# Upper Rim Urea Derivative of Calix[4]diquinone : $H_2PO_4^-$ Ion Selective Receptor

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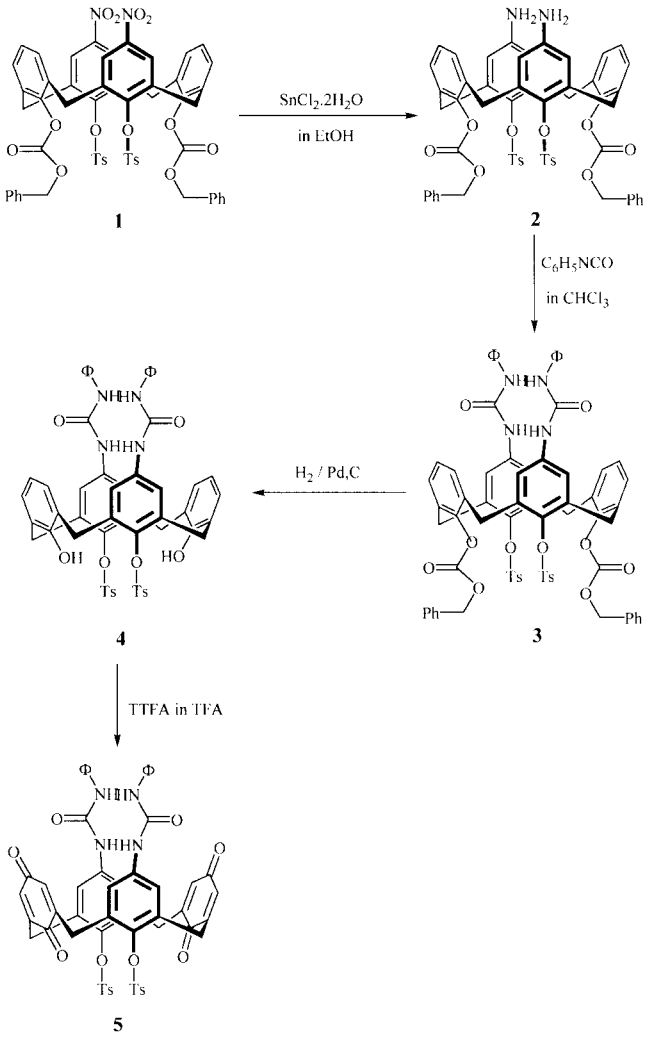
For the development of advancing chemical sensor technology considerable interest is being shown in the incorporation of organic and transition metal redox-active centers into various macrocylic compounds such as crown ether, cryptand and calixarene.[1-3] Beer reported several examples of anion receptors based on cobalticinium,[4,5] and ruthenium (II)[6,7] derivatives. Quinones play a key role in photosynthetic energy conversion.[8] They are the ultimate electron acceptors in the cascade of electron-transfer reaction initiated when photosynthetic reaction centers are excited.

Several excellent quinone and anthraquinone based redox-switchable ligands for cations were developed by Gokel and Echegoyen.[9-11] But quinone based redox-switchable hosts for anions were not reported at all. Recently we first reported[12] a urea derivative of calix[4]diquinone which showed a high selectivity for $HSO_4^-$. Two urea units were introduced at the lower rim of calix[4]arene. Here we reported the second urea derivative of calix[4]diquinone, which was utilizing at the upper rim of calixarene for the introduction of urea groups and studied the electrochemical and complexation behavior. This novel neutral anion receptor binds anions through hydrogen bonding and shows a high selectivity with $H_2PO_4^-$ over $CH_3CO_2^-$, $Cl^-$ and $HSO_4^-$.

