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Influence of laterally attached alkyl groups on the conformational behaviour of a basic calix[4]arene: combined NMR, molecular mechanics and X-ray study

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Three new calixarenes **3**–**5** featuring an alkyl residue of different chain lengths attached to one of the central ring methylene groups of the basic calix[4]arene **1** have been prepared. A systematic study that includes also the lower homologous compound **2** showing the effect of the alkyl substitution on the conformational behaviour of the calixarene framework in comparison with the unsubstituted parent compound **1** is reported. The application of special 2D NMR techniques, 2D-EXSY and ROESY methods at various temperatures establishes that calixarenes **2**–**5** adopt the *partial cone* conformation of lower symmetry and far less the symmetric *cone* and *1,2-alternate* conformations. In solution, they undergo a fast interconversion with relatively low activation energies of about 15 kcal/mol at room temperature. The conformer distribution is well reproduced by molecular mechanistic calculations (MMFF94), indicating the present conformers to assume the lowest steric energies. A single-crystal X-ray structure of the lateral ethyl derivative **2** corroborates these results, showing the molecule in a sterically favourable *partial cone* conformation.

Keywords: calixarenes; lateral substitution; synthesis; conformational study; solution 2D NMR measurements; X-ray crystal structure

Introduction

Calixarenes and their derivatives are an important class of compounds that have been extensively investigated regarding their supramolecular recognition properties during the past two decades (*1*). Calixarenes have also emerged as very attractive building blocks for the development of highly ingenious functional systems and devices (*2*). In both of these respects, much work has been dedicated to the synthesis of calixarenes modified on the upper and lower rims, giving rise to an enormous variety of compound structures (*3*). Homocalixarenes (*4*), thiacalixarenes (*5*) and others (*1*), where the bridging methylene units of the conventional calixarene framework are completely replaced by modifying organic groups or hetero-atoms, represent further currently studied yet rather well-known types of structural modifications of the calixarene family (*6*). By way of contrast, calixarenes featuring a substitution of only one of the methylene bridges are presently rare (*7*), although these laterally substituted calixarenes may open interesting aspects of calixarene chemistry including linked constructions of oligotopic receptors (*8*), as well as systems distinguished by particular anchoring of the calixarene to a specific target or support (*2*, *9*). As a result, the conformational behaviour of this particular compound type is also studied only fragmentarily in a few cases of modified tetrahydroxycalix[4]- and -calix[5]arenes (*7c,d*). This warrants dealing with the conformational property of laterally monosubstituted calixarenes more broadly. Hence, a series of calixarenes that feature a lateral substitution of alkyl groups of different chain lengths and include a well-known parent compound were considered for this purpose. The concrete system of compounds, which was chosen for this study, as specified in Figure 1, covers the tetra-*tert*-butyltetramethoxycalix[4]arene (**1**) as the reference and **2**–**5** as the test compounds. This shows an advantage since the conformational behaviour of **1** is known rather detailed from previous work (*10*). Moreover, for the synthesis of **2**–**5**, one can follow a literature method elaborated for calixarene **2** by Scully et al. (*7a*). The conformational properties of **2**–**5**, which are described here, were determined from a detailed solution NMR study. This involves measurements at various temperatures and uses special 2D NMR techniques to yield a full description of the conformer distribution and the free activation energies of conformational interconversion. We also report on the crystal structure of the corresponding laterally ethyl-monosubstituted calixarene **2**, being the first crystal structure of a laterally monosubstituted tetramethoxycalix[4]arene.

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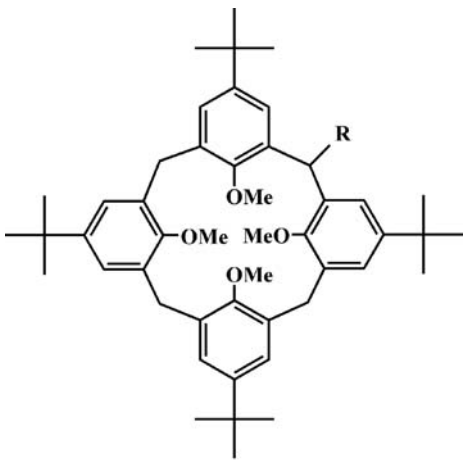


1 R = H
2 R = C_2H_5
3 R = *n*-C_3H_7
4 R = *n*-C_5H_{11}
5 R = *n*-$C_{10}H_{21}$

Figure 1. Compounds studied in this paper.

Results and discussion

Synthesis

Calixarene **1**, which is the basic compound for the synthesis of **2**–**5**, was obtained from a two-stage methylation reaction of 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrahydroxycalix[4]arene (*11*) using in a starting phase-transfer process sodium hydroxide, dimethyl sulphate and tetrabutylammonium bromide to yield the intermediate compound with two distal methyl groups, followed by treatment with sodium hydride and iodomethane in a final methylation step (*12*). A corresponding one-step methylation method of the parent tetrahydroxycalixarene with sodium hydride and iodomethane, described in the literature (*10a*, *13*), did not prove competitive in its result. The target calixarenes **2**–**5** featuring different laterally substituted alkyl groups were prepared by deprotonation of **1** with *n*-butyllithium and reaction with respective alkyl halides following the procedure described by Scully et al. (*7a*).

