Brief Communications

Reactions of trialkyl(aryl)phosphonium-substituted acetals with resorcinol and its derivatives

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The reactions of 2-tributylphosphonioacetaldehyde acetal with resorcinol and 2-methylresorcinol in an acidic aqueous-ethanol medium afford calix[4]resorcinols containing four tributylphosphonium groups at the lower rim. The corresponding reactions of the triphenylphosphonium analog give phosphonium salts containing the 2,2-diarylethyl moiety.

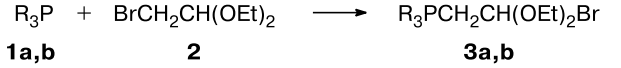
Key words: phosphonium salts, acetals, resorcinol, condensation, calixarenes.

The chemistry of calixarenes and, in particular, of calix[4]resorcinols currently receives considerable attention from researchers.[1—3] The main method for the synthesis of calix[4]resorcinols is based on the tetramerization of aliphatic and aromatic aldehydes with resorcinol in acidic aqueous-alcohol media.[4,5] Numerous O-phosphorylated derivatives with different compositions and structures have been synthesized; however, data on calixarenes C-phosphorylated at the lower rim are scarce.[6] This is associated with the fact that methods for the direct C-phosphoylation of the calixarene core are lacking, and it is hardly probable that they will be developed in the nearest future.

Recently, we have formed for the first time a phosphorus-containing calixarene matrix by the acid-catalyzed reaction of resorcinol with available phosphorus-containing α-phosphonoacetals.[7—11] It appeared that calixarenes containing acidic phosphonate groups are efficient extracting agents for ions of lanthanum group metals from acidic solutions.[12]

The aim of the present study was to synthesize calix[4]resorcinols containing phosphonium groups at the lower rim. The presence of these groups in the molecule should improve their solubility and have an effect on the character of aggregation in organic solvents and biological activity. The alkylation of tributyl- and triphenylphosphines **1a**,**b** with α-bromoacetal **2** afforded the key phosphonium-substituted acetals **3a**,**b** (Scheme 1).

Scheme 1



3: R = Bu (**a**), Ph (**b**)

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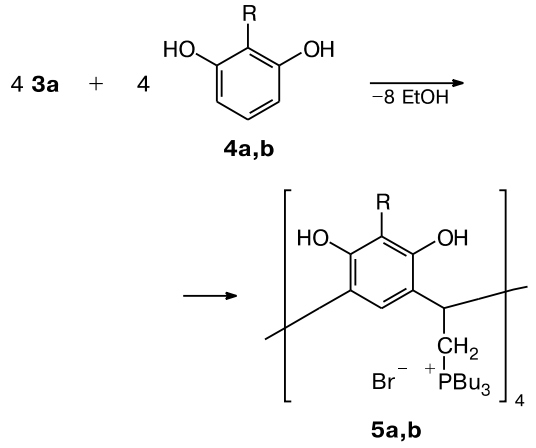
Phosphonium salts **3a** and **3b** are oily compounds characterized by singlets at δ 31.5 and 21.1, respectively, in the ^{31}P NMR spectra. Due to the salt structure of these compounds, their ^{1}H NMR spectra show poorly resolved broadened signals, and only the group analysis of protons can be performed based on the chemical shifts without taking into account their fine structure.

The condensation of acetal **3a** with resorcinol and 2-methylresorcinol **4a**,**b** was performed by heating them for a short period of time in an acidic aqueous-ethanol medium, which resulted in the formation of calixarenes **5a**,**b** containing four phosphonium moieties (Scheme 2).

