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Kinetics and Thermodynamics of Ni^{2+} Complexation by Lasalocid (X-537A) in MeOH

J. GARCIA-ROSAS and H. SCHNEIDER

Max-Planck-Institut für biophysikalische Chemie, Am Fassberg, D-3400 Göttingen, F.R.G.

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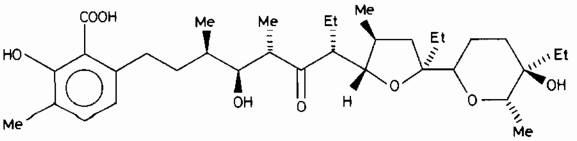
The formation and dissociation rate constants of the nickel complex of lasalocid (X-537A) in methanol have been determined using the stopped-flow method, by monitoring the change in conductance involved in the complexation reaction. From the corresponding activation parameters, the enthalpy and entropy of formation of the complex have been obtained. The results are compared with those reported in the literature from NMR and circular dichroism studies. Also, the stability constant of the sodium–lasalocid complex in methanol has been determined using a conductimetric technique.

Introduction

The polyether antibiotic lasalocid A, or X-537A, is a carboxylic ionophore which presents complexing properties towards a variety of metal ions, as well as primary and secondary ammonium ions [1, 2]. Numerous NMR [3–6], X-ray [7] and circular dichroism [8–10] studies of X-537A and its complexes have been reported. Recently a spectroscopic study on the interaction of lasalocid with lanthanide ions has appeared in the literature [11]. The stability constants for some lasalocid metal complexes in methanol and ethanol have been measured [9, 12]. Kinetic studies of the complexation of metal ions by carboxylic ionophores are, however, very scarce [13, 14]. These studies are important in relation to the process of transport of ions through membranes by carrier molecules with considerable biological activity. The complexation of the nickel ion is of interest in the field of biology as well as in solution chemistry. The selective uptake of nickel ions by certain plants is described elsewhere [15]. Theories of ion–solvent interactions and solvation–desolvation mechanisms have made widely use of kinetic data for Ni^{2+} complexation by several ligands [16, 17].



In this work we report a stopped-flow study in which the formation and dissociation rate constants of Ni^{2+} complex of lasalocid in methanol have been determined. The dissociation rate for the complex has been measured before (by NMR line-broadening spectroscopy), with the formation rate constant obtained as the product of the dissociation rate and stability constants [13]. However, the reported values for the corresponding kinetic parameters differ from ours, particularly those corresponding to the energetics of the transition state. Therefore we consider it of interest to report the results obtained from a more straightforward technique. These results are discussed in terms of known solvent exchange models.

The value of the stability constant of the nickel complex has been determined as the ratio of the formation and dissociation rate constants. The values for the enthalpy and entropy of complexation have been obtained by combining the corresponding activation parameters for the formation and dissociation reactions. Also, as part of our study we have determined the stability constant of the Na^+ lasalocid complex by a conductimetric method.

Experimental

Lasalocid was obtained as the sodium salt from Aldrich Chem. Co. It was recrystallized twice from methanol and dried under vacuum. Its melting point was 171–172 °C. Nickel solutions in MeOH were prepared from the corresponding hydrated nitrate and dried over molecular sieves. Methanol was obtained from Merck (dried AR, max. 0.01% H_2O).

The complexation reactions were monitored using a stopped-flow apparatus with conductimetric detection. Solutions of the partially dissociated sodium salt of lasalocid (NaL) and Ni^{2+} in MeOH were mixed in the stopped-flow. The following reactions are assumed to occur, eqns. (1), (2), with an overall change in the number of ionic species.

$$\mathrm{NaL} \overset{K_{\mathrm{NaL}}^{-1}}{\rightleftharpoons} \mathrm{Na^+} + \mathrm{L^-} \qquad (1)$$

