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DETERMINATION OF COORDINATION SITES IN POLYETHER PHOSPHORYL LIGANDS USING MODEL COMPOUNDS

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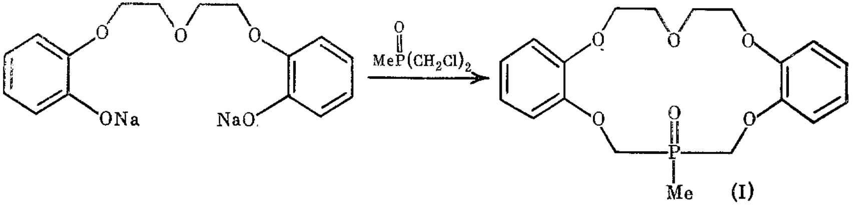
The macrocyclic polyethers are well known as complexing agents for cationic alkali and alkaline earth metals [1]. Efforts to improve their complexing abilities has led to the synthesis of macrocycles containing in addition to the ether oxygen atoms most nucleophilic donor sites, including phosphoryl groups. At the present time a large number of macrocycles are known that contain one or more phosphoryl groups [2, 3]. Their complexing ability has been studied [4], and in some cases the means by which the metal is coordinated with the macrocyclic ligands in the compounds has been determined [5, 6].

The aim of this work was to synthesize a new phosphoryl-containing macrocyclic compound and to determine by the use of model compounds the coordination sites in it and in some noncyclic phosphoryl-containing ligands in the interaction between 2,4-dinitrophenol and the alkali metals. The macrocyclic oxide of phosphine (I) is the analog of a macrocycle containing a phosphonate group [2] obtained by alkylation of the disodium derivative bis-(2-(o-oxyphenoxy)diethyl)ether by the oxide of methyldi(chloromethyl)phosphine (mechanism I). By reaction of the latter with the Na-salt of o-methoxyphenol, the acyclic analog (II) of ligand (I) was synthesized.

Scheme I



Models of a number of acyclic complexing agents previously obtained by us [7] were prepared by reacting the corresponding phenolates of alcoholates with tosyls, halide-containing compounds (cf. Reaction 2). For example, the dioxide (III) forms as a result of the reaction of the Na-salt of o-(2-diphenylphosphinylethyl)phenol with the bistosylate of diethylene glycol. The reaction of 1,5-dibromopentane with the Na-salt of o-diphenylphosphinylmethoxyphenol yields compound (IV). As a result of the reactions depicted in Fig. 2, the dioxide (VII) is obtained from the Li alcoholate (V) and its tosylate (VII). Compounds (VIII), (IX) (Table 1), segments of the macrocycle (I), were obtained by a previously described method [8, 9].

The stability constants of the synthesized compounds with cationic alkali metals were determined by an electrical conductivity method (cf. Table 1). The constancy of the values for the stability constants of the crown-ether complexes (I) for all of the alkali metals studied, except cesium, should be noted. The macrocycle (I) proved to be more effective than its acyclic analog (II). The smallest difference in the stability constants is observed for the reaction with Li^+, which is apparently related with the preferred coordination of the P=O group with some fractional participation in the case of the crown ether of the central ether oxygen atom. This explanation is consistent with PMR data obtained by us earlier [6].

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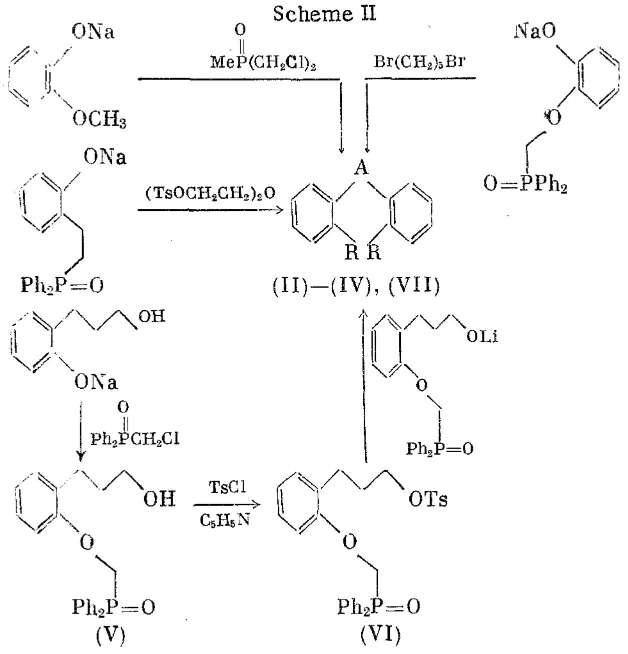
Scheme II



