



Synthesis and Structure of a Bis-calix[4]arene with an *o*-Xylene Linkage

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Abstract

The reaction of *p*-*tert*-butyl calix[4]arene **1** with α, α' -dibromo-*o*-xylene in basic conditions leads to two new compounds. One of them is a bis-calix[4]arene, whose crystal structure has been determined.

Introduction

The burgeoning family of multi-, and more particularly double-, calixarenes, is one of the consequences of the fruitful development of calixarene chemistry during the last 50 years [1]. Double calix[4]arenes have been designed as a synthetic challenge as well as to provide the chemists with molecular receptors presenting special properties due to their molecular ditopic structure. For example, amide-bridged bis-calix[4]arenes connected via the narrow rim formed dinuclear $\text{Eu}^{3+}/\text{Eu}^{3+}$ and $\text{Eu}^{3+}/\text{Nd}^{3+}$ complexes displaying $\text{Eu}^{3+} \rightarrow \text{Nd}^{3+}$ energy transfer [2]. Similarly, a doubly-bridged bis-calix[4]arene connected via the narrow rim with two metal binding sites shows metal oscillation between the two binding sites [3].

In the present communication we describe the preparation of calixarenes **2** and **3**. The bis-calixarene structure of **2** has been ascertained by single-crystal X-ray diffraction.

Experimental

Synthesis

All reagents were commercial and used without further purification. *p*-*tert*-Butyl calix[4]arene **1** was prepared according to the literature [4]. The melting points were taken on a Büchi apparatus in a capillary sealed under nitrogen. Silica columns were prepared with Kieselgel SiO₂ 60 (40–63 μm) Merck (1.11567.1000). ¹H-NMR spectra were recorded at 200 MHz on a Bruker SY200 spectrometer. The solvents are specified in the experimental section. Chemical shifts are given as δ values in ppm relative to TMS ($\delta = 0.00$). The FAB-MS spectra were obtained on a VG-Analytical ZAB HF apparatus. Elemental analyses were determined

at the Centre de Microanalyse of the Institut de Chimie de Strasbourg.

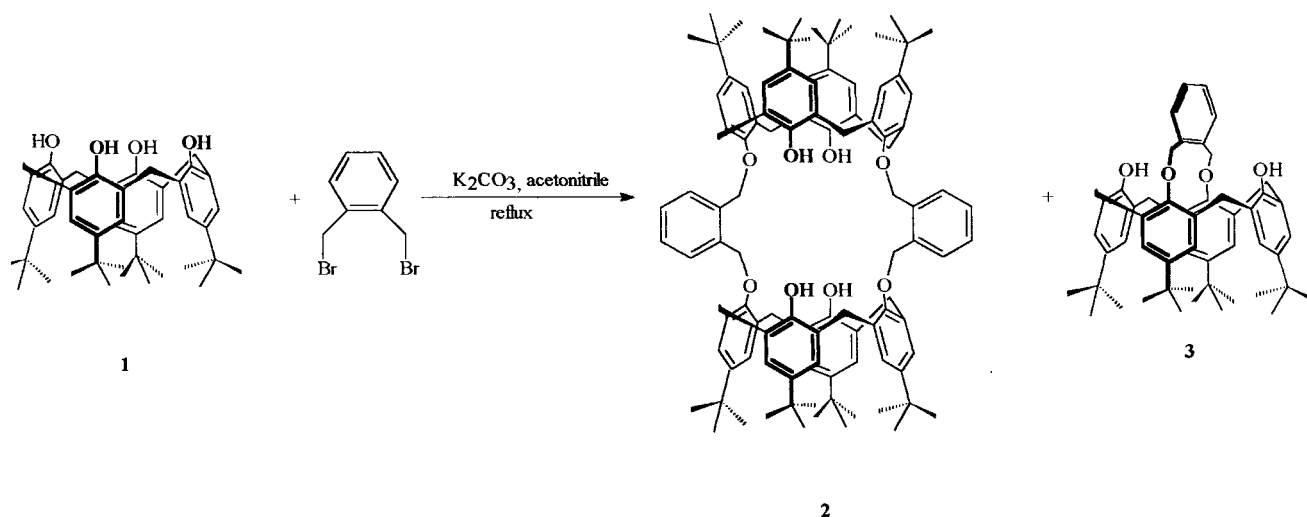
Preparation of **2** and **3**

A sample of 1.29 g (2.00 mmol) of *p*-*tert*-butylcalix[4]arene **1** and 0.415 g (3.00 mmol) of K₂CO₃ was stirred for 30 minutes at room temperature in 150 mL of acetonitrile. Then 0.528 g (2.00 mmol) of α, α' -dibromo-*o*-xylene was added. The mixture was refluxed for 4 days. The solvents were removed to dryness and the residue dissolved in dichloromethane. Water was added and the mixture was acidified with concentrated hydrochloric acid to pH \sim 2. The organic layer was dried over Na₂SO₄, filtered and concentrated to give a residue which was purified by column chromatography (hexane/dichloromethane: 60/40) to afford 0.422 g (28%) of **2** and 0.030 g (2%) of **3**:

