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Conformational studies of calix[5]arenes containing a single alkanediyl bridge †

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Six new calix[5]arenes substituted at one of the methylene bridges by methyl, ethyl, isopropyl, *tert*-butyl, *p*-tolyl and *p*-nitrophenyl have been synthesised by heat induced (3+2) fragment condensation of a linear trimer with the corresponding bishydroxymethylated alkanediyl diphenols in boiling xylene. These conditions give the calix[5]arenes more reliably in about 20–30% yield, while the corresponding condensation with bisbromomethylated alkanediyl diphenols leads to complex mixtures from which sometimes only a calix[8]arene could be isolated. In agreement with molecular mechanics calculations the calix[5]arenes prefer the cone conformation with an equatorial position of the alkyl or aryl substituent at the bridge. From variable temperature ^{1}H NMR spectroscopy the conformational equilibria and the energy barriers for the cone-to-cone ring inversion have been determined. Single crystal X-ray analyses have been performed for the calix[5]arene substituted by *tert*-butyl and for the corresponding *tert*-butyl substituted dinuclear precursor.

Introduction

In comparison to calix[4]- and calix[6]arenes the chemistry of calix[5]arenes is less developed.[1] This may be partly due to the fact that calix[5]arenes are not quite as easily available in larger quantities,[2] and that selective chemical modifications are more complicated for regio- and stereochemical reasons.[3] On the other hand, calix[5]arenes are attractive, since in contrast to calix[6]arenes their conformational mobility can still be restricted by attachment of sufficiently large residues[4] at the phenolic oxygens, while their cavity is larger than that of calix[4]arenes.[5]

Calix[5]arenes with free phenolic hydroxy groups assume in solution according to their NMR spectra a cone conformation with apparent five-fold symmetry. *tert*-Butylcalix[5]arene for instance shows at low temperature (<−30 °C) one singlet for the *tert*-butyl and for the aromatic protons and one pair of doublets for the methylene protons. Like with calix[4]arenes a singlet for the methylene protons found at higher temperature (>30 °C) is interpreted by a rapid cone-to-cone interconversion. The energy barrier for this process, which may be derived from variable temperature NMR studies, is usually lower by about 2.5 kcal mol^{-1} in comparison to the corresponding calix[4]arenes, which is in agreement with the larger ring size.[1]

A cone conformation was found also in the crystalline state for various calix[5]arenes independent of the substituent in the *para*-position and of the guest included in the cavity.[6] O–O-Distances up to 2.85–2.9 Å as compared to about 2.65 Å found for calix[4]arenes are in agreement with weaker intramolecular hydrogen bonds. More or less distorted cone-conformations are also found for the anions of *p*-sulfonatocalix[5]arene[7] and for a calix[5]arene in which one hydroxy group is replaced by bromine.[8]

Calix[4]arenes still adopt the expected cone conformation if one or two methylene bridges are substituted by an alkyl or aryl group.[9,10] From the two diastereomeric cone conformations with this substituent positioned equatorially or axially, the conformation with an equatorial position is predominant for aliphatic residues, while no pronounced preference was observed for aromatic ones. Variable temperature NMR studies revealed that the barrier of the ring inversion is (slightly) increased by an aliphatic substituent at the bridge. We were interested to know if similar conformational effects can be detected also in calix[5]arenes containing an alkanediyl bridge. Recently Sartori *et al.* reported that in calix[5]arenes substituted at one of the methylene bridges by an aryl group the equatorial conformer is preferred,[11] a result which is in surprising contrast to analogous calix[4]arenes.[9]

Results and discussion

Syntheses

Since no synthetic strategy for a direct and selective substitution of the methylene bridges is known, we tried to prepare the desired calix[5]arenes by (3+2) fragment condensation of a linear trimer with a bisbromo- or bishydroxymethylated dimer as outlined in Scheme 1.

We did not anticipate a significant influence of the substituents in the *para*-position. Therefore we chose two different *para*-

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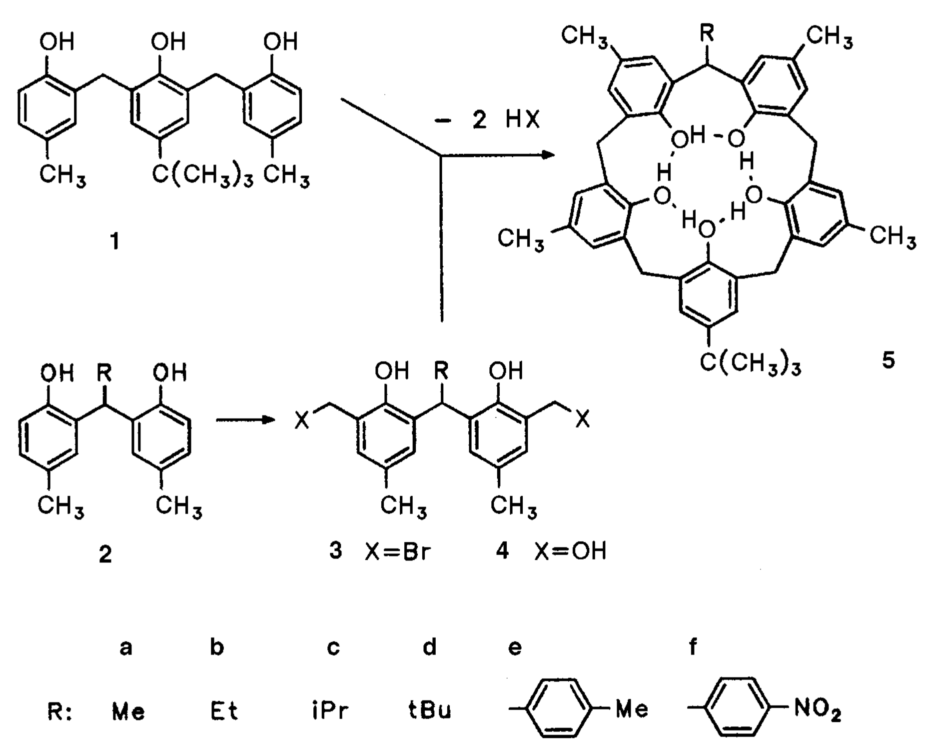
† Full crystallographic details, excluding structure factor tables, have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 2*, available *via* the RSC Web page (http://www.rsc.org/authors). Any request to the CCDC for this material should quote the full literature citation and the reference number 188/140.



Scheme 1 Alkanediyl bridged calix[5]arenes by (3+2) fragment condensation.

substituents (methyl and *tert*-butyl) in order to spread the NMR signals in the final calix[5]arene. The linear trimer **1** is easily obtained in large quantities by condensation of bisbromo- or bishydroxymethylated *p*-*tert*-butylphenol with an excess of *p*-cresol. The necessary bisbromomethylated dimers **3a**–**f** are conveniently prepared by condensation of the appropriate aldehyde with an excess of *p*-cresol (70–80%) and subsequent bromomethylation (75–85%).[9] Reaction of **2** with formaldehyde under alkaline conditions gives the bishydroxymethylated dimers **4**.

Unfortunately the (3+2) fragment condensation using bisbromomethylated dimers **3** is less clear than the (2+2) condensation, where the desired calix[4]arene is obviously the only (or at least the main) macrocyclic product which consequently is easily isolated by column chromatography.[9] Mixtures of several products with similar chromatographic behaviour are formed in the condensation of **1** with **3a**–**f** from which the desired calix[5]arenes could be isolated only in the case of **5c**,**d** after repeated chromatographic separations (11–13% of the chromatographically and spectroscopically pure product after a final recrystallization). Calix[8]arenes (see below) could be isolated as a side product (**6c**,**d**) or as the only identifiable product (**6a**,**b**,**e**) in about 3% yield.

