

217. Metal Complexes with Macrocyclic Ligands

Part XX¹⁾

Influence of Coordinated Ligands onto the Complexation Rate of Ni²⁺ with 1,4,8,11-Tetraazacyclotetradecane

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(8.VIII.84)

Summary

The kinetics of the reaction between 1,4,8,11-tetraazacyclotetradecane (Cy) and Ni²⁺ in the presence of a series of ligands L = fluoride, acetate, glycolate, oxalate, malonate, succinate, methanetriacetate, 1,3,5-cyclohexanetriacetate, tricarballylate, picolinate, glycinate, iminodiacetate, nitrilotriacetate, *N,N'*-ethylenediiminodiacetate, ammonia, pyridine, ethylenediamine, 1,3-propanediamine and diethylenetriamine were studied by pH-static and spectrophotometric methods at 25° and *I* = 0.5. By analysis of the log *k*/log [L] and/or log *k*/pH profiles the resolved bimolecular rate constants $k_{\text{CyH}_n}^{\text{NiL}_m}$ (Table 3) were determined using a non-linear least-square fitting procedure. Practically for all systems the rate constant $k_{\text{CyH}}^{\text{NiL}}$, describing the reaction between the 1:1 Ni²⁺ complex and the monoprotonated form of the macrocycle, was obtained. In some cases, however, also $k_{\text{CyH}_2}^{\text{NiL}}$ and $k_{\text{Cy}}^{\text{NiL}}$ were found. Since the experimental conditions were chosen so that NiL was mainly formed, the reactivity of NiL₂ was generally not measurable. The effect of the number of coordinated donor groups in NiL and of the charge of NiL on $k_{\text{CyH}}^{\text{NiL}}$ is discussed. Both effects seem to indicate that for the reaction between NiL and CyH⁺ first bond formation is not the rate-determining step.

Introduction. – The kinetics of metal-ion complexation by tetraazamacrocycles has been studied under variation of the ring size [2] [3], the degree of substitution [4] and protonation. In general, one has to differentiate between protonated and non-protonated species of the macrocycle, when complexation rates are discussed. So it was found that in strongly alkaline solution Cu(OH)₃⁻ and Cu(OH)₄²⁻ react with open-chain and cyclic tetraamines at similar rates, indicating that the same mechanism is involved [5]. Studies in organic solvents also show that the complexation of Ni²⁺ with open-chain and cyclic N₄-ligands is governed by the solvent-exchange rate independently of the nature of the ligand [6]. This was also found for a series of N₂O₂-macrocycles in MeOH [7] and for S₄-macrocycles in H₂O/EtOH mixtures [8]. In contrast to this, mono- (CyH⁺; Cy = 1,4,8,11-tetraazacyclotetradecane) and diprotonated (CyH₂²⁺) tetraazama-

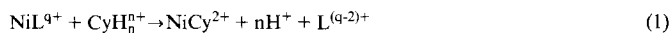
¹⁾ Part XIX: [1].

crocycles have slower complexation rates than what one would expect from analogous open-chain tetraamines or from solvent-exchange rates assuming that the *Eigen* mechanism is effective [9]. These observations have given rise to a long discussion about the possible reasons for the lower reactivity of the protonated species CyH^+ or CyH_2^{2+} in H_2O . Thus 1) second bond formation as rate-determining step [9], 2) steric effects [10], 3) electrostatic repulsion of the positively charged species M^{2+} and CyH_n^{n+} [5], and 4) conformational changes [2] have been put forward. In principle, each one or a combination of these effects can explain the lower reactivity of protonated macrocycles, but up to now it is not clear to which degree they are involved. Effects 2 and 3 mainly influence K_{os} , the outer-sphere stability constant, but not $k_{\text{H}_2\text{O}}$, the solvent-exchange rate. In mechanism 1 k_{obs} is determined by the rate of chelate ring closure which contains the rate constant of first bond formation and dissociation as well as that of second-bond formation. Explanation 4 is practically only dependent on the special properties of the macrocycle, whereby the conformation of the free ligand and that of the form able to bind the metal ion could be in a rapid pre-equilibrium before the rate-determining step, or if the conformation change is slow, could determine the overall rate of complexation.

