coupled product **15** in only 24% yield, while it was found as shown in Scheme VI that the addition of CTMS and Et_3N into this reaction system brought about the increase in the yield (78%) of **15**.[26] Under the latter reaction conditions, the coupling of dienol ether **16** with **1c** also gave the corresponding coupled product **17** in 70% yield (Scheme VII).

The fact that the acidic hydrolysis of the coupling product **15** or **17** forms the corresponding ketone **20** or aldehyde **21** indicates that the dienol ether **14** or **16** behaves in this coupling reaction as the equivalent for the anion **18** or **19** in which the negative charge is located at the β- or γ-position of the carbonyl group.

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[26] The cathodic solution of DMF (20 mL) containing CTMS (10 mmol), Et_3N (10 mmol), Bu_4NBF_4 (5 mmol), **14** or **16** (2 mmol), and **1c** (10 mmol) was electrochemically reduced under similar conditions described in ref 16.

Octamethylcalix[4]arene

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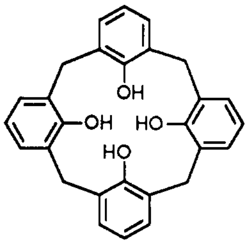
Summary: The sterically crowded octamethylcalix[4]arene (**2**) was synthesized in one step and shown to exist in a relatively flexible "boat" conformation.

Sir: In recent years extensive research has been carried out on macrocyclic hosts capable of including small guest molecules in their cavities.[1] A noteworthy family of these synthetic macrocycles consists of cyclic arrays of *n* phenol moieties linked by methylene groups. These compounds are commonly referred to by the trivial name (coined by Gutsche) "calix[*n*]arenes".[2] *p-tert*-butylcalix[*n*]arenes (*n* = 4, 5, 6, and 8) can be prepared in one step by base-catalyzed condensation of *p-tert*-butylphenols and formaldehyde under different experimental conditions.[3] In addition, several multistep syntheses have been developed for the synthesis of calixarenes.[4]

The conformational behavior of calix[4]arenes is commonly analyzed in terms of four conformations: cone, partial cone, and 1,3- and 1,2-alternate.[2,5] Spectroscopic evidence as well as X-ray diffraction data show that the parent compound (**1**) and its *p*-alkyl derivatives exist in solution as well as in the crystalline state in the cone conformation.[2,6] The energetic preference for the cone conformation is ascribed to the existence of a cyclic intramolecular hydrogen bond.

We report the (serendipitous) one-step preparation of the previously unknown sterically crowded octamethylcalix[4]arene (**2**),[7] a compound which displays novel conformational properties. Our initial goal was to synthesize **3** in which the OH groups are arranged in a *extra*-annular fashion (i.e. located in the outer periphery). However, when a solution of 2,6-dimethyl-4-hydroxybenzyl alcohol[8] (**4**) in nitrobenzene at 90 °C was treated with 0.5 equiv of $AlCl_3$ instead of the expected calixarene **3**,[9] we isolated an isomeric calixarene **2** (with *intra*-annular OH groups) as the sole product in 28% (not optimized) yield.[10] This remarkably simple preparation of **2** is notable since no one-step, synthetically useful cyclization of benzylic alcohols to yield calixarenes with *intra*-annular OH groups has been reported previously.[11] The reaction probably involves the rearrangement of **4** to 2,4-dimethyl-6-hydroxybenzyl alcohol[12] (**5**) prior to the tetramerization. Indeed, when **5** was submitted to the reaction conditions, **2** was obtained in ca. 50% yield.



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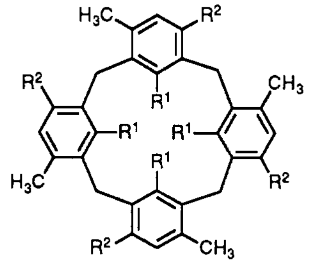
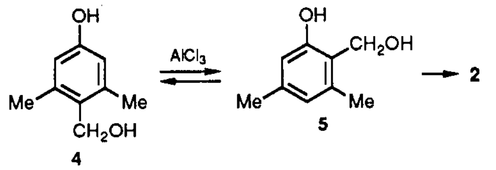


2: R^1 = OH; R^2 = Me
3: R^1 = Me; R^2 = OH



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[2] For reviews, see: Gutsche, C. D. *Acc. Chem. Res.* **1983**, *16*, 161. Gutsche, C. D. *Topics in Current Chemistry*; Springer-Verlag: Berlin, 1984; Vol. 123, p 1. Gutsche, C. D. in ref 1a, p 93. Shinkai, S. *Pure Appl. Chem.* **1986**, *58*, 1523.

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[7] CAS name for **2**: 4,6,10,12,16,18,22,24-octamethylpentacyclo-$[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]$octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23-dodecaene-25,26,27,28-tetrol.