The urea derivative calix[4]arene **3** was obtained by the reaction of diaminocalix[4]arene **2** which was prepared by the reduction of dinitrocalix[4]arene **1**[13-15] with $SnCl_2$, and phenylisocyanate in high yield as shown in Scheme 1. After removing benzyloxycarbonyl group with $H_2$ in the presence of palladium charcoal, oxidation to quinone was conducted with TTFA (thallium trifluoroacetate) in trifluoroacetic acid to afford the urea derivative calix[4]quinone **5** in 30% yield. The $^1$H NMR spectrum of **5** in DMSO-$d_6$ shows a pair of doublets at $\delta$ 3.54 and 2.97 for the bridge methylene protons, two singlets at $\delta$ 6.85 and 6.78 for the aromatic and quinone protons, and two singlets at $\delta$ 8.32 and 8.20 for the urea NH protons, indicating that **5** exist as a cone conformation.

The anion binding properties were investigated by the proton NMR titration in DMSO-$d_6$ solution in the presence of various anions such as tetrabutylammonium (TBA) chloride, bromide, dihydrogen phosphate, benzoate, hydrogen sulfate and acetate. In proton NMR experiments a large downfield shift of two singlets NH proton resonances at $\delta$ 8.32 and 8.20 and the moderate upfield shift of two singlet at $\delta$ 6.85 and 6.78 were observed upon addition of TBA $H_2PO_4^-$ anion to host solution as shown in Figure 1. Also the moderate up and down field shift of phenyl resonances attached directly with urea nitrogen was noticeable. Particularly two singlets at $\delta$ 8.32 and 8.20 for the urea NH signals shifted rapidly at around $\delta$ 10.2 and 10.0 upon addition of 1 equivalent TBA $H_2PO_4^-$. Further addition of $H_2PO_4^-$ caused an only very slight downfield shift. Any further significant change was not observed after one equivalent of TBA $H_2PO_4^-$, suggesting that **5** complexed with dihydrogen phosphate ion 1 : 1 solution stoichiometry. Large chemical shift change of the NH protons in the presence of anion indicates that the anions bind the urea protons directly. Calixarene phenyl and quinone proton signals shifted upfield upon addition of anion, suggesting that the anions do not bind directly with aromatic protons.




**Scheme 1**. Synthesis of a urea derivative of calix[4]diquinone.

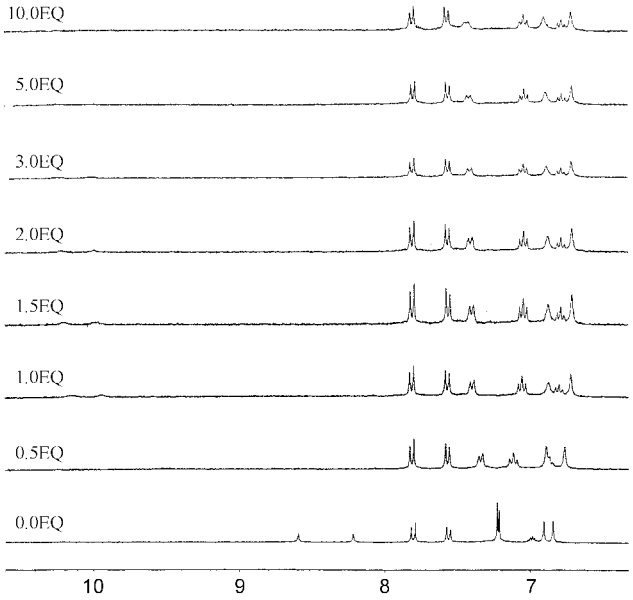



**Figure 1**. The partial $^1$H NMR spectra of **5** in the presence of TBA $H_2PO_4^-$ in DMSO-$d_6$. Numbers at the left side indicate the equivalent amounts of $H_2PO_4^-$ added.

The association constants of the various anions to the receptors are obtained from the resulting titration curves using EQ-NMR[16] and these values are presented in Table 1. A high selectivity for $H_2PO_4^-$ was observed for the urea derivative of calix[4]diquinone **5**. The influence of quinone moieties for the anion binding might be the important factor for the selectivity of dihydrogen phosphate through the hydrogen bond with carbonyl oxygen with OH proton in $H_2PO_4^-$. But we do not have the evidence at this point.

