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Crystal and solution structures of 25,27-diethoxycarbonylmethoxy-26,28-dimethoxy-*t*-butylcalix[4]arene

Peter J. Duggan,* Sarah L. Sheahan and Melanie L. Szydzik

Department of Chemistry, Monash University, Clayton, Melbourne, Victoria, 3800, Australia

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Abstract

The crystal and solution structures of diethoxycarbonylmethoxy-26,28-dimethoxy-*t*-butylcalix[4]arene (**2**) have been determined. This diester (**2**) adopts the less common partial cone conformation in the solid state, but in solution, **2** is fluxional at room temperature. Variable temperature ^1H NMR spectroscopy shows that at 250 K in CDCl_3 , **2** exists in a cone and a partial cone in a ratio of 43:57. © 2000 Elsevier Science Ltd. All rights reserved.

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The highly ordered structure of calixarenes makes them extremely useful in the study of molecular recognition and supramolecular processes and as a result, they have found a number of practical applications.¹ By far the most commonly described calixarene is *p*-*tert*-butylcalix[4]arene (**1**). Calix[4]arenes are known to exist in a range of conformations including the cone, the partial cone, the 1,2-alternate and the 1,3-alternate structures.¹ It is critical that the conformation adopted by a given calixarene is known, as this determines its recognition properties. The diester (**2**) in particular, has seen application in ion selective electrodes,² and as a direct precursor to sensitising lanthanide chelators.³ The diacid (**3**), derived from **2**, is a selective sodium extractant,⁴ and has recently been used as a component in sugar permeable plasticised liquid membranes.⁵ Despite the obvious importance of **2**, no structural studies of this compound have been described. A major reason for this is that the NMR spectra of **2** at room temperature show considerable broadening. Herein, we report the results of an X-ray analysis of crystalline **2** and a variable temperature NMR study of its solution structures.

Fig. 1 shows the solid state molecular structure that we have determined for **2**. No entrapped solvent could be detected within the crystal structure. Examination of the packing diagram (not shown) revealed that the crystal is devoid of any significant intermolecular bonding interactions such as pi–pi stacking or hydrogen bonding. The diester **2** clearly crystallises in the less common¹ partial cone conformation, with three aromatic rings being within 3.5° of being parallel, and of these, the ring bearing the methoxy group is inverted relative to those bearing the ester groups. The two aromatic rings bearing the methoxy groups sit at an angle of 67.3° to each other. The tilted ring appears to adopt this conformation so

* Corresponding author. Fax: +61-3-9905 4597; e-mail: peter.duggan@sci.monash.edu.au (P. J. Duggan)

as to place the methoxy group within the vacant calixarene cavity. The overall structure shows close similarity to the partial cones of the tetraacetate (**4**)^{6a} and 25,27-di(allyloxy)-5,17-di-*t*-butyl-26,28-dimethoxycalix[4]arene^{6b} reported by Andreotti et al. and by Harrowfield, Mocerino and co-workers, respectively.

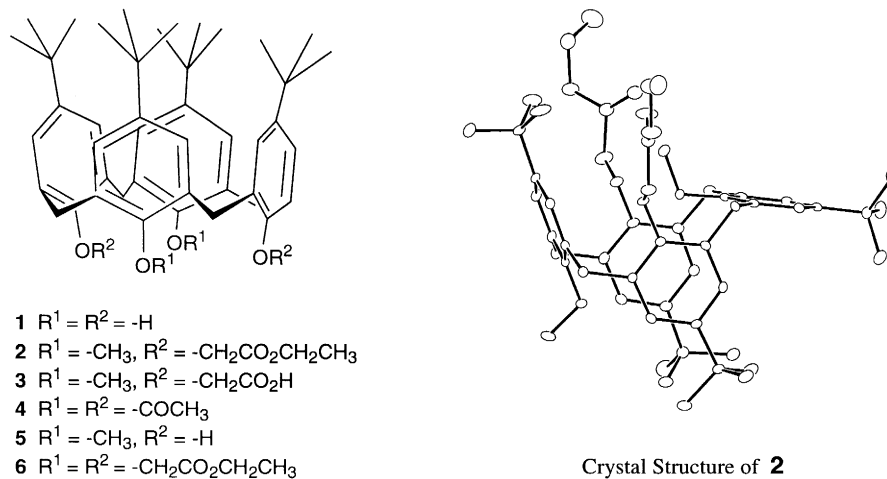


Fig. 1.