2 m.p. > 260 °C; ¹H-NMR (CDCl₃): δ = 8.57 (s, 4H, OH), 7.62–7.58 (m, 4H, xylene H), 7.25–7.20 (m, 4H, xylene H), 7.00 (s, 8H, ArH), 6.90 (s, 8H, ArH), 5.77 (s, 8H, O—CH₂-xylene), 4.81 (d, 8H, $J = 12.9$ Hz, Ar—CH₂—Ar), 3.20 (d, 8H, $J = 12.9$ Hz, Ar—CH₂—Ar), 1.20 (s, 36H, C(CH₃)₃), 1.15 (s, 36H, C(CH₃)₃); FAB-MS m/z 1502.12 (MH⁺); Anal. Calcd for C₁₀₄H₁₂₄O₈: C, 83.16; H, 8.32. Found: C, 83.27; H, 8.24.

3 m.p. > 260 °C (dec.); ¹H-NMR (CDCl₃): δ = 8.49–8.45 (m, 2H, xylene H), 7.60–7.56 (m, 2H, xylene H), 7.34 (s, 2H, OH), 7.02 (s, 4H, ArH), 6.78 (s, 4H, ArH), 5.07 (s, 4H, O—CH₂-xylene), 3.26 (d, 4H, $J = 13.1$ Hz, Ar—CH₂—Ar), 2.88 (d, 4H, $J = 13.1$ Hz, Ar—CH₂—Ar), 1.28 (s, 18H, C(CH₃)₃), 0.93 (s, 18H, C(CH₃)₃); FAB-MS m/z 751.4 (MH⁺); Anal. Calcd for C₅₂H₆₂O₄: C, 83.16; H, 8.32. Found: C, 83.11; H, 8.49.

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Scheme 1. Preparation of **2** and **3**.

Crystallography

Crystals of (**2**) suitable for X-ray analysis were obtained by the technique of vapor diffusion of methanol into a chloroform solution.

The data were collected at 100(2) K on a Nonius Kappa-CCD area detector diffractometer [5] using graphite-monochromated Mo K α radiation (0.71073 Å). The crystal was introduced in a Lindemann glass capillary with a protecting ‘Paratone’ oil (Exxon Chemical Ltd.) coating. The unit cell parameters were determined from the reflections collected on ten frames and were then refined on all data. The data were processed with DENZO-SMN [6]. The structure was solved by direct methods with SHELXS-97 [7] and subsequent Fourier-difference synthesis and refined by full-matrix least-squares on F^2 with SHELXL-97 [8]. Three *tert*-butyl groups were found disordered as well as two out of the four methanol molecules, one over two sites sharing the same carbon atom, and the other over four positions arranged in a square. All non-hydrogen atoms were refined with anisotropic displacement parameters, except the disordered ones, those of one methanol molecule and those of the chlorine atoms of the solvent chloroform molecule (the latter behaving badly upon refinement). All hydrogen atoms were introduced at calculated positions, except in the disordered parts and those bound to oxygen atoms (which were not found on the Fourier-difference map). All hydrogen atoms were treated as riding atoms with an isotropic displacement parameter equal to 1.2 (CH, CH₂) or 1.5 (CH₃) times that of the parent atom. The very low quality of the crystals and the disorder present in several parts of the structure resulted in a rather low-precision structure determination. The geometry of the calixarene is however known without ambiguity. Refinement of 1140 parameters on 16724 independent reflections out of 35854 measured reflections ($R_{\text{int}} = 0.089$) led to $R_1 = 0.122$, $wR_2 = 0.289$, $s = 1.029$, $\Delta\rho_{\text{max}} = 0.956 \text{ e \AA}^{-3}$. The molecular plot was drawn with SHELXTL [9]. All calculations were performed on a Silicon Graphics R5000 workstation. Crystal data: C₁₀₉H₁₄₁Cl₃O₁₂, $M = 1749.57$, triclinic, space group $P - 1$, $a = 14.499(1)$,

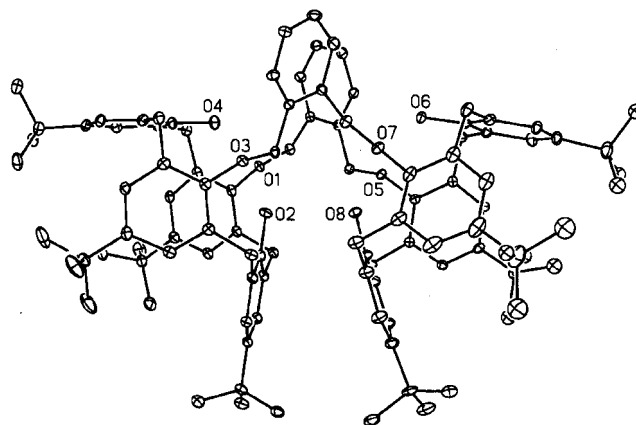


Figure 1. View of the bis-calix[4]arene moiety in compound **4**. Hydrogen atoms and solvent molecules omitted for clarity. Only one position of the disordered *tert*-butyl groups is represented.

