Pergamon

Tetrahedron, Vol. 53, No. 47, pp. 16195-16204, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)10078-3

Conformational Control in the Synthesis of Mixed Tetraethers of Calix[4]arene. Part 2.

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Abstract: A series of mixed tetraethers of calix[4]arene and p-*tert*-butylcalix[4]arene in which two distal substituents are methyl and the other two 1-alkenyl groups with 3, 4 and 5 carbon atom chains have been prepared by two routes which differ in the order in which the groups (methyl or alkenyl) were introduced. The ethers of p-*tert*-butylcalix[4]arene were isolated as a mixture of cone (minor) and partial cone (major) conformations in dynamic equilibrium. For the ethers of calix[4]arene the conformational outcome depended on the method of synthesis. Up to three conformations could be detected: a cone, a partial cone with an anisyl unit inverted, and a partial cone with an alkenyl-bearing ring inverted. ^{1}H NMR analysis of the complexes formed between these ethers and alkali metal iodides showed that both cone and partial cone complexes of the p-*tert*-butylcalix[4]arene tetraethers could be detected with lithium iodide, but only cone complexes with the calix[4]arene derivatives. Sodium iodide complexes were also formed with both sets of compounds but in all cases only the cone complex was detected. © 1997 Elsevier Science Ltd.

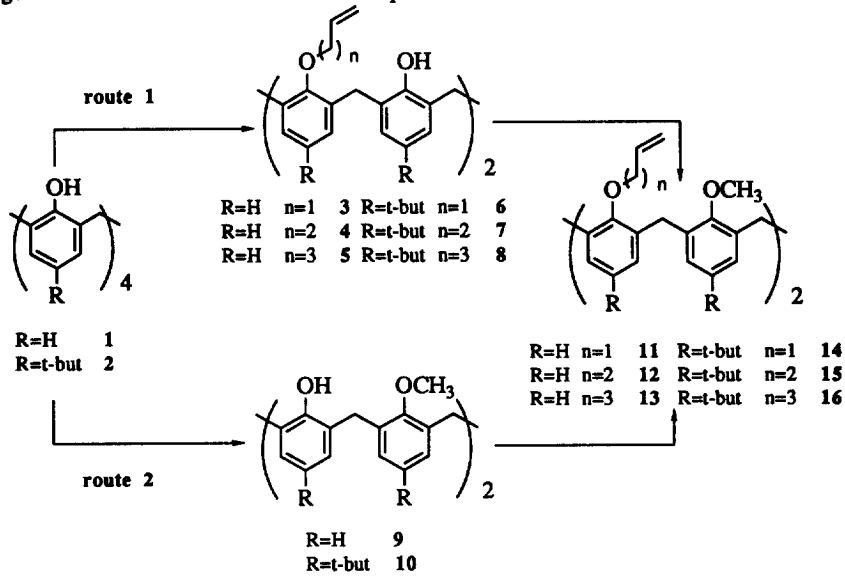
INTRODUCTION

In a recent paper[1] we described novel conformational aspects of the synthesis of mixed tetraethers of calix[4]arene **1**[2] in which two distal substituents were methyl acetates and the other two 1-alkenyl groups with 3-6 carbon atoms in the chain. The synthesis revealed that the final conformational outcome depended on the *order* in which the groups (alkenyl or acetate) were introduced on the lower rim. Conformational interconversion was not observed in any of the products, confirming that the substituents on the phenolic oxygen atoms were too large to pass through the calixarene annulus at ordinary temperatures. Cone (major) and 1,3-alternate (minor) conformations resulted when the alkenyl groups were introduced first followed by the ester groups, but when the order was reversed only partial cone conformers were formed. This difference was interpreted on the basis of a template effect operating at the fourth, and final alkylation stage and involving the sodium counterion of the base used in the alkylation. Additional features of these alkylation reactions have now been uncovered during a study on the conformational outcome of introducing methyl ethers in combination with alkenyl ethers on the lower rim of calix[4]arene **1** and its p-*tert*-butyl analogue **2**. This combination was chosen because one of the groups, the small methoxy group, is known to be capable of rotation through the annulus at room temperature[3] whereas the larger alkenyloxy group, as we showed earlier, is too large to allow rotation and consequently it freezes conformationally the aromatic subunit to which it is attached. p-*tert*-Butylcalix[4]arene **2** was included in the study to determine if there are any long range effects arising from the nature of the upper rim on the

conformational outcome. As we have shown elsewhere these mixed tetraether derivatives are useful building blocks for the synthesis of bridged and oligocalixarenes via ruthenium-catalysed olefin metathesis.[4]

