

Synthesis and Crystallographic Studies of a Calix[4]arene with a 1,3-Alternate Conformation

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25,27-Bis(ethoxycarbonylmethoxy)-26,28-bis(2-pyridylmethoxy)-5,11,17,23-tetra-*tert*-butylcalix[4]arene with a 1,3-alternate conformation (1,3-alternate-2) has been synthesized. Dynamic ¹H NMR spectroscopy has established that the conformation is immobilized (*i.e.*, the oxygen-through-the-annulus rotation is inhibited). The single crystal was grown from acetonitrile and analysed by X-ray crystallography. It was found that the structural characteristics of a 1,3-alternate conformation are (i) the four phenyl rings are more or less parallel to each other, the dihedral angles between the four phenyl rings and the mean plane of the four methylene groups being 93.5, 100.4, 101.4 and 106.1°, (ii) the ArCH₂Ar bond angles are more expanded than those for other conformations and (iii) 1,3-alternate-2 in solution adopts C₂ symmetry whereas in the solid state it is less symmetrical because of the unsymmetrical orientation of the ester and the pyridyl substituents. This is a rare example of the X-ray crystallographic analysis of 1,3-alternate calix[4]arenes.

Calix[*n*]arenes are a class of cavity-shaped macrocycles composed of *n* molecules of phenol and *n* molecules of formaldehyde. The X-ray crystallographic studies of calix[*n*]arenes have been continuously reported by Atwood *et al.*,¹⁻⁴ Andreetti *et al.*,⁴⁻⁸ and others.^{9,10} In calix[*n*]arenes there exist four possible conformational isomers: cone, partial cone, 1,2-alternate and 1,3-alternate, but the previous examples have exclusively dealt with the cone conformation. In particular, X-ray crystallographic studies of the 1,2- and 1,3-alternate conformers are very limited.¹¹ The trend is associated with the ease of the synthesis of cone conformers and with the extreme difficulty of the synthesis of 1,2- and 1,3-alternate conformers.¹² With regard to the 1,3-alternate conformation, there exists only one example: 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetramethoxycalix[4]arene, the conformation of which is not immobilized,^{11,13-15} was crystallized as a complex with EtAlCl₂ to give a 1,3-alternate conformer.† It is known that calix[4]arenes with a cone-shaped cavity are capable of including small guest molecules.¹⁻¹⁰ One can expect, however, that there exists a rich inclusion chemistry and a novel stereochemistry for the conformations other than cone. This encouraged us to attempt X-ray crystallographic studies on conformational isomers other than cone.¹⁵

Previously, we allowed 25,27-dihydroxy-26,28-bis(2-pyridylmethoxy)-5,11,17,23-tetra-*tert*-butylcalix[4]arene (**1**) to react with ethyl bromoacetate in *N,N*-dimethylformamide (DMF) in the presence of K₂CO₃.¹⁶ On TLC separation we observed two major spots and one minor spot. The two major spots were identified as the cone and partial cone conformations of 25,27-bis(ethoxycarbonylmethoxy)-26,28-bis(2-pyridylmethoxy)-5,11,17,23-tetra-*tert*-butylcalix[4]arene (**2**) by ¹H NMR spectroscopy, but the minor spot remained unidentified because of the low yield.¹⁶ We repeated this reaction and collected the minor spot: the ¹H NMR spectrum of the sample thus obtained

established that this compound adopts a 1,3-alternate conformation, a rare conformation among calix[4]arenes. In this paper, we report a rare example of the X-ray crystallographic study of the 1,3-alternate calix[4]arene.

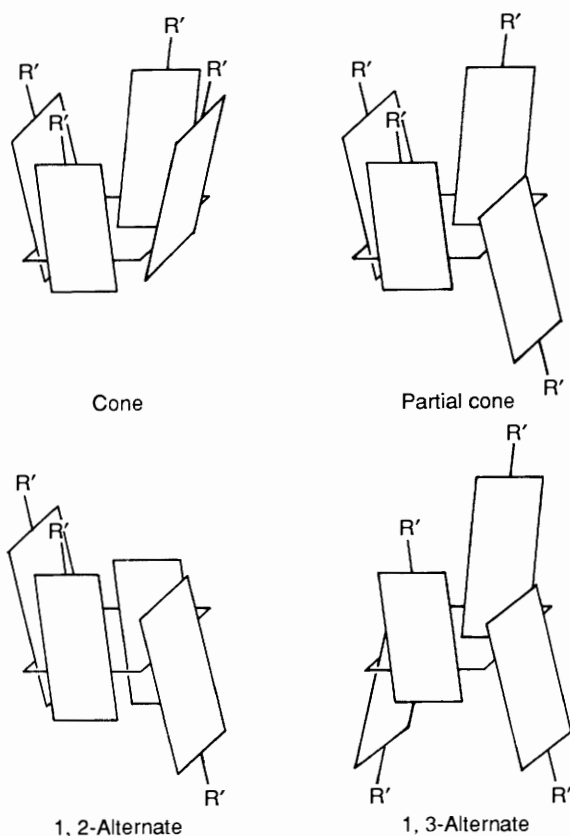
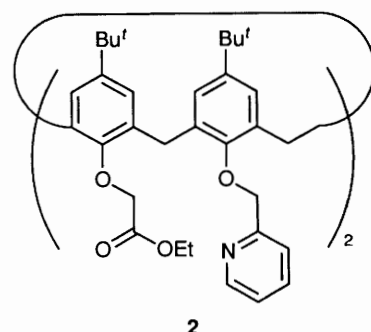
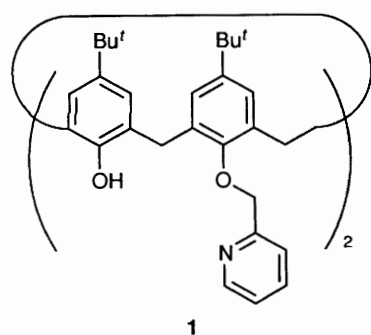
Experimental

