161. Metal Complexes with Macrocyclic Ligands

Part XXXIV[1])

Geometrical and Conformational Changes during the On/Off Reaction of the Side Chain in the Cu^{II} Complex of 11-(3-Aminopropyl)-1,4,7,11-tetraazacyclotetradecane

by **André Schiegg**, **Andreas Riesen**, and **Thomas A. Kaden***

Institut für Anorganische Chemie, Universität Basel, Spitalstr. 51, CH–4056 Basel

(30.VIII.91)

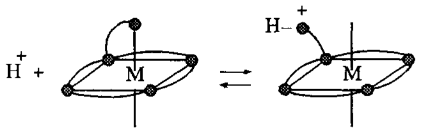
Solution studies of the Cu^{2+} complex with 11-(3-aminopropyl)-1,4,7,11-tetraazacyclotetradecane (L) indicate that, depending on the pH and on the age of the solution, different species are present. Dissolving the solid $[CuL](ClO_4)_2$ in slightly acidic solution gives the protonated complex **AH**, characterized by an absorption maximum at 574 nm, by a relatively fast proton-induced dissociation kinetics and by the typical colour change in basic solution to give the deprotonated form **A** with coordinated side chain. **AH** slowly interconverts in acidic solution to a new species **BH**, which has an absorption maximum at 547 nm, and which is kinetically more stable against acid dissociation and shows no coordination of the amino group of the side chain. In alkaline solution, however, the deprotonated form **B** delivers **A** in a base induced reaction. The X-ray diffraction studies of **A** and **BH** allow to determine the geometry of the metal ion and the configuration of the macrocycle. In **A**, the Cu^{2+} is pentacoordinated by the five N-atoms of the ligand and the macrocycle is in the *RRSR* configuration, whereas in **BH** the Cu^{2+} is octahedrally coordinated by the four N-atoms of the macrocycle and two axial perchlorate O-atoms with the macrocycle in the *RRRS* configuration. The amino group of the side chain is protonated and not coordinated. Thus, the on/off equilibrium of the side chain not only changes the geometry of the metal ion, as is generally found, but also alters the macrocyclic moiety.

Introduction. – When we discovered the on/off reaction (*1*) of mono-*N*-functionalized macrocycles having a ligating group in their side chain, we discussed the fact, that the additional donor group changes the geometry of the metal ion and thus its chemical and physical properties [2]. At that time we supposed that this would not alter the basic structure of the metal/macrocycle moiety, since tetraazamacrocyclic complexes are in general kinetically stable, whereas the side-chain donor group forms a kinetically labile bond. In the meantime, a large number of such reactions have been described, and in several cases the structure of the metal complex with the coordinated side chain and that of the parent compound with no side chain are known [3]. Smaller deviations between these structures have been observed and discussed [4]. Probably the structural changes are mainly due to the fact that, when the donor group becomes cooordinated, the side chain sterically interacts with the macrocyclic backbone and partially modifies its structure.

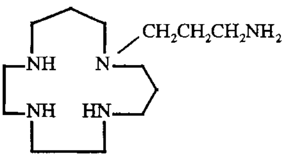
Studying a tetraazamacrocycle of this type (L), which carries a 3-aminopropyl side chain, we have observed for the first time that the on/off *Equilibrium 1* can have drastic

---

[1]) Part XXXIII: [1].



(1)



L

consequences not only for the metal-ion geometry, but also for the configuration of the macrocyclic ring.

Experimental. – *X-Ray Diffraction.* The complex $[CuL](ClO_4)_2$ (**A**) was prepared as described in [1]. Recrystallization from MeOH gave crystals suitable for the diffraction study.

