presence of SDS, while the latter solution fluoresces at high pH with little dependence of the emission intensity on the presence of SDS. These different properties of diazepam and chlorodiazepoxide on pH can be used to facilitate the design of micelle-improved chemical analysis of the drugs.

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

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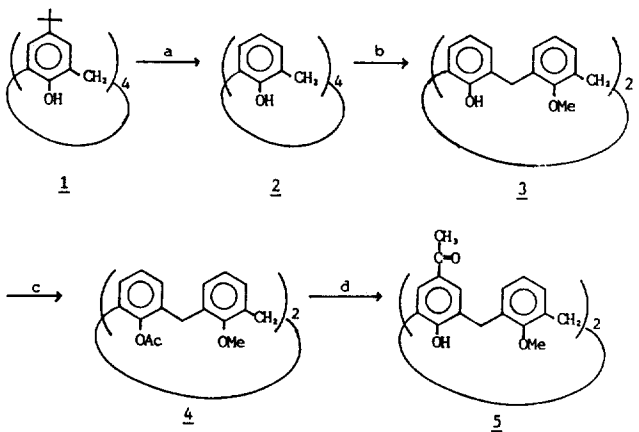
A method is described for the selective functionalization of calix[4]arene at the para positions of the phenyl rings. The diametrically substituted calix[4]arene dimethyl ether **3**, obtained from the treatment of calix[4]arene **2** with methyl iodide in the presence of K_2CO_3, is converted to the diacetyloxy calix[4]arene dimethyl ether **4**. This compound undergoes Fries rearrangement to yield the diametrically *p*-diacetylcalix[4]arene dimethyl ether **5** in 68% yield.

Introduction

The functionalization of calixarenes on the phenyl rings has attracted our attention[1] and that of several research groups[2,3] because of the possibility of easily obtaining new host molecules for the complexation of ions and neutral molecules or new type of enzyme mimics. Although several routes have been developed to introduce functional groups at the para positions of the phenyl rings, they all lead to tetra-substituted calix[4]arenes, having the same substituent at all the para positions. The stepwise route to give access to differently substituted calix[4]arenes were developed by Gutsche and No[4] and Böhmer *et al.*[5], but the methods are relatively long, tedious and low with respect to yield. The purpose of the present work is to exploit the possibility of adapting the short synthesis to the preparation of selectively functionalized calixarenes which can be used for the synthesis of calixarenes containing more than two different functional groups. Here we report the synthesis of diametrically substituted *p*-diacetylcalix[4]arene dimethyl ether **5** as shown on scheme.



Reagents: a. $AlCl_3$/Benzene, b. MeI/K_2CO_3/Acetone, c. Ac_2O/H^+, d. $AlCl_3$

Scheme

When calix[4]arene **2**, obtained in 74% yield[1a] by $AlCl_3$-catalyzed removal of the *tert*-butyl groups from *p*-*tert*-butylcalix[4]arene which was prepared readily[6], was reacted with methyl iodide in the presence of K_2CO_3 in reluxing acetone, 75% yield of the diametrically substituted calix[4]arene dimethyl ether **3** was isolated. Recently Reinhoudt[7] reported the preparation of compound **3** by reacting the compound **2** with methyl tosylate in refluxing acetonitrile. To acetylate the remaining two hydroxyl groups compound **3** was treated with acetic anhydride and sulfuric acid as catalyst to give the desired product **4** in 92% yield as a mixture of three conformers, which was used for Fries rearrangement reaction without separation of each conformer. When a solution of compound **4** and $AlCl_3$ in nitrobenzene was stirred overnight at room temperature, the rearranged product **5** was obtained in 68% yield. The rearrangement was confirmed by spectral comparison. In IR spectrum, the OH-stretching band was appeared and the position of carbonyl stretching band was shifted from 1735 cm^{-1} of ester to 1670 cm^{-1} of aromatic ketone. ^{1}H-NMR spectrum also showed the resonance peak of OH protons, and that of methyl protones adjacent to carbonyl was shifted from 1.53 ppm of ester to 2.50 ppm of ketone. The ^{1}H-NMR spectrum showed a typical AB quartet for the methylene bridge protons at 4.33 and 3.49 ppm (J = 13Hz), indicating that compound **5** exists in cone conformation.[8]

Experimental

IR spectra were obtained by using a Shimazu IR-435 spectrophotometer, and ^{1}H-NMR spectra were recorded on Varian EM-360A instrument with TMS as internal standard. Melting points were measured in sealed capillary tube using Sybron thermolyne apparatus with polarizing microscope and were not corrected.