RESULTS AND DISCUSSION

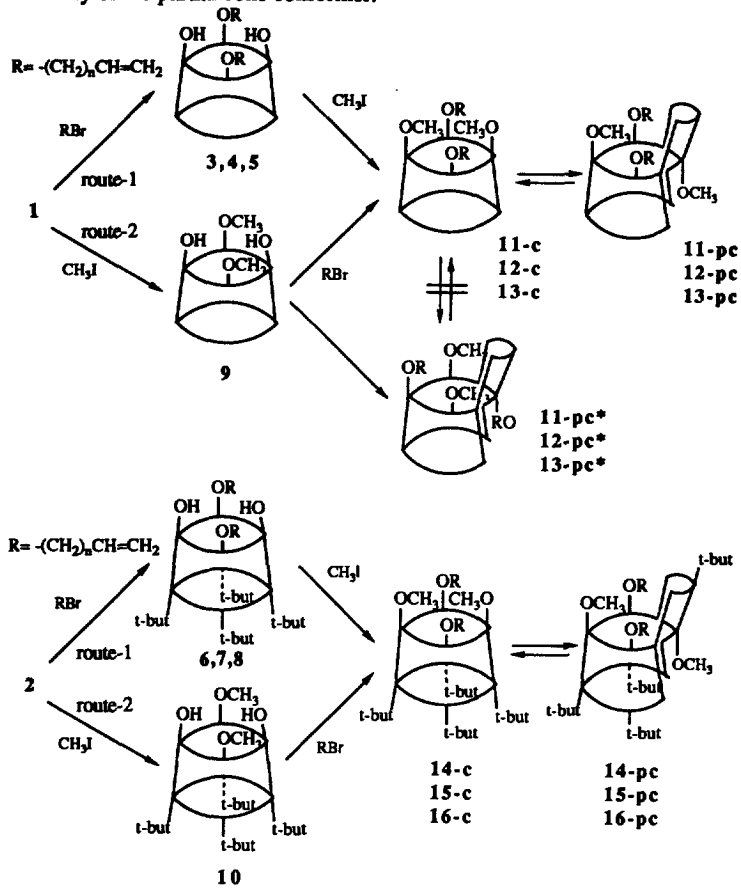
The compounds **11-16** discussed here possess an $A^{\alpha\beta}B^{\alpha}A^{\alpha\beta}B^{\alpha}$ patern, indicating that pairs of identical substituents are distal rather than proximal, i.e. diagonally opposite to each other with only the A substituent capable of rotation through the annulus. As before, the syntheses differ in the order in which the groups were introduced. Route-1 refers to the sequence of alkylation with the appropriate 1-alkenyl bromide (potassium carbonate in acetone) to afford diethers **3-5** from **1** and **6-8** from **2**, followed by dimethylation with methyl iodide (sodium hydride in THF) to afford the fully substituted tetraethers. Route-2 was the converse with dimethylation first (potassium carbonate in acetone) to form **9** from **1** and **10** from **2**, followed by dialkylation using the stronger base NaH in THF. These reaction sequences are summarised in Schemes 1 and 2.



Scheme 1

Whereas both methods produced identical results for the three ethers **14-16** in the p-*tert*-butyl series, this was not so for ethers **11**, **12** and **13** in the dealkylated series (vide infra). Ethers **14-16** were isolated as a mixture of cone (c) and partial cone (pc) conformers in dynamic equilibrium on the NMR time scale. The ^1H NMR spectrum of each compound between 0 and -60°C contained two distinct sets of resonances indicating the presence of these two conformers. The presence of different signals for each methoxy group indicated that the pc conformer was that with an anisyl subunit in the inverted position. Furthermore, the hydrogen atoms of the methylene groups adjacent to the oxygen atoms in the alkenyl chains in the pc conformer were clearly non-equivalent. Direct integration of the ^1H NMR signals showed that the pc conformer was the dominant component of the mixture at -60°C for all three tetraethers (Table 1), although the length of the alkenyl chain does have some influence on the isomer ratio in as much as the C_4 and C_5 homologs have slightly more preference for the cone

form than the C_3 counterpart. The behaviour of dialkyl ethers **6**, **7** and **8** on methylation is reminiscent of the behaviour of the corresponding 1,3-diethyl ether of p-*tert*-butylcalix[4]arene. Reinhoudt et al.[5] found that dimethylation of this compound in the cone conformation with methyl iodide in THF/DMF using sodium hydride as base furnished a 80:20 equilibrium mixture of partial cone and cone conformations, confirming the greater thermodynamic stability of the partial cone conformer.



Scheme 2

For ethers **11-13** the conformational outcome depends on the method of synthesis. Thus, when route-1 was employed, a mixture of cone (c) and partial cone (pc) conformers, again in a dynamic equilibrium, was produced and, as with tetraethers **14-16** above, the pc conformer was that with an anisyl subunit inverted. However, unlike the p-*tert*-butyl series, there is no longer a clear preference for the pc conformer at equilibrium (Table 1). Although the origin of the effects are unclear, the data indicate that a para-hydrogen substituent increases the stability of the cone conformation as does the length of the two alkenyl chains on the lower rim. However, when the same ethers, i.e. **11-13**, were synthesised by route-2 the results were rather different. In this case three conformational isomers were obtained, the c and pc conformers previously encountered in route-1 plus a new partial cone conformer, designated pc*, in which one of alkenyl-bearing aromatic moieties occupies the

