



Solvation of Calix[4]arene-bis-crown-6 Molecules^{*,**}

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Abstract

Single crystal X-ray diffraction analyses of calix[4]arene-bis-crown-6 (**1**) and calix[4]arene-bis-benzocrown-6·1,2-dichloroethane (**2**) are reported. These structures offer an opportunity to study the conformation of calix[4]arene-bis-crown-6 molecules in the absence of solvent, and when very weakly solvated. These structures exhibit different conformations of the crown ring, and limited flexibility of the calix[4]arene, but do not show solvent or crown inclusion in the calix[4]arene cavity. Comparisons to similar structures are made, and the implications for cesium binding are discussed.

Introduction

Understanding the nature of ion solvation is important to understanding the relative inclination for a specific ion to cross an aqueous/non-aqueous phase barrier. More directly stated, the higher the energy of hydration for an ion, the more difficult it will be to move this ion into non-polar media where solvation of an ion is ordinarily much weaker. Generally, this trend follows the charge/size ratio: the larger this ratio, the more difficult it will be to extract the ion from aqueous solution [1, 2]. We have called this monotonic trend “bias”, and are currently engaged in research directed towards altering this predetermined selectivity [3–5].

On the other side of the phase barrier, solvation of the host molecule and its complexes plays a similar, but often neglected role. The host molecule is solvated in the organic media (diluent), and this solvation is, at least partially, disrupted by the arrival and coordination of the guest species. This disruption represents an energy penalty that may be more or less compensated by subsequent solvation of the host-guest complex. What if the host molecule contained a volume of space that was inaccessible to solvent molecules, but would allow guest species into this space? Likely, this would enhance the extraction strength towards those guests, as there would be no desolvation required in the protected cavity [6].

Calix[4]arene-bis-crown-6 host molecules (Figure 1) have recently demonstrated extraordinary extraction strength and selectivity towards the cesium ion [7–13]. Much of this work has focussed on the dramatic selectivity of these molecules, but their high extraction strength is equally impressive when compared to simple crown ether molecules [13]. Part of the high extraction strength towards cesium may be due to the difficulty of solvating the interior faces of the calix[4]arene with simple solvent molecules. As has been structurally demonstrated, cesium binding to the crown cavity also establishes cation- π interactions within the interior of the calix[4]arene, in effect, filling a vacuum by “solvating” this relatively inaccessible area of the host molecule [12, 14–17].

In the absence of a guest species, the structures of most crown ether molecules collapse in on themselves to fill the void created [18]. Thinking that this could be a way that calix[4]arene-crown-6 molecules might be able to self-solvate the interior of the calix[4]arene cavity, we sought to determine crystal structures of uncomplexed calix[4]arene-bis-crown-6 molecules. The results are reported herein.

Experimental

X-ray data collection, structure determination, and refinement

General

The calix-crown ether compounds were obtained from a commercial source (Acros), and used as supplied. The structures were determined by single-crystal X-ray diffraction methods. Intensity data for both compounds were collected on a Bruker AXS Smart 1000 X-ray diffractometer equipped

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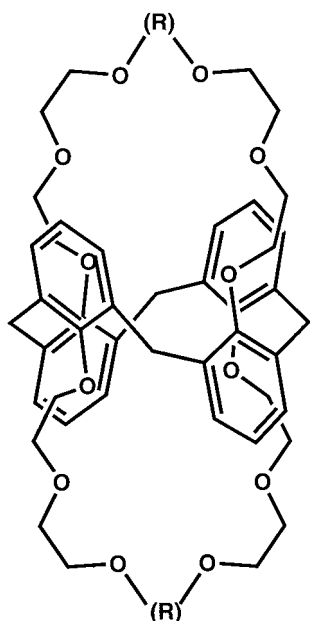


Figure 1. Schematic representation of calix[4]arene-bis-crown-6 molecules. R = ethylene (1), 1,2-phenylene (2), 2,3-naphthylene [11].

