Pergamon

Tetrahedron Letters, Vol. 37, No. 23, pp. 4039-4042, 1996

0040-4039/96 $15.00 + 0.00

PII: S0040-4039(96)00756-3

Structures of Bridged Calix[6]arenes Bearing a Bromide Functionality in the Cavity

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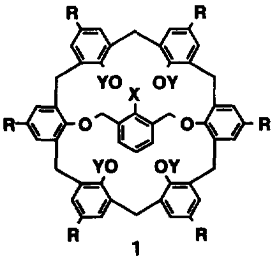
Abstract: The structures of bridged calix[6]arenes **1a** and **1b** were investigated. Whereas **1a** was found to take a structure where the bridging unit lies below the calix[6]arene macroring with a cone conformation, its tetramethyl ether **1b** adopts the 1,2,3-alternate conformation with the central bromide functionality pointing into the cavity, as revealed by X-ray crystallographic analysis.

Calixarenes have been widely utilized as a versatile building block for the construction of elaborately functionalized molecular systems.[1] While the cavities of calixarenes have so far been utilized mostly as a complexing site, they recently attract increasing attention as a new type of reaction environment which regulates the reactivities of an intracavity functional group in a unique fashion. We have been investigating the development of a reaction environment based on the bridged calix[6]arene **1** and previously reported the unique photoreaction of an azide bearing this framework.[2] Very recently, we also reported that the molecular architecture of **1** is quite effective for the stabilization of highly reactive species such as a sulfenic acid.[3] The concave pyridines bearing a framework similar to **1** were reported by Lüning et al.[4] In order to use these compounds as a molecular system with various functions, it is prerequisite for their structural features to be fully clarified. However, there have been only a few reports on the structural behavior of the calix[6]arenes bridged by an aromatic unit.[5] In this communication, we describe the structural features of bridged calix[6]arenes **1a** and **1b** bearing an intracavity bromide functionality investigated by some different techniques.[6]



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	X	Y	R
a	Br	H	*t*-Bu
b	Br	Me	*t*-Bu
c	H	H	*t*-Bu

The 1,4-bridged product **1a** was prepared by the reaction of *p-tert*-butylcalix[6]arene (**2**) with 2-bromo-1,3-bis(bromomethyl) benzene[7] in the presence of KOH in THF-DMF (concentration of **2** was 2.5 mmol/l) in a relatively good yield of 73%. Methylation of **1a** with KH and methyl iodide afforded the tetramethyl ether **1b** in a yield of 55%. The ^{1}H NMR spectra of **1a** ($CDCl_2CDCl_2$) at 0 °C (Figure 1c) showed three singlets (1:1:1 ratio) for *tert*-butyl groups, four pairs of doublets for $ArCH_2Ar$ methylenes (ratio 1:1:2:2), one pair of doublets for $ArCH_2O$ methylenes, and two singlets at δ 8.84 and 9.01 for hydroxyl groups. This spectral pattern indicates the *Cs* symmetry of the molecule and can be most reasonably explained by assuming a structure where the bridging *m*-xylenyl unit lies below the calix[6]arene macroring with a cone conformation in such a way that it forms the bottom of the cone (Scheme 1). The resonances of the hydroxyl protons appearing at fairly low fields are consistent with the strong hydrogen bonding interactions which are expected for the conformation of Scheme 1. This interpretation is corroborated by the molecular mechanics calculation of **1a** using AMBER* force field.[8] Figure 2 shows the lowest energy structure of **1a**, which is in good agreement with the conformation suggested by the NMR analysis. The pinched cone conformation of the calix[6]arene ring of **1a** has a striking resemblance to the molecular structures of the parent calix[6]arene **2** obtained by X-ray analysis[9] and molecular mechanics calculations.[10] The calculation of the bridged calix[6]arene **1c** without a central functionality[8] gave the lowest energy structure quite similar to that of **1a**. These results indicate that the parent calix[6]arene **2** can be bridged by a *m*-xylenyl unit without altering its conformation which is stabilized by a network of the strong hydrogen bondings between the hydroxyl groups. Therefore, a tetrahydroxy compound, such as **1a**, with the bridging *m*-xylenyl unit lying below the cone of the calix[6]arene skeleton is not considered to be suitable for the construction of a reaction environment for the central functionality.

