Synthesis and X-Ray Molecular Structures of *p-tert*-Butylcalix[4]arenes with Diamide Bridges Spanning the 1,3-(Distal) Positions on the Lower Rim

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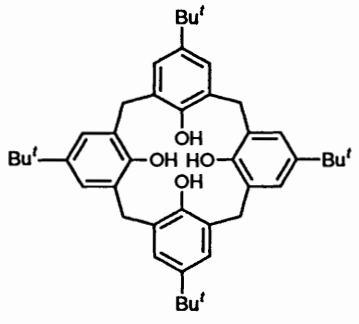
Reaction of a 1,3-diacid dichloride **1d** of *p-tert*-butylcalix[4]arene with various aliphatic diamines including diaza-15-crown-5 and diaza-18-crown-6 yields calixarenes capped by diamide bridges, in yields of 19–95%. The tendency for capping is so pronounced with ethylenediamine that cyclic diamide **2a** is formed even in the presence of an excess of diamine. Crystals of the ethylenediamine adduct **2a** and of the *N,N'*-dimethylethylenediamine adduct **2c** were studied by X-ray diffraction. Crystals of adduct **2a** are monoclinic, space group *C*2/*c*, $a = 36.140(4)$, $b = 11.879(3)$, $c = 25.801(6)$ Å, $\beta = 114.66(2)°$ with $R = 0.077$ for 3044 observed reflections. Crystals of adduct **2c** are triclinic, space group *P*1, $a = 10.272(2)$, $b = 12.474(3)$, $c = 19.351(4)$ Å, $\alpha = 93.799(18)$, $\beta = 95.524(15)$, $\gamma = 91.584(18)°$ with $R = 0.076$ for 2317 observed reflections. While adduct **2a** includes a molecule of dichloromethane in its hydrophobic cavity, the distortion of the cone conformation in adduct **2c** is too severe to allow the inclusion of a guest. This distorted chiral conformation of adduct **2c** (C_2 symmetry) is also stable in solution at room temperature.

Calixarenes are readily amenable to chemical modification at the phenolic hydroxy groups, leading to molecules with selective host–guest properties.[1] In particular, the easy accessibility of *p-tert*-butylcalix[4]arene[2] has made this member of the series increasingly popular as a building block or platform for assembling more elaborate structures with ligating side-arms or podands. Several tetra- and di-substituted calix[4]arenes have been synthesized, some of which are now well established as selective receptors for metal cations.[3–6]

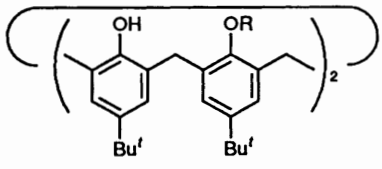
More elaborate structures are now beginning to emerge, including molecules with two or even three calixarene subunits. Recent examples include two calixarenes joined by a single bridge,[7] the singly bridged calixcrowns [poly(oxyethylene) bridge],[8–10] calixspherands (*m*-teranisyl bridge),[11] and double and triple calixarenes with metallocene (ferrocene) bridges.[12] Use of various conformationally constrained spacers such as phthaloyl dichloride or biphenyl-4,4'-disulfonyl dichloride led to the formation of 1,2-bridged single calixarenes and bridged triple calixarenes,[13,14] respectively. The two most recent examples of double calixarenes use glycol chains to provide the links. In one, two calix[4]arenes in the cone conformation are linked by three chains on the lower rim.[15] The second is more complex, having two calixcrowns in the 1,3-alternate conformation connected by two glycol bridges.[16]

The reaction to produce all of these examples is that between the parent *p-tert*-butylcalix[4]arene and an activated bifunctional reagent such as a diacid dichloride, an oligoethylene glycol ditosyl ester or a bis-bromomethylated teranisyl system. Different calixarene conformations are possible from this approach since *p-tert*-butylcalix[4]arene is conformationally mobile and may react so as to lead to more than one conformationally stable product.[16]

We have developed an alternative strategy for the synthesis of larger calixarene structures. Rather than use the parent calix[4]arene with four free phenolic groups, we have taken the easily prepared *syn*-1,3-diacid dichloride of *p-tert*-butylcalix[4]arene **1d** and combined it with various bifunctional



1a



	R
1b	CH_2CO_2Et
1c	CH_2CO_2H
1d	CH_2COCl
1e	$CH_2CONHCH_2CH_2NH_2$
1f	CH_2CO_2Me
1g	CH_2CN

amines to form diamides. In this way we can restrict the possible products to those containing 1,3-*syn*-bridged calixarene substructures. Although we expected to obtain doubly bridged double calixarenes by this approach, we were aware also of the possibility of producing bridged single calixarenes or triple calixarenes or mixtures of all three. A recently published similar strategy[17] involving reaction of 1,3-diesters of calix[4]arene with bifunctional amines led exclusively to singly bridged calixarenes, which for convenience in this paper we shall call capped calixarenes.

