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Conformational Preferences of *O*-Substituted Oxacalix[3]Arenes

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A tripicolyl derivative of *p-tert*-butyloxacalix[3]arene has been synthesized and characterized. The compound crystallizes, as the 0.5 $CH_3OH \cdot 0.5\ H_2O$ complex, in the monoclinic space group $P2_1/c$ with $a = 14.158(7)$, $b = 14.196(7)$, $c = 27.612(12)$ Å, $\beta = 103.53(1)°$, and $D_c = 1.083\ g\,cm^{-3}$ for Z = 4. Refinement based on 8738 observed reflections gave a final R value of 0.062. The tris(diethylacetamide) derivative of *t*-butyloxacalix[3]arene has been prepared in high yield and structurally characterized in two forms. A desolvated form crystallizes in the monoclinic space group $P2_1/n$ with $a = 22.062(2)$, $b = 11.028(11)$, $c = 22.357(3)$ Å, $\beta = 103.78(1)°$, and $D_c = 1.152\ g\,cm^{-3}$ for $Z = 4$. Refinement based on 6284 observed reflections gave a final R value of 0.107. A solvated compound crystallizes with 2 molecules of DMF in the triclinic space group $P\bar{1}$ with $a = 13.5598(6)$, $b = 13.6343(5)$, $c = 19.3443(9)$ Å, $\alpha = 76.938(1)$, $\beta = 77.873(1)°$, $\gamma = 61.699(1)°$, and $D_c = 1.159\ g\,cm^{-3}$ for $Z = 2$. Refinement based on 8414 observed reflections gave a final *R* value of 0.064. Conformational preferences of these compounds have been modelled by computational methods. The results of these simulations support the ratios of cone:partial cone conformers found experimentally.

Keywords: Macrocycles, calixarenes, crystallography, molecular modelling

INTRODUCTION

Hexahomotrioxacalix[3]arenes (hereafter referred to as oxacalix[3]arenes) are a subset of the calixarene group of macrocycles and were first reported in 1962 [1]. Despite intermittent attempts to improve the syntheses of these compounds [2–6] they have remained largely overlooked as subjects for investigation in the field of supramolecular chemistry. Recently there has been renewed interest in *O*-substituted derivatives with a view to the separation of alkali metal [7, 8] and ammonium salts [9–11].

Oxacalix[3]arenes have a cavity defined by an eighteen membered ring, reminiscent of flexible macrocycles such as 18-crown-6 and the more rigid spherands [12] and torands [13, 14] (Fig. 1). This makes the oxacalix[3]arene cavity slightly larger and more flexible than the more commonly encountered calix[4]arenes. The threefold symmetry, large cavity and combination of ethereal and phenolic oxygen atoms all favour the increased application of oxacalix[3]arenes to problems of molecular recognition and complexation of

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*Corresponding author.

