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Potentiometric and Thermodynamic Studies of 4-(1*H*-Indol-3-yl)butanoic Acid and Its Metal Complexes

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The proton−ligand dissociation constants of 4-(1*H*-indol-3-yl)butanoic acid and the stability constants of its metal−ligand complexes with (Mn^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}, and UO_2^{2+}) have been determined potentiometrically in 0.1 $mol \cdot dm^{-3}$ (KCl) and 10 % (by volume) ethanol−water mixture and at (298, 308, and 318) K. The order of the stability constants of the formed complexes increases in the sequence Mn^{2+}, Co^{2+}, Ni^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}, Cu^{2+}, and UO_2^{2+}. The effect of temperature was studied, and the corresponding thermodynamic parameters (ΔG, ΔH, and ΔS) were derived and are discussed. The dissociation process is nonspontaneous, endothermic, and entropically unfavorable. The formation of the metal complexes has been found to be spontaneous, endothermic, and entropically favorable.

Introduction

Indol and its derivatives represent an interesting group of heterocyclic compounds, because of their unusual chemical structure and interesting biological properties. 4-(1*H*-Indol-3-yl)butanoic acid enhances the growth and development of food crops and ornamentals when applied to soil, cuttings, or leaves.[1−4] As part of our continuous work reporting on the determination of dissociation and stability constants of some organic compounds and their metal complexes by potentiometric techniques,[5−8] we report here the dissociation constant of 4-(1*H*-indol-3-yl)butanoic acid and the stability constants of its complexes with Mn^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}, and UO_2^{2+} at different temperatures. Furthermore, the corresponding thermodynamic functions of complexation are evaluated and discussed.

Experimental Section

Reagents and Materials. 4-(1*H*-Indol-3-yl)butanoic acid (Figure 1) from Aldrich was used as received, and a 0.001 $mol \cdot dm^{-3}$ solution was prepared by dissolving an accurate weight of the solid in ethanol (Analar). Metal ion solutions (0.0001 $mol \cdot dm^{-3}$) were prepared from Analar metal chlorides in bidistilled water and standardized with ethylenediaminetetraacetic acid (EDTA).[9] The system was maintained at an ionic strength of 1 $mol \cdot dm^{-3}$ (KCl) in bidistilled water as a supporting electrolyte. A carbonate-free sodium hydroxide solution in a 10 % (by volume) ethanol−water mixture was used as titrant and standardized against oxalic acid (Analar). In the experiment, a solution of 0.001 $mol \cdot dm^{-3}$ (HCl) in bidistilled water was used.

Potentiometric Measurements. The pH measurements were performed with a Metrohm 836 Titrando (KF and potentiometric titrator) equipped with a combined porolyte electrode. The pH meter readings in the nonaqueous medium were corrected.[10] The electrode system was calibrated according to the method of Irving et al.[11] All titrations have been carried out between pH 3.0 and 11.0. The apparatus, general conditions, and methods of calculation were the same as in previous work.[5−8] The following mixtures (i−iii) were prepared and titrated potentiometrically at 298 K against standard 0.002 $mol \cdot dm^{-3}$ (NaOH) in a 10 % (by volume) ethanol−water mixture:

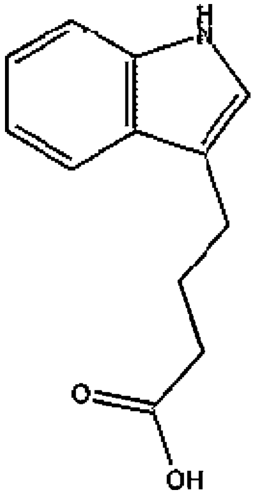

Figure 1. Structure of 4-(1*H*-indol-3-yl)butanoic acid.

(i) 5 cm^3 0.001 $mol \cdot dm^{-3}$ (HCl) + 5 cm^3 1 $mol \cdot dm^{-3}$ (KCl) + 5 cm^3 ethanol.

(ii) 5 cm^3 0.001 $mol \cdot dm^{-3}$ (HCl) + 5 cm^3 1 $mol \cdot dm^{-3}$ (KCl) + 5 cm^3 0.001 $mol \cdot dm^{-3}$ ligand.

