Chiral Quadridentate Ligands based on Amino Acids: Template Syntheses and Properties of the Free Ligands and Their Transition-metal Complexes‡

Jozsef Balla,[a] Paul V. Bernhardt,[a] Peter Buglyo,[a] Peter Comba,*,†,[a] Trevor W. Hambley,[b] Reto Schmidlin,[a] Sandra Stebler[a] and Katalin Várnagy[a]

[a] *Institut für Anorganische Chemie, Universität Basel, Spitalstrasse 51 4056 Basel, Switzerland*

[b] *School of Chemistry, University of Sydney, New South Wales 2006, Australia*

The copper(II)-directed condensation of amino acids with formaldehyde and nitroethane has produced new open-chain quadridentate ligands stereoselectively and in generally high yield. The free ligands with pendant amine substituents may be isolated by zinc reduction of the copper(II) complexes. The reactions studied employed optically pure L-amino acids with non-co-ordinating side chains, racemic amino acids with non-co-ordinating side chains, amino acid mixtures and β-amino acids. The quadri- and quinquedentate ligands form very stable complexes with transition-metal ions, with their copper(II) complexes being generally stable down to pH ≈ 1. The isolation and spectroscopic properties (UV/VIS, IR, NMR and EPR) of cobalt(III) and copper(II) complexes of some of the amino acid-based ligands are reported. Condensation of racemic and mixed amino acids led to one out of three possible quadridentate ligands, and this stereoselectivity is interpreted based on a model involving the co-ordination of an organic nitro group. This mechanism is supported by qualitative molecular mechanics calculations. The crystal structures of the condensation products with β-alanine, ([Cu(mnp-β-ala)]·5H_2O (mnp-β-ala = 6-methyl-6-nitro-4,8-diazaundecanedioate), and the Zn–HCl reduction product of the condensation with glycine [Cu(Hampgly)Cl]·2H_2O (ampgly = 5-amino-5-methyl-3,7-diazanonanedioate), have been determined. In the former structure the Cu^{II} is in a distorted trigonal-bipyramidal environment with the fifth site being a co-ordinated carboxylate oxygen from an adjacent molecule, while in the latter Cu^{II} has a square-pyramidal co-ordination with an apical chloride ligand.

Chiral transition-metal complexes are of considerable interest in areas such as a racemate separation, stereoselective catalysis and biomimetic chemistry. In a number of reactions amino acids have been found to be readily available and useful building blocks for the synthesis of chiral ligands.[1–4] We have reported recently examples of stereoselective, copper(II)-directed condensations of chiral bidentate ligands with formaldehyde and nitroethane which afford chiral quadridentate ligands co-ordinated to copper(II) ions **1** in high yield (Scheme 1). The systems reported so far are based on glycine, L-alanine, D,L-alanine, L-phenylalanine[5] and the amino acid derivative 2-(*S*)-aminomethylpyrrolidine,[6] where, in addition to the copper(II) complexes, the metal-free nitro-substituted ligands H_2mnpama were isolated, but shown to be unstable as free bases. In solutions of the copper(II) species [Cu(mnpama)] **1** and [Cu(ampama)] **2** with condensed glycine and glycine–L-alanine mixtures we observed the formation of dimeric species in equilibrium with the respective monomers, and the solution structure of these weakly coupled dinuclear copper(II) complexes has been solved with a combination of EPR spectroscopy, spectra simulations and molecular mechanics calculations.[7]

We present now details of the template syntheses of [Cu(mnpama)] **1**, based on an additional optically pure L-amino acid with a non-co-ordinating side chain (L-valine), racemic amino acids with non-co-ordinating side chains (D,L-phenylalanine, D,L-valine, D,L-leucine and, D,L-3-methylvaline), mixed amino acids (glycine–L-alanine) and β-amino acids (β-alanine and D,L-3-aminobutyric acid). Also discussed are the reduced amino-substituted products [Cu(ampama)] **2**. The ligands H_2ampama have been characterized spectroscopically and by the co-ordination of (*S*),(*S*)-ampala to Co^{III}. The copper complexes [Cu(mnpama)] **1** and [Cu(ampama)] **2** exhibit high stability for acyclic complexes, and their properties are discussed based on their solution spectra. Also reported are the crystal structures of the distorted trigonal-bipyramidal complex [Cu(mnp-β-ala)]·5H_2O (mnp-β-ala = 6-methyl-6-nitro-4,8-diazaundecanedioate) and the square-pyramidal complex [Cu(Hampgly)Cl]·2H_2O (ampgly = 5-amino-5-methyl-3,7-diazanonanedioate).

Of some interest is the fully selective formation of one out of three possible isomers resulting from the template condensation of racemic and mixed amino acids.[5] Some, but not full, selectivity has been reported in a similar condensation using $[Cu(en)_2]^{2+}$ (en = 1,2-diaminoethane).[8] Based on the thoroughly studied example involving D,L-alanine, a mechanism is proposed which involves the co-ordination of the nitro group of $CH_3CH_2NO_2$ to copper(II), and this is supported by independent structural data on copper(II) complexes with similar ligand systems[9] and qualitative molecular mechanics calculations.

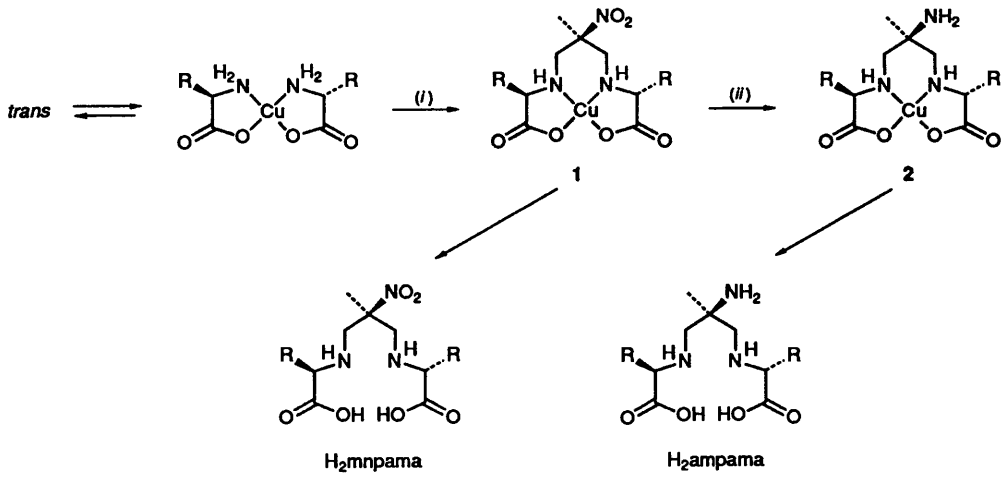
Experimental

Materials.—All reagents were of analytical purity used as purchased. **CAUTION**: Although we never have experienced any problems, perchlorate salts are potentially explosive.

Syntheses.—Template condensation. The condensation products [Cu(mnpama)] **1** were obtained essentially as reported[5]

† *Present address:* Anorganisch-Chemisches Institut, Universität Heidelberg, im Neuenheimer Feld 270, 6900 Heidelberg, Germany.

