# Synthesis and Conformational Characteristics of Inherently Chiral Monoalkyl Ethers of *p-tert*-Butyldihomooxacalix[4]arene

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The synthesis of four inherently chiral monoalkyl ethers (methyl, ethyl, allyl, and benzyl), derived from *p-tert*-butyldihomooxacalix[4]arene, is described. Their conformational features were studied by variable temperature $^1$H NMR spectroscopy in solvents with different polarity, such as chloroform (or $CDCl_2CDCl_2$), acetone, DMSO, and pyridine. Coalescence temperatures and $\Delta G^{\ddagger}$ were determined in $CDCl_2CDCl_2$ and pyridine solutions. Monomethyl ether has a $T_c$ of 86 °C in $CDCl_2$-$CDCl_2$ and of −8 °C in pyridine, and the other derivatives are conformationally immobilized ($\Delta G^{\ddagger} \gg 20$ kcal mol$^{-1}$ in both solvents). The cone conformation, obtained for all monoethers, was confirmed by $^{13}$C and NOESY spectra and also from a series of NOE 1D experiments. Complete assignment of both proton and carbon NMR spectra was achieved for the monomethyl ether by a combination of COSY, HMQC, and selective INEPT experiments, in chloroform at room temperature. Inherent chirality for all compounds was demonstrated by the addition of Pirkle's reagent to $CDCl_3$ solutions of monoethers derivatives, causing duplication of the NMR proton signals.

## Introduction

Calixarenes are a versatile class of macrocyclic compounds, which after suitable functionalization of the edges can act as host−guest receptors and carriers.[1−3] One of the main interests in calixarenes as host molecules is their potential ability for chiral recognition. Chiral derivatives can be obtained by the introduction of chiral residues either at the upper or lower rim of the calixarene framework.[4−6] However, due to the nonplanarity of the molecule, calixarenes can display inherent chirality.[7] For calix[4]arenes, the most studied members of this family of compounds, intrinsic chirality can be attained with, at least, three different substituents at the lower rim (including the OH group) if the molecule adopts a cone conformation, and with a minimum of two different substituents if one of them is inverted.[8,9] Furthermore, the resulting chiral calix[4]arenes must be conformationally rigid, to be resolved into their enantiomers.

The large number of possible *O*-alkylation products of dihomooxacalix[4]arenes,[10−13] compounds where a methylene bridge (−$CH_2$−) is replaced by a dimethyleneoxa bridge (−$CH_2OCH_2$−), together with the lower symmetry of the molecule, results in more possibilities for getting chiral derivatives. Thus, a tetraalkylated dihomooxacalix[4]arene (Figure 1) may be inherently chiral if it exists in a partial cone conformation (totally asymmetric) or in the 1,2-alternate B or 1,3-alternate conformations ($C_2$ symmetry axis),[14] and if the OR group is big enough to suppress the oxygen-through-the-annulus conformational inversion. When the dihomooxacalix[4]arene adopts a

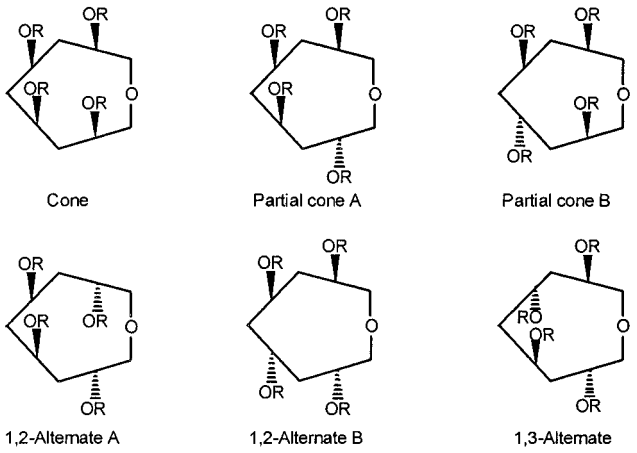


**Figure 1.** Conformations of dihomooxacalix[4]arenes.

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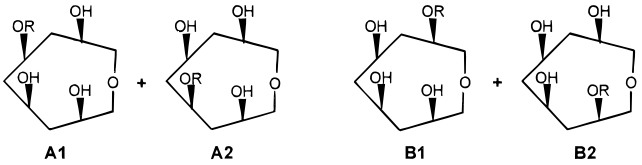
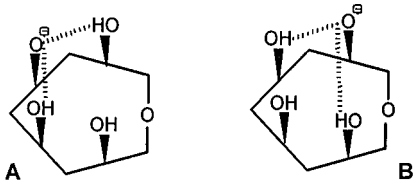


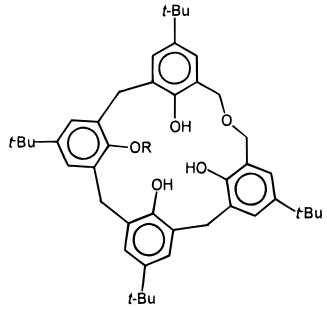

**Figure 2.** Possible enantiomers from racemic monoethers **1b**−**e** in the cone conformation.

**Scheme 1**




cone conformation, the intrinsic chirality can be attained with only two different substituents, including the OH group.

