that the second step is a rearrangment reaction of the intermediate involving M–N bond inversion. The complex $[ML]^{2+}$, finally formed, is a thermodynamically more stable stereoisomer of the intermediate $[ML]_{int}^{2+}$.

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Registry No. L[1], 295-37-4; L[2], 53118-99-3; L[3], 121187-41-5; L[4], 67707-85-1; L[5], 41203-22-9; Ni, 7440-02-0; Cu, 7440-50-8.

Contribution from Anorganische Chemie III, Eduard-Zintl-Institut
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Kinetic Studies of Nickel(II) and Copper(II) Complexes with N_4 Macrocycles of the Cyclam Type. 2. Kinetics and Mechanism of Complex Formation with Different C-Alkylated 1,4,8,11-Tetraazacyclotetradecanes

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Received April 5, 1991

The relative pK_a values of the species LH^+ (p$K_a(1)_r$) and LH_2^{2+} (p$K_a(2)_r$) were determined for six cyclic tetraamines L^6 (=1,4,8,11-tetraazadibenzo[*b,i*]cyclotetradecane), L^7 (=TMBC = 1,4,8,11-tetramethyl-1,4,8,11-tetraazadibenzo[*b,i*]cyclotetradecane), L^8 (=Tet A = *meso*-5,5,7,12,12,14-hexamethyl-1,4,8,11-tetraazacyclotetradecane), L^9 (=Tet B = *rac*-5,5,7,12,12,14-hexamethyl-1,4,8,11-tetraazacyclotetradecane), L^{10} (=*meso*-5,12-dimethyl-1,4,8,11-tetraazacyclotetradecane), and L^{11} (=*meso*-5,12-dimethyl-*meso*-7,14-diphenyl-1,4,8,11-tetraazacyclotetradecane) by potentiometric titration in *N,N*-dimethylformamide (=DMF). p$K_a(1)_r$ and p$K_a(2)_r$ are not significantly affected by C-alkylation within the series of ligands L^6–L^{11}. Spectrophotometry and multiscan stopped-flow spectrophotometry was used to study the kinetics of complex formation of M^{2+} ions (M = Ni, Cu) with L^6–L^{11} in DMF at $I = 0.1$ M ($NaClO_4$) in the temperature ranges 293–313 K (Ni) and 215–263 K (Cu), respectively. Complex formation is found to be a two-step process with an initial fast second-order reaction (first-order in both $[M^{2+}]_0$ and $[L]_0$, rate constant k_1), generating an intermediate species $[ML]_{int}^{2+}$, and a subsequent slower first-order reaction (rate constant k_2), in which the intermediate is converted to the product $[ML]^{2+}$. The activation parameters ΔH^* and ΔS^* of the k_1 step are reported for systems M^{2+}/L^{6-11}. At 303 K and for M = Ni, rate constant k_1 ranges from 1040 (L^{10}) to 0.057 $M^{-1}\,s^{-1}$ (L^7), whereas rate constant k_2 lies in the range 1.5×10^{-3} (L^{11}) to $0.08 \times 10^{-3}\ s^{-1}$ (L^9). For M = Cu, k_1(218 K) ranges from 14.4×10^4 (L^9) to 0.0283 $M^{-1}\,s^{-1}$ (L^7), and k_2(303 K) ranges from 83.7×10^{-3} (L^7) to $0.54 \times 10^{-3}\ s^{-1}$ (L^{10}). The characteristics of the visible absorption spectra of the intermediates $[ML]_{int}^{2+}$ and products $[ML]^{2+}$ are presented. They clearly indicate square-planar N_4 coordination of L in the intermediates as well as in the products. Only the nickel species formed with L^6 and L^7 are different in that the ligand is probably folded. The kinetic data obtained are not in line with the interpretation that intermediate formation follows the classical Eigen–Wilkins mechanism with the formation of the first M–N bond being rate-controlling. They suggest instead the operation of a mechanism with conformational changes in the ligands affecting rate control (Eigen–Winkler mechanism).

Introduction

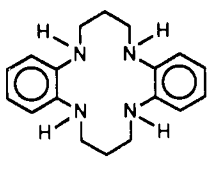
As shown in the preceding contribution,[1] complex formation of divalent transition metal ions M^{2+} (M = Ni, Cu) with the tetraaza macrocycle cyclam (=L^1)[2] and differently N-methylated cyclam ligands (L^2–L^5)[2] in the aprotic solvent DMF (=*N,N*-dimethylformamide) is a two-step process according to (1) and (2).

$$M^{2+} + L \xrightarrow{k_1\ (M^{-1}\,s^{-1})} [ML]_{int}^{2+} \tag{1}$$

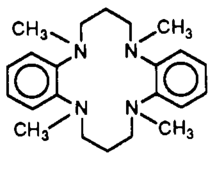
$$[ML]_{int}^{2+} \xrightarrow{k_2\ (s^{-1})} [ML]^{2+} \tag{2}$$

The visible spectra of the intermediates $[ML]_{int}^{2+}$, formed according to (1), clearly indicate square-planar N_4 coordination.[1] Second-order rate constant k_1 correlates with the pK_a of the second-basic nitrogen of ligands L^1–L^5, which suggests the formation of the second M–N bond to be the rate-controlling step in the formation of $[ML]_{int}^{2+}$.[1] There is strong experimental evidence in support of reaction 2 being an isomerization step, in which the thermodynamically less stable intermediate forms the more stable stereoisomer $[ML]^{2+}$ via M–N bond inversion.[1]

