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Effective Synthesis of β-Ketophosphonate Derivatives of Calix[4]resorcinolarenes

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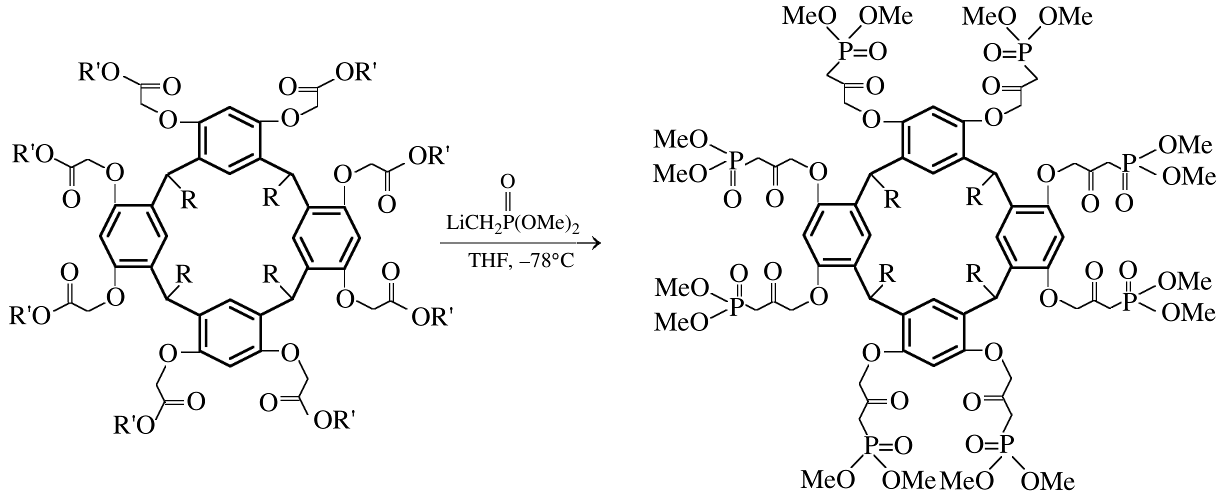
Abstract—An effective method for introduction of β-phosphonate fragments to a calix[4]resorcinolarene matrix is presented octa(ketophosphonate)calix[4]resorcinolarenes are prepared. The effectiveness of 2,8,14,20-tetramethyl-4,6,10,12,16,18,22,24-octa[3-(dimethoxyphosphoryl)-2-oxopropyl]calix[4]-resorcinolarene for extraction of lanthanum ions from water to chloroform in the presence of picrate ions, accompanied by formation of a complex is demonstrated.

Phosphorus-containing calixarenes have been intensively studied over the last years [1]. Noteworthy is their ability to behave as atypical multicenter ligands for silver, copper, gold, and platinum ions, involving them into clusters [2, 3]. Unlike classical calixarenes, phosphorus-containing calix[4]resorcinolarenes have been much poorer explored, and most emphasis has been put on the introduction of phosphorus into the upper calixarene rim via functionalization of hydroxy groups. Application of such phosphorus derivatives is restricted by their sensitivity to hydrolysis by the P–OAr bond. However, the hydrolytic stability of phosphorus-containing calix[4]resorcinolarenes can be increased by introduction of a phosphorus fragment via P–C bond formation. In the preceding communication [4] we have described the preparation of aminophosphonate calix[4]resorcinolarene derivatives and their successful application for lanthanum extraction.

Here we report on a convenient and an effective method for introduction of β-ketophosphonate fragments to a calix[4]resorcinolarene matrix (compounds **III** and **IV**). As starting compounds we used esters **I** and **III**, obtained by reaction of monobromoacetates with calix[4]resorcinolarenes [5], and dimethyl (lithiomethyl)phosphonate obtain, in its turn, from the corresponding phosphonate with BuLi [6].



R = CH_3, R' = C_2H_5 (**I**); R = C_8H_{17}, R' = CH (**II**); R = CH_3 (**III**), C_8H_{17} (**IV**).