In this paper is reported the synthesis and characterization of four inherently chiral monoalkyl ethers (methyl **1b**, ethyl **1c**, allyl **1d**, and benzyl **1e**) of *p-tert*-butyldihomooxacalix[4]arene. Their conformational behavior was also studied by variable temperature $^1$H NMR spectroscopy.



| 1 | R |
|---|---|
| a | H |
| b | $CH_3$ |
| c | $CH_2CH_3$ |
| d | $CH_2CH{=}CH_2$ |
| e | $CH_2C_6H_5$ |

## Results and Discussion

**Synthesis.** Monoalkyl ethers of *p-tert*-butylcalix[4]arene have been synthesized by different methods,[15−18] but all monoethers **1b**−**e** were prepared by direct monoalkylation of *p-tert*-butyldihomooxacalix[4]arene **1a**, with 1 equiv of NaH and <2 equiv of alkyl halide in refluxing THF−DMF (10:1 v/v). This reaction yields a mixture of the monoalkylated product and the unreated **1a**. Separation by flash chromatography gives the racemic monoether **A1**+**A2** (Figure 2) in moderate yield.

An explanation for the preferential formation of racemate **A**, where the negative charge of the phenoxide anion formed is more strongly stabilized by the hydrogen bonds than in racemate **B**, is possibly the smaller distance between the phenoxide anion and the OH groups, in racemate A (Scheme 1).

**Conformational Behavior of Monoethers 1b−e.** Conversion of **1a** to its monoethers derivatives (**1b**−**e**) reduces drastically the conformational mobility, as a result of a combined effect of strong intramolecular hydrogen bonding with the steric hindrance of the OR groups. This reduction of conformational mobility increases with the size of the OR group.

**Table 1. Conformational Characteristics of *p-tert*-Butyldihomooxacalix[4]arene Monoethers**

| compound | conformation | $T_c$ (°C) | $\Delta G^{\ddagger}$ (kcal mol$^{-1}$)[a] | solvent |
|---|---|---|---|---|
| methyl (**1b**) | cone | 86 | 16.6 | $CDCl_2CDCl_2$ |
| | cone | 23 | 13.6 | acetone |
| | cone | −8 | 12.0 | pyridine |
| ethyl (**1c**) | cone | ≫130 | ≫20 | $CDCl_2CDCl_2$ |
| | cone | ≫110 | ≫20 | pyridine |
| allyl (**1d**) | cone | ≫130 | ≫20 | $CDCl_2CDCl_2$ |
| | cone | ≫110 | ≫20 | pyridine |
| benzyl (**1e**) | cone | ≫130 | ≫20 | $CDCl_2CDCl_2$ |
| | cone | ≫110 | ≫20 | pyridine |

[a] An average value of the rates of inversion ($K_c$) at the coalescence temperature for the different types of methylene groups ($CH_2OCH_2$ and $ArCH_2Ar$), was used in the determination of $\Delta G^{\ddagger}$.

In monoalkylated derivatives (**1b**−**e**) the strength of the hydrogen bonding is reduced comparatively with that of parent compound **1a**, but still effective as has been shown for monomethyl ether of *p-tert*-butylcalix[4]arene.[19,20]

The coalescence temperatures ($T_c$) and free energies of activation to conformational inversion ($\Delta G^{\ddagger}$) for the monoethers **1b**−**e** were determined, and the results are shown in Table 1.

All monoethers show a fixed conformation at room temperature, as inferred from the set of five AB quartets for the $CH_2$ bridge protons, in chloroform. The $^1$H NMR spectra also display four singlets for the *tert*-butyl groups, four pairs of doublets for the aromatic protons, and three sharp singlets for the OH groups.

Their $^{13}$C NMR spectra show a pattern containing 24 downfield resonances arising from the aromatic carbons, two midfield resonances arising from the methylene carbons $\boldsymbol{C}H_2O\boldsymbol{C}H_2$, and 11 upfield resonances arising from the quaternary carbons $\boldsymbol{C}(CH_3)$ (4 lines), the Me carbons of the *t*-Bu groups $C(\boldsymbol{C}H_3)$ (4 lines), and the methylene carbons $Ar\boldsymbol{C}H_2Ar$ (3 lines). For all monoethers **1b**−**e**, the three $Ar\boldsymbol{C}H_2Ar$ resonances appear in the range 30−33 ppm evidencing the cone conformation, according to the rule proposed by Mendoza.[21] The cone conformation was further substantiated by proton−proton correlations observed in the NOESY spectrum of **1b**. For the other derivatives, this conformation was also confirmed by a series of NOE 1D experiments.

The position of the alkyl group (enantiomers **A1**+**A2**) in monomethyl ether **1b** was achieved by exhaustive NMR studies. The other derivatives (**1c**−**e**) bear the OR groups in the same position, since their proton and $^{13}$C spectra are very similar to those of derivative **1b**.

The analogous monoethers from *p-tert*-butylcalix[4]arene[15,22] and from *p-tert*-butylcalix[5]arene[23] also show a cone conformation in solution.

Evidence of chirality for monoethers **1b**−**e** was provided by the addition of an excess of Pirkle's reagent, (*S*)-

