Complexation of Macrocyclic Compounds with Organic Molecules: 1 Pyridoxine Hydrochloride in Dimethylsulfoxide.

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The complexation behavior of pyridoxine hydrochloride with certain oxa- and thia-crown ethers in dimethylsulfoxide has been studied by conductometric and polarographic techniques. The vitamin is observed to form complexes with six-membered coronand rings of the crown ethers. The conductivity studies indicate 1:1 complex formation between the vitamin and the crown ether. The nature of the atoms (oxygen and sulpur) in the coronand ring is observed to affect the stability of the complex. The limiting ionic conductivity of the complexed vitamin is also reported. In addition, complexation studies of pyridoxine hydrochloride were carried out by polarography, and the results obtained compared well with those obtained by conductivity measurements.

Introduction

Vitamins are biologically active organic compounds with a diverse chemical nature. The vitamins of the B group are water-soluble compounds and contain the pyridine ring in their molecules. Out of the six forms of vitamin B6, pyridoxine was the first to be isolated and is essential in the human diet for the metabolism of amino acids and the maintenance of body cells.[1] Deficiency of this vitamin causes retarded growth, insomnia, general weakness, and skin lesions. Since the time Pedersen published the first report on crown compounds in 1967,[2] these compounds have been considered for a wide range of applications including enzyme models, biophysics, and medicine.[3] Although thermodynamic studies on cation−crown ether complexation started immediately after the first synthesis of the ligands, most of the work has been concentrated in the area of alkali, alkaline earth, and some heavy metal cation complexes. We have recently reported the complexation behavior of certain metal ions with crown ethers in mixed solvent media.[4,5] Molecular recognition by specific noncovalent interactions is crucial in biological systems. The interaction of pyridoxine hydrochloride (pyridoxine HCl) with some transition-metal ions[6−10] and it's metal binary complexes with certain amino acids have been extensively studied.[11−13] However, survey of the literature revealed absence of the complexation studies of the vitamin with polyether macrocycles.

Dimethylsulfoxide (DMSO), a dipolar aprotic solvent has found applicability as a physiological and pharmacological substrate.[14] It has a moderate viscosity (1.996 mPa s at 25 °C), a fairly high relative permittivity (46.68 at 25 °C), and extensive dissolving power. DMSO was thus chosen for study considering the solubility criteria of the water insoluble crown ethers. In the present work, an attempt has been made to study the complexation behavior of the vitamin with six-membered and eight-membered oxa-crown ethers and hexathia-crown ether in DMSO, and the concentration stability constants of the complexes so formed are reported. The macrocyclic compounds studied were 18-crown-6, dibenzo-18-crown-6, dicyclohexano-18-crown-6, dibenzo-24-crown-8, and 1,4,7,10,13,16-hexathiacyclooctadecane. The biological media in general are considered to be near aqueous media. However, certain reports highlight the lipophilic nature of the biological matrix and are better represented by nonaqueous media. Hence, the equilibrium studies of pyridoxine hydrochloride with crown ethers in DMSO as solvent would provide a better understanding of these systems.

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Experimental Section

Solvents and Reagents. The purification and storage of DMSO have been described elsewhere.[15] Pyridoxine HCl purchased from Sigma (USA) was used as such. The macrocycles, viz., 18-crown-6 (18C6), dibenzo-18-crown-6 (DB18C6), and dibenzo-24-crown-8 (DB24C8), were purchased from Aldrich (USA), 1,4,7,10,13,16-hexathiacyclooctadecane (hexathia) from Aldrich (Germany), and dicyclohexano-18-crown-6 (DCH18C6) from Fluka (Switzerland) and used as supplied. Tetraethylammonium perchlorate (TEAP) was prepared by adding a slight excess of perchloric acid (70% Loba, GR) to tetraethylammonium hydroxide (Sisco, India). The precipitate was washed several times with water to obtain the filtrate free from acid. The product thus obtained was recrystallized twice from water, dried in a vacuum, and used as supporting electrolyte. Mercury used for the working electrode was triply distilled under reduced pressure. The reference electrode used for the polarographic studies in DMSO consisted of replacing the inner solution of the conventional Ag/AgCl electrode (No. 6.1414.010, Metrohm, Netherlands) with saturated LiCl in ethanol[16] and the outer chamber with saturated solution of tetramethylammonium chloride (TMACl) in pure DMSO.

