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Reaction of Tetramethylcalix[4]resorcinolarene with 3,5-Di-*tert*-butyl-4-hydroxybenzyl Acetate

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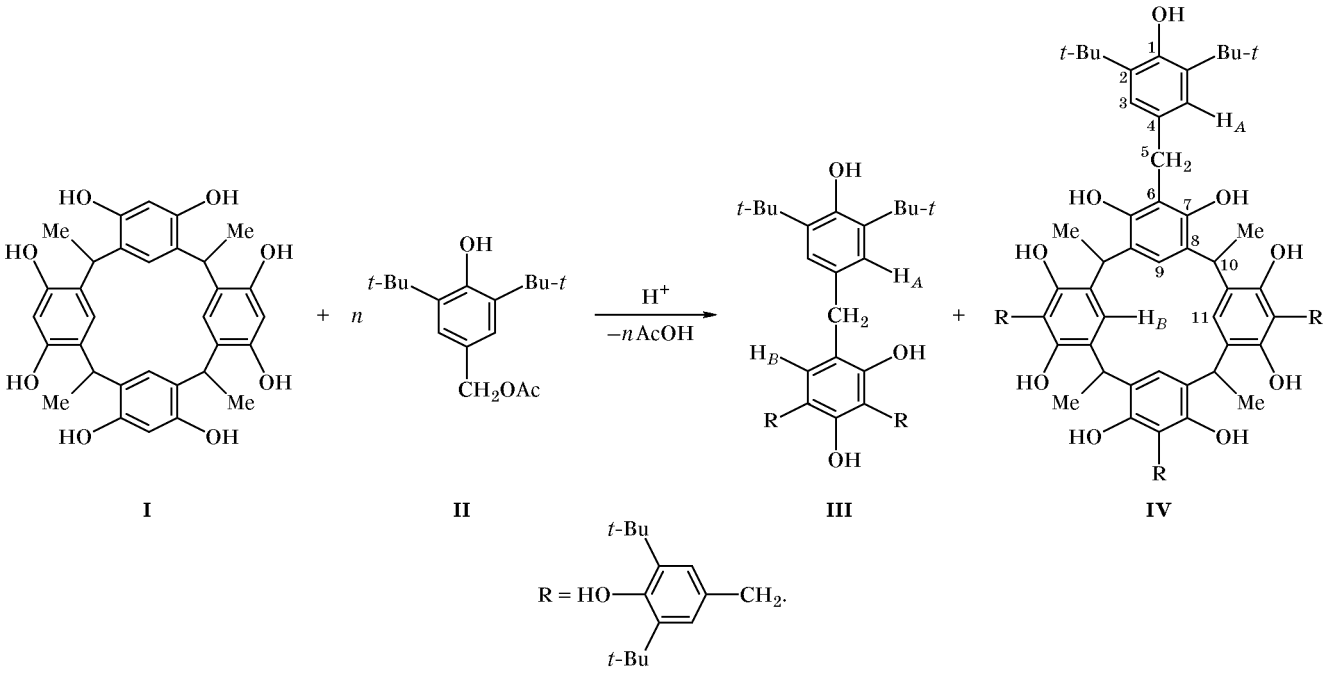
Abstract—Upper-rim modification of tetramethylcalix[4]resorcinolarene with 3,5-di-*tert*-butyl-4-hydroxybenzyl fragments is accompanied by unusual decomposition of the macroring in the modified product with formation of 2,4,6-tris(3,5-di-*tert*-butyl-4-hydroxybenzyl)resorcinol.

Study of the antioxidizing properties of calix[4]resorcinolarene **I** and some its derivatives showed the possibility for creation of a new group of highly efficient calixarene-based inhibitors of thermooxidative polymer degradation [1]. Modification of calixarene **I** through introduction of sterically hindered phenolic fragments into the aromatic rings may be promising from the viewpoint of increasing the antioxidizing activity.

We have studied the reaction of calix[4]resorcinolarene **I** with 3,5-di-*tert*-butyl-4-hydroxybenzyl acetate (**II**); the use of the latter makes it possible to introduce sterically hindered phenolic fragments into molecules of various compounds [2]. The reaction was carried out in the presence of a strong mineral acid ($HClO_4$, H_2SO_4), and it led to formation of a mixture containing 70% of 2,4,6-tris(3,5-di-*tert*-butyl-4-hydroxybenzyl)resorcinol (**III**) and 30% of 5,11,17,19-

Scheme 1.



