Synthesis and Catalytic Activity of a New Class of Cyclophosphazenic Polypodands

Maria Paola Bullitta, Elias Maccioni, Luciana Corda
and Gianni Podda*

Dipartimento Farmaco Chimico Tecnologico,
Via Ospedale 72, I-09124 Cagliari, Italy
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A new class of solid-liquid phase-transfer catalysts (SL-PTC) has been prepared by the reaction of octachlorocyclotetraphosphazatetraene and polyethylene glycol monoalkyl ether. These polypodands are found to be powerful metal cation complexing agents and very efficient catalysts in anion promoted reactions (*e.g.* nucleophilic substitution and reduction reactions).

The synthesis and complexing properties of open-chain ligands (podands) has been studied extensively in the recent years and some interesting reviews regarding this field have appeared [1-5]. Polypodands of the acyclic type form stable complexes with alkali and alkaline-earth metal salts [1]. This property is based on cavity size, donor atom type and size and nature of the R groups [5].

Previously, we reported the high-yield synthesis of a series of polypodands and investigated their catalytic abilities in phase-transfer reactions [6a-d]. In general, these systems possess a powerful complexing ability and high catalytic activity in anion-promoted reactions, particularly under solid-liquid PTC conditions [6c-d].
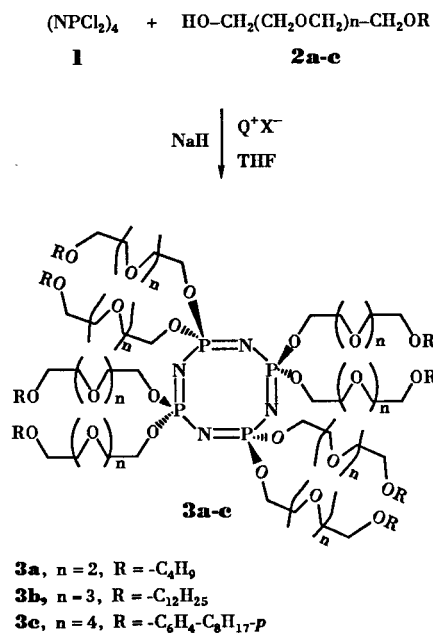
Our attention is now focussed on the preparation of new polypodands with several polyether chains and a higher number of donor atoms for selective cation complexation. In the present paper, we report the synthesis of a new class of polypodands in which several polyether chains, with different end groups, are linked to the same centre. Some examples of the application of the new ligands as phase-transfer catalysts in anion-promoted reactions are also reported.

Results and Discussion.

The reactions of eight-membered ring systems, such as octachlorocyclotetraphosphazatetraene ($N_4P_4Cl_8$), with monofunctional substrates have received little attention, as compared to the lower homologue, hexachlorocyclotriphosphazatriene ($N_3P_3Cl_6$). Octachlorocyclotetraphosphazatetraene is very reactive towards nucleophilic reagents giving a large number of products [7].

In this study, polypodands **3a-c** were synthesized [6] by reacting octachlorocyclotetraphosphazatetraene, ($N_4P_4Cl_8$, **1**) with the sodium salt of the appropriate oligoethylene glycol monoalkylether **2a-c** under vigorous stirring (Scheme I). The reaction mixture was purified by column chromatography on silica gel to afford **3a-c** as viscous liquids in 18-45% yields. The structures proposed for polypodands **3a-c** are consistent with their ir, ^1H nmr and ^{31}P nmr spectra.

Scheme 1

$$(NPCl_2)_4 \quad + \quad HO-CH_2(CH_2OCH_2)n-CH_2OR$$
$$\mathbf{1} \qquad\qquad\qquad \mathbf{2a\text{-}c}$$

NaH | Q^+X^-
THF

3a-c

3a, n = 2, R = -C_4H_9
3b, n = 3, R = -$C_{12}H_{25}$
3c, n = 4, R = -C_6H_4-C_8H_{17}-p

The ir spectra of all compounds show two characteristic bands located at 1240 cm^{-1} and 1050 cm^{-1}. These are attributable to the P=N and C-O vibrations, respectively, in agreement with the literature data [6]. The ^{31}P nmr spectra of **3a-c** show a singlet peak between 2.60 and 2.72 ppm. The singlet peak of starting octachlorotetracyclophosphazatetraene (**1**) appears at −6.5 ppm [7]. The polypodands **3a-c** are soluble in low polar organic media and can be used as phase-transfer catalysts. In agreement with polypodands **4a-c** previously reported [6], the new ligands **3a-c** differ in their complexing abilities. Complexation was measured by stirring a chlorobenzene solution of ligands **3a-c** with 100 molar equivalents of inorganic salts M^+Y^-(M^+ = Na^+, K^+, Rb^+; Y^- = I^-, Br^-) as the solid phase (Table 1).