Procedures

Conductivity Measurements. All conductivity measurements[17] were made in a conventional way using a dip-type cell (cell constant 0.940 cm^{-1}) with lightly platinised electrodes at (25 ± 0.05) °C. A Toshniwal digital autoranging conductivity meter (Chemito130) was used in the measurements. The conductivity meter was regularly calibrated using standard potassium chloride solutions. As a general procedure, a measured volume of solvent was

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taken in the cell and the conductivity was measured. Thereafter, the increments of stock vitamin solution were made, and the conductivity was measured after every increment. The solvent conductivity was subtracted from the solution conductivity for the calculation of molar conductivity. The uncertainty in the measurement of conductivities was $\pm 0.1\ \mu S \cdot cm^{-1}$.

Step 1: Determination of the Limiting Molar Conductivity (Λ_0) and Association Constant of the Vitamin in DMSO. The conductivity of a measured volume of DMSO was determined, and then the increments of the vitamin stock solution ($\sim 2 \times 10^{-2}$ M) were added to the cell using a microliter syringe buret. The conductivity of the solution in the cell was measured after each transfer.

Step 2: Determination of the Concentration Stability Constant (K_{VHL^+}) of the Vitamin and Crown Ether Complex. A solution of the vitamin in DMSO was placed in the cell, and the conductivity was measured. Step-by-step increments of the crown ether stock solution ($\sim 2 \times 10^{-2}$ M) in DMSO were effected by a rapid transfer using a microliter syringe buret until the total concentration of crown ether was approximately three times greater than that of the vitamin. The conductivity of the solution was measured after each transfer of crown ether solution.

Step 3: Determination of Λ_0 of VHL. A solution of crown ether ($\sim 2 \times 10^{-3}$ M) in DMSO was placed in the cell, and the conductance of the solution was measured. Then a step-by-step increase in the concentration of the vitamin was effected by a rapid transfer of the vitamin solution ($\sim 2 \times 10^{-2}$ M) in DMSO to the cell until the concentration of vitamin becomes approximately twice as large as that of the crown ether. The conductivity of the solution was measured after each transfer of vitamin solution.

Polarographic Measurements. The polarographic system used for the studies was Electrochemical Work Station, model Autolab 30; the electrode assembly was a 663 VA stand with GPES computer software for recording and analyses of the polarograms, supplied by Eco Chemie, The Netherlands. The three-electrode cell comprising mercury as working, graphite as auxiliary, and $Ag|AgCl|LiCl_{sat}$-(EtOH)|$TMACl_{sat}$(DMSO) as a reference electrode was used for the measurements. A polarogram of the solution containing the supporting electrolyte (0.05 M TEAP) was run before every experiment. A solution of the vitamin was placed in the sample cup and polarogram was run. Step-by-step increments of the crown ether stock solution was effected until the total concentration of the crown ether was approximately thrice the concentration of the vitamin. After each addition, polarograms were recorded at a scan rate of 10 mV/s and pulse amplitude of 100 mV.

Theory

Conductivity Data Analysis. The conductivity data of pyridoxine HCl in DMSO were analyzed using the Fuoss (1978) conductance−concentration equation[18] and the Fuoss computer program. The limiting molar conductance (Λ_0), association constant (K_A), and cosphere diameter (R) have been discussed earlier[17] based on the following equilibrium

$$VHCl \rightleftharpoons VH^+ + Cl^- \qquad (1)$$

The treatment of conductivity data for the complexation of certain crown ethers with alkaline earth metals has been reported earlier.[19] An analogous approach for the complexation of the vitamin (VHCl) and crown ether (L) may be considered as

$$\underset{\alpha[VH]_t}{VH^+} + \underset{[L]_t - (1-\alpha)[VH]_t}{L} \rightleftharpoons \underset{(1-\alpha)\,[VH]_t}{VHL^+} \qquad (2)$$

where $[VH]_t$, $[L]_t$, and α are the total concentration of cation, the total concentration of crown ether, and the fraction of the uncomplexed cation, respectively. Accordingly, the thermodynamic stability constant K_{VHL^+}' is given by

$$K'_{VHL^+} = [VHL]f_{VHL^+}/[VH]f_{VH^+}[L]f_L \qquad (3)$$

where [VHL], [VH], and [L] are the concentrations of complexed cation, uncomplexed cation, and uncomplexed crown ether respectively, while f_{VHL^+}, f_{VH^+}, and f_L are the corresponding activity coefficients. The concentration stability constant K_{VHL^+}, which is reported, since f_{VHL^+} and f_{VH^+} are unknown, is given by

$$K_{VHL^+} = K'_{VHL^+}f_{VH^+}/f_{VHL^+} = [VHL]/[VH]\ [L] = (1-\alpha)/\alpha[L] \qquad (4)$$

where f_L is assumed to be unity.

