Chinese Journal of Chemistry, **2004**, *22*, 1372—1376 **Article**

Amide-based Fluorescent Macrocyclic Anion Receptors

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Two fluorescent anion receptors (**1** and **2**) based on amide macrocycle were synthesized and corresponding fluorescence quenching induced by anion complexation was observed in different degree. Receptors form 1∶1 complexes with anions by hydrogen bonding interactions. Receptor **1** bound anions in the order of F^->Cl^-> $H_2PO_4^-$ >CH_3COO^->>Br^-, I^- and receptor **2** showed high selectivity to F^- over other anions.

Keywords macrocyclic polyamine, synthesis, fluorescence, anion recognition

Introduction

Interest in the selective recognition and sensing of anionic species continues to attract the attention of supramolecular chemistry community.[1] The importance of anions in chemical and biological process can not be underestimated. It is well known that in nature neutral proteins bind anions only via hydrogen bonding interactions.[2] Several anion receptors have been constructed from five-membered heterocycle,[3] amide,[4] (thio) urea,[5] since these groups form relatively strong NH···anion hydrogen bonds with anions.

The design and synthesis of fluorescence-based anion receptors have a potentially abundant use for on-line and real time detection of physiologically important anions and environmental monitoring of harmful anionic pollutants, because any fluorescent change induced by anion complexation is highly sensitive and easily detectable. The simplest fluorescent anion receptors are multi-component system consisting of a signaling unit (fluorophore) and a guest binding site (receptor) and the two are usually linked via a spacer.[6] In recent decades, a variety of artificial anion receptors coordinating anion by amide macrocycles have been reported, however, simple and easily synthesized fluorescent anion receptors based on amide macrocycles remain rare.[7]

Here, we report the synthesis of two typical PET (photoinduced electron transfer) fluorescent receptors **1** and **2** consisting of an amide macrocycle with a pendant anthracene, and their binding behaviors with anions were investigated by fluorescence, UV-vis and ^{1}H NMR spectra.

Results and discussion

Synthesis of receptors 1 and 2

The synthetic routes of receptors **1** and **2** are outlined in Scheme 1. Compound **5** was purified by recrystallization from ethanol.

Fluorescence spectral study

The binding properties of receptor **1** or **2** with anions were investigated by fluorescence spectra. Free receptors **1** and **2** showed similar fluorescence emission bands with a maximum at 414 nm. The complexation of receptors with anions resulted in fluorescence quenching of receptors to different extent.

In the absence of anions, the fluorescence emission spectra of **1** consisted of three sharp bands at 390, 414, 438 nm, with a shoulder at 467 nm. Addition of F^- effectively quenched the fluorescence emission of **1** due to its small size and high charge density. Upon addition of F^- to the solution of **1** in about 4-fold, emission intensity of **1** was remarkably decreased to about 50% due to the formation of anion-receptor complex (Figure 1), however, in the presence of other anions the fluorescence quenching of **1** was weak (Figure 2). Introducing about 40-fold of Cl^-, $H_2PO_4^-$, CH_3COO^- to the solution of **1** led to fluorescence quenching to about 66%, 50%, 52%, respectively. Addition of a great excess of Br^- and I^- did not cause significant fluorescence quenching of **1**, ruling out the possibility of quenching by heavy atom effect. In the presence of anions, there was no evident spectral change (for example, no spectral shift or formation of new emission bands) of **1** except original three bands.

Free receptor **2** showed similar fluorescence emission bands to **1**. The fluorescence quenching of **2** was