$b = 18.390(2)$, $c = 19.050(2) \text{ \AA}$, $\alpha = 77.530(4)$, $\beta = 79.227(4)$, $\gamma = 87.104(4)^\circ$, $V = 4871.8(8) \text{ \AA}^3$, $Z = 2$, $D_c = 1.193 \text{ g cm}^{-3}$, $\mu = 0.155 \text{ mm}^{-1}$, $F(000) = 1884$.

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication No. CCDC-171075. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: <http://www.ccdc.cam.ac.uk>).

Discussion

As indicated in Scheme 1, *p*-*tert*-butyl calix[4]arene **1** was refluxed in acetonitrile for 30 min with 1 equivalent of α, α' -dibromo-*o*-xylene in the presence of K_2CO_3 in excess. After work up (see experimental), the residue was chromatographed on silica column with a 60/40 mixture of hexane/dichloromethane as eluent to give calixarene derivatives **2** and **3** in 28% and 2% yields, respectively. The cone conformation of the calixarenic moieties of **2** and **3** were

deduced from their $^1\text{H-NMR}$ spectra. Characteristic AB systems were observed at 3.20 ppm and 4.81 ppm (with $J = 12.9$ Hz) and 2.88 ppm and 3.26 ppm (with $J = 13.1$ Hz) for **2** and **3** respectively. The 1,3-alkylation of the calix[4]arene units was shown by the presence of two singlets at 1.15 ppm and 1.20 ppm for the *p-tert*-butyl groups in **2** and 0.93 ppm and 1.28 ppm for the ones of **3**. From the integration ratios the degree of condensation in **2** and **3** could not be deduced. The [2 + 2] structure of **2** as compared to the [1 + 1] of **3** was deduced from the FAB-MS spectra giving $m/z = 1502.12$ (MH^+) for **2** and $m/z = 751.4$ (MH^+) for **3**.

The dimeric structure of **2** was confirmed by the determination of the crystal structure of the adduct (BisC4)-4MeOH· CHCl_3 , **4**, which crystallizes in the triclinic space group $P-1$, with one complete molecule in the repeat unit (Figure 1). The two calix[4]arene units are not positioned in a face-to-face quasi-parallel fashion, as observed in the closely related compound in which the *o*-xylene links of **4** are replaced by *m*-benzoic acid units [10]. The dihedral angle between the mean planes defined by the four methylene carbon atoms of each calixarene in **4** is $72.2(1)^\circ$, which results in two aromatic rings, one in each calixarene unit (bound to O2 and O8), to be nearly parallel [dihedral angle $25.5(4)^\circ$], but the large distance between the centroids of those two rings (4.552 \AA) precludes any strong interaction. As a consequence, **4** does not possess a pseudo binary axis parallel to the main axis of the calixarenes, but one bisecting the two mean planes. A similar conformation has been found in a double *p-tert*-butylcalix[4]arene bridged by two ether chains $\text{O}—[(\text{CH}_2)_2—\text{O}]_3—$ [11], with a dihedral angle between the two mean planes of 84.34° . The two aromatic rings of the links in **4** are nearly parallel to each other [dihedral angle $15.1(4)^\circ$]. They are not facing each other, but are shifted one with respect to the other along their mean plane and the distance between their centroids is 4.946 \AA . The conformation of the calixarenes is the usual cone one, with

dihedral angles between the aromatic rings and the mean plane of $70.2(2)$, $43.3(2)$, $71.5(2)$, $56.1(1)^\circ$ for the first unit and $63.2(1)$, $61.7(2)$, $66.2(2)$, $54.4(2)^\circ$ for the second one. These angles span a wider range in the first case, in which two diametrically opposed rings are more “vertical” than the other ones, whereas the second calixarene is a more regular cone. The unsubstituted phenolic groups are likely involved in hydrogen bonds with the neighbouring oxygen atoms, with $\text{O} \cdots \text{O}$ distances in the range $2.710(6)$ – $3.027(6) \text{ \AA}$. One of them (O4) is also possibly linked to a chlorine atom of the chloroform molecule [$\text{O} \cdots \text{Cl}$ $3.040(6) \text{ \AA}$]. A methanol molecule is included in each cavity (one of them disordered), as frequently observed.

Future work is directed toward: (a) using the structure of **2** for creating higher molecular structures; (b) carrying out metal cation complexation studies with **2** and **3** in order to find new selectivities.

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