Metal Complexes of Macrocyclic Ligands

Part XLVII[1])

Copper(II) and Nickel(II) Complexes of '*trans*'-Difunctionalized Tetraaza Macrocycles

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Reductive cleavage of the bis-aminal **1** of 1,4,8,11-tetraazacyclotetradecane allows a new synthesis of 1,8-dimethyl-1,4,8,11-tetraazacyclotetradecane (**3**), which is an ideal starting compound for preparing '*trans*'-difunctionalized derivatives. Thus, **3** was reacted to give the macrocyclic diacetonitrile **5** and dipropanenitrile **9**. These were reduced with *Raney*-Ni and H_2 to the corresponding diamines **6** and **10**, respectively. In addition, **5** was selectively hydrolysed to the diacetamide **7** and fully hydrolysed to the diacetic acid **8**. The Cu^{2+} and Ni^{2+} complexes of these new ligands were prepared and their spectral and structural properties studied. Whereas **3** yielded square planar species, the functionalized derivatives gave penta- or hexacoordinate complexes. The ligands with amino groups in their side chains (**6** and **10**) formed square planar species at acidic pH (amino groups protonated), but pentacoordinate geometries resulted at alkaline pH, where one amino group underwent coordination. In contrast, the diacetic acid **8** gave distorted octahedral Cu^{2+} and Ni^{2+} complexes.

Introduction. – The functionalization of tetraazamacrocycles has given to coordination chemists many new and interesting ligands [2]. Beside *C*-functionalization, which is, in general, more difficult to achieve, *N*-functionalization with side chains carrying ligating groups has been developed to the extent that macrocycles with high selectivity and high thermodynamic and kinetic stability can now be prepared.

The easiest synthetic approach is persubstitution, in which all four N-atoms of the macrocycle are alkylated or acylated. Examples with carboxylate [3], amine [4], pyrazole [5], pyridine [6], hydroxo [7], and phosphonate [8] donors have been described.

Synthetically more demanding is the preparation of mono-, di-, or trisubstituted derivatives. Several approaches have been tested. Thus, for monosubstituted derivatives, the selective alkylation [9], the protection with three easily-to-cleave-off groups, and the template synthesis with compounds already functionalized have been described [10]. The protection of three N-atoms can be achieved in several ways. Using Me groups, which of course cannot be cleaved off any more, one can introduce one side chain at the non-methylated N-atom, whereby macrocycles with tertiary amino groups result [11]. On the other side, one can also use protecting groups, such as tosyl [12] or (*tert*-butoxy)carbonyl(Boc) [13], or use 3-N-bridged derivatives containing P or B [14][15], $Cr(CO)_3$ as well as $Mo(CO)_3$ [16], or CH [17]. The *N*-alkylation can be achieved with all these compounds followed by deprotection to give mono-*N*-functional derivatives.

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The 3-N-bridged derivatives have also been used to prepare trisubstituted macrocycles, since they allow to introduce orthogonal *N*-protecting functions, and, thus, after removing of the protection at the three N-atoms, one has a monoprotected derivative [17].

Disubstitution can be realized starting from dimethyl derivatives, whereby '*cis*' [18] and '*trans*' [19] isomers have been used, or by introducing tosyl [20] as protecting groups ('*cis*' and '*trans*' refer to the relative position of two (substituted) N-atoms in a (metal-free) macrocyclic ligand). In addition, selective dialkylation seems also possible. An especially interesting example has been published by *Anelli et al.* [21] with the preparation of selectively substituted '*trans*' derivatives of 1,4,7,10-tetraazacyclododecane.

Since relatively few compounds of this type have been studied in the case of 1,4,8,11-tetraazacyclotetradecane, we have developed a new synthesis for the 1,8-dimethyl derivative, which allows the selective introduction of two side chains in '*trans*' position.

