Novel Building Blocks for Oligonuclear Copper Complexes Derived from β-Ketoenamines of Histidine

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Dedicated to Prof. Dr. Egon Uhlig on the Occasion of his 70th Birthday

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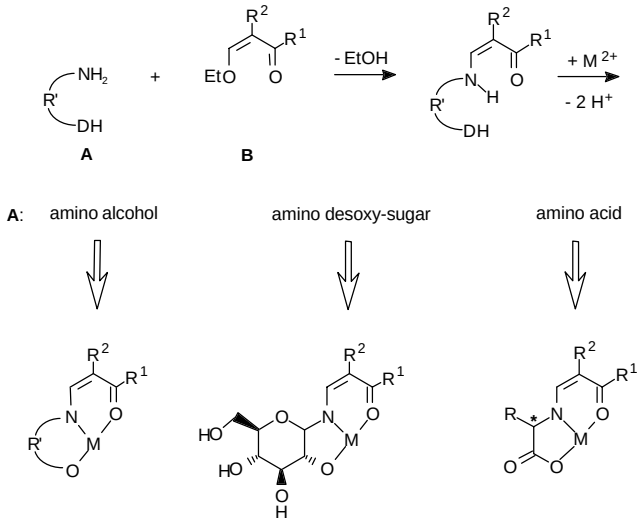
Abstract. Condensation products of *L*-histidine with the 3-oxoenolethers diethyl-ethoxymethylene-malonate (**1**) and ethyl-ethoxymethylene-cyanoacetate (**2**) react with copper(II) as di-anionic ligands to give neutral 1:1 complexes Cu-**His1** and Cu-**His2**. Both complexes crystallize as oligonuclear units, even from strongly donating solvents like N-methylimidazole (Meim) (Cu-**His1**) and pyridine (Cu-**His2**). X-ray structure analyses show supramolecular structures, formed of two (Cu-**His1**) or four (Cu-**His2**) formula units of the complex, which arrange to macrocycles by means of intermolecular coordination of the imidazole-N. Strong H-bridges result in a face-to-face orientation of the hydrophilic sites of two great rings. ESI-MS investigations in pyridine solution give evidence for the existence of dimeric, tetrameric and – in case of Cu-**His2** – trimeric units, besides the monomeric adducts with one pyridine. In contrast to the dimeric or tetrameric ("cubane-like") copper(II) complexes of amino alcohols and their β-ketoenamines, the complexes Cu-**His1** and Cu-**His2** show no significant spin coupling from room temperature down to 4 K. The complexes Cu-**His1** and Cu-**His2** give no electrochemically reversible $Cu^{II/I}$ reduction in pyridine. However, the isolation of a stable diamagnetic copper(I) complex of the methylester derivative, Cu^{I}-**HisMe1**, supports the assumption, that similar histidine-derived copper complexes should display reversible redox behaviour and catalytic activity in reactions with O_2.

Copper is next to iron the most important biometal for the binding and activation of molecular oxygen [1]. Many copper enzymes involved in the metabolism of dioxygen contain dinuclear copper centers as active sites [1, 2], *e.g.* catechol oxidase [3], tyrosinase [4], and the O_2 carrying hemocyanins [4]. Other copper proteins are based on higher oligonuclear units [5], *e.g.* ascorbat oxidase [6] and laccase [7]. In the past few years, a large variety of "biomimetic" oligonuclear copper complexes have been synthesized, aiming to model the biological systems and to evaluate the catalytic potential of simpler synthetic compounds with similar structural features [8, 9].

Apart from these "bioinspired"current developments, the chemistry of oligonuclear copper complexes has a long tradition: In 1955, Hein and Beerstecher [10] described the *O*-bridged dinuclear structure and the markedly reduced paramagnetism of copper(II) complexes with deprotonated aminoalcohols, $[Cu(aminol\text{-}H)X]_2$ (X^-: halide). Uhlig *et al.* observed similar properties with complexes of pyridine derivatives [11, 12] and described relationships between the spin–spin coupling and the degree of oligomerization in copper(II) complexes of deprotonated aminoalcohols [13]. Such earlier contributions constituted one starting point for extensive subsequent investigations in the field of "magnetically anomalous" copper(II) complexes [14].

In our approach (scheme 1), we use deprotonated condensation products of a functionalized primary amine



Scheme 1 Building blocks for oligonuclear metal complexes derived from 3-oxo-1-enamines.

