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 tetrakis-(azidosulfonyl)calix[4]arenes with 2-cyanoacetamides afforded the product of the Dimroth rearrangement, namely tetrakis-(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.

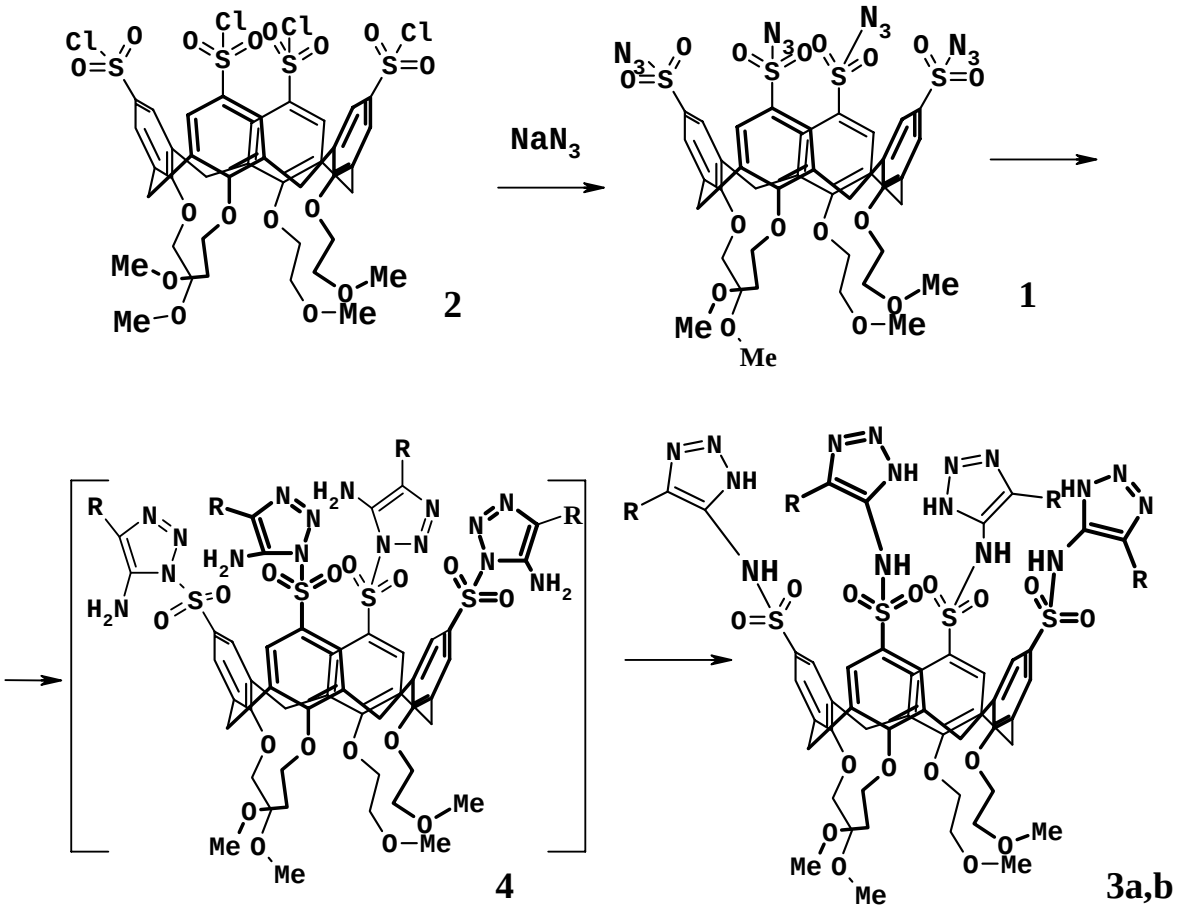
Keywords: Calix[4]arenes, anion-receptors, 1,2,3-triazoles, Dimroth rearrangement

Introduction

Calix[4]arenes[1,2] 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 anions[3] by synthetic receptors based on the calixarenes still remains relatively unexplored. Thus, the introduction of activated amides[4] 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, thiourea[5] and sulfonamide[6] 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)[6] 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 ^{1}H-NMR spectra of **3a,b** indicates the presence of four $NHSO_2$ 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**.



