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Structure–alkali metal cation complexation relationships for macrocyclic PNP-lariat ether ligands†

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Water-insoluble, mono- and diarmed PNP-lariat ethers containing various aryloxy and regioisomerically-positioned binaphthylylenedioxy substituents linked to the phosphorus atoms of the cyclophosphazene ring *via* oxygen atoms are synthesized by regioselective, sodium ion-assisted arylolysis of tetrachloro-16-PNP-6 crown ether **1**. Heterogeneously-substituted, mixed aryloxy-amino PNP-lariat ethers and bis-lariat ethers with two different substituents linked to the PNP-macrocycle *via* an oxygen and a nitrogen atom are prepared by stepwise arylolysis and aminolysis reactions of **1**. The alkali-metal cation complexation behavior of the PNP-lariat ethers is evaluated in solvent polymeric membrane electrodes. The PNP-lariat and bis-lariat ethers exhibit pronounced selectivity for large alkali metal cations (Rb^+ and Cs^+) over small ones (Li^+ and Na^+). The selectivity is influenced by the configuration of the crown ether ring and the number of oxygen donor atoms in the ligand. For some PNP-lariat ethers, evidence for formation of 2 : 1 (ligand–metal ion) complexes with Rb^+ and Cs^+ is provided by ESI-MS.

Introduction

Lariat ethers are crown ethers with sidearms that contain electron-donating substituents. The donor atoms in these sidearms may cooperate with those in the macrocyclic skeleton to provide three-dimensional coordination of a ring-bound cation.[1,2] The complexation behavior of lariat ethers resembles natural ionophores that transport metal ions through cell membranes.

The mechanism of metal ion binding by lariat ethers and their metal ion selectivity has been investigated in many laboratories. Of particular interest has been the type and number of sidearms and the donor atoms contained therein, as well as the type of atom to which the sidearm is joined to the ring (the so-called pivot atom).[2–9] To date, structure–property relationships have been explored for C-pivot and N-pivot lariat ethers. Recently, PNP-crown compounds with oxy[10–13] and with amino[14–16] substituents linked to the macrocyclic phosphorus atoms of cyclophosphazene rings (*i.e.*, P-pivot PNP-lariat ethers) have been reported. However, information about their complexation behavior is limited primarily to simple TLC screening of metal ion binding abilities.[11,15,17,18] Only for a single representative of this type of lariat ether, a tetrapyrrolidinyl-PNP-crown derivative, have potentiometric and crystallographic results for metal ion binding been reported.[19,20]

A versatile precursor for this type of P-pivot lariat ether is tetrachloro-PNP-crown **1**,[21,22] a functional crown ether with a chlorocyclophosphazene subunit built into the macrocyclic polyether skeleton and four reactive chlorines linked to phosphorous atoms. Incorporation of the PNP-fragment of the N_3P_3 ring into the crown ether structure introduces some degree of preorganization. The nitrogen in the macrocycle ring is only weakly electron-donating due to resonance interactions within the N_3P_3 ring. However, the electron donicity of the nitrogen donor of this P–N=P unit in **1** can be significantly increased by introduction of electron-donating substituents at the phosphorus atoms. Numerous non-crown cyclophosphazene derivatives are known to display complexation ability, particularly towards transition metal ions, when strongly electron-donating substituents are linked to phosphorus atoms, enhancing the basicity of the nitrogen atom.[23–25] Recently we reported direct participation of the nitrogen atom of the PNP-crown unit in complexation of Ag^+ by a tetrapyrrolidinyl derivative of **1**, but not for Na^+ or K^+.[15,16]

Our earlier studies of the supramolecularly-assisted substitution reactions of reactive tetrachloro-PNP-crown precursor **1** have shown that it can be readily converted into aryloxy-[10–13] and amino-derivatives.[14–16] In this work, we have synthesized several additional PNP-lariat ethers with one or four aryloxy substituents, as well as new heterogeneously substituted PNP-lariat and bis-lariat ethers with both aryloxy and amino substituents proximate to the macrocyclic polyether unit. To probe the influence of ligand structure upon alkali metal cation complexation, we have investigated the responses of PNP-lariat ethers in solvent polymeric membrane electrodes. ESI-MS was utilized to determine the stoichiometries of some PNP-lariat ether–alkali metal cation complexes.

Results and discussion

Synthesis of PNP-lariat ethers

The macrocyclic rings of the PNP-lariat ethers contain –P–N̲= P– subunits derived from the triphosphazene ring system,

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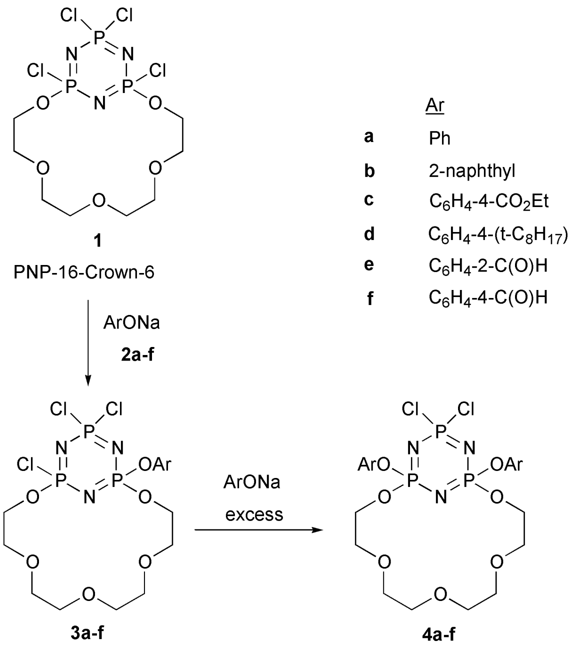
† Electronic supplementary information (ESI) available: diagnostic ^{31}P NMR and ^1H NMR spectral data and combustion analyses for new PNP-lariat and bis-lariat ethers. See http://www.rsc.org/suppdata/p2/b1/b110415b/

