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A novel calix[4]arene fluorescent receptor for selective recognition of acetate anion

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Abstract—A novel bridged fluorescent calix[4]arene with 1,8-diaminoanthracene and glycine at the upper rim has been prepared, which exhibited selective recognition towards AcO^- over other anions such as F^-, Cl^-, Br^-, $H_2PO_4^-$, NO_3^-, I^- and HSO_4^- by fluorescence spectroscopy and ^1H NMR method.

The development of design and synthesis of new artificial receptors for selective anion recognition is increasingly topical field in supramolecular chemistry because of the important roles of anion in biomedicinal and chemical processes.[1] As one of the attractive molecules in anion recognition, calixarene can construct additional recognition sites in advantage of its unique three-dimensional structure. It is well known that activated amides[2] and (thio)ureas[3] can interact with anions through the formation of hydrogen bond between the active N–H and anions. Hence, potential cavity for anion recognition could be formed by the introduction of amido groups to calixarene.[4] On the other hand, sensors based on anion-induced changes in fluorescence appear to be particularly attractive due to the high detections limit and simplicity of fluorescence. However, to the best of our knowledge, there are few examples of fluoroionphores based on calixarenes developed for anion recognition in recent years.[5] Previously, we reported on the cone calix[4]arene conformer bearing alanine and dansyl on upper rim that exhibited a good recognition to F^-.[6] In this letter, we report the synthesis and anion coordination investigation of a new bridged fluorescent calix[4]arene based amide receptor with anthracene as fluorophore.

The new fluorescent molecule **6** was synthesized as outlined in Scheme 1. As described in the literature,[7] this 1,8-diaminoanthracene **2** was obtained in 30% by treating 1,8-dinitroanthraquinone **1** with sodium borohydride in isopropanol at reflux for 48 h.[8] The *N*-Boc-glycine was converted to the mixed anhydride intermediately by the treatment of isobutyl chloroformate/Et_3N, and to this was added compound **2** to give compound **3** in one-pot.[9] The Boc protecting group was removed by the treatment of crude **3** with TFA at room temperature to give compound **4**. The calix[4]arene bisacid **5**[10] was converted to calix[4]arene biscarbonyl chloride using $SOCl_2$ and then coupled with compound **4** gave the desired fluorescent molecule **6** in 30% yield. The structure of **6** in cone conformation was confirmed by ^1H (including D_2O exchange) and ^{13}C NMR, 2D ^1H–^1H COSY, MALDI-TOF MS spectroscopy and elemental analysis.[11]

The fluorescence spectra were recorded from a solution (1×10^{-5} M) of the compound **6** in CH_3CN (0.4% v/v $CHCl_3$) on excitation at 370 nm and emission at 438 nm, respectively. In each case the counter cation was tetrabutylammonium. As shown in Figure 1, the fluorescence intensity of **6** at 438 nm was gradually quenched as the anion concentration increased. When the concentration of AcO^- increased to 30 equiv, the fluorescent intensity was reduced to 44% of the initial one. In the case of F^-, the spectral changes of **6** were similar to but smaller than those of AcO^-. From Stern–Volmer plot (the fluorescence quenching followed the Stern–Volmer equation),[12] host **6** formed 1:1 stoichiometric solution complexes with AcO^- and F^-, and the association constants were estimated 3200 and 800 M^{-1}, respectively.

Keywords: Calix[4]arene; Anion recognition; Hydrogen bond.

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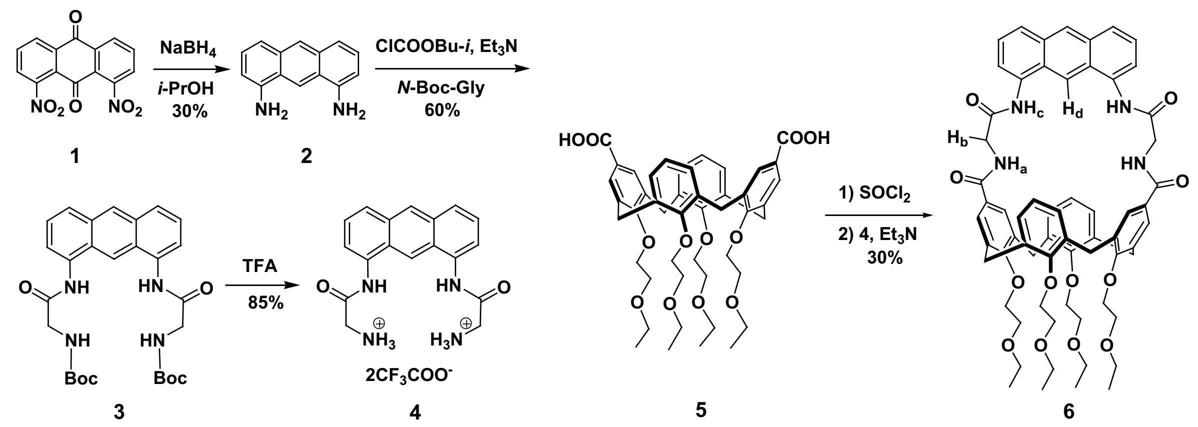


Scheme 1.

