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In Vacuo and *in Crystal* Molecular-Mechanical Modeling of Copper(II) Complexes with Amino Acids

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Two molecular mechanics models, model 7 (described earlier) and model 8 (described here), have been used to calculate the geometries of nine copper(II) complexes with α-amino acids and their N-alkylated derivatives and the diastereoselectivity in the copper(II)/*N,N*-dimethylvaline system. Interactions inside the copper(II) coordination sphere are modeled by a repulsive coulombic potential among nonbonded atoms of the copper(II) coordination polyhedron and a harmonic bond-stretching potential between metal and ligand atoms. The models differ in the nonbonded part of the conformational potential: a Buckingham function (model 7) is replaced by a Lennard−Jones 12-6 function and electrostatic potential in model 8, in order to perform crystal calculations by the Consistent Force Field (CFF) program. The potential energy parameter set of model 8 is optimized on X-ray crystal structures and selected vibrational frequencies. *In vacuo* (models 7 and 8) and *in crystal* (model 8) calculations of the geometries of the copper(II) complexes are compared with their X-ray crystal structures. An optimized parameter set of model 8, the M8-kr47 force field, reproduces the unit cell volumes in a range from −8% to +4%. Significantly better reproduction of the copper(II) coordination polyhedron geometries is obtained with model 8 by an *in crystal* than an *in vacuo* approximation, especially for molecules with distorted copper(II) coordination. Model 8 is better in reproducing the bond lengths ($\mathrm{rms}(\Delta b) = 0.031$ Å) and the torsional angles ($\mathrm{rms}(\Delta\varphi) = 8.4°$) but yields worse agreement between the experimental and the calculated valence angles than model 7 ($\mathrm{rms}(\Delta\vartheta) = 2.3°$). The overall similarity is reproduced equally well by the both models ($\mathrm{rms}(\Delta r) = 0.163$ Å). The M8-kr47 reproduces the diastereoselectivity within experimental error, while model 7 overestimates it.

Introduction

For some time, we have been interested in the modeling of structural and thermodynamical properties of the complexes formed by copper(II) with amino acids and amino acid derivative ligands, so as to contribute to better understanding of the structure and function of the copper proteins. Our special attention has been given to a simulation of the distortion of a copper(II) coordination polyhedron.[2−7] The distortion is connected with the redox potential of the copper proteins.[8]

The copper(II) chelates with N-alkylated α-amino acids were found to be most interesting, for two reasons. Their red crystal modifications consist of discrete molecules held together by van der Waals interactions.[9−11] As the interactions between the molecules in the crystal lattice were presumably very weak (there are no intermolecular contacts closer than 3.2 Å), the lack of additional interactions due to chelation or hydrogen bonding made this type of compounds nearly ideally suited for the study of molecular conformation in the absence of influence from neighboring molecules in the crystal lattice.

The second reason is a considerable stereoselectivity effect observed in these compounds.[12] The effect is seldom observed in copper(II) complexes with bidentate amino acids.[13] In fact, it cannot be observed unless amino acids have bulky side chains, and it was predicted to be due to the side-chains' intramolecular interactions.[12] If the stereoselectivity is measured in poorly solvating solvents incapable of coordination (e.g. chloroform), it can be explained in terms of the conformational Gibbs free energy difference between LL- and DL- diastereomers of the same bonding isomers. All other factors can be neglected which, again, makes these systems almost ideally suited for evaluation and adaptation of an empirical force field for amino acidato complexes.

The thermodynamic stereoselectivity is closely connected with the plasticity[14] (nonrigidity) of the copper(II) coordination sphere. Because of the property of plasticity, the copper(II) coordination polyhedron can easily distort in order to avoid and suppress the intramolecular strain. The plasticity of the

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(2) Raos, N.; Simeon, Vl. *Croat. Chem. Acta* **1985**, *58,* 127.

(3) Sabolović, J.; Raos, N.; Rasmussen, Kj. *Croat. Chem. Acta* **1989**, *62,* 495.

(4) Sabolović, J.; Raos, N. *Polyhedron* **1990**, *9,* 1277.

(5) Sabolović, J.; Raos, N. *Polyhedron* **1990**, *9,* 2419.

(6) Sabolović, J.; Raos, N.; Rasmussen, Kj. *Polyhedron* **1991**, *10,* 2079.

(7) Sabolović, J. *Polyhedron* **1993**, *12,* 1107.

