Effect of Carboxylate Ligands on the Rate of Co^{2+} Incorporation into 1,4,8,11-Tetraazacyclotetradecane

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(Received February 16, 1989; revised June 17, 1989)

The mechanism of metal ion incorporation into tetraazamacrocycles has been discussed in several papers, taking into account the ring size [1], the degree of substitution [2] and the type of protonation [3]. The studies in aqueous solution have shown that, in general, the protonated forms CyH_2^{2+} and CyH^+ are the reactive ones. Especially in the case of CyH_2^{2+} electrostatic effects play an important role and can slow down the rate by several orders of magnitude.

We have previously observed that the addition of ligands, which form complexes with a smaller positive charge, increases the rate for Cu^{2+} and Ni^{2+} and have shown that there is a non-linear correlation between the log of the rate constant and the log of the stability constant of the complex [4, 5]. In continuation of these studies, we present here results on the rate of complexation of Co^{2+} with 1,4,8,11-tetraazacyclotetradecane (Cy) in the presence of a series of additional ligands with carboxylic groups, such as α-picolinic, glycolic, malonic and tricarballylic acid.

Experimental

1,4,8,11-Tetraazacyclotetradecane (Cy) was prepared according to the literature; melting point 184–186 °C (185–186° [6]). All other chemicals were of analytical grade and were used without further purification.

The kinetics of the complexation of Co^{2+} and Cy were studied by a pH-stat technique (Metrohm) following the release of protons according to eqn. (1), whereby L = α-picolinate, glycolate, malonate or tricarballylate.

$$CoL_m + CyH_n^{n+} \longrightarrow Co(Cy)^{2+} + mL + nH^+ \qquad (1)$$

Typical concentrations were: $[L]_{tot} = 1.6 \times 10^{-3}$ to 1.6×10^{-2} M, $[Cy]_{tot} = 8 \times 10^{-4}$ M, $[Co^{2+}]_{tot} = 8 \times 10^{-3}$ M, $I = 0.5$ M (KNO_3), $T = 25.0 \pm 0.5$ °C, under N_2 atmosphere to prevent oxidation of Co^{2+}. The pH, measured with a calibrated glass electrode, was chosen so that no $Co(OH)_2$ precipitation occurred.

The rate constants were calculated from 20 to 30 points of the pH-stat curves using the program ELORMA [7] for pseudo-first-order reactions ($[Co^{2+}]_{tot} \gg [Cy]_{tot}$). The error in k_{obs} was smaller than 5% for duplicates.

Results and Discussion

The incorporation rate of Co^{2+} into Cy, measured in the presence of an additional ligand L, is a bimolecular reaction (between Co^{2+} and Cy) but is also dependent on the pH and [L] concentration. For the four ligands studied, log k_{obs}/log[L] profiles at different pH values are more or less complicated, depending on the species CoL_m, on their reactivity, and on the protonated form of the macrocycle CyH_n^{n+} (Figs. 1–4). The shape of these curves can be fitted with Scheme 1, which takes into account all the possible species present in solution.

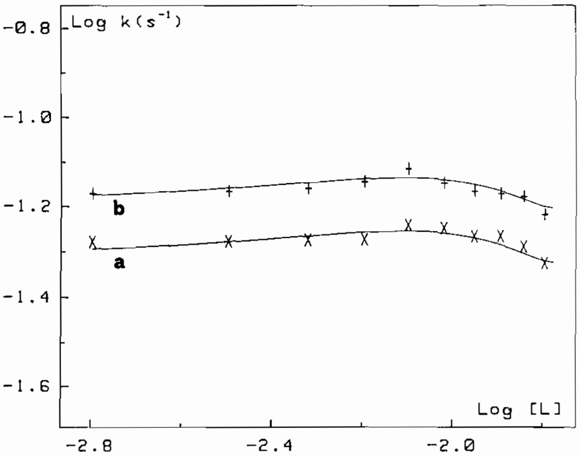
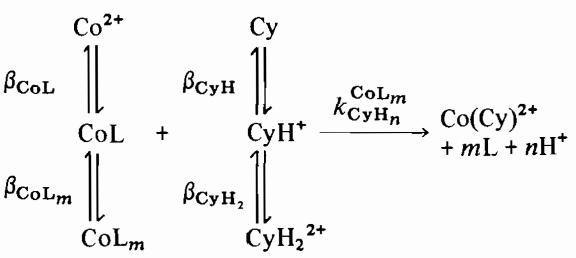


Fig. 1. Log k_{obs}/log [L] profile for L = Pic at pH 7.22 (a) and 7.34 (b) and $[Co^{2+}] = 8 \times 10^{-3}$ M. The curves are calculated with the rate constants of Table 2.