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$$Ni^{2+} + L^- \underset{k_d}{\overset{k_f}{\rightleftharpoons}} NiL^+ \tag{2}$$

where L^- is the lasalocid ion. To obtain first-order conditions, NaL was used in excess. Total concentrations were $5.2 \times 10^{-4} \leqslant [NaL]_T \leqslant 2.7 \times 10^{-3}$ *M*, $1.0 \times 10^{-4} \leqslant [Ni(NO_3)_2]_T \leqslant 2.0 \times 10^{-4}$ *M* (at these concentrations the amount of protonated ligand HL is negligible). The rate constants were measured at 0.0, 5.1 and 10.0 °C. The rate constant at 25 °C was obtained by extrapolation using the corresponding activation parameters. During the measurements it was observed that the platinum electrodes of the cell were covered by a thin white film left by the NaL solutions, particularly the most concentrated ones. Pure methanol had to be flushed continuously.

The stability constant K_{NaL}, defined by eqn. (3), was determined from measurements of the conductance of NaL solutions at different concentrations using a Wayne-Kerr Bridge (B642).

$$K_{NaL} = \frac{[NaL]}{[Na^+][L^-]} \tag{3}$$

The value of K_{NaL} was obtained following the procedure proposed by King [18] for the determination of acidity constants from conductance measurements. This method is based on Shedlovsky's equation for conductance of 1:1 electrolytes [19]. An appropriate form of this equation is given by (4), where c_i, c are the ionic and

$$\Lambda + S\sqrt{c_i} = \Lambda^\infty - K\,\frac{\Lambda^2 c(10^{-2A\sqrt{c_i}})}{\Lambda^\infty - S\sqrt{c_i}} \tag{4}$$

total concentrations respectively, Λ is the equivalent conductance, Λ^∞ the limiting equivalent conductance, K is the stability constant, and A, S are parameters given by

$$A = \frac{1.823 \times 10^6}{(\epsilon T)^{1.5}} \tag{5}$$

$$S = B_1\Lambda^\infty + B_2 \tag{6}$$

$$\text{where } B_1 = \frac{8.204 \times 10^5}{(\epsilon T)^{1.5}} \tag{7}$$

$$\text{and } B_2 = \frac{82.5}{\eta(\epsilon T)^{0.5}} \tag{8}$$

In the above equations, ϵ is the dielectric constant, T is the temperature and η is the viscosity. An iterative procedure was used to obtain consistent values of Λ^∞ and c_i in eqn. (4). From a plot of $\Lambda + S\sqrt{c_i}$ *vs.* $\dfrac{\Lambda^2 c(10^{-2A\sqrt{c_i}})}{\Lambda^\infty - S\sqrt{c_i}}$, the value of K was obtained from the slope and Λ^∞ from the intercept (Fig. 1).

Results

Stability Constant of NaL

Values of $\log K_{NaL} = 2.83$ and $\Lambda^\infty = 89.8\ \Omega^{-1}\ cm^2\ eq^{-1}$ at 25 °C and $\log K_{NaL} = 2.79$ and $\Lambda^\infty = 75.3\ \Omega^{-1}\ cm^2\ eq^{-1}$ at 13 °C were obtained. The value of K_{NaL} is in good agreement with that obtained from circular dichroism measurements, $\log K_{NaL} = 2.57$ at 25 °C [9].

Formation and Dissociation Rates of NiL⁺

It can be shown that the kinetic equation corresponding to reactions (1), (2) is given by eqn. (9), where x is the reaction

$$-\frac{dx}{dt} = \left(\frac{k_f[NaL]_T\gamma_\pm^4}{1 + K_{NaL}[Na^+]} + k_d\right)x \tag{9}$$

variable, $[NaL]_T$ is the total concentration of NaL (dissociated and undissociated) and $\gamma_\pm$ is the mean ionic activity coefficient. The observed first-order rate constant (k_e) is then given by (10):

$$k_e = \frac{k_f[NaL]_T\gamma_\pm^4}{1 + K_{NaL}[Na^+]} + k_d \tag{10}$$

Therefore a plot of k_e against $\dfrac{[NaL]_T\gamma_\pm^4}{1 + K_{NaL}[Na^+]}$ should be a straigth line (Fig. 2) whose intercept is k_d, the dissociation rate constant of NiL^+, and whose slope is k_f, the formation rate constant of the NiL^+ complex corrected to zero-ionic strength through the activity coefficient. The mean ionic activity coefficients were calculated using Davies' equation [20]. $\gamma_\pm$ is given by eqn. (11), where I is

$$\gamma_\pm = 10^{-A\left(\frac{I^{1/2}}{I^{1/2} + 1} - 0.31\right)} \tag{11}$$

the ionic strength and A is the Debye–Hückel parameter given by eqn. (5).

