4. Metal Complexes with Macrocyclic Ligands. XV[1]). The Complexation Kinetics of Open Chain and Cyclic Tetraazaligands with Ni^{2+} in DMSO and DMF

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Summary

The complexation kinetics of 2,6,9,13-tetraazatetradecane (**1**), 1,4,8,11-tetraazacyclotetradecane (**2**) and *N,N',N'',N'''*-tetramethyl-1,4,8,11-tetraazacyclotetradecane (**3**) with Ni^{2+} were studied by the stopped-flow technique in DMSO and DMF. The bimolecular rate constants k_L^{Ni} *(Table 2)* follow in both solvents the order **1**$\gtrsim$**2**>**3**. The similar complexation rates of **1** and **2** in their unprotonated form indicate that for both the open chain and the cyclic ligand the same mechanism holds. By comparison with the solvent exchange the rate determining step of the complexation is the dissociation of the first solvent molecule in the outer-sphere complex. The lower reactivity of **3** is probably due to steric effects.

In the case of **2** a second step in the complexation process was observed and explained by a rearrangement of the ligand already coordinated to the metal ion.

The complexation kinetics of cyclic tetraazaligands with Co^{2+}, Ni^{2+}, Cu^{2+} and Zn^{2+} have been studied in aqueous solution [2]. In the pH region accessible to such measurements generally LH^+, the monoprotonated form of the ligand, is the reactive species. Thus the bimolecular rate constants k_{LH}^M can be obtained. These are considerably smaller than one would expect from the water exchange rates of the corresponding metal ions and also smaller than the values obtained for monoprotonated tetraaza open chain ligands. Several reasons for it have been put forward: second bond formation as the rate determining step [3], steric effects [4], electrostatic repulsion [5] and conformational changes [2].

By contrast, the reactivity of non-protonated open chain and cyclic ligands does not seem to differ significantly. A study of the complexation of Cu^{2+} with polyamines in strongly alkaline solutions, where $Cu(OH)_3^-$ and $Cu(OH)_4^{2-}$ are the species present, shows similar rate constants for cyclic and open chain ligands [5]. The authors conclude that the rate determining step is, in both cases, the solvent exchange. Similarly the complex formation of Ni^{2+} with a series of N_4-macrocycles in CH_3CN [6] and that with two N_2O_2-donor macrocylces in methanol [7] is con-

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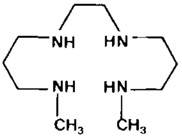
trolled by the rate of solvent exchange. To gain a deeper insight in this type of reactions we have studied the complex formation rates of the three ligands **1**, **2** and **3** with Ni^{2+} in DMSO and DMF.



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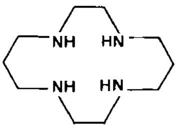

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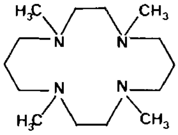

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Experimental Part. - Melting points are not corrected. NMR.-spectra were run on a *VARIAN EM 360* spectrometer with TMS or 3-(Trimethylsilyl)-propanesulfonate as internal standard. The synthesis of 1,4,8,11-tetraazacyclotetradecane [8] and *N,N′,N″,N‴*-tetramethyl-1,4,8,11-tetraazacyclotetradecane [9] was performed according to the literature.

N,N′,N″,N‴-*Tetratosyl-2,6,9,13-tetraazatetradecane* (**4**). To a solution of 3.0 g (0.13 mol) sodium in 600 ml abs. MeOH 47.5 g (0.06 mol) *N,N′,N″,N‴*-tetratosyl-1,5,8,12-tetraazadodecane [10] were added and the mixture heated until the compound was dissolved. The solvent was evaporated and the disodium salt was then treated twice with 50 ml abs. benzene, which was distilled off. The dry product was dissolved in 700 ml abs. DMF, heated to 120° and reacted with 28.4 g (0.20 mol) CH_3I in 200 ml DMF, which were added during in 1 h. The mixture was kept for 4 h at 120°, then the solvent was taken off on a rotary evaporator. The residue was cristallized from $CHCl_3$/EtOH giving 22.5 g (46%) **4**, m.p. 125-128°. - ^{1}H-NMR. ($CDCl_3$): 1.83 (*m*, 4 H, 2 $CH_2-CH_2-CH_2$); 2.41 (*s*, 12 H, 4 $H_3C-Ar.$); 2.67 (*s*, 6 H, 2 H_3C-N); 3.0 (*m*, 12 H, 6 H_2C-N); 7.2-7.8 (*m*, 16 H, arom. H).

