

## MACROCYCLIC LIGANDS ON POLYMERS

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**Abstract:** The ion binding properties of linear polymers carrying crown ether ligands as pendent groups are reviewed. The polymers often exhibit selective cation binding different from that of their monomeric crown analogues. One of the polymers, poly(vinylbenzo-18-crown-6), behaves in water as a neutral poly-soap and strongly interacts with organic anions. The binding is enhanced and also can be regulated by charging the polymer with crown complexable cations. This polymer also catalyzes solvent sensitive reactions by a micellar type mechanism. In the decarboxylation of 6-nitrobenzisoxazole-3-carboxylate in water the substrate bound to the  $\text{Cs}^+$  charged poly(crown ether) decomposes 14000 times more rapidly than in water. In benzene the decarboxylation is also accelerated by poly(crown ethers), but in this case as a result of anion activation. Poly-(crown ethers) were also found to form polysalt complexes in water with several polyanions in the presence of crown complexable cations. In the absence of salts, complexes can be formed with polyacids through hydrogen bonding.

### INTRODUCTION

The development of macrocyclic ligands of the crown ether (1) or cryptand (2) type and of the acyclic podands (3) has been of interest to investigators in many fields of chemistry. These compounds, with their multiple and strategically located binding sites, are especially effective in the selective complexation of spherical cations, notably the alkali and alkaline earth cations, both of which play a vital role in many chemical and biological processes. Moreover many of the macrocyclic ligands interact with organic cations such as primary ammonium and diazonium ions, and even with neutral molecules such as urea and acetonitrile. The synthesis of macrocycles with chiral recognition properties (4-7) has extended their use to the resolution of racemic mixtures and to the mimicry of enzyme systems (8,9). Further developments in macrobicyclic and tricyclic cryptands (2) led to anion inclusion complexes (10) as well as binuclear complexes where small molecules can be inserted between two bound cations fixed at a specific distance in the cryptate complex (11).

Physical and chemical properties of ions and ion pairs frequently change on interaction with ligands such as their solubility in apolar media, their conductivity behavior, optical spectrum, dipole moment, nuclear magnetic and electron spin resonance spectrum, reactivity, etc. In media where ion pairing is dominant the binding of a macrocycle to the cationic part of an ion pair may result in the formation of a more ionic bond, a breakdown of aggregates, a change in interionic ion pair distance or free ion dissociation, or a combination of these (12-15). This in turn can dramatically affect the reactivity of carbanions, alkoxides, sulfides, carboxylates and other nucleophiles, particularly in non-anion solvating media (15,16). Numerous studies on the structure of ion and ion pair complexes with macrocyclic ligands in both solid state and solution have been published, and other applications in the field of mediated ion transport, ion exchangers and catalysts for organic reactions are well documented.

In several applications the ligands have been anchored to polymeric networks to facilitate quick recovery of the chelating agents and to prevent product contamination by the ligands which are often difficult to remove. Such materials have been developed, among others, by Blasius and his coworkers (17) and by Montanari et al (18) for ion exchange purposes and as catalysts. In our own work dealing with poly(crown ethers) we have chiefly been concerned with the development and study of well characterized linear polymers containing crown ligands as pendent groups (polymers with crown moieties incorporated in the backbone of the macromolecule have also been reported (19)). Attaching crown ligands to a polymer chain can change their cation binding properties due to the proximity of other crown ligands or comonomer substituents. Also, the dissolution of the neutral poly(crown ethers) in a salt solution of crown complexable cations produces a polycation of variable charge density, depending on the nature of the cation, the salt concentration, solvent and temperature. Systems of this kind are useful to study ion and ion pair binding to neutral macro-

molecules and the factors affecting such interactions. In the course of these investigations it was observed that one of the polymers, poly(vinylbenzo-18-crown-6), behaves as a polysoap when dissolved in water, binding organic anions to its apolar polymer domain. This binding, hydrophobic in nature in the absence of charge on the polymer, can be regulated by crown complexable cations. When the organic anion undergoes a solvent dependent reaction, such as the decarboxylation of 6-nitrobenzisoxazole-3-carboxylate, the polymer acts as a catalyst by binding the anion to a more reactive environment. In this paper we will discuss some of the interesting properties of poly(crown ethers) pertaining to their cation and especially anion binding, their catalytic properties, and their tendency to form polysalt complexes in aqueous media.

#### SYNTHESIS AND CATION BINDING PROPERTIES OF POLY(CROWN ETHERS)

The two crown monomers most frequently used in our work are 4'-vinylbenzo-15-crown-5 and 4'-vinylbenzo-18-crown-6, the synthesis of which were reported (20,21). The monomers easily convert to linear high molecular weight polymers by a normal radical (ABIN/benzene) or anionic living polymer type (in tetrahydrofuran at low temperature) polymerization (20). The two homopolymers have been abbreviated as P15C5 and P18C6 (Figure 1A). Random type

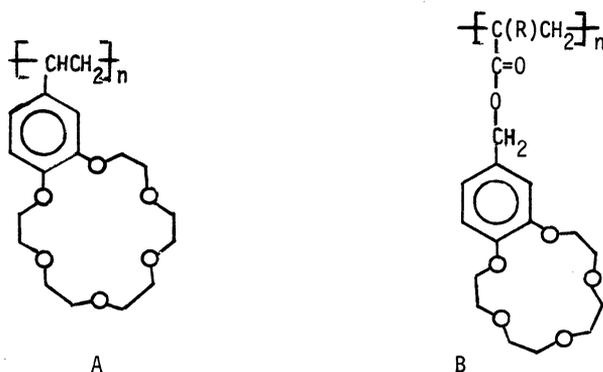


Figure 1: Structures of poly(vinylbenzocrown ethers) and poly(crown acrylates).

copolymers of the vinyl(crown ethers) with styrene were made radically, the reactivity ratios being close to unity (22). Block copolymers can be synthesized by anionic polymerization with styrene, vinylpyridine, ethyleneoxide or methylmethacrylate as comonomer. Also prepared were crown ester monomers derived from acrylic and methacrylic acid, and the polymers of which (Figure 1B) were used in the study of polysalt complexes (23). Most polymers used in our work had number average molecular weights in the range of 35,000 to 100,000. The poly(vinylbenzocrown ethers) are soluble in solvents such as benzene, chloroform and tetrahydrofuran, but fair to poor in the more polar solvents, an exception being the rather high solubility of P18C6 in water, 8 g/100 ml (20). The latter polymer exhibits inverse temperature solubility in water, the cloud point being 37<sup>o</sup> C. Its micellar character causes it to bind organic molecules.