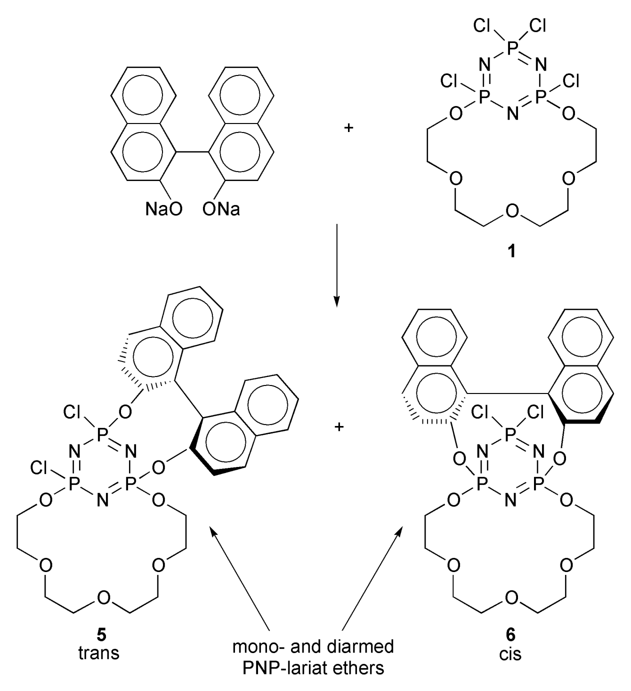
which allows the attachment of oxygen or nitrogen nucleophiles to the crown-bearing phosphorus atoms. In the current study, the substituents are aryloxy groups or a combination of aryloxy and amino groups. Previously, we have shown that both aryloxy and amino substituents can be introduced regioselectively into the PNP-crown structure by supramolecularly-assisted nucleophilic substitution reactions of the precursor tetrachloro-PNP-crown **1** with sodium aryloxide[10–13] or amine[14–16] nucleophiles, respectively.



Scheme 1 Synthesis of monoaryloxy-substituted PNP-lariat ethers **3a**–**f** and tetrakis(aryloxy)-substituted PNP-lariat ethers **4a**–**f.**

We have reported the synthesis of monoaryloxy-substituted PNP-lariat ethers **3a** and **3b** by reactions of one equivalent of phenoxide and 2-naphthoxide, respectively, with **1** (Scheme 1).[12] Also, tetraaryl-subsituted PNP lariat ethers **4a** and **4b** were prepared by reactions of six equivalents of the corresponding aryloxide with **1** (Scheme 1).[22] For investigation of steric and inductive effects of substituents on metal ion complexation by the PNP-lariat ethers, analogs **3c**–**f** and **4c**–**f** have now been synthesized similarly by reactions of **1** with the aryloxides derived from ethyl 4-hydroxybenzoate, 4-*tert*-octylphenol, 2-hydroxybenzaldehyde and 4-hydroxybenzaldehyde, respectively. Diagnostic ^{31}P NMR spectral data[16,26] for **3c**–**f** and **4c**–**f** that verify the substitution pattern and stereochemistry, as well as combustion analysis and ^{1}H NMR spectral data for these new PNP-lariat ethers are given in the supplementary information.†

It should be noted that attempts to prepare bis(aryloxy)-substituted analogs of **3a** and **3b** by reactions of **1** with two equivalents of phenoxide and 2-naphthoxide, respectively, gave complicated mixtures of products from substitution at the crown-bearing and non-crown phosphazenic phosphorus atoms.[12] However, the two aryloxy substituents remote from the crown units in **4a**–**f** should have only minor influence on a metal ion complexed by the polyether portion of the ligand. Therefore, compounds **4a**–**f** may be considered as "diarmed" PNP-lariat ethers.



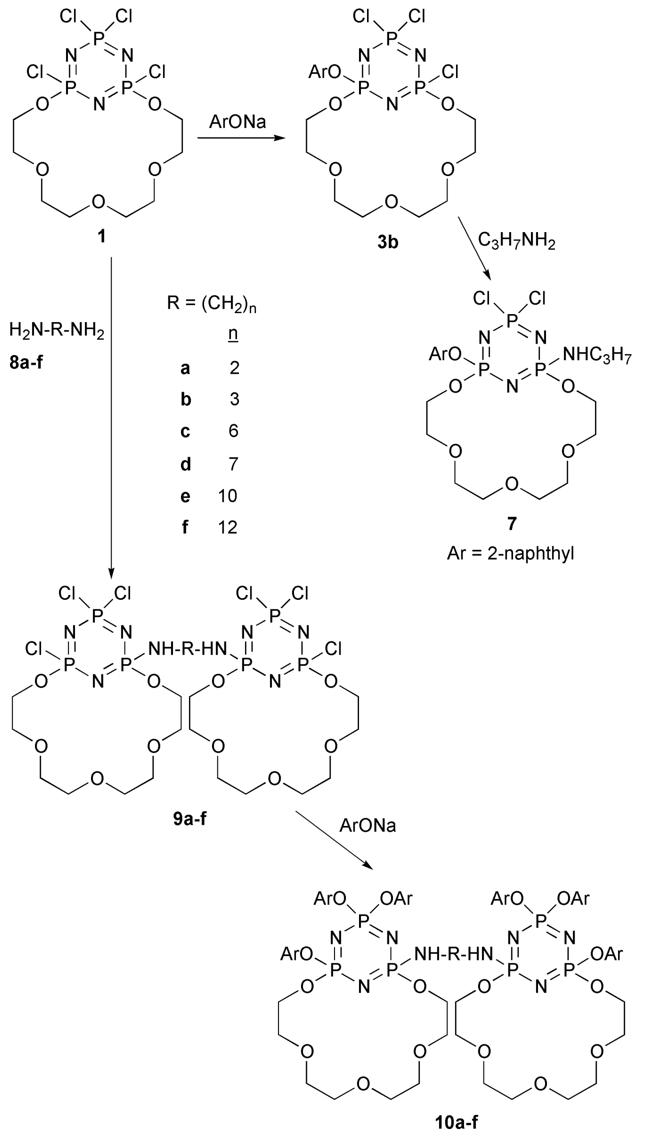
Scheme 2 Synthesis of isomeric 1,1′-bi-2-naphthoxy-PNP lariat ethers **5** and **6**.