Conformational study

Conformational predominance and conformational flexibility are important structural parameters of a calixarene molecule, being decisive of its supramolecular behaviour both in solution and solid state (*1–3*). While the so-called *cone* conformation, providing a spacious cavity structure, is perhaps the most frequent conformation of the existing calixarenes (*1*, *14*), the other types of molecular conformations, including *partial cone*, *1,2-* and *1,3-alternate* conformations, are somewhat more rarely found though not less important for a designed purpose (*15*). As a rule, these conformations are mainly determined by the ring size or the nature and the space required for the substituents being present at the upper and lower rims of the calixarene molecule. Conformational property will also depend on the physical condition, including the type of the solvent as well as the presence of a proper guest molecule. However, in no manner, *O*-alkylated calixarenes that feature an alkyl residue laterally attached to one of the methylene groups of the central ring have been studied conformationally. Only analogous tetrahydroxycalixarenes were taken for a corresponding study (*7c,d*).

A well-known molecular structure is that of the tetra-*tert*-butyltetramethoxycalix[4]arene (**1**), which was chosen as the parent compound for the test. According to the NMR data (*10*), **1** in a solution of $CDCl_3$ exists in equilibrium of all four conventional conformers of which the *partial cone* conformation is the preferred one. A *partial cone* conformer is also reported for the solvent-free calixarene **1** (*16*) as well as for the furan (*17*) and dichloromethane (*18*) inclusion compounds in the solid state, while a corresponding sodium complex shows a *cone* conformation both in the crystal structure and in $CDCl_3/CD_3CN$ solution due to the coordination of the sodium ion (*10b*). Thus, it is clear that a potential change of the conformational behaviour in the present cases of calixarenes, in comparison with **1**, is attributed to the laterally substituted alkyl groups.

A complex pattern of signals in the NMR spectra of the alkyl-substituted calixarenes **2**–**5** in both $CDCl_3$ and tetrachloroethane-d_2 (TCl-d_2) at various temperatures indicates that the compounds exist in different conformers, as demonstrated exemplary for the lateral propyl derivative **3** in Figure 2. To minimise the signal broadening and to separate the overlapping region of methine and methylene signals, we carried out the NMR experiments at an optimised temperature of 269 K, yielding three different signals for the methine protons between 4.47 and 4.79 ppm in $CDCl_3$ for compounds **2**–**5**. Detailed 2D NMR measurements using COSY-, $^1H/^{13}C$-correlated HSQC (*19*), HMBC (*20*) as well as NOESY and ROESY experiments gave a full determination of conformers (specified in Figure 3; ^1H and ^{13}C chemical shifts are summarised in Tables S1–S4 of the Supplementary Material). A special denotation of the calixarene scaffold in the three observed conformations is illustrated in Figure 3, indicating similarities in the chemical shift for different pairs of atoms.

Depending on the alignment of the four arene units with reference to the lateral substituent, there are 16 different conformational isomers possible (Figure 4). Six of them are mirror images of each other resulting in identical NMR spectra. The 2D experiments show that the laterally substituted *n*-alkyl calixarenes, studied here, exist mainly in one *partial cone* conformation (*pacoD* in Figure 4), with an equatorial substituent between two *syn*-orientated arene

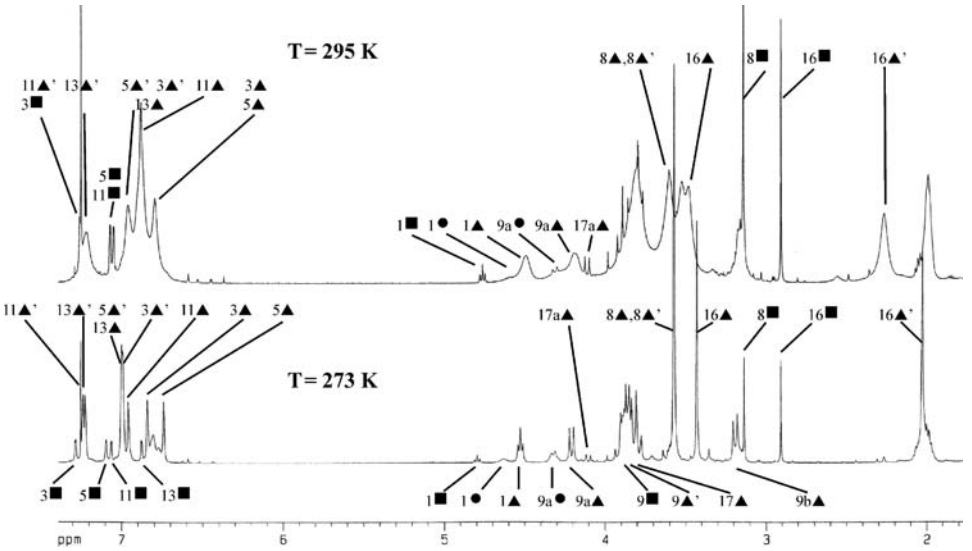
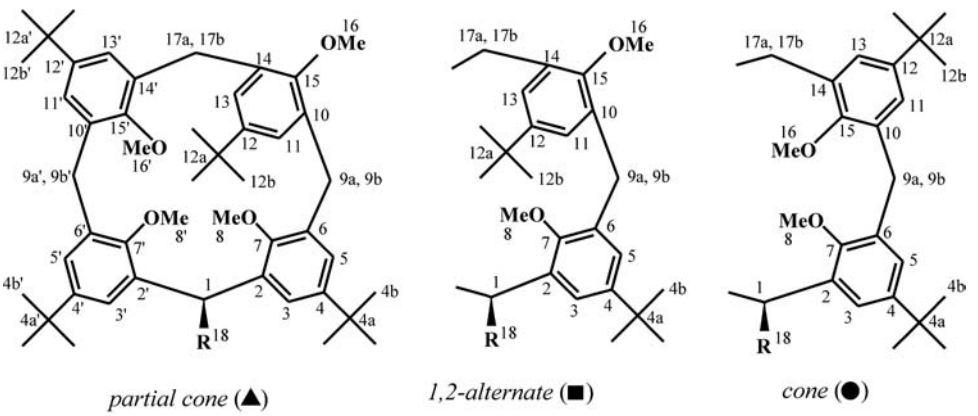


Figure 2. ^{1}H NMR spectra of **3** in $CDCl_3$ at $T = 269$ and 295 K.