The conductivity (κ) of a solution containing pyridoxine HCl and crown ether is written as

$$\kappa = k_{VH} + k_{VHL} \qquad (5)$$

where k_{VH} and k_{VHL} are the conductivities of the vitamin and vitamin−crown ether, respectively. The respective molar conductivities are given by

$$\Lambda_{VH} = k_{VH}/[VH] = k_{VH}/\alpha[VH]_t \qquad (6)$$

$$\Lambda_{VHL} = k_{VHL}/[VHL] = k_{VHL}/(1-\alpha)[VH]_t \qquad (7)$$

Equation 5 may be written in terms of molar conductance (Λ) by considering the total concentration $[VH]_t$ via eqs 6 and 7, to give

$$\Lambda = \kappa/[VH]_t = \alpha\Lambda_{VH} + (1-\alpha)\Lambda_{VHL} \qquad (8)$$

The correction for the viscosity changes is neglected, as the crown ether concentration was kept low. By use of eqs 4 and 8, one obtains

$$K_{VHL^+} = (\Lambda_{VH} - \Lambda)/\{(\Lambda - \Lambda_{VHL})\ [L]\} \qquad (9)$$

where

$$[L] = [L]_t - [VH]_t(\Lambda_{VH} - \Lambda)/(\Lambda_{VH} - \Lambda_{VHL})$$

The Λ_{VHL} value is estimated from the Λ values at the point of a large $[L]_t$ to $[V]_t$ ratio. By use of the Λ_{VHL} value, the K_{VHL^+} value in eq 9 is calculated.

The procedure for obtaining the limiting ionic conductivity is as follows:

From the principle of mass balance, the total concentration can be written as

$$[V]_t = [VH] + [VHL] \qquad (10)$$

$$[L]_t = [L] + [VHL] \qquad (11)$$

Table 1. Molar Conductivity, Λ, at Concentration *c* of Pyridoxine + 18C6 in Pure DMSO by Steps 1, 2, and 3

step 1		step 2		step 3	
$10^3 c[VH]_t$/mole·dm^{-3}	Λ/S·cm^2·mol^{-1}	$c[L]_t/c[VH]_t$	Λ/S·cm^2·mol^{-1}	$10^3 c[VH]_t$/mole·dm^{-3}	Λ/S·cm^2·mol^{-1}
2.116	27.15	0.113	35.12	0.202	31.70
3.065	25.89	0.227	35.17	0.400	31.62
4.859	24.36	0.340	35.20	0.595	30.87
6.528	22.96	0.453	35.24	0.785	30.63
10.229	20.95	0.566	35.26	0.972	29.89
13.379	19.30	0.680	35.33	1.156	29.47
17.312	18.09	0.793	35.35	1.513	28.86
20.566	17.18	0.906	35.41	1.856	28.10
		1.019	35.47	2.188	27.45
		1.133	35.58	2.508	26.90
		1.246	35.62	2.817	26.40
		1.359	35.67	3.115	25.96
		1.472	35.82	3.403	25.79
		1.586	35.91	3.682	25.35
		1.699	35.99	3.952	25.04
		1.926	36.15		
		2.152	36.18		

On combination of eq 4 with eqs 10 and 11, the following quadratic equation is obtained

$$K_{VHL^+}[VHL]^2 - \{1 - K_{VHL^+}([V]_t + [L]_t)\}[VHL] + K_{VHL^+}[V]_t[L]_t = 0 \quad (12)$$

The [VH] value is obtained from eq 10 using the [VHL] value calculated from eq 12 at a particular concentration of vitamin $[V]_t$ and crown ether $[L]_t$. The k_{VH} value in eq 5 at this [V] point can be obtained from the Λ_{VH} vs $[VH]^{1/2}$ plot. Then the Λ_{VHL} value at the corresponding [VHL] point can be calculated from eqs 5 and 7 using this k_{VH} value and organized in the form of a Λ_{VHL} vs $[VHL]^{1/2}$ plot. The limiting molar conductance (Λ_0) of the vitamin−crown ether is determined by extrapolation of the plot generated in the above manner. The limiting ionic conductivity (λ_0-(VHL^+)) of the vitamin−crown ether is obtained by using $\lambda_{0,Cl^-} = 24.4$ S·cm^2·mol^{-1}.[20]

