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NMR Titration, Potentiometry and Extraction Studies of Some Acyclic Polyethers with Aromatic End-Groups

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Acyclic ionophore antibiotics including monensin, nigericine and grisorixin wrap themselves around the cation, in a manner very similar to the cyclic species.¹ The acyclic oligoethers, called podands, can be obtained simply and cheaply; there is no need for high-dilution or template effects in preparation.^{2,3} Furthermore, some podands with aromatic end-groups wrap themselves around the cations such as, Na⁺ and Rb⁺ ions in a helical manner to make pseudo-cycle both in solid⁴ and solution⁵ states. Vögtle's group has synthesized numerous such open-chain hosts containing nitrogen donors in aromatic end-groups.⁶ In spite of these benefits, less attention was paid to their thermodynamic, structural informations and applications in solution.⁷

Results and Discussion

In this study, we have investigated the cationic interactions of some serial podands (I-VIII) having sulfurs or asymmetric end-groups shown in Figure 1 by means of pmr titrations^{8,9} and potentiometry. The stoichiometries and other informations have obtained by plotting the chemical shift changes as a function of host/guest mole ratio shown as in Figure 2. According to Figure 2, all of the cation induced shift varies linearly with the mole ratio until the ratio of 1:1 reached and no more shifts were observed above 1. From these breaks, it could be deduced that all of podands in Figure 1 form 1:1 complexes with cations.

Since the cation induced shifts of host protons depend mainly on the strength of the interaction between the nearest neighboring donor atoms and guest ions, it is to be expected that the magnitude of chemical shift variation is a sensitive probe of interactions in the same host for a given guest ion.^{8,9} For example, by the comparison of slopes in Figure

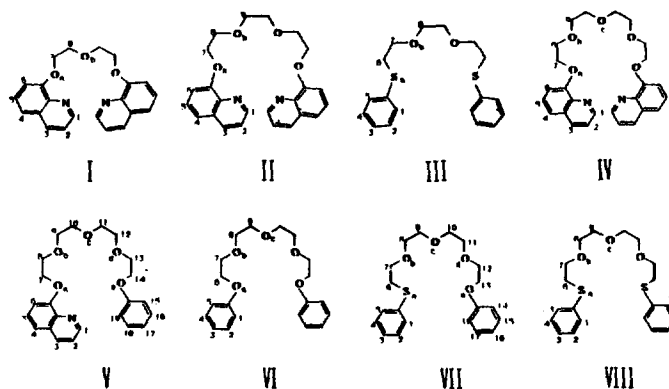


Figure 1. The structures of podands used in this study.

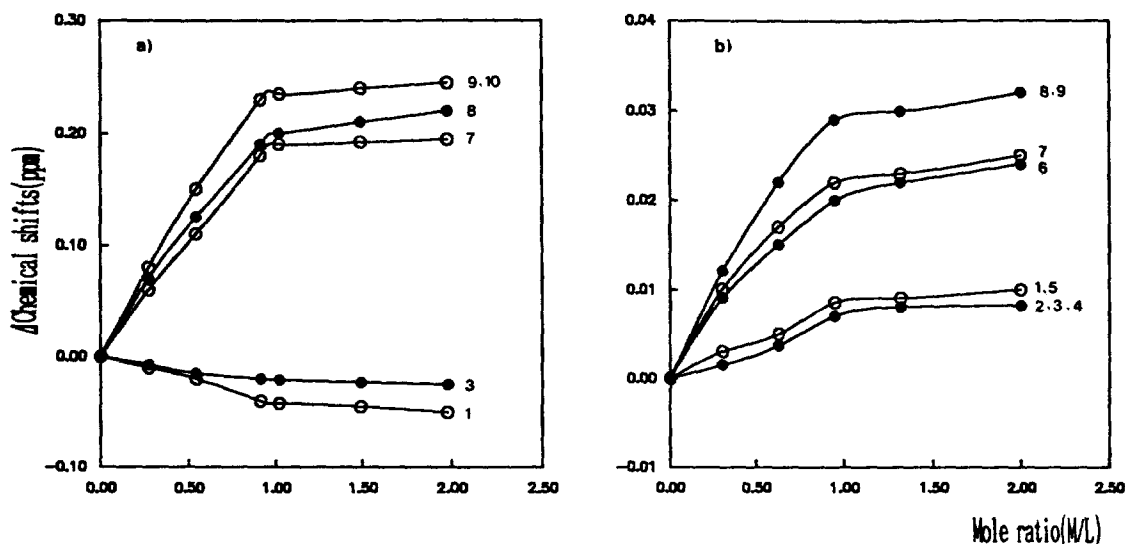


Figure 2. Observed chemical shifts of the protons on podands in acetone- d_6 /DMSO- d_6 (7 : 3 v/v) as a function of the mole ratio, a) NaClO₄/IV and b) NaClO₄/VI.