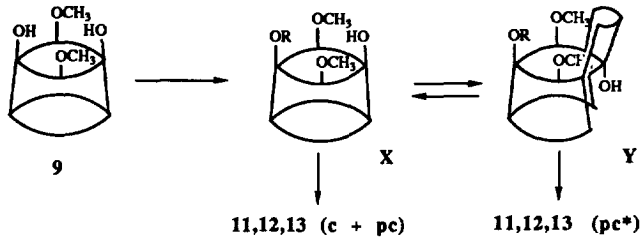
inverted position. For this third conformer the ^1H NMR spectrum exibited one signal for the two methoxy groups indicating that they were equivalent, but different signals for the two sets of methylene groups of the two alkenyl substituents consistent with one being in the inverted position. Further ^1H NMR measurements at different temperatures down to -60°C showed that the cone and the partial cone isomers were in a dynamic equilibrium with the pc conformation predominating for the diallyl derivative **11**, but of equal stability with the cone conformation for the longer chain derivative **12** and **13**. Thus, the trend observed earlier in Table 1 of a shift towards more cone conformer at equilibrium with increasing chain length is maintained. However, the proportion of the pc* conformer to the combined proportions of the other two conformers for **11-13** did not vary with temperature indicating that the former was not a participant in the equilibration of the latter. This fact confirms that over the temperature range measured the pc* conformations of **11-13** are fixed and incapable of isomerisation to other conformations as this would require passage of an alkenyl group through the annulus. For compounds **12** and **13** the pc* conformer was the major reaction product; for **11** it represented 50% of the total.

Table 1. Distribution of Conformational Isomers of Tetraethers **11-16** at -60°C as Function of Synthetic Route.

	compound	route	c		pc		pc*
From 2	**14**	1=2	15%	⇌	85%		—
	15	1=2	27%	⇌	73%		—
	16	1=2	25%	⇌	75%		—
From 1	**11**	1	25%	⇌	75%		—
	11	2	14%	⇌	36%	⇌	50%
	12	1	48%	⇌	52%		—
	12	2	9%	⇌	9%	⇌	82%
	13	1	55%	⇌	45%		—
	13	2	14%	⇌	14%	⇌	72%

As we have already mentioned, the conformational outcome of tetrasubstitution of calix[4]arenes on the lower rim can be influenced by several factors. In the examples presented here a combination of three factors may explain the results. When route-1 is used the dialkylated intermediates **6-8** and **3-5** are all produced as stable cone conformations, but this does not preclude conformational isomerization during further alkylation. For example, Gutsche and Reddy[6] have shown that while the 1,3-(distal)dibenzyl ether of **2** is conformationally fixed in the cone conformation, on further derivatization with benzyl bromide, non-equilibrating cone and partial cone tetrabenzyl ethers were produced. Since partial cone product requires ring inversion it was assumed that this only occurred with the aryl ring containing the free OH group. Applying the same assumption to the dimethylation of **6-8** and **3-5**, we can conclude that three products are possible, *viz.* cone, partial cone, and 1,3-alternate. In the event, the equilibrating mixture contains the more stable partial cone and cone conformers without detectable amounts of the 1,3-alternate form. This situation is obtained regardless of whether the para-substituent is *tert*-butyl or hydrogen. However, when route-2 was employed different mixtures of conformers were obtained depending, not on the conformations of the dimethyl ether intermediates **9** and **10** which were cone in both cases, but on the nature of the para-substituent. Whereas in the p-*tert*-butyl series routes 1 and 2 produced identical results, in the para-hydrogen series, route-2 follows two kinetically controlled pathways from a common

intermediate **X**, as shown in Scheme 3, one leading to a pair of cone and partial cone isomers and the other to a single but different partial cone isomer (pc*). For the former, one cannot deduce if there is a kinetic preference for either isomer in formation as the two are in dynamic equilibrium. While it is unclear as to how a para-hydrogen substituent promotes the pc* product formation this isomer must be derived from a trialkylated precursor with the final free OH group (or its anion) in the inverted position as in **Y** in Scheme 3. If one assumes a rapid reversible isomerisation between **X** and **Y** then the two sets of products simply reflect the relative rates of the final alkylation of **X** and **Y**, provided that the rate of inversion exceeds the rates of alkylation. The presence of para-hydrogen substituents may for steric reasons facilitate the alkylation of the OH in the inverted position, i.e. **Y**, leading to a preference for the pc* isomer. The para-hydrogen substituents may also promote the isomerisation of **X** to **Y** as there is less likelihood of solvent molecules being within the cavity of the calixarene compared with the *tert*-butyl counterpart.



