Journal of Inclusion Phenomena and Molecular Recognition in Chemistry **28:** 315–323, 1997.

Complex Formation of Some Anilinium Ion Derivatives with 18-Crown-6, 1,10-diaza-18-crown-6 and Cryptand C222 in Acetonitrile, Dimethylformamide and their 1 : 1 Mixture

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(Received: 16 July 1996; in final form: 6 November 1996)

Abstract. The complexation reactions between the protonated salts of aniline, *o*-hydroxy aniline, *o*-amino aniline and 2,3-benzo aniline (α-naphthylamine) and macrocyclic ligands 18-crown-6,1,10-diaza-18-crown-6 and cryptand C222 have been studied conductometrically in acetonitrile, dimethylformamide and their 1 : 1 (mol–mol) mixture at 25 °C. Formation constants of the resulting 1 : 1 complexes were determined from the computer fitting of the molar conductance-mole ratio data. In all cases studied, the stability of the complexes decreases in the order C222 > 1,10-diaza-18-crown-6 > 18-crown-6. There is also an inverse relationship between the stabilities of the complexes and the Gutmann donor number of the solvents. It was found that, in the aromatic anilinium series used, increasing the bulkiness of the organic substituent in the ortho position results in a loss of complex stability.

Key words: Anilinium derivatives, macrocyclic ligands, complexation, conductance, solvent effect.

1. Introduction

It is well known that amine transport plays an important role in biological systems [1,2]. Amine groups are also constituents of many biologically important compounds such as amino acids and drugs whose transport mechanisms across membranes is largely unknown. On the other hand, organic amines are known to block either sodium ion or potassium ion in nerve channels and, in some cases this results in the death of the organisms [3, 4]. Thus, during the past two decades, considerable attention has been given to the interaction between different protonated amines and macrocyclic ligands, that serve as interesting model compounds for the study of the molecular effect on membrane permeability [5–15].

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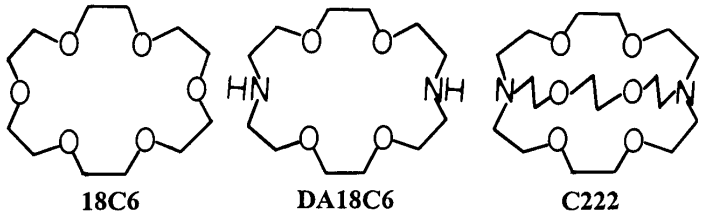

Figure 1. Structures of the ligands.

We have recently reported the thermodynamics of complexation of the ammonium ion and some other protonated amines with several crown ethers and cryptands in nonaqueous and mixed solvents [13–15]. In this paper we report a conductance study of the interaction between anilinium (An^+), *o*-hydroxy anilinium (HAn^+), *o*-amino anilinium (AAn^+) and 2,3-benzo anilinium (BAn^+) ions and 18-crown-6 (18C6), 1,10- Diaza-18-crown-6 (DA18C6) and cryptand C222 in acetonitrile (AN), dimethylformamide (DMF) and their 1 : 1 mixture. Structures of the macrocyclic ligands used are shown in Figure 1.

2. Experimental

All chemicals used were of the highest purity available from Merck chemical company. Nitrate salts of An^+, HAn^+, AAn^+ and BAn^+ ions were prepared from the 1 : 1 interaction of nitric acid with aniline, 2-aminophenol, *o*-phenylenediamine and α-naphthylamine, respectively. The resulting nitrate salts were recrystallized three times from triply distilled deionized water and vacuum dried at 60 °C over P_2O_5 for 72 h. The macrocyclic ligands 18C6, DA18C6 and C222 were purified and dried using previously reported methods [16,17]. Reagent grade AN and DMF were purified and dried by the previously described procedures [18]. The conductivities of the solvents were less than 1.0×10^{-7} S^{-1} cm^{-1}.

