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LETTERS TO THE EDITOR

Phosphorylation of Octa-2-hydroxyethylated Calix[4]resorcinol

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Supramolecular chemistry has provided numerous examples of macrocyclic structures acting as *hosts* for organic molecules, the process being a basis for the macrocycles application in molecular recognition. In particular, such structures include calixarenes [1], attractive building blocks containing symmetric cavities of easily tunable size [2, 3]. They can be functionalized [3, 4] and used to form the large-scale spatially organized structures [5].

A promising method of the calixarene molecules modification is phosphorylation of four-coordinated phosphorus derivatives, allowing the phosphoryl group to be introduced into the molecule. Compounds of this type can be of interest as complexing agents and biologically active substances.

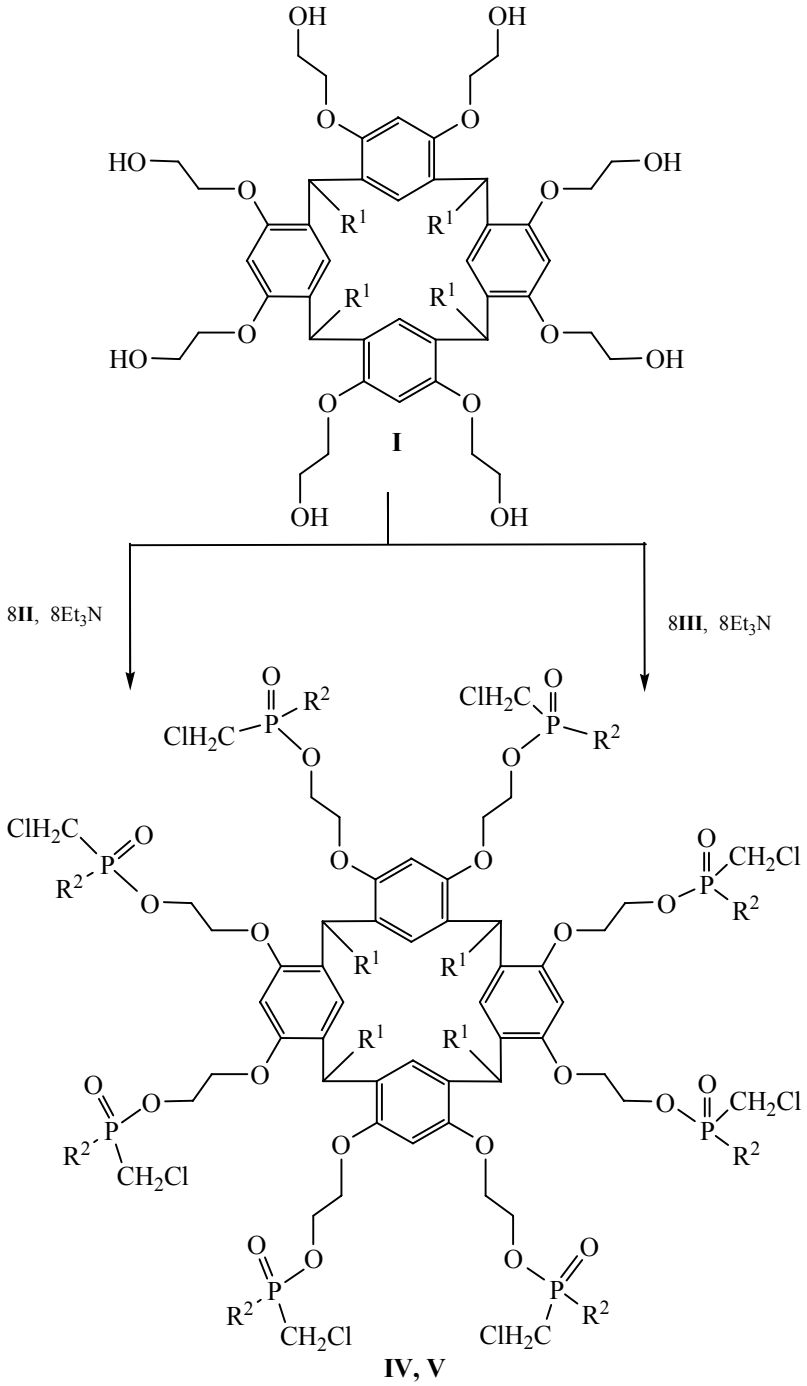
Octa-2-hydroxyethylcalix[4]resorcinol **I** was selected as a model compound to test the approach. Bis(chloromethyl)phosphinic acid chloride **II** and chloromethylphosphonic acid dichloride **III** were used as the phosphorylating agents. The approach potentially allows simultaneous introduction of phosphoryl groups (important for the complexes formation) and chloromethyl groups (sites of further modification of the calixarenes obtained) [6]. Interaction of calixarene **I** with acid chlorides **II** and **III** was carried out in chloroform solution in the presence of triethylamine. With chloride **II**, calixarene **IV** containing bis(chloromethyl)phosphinate groups was obtained with yield of 75%; in the case of chloride **III** the reaction product was calixarene **V** bearing fragments of chloromethylphosphonic acid. This result was apparently due to hydrolysis of the formed chloromethyl chlorophosphonates (Scheme 1).

