

SYNTHESIS AND ¹H NMR COMPLEXATION STUDY OF THIACALIX[4]ARENE TETRAACETATES

Pavel LHOTÁK^{a1,*}, Václav ŠTASTNÝ^{a2}, Petra ZLATUŠKOVÁ^{a3}, Ivan STIBOR^{a4},
Veronika MICHLOVÁ^{b1}, Marcela TKADLECOVÁ^{b2}, Jaroslav HAVLÍČEK^{b3}
and Jan SÝKORA^c

^a Department of Organic Chemistry, Prague Institute of Chemical Technology, Technická 5,
166 28 Prague 6, Czech Republic; e-mail: ¹ lhotakp@vscht.cz, ² stastnyv@vscht.cz,
³ zlatuskp@vscht.cz, ⁴ stibori@vscht.cz

^b Department of Analytical Chemistry, Prague Institute of Chemical Technology, Technická 5,
166 28 Prague 6, Czech Republic; e-mail: ¹ michlovv@vscht.cz, ² tkadlecm@vscht.cz,
³ havlicej@vscht.cz

^c Department of Solid State Chemistry, Prague Institute of Chemical Technology, Technická 5,
166 28 Prague 6, Czech Republic; e-mail: sykoraj@vscht.cz

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Dedicated to Professor Otakar Červinka on the occasion of his 75th birthday.

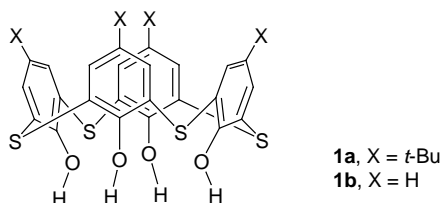
Alkylation of thiacalix[4]arenes with ethyl bromoacetate led to high yields (≈60%) of corresponding tetraacetates in various conformations (cone, partial cone, 1,3-alternate) depending strictly on the carbonate (Na, K, Cs) used for the reaction. The complexation ability of new compounds was studied by ¹H NMR.

Key words: Calixarenes; Thiacalixarenes; Alkylation; NMR spectroscopy; X-Ray diffraction; Complexation; Alkali metal cations.

Calix[*n*]arenes, the well-known cyclic oligomers of 4-substituted phenols and formaldehyde, have drawn much attention during the last decade¹. Because of their simple one-pot preparation, enabling large scale synthesis, and due to their unique molecular framework with the “shaping” and “tuning” possibilities, they became very popular as complexation agents, molecular scaffolds and/or useful building blocks in the construction of more elaborated molecular systems in supramolecular chemistry².

Very recently, the synthesis of new type of calix[4]arene bearing four sulfur atoms instead of methylene bridges has been described^{3–9}. The tetraalkylated derivatives of so-called thiacalix[4]arene **1** were found to possess interesting conformational behaviour both in solution¹⁰ and in the

solid state¹¹. So far, the 1,3-alternate conformer was the only isomer prepared by direct alkylation of parent calixarenes **1a** and **1b**. Therefore, the aim of our research was the preparation of other conformers, which could serve as a starting material and suitable building blocks for the preparation of more sophisticated structures.



Since the introduction of four simple alkyl groups (methyl to butyl) led only to the 1,3-alternate conformation¹¹, we have attempted using of acetate groups which should possess a much higher complexation ability and, consequently, which could serve as templating units in the alkylation reaction (Fig. 1). The alkylation of **1a** and **1b** with an excess of ethyl bromoacetate¹² was carried out in the boiling acetone (3 days) in the presence of various alkali metal carbonates (Na_2CO_3 , K_2CO_3 , Cs_2CO_3). Under these conditions, the expected tetraalkylated derivatives in the form of immobilised conformers were obtained (Scheme 1). It was found that the crude reaction mixtures generally contain three basic conformers **2**, **3** and **4** (cone, partial cone and 1,3-alternate, respectively), the yields of which strongly depend on the metal used in the reaction.

The alkylation of **1a** carried out in the presence of Cs_2CO_3 led to a high yield (68%) of substantially pure 1,3-alternate conformer **4a**, which was very simply isolated from the crude reaction mixture by precipitation¹² of a chloroform extract with methanol. In the mother liquor we have proved

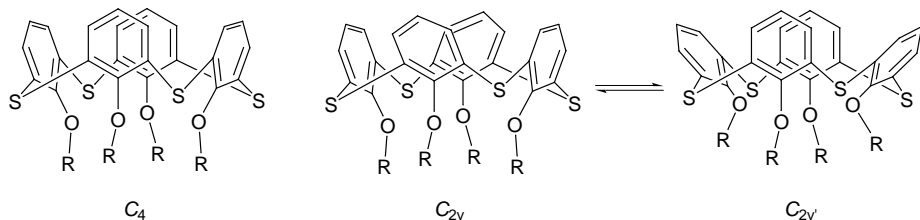
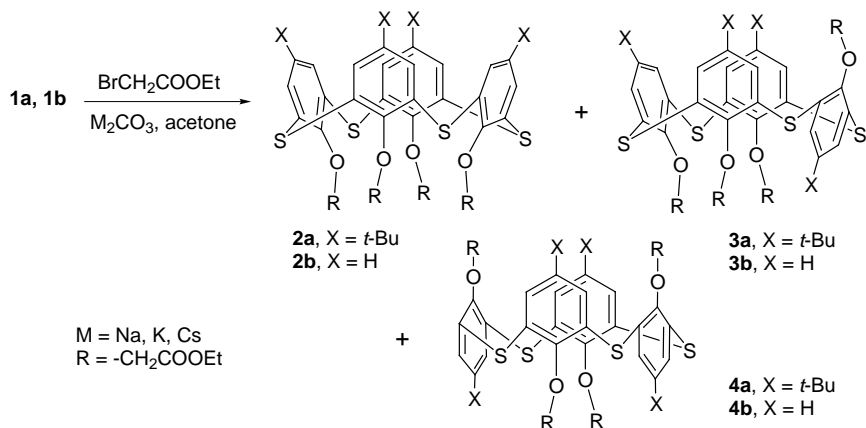