$$\mathrm{R{=}OCH_3,\ A{=}OCH_2\overset{Me}{\overset{|}{P}}(O)CH_2O\ (II);\ R{=}Ph_2\overset{O}{\overset{\|}{P}}CH_2CH_2,}$$

$$\mathrm{A{=}(OCH_2CH_2)_2O\ (III);\ R{=}Ph_2\overset{O}{\overset{\|}{P}}CH_2O,\ A{=}O(CH_2)_5O\ (IV);}$$

$$\mathrm{R{=}Ph_2\overset{O}{\overset{\|}{C}}H_2O,\ A{=}(CH_2CH_2CH_2)_2O\ (VII).}$$

With the transition to cations of larger radius, other donor sites on the ligand (I) become capable of participating in the coordination, as a result of which the stability of the compounds does not change, despite its common tendency to decrease. It should be noted that the complexation ability and selectivity of the phosphoryl-containing macrocycle are inferior to those of dibenzo-18-crown-6, as well as those of phosphoryl-containing podands [7].

In the acyclic ligands (III), (IV), and (VII), the ether oxygens are replaced alternately by methylene groups. Comparing the stability constants of complexes of these compounds with analogous data [10] for the previously studied podand (X) it can be seen that in the case of lithium the values are similar. This is evidence of the preferred participation of the oxygen of the phosphoryl groups in coordination with Li^+. The complex of ligand (III) with lithium is somewhat more stable, possibly owing to the greater basicity of the phosphoryl groups without neighboring pyrocatechol rings. The absence of either a central diethylene glycol oxygen or pyrocatechol oxygens leads to a decrease in the stability constants of complexes of these ligands with Na^+, K^+, and Cs^+ by 1 or 2 orders of magnitude. Apparently, in complex formation with cations having ionic radii greater than that of Li^+, the ether oxygens, in addition to the P=O groups, are involved in the coordination with the metal.

The mono-oxide (VIII) forms the most stable complexes with lithium; as the ionic radius of the cation increases, the interaction with the metal weakens. The stability of the complexes with ligand (II) is higher than with ligand (VIII) owing to the participation of complexing terminal CH_3O groups. Apparently, a pseudocyclic effect is involved here [9] that stabilizes the complex formed. Compound (IX), which does not contain a phosphoryl group, forms less stable complexes with lithium than ligands (II) and (VIII), from which it can be concluded that the more nucleophilic phosphoryl group oxygens are preferred in this complexation reaction. Podand (IX), which mimics the structure of dibenzo-18-crown-6 to a considerable degree, like the latter manifests a fairly high selectivity in this solvent for Na^+, but forms less stable complexes.

EXPERIMENTAL

The reactions were carried out under dry Ar. The PMR spectra of compounds (I)-(IV) were recorded on a Varian HA-100 spectrometer (standard HMDS, solvent $CHCl_3$); the PMR spectra of

TABLE 1. Logarithms of the Stability Constants of the Complexes $[ML]^+$ of Ions of Alkali Metals (M^+) with Compounds (I)-(IV), (VII)-(X) (L)