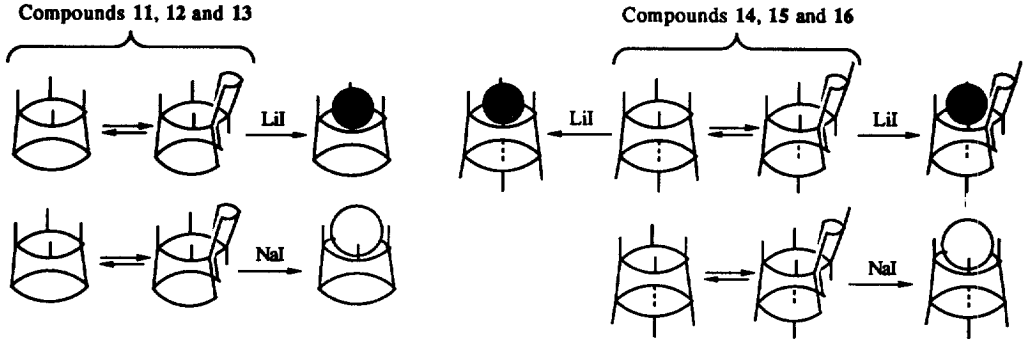
Scheme 3

Complexation Studies

In view of the conformational diversity of these new unsymmetrically substituted tetraethers it became of interest to examine their behaviour in complexation with alkali cations. Previous studies by Chang and Cho[7] have established that simple tetraalkyl derivatives of p-*tert*-butylcalix[4]arene, e.g. **2**, have the ability to extract Na^+ and K^+ ions from water into dichloromethane, though the extraction levels (6 and 3%) are significantly less than those observed with other oxygenated calix[4]arene derivatives.[8]

Blinx and Detellier[9] have examined the kinetics and mechanism of complexation of sodium tetraphenylborate by p-*tert*-butylcalix[4]arenetetramethyl ether in a mixture of chloroform and acetonitrile using ^{23}Na and ^1H NMR measurements. The results show the formation of a 1:1 complex with the calixarene fixed in the cone conformation, with exchange of the sodium cation between the solvated and complexed sites following a dissociation / recombination mechanism. In general, complexation processes with calixarenes can be conveniently followed by ^1H and /or ^{13}C NMR measurements as a consequence of the large spectral differences between the host and the complex. Solutions of each calixarene in $CDCl_3$ were treated with alkali iodide (excess). After several days at room temperature the heterogeneous mixture was filtered and the ^1H NMR spectrum recorded. The behaviour of compounds **14**, **15** and **16** (those with p-*tert*-butyl groups) shows that two types of Li^+ complexes are produced: one in which the calixarene is frozen in a cone conformation and a second in which the calixarene is in a partial cone conformation. These are shown iconographically in Scheme 4. The Li^+ pc complex is preferred. The larger Na^+ ion also forms complexes with ethers **14**, **15** and **16**, but only in the cone conformation. Thus, as the complexation process proceeds the equilibrium that exists between cone and pc conformation shifts in favour of the former. No ^1H NMR changes occurred with potassium iodide suggesting that this cation is too large to be accommodated by a calix[4]arene tetraether. In the case of compounds **11**, **12**

and **13** (obtained as a mixture of cone (c) and partial cone (pc) by route-1) cations Li^+ and Na^+ are both complexed by the cone conformer and again the equilibrium between cone and pc conformers shifts in favour of the former. Potassium ion is not complexed.



Scheme 4

From the experimental results it seems that Li^+ prefers to be allocated as a cone complex. In fact this is the only conformation obtained for the lithium complexes of compounds **11**, **12** and **13**. However, steric hindrance between the *tert*-butyl groups of compounds **14**, **15** and **16** may explain why partial cone complex is observed in these cases. Energies may be such that it is favourable to lose some binding energy of the 4-oxygen co-ordination sphere, in forming a 3-oxygen partial cone, in order to reduce the steric hindrance between the bulky alkyl groups. As there is none of this hindrance in compounds without *tert*-butyl groups it is preferential for the complexes to exist in the more stable 4-oxygen cone conformation sphere. Sodium can only be complexed by the 4-oxygen cavity, and therefore the equilibrium cone-partial cone moves to the former when the complexation takes place.

EXPERIMENTAL SECTION

Melting points were determined with an Electrothermal Reicter Melting Point apparatus. ^1H NMR spectra were recorded on General Electric QE 300 (^1H 300 MHz) and General Electric omega 500 (^1H 500 MHz) instruments with Me_4Si as internal standard. Spectrometric mass measurements (F.A.B.) were carried out with a V.G. Organic Autospec mass spectrometer using a L.S. I. M. S. source. Analytical TLC were performed on silica gel plates (SiO_2, Merck, 60 F_{254}), while silica gel 60 (SiO2, Merck, flash chromatography) was used for preparative column chromatography. Microanalyses were carried out by the Microanalysis Service of the School of Chemistry at The Queen's University of Belfast. Alkenyl bromides and methyl iodide were acquired from Aldrich and were used without further purification. Compounds **3-5** were prepared by a published procedure.[1]

Synthesis of 25,27-dialkenyl-26,28-dimethoxycalix[4]arene derivatives.

Route-1. Synthesis of 25,27-dialkenyl-26,28-dimethoxycalix[4]arenes 11-13.