2: R = $CH_2^{19}CH_3$

3: R = $CH_2^{19}CH_2^{20}CH_3$

4: R = $CH_2^{19}CH_2^{20}CH_2^{21}CH_2^{22}CH_3$

5: R = $CH_2^{19}CH_2^{20}CH_2^{21}CH_2^{22}CH_2^{23}CH_2^{24}CH_2^{25}CH_2^{26}CH_2^{27}CH_3$

Figure 3. Denotation of atoms of the conformers of **2**–**5** studied in this paper.

units, and also as *1,2-alternate* (*alt2C* in Figure 4) and *cone* (*coneB* in Figure 4) conformers (Scheme 1), which are revealed in the region of the OCH_3 groups of the HSQC spectrum (Figure 5). In the ROESY spectrum (Figure 6), all conformers possess stronger positive cross-peaks between the axial methine H-1 protons in the bridge and the near H-8 protons of the methoxy groups than between these protons and the H-3 protons of the same aromatic rings, indicating the vicinity of one of the methoxy groups on the lower rim to H-1. Further characteristic-specific interactions between aromatic protons of the calixarene and protons of OCH_3 or *tert*-butyl groups neighbouring the methylene bridge are marked in Figure 6. These correlations suggest the orientation of arene units of the calixarene ring for each individual isomer. For example, the *paco* isomer is characterised by the cross-peaks 8▲′/11▲′, 16▲/13▲, 16▲′/5▲′ and 16▲′/13▲, and the *1,2-alternate* species by the 8■/11■ and 8■/13■ relation.

Furthermore, in Figure 6, negative cross-peaks between different H-1 proton signals can be observed due to chemical exchange processes in the form of a dynamic interconversion of conformers. To extract the rate constants for the conformational chemical exchange (k_{chem}), the 2D-EXSY method (*21*) was used, and thus the free activation energies $\Delta G^{\#}$ of the interconversion have been calculated (Table 1). Interestingly, compounds **2**–**5** display a fast

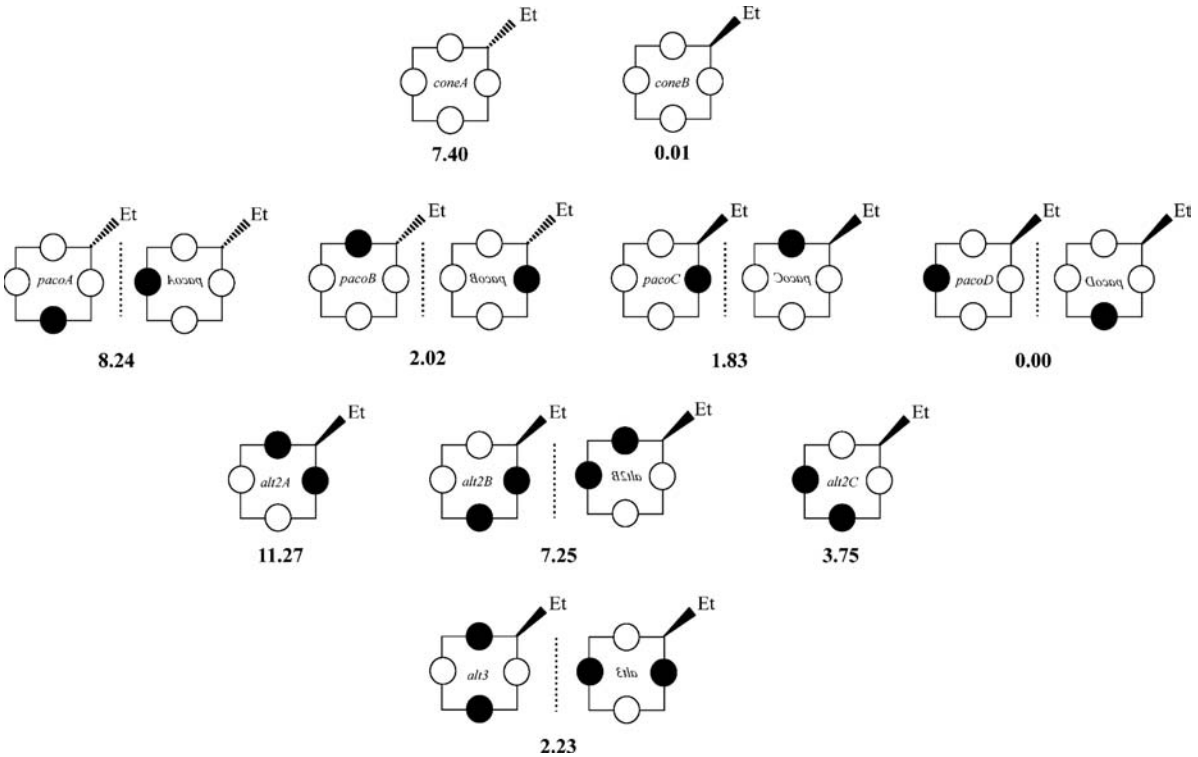
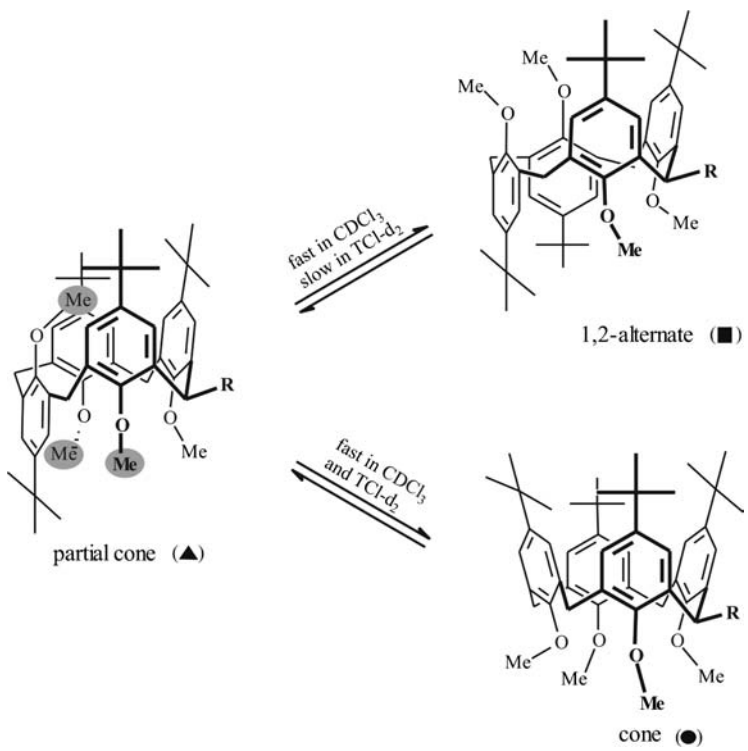