(iii) 5 cm^3 0.001 $mol \cdot dm^{-3}$ (HCl) + 5 cm^3 1 $mol \cdot dm^{-3}$ (KCl) + 5 cm^3 0.001 $mol \cdot dm^{-3}$ ligand + 10 cm^3 0.0001 $mol \cdot dm^{-3}$ metal chloride.

For each mixture, the volume was made up to 50 cm^3 with bidistilled water before the titration. These titrations were repeated for temperatures of (308 and 318) K. The temperature was controlled to within ± 0.05 K by circulating thermostatted water (JULABO f34-ED) through the double-walled glass vessel. The cell was equipped with a magnetic stirrer.

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Table 1. Thermodynamic Functions for the Dissociation of 4-(1*H*-Indol-3-yl)butanoic Acid in a 10 % (by Volume) Ethanol−Water Mixture in the Presence of 0.1 mol·dm^{-3} KCl at Different Temperatures[a]

	dissociation constant		free energy/kJ·mol^{-1}		enthalpy/kJ·mol^{-1}		entropy/J·mol^{-1}·K^{-1}	
temp./K	pK_1^H	pK_2^H	ΔG_1	ΔG_2	ΔH_1	ΔH_2	$-\Delta S_1$	$-\Delta S_2$
298	9.50 (0.10)	4.70 (0.10)	54.21	26.82	29.04	29.95	279.36	190.50
308	9.34 (0.10)	4.54 (0.09)	55.08	26.77			273.12	184.16
318	9.18 (0.10)	4.37 (0.09)	55.89	26.61			267.08	177.86

[a] Standard deviations are given in parentheses.

Table 2. Stepwise Stability Constants for ML and ML$_2$ Complexes of 4-(1*H*-Indol-3-yl)butanoic Acid in a 10 % (by Volume) Ethanol−Water Mixture in the Presence of 0.1 mol·dm^{-3} KCl at Different Temperatures[a]

	298 K		308 K		318 K	
M^{n+}	log K_1	log K_2	log K_1	log K_2	log K_1	log K_2
Mn^{2+}	8.12 (0.10)	5.30 (0.11)	8.27 (0.09)	5.45 (0.10)	8.43 (0.10)	5.59 (0.12)
Co^{2+}	8.20 (0.09)	5.36 (0.10)	8.36 (0.13)	5.52 (0.12)	8.52 (0.11)	5.67 (0.09)
Ni^{2+}	8.29 (0.12)	5.45 (0.10)	8.45 (0.11)	5.60 (0.10)	8.61 (0.12)	5.76 (0.10)
Cu^{2+}	8.60 (0.11)	5.75 (0.10)	8.74 (0.12)	5.89 (0.09)	8.91 (0.11)	6.04 (0.12)
Zn^{2+}	8.35 (0.09)	5.52 (0.13)	8.50 (0.10)	5.67 (0.14)	8.66 (0.10)	5.82 (0.11)
Cd^{2+}	8.45 (0.12)	5.62 (0.10)	8.63 (0.10)	5.78 (0.10)	8.80 (0.10)	5.95 (0.13)
Hg^{2+}	8.50 (0.09)	5.67 (0.10)	8.66 (0.10)	5.82 (0.09)	8.83 (0.10)	5.97 (0.10)
UO_2^{2+}	8.75 (0.10)	5.87 (0.09)	8.91 (0.10)	6.02 (0.11)	9.07 (0.10)	6.17 (0.09)

[a] Standard deviations are given in parentheses.

Results and Discussion

The interaction of a metal with an electron donor atom of a ligand is usually followed by the release of H$^+$. Alkaline potentiometric titrations are based on the detection of the protons released upon complexation. The main advantage of this technique compared to other methods is that from the titration curves it is possible to follow complexation continuously as a function of pH and to detect the value exactly at which pH complexation takes place. Furthermore, it is possible to calculate the pK_a values, the dissociation constants, and the stability constants. The following equilibria were used for the determination of the pK_a values and the stability constants:

$$H_2A = HA^- + H^+$$

$$HA^- = A^{2-} + H^+$$

$$H_2A + M^{2+} = MA + 2H^+$$

$$H_2A + MA = MA_2^{\ 2-} + 2H^+$$

H_2A represents an 4-(1*H*-indol-3-yl)butanoic acid molecule, which bears two dissociable H$^+$, while M^{2+} are divalent metal ions.