(8) (a) Colman, P. M.; Freeman, H. C.; Guss, J. M.; Murata, M.; Norris, V. A.; Ramshaw, J. A. M.; Venkatappa, M. P. *Nature* **1978**, *272,* 319. (b) Roberts, V. A.; Fisher, C. L.; Redford, S. M.; Mcree, D. E.; Parge, H. E.; Getzoff, E. D.; Tainer, J. A. *Free Radical Res. Commun.* **1991**, *12−13,* 269. (c) Eichhorn, G. L., Ed. *Inorganic Biochemistry*; Elsevier Scientific Publishing Company: Amsterdam, London, and New York, 1973; Vol. 2.

(9) Kaitner, B.; Kamenar, B.; Paulić, N.; Raos, N.; Simeon, Vl. *J. Coord. Chem.* **1987**, *15,* 373.

(10) Kaitner, B.; Paulić, N.; Raos, N. *J. Coord. Chem.* **1991**, *22,* 269.

(11) Kaitner, B.; Ferguson, G.; Paulić, N.; Raos, N. *J. Coord. Chem.* **1992**, *26,* 105.

(12) (a) Davankov, V. A.; Rogozhin, S. V.; Kurganov, A. A.; Zhuchkova, L. Ya. *J. Inorg. Nucl. Chem.* **1975**, *37,* 369. (b) Davankov, V. A.; Rogozhin, S. V.; Struchkov, Yu. T.; Alexandrov, G. G.; Kurganov, A. A. *J. Inorg. Nucl. Chem.* **1976**, *38,* 631.

(13) (a) Gillard, R. D.; Irving, H. M.; Parkins, R. M.; Payne, N. C.; Pettit, L. D. *J. Chem. Soc. A* **1966**, 1159. (b) Simeon, Vl.; Weber, O. A. *Croat. Chem. Acta* **1966**, *38,* 161. (c) Barnes, D. S.; Pettit, L. D. *J. Inorg. Nucl. Chem.* **1971**, *33,* 2177.

(14) (a) Gažo, J.; Bersuker, I. B.; Garaj, J.; Kabašová, M.; Kohut, J.; Langfelderová, H.; Melník, M.; Serátor, M.; Valach, F. *Coord. Chem. Rev.* **1976**, *19,* 253. (b) Bersuker, I. B. *The Jahn-Teller Effect and Vibronic Interactions in Modern Chemistry*; Plenum Press: New York, 1984.

coordination sphere is connected with the electron configuration of the copper ion and is due to the Jahn−Teller effect or the pseudo-Jahn−Teller effect. A consequence is the variability of the spatial arrangement of the same ligands around copper (distortion isomerism).[14]

In an attempt to model the distortion of the copper(II) polyhedron, several molecular mechanics models have been proposed.[3−7,15] Among them, the electrostatic models (model 6 and model 7) gave the best agreement with the crystal structures of a series of tetracoordinated copper(II) amino acidates.[5,7]

Model 7[7] was chosen for further force field development. Because the only available experimental structures were those determined by X-ray diffraction, the main idea was to modify model 7 in order to simulate the molecular conformations in crystalline surroundings as well as in the *in vacuo* approximation. The aim of a new model (model 8) is to determine a force field by optimization of the empirical parameters with respect to experimental data, that will reproduce well not only the properties of the copper(II) complexes with N-alkylated amino acids (group I molecules) but also with other amino acids that have the same *trans*-CuN_2O_2 coordination polyhedron but a crystal structure such that an intermolecular influence on the geometry of the central atom coordination should be expected (group II molecules).

Methods

Conformational Energy. The conformational (strain) potential energy was calculated from the following basic formula:

$$V = \frac{1}{2}\sum_i k_{b,i}(b_i - b_{0,i})^2 + \frac{1}{2}\sum_j k_{\vartheta,j}(\vartheta_j - \vartheta_{0,j})^2 + \frac{1}{2}\sum_k k_{\chi,k}\chi_k^{\,2} + \frac{1}{2}\sum_l V_{\varphi,l}(1 \pm \cos n_l\varphi_l) + \sum_{m>n}\frac{q_m q_n}{\epsilon_r r_{mn}} + V_{NB} \quad (1)$$

Here b, ϑ, φ, χ and r are bond lengths, valence, torsional, and out-of-plane angles, and nonbonded distances. k_b is an empirical parameter for bond stretching, k_ϑ for valence angle bending and k_χ for the out-of-plane deformational potential for the carboxyl groups. Torsional interactions are specified with V_φ and n (height and multiplicity of the torsional barrier, respectively). q is a charge parameter for the atoms of the coordination polyhedron (see below) and ϵ_r is the dielectric constant. The part of the strain potential energy which is different for two electrostatic models, model 7 and the new model 8, is the nonbonded potential, V_{NB}. Intramolecular interactions separated by three or more bonds are considered nonbonded.

