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Synthesis and Crystal Structure of an *O*-Silylated Hexahomotriazacalix[3]arene

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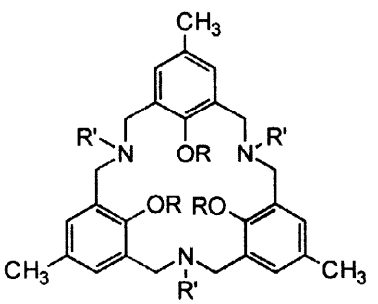
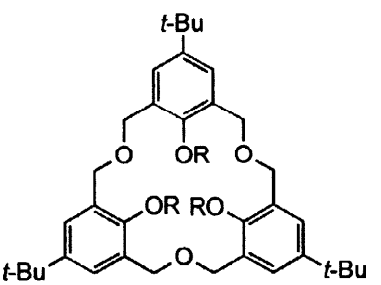
Abstract: The first synthesis of an *O*-silylated derivative of a hexahomotriazacalix[3]arene has been achieved using 1-(trimethylsilyl)imidazole (TMSIM), 1,1,1,3,3,3-hexamethyldisilazane (HMDS), or bis(trimethylsilyl)trifluoroacetamide (BSTFA) in acetronitrile. The cone isomer was formed selectively using TMSIM and HMDS; whereas a cone / partial cone mixture was obtained using BSTFA.

Recently, we reported the synthesis, crystal structure and host-guest chemistry of *N*-(methoxycarbonyl)-methyhexahomotriazacalix[3]arene **1**.[1] The hexahomotriazacalix[3]arene macrocycle will be abbreviated to azacalix[3]arene in this paper. Macrocycle **1** showed no significant binding to alkali metal ions. The lack of binding was proposed to be due to the strong intramolecular hydrogen-bonding interactions between the phenol groups and the nitrogens which was observed in the crystal structure. Previous studies have reported that *O*-alkylation of the phenolic oxygens in calixarenes and related macrocycles results in significantly higher affinities toward alkali and alkylammonium ions.[2-5] Modification of the phenolic oxygens in the azacalix[3]arene **1** will eliminate the intramolecular hydrogen bonding, enhance the coordination ability of the phenolic oxygens, and lock the macrocycle into either a cone or partial-cone conformation.





1. R = H; R' = $CH_2CO_2CH_3$
2. R = CH_2-2-pyridyl; R' = CH_2Ph.
3. R = $Si(CH_3)_3$; R' = $CH_2CO_2CH_3$

4. R = H

There has only been one report of the synthesis of an *O*-modified azacalix[3]arene **2** by Takemura and co-workers;[4,5] the cone vs. partial-cone selectivity of the *O*-alkylation reaction was not reported. In this manuscript we report the *O*-silylation of azacalix[3]arene **1**, the dependence of the cone vs. partial-cone selectivity on the reaction conditions, and the crystal structure of the cone conformer of the *O*-silylated azacalix[3]arene **3a** (Fig. 1). This is the first crystal structure of an *O*-modified azacalix[3]arene.

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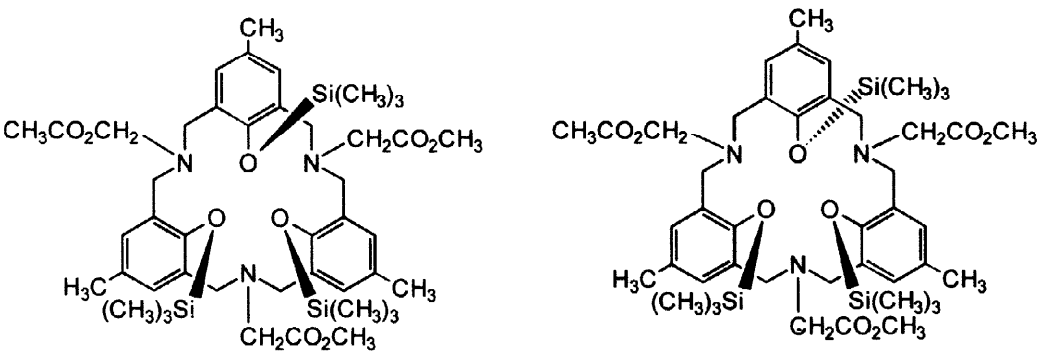
RESULTS AND DISCUSSION

The reaction of azacalix[3]arene **1** with TMSIM (1-(trimethylsilyl)imidazole) for 24 h in acetonitrile at room temperature gave an 82% yield of the pure cone isomer **3a** (Fig. 1). Similarly, the reaction of **1** with HMDS (1,1,1,3,3,3-hexamethyldisilazane) for 3 days in acetronitrile at room temperature also yielded the cone isomer **3a**. In contrast, treatment of **1** with BSTFA (bis(trimethylsilyl)trifluoroacetamide) for 5 h in acetonitrile at room temperature resulted in a mixture of the cone isomer **3a** and the partial-cone isomer **3b** in a 1: 1.5 ratio, respectively, based on the ^{1}H NMR spectra of this mixture. It is interesting to note that the *O*-silylation of the hexahomotrioxacalix[3]arene macrocycle **4**[6] exhibits a marked preference for the formation of the partial-cone isomer under all conditions that were examined. Since the crystal structure of azacalix[3]arene **1** exhibits a cone conformation, it is possible that hydrogen-bonding may fix mono- and disilylated intermediates in a cone conformation. The hexahomotrioxacalix[3]arene macrocycles **4** do not possess as strong hydrogen bonding as azacalix[3]arene **1**; as a result, partially alkylated intermediates would not be as stabilized in the cone conformer allowing the partial-cone isomer to form.