We have previously indicated that the electrostatic repulsion (effect 3) becomes very important for diprotonated species CyH_2^{2+} , since there is a correlation between the rate of complex formation with Cu^{2+} and the third protonation constant of the macrocycle for a series of tetraazamacrocycles of different ring size [2]. However, for CyH^+ the question is still open. Thus, we have undertaken a new study of the rate of complex formation of Cy with a series of Ni^{2+} -complexes of mono- and polydentate ligands, having different charges and donor atoms, hoping to gain a deeper insight into the mechanism of complexation with the monoprotinated species CyH^+ .

Experimental. – *cis,cis*-1,3,5-Cyclohexanetricarboxylic acid [11], 2-(carboxymethyl)glutaric acid [12] and Cy [13] were prepared according to the literature. All other chemicals were purchased and used without further purification (analytical grade).

The kinetics of the complexation of Cy with Ni^{2+} in the presence of $\text{L} =$ fluoride, pyridine, acetic, picolinic, tricarballic, malonic, oxalic and glycolic acid were measured with a pH-stat by titrating with 0.04M NaOH the protons released during the complexation according to (1). The concentrations are given in Table 1.



The pH of the mixture containing all components except Ni^{2+} was set between 7 and 8, and then Ni^{2+} was added to start the reaction. From the curves of base consumption *vs.* time, the pseudo-first-order rate constants (since $[\text{Ni}^{2+}]_{\text{tot}} \geq 10[\text{Cy}]_{\text{tot}}$) were computed. Duplicates agreed better than 3% standard deviation.

The other reactions with $\text{L} =$ methanetricarboxylic acid, *cis,cis*-1,3,5-cyclohexanetricarboxylic acid, *N,N'*-ethylenediiminodiacetic acid, succinic acid, NH_3 , ethylenediamine, 1,3-propanediamine, diethylenetriamine and glycine were measured spectrophotometrically at the absorption maximum of NiCy^{2+} (450 nm) using a *Varian Techtron* 635 spectrophotometer equipped with a mixing device which allows to mix the reactants in less than 0.5 sec directly in a flow cell. The analog signal of the spectrophotometer was digitalized through an A/D converter (8 bit, 100 Hz) and read in constant time intervals by a *Dolphin* microprocessor. At the end of the experiment the absorbancy values were stored on magnetic tape from which they were transferred to an *Apple II* for calculation [14]. The 'best' experimental conditions (Table 1) to measure the reactivity of NiL were determined by a program which calculates the species distribution as function of the pH, using the protonation constant β_{LH_p} and the stability constants β_{NiL_m} .

Table 1. *Experimental Conditions for the Kinetics of Reaction 1*

| L ^{a)} | 10 ² [L] | pH | Method | Buffer ^{b)} |
|---------------------|---------------------|--------------------|--------|----------------------|
| F ⁻ | 0.5–1.0 | 7.5, 7.79 | c) | |
| Ac ⁻ | 0.5–3.0 | 7.49, 7.66, 7.75 | c) | |
| GloI ⁻ | 0.16–1.6 | 7.75, 7.87 | c) | |
| Ox ²⁻ | 0.16–1.6 | 7.61, 7.80 | c) | |
| Mal ²⁻ | 0.16–1.6 | 7.59, 7.79 | c) | |
| Suc ²⁻ | 0.8–4.0 | 7.76, 7.86 | d) | Coll |
| Metri ³⁻ | 3.0–4.0 | 7.52, 7.77 | d) | Coll |
| Cytri ³⁻ | 2.8–3.6 | 7.53, 7.64 | d) | Coll |
| Tri ³⁻ | 0.16–1.6 | 7.50, 7.70, 7.90 | c) | |
| Pic ⁻ | 0.16–1.6 | 7.51, 8.00, 8.20 | c) | |
| Gly ⁻ | 3.0–4.4 | 8.91 | d) | <i>t</i> -BA |
| | 2.0 | 9.0–10.0 | d) | <i>t</i> -BA |
| IDA ²⁻ | 2.0–4.0 | 9.91, 10.17 | d) | <i>t</i> -BA |
| | 2.8 | 9.5–11.0 | d) | <i>t</i> -BA |
| NTA ³⁻ | 2.0–3.6 | 9.08, 9.45, 9.85 | d) | <i>t</i> -BA |
| | 2.8 | 9.0–11.0 | d) | <i>t</i> -BA |
| EDDA ²⁻ | 2.4–3.6 | 9.65, 10.09 | d) | <i>t</i> -BA |
| | 2.0 | 10.0–11.0 | d) | <i>t</i> -BA |
| NH ₃ | 0.6–1.0 | 7.60, 7.75 | d) | Coll |
| py | 0.5–1.0 | 7.53, 7.73 | c) | |
| en | 2.8–3.6 | 9.03 | d) | <i>t</i> -BA |
| | 2.0 | 9.2–9.8 | d) | <i>t</i> -BA |
| pn | 2.8–3.6 | 8.06 | d) | Coll |
| | 2.0 | 7.8–8.4 | d) | Coll |
| dien | 2.4–3.6 | 9.59, 10.10, 10.40 | d) | <i>t</i> -BA |
| | 2.8 | 9.5–11.0 | d) | <i>t</i> -BA |