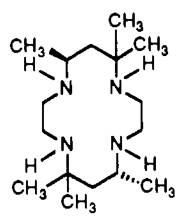
In the present contribution the kinetic investigation of complex formation with N-methylated cyclam derivatives L^2–L^5 is extended to C-alkylated cyclam derivatives L^6–L^{11}.[3] The study was undertaken (i) to provide data for a comparison of the kinetic effect of C-alkylation vs N-alkylation and (ii) to address the question of ligand-controlled kinetics vs metal-controlled kinetics on the basis of the data obtained for nickel(II) and copper(II) reacting



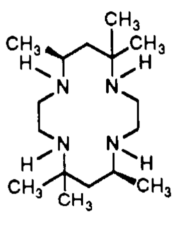
L^6



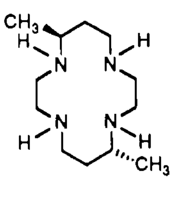
L^7 (TMBC)



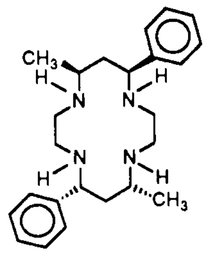
L^8 (TET A)



L^9 (TET B)



L^{10}



L^{11}

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(1) Röper, J. R.; Elias, H. *Inorg. Chem.*, preceding paper in this issue.

(2) Abbreviations used: L^1 = cyclam = 1,4,8,11-tetraazacyclotetradecane; L^2 = 1-methyl-1,4,8,11-tetraazacyclotetradecane; L^3 = 1,4-dimethyl-1,4,8,11-tetraazacyclotetradecane; L^4 = 1,4,8-trimethyl-1,4,8,11-tetraazacyclotetradecane; L^5 = TMC = 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane.

(3) Abbreviations used: L^6 = 1,4,8,11-tetraazadibenzo[*b,i*]cyclotetradecane; L^7 = TMBC = 1,4,8,11-tetramethyl-1,4,8,11-tetraazadibenzo[*b,i*]-cyclotetradecane; L^8 = Tet A = *meso*-5,5,7,12,12,14-hexamethyl-1,4,8,11-tetraazacyclotetradecane; L^9 = Tet B = *rac*-5,5,7,12,12,14-hexamethyl-1,4,8,11-tetraazacyclotetradecane; L^{10} = *meso*-5,12-dimethyl-1,4,8,11-tetraazacyclotetradecane; L^{11} = *meso*-5,12-dimethyl-*meso*-7,14-diphenyl-1,4,8,11-tetraazacyclotetradecane.

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Table I. Visible Absorption Spectra of Complexes $[ML]_{int}^{2+}$ and $[ML]^{2+}$ (M = Ni, Cu) in DMF (303 K; $c = 5 \times 10^{-3}$)

	λ_{max}, nm (ϵ_{max}, $M^{-1}\ cm^{-1}$)			
	$[NiL]_{int}^{2+}$	$[NiL]^{2+}$	$[CuL]_{int}^{2+}$	$[CuL]^{2+}$
L^6	425 (77), 550 (sh), 639 (135), 702 (180)	not det	549 (210)	not det
L^7	396 (21), 661 (5), 728 (sh)	396 (20), 668 (4), 728 (sh)	645 (246)	585 (249)
L^8	376 (10), 453 (68), 600 (sh)	459 (75)	638 (170)	520 (139)
L^9	367 (sh), 453 (70)	367 (14), 454 (58), 582 (5)	546 (140)	600 (131)
L^{10}	340 (10), 440 (47)	340 (9), 442 (36)	530 (103)	530 (112)
L^{11}	330 (28), 448 (29), 518 (sh)	330 (27), 448 (10), 518 (11)	546 (135)	539 (141)

Table II. Half-Neutralization Potentials (HNP), Relative pK_a Values of the Ligands L^6–L^{11} in DMF, and Second-Order Rate Constant k_1 for Reaction 1 with M = Ni and Cu

	L^1[a]	L^6	L^7	L^8	L^9	L^{10}	L^{11}
HNP(1), mV[b]	−181 ± 13	*c*	*c*	−210 ± 1.8	−246 ± 4.7	−183 ± 4	−145 ± 0.06
HNP(2), mV[b]	−75 ± 0.2	*c*	*c*	−63 ± 3.0	−86 ± 0.6	−66 ± 9	−21 ± 5.9
p$K_a(1)_r$	9.3 ± 0.2			9.8 ± 0.03	10.4 ± 0.08	9.3 ± 0.07	8.7 ± 0.001
p$K_a(2)_r$	7.5 ± 0.03			7.3 ± 0.05	7.7 ± 0.01	7.3 ± 0.15	6.6 ± 0.1

[a] Data for L^1 were taken from ref 1. [b] At 298 K. [c] Protonation not to be observed.

with the same set of ligands L. The background for the latter question is the expectation that, if the Eigen–Wilkins mechanism were operative, the ratio $k_1(Cu):k_1(Ni)$ should be of the same size for all ligands L and correspond to the ratio for solvent exchange.