[8] Auwers, K. *Ber.* **1907**, *40*, 2524.

[9] It has been reported that treatment of 2,6-dimethyl-4-methoxybenzyl alcohol with $AlCl_3$ yields the tetramethyl tetraether of **3**: Wu, T.-T.; Speas, J. R. *J. Org. Chem.* **1987**, *52*, 2330.

[10] Preparation of **2**. To a solution of **4** (0.5 g, 0.33 mmol) in 55 mL of $C_6H_5NO_2$ at 90 °C was added 0.277 mg of $AlCl_3$. After the mixture was stirred for 2 h, water was added, and the mixture was stirred at room temperature for 1 h. The phases were separated, and the organic phase was filtered through a sintered-glass funnel (no. 3). The filtrate was washed twice with water, and the organic phase was dried ($MgSO_4$). Evaporation of the solvent under low pressure yielded almost pure **2**. Recrystallization from DMF afforded 170 mg of **2**·DMF (28%). A solvent-free sample could be obtained by sublimation under reduced pressure: mp 330–332 °C; MS (EI, 70 eV) *m/z* 536 (M, 36), 135 ([M − (2,3,5-$Me_3C_6H_2OH$ − H)], B). Anal. Calcd for $C_{36}H_{40}O_4$: C, 80.56; H, 7.51. Found: C, 80.70; H, 7.38.

[11] $TiCl_4$-catalyzed alkylations have been used for the preparation of calixarenes, e.g. by reaction of 2,6-bisbromomethylated phenols with phenols. See for example ref 4b.

[12] Finn, S. R.; Musty, J. W. G. *J. Appl. Chem.* **1951**, *1*, 182.

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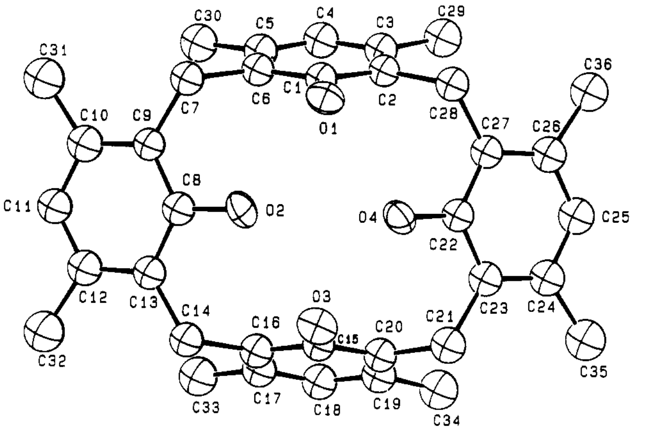

Figure 1. Numbering scheme of the octamethylcalix[4]arene (2). The associated DMF molecule was omitted for clarity.

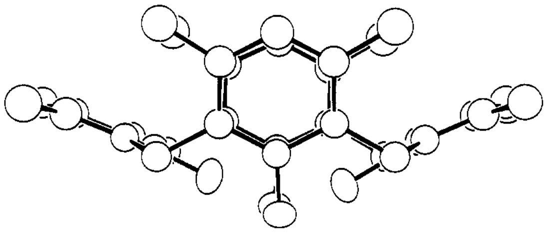

Figure 2. Side view of the octamethylcalix[4]arene (2).

Inspection of CPK molecular models suggests that a symmetric (C_{4v}) cone conformation should be unattainable for 2 due to the steric repulsions between the methyl groups. The models suggest that 2 should adopt a "boat" shapped C_{2v} conformation in which two opposite rings (i.e. in a 1,3-relation) are nearly coplanar to the mean macrocyclic plane whereas the two remaining rings are nearly perpendicular to it. Since this conformation was previously observed for *extra*-annular octahydroxycalix[4]arenes and their derivatives[13] but it is unprecedented for unbridged *intra*-annular ones,[14] we decided to determine the conformation of 2 in the solid state. Slow evaporation of a DMF solution of 2 at room temperature yielded crystals of 2·DMF (1:1) suitable for X-ray analysis. The X-ray structure of a single crystal of 2 was solved and refined by standard least-square procedures in the space group $P\bar{1}$.[15]