The neutral poly(crown ethers), when dissolved in a solution of crown complexable cations are converted into polycations as demonstrated by the strong enhancement of the reduced viscosity on lowering the concentration of the polymer-salt mixture. This behavior, typical for a polyelectrolyte, is depicted in a somewhat different fashion in Figure 2, where  $\eta_r$  is plotted versus the cation to crown ratio. The increased charge density on the polymer at higher cation to crown ratios expands the chain but this is eventually offset by the screening effect of the counterions, causing  $\eta_r$  to pass through a maximum. The value of this maximum increases in the order  $\text{Na}^+ < \text{K}^+ < \text{Cs}^+$  for P18C6 and  $\text{Na}^+ < \text{Cs}^+ < \text{K}^+$  for P15C5. These orders reflect the binding efficiencies of the two polymers for the respective cations, a result confirmed from conductance data in methyl ethyl ketone (22) as well as from potentiometric (24), optical (25) and extraction (20,26) measurements. The high binding constants found for P15C5/ $\text{K}^+$  and P18C6/ $\text{Cs}^+$  result from the cooperative effect of two ligands interacting with the same cation. Such sandwich type complexes are frequently found when the cation diameter exceeds that of the crown cavity, e.g., for benzo-15-crown-5  $\text{K}^+$  (27) or for 18-crown-6/ $\text{Cs}^+$  (28).

The binding of a cation to a poly(crown ether) may differ considerably from its binding to the corresponding monomeric crown ether, even when only 1:1 complexes are formed. For example, the binding constant for  $\text{Na}^+$  to 4'-methylbenzo-18-crown-6 in water is 27  $\text{M}^{-1}$  compared with only 1.2 for P18C6, most likely as a result of different desolvation requirements for the cation prior to the binding (24). Moreover, the binding decreases as the charge density on the poly(crown ether) increases (see below). In a non-cation

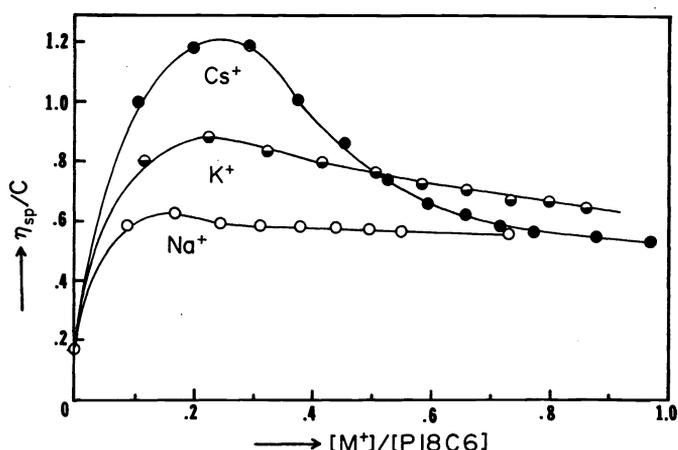


Figure 2: Dependence of reduced viscosity of P18C6 on the cation to crown ratio for different cations; solvent: THF/MeOH (1/1 by volume);  $T = 25^{\circ}\text{C}$ ;  $[\text{P18C6}] = 0.106\text{ g/dl}$ ; (●)CsCl; (◐)KCl; (○)NaCl.

solvating medium the binding constants for corresponding monomeric and polymeric crown ethers do not differ much as long as 1:1 complexes are formed, the charge density on the polymer is low, and no other groups in the polymer chain interfere with the binding. This is demonstrated from extraction experiments involving the picrate salt/ $\text{H}_2\text{O}/\text{CHCl}_3$  system, some of the data being shown in Table I (26). Note that the constant  $K_e$

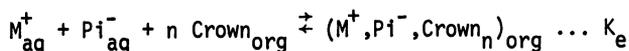
Table I. Extraction Equilibrium Constants of Sodium and Potassium Picrate for  $\text{H}_2\text{O}/\text{CHCl}_3$  at  $20^{\circ}\text{C}$  with Crown Ethers and their Polymers (Ref. 26)<sup>a</sup>

Crown <sup>b</sup>	$K_e \times 10^{-3} \text{ M}^{-2}$	
	Sodium Picrate	Potassium Picrate
B15C5	3.7	0.42
P15C5	5.5	2.3
SP15C5 (20%)	4.1	45
B18C6	2.3	240
P18C6	5.6	550
SP18C6 (20%)	1.7	150

<sup>a</sup> $[\text{NaPi}]$  in water  $10^{-2}\text{ M}$ ;  $[\text{KPi}] = 10^{-3}$  to  $3 \times 10^{-3}\text{ M}$ ;  $[\text{Crown}]$  in  $\text{CHCl}_3$  between  $10^{-4}$  and  $4 \times 10^{-4}\text{ M}$ .

