HSO_4^- Anion Selective Urea Calix[4]diquinone Receptor

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Introduction

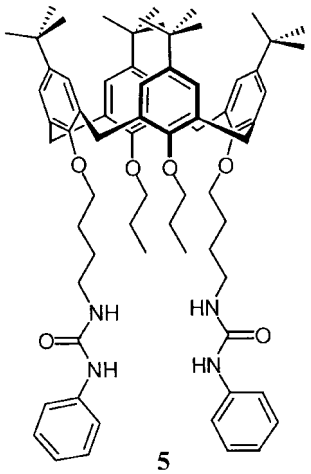
The various macrocyclic compounds such as crown ether and calixarene[1-3] containing redox-active centers have been utilized for the development of advancing chemical sensor technology. Several excellent quinone and anthraquinone based redox-switchable ligands for cations were developed by Gokel and Echegoyen.[4-6] But quinone based redox-switchable hosts for anions were not reported at all until recently. The urea and thiourea groups have been used in the development of neutral receptors, because the hydrogen bond is directional in character and orientation of the hydrogen bond donors can provide the selective anion recognition. Recently we reported[7] a lower rim urea derivative of calix[4]diquinone for the first time, which showed a high selectivity for HSO_4^-. Also the upper rim urea derivative[8] of calix[4]diquinone was synthesized, which showed a high selectivity with $H_2PO_4^-$ over $CH_3CO_2^-$, Cl^- and HSO_4^-.

In order to develop the series of anion redox receptors, here we report the calix[4]diquinone receptor **4** having two urea moieties in farther distance from quinone and investigated the complexation behavior with anions. This novel anion receptor **4** binds anions through hydrogen bonding and also shows high selectivity for HSO_4^- over $H_2PO_4^-$, Cl^- and $CH_3CO_2^-$.

Results and Discussion

By taking advantage of a selective 1,3-alkylation, 1,3-bis(cyanopropyl)oxycalix[4]arene **1** was prepared by the reaction of *p-t*-butylcalix[4]arene and 4-bromobutyronitrile in the presence of K_2CO_3.[9] Reduction with $LiAlH_4$ yielded the corresponding aminocalix[4]arene **2**, which was transformed into urea derivative **3** when treated with phenylisocyanate. Finally reaction of calixarene **3** with TTFA (thallium trifluoroacetate) in trifluoroacetic acid afforded the urea derivative calix[4]diquinone **4** in 46% yield (Scheme 1). The ^1H NMR spectrum of **4** showed a pair of doublets at δ 4.20 and 3.10 for the bridge methylene protons and a singlet and a triplets at δ 7.86 and 6.34 for the four urea N-H protons. Four quinone protons signal appeared at δ 6.71 as a singlet. The ^{13}C NMR spectrum of **4** indicated that **4** existed as a cone based on the bridge carbon signal at δ 30.6.[10]

The anion coordination properties were investigated by the proton NMR titration in $CDCl_3$ solution in the presence of various anions such as tetrabutylammonium (TBA) chloride, bromide, dihydrogen phosphate, hydrogen sulfate, and acetate. In proton NMR experiments a large downfield shift of a singlet NH proton resonance at δ 7.86 was observed upon addition of TBA hydrogen sulfate to host **4** solution as shown in Figure 1 upon addition of 1 equivalent TBA HSO_4^-. Further addition of HSO_4^- caused an only slight downfield shift. Any further significant change was not observed after one equivalent of TBA HSO_4^-, suggesting that **4** complexed with hydrogen sulfate ion 1 : 1 solution stoichiometry. Large chemical shift change of the NH protons in the presence of anion suggests that the anions bind the urea protons directly. The association constants of the various anions to the receptors are obtained from the resulting titration curves using EQ-NMR[11] and these values are presented in Table 1.



