 with F^- were performed by UV–Vis spectroscopy in DMSO to investigate the binding abilities of receptor 1 with F^-. As shown in Figure 2, the absorption spectra of the solution of receptor 1 were recorded during the course of the titration with different concentrations of F^- in DMSO. Upon the gradual addition of F^-, the absorption peak disappeared at 332 nm, whereas, a new absorption peak appeared at 380 nm, the intensity of the absorption peak at 277 nm was enhanced. The linear relationship between $(A_0–A)^{-1}$ vs $(C_{F-})^{-1}$ obtained in the Benesi–Hildebrand plot[19,20] indicated the formation of a 1:1 complex between receptor 1 and fluoride ions by hydrogen-bonding interactions.

Similar variations in receptors 2–4 were observed upon the gradual addition of F^-. The binding constants for receptors 1–4 with F^- were calculated; the results are reported in Table 1.

Moreover, the addition of the protonic solvent H_2O destroyed the hydrogen-bonding interactions of receptors 1–4 with F^-, and reversed the molecular structure of receptors 1–4. For example, the changes in the absorption spectra of receptor 1 upon the addition of F^- disappeared upon the addition of water, as shown in Figure 1S.

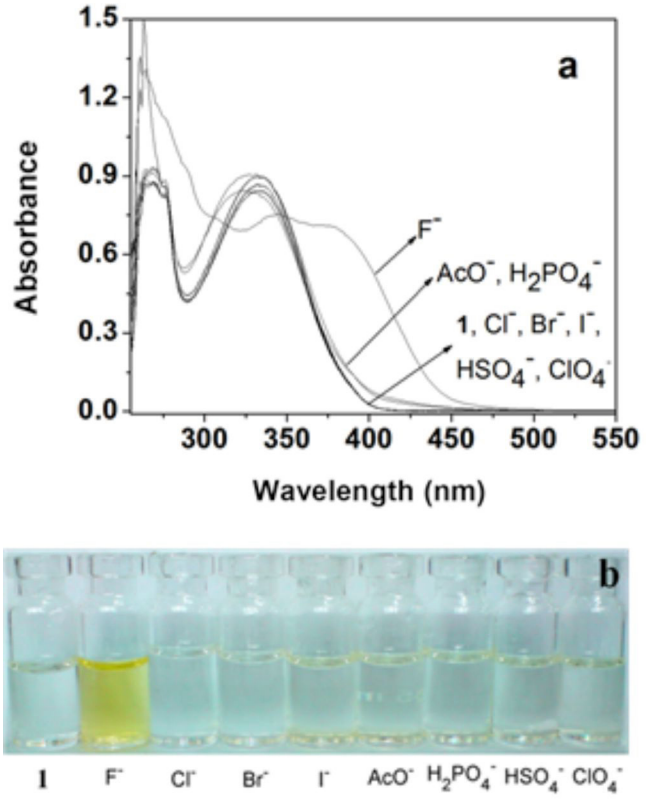

Figure 1. *Changes in the UV-Vis absorption spectra (a) (2.5 × 10^{-5} mol L^{-1}) and colour (b) (5.0 × 10^{-5} mol L^{-1}) of receptor 1 in DMSO solution upon the addition of 200 equiv. of various anions*

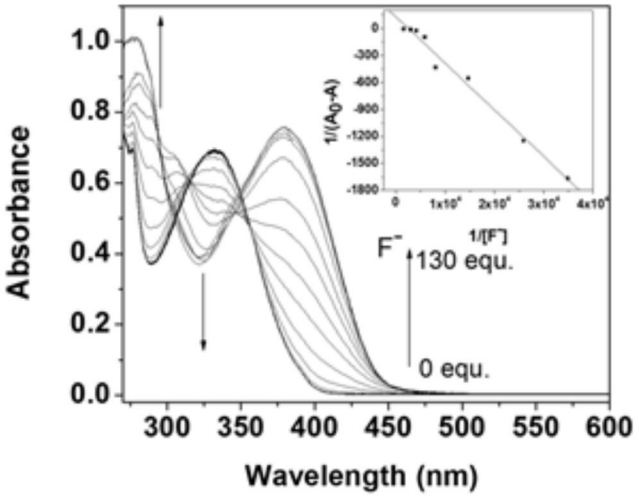

Figure 2. *Changes in the UV-Vis absorption spectra of receptor 1 (3.0 × 10^{-5} mol L^{-1}) upon addition of F^-*