Conductivity measurements were carried out with a Metrohm 660 conductivity meter. A dip-type conductivity cell, made of platinum black, with a cell constant of 0.8210 cm^{-1} was used. In all measurements the cell was thermostated at 25.00 $\pm$ 0.05 °C using a Phywe immersion thermostat.

In a typical experiment, 50 mL of anilinium nitrate solution (1.0×10^{-4} M) was placed in the titration cell, thermostated to 25 °C, and the conductance of the solution measured. Then, a known amount of the macrocycle solution was added in a stepwise manner using a calibrated micropipette. The conductance of the solution was measured after each addition. Addition of the ligand was continued until the desired ligand-to-cation mole ratio was achieved.

The 1 : 1 binding of the protonated amines with macrocyclic ligands can be expressed by the following equilibrium:

$$M^+ + L \overset{K_f}{\rightleftharpoons} ML^+. \tag{1}$$

The corresponding equilibrium constant, K_f, is given by

$$K_f = \frac{[\mathrm{ML}^+]}{[\mathrm{M}^+][\mathrm{L}]} \cdot \frac{f(\mathrm{ML}^+)}{f(\mathrm{M}^+)f(\mathrm{L})}, \tag{2}$$

where $[\mathrm{ML}^+]$, $[\mathrm{M}^+]$, [L] and f represent the equilibrium molar concentrations of complex, free cation, free ligand and the activity coefficients of the species indicated, respectively. Under the dilute conditions used, the activity coefficient of the uncharged ligand, $f(\mathrm{L})$ can be reasonably assumed as unity [13,14,19,20]. The use of the Debye–Hückel limiting law of 1 : 1 electrolytes [21] leads to the conclusion that $f(\mathrm{M}^+) \sim f(\mathrm{ML}^+)$, so the activity coefficients in Equation (2) cancel out.

Thus the complex formation constant in terms of the molar conductance can be expressed as [22,23]:

$$K_f = \frac{\mathrm{ML}^+]}{[\mathrm{M}^+][\mathrm{L}]} = \frac{(\Lambda_\mathrm{M} - \Lambda_\mathrm{obs})}{(\Lambda_\mathrm{obs} - \Lambda_\mathrm{ML})[\mathrm{L}]}, \tag{3}$$

where

$$[\mathrm{L}] = C_\mathrm{L} - \frac{C_\mathrm{M}(\Lambda_\mathrm{M} - \Lambda_\mathrm{obs})}{(\Lambda_\mathrm{M} - \Lambda_\mathrm{ML})}. \tag{4}$$

Here, Λ_M is the molar conductance of the protonated amine before addition of ligand, Λ_ML the molar conductance of the complexed amine, Λ_obs the molar conductance of the solution during titration, C_L the analytical concentration of the macrocycle added, and C_M, the analytical concentration of the amine salt. The complex formation constant, K_f, and the molar conductance of the complex, Λ_ML, were obtained by computer fitting of Equations (3) and (4) to the molar conductance–mole ratio data using a nonlinear least-squares program KINFIT [24].

3. Results and Discussion

In order to evaluate the influence of adding macrocyclic ligands on the molar conductance of the protonated amines used, in AN, DMF and AN-DMF (1 : 1) solutions, the conductivity at a constant salt concentration (1.0×10^{-4} M) was monitored while increasing the macrocycle concentration at 25 °C. The resulting molar conductance vs. macrocycle/cation mole ratio plots are shown in Figures 2–4. It is obvious that, in all cases studied, addition of the macrocyclic ligand to the protonated amine solutions caused a rather large and continuous decrease in the molar conductance of the solutions, indicating the lower mobility of the complexed cations compared to the free ones. However, in the AN-DMF mixture, the difference between the molar conductances of the free and complexed cations for the DA18C6–HAn^+ system was so low that the variations in molar conductance

