Phosphorus-containing podands

11. Synthesis of bis(*ortho*-diphenylphosphinyl)benzyl ethers of oligoethylene glycols and their complexing properties with respect to alkali metal cations

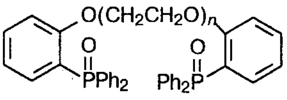
*A. N. Bovin, V. I. Evreinov, Z. V. Safronova, and E. N. Tsvetkov**

Institute of Physiologically Active Compounds, Russian Academy of Sciences,
142432 Chernogolovka, Moscow Region, Russian Federation

A number of monopodands having *o*-diphenylphosphinyl terminal groups were synthesized by alkylating sodium derivatives of oligoethylene glycols with *o*-(bromomethyl)phenyldiphenylphosphine. The stability constants of the complexes of these ligands with alkali metal cations at 25 °C were determined conductometrically in a THF—chloroform solution (4:1, v/v). The complexing ability of monopodands with respect to the cations studied increases monotonically as the number of electron-donating sites increases (from 3 to 8) for all of the cations except Li^+ and, to some extent, Na^+. In the case of Li^+ a smooth decrease in the stability of the complexes is observed. The monopodands obtained in this work differ drastically in this regard from their structural isomers, bis[*o*-(diphenylphosphinylmethyl)phenyl] ethers of oligoethylene glycols, which had been studied previously.

Key words: monopodand; phosphine oxide; conductometry; alkali metal cations; stability constants of complexes.

Among the phosphoryl-containing monopodands thus far studied the most efficient complexing agents towards alkali metal cations are ligands **1** and **2** which contain conformationally rigid phosphine oxide type terminal groups, namely *o*-(diphenylphosphinyl)phenyl[2] and *o*-(diphenylphosphinylmethyl)phenyl[3] groupings.



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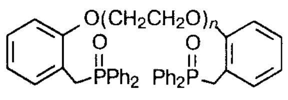


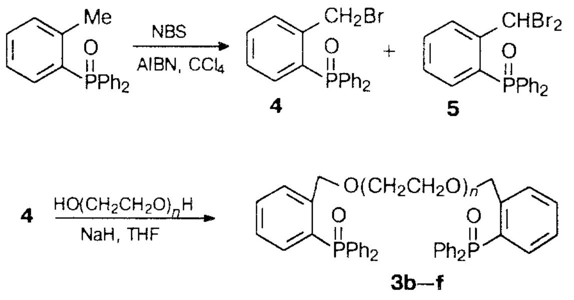
2

n = 0 (**a**), 1 (**b**), 2 (**c**), 3 (**d**), 4(**e**), 5 (**f**)

Although the stability of the complexes formed by podands **2** is somewhat lower than that of **1**, the former ligands are more ion-selective (mainly with respect to Li^+ and Na^+ cations).

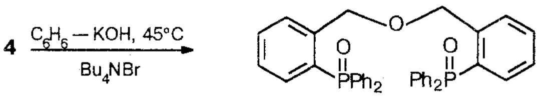
The purpose of this work was to synthesize the structural isomers of the podands **2**, namely, the bis[*o*-(diphenylphosphinyl)benzyl] ethers of oligoethylene glycols **3a—f** (Scheme 1) and to study their complexing properties in respect to alkali metal cations. Compounds **3b—f** were synthesized in 50—70 % yields by alkylating sodium derivatives of the corresponding oligoethylene glycols with *o*-(bromomethyl)phenyldiphenylphosphine oxide (**4**) in THF. Compound **4** was in its turn prepared in 71 % yield by the reaction of diphenyl(*o*-tolyl)phosphine oxide with N-bromosuccinimide. This reaction afforded also 7 % of *o*-(dibromomethyl)phenyldiphenylphosphine oxide (**5**) as a side product.

