Articles

Why Are Copper(II) Amino Acid Complexes Not Planar in Their Crystal Structures? An *ab Initio* and Molecular Mechanics Study

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This paper presents geometries of copper(II) chelates with L-alanine, L-leucine, and L-*N*,*N*-dimethylvaline optimized by the hybrid density functional method B3LYP. According to the molecular quantum mechanics results, a square-planar copper(II) coordination geometry is electronically favored *in vacuo*. Deviations from the planar configuration observed in the crystal state should be attributed to sterical intramolecular and/or intermolecular effects. This paper proposes a new molecular mechanics model for tetracoordinated copper(II) amino acidates to investigate these effects in detail. The empirical parameter set for the selected potential energy functions was optimized both with respect to the X-ray crystal structures (internal coordinates and unit cell constants) and with respect to the quantum mechanically derived valence angles around copper. To test this newly developed force field (FF), the equilibrium geometries of 10 molecules are predicted *in vacuo* and in approximate crystalline surrounding. The results were compared with their *ab initio* and experimental crystal structures, respectively. The unit cell volumes were reproduced in a range from −7.0% to 2.1%. The total root-mean-square deviations between the experimental and FF in crystal internal coordinates were 0.017 Å in the bond lengths, 2.2° in the valence angles, and 3.6° in the torsion angles. The force field is capable of reproducing the changes in the chelate rings' torsion angles caused by the crystal packing forces and successfully explains the nonplanarity of Cu(II) amino acid complexes in their crystal structures.

1. Introduction

Copper is an essential metalloelement, needed for normal metabolic processes in cells.[1−3] Many enzymes, such as cytochrome *c* oxidase, superoxide dismutase, tyrosinase, dopamine-β-monooxygenase, lysil oxidase, ascorbate oxidase, and amine oxidases, require copper in the active sites to be biochemically active. In blood plasma or serum copper is present in ceruloplasmin and in complexes with albumin and amino acids. These complexes, which are electrically neutral, lipophilic and diffusible molecules, in nondisease state regulate the copper-dependent homeostatic processes.[3]

Copper(II) complexes with amino acids and amino acid derivative ligands are supposed to be good model compounds for the metal−ligand sites at proteins. They are also considered as potentially good models for mimicking the superoxide dismutase activity. So far, their only experimentally available structures have been those determined by X-ray diffraction.

Generally, the ligand arrangements around the binding sites for copper ions in proteins are unsymmetrical, being an intermediate between planar and tetrahedral configurations.[1,2] In tetracoordinated copper(II) amino acidates, which are the subject of the present study, the central metal atom has either an irregular square-planar, a distorted planar or a flattened tetrahedral coordination geometry, as determined by the X-ray diffraction measurements.[4−11]

The copper(II) coordination polyhedron can distort easily. The "softness" ("plasticity") of the copper(II) coordination sphere is stereochemical manifestation of the Jahn−Teller or pseudo Jahn−Teller effects in a sense that the Jahn−Teller center (i.e. copper(II)) allows a distorted configuration with several equally probable directions of distortions.[12−14] In the absence of external

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perturbations, the coordination sphere plasticity results in continuous transitions between equivalent directions of distortions. The crystal environment of a given coordination center may be the external factor stabilizing one of many distorted configurations.

For a long time molecular mechanics was the only method available for modeling structural and thermodynamical properties of the copper(II) amino acidates.[15−17] Nowadays, the increasing computing power and the development of hybrid density functional methods make it possible to optimize the geometries of these molecules quantum mechanically at a level that even includes an approximate treatment of dynamic electron correlation. Still, the high level quantum chemical calculations on metal-biomolecule complexes are rare.[18−20] The impressive reliability of the hybrid density functional method for the description of copper and other 3d transition metals has been shown in numerous studies.[21−29] *Ab initio* derived geometries *in vacuo* compared with the experimental crystal data can clarify the influence of the crystal environment on the copper(II) coordination sphere. With molecular mechanics calculations, on the other side, it is possible to obtain equilibrium molecular conformations by explicit incorporation of the environmental effects into the calculations. The comparison of molecular mechanics results with the X-ray crystal data and *ab initio* geometries should be an excellent test for the molecular mechanics model validity.

Several approaches in molecular-mechanical modeling of copper(II) complexes and of the copper(II) coordination shere plasticity have been established.[16,30−32] The variability of the valence angles around copper(II) has been described either explicitly by valence-angle bending potential using different analytical functions,[30,33−41] or by nonbonded interactions between ligand atoms (points-on-a-sphere method)[31] modeled with van der Waals and/or electrostatic potentials.[17,32,42−49] Attempts to calculate the magnitude and direction of the Jahn−Teller distortion in Cu(II)-N_6 compounds were made by adding an energy term to mimic the Jahn−Teller stabilization energy to the strain energy of a molecule.[43] A similar but more general approach, which was attempted to handle any coordination number and molecular geometry or ligand type with a single empirical parameter set, adds a d orbital stabilization energy to the conformational potential.[17,44−46] The d orbital stabilization energy is calculated by means of a ligand field model and explicitly treats the electronic effects arising from changes in the d orbital energies.

A common way to develop the force fields for compounds with copper(II) has been to incorporate implicitly the effects of surrounding environment on an average basis into the parameter set. On the contrary, our approach is to calculate the environmental effects explicitly, i.e., to derive a “vacuum-like” potential applicable to both gas phase (isolated molecules) and condensed phase simulations (by accounting the influence of the crystal packing forces).

The first simulations of molecular conformations of tetracoordinated copper(II) chelates in crystalline surroundings with a molecular mechanics model revealed them as different from the conformations calculated for isolated molecules.[49] *In vacuo* calculations gave a much more distorted copper(II) coordination polyhedron (a distorted tetrahedron) than did crystal calculations. As the simulations in crystals gave the geometries of copper(II) coordination close to the experimentally observed ones, a possible conclusion was that the model described the real situation quite well, i.e., that the influence of intermolecular interactions was considerable, and that the copper(II) coordination might be more distorted in nonpolar solution.

However, this paper presents results of the geometry optimizations of three copper(II) amino acid complexes up to the B3LYP/LanL2DZ+(d) level of theory. Unexpectedly, the obtained copper(II) coordination polyhedra are less distorted *in vacuo* than in the crystal state, which is just the opposite behavior to the above-mentioned molecular mechanics prediction. Therefore, a new molecular mechanics model was developed. Ten copper(II) chelates with the same *trans*-N_2O_2 copper(II) coordination polyhedron were selected for modeling. The force field was optimized on experimental data of five molecules and on the *in vacuo ab initio* copper(II) coordination geometry of three molecules. The aim of this work was to derive a force field suitable for reproduction and prediction of properties of a whole class of compounds of our interest, namely

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amino acids complexed to Cu(II). The goal is to contribute to a better understanding of the structure and function of copper−biomolecule complexes, and also to predict a ligand which may be effective in transporting copper ions to the sites in biological systems where their pharmacological and biochemical activity would be of the utmost need.

2. Methods and Calculations

2.1. Molecular Quantum Mechanics. All *ab initio* calculations were done using the Gaussian94 series of programs[50] applying the hybrid density functional method B3LYP[51] within a restricted open shell approach. Dunning/Huzinaga full double-ζ (D95)[52] was used as a basis set for first row elements and Los Alamos effective core potential (ECP) plus double-ζ (DZ)[53−55] for Cu. This combination of basis sets corresponds to the LanL2DZ basis set keyword in Gaussian94[50] and therefore the approach will be called B3LYP/LanL2DZ in this paper. Further on, polarization functions[56] were added to carbon, oxygen and nitrogen (this approach is named B3LYP/LanL2DZ(d) below). Finally, diffuse functions[57] were augmented to the first row elements (denoted as B3LYP/LanL2DZ+(d) throughout this paper).