‡ *Supplementary data available:* see Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1993, Issue 1, pp. xxiii–xxviii.



Scheme 1 (*i*) CH_2O, $EtNO_2$, base; (*ii*) Zn, HCl, Cu^{2+}, base

for [Cu(mnpgly)] (mnpgly = 5-methyl-5-nitro-3,7-diazanonanedioate), [Cu{(*S,S*)-mnpala}]·H_2O [(*S,S*)-mnpala = (2*S*,8*S*)-2,5,8-trimethyl-5-nitro-3,7-diazanonanedioate), [Cu{(*R,S*)-mnpala}]·H_2O [(*R,S*)-mnpala = (2*R*,8*S*)-2,5,8-trimethyl-5-nitro-3,7-diazanonanedioate) and [Cu{(*S,S*)-mnpphe}]·H_2O [(*S,S*)-mnpphe = (2*S*,8*S*)-2,8-dibenzyl-5-methyl-5-nitro-3,7-diazanonanedioate].

For the above and the following compounds the copper(II) bis-(amino acid) complexes were refluxed for 5 h in methanolic solution with 4 equivalents of triethylamine, 1 equivalent of nitroethane and 2 equivalents of formaldehyde. Variations included the use of an excess of reagents (two-fold) in the case of the β-amino acids and the isolation of all the products by crystallization. The racemic and mixed amino acid condensation products are far less soluble than the analogues with optically pure amino acids, and recrystallization from hot saturated aqueous solutions for the less-soluble racemic amino acids or chromatography {medium-pressure liquid chromatography MPLC [2 bar (2 × 10^5 Pa)], Silica gel 60, ethanol–acetone (1 : 1)} may be performed if desired. The products were characterized spectroscopically [IR (NO_2 stretching at ≈1550 (ν_{asym}) and ≈1360 cm^{-1} (ν_{sym})], VIS and EPR, see Table 6], by elemental analyses and (in some cases, see below) by X-ray analysis and by isolation and NMR spectroscopy of the metal-free ligands (nitro- and corresponding amino-derivatives).

[Cu{(*S,S*)-mnpval}]·5H_2O [(*S,S*)-mnpval = (2*S*,8*S*)-2,8-diisopropyl-5-methyl-5-nitro-3.7-diazanonanedioate]; yield 5% (Found: C, 34.5; H, 5.8; N, 8.9. Calc. for $C_{14}H_{35}CuN_3O_{11}$: C, 34.1; H, 7.3; N, 8.7%). [Cu{(*R,S*)-mnpphe}]·0.5H_2O [(*R,S*)-(mnpphe = (2*R*,8*S*)-2,8-dibenzyl-5-methyl-5-nitro-3,7-diazanonanedioate]: yield 61% (Found: C, 52.9; H, 5.1; N, 8.4. Calc. for $C_{22}H_{24}CuN_3O_{6.5}$: C, 52.9; H, 5.2; N, 8.4%). [Cu{(*R,S*)-mnpval}]·3H_2O [(*R,S*)-mnpval = (2*R*,8*S*)-2,8-diisopropyl-5-methyl-5-nitro-3,7-diazanonanedioate]: yield 22% (Found: C, 37.1; H, 6.3; N, 9.3. Calc. for $C_{22}H_{29}CuN_3O_9$: C, 37.6; H, 6.5; N, 9.4%). [Cu{(*R,S*)-mnpleu}]·4H_2O [(*R,S*)-mnpleu = (2*R*,8*S*)-5-methyl-2,8-bis(2-methylpropyl)-5-nitro-3,7-diazanonanedioate]: Yield 34% (Found: C, 42.9; H, 7.0; N, 9.2. Calc. for $C_{22}H_{27}CuN_3O_{10}$: C, 42.0; H, 7.0; N, 9.2%). [Cu{(*R,S*)-mnptleu}]·H_2O [(*R,S*)-mnptleu = (2*R*,8*S*)-2,8-bis(1,1-dimethylethyl)-5-methyl-5-nitro-3,7-diazanonanedioate]: Yield 34% (Found: C, 44.2; H, 6.9; N, 9.7. Calc. for $C_{22}H_{25}CuN_3O_7$: C, 43.7; H, 6.8; N, 9.6%). [Cu{(*S*)-mnpglyala}]·2H_2O [(*S*)-mnpglyala = (2*S*)-2,5-dimethyl-5-nitro-3,7-diazanonanedioate]: yield 42% (Found: C, 30.0; H, 5.4; N, 11.5. Calc. for $C_9H_{19}CuN_3O_8$: C, 30.0; H, 5.3; N, 11.6%). [Cu(mnp-β-ala)]·5H_2O: yield 46% (Found: C, 28.1; H, 6.3; N, 9.1. Calc. for $C_{10}H_{27}CuN_3O_{11}$: C, 28.0; H, 6.3; N, 9.8%). [Cu{(*R,S*)-mnpaba}]·0.5H_2O [(*R,S*)-mnpaba = (3*R*,9*S*)-3,6,9-trimethyl-6-nitro-4,8-diazaundecanedioate]: yield 28% (Found: C, 38.6; H, 5.8; N, 11.4. Calc. for $C_{12}H_{22}CuN_3O_{6.5}$: C, 38.3; H, 5.9; N, 11.2%).

Metal-free ligands and nitro-reduction products. Some metal-free nitro-substituted ligands H_2mnpama were isolated as described earlier,[5] *via* precipitation of Cu^{2+} with $[Fe(CN)_6]^{4-}$ in acidic aqueous solution followed by isolation of the hydrochloride salt of the ligand after chromatographic purification (Dowex 1 × 2) of the solution. The ligands based on racemic amino acids [(*S,R*) isomer, see Scheme 2] have potential C_s symmetry whereas both the ligands based on optically pure amino acids and on amino acid mixtures are asymmetrical, thus isomeric purity may therefore be tested by ^{13}C NMR spectroscopy. The entire reaction mixture from the condensation leading to [Cu{(*R,S*)-mnpala}] was treated as above and the solution containing the metal-free ligand and side products was analysed by ^{13}C NMR spectroscopy. The NMR data for all nitro-substituted metal-free ligands are in Table 1.

Reduction of the pendant NO_2 group was generally achieved by addition of 10 equivalents of zinc powder to a warm aqueous solution of [Cu(mnpama)] **1**. After 0.5 h of vigorous stirring the decolourized solution was filtered, and addition of an excess (two-fold) of $Cu(NO_3)_2$·3H_2O afforded a blue solution of [Cu(ampama)] **2**. The solution was diluted (water, *ca.* 20-fold), the pH adjusted to ≈3 (protonation of the pendant amine), and then sorbed onto a column of SP-Sephadex C25 cation-exchange resin. The pure complexes were eluted with NaCl or $NaClO_4$ (0.1 mol dm^{-3}) and precipitated as chloride or perchlorate salts, respectively.

