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Anion receptor with four imidazolium rings on the glycoluril

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Abstract—We have synthesized a new anion receptor with four imidazolium groups attached on the glycoluril. The receptor binds halide and acetate in 1:2 stoichiometry and acetate has the highest affinity for this new receptor among the anions we investigated.

Hydrogen bond between C(2)–H in imidazolium rings and guest anion is currently accepted as an important anion binding interaction. Various types of spatial arrangement of imidazolium rings on the suitable spacer produced tweezer type imidazolium receptor,[1] tripodal imidazolium receptor[2] and cyclic imidazolium receptor.[3] Recently, Yoon and co-workers reported a receptor of four imidazolium groups appending cavitand moiety, which has affinity towards dicarboxylates.[4] To develop a new imidazolium group based anion receptor, we have designed receptor **1**, which utilizes glycoluril as a spacer for four imidazolium groups. In this receptor, four imidazolium groups are arranged at the corner of the glycoluril. Here, we would like to report the synthesis and binding properties of receptor **1** with various anions.

The synthesis of anion receptor **1** started from the compound **2**. Compound **2** was synthesized following the literature method.[5] The compound **2** was reacted with sodium hydride and imidazole at 80 °C in DMF to give the compound **3** in 79% yield. Then compound **3** was refluxed with excess ethyl bromide for 12 h. Anion exchange with ammonium hexafluorophosphate gave the expected compound **1** in 70% yield (Scheme 1). All compounds are characterized with ^{1}H NMR, ^{13}C NMR and HRMS.[6]

The complexation ability of receptor **1** was measured by standard ^{1}H NMR titration experiments in 10% DMSO-d_6 in CD_3CN using a constant host concentration (4 mM) and increasing concentrations of anions (0.1–10 equiv). The chemical shift data were analyzed by EQNMR.[7] The addition of tetrabutylammonium halide salts to the solution of receptor **1** in 10% DMSO-d_6 in CD_3CN resulted in downfield shifts in C(2) proton of imdazolium moieties. In case of chloride ion, C(2) protons originally resonating at $\delta = 8.81$ were shifted to $\delta = 10.07$ upon addition of 3 equiv of chloride ion, which indicates that all four C(2) proton are involved in binding events. Although we expected 1:1 binding, the Job plot experiments showed 1:2 binding stoichiometry for chloride (Fig. 2). The association constant calculated from the chemical shift change of C(2)–H of imidazolium ring was $1.5 \times 10^6 \pm 1.2 \times 10^3\ M^{-2}$ ($\beta_2 = K_1K_2$). Job plot for other halides also showed 1:2 stoichiometry irrespective of the size of the halides. The association constants ($\beta_2 = K_1K_2$) were calculated as $1.8 \times 10^6 \pm 4.6 \times 10^4$ for fluoride, $4.8 \times 10^5 \pm 1.1 \times 10^4$ for bromide and $3.1 \times 10^5 \pm 4.6 \times 10^4$ for iodide.

We expected that the four C(2)–H in imidazolium rings attached at the corner of glycoluril would form a cavity and point to the anion located at the centre of the concave structure of glycoluril. The shape and size of the cavity seemed to be suitable for spherical halide ions. Therefore, we expected receptor **1** would bind halide ion in 1:1 fashion. The expected energy minimized structure of receptor **1** and iodide is shown in Figure 1 (Cache 3.2 MOPAC calculation). However, it was found that receptor **1** binds with anions in 1:2 fashion. Even though receptor **1** has space enough to capture halide inside the cavity which is made of four imidazolium rings, receptor **1** binds halides only 1:2 fashion. Receptor **1** does not seem to like to locate four imidazolium rings closely. Each imidazolium ring has +1 positive charge. When they are located closely to bind with one halide ion, +3 positive charges exist in small area. Therefore, we