Scheme 2



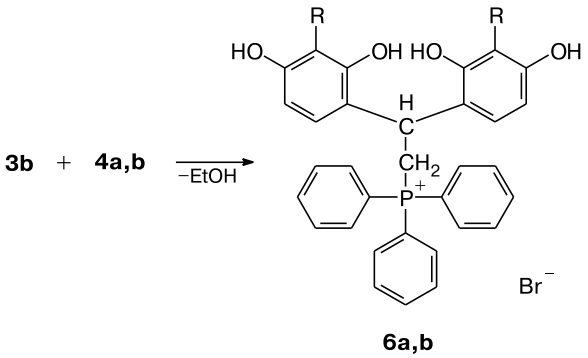
4, 5: R = H (**a**), Me (**b**)

The formation of cyclic products **5a**,**b** is evidenced by the fact that signals for the *ortho*-protons of the aromatic rings are absent in the ^{1}H NMR spectra. Compounds **5a**,**b** are pale-yellow powders soluble in alcohols, DMSO, and DMF, as well as in mixtures of these solvents with water. The ^{31}P NMR spectra of products **5a**,**b** show one signal at δ 33—34.

It appeared that the synthetic result of the reactions of resorcinol and 2-methylresorcinol with phosphonium-substituted acetals substantially depends on the structures of the latter. The reactions of compound **3b** with compounds **4a**,**b** in an acidic aqueous-ethanol medium produce phosphonium salts containing the 2,2-diarylethyl moiety (Scheme 3).

The formation of adducts **6a,b** instead of the expected calix[4]resorcinols is apparently associated with the steric effect of three phenyl rings that are present in the molecules. This reaction in an aprotic solvent (dichloromethane) in the presence of trifluoromethanesulfonic acid gives the same products. Compounds **6a,b** are pale-yellow powders soluble in ethanol, DMF, and DMSO. The ^{31}P NMR spectra of these compounds show one signal at δ 21. Recently, compounds structurally similar to phosphonium salts **6a,b** have been synthesized by the reactions of diethyl 2,2-diethoxyethylphosphonate with anisol and 1,3-dimethoxybenzene, respectively, in dichloromethane in the presence of trifluoromethanesulfonic acid.[13]

Scheme 3



6: R = H (**a**), Me (**b**)

Experimental

The ^{1}H NMR spectra were recorded on Bruker Avance-600 instruments (600 MHz) in $CDCl_3$ and CD_3OD. The ^{31}P NMR spectra were measured on a Bruker MSL-400 Fourier-transform spectrometer (100.62 MHz). The NMR experiments were carried out in solutions (10 mmol L^{-1}) at 303 K with the use of an inverse sensor with a *z*-gradient coil (5 mm). The chemical shifts δ are given with respect to the signals of the residual protons of the deuterated solvent (^{1}H) and 85% H_3PO_4 as the external standard (^{31}P). The mass spectra were obtained on a MALDI-2 V-5.2.0 instrument (1,8,9-trihydroxyanthracene as the matrix).

***P*,*P*,*P*-Tributyl-*P*-(2,2-diethoxyethyl)phosphonium bromide (3a).** A mixture of tributylphosphine (7.53 g, 0.037 mol) and 1-bromo-2,2-diethoxyethane (**2**) (11.02 g, 55.9 mmol) was kept under argon at 80 °C for 4 h. An excess of the reactant was distilled off using a vacuum oil pump. The oily residue was triturated with diethyl ether, the solvent was removed, and the product was kept *in vacuo* to a constant weight. Product **3a** was synthesized in a yield of 8.3 g (56%). Found (%): P, 7.59. $C_{18}H_{40}BrO_2P$. Calculated (%): P, 7.76. ^{1}H NMR ($CDCl_3$), δ: 0.28 (m, 9 H, Me); 0.52 (m, 6 H, Me); 0.82 (m, 6 H, $PCH_2CH_2C\underline{H}_2$); 0.92 (m, 6 H, $PCH_2C\underline{H}_2$); 1.79 (m, 6 H, $PC\underline{H}_2CH_2$); 2.29 (m, 2 H, $PC\underline{H}_2CH$); 2.96 (m, 2 H, —OCH_2); 3.07 (m, 2 H, OCH_2); 4.33 (m, 1 H, CH). ^{31}P NMR ($CDCl_3$), δ: 31.5.