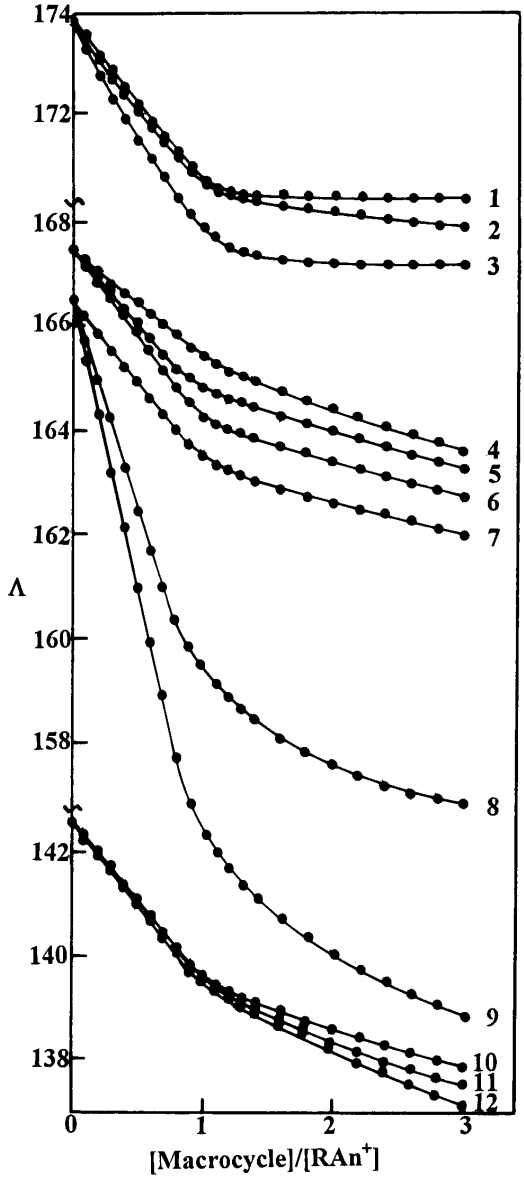

Figure 2. $\Lambda(S^{-1}\ cm^2\ mol^{-1})$ vs. [macrocycle]/[RAn^+] curves in acetonitrile at 25°: (1) An^+–DA18C6, (2) An^+–C222, (3) An^+-C222, (4) HAn^+–18C6, (5) HAn^+–DA18C6, (6) HAn^+–C222, (7) AAn^+–C222, (8) AAn^+–DA18C6, (9) AAn^+–18C6, (10) BAn^+–DA18C6, (11) BAn^+–C222, (12) BAn^+–18C6.

could not be measured accurately; thus, the results for this system are not included in Figure 3 and Table I.