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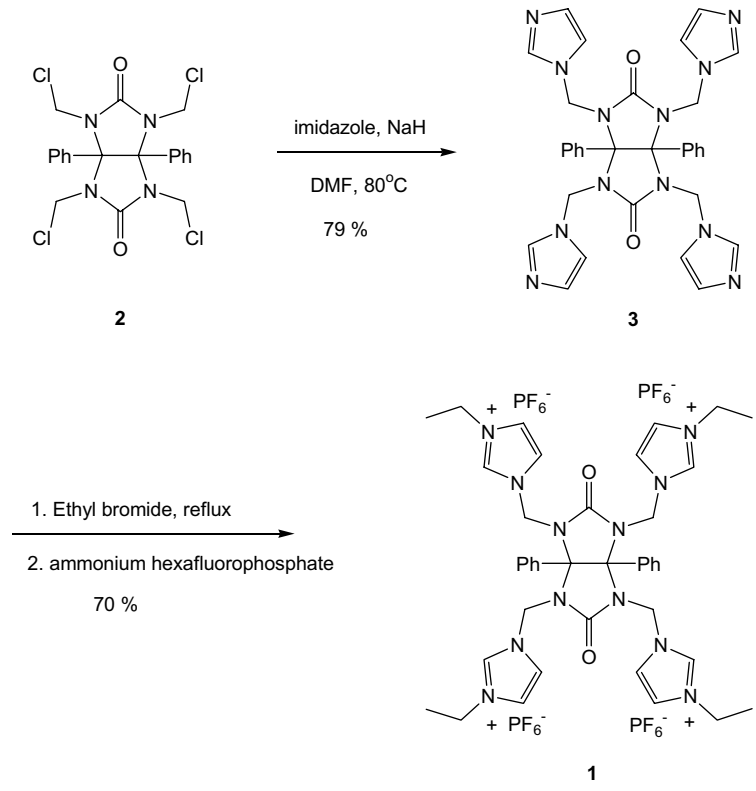

Scheme 1. The synthetic procedure for the anion receptors **1**.

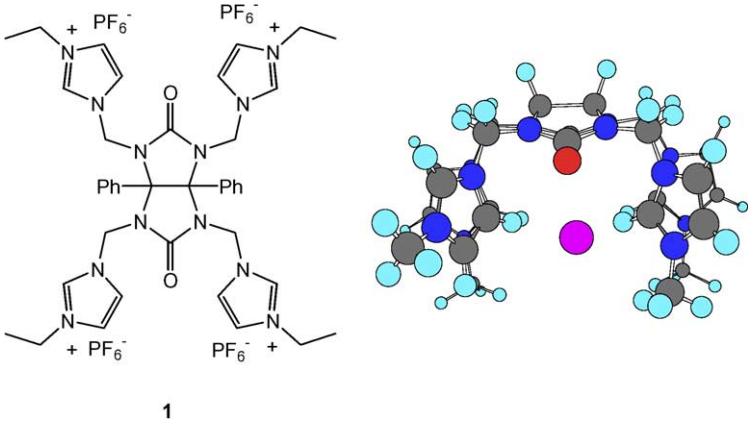

Figure 1. The expected energy minimized structure of receptor **1** and iodide (Cache 3.2 MOPAC calculation). The aromatic rings of glycoluril are omitted for clarity.

propose that receptor **1** chooses to bind halides in 1:2 stoichiometry due to the repulsion of these positive charges. This phenomenon extends to acetate. The binding of acetate was strong enough that binding curve and Job plot clearly demonstrated the 1:2 stoichiometry of complex (Figs. 2 and 3). The association constant was $2.9 \times 10^6 \pm 8.7 \times 10^4$ ($\beta_2 = K_1K_2$). As receptor **1** formed 1:2 complex with acetate, we investigated the binding of dicarboxylate with the receptor **1**. Job plot study of oxalate, malonate, adipate, isophthalate and terephthalate showed a mixed stoichiometry. However, succinate and glutarate showed 1:1 stoichiometry (Fig. 4). The association constants in 10% DMSO-d_6 in CD_3CN were calculated $1.8 \times 10^3 \pm 72$ for succinate and $2.7 \times 10^3 \pm 112$ for glutarate. Molecular modeling showed that receptor **1** does not have optimum geometry for succinate and glutarate. Receptor **1** has to be twisted to bind these dicarboxylates and the hydrogen bond angles are in the range of 130–170°. Therefore, receptor **1** has low association constants for succinate and glutarate (Fig. 4).

Other anions such as HSO_4^- and CN^- also showed a mixed stoichiometry. Therefore, it was not possible to obtain accurate association constants for these anions.

In conclusion, we have synthesized a new anion receptor **1** with four imidazolium groups attached on the glycolu-

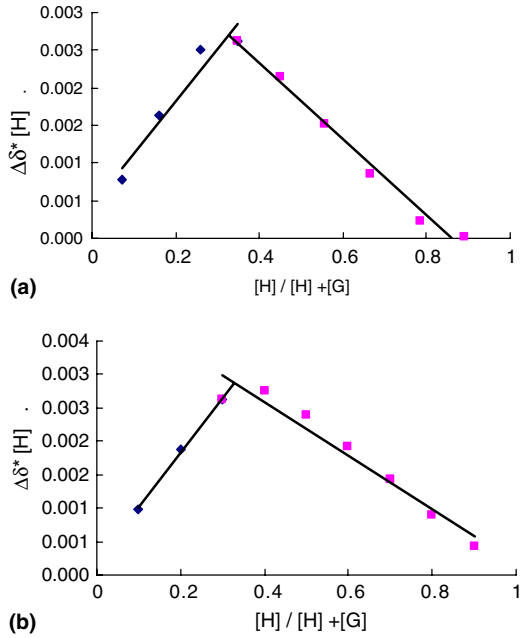

Figure 2. The Job plots of **1** and (a) tetrabutylammonium chloride (b) tertabutylammonium acetate.