Syntheses.—Compound **2** was synthesized from compound **1** by two different methods: (i) the reaction with ethyl bromoacetate in DMF (dimethylformamide) in the presence of K₂CO₃ and (ii) the reaction with ethyl bromoacetate in acetone in the presence of Cs₂CO₃.

Method (i). Compound **1** (1.5 g; 1.8 mmol) was treated with ethyl bromoacetate (3.0 g; 18 mmol) in the presence of K₂CO₃ (11 g) in anhydrous DMF at 75 °C for 14 h. After cooling, the reaction mixture was poured into chloroform, washed with water, and dried over MgSO₄. The solution was concentrated *in vacuo*, the residue being subjected to TLC separation [silica gel, hexane-ethyl acetate (3:2 v/v)]. The spots at R_f = 0.15 (m.p. 144–145 °C, yield 32%) and R_f = 0.60 (m.p. 211–213 °C, yield 7.7%) were identified as cone-**2** and partial-cone-**2**, respectively.¹⁶ The remaining spot at R_f = 0.75 was 1,3-alternate-**2**; yield 1.1%, m.p. 271–273 °C; ν_{max}(Nujol)/cm⁻¹ 1770 (C=O) and no ν_{OH}; δ_H(CDCl₃, 30 °C) 0.78 and 1.27 (Bu^t, 2 × s, 18 H each), 1.17 (CH₃, t, 6 H), 3.40 (OCH₂CO, s, 4-H), 3.66 and 4.05 [ArCH₂Ar, 2 × d (J 16), 4 H each], 4.05 (COOCH₂, q, 4 H), 4.76 (OCH₂Py, s, 4 H), 6.71 and 7.13 (ArH, 2 × s, 4 H each), 6.58, 7.17, 7.60 and 8.51 (PyH, m, d, m, d, respectively, 2 H each). (Found: C, 76.2; H, 7.95; N, 2.55. C₆₄H₇₈N₂O₈ requires C, 76.62; H, 7.84; N, 2.79%).

Method (ii). Compound **1** (4.42 g; 5.32 mmol) and Cs₂CO₃ (17.3 g; 26.6 mmol) in anhydrous acetone (300 cm³) were heated under reflux for 1 h under a nitrogen stream. To this solution was added ethyl bromoacetate (8.88 g; 53.2 mmol) and the reflux heating was continued for 3 h. After cooling, the mixture was poured into water, the precipitate being collected by filtration. The solid was dissolved in chloroform. The chloroform solution was washed with water and dried over MgSO₄. After filtration, the filtrate was concentrated under reduced pressure, the residual solid being subjected to TLC separation [silica gel, hexane-ethyl acetate (3:2 v/v)]. We thus obtained 1,3-alternate-**2** in 42.7% yield and partial-cone-**2** in 18.0% yield. The

† Atwood and Bott briefly describe in their review article that tetrasodium 5,11,17,23-tetrasulfonato-25,26,27,28-tetramethoxycalix[4]arene is crystallized from water as a 1,3-alternate conformer (see Ref. 10). We also found that this calix[4]arene and 5,11,17,23-tetrakis(trimethylammoniomethyl)-25,26,27,28-tetramethoxycalix[4]arene adopts the 1,3-alternate conformation in water (K. Sisido and S. Shinkai, to be submitted).



analytical data for 1,3-alternate-**2** are similar to those described in method (i).

X-Ray Analysis.—The crystals were grown in acetonitrile solvent. Crystal dimensions used were 0.2 mm radii. Integral intensities were collected by using graphite-monochromatized Cu-K α radiation by the ω -2 θ scan technique up to $2\theta = 120^\circ$. Two standard reflections were monitored every 7200 s and a 0.012% decrease in its intensity per hour was noted. Of the 8926 reflections measured, the number of reflections observed was 6530 [$I > 3\sigma(I)$], where σ is the standard deviation observed

Table 1 Crystal data

Chemical formula	C ₆₄ H ₇₈ N ₂ O ₈
<i>F</i> _w	1003.33
Crystal system	triclinic
Space group	<i>P</i> $\bar{1}$
Cell dimensions	
<i>a</i> /Å	14.0330(18)
<i>b</i> /Å	20.5253(27)
<i>c</i> /Å	11.0414(14)
α /deg	101.36(1)
β /deg	111.23(1)
γ /deg	81.72
<i>Z</i>	2
<i>D</i> _c /g cm ⁻³	1.150
<i>R</i> (%)	11.2

from the counting statistics]. The structure was solved by direct methods (MULTAN 78) and then refined by the full-matrix least-squares procedure with anisotropic thermal parameters. Hydrogen atoms were not included in refinement. The final *R* value was 11.2% and the final difference Fourier height maximum was 0.816 eÅ⁻³.