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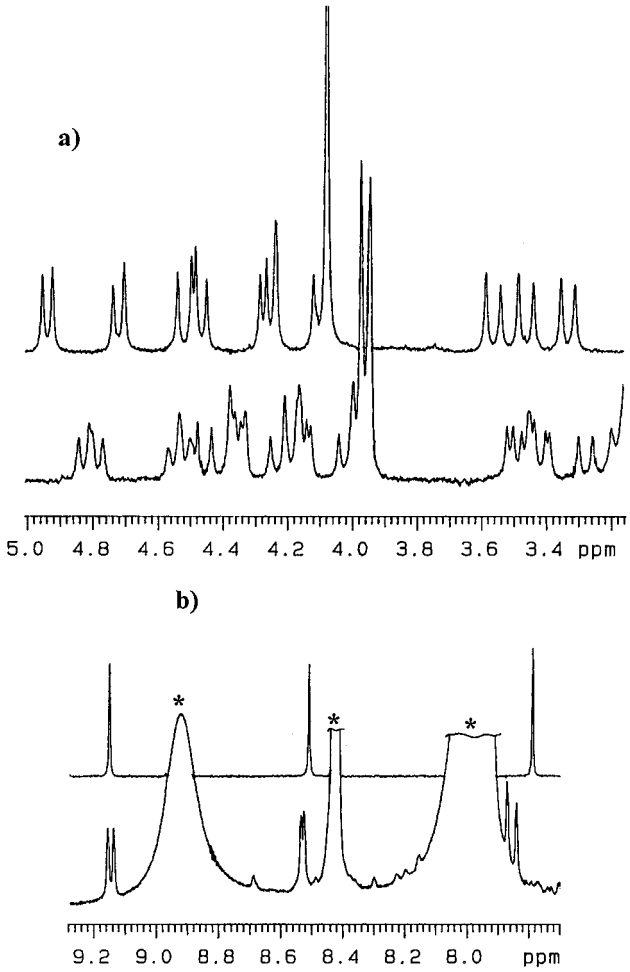


**Figure 3.** Partial 300 MHz $^1$H NMR spectra in $CDCl_3$ at 22 °C in the absence (top) or in the presence (bottom) of Pirkle's reagent (* Pirkle's peaks): (a) monomethyl **1b**, (b) monoallyl **1d**.

(+)-2,2,2-trifluoro-1-(9-anthryl)ethanol, to a $CDCl_3$ solution of each calixarene, causing duplication of proton signals. This effect was observed for all monoethers, although the complexity in some regions of the spectra do not allow the observation of separated signals. For example, the splitting patterns for the $CH_2$ or OH groups of compound **1b** and **1d**, respectively, are shown in Figure 3.

**Monomethyl Ether.** Compound **1b** shows, in chloroform at room temperature, a fixed cone conformation. As the temperature is raised, the five pairs of doublets arising from the $CH_2$ bridge protons in the $^1$H NMR spectrum broaden and then at 130 °C in $CDCl_2CDCl_2$ collapse into two sharp and one broad singlets (Figure 4a). In this solvent, derivative **1b** has a coalescence temperature of 86 °C corresponding to an energy barrier to conformational inversion ($\Delta G^{\ddagger}$) of 16.6 kcal mol$^{-1}$.

When the nonpolar solvents $CDCl_3$ or $CDCl_2CDCl_2$ are replaced by the more polar and basic solvent pyridine, the $T_c$ of **1b** falls to −8 °C, corresponding to a $\Delta G^{\ddagger}$ of 12.0 kcal mol$^{-1}$. The considerable lowering in $\Delta G^{\ddagger}$ value is the result of disruption of the intramolecular hydrogen bonding that contributes to hold the calixarene in the cone conformation. At 110 °C the conformational mobility is complete, as indicated by the five sharp singlets in a 1:1:1:1:1 ratio for the methylenic protons ($\delta$ 4.55, 4.47

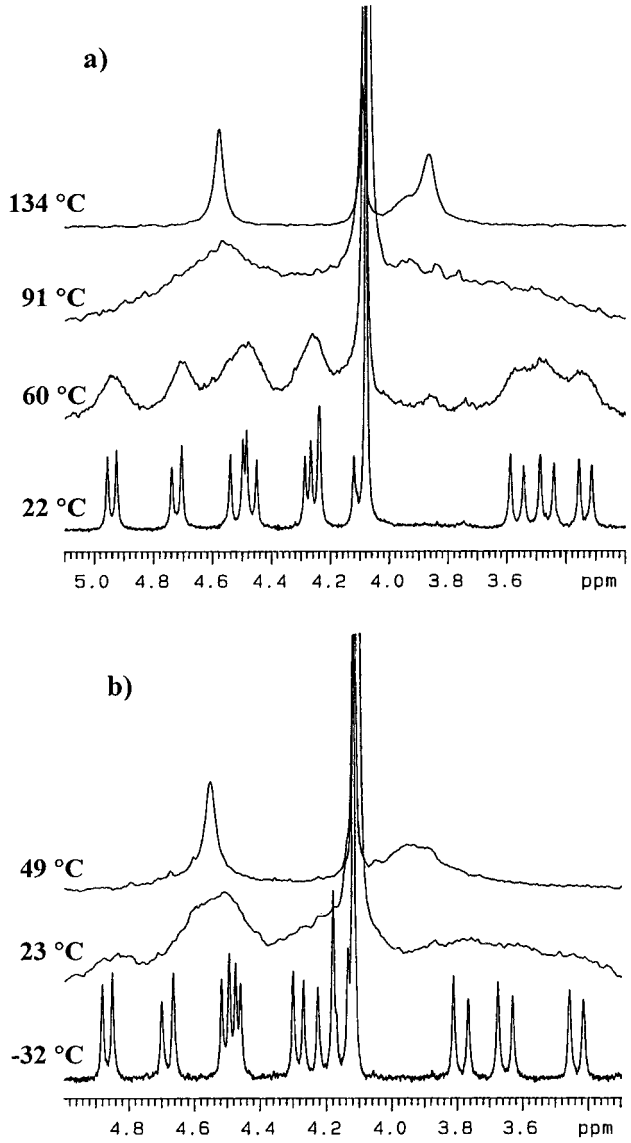


**Figure 4.** Variable temperature $^1$H NMR spectra of monomethyl ether **1b** at 300 MHz: (a) $CDCl_3$ or $CDCl_2CDCl_2$, (b) acetone.

for $CH_2OCH_2$, and 4.19, 4.13 and 4.12 for $ArCH_2Ar$) shown in Figure 5.