Figures 1 and 2 show two views of the conformation of 2 in the crystal (a "boat" conformation). The dihedral angles between the least-squares planes of the aryl groups and the plane defined by C(7), C(14), C(21), and C(28) are 72°, 22°, 69°, and 26°, respectively. One molecule of DMF is hydrogen-bonded to one of the OH groups (O(1)). In contrast with other unbridged calix[4]arenes reported in the literature, the four oxygen atoms are not located on a single plane but in a somewhat distorted tetrahedral arrangement in which two oxygens (O(2) and O(4)) are located inside the molecular cavity. The distances between neighboring oxygen atoms are 2.64 (1) (O(3)–O(4)), 2.71 (1) (O(2)–O(3)), 2.73 (1) (O(1)–O(4)), and 2.77 (1) Å (O(1)–O(2)). Since the conventional van der Waals oxygen radius is 1.4 Å and O···O contact distances of 2.8 Å are extremely rare,[16] these distances seem to indicate hydrogen bonding interactions. The O–O distances of 2 (excluding O(3)–O(4)) are significantly longer than the corresponding distances found for 1 and its *p*-alkyl derivatives. Interestingly, only three protons are available to hydrogen bond the four OH oxygens since the O(1) proton is hydrogen bonded to DMF. It seems possible that the observed structure represents the unresolved average between two structures having heterodirectional cyclic hydrogen bonds (i.e. O(2) → O(3) → O(4) → O(1) and O(4) → O(3) → O(2) → O(1)).

The ^{1}H NMR spectrum (200.13 MHz) of an unsolvated sample of 2 in $CDCl_3$ at room temperature displays single signals for each of the aromatic, methylene, methyl, and OH protons and is in accord with a conformationally mobile species on the NMR time scale.[17] In the same solvent, 1 exists at room temperature in a frozen cone conformation on the NMR time scale.[18] The ^{1}H NMR spectrum of 2 in $CDCl_3/CD_2Cl_2$ displays at 192 K two signals each for the methyls, OH groups, and aromatic protons, whereas the methylene protons appear as a single broad AB quartet, in agreement with a frozen "boat" conformation in solution. A dynamic NMR analysis indicates that the barrier for the ring inversion process is 10.7 kcal mol^{-1}. The increased flexibility of 2 compared to 1 can be tentatively ascribed to its increased ground-state energy as well as to the stronger intramolecular hydrogen bonds in 1 (as evidenced by its shorter O–O distances) which hold the cone conformation.

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Registry No. 2, 123775-99-5; 2·DMF, 123776-00-1; 3, 123776-01-2; 4, 28636-93-3; 5, 67730-49-8.

Supplementary Material Available: Tables of positional parameters, bond lengths, bond angles, and thermal parameters for 2 (9 pages); table of structure factors for 2 (13 pages). Ordering information is given on any current masthead page.

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(13) Erdtman, H.; Hogberg, S.; Abrahamsson, S.; Nilsson, B. *Tetrahedron Lett.* **1968**, 1679. Stevens, K. *Acta Crystallogr.* **1976**, *B32*, 847.

(14) Calix[4]arenes bridged by an alkyl chain at the para position of two opposite phenol rings distort from a "cone" into a "boat" conformation. The shorter the methylene chain, the larger is the distortion. Paulus, E.; Bohmer, V.; Goldmann, H.; Vogt, W. *J. Chem. Soc., Perkin Trans. 2* **1987**, 1609. Goldmann, H.; Vogt, W.; Paulus, E.; Bohmer, V. *J. Am. Chem. Soc.* **1988**, *110*, 6811.

(15) Crystallographic data for 2: $C_{36}H_{40}O_4{\cdot}C_3H_7NO$ $M = 609.8$, triclinic, space group $P\bar{1}$, $a = 9.668$ (3) Å, $b = 18.659$ (5) Å, $c = 9.594$ (3) Å, $\alpha = 102.61$ (8), $\beta = 104.86$ (7), $\gamma = 92.78$ (8)°, $V = 1622.4$ (9) Å^3, $Z = 2$, $\rho_{calc} = 1.25$ g cm^{-3}, μ(Mo Kα) = 0.46. Data were measured on a PW1100/20 Philips Four-Circle computer-controlled diffractometer. Intensities were corrected for Lorentz and polarization effects. All non-hydrogen atoms were found by using the results of the SHELXS-86 direct method analysis. After several cycles of refinements the positions of the hydrogen atoms were calculated and added with a constant isotropic temperature factor of 0.05 Å^2 to the refinement process. R and R_w after refinement were 0.090 and 0.116, respectively.

(16) Murray-Rust, P.; Gluker, J. P. *J. Am. Chem. Soc.* **1984**, *106*, 1018.

(17) ^{1}H NMR spectrum (200.13 MHz, $CDCl_3$, room temperature): δ 2.25 (s, 24 H, CH_3), 3.80 (s, 8 H, CH_2), 6.51 (s, 4 H, Ar-H), 8.19 (s, 4 H, OH). ^{13}C NMR (50.32 MHz, $CDCl_3$, room temperature): δ 20.0, 24.5, 122.6, 125.3, 135.4, 152.5.

(18) Gutsche, C. D.; Bauer, L. J. *J. Am. Chem. Soc.* **1985**, *107*, 6052.