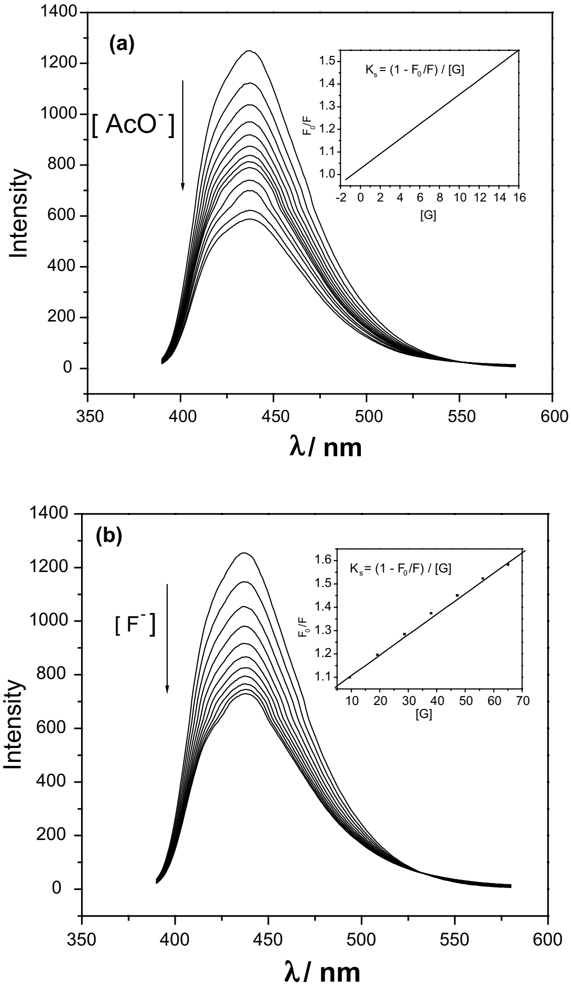


Figure 1. Fluorescence emission spectra of **6** (1×10^{-5} M) in the presence of (a) AcO^-, (b) F^- in CH_3CN (0.4% v/v $CHCl_3$). The concentration of AcO^-: 0, 2.5, 5.0, 7.5, 10.0, 12.5, 15.0, 17.5, 20.0, 25.0, 30.0, 40.0, 50.0×10^{-5} M^{-1}. The concentration of F^-: 0, 10.0, 20.0, 30.0, 40.0, 50.0, 60.0, 70.0, 80.0, 90.0, 100.0×10^{-5} M^{-1}; $\lambda_{ex} = 370$ nm. Anions used were in the form of their n-Bu_4N^+ salts.

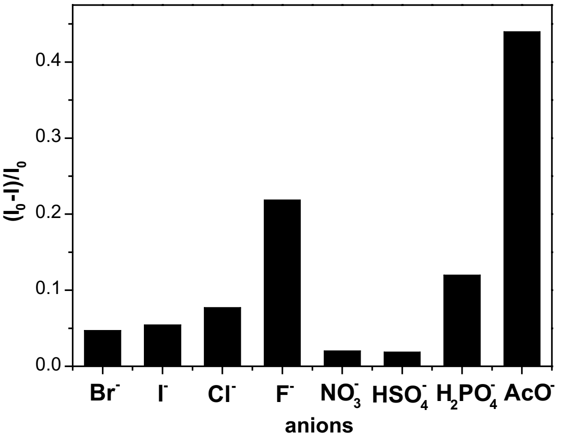


Figure 2. Fluorescence quench ratio $(I_0 - I)/I_0$ of the compound **6** with various anions (n-Bu_4N^+ salts) in CH_3CN (0.4% v/v $CHCl_3$) at $\lambda_{ex} = 370$ nm.

The compound **6** showed good selectivity for AcO^- over the other anions (Fig. 2). No significant fluorescence intensity changes were observed on the addition of 30 equiv of Cl^-, Br^-, $H_2PO_4^-$, NO_3^-, I^- or HSO_4^-. Although a decrease of fluorescence intensity was observed upon the addition of $H_2PO_4^-$, it corresponded to only 30% the amount of that caused by AcO^-.