In acetone (Figure 4b), a solvent of medium polarity, the fixed cone conformation is reached at ca. −20 °C, as indicated by the same methylenic protons pattern. The coalescence temperature, in this solvent, is 23 °C and the corresponding $\Delta G^{\ddagger}$ 13.6 kcal mol$^{-1}$.

The assignment for both proton and carbon spectra (Table 2) was obtained from cross-peak correlations in the COSY spectrum (Figure 6) and by the analysis of a HMQC spectrum correlating directly bonded $^1$H and $^{13}$C nuclei. Identification of some quaternary carbons was done by selective INEPT, that correlates protons and carbons two or three bonds away.

The position of the methyl substituent in compound **1b** was deduced by proton−proton correlations observed in the NOESY spectrum, which have also confirmed the cone conformation of this derivative in chloroform at room temperature. Figure 7 shows the most relevant NOE enhancements used in these assignments.

**Monoethyl and Monoallyl Ethers.** Analysis of variable temperature $^1$H NMR spectra of both compounds

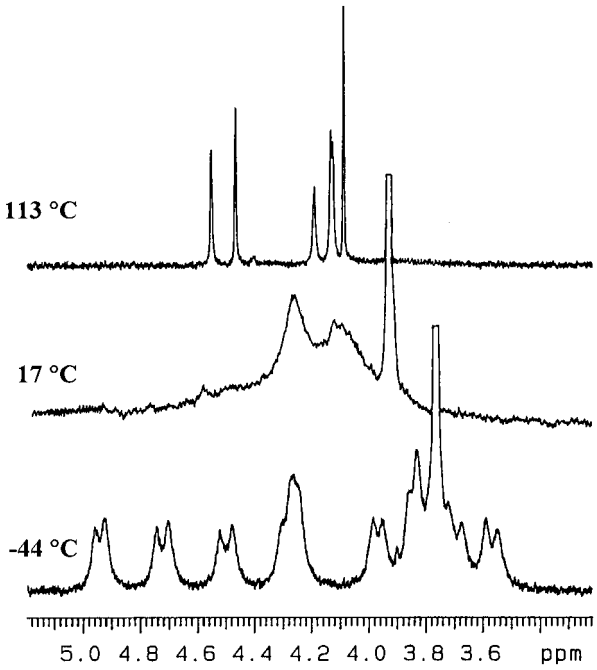


**Figure 5.** Variable temperature $^1$H NMR spectra of monomethyl ether **1b** in pyridine at 300 MHz.

**Table 2. Chemical Shifts ($\delta$) of Protons and Carbons of 1b**

| atom | $\delta_C$ | $\delta_H$ (eq), (ax) |
|---|---|---|
| 2 | 72.28 | 4.46, 4.72 |
| 4 | 71.75 | 4.25, 4.94 |
| 10 | 31.36 | 3.46, 4.27 |
| 16 | 32.57 | 3.56, 4.10 |
| 22 | 29.85 | 3.34, 4.52 |
| 6 | 125.69 | 6.98 |
| 8 | 128.15 | 7.30 |
| 12 | 125.89 | 7.13 |
| 14 | 125.48 | 7.11 |
| 18 | 125.19 | 7.08 |
| 20 | 126.76 | 7.04 |
| 24 | 127.41 | 7.30 |
| 26 | 123.56 | 6.90 |
| 7′ | 31.42 | 1.24 |
| 13′ | 31.50 | 1.24 |
| 19′ | 31.14 | 1.14 |
| 25′ | 31.60 | 1.28 |
| 27 | 152.63 | 7.86 |
| 28 | 150.56 | 4.08 |
| 29 | 147.74 | 9.20 |
| 30 | 151.25 | 8.52 |

**1c** and **1d** reveals that they are conformationally immobile calixarenes. Derivatives **1c** and **1d** show little change in their spectral patterns over the temperature ranges 20 to 130 °C in $CDCl_3$ or $CDCl_2CDCl_2$ and 20 to 110 °C in pyridine (Figure 8). This indicates a $T_c \gg 130$ °C and a $T_c \gg 110$ °C ($\Delta G^{\ddagger} \gg 20$ kcal mol$^{-1}$) for both compounds in $CDCl_2CDCl_2$ and pyridine, respectively. In DMSO the cone conformation of monoether **1d** remains unchanged up to temperatures as high as 120 °C, while for **1c** the $CH_2$ bridge doublets start to broaden at this temperature.

The very high energy barrier to conformational inversion in **1c** and **1d**, even in pyridine, indicates that the steric hindrance effect of the alkyl substituent and in a lesser extent the intramolecular hydrogen bonding play an important role in reducing the conformational mobility.