Experimental. – 1. *General.* Compound 1,4,8,11-tetraazatricyclo[9.3.1.1.^{4,8}]hexadecane (**1**) was prepared according to [22]. Solns. were evaporated in a rotatory evaporator. ^{1}H- and ^{13}C-NMR Spectra: *Varian Gemini 300*; δ in ppm rel. to $SiMe_4$ as internal standard for $CDCl_3$ or sodium 3-(trimethylsilyl)propane-1-sulfonate for D_2O soln. TLC: aluminium oxide *60 F_{254}* neutral (*Merck*, type *E*) or silica gel *60 F_{254}* (*Merck*). Flash chromatography (FC): silica gel *60* (0.04–0.06 mm, 230–400 mesh, *Merck*); method of *Still et al.* [23]. M.p.: *Büchi 535*; not corrected. GC/MS: *Hewlett-Packard* (mass-selective detector *5971*, gas chromatograph *5890* series II); column 'Me_2Si', 12 m. FAB-MS: *VG 70–250;* nitrobenzyl alcohol as matrix, *m/z* (rel. %). Elemental analysis were performed by the analytical laboratory of *Ciba-Geigy AG*, Basel.

2. *Ligands. 4-Methyl-1,4,8,11-tetraazabicyclo[9.3.1]pentadecane* (**2**). To a soln. of **1** (5.0 g, 22.3 mmol) in abs. EtOH (150 ml), 10% Pd/C (450 mg) was added. The mixture was hydrogenated (60 atm) at r.t. for 96 h. Then, it was filtered over *Celite* and evaporated yielding a light yellow oil (5.0 g). This was purified by FC (silica gel *60*, 50 × 8 cm, EtOH/25% NH_3 soln. 11 : 2). The fractions were analysed by TLC (EtOH/25% NH_3 soln. 7 : 3) and GC/MS: 229 ($[M+2H]^+$), 227 ($[M+H]^+$), 226 (M^+).

1,8-Dimethyl-1,4,8,11-tetraazacyclotetradecane (**3**). To a soln. of **1** (5.0 g, 22.3 mmol) in abs. EtOH (250 ml) at −10°, *Raney*-Ni (5.0 g) and liq. NH_3 (100 ml) were added. The mixture was hydrogenated (130 atm) at 60° for 336 h. Then it was filtered and evaporated giving a yellow oil (4.8 g) which was analysed by GC/MS: two main products **4** (50%) and **3** (43%) as well as a small quantity of by-products (7%). The oil was purified by FC (silica gel *60*, 50 × 8 cm, EtOH/25% NH_3 soln. 11 : 2): 2.0 g (40%) of crystalline **3**. The compound was sublimed at 50°/0.1 mbar. M.p. 25–30°. ^{1}H-NMR ($CDCl_3$): 1.80 (*q*, $CH_2CH_2CH_2$); 2.24 (*s*, MeN); 2–3 (NH); 2.46, 2.52, 2.73, 2.77 (4*t*, CH_2N). ^{13}C-NMR ($CDCl_3$): 25.55 ($CH_2CH_2CH_2$); 42.06 (MeN); 47.17, 49.82, 56.69, 57.12 (NCH_2N). Anal. calc. for $C_{12}H_{28}N_4 \cdot 0.25\ H_2O$ (232.89): C 61.89, H 12.24, N 24.06; found: C 62.17, H 12.18, N 23.99.

The tetrahydrochloride was prepared by treating **3** (220 mg) with 18% HCl soln. (8 ml) and so much EtOH until crystallization began. After cooling to −10°, the crystals were filtered and washed with abs. EtOH. ^{1}H-NMR (D_2O): 2.22 (*q*, $CH_2CH_2CH_2$); 3.04 (*s*, MeN); 3.44, 3.53 (2*t*, CH_2N); 3.70, 3.73 (2*s*, CH_2N). ^{13}C-NMR (D_2O): 20.65 ($CH_2CH_2CH_2$); 45.03 (MeN); 39.63, 43.82, 49.04, 52.71 (CH_2N). Anal. calc. for $C_{12}H_{28}N_4 \cdot 3.95$ HCl (372.76): C 38.67, H 8.64, Cl 37.66, N 15.03; found: C 38.65, H 8.74, Cl 37.54, N 15.27.

