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Articles

A New Carboxylate Selective Anion Receptor Utilizing Amide and Carbamate Hydrogens

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A new anion receptor utilizing carbamate functionality as hydrogen bonding site has been designed and synthesized. This new receptor **2** has two amide hydrogens and two carbamate hydrogens anchored at 1,8-position of anthracene. These four hydrogens form a concave structure for the anions and the receptor **2** was found to be a selective receptor for acetate among the anions investigated.

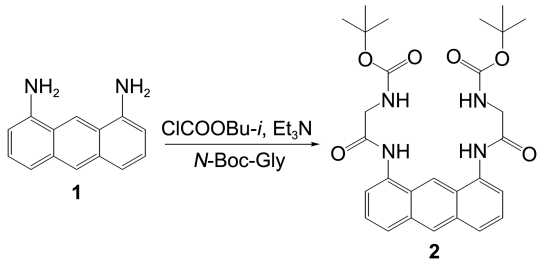
Key Words : Anion receptor, Amide, Carbamate, Hydrogen bonds, Anthracene

Introduction

There have been considerable efforts to develop efficient artificial receptors for anion recognition and sensing as anions play a major role in biological, medical, environmental, and chemical sciences.[1] As anions display wide range of geometries, design and synthesis of artificial receptors that exhibit high binding affinity and selectivity to a targeted anion still remain a great challenge. The design of complementary structural components that show good recognition properties requires building in relatively strong and directional adhesive forces. Among various noncovalent interactions, hydrogen-bonding interactions are particularly useful and effective in this regard. Receptors bearing functional groups such as amides,[2] ureas,[3] thioureas,[4] imidazolium[5] and positively charged groups[6] have been widely used to recognize anions *via* hydrogen-bonding interactions. To achieve high binding affinity and good selectivity, hydrogen bonding moieties are arranged in space in a rigid and convergent manner. In addition, receptors bearing multiple hydrogen bonding moieties have been shown to be useful to promote cooperative binding, which would result in enhanced binding affinity.[7] In addition to these functional groups, carbamate functionality has been successfully utilized as a new hydrogen bonding moiety.[8] To extend the scopes of carbamate functionality as an anion binding moiety, we have designed the receptor **2**, which has amide groups and carbamate groups to provide convergent hydrogen bonds.

The new receptor **2** has two amide hydrogens and two carbamate hydrogens anchored at 1,8-position of anthracene. These four hydrogens form a concave structure for the anions and the receptor **2** was found to be a selective receptor for acetate. Recognition of carboxylate anions and carboxylic acids by synthetic receptors is one of most important research areas due to the their presence in a variety of biomolecules such as amino acids and the huge application in pharmaceutical science.[9] The binding phenomena of the receptor **2** could be monitored by fluorescence spectra, and ^{1}H NMR.

The synthesis of the new receptor **2** was obtained as outlined in Scheme 1. 1,8-diaminoanthracene **1** was obtained following literature method.[10] This compound **1** was added to the mixture of *N*-(*tert*-butoxycarbonyl)glycine, isobutyl chloroformate and triethylamine to give a desired



Scheme 1. The synthetic scheme for the anion receptor **2**.

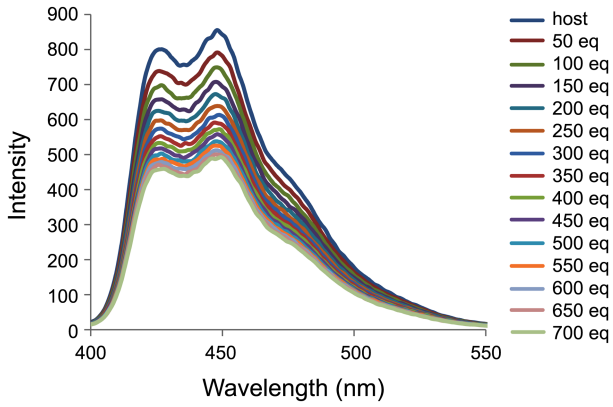


Figure 1. The change of fluorescence spectra in the receptor **2** when tetrabutylammonium acetate was added.