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Table 1. ^{1}H and ^{31}P NMR spectra of compounds **I–IV**

Comp. no.	^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz)										^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm
	$POCH_3$	H_2O	CH_{Ar}	CHC_8H_{17} [$CHCH_3$]	CH_2	CH_2P	OCH_3 [OCH_2CH_3]	$CHCH_3$ [$CH_2C_7H_{15}$]	$(CH_2)_6$ [OCH_2CH_3]	$(CH_2)_6CH_3$	
I	–	–	6.7 s, 6.24 s	[4.7 q (*J* 7.08)]	4.3 s	–	[4.2 q (*J* 7.081)]	1.46 d (*J* 7.08)	[1.2 t (*J* 7.081)]	–	–
II	–	–	6.54 s, 6.12 s	4.5 t (*J* 7.33)	4.2 s	–	3.68 s	[1.24 br]	1.2–1.16 m	0.78 t (*J* 6.68)	–
III	3.76–3.63 m	7.76 br	6.57 s, 6.19 s	[4.63 q (*J* 6.92)]	4.8 s	3.36–3.29 m	–	1.42 d (*J* 6.95)	–	–	23.72, 23.26
IV	3.54–3.45 m	7.0 br	6.4 br, 5.9 br	4.6–4.5 br	4.34 s	3.13 br	–	[1.58 br]	1.22–0.99 m	0.61 br	23.4 br

The methylenephosphonate group was easily introduced by stepwise addition of $LiCH_2P(O)(OMe)_2$ in THF at –78°C under argon to a solution of calixarene **I**, **II**. The ^{31}P NMR spectra of the prepared compounds contain signals at δ_P 23.4 (**IV**) and 23.72 and 23.26 ppm (**III**). The observation of two signals in the latter case suggests that compound **III** is conformationally inhomogeneous, whereas in compound **IV** inversion processes are hindered due to the presence of a long aliphatic "tail" (C_8H_{17}). Analysis of the mass spectra (MALDI–TOF) showed that the products are complexes of with one water molecule: compound **III**: found 1874 (100%, $M + H_2O$, calculated 1856 + 18); compound **IV**: found 2266 (100%, $M + H_2O$, calculated 2248 + 18). The complex formation is confirmed by the appearance in the ^{1}H NMR spectra of broad proton signals of water at δ 7.76 (**III**) and 7.0 ppm (Table 1).

We studied lanthanum extraction from water (pH 5.5) to chloroform by compound **III** (L) in the presence of excess sodium picrate. The lanthanum concentration in the water phase was determined by spectrophotometry using Xylenol Orange [7]. The stoichiometry of the complex formed, namely, the number of extractant molecules coordinating one lanthanum ion (*n*) was determined by graphical solution of the following equation:

$$K_{ex} = \alpha/[(1 - \alpha)(C^0_L - n\alpha C^0_{LaCl_3})^n(C_{NaPic})^3_{init}].$$

Here $C^0_{LaCl_3}$ and C^0_L are the initial concentrations of lanthanum chloride and compound **III** (L), respectively; $\alpha = E^{3+}_{La}/100$; and E^{3+}_{La} is the degree of lanthanum extraction.

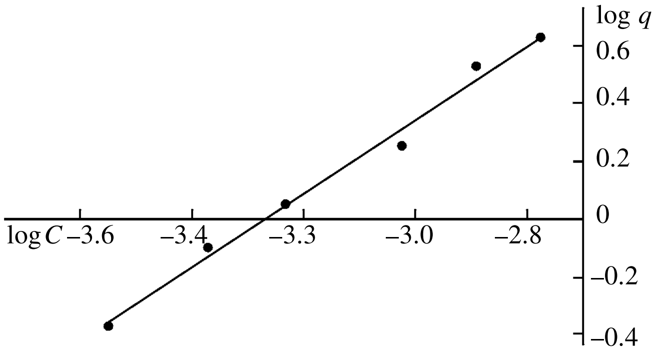
Table 2. Dependence of the degree of La^{3+} extraction and the log *q* and log *C* values on the ligand L concentration in the organic phase[a]

$C_L \times 10^{-4}$, M	E^{3+}_{La}, %	log *q*	–log *C*
4	30	–0.368	3.553
6	44	–0.105	3.373
8	53	0.052	3.231
12	64	0.250	3.025
16	77	0.525	2.889
20	81	0.630	2.776

[a] C_{LaCl_3} 4×10^{-4}, C_{NaPic} 3×10^{-2} M

Analysis of the dependence of log *q* [where $q = \alpha/(1 - \alpha)$] on $\log C = (C^0_L - n\alpha C^0_{LaCl_3})$ (Table 2, figure) shows that at ligand concentrations of 4×10^{-4}–2×10^{-3} M and lanthanum chloride and sodium picrate concentrations of 4×10^{-4} and 3×10^{-2} M, respectively, a 1 : 1 $(LaPic_3)(L)$ complex with the extraction constant K_{ex} 7.4×10^7 M^{-4} prevails.