Figure 4. Possible conformers of **2** with sterical energy differences (in kcal/mol) relative to the most stable partial cone (*pacoD*) conformation. The filled and unfilled circles represent an 'up' or 'down' orientation of the methoxy groups, respectively. Mirror images are separated by a broken line and indicated by inverted letters.



Scheme 1. Conformational isomers and conformational behaviour in solution of the laterally alkyl-substituted calixarenes **2**–**5** (R as specified in Figure 1).

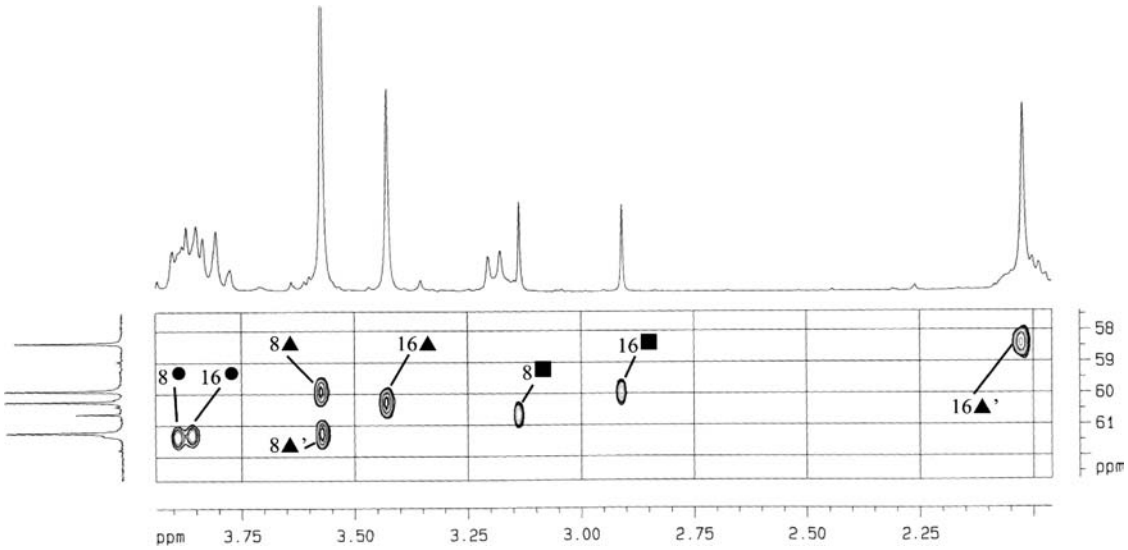


Figure 5. HSQC spectrum of **3** in $CDCl_3$ at 265 K (region of OCH_3 only).