(component A; D = anionic substituent with O, S or N as additional donor) and a substituted 3-oxo-enol (component B; preferably as its enol-ether) as potential tridentate, dianionic chelate ligands L^{2-}. Their neutral 1:1 complexes with copper(II), CuL, are coordinatively highly unsaturated and tend to oligomerize spontaneously leading to oligonuclear structures. The bridge R' and the substituents $R^{1,2}$ can be used to control the electronic properties of the donor set and partly the bulkiness of the ligand very efficiently.

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The complexes derived from condensation products of aminoethanol and acetylacetone [15] were the first tetranuclear chelate complexes of copper [16] and nickel [17] with a "cubane-like" $[M_4O_4]$ core. The magnetic behaviour of such complexes depends strongly on the bridge R' and slightly on the substituents $R^{1,2}$ [18]. Particularly interesting structural and magnetic features have been found with complexes derived from amino desoxy-sugars which are under investigation presently [19]. First prototypes with derivatives of an amino acid have been synthesized and magnetically characterized ten years ago [18]. We present here the first established structures of oligonuclear copper(II) complexes with the 3-oxo-enamine derivatives of histidine, Cu-**His1** and Cu-**His2**. Histidine is of particular interest as part of such structures because of its essential role as ligand in copper proteins [1–7]. The copper(I) complex with a monoanionic ligand derived from histidine methylester, Cu-**HisMe1**, will be described additionally.

Experimental

Syntheses

$Cu(ac)_2 \cdot H_2O$ (ac = acetate), *L*–histidine (**His**), *L*–histidine methylester · 2HCl (**HisMe**), diethyl(ethoxymethylene) malonate (**1**) and ethyl(ethoxymethylene)cyanoacetate (**2**), *N*-methylimidazole (MeIm) and pyridine were bought from Merck and used without further purification. $[Cu(MeCN)_4]ClO_4$ was prepared by methods from literature [20]. Methanol was dried over activated magnesium. The syntheses of the Cu(I)-complex were performed under an argon atmosphere.

[Diethyl({[1-carboxy-κO-2-(1H-imidazol-4-yl)ethyl]amino-κN}methylene)malonato(2-)-κO']copper(II) (**Cu-His1**)

1.4 g **1** (6.45 mmol) in 50 mL methanol was added to a solution of 1.0 g *L*-histidine (6.45 mmol) and an equimolar amount of sodium-methanolate in 50 mL dried methanol. The reaction mixture was heated on reflux for 15 min, and 1.9 g $Cu(ac)_2 \cdot H_2O$ (6.45 mmol) in 100 mL methanol was dropped to the reaction mixture. The resulting pale blue precipitate was filtered off, washed with methanol, and dried at 80 °C *in vacuo*. Yield 2.3 g (92%). Crystals were obtained by diffusion of toluene into a solution of Cu-**His1** in MeIm.

$CuC_{14}H_{17}N_3O_6$ (386.9)
Found: C 43.00 H 4.42 N 10.96 Cu 16.46
Calcd.: C 43.47 H 4.43 N 10.86 Cu 16.43.

(N-{[(Z)-2-Cyano-2-(ethoxycarbonyl-κO)vinyl]amino-κN}-L-histidinato(2–)-κO)copper(II) monohydrate; (Cu-**His2** · H_2O)

1.1 g **2** (6.45 mmol) in 50 mL methanol was added to a solution of 1 g *L*–histidine (6.45 mmol) and an equimolar amount of sodium-methanolate in 50 mL dried methanol. The reaction mixture was heated on reflux for 15 min and 1.9 g $Cu(ac)_2 \cdot H_2O$ in 100 mL methanol was added dropwise to the reaction mixture. The resulting green blue precipitate was filtered off, washed with methanol, and dried *in vacuo*. The product contains one H_2O. Yield 2.2 g (94%).

$CuC_{12}H_{14}N_4O_5$ (357.8)
Found: C 39.94 H 4.04 N 15.79 Cu 17.92
Calcd.: C 40.28 H 3.94 N 15.66 Cu 17.76 .

The anhydrous complex was prepared by drying *in vacuo* over P_2O_5.

$CuC_{12}H_{12}N_4O_4$ (339.8)
Found: C 41.19 H 3.68 N 16.28 Cu 18.58
Calcd.: C 42.41 H 3.56 N 16.49 Cu 18.70.

Crystals were obtained by diffusing hexane into a pyridine solution of Cu-**His2**.