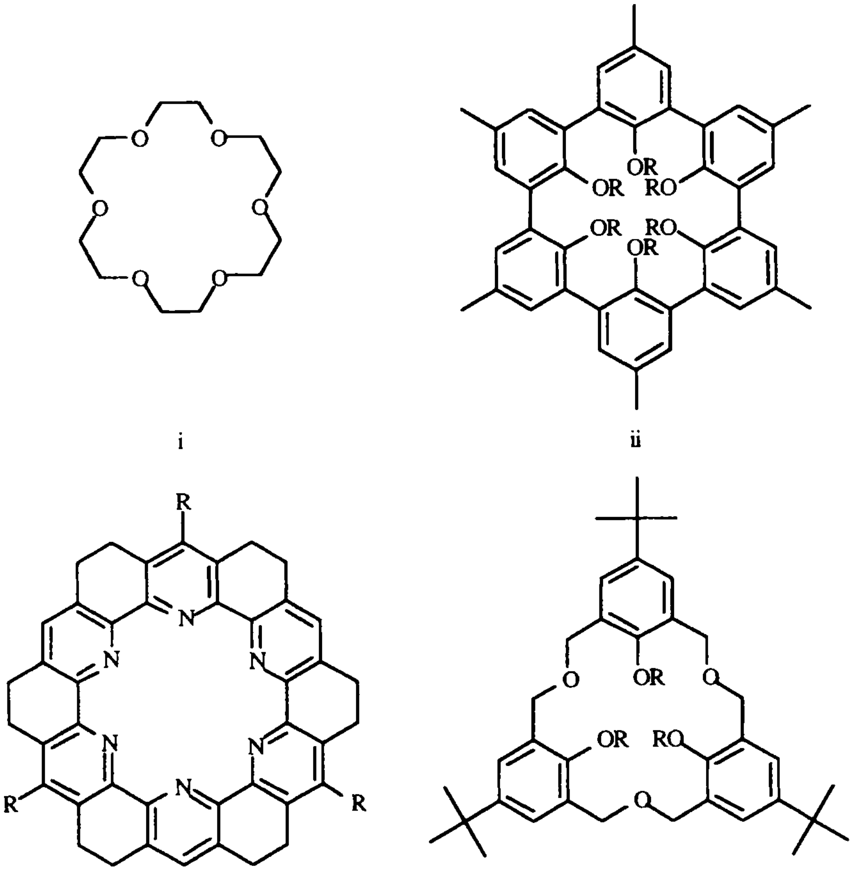

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FIGURE 1 Eighteen membered macrocycles; (i) 18-crown-6, (ii) spherand, (iii) torand (R = *n*-butyl[12] or H[13]) and (iv) *p-tert*-butyloxacalix[3]arene.

metal ions. The unique donor atom environment afforded by the oxacalix[3]arenes is expected to imbue them with characteristics of both calixarenes and crown ethers, particularly with respect to their inclusion complexes. Hampton has shown that *p-tert*-butyloxacalix[3]arene (1) can complex both transition metals [15] and lanthanide metal ions [16] *via* the phenolic oxygens. The *p*-methyl analogue binds transition metals [17] and Fuji has shown that oxacalix[3]arenes can complex C_{60} through complementary recognition between the fullerene and oxacalix [3]arene threefold symmetry elements [18]. The major drawback to more widespread application of oxaxalix[3]arenes to host-guest chemistry is the shallowness of the macrocyclic cavity [19]. One solution to this problem is to extend the cavity through *O*-alkylation of the phenolic rings. To investigate this principle we have appended picolyl groups to the lower rim of the oxacalix [3]arene using a synthetic approach which has proven successful in the case of calix[4]arenes [20]. In addition, we report X-ray structures of a tris(diethylacetamide) derivative, the first *O*-substituted oxacalix[3]arene to retain a cone conformation following reaction of the three lower rim phenolic oxygens with bulky alkyl groups.

RESULTS AND DISCUSSION

Syntheses

The treatment of *p-tert*-butyloxacalix[3]arene (**1**) with excess picolyl chloride hydrochloride in dimethylformamide in the presence of sodium hydride afforded the tripicolyl derivative (**2**) in 68% yield. As with other substituted oxacalix[3]arenes, [7–11,24,25] **2** was obtained in a partial cone conformation as indicated by ^{1}H NMR and later confirmed by X-ray crystallography. This is in contrast with the reaction of *p-tert*-butylcalix[4]arene and picolyl chloride which, under the same conditions, yields the cone conformer exclusively. Attempts to prepare complexes with various metals by heating stoichiometric mixtures of **2** with several metal salts (zinc acetate, cuprous iodide, europium nitrate and uranyl nitrate) in dimethylformamide resulted in X-ray quality crystals. Structure determination showed that the crystals were not of metal complexes, however, but of the free ligand in a partial cone conformation. The tris(diethylacetamide) derivative (**3**) was first reported by Shinkai [8] and, based upon ^{1}H NMR evidence, a cone conformation was assigned. The compound was recrystallized from both acetonitrile and dimethylformamide to give two distinctly different crystalline forms.

Crystallography

The structure of **2** (Fig. 2) shows a 'self-inclusion' complex (as observed in analogous calix[4]arene derivatives [20,26]) in which one of the pendent pyridines is positioned between two *tert*-butyl groups with the nitrogen lone pair directed into the cavity and approaching an ethereal oxygen atom at a distance of 3.7 Å. This conformation explains the shielding of hydrogens on one pyridine ring observed in the proton NMR spectrum. Indeed the effect is so marked that the two methylene hydrogens next to the self-included pyridine appear as a doublet ($J = 26.5$ Hz) almost 2 ppm upfield of the four hydrogens in analogous positions on the two other rings. The phenolic rings are between 5.7 and 6.3 Å apart compared to 6.8 Å for **1** [19] giving a slightly smaller and less symmetrical cavity presumably due to the inversion of one phenolic ring. Unlike **1**, which crystallizes without solvent, both water and methanol (each 50% disordered) are found in crystalline **2**. Neither solvent has a strong association with the macrocycle which is surprising as the sample used in the X-ray determination was precipitated from a water/methanol solution and refluxed in dimethylformamide without displacing the original solvents. The idealized geometry for oxacalix[3]arenes is observed in the structure of the parent macrocycle, **1**, and gives torsion angles around the cavity of $g^+, g^-, g^+, g^-, g^+, g^-$ when starting from the O-substituted carbon in a phenol ring (see Tab. V) using the designations $g^+ = gauche^+, g^- = gauche^-, a = anti$ and $s = syn$. The torsion angles around for **2** are, by contrast, $g^+, g^+, g^-, g^+, g^-, g^-$ giving an overall saddle shape to the macrocycle.