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrahydroxycalix[4]arene 1 was prepared in 52% yield from *p*-*tert*-butylphenol and formaldehyde as described on the literature[6].

25,26,27,28-Tetrahydroxycalix[4]arene 2 was prepared in 74% yield by $AlCl_3$-catalyzed removal of the *tert*-butyl groups from the compound **1** following published procedure[1a].

25,27-Dihydroxy-26,28-dimethoxycalix[4]arene 2. A solution of compound **2** (1.00g, 2.36 mmole) in acetone (100 m*l*) was treated with 1.30g (4 mole equivalent of **2**) of anhydrous K_2CO_3. To this suspension methyl iodide was added dropwise, then the reaction mixture was refluxed for 6 hr. After removal of acetone by evaporation, the residue was acidified with 1N-HCl, then extracted with chloroform. The organic layer was collected, washed with water, dried over anhydrous $MgSO_4$, and evaporated chloroform to dryness to yield slightly pale-yellow solid which was recrystallized from *n*-butanol to give 0.80g (75%) of colorless crystalline solid; mp 301-303 °C; IR(KBr) 3120 cm^{-1} (OH stretching); ^{1}H-NMR ($CDCl_3$) δ7.80 (s, 2H, OH), 7.02-6.61 (m, 12H, ArH), 4.34 (d, 4H, J = 13 Hz, CH_2), 4.00 (s, 6H, OCH_3), 3.30 (d, 4H, J = 13 Hz, CH_2).

25,27-Diacetyloxy-26,28-dimethoxycalix[4]arene 4. A solution of compound **3** (0.90g, 2.0 mmole) in 30 m*l* acetic anhydride was added 1-2 drops of conc sulfuric acid. The mixture was heated under reflux for 1.5 hr, poured into 100 m*l* cold water and then stirred for a while. The resulting precipitate was collected by filtration, washed with water, and dried to give slightly brown solid, which was recrystallized from benzene to yield 0.98g (92%) of a mixture of three compounds as colorless crystalline solid. According to IR and ^{1}H-NMR spectrum these compounds are conformers of the desired product, and used in the Fries rearrangement reaction without futher separation: mp 273-275 °C; IR (KBr) 1735 cm^{-1} (C=O stretching); ^{1}H-NMR ($CDCl_3$) δ7.40-6.77 (m, 12H, ArH), 4.02-3.12 (m, 8H, CH_2), 3.62 (s, 6H, OCH_3), 1.53 (s, 6H, $COCH_3$).

5,17-Diacetyl-26,28-dihydroxy-25,27-dimethoxycalix[4]arene 5. A solution of compound **4** (0.56g, 1.04 mmole) in nitrobenzene (60 m*l*) was treated with $AlCl_3$ (2.09g) and the mixture was stirred for overnight at room temperature. The resulting mixture was treated with water, and nitrobenzene was removed by steam distillation. The residue was collected, crushed into powder, washed with water, dried and then boiled with 30 m*l* of benzene. The flash chromatographic separation (eluent was 2:5 mixture of acetone and hexane) of the benzene-insoluble material furnished 0.38g (68%) of crystalline solid; mp 354-335 °C (decompose, softening and sublimation at around 340 °C); IR(KBr) 3250 cm^{-1} (OH stretching), 1680 (C=O stretching); ^{1}H-NMR ($CDCl_3$) δ8.53 (s, 2H, OH), 7.84, 7.43 and 6.91 (s, 10H, ArH), 4.33 (d, 4H, J = 13 Hz, CH_2), 3.98 (s, 6H, OCH_3), 3.49 (d, 4H, J = 13 Hz, CH_2), 2.50 (s, 6H, $COCH_3$).

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