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Thermodynamics of complexation of some transition metal ions by salicylaldehyde carbohydrazone pyridinium chloride and diacetyl carbohydrazone pyridinium chloride

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Abstract

The proton–ligand dissociation constants pK_a^H of salicylaldehyde carbohydrazone pyridinium chloride (SGP) and diacetyl carbohydrazone pyridinium chloride (DGP) and the stepwise stability constants of their complexes with Fe^{3+}, Cu^{2+}, Hg^{2+}, Ni^{2+} and Pb^{2+} have been determined pH-metrically in aqueous solution at different temperatures. Values of $\bar{n}_A$, $\bar{n}$ and pL have been calculated by Bjerrum and Calvin's method, as adapted by Irving and Rossotti. The relative stabilities of the complexes formed were: $Fe^{3+} > Cu^{2+} > Pb^{2+} > Ni^{2+} > Hg^{2+}$. The thermodynamic functions ΔG, ΔH, ΔS and ΔC_p have been determined. The negative values of free energy change for all chelates indicate that the complex formation reactions are spontaneous. The enthalpy change values are negative indicating that the complexation reactions have an exothermic nature. The complex formation in all cases is entropically favourable due to the positive entropy change values. The ΔC_p values are zero over the temperature range studied because the plots of $\log K$ versus $1/T$ are linear in all cases. The ratios of metal to ligand were determined conductometrically.

INTRODUCTION

In our previous studies [1, 2], a microcalorimetric technique was used to derive the stability constants and the thermodynamic parameters for the binding of α-cyclodextrin with many straight chain alkanols and α,ω-alkanediols in aqueous solution. In continuation of our studies, here we report the formation constants and the thermodynamic parameters for the complexes formed between salicylaldehyde Girard-P hydrazone (SGP) or diacetyl Girard-P hydrazone (DGP) and some transition metal ions as determined by potentiometry. Metal-ion complex formations are among the most prominent interactions in nature [3, 4]. Binding by metal ions and proteins can influence the biological action of medicinal agents. Of

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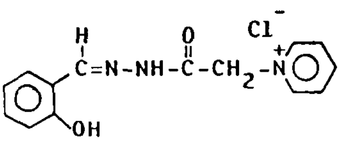
particular importance in pharmacy and medicine is the relationship between complexation and the absorption and distribution of a drug in the body and the way in which complexation influences the onset and duration of drug action [5].

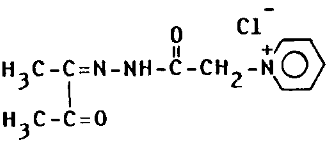
The choice of the hydrazones as ligands and of Cu^{2+}, Ni^{2+}, Fe^{3+}, Hg^{2+} and Pb^{2+} as metal ions is owing to the reported tuberculostatic activity of aroyl hydrazones [6]. Their mode of action has been attributed to the formation of stable chelates with the transition metals present in the cell. Such processes inhibit a great many of the vital enzymatic reactions catalysed by these transition ions [7]. It is interesting to study the hydrazone complexes of Cu^{2+}, Fe^{3+}, and Ni^{2+} ions which are normally present in the human body. In addition Hg^{2+} and Pb^{2+} were chosen as toxic metals, following Albert's classification of metal binding agents with chemotherapeutic activity into antidotes and antibacterial agents [8].

EXPERIMENTAL

The ligands were prepared as described previously [9] and were recrystallized from ethanol.



SGP



DGP

Solutions of metal ions were prepared by weighting AnalaR chlorides into deionized water; the solutions were standardized complexometrically by EDTA [10]. Carbonate-free sodium hydroxide solution was prepared [10] and standardized against AnalaR oxalic acid. KCl was used to maintain constant ionic strength ($\mu = 0.1$). Bjerrum and Calvin's method, as adapted by Irving and Rossotti [11], was used to determine the average number of protons associated with a reagent molecule $\bar{n}_A$, the average number of ligand molecules attached per metal ion $\bar{n}$, and the free ligand exponent pL. From these values, the protonation constants of the ligand as well as the formation constants of the metal complexes in aqueous solution can easily be calculated by different computational methods [12, 13].