Results

The crystal data, bond lengths, bond angles and atomic coordinates of 1,3-alternate-**2** are summarized in Tables 1, 2, 3 and 4, respectively. The side view and top view of the ORTEP drawing are shown in Figs. 1 and 2, respectively. The unit cell containing two 1,3-alternate-**2** molecules is illustrated in Fig. 3. Full lists of bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details of the deposition scheme see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 2*, 1992, issue 1.

Discussion

The conformation of calix[4]arene derivatives can be readily identified by ¹H NMR spectroscopy: the ArCH₂Ar methylene protons provide the splitting patterns characteristic of each conformer. For example, the methylene protons in 1,3-alternate 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrapropoxycalix[4]-arene appear, as expected from its symmetry, as a singlet at 3.80 ppm (CDCl₃, 25 °C).^{12,15} The ¹H NMR spectrum of **2** was unaffected by temperature, indicating that the conformation is immobilized. The conformation which provides a pair of doublets for the ArCH₂Ar' methylene protons is ascribed either to cone-**2** or to 1,3-alternate-**2**. According to Gutsche,¹⁷ the $\Delta\delta$ value for a true cone is *ca.* 0.9 and becomes smaller when the phenol unit is flattened. The methylene protons in 1,3-alternate-**2** appear as a pair of doublets with $\Delta\delta = 0.39$. This supports the view that this methylene group is flanked by two *anti* phenyl units and this compound adopts a 1,3-alternate conformation.* The results also show that 1,3-alternate-**2** basically possesses C₂ symmetry in solution.

The X-ray analysis data showed a relatively large final difference Fourier height maximum (0.816 eÅ⁻³) and a relatively high *R* value (0.112). In the residual electron density we could not find any poly(nonhydrogen)atomic molecule. This implies that inclusion of solvent molecules does not occur, and if any, they are probably water molecules. On the other hand, it was very difficult to improve the *R* value further. Disorder was not

* The methylene protons in cone-**2** also appeared as a pair of doublets but the $\Delta\delta$ value (1.52) was much greater than that for 1,3-alternate-**2**, indicating that this methylene group is flanked by two *syn* phenyl units.

Table 2 Bond lengths (Å) with estimated standard deviations in parentheses

Atom 1-Atom 2	Distance	Atom 1-Atom 2	Distance	Atom 1-Atom 2	Distance
C(24)-O(4)	1.484(6)	C(40)-C(29)	1.524(6)	C(1)-C(2)	1.414(7)
C(24)-C(25)	1.488(9)	C(40)-C(41)	1.534(8)	C(1)-C(6)	1.396(6)
O(4)-C(23)	1.339(6)	C(26)-C(19)	1.522(7)	C(2)-C(3)	1.404(5)
O(13)-C(12)	1.398(11)	C(26)-C(27)	1.531(7)	C(3)-C(4)	1.401(6)
C(13)-N(1)	1.323(7)	C(21)-C(17)	1.514(6)	C(4)-C(5)	1.393(6)
C(12)-C(11)	1.412(12)	C(21)-C(59)	1.592(12)	C(5)-C(6)	1.384(5)
O(3)-C(23)	1.200(7)	C(21)-C(60)	1.507(10)	C(15)-C(16)	1.383(6)
C(23)-C(22)	1.478(7)	C(21)-C(61)	1.515(11)	C(15)-C(20)	1.405(7)
C(22)-O(2)	1.430(6)	C(47)-C(43)	1.531(6)	C(16)-C(17)	1.411(8)
O(2)-C(20)	1.403(5)	C(47)-C(62)	1.537(9)	C(17)-C(18)	1.390(8)
C(33)-C(31)	1.526(6)	C(47)-C(63)	1.540(10)	C(18)-C(19)	1.413(6)
C(33)-C(56)	1.526(9)	C(47)-C(64)	1.558(8)	C(19)-C(20)	1.387(7)
C(33)-C(57)	1.553(11)	O(5)-C(34)	1.466(8)	C(27)-C(28)	1.390(6)
C(33)-C(58)	1.500(11)	O(5)-C(28)	1.394(5)	C(27)-C(32)	1.395(6)
C(49)-C(48)	1.478(10)	C(34)-C(35)	1.495(7)	C(28)-C(29)	1.405(6)
C(49)-O(7)	1.300(8)	C(35)-N(2)	1.313(9)	C(29)-C(30)	1.378(6)
C(49)-O(8)	1.190(9)	C(35)-C(39)	1.405(10)	C(30)-C(31)	1.410(6)
C(48)-O(6)	1.431(7)	C(36)-C(37)	1.388(14)	C(31)-C(32)	1.405(6)
O(6)-C(46)	1.388(5)	C(36)-N(2)	1.359(9)	C(41)-C(42)	1.391(5)
C(7)-C(1)	1.532(6)	C(37)-C(38)	1.417(12)	C(41)-C(46)	1.402(7)
C(7)-C(54)	1.530(10)	C(38)-C(39)	1.400(8)	C(42)-C(43)	1.410(8)
C(7)-C(53)	1.488(12)	O(1)-C(8)	1.444(7)	C(43)-C(44)	1.388(7)
C(7)-C(55)	1.511(12)	O(1)-C(4)	1.391(4)	C(44)-C(45)	1.386(5)
C(14)-C(3)	1.515(6)	C(8)-C(9)	1.504(6)	C(45)-C(46)	1.387(7)
C(14)-C(15)	1.528(8)	C(9)-N(1)	1.335(9)	O(7)-C(51)	1.495(15)
C(50)-C(5)	1.534(6)	C(9)-C(10)	1.416(9)	C(51)-C(52)	1.36(2)
C(50)-C(45)	1.544(7)	C(11)-C(10)	1.394(8)		