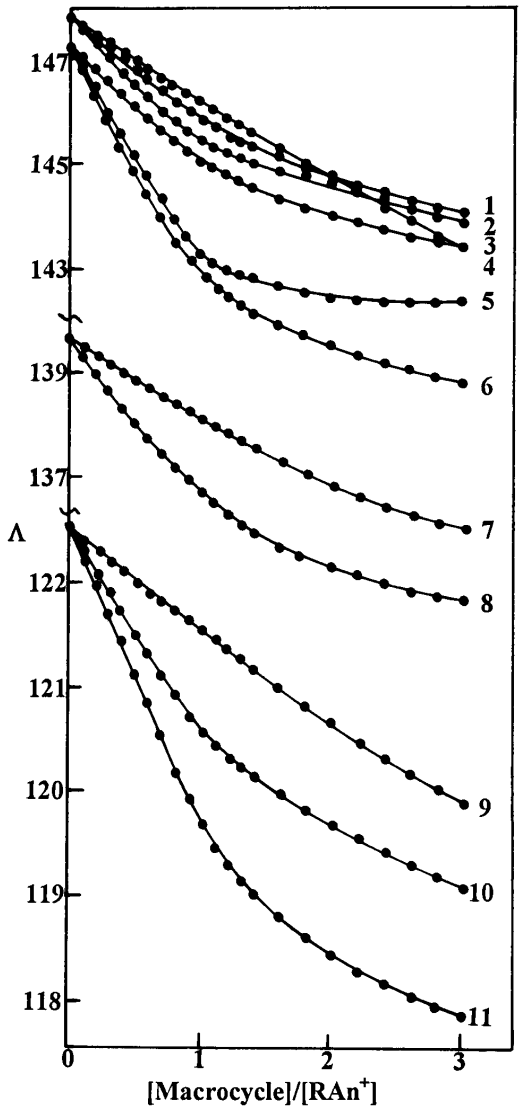

Figure 3. $\Lambda(S^{-1}\ cm^2\ mol^{-1})$ vs. [macrocycle]/[RAn^+] in acetonitrile-dimethylformamide at 25 °C: (1) AAn^+–DA18C6, (2) AAn^+–C222, (3) AAn^+–18C6, (4) An^+–18C6, (5) An^+–C222, (6) An^+–DA18C6, (7) HAn^+–18C6, (8) HAn^+–C222, (9) BAn^+–18C6, (10) BAn^+–DA18C6, (11) BAn^+–C222.

From Figures 2–4 it is seen that, in most cases studied, and especially in AN solution, the slopes of the corresponding molar conductance–mole ratio plots change sharply at the point where the ligand to cation mole ratio is one, emphasizing the formation of a relatively stable 1 : 1 complex between the macrocyclic ligands and the protonated amines used. However, in DMF solution (Figure 4), in some

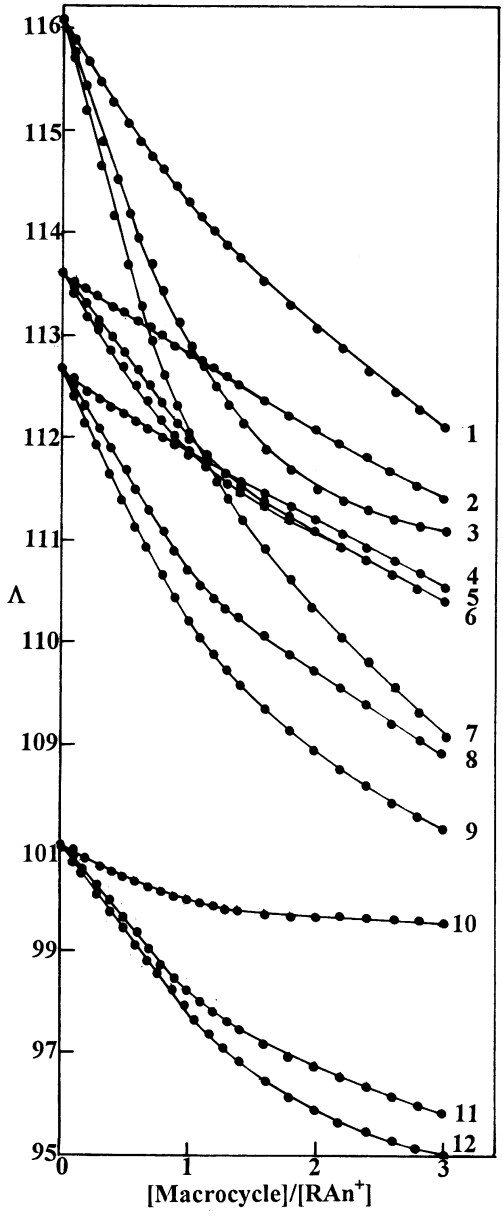

Figure 4. $\Lambda(S^{-1}\ cm^2\ mol^{-1})$ vs. [macrocycle]/[RAn^+] in dimethylformamide of 25 °C: (1) An^+–18C6, (2) HAn^+–18C6, (3) An^+-C222, (4) AAn^+–18C6, (5) HAn^+–C222, (6) HAn^+–DA18C6 (7) An^+–DA186C6, (8) AAn^+–C222, (9) AAn^+–DA18C6, (10) BAn^+–DA18C6, (11) BAn^+–C222, (12) BAn^+–DA18C6.