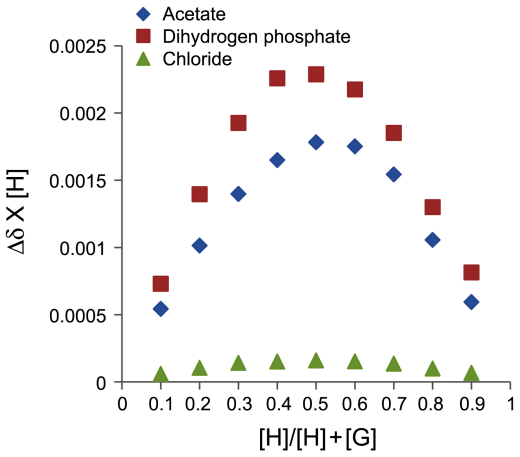


Figure 2. The Job plots of **2** with tetrabutylammonium acetate, tetrabutylammonium dihydrogen phosphate and tetrabutylammonium chloride using ^{1}H NMR.

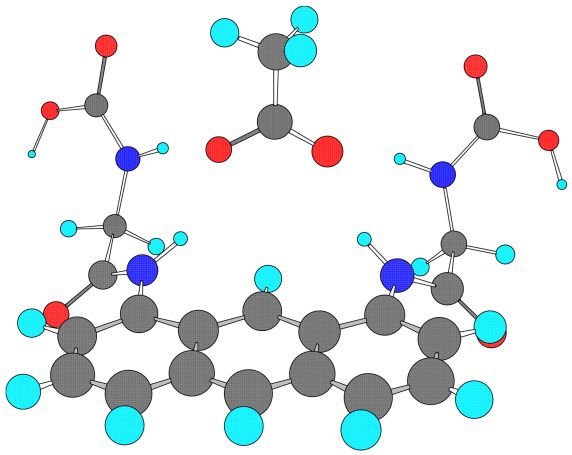


Figure 4. The energy minimized structure of 1:1 complex between receptor **2** and acetate (Cache 3.2 MOPAC calculation); BOC groups are omitted for clarity.

compound **2** in 86% yield.[11]

The receptor **2** displayed strong fluorescence emission in DMSO as shown in Figure 1. The excitation and emission wavelength were 386 and 448 nm, respectively. The association between the receptor **2** and Y shaped acetate was investigated first by fluorescence titration. The fluorescence change of the receptor **2** was monitored in DMSO. The intensity of emission spectrum from 2 μM solution of the receptor **2** gradually decreased as the concentration of tetrabutylammonium acetate salts was increased (50-700 equiv.), which indicates the association between the receptor **2** and acetate. For example, when the concentration of acetate increased to 50 equivalents, the fluorescence intensity was reduced to 17% of the initial one. The fluorescence quenching effect was possibly due to the photo-induced electron transfer (PET) process between the anthracene moiety and the binding site. The stoichiometry between the receptor **2** and acetate was determined by Job plot using ^{1}H NMR, which showed evident 1:1 stoichiometry (Figure 2).[12] A Benesi-Hildebrand plot by use of change in the 448 nm fluorescence intensity gave association constants.[13] From the experiments, the receptor **2** showed association constant 1.2 × 10^3 for acetate in DMSO.

The complexation ability of the receptor **2** to the acetate was also measured by standard ^{1}H NMR titration experiments in DMSO-d_6 using a constant host concentration (2 mM) and increasing concentrations of anions. (1-15 equiv. Figure 3) The addition of tetrabutylammonium acetate salt to the solution of 2 mM in DMSO-d_6 resulted in downfield shifts in both the amide N-H hydrogen and carbamate N-H hydrogen. The amide and carbamate peak in the receptor **2** without acetate salt appeared at 10.06 ppm and 7.10 ppm respectively in DMSO-d_6. Both amide and carbamate peaks moved until 11.30 ppm and 7.37 ppm respectively with 15 equivalent of acetate. No further shifts were observed. This phenomenon indicated that all the 4 hydrogens from amide and carbamate involved in bonding with acetate ion. In addition, 9-H of anthracene peak appearing at 8.84 ppm moved until 9.38 ppm, which indicated participation of aromatic hydrogen in the binding event. Therefore, the signals of these groups were used to determine the association constant for receptor **2** and acetate. The chemical shift data were analyzed by EQNMR.[14] The association constant calculated from ^{1}H NMR titration gave 1.3 × 10^3 for acetate,

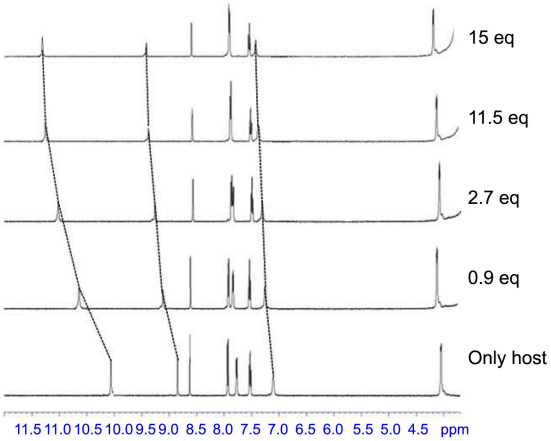


Figure 3. ^{1}H NMR spectra of 2 mM of **2** with increased amounts of tetrabutylammonium aceate in DMSO-d_6. The shift of amide and carbamate N-H peaks are designated by dotted lines.

