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Evaluation of stepwise complexation constants of biologically active ligand with lanthanon ions

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Abstract

The stabilities of the chelates formed by 2-acetylpyridine thiosemicarbazone with La(III), Pr(III), Nd(III), Gd(III), Sm(III), Tb(III), Dy(III) and Ho(III) have been determined pH-metrically in 75% (v/v) ethanol at various ionic strengths of $NaClO_4$ and at different temperatures. The thermodynamic stability constants and other thermodynamic functions are also reported. The trends in the stability constants for lanthanon(III) complexes has been found to be La(III) < Pr(III) < Nd(III) < Sm(III) < Gd(III) < Tb(III) < Dy(III) < Ho(III).

INTRODUCTION

Thiosemicarbazones are compounds which act as complexing agents for various metal ions. They have many analytical applications and they are also of interest in various biological systems. 2-Acetylpyridine thiosemicarbazone has been used for the spectrophotometric determination of Cu(II), Ni(II) [1], Fe(II) [2] and Au(III) [3]. 2-Acetylpyridine thiosemicarbazone (2-APT) has also been used as an inhibitor of ecdysis in oncopeltus [4]. Domagk et al. [5] reported for the first time the antitubercular activity of metal thiosemicarbazones; for example, Conteben in the form of tablets and Solvoteben in the form of injections act as antitubercular agents. Thiosemicarbazones have been found to be active in preventing the growth of fungi. They also act as good insecticides, pesticides [6] and fungicides [7,8]. The metal thiosemicarbazones are active against smallpox [9], influenza [10], protozoa [11] and certain kinds of tumours [12]. Keeping this in view, 2-APT has been chosen for an investigation of its chelating behaviour towards lanthanons.

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EXPERIMENTAL

2-Acetylpyridine thiosemicarbazone (2-APT) was prepared by reacting the requisite amounts of thiosemicarbazide hydrochloride (Fluka AnalaR) dissolved in ethanol and equimolar amounts of 2-acetylpyridine (Fluka AnalaR). The reaction mixture was boiled under reflux for 6 to 8 h on a water bath and then cooled overnight in a freezer. The brown solid was recovered by filtration. The compound was recrystallized from ethanol and its solution was prepared in ethanol. Tetramethylammonium hydroxide (TMAH) (E. Merck A.G. Darmstadt) in 75% ethanol was used as titrant.

Perchloric acid was standardized and was diluted to the required molarity (0.1 M) with conductivity water; $NaClO_4$ (Riedel) was used to maintain the ionic strength constant.

The solutions of lanthanon(III) ions, namely La(III), Pr(III), Nd(III), Sm(III), Gd(III), Tb(III), Dy(III) and Ho(III), were prepared and standardized by conventional methods.

A digital pH meter (ECIL model pH 5651) in conjunction with a glass electrode was used for pH measurements. The pH meter was standardized with potassium hydrogenphthalate and phosphate buffers before performing the titrations.

All measurements were made at a temperature maintained constant by using an MLW (NBE type) thermostat (FRG).

The method of Bjerrum and Calvin [13,14] as modified by Irving and Rossotti [15] was used to determine the $\bar{n}$ and pL values. The stability constants were computed on a VAX 11/750 computer (USA) using a weighted least squares method modelled on that of Sullivan et al. [16].

pH titration procedure

Investigations were carried out at four different ionic strengths, namely 0.02 M, 0.05 M, 0.1 M and 0.2 M $NaClO_4$ at 25°C, and at 0.1 M at 35 ± 0.5, 40 ± 0.5 and 50 ± 0.5°C. For each set of experiments, the final volume was made up to 20 cm^3, maintaining the 75% (v/v) ethanol–water medium.

The concentrations of $HClO_4$, 2-APT and metal ions in the aforesaid volumes were 0.01 M, 0.00515 M and 0.00051 M, respectively. Each set of solutions was titrated against 0.1 M TMAH in 75% (v/v) ethanol. The titrations were carried out in a covered double walled glass cell in an atmosphere of N_2, which was presaturated with the solvent (75% ethanol–water) before being passed into the reaction solution.

RESULTS AND DISCUSSION

For calculation of $\bar{n}$ and pL values, we have taken the final volume as 19.40 instead of 20 ml owing to volume contraction in ethanol–water

TABLE 1

Stability constants of lanthanon(III) complexes of 2-APT at different ionic strengths (temp. = 25 ± 0.5°C)

	La(III)	Pr(III)	Nd(III)	Sm(III)	Gd(III)	Tb(III)	Dy(III)	Ho(III)
$\mu = 0.2$ M $NaClO_4$, $pK_1 = 10.15$								
log K_1	6.82	7.05	7.38	7.51	7.60	7.86	7.88	7.95
log K_2	6.76	6.78	6.80	6.98	7.15	7.25	7.31	7.59
log β_2	13.58	13.83	14.18	14.49	14.75	15.11	15.19	15.54
S_{min}	0.1186	0.1780	0.0864	0.1369	0.0298	0.0067	0.1392	0.1186
$\mu = 0.1$ M $NaClO_4$, $pK_1 = 10.36$								
log K_1	6.94	7.12	7.54	7.57	7.66	7.81	7.93	8.02
log K_2	6.59	6.86	6.69	7.01	7.25	7.39	7.43	7.68
log β_2	13.53	13.98	14.23	14.58	14.91	15.20	15.36	15.70
S_{min}	0.0679	0.1235	0.0493	0.1176	0.0687	0.1897	0.1496	0.0298
$\mu = 0.05$ M $NaClO_4$, $pK_1 = 10.54$								
log K_1	7.02	7.33	7.59	7.63	7.79	8.06	8.08	8.15
log K_2	6.73	6.79	6.90	7.10	7.34	7.43	7.52	7.79
log β_2	13.75	14.12	14.49	14.73	15.13	15.49	15.60	15.94
S_{min}	0.2618	0.1589	0.0160	0.0376	0.1206	0.0273	0.1582	0.0981
$\mu = 0.02$ M $NaClO_4$, $pK_1 = 10.80$								
log K_1	7.14	7.40	7.74	7.84	7.95	8.06	8.24	8.26
log K_2	6.90	7.13	7.25	7.26	7.50	7.67	7.77	7.94
log β_2	14.04	14.53	14.99	15.10	15.45	15.73	16.01	16.20
S_{min}	0.1384	0.2869	0.0648	0.4191	0.0116	0.1780	0.0108	0.1683