[Cu(Hampgly)]Cl·2H_2O: yield 21% (Found: C, 27.2; H, 5.7; Cl, 10.0; N, 12.0. Calc. for $C_8H_{20}ClCuN_3O_6$: C, 27.2; H, 5.7; Cl, 10.0; N, 11.9%). [Cu{(*S,S*)-Hampala}]ClO_4·1.5H_2O [(*S,S*)-ampala = (2*S*,8*S*)-5-amino-2,5,8-trimethyl-3,7-diazanonanedioate]: yield 29% (Found: C, 27.9; H, 5.3; Cl, 8.6; N, 10.0. Calc. for $C_{10}H_{23}ClCuN_3O_{9.5}$: C, 27.5; H, 5.3; Cl, 8.1, N, 9.6%). [Cu{(*R,S*)-Hampala}]Cl·2H_2O [(*R,S*)-ampala = (2*R*,8*S*)-5-amino-2,5,8-trimethyl-3,7-diazanonanedioate]:yield 21% (Found: C, 31.9; H, 6.6; Cl, 8.7; N, 10.8. Calc. for $C_{10}H_{24}ClCuN_3O_6$: C, 31.5; H, 6.3; Cl, 9.3; N, 11.0%). [Cu{(*S,S*)-Hampphe}]ClO_4·2H_2O [(*S,S*)-ampphe = (2*S*,8*S*)-5-amino-2,8-dibenzyl-5-methyl-3,7-diazanonanedioate]: yield 19% (Found C, 43.9; H, 5.6; Cl, 6.1; N, 6.8. Calc. for $C_{22}H_{32}ClCuN_3O_{10}$: C, 44.2; H, 5.4; Cl, 5.9; N, 7.0%).

The hydrochloride salts of the amine-substituted metal-free ligands H_2ampama were prepared from the purified $[Cu(Hampama)]^+$ complexes. After addition of an excess (10-fold) of Zn to warm aqueous solutions of the complexes the decolourized solutions were filtered after 0.5 h. The Zn^{2+} was removed as $Zn(OH)_2$ at pH 7, and the solutions were then diluted (water) and the pH adjusted to 3. These solutions were sorbed onto a column of SP-Sephadex C25 cation-exchange resin to remove

further Zn^{2+}, and the metal-free ligands were then eluted with water at pH ≈3. The aqueous solutions of H_2ampama were evaporated under reduced pressure, and the solid dissolved in methanol. Free H_2ampama hydrochloride salts were isolated by addition of small amounts of HCl and diethyl ether. The ^{13}C NMR resonances are presented in Table 1.

The complex [Co{(*S*,*S*)-ampala}(OH)]·2H_2O was obtained by air oxygenation (12 h) of an aqueous solution (200 cm^3, pH 7) containing (*S*,*S*)-H_2ampala·HCl (2.49 g, 8.86 mmol), $CoCl_2$·6H_2O (3.55 g, 14.9 mmol) and charcoal (1 g). After filtration, the resulting red solution was passed over a column charged with SP Sephadex C25 (Na^+ form), and the major red band did not show any retention (no retention was observed on an anion-exchange column either). The aqueous solution was evaporated to near dryness to afford a purple solid (0.83 g, 2.3 mmol, 26%) (Found: C, 33.4; H, 6.4; Cl, 0.9; N, 11.9. Calc. for $C_{10}H_{24}CoN_3O_7$: C, 33.6; H, 6.5; Cl, 0.0; N, 11.8%). Electronic spectrum (water, pH 3): ν_{max} 19 250 (214) and 27 400 cm^{-1} (ε 187 dm^3 mol^{-1} cm^{-1}).

Measurements and Calculations.—The UV/VIS/NIR spectra were recorded on a Cary 2300 or on a Hewlett-Packard 8450A spectrophotometer, and IR spectra (KBr pellets) on a Perkin Elmer FTIR 1600 instrument. The EPR spectra [dimethylformamide–water (1:2), 298 or 77 K] were obtained with a Varian E9 spectrometer fitted with a E101 microwave bridge, a variable-temperature control unit, a Bruker ER035 Gaussmeter and a Marconi Instruments 2440 microwave counter. The spectra were analysed by simulations with EPR50F.[10] Proton-decoupled ^{13}C NMR spectra were measured on a Varian GEMINI 300 instrument at 75 MHz with dioxane or sodium 3-trimethylsilyltetradeuteriopropionate, as internal standard. A Büchi 681 chromatography system was used for MPLC. Microanalyses were obtained from Ciba-Geigy, Basel.

Molecular mechanics calculations involved the generation of trial coordinates with the molecular graphics package SMILE[11] and subsequent refinement of the structures with the strain-energy-minimization program MOMEC-87,[12] using a recently developed force field.[13] Optimized structures were plotted with ORTEP.[14]

Crystal Structure Determinations.—Cell constants for both structures were determined by least-squares fits to the setting parameters of 25 independent reflections, measured and refined on an Enraf-Nonius CAD4F diffractometer employing graphite-monochromated Mo-Kα radiation. Intensity data for [Cu(mnp-β-ala)]·5H_2O {[Cu(Hampgly)Cl]·2H_2O} were collected in the range $1 < \theta < 27.5°$ {$1 < \theta < 25°$}, using an ω {ω–θ} scan mode. The scan width and horizontal counter aperture employed were $1.50 + 0.34 \tan\theta$ {$0.7 + 0.35 \tan\theta$} and $2.70 + 1.05 \tan\theta$ {$2.20 + 1.05 \tan\theta$}, respectively. Data reduction and application of Lorentz, polarization and absorption (maximum 1.181, minimum 1.048 {1.287, 1.170}) corrections were carried out using the Enraf-Nonius Structure Determination Package.[15] The structures were solved by direct methods using SHELXS 86[16] and the solution was extended by Fourier methods with SHELX 76.[17] Hydrogen atoms were included at calculated sites with group isotropic thermal parameters, and all other atoms were refined anisotropically. Scattering factors and anomalous dispersion terms used for Cu were taken from ref. 18 and all others used were those supplied in SHELX 76.[17] The structures were drawn using ORTEP.[14] The atom numbering schemes are given in Figs. 2 and 3, and final atomic coordinates and bond lengths and angles are listed in Tables 2–5.

Additional material available from the Cambridge Crystallographic Data Centre comprises H-atom coordinates and thermal parameters.

Crystal data. [Cu(mnp-β-ala)]·5H_2O. $C_{10}H_{27}CuN_3O_{11}$, M = 428.89, tetragonal, space group $I4_1/a$, a = 20.135(5), c = 18.104(4) Å, U = 7339.9 $Å^3$, Z = 16, D_c = 1.552 g cm^{-3}, μ(Mo-Kα) = 12.15 cm^{-1}, λ(Mo-Kα) = 0.710 69 Å, F(000) = 3600, N = 4575, N_o 1455, h 0–26, k 0–26, l 0–23, R = 0.049, R' = 0.044, $w = 2.27/[\sigma^2(F_o)]$, residual extrema 0.5, −0.4, e $Å^{-3}$.