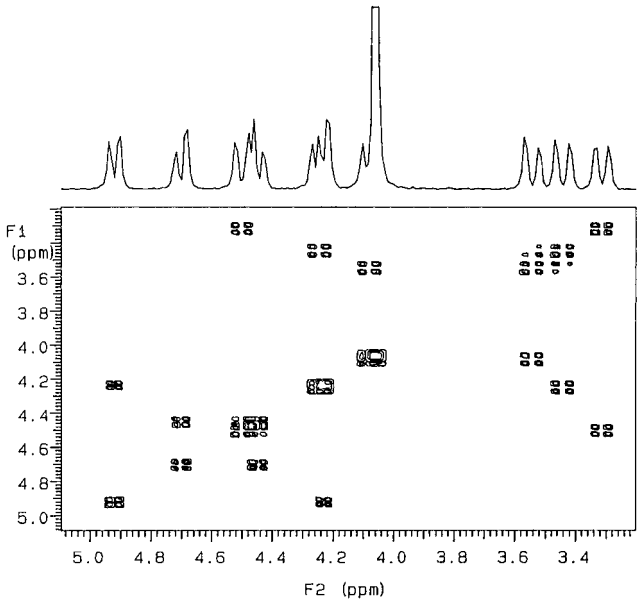


**Figure 6.** $^1$H NMR and COSY spectra of compound **1b** in $CDCl_3$ at 22 °C and 300 MHz.

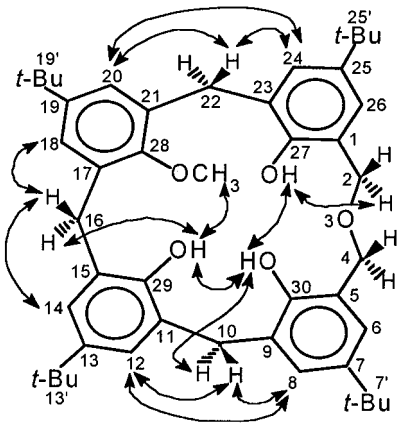


**Figure 7.** Relevant NOE enhancements used to prove the position of methyl group and the cone conformation in **1b**.

Reinhoudt *et al.*[20] found that the strength of the hydrogen bonds in partly methylated calix[4]arenes in the cone conformation is influenced by the exact geometry of the cone. In compound **1c**, saturation of the $CH_3$ protons of the ethyl group shows a much bigger NOE enhancement on the OH at $\delta$ 9.38 than on the OH at $\delta$ 7.86. This suggests a geometry of the cone conformation in which the $CH_3$ of the ethyl group points inside the cavity. The allyl group in compound **1d** must have a very similar orientation, since the OH group at $\delta$ 9.15 is the only that gives NOE effect on the protons of the allyl group.

**Monobenzyl Ether.** In a first synthesis of compound **1e**, using benzyl chloride as alkylating agent, >1 equiv of NaH and ca. 24 h of reflux, a mixture of the two monoethers **A** and **B** was obtained in a 1:1 ratio, even after flash and preparative chromatographies. This is confirmed by the proton spectrum, where the peaks of the two isomers **A** and **B** are seen (Figure 9). After eluting the preparative plate several times, monoether **A** was obtained pure.

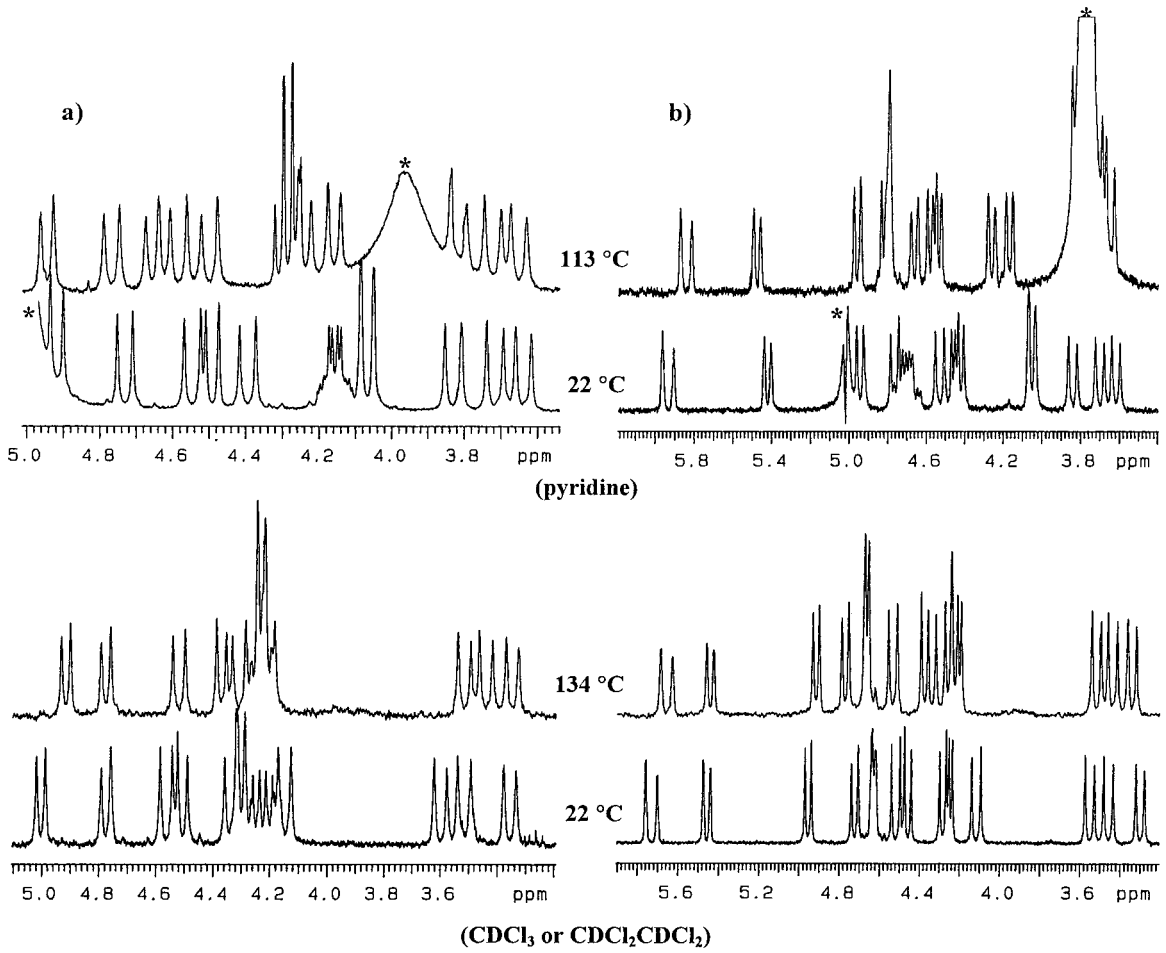


**Figure 8.** Variable temperature $^1$H NMR spectra at 300 MHz: (a) monoethyl ether **1c**, (b) monoallyl ether **1d**. (* Residual peak from saturation of water).

