Complexation of Some Transition Metal Ions with Benzooxazole Sulfamethazine: A Potentiometric and Thermodynamic Studies in Aqueous Solution

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Abstract— The interaction of Mn^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, La^{3+}, Ce^{3+}, UO_2^{2+} and Th^{4+} ions with benzooxazole sulfamethazine (BOSM) have been studied in aqueous solution. The proton-ligand dissociation constant of benzooxazole sulfamethazine and metal-ligand stability constants of its complexes with metal ions (Mn^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, La^{3+}, Ce^{3+}, UO_2^{2+} and Th^{4+}) have been determined potentiometrically in 0.1 mol dm^{-3} KCl and 40 % (by volume) DMF–water mixture and at (298, 308 and 318) K. The stability constants of the formed complexes increases in the order Mn^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, La^{3+}, Ce^{3+}, UO_2^{2+} and Th^{4+}. The effect of temperature was studied and the corresponding thermodynamic parameters (ΔG, ΔH and ΔS) were derived and discussed. The dissociation process is non-spontaneous, endothermic and entropically unfavourable. The fotmation of the metal complexes has been found to be spontaneous, exothermic and entropically favourable.

Keywords — Benzooxazole sulfamethazine, Stability constants and thermodynamics.

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1 INTRODUCTION

Sulfonamides were the first effective chemotherapeutic agents to be employed systematically for the prevention and cure of bacterial infections [1]. Sulfonamide and azosulfonamide derivatives have been found to be biologically versatile anticancer, antimalarial and antitubercular drugs [2]. Their metal complexes are highly antibacterial and antifungal [3]. Although potentiometric studies of azo compounds have been studied extensively [4-6], little attention including azo compounds formed by interaction of benzooxazole and sulfonamides as ligands has been reported [7]. In continuation of earlier work [8-10], we report here the dissociation constant of BOSM and the stability constants of its complexes with Mn^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, La^{3+}, Ce^{3+}, UO_2^{2+} and Th^{4+} at different temperatures. Furthermore, the corresponding thermodynamic functions are evaluated and discussed.

2 EXPERIMENTAL SECTION

Benzooxazole sulfamethazine [4-((benzo[d]oxazol-2-ylthio)diazenyl)-N-(4,6-dimethyl pyrimidin-2-yl)benzenesufon amide] (Fig. 1) was prepared as previously described, using standard procedures [7,11]. The purity was checked by elemental analysis, IR and ^1H NMR spectra.
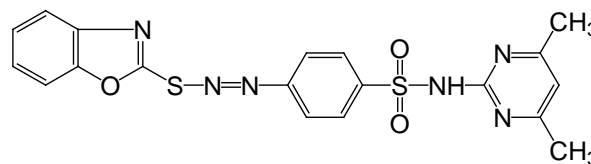
(Fig. 1)

Stock solution of (0.001 mol dm^{-3}) of BOSM was prepared by dissolving an accurately weighed amount of the solid in DMF (Analar). Metal ion solutions of about (0.0001 mol

dm⁻³) were prepared from Analar metal chlorides in bidistilled water and standardized with EDTA [12]. Solutions of 0.001 mol dm⁻³ HCl and 1 mol dm⁻³ KCl were also prepared in bidistilled water. A carbonate-free sodium hydroxide solution in 40 % (by volume) DMF–water mixture was used as titrant and standardized against oxalic acid (Analar).

The apparatus, general conditions and methods of calculation were the same as in previous work [8-10]. The following mixtures (i) – (iii) were prepared and titrated potentiometrically at 298 K against standard 0.002 mol dm⁻³ NaOH in a 40 % (by volume) DMF–water mixture:

i) 5 cm³ 0.001 mol dm⁻³ HCl + 5 cm³ 1 mol dm⁻³ KCl + 20 cm³ DMF.

ii) 5 cm³ 0.001 mol dm⁻³ HCl + 5 cm³ 1 mol dm⁻³ KCl + 15 cm³ DMF + 5 cm³ 0.00l mol dm⁻³ ligand.

iii) 5 cm³ 0.001 mol dm⁻³ HCl + 5 cm³ l mol dm⁻³ KCl + 15 cm³ DMF + 5 cm³ 0.001 mol dm⁻³ ligand + 5 cm³ 0.0002 mol dm⁻³ metal chloride.