2,6,9,13-Tetraazatetradecane-tetrahydrobromide (**5**). A suspension of 5.0 g (6.1 mmol) **4** in 45 ml 33% HBr-solution in glacial acetic acid and 4.7 g (49 mmol) phenol was treated for 20 h at 60°. The clear solution was cooled and 2.5 g (78%) **5** were obtained. Recristallisation from MeOH/H_2O/ether gave 2.2 g **5**, m.p. 269-271°. - ^{1}H-NMR. (D_2O): 2.10 (*qi*, 4 H, 2 $CH_2-CH_2-CH_2$); 2.69 (*s*, 6 H, 2 H_3C-N); 3.3-3.5 (*m*, 12 H, 6 H_2C-N).

$C_{10}H_{30}Br_4N_4$	Calc.	C 22.83	H 5.75	Br 60.76	N 10.65%
(525.99)	Found	„ 22.88	„ 5.55	„ 60.47	„ 10.54%

The free base **1** was obtained by dissolving the tetrahydrobromide **5** in water and running the solution over *Dowex*-1 in its OH^--form. The eluate was evaporated and the remaining solid was dried at 0.08 Torr for 2 h. $Ni(ClO_4)_2 \cdot 6\,H_2O$ *(p.a. Fluka)* was recristallized from water and dehydrated to $Ni(ClO_4)_2 \cdot H_2O$ by heating the hexasolvate to 75-90° at 0.5 Torr over P_2O_5 [11]. DMSO and DMF *(Merck, Uvasol)* were dried over CaH_2 and distilled under N_2 at 0.15 Torr before use.

Kinetics. - Solutions of $Ni(ClO_4)_2 \cdot H_2O$ and of the ligands were prepared in a dry box under N_2 and transferred to the stopped-flow syringes without coming in contact to moist air. The effective Ni^{2+}-concentration was determined by complexometry with murexide as indicator [12]. The measurements were run on a *Canterbury SF-3A* (1 cm cuvette) stopped-flow spectrometer, which was interfaced through a *Datalab DL 901* transient recorder to a *Hewlett-Packard* top desk computer HP 9820 [13]. The wave-lenghts are given in nm, the ε-values in $M^{-1}\,cm^{-1}$.

The complexation reaction of **1**, **2** and **3** were followed at 356 ($\varepsilon = 21$), 450 ($\varepsilon = 20$) and 503 ($\varepsilon = 87$) in DMF and at 365 ($\varepsilon = 24$), 450 ($\varepsilon = 33$) and 503 ($\varepsilon = 132$) in DMSO, respectively. Typical concentrations were $2 \cdot 10^{-4} - 10^{-3}$ M ligand and $8 \cdot 10^{-3} - 2.5 \cdot 10^{-2}$ M Ni^{2+}. The Ni^{2+}-concentration always was in an at least 10-fold excess in order to have pseudo-first order reactions.

The temperature dependences were measured between 5° and 35° in DMF and between 15° and 35° in DMSO.

Results. - The kinetics of complex formation between **3** and Ni^{2+} in DMF and DMSO are bimolecular processes, which can be described by the equ. (1). The rate constants, determined under pseudo-first order condition using an excess of

$$v_f = k_L^{Ni}[Ni^{2+}] \cdot [L] \qquad (1)$$

Ni^{2+}, have been converted to second order rate constants *(Table 1)*.