with a CCD area detector, graphite-monochromated Mo radiation ($K_{\alpha} = 0.71073 \text{ \AA}$) and an upgraded Nicolet LT-2 low temperature device. Suitable crystals were coated with paratone oil (Exxon) and mounted on a glass fiber. Data collection nominally covered over a hemisphere of reciprocal space by combining four sets of exposures. Each exposure set consisted of 606 individual frames. The first three sets had a different ϕ angle (0, 120 and 240°) with each exposure covering 0.3° in ω . The fourth set was a ϕ -scan with each exposure covering 0.3° in ϕ . Unit cell refinement and data reduction were performed by SAINT [19], and an empirical absorption correction applied (SADABS [20]). The structures were solved by direct methods, and expanded using Fourier techniques (SHELXTL [21]). All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were placed in calculated positions, refined using a riding model, and given an isotropic displacement parameter equal to 1.2 times the equivalent isotropic displacement parameter of the atom to which they were attached. Full-matrix least-squares refinement against $|F|^2$ of the quantity $\sum w(F_o^2 - F_c^2)^2$ was used to adjust the refined parameters. Final geometric analysis was performed by PLATON [22]. A summary of parameters associated with the structure determinations is given in Table 1.

Calix[4]arene-bis-crown-6 (1)

X-ray quality crystals were obtained by recrystallization from ethyl acetate. Determination of the absolute structure proved inconclusive, as the Flack parameter [23] refined to a value of 0.9(8).

Calix[4]arene-bis-benzocrown-6-1,2-dichloroethane (2)

Single crystals of **2** were obtained from slow evaporation of a 1,2-dichloroethane (1,2-DCE) solution. The 1,2-DCE molecule is disordered, and was modeled over two sites (57:43). Refinement of the 1,2-DCE atoms was restrained so that

Table 1. Crystal data and summary of intensity data collection and structure refinement

Compound	1	2
Formula	C ₄₈ H ₆₀ O ₁₂	C ₅₈ H ₆₄ Cl ₂ O ₁₂
Formula Weight	829.0	1024.0
Temp., °C	-100	-110
Max. crystal dimensions (mm ³)	0.39 × 0.31 × 0.22	0.38 × 0.21 × 0.15
Crystal System	Tetragonal	Orthorhombic
Space Group	<i>P</i> 4 ₃ 2 ₁ 2	<i>P</i> 2 ₁ 2 ₁ 2 ₁
<i>a</i> (Å)	14.7405(5)	11.026(4)
<i>b</i> (Å)		17.718(6)
<i>c</i> (Å)	39.5876(18)	26.544(9)
<i>V</i> (Å ³)	8601.7(6)	5186(3)
<i>Z</i>	8	4
<i>D</i> _{calc} (g cm ⁻³)	1.28	1.31
μ (cm ⁻¹)	0.91	1.89
θ range (deg)	1.4 ≤ θ ≤ 28.3	1.3 ≤ θ ≤ 24.7
Reflections measured	94330	51244
Independent reflections	10654 [<i>R</i> _{int} = 0.059]	8832 [<i>R</i> _{int} = 0.093]
<i>R</i>	0.042	0.050
<i>R</i> _w	0.119	0.112
GOF	0.98	1.10
Largest feature in final diff. map (e ⁻ Å ⁻³)	0.33	0.79

chemically equivalent bond distances and angles are similar. Additionally, the thermal parameters for all disordered atoms were restrained to be similar to their nearest neighbor, or any atom within 0.7 Å. Despite these restraints, two of the disordered atoms (Cl2B and C58A) exhibited unusual elongation, likely a result of further, unresolved disorder. The highest peak of residual electron density (0.8 e/Å³) is located near one of the crown rings, and may suggest conformational disorder of that crown ring, but is not found in a chemically reasonable location (near C45). The second highest peak is <0.5 e/Å³, and is located near the disordered 1,2-DCE molecule. The absolute structure was correctly determined, as indicated by the Flack parameter [23] of -0.02(10).

Results and discussion

The structures of calix[4]arene-bis-crown-6 (**1**) and calix[4]arene-bis-benzocrown-6-1,2-dichloroethane (**2**) are depicted in Figures 2 and 3 respectively. In general, the bond distances and angles observed in these two structures are consistent with expected values [24]. For example, the C_{sp³}—O distances for **1** average 1.418 Å while ranging from 1.394(3) to 1.445(2) Å. A complete listing of bond distances and angles are available as part of the supplementary data.