FIG. 1
 C_{2v} - C_{2v} interconversion of tetrasubstituted thiacalix[4]arenes

small amount of two other conformations, **2a** and **3a** (in overall yields 0.5 and 8%, respectively). The situation is shown in Table I. The same reaction with Na_2CO_3 gave cone derivative **2a** (75%) as a main product again after



SCHEME 1

TABLE I
Synthesis and isolation of thiacalix[4]arene tetraacetates **2**, **3** and **4**

Carbonate	Parameter	Precipitate		Filtrate	
		from 1a	from 1b	from 1a	from 1b
Na_2CO_3	overall yield, %	75	65	1.5	8
	content of conformers, %	2a/3a/4a 100/0/0	2b/3b/4b 87/13/0	2a/3a/4a 44/33/23	2b/3b/4b 31/44/25
	isolated, %	75/0/0	55/0/0 ^a		
K_2CO_3	overall yield, %	69	58	14	11
	content of conformers, %	2a/3a/4a 6/80/14	2b/3b/4b 3/79/18	2a/3a/4a 50/50/50	2b/3b/4b 30/55/15
	isolated, %	0/62/0 ^b	0/48/0 ^b		
Cs_2CO_3	overall yield, %	68	70	8	8
	content of conformers, %	2a/3a/4a 0/0/100	2b/3b/4b 0/0/100	2a/3a/4a 0/85/15	2b/3b/4b 0/74/26
	isolated, %	0/0/68	0/0/70		

^a Isolated by repeated precipitation from a CH_2Cl_2 -methanol mixture. ^b Isolated by column chromatography using the whole reaction mixture (precipitate and filtrate combined).

simple precipitation, while the mother liquor contains very small amounts of all three conformers **2a**, **3a** and **4a** (lower than 1% of each). The most complex situation was observed in case of K_2CO_3 , where the precipitate contains all the three conformations **2a**, **3a** and **4a** in an approximate molar ratio of 6 : 80 : 14. Consequently, the partial cone conformer **3a** was isolated in 62% by column chromatography (silica gel) of the whole reaction mixture. These results are comparable with the recently described synthesis¹² of compounds **2a–4a**. Nevertheless, we have analysed the reaction mixtures in more details^{12b} showing the exact contents of appropriate conformers. Furthermore, our procedure yields the proposed products without the use of column chromatography^{12a} (**2a**, **4a**) only after a simple precipitation from the crude reaction mixture. It enables the preparation of the above noticed compounds in a large scale (up to 30 g of starting thiacalixarene **1a**), as was proved by us.

The above facts indicate the crucial role of the metal template in the formation of appropriate conformations. Similar effects are known from the chemistry of “classic” calix[4]arene, nevertheless, the selectivity is not so high, especially in the case of 1,3-alternate conformation. It is well-known that the *tert*-butylcalix[4]arene gives with Cs_2CO_3 almost the pure partial cone isomer and the 1,3-alternate is inaccessible by direct alkylation¹³. On the other hand, thiacalix[4]arene **1a** gives smoothly high yields of this conformer. A possible explanation can be based on the fact that the size of template cation match the size of the cavity formed by thiacalixarene, which is obviously bigger than that in a “classic” calixarene. While the Na^+ ion corresponds to the size of cone cavity and can be accommodated amongst four ester groups, the Cs^+ ion is clearly too big for such a binding mode. Instead, the cesium cation prefers 1,3-alternate conformation where the sterical repulsion is minimised. The potassium cation represents a kind of intermediate situation.

It was shown¹³ in the chemistry of classical calix[4]arene, that the removing of *tert*-butyl groups leads to dramatic changes in the conformational preferences in the alkylation reaction using ethyl bromoacetate. Thus, *tert*-butylcalix[4]arene gives with K_2CO_3 a mixture of cone and partial cone derivatives in the 96 : 3 ratio, while calix[4]arene under the identical conditions yields a complex mixture of cone, partial cone and 1,3-alternate conformations in the 33 : 46 : 21 ratio. Consequently, we have tested the behaviour of de-*tert*-butylated thiacalix[4]arene **1b** in the same reaction. Surprisingly, our results indicate the same type of the conformational preferences as observed for **1a** (albeit not so pronounced) during the alkylation

of **1b**. Thus, with Na_2CO_3 used as a base, a mixture of **2b** and **3b** in the 87 : 13 molar ratio was obtained in 65% overall yield (after precipitation with methanol) while K_2CO_3 gave a precipitate consisting of all the three conformations **2b/3b/4b** in the 3 : 79 : 18 ratio. A simple reprecipitation did not lead to pure products. Hence, isomers **2b** and **3b** were isolated by column chromatography on silica gel in 55 and 48% yields, respectively. The alkylation with Cs_2CO_3 gave mixture of partial cone **3b** and 1,3-alternate **4b** compounds which yielded pure **4b** (70%) by reprecipitation from a CH_2Cl_2 -methanol mixture.

