The Dimroth rearrangement of 1,2,3-triazoles in the synthesis of anion receptors based on calix[4]arenas

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Dedicated to Professor Oleg N. Chupakhin on the occasion of his 70th birthday
(received 20 July 04; accepted 18 Aug 04; published on the web 27 Aug 04)

Abstract
Reaction of tetrais-(azidosulfonyl)calix[4]arenes with 2-cyanoacetamides afforded the product of the Dimroth rearrangement, namely tetrais-(1,2,3-triazole-5-aminosulfonyl) calix[4]arenes. The complexation of the 1,2,3-triazolesulfonamide calixarene hybrids with anions was studied by NMR titration, and association constants were determined.

Keywords: Calix[4]arenes, anion-receptors, 1,2,3-triazoles, Dimroth rearrangement

Introduction
Calix[4]arenes1,2 are macrocyclic compounds which are used widely in supramolecular chemistry for the construction of various receptors for the complexation of charged or neutral molecules. Their unique three-dimensional structures with almost unlimited derivatization abilities, and the tunable shape of the molecules, make calixarenes ideal candidates for building blocks and/or molecular scaffolds in the design of new and more sophisticated molecules. Whereas cation complexation has been studied extensively for a long time, the recognition of anions3 by synthetic receptors based on the calixarenes still remains relatively unexplored. Thus, the introduction of activated amides4 into the upper rim of calixarene derivatives, pre-organized in the cone conformation, led to receptors’ interacting with anions by hydrogen bonds. Other moieties used frequently for anion recognition are urea, thiourea5 and sulfonamide6 units. In the present paper we report anion receptors based on 1,2,3-triazole–calixarene hybrids.
**Results and Discussion**

The starting azidosulfonylcalixarene, 1, was obtained in 55% yield by reaction of chlorosulfonylcalix[4]arene 2 (cone conformation) with sodium azide. The cycloaddition of arylsulfonyl azides to cyanoacetamides led to 1-arylsulfonyl-5-amine-1,2,3-triazoles: the latter can be transformed by Dimroth rearrangement into 1H-5-arylsulfonylamino-1,2,3-triazole. We have shown that the treatment of azidosulfonylcalix[4]arene 1 with N-phenyl- and N-cyclohexyl-2-cyanoacetamides at 40°C in solution in the presence of an equivalent of EtONa for 15 h gave the tetrakis((1H-1,2,3-triazol-5-amine)sulfonyl)calix[4]arenes 3a,b in 38 and 60% yields, respectively. The ¹H-NMR spectra of 3a,b indicates the presence of four NHSO₂ protons at 6.52 ppm and four NH protons at 10–11 ppm. Reaction under the same conditions of the tosyl azide and N-phenyl-2-cyanoacetamide also led to the product of Dimroth rearrangement, namely 1H-5-tosylamino-1,2,3-triazole-4-N-phenylcarboxamide, 5.

![Chemical structures](image)

**R = CONHPh** (a), **CONHC₆H₁₄cyclo** (b)

Because the sulfonamide calix[4]arenes are known to form complexes with anions, we proposed the use of tetrakis((1H-1,2,3-triazol-5-amine)sulfonyl)calix[4]arenes 3a,b as neutral
anion- receptors. A $^1$H- NMR spectroscopic study revealed that, upon addition of tetrabutylammonium salt to a solution of 3a,b in CDCl$_3$, downfield shifts occur in the resonance corresponding to the sulfonamido NH protons (e.g., 8.45 ppm–10.60 ppm, see Figure 1), consistent with the formation of hydrogen bonds. The host–guest complex at 1:1 stoichiometry was determined by Job plots (maxima at mole fractions of 0.5). The association constants $K$ of 3a,b (and of reference compounds 5 and 6) with the tetrabutylammonium salt of NO$_3^-$, Cl$^-$ have been determined by $^1$H-NMR titration experiments, and are summarized in Table 1.

![Figure 1. Titration curve for addition of Bu$_4$NCl to 3a in CDCl$_3$ at 298$^\circ$C.]

<table>
<thead>
<tr>
<th>Complex</th>
<th>Anions $^b$</th>
<th>Cl$^-$</th>
<th>NO$_3^-$</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>850</td>
<td>450</td>
<td></td>
</tr>
<tr>
<td>3b</td>
<td>720</td>
<td>510</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>21</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>6$^c$</td>
<td>360</td>
<td>240</td>
<td></td>
</tr>
</tbody>
</table>

The influence of the present eight pre-organized binding sites is very clear, from comparing the $K$ values of 3a,b with that of reference compound 4. Also, the presence of the four NH-heterocycle- protons of 3a,b in addition to the four sulfonamide ones in the tetrakis-(propylaminosulfonyl)- calix[4]arenes, 5$^4$, increases $K_{\text{ass}}$. 

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$^a$ The error is <5%. $^b$ The counter-ion is Bu$_4$N$^+$. $^c$ Result from ref. 6.
Conclusions

Anion-receptors based on the sulfamoylcalix[4]arenes and 1,2,3-triazoles have been prepared. The key step of this synthesis is the Dimroth rearrangement of a 5-amino-1-arylsulfonyl-1,2,3-triazole to a 5-arylsulfonamino-1H-1,2,3-triazole. The association constants were determined.

