A cyclopendant complexon based on dibenzo-18-crown-6

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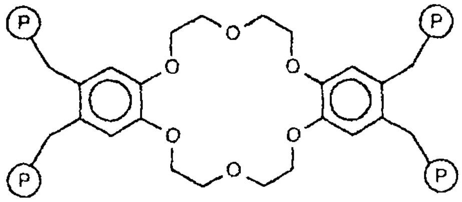
A derivative of dibenzo-18-crown-6 containing dihydroxyphosphorylmethyl groups in the 4, 5, 4′, and 5′ positions of the benzene ring has been synthesized. Unlike dibenzo-18-crown-6, its phosphorylated derivative does not form stable complexes with cations of alkali and alkaline-earth metals. Complexes with transition metals are water-insoluble in most cases.

Key words: crown polyethers, synthesis, complexation, acid-base properties, potentiometric titration.

Dibenzo-18-crown-6 is one of the most accessible and well-studied polyethers. Several complex-forming reagents containing additional (pendant) coordinating groups were obtained from it.[1,2] These compounds were studied as ligands[1] for alkali metals and Co^{2+} and as extractants[2] for alkali and alkaline-earth elements. Crown polyethers containing phosphonic groups are virtually unstudied. Only data on the synthesis of mono- and diphosphonic acids with the amino-substituted crown-polyether fragment[3] and on their complex-forming properties with respect to the Na^+ ion are available.

Previously, based on dibenzo-18-crown-6, we have synthesized[4] ligand **1** containing diphenylphosphinylmethyl groups as pendant ones.



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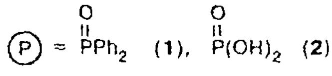
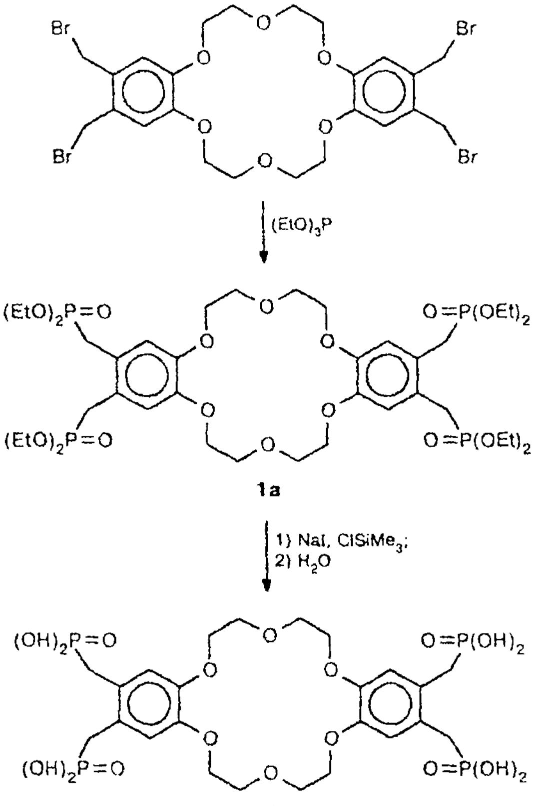


$$\text{Ⓟ} = \overset{O}{\overset{\|}{P}}Ph_2\ (\mathbf{1}),\quad \overset{O}{\overset{\|}{P}}(OH)_2\ (\mathbf{2})$$

The study of its complex-forming properties showed[5] that alkali metal cations are bound by O atoms to the dibenzo-18-crown-6 cycle, and the Co^{2+} ion is bound by O atoms of phosphoryl groups. Both types of donor atoms participate simultaneously in coordination with the cations studied.[5]

Scheme 1



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In this work, we studied the analog of compound **1** containing acidic dihydroxyphosphoryl groups instead of neutral diphenylphosphoryl groups: complexon **2**, which was synthesized according to the Scheme 1.

Interaction of tetrakis(bromomethyl)dibenzo-18-crown-6 with triethyl phosphite (the Arbuzov reaction) gave the corresponding tetraphosphonate, which was subsequently transformed into octakis(trimethyl-

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[†] Deceased.