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A high selectivity for HSO_4^- was observed for the urea derivative of calix[4]diquinone **4**. The influence of the hydrogen bond in **4** with HSO_4^- could be a major factor, comparing the K values of **4** with those of the corresponding urea derivative **5**[9] which exhibited a high selectivity for spherical anions, in the order $Cl^- > Br^- > I^-$, and very weak binding with tetrahedral HSO_4^- and $H_2PO_4^-$. The relatively low affinity toward HSO_4^- compared with previous urea derivative[7] can be attributed to the relatively long distance between quinone oxygen and urea N-H proton, which could play a significant role as the additional binding. The receptor **3** also exhibits remarkable thermodynamic stability for HSO_4^- as shown in Table 1. The partial ^1H NMR spectra of **3**

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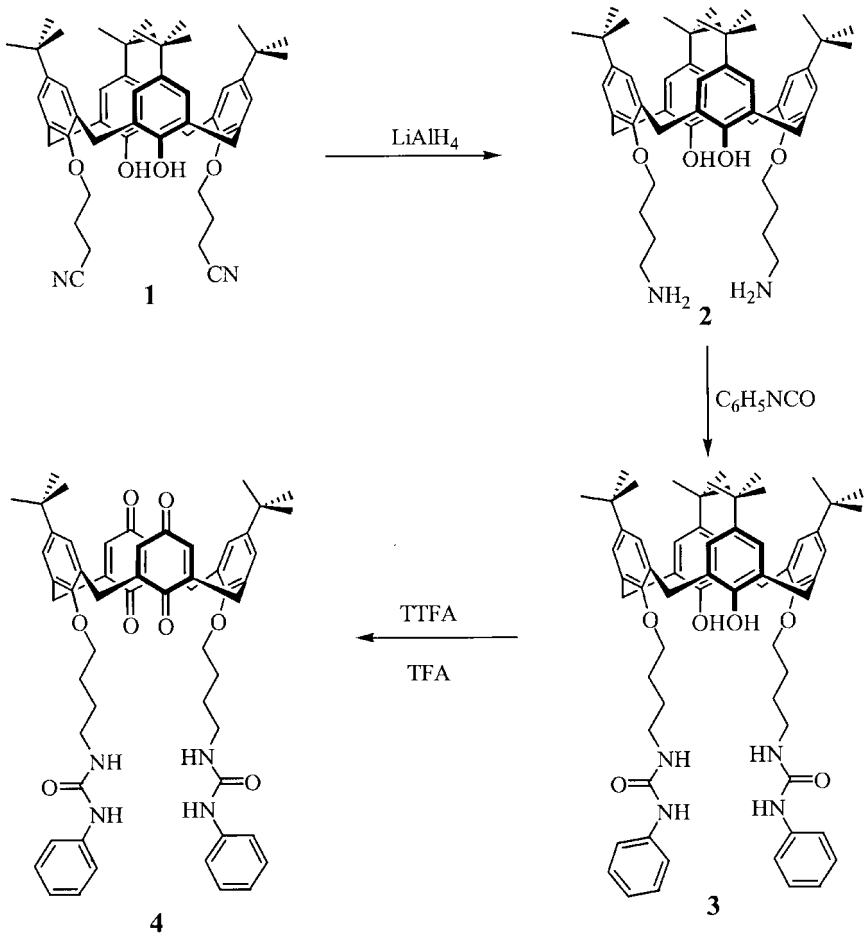

Scheme 1. Synthesis of redox switchable anion receptor.