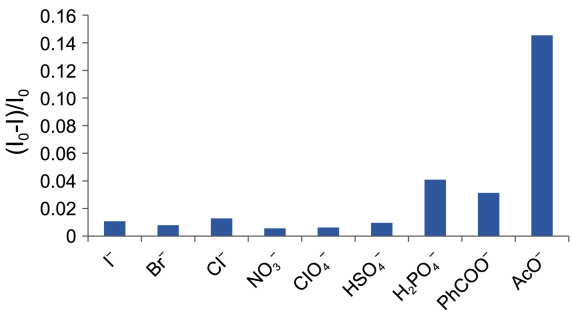


Figure 5. Fluorescence quench ratio (I_0–I)/I_0 of the compound **2** (2 μM) with various anions (n-Bu_4N^+ salts, 100 equivalents) in DMSO at λ_{ex} = 386 nm and λ_{em} = 448 nm.

Table 1. The association constants (M^{-1}) of the receptor **2** and various anions in DMSO

Anion	Ka from Fluorescence titration	Ka[a] from ^{1}H NMR titration
$CH_3CO_2^-$	1.2×10^3	1.3×10^3
$H_2PO_4^-$	6.4×10^2	
$PhCO_2^-$	3.0×10^2	
Cl^-	2.8×10^2	
Br^-	1.3×10^2	
I^-	1.1×10^2	
HSO_4^-	1.5×10^2	
NO_3^-	Nb[a]	
ClO_4^-	Nb	

[a]nonbinding

which is similar value from the fluorescence titration. The possible binding mode and energy minimized structure of receptor **2** and acetate were shown in Figure 4.

The receptor **2** also showed 1:1 stoichiometry for the spherical halides and tetrahedral shape anions such as dihydrogen phosphate. Among the anions investigated, the receptor **2** showed good selectivity for acetate over the other anions. The florescence intensity changes were the most significant with acetate (Figure 5). Among the anions with same geometry, the association constants simply reflected basicity of anion. For example, dihydrogen phosphate showed higher association constant than that of hydrogen sulfate. Halides generally showed weak association constant with receptor **2**. Probably, the cavity formed by 4 hydrogens was too large to accommodate halide ions. The results are summarized in and Table 1.

In summary, we have designed and synthesized a novel carboxylate fluorescent receptor based on two amide hydrogens and two carbamate hydrogens anchored at 1,8-position of anthracene. Fluorescence spectra clearly showed that receptor **2** is a good sensor in the selective recognition for acetate over other anions such as I^-, Br^-, Cl^-, HSO_4^-, $H_2PO_4^-$, ClO_4^- and NO_3^-.

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11. **Synthesis of compound 2**: Isobutyl chloroformate (826 mg, 6.05 mmol), *N*-(*tert*-butoxycarbonyl)glycine (1060 mg, 6.05 mmol) and triethylamine (612 mg, 6.05 mmol) in dried dichloromethane at 0 °C were stirred for an hour. Then to this solution was added 1,8-diaminoanthracene (450 mg, 2.16 mmol) and the reaction mixture was stirred for 3 hours. After the solvent was evaporated at reduced pressure, the residue was chromatographed on the silicagel with 3% methanol in dichloromethane. ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.07 (s, 2H), 8.86 (s, 1H), 8.62 (s, 1H), 7.93 (d, 2H, J = 8.5 Hz), 7.78 (d, 2H, J = 7 Hz), 7.53 (t, 2H, J = 7.5 Hz), 7.11 (s, 2H), 4.07 (d, 4H, J = 5.5 Hz), 1.43 (s, 18H) ^{13}C NMR (500 MHz, DMSO-d_6) 169.0, 156.0, 133.3, 131.6, 126.8, 125.7, 125.5, 124.9, 120.0, 116.3, 78.1, 43.8, 28.2 FAB MS *m/z* (M^+): calcd, 522.25, found, 522.21
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