Compound	R	A	Li+	Na+	K+	Cs+
(I)	–	–	3,26	3.29	3,29	2,56
(II)	OCH_3	$OCH_2\overset{Me\quad O}{P}CH_2O$	2,65	2.25	1,88	1,78
(III)	$Ph_2\overset{O}{\overset{\|}{P}}CH_2CH_2$	$(OCH_2CH_2)_2O$	4,05	2,95	2,11	–
(IV)	$Ph_2\overset{O}{\overset{\|}{P}}CH_2O$	$O(CH_2)_5O$	3,46	2,60	2,11	1,30
(VII)	$Ph_2\overset{O}{\overset{\|}{P}}CH_2O$	$(CH_2CH_2CH_2)_2O$	3,18	2,28	1,51	≤1
(VIII)	H	$OCH_2\overset{Me\quad O}{P}CH_2O$	2,05	1,57	≤1	–
(IX)	OCH_3	$(OCH_2CH_2)_2O$	1,65	2.86	2,19	1,68
(X)	$Ph_2\overset{O}{\overset{\|}{P}}CH_2O$	$(OCH_2CH_2)_2O$	3,65	4,01	4,19	3,50
	Dibenzo-18-crown-6		4,06	5.60	4,66	3,27

compounds (V)-(VII) were recorded on a Bruker WM-250 spectrometer (HMDS standard, solvent $CDCl_3$), and the NMR spectra of $^{31}P-\{^1H\}$ on a Bruker HX-90 spectrometer (36.43 MHz) in the pulsed mode (standard, 85% H_3PO_4; the same solvent was used as for the PMR spectra). The down-field shifts were taken as positive. The melting points were measured using short-range Anschutz thermometers. The yields, constants, and analytical data for the compounds synthesized are summarized in Table 2.

1,2,8,9-Dibenzo-5-phospha-5-oxy-5-methyl-16-crown-6 (I). To a solution of MeONa, obtained from 0.5 g Na and 30 ml anhydrous MeOH, was added 3.0 g of bis-(o-(oxyphenoxy)di-ethyl) ether [11]. The mixture was boiled for 30 min and evaporated under vacuum. The residue was held for 1 h at a vacuum of 1 mm Hg at 90-100°C. To a suspension of the salt in 60 ml of anhydrous o-xylene, a solution of 1.7 g of methyldi(chloromethyl)phosphinic oxide [12] in 18 ml of a mixture of DMF-o-xylene (1:5) was added dropwise over the course of 1.5 h as the solution was boiled. The mixture was boiled for 13 h and evaporated under vacuum. The residue was treated with a 20% water—alcohol solution of NaOH and extracted with chloroform. The extract was washed with dil. HCl, a solution of $NaHCO_3$, and water, and dried with Na_2SO_4. The solvent was evaporated off under vacuum. After recrystallization of the residue the yield was 0.6 g (I). The molecular weight, as determined by mass spectrometry, was 378 (calculated, 378).

Methyldi(o-methoxyphenoxymethyl)phosphine Oxide (II). To a solution of MeONa, obtained from 0.6 g Na and 15 ml anhydrous MeOH, was added 3.1 g o-methyoxyphenol, and the solution evaporated under vacuum (cf. above). To a suspension of the salt in 25 ml anhydrous o-xylene, a solution of 2.0 g of methyldi(chloromethyl)phosphine oxide in 5 ml of anhydrous DMF was added dropwise at a temperature of 90-100°C. The mixture was boiled for 4.5 h and evaporated under vacuum. The residue was diluted in 40 ml chloroform and washed with water, 5% NaOH, and water. The extract was dried with Na_2SO_4, and the solvent driven off under vacuum. The residue was recrystallized; the yield of (II) was 3.5 g.

Diethylene Glycol bis(o-2-Diphenylphosphinylethylphenyl)ether (III). To a solution of MeONa obtained from 0.2 g Na and 100 ml anhydrous MeOH was added 5.0 g of o-(2-diphenylphosphinylethyl)phenol [13]; the mixture was boiled 30 min and evaporated under vacuum. To the residue was added 30 ml anhydrous o-xylene and 1.5 g diethylene glycol bistosylate [14] at 100°C. The mixture was boiled 5 h, and evaporated down under vacuum. The residue was diluted with chloroform, and the solution was washed with water, 5% NaOH, and water. The extract was dried with Na_2SO_4, and the solvent was driven off under vacuum. The residue was recrystallized; the yield of (III) was 2.2 g.