Titrations were carried out at constant temperature. This was adjusted to ±0.05°C by circulating water from an ultrathermostat (Kotterman 4130, Germany) through the annular space of a double-walled Pyrex titration cell of 50 ml capacity. Alkali was added from a microburette (5 ml). The contents of the titration vessel were stirred magnetically. The pH-meter readings were measured to 0.01 units with an Orion Research model 601 A/digital ionalyzer, standardized before and checked after each titration with buffer solutions produced by Fisher (New Jersey, USA). The following solutions were titrated potentiometrically by successive additions of 0.1 ml standardized 0.02 M sodium hydroxide.

(1) 5 ml HCl (10^{-2} M) + 5 ml KCl (1 M)
(2) 5 ml HCl (10^{-2} M) + 5 ml KCl (1 M) + 5 ml ligand (10^{-2} M)
(3) 5 ml HCl (10^{-2} M) + 5 ml KCl (1 M) + 5 ml ligand (10^{-2} M)
+ 5 ml metal chloride (10^{-3} M)

Before the titrations, all the above solutions were made up to 50 ml with deionized water. The titrations were repeated for temperatures of 288.15, 298.15 and 308.15 K. Titrations were carried out for ligand:metal ion ratios ranging from 10 to 1, in order to satisfy the maximum coordination possibility of the metal ions. In the case of Cu^{2+}, titrations were also carried out with twice the metal concentration described above, but the stability constant obtained did not differ by more than 0.2% from that determined at the lower metal concentration.

For the conductomeric measurements, a YSI model 35 conductance meter connected with a dipping cell (cell constant = 1) was used. In the conductometric titrations, 25 ml of 10^{-3} M metal chloride were titrated with 10^{-2} M ligand solution at 298.15 K.

RESULTS AND DISCUSSION

The proton–ligand system

To calculate the stepwise and overall stability constants of the metal chelates, the proton–ligand formation constant must be known. The acid dissociation constants of the ligands were calculated from the titration curves of the acid in the presence and absence of ligand. The formation curves at 298.15 K, Fig. 1, for the proton–ligand systems were extended between 0 and 1 (for DGP) and between 0 and 2 (for SGP) in the $\bar{n}_A$ scale. These values indicate that DGP has one dissociable proton (the enolized hydrogn ion of NH in the hydrazone moiety), whereas SGP has two (the enolized hydrogn ion of NH in the hydrazone moiety and the phenolic OH). From these curves, one can obtain directly the protonation constants $\log K_1^H$ and $\log K_2^H$ by interpolation at $\bar{n}_A = 0.5$ and 1.5, respectively. These values have also been evaluated by the least-squares technique [12, 13]

$$\frac{\bar{n}_A}{(1-\bar{n}_A)[H^+]} = \frac{1}{K_1} + \frac{1}{K_1K_2}\frac{(2-\bar{n}_A)[H^+]}{(1-\bar{n}_A)} \tag{1}$$

where

$$K_1 = \frac{[HL^-][H^+]}{[H_2L]} \qquad K_2 = \frac{[H^+][L^{2-}]}{[HL^-]}$$

The protonation constants obtained are given in Tables 1 and 2.

