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Tetraalkylated 2,8,14,20-Tetrathiacalix[4]arenes: Novel Infinite Channels in the Solid State

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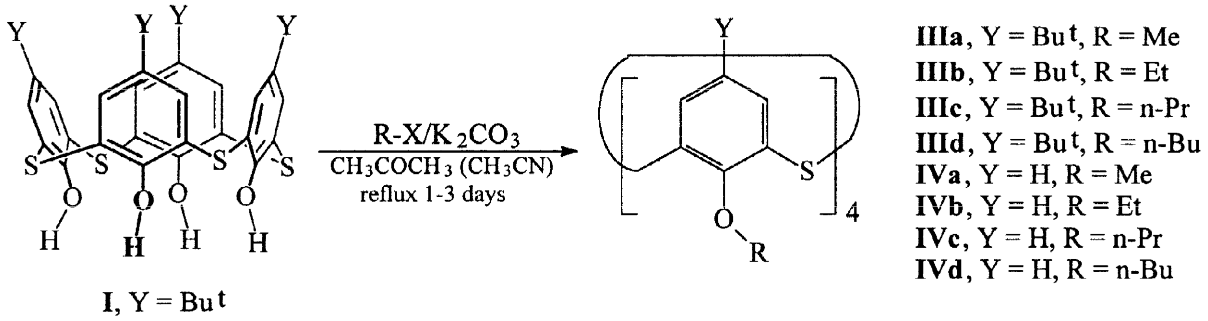
Abstract: The synthesis of new tetraalkylated derivatives of 2,8,14,20-tetrathiacalix[4]arenes was achieved by the refluxing of thiacalixarenes in acetone or acetonitrile with the alkylation agent (R-I, R-Br) in the presence of K_2CO_3 or Cs_2CO_3. The structure of the tetraalkylated thiacalix[4]arenes was studied by means of ^1H NMR experiments proving the *1,3-alternate* conformation under measurement conditions ($CDCl_3$, room temperature). The same conformation was established by X-ray analysis in the solid state where these derivatives create nice infinite channels.

Keywords: Calixarenes; Alkylation; X-Ray crystal structure

During the last decade, calix[n]arenes,[1,2] a family of macrocyclic oligophenols, have attracted much attention because of their unique molecular structure and simple one-pot preparation. Indeed, calix[4]arene has proved to be very important building block in supramolecular chemistry.[3] The easy chemical transformability of this molecule together with its „tuneable“ molecular shape (conformation), makes calix[4]arene very attractive for molecular design. There are many examples in the literature dealing with the use of calix[4]arene as a molecular scaffold for the synthesis of more elaborate molecules, supramolecular assemblies, sensors, receptors etc. This was facilitated by the well developed chemistry of calix[4]arene, the best developed, so far, in the calix[n]arene family.

In this respect, the recently prepared thiacalixarenes[4,5] **I** and **II** represent very promising molecules with many potential applications in the above mentioned fields. Compounds **I** and **II** not only have similar chemistry to that of calix[4]arene, but also the presence of the four sulphur atoms should bring some new



I, Y = Bu^t
II, Y = H

IIIa, Y = Bu^t, R = Me
IIIb, Y = Bu^t, R = Et
IIIc, Y = Bu^t, R = n-Pr
IIId, Y = Bu^t, R = n-Bu
IVa, Y = H, R = Me
IVb, Y = H, R = Et
IVc, Y = H, R = n-Pr
IVd, Y = H, R = n-Bu

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features into the chemistry of „classical“ calixarenes. Hence, the aim of our work was the study of simple chemical transformations of the basic skeleton *via* alkylation reactions of the lower rim (OH groups).

The alkylation of **I** when carried out by the procedure commonly used in calix[4]arene chemistry (DMF, NaH/PrI (excess)) did not lead to the proposed product and, after 48 h at room temperature, gave only unreacted thiacalixarene. Similarly, heating under reflux in THF:DMF (5:1) mixture (5 days) gave only traces of products. Propylation in DMF at 90°C (24 h) yielded a complex reaction mixture including several alkylated products and the starting compound **I**, from which the tetraalkylated compound **IIIc** was isolated, but only in low yield (18%), using preparative TLC.

Surprisingly, the alkylation of **I** with an excess of methyl iodide in the presence of K_2CO_3 in refluxing acetone (24 h) gave the expected derivative **IIIa** smoothly in excellent yield (91%). The influence of the cation used in the base was demonstrated during the preparation of tetrapropyl derivative **IIIc**. The reaction[6] in acetone at reflux (48 h) using various carbonates (Cs_2CO_3, K_2CO_3, Na_2CO_3) led to the proposed product **IIIc** in 70%, 65% and 0%, respectively[7]. The use of acetonitrile as solvent gave worse results (50% yield for **IIIc** using K_2CO_3). As was shown by the preparation of tetraalkylated products **IIIa-d** and **IVa-d**, the reaction is general for both *tert*-butylthiacalix[4]arene **I** and its de-*tert*-butylated derivative **II.** The above-mentioned products were obtained by this method using K_2CO_3 and acetone in good yields ranging from 45% to 92%.