From the values of k_f and k_d at different temperatures, the corresponding activation parameters and values of k_f and k_d at 25 °C were obtained (Table I). The stability constant of NiL^+ can be calculated as $K_{NiL^+} = k_f/k_d$ and the enthalpy and entropy of complexation are given by $\Delta H^\circ = \Delta H_f^\ddagger - \Delta H_d^\ddagger$ and $\Delta S^\circ = \Delta S_f^\ddagger - \Delta S_d^\ddagger$, respectively (Table II).

Tables I and II include the reported values as given in references [9] and [13]. However there

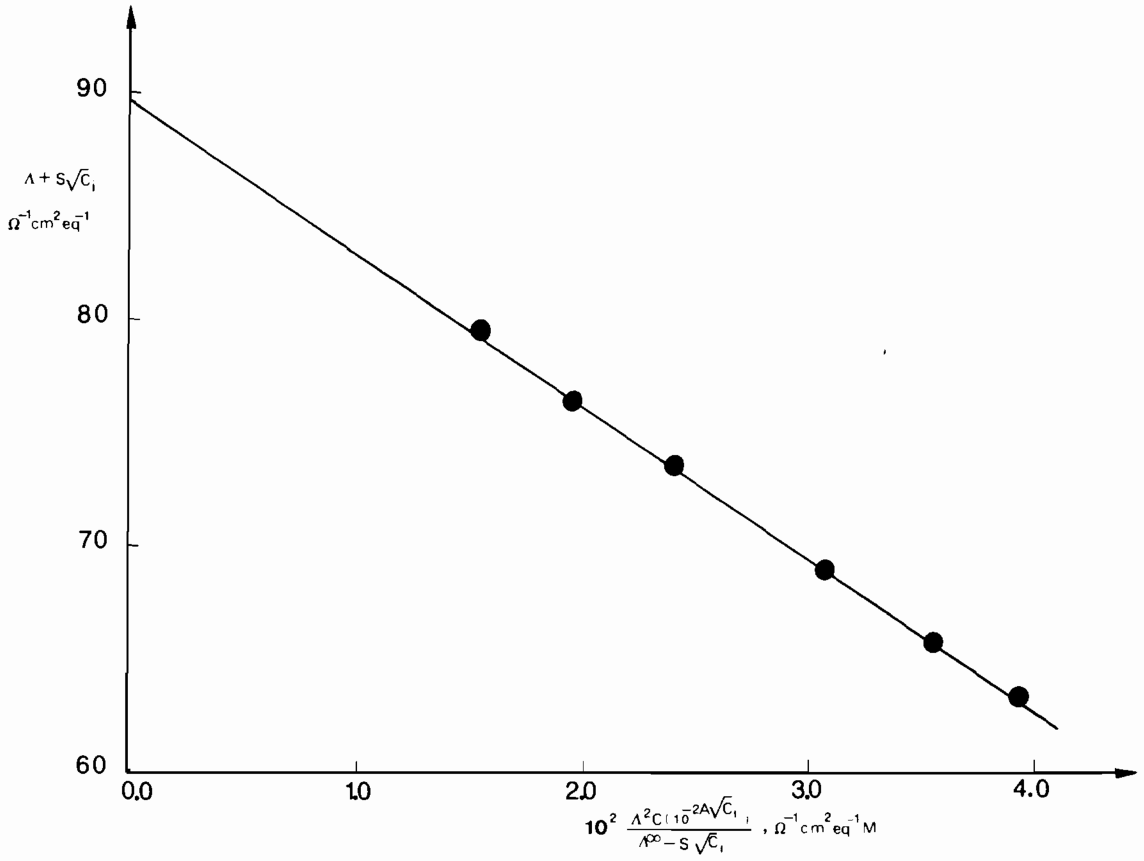

Fig. 1. Equivalent conductivity as a function of concentration for the sodium complex of lasalocid (T = 25 °C).