Scheme 1



n = 1 (**b**), 2 (**c**), 3 (**d**), 4(**e**), 5 (**f**)

The simplest ligand, **3a** (n = 0), was obtained by the alkaline hydrolysis (60 % KOH solution) of bromide **4** under the conditions of phase transfer catalysis.



3a

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* For part 10, see ref. 1.

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Scheme 2

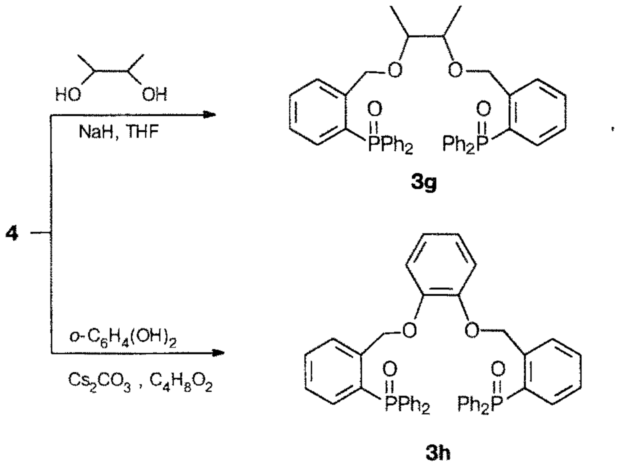

Table 1. Logarithms of stability constants (log*k*) of alkali metal cations M^+L with monopodands **3a—h** in a THF—$CHCl_3$ solvent mixture (4:1, v/v) at 25 °C

Ligand	*n*	Li^+	Na^+	K^+	Rb^+	Cs^+
3a	0	5.5	4.1	3.2	2.9	2.7
3b	1	5.2	4.5	3.2	2.9	2.4
3c	2	5.3	5.0	3.9	3.4	2.8
3d	3	5.2	5.2	4.4	4.2	3.7
3e	4	4.9	5.5	4.8	4.5	3.9
3f	5	4.6	5.4	5.3	5.0	4.3
3g	1	4.9	4.2	3.1	2.7	2.3
3h	1	4.3	3.4	2.4	2.2	1.9

In order to examine the effect of the structure of the polyether chain in podand **3b** on its complexing ability we synthesized the isodentate analogs of **3b**, compounds **3g** and **3h**, by alkylating (±)-2,3-butanediol or pyrocatechol with the benzylic bromide **4** (Scheme 2).

The complexing ability of monopodands **3a—h** with respect to alkali metal cations was estimated on the basis of the logarithms of the stability constants (log*k*) of the complexes M^+L. These values were determined conductometrically in a THF—$CHCl_3$ solvent mixture (4:1, v/v) at 25 °C. We compared the complexing properties and selectivity of monopodands **3** with those of their structural isomers **2b—f** described previously.[3]

The resulting logarithms of the stability constants (log*k*) for the M^+L complexes of compounds **3a—h** with alkali metal cations are given in Table 1. Fig. 1,*a* shows the dependence of log*k* on the number (*n*) of CH_2CH_2O fragments in the polyether chain of a ligand (**3a—f**) and on the total number (*m*) of electron-donating sites in its molecule. For comparison in Fig. 1,*b* we present the similar dependence found previously for the structural isomers **2b—f**.