Polarographic Studies. The determination of stability of complexes by polarography is based on the fact that on complexation the half-wave potential is shifted to more negative potentials.[21] The relation between the shift in the half wave potential and the stability constant is as follows

$$\Delta E_{1/2} = (E_{1/2})_s - (E_{1/2})_c = (0.05916/n) \log B_p + (0.05916p/n) \log C_x \quad (13)$$

where $(E_{1/2})_s$ and $(E_{1/2})_c$ are the half-wave potentials of the free and complexed cations, respectively, B_p is the stability constant, C_x the total ligand concentration, and "p" is the ligand-to-vitamin ratio. The half-wave potential obtained by sampled DC can be correlated to the peak potential (E_p) as obtained by differential pulse polarography (DPP) by the following equation

$$E_{1/2} = E_p + \Delta E/2 \quad (14)$$

As the shift in peak potentials can be measured more accurately than the half-wave potentials, eq 13 can be replaced by

$$\Delta E_p = (E_p)_s - (E_p)_c = (0.05916/n) \log B_p + (0.05916p/n) \log C_x \quad (15)$$

Equation 15 indicates that the plot of ΔE_p vs log C_x would provide the value of $(0.05916/n)$ log B_p as intercept and $0.05916p/n$ as slope. These plots are used to calculate the stability constants.[5]

Table 2. Molar Conductivity, Λ, at Concentration c of Pyridoxine + DB18C6 in Pure DMSO by Steps 2 and 3

step 2		step 3	
$c[L]_t/c[VH]_t$	Λ/S·cm^2·mol^{-1}	$10^3 c[VH]_t$/mol·dm^{-3}	Λ/S·cm^2·mol^{-1}
0.184	31.00	0.198	35.07
0.361	31.17	0.393	34.63
0.541	31.34	0.584	33.77
0.722	31.51	0.771	32.97
0.902	31.63	0.954	32.29
1.083	31.85	1.134	32.01
1.263	31.91	1.484	30.73
1.444	31.97	1.821	29.81
1.624	32.02	2.147	29.02
1.805	32.07	2.461	28.37
2.045	32.09	2.764	27.93
2.286	32.16	3.057	27.48
2.526	32.17	3.340	26.74
2.767	32.17		
3.028	32.14		

Results and Discussion

The values of limiting molar conductance, Λ_0, $\lambda_0(VHL^+)$, and K_A for pyridoxine HCl have been reported earlier.[17] It has been observed that the K_A value of the vitamin in DMSO is fairly high and that the pyridoxine cation is extensively solvated by DMSO as observed by the rapid decrease in the Walden product with increasing content of DMSO.[17]

The conductometric data for the vitamin by steps 1−3 are given in Tables 1−4. Figure 1 represents the results of the studies on the pyridoxine cation complexation with DB18C6 by conductometric method. Figure 2 represents the limiting molar conductance plot of pyridoxine+DB18C6 (Λ_0 vs $[VL^{n+}]^{1/2}$). The plot of Λ vs $[L]_t/[VH]_t$ did not exhibit any inflection for DB24C8, indicating the absence of formation of any complex. It was observed that the Λ value increases with an increase in $[L]_t/[VH]_t$ for all the complexes of pyridoxine with the 18-membered crowns. Such observation implies that the conductivity of the complexed ion is larger than that of the simple uncomplexed ion and can be explained as follows:

It has been already shown that the pyridoxine cation is extensively solvated by the solvent, viz., DMSO. On account of the strong solvation of the cation and less solvated complex with the small crown ether, the moving entity of the complex may be less bulky and more mobile. Hence

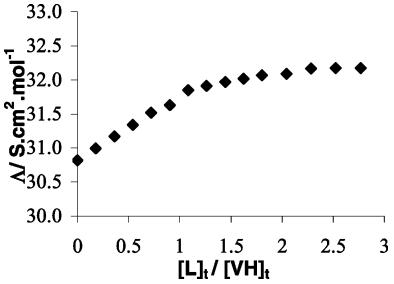

Figure 1. Plot of Λ vs $[L]_t/[VH]_t$ for the DB18C6 + pyridoxine system.