The ^1H NMR spectra of compounds **2a**, **3a** and **4a** were measured in CDCl_3 . The simplest conformer assignment is in the case of partial cone derivative **3a** where the expected splitting pattern can be found, such as the set of two singlets and two doublets (*meta* interactions) in the aromatic region. The splitting pattern of **2a** and **4a** is the same, showing high symmetry of both isomers. Therefore, for the assignment of appropriate conformation, a ^1H NOE experiment (DPFGSE-NOE)¹⁴ was measured. In the spectrum of **4a**, we observed strong interactions between the O- CH_2 -CO groups (4.61 ppm) and aromatic hydrogens (7.49 ppm), which are possible only for 1,3-alternate conformation. Accordingly, no such interaction was obtained for **2a**. Another indirect evidence for the assignment of **2a** and **4a** is a 0.5 ppm difference (0.36 ppm for **2b** and **4b**) between the chemical shifts of the $-\text{CH}_2\text{CO}-$ groups: 5.17 versus 4.61 ppm. The significant high-field shift for 1,3-alternate is apparently caused by the proximity of the above mentioned group and the aromatic system (magnetic anisotropy of aromatic ring). The spectra of de-*tert*-butylated derivatives **2b-4b** also possess the corresponding splitting patterns. The interesting behaviour was observed with **2b** where broad signals in the aromatic part of the spectrum indicate the presence of an additional dynamic process at room temperature. As we found very recently, this can be ascribed to the C_{2v} - $C_{2v'}$ interconversion between so called pinched cone conformations of tetra-substituted cone derivatives¹⁵ (Fig. 1). The apparent C_4 symmetry of **2b** observed at ambient temperature (Fig. 2a, 28 °C) is in fact the result of averaging due to the rapid equilibrium between the two pinched cone conformers. As obvious from Fig. 2, the lowering of the temperature leads to the extensive line broadening in the ^1H NMR spectrum (0 °C, Fig. 2b), and finally to the formation of two sets of signals corresponding to the lower C_{2v} symmetry of pinched cone conformation (-60 °C, Fig. 2d). The relatively high coalescence temperature of this process (ca -10 °C) indicates the much higher activation energy of pinched cones interconversion as

compared with classical calix[4]arenes (in acetate derivatives this process has never been observed)¹⁶.

The structure of **2b** was also confirmed by X-ray analysis of single crystal. As shown in Figs 3 and 4, cone derivative possesses typical pinched cone conformation with two opposite phenyl rings facing each other (interplanar angle 39°) in the cavity and two flattened rings (interplanar angle 108°) oriented outside the cavity. As expected, the cavity of **2b** is somewhat bigger than that in the corresponding cone tetraacetate of "classic" calix[4]arene. Thus, the distances between two neighbouring sulfur atoms (S1–S2) and between two opposite sulfur atoms (S1–S3) are 5.48 and 7.67 Å, respectively, while the typical distances between corresponding CH₂ groups in the cone conformation¹⁷ of 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis[(ethoxycarbonyl)methoxy]calix(4)arene are 5.11 and 7.16 Å.

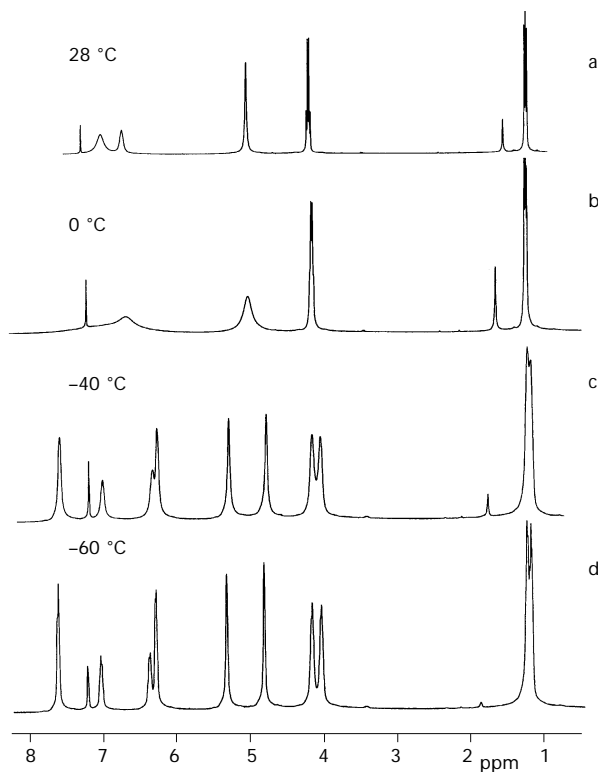


FIG. 2
Temperature dependent ¹H NMR spectra of **2b** (CDCl₃, 500 MHz)