Experimental Section

General Procedures. NMR chemical shifts were recorded with a Bruker WH-250 spectrometer at 250 MHz, CDCl₃ solution, and are given in δ units. All reaction mixtures and products were examined by TLC on DC-Plastikfolen Kieselgel-60 F-254 plates. Melting points are uncorrected. All reagents are commercially available (Aldrich, Acros) and were used without further purification. The calix[4]arenes 2, 6 were prepared as described.⁶

25,26,27,28-Tetrakis(methoxyethoxy)-5,11,17,23-tetrakis(azidosulfonyl)calix[4]arene (1). A mixture of chlorosulfonyl calix[4]arenes 2 (1.16 g, 1 mmol) and sodium azide (0.65 g, 10 mmol) in 50 ml ethanol was stirred at room temperature for 4 h. The precipitate was filtered off, and the ethanol removed under vacuum at 35°C. To the residue was added CH₂Cl₂ (50 ml), the solution washed with water (4x100 ml), and the solvent removed under vacuum at 35°C. Yield 55%, m.p. 137°C (decomp.) ¹H-NMR (CDCl₃, δ, ppm): 7.54 (8H, s, ArH), 5.13 (4H, d, J=3.7 Hz, 4xCHAr), 3.38 (8H, t, J=4.4 Hz, 4xOCH₂), 3.80 (8H, t, J=4.4 Hz, 4xOCH₂), 3.56 (4H, d, J=13.7 Hz, 4xCHAr), 3.33 (12H, s, 4xOMe). Anal. Calc. for C₄₀H₄₄N₁₂O₁₆S₄, C 44.60, H 4.12, N 15.60, S 11.91. Found: C 44.37, H 3.98, N 16.00, S 11.60%.

25,26,27,28-Tetrakis(methoxyethoxy)-5,11,17,23-tetrakis(N-(4-N-phenylcarbamoyl-1H-1,2,3-triazol-4-yl)sulfamoyl)calix[4]arene (3a). To a mixture of the calix[4]arene 1 (119 mg, 0.1 mmol) and N-phenyl-2-cyanoacetamide (66 mg, 0.4 mmol) in 5 ml ethanol, was added sodium ethoxide (32 mg, 40.4 mmol), and the reaction mixture was stirred at 40°C for 15 h. The precipitate was filtered and recrystallized from ethanol. Yield 55%. mp 249°C decomp. ¹H-NMR (CDCl₃, δ, ppm): 10.5–12.0 (4H, br., NH), 10.23 (4H, br. s, NH), 7.0–8.0 (28H, m, ArH), 6.52 (4H, s, NH), 5.10 (4H, d, J=14.1 Hz, 4xCHAr), 4.83 (8H, t, J=4.3 Hz, 4xOCH₂), 3.78 (8H, t, J=4.3 Hz, 4xOCH₂), 3.55 (4H, d, J=14.1 Hz, 4xCHAr), 3.19 (12H, s, 4xOMe). Anal. Calc. for C₇₆H₇₆N₂₀O₂₀S₄: C 53.14, H 4.46, N 16.31, S 7.47. Found: C 53.11, H 4.58, N 16.59, S 7.46%.

25,26,27,28-Tetrakis(methoxyethoxy)-5,11,17,23-tetrakis(N-(4-N-cyclohexylcarbamoyl-1H-1,2,3-triazol-4-yl)sulfamoyl)calix[4]arene (3b). Yield 0.1 g (60%). mp 217°C. ¹H-NMR (CDCl₃, δ, ppm): 10.5–12.0 (4H, br., NH), 10.20 (4H, br. s, NH), 7.54 (8H, s, ArH), 6.56 (4H, s, NH), 5.13 (4H, d, J=13.7 Hz, 4xCHAr), 4.38 (8H, t, J=4.1 Hz, 4xOCH₂), 3.88 (8H, t, J=4.1 Hz, 4xOCH₂), 3.56 (4H, d, J=13.7 Hz, 4xCHAr), 3.34–3.38 (4H, m, CH), 3.20 (12H, s, 4xOMe), 1.2–2.2 (40H, m, CH). Anal. Calc. for C₇₆H₁₀₀N₂₀O₂₀S₄: C 52.40, H 5.79, N 16.08, S 7.36. Found: C 52.66, H 5.45, N 16.20, S 7.45%.
Determination of association constants. The measurements were performed by $^1$H-NMR titration experiments in CDCl$_3$ at 298°C using a concentration of 4 mM and a varying guest concentration of 0.3–30 mM. For each $K$ value determination 4–8 different guest concentrations were taken. The chemical shift of the SO$_2$NH signal was used as the probe. The $K$ values were calculated by non-linear regression as described in ref. 7.

Acknowledgments

This research was made possible in part by grants No. 04-03-96143 and No. 04-03-96104 of the Russian Foundation for Basic Research.

References