The Synthesis of Selectively Substituted *p*-Diacetylcalix[4]arene

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Friedel–Crafts acetylation of the calix[4]arene dimethyl ether (**2**) gives diametrically substituted *p*-diacetylcalix[4]arene dimethyl ether (**3**), which was demethylated to produce selectively substituted *p*-diacetylcalix[4]arene (**4**).

The introduction of functional groups at the *para* positions of calixarenes has attracted our attention[1] and that of several groups[2,3] because of the possibility of easily obtaining new host molecules for the complexation of ions and neutral molecules or a new type of enzyme mimics. Although several short synthetic routes have been developed to introduce functional groups into the phenyl rings, they all lead to tetra-substituted calix[4]arenes, having the same substitutent at all the *para* positions. The stepwise routes giving access to differently substituted calix[4]arenes were developed by

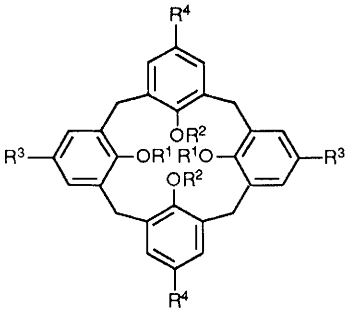

Table 1. Selectively substituted p-diacetylcalix[4]arenes (1)—(7).

Compound	R^1	R^2	R^3	R^4
(**1**)	H	H	H	H
(**2**)	Me	H	H	H
(**3**)	Me	H	COMe	H
(**4**)	H	H	COMe	H
(**5**)	Me	COMe	H	H
(**6**)	Me	H	H	COMe
(**7**)	Me	H	COPh	H

Gutsche and No[4] and Böhmer *et al.*,[5] but the methods are relatively long and tedious, producing low yields.

The purpose of the present work is to exploit the possibility of adapting the short synthesis to the preparation of selectively substituted calix[4]arenes which can be used for the synthesis of calix[4]arenes containing more than two different functional groups. In this regard, recently Reinhoudt and coworkers[6] reported that the difference in reactivity of phenyl rings of the diametrically dimethoxylated calix[4]arene can be utilized for the selective functionalization of calixarenes. Here we report the synthesis of selectively substituted p-diacetylcalix[4]arene using the reactivity difference of phenyl rings as shown in Table 1.

When calix[4]arene (**1**),[7] obtained by $AlCl_3$-catalysed removal of the t-butyl groups from p-t-butylcalix[4]arene,[8] was reacted with methyl iodide in the presence of K_2CO_3 in refluxing acetone, 75% yield of compound (**2**) was isolated. Reinhoudt[6] synthesized the same compound by reacting compound (**1**) with methyl tosylate in refluxing acetonitrile. When a solution of compound (**2**) in CH_2Cl_2 was stirred with acetyl chloride in the presence of $AlCl_3$, compound (**3**) was produced in 63% yield. The p-acetylation was confirmed by IR and ^1H NMR spectroscopies. In the IR spectrum, the OH stretching band remained and the carbonyl band appeared at $1680 \, cm^{-1}$, indicating the aromatic ketone rather than ether. In the ^1H NMR spectrum, the resonance peak from methyl protons adjacent to the carbonyl group was observed at δ 2.53, whereas that of ester usually appears at around δ 1.50. The typical AB quartet pattern of the ^1H NMR resonance peaks of the methylene bridge protons at δ 4.29 and 3.45 (J 13 Hz), indicates that compound (**3**) exists in the cone conformation.[9]

Comparisons of physical data of this compound with isomeric compound (**6**), which was prepared by the Fries rearrangement of corresponding diacetoxycalix[4]arene (**5**), supports the suggested structure of compound (**3**), in which two acetyl groups are introduced into anisole rings rather than phenol rings. It was reported[10] that the treatment of the calix[4]arene (**1**) with acetyl chloride under Friedel–Crafts conditions resulted in O-acetylation, producing the ester, rather than p-acetylation, and the resulting ester failed to undergo further reaction at the *para* positions. However, when calix[4]arene tetramethyl ether was treated under the same conditions, C-acetylation at the *para* positions occurred with concomitant partial demethylation. Reinhoudt[6] reported that bromination, nitration, or the Mannich reaction exclusively took place at the phenol rings rather than the anisole rings of compound (**2**). The C-benzoylated compound (**7**) was isolated in 67% yield by treating compound (**2**) with benzoyl chloride under the same conditions, and exists in a cone conformation. When compound (**3**) was treated with BBr_3[2a,11] in CH_2Cl_2 at room temperature, methyl groups were cleaved to give p-diacetylcalix[4]arene (**4**) in 85% yield.

We conclude that diametrically substituted p-diacetylcalix[4]arene (**4**) can be prepared by selective Friedel–Crafts acetylation of the selectively substituted dimethoxycalix[4]arene (**2**). We are currently studying the introduction of further functional groups into the compounds obtained in this investigation.

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