4,11-Dimethyl-1,4,8,11-tetraazacyclotetradecane-1,8-diacetonitrile (**5**). To a stirred soln. of **3** (2.0 g, 8.8 mmol) and 37% formaldehyde soln. (1.6 ml, 17.9 mmol) in H_2O (15 ml), cooled to 0°, KCN (1.45 g, 22.3 mmol) in H_2O (15 ml) was slowly added. The soln. was kept overnight at r.t., then alkalinized with NaOH, and extracted with CH_2Cl_2 (5 × 30 ml). The org. phase was dried (Na_2SO_4), filtered, and evaporated. The product was recrystallized from EtOH to give colourless crystals (2.0 g, 78%) which were dried under high vacuum. M.p. 137–138°. ^{1}H-NMR ($CDCl_3$): 1.61 (*q*, $CH_2CH_2CH_2$); 2.19 (*s*, 2 MeN); 2.41, 2.45, 2.62, 2.64 (4*t*, CH_2N); 3.63 (*s*, NCH_2CN). ^{13}C-NMR ($CDCl_3$): 24.77 ($CH_2CH_2CH_2$); 42.35 (NCH_2CN); 43.13 (MeN); 50.38, 51.10, 52.97, 54.50 (CH_2N); 114.99 (CH_2CN). FAB-MS: 308 (18, $[M+2H]^+$), 307 (100, $[M+H]^+$), 306 (32, M^+). Anal. calc. for $C_{16}H_{30}N_6$ (306.45): C 62.71, H 9.87, N 27.42; found: C 62.60, H 9.84, N 27.51.

4,11-Dimethyl-1,4,8,11-tetraazacyclotetradecane-1,8-diethanamine Hexahydrochloride (**6**·6 HCl). To a cooled soln. of **5** (1 g, 3.26 mmol) in EtOH (200 ml), *Raney*-Ni (5 g) and liq. NH_3 (*ca.* 50 ml) were added. The mixture was hydrogenated (70 atm, 45°) for 1 week in an autoclave. The catalyst was filtered off and the solvent evaporated. The remaining yellow oil (*ca.* 1 g) was dissolved in conc. HCl soln. and the crystallization induced by addition of EtOH. The hydrochloride was filtered, washed with cold EtOH, and dried: 1 g (75%). ^{1}H-NMR (D_2O): 2.14 (*q*, $CH_2CH_2CH_2$); 3.01 (*s*, MeN); 3.14, 3.24, 3.35, 3.39, 3.46 (5*t*, NCH_2CH_2); 3.63 (*t*, $CH_2CH_2NH_2$). ^{13}C-NMR (D_2O): 22.29 ($CH_2CH_2CH_2$); 37.71 ($CH_2CH_2NH_2$); 44.94 (MeN); 48.14, 51.61, 51.67, 53.50, 53.95 (CH_2N). Anal. calc. for $C_{16}H_{38}N_6 \cdot 5.8\ HCl \cdot 0.8\ H_2O$ (540.93): C 35.53, H 8.46, Cl 38.11, N 15.54; found: C 35.56, H 8.49, Cl 38.07, N 15.46.

4,11-Dimethyl-1,4,8,11-tetraazacyclotetradecane-1,8-diacetamide (**7**). To hydrolyze both nitrile groups, **5** was treated with $Cu(ClO_4)_2$ (1 g in DMF (3 ml)) and 0.1M NaOH (15 ml) overnight. Then KCN (2.12 g) was added to demetallate the macrocycle, and the soln. was extracted wtih CH_2Cl_2. From this soln., **7** (0.4 g, 36%) crystallized on standing. M.p. 210–215°. ^{1}H-NMR ($CDCl_3$): 1.60 (*q*, $CH_2CH_2CH_2$); 2.14 (*s*, MeN); 2.41, 2.53, 2.56, 2.60 (4*t*, CH_2CH_2N); 3.08 (*s*, NCH_2CONH_2); 5.36, 9.16 (NCH_2CONH_2). ^{13}C-NMR ($CDCl_3$): 26.05 ($CH_2CH_2CH_2$); 42.58 (MeN); 53.33, 54.96, 55.07, 57.20, 59.34 (CH_2N); 176.90 ($CONH_2$). FAB-MS: 344 ($[M+2H]^+$), 343 ($[M+H]^+$). Anal. calc. for $C_{16}H_{34}N_6O_2 \cdot 0.5\ H_2O$ (351.50): C 54.67, H 10.04, N 23.9; found: C 54.78, H 9.89, N 23.65.