Diethyl({[2-(1H-imidazol-4-yl)-1-(methoxycarbonyl)ethyl]-amino}methylene)malonate; (H-**HisMe1**)

To a solution of 7.3 g *L*-histidine-methylester · 2HCl (30.15 mmol) and 2.4 g NaOH (60.3 mmol) in 240 mL methanol 6.52 g **1** was added. The reaction mixture was heated on reflux for 5 min and then concentrated to 30 mL. Under stirring and cooling with ice 300 mL water was slowly dropped into the reaction mixture. The resulting white precipitate was filtered off, repeatedly washed with water, and dried *in vacuo*. Yield 7.4 g (72%); *m.p.* 123 °C. – ^{1}H NMR ($\delta_{H/ppm}$= 200 MHz; $CDCl_3$, Si_2Me_6): 1.21 [3H, t, *J*(HH) 7.2 Hz, CH_3], 1.26 [3H, t, J(HH) 7.2 Hz, CH_3], 2.98–3.26 [2H, m, CH_2], 3.73 [3H, s, O–CH_3], 4.09 [2H, q, *J*(HH) 7.2 Hz, O–CH_2], 4.16 [2H, q, *J*(HH) 7.2 Hz, O–CH_2], 4.24–4.43 [1H, m, N–CH], 6.78 [1H, s, imidazole], 7.51 [1H, s, imidazole], 7.71 [1H, d, *J*(HH) 14 Hz, C=CH-N], 9.43 [1H, m, NH].

$C_{15}H_{21}N_3O_6$ (339.4) Found: C 52.89 H 6.48 N 12.13
Calcd.: C 53.09 H 6.24 N 12.38.

[Diethyl({[2-(1H-imidazol-4-yl)-1-(methoxycarbonyl)ethyl]-amino}methylene)malonato]copper(I); (Cu^I-**HisMe1**)

To a solution of 1.00 g H-**HisMe1** (2.95 mmol) and 0.96 g $[Cu(MeCN)_4]ClO_4$ (2.95 mmol) in 70 mL methanol, 2.9 mL of a 1M methanolic solution of sodium-methanolate was slowly added. The reaction mixture was stirred for 30 min. The resulting oil was separated from the methanolic solution and repeatedly washed with methanol. The complex was isolated as white powder after drying *in vacuo.* The dry complex is moderately air sensitive and strongly so in solution. Yield 1.3 g (86%). – ^{1}H NMR ($\delta_{H/ppm}$ = 200 MHz; D_6-dioxane, Si_2Me_6): 1.16 [6H, m, CH_3], 3.11 [2H, m, CH_2], 3.32 [3H, s, O–CH_3], 3.99–4.17 [2H, m, O–CH_2], 4.72 [1H, m, N–CH], 6.70 [1H, s, imidazole], 7.46 [1H, s, imidazole], 7.83 [1H, d, *J*(HH) 14 Hz, C=CH–N], 9.28 [1H, m, NH]. – MS (*m/z*; chemical ionization, H_2O): 679 [M_2^+, base peak], 340 [M^+], 295 (M^+–C_2H_5O).

$CuC_{15}H_{20}N_3O_6$ (401.9)
Found: C 44.54 H 5.03 N 10.33 Cu 15.57
Calcd.: C 44.83 H 5.02 N 10.46 Cu 15.81.

Crystal Structure Determination

The intensity data for the compounds were collected on a Nonius KappaCCD-diffractometer, using graphite-monochromated Mo-K_α radiation. Data were corrected for Lorentz polarization, but not for absorption effects [21].

Only parts of the structures could be solved by direct meth-

ods (SHELXS [22]) and refined by full-matrix least squares techniques against Fo^2 (SHELXL-97 [23]). The complete structures could not be resolved for both compounds. Approximately 50% of the unit cell volume is occupied by the copper complex. The remainder exhibits some electron density which, however, could not be interpreted. The scattering power of the crystals and the resolution of the Mo-K_α radiation were not sufficient to resolve the structure parts of these holes [1]). Investigations with copper and synchrotron radiation, respectively, are under way, and the results will be published elsewhere. XP (SIEMENS Analytical X-ray Instruments, Inc.) was used for structural representations.

Crystal Data for Cu-**His1**(· solv): "$C_{28}N_6O_{12}Cu_2$" [2]), green prism, size 0.31 × 0.22 × 0.18 mm^3, monoclinic, space group C2, a = 23.049(4), b = 23.906(4), c = 16.754(3) Å, β = 131.77(3)°, V = 6885(2) Å^3, T = −90 °C, 6494 reflections in h(−28/19), k(−34/20), l(−19/24), measured in the range 1.46° ≤ Θ ≤ 30.81°, completeness Θ_{max} = 74.4%, 5348 independent reflections, R_{int} = 0.079, 3498 reflections with $F_o > 4\sigma(F_o)$, largest difference peak and hole: 1.62/−1.34 eÅ^{-3}.

