23. Metal Complexes with Macrocyclic Ligands

Part XLI[1])

Nickel(II) and Copper(II) Complexes with Mono-*N*-functionalized Dithiadiazamacrocycles

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Three N_2S_2 macrocycles (**3**, **10**, **12**) carrying an amino group as a pendant arm have been synthesized and their complexation properties towards Ni^{2+} and Cu^{2+} studied. The crystal structures of the Cu^{2+} complexes with 10-methyl-1,4-dithia-7,10-diazacyclododecane-7-ethanamine (**3**) and 11-methyl-1,4-dithia-8,11-diazacyclotetradecane-8-ethanamine (**10**) show that, in both cases, the Cu^{2+} is pentacoordinated by the four donor atoms of the macrocycle and the amino group of the side chain. In aqueous solution, however, two forms of the complexes with stoichiometries [MLH] and [ML] (M = Cu^{2+} or Ni^{2+}) have been observed. In [MLH], the amino group is protonated and does not bind to the metal ion, whereas in [ML] the amino group is bound, and a pentacoordinated geometry results. The pK_a values for the equilibrium $[ML] + H^+ \rightleftharpoons [MLH]^+$ decrease in the order **12** > **10** > **3**, indicating that the 2-aminoethyl side chain binds better to the Cu^{2+} than the 3-aminopropyl side chain. Cyclic voltammetry for the Cu^{2+}/Cu^+ pair shows that the 2-aminoethyl pendant arm stabilizes the Cu^{2+} oxidation state, when the metal ion is in the 14-membered ring (**10**), whereas it stabilizes Cu^+ for the 12-membered macrocycle (**3**).

Introduction. – One of several trends in the development of macrocyclic chemistry has been the functionalization by pendant arms carrying functional groups [2]. If these groups have donor atoms, which can coordinate to the metal ion, this allows to enlarge the coordination number of the metal ion, to change its coordination geometry, and thus influence its properties in a very general way [3]. Pendant chains have also been used to covalently attach the macrocyclic moiety to solid supports to make ion exchangers [4], or to proteins to label monoclonal antibodies [5]. Functionalization can be introduced either at the N- or C-atoms of the ring. In the first case, which is synthetically easier, the secondary N-atom is changed into a tertiary one, thus making it a poorer donor, whereas in the second case the functionalization does not change the N-atoms, so that the macrocycle retains its full coordinative properties.

Although examples of functionalized ligands of both types have been described for crown ethers [6], for N,O macrocycles [7], and polyaza cycloalkanes [2], much less is known about the properties of functionalized thiaaza systems. Examples of it can be found in N_2S macrocycles, which have been substituted at the N-atoms by two acetate groups [8] or by two 2-methylpyridyl side chains [9].

In view of a more systematic study of such ligands, we have prepared a series of mono-*N*-functionalized N_2S_2 macrocycles with 12- and 14-members carrying one aminoalkyl side chain (**3**, **10**, and **12**).

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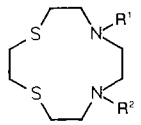
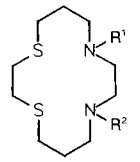


1 $R^1 = R^2 = H$
2 $R^1 = H$, $R^2 = CH_3$
3 $R^1 = (CH_2)_2-NH_2$, $R^2 = CH_3$



4 $R^1 = R^2 = H$
7 $R^1 = H$, $R^2 = CH_3$
8 $R^1 = R^2 = CH_3$
10 $R^1 = (CH_2)_2-NH_2$, $R^2 = CH_3$
12 $R^1 = (CH_2)_3-NH_2$, $R^2 = CH_3$

Experimental. – *General.* The starting compounds were either purchased or prepared according to the literature and characterized by m.p., and IR and NMR spectra: *10-methyl-1,4-dithia-7,10-diazacyclododecane-7-ethanamine* (**3**) [1] and *2,2'-[(ethane-1,2-diyl)bis(thio)]bis[propanoic acid]* (**5**) [10]. FC = flash chromatography. Uncorrected m.p.: *Büchi-510* apparatus. IR Spectra: *Pye Unicam SP3-100, Philips*; KBr pellets or films on NaCl plates. ^{1}H- and ^{13}C-NMR Spectra: *Varian-Gemini-300* instrument; δ in ppm rel. to Me_4Si or 3-(trimethylsilyl)-propane sulfonate as internal standard (0 ppm). Elemental analyses were performed by the analytical laboratory of *Ciba AG*, Basel.