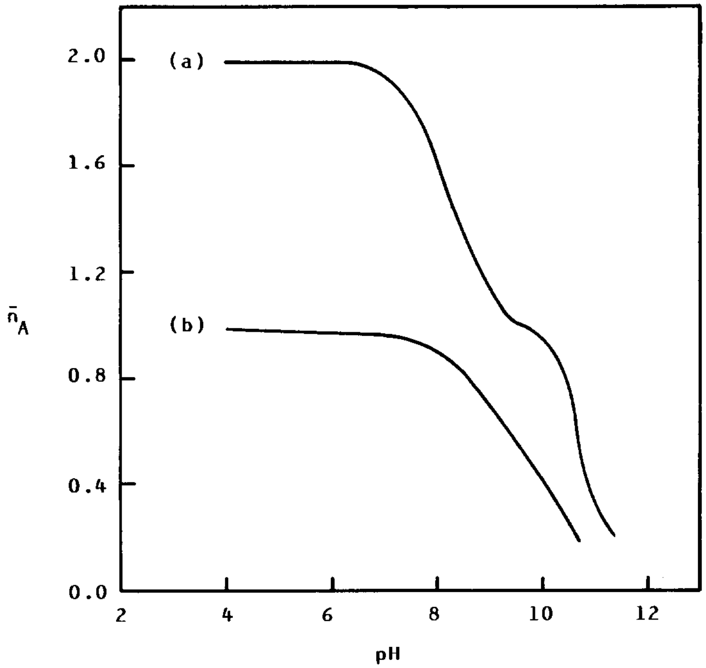


Fig. 1. Formation curves of the proton–ligand system of (plot a) SGP, and (plot b) DGP at 298.15 K.

Inspection of these tables reveals that DGP has a lower pK_1^H value than SGP; this can be attributed to the decrease in electron density on the hydrazone moiety caused by the –M effect of the carbonyl group in DGP. This leads to the conclusion that the removal of a hydrazone–moiety proton from DGP is easier than from SGP, confirming that DGP has a lower basic character.

Metal–ligand system

The respective metal ions in the presence of both ligands were titrated against NaOH solution and the results are represented graphically in Figs. 2 and 3. It can be seen that there is a clear separation between the titration curves of the metal complex and of the ligands. These results indicate the release of protons due to complexation. The possible formation of metal hydroxide is excluded because no precipitate was observed in the titration vessel. Values of $\bar{n}$ and pL were obtained according to Irving and Rossotti [11]

$$\bar{n} = \frac{(V_3 - V_2)(N^0 + E^0)}{(V_0 + V_1)T^0_{\mathrm{CM}}\bar{n}_{\mathrm{A}}} \qquad (2)$$

$$\mathrm{p}L = \log\left[\frac{\sum_0^n \beta_{\mathrm{n}}^{\mathrm{H}}[\mathrm{H}^+]^n(V_0 + V_3)}{(T^0_{\mathrm{CL}} - \bar{n}T^0_{\mathrm{CM}})V_0}\right] \qquad (3)$$

TABLE 1

Formation constants of some metal ion chelates formed with SGP and DGP calculated by different computational methods at 288.15 K

Cation	Computational method	Formation constants			
		SGP		DGP	
		$\log K_1$	$\log K_2$	$\log K_1$	$\log K_2$
H^+	Half $\bar{n}$	11.01	8.43	9.98	–
	Average value	11.06	8.50	9.95	–
	Least-squares fitting	10.93	8.42	9.98	–
	Mean	11.00	8.45	9.97	–
Fe^{3+}	Half $\bar{n}$	9.45	7.45	8.30	6.50
	Successive approximation	9.25	7.40	8.22	6.52
	Least-squares fitting	9.34	7.38	8.20	6.56
	Mean	9.33	7.41	8.24	6.54
Cu^{2+}	Half $\bar{n}$	8.80	7.01	7.61	6.08
	Mid-point	8.77	6.79	7.66	5.92
	Least-squares fitting	8.73	6.96	7.59	6.00
	Mean	8.70	6.92	7.62	6.00
Ni^{2+}	Half $\bar{n}$	6.85	5.71	5.85	4.82
	Mid-point	8.70	5.79	5.79	4.77
	Least-squares fitting	8.72	5.69	5.82	4.78
	Mean	6.76	5.73	5.82	4.79
Pb^{2+}	Half $\bar{n}$	7.68	6.23	6.70	5.28
	Successive approximation	7.58	6.10	6.63	5.23
	Least-squares fitting	7.57	6.21	6.62	5.24
	Mean	7.61	6.18	6.65	5.25
Hg^{2+}	Half $\bar{n}$	6.18	5.08	5.09	4.26
	Correction term	6.02	5.16	5.21	4.32
	Least-squares fitting	6.07	5.10	5.14	4.32
	Mean	6.09	5.11	5.15	4.30

where V_1, V_2 and V_3 denote the volume of alkali required to reach the same pH in the titration of mixtures (1), (2) and (3), respectively, V_0 is the initial volume of titrated solution (50 ml), N^0 the normality of the alkali, E^0 the initial concentration of the free acid, T^0_{CM} the total metal ion concentration, T^0_{CL} the total ligand concentration and β^H_n the overall proton–ligand formation constant value. The maximum value of $\bar{n}$ in all cases was found to be ≈ 2, confirming the formation of both ML and ML_2 types of complexes. The $\bar{n}$ and pL values were utilized to calculate successive stability constants