Fig. 1,*a* indicates that an increase of *m* in a molecule of ligand **3** brings about an increase in its complexing ability in relation to all of the alkali metal cations except Li^+ and, to some extent, Na^+. The stability of a complex of a monopodand **3** with K^+, Rb^+, or Cs^+ is always higher than that of the complex derived from the corresponding **2**, which is probably due to the higher basicity of the «benzyl» ether oxygen atoms in compounds **3a—f** in comparison with the «phenyl» ether oxygen atoms in isomers **2**. On the other hand, in the case of Li^+, the stability of the complexes decreases monotonically as the number of electron-donating sites in the ligand increases, and the highest log*k* value (5.5) is observed for the shortest ligand, **3a**. Notice that for the series **2b—f** as well as for podands **1** the curves of log*k* *vs* *n* for the Li^+ and Na^+ cations display sharp maxima, whereas in the case of ligands **3** there are no such extrema on the curves.[2,3] The results obtained imply that while the insertion of a CH_2 group between the P=O group and the phenyl ring lowers the stability of the Li^+ complex only slightly while the selectivity of the monopodands with respect to Li^+ is retained or even increased (compounds **2b—f**), the incorporation of the same group between the phenyl ring and the phenoxyl oxygen atom (compounds **3a—f**) completely levels the selectivity relative to both Li^+ and Na^+. Apparently, in order for a monopodand to form a stable complex with lithium it must have a triethylene glycol diphenyl ether moiety with substituents with effective donating sites in the *ortho*-positions of both benzene rings.

Isodentate analogs of monopodands **3b**, compounds **3g,h**, are characterized by distinct basicity of the oxygen atoms in the polyether chain which is higher for ligand **3g** and lower in the case of **3h**. Nevertheless, both ligands form less stable complexes with all of the alkali metal cations. In the former case the observed slight lowering of the stability of the complex is apparently due to shielding of the ether O atoms by methyl groups which is not counterbalanced by the increase in the electron-donating properties of these O atoms caused by the inductive effect of the alkyl substituents. The introduction of a methyl group into an ethylene glycol moiety of crown ethers does not usually result in an increase in the stability of their complexes with metal cations.[6,7] However, in some cases it increases the selectivity of these ligands towards cations of small radii.[7] In our case the selectivity of monopodand **3g** differs little from that of compound **3b**.

In the case of ligand **3h** the stability of the complexes is considerably lower than in the case of **3g**. The replacement of the ethylene glycol moiety in **3b** by the pyrocatechol fragment (**3h**) does not cause any change in the selectivity of the ligand.

Thus, the absence of pronounced extrema on the curves of the log*k* dependence on the length of the polyether chain of the ligand with *n* ranging from 0 to 5 can be regarded as the key feature of the complexing properties of monopodands **3a—f**. In this respect compounds **3a—f** are similar only to monopodands of the general formula