<sup>b</sup>B15C5 refers to 4'-methylbenzo-15-crown-5; SP15C5 (20%) denotes a copolymer of styrene with 20 mole percent of 4'-vinylbenzo-15-crown-5, etc.; see also text.

which describes the equilibrium



does not significantly change when the polymeric crown ethers are replaced by the two monomeric analogues 4'-methylbenzo-15-crown-5 and 4'-methylbenzo-18-crown-6. Some assistance of neighboring oxygen atoms in the cation binding may be indicated from the somewhat higher values obtained for the homopolymers. On the other hand, larger differences are found when a 2:1 crown cation complex is formed such as for  $\text{K}^{+}$  with the 15-crown-5 polymers (Table I). The close proximity of the two crown ligands facilitates formation of the sandwich type complexes. Experiments with bis(crown ethers) containing two crown ligands at each end of a short chain reveal that an optimum distance exists

between the ligands for maximum cation binding efficiency (29). This is also apparent from the higher binding constants found for the SP15C5 (20%) copolymer compared with the homopolymer. Steric hindrance in the latter polymer on complexing  $K^+$  may also be a problem.

The complex between a cation and a crown polymer may be intra or intermolecular when two ligands are involved. The latter mode leads to cross linking and high viscosities of the polymer solutions. The probability of intermolecular complexation, at constant polymer concentration increases at higher crown content of the polymer chain. It also is enhanced when at constant crown concentration the spacing between crown ligands on a chain is increased. The first effect is demonstrated in Figure 3, showing a greater maximum viscosity at constant polymer concentration for a polymer with higher crown content. As expected, the maximum occurs at a cation to crown ratio close to 0.5. At higher ratios the 2:1 complexes are replaced by 1:1 complexes, thereby removing the crosslinks.

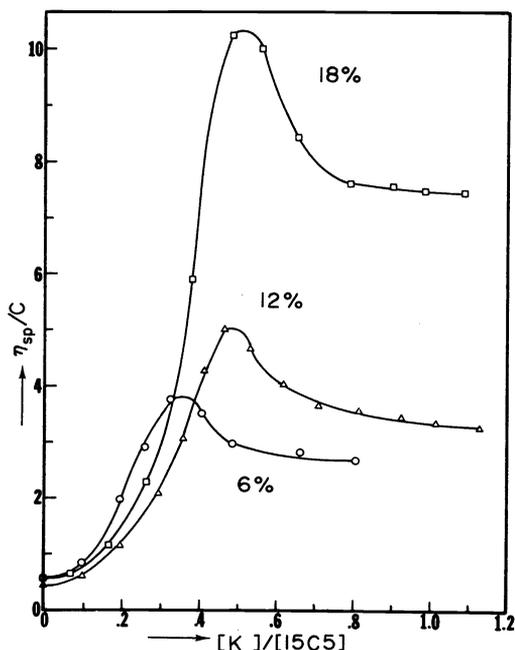


Figure 3: Dependence of reduced viscosity of styrene/vinylbenzo-15-crown-5 copolymers (SP15C5) on the cation to crown ratio (molar ratio of  $KBPh_4$  to crown monomer units). Solvent: methyl ethyl ketone;  $T = 25^\circ C$ ;  $[Polymer] = 8 \text{ g/dl}$  (O)SP15C5 (6%); ( $\Delta$ )SP15C5 (12%); ( $\square$ )SP15C5 (18%).

#### BINDING OF ORGANIC SOLUTES TO POLY(CROWN ETHERS)

Several non-ionic polymers are known to bind organic solutes in aqueous media, the best known examples being poly(vinylpyrrolidone) (30-32) and bovine serum albumin (33,34). The driving force of the binding is frequently hydrophobic in nature, but electrostatic forces, charge transfer interactions and hydrogen bonding may play a role as well. While exploring the anion dependence of the cation binding to P18C6 in water we observed a shift in the spectrum of picrate anions on addition of P18C6 (25,35). Further investigations showed an unusual strong affinity of P18C6 for organic anions such as picrate, tetraphenylboron, dodecylsulfate, dyes, etc. As pointed out earlier, P18C6 has a comparatively high solubility in water in spite of its polystyrene backbone, and exhibits inverse temperature solubility. Its low intrinsic viscosity suggests that in water the polymer assumes a tightly coiled conformation. It resembles a micelle with an apolar polystyrene like core and with crown units exposed to the solvent to keep the particle in solution by hydrogen bonding of crown oxygen atoms to water molecules.

The binding of picrate anions can be measured spectrophotometrically, the absorption maximum of the bound species being 384 nm as compared to 355 nm in water. The absorption band of the bound anion is nearly identical to that of the free picrate anion or of its

loose ion pair in solvents such as THF or acetone. Several other organic species undergo spectral shifts on binding such as 2-cyano-5-nitrophenolate (the decomposition product of 6-nitrobenzisoxazole-3-carboxylate), methyl orange, phenolphthaleine, chrysophenine and 2-(4'-hydroxybenzeneazo)benzoate. A hypsochromic shift is found for methyl orange from 460 nm in water to 435 nm for the bound anion. The interactions with P18C6, at least for picrate and methyl orange, can be described by a rearranged form of the Langmuir isotherm (36)

$$1/r = 1/n + 1/nKa \quad (1)$$

where  $1/r$  is the ratio of total crown monomer base units to bound solute,  $a$  denotes the free solute concentration and  $1/n$  represents the minimum number of crown units required to bind a solute molecule. The constant  $K$  is the intrinsic binding constant and  $K_1 = nK$  is the first binding constant. As long as no cations are bound to P18C6 under the prevailing conditions, plots of  $1/r$  versus  $1/a$  are found to be good straight lines for both picrate and methyl orange over a temperature range of 5° C to 35° C. The linear relationship means that binding of an anion to P18C6 is not affected by already bound anions. This is not surprising since at 25° C a maximum of only 5 picrate anions and even less methyl orange anions can be bound to a polymer of DP 200, hence mutual anion repulsion can probably be neglected.