The protonated form **BH** was obtained, when a soln. of $[CuL](ClO_4)_2$ (2.0 g) in 30 ml of H_2O adjusted to pH 2 with $HClO_4$ and treated with an excess of $NaClO_4$ was slowly evaporated over $CaCl_2$ in a desiccator. Thereby, two sorts of crystals were obtained: *a*) light-violet needles of composition $[Cu(LH)](ClO_4)_3 \cdot 3\ H_2O$, orthorhombic, $P2_12_12_1$ with $a = 7.485(4)$, $b = 9.837(2)$, and $c = 35.841(7)$ Å. This structure was partially solved, but due to disorder did not give an acceptable R value; *b*) dark-violet prisms of composition $[Cu(LH)](ClO_4)_3 \cdot NaClO_4$ (**BH**), the structure of which will be discussed below.

The crystal data and parameters of the data collection for the two complexes **A** and **BH** are given in *Table 1*. Unit cell parameters were determined by accurate centering of 25 independent strong reflections by the least-squares method. Four standard reflections monitored every h during data collection showed no significant variation of the intensity. The raw data set was corrected for polarization effects, but no correction for absorbance was applied. The structures were solved by *Patterson* techniques using the program SHELXS-86 [5]. Anisotropic least-squares refinements were carried out on all non-H-atoms. H-Atoms are in calculated positions with C–H distance of 1.08 Å and fixed isotropic thermal parameters. Scattering factors are from *Cromer* and *Mann* [6] or given in the SHELX-76 program [5]. Fractional coordinates are deposited at the *Cambridge Crystallographic Data Centre.*

pH Titrations were performed with the automatic titrator unit described in [7]. Solns. of $2.5 \cdot 10^{-3}$ M complex **AH** or **BH** or a mixture of both in 0.5M KNO_3 were titrated with 0.4M NaOH under N_2 at 25.0°. The curve fitting and the determination of the log K_H values was accomplished with the program TITFIT [8].

Spectra were measured on a *Cary 118C* spectrophotometer in 1-cm thermostatted cells at 25°. The dissociation kinetics of the protonated complexes **AH** and **BH** were followed with a *Techtron 635* spectrophotometer equipped with a mixing device, which allows to inject the two reactants directly into a 1-cm flow-cell. Solns. of 10^{-3} M Cu^{2+} complex and HNO_3 of different concentration (0.005–1M), both adjusted to $I = 0.5$M with KNO_3, were reacted and the dissociation kinetics were followed at 575 nm. Spectrophotometric measurements were also used to follow the kinetics of the interconversion **B** to **A** of the two basic forms as a function of $[OH^-]$, which was varied between 0.05 and 0.5M using NaOH and KNO_3 to adjust $I = 0.5$M. The pseudo-first-order ($[OH^-]$ = const.) rate constant were calculated with the program SANYO [9].

Results and Discussion. – In general, functionalized macrocycles give complexes, which, depending on the pH of the solution, have a deprotonated coordinated side chain, or a protonated noncoordinated one (*1*). This structural change is accompanied by a shift of λ_{max} from that of the MN_4 chromophore given by the metal/tetraazamacrocycle unit to

Table 1. *Crystal Data and Parameter of Data Collection for [CuL](ClO_4)$_2$* (**A**) *and [CuLH](ClO_4)$_3$ · $NaClO_4$* (**BH**)

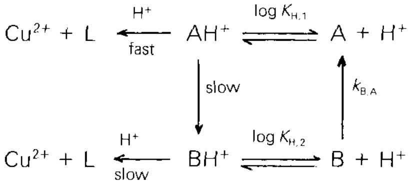
	Compound	
	A	**BH**
Formula	$C_{13}H_{31}Cl_2CuN_5O_8$	$C_{13}H_{32}Cl_4CuN_5NaO_{16}$
Crystal system	orthorhombic	triclinic
Space group	$P2_1an$	$P\bar{1}$
a [Å]	9.400(5)	9.130(1)
b [Å]	15.200(2)	14.751(4)
c [Å]	15.376(1)	13.372(3)
α [deg]	90	88.10(2)
β [deg]	90	106.14(1)
γ [deg]	90	126.99(2)
Z; V [Å^3]	4; 2196.9	2; 1360.6
Θ_{max} [deg]	25	27
Radiation	MoK_α	MoK_α
Scan type	$\omega/2\Theta$	$\omega/2\Theta$
Collected reflections	$+h, +k, +l$	$\pm h, \pm k, +l$
μ [cm^{-1}]	12.16	12.11
F(000)	1084	756
No. of indep. refl.	2229	5919
No. of refl. in refin.	1398	4148
No. of variables	263	376
Observations/variables	5.3	11.0
Largest peak of ΔF [e/Å^3]	0.44	0.73
Final R	0.053	0.052
Final R_w	0.055	0.059
Weighting scheme	$1.29/[\sigma^2 + 1.45 \cdot 10^{-3}F^2]$	$0.82/[\sigma^2 + 1.46 \cdot 10^{-3}F^2]$