Like with a calix[4]resorcinolarene containing carbamoyl phosphine oxide moieties [8], the effective extraction is ensured by the complex-forming ability of chelate ketophosphonate substituents fixed on the calix[4]resorcinolarene frame.



Plot of log *q* vs. log *C*. $y = 1.2735x + 4.1643$; R^2 0.9915.

EXPERIMENTAL

All reactions were performed under argon using Schlenk vessels. The ^{1}H and ^{31}P NMR spectra were recorded on a Unity-300 spectrophotometer (300 and 121 MHz) for 10–15% solutions against internal TMS and external 85% H_3PO_4. The mass spectra were obtained on a MALDI-TOF Kratos Kompact MALDI II instrument.

Dimethyl (lithiomethyl)phosphonate was prepared by the procedure in [6] and esters **I** and **II**, by the procedure in [5].

2,8,14,20-Tetramethyl-4,6,10,12,16,18,22,24-octa[3-(dimethoxyphosphoryl)-2-oxopropyl]calix[4]resorcinolarene (III). A solution of *n*-butyllithium (13.4 ml or 21.44 mmol of a 1.6 M solution in hexane) was added with vigorous stirring under argon at –78°C over the course of 1 h to a solution of 2.1 g of dimethyl methylphosphonate in 200 ml of THF. After 1-h stirring, a solution of 2 g of calix[4]resorcinolarene **I** in 50 ml of THF was added in one portion, and the mixture was stirred for 50 h at room temperature. The solvent was removed in a vacuum, the residue was treated with a mixture of ethyl acetate (2 × 100 ml) and 5 N HCl (2 × 150 ml), the organic layer was separated, and dried over $MgSO_4$. The solvent was removed in a vacuum to leave 2.08 g (69%) of compound **III** as a thick yellow oil which crystallized after 7 days.

2,8,14,20-Tetraoctyl-4,6,10,12,16,18,22,24-octa[3-(dimethoxyphosphoryl)-2-oxopropyl]calix[4]resorcinolarene (IV). A solution of *n*-butyllithium (24 ml or 38.4 mmol of a 1.6 M solution in hexane) was added with vigorous stirring under argon at –78°C over the course of 1 h to a solution of 3.6 g of dimethyl methylphosphonate in 250 ml of THF. After 1-h stirring, a solution of 4 g of calix[4]resorcinolarene **II** in 50 ml of THF was added in one portion, and the mixture was stirred for 50 h at room temperature. The solvent was removed in a vacuum, the residue was treated with ethyl acetate (2 × 100 ml) and 5 N HCl (2 × 150 ml), the organic layer was separated and dried over $MgSO_4$. The solvent was removed in a vacuum to leave 4.68 g (79%) of compound **IV** as a thick yellow oil.

Extraction. Chemically pure grade $LaCl_3 \cdot 6H_2O$ and pure grade NaPic were used. The concentration of La(III) in the initial solution was determined by trilonometry with Thymol Blue and Xylenol Orange as indicators [9]. Extraction was performed by the following procedure. To 5 ml of aqueous $LaCl_3$ (4×10^{-4} M) and NaPic (3×10^{-2} M) (pH 5.5) we added 5 ml of a chloroform solution of compound **III** (4×10^{-4}–2×10^{-3} M). The two-phase system was stirred magnetically stirred in a closed flask for3 h. The concentration of $LaPic_3$ in the aqueous phase was determined by spectrophotometry with Xylenol Orange as indicator [7] at pH 6.0 in an acetic acid–acetate buffer. The pH values were measured on an I-130 pH-meter. The electronic absorption spectra were measured on a UV-Vis instrument.

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