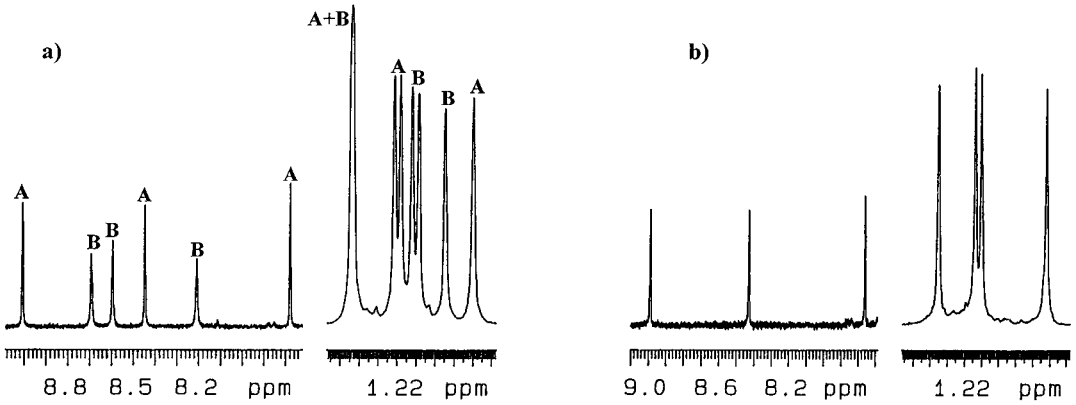


**Figure 9.** Partial 300 MHz $^1$H NMR spectra (OH and *t*-Bu regions) of monobenzyl ether **1e** in $CDCl_3$ at 22 °C. (a) Mixture of monoethers **A** and **B**, (b) Only monoether **A**.

In a second synthesis, using benzyl bromide and 1 equiv of NaH, a single pair of enantiomers (**A1**+**A2**) was obtained, as for the other monoethers.

Compound **1e** is also conformationally fixed and has $\Delta G^{\ddagger}$ values in either $CDCl_2CDCl_2$ or pyridine that are too high to be measured by variable temperature $^1$H NMR spectroscopy.

## Conclusions

The synthesis of monoethers **1b**−**e** only produced the pair of enantiomers **A1**+**A2**, which are seen in the $^1$H NMR spectra by the addition of Pirkle's reagent to the $CDCl_3$ solutions of each calixarene.

As for *p-tert*-butylcalix[4]arene, the introduction of just one methyl group in dihomooxacalix[4]arene **1a** reduces drastically the conformational mobility. With an alkyl group bigger than the methyl, the monoethers are conformationally fixed in a cone conformation, even in pyridine as solvent.

The very high energy barrier to conformational inversion in these monoethers is assumed to be mostly the result of steric hindrance effects of the alkyl group

substituent and in a lesser extent of intramolecular hydrogen bonding among the OH groups.

## Experimental Section

All chemicals were reagent grade and were used without further purification. Chromatographic separations were performed on Merck silica gel 60 (particle size 40−63 $\mu$m, 230−400 mesh). Melting points were measured on an Electrothermal 9200 apparatus and are uncorrected. $^1$H and $^{13}$C NMR spectra were recorded on a Varian Unity 300 spectrometer with TMS as internal reference. The NOE 1D difference spectra were acquired with a saturation delay of 5 s and 256 transients. The conventional COSY 45 and the phase sensitive NOESY experiments were collected as a 256 × 2K complex points. The NOESY spectrum was acquired with a mixing time of 1 s. The one bond HMQC spectrum was acquired with carbon decoupling, a delay in the BIRD pulse optimized for an average 145 Hz coupling, and as 256 × 2K complex points. The long-range delays in selective INEPT spectra were optimized for 8 Hz. All temperatures were corrected to MeOH or ethylene glycol, and the readouts are considered accurate to ±1 °C. FAB mass spectra were obtained on a VG Trio 2000 quadrupole instrument, using *m*-nitrobenzyl alcohol as a matrix.

**General Procedure for Monoalkylation of *p-tert*-Butyldihomooxacalix[4]arene (1a).** A suspension of 1 g (1.48 mmol) of *p-tert*-butyldihomooxacalix[4]arene (**1a**) and 0.059 g (1.48 mmol) of NaH (60% oil dispersion) in 55 mL of THF/DMF (10:1, v/v) was stirred in an atmosphere of $N_2$. After nearly 10 min, the alkylating agent (ca. 2.50 mmol, iodide for compounds **1b** and **1c**, and bromide for the other two) was added, and the reaction mixture was refluxed and stirred for nearly 15 h. After cooling, the solvent was evaporated, and the residue was poured into 100 mL of water. The material that precipitated was removed by filtration, washed with water, and then subjected to flash chromatography ($SiO_2$, eluent $CH_2Cl_2$/*n*-heptane, 2:1 ratio for **1b** that was progressively decreased until a 1:1 ratio for **1e**).