Table 3. Molar Conductivity, Λ, at Concentration *c* of Pyridoxine + DCH18C6 in Pure DMSO by Steps 2 and 3

step 2		step 3	
$c[L]_t/c[VH]_t$	Λ/S·cm²·mol⁻¹	$10^3c[VH]_t$/mol·dm⁻³	Λ/S·cm²·mol⁻¹
0.101	33.08	0.393	36.05
0.202	33.15	0.584	35.83
0.302	33.16	0.771	35.31
0.403	33.22	0.954	34.81
0.504	33.27	1.134	34.40
0.605	33.32	1.484	33.29
0.706	33.41	1.822	32.39
0.807	33.51	2.147	31.82
0.907	33.59	2.461	31.09
1.008	33.62	2.764	30.43
1.109	33.64	3.057	29.97
1.210	33.61	3.340	29.35
1.311	33.63	3.614	28.89
1.411	33.63	3.879	28.54
1.512	33.64		
1.613	33.63		
1.714	33.63		
1.815	33.68		
1.915	33.66		
2.016	33.69		

Table 4. Molar Conductivity, Λ, at Concentration *c* of Pyridoxine + Hexathia in Pure DMSO by Steps 2 and 3

step 2		step 3	
$c[L]_t/c[VH]_t$	Λ/S·cm²·mol⁻¹	$10^3c[VH]_t$/mol·dm⁻³	Λ/S·cm²·mol⁻¹
0.197	33.04	0.393	33.04
0.295	33.11	0.584	33.04
0.394	33.23	0.771	32.54
0.492	33.34	0.954	31.63
0.590	33.40	1.311	29.89
0.689	33.56	1.655	28.45
0.787	33.66	1.986	27.69
0.885	33.86	2.306	27.23
0.984	33.96	2.614	26.93
1.082	33.94	2.912	26.54
1.181	33.97	3.199	26.25
1.377	34.07	3.478	25.79
1.476	34.14	3.747	25.51
1.672	34.16	4.008	25.25
1.869	34.28		
2.066	34.32		
2.164	34.30		

the conductivity of the less solvated complex is larger than that of the strongly solvated uncomplexed ion.

In all cases, a clear break point at $[L]_t/[VH]_t \approx 1$ is observed for all the pyridoxine−crown ether complexes studied, as evident by a representative plot for the pyridoxine + DB18C6 system given in Figure 1. It is observed from this figure that the Λ values continue to increase with the addition of crown ether until the ratio $[L]_t/[VH]_t$ reaches close to 1. Thereafter, further increase in crown ether concentration does not show any change in conductivity, indicating 1:1 complexation. Additional complexes such as the 2:1 complex VHL_2^+ are not considered in the present

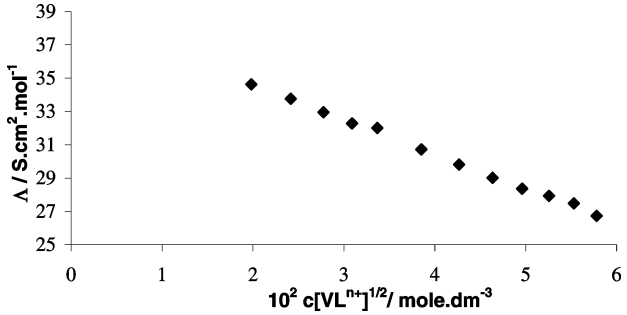

Figure 2. Plot of Λ of complex vs $10^2c[VL^{n+}]^{1/2}$/mole·dm^{-3} for the DB18C6 + pyridoxine system.