Even though atomic charges are not physical observables and therefore cannot be seen as results of rigid molecular quantum mechanics, they provide a very helpful tool to analyze the distribution of electron and spin density. Especially if the systems under consideration are simultaneously investigated at quantum mechanical and at classical level, atomic charges derived from quantum mechanics can provide significant help for the proper description of electrostatics in the frame of classical mechanics. Among the various schemes to distribute the electron density to the nuclei, the Natural Bond Orbital (NBO) analysis has been proved to be rather independent from basis sets and fruitful for chemical intuition.[58−65] Therefore, the wave function with respect to the electron density resulting from molecular quantum mechanics was investigated by Natural Population Analysis (NPA) using the NBO Version 3.1 program (by E. D. Glending, A. E. Reed, J. E. Carpenter, and F. Weinhold), which is distributed together with the Gaussian94 series of programs.

Numerous benchmark studies on small copper systems[22−26] proved that the B3LYP method can reliably describe Cu in all oxidation states at an accuracy comparable to very expensive high level *ab initio* methods (like MP4 and CCSD(T)) that would not be feasible for large systems as the ones investigated in this study. Especially good match was obtained for structural data, which confirms the high reliability of the B3LYP method for geometry optimizations. Therefore, a very reliable description of the copper(II) amino acidates which are much larger molecules that the ones investigated by the benchmark studied[22−26] can be expected with confidence. The assumed reliability is also confirmed by the recent theoretical study for the [glycine-Cu]$^+$ system.[20] The comparison between the metal−animo acid geometries optimized at the second-order Møller−Plesset perturbation (MP2) and B3LYP levels of theory showed excellent agreement within the glycine fragment, with the largest differences being ca. 0.01 Å and 1°, and with differences in Cu−O and/or Cu−N distances in the 0.03−0.06 Å range.[20]

2.2 Molecular Mechanics. The conformational (strain) potential energy is calculated from the following basic formulas:

$$V_{\text{total}} = V_{\text{b}} + V_\theta + V_\phi + V_\chi + V_{\text{nb}} + V_{\text{cp}} \tag{1}$$

$$V_{\text{b}} = \sum_{\text{all bonds}} D_{\text{e}}(\mathrm{e}^{-2\alpha(b-b_0)} - 2\mathrm{e}^{-\alpha(b-b_0)})$$

$$V_\theta = \sum_{\substack{\text{all valence angles}\\ \text{except around metal}}} \frac{1}{2}k_\theta(\theta - \theta_0)^2$$

$$V_\phi = \sum_{\substack{\text{one torsion}\\ \text{per bond}}} \frac{1}{2}V_n(1 \pm \cos n\phi)$$

$$V_\chi = \sum_{\text{all oop}} \frac{1}{2}k_\chi \chi^2$$

$$V_{\text{nb}} = \sum_{\substack{i<j\\ \text{atoms more than}\\ \text{two bonds apart}}} (A_iA_jr_{ij}^{-12} - B_iB_jr_{ij}^{-6} + q_iq_j\epsilon_r^{-1}r_{ij}^{-1})$$

$$V_{\text{cp}} = \sum_{\substack{k<l\\ \text{nonbonded atoms}\\ \text{of the copper(II)}\\ \text{coordination polyhedron}}} q_kq_l\epsilon_r^{-1}r_{kl}^{-1}$$

Here b, θ, ϕ, χ, and r are bond lengths, valence, torsion, and out-of-plane angles, and nonbonded distances. D_{e}, α, and b_0 are empirical parameters for bond stretching (a Morse function), k_θ and θ_0 for valence-angle bending, and k_χ for the out-of-plane deformational potential for the carboxyl groups. Torsional interactions are specified with V_n and n (height and multiplicity of the torsional barrier, respectively). A and B are one-atom empirical parameters for the van der Waals interactions (a Lennard-Jones 12−6 function). q is a charge parameter and ϵ_r is the dielectric constant. Intramolecular interactions separated by three and more bonds are considered nonbonded. Intermolecular atom−atom interactions are calculated with the same functional forms and empirical parameters as the intramolecular nonbonded interactions, V_{nb}. The last term in eq 1, V_{cp}, stands for the repulsive electrostatic potential between the nonbonded atoms of the metal coordination polyhedron. Therefore, the interactions inside the copper(II) coordination sphere are modeled with the Morse potential between the copper and ligand atoms, V_{b}, and the Coulombic potential between the ligand atoms, V_{cp}. It is a model without any explicit angle-bending potential for the angles around copper.

The choice of the potential energy functions is the same as in the previously described and analyzed model,[49] except that the Morse potential is chosen instead of a harmonic function for modeling the bond potential. The reasons for selecting the Morse potential over the quadratic function are: the harmonic potential could not reproduce the diversities in the Cu−N and Cu−O bond lengths, and the satisfactory performance of several force fields which use Morse potentials.[45,66−69]

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Table 1. Crystallographic Data for Copper(II) Complexes with α-Amino Acids and Amino Acid Derivative Ligands

label	compound	Bravais type	space group	Z	coordination geometry	ref
(A)	bis(L-*N*,*N*-dimethylvalinato)copper(II)	orthorhombic	$P2_12_12_1$	4	flattened tetrahedron	4
(B)	bis(D,L-*N*,*N*-dimethylvalinato)copper(II)	monoclinic	$P2_1/c$	2	irregular square-planar	5
(C)	bis(α-aminoisobutyrato)copper(II)	monoclinic	$P2_1/c$	2	irregular square-planar	6
(D)	bis(L-alaninato)copper(II)	monoclinic	$P2_1$	2	distorted planar	7
(E)	bis(D,L-*N*,*N*-diethylalaninato)copper(II)	triclinic	$P1$	1	irregular square-planar	8
(F)	bis(L-leucinato)copper(II)	monoclinic	$P2_1$	2	distorted planar	9
(G)	bis(L-2-aminobutyrato)copper(II)	monoclinic	$P2_1$	2	distorted planar	10
(H)	bis(D,L-2-aminobutyrato)copper(II)	monoclinic	$P2_1/c$	2	irregular square-planar	9
(I)	bis(L-*N*,*N*-dimethylisoleucinato)copper(II)	monoclinic	$P2_1$	2	flattened tetrahedron	11
(J)	bis(1-aminocyclopentanecarboxylato)copper(II)	monoclinic	$P2_1/a$	2	irregular square-planar	7

The molecular mechanics model fits into a group of our electrostatic models[47−49] or points-on-a-sphere models. Originally, as we dealt with four-coordinate compounds, two dummy atoms imagined to represent an electron pair placed half above and half below the coordination plane were supposed to be part of the copper(II) coordination polyhedron.[47] However, the active role of the dummy atoms in the nonbonded interactions[49] appeared to be a disadvantage of the model because the equilibrium conformations of a molecule depended mostly on their initial positions. The problem was more pronounced in the copper(II) complexes with apically coordinated oxygens from the neighboring molecules in the crystal lattice.[49] Subsequent calculations of the intermolecular Cu−O distances revealed them to be overestimated by more than 0.5 Å, as the dummy atoms prevented the carboxyl oxygens from surrounding molecules to come close to the copper atom. Consequently, the dummy atoms were dropped out.