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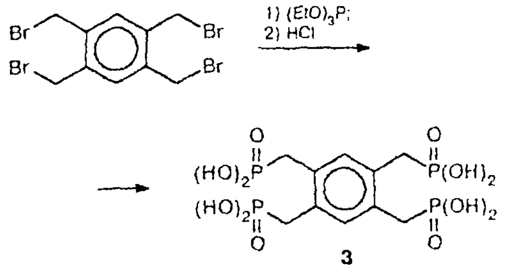
silyl)ether hydrolyzed by water without isolation to form acid **2**.

Complexon **2** is a high-melting colorless crystalline substance, which is very poorly soluble in water.

Acid-base and complex-forming properties of compound **2** were studied by pH-metric titration in water. For comparison, we studied acid **3** with the same number of phosphonic groups but without a cyclic fragment of crown polyether. It was also synthesized by the Arbuzov reaction of 1,2,4,5-tetrakis(bromomethyl)benzene with triethyl phosphite followed by hydrolysis of the intermediate phosphonate with concentrated HCl.



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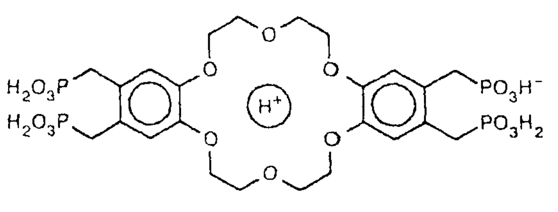
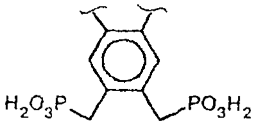
The pK_a values of acids **2** and **3** calculated by the known program[6] on a BESM-6 computer are presented in Table 1.

The neutralization curve of acid **3** exhibits two buffer regions: $0 < a < 4$ and $4 < a < 8$ (a is the number of moles of KOH per mole of the acid). It can be assumed that the first buffer region corresponds to dissociation of four protons of PO_3H_2 groups, and the second region reflects dissociation of four protons of PO_3H^- groups. The pK_7 and pK_8 values of acid **3** are low. Most likely, hydrogen bonds with the participation of protons of two adjacent phosphonic groups are not formed in this case, unlike the case of methylenediphosphonic acid (pK_4 = 10.42).[8] For acid **2**, the first buffer region corresponds to the dissociation of only three protons, which may indicate that the solution contains the following zwitterion:



The very high pK_7 and pK_8 values of acid **2** (the pH-metric titration method used in this work does not allow one to determine reliable values of pK_8) are most likely explained by the existence of intramolecular hydrogen bonds. Thus, the presence of the macrocyclic fragment of crown polyether in the molecule of complexon **2** results in a substantial change in the mechanism of its dissociation as compared to that of acid **3**.

Titration of acid **2** with a solution of Me_4NOH in the Me_4NCl medium in the presence of equimolar amounts of Li^+, Na^+, K^+, Mg^{2+}, Ca^{2+}, Sr^{2+}, and Ba^{2+} ions showed no noticeable complexation with these cations. Most likely, the effect of four methylphosphonic groups decreases substantially the nucleophilicity of O atoms of the macrocycle, and the fragment



is unable to form stable complexes with ions of alkali and alkaline-earth elements (see, *e.g.*, Refs. 9 and 10). Note that butylenediphosphonic acid with a bridge of C atoms between phosphonic groups, which has the same length as the fragment presented above, forms ML complexes with Mg^{2+}, Ca^{2+}, and Ba^{2+} ions, and the logarithms of their stability constants are equal to 2.77, 2.54, and 2.28, respectively.[11]

Based on the neutralization curves, we can assert that complexon **2** forms complexes with cations of bivalent transition metals and Fe^{3+}, La^{3+}, and other ions. However, stability constants of the majority of these complexes cannot be calculated because of their restricted solubility in water. Fe^{3+}, La^{3+}, Eu^{3+}, and Pb^{2+} ions give insoluble complexes; Cu^{2+}, Co^{2+}, Ni^{2+}, Mn^{2+}, Zn^{2+}, and Cd^{2+} ions form insoluble complexes after addition of 4 equiv. of KOH.