Electrostatic Models. Model 7. The model was termed electrostatic because of the assumption that repulsive coulombic interactions among the nonbonded atoms of the coordination polyhedron determine its shape.[7] No charge was supposed to reside on the atoms outside the coordination sphere. The coordination polyhedron was defined by five real atoms (M, N, N′, O, and O′) situated in the plane of the chelate rings, and two "dummy" ligand atoms (denoted X and X′), imagined to represent an electron pair placed half above and half below the plane. As a counterbalance to these coulombic interactions between all nonbonded atoms of the coordination polyhedron only harmonic bond-stretching interactions between the ligand atoms and the metal atom were considered. Therefore, it is a model without any explicit angle-bending potential for the angles around copper.

Nonbonded van der Waals interactions were modeled by a Buckingham function

$$V_{NB} = \sum_i [a_i \exp(-b_i r_i) - c_i r_i^{-6}] \quad (2)$$

where a, b, and c are empirical atom pair parameters.

Model 8. The interactions inside the copper(II) coordination polyhedron are the same as in model 7: harmonic bond-stretching between metal and six ligand atoms (two of them are "dummy" atoms), and repulsive coulombic interactions among the nonbonded atoms.

The difference between the models originates in nonbonded potential: a Lennard−Jones 12-6 function is chosen instead of Buckingham function; charges, q, are placed on all atoms and, consequently, electrostatic nonbonded interactions are introduced

$$V_{NB} = \sum_{i>j}\left(\frac{A_iA_j}{r_{ij}^{12}} - \frac{B_iB_j}{r_{ij}^{\,6}} + \frac{q_iq_j}{\epsilon_r r_{ij}}\right) \quad (3)$$

where A and B are one-atom empirical parameters.

Comparison of the Structures. The root-mean-square deviation, rms, between experimental and theoretical structures was calculated from

$$\mathrm{rms}(\Delta Y) = \left(\frac{1}{N}\sum_{i=1}^{N}(\Delta Y_i)^2\right)^{1/2} \quad (4)$$

where Y stands for internal coordinate, interatomic distance, unit cell constant or the lattice unit cell volume. ΔY is the difference $Y_{exp} - Y_{calc}$ between an experimentally measured observable and the corresponding calculated value.

Calculation of the Diastereoselectivity Effect. The average Gibbs free energy of the diastereomer (MLL or MDL) was calculated from the formula

$$\langle G\rangle = \frac{\sum_i G_i\omega_i}{\sum_i \omega_i} \quad (5)$$

where G_i is the Gibbs free energy, and ω_i is the statistical weight of the ith conformer calculated from the Boltzmann distribution formula. Details of the calculations were given elsewhere.[15]

Experimental Data

We have selected nine substances for modeling. The experimental data that the theoretical results have been compared with are the X-ray structures of nine tetracoordinated copper(II) amino acidates with *trans*-N_2O_2 copper(II) coordination and the diastereoselectivity effect of bis(*N*,*N*-dimethylvalinato)copper(II). We note that the complexes are neutral molecules. Their structural formulas are given in Figure 1.

With respect to the interactions among the molecules in the crystal lattice, the nine molecules can be divided into two groups. The molecules of group I are bis(L-*N*,*N*-dimethylisoleucinato)copper(II),[10] bis(L-*N*,*N*-dimethylvalinato)copper(II),[9] and bis(D,L-*N*,*N*-diethylalaninato)copper(II).[11] In crystals these three molecules are held together only by van der Waals forces. The two first of them have distorted copper(II) coordination (a flattened tetrahedron), while the third has an irregular square-planar one, without any noticeable apical coordination. It is supposed that the distortion is a result of intramolecular strain rather than intermolecular interactions in the crystals.

The other six molecules (group II) are bis(L-leucinato)copper(II),[16] bis(L-alaninato)copper(II),[17] bis(L-2-aminobutyrato)copper(II),[18] bis(D,L-2-aminobutyrato)copper(II),[16] bis(α-aminoiso-bu

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(15) Raos, N.; Niketić, S. R.; Simeon, Vl. *J. Inorg. Biochem.* **1982**, *16*, 1.