4,11-Dimethyl-1,4,8,11-tetraazacyclotetradecane-1,8-diacetic Acid Tetrahydrochloride (**8**·4 HCl). A soln. of **5** (1 g, 3.26 mmol) and LiOH (0.69 g) in H_2O (40 ml) was heated to reflux for 14 d. Then the soln. was acidified with 2M HCl and filtered and the residue purified by ion-exchange chromatography (*Dowex 2*, 0.2M HCl): **8**·4HCl (0.7 g, 44%). FAB-MS: 346 ($[M+2H]^+$), 345 ($[M+H]^+$), 344 (M^+). ^{1}H-NMR (D_2O): 2.08 (*q*, $CH_2CH_2CH_2$); 2.96 (*s*, MeN); 3.31, 3.44, 3.46, 3.54 (4*t*, CH_2N); 3.73 (*s*, NCH_2COOH). ^{13}C-NMR ($CDCl_3$): 27.86 ($CH_2CH_2CH_2$); 48.52 (NCH_2COOH); 55.92 (MeN); 58.79, 60.06, 60.21, 61.66 (CH_2N); 181.28 (NCH_2COOH). Anal. calc. for $C_{16}H_{32}N_4O_4 \cdot 4\ HCl \cdot 2.2\ H_2O$ (529.94): C 36.26, H 7.68, Cl 26.76, N 10.57; found: C 36.04, H 7.76, Cl 26.83, N 10.75.

4,11-Dimethyl-1,4,8,11-tetraazacyclotetradecane-1,8-dipropanenitrile (**9**). To a soln. of **3** (1.7 g, 7.4 mmol) in EtOH (50 ml), acrylonitrile (2 ml, 30.0 mmol) was added. The mixture was stirred overnight at r.t. and then evaporated to give a crude product which was recrystallized from EtOH: 2.1 g (84%). M.p. 74°. ^{1}H-NMR ($CDCl_3$): 1.62 (*q*, $CH_2CH_2CH_2$); 2.20 (*s*, MeN); 2.45, 2.47, 2.47, 2.58, 2.60 (5*t*, CH_2N); 2.80 (*t*, NCH_2CH_2CN). ^{13}C-NMR ($CDCl_3$): 16.04 ($CH_2CH_2CH_2$); 24.98 (CH_2CH_2CN); 43.41 (MeN); 50.47, 51.32, 51.51, 54.57, 54.83 (CH_2N); 119.28 (CH_2CN). FAB-MS: 336 ($[M+2H]^+$), 335 ($[M+H]^+$), 334 (M^+). Anal. calc. for $C_{18}H_{34}N_6$ (334.51): C 64.53, H 10.24, N 25.12; found: C 64.65, H 10.24, N 25.37.

4,11-Dimethyl-1,4,8,11-tetraazacyclotetradecane-1,8-dipropanamine Hexahydrochloride (**10**·6 HCl). Same procedure as for **6**: 1.4 g (83%). ^{1}H-NMR (D_2O): 2.26 (*q*, $CH_2CH_2CH_2$); 3.13 (*s*, MeN); 3.17, 3.48 (2*t*, NCH_2CH_2); 3.62 (*m*, NCH_2CH_2); 3.90 (*s*, NCH_2CH_2). ^{13}C-NMR (D_2O): 19.19 ($CH_2CH_2CH_2$); 24.68 (NCH_2CH_2); 38.64 (MeN); 44.99, 45.71, 46.85, 49.52, 51.63, 54.88 (NCH_2CH_2). Anal. calc. for $C_{18}H_{42}N_6 \cdot 5.8\ HCl \cdot 1.2\ H_2O$ (575.67): C 37.56, H 8.79, Cl 35.72, N 14.60; found: C 37.68, H 8.73, Cl 35.74, N 14.46.

8,11-Dimethyl-1,4,8,11-tetraazacyclotetradecane-1,4-diacetic Acid Tetrahydrochloride (**11**·4 HCl). A soln. of 8,11-dimethyl-1,4,8,11-tetraazacyclotetradecane-1,4-diacetonitrile [24] (1 g, 3.26 mmol) and LiOH (0.69 g) in H_2O (40 ml) was refluxed for 2 weeks. The soln. was acidified with 2M HCl, whereby the product precipitated. It was purified by ion-exchange chromatography (*Dowex 2 × 4*): 0.6 g (35%). FAB-MS: 346 ($[M+2H]^+$), 345 ($[M+H]^+$), 344 (M^+). ^{1}H-NMR (D_2O): 2.19 (*q*, $CH_2CH_2CH_2$); 3.02 (*s*, MeN); 3.25, 3.50 (2*t*, CH_2N); 3.38, 3.77 (2*s*, CH_2N); 3.88 (*s*, NCH_2COOH). ^{13}C-NMR ($CDCl_3$): 22.44 ($CH_2CH_2CH_2$); 44.89 (MeN); 49.19, 52.94, 53.92, 54.75, 57.69 (CH_2N); 174.00 (COOH). Anal. calc. for $C_{16}H_{32}Cl_4N_4O_4 \cdot 0.75\ H_2O$ (521.83): C 36.83, H 7.63, Cl 27.18, N 10.74; found: C 37.01, H 7.46, Cl 26.97, N 10.86.