Molecular mechanics calculations were performed with the Consistent Force Field (CFF) program for conformational analysis,[70−72] which was further modified to cope with the electrostatic models. Crystal simulations were carried out by using the Williams variant of the Ewald lattice summation method[73,74] with a spherical and abrupt cutoff limit of 14 Å and convergence constants of 0.2 $Å^{-1}$, 0.2 $Å^{-1}$, and 0.0 for Coulomb, dispersion, and repulsion lattice summation terms. The parameters for the set of potential energy functions were determined by combining trial and error guesses with the optimization algorithm which is a variant of the general least-squares method (the Levenberg−Marquardt algorithm).[71,72]

3. Experimental Data

Ten X-ray crystal structures of the copper(II) amino acidato complexes with the same *trans*-CuN_2O_2 coordination polyhedron and the same atom types were selected for modeling (Table 1 and Figure 1). The compounds are electrically neutral molecules.

The 10 molecules differ with respect to the shape of the copper(II) coordination polyhedron (Table 1) and with respect to the types of intermolecular interactions in the crystal state. Four of them are copper(II) complexes with N-alkylated amino acids, bonded only by van der Waals interactions and without any noticeable apical coordination to the copper.[4,5,8,11] The other six molecules have the crystal organization as follows: they are arranged in isolated two-dimensional sheets, linked to each other within the sheet by a net of relatively weak N−H···O hydrogen bonds and also by intermolecular Cu−O interactions, completing an elongated octahedral coordination around copper.[6,7,9,10] The distances between the copper and the carboxyl oxygens of the neighboring molecules are in a range from 2.629 Å (in bis(L-leucinato)copper(II)[9]) to 3.116 Å (in bis(1-aminocyclopentanecarboxylato)copper(II)[7]). The two-dimensional sheets are held together by van der Waals interactions.

4. Results and Discussion

4.1. Quantum Mechanics. We applied the B3LYP method to study three molecules with distorted copper(II) coordination geometry, bis(L-*N*,*N*-dimethylvalinato)copper(II), bis(L-alaninato)copper(II), and bis(L-leucinato)copper(II). Bis(L-alaninato)copper(II) was chosen as the smallest molecule, bis(L-leucinato)copper(II) is the compound with the largest amino acid residue, and bis(L-*N*,*N*-dimethylvalinato)copper(II) has the most distorted copper(II) coordination polyhedron of the 10 copper(II) chelates. Their geometries were optimized at the B3LYP/LanL2DZ level of theory. Bis(L-*N*,*N*-dimethylvalinato)copper(II) and bis(L-leucinato)copper(II) were also optimized with additional polarization functions (B3LYP/LanL2DZ(d) level of theory, the first molecule) and additional diffuse functions on nitrogens, carbons and oxygens (B3LYP/LanL2DZ(d)+, the second molecule). All geometry optimizations were started from the experimental molecular structures and were made without symmetry constraints, i.e., all degrees of freedom were optimized.

Adding the diffuse and polarization functions yields the N−C bond lengths and the bond distances between the atoms of the carboxyl group closer to the experimental values (for the N−C bonds by up to 0.019 Å, C−O by 0.029 Å, and C═O by 0.024 Å), lengthening of the Cu−N bonds (by 0.015 Å) and shortening of the Cu−O bonds (by 0.010 Å) for bis(L-*N*,*N*-dimethylvalinato)copper(II), and changes in the valence and torsion angles not larger than 3.3° and 3.1°, respectively. Unless explicitly stated otherwise, the LanL2DZ(d) and LanL2DZ(d)+ structures are used for comparisons with the experimental and molecular mechanics results.

The comparison of the experimental data with the *ab initio* calculated equilibrium geometries offers first indications about the strength of intermolecular interactions in the geometry of copper(II) amino acidato complexes.

The copper(II) coordination polyhedra of the three molecules are less distorted *in vacuo* than in the crystal state. The difference in the spatial arrangements of the ligands around the metal is more pronounced for bis(L-*N*,*N*-dimethylvalinato)copper(II) than for the other two molecules (Table 2 and Figure 2). On the other side, the chelate rings' torsion angles of the first molecule are almost unchanged (the maximum difference is 8.6°), while the changes in some torsions are significant for the copper complexes with L-alanine and L-leucine (up to 20°), pointing out a possibility of different conformations in the condensed and gaseous phases (Table 3).

The electronic configuration on the copper and four ligand atoms is very similar for all three studied systems (Table 4). As bis(L-alaninato)copper(II) and bis(L-leucinato)copper(II) have

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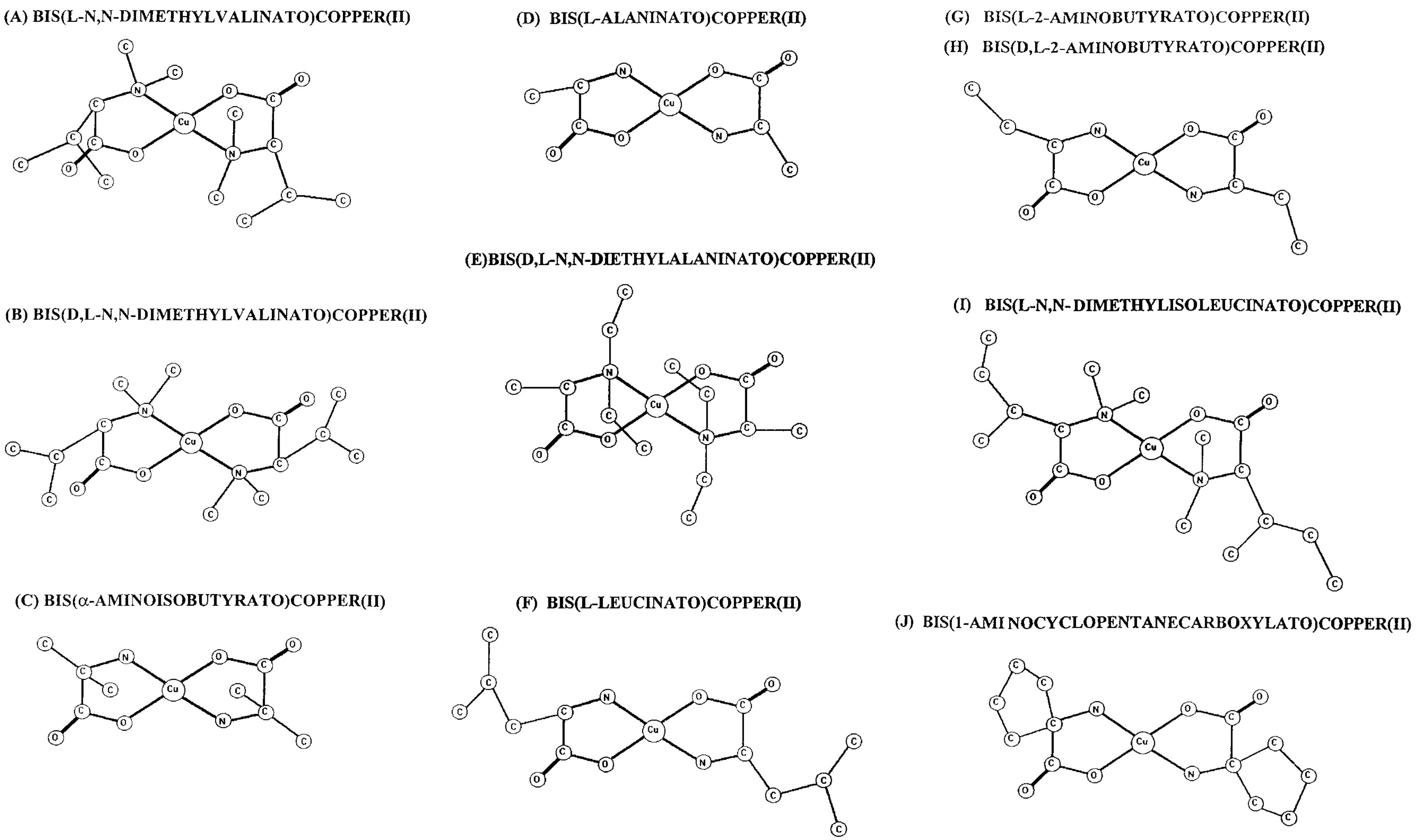

Figure 1. Copper(II) complexes with α-amino acids and amino acid derivative ligands studied in this work (hydrogens are omitted for clarity).