The ^{1}H NMR spectra of derivatives **IIIb-d** and **IVc,d** are extremely simple and show the presence of one conformer, which is stable in the NMR time scale under measurement conditions (-80 to 100°C). For instance, the one singlet observed for the aromatic hydrogens (δ 7.36 ppm) in the spectrum of **IIIb** together with the single set of signals for the $-CH_2-$ (3.95 ppm) and $-CH_3$ (0.66 ppm) groups indicate the high symmetry of the product. The significant up-field shift of the methyl group (due to the magnetic anisotropy of the aromatic rings) is indicative of a *1,3-alternate* conformation. To support this assumption, the ^{1}H NOE Diff experiment was measured for **IIIb**. It clearly showed the interactions of the $-CH_2-$ group and the aromatic hydrogens, proving the *1,3-alternate* conformation of this compound in $CDCl_3$ solution. In all the above-described reaction products **III** and **IV** were isolated as only one tetraalkylated conformer. This could be explained by the fact, that the alkyl groups used for the reaction are not bulky enough to „freeze“ rotation of the phenolic units and the *1,3-alternate* conformation is the most stable conformer from the thermodynamic point of view.

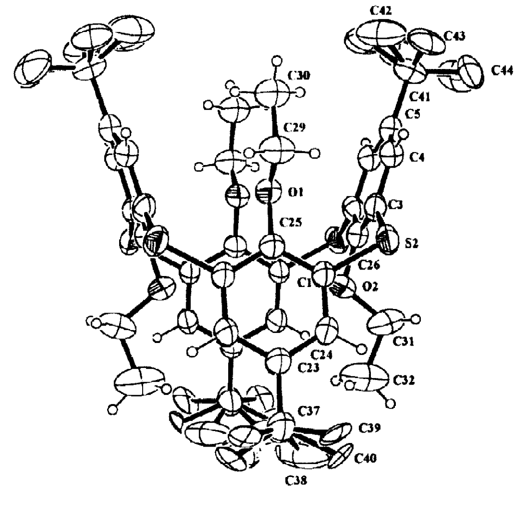

Figure 1: ORTEP drawing of **IIIb**.

In order to gain more information about conformational properties, we attempted a study of the novel tetraalkylated thiacalix[4]arenes **III** and **IV** by X-ray diffraction methods on suitable monocrystals. Surprisingly, in all measured cases (**IIIb**, **IIIc**, **IVb**) these derivatives adopt the *1,3-alternate* conformation also in the solid state. In this article we present detailed structural information of 25,26,27,28-tetraethoxy-5,11,17,23-tetra-*tert*-butyl-2,8,14,20-tetra-thia-calix[4]arene **IIIb**[8] (Figure 1). Suitable monocrystals of **IIIb** were obtained upon slow evaporation of ethyl acetate-dichloromethane solution in the form of a CH_2Cl_2 clathrate. Molecules adopt the *1,3-alternate* conformation with approximate $\bar{4}2m$ symmetry. It is noteworthy that the angle between opposing pairs of thiacalixarene phenyl rings significantly differs from ideal parallelism, in contrast with *1,3-alternate* conformers of „classical" calix[4]arenes[9]. In **IIIb** the lower rims are inclined to each other causing interplanar angles of 30(3)° and 36(2)°. The diameter of inner cavity measured in the mean plane of molecule (created by the four sulphur atoms) is obviously larger than that in corresponding calix[4]arenes. The distances between the two distal and the two proximal sulphur atoms are approximately 7.8 Å and 5.5 Å, respectively, while the typical distances between corresponding CH_2 groups in calix[4]arene *1,3-alternate*[9f] are 7.1 Å and 5.0 Å.

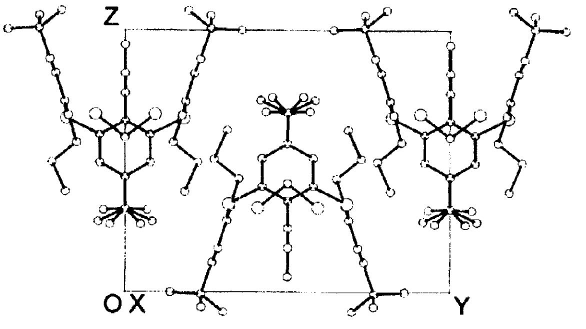

Figure 2: Crystal packing (view along x-axis).