Intrinsic binding constants for picrate and methyl orange to P18C6 are given in Table II, together with the  $1/n$  values and the thermodynamic parameters. The affinity of neutral P18C6 for organic solutes compares favorably with that of bovine serum albumin and poly(vinylpyrrolidone). The binding constant,  $K_1^*$  of methyl orange with P18C6 is larger by factors 12 and 5, respectively, compared with the two latter polymers. The considerable increase in entropy on binding methyl orange to P18C6 is consistent with results reported for other polymers, and indicates that the interaction is hydrophobic in nature. The binding of picrate is exotropic, and more exothermic than for methyl orange. Charge transfer or polar forces may play here a more dominant role, as has also been found in the binding of *p*-nitrophenolate to  $\alpha$ -cyclodextrin (37) and for other dyes (38).

Table II. Binding Constants of Sodium Picrate and Methyl Orange to Poly(vinylbenzo-18-crown-6) in Water (Ref. 25)<sup>a</sup>

Temp °C	$K \times 10^{-3} M^{-1}$	$K_1 \times 10^{-3} M^{-1}$	$K_1^* \times 10^{-3} (10^5 \text{ g})$	$1/n$
<u>Sodium Picrate</u>				
$\Delta H = -11.9 \pm 1 \text{ kcal/mole}; \Delta S = -17 \pm 4 \text{ e.u.}$				
35	51	1.17	347	44
25	134	3.19	945	42
17.5	170	4.85	1430	35
0	673	20.9	6190	32
<u>Methyl Orange</u>				
$\Delta H = -3.9 \pm 0.2 \text{ kcal/mole}; \Delta S = 9.7 \pm 1.5 \text{ e.u.}$				
25	96	1.13	334	85
15	118	1.28	379	92
5	152	1.71	504	89

<sup>a</sup>The constants  $K, K_1$  and  $K^*$  refer to the intrinsic binding constant in  $M^{-1}$ , the first binding constant in  $M^{-1}$  and the first binding constant expressed in  $10^5 \text{ g}$  of polymer, respectively.  $\Delta H$  and  $\Delta S$ , calculated from  $\log K$  vs  $1/T$  plots, refer to the reaction: solute + P18C6  $\rightleftharpoons$  P18C6 bound solute.

The values of  $1/n$  are large, especially for methyl orange. For a P18C6 chain of  $DP \approx 200$  ( $M_n = 67000$ ) a maximum of only five picrate anions can be accommodated and only two to three for methyl orange. The same values are obtained by measuring the amount of solute bound under saturation condition, i.e., at high solute concentration. It is not certain what determines  $1/n$ , but anion size may be an important factor. The tightly coiled chain must slightly expand to accommodate the solute molecules and this requires energy. This may be one reason why  $1/n$  is smaller (i.e., more anions can be accommodated) at lower temperatures or when the polymer chain is charged with cations. Under these conditions the chain slightly expands as shown from viscosity measurements.

Cation effect on solute binding. One of the unique features of P18C6 in comparison with other solute binding polymers concerns its ability to regulate the absorption of organic anions by means of crown complexable cations. The positive charge density will superimpose on the hydrophobic interaction an electrostatic force which then greatly enhances the

binding of anions. The extra amount of anion bound, at least in the case of picrate anions, is nearly proportional to the charge density on the polymer chain as expressed in terms of the number of cations bound divided by the total number of available crown ligands (39). The extent of anion binding is cation specific since cation binding to P18C6 differs significantly. Potentiometric measurements (24) yield binding constants in water of  $1.2 \text{ M}^{-1}$  for  $\text{Na}^+$ ,  $35 \text{ M}^{-1}$  for  $\text{K}^+$  and  $110 \text{ M}^{-1}$  for  $\text{Cs}^+$  (the latter actually is determined spectrophotometrically (25)). These values vary with charge density. For example, more detailed measurements on the system P18C6/KCl in water reveal that the binding constant of  $\text{K}^+$  to P18C6 changes from  $55 \text{ M}^{-1}$  at about zero charge density to a nearly constant value of  $20 \text{ M}^{-1}$  above a ratio of  $\text{K}^+$  bound/(crown total) equal to 0.15. The values are nearly independent of ionic strength, at least up to  $0.5 \text{ M LiCl}$  (39).

The effect of addition of  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Cs}^+$  and  $\text{NH}_4^+$  on picrate binding is depicted in Figure 4. Picrate absorbed in the absence of salt represents the amount bound to the neutral polymer at  $[\text{Pi}] = 1 \times 10^{-5} \text{ M}$  and  $[\text{P18C6}] = 5 \times 10^{-4} \text{ M}$ . Even small quantities of  $\text{Cs}^+$  are sufficient to affect complete binding of picrate, assuming of course that no saturation

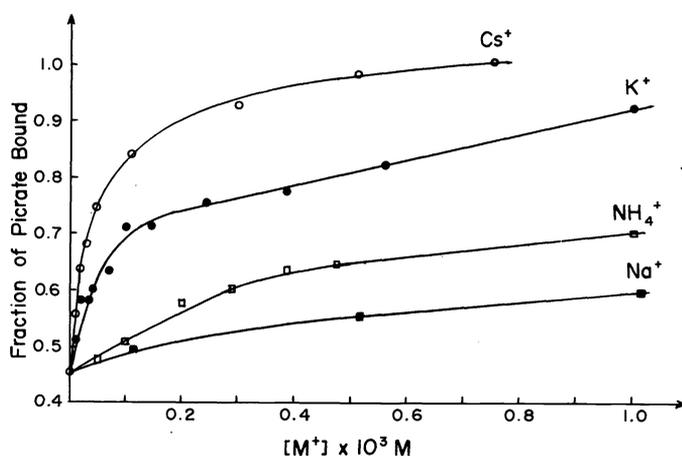


Figure 4: Effect of different cations on the fraction of sodium picrate bound to P18C6 in water;  $[\text{NaPi}] = 1 \times 10^{-5} \text{ M}$ ;  $[\text{P18C6}] = 5 \times 10^{-4} \text{ M}$ ; (O) CsCl; (●) KCl; (□)  $\text{NH}_4\text{Cl}$ ; (■) NaCl;  $T = 25^\circ \text{ C}$ . (Ref. 25).