TABLE 2

Thermodynamic parameters and stepwise stability constants for ML and ML_2 chelates at various temperatures

Cation	Temperature (K)						Free energy change (kJ mol^{-1})		Enthalpy change (kJ mol^{-1})		Entropy change (J K^{-1} mol^{-1})	
	288.15		298.15		308.15							
	$\log K_1$	$\log K_2$	$\log K_1$	$\log K_2$	$\log K_1$	$\log K_2$	$-\Delta G_1$	$-\Delta G_2$	$-\Delta H_1$	$-\Delta H_2$	ΔS_1	ΔS_2
Salicylaldehyde carbohydrazone pyridinium chloride (SGP)												
H^+	11.00	8.45	10.75	8.22	10.51	8.01	−61.37	−46.93	−41.57	−37.38	−66.4	−32.0
Fe^{3+}	9.33	7.41	9.07	7.19	8.80	7.00	51.78	41.05	45.02	34.83	22.7	20.9
Cu^{2+}	8.70	6.92	8.49	6.72	8.27	6.54	48.47	38.37	36.53	32.28	40.1	20.4
Ni^{2+}	6.76	5.73	6.59	5.55	6.41	5.39	37.62	31.69	29.73	28.88	26.5	9.4
Pb^{2+}	7.61	6.18	7.46	6.00	7.32	5.84	42.59	34.25	24.63	28.88	60.2	18.0
Hg^{2+}	6.09	5.11	5.95	4.97	5.82	4.84	33.97	28.37	22.94	22.94	37.0	18.2
Diacetyl carbohydrazone pyridinium chloride (DGP)												
H^+	9.97	–	9.74	–	9.53	–	−55.61	–	−37.38	–	−61.1	–
Fe^{3+}	8.24	6.54	8.00	6.38	7.79	6.20	45.67	36.42	38.23	28.88	25.0	25.3
Cu^{2+}	7.62	6.00	7.41	5.85	7.19	5.68	42.30	33.40	36.53	27.18	19.4	20.9
Ni^{2+}	5.82	4.79	5.65	4.65	5.50	4.50	32.14	26.55	27.18	24.63	16.6	6.4
Pb^{2+}	6.65	5.25	6.46	5.11	6.28	4.95	36.88	29.17	31.43	25.48	18.3	12.4
Hg^{2+}	5.15	4.30	5.00	4.17	4.86	4.03	28.26	23.81	24.63	22.94	12.2	2.9

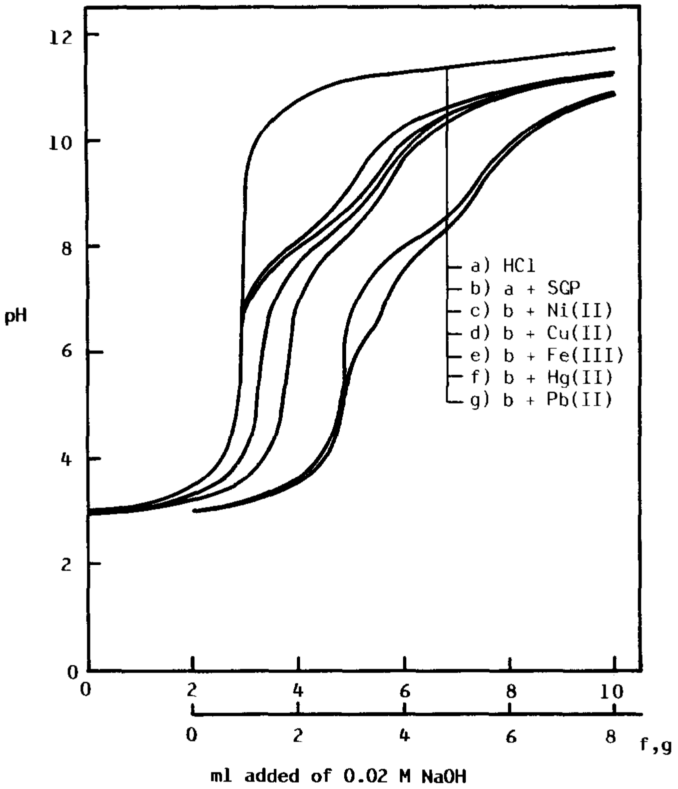


Fig. 2. Potentiometric titration curves for SGP in the presence of various metal ions at 288.15 K.