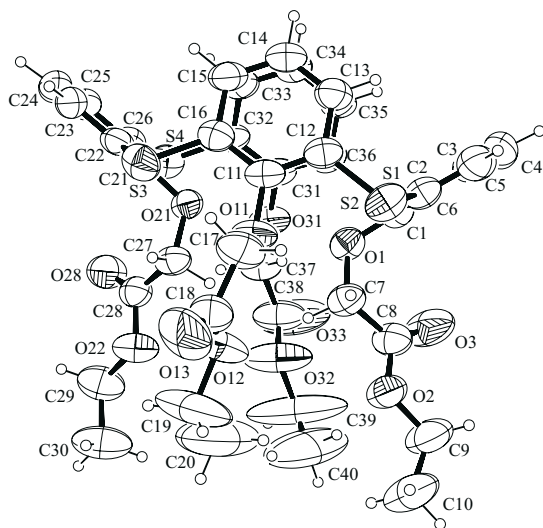


FIG. 3
ORTEP drawing of X-ray structure of **2b**

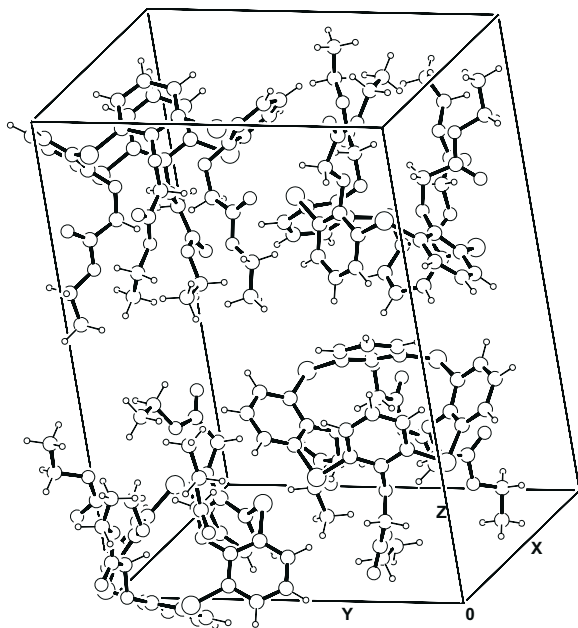


FIG. 4
Molecular packing of **2b**

A complexation study of **2a–4a** reveals that all novel compounds interact with alkali metal cations. The interactions were studied by ^1H NMR spectroscopy (300, 400 or 500 MHz, CDCl_3 : CD_3CN is 4 : 1, v/v) using standard NMR titration experiments, where the ligand concentration was kept constant while the concentration of salts (picrates) was changed to achieve at least a twenty-fold excess.

The titration experiments could be subdivided into three general groups: (i) slow-exchange conditions, (ii) fast-exchange conditions and (iii) intermediate conditions. Under the slow-exchange conditions, two sets of signals were observed in the spectra, assignable to the complexed and uncomplexed ligand. In all the cases studied, the formation of only the 1 : 1 complexes was observed as indicated by characteristic doubling of appropriate signals. Figure 5 shows this situation after an addition of sodium picrate to a solution of **2a** at 298 K. Similar behaviour was also found for the **2a** : K^+ system at 230 K, while at room temperature, only unresolved broad diffuse peaks were obtained, which corresponds to the above-noticed item (iii).

All experiments carried out with 1,3-alternate conformation of **4a** at room temperature also possessed typical features of intermediate conditions: very broad, insufficiently resolved peaks, unacceptable for the direct integration. Hence, to achieve better resolution with **4a**, measurement at lower temperatures was used: Na^+ (260 K), K^+ (270 K), Rb^+ (230 K) and Cs^+

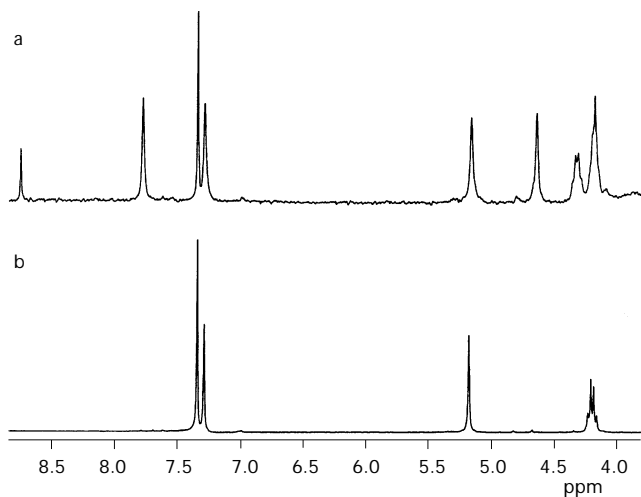


FIG. 5
Partial ^1H NMR spectrum of **2a** (300 MHz, 298 K, CDCl_3): a after addition of Na^+Pic^- , b free **2a**

(230 K). The lower symmetry of ^1H NMR spectra of the complexes indicates an unsymmetrical complexation, with the metal cation held by two acetate units at one side of the molecule. An example of the complex formation for the **4a** : Rb^+ system is depicted in Fig. 6. In all the above-mentioned measurements, simple integration of appropriate signals led directly to the concentration of complexed and uncomplexed thiacalixarene species in the measured solution. The corresponding complexation constants were then obtained as an average value from several independent measurements; they are collected in Table II.