Experimental Section

Ligands. Macrocycles L^6–L^{11} were prepared as described in the literature.[4]

The experimental details concerning solvent, metal salts, instrumentation, potentiometric titrations, and kinetic measurements were described.[1] Unless otherwise stated, the kinetic experiments were carried out under stoichiometric conditions ($[M^{2+}]_0 = [L]_0$) and the absorbance/time data fitted to eqs 5 and 7, respectively, given in ref 1. Complex formation was followed by monitoring the increase in absorbance at 435–455 nm (systems Ni^{2+}/L^7–L^{11}), 708–716 nm (system Ni^{2+}/L^6), 530–550 nm (systems Cu^{2+}/L^6, L^9–L^{11}), 587 nm (system Cu^{2+}/L^7), and 626–657 nm (system Cu^{2+}/L^8).

Results and Discussion

General Kinetic Results. The reaction of ligands L^6–L^{11} with Ni^{2+} ions in DMF was studied at 293–313 K, whereas in the case of Cu^{2+} ions the temperature had to be lowered to 218–263 K. Complex formation is biphasic for both nickel and copper. An initial fast reaction, leading to an intermediate $[ML]_{int}^{2+}$, is followed by a considerably slower reaction, which generates the spectrum of the product $[ML]^{2+}$. As an example, Figure 1 shows the spectral changes associated with the formation of the intermediate $[CuL^6]_{int}^{2+}$ at 218 K.

The absorbance/time data describing the initial reaction correspond to a second-order reaction (first-order in both $[M^{2+}]$ and [L]), whereas those describing the subsequent slow reaction fit a first-order reaction. As found for the ligands L^1–L^5 already,[1] complex formation with ligands L^6–L^{11} is thus adequately described by reactions 1 and 2 (M = Ni, Cu).

Visible Absorption Spectra of the Intermediates and Products. For both nickel and copper the formation of the intermediate species $[ML]_{int}^{2+}$ is fast compared to their rearrangement, so that the spectra of the intermediates are easily accessible (see Table I). Except for the two dibenzocyclam ligands L^6 and L^7, the characteristic absorptions of the species $[NiL^{8-11}]_{int}^{2+}$ and $[NiL^{8-11}]^{2+}$ are very similar to those found with the ligands L^1–L^5 previously.[1] Without repeating the detailed discussion presented earlier,[1] one is allowed to conclude, therefore, that in the complexes $[NiL^{8-11}]^{2+}$ as well as in the intermediates $[NiL^{8-11}]_{int}^{2+}$ the N_4 macrocycle is bound to the nickel in a square-planar fashion, with one or two additional DMF molecules being coordinated in axial positions. The relatively small changes in absorption associated with the slow reaction $[NiL]_{int}^{2+} \rightarrow [NiL]^{2+}$ (see Table I) are compatible with the interpretation[1] that this reaction is an isomerization step which does not change the donor atom arrangement around the nickel.

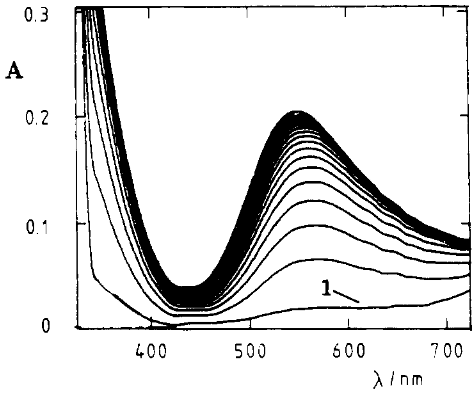

Figure 1. Formation of the intermediate $[CuL^6]_{int}^{2+}$ in DMF as monitored by multiscan stopped-flow spectrophotometry at 218 K ($[Cu^{2+}]_0 = [L^6]_0 = 2.7 \times 10^{-3}$ M; spectrum 1 taken after 10 ms; $\Delta t = 0.66$ s).

The visible spectra obtained for the nickel complexes with the ligands L^6 (=dibenzocyclam) and L^7 (=1,4,8,11-tetramethyldibenzocyclam) are somewhat different. It was shown by X-ray structure analysis[5] that in the complex $[NiL^7](NO_3)_2$ the macrocycle is folded, thus providing two cis positions for the coordination of a nitrate ion in a bidentate fashion. It could well be therefore that the somewhat exceptional spectra of complexes $[NiL^6]^{2+}$ and $[NiL^7]^{2+}$ (and of the corresponding intermediates) are due to cis-octahedral coordination in the sense that the nickel is coordinated by the folded macrocycle and two cis-oriented DMF molecules.