[Cu(Hampgly)Cl]·2H_2O. $C_8H_{20}ClCuN_3O_6$, M = 353.26, monoclinic space group $P2_1/c$, a = 7.782(2), b = 14.005(3), c = 13.060(2) Å, β = 105.32(2), U = 1372.7 $Å^3$, Z = 4, D_c = 1.709 g cm^{-3}, μ(Mo-Kα) = 18.15 cm^{-1}, λ(Mo-Kα) = 0.710 69 Å, F(000) = 732, N = 2634, N_o = 2312, h −9 to 9, k 0–16, l 0–15, R = 0.024, R' = 0.028, $w = 1.55/[\sigma(F_o) + 0.000\,216F_o^2]$, residual extrema 0.3, −0.2 e $Å^{-3}$.

Results and Discussion

The copper(II)-directed condensation of *cis*-disposed primary amines with formaldehyde and nitroethane has been shown in many cases to be a general and quick method for the preparation of acyclic and macrocyclic mono- and bi-nucleating ligands having primary and secondary amine, pyridyl, hydroxo, carboxylato, thiaether and nitro donors.[8,9,19–23] More recently we have used this template synthesis for the preparation of chiral ligands,[5,6,24] however the nitro-substituted metal-free ligands are notoriously unstable in neutral or basic solution[25] and this clearly is a drawback for their use in co-ordination chemistry. We report here a general method for the isolation of the stable amino-substituted metal-free ligands and their co-ordination chemistry. There are many possible ways to modify the amine substituents of the central carbon atom of the six-membered chelate ring (the cap), and this is preparative chemistry which is currently being studied.[26]

Syntheses.—The yields of the condensation products (not optimized) are generally high and largely dependent on the relative solubilities of the bis(amino acidato)copper(II) starting materials and the condensed products. Reaction in water instead of methanol has been studied in some cases, and leads to appreciable yields of amino acid derivatives without hydrophobic side chains. However, with less-polar amino acids such as L-phenylalanine and L-valine the bis(amino acidato)-copper(II) complexes were not sufficiently soluble in aqueous solution. We have recently shown that the copper(II)-directed condensation of co-ordinated potentially tridentate ligands is also feasible,[27] and the syntheses presented here might therefore be extended to amino acids with co-ordinating side chains.

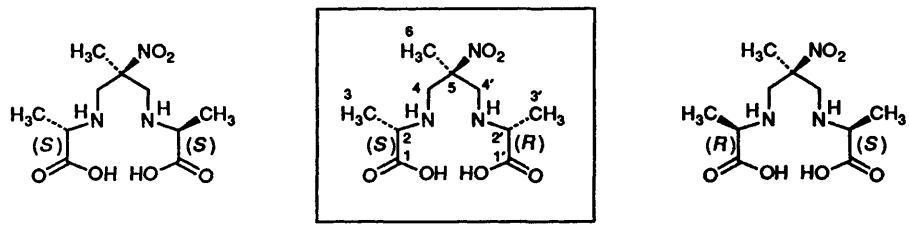
The copper(II) products [Cu(mnpama)] **1** are precipitated from the reaction mixture and purified by recrystallization. The earlier proposed purification of the reaction mixture by ion-exchange chromatography[5] (separation from charged side products) or by MPLC (silica gel) does not improve the yield significantly. The condensation products involving racemic or mixed amino acids are generally much less soluble than the corresponding products with optically pure amino acids. The reason for this is not obvious. The three extant structures [Cu(mnpgly)], [Cu{(*S*,*S*)-mnpala}]·H_2O and [Cu{(*R*,*S*)-mnpala}][5] reveal that the one based on the racemic starting material (D,L-alanine) is six-co-ordinate, with a chain structure resulting from co-ordination by carboxylate oxygen atoms of adjacent molecules in the axial co-ordination sites. In the remaining two structures the copper(II) ion is only five-co-ordinate. This indicates that for products based on optically pure amino acids (and in fact also with the ligand conformation adopted by the glycine condensation product) one axial site is blocked, which effectively discourages the formation of polymeric structures and therefore leads to greater solubility.

In the case of [Cu{(*S*,*S*)-mnpala}] it was shown experimentally that the condensation proceeds with full retention of optical purity.[5] This is not surprising in view of the inherently slow kinetics of epimerization of co-ordinated amino acids under the conditions employed in this work.[28] Although stereoretention was not experimentally determined in the other cases, in view of the stereoselective formation of the mixed-ligand isomer of the copper(II) complex (see below), the comparable low solubility and the strikingly different NMR

Table 1 ^{13}C-NMR data of the metal-free ligands mnpama and ampama *

Ligand	1/1'	2/2'	3/3'	4/4'	5	6
H_2mnpgly·2HCl	169.07	51.50		48.71	85.77	19.50
H_2mapgly·3HCl	173.63	50.66		54.84	51.84	21.13
(*S*)-H_2mnpglyala·2HCl	169.09/172.08	52.04/58.00	14.77	49.25/50.50	86.16	20.18
(*S,S*)-H_2mnpala·2HCl	171.78/171.82	57.31/57.35	13.94/13.99	49.87/49.96	85.73	19.41
(*S,S*)-H_2ampala·3HCl	176.38/176.53	58.94/58.94	16.02/16.06	53.09/53.24	52.00	20.92
(*R,S*)-H_2mnpala·2HCl	171.73	57.51	14.01	49.98	85.80	19.37
(*R,S*)-H_2ampala·3HCl	176.59	58.87	15.90	53.09	51.63	21.39
(*S,S*)-H_2ampphe·3HCl	172.17/172.97	62.38	32.24/32.98 127.80/127.86; 129.06/129.22; 129.45/129.53; 134.54/134.67	53.04/53.20	53.19	19.48

* For atom numbering see Scheme 2; for abbreviations see Experimental section.



Scheme 2

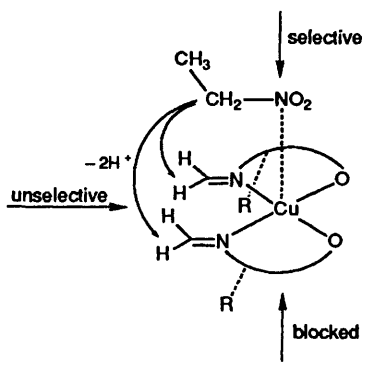


Fig. 1 Model for the stereoselective formation of [Cu(mnpama)] with racemic amino acids or amino acid mixtures. The drawing is general for the various mechanistic possibilities given in the text

characteristics of the metal-free ligands (Table 1), it seems unlikely that any racemization would have remained undetected in the isolated free ligands.

