Synthesis and structural analysis of mercaptothiacalix[4]arene

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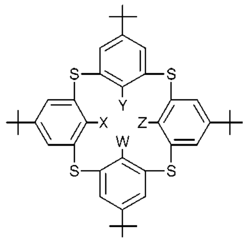
The synthesis of *p-tert*-butyltetramercaptotetrathiacalix[4]arene 1 bearing eight sulfur atoms was achieved in high overall yield (80%); the synthetic strategy used was based on the synthesis of *p-tert*-butyltetrathiacalix[4]arene 2, treatment of the latter with *N,N*-dimethylthiacarbamoyl chloride under mild conditions, thermal transposition of the *O*-thiacarbamoyl into the *S*-thiacarbamoyl derivatives in quantitative yield and deprotection of the sulfur centres by treatment with hydrazine hydrate; the conformation of compound 1 was investigated in the solid state by X-ray diffraction on a single crystal, which revealed that compound 1 adopts the 1,3-alternate conformation.



1 X = Y = Z = W = SH
2 X = Y = Z = W = OH
3 or **4** X = Z = OH, Y = W = $OCSNMe_2$
5, **6** or **7** X = OH, Y = Z = W = $OCSNMe_2$
8 or **9** X = Y = Z = W = $OCSNMe_2$
10 or **11** X = Y = Z = W = $SCONMe_2$

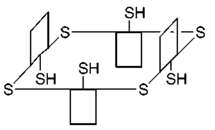
Calixarenes, and in particular, calix[4]arene derivatives are among the most used macrocyclic frameworks.[1] The increasing interest in calixarenes is due to the almost endless structural as well as functional possibilities that such backbones allow to explore. Indeed, one may not only elaborate new compounds by modifying the upper and/or the lower rim of the calix unit, but one may also replace the methylene junction between the aromatic moieties by other elements or groups. Recently, the synthesis[2] and the structural analysis[3] of thiacalix[4]arenes, which are a new class of calix[4]arene derivatives, based on the substitution of the CH_2 groups linking the aromatic rings by sulfur atoms was reported.[4] Furthermore, the partial as well as complete oxidation of the thioether junctions into sulfoxide[5] and sulfone[6] respectively was achieved. For the parent calix[4]arene derivatives, the binding of metal cations[1] and main group elements such as silicon[7] takes place at the lower rim through the OH groups. For the thiacalixarene derivatives, it has been demonstrated that upon replacement of the methylene groups by sulfur atoms, the number of coordination sites increases leading thus to a large diversity in the coordination properties.[8] For sulfur containing calixarenes, the synthesis of di[9]- and tetra[10,11]-mercapto calix[4]arenes, in which two and four OH groups were replaced by two and four SH groups, respectively, as well as their ability to bind mercury cation was reported. More recently, other examples of dimercapto calix[4]arene derivatives bearing two long alkyl chains was achieved and their ability to extract selectively Hg^{2+} cations from water into $CHCl_3$ was demonstrated.[12] We believe that ligand **1**, which is based on the thiacalixarene framework and bears four SH groups, may be of great interest for both its coordination features and as a backbone for the elaboration of other ligands.

Here we report the first synthesis and the solid state X-ray structure of tetramercaptotetrathiacalix[4]arene **1**.

The synthesis of **1** was first attempted by treatment of *p-tert*-butylthiophenol by S_8 under the same conditions as those used for the preparation of thiacalixarene **2**.[2] Unfortunately, no condensation reaction could be detected using these conditions. The synthesis of **1** was then based on the preparation of the tetrathiacalixarene **2**[2] and subsequent transformation of all four OH groups into SH functionalities. The key step in the strategy used was the thermal Newman–Kwart rearrangement of the $OCSNMe_2$ groups into $SCONMe_2$,[9–11,13,14] followed by the generation of the SH groups. In a first attempt, compound **2** was treated with *N,N*-dimethylthiacarbamoyl chloride ($ClCSNMe_2$) in diglyme at 180 °C[10] and in the presence of NaH as base. Unfortunately, the condensation generated a variety of di- and tri-substituted derivatives. No tetra substituted conformer could be isolated from the ensuing complicated mixture. However, dithiacarbamate compounds **3** (10%) and **4** (10%) and trithiacarbamate compounds **5** (10%), **6** (10%) and **7** (8%) were isolated and structurally characterised either by 2-D NMR or by X-ray diffraction on single crystals in the case of **4**–**6**. In order to generate the tetra-substituted derivatives, one could, as previously reported for tetramercaptocalix[4]arene,[10] treat further the di- or tri-substituted compounds above by $ClCSNMe_2$; instead, the formation of the tetra-substituted compounds was investigated under other basic and solvent conditions. It was found that the treatment of **2** with $ClCSNMe_2$ in refluxing acetone in the presence of K_2CO_3 afforded two tetra-substituted compounds **8** (12%) and **9** (80%). Whereas the structure of **8** was elucidated in the solid state by X-ray diffraction on a single crystal, the conformation of compound **9** was studied by 2-D NMR methods.