^{a)} Abbreviations for L: F⁻, fluoride; Ac⁻, acetate; GloI⁻, glycolate; Ox²⁻, oxalate; Mal²⁻, malonate; Suc²⁻, succinate; Metri³⁻, methanetriacetate; Tri³⁻, tricarballylate; Cytri³⁻, *cis,cis*-1,3,5-cyclohexanetricarboxylate; Pic⁻, picolinate; Gly⁻, glycinate; IDA²⁻, iminodiacetate; NTA³⁻, nitrilotriacetate; EDDA²⁻, *N,N'*-ethylenediamine diacetate; py, pyridine; en, ethylenediamine; pn, 1,3-propanediamine; dien, diethylenetriamine; trien, triethylenetetraamine.

^{b)} Buffer abbreviations: *t*-BA, *tert*-butylaminoethanol; Coll, 2,4,6-collidine.

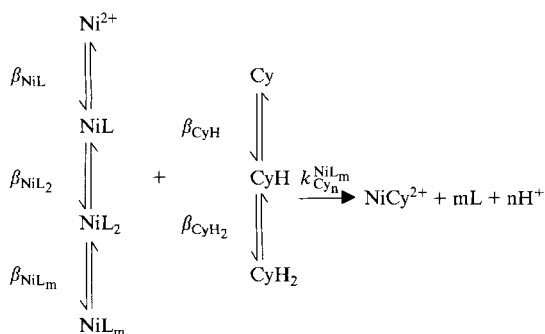
^{c)} [Ni²⁺]_{tot} = 8 · 10⁻³ M, [Cy]_{tot} = 8 · 10⁻³ M, pH-stat method.

^{d)} [Ni²⁺]_{tot} = 2 · 10⁻² M, [Cy]_{tot} = 2 · 10⁻³ M, spectrophotometric method.

Results. – The incorporation rate of Ni²⁺ into Cy has been measured in the presence of different ligands L at selected pH values. Depending on the ligand and on the complexes formed by it, more or less complicated log *k*_{obs}/log [L] profiles were obtained. Three of these, exemplifying also the other reactions, are shown in *Fig. 1–3*. The shape of these curves can be fully understood, and the experimental points can be satisfactory fitted by taking into account the different complexes NiL_m and their different reactivities towards CyH⁺, the monoprotonated form of the macrocycle, and/or Cy, the free cyclic tetraamine. Thus, the *Scheme* can be proposed.

To describe the chemical equilibria in the *Scheme* the *Eqns. 2–4* are necessary, [Ni²⁺]_{tot}, [L]_{tot} and [Cy]_{tot} representing the analytical concentrations of the three species, the β-values being the overall protonation and complexation constants and for m = p = n = 0 β_{Ni} = β_L = β_{Cy} = 1. Assuming that Ni²⁺ and the complexes NiL_m can react with different forms of the macrocycle CyH_n⁺, one can write *Eqn. 5* for the formation kinetics.

Scheme



$$[\text{Ni}^{2+}]_{\text{tot}} = [\text{Ni}^{2+}] \sum_m \beta_{\text{NiL}_m} \cdot [\text{L}]^m \quad (2)$$

$$[\text{L}]_{\text{tot}} = [\text{L}] \sum_p \beta_{\text{LH}_p} [\text{H}^+]^p + [\text{Ni}^{2+}] \sum_m m \cdot \beta_{\text{NiL}_m} \cdot [\text{L}]^m \quad (3)$$

$$[\text{Cy}]_{\text{tot}} = [\text{Cy}] \sum_n \beta_{\text{CyH}_n} \cdot [\text{H}^+]^n \quad (4)$$

$$\frac{d[\text{NiCy}]}{dt} = \sum_n \sum_m k_{\text{CyH}_n}^{\text{NiL}_m} \cdot [\text{NiL}_m] \cdot [\text{CyH}_n] \quad (5)$$