Table 1. *Experimental conditions and rate constants for the complexation of* **2** *and* **3** *with* Ni^{2+} *in DMSO and DMF*

	Ligand **2**					Ligand **3**			
	$[Ni^{2+}]$ $\times 10^2$	[L] $\times 10^3$	T (°C)	$k^{L}_{Ni}(M^{-1}s^{-1})$ $\times 10^3$ [a]	$k_{int}(s^{-1})$[a]	$[Ni^{2+}]$ $\times 10^2$	[L] $\times 10^3$	T (°C)	$k^{L}_{Ni}(M^{-1}s^{-1})$ [a]
DMSO	2.0	0.3	25.0	1.58	2.45	2.0	1.0	25.0	5.18
	1.5	0.3	25.0	1.63	2.35	1.5	1.0	25.0	5.60
	1.0	0.3	25.0	1.66	2.36	1.0	1.0	25.0	5.36
	0.8	0.4	14.8	0.84		2.5	0.88	14.8	1.54
	0.8	0.4	20.0	0.98		2.5	0.88	20.0	3.33
	0.8	0.4	25.2	1.61		2.5	0.88	25.2	5.02
	0.8	0.4	30.4	2.52		2.5	0.88	30.4	7.80
	0.8	0.4	34.4	2.78		2.5	0.88	34.4	12.80
DMF	2.0	0.2	25.0	1.85	0.33	2.0	1.0	25.0	79.4
	1.5	0.2	25.0	1.71	0.34	1.5	1.0	25.0	80.3
	1.0	0.2	25.0	1.86	0.30	1.0	1.0	25.0	81.1
	0.87	0.2	5.2	0.84		2.5	0.9	9.7	27.2
	0.87	0.2	15.8	1.48		2.5	0.9	14.8	41.3
	0.87	0.2	20.2	1.75		2.5	0.9	20.7	62.0
	0.87	0.2	26.2	1.95		2.5	0.9	27.8	99.3
	0.87	0.2	32.5	2.89		2.5	0.9	30.4	112

[a] Mean values of 3 to 5 measurements.

To fit the experimental curve of the reaction between **2** and Ni^{2+} in DMF and DMSO two exponentials were necessary. This was achieved by a non-linear last square fit using the *Newton-Gauss-Marquardt* algorithm [14]. The faster reaction is $[Ni^{2+}]$-dependent and can also be described by equ. (1) whereas the second, slower process is independent of $[Ni^{2+}]$ (see *Table 1*). The whole complexation process was therefore interpreted by two consecutive steps. First an intermediate $(NiL^{2+})_{int}$ is formed which then converts to the thermodynamically more stable product (see equ. 2).

$$Ni^{2+} + L \xrightarrow{k^{Ni}_{L}} (NiL^{2+})_{int} \xrightarrow{k_{int}} NiL^{2+}. \qquad (2)$$

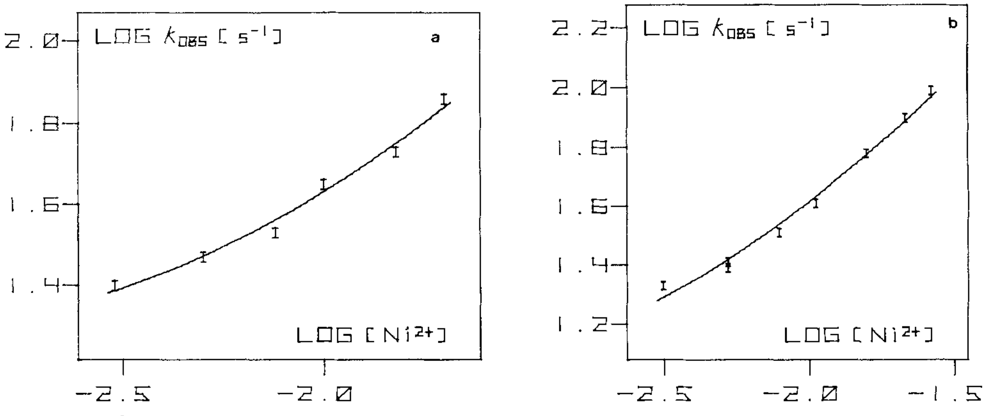

Figure. *$[Ni^{2+}]$-Dependence of the observed rate constant* k_{obs} *for the complexation with* **1** *in DMSO (a) and DMF (b).* The curves were calculated with $k_{obs} = k^{Ni}_{L}[Ni^{2+}] + k_{NiL}$ and the values given in *Table 2*.

In the case of the open chain ligand **1** the pseudo-first order rate constants were not linearly dependent on $[Ni^{2+}]$ (*Fig. 1a* and *1b*) indicating that under our experimental conditions the dissociation also was involved. In this case $k_{obs}=k_L^{Ni}[Ni^{2+}]+k_{NiL}$ [15]. By fitting the experimental points of *Figures 1a* and *1b* both k_L^{Ni} and k_{NiL} can be obtained *(Table 2)*.