The electrochemical property of **5** was investigated using cyclic voltammetry. Calix[4]diquinone **5** 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 **5** solutions occurred cathodic shifts of quinone/semiquinone redox couple with the relative magnitudes following the order $H_2PO_4^- > C_6H_5COO^- > CH_3COO^-$, $Cl^-$, $HSO_4^-$, $Br^-$. The most significant results were observed with $H_2PO_4^-$ anion. Cathodic shifts of calix[4]diquinone **5** in the presence of anions are summarized in Table 1. The addition of dihydrogen phophate anion caused a 94 mV cathodic shift in the quinone/semiquinone redox couple.

**Table 1**. Stability constants ($K_a$) and cathodic shifts of calix[4]-diquinone **5** in the presence of anions in DMSO

| Anion | $K$/dm$^3$ mol$^{-1}$ | $\Delta E$ (mV) |
|---|---|---|
| $Cl^-$ [a] | 53 | ~0 |
| $Br^-$ | 0 | ~0 |
| $HSO_4^-$ | 100 | ~0 |
| $CH_3COO^-$ | 840 | ~0 |
| $PhCOO^-$ | 2430 | 53 |
| $H_2PO_4^-$ | 13900 | 94 |

[a] Tetrabutylammonium salts. Errors estimated to be < 10%.

In summary, we developed a urea derivative of calix[4] diquinone from the upper rim and it showed a high selectivity for $H_2PO_4^-$.

## Experimental Section

**5,17-Dinitro-25,27-bis(benzyloxycarbonyloxy)-26,28-bis-(tosylsulfonyloxy) calix[4]arene (1)**. Following the procedure previously reported,[15] **1** was prepared from calix[4]-arene by the three step reaction sequence. mp. 215-218 °C.[15]

**5,17-Diamino-25,27-bis(benzyloxycarbonyloxy)-26,28-bis(tosylsulfonyloxy) calix[4]arene (2)**. To a 0.98 g (0.9 mmol) of **1** in 50 mL of ethanol, 2.0 g $SnCl_2 \cdot 2H_2O$ (9 mmol) was added and the mixture was refluxed for 12 h. Neutralized with NaOH solution and extracted with $CH_2Cl_2$. After removing the solvent, the residue was triturated with MeOH. Recrystallization from $CHCl_3$-$CH_3OH$ gave 0.57 g (61%) of **2**. mp. 218-220 °C; $^1$H NMR ($CDCl_3$) $\delta$ 7.76 (d, 4H, $J$ = 7.14 Hz, ArH) $\delta$ 7.48 (t, 4H, $J$ = 14.6 Hz, ArH) $\delta$ 7.39 (t, 4H, $J$ = 7.11 Hz, ArH) $\delta$ 7.30, $\delta$ 7.07 (a pair of d, 8H, $J$ = 8.3 Hz, TsH) $\delta$ 6.99-6.90 (m, 8H, ArH) $\delta$ 5.95 (s, 4H, $ArNH_2$) $\delta$ 5.55 (s, 4H, $OCH_2Ar$) $\delta$ 3.79, $\delta$ 2.67 (a pair of d, 8H, $J$ = 13.6 Hz, $ArCH_2Ar$) $\delta$ 2.38 (s, 6H, $CH_3$). $^{13}$C NMR ($CDCl_3$) $\delta$ 155.3 (-CO) $\delta$ 148.0, 144.6, 143.6, 136.7, 136.5, 135.1, 135.0, 132.6, 129.5, 129.2, 129.0, 128.6, 128.5, 128.2, 125.74 and 116.0 (Ar) 70.8 ($OCH_2Ar$) $\delta$ 31.0 ($ArCH_2Ar$) $\delta$ 21.7 ($CH_3$).