that of MN_4X, X being the donor group of the side chain [3]. Thus, these reactions can easily be followed by spectrophotometric titrations, from which the spectra of the two forms and the protonation constant log K_H, describing *Equilibrium 1* can be obtained.

In the case of the Cu^{2+} complex with L, the situation is more complicated. Depending on the pH and on the age of the solution, four species instead of only two can be observed. Two of them are protonated forms (**AH**, **BH**), the other two deprotonated ones (**A**, **B**), thus giving two acid-base equilibria with two different log K_H values (see the *Scheme*).

If one dissolves the solid [CuL](ClO_4)$_2$ (**A**) in a slightly acidic solution, one finds for the protonated form **AH** an absorption maximum at 574 nm (*Fig. 1*). This species shows the typical colour change, when the pH is increased above 6. The observed log $K_{H,1}$ = 6.17 and the shift of λ_{max} to 733 nm with a shoulder at 618 nm are in complete agreement with

Scheme. *Equilibria and Reactivity of the Two Isomers* **AH**/**A** *and* **BH**/**B**



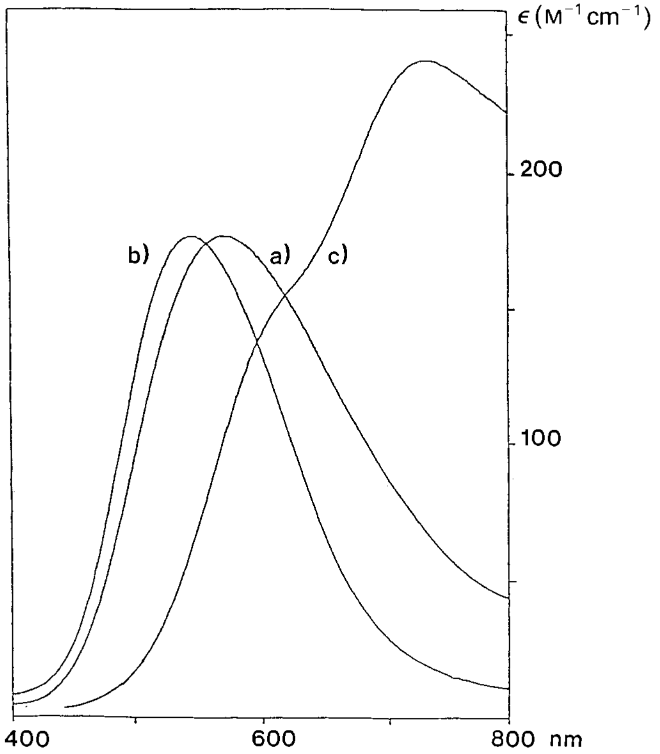


Fig. 1. *Spectra of the Cu*$^{2+}$ *complexes with L* a) *in fresh acidic solution* (**AH**), b) *in old acidic solution* (**BH**), *and* c) *alkaline solution* (**A**)

the on/off equilibrium, in which the amino group of the side chain binds axially to the Cu^{2+} [1]. Similarly, the potentiometric titration of **AH** gives log $K_{H,1}$ = 6.15(2) in good accordance with the spectrophotometric value.