Table 1. Stoichiometries and Relative Donor Strength of Podand Complexes

Host	Guest	H : G	$\Delta\delta$ /mole ratio	Donor strength
I	Li ⁺	1 : 1	H ₈ >H ₇ >H ₁	O _b >O _a >N
II	Na ⁺	1 : 1	H ₁ >H ₇ >H _{8,9}	N>O _a >O _b
	K ⁺	1 : 1	H ₁ >H ₇ >H ₈ >H ₉	N>>O _a >O _b
	NH ₄ ⁺	1 : 1	H ₁ >H ₇ >H ₈ >H ₉	N>>O _a >O _b
	CH ₃ NH ₃ ⁺	1 : 1	H ₁ >H ₇ >H _{8,9}	N>>O _a >O _b
IV	Na ⁺	1 : 1	H _{9,10} >H ₈ >H ₇ >H ₃ >H ₁	O _c >O _b >O _a >N
	K ⁺	1 : 1	H ₁ >H ₇ >H ₈ >H _{9,10}	N>>O _c >O _b >O _a
	NH ₄ ⁺	1 : 1	H ₁ >H ₇ >H ₈ >H _{9,10}	N>>O _a >O _b >O _c
	CH ₃ NH ₃ ⁺	1 : 1	H ₁ >H ₇ >H ₈ >H _{9,10}	N>>O _a >O _b >O _c
V	Li ⁺	1 : 1	H ₁ >H ₇ >H ₈ >H ₉ >H _{10,11}	N>O _a >O _b >O _c
	Na ⁺	1 : 1	H _{10,11} >H ₁ >H _{3,7} >H ₁₄	O _c >N>O _a >O _b
	K ⁺	1 : 1	H _{10,11} >H ₈ >H ₉ >H ₇ >H ₁₃ >H ₁ >H ₁₄	O _c >O _b >O _a >O _d >N>O _c
	NH ₄ ⁺	1 : 1	H ₁ >H _{7,10,11}	N>H _{7,10,11}
VI	Na ⁺	1 : 1	H ₈ >H ₇ >H ₆ >H ¹	O _c >O _b >>O _a
	K ⁺	1 : 1	H ₆ >H _{8,9} >H ₇	O _a >O _c >O _b
VIII	K ⁺	1 : 1	H _{8,9} >H ₇ >H ₆	O _c >O _b >S _a
	NH ₄ ⁺	1 : 1	H _{8,9} >H ₇ >H ₆	O _c >O _b >S _a
	Ag ⁺	1 : 1	H ₆ >>H _{8,9} >H ₇	S _a >>O _c >O _b

2, it could be deduced that the donor strengths of atoms in IV and VI which have C₂ symmetry for Na⁺ ion are in the order of O_c>O_b>O_a>N and O_c>O_b>O_a, respectively. So the Na⁺ ion does not equally interact with donor atoms but preferentially does with the oxygens rather than nitrogen atoms in case of IV. Furthermore among the oxygens, the central oxygen (O_c) behaves as the strongest donor rather than other two oxygens (O_b and O_a) in both cases. These results could be explained in terms of electronegativity of heteroatoms because the electronegativity of aromatic oxygens have smaller than that of aliphatic oxygens.⁴ These results are also supported by the solid structure of the similar system.¹⁰ But according to Table 1 for the larger ions such as K⁺ ion, nitrogen act as the strongest donor.

The nitrogen atoms in quinoline also act as the strongest

donors especially for the ammonium and methylammonium ions due to the hydrogen bond between ⁺N-H...N. Lehn¹¹ also reported that alkylammonium ion interacts with [18]-N₃O₃ about 30 times more strongly than [18]-O₆, since ⁺N-H...N hydrogen bonding is stronger than ⁺N-H...O hydrogen bonding.