Complexes of acid **3** with Ca^{2+}, Sr^{2+}, Ba^{2+}, Co^{2+}, and Cu^{2+} cations possess higher solubility. The stability constants of these complexes are presented in Table 2.

The data obtained suggest that more than two phosphonic groups participate simultaneously in coordination on complexation of acid **3** with cations. However, this problem should be additionally studied.

Table 1. Dissociation (concentration) constants of acids **2** and **3** (25 °C, μ = 1.0 (KNO_3))

pK_i	Compound **2**	Compound **3**
pK_1	<1	<1
pK_2	<2	<2
pK_3	2.0	1.5
pK_4	6.38	2.96
pK_5	7.75	6.36
pK_6	9.07	7.07
pK_7	11.9	8.37
pK_8	12	9.03

Note. Errors in determination of the constants were found as described previously;[7] their values for acid **2**: ±0.02 for pK_4—pK_6 and ±0.15 for pK_3—pK_7; for acid **3**: ±0.02 for pK_4—pK_8 and ±0.15 for pK_3.

Table 2. Logarithms of stability constants of complexes of acid 3 (25 °C, μ = 0.1 (KCl))

Cat-ion	MH_4L	MH_3L	MH_2L	MHL	ML	M_2H_2L	M_2HL	M_2L
Ca^{2+}	—	—	—	[a]	[a]	—	3.97	4.42
Co^{2+}	—	—	4.05	5.23	5.95	4.45	6.74	8.38
Cu^{2+}	4.2	6.6	8.7	10.7	12.3	[b]	[b]	[b]

Note. Sr^{2+} and Ba^{2+} ions with complexon 3 form less stable complexes than the Ca^{2+} ion. Errors in determination of the constants were found as described previously;[7] for Ca^{2+} and Co^{2+}, they are equal to ±0.04; for Cu^{2+}, it is equal to ±0.13.

[a] The constants were not calculated due to their low values.

[b] Precipitate.

Experimental

Tetrakis(diethoxyphosphorylmethyl)dibenzo-18-crown (1a). A mixture of tetrakis(bromomethyl)dibenzo-18-crown-6 [12] (6.0 g) and triethyl phosphite (7.0 g) in xylene (40 mL) was heated at 150 °C for 30 min in an N_2 flow. Half of the solvent was evaporated, and the residue was cooled and diluted with ether. The precipitate was crystallized from benzene to obtain compound **1a** in 51% yield (4.0 g), m.p. 199—200 °C. Found (%): C, 50.1; H, 7.2; P, 12.9. $C_{40}H_{68}O_{18}P_4$. Calculated (%): C, 50.0; H, 7.1; P, 12.9.

Tetrakis(dihydroxyphosphorylmethyl)dibenzo-18-crown-6 (2). A modified procedure was used.[13] Me_3SiCl (7.2 g) was added to a stirred solution of compound **1a** (5.3 g) and NaI (9.95 g) in MeCN (45 mL) at 20 °C. After 15 min the mixture was heated to 40 °C, kept for 40 min, and cooled to 20 °C; water (50 mL) was added after 15 h. The mixture was stirred, and the precipitate that formed was separated, washed with ethanol, and crystallized from water. Compound **2** was obtained in 56.6% yield (2.3 g), decomp. temp. >310 °C. Found (%): C, 39.5; H, 4.9; P, 17.1. $C_{24}H_{36}O_{18}P_4$. Calculated (%): C, 39.1; H, 4.9; P, 16.8. Neutralization equivalent: found 741; calculated 736.4.