If a slightly acidic solution of **AH** is left at room temperature for 1 to 2 weeks, a shift of the absorption maximum from 574 nm to 547 nm is observed. The new species **BH** shows properties, which are distinctly different from those of **AH**. So, **BH** is kinetocally much more stable against H$^+$ than **AH** (*Fig. 2*). Fresh solutions containing **AH** dissociate at pH < 1 to Cu^{2+} and the protonated macrocycle, whereas old solutions containing **BH** only slowly react at this pH. In addition, when a solution of **BH** is titrated with base to study the on/off equilibrium, no colour change is observed spectrophotometrically, although the potentiometric titration gives log $K_{H,2}$ = 9.55(2). We, thus, infer that in **BH** the ammonium proton of the side chain can indeed be titrated, but that the resulting amino group is not able to coordinate to the Cu^{2+} ion.

If one waits for a certain time δt at the end of the potentiometric titration of **BH** at pH 11 before adding 1 equiv. of acid in order to titrate the complex again, one observes that different amounts of the two forms **AH** and **BH** are present in solution, which can be distinguished by their log K_H values (*Fig. 3*). For δt = 10, 30, and 130 min, the amount of **AH** was found to be 34, 56, and 86%, respectively.

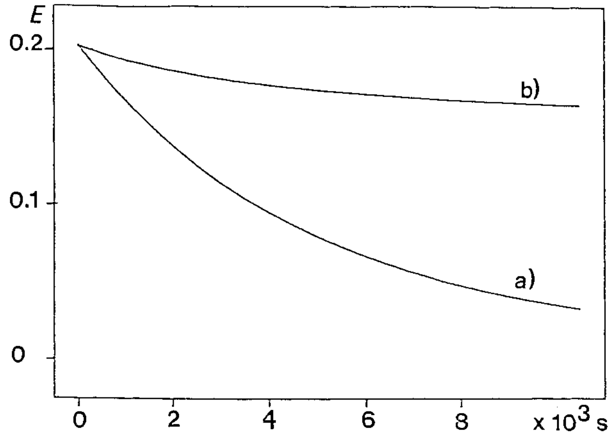


Fig. 2. *Dissociation kinetics of the two isomers* **AH** (a) *and* **BH** (b) *at pH = 0.33, at I = 0.5* M *(KNO$_3$) and 25.0°*

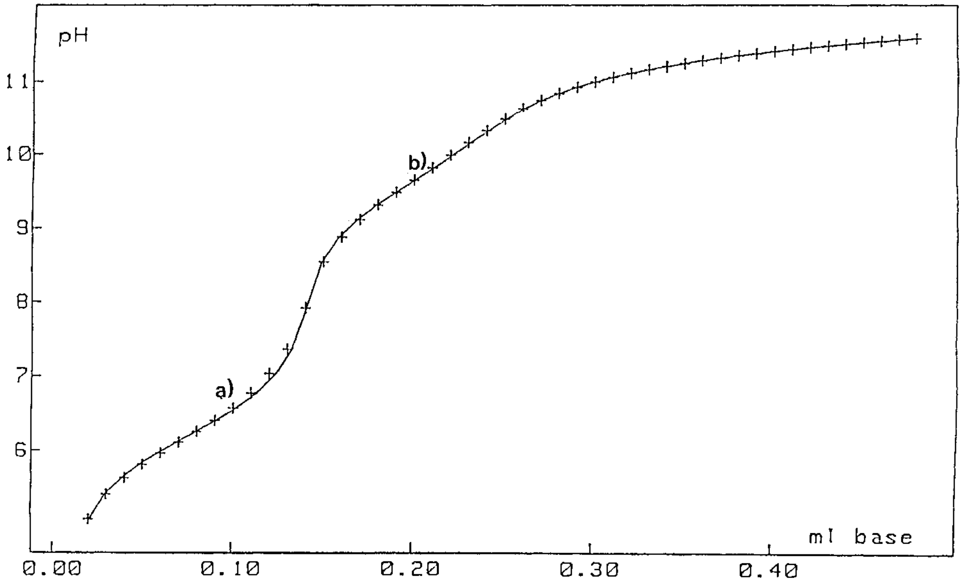


Fig. 3. *Titration of a mixture of the two forms* **AH** *and* **BH** *of the Cu^{2+} complex with L.* The curve was calculated assuming 56% **AH** and 44% **BH** and using the log K_H values of 6.17 and 9.55 for the two species, respectively.