A similar observation was reported recently by No and Kwan[12] who showed, however, that the heat induced (3+2) fragment condensation using hydroxymethylated dimers in refluxing xylene gave a less complex reaction mixture,[13] from which the calix[5]arene was easily isolated by column chromatography in yields of 20–25%. Using analogous conditions the calix[5]arenes **5a**,**b**,**e**,**f** could be prepared in yields of up to 30%. Obviously this heat induced condensation using hydroxymethylated compounds is the method of choice for the directed synthesis of calix[5]arenes, since Sartori *et al.*[11] described the synthesis of four examples similar to **5e**,**f** by a (4+1) fragment condensation (18–28%).

The structural assignment of **5a**–**f** is mainly based on spectroscopic arguments (compare the ^{1}H NMR data in Table 6) and for **5d** it is additionally corroborated by single crystal X-ray analysis (see below). In all cases a molecular ion consistent with the proposed structure was found in the mass spectrum and, more importantly, no peaks corresponding to calix[*n*]arenes with a different ring size ($n = 4,6,7,8$; see below) or (for $n = 5$) with a different substitution pattern could be detected.

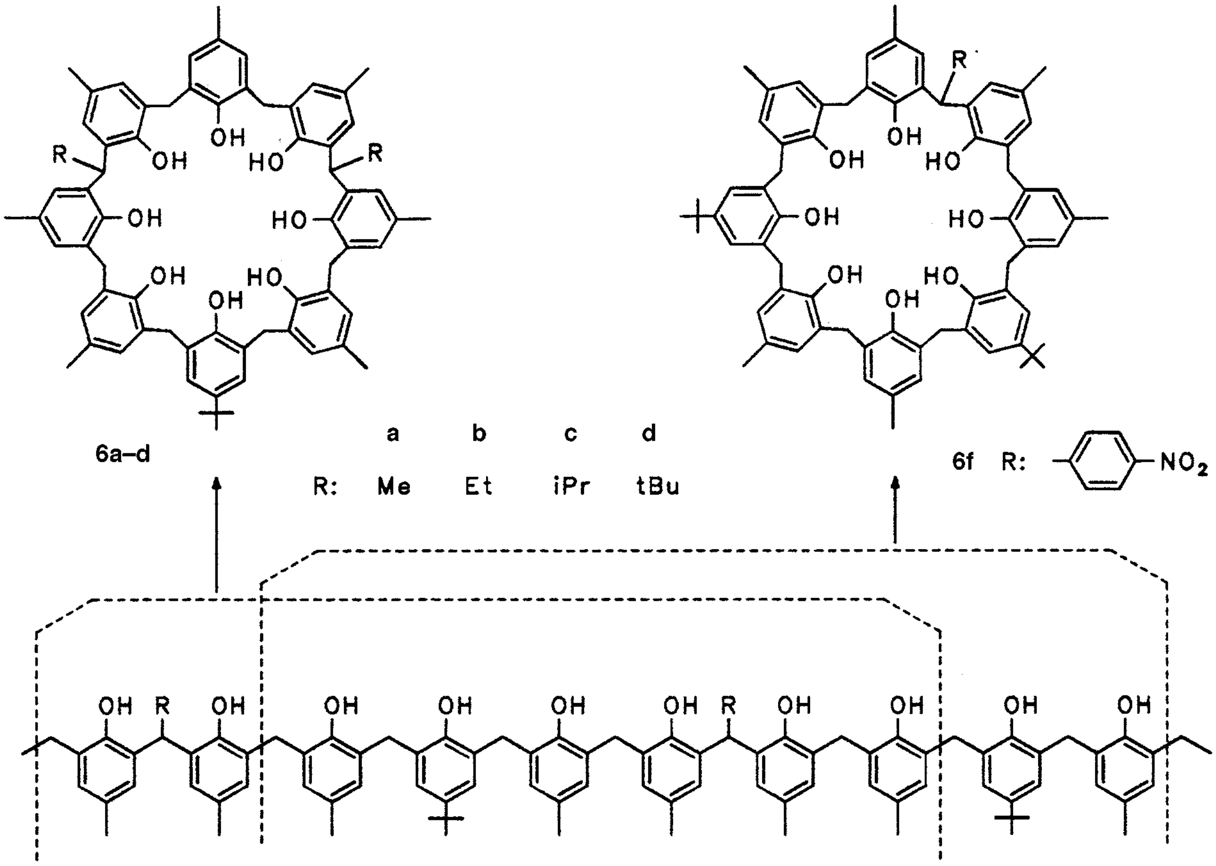
The identification of compounds **6** as calix[8]arenes is based on their field desorption (FD) and chemical ionization (CI) mass spectra, which also show that **6a**–**d** contain two alkylidene bridges (-CHR-) and one *p*-*tert*-butylphenol unit, while **6f** contains one *p*-nitrophenyl substituted bridge and two *p*-*tert*-butylphenol units. (A small peak in the CI mass spectra of **6a** and **6b** can be interpreted as a calix[8]arene with a structure analogous to **6f**.) Both structures are compatible with a section of a linear oligomer formed by "regular" condensation of **1** and **3**, as indicated in Scheme 2.

Although mechanistic conclusions based on products isolated in 3% yield should be drawn cautiously, this result suggests that a single "*ipso*-attack" of a benzyl cation (in a "back-biting" reaction) is responsible for the formation of these calix[8]arenes while indications for a complete "scrambling" of the phenolic units are not found.

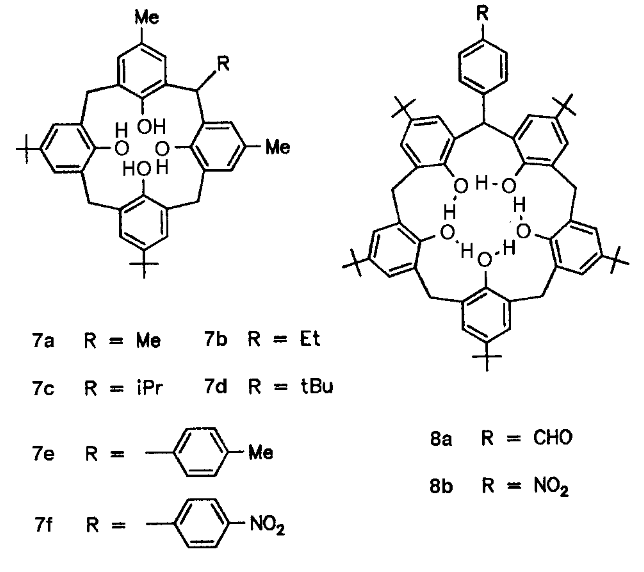
^{1}H NMR studies

The ^{1}H NMR spectrum of calix[5]arene **5a** displays three signals for the OH groups (ratio 1 : 2 : 2), four signals (singlets or pseudo-singlets) for the aromatic protons, two very close singlets for the *p*-methyl groups and one singlet for the *p*-*tert*-butyl group. The protons of the methylene bridges appear as two pairs of overlapping doublets which can be attributed to the axial and equatorial protons, while the ethylidene bridge gives rise to a quartet and a doublet with the expected ratio of 1 : 3. Similar NMR spectra, consistent with the presence of a single cone conformation were observed for the calix[5]arenes **5b**–**f**, although in some cases some signals coincide by accidental isochrony.

The doublets for the axial and equatorial methylene protons of **5a**–**d** are separated by 0.62–0.65 ppm, a value smaller than the one observed for analogous alkylidene calix[4]arenes like **7a**–**d** (*ca.* 0.8 ppm). This is largely due to the less pronounced downfield shift of the axial methylene protons (*ca.* 4.00–4.05 ppm in **5** in contrast to 4.20–4.25 ppm in **7**).[14] As previously analysed for **7a**–**f**[9] the alkylidene groups lead to unequivalent pairs of protons within the methylene groups, which are



Scheme 2 Calix[8]arenes as sections of a linear polycondensate.