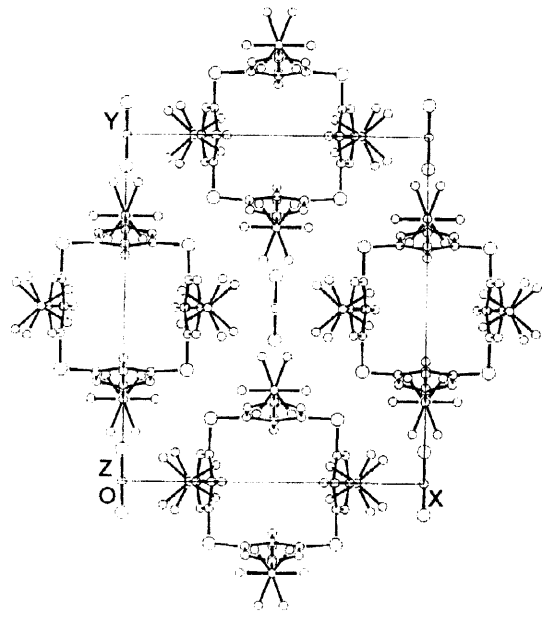

Figure 3: Crystal packing (view along z-axis).

The *1,3-alternate* conformer of **IIIb** creates square box-shaped cavities that are packed parallel to each other in the crystal and form very nice infinite channels. The free space outside these channels (again in the form of channels with approximately the same diameter) is occupied by dichloromethane guest molecules (Figures 2 and 3).

In conclusion, the alkylation of thiacalixarenes **I** and **II** has yielded tetraalkylated products that prefer a *1,3-alternate* conformation in the solid state, and could have potential use in crystal engineering and molecular design.

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6. Representative procedure for the alkylation of thiacalixarenes: The mixture of derivative **I** (1 mmol), potassium carbonate (20 mmol) and propyl iodide (20 mmol) was stirred under reflux in 20 ml of acetone for 2 days. The reaction mixture was poured into diluted hydrochloric acid and extracted with chloroform. The organic layer was washed with water, dried over $MgSO_4$ and evaporated to yield crude product. Recrystallization from an ethyl acetate-acetone-$CHCl_3$ mixture gave pure derivative **IIIc** (65%) as white crystals, m.p.> 350°C. ^1H NMR spectrum ($CDCl_3$, 298 K, 300 MHz): δ 0.62 (t, 12H, J=7.1 Hz, CH_3), 1.00 (m, 8H, -$\underline{CH_2}$-CH_3), 1.25 (s, 36H, t-But), 3.80 (q, 8H, J=7.7 Hz, O-CH_2-), 7.30 (s, 8H, H-arom). EA calcd. for $C_{52}H_{72}O_4S_4$: C, 70.22; H, 8.16; S, 14.42%. Found C, 70.03; H, 8.10; S, 14.04%.
7. In case of Na_2CO_3 the reaction mixture consists of unreacted starting compound **I** and very small amount of product **IIIc** (~ 2% by ^1H NMR).
8. *X-ray data for* **IIIb**: $C_{48}H_{64}O_4S_4.CH_2Cl_2$, M = 918.16, orthorhombic, space group *Pmmn*, a = 13.228(2), b = 15.318(2), c = 12.536(1) Å, Z = 2, U = 2540.1(5) Å^3, D_c = 1.200 gcm^{-3}, $\mu(Cu\ K\alpha)$ = 2.99 mm^{-1}, crystal dimensions of 0.11x0.21x0.29 mm. Data were measured at 293 K on an Enraf-Nonius CAD4 diffractometer with graphite monochromated Cu-Kα radiation. The structure was solved by direct methods and anisotropically refined by full matrix least-squares on F^2 to final R = 0.093 and $R_w(F^2)$ = 0.233 using 2042 independent reflections (θ_{max} = 59.9°). Hydrogen atoms were found from expected geometry and were not refined. *tert*-Butyl groups were disordered and modeled in terms of two sets of rotationally disordered sites with equal occupancies. Absorption was neglected. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.
9. We are aware of only several examples of X-ray structures of O-alkylated calix[4]arenes in the *1,3-alternate* conformation: a) A. Vrielink, P.W. Codding, C. D. Gutsche, Lee-Gin Lin, *J. Inclusion Phenom.*, **1986**, *4*, 199; b) Bott S. G., Coleman A. W., Atwood J. L., *J. Inclusion Phenom.*, **1987**, *5*, 747; c) See K. A., Fronczek F. R., Watson W. H., Kashyap R. P., Gutsche C. D., *J. Org. Chem*, **1991**, *56*, 7256-7268; d) Schätz R., Weber C., Schilling G., Oeser T., Huber-Patz U., Irngartinger H., *Liebigs Ann. Chem.*, **1995**, 1401-1408; e) Fujimoto K., Nishiyama N., Tsuzuki H., Shinkai S., *J. Chem. Soc., Perkin Trans. 2,* **1992**, 643-648; f) Verboom W., Datta S., Asfari Z., Harkema S., Reinhoudt D. N., *J. Org. Chem*, **1992**, *57*, 5394-5398; g) Delague X., Harrowfield J. M., Hosseini M. W., Mocerino M., Skelton B., White A. H., *Aust. J. Chem.*, **1998**, *51*, 111-121.