analysis. In the current studies, we are confining our discussion to 1:1 complexes. In case of the benzo-substituted crown ethers, such behavior is not observed probably due to the steric hindrance imparted by the bulky substituents. The site of the interaction of the vitamin with the crown ether may be the pyridine ring with the N atom of the ring approaching the crown cavity with the vitamin molecule being directly perpendicular to the plane of the crown ether. The interactions of amino acids with oxa-crown ethers have been well studied.[22] In these cases, NH_3^+ of an amino acid, each H atom interacts with one O atom of the crown ether via hydrogen bonding and the N atom bonds with three O atoms via electrostatic attraction. A full participation of all macrocyclic donor atoms with the complexed cation is expected to give the highest possible stability to the resulting complex. This does not seem to be the case with pyridoxine since only nitrogen in the pyridine ring is available for complexation. Such behavior is reflected in the weak stability of the complexes. Because of the greater solvation of the cation, the stability of complex in the particular medium decreases, i.e., the solvation of the cations influences the stabilities of the complexes formed. Such a study on the strength of solvation of the metal ion was studied by Buschmann and Schollmeyer.[23] Also, with greater dissociation of the molecule, the cation can react more easily with the crown ether. Although the impetus for dissociation is the electronegative chloride anion, pyridoxine HCl being a highly associated molecule in DMSO, the interaction of the cation with the crown becomes difficult, thus decreasing the stability of the complex. A summary of the results, i.e., stability constants and limiting ionic conductivities of the complexes obtained from the complexation studies are given in Tables 5. As seen from the results, pyridoxine HCl does form complexes with six-membered coronand ring systems. The substitution of oxygen by sulfur in the coronand ring is observed to increase the stability of the complex. The stability constant values of pyridoxine HCl with 18C6 and DCH18C6 are observed to be almost similar, whereas in the case of DB18C6, the complex shows greater stability. Such behavior has been observed earlier in the case of transition-metal ions.[24] A relatively higher stability with DB18C6 could be due to the unsaturated benzo-group substituent, which is electron rich and thus favoring interaction with the cation.

Polarographic studies showed that, in pure DMSO, pyridoxine HCl exhibits a single irreversible reduction peak. The reduction may be either due to catalytic hydrogen evolution or direct attack on the pyridine ring[25] as shown in Scheme 1.

The negative shift in the E_p value of the vitamin on addition of crown ether indicates that the electroactive site of the vitamin is involved in the interaction with the ligand. The effect of hexathia on the reduction peak of pyridoxine

Scheme 1

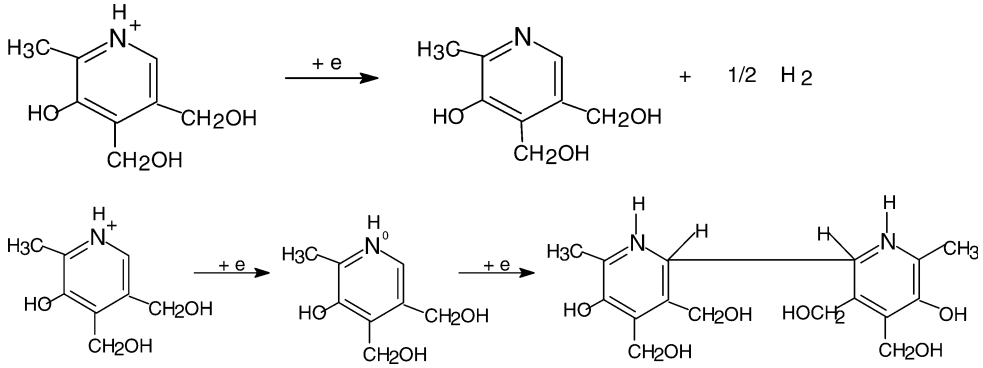

Table 5. Limiting Ionic Conductivities, $\lambda_0(VHL^+)$ and Concentration Stability Constants, $\log(K_{VHL^+})$ for Pyridoxine + Crown Ether Complexes by Conductometry

pyridoxine cation	$\lambda_0(VHL^+)$/S·cm²·mol⁻¹	$\log(K_{VHL^+}$/mol·dm⁻³)[a]
18C6	10.05	0.61
DB18C6	14.00	1.48
DCH18C6	16.03	0.78
hexathia	12.91	0.85

[a] In all the cases, the standard deviation was <0.06 ($5 \le n \le 9$).

Table 6. Summary of the Concentration Stability Constants, $\log(K_{VHL^+})$ of Pyridoxine + Crown Ether Complexes by Different Methods[a]

crown ether	conductometric method	polarographic method
18C6	0.61	0.46
DB18C6	1.48	1.29
DCH18C6	0.71	0.51
hexathia	0.85	0.84

[a] In all the cases, the standard deviation was <0.06 ($5 \le n \le 9$).