An addition of metal (Li, Na, K, Rb) picrates into a solution of partial cone derivative **3a** at room temperature resulted in the induced chemical shifts of signals – a typical feature of the fast-exchange conditions. As follows from Fig. 7, an addition of NaPic to a solution of **3a** in a CDCl_3 : CD_3CN (4 : 1, v/v) mixture caused a visible shift of aromatic protons in both calix[4]arene subunits (≈ 75 Hz). The plot of the induced chemical shifts *versus* the added metal concentration led to common titration curves corresponding to the formation of the 1 : 1 complex. The stoichiometry of the complexation was also proved using standard Job's plot procedure (Fig. 8). The complexation constants under the fast-exchange conditions were computed using nonlinear-regression curve-fitting program; they are collected in Table II. Regarding the absolute values of the

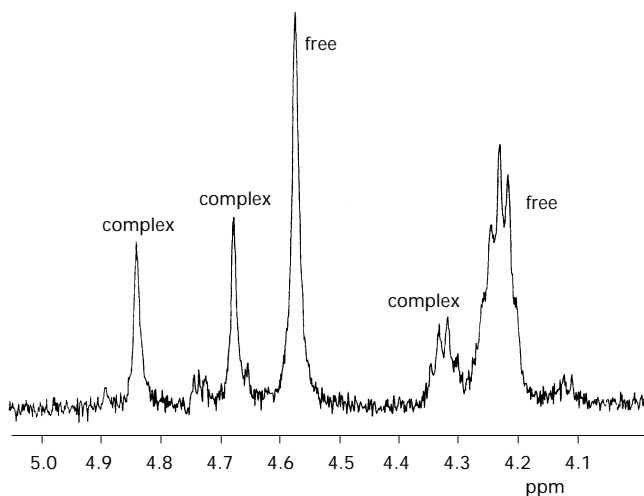


FIG. 6

Partial ^1H NMR spectrum of **4a** (CDCl_3 : CD_3CN is 4 : 1, v/v) after addition of Rb^+Pic^- (500 MHz, 230 K, CDCl_3)

TABLE II
Complexation constants K (in $\text{mol}^{-1} \text{dm}^3$) for metal picrates in $\text{CDCl}_3 : \text{CD}_3\text{CN}$ (4 : 1, v/v), temperatures (in K) are indicated in parentheses

Compound	Li ⁺	Na ⁺	K ⁺	Rb ⁺	Cs ⁺
2a	$>10^4$ (298) ^b	$6\,600 \pm 1\,100$ (298) ^c	320 ± 30 (230) ^c	0^a (298)	0^a (298)
3a	$3\,500 \pm 1\,500$ (298) ^b	$7\,040 \pm 740$ (298) ^b	$31\,000 \pm 5\,000$ (298) ^b	$>10^4$ (298) ^b	0^a (298)
4a	0^a (298)	$5\,500 \pm 2\,300$ (260) ^c	$4\,800 \pm 200$ (270) ^c	$8\,500 \pm 3\,100$ (230) ^c	210 ± 30 (230) ^c
2b	$1\,120 \pm 210$ (298) ^b	$2\,870 \pm 690$ (298) ^b	0^a (298)	0^a (298)	0^a (298)
3b	0^a (298)	0^a (298)	0^a (298)	0^a (298)	0^a (298)
4b	0^a (298)	0^a (298)	100 ± 80 (298) ^{b,d}	680 ± 160 (298) ^{b,d}	$1\,590 \pm 800$ (298) ^{b,d}

^a No changes were observed in the ^1H NMR spectrum. ^b Fast-exchange conditions. ^c Slow-exchange conditions. ^d $\text{CDCl}_3 : \text{CD}_3\text{CN}$ (1 : 1, v/v).

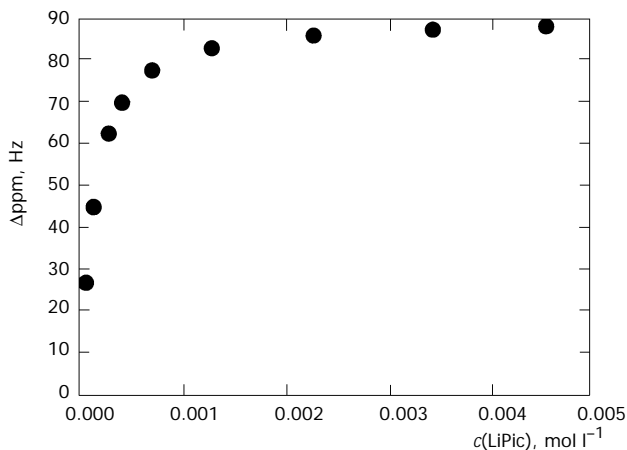


FIG. 7

Typical titration curve of **3a** with Li^+Pic^- (500 MHz, 298 K, $\text{CDCl}_3 : \text{CD}_3\text{CN}$, $c(\mathbf{3a}) = 1 \cdot 10^{-4} \text{mol dm}^{-3}$)

complexation constants, Table II indicates some trends – each conformer **2a–4a** possesses the highest selectivity towards a specific cation, the size of which depends on the shape of the calixarene cavity. While the cone conformer **2a** shows the highest selectivity to Li^+ ($K > 10^4 \text{ mol}^{-1} \text{ dm}^3$) and Na^+ ($K = 6\,600 \text{ mol}^{-1} \text{ dm}^3$), the 1,3-alternate **4a** prefers much larger Rb^+ cation ($K = 8\,500 \text{ mol}^{-1} \text{ dm}^3$). The selectivity of the measured complexation generally corresponds to the preferences obtained in the alkylation reactions.