A qualitative analysis of the copper spectra obtained with the ligands L^6–L^{11} (see Table I) reveals the following: (i) both the intermediates $[CuL]_{int}^{2+}$ and the final products $[CuL]^{2+}$ show just one broad absorption; (ii) the absorptivities of corresponding intermediates and products differ not very much; (iii) the step intermediate → product is associated with either a small blue-shift (L^7, L^8), red-shift (L^9) or, for ligands L^{10} and L^{11}, no considerable shift in λ_{max} at all. Taking into account the results of X-ray structure analysis of complexes such as $[CuL^7](ClO_4)_2$[6] and $[CuL^8](ClO_4)_2$,[7] the interpretation of these spectroscopic findings is straightforward in the sense that they clearly point to more or less square-planar N_4Cu coordination in the products $[CuL^{6-11}]^{2+}$ as well as in the intermediates $[CuL^{6-11}]_{int}^{2+}$. One has to consider

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(4) (a) L^6: Hiller, H.; Dimroth, P.; Pfitzner, H. *Liebigs Ann. Chem.* **1968**, *717*, 137. (b) L^7: Borch, R. F.; Hassid, A. I. *J. Org. Chem.* **1972**, *37*, 1673. (c) L^8, L^9: Hay, R. W.; Lawrance, G. A.; Curtis, N. F. *J. Chem. Soc., Perkin Trans. 1* **1975**, 591. (d) L^{10}: Hay, R. W.; Piplani, D. P. *J. Chem. Soc., Dalton Trans.* **1977**, 1956. (e) L^{11}: Hideg, K.; Lloyd, D. *J. Chem. Soc. C* **1971**, 3441.

(5) Grewe, R.; Paulus, H.; Elias, H. *Z. Naturforsch.* **1984**, *39b*, 903.

(6) Klaehn, D.-D.; Paulus, H.; Grewe, R.; Elias, H. *Inorg. Chem.* **1984**, *23*, 483.

(7) Clay, R.; Murray-Rust, J.; Murray-Rust, P. *J. Chem. Soc., Dalton Trans.* **1979**, 1135.

additionally that, according to (3), coordination of a solvent

$$[CuL]^{2+} + DMF \rightleftharpoons [CuL(DMF)]^{2+} \quad K \qquad (3)$$

molecule and thus formation of five-coordinate copper is favored (K = 30.9 M^{-1} for L = L^5, for example[1]). Since the intermediate complexes $[CuL]_{int}^{2+}$ are also subject to this type of solvation, it becomes understandable as to why the reaction of the copper intermediates is associated with either a blue-shift, red-shift, or no considerable shift (L^{10}, L^{11}) at all.

In summary, the visible spectra of the species $[NiL^{6-11}]_{int}^{2+}$ and $[CuL^{6-11}]_{int}^{2+}$ indicate convincingly that the intermediates as well as the finally formed complexes $[NiL^{6-11}]^{2+}$ and $[CuL^{6-11}]^{2+}$ are of square-planar N_4M coordination geometry. The nickel species formed with the two dibenzo derivatives of cyclam, L^6 and L^7, are somewhat exceptional with the macrocyclic ligand being probably folded.

Relative pK_a Values. Table II summarizes the half-neutralization potentials and relative pK_a values[8] obtained for ligands L^6–L^{11}. Only two deprotonation steps are observed upon titration of DMF solutions of the ligands (acidified with F_3CSO_3H) with $[Bu_4N]OH$. p$K_a(1)_r$ characterizes the most basic nitrogen N(1) in L, and p$K_a(2)_r$, correspondingly the second-basic one, N(2).

Ligands L^6 and L^7 are obviously so little basic that they are not protonated by F_3CSO_3H in DMF at all. It is found, for L^8–L^{11}, that p$K_a(1)_r$ and p$K_a(2)_r$ differ by ca. 2.0 (L^{10}, L^{11}) or 2.5 (L^8, L^9) pK units. p$K_a(1)_r$ and p$K_a(2)_r$, respectively, are highest for L^9 and lowest for L^{11}. As to be expected, the stereoisomers L^8 (Tet A) and L^9 (Tet B) agree in both p$K_a(1)_r$ and p$K_a(2)_r$.

The general finding is therefore that C-methylation of cyclam does not affect the pK_a values substantially. As a matter of fact, the pK_a data obtained for L^1 = cyclam are rather close to those found for the C-methylated derivatives L^8–L^{10} (see Table II). C-phenylation as in ligand L^{11}, however, reduces both p$K_a(1)_r$ and p$K_a(2)_r$ by approximately one pK unit.

Kinetics of Complex Formation. Table III summarizes the kinetic parameters k_1, k_2, and $\Delta H^{\ddagger}/\Delta S^{\ddagger}$ (for the k_1 step) for both nickel and copper. Proof for the first step to be a second-order reaction and for the second step to be a first-order reaction comes from the fact that the A/t data can be well fitted to eqs 5 and 7, respectively, given in ref 1.

For M = Ni, rate constant k_1 covers a wide range from 1040 (L^{10}) to 0.057 M^{-1} s^{-1} (L^7). One can clearly see, however, that ligands L^6 and L^8–L^{11} form a group with k_1 lying in the rather narrow range 106 (L^6)–1040 (L^{10}) M^{-1} s^{-1}, whereas L^7, the tetra-N-methylated dibenzo derivative of cyclam, is an exceptionally slow reacting ligand. In the final isomerization step, however, this ligand is no longer an exception in the sense that $k_2(L^7)$ is rather close to $k_2(L^8–L^{11})$. The data for k_2 lie in the range 0.080 × 10^{-3} (L^9)–1.5 × 10^{-3} (L^{11}) s^{-1}.