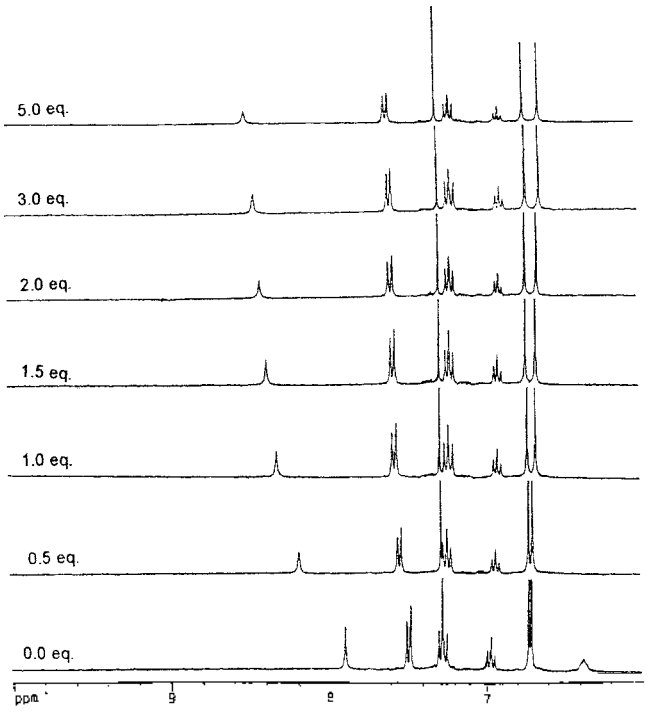

Figure 1. The partial ^{1}H NMR spectra of **4** in the presence of TBA (tetrabutylammonium) HSO_4^- in $CDCl_3$. Numbers at the left side indicate the equivalent amounts of HSO_4^- added.

Table 1. Stability constants (K_a) in $CDCl_3$ and cathodic shifts in the presence of anions in CH_3CN

Anion	K/dm^{3}mol^{-1}			ΔE (mV)
	3	**4**	**5**[a]	**4**
Cl^-[b]	80	52	7105	10
Br^-	–	16	2555	<5
I^-	–	–	605	0
ClO_4^-	–	–	–	<6
HSO_4^-	2,990	1170	–	110
$H_2PO_4^-$	410	605	–	100
$CH_3CO_2^-$	414	254	–	20

[a]Stability constants of **5** were taken from Reinhoudt *et al.*[9] [b]Tetabutylammonium salts. Errors estimated to be <10%.

upon titration of TBA (tetrabutylammonium) HSO_4^- in $CDCl_3$ are presented in Figure 2. Obviously OH protons of calix[4]arene **3** help the HSO_4^- binding, presumably by the additional hydrogen bond with HSO_4^-. Hydroxy proton signal was observed at δ 6.98 in the absence of anions. Continuous downfield shift of OH proton resonance at δ 6.98 was observed upon addition of HSO_4^- to the $CDCl_3$ solution of **3**. Downfield shift suggests that calixarene OH protons form a hydrogen bond with anions. The receptor **3** shows a high selectivity for HSO_4^- over Cl^-, $H_2PO_4^-$, and

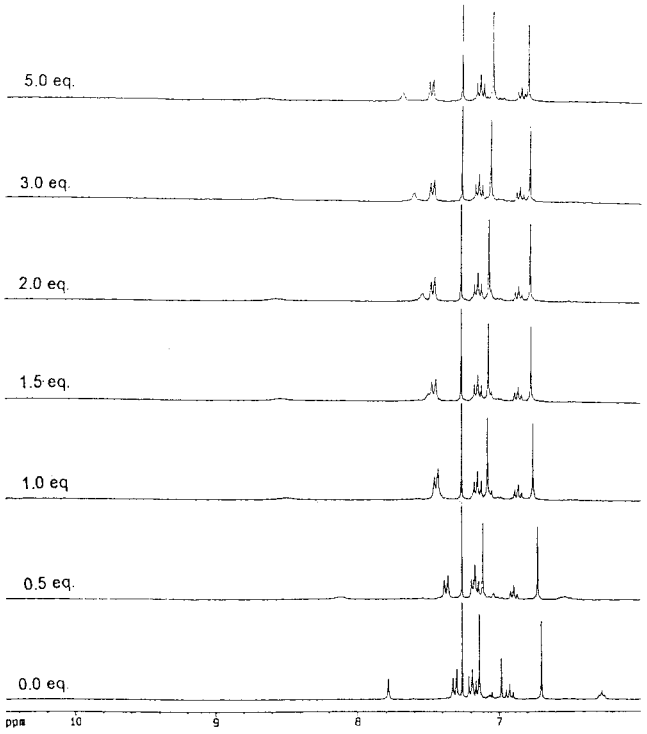

Figure 2. The partial ^{1}H NMR spectra of **3** in the presence of TBA (tetrabutylammonium) HSO_4^- in $CDCl_3$. Numbers at the left side indicate the equivalent amounts of HSO_4^- added.

CH_3COO^- as observed with receptor **4** presumably due to the additional hydrogen bond with hydroxy proton.