In a few cases the effect of water added to abs. DMF and DMSO was checked. Up to 10 M water there was only a 10% change in the rate constants.

The temperature dependence of k_L^{Ni} was also investigated and the activation parameters $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ were calculated as usual. The results are given in *Table 2* together with the mean values of the rate constants.

Table 2. *Rate constants and activation parameters for the complexation of* **1**, **2** *and* **3** *with* Ni^{2+} *in DMSO and DMF at 25°*

Solvent	Ligand	k_{NiL}^{L} ($M^{-1}s^{-1}$)	$\Delta E^{\ddagger}$ ($kJ\,mol^{-1}$)	$\Delta S^{\ddagger}$ ($JK^{-1}mol^{-1}$)	k_{NiL} or k_{int} (s^{-1})
DMSO	**1**	$(2.6\pm0.2)\cdot10^3$	-	-	16.5 ± 1.5
	2	$(1.6\pm0.1)\cdot10^3$	47 ± 5	-25 ± 17	2.3 ± 0.2
	3	5.2 ± 0.1	73 ± 5	13 ± 13	-
DMF	**1**	$(3.2\pm0.2)\cdot10^3$	-	-	9.5 ± 1.2
	2	$(1.8\pm0.1)\cdot10^3$	28 ± 2	-87 ± 9	0.32 ± 0.01
	3	80 ± 3	46 ± 1	-53 ± 5	-

Discussion. - In the present study we have measured the complexation of **1**, **2** and **3** with Ni^{2+} to compare their reactivities and investigate whether the same step is rate determining for the cyclic and open chain ligands.

It is generally assumed that substitution reactions in non-aqueous solvents follow the dissociative model proposed for the complexation of divalent metal ions in water [16]. Thus the solvent exchange rate k_{sol} and the stability of the outer-sphere complex K_{os} govern the reactivity and $k_{obs}=K_{os}\cdot k_{sol}$. The rate constants of the complexation of **1** and **2** in DMSO and DMF are similar to each other and assuming $K_{os}=0.1-0.5\,M^{-1}$ also comparable to the solvent exchange rates ($k_{DMSO}^{Ni}=3.2-9.3\cdot10^3\,s^{-1}$, $k_{DMF}^{Ni}=3.8-7.7\cdot10^3\,s^{-1}$ [17]). Thus for the metal complex formation with **1** and **2** the same step, the substitution of the first solvent molecule, is rate determining.

Ligand **3** is less reactive with Ni^{2+} in both solvents, its rates of complexation being 20-250 times lower than those of **2**. The methyl groups attached to the N-atoms sterically inhibit to a large degree the reaction. This is expected from the results of *Rorabacher et al.* [4], who in a series of *N*-alkylated open-chain amines have observed a strong influence of the degree of alkylation at the *N*-atoms on the complexation rates.

Beside the bimolecular complexation **2** additionally shows a second step in DMSO and DMF. We interpret this by postulating an intermediate with an absorption spectrum similar to that of the end product but a lower molar absorptivity. We do not think that the second process can be second or even third bond formation, since the intermediate already exhibits square planar coordination geometry which for Ni^{2+} is only attained in a rather strong ligand field of four *N*-atoms [18]. The second reaction can, however, be explained by a rearrangement of the ligand already coordinated to the Ni^{2+}-ion. The first complex $(NiL^{2+})_{int}$ (2) is not the thermodynamically most stable form and probably isomerizes through *N*-inversion to a more stable product or a mixture of isomers. Similar reactions have been observed in MeOH for the complexation with a N_2O_2-macrocycle [7] and in CH_3CN for a series of tetraaza-ligands [6].

The results obtained by *Hay et al.* [6] in CH_3CN and those of this paper in DMSO and DMF clearly show that there is no difference in reactivity between the cyclic and the open chain tetraazaligands: the first ones are flexible enough so that first bond formation is the rate determining step of the complexation as for the latter. This is in contrast to the observation that in water, where the monoprotonated forms are the reactive species, cyclic and open chain ligands significantly differ in their complexation rates [2].

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