In a 2-neck round-bottom flask **3**, **4** or **5** (1.4 mmol) was dissolved in 20 ml of dry THF. To this solution a large excess of NaH (5.68 mmol) and methyl iodide (5.68 mmol) were added. The mixture was stirred and refluxed under nitrogen. The progress of the reaction was monitored by silicaTLC. After cooling the mixture

some drops of water were added. The solvent was evaporated and the crude material dissolved in dichloromethane. The inorganic precipitate was separated by filtration and the organic solution washed with water and dried with $MgSO_4$. The solid obtained after removing the solvent was recrystallised from ethanol in the case of compound **11** or from dichloromethane-methanol for compounds **12** and **13** to yield a white crystalline solid. **11** (98%). m.p. 173-174°C., **12** (95%). m.p. 89-91°C., **13** (99%). m.p. 108-109 °C.

11: 2 isomers (c) n=1 + (pc) n=1, ^{1}H NMR -60°C($CDCl_3$): δ 7.35-6.38 (set of signals, ArH, 12H cone + 12H partial cone), 6.23 (m, -CH=, 2H cone), 6.10 (m, -CH=, 2H partial cone), 5.66 (dd, =CH, 2H cone, J=17Hz, J=2Hz), 5.56 (dd, =CH, 2H partial cone, J=17 Hz, J=2Hz), 5.31 (d broad, =CH, 2H cone + 2H partial cone), 4.39 (m, OCH_2, 2H partial cone), 4.34 (d, $ArCH_2Ar$, 4H cone, J=13Hz), 4.28 (d, OCH_2, 4H cone, J=4Hz), 4.17 (m, OCH_2, 2H partial cone), 4.03 (d, $ArCH_2Ar$, 2H partial cone, J=13Hz), 3.95 (s, OCH_3, 6H cone), 3.74 (s, OCH_3, 3H partial cone), 3.70 (s, $ArCH_2Ar$, 2H partial cone), 3.24 (d, $ArCH_2Ar$, 4H cone, J=13Hz), 3.15 (d, $ArCH_2Ar$, 2H partial cone, J=13Hz), 3.05 (s, OCH_3, 3H partial cone). Anal. Calcd. for $C_{36}H_{36}O_4$: C, 81.17, H, 6.81. Found: C, 81.21, H, 6.71.

12: 2 isomers (c) n=2 + (pc) n=2,^{1}H NMR -60°C($CDCl_3$): δ 7.36-6.36 (set of signals, ArH, 12H cone + 12H partial cone), 6.12 (m, -CH=, 2H cone), 6.00 (m, -CH=, 2H partial cone), 5.25-5.10 (m, =CH, 4H cone + 4 partial cone) , 4.33 (d, $ArCH_2Ar$, 4H cone, J=13Hz), 4.04 (d, $ArCH_2Ar$, 2H partial cone, J=13Hz), 3.93 (s, OCH_3, 6H cone), 3.90-3.63 (set of signals, OCH_2 4H cone, OCH_2 4H partial cone, $ArCH_2Ar$, 4H partial cone, OCH_3 3H partial cone), 3.23 (d, $ArCH_2Ar$, 4H cone, J=13Hz), 3.15 (d, $ArCH_2Ar$, 2H partial cone, J= 13Hz), 2.98 (s, OCH_3, 3H partial cone), 2.70-2.61 (m, CH_2, 4H cone + 4H partial cone). Anal. Calcd. for $C_{38}H_{40}O_4$: C, 81.39, H, 7.19. Found: C, 81.29, H, 7.25.

13: 2 isomers (c) n=3 + (pc) n=3,^{1}H NMR -60°C($CDCl_3$): δ 7.32-6.31 (set of signals, ArH, 12H cone + 12H partial cone), 5.93 (m, -CH=, 2H cone + 2H partial cone), 5.10 (m, =CH, 4H cone + 4 partial cone), 4.34 (d, $ArCH_2Ar$, 4H cone, J=13Hz), 4.06 (d, $ArCH_2Ar$, 2H partial cone, J=13Hz), 3.95 (s, OCH_3, 6H cone),3.73 (t, OCH_2, 4H cone, J=6Hz), 3.66 (set of signals, $ArCH_2Ar$ 4H partial cone, OCH_2 4H partial cone, OCH_3 3H partial cone), 3.21 (d, $ArCH_2Ar$, 4H cone, J=13Hz), 3.15 (d, $ArCH_2Ar$, 2H partial cone, J= 13Hz), 3.02 (s, OCH_3, 3H partial cone), 2.40 (m, CH_2, 4H cone), 2.30 (m, CH_2, 4H partial cone), 2.02 (m, CH_2, 4H cone), 1.75 (m, CH_2, 4H partial cone). Anal. Calcd. for $C_{40}H_{44}O_4$: C, 81.60, H, 7.53. Found: C, 81.61, H, 7.51.

Route-2. Synthesis of 25,27-dimethoxy-26,28-dihydroxycalix[4]arene ***9****.*

1 (1.18 mmol) was placed in a 2-neck round-bottom flask with 20 ml of dry acetone. To this mixture K_2CO_3 (2.36 mmol) and a large excess of methyl iodide (9.5 mmol) were added. The mixture was refluxed under nitrogen for 72 h. After cooling the reaction mixture was filtered and the solvent evaporated. The solid obtained was redissolved in dichloromethane and filtered again to separate the inorganic solid. After removing the solvent, the crude material was recrystallised from dichloromethane-methanol to yield compound **9** (75%).