The electrochemical property of **4** in acetonitrile also was investigated using cyclic voltammetry. Calix[4]diquinone **4** is initially reduced to semiquinone-quinone by one electron transfer, and then reduced to semiquinone-semiquinone at more negative potential. The addition of anions to calix[4]-diquinone **4** solutions occurred cathodic shifts of quinone/semiquinone redox couple with the relative magnitudes following the order HSO_4^- > $H_2PO_4^-$ > CH_3COO^- > Cl^- > Br^-, I^-, ClO_4^-. The most significant result also was observed with HSO_4^- anion. The addition of hydrogen sulfate anion causes a 110 mV cathodic shift in the quinone/semiquinone redox couple. This large cathodic shift indicates a strong stabilization of calix[4]diquinone **4** in the presence of hydrogen sulfate anion. This result indicates that hydrogen sulfate anion coordinates to the NH protons of calix[4]-diquinone **4** and also bonds to quinone moiety by hydrogen bonding.

Experimental Section

5,11,17,23-Tetra-*tert*-butyl-25,27-bis(cyanopropyloxy)-26,28-dihydroxycalix[4]arene (1). To a stirred solution of 5.0 g (7.72 mmol) of *p-tert*-butylcalix[4]arene and 1.28 g (9.26 mmol) of K_2CO_3 in 80 mL of CH_3CN, 2.4 g (16.2 mmol) of 4-bromobutyronitrile was added and the mixture was refluxed for 5 days. The solvent was evaporated and the residue was taken up in CH_2Cl_2 (300 mL), washed with 1 N HCl (100 mL), H_2O (50 mL), and brine (50 mL), and dried with $MgSO_4$. The solvent was evaporated and the residue was recrystallized from $CHCl_3$/MeOH to yield a white solid (1.0 g, 70%). mp ≥ 300 °C; IR (KBr) 2247 cm^{-1} (CN); ^{1}H NMR ($CDCl_3$) δ 7.39 (s, 2H, -OH), 7.06 (s, 4H, ArH), 6.88 (s, 4H, ArH), 4.17 and 3.39 (pair of d, 8H, $ArCH_2Ar$, J = 12.5 Hz), 4.09 (t, 4H, $-OCH_2-$, J = 6.3 Hz), 3.03 (t, 4H, $-CH_2CN$, J = 6.9 Hz), 2.32 (m, 4H, $-CH_2-$), 1.28 and 1.00 (two s, 36H, $-C(CH_3)_3$); ^{13}C NMR ($CDCl_3$) δ 150.3, 148.8, 147.6, 142.1, 132.5, 127.5, 125.8, and 125.3 (Ar), 119.4 (-CN), 73.3 ($-OCH_2-$), 34.0, 33.9, 31.8, 31.7, 31.0, 26.6 and 14.2 ($ArCH_2Ar$, $-CH_2CH_2-$ and $-C(CH_3)_3$).

5,11,17,23-Tetra-*tert*-butyl-25,27-bis(4-aminobutyloxy)-26,28-dihydroxycalix[4]arene (2). To a vigorously stirred solution of 2.5 g (3.2 mmol) of dinitrile **1** in 150 mL of diethyl ether, a slurry of 1 g (28 mmol) of $LiAlH_4$ was added portionwise and the reaction mixture was refluxed for 5 h. After the reaction flask was immersed into an ice-water bath, the excess $LiAlH_4$ was destroyed by careful addition of wet benzene (100 mL) and water (5 mL). The clear organic layer was decanted and the inorganic salts were washed with benzene. The combined organic layers were evaporated to dryness to afford diamine **2** (2.3 g, 91%) as a white solid which was pure enough to be used in the next step. mp 155-157 °C; ^{1}H NMR ($CDCl_3$) δ 7.59 (s, 2H, -OH), 7.04 (s, 4H, ArH), 6.81 (s, 4H, ArH), 4.27 and 3.30 (pair of d, 8H, $ArCH_2Ar$, J = 13 Hz), 3.99 (t, 4H, $-OCH_2-$, J = 6.3 Hz), 2.86 (t, 4H, $-CH_2N-$, J = 6.9 Hz), 2.05 and 1.84 (m, 8H, $-CH_2CH_2-$), 1.28 and 0.97 (s, 36H, $-C(CH_3)_3$); ^{13}C NMR ($CDCl_3$) δ 150.6, 149.9, 146.8, 141.5, 132.6, 127.8, 125.5, and 125.1 (Ar), 76.2 ($-OCH_2-$), 41.9 ($-CH_2N-$), 33.9, 33.8, 31.7, 31.5, 31.0, 30.2 and 27.4 ($ArCH_2Ar$, $-CH_2CH_2-$ and $-C(CH_3)_3$).