Stereoselectivity.—The copper(II)-directed condensation of mixed amino acids (including racemic amino acids and also other chiral bidentate ligands[6]) with formaldehyde and nitroethane leads with 100% selectivity to one out of the three possible isomers (Scheme 2). A comparison of physical properties [solubility of the copper(II) complexes and NMR spectra of the metal-free ligands] of the mixed-ligand products with those obtained of the corresponding pure ligands indicated that mixed-ligand species were formed. From the crystal structure of [Cu{(*R,S*)-mnpala}]·H_2O it emerged that the selectively formed product has the amino acid substituents oriented *anti* to the nitro substituent of the six-membered chelate ring [(*S,R*) isomer].[5]

The fact that the only condensation product detected in the case of [Cu(mnpala)], starting with racemic alanine, was [Cu{(*R,S*)-mnpala}] (crystallized product *and* filtrate) indicated that the stereoselectivity is not merely due to removal of the least-soluble product from a reaction mixture. The observed stereoselectivity must then occur during the condensation reaction. Here, the nitroethane anion attacks the co-ordinated imines or carbinolamines,[29] formed *via* reaction of two formaldehyde molecules with two *cis*-disposed deprotonated amines, and, in case of the imine intermediate, *via* subsequent elimination of water.[19] With racemic amino acids, one side of the chromophore of the bis(imine) intermediate is blocked (see Fig. 1). This must lead to some stereoselectivity if nitroethane is oriented towards the chromophore. This implicates the involvement of an intermediate in the mechanism, which exhibits a co-ordinated nitro group in the axial site *anti* to the amino acid substituents. Co-ordination of organic nitro groups to copper(II) has been shown experimentally in crystal structures involving fragments similar to the ones discussed here,[9] and it was also implied by IR spectroscopy.[30–32] The fact that the only product detected upon condensation of a 1:1 L-alanine–glycine mixture was [Cu(mnpglyala)], indicates that a minimum of one methyl is enough to block one face of the bis(imine) intermediate.

The proposed mechanism is supported by molecular mechanics calculations. We stress that these results can only be of qualitative nature since the reaction sequence leading to the condensation product is not exactly known. That is, there is no way to decide whether the stereoselectivity results from the condensation of a co-ordinated molecule of nitroethane with both imines or carbinolamines or from the reaction of an uncoordinated molecule of nitroethane with one co-ordinated imine or carbinolamine function followed by co-ordination of the nitro group in this intermediate and subsequent stereoselective ring closure. Owing to these ambiguities we decided to study the stability of the final copper(II) complex with a co-ordinated nitro group common to all the possibilities. Three possible structures were included in the calculations, one leading to (*R,R*)/(*S,S*)-type ligands and the others to the two possible mixed-ligand isomers (*S,R*) and (*R,S*), respectively. The calculated structure leading to the observed species [(*S,R*) isomer] was more stable than that calculated for the formation of an (*R,R*)/(*S,S*)-product mixture, and the structure leading to the other mixed-ligand species (*R,S*) was less stable again. This is supportive of the proposed mechanism.

The proposed mechanism for the stereoselective template condensation, involving co-ordination of the nitroethane anion substrate, is further supported by the fact that the stereoselectivity is reduced in the presence of species competing for axial co-ordination at the copper(II) intermediates:

Table 2 Positional parameters (× 10^4) for [Cu(mnp-β-ala)]·5H_2O

Atom	x	y	z
Cu	2183(1)	4674(1)	7895(1)
O(1)	1769(3)	4968(3)	83(3)
O(2)	2174(3)	4843(3)	8976(3)
C(1)	1709(4)	5019(4)	9414(4)
C(2)	1068(4)	5289(4)	9103(5)
C(3)	1064(4)	5492(5)	8302(5)
N(1)	1236(3)	4944(3)	7788(4)
C(4)	747(4)	4411(4)	7824(5)
C(5)	831(4)	3847(4)	7266(5)
C(6)	1500(4)	3515(4)	7259(5)
N(2)	2073(3)	3964(3)	7112(4)
C(7)	2684(4)	3550(4)	7023(5)
C(8)	3282(4)	3982(4)	6842(5)
C(9)	3505(4)	4430(4)	7461(5)
O(3)	3131(3)	4514(3)	8025(3)
O(4)	4054(3)	4702(3)	7404(4)
N(3)	682(4)	4100(5)	6478(5)
O(5)	679(4)	3692(4)	5993(4)
O(6)	556(4)	4691(4)	6393(4)
C(10)	304(5)	3319(5)	7436(6)
O(7)	4413(5)	−93(6)	4099(5)
O(8)	4195(5)	3800(5)	1685(5)
O(9)	520(4)	4002(4)	2669(5)
O(10)	944(4)	2230(4)	1318(6)
O(11)	1197(7)	2525(8)	2877(8)
O(11′)	3695(35)	2184(33)	1903(41)
O(12)	4800(23)	2045(22)	1622(25)

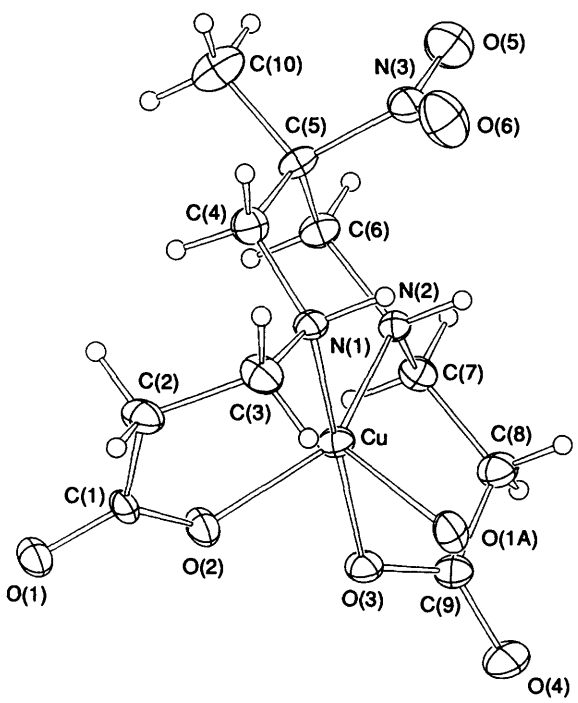


Fig. 2 An ORTEP plot of [Cu(mnp-β-ala)]·5H_2O from the crystal structure analysis

condensation of $[Cu(en)_2]^{2+}$ with formaldehyde and nitroethane leads in aqueous methanol to a mixture of macrocyclic products with the fused nitro substituents in a *trans* (80) or *cis* (20%) orientation.[8] Under strictly anhydrous conditions the observed stereoselectivity is 100%.

A similar face selectivity with this and other asymmetrical and chiral quadridentate ligands, based on various amino acid mixtures, might lead to stereoselective co-ordination of substrates to the corresponding four- or five-co-ordinated transition-metal complexes, and to stereoselective reactions on the co-ordinated substrates, and these ideas are being pursued.