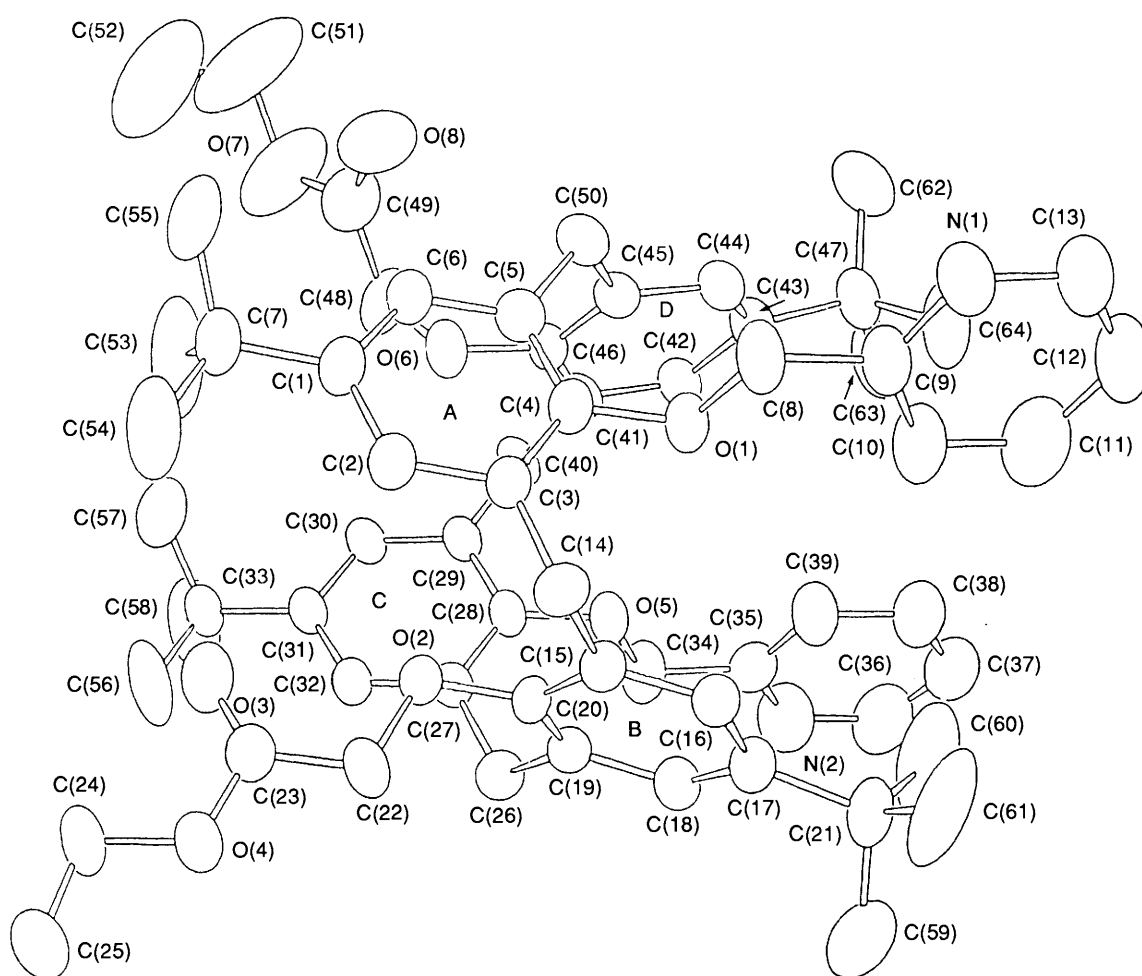
**Fig. 1** Side view of the ORTEP drawing of 1,3-alternate-2