Reaction of the bis(aryloxide) derived from 1,1′-bi-2-naphthol with **1** gave regioisomeric binaphthylylenedioxy derivatives **5** and **6**, that have one or both ends, respectively, of the dioxyarylene substituent linked to the PNP-macrocycle (Scheme 2).[10,11] Diarmed PNP-lariat ether **6** has two chlorine atoms on the remote phosphorus atom and therefore can be regarded as a model compound for the series **4a**–**f** that is undisturbed by remote, electron-donating aryloxy substituents. On the other hand, regioisomer **5** resembles the monoaryloxy-substituted PNP-lariat ether **3b**. However, **5** has only two unsubstituted chlorine atoms (compared with three in **3b**) and should be more strained and sterically crowded.

In the earlier work, we obtained solid-state structures for **5** and **6** that show the linkage of the polyether rings to the N_3P_3 unit is trans in **5** and cis in **6**. This results from inversion of the initial *cis*-configuration of **1** that accompanies each S_N2 substitution at the macrocycle-bearing phosphorus atoms.[10,11] Based upon comparative ^{31}P NMR studies and the recent correlations between structure and the ^{31}P NMR spectrum reported by Davies *et al.* for configurational cyclophosphazenic isomers,[16] we ascribe a *trans*-configuration of the PNP-macrocycle to all monoarmed PNP-lariat ethers and the *cis*-configuration to the diarmed derivatives.

Although we had intended to investigate the metal ion complexation properties for similar pairs of amino-substituted, mono- and "diarmed" PNP-lariat ethers, such compounds were found to be either hydrolytically unstable or water-soluble which precluded their application in solvent polymeric membrane electrodes.

As the third series of PNP-lariat ethers for investigation, we have now synthesized hitherto unreported, hydrolytically stable PNP-lariat ether **7** and bis-lariat ethers **10a**–**f** that have one aryloxy and one amine substituent linked to the PNP-macrocycle (Scheme 3). This new type of heterogeneously disubstituted PNP-lariat ether was prepared by arylolysis followed by aminolysis for **7** and aminolysis followed by arylolysis for **10a**–**f**. Earlier we observed that hydrogen bonding-driven regioselectivity in aminolysis of **1** occurs for both mono- and disubstitution at the PNP-macrocycle,[14–16] whereas metal ion-catalysed, regio-controlled arylolysis of **1** is limited to its first macrocyclic chloride function.[10–13] To achieve regioselective introduction of both amino and 2-naphthyloxy functions at positions adjacent to the PNP-crown unit, disubstitution of the tetrachloro-PNP-crown precursor **1** began with arylolysis to regioselectively obtain the mono-2-naphthoxy derivative **3b**, that subsequently was reacted with 1-aminopropane to form the mixed aryloxy-amino-PNP-lariat ether **7**. Per(2-naphthyloxy) diamino-bridged derivatives **10a**–**f** were obtained in almost quantitative yields by complete arylolysis of their earlier reported diamino-bridged precursors **9a**–**f**.[14] It was anticipated that such replacement of the active chlorine atoms in **9a**–**f** with 2-naphthoxy groups would increase their lipophilicity and



Scheme 3 Synthesis of heterogeneously-substituted PNP-lariat ether **7** and bis-PNP-lariat ethers **10a**–**f**.

hydrolytic stability. Diagnostic ^{31}P NMR spectral data[16,26] for **7** and **10a**–**f**, as well as combustion analysis and ^{1}H NMR spectral data for these new PNP-lariat and bis-lariat ether compounds are given in the supplementary information.†

Both **7** and **10a**–**f** PNP-lariat compounds have the same type of mixed naphthoxy-amino substituents linked to the two sides of the PNP-macrocycle. Thus, the hetero-diarmed compound **7** might be regarded as a monomeric model for the heterogeneously disubstituted, diamino-bridged PNP-bis-lariat ethers **10a**–**f**, keeping in mind the difference at the non-macrocyclic phosphorus atom, which bears two chlorine atoms in the former and two 2-naphthoxy groups in the latter. (This difference resembles that for the diarmed aryloxy lariat ethers **4b** and **6** with the latter having unsubstituted chloride functions at the non-crown phosphorus atom and the former **4b** bearing two 2-naphthoxy substituents in this position.)

Alkali metal cation complexation by PNP-lariat ethers

A variety of experimental methods has been utilized to assess metal ion complexation by macrocyclic multidentate ligands.[27] A commonly employed method involves incorporation of the ionophore into a solvent polymeric membrane and measuring the response of an electrode assembly containing this membrane to aqueous solutions containing two metal ion species.[28] This is a particularly useful method for screening the effects of structural variation within a series of ligands upon their metal ion complexation selectivity.[4,5] For the current study, the PNP-lariat and bis-lariat ethers were incorporated into *ortho*-nitrophenyl octyl ether (NPOE)-plasticized PVC membranes.[4,5] Responses of electrodes containing the membranes to pairs of alkali metal cations in aqueous solutions were determined by the fixed interference method[29,30] to give $-\log K_{\mathrm{M1,M2}}^{\mathrm{Pot}}$ values, for which a larger number reflects greater selectivity for the best-complexed metal ion over the interfering metal ion.

