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## 218. Metal Complexes with Macrocyclic Ligands. X<sup>1)</sup>. On the Metal Complexation Kinetics of two N<sub>4</sub>-Macrocycles containing a Pyridine Ring

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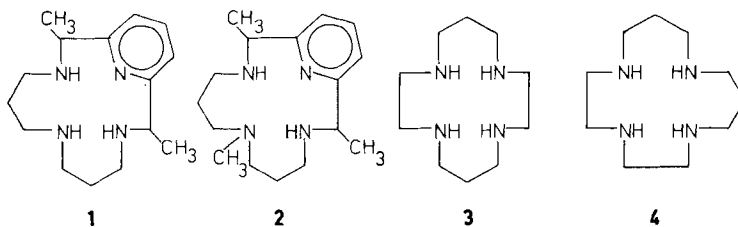
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### Summary

The complexation kinetics of the two macrocycles **1** and **2** with Co<sup>2+</sup>, Ni<sup>2+</sup>, Cu<sup>2+</sup> and Zn<sup>2+</sup> have been measured by pH-stat techniques. The rates are first order in metal and ligand concentration and depend upon the pH. This results from the different reactivities of the various protonated species of the macrocyclic tetraamines. The resolved rate constants are given in *Table 2*.

In comparison with other 14-membered cyclic aliphatic tetraazasystems **1** and **2** react more slowly with metal ions. This might be a consequence of the more rigid structure induced by the pyridine ring.

The kinetics of complex formation between transition metal ions and macrocyclic ligands have been studied from the view point of ring size [2], of steric effects at the coordinating amino groups [3] and at the carbon atoms of the ring [4] and of electrostatic interactions [5]. All these factors seem to affect to some degree the rate of complexation, which for the protonated species of the macrocycles is slower than that of analogous open chain polyamines.



<sup>1)</sup> Part IX, see [1].

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The hypothesis put forward in the first study of such reactions [6], that the energy of rotation necessary to bring the second nitrogen atom into the coordination sphere of the metal ion might increase the activation energy so that second bond formation becomes the rate determining step, is still an attractive explanation for the slow complexation rate. The flexibility of the macrocycle can be influenced by introducing more rigid structural elements in the ring. We have now studied the complexation of two cyclic tetraazasystems in which one amino group has been replaced by a pyridine nitrogen (structures **1** and **2**).

**Experimental Part.** - *meso*-2,12-Dimethyl-3,7,11,17-tetraazabicyclo[11.3.1]heptadeca-1(17),13,15-trien (**1**) [7] and 2,7,12-trimethyl-3,7,11,17-tetraazabicyclo[11.3.1]heptadeca-1(17),13,15-trien (**2**) [8] were synthesized according to the literature and characterized by elementary analysis, NMR, and IR spectra. Analytical grade chemicals were used without further purification.  $T = 25 \pm 0.01^\circ$  and  $I = 0.5$  (KCl).

The  $pK^H$  values of the cyclic tetraamines were obtained by titrating under nitrogen 4 ml  $10^{-2}M$  amine in 0.5M KCl with 0.2M HCl on a *Metrohm* Compensator E 388 with a glass electrode calibrated with two buffers. Duplicate did not differ by more than 0.01 pH unit in their buffer regions.

The kinetics were followed with a pH-stat (Combititrator 3 D *Metrohm*) by titrating with 0.025M NaOH the protons released during the complexation. Typical concentrations were  $2 \cdot 10^{-4}M$  ligand, 0.5M KCl and  $2 \cdot 10^{-3} - 10^{-2}M$  metal ion in 50 ml water. Since an excess of metal ion was used the curves were calculated with a program for first-order reactions. For  $Cu^{2+}$  at high pH the complexation was so fast that a lower excess of  $Cu^{2+}$  had to be used and the rate constants were therefore calculated using a program for second order reactions. The agreement between duplicates was better than 5%.

**Results and Discussion.** - The  $pK^H$  values of **1** and **2** obtained from the potentiometric titrations by the computer program VARIAT [9] are given in *Table 1* together with those of 1,4,8,11-tetraazacyclotetradecane (**3**) and 1,4,7,11-tetraazacyclotetradecane (**4**).

The values are typical for a 14-membered macrocycle with two proximal propylene bridges as **4** and distinctly different from those of **3**.

The kinetics of complex formation are first order in ligand and metal ion and are a function of the pH (*Fig. 1* and *2*). The pH dependence of  $k_{obs}$  can be resolved by assuming that the various protonated species of the cyclic polyamines react at different rates with the metal ion. Under the pH conditions the kinetics were studied **1** and **2** are present as  $LH_3^{3+}$  and  $LH_2^{2+}$ . This, however, does not exclude that  $LH^+$  or even L are reactive species. Thus, the following reactions must be considered (1).