is a sign error in the reported value of ΔH°, since a negative enthalpy of complexation should correspond to a complex whose stability constant increases with decreasing temperature. Therefore, the reported values of ΔS°, $\Delta H_f^\ddagger$ and $\Delta S_f^\ddagger$, which have been derived from the value of ΔH°, have been corrected and are given in the tables for comparison. The reported values of ΔH° and ΔS° have been obtained from circular dichroism measurements of the stability constant at different temperatures. These values are in good agreement with ours, obtained from kinetic measurements. However, the reported values for the entropy and enthalpy of activation differ radically from those obtained in the present work.

Discussion

In terms of the Eigen–Wilkins mechanism [21, 22], the complexation reaction involves the formation of an outer-sphere complex followed by the release of the solvent molecules (S) from the metal ion, eqn. (12).

$$[M(S)]^{2+} + L^- \overset{K_o}{\rightleftharpoons} [M(S)^{2+} \ldots L^-] \xrightarrow{k_1} ML^+ + S \qquad (12)$$

The overall formation rate constant is given by the product $K_o{\cdot}k_1$, where K_o is the equilibrium constant for the formation of the outer-sphere complex and k_1 is the rate constant for the rate-determining step, which involves the substitution of solvent molecules by ligand binding sites in the inner-sphere shell of the cation. Values of $K_o{\cdot}k_1$, $\Delta H^\ddagger_{K_o \cdot k_1}$ and $\Delta S^\ddagger_{K_o \cdot k_1}$ for complexation reactions of Ni^{2+} by anions such as SCN^-, Cl^-, CF_3COO^-, CCl_3COO^-, $CHCl_2COO^-$, CH_2ClOO^- and CH_3COO^- in MeOH are reported in the literature [23]. These values range from 0.7×10^5 to 2.5×10^5 M^{-1} s^{-1} for $K_o{\cdot}k_1$, 17 to 20 kcal mol^{-1} for $\Delta H^\ddagger_{K_o \cdot k_1}$ and 25 to 35 cal mol^{-1} deg^{-1} for $\Delta S^\ddagger_{K_o \cdot k_1}$. The activation parameters which we have determined for the formation reaction of NiL^+ (Table I) are also in these ranges.

If we assume that the constant for the rate determining step (k_1) is the rate constant of solvent exchange for $Ni^{2+}(k_o)$, we can estimate K_o. The value of k_o for Ni^{2+} in MeOH is 10^3 s^{-1} [24]. This gives a value of $K_o = k_f/k_o = 6 \times 10^2$ M^{-1}. If we consider only simple electrostatic interactions, Fuoss' equation (13) [25] can be used to calculate K_o.

$$K_o = (4/3)\pi N a^3 \exp(-z_+ z_- e_o^2/\epsilon a k T) \qquad (13)$$

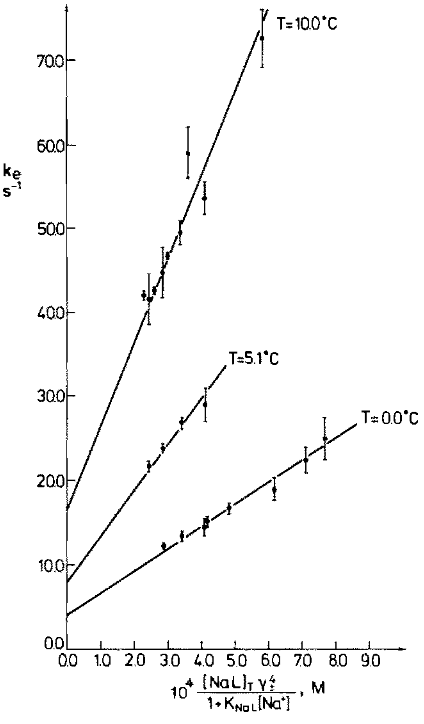

Fig. 2. Observed rate constant as a function of the total concentration of NaL.

where N is the Avogadro number; z_+, z_- are the ionic charges; e_0 is the electronic charge, k is the Boltzmann constant, ϵ is the dielectric constant, and a is the distance of closest approach of the ions.