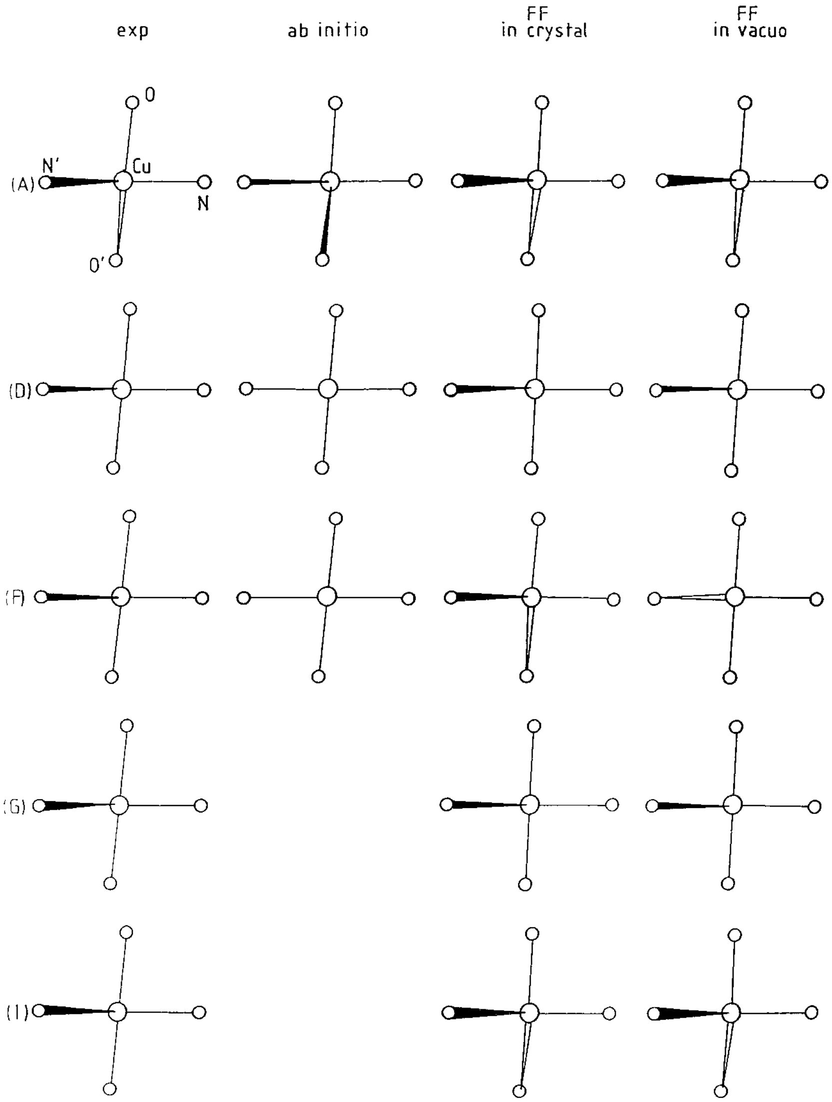

Figure 2. Coordination polyhedra of five molecules with distorted copper(II) coordination geometry: (A) bis(L-*N*,*N*-dimethylvalinato)copper(II); (D) bis(L-alaninato)copper(II); (F) bis(L-leucinato)copper(II); (G) bis(L-2-aminobutyrato)copper(II); (I) bis(L-*N*,*N*-dimethlyisoleucinato)copper(II).

almost an irregular square-planar *in vacuo* copper(II) coordination, the former result implies that the planar coordination is electronically favored in all three examined molecules,[75] and that the deviations from planarity may be attributed to the sterical (intramolecular or/and intermolecular) effects. It might be that the van der Waals interactions between the bulky alkyl groups attached to the nitrogens in bis(L-*N*,*N*-dimethylvalinato)copper(II) cause the distortion of the copper(II) coordination polyhedron from the electronically favored planar geometry. Additional strain imposed by the crystal packing forces might indirectly (as there is no apical coordination to the metal) cause further distortion of the polyhedron, i.e., the changes inside the copper(II) coordination sphere due to its property of plasticity (flexibility) may be more favored energetically than the changes in the torsion angles.

As the three molecules are rather different, we expect that similar effects could be found for all molecules of the same class.

4.2. Molecular Mechanics. Potential Energy Parameter Set. The introduction of the new potential energy function form (the Morse potential) and the removal of the dummy atoms from the studied systems called for changes in the potential energy parameter set. The dummy atom force field, M8-kr47,[49] was taken as an initial empirical parameter set for parameters' optimization in the valence-angle bending, torsion, out-of-plane bending and nonbonded part of the conformational potential V_{total} (eq 1). Four equilibrium θ_0, those for the O$-$C(sp^2)$=$O, C$-$C(sp^2)$=$O, C$-$C(sp^2)$-$O, and C(sp^2)$-$O$-$Cu valence angles, and the multiplicity for the C$-$C(sp^2) torsion were changed to be close to their usual experimental values. The initial values for Morse potential parameters were taken from the literature.[45,66]

Although the infrared spectra of several molecules have been recorded, the assignment of the frequencies is not possible (except for the C$-$H and C$=$O bond stretching) without extensive studies of vibrational spectra. Furthermore, only the crystal spectra were recorded, a case that the CFF program still cannot treat in a proper way. Therefore, the X-ray crystal structures have been chosen as the only experimental data on which to optimize the parameters.

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(75) Several starting structures of bis(glycinato)copper(II) with differently distorted coordination polyhedron were additionally tested for another local minima. Only the planar minimum was found in the trans orientation of the two glycine ligands.