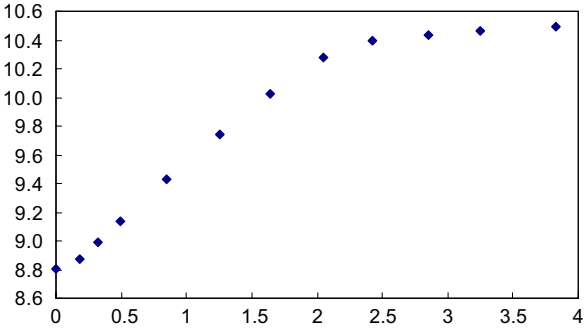

Figure 3. Changes in the C(2)–H of imidazolium ring in receptor **1** with increasing acetate concentrations.

ril. They bind halide and acetate in 1:2 stoichiometry and acetate has the highest affinity for this new receptor among the anions we investigated.

References and notes

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6. Compound **3**: ^{1}H NMR ($CDCl_3$) 7.47 (s, 4H) 7.12 (m, 14H) 6.27 (d, 4H, $J = 7.8$) 5.36 (d, 4H, $J = 14.4$) 5.10 (d, 4H, $J = 14.4$); ^{13}C(DMSO-d_6) δ 163.89, 142.63, 135.46, 134.79, 134.09, 133.38, 123.95, 93.05, 57.72; HRMS (FAB) calculated for $C_{32}H_{30}N_{12}O_2H^+$: 615.2694. Found: 615.2639. Compound **1**: ^{1}H NMR (CD_3CN) 8.64 (s, 4H) 7.50 (t, 4H, $J = 1.85$) 7.43 (t, 4H, $J = 1.85$) 7.26 (t, 2H, $J = 7.40$) 7.05 (t, 4H, $J = 7.40$) 6.50 (d, 4H, $J = 7.50$) 5.62 (d, 4H, $J = 14.80$) 5.52 (d, 4H, $J = 14.80$) 4.25 (q, 8H, 7.30) 1.49 (t, 12H, $J = 7.30$); ^{13}C(CD_3CN) δ 158.77, 136.56, 136.36, 131.40, 129.63, 128.95 123.13, 123.00, 89.70, 55.91, 45.90, 12.79; HRMS (FAB) M−PF_6 calculated for $C_{40}H_{50}N_{12}P_3F_{18}$: 1165.3106. Found: 1165.3159.
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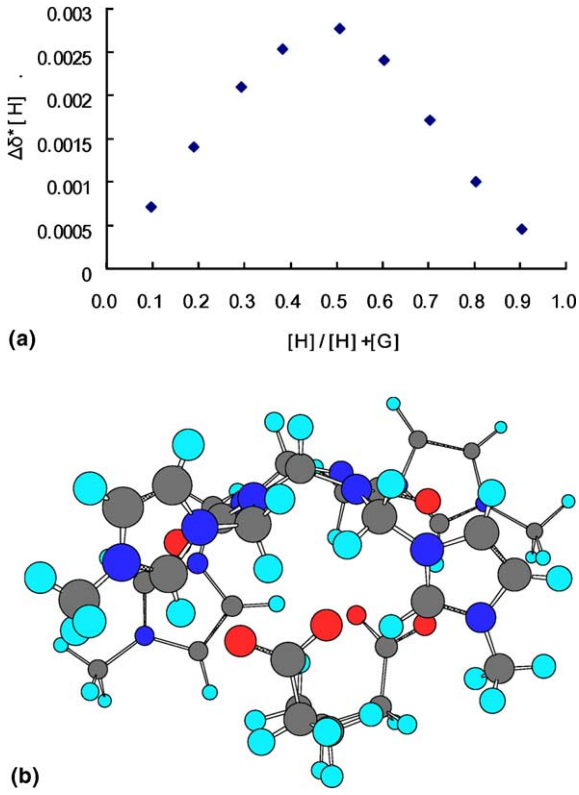

Figure 4. The Job plot of glutarate (a) and energy minimized structure of of receptor **1** and glutarate (b) (Cache 3.2 MOPAC calculation). The aromatic rings of glycoluril are omitted for clarity.