Although it is very useful to know the solid state structure adopted by macrocyclic ligands such as **2**, the application of such compounds is almost invariably in solution. Consequently, we have undertaken a study of the solution structure of **2**. The room temperature ¹H NMR spectra of **2** in CDCl₃, *d*₆-DMSO and *d*₆-acetone show considerable broadening and none were useful in the determination of the solution conformation of **2**. We therefore conducted variable temperature NMR experiments on a sample of the crystal used for X-ray analysis, recording spectra in CDCl₃ from 330 K down to 250 K and in *d*₆-DMSO from 330 K up to 410 K (Fig. 2). As the temperature was lowered, the proton resonances become sharper and better resolved, with the sharpest spectrum observed at 250 K. Closely related compounds (**1**, **3**, **5**) show high symmetry in solution, yielding room temperature ¹H NMR spectra characteristic of calix[4]arenes in the cone conformation. By contrast, the spectrum of **2** at 250 K is considerably more complicated. This spectrum is consistent with the presence of a combination of predominantly two solution forms of **2**, one of which (43%) is the cone conformation, and the other (57%) is a partial cone closely related to the solid state conformation. The spectrum at 250 K was fully assigned (see Experimental) after examination of a COSY spectrum recorded at the same temperature. The peaks assigned to the benzylic protons of the partial cone are of particular note. These occur as two pairs of doublets at δ 3.73 and 3.88 ppm, and δ 3.12 and 4.64 ppm. The former resonances correspond to the methylene protons between the aromatics which are almost orthogonal, whereas the latter correspond to the methylene protons that are flanked by the aromatic rings that are parallel.⁷

Fig. 2 also shows the effect on the ¹H NMR spectrum of **2** when it is heated in *d*₆-DMSO.⁸ A fully resolved spectrum was obtained once 410 K was reached. This spectrum most likely results from an averaging of the spectra of a number of rapidly equilibrating forms, yielding a spectrum reminiscent of a cone. When the sample was brought back to room temperature, an identical spectrum to that observed prior to heating was obtained, indicating the reversibility of the process.

In summary, we have shown that the calix[4]arene diester (**2**) crystallises in a partial cone conformation similar of that found for two related calix[4]arenes.⁶ In solution, **2** shows significant structural mobility at room temperature, but at 250 K in CDCl₃, **2** exists in two main conformations, the cone and apparently the same partial cone as that observed in the solid state, in a ratio of 43:57. At 410 K in *d*₆-DMSO, a fully

