Water-soluble poly(diazacrown ethers): evidence for a polymer-sandwich complex with barium

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The synthesis of water-soluble polymers containing a [22] diazacrown ether in the backbone is described. These compounds are obtained by polycondensation of the cyclic diamine [22] with epichlorohydrin or diepoxyoctane. The cation binding properties of these polymers are studied by ^{13}C n.m.r. spectroscopy and potentiometry, and the results compared with those of the monomeric analogues. The two polymers do not exhibit typical polyelectrolyte behaviour: each ligand unit in the chain is independent as far as basicity constants and stability of the complexes formed are concerned. In general, 1:1 complexes are observed in water with all the studied cations (Ca, Ba, Sr, Cu, Zn), except for the diepoxyoctane polymer where, in presence of barium, a 2:1 sandwich polymeric complex is obtained. By comparing with the other ligands studied, it is shown that this unique structure is due to the particular polymeric nature of this ligand.

INTRODUCTION

We recently reported the synthesis and binding properties of liposoluble polymers containing diazacrown ethers in the backbone[1,2]. By comparison with the properties of the monomeric analogues, we have shown that the binding properties were dependent not only on the nature of the incorporated cyclic ligand, but also on the nature of the bridge leading to the polymeric structure. In these studies, only complexes of 1:1 ligand: cation stoichiometry were observed. However, the formation of 2:1 complexes has been observed or proposed in several studies, i.e. Pedersen[3] and Frensdorff[4] for the 15–5 and 18–6 crown ethers with K^+ and Cs^+ cations in methanol and Smid[5] for the 15–5 polymer with K^+ in methylene chloride. In this latter case, this remarkable detail is due partly to the fact that the poly(crown ether) can form complexes intramolecularly by cooperative action of two adjacent pendant crown ether moities. Recently Kimura *et al.*[6] studied the effect of the tacticity of these types of polymers on such stoichiometry.

In this paper, we describe the synthesis of water-soluble polymers obtained by polycondensation of the cyclic diamine [22] with epichlorohydrin or diepoxyoctane. Binding properties are studied by potentiometry and ^{13}C n.m.r. spectrometry. We will see that, in one case, a 2:1 complex is observed, which leads to a sandwich polymeric structure.

EXPERIMENTAL

Synthesis of poly(N, 2(hydroxy)propane [22] diazacrown ether), p[22]EpiC

6.8 ml (50.4 mmol) of triethylamine (Merk; distilled over KOH) and 3.95 ml (50.4 mmol) of epichlorohydrin (Prolabo, distilled before using) was added under nitrogen and stirred into a solution of 13.22 g (50.4 mmol) of diamine [22] (Kriptofix [22] (Merk, recrystallized in dry heptane) in 25 ml of dry methanol.

After 24 h of heating under reflux, the solvent was evaporated and the residue dried overnight under vacuum. The product was extracted with 3 x 100 ml dry THF. After evaporation of THF, 20 ml NEt_4OH solution (Merk) was added and this solution extracted with 5 x 500 ml chloroform. The product was obtained by evaporation of $CHCl_3$ and dried overnight under vacuum to yield 15 g (90%).

Tonometric analysis gave $M_n = 1500$, indicating an average of 4–5 ligand units in the polymeric chain.

Anal. calcd. for $H(C_{15}H_{30}N_2O_5)_4Cl$: C, 55.04; H, 9.24; N, 8.56; O, 24.44; Cl, 2.63. Found: C, 54.82; H, 9.90; N, 8.48; O, 24.70; Cl, 1.80.

Synthesis of poly(N, 2, 7(dihydroxy)octane [22] diazacrown ether), p[22]EpiO

4.07 g (28.6 mmol) of diepoxyoctane (Polysciences, distilled under reduced pressure before use) was added to a solution of 7.50 g (28.6 mmol) of diamine [22] in 18 ml of dry CH_3OH and 2 ml of dry THF under nitrogen and stirring. After heating under reflux for 72 h, the solvents were evaporated and the residue was extracted with 10 ml $CHCl_3$ and precipitated in 1 l heptane. After filtration and drying under vacuum, 10.6 g (90%) was obtained. G.p.c. analysis in THF gives $M_n = 4300$ with $M_w/M_n = 1.72$ indicating an average of 10 ligand units in the polymeric chain.