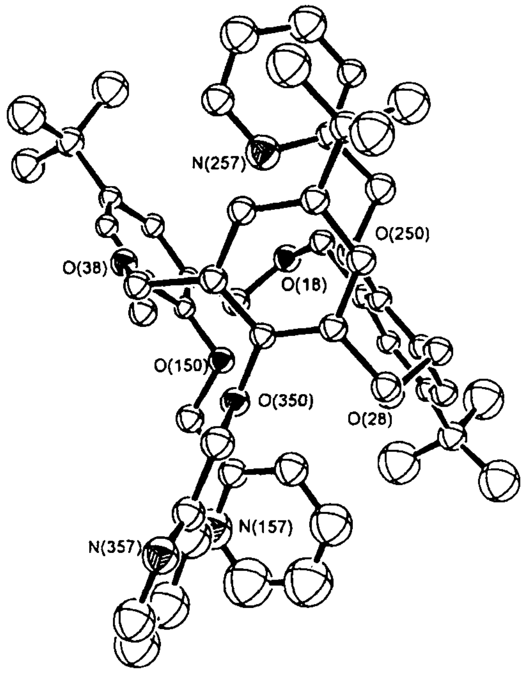


FIGURE 2 Molecular structure of $2 \cdot 0.5\ H_2O \cdot 0.5\ CH_3OH$.

Compound **3** was recrystallized from acetonitrile to yield colourless needles suitable for X-ray analysis. The structure (Fig. 3) shows **3** to exist in a cone conformer, however, the cavity is greatly distorted from an ideal cone geometry with torsion angles of s, g^+, g^-, g^+, s, g^+. As a result one of the *p-tert*-butylphenol rings is tilted in towards the macrocyclic cavity hindering any solvent or cation encapsulation. The ring tilt also has the effect of directing one of the diethylacetamide nitrogens away from the cavity. The distortion is evident with phenolic ring centroids 4.4, 4.9 and 6.4 Å apart. The amide nitrogens are between 5.7 and 6.0 Å apart giving a secondary cavity at a distance of 5.8 Å from the upper rim. The nitrogen directed away from the cavity is, however, slightly closer to the upper rim (5.5 Å) than the others. Such distortion is undoubtedly due to crystal packing and is similar to that observed in the X-ray structure of *p-tert*-butylcalix[4]arenetetra(diethylacetamide) [31].

A similar geometry was found for **3** which had been recrystallized from dimethylformamide. A solution of **3** in dimethylformamide was cooled to −10°C for several weeks whereupon large colourless blocks formed. These blocks effloresced when removed from solvent at room temperature so an X-ray structural determination was undertaken at −150°C. The structure shows that each oxacalix[3]arene is associated with two molecules of dimethylformamide residing outside the cavity which, as with the solvent free structure, is in the cone conformation. Again the torsion angles are greatly distorted from the ideal with g^-, a, g^-, g^+, g^-, a observed. An expanded view of the compound reveals that the solvent molecules form channels in two dimensions between bilayers of oxacalix[3]arenes (Fig. 4) which are in turn separated solely by weak van der Waals forces. This remarkable level of solvation explains the unstable nature of the complex in the solid state.

Molecular Modelling Studies

The mechanism behind *O*-substitution is important as the ability to form cone conformers is central to the application of oxacalix[3]arenes to inclusion chemistry. For this reason we decided to see if molecular modelling techniques could

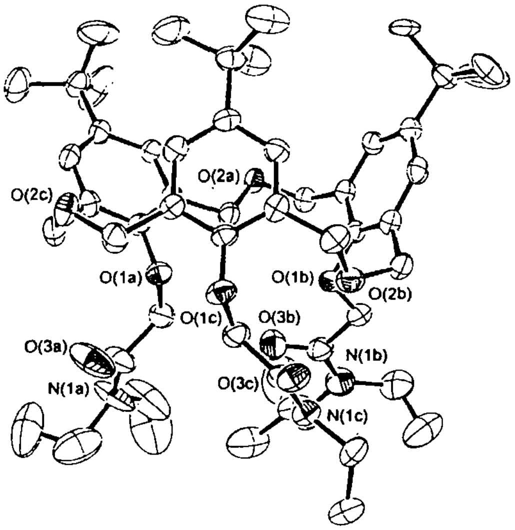


FIGURE 3 Molecular structure of 3.