Table 1 Yields, m.p.s and ^{1}H NMR data for lower rim-capped calixarenes **2a–2j**

Compound	Yield (%)	M.p. (°C)[a]	^{1}H NMR spectral data (δ) Bu^t	$ArCH_2Ar$	OCH_2	ArH	OH	NH
2a	95	270–290 (d)	1.14, 1.23	3.46, 4.14	4.51	7.05	8.3	8.57
2b	74	194–200	1.12, 1.23	3.46, 4.09	4.52	7.02, 7.06	8.37	8.89
2c	21	308–320 (d)	0.866, 1.29	2.64–6.08 6 doublets		6.54 7.1	8.61,	
2d	52	300 (d)	1.06, 1.21	2.80–6.20[b]		6.85–7.07 4 doublets	8.09	
2e	34	215 (d)	1.19 (18 H), 1.07 (9 H), 1.04 (9 H)	3.10–5.49[b]		6.73–7.07	8.62, 8.58	
2f	19	278–280	1.01 (18 H), 1.24 (9 H), 1.26 (9 H)	3.05–5.70[b]		6.61–7.07	7.46, 8.02	
2g	32	275–276	0.85, 1.30	3.35, 4.13	4.48	6.69, 7.1	6.4	8.30
2h	22	242–244	0.84, 1.32	3.34, 4.17	4.46	6.63, 7.1	5.96	8.31
2i	35	235–236	0.88, 1.30	3.36, 4.22	4.51	6.69, 6.09	6.31	8.31
2j	31	208–213	0.94, 1.26	3.36, 4.26	4.53	6.78, 7.05	7.13	8.44

[a] (d) = with decomposition. [b] Peaks cannot be assigned due to a complex pattern for the bridge protons.

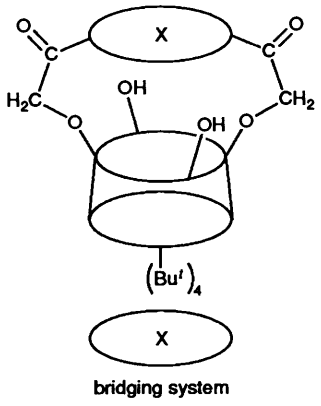
Results and Discussion

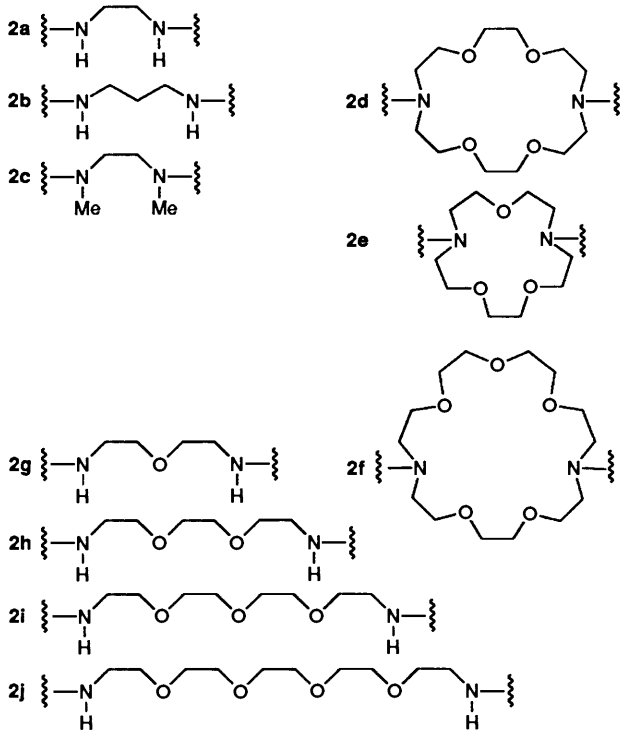
Diacid dichloride **1d** was prepared by a published procedure which involves conversion of *p-tert*-butylcalix[4]arene **1a** into the 1,3-diester **1b**, hydrolysis of the latter to diacid **1c** followed by exposure to thionyl chloride.[18] A standard procedure adopted for all cyclisation reactions involved the simultaneous addition, *via* a perfusor injector, of a solution of diacid dichloride **1d** (2 mmol) in benzene and of a solution of diamine (2 mmol) in benzene during 5 h to a stirred solution of triethylamine (4.4 mmol) in benzene at room temperature. With the exception of the ethylenediamine adduct **2a**, which was formed in very high yield and required little purification, the products were isolated and purified by flash chromatography. The diamines used and the products isolated are summarised in Table 1. Mass spectrometric analysis showed that capped single calixarenes were the predominant, if not the exclusive, products in all cases. Double or larger calixarenes were not isolated, although their formation in small amounts, which seemed probable, cannot be ruled out. We can say, however, that compound **2a**, which previously had been identified as a double calixarene on the basis of a small peak in the mass spectrum,[14] is indeed a capped single calixarene whose structure has now been confirmed by X-ray diffraction analysis. A deliberate effort was made to form the bridged double calixarene *via* the diamide diamine **1e** through use of a large excess of ethylenediamine in two different modes: (a) with the diacid dichloride **1d** and (b) with the dimethyl diester **1f** in 50 : 50 toluene–methanol. In both cases use of a 10-fold excess of diamine did not prevent the capping reaction, compound **2a** being produced in > 90% yield, while no doubly substituted calixarene **1e** was found.