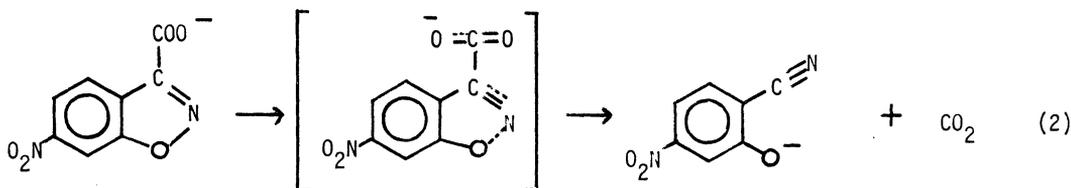
occurs, i.e.,  $[\text{P18C6}]/[\text{Pi}] > 1/n$ . The efficiency of different cations to promote anion binding reflects their ability to complex with P18C6. The plot of Figure 3 may be used to measure spectrophotometrically the binding constants of those cations which cannot easily be determined potentiometrically. The quantity of bound picrate can be correlated with the charge density,  $\text{K}^+$  bound/total crown (calculated from the known binding constant of  $\text{K}^+$  to P18C6). For any monovalent cation,  $\text{M}^+$ , the amount of picrate bound is then determined as a function of  $[\text{M}^+]$ . Assuming that the electrostatic potential generated by the cation binding is cation independent and only a function of the number of charges, given by  $\text{DP} \times \text{ratio bound } \text{M}^+/\text{total crown}$ , one can calculate this ratio at different  $\text{M}^+$  concentrations by comparing the quantity of bound picrate with that bound in the presence of  $\text{K}^+$ . In this way one arrives at  $K(\text{Na}^+) = 1.4 \text{ M}^{-1}$ , close to the potentiometric value  $1.2 \text{ M}^{-1}$ . Compared at the same total salt concentration the order of binding to P18C6 is  $\text{Cs}^+ > \text{Rb}^+ \sim \text{Tl}^+ > \text{K}^+ > \text{NH}_4^+ > \text{Ag}^+ > \text{Na}^+ \gg \text{Li}^+$ . This sequence roughly parallels the hydration enthalpies of the ions.  $\text{Mg}^{++}$  and  $\text{Ca}^{++}$  have little effect on the binding, but  $\text{Ba}^{++}$  is comparable to  $\text{K}^+$ . Actually, at lower salt concentrations  $\text{Ba}^{++}$  is more effective than  $\text{K}^+$  when the amount of bound picrate is plotted as a function of salt concentration. For equal ratios of bound cation to total crown the electrostatic potential is, of course, twice as high for  $\text{Ba}^{++}$  as for  $\text{K}^+$ .

It may be interesting to mention that while at  $0.1 \text{ M KCl}$  all picrate is bound at  $[\text{P18C6}] = 5 \times 10^{-4} \text{ M}$  and  $[\text{Pi}] = 1 \times 10^{-5} \text{ M}$ , spectral observations indicate that the fraction of bound picrate appears to decrease considerably above  $0.3 \text{ M KCl}$ . The same has been found for other anions such as 2-cyano-5-nitrophenolate. However, dialysis experiments show that no picrate is released. Apparently, the high charge density on P18C6 at high KCl concentration eventually forces the chain to slightly expand. This permits water molecules to penetrate the polymer domain and to hydrate at least some of the picrate anions, causing the

spectrum to change. Picrate anions can easily be removed from the polymer domain by anions such as dodecyl sulfate or tetraphenylboron, even at very low concentrations of these solutes. Such experiments make it possible to measure the binding constants of anions whose spectra do not change on binding.

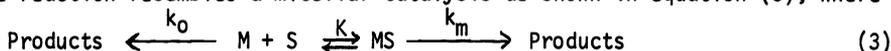
#### CATALYSIS WITH POLY(CROWN ETHERS)

**Catalysis of solvent sensitive reactions.** The property of P18C6 to bind solutes in water induced us to evaluate its effectiveness to catalyze solvent sensitive reactions. Several such reactions are known, and we chose the decarboxylation of 6-nitrobenzoxazole-3-carboxylate (equation 2), a clean unimolecular reaction whose product, 2-cyano-5-



nitrophenolate, can easily be monitored spectrophotometrically. The reaction, studied in detail by Kemp et al. (40,41) is a concerted intermediateless  $E_2$  elimination, slow in water, more rapid in media such as benzene and tetrahydrofuran, and extremely fast in hexamethylphosphoramide, the difference in rate constant between the latter solvent and water being a factor  $10^8$ . Catalysis in water was already accomplished by means of cationic micelles such as cetyltrimethylammonium bromide (42,43) and more recently by synthetic polymers (44,45).