8-Methyl-1,4-dithia-8,11-diazacyclotetradecane-7,12-dione (**6**). To **5** (13 g, 54.5 mmol), $SOCl_2$ (*puriss.*, 61.2 ml, 0.84 mol) was added. After complete dissolution, the mixture was stirred at 40° for 1 h, the excess $SOCl_2$ distilled off at 11 Torr, and the residue treated twice with toluene (50 ml), which was distilled off to remove the last traces of $SOCl_2$. The diacyl dichloride was kept under N_2, at 4° and then used for the cyclization. The cyclization was performed using a high-dilution apparatus (*Normag AG*) under dry N_2 at −10° to 0°. To toluene (1 l), the toluene solns. (500 ml) of the diacyl dichloride (54.5 mmol), and of *N*-methylethane-1,2-diamine (109 mmol) were added simultaneously and dropwise at a rate of *ca.* 15–20 drops/20 s. After complete addition, the two dropping funnels were rinsed with dry toluene (50 ml). The mixture was then filtered, the solid dissolved in H_2O and extracted 5 times with CH_2Cl_2. The product from the CH_2Cl_2 phase (dried and evaporated) was combined with that of the evaporated toluene phase from the reaction. The crude product was purified by FC (silica gel, CH_2Cl_2/MeOH 10:1) and recrystallized from EtOH/Et_2O: **6** (5.27 g, 35%). M.p. 115–116°. IR (KBr): 3365 (NH), 2970 (CH), 1660, 1540 (CON). Anal. calc. for $C_{11}H_{20}N_2O_2S_2$: C 47.80, H 7.29, N 10.14, O 11.58, S 23.20; found: C 47.62, H 7.29, N 10.28, O 11.70, S 23.26.

8-Methyl-1,4-dithia-8,11-diazacyclotetradecane Bis(hydrochloride) (**7**·2 HCl). Compound **6** (6 g, 21.71 mmol) in THF (80 ml) was purged with N_2 (1 h), treated with 1M diborane (60 mmol) in THF at r.t., and heated under reflux. After 6 h, the soln. was cooled to r.t., treated again with 1M diborane (60 mmol) in THF, and heated under reflux for 22 h. After repeating this treatment for a third time (1M diborane (40 mmol) in THF, 6 h heating under reflux), the excess of diborane was destroyed by addition of MeOH under stirring at r.t. (1 h). The mixture was evaporated, the residue taken up with MeOH/H_2O/conc. HCl soln. 78:42:18, and heated under reflux for 4 h. The soln. was evaporated, the residue treated with 6M KOH (40 ml), and extracted 5 times with CH_2Cl_2, the org. phase was dried (Na_2SO_4) and evaporated. The crude product was dissolved in MeOH (50 ml), treated with conc. HCl (5 ml), and evaporated. Recrystallization from MeOH gave pure **7**·2 HCl (4.67 g, 67%). M.p. 229–232° (dec.). ^{1}H-NMR (D_2O): 2.15 (*m*, $CH_2CH_2CH_2$); 2.80 (*t*, 2 SCH_2); 3.00 (*s*, SCH_2CH_2S); 3.05 (*s*, MeN); 3.40 (2*t*, 2 $NCH_2CH_2CH_2$); 3.70 (*s*, NCH_2CH_2N). Anal. calc. for $C_{11}H_{26}Cl_2N_2S_2$: C 41.11, H 8.16, Cl 22.07, N 8.72, S 19.95; found: C 41.44, H 8.06, Cl 22.00, N 8.82, S 19.94.

11-Methyl-1,4-dithia-8,11-diazacyclotetradecane-8-acetonitrile Hydroperchlorate (**9**·$HClO_4$). A soln. of 35% formaldehyde (4.94 ml, 62.2 mmol) was added to a suspension of **7** (3.09 g, 12.45 mmol) in H_2O (40 ml) at 0°. Addition of AcOH (9.2 ml) gave a clear soln. which was reacted with KCN (4.04 g, 62.2 mmol) in H_2O. After stirring for 1 h at r.t., the mixture was treated with solid NaOH and then extracted 5 times with CH_2Cl_2. The org. phase was dried and evaporated. The crude product was dissolved in EtOH, and a soln. of $HClO_4$ in H_2O was added. Then the solvent was evaporated and the crude product recrystallized first from EtOH and then from H_2O: **9**·$HClO_4$ (4.44 g, 92%). M.p. 119–121°. IR (KBr): 2230 (CN). ^{13}C-NMR (CD_3CN): 24.45, 26.05 ($CH_2CH_2CH_2$); 29.15, 29.80, 32.05, 33.00 (4 CH_2S); 41.40, 41.90 (MeN, NCH_2CN); 50.00, 51.30, 55.70, 57.05 (4 CH_2N); 116.5 (CH_2CN). Anal. calc. for $C_{13}H_{26}ClN_3O_4S_2$: C 40.25, H 6.75, Cl 9.14, N 10.83; found: C 40.23, H 6.85, Cl 9.06, N 10.85.

11-Methyl-1,4-dithia-8,11-diazacyclotetradecane-8-ethanamine Tris(picrate) (**10**·3 $C_6H_3N_3O_7$). *Raney*-Ni (5 g) was added to **9** (3 g, 10.44 mmol) in dry EtOH (30 ml). The soln. was cooled, treated with liq. NH_3, and hydrogenated at 50 atm for 96 h in the autoclave. The catalyst was filtered off and the solvent evaporated. After adding 1M NaOH (20 ml) and KCN (2 g), the crude product was extracted 5 times with CH_2Cl_2. The org. phase was dried (Na_2SO_4), evaporated, and the residue was submitted to FC (silica gel, MeOH/25% NH_3 soln. 23:2): **10** (1.76 g, 58%).