Table 1. *Ks* and *R* values of receptors 1-4 with F^- in DMSO

Receptor		1	2	3	4
F^-	*Ks* (L mol^{-1})	2530	537	168	621
	R	0.9925	0.9929	0.9958	0.9957

Receptor 5 can selectively recognize F^-, AcO^- and $H_2PO_4^-$ in DMSO via obvious spectral changes and favourable colour changes, as shown in Figure 3. Two new peaks appeared at 379 and 406 nm,

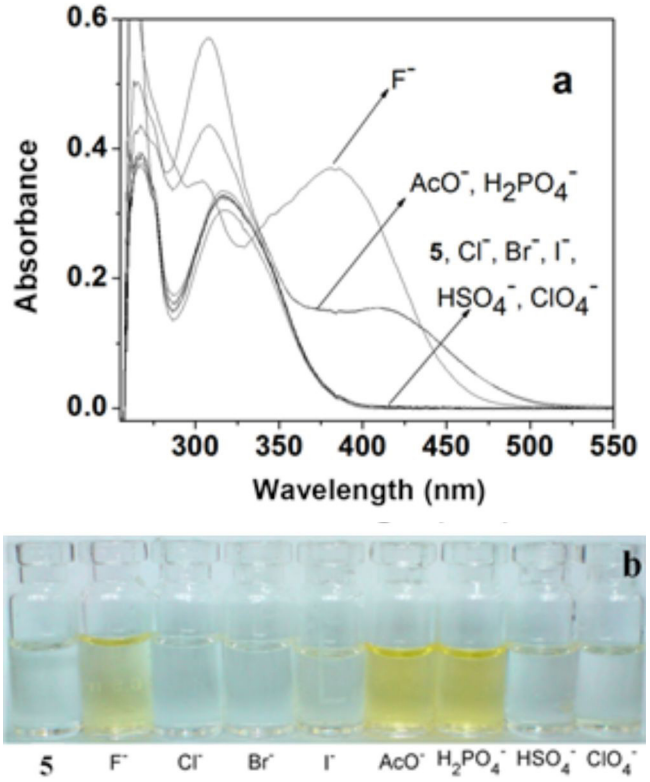

Figure 3. *Changes in the UV-Vis absorption spectra (a) (2.5×10^{-5} mol L^{-1}) and colour (b) changes (5.0×10^{-5} mol L^{-1}) of receptor 5 in DMSO solution upon the addition of 200 equiv. of various anions*

which are associated with the colour change from colourless to yellow.

Moreover, the interactions of receptor 5 with anions were studied in detail using UV-Vis spectroscopic titration techniques, as shown in Figure 4. Upon the gradual addition of F^-, the intensity of the absorption peak at 317 nm decreased and a discernible bathochromic shift occurred from 317 nm to 322 nm, as shown in Figure 4(a). Two new absorption peaks were observed at 275 and 379 nm. Figures 4(b) and 4(c) show the changes in absorption spectra of receptor 5 upon the addition of AcO^- and $H_2PO_4^-$, respectively. The intensity of the peak at 317 nm decreased, whereas a new peak emerged at 406 nm. A discernible blue shift occurred from 317 nm to 310 nm. Isosbestic points appeared at 307 and 350 nm. Similarly, the linear relationship of $(A_0–A)^{-1}$ vs $(C_{anions})^{-1}$ obtained in the Benesi–Hildebrand plot indicated the formation of 1:1 complexes between receptor 5 and anions, which was the best reason for inducing these variations of spectra and colour changes.

Interestingly, receptor 5 can even selectively recognize F^- over AcO^-, $H_2PO_4^-$ and other anions by a favourable colour change of colourless-to-yellow in DMSO–water binary solution, as shown in Figure 5. The interactions of receptor 5 with F^- in DMSO–H_2O binary solution were studied in detail using UV-Vis spectroscopic titration techniques, as shown in Figure 2S. Similarly, the binding constants for receptor 5 and anions in DMSO and DMSO–H_2O binary solution were calculated, respectively; the results are reported in Table 2.