7a R = Me 7b R = Et

7c R = iPr 7d R = tBu

7e R = Me

7f R = NO_2

8a R = CHO

8b R = NO_2

Table 1 Chemical shifts for the methine protons -CHR- in mono-alkanediyl bridged calix[4]- and calix[5]arenes **7** and **5** ($CDCl_3$, 400 MHz)

Substituent		Compound 7[a]	Compound 5
CH_3	**a**	4.70	4.55
CH_2CH_3	**b**	4.35	4.19
$CH(CH_3)_2$	**c**	4.03	3.88
$C(CH_3)_3$	**d**	4.53	4.43
p-C_6H_4-CH_3	**e**	6.07/5.24[b]	5.90,[c] 5.23[d]
p-C_6H_4-NO_2	**f**	6.11/5.27[b]	5.95,[c] 5.27[d]

[a] Values from ref. 9. [b] Two diastereomeric cone-conformations with axial/equatorial methine proton. [c] Major conformer. [d] Minor conformer.

diastereotopic even under fast cone-to-cone inversion conditions. The large splitting observed for the methylene protons and the overall similarity of the NMR spectra suggest that compounds **5** adopt a cone conformation like **7**.

The methine protons of the alkylidene bridges in **5a–d** (Table 1) also show chemical shifts similar to those found for the corresponding calix[4]arenes **7a–d** (again an upfield shift by 0.1–0.2 ppm is observed for **5** in comparison to **7**). This is ascribed to an axial position of the methine proton, which was additionally confirmed for **5b** by a 2D NOESY spectrum displaying a NOE cross peak of the methine signal with an OH signal. Consequently, the alkyl substituents must adopt an equatorial position, and this conformer is dubbed "equatorial".

Raising the temperature resulted for **5a–c** (in $CDCl_2CDCl_2$) in broadening of the methylene and methine signals followed by resharpening. This behaviour is characteristic of the exchange with a hidden partner, *i.e.* a dynamic process involving a conformationally biased system.[15] No effect could be detected for **5d** in the range of 275–400 K, suggesting that the conformational equilibrium is too strongly biased towards the preferred (equatorial) form. On the basis of the maximum broadening of the methine proton (ω) and of the corresponding temperature (T_m), the conformational data in Table 2 were calculated.

The free energy differences of the axial and equatorial conformations of **5a–c** (2.5–2.6 kcal mol^{-1}) are identical within the experimental error, while the lack of broadening observed for **5d** indicates that the population of the equatorial conformer is even larger. While the barriers of the equatorial→axial transition (a process which involves a cone-to-cone inversion) are identical for **5a** and **5b** (16.1–16.2 kcal mol^{-1}) a slightly higher barrier (17.0 kcal mol^{-1}) results for **5c**. All these barriers are larger than for *p*-*tert*-butylcalix[5]arene (13.2 kcal mol^{-1}).[16,17] The conformational behaviour is identical to that found for **7a–d**, where the largest barrier was determined for the isopropyl

Table 2 Conformational data for the monoalkanediyl bridged calix[5]arenes **5**

Compound	T_m/K[a]	ω/Hz[b]	$K_{eq/ax}$	$\Delta G°$/kcal mol^{-1}	$\Delta G^{\ddagger}_{eq\text{-}ax}$/kcal mol^{-1}
5a (R = Me)[c]	310	3.6	71	2.6	16.2
5b (R = Et)[c]	310	4.5	57	2.5	16.1
5c (R = *i*Pr)[c]	330	5.6	45	2.5	17.0
5e (R = *p*-MeC_6H_4)[d]	270	23.2	10.7 (11.7[e])	1.3 (1.0[e])	13.1
5f (R = *p*-$NO_2C_6H_4$)[d]	275	23.7	10.6 (11.7[e])	1.3 (1.0[e])	13.3

[a] Temperature of maximum broadening. [b] Maximum width of the methine signal. [c] In $CDCl_2CDCl_2$. [d] In $CDCl_3$. [e] Value obtained by integration of the methine protons of both conformers at 210 K.

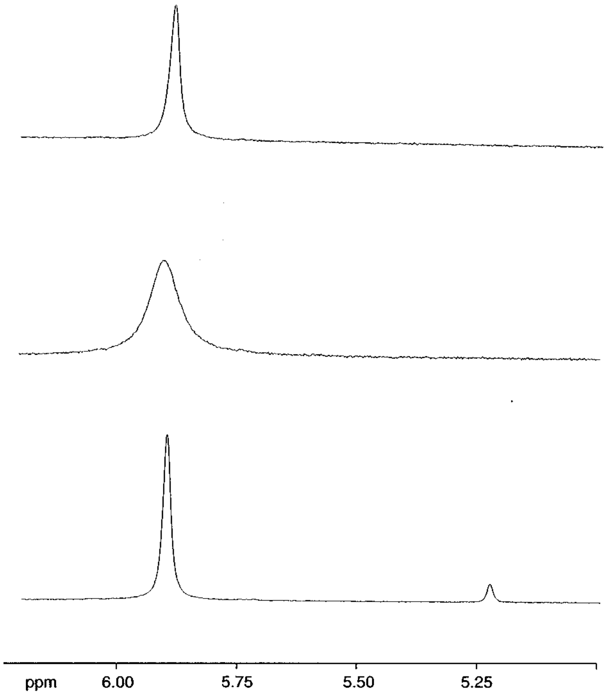


Fig. 1 From bottom to top: methine region of the ^1H NMR spectra (400 MHz, $CDCl_3$) of **5e** at 210 K (slow exchange), 270 K (T_m) and 298 K (fast exchange). The major and minor signals observed at 210 K correspond to the equatorial and axial conformers of **5e**.

substituted **7c**,[9] while the presence of an alkanediyl group does not seem to affect the rotational barrier in *exo*-calix[4]arenes.[14]

The ^1H NMR spectra of calix[5]arenes **5e** and **5f** at 210 K are very similar and display (in contrast to **5a**–**d**) signals for a major and a minor conformer in a ratio of 11.7 : 1, as determined by integration of the two methine protons (Fig. 1). Cross peaks were found in the NOESY spectrum of **5e** between the OH and methine protons, suggesting an axial location of the latter, and indicating that in the major conformer the substituent is located in an equatorial position. From the maximum width of the methine signal at T_m (Table 2 and Fig. 1) nearly identical equilibrium constants ($K_{eq/ax}$ = 10.6 and 10.7) were estimated for **5e** and **5f** at their respective T_m. These $K_{eq/ax}$ values are somewhat smaller than those determined for calix[5]arenes **8a**,**b** in CD_2Cl_2 ($K_{eq/ax}$ = 24 and 32).[11]

The barriers for the eq→ax transition of **5e** and **5f** are nearly identical ($\Delta G^{\ddagger}$ = 13.1 and 13.3 kcal mol^{-1}). They are lower than the barriers for **5a**–**c** and similar to those reported for **8a** and **8f** ($\Delta G^{\ddagger}$ = 13.5 and 13.2 kcal mol^{-1}). These data indicate that the *para*-substituent on the aryl ring of the bridge has only a minor effect on the conformational equilibria and the rotational barrier.

Single crystal X-ray structures

Single crystals of the calix[5]arene **5d** and of the corresponding alkanediyl bridged dimer **2d** have been obtained by recrystallization from $CHCl_3$–methanol and $CHCl_3$–*n*-hexane, respectively. Details of the X-ray experimental conditions, cell data, structure solution and refinement are collected in Table 3. The molecular conformation of **5d** and a section of its crystal lattice are shown in Figs. 2 and 3, while the conformation of **2d** and its arrangement to hydrogen bonded dimers is illustrated by Fig. 4.