To obtain the picrate, **10** (200 mg, 0.69 mmol) was dissolved in EtOH (10 ml) and treated with a sat. EtOH soln. (1.5 ml) of picric acid. The yellow precipitate was filtered off and recrystallized from MeCN/Et_2O: **10**·3 $C_6H_3N_3O_7$ (0.4 g, 60%). Anal. calc. for $C_{31}H_{38}N_{12}O_{21}S_2$: C 38.04, H 3.91, N 17.17, S 6.55; found: C 38.27, H 4.02, N 17.05, S 6.64.

8-Methyl-1,4-dithia-8,11-diazacyclotetradecane-11-propanenitrile Bis(hydrochloride) (**11**·2 HCl). To a soln. of **7** (1.16 g, 4.67 mmol) in acrylonitrile (15 ml), 10 drops AcOH were added. After heating under reflux for 72 h, evaporation of the solvent gave **11** (1.41 g, 100%). IR (film): 2220 (CN). The crude product was purified by bulb-to-bulb distillation (175–190°). A small amount (the rest was used for the preparation of **12**) was dissolved in EtOH and treated with conc. HCl. After evaporation of the solvent and recrystallization from i-PrOH, hygroscopic **11**·2 HCl was obtained. ^{1}H-NMR (D_2O): 2.10 (*m*, $CH_2CH_2CH_2$); 2.70 (*t*, 2 SCH_2); 2.90 (*s*, SCH_2CH_2S); 3.00 (*s*, MeN); 3.10 (*t*, CH_2CH_2CN); 3.40 (2*t*, $NCH_2CH_2CH_2$); 3.60 (*t*, CH_2CH_2CN); 3.70 (*s*, NCH_2CH_2N). ^{13}C-NMR (D_2O): 21.55 (CH_2CN); 30.90, 35.00, 35.15, 38.50, 38.60, 49.65, 53.55, 55.40, 57.70, 58.65, 62.15 ($CH_2CH_2CH_2$, CH_2X, MeN). Anal. calc. for $C_{14}H_{28}N_3S_2$·1.8 HCl·0.8 H_2O: C 43.95, H 8.27, Cl 16.68, N 10.98, H_2O 3.76; found: C 44.23, H 7.95, Cl 16.91, N 11.01, H_2O 3.90.

8-Methyl-1,4-dithia-8,11-diazacyclotetradecane-11-propanamine (**12**). *Raney*-Ni (1.6 g) was added to **11** (1 g, 3.317 mmol) in dry EtOH (10 ml). The soln. was cooled, treated with liq. NH_3, and hydrogenated at 80 atm for 96 h in the autoclave. The catalyst was filtered off and the solvent evaporated. After adding 1M NaOH (10 ml) and KCN (2.5 g), the crude product was extracted 5 times with CH_2Cl_2. The org. phase was dried (Na_2SO_4) and evaporated, and the residue was submitted to FC (silica gel, MeOH/25% NH_3 24:1): **12** (0.3 g, 30%). ^{1}H-NMR ($CDCl_3$): 1.75 (*quint.* 2 $CH_2CH_2CH_2$); 2.20 (*s*, MeN); 2.55 (*m*, 9 CH_2); 2.70 (*s*, NCH_2CH_2N).

General Procedure for the Syntheses of the Cu^{II} and Ni^{II} Complexes. ***CAUTION:*** *Although no problems were encountered in this work, perchlorates are potentially explosive and should be prepared only in small quantities and handled with care.* $Cu(ClO_4)_2·6\ H_2O$ or $Ni(ClO_4)_2·6\ H_2O$ was dissolved in H_2O or dry EtOH and added to an equimolar soln. of the ligand as free base in H_2O, dry EtOH, or dry MeOH. The precipitate thereby formed was dissolved in H_2O, MeCN, or a mixture of these two solvents, and the insoluble $M(OH)_2$ was filtered off. After evaporation of the solvent the crude product was recrystallized.

(10-Methyl-1,4-dithia-7,10-diazacyclododecane-7-ethanamine)copper(II) Diperchlorate ([Cu(**3**)]$(ClO_4)_2$). Recrystallization from EtOH/H_2O gave dark blue crystals. Characterized by X-ray diffraction (see below).

(11-Methyl-1,4-dithia-8,11-diazacyclotetradecane-8-ethanamine)copper(II) Diperchlorate ([Cu(**10**)]$(ClO_4)_2$). Recrystallization from H_2O gave blue-green crystals. Anal. calc. for $C_{13}H_{29}Cl_2CuN_3O_8S_2$: C 28.19, H 5.28, Cl 12.80, Cu 11.47, N 7.59, S 11.58; found: C 28.36, H 5.45, Cl 12.66, Cu 11.70, N 7.71, S 11.42.

(11-Methyl-1,4-dithia-8,11-diazacyclotetradecane-8-ethanamine)nickel(II) Diperchlorate ([Ni(**10**)]$(ClO_4)_2$). Recrystallization from H_2O gave violet crystals. Anal. calc. for $C_{13}H_{29}Cl_2N_3NiO_8S_2$: C 28.44, H 5.32, Cl 12.91, N 7.65, S 11.68; found: C 28.64, H 5.41, Cl 12.87, N 7.74, S 11.66.