of metal complexes using the usual computational methods [12, 13], such as half-$\bar{n}$ values, successive approximation and correction term. The stepwise formation constants were also determined graphically using a linear least-squares treatment equation, after Irving and Rossotti [11, 12]

$$\frac{\bar{n}}{(1-\bar{n})[\mathrm{L}]} = K_1 + \beta_2\left(\frac{2-\bar{n}}{1-\bar{n}}\right)[\mathrm{L}] \tag{4}$$

These values are also recorded in Tables 1 and 2. It was found that the stability constants calculated by the different methods are in good agreement with those derived from eqn (4).

The number of vacant sites of the metal ion or its coordination number plays an important role in the binding with the ligand. These sites are more freely available for the binding of a first ligand than for a second. Hence, in none of the investigated complexes is $K_2 > K_1$, i.e. $\log K_1 - \log K_2$ values are usually positive. In the present study, this value lies between 0.83 and 2.55 log K units. Inspection of Table 2 indicates that the order of increasing stability constants for the metal ions with both ligands under investigation is: $Fe^{3+} > Cu^{2+} > Pb^{2+} > Ni^{2+} > Hg^{2+}$, which is in accordance with Irving

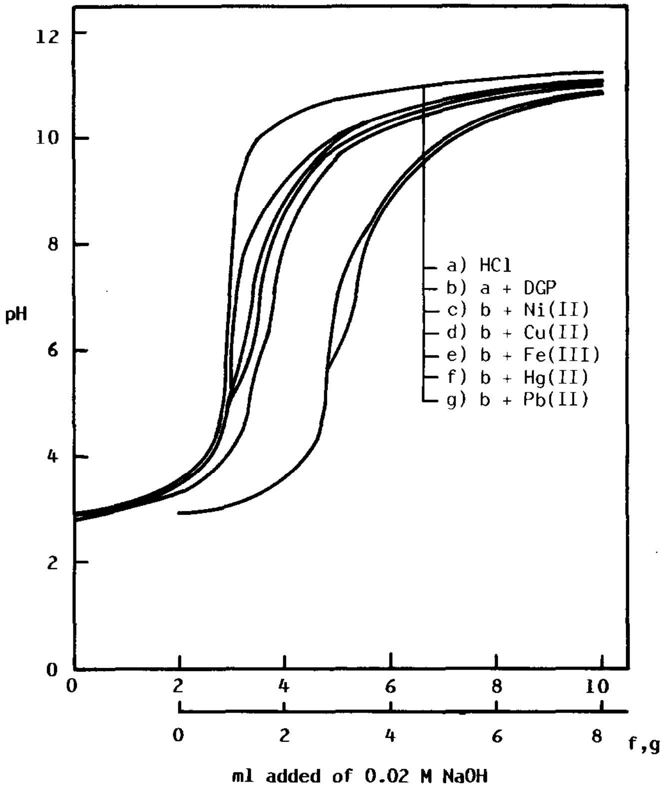


Fig. 3. Potentiometric titration curves for DGP in the presence of various metal ions at 298.15 K.

and Williams [14]. Also the values of $\log K_1$ or $\log K_2$ for a given metal ion with both SGP and DGP follow the order SGP > DGP, which is the same order of the basicity of the ligands.