Quite a different situation was found for the tetraacetates **2b**, **3b** and **4b**, derived from de-*tert*-butylated thiacalix[4]arene. In general, the complexation ability of these compounds is suppressed if compared with that of *tert*-butyl derivatives **2a–4a**. The cone derivative **2b** interacts only with Li^+ ($K = 1\,120 \text{ mol}^{-1} \text{ dm}^3$) and Na^+ ($K = 2\,870 \text{ mol}^{-1} \text{ dm}^3$) cations, while the addition of KPic did not induced any visible changes in NMR spectra. Interestingly, the pinched cone–pinched cone interconversion is influenced by the presence of Na^+ . The addition of 1 equivalent of sodium picrate to the solution of **2b** in $\text{CDCl}_3 : \text{CD}_3\text{CN}$ (4 : 1, v/v) suppressed the coalescence temperature of this process, obviously due to the fact that the C_4 symmetry is stabilised by the complexation (Figs 9a, 9b show the situation at $-40 \text{ }^\circ\text{C}$). Subsequent lowering of the temperature led finally to the slow-exchange conditions and to the separated signals for the complex (C_4 symmetry) and the pinched cone conformers (C_{2v} symmetry) at $-80 \text{ }^\circ\text{C}$, Fig. 9c. To the best of our knowledge, this is the first example of such an equilibrium observed in the whole calixarene chemistry.

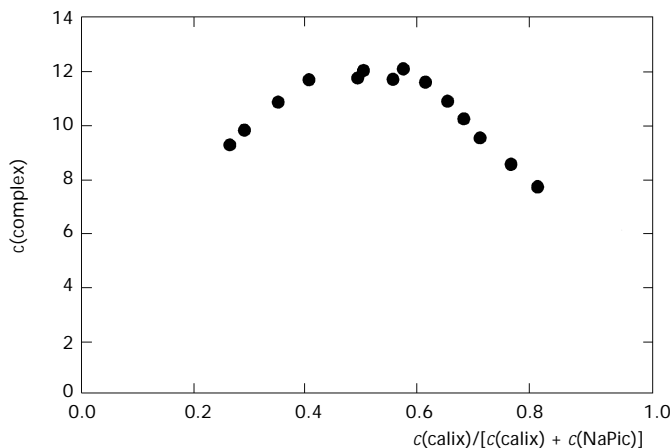


FIG. 8

Job's plot for the **3a**: Na^+Pic^- system ($\text{CDCl}_3 : \text{CD}_3\text{CN}$ is 4 : 1, v/v, $c = 2 \cdot 10^{-3} \text{ mol dm}^{-3}$)

Very unexpected results were obtained for the partial cone conformer **3b**. Under the conditions used for the measurement ($\text{CDCl}_3 : \text{CD}_3\text{CN}$ 4 : 1, 298 K, 500 Hz) no changes in spectra were observed after addition (up to 20 equivalents) of the corresponding picrates (<10 Hz). This indicates unprecedentedly low (if any) complexation constants in this case. Probably, the partial cone derivative **3b** adopts such a conformation that does not enable efficient complexation with spherical cations. 1,3-Alternate conformer **4b** prefers larger cations with the highest selectivity towards Cs^+ ($K = 1\,590 \text{ mol}^{-1} \text{ dm}^3$).

In conclusion, the alkylation of thiacalixarenes **1a** and **1b** with ethyl bromoacetate gives high yields of tetraalkylated products **2–4** immobilised in the defined conformations, depending on the cation used for the reaction. These conformers represent valuable building blocks for the design of novel thiacalixarene-based receptors. The complexation study revealed an interesting behaviour of these compounds, especially the pinched cone-pinchd cone interconversion of **2b** and its suppression by cation added. The synthetic exploitation of new derivatives is currently under investigation.

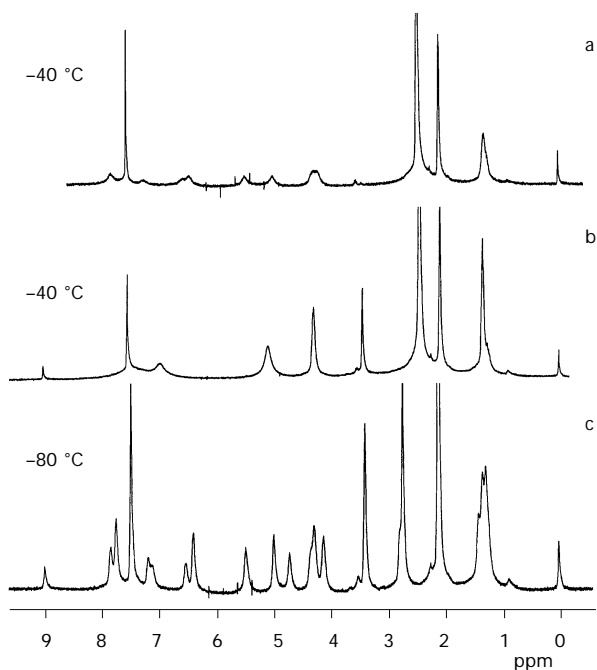


FIG. 9

^1H NMR spectra of **2b** in $\text{CDCl}_3 : \text{CD}_3\text{CN}$ (4 : 1, v/v): a free **2b** (3 mol dm^{-3}), b the same sample after addition of NaPic (1 equivalent), c sample as in b at lower temperature

EXPERIMENTAL

Melting points were determined on a Boetius block (Zeiss Jena, Germany) and are not corrected. The IR spectra (ν_{\max} in cm^{-1}) were measured on an FT-IR spectrometer Nicolet 740 in KBr. ^1H NMR spectra were obtained on a Bruker 400 in CDCl_3 using TMS (δ 0 ppm) as an internal standard. Chemical shifts are given in ppm (δ -scale), coupling constants (J) in Hz. The purity of the substances and the reaction courses were monitored by TLC using Silufol and Alufol plates (Kavalier, Votice, Czech Republic). Column preparative chromatography was carried out on a silica gel Merck (60/100).