Table 1 presents the results of potentiometric ion-selectivity measurements ($-\log K_{\mathrm{Rb,M}}^{\mathrm{Pot}}$) values for the aryloxy-substituted mono- (**3a**–**f** and **5**) and diarmed (**4a**–**f** and **6**) PNP-lariat ethers that contain one and two aryloxy groups, respectively, in close proximity to the crown structure. The series of diarmed PNP-lariat ethers **4a**–**f** also bear aryloxy substituents at the remote non-macrocyclic P-atom; whereas **6** has unsubstituted chlorines at that site. On the other hand, the monoarmed PNP-lariat ethers **3a**–**f** each contain three unsubstituted chlorines; whereas in **5** one of the chlorines on the non-macrocyclic phosphorus atom in the N_3P_3 ring has been replaced by an aryloxy substituent.

It is immediately apparent that solvent polymeric membrane electrodes containing the PNP-lariat ethers exhibit pronounced selectivity for large alkali metal cations (Rb^+ and Cs^+) over the smaller Na^+ and particularly Li^+. Further inspection of the data reveals that the selectivity for the large alkali metal cations is greater for the diarmed ligands **4a**–**f** and **6** than for the mono-armed ligands **3a**–**f** and **5**.

The observed selectivity of the mono- and diarmed PNP-lariat ethers for large alkali metal cations (Rb^+ and Cs^+) is inconsistent with the concept of maximum metal ion binding for the metal ion that best fits within the crown cavity, since a 16-crown-5 ring is much too small to accommodate Rb^+ or Cs^+. As recognized by Hancock[3,6] and others,[2] the determining factors for selectivity with flexible ligands such crown and lariat ethers are the total number of oxygen atoms in the ligand and the size of the chelate ring formed on metal ion complexation. Molecular mechanics calculations suggest that the larger is the number of oxygen donor atoms in a molecule the greater is the selectivity for large metal ions, irrespective of whether the oxygen is part of the macrocyclic ring or located in a sidearm.[3]

Structural differences between these two groups of PNP-lariat ethers are delineated in the second–fifth columns of Table 1 in terms of the configuration of the crown ring, the total number of aryloxy substituents, the number of aryloxy substituents proximal to the PNP-crown structure, and the total number of lariat-type oxygen atoms (crown oxygens + oxygens in aryloxy groups adjacent to the crown structure), respectively. As a group, the monoarmed PNP-lariat ethers **3a**–**f** and **5** have a twisted *trans*-configuration of the crown ring. Also, the single proximate aryloxy substituent gives a total of six oxygens that are potentially available for metal ion complexation. On the other hand, each of the diarmed PNP-lariat ethers **4a**–**f** and **6** has a *cis*-configuration of the crown ring and a total of seven oxygens that could be involved in metal ion complexation.

From this structural analysis and the data contained in Table 1, it is concluded that a *cis*-configuration of the crown ring and increasing the number of potential oxygen donor atoms enhance selectivity of PNP-lariat ethers for large alkali metal cations (Rb^+ and Cs^+) over small ones. Another factor that could favor the large metal ion selectivity of aryloxy-substituted diarmed PNP-lariat ethers is increased metal ion–π interactions with the aromatic rings of the substituents. Such interactions between large, soft alkali metal cations and aromatic compounds are well-known.[31,32]

In Table 1, comparison of the alkali metal cation selectivities observed for PNP-lariat ethers **3a**–**f** with **5** and for **4a**–**f** with **6** verifies the earlier supposition that only substituents linked directly to the macrocycle-bearing phosphorus atoms will noticeably affect the selectivity. Whether chlorine or

Table 1 Potentiometric selectivities for Rb^+ over other alkali metal cations for monoaryloxy-substituted PNP-lariat ethers **3a–f**, tetraaryloxy-substituted PNP-lariat ethers **4a–f**, and binaphthylylenedioxy PNP-lariat ethers **5** and **6**

Ligand					$-\log K_{Rb,M}^{Pot}$				
	Config.[a]	n[b]	m[c]	x[d]	Li^+	Na^+	K^+	Rb^+	Cs^+
3a	*trans*	1	1	6	1.71 ± 1.04	1.08 ± 0.04	0.32 ± 0.01	0.00	−0.05 ± 0.02
3b	*trans*	1	1	6	1.66 ± 0.04	1.03 ± 0.01	0.25 ± 0.02	0.00	−0.09 ± 0.01
3c	*trans*	1	1	6	1.78 ± 0.03	1.12 ± 0.03	0.31 ± 0.01	0.00	0.03 ± 0.01
3d	*trans*	1	1	6	1.74 ± 0.01	1.14 ± 0.02	0.37 ± 0.02	0.00	−0.03 ± 0.02
3e	*trans*	1	1	6	1.94 ± 0.05	1.07 ± 0.01	0.20 ± 0.04	0.00	−0.03 ± 0.02
3f	*trans*	1	1	6	1.74 ± 0.03	1.12 ± 0.01	0.28 ± 0.02	0.00	−0.10 ± 0.03
4a	*cis*	4	2	7	4.03 ± 0.02	2.91 ± 0.01	0.80 ± 0.04	0.00	0.06 ± 0.02
4b	*cis*	4	2	7	3.80 ± 0.04	2.60 ± 0.04	0.80 ± 0.02	0.00	0.13 ± 0.02
4c	*cis*	4	2	7	4.00 ± 0.05	2.50 ± 0.04	0.62 ± 0.02	0.00	0.01 ± 0.02
4d	*cis*	4	2	7	3.20 ± 0.03	1.88 ± 0.04	0.36 ± 0.02	0.00	−0.27 ± 0.02
4e	*cis*	4	2	7	3.25 ± 0.05	1.16 ± 0.02	0.38 ± 0.01	0.00	−0.07 ± 0.01
4f	*cis*	4	2	7	3.54 ± 0.05	2.13 ± 0.02	0.42 ± 0.02	0.00	−0.12 ± 0.00
5	*trans*	2[e]	1	6	1.89 ± 0.01	1.03 ± 0.03	0.27 ± 0.02	0.00	0.07 ± 0.01
6	*cis*	2[e]	2	7	3.97 ± 0.01	2.98 ± 0.032	0.19 ± 0.03	0.00	0.75 ± 0.03