$$Ph_2P(O)CH_2CH_2O(CH_2CH_2O)_nCH_2CH_2P(O)Ph_2$$

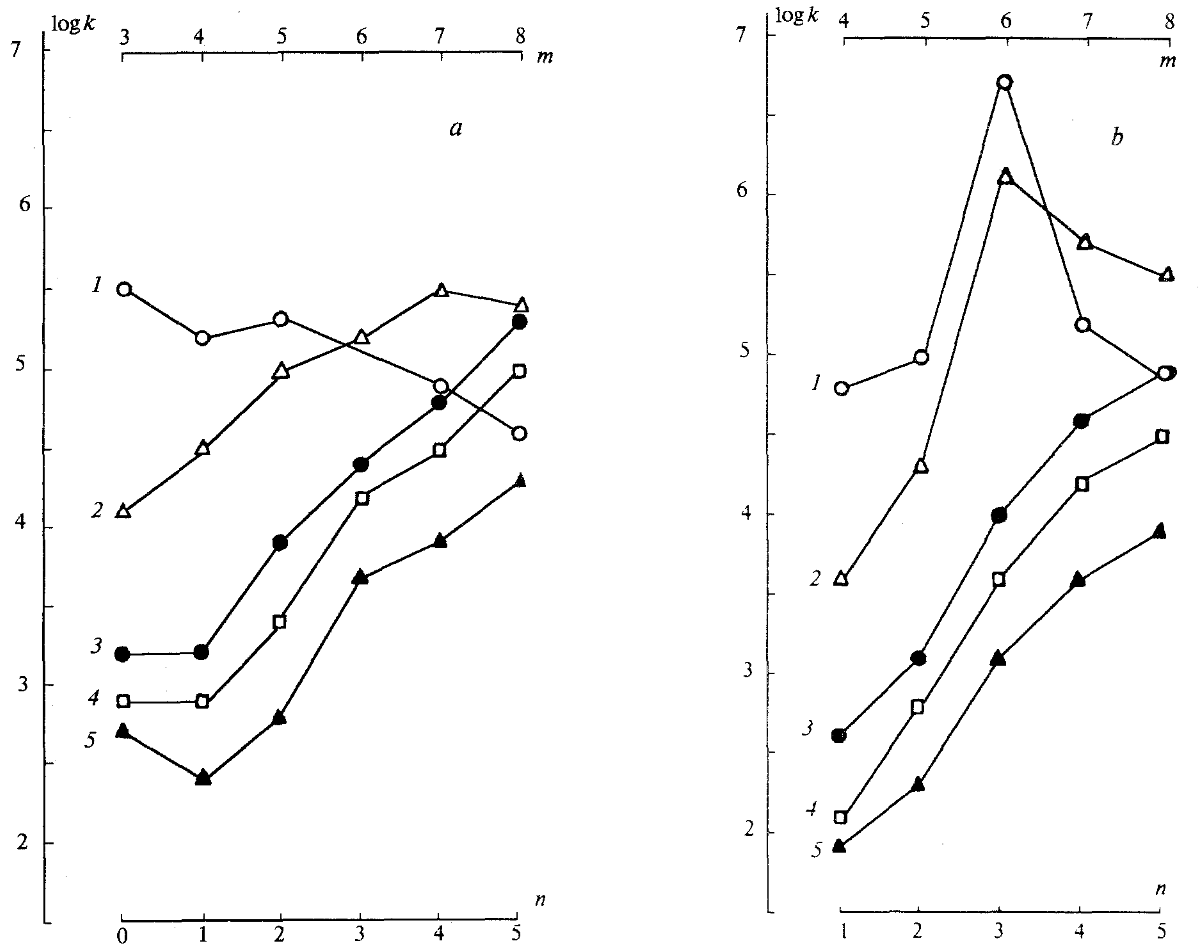

Fig. 1. The dependence of the logarithms of the stability constants (*k*) of complexes of alkali metal cations with bis[*o*-(diphenylphosphinyl)benzyl] (**3**) (*a*) and bis[*o*-(diphenylphosphinylmethyl)phenyl][3] (**2**) (*b*) on the length of the polyether chain (*n*) and on the number of electron-donating sites in the ligand (*m*): Li^+ (*1*); Na^+ (*2*); K^+ (*3*); Rb^+ (*4*); Cs^+ (*5*).

previously studied by us[8] which have a conformationally mobile terminal group, except that ligands **3a—f** possess lower complexing ability with respect to Li^+ and Na^+ cations.

Experimental

^1H and ^{31}P NMR spectra were recorded on a Bruker CKhR-200 spectrometer in $CDCl_3$ as a solvent unless specified otherwise and referred to internal TMS and external 85 % H_3PO_4 standards. Melting points were determined on a Boetius RNMK 05 instrument. Column chromatography was carried out using silica gel L (100—250 μ), TLC was performed on Silufol plates employing ethyl acetate as the eluent. All of the reactions were carried out under dry Ar. Yields, physical properties, averaged data of elemental analysis, and the data of the NMR spectra for compounds **3a—h** are given in Table 2.