The structure of **2** is a bit unusual in that it exhibits no C—H...O hydrogen bonds between the 1,2-dichloroethane (1,2-DCE) solvent molecule and the crown oxygen atoms. All previous structures of calix[4]arene-bis-crown-6 molecules crystallized from polar solvents are inclusion complexes, i.e., the electropositive portion of the solvent clearly

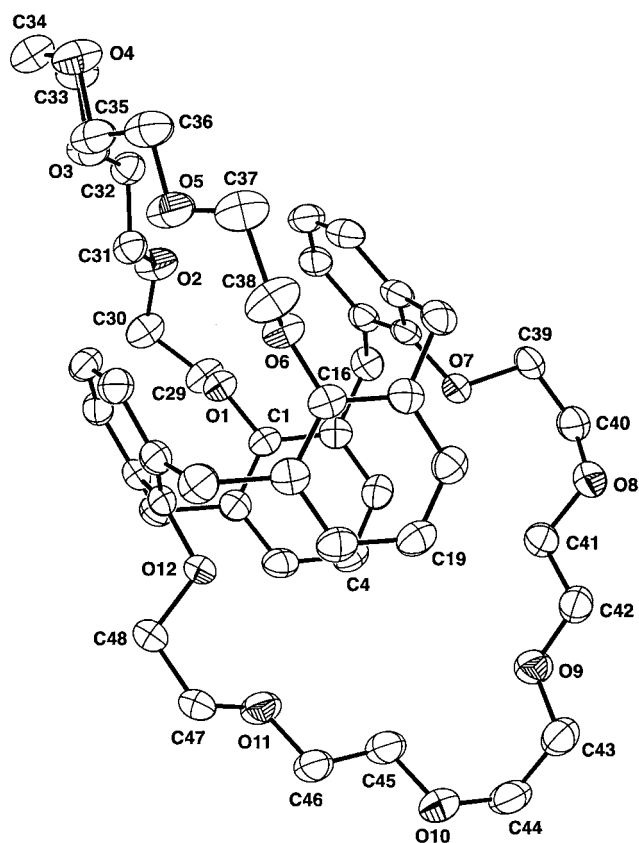


Figure 2. ORTEP representation with 50% probability ellipsoids of calix[4]arene-bis-crown-6 (**1**). Unlabelled atoms are carbon. Hydrogen atoms are omitted for clarity.

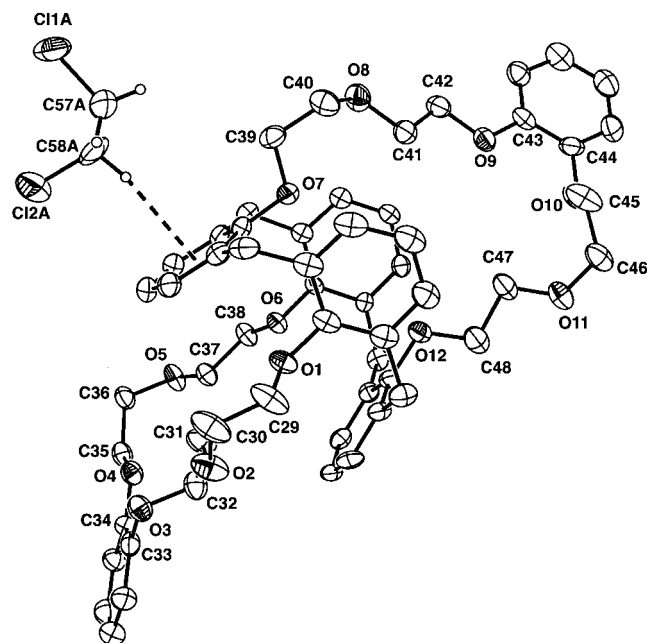


Figure 3. ORTEP representation with 50% probability ellipsoids of calix[4]arene-bis-benzocrown-6,1,2-dichloroethane (**2**). Unlabelled atoms are carbon. Hydrogen atoms, except those on the 1,2-dichloroethane molecule, and the minor disorder component are omitted for clarity.