[a] Configuration of the polyether macrocycle relative to the N_3P_3 ring. [b] Total number of OAr substituents in the ligand. [c] Number of OAr substituents proximal to the PNP-crown unit. [d] Number of lariat-type oxygen atoms, capable of cooperating in coordination of metal cations (crown oxygens + oxygens of the side arms, adjacent to the crown structure). [e] The two halves of the conjugated binaphthylylenedioxy substituent are considered as two separate aryloxy substituents linked to the different phosphorus atoms in the N_3P_3 ring.

Table 2 Potentiometric selectivities for Rb^+ over other alkali metal cations for homogeneously-substituted tetra-2-naphthoxy-PNP-lariat ether **4b** and heterogeneously-substituted PNP-lariat ether **7** and PNP-bis-lariat ethers **10a–f**

Ligand			$-\log K_{Rb,M}^{Pot}$				
	x[a]	y[b]	Li^+	Na^+	K^+	Rb^+	Cs^+
4b	1	—	3.80 ± 0.04	2.60 ± 0.04	0.80 ± 0.02	0.00	0.13 ± 0.02
7	1	3	4.41 ± 0.04	2.44 ± 0.04	0.77 ± 0.02	0.00	−0.04 ± 0.02
10a	2	2	3.68 ± 0.06	2.20 ± 0.04	0.33 ± 0.02	0.00	0.01 ± 0.03
10b	2	3	3.95 ± 0.05	2.67 ± 0.03	0.45 ± 0.02	0.00	−0.01 ± 0.03
10c	2	6	4.34 ± 0.04	2.70 ± 0.01	0.89 ± 0.03	0.00	0.17 ± 0.01
10d	2	7	3.91 ± 0.02	2.54 ± 0.02	0.68 ± 0.02	0.00	0.16 ± 0.02
10e	2	10	3.92 ± 0.03	2.54 ± 0.01	0.65 ± 0.02	0.00	0.22 ± 0.04
10f	2	12	4.34 ± 0.03	2.75 ± 0.03	0.86 ± 0.05	0.00	0.25 ± 0.02

[a] Number of the PNP-lariat-ether units in the molecule. [b] Number of carbon atoms in the polymethylene chain of the 1,ω-diamino side arm.

aryloxy groups are attached to the remote phosphorus has no perceptible influence on selectivity.

Table 2 presents the results of potentiometric ion-selectivity ($-\log K_{Rb,M}^{Pot}$) values for the heterogeneously-substituted, diarmed PNP-lariat ether **7** and the mixed PNP-bis-lariat ethers **10a–f** in which the length of the spacer between two PNP units is systematically varied. In this series of diarmed PNP compounds, one substituent on each PNP-crown unit is a 2-naphthoxy group and the other is an alkylamine group. For ease of comparison, data is included also for the tetra-2-naphthoxy-substituted ligand **4b** that is considered as a homogeneously-substituted, diarmed PNP-lariat ether.

Comparison of the results for the homogeneously- and heterogeneously-substituted diarmed PNP-lariat ethers **4b** and **7**, respectively, reveals that replacing one of the aryloxy substituents in the former with a propylamino group in the latter has no appreciable effect on selectivity for complexation of alkali metal cations. The essentially identical selectivities observed with PNP-lariat ether **7** and PNP-bis-lariat ethers **10a–f** that have two-, three-, six-, seven-, ten- and twelve-carbon spacers between the two PNP units reveal that there is no cooperativity of these two units in complexation of alkali metal cations by the bis-lariat ether ligands. Thus for diarmed ligands with *cis*-configurations of the PNP-crown portion, neither replacing an oxygen-containing substituent with an alkylamine group nor linking the two heterogeneously substituted PNP units together significantly alters the selectivity of alkali metal cation complexation.

To gain insight into the stoichiometry of alkali metal cation-PNP-lariat ether complexes, electrospray ionization mass spectrometric (ESI-MS) measurements were performed on methanolic solutions of diarmed PNP-lariat ethers in the presence of alkali metal cations. Table 3 presents the results obtained for methanolic solutions of tetra-2-naphthoxy-substituted PNP-lariat ether **4b** with Rb^+ and with Cs^+, the best complexed alkali metal cations in the solvent polymeric membrane electrode studies, at 1 : 2, 1 : 1 and 2 : 1 ligand : cation molar ratios. For both of the large alkali metal cations and all three molar ratios, peaks for 1 : 1 and 2 : 1 (**4b**/metal ion) complexes were observed. Although no clear pattern of influence of the ligand : cation molar ratio on the relative proportions of 1 : 1 and 2 : 1 complexes was evident, 2 : 1 complexes usually predominated. Thus, the importance of 2 : 1 "sandwich" complexes of the lariat ether with the oversized metal ions is established for diarmed PNP-lariat ether **4b**. Since formation of 2 : 1 complexes with lipophilic macrocyclic multidentate ligands is expected to be even higher in non-polar media,[28] the proportion of such complexes should be enhanced in the solvent polymeric membranes. Subsequently, additional ESI-MS measurements were performed for equimolar methanolic solutions of **4b** with Li^+, Na^+ and K^+. As shown by the data in Table 4, only 1 : 1 complexes of **4b** with these smaller alkali metal cations were observed. Thus, results of the ESI-MS experiments conducted with this diarmed PNP-lariat ether suggest that the selectivity for large alkali metal cations (Rb^+ and Cs^+) observed in the solvent polymeric membrane elec-