TABLE 2. Yields, Constants, and Analytical Data for the Compounds Synthesized

Compound	Yield, %*	mp, °C (solvent for recystallization)	Found, %			Empirical formula	Calculated, %			PMR spectra δ, ppm)						^{31}P NMR spectra, (δ, ppm)
			C	H	P		C	H	P	CH_3, d	J_{PH}, Hz or CH_2, m	C_2H_4, m or CH_2, m	CH_2, d	I_{PH}, or J_{PH}, Hz	aromatic protons	
(I)	15	172.5–173 (AcOEt – MeOH)	60.3	6.2	7.8	$C_{19}H_{23}O_6P$	60.3	6.1	8.2	1.83 (3H)	13	3.98 (8H)	4.39 d.d. 4.65 d.d.	13 8 13	6.88 m (8H)	41.15
(II)	84	92.5–93 (C_6H_6 – hexane	60,7	6,1	8,9	$C_{17}H_{21}O_5P$	60,7	6.3	9,2	1,75 (3H)	13	–	4.48 m (4H)	–	6.76–7,04 m (8H)	42.09
(III)	65	164–165 (*i*-PrOH)	73.9	6.1	8.6	$C_{44}H_{44}O_5P_2$	73,9	6.2	8,7	–	–	2.72 (8H) 3.91 (8H)	–	–	6.66–7,18 m (8H), 7.36–7,80 m (20H) †	35.99 †
(IV)	62	87.5–88.5 (AcOEt)	72.0	5,9	8.8	$C_{43}H_{42}O_6P_2$	72,1	5.9	8,6	1.74 (6H), 3.84 (4H)			4.72 (4H)	6	6.83 m(8H), 7.40 m(12H), 7.96 m (8H)	26.42
(V)	73	81.5–82 (C_6H_6 – hexane	72.2	6,2	8.5	$C_{22}H_{23}O_3P$	72.1	6,3	8.4	1.60 (2H), 2.54 t (2H,), 3.46 t (2H)			4.69 (2H)	7.5	6.89 m(2H), 7.11m (2H), 7.50 m (6H), 7.84 m (4H)	28.75
(VI)	63	Liquid	66.7	5.7	5.6	$C_{29}H_{29}O_5P$	66.9	5.6	5,9	1,58 (2H), 2.40 m (CH_2, CH_3, 5H), 3.79 t (2H)			4,72 (2H)	7	6.80–8.00 m (18H)	29.81
(VII)	49	Liquid	73.6	6,2	8,4	$C_{44}H_{44}O_5P_2$	73.9	6,2	8.7	1,57 (4H), 2.45 t (4H), 3.14 t (4H)			4.71 (4H)	8	6.90 m (4H), 7,07 m (2H), 7.16 m (2H), 7.48 m(12H), 7.86 m (8H)	28.93

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*The yield is given for the product obtained after recrystallization; the melting point of this product did not differ from that of the sample analyzed by more than 5°C.

†This spectrum was recorded in CD_3OD.

1,5-Bis-(o-diphenylphosphinylmethoxyphenoxy)pentane (IV). To a solution of MeONa obtained from 0.2 g Na and 15 ml anhydrous MeOH was added 3.0 g of o-diphenylphosphinylmethoxyphenol [7]; the mixture was evaporated under vacuum (cf. synthesis of (I)). To the pulverized phenolate was added 20 ml anhydrous toluene and 1.1 g 1.5-dibromopentane at 100°C. The mixture was boiled 8 h and evaporated under vacuum. The residue was dissolved in 40 ml chloroform, and the solution was washed with water, 5% NaOH, and water. The extract was dried with Na_2SO_4, and the solvent was driven off under vacuum. Chromatography was performed on the residue (3.8 g) on a column packed with silica gel L (eluant:ethyl acetate). After evaporation of the eluate and recrystallization of the residue, 2.1 g of (IV) was obtained.