(8-Methyl-1,4-dithia-8,11-diazacyclotetradecane-11-propanamine)copper(II) Diperchlorate ([Cu(**12**)]$(ClO_4)_2$). Recrystallization from H_2O and from EtOH/H_2O gave blue crystals. Anal. calc. for $C_{14}H_{31}Cl_2CuN_3O_8S_2$: C 29.60, H 5.50, Cu 11.20, N 7.40; found: C 29.72, H 5.54, Cu 11.10, N 7.55.

(8-Methyl-1,4-dithia-8,11-diazacyclotetradecane-11-propanamine)nickel(II) Diperchlorate ([Ni(**12**)]$(ClO_4)_2$). Recrystallization from EtOH and from MeCN/EtOH/H_2O gave blue crystals. Anal. calc. for $C_{14}H_{31}Cl_2N_3NiO_8S_2$: C 29.86, H 5.55, N 7.46, Ni 10.42; found: C 30.07, H 5.64, N 7.57, Ni 10.40.

X-Ray Diffraction. The crystal data and parameters of the data collection of [Cu(**3**)]$(ClO_4)_2$ and [Cu(**10**)]$(ClO_4)_2$ are given in *Table 1*. Unit cell parameters were determined by accurate centring of 25 independent strong reflections by the least-squares method. The raw data set was corrected for polarization effects. For [Cu(**3**)]$(ClO_4)_2$, the absorption correction was determined by psi-scans. The structure of [Cu(**10**)]$(ClO_4)_2$ was solved by *Patterson* technique using the program SHELX-86 [11] and the structure of [Cu(**3**)]$(ClO_4)_2$ by direct methods using the program SIR-92 [12]. Anisotropic least-square refinements were carried out on all non-H-atoms using the program CRYSTALS [13]. H-Atoms are in calculated positions with C–H distance of 0.96 Å and fixed isotropic thermal parameters. Scattering factors are taken from *International Tables for Crystallography, Vol. IV* [14].

Table 1. *Crystal Data and Parameter of Data Collection for* $[Cu(\mathbf{3})](ClO_4)_2$ *and* $[Cu(\mathbf{10})](ClO_4)_2$

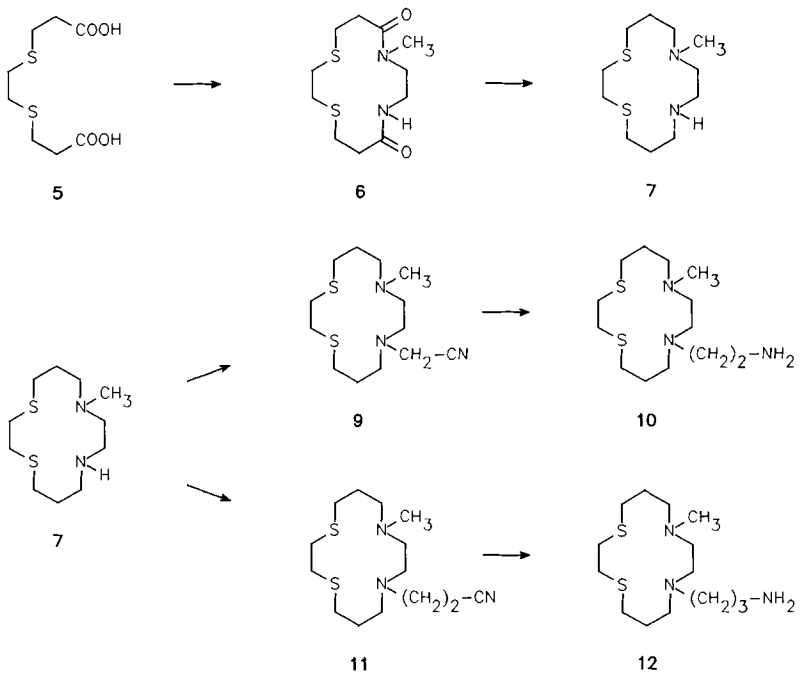
	$[Cu(\mathbf{3})](ClO_4)_2$	$[Cu(\mathbf{10})](ClO_4)_2$
Formula	$C_{11}H_{25}Cl_2CuN_3O_8S_2$	$C_{13}H_{29}Cl_2CuN_3O_8S_2$
Mol. weight [$gmol^{-1}$]	525.900	553.954
Temp. [K]	298	298
Crystal size [mm]	0.10 × 0.18 × 0.30	0.20 × 0.33 × 0.38
Absorption coeff. [cm^{-1}]	63.48	14.37
Crystal system	monoclinic	monoclinic
Space group	$P2_1/c$ (No. 14; [16])	$P2_1/c$ (No. 14; [16])
a [Å]	8.994 ± 0.002	10.042 ± 0.003
b [Å]	17.571 ± 0.002	15.677 ± 0.003
c [Å]	12.996 ± 0.002	14.356 ± 0.002
α [deg]	90	90
β [deg]	101.55 ± 0.01	97.18 ± 0.01
γ [deg]	90	90
Z; V [Å^3]	2012.1 ± 0.5	2242.4 ± 0.8
Calc. density [gcm^{-3}]	1.736	1.641
Θ_{max} [deg]	77.5	28
Radiation	CuK_α, 1.54178 Å	MoK_α, 0.71069 Å
Scan type	$\omega/2\Theta$	$\omega/2\Theta$
$F(000)$	1084	1148
No. of indep. refl.	4212	3497
No. of refl. in refin.	3340	1927
No. of variables	281	317
Last max./min.	+1.04/−0.75	+0.77/−0.45
Final R	5.97	6.49
Final R_w	7.12	6.93
Weighting scheme	weight·$[1-(\Delta(F)/6\sigma F)^2]^2$	weight·$[1-(\Delta(F)/6\sigma F)^2]^2$