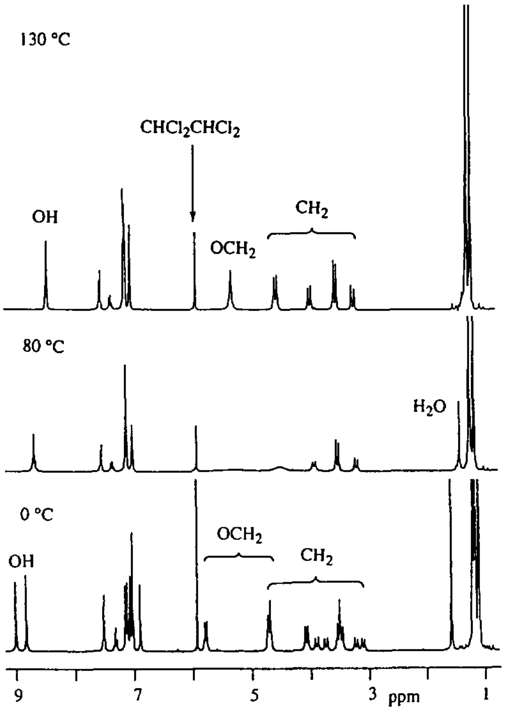
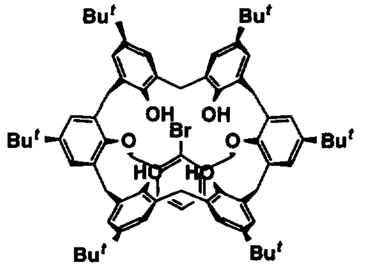


Figure 1. ^{1}H NMR spectra of **1a** in CDCl$_2$CDCl$_2$.

An increase in temperature induces a spectral change shown in Figure 1. The spectral pattern at 130 °C (Figure 1a) shows the complete equivalence of the four non-bridged phenolic rings, which can be explained by assuming that at high temperatures the central aromatic ring undergoes a rapid swinging motion with the bromide functionality passing through the annulus. From the coalescence temperature for the *tert*-butyl and hydroxyl resonances, a $\Delta G^‡$ value of 16 kcal mol^{-1} is calculated for this process.

Scheme 1.



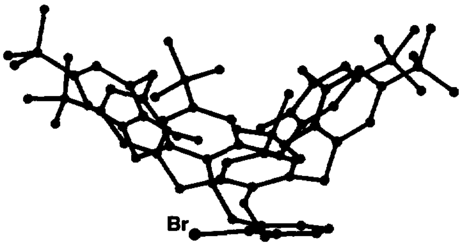


Figure 2. Lowest energy structure of **1a**.

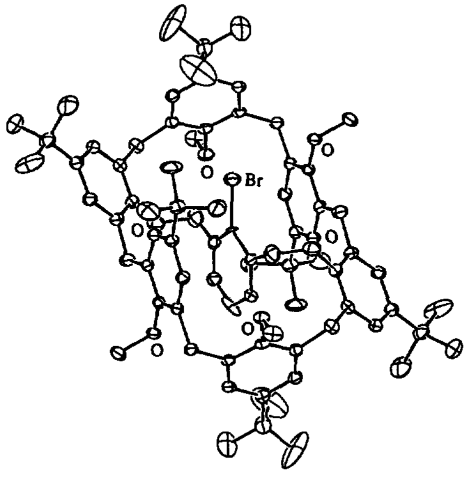


Figure 3. ORTEP drawing of the structure of **1b**.

