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LETTERS

Urea derivative of calix[4]diquinone: HSO_4^- ion selective receptor

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Abstract

Urea derivative of calix[4]diquinone **3** has been synthesized in two steps via urea formation and oxidation of **1**. Anion–ligand interactions were studied by ^1H NMR and electrochemical analysis and showed a good affinity between receptor **3** and HSO_4^-. © 1999 Elsevier Science Ltd. All rights reserved.

A redox-switchable receptor is a compound capable of forming a complex with a given substrate in such a way that the thermodynamic stability of the complex is determined by the oxidation state of the receptor. In pursuit of advancing chemical sensor technology considerable interest is being shown in the incorporation of organic and transition metal redox-active centers into various macrocylic frameworks such as crown ether, cryptand and calixarene.[1] Selective binding of ions is an important aspect of ion detection and ion transport. Selective complexation of anions is more demanding than that of cations due to low charge density and strong solvation. Furthermore, it has to be kept in mind that anions are subject to pH-dependent acid–base equilibria.[2] Beer et al. reported several examples of anion receptors based on cobalticinium,[3] and ruthenium(II)[4] derivatives and Reinhoudt et al. published several reports on neutral anion receptors of urea[5] and sulfone amide[6] derivatives of calixarene.

In nature, sulfate and phosphate binding proteins are very important receptors for the active transport systems in the cell.[7] It is known that prokaryotic, periplasmic phosphate and sulfate binding proteins can bind anions with high selectivity, exclusively by the formation of hydrogen bonds. They exhibit selectivities of more than 10^5 for binding phosphate over sulfate and of sulfate over phosphate, respectively.[8]

Quinones play a key role in photosynthetic energy conversion.[9] They are the ultimate electron acceptors in the cascade of electron-transfer reactions initiated when photosynthetic reaction centers are excited. Incorporating anion binding urea and electron accepting quinone moieties into the calix[4]arene framework, we synthesized a urea derivative[10,11] of calix[4]diquinone **3** and studied the electrochemical and complexation behavior. This novel neutral anion receptor binds anions through hydrogen bonding and shows high selectivity with HSO_4^- over $H_2PO_4^-$, Cl^- and $CH_3CO_2^-$.

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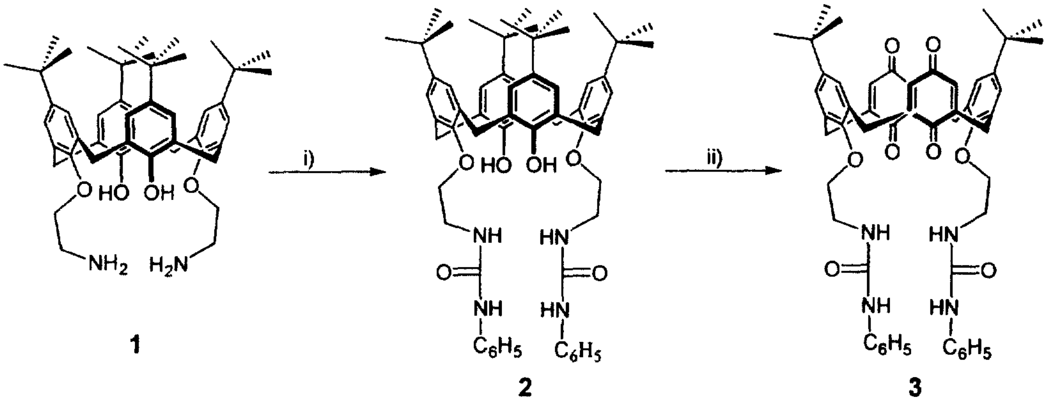
The urea derivative calix[4]arene **2** was obtained by the reaction of bis-(2-aminoethyl)calix[4]arene **1**[12] and phenylisocyanate in 90% yield.[13] Reaction of calixarene **2** with thallium trifluoroacetate (TTFA) in trifluoroacetic acid afforded the urea derivative calix[4]diquinone **3** in 40% yield (Scheme 1).[14] At low temperature a mixture of cone and partial cone conformers of **3** was observed as seen previously from the diester and diamide derivatives of a calix[4]diquinone.[15,16]



i) $C_6H_5N{=}C{=}O$, ii) $Tl(O_2CCF_3)_3$ in CF_3CO_2H

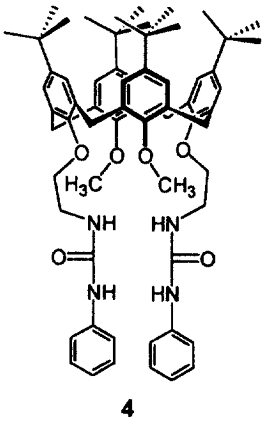
Scheme 1.