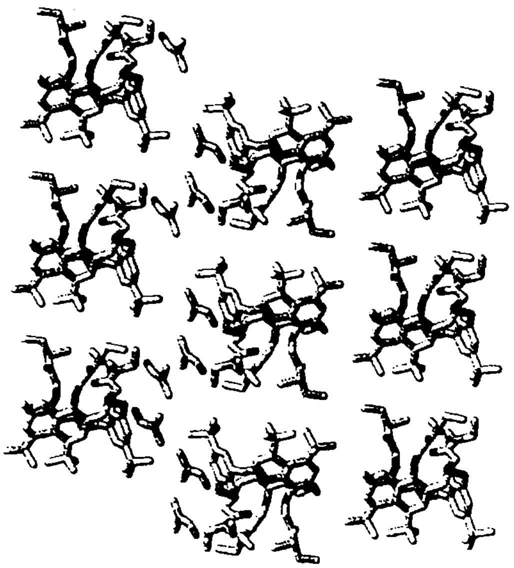


FIGURE 4 Expanded view of 3·2 DMF showing solvent channels.

be applied to the oxacalix[3]arenes as successfully as they had been to calix[n]arenes [27] and crown ethers [28,29]. Our approach to modelling the oxacalix[3]arenes mirrors that which we have used in previous work, that is, it uses simple molecular mechanics forcefields to see how well they simulate experimental data [30]. In this case it proved necessary to generate and analyse large numbers of conformers in a complete grid search for each compound studied. In order to keep the computational time to a minimum fairly severe acceptance criteria were adopted to reduce the number of conformers from the 120932352 generated from each grid search to a more manageable 100 to 200 which were eventually used in the analysis. The object of this was to scan all the possible conformers yet retain a large element of randomness in those accepted. The method used required breaking one bond in the oxacalix[3]arene and treating it as an acyclic molecule. By retaining those conformers in which two carbon termini were within reasonable bonding distances and angles of each other we would expect to be left with those structures which were essentially cyclic. Reforming the bond and optimising the geometry (through a combination of molecular dynamics and molecular mechanics) gave the final structures from which conformational preferences were determined. Occasional high energy structures resulted where reforming the broken bond had resulted in a twisted, rather than cyclic, geometry. These structures, which increased in occurrence as the size and number of substituents increased, were removed from the final data set used to generate cone : partial cone ratios.

It has been shown that the parent oxacalix[3]arenes are fluxional on the NMR timescale (all protons appear as singlets) as the phenolic hydroxyl group can rotate through the macrocyclic annulus, however, if any substituent more bulky than a methyl group is appended to the lower rim, free rotation ceases yielding partial cone conformers [9]. Conversely, the most stable solid state structure is a cone, apparently locked in position by a hydrogen bonding network [19].

The mechanism of *O*-substitution is presumed to start with one phenolic group being deprotonated by a base (sodium in the case of **2** and **3**) with initial attack occuring at the phenoxide as the macrocycle is held in a cone conformation [7]. This conformation of the monoanion is sterically less demanding for the initial approach of the first picolyl or diethylacetamide group than a partial cone conformation as the incoming reactant does not have to contend with crowding by two *tert*-butyl groups. Once the first phenolic group reacts to form the monosubstituted compound it has been proposed that a second phenol group (possibly as the phenoxide) rotates through the annulus such that the second substituent reacts to give a partial cone configuration. Finally a third substituent approaches from either end of the macrocycle (there is now no preference for attack based on steric considerations) to give the partial cone conformer. At any stage of this process free phenolic groups may pass through the annulus to become susceptible to attack. Thus, if we ignore steric effects, there is an equal chance of a second substituent adding from either direction. In the final stage a third substituent can only react to form the partial cone conformer. In contrast, there is an equal chance of forming the cone or partial cone conformer from the disubstituted cone precursor. This gives a predicted ratio of 25 : 75 cone : partial cone conformer overall through the above routes illustrated in Figure 5.

We have investigated the conformational preferences of parent (unsubstituted) *p-tert*-butyloxacalix[3]arene (**1**), *p*-methyloxacalix[3]arene, mono-, di- and tripicolyl substituted *p-tert*-butyloxacalix[3]arene (**2**), and *p-tert*-butyloxacalix[3]arenetris(diethylacetamide) (**3**). The results are given in Table III.