Addition of P18C6 to an aqueous solution of the carboxylate does indeed speed up the decomposition as a fraction of the anion becomes bound to the more reactive polymer domain (35,46). The reaction resembles a micellar catalysis as shown in equation (3), where S



and MS refer to the free and bound carboxylate, respectively,  $M = [C]/N$  denotes the concentration of "free binding sites," C the [free crown ligand] and N the number of crown units involved in the binding of a carboxylate anion. K denotes the intrinsic binding constant of carboxylate to P18C6, and  $k_0$  and  $k_m$  are the respective decarboxylation rate constants for free and bound anion. When only a small fraction of binding sites are occupied, the observed rate constant  $k(\psi)$  is given by equation (4). If conditions are chosen such that

$$\frac{1}{k_\psi - k_0} = \frac{1}{k_m - k_0} + \frac{N}{(k_m - k_0) K C} \quad (4)$$

the total carboxylate concentration,  $S_0$ , far exceeds that of the available binding sites, i.e.,  $S_0 \gg C_0/N$ , the steady state relationship shown in equation (5) is valid:

$$C_0 / (k_\psi - k_0) = N / k_m K + N S_0 / k_m \quad (5)$$

A detailed investigation (46) reveals that both equations are obeyed in the P18C6/water/carboxylate system. By combining the results of equations (4) and (5) the binding constant K and the ratio  $N/k_m$  are obtained. N was found to be nearly identical to the  $1/n$  value reported for picrate binding (Table II). K and  $k_m$  values are shown in Table III. The rate constant  $k_0$  in water at 25° C is only  $3 \times 10^{-6} \text{ sec}^{-1}$ . Note that the binding constant for carboxylate is much lower than for picrate (Table II), apparently as a result of a lower binding entropy,  $\Delta S$  being -26 e.u. and  $\Delta H = -11.3 \text{ kcal/mole}$ . The catalytic factor for neutral P18C6, given by  $k_m/k_0$ , is equal to 2300 at 25° C. The  $\Delta H^\ddagger$  is 21.1 kcal/mole and  $\Delta S^\ddagger$  is 2.3 e.u. compared to  $\Delta H^\ddagger = 32 \text{ kcal/mole}$  and  $\Delta S^\ddagger = 19 \text{ e.u.}$  in water.

**Effect of cation.** Carboxylate binding, similar to picrate, can be regulated by crown complexable cations.  $\text{Cs}^+$ , as expected from the picrate results, is the most effective cation in promoting the catalytic effect of P18C6. In Figure 5 the observed rate constant  $k(\psi)$  is plotted versus the salt concentration. For ratios [P18C6]/[carboxylate] = 20 the binding sites become saturated, but enough are available at a ratio of 50, and under these conditions the maximum rate constant  $k_m$  at 25° C obtained with CsCl is larger by a factor 14000 compared with the decarboxylation rate constant in water. This acceleration is considerably higher than previously found for ordinary micelles (highest catalytic factor reported is 400 (42) and also larger than for laurylated polyethylenimines (a factor of 1300 was found for this system) (44). The high reactivity results from the

Table III. Intrinsic Binding Constants and Decarboxylation Rate Constants for 6-Nitrobenzoxazole-3-carboxylate Bound to Poly(vinylbenzo-18-crown-6) in Water (Ref. 46)

Temp °C	[KCl] × 10 <sup>3</sup> , M	[CsCl], M	k <sub>m</sub> × 10 <sup>4</sup> , sec <sup>-1</sup>	K, M <sup>-1</sup>
5			5.96	1350
5		0.2	55	
15			21.3	720
15		0.2	154	
25			69	340
25		0.2	420	
25	0.50		60	610
25	1.00		92	780
25	2.00		89	~2500
25	4.00		110	

binding of carboxylate to a more reactive environment, and it is worth noting that the k<sub>m</sub> of carboxylate bound to neutral P18C6 is close to the decarboxylation rate constant found by Kemp *et al* in benzene (40). The even higher reactivity of Cs<sup>+</sup> charged P18C6 (activation parameters ΔH<sup>‡</sup> = 16.1 kcal/mole and ΔS<sup>‡</sup> = -10.7 e.u.) is consistent with results of other investigators involving positively charged micelles and polymers (42,44). The decrease in k(ψ) observed at very high salt concentration (see Figure 4) may be of the same origin as suggested earlier for a similar phenomenon involving the picrate spectrum. The highly charged polymer may slightly swell, permitting water molecules to stabilize some of the bound carboxylate.

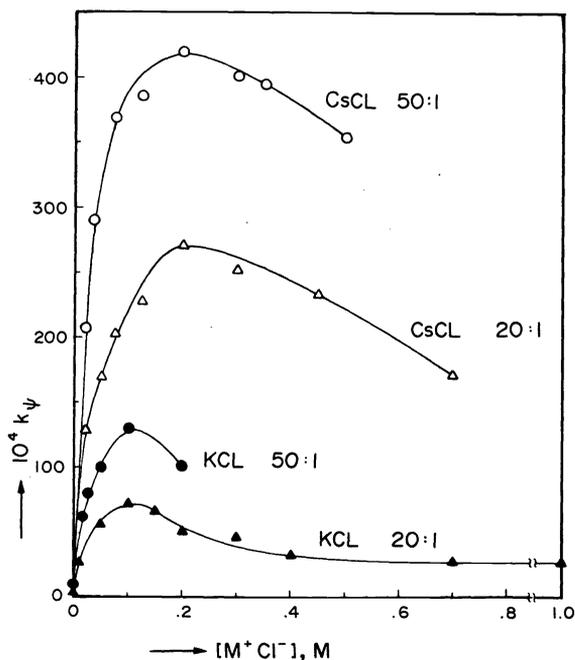


Figure 5: Observed rate constant,  $k_{\psi}$ , of decarboxylation of 6-nitrobenzoxazole-3-carboxylate in water in the presence of P18C6 as a function of salt concentration at different ratios  $r = [\text{P18C6}]/[\text{carboxylate}]$ ;  $T = 25^{\circ}\text{C}$ ; (○) CsCl,  $r = 50$ ; (Δ) CsCl,  $r = 20$ ; (●) KCl,  $r = 50$ ; (▲) KCl,  $r = 20$ . (Ref. 46).