Crystal Data for Cu-**His2** · 1/2 pyridine (· solv): "$C_{54}N_{18}O_{16}Cu_4$" [2]) (tetranuclear unit −4 methyl + 2 pyridine) green prism, size 0.42 × 0.31 × 0.22 mm^3, tetragonal, space group $I4_122$, a = 29.820(3), b = 29.820(3), c = 55.669(7) Å, V = 49503(9) Å^3, T = −90 °C, 38123 reflections in h(−42/41), k(−29/29), l(−59/38), measured in the range 1.21° ≤ Θ ≤ 30.10°, completeness Θ_{max} = 81.6 %, 26848 independent reflections, R_{int} = 0.093, 13346 reflections with $F_o > 4\sigma(F_o)$, largest difference peak and hole: 1.62/−1.39 eÅ^{-3}.

Further Instrumentation

EPR spectra were recorded in frozen solutions (c = 0.001 g mol^{-1}) on a conventional X-band spectrometer EPS 300E (Fa. Bruker) at a temperature of T = 77 K.

The solid-state magnetic susceptibilities were measured by SQUID method on a Quantum Design MRMS 2. Diamagnetic corrections for the ligands were accounted for by methods described in the literature [24].

The mass spectra were recorded on a Finnigan MAT spectrometer MAT 95 XL (FAB: Cs-FAB-Gun, 20 kV, solution in 3-nitro-benzylalcohol; ESI: solution (1 gL^{-1}) in methanol/chloroform 90/10 Corona-Voltage 3kV; in pyridine Corona-Voltage 4 kV). For improvement of detection and to standardize all measurements, traces of $KClO_4$ were added to all solutions. Thus, in most cases the potassium adducts of the species were detected instead of the protonated forms.

^{1}H NMR spectra: NMR spectrometer Bruker type AC 200, (200 MHz). Elemental analysis: Analysator Leco, type CHNS-932.

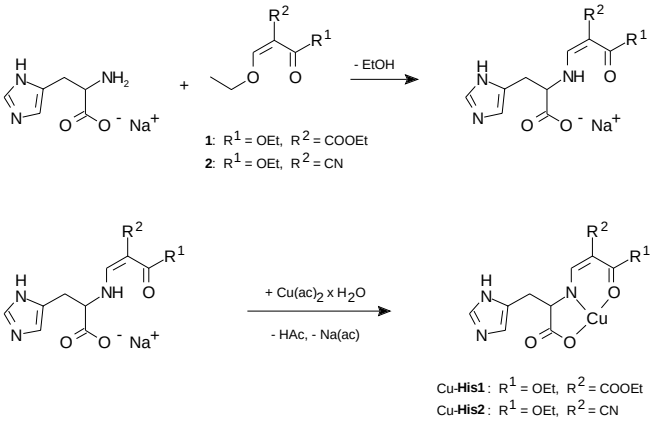
Results and Discussion

Syntheses

The β-ketoenoles or their enolethers of the general type B (scheme 1) react with all sufficiently basic primary amines yielding the corresponding enamines in a strongly exergonic and nearly quantitative reaction. This is a special advantage in comparison with (unsymmetrically substituted) β-diketones or aromatic derivatives (*e.g.* pyridoxal [25]), which often give mixtures of isomers or cyclic condensation products. In the case of amino acids, the *zwitterion* must be converted to the anion to release the basic amino group. Using this procedure, we synthesized the 3-oxo-enamines of *L*-histidine (and subsequently their 1:1 copper complexes) from the enolethers B with the following combinations of substituents R^1/R^2:

Me/COOEt Me/COMe Me/COPh Ph/COOEt OEt/COOEt(**1**) OEt/CN(**2**).

The following discussion will focus on **1** and **2**, because in these cases only the structure of the copper complexes could be solved by X–ray analysis. The condensation of **1** and **2** with the sodium salt of *L*-histidine (scheme 2) also takes place without complications, although these both 3-oxoenolethers are the weakest elec-



Scheme 2 Synthesis of formally tricoordinated copper(II) complexes, derived from 3-oxo-1-enaminates of histidine. The imidazole N<u>H</u> is arbitrarily localized at the δ-N as in the cyclic oligomers of the complexes.

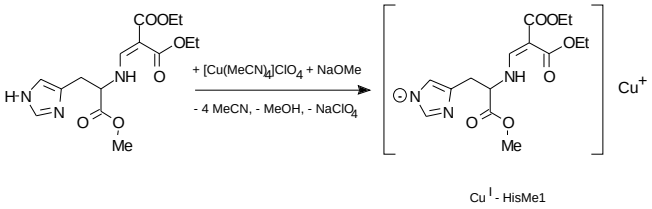
trophiles within the row given above. The free ligands H_2-**His1** and H_2-**His2** can be isolated from aqueous solutions of their hygroscopic sodium salts, NaH-**His1** and NaH-**His2**, by slow addition of an acid. The oily products have not been characterized in detail. The best way to synthesize the pale blue copper complexes Cu-**His1** and Cu-**His2** is the *in situ* condensation of the corresponding 3-oxo-enoles **1** and **2**, respectively, with *L*-histidine in 1:1 mole ratio in presence of an equimolar amount of sodium methoxid in methanol, followed by addition of the equimolar amount of $Cu(ac)_2 \cdot H_2O$ in methanol.