The ^{1}H NMR spectra of compounds **2a**, **b** and **g–j** could be assigned completely and are fully consistent with capped structures all in the cone conformation. Compounds **2a** and **2h** were identical with those obtained by the 1,3-diester reaction with difunctional amines.[17] The general spectral features are: two singlets for the *tert*-butyl protons and two singlets for the aromatic protons; two doublets for the methylene protons, $ArCH_2Ar$ (indicating the equivalence of all four methylene groups); a singlet each for the $-OCH_2CO$-protons and OH protons; a broad triplet for the NH protons; and usually a sharply defined multiplet for the methylene moieties of the bridge. Interestingly, the signals for the aromatic protons of adduct **2a** coincide, forming a singlet at δ 7.05. All ^{1}H NMR chemical shifts are summarised in Table 1.

Although compounds **2a** and **2c** differ by only two methyl groups, this difference has a profound effect on their molecular conformations, which is evident from the ^{1}H NMR data. One pair of doublets is the expected pattern for the H_A and H_B protons in the $ArCH_2Ar$ moiety of a symmetrical 1,3-*syn*-disubstituted calix[4]arene (C_{2v} symmetry). In contrast, the H_A and H_B protons in **2c** appear in a pattern of four doublets and the OCH_2 protons appear as two doublets rather than the usual singlet. Furthermore, the aromatic protons exhibit three signals, a split singlet (2H + 2 H) and a singlet (4 H). This information suggests that compound **2c** has four different types of aromatic protons and, though less symmetrical than the C_{2v} symmetry shown by adduct **2a**, it does possess elements of symmetry and should be chiral. In summary, the ^{1}H NMR data strongly suggest that adduct **2c** is a very rigid molecule with a conformationally immobile bridge. Further ^{1}H NMR studies using Pirkle's reagent revealed a clear doubling up of most of the signals, the most prominent being the H_A, H_B and $-OCH_2CO$ protons. This result further indicates that compound **2c** is chiral in solution.

X-Ray diffraction analysis was used to probe the solid-state conformations of adducts **2a** and **2c**. Calixarene **2a** adopts a relatively open distorted cone conformation in the solid state (Fig. 1) and this molecule also has approximate (non-crystallographic) two-fold symmetry. The major conformation-determining features in this molecule are the presence of (a) two intramolecular N–H···O hydrogen bonds between the diamide NH groups and the proximal phenolic OH groups [N(4)···O(B) 3.34(1) Å and N(7)···O(D) 3.07(1) Å] and (b) two intramolecular O–H···O hydrogen bonds between the phenolic oxygens and the proximal ethereal oxygens [O(B)···O(C) 2.70(1) Å and O(D)···O(A) 2.71 Å]. The conformation of adduct **2a** is defined by the angles which the aromatic rings make with the plane of the four CH_2 moieties which link them, *viz.* 115.9(2)° (A), 130.9(2)° (B), 109.9(2)° (C) and 129.9(2)° (D). Two opposite rings (A and C) are at an angle





of 45.8(2)° to each other, while phenolic rings B and D are close to being normal to one another [interplanar angle 80.8(2)°], all rings being tilted so that their *tert*-butyl groups are pitched away from the calix cavity. This conformation leads to O · · · O separations of 4.47(1) Å between the ethereal oxygens O(A) and O(C) and 3.50(1) Å between the phenolic oxygens O(B) and O(D). The conformation adopted by adduct **2a** creates a cavity which is large enough to accommodate a solvent molecule and this is what we observe. A dichloromethane molecule is encapsulated in the calixarene cavity as shown in Fig. 2 [with intermolecular contacts Cl(1) · · · {C(1) to C(6)} in the range 3.51(2)–3.88(2) Å and Cl(2) · · · {C(9A), C(9B) C(4B)} in the range 3.89(2)–3.99(2) Å]. Another dichloromethane molecule of solvation is present in the lattice near the carbonyl oxygen O(3) [O(3) · · · Cl 3.10(2) Å].