The k_1 data obtained for M = Cu at reduced temperature (218 K) reflect the same pattern as observed for M = Ni. The reaction with ligand L^7 is extremely slow (k_1 = 0.0283 M^{-1} s^{-1} at 218 K), whereas ligands L^8–L^{11} form a group of much faster reacting ligands with k_1 ranging from 1.67 × 10^4 (L^{11}) to 14.4 × 10^4 M^{-1} s^{-1} (L^9). In contrast to the reaction with Ni^{2+} ions, dibenzocyclam (L^6) reacts with copper rather slowly (k_1 = 133 M^{-1} s^{-1}). Rate constant k_2 for the final step, determined at 303 K, lies in the rather narrow range 0.54 × 10^{-3} (L^{10})–83.7 × 10^{-3} (L^7) s^{-1} and is thus close to the corresponding data obtained for nickel (see Table III).

Mechanism of Intermediate Formation According to (1). Within the series of ligands L^1–L^{11}, cyclam = L^1 is the fastest reacting ligand. Its rate of intermediate formation with nickel is compatible with the classical I_d mechanism (rate control through solvent exchange).[1] On the basis of k_{ex} = 5.9 × 10^{-3} s^{-1} for solvent exchange in $[Ni(DMF)_6]^{2+}$ [9] and $k_1(L^1)$ = 7.9 × 10^3 M^{-1} s^{-1} (see Table III) one obtains $K_{os} \approx k_1/k_{ex}$ = 1.3 M^{-1}, which is of acceptable size for outer-sphere complex formation in an organic solvent such as DMF.[10]

Table III. Rate Constants and Activation Parameters for Complex Formation in DMF According to Reactions 1 and 2[a,b]

	L^1	L^2	L^3	L^4	L^5	L^6	L^7	L^8	L^9	L^{10}	L^{11}
					M = Ni[c]						
$10^{-2}k_1$ at 303 K, M^{-1} s^{-1}	79.0 ± 5.3	23.0 ± 2.5	12.6 ± 1.6	5.50 ± 0.07	0.610 ± 0.001	1.06 ± 0.07	0.000 57 ± 0.000 087[d]	1.96 ± 0.13	9.76 ± 0.28	10.4 ± 0.4	3.74 ± 0.27
10^3k_2 at 303 K, s^{-1}	256 ± 7	0.186 ± 0.001	0.90 ± 0.01	0.100 ± 0.003	0.580 ± 0.003	*e*	0.18 ± 0.01	0.30 ± 0.01	0.080 ± 0.001	0.41 ± 0.15	1.5 ± 0.7
$\Delta H^{\ddagger}$, kJ mol^{-1}	20 ± 2	77 ± 5	79 ± 7	63 ± 2	60 ± 6	65 ± 3	not det	83 ± 4	56 ± 3	57 ± 3	84 ± 15
$\Delta S^{\ddagger}$, J mol^{-1} K^{-1}	−105 ± 7	74 ± 16	75 ± 23	15 ± 8	−10 ± 18	8 ± 11	not det	73 ± 12	−2 ± 10	1 ± 10	85 ± 50
					M = Cu[a,f]						
$10^{-2}k_1$ at 218 K, M^{-1} s^{-1}	*g*	*g*	*g*	*g*	72.8 ± 2.1	1.33 ± 0.02	0.000 283 ± 0.000 000 6[h]	313 ± 98	1440 ± 44	478 ± 40	167 ± 47
10^3k_2 at 303 K, s^{-1}	not det	not det	not det	1.43 ± 0.02	5.40 ± 0.03	*e*	83.7 ± 0.1[i]	2.8 ± 1.9	3.4 ± 0.15	0.54 ± 0.06	7.87 ± 0.08
$\Delta H^{\ddagger}$, kJ mol^{-1}					15.0 ± 6.0	49 ± 1	45 ± 1	not det	not det	18 ± 8	20 ± 8
$\Delta S^{\ddagger}$, J mol^{-1} K^{-1}					−101 ± 28	25 ± 3	−65 ± 2	not det	not det	−67 ± 36	−68 ± 33

[a] The data for ligands L^1–L^5 were taken from ref 1. [b] The activation parameters, as determined from the temperature dependence of rate constant k_1, refer to reaction 1. [c] Experiments carried out at $[Ni^{2+}]_0$ = $[L]_0$ = 4 × 10^{-3} M at five–six temperatures in the range 293–313 K. [d] Determined under pseudo-first-order conditions at $[L^7]_0$ = 4 × 10^{-3} M and $[Ni^{2+}]_0$ = 4 × 10^{-2}–0.1 M. [e] Not determined because of slow oxidative decomposition of the complex in aerated solution. [f] Experiments carried out at $[Cu^{2+}]_0$ = $[L]_0$ = 3 × 10^{-3} M (L^6) or 4 × 10^{-4} (L^8–L^{11}) at five-six temperatures in the range 215–233 K (L^{10}, L^{11}) or 218–263 K (L^6). [g] Too fast for stopped-flow monitoring at 218 K. [h] Kinetic experiments carried out under pseudo-first-order conditions at $[L^7]_0$ = 4 × 10^{-3} M and $[Cu^{2+}]_0$ = 4 × 10^{-2} M in the range 308–253 K at six temperatures; k_1(Cu) = 0.0283 M^{-1} s^{-1} obtained by extrapolation to 218 K. [i] At 298 K.

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(8) Calculation of the relative pK_a values is described in ref 1.