Anal. calcd. for $(C_{20}H_{40}N_2O_6)_n$: C, 59.38; H, 9.96; N, 6.93; O, 23.73. Found: C, 58.95; H, 9.90; N, 6.64; O, 23.63.

Potentiometric titrations

These were performed according to a procedure (7) described previously using an Orion-701 potentiometer, an

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Table 1 Chemical shifts of ^{13}C m.m.r. signals for p[22] EpiC with $Ba(NO_3)_2$ in D_2O at 70°C (in ppm) (22.63 MHz, TSM)

		Ligand: Ba^{2+} ratios		
Carbon	Free ligand	2:1	1:1	1:2
a	71.0	71.2	71.4	71.4
b	70.1	69.9	69.8	69.8
c	55.4	55.4	55.4	55.4
d	60.7	59.7	58.7	58.8
e	68.1	67.8	67.4	67.4

automatic Mettler titration apparatus, a combined Metrohm EA 120X electrode and a salt bridge containing 0.1 M NMe_4Cl solution. All measurements were performed under argon in a 20 ml microcell, thermostatically controlled at 20°C.

A back-titration procedure was used. The previously acidified solution of ligand was titrated with NMe_4OH in the presence of NMe_4Br (0.1 M) in order to maintain a nearly constant ionic strength. For the determination of the stability constants of the complexes, the titration was performed in the presence of excess cations (nitrate salts).

The analysis of the titration curves is performed by a computer program[8] adapted by Simon[9] and Vitali[10].

^{13}C n.m.r. spectroscopy

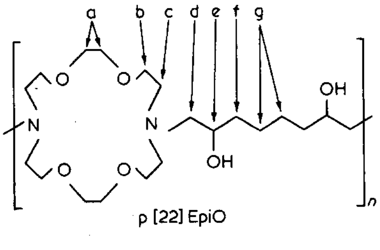
Spectra were run in 0.5 M solutions in D_2O at 70°C on a Bruker XG 90 spectrometer operating at 22.63 MHz. The spectral conditions were: pulse width, 6 μs; points 4K18 K; width 100 Hz; acquisition time, 6000 s. All chemical shifts were determined with TMS as a reference. EBuOH was added as an additional reference.

Viscosity measurements

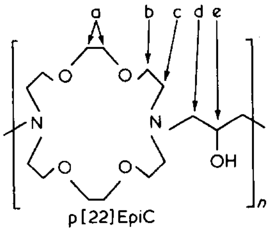
These were made in THF at 25°C in an automatic capillary viscometer[11].

RESULTS AND DISCUSSION

The polycondensation of the diamine [22] with epichlorohydrin or diepoxyoctane gives water-soluble polymers whose repeat unit structures are depicted below:



p [22] EpiO



p[22]EpiC

N.m.r. spectroscopy

^{13}C n.m.r. spectroscopy permits direct observation of the formation of the complexes between macrocycle compounds and cations[12]. The spectra of the free ligand and the complexes are different; and in operating with different cation: ligand ratios, it is possible generally to determine the stoichiometry of the complexes. Such experiments were done for the two polymeric ligands in D_2O with Ca^{2+} and Ba^{2+} cations. Some results showing the chemical shifts obtained as a function of the ligand: cation ratios are in *Tables 1, 2* and *3*.

For p[22] EpiO with Ca^{2+}, and p[22] EpiC with Ba^{2+}, a maximum shift is observed for a 1:1 complex. This is in agreement with results obtained with the monomeric analogue molecules[7]. For p[22] EpiO with Ba^{2+}, the maximum 2:1 stoichiometry is obtained. Further, a splitting of the spectrum is observed (*Figure 1*), indicating the coexistence of two species with a slow exchange typical of very stable complexes[12].