I **II** **III** **IV**

R = HO—(*t*-Bu, *t*-Bu, CH_2).

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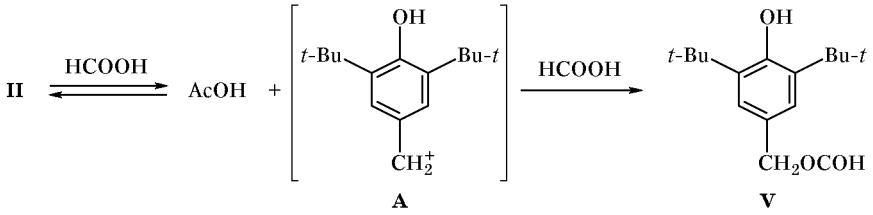
Scheme 2.



A V

tetrakis(3,5-di-*tert*-butyl-4-hydroxybenzyl)-4,6,10,12,-16,18,22,24-octahydroxy-2,8,14,20-tetramethylpentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacosa-1(25),3,5,7(28),-9,11,13(27),15,17,19(26),21,23-dodecaene (**IV**).

When the reaction was performed in the presence of formic acid as acid catalyst (which promotes fast and quantitative transformation of benzyl acetate **II** into benzyl formate **V**), the product ratio considerably changed: the mixture contained 30% of **III** and 70% of **IV**. The formation of compound **III** in the reaction of calixarene **I** with benzyl acetate **II** seems to be surprising. This is the first example of cleavage of the calix[4]resorcinolarene macroring by the action of electrophile. Taking into account that such cleavage does not occur in the binary system calixarene **I**–perchloric (or formic) acid, we presume that compound **III** is formed as a result of exhaustive benzylation of calixarenes **I** and/or **IV** with benzyl cation **A** generated during the process (Scheme 2). In fact, after storage of a solution of compounds **IV** and **II** (at a ratio of 1:8) in acetone in the presence of perchloric acid, signals belonging to calixarene **IV** [($CDCl_3$), δ, ppm: 1.74 d (12H, Me, ^3J = 7.0 Hz), 4.60 q (4H, CH, ^3J = 7.0 Hz), 6.34 s (8H, OH)] disappear almost completely from the ^{1}H NMR spectrum of the mixture, but those corresponding to compound **III** appear, δ, ppm: 3.80 s (4H, CH_2), 3.92 s (2H, CH_2), 4.85 s (2H, OH), 6.93 s (1H, H_{arom}). An analogous pattern was observed for dilute solutions of **IV** and **II** in formic acid.

Decomposition of the calixarene ring, which was accompanied by disappearance of the methyl proton doublet at δ 1.74 ppm and CH proton quartet at δ 4.60 ppm, also occurred when a solution of calixarene **IV** in formic acid containing no acetate **II** was stored for several days. In this case, the process was slower.

Thus we can conclude that the reaction of calixarene **I** with benzyl acetate **II** gives compound **III** as a result of cleavage of the calixarene macroring in product **IV** by the action of electrophiles: benzyl carbocation **A** and acid catalyst. Presumably, the observed sensitivity to electrophiles under mild conditions is a specific property of resorcinol systems. For example, bis(3,5-di-*tert*-2-hydroxy-butylphenyl)-methane and bis(3-*tert*-butyl-2-hydroxy-5-methylphenyl)methane are stable toward benzyl acetate **II** in formic acid. The stability of calixresorcinolarene **I** to mineral acids [3] may be explained by differences in the supramolecular structure of compounds **I** and **IV**.

The structure of products **III** and **IV** was proved by the ^{1}H and ^{13}C NMR spectra and by independent synthesis of compound **III** from resorcinol and benzyl acetate **II**.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded on a Varian Gemini 200 spectrometer at 200 (^{1}H) and 50 MHz (^{13}C) using the solvent signals as reference ($CDCl_3$, acetone-d_6).