[1]) Similar problems are typical for crystals with high content of solvent molecules [25], *e.g.* metal complexes of oligo- and polypeptides. Because of this uncertainty, the data files have not yet been sent to a data bank. The resolved parts of the structure are, however, doubtless. The present files can be requested from the authors in the meantime.

[2]) Only the doubtless localized atoms are summarized.

The solvent free complex Cu-**His1** is moderately soluble in $HCCl_3$ and alcohols and shows good solubility in coordinating solvents like pyridine and MeIm. The complex Cu-**His2** was obtained as adduct with one molecule water. Drying over P_2O_5 yields the anhydrous derivative. This product takes up reversibly water from air to give the hydrate. All attempts to isolate stable stoichiometric adducts with *N*-bases have failed: Cu-**His1** crystallizes even from *N*-methyl-imidazole without additionally coordinated MeIm, and the crystals of Cu-**His2** with pyridine are only stable in pyridine containing solution or in an atmosphere saturated with pyridine vapour. In dried state, the crystals lose their pyridine rapidly, and afterwards they only contain substoichiometric residues.

To synthesize the copper(I) complex Cu-**HisMe1** of the methylated derivative H-**HisMe1**, the pure free ligand was prepared *via* condensation of *L*-histidine methylester with **1**. Reaction with $[Cu(CH_3CN)_4]ClO_4$ in presence of sodium methoxid in a 1:1:1 mole ratio in methanol under argon leads to Cu-**HisMe1** (scheme 3). The complex is oxidized, and coloured pale green on air.



Scheme 3 Synthesis of a copper(I) complex derived from histidine methyl ester (exact structure unknown).

In contrast to the copper(II) derivatives, the ligand in Cu^{I}-**HisMe1** seems to be deprotonated on the imidazole nitrogen and not on the enamine nitrogen of the tautomeric Schiff base (see formula in scheme 3). The ^1H NMR spectrum of the copper(I) complex shows the enamine proton with the typical coupling pattern of two different neighbouring protons. This is the first example of a complex wherein the enamine function of such a Schiff base-type ligand is not deprotonated.

Structures of Cu-His1 (· solv) and Cu-His2 · 0.5 py (· solv)

The formula units of our copper(II) complexes are closely related to copper complexes derived from Schiff bases of *L*-histidine with salicylaldehyde, 3-(hydroxymethylene)camphor and similar hydroxyaldehydes. The derivatives of salicylaldehyde can be interpreted as a special case of our structures with $R^1 + R^2$ = benzo. Transition metal complexes of such Schiff base ligands derived from various amino acids have been extensively studied for many years [25–31]. A large number of X-ray [27–30] and neutron diffraction [31] studies prove, that the metal atom reaches its normal coordination numbers of 4, 5 or 6 (in a strongly distorted octahedron) either by incorporation of an additional ligand (N-bases [27, 30], water [28–31]) or by intermolecular coordination forming polymeric chains [28, 29] (often stabilized by a network of H-bridges). Presently, however, there are no X-ray analyses of copper complexes with Schiff bases of *L*-histidine (with exception of the cyclic derivative of pyridoxal [25]) – although this amino acid has attracted much attention as part of such structures [26], because it acts as an essential ligand in nearly all copper proteins. We introduce here X-ray structure determination of copper complexes with Schiff base-type ligands derived from *L*-histidine.

The crystals of Cu-**His1** and Cu-**His2** were obtained from *N*-methylimidazole and pyridine, respectively. Surprisingly, even under competition of these strongly donating *N*-bases, both complexes organize into macrocyclic oligonuclear structures (instead of monomeric adducts), which are built from two and four mono-molecular units, respectively. The basic structural motifs are shown in Figures 1 and 2. In both cases, the monomeric building blocks are linked by intermolecular coordination of the ε-nitrogen of histidine.