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, perchlorate, hydrogen sulfate, and acetate. In proton NMR experiments a large downfield shift of broad singlet NH proton resonance at δ 7.83 and the slight downfield shift of doublet *ortho* protons at δ 7.52 of the phenyl group were observed upon addition of TBA anions to the host solution. In particular, a singlet at δ 7.83 for the amide NH signal shifted rapidly at around δ 8.6 upon addition of 1 equivalent TBA HSO_4^-. Further addition of HSO_4^- caused only a slight downfield shift. Any further significant change was not observed after 1 equivalent of TBA HSO_4^-, suggesting that **3** complexed with the hydrogen sulfate ion 1:1 solution stoichiometry. A large chemical shift change of the NH protons in the presence of anions 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[17] and these values are presented in Table 1. Interestingly, a selectivity for HSO_4^- was observed for the derivative of calix[4]diquinone **3**. The influence of the hydrogen bond with quinone moieties with HSO_4^- is very clear comparing the *K* values of **3** with those of the corresponding urea derivative **4**.[18] For HSO_4^- **3** shows the highest *K* values which could be due to the presence of OH protons in anions. The electrochemical property of **3** was investigated using cyclic voltammetry.[19] Calix[4]diquinone **3** is initially reduced to semiquinone/quinone by one electron transfer, and then reduced to semiquinone/semiquinone at a more negative potential. The addition of anions to calix[4]diquinone **3** solutions resulted in cathodic shifts of the 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 was observed with HSO_4^- anion. The addition of hydrogen sulfate anion caused a 140 mV cathodic shift in the quinone/semiquinone redox couple. This large cathodic shift signifies a strong stabilization of calix[4]diquinone **3** in the presence of hydrogen sulfate anion. This result indicates that hydrogen sulfate anion coordinates to the NH protons of calix[4]diquinone **3** and also bonds to quinone moiety by hydrogen bonding.

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

	K /dm$_3$ mol^{-1}		ΔE(mV)
Anion	**3**	**4**	**3**
Cl^-	830	2540	15
Br^-	270	1632	<5
ClO_4^-	85	-	<5
HSO_4^-	2570	303	140
$H_2PO_4^-$	1010	250	110
$CH_3CO_2^-$	990	528	40

*The first cathodic peak potential of **3** is -0.42 V vs Ag/AgCl.



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Acknowledgements

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13. Compound **2**: To a 0.5 g (0.68 mmol) of **1** in 20 mL of CH_2Cl_2, 0.15 mL of phenylisocyanate was added and the mixture stirred overnight under a nitrogen atmosphere. After removing the solvent, the residue was triturated with MeOH.

Recrystallization from $CHCl_3$–CH_3OH gave 0.59 g (90%) of **2**. ^{1}H NMR ($CDCl_3$) δ 8.71 (s, 2H, -OH), 7.17–7.28 (m, 8H, ArH), 7.12 (br t, 2H, -NH), 7.01 and 7.07 (two s, 8H, ArH), 6.81 (s, 2H, -HN-), 4.24 and 3.42 (a pair of d, 8H, $ArCH_2Ar$), 4.11 (t, 4H, $-OCH_2-$), 3.85 (q, 4H, $-CH_2N-$), 1.26 and 1.12 (two s, 36H, $-C(CH_3)_3$). ^{13}C NMR ($CDCl_3$) δ 155.9 (-NHCONH-), 149.0, 148.6, 148.3, 143.5, 138.8, 133.0, 128.9, 127.9, 126.2, 125.8, 123.1 and 120.3 (Ar), 76.2 ($-OCH_2-$), 40.2 ($-CH_2N-$), 34.2, 34.0, 32.1, 31.6 and 31.1 ($ArCH_2Ar$ and $-C(CH_3)_3$).

14. Compound **3**: To a 1.0 g (1 mmol) of **2** in 15 mL of trifluoroacetic, 1.2 g of TTFA (2 mmol) was added and the mixture stirred for 2 h in the dark under a nitrogen atmosphere. The solvent was then removed and the residue poured onto ice/water (50 ml). The product was then extracted into chloroform (100 ml). The solvents were removed. The crude products were purified by column chromatography (eluent, $CHCl_3$:MeOH=20:1) to give a yellow power (0.30 g, 34%). Mp 157–158°C. ^{1}H NMR ($CDCl_3$) d7.83 (s, 2H, -NH), 7.52 (d, 4H, ArH, J=7.5 Hz), 7.20 (t, 4H, ArH, J=7.5 Hz), 6.96 (t, 2H, ArH, J=7.5 Hz), 6.84 (s, 4H, ArH), 6.77 (s, 4H, ArH), 6.28 (s, 2H, -NH), 3.75 and 3.24 (pair of d, 8H, $ArCH_2Ar$, J=13 Hz),), 3.73 (br s, 8H, $-CH_2CH_2-$), 1.10 (s, 18H, $-C(CH_3)_3$). ^{13}C NMR ($CDCl_3$) d185.7, 155.6 and 152.9 (-CO), 148.2, 147.1, 139.5, 132.7, 129.1, 128.9, 127.1, 122.6 and 119.2 (Ar), 73.9 ($-OCH_2-$), 40.2 ($-CH_2N-$), 34.1 and 31.3 ($-C(CH_3)_3$), 29.7 ($ArCH_2Ar$).
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19. Acetonitrile as a solvent and $(n\text{-}Bu_4)NBF_4$ as the supporting electrolyte were used for the voltametric measurements and were accomplished with a three electrode potentiostat (BAS 100B/W). A platinum wire electrode was used as an auxiliary electrode, and an Ag/AgCl electrode supplied by BAS was used as a reference electrode. A 3.0 mm diameter glassy carbon was employed as a working electrode.