Alkylation of Thiacalixarene **1a**. General Procedure

A mixture of compound **1a** (1.5 mmol), an appropriate carbonate (10 mmol) and ethyl bromoacetate (20 mmol) was stirred under reflux in acetone (20 ml) for 3 days. The reaction mixture was poured into water and extracted with chloroform. The organic layer was washed with water, dried over anhydrous MgSO_4 and evaporated to dryness. The residue was dissolved in CH_2Cl_2 (5 ml) and precipitated from a great excess of methanol (100 ml) to yield crude products. The overall yields of the precipitate and the product from the filtrate (after evaporation to dryness), together with the contents of appropriate conformers are collected in Table I.

5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetrakis[(ethoxycarbonyl)methoxy]-2,8,14,20-tetrathiacalix[4]arene (cone) (2a). Carbonate used: Na_2CO_3 ; yield 75%; m.p. 173–175 °C (methanol- CHCl_3) (ref. ^{12a}: 180.0–180.6 °C, ref. ^{12b}: 165–167 °C). ^1H NMR (CDCl_3): 1.08 (s, 36 H, *t*-Bu); 1.27 (t, 12 H, $J = 7.3$, $-\text{CH}_2\text{CH}_3$); 4.20 (q, 8 H, $J = 7.1$, $-\text{CH}_2\text{CH}_3$); 5.17 (s, 8 H, O- CH_2 -COOEt); 7.28 (s, 8 H, H arom.). IR (KBr): 1 754, 1 730. For $\text{C}_{56}\text{H}_{72}\text{O}_{12}\text{S}_4$ (1 065.5) calculated: 63.13% C, 6.81% H, 12.04% S; found: 62.87% C, 6.73% H, 12.12% S.

5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetrakis[(ethoxycarbonyl)methoxy]-2,8,14,20-tetrathiacalix[4]arene (partial cone) (3a). Carbonate used: K_2CO_3 ; isolated by column chromatography on silica gel using a petroleum ether- CHCl_3 mixture as an eluent in 62% yield; m.p. 205–207 °C (ethyl acetate- CHCl_3) (ref. ^{12a}: 212.0–212.8 °C, ref. ^{12b}: 202–204 °C). ^1H NMR (CDCl_3): 1.04 (s, 18 H, *t*-Bu); 1.13 (t, 3 H, $J = 7.1$, $-\text{CH}_2\text{CH}_3$); 1.27 (t, 6 H, $J = 7.1$, $-\text{CH}_2\text{CH}_3$); 1.31 (s, 9 H, *t*-Bu); 1.32 (t, 3 H, $J = 7.1$, $-\text{CH}_2\text{CH}_3$); 1.42 (s, 9 H, *t*-Bu); 3.97 (q, 2 H, $J = 7.1$, $-\text{CH}_2\text{CH}_3$); 4.15–4.30 (m, 6 H, $J = 7.1$, $-\text{CH}_2\text{CH}_3$); 4.64 (s, 2 H, O- CH_2 -COOEt); 4.69 (d, 2 H, $J = 15.4$, O- CH_2 -COOEt); 4.73 (s, 2 H, O- CH_2 -COOEt); 4.77 (d, 2 H, $J = 15.4$, O- CH_2 -COOEt); 7.01 (d, 2 H, $J = 2.7$, H arom.); 7.52 (d, 2 H, $J = 2.7$, H arom.); 7.54 (s, 2 H, H arom.); 7.85 (s, 2 H, H arom.). IR (KBr): 1 764. For $\text{C}_{56}\text{H}_{72}\text{O}_{12}\text{S}_4$ (1 065.5) calculated: 63.13% C, 6.81% H, 12.04% S; found: 63.03% C, 6.84% H, 11.94% S.

5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetrakis[(ethoxycarbonyl)methoxy]-2,8,14,20-tetrathiacalix[4]arene (1,3-alternate) (4a). Carbonate used: Cs_2CO_3 ; yield 68%; m.p. 314–318 °C (ethyl acetate- CHCl_3) (ref. ^{12a}: 329.5–331.0 °C, ref. ^{12b}: >260 °C). ^1H NMR (CDCl_3): 1.24 (s, 36 H, *t*-Bu); 1.27 (t, 12 H, $J = 7.1$, $-\text{CH}_2\text{CH}_3$); 4.21 (q, 8 H, $J = 7.1$, $-\text{CH}_2\text{CH}_3$); 4.61 (s, 8 H, O- CH_2 -COOEt); 7.49 (s, 8 H, H arom.). IR (KBr): 1 768, 1 731. For $\text{C}_{56}\text{H}_{72}\text{O}_{12}\text{S}_4$ (1 065.5) calculated: 63.13% C, 6.81% H, 12.04% S; found: 63.39% C, 7.01% H, 11.99% S.

Alkylation of Thiacalixarene **1b**. General Procedure

A mixture of compound **1b** (0.6 mmol), an appropriate carbonate (6 mmol) and ethyl bromoacetate (12 mmol) was stirred under reflux in acetone (15 ml) for 3 days. The reaction

mixture was poured into water and extracted with chloroform. The organic layer was washed with water to neutral pH, dried over anhydrous MgSO_4 and evaporated to dryness. The residue was dissolved in CH_2Cl_2 (2 ml) and precipitated with methanol (50 ml) to yield crude products. The overall yields of the precipitate and product from the filtrate (after evaporation to dryness), together with the contents of appropriate conformers are collected in Table I.