Spectrophotometric Titrations. The titrations of the complexes $[CuL]^{2+}$ (L = **10** and **12**) with 0.1M HNO_3 were run at 25 ± 0.1° and $I = 0.5$ (KNO_3) on the automatic computer-controlled titrator, consisting of an UV/VIS spectrophotometer (*Pye Unicam PU 8800*, *Philips*), a *Metrohm 605* potentiometer, a *Metrohm 665* dosimat with a combined glass electrode, and an *AT-286* computer [15]. The buffer solns. (pH 4.00 and 7.00) for electrode calibration were also from *Metrohm*. The spectra were measured between 450 and 800 nm. To stabilize the pH, 10^{-2} M $ClCH_2COO^-$ and 2,6-lutidine was used as a buffer for L = **10** and L = **12**, respectively. The complex concentration at the beginning of the titration was 10^{-3}–$3.0 \cdot 10^{-4}$ M. The data were evaluated with the program SPECFIT [16]. In addition, spectra of the complexes (10^{-3}–10^{-4} M) were measured with a *Perkin-Elmer Lambda 2* spectrophotometer in 1-cm cells. The pH values were adjusted with HNO_3 or NaOH to the desired value.

Cyclic Voltammetry. The cyclic voltammetry was measured in aq. soln. with $[CuL]^{2+} = 4 \cdot 10^{-4}$ M and 0.2M $NaClO_4$ as electrolyte, using a *Metrohm VA* scanner *E 612* and a *Metrohm VA* detector *E 611* with a three-electrode cell: working electrode Pt, auxiliary electrode Pt, reference electrode calomel with NaCl bridge. Cyclic voltammograms were recorded with 2–10 mV s^{-1} scan rate covering about 800 mV.

Results and Discussion. – *Synthesis of the Ligands* (see *Scheme*). The cyclization of α,ω-dicarboxylic acids as dichlorides with *N*-methylethane-1,2-diamine follows the previously described high-dilution procedure to give cyclic diamides [17]. These were then reduced with B_2H_6 in THF to the corresponding cyclic diamines. The introduction of one pendant side chain, applying either the *Strecker* synthesis with KCN and CH_2O for **9** or the 1,4-addition of acrylonitrile for **11**, is an easy task, since there is only one secondary amino group to be substituted. Reduction of the CN group with *Raney*-Ni/H_2 produces the N_2S_2 macrocycles with either one 2-aminoethyl (**10**) or one 3-aminopropyl (**12**) side chain.

Scheme



Structures of the Cu^{2+} Complexes. Two of the ligands gave crystalline Cu^{2+} complexes ideal for an X-ray diffraction study. The structure of the Cu^{2+} complex with the 12-membered macrocycle **3** shows a pentacoordinate Cu^{2+} surrounded by three N- and two S-atoms (*Fig. 1*). The geometry is in between that of a trigonal bipyramid with S(1)–Cu–N(1) as axis (bond angle 161°) and that of a square pyramid with a somewhat distorted N_2S_2 plane (deviations of ±0.2 Å) and N(3) as axial ligand. The macrocycle is in the *trans-I*-configuration, if we take into account that the side chain, the *N*-Me group (C(13)) and the free electron pairs of the two S-atoms all point in the same direction. The bond lengths Cu–N (2.03–2.09 Å) and Cu–S (2.32–2.37 Å) are normal (*Table 2*).

Table 2. *Selected Bond Lengths* [Å] *and Angles* [°] *for [Cu(**3**)](ClO$_4$)$_2$ and the Major Form of [Cu(**10**)](ClO$_4$)$_2$*

	$[Cu(\mathbf{3})]^{2+}$	$[Cu(\mathbf{10})]^{2+}$		$[Cu(\mathbf{3})]^{2+}$	$[Cu(\mathbf{10})]^{2+}$
Cu–N(1)	2.034(4)	2.059(7)	S(1)–Cu–S(2)	84.23(5)	86.1(1)
Cu–N(2)	2.095(3)	2.087(7)	S(1)–Cu–N(1)	161.8(1)	178.6(2)
Cu–N(3)	2.093(4)	2.128(7)	S(2)–Cu–N(1)	87.9(1)	92.5(2)
Cu–S(1)	2.320(1)	2.310(3)	S(1)–Cu–N(2)	88.7(1)	93.7(2)
Cu–S(2)	2.375(1)	2.379(3)	S(2)–Cu–N(2)	140.1(1)	148.6(2)
			N(1)–Cu–N(2)	86.8(1)	87.6(3)
			S(1)–Cu–N(3)	112.1(1)	95.7(2)
			S(2)–Cu–N(3)	105.9(1)	99.3(2)
			N(1)–Cu–N(3)	85.9(2)	84.3(3)
			N(2)–Cu–N(3)	113.1(2)	112.0(3)