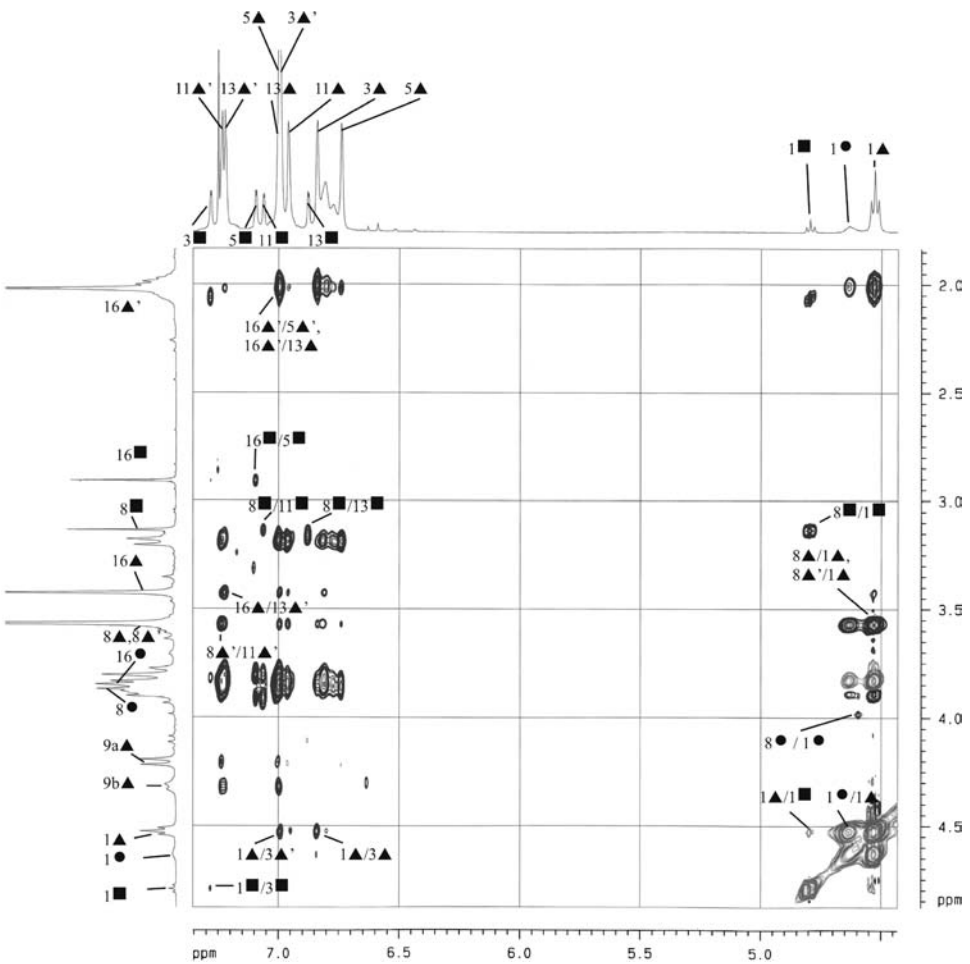


Figure 6. Part of the ROESY spectrum of **3** in $CDCl_3$ at 265 K.

Table 1. (a) Rate constants k_{chem} and (b) free activation energies $\Delta G^{\#}$ of conformational interconversion according to the methine protons H-1 of compounds **2**–**5** and for comparison of compound **1**, calculated by the 2D-EXSY method.

	2				**3**				**4**	**5**
Interconversion	$CDCl_3$, 295 K	$CDCl_3$, 264 K	TCl-d_2, 295 K	TCl-d_2, 263 K	$CDCl_3$, 295 K	$CDCl_3$, 263 K	TCl-d_2, 295 K	TCl-d_2, 260 K	$CDCl_3$, 265 K	$CDCl_3$, 265 K
(a) k_{chem} (s^{-1})										
paco/cone	Fast	18.9	Fast	–	Fast	18.2	Fast	–	15.9	19.5
paco/1,2-alt.	52.0	0.82	14.4	0.7	14.5	0.5	7.3	0.4	0.5	1.3
(b) $\Delta G^{\#}$ (kcal/mol)[a,b]										
paco/cone	–	13.8	–	–	–	13.7	–	–	13.9	13.7
paco/1,2-alt.	14.9	15.4	15.7	15.6	15.7	15.6	16.1	15.6	15.7	15.2

[a] Interconversion *paco/1,2-alt.* for **3** at coalescence in TCl-d_2 (360 K): 17.5 kcal/mol.
[b] Interconversion *paco/1,2-alt.* for unsubstituted compound **1** at coalescence in TCl-d_2 (363 K): 16.4 kcal/mol.

partial cone/cone interconversion involving values of free activation energy rather comparable to the reported ~13 kcal/mol for the laterally unsubstituted prototype calixarene **1** in the same solvent (*10a*). The observed influence of the solvent and the temperature on the conformational behaviour is in agreement with the common expectation. In this connection, the conformational reorientation was found to be faster at higher temperature and retarded in solution of the larger and less polar solvent molecules of TCl-d_2 compared to $CDCl_3$.

The conformer distribution of **1**–**5**, summarised in Table 2, shows that the *partial cone* conformation predominates the present series of tetra-*tert*-butyltetramethoxycalix[4]arenes in $CDCl_3$, varying only little by introduction of the lateral alkyl substituents, i.e. the predominance of the *partial cone* conformation is only slightly affected. Nevertheless, its frequency decreases to some extent for the benefit of the rarely occurring *cone* and *1,2-alternate* structures in the following manner. With increasing chain length, the ratio of the *partial cone* conformation remains nearly unchanged, while the *cone* conformation decreases and the *1,2-alternate* conformation increases. However, as contrasted with the prototype calixarene **1**, for none of the studied compounds a *1,3-alternate* conformation was detected. This points to a predominance of thermodynamically stable conformers and suggests the avoidance of an isoclinal arrangement of the lateral substituent, presumably for energetic reasons.

