147. Metal Complexes with Macrocyclic Ligands, V[1]). Formation and Dissociation Kinetics of the Pentaco-ordinated Ni^{2+}, Cu^{2+}, Co^{2+} and Zn^{2+} Complexes with 1,4,8,11-Tetramethyl-1,4,8,11-tetraazacyclotetradecane

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Summary. The formation and dissociation kinetics of the pentaco-ordinated Cu^{2+}, Ni^{2+}, Co^{2+} and Zn^{2+} complexes with 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane (4-MeCyclam-14) was studied by pH-stat techniques and spectrophotometrically. The rates of the reactions between 4-MeCyclam-14 and each of the four metal ions, although slower than normal complexations by a factor of $10^3 - 10^4$, closely follow the order $Cu^{2+} > Zn^{2+} > Co^{2+} > Ni^{2+}$, found for the rate of water exchange. This implies that beside water exchange an other constant factor plays an important role in the rate determing step. The dissociation of the pentaco-ordinated 4-MeCyclam-14 complexes is acid catalyzed. The limiting rate for acid dissociation is not reached even in 2.5 M HNO_3 in the case of $Ni(4\text{-MeCyclam-14})^{2+}$. From the formation and dissociation rates stability constants have been calculated, which do not show any macrocyclic effect.

Although the complexation kinetics of transition metal ions with macrocyclic tetraaza-ligands has been studied [1]–[3], little is known about their dissociation, since most of these compounds dissociate very slowly even under extreme conditions. For example the Ni^{2+} complex of 1,4,8,11-tetraazacyclotetradecane (Cyclam-14) is decomposed by 12 M HCl at 100° with a half time of several minutes [4]. Similarly the dissociation of the square planar complex Cu(tet a) (red) with 6.1 M HCl is very slow [3].

During our studies with macrocycles we have observed that beside the square planar or octahedral complexes formed by most of these ligands, a series of pentaco-ordinated compounds which are kinetically less stable against acids is obtained with 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane (4-MeCyclam-14) [5]. We have now studied the kinetics of the dissociation of the Ni^{2+}, Cu^{2+}, Co^{2+} and Zn^{2+} complexes with 4-MeCyclam-14. From the rates of formation and dissociation we have calculated the stability constants of these complexes.

Experimental. – *Reagents.* 4-MeCyclam-14 was synthesized as described in the literature [1], all other reagents were of analytical grade. Metal complex solutions ($3 \cdot 10^{-3} - 10^{-2}$ M) were prepared by reaction of 4-MeCyclam-14 with a 10% excess of metal salt (except Zn^{2+} for which exactly one equivalent was used) at pH 5–7 and 80°. The pH was kept constant either manualy or with a pH-stat until no pH change could be detected and in the case of Ni^{2+}, Cu^{2+} and Co^{2+} until the absorption spectra remained constant. Thereafter the excess of unreacted metal ion was precipitated as hydroxide and the solution adjusted to the desired pH and volume.

Kinetics. – The formation of the Co^{2+} and Zn^{2+} complexes with 4-MeCyclam-14 was followed under pseudo-first order condition at 25° and 40° with a pH-stat Combititrator 3D (*Metrohm*) as described before [1]. The dissociation of the Cu^{2+}, Ni^{2+} and Co^{2+} complexes was measured

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[1]) Part IV see [1].

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spectrophotometrically by mixing metal complex solutions with HNO_3 of different concentrations. The reactions were followed on a *Techtron* 635 spectrophotometer equipped with a device, which allows to mix solutions in 0.5 seconds (Co^{2+}), on a *Durrum* stopped flow instrument (Ni^{2+}) and on a *Bausch & Lomb* Spectronic 600 E (Cu^{2+}, Ni^{2+}) at 650 nm ($\varepsilon = 243\,M^{-1}\,cm^{-1}$) for $Cu(4\text{-MeCyclam-14})^{2+}$, at 470 nm ($\varepsilon = 21.5\,M^{-1}\,cm^{-1}$) for $Co(4\text{-MeCyclam-14})^{2+}$ and at 395 nm ($\varepsilon = 77\,M^{-1}\,cm^{-1}$) for $Ni(4\text{-MeCyclam-14})^{2+}$ either at 25° or 40° and $I = 0.5$ or 1 (KNO_3). The dissociation of $Ni(4\text{-MeCyclam-14})^{2+}$ was also studied using Cu^{2+} as a scavenger in the pH-range 2.5–4.6 in 0.01 M acetate, chloroacetate and dichloroacetate buffers at 40°.