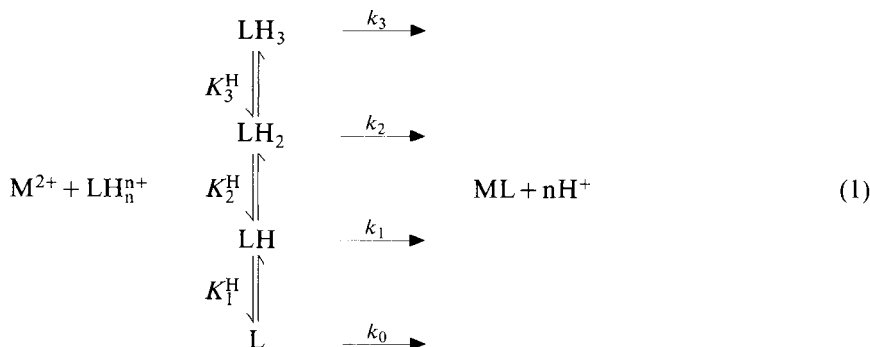


Table 1.  $pK^H$  values of **1**, **2**, **3** and **4** at 25° and  $I=0.5$ 

	$pK_1^H$	$pK_2^H$	$pK_3^H$	Ref.
<b>1</b>	10.08	9.09	5.35	
<b>2</b>	10.21	8.92	5.21	
<b>3</b>	11.83	10.76	< 2	[2]
<b>4</b>	11.29	10.19	4.32	[2]

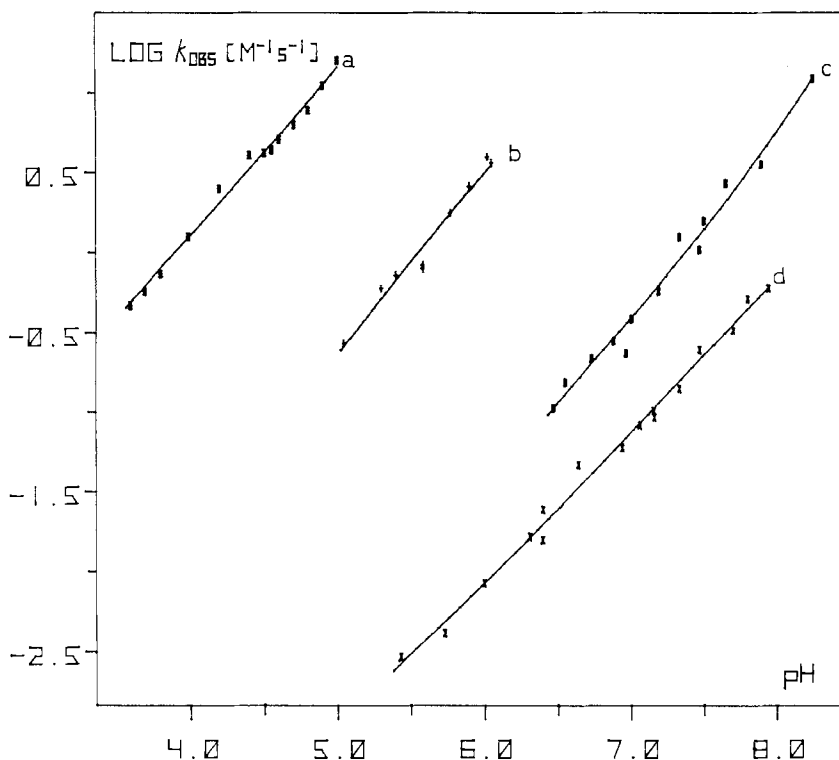


Fig.1. pH dependence of  $k_{obs}$  for the complexation of **1** with a)  $Cu^{2+}$ , b)  $Zn^{2+}$ , c)  $Co^{2+}$  and d)  $Ni^{2+}$  (at 40°). The curves are calculated with the rate constants of Table 2 and the size of the experimental points corresponds to  $\sigma_y$ .