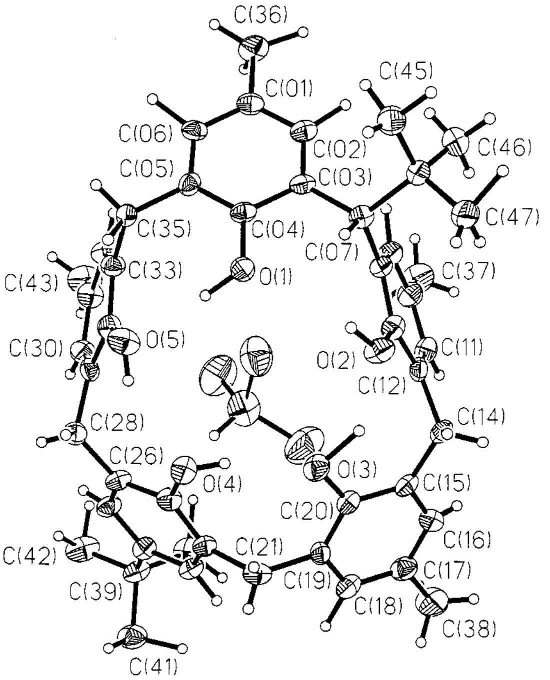


Fig. 2 Molecular conformation and numbering scheme of calix[5]-arene **5d**. Only the included chloroform is shown. Thermal ellipsoids are drawn on a 30% level.

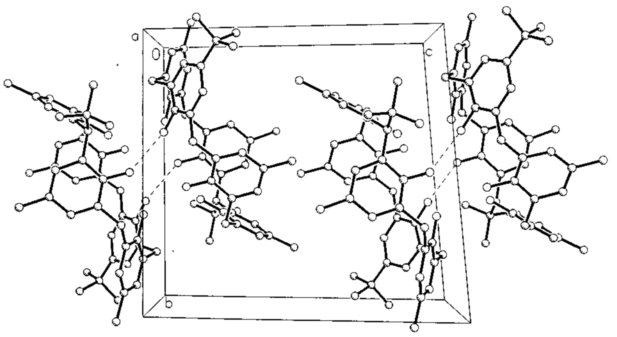


Fig. 3 Packing of calix[5]arene **5d**; hydrogen atoms and included chloroform and methanol are omitted.

As expected, **5d** is found in a cone-like conformation in which the *tert*-butyl group at the bridge assumes the equatorial position. Like in X-ray structures of calix[5]arene derivatives all five bridging carbon atoms (C07, C14, C21, C28, C35) are not really coplanar (rms = 0.234 Å). From five possibilities to define a best plane through four of these bridging carbons one is distinctly better (C7, C14, C28, C35, rms = 0.031 Å) than the other

Table 3 Summary of crystal data, data collection, structure solution and refinement details

	2d[a]	**5d**[b]
(a) Crystal data		
Formula	$C_{19}H_{24}O_2$	$C_{47}H_{54}O_5 \cdot CHCl_3 \cdot CH_3OH$
Formula weight	284.38	850.31
Colour, habit	Colourless, block	Colourless
Crystal size/mm^3	0.41 × 0.41 × 0.35	0.35 × 0.21 × 0.07
Crystal system	Triclinic	Triclinic
a/Å	7.993(1)	11.408(1)
b/Å	8.566(1)	14.994(1)
c/Å	12.851(1)	15.054(1)
α/°	93.60(1)	83.57(1)
β/°	98.92(1)	79.46(1)
γ/°	107.54(1)	67.94(1)
V/Å^3	823.2(4)	2343.7(7)
Space group	$P\bar{1}$	$P\bar{1}$
Z	2	2
F(000)	308	904
D_{calc}/g cm^{-3}	1.147	1.205
μ/mm^{-1}	0.07	0.24
(b) Data acquisition[a]		
Temp./K	294(1)	293(2)
Unit-cell reflcns	25	1389
θ-Range of data collect./°	2.51 to 26.91	1.95 to 21.97
hkl Range of reflcns	−10/9; 0/10; −16/16	−12/11; −15/15; −15/14
Reflcns measured	3572	5694
Unique reflcns (R_{int})	3572	5130 (0.0482)
Reflcns with $I > 2\sigma(I)$	2432	2363
(c) Structure solution and refinement		
Solution method	Direct methods	Direct methods
Refinement on	F^2	F^2
Data/restraints/parameters	3572/0/198	5120/0/536
H-atom treatment	Riding	Riding (except O-H)
Ext. coeff.	0.047(6)	0.010(2)
Weights:		
k in $w = 1/[\sigma^2(F_o^2) + k]$ $[P = (F_o^2 + 2F_c^2)/3]$	$(0.0582P)^2 + 0.0635P$	$(0.122P)^2$
R(obs, F), R_wF^2(all), g.o.f.	0.0400, 0.1206, 1.098	0.0778, 0.2413, 0.957
Density range in final Δ-map/e Å^{-3}	−0.12, 0.17	−0.25, 0.43
Max final shift/error ratio	0.009	0.000

[a] Data collection on an Enraf Nonius CAD-4 diffractometer with graphite monochromatised Mo-Kα radiation (λ 0.7107 Å). All calculations were done on an IBM Aptiva 166 MHz system with the NRCVAX system of programs (E. J. Gabe, Y. Le Page, J.-P. Charland, F. L. Lee and P. S. White, *J. Appl. Crystallogr.*, 1989, **22**, 384) for refinement with observed data on F, or with SHELXL-93 (G. M. Sheldrick, 1993) for refinement with all data on F^2. [b] Reflections were measured on a computer controlled three circle diffractometer with a CCD area detector (Siemens): Mo-Kα radiation (rotating anode with 0.5 × 5 mm focus). Solution of the phase problem and the least squares refinement of the structure parameters by the SHELX-97 programs (G. M. Sheldrick, Program for the Solution and Parameter Refinement of Crystal Structures, University of Göttingen, Germany, 1997). The coordinates of the H-atoms were calculated (except those on oxygen).

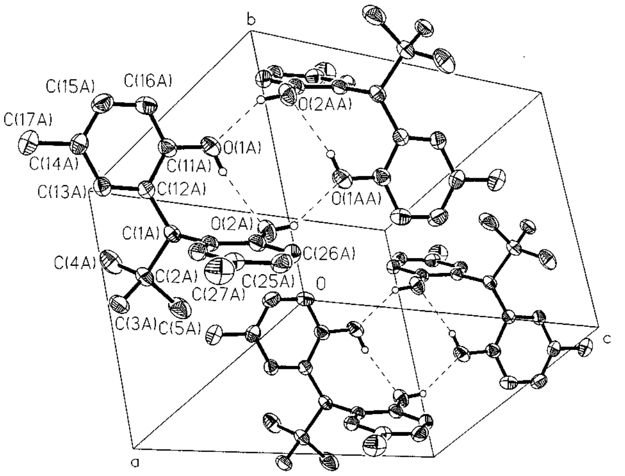


Fig. 4 Molecular conformation, numbering scheme and packing of dimer **2d**. Thermal ellipsoids are drawn on a 30% level.

four (rms = 0.143–0.273 Å). Thus, the conformation may be described by the inclination of the phenolic units with respect to this major plane (M), and the minor plane (m) defined by C14, C21, and C28. The dihedral angle between both planes (M,m) is 17.3° with the OH groups on the concave side.[18] These inclination angles and further conformational parameters are collected in Table 4 and compared with the corresponding values of the dimer **2d**.