2,4,6-Tris(3,5-di-*tert*-butyl-4-hydroxybenzyl)-resorcinol (III). *a*. To a solution of 1 g (0.002 mol) of calixarene **I** and 4.1 g (0.0148 mol) of benzyl acetate **II** in 20 ml of acetone we added 0.08 ml of 72% perchloric acid. The mixture was kept for 24 h at 20°C and poured into water. The precipitate was filtered off, washed with water until neutral reaction, and dried for 2 days at 20°C. We thus obtained 3.4 g of a product which, according to the ^{1}H NMR data, was a mixture of compounds **III** and **IV** at a ratio of 70:30. By recrystallization from hexane we isolated 1.2 g (35%) of compound **III**, mp 153–154°C; published data [3]: mp 151–154°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.42 s (54H, CMe_3), 3.80 s (4H, CH_2), 3.92 s (2H, CH_2), 4.85 s (2H, OH), 5.09 s (1H, OH), 5.16 s (2H, OH), 6.93 s (1H, H_B), 7.12 s (1H, H_A). Found, %: C 79.85; H 9.70. $C_{51}H_{72}O_5$. Calculated, %: C 80.10; H 9.42.

b. To a solution of 70 g (0.252 mol) of ester **II** and 9.23 g (0.084 mol) of resorcinol in 140 ml of acetic acid we added under stirring at 50°C 0.35 ml of 72% of perchloric acid in a dropwise manner. The mixture was heated for 1 h and was then stirred for 3 h at room temperature. The precipitate was filtered off, washed with a small amount of acetic acid and with water, and dried in air. We thus obtained 55 g (85.5%) of compound **III** with mp 153–154°C.

5,11,17,19-Tetrakis(3,5-di-*tert*-butyl-4-hydroxybenzyl)-4,6,10,12,16,18,22,24-octahydroxy-2,8,14,-20-tetramethylpentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]-octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),-21,23-dodecaene (IV). Formic acid, 65 ml, was added to a solution of 3 g (0.0055 mol) of calixarene **I** and 6.9 g (0.0248 mol) of ester **II** in 55 ml of acetone. The mixture was kept for 24 h at 20°C, poured into 100 ml of water, and neutralized with a solution of sodium hydrogen carbonate to pH 5–6. The precipitate was filtered off, washed with water, and dried in air. We obtained 7.75 g of a product which, according to the ^{1}H NMR data, was a mixture of compounds **III** and **IV** at a ratio of 30 : 70. The product was dissolved in 25 ml of benzene, and 170 ml of hexane was added to precipitate 2.6 g (33%) of compound **IV**, mp 230°C (decomp.). ^{1}H NMR spectrum, δ, ppm: in $CDCl_3$: 1.39 s (72H, CMe_3), 1.77 d (12H, Me, ^3J = 7.0 Hz), 3.89 s (8H, CH_2), 4.60 q (4H, CH, ^3J = 7.0 Hz), 5.08 s (4H, OH), 6.34 s (8H, OH), 7.00 s (8H, H_A), 7.33 s (4H, H_B); in acetone-d_6: 1.37 s (72H, CMe_3), 1.73 d (12H, Me, ^3J = 7.0 Hz), 3.89 s (8H, CH_2), 4.60 q (4H, CH, ^3J = 7.0 Hz), 5.72 s (4H, OH), 7.18 s (8H, H_A), 7.52 s (4H, H_B), 7.88 s (8H, OH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 20.5 q (C^{11}, $^1J_{CH}$ = 125.0 Hz), 28.3 d (C^{10}, $^1J_{CH}$ = 130.0 Hz), 29.4 t (C^5, $^1J_{CH}$ = 90.0 Hz), 30.2 q (C**Me**$_3$, $^1J_{CH}$ = 120.0 Hz), 34.3 s (**C**Me_3), 114.0 s (C^8), 121.6 d (C^9, $^1J_{CH}$ = 150.0 Hz), 125.0 d (C^3, $^1J_{CH}$ = 150.0 Hz), 125.5 s (C^6), 128.9 s (C^4), 136.5 s (C^2), 149.0 s (C^7), 152.6 s (C^1). Found, %: C 77.65; H 8.65. $C_{92}H_{120}O_{12}$. Calculated, %: C 77.97; H 8.47.

Transformations of calixarene IV in acid medium. A solution of 0.1 g (7×10^{-5} mol) of calixarene **IV** and 0.155 g (5.6×10^{-4} mol) of ester **II** in 10 ml of acetone and 10 ml of formic acid (or in 10 ml of acetone containing one drop of perchloric acid) was kept for 24 h at 20°C, poured into water, and neutralized with a solution of $NaHCO_3$. The precipitate was filtered off, washed with water, and dried. The product was analyzed by ^{1}H NMR spectroscopy.

Transformation of calixarene IV in formic acid in the absence of ester II was effected as described above. The mixture was kept for 6 days at 20°C. Calixarene **I** did not change under these conditions, as well as in acetone in the presence of perchloric acid, and it was recovered from the reaction mixture.

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