In Fig. 4, the values of $\log K_1$ for SGP chelates are plotted versus the corresponding $\log K_1$ values for DGP chelates at different temperatures. By linear regression of the data in Fig. 4, the following relations are obtained at 288.15, 298.15 and 308.15 K, respectively.

$$\log K_1 \text{ (SGP chelates)} = 0.81 + 1.03 \log K_1 \text{ (DGP chelates)}$$

$$\log K_1 \text{ (SGP chelates)} = 0.86 + 1.02 \log K_1 \text{ (DGP chelates)}$$

$$\log K_1 \text{ (SGP chelates)} = 0.92 + 1.01 \log K_1 \text{ (DGP chelates)}$$

It can be seen that, at each temperature, a linear relation is obtained with a correlation coefficient ≈ 1. The intercepts are found to be 0.81, 0.86 and 0.92 at 288.15, 298.15 and 306.15 K, respectively. These values correspond approximately to the basicity difference ΔpK_1^H, where

$$\Delta pK_1^H = [pK_1^H(\text{SGP}) - pK_1^H(\text{DGP})]$$

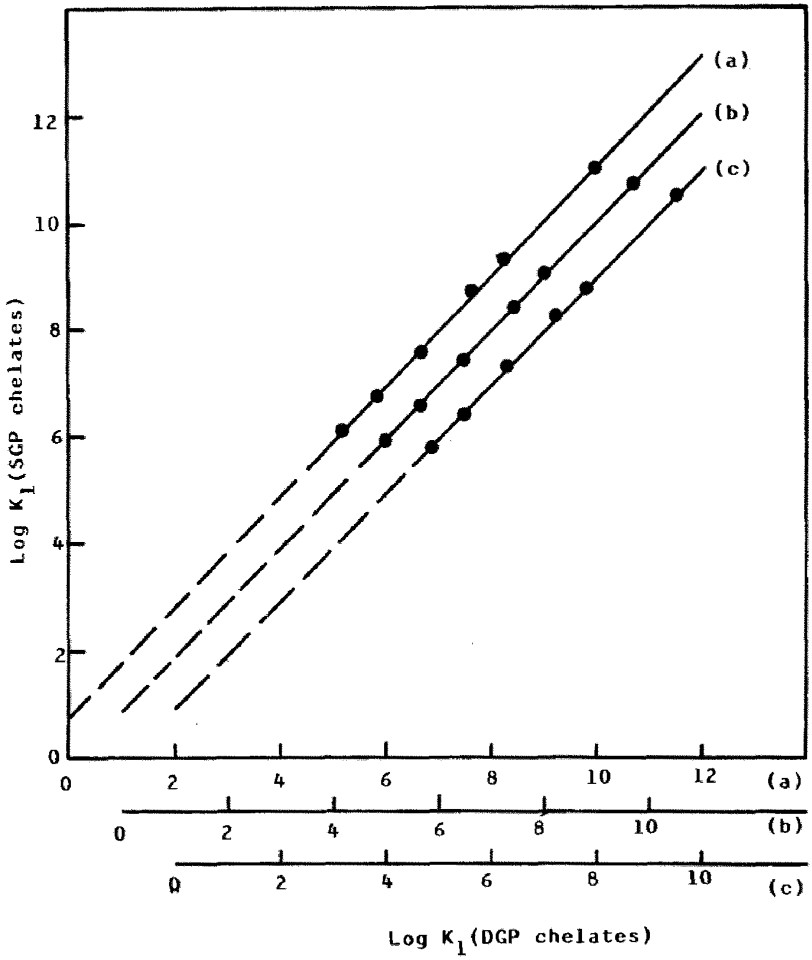


Fig. 4. Plots of log K_1 for various cation–SGP chelates versus log K_1 for various cation–DGP chelates at (plot a) 288.15 K, (plot b) 298.15 K, and (plot c) 308.15 K.

The ΔpK_1^H values are 1.03, 1.01 and 0.98 at 288.15, 298.15 and 308.15 K, respectively. This indicates that the basicity of the ligands is the main factor governing the stabilization of the SGP and DGP chelates.

Effect of temperature and thermodynamic functions

The effect of temperature on the acid dissociation constants of the ligands and the stepwise stability constants of their chelates with the investigated metal ions was studied using a pH-metric technique in aqueous solution.