***P*-(2,2-Diethoxyethyl)-*P*,*P*,*P*-triphenylphosphonium bromide (3b).** By analogy with the synthesis of compound **3a**, oily product **3b** was pepared in a yield of 1.0 g (55%) from triphenylphosphine (3 g, 1.5 mmol) and reactant **2** (3.4 g, 17.3 mmol). Found (%): P, 6.66. $C_{24}H_{28}BrO_2P$. Calculated (%): P, 6.75. ^{31}P NMR ($CDCl_3$), δ: 21.1. In subequent reactions, compound **3b** was used without additional purification.

4,6,10,12,16,18,22,24-Octahydroxy-2,8,14,20-tetrakis(tributylphosphoniomethyl)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 tetrabromide (5a). A mixture of resorcinol (0.74 g, 6.8 mmol), water (14 mL), ethanol (14 mL), concentrated hydrochloric acid

(5 mL), and salt **3a** (2.7 g, 6.8 mmol) was kept at 50 °C for 1 h and then at 20 °C for 7 days. The solvent was distilled off. The oily product was triturated with diethyl ether, filtered, and dried *in vacuo* (1 h, 40 °C, 0.04 Torr) to a constant weight. Compound **5a** was obtained in a yield of 2.3 g (82%) as a beige powder, m.p. 185—190 °C. Found (%): C, 56.75; H, 8.17; Br, 19.60; P, 7.40. $C_{80}H_{136}Br_4O_8P_4$. Calculated (%): C, 57.55; H, 8.15; Br, 19.18; P, 7.43. ^{1}H NMR (CD_3OD), δ: 0.91 (m, 36 H, Me); 1.40 (m, 48 H, CH_2); 1.91 (m, 24 H, $PC\underline{H}_2CH_2$); 2.30 (m, 8 H, $PC\underline{H}_2CH$); 4.86 (m, 4 H, CH); 6.61 (br.s, 4 H, *o*-CH_{Ar}); 7.08 (br.s, 4 H, *m*-CH_{Ar}). ^{31}P NMR (CD_3OD), δ: 33.3. MALDI-MS: 1348 $[M - 4\ Br^-]^{4+}$.

4,6,10,12,16,18,22,24-Octahydroxy-2,8,14,20-tetrakis(tributylphosphoniomethyl)-5,11,17,23-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 tetrabromide (5b). By analogy with the synthesis of compound **5a**, product **5b** was prepared from 2-methylresorcinol (0.78 g, 6.3 mmol), water (14 mL), ethanol (14 mL), concentrated hydrochloric acid (5 mL), and salt **3a** (2.5 g, 6.3 mmol) in a yield of 1.42 g (53%) as a pale-orange powder, m.p. 181—185 °C. Found (%): C, 57.60; H, 8.58; P, 6.76. $C_{84}H_{144}Br_4O_8P_4$. Calculated (%): C, 58.33; H, 8.33; P, 7.18. ^{1}H NMR (DMSO-d_6), δ: 0.75 (m, 36 H, Me); 1.25 (m, 48 H, CH_2); 1.76 (br.s, 12 H, Me); 2.07 (m, 24 H, $PC\underline{H}_2CH_2$); 2.50 (m, 8 H, $PC\underline{H}_2CH$); 4.35 (m, 4 H, CH); 6.69 (br.s, 4 H, *m*-H_{Ar}). ^{31}P NMR (DMSO-d_6), δ: 33.8. MALDI-MS: 1408 $[M - 4\ Br^-]^{4+}$.