(9) Matwiyoff, N. A. *Inorg. Chem.* **1972**, *11*, 1688.

Table IV. Comparison of Rate Constants Obtained for Corresponding Nickel and Copper Complexes

	$k_1(Cu):k_1(Ni)$ at 303 K[a]	$k_2(Cu):k_2(Ni)$ at 303 K[b]
L^5	1.7×10^3	9.3
L^6	3.4×10^3	
L^7	0.73×10^3	4.7×10^2[c]
L^8		9.3
L^9		43
L^{10}	1.0×10^3	1.3
L^{11}	1.4×10^3	5.2
MeOH[d]	2.2×10^4[d]	

[a] Data for $k_1(Ni)$ taken from Table III; data for $k_1(Cu)$ at 303 K calculated with the activation parameters listed in Table III. [b] Data for k_2 taken from Table III. [c] The number for $k_2(Cu)$ used to calculate this value refers to 298 K instead of 303 K. [d] Ratio $k_{ex}(Cu):k_{ex}(Ni)$ for methanol exchange.[12,13]

Rate constants k_1 obtained for intermediate formation of nickel with the C-alkylated cyclam derivatives L^6–L^{11} at 303 K are clearly smaller than k_1 obtained for cyclam (see Table III). The ratio $k_1(L^x):k_1(L^1) = \alpha(L^x)$ follows sequence (4), which means

$$\alpha(L^1):\alpha(L^6):\alpha(L^7):\alpha(L^8):\alpha(L^9):\alpha(L^{10}):\alpha(L^{11}) = 1:1.3 \times 10^{-2}:7.2 \times 10^{-6}:2.5 \times 10^{-2}:1.2 \times 10^{-1}:1.3 \times 10^{-1}:4.7 \times 10^{-2} \quad (4)$$

that the formation of the intermediates $[NiL^{6-11}]_{int}^{2+}$ is at least by a factor of 10–100 slower than expected on the basis of solvent loss being rate-controlling. The reaction with L^7 is extremely slow.

Qualitatively, the reactivity pattern found for the reaction of copper with L^6–L^{11} at 218 K is the same as found for nickel, in that $k_1(L^7) \ll k_1(L^6) < k_1(L^8) < k_1(L^9) > k_1(L^{10}) > k_1(L^{11})$ (see Table III). In line with this the activation parameters ΔH^* and ΔS^*, as available for both nickel and copper reacting with L^5, L^6, L^{10}, and L^{11}, add up to ΔG^* values (298 K) with a more or less constant difference $\Delta(\Delta G^*) = \Delta G^*(Ni,L^x) - \Delta G^*(Cu,L^x)$ of about 18–20 kJ mol^{-1}.

Rate constant k_{ex} for solvent exchange in $[Cu(DMF)_6]^{2+}$ is hitherto unknown, unfortunately. For methanol, both $k_{ex}(Cu)$ and $k_{ex}(Ni)$ were determined.[12,13] On the basis of the reported activation parameters[12] one arrives at $k_{ex}(Cu)/k_{ex}(Ni) = 2.2 \times 10^4$ for the relative rates of methanol exchange at 303 K. Assuming that this ratio is a reasonable lower limit[14] for DMF as well, one realizes that the experimentally obtained ratio $k_1(Cu):k_1(Ni)$ (see Table IV) is at least by a factor of 10 smaller.

The mechanism to be suggested for intermediate formation according to (1) has thus to rationalize the following experimental facts: (i) intermediate formation of nickel with ligands L^6–L^{11} is clearly slower than expected for DMF exchange in $[Ni(DMF)_6]^{2+}$ being rate-limiting; (ii) for a given ligand, the ratio $k_1(Cu):k_1(Ni)$ is smaller than the ratio $k_{ex}(Cu):k_{ex}(Ni)$ for DMF exchange. Both facts suggest the operation of a mechanism which involves metal-based processes as well as ligand-based processes.

Interestingly enough, the present results obtained with N_4 macrocycles are rather similar to those obtained with crown ethers and cryptands, reacting with alkali metal ions and alkaline earth metal ions in organic media.[16] It was found, for example, that complex formation of alkali metal cations with dibenzo-30-crown-10 in methanol was much slower than expected from solvent exchange rate constants.[16] This finding was rationalized by suggesting that conformational change in the ligand was involved in rate control. The experimental results obtained in complex formation studies with a variety of crown ethers (including biologically relevant ligands such as valinomycin) and rigid cryptands led to the so-called Eigen–Winkler mechanism[16–18] (an extension of the Eigen–Wilkins mechanism). This mechanism takes into account that both solvent substitution on the metal cation and ligand rearrangement may influence the energy profile of the overall complex formation process. Equation 5 shows schematically that, after pre-association, the formation of the first metal–ligand bond, associated with the loss of a solvent molecule in the first coordination sphere of the metal, leads to the species MC^{n+}. The formation of this species is not necessarily rate-controlling, since a conformational change in the partially bonded ligand C may be required before the product $\{MC^{n+}\}$ with the fully complexed metal is formed.

$$M^{n+} + C \rightleftharpoons M^{n+}\cdots C \rightleftharpoons MC^{n+} \rightleftharpoons \{MC^{n+}\} \quad (5)$$