The dissociation constants of DGP and SGP were calculated at various temperatures and are recorded in Table 2. Inspection of these values reveals that the pK^H values decrease with increasing temperature from

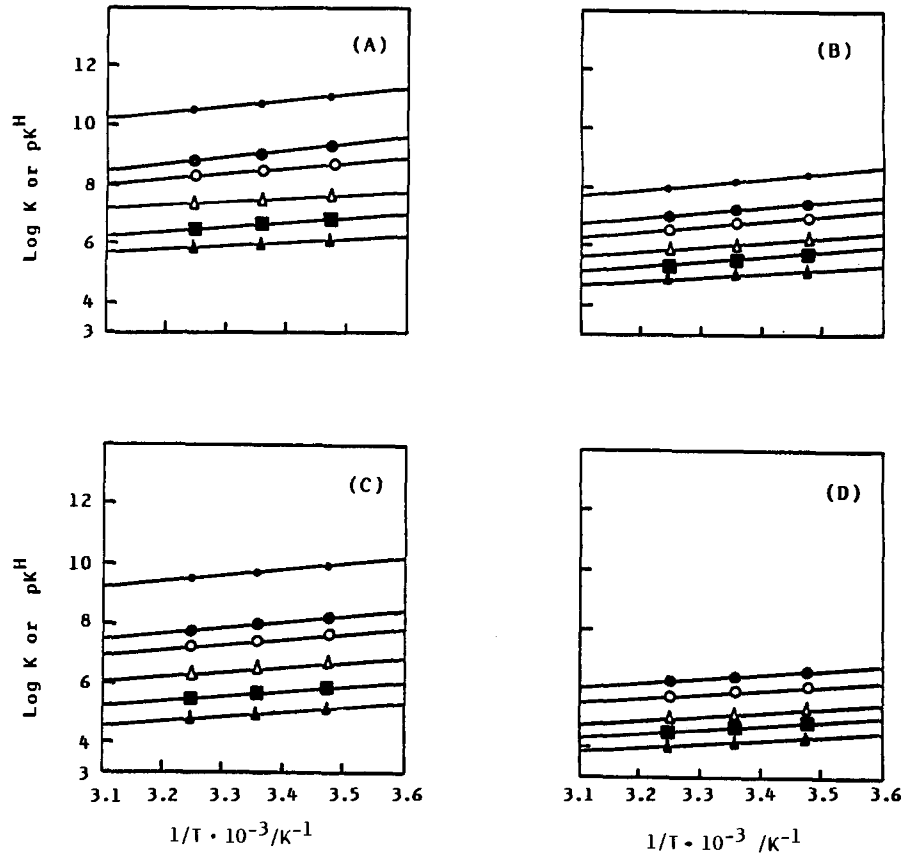


Fig. 5. Temperature dependence of dissociation and stability contants plots. (A) Log K_1^H vs. $1/T$ plots of SGP and log K_1 vs. $1/T$ plots for its chelates. (B) Log K_2^H vs. $1/T$ plots of SGP and log K_2 vs. $1/T$ plots for its chelates. (C) Log K_1^H vs. $1/T$ plots of DGP and log K_1 vs. $1/T$ plots for its chelates. (D) Log K_2 vs. $1/T$ plots for DGP chelates. Symbols: •, dissociation constant; ●, Fe(III); ○, Cu(III); △, Pb(II); ■, Ni(II); ▲, Hg(II).

288.15 to 308.15 K, in accordance with the weakly acidic nature of the ligands studied. This means that by increasing the temperature the acidity of the ligand increases. The enthalpy change ΔH for the dissociation of the DGP and SGP can be deduced from the slope of the plot of the pK^H versus $1/T$ plot (Fig. 5). The corresponding free energy change ΔG and the entropy change ΔS for such dissociations were calculated using the following well-known relationships

$$\Delta G = -2.303RT \log K^H = 2.303RT\text{p}K^H \quad (5)$$

$$\Delta G = \Delta H - T\Delta S \quad (6)$$

The dissociation thermodynamic parameters are summarized in Table 2. The positive values of ΔH indicate that the dissociation of DGP and SGP in aqueous solution is endothermic, as expected for the dissociation of weak acids, and a rise in temperature enhances the dissociation of the ligands. The positive values of ΔG reveal that the dissociations of the studied ligands are not spontaneous. The negative values of entropy change are owing to increased order as a result of a solvation process, which can be explained as the sum total of the bound water molecules with the dissociated ligand being more than the water molecules originally accompanying the undissociated form.