Calixarene **2c** adopts a distorted cone conformation in the solid state (Fig. 3) and has approximate (non-crystallographic) two-fold symmetry. The major conformation-determining features in this molecule are the presence of two intramolecular O–H · · · · O hydrogen bonds between the phenolic OH groups and the proximal carbonyl oxygens of the diamide function [O(B) · · · O(3) 2.70(1) Å and O(D) · · · O(11) 2.68(1) Å]. The conformation of adduct **2c** is defined by the angles which the

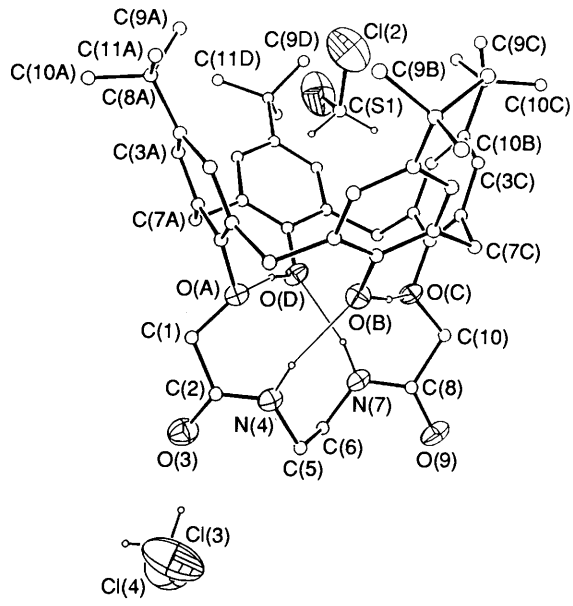


Fig. 1 A view of compound **2a** showing the hydrogen-bonding pattern, the general conformation with the dichloromethane molecules of solvation, and our numbering scheme. For clarity, H-atoms are omitted (except those involved in hydrogen bonding), C-atoms are shown as small spheres of an arbitrary size, and the Cl-, N- and O-atoms are shown as thermal ellipsoids drawn at the 35% probability level.

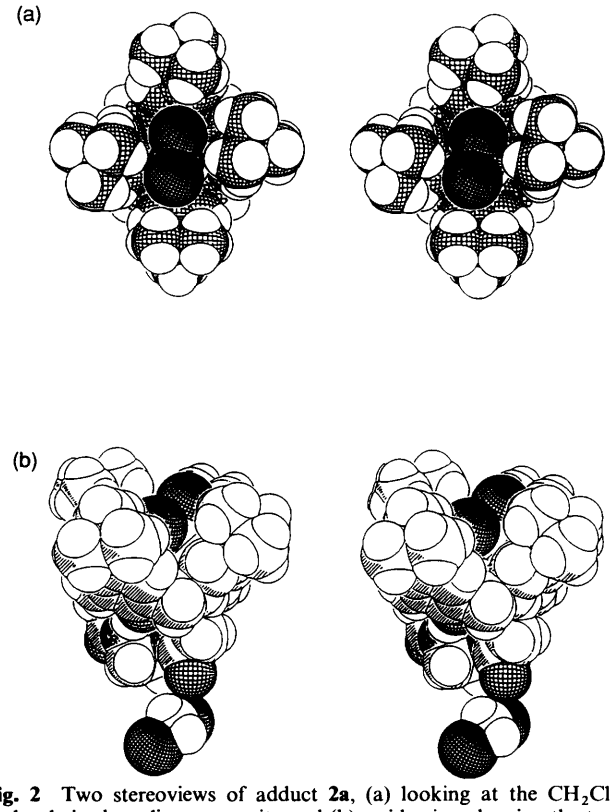


Fig. 2 Two stereoviews of adduct **2a**, (a) looking at the CH_2Cl_2 molecule in the calixarene cavity and (b) a side view showing the two CH_2Cl_2 molecules and the general conformation with the atoms drawn as van der Waals spheres

aromatic rings make with the plane of the four CH_2 moieties which link them, *viz.* 130.5(2)° (A), 97.8(2)° (B), 128.6(2)° (C) and 91.9(2)° (D) (interplanar angles > 90° indicate that the ring system is tilted so that its *tert*-butyl group is directed away from the ring cavity). Two opposite rings (A and C) are close to being normal to one another [interplanar angle 79.2(3)°] while

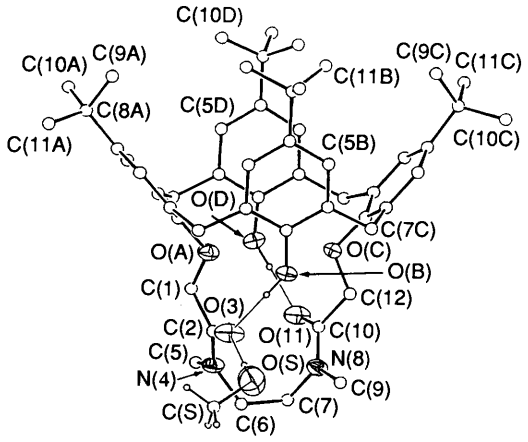


Fig. 3 A view of compound **2c** showing the hydrogen-bonding pattern, the general conformation, and our numbering scheme. For clarity, H-atoms are omitted (except those involved in hydrogen bonding), C-atoms are shown as small spheres of an arbitrary size, and the N- and O-atoms are shown as thermal ellipsoids drawn at the 35% probability level.