Table 3 Bond lengths (Å) and angles (°) for [Cu(mnp-β-ala)]·5H_2O

O(1A)–Cu	2.275(5)	O(2)–Cu	1.986(6)
N(1)–Cu	1.992(6)	N(2)–Cu	2.025(6)
O(3)–Cu	1.950(5)	C(1)–O(1)	1.222(9)
C(1)–O(2)	1.277(9)	C(2)–C(1)	1.508(11)
C(3)–C(2)	1.508(12)	N(1)–C(3)	1.485(10)
C(4)–N(1)	1.457(9)	C(5)–C(4)	1.529(11)
C(6)–C(5)	1.504(10)	N(3)–C(5)	1.543(12)
C(10)–C(5)	1.533(11)	N(2)–C(6)	1.491(9)
C(7)–N(2)	1.494(9)	C(8)–C(7)	1.522(11)
C(9)–C(8)	1.507(11)	O(3)–C(9)	1.281(10)
O(4)–C(9)	1.238(10)	O(5)–N(3)	1.203(9)
O(6)–N(3)	1.226(9)		
O(2)–Cu–O(1A)	95.0(2)	N(1)–Cu–O(1A)	87.9(2)
N(1)–Cu–O(2)	92.3(2)	N(2)–Cu–O(1A)	120.9(2)
N(2)–Cu–O(2)	144.1(3)	N(2)–Cu–N(1)	91.1(2)
O(3)–Cu–O(1A)	86.4(2)	O(3)–Cu–O(2)	85.3(2)
O(3)–Cu–N(1)	173.6(3)	O(3)–Cu–N(2)	94.3(2)
C(1)–O(2)–Cu	131.8(5)	C(2)–C(1)–O(2)	119.7(7)
O(1)–C(1)–O(2)	121.3(7)	O(1)–C(1)–C	119.0(8)
C(3)–C(2)–C(1)	117.5(7)	N(1)–C(3)–C(2)	113.6(8)
C(3)–N(1)–Cu	111.3(5)	C(4)–N(1)–Cu	116.2(5)
C(4)–N(1)–C(3)	111.2(7)	C(5)–C(4)–N(1)	116.2(7)
C(6)–C(5)–C(4)	115.8(7)	N(3)–C(5)–C(4)	110.1(7)
N(3)–C(5)–C(6)	108.3(7)	C(10)–C(5)–C(4)	107.8(7)
C(10)–C(5)–C(6)	108.2(7)	C(10)–C(5)–N(3)	106.3(7)
N(2)–C(6)–C(5)	115.1(7)	C(6)–N(2)–Cu	112.8(5)
C(7)–N(2)–Cu	112.3(5)	C(7)–N(2)–C(6)	108.5(6)
C(8)–C(7)–N(2)	110.8(6)	C(9)–C(8)–C(7)	114.7(7)
O(3)–C(9)–C(8)	119.7(8)	O(4)–C(9)–C(8)	118.1(8)
O(4)–C(9)–O(3)	112.2(9)	C(9)–O(3)–Cu	120.1(5)
O(5)–N(3)–C(5)	116.8(9)	O(6)–N(3)–C(5)	118.5(8)
O(6)–N(3)–O(5)	124.7(9)		

The complexes [Cu(mnpglyala)] and [Cu(Hampglyala)]$^+$ are, apart from the glycine-based condensation products, the only species for which dinuclear copper(II) complexes have been observed in solution, and this is a result which also has been supported by molecular mechanics calculations.[7]

Molecular Structures.—[Cu(mnp-β-ala)]·5H_2O. The structure of [Cu(mnp-β-ala)]·5H_2O defines the chromophore as distorted trigonal bipyramidal. A drawing of the complex with the atom numbering scheme appears in Fig. 2, and selected bond lengths and angles are given in Table 3. The amine nitrogen of one β-alanine subunit and the carboxylate oxygen of the other occupy the axial positions with a N–Cu–O angle of 173.6°. The remaining two ligand donor atoms, together with a carboxylate oxygen atom from an adjacent molecule, define the trigonal plane. The copper(II) centre is displaced from this plane by 0.02 Å. The trigonal angle involving the two oxygen ligands is compressed to 95°, while that defined by the copper(II) and the oxygen and nitrogen atoms of the co-ordinated mnp-β-ala is expanded to 144°. The axial bonds are significantly shorter than those in the trigonal plane: Cu–N (axial/in-plane) 1.992/2.025; Cu–O (axial/in-plane) 1.950/1.992 Å.

[Cu(Hampgly)Cl]·2H_2O. The molecular structure of [Cu(Hampgly)Cl] with the atom numbering scheme is presented in Fig. 3, and selected bond lengths and angles are collected in Table 5. The co-ordination geometry of the copper(II) chromophore is square pyramidal with the metal displaced by 0.18 Å from the CuN_2O_2 plane towards the apical chloride. The structure is, as expected, very similar to those of [Cu(mnpama)] with ama = gly, (*S*,*S*)-ala and (*R*,*S*)-ala[5] (Cu–N_{av} 1.994 *vs.* 1.986, Cu–O_{av} 1.958 *vs.* 1.923, Cu–(axial ligand) 2.630 *vs.* 2.651 Å).

Solution Spectroscopy of the Copper(II) Complexes.—Spectroscopic data for [Cu(mnpama)] **1** and [Cu(ampama)] **2** are given in Table 6. The d–d and EPR spectra for all [Cu(mnpama)] and [Cu(ampama)] complexes involving α-

Table 4 Positional parameters (× 10^4) for [Cu(Hampgly)Cl]·$2H_2O$

Atoms	*x*	*y*	*z*
Cu	4 077(1)	9 676(1)	1 549(1)
Cl	6 298(1)	9 420(1)	3 433(1)
O(1)	2 999(2)	8 401(1)	1 374(1)
O(2)	830(2)	7 563(1)	1 753(1)
O(3)	5 984(2)	9 327(1)	902(1)
O(4)	8 383(2)	9 928(1)	531(1)
N(I)	1 919(2)	10 032(1)	2 006(1)
N(2)	4 838(2)	11 017(1)	1 382(1)
N(3)	2 615(3)	2 555(1)	2 999(2)
C(1)	1 737(3)	8 301(2)	1 806(2)
C(2)	1 393(3)	9 147(2)	2 458(2)
C(3)	2 064(3)	10 861(2)	2 713(2)
C(4)	2 635(3)	11 761(2)	2 217(2)
C(5)	4 574(3)	11 717(2)	2 163(2)
C(6)	6 712(3)	10 961(2)	1 339(2)
C(7)	7 086(3)	10 007(2)	887(2)
C(8)	1 338(3)	12 034(2)	1 173(2)
O(5)	5 167(3)	7 986(2)	5 034(2)
O(6)	1 923(3)	6 312(2)	209(2)