Interesting is also the observation that in alkaline solution **B** slowly interconverts to **A** in a base-dependent reaction, which follows the rate law (*2*) with $k_{B,A} = 6.8 \cdot 10^{-2}\ \text{M}^{-1}\text{s}^{-1}$ at 25°. This base-induced reaction is typical for a *N*-isomerisation through a conjugate base mechanism [10].

$$v_{B,A} = k_{B,A} \cdot [B] \cdot [OH^-] \qquad (2)$$

From this, we infer that the pairs **AH**/**A** and **BH**/**B** must be isomers, which differ from each other by their *N*-configuration. **BH** is the most stable form at low pH, whereas **A** is preferentially formed at high pH. So, a configurational change takes place from acidic solutions containing **BH** to alkaline ones with **A**, the driving force being the additional energy of the new Cu–N bond formed with the amino group of the side chain.

To understand this from a structural point of view, we shall now discuss the X-ray diffraction results of **A** and **BH**. In **A**, the amino group of the side chain is bound to the Cu^{2+}, thus giving a pentacoordinate arrangement. The geometry can be described either as a distorted trigonal bipyramid or a distorted square pyramid (*Fig. 4*), in which all of the five N-atoms of the ligand are bound.

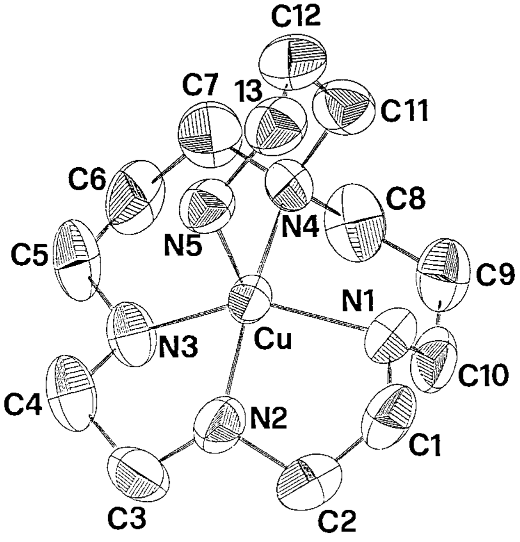


Fig. 4. *Structure and atom numbering of the* Cu^{2+} *complex* **A**

Whereas the N(2)–Cu–N(4) bond is nearly linear (171°), as one would expect for a trigonal bipyramid, the angles in the equatorial plane are very different from the ideal value of 120°, the N(1)–Cu–N(3) being larger (143°), and the other two N(3)–Cu–N(5) and N(5)–Cu–N(1) being smaller (107° and 110°, respectively). The metal–N bonds are 2.04–2.08 Å for the macrocycle, whereas that to the side-chain amino groups is somewhat longer with 2.14 Å (*Table 2*).

Table 2. *Selected Bond Lengths* [Å] *and Angles* [°] *for* $[CuL](ClO_4)_2$ (**A**)

Cu–N(1)	2.041(10)	N(1)–Cu–N(3)	142.9(4)
Cu–N(2)	2.043(10)	N(2)–Cu–N(4)	170.8(4)
Cu–N(3)	2.083(10)	N(5)–Cu–N(1)	109.5(4)
Cu–N(4)	2.053(9)	N(5)–Cu–N(2)	95.4(4)
Cu–N(5)	2.136(9)	N(5)–Cu–N(3)	106.6(4)
		N(5)–Cu–N(4)	93.7(4)