When the complexation constants β_{NiL_m} are introduced *Eqn. 6* results.

$$\frac{d[\text{NiCy}]}{dt} = [\text{Ni}^{2+}] \sum_n \sum_m k_{\text{CyH}_n}^{\text{NiL}_m} \cdot \beta_{\text{NiL}_m} \cdot [\text{L}]^m \cdot [\text{CyH}_n] \quad (6)$$

$[\text{CyH}_n]$ can be calculated from *Eqn. 4* and the value obtained from *Eqn. 7* can now be introduced in *Eqn. 6* to give *Eqn. 8*.

$$[\text{CyH}_n] = [\text{Cy}] \cdot \beta_{\text{CyH}_n} \cdot [\text{H}^+]^n = \frac{[\text{Cy}]_{\text{tot}} \cdot \beta_{\text{CyH}_n} \cdot [\text{H}^+]^n}{\sum_n \beta_{\text{CyH}_n} \cdot [\text{H}^+]^n} \quad (7)$$

$$\frac{d[\text{NiCy}]}{dt} = \frac{\sum_n \sum_m k_{\text{CyH}_n}^{\text{NiL}_m} \cdot \beta_{\text{NiL}_m} \cdot \beta_{\text{CyH}_n} \cdot [\text{L}]^m \cdot [\text{H}^+]^n}{\sum_n \beta_{\text{CyH}_n} \cdot [\text{H}^+]^n} \cdot [\text{Cy}]_{\text{tot}} \cdot [\text{Ni}^{2+}] \quad (8)$$

By comparing *Eqn. 8* with the observed rate constant k_{obs} of *Eqn. 9*, the final *Eqn. 10* is obtained. From *Eqn. 10* one sees that $[\text{Ni}^{2+}]$ and $[\text{L}]$ must be known to calculate k_{obs} . These can be determined from *Eqn. 2* and *3* by an iterative *Newton-Raphson* procedure

Table 2. Protonation and Ni²⁺ Stability Constants of the Ligands L Used for the Calculation of Species Distribution

| L ^{a)} | Protonation constants | | | Stability constants | | | Ref. |
|---------------------|-----------------------|-----------------|-----------------|---------------------|---------------------|---------------------|------|
| | LH | LH ₂ | LH ₃ | NiL | NiL ₂ | Other | |
| F ⁻ | 2.93 | | | 1.10 | | | [15] |
| Ac ⁻ | 4.64 | | | 1.12 | 1.81 | | [16] |
| Glol ⁻ | 3.61 | | | 1.69 | 2.70 | | [17] |
| Ox ²⁻ | 3.65 | 4.88 | | 5.30 | 7.64 | | [16] |
| Mal ²⁻ | 5.10 | 7.84 | | 3.20 | | | [16] |
| Suc ²⁻ | 5.21 | 9.21 | | 1.60 | | | [16] |
| Metri ³⁻ | 4.81 | 8.91 | 12.21 | 1.86 | | b) | [18] |
| Cytri ³⁻ | 4.96 | 9.29 | 13.04 | 1.41 | | b) | [18] |
| Tri ³⁻ | 5.95 | 10.58 | 14.08 | 2.70 | | b) | [23] |
| Pic ⁻ | 5.44 | 7.04 | | 6.40 | 11.90 | | [16] |
| Gly ⁻ | 9.70 | 12.31 | | 5.65 | 10.51 | 13.95 ^{c)} | [19] |
| IDA ²⁻ | 9.33 | 11.91 | | 8.19 | 14.30 | | [19] |
| NTA ³⁻ | 9.45 | 12.05 | 14.02 | 11.54 | 16.24 | | [16] |
| EDDA ²⁻ | 9.57 | 16.05 | | 13.50 | 18.25 ^{d)} | | [16] |
| NH ₃ | 9.25 | | | 2.80 | 4.85 | 6.51 ^{c)} | [16] |
| py | 5.21 | | | 1.78 | 2.82 | 3.12 ^{c)} | [16] |
| en | 10.14 | 17.56 | | 7.60 | 14.08 | 19.11 ^{c)} | [16] |
| pn | 10.62 | 19.74 | | 6.39 | 10.78 | 12.01 ^{c)} | [16] |
| dien | 10.03 | 19.27 | 23.86 | 10.70 | 18.90 | | [16] |

a) For the abbreviations for L, see Footnote a, Table 1.

b) β_{NiLH} and β_{NiLH_2} were not taken into account since the measurements were done at pH > 7, where these species do not exist.