The degree of binding is evident from the results in Table 1 and Table 2. The association constants of receptors with anions (*Ks*) decrease in the order receptor 5 > 1 > 4 > 2 > 3. Receptor 5 can even selectively recognize F^- in DMSO–H_2O binary solution; however, similar binding ability is not exhibited by other receptors upon the addition of F^- under the same conditions. Receptor 5 likely offers a greater number of sites suitable for binding F^- and enhances the binding ability; the complex between receptor **5** and

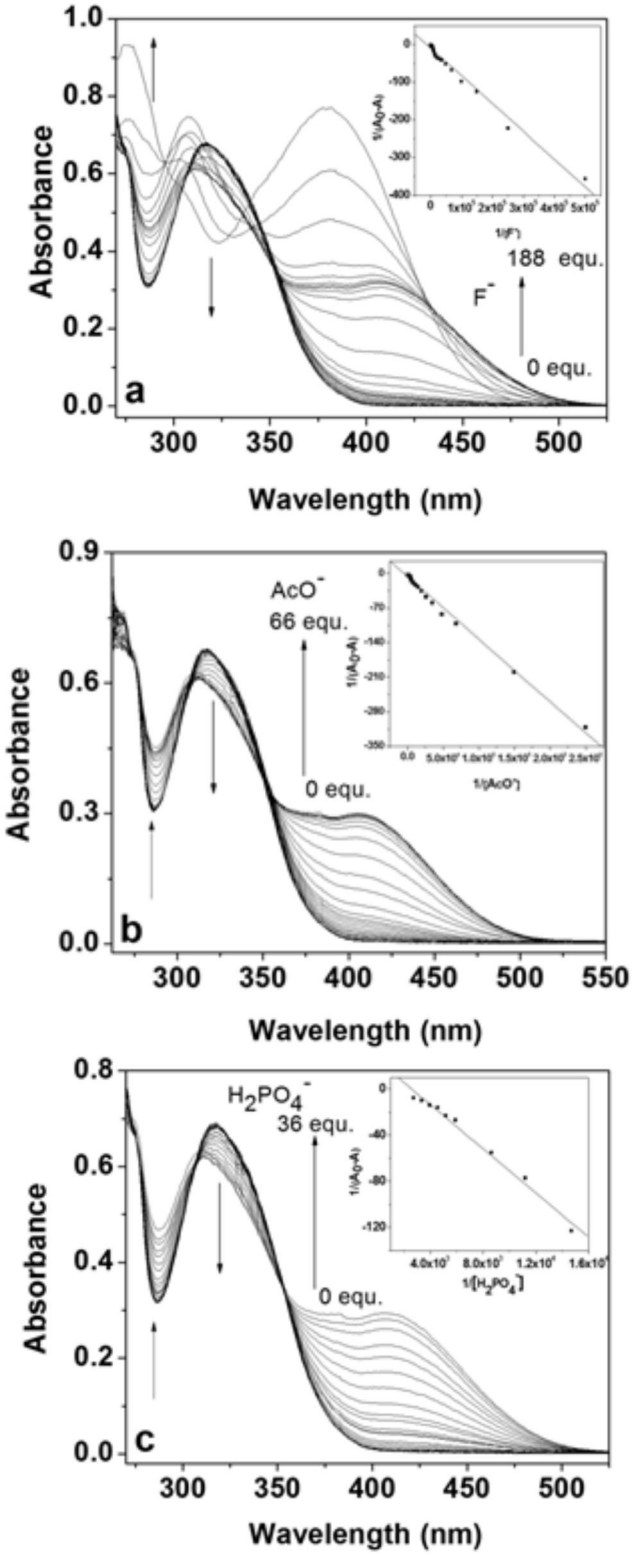

Figure 4. *Changes in the UV-Vis absorption spectra of receptor 5 upon the addition of F^- (a), AcO^- (b) and $H_2PO_4^-$ (c) in DMSO*

F^- by multiple hydrogen-bonding interactions formed in DMSO–H_2O binary solution which was evident by a favourable colour change of colourless-to-yellow.

