



Properties of a Tetrahomodioxacalix[6]arene Derivative

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Abstract

The synthesis and X-ray crystal structure of a novel tetrahomodioxacalix[6]arene hexamethylester **2** are presented. Preliminary investigations of alkali metal ion complexation showed that **2** is a poor extractant with selectivity for lithium.

Introduction

Calixarenes are macrocyclic molecules readily accessible in large quantities by condensation of formaldehyde with *p*-alkylphenols under alkaline [1–3] or acid [1b] conditions.

Since the first report of Gutsche on their full characterization, much work has been devoted to the study of *O*-derivatives of calixarenes and more particularly to *O*-alkylated calixarenes bearing carbonyl functions [4]. The introduction of ester functions was originally intended to mimic the natural ionophore valinomycin which binds K^+ selectively through its ester carbonyls [4]. In this context, the extraction data of alkali cations with the tetraalkylesters of calix[4]arenes and the hexaalkylesters of calix[6]arene derivatives reveal that the former extract all alkali cations with a distinct preference for Na^+ [5] while the latter show a distinct shift away from Na^+ and K^+ with a maximum affinity for Cs^+ [5, 6]. Upon complexation of K^+ [7, 8] and Cs^+ [9], the hexabutylester of calix[6]arene adopts a regular cone conformation with C_6 symmetry, while the hexaethyl-ester adopts a distorted cone conformation when complexing K^+ and a C_{3v} symmetry when Cs^+ is included in the cavity [10].

Oxacalixarenes [11, 12] are a family of calixarenes in which the methylene bridges are replaced totally or partially by $-CH_2-O-CH_2-$ groups. By analogy with calixarenes, ester derivatives have been prepared by alkylation of oxacalixarenes at the phenol functions, namely a trimethylester

from *p*-*tert*-butyltrihomooxacalix[3]arene [13], and a tetraester from *p*-*tert*-butyltetrahomodioxacalix[4]arene [14] and also from its *p*-phenyl analogue [15].

Very recently one of us has reported the synthesis of a series of homooxacalixarenes larger than those already known [16]. In particular *p*-*tert*-butyltetrahomodioxacalix[6]arene **1** was obtained in quantities large enough to allow extensive investigations. The interest in the molecular structure of **1** is that this molecule has some features of both *p*-*tert*-butyltetrahomodioxacalix[4]arene and *p*-*tert*-butylcalix[6]arene, though with a larger cavity than the latter. In the present short communication we report the synthesis of *p*-*tert*-butyltetrahomodioxacalix[6]arene hexamethylester **2** by *O*-alkylation of *p*-*tert*-butyltetrahomodioxacalix[6]arene **1**. The crystal structure of **2** as a chloroform solvate has been determined and preliminary studies of the complexation of alkali metal picrates are reported.

The preparation of **2** is illustrated in Scheme 1. Under a nitrogen atmosphere, *p*-*tert*-butyltetrahomodioxacalix[6]arene **1** was reacted with 8 equivalents of methyl bromoacetate in the presence of cesium carbonate in refluxing acetonitrile for 38 hours to produce the corresponding hexamethylester **2** in 83% yield [17].

Elemental analyses and FAB(+) MS were in agreement with the proposed formula $C_{86}H_{112}O_{20}$. The 1H -NMR spectrum of **2** in $CDCl_3$ showed one singlet at 3.96 ppm characteristic of *Ar-CH_2-Ar* methylene protons, one singlet at 4.49 ppm for *Ar-CH_2-O* protons, two singlets at 3.06 and 3.63 ppm in a 1 : 2 ratio for the $-O-CH_3$ protons, one AB system