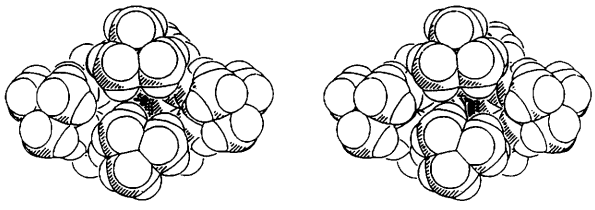


Fig. 4 A stereoview of the congested calixarene cavity of adduct **2c** with all atoms drawn as van der Waals spheres

phenolic rings B and D are almost parallel [interplanar angle 9.6(3)°], both rings B and D being tilted so that their *tert*-butyl groups are pitched slightly away from the calix cavity. This conformation leads to O···O separations of 3.75 Å between O(A) and O(C) and 5.20 Å between O(B) and O(D). The O···O distances between adjacent phenolic and ethereal O atoms are in the range 3.13(1)–3.29(1) Å. The conformation thus adopted by adduct **2c** effectively precludes a solvent molecule being encapsulated in the cavity (views into the cavity are in Fig. 4). It can be seen that it would not be possible to encapsulate a small molecule within the cup of adduct **2c** because of the locked conformation which results in the separation of the *tert*-butyl carbon atoms of rings B and D [C(11B)···C(11D) 4.23 Å, corresponding H···H separation 2.47 Å] being just greater than the sum of the relevant van der Waals radii (4.0 and 2.4 Å, respectively). In accord with this, the methanol of solvation {which is hydrogen bonded to the carbonyl oxygen O(3) [O(3)···O(S) 2.84(1) Å]} is *exo* to the calixarene cavity.

While molecules **2a** and **2c** both have distorted cone conformations, they are significantly different because of the different intramolecular hydrogen-bonding interactions. This results in the phenolic rings in molecule **2c** being almost parallel to each other, whereas in compound **2a** they are almost normal to one another. A recent study of a dinitrile derivative of 5,11,17,23-tetra-*tert*-butyl-25,27-bis(cyanomethoxy)-26,28-dihydroxycalix[4]arene[18] **1g** reports a conformation similar to that found here for compound **2a**, with the phenolic rings almost normal to each other. The diamide function linking the ethereal oxygens in adduct **2a** causes the calixarene cage to have a more open conformation than was found in compound **1g**.

The conformation adopted by the diamide functions linking O(A) and O(C) in both structures are determined by intramolecular hydrogen bonding. Unlike the carbonyl oxygens in adduct **2c**, which are oriented towards the calixarene cavity and are involved in intramolecular hydrogen bonding, both carbonyl oxygens in adduct **2a** are directed away from the calixarene cavity and are not involved in hydrogen bonding. As a consequence of this, the conformations of the diamide $-CH_2-C(O)-N-CH_2-CH_2-N-C(O)-CH_2-$ chains are significantly different between compounds **2a** and **2c**, although the $-N-CH_2-CH_2-N-$ moieties both have *gauche* conformations. The $-O-CH_2-C(O)-N-$ torsion angles in compound **2c** are $-151(1)°$ and $-159(1)°$; the corresponding values in adduct **2a** are 23.3(4)° and 27.1(4)°; the -N-C-C-N- torsion angles are 70.6(8)° in **2c** and 59.2(6)° in **2a**. The molecular dimensions of both compounds (bond angles are summarised in Tables 2 and 3) are in accord with previously reported values for the various bond types and are unexceptional. All the calixarene contacts correspond to normal van der Waals interactions. In the crystal lattice, the molecules pack in double layers which have the diamide chains adjacent; this results in sheets of *tert*-butyl carbon atoms being on the face of each double layer.

The locked conformation adopted by adduct **2c** effectively precludes a solvent molecule being encapsulated within the cavity, whereas compound **2a** has a more open cone conformation in the solid state. In accord with this, the methanol of solvation is *exo* to the calixarene cavity in adduct **2c**, while there are two dichloromethane molecules in adduct **2a**, one encapsulated within the cavity, the other *exo* to the cavity. The enclathration of a suitable guest molecule within the calix cavity has been observed previously in relatively open calixarene conformations, *e.g.* acetonitrile in tetraethyl *p-tert*-butylcalix[4]arene tetracarbonate.[19] The encapsulated CH_2Cl_2 molecule in adduct **2a** has a very similar environment to that reported recently by Atwood *et al.*[20] for a CH_2Cl_2 molecule enclathrated in a *p-tert*-butylcalixarene with dichloromethane H···π-arene contact distances of 2.61 and 2.76 Å (assuming a C–H distance of 1.08 Å). The crystal structures of some hemicarcerands and hemicarceplexes readily demonstrate the encapsulation of small molecules (MeCN or CH_2Cl_2) inside the host cavity,[21] with solvent molecules also present in the lattice.