Table 3 Molecular ions observed in the ESI-MS spectra for methanolic solutions of PNP-lariat ether **4b** with Rb^+ and Cs^+

Cation	Molar ratio [**4b**]/[cation]	Molecular ions observed in the ESI-MS spectrum	Relative intensities of the peaks for the 1 : 1 to 1 : 2 complexes
Rb^+	1 : 1	$(L + Rb)^+$, $(2L + Rb)^+$	1 : 2.5
	1 : 2	$(L + Rb)^+$, $(2L + Rb)^+$	1 : 4.6
	2 : 1	$(L + Rb)^+$, $(2L + Rb)^+$	1 : 4.4
Cs^+	1 : 1	$(L + Cs)^+$, $(2L + Cs)^+$	1 : 2.8
	1 : 2	$(L + Cs)^+$, $(2L + Cs)^+$	1 : 0.6
	2 : 1	$(L + Cs)^+$, $(2L + Cs)^+$	1 : 2.0

Table 4 Molecular ions observed in the ESI-MS for equimolar methanol solutions of PNP-lariat ether ligands **4a**–**d** with alkali metal salts

	Molecular ions observed				
Ligand	Li^+	Na^+	K^+	Rb^+	Cs^+
4a	$(L)^+$, $(L + Li^+)$	$(L + Na)^+$	$(L + K)^+$, $(2L + K)^+$	$(L + Rb)^+$, $(2L + Rb)^+$	$(L + Cs)^+$, $(2L + Cs)^+$
4b	$(L + Li)^+$	$(L + Na)^+$	$(L + K)^+$	$(L + Rb)^+$, $(2L + Rb)^+$	$(L + Cs)^+$, $(2L + CS)^+$
4c	$(L + Li)^+$	$(L)^+$	$(L + Na)^+$, $(L + K)^+$, $(2L + Na)^+$	$(L + Rb)^+$	$(L)^+$, $(L + Cs)^+$
4d	$(L)^+$, $(L + Li)^+$	$(L + Na)^+$	$(L + Na)^+$, $(L + K)^+$, $(2L + Na)^+$	$(L)^+$, $(L + Rb)^+$	$(L + Cs)^+$

trode experiments results from formation of 2 : 1 sandwich complexes of the PNP-lariat ethers with Rb^+ and Cs^+.

To explore the generality of this postulation, additional diarmed PNP-lariat ethers with four phenoxy (**4a**), 4-(ethoxycarbonyl)phenoxy (**4c**), and 4-*tert*-octylphenoxy (**4d**) substituents were examined. Species detected in the ESI-MS spectra for equimolar methanolic solutions of each ligand with each of the five alkali metal cations are identified in Table 4. For **4a**, both 1 : 1 and 2 : 1 complexes were noted with K^+, Rb^+, and Cs^+. With Li^+ and Na^+, only complexes with 1 : 1 stoichiometries were observed. Overall, the ESI-MS results for diarmed PNP-lariat ethers **4a** and **4b** with phenoxy and 2-naphthoxy substituents, respectively, are quite similar. This is in agreement with the very similar responses of these two ligands when incorporated into solvent polymeric membrane electrodes (see Table 1). However, the stoichiometries observed from diarmed PNP-lariat ethers **4c** and **4d** that have *para*-substituted phenoxy substituents are quite different from those found for **4a** and **4b**. Thus for diarmed PNP-lariat ethers **4c** and **4d**, only complexes of 1 : 1 stoichiometry are noted with Rb^+ and Cs^+. This result indicates that the presence of *para*-substituents interferes with the formation of 2 : 1 complexes for the large alkali metal cations. Seemingly this would suggest that the large alkali metal cation selectivities observed for diarmed PNP-lariat ethers **4c** and **4d** in solvent polymeric membrane electrodes would be lower than those for **4a** and **4b**. As can be seen from the data in Table 1, this expected lower selectivity is evident for **4d**, but not for **4c**.

Conclusions

From the precursor tetrachloro-PNP-crown **1** in which $-O(CH_2CH_2O)_3CH_2CH_2O-$ links two phosphorus atoms in the triphosphazene ring, a variety of P-pivot lariat and bis-lariat ethers are prepared by attaching one or two aryloxy groups or one aryloxy and one alkylamino group to the crown-bearing phosphorus atoms. When incorporated into solvent polymeric membrane electrodes, these PNP-lariat and bis-lariat ethers exhibit selectivities for large alkali metal cations (Rb^+ and Cs^+) over the small alkali metal cations (Li^+ and Na^+). This selectivity is enhanced when the crown ring has a *cis*-configuration and the number of oxygen donor atoms in the sidearms is increased. Results for ESI-MS experiments performed with methanolic solutions of some diarmed PNP-lariat ethers and Rb^+ and Cs^+ demonstrate the presence of 2 : 1 (ligand–metal ion) complexes. Preferred formation of 2 : 1 sandwich complexes of PNP-lariat ethers with the oversized metal cations is suggested to be an important causitive factor for the large alkali metal cation selectivity observed in the solvent polymeric membrane electrode system.