Table I. Formation constants of different anilinium ion derivatives with macrocycles 18C6, DA18C6 and C222 in various solvent systems at 25 °C.

Macrocycle	Solvent	log K_f			
		An^+	AAn^+	HAn^+	BAn^+
18C6	AN	4.95 ± 0.04	4.49 ± 0.03	4.32 ± 0.04	3.87 ± 0.05
	AN + DMF	4.03 ± 0.05	3.10 ± 0.10	3.37 ± 0.02	> 2.5
	DMF	3.42 ± 0.03	2.63 ± 0.07	2.61 ± 0.03	>2.5
DA18C6	AN	4.98 ± 0.05	4.81 ± 0.07	4.44 ± 0.04	4.37 ± 0.04
	AN + DMF	4.32 ± 0.07	3.85 ± 0.05	–	4.02 ± 0.05
	DMF	4.15 ± 0.07	3.75 ± 0.06	3.77 ± 0.03	3.71 ± 0.07
C222	AN	5.48 ± 0.07	5.26 ± 0.07	4.46 ± 0.05	4.10 ± 0.04
	AN + DMF	4.85 ± 0.05	4.46 ± 0.04	4.41 ± 0.05	3.89 ± 0.04
	DMF	4.35 ± 0.05	3.92 ± 0.02	3.94 ± 0.02	3.54 ± 0.05

cases the relatively large decrease in molar conductance of the protonated amines upon addition of the macrocyclic ligands does not show any tendency of leveling off even at mole ratios of about 3, indicating the formation of weaker complexes.

The stability constants of the resulting 1 : 1 complexes were determined by the computer fitting of Equations (3) and (4) to the molar conductance–mole ratio data and the results are summarized in Table I. The assumed 1 : 1 stoichiometry for the resulting complexes was further supported by the fair agreement between the observed and calculated molar conductances. It should be noted that, in AN and DMF as solvents of intermediate dielectric constants (with respective ϵ values of 36.1 and 38.0) and relatively high donor numbers (with respective DNs of 14.1 and 26.6) [25], it was assumed that the association to ion pairs is negligible under the highly dilute experimental conditions [14,26]. The macrocycle concentration in solutions was also sufficiently low (3.0×10^{-4} M) to avoid corrections for viscosity changes. It is interesting to note that the molar conductance of each protonated amine nitrate solution in the solvents used decreases in the order AN > AN + DMF > DMF (see Figures 2–4), mainly due to the relatively large differences between the viscosities of the two solvents (i.e. 0.34 for AN and 0.80 for DMF).

From Table I, it is readily evident that the nature of the solvent has a very fundamental influence on the stability of the resulting 1 : 1 complexes between the protonated amines and the macrocyclic ligands used. Since in the complexation process, the ligand must compete with solvent molecules for the cations, variation of the solvent properties is expected to change the apparent binding abilities of the complexes. Actually, there is an inverse relationship between the stability of the complexes and the solvating power of the solvents, as expressed by the Gutmann donor number, DN [25]. That is, the stability of all protonated amine-macrocycle complexes decreases in the order AN > AN-DMF > DMF. There are several earlier reports which clearly indicate the same type of solvent effect on the stabilities of various cation-macrocycle complexes [13,16,27–33].