The stepwise stability constants of the complexes formed at different temperatures were calculated as described previously and are given in Table 2. These values decrease with increasing temperature indicating that the complexation process is favourable at lower temperatures. The stepwise thermodynamic parameters ΔG_1, ΔG_2, ΔH_1, ΔH_2, ΔS_1 and ΔS_2 for the chelate compounds were calculated by a procedure similar to that used for the dissociation of the ligands. These values are recorded in Table 2. Inspection of these values reveals that:

(1) All values of ΔG are negative indicating the spontaneous character of the chelation processes.

(2) The negative values of ΔH show that the chelation process is accompanied by generation of heat and that the process is exothermic, indicating that the complexation reactions are favourable at lower temperatures.

(3) The positive entropy change is characteristic of chelation. It occurs because the water molecules arranged in an orderly fashion around the ligand and metal ion have acquired a more random configuration on chelation, as in hydrophobic bonding [15]. This is referred to as a gain in configurational entropy. For complexing DGP (HL) with cupric ion (Cu^{2+}), the ions (L^- and Cu^{2+}) are normally hydrated with a certain number of water molecules in aqueous solution, and these are squeezed out when the complex is formed. Thus, the ordered arrangement of the solvent around the ions is lost and the entropy of the system increases. The process is represented as

$$Cu^{2+} \cdot (H_2O)_x + 2L^- \cdot (H_2O)_y = CuL_2 + z(H_2O) \qquad \Delta S \approx +\text{value}$$

in which x and y are the number of H_2O molecules bound and z is the number of free waters in solution.

The plots of the logarithms of the stability constants against reciprocal temperature (Fig. 5) are linear in all the systems, which indicates that the values of ΔC_P are equal to zero [16].

CONDUCTOMETRIC TITRATION

The stoichiometry of the complexes formed between metal ions and SGP or DGP has been determined using conductometric titration. The plots of the specific conductance values, after correction for the dilution effect,

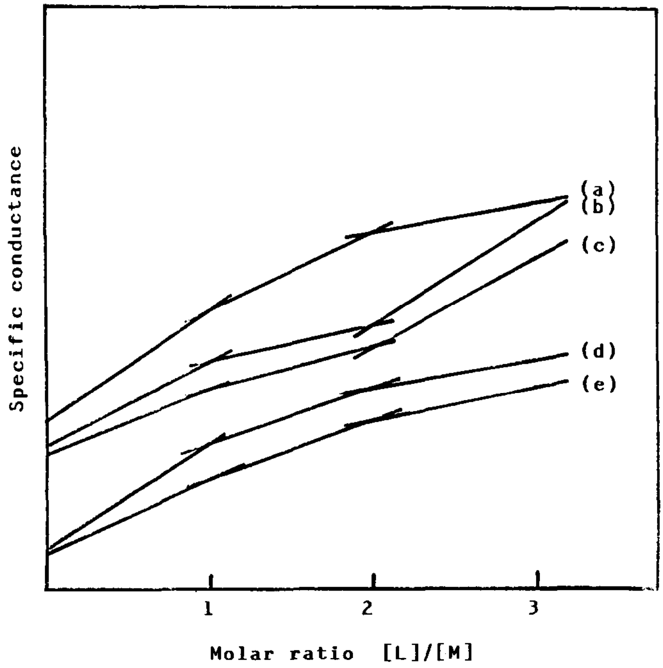


Fig. 6. Conductometric titration curves for (plot a) $FeCl_3$, (plot b) $PbCl_2$, (plot c) $HgCl_2$, (plot d) $CuCl_2$, and (plot e) $NiCl_2$ with SGP at 298.15 K.

against the molar ratio of the complexes, shown in Fig. 6, are characterized by two sharp breaks denoting the formation of both molar ratios 1:1 and 1:2 (M:L), in good agreement with the results determined by potentiometric measurements. Also, these curves are characterized by an increase in the conductance of the solution during complex formation which can be ascribed to the liberation of H^+ ions from the ligands through displacement by the metal ions.

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