The dissociation of the Zn^{2+} complex was measured in 0.01 M acetate buffers by reacting the free Zn^{2+} ion with Xylenolorange [6] and following the optical density at 570 nm ($\varepsilon = 2.29 \cdot 10^4\,M^{-1}\,cm^{-1}$). In the case of reactions run below pH 5, aliquots containing 0.1–2 μg Zn^{2+}/ml were withdrawn at different times and mixed with 0.005% Xylenolorange in 0.05 M α-picoline buffer pH 5.5. The optical density was measured immediatly. Above pH 5, where the complex of Zn^{2+} with Xylenolorange is fully formed, Xylenolorange was added to the reaction solution. Both methods gave above pH 5 the same results indicating that Xylenolorange did not interfere with the dissociation reaction. Activation energies were obtained from kinetics measurements run between 20° and 50°. The rate constants and the activation energies were calculated using appropriate programms for a desk computer.

Results and Discussion. – *Complex Formation.* The kinetics of complex formation between 4-MeCyclam-14 and Co^{2+} or Zn^{2+} is proportional to $[M^{2+}]_{tot}$, to $[4\text{-MeCyclam-14}]_{tot}$ and inversely proportional to $[H^+]$ (1). (Fig. 1). Since in the pH range, in which the reaction was studied, the ligand exists as LH_2^{2+} [1], the inverse

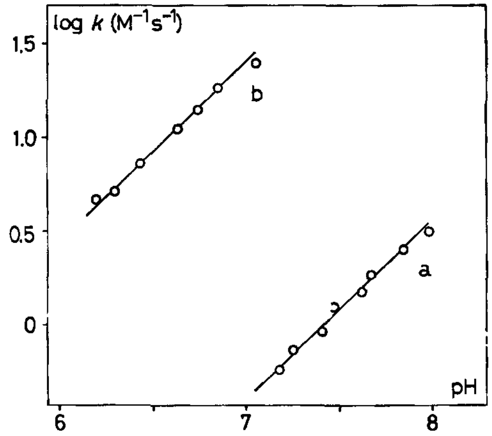

Fig. 1. *pH-Dependence of the formation of the a) Co^{2+} (40°) and b) Zn^{2+} (25°) complexes with 4-Me Cyclam-14 at $I = 0.5$*

$$\frac{d[ML]}{dt} = k_{+}\,[M^{2+}]_{tot}\,[4\text{-MeCyclam-14}]_{tot}/[H^{+}] \qquad (1)$$

proportionality to $[H^+]$ indicates that LH^+ is the reactive species. With pK_2^H, the second protonation constant of 4-MeCyclam-14, one can then determine the bimolecular rate constants $k_M^{HL} = k_+ K_2^H$ (Table 1).

The k_M^{HL} values for the four metal ions studied, although much smaller than those generally observed for normal complexations, follow the order $Cu^{2+} > Zn^{2+} > Co^{2+} > Ni^{2+}$, found for the rate of water exchange of these metal ions [7]. In addition the

Table 1. *Rate constants, activation energies and* Arrhenius *constants for the formation and dissociation of the Cu^{2+}, Ni^{2+}, Co^{2+} and Zn^{2+} complexes with 4-MeCyclam-14 at 25° and $I = 0.5$*

Metal ion	k_M^{HL} ($M^{-1}\ s^{-1}$)	ΔE^* (kcal/mol)	log A ($M^{-1}\ s^{-1}$)	k_H^{ML} ($M^{-1}\ s^{-1}$)	ΔE^* (kcal/mol)	log A ($M^{-1}\ s^{-1}$)
Cu^{2+}	$2.9\ 10^{5}$ a)	19.6 a)	19.9 a)	$6.7\ 10^{-3}$ ($k_{H_2}^{ML} = 0.33$ c))	9.6 b)	
Ni^{2+}	1.4 a)	18.4 a)	13.7 a)	$2.9\ 10^{-2}$ ($k^{ML} = 2.2\ 10^{-4}$ d))	11.1	6.6
Co^{2+}	1.6 10	19.8	15.8	2.5	11.2	8.6
Zn^{2+}	$4.5\ 10^{3}$	18.8	17.5	3.6 10	11.8	10.2

a) See [1]. b) At pH = 1.35. c) In $M^{-2}\ s^{-1}$. d) In s^{-1} at 40°.

ratio $k_M^{HL}/k_M^{H_2O}$ is practically constant and equal to $10^{-3} - 10^{-4}$. These two observations together imply that water exchange coupled with an other constant factor, able to slow down the rate by 3 or 4 orders of magnitude, must be involved in the rate determing step of the complexation of these metal ions with 4-MeCyclam-14. In a previous paper [1] we have indicated that this is probably not due to steric effects. A more probable reason for the slow reaction could be a conformation change of the ligand. Whether this change occurs in a rapid pre-equilibrium before the complexation step or takes place in an intermediate in which the metal ion is already coordinated to one or more nitrogen atoms of the ligand [2] is difficult to decide at the moment.