**Catalysis by anion activation.** Most studies on the catalytic effect of crown ethers involve their role as anion activators (15). We have studied the decarboxylation reaction (equation 2) in benzene in the presence of 4'-methylbenzo-18-crown-6 (MB18C6)

and of copolymers of styrene and 4'-vinylbenzo-18-crown-6 (47). The potassium carboxylate is formed on mixing potassium-*t*-butoxide and 6-nitrobenzoxazole-3-carboxylic acid in benzene, but the reaction cannot be observed in the absence of crown as the salt appears to precipitates. The solution remains homogeneous when excess crown is present (either in the acid or butoxide solution). The decarboxylation into the phenolate (equation 2) is independent of crown, butoxide or acid concentration as long as butoxide and crown are in excess. This indicates that the carboxylate is formed instantaneously. The rapid, unimolecular decomposition can be monitored in a Durrum stop flow spectrophotometer. The results are shown in Table IV.

Table IV. Effect of Benzo-18-crown-6 Content on the Poly(Crown Ether) Catalyzed Decarboxylation of Potassium-6-Nitrobenzoxazole-3-carboxylate in Benzene at 25° C<sup>a</sup>

% crown	k, sec <sup>-1</sup>	$\lambda_m^b$
MB18C6	0.14	444
1.65	0.13	444
5.5	0.13	445
9.1	0.17	446
19.1	0.21	447
47.9	0.54	448
100	0.90	450
cryptand 2,2,2	4.8	454

<sup>a</sup>Conditions: [Acid] =  $5 \times 10^{-4}$  M; [*t*-butoxide] =  $2 \times 10^{-3}$  M; [crown] =  $5 \times 10^{-3}$  M. For the 1.65% and 5.5% copolymers all concentrations were lower by a factor 4. MB18C6 refers to 4'-methylbenzo-18-crown-6 and crown percentages are mole percent of 4'-vinylbenzo-18-crown-6 monomer in their copolymers with styrene.

<sup>b</sup>Wavelength maximum of the product, potassium 2-cyano-5-nitrophenolate in the reaction mixture.

The data show a higher rate constant at increased crown content in the polymer, but compared with the monomeric analogue MB18C6 the rate enhancement is only a factor seven. The increase is probably associated with a slight increase in the interionic ion pair distance of the bound carboxylate as a higher crown content will make it sterically more difficult for the anion to associate with the bound cation. An increased ion pair distance would tend to destabilize the reactant more than its delocalized transition state. The larger ion pair distance for the reactant cannot be observed directly, but the effect is apparent in the phenolate product (Table IV). Its absorption maximum shifts to higher wavelength on increasing the crown content. Such shifts are frequently associated with an increased interionic ion pair distance (13) and was also observed for picrate salts (26). The increase in rate could in part be a result of a changing environment since the carboxylate will be close to the oxygen containing crown ligands but any such effect would be much smaller than observed in the aqueous system (previous section). We attempted to use copolymers of styrene and 4'-vinylbenzo-15-crown-5 since polymers with a 15-crown-5 moiety form 2:1 complexes with K<sup>+</sup> and tend to form loose ion pairs with salts such as picrates (26,29). However, precipitation occurred in all these systems, and no reliable measurements were possible. A rather large increase in interionic distance can be accomplished by adding cryptand 2,2,2 (note the higher absorption maximum for the cryptated phenolate product). The cryptated carboxylate ion pair has a decarboxylation rate constant of 4.7 sec<sup>-1</sup> (or 8.7 sec<sup>-1</sup> at 30° C) more than 30 times higher than found for the MB18C6 complexed ion pair (Table IV). It is also about 2000 times higher than the decarboxylation rate constant reported in benzene by Kemp et al ( $k \approx 5 \times 10^{-3}$  sec<sup>-1</sup> at 30° C). Their value refers to the carboxylate salt with tetramethylguanidinium as counterion. Apparently the latter salt is a rather tight ion pair in benzene.

#### POLY(CROWN ETHER) COMPLEXES WITH MACROMOLECULES

Polysalt complexes. Formation of complexes between polyions of opposite charge is a phenomenon common to both synthetic and natural polymers (48). In the course of an investigation on the biological activity of poly(vinylbenzo-18-crown-6) it was observed that this water soluble polymer strongly inhibits the reverse transcriptase activity of virions of murine leukemia (49). The neutral poly(crown ether) interacts with poly(riboadenylate) and renders it inactive as a template for the elongation of nucleotides. When crown complexable cations such as K<sup>+</sup> are present the charged poly(crown ether) coprecipitates with the poly(riboadenylate) as a polysalt complex.

More recent work (23,24) has demonstrated that in the presence of certain salts P18C6 as well as poly(crown acrylates) form insoluble polysalt complexes with polyanions such as sodium carboxymethylcellulose (CMC), poly(styrenesulfonate) and poly(acrylates). In addition to variables such as chain length, charge density, chain conformation and chain flexibility, charge equivalence constitutes an important factor in controlling the formation and ultimate structure of a polysalt complex (48). This appears to be also the case in our systems. For example, addition of KCl to an aqueous, homogeneous mixture of CMC and P18C6 with a ratio of crown/COO<sup>-</sup> = 2 produces an insoluble complex, with maximum precipitation occurring at 0.1 M KCl. At higher KCl concentration the amount of precipitated P18C6 decreases again until at 0.5 M KCl the solution remains clear. As depicted in Figure 6, the [KCl] at which the maximum is reached depends on the initial ratio CMC/P18C6. Note that at a low ratio a decrease in [KCl] causes increased P18C6 precipitation, while at higher CMC/P18C6 ratios the reverse is observed.