Table 2. Copper(II) Coordination Polyhedra Angles of the Experimental X-ray Crystal and *ab Initio in Vacuo* Structures, and of the Structures Obtained by the Force Field (FF) *in Vacuo* and in Crystal[a]

			FF	
	expt	*ab initio*	in crystal	*in vacuo*
Bis(L-*N*,*N*-dimethylvalinato)copper(II)				
N−Cu−N′	161.4	172.5	158.5	160.6
N−Cu−O	84.3	84.2	85.9	86.1
N−Cu−O′	97.2	95.3	96.1	94.6
N′−Cu−O	95.3	95.3	95.5	94.6
N′−Cu−O′	84.5	84.2	85.9	86.1
O−Cu−O′	175.7	171.9	171.1	176.1
O′N′NO	156.3	179.9	149.3	156.1
β	170.3	169.4	171.5	169.4
Bis(L-alaninato)copper(II)				
N−Cu−N′	175.5	179.8	173.4	174.2
N−Cu−O	83.8	85.0	86.8	86.7
N−Cu−O′	95.5	94.9	92.0	93.9
N′−Cu−O	96.2	94.8	95.4	93.0
N′−Cu−O′	84.4	85.3	85.7	86.5
O−Cu−O′	179.2	179.4	178.6	179.1
O′N′NO	175.8	−179.4	174.4	173.3
β	176.7	179.6	174.9	176.5
Bis(L-leucinato)copper(II)				
N−Cu−N′	174.6	179.6	170.0	176.7
N−Cu−O	84.2	84.4	85.5	86.9
N−Cu−O′	95.6	95.7	94.8	92.6
N′−Cu−O	96.0	95.3	93.5	93.9
N′−Cu−O′	84.2	84.6	87.1	86.5
O−Cu−O′	179.7	179.8	174.5	178.0
O′N′NO	174.7	180.0	164.3	−178.7
β	176.2	179.7	176.9	−176.4

[a] The valence angles, a "torsion" angle O′N′NO, and a distortion angle β are expressed in degrees. The distortion coordinate β is defined as an angle between the bisectors of the two N−Cu−O angles in opposite chelate rings.

Table 3. Chelate Rings' Torsion Angles (in degrees) of the Experimental X-ray Crystal and *ab Initio in Vacuo* Structures, and of the Structures Obtained by the Force Field (FF) *in Vacuo* and in Crystal[a]

			FF	
	expt	*ab initio*	in crystal	*in vacuo*
Bis(L-*N*,*N*-dimethylvalinato)copper(II)				
OCuNC	−156.7	−151.4	−156.4	−154.7
O′CuN′C′	−152.2	−151.3	−154.1	−154.7
CCNCu	−86.6	−92.4	−87.8	−89.7
CCCN	−175.9	−167.3	−178.6	−176.1
OKCN	−31.0	−29.6	−32.5	−31.0
CuOKC	7.4	10.7	10.5	11.0
C′C′N′Cu	−95.1	−92.5	−93.1	−89.7
C′C′C′N	−169.2	−167.3	−174.3	−176.1
O′K′C′N′	−25.2	−29.4	−27.0	−30.9
CuO′K′C′	7.5	10.6	9.4	10.9
KOCuN	12.3	7.1	9.3	7.7
K′O′CuN′	8.3	7.1	7.1	7.8
Bis(L-alaninato)copper(II)				
OCuNC	27.8	17.8	23.4	16.1
O′CuN′C′	−13.5	−14.6	−16.0	−16.3
CCNCu	−166.9	−149.1	−158.7	−143.6
OKCN	36.5	19.4	35.2	17.9
CuOKC	−13.7	−4.9	−14.7	−4.2
C′C′N′Cu	−99.9	−102.4	−97.3	−96.9
O′K′C′N′	−19.0	−15.3	−19.5	−18.8
CuO′K′C′	8.4	3.2	6.4	5.2
KOCuN	−8.2	−7.5	−5.5	−7.1
K′O′CuN′	3.0	6.7	5.7	6.7
Bis(L-leucinato)copper(II)				
OCuNC	−19.4	−20.7	−19.4	−22.7
O′CuN′C′	27.1	16.5	22.6	15.9
CCNCu	−87.8	−91.9	−92.3	−85.9
CCCN	176.6	179.5	176.8	170.8
OKCN	−29.8	−26.7	−25.0	−34.7
CCCC	−174.9	−176.2	−175.6	−175.3
CuOKC	14.0	9.7	8.9	15.0
C′C′N′Cu	−166.2	−146.7	−158.0	−142.7
C′C′C′N′	−72.5	−63.5	−58.3	−57.4
O′K′C′N′	36.3	16.2	37.2	17.6
C′C′C′C′	176.9	173.1	177.6	172.4
CuO′K′C′	−13.7	−2.5	−17.3	−4.3
KOCuN	3.3	6.5	6.2	5.0
K′O′CuN′	−7.9	−8.2	−3.6	−6.9

[a] Symbol K stands for the planar carbon atom of the carboxyl group.

Table 4. Valence Electron Configurations by NPA with the Basis Set LanL2DZ for the Atoms of the Copper(II) Coordination Polyhedron

atom	population
Bis(L-*N*,*N*-dimethylvalinato)copper(II)	
Cu	4s (0.26) 3d (9.41) 4p (0.02)
N	2s (1.34) 2p (4.27) 3p (0.02)
O	2s (1.74) 2p (5.15) 3p (0.01)
Bis(L-alaninato)copper(II)	
Cu	4s (0.33) 3d (9.39) 4p (0.02)
N	2s (1.44) 2p (4.51) 3p (0.02)
O	2s (1.76) 2p (5.09) 3p (0.01)
Bis(L-leucinato)copper(II)	
Cu	4s (0.33) 3d (9.39) 4p (0.01)
N	2s (1.44) 2p (4.50) 3p (0.02)
O	2s (1.74) 2p (5.13) 3p (0.01)

The conformational potential energy was minimized as a molecule was in the crystalline surroundings, by taking intermolecular interactions into account. The empirical parameters were optimized with respect to the experimental data (internal coordinates and unit cell constants) of five molecules: bis(L-*N*,*N*-dimethylvalinato)copper(II), bis(D,L-*N*,*N*-dimethylvalinato)copper(II), bis(α-aminoisobutyrato)copper(II), bis(L-alaninato)copper(II), and bis(D,L-*N*,*N*-diethylalaninato)copper(II). The θ_0 and n parameters as well as D_e, α, and b_0 for the C−H and N−H bonds were kept unchanged during the optimization process. The new parameters were tested on another five molecules.

The preliminary calculated geometries by the crystal simulator without the dummy atoms were encouraging. Good reproduction of the crystal structures was possible. However, for isolated molecules, without the influence of intermolecular interactions, the copper(II) coordination polyhedron distorted from an irregular square-planar one toward a distorted tetrahedron. Besides, a problem of many minima occurred at the parameter hypersurface, i.e., many different combinations of the parameter set yielded similar results. Restricting the parameter hyperspace with additional data on which to optimize the parameters was necessary.

The solution of the problem has been looked for in the *ab initio* calculated structures: The *ab initio* results revealed that the distorted *in vacuo* copper(II) coordination polyhedra by the force field were "false" minima, i.e., as already mentioned, *in vacuo* copper(II) coordination geometries are less distorted than in the crystal state. Therefore, the *ab initio* data were used as additional condition for restricting the parameter hyperspace on our way to finding a suitable force field.