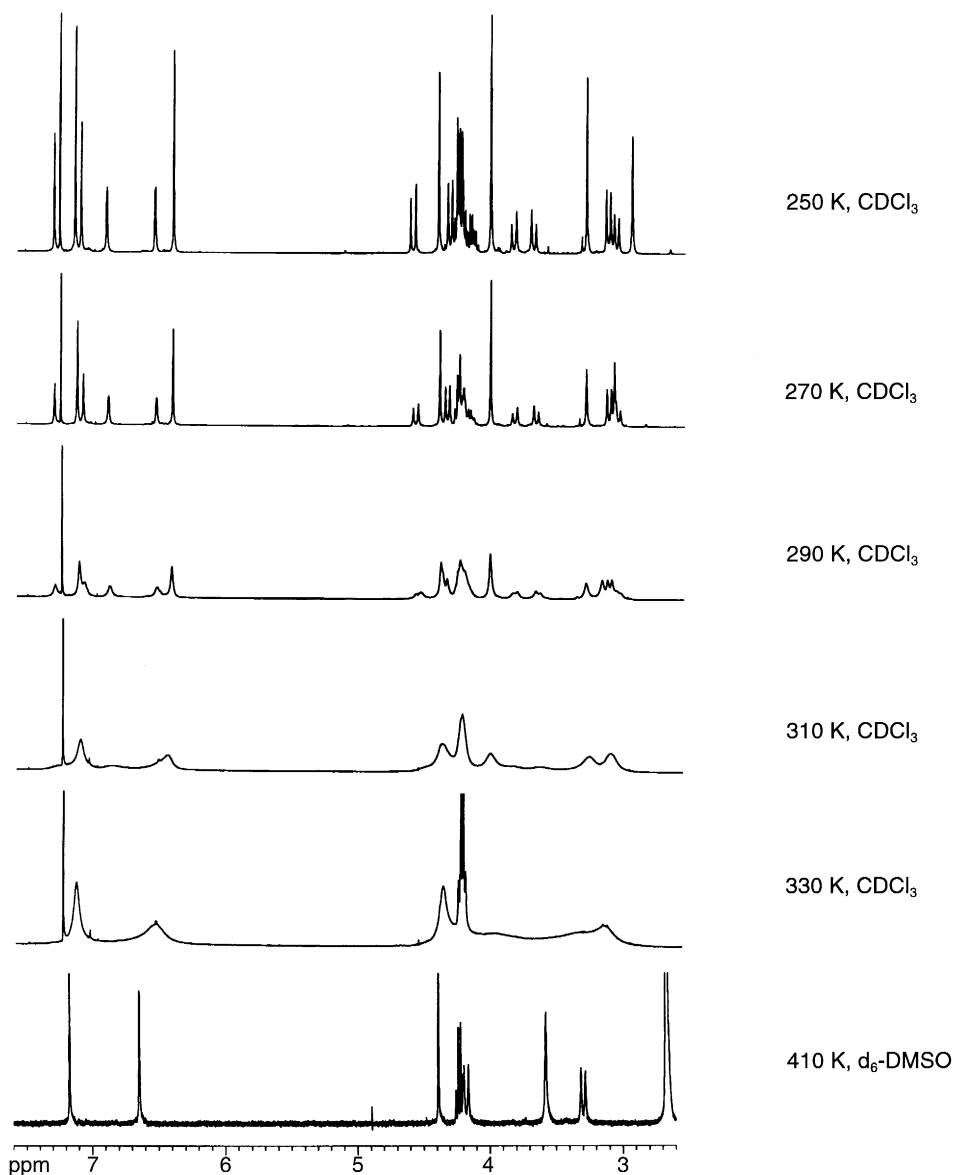


Fig. 2. Partial variable temperature 400 MHz ^1H NMR spectra recorded for **2** in CDCl_3 and d_6 -DMSO

averaged spectrum reminiscent of a calix[4]arene cone spectrum is obtained. The high proportion of the partial cone seen in solution for **2** explains why this ligand was observed to be a 'defective' ionophore in ion selective electrodes, where greater sodium selectivity occurs when the oxygen ligands are all able to coordinate to the metal ion.²

1. Experimental

5,11,17,23-Tetra-*tert*-butyl-25,27-diethoxycarbonylmethoxy-26,28-dimethoxycalix[4]arene (**2**). The diester (**2**) was prepared in 82% yield from the dimethyl ether (**5**)⁹ following a procedure similar to that described by Sabbatini, and Ungaro.³ The crude product partially crystallised as colourless prismatic

columns. The residual oil was crystallised from DCM/methanol yielding a mixture of fine white and larger colourless rhombic crystals. Both sets of colourless crystals were subjected to X-ray analysis and were found to have identical unit cell dimensions, m.p. 158–159°C, (lit.,⁴ 213–214°C); $\nu_{\max}/\text{cm}^{-1}$ (KBr) 2961s, 1763s, 1602m, 1480s; δ_{H} (Bruker DRX 400 MHz; CDCl_3 ; Me_4Si ; 250 K) 0.80 (7.74 H, s, *t*-Bu cone), 1.04 (10.26 H, s, *t*-Bu par. cone), 1.20–1.40 (24.0H, m, *t*-Bu cone and par. cone, $-\text{CH}_2\text{CH}_3$ cone and par. cone), 3.00 (1.71H, s, $-\text{OCH}_3$ par. cone), 3.12 (1.14H, d, *J* 14.2, Ar- CH_2 -Ar par. cone), 3.18 (1.72H, d, *J* 12.6, Ar- CH_2 -Ar cone), 3.34 (1.71H, s, $-\text{OCH}_3$ par. cone), 3.73 (1.14H, d, *J* 14.0, Ar- CH_2 -Ar par. cone), 3.88 (1.14H, d, *J* 14.0, Ar- CH_2 -Ar par. cone), 4.06 (2.58H, s, $-\text{OCH}_3$ cone), 4.14–4.33 (6.28H, m, $-\text{CO}_2\text{CH}_2$ - cone and par. cone, $-\text{CH}_2\text{CO}_2$ - par. cone), 4.36 (1.72H, d, *J* 12.6, Ar- CH_2 -Ar cone), 4.45 (1.72 H, m, $-\text{CH}_2\text{CO}_2$ - cone), 4.64 (1.14H, d, *J* 14.2, Ar- CH_2 -Ar par. cone), 6.43 (1.71 H, s, ArH cone), 6.57 (1.14 H, d, *J* 2.3, ArH par. cone), 6.93(1.14 H, d, *J* 2.3, ArH par. cone), 7.11 (1.14 H, s, ArH par. cone), 7.16 (1.71 H, s, ArH cone), 7.32 (1.14 H, s, ArH par. cone); *m/z* (ESI⁺, MeOH:DCM, 3:1): 871.52 ([M+Na]⁺), 887.49 ([M+K]⁺); HRMS (Bruker BioApex 47e FTMS, ESI⁺): found; *m/z* 871.5101, $\text{C}_{54}\text{H}_{72}\text{O}_8$ Na requires 871.5125.

Crystal structure determination of **2**. A crystal of **2** was mounted on a glass fibre, before being cooled in the cold gas stream of the diffractometer (Nonius Kappa CCD area detector with graphite monochromated Mo-K α radiation). Crystal data: $\text{C}_{54}\text{H}_{72}\text{O}_8$, *M*=849.16, prismatic, *a*=9.7735(2), *b*=21.8545(3), *c*=23.4285(5), β =91.791(1)°, *U*=5001.8(1) Å³, *T*=123±1 K, space group *P* 2₁/n (no. 14), *Z*=4, $\mu(\text{Mo-K}\alpha)$ =0.074mm⁻¹, 58015 reflections measured, 14540 unique (*R*_{int}=0.086). The final *wR* (*F*²) was 0.046 (observed data).

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