Another interesting thing is every resonances significantly shifted downfield upon cation binding, consistent with coordination to the cations but exceptionally the protons of the quinoline groups are shifted upfield in IV-Na⁺ complexes shown as Figure 2a. This difference in the direction of chemical shift change is understood by considering the difference between the proposed structures as illustrated in Figure 3a and 3b, respectively. This unusual behavior is perhaps due to a helical conformation of the complex with par-

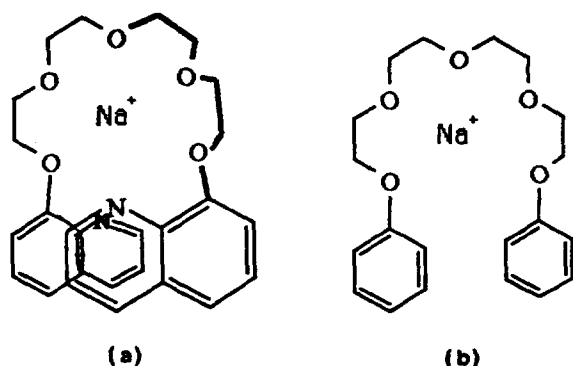


Figure 3. Proposed structures of a) Na^+ -IV and b) Na^+ -VI complexes in solution.

Table 2. Log K of Podand Complexes with Ag^+ Ion in Methanol at 25.0 °C

Podand	log K	Podand	log K
I	7.04	II	7.15
III	5.90	IV	7.69 (7.02) ¹³
V	4.16	VI	<2
VII	3.88	VIII	5.50

tial stacking¹² of the quinoline groups, as found in the solid state structure of a complex⁴. The overlap between the two quinoline groups of IV is the cause for the upfield shift of the quinoline signals in case of IV- Na^+ complex since the shielding zone of the quinoline group covers each other.

In order to determine the stability constants of complexes with Ag^+ ion, the potentiometric titrations shown as in Figure 3 were very successful because of the Ag^+ -ISE (Orion 94-16) responses nearly Nernstian in methanol and the computer curve-fitting program, KINFIT¹⁴ gave the quite reasonable results in accuracy.

Comparing the stability constants of the Ag^+ ion with 18-crown-6 (log K ; 4.57)¹⁵ and the podands in Table 2, the nitrogen containing podands showed higher stabilities than 18-crown-6. So the symmetric two quinoline groups in I, II and IV stabilize the Ag^+ ion complexes very effectively. Otherwise, the Q_2O_n -types (Q =quinoline, $n=3, 4$ and 5) show no maximum selectivity with n because the podand complexes are not rigid and relatively flexible in solution. So the "ion-in-the hole" model is not acceptable in podand complexes. Substitutions of one or two sulfurs for oxygens in ether ring produce dramatic effect on log K for complexations with Ag^+ ion. As expected, the sulfur atoms act as soft base to enhance the stability toward the Ag^+ ion, classified as a soft acid.¹⁶

From the combinations of measured log K and NMR titration data, our conclusion is that the bond strength between Ag^+ ion and the different donor atoms decreases in the order: $\text{N} > \text{S} > \text{O}$, and end-groups decreases in the order: quinoline > phenyl. And asymmetric podands such as V and VII showed moderate affinity for Ag^+ ion compared to their analogues.

We also carried out the extractions of some cation picrates including group IA, IIA, NH_4^+ , Ag^+ , Tl^+ and some heavy metal ions from water to chloroform phase by using these

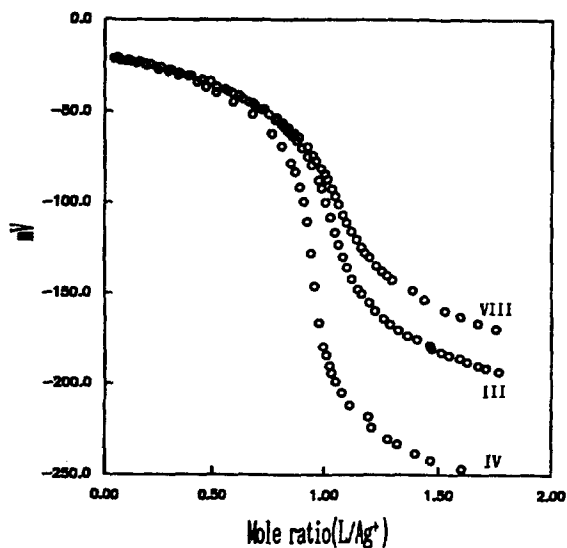


Figure 4. Potentiometric titration curves of some podands with AgClO_4 using Ag^+ -ISE in methanol at 25.0 °C.

podands. We found that II and IV showed higher extractivities for Ag^+ ion (86.8 and 86.6%, respectively) and Pb^{2+} ion (88.1 and 68.9%, respectively) than any other cations. But sulfur containing podands such as III, VII and VIII showed poor extractivities for Ag^+ ion unlike the stability values. And most podands showed poor extractivities for group IA ions (0-5%). The extraction and membrane transport experiments using any other new podands including Figure 1 are also accomplishing in our laboratory, and their results will be discussed in following issue of this paper.