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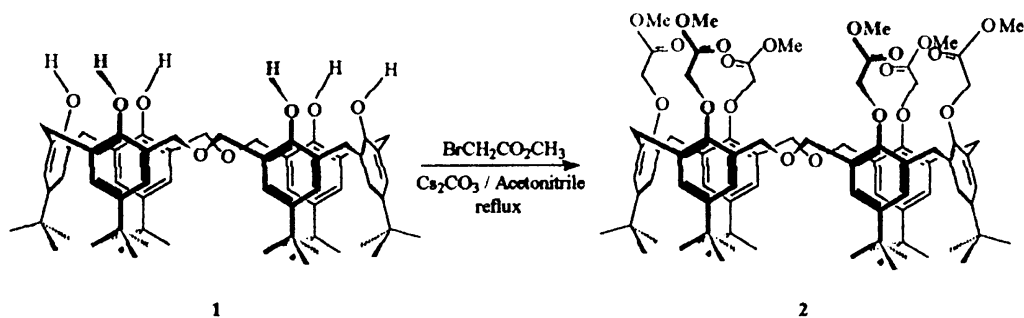
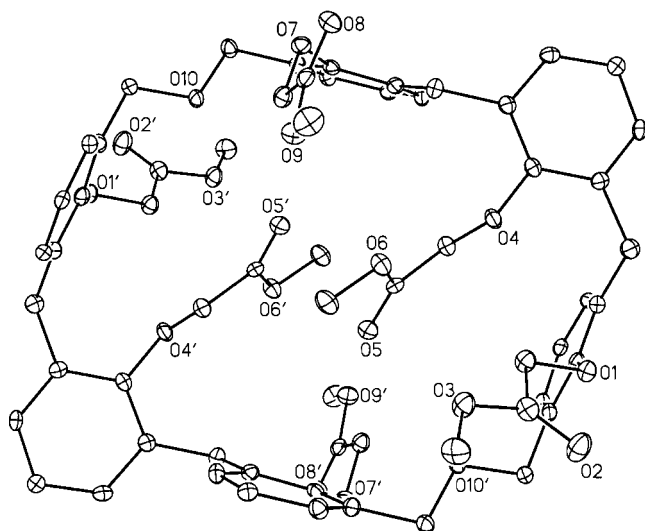
Scheme 1. Preparation of **2**.

Figure 1. View of the molecular structure of **2**. Hydrogen atoms, *tert*-butyl groups and solvent molecules are omitted. Primed atoms are related to unprimed ones by the symmetry centre. Thermal ellipsoids are drawn at the 30% probability level.

for 8 aromatic protons and one singlet for the other 4 aromatic protons [17]. The conformation could be “cone” or “1,2,3-alternate”. Only the cone conformation is represented in Scheme 1.

Crystal structure

2.2 CHCl_3 crystallizes with only half a molecule and one chloroform molecule in the asymmetric unit [18]. The centrosymmetric molecule is represented in Figure 1.

In the case of calix[6]arene derivatives, two extreme conformations are frequently encountered, with more or less distortion: the *pinched cone* with C_{2v} symmetry and the centrosymmetric 1,2,3-*alternate* or *double partial cone* with C_i symmetry. In the case of *p-tert*-butylcalix[6]arene and calix[6]arene, the passage from the first to the second of these two forms has been shown to depend on the disruption of the intramolecular hydrogen bonding cyclic array (as observed in the first form) by solvents possessing hydrogen bonding ability [20] or by partial deprotonation [21]. Two perturbing factors are present in **2** with respect to the *R*-calix[6]arene case: the replacement of two methylene bridges by two $-\text{CH}_2-\text{O}-\text{CH}_2-$ bridges, which confers a greater flexibility to the molecule, and the presence of

six *O*-substituents, which eliminates all intramolecular hydrogen bonds. The resulting conformation is analogous to the 1,2,3-*alternate* one in calix[6]arenes, the two half-cones being separated by the ether bridges. However, this conformation is much distorted, since two diametrically opposed ester substituents are located inside the calixarene cavity, the corresponding aromatic rings being nearly parallel to the mean plane of the molecule. If the mean plane is defined by the eight methylene carbon atoms (notwithstanding a strong rms deviation of 0.53 Å), the dihedral angles corresponding to the three rings of the asymmetric unit are 76.01(9), 19.8(2) and 88.26(7)°. The conformation can also be described, as proposed by Kanamathareddy and Gutsche [22], by the sequence (u,u,o,u,d,do,d) and can thus be described as a flattened 1,2,3-*alternate* form, as observed for various calix[6]arene derivatives [20, 23]. Such a self-inclusion of lower rim substituents has already been observed with similar conformations [23–25]. In various *p-tert*-butylcalix[6]arene derivatives, the cavity has been shown to be occupied by two opposite allyl [23a] or ethoxycarbonylmethyl [23b] groups. In another calix[6]arene derivative, the self-inclusion of three 1,3,5-methoxy substituents has been attributed to weak $\text{CH}\cdots\pi$ interactions, and was shown to result in a reduction of the conformational flexibility [24]. The self-inclusion of one methoxy substituent in a calix[4]arene derivative has been shown to have a significant influence on the conformer energy and may prevent inclusion of a polyhapto-bound metal ion such as Ag(I) [25]. In this case, the $\text{CH}_3\cdots\pi$ interactions were seemingly not at the origin of the self-inclusion. This is also the case in the present compound, since the distances between the included groups and the aromatic rings are larger than 4.1 Å. Although the origin of this self-inclusion is unknown, the hypothesis can be made that dipole-dipole interactions between the two head-to-tail ester groups, with a minimum separation of ~ 2.9 Å, could play some role.