MM calculation

To evaluate the steric influence of the lateral alkyl substituent, relative energies of the different conformers of **2** as a model compound, summarised in Figure 4, were determined using the MMFF94 force field (*22*) as implemented in the SYBYL software. As proven by previous mechanistic studies (*7d*), all conformations with an axial arrangement of the lateral substituent are energetically discriminated due to their higher angle bending energy. The predominance of the *partial cone* conformation resulting from the NMR experiments, bearing the lateral substituent in an equatorial position between *syn*-orientated arene units in solution (*pacoD*), may thus be explained with the avoidance of repulsion between the α-C-atom of the lateral alkyl moiety and the neighbouring methoxy groups, indicated by their low sterical energies (Table 3). Analogously, the frequency and stability of the *coneB* conformer detected by NMR can be assumed due to its similar low ground state energy. It is also shown that the energy gap between the *1,2-alternate* (*alt2C*) and the *1,3-alternate* conformer is small, giving evidence of their potential presence in solution. The fact that only the *1,2-alternate* conformer is detected in the NMR could result from its higher energy gap to the lowest energy *partial cone* conformer (~3.8 kcal/mol for *alt2C*)

Table 2. Mole fractions of conformers for compounds **1–5** in solution.

	1				**2**				**3**			**4**	**5**
Conformer	$CDCl_3$, 295 K	$CDCl_3$, 265 K	TCl-d_2, 295 K	TCl-d_2, 263 K	$CDCl_3$, 295 K	$CDCl_3$, 261 K	TCl-d_2, 295 K	TCl-d_2, 260 K	$CDCl_3$, 295 K	$CDCl_3$, 261 K	TCl-d_2, 295 K	TCl-d_2, 260 K	$CDCl_3$, 264 K	$CDCl_3$, 263 K
paco (▲,▲′)	85	84	83	84	90	74	88	79	88	72	87	80	73	71
cone (■)	7	9	6	6	–	17	–	10	–	17	–	10	16	15
1,2-alt. (●)	8	7	10	9	10	9	12	11	12	10	13	10	11	14

Table 3. Relative energies (in kcal/mol) for possible conformers of ethyl compound **2** obtained by the MMFF94 force field (SYBYL) and calculated populations.

Conformation	Relative energy (kcal/mol)	Relative to *pacoD* (kcal/mol)	Population (%)
coneA	225.76	0.01	47.13
coneB	233.15	7.40	–
pacoA	233.99	8.24	–
pacoB	227.77	2.02	1.58
pacoC	227.58	1.83	2.18
pacoD	225.75	0.00	47.93
alt2A	237.02	11.27	–
alt2B	233.00	7.25	–
alt2C	229.50	3.75	0.08
alt3	227.98	2.23	1.11

leading to separate signals, whereas the interconversion to the *1,3-alternate* conformer is too fast on the NMR time scale.

Crystal structure of compound 2·CHCl₃

In order to compare the conformational results from the solution NMR study with the conformational behaviour in the solid state, we tried to obtain suitable crystals of compounds **2**–**5** for the X-ray study. Unfortunately, we were unsuccessful in obtaining high-quality crystals in the case of **3**–**5**, presumably due to the high flexibility of the rather extended alkyl chains. However, the corresponding laterally ethyl-substituted compound **2** yielded colourless crystals (space group $Pca2_1$) from a solvent mixture of methanol and chloroform (2:1) suitable for the X-ray study (Table 4). The crystals were analysed to be a stoichiometric 1:1 solvate with chloroform. Not surprisingly, also in the solid state, one low-energy *partial cone* conformer bearing the lateral substituent in an equatorial position between *syn*-orientated arene units is found (Figure 7). This result is in agreement both with the predominance of the *partial cone* conformation in solution and with the lowest energy conformer (*pacoD*) from the MM calculation.

Selected conformational parameters of the calixarene molecule **2** are summarised in Table S5. The opposite phenyl rings A and C differ only little from coplanarity [8.9° (1)], while the aromatic rings B and D are orientated in an angle of 42.8° (1). Similar to a comparable 2:1 solvate of the lateral unsubstituted calixarene **1** with dichloromethane (*18*), the methoxy group of ring D points outwards and maintains no interactions with the other rings. In consequence of the compact structure caused by the *partial cone* conformer, the calixarene does not allow a cavitate inclusion of solvent molecules, which are therefore located interstitially in the crystal lattice. With reference to the crystal packing, the calixarene molecules are orientated translatory staggered along the crystallographic *b*-axis (Figure 8). Corresponding to the non-polar character of the calixarene, the interactions are limited to weak C–H···π

Table 4. Crystal data and selected details of the data collection and refinement calculations of compound **2**·$CHCl_3$.

Compound	**2**·$CHCl_3$
Empirical formula	$C_{51}H_{69}Cl_3O_4$
Formula weight (g/mol)	852.4
Crystal system	Orthorhombic
Space group	$Pca2_1$
a (Å)	23.9269(5)
b (Å)	16.8437(4)
c (Å)	12.6634(3)
α (°)	90.00
β (°)	90.00
γ (°)	90.00
V (Å^3)	5103.6(2)
Z	4
F (000)	1832
D_c (mg m^{-3})	1.109
μ (mm^{-1})	0.219
Data collection	
Temperature (K)	93(2)
No. of collected reflections	57,108
Within the θ limit (°)	1.21–28.10
Index ranges $\pm h$, $\pm k$, $\pm l$	−31/31, −22/21, −16/10
No. of unique reflections	9944
R_{int}	0.0968
Refinement calculations: full-matrix least squares on all F^2 values	
Weighting expression, w[a]	$[\sigma^2(F_o^2) + (0.1788P)^2 + 4.6405P]^{-1}$
No. of refined parameters	537
No. of F values used [$I > 2\sigma(I)$]	8817
Final R indices	
R ($=\Sigma\lvert\Delta F\rvert/\Sigma\lvert F_o\rvert$)	0.0843
wR on F^2	0.2405
S (=Goodness of fit on F^2)	1.092
Final $\Delta\rho_{max}/\Delta\rho_{min}$ (e Å^{-3})	0.000

[a] $P = (F_o^2 + 2F_c^2)$.

contacts (*23*) involving guest and calixarene molecules [d(C1GA···centroid C) = 3.569 (1) Å] or the calixarene molecules among each other [d(C33···centroid B) = 3.486 (1) Å], as specified in Table S6.