The various steps shown in eq 5 and the experimental findings described in the preceding paper[1] can provide an explanation for the kinetic results obtained. If, as shown schematically by reactions 6–10 (charges omitted; M = Cu, Ni; S = solvent), the formation

$$MS_6 + L \rightleftharpoons MS_{6},L \quad K_{OS} \quad (6)$$

$$MS_{6},L \rightleftharpoons S_5M\text{–}(L) + S \quad K_b \quad (7)$$

$$S_5M\text{–}(L) \xrightleftharpoons{K_{con}} S_5M\text{–}(L^*) \;(\xrightleftharpoons{k_c(rds)})\; S_4M{=}(L) + S \quad (8)$$

$$S_4M{=}(L) \xrightarrow{fast} S_3M{\equiv}(L) \xrightarrow{fast} S_2ML + 2S \quad (9)$$

$$S_2ML \rightleftharpoons S + SML \rightleftharpoons 2S + ML\ (=[ML]_{int}) \quad (10)$$

of the second M–N bond (step 8) is rate-controlling,[1] the second-basic nitrogen N(2) has to get close enough to the metal. The macrocycle L in the species S_5M–(L), as bound to the metal by a single M–N(1) bond, is subject to conformational changes, and there is only an equilibrium concentration of properly oriented N(2) atoms in the form of the species S_5M–(L^*). Rate control through reaction 8 would then mean that the experimentally obtained rate constant k_1, according to (11), is a composite parameter with rate constant k_c supposed to be close to k_{ex}.

$$k_1 = K_{os}K_bK_{con}k_c \quad (11)$$

Reaction scheme (6)–(10) still implies that loss of solvent molecules from the primary solvation shell of the metal plays a key role in the process of intermediate formation. It implies in addition, however, that conformational changes in the ligand, necessary for the closure of the first chelate ring, can become rate-affecting. It should be pointed out that the formation of the third and fourth M–N bond according to (9) is assumed to be a fast, quasi-irreversible consecutive process. The species S_2ML, which is subject to desolvation according to (10), corresponds to the intermediate $[ML]_{int}^{2+}$ of the preceding discussion.

In the mechanism given by (6)–(9), equilibrium constant K_{con} is the critical parameter to explain the finding that $\alpha(L^1) > \alpha(L^{6-11})$ (see (4)). Increasing C-alkylation and/or N-methylation of cyclam obviously reduces the conformational flexibility of the ligand so much that, due to K_{con} being small, the formation of the second M–N bond according to (8) is not only controlled by the rate of solvent loss from the species S_5M–(L). Ligand L^7, the tetra-N-methylated derivative of dibenzocyclam, is an example

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(10) For the outer-sphere interaction of M^{2+} cations with neutral monodentate ligands in water, theoretical calculations[11] lead to $K_{os} = 0.15$ M^{-1}.

(11) Wilkins, R. G. *The Study of Kinetics and Mechanism of Reactions of Transition Metal Complexes*; Allyn and Bacon: Boston, MA, 1974; p 183.

(12) Helm, L.; Lincoln, S. F.; Merbach, A. E.; Zbinden, D. *Inorg. Chem.* **1986**, *25*, 2550.

(13) Luz, Z.; Meiboom, S. *J. Chem. Phys.* **1964**, *40*, 2686.

(14) It is found for divalent transition metal ions such as Mn^{2+}, Fe^{2+}, Co^{2+}, and Ni^{2+} that DMF exchange is faster than methanol exchange by an averaged factor of approximately 13.[15] The application of this factor to $k_{ex}(Cu) = 3.09 \times 10^7$ s^{-1} for methanol[13] would lead to $k_{ex}(Cu) \approx 3.9 \times 10^8$ s^{-1} for DMF and, hence, to the ratio $k_{ex}(Cu) \times k_{ex}(Ni) \approx 1 \times 10^5$ for DMF.

(15) Van Eldik, R., Ed. *Inorganic High Pressure Chemistry*; Elsevier: Amsterdam, 1986; p 87.

(16) An excellent summary on this topic is to be found in: Burgess, J. *Ions in Solution*; Ellis Horwood: Chichester, England, 1988; Chapter 10.5.

(17) Eigen, M.; Winkler, R. In *The Neurosciences*: *Second Study Program*; F. O. Schmitt, Ed.; Rockefeller University: New York, 1970.

(18) For the development and coining of the term "Eigen-Winkler mechanism" see: (a) Wallace, W.; Chen, C.; Eyring, E. M.; Petrucci, S. *J. Phys. Chem.* **1985**, *89*, 1357; (b) Petrucci, S.; Adamic, R. J.; Eyring, E. M. *J. Phys. Chem.* **1986**, *90*, 1677; (c) Eggers, F.; Funck, T.; Richmann, K. H.; Schneider, H.; Eyring, E. M.; Petrucci, S. *J. Phys. Chem.* **1987**, *91*, 1961.

for extremely reduced flexibility (K_{con} very small) and, correspondingly, low reactivity (k_1 very small). On the other hand, the nonsubstituted macrocycle cyclam = L^1 is so flexible that there is obviously no ligand-based rate retardation. This means that the k_1 data obtained for systems Ni^{2+}/L^{1-11} indeed suggest a changeover in mechanism for intermediate formation. The data obtained for L^1 are compatible with rate control through solvent loss according to (7) (Eigen–Wilkins mechanism). The data obtained for the less flexible ligands L^2–L^{11}, however, are more or less ligand-affected in the sense that intermediate formation is a concerted process, in which both solvent substitution and ligand rearrangement are important (Eigen–Winkler mechanism).