Structure and composition of compounds **IV** and **V** were confirmed by IR, NMR spectroscopy, and elemental analysis.

Octa-2-hydroxyethylated calix[4]resorcinol **I** was synthesized as described in [7].

4,6,10,12,16,18,22,24-Octakis[2-di(chloromethyl)-phosphoryloxyethoxy]-2,8,14,20-tetranonylpentacyclo-[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). 0.60 g of triethylamine and a solution of 1.08 g of the acid chloride **II** in 3 mL of chloroform were added upon stirring to a solution of 1 g of **I** in 10 mL of chloroform. The reaction mixture was kept at 40°C for 4 h. After the solvent removal, the residue was dissolved in dioxane, and triethylamine hydrochloride was filtered off. The filtrate was evaporated. The residue was dried in vacuum. Yield 1.56 g (84%), viscous liquid. IR spectrum, ν, cm^{-1}: 1299 (P=O), 1583, 1610 (arom.). ^{1}H NMR spectrum, δ, ppm, (*J*, Hz): 0.88 t (12H, CH_3, $^3J_{HH}$ 6.83), 1.25 m [56H, $(CH_2)_7$], 1.82 m (8H, CH_2), 3.56–4.38 br.m (32H, OCH_2CH_2, CH_2Cl), 4.52 t (4H, CH, $^3J_{HH}$ 7.51), 6.40 s (4H, ArH), 6.71 s (4H, ArH). ^{13}C NMR spectrum, δ_C, ppm, (*J*, Hz): 14.09 q (CH_3, $^1J_{CH}$ 124.25), 22.68 t (CH_2, $^1J_{CH}$ 125.70), 28.31 t (CH_2, $^1J_{CH}$ 125.34), 29.40 t (CH_2, $^1J_{CH}$ 126.06), 29.85 t (CH_2, $^1J_{CH}$ 126.06), 30.23 t (CH_2, $^1J_{CH}$ 129.69), 31.94 t (CH_2, $^1J_{CH}$ 130.42), 32.61 t (CH_2, $^1J_{CH}$ 126.16), 33.31 t (CH_2, $^1J_{CH}$ 149.68), 35.15 t (CH_2Cl, $^1J_{CH}$ 149.31), 35.53 d (C^1, $^1J_{CH}$ 126.79), 65.11 t ($ArOCH_2$, $^1J_{CH}$ 147.50), 68.54 t (CH_2OP, $^1J_{CH}$ 144.23), 101.32 d (C^7, $^1J_{CH}$ 150.68), 126.63 d (C^4, $^1J_{CH}$ 152.58), 127.81 s ($C^{2,6}$), 154.51 s ($C^{3,5}$). ^{31}P NMR spectrum, ($CDCl_3$): δ_P 41.03 ppm. Found, %: C 45.95; H 6.05; Cl 22.58; P 9.85.

Scheme 1.



$R^1 = C_9H_{19}$; $R^2 = CH_2Cl$ (**IV**), OH (**V**).

$C_{96}H_{152}Cl_{16}O_{24}P_8$. Calculated, %: C 46.02; H 6.12; Cl 22.64; P 9.89. Mass spectrum (MALDI-TOF), *m*/*z* (I_{rel}, %): 2525.43 $[M + Na]^+$, 2541.46 $[M + K]^+$.

4,6,10,12,16,18,22,24-Octakis(2-hydroxychloromethylphosphoryloxyethoxy)-2,8,14,20-tetranonylpentacyclo[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) was prepared similarly from 1.0 g of **I**, 0.60 g of triethylamine and 1.00 g of the acid chloride **III**. Yield 1.36 g (82%), powder, mp 146°C. IR spectrum, ν, cm^{-1}: 1296 (P=O), 1584, 1611 (arom.), 2290 br. (P–OH). ^1H NMR spectrum, δ, ppm, (*J*, Hz): 0.84 br. s (12H, CH_3), 1.33 m [56H, $(CH_2)_7$], 1.83 m (8H, CH_2), 3.90–4.20 br.m (48H, OCH_2CH_2, CH_2Cl), 4.54 br. s (4H, CH), 6.12 s (4H, ArH), 6.45 s (4H, ArH). ^{31}P NMR spectrum, ($CDCl_3$): δ_P 18.56 ppm. Found, %: C 46.85; H 6.50; Cl 12.45; P 11.00. $C_{88}H_{144}Cl_8O_{32}P_8$. Calculated, %: C 47.07; H 6.46; Cl 12.63; P 11.04. Mass spectrum (MALDI-TOF), *m*/*z* (I_{rel}, %): 2267.46 $[M + Na]^+$, 2283.57 $[M + K]^+$.

^1H (400.13 MHz) and ^{31}P (161.94 MHz) NMR spectra were recorded with a Bruker MSL-400 spectrometer. ^{13}C NMR spectra were taken using a Bruker Avance 600 spectrometer operating at 150 MHz. The signals of residual protons of the deuterated solvent ($CDCl_3$) were used as reference. IR spectra were registered with a Bruker Vector 22 IR Fourier spectrometer at 400–4000 cm^{-1} (paraffin oil). Mass spectra (MALDI-TOF) were obtained with an ULTRAFLEX III TOF/TOF Bruker instrument using *p*-nitroaniline as a matrix.

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