3. *Copper(II) Complexes.* The Cu^{2+} complexes were obtained by mixing equimolar amounts of $Cu(ClO_4)_2 \cdot 6H_2O$ and ligand in EtOH or H_2O and gentle heating.

(1,8-Dimethyl-1,4,8,11-tetraazacyclotetradecane)copper(II) Diperchlorate ([Cu(**3**)]$(ClO_4)_2$): Blue-violet crystals (47%) from EtOH. Anal. calc. for $C_{12}H_{28}Cl_2CuN_4O_8$ (490.83): C 29.37, H 5.75, Cl 14.45, Cu 12.95, N 11.41; found: C 29.06, H 5.69, Cl 14.51, Cu 12.9, N 11.35.

(4,11-Dimethyl-1,4,8,11-tetraazacyclotetradecane-1,8-diacetamide)copper(II) Diperchlorate Hemihydrate ([Cu(**7**)]$(ClO_4)_2 \cdot 0.5\ H_2O$): Blue crystals (48%) from EtOH. Anal. calc. for $C_{16}H_{34}Cu_2Cl_2N_6O_{10}$ (604.94): C 31.77, H 5.67, Cl 11.72, Cu 10.50, N 13.89; found: C 31.80, H 5.62, Cl 12.16, Cu 10.2, N 13.58.

(4.11-Dimethyl-1,4,8,11-tetraazacyclotetradecane-1,8-diacetic Acid)copper(II) Diperchlorate Dihydrate ([Cu(**8**)]$(ClO_4)_2 \cdot 2\ H_2O$): Blue crystals (41%) from H_2O after acidifying to pH 1 with $HClO_4$. Anal. calc. for $C_{16}H_{32}Cl_2Cu_2N_4O_{12} \cdot 2\ H_2O$ (642.93): C 29.89, H 5.64, Cl 11.03, Cu 9.88, N 8.71, O 34.84; found: C 30.00, H 5.39, Cl 10.85, Cu 9.90, N 8.84, O 35.02.

(8,11-Dimethyl-1,4,8,11-tetraazacyclotetradecane-1,4-diacetic Acid)copper(II) Diperchlorate Monohydrate ($[Cu(\mathbf{11})](ClO_4)_2]\cdot 1.2\ H_2O$): Blue crystals (31%) from H_2O at pH 6–7. Anal. calc. for $C_{16}H_{32}Cl_2Cu_2N_4O_{12}\cdot 1.2\ H_2O$ (628.52): C 30.58, H 5.52, Cl 11.28, Cu 10.11, N 8.91; found: C 30.53, H 5.54, Cl 11.54, Cu 9.82, N 8.92.

4. *Nickel(II) Complexes.* The Ni^{2+} complexes were prepared by mixing equimolar amounts of $Ni(ClO_4)_2$ and ligand, and adjusting the pH to the desired value.

Results and Discussion. – The bis-aminal **1** of 1,4,8,11-tetraazacyclotetradecane has been described [22], but no application from the synthetic point of view were reported until recently. We now studied the reductive cleavage of **1** using different reagents. The results (*Table 1*) show that, depending on the reaction conditions, either the monomethyl monoaminal **2** (*Scheme 1*, *Conditions a*) or the two isomeric dimethyl derivatives with '*trans*' and '*cis*' structures **3** and **4**, respectively (*Conditions b*) were formed. Especially interesting is the observation that the reduction of the two animal groups occurs stepwise so that, *e.g.*, with 10% Pd/C under H_2, the intermediate **2** was produced in 90% yield. If, however, one is interested in the complete reduction, the hydrogenation with *Raney*-Ni can be used which yielded the two dimethyl isomers **3** and **4**, with a slight excess of the '*trans*' compound **3** and a minimum of by-products. The separation of the isomers was achieved by FC (EtOH/25% NH_3 soln. 6:1) and gave pure products (by GC/MS).