The three remaining capped calixarenes synthesized in this study, compounds **2d**, **2e** and **2f**, are in fact calixcryptands, each with two phenolic groups at the base of a new cavity defined by the lower rim of the calixarene and the azacrown ring. The ^1H NMR spectra of compounds **2d–2f**, unlike those of compounds **2a–c** and **2g–j**, are complex and were only partly assigned. The pattern of the methylene protons in the azacrown moiety totally obscures the calixarene signals in the δ 3–5 region. Compound **2d** exhibits two doublets representing the $ArCH_2Ar$ protons and two singlets for the *tert*-butyl groups with four doublets in the aromatic region, an arrangement very like that in complex **2c** and indicative of a possible chiral conformation. A CPK model of compound **2d** suggests that it has an extremely rigid and inflexible structure. Compounds **2e** and **2f**, owing to their asymmetric nature, both display three *tert*-butyl singlets in the ^1H spectrum (relative intensities 2:1:1) and two hydroxy proton signals. The aromatic regions of the spectra in both again are complex consisting of multiplets between δ 6.73 and 7.07 for adduct **2e** and between δ 6.61 and 7.07 for adduct **2f**.

Compounds **2d–2f** are calixcryptands with well defined hydrophilic cavities on the lower rim in addition to the hydrophobic cavities defined by the upper rim. Preliminary work on their properties shows that the amide groups can be reduced to amino groups giving structures whose receptor properties are under investigation.

Experimental

M.p.s. were determined on a Thomas Hoover apparatus and are uncorrected. ^1H NMR spectra were recorded at 400 MHz on a Bruker WP 400 instrument with $SiMe_4$ as internal

Table 2 Summary of cell parameters, data collection and refinement details

Compound	$C_{52}H_{68}N_2O_6 \cdot CH_3OH$ **2c**	$C_{50}H_{64}N_2O_6 \cdot 1.25CH_2Cl_2$ **2a**
Formula	$C_{53}H_{72}N_2O_7$	$C_{51.25}H_{66.5}Cl_{2.5}N_2O_6$
M	849.2	895.2
Colour, habit	Colourless block	Colourless block
Crystal size (mm)	0.30, 0.30, 0.30	0.40, 0.50, 0.35
Crystal system	Triclinic	Monoclinic
a(Å)	10.272(2)	36.140(4)
b(Å)	12.474(3)	11.879(3)
c(Å)	19.351(4)	25.801(6)
α(°)	93.80(2)	
β(°)	95.52(2)	114.66(2)
γ(°)	91.58(2)	
V(Å^3)	2461(1)	10 066(4)
Space group	$P\bar{1}$	$C2/c$
Z	2	8
F(000)	912	3828
D_{calc} (g cm^{-3})	1.15	1.18
μ (cm^{-1})	0.7	5.0
2θ-range (°)	4–45	4–101
2θ-range for setting angles (°)	22–28	15–53
Temperature (T/°C)	21	21
Radiation	Mo-Kα (λ 0.7093 Å)	Cu-Kα (λ 1.5406 Å)
Reflections measured	6419	10 989
Unique reflections		5362
Reflections with $I > 3\sigma(I)$	2317 [2.5 $\sigma(I)$]	3044
No. of variables in LS	559	577
Least-squares type	Full-matrix	Full-matrix
p in weights	0.0015	0.003
R, R_w, GoF,	0.076, 0.088, 1.46	0.077, 0.109, 1.71
Density in final Δ-map (e Å^{-3})	−0.24, +0.37	−0.38 to 0.36
Final shift/error ratio	0.006	0.08

Table 3 Summary of bond lengths (Å) (range and mean) for **2a**·1.25CH_2Cl_2

Bond	Range	Mean
C^{ar}–$O^{(phen)}$	1.370(10)–1.375(10)	1.372(10)
C^{ar}–$O^{(ether)}$	1.405(10)–1.415(9)	1.410(10)
C^{sp^3}–O	1.439(9)–1.439(11)	1.439(10)
C^{sp^3}–C^{sp^2}	1.491(13)–1.517(14)	1.504(14)
C^{sp^2}=O	1.230(14)–1.233(11)	1.231(13)
C^{sp^2}–N	1.293(14)–1.334(13)	1.313(14)
C^{sp^3}–N	1.441(14)–1.467(12)	1.454(13)
C^{sp^3}–$C^{sp^3(in\ diamide)}$	1.512(14)	
C^{ar}–C^{ar}	1.368(14)–1.416(11)	1.389(12)
C^{ar}–C^{sp^3}	1.497(11)–1.554(13)	1.518(11)
C^{sp^3}–$C^{Bu^t\ methyl}$	1.447(19)–1.575(16)	1.508(16)
C^{sp^3}–$Cl^{(CH_2Cl_2)}$	1.54(4)	

standard and $CDCl_3$ as solvent. Mass spectra and accurate masses were measured with a VG Autospec mass spectrometer. Flash chromatography was performed using a Rhone–Poulenc silica gel C-60-H (40–60μm).