Table 2. Hydrogen-bond distances (Å) and angles (deg)^a

	D—H...A	H _⊥ ^b	H...A	D...A	∠D—H...A
1	C35—H35A...O3		2.39	3.047(3)	123
1	C36—H36B...O2 ⁱ		2.43	3.178(3)	132
1	C45—H45B...O9		2.44	3.032(3)	118
1	C46—H46A...O8 ⁱⁱ		2.37	3.208(3)	142
2	C31—H31A...O1		2.44	3.046(6)	119
2	C32—H32A...O4		2.40	2.999(5)	118
2	C45—H45A...O9		2.42	3.005(6)	117
2	C58A—H58B...Cg2 ^c	2.62	2.65	3.628(17)	169

^aNo esd's are given for some values because the positional parameters of H atoms were not refined. Symmetry codes: (i) $\frac{3}{2} - x, \frac{1}{2} + y, \frac{7}{4} - z$; (ii) $\frac{1}{2} + x, \frac{3}{2} - y, \frac{5}{4} - z$.

^bH_⊥ is the perpendicular distance between the H atom and the arene plane.

^cCg2 refers to the calculated centroid of the calix arene ring C8-13.

interacts with the crown ring [12]. One of the hydrogen atoms (H57B) on 1,2-DCE makes a close contact with one of the calixarene rings, as illustrated in Figure 3. This contact is close enough to be considered a C—H... π hydrogen bond and demonstrates solvation of the exterior of the calix[4]arene by 1,2-DCE instead of the crown cavity. It also suggests that 1,2-DCE is unable to compete with the intramolecular C—H...O interactions of the collapsed crown ring. The metrical parameters for this interaction are presented in Table 2.

These structures are similar to the only other published structure of a non-complexed calix[4]arene-bis-crown-6 molecule: calix[4]arene-bis-naphthocrown-6-toluene [11]. In all three structures, the crown cavity is partially collapsed in on itself. While this is typically observed for large uncomplexed crown-ether molecules [18], the extent of collapse is much less pronounced in these structures, presumably due to the rigidity enforced by the calix[4]arene platform. By closing in on itself, the crown allows some of its slightly electropositive H atoms to come within contact distance of some of its oxygen atoms. Those interactions, as well as intermolecular C—H...O hydrogen bonds, with the shortest distances and reasonable directionality, are listed in Table 2. These interactions, while weak [25], undoubtedly influence the observed conformation of the crown ether portion of the molecule.

The greatest conformational variability between the two structures presented here is observed in the crown ether segments. The relative arrangement of these rings can be determined by examination of their torsion angles (Table 3) [18, 26]. The two crown portions in **1** exhibit the same conformation, albeit inverted ($g^+ \leftrightarrow g^-$), while the crown fragments for **2** have two distinct conformations. Even ignoring the two near zero torsion angles imposed by the crown-benzo groups in **2**, its two crown conformations are different from that observed in **1**. None of the three conformations seen here match the two observed for the previously published calix[4]arene-bis-naphthocrown-6-toluene [11], giving a total of five distinct crown conformations for uncomplexed calix[4]arene-biscrown-6 molecules, suggesting that several low-energy conformations are possible for

Table 3. Selected torsion angles (deg)