The data given in Table I clearly indicate that, in the case of all anilinium ion derivatives used, the stability of the resulting 1 : 1 complexes decreases in the order C222 > DA18C6 > 18C6. It is well known theoretically [34,35] and experimentally [36] that in R—NH_3^+ ions the positive charge is distributed over the H atoms and not located on the central nitrogen atom, as implied by the valence bond picture. Thus, the binding of R—NH_3^+ ions with macrocyclic ligands would occur via H-bonding between the amine hydrogen atoms of the cation and the electron donating hetero atoms of the macrocyclic rings. As reported previously [5,7,12,37], the tetrahedral NH_4^+ and R—NH_3^+ ions can nicely bind to three of the six available oxygen atoms in the 18C6 ring to form a stable complex. In this case, the R group (which could be an H group in the case of the NH_4^+ ion) presumably protrudes upward from the center, and perpendicular to, the plane of the oxygens. Since it is well known that N^+—H· · ·N hydrogen bonding is stronger than N^+—H· · ·O [12,38,39], it is not surprising to observe a significant increase in the stability of the R—NH_3^+ complexes by substitution of two oxygen atoms by two nitrogens in the 18C6 macrocyclic ring. On the other hand, connection of a —$CH_2CH_2OCH_2OCH_2CH_2$— bridge onto the DA18C6 ring results in the formation of a rigid macrobicyclic ligand C222 with a conformation more suitable for the formation of a 1 : 1 complex with the protonated amines used. It should be noted that, such a 'cryptate effect', which results in an enhanced stability of ammonium complexes with different cryptands over the corresponding aza crowns, has already been reported in the literature [10].

As is obvious from Table I, in almost all cases studied, and in all solvent systems used, the sequence of stability of the resulting 1 : 1 complexes follows the order $An^+ > AAn^+ > HAn^+ > Ban^+$. It is well known that, in the host–guest interactions between macrocyclic ligands and different cations, a number of host–guest parameters play a fundamental role. The important structural properties of macrocyclic ligands as host include cavity size, type and number of donating atoms in the ring, nature of the ring substituent and ring conformation [2,7]. On the other hand, due to different binding mechanisms involved, the guest parameters for organic ammonium ions differ from those of metal ions. In the cation–ligand binding process, metal ions penetrate inside the macrocyclic cavity, whereas the binding of the organic ammonium ions occurs via a hydrogen bonding to the available ring donor atoms [7,12,37]. Thus, the important guest parameters of organic ammonium ions include the number of hydrogen atoms available for H-bonding, steric hindrance to ligand–cation approach by the organic moiety of the guest and electronic effects on the H-bonding donicity of the guest.

The steric bulk will be a hindrance to the host–guest complexation only in as much as it is allowed to interfere directly with the site of complexations. Consequently, the substitution of different organic groups in the *ortho* position of the anilinium ion is expected to largely influence the stability of the resulting macrocyclic complexes. As seen from the observed stability sequence, increasing the organic bulk in the *ortho* position results in a loss of complex stability, while the

resulting complexes do not seem to demonstrate a high degree of sensitivity to the electronic effect. A similar conclusion has been reached before [7].