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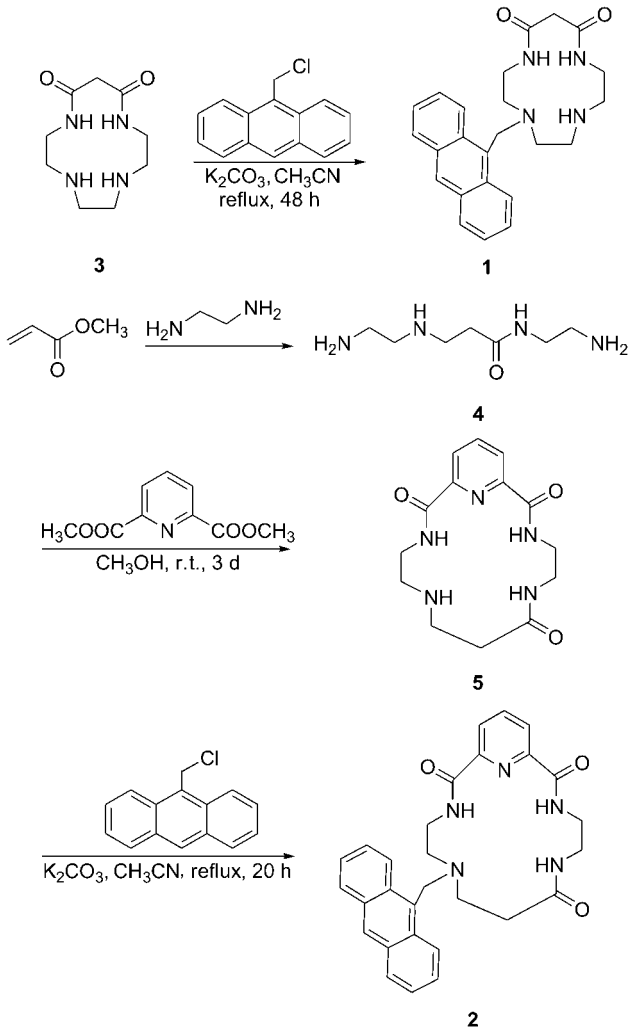
Scheme 1 Synthesis of receptors **1** and **2**



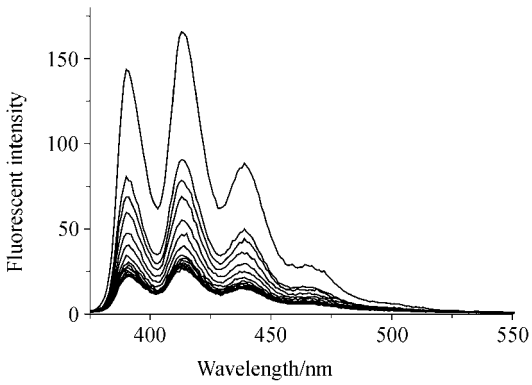


Figure 1 Fluorescent spectra of **1** (5×10^{-6} mol•L^{-1}) with F^- in $CHCl_3$. The equiv. of F^- are: 0, 4, 8, 12, 16, 20, 24, 40, 45, 50, 60, 80, 120, 160, 200, λ_{ex}=368 nm.

weaker than that of **1** in the presence of the same anions. Upon gradual addition of F^- to the solution of **2**, emission intensity of **2** was gradually decreased (Figure 3). Addition of other anions (Cl^-, Br^-, I^-, $H_2PO_4^-$, CH_3COO^-) did not change the emission intensity of **2** at all. The high selectivity of **2** for F^- might be due to the relatively rigid macrocycle consisting of -NH-CO- linked by a pyridine subunit.

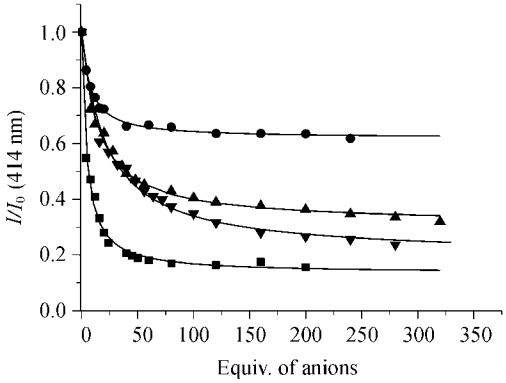


Figure 2 Changes of I/I_0 of **1** at 414 nm upon addition of anions in $CHCl_3$, [**1**]: 5×10^{-6} mol•L^{-1}, (■F^-, ●Cl^-, ▲H_2PO4^-, ▼ CH_3COO^-). The lines are fitting curves. The correlation coefficients of non-linear curve fitting are 0.9952, 0.9979, 0.9954 and 0.9946, respectively.

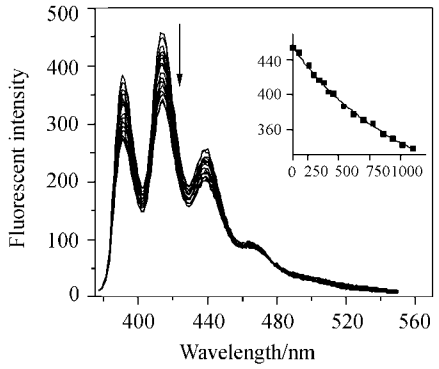


Figure 3 Fluorescent spectra of **2** (5×10^{-6} mol•L^{-1}) with F^- in $CHCl_3$. The equiv. of F^- are: 0, 48, 128, 168, 208, 248, 288, 328, 408, 488, 568, 648, 728, 808, 888, 968. λ_{ex}=368 nm. Inset: Change of fluorescent intensity of **2** at 414 nm upon addition of F^-. The lines are fitting curves. The correlation coefficient of non-linear curve fitting is 0.9986.