This comparison with **2d** reveals a striking similarity with the respective section of **5d**, especially the bond and torsion angles are very similar. The intramolecular O···O-distance in **2d** is distinctly shorter, however, than the distance O1···O2 in **5d**. In general the intramolecular O···O distances of **5d** (average 3.04 Å) are much longer than in other calix[5]arenes.[19,20] This cannot be simply caused by the substituent at the bridge, since an average O···O-distance of 2.796 Å was also found for calix[5]arene **8b** substituted at one bridge by *p*-nitrophenyl.[11] A possible explanation may be found in the packing of **5d**. As Fig. 3 shows, two molecules of **5d**, symmetry related by an inversion centre have two intermolecular O···O distances (O2···O4A = O2A···O4 = 2.804 Å) which are shorter than all the intramolecular O···O distances. Presumably by this intermolecular hydrogen bonding[20] the intramolecular hydrogen bonds are weakened, especially the hydrogen bond between O1 and O2.

Table 4 Conformational parameters of calix[5]arene **5d** and the dimer **2d**. Dihedral (interplanar) angles δ refer to the indicated planes, torsion angles φ and χ around the Ar–C bonds include the intraannular (OH-substituted) C-atom, the bond angles β refer to the carbon atoms attached to the bridge

Planes[a]	AM	BM	Cm	Dm	EM	
δ_1/°	138.9	97.4	113.0	120.3	107.2	
Planes[a]	AB	BC	CD	DE	EA	**2d**
δ_2/°	108.4	115.4	120.2	123.6	112.2	102.9
Atom	C7	C14	C21	C28	C35	**2d**
φ/°	82.6	114.9	90.2	89.7	113.6	79.8
χ/°	−127.9	−75.4	−103.5	−109.6	−82.0	−115.8
β/°	111.0	116.3	115.4	116.7	113.0	109.6
	114.2/117.7					114.1/119.5
O···O-	O1/O2	O2/O3	O3/O4	O4/O5	O5/O1	**2d**
Distance/Å	3.370	2.962	2.847	3.067	2.942	2.989

[a] The following planes are used: A = C01-C06, B = C08-C13, C = C15-C20, D = C22-C27, E = C29-C34, M = C07,C14,C28,C35, m = C14,C21,C28.

Table 5 Results of the molecular mechanics calculations on the monoalkanediyl calix[5]arenes **5** obtained with the Tripos force field[a]

R	$\Delta E_{\text{ax-eq}}$	ΔE_{bend}	ΔE_{bnd}	ΔE_{nbnd}
Methyl	2.45	2.30	2.91	−0.46
Ethyl	2.38	2.28	2.93	−0.55
Isopropyl	2.28	2.25	2.92	−0.64
tert-Butyl	4.08	3.73	5.28	−1.20
Phenyl	1.34	1.73	2.09	−0.75
p-Tolyl	1.34	1.73	2.10	−0.76
p-Nitrophenyl	1.23	1.70	2.09	−0.86
2,4-Dinitrophenyl	0.96	1.19	1.29	−0.33

[a] All energies in kcal mol^{-1}. The abbreviations denote the following: $\Delta E_{\text{ax-eq}}$ = total energy difference between the axial and equatorial isomer, ΔE_{bend} = difference of the angle bending energies, ΔE_{bnd} = difference of the bonding energies (sum of bond stretching, angle bending, torsional and out-of-plane energies), ΔE_{nbnd} = difference of the nonbonding energies from van der Waals and electrostatic interactions.

Molecular mechanics studies

Force field calculations of alkanediyl calix[5]arenes were performed independently of the experimental studies. Table 5 lists for selected examples the calculated energy differences of equatorial and axial conformers.

Like with the corresponding alkanediyl bridged calix[4]arenes **7** an energetic preference exists for the equatorial position of substituents. By far the highest energy differences are found for R = *t*-Bu (about 4 kcal mol^{-1}) while lower and nearly equal values result for R = Me, Et and *i*-Pr (2.2–2.4 kcal mol^{-1}), which is completely in agreement with the conformational studies reported above. The less favoured axial arrangement of alkyl substituents is due to the steric strain induced by the repulsion between the phenolic hydroxy groups and the substituent (H or Me) at the sp^3-carbon attached to the bridge. This effect is particularly pronounced in the case of the *tert*-butyl substituted calix[5]arene where the repulsion leads to a distortion of the tetrahedral arrangement of the bridging methine carbon (bond angles between 98.6° and 118.7°), to a strong deviation of the calixarene scaffold from the five-fold starting symmetry and even to a pronounced weakening of the circular hydrogen bonding system (O···O distances between 2.70 and 3.31 Å). Similar distortions are observed for *ortho*-substituted aryl residues (like 2,4-dinitrophenyl) in both the equatorial and the axial position, while a "regular shape" of the calix[5]arene is more or less maintained for all of the other calculated structures.

Lower energy differences in comparison to alkyl groups are found for aryl substituents for which only four typical examples are included in Table 5. (Various *para*-substituted phenyl substituents lead to nearly identical results.) However, these energy differences are up to 1 kcal mol^{-1} higher for the calix[5]arenes than for the corresponding calix[4]arenes which again is in good agreement with the experimentally determined values.

An explanation for this predominantly equatorial arrangement of aryl substituents requires a detailed analysis of the calculated geometries. In the case of the alkanediyl calix[4]arenes the axial position of an aryl group is energetically less destabilised due to its planar geometry than that of an alkyl residue. However, an aryl substituent is energetically destabilised in the equatorial arrangement by the repulsion between its *ortho*-positions and the adjacent phenolic moieties while an alkyl group is less hindered in this arrangement. As a result, both the equatorial and the axial conformers of an aryl substituted calix[4]arene are energetically nearly equivalent.

In the case of the calix[5]arenes the axial isomer is very similar to that of the corresponding calix[4]arene with respect to the geometric parameters of the methine bridge. For the equatorial isomer, however, the widening of the Ar–C–Ar bond angles and the slightly larger tilt of the phenolic rings with respect to the mean plane through the methylene carbon atoms in calix[5]arenes compared to calix[4]arenes (if "ideal" C_5 and C_4-symmetrical structures are considered) lead to a slightly larger distance between the *ortho*-positions of the substituent and the adjacent phenolic rings (compare Fig. 5). For example, the distance between the *ortho*-protons of a phenyl-substituted calix[5]arene and the centroids of the adjacent phenolic rings is larger by about 0.2 Å and hence the steric strain of the equatorial isomer is reduced. This is manifested also in the bond angles around the bridging methine carbon which are close to the usual values of the unsubstituted calix[5]arene while for the corresponding aryl substituted calix[4]arenes larger deviations are observed.

Experimental

Syntheses

The preparation of alkanediyl bridged dimers **2** and of the bisbromomethylated compounds **3** derived from them has been described before.[9] The following procedures for the hydroxymethylation are not optimised, and the yields of bishydroxymethylated compounds **4** should be improvable in some cases. The trimer **1** was prepared in analogy to the literature[12] by acid catalysed condensation of bishydroxymethylated *p*-*tert*-butylphenol with excess *p*-cresol.

Column chromatographic separations were done with silica gel (0.015–0.4 mm) using the solvent indicated for the individual case. Prefabricated silica plates (Merck 60 PF$_{254}$) were used for TLC analysis using CHCl$_3$, CHCl$_3$–acetone 10:1 or hexane–acetone 6:1 as eluent. Routine ^{1}H NMR spectra were recorded on a Bruker AC 200 MHz. *J* Values are given in Hz.