Experimental

General. The $^1\text{H-NMR}$ spectra were recorded with a Bruker AW80 (80 MHz) NMR spectrometer. The Chemical shifts are recorded from TMS, and $\text{AC-d}_6/\text{DMSO-d}_6$ (7:3 v/v) mixed solvent was used in NMR experiments. The IR spectra were recorded with a Hitachi 270-50 spectrophotometer.

Preparations of 'Podands'; Symmetric Podands.

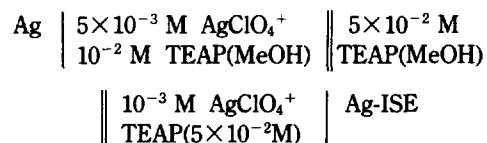
1,11-Dichloro-3,6,9-trioxaundecane or 1,8-dichloro-3,6-dioxaoctane (25 mmol) dissolved in 25 ml ethanol (or butanol) was added dropwise within 30 min and under stirring to refluxing solution of 8-hydroxyquinoline, phenol or thiophenol (50 mmol) and KOH (50 mmol) in 100 ml of ethanol or butanol. The mixture was refluxed for 20 h and was then allowed to cool to room temperature. After filtration of the precipitate and the solvent was removed by distillation under vacuum, chloroform was added to the viscous oil to dissolve. In order to separate unreacted, the mixture was extracted several times with dilute NaOH and washed with water. The organic layer was concentrated by distillation under vacuum. Chromatography on silica gel with chloroform/ethanol gave the pure products.

Asymmetric Podands. 1,11-Dichloro-3,6,9-trioxaundecane (400 mmol) dissolved in 200 ml butanol was added under stirring to refluxing solution of 8-hydroxyquinoline, or thiophenol (50 mmol) and KOH (50 mmol) in 200 ml butanol. The mixture was refluxed for 20 h. The procedure for

the workup was the same as for symmetric podands. The adduct with one aromatic end group was purified by fractional distillation under vacuum. Again, 8-hydroxyquinoline or thiophenol (20 mmol) and KOH (20 mmol) were dissolved in 100 ml of boiling butanol. After adduct (200 mmol) was added, the mixture was refluxed for 20 h. The final product (V, VIII) was purified by chromatography on silica gel.

NMR titrations. Chemical shifts of each protons among podands were determined by a frequency counter within an error of ± 0.2 Hz, relative to TMS zero locking. The use of AC-d₆/DMSO-d₆ mixtures as the solvents in NMR titration was based on the solubility considerations. A sample tube containing a few mg of podand in a known volume of solvent was first loaded into the probe and spectrum was taken. The sample was then unloaded, added to the sample tube with a small amount of the solid salt, reloaded into the probe, and another spectrum was taken. This process was repeated until no significant change was observed in observed in successive spectra. Usually seven to ten spectra were taken for each of the experiment. The concentrations of podands were held constant at about 5×10^{-2} M and salt concentrations varied from 0.0 M to approximately 0.1 M.

Potentiometry. All potentiometric titrations were done with Ag-ISE (Orion 94-16) in anhydrous methanol. The double junction type reference electrode was used. The general construction of the cell used for the measurements was as follows.



Titrations were carried out in an all-glass cell thermostated to 25 ± 0.1 °C. Titrant was added from 2 to 5 ml microburets calibrated. The data were analyzed using a nonlinear least-square program, KINFIT 4¹⁴ to fit the calibration curves for calculating the stability constants.

Extraction. The chloroform solution of the podand (5.0 ml, 3.0×10^{-3} M) and the aqueous solution of cationic picrate (5.0 ml, 3.0×10^{-3} M) were placed in volumetric flask, and

the flask were shaken in thermostated incubator for 30 min at 25 ± 0.2 °C. The concentration of metal picrate in the water phase was determined from its absorption at 356 nm.

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