UV-vis spectral study

Upon complexation, changes in the UV-vis spectra of anthracene moiety were only minor for **1** (peaks at 334, 351 369, 389 nm) and **2** (peaks at 335, 351, 370, 390 nm) in the presence of anions (Figure 4), which implied that a PET process occurred with anion binding.[6a,8] The presence of methylene spacer acting as the insulating role minimized any ground interactions between the fluorophore and the anion receptor. It was proposed that upon anion recognition, the rate of electron transfer from the HOMO of the amide-anion complex to the anthracene excited state enhanced, which caused the fluorescence emission to be quenched or "switched off",[9] and a little change of UV-vis spectra in the complexation.

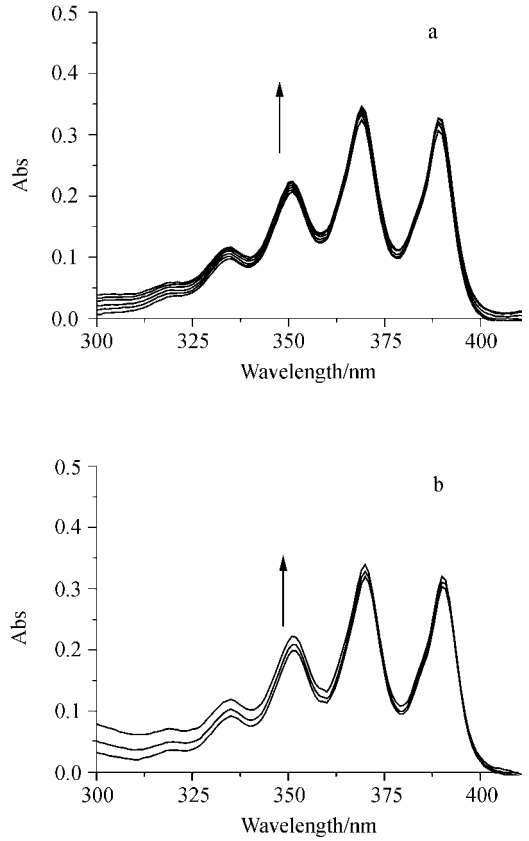


Figure 4 Absorption spectra of receptors (2.5×10^{-5} mol•L^{-1}) with F^- in $CHCl_3$. (a) **1** and F^-. Equivalent of F^-: 0, 50, 100, 200, 300 and 400; (b) **2** and F^-. Equivalent of F^-: 0, 200 and 400.

^{1}H NMR spectral study

The ^{1}H NMR spectra of receptors **1** and **2** show dramatic changes in the presence of anions. Receptor **1** shows two signal peaks of amide proton at δ: 5.39 and 8.57 and receptor **2** shows three signal peaks of amide proton at δ: 5.03, 8.95, and 9.14. In the presence of anions, the signals of amide protons disappear, illustrating that the recognition of receptors for anions is caused by multiple hydrogen bonding interactions.[10] Anion complexation induced upfield shift of $ArCH_2$ proton signal. For example, upon addition of F^-, the $ArCH_2$ peak of **1** shifted from δ: 4.63 to 4.50, and the peak of **2** shifted from δ: 4.49 to 4.39. Moreover, the chemical shifts of anthracene proton changed too. The anthracene proton signals of free receptor **1** showed multiple peaks, including δ: 7.45—7.59 (m, 4H), 8.03 (d, J=8 Hz, 2H), 8.42 (d, J=8 Hz, 2H) and 8.44 (s, 1H). In the presence of F^-, the peaks shifted to δ: 7.32 (t, J=7.8 Hz, 2H), 7.53 (t, J=7.8 Hz, 2H), 7.82 (d, 2H), 8.24 (s, 1H) and 8.37 (d, J=7.8 Hz, 2H) respectively. It would be attributed to the changes of chemical environment on protons of anthracene in the complexation.

Determination of association constants and stoichiometric ratio

For the complex of 1∶1 stoichiometry, the following relation could be derived easily as reported formerly:[11]

$$I/I_0=1+0.5\Delta\varepsilon\left\{\left[c_H+c_G+\frac{1}{K_{ass}}-\left[\left(c_H+c_G+\frac{1}{K_{ass}}\right)^2-4c_Hc_G\right]^{1/2}\right]\right\}/I_0$$

where I is the fluorescence intensity, and c_H or c_G is the overall concentration of host or anion guest correspondingly.