Table 6 ^{1}H NMR data (δ_H in ppm, J in Hz) for calix[5]arenes **5** (400 MHz, $CDCl_3$)

Proton	**5a**[a]	**5b**[a]	**5c**[a]	**5d**[a]	**5e**[b]	**5f**[b]
OH	8.78 (s, 1 H) 8.74 (s, 2 H) 8.52 (s, 2 H)	8.76 (s, 1 H) 8.74 (s, 2 H) 8.47 (s, 2 H)	8.72 (s, 2 H) 8.70 (s, 2 H) 8.37 (s, 2 H)	8.55 (s, 2 H) 8.50 (s, 1 H) 7.87 (s, 2 H)	8.72 (s, 2 H) 8.68 (s, 1 H) 8.33 (s, 2 H)	8.70 (s, 3 H) 8.42 (s, 2 H)
ArH	7.16 (s, 2 H) 7.02 (s, 2 H) 6.97 (s, 4 H) 6.94 (s, 2 H)	7.17 (s, 2 H) 6.97 (s, 6 H) 6.93 (s, 2 H)	7.16 (s, 2 H) 6.96 (s, 6 H) 6.91 (s, 2 H)	7.15 (s, 4 H) 6.95 (s, 4 H) 6.91 (s, 2 H)	7.17 (s, 2 H) 6.99 (s, 6 H) 6.86 (s, 2 H)	7.18 (s, 2 H) 7.03 (s, 2 H) 7.01 (s, 4 H) 6.74 (s, 2 H)
CHR	4.56 (q, J 6.8, 1 H)	4.21 (t, J 7.5, 1 H)	3.88 (d, J 11.1, 1 H)	4.42 (s, 1 H)	5.92 (s, 1 H)[c]	5.97 (s, 1 H)[c]
CH_2(ax)	4.09 (d, J 14.0, 2 H) 4.07 (d, J 14.0, 2 H)	4.10 (d, J 13.9, 2 H) 4.08 (d, J 13.9, 2 H)	4.09 (d, J 14.1, 4 H)	4.09 (d, J 14.3, 4 H)	4.06 (d, J 13.6, 4 H)	4.06 (d, J 13.6, 4 H)
CH_2(eq)	3.46 (d, J 14.5, 2 H) 3.43 (d, J 14.5, 2 H)	3.46 (d, J 14.4, 2 H) 3.42 (d, J 14.4, 2 H)	3.44 (d, J 14.1, 2 H) 3.40 (d, J 14.1, 2 H)	3.43 (d, J 14.0, 2 H) 3.39 (d, J 14.0, 2 H)	3.46 (d, J 13.6, 4 H)	3.46 (d, J 13.6, 4 H)
CH_3	2.22 (s, 12 H)	2.22 (s, 12 H)	2.21 (s, 12 H)	2.20 (s, 12 H)	2.21 (s, 6 H) 2.15 (s, 6 H)	22.2 (s, 6 H) 2.17 (s, 6 H)
$C(CH_3)_3$	1.27 (s, 9 H)	1.27 (s, 9 H)	1.26 (s, 9 H)	1.26 (s, 9 H)	1.25 (s, 9 H)	1.25 (s, 9 H)
R	1.53 (d, J 7.0, 3 H)	1.99 (q, J 7.3, 2 H) 0.77 (t, J 7.5, 3 H)	2.44 (m, 1 H) 0.76 (d, J 6.5, 6 H)	1.03 (s, 9 H)	7.06 (d, J 7.6, 2 H) 6.91 (s, 2 H) 2.31 (s, 3 H)	8.09 (d, J 8.1, 2 H) 7.22 (d, 2 H)

[a] At rt. [b] Chemical shifts for the major conformer at 210 K. [c] The methine proton of the minor isomer resonates at 5.24 (**5e**) or 5.29 (**5f**) ppm.

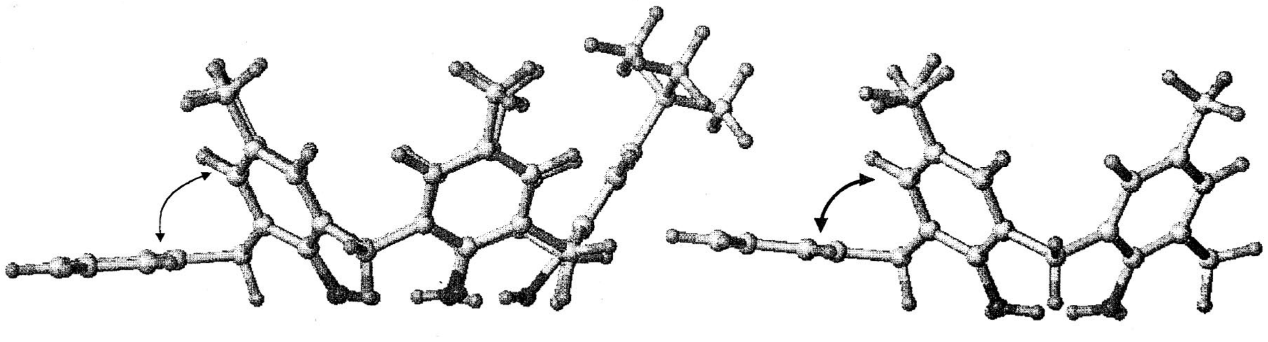


Fig. 5 Stick and ball representation of the minimised equatorial isomers of a phenyl-substituted calix[5]- (left) and calix[4]arene (right). Repulsions are symbolised by arrows.

The ^{1}H NMR data (Bruker DRX 400 MHz) for calix[5]arenes **5a–f** are collected in Table 6.

6,6′-Dihydroxymethyl-4,4′-dimethyl-2,2′-(ethane-1,1-diyl)-diphenol (4a). The dimer 4,4′-dimethyl-2,2′-(ethane-1,1-diyl)-diphenol (**2a**, 4.85 g, 0.02 mol) was dissolved in a solution of NaOH (1.76 g, 0.044 mol) in 20 mL water, formaldehyde (36 mL of a 37% aqueous solution, 0.44 mol) was added and the mixture kept at 40 °C for two days. A crystalline precipitate was filtered, dissolved in water (20 mL)–methanol (70 mL) and the solution dropped in diluted hydrochloric acid, to give the bishydroxymethylated dimer as a white precipitate which was carefully washed with water and dried (3.7 g). An additional quantity (1.5 g), according to TLC ($CHCl_3$–methanol 10 : 1) even purer, was obtained from the first alkaline filtrate. An analytically pure sample was obtained by recrystallisation from $CHCl_3$. Yield 45%, mp 139–140°C; found: C, 69.5; H, 7.4; $C_{18}H_{22}O_4 \cdot 0.5H_2O$ requires C, 69.45; H, 7.45; δ_H (200 MHz, $CDCl_3$) 8.10 (2 H, br s, OH), 7.04, 6.67 (2 H each, s, ArH), 4.67 (4 H, s, CH_2), 4.64 (1 H, q, J 7, CH), 2.22 (6 H, s, Ar-CH_3), 1.60 (3 H, d, J 7, CH-CH_3).

6,6′-Dihydroxymethyl-4,4′-dimethyl-2,2′-(propane-1,1-diyl)-diphenol (4b). Synthesis in analogy to **4a**; an analytical sample was obtained by column chromatography ($CHCl_3$–methanol 10 : 1) or by recrystallisation from $CHCl_3$–light petroleum. Yield 50%, mp 133–134 °C; found: C, 72.25; H, 7.6; $C_{19}H_{24}O_4$ requires C, 72.15; H, 7.65; δ_H (200 MHz, $CDCl_3$) 8.13 (2 H, br s, OH), 7.01, 6.68 (2 H each, s, ArH), 4.68 (4 H, s, CH_2-OH), 4.33 (1 H, t, J 8, CH-CH_2), 2.22 (6 H, s, Ar-CH_3), 2.09 (2 H, p, J 7, CH-CH_2-CH_3), 0.87 (3 H, t, J 7, CH_2-CH_3).