The empirical parameters were reoptimized to reproduce the experimental data as well as the *ab initio in vacuo* copper(II) coordination geometry. The difference in the crystal packing forces between the copper(II) complexes with N-alkylated amino acids and other amino acid complexes were simulated by

Table 5. Potential Energy Parameter Set[a,b]

bond	D_e	α	b_0	bond	D_e	α	b_0
Cu−N	219.414	1.195	1.989	K−Q	54.684	3.456	1.230
N−C	52.471	3.029	1.465	C−K	114.167	3.609	1.522
C−C	162.361	4.051	1.527	K−O	59.168	2.500	1.299
C−H	101.600	1.800	1.090	Cu−O	85.768	1.850	1.901
N−H	93.000	2.500	1.010				

angle	k_θ	θ_0	angle	k_θ	θ_0
Cu−N−H	16.682	1.911	C−N−C	209.726	1.911
Cu−N−C	10.000	1.911	K−C−H	157.557	1.911
N−C−C	191.439	1.911	N−C−K	234.054	1.911
N−C−H	120.860	1.911	C−C−K	163.683	1.911
H−N−H	47.951	1.911	O−K−Q	276.728	2.164
H−C−H	111.182	1.911	C−K−Q	274.949	2.094
C−N−H	120.093	1.911	C−K−O	195.995	2.025
H−C−C	154.313	1.911	K−O−Cu	317.232	2.007
C−C−C	281.007	1.911			

torsion	V_n	n	torsion	V_n	n
−C−C−	3.700	3.000	−O−K−	7.580	−2.000
−C−N−	1.015	3.000	−C−K−	0.520	12.000
−O−Cu−	2.760	−4.000	−Cu−N−	0.350	12.000

out-of-plane torsion	k_χ
Q(K−C−O)	95.277

nonbonding	A	B	nonbonding	A	B
H(C)	98.676	4.390	O	751.741	39.667
H(N)	220.000	6.663	Q	239.448	22.050
C	845.174	16.040	Cu	895.565	42.158
N	308.461	12.001	K	261.913	24.053

charge parameters	q	charge parameters	q	charge parameters	q
H	−0.109	Q	−0.097	N	−0.850
C	−0.399	Cu	0.870	O	−1.111
K	−0.138				

[a] Uncommon symbols: K, planar carbon atom; Q, double-bonded oxygen atom. [b] Units are as follows: D_e, kcal mol^{-1}; α, Å^{-1}; b_0, Å; k_θ, kcal mol^{-1} rad^{-2}; θ_0, rad; V_n, kcal mol^{-1}; V_χ, kcal mol^{-1} rad^{-2}; A, (kcal mol^{-1} Å^{12})$^{1/2}$; B, (kcal mol^{-1} Å^{6})$^{1/2}$; q, in electron units (the expression for electrostatic interactions has to be multiplied by 332.091 kcal mol^{-1} Å in order to be in kcal mol^{-1}, and the dielectric constant is equal to 2).

Table 6. Charge Assignment by the CFF Program Using the Charge Parameters Given in Table 5, and Charges Obtained by the NPA Method with the LanL2DZ Basis Set (Average Values)

	charges/*e*			charges/*e*	
atom	FF	NPA	atom	FF	NPA
Bis(D,L-*N*,*N*-dimethylvalinato)copper(II), Bis(L-*N*,*N*-dimethylvalinato)copper(II)					
Cu	1.011	1.310	$C^{1,2}(H_3)$	0.282	−0.371
N	−0.709	−0.624	$C^{\alpha}(H)$	0.064	−0.122
O	−0.970	−0.894	$C^{\beta}(H)$	−0.149	−0.195
K	0.492	0.890	$C^{\gamma,\delta}(H_3)$	0.069	−0.598
Q	−0.391	−0.673	H(C)	0.032	0.207
Bis(α-aminoisobutyrato)copper(II)					
Cu	1.005		C^{α}	−0.051	
N	−0.715		$C^{\beta,\gamma}(H_3)$	0.063	
O	−0.976		H(C)	0.026	
K	0.486		H(N)	0.433	
Q	−0.397				
Bis(L-alaninato)copper(II)					
Cu	1.006	1.259	$C^{\alpha}(H)$	0.058	−0.105
N	−0.714	−0.970	$C^{\beta}(H_3)$	0.064	−0.656
O	−0.975	−0.860	H(C)	0.027	0.232
K	0.487	0.811	H(N)	0.433	0.430
Q	−0.396	−0.636			
Bis(D,L-*N*,*N*-diethylalaninato)copper(II)					
Cu	1.011		$C^{1,3}(H_2)$	0.173	
N	−0.709		$C^{2,4}(H_3)$	0.069	
O	−0.970		$C^{\alpha}(H)$	0.064	
K	0.492		$C^{\beta}(H_3)$	0.069	
Q	−0.391		H(C)	0.032	
Bis(L-leucinato)copper(II)					
Cu	1.005	1.260	$C^{\alpha}(H)$	0.057	−0.105
N	−0.715	−0.971	$C^{\beta}(H_2)$	−0.046	−0.444
O	−0.976	−0.878	$C^{\gamma}(H)$	−0.155	−0.195
K	0.485	0.909	$C^{\delta,\epsilon}(H_3)$	0.063	−0.639
Q	−0.397	−0.690	H(C)	0.026	0.217
			H(N)	0.432	0.426
Bis(L-2-aminobutyrato)copper(II), Bis(D,L-2-aminobutyrato)copper(II)					
Cu	1.005		$C^{\alpha}(H)$	0.058	
N	−0.715		$C^{\beta}(H_2)$	−0.046	
O	−0.976		$C^{\gamma}(H_3)$	0.063	
K	0.486		H(C)	0.026	
Q	−0.397		H(N)	0.433	
Bis(L-*N*,*N*-dimethylisoleucinato)copper(II)					
Cu	1.010		$C^{1,2}(H_3)$	0.281	
N	−0.710		$C^{\alpha}(H)$	0.063	
O	−0.971		$C^{\beta}(H)$	−0.150	
K	0.491		$C^{\gamma,\epsilon}(H_3)$	0.068	
Q	−0.392		$C^{\delta}(H_2)$	−0.041	
			H(C)	0.031	
Bis(1-aminocyclopentanecarboxylato)copper(II)					
Cu	1.018		C^{α}	−0.038	
N	−0.702		$C^{\beta,\gamma}(H_2)$	−0.033	
O	−0.963		$C^{\delta,\epsilon}(H_2)$	−0.033	
K	0.499		H(C)	0.039	
Q	−0.384		H(N)	0.446	

[a] H(C) and H(N) stand for hydrogens bonded to carbon and nitrogen, respectively; $C^i(H_j)$ denotes carbon of alkyl groups for $i = 1, 2, 3, 4$ or carbon of the amino acid residue for $i = \alpha, \beta, \gamma, \delta, \epsilon$; j denotes the number of H atoms bonded to the carbon.

separating the Lennard-Jones parameters for the hydrogens bonded to the nitrogens and those bonded to the carbons. The parameters were optimized with respect to the experimental data (bond lengths, valence and torsion angles, and unit cell dimensions) of the same five molecules and also with respect to the valence angles around the copper obtained by the *ab initio* calculations of the three molecules (bis(L-*N*,*N*-dimethylvalinato)-copper(II), bis(L-alaninato)copper(II), and bis(L-leucinato)copper(II), Table 2). The parameters were systematically tested on other molecules. The final force field (FF) is given in Table 5.