For each mixture, the volume was made up to 50 cm³ with bidistilled water before the titration. For each system three replicate measurements were carried out under nitrogen atmosphere. These titrations were repeated for temperatures of 308 K and 318 K. The temperature was controlled to within ± 0.05 K by circulating thermostated water (Neslab 2 RTE 220) through the outer jacket of the vessel. The pH measurements were performed with a HANNA instruments model 211 pH-meter accurate to ± 0.01 units. The term pH is in this work defined as –log [H⁺]. The pH–meter readings in the non–aqueous medium were corrected [13]. The electrode system was calibrated according to the method of Irving et al. [14].

3. Results and discussion

The average number of the protons associated with the ligand (BOSM) at different pH values, $\bar{n}_A$, was calculated from the titration curves of the acid in the absence and presence of OSM. Applying eq. 1:

$$\bar{n}_A = Y + \frac{(V_1 - V_2)(N° + E°)}{(V° + V_1) TC°_L} \qquad (1)$$

where Y is the number of available protons in BOSM ($Y=1$) and 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 cm³) of the mixture, $TC°_L$ is the total concentration of the reagent, $N°$ is the normality of sodium hydroxide solution and $E°$ is the initial concentration of the free acid. Thus, the formation curves ($\bar{n}_A$ vs. pH) for the proton-ligand systems were constructed and found to extend between 0 and 1 in the $\bar{n}_A$ scale. This means that BOSM has one ionizable proton (the enolized hydrogen ion of the sulphonamide group, pK^H) [4]. Different computational methods [15] were applied to evaluate the dissociation constant. Two replicate titrations were performed and the average values obtained are listed in Table 1. The completely protonated form of BOSM has one dissociable proton, that dissociates in the measurable pH range.

Table 1. Thermodynamic functions for the dissociation of BOSM in 40 % (by volume) DMF–water mixture and 0.1 mol dm⁻³ KCl at different temperatures.

T/K	Dissociation constant pK^H	Gibbs energy / kJ mol⁻¹ ΔG_1	Enthalpy / kJ mol⁻¹ ΔH_1	Entropy / J mol⁻¹ K⁻¹ $-\Delta S_1$
298	5.56	31.72		16.48
308	5.41	31.90	26.81	16.53
318	5.25	31.97		16.23

The formation curves for the metal complexes were obtained by plotting the average number of ligands attached per metal ion ($\bar{n}$) vs. the free ligand exponent (pL), according to Irving and Rossotti [16]. 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:

$$\bar{n} = \frac{(V_3 - V_2)(N^\circ + E^\circ)}{(V^\circ + V_2)\,\bar{n}_A\,TC^\circ_M} \qquad (2)$$

and

$$pL = \log_{10}\frac{\sum_{n=0}^{n=J}\beta^H_n\left[\frac{1}{\text{anti log pH}}\right]^n}{TC_L^\circ - \bar{n}TC_M^\circ}\cdot\frac{V^\circ + V_3}{V^\circ} \qquad (3)$$

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 metal-ligand stability constants were determined using different computional methods [17,18]. The values of the stability constants (log K_1 and log K_2) are given in Table 2.

Table 2. Stepwise stability constants for ML and ML$_2$ complexes of BOSM in 40 % (by volume) DMF–water mixtures and 0.1 mol dm^{-3} KCl at different temperatures.

M^{n+}	298 K		308 K		318 K	
	log K_1	log K_2	log K_1	log K_2	log K_1	log K_2
Mn^{2+}	6.10	5.19	5.92	5.05	5.73	4.90
Co^{2+}	6.30	5.35	6.12	5.21	5.92	5.07
Ni^{2+}	6.40	5.51	6.21	5.36	6.02	5.20
Cu^{2+}	6.70	5.77	6.52	5.60	6.33	5.42
La^{3+}	6.85	5.98	6.66	5.80	6.45	5.63
Ce^{3+}	6.90	6.05	6.72	5.85	6.54	5.67
UO_2^{2+}	7.11	6.20	6.90	6.03	6.69	5.83
Th^{4+}	7.40	6.55	7.18	6.32	6.96	6.13

The following general remarks can be pointed out:

(*i*) The maximum value of $\bar{n}$ was ~ 2 indicating the formation of 1 : 1 and 1 : 2 (metal : ligand) complexes only [19].