Diacid dichloride **1d** was prepared from *p-tert*-butylcalix[4]-arene according to the published procedure.[18] The diamines used are commercially available (Merck–Schuchardt) or were prepared as formerly described.[22] Light petroleum refers to the fraction boiling in the range 40–60 °C.

Cyclisation of Compound **1d** *with Diamines. General Procedure.*—A solution of compound **1d** (1.6 g, 2 mmol) in dry benzene (40 cm^3) and a solution of the diamine (2 mmol) in dry benzene (40 cm^3) were added simultaneously *via* 2 syringes to a stirred solution of triethylamine (0.61 cm^3, 4.4 mmol) in dry benzene (200 cm^3) at room temperature. The addition time was approximately 5 h in each case. When the addition was completed, the solution was filtered, and concentrated at reduced pressure. The solid residue was purified by flash chromatography over silica and subsequent recrystallisation, with the exception of compound **2a** which was purified directly by recrystallisation, to afford the pure bisamides. The following compounds were thus prepared.*

Compound **2a**[17], adduct with ethylenediamine, 95% yield, m.p. 270–290 °C (decomp.) (from methanol–dichloromethane).

Compound **2b**, adduct with trimethylene diamine [chromatographic eluent: (1:1) chloroform–acetone], 74% yield, m.p. 194–200 °C (from acetone) (Found: M$^+$, 802.4881. Calc. for $C_{51}H_{66}N_2O_6$: M, 802.4920).

Compound **2c**, adduct with *N,N'*-dimethylethylenediamine [chromatographic eluent: (1:1) dichloromethane–ethyl acetate], 21% yield, m.p. 308 °C (decomp.) (from methanol–dichloromethane) (Found: M$^+$, 816.5049. $C_{52}H_{68}N_2O_6$ requires M, 816.5077) (Found: C, 74.6; H, 8.3; N, 3.1. $C_{52}H_{68}N_2O_6 \cdot CH_3OH$ requires C, 75.0; H, 8.6; N, 3.3%).

Compound **2d**, adduct with 1,4,10,13-tetraoxa-7,16-diazacyclooctadecane (chromatographic eluent: ethyl acetate), 52% yield, m.p. 300 °C (decomp.) (from methanol–dichloromethane) (Found: M$^+$, 990.7. $C_{60}H_{82}N_2O_{10}$ requires M, 990.7) (Found: C, 71.4; H, 8.4; N, 2.4. $C_{60}H_{82}N_2O_{10} \cdot CH_3OH$ requires C, 71.6; H, 8.5; N, 2.7%).

Compound **2e**, adduct with 1,4,10-trioxa-7,13-diazacyclopentadecane (chromatographic eluent: ethyl acetate), 34% yield, m.p. 218 °C (decomp.) (from cyclohexane–dichloromethane) (Found: M$^+$, 946.9. $C_{58}H_{78}N_2O_9$ requires M, 946.9) (Found: C,

* Carbon values in microanalysis are frequently low for calixarenes with cavities capable of retaining solvent molecules.[23] Compounds **2c**–**2f**, **2g**, **2i and 2j** give acceptable microanalysis only if one assumes that there is one molecule of methanol of crystallisation (used in flash chromatography and recrystallisation) in the case of compounds **2c**, **2d**, **2f**, **2g**, **2i** and **2j**, and one molecule of ethyl acetate (used in flash chromatography in the case of compound **2e**) present in the sample.

Table 4 Summary of bond lengths (Å) for **2c**·MeOH

Bond	Range	Mean
C^{ar}–$O^{(phen)}$	1.334(13)–1.357(12)	1.346(13)
C^{ar}–$O^{(ether)}$	1.391(13)–1.396(12)	1.394(13)
C^{sp^3}–O	1.374(17)–1.430(13)	1.403(17)
C^{sp^3}–C^{sp^2}	1.513(17)–1.515(13)	1.514(17)
C^{sp^2}=O	1.224(17)–1.234(15)	1.229(17)
C^{sp^2}–N	1.333(15)–1.337(15)	1.335(15)
C^{sp^3}–N	1.454(16)–1.463(15)	1.458(15)
C^{sp^3}–$C^{sp^3(in\ diamide)}$	1.508(19)	
C^{ar}–C^{ar}	1.355(18)–1.409(16)	1.387(17)
C^{ar}–C^{sp^3}	1.511(16)–1.536(16)	1.527(16)
C^{sp^3}–$C^{Bu^t\ methyl}$	1.386(23)–1.537(21)	1.462(23)
C^{sp^3}–$OH^{(methanol)}$	1.374(17)	

71.8; H, 8.2; N, 2.6. $C_{58}H_{78}N_2O_9$·$C_3H_8O_2$ requires C, 71.9; H, 8.4; N, 2.7%).