Table 3 Bond angles (deg) with estimated standard deviations in parentheses

Atom 1-Atom 2- Atom 3	Angle	Atom 1-Atom 2- Atom 3	Angle
O(4)-C(24)-C(25)	107.2(5)	C(1)-C(7)-C(53)	109.5(5)
C(24)-O(4)-C(23)	117.2(4)	C(1)-C(7)-C(55)	110.5(5)
C(12)-C(13)-N(1)	122.5(7)	C(54)-C(7)-C(53)	104.7(7)
C(13)-C(12)-C(11)	118.7(6)	C(54)-C(7)-C(55)	110.5(6)
O(4)-C(23)-O(3)	122.2(4)	C(53)-C(7)-C(55)	108.7(7)
O(4)-C(23)-C(22)	109.6(4)	C(3)-C(14)-C(15)	112.9(4)
O(3)-C(23)-C(22)	128.2(5)	C(5)-C(50)-C(45)	115.0(4)
C(23)-C(22)-O(2)	109.2(4)	C(29)-C(40)-C(41)	114.8(4)
C(22)-O(2)-C(20)	110.3(3)	C(19)-C(26)-C(27)	114.9(5)
C(31)-C(33)-C(56)	111.7(5)	C(17)-C(21)-C(59)	109.0(5)
C(31)-C(33)-C(57)	108.5(5)	C(17)-C(21)-C(60)	111.1(5)
C(31)-C(33)-C(58)	109.5(5)	C(17)-C(21)-C(61)	113.5(5)
C(56)-C(33)-C(57)	105.3(6)	C(59)-C(21)-C(60)	108.3(7)
C(56)-C(33)-C(58)	113.4(6)	C(59)-C(21)-C(61)	102.5(6)
C(57)-C(33)-C(58)	108.2(7)	C(60)-C(21)-C(61)	111.9(6)
C(48)-C(49)-O(8)	109.7(7)	C(43)-C(47)-C(62)	107.2(4)
C(48)-C(49)-O(8)	129.1(6)	C(43)-C(47)-C(63)	112.9(5)
O(7)-C(49)-O(8)	121.1(7)	C(43)-C(47)-C(64)	109.9(4)
C(49)-C(48)-O(6)	112.5(6)	C(62)-C(47)-C(63)	109.9(5)
C(48)-C(35)-C(46)	115.6(3)	C(62)-C(47)-C(64)	110.0(6)
C(1)-C(7)-C(54)	112.7(5)	C(63)-C(47)-C(64)	107.0(5)
C(34)-O(5)-C(28)	111.8(4)	C(50)-C(5)-C(4)	122.8(3)
O(5)-C(34)-C(35)	108.6(6)	C(50)-C(5)-C(6)	118.5(4)
C(34)-C(35)-N(2)	112.5(6)	C(4)-C(5)-C(6)	118.7(4)
C(34)-C(35)-C(39)	123.7(6)	C(1)-C(6)-C(5)	122.9(4)
N(2)-C(35)-C(39)	123.8(5)	C(14)-C(15)-C(16)	120.9(5)
C(37)-C(36)-N(2)	124.5(8)	C(14)-C(15)-C(20)	121.1(4)
C(36)-C(37)-C(38)	116.9(6)	C(16)-C(15)-C(20)	118.0(5)
C(37)-C(38)-C(39)	118.9(8)	C(15)-C(16)-C(17)	122.4(5)
C(8)-O(1)-C(4)	111.4(4)	C(21)-C(17)-C(16)	121.9(5)
O(1)-C(8)-C(9)	108.4(5)	C(21)-C(17)-C(18)	120.5(5)
C(8)-C(9)-N(1)	114.7(5)	C(16)-C(17)-C(18)	117.6(4)
C(8)-C(9)-C(10)	122.6(5)	C(17)-C(18)-C(19)	121.4(5)
N(1)-C(9)-C(10)	122.5(5)	C(26)-C(19)-C(18)	119.9(5)
C(12)-C(11)-C(10)	118.6(7)	C(26)-C(19)-C(20)	121.4(4)
C(7)-C(1)-C(2)	122.5(4)	C(18)-C(19)-C(20)	118.5(5)
C(7)-C(1)-C(6)	120.3(4)	O(2)-C(20)-C(15)	119.9(4)
C(2)-C(1)-C(6)	117.2(4)	O(2)-C(20)-C(19)	118.7(4)
C(1)-C(2)-C(3)	121.4(4)	C(15)-C(20)-C(19)	121.4(4)
C(14)-C(3)-C(2)	119.9(4)	C(26)-C(27)-C(28)	122.9(4)
C(14)-C(3)-C(4)	121.4(3)	C(26)-C(27)-C(32)	118.2(4)
C(2)-C(3)-C(4)	118.7(4)	C(28)-C(27)-C(32)	118.8(4)
O(1)-C(4)-C(3)	119.8(4)	O(5)-C(28)-C(27)	119.4(4)
O(1)-C(4)-C(5)	119.1(3)	O(5)-C(28)-C(29)	119.4(3)
C(3)-C(4)-C(5)	121.1(4)	C(27)-C(28)-C(29)	121.2(4)
C(40)-C(29)-C(28)	121.7(4)	C(42)-C(43)-C(44)	116.9(4)
C(40)-C(29)-C(30)	120.0(4)	C(43)-C(44)-C(45)	122.8(5)
C(28)-C(29)-C(30)	118.3(4)	C(50)-C(45)-C(44)	119.0(5)
C(29)-C(30)-C(31)	122.7(4)	C(50)-C(45)-C(46)	122.4(3)
C(33)-C(31)-C(30)	120.5(4)	C(44)-C(45)-C(46)	118.5(5)
C(33)-C(31)-C(32)	122.6(4)	O(6)-C(46)-C(41)	121.3(4)
C(30)-C(31)-C(32)	116.9(4)	O(6)-C(46)-C(45)	117.8(4)
C(27)-C(32)-C(31)	121.9(4)	C(41)-C(46)-C(45)	120.9(4)
C(40)-C(41)-C(42)	118.0(5)	C(49)-O(7)-C(51)	117.9(8)
C(40)-C(41)-C(46)	123.7(4)	O(7)-C(51)-C(52)	101.0(1)
C(42)-C(41)-C(46)	118.3(5)	C(13)-N(1)-C(9)	119.5(6)
C(41)-C(42)-C(43)	121.8(5)	C(9)-C(10)-C(11)	118.0(7)
C(47)-C(43)-C(42)	122.2(5)	C(35)-N(2)-C(36)	117.5(8)
C(47)-C(43)-C(44)	120.9(5)	C(35)-C(39)-C(38)	118.4(7)