R = CONHPh (**a**), $CONHC_6H_{11}$cyclo (**b**)

Because the sulfonamide calix[4]arenes are known to form complexes with anions, we proposed the use of tetrakis((1*H*-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.

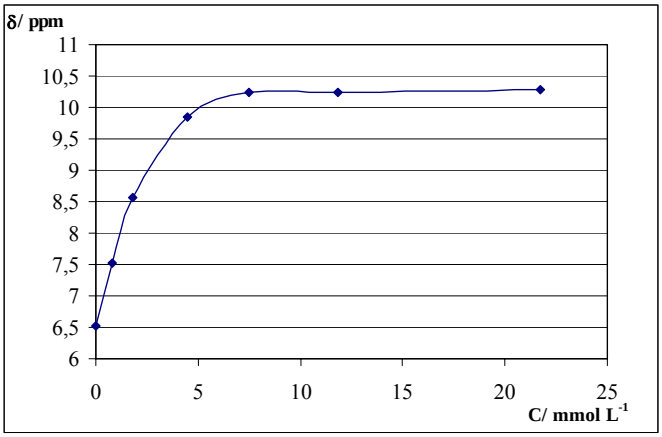
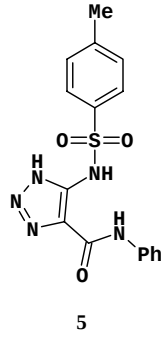


Figure 1. Titration curve for addition of Bu_4NCl to **3a** in $CDCl_3$ at 298°C.

Table 1. Association constant (K, M^{-1}, $CDCl_3$) of complexation of **3a,b, 5, 6** with anions[a]

Complex	Anions [b]	
	Cl^-	NO_3^-
3a	850	450
3b	720	510
5	21	12
6[c]	360	240



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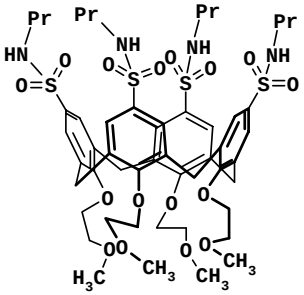

6

[a] The error is <5%. [b] The counter-ion is Bu_4N^+. [c] Result from ref. 6.

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_{ass}.

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-arylsulfonylamino-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, $CDCl_3$ 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 35ºC. To the residue was added CH_2Cl_2 (50 ml), the solution washed with water (4x100 ml), and the solvent removed under vacuum at 35ºC. Yield 55%, m.p. 137ºC (decomp.) ^{1}H-NMR ($CDCl_3$), δ 7.54 (8H, s, ArH), 5.13 (4H, d, J=3.7 Hz, 4xCHAr), 3.38 (8H, t, J=4.4 Hz, 4xOCH_2), 3.80 (8H, t, J=4.4 Hz, 4xOCH_2), 3.56 (4H, d, J=13.7 Hz, 4xCHAr), 3.33 (12H, s, 4xOMe). Anal. Calc. for $C_{40}H_{44}N_{12}O_{16}S_4$, 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-1*H*-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 40ºC for 15 h. The precipitate was filtered and recrystallized from ethanol. Yield 55%. mp 249ºC decomp. ^{1}H-NMR ($CDCl_3$, 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, 4xOCH_2), 3.78 (8H, t, J=4.3 Hz, 4xOCH_2), 3.55 (4H, d, J=14.1 Hz, 4xCHAr), 3.19 (12H, s, 4xOMe). Anal. Calc. for $C_{76}H_{76}N_{20}O_{20}S_4$: 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-1*H*-1,2,3-triazol-4-yl)sulfamoyl)calix[4]arene (3b). Yield 0.1 g (60%). mp 217ºC. ^{1}H-NMR ($CDCl_3$, 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, 4xOCH_2), 3.88 (8H, t, J=4.1 Hz, 4xOCH_2), 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 $C_{76}H_{100}N_{20}O_{20}S_4$: 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^{o}C using a concentration of 4 m*M* and a varying guest concentration of 0.3–30 m*M*.[4] For each *K* value determination 4–8 different guest concentrations were taken. The chemical shift of the SO_2NH 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.

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