Viscosity behaviour

Considering the relatively high concentration (0.5 M) used in n.m.r. spectroscopy, it is possible that the formation of 2:1 complexes is the result of an intermolecular process. As n.m.r. measurements of more dilute solutions is difficult, we have studied the viscosmetric behaviour of the solutions. An intermolecular process must lead to the formation of a loose gel (high viscosity) or of aggregates (low viscosity); on dilution, the destruction of such structures must induce a dramatic change of viscosity. The intrinsic viscosity of the [22] EpiO polymer has been measured in water at pH 10 in the presence of a buffer and 0.1 M NMe_4Br. In the absence or presence of barium salt, a normal plot of reduced viscosity *versus* polymer concentration is observed; the dilution does not affect the configuration of the polymer. In addition, the $[\eta]$ value of 0.15 dl g^{-1} obtained without salt decreases to 0.12 dlg^{-1} in the presence of barium nitrate, whatever the ligand: Ba ratio (2:1 or 1:1). Firstly, the fact that the viscosity stays the same for 2:1 and 1:1 ratio confirms the n.m.r. result. Secondly, the decrease in viscosity in the presence of Ba^{2+} clearly indicates that there is a contraction of the polymer, as might be expected for the case of an intramolecular sandwich structure. In general cases, the binding of cations by a polymeric ligand leads to an increase of viscosity[5].

Table 2 Chemical shifts of ^{13}C n.m.r. signals for p[22] EpiO with $Ca(NO_3)_2$ in D_2O at 70°C (in ppm) (22.63 MHz, TSM)

		Ligand: Ca^{2+} ratios		
Carbon	Free ligand	2:1	1:1	1:2
a	71.4	70.9	70.4	70.4
b	70.3	70.2	70.0	70.0
c	55.6	54.8	54.1	54.1
d	62.4	62.2	62.1	62.1
f	36.1	35.7	35.3	35.3
g	26.5	26.3	26.1	26.1

Table 3 Chemical shifts of ^{13}C n.m.r. signals for p[22] EpiO with $Ba(NO_3)_2$ in D_2O at 70°C (in ppm) (22.63 MHz, TSM)

		Ligand: Ba^{2+} ratios		
Carbon	Free ligand	2:1	1:1	1:2
a	71.4	71.1 70.4	71.2 70.6	71.2 70.6
b	70.3	70.0 69.5	70.0 69.4	70.0 69.5
c	55.6	56.1 55.4	56.4 55.4	56.4 55.4
d	62.4	61.7 61.0	61.7 60.7	61.7 60.7
f	36.1	35.7	35.8	35.3
g	26.5	25.9	25.9	25.9