1,2,4,5-Tetrakis(dihydroxyphosphorylmethyl)benzene (3). A mixture of 1,2,4,5-tetrakis(bromomethyl)benzene[14] (2.5 g) and triethyl phosphite (6.0 g) was heated at 140—180 °C with weak boiling for 1 h. An excess of phosphite was distilled off, and the residue was refluxed for 6 h with conc. HCl (15 mL). The precipitate of **3** formed on cooling was crystallized from aqueous ethanol. The yield of compound **3** was 95% (2.4 g), decomp. temp. >350 °C. Found (%): C, 26.6; H, 4.1; P, 27.1. $C_{10}H_{18}O_{12}P_4$. Calculated (%): C, 26.5; H, 4.0; P, 27.3. Neutralization equivalent: found 460; calculated 454.1.

Potentiometric titration was performed according to the previously described procedure[7] on an OP-208 pH-meter (Hungary) with an accuracy of ±0.01 pH units at 25 °C. The concentration of acid and metal nitrate in the starting solutions was 0.005 mol L^{-1}; ionic strength μ = 1.0 (1.0 *M* KNO_3) at the half-neutralization point. The titration curves contained 40—60 experimental points and were repeated twice; pK_a was determined as the average of three independent titrations. The errors presented for the dissociation constants in Table 1 were determined as half-sums of deviations obtained by shifting the experimental titration curve by the value of possible error of the pH-meter (±0.01 pH units). Errors of determination of stability constants in Table 2 were found by the same way. Dissociation and stability constants of the complexes were calculated by the known program[6] on a BESM-6 computer.

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References

1. K. B. Yatsimirskii, E. I. Sinyavskaya, L. V. Tsymbal, I. Ya. Postovskii, V. A. Popova, and I. V. Podgornaya, *Zh. Neorg. Khim.*, 1983, **28**, 946 [*J. Inorg. Chem. (USSR)*, 1983, **28** (Engl. Transl.)].
2. N. L. Luk'yanenko, A. V. Bogatskii, V. N. Pastushok, E. Yu. Kulygina, L. R. Berdnikova, and M. U. Mamina, *Khim. Geterotsikl. Soedin.*, 1981, 599 [*Chem. Heterocycl. Compd.*, 1981 (Engl. Transl.)].
3. M. Tazari, K. Nita, and M. Takagi, *Chem. Lett.*, 1982, 571.
4. G. V. Bodrin, M. I. Kabachnik, N. E. Kochetkova, T. Ya. Medved', B. F. Myasoedov, Yu. M. Polikarpov, and M. K. Chmutova, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1984, 1841 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1984, **33**, 1682 (Engl. Transl.)].
5. K. B. Yatsimirskii, M. I. Kabachnik, E. I. Sinyavskaya, L. V. Tsymbal, T. Ya. Medved', G. V. Bodrin, and Yu. M. Polikarpov, *Zh. Neorg. Khim.*, 1985, **30**, 976 [*J. Inorg. Chem. (USSR)*, 1985, **30** (Engl. Transl.)].
6. N. I. Voronezheva, Yu. V. Rudyak, N. M. Dyatlova, and A. I. Grigor'ev, *Koord. Khim.*, 1980, 991 [*Sov. J. Coord. Chem.*, 1980 (Engl. Transl.)].
7. M. I. Kabachnik, T. Ya. Medved', Yu. M. Polikarpov, B. K. Shcherbakov, F. I. Bel'skii, E. I. Matrosov, and M. P. Pasechnik, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1984, 835 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1984, **33** (Engl. Transl.)].
8. R. R. Irani and K. Moedritzer, *J. Phys. Chem.*, 1962, **66**, 1349.
9. J.-P. Behr, J.-M. Lehn, and P. J. Nierling, *J. Chem. Soc., Chem. Commun.*, 1976, 621.
10. H. K. Frensdorff, *J. Am. Chem. Soc.*, 1971, **93**, 600.
11. G. Schwarzenbach, P. Ruckstuhl, and J. Zurc, *Helv. Chim. Acta*, 1951, **34**, 455.
12. A. Cygan, J. F. Biernat, and H. Chadzyńsky, *Pol. J. Chem.*, 1979, **53**, 929.
13. T. Morita, Y. Okamoto, and H. Sakurai, *Tetrahedron Lett.*, 1978, 2523.
14. J. T. Stapler and J. Bornstein, *J. Heterocycl. Chem.*, 1973, **10**, 983.

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