c) β_{NiL_3} .

d) Determined from our kinetics measurements.

using β_{LH_p} and β_{NiL_m} values taken from the literature (Table 2). Once [Ni²⁺] and [L] have been obtained, the $k_{\text{CyH}_n}^{\text{NiL}_m}$ values can be calculated from Eqn. 10 by a non-linear least-square curve fitting program, using $\log \beta_{\text{CyH}} = 11.83$ and $\log \beta_{\text{CyH}_2} = 22.59$ [2]. The values of $k_{\text{CyH}_n}^{\text{NiL}_m}$ are given in Table 3 together with their standard deviations. The curves of Fig. 1–3, calculated with the 'best' parameters, and the values of $\sigma_{\log k_{\text{obs}}}$ show the quality of the fit.

$$\frac{d[\text{NiCy}]}{dt} = k_{\text{obs}}[\text{Cy}]_{\text{tot}} = k'_{\text{obs}}[\text{Ni}^{2+}]_{\text{tot}}[\text{Cy}]_{\text{tot}} \quad (9)$$

$$k_{\text{obs}} = \frac{[\text{Ni}^{2+}] \sum_n \sum_m k_{\text{CyH}_n}^{\text{NiL}_m} \cdot \beta_{\text{NiL}_m} \cdot \beta_{\text{CyH}_n} \cdot [\text{L}]^m \cdot [\text{H}^+]^n}{[\text{Ni}^{2+}]_{\text{tot}} \cdot \sum_n \beta_{\text{CyH}_n} \cdot [\text{H}^+]^n} \quad (10)$$

Discussion. – The kinetics of Reaction 1 have been measured between pH 7 and 11. In this pH range CyH₂²⁺ is the main species, although at pH > 10 CyH⁺ and Cy are also present. Despite it, the rate constants $k_{\text{CyH}_2}^{\text{NiL}_m}$ are rare and only found for complexes NiL_m, which bear a strongly negative charge (L = Tri, Metri, Cytri). Generally, CyH⁺

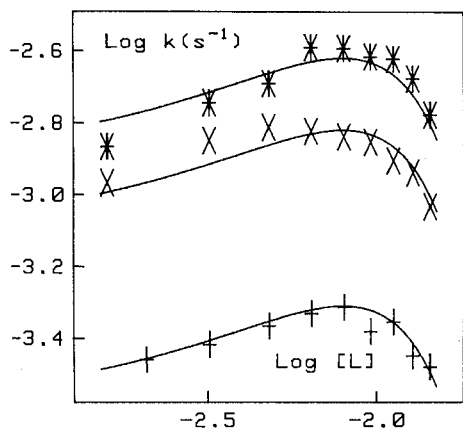


Fig. 1. $\log k/\log [L]$ profiles for $L = \text{Pic}$ at pH 7.46, 7.95 and 8.14 (from bottom to top) and $[\text{Ni}^{2+}] = 8 \cdot 10^{-3} \text{M}$. Curves calculated with the rate constants of Table 3.

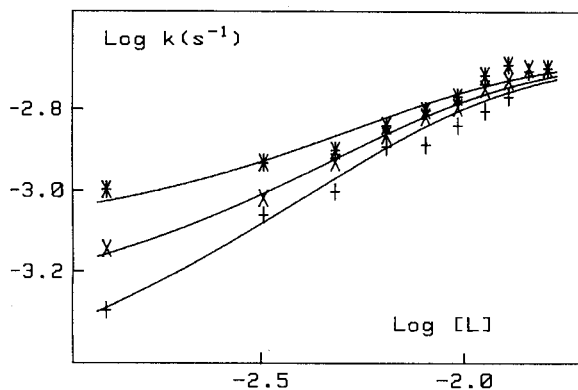


Fig. 2. $\log k/\log [L]$ profiles for $L = \text{Tri}$ at pH 7.50, 7.70 and 7.90 (from bottom to top) and $[\text{Ni}^{2+}] = 8 \cdot 10^{-3} \text{M}$. Curves calculated with the rate constants of Table 3.