References

1. Yu. A. Ovchinnikov, V. T. Ivanov, and A. M. Shkrob: *Membrane-Active Complexones*, Elsevier, New York (1974).
2. R. M. Izatt, N. E. Izatt, B. E. Rossiter, and J. J. Christensen: *Science* **199**, 994 (1978), and references therein.
3. K. A. Rubinson: *J. Chem. Educ.* **54**, 345 (1977).
4. D. F. Martin and B.B. Martin: *J. Chem. Educ.* **53**, 614 (1976).
5. R. M. Izatt, J. D. Lamb, B. E. Rossiter, N. E. Izatt, and J. J. Christensen: *J. Chem. Soc., Chem. Commun.*, 386 (1978).
6. J. L. Roberts, R. E. McClintock, Y. El-Omrani, and J. W. Larson: *J. Chem. Eng. Data* **24**, 79 (1979).
7. R. M. Izatt, J. D. Lamb, N. E. Izatt, B. E. Rossiter, J. J. Christensen, and B. L. Haymore: *J. Am. Chem. Soc.* **101**, 6273 (1979).
8. J. D. Lamb and R. M. Izatt: *J. Am. Chem. Soc.* **102**, 479 (1980).
9. R. A. Schultz, E. Schlegel, D. M. Dishong, and G. W. Gokel: *J. Chem. Soc., Chem. Commun.*, 242 (1982).
10. E. Graf, J. P. Kintzinger, J. M. Lehn, and J. L. Moigne: *J. Am. Chem. Soc.* **104**, 1672 (1982).
11. R. A. Schultz, B. D. White, D. M. Dishong, K. A. Arnold, and G. W. Gokel: *J. Am. Chem. Soc.* **107**, 6659 (1985).
12. C. Y. Zhu, R. M. Izatt, J. S.. Bradshaw, and N. K. Dalley: *J. Incl. Phenom.* **13**, 17 (1992).
13. M. Hasani and M. Shamsipur: *J. Incl. Phenom.* **16**, 123 (1993).
14. M. Hasani and M. Shamsipur: *J. Solution Chem.* **23**, 721 (1994).
15. M. R. Ganjali and M. Shamsipur: *J. Incl. Phenom.* **23**, 41 (1995).
16. S. Kashanian and M. Shamsipur: *Inorg. Chim. Acta* **155**, 203 (1989).
17. H. Parham and M. Shamsipur: *Polyhedron* **11**, 987 (1992).
18. M. S. Greenberg and A. I. Popov: *Spectrochim. Acta* **31A**, 697 (1975).
19. K. M. Tawarah and S. A. Mizyed: *J. Solution Chem.* **18**, 387 (1989).
20. A. J. Smetana and A. I. Popov: *J. Chem. Thermodyn.* **11**, 1145 (1979).
21. P. Debye and H. Hückel: *Phys. Z.* **24**, 305 (1928).
22. Y. Takeda: *Bull. Chem. Soc. Jpn.* **56**, 3600 (1983).
23. D. P. Zollinger, E. Bulten, A. Christenhuse, M. Bos, and W. E. Van der Linden: *Anal. Chim. Acta* **198**, 207 (1987).
24. V. A. Nicely and J. L. Dye: *J. Chem. Educ.* **48**, 443 (1971).
25. V. Gutmann: *The Donor-Acceptor Concepts of Molecular Interactions*, Plenum, New York (1978).
26. G. J. Janz and R. P. T. Tomkins: *Nonaqueous Electrolyte Handbook*, Vol. 1, Academic Press, New York (1972).
27. A. Rouhollahi, M. Shamsipur, and M. K. Amini: *Talanta* **41**, 1465 (1994).
28. A. Jabbari, M. Hasani, and M. Shamsipur: *J. Incl. Phenom.* **15**, 329 (1993).
29. M. K. Amini and M. Shamsipur: *Inorg. Chim. Acta* **183**, 65 (1991).
30. L. L. Soong, G. E. Leroi, and A. I. Popov: *Inorg. Chem.* **29**, 1366 (1990).
31. J. D. Lin and A. I. Popov: *J. Am. Chem. Soc.* **103**, 3773 (1981).
32. M. Shamsipur and A. I. Popov: *J. Am. Chem. Soc.* **101**, 4051 (1979).
33. E. Mei, A. I. Popov, and J. L. Dye: *J. Phys. Chem.* **81**, 1677 (1977).
34. A. Pullman and A. M. Armbruster: *Chem. Phys. Lett.* **36**, 558 (1975).
35. P. Kollmann: *J. Am. Chem. Soc.* **99**, 4875 (1977).
36. J. F. Griffin and P. Coppens: *J. Am. Chem. Soc.* **97**, 3496 (1975).
37. D. J. Cram and J. M. Cram: *Science* **183**, 808 (1974).
38. J. M. Lehn and P. Vierling: *Tetrahedron Lett.* 1323 (1980).
39. J. N. Vinogradov and R. H. Linnell: *Hydrogen Bonding*, Van Nostrand Reinhold, New York, Ch. 5 (1971).