Synthesis of calix[4]resorcinarenes with phosphorylaryl substituents at the lower rim of the molecule

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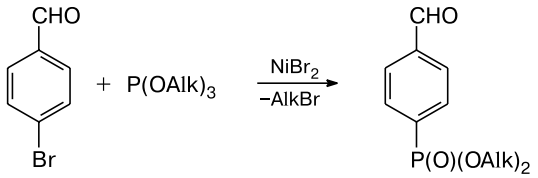
Reaction of resorcinarenes with 4-phosphorylbenzaldehydes afforded calix[4]resorcinarenes, bearing phosphorylaryl substituents at the lower rim of the molecule.

Key words: resorcinarenes, phosphonates, condensation, calix[4]resorcinarenes.

One of the most promising and fast developing trends in organic chemistry is exploration of calix[*n*]arenes, in particular, calix[4]resorcinarenes.[1] This is due to the simplicity of their synthesis and the ability to form complexes of the "guest—host" type with various organic compounds and metal ions, as well as the tendency to self-association, leading to supramolecular ensembles. All the properties described above make this class of compounds very prospective from the point of view of creation of new types of complex-forming agents and the metal ions extragents, as well as new catalytic systems. In this connection, the functionalized and, especially, phosphorylated derivatives are of particular interest.

The data on phosphorus-containing calixarenes are recently reviewed,[2] indicating that a large number of *O*-phosphorylated derivatives of various composition and structure were obtained by far, whereas calixarenes, *C*-phosphorylated at the lower rim of the molecule, were not studied. This is no wonder, since a direct phosphorylation of calixarene framework can hardly afford the target products. Recently,[3,4] we accomplished for the first time a one-step construction of the phosphorus-containing calixarene matrix by the acid-catalyzed reaction of resorcinarene and phosphorus-containing acetal. As a result, the first representative of calix[4]resorcinarenes, bearing phosphinoylalkyl fragments at the lower rim of the molecule, was synthesized. Taking into account the literature data,[5,6] it was reasonable to suppose that the similar in structure *C*-phosphorylarylated calixarenes can be obtained by involvement of phosphorylated benzaldehyde into the condensation with resorcinarene or its derivatives. The synthesis of 4-(diethoxyphosphoryl)benzaldehyde (**1**) and 4-(diisopropoxyphosphoryl)benzaldehyde (**2**) was accomplished on the basis of the earlier[7—10] developed method of the introduction of phosphorus-containing structural fragments into aromatic systems,[7—10] *viz.*, the catalytic reaction of trialkyl phosphites with 4-bromobenzaldehyde (Scheme 1).

Scheme 1



1, 2

Alk = Et (**1**), Pr^i (**2**)

The heating of equimolar amounts of aldehydes **1** or **2** and resorcinarene (**3a**) (or 2-methylresorcinarene (**3b**)) under acidic conditions leads to calix[4]resorcinarenes **4a,b** and **5a,b**, bearing four phosphorylphenyl fragments at the lower rim of the molecule (Scheme 2).

The structure of compounds isolated was confirmed by IR, ^{1}H and ^{31}P spectroscopy and mass spectrometry methods, their composition, by elemental analysis.

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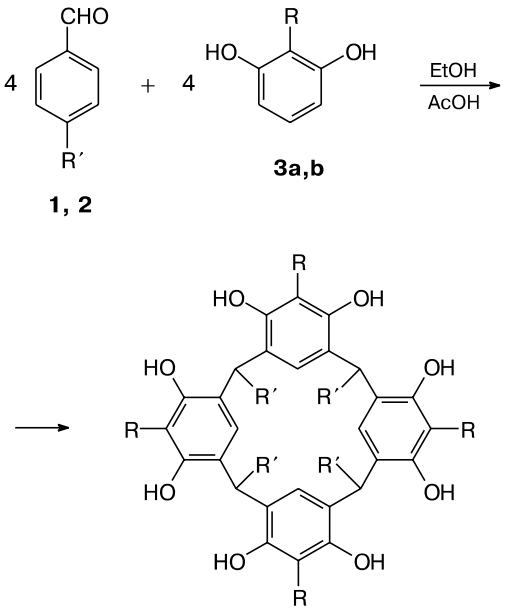
Scheme 2



R = H (**a**), Me (**b**); R′ = $C_6H_4P(O)(OEt)_2$-4 (**1**, **4**), $C_6H_4P(O)(OPr^i)_2$-4 (**2**, **5**)

Experimental

^1H and ^{31}P NMR spectra were recorded on a Bruker MSL-400 spectrometer (400.13 and 166.93 MHz, respectively). The δ values were calculated relatively to the signals of residual protons of DMSO-d_6 (^1H) or of the external standard, 85% aq. H_3PO_4 (^{31}P). IR spectra were recorded on a Specord M-80 spectrometer in the region 450—4000 cm^{-1}. Crystalline samples were studied in Nujol mulls. Mass spectra were recorded on a MALDI 2 V5.2.0 instrument (1,8,9-trihydroxyanthracene as the matrix).