Table 5 Bond lengths (Å) and angles (°) for [Cu(Hampgly)Cl]·$2H_2O$

Cl–Cu	2.630(1)	O(1)–Cu	1.960(1)
O(3)–Cu	1.955(1)	N(1)–Cu	1.988(2)
N(2)–Cu	1.999(2)	C(1)–Cu	2.730(2)
C(7)–Cu	2.742(2)	C(1)–O(1)	1.263(3)
C(1)–O(2)	1.243(3)	C(7)–O(3)	1.285(3)
C(7)–O(4)	1.223(3)	C(2)–N(1)	1.476(3)
C(3)–N(1)	1.469(3)	C(5)–N(2)	1.469(3)
C(6)–N(2)	1.476(3)	C(4)–N(3)	1.513(3)
C(2)–C(1)	1.524(3)	C(4)–C(3)	1.536(3)
C(5)–C(4)	1.530(3)	C(8)–C(4)	1.515(3)
C(7)–C(6)	1.519(3)		
O(1)–Cu–Cl	98.1(0)	O(3)–Cu–Cl	89.1(0)
O(3)–Cu–O(1)	94.1(1)	N(1)–Cu–Cl	98.7(1)
N(1)–Cu–O(1)	84.0(1)	N(1)–Cu–O(3)	172.1(1)
N(2)–Cu–Cl	95.1(1)	N(2)–Cu–O(1)	166.7(1)
N(2)–Cu–O(3)	84.6(1)	N(2)–Cu–N(1)	95.5(1)
C(1)–O(1)–Cu	114.0(1)	C(7)–O(3)–Cu	114.0(1)
C(2)–N(1)–Cu	104.7(1)	C(3)–N(1)–Cu	117.1(1)
C(3)–N(1)–C(2)	113.3(2)	C(5)–N(2)–Cu	116.8(1)
C(6)–N(2)–Cu	106.2(1)	C(6)–N(2)–C(5)	112.5(2)
O(2)–C(1)–O(1)	124.3(2)	C(2)–C(1)–O(1)	115.8(2)
C(2)–C(1)–O(2)	119.8(2)	C(1)–C(2)–N(1)	108.7(2)
C(4)–C(3)–N(1)	111.5(2)	C(3)–C(4)–N(3)	105.2(2)
C(5)–C(4)–N(3)	104.3(2)	C(5)–C(4)–C(3)	112.6(2)
C(8)–C(4)–N(3)	107.4(2)	C(8)–C(4)–C(3)	112.9(2)
C(8)–C(4)–C(5)	113.6(2)	C(4)–C(5)–N(2)	112.3(2)
C(7)–C(6)–N(2)	110.7(2)	O(4)–C(7)–O(3)	124.0(2)
C(6)–C(7)–O(3)	116.7(2)	C(6)–C(7)–O(4)	119.3(2)

amino acids are very similar to each other, and typical for a square-planar CuN_2O_2 co-ordination geometry with one or two weakly bound axial ligands. This is in agreement with the known crystal structures of [Cu(mnpgly)], [Cu{(*S*,*S*)-mnpala}] and [Cu{(*R*,*S*)-mnpala}]·H_2O[5] and of [Cu(Hampgly)Cl]·$2H_2O$. The chromophores of the dinuclear species [{Cu(mnpgly}$_2$], [{Cu(ampgly)}$_2$], [{Cu(mnpglyala)}$_2$] and [{Cu(ampglyala)}$_2$] are also similar, and this is in agreement with molecular mechanics calculations.[7]

The two complexes with co-ordinated condensed β-amino acids, [Cu(mnp-β-ala)] and [Cu{(*R*,*S*)-mnpaba}], show a marked red shift of their d–d maxima relative to the α-amino acid analogues, and a significant reduction of the hyperfine coupling constant $A_{\|}$. This implies an appreciable distortion of the central chromophore. Based on the structural and spectroscopic properties of a series of copper(II) complexes with N_4 macrocyclic ligands of varying hole sizes,[9,33] a tetrahedral distortion of the CuN_2O_2 core accompanying the change from a

Table 6 Spectroscopic data of the copper(II) complexes of nitro- and amino-capped amino acids

	$g_{\|}$	$g_{\perp}$	$A_{\|}$/ 10^{-4} cm^{-1}	$A_{\perp}$/ 10^{-4} cm^{-1}	$\tilde{\nu}_{VIS}$/ cm^{-1}
[Cu(mnpgly)]*					16 200
[Cu(Hampgly)]$^+$*					16 100
[Cu{(*S*)-mnpglyala}]*					16 300
[Cu{(*S*,*S*)-mnpala}]	2.24	2.06	194	22	16 700
[Cu{(*S*,*S*)-Hampala}]$^+$	2.24	2.06	192	27	16 400
[Cu{(*R*,*S*)-mnpala}]	2.24	2.05	201	21	16 450
[Cu{(*R*,*S*)-Hampala}]$^+$	2.25	2.07	191	22	15 300
[Cu{(*S*,*S*)-mnpphe}]	2.24	2.06	192	20	16 900
[Cu{(*S*,*S*)-Hampphe}]$^+$	2.24	2.06	189	18	16 340
[Cu{(*R*,*S*)-mnpphe}]	2.23	2.05	196	19	15 800
[Cu{(*S*,*S*)-mnpval}]	2.23	2.05	196	18	15 430
[Cu{(*R*,*S*)-mnpval}]	2.23	2.05	202	20	15 340
[Cu{(*R*,*S*)-mnpleu}]	2.25	2.06	189	22	16 300
[Cu{(*R*,*S*)-mnptleu}]	2.22	2.05	201	18	16 200
[Cu(mnp-β-ala)]	2.29	2.07	174	23	14 800
[Cu{(*R*,*S*)-mnpaba}]	2.27	2.08	178	24	15 000

* In equilibrium with a dinuclear species (see text)

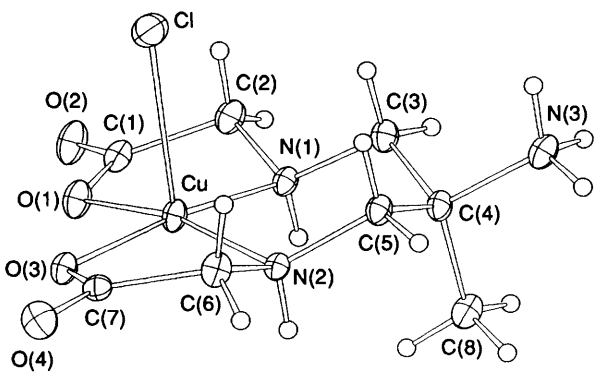


Fig. 3 An ORTEP plot of [Cu(Hampgly)Cl]·$2H_2O$ from the crystal structure analysis

5,6,5- to a 6,6,6-membered chelate ring system was expected. This is also in agreement with the crystal structure of [Cu(mnp-β-ala)]·$5H_2O$, which may be interpreted as monocapped distorted tetrahedral. We believe that the expansion of the N(1)–Cu–O(3) angle, leading to a trigonal-bipyramidal rather than a capped tetrahedrally distorted co-ordination geometry, is due to the steric requirements of the second [Cu(mnp-β-ala)] molecule, bound through its O(1) carboxylate oxygen atom as the fifth ligand to the copper(II) centre. This is supported by molecular mechanics calculations: a five- and a six-co-ordinated species with one or two apical water ligands have been calculated to model the situation in aqueous solution. Plots of the calculated and the experimental structures are given together with structural and thermodynamic parameters in Fig. 4. The calculations indicate that, in solution, [Cu(mnp-β-ala)] is probably six-co-ordinated. This is also in agreement with the solution spectroscopic data, which indicate a considerable tetrahedral distortion of the central chromophore.

Co-ordination Chemistry of the Metal-free Ligands.—The potentially quinquedentate ligands ampama form stable complexes with Cu^{II} and Co^{III}. For octahedrally co-ordinating metal ions a number of different configurations, including α and β isomers of the 5,6,5-membered chelate rings, four- and five-co-ordination of the ligand and various orientations of the amino acid side chains are possible. The exact co-ordination geometry of [Co{(*S*,*S*)-ampala}(OH)] has not been identified so far. However, its stoichiometry and spectroscopic data indicate that the species isolated is a hydroxo complex with (*S*,*S*)-ampala acting as a quinquedentate ligand.