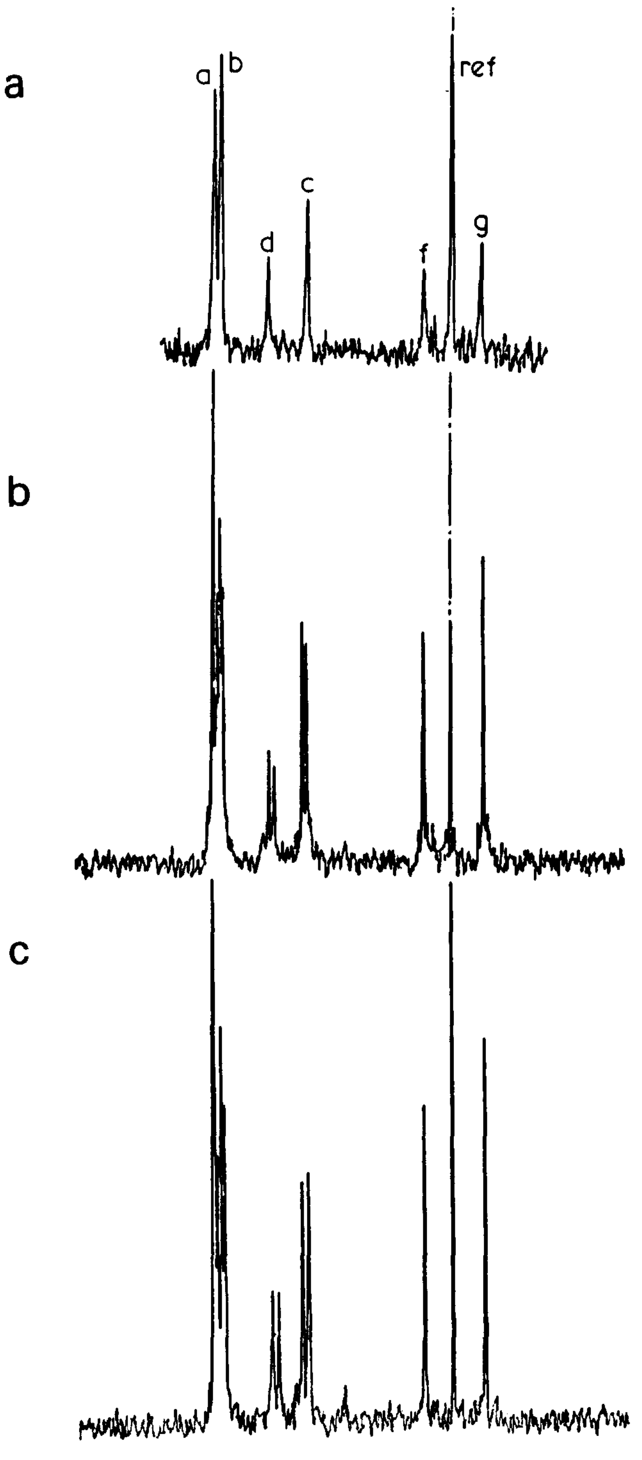


Figure 1 ^{13}C n.m.r. spectra of p[22] EpiO and its complexes with $BaNO_3$ in D_2O at 70°C (22.63 MHz, TSM). A, Free ligand; B, 2L: 1 Ba; C, 1L: 1 Ba or 1L: 2 Ba

In summary, n.m.r. and viscometric measurements demonstrate the formation of a polymeric sandwich complex with Ba^{2+}. To our knowledge, this is the first direct observation of such a structure in water. Of particular interest is that this unique structure is only obtained with the [22] EpiO polymer. This observation demonstrates that a ring size (r = 1.40 Å) too small to accommodate the cation is not a sufficient condition for 2:1 complex formation, and that the presence of flexible (CH_2) bridges permits and stabilizes the sandwich structure.

Stability constants

Using the fact that the nitrogen atoms of the ring participate in the complexation of cations and become more difficult to protonate, it is possible to determine the stability constants of complexes in water by potentiometric titrations[12]. A first titration without cations leads to the determination of the two basicity constants K_1 and K_2, corresponding to the equilibrium:

$$L + H^+ \overset{K_1}{\rightleftarrows} LH^+$$

$$LH^+ + H^+ \overset{K_2}{\rightleftarrows} LH_2^{2+}$$

with

$$K_1 = \frac{[LH^+]}{[L]\ [H^+]}$$

and

$$K_2 = \frac{[LH_2^{2+}]}{[LH^+]\ [H^+]}$$

A second titration in the presence of cations allows determination of the stability constants of the complexes according to the equilibrium:

$$L + M^{n+} \overset{K_{s1}}{\rightleftarrows} LM^{n+} \qquad (1)$$

$$LM^{n+} + L \overset{K_{s2}}{\rightleftarrows} LM^{n+}L \qquad (2)$$

with

$$K_{s1} = \frac{[LM^{n+}]}{[L]\ [M^{n+}]}$$

and

$$K_{s2} = \frac{[LM^{n+}L]}{[LM^{n+}]\ [L]}$$

Also

$$K'_{s2} = K_{s1} \times K_{s2}$$

(All the constants considered are 'concentration' constants assuming the activity coefficients of the species equal to one).