9: ^{1}H NMR ($CDCl_3$): δ 7.75 (s, OH, 2H), 7.08 (d, ArH, 4H), 6.90 (d, ArH, 4H), 6.75 (m, ArH, 4H), 4.30 (d, $ArCH_2Ar$, 4H), 4.00 (s, OCH_3, 6H), 4.45 (d, $ArCH_2Ar$, 4H). MS (FAB): m/z 526 (M^++1).

Synthesis of 25,27-dialkenyl-26,28-dimethoxycalix[4]arenes ***11-13****.*

In a 2-neck round-bottom flask bearing a nitrogen atmosphere **9** (0.89 mmol) was dissolved in 15 ml of dry THF containing a large excess of NaH. To this mixture an excess of the corresponding alkenyl bromide (allyl bromide, 4-bromobutene or 5-bromopentene) was added. The mixture was refluxed 48 h for compound **11** and

72 h for compounds **12** and **13**. After cooling some drops of water were carefully added. The mixture was filtered and the inorganic solid was washed with an additional portion of dichloromethane. The organic phases were evaporated and the crude material redissolved in dichloromethane and washed with water. The organic phase was then dried with $MgSO_4$ and evaporated to dryness. In the case of compound **11**, the crude material was recrystallised from ethanol to obtain **11** as a white solid crystals (83%). m.p. 160-161°C. Compounds **12** and **13** were purified by cc (silica flash, hexane-ethyl acetate rising polarity from 2% to 6%). **12** (51%). m.p. 146-147°C. **13** (77%). m.p. 96-97°C. These three compounds obtained by route-2 showed similar microanalyses to the corresponding compounds obtained by route-1. TLC analysis showed separables spots for the conformationally fixed **11-13** pc* isomers.

11: 3 isomers (c) n=1 + (pc) n=1 + (pc*) n=1, ^1H NMR -60°C($CDCl_3$). Only listed are the signals corresponding to the pc*: δ 7.35-6.93 (set of signals, ArH, 12H), 5.90 (m, -CH=, 1H), 5.65 (m, -CH=, 1H), 5.17 (m, =CH, 2H), 4.94 (s+d, =CH, 2H), 4.24 (d, OCH_2, 2H, J=6Hz), 4.07 (d, $ArCH_2Ar$, 2H, J=13Hz), 3.98 (d, OCH_2, 2H, J=6Hz), 3.72 (d+d, $ArCH_2Ar$, H, J=13H), 3.63 (s, OCH_3, 6H), 3.15(d, ArCH2Ar, 2H, J=13Hz).

12: 3 isomers (c) n=2 + (pc) n=2 + (pc*) n=2, ^1H NMR -60°C($CDCl_3$). Only listed are the signals corresponding to the pc*: δ 7.38-6.35 (set of signals, ArH, 12H), 5.80 (m, -CH=, 2H), 5.26-4.96 (set of signals, =CH, 4H), 4.10 (d, $ArCH_2Ar$, 2H, J=13Hz), 3.63 (s, OCH_3, 6H), 3.61 (t, OCH_2, 2H, J=8Hz), 3.47 (t, OCH_2, 2H, J=8Hz), 3.15 (d, $ArCH_2Ar$, 2H, J=13Hz), 2.40 (m, CH_2, 2H), 2.12 (m, CH_2, 2H).

13: 3 isomers (c) n=3 + (pc) n=3 + (pc*) n=3, ^1H NMR -60°C($CDCl_3$). Only listed are the signals corresponding to the pc*: δ 7.31-6.20 (set of signals, ArH, 12H), 5.80 (m, -CH=, 2H), 5.07-4.91 (m, =CH, 4H), 4.01 (d, $ArCH_2Ar$, 2H, J=13Hz), 3.59 (s, OCH_3, 6H), 3.42 (t, OCH_2, 2H, J=7Hz), 3.38 (t, OCH_2, 2H, J=7Hz), 3.13 (d, $ArCH_2Ar$, 2H, J=13Hz), 2.01 (m, CH_2, 4H), 1.64 (m, CH_2, 2H), 1.52 (m, CH2, 2H).

Synthesis of 5,11,17,23-tetra-tert-butyl-25,27-dialkenyl-26,28-dimeyhoxycalix[4]arene dervatives.

Route-1. Synthesis of 5,11,17,23-tetra-t-butyl-25,27-dialkenyl-26,28-dihydroxy calix[4]arenes ***6-8***.

In a 2-neck round-bottom flask **2** (1.54 mmol) was dissolved in 15-20 ml of dry acetone. To this mixture K_2CO_3 (3.4 mmol) and the corresponding alkenyl bromide (allyl bromide for compound **6**, 4-bromobutene for compound **7** and 5-bromopentene for compound **8**) (5 mmol) were added. The mixture was refluxed under nitrogen for 72-120 h. The reaction was worked up in the same way as for products **3**, **4** and **5**. Compounds **6**, **7** and **8** were obtained as white crystalline solids. **6** (82%), **7** (80%), **8** (76.5%).