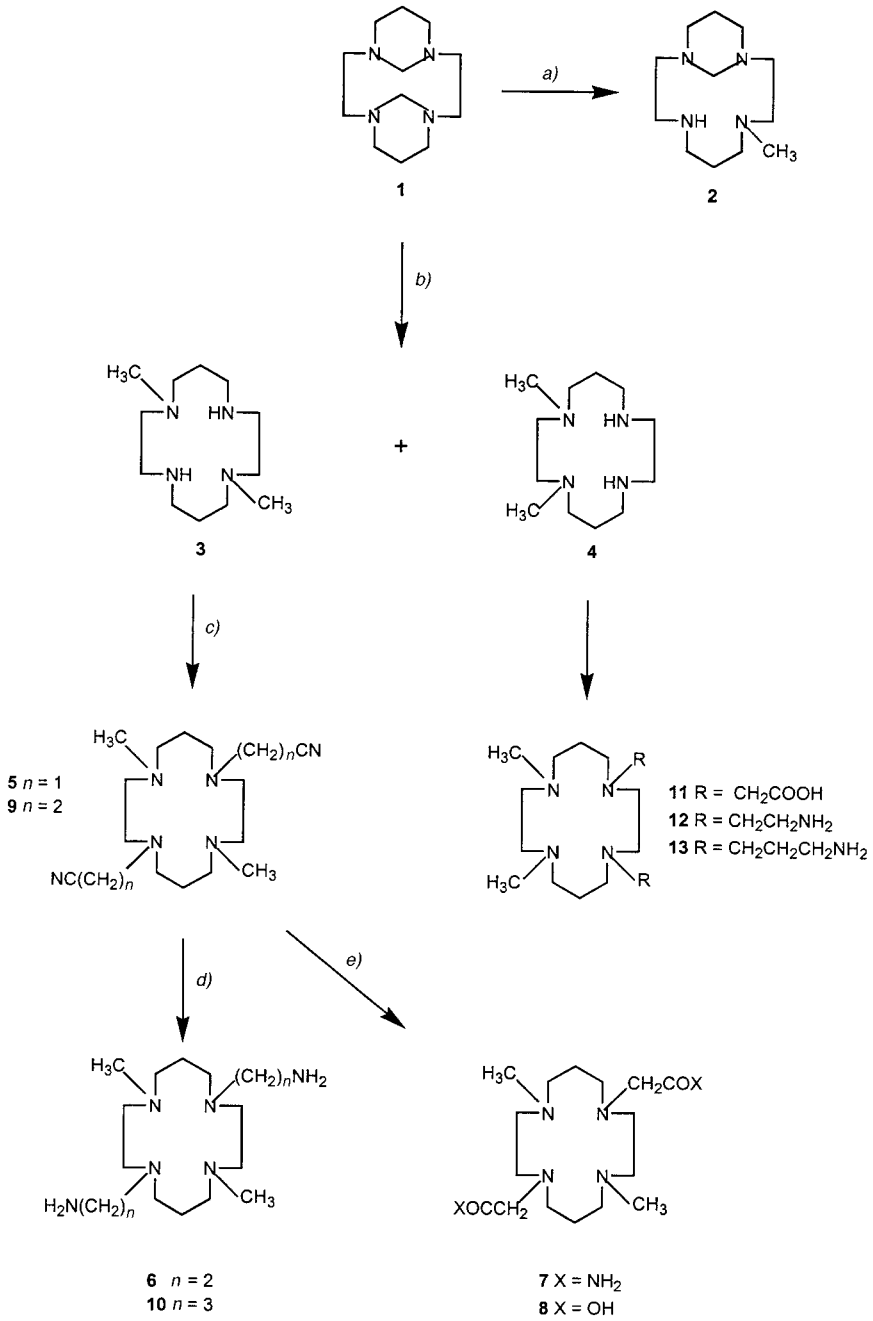
The '*cis*'-compound **4** has been prepared by a template reaction with good yields, and this is of course the easiest way [25]. The '*trans*' derivative **3** has also been described with an overall yield of 28% [19]. In contrast, we now prepared 40% of pure '*trans*' isomer **3** in a two-step synthesis with a relatively simple purification procedure. Both '*cis*' and '*trans*' derivatives allow to selectively prepare bis-functionalized macrocycles. Whereas several compounds with '*cis*' structure have been described [18], only the diacetate has been prepared in the '*trans*' series [19].