**5,17-Di(*N'*-phenylureido)-25,27-bis(benzyloxycarbonyl-oxy)-26,28-bis(tosylsulfonyloxy)calix[4]arene (3)**. To a 1.0 g (0.97 mmol) of **2** in 50 mL of chloroform, 0.23 g of phenylisocyanate was added and the mixture was stirred for overnight. Additional 50 mL of $CHCl_3$ was added and washed with water three times. After removing the solvent, the residue was triturated with MeOH. Recrystallization from $CHCl_3$-$CH_3OH$ gave 0.87 g (71%) of **3**. mp. 202-204 °C; $^1$H NMR (DMSO-$d_6$) $\delta$ 8.52 (s, 2H, NH) $\delta$ 8.47 (s, 2H, NH) 7.74 (d, 4H, $J$ = 7Hz, ArH) $\delta$ 7.52-7.41 (m, 8H, ArH) $\delta$ 7.29 (d, 8H, $J$ = 8.43 Hz, ArH) $\delta$ 7.24-7.17 (m, 12H, ArH) $\delta$ 6.99 (s, 4H, ArHN) $\delta$ 6.97-6.90 (m, 4H, ArH) $\delta$ 5.49 (s, 4H, $OCH_2Ar$) $\delta$ 3.67, 2.87 (a pair of d, 8H, $J$ = 13.3 Hz, $ArCH_2Ar$) 2.38 (s, 4H, $CH_3$). $^{13}$C NMR ($CDCl_3$) $\delta$ 155.0, 152.7 (-CO) $\delta$ 148.1, 145.1, 139.2, 138.5, 136.8, 136.6, 135.4, 134.9, 132.1, 129.7, 128.9, 128.7, 128.6, 128.2, 126.0, 122.4, 118.5 and 118.2 (Ar) $\delta$ 70.6 ($OCH_2Ar$) $\delta$ 31.0 ($ArCH_2Ar$) $\delta$ 21.7 ($CH_3$).

**5,17-Di(*N'*-phenylureido)-25,27-dihydroxy-26,28-bis(tosyl-sulfonyloxy)calix[4]arene (4)**. A 1.0 g of **3** in 50 mL of THF and ethanol mixture (3 : 7) was treated with $H_2$ under 60 psi in the presence of Pd/C. After removing catalyst and solvent, 0.73 g (92%) of **4** was obtained as a colorless powder. mp. 198-200 °C; $^1$H NMR ($CDCl_3$) $\delta$ 7.7 (d, 4H, $J$ = 7.5 Hz, TsH) $\delta$ 7.3 (d, 4H, $J$ = 7.5 Hz, TsH) $\delta$ 7.2-6.4 (br m, 22H, ArH, NH) $\delta$ 6.25 (br s, 2H, NH) $\delta$ 5.2 (br s, 2H, OH) $\delta$ 3.9, $\delta$ 3.0 (a pair of d, 8H, $J$ = 12 Hz, $ArCH_2Ar$) $\delta$ 2.45 (s, 6H, $CH_3$). $^{13}$C NMR ($CDCl_3$) $\delta$ 152.7 (-CO) $\delta$ 152.6, 146, 139.4, 139, 137.6, 135, 132, 130, 129.8, 128.8, 128.7, 122.5, 120, 118.6 and 118 (ArH) $\delta$ 31.6 ($ArCH_2Ar$) $\delta$ 21.7 ($CH_3$).