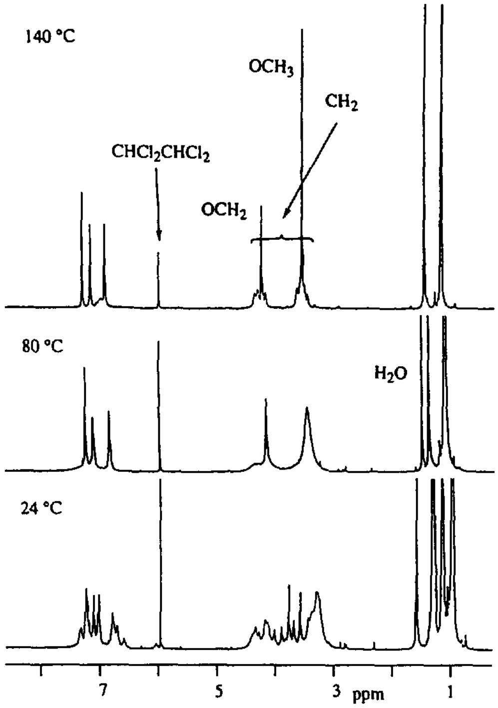


Figure 4. ^1H NMR spectra of **1b** in $CDCl_2CDCl_2$.

The tetramethyl ether **1b** showed a conformational behavior quite different from its precursor **1a**. X-ray crystallographic analysis[11] revealed that **1b** adopts the (**u**,u,d,d,d,u)[12] 1,2,3-alternate conformation (Figure 3) similarly to the bridged calix[6]arene bearing a sulfenic acid functionality which we reported recently.[3] The bromide functionality is directed into the cavity and surrounded by the parent macrocycle. A molecular mechanics calculation of **1b**[8] afforded the lowest energy structure which is in good agreement with that determined by X-ray analysis. The ^1H NMR spectrum of **1b** at room temperature shows complex and broadened signals (Figure 4c). At high temperatures above 120 °C, the signals get resolved and at 140 °C were observed two *tert*-butyl resonances (ratio 2:1), a singlet for OMe protons, two pairs of doublets for $ArCH_2Ar$ methylenes (ratio 1:2), and a singlet for $ArCH_2O$ methylenes (Figure 4a). This spectral pattern indicates that at high temperatures **1b** undergoes the flipping motion of the anisolic rings with the OMe groups passing through the annulus, which results in the equivalence of these rings on the NMR time-scale.

The results described here indicate that, in the case of the bridged calix[6]arenes of type 1, the *O*-alkylated form is better suited for a reaction field of the central functionality. Further investigation is currently in progress on how the functional groups on the upper and lower rims and on the central bridge exert an influence on the conformational behavior of the molecule.

Acknowledgments: This work was supported by Grants-in-aid for Scientific Research (No. 06453062 and 07854035) from the Ministry of Education, Science and Culture, Japan.

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11. Crystallographic data for **1b**·$2C_6H_5CH_3$: FW = 1391.70, *triclinic*, space group $P\bar{1}$, a = 12.495(3) Å, b = 15.238(3) Å, c = 11.535(3) Å, α = 111.68(1) °, β = 100.73(1) °, γ = 90.14(1) °, V = 1992.2(9) Å^3, Z = 1, D_{calcd} = 1.160 g/cm^3, μ = 11.83 cm^{-1}. The intensity data were collected on an Enraf-Nonius CAD-4 diffractometer with CuKα radiation (λ = 1.5418 Å), and the structure was solved by direct methods (*MULTAN 78*) using a program system *UNICS III*. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. The final cycle of full-matrix least-squares refinement was based on 4692 observed reflections [$I > 3.00\sigma(I)$] and 478 variable parameters with R (Rw) = 0.079 (0.091). Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.
12. For the conformational notations, see ref 5a.

(*Received in Japan* 18 *March* 1996; *revised* 15 *April* 1996; *accepted* 17 *April* 1996)