The data for the parent oxacalix[3]arenes show a tendency towards the statistical distribution of conformers even though the stabilizing presence of hydrogen bonding (which was

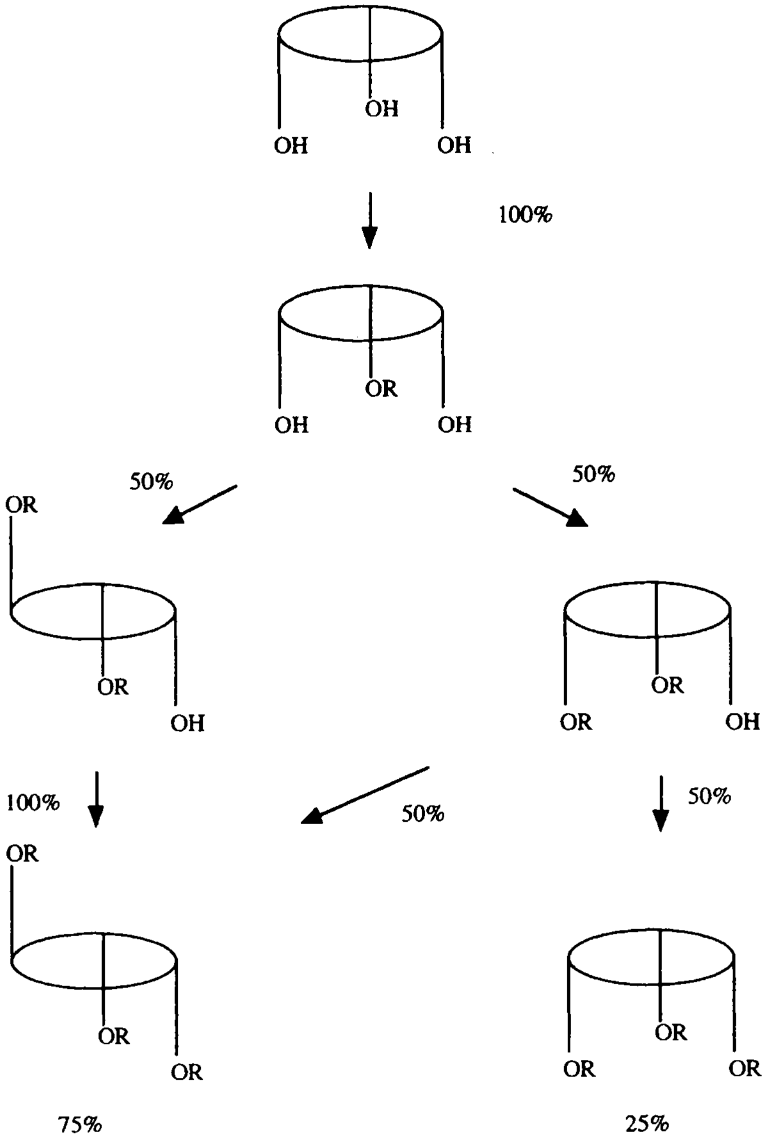


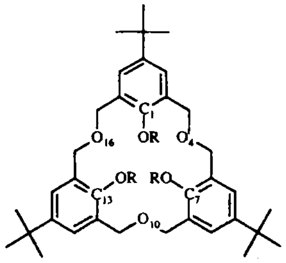
FIGURE 5 Pathways for *O*-substituted oxacalix[3]arene formation.

allowed for by the mechanics program) would be expected to favour the cone conformer. In fact the lowest energy conformer is in the partial cone configuration, however, the energy differences between cone and partial cone conformers are small and 40% of the lowest energy structures do adopt a cone. We have remarked upon this phenomenon in relation to stable conformers of another cyclic ligand with threefold symmetry, thiacrown 9ane[S]$_3$, where the lowest energy conformer is not that observed in the X-ray structure but is consistent with electron diffraction data [30]. The effect of packing is usually cited as the reason discrepancies between solid state structures and those in the gas phase, solution or derived from theoretical models.