**7,13,19,25-Tetra-*tert*-butyl-28-methoxy-27,29,30-trihydroxy-2,3-dihomo-3-oxacalix[4]arene (1b).** It was obtained in 57% yield: mp 246−247 °C; $^1$H NMR ($CDCl_3$) $\delta$ 9.20, 8.52, 7.87 (3s, 3H, OH), 7.30 (2d, 2H, $J$ = 2.4 Hz, ArH), 7.13, 7.11, 7.09, 7.04, 6.97, 6.90 (6d, 6H, $J$ = 2.4 Hz, ArH), 4.94 (d, 1H, $J$ = 8.9 Hz, $CH_2OCH_2$), 4.72 (d, 1H, $J$ = 9.6 Hz, $CH_2OCH_2$), 4.52 (d, 1H, $J$ = 12.9 Hz, $ArCH_2Ar$), 4.47 (d, 1H, $J$ = 9.6 Hz, $CH_2OCH_2$), 4.27 (d, 1H, $J$ = 13.9 Hz, $ArCH_2Ar$), 4.25 (d, 1H, $J$ = 8.9 Hz, $CH_2OCH_2$), 4.10 (d, 1H, $J$ = 13.7 Hz, $ArCH_2Ar$), 4.08 (s, 3H, $OCH_3$), 3.56 (d, 1H, $J$ = 13.7 Hz, $ArCH_2Ar$), 3.46 (d, 1H, $J$ = 13.9 Hz, $ArCH_2Ar$), 3.34 (d, 1H, $J$ = 12.9 Hz, $ArCH_2Ar$), 1.28, 1.14 (2s, 18H, $C(CH_3)_3$), 1.24 (s, 18H, $C(CH_3)_3$); $^{13}$C NMR ($CDCl_3$) $\delta$ 152.6, 151.3, 150.6, 147.74, 147.70, 143.6, 142.5, 141.6, 132.7, 131.3, 128.5, 127.4, 126.62, 126.55, 122.6 (Ar), 128.2, 127.4, 126.8, 125.9, 125.7, 125.5, 125.2, 123.6 (ArH), 72.3, 71.8 ($CH_2OCH_2$), 63.5 ($OCH_3$), 34.2, 33.9 (***C***$(CH_3)_3$), 32.6 ($ArCH_2Ar$), 31.6, 31.5, 31.4, 31.1 (C(***C***$H_3)_3$), 31.4, 29.9 ($ArCH_2Ar$); MS *m*/*z* 692. Anal. Calcd for $C_{46}H_{60}O_5$: C, 79.73; H, 8.73. Found: C, 79.47; H, 8.76.

**7,13,19,25-Tetra-*tert*-butyl-28-ethoxy-27,29,30-trihydroxy-2,3-dihomo-3-oxacalix[4]arene (1c).** It was obtained in 36% yield: mp 247−248 °C; $^1$H NMR ($CDCl_3$) $\delta$ 9.38, 8.59, 7.86 (3s, 3H, OH), 7.36 (2d, 2H, $J$ = 2.2 Hz, ArH), 7.19, 7.16, 7.13, 7.09, 7.02, 6.94 (6d, 6H, $J$ = 2.2 Hz, ArH), 5.01 (d, 1H, $J$ = 9.4 Hz, $CH_2OCH_2$), 4.78 (d, 1H, $J$ = 9.9 Hz, $CH_2OCH_2$), 4.56 (d, 1H, $J$ = 12.7 Hz, $ArCH_2Ar$), 4.51 (d, 1H, $J$ = 9.9 Hz, $CH_2OCH_2$), 4.34 (d, 1H, $J$ = 13.6 Hz, $ArCH_2Ar$), 4.30 (d, 1H, $J$ = 9.4 Hz, $CH_2OCH_2$), 4.23 (m, 2H, $OCH_2CH_3$), 4.15 (d, 1H, $J$ = 13.5 Hz, $ArCH_2Ar$), 3.60 (d, 1H, $J$ = 13.5 Hz, $ArCH_2Ar$), 3.52 (d, 1H, $J$ = 13.6 Hz, $ArCH_2Ar$), 3.36 (d, 1H, $J$ = 12.7 Hz, $ArCH_2Ar$), 1.75 (t, 3H, $OCH_2CH_3$), 1.32, 1.19 (2s, 18H, $C(CH_3)_3$), 1.29 (s, 18H, $C(CH_3)_3$); $^{13}$C NMR ($CDCl_3$) $\delta$ 152.7, 151.3, 149.5, 147.9, 147.5, 143.5, 142.5, 141.5, 132.9, 131.4, 128.6, 127.5, 126.6, 122.7, 122.6 (Ar), 128.1, 127.4, 126.6, 125.9, 125.7, 125.5, 125.0, 123.6 (ArH), 72.3, 72.2 ($CH_2OCH_2$), 71.7 ($OCH_2CH_3$), 34.2, 33.9, (***C***$(CH_3)_3$), 32.9 ($ArCH_2Ar$), 31.6, 31.5, 31.4, 31.2 (C(***C***$H_3)_3$), 31.3, 30,0 ($ArCH_2Ar$), 15.4 ($OCH_2CH_3$); MS *m*/*z* 706. Anal. Calcd for $C_{47}H_{62}O_5$: C, 79.85; H, 8.84. Found: C, 79.73; H, 9.05.