Reaction sequence (6)–(9) does not provide a simple explanation for the finding that $k_1(Cu)/k_1(Ni) < k_{ex}(Cu)/k_{ex}(Ni)$. Since K_{os} and K_{con} should be of practically equal size for both copper and nickel, one has to consider the ratio $K_b(Cu):K_b(Ni)$ as a critical parameter. Monodentate nitrogen ligands such as NH_3 coordinate copper better than nickel. Since K_b describes complex formation with L as monodentate ligand, one would expect therefore the ratio $K_b(Cu):K_b(Ni)$ to be >1 and not <1, as it would help to interpret the experimental findings. So, one is left with doubts concerning the basic assumption that the rate of DMF exchange in the species $S_5M-(L)$ corresponds to that in the fully solvated species MS_6. Looking, for example, at the rate constant k_{ex} for water exchange in the species $M(H_2O)_6^{2+}$, $M(H_2O)_5(NH_3)^{2+}$, and $M(H_2O)_5Cl^+$ for M = Ni and Co, one finds that the ratio $k_{ex}(Co):k_{ex}(Ni)$ is greater for the chloro species than for the other species.[19] This might be an indication for what is happening with the lability of the DMF molecules in the species $S_5Cu-(L)$ and $S_5Ni-(L)$ (see (7)). Additional arguments can come from the fact that the Cu^{2+} ion is a Jahn–Teller system. This might mean that solvent exchange on the Cu^{2+} ion is a rather complex matter per se. It would be of great interest therefore to have more experimental information on solvent lability in the species $[Cu(DMF)_6]^{2+}$.

Mechanism of Intermediate Rearrangement According to (2). The data obtained for first-order rate constant k_2, describing the slow reaction of the intermediates $[NiL^{7-11}]_{int}^{2+}$, are rather close to those obtained for the intermediates $[NiL^{1-5}]_{int}^{2+}$ (see Table III). For L^5 the experimental findings clearly prove[1] that the k_2 step corresponds to the isomerization process *RSRR* → *RSRS* via Ni–N bond inversion. It is thus reasonable to interpret the reactions $[NiL^{7-11}]_{int}^{2+} \rightarrow [NiL^{7-11}]^{2+}$ as also being rearrangement steps, in which Ni–N bond inversion converts the intermediates into the thermodynamically more stable products. The stereochemical details of these conversions have yet to be studied.

The first-order reaction of the copper intermediates $[CuL^{7-11}]_{int}^{2+}$ is also surprisingly slow (see Table III). As shown in Table IV, the ratio $k_2(Cu):k(Ni)$ for ligands L^8–L^{11} and L^5 is of the order of 1–10 only. Such a small dependence on the metal suggests strongly that the slow reactions of the copper intermediates $[CuL^{7-11}]_{int}^{2+}$, as in the case of the corresponding nickel intermediates, are also isomerization reactions involving Cu–N bond inversion.

For L^7 the ratio $k_2(Cu):k_2(Ni)$ is 470 and thus exceptionally high (see Table IV). This result is not quite unexpected. In the discussion of the visible absorption spectra it was pointed out that in the species $[NiL^7]_{int}^{2+}$ and $[NiL^7]^{2+}$ the ligand might be present in a folded form. If the ligand coordinates copper in a square-planar fashion and nickel in a folded form, the nature of the corresponding isomerization processes will be different.

Conclusions

The C-alkylated N_4 macrocycles L^6–L^{11} react with nickel(II) and copper(II) in DMF in a two-steo process (rate constants k_1 and k_2) according to (1) and (2). The first step (second-order reaction) leads to a thermodynamically unstable intermediate with square-planar N_4 coordination, which rearranges in the second step (first-order reaction) to form the stable complex $[ML]^{2+}$. The pattern of reactivity, as found for the various ligands in the first step, is rather similar for nickel and copper, although intermediate formation with copper is much faster than with nickel. The size of rate constant $k_1(Ni)$ is not compatible with a mechanistic interpretation according to the classical Eigen–Wilkins mechanism, i.e. with formation of the first Ni–N bond being rate-controlling. It is suggested that formation of the second Ni–N bond is controlling the rate of intermediate formation and that conformational changes in the rigid macrocycles L are rate-reducing. So, the mechanistic interpretation of the process of intermediate formation is rather close to the Eigen–Winkler mechanism, as developed for complex formation with crown ethers and cryptands. The ratio $k_1(Cu):k_1(Ni)$, which is found to be of the order of 10^3 at 303 K, is smaller than the estimated ratio $k_{ex}(Cu):k_{ex}(Ni)$ for DMF exchange. The rearrangement of the intermediates, a comparatively slow stereochemical isomerization process with half-lives in the minute range at 303 K, is rather little affected by N-alkylation or C-alkylation of L. The copper intermediates rearrange only slightly faster than their nickel analogues.

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[19] Burgess, J. *Metal Ions in Solution*; Ellis Horwood: Chichester, England, 1978; p 332.