Hydrophosphinoyl derivatives of calix[4]resorcinarenes

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Calix[4]resorcinarene reacts with *N,N,N′,N′*-tetraethyl-*P*-ethylphosphonous diamide to give dioxaphosphocines, whose hydrolysis with "intracavity" water yields phosphinoyl derivative of calix[4]resorcinarene.

Key words: calix[4]resorcinarene, phosphorylation, hydrolysis, phosphinates.

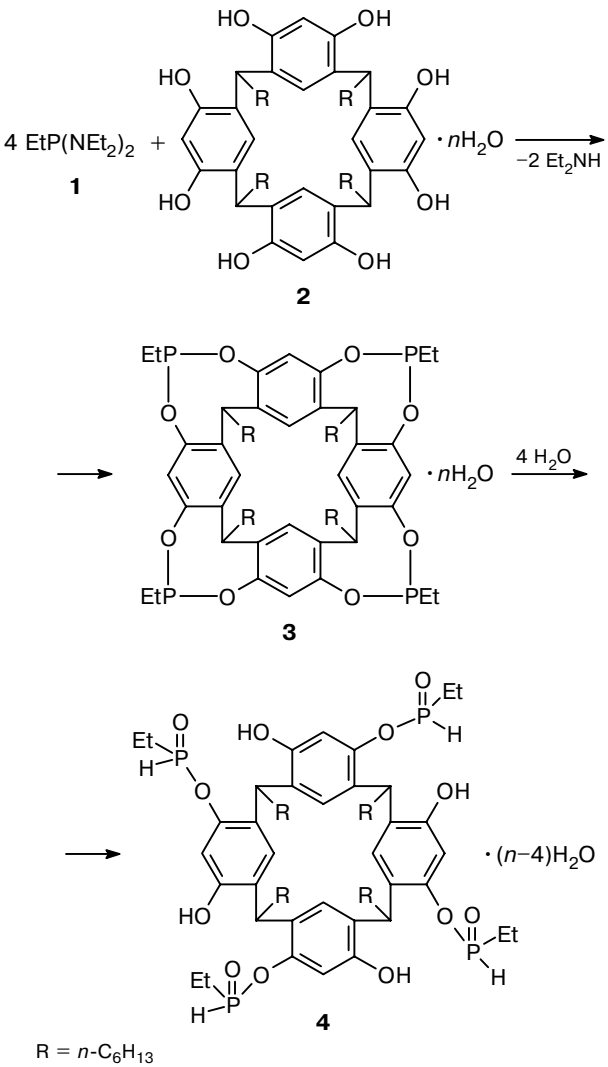
The chemistry of calixarenes, cyclic condensation products of phenols with aldehydes, has been developing rapidly for the last two decades. Calixarenes are easily available compounds, whose reactive centers allow them to be structurally modified. The phosphorylation of the hydroxy groups of calixarenes has been studied intensively since the 1990s; the results obtained are reviewed in Ref. 1. The phosphorylating agents were mainly acid chlorides of the four-coordinate phosphorus, and the resulting phosphates (phosphonates or phosphinates) cannot, as a rule, undergo further transformations. In our opinion, progress in the chemistry of *O*-phosphorylated calixarenes is associated with the incorporation of reactive phosphorus-containing groups, *e.g.*, P—H, into their molecules. Chemical transformations of such objects can give rise to promising complexation agents which combine a macrocycle (the formation of "guest—host" complexes) and chelating fragments, to new organoelement molecular container-type compounds with unusual properties, *etc.* No phosphinoyl derivatives of calix[4]resorcinarenes have been described so far.

Earlier, we have studied the reactions of calix[4]resorcinarenes with methyl and ethyl phosphodiamidites and noted that the resulting macrocyclic phosphites are oxidized very easily with atmospheric oxygen to the corresponding cyclophosphates.[2] In this study, *N,N,N′,N′*-tetraethyl-*P*-ethylphosphonous diamide (**1**) was used as a phosphorylating agent.

Results and Discussion

We synthesized calixarene (**2**) and made it to react with amide **1** (1 : 4) in toluene at 20 °C (Scheme 1). According to ^{31}P NMR data, four hours after the reaction started, the reaction mixture contained the starting amide **1** (δ 90) and also phosphorylated calixarenes **3** (δ 189.1 and 191.5) and **4** (δ 24.8, $^{1}J_{P,H}$ = 500 Hz). The mixture was heated in an atmosphere of argon at 110 °C

Scheme 1



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for 2 h. As a result, the ^{31}P NMR spectra no longer contained signals for compounds **1** and **3**, showing only a signal for the final hydrogen phosphinate **4**, which was isolated and characterized by ^{1}H and ^{31}P NMR spectra and elemental analysis.