***P*-[2,2-Bis(2,4-dihydroxyphenyl)ethyl]-*P*,*P*,*P*-triphenylphosphonium bromide (6a).** A mixture of resorcinol (1.0 g, 9.2 mmol), ethanol (3 mL), water (10 mL), concentrated hydrochloric acid (3 mL), and salt **3b** (2.10 g, 4.6 mmol) was kept at 50 °C for 1 h and then at 20 °C for 7 days. The solvent was distilled off. The residue was reprecipitated from ethanol into diethyl ether and kept *in vacuo* (0.5 h, 40 °C, 0.04 Torr) to a constant weight. Product **6a** was obtained in a yield of 2.0 g (75%) as a pale-yellow powder, m.p. 198—202 °C. Found (%): C, 65.95; H, 4.82; P, 5.72. $C_{32}H_{28}BrO_4P$. Calculated (%): C, 65.41; H, 4.77; P, 5.28. ^{1}H NMR (CD_3OD), δ: 4.11 (dd, 2 H, PCH_2, $^2J_{PH}$ = 12.29 Hz, $^3J_{HH}$ = 6.97 Hz); 4.92 (dt, 1 H, CH, $^3J_{PH}$ = = 11.74 Hz, $^3J_{HH}$ = 6.97 Hz); 6.09 (dd, 2 H, *m*-H_{Ar}, $^5J_{PH}$ = = 2.20 Hz, $^3J_{HH}$ = 8.43 Hz); 6.14 (d, 2 H, *o*-CH_{Ar}); 6.79 (d, 2 H, *o*-CH_{Ar}, $^3J_{HH}$ = 8.44 Hz); 7.65 (m, 15 H, Ph). ^{31}P NMR (CD_3OD), δ: 20.9.

***P*-[2,2-Bis(2,4-dihydroxy-3-methylphenyl)ethyl]-*P*,*P*,*P*-triphenylphosphonium bromide (6b).** *A* (the ratio of the starting reactants was 1 : 1). A solution of salt **3a** (0.79 g, 1.72 mmol) in ethanol (2 mL) was added dropwise with stirring to a mixture of 2-methylresorcinol (0.21 g, 1.72 mmol), ethanol (2 mL), water (4 mL), and concentrated hydrochloric acid (2 mL). The reaction mixture was heated with stirring (0.5 h, 50 °C) and kept at 20 °C for 7 days. After distillation of the solvent, the product (oil) was reprecipitated from ethanol into diethyl ether and dried *in vacuo* (40 °C, 0.04 Torr) to a constant weight. The product was obtained in a yield of 0.37 g (75%) as a gray-yellow powder, m.p. 220—223 °C. Found (%): C, 66.07; H, 5.19; Br, 13.12; P, 4.96. $C_{34}H_{32}BrO_4P$. Calculated (%): C, 66.34; H, 5.20; Br, 13.010; P, 5.04. ^{1}H NMR (CD_3OD), δ: 1.95 (s, 6 H, Me); 4.14 (dd, 2 H, PCH_2, $^2J_{PH}$ = 12.11 Hz, $^3J_{HH}$ = 6.97 Hz); 5.13 (dt, 1 H, CH, $^3J_{PH}$ = 12.84 Hz, $^3J_{HH}$ = 6.79 Hz); 6.19 (d, 2 H, *m*-H_{Ar}, $^3J_{HH}$ = = 8.47 Hz); 6.74 (d, 2 H, *o*-H_{Ar}, $^3J_{HH}$ = 8.52 Hz); 7.69 (m, 15 H, Ph). ^{31}P NMR (CD_3OD), δ: 21.4.

B (the ratio of the starting reactants was 2 : 1). Product **6b** was synthesized in the same fashion by the reaction of 2-methylresorcinol (4.32 g, 34.9 mmol) with salt **3a** (8.00 g, 17.4 mmol) in dichloromethane (70 mL) in the presence of trifluoroacetic acid (10 mL) in a yield of 7.5 g (70%), m.p. 220—223 °C. Found (%): C, 66.07; H, 5.19; Br, 13.12; P, 4.96. $C_{34}H_{32}BrO_4P$. Calculated (%): C, 66.34; H, 5.20; Br, 13.010; P, 5.04. The ^{1}H and ^{31}P NMR spectra of the product synthesized according to the method *A* are identical to those of the product prepared by the method *B*.

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