For the case of NiL^+ in MeOH at 25 °C: $z_+ = 2$, $z_- = -1$ and $\epsilon = 3.627 \times 10^{-9}$ C^2 N^{-1} m^2. Table III shows the values of K_0 for different values of a. As can be seen from this table, K_0 depends appreciably on the value assumed for a. Thus, for $K_0 = 6 \times 10^2$ a value of a = 4.3 Å corresponds. This value is smaller than that used by other authors to determine values of K_0 from the Fuoss equation for complexes of Ni^{2+} in methanol (6 Å, Dickert *et al.* [26]). For a = 6 Å corresponds a value of $K_0 = 1.7 \times 10^2$ M^{-1} (Table III). It has been suggested, however, that different values of $K_0 \cdot k_1$ for different ligands having the same charge, may not be due to different values of K_0 but rather to different values of k_1 [23]. In this case, k_1 would be given by the rate of solvent exchange plus a contribution from a mechanism involving a ligand-assisted desolvation [27]. This mechanism could be, for example, an inner molecular proton transfer in the outer-sphere complex, eqn. (14).

$$[Ni(CH_3OH)L]^+ \rightarrow [Ni(CH_3O)HL]^+ \rightarrow NiL^+ + CH_3OH \quad (14)$$

Recently, a number of studies on $BeSO_4$ by means of proton magnetic resonance and relaxation techniques have attempted to prove the existence of such ligand-assisted mechanisms [28]. In any case, the high formation rate of the complex speaks in favour of a great conformational flexibility of the ligand [11].

TABLE I. Rate Constants and Activation Parameters for the Complexation of Ni^{2+} by Lasalocid in MeOH at 25 °C.

	k_f (M^{-1} s^{-1})	$\Delta H_f^\ddagger$ (kcal mol^{-1})	$\Delta S_f^\ddagger$ (cal mol^{-1} deg^{-1})	k_d (s^{-1})	$\Delta H_d^\ddagger$ (kcal mol^{-1})	$\Delta S_d^\ddagger$ (cal mol^{-1} deg^{-1})
This work	(6.0 ± 0.2) × 10^5	19.4 ± 0.6	32.9 ± 1.9	(1.2 ± 0.3) × 10^2	21.6 ± 0.8	23.5 ± 2.5
Reported value[a]	(2.2 ± 0.4) × 10^6	6.8 ± 1.5	−8 ± 7	(2.4 ± 0.4) × 10^2	4.5 ± 1.5	−32 ± 6
Reported value after correction[b]	–	2.2 ± 1.5	−22 ± 7	–	–	–

[a]Degani and Friedman, ref. [13]. [b]See text.

TABLE II. Stability Constant and Thermodynamic Parameters for the Complexation of Ni^{2+} by Lasalocid in MeOH at 25 °C.

	log K_s (K_s in M^{-1})	ΔH^o (kcal mol^{-1})	ΔS^o (cal mol^{-1} deg^{-1})
This work	3.7 ± 0.2	−2.2 ± 0.8	9.4 ± 2.5
Reported value[a]	3.96	2.3 ± 0.1	26 ± 1
Reported value after correction[b]	–	−2.3 ± 0.1	10.4 ± 1

[a]Degani and Friedman, ref. [9]. [b]See text.

TABLE III. Values of K_0 in MeOH at 25 °C.

a (Å)	4	5	6
K_0 (M^{-1})	8.7×10^2	3.1×10^2	1.7×10^2

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