Experimental

Synthesis

Materials. Sodium hydride, salicylaldehyde, 4-hydroxybenzaldehyde, 4-*tert*-octylphenol (Aldrich), and ethyl 4-hydroxybenzoate (Sigma) were used as received. The 1-aminopropane and 1,ω-diaminoalkane reactants (Fluka) were used as received. THF (POCh, Gliwice, Poland) was distilled over CuCl, then over calcium hydride, and finally twice over a sodium–potassium alloy under an atmosphere of dry argon. Hexane (Merck) was used without purification. The 1,3-[oxybis(ethyleneoxyethyleneoxy)]-1,3,5,5-tetrachlorocyclotriphosphazatriene (**1**) was synthesized and purified as previously reported.[22] PNP-lariat ethers **3a**, **3b**, **4a**, **4b**, **5**, and **6** were prepared by reported methods.[10–12,20]

Methods. ^1H NMR spectra were recorded on a Varian VXR 300 spectrometer in $CDCl_3$ with TMS as the internal reference (unless specified otherwise). ^{31}P NMR spectra were recorded in $CDCl_3$ with 85% H_3PO_4 as the external reference with positive shifts downfield from the reference on the same spectrometer operating at 121 MHz. In most cases, both proton-coupled and proton-decoupled ^{31}P NMR spectra were obtained. ESI-MS analysis was performed with a Finnigan LCQ ion trap spectrometer. A solution of the sample was introduced into the ESI-MS source by continuous infusion with a syringe pump at a rate of 3 $\mu l\ min^{-1}$. The ESI-source was operated at 4.25 kV and the capillary heater was set to 200 °C. The experiments were performed in the positive ion-mode.

Flash column chromatography was performed on silica gel (230–400 mesh, Macherey-Nagel) with hexane–THF or chloroform–methanol as eluents. TLC analyses were conducted on Merck pre-coated silica gel 60 plates.

All reactions were performed under a dry argon atmosphere.

General procedure for regioselective synthesis of *gem*-to macrocycle mono-aryloxy-substituted PNP-lariat ethers 3c–f. The monoaryloxy-substitution reactions were carried under the optimized reaction conditions reported for the synthesis of **3a** and **3b**.[12]

To a solution of 1,3-[oxybis(ethyleneoxyethyleneoxy)]-1,3,5,5-tetrachlorocyclotriphosphazatriene (**1**) (0.469 g, 1.0

mmol) and ArOH (1.0 mmol) in dry THF (40 ml) in a 100 ml, 4-necked flask equipped with a magnetic stirrer, reflux condenser, and argon inlet, NaH (60% oil suspension, 0.040 g, 1.0 mmol) was added. The reaction mixture was stirred for 2 h at room temperature with the progress of the reaction monitored by TLC with hexane–THF (3 : 1) as eluent and pyridine-*m*-toluidine (1 : 1) (for all chlorine-containing cyclophosphazene-derivatives) and I_2 vapor (for multiple bond-containing compounds) as developing reagents. The reaction mixture was filtered and the THF was evaporated *in vacuo* to give a colorless oil that was extracted with benzene (50 ml). The benzene-soluble material containing predominantly the monosubstitution product (**3c**, approx. 83%; **3d**, approx. 78%; **3e**, approx. 99%; and, **3f**, approx. 99%, as inferred from the ^{31}P NMR spectrum of the crude product) was chromatographed on silica gel with hexane–THF (2 : 1) as eluent. Products **3c**–**f** were separated in pure form and characterized, which allowed estimation of the composition of the crude reaction product mixture from the ^{31}P NMR spectrum by comparing intensities of the AMX signals corresponding to the mono-oxy-substituted derivatives **3c**–**f** to the overall ^{31}P NMR signal intensities, as previously reported for **3a** and **3b**.[12]

The ^{31}P and ^{1}H NMR spectral data and combustion analysis data for **3c**–**f** are given in the supplementary information.†

General procedure for the synthesis of *gem*-to macrocycle tetraaryloxy-substituted PNP-lariat ethers 4c–f. New compounds **4c**–**f** were obtained by the method of preparation previously reported for the synthesis of **4a** and **4b**.[22]

Into a 250 ml, 4-necked flask equipped with a mechanical stirrer, reflux condenser, and argon inlet was placed 1,3-[oxybis(ethyleneoxyethyleneoxy)]-1,3,5,5-tetrachlorocyclotriphosphazatriene (**1**) (0.469 g, 1.0 mmol), the appropriate ArOH (6.0 mmol), 60% NaH (0.24 g, 6.0 mmol) and 50 ml of dry THF. The reaction was conducted with stirring at 20 °C for 3 h (for **4c** and **4f**) or 24 h (for **4d** and **4e**) to afford complete replacement of the chlorine atoms with aryloxy groups. The mixture was filtered and the filtrate was evaporated *in vacuo*. The residue was extracted with benzene. Excess ArOH was removed by extraction of the benzene solution with aqueous NaOH and then with distilled water. The benzene solution was dried over anhydrous Na_2SO_4 and evaporated *in vacuo* to provide the desired product as a colorless or pale yellow viscous oil in 70–90% yield.