Table 1

Complexation [a] by Polypodands 3a-c and 4a-c under SL-PTC Conditions at 60° [b]

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MI	3a	3b	3c	4a [c]	4b [c]	4c [c]
NaI	88	440	510	70	390	420
KI	17	87	92	6	82	97
RbI	10	48	74	3	47	58
NaBr	-	14	19	-	17	18

[a] Defined as moles of My complexed/moles of ligand x 100. [b] A chlorobenzene solution (20 ml) of the ligand (0.5-4 x $10^{-2}M$) and 100 molar equivalents of the inorganic salt MY as solid phase. [c] Ref [6].

As shown in Table 1, complexation increases in the order **3a** < **3b** < **3c**. Also, ligands **3a-c** are only slightly better than **4a-c** probably due to an increase in number of pendant arms and of donor atoms. The extent of complexation depends on the size of the cation. Complexation decreases on increasing the size of the cation ($Na^+ > K^+ > Rb^+$). Also complexation greatly decreases on changing the anion from I^- to Br^- (Table 1). Polypodands **3b** and **3c** show about the same complexing ability.

The catalytic activity of polypodands **3a-c** under solid-liquid phase transfer catalysis conditions (SL-PTC) was evaluated in nucleophilic substitution reactions by I^- on n-octylbromide (eq 1), by I^- or Br^- on n-octyl methanesulfonate (eq 2-3), and in the reduction of 2-octanone to the corresponding 2-octanol by sodium borohydride (eq 4).
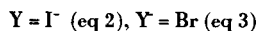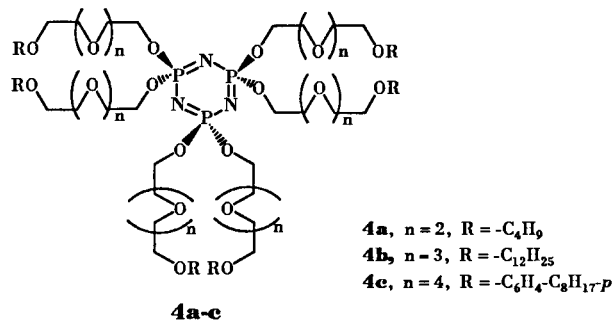
$$n\text{-}C_8H_{17}Br + M^+I^- \longrightarrow n\text{-}C_8H_{17}I + M^+Br^- \quad (1)$$

$$n\text{-}C_8H_{17}OMes + M^+Y^- \longrightarrow n\text{-}C_8H_{17}Y + MesO^-M^+ \quad (2\text{-}3)$$

$$Y = I^- \text{ (eq 2)}, Y = Br \text{ (eq 3)}$$

$$n\text{-}C_6H_{13}COCH_3 + NaBH_4 \longrightarrow n\text{-}C_6H_{13}CHOHCH_3 \quad (4)$$

Table 2

Catalytic Activity of Polypodands 3a-c and 4a-c in Reaction 1, where M+ = Na+, K+ and Rb+ and using SL-PTC Conditions at 60° [a]

Reaction Time (hours) [b]

MI	3a	3b	3c	4a [c]	4b [c]	4c [c]
NaI	5	2	2	12	6	5
KI	8	6	5	12	7	7
RbI	10	9	7	28	12	12

[a] A 5 ml chlorobenzene solution containing 5 mmoles of 1-bromo-octane, 0.25 mmole of catalyst with 25 mmoles of MI as the solid phase. [b] Conversion >95% by glc analysis. [c] ref [6c,d].