**5,17-Di(*N'*-phenylureido)-26,28-bis(tosylsulfonyloxy)calix-[4]-25,27-diquinone (5)**. To a 0.30 g (0.97 mmol) of **4** in 15 mL of trifluoroacetic acid, 0.40 g of TTFA (thallium trifluoroacetate) was added and the mixture was stirred for 12 h under the nitrogen atmosphere. After removing the solvent, the residue was separated by the column chromatography (eluent : chloroform : methanol = 100 : 1) to give 0.10 g (30%) of **5** as a pale yellow powder. mp. 186-188 $^{o}$C; $^{1}$H NMR (DMSO) $\delta$ 8.32 (br s, 2H, NH) $\delta$ 8.20 (br s, 2H, NH) $\delta$ 7.75 (d, 4H, $J$ = 9 Hz, TsH) $\delta$ 7.50 (d, 4H, $J$ = 9 Hz, TsH) $\delta$ 7.16 (two s, 8H, ArH) $\delta$ 6.90 (m, 2H, ArH) $\delta$ 6.85 (s, 4H, quinone H) $\delta$ 6.78 (s, 4H, ArHN) $\delta$ 3.54, $\delta$ 2.97 (a pair of d, 8H, $J$ = 14 Hz, $ArCH_2Ar$) $\delta$ 2.45 (s, 6H, $CH_3$) $^{1}$H NMR ($CDCl_3$) $\delta$ 7.70 (d, 4H, $J$ = 7.9 Hz, TsH) $\delta$ 7.46 (br , 2H, NH) $\delta$ 7.30 (d, 4H, $J$ = 7.9 Hz, TsH) $\delta$ 7.27 (s, 2H, ArH) $\delta$ 7.10 (s, 8H, ArH) $\delta$ 6.95 (br s, 2H, NH) $\delta$ 6.68 (s, 4H, quinone H) $\delta$ 6.41 (s, 4H, ArHN) $\delta$ 3.60, $\delta$ 2.90 (a pair of d, 8H, $J$ = 14 Hz, $ArCH_2Ar$) $\delta$ 2.44 (s, 6H, $CH_3$). $^{13}$C NMR (DMSO-$d_6$) $\delta$ 188, 184 (-CO) $\delta$ 152, 147.4, 146, 139.3, 139, 137.8, 132.5, 132.1, 131.9, 130.5, 128.6, 128, 121.7 and 118 (Ar) $\delta$ 30 ($ArCH_2Ar$) $\delta$ 21 ($CH_3$).

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## References

1. Minami, T.; Shinkai, S.; Manabe, O. *Tetrahedron Lett.* **1982**, *23*, 5167.
2. Vögle, F.; Oepen, G. *Liebigs Ann. Chem.* **1979**, 1094.
3. Beer, P. D.; Drew, M. G. B.; Hazlewood, C.; Hesek, D.; Hodacova, J.; Stokes, S. E. *J. Chem. Soc. Chem. Comm.* **1993**, 229.
4. Beer, P. D.; Drew, M. G. B.; Hesek, D.; Nam, K. C. *Chem. Comm.* **1997**, 107.
5. Beer, P. D.; Drew, M. G. B.; Hodacova, J.; Stokes, S. E. *J. Chem. Soc., Dalton Trans.* **1995**, 3447.
6. Szemes, F.; Hesek, D.; Chem, Z.; Dent, S. W.; Drew, M. G. B.; Goulden, A. J.; Graydon, A. R.; Grieve, A.; Mortimer, R. J.; Wear, T.; Weightman, J. S.; Beer, P. D. *Inorg. Chem.* **1996**, *35*, 5868.
7. Beer, P. D.; Dent, S. W. *Chem. Comm.* **1998**, 825.
8. Gunner, M. R. *Curr. Top. Bioenergetics* **1991**, *16*, 319.
9. Gustowski, D. A.; Delgado, M.; Gatto, V. J.; Echegoyen, L.; Gokel, G. W. *J. Am. Chem. Soc.* **1986**, *108*, 7553.
10. Chen, Z.; Schall, O. F.; Alcala, M.; Li, Y.; Gokel, G. W.; Echegoyen, L. *J. Am. Chem. Soc.* **1992**, *114*, 444.
11. Echegoyen, L. E.; Yoo, H. K.; Gatoo, V. J.; Gokel, G. W. *J. Am. Chem. Soc.* **1989**, *111*, 2440.
12. Nam, K. C.; Kang, S. O.; Jeong, H. S.; Jeon, S. *Tetrahedron Lett.* **1999**, *40*, 7343.
13. Beer, P. D.; Gale, P. A.; Hesek, D. *Tetrahedron Lett.* **1995**, *36*, 767.
14. Hesek, D.; Inoue, Y.; Drew, M. G. B.; Beer, P. D.; Hembury, G. A.; Ishida, H.; Aoki, F. *Organic Lett.* **2000**, 2237.
15. Beer, P. D.; Hesek, D.; Nam, K. C. *Organometallics* **1999**, *18*, 3933.
16. Hynes, M. J. *J. Chem. Soc., Dalton Trans.* **1993**, 311.