Dissociation Constants. The average number of the protons associated with the reagent molecule, $\bar{n}_A$, was determined at different pH values applying the following eq 1:

$$\bar{n}_A = Y + \frac{(V_1 - V_2)(N^o - E^o)}{(V^o - V_1)TC^o_L} \tag{1}$$

where Y is the number of available protons in 4-(1*H*-indol-3-yl)butanoic acid ($Y = 2$), V_1 and V_2 are the volumes of alkali required to reach the same pH on the titration curve of hydrochloric acid and reagent, respectively, $V°$ is the initial volume (50 cm^3) of the mixture, TC°$_L$ is the total concentration of the reagent, $N°$ is the normality of the sodium hydroxide solution, and $E°$ is the initial concentration of the free acid. The titration curves ($\bar{n}_A$ vs pH) for the proton−ligand systems were constructed and found to extend between 0 and 2 on the $\bar{n}_A$ scale. This means that 4-(1*H*-indol-3-yl)butanoic acid has two dissociable protons (the hydrogen ion of the NH in indol moiety, pK_1^H,[12] and the −COOH group, pK_2^H). Different computional methods[13] were applied to evaluate the dissociation constants. Three replicate titrations were performed; the average values obtained are listed in Table 1.

Metal−Ligand Stability Constants. The stability constants of binary complexes of 4-(1*H*-indol-3-yl)butanoic acid with some divalent metal ions were determined by plotting the average number of ligands attached per metal ions ($\bar{n}$) versus the free ligand exponent (pL), according to Irving and Rossotti.[14] The average number of the reagent molecules attached per metal ion, $\bar{n}$, and free ligand exponent, pL, can be calculated using eqs 2 and 3:

$$\bar{n} = \frac{(V_3 - V_2)(N^o + E^o)}{(V^o + V_2)\bar{n}_A TC^o_M} \tag{2}$$

and

$$pL = \log_{10} \frac{\sum_{n=O}^{n=J} \beta^H_n \left(\frac{1}{[H^+]}\right)^n}{TC^o_L - \bar{n}TC^o_M} \cdot \frac{V^o + V_2}{V^o} \tag{3}$$

where TC°$_M$ is the total concentration of the metal ion present in the solution, β^H_n is the overall proton-reagent stability constant. V_1, V_2, and V_3 are the volumes of alkali required to reach the same pH on the titration curves of hydrochloric acid, organic ligand, and complex, respectively. These curves were analyzed, and the successive stability constants were determined using different computational methods.[15,16] The maximum value of $\bar{n}$ was ∼2 indicating the formation of 1:1 and 1:2 (metal: ligand) complexes only.[17] The metal ion solution used in the present study was very dilute ($2 \cdot 10^{-5}$ mol·dm^{-3}); hence, there was no possibility of formation of polynuclear complexes.[18,19] The metal titration curves were displaced to the right-hand side of the ligand titration curves along the volume axis, indicating proton release upon the complex formation of the metal ion with the ligand. The large decrease in pH for the metal titration curves relative to ligand titration curves points to the formation of strong metal complexes.[20,21]

The values of the stability constants (log K_1 and log K_2) are given in Table 2. The stability of the chelates increases in the order Mn^{2+}, Co^{2+}, Ni^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}, Cu^{2+}, and UO$_2^{2+}$.[22−24] This order largely reflects that the stability of Cu^{2+} complexes are considerably larger as compared to other metals of the 3d series. Under the influence of both the polarizing ability of the

Table 3. Thermodynamic Functions for ML and ML_2 Complexes of 4-(1*H*-Indol-3-yl)butanoic Acid in 10 % (by Volume) Ethanol−Water Mixture and 0.1 $mol \cdot dm^{-3}$ KCl

