# Selectively Dehydroxylated Calix[4]arenes and 1,3-Dithiocalix[4]arenes; Novel Classes of Calix[4]arenes

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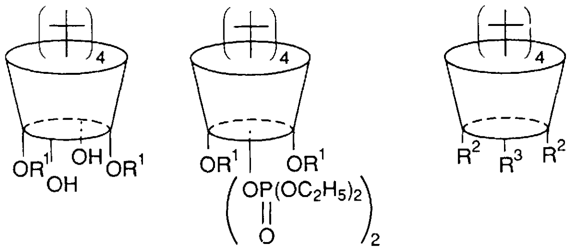
Selective modification of calix[4]arenes either by selective dehydroxylation *via* the reductive removal of phosphate(s), or *via* the Newman–Kwart rearrangement of 1,3-bis(dimethylthiocarbamoyl)calix[4]arenes yields calix[4]arenes **3** and 1,3-dithiocalix[4]arenes **6**, respectively.

Calix[4]arenes[1] can easily be functionalised both at the phenolic OH groups (lower rim) and, after removal of the t-butyl groups, at the *para* positions of the phenol rings (upper rim). Recently we reported *e.g.* the regioselective introduction of two substituents at the upper rim[2] and the 1,3-*O*-alkylation of the lower rim.[3] Subsequently, we have also studied the selective modification of calix[4]arenes at the diametrical (1,3-) positions, either *via* removal of two phenolic groups or *via* replacement of two of the original oxygen atoms by sulphur. The complete dehydroxylation of *p*-t-butylcalix[*n*]arenes (*n* = 4 and 8) by reductive cleavage of the corresponding diethyl phosphate esters, very recently published by Goren and Biali,[4] prompts us to present our preliminary results on the selective modification of the lower rim.

Using a slightly modified literature procedure[5,6] we reacted *p*-t-butylcalix[4]arene **1a**[7] with 4 equiv. of diethyl chlorophosphate in tetrahydrofuran (THF) in the presence of $K_2CO_3$ as a base to give selectively the 1,3-diphosphorylated calix[4]arene **2a**†,‡ in 74% yield. Analogously **2b** was obtained in 76% yield starting from 1,3-dimethoxycalix[4]arene **1b**[3] using NaH as a base. The $^1H$ NMR spectrum of **2b** shows, in addition to one singlet at δ 3.04 ($OCH_3$), two ABq patterns at δ 4.48 and 3.77 (*J* 17.3 Hz) and δ 4.46 and 3.25 (*J* 13.1 Hz), which indicates that **2b** is present in the 1,2-alternate conformation.[8] To the best of our knowledge only Atwood *et al.*[9] and Gutsche *et al.*[10] have isolated a calix[4]arene in the 1,2-alternate conformation.

Reaction of **2a** with 6 equiv. of potassium in liquid ammonia at −60 °C[5,6] gave, after chromatography, the bis(dehydroxylated) **3a** and the mono(dehydroxylated) calix[4]arene **3b** as crystalline compounds in yields of 71 and 14%, respectively.§ The formation of **3b** is due to partial hydrolysis of one of the phosphate moieties. The singlet at δ 3.92 (**3a**) and the two singlets (1 : 1 ratio) at δ 3.91 and 3.86 (**3b**) of the methylene bridge protons in the $^1H$ NMR spectra indicate that these molecules are flexible. Reaction of **2b** with potassium in liquid ammonia afforded the bis(dehydroxylated) dimethoxycalix[4]arene **3c** as a 83 : 17 mixture of 1,3-*syn*-(1,3-alternate like) and 1,3-*anti*-configurations¶ in a yield of 55%. Varying the temperature from −20 °C to 60 °C did not influence this ratio. The presence of one singlet at δ 3.02 ($OCH_3$), and one ABq at δ 4.18 and 3.59 (*J* 14.9 Hz, $ArCH_2Ar$) and two singlets at δ 1.38 and 1.14 ($Bu^t$) indicates the predominant 1,3-*syn*-configuration. The 1,3-*anti*-configuration exhibits a corresponding $^1H$ NMR spectrum, however, with two striking differences, *viz.* a singlet of the methoxy group at δ 3.20 and an aromatic singlet at δ 5.95 (δ 6.30 in the 1,3-*syn*).