Conclusions

According to the literature (*1*, *7*), calixarenes showing a substitution of a single methylene bridge, especially in the case of an alkyl substitution, are a rather low developed class of compounds. As derivatives of the archetype tetramethoxycalix[4]arene **1**, only the first two members of the potential compound series, i.e. the methyl and ethyl (**2**) derivatives, have previously been synthesised and preliminarily described regarding their conformational behaviour. With the present calixarenes **3**–**5** featuring the corresponding mode of lateral substitution but using higher alkyl groups of different chain lengths, new examples of this particular compound type have now been made available. They enable to perform a first systematic study of the influence of the given alkyl groups on the conformational property of the tetramethoxycalix[4]arene system.

The following main conclusions can be obtained from this study. (1) The lateral attachment of an alkyl residue to one of the central ring methylene groups of the basic calixarene **1** has no substantial consequence on the conformational behaviour. That is, independent of the chain length, a respective substitution of an alkyl group does not hamper the predominance of the *partial cone* conformation of **1** in chloroform solution, as proven by NMR spectroscopy. This particular conformation was also found to be low energetic in the calculated sterical energies. Moreover, the crystal structure of compound **2** in its solvated form with chloroform is in structural agreement, showing the *partial cone* conformation in the crystalline state. (2) As against the unsubstituted calixarene **1**, the free activation energy for the conformational interconversion of **2**–**5** in solution is found to be only moderately higher. Hence, it is shown that (3) an alkyl substitution of one of the hydrogen atoms of a methylene group between the flanking aryl residues of the central ring offers a very promising possibility for the coupling of a basic tetramethoxycalix[4]arene structural element to spacer or linker units in order to realise future developments of new complex framework structures without substantial impairment of the initial calixarene conformation, while corresponding modifications at the upper and lower rim sites normally result in distinct changes of the conformational behaviour.

Future work is required to explore the effect of more than one laterally attached alkyl group or of a substituent containing polar or functional units in the side chain. Investigations in this direction are the aim of our group.

Experimental

Materials

1-Iodopropane (Fluka, Buchs, Switzerland), 1-iodopentane (Acros, Morris Pla, NJ, USA) and 1-bromodecane (Fluka) were used as received. The *n*-BuLi (1.6 M in hexane) was purchased from Acros. Analytical TLC was performed on precoated silica gel plates (60 F_{254}; Merck, Darmstadt, Germany). Organic solvents were purified by standard procedures (*24*).

Techniques

Melting points were determined with a hot-stage microscope (VEB Dresden Analytik, Dresden, Germany) and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded using a Bruker DRX 500 spectrometer. The chemical shifts (δ) are reported in ppm relative to TMS = 0 ppm. Mass spectra were recorded with EI-MS (Finnigan MAT 8200). The elemental analyses were performed with a Heraeus CHN rapid analyser.

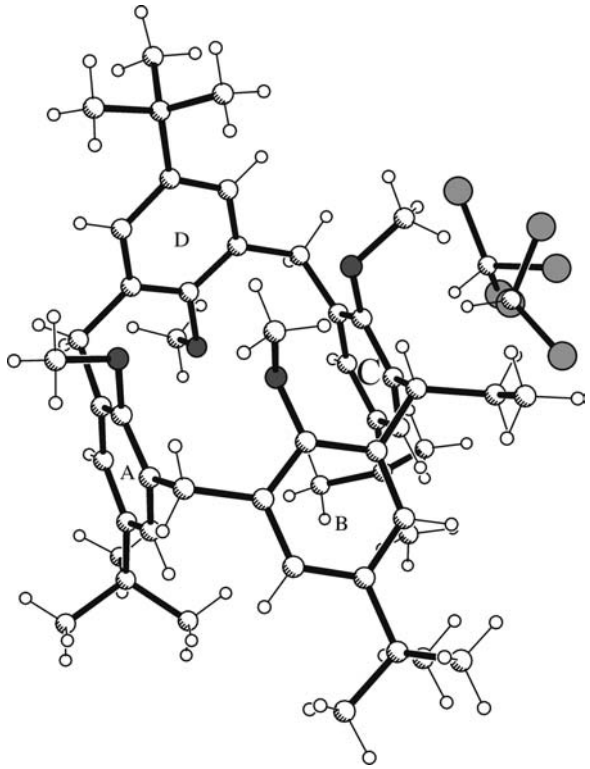


Figure 7. Molecular structure of the solvate compound **2**· $CHCl_3$.