found in the present crystal. Calix[4]arenes feature the structure in which benzene rings are linked by a central band and substituents are splayed out from the central axis like a skirt.^{15,18,19} This structure allows the facile molecular motion of terminal atoms. As shown in Fig. 1, in fact, O(7), C(51) and C(52) in an ester group and C(53), C(54), C(59), C(60) and C(61) in *tert*-butyl groups have very large vibration parameters. Similar vibrational characteristics of calix[4]arenes are seen in related systems.^{15,18,19} We thus consider that the difficulty in

Table 4 Atomic co-ordinates and their estimated standard deviations

Atom	x	y	z
C(24)	0.2263(5)	0.1385(3)	0.0407(6)
O(4)	0.3180(3)	0.1164(2)	0.1478(4)
C(13)	0.7064(5)	0.0559(4)	1.3027(6)
C(12)	0.8004(5)	0.0729(4)	1.3063(6)
O(3)	0.2775(4)	0.1970(3)	0.2920(4)
C(23)	0.3341(4)	0.1504(3)	0.2692(5)
C(22)	0.4277(4)	0.1211(3)	0.3624(5)
O(2)	0.4516(2)	0.1625(2)	0.4882(3)
C(33)	0.3323(4)	0.4063(3)	0.3707(5)
C(49)	0.2459(5)	0.4195(3)	0.8730(6)
C(48)	0.3339(4)	0.4155(3)	0.8277(6)
O(6)	0.3890(2)	0.3512(2)	0.8294(3)
C(7)	0.1207(4)	0.2091(3)	0.5635(5)
C(14)	0.4615(4)	0.0665(2)	0.6542(5)
C(50)	0.4041(4)	0.2585(2)	0.9997(4)
C(40)	0.5644(4)	0.4233(2)	0.8470(4)
C(26)	0.6235(4)	0.2281(2)	0.5061(5)
C(21)	0.8491(4)	0.0567(3)	0.7798(5)
C(47)	0.7449(4)	0.3463(3)	1.2904(5)
O(5)	0.6816(2)	0.3053(2)	0.7692(3)
C(34)	0.7724(4)	0.3342(3)	0.7729(6)
C(35)	0.8624(4)	0.3129(3)	0.8847(5)
C(36)	1.0358(5)	0.3158(5)	0.9870(8)
C(37)	1.0391(5)	0.2805(4)	1.0837(7)
C(38)	0.9455(5)	0.2582(4)	1.0748(7)
O(1)	0.5240(2)	0.1434(2)	0.9150(3)
C(8)	0.5186(4)	0.0977(3)	0.9961(5)
C(9)	0.6207(4)	0.0923(3)	1.1045(5)
C(11)	0.8028(5)	0.1020(4)	1.2019(8)
C(1)	0.2289(3)	0.1903(3)	0.6549(5)
C(2)	0.2937(3)	0.1376(2)	0.6159(5)
C(3)	0.3929(3)	0.1218(2)	0.7011(4)
C(4)	0.4276(3)	0.1597(2)	0.8268(4)
C(5)	0.3672(3)	0.2139(2)	0.8654(4)
C(6)	0.2692(3)	0.2276(2)	0.7796(4)
C(15)	0.5567(3)	0.0917(2)	0.6479(4)
C(16)	0.6540(4)	0.0665(2)	0.7172(4)
C(17)	0.7435(4)	0.0897(2)	0.7160(5)
C(18)	0.7317(4)	0.1435(2)	0.6513(5)
C(19)	0.6335(3)	0.1710(2)	0.5805(4)
C(20)	0.5481(3)	0.1415(2)	0.5728(4)
C(27)	0.5630(3)	0.2915(2)	0.5468(4)
C(28)	0.5929(3)	0.3273(2)	0.6736(4)
C(29)	0.5357(3)	0.3856(2)	0.7067(4)
C(30)	0.4536(4)	0.4096(2)	0.6080(4)
C(31)	0.4216(4)	0.3763(2)	0.4771(4)
C(32)	0.4773(4)	0.3160(2)	0.4503(4)
C(41)	0.5628(4)	0.3830(2)	0.9494(4)
C(42)	0.6486(4)	0.3816(2)	1.0630(4)
C(43)	0.6567(4)	0.3423(2)	1.1582(4)
C(44)	0.5782(4)	0.3013(2)	1.1291(4)
C(45)	0.4904(3)	0.3026(2)	1.0187(4)
C(46)	0.4809(3)	0.3465(2)	0.9334(4)
C(25)	0.2202(5)	0.0901(4)	-0.0810(6)
O(7)	0.1876(4)	0.4737(3)	0.8454(7)
C(54)	0.6904(6)	0.1629(5)	0.4308(9)
O(8)	0.2247(4)	0.3812(2)	0.9254(5)
C(53)	0.1171(7)	0.2763(4)	0.5300(9)
C(51)	0.1015(7)	0.4914(6)	0.898(1)
C(55)	0.0431(5)	0.2105(6)	0.6298(8)
C(52)	0.0193(9)	0.4770(9)	0.787(2)
C(62)	0.6994(5)	0.3793(4)	1.3973(6)
C(63)	0.8315(5)	0.3865(3)	1.2961(6)
C(64)	0.7936(5)	0.2749(3)	1.3157(7)
C(56)	0.3001(7)	0.3575(4)	0.2422(7)
C(57)	0.2373(6)	0.4196(6)	0.4153(8)
C(59)	0.9050(6)	0.0365(5)	0.6739(9)
C(58)	0.3590(7)	0.4717(4)	0.3553(8)
C(60)	0.9134(7)	0.1035(5)	0.894(1)
C(61)	0.8469(6)	-0.0098(4)	0.818(1)
N(1)	0.6203(4)	0.0635(3)	1.2027(5)
C(10)	0.7115(4)	0.1114(3)	1.0981(6)
N(2)	0.9487(4)	0.3329(4)	0.8895(6)
C(39)	0.8557(5)	0.2748(3)	0.9734(6)