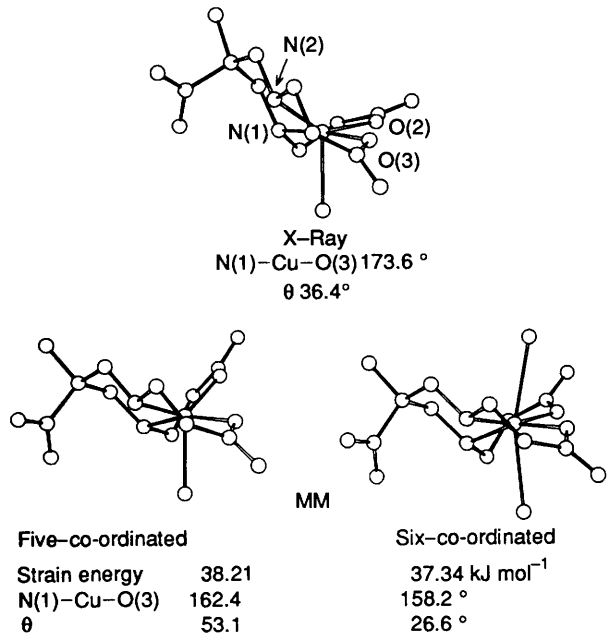


Fig. 4 ORTEP plots of the experimentally observed and of the calculated five- and six-co-ordinate structures of [Cu(mnp-β-ala)] (for the complete atom numbering scheme see Fig. 2). Tetrahedral twist angle θ: 0° for square-planar geometry, 90° for tetrahedral

Transition-metal complexes with high stabilities are of increasing importance in various fields of medical chemistry (treatment of Wilson's disease, nuclear medicine, magnetic resonance imaging, *etc.*). The copper(II) complexes of mnpama and ampama are stable in acidic aqueous solutions (pH $\geqslant$ 1). This is rather unusual co-ordination chemistry for open-chain amino acid ligands and might lead to applications of the series of easily available ligands described here, both with copper(II) and a range of other metal ions.

Acknowledgements

Generous financial support by the Swiss National Science Foundation (Grants 20-28522.90, 70UP-029676 and 70UP-031551) is gratefully acknowledged.

References

1 T. R. Wagler and C. J. Burrows, *Tetrahedron Lett.*, 1988, **29**, 5091.
2 T. R. Wagler, Y. Fang and C. J. Burrows, *J. Org. Chem.*, 1989, **54**, 1584.
3 T. Murakami and C. Koichi, *Bull. Chem. Soc. Jpn.*, 1986, **59**, 3675.
4 S. Kitagawa, T. Murakami and M. Hatano, *Inorg. Chem.*, 1975, **14**, 2347.
5 P. Comba, T. W. Hambley, G. A. Lawrance, L. L. Martin, P. Renold and K. Várnagy, *J. Chem. Soc., Dalton Trans.*, 1991, 277.
6 P. V. Bernhardt, P. Comba, T. W. Hambley, L. L. Martin, K. Várnagy and L. Zipper, *Helv. Chim. Acta*, 1992, **75**, 145.
7 P. V. Bernhardt, P. Comba, T. W. Hambley, S. S. Massoud and S. Stebler, *Inorg. Chem.*, 1992, **31**, 2644.
8 P. V. Bernhardt, P. Comba, T. W. Hambley, G. A. Lawrance and K. Várnagy, *J. Chem. Soc., Dalton Trans.*, 1992, 355.
9 P. Comba, N. F. Curtis, G. A. Lawrance, M. A. O'Leary, B. W. Skelton and A. H. White, *J. Chem. Soc., Dalton Trans.*, 1988, 2145.
10 P. A. Martinelli, G. R. Hanson, J. S. Thompson, B. Holmquist, J. R. Pilbrow and B. L. Vallee, *Biochemistry*, 1988, **28**, 225.
11 D. Eufri and A. Sironi, *J. Mol. Graphics*, 1989, **7**, 165.
12 T. W. Hambley, MOMEC-87, A Program for Strain Energy Minimization, University of Sydney, 1987.
13 P. V. Bernhardt and P. Comba, *Inorg. Chem.*, 1992, **31**, 2638.
14 C. K. Johnson, ORTEP, A Thermal Ellipsoid Plotting Program, Oak Ridge National Laboratories, Oak Ridge, TN, 1965.
15 Enraf-Nonius Structure Determination Package, Enraf-Nonius, Delft, 1985.
16 G. M. Sheldrick, SHELXS 86, A Program for Crystal Structure Solution, University of Göttingen, 1986.
17 G. M. Sheldrick, SHELX 76, A Program for X-Ray Crystal Structure Determination, University of Cambridge, 1976.
18 D. T. Cromer and J. T. Waber, *International Tables for X-Ray Crystallography*, Kynock Press, Birmingham, 1974, vol. 4.
19 P. Comba, T. W. Hambley and G. A. Lawrance, *Helv. Chim. Acta*, 1985, **68**, 2332.
20 P. Comba, N. F. Curtis, G. A. Lawrance, A. M. Sargeson, B. W. Skelton and A. H. White, *Inorg. Chem.*, 1986, **25**, 4260.
21 P. Comba, G. A. Lawrance, M. Rossignoli, B. W. Skelton and A. H. White, *Aust. J. Chem.*, 1988, **41**, 773.
22 P. Comba, G. A. Lawrance, T. M. Manning, A. Markiewicz, K. S. Murray, M. A. O'Leary, B. W. Skelton and A. H White, *Aust. J. Chem.*, 1990, **43**, 69.
23 P. V. Bernhardt, P. Comba, L. R. Gahan and G. A. Lawrance, *Aust. J. Chem.*, 1990, **43**, 2035.
24 P. V. Bernhardt, P. Comba, B. L. Elliott, G. A. Lawrance, M. A. O'Leary, G. Wei and E. N. Wilkes, unpublished work.
25 G. A. Lawrance, M. A. O'Leary, B. W. Skelton, F. Woon and A. H. White, *Aust. J. Chem.*, 1988, **41**, 1533.
26 P. V. Bernhardt and P. Comba, *J. Chem. Soc., Chem. Commun*, 1993, 113.
27 P. V. Bernhardt, P. Comba, A. Mahu-Rickenbach, S. Steiner, S. Stebler, K. Várnagy and M. Zehnder, *Inorg. Chem.*, 1992, **31**, 4194.
28 G. G. Smith, A. Khatib and G. S. Reddy, *J. Am. Chem. Soc.*, 1983, **105**, 293.
29 T. F. Cummings and J. R. Shelton, *J. Org. Chem.*, 1960, **25**, 419.
30 W. L. Driessen and W. L. Groeneveld, *Recl. Trav. Chim. Pays-Bas*, 1969, **88**, 491.
31 W. L. Driessen and W. L. Groeneveld, *Recl. Trav. Chim. Pays-Bas*, 1969, **88**, 620.
32 W. L. Driessen, L. M. van Geldrop and W. L. Groeneveld, *Recl. Trav. Chim. Pays-Bas*, 1970, **89**, 1271.
33 P. V. Bernhardt, P. Comba, T. W. Hambley, M. A. Hitchman and H. Stratemeier, unpublished work.

Received 16*th October* 1992; *Paper* 2/05542B