6: ^1H NMR ($CDCl_3$): δ 7.42 (s, OH, 2H), 7.10 (s, ArH, 4H), 6.80 (s, ArH, 4H), 6.22 (m, -CH=, 2H), 5.72 (d, =CH, 2H), 5.38 (d, =CH, 2H), 4.46 (d, OCH_2, 4H), 4.25 (d, $ArCH_2Ar$, 4H), 3.25 (d, $ArCH_2Ar$, 4H), 1.25 (s, t-but, 18H), 0.95 (s, t-but, 18H). MS (FAB): m/z 730 (M^++1).

7: ^1H NMR ($CDCl_3$): δ 7.55 (s, OH, 2H), 7.08 (s, ArH, 4H), 6.84 (s, ArH, 4H), 6.20 (m, -CH=, 2H), 5.28 (d, =CH, 2H), 5.16 (d, =CH, 2H), 4.25 (d, $ArCH_2Ar$, 4H), 4.05 (t, OCH_2, 4H), 3.30 (d, $ArCH_2Ar$, 4H), 2.76 (m, CH_2, 4H), 1.30 (s, t-but, 18H), 0.95 (s, t-but, 18H). MS (FAB): m/z 758 (M^++1).

8: ^1H NMR ($CDCl_3$): δ 7.80 (s, OH, 2H), 7.15 (s, ArH, 4H), 6.85 (s, ArH, 4H), 5.92 (m, -CH=, 2H), 5.20 (d, =CH, 2H), 5.05 (d, =CH, 2H), 4.30 (d, $ArCH_2Ar$, 4H), 4.00 (t, OCH_2, 4H), 3.30 (d, $ArCH_2Ar$, 4H), 2.50 (m, CH_2, 4H), 2.10 (m, CH_2, 4H), 1.30 (s, t-but, 18H), 1.00 (s, t-but, 18H). MS (FAB): m/z 786 (M^++1).

Synthesis of 5,11,17,23-tetra-t-butyl-25,27-dialkenyl-26,28-dimethoxy calix[4]arenes 14-16.

From products **6**, **7** and **8** an identical procedure to that for the synthesis of **11**, **12** and **13** (route-1) was followed. In each case the crude material was easily purified by recrystallisation from dichloromethane-methanol. **14** (98%). m.p. 189-190°C. **15** (65%). m.p. 154-155°C. **16** (82%). m.p. 168-169°C.

14: 2 isomers (c) n=1 + (pc) n=1,^{1}H NMR -60°C($CDCl_3$): δ 7.23 (s, ArH, 2H partial cone), 7.16 (s, ArH, 4H cone), 7.11 (s, ArH, 2H partial cone), 6.93 (d, ArH, 2H partial cone, J=2Hz), 6.56 (d, ArH, 2H partial cone, J=2Hz), 6.41 (s, ArH, 4H cone) 6.25 (m, -CH=, 2H cone), 6.09 (m, -CH=, 2H partial cone), 5.65 (d broad, =CH, 2H cone), 5.41 (d broad, =CH, 2H partial cone, J=16 Hz), 5.30 (d, =CH, 2H cone), 5.24 (d, =CH, 2H partial cone, J=11Hz), 4.36 (dd, OCH_2, 2H partial cone, J=12Hz, J=6Hz), 4.27 (d, $ArCH_2Ar$, 4H cone, J=13Hz), 4.24 (d, OCH_2, 4H cone, J=5Hz), 4.10 (dd, OCH_2, 2H partial cone, J=12Hz, J=6Hz), 4.02 (d, $ArCH_2Ar$, 2H partial cone, J=14Hz), 3.90 (s, OCH_3, 6H cone), 3.77 (d, $ArCH_2Ar$, 2H partial cone, J=14Hz), 3.70 (d, $ArCH_2Ar$, 2H partial cone, J=14Hz), 3.19 (s, OCH_3, 3H partial cone), 3.14 (d, $ArCH_2Ar$, 4H cone, J=13Hz), 3.09 (d, $ArCH_2Ar$, 2H partial cone, J=14Hz), 2.95 (s broad, OCH_3, 3H partial cone), 1.35 (s, t-but, 9H partial cone), 1.33 (s, t-but, 18H cone), 1.32 (s, t-but, 9H partial cone), 1.05 (s, t-but, 18H partial cone), 0,78 (s, t-but, 18H cone). Satisfactory analysis could not be obtained due to solvent retention.