Complex Dissociation. – The dissociation kinetics of the pentaco-ordinated Cu^{2+}, Ni^{2+}, Co^{2+} and Zn^{2+} complexes with 4-MeCyclam-14 was studied at acid pH. The rate law contains several terms (2). For

$$-\frac{d[ML]}{dt} = k^{ML}[ML] + k_H^{ML}[ML][H^+] + k_{H^2}^{ML}[ML][H^+]^2 \qquad (2)$$

M = Zn^{2+} and Co^{2+} only the term proportional to $[H^+]$ was observed, whereas for M = Cu^{2+} both $k_{H^2}^{ML}$ and k_H^{ML} and for M = Ni^{2+} k^{ML} and k_H^{ML} were found (Fig. 2 and 3). The rate constants are given in Table 1 together with their activation energies and *Arrhenius* constants. The dissociation of the Ni^{2+} complex was studied in more details over a broad range of proton concentrations. Up to 2.5 M HNO_3 there was no indication that the limiting rate, which for open chain amines generally occurs at 0.05 – 0.2 M $[H^+]$ [8] was reached.

Let us assume that the dissociation for the pentaco-ordinated $Ni(4\text{-}MeCyclam\text{-}14)^{2+}$ proceeds by the generally accepted dissociation mechanism for chelate compounds [9] (Fig. 4). Applying the steady-state aproximation to the intermediate and assuming that $k_{-1} < k_2 + k_3[H^+]$, the rate of dissociation becomes (3) in agreement with the rate law experimentally found.

$$k_- = \frac{k_1}{k_{-1}}(k_2 + k_3[H^+]). \qquad (3)$$

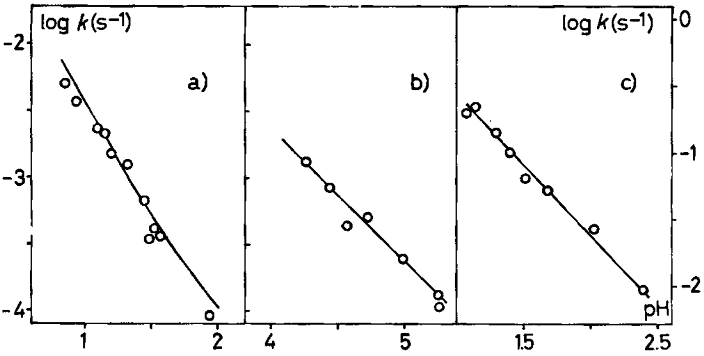

Fig. 2. *pH-Dependence of the dissociation of a)* $Cu(4\text{-}MeCyclam\text{-}14)^{2+}$ *b)* $Zn(4\text{-}MeCyclam\text{-}14)^{2+}$ *and c)* $Co(4\text{-}MeCyclam\text{-}14)^{2+}$ *at 25° and* $I = 0.5$ (KNO_3)

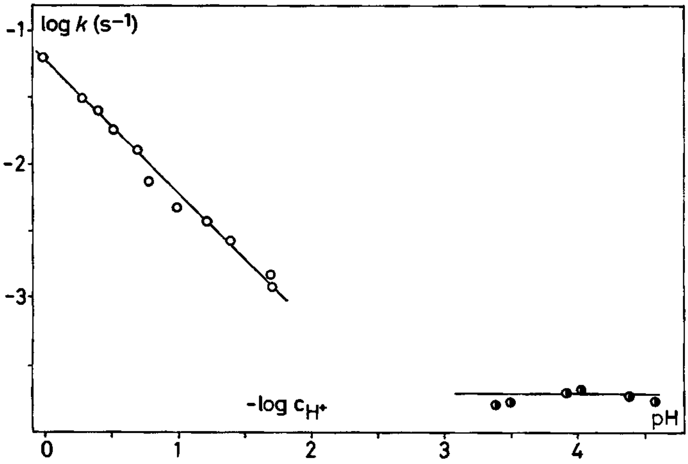

Fig. 3. *pH-Dependence of the dissociation of* $Ni(4\text{-}MeCyclam\text{-}14)^{2+}$ *at 40° and* $I = 1$ (KNO_3) *in the presence of* HNO_3 (○) *and* Cu^{2+} (◑) *as scavenger*

The fact that the non-coordinated amino group in the intermediate is not protonated and the low rate of the dissociation are indicative that we have a situation very similar to the one observed for the dissociation of the Ni^{2+} complex with *cis,cis*-1,3,5-triaminocyclohexane [10]. The dissociation of the first Ni-N bond is coupled with a conformational change across a potential barrier, whose height is between that found for open chain ligands and that of the even more robust square planar Ni^{2+} complex with Cyclam-14.