The non-linear curve fitting results were summarized in Figures 2 and 3. All of the correlation coefficients were larger than 0.99, indicating that receptors (**1** and **2**) and anions formed 1∶1 complexes.[11] The calculated association constants are listed in Table 1. It was deduced from the association constants that receptor **1** bound anions in the order $F^->Cl^->H_2PO_4^->CH_3COO^->>Br^-$, I^- and receptor **2** showed better selectivity to F^- over other anions in spite of less affinity.

Table 1 Association constants K_{ass} (L•mol^{-1}) of receptors **1** and **2** with anions[a] in $CHCl_3$

Anion	K_{ass}(L•mol^{-1})	
	receptor **1**	receptor **2**
F^-	$(4.93\pm0.40)\times10^4$	$(1.46\pm0.12)\times10^2$
Cl^-	$(2.93\pm0.16)\times10^4$	[b]
$H_2PO_4^-$	$(1.39\pm0.09)\times10^4$	[b]
CH_3COO^-	$(9.30\pm0.67)\times10^3$	[b]
Br^-	[b]	[b]
I^-	[b]	[b]

[a] Anions were used as their tetrabutylammonium salts. [b] The changes of the spectra were too small to calculate the association constants precisely.

Conclusion

The neutral anion receptors **1** and **2** based on amide macrocycle were synthesized easily. **1** and **2** both form 1∶1 complex with anions by hydrogen bonding interactions. Upon anion complexation, the fluorescent intensities of receptors **1** and **2** were quenched possibly due to PET process. Receptor **1** bound anions in the order $F^->Cl^->H_2PO_4^->CH_3COO^->>Br^-$, I^- and receptor **2** showed higher selectivity to F^- over other anions. The fluorescent quenching of receptor **2** induced by anion recognition is promising to be used as fluorescent chemosensors for F^-.

Experimental

Materials

Methanol was distilled after refluxing with magne-

sium. Acetonitrile was distilled after refluxing with phosphorus pentoxide. Potassium carbonate was baked at 500 ℃ for 4 h before use. All other commercially available reagents were used without further purification. The anions were used as their tetrabutylammonium salts. **3**[12] and **4**[13] were synthesized according to literature.

Melting points were measured on a Reichert 7905 melting-point apparatus (uncorrected). The infrared spectra were performed on a Nicolet 670 FT-IR spectrophotometer. The mass spectra were recorded on a ZAB-HF-3F spectrometer or Finnigan LCQ advantage spectrometer. Elemental analyses were determined by a Perkin-Elmer 204B elemental autoanalyzer. ^{1}H NMR spectra were recorded on a Varian Mercury VX-300 MHz spectrometer. UV-vis spectra were taken on a TU-1901 spectrometer. Fluorescence spectra were obtained on a Schimadzu RF-5301 spectrometer.

Synthesis

Receptor 1: Under nitrogen atmosphere, a solution of 9-chloromethylanthracene (1.13 g, 5 mmol) in dry CH_3CN (100 mL) was added dropwise to a solution of **3** (1.07 g, 5 mmol) in dry CH_3CN (100 mL) in the presence of an excess amount of K_2CO_3 (3.45 g, 25 mmol) at reflux. The reaction mixture was heated at reflux and stirred for about 48 h under nitrogen atmosphere. After filtration, the filtrate was evaporated to dryness, and the residue was dissolved in water and then extracted with $CHCl_3$ (50 mL×4). The combined $CHCl_3$ solution was dried by anhydrous sodium sulfate, evaporated, and purified by column chromatography on neutral Al_2O_3 by eluting with $CHCl_3$-CH_3OH (100∶2) to give receptor **1** as pale yellow solid (0.73 g, yield 36.1%). m.p. 167—169 ℃; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.68 (br, 1H, NH), 1.78 (t, J=5 Hz, 2H, NCH_2), 2.43—2.50 (m, 4H, NCH_2), 2.88 (t, J=5 Hz, 2H, NCH_2), 2.97—3.03 (m, 2H, $CONCH_2$), 3.28 (s, 2H, $COCH_2CO$), 3.51—3.56 (m, 2H, $CONCH_2$), 4.63 (s, 2H, $ArCH_2$), 5.39 (br, 1H, CONH), 7.45—7.59 (m, 4H), 8.03 (d, J=8 Hz, 2H), 8.42 (d, J=8 Hz, 2H), 8.44 (s, 1H), 8.57 (br, 1H, CONH); IR (KBr) ν: 3315, 1679, 1632, 1560, 1260, 732 cm^{-1}. FAB-MS *m/z* (%): 405 (M^++1, 11). Anal. calcd for $C_{24}H_{28}N_4O_2$: C 71.25, H 6.99, N 13.85; found C 71.13, H 6.97, N 13.94.