To functionalize the '*trans*' derivative **3**, we introduced side chains with nitrile groups either using *Strecker*'s synthesis or by addition of acrylonitrile (*Scheme 1*). The obtained dinitriles **5** and **9**, respectively, are ideal intermediates since they could either be reduced to the diamines **6** and **10**, respectively, using *Raney*-Ni/H_2 in the presence of liquid NH_3, or in the case of **5**, be hydrolysed to the diacetic acid **8** or the diacetamide **7**. This last reaction was performed overnight using the Cu^{2+} complex of **5** dissolved in 0.1M NaOH and resembles that previously described for the hydrolysis of 1,4,8,11-tetraazacyclotetradecane-1-acetonitrile [18] which also stopped at the amide state. For the preparation of the diacetic acid **8**, prolonged hydrolysis with LiOH at reflux temperature was necessary.

All of the new ligands were complexed with Cu^{2+} and Ni^{2+} in order to compare their properties with the analogous '*cis*' derivatives. The UV/VIS spectra allow to discuss their structures in solution (*Table 2*). The Cu^{2+} and Ni^{2+} complexes of the '*trans*'-dimethyl ligand **3** show spectral properties typical for a square-planar geometry. Thus, the absorption maximum at 542 nm for $[CuL]^{2+}$ is typical for a square planar CuN_4 chromophore and is comparable with that of the Cu^{2+} complex of the corresponding '*cis*' ligand with λ_{max} 540 nm [26]. Similarly, the observation that only one band at 457 nm is found for the Ni^{2+} complex of **3** is a clear indication for its square-planar coordination geometry (*cf.* 460 nm for the Ni^{2+} complex of **4** [26]).

For the complexes of the '*trans*'- and '*cis*'-diacetic acids **8** and **11**, the structures must be different. The known X-ray structure of $[Cu(\mathbf{8})]^{2+}$ shows that a distorted octahedral

Scheme 1



a) H_2, 10% Pd/C, EtOH. *b*) *Raney*-Ni, liq. NH_3, EtOH. *c*) 37% CH_2O/H_2O, KCN, H_2O; or MeCN, EtOH. *d*) *Raney*-Ni, liq. NH_3, EtOH. *e*) 1. $Cu(ClO_4)_2$, DMF, 0.1M NaOH; 2. KCN for **7**; LiOH, H_2O for **8**.

Table 1. *Reductive Cleavage of* **1** *with Different Reagents and Yields of the Products*

Reagent	Conditions	Products	Ratio in %[a])
HCOOH	72 h reflux ($EtOH/H_2O$)	**2**/SP[b])	61:24
NaOH/Zn	1 h reflux (EtOH)	**2**/SP[b])	–
$NaBH_4$	2 h reflux ($EtOH/H_2O$)	**4/3**	54:37
$NaBH_4/NaHCO_3$	2 h reflux ($EtOH/H_2O$)	**4/3**	52:43
$LiAlH_4$	Et_2O	**1**	100
10% Pd/C	55°/130 atm H_2/136 h	**1**, **2**	4:90
Raney-Ni, abs. EtOH	50°/120 atm H_2/144 h	**4/3**	45:47
Raney-Ni, NH_3	50°/120 atm H_2/144 h	**4/3**	44:51

[a]) Determined by GC/MS. [b]) Unknown by-product.

Table 2. *Absorption Spectra of the* Cu^{2+} *and* Ni^{2+} *Complexes with Ligands* **3**, **6**, **10**, **11**, *and* **8**

Ligand	λ_{max} [nm] (ε[M^{-1} cm^{-1}])	
	$[CuL]^{2+}$	$[NiL]^{2+}$
3	542 (209)	457 (47)
6	668 (249)	602 (42), 381 (101)
10	735 (246)	651 (23), 399 (55)
11	638 (106)	948 (9), 582 (7), 368 (12)
8	621 (133)	1018 (13), 576 (7), 373 (8)

N_4O_2 donor set is present [27]. A similar structure is probably also present in the '*cis*' derivative since its absorption spectrum is very similar. Both Ni^{2+} complexes of **8** and **11** show spectra which are typical for octahedral high-spin Ni^{2+}.