4-Diethoxyphosphorylbenzaldehyde (1). A mixture of triethyl phosphite (13.5 g, 81 mmol), 4-bromobenzaldehyde (15 g, 81 mmol), and $NiBr_2$ (0.35 g, 1.6 mmol) was kept for 4 h at 170 °C. Ethyl bromide (5.84 g, 97%) was distilled off during the reaction. After fractional distillation *in vacuo*, compound **1** was obtained (10.2 g, 52%), b.p. 134 °C (0.05 Torr). Found (%): C, 54.00; H, 5.99; P, 12.35. $C_{11}H_{15}O_4P$. Calculated (%): C, 54.55; H, 6.19; P, 12.81. IR, ν/cm^{-1}: 1210 (P=O); 1715 (CHO). ^1H NMR, δ: 1.25 (t, 6 H, Me, J = 7.0 Hz); 4.10 (m, 4 H, CH_2); 7.93, 8.03 (both d, 2 H each, C_6H_4, J = 8.4 Hz); 10.21 (s, 1 H, CHO). ^{31}P NMR, δ: 17.00.

4-Diisopropoxyphosphorylbenzaldehyde (2). A mixture of triisopropyl phosphite (11 g, 54 mmol), 4-bromobenzaldehyde (10 g, 54 mmol), and $NiBr_2$ (0.354 g, 1.6 mmol) was kept for 4 h at 170 °C. Isopropyl bromide (3.6 g, 56%) was distilled off during the reaction. After fractional distillation *in vacuo*, compound **2** was obtained (6.3 g, 48%), b.p. 126 °C (0.05 Torr). Found (%): C, 56.90; H, 6.99; P, 11.18. $C_{13}H_{19}O_4P$. Calculated (%): C, 57.77; H, 7.03; P, 11.48. IR, ν/cm^{-1}: 1212 (P=O); 1716 (CHO). ^1H NMR, δ: 1.02, 1.05 (both d, 12 H, $CH(C\underline{H}_3)_2$); 4.56 (m, 2 H, $C\underline{H}(CH_3)_2$); 7.95, 8.05 (both d, 2 H each, C_6H_4, J = 8.4 Hz); 10.31 (s, 1 H, CHO). ^{31}P NMR, δ: 17.00.

4,6,10,12,16,18,22,24-Octahydroxy-2,8,14,20-tetrakis[4-diethoxyphosphorylphenyl]pentacyclo[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 (4a). Phosphonate **1** (4.39 g, 1.8 mmol) was gradually and with stirring added to a cooled to 10 °C solution of resorcinarene (2 g, 1.8 mmol) in 95% aqueous EtOH (30 mL) and glacial acetic acid (4.68 mL). The reaction mixture was kept for 40 h at 60 °C. The precipitate formed was washed with ethanol and kept *in vacuo* (40 °C, 0.06 Torr) until the weight was constant to obtain compound **4a** (1.9 g, 73%), m.p. 275 °C (decomp.). Found (%): C, 60.71; H, 5.22; P, 9.00. $C_{68}H_{76}O_{20}P_4$. Calculated (%): C, 61.07; H, 5.68; P, 9.28. IR, ν/cm^{-1}: 1210 (P=O); 3300—3400 (OH). ^1H NMR, δ: 1.25 (t, 24 H, Me, J = 7.0 Hz); 3.98 (m, 16 H, CH_2); 5.69 (s, 4 H, CH); 6.17 (s, 4 H, O-CH_{Ar}, C_6H_2); 6.84 (s, 4 H, m-CH_{Ar}, C_6H_2); 7.30 (d, 8 H, O-CH_{Ar}, C_6H_4, J = 8.0 Hz); 7.33 (d, 8 H, m-CH_{Ar}, C_6H_4, J = 8.0 Hz); 8.54 (s, 8 H, OH). ^{31}P NMR, δ: 20.98. MS: m/z 1359 [M + Na].