Compound 5: After a methanol solution (250 mL) of **4** (1.74 g, 0.01 mol) and 2, 6-dimethylester pyridine (1.94 g, 0.01 mol) was stirred at room temperature under nitrogen atmosphere for 3 d, the reaction solvent was removed by evaporation to give compound **5** as white solid, which was purified by recrystallization from ethanol: yield 1.62 g (53.1%). m.p. 204—205 ℃; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.62 (br, 1H, NH), 2.47 (t, J=5 Hz, 2H, NCH_2), 2.87 (t, J=5 Hz, 2H, NCH_2), 3.00 (t, J=5 Hz, 2H, $COCH_2$), 3.58—3.62 (m, 4H, $PyCONCH_2$), 3.71 (t, J=5 Hz, 2H, $CONCH_2$), 6.21 (br, 1H, CONH), 7.97 (t, J=8 Hz, 1H, PyH), 8.22 (d, J=8 Hz, 1H, PyH), 8.27 (d, J=8 Hz, 1H, PyH), 9.06 (br, 1H, CONH), 9.14 (br, 1H, CONH); IR (KBr) ν: 3336, 3288, 3258, 1676, 1655, 1552, 1263, 739, 645 cm^{-1}. FAB-MS *m/z* (%): 306 (M^++1, 100). Anal. calcd for $C_{14}H_{19}N_5O_3$: C 55.06, H, 6.28, N, 22.94; found C 55.15, H 6.34, N, 22.85.

Receptor 2: Under nitrogen atmosphere, a solution of 9-chloromethylanthracene (1.13 g, 5 mmol) in dry CH_3CN (60 mL) was added to a solution of **5** (1.53 g, 5 mmol) in dry CH_3CN (60 mL) in the presence of an excess amount of K_2CO_3 (5.39 g, 39.1 mmol) at reflux. The reaction mixture was heated at reflux and stirred for about 20 h under nitrogen atmosphere. After filtration, the filtrate was evaporated to dryness, and the residue was dissolved in water and then extracted with $CHCl_3$ (50 mL×4). The combined $CHCl_3$ solution was dried by anhydrous sodium sulfate, evaporated, and purified by column chromatography on neutral Al_2O_3 by eluting with $CHCl_3$-CH_3OH (100∶2, V∶V) to give receptor **2** as pale yellow solid (2.12 g, yield 85.7%). m.p. 237—239 ℃; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.92 (t, J=5 Hz, 2H, NCH_2), 2.80 (t, J=5 Hz, 2H, NCH_2), 2.98 (t, J=5 Hz, 2H, $COCH_2$), 3.19—3.22 (m, 4H, $PyCONCH_2$), 3.76 (t, J=5 Hz, 2H, $CONCH_2$), 4.49 (s, 2H, $ArCH_2$), 5.03 (br, 1H, CONH), 7.04 (t, J=8 Hz, 2H, ArH), 7.28 (t, J=8 Hz, 2H, ArH), 7.85—8.31 (m, 8H, PyH, ArH), 8.95 (br, 1H, CONH), 9.14 (br, 1H, CONH); IR (KBr) ν: 3332, 3288, 1681, 1659, 1536, 1447, 1282, 1235, 756 cm^{-1}. ESI-MS *m/z* (%): 496.1 (M^++1, 100). Anal. calcd for $C_{29}H_{29}N_5O_3$: C 70.27, H 5.91, N 14.13; found C 70.36, H 6.00, N 14.04.

Binding studies

The studies on binding properties of **1** and **2** were carried out in $CHCl_3$ or $CDCl_3$. UV-vis spectral study was carried out with a series of 2.5×10^{-5} mol•L^{-1} solutions of receptors containing different amounts of anions. The fluorescence titration was performed with a series of 5×10^{-6} mol•L^{-1} solutions of receptors containing different amounts of anions **1**: the excited wavelength was 368 nm, and the excitation and emission slit width were 3 nm; **2**: the excited wavelength was 368 nm, and the excitation and emission slit width were 5 nm. ^{1}H NMR study was recorded as adding equiv. of anions into receptors (10^{-2} mol•L^{-1}).

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