Scheme 1.

From this one can derive the general rate law expression, eqn. (2), as described in ref. 4.

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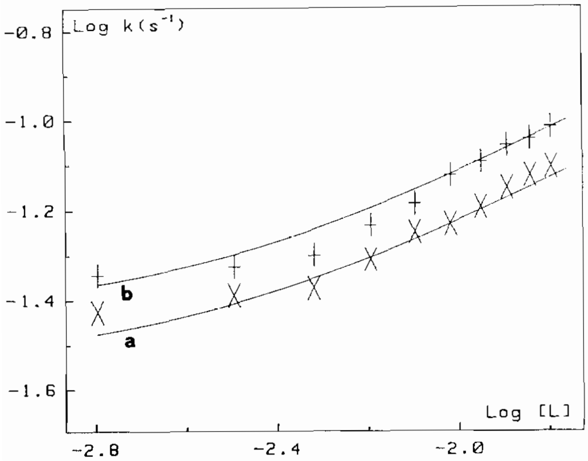

Fig. 2. Log k_{obs}/log [L] profile for L = Glyc at pH 6.97 (a) and 7.08 (b) and $[Co^{2+}] = 8 \times 10^{-3}$ M. The curves are calculated with the rate constants of Table 2.

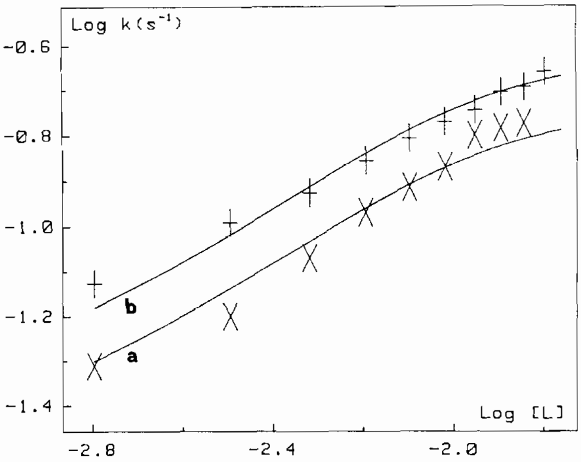

Fig. 3. Log k_{obs}/log [L] profile for L = Mal at pH 6.94 (a) and 7.06 (b) and $[Co^{2+}] = 8 \times 10^{-3}$ M. The curves are calculated with the rate constants of Table 2.

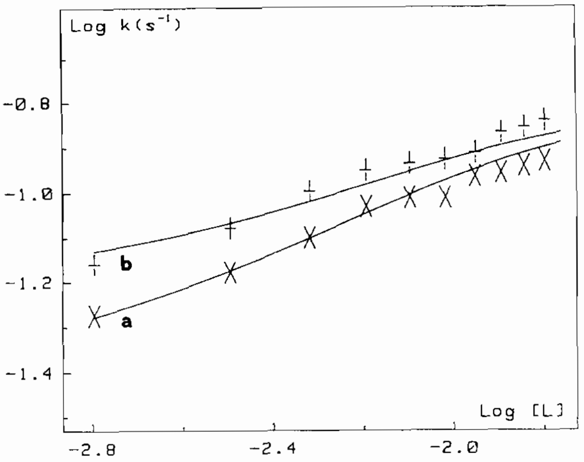

Fig. 4. Log k_{obs}/log [L] profile for L = Tri at pH 7.02 (a) and 7.24 (b) and $[Co^{2+}] = 8 \times 10^{-3}$ M. The curves are calculated with the rate constants of Table 2.