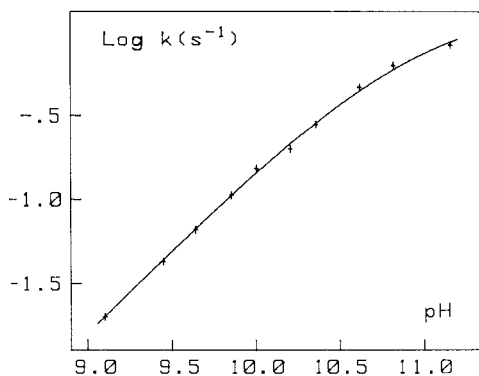
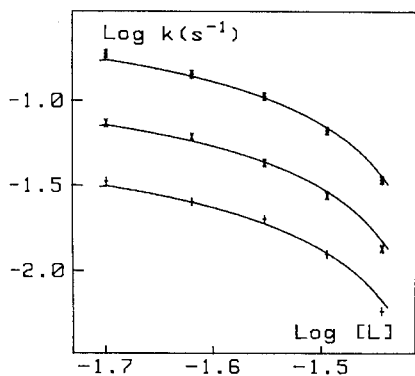


Fig. 3. $\log k/\log [L]$ and $\log k/\text{pH}$ profiles for $L = \text{NTA}$ at $[\text{Ni}^{2+}] = 2 \cdot 10^{-2} \text{M}$. Left: pH 9.08, 9.45 and 9.85 (from bottom to top). Right: $[\text{NTA}] = 2.8 \cdot 10^{-2} \text{M}$.

Table 3. Rate Constants ($\text{M}^{-1}\text{s}^{-1}$) and Standard Errors (in brackets) for the Reactions in the Scheme at 25° and $I = 0.5$ (KNO_3)

| L ^{a)} | $k_{\text{CyH}}^{\text{Ni}}$ | $k_{\text{CyH}}^{\text{NiL}}$ | Other | N _{exp.} ^{b)} | $10^2 \cdot \sigma^c)$ |
|---------------------|------------------------------|-------------------------------|--|---------------------------------|------------------------|
| F ⁻ | 57(2) | 196(11) | | 26 | 1.0 |
| Ac ⁻ | 52(2) | 157(7) | ^{d)} | 21 | 2.7 |
| GloI ⁻ | 57(6) | 340(20) | ^{d)} | 18 | 1.8 |
| Ox ²⁻ | 58(4) | 260(8) | $k_{\text{CyH}}^{\text{NiL}_2} = 363(18)$ | 20 | 2.2 |
| Mal ²⁻ | 60(8) | 501(10) | | 19 | 2.4 |
| Suc ²⁻ | 56 ^{e)} | 820(10) | | 20 | 1.4 |
| Metri ³⁻ | 56 ^{e)} | 590(40) | $k_{\text{CyH}_2}^{\text{NiL}} = 0.15(5)$ | 12 | 1.0 |
| Cytri ³⁻ | 55 ^{e)} | 610(30) | $k_{\text{CyH}_2}^{\text{NiLH}} = 0.16(2)$ | 10 | 0.8 |
| Tri ³⁻ | 58(2) | - | $k_{\text{CyH}_2}^{\text{NiL}} = 0.28(1)$ | 28 | 2.1 |
| Pic ⁻ | 57(7) | 139(7) | $k_{\text{CyH}}^{\text{NiL}_2} = 54(5)$ | 28 | 3.6 |
| Gly ⁻ | | 195(5) | ^{f)} | 11 | 3.6 |
| IDA ²⁻ | | 55(1) | ^{f)} | 19 | 4.0 |
| NTA ³⁻ | | 75(1) | $k_{\text{Cy}}^{\text{NiL}} = 131(13)^f)$ | 26 | 2.3 |
| EDDA ²⁻ | | 2.2(2) | $k_{\text{Cy}}^{\text{NiL}} = 63(3)^f)$ | 16 | 3.5 |
| NH ₃ | 52(2) | 75(6) | ^{d)} | 13 | 2.6 |
| py | 50(3) | 27(4) | ^{d)} | 15 | 3.0 |
| en | | 75(2) | ^{f)} | 12 | 3.5 |
| pn | | 43(1) | ^{d)} | 10 | 2.5 |
| dien | | 33(1) | ^{f)} | 20 | 4.2 |

^{a)} For the abbreviations for L, see Footnote a, Table 1. ^{b)} Number of experiments. ^{c)} σ is the standard deviation in $\log k_{\text{obs}}$ after fitting with the best parameters. ^{d)} $k_{\text{CyH}}^{\text{NiL}_2}$ could not be determined since the reaction conditions were chosen so that $[\text{NiL}_2] < 0.1[\text{NiL}]$. ^{e)} These values were kept constant during the fitting procedure. ^{f)} $k_{\text{CyH}}^{\text{NiL}_2} < k_{\text{CyH}}^{\text{NiL}}/100$, for the calculation $k_{\text{CyH}}^{\text{NiL}_2} = 0$.