Table 4 Basicity constants of polymeric ligands and models in water at 20°C in presence of 0.1 M NMe_4Br

	Ligands			
	p[22] EpiC	[22] $(CH_3)_2^a$	p[22] EpiO	[22] $(EtOH)_2^a$
pK_1	8.33(4)	9.56(1)	8.76(2)	8.44(1)
pK_2	4.75(4)	7.59(1)	6.78(2)	6.88(1)

The values in parentheses are the standard deviations
[a] according to ref 7

Table 5 Stability constants, log K_s, of the poly(crown ether) complexes in water at 20°C in presence of 0.1 M NMe_4Br

Cation	Ionic radius (Å)	Log K_{s1}			
		[22] $(CH_3)_2$[a]	[22] $(EtOH)_2$[a]	p[22] EpiC	p[22] EpiO
Ca^{2+}	1.06	2.4	3.7	2.4	3.7
Sr^{2+}	1.27	4.2	4.3	2.9	4.2
Ba^{2+}	1.43	3.8	5.3	3.6	9.7[b]
Cu^{2+}	0.92			6.7	7.3
Cd^{2+}	1.03		7.1	5.6	6.6

[a] According to ref 7

[b] $K_{s'2'}$ calculated for 2:1 complex

However, the case of a polymeric ligand must be considered in more detail. A polyelectrolyte effect due to the interactions between the ionizable groups, affects the determination of pK; and only *apparent* pK can be calculated. For a non-macromolecular electrolyte with two ionizable groups, it can be demonstrated[13] that, at any moment of the titration, the concentration of free H^+ is given by:

$$pH = \frac{pK_1 + pK_2}{2} + \log\left[\frac{2(2-\bar{n})}{[R^2(1-\bar{n})^2 + 4\bar{n}(2-\bar{n})]^{1/2} - R(1-\bar{n})}\right] \quad (3)$$

with

$$\log R = \frac{pK_1 - pK_2}{2}$$

and

$$\bar{n} = \frac{H_0 - H}{L_0}$$

where L_0 is the initial concentration of ligand and H_0 the total concentration in H^+.

For a polyelectrolyte, equation (3) is not generally valid, and an additional term varying with the ionization degree must be added. The use of equation (3) leads here to *apparent* pK_1 and pK_2, whose values vary with $\bar{n}$. When the quantity pH −log[X] calculated from the experimental titration curves of the two polymers is plotted over $\bar{n}$, no variation is observed, showing that the two polymers do not exhibit typical polyelectrolyte behaviour. Although similar behaviour has been observed with polyamines containing diacylpiperazine groups[14], this independence of the repeating units is possibly due to the presence of the monocycles sheltering the positive charges on the protonated nitrogens.

In *Table 4*, the basicity constants of the two polymers are given, together with those previously obtained for the analogous molecules. It can be seen that the polymer structure does not influence the pK values of the [22] EpiO ligand containing the same unit as the analogue [22] $(EtOH)_2$. A lower basicity is observed for the second amine group of the polymer [22] EpiC; here, each crown unit is separated by only three carbons. The OH group in the middle can interact easily with the unprotonated nitrogen, leading to a decrease of its basicity.

Table 5 lists the pK_{s1} values of the polymeric ligand complexes with alkaline earth, Cu and Cd cations. K'_{s2} has been calculated for p[22] EpiO with Ba^{++}. Except for the latter case, the binding properties of the polymer p[22] EpiO are similar to those of the analogue [22] $(EtOH)_2$, showing that the polymeric chain does not affect the stability of the complexes formed with cations whose size is inferior to that of the ring. For [22] EpiC, the situation is more complex to analyse because the basic structure is between that of the two analogues. Strontium is poorly complexed and no explanation is evident.

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