^{1}H NMR spectral studies

To further investigate the interactions between receptor 5 and

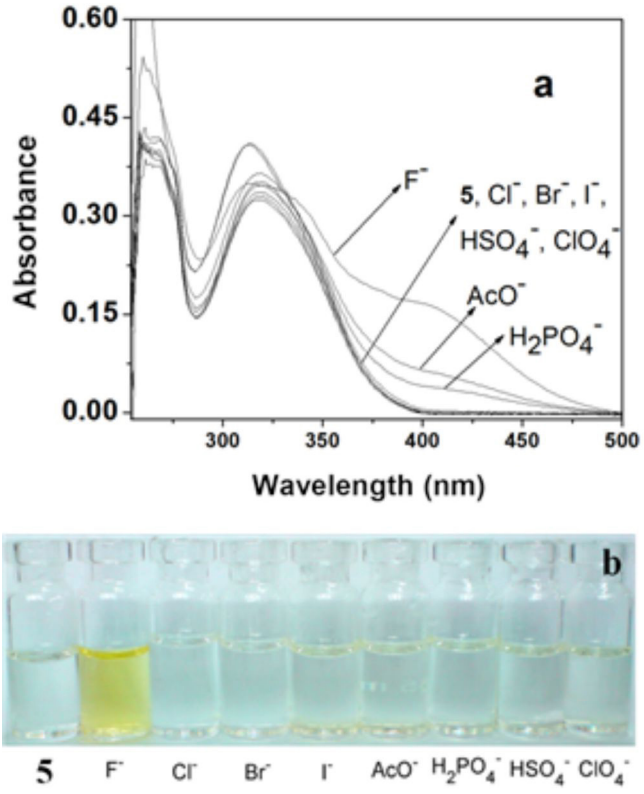

Figure 5. *Changes in the UV-Vis absorption spectra (a) (2.5 × 10^{-5} mol L^{-1}) and colour (b) (5.0 × 10^{-5} mol L^{-1}) of receptor 5 in DMSO–H_2O (9:1, v/v) solution upon the addition of 200 equiv. of various anions*

Table 2. *Ks* and *R* values of receptor 5 with anions in DMSO and DMSO–H_2O (9:1, v/v) solution

		F^-	AcO^-	$H_2PO_4^-$
DMSO	*Ks* (L mol^{-1})	11200	5310	2605
	R	0.9918	0.9964	0.9930
DMSO–H_2O (9:1, v/v)	*Ks* (L mol^{-1})	2600	-	–
	R	0.9892	–	–

F^-, we conducted ^{1}H NMR titration experiments with receptor 5 and F^- in DMSO-d_6, as shown in Figure 3S. The addition of 0.2 equiv. of F^- caused drastic decreases and large downfield shifts of the N–H protons of receptor 5, and the signals of the N–H protons of receptor 5 almost vanished upon the addition of 1 equiv. of F^-, which suggests that a complex may have formed by multiple hydrogen-bonding interactions between receptor 5 and F^-. Considering the aforementioned observations, the possible binding modes of receptor 5 with F^- are illustrated in Scheme 1S.

CONCLUSIONS

A series of novel compounds based on *N*-(indol-3-ylglyoxylyl) benzylamine were designed and synthesized as anion receptors. UV–Vis absorption spectroscopy revealed that the aryl and aliphatic amines derivatives of *N*-(indol-3-ylglyoxylyl)benzylamine can bind with F^- via multiple hydrogen-bonding interactions, whereas the interactions of these receptors with Cl^-, Br^-, I^-, AcO^-, $H_2PO_4^-$, HSO_4^- and ClO_4^- were too weak to enable the measurement of the association constants by UV spectroscopy in diluted solutions. Notably, the hydrazine hydrate derivative receptor exhibited excellent selectivity towards F^-, AcO^- and $H_2PO_4^-$ by colour changes from colourless to yellow in DMSO. The framework supplies a greater number of binding points for anions and can recognize fluoride ions selectively in DMSO–H_2O binary solution by a colour change from colourless to yellow, which result in excellent naked-eye detection of fluoride ions. More detailed studies of the binding mechanism between receptor 5 and anions are under investigation.

ACKNOWLEDGEMENTS

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SUPPLEMENTARY MATERIAL

The detailed characterization data for receptor 1–5, UV absorption spectra of receptor 1 in DMSO–H_2O (9:1, v/v) solution upon the addition of various anions, UV absorption spectra of receptor 5 in DMSO–H_2O (9:1, v/v) solution upon the addition of various anions, ^{1}H NMR titration of receptor 5 in the presence of F^- in DMSO-d_6, possible binding modes of receptor 5 with fluoride ions are available. Supplementary material associated with this article can be found, in the online version, at http://www.quimicanova.sbq.org.br/.

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