is the reactive species and, thus, values for $k_{\text{CyH}}^{\text{NiL}}$ were obtained for practically all systems. Only in a few cases, when the pH was high enough, $k_{\text{Cy}}^{\text{NiL}}$ was also observed. Since our experimental conditions were chosen so that NiL was the predominant species, the reactivity of the 1:2 or 1:3 complexes could not be determined except for L = Pic and Ox. For many of the other ligands an upper limit was estimated from the value $k_{\text{CyH}}^{\text{NiL}}$ and the maximal amount of NiL₂ present.

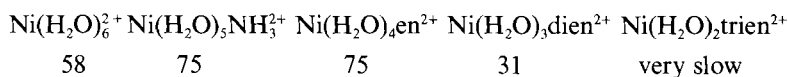
Fig. 1-3 show the different shapes of the $\log k_{\text{obs}}/\log [\text{L}]$ profiles obtained. Qualitatively they can be understood as follows. In Fig. 1 for Pic as ligand, we see at low $\log [\text{L}]$ a plateau corresponding to the reactivity of Ni²⁺. The larger $\log [\text{L}]$ becomes the more 1:1 complex NiL is formed, which in this case has a higher reactivity than Ni²⁺. Thus, an increase of $\log k_{\text{obs}}$ is found. When the concentration of L exceeds the 1:1 ratio also some 1:2 complex is formed and since it has a lower reactivity compared to that of the 1:1 complex a drop in $\log k_{\text{obs}}$ is observed. The curves at different pH are parallel to each other, indicating that for all pH the protonated form CyH⁺ is the reactive species. Fig. 2 (L = Tri) shows a different case since the curves at different pH values do not run parallel to each other. This indicates that at low $\log [\text{L}]$, Ni²⁺ is reacting with CyH⁺, whereas at higher $\log [\text{L}]$ the 1:1 complex reacts with CyH₂²⁺, which at these pH values is present at nearly 100%. The third example with L = NTA shows measurements which have been done at high pH, where no free Ni²⁺ exists any more. These reaction conditions had to be chosen for complexes which only form at high pH and have relatively low reactivities. The curves start with a plateau corresponding to the reactiv-

ity of the completely formed complex NiL, and show with increasing log [L] a decreasing log k_{obs} since a nonreactive 1:2 complex is formed. The pH dependence between 9 and 11 clearly shows that CyH⁺ and at high pH Cy both are reactive. The other ligands gave log $k_{\text{obs}}/\log [L]$ or log k_{obs}/pH profiles similar to the three types described above although sometimes one of the aspects is missing. So the dependencies for L = Ac, Glol, Ox, Mal, Suc, NH₃ and py are similar to Fig. 1, for L = Metri and Cytri to Fig. 2 and for L = IDA, EDDA, en, pn, dien and Gly to Fig. 3.

The pH- and log [L] profiles can be quantitatively explained by assuming that the different Ni²⁺-species react with either CyH₂²⁺, CyH⁺ or Cy in a bimolecular step (Scheme). The large variety of ligands, which differ in their charge and in the nature and number of coordinating groups, allows to extract some general conclusion for this type of reactions.

The Charge Effect on $k_{\text{CyH}}^{\text{NiL}}$. Since NiL reacts with a positively charged species such as CyH⁺, one expects that the lower the positive charge of NiL the faster the complexation reaction. In accordance with this, one finds with a series of carboxylate ligands that the rate changes from 56M⁻¹s⁻¹ for Ni²⁺, to 157M⁻¹s⁻¹ for Ni(Ac)⁺ to 266M⁻¹s⁻¹ for Ni(Ox) and to 590M⁻¹s⁻¹ for Ni(Tris)⁻. Thus, on going from a species with charge +2 to one with -1, the rate constant increases by a factor of about 10. Similarly, if one keeps the number of coordinated donor groups constant and varies the charge the same trend is observed: 75M⁻¹s⁻¹ for Ni(en)²⁺, 195M⁻¹s⁻¹ for Ni(Gly)⁺ and 260M⁻¹s⁻¹ for Ni(Ox). In addition, there are, however, more subtle effects as shown by the complexes with the three dicarboxylic acids: 260M⁻¹s⁻¹ for Ni(Ox), 501M⁻¹s⁻¹ for Ni(Mal) and 820M⁻¹s⁻¹ for Ni(Suc). Thus, not only the charge of the species, but also the size of the chelate ring seems to play a but small role. The electrostatic effects observed for the reaction of CyH⁺ with different complexes NiL are relatively small, compared to charge effects found for analogous reactions with Ni²⁺ [20].