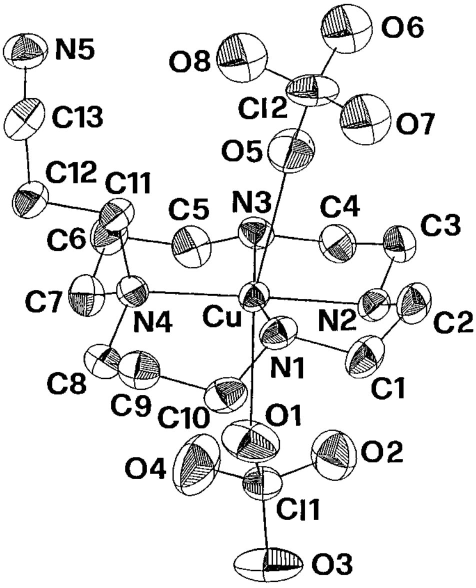


Fig. 5. *Structure and atom numbering of the Cu^{2+} complex* **BH**

The X-ray structure of **BH**, the thermodynamically stable form in acidic solution, shows a Cu^{2+} ion in a distorted octahedral environment, coordinated by the four N-atoms of the macrocycle and two ClO_4^- ions. The amino group of the side chain is protonated and not involved in coordination (*Fig. 5*). The calculated best plane through the four N-atoms gives deviations of ±0.14 to ±0.17 Å for the N-atoms and the Cu^{2+} is displaced from it by 0.12 Å towards O(1). The macrocycle is folded along the N(2)–Cu–N(4) axis, the angles N(2)–Cu–N(4) and N(1)–Cu–N(3) being 178° and 161°, respectively. The equatorial Cu–N bonds are 2.01–2.04 Å, and the axial Cu–O bonds are 2.53 and 2.67 Å (*Table 3*).

A comparison between the two structures of **A** and **BH** shows that the binding of the side chain amino group not only modifies the coordination geometry of the metal ion, but also involves a configurational rearrangement of the macrocycle. Both in **A** and in **BH**, the macrocycle is in the *trans-II*-configuration [11]. However, following the numbering of the N-atoms the sequence is *RRSR* for **A** and *RRRS* for **BH** (*Fig. 6*). The latter configuration, observed in the low-spin Ni^{2+} complex of the parent compound 1,4,7,11-tetraazacyclotetradecane [12] and in the binuclear Ni^{2+} complexes, in which the two macrocyclic

Table 3. *Selected Bond Lengths* [Å] *and Angles* [°] *for* $[CuLH](ClO_4)_3 \cdot NaClO_4$ (**BH**)

Cu–N(1)	2.038(4)	N(1)–Cu–N(3)	161.4(2)	O(1)–Cu–N(4)	93.2(2)
Cu–N(2)	2.008(4)	N(2)–Cu–N(4)	178.3(2)	O(5)–Cu–N(1)	78.0(2)
Cu–N(3)	2.039(4)	O(1)–Cu–O(5)	167.3(2)	O(5)–Cu–N(2)	83.2(2)
Cu–N(4)	2.042(4)	O(1)–Cu–N(1)	106.0(2)	O(5)–Cu–N(3)	85.6(2)
Cu–O(1)	2.528(4)	O(1)–Cu–N(2)	85.1(2)	O(5)–Cu–N(4)	98.4(2)
Cu–O(5)	2.673(4)	O(1)–Cu–N(3)	88.2(2)		