		Gibbs energy/ $kJ \cdot mol^{-1}$		enthalpy/ $kJ \cdot mol^{-1}$		entropy/ $J \cdot mol^{-1} \cdot K^{-1}$	
M^{n+}	T/K	$-\Delta G_1$	$-\Delta G_2$	ΔH_1	ΔH_2	ΔS_1	ΔS_2
Mn^{2+}	298	46.33	30.24	28.13	26.31	249.87	189.77
	308	48.77	32.14			249.68	189.77
	318	51.33	34.04			249.87	189.78
Co^{2+}	298	46.79	30.58	29.04	28.13	254.46	197.01
	308	49.30	32.55			254.35	197.01
	318	51.88	34.52			254.47	197.01
Ni^{2+}	298	47.30	31.10	29.04	28.13	256.17	198.76
	308	49.83	33.02			256.07	198.54
	318	52.42	35.07			256.16	198.74
Cu^{2+}	298	49.07	32.81	28.13	26.31	259.06	198.39
	308	51.54	34.73			258.67	198.18
	318	54.25	36.78			259.06	197.83
Zn^{2+}	298	47.64	31.50	28.13	27.22	254.26	197.05
	308	50.13	33.44			254.10	196.95
	318	52.73	35.44			254.28	197.04
Cd^{2+}	298	48.21	32.07	31.76	29.95	268.36	208.12
	308	50.89	34.09			268.34	207.79
	318	53.58	36.23			268.36	208.11
Hg^{2+}	298	48.50	32.35	29.95	27.22	263.26	199.90
	308	51.07	34.32			263.05	199.81
	318	53.76	36.35			263.24	199.91
UO_2^{2+}	298	49.93	33.49	29.04	27.22	265.00	203.72
	308	52.54	35.50			264.87	203.64
	318	55.22	37.57			264.97	203.74

metal ion[25] and the ligand field,[26] Cu^{2+} will receive some extra stabilization due to the tetragonal distortion of octahedral symmetry in its complexes. The greater stability of Cu^{2+} complexes is produced by the well-known Jahn−Teller effect.[27]

Effect of Temperature. The dissociation constant (pK^H) for 4-(1*H*-indol-3-yl)butanoic acid as well as the stability constants of its complexes with Mn^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}, and UO_2^{2+} have been evaluated at (298, 308 and 318) K and are given in Tables 1 and 3. The enthalpy change (ΔH) for the dissociation and complexation process was calculated from the slope of the plot pK^H or $\log K$ versus $1/T$ using the graphical representation of van't Hoff (eqs 4 and 5):

$$\Delta G = -3.03RT \log K = \Delta H - T\Delta S \qquad (4)$$

or

$$\log K = (-\Delta H/2.303R)(1/T) + (\Delta S/2.303R) \qquad (5)$$

From the ΔG and ΔH values one can deduce the ΔS using the well-known relationships 4 and 6:

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

where $R = 8.314\ J \cdot K^{-1} \cdot mol^{-1}$ is the gas constant, K is the dissociation constant for the ligand or the stability constant of the complex, and T is the absolute temperature.

The thermodynamic parameters of the dissociation process of 4-(1*H*-indol-3-yl)butanoic acid are recorded in Table 1. Inspection shows that the pK^H values decrease with increasing temperature; that is, the acidity of the ligand increases, suggesting that the dissociation process is endothermic and increases with increasing temperature. This is verified from the positive values of ΔH. The positive value of ΔG reveals that the dissociation process is not spontaneous.[27] The negative value of ΔS is obtained due to the increased order as a result of the solvation process.

The thermodynamic parameters of the stepwise stability constants of the complexes are recorded in Table 3. It is known that the divalent metal ions exist in solution as octahedrally hydrated species,[16] and the obtained values of ΔH and ΔS can then be considered as the sum of two contributions: (a) release of H_2O molecules, and (b) metal−ligand bond formation. An examination of these values shows that the stepwise stability constants ($\log K_1$ and $\log K_2$) for the complexes increase with increasing temperature, suggesting that the complex formation is endothermic (positive values of ΔH) and favorable at higher temperatures.[28] The negative value of ΔG reveals that all complexes under investigation are formed spontaneously in solution.[29] The entropy values, ΔS, for all complexes are positive, indicating that the disorder of the system increases much more rapidly than the increase in the order taking place in the chelation.[6]

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