In order to investigate the nature of anion coordination, NMR experiments were carried out in DMSO-d_6. A partial ^1H NMR spectrum is shown in Figure 3, and each peak was assigned based on the 2D COSY spectrum. As expected, we observed the ^1H NMR spectral changes on addition of 2 equiv of the tetrabutylammonium salts of AcO^-, F^- and $H_2PO_4^-$ in DMSO-d_6 while no spectral changes were observed upon the addition of NO_3^-, Cl^-, Br^-, I^- or HSO_4^- in the same condition. Notably, when AcO^-, F^- and $H_2PO_4^-$ were added, the signal of H_c shifted downfield ($\Delta\delta = 1.23$, 0.54 and 1.39, respectively), indicating the formation of hydrogen bonds between the anthracene–NH and anions. Moreover, H_d (9-position proton of anthracene) showed a downfield shift ($\Delta\delta = 0.44$, 0.16 and 0.27, respectively),[13] from which we presume that H_d also participated in the formation of hydrogen bonds with anions. Other anthracene proton signals showed almost no changes.

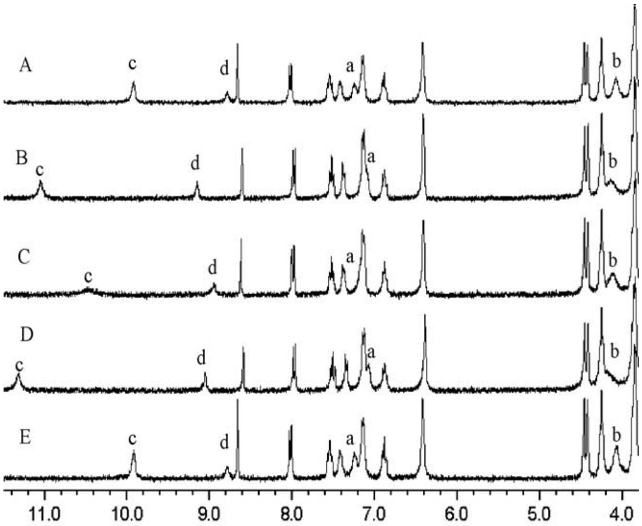
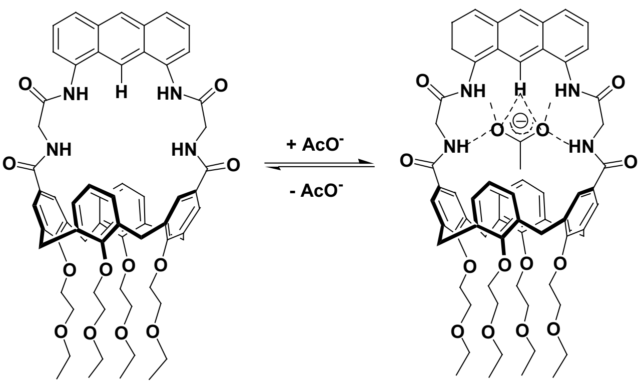


Figure 3. Partial ^{1}H NMR (300 MHz) spectra of host **6** (1.1×10^{-3} M) in DMSO-d_6. (A) Host **6**; (B) **6**+2 equiv of AcO^-; (C) **6**+2 equiv of F^-; (D) **6**+2 equiv of $H_2PO_4^-$; (E) **6**+2 equiv of NO_3^-. Anions used were in the form of their n-Bu_4N^+ salts.



Scheme 2. Possible binding model of **6** with AcO^-.

In addition, a slight upfield shift of H_a and downfield shift of H_b were observed, possibly due to the affection of n-Bu_4N^+ cation as well as the rigid conformation of host **6**. A probable structure for complex with **6** was shown in Scheme 2.

In summary, we have synthesized a novel anion fluorescent receptor based on calix[4]arene. The studies of fluorescence spectra clearly showed that receptor **6** is a good sensor in the selective recognition for AcO^- over other anions examined as F^-, Cl^-, Br^-, $H_2PO_4^-$, NO_3^-, I^- and HSO_4^- via a PET process. From ^{1}H NMR spectra, host **6** could recognize anions due to the formation of hydrogen bonds between NH, 9-H of anthracene and anions.