(*ii*) The metal ion solution used in the present study was very dilute (2 x 10^{-5} mol dm^{-3}), hence there was no possibility of formation of polynuclear complexes [20,21].

(*iii*) The metal titration curves were displaced to the right-hand side of the ligand titration curves along the volume axis, indicating proton release upon complex formation of the metal ion with the ligand. The large decrease in pH for the metal titration curves relative to ligand titration curves point to the formation of strong metal complexes [22,23].

(i*v*) For the same ligand at constant temperature, the stability of the chelates increases in the order Mn^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, La^{3+}, Ce^{3+}, UO$_2^{2+}$ and Th^{4+} [24,25].

The dissociation constant (pK^H) for BOSM, as well as the stability constants of its complexes with Mn^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, La^{3+}, Ce^{3+}, UO$_2^{2+}$ and Th^{4+} have been evaluated at 298 K, 308 K, and 318 K, and are given in Tables 1 and 3, respectively.

Table 3. Thermodynamic functions for ML and ML_2 complexes of BOSM in 40 % (by volume) DMF–water mixture and 0.1 mol dm^{-3} KCl.

M^{n+}	T/K	Gibbs energy / kJ mol^{-1}		Enthalpy / kJ mol^{-1}		Entropy / J mol^{-1} K^{-1}	
		$-\Delta G_1$	$-\Delta G_2$	$-\Delta H_1$	$-\Delta H_2$	ΔS_1	ΔS_2
Mn^{2+}	298	34.81	29.61			26.85	13.69
	308	34.91	29.78	26.81	25.53	26.30	13.80
	318	34.89	29.83			25.41	13.52
Co^{2+}	298	35.95	30.53			26.41	12.48
	308	36.09	30.72	28.08	26.81	26.01	12.69
	318	36.05	30.87			25.06	12.77
Ni^{2+}	298	36.52	31.44			26.17	13.42
	308	36.62	31.61	28.72	27.44	25.65	13.54
	318	36.65	31.66			24.94	13.27
Cu^{2+}	298	38.23	32.92			19.06	11.81
	308	38.45	33.02	32.55	29.40	19.16	11.75
	318	38.54	33.00			18.84	11.32
La^{3+}	298	39.08	34.12			28.32	15.97
	308	39.28	34.20	30.64	29.36	28.05	15.71
	318	39.27	34.28			27.14	15.47
Ce^{3+}	298	39.37	34.52			27.18	15.20
	308	39.63	34.50	31.27	29.99	27.14	14.64
	318	39.82	34.52			26.89	14.25
UO_2^{2+}	298	40.57	35.38			20.50	12.38
	308	40.69	35.56	34.46	31.69	20.23	12.56
	318	40.73	35.50			19.72	11.98
Th^{4+}	298	42.22	37.37			13.19	11.31
	308	42.34	37.27	38.29	34.00	13.15	10.62
	318	42.38	37.32			12.86	10.44

The enthalpy (ΔH) for the dissociation and complexation process was calculated from the slope of the plot pK^H or $\log K$ vs. $1/T$ using the graphical reperesentation of *van't Hoff* eqs. 4 and 5:

$$\Delta G = -2.303\ RT \log K = \Delta H - T\ \Delta S \qquad (4)$$

or

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

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

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

All thermodynamic parameters of the dissociation process of BOSM are recorded in Table 1. From these results the following conclusions can be made:

(*i*) The pK^H values decrease with increasing temperature, i.e. the acidity of the ligand increases [10].

(*ii*) A positive value of ΔH indicates that dissociation is accompanied by absorption of heat and the process is endothermic.

(*iii*) A positive value of ΔG indicates that the dissociation process is not spontaneous [26].

(*iv*) A negative value of ΔS is obtained due to the increased order as a result of the solvation process.

All the thermodynamic parameters of the stepwise stability constants of complexes are recorded in Table 3. It is known that the divalent metal ions exist in solution as octahedrally hydrated species [18] 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. Examination of these values shows that:

(*i*) The stability constants ($\log K_1$ and $\log K_2$) for BOSM complexes decrease with increasing temperature [9].

(*ii*) The negative value of ΔG for the complexation process suggests the spontaneous nature of such processes.

(*iii*) The ΔH values are negative, meaning that these processes are exothermic and favourable at lower temperature.

(*iv*) The ΔS values for the complexes are positive, confirming that the complex formation is entropically favourable [8].

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