***o*-(Bromomethyl)phenyldiphenylphosphine oxide (4) and *o*-(dibromomethyl)phenyldiphenylphosphine oxide (5).** A mixture of 40.0 (220 mmol) of N-bromosuccinimide and 1.5 g of aza-bis-isobutyric acid dinitrile was added portionwise every 30 min to a stirred and refluxed solution of diphenyl(*o*-tolyl)phosphine oxide (50.5 g, 170 mmol) in 400 mL of CCl_4; the course of the reaction was followed by TLC. After 4 h the reaction mixture was cooled, the precipitate was separated, and the mother liquor was concentrated *in vacuo*. Column chromatography of the residue (benzene as the eluent) afforded 5.0 g of dibromide **5**, yield 7 %, m.p. 147—149 °C, R_f 0.75. ^1H NMR, δ: 7.00—7.30 (m, 2 H); 7.50 (m, 10 H); 7.70 (m, 1 H); 7.95 (s, 1 H, $CHBr_2$); 8.15 (m, 1 H). ^{31}P NMR, δ: 32.52. Found (%): C, 50.2; H, 3.6; Br, 34.9; P, 7.1. $C_{19}H_{15}Br_2OP$. Calculated (%): C, 50.7; H, 3.4; Br, 35.5; P, 6.9.

Further elution (benzene—acetone, 10:1) gave 45.0 g of bromide **4**. Yield 71 %, m.p. 114—116 °C (*cf.* ref. 4), R_f 0.57. ^1H NMR (C_6D_6), δ: 5.18 (s, 2 H, CH_2); 6.80—7.20 (m, 10 H); 7.45—7.85 (m, 4 H). ^{31}P NMR (C_6D_6), δ: 29.81.

1,3-Bis(*o*-diphenylphosphinylphenyl)-2-oxapropane (3a). A mixture of bromide **4** (3.7 g, 10 mmol) and tetrabutylammonium bromide (0.5 g) in 40 mL of benzene and 30 mL of 60 % KOH was vigorously stirred for 4 h at 40—50 °C; the course of the reaction was followed by TLC. The reaction mixture was cooled to 20 °C, and the precipitate was separated and washed with water. The benzene solution was washed with water, dried

Table 2. Characteristics of podands **3a—h**

Com-pound	Yield (%)	M.p./°C (recrystallization solvent)	Found/Calculated (%)			Molecular formula	^{1}H NMR, δ			^{31}P NMR, δ
			C	H	P		ArCH$_2$O (s, 4 H)	(CH$_2$CH$_2$O)$_n$ (m, 4 H)	H arom. (m)	
3a	66	193—194(dioxane—methyl ethyl ketone)	76.2 76.2	5.5 5.4	10.5 10.4	$C_{38}H_{32}O_3P_2$	4.65	—	6.96 (2 H); 7.15 (6 H); 7.40—7.70 (20 H)	31.98
3b	80	155—158 (methyl ethyl ketone)	74.4 74.7	5.9 5.7	9.7 9.6	$C_{40}H_{36}O_4P_2$	4.80	3.25(s)	7.04 (2 H); 7.22 (2 H); 7.40—7.68 (22 H); 7.77 (2 H)	32.10
3s	50	102—104 (ether—toluene)	73.1 73.5	6.0 5.9	8.8 9.0	$C_{42}H_{40}O_5P_2$	5.19	3.24; 3.38	6.84 (t, 2 H); 7.05 (12 H); 7.20 (4 H); 7.70 (dd, 8 H); 7.89 (dd., 2 H)	29.57[a]
3d	70	Viscous oil	71.9 72.3	6.0 6.1	8.3 8.5	$C_{44}H_{44}O_6P_2$	5.19	3.30; 3.40 (8 H)	6.85 (t, 2 H); 7.05 (12 H); 7.18 (2 H); 7.25 (t, 2 H); 7.71 (dd, 8 H); 7.92 (dd, 2 H)	29.57[a]
3e	61	The same	70.9 71.3	6.4 6.2	8.0 8.0	$C_{46}H_{48}O_7P_2$	5.17	3.31; 3.42 (12 H)	6.90 (t, 2 H); 7.03—7.20 (14 H); 7.27 (t, 2 H) 7.71 (dd, 8 H); 7.9 (dd, 2 H)	29.57[a]
3f	68	The same	69.9 70.4	6.7 6.4	7.3 7.6	$C_{48}H_{52}O_8P_2$	5.18	3.32; 3.42 (12 H); 3.50 (s, 4 H)	6.88 (2 H); 7.10 (12 H);7.18 (2 H); 7.27 (t, 2 H); 7.69 (dd, 8 H); 7.88 (2 H)	29.40[a]
3g	65	The same	74.9 75.2	6.1 6.0	8.8 9.2	$C_{42}H_{40}O_4P_2$	4.70[b] (d, 2 H) 4.86[b] (d, 2 H)	3.26 (2 H, CHMe); 0.82 (d, 6 H, Me)[c]	7.03 (2 H); 7.21 (2 H); 7.40—7.80 (24 H)	31.98
3h	79	180—183 (methyl ethyl ketone)	76.6 76.5	5.2 5.3	9.1 9.0	$C_{44}H_{36}O_4P_2$	5.48	—	6.49 (2 H); 6.62 (2 H, *o*-$C_6H_4O_2$); 7.10 (2 H); 7.23 (t, 2 H); 7.48 (14 H); 7.66 (dd, 8 H); 7.88 (dd, 2 H)	31.80