The rate of formation is then given by (2). With (3)

$$v_f = k_{obs} [M^{2+}] [L]_{tot} = [M^{2+}] \cdot \sum_{i=0}^3 k_i [LH_i^{i+}] \quad (2)$$

one obtains for  $k_{obs}$  equation (4), where  $\beta_i$  are the overall protonation constants ( $\beta_i = \prod_{j=1}^i K_j^H$ ).

$$[L]_{tot} = \sum_{i=0}^3 [LH_i] = [L] \sum_{i=0}^3 \frac{[H^+]^i}{\beta_i} \quad \text{with } \beta_0 = 1 \quad (3)$$

$$k_{obs} = \frac{\sum_{i=0}^3 k_i \frac{[H^+]^i}{\beta_i}}{\sum_{i=0}^3 \frac{[H^+]^i}{\beta_i}} \quad \text{with } \beta_0 = 1 \quad (4)$$

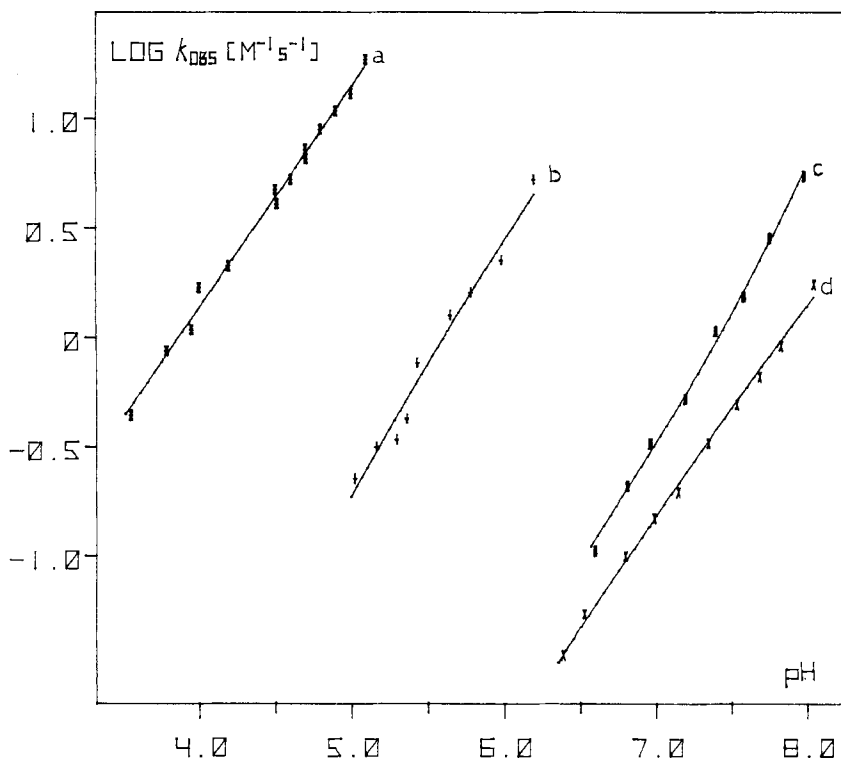


Fig. 2. pH dependence of  $k_{obs}$  for the complexation of **2** with a)  $\text{Cu}^{2+}$ , b)  $\text{Zn}^{2+}$ , c)  $\text{Co}^{2+}$  and d)  $\text{Ni}^{2+}$  (at  $40^\circ$ ). The curves are calculated with the rate constants of Table 2 and the size of the experimental points corresponds to  $\sigma_y$ .

The pH dependences have been fitted with equations of the type (4) using the  $\text{pK}^{\text{H}}$  values of Table 1 and the smallest set of  $k_i$  values. The computation was done on a desk computer HP 9821 with a non-linear least square program based on Marquardt's version [10] of the Newton-Gauss approximation [11].

To exemplify what we understand under the smallest set of best rate constants let us discuss the fitting of the pH dependence of **2** with  $\text{Co}^{2+}$ . In a first approximation only  $k_1$  was considered as parameter (Fig. 3). This gave a square sum of 0.0954 with 7 degrees of freedom (D.F.) and a standard deviation  $\sigma=0.117$ , which is unsatisfactory for such measurements. We then tried the curve fitting with  $k_1$  and  $k_0$  (Fig. 3). In this case the square sum is 0.0086 with 6 D.F. and  $\sigma=0.037$ . In order to prove whether the fitting with two parameters is better than that with one the F-test is used [12]. In our case  $F=0.0954 \times 6 / (0.0086 \times 7) = 9.51$  which represent a significant improvement even with a 1% uncertainty level ( $F_{0.01} = 8.26$ ).