3a (cone isomer) **3b** (partial cone)

Fig. 1

An X-ray crystal structure[7] was determined for isomer **3a** to confirm its cone conformation. As evidenced in the ORTEP diagram in Fig. 2, all three of the TMS groups are on the same face of the macrocycle, consistent with a cone conformation for this compound. Two of the aryl rings are essentially parallel and separated by 3.86 Å; the third aryl ring is nearly perpendicular to the other aryl rings. Although the macrocycle possesses a cone conformation, the severe distortion of the macrocycle due to the three bulky trimethylsilyl groups results in a cavity which is too small for the inclusion of molecules.

SYNTHESIS

An excess of TMSIM (36 μL 0.25 mmol) was added to a solution of 50 mg of macrocycle **1** (0.071 mmol) in 5 mL of acetonitrile under nitrogen. After 24 h, the white precipitate was collected, washed with

acetonitrile, and dried *in vacuo* overnight. Isomer **3a** was obtained by recrystallization from chloroform and acetonitrile in 82% yield. The ^{1}H NMR and CHN elemental data were in accordance with the assigned structure.[8] X-ray quality crystals of **3a** were obtained by the slow crystallization of **3a** from chloroform and acetonitrile.

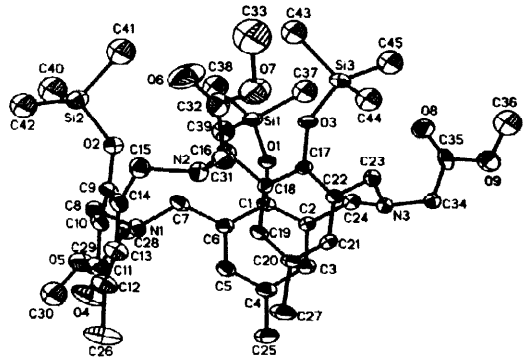


Fig. 2. X-Ray crystal structure for the cone conformation of tris(trimethylsilyl)azacalix[3]arene **3a**

NMR STUDIES

The ^{1}H NMR spectrum of **3a** in d_6-acetone consisted of a singlet for the aryl protons, a pair of doublets for the macrocycle methylene protons, one singlet for the *p*-methyl groups, one singlet for the three methylene groups in the nitrogen substituents, and one TMS singlet. The ^{1}H NMR spectra of mixtures of **3a** and **3b** formed in the reaction of **1** with BSTFA in CD_3CN consisted of six doublets for the methylene protons in the partial-cone isomer **3b** overlapping a pair of doublets for the cone isomer **3a**, three singlets for the aryl protons, three singlets for the *p*-methyl groups, three singlets for the methylene groups in the nitrogen substituents, and three TMS singlets. These spectra are consistent with the anticipated C_{3v} and C_s symmetry of **3a** and **3b**, respectively. There was no change in the ^{1}H NMR spectrum of pure cone isomer **3a** when the temperature was lowered to 210° K or raised to 335° K. This indicates that it is not possible for the cone **3a** and partial-cone **3b** isomers to equilibrate in this temperature range.

CONCLUSION

The *O*-silylation of azacalix[3]arene **1** results in the preferential formation of the cone conformer **3a** which exhibits no equilibration with the partial-cone isomer **3b**. Although the reaction is selective for only the cone conformer **3a**, an X-ray structure determination indicates that *O*-silylated macrocycle does not possess a large enough cavity for host-guest chemistry. We are currently examining the *O*-alkylation of the azacalix[3]arenes **1** and the host-guest chemistry of the *O*-modified macrocycles.

ACKNOWLEDGMENTS

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6. Hampton, P. D.; Daitch, C. E.; Duesler, E. N. *New J. Chem.* **1996**, *20*, 427-437.
7. Crystal structure for **3a**: ($C_{45}H_{69}N_3O_9Si_3$), M 880.3, monoclinic, space group $P2_1/c$, a 18.358(6), b 13.111(4), c 21.943(8) Å, β 102.70(2)°, V 5147(4)Å^3, D_c 1.136 Mg/m^3, Z 4, μ Mo 1.43 cm^{-1}. Crystal size 0.34 by 0.43 by 0.46 mm, 2θmax 43°, min. and max. transmission factors 0.93 and 0.94. The number of reflexions was 3679 considered observed out of 5922 unique data, with R (int) 2.72%. Final values of R, R_w were 6.80, 5.88% for the observed data.
8. Analytical and spectroscopic data for compound **3a**. Analytical calculation for $C_{45}H_{69}O_9N_3Si_3$: C, 61.39; H, 7.90; N, 4.77. Found: C, 60.99; H, 7.79; N, 4.67. ^{1}H NMR (d_6-acetone, 250 MHz) δ 6.73 (s, 6H, Ar*H*), 3.82 (d, J = 14.1 Hz, 6H, ArCH_2N), 3.49 (d, J = 14.1, 6H, ArCH_2N), 3.67 (s, 6H, CH_2CO), 3.51 (s, 9H, OCH_3), and 0.24 (s, 27H, Si(CH_3)$_3$). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 172.5, 148.5, 130.4, 130.2, 129.6, 129.4, 129.2, 58.5, 52.5, 20.6, 20.0, 1.1.