4,6,10,12,16,18,22,24-Octahydroxy-5,11,17,23-tetramethyl-2,8,14,20-tetrakis[4-diethoxyphosphorylphenyl]pentacyclo[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 (4b). Phosphonate **1** (1.94 g, 0.8 mmol) was gradually and with stirring added to a cooled to 10 °C solution of 2-methylresorcinarene **3b** (1 g, 0.8 mmol) in 95% EtOH (15 mL) and glacial AcOH (2.34 mL). The reaction mixture was kept for 45 h at 60 °C. The precipitate formed was washed with ethanol and kept *in vacuo* (40 °C, 0.06 Torr) until the weight was constant to obtain compound **4b** (1.8 g, 64%), m.p. 250 °C (decomp.). Found (%): C, 61.81; H, 5.72; P, 8.55. $C_{72}H_{84}O_{20}P_4$. Calculated (%): C, 62.07; H, 6.03; P, 8.91. IR, ν/cm^{-1}: 1200 (P=O); 3300—3400 (OH). ^1H NMR, δ: 1.24 (t, 24 H, Me, J = 7.0 Hz); 1.82 (s, 12 H, ArMe); 4.00 (m, 16 H, CH_2); 5.51 (s, 4 H, CH); 6.84 (s, 4 H, m-CH_{Ar}, C_6H); 7.27 (d, 8 H, O-CH_{Ar}, C_6H_4, J = 8.0 Hz); 7.30 (d, 8 H, m-CH_{Ar}, C_6H_4, J = 8.0 Hz); 8.00 (s, 8 H, OH). ^{31}P NMR, δ: 19.56. MS: m/z 1392 [M + Na].

4,6,10,12,16,18,22,24-Octahydroxy-2,8,14,20-tetrakis[4-diisopropoxyphosphorylphenyl]pentacyclo[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 (5a). Phosphonate **2** (2 g, 7.75 mmol) was gradually and with stirring added to a cooled to 10 °C solution of resorcinarene **3a** (0.853 g, 7.75 mmol) in 95% aq. EtOH (14 mL) and glacial acetic acid (2.15 mL). The reaction mixture was kept for 40 h at 60 °C. The precipitate formed was washed with ethanol and kept *in vacuo* (40 °C, 0.06 Torr) until the weight was constant to obtain compound **5a** (1.5 g, 53%), m.p. > 190 °C (decomp.). Found (%): C, 62.4; H, 6.0; P, 7.75. $C_{76}H_{92}O_{20}P_4$. Calculated (%): C, 62.98; H, 6.35; P, 8.56. IR, ν/cm^{-1}: 1200 (P=O); 3300—3400 (OH). ^1H NMR, δ: 1.07, 1.10 (both d, 48 H, Me, J = 7 Hz); 4.56 (m, 8 H, CH); 5.65 (s, 4 H, CH); 6.12 (s, 4 H, O-CH_{Ar}, C_6H_2); 6.20 (s, 4 H, m-CH_{Ar}, C_6H_2); 7.00 (d, 8 H, O-CH_{Ar}, C_6H_4, J = 8.1 Hz); 7.50 (d, 8 H, m-CH_{Ar}, C_6H_4, J = 8.1 Hz); 8.90 (s, 8 H, OH). ^{31}P NMR, δ: 17.05.

4,6,10,12,16,18,22,24-Octahydroxy-5,11,17,23-tetramethyl-2,8,14,20-tetrakis[4-diisopropoxyphosphorylphenyl]pentacyclo[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 (5b). Phosphonate **2** (1.93 g, 7.14 mmol) was gradually and with stirring added to a cooled to 10 °C solution of 2-methylresorcin-

arene **3b** (0.886 g, 7.14 mmol) in 95% aq. EtOH (14 mL) and glacial acetic acid (2.15 mL). The reaction mixture was kept for 60 h at 60 °C. The precipitate formed was washed with ethanol and kept *in vacuo* (40 °C, 0.06 Torr) until the weight was constant to obtain compound **5b** (1.69 g, 65%), m.p. > 185 °C (decomp.). Found (%): C, 63.4; H, 6.41; P, 7.92. $C_{80}H_{100}O_{20}P_4$. Calculated (%): C, 63.82; H, 6.64; P, 8.24. IR, ν/cm^{-1}: 1200 (P=O); 3300—3400 (OH). ^{1}H NMR, δ: 1.10, 1.20 (both d, 48 H, Me, J = 7 Hz); 2.08 (s, 12 H, ArMe); 4.65 (m, 8 H, CH); 5.60 (s, 4 H, CH); 6.40 (s, 4 H, *m*-CH_{Ar}, C_6H); 6.90 (d, 8 H, *O*-CH_{Ar}, C_6H_4, J = 8.1 Hz); 7.49 (d, 8 H, *m*-CH_{Ar}, C_6H_4, J = 8.1 Hz); 8.93 (s, 8 H, OH). ^{31}P NMR, δ: 16.51.

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