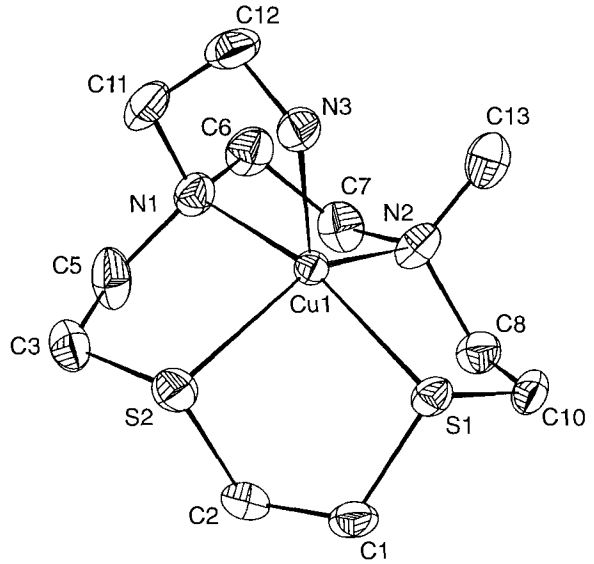


Fig. 1. *ORTEP Drawing and atom numbering of* $[Cu(\mathbf{3})](ClO_4)_2$

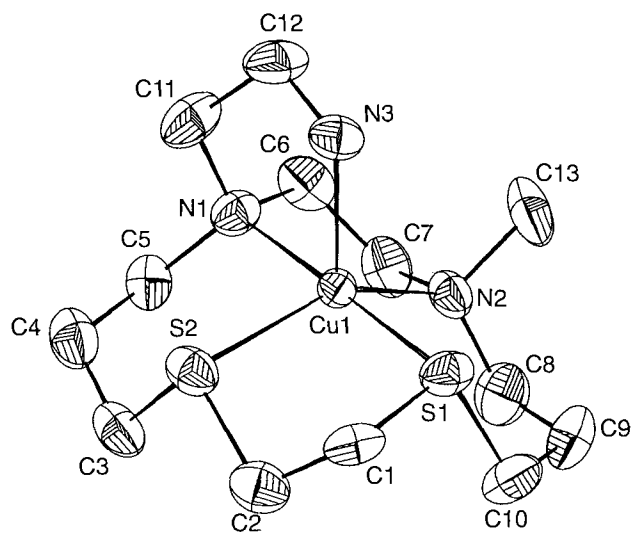


Fig. 2. *ORTEP Drawing and atom numbering of* $[Cu(\mathbf{10})](ClO_4)_2$

The Cu^{2+} complex of **10** shows a disordered structure with an occupation of 78:22 for the two molecules. The disorder is mainly due to the position of S(2) and the C(1)–C(2) and C(3)–C(4)–C(5) chains attached to it. In the major form (*Fig. 2*), the six-membered ring formed by Cu, S(2), C(3), C(4), C(5), N(1) is in the chair conformation, whereas the same ring is in the twist conformation in the minor form. In both forms, the Cu^{2+} is

pentacoordinate in a distorted trigonal bipyramidal geometry, the axis being given by N(1), Cu, and S(1) with an angle of 178.6°, and the equatorial donor atoms being S(2), N(2), and N(3). The best plane through these atoms and the Cu^{2+} gives only small deviations of ±0.01–0.03 Å.

Whereas bond lengths are normal for Cu–N (2.02–2.12 Å) and Cu–S (2.3–2.4 Å; *Table 2*), the angles in the trigonal plane strongly differ from the ideal value of 120°: N(2)–Cu–S(2) is 148.6°, N(2)–Cu–N(3) is 112.0°, and S(2)–Cu–N(3) is 99.3°.

In the major form, the side chain, the *N*-Me group (C(13)) as well as the free electron pairs of the two S-atoms all point in the same direction, so that the ligand is in the *trans-I*-configuration, and this recalls structures observed for several derivatives of 1,4,8-trimethyl-1,4,8,11-tetraazacyclotetradecane [18]. In the minor form, the configuration of the macrocycle is *trans-II*.

Studies in Aqueous Solution. The absorption spectra of the Cu^{2+} and Ni^{2+} complexes were measured at different pH values. In the case of the ligands **10** and **12**, a pH-dependent equilibrium between [MLH] (low pH) and [ML] (high pH) occurs, whereas for **3** no spectral change is observed, since the complex dissociates at low pH. At low pH, the amino group of the side chain is protonated, and thus cannot bind to the metal ion. In the case of the 14-membered rings **10** and **12**, square-planar coordination geometries result with typical absorption characteristics for Cu^{2+} and Ni^{2+} (*Table 3*). At high pH, deprotonation of the ammonium group of the side chain gives a potential new donor in form of the amine, which coordinates to the metal ion. Indeed, the absorption spectra show the geometry change and indicate pentacoordination for Cu^{2+} as well as for Ni^{2+} (*Table 3*). In

Table 3. *Spectral Properties* (λ_{max} in nm and ε values in M^{-1} cm^{-1}) *and* pK_a *Values of the* Ni^{2+} *and* Cu^{2+} *Complexes with* **3**, **10**, *and* **12**