medium. The values of $\bar{n}_H$ were calculated at various pH values from the titration curves. The pK_a of the ligand was obtained by plotting $\log[\bar{n}_H/(1 - \bar{n}_H)]$ vs. pH; the values thus obtained are 10.80, 10.60, 10.39 and 10.16 at $\mu = 0.02$ M, 0.05 M, 0.1 M and 0.2 M $NaClO_4$ respectively at 25°C. The pK_a values of the ligand at 35 ± 0.5, 40 ± 0.5 and 50 ± 0.5°C ($\mu = 0.1$ M $NaClO_4$) were found to be 10.18, 10.06 and 9.90 respectively.

In these studies the values of dissociation constants (pK_a) were found to decrease with increasing ionic strength of the medium, in agreement with the Debye–Hückel equation [17]

$$pK_a - \left[A\sqrt{\mu}/\left(1 + \alpha\sqrt{\mu}\right)\right] + C = pK_a$$

A similar trend has been obtained for the stability of chelates. The order of the stability constants for the metal chelates of 2-APT was found to be La(III) < Pr(III) < Nd(III) < Sm(III) < Gd(III) < Tb(III) < Dy(III) < Ho(III). The log K_1, log K_2, log β_2 and S_{min} values at 25 ± 0.5°C for the trivalent ion chelates at different ionic strengths are summarized in Table 1.

These studies reveal that the stability constants decrease as the temperature increases, along with the pK_a values. The log K_1, log K_2, log β_2 and S_{min} values at different temperatures ($\mu = 0.1$ M) are given in Table 2.

TABLE 2

Stability of lanthanon complexes of 2-APT at different temperatures ($\mu = 0.1$ M $NaClO_4$)

	La(III)	Pr(III)	Nd(III)	Sm(III)	Gd(III)	Tb(III)	Dy(III)	Ho(III)
Temp. = 50 ± 0.5°C, $pK_1 = 9.90$								
$\log K_1$	6.70	6.91	7.20	7.32	7.50	7.79	7.80	7.84
$\log K_2$	6.38	6.68	6.74	6.80	7.05	7.26	7.22	7.49
$\log \beta_2$	13.08	13.63	14.04	14.12	14.55	15.05	15.02	15.33
S_{min}	0.1725	0.1986	0.0750	0.1108	0.1687	0.0645	0.1486	0.1486
Temp. = 40 ± 0.5°C, $pK_1 = 10.06$								
$\log K_1$	6.74	6.95	7.23	7.35	7.66	7.82	7.85	7.90
$\log K_2$	6.45	6.71	6.74	7.03	7.13	7.01	7.26	7.53
$\log \beta_2$	13.19	13.66	13.97	14.38	14.79	14.83	15.11	15.43
S_{min}	0.1894	0.2133	0.1368	0.1274	0.0642	0.0576	0.1233	0.1435
Temp. = 35 ± 0.5°C, $pK_1 = 10.18$								
$\log K_1$	6.80	7.04	7.38	7.42	7.72	7.88	7.90	7.92
$\log K_2$	6.50	6.77	6.79	6.91	6.97	7.07	7.30	7.58
$\log \beta_2$	13.30	13.81	14.17	14.33	14.69	14.95	15.20	15.51
S_{min}	0.2163	0.1931	0.0689	0.1826	0.0956	0.0067	0.1079	0.1346

The results show that the stability of metal chelates increases regularly from La(III) to Ho(III). For these chelates $\bar{n}$ values greater than 2.0 have not been obtained. We therefore conclude that not more than two chelates, i.e. 1 : 1 and 1 : 2 (M : L) are formed in each system. In view of the very low (5.0×10^{-4} M) concentration of metal ions used in the titration, it has been assumed that the possibility of polynuclear complex formation is negligible. The overall free energy, enthalpy and entropy changes at 25 ± 0.5°C are reported in Table 3. The results indicate that the values of ΔH and ΔG are negative, showing that chelate formation takes places spontaneously and with the liberation of energy.

TABLE 3

Thermodynamic functions of lanthanon(III) complexes of 2-APT at $\mu = 0.1$ M $NaClO_4$ and temp. 25 ± 0.5°C

Metal ion	$-\Delta G$ (kJ mol^{-1})	$-\Delta H$ (kJ mol^{-1})	$-\Delta S$ (kJ K^{-1} mol^{-1})
La(III)	40.9	21.0	0.66
Pr(III)	42.6	19.1	0.07
Nd(III)	43.5	17.1	0.08
Sm(III)	44.7	19.1	0.08
Gd(III)	44.9	22.9	0.07
Tb(III)	45.8	15.2	0.10
Dy(III)	46.4	21.8	0.05
Ho(III)	47.4	22.9	0.07

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