TABLE I Crystal data and summary of data collection

Compound	2 · 0.5 H_2O · 0.5 CH_3OH	3	3 · 2 DMF
Formula	$C_{54.5}H_{66}N_3O_7$	$C_{54}H_{81}N_3O_9$	$C_{60}H_{95}N_5O_{11}$
Mol. weight	875.14	916.22	1062.41
$T(K)$	293(2)	293(2)	123(2)
Wavelength (Å)	0.71070	0.71070	0.71070
Space group	$P21/c$	$P21/n$	P-1
Cell constants			
a, Å	14.158(7)	22.062(2)	13.5598(6)
b, Å	14.196(7)	11.028(11)	13.6343(5)
c, Å	27.612(12)	22.357(3)	19.3443(9)
α, deg	90	90	76.938(1)
β, deg	103.53(1)	103.78(1)	77.873(1)
γ, deg	90	90	61.699(1)
V, $Å^3$	5395.5	5282.9	3045.2
Molecules/unit cell	4	4	2
D_c, mg m^{-3}	1.083	1.152	1.159
Absorption coefficient (mm^{-1})	0.070	0.077	0.079
$F(000)$	1896	1992	1156
Crystal size (mm)	0.2×0.15×0.15	0.4×0.1×0.1	0.3×0.2×0.2
θ range, deg	2.80 to 25.38	2.66 to 22.50	3.48 to 26.00
Index ranges	$-16 \leq h \leq 16$ $0 \leq k \leq 15$ $0 \leq l \leq 32$	$0 \leq h \leq 23$ $0 \leq k \leq 11$ $-24 \leq l \leq 23$	$-16 \leq h \leq 16$ $-16 \leq k \leq 16$ $-23 \leq l \leq 23$
Reflections collected/unique	16508/8738 [R(int) = 0.0779]	39146/6284 [R(int) = 0.1020]	25825/11153 [R(int) = 0.0522]
Data/restraints/parameters	8738/0/587	6284/0/632	11153/0/704
Goodness of fit on F^2	0.791	1.052	1.028
Final R indices $[I > 2\sigma(I)]$	$R_1 = 0.062$ $wR_2 = 0.189$	$R_1 = 0.107$, $wR_2 = 0.245$	$R_1 = 0.064$, $wR_2 = 0.149$
R indices (all data)	$R_1 = 0.088$, $wR_2 = 0.211$	$R_1 = 0.168$, $wR_2 = 0.277$	$R_1 = 0.088$, $wR_2 = 0.164$
Largest diff. peak and hole ($Å^{-3}$)	0.20 and −0.18	0.35 and −0.37	0.58 and −0.33

TABLE II Comparison of torsion angles for oxacalix[3]arenes 1, 2 and 3



Compound	Torsion angles (degrees)						Ref.
	C_1-O_4	O_4-C_7	C_7-O_{10}	$O_{10}-C_{13}$	$C_{13}-O_{16}$	$O_{16}-C_1$	
1	−62.5	64.5	−58.3	58.3	−64.6	62.5	19
2	89.4	76.3	−94.7	152.5	−107.8	−152.0	[a]
3	−178.0	91.4	−64.5	77.1	−163.8	89.3	[a]
3 · 2 DMF	−82.7	171.9	−68.3	70.0	−91.8	178.1	[a]

[a] This work.

The statistically expected distribution is also observed for the mono-, di- and tripicolyl derivatives of *p-tert*-butyloxacalix[3]arene where the orientations of the unsubstituted phenolic groups are considered when assigning conformations. As expected the final distribution for

TABLE III Summary of conformational searching for oxacalix[3]arenes and their O-alkylated derivatives

Compound	Low energy conformers (% of total used)	Conformer	
		% cone	% partial cone
p-Methyloxacalix[3]arene	154 (77)	19	81
p-*t*-Butyloxacalix[3]arene	167 (83)	25	75
Picolyl-*p*-*t*-butyloxacalix[3]arene	123 (80)	27	73
Dipicolyl-*p*-*t*-butyloxacalix[3]arene	135 (74)	25	75[a]
Tripicolyl-*p*-*t*-butyloxacalix[3]arene	79 (49)	24	76
Tris(diethylacetamide)- *p*-*t*-butyloxacalix[3]arene	(1)[b] 78(72)	40	60
	(2)[b] 119 (81)	34	66

[a] The distribution of conformers between *anti* picolyl groups (which can only yield alternate conformers upon further reaction) and *syn* picolyl groups (which yield alternate and cone conformers in a 50:50 ratio) is 57:43, mirroring the theoretical distribution of 50:50.