	L = **3**	L = **10**	L = **12**
[NiL]		370 (70), 570 (43)	380 (230), 590 (120)
[NiLH]		460 (75)	480 (200)
[CuL]	650 (700)	360 (6800), 650 (600)	360 (7300), 650 (700)
[CuLH]	[a])	580 (700)	575 (809)
pK_a	< 2	3.17 ± 0.06	6.59 ± 0.01

[a]) Upon acidification, the complex dissociates.

the case of Cu^{2+}, the absorption maxima shift from 580 and 575 nm to 650 nm and 650 nm for **10** and **12**, respectively. The shift to longer wavelengths is typical for an additional axial coordination to Cu^{2+} [19]. In the case of Ni^{2+}, the absorption characteristics change from a one-band spectrum, typical for D_{4h} symmetry [20], to a two-band spectrum with relatively large ε values, which has been observed for pentacoordinated macrocyclic Ni^{2+} species [21].

For the Cu^{2+} complexes the pH dependence of the spectra was quantitatively studied using spectrophotometric titrations (*Fig. 3*). The acid-base reaction (*Eqn. 1*), where a_H is the proton activity, was used to fit the data and thereby obtain the molar absorptivities of the two species [CuL] and [CuLH], and the K_a values. The results (*Table 3*) show that, in the case of the shorter 2-aminoethyl chain (**10**), it is more difficult to protonate the

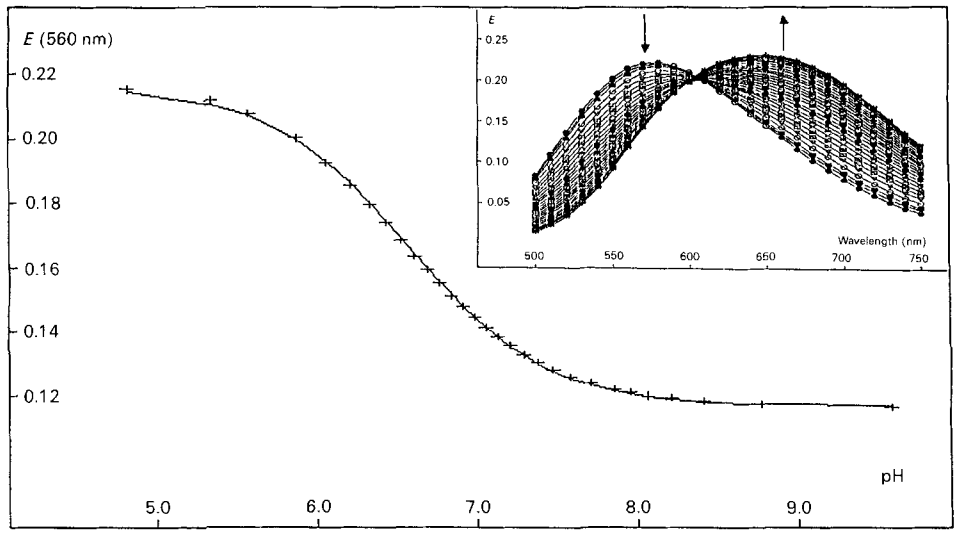


Fig. 3. *Spectrophotometric titration of* $[Cu(\mathbf{12})]^{2+}$ *with* HNO_3. Absorptivity at 560 nm as a function of pH: +: experimental points, −: calculated curve. Insert: Development of the spectra during the titration.

coordinated amino group than for the longer 3-aminopropyl pendant chain (**12**). Between the 12- and the 14-membered macrocycle, there is a difference in that the amino group of **3** cannot be protonated at low pH without dissociation of the complex.

$$CuL + H^+ \rightleftharpoons CuLH^+; \quad K_a = [CuLH]/[CuL] \cdot a_H \qquad (1)$$

The cyclic voltammetry of the Cu^{2+}/Cu^+ redox process is a good indication of the relative stability of the Cu^{2+} and Cu^+ species. As previously observed for the unsubstituted N_2S_2 macrocycles, the 14-membered ring **4** stabilizes Cu^{2+} as compared to Cu^+ [22]. This stems from the fact that the 14-membered ring is ideal to give square-planar geometry, which is typical for Cu^{2+}, whereas the 12-membered ring **1** is too small to encompass the metal ion. Stepwise substitution of the secondary amino groups in **4** by Me groups to give **7** and **8** increases the E_0 value and thus destabilizes the Cu^{2+} state compared to Cu^+ (*Table 4*).

Table 4. *Redox Potentials (vs.* SHE) *for the* Cu^{2+}/Cu^+ *Pair, as Determined by Cyclic Voltammetry of the* Cu^{2+} *Complexes in Aqueous Solution* (0.2M $NaClO_4$)

Ligand	14-Membered ring[a])	12-Membered ring[a])
$R^1 = R^2 = H$ (**4** and **1**)	84 (70)[b]) [22]	116 (52)[b]) [22]
$R^1 = H$, $R^2 = CH_3$ (**7**)	108 (133)	
$R^1 = R^2 = CH_3$ (**8**)	176 (173)	
$R^1 = CH_3$, $R^2 = (CH_2)_2NH_2$ (**10** and **3**)	29 (70)	151 (60)
$R^1 = CH_3$, $R^2 = (CH_2)_3NH_2$ (**12**)	118 (107)	

[a]) Potential in mV (peak-peak separation ΔE).
[b]) 0.2M Na_2SO_4.