	1	2
O(1)–C(29)–C(30)–O(2)	64.5(2)	69.5(6)
C(29)–C(30)–O(2)–C(31)	–97.7(2)	–85.4(6)
C(30)–O(2)–C(31)–C(32)	–164.27(17)	–174.3(4)
O(2)–C(31)–C(32)–O(3)	170.25(17)	78.6(5)
C(31)–C(32)–O(3)–C(33)	–177.15(18)	173.1(4)
C(32)–O(3)–C(33)–C(34)	–178.31(19)	–72.3(5)
O(3)–C(33)–C(34)–O(4)	77.3(3)	2.7(6)
C(33)–C(34)–O(4)–C(35)	–77.0(3)	–174.4(3)
C(34)–O(4)–C(35)–C(36)	175.80(18)	172.7(3)
O(4)–C(35)–C(36)–O(5)	–177.69(17)	86.3(4)
C(35)–C(36)–O(5)–C(37)	165.16(19)	–81.3(5)
C(36)–O(5)–C(37)–C(38)	–171.03(18)	–158.1(3)
O(5)–C(37)–C(38)–O(6)	55.6(3)	171.2(3)
O(7)–C(39)–C(40)–O(8)	–65.3(2)	69.3(5)
C(39)–C(40)–O(8)–C(41)	96.9(2)	–102.7(5)
C(40)–O(8)–C(41)–C(42)	166.50(17)	–162.5(4)
O(8)–C(41)–C(42)–O(9)	–168.87(16)	–178.0(3)
C(41)–C(42)–O(9)–C(43)	178.60(18)	–167.8(3)
C(42)–O(9)–C(43)–C(44)	179.26(19)	170.2(4)
O(9)–C(43)–C(44)–O(10)	–79.1(2)	6.5(6)
C(43)–C(44)–O(10)–C(45)	75.3(3)	–73.3(6)
C(44)–O(10)–C(45)–C(46)	178.48(19)	–172.3(4)
O(10)–C(45)–C(46)–O(11)	177.81(17)	–52.9(6)
C(45)–C(46)–O(11)–C(47)	–159.12(19)	–56.9(5)
C(46)–O(11)–C(47)–C(48)	171.70(18)	–158.9(4)
O(11)–C(47)–C(48)–O(12)	–56.7(3)	–179.3(3)
Cl(1A)–C(57A)–C(58A)–Cl(2A)		55(3)
Cl(1B)–C(57B)–C(58B)–Cl(2B)		52(4)

these sorts of molecules. None of these five crown conformations match the two conformations that are observed in several structures of calix[4]arene-biscrown-6-type molecules binding either alkali metal ions or polar solvents. The binding conformations in these host–guest complexes always exhibit *gauche* O–C–C–O angles, and *anti* C–O–C–C angles [12, 17]. This suggests that some conformational reorganization of the ligand is required for binding.

The conformation of the calix[4]arene portion of these molecules has significantly less flexibility, mostly because the dual crown substitution locks it in the 1,3-alternate conformation [27]. The primary perturbation observed is in the interarene angle between opposing benzo groups. That is to say that each benzo group of the calix[4]arene fragment can pivot about its two C_{arene}–CH₂ bonds. These interarene angles are 26.6(2)° and 25.1(2)° for **2** which are similar to those observed (17.6–30.9°) in calix[4]arene-bis-crown-6 complexes of alkali metal ions or polar solvents [12]. In contrast, the interarene angles observed for **1** are –12.4(1)° and –12.5(1)°, where the negative sign indicates that the arene rings have tilted such that the carbon atoms *para* to the phenolic group (e.g., C4 and C19) are closer to each other than those *ipso* (e.g., C1 and C16). It is interesting to consider that substitution of the crown ethylene group farthest

from the calix[4]arene with a benzo group might have such a dramatic effect on the calix conformation.

While the crown portions of **1** and **2** are collapsed inward, the interior of the calix[4]arene cavity remains empty. This void is relatively small; the distances between the centroids of opposing arene groups vary from 5.118(1) to 5.710(2) Å in the structures reported here. As might be expected from the way these arene groups pivot, this distance correlates roughly with the interarene angle. These distances clearly indicate that there is insufficient room for solvent inclusion, inhibiting the solvation of the interior faces of the arene rings, even by such small solvent molecules such as 1,2-dichloroethane, toluene, acetonitrile, and nitromethane, which are all observed well outside of the calix[4]arene cavity in **2** and previously reported structures [11, 16, 28]. Additionally, the rings are too far apart to “ π -stack” with each other through the calix cavity, preventing one final possible method of self-solvation. The only known structures demonstrating bonding interactions to the interior of the calix[4]arene are those binding alkali metal ions, which can form cation- π bonds to the interior arene faces [12]. This suggests that at least part of the unusually strong extraction of cesium by calix[4]arene-bis-crown-6 molecules is due to cesium’s ability to “solvate” the interior of the calix[4]arene without having to pay for it by desolvating the cavity prior to coordination. This line of reasoning is further supported by a recent paper that notes that cesium extraction strength is significantly diminished when one crown fragment is removed [29], allowing significant freedom of movement (and presumably greater access for solvation) of two of the four calix[4]arene rings.

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