[b] See text.

the trisubstituted oxacalix[3]arene approaches the statistical 25:75 cone:partial cone ratio. This is in agreement with reported yields of trisubstituted oxacalix[3]arenes where sodium has been used as the deprotonating base. There is only one example in which a yield greater than 75% has been claimed for a product in the partial cone conformation and no examples exist where the cone conformer has been isolated in greater than 25% yield. Deviations from these statistical values only occur when larger alkali metals are employed in O-substitution. The 68% yield of **2** as the partial cone conformer is also in line with the computational prediction, however, when we prepared **3** we were surprised to be able to obtain it in 44% yield following recrystallization. The literature yield was 23%, in agreement with a statistically predicted 25% yield. This derivative was modelled, subjecting it to the same parameters as all other compounds in this study, and a non-statistical distribution of cone:partial cone was observed. An initial ratio of 40:60 cone:partial cone based on 78 optimised structures was unexpected so a second simulation, generating conformers from a different starting geometry, was run and gave a 34:66 cone:partial cone ratio from 119 optimised structures. While neither of these simulations prediced the 44% yield of **3** in the cone conformer, they both reflect a greater than statistical likelihood of obtaining **3** in that conformation. We speculate that the reasons for the apparent success of the simulation include the ability of the diethylacetamide groups to thread through the macrocyclic annulus (as observed in some high energy conformers generated during the simulation) and the apparent similarity in the way that the program considers the volumes of *p*-*tert*-butyl and diethylacetamide groups. The increased experimental yield has been ascribed to interactions between solvent, Na^+, diethylacetamide groups on the partially substituted oxacalix[3]arene and free *N*,*N*′-diethylchloroacetamide [8].

In conclusion, we have prepared a new tripicolyl *t*-butyloxacalix[3]arene derivative, charaterized it by X-ray crystallography and shown it to be in the partial cone conformation. The conformational preference observed for this compound has been accurately modelled using relatively unsophisticated computational methods. The tris(diethylacetamide) derivative of *p*-*tert*-butyloxacalix[3]arene has been prepared in high yield, characterized crystallographically (in both solvated and desolvated forms) and modelled computationally. The results of the molecular simulation support the non-statistical ratio of cone:partial cone conformers found experimentally. Through these results we have demonstrated the power of conformational searching and molecular mechanics in predicting the ratio of cone: partial cone conformers for *O*-substituted oxacalix[3]arenes.

EXPERIMENTAL

Syntheses

Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker AM360 instrument in $CDCl_3$ solution at 360 MHz (^1H) and 90 MHz (^{13}C). Chemical shifts (parts per million downfield from internal Me_4Si) are reported in the following order: chemical shift, spin multiplicity (br = broad, *s* = singlet, *d* = doublet, *t* = triplet, *q* = quartet, *m* = multiplet), coupling constant (Hz) and integration. Infrared (IR) spectra were recorded on Perkin Elmer 1720-X FTIR spectrophotometer. IR spectral bands are reported in cm^{-1}. Mass spectrometry was performed at King's College and elemental analysis at the University of Kent, UK. The melting point is uncorrected.

Reagents were purchased from Aldrich Chemical Company and were used without further purification. 7,15,23-Tri-*tert*-butyl-25,26,27-trihydroxy-2,3,10,11,18,19-hexahomo-3,11,19-trioxacalix[3]arene (**1**) was prepared as reported in the literature [3].