3-(o-Diphenylphosphinylmethoxyphenyl)propanol (V). To a solution of MeONa obtained from 0.5 g Na and 10 ml anhydrous MeOH, a solution of 3.3 g 3-(o-oxyphenyl)propanol [15] in 10 ml anhydrous MeOH was added dropwise. The mixture was boiled 30 min and evaporated under vacuum (cf. synthesis of (I)). To the residue was added 30 ml anhydrous o-xylene and 4.5 g diphenylchloromethylphosphine oxide [16]. The mixture was boiled 9 h and evaporated under vacuum. The residue was dissolved in chloroform, and the solution was washed with water, 5% NaOH, and water. The extract was dried with Na_2SO_4, and the solvent was driven off under vacuum. The residue was recrystallized; the yield of (V) was 4.8 g.

3-(o-Diphenylphosphinylmethoxyphenyl)propyltosylate (VI). To a solution of 2.6 g TsCl in 5 ml anhydrous Py, a solution of 5.0 g (V) in 8 ml anhydrous Py was added dropwise at 0-5°C over the course of 2 h. The mixture was held at 0°C for 1 h and at 20°C for 3 h, and poured into a mixture of crushed ice (20 g) and HCl (6 ml). The oil that separated out was extracted with benzene. The extract was washed with dilute HCl, Na_2CO_3 solution, and water, and then dried with Na_2SO_4. The solvent was driven off under vacuum. The residue (5.5 g) was separated by chromatography on a column with silica gel L (eluant: ethyl acetate). After evaporation of the eluate, 4.2 g of (VI) was obtained.

Bis(3-o-diphenylphosphinylmethoxyphenylpropyl)ether (VII). To a solution of 2.6 g (V) in 25 ml anhydrous benzene, 7.8 ml of a 1 N solution of BuLi in benzene was added; to the mixture was added a solution of 3.5 g (VI) in 10 ml anhydrous benzene. The mixture was boiled for 14 h and evaporated under vacuum. To the residue was added chloroform; the solution was washed with water, 5% NaOH, and water. The extract was dried with Na_2SO_4 and evaporated under vacuum. The residue (3.7 g) was dissolved in 8 ml anhydrous benzene, and 3 ml phenyl isocyanate was added.* The solution was boiled for 10 h, and half of the solvent driven off under vacuum. The residue was separated on a chromatographic column of silica gel L. The contaminants were eluted with ethyl acetate, and the main product (the third fraction) with a mixture of ethyl acetate and MeOH (9:1). After evaporation of the solution, 2.4 g of (VII) was obtained.

Measurements. The electrical conductivity of the solutions was measured using an R-5010 a.c. bridge in a thermostatted (25 ± 0.1°C) cell with platinized platinum electrodes. The cell constant was 0.20. The solvent used was a mixture of THF and $CHCl_3$ (4:1), and the salts were the 2,4-dinitrophenolates of the alkali metals. The method used to determine the stability constants of the complexes [17] was to measure the electrical conductivity of the solutions at a constant concentration of the salt of the metal with varying concentrations of the ligand. The error in the determination of the resistance was ±3%. All operations involved in measuring the electrical conductivity were carried out in air.

CONCLUSIONS

1. The oxide of the macrocyclic phosphine and its acyclic analog have been synthesized, as well as complexing agents of the monopodand type.

2. By using model compounds it has been shown that when the phosphoryl-containing macrocycle complexes with the lithium ion, the phosphoryl group oxygen and, apparently, the central ethereal oxygen, participate in the coordination. For ions of greater radius, the ether oxygens only are involved.

3. In the phosphoryl-containing podands, coordination with the lithium ion via the phosphoryl groups is preferred. In complex formation with ions of larger radii, the ether oxygens participate in the coordination.

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*The phenyl isocyanate was needed to bind the unreacted starting alcohol, the content of which was ~20% according to PMR data.

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