Compound **2f**, adduct with 1,4,7,13,16-pentaoxa-10,19-diazacycloundecosane [chromatographic eluent: (9:1) dichloromethane–methanol], 19% yield, m.p. 278–280 °C (from methanol–dichloromethane); *m/z* (FAB) M^+, 1036 (Found: C, 70.9; H, 8.5; N, 2.6. $C_{62}H_{86}N_2O_{11}$·CH_3OH requires C, 71.2; H, 8.5; N, 2.6%).

Compound **2g**, adduct with 1,5-diamino-3-oxapentane (chromatographic eluent: ethyl acetate), 32% yield, m.p. 275–276 °C (from methanol–dichloromethane) (Found: M^+, 832.5056. $C_{54}H_{68}N_2O_7$ requires *M*, 832.5027) (Found: C, 73.5; H, 8.3; N, 3.0. $C_{52}H_{68}N_2O_7$·CH_3OH requires C, 73.6; H, 8.4; N, 3.2%).

Compound **2h**,[17] adduct with 1,8-diamino-3,6-dioxaoctane [chromatographic eluent: (20:1) dichloromethane–methanol], 22% yield, m.p. 242–244 °C (from light petroleum–chloroform) (Found: M^+, 876.9; C, 73.6; H, 8.5; N, 3.1%. $C_{54}H_{72}N_2O_8$ requires *M*, 876.9; C, 74.0; H, 8.3; N, 3.2%).

Compound **2i**, adduct with 1,11-diamino-3,6,9-trioxaundecane [chromatographic eluent: (1:1) chloroform–acetone], 35% yield, m.p. 235–236 °C (from methanol–dichloromethane) (Found: M^+, 920.6. $C_{56}H_{76}N_2O_9$ requires *M*, 920.6) (Found: C, 72.0; H, 8.2; N, 2.7. $C_{56}H_{76}N_2O_9$·CH_3OH requires C, 71.8; H, 8.5; N, 2.9%).

Compound **2j**, adduct with 1,14-diamino-3,6,9,12-tetraoxatetradecane [chromatographic eluent: (25:1) chloroform–methanol], 31% yield, m.p. 208–213 °C (from cyclohexane) (Found: M^+, 964.0. $C_{58}H_{80}N_2O_{10}$ requires *M*, 964.0) (Found: C, 71.4; H, 8.4; N, 2.7. $C_{58}H_{80}N_2O_{10}$·CH_3OH requires C, 71.1; H, 8.5; N, 2.8%).

X-Ray Structure Determination.—Structure analysis. The cell parameters, data collection and refinement details for adducts **2a** and **2c** are summarised in Table 4. Intensities of 3 reflections measured every 2 h showed no decay. The structures were solved by direct methods (using the NRCVAX[24] programs), which initially revealed most of the non-hydrogen atoms. Refinement was by full-matrix least-squares refinement calculations on *F*, initially with isotropic and finally with anisotropic thermal parameters. Hydrogen atoms bonded to carbon were clearly visible in the difference maps computed at various stages of refinement, and were positioned on geometric grounds (C–H 0.95 Å) and included as riding atoms in the structure factor calculations. In structure **2c**, difference maps showed the presence of a methanol of solvation *exo* to the calixarene cavity and hydrogen-bonded to a carbonyl oxygen. The hydroxy group H-atoms [H(OA) on O(A), H(OC) on O(C) and H(OS) on the methanol oxygen O(S)] were also clear in difference maps and were positioned as riding atoms on the respective oxygens and directed towards the appropriate carbonyl oxygen [O(3) or O(11)]. The terminal C-atoms of the *tert*-butyl groups on rings A, B and D are markedly anisotropic, but there was no indication from difference maps of more than one conformation being clearly adopted. In structure **2a**, the presence of two dichloromethane molecules of solvation was clear in early difference maps, but it was obvious from the peak heights that they were not present with unit occupancy. The occupancy factors for the two CH_2Cl_2 molecules were determined during initial isotropic refinement and were fixed before anisotropic refinement. The two hydroxy group and two amide H-atoms were more clearly resolved in difference maps than were the hydroxy group H-atoms in structure **2c** and their co-ordinates were obtained directly from the difference maps.

Scattering factors were taken from International Tables.[25] All calculations were performed on a Silicon Graphics 4D-35TG workstation using the NRCVAX programs. Details of molecular geometry are given in Tables 2 and 3 respectively. Figs. 1–4 are views of the molecules prepared with the aid of ORTEP II[26] and PLUTON.[27]

Additional material available from Cambridge Crystallographic Data Centre* comprises thermal parameters, fractional coordinates, H-atom co-ordinates, mean-plane data and selected torsion angles. Copies of the structure-factor listing are available from the authors.

* For details of the deposition scheme, see 'Instructions for Authors,' *J. Chem. Soc., Perkin Trans. 1*, in the January issue.

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