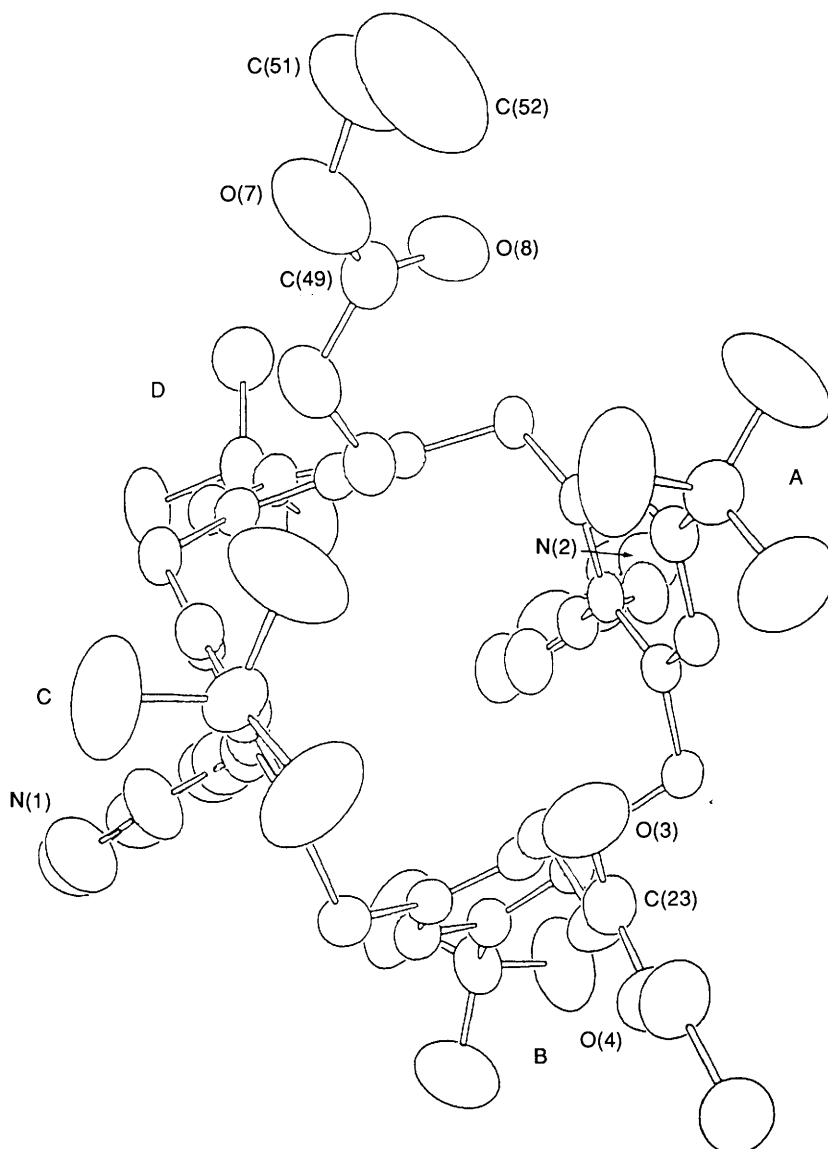


Fig. 2 Top view of the ORTEP drawing of 1,3-alternate-2

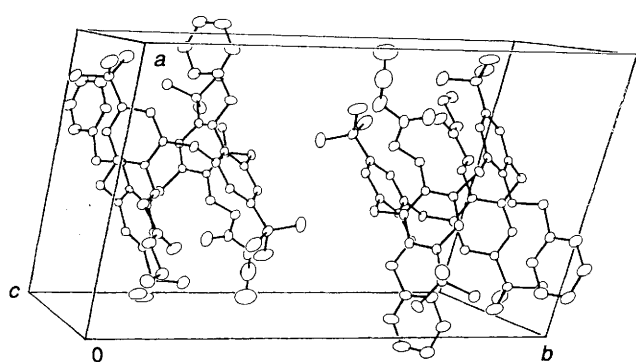


Fig. 3 Unit cell containing two 1,3-alternate-2 molecules

improving the R value is related to the large vibrational parameters.