Alkali metal ion complexation

Preliminary complexation studies of hexamethyl ester **2** with alkali metal picrates were realized by means of proton nuclear magnetic resonance spectroscopy. After a period of 2 weeks reaction between solid alkali picrates and a chloroform solution of **2** the ratio of metal to ligand in solution, as estimated by integration of the picrate proton resonance

versus those of the aromatics of **2**, was 1 : 5 for lithium and 1 : 8 for sodium while no picrate signal was observed for potassium, rubidium and cesium. This was indicative of the poor ability of ligand **2** to extract alkali cations and is in contrast with the observation of a selectivity for cesium of the related hexaethylester calix[6]arene [4]. The poor ability of extraction is probably due to a macrocyclic frame too large to fit the size and geometry required for efficient complexation. That lithium is preferred during extraction, although it is the smallest cation, may be explained by the formation of binuclear species if one considers ligand **2** as a ditopic receptor composed of two "homooxacalix[3]" subunits attached by ether linkages. Future work is directed to the use of **2** as a "bi-anchorage" platform for synthesis of ditopic receptors.

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- General:** Mp., capillaries under nitrogen, Büchi 500. TLC plates silica gel 60 F₂₅₄ Merck. ¹H-NMR in CDCl₃, Bruker SY200 (δ in ppm, J in Hz), FAB(+) MS, VG-Analytical ZAB HF. Elemental analyses performed at the Service de Microanalyse of the Institut de Chimie de Strasbourg.
Preparation of 2: *p-tert*-butyltetrahomodioxacalix[6]arene **1** (3.004 g, 2.91 mmol), Cs₂CO₃ (3.930 g, 12.06 mmol) and CH₃CN (270 ml) were stirred for 1 h at room temperature under N₂. Then, BrCH₂CO₂CH₃ (3.724 g, 24.34 mmol) was added. After refluxing for 38 h, the solvents were evaporated to dryness and the residue was dissolved in CH₂Cl₂ and precipitated with CH₃OH to give the hexamethylester derivative **2** (3.514 g, 83%) as a white solid. Mp. 210–211 °C. R_f = 0.61 (95/5 CH₂Cl₂-acetone). ¹H-NMR (200 MHz, CDCl₃) 7.14 (s, 4H, ArH_{meta}), 7.10 (d, J = 2.4 Hz, 4H, ArH_{meta}), 6.97 (d, J = 2.4 Hz, 4H, ArH_{meta}), 4.49 (s, 8H, ArCH₂O), 4.35 (s, 8H, ArOCH₂), 3.96 (s, 8H, ArCH₂Ar), 3.83 (s, 4H, ArOCH₂), 3.63 (s, 12H, OCH₃), 3.06 (s, 6H, OCH₃), 1.25 (s, 18H, C(CH₃)₃), 1.12 (s, 36H, C(CH₃)₃). FAB(+) MS, m/z 1465.7 (M⁺). Anal. Calcd. for C₈₆H₁₁₂O₂₀·3CH₃OH: C, 68.44; H, 8.00. Found.: C, 68.11; H, 7.99%.
- Crystal data for 2.2CHCl₃:** C₈₈H₁₁₄Cl₆O₂₀, M = 1704.49, triclinic, space group $P1\bar{1}$, a = 12.4479(13), b = 14.5943(14), c = 15.1464(9) Å, α = 113.208(5), β = 95.168(6), γ = 114.877(4)°, V = 2183.6(3) Å³, Z = 1, D_c = 1.296 g cm⁻³, μ = 0.266 mm⁻¹, F(000) = 904. Data collected at 110(2) K on a Nonius Kappa-CCD area-detector diffractometer with Mo- $K\alpha$ radiation. No absorption correction. Structure solved by direct methods. Hydrogen atom of the chloroform molecule found on the Fourier-difference map and introduced as a riding atom. All other hydrogen atoms included at calculated positions as riding atoms. All non-hydrogen atoms refined anisotropically. Refinement by full-matrix least-squares on F^2 . R_1 = 0.065 (wR_2 = 0.118). All calculations have been done with SHELXTL [19].
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