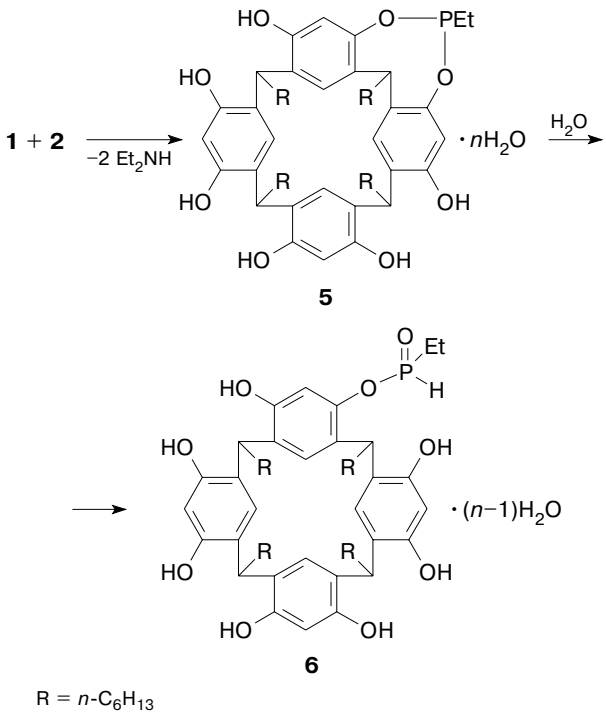
Since the starting calixarene contains eight hydroxy groups and thus can produce regioisomers, the structure of the final product **4** was determined using ^{1}H NMR spectroscopy. The *ortho* and *meta* protons of the aromatic rings of calixarenes (relative to the hydroxy groups) are very sensitive to the presence of *ortho*-substituents. In symmetrical molecules, all of the four *ortho*- and four *meta*-protons are equivalent, giving only two singlets in the ^{1}H NMR spectra. If four substituents (*e.g.*, dialkoxyphosphoryl groups) are localized on two aromatic rings, then the *ortho*- and *meta*-protons become nonequivalent, and four singlets appear in the ^{1}H NMR spectrum.[3] The ^{1}H NMR spectrum of compound **4** exhibits two singlets at δ 6.38 and 7.40 with an intensity ratio of 1 : 1 for the *ortho*- and *meta*-protons, thus confirming its symmetrical structure.

According to the published X-ray structural data, the molecular cavity of calixarene can contain from one to several tens of bound water molecules, which are involved in a complicated system of hydrogen bonds with the phenolic OH groups.[4] Note that water cannot be removed completely from the calixarene cavity by chemical methods. The ^{1}H NMR spectra of some calixarenes and their derivatives show a broadened singlet at δ 3.0—3.5 for the protons of "intracavity" water. In many other cases, such spectral identification is however impossible, probably, because of specific intramolecular hydrogen bonding in calixarenes and cavitands.

In the first stage of the reaction under discussion, the starting calixarene **2** is phosphorylated to give cavitand **3** containing four dioxaphosphocine fragments. Its subsequent hydrolysis by "intracavity" water in boiling toluene yields the final calixarene **4** with four phosphinoyl fragments. The residual amount of water in compound **4** could not be determined by spectroscopic methods. "Intracavity" water in the starting calixarene **2** also produces no ^{1}H signals, but its presence was confirmed by transformations of strongly hydrolyzable alkenyl phosphites into phosphinoyl compounds in an inert atmosphere free of atmospheric moisture.

It is noteworthy that one phosphite (phosphonite or phosphinite) fragment cannot, as a rule, be introduced into the calixarene molecule by conventional methods. For example, it was found[5] that the phosphorylation of calixarenes with hexaalkylphosphorous triamides yields, depending on the ratio of the reagents and on the nature of substituent R in the bridging fragment of the molecule, mixtures of linear and cyclic products differing in the number of phosphorus-containing groups and of variable compositions. We found that the reaction of compound **1** with equimolar amount of calixarene **2** first produces cyclic phosphonite (**5**) (δ_P 188.8), which is hydrolyzed by "intracavity" water to give the final product (**6**) containing a single phosphinoyl group (δ_P 26.6, $^{1}J_{P,H}$ = 499 Hz) in high yield either upon heating in toluene or upon prolonged storage (Scheme 2). The molecule of **6** is non-symmetrical; as a result, its methine protons are nonequivalent, giving a multiplet at δ 4.45—4.55 in the ^{1}H NMR spectrum. The ^{1}H NMR spectrum of **6** also contains two singlets at δ 6.33 and 6.50 (an intensity ratio of 3 : 1) for the *ortho*-protons of the benzene rings and two singlets at δ 7.30 and 7.45 (3 : 1) for the *meta*-protons.