Based on the observation mentioned above, in order to study the role of alkali metal cations M^+ present in M_2CO_3 (M = Li, Na, K and Cs) on the yield of formation of the tetra-substituted compounds, a systematic investigation was undertaken. Whereas for Li^+ cation, 30% of the disubstituted compound **4** and 5% of the trisubstituted conformer **6** were obtained, in the presence of Na^+, 30% of **4** and 3% of **7** were isolated. For Cs^+ as for K^+, 12% of **8** and 80% of **9** were obtained. The effect of alkali metal cations on the alkylation of **2** has been previously investigated.[15] In marked contrast with *p-tert*-butylcalix[4]arene for which under the same conditions no tetra substituted derivative could be obtained, for tetrathiacalixarene **2**, the tetra-substituted conformers were formed in 92% yield under rather mild conditions.

Since for the final compound **1**, the SH groups may freely pass though the annulus of the calix, we believed that it was not necessary to separate the 1,2-alternate **8** and the 1,3-alternate **9** conformers. Thermal rearrangement was thus performed in quantitative yield on the purified mixture of the two conformers **8** and **9** at 300 °C *in vacuo*. As expected, two transposed



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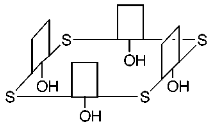

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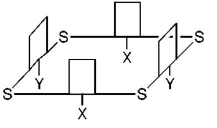
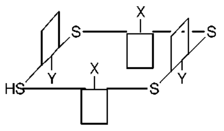
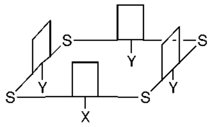


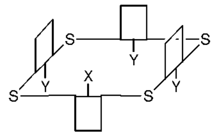
3 X = OH, Y = OCSNMe$_2$



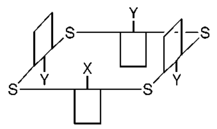
4 X = OH, Y = OCSNMe$_2$



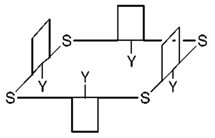
5 X = OH, Y = OCSNMe$_2$



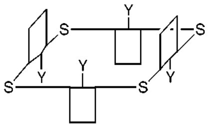
6 X = OH, Y = OCSNMe$_2$



7 X = OH, Y = OCSNMe$_2$



8 Y = OCSNMe$_2$
10 Y = SCONMe$_2$



9 Y = OCSNMe$_2$
11 Y = SCONMe$_2$

conformers **10** and **11** were obtained. The final deprotection of the sulfur groups leading to the desired compound **1** was first attempted under reductive conditions using LiAlH$_4$ in either refluxing THF for 2 h, and at room temperature for 3 h. In both cases, 50 and 75% of an undesired compound in which three out of four SCONMe$_2$ units were transformed into SH groups was obtained. Refluxing the mixture in THF for a longer period of time resulted in the decomposition of the mixture of conformers. Finally, the desired compound **1** could be obtained in 90% yield upon treatment of the mixture of **10** and **11** by hydrazine hydrate at 100 °C for 18 h. It is worth noting that starting from **2**, the overall yield for the synthesis of **1** was 80%.

In CDCl$_3$ solution at 25 °C, the ^{1}H NMR spectrum of **1** was extremely simple and comprised a singlet (δ 7.84) corresponding to the aromatic protons and two other singlets at δ 1.25 and 4.72 corresponding to the *tert*-butyl and SH groups, respectively. Owing to the absence of the methylene groups, using only NMR observations, the differentiation between the cone and 1,3-alternate conformers is not feasible. However, the solid state conformation of **1** could be studied by X-ray diffraction on a single crystal (Fig. 1).† In marked contrast with the parent compound **2** which adopts the cone conformation in the crystalline phase,[3] compound **1** adopts the 1,3-alternate conformation in the crystalline phase. The aromatic rings located on the same face of the ligand are almost parallel. The average C–S and C–SH distances are 1.78 and 1.76 Å, respectively.

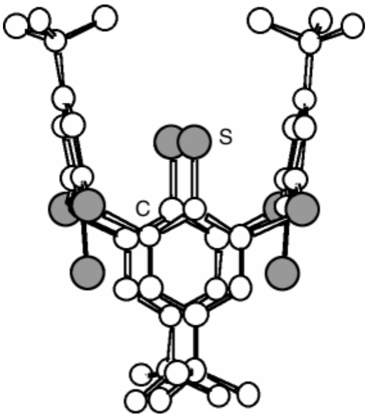


Fig. 1 : X-Ray analysis of *p-tert*-butyltetramercaptotetrathiacalix[4]arene **1**. For the sake of clarity, H atoms and solvent molecules are not represented (for distances see text).

In conclusion, a fast and efficient synthesis of compound **1** was achieved. In the solid state, it was shown that **1** adopts the 1,3-alternate conformation. The complexation ability of **1** towards transition metal cations is currently under investigation.

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Notes and references

† *Crystallographic data* for **1** (colourless crystals, 173 K), C$_{121}$H$_{139}$Cl$_2$OS$_{24}$, M = 2449.90, triclinic, space group $P\bar{1}$, a = 14.9058(4), b = 18.8600(4), c = 24.5600(7) Å, α = 84.044(2), β = 80.888(2), γ = 78.386(2)°, U = 6659.2(4) Å^3, Z = 2, D_c = 1.22 g cm^{-3}, Mo-Kα graphite kappaCCD, μ = 0.470 mm^{-1}, 12582 data with $I > 3\sigma(I)$, R = 0.077, R_w = 0.096. The disordered *tert*-butyl groups were refined isotropically over two sites with 50% occupancy. CCDC 182/1421. See http://www.rsc.org/suppdata/cc/1999/2169/ for crystallographic files in .cif format.

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