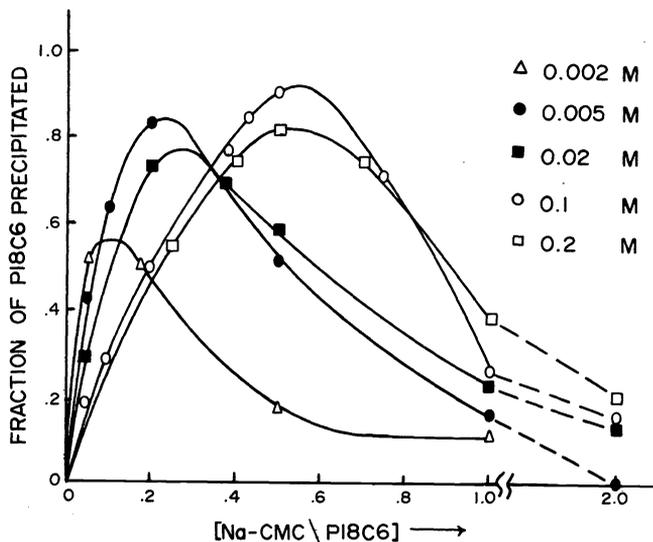


Figure 6: Polysalt complex between poly(vinylbenzo-18-crown-6) and sodium carboxymethylcellulose. Plot of P18C6 precipitated versus CMC/P18C6 ratio at concentrations of KCl equal to: ( $\Delta$ ) 0.002M; ( $\bullet$ ) 0.005M; ( $\blacksquare$ ) 0.02 M; ( $\circ$ ) 0.1 M; ( $\square$ ) 0.2 M. (Ref. 24).

The complex formation is a result of electrostatic interactions between the fixed charges on the polyanion and the mobile charges on the poly(crown ether). Maximum precipitation in polyanion-polycation systems generally occurs when charge equivalence is reached (48). The charge density on the poly(crown ether) is a function of the type of cation, its concentration and [P18C6]. Hence, the amount of complex formed is expected to depend on these variables (Figure 6). From the known binding constant of K<sup>+</sup> with P18C6 it could be demonstrated that at a CMC/P18C6 ratio of 0.5 maximum precipitation indeed occurs at about 0.1 M KCl. At 0.005 M KCl the average segment length of free crown ligands between points of charge interaction is much larger. Therefore, less CMC is needed to reach the point of charge equivalence and maximum P18C6 precipitation.

Screening of the polyion charges by counterions reduces the electrostatic interactions. It can cause dissolution of a polysalt complex at high salt concentration or it may prevent its formation. For example, no precipitate is formed when NaCl is added. The binding constant of Na<sup>+</sup> with P18C6 is low compared with K<sup>+</sup>, and at 0.15 M NaCl the charge density on P18C6 is the same as at 0.005 M KCl. However, while with 0.005 M KCl precipitation occurs, the solution remains homogeneous at 0.15 M NaCl. Apparently, the small number of charges on the P18C6 are effectively screened by the Cl<sup>-</sup> counterions, causing a weakening in the electrostatic interactions with the polyanion charges. The same is observed at 0.005 M KCl when 0.1M (CH<sub>3</sub>)<sub>4</sub>N<sup>+</sup>Cl<sup>-</sup> is added. The tetramethylammonium cation does not bind to P18C6, hence, the system should behave similar to that of 0.1 M NaCl, which is indeed the case. The nature of the anion also influences the precipitation. At constant CMC/P18C6 and [KCl] = 0.1 M, the amount of P18C6 precipitated decreases in the order OH<sup>-</sup> ~ Cl<sup>-</sup> > Br<sup>-</sup> > I<sup>-</sup>. It is also interesting to note that when picrate anions are bound to P18C6 in the presence of 0.1 M KCl (see previous section), addition of CMC causes the picrate to precipitate with the P18C6.

Complexes with polyacids. Neutral polymers have also been observed to form complexes. An example is the interactions of poly(ethyleneoxide) with polyacids through hydrogen bonding (50). A complex of this type appears to be formed on mixing aqueous solutions of P18C6 and poly(acrylic acid) (PAA) or poly(methacrylic acid) (PMAA). The results are shown in figure 7. At 0.1 M KOH the polyacid is nearly completely ionized, and a

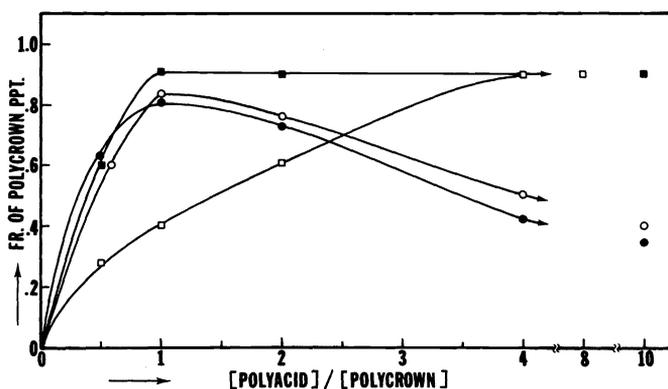


Figure 7: Complexes between P18C6 and poly(acrylic acid) (PAA) and poly(methacrylic acid) (PMAA). Plot of P18C6 precipitated versus ratio of [poly acid]/[poly crown]. Systems: (□) P18C6/PAA, 0.1 M KCl; (■) P18C6/PAA, 0.01 M HCl; (●) P18C6/PAA, 0.1 M KOH; (○) P18C6/PMAA, 0.1 M KOH. (Ref. 23).

polysalt complex is formed with maximum precipitation occurring at a ratio of poly acid/poly crown  $\approx 1$ . A charged poly(crown ether) is also formed in 0.1 M KCl, but with the pH being about 7, only a fraction of the COOH groups are ionized and maximum P18C6 precipitation occurs at polyacid/poly crown  $\approx 4$ . No ionization occurs in 0.01 N HCl, yet in the absence of  $K^+$  nearly all P18C6 precipitates at a COOH/crown ratio of 1. Both polymers are neutral and hydrogen bonding is most likely responsible for the formation of this insoluble complex, with one COOH group bonded to one crown unit.

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