**7,13,19,25-Tetra-*tert*-butyl-28-alloxy-27,29,30-trihydroxy-2,3-dihomo-3-oxacalix[4]arene (1d).** It was obtained in 51% yield: mp 209−210 °C; $^1$H NMR ($CDCl_3$) $\delta$ 9.15, 8.51, 7.79 (3s, 3H, OH), 7.30 (2d, 2H, $J$ = 2.4 Hz, ArH), 7.13, 7.10, 7.08, 7.04, 6.97, 6.89 (6d, 6H, $J$ = 2.4 Hz, ArH), 6.32 (m, 1H, HC═), 5.73 (m, 1H, trans $H_2C$═, $J$ = 17.1 Hz), 5.46 (m, 1H, cis $H_2C$═, $J$ = 10.5 Hz), 4.96 (d, 1H, $J$ = 9.3 Hz, $CH_2OCH_2$), 4.73 (d, 1H, $J$ = 10.1 Hz, $CH_2OCH_2$), 4.63 (m, 2H, $OCH_2C$═), 4.52 (d, 1H, $J$ = 12.8 Hz, $ArCH_2Ar$), 4.46 (d, 1H, $J$ = 10.1 Hz, $CH_2OCH_2$), 4.28 (d, 1H, $J$ = 13.7 Hz, $ArCH_2Ar$), 4.25 (d, 1H, $J$ = 9.3 Hz, $CH_2OCH_2$), 4.12 (d, 1H, $J$ = 13.5 Hz, $ArCH_2Ar$), 3.55 (d, 1H, $J$ = 13.5 Hz, $ArCH_2Ar$), 3.46 (d, 1H, $J$ = 13.7 Hz, $ArCH_2Ar$), 3.30 (d, 1H, $J$ = 12.8 Hz, $ArCH_2Ar$), 1.27, 1.14 (2s, 18H, $C(CH_3)_3$), 1.24 (s, 18H, $C(CH_3)_3$); $^{13}$C NMR ($CDCl_3$) $\delta$ 152.8, 151.3, 149.4, 147.8, 147.7, 143.5, 142.5, 141.5, 132.9, 131.4, 128.6, 127.4, 126.61, 126.56, 122.7, 122.6 (Ar), 132.5, 128.2, 127.4, 126.8, 125.9, 125.7, 125.5, 125.1, 123.6 (HC═ and ArH), 119.1 ($H_2C$═), 77.0 ($OCH_2C$═), 72.3, 71.7 ($CH_2OCH_2$), 34.2, 33.9 (***C***$(CH_3)_3$), 32.9 ($ArCH_2Ar$), 31.6, 31.5, 31.4, 31.2 (C(***C***$H_3)_3$), 31.4, 30.1 ($ArCH_2Ar$); MS *m*/*z* 718. Anal. Calcd for $C_{48}H_{62}O_5$: C, 80.18; H, 8.69. Found: C, 79.75; H, 8.74.

**7,13,19,25-Tetra-*tert*-butyl-28-benzoxy-27,29,30-trihydroxy-2,3-dihomo-3-oxacalix[4]arene (1e).** It was obtained in 32% yield: mp 155−156 °C; $^1$H NMR ($CDCl_3$) $\delta$ 8.99, 8.43, 7.76 (3s, 3H, OH), 7.66 (2d, 2H, $OCH_2ArH$), 7.48−7.38 (m, 3H, $OCH_2ArH$), 7.27, 7.26, 7.09, 7.06, 7.05, 7.04, 6.94, 6.87 (8d, 8H, $J$ = 2.5 Hz, ArH), 5.21 (d, 1H, $J$ = 11.5 Hz, $OCH_2Ar$), 5.06 (d, 1H, $J$ = 11.5 Hz, $OCH_2Ar$), 4.94 (d, 1H, $J$ = 9.3 Hz, $CH_2OCH_2$), 4.71 (d, 1H, $J$ = 10.3 Hz, $CH_2OCH_2$), 4.56 (d, 1H, $J$ = 12.9 Hz, $ArCH_2Ar$), 4.44 (d, 1H, $J$ = 10.3 Hz, $CH_2OCH_2$), 4.23 (d, 1H, $J$ = 9.3 Hz, $CH_2OCH_2$), 4.17 (d, 1H, $J$ = 13.8 Hz, $ArCH_2Ar$), 4.01 (d, 1H, $J$ = 13.5 Hz, $ArCH_2Ar$), 3.46 (d, 1H, $J$ = 13.5 Hz, $ArCH_2Ar$), 3.39 (d, 1H, $J$ = 13.8 Hz, $ArCH_2Ar$), 3.26 (d, 1H, $J$ = 12.9 Hz, $ArCH_2Ar$), 1.25, 1.21, 1.20, 1.12 (4s, 36H, $C(CH_3)_3$); $^{13}$C NMR ($CDCl_3$) $\delta$ 152.8, 151.2, 149.4, 147.81, 147.77, 143.4, 142.4, 141.5, 136.1, 132.9, 131.4, 128.5, 127.4, 126.5, 126.4, 122.7, 122.6 (Ar), 128.9, 128.5, 128.2, 127.4, 126.8, 125.8, 125.7, 125.5, 125.1, 123.6 (ArH), 78.5 ($OCH_2Ar$), 72.2, 71.7 ($CH_2OCH_2$), 34.2, 33.9 (***C***$(CH_3)_3$), 32.8 ($ArCH_2Ar$), 31.6, 31.5, 31.4, 31.2 (C(***C***$H_3)_3$), 31.3, 30.2 ($ArCH_2Ar$); MS *m*/*z* 768. Anal. Calcd for $C_{52}H_{64}O_5$: C, 81.21; H, 8.39. Found: C, 81.03; H, 8.28.

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