Scheme 2



Experimental

^{1}H NMR spectra were recorded on a Tesla BS-567A instrument (100 MHz) with Me_4Si as the internal standard. ^{31}P NMR spectra were recorded on a Bruker MSL-400 instrument (166.93 MHz) with 85% H_3PO_4 as the external standard. IR spectra were recorded on a UR-20 spectrometer in the range 400—3600 cm^{-1} (suspensions in Vaseline oils).

Amide **1** was prepared according to the known procedure.[6]

2,8,14,20-Tetrahexylpentacyclo[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-dodecaen-4,10,16,22,16,18,22,24-octol (2). Heptanal (114 g, 1 mol) was added with stirring over 1.5 h to a mixture of resorcinol (110 g, 1 mol), EtOH (500 mL), water (500 mL), and conc. HCl (250 mL). The reaction mixture was heated at 50 °C for 1 h and kept at 20 °C for 7 days. The precipitate that formed was filtered off, washed several times with water, and recrystallized from EtOH. The product was dried at 150 °C (1—2 Torr) for 7 days to give compound **2** (194 g, 94%), m.p. >350 °C. Found (%): C, 75.12; H, 8.79. $C_{52}H_{72}O_8$. Calculated (%): C, 75.72; H, 8.73. ^{1}H NMR, δ: 0.89 (m, 12 H, C$\underline{H}_3(CH_2)_5$);

1.29 (m, 32 H, Me(C$\underline{H}_2$)$_4$CH$_2$); 2.29 (m, 8 H, C$\underline{H}_2$CH); 4.28 (t, 4 H, C$\underline{H}$CH$_2$, $J_{H,H}$ = 7.3 Hz); 6.23 (s, 4 H, *o*-H arom.); 7.25 (s, 4 H, *m*-H arom.); 8.50 (s, 8 H, $\underline{H}$O).

2,8,14,20-Tetrahexyl-4,10,16,22-tetrahydroxypentacyclo[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-6,12,18,24-tetrayl tetrakis(ethylphosphinate) (4). Amide **1** (0.49 g, 2.4 mmol) was added with stirring to a solution of calixarene **2** (0.5 g, 0.6 mmol) in 30 mL of anhydrous toluene. The solution was kept at 20 °C for 2 h and then heated at 110 °C for 2 h. The solvent was removed, and the residue was washed three times with benzene and dried at 80 °C (1—2 Torr) for 2 h. The yield of compound **4** was 0.52 g (76%), m.p. 69 °C. Found (%): C, 64.08; H, 8.16; P, 10.07. $C_{60}H_{92}O_{12}P_4$. Calculated (%): C, 63.82; H, 8.15; P, 10.99. IR, ν/cm^{-1}: 1280 (P=O); 1600—1610 (CH arom.); 2520 (P—H); 3200 (OH). ^{1}H NMR, δ: 0.54 (m, 12 H, C$\underline{H}_3$CH$_2$P); 0.87 (m, 12 H, C$\underline{H}_3$(CH$_2$)$_5$); 1.27 (m, 32 H, Me(C$\underline{H}_2$)$_4$CH$_2$); 2.18 (m, 8 H, PC$\underline{H}_2$Me); 2.38 (m, 8 H, C$\underline{H}_2$CH); 4.24 (t, 4 H, C$\underline{H}$CH$_2$); 6.38 (s, 4 H, *o*-H arom.); 7.06 (s, 4 H, $\underline{H}$O); 7.40 (s, 4 H, *m*-H arom.).

2,8,14,20-Tetrahexyl-4,6,10,12,16,18,22-heptahydroxypentacyclo[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-dodecaen-24-yl ethylphosphinate (6) was obtained as described above for compound **4** from calixarene **2** (0.4 g, 0.48 mmol) and amide **1** (0.099 g, 0.48 mmol), yield 0.36 g (82%), m.p. 106 °C. Found (%): C, 70.93; H, 8.33; P, 3.52. $C_{54}H_{77}O_9P$. Calculated (%): C, 72.00; H, 8.55; P, 3.44. ^{1}H NMR, δ: 0.56 (t, 3 H, C$\underline{H}_3$CH$_2$P); 0.82 (t, 12 H, C$\underline{H}_3$(CH$_2$)$_5$); 1.22—1.48 (m, 32 H, Me(C$\underline{H}_2$)$_4$CH$_2$); 2.18 (m, 2 H, C$\underline{H}_2$Me); 2.80—2.93 (m, 8 H, C$\underline{H}_2$CH); 4.45—4.55 (m, 4 H, C$\underline{H}$CH$_2$); 6.33 (s, 3 H, *o*-H arom.); 6.50 (s, 1 H, *o*-H arom.); 7.30 (s, 3 H, *m*-H arom.); 7.45 (s, 1 H, *m*-H arom.); 7.09 (s, 7 H, $\underline{H}$O).

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