4a, n = 2, R = -C₄H₉ → 4a, n = 2, R = $-C_4H_9$
4b, n = 3, R = $-C_{12}H_{25}$
4c, n = 4, R = $-C_6H_4\text{-}C_8H_{17}\text{-}p$

4a-c

The reactions shown in eq 1-4 were carried out in a chlorobenzene-solid salt two-phase system using 0.05 molar equivalents of the ligand and a 5:1 inorganic salt:substrate molar ratio. The reactions (up to 95-98% of conversion) were monitored by glc analysis of the organic phase with respect to an internal standard. Reaction times needed to convert 95% or more of the reactant to product. This activity was compared to the catalytic activity of polypodands **4a-c** [6]. The results are reported in Tables 2-4.

Table 3

Catalytic Activity of Polypodands 3a-c and 4a-c in Reactions 2 and 3, where Y⁻ = I⁻ and Br⁻ and M⁺ = Na⁺, K⁺ and Rb⁺ under SL-PTC Conditions at 60° [a]

Reaction Time (hours) [b]

MY	3a	3b	3c	4a [c]	4b [c]	4c [c]
NaI	0.50	0.20	0.20	1.5	0.75	0.50
NaBr	30	28	28	-	32	32
KI	3	1	1	4	2	2
RbI	6	2.50	2	12	3	2.50

[a] Same amounts of substrate, catalyst and inorganic salt as reported in Table 2, footnote [a]. [b] Conversions > 95%, by glc analysis. [c] Ref [6c,d].

Table 4

Catalytic Activity of Polypodands 3a-c and 4a-c in Reaction 4 under SL-PTC Conditions at 60°C [a]

Catalyst	Reaction Time (hours) [b]
3a	2.50
3b	2
3c	1.50
4a [c]	8
4b [c]	4
4c [c]	3

[a] Experimental details are the same as in Table 2, footnote [a]; but 2:1/sodium borohydride:substrate molar ratio. [b] Conversions > 98% by glc analysis. [c] Ref [6c,d].

As shown in the tables, the catalytic efficiency of polypodands **3a-c** was higher than that for ligands **4a-c**. The highest reaction rates were found with the sodium cation and the methanesulfonate anion (rates are faster for eq 2 and 3, see Table 3). This behaviour seems to be related to the size of the cation and to the nature of the nucleophile. The cavity size effect is more pronounced in the eight-arm polypodands **3b** and **3c** than in six-arm polypodand **4b** and **4c** containing the same ethyleneoxy chains and the same end groups.

The reduction reaction of 2-octanone to give 2-octanol was performed in a chlorobenzene solid sodium borohydride two phase system in the presense of catalytic amounts of polypodands **3a-c** (eq 4). As shown in Table 4, the catalytic efficiency of ligands **3a-c** is higher than that of ligands **4a-c**.

In conclusion, the easy synthesis and high complexing ability make this new class of open-chain ligands a valid alternative to other more widely used analogues.

EXPERIMENTAL

All the solvents were Carlo Erba reagent grade and used after fractional distillation. Tetrahydrofuran (THF) was distilled over sodium and then over lithium aluminum hydride under an atmosphere of dry nitrogen and immediately used. Tetrabutylammonium bromide, *n*-octyl bromide, 2-octanone, triethylene glycol monobutyl ether, tetraethylenglycole monododecyl ether and pentaethylene glycol mono-[*p*-octylphenyl] ether were commercially available and used as purchased. *n*-Octyl methanesulfonate, bp 112-114° (2 Torr), n_D^{20} 1.4398 was prepared according as reported [9]. All inorganic salts were Analar grade commercial products used without further purification. Octachlorocyclotetraphosphazatetraene were purchased from Shin Nisso Kato Co. Ltd. and used without further purification. Merck silica gel (70-230 mesh) was used for column chromatography. The tlc were performed on Merck silica gel 60F 254 precoated plates.

The ir spectra were measured with a Perkin Elmer 157 spectrometer and the ^{1}H nmr spectra were recorded on a Varian EM 360L spectrometer (60 MHz) using TMS as an internal standard. The ^{31}P nmr spectra were performed at 200 or 300 MHz using 85% phosphoric acid as an external standard. Microanalyses (C,H,N) were carried out on a Carlo Erba Model 1106 Elemental Analyzer.

Solid-liquid phase transfer reactions in the presence of catalyst **3a-c** were carried out as described previously [6a-d]. Glc analyses were performed on a Carlo Erba HR GC 5300 flame-ionization instrument (SE-30, 3% on Chromosorb, Carbowax 20M and a capillary column SP-2100 (Supelco, Inc.). Potentiometric titrations were carried out with a Methrom 670 titroprocessor using silver electrodes.