Replacing one Me group of **8** by an aminoalkyl side chain decreases E_0 drastically for **10** with the shorter chain and somewhat less for **12** with the longer one. The value of E_0 for the 2-aminoethyl-substituted ligand **10** is such, that the potential is even lower than that of the unsubstituted macrocycle **4**. In contrast, the potential of the Cu^{2+}/Cu^{+} pair in the 12-membered ring **3** is higher by 45 mV than that of the unsubstituted macrocycle **1**. This is a clear indication that the geometry offered by the smaller macrocycle, even with an additional coordinating group in the side chain, is more suitable than that of the 14-membered ring for stabilizing the Cu^{+} with respect to the Cu^{2+} oxidation state. A detailed discussion of the decrease of E_0 with increasing *N*-substitution degree and of the effect of introducing a side chain would require structural information on both Cu^{2+} and Cu^{+} species. Whereas the structure of the Cu^{2+} complexes has been characterized (*vide supra*), no such information is available for the Cu^{+} species.

In summary, the results obtained show that the chemistry of mono-*N*-functionalized N_2S_2 macrocycles does not significantly differ from that of the analogous N_4 compounds [2]. However, their potential to stabilize Cu^{+} is an interesting new feature, which can be used to model biological systems.

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REFERENCES

[1] P. C. Riesen, Th. A. Kaden, *Helv. Chim. Acta* **1995,** *78,* 1325.
[2] Th. A. Kaden, *Topics Curr. Chem.* **1984,** *121,* 157; P. Bernhardt, G. A. Lawrence, *Coord. Chem. Rev.* **1990,** *104,* 297; Th. A. Kaden, in 'Crown Compounds towards Future Application', Ed. S. R. Cooper, VCH Publishers, New York, 1992, p. 135; Th. A. Kaden, in 'Advances in Supramolecular Chemistry', Ed. G. W. Gokel, JAI Press Inc., Greenwich, 1993, Vol. 3, p. 65.
[3] Th. A. Kaden, *Comments Inorg. Chem.* **1990,** *10,* 25.
[4] I. Schmid, R. Sintra, *Topics Curr. Chem.* **1984,** *121,* 105.
[5] D. Parker, *Chem. Brit.* **1990,** *26,* 942; Th. A. Kaden, *Nachr. Chem. Techn. Lab.* **1990,** *38,* 728.
[6] R. A. Schultz, D. M. Dishong, G. W. Gokel, *J. Am. Chem. Soc.* **1982,** *104,* 625; M. Tagaki, H. Nakamura, *J. Coord. Chem.* **1986,** *15,* 53.
[7] K. Krakowiak, J. D. Bradshaw, D. J. Zamecka-Krakowiak, *Chem. Rev.* **1989,** *89,* 929.
[8] D. M. Wambeke, W. Lippens, G. H. Herman, A. M. Goeminne, *Bull. Soc. Chim. Belges* **1993,** *102,* 593; D. M. Wambeke, W. Lippens, G. H. Herman, A. M. Goeminne, *J. Chem. Soc., Dalton Trans.* **1993,** *13,* 2017.
[9] K. Wasielewski, R. Mattes, *Acta Crystallogr., Sect. C* **1990,** *46,* 1826.
[10] N. Yoda, *Makromol. Chem.* **1962,** *56,* 36.
[11] G. M. Sheldrick, 'SHELXS 86', Universität Göttingen, 1986.
[12] A. Altomare, G. Gascarano, C. Giacovazzo, A. Guagliardi, M. C. Burla, G. Polidori, M. Camalli, *J. Appl. Cryst.* **1994,** *27,* 435.
[13] D. Watkin, 'CRYSTALS', Crystallographic Laboratory, Oxford, 1990.
[14] 'International Tables of Crystallography', Kynoch Press, Birmingham, 1974, Vol. IV.
[15] G. Hänisch, Th. A. Kaden, A. D. Zuberbühler, *Talanta* **1979,** *26,* 563.
[16] H. Gampp, M. Maeder, Ch. J. Meyer, A. D. Zuberbühler, *Talanta* **1985,** *32,* 257.
[17] L. Siegfried, Th. A. Kaden, *Helv. Chim. Acta* **1984,** *67,* 29.
[18] D. Tschudin, A. Riesen, Th. A. Kaden, *Helv. Chim. Acta* **1989,** *72,* 131.
[19] E. J. Billo, *Inorg. Nucl. Chem. Lett.* **1974,** *10,* 613; A. A. Kurganov, V. A. Davankoff, *ibid.* **1976,** *12,* 743.
[20] A. B. Lever, 'Inorganic Electronic Spectroscopy', Elsevier Publishing Company, Amsterdam, 1968.
[21] M. Micheloni, P. Paoletti, S. Bürki, Th. A. Kaden, *Helv. Chim. Acta* **1982,** *65,* 587.
[22] K. P. Balakrishnan, Th. A. Kaden, L. Siegfried, A. D. Zuberbühler, *Helv. Chim. Acta* **1984,** *67,* 1060.