Acknowledgements

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9. To a cold solution (−15 °C) of *N*-Boc-glycine acid (1.307 g, 7.47 mmol) and Et_3N (1.04 mL, 7.47 mmol) in dry CH_2Cl_2 (20 mL), isobutyl chloroformate (1.020 g, 7.47 mmol) was added. After the mixture was stirred for 1 h, compound **2** (0.555 g, 2.67 mmol) was added. Then the mixture was allowed to slowly warm to rt and stirred for 24 h. The precipitate was filtered and washed with EtOAc. The solid was recrystallized from THF–EtOAc to give a yellow product in 60% yield. Mp: 238–239 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 10.09 (s, 2H, NH), 8.86 (s, 1H, AnH), 8.63 (s, 1H, AnH), 7.93 (d, $J = 8.55$ Hz, 2H, AnH), 7.78 (d, $J = 7.17$ Hz, 2H, AnH), 7.53 (t, $J = 8.01$ Hz, 2H, AnH), 7.13 (t, $J = 5.82$ Hz, 2H, CH_2NH), 4.06 (d, $J = 5.82$ Hz, 4H, CH_2NH), 1.42 (s, 18H, $C(CH_3)_3$); ^{13}C NMR (75 MHz, DMSO-d_6): δ 168.9, 156.0, 133.3, 131.6, 126.7, 125.6, 125.4, 124.9, 120.0, 116.3, 78.0, 43.7, 28.1; MALDI-TOF MS: $m/z = 545.4$ ($M+Na^+$). Anal Calcd for $C_{28}H_{34}O_6N_4$: C, 64.35; H, 6.56; N, 10.72. Found: C, 64.15; H, 6.71; N, 10.40.
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11. To a solution of **4** (0.436 g, 0.84 mmol) and Et_3N (0.6 mL, 4.18 mmol) in dry CH_2Cl_2 (140 mL) was added dropwise **5** chloride (0.648 g, 0.84 mmol) in dry CH_2Cl_2 (20 mL). The mixture was stirred overnight at rt and quenched by adding 5% Na_2CO_3 aqueous solution. The organic layer was separated, washed with water, dried over Na_2SO_4. After removal of the solvent in vacuo, the residue was

chromatographed (CH_2Cl_2/acetone, from 3:1 to 1:1, v/v) to give a yellow product in 30% yield. Mp > 300 °C; ^1H NMR (300 MHz, DMSO-d_6): δ 9.92 (s, 2H, AnN*H*), 8.78 (s, 1H, An*H*), 8.66 (s, 1H, An*H*), 8.02 (d, $J = 8.49$ Hz, 2H, An*H*), 7.54 (t, 2H, $J = 7.17$ Hz, An*H*), 7.42 (br, 2H, An*H*), 7.24 (br, 2H, $CH_2N\mathit{H}$), 7.14 (d, 4H, $J = 5.88$ Hz, Ar*H*), 6.87 (t, 2H, $J = 7.47$ Hz, Ar*H*), 6.41 (s, 4H, Ar*H*), 4.44 (d, $J = 12.87$ Hz, 4H, H_{ax} of $ArC\mathit{H}_2Ar$), 4.24 (t, $J = 5.9$ Hz, 4H, $OC\mathit{H}_2CH_2O$), 4.07 (br, 2H, $C\mathit{H}_2NH$), 3.83–3.85 (m, 4H, $OC\mathit{H}_2CH_2O$, 4H, $OCH_2C\mathit{H}_2O$), 3.73 (t, $J = 4.26$ Hz, 4H, $OCH_2C\mathit{H}_2O$), 3.52 (q, $J = 6.87$ Hz, 4H, $C\mathit{H}_2CH_3$), 3.45 (q, $J = 7.05$ Hz, 4H, $C\mathit{H}_2CH_3$), 3.14 (d, $J = 13.59$ Hz, 4H, H_{eq} of $ArC\mathit{H}_2Ar$), 1.16 (t, $J = 6.96$ Hz, 6H, $CH_2C\mathit{H}_3$), 1.07 (t, $J = 6.96$ Hz, 6H, $CH_2C\mathit{H}_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.0, 167.1, 157.7, 157.0, 135.6, 133.5, 132.8, 128.9, 127.7, 127.0, 126.9, 125.5, 124.2, 122.0, 118.0, 74.0, 72.1, 69.4, 69.3, 66.4, 66.0, 44.5, 30.6, 15.3, 15.1; MALDI-TOF MS: *m*/*z* = 1087.2 ($M{+}H^+$); 1109.2 ($M{+}Na^+$); 1125.1 ($M{+}K^+$). Anal Calcd for $C_{64}H_{70}O_{12}N_4{\cdot}0.5H_2O$: C, 70.12; H, 6.53; N, 5.11. Found: C, 69.99; H, 6.55; N, 5.05.

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