Especially interesting are the spectral properties of the complexes with **6** and **10**, which have two alkanamine side chains. The spectra at alkaline pH are typical for pentacoordinated species. In the case of the Cu^{2+} complexes, the relatively high ε values and the maxima at longer wavelengths are indicative for it. In the case of the Ni^{2+} complexes, the two bands with relatively high ε values also indicate pentacoordination for Ni^{2+}.

Since the spectra of these species are strongly pH-dependent, we run spectrophotometric pH titrations which were fitted assuming the equilibria described by *Eqns. 1* and *2*.

$$[CuL]^{2+} + H^+ \rightleftharpoons [CuLH]^{3+};\ K_1 \quad (1)$$

$$[CuLH]^{3+} + H^+ \rightleftharpoons [CuLH_2]^{4+};\ K_2 \quad (2)$$

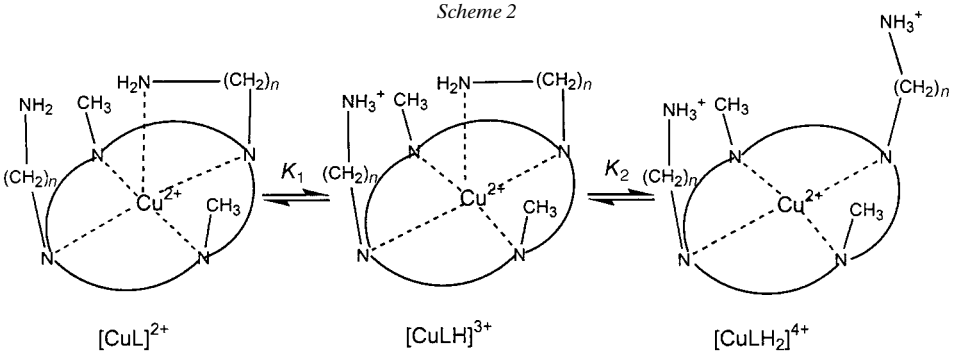
For the complexes **6** and **10**, the log K_1 values are high and typical for the protonation of a free amine (*Table 3*). The spectral changes in going from $[CuL]^{2+}$ to $[CuLH]^{3+}$ are only minor so that the log K_1 values must be associated with the protonation of a free, uncoordinated amino group. The second protonation log K_2 is strongly dependent on the chain length and induces a strong shift in λ_{max}, indicating that, through protonation, the ligand field around the Cu^{2+} is changed. A similar behaviour was observed for the Cu^{2+} complexes of diamines **12** and **13** [28] (see *Table 3*).

Table 3. *Absorption Spectra and log* K_H *Values of the Species Formed with the Macrocycles* **6**, **10**, **12** [28], *and* **13** [28] *Carrying Two Alkanamine Side Chains*

Ligand		$[CuL]^{2+}$	$[CuLH]^{3+}$	$[CuLH_2]^{4+}$
12 [28]	λ ($\in$)	683 (336)	672 (280)	–
	log K_H		8.17 (1)	< 3
6	λ ($\in$)	659 (254)	669 (249)	–
	log K_H		8.25 (1)	< 3
13 [28]	λ ($\in$)	743 (321)	739 (315)	651 (260)
	log K_H		9.45 (1)	6.71 (1)
10	λ ($\in$)	748 (261)	751 (255)	654 (227)
	log K_H		9.52 (2)	7.04 (2)

To explain the results of the photospectrometric pH titrations, we propose *Scheme 2* in which the protonations and concomitant structural processes are depicted. $[CuL]^{2+}$ is pentacoordinated, the four N-atoms of the macrocycle and one alkanamine side chain being involved in coordination. The other alkanamine side chain is free and does not coordinate. Addition of the first proton takes place at this NH_2 group with a minor change in the absorption spectrum. In the second step, however, the coordinated NH_2 group is protonated and, depending on the alkane chain length, the process is more or less easy. Through protonation, the resulting ammonium group dissociates from Cu^{2+} so that a square-planar species results, as indicated by the spectral properties.

Scheme 2



In conclusion, it is interesting to note that the difunctionalized macrocycles can give so many different coordination geometries with Ni^{2+} and Cu^{2+}. In particular, it is not clear yet why the macrocyclic diacetic acids give *trans*-octahedral geometry with a *trans-III* configuration of the macrocycle, whereas the macrocyclic dialkanamine ligands form pentacoordinate species with *trans-I* configuration of the N-atoms

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