Effect of the Coordinated Donor Atoms on $k_{\text{CyH}}^{\text{NiL}}$. The effect of the number of occupied coordination sites by the ligand L on the rate is best looked at in the series of amine ligands since this is not accompanied by a change in charge. Let us discuss the rate constants $k_{\text{CyH}}^{\text{NiL}}$ (M⁻¹s⁻¹) for the following series:



There is practically no effect up to two N-atoms, then a small decrease for three N-donors and an extremely sharp drop after the fourth NH₂-group has coordinated.

The following examples also shows the same trend. For complexes with unidentate and bidentate ligands such as NiAc⁺, NiGly⁺ and NiPic⁺ with rate constants of 157, 195 and 139M⁻¹s⁻¹, respectively, there is practically no change in reactivity. However, a decrease in $k_{\text{CyH}}^{\text{NiL}}$ is found on going from Ni(IDA) (3 donors) to Ni(EDDA) (4 donors) with rate constants of 49 and 2.6M⁻¹s⁻¹, respectively.

Mechanism of the Reaction. It is generally accepted that ligand-ligand substitutions proceed stepwise through a ternary complex in which both the incoming and the expelled ligands are simultaneously coordinated to the metal ion [21]. Depending on the nature of L, the rate-determining step can be at the beginning of the reaction sequence, along the series of steps or even at the very end (Eqn. 11)



To discuss this, several points must be considered. First, a coordinated ligand reduces the number of replacable H_2O -molecules and, therefore, a reduction in the rate by a corresponding statistical factor is expected. Secondly, the coordinated ligand L can alter the overall charge so that in respect to $\text{Ni}(\text{H}_2\text{O})_6^{2+}$ the outer-sphere stability constant K_{os} is changed. Third, it has been shown that coordinated ligands influence the solvent exchange rate. Thus, a correlation between the number of coordinated NH_2 -groups and the H_2O -exchange or ligand-substitution rate has been observed for Ni^{2+} [22]. Fourth, ring closure could become important when the incoming ligand needs a high activation energy for internal rotation. Finally, breaking of bonds of the leaving ligand could become rate-determining when several coordination sites are blocked. If we now concentrate on the results described above for $k_{\text{CyH}}^{\text{NiL}}$, we find only a small electrostatic effect reflected in a factor of 2–5 per charge unit. This would indicate that charge effects cannot alone explain the lower reactivity of CyH^+ compared to that of analogous monoprotonated open-chain tetraamines as was proposed [5]. In addition, the number of coordinated NH_2 -groups practically has no effect on the rate constant $k_{\text{CyH}}^{\text{NiL}}$. Both seem to indicate that first bond formation, or better dissociation of the first H_2O -molecule does not play the same role for CyH^+ as generally for open-chain ligands. In addition, inhibition of the ligand-substitution rate is found for ligands with three or more coordinating groups.

Thus, all the typical features for first bond formation generally found for other Ni^{2+} -complexes are not observed here. This again opens the discussion about the rate-determining step in the complexation with macrocyclic polyamines. To discuss it, one carefully has to differentiate between the different protonated forms CyH_2^+ , CyH^+ , and Cy, and the arguments have to be specific for each species. We have previously indicated that the electrostatic repulsion in the formation of the outer-sphere complex probably is the main reason for the slowness in the formation reaction with the diprotonated form CyH_2^+ . On the other side, it was shown by studies in strongly alkaline solution [5] and in non-aqueous solvents [6], where Cy is the reacting species, that the free cyclic amine reacts as fast as analogous open-chain ligands when no steric hindrance is present. The question remains open why the monoprotonated form CyH^+ behaves differently from open-chain analogs. Does eventually an internal H-bond stabilize CyH^+ in a conformation which is not reactive so that CyH^+ has to restructure itself before complexation can occur? Or is a conformation change necessary after first bond formation has taken place? The present study although it clearly demonstrates the effects governing the reactivity of CyH^+ cannot prove in a definitive way the different hypotheses postulated.

This study was supported by the *Swiss National Science Foundation* (Project No. 2.021-0.83) and this is gratefully acknowledged.

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