6,6′-Dihydroxymethyl-4,4′-dimethyl-2,2′-(4-tolylmethanediyl)-diphenol (4e). Synthesis in analogy to **4a**; an analytical sample was obtained by column chromatography ($CHCl_3$–methanol 10 : 1). Yield 45%, mp 159–161 °C; found: C, 74.45; H, 6.55; $C_{24}H_{26}O_4 \cdot 0.5H_2O$ requires C, 74.4; H, 7.0; δ_H (200 MHz, $CDCl_3$) 7.2 (2 H, s, OH), 7.08, 7.01 (2 H each, d, J 8.3, ArH), 6.74, 6.67 (2 H each, s, ArH), 6.00 (1 H, s, CH), 4.75 (4 H, s, CH_2), 2.31 (3 H, s, CH_3), 2.16 (6 H, s, CH_3).

6,6′-Dihydroxymethyl-4,4′-dimethyl-2,2′-(4-nitrophenyl-methanediyl)diphenol (4f). Synthesis and purification in analogy to **4a**. Yield 55%, mp 120 °C (softening around 75 °C); δ_H (200 MHz, $CDCl_3$) 8.11 (2 H, d, J 8, ArH), 7.57 (2 H, s, OH), 7.27 (2 H, d, J 9, ArH), 6.75, 6.57 (2 H each, s, ArH), 6.19 (1 H, s, CH), 4.81 (4 H, s, CH_2), 2.16 (6 H, s, CH_3).

Condensation of trimer 1 with bishydroxymethylated dimers 4a,b,e,f. A suspension of 4 mmol (1.56 g) of the trimer **1** (2,6-bis[(2-hydroxy-5-methyl)benzyl]-4-*tert*-butylphenol[12]) and the bishydroxymethylated dimer **4** (4 mmol) in dry xylene (80 mL) was heated under argon to form a clear solution which was refluxed for 3 days. The solvent was evaporated and the residue submitted to column chromatography (*n*-hexane–acetone 6 : 1).

The first fractions consisted of TLC-pure calix[5]arene which was recrystallized from chloroform–methanol. **Calix[5]arene 5a**: yield 0.510 g (19.5%); mp 235 °C; FD-MS: *m*/*z* 656.7 (M^+), **calix[5]arene 5b:** yield 0.81 g (30%); mp 232–234 °C; FD-MS: *m*/*z* 670.7 (M^+), **calix[5]arene 5e:** yield 0.79 g (27%); mp 206–208 °C (decomp.); FD-MS *m*/*z* 732.8 (M^+), **calix[5]arene 5f**: yield 0.55 g (18%); mp 223–225 °C; FD-MS 763.8 (M^+).

Condensation of trimer 1 with bisbromomethylated dimers 3a–d,f. A solution of 5 mmol (1.95 g) of **1** (2,6-bis[(2-hydroxy-5-methyl)benzyl]-4-*tert*-butylphenol[12]) and 5.5 mmol of the corresponding bisbromomethylated 4,4′-dimethyl-2,2′-(alkanediyl)diphenol **3** in 200 ml dioxane was added dropwise under nitrogen over 4 h to a well stirred solution of 1 ml conc. H_2SO_4 in 300 ml dioxane at 60 °C. Afterwards the mixture was refluxed for three days, the solvent was evaporated and the calix[5]- and calix[8]arenes were isolated by column chromatography with $CHCl_3$–CCl_4 mixtures as eluents. All products were finally recrystallized from $CHCl_3$–MeOH. **Calix[5]arene 5c:** yield 440 mg (12.9%), mp 257–258 °C; FD-MS: *m*/*z* 684.7 (M^+), **calix[5]arene 5d:** yield 380 mg (10.9%), mp 240–242 °C; FD-MS: *m*/*z* 698.5 (M^+), **calix[8]arene 6a:** yield 85 mg, mp 372–373 °C; δ_H (200 MHz, $CDCl_3$) 9.51, 9.47, 9.42, 9.36 (4 × s, 8 H, OH), 7.15 (s, 2 H, ArH), 7.00, 6.94, 6.89 (s, 14 H, ArH), 4.85 (q, 2 H, *J* 6.8, CH), 4.2–4.4 (m, 6 H, CH_2), 3.3–3.5 (m, 6 H, CH_2), 2.23, 2.21 (2 × s, 21 H, Ar-CH_3), 1.56 (d, 6 H, CH_3 {+H_2O}), 1.27 (s, >9 H, $C(CH_3)_3$); CI-MS: *m*/*z* 1029.9 (M^+). [A peak at 1057.9 can be interpreted as calix[8]arene with two *p*-*t*-Bu groups and one -CHMe- bridge.] **Calix[8]arene 6b**: yield 120 mg, mp 368–370 °C; δ_H (200 MHz, $CDCl_3$) 9.56, 9.49, 9.46, 9.33 (4 × br s, 8 H, OH), 7.17 (s, 2 H, ArH), 6.96, 6.90 (2 × s, 14 H, ArH), 4.54 (t, 2 H, *J* 7, CH), 4.2–4.4 (m, 6 H, CH_2), 3.3–3.5 (m, 6 H, CH_2), 2.22 (s, 21 H, $ArCH_3$), 2.08 (m, 4 H, CH_2), 1.28 (s, 9 H, $C(CH_3)_3$), 0.85 (t, 6 H, *J* 6.9, CH_3); CI-MS: *m*/*z* 1058.0 (M^-). [A peak at 1071.9 can be interpreted as calix[8]arene with two *p*-*t*-Bu groups and one -CHEt- bridge.] **Calix[8]arene 6c**: yield 68 mg, mp 239–245 °C, δ_H (200 MHz, $CDCl_3$) 9.25–9.65 (8 H, OH), 7.17 (s, 2 H, ArH), 6.85–7.0 (14 H, ArH), 4.2–4.4 (m, 2 H, ArCHAr + 6 H, CH_2), 3.35–3.5 (m, 6 H, CH_2), 2.58 (m, 2 H, $CH(CH_3)_2$), 2.25, 2.23, 2.21 (3 × s, 21 H, $ArCH_3$), 1.29 (s, 9 H, $C(CH_3)_3$), 0.8–0.87 (m, 12 H, $CH(CH_3)_2$); CI-MS: *m*/*z* 1087.6 (MH^+). **Calix[8]arene 6d**: yield 92 mg, decomp. 420 °C, δ_H (200 MHz, $CDCl_3$) 9.53, 9.47 (2 × s, 4 H, OH), 8.90, 8.82 (2 × br s, 4 H, OH), 7.17, 7.13 (2 × s, 4 H, ArH), 6.98, 6.96, 6.92 (3 × s, 12 H, ArH), 4.78 (s, 2 H, CH), 4.36–4.23 (m, 6 H, CH_2), 3.50–3.35 (m, 6 H, CH_2), 2.25, 2.23 (2 × s, 21 H, CH_3), 1.29 (s, 9 H, $ArC(CH_3)_3$), 1.09 (s, 18 H, $C(CH_3)_3$); CI-MS: *m*/*z* 1115.6 (MH^+), 1114.5 (M^-). **Calix[8]arene 6f**: yield 83 mg, decomp. 264 °C ($CHCl_3$–MeOH), δ_H (200 MHz, $CDCl_3$) 9.53, 9.46, 9.43, 9.38 (4 × s, 8 H, OH), 8.06, 7.42 (2 × d, 2 H each, *J* 8.7, $Ar(NO_2)H$), 7.17, 7.01 (2 × d, *J* 1.5, 2 H each, ArH), 6.92 (s, 4 H, ArH), 6.79 (s, 2 H, ArH), 6.72 (s, 4 H, ArH), 6.70 (s, 2 H, ArH), 6.33 (s, 1 H, CH), 4.34–4.15 (m, 7 H, CH_2), 3.50–3.44 (m, 4 H, CH_2), 2.97–2.87 (br, 3 H, CH_2), 2.26 (s, 6 H, CH_3), 2.21 (s, 12 H, CH_3), 1.29 (s, 18 H, $C(CH_3)_3$); FD-MS: *m*/*z* 1166.4 (MH^+).