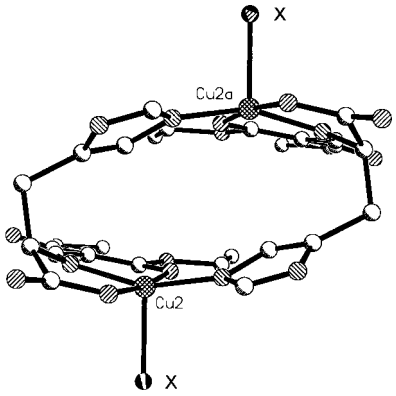


Fig. 1 Dinuclear macrocyclic structure of Cu–**His1**. X is the unknown part of the structure.

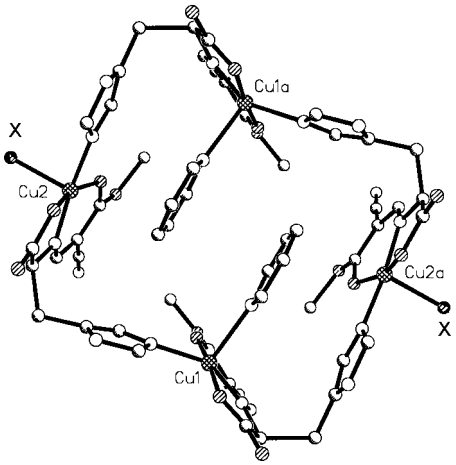


Fig. 2 Tetranuclear macrocyclic structure of Cu–**His2** · 0.5 pyridine. The terminal methyl of the ethoxy substituents could not doubtless been localized and is not given. X is the unknown part of the structure.

Each copper achieves a coordination number five in a strongly distorted square-pyramidal polyhedron by coordination of this histidine-*N*, the typical tridentate [O, N, O]$^{2-}$ donor set of the chelate ligand, and a monodentate ligand X. The identity of this additional ligand could not be proved with certainty in each case. In Cu-**His2**, two of the four copper atoms are coordinated by weakly-bound pyridine molecules, which are directed into the hole of the supramolecular framework (Fig. 2). The metal–donor bond lengths vary between approximately 1.85–1.90 (enamine-*N*), 1.95 (carboxylate-*O*), 2.00 (carbonyl–*O*), 1.98–2.05 (imidazole-*N*) and 2.3–2.4 Å (X; axial pyridine-N). The Cu–Cu distances within the macrocycles amount to 4.8 Å for the dimer of Cu-**His1** and 6.3 (Cu1–Cu2a), 7.1(Cu1–Cu2), 8.4 (Cu1–Cu1a), and 10.4 Cu2–Cu2a) Å for the tetramer of Cu–**His2**.

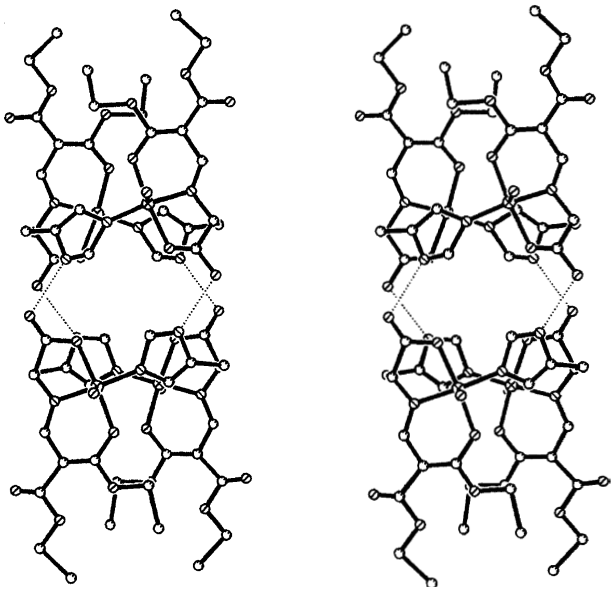


Fig. 3 Stereoview of the H-bridged face-to-face orientation of the two dinuclear units of Cu–**His1**.

In both complexes, the hydrophilic groups are located on one side of the great ring, and the more hydrophobic ethoxy groups of the six-membered chelate ring are on the other side. This orientation leads to a face-to-face dimerization of the macrocycles, assisted by strong H-bridges between the imidazole–NH and the non-coordinated carboxylate–O (O–N-distance 2.75 Å). Figure 3 illustrates this type of dimerization in Cu-**His1**.

The cyclic oligonuclear structures of Cu-**His1** and Cu-**His2** are unlike all known structures of metal complexes with Schiff bases of amino acids. They are, however, closely related to several complexes of dipeptides with histidine. For instance, β-alanyl-histidinato(2-)copper(II) forms a imidazole-bridged cyclic dimer [32] like Cu-**His1**, and the zinc complex of glycylhistidine [33] consists of similar subunits. A cyclic tetranuclear structure like that of Cu-**His2** has been described for a complex derived from glycylhistidine and gold(III) [34].