The best  $k_i$  values of **1** and **2** together with those of **3** and **4** are collected in Table 2. The results show that although  $\text{LH}_3^{3+}$  is the predominant species below pH 5 its reactivity is too low to be measured. In contrast  $\text{LH}_2^{2+}$  and  $\text{LH}^+$  are both reactive. The ratio  $k_1/k_2$  is  $10^3$ - $10^4$  which is larger than what is generally found for linear polyamines [13], but typical for cyclic ligands [2-4]. The large ratio  $k_1/k_2$  is indicative

Table 2. Rate constants ( $M^{-1}s^{-1}$ ) for the complexation of **1**, **2**, **3** and **4** with  $Co^{2+}$ ,  $Ni^{2+}$ ,  $Cu^{2+}$  and  $Zn^{2+}$  at  $25^\circ$  and  $I=0.5$ 

		<b>1</b>	<b>2</b>	<b>3</b> [2]	<b>4</b> [2]
$Co^{2+}$	$10^{-3}k_0$	$3.5 \pm 1.3$	$5.2 \pm 0.7$	19000	-
	$10^{-1}k_1$	$4.7 \pm 0.4$	$2.5 \pm 0.1$	150	100
$Ni^{2+}$	$k_1$	$9.3 \pm 0.4$	$13.0 \pm 0.3^a)$ ( $2.6 \pm 0.06^b)$	53	240
	$10^3 k_2$	$2.9 \pm 0.6$	-	-	-
$Cu^{2+}$	$10^{-5}k_1$	$2.3 \pm 0.5$	$1.2 \pm 0.2$	18	-
	$k_2$	$29 \pm 1$	$22 \pm 1$	0.39	190
$Zn^{2+}$	$10^{-3}k_1$	$4.2 \pm 0.5$	$2.6 \pm 0.3$	50	74
	$k_2$	$0.42 \pm 0.15$	$0.19 \pm 0.09$	-	-

a) At  $40^\circ$ . b) Calculated from the value at  $40^\circ$  with  $\Delta E^* = 104 \text{ kJ. mol}^{-1}$ .

for a more important electrostatic interaction between  $M^{2+}$  and  $LH_2^+$  than for  $M^{2+}$  and  $LH^+$ . For **1** and **2** the complexation rates follow the usual order  $Cu^{2+} > Zn^{2+} > Co^{2+} > Ni^{2+}$ , which parallels the solvent exchange rates [14].

In comparison with **3** and **4** the two macrocycles with a pyridine ring react more slowly. However, the effect of introducing a pyridine ring is not a dramatic one, the

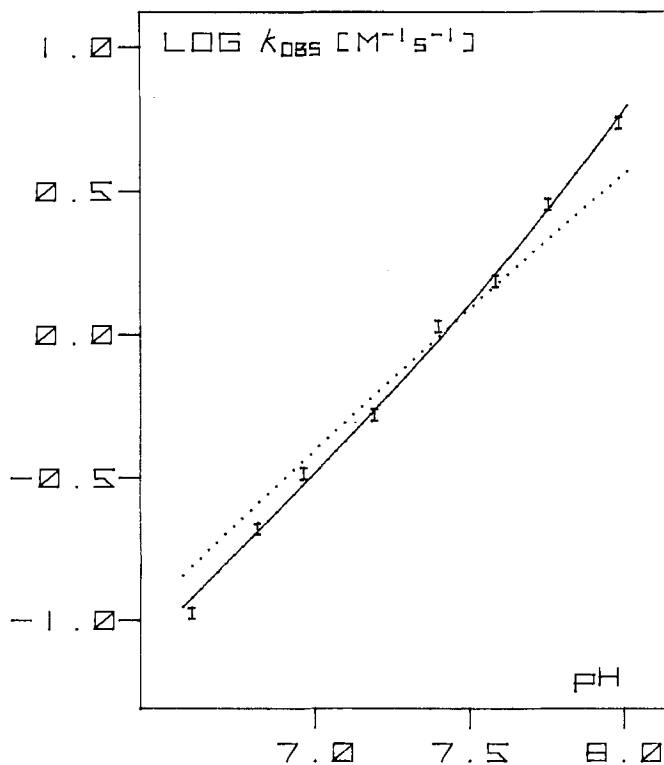


Fig. 3. Comparison of the fitting of the pH dependence of  $k_{obs}$  for **2** with  $Co^{2+}$  considering only  $k_1$  (....) or  $k_0$  and  $k_1$  (—).

rates being only 10–100 times smaller. Whether these differences reflect the lower flexibility of the macrocycle or are due to steric effects cannot be stated at the moment. It is, however, clear that more rigid rings must be studied to answer this question.

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## 219. Metal Complexes with Macrocyclic Ligands. XI<sup>1)</sup>. Ring Size Effect on the Complexation Rates with Transition Metal Ions

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### Summary

The 12–16 membered tetraazamacrocycles 1–6 were synthesized, their protonation constants and complexation kinetics measured at 25° and  $I=0.5$ . The results of *Table 1* show that  $pK_3^H$  is strongly influenced by the ring size whereas  $pK_2^H$  and  $pK_1^H$  are relatively insensitive to it. This can be understood in terms of electrostatic interactions of the positive charges when located on adjacent amino groups.

The kinetics of complex formation between the macrocyclic ligands and several transition metal ions have been studied by pH-stat and stopped-flow techniques

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