25,26,27,28-Tetrakis[(ethoxycarbonyl)methoxy]-2,8,14,20-tetrathiocalix[4]arene (cone) (2b). Carbonate used: Na_2CO_3 ; isolated by reprecipitation from CH_2Cl_2 -methanol mixture in 55% yield; m.p. 116–117 °C (methanol- CHCl_3). ^1H NMR (CDCl_3): 1.26 (t, 12 H, $J = 7.2$, $-\text{CH}_2\text{CH}_3$); 4.20 (q, 8 H, $J = 7.1$, $-\text{CH}_2\text{CH}_3$); 5.04 (s, 8 H, O- CH_2 -COOEt); 6.71 (brs, 4 H, H-*para*); 7.00 (brs, 8 H, H-*meta*). IR (KBr): 1 754, 1 732. For $\text{C}_{40}\text{H}_{40}\text{O}_{12}\text{S}_4$ (841.0) calculated: 57.13% C, 7.79% H, 15.25% S; found: 57.57% C, 7.73% H, 15.22% S.

25,26,27,28-Tetrakis[(ethoxycarbonyl)methoxy]-2,8,14,20-tetrathiocalix[4]arene (partial cone) (3b). Carbonate used: K_2CO_3 ; isolated by column chromatography on silica gel using petroleum ether- CHCl_3 mixture as an eluent in 48% yield; m.p. 164–165 °C (ethyl acetate- CHCl_3). ^1H NMR (CDCl_3): 1.20 (t, 3 H, $J = 7.1$, $-\text{CH}_2\text{CH}_3$); 1.33 (t, 6 H, $J = 7.2$, $-\text{CH}_2\text{CH}_3$); 1.42 (t, 3 H, $J = 7.1$, $-\text{CH}_2\text{CH}_3$); 4.01 (q, 2 H, $J = 6.6$, $-\text{CH}_2\text{CH}_3$); 4.10 (s, 2 H, O- CH_2 -COOEt); 4.27 (q, 6 H, $J = 7.1$, $-\text{CH}_2\text{CH}_3$); 4.40 (q, 3 H, $J = 7.1$, $-\text{CH}_2\text{CH}_3$); 4.70 (s, 4 H, O- CH_2 -COOEt); 4.81 (s, 2 H, O- CH_2 -COOEt); 6.65 (t, 2 H, $J = 7.7$, H-*para*); 6.78 (d, 2 H, $J = 8.1$, H-*meta*); 6.90 (t, 2 H, $J = 6.7$, H-*para*); 7.15 (t, 2 H, $J = 6.6$, H-*para*); 7.46 (d, 2 H, $J = 8.2$, H-*meta*); 7.70 (d, 2 H, $J = 7.7$, H-*meta*); 7.96 (d, 2 H, $J = 7.7$, H-*meta*). IR (KBr): 1 755, 1 733. For $\text{C}_{40}\text{H}_{40}\text{O}_{12}\text{S}_4$ (841.0) calculated: 57.13% C, 7.79% H, 15.25% S; found: 57.07% C, 7.84% H, 15.04% S.

25,26,27,28-Tetrakis[(ethoxycarbonyl)methoxy]-2,8,14,20-tetrathiocalix[4]arene (1,3-alternate) (4b). Carbonate used: Cs_2CO_3 ; yield 70%; m.p. 194–195 °C (ethyl acetate- CHCl_3). ^1H NMR (CDCl_3): 1.39 (t, 12 H, $J = 7.1$, $-\text{CH}_2\text{CH}_3$); 4.34 (q, 8 H, $J = 7.1$, $-\text{CH}_2\text{CH}_3$); 4.68 (s, 8 H, O- CH_2 -COOEt); 6.83 (t, 4 H, $J = 7.7$, H-*meta*); 7.60 (d, 8 H, $J = 7.7$, H-*para*). IR (KBr): 1 756, 1 731. For $\text{C}_{40}\text{H}_{40}\text{O}_{12}\text{S}_4$ (841.0) calculated: 57.13% C, 7.79% H, 15.25% S; found: 57.59% C, 7.81% H, 14.99% S.

X-Ray Measurement

X-Ray data for $\text{C}_{40}\text{H}_{40}\text{O}_{12}\text{S}_4$, $M = 840.988 \text{ g mol}^{-1}$, orthorhombic system, space group $P2_12_12_1$, $a = 12.016(1)$, $b = 16.245(1)$, $c = 21.598(1) \text{ \AA}$, $Z = 4$, $V = 4215.8(4) \text{ \AA}^3$, $D_c = 1.325 \text{ g cm}^{-3}$, $\mu(\text{CuK}\alpha) = 2.53 \text{ mm}^{-1}$, crystal dimensions $0.08 \times 0.15 \times 0.4 \text{ mm}$. Data were measured at 293 K on an Enraf-Nonius CAD4 diffractometer with graphite monochromated $\text{CuK}\alpha$ radiation. The structure was solved by direct methods¹⁸ and anisotropically refined by full-matrix least-squares on F (ref.¹⁹) to final $R = 0.051$ and $R_w = 0.05$ using 2 956 independent reflections ($\theta_{\text{max}} = 67.94^\circ$). Hydrogen atoms were found from the expected geometry; they were not refined. Psi scan was used for the absorption correction. Crystallographic data for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC-139288. Copies of the data can be obtained free of charge on application to CCDC, e-mail: deposit@ccdc.cam.ac.uk.

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