Cyclophosphazenic polypodands **4a-c** were prepared according to a previously reported procedure [6].

General Procedure for the Synthesis of **3a-c**.

All the reported preparations were performed under strictly anhydrous conditions according to the following standard procedure. Sodium hydride (0.17 mole as an 80% dispersion in mineral oil) was suspended in dry THF (50 ml) and the suspension was stirred at room temperature under a nitrogen atmosphere for 1 hour. To this suspension, a solution of the appropriate polyoxyethylene glycol monoalkylether (0.088 mole) and tetrabutylammonium bromide (1 g) in THF (150 ml) was added dropwise and the mixture was stirred for 6 hours at reflux. To the solution of the sodium salt, a solution of octachlorocyclotetraphosphazatetraene (NPCl$_2$)$_4$ (0.073 mole) was added over thirty minutes and the mixture was stirred for two days at reflux. The precipitated sodium chloride was filtered and washed with dichloromethane. The combined organic phases were evaporated *in vacuo* to give an oily residue. The residue was purified by column chromatography (silica gel) first using dichloromethane as eluent to remove the excess of polyoxyethylene glycol monoalkyl ether and then dichloromethane/methanol (20:1) to give pure **3a-c** as colorless oils.

The specific detail of compounds **3a-c** thus prepared are given below.

Octakis[butoxytris(ethoxy)]cyclotetraphosphazatetraene (**3a**).

A pale yellow oil (45%) was isolated; n_D^{25} 1.4649; ir (neat): 2940, 2870, 1430, 1360, 1310, 1255, 1200, 1130, 1100, 1050, 980, 845, 740 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 4.02-3.60 (m, 112 H) 1.42-0.83 (m, 56 H) ppm; ^{31}P nmr [7,8] (deuteriochloroform, 85% phosphoric acid): a single peak at δ 2.60.

Anal. Calcd. for $C_{80}H_{168}N_4O_{32}P_4$: C, 52.68; H, 9.31; N, 3.05. Found: C, 52.73; H, 9.30; N, 3.07.

Octakis[dodecyloxytetrakis(ethoxy)]cyclotetraphosphazatetraene (**3b**).

A pale yellow oil (30%) was isolated; n_D^{25} 1.4585; ir (neat); 2930, 2840, 1460, 1340, 1300, 1240, 1100, 1050, 970, 840, 720 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 4.00-3.63 (m, 144 H), 1.23-0.76 (m, 184 H); ^{31}P nmr [7,8] (deuteriochloroform, 85% phosphoric acid): a single peak at δ 2.64.

Anal. Calcd. for $C_{160}H_{328}N_4O_{40}P_4$: C, 62.40, H, 10.82; N, 1.80. Found: C, 62.44; H, 10.80; N, 1.82.

Octakis[(*p*-octyl)phenoxypentakis(ethoxy)]cyclotetraphosphazatetraene (**3c**).

A pale yellow oil (18%) was isolated; n_D^{25} 1.5035; ir (neat); 3020, 2960, 2840, 1600, 1570, 1500, 1450, 1360, 1290, 1240, 1180, 1130, 1050, 940, 820, 730 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 6.80-7.20 (m, 32 H), 4.40-3.50 (m, 160 H), 0.65-1.8 (m, 136 H); ^{31}P nmr [7,8] (deuteriochloroform, 85% phosphoric acid): a single peak at δ 2.74.

Anal. Calcd. for $C_{192}H_{328}N_4O_{48}P_4$: C, 64.26; H, 9.21; N, 1.56. Found: C, 64.30; H, 9.22; N, 1.56.

Complexation by Polypodands **3a-c**.

The extent of complexation by polypodands **3a-c** under SL-PTC conditions was determined by stirring 20 ml of a standardized chlorobenzene solution of **3a-c** (0.5- 4 x 10^{-2} *M*) with 100 molar equivalents of an inorganic salt MY (M$^+$ = Na$^+$, K$^+$, Rb$^+$; Y$^-$ = I$^-$, Br$^-$), as a solid phase, in a flask thermostated at 60°. The system was stirred for 2-3 hours, then kept without stirring for an additional thirty minutes to allow good separation of the two phases. A 5 ml sample of the organic phase was centrifuged and titrated with 0.01N silver nitrate solution. The results are in Table 1.

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