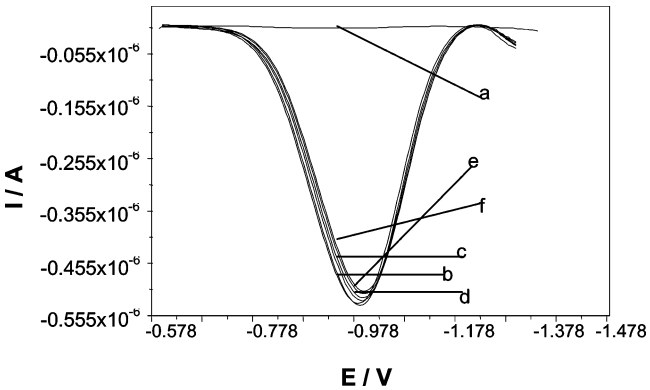

Figure 3. Effect of hexathia on the reduction peak by DPP. a, blank (0.05 M TEAP); b, pure vitamin, concentration = 1.235×10^{-3} M; c, L_1, concentration = 4.752×10^{-4} M; d, L_2, concentration = 7.677×10^{-4} M; e, L_3, concentration = 1.302×10^{-3} M; f, L_4, concentration = 2.400×10^{-3} M.

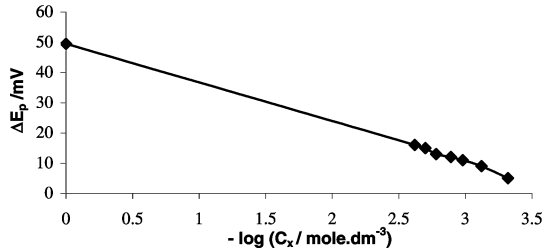

Figure 4. Plot of ΔE_p vs $-\log C_x$ for the hexathia + pyridoxine system.

by DPP is shown in Figure 3. The plot of ΔE_p vs $-\log C_x$ for the pyridoxine−hexathia is shown in Figure 4. It is observed from Figure 3 that the negative shift in the peak potential of the vitamin on progressive addition of crown ether is continued up to $[L]_t \approx [VH]_t$ and further increase in crown ether concentration does not show any shift in peak potential, indicating 1:1 complexation. The same behavior is observed for all crown ethers. Table 6 summarizes the concentration stability constants obtained by conductometric and polarographic methods. It is noticed from the table that all the polarographic values are less than conductometric ones. It may be due to the presence of the supporting electrolyte, viz., 0.05 M TEAP, in the polarographic measurements, which affects the complexation equilibria. However, the close agreement between the results gives an accurate indication of the stability of the complexes.

Literature Cited

(1) Kaplan, L. A.; Pesce, A. J. *Clinical Chemistry*; C. V. Mosby: St. Louis, 1989; 555.
(2) Pedersen, C. J. Cyclic Polyethers and Their Complexes with Metal Salts. *J. Am. Chem. Soc.* **1967**, *89*, 7017−7036.
(3) Glendening, E. D.; Feller D.; Thompson, M. A. An ab Initio Investigation of the Structure and Alkali Metal Cation Selectivity of 18-Crown-6. *J. Am. Chem. Soc.* **1994**, *116*, 10657−10669.
(4) Ijeri, V. S.; Srivastava, A. K. Complexation of Macrocyclic Compounds with Metal Ions: 1. Cd(II), Pb(II), Co(II), Mn(II), and Ag(I) in 40 Volume % Ethanol + Water. *J. Chem. Eng. Data*. **2002**, *47*, 346−350.
(5) Samant, R. A.; Ijeri, V. S.; Srivastava, A. K. Complexation of Macrocyclic Compounds with Metal Ions: 2. Mg(II), Ca(II), Sr(II), Ba(II), Cu(II), and Ag(I) in 20 Mass % Propylene Carbonate + Ethylene Carbonate. *J. Chem. Engg. Data*. **2003**, *48*, 203−207.
(6) Lopes, M. H.; Novais, A. Complexes of Biological Interest. II. Polarographic Determination of Formation Constants of Cd(II) with B6 using De Ford and Hume Methods. *Rev. Port. Farm* **2000**, *50*, 151−159.
(7) Shabilaloc, A. A.; Saidalieva, A. K.; Shadmanov, K. K. Mixed-Ligand Coordination Compounds of Cobalt (II) with Pyridoxine and Vitamin B3 and Its Isomer. *Uzb. Khim. Zh.* **1998**, *1*, 16−19.
(8) Dobrynina, N. A.; Nikolaeva, L. S.; Petrosyan, A. G. Complexation of Rare Earth Elements with Pyridoxine. *Zh. Neorg. Khim.* **1999**, *44*, 1160−1164.
(9) Zhu, Y. C.; Zhang, M. Q.; Wu, J. G.; Deng, R. W. The Study of Equilibrium and Formation Constants of Some Transition Metal Complexes with Vitamin B6 in Solution by Potentiometry. *Chem. Pap.* **2001**, *55*, 229−232.
(10) Lopes, M. H.; Costa, M. Graphic Method for the Determination of the Number of Species in Solutions of Complexes of Vitamin B6 and Metallic Cations Using Spectrophotomertic Data. *Rev. Port. Farm.* **1998**, *48*, 105−108.
(11) Khan, F.; Sahu, P. Thermodynamic Consideration in Complex Formation of [Cd−L-Amino Acidate−Vitamin B6] system. *J. Inst. Chem.* **2000**, *72*, 127−128.
(12) Shuaib, N. M.; Marafie, H. M.; Othman, A.-F.; El-Ezaby, M. S. Complexes of Vitamin B6. 23. Interaction of Some Tertiary Ligating Amino Acids with the Binary Complexes of Ni(II) or Cu(II) and Pyridoxamine. *J. Chem. Eng. Data* **1999**, *44*, 1348−1354.