Stability Constants. – Equilibrium measurements with macrocyclic ligands are difficult because of the slow rate with which the equilibrium is attained. However, from their kinetics of formation and dissociation one can calculate the stability constants K_{ML} (4).

$$K_{ML} = \frac{k_M^{HL}}{k_{ML}^H\, K_1^H} = \frac{[ML]}{[M][L]}\,. \qquad (4)$$

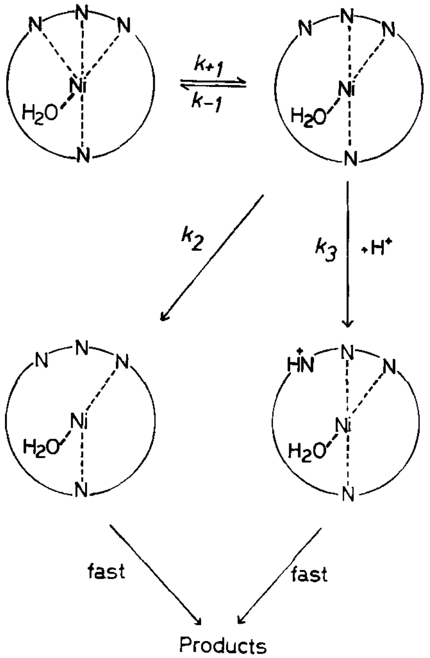

Fig. 4. *Scheme for the dissociation of Ni(4-MeCyclam-14)$^{2+}$*

The values of log K_{ML} for the Cu^{2+}, Ni^{2+}, Co^{2+} and Zn^{2+} complexes of 4-MeCyclam-14 are given in Table 2 together with those of Trien and Tren. Although the geometries of the complexes formed with 4-MeCyclam-14, Trien and Tren are quite different, the complexes with the macrocyclic ligand are equally or less stable than those with the other tetraamines. For these pentaco-ordinated metal complexes no macrocyclic effect [10] is found.

Table 2. *Stability constants of the complexes of 4-MeCyclam-14, Trien and Tren with Cu^{2+}, Ni^{2+}, Co^{2+} and Zn^{2+}*

log K_{ML}

Metal ion	4-MeCyclam-14[a]	TRIEN[b] [c]	TREN[b] [d]
Cu^{2+}	17.7	20.4	18.8
Ni^{2+}	11.8	14.0	14.8
Co^{2+}	10.9	11.0	12.8
Zn^{2+}	12.2	12.1	14.65

[a] 25°, I = 0.5. [b] 20°, I = 0.1. [c] *G. Schwarzenbach*, Helv. *33*, 974 (1950). [d] *J. E. Prue & G. Schwarzenbach*, Helv. *33*, 963 (1950).

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148. Etude par spectrométrie de masse des O-isopropylidène-1,2-*thréo*- et -*érythro*-furannoses et des quatre désoxy-5-O-isopropylidène-1,2-pentofurannoses

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Summary. The mass spectra of the O-isopropylidene derivatives of *threo*- and *erythro*-furanose and those of the four C(4) methylated stereoisomers have been studied. Fragmentation modes based upon deuterium labelling, metastable peaks and high-resolution measurements are proposed. Each stereoisomer can be characterized by its low-resolution mass spectrum.

Ce mémoire décrit une étude de la fragmentation des substances représentées dans la Figure 1. Cette étude a été effectuée à l'aide des spectres de masse des molé-

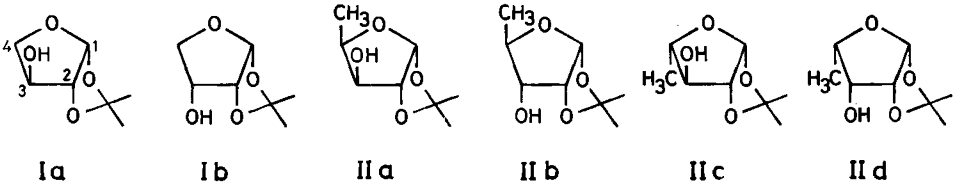

Fig. 1. *Composés étudiés*

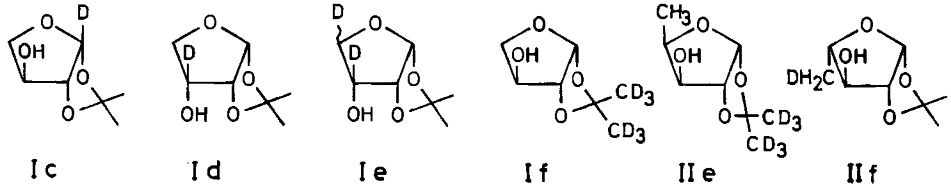

Fig. 2. *Substances deutériées utilisées*