Phenols can be transformed into the corresponding thiophenols *via* the corresponding *O*-aryl dialkylthiocarbamates and *S*-aryl dialkylthiocarbamates.[11] We have used this Newman–Kwart rearrangement for the transformation of the bis(dehydroxylated) calixarene **3a** and the 1,3-dimethoxycalix[4]arene **1b** to the 1,3-dithiocalix[4]arenes **6a** and **6b**, respectively. Reaction of **3a** and **1b** with 2.5 equiv. of *N*,*N*-dimethylthiocarbamoyl chloride in *N*,*N*-dimethylformamide (DMF) in the presence of NaH as a base gave the *O*-dimethylthiocarbamates **4a** and **4b** in yields of 86 and 87%, respectively. Heating compounds **4a** and **b** at 320 °C for 4 h

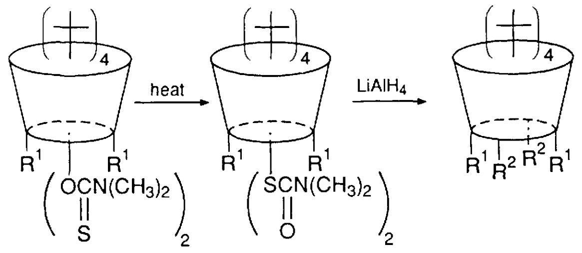


**1** **a**; $R^1$ = H
**b**; $R^1$ = $CH_3$

**2** **a**; $R^1$ = H
**b**; $R^1$ = $CH_3$
**c**; $R^1$ = $P(O)(OC_2H_5)_2$

**3** **a**; $R^2$ = OH, $R^3$ = H
**b**; $R^2$ = $R^3$ = OH
**c**; $R^2$ = $OCH_3$, $R^3$ = H
**d**; $R^2$ = H, $R^3$ = OH
**e**; $R^2$ = $R^3$ = H

**Fig. 1**



**4** **a**; $R^1$ = H
**b**; $R^1$ = $OCH_3$

**5** **a**; $R^1$ = H
**b**; $R^1$ = $OCH_3$

**6** **a**; $R^1$ = H, $R^2$ = SH
**b**; $R^1$ = $OCH_3$, $R^2$ = SH
**c**; $R^1$ = $OCH_3$, $R^2$ = $SCH_3$

**Scheme 1**

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† Satisfactory analytical and spectral data were obtained for all new compounds.

‡ For reasons of simplicity the positions of the original OH groups in **1** are numbered as 1, 2, 3 and 4.

§ The corresponding reaction with the tetraphosphate **2c**[4] gave the tris(dehydroxylated)-**3d** and the tetrakis(dehydroxylated) calix[4]arene **3e**[4] in yields of 23 and 41%, respectively. These results demonstrate that in addition to the complete dehydroxylated calix[4]arene **3e**[4] the mono-, di- and tri-hydroxycalix[4]arenes (**3d**, **3a** and **3b**, respectively) are easily accessible.

¶ *anti* Implies that the two methoxy groups are at opposite sites of the molecule.

under argon afforded the rearranged *S*-dimethylthiocarbamates **5a** and **b** in yields of 64 and 90%, respectively. According to their $^1$H NMR spectra ‖ both **4a** and **5a** exist as a 1 : 1 mixture of the 1,3-*syn*- and 1,3-*anti*-configurations in which the unsubstituted phenyl rings can freely rotate. Both compounds **4b** and **5b** exist in a mixture of the 1,2-alternate and the partial cone conformations, in which the carbamate moieties are in the *anti*-position, in ratios of 5.4 : 1 and 3.2 : 1, respectively. The 1,2-alternate conformations display similar patterns in the $^1$H NMR spectra as **2b**, whereas the partial cones are recognized by the 2 : 1 : 1 ratio of the t-butyl signals and one methoxy signal. Reduction of *S*-dimethylthiocarbamate **5a** with $LiAlH_4$[12] in refluxing THF for 14 h under argon afforded the 1,3-dimercaptocalix[4]arene **6a** in a yield of 85%. In contrast to 1,3-dihydroxycalix[4]arene **3a**, **6a** exists as a 87 : 13 mixture of 1,3-*syn*- and 1,3-*anti*-configurations as followed from a corresponding $^1$H NMR spectrum (SH at δ 2.50 and 2.76, respectively) as that of **3c**. Treatment of *S*-dimethylthiocarbamate **5b** with $LiAlH_4$ for 2 days afforded the 1,3-dimercapto-2,4-dimethoxycalix[4]arene **6b** as a complicated mixture of conformers. However, methylation of **6b** with methyl iodide in a 1 : 1 mixture of dichloromethane and acetonitrile in the presence of $K_2CO_3$ gave the 1,3-dimethoxy-2,4-bis(methylthio)calix[4]arene **6c** in 40% overall yield (from **5b**). The $^1$H NMR spectrum shows the characteristic patterns[1] of a partial cone (with a methylthio group in the cavity) and a cone conformation in a ratio of 3 : 2. Compounds **6b** and **6c** represent the first examples of 'mixed' calix[4]arenes having two different (substituted) heteroatoms at the lower rim.

In principle both types of novel calix[4]arene derivatives **3** and **6** will give rise to a variety of novel applications in calixarene chemistry. We are currently studying the (selective) replacement of the hydroxy functions in calix[4]arenes by other functionalities.

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‖ For instance, for **5a**, two ABq patterns (ratio 1 : 1) are present of the methylene bridge protons at δ 4.37 and 3.79 (*J* 15.0 Hz) and 4.30 and 3.87 (*J* 14.7 Hz) and four singlets of the t-butyl groups (ratio 1 : 1 : 1 : 1) at δ 1.39, 1.36, 1.19 and 1.14.

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