7,15,23-Tri-*tert*-butyl-25,26,27-tri(2-pyridylmethoxy)-2,3,10,11,18,19-hexahomo-3,11,19-trioxacalix[3]arene (2). Following the procedure of Pappalardo [20] for *O*-alkylation of calix[4]arenes, oxacalix[3]arene **1** (520 mg, 0.9 mmol) was dissolved in anhydrous dimethylformamide (20 mL) and stirred under a dry nitrogen atmosphere. Sodium hydride (1.60 g, 30 mmol [50% dispersion in oil]) was added and the reaction mixture stirred for 30 minutes. Picolyl chloride hydrochloride (2.22 g, 13 mmol) was added, complete transfer being facilitated by washing residual solids into the reaction vessel with further anhydrous dimethylformamide (10 mL). The mixture was heated to 60°C and stirred for 24 hours, maintaining a temperature between 55 and 65°C. After 24 hours methanol (2 mL) was added dropwise to quench any unreacted sodium hydride. The reaction mixture was poured into distilled water (100 mL), stirred until a flocculent precipitate appeared and left overnight at 4°C to complete precipitation. Recrystallization of this material from methanol (20 mL) gave 523 mg (68%) of **2** as small colourless crystals, m.p. 166–8°C. IR (CH_2Cl_2 mull) 3436, 3055, 2987, 1484, 1201, 1074, 896. ^1H NMR δ 0.98 (s, 18H, CMe_3), 1.15 (s, 9H, CMe'_3). 2.92 (d, J = 26.5, 2H, OCH_2Py'), 4.11 (s, 1H, 3-PyH′), 4.14 (d, J = 10.6, 2H, CH_2O), 4.21 (d, J = 12.4, 2H, CH_2O), 4.27 (d, J = 10.6, 2H, CH_2O), 4.52 (d, J = 10.7, 2H, CH_2O), 4.69 (ABq, J = 13.3, 4H, OCH_2Py), 4.83 (d, J = 12.4, 2H, CH_2O), 4.97 (d, J = 10.6, 2H, CH_2O), 7.01 (m, 3H, 3-PyH and 4-PyH′), 7.06 (m, 1H, 5-PyH′, 7.17 (d, J = 2, 4H, ArH), 7.23 (d, J = 2, 2H, ArH′), 7.31 (m, 2H, 5-PyH), 7.37 (m, 2H, 4-PyH), 7.56 (m, 1H, 6-PyH′) and 8.33 (m, 2H, 6-PyH). ^{13}C NMR (proton decoupled) δ 31.09, 31.34, 33.99, 34.26, 62.64, 66.35, 67.97, 76.02, 121.31, 121.73, 122.01, 127.22, 127.36, 128.28, 129.49, 130.11, 130.99, 136.60, 137.40, 146.12, 146.65, 147.87, 148.25, 153.31, 154.55, 156.80 and 157.21. FAB mass spectrum (thioglycerol matrix) *m/e* 851 $(M + H)^+$. Anal. Calcd. For $2 \cdot 0.5\ H_2O \cdot 0.5\ CH_3OH$ ($C_{54.5}H_{66}\ N_3O_7$): C; 74.80, H; 7.60, N; 4.80. Found: C; 74.89, H; 7.63, N; 5.35.

7,15,23-Tri-*tert*-butyl-25,26,27-tri(*N*,*N*-diethylaminocarbonyl-methoxy)-2,3,10,11,18,19-hexahomo-3,11,19-trioxacalix[3]arene (**3**) was prepared from (**1**) in accordance with literature procedures with the exception that the crude material was recrystallized from acetonitrille to give **3** in 44% yield (lit. 23% from methanol [8]). Crystals suitable for X-ray diffraction were grown as colourless needles from dilute acetonitrile solution. Recrystallization from dimethylformamide yielded colourless blocks which effloresced above 0°C.

X-ray Data

X-ray single crystal intensity data for **2** $\cdot$ 0.5 H_2O $\cdot$ 0.5 MeOH were measured using a MAR research Image Plate System and data analysis carried out with the XDS program [21]. Data for **3** and **3** $\cdot$ 2DMF were measured using a Nonius $^{\text{Kappa}}$CCD diffractometer with data analysed by the DENZO package. All three structures were solved using direct methods (SHELX86[22] for **2** $\cdot$ 0.5 H_2O $\cdot$ 0.5 MeOH, SHELXS-97 for **3** and **3** $\cdot$ 2DMF). Refinement on F^2 using SHELXL [23] led to an R of 0.062 for **2** $\cdot$ 0.5 H_2O $\cdot$ 0.5 MeOH and, using SHELXL-97 and RES2INS, to an R of 0.107 for **3** and 0.064 for **3** $\cdot$ 2 DMF. Details of the crystal data and summaries of the data collection are given in Table I. Other crystollographic details are available from P. J. C.

Computational Details

Calculations were performed using Chem-X (Chemical Design Ltd) on an IBM compatible personal computer. An oxacalix[3]arene structure was generated using 3D Sketch and energy minimised using the ALLATOMS forcefield with Gasteiger charges applied. A bond (C_{aryl} to C_{alkyl}) was removed from the resultant structure to given an initial conformer from which to start analysis. Charges were removed and a conformational path set between the terminal C_{aryl} and C_{alkyl} atoms. Acceptance criteria were set such that only conformers in which the terminal carbon atoms were between 1.48 and 1.52 Å and in which the C_{alkyl}—C_{aryl}—C_{aryl} bond angle was between 118 and 122° would be retained. This reduced the data set from 120932352 to a more manageable 100 to 200 structures. Once the data set was identified, the terminal C_{aryl} to C_{alkyl} bond was replaced, Gesteiger charges generated and the structure optimised using a combination of molecular dynamics and molecular mechanics until energy covergence occurred. Finally, structures more than double the energy of the minimum value recorded were discarded from each simulation data set. This removed a small number of structures which were unreasonably high in energy. The resulting structures were inspected and assigned as cone or partial cone conformations depending on the *O*-substituents' positions relative to a plane defined by the centroids of the three linked aromatic rings.

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