The crystal structure of 1,3-alternate-2 is not as symmetrical as that in solution. It is seen from Fig. 2 that two pyridine nitrogens are turned towards the *exo*-annulus direction: the dihedral angles between the least-squares plane of the benzene ring and that of the pyridine ring are 104.4° for phenyl unit A

and 94.7° for phenyl unit C. Probably, this orientation is favoured because of electrostatic repulsion between lone pair electrons on the nitrogen atoms. In contrast, one of the two residual ester carbonyl groups (in phenyl unit B) is turned towards the *endo*-annulus direction with a dihedral angle of 92.4° between the least-squares plane of the benzene ring and that of the ester carbonyl group [$\text{CH}_2\text{-C}(\text{C}=\text{O})\text{O}$] whereas the other ester carbonyl group (in phenyl unit D) is turned towards the *exo*-annulus direction with a dihedral angle of 58.5° . We previously found, on the basis of ^1H NMR measurements, that when an equimolar amount of alkali metal cation such as Li^+ or Na^+ is mixed with 1,3-alternate-2, the metal cation is predominantly bound to the ester side, and not to the pyridine side.¹⁸ The crystal structure in Fig. 2 indicates that one ester group (in phenyl unit B) is already pre-organized so that it can bind the metal cation and another ester group (in phenyl unit D) is considerably mobile, as expected from the large temperature factors for O(7), C(51) and C(52) [$U(1,1) = 0.121, 0.140$ and 0.111 and $U(3,3) = 0.300, 0.43$ and 0.39 , respectively; see the large ellipsoids for these atoms in Fig. 2]. These structural features of 1,3-alternate-2 lead to the facile association of these two ester groups with alkali metal cations.

It is known that the dihedral angles between the four phenyl rings and the mean plane of the four methylene groups are

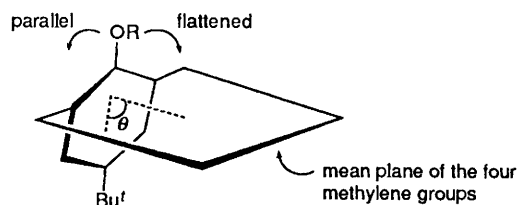


Fig. 4 Definition of the dihedral angle (θ) between a phenyl ring and the mean plane of the four methylene groups

markedly different among the four conformers of calix[4]arene derivatives and sensitively reflect their structural features. In cone calix[4]arenes with C_4 symmetry the dihedral angles are held at $121\text{--}125^\circ$.^{5-8,19} In 1,3-di-*O*-alkylated cone calix[4]arenes the two RO groups are more or less parallel to each other while the two OH groups are flattened (for the definition of the dihedral angle see Fig. 4).²² As a result, the dihedral angles for the RO-appended phenyl groups are $87\text{--}104^\circ$ while those for the OH-appended phenyl groups are $136\text{--}148^\circ$.²⁰ In a partial cone conformation, the dihedral angles for an inverted phenyl unit are $-83\text{--}-92^\circ$ and those for two phenyl units flanking the inverted phenyl unit are $85\text{--}95^\circ$.^{11,15,20} On the other hand, the dihedral angles for the residual phenyl unit which occupies the distal position to the inverted phenyl unit are $138\text{--}145^\circ$.^{11,15,20} The results show that three phenyl units are almost parallel while the residual phenyl unit is considerably flattened. What kind of structural features can we therefore expect for a 1,3-alternate confirmation? The computation of positional parameters resulted in the following dihedral angles between the four phenyl rings and the mean plane of the four methylene groups: 93.5° for phenyl unit A, 100.4° for phenyl unit B, 101.4° for phenyl unit C and 106.1° for phenyl unit D. The result implies that the four phenyl units in a 1,3-alternate conformation are characteristically parallel to each other. We previously estimated the most stable structure for 1,3-alternate 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetramethoxycalix[4]arene by a computational method.²¹ The dihedral angles between the four phenyl rings and the mean plane of the four methylene groups are $88.17\text{--}88.21^\circ$,²¹ indicating that in a 1,3-alternate conformation the parallel orientation minimizes the steric energy.

Also interesting are the ArCH₂Ar bond angles. Previous X-ray data show that those for a cone are $112\text{--}123^\circ$ and those for a partial cone are $111\text{--}112^\circ$.^{5-8,11,15,20} In 1,3-alternate-2, on the other hand, the ArCH₂Ar' bond angles are enlarged (although only slightly) to 112.9 , 114.8 , 114.9 and 115.0° . The bond angles estimated by a computer for 1,3-alternate 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetramethoxycalix[4]arene are $112.04\text{--}112.16^\circ$.²¹ At present, it is not clear if the enlarged bond angle is characteristic of a 1,3-alternate conformation or if this is just due to the bulky *O*-substituents in the present system.

In conclusion, the present study has demonstrated the first X-ray crystallographic analysis of a conformationally-immobilized 1,3-alternate calix[4]arene. The structural characteristics

are summarized as follows: (i) the four phenyl rings are more or less parallel to each other, (ii) the ArCH₂Ar bond angles are more expanded than those for other conformations and (iii) in contrast to the apparent C_2 symmetry in solution, 1,3-alternate-2 in the solid state is less symmetrical. The results may be of great significance in understanding the relative stability of the four possible conformational isomers of calix[4]arenes.

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Paper 1/05882G

Received 19th November 1991

Accepted 17th January 1992