In the CFF program, the fractional charges are not assigned by their parameter values, but redistributed by a special algorithm, keeping the total charge on the molecules neutral and distributing fractional charges in a manner supposed to mimic *ab initio* results.[72] The assignments of the charges due to the charge parameters given in Table 5 are in Table 6. Table 6 also shows the NPA charges calculated for the three molecules. The NPA values were used as a guideline for selecting initial charge parameters prior to the parameters' reoptimization. Another tool for deriving the charge values can be the electrostatic potential fit model.[76] Since the electrostatic potential derived charges rely mostly on the van der Waals surface of a molecule, the approach might suffer from linear dependencies between the charges assigned to the atoms "buried" inside the

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Table 7. Means and Standard Deviations of the Cu−N and Cu−O Bond Lengths for 10 Copper(II) Complexes[a]

			FF	
	expt	*ab initio*	in crystal	*in vacuo*
Cu−N	1.998(20)	2.050(20)	1.999(17)	1.999(18)
Cu−O	1.931(24)	1.917(4)	1.926(3)	1.915(6)
group I				
Cu−N	2.021(9)	2.079(0)	2.017(11)	2.019(11)
Cu−O	1.905(9)	1.916(0)	1.928(1)	1.922(1)
group II				
Cu−N	1.984(7)	2.036(3)	1.986(4)	1.986(2)
Cu−O	1.949(10)	1.917(5)	1.925(3)	1.910(1)
Cu−O (axial)	2.85(17)		2.74(17)	

[a] Group I: four copper(II) complexes with N-alkylated amino acids. Group II: six molecules with apical coordination to the metal atom in the crystal state. All values are in Å.

bulky compounds under considerations and the atoms closer to the molecule surface. As in our model the electrostatic interactions are assumed to have an important role in repulsions of nonbonded atoms of the copper(II) coordination polyhedron (besides being part of the nonbonded potential, eq 1), the reasonable guesses for the charges of the "buried" coordination polyhedron atoms were of importance. Therefore, a unique charge partitioning scheme as NPA was chosen for initial charge parameter guesses.

Comparison of Experimental and Theoretical Structures. The ability of the model to reproduce structural properties was examined. The equilibrium geometries of the 10 copper(II) chelates were calculated in the vacuum and in the condensed phase approximations. Only experimentally derived atomic coordinates were used as the starting points for geometry optimizations. The minimum structures, FF in crystal and FF *in vacuo*, were compared with the X-ray crystal data and the gas phase conformations obtained by the B3LYP approach, respectively. The efficiency of the force field was compared to that of the dummy atoms' M8-kr47 force field.[5,49]

As the differences between the experimental and the *ab initio* structures are almost all contained in the copper(II) coordination sphere and in the chelate rings' torsion angles, the ability of the force field to reproduce these changes was investigated.

Crystal Lattice Simulations. The experimental lattice constants and volumes were compared with the values calculated by the crystal simulator. The unit cell volumes are reproduced in a range from −7.0% to 2.1%. The rms deviations in the unit cell constants are 0.340 Å for a, b and c constants, and 2.3° for α, β, and γ unit cell angles. The rms of the unit cell volumes is 22.4 Å^3. In comparison with the results obtained with the dummy atoms,[5,49] the present force field reproduces the unit cell constants about 65% and the unit cell volumes 55% better than the M8-kr47 force field.

Reproduction of the Cu−N and Cu−O Bond Lengths. The bond distances between the copper and four ligand atoms show the greatest variability among the bond lengths of the 10 copper(II) amino acidates. The experimental Cu−N bonds range from 1.977 to 2.033 Å, while the Cu−O bonds differ by 0.068 Å, having the values from 1.886 to 1.954 Å. Thus, the Cu−O bonds are slightly shorter than the Cu−N bonds, the difference being higher for the copper complexes with N-alkylated amino acids (Table 7).

The Morse potential simulates very well the diversity in the Cu−N distances, and yields slightly worse but still good reproduction of the Cu−O bonds (Table 7, FF in crystal). While Cu−N are almost the same by FF *in vacuo* as in crystal for all molecules, the Cu−O distanced are longer in crystal than *in vacuo* for the molecules with the apical copper(II) coordination in the crystal state (group II, Table 7). *In vacuo*, these molecules are not under the influence of the intermolecular interactions which may cause pulling away the in-plane oxygens from the metal atom.

Table 8. Means and Standard Deviations of the Angles around Copper for 10 Molecules (in degrees)[a]

		FF	
	expt	in crystal	*in vacuo*
N−Cu−N′	175.2 (6.3)	173.8 (7.5)	174.8 (7.2)
N−Cu−O	84.1 (0.3)	86.0 (0.5)	86.4 (0.4)
N−Cu−O′	96.0 (0.5)	94.3 (1.1)	93.7 (0.7)
N′−Cu−O	95.9 (0.3)	94.4 (0.6)	93.8 (0.5)
N′−Cu−O′	84.2 (0.3)	85.9 (0.5)	86.4 (0.3)
O−Cu−O′	179.2 (1.3)	177.9 (3.1)	178.8 (1.5)
O′N′NO	174.6 (7.8)	171.9 (10.6)	174.2 (9.2)
β	177.1 (3.5)	177.1 (3.3)	177.9 (4.0)

[a] The angles are defined in Table 2.

The Cu−O values by the FF *in vacuo* agree with the *ab initio* mean of the three molecules' Cu−O bonds (Table 7). On the contrary, the FF does not follow the *ab initio* lengthening of the Cu−N bonds.

The mean of the intermolecular FF in crystal Cu−O distances is in the range of mean distances between the copper and the axial carboxyl oxygens in the real crystal structures (group II, Table 7).

The root-mean-square deviations between the experimental and FF in crystal bond distances are 0.009 Å for Cu−N, 0.028 Å for in plane Cu−O, and 0.15 Å for the intermolecular Cu−O distances.

Simulation of Copper(II) Coordination Polyhedra Distortion. A comparison of experimental and theoretical values of the eight angles that describe the shape of the copper(II) coordination polyhedron by means of average values and standard deviations is given in Table 8. The FF values of the coordination polyhedron angles for bis(L-*N*,*N*-dimethylvalinato)copper(II), bis(L-alaninato)copper(II), and bis(L-leucinato)copper(II) are gathered together with the corresponding experimental and *ab initio* ones in Table 2.

The force field retains the planarity of the molecules that have the irregular square-planar copper(II) coordination in the real crystal state (Table 1). The planarity is preserved by the simulations in the crystalline surroundings as well as for the isolated molecules.

The shapes of the distorted copper(II) coordination polyhedra (Figure 2) obtained by FF are less distorted *in vacuo* than in crystal. With this respect, the force field performance follows the relationship between the *ab initio* and X-ray results (Table 8). However, the extent of the distortion from the isolated molecule to the crystalline structure is not exactly reproduced. That refers especially to bis(L-*N*,*N*-dimethylvalinato)copper(II), where the *in vacuo* coordination polyhedron resembles the experimental polyhedron rather than the *ab initio* one (Table 2, Figure 2).

The crystal reproduction of the copper(II) coordination polyhedron angles is better by the present force field than by the dummy atom M8-kr47 force field (2.0° and 2.4° rather than 3.5° and 4.5° for $\mathrm{rms}(\Delta\theta)$ and $\mathrm{rms}(\Delta\theta,\Delta\varphi_{\mathrm{ONNO}},\Delta\beta)$, respectively) and comparable to the values obtained by the electrostatic model 7[48] that has the environmental effects built into the parameter set ($\mathrm{rms}(\Delta\theta) = 1.9°$ and $\mathrm{rms}(\Delta\theta,\Delta\varphi_{\mathrm{ONNO}},\Delta\beta) = 2.3°$).

Chelate Ring Torsions. The FF *in vacuo* and in crystal torsion angles for bis(L-*N*,*N*-dimethylvalinato)copper(II), bis(L-alaninato)copper(II), and bis(L-leucinato)copper(II) are given in Table 3, in line with corresponding experimental and *ab initio* values.

The torsion angles of the first two molecules were part of the experimental data on which the force field was optimized. This may explain the matching of the experimental and calculated torsions of these two molecules (the rms errors are 2.4° and 3.5°, respectively). Nevertheless, the force field reproduces well the torsions in the crystal of the third molecule (rms($\Delta\varphi$) = 5.3°), and also yields good *in vacuo* reproduction of the *ab initio* angles for all three molecules. The rms deviations between the *ab initio* and FF *in vacuo* chelate rings' torsion angles are 4.1°, 2.9°, and 4.4°, respectively. These results point out that the force field is capable simulating the influence of the intermolecular interactions on changing the geometry of the chelate rings in a proper way. Besides, it is a proof that the changes between the *ab initio* and experimental structures can be explained by the crystal packing effects.