15: 2 isomers (c) n=2 + (pc) n=2,^{1}H NMR -60°C($CDCl_3$): δ 7.28 (s, ArH, 2H partial cone), 7.18 (s, ArH, 4H cone), 7.10 (s, ArH, 2H partial cone), 6.95 (d, ArH, 2H partial cone, J=2Hz), 6.59 (d, ArH, 2H partial cone, J=2Hz), 6.41 (s, ArH, 4H cone) 6.12 (m, -CH=, 2H cone), 5.93 (m, -CH=, 2H partial cone), 5.21 (d, =CH, 2H cone, J=17Hz), 5.13 (d, =CH, 2H cone + 2H partial cone, J=17 Hz), 5.06 (d, =CH, 2H partial cone, J=10Hz), 4.28 (d, $ArCH_2Ar$, 4H cone, J=13Hz), 4.07 (d, $ArCH_2Ar$, 2H partial cone, J=13Hz), 3.97 (m, OCH_2, 2H partial cone), 3.92 (s, OCH_3, 6H cone), 3.82-3.72 (m, ArCH2Ar, 4H partial cone + OCH_2, 4H cone), 3.58 (m, OCH_2, 2H partial cone), 3.19 (s, OCH_3, 3H partial cone), 3.16 (d, $ArCH_2Ar$, 4H cone, J=13Hz), 3.11 (d, $ArCH_2Ar$, 2H partial cone, J=13Hz), 2.85 (s broad, OCH_3, 3H partial cone), 2.71 (m, CH_2, 4H cone), 2.64 (m, CH2, 4H partial cone), 1.42 (s, t-but, 9H partial cone), 1.35 (s, t-but, 18H cone), 1.33 (s, t-but, 9H partial cone), 1.06 (s, t-but, 18H partial cone), 0,79 (s, t-but, 18H cone). Anal. Calcd. for $C_{54}H_{72}O_4$: C, 82.61, H, 9.24. Found: C, 82.71, H, 9.00.

16: 2 isomers (c) n=3 + (pc) n=3,^{1}H NMR -60°C($CDCl_3$): δ 7.29 (s, ArH, 2H partial cone), 7.18 (s, ArH, 4H cone), 7.12 (s, ArH, 2H partial cone), 6.94 (d, ArH, 2H partial cone, J=2Hz), 6.55 (d, ArH, 2H partial cone, J=2Hz), 6.41 (s, ArH, 4H cone), 5.91-5.85 (m, -CH=, 2H cone + 2H partial cone), 5.12 (d, =CH, 2H cone, J=17Hz), 5.55 (d, =CH, 2H cone + 2H partial cone, J=17 Hz), 5.02 (d, =CH, 2H partial cone, J=11Hz), 4.28 (d, $ArCH_2Ar$, 4H cone, J=13Hz), 4.05 (d, $ArCH_2Ar$, 2H partial cone, J=13Hz), 3.95 (s, OCH_3, 6H cone), 3.86 (m, OCH_2, 2H partial cone), 3.73 (m, ArCH2Ar, 4H partial cone + OCH_2, 4H cone), 3.53 (m, OCH_2, 2H partial cone), 3.20 (s, OCH_3, 3H partial cone), 3.16 (d, $ArCH_2Ar$, 4H cone, J=13Hz), 3.11 (d, $ArCH_2Ar$, 2H partial cone, J=13Hz), 2.95 (s broad, OCH_3, 3H partial cone), 2.39-190 (5m, CH_2, 8H cone + 8H partial cone), 1.40 (s, t-but, 9H partial cone), 1.36 (s, t-but, 18H cone), 1.34 (s, t-but, 9H partial cone), 1.04 (s, t-but, 18H partial cone), 0,78 (s, t-but, 18H cone). Anal. Calcd. for $C_{56}H_{76}O_4$: C, 82.71, H, 9.42. Found: C, 82.84, H, 9.62.

Route-2. Synthesis of 5,11,17,23-tetra-t-butyl-25,27-dimethoxy-26,28-dihydroxycalix[4]arenes 10.

2 6.16 (mmol) was refluxed under nitrogen in 40 ml of dry acetone with K_2CO_3 (13.5 mmol) and an excess of methyl iodide (28 mmol). After 72 h the cooled reaction was filtered and the filtrate was concentrated, redissolved in dichloromethane and filtered again. The organic solution was then evaporated and the crude material was recrystallised from dichloromethane-methanol to obtain **10** as a white crystalline solid (86%).

10: ^{1}H NMR ($CDCl_3$): δ 7.18 (s, OH, 2H), 7.05 (s, ArH, 4H), 6.75 (s, ArH, 4H), 4.28 (d, $ArCH_2Ar$, 4H), 3.98 (s, OCH_3, 6H), 3.35 (d, $ArCH_2Ar$, 4H), 1.30 (s, t-but, 18H), 0.95 (s, t-but, 18H). MS (FAB): m/z 678 (M^++1).

Synthesis of 5,11,17,23-tetra-t-butyl-25,27-dialkenyl-26,28-dimethoxy calix[4]arenes ***14-16.***

From **10**, compounds **14**, **15** and **16** were obtained in the same way as **11**, **12** and **13** were from **9**. Purification was accomplished by recrystallisation from dichloromethane-methanol to yield the products as white crystalline solids. **14** (69%). **15** (45%). **16** (62%). The corresponding ^{1}H NMR of these compounds showed the same signals as those obtained for the same set of products by route-1 indicating that an identical mixture of conformers was present. These compounds showed similar microanalysis and identical melting point values to the corresponding compounds obtained by route-1.

ACKNOWLEDGEMENT

We thank D.E.N.I. for a Distinction award to J. K. B. and the EPSRC for a postdoctoral award to M. P.

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(*Received in UK* 25 *July* 1997; *revised* 15 *September* 1997; *accepted* 18 *September* 1997)