This similarity is obviously due to the analogy between the peptide group and the enamine function, which can be interpreted as a vinylogous amide. Both are easily deprotonated on complexation. The coordinated terminal amino group of dipeptides is replaced by the coordinated 3-oxo function in our complexes.

Mass spectrometry

Crystals used for structure analyses are the least soluble species under the conditions of the MeIm–toluene system – therefore we cannot exclude that other structure types exist in solution. The complexes Cu-**His1** and Cu-**His2** were investigated in detail by mass spectrometric methods (FAB, ESI) in different solvents. The results are collected in Tab. 1, and typical spectra of Cu-**His1** are documented in Figure 4.

The moderate solubility of Cu-**His1** in $HCCl_3$ and alcohols indicates that an oligomeric structure is more like-

Table 1 Mass spectroscopic data of Cu-**His1** and Cu-**His2**

		Method	*m/z* (intensity in %) [b]
Cu-**His1**	FAB (nba [a])	342.2 (100)	M – 45 + H^+
		775.4 (17)	2 × M + H^+
		1223.4 (67)	4 × M – (7 × 46) + H^+
		1547.6 (76)	4 × M + H^+
	ESI in $HCCl_3/CH_3OH$	813.4 (100)	2 × M + K^+
		1585.4 (32)	4 × M + K^+
	ESI in pyridine	466.3 (100)	M + py + H^+
		504.2 (50)	M + py + K^+
		813.3 (57)	2 × M + K^+
		852.4 (18)	2 × M + py + H^+
		1199.5 (16)	3 × M + K^+
		1585.5 (20)	4 × M + K^+
Cu-**His2**	FAB (nba [a])	– [c]	
	ESI in $HCCl_3/CH_3OH$	– [c]	
	ESI in pyridine	378.5 (93)	M + K^+
		457.2 (100)	M + py + K^+
		717.2 (23)	2 × M + K^+
		1397.5(4)	4 × M + K^+

[a]) nba - nitro-benzylethanol; [b]) data correspond to the most intensive peak of the isotope pattern; [c]) insoluble in the solvent.

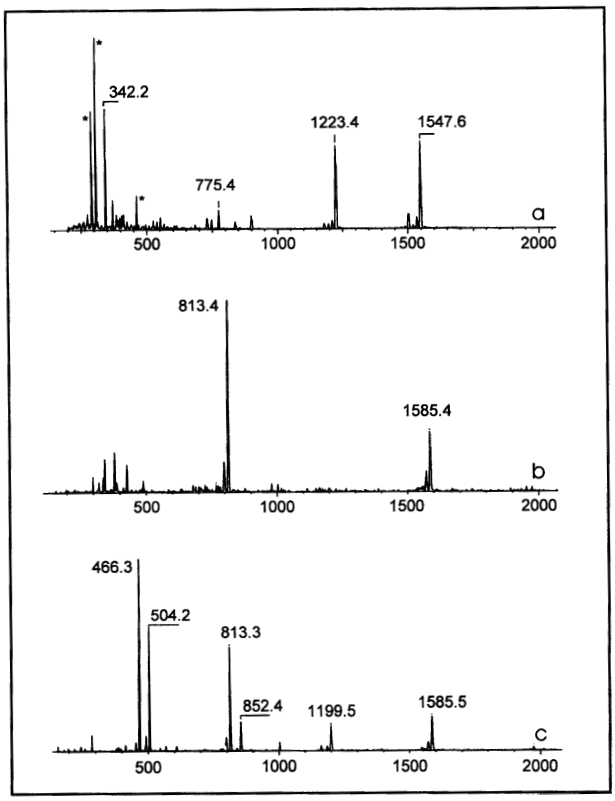


Fig. 4 Mass spectra of Cu-**His1**: a) FAB technique with nitrobenzylalcohol (nba), *signals of nba; b) ESI technique ($HCCl_3$/MeOH); c) ESI technique (pyridine).

ly than a acyclic polymer one. In the FAB spectrum we detected the signals of the tetramer (*m/z* = 1547) or its tetrameric fragments, respectively, with high intensity besides the base peak of the monomeric fragment with M - 45. The signal of the dimer was observed as well. The milder conditions of the ESI technique (in $HCCl_3$/methanol) results in a spectrum with signals of the unfragmented dimer and tetramer (detected as K^+ adducts – cf. experimental part – not with the signal of the monomer. This reflects the crystal structure of the complex, which shows that two cyclic dimers form a tetramer by hydrogen bridges. The good donor pyridine can split and reorganize these structures, hence peaks of the mono pyridine adduct dominate the spectra. Despite this predominance, the signals of the dimer (with and without pyridine), trimer and tetramer were also detected. The signal intensity of the higher oligomers – especially of the trimer, is lower than that of the dimeric structure.