(13) Sharma, G.; Chandel, C. P. S. Electrochemical Studies on Mixed Ligand Complexes of Cadmium Ion with Some Dicarboxylic Acids and Pyridoxine (Vitamin B6). *Asian J. Chem.* **2002**, *14*, 23−33.
(14) Fox, M. F.; Whittingham, K. P. Component Interactions in Aqueous Dimethylsulphoxide. *J. Chem. Soc., Faraday Trans. 1* **1975**, *71*, 1407−1412.
(15) Srivastava, A. K.; Jagasia, I. M. Conductance Behaviour of Certain Potassium Alkyl Xanthates in Dimethylsulphoxide + Water at 25 °C. *J. Electroanal. Chem.* **1995**, *385*, 171−175.
(16) Lubert, K. H.; Wagner, M.; Olk, R.-M. Voltammetric Characterization of an Insoluble Tetrathiafulvalene Derivative by Means of Modified Carbon Paste Electrode. *Anal. Chim. Acta* **1996**, *336*, 77−84.
(17) Srivastava, A. K.; Shivdas, R. Conductance Behaviour of Pyridoxine Hydrochloride in Dimethylsulphoxide + Water at 25 °C. *J. Electroanal. Chem.* **1995**, *399*, 235−238.
(18) Fuoss, R. M. Conductance-Concentration Function for the Paired Ion Model. *J. Phys. Chem.* **1978**, *82*, 2427−2440.
(19) Srivastava, A. K.; Tiwari, B. Behaviour of Alkaline Earth Metals and Silver Perchlorates and Their Complexes with Some Crown Ethers in Propylene Carbonate. *J. Electroanal. Chem.* **1992**, *325*, 301−311.
(20) Conway, B. E.; Bockris, J. O'M. *Modern Aspects of Electrochemistry*; Butterworth: London, 1972.
(21) Irwing, H. The Stability of Metal Complexes and Their Measurements Polarographically. In *Advances in Polarography*; Langmuir, I. N., Ed.; Pergamon Press: New York, 1960.
(22) Danil de Namor, A. F.; Ritt, M.; Schwing- Weill, M.; Arnaud-Neu F.; Lewis, D. F. V. Solution Thermodynamics of Amino Acid-Cryptand 222 Complexes in Methanol and Ethanol. *J. Chem. Soc., Faraday Trans.* **1991**, *87*, 3231−3239.
(23) Buschmann, H.-J.; Schollmeyer, E. The Complexation Reaction of 18-Crown-6 with Ag^+ in Different Solvents Studied by Potentiometric and Calorimetric Methods. *Inorg. Chim. Acta* **2000**, *298*,-120−122.
(24) Izatt, R. M.; Bradshaw, J. S.; Nielsen, S. A.; Lamb, J. D.; Christensen, J. J. Thermodynamic and Kinetic Data for Cation-Macrocycle Interaction. *Chem. Rev.* **1985**, *85*, 271−339.
(25) Mann, C. K. and Barnes, K. K. *Electrochemical Reactions in Nonaqueous Systems*; Marcel Dekker: New York, 1970.

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