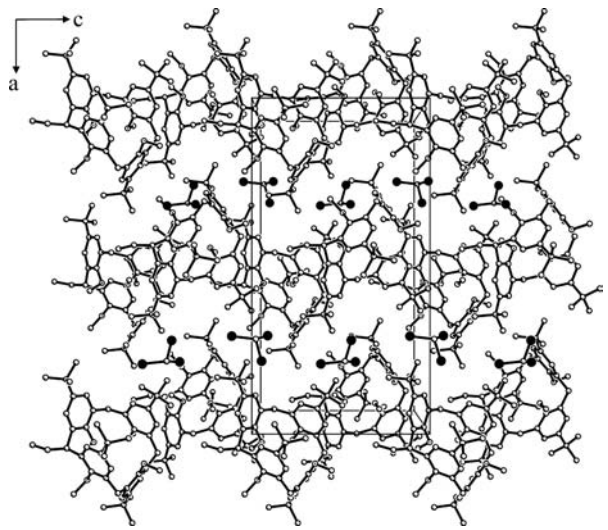


Figure 8. Packing diagram of **2**· $CHCl_3$ viewed down the *b*-axis, illustrating the strands of calixarene molecules and localisation of the solvent molecules.

Synthesis of 5,11,17,23-tetra-tert-butyl-25,26,27,28-tetramethoxycalix[4]arene (1)

A mixture of 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrahydroxycalix[4]arene (*11*), NaOH (aqueous, 50 p.c.), dimethyl sulphate and tetrabutylammonium bromide in toluene was reacted following a known procedure (*12*). Recrystallisation from MeOH–$CHCl_3$ (1:1) yielded 60% of intermediate 5,11,17,23-tetra-*tert*-butyl-26,28-dihydroxy-25,27-dimethoxycalix[4]arene as a colourless solid, mp 235–238°C. Following the literature protocol (*13*), this compound was caused to react with NaH and iodomethane to afford 67% of calixarene **1** as a colourless solid, mp 242–244°C (lit. (*12*) 242–243°C).

General procedure for the synthesis of the laterally monoalkylated calix[4]arenes (2–5)

The synthesis of products **2**–**5** follows the protocol described by Scully et al. (*7a*). To a stirred solution of **1** (1.0 mmol) in dry THF (30 ml), *n*-BuLi (1.6 N in *n*-hexane, 2.9 ml, 4.6 mmol) was added at room temperature under argon. After having stirred for 30 min, the respective 1-halogenalkane (8.0 mmol) was added via a syringe to the solution, causing a change of its colour from red to yellow. Stirring was continued for 1 h. The solvent was removed under reduced pressure and the residue partitioned into water–dichloromethane (1:1, 60 ml). The organic layer was washed with water (2× 30 ml), dried ($MgSO_4$) and evaporated under reduced pressure. Recrystallisation from MeOH yielded the products as colourless solids. Experimental, MS and elemental analysis data of the individual compounds are specified below. For the detailed 2D NMR experiments, all substances were dried for 24 h under vacuum at 50°C. The respective NMR data of **2**–**5** are given in the Supplementary Material (Tables S1–S4). The NMR data for **2** correspond to the literature (*7a*).

5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetramethoxy-2-ethylcalix[4]arene (2)

1-Bromoethane was used. Yield 0.42 g (57%), mp 183–185°C [lit. (*7a*) 184–186°C].

5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetramethoxy-2-n-propylcalix[4]arene (3)

1-Iodopropane was used. Yield 0.34 g (46%), mp 132–135°C. Anal. Calcd for $C_{51}H_{70}O_4$ 0.5 MeOH: C 81.06, H 9.51. Found: C 80.99, H 9.78%. MS (70 eV), *m*/*z* (%): 747 (M^+, 100), 748 (52), 358 (35), 177 (28).

5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetramethoxy-2-n-pentylcalix[4]arene (4)

1-Iodopentane was used. Yield 0.35 g (47%), mp 76–80°C. Anal. Calcd for $C_{53}H_{74}O_4$: C 82.12, H 9.62. Found: C 82.15, H 9.80%. MS (70 eV), *m*/*z* (%): 775 (M^+, 100), 776 (64), 372 (43), 177 (14).

5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetramethoxy-2-n-decylcalix[4]arene (5)

1-Bromodecane was used. Yield 0.37 g (44%), mp 139–144°C. Anal. Calcd for $C_{58}H_{84}O_4$ 1.5 MeOH: C 80.00, H 10.15. Found: C 79.85, H 9.88%. MS (70 eV), *m/z* (%): 845 (M^+, 100), 846 (63), 407 (42), 177 (32).

X-ray crystallography

Crystals of **2** suitable for X-ray diffraction analysis were obtained by slow recrystallisation from methanol–chloroform (2:1) solution. The intensity data were collected on a Bruker APEX II diffractometer with Mo Kα radiation ($\lambda = 0.71073$ Å) using ω- and ϕ-scans. Reflections were corrected for background and Lorentz polarisation effects. Preliminary structure models were derived by application of direct methods (*25*) and were refined by full-matrix least-squares calculation based on F^2 for all reflections (*26*). All hydrogen atoms were included in the models in calculated positions and were refined as constrained to bonding atoms. Relevant crystal data together with the refinement details are listed in Table 4.

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre (No. CCDC 748215). Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK. Fax (+44) 1223-336-033; E-mail: deposit@ccdc.cam.ac.uk or www.ccdc.cam.ac.uk.

Supplementary Material

^{1}H and ^{13}C NMR data of **2**–**5** in $CDCl_3$ and TCl-d_2, selected conformational parameters and geometric parameters of potential hydrogen bond-type interactions from the crystal structure of **2**·$CHCl_3$ are available as Supplementary Material, available online.

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