Cu-**His2** is insoluble in weak or non coordinating solvents, therefore a measurement was only possible in pyridine. The presumably polymeric structure is obviously split in this strongly coordinating solvent, and subsequently the oligonuclear cyclic structures can be organized. The peaks of the monomer, the pyridine adduct of the monomer, the dimer, and, with very low intensity, the tetramer were found. The crystallization of the structurally characterized tetramer is probably favoured by solubility effects in the system pyridine/*n*-hexane.

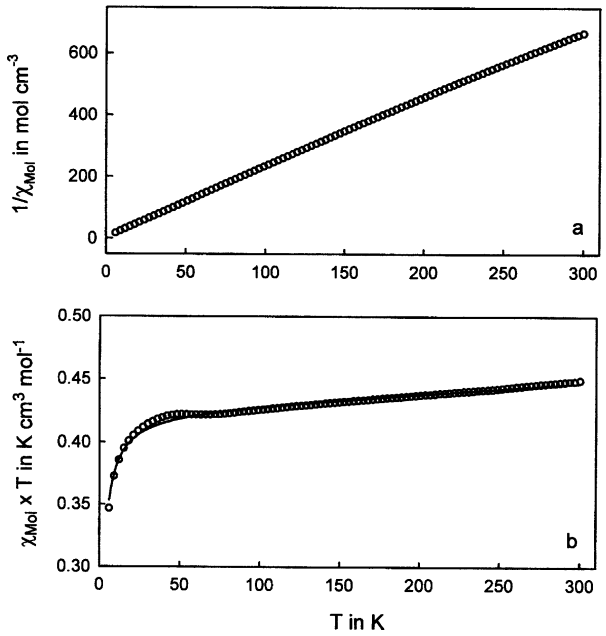


Fig. 5 Magnetic susceptibility of solvent free Cu-**His1**: a) reverse molar susceptibility plotted *versus* temperature. b) $c_M \times T$ plotted versus temperature. The solid line is calculated from a fit of the data to the Curie-Weiss expression considering the temperature independent paramagnetism (TIP).

Magnetic Susceptibility

In the case of the solvent free Cu-**His1**, the magnetic susceptibility was measured from 300 K down to 4 K at a magnetic field of 1 T. Figure 5 depicts the plot $1/\chi_M$ *vs*. *T* (a) and the plot $\chi_M \times T$ *vs*. *T* (b). Both plots show the typical Curie–Weiss behaviour of a copper complex with S = 1/2 ground state (μ_{eff} = 1.92 μ_B at 300 K). The data in plot b were fitted to $\chi_M \times T = (C/(T-\Theta)+\mathrm{TIP}) \times T$ with C = 0.428 Kcm^{-3}mol and Θ = –1.36 K (considering the temperature independent paramagnetism, TIP, of 6×10^{-5} K cm^{-3} mol for Cu [24]). The results give no hints to antiferromagnetic interaction between the copper centers in the oligonuclear structures. This is not surprising because the distances between the copper centers are too great for direct interactions, and the π-conjugation of the ligand is interrupted by the methylene groups of histidine. The slight negative value of the Weiss constant point out the very weak intermolecular interactions in solid state.

EPR-Spectroscopy

The EPR-spectra of the copper(II) complexes in frozen solutions at 77 K show merely one broad signal that occurs for Cu-**His1** in $HCCl_3$ at a surprising low *g*-value: Cu-**His1** ($HCCl_3$) *g* = 2.078; Cu-**His1** (pyridine) *g* = 2.105; Cu-**His2** (pyridine) *g* = 2.115. The typical *g*-val-

ue anisotropy and the hyperfine coupling of the copper nucleus were not found. The observation of only one unresolved signal could be due to the existence of copper centers with different orientation of the coordination polyhedrons in the (cyclic) oligomer or to different but still alike species, *e.g.* pyridine adducts, dimers, trimers or tetramers (*cf.* mass spectrometry), in the solution.

Redox Behaviour

The complexes Cu-**His1** and Cu-**His2** could be studied in pyridine only, since the solubility is too poor in other solvents suitable for cyclovoltammetry . Under these conditions, no reversible $Cu^{II/I}$ reduction could be observed because the Cu(I) disproportionates. However, the isolation of a stable diamagnetic copper(I) complex of the methylester derivative, Cu^{I}-**HisMe1**, supports the assumption that similar histidine-derived copper complexes should have reversible redox behaviour and catalytic activity in reactions with dioxygen. Attempts to optimize the complexes with regard to these properties are under way.

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