$$\frac{d[\mathrm{Co(Cy)}]}{dt} = \frac{\Sigma_m \Sigma_n k^{\mathrm{CoL}_m}_{\mathrm{CyH}_n} \beta_{\mathrm{CoL}_m} \beta_{\mathrm{CyH}_n} [\mathrm{L}]^m [\mathrm{H}]^n}{\Sigma_n \beta_{\mathrm{CyH}_n} [\mathrm{H}^+]^n} \times [\mathrm{Cy}]_{\mathrm{tot}} [\mathrm{Co}^{2+}]_{\mathrm{tot}} \qquad (2)$$

from which eqn. (3) follows

$$k_{\mathrm{obs}} = \frac{[\mathrm{Co}^{2+}] \, \Sigma_n \Sigma_m k^{\mathrm{CoL}_m}_{\mathrm{CyH}_n} \beta_{\mathrm{CoL}_m} \beta_{\mathrm{CyH}_n} [\mathrm{L}]^m [\mathrm{H}^+]^n}{\Sigma_n \beta_{\mathrm{CyH}_n} [\mathrm{H}^+]^n} \qquad (3)$$

with $\beta_{\mathrm{Co}} = \beta_{\mathrm{Cy}} = 1$ for $m = n = 0$. The free concentrations of Co^{2+} and L were calculated by the Newton–Raphson method using the protonation and stability constants taken from the literature (Table 1). The bimolecular rate constants $k^{\mathrm{CoL}_m}_{\mathrm{CyH}_n}$ were then determined by fitting k_{obs} with eqn. (3) by a non-linear least-squares program. The quality of the fit can be seen from Figs. 1–4 and from the values of $\sigma_{\log k_{\mathrm{obs}}}$ given in Table 2.

The results of Table 2 show that beside the free metal ion (Co^{2+}) the 1:1 complexes (CoL) and, in one case, also CoL_2 can react with the monoprotonated form of the macrocycles CyH^+. Only in the case of tricarballylic acid was a bimolecular path involving CyH_2^{2+} found, probably because the 1:1 complex $Co(Tri)^-$ has a negative charge, which makes a reaction with a dipositive ion CyH_2^{2+} electrostatically favourable.

TABLE 1. Protonation and Co^{2+} stability constants of the ligands L used for the calculation of the species distribution

Ligand L[a]	Protonation constants			Stability constants		Reference
	$\log \beta_{\mathrm{LH}}$	$\log \beta_{\mathrm{LH}_2}$	$\log \beta_{\mathrm{LH}_3}$	$\log \beta_{\mathrm{CoL}}$	$\log \beta_{\mathrm{CoL}_2}$	
Pic	4.95			6.00	10.80	8
Glyc	3.57			1.48		9
Mal	5.08	7.65		2.66		9
Tri	5.95	10.58	14.08	2.44		8

[a] Pic = α-picolinate, Glyc = glycolate, Mal = malonate, Tri = tricarballylate.

TABLE 2. Bimolecular rate constants (M^{-1} s^{-1}) and standard errors (in parentheses) for the reactions of eqn. (1) at 25 ℃ and $I = 0.5$ M (KNO_3)

Ligand	$k_{\mathrm{Co}}^{\mathrm{CyH}}$	$k_{\mathrm{CoL}}^{\mathrm{CyH}}$	$k_{\mathrm{CoL_2}}^{\mathrm{CyH}}$	$k_{\mathrm{CoL}}^{\mathrm{CyH_2}}$	N[a]	σ[b]
Pic	$2.1(1) \times 10^4$	$2.6(1) \times 10^4$	$2.0(1) \times 10^4$		20	0.013
Glyc	$2.1(1) \times 10^4$	$1.5(1) \times 10^5$			20	0.026
Mal	$2.1(2) \times 10^4$	$1.6(1) \times 10^5$			19	0.030
Tri	$2.5(1) \times 10^4$			20(1)	20	0.023

[a] Number of experiments. [b] σ is the standard deviation of log k_{obs} after fitting with the values of this Table.

For CyH^+, the charge plays a relatively small role. The less positive the charge of the complex the faster the complexation rate with the macrocycle. These results are fully consistent with those previously found for Ni^{2+} [4] and Cu^{2+} [5] and, as discussed there, we must assume that at least one intermediate must be a mixed-ligand complex, in which both the additional ligand L and the macrocycle Cy are coordinated. The pH-stat measurements, however, did not allow the detection of any such species. Finally, one can also note that the rates for the Co^{2+} complexes are between those of the Cu^{2+} and the Ni^{2+} complexes, as expected from the solvent exchange rate of these ions.

Acknowledgement

This work was supported by the Swiss National Science Foundation (Project 20.5372.87) and this is gratefully acknowledged.

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