NMR measurements

Conformational equilibria were studied on a Bruker DRX 400 MHz NMR spectrometer using the "hidden partner" approximation.[15] The maximum broadening of a signal (ω_{max}) is defined as ($\omega_{obs} - \omega_0$) where ω_{obs} is the measured maximal linewidth and ω_0 is the linewidth in the absence of exchange. The value of ω_{max} is related to the chemical shift difference of a given group in the exchanging conformations ($\Delta\nu$) and the mole fraction (p) of the less stable conformer ($p\Delta\nu = \omega_{max}$). At the temperature of maximum broadening (T_m) the rate constant for the conversion of the more stable to the less stable conformer is given by $k = 2\,\pi p\Delta\nu$. In all cases T_m and $\Delta\nu$ values for the signal of the methine proton at the bridge were used. For **4a**–**c** the $\Delta\nu$ value (the difference between the chemical shifts of the methine proton of the equatorial and axial conformation) was estimated from the chemical shift difference between the equatorial and axial methylene protons. The $\Delta\nu$ values for **4e** and **4f** (271.6 and 275.1 Hz, respectively) were measured at 210 K in the slow exchange spectrum and used for the estimation of the conformational equilibria at T_m.

Calculations

The computational studies were performed with the SYBYL 6.0 software including the TRIPOS force field using some modified parameters.[21] The optimisations were performed using a distance-dependent dielectric with $\varepsilon = 1$ until the rms energy gradient was less than 0.001 kcal mol^{-1} $Å^{-1}$ using the Powell minimiser included in the SYBYL/MAXIMIN2 routine. The Gasteiger–Hückel method[22] was used for the calculation of the partial charge distribution of the molecules. A nearly C_5-symmetrical calix[5]arene conformer was chosen as starting structure for the generation of the alkanediyl-substituted compounds.

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References

1 For a review on calixarenes see: V. Böhmer, *Angew. Chem.*, 1995, **107**, 785; *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 713.

2 Up to 20% are available by a one-pot reaction: D. R. Stewart and C. D. Gutsche, *Org. Prep. Proc. Int.*, 1993, **25**, 137; see also K. Iwamoto, K. Araki and S. Shinkai, *Bull. Chem. Soc. Jpn.*, 1994, **67**, 1499.

3 For example, the number of partially *O*-alkylated derivatives, as well as the number of potential conformational isomers in a completely *O*-alkylated product is higher than with calix[4]arenes.

4 D. R. Stewart, M. Krawieck, R. P. Kashyap, W. H. Watson and C. D. Gutsche, *J. Am. Chem. Soc.*, 1995, **117**, 586.

5 For recent examples of guest binding in the cavity of calix[5]arene derivatives see: (*a*) T. Haino, M. Yanase and Y. Fukazawa, *Tetrahedron Lett.*, 1997, **38**, 3739; (*b*) T. Haino, M. Yanase and Y. Fukazawa, *Angew. Chem.*, 1998, **110**, 1004; *Angew. Chem., Int. Ed. Engl.*, 1998, **37**, 997; (*c*) S. Pappalardo and M. F. Parisi, *J. Org. Chem.*, 1996, **61**, 8724; (*d*) R. Arnecke, V. Böhmer, R. Cacciapaglia, A. Dalla Cort and L. Mandolini, *Tetrahedron*, 1997, **53**, 4901; (*e*) F. Arnaud-Neu, S. Fuangswasdi, A. Notti, S. Pappalardo and M. F. Parisi, *Angew. Chem.*, 1998, **110**, 120; (*f*) see also J. W. Steed, C. P. Johnson, R. K. Juneja, R. S. Burkhalter and J. L. Atwood, *Supramol. Chem.*, 1996, **6**, 235.

6 See for instance: (*a*) J. F. Gallagher, G. Ferguson, V. Böhmer and D. Kraft, *Acta Crystallogr., Sect. C*, 1994, **50**, 73; (*b*) M. Perrin and S. Lecocq, *J. Inclusion Phenom. Mol. Recognit. Chem.*, 1991, **11**, 171.

7 (*a*) J. W. Steed, C. P. Johnson, C. L. Barnes, R. K. Juneja, J. L. Atwood, S. Reilly, R. L. Hollis, P. H. Smith and D. L. Clark, *J. Am. Chem. Soc.*, 1996, **117**, 11 426; (*b*) C. P. Johnson, J. L. Atwood, J. W. Steed, C. B. Bauer and R. D. Rogers, *Inorg. Chem.*, 1996, **35**, 2602.

8 J. M. Van Gelder, O. Aleksiuk and S. E. Biali, *J. Org. Chem.*, 1996, **61**, 8419.

9 S. E. Biali, V. Böhmer, S. Cohen, G. Ferguson, C. Grüttner, F. Grynszpan, E. F. Paulus, I. Thondorf and W. Vogt, *J. Am. Chem. Soc.*, 1996, **118**, 12 938.

10 G. Sartori, R. Maggi, F. Bigi, A. Arduini, A. Pastorio and C. Porta, *J. Chem. Soc., Perkin Trans. 1*, 1994, 1657.

11 M. Bergamaschi, F. Bigi, M. Lanfranchi, R. Maggi, A. Pastorio, M. A. Pellinghelli, F. Peri, C. Porta and G. Sartori, *Tetrahedron*, 1997, **53**, 13 037.

12 K. No and K. M. Kwan, *Synthesis*, 1996, 1293.

13 Compare also T. Haino, T. Harano, K. Matsumura and Y. Fukazawa, *Tetrahedron Lett.*, 1996, **36**, 5793.

14 This downfield shift of the axial protons in the cone conformation of *endo*-calix[4]arenes is caused by the proximity to the OH groups, since in *exo*-calix[4]arenes the equatorial protons appear at lower field. See: S. E. Biali, V. Böhmer, J. Brenn, M. Frings, I. Thondorf, W. Vogt and J. Wöhnert, *J. Org. Chem.*, 1997, **62**, 8350.

15 F. A. L. Anet and V. J. Basus, *J. Magn. Reson.*, 1978, **32**, 339. For papers using this method see for example: S. P. Adams and H. W. Whitlock, *J. Am. Chem. Soc.*, 1982, **104**, 1602; D. Casarini, L. Lunazzi and D. Macciantelli, *J. Chem. Soc.*, *Perkin Trans. 2*, **1985**, 1839.

16 C. D. Gutsche and L. J. Bauer, *J. Am. Chem. Soc.*, 1985, **107**, 6052.

17 An unusually high energy barrier of 17.3 kcal mol^{-1} was found for a "resorcinol derived" calix[5]arene consisting of five 2,4-dihydroxybenzophenone units: M. Tabatabai, W. Vogt, V. Böhmer, G. Ferguson and E. F. Paulus, *Supramol. Chem.*, 1994, **4**, 147.

18 This conformation can be designated as TTTtt(17.3), see I. Thondorf and J. Brenn, *J. Chem. Soc.*, *Perkin Trans. 2*, 1997, 2293.

19 J. F. Gallagher, G. Ferguson, V. Böhmer and D. Kraft, *Acta Crystallogr.*, *Sect. C*, 1994, **50**, 73; and references cited there.

20 For a recent example with an average O···O-distance of 2.955 Å see: L. Dumazet, N. Ehlinger, F. Vocanson, S. Lecocq, R. Lamartine and M. Perrin, *J. Inclusion Phenom. Mol. Recognit. Chem.*, 1997, **29**, 175.

21 I. Thondorf, G. Hillig, W. Brandt, J. Brenn, A. Barth and V. Böhmer, *J. Chem. Soc.*, *Perkin Trans. 2*, 1994, 2259.

22 (*a*) J. Gasteiger and M. Marsili, *Tetrahedron*, 1980, **36**, 3219; (*b*) M. Marsili and J. Gasteiger, *Croat. Chem. Acta*, 1980, **53**, 601.

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