5,11,17,23-Tetra-*tert*-butyl-25,27-bis[(N-phenylureido)-butyloxy]-26,28-dihydroxycalix[4]arene (3). To a 2 g (2.5 mmol) of **2** in 70 mL of CH_2Cl_2, 0.5 mL (5 mmol) of phenylisocyanate was added and the mixture was stirred at room temperature for 3 h. After removing the solvent, the residue was triturated with MeOH yielding a pure white solid (1.8 g, 70%). mp 163-165 °C; ^{1}H NMR ($CDCl_3$) δ 7.81 (s, 2H, -OH), 7.30 (d, 4H, ArH, J = 7.6 Hz), 7.18 (t, 4H, ArH, J = 8.4 Hz), 7.15 (s, 4H, ArH), 7.02 (s, 2H, -NH), 6.92 (t, 2H, ArH, J = 7.4 Hz), 6.71 (s, 4H, ArH), 6.30 (t, 2H, -NH, J = 5.6 Hz), 4.21 and 3.38 (pair of d, 8H, $ArCH_2Ar$, J = 13.3 Hz), 3.97 (t, 4H, $-OCH_2-$, J = 6 Hz), 3.46 (q, 4H, $-CH_2N-$, J = 6 Hz), 1.99 and 1.84 (m, 8H, $-CH_2CH_2-$), 1.34 and 0.88 (s, 36H, $-C(CH_3)_3$); ^{13}C NMR ($CDCl_3$) δ 156.7 (-CO), 149.9, 149.5, 147.2, 142.9, 139.7, 131.8, 129.2, 128.9, 128.1, 125.6, 125.4, 122.0, 118.5 and 115.1 (Ar), 77.3 ($-OCH_2-$), 39.4 ($-CH_2N-$), 33.9, 33.8, 31.7, 31.5, 30.9, 27.3 and 26.5 ($ArCH_2Ar$, $-CH_2CH_2-$ and $-C(CH_3)_3$).

5,17-Di-*tert*-butyl-26,28-bis[(N'-phenylureido)butyl]oxy-calix[4]-25,27-diquinone (4). To a 0.2 g (0.2 mmol) of **3** in 15 mL of trifluoroacetic acid, 0.5 g of thallium trifluoro-acetate (0.92 mmole) was added and the mixture stirred for 15 hours in the dark under the nitrogen atmosphere. The solvent was then removed and the residue poured onto ice/water (50 mL). The product was then extracted into chloro-

form (100 mL). After removing the solvent, the crude products were purified by the column chromatography (eluent, $CHCl_3$: MeOH = 20 : 1) to give a yellow powder **4** (86 mg, 46%). mp 151-152 °C; ^{1}H NMR ($CDCl_3$) δ 7.86 (s, 2H, -NH), 7.46 (d, 4H, ArH, J = 7.8 Hz), 7.25 (t, 4H, ArH, J = 7.8 Hz), 6.95 (t, 2H, ArH, J = 7.8 Hz), 6.71 (s, 8H, ArH), 6.34 (s, 2H, -NH), 4.20 and 3.10 (a pair of d, 8H, $ArCH_2Ar$, J = 12.9 Hz), 3.69 (t, 4H, -OCH_2-, J = 4.8 Hz), 3.40 (q, 4H, -NCH_2-, J=5.7 Hz), 1.87 (m, 8H, -CH_2-), 1.03 (s, 18H, -$C(CH_3)_3$); ^{13}C NMR ($CDCl_3$) δ 188.1 and 185.9 (-CO), 156.6 (-NHCONH-), 152.8, 148.9, 146.3, 139.9, 132.2, 129.0, 125.5, 121.9 and 118.4 (Ar), 75.7 (-OCH_2-), 39.3 (-CH_2N-), 34.0 and 31.2 (-$C(CH_3)_3$), 30.6 ($ArCH_2Ar$), 27.2 and 26.9 (-CH_2-).

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