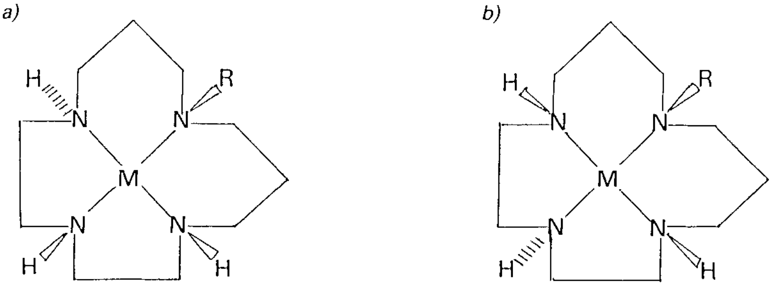


Fig. 6. *Conformation of the macrocycle in* **AH** (a) *and in* **B** (b)

rings are bridged either by an ethylene or a *p*-xylylene group [13], is probably the thermodynamically most stable configuration for this macrocycle. The other configuration *RRSR* has not yet been observed for this macrocycle, but is apparently required in order to allow the coordination of the amino group of the side chain.

This is to our knowledge the first example, in which the coordination of the donor group of the side chain not only modifies the geometry of the metal ion, as has been found in similar compounds, but also alters the configuration of the kinetically stable metal/macrocycle unit.

The support of this work by the *Swiss National Science Foundation* (Project No. 20-27936.89) is gratefully acknowledged.

REFERENCES

[1] A. Schiegg, Th. A. Kaden, *Helv. Chim. Acta* **1990**, *73*, 716.

[2] T. J. Lotz, Th. A. Kaden, *J. Chem. Soc., Chem. Commun.* **1977**, 15; *Helv. Chim. Acta* **1978**, *61*, 1376.

[3] W. Schibler, Th. A. Kaden, *J. Chem. Soc., Chem. Commun.* **1981**, 603; A. K. Basak, Th. A. Kaden, *Helv. Chim. Acta* **1983**, *66*, 2086; M. Hediger, Th. A. Kaden, *ibid.* **1983**, *66*, 861; B. Korybut-Daszkiewicz, *J. Chem. Soc., Chem. Commun.* **1985**, 192; N. W. Alcock, E. H. Curzon, P. Moore, H. A. A. Omar, C. Pierpoint, *J. Chem. Soc., Dalton Trans.* **1985**, 1361; E. K. Barefield, K. A. Foster, G. M. Freeman, K. D. Hodges, *Inorg. Chem.* **1986**, *25*, 4663; M. Studer, Th. A. Kaden, *Helv. Chim. Acta* **1986**, *69*, 2081; P. S. Pallavicini, A. Perotti, A. Poggi, B. Seghi, L. Fabbrizzi, *J. Am. Chem. Soc.* **1987**, *109*, 5139; D. Tschudin, A. Basak, Th. A. Kaden, *Helv. Chim. Acta* **1988**, *71*, 100.

[4] Th. A. Kaden, *Comments Inorg. Chem.* **1990**, *10*, 25.

[5] G. M. Sheldrick, SHELX-76 and SHELXS-86. Computer programs for crystal structure determination, University of Göttingen.

[6] D. T. Cromer, J. B. Mann, *Acta Crystallogr., Sect. A* **1968**, *24*, 321.

[7] H. Gampp, M. Maeder, A. D. Zuberbühler, Th. A. Kaden, *Talanta* **1980**, *27*, 573.

[8] A. D. Zuberbühler, Th. A. Kaden, *Talanta* **1982**, *29*, 201.

[9] H. Gampp, M. Maeder, A. D. Zuberbühler, *Talanta* **1980**, *27*, 1037.

[10] E. J. Billo, *Inorg. Chem.* **1987**, *26*, 3224; D. Tschudin, Th. A. Kaden, *Helv. Chim. Acta* **1989**, *72*, 313; R. W. Hay, C. Y. Quan, *Inorg. Chim. Acta* **1991**, *180*, 147.

[11] For the nomenclature see for example: B. Bosnich, C. K. Poon, M. L. Tobe, *Inorg. Chem.* **1965**, *4*, 1102.

[12] J. C. A. Boyens, *Acta Crystallogr., Sect. C* **1983**, *39*, 846.

[13] R. Schneider, A. Riesen, M. Zehnder, Th. A. Kaden, *Helv. Chim. Acta* **1986**, *69*, 53.