Errors in Internal Coordinates Calculations. Bond Lengths. The rms deviations for the experimental and FF in crystal bond lengths range from 0.008 Å up to 0.028 Å. The maximum difference of 0.067 Å is obtained for the short N−C(alkyl) (=1.435 Å) bond length of bis(D,L-*N*,*N*-diethylalaninato)copper(II). The bond distances do not change much from the FF in crystal to the FF *in vacuo* conformations. The exceptions are the Cu−O bond lengths of the molecules with apical coordination to the copper in the crystal state. They are shorter *in vacuo* up to 0.014 Å. The total rms deviation between the experimental and FF in crystal bond lengths is 0.017 Å (compared to the M8-kr47 value of 0.029 Å).

Valence Angles. The total rms error in the valence angles is 2.2° (2.3° by M8-kr47). The differences in the valence angles are the largest for the Cu−N−C(alkyl) angles of the copper(II) complexes with N-alkylated amino acids, when comparing the experimental data with the FF in crystal valence angles, and for the Cu−N−H when comparing the FF in crystal and FF *in vacuo* calculated angles. The copper(II) coordination geometry appears to be dependent on the valence angles constituted by the copper, the nitrogen and the atom bonded to the nitrogen. To get the best feasible reproduction of the copper(II) coordination geometry, the k_θ empirical parameters for valence-angle bending of these angles have to be small, i.e., an increase in k_θ renders the reproduction of the angles around the central metal atom. In the real crystal structures the Cu−N−C(alkyl) angles appear to have the values from 100° to 118° (a range rather inappropriate to be modeled by the harmonic function), while the force field conditions them to be from 92° to 121°. The maximum difference is 11.8° for one of the two Cu−N−C(alkyl) angles for bis(D,L-*N*,*N*-dimethylvalinato)copper(II). Even higher deviations from the equilibrium θ_0 (=109.47°) occur for the Cu−N−H angles in the other compounds. For instance, by placing bis(D,L-2-aminobutyrato)copper(II) into crystalline surroundings, the intermolecular interactions cause the Cu−N−H values to shift from 102° and 93° (*in vacuo*) to 130° and 69° (in crystal). The Cu−N−H angles are also poorly reproduced when comparing their FF *in vacuo* with *ab initio* values for bis(L-alaninato)copper(II) and bis(L-leucinato)copper(II). The angles result reduced by 17.4° and 19.7°, respectively. No internal coordinates containing hydrogens were included into the parameters' optimization process. This could be the reason for poor reproduction of the Cu−N−H angles, i.e., the hydrogens bonded to the nitrogens can adopt any position that leaves the internal coordinates on which the parameters were optimized close to their experimental values.

Torsion Angles. The crystalline torsion angles are well reproduced by the force field. The rms deviations are from 2.7° to 3.9°, and the total rms error over 10 molecules is 3.6° (8.3° with M8-kr47). The maximum difference is 14.2° in comparison to 27.1° by the M8-kr47 force field.

In vacuo torsions are almost of the same values as the FF in crystal ones for the four bis(*N*,*N*-alkylamino acidato)copper(II) complexes. For the other molecules, the maximum differences between the FF vacuum and crystal structures are from 7° up to 65.5°, indicating a change in conformations for some of the compounds.

To sum up, the presented force field better reproduces the internal coordinates, crystal lattice organizations, as well as the diversity in the copper(II) coordination geometry *in vacuo* and in crystal than the dummy atoms force field, and, as such, it is better suited for further calculations.

4.3. Energy Difference between Planar and Nonplanar Copper(II) Amino Acid Complexes. The difference between FF *in vacuo* conformational strain energies of the planar bis(D,L-*N*,*N*-dimethylvalinato)copper(II) and the distorted bis(L-*N*,*N*-dimethylvalinato)copper(II) equals −1.4 kJ mol^{-1}. The two isomers' energy difference can be discussed with respect to the stereoselectivity (or, more specificaly, enantioselectivity) effect of the system copper(II)/*N*,*N*-dimethylvaline determined experimentally through polarimetric titration in chloroform solution.[77] The stereoselectivity effect measures which complex is thermodynamically more stable, the meso-structure, CuDL, or equally paired optically active structure, CuLL and CuDD, where the amino acid enantiomers are signified by D and L. In chloroform, the DL complex was determined as the prevailing species (the effect is 3.45 ± 0.55 kJ mol^{-1}),[77] and therefore thermodynamically more stable. If the effect is expressed by means of a difference between the Gibbs free energies of the two isomers,[15] the FF calculations give again the LL complex energetically favored, by 2.2 kJ mol^{-1}. The Gibbs free energies were calculated for 21 conformers of each LL and DL complexes, by taking vibrational contributions to the thermodynamic functions[72] at 298.16 K into account. For both molecules, the most stable conformer corresponds to the same one found by the X-ray diffraction measurements, with the probability of its occurrence calculated to be 0.99.

Interesting to note, the enantioselectivity effect was not observed in copper(II) amino acidates unless amino acids had bulky N-substituents, and it was predicted to be due to the steric interligand interactions.[15,77] In line with the prediction, the difference between the FF strain energies of the two bis(*N*,*N*-dimethylvalinato)copper(II) molecules comes mainly from the Lennard-Jones potential energy contributions, giving less repulsive interactions in the LL than the DL complex. Obviously, the FF *in vacuo* distortion of the copper(II) coordination polyhedron reduces the repulsions caused by close interatomic contacts. With this respect, the flatteness of the potential energy surface in vicinity of the *trans*-planar minimum is well simulated. However, it seems reasonable to assume that more planar copper(II) coordination geometry than the one predicted with the FF force field should yield distorted geometry less energetically favored to the planar one. From this viewpoint, better quantitative reproduction of the copper(II) coordination polyhedon calls for further improvement of the molecular mechanics model.

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5. Conclusions

We have presented the results of the *ab initio* and molecular mechanics studies of a series of tetracoordinated copper(II) chelates with α-amino acids in which three different shapes of the copper(II) coordination polyhedron were observed in the crystal state. According to the *ab initio* results, a square-planar copper(II) coordination geometry is an electronically favored structure for bis(amino acidato)copper(II) complexes. If there is no steric hindrance present in a molecule (as can be close contacts between bulky alkyl groups replacing the hydrogens of the amino group), it remains planar. The comparison of the experimental crystalline structures with the *ab initio in vacuo* derived equilibrium geometries points out that a strain imposed by symmetrical arrangement of molecules in the crystal lattice can be alleviated either by distortion of the copper(II) coordination polyhedron or/and by changing the geometry of the chelate rings. These changes can be calculated and reproduced with a set of relatively simple analytical functions (defined by carefully selected parameters) that describe the conformational potential energy of a molecule and van der Waals and hydrogen bonding interactions between the molecules.

Supporting Information Available: Listings of root-mean-square deviations and maximum errors in bond lengths, valence and torsional angles for the 10 molecules (comparison of experimental and *ab initio* data, comparison of experimental and FF in crystal data, comparison of FF in crystal and FF *in vacuo* internal coordinates), and of experimental and theoretical lattice constants, unit cell volumes and comparison of the volumes. This material is available free of charge via the Internet at http://pubs.acs.org.

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