The ^{31}P and ^{1}H NMR spectral data and combustion analysis data for **4c**–**f** are given in the supplementary information.†

Regioselective synthesis of *gem*-to macrocycle di-hetero-substituted PNP-lariat ether 7. A solution of 1,3-[oxybis(ethyleneoxyethyleneoxy)]-1,3,5,5-tetrachlorocyclotriphosphazatriene (**1**) (0.469 g, 1.0 mmol) and 2-naphthol (**2b**) (0.144 g, 1.0 mmol) in dry THF (80 ml) was placed in a 200 ml, 4-necked flask equipped with a magnetic stirrer, reflux condenser, and argon inlet. NaH (60% oil suspension, 0.040 g, 1.0 mmol) was added and the mixture was stirred at room temperature for 2 h. Progress of the reaction was monitored by TLC with hexane–THF (2 : 1) as eluent. A solution of 1-aminopropane (0.118 g, 2.0 mmol) in 80 ml of hexane was added dropwise and the reaction mixture was stirred at room temperature for the 3 h. The reaction mixture was filtered and the THF was evaporated *in vacuo* to provide a colorless oil (0.56 g, 93% yield of crude product containing approx. 85% of **7** by ^{31}PMR spectroscopy) that was chromatographed on silica gel with hexane–THF (2 : 1) as eluent to give **7**; *m*/*z* 559 (M^+ for $C_{21}H_{31}O_6N_4P_3Cl_2$). The ^{31}P and ^{1}H NMR spectral data and combustion analysis data for **7** are given in the supplementary information.†

One-pot synthesis of bis-PNP-lariat ethers 10a–f. To a solution of **1** (0.934 g, 2.0 mmol) in hexane (75 ml) in a 250 ml, 3-necked flask, a solution of the appropriate diamine (2.0 mmol) in dry THF (75 mL) was added dropwise from an addition funnel. The mixture was stirred at room temperature for 3 h to give the previously reported[14] diamino-bridged bis-PNP-crowns **9a**–**f**. A solution of 2-naphthol (0.864 g, 6.0 mmol) in 100 ml of dry THF and then NaH (60% oil dispersion, 0.24 g, 6.0 mmol) were added and the mixture was stirred vigorously at room temperature for 2 h. The mixture was filtered and the filtrate was evaporated *in vacuo*. The resultant colorless oil was dissolved in benzene (50 ml) and extracted several times with aqueous KOH to remove the excess of 2-naphthol and then with distilled water. The organic layer was dried over anhydrous Na_2SO_4, concentrated to 5 ml and chromatographed on silica gel with THF–hexane (2 : 3) as eluent. Yields of the per-(2-naphthoxy) 1,*n*-diamine bridged bis-PNP-lariats **10a**–**f** varied from 7% ($n = 2$) to 48% ($n = 10$). The low yield of **10a** is ascribed to loss of the polar product into the aqueous phase during workup. Products **10a**–**f** were found to be stable in air for extended periods of time. The ^{31}P and ^{1}H NMR spectral data and combustion analysis data for **7** are given in the supplementary information.†

Potentiometric measurements

Reagents. Lithium chloride (99 + %), caesium chloride (99+%), and rubidium chloride (99+%) were obtained from Alfa Aesar. Sodium chloride (99.9%) and potassium chloride (99.9%) were purchased from Fisher. Poly(vinyl chloride) (PVC) with an average polymerization degree of 1100 was purchased from Wako Pure Chemical Industries (Osaka, Japan). *o*-Nitrophenyl octyl ether (NPOE) and potassium tetrakis(*p*-chlorophenyl)borate (KTpClPB) were obtained from Dojindo Laboratories (Kumamoto, Japan). Deionized water, which was used to prepare all of the aqueous solutions and to rinse the glassware, was prepared by passing distilled water through three Barnstead combination ion-exchange cartridges in series. Reagent grade tetrahydrofuran (THF) was dried by distillation from sodium metal.

Preparation of PVC membranes. The ligand (5.0 mg), NPOE (100 mg, the membrane solvent), PVC (50 mg), and KTpClPB (1.0 mg) were dissolved in 1.5 ml of THF. (The bulky anionic group in KTpClPB minimizes interference by lipophilic sample anions, facilitates the interfacial cation-exchange reaction, and reduces the surface resistance of the membrane.) A poly(tetrafluoroethylene) (PTFE) membrane support (purchased from Denki Kagaku Keiki (DKK) Co., Tokyo, Japan) was dipped first in THF, then in the solution, and mounted in the PVC tube. Two drops of the THF solution were placed onto the membrane support with a microsyringe and allowed to evaporate for at least 30 min. This application and evaporation sequence was repeated six times. Then the membrane was allowed to stand for 24 h to allow the THF to evaporate completely. The resultant PVC tube with the coated PTFE membrane support was fixed on a Denki Kagaku Keiki (DKK, Musashino, Tokyo, Japan) No. 7900 electrode body. The electrode was conditioned by soaking in 0.10 M solution of the primary ion chloride for 12 h before use. For each ligand, two membrane electrodes were prepared.

Measurements. Aqueous solutions containing 0.001 mol dm^{-3} to 0.5 mol dm^{-3} primary ion and a background concentration of the other alkali metal chloride as the interfering ion were prepared with deionized water. The background concentrations of interfering ions were: 0.5, 0.1, or 0.001 mol dm^{-3} for Li^+; 0.1 mol dm^{-3} for Na^+; and 0.01 mol dm^{-3} for K^+ and Cs^+. Potentiometric measurements with a membrane electrode were carried out at 23–25 °C with a voltage meter (Fisher Scientific Accumet 50 pH meter), a double junction Ag–AgCl reference electrode (DKK Number 4083), and a magnetic stirrer to agitate the sample solution. The electrode cell was Ag–AgCl/

0.10 mol dm^{-3} RbCl/PVC membrane/sample solution/0.10 mol cm^{-3} NH_4NO_3/4.0 mol dm^{-3} KCl/Ag–AgCl. Single ion activities were obtained from the concentrations according to Debye-Hückel equation. The selectivity coefficients (log $K_{N,M}^{Pot}$) were determined by the fixed interference method.[29,30] For a given polymeric membrane system, the potentiometric selectivity was determined twice for each of two independently prepared membranes. The average value for the potentiometric selectivity was calculated from the values obtained for the four measurements.

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