[a] In C_6D_6. [b] $^2J_{HH}$ = 13.5 Hz. [c] $^3J_{HH}$ = 6 Hz.

with Na_2SO_4, and evaporated *in vacuo*. The residue was triturated with methyl ethyl ketone, and the resulting precipitate was separated. Combined precipitates were recrystallized to yield 2.0 g of monopodand **3a**.

1,6-Bis(*o*-diphenylphosphinylphenyl)-2,5-dioxahexane (3b); 1,9-bis(*o*-diphenylphosphinylphenyl)-2,5,8-trioxanonane (3c); 1,12-bis(*o*-diphenylphosphinylphenyl)-2,5,8,11-tetraoxadodecane (3d); 1,15-bis(*o*-diphenylphosphinylphenyl)-2,5,8,11,14-pentaoxapentadecane (3e); 1,18-bis(*o*-diphenylphosphinylphenyl)-2,5,8,11,14,17-hexaoxanonadecane (3f); 1,6-bis(*o*-diphenylphosphinylphenyl)-3,4-dimethyl-2,5-dioxahexane (3g). A mixture of NaH (0.6 g, 14 mmol) and the corresponding diol (6 mmol) in 30 mL of anhydrous THF was stirred for 10 min at 20—40 °C. Bromide **4** (5.6 g, 15 mmol) was added to the mixture, which was then stirred for additional 3 h; the course of the reaction was followed by TLC. The precipitate was separated and the filtrate was evaporated *in vacuo*. Recrystallization of the residue afforded **3b**. Monopodands **3c—g** were purified by column chromatography (benzene—*i*-PrOH mixture as the eluent).

1,2-Bis(*o*-diphenylphosphinylphenylmetoxy)benzene (3h). A mixture of bromide **4** (4.4 g, 12 mmol), pyrocatechol (0.6 g, 6 mmol), and Cs_2CO_3 (6.5 g, 20 mmol) in 20 mL of anhydrous dioxane was refluxed for 1 h. The mixture was cooled, the precipitate was separated, and the solvent was evaporated *in vacuo*. The residue was dissolved in 20 mL of benzene, washed twice with 20 mL of water, dried with Na_2SO_4, and evaporated *in vacuo*. Recrystallization of the residue from methyl ethyl ketone gave 3.0 g of monopodand **3h**.

Conductometric measurements were carried out in a THF—$CHCl_3$ solution (4:1, v/v) according to a procedure described previously.[5] Alkali metal 2,4-dinitrophenoxides were used in the measurements. Random error (±2*s*, where *s* is the standard deviation) in determining log*k* of the complexes of ligands **3** with alkali metal cations was less than ±0.1 log. units. The contents of ionogenic impurities in the ligands were checked by conductometry.

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