(16) Fewcett, T. G.; Ushay, M.; Rose, J. P.; Lalancette, R. A.; Potenza, J. A.; Schugar, H. *J. Inorg. Chem.* **1979**, *18*, 327.

(17) Hitchman, M. A.; Kwan, L.; Engelhardt, L. M.; White, A. H. *J. Chem. Soc. Dalton Trans.* **1987**, 457.

(18) Levstein, P. R.; Calvo, R.; Castellano, E. E.; Piro, O. E.; Rivero, B. E. *Inorg. Chem.* **1990**, *29*, 3918.

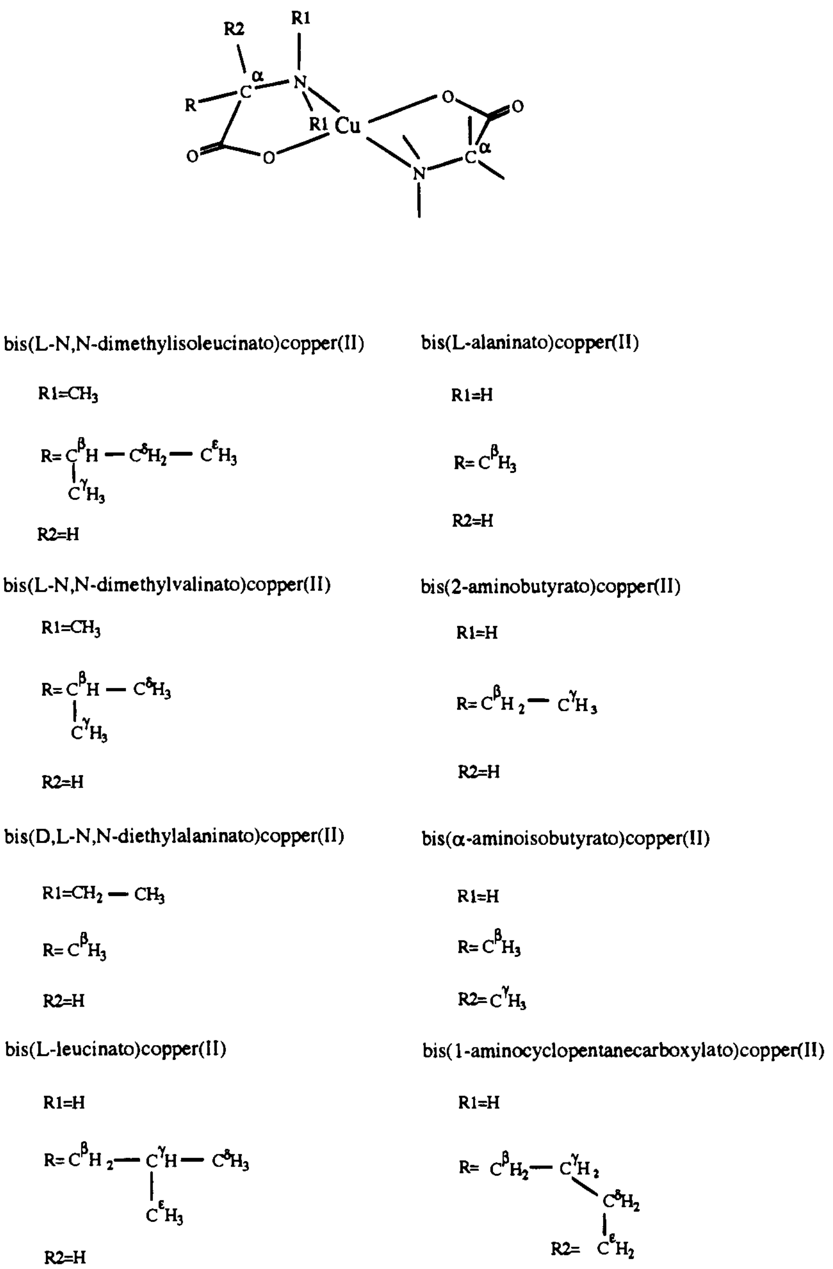

Figure 1. Copper(II) complexes with α-amino acids and their N-alkylated derivatives studied in this work.

tyrato)copper(II),[19] and bis(1-aminocyclopentanecarboxylato)copper(II).[17] The first three complexes of group II have a distorted planar coordination and the three others an irregular square-planar copper(II) coordination. The crystal organization of group II molecules is as follows: the structures consist of tetragonally coordinated Cu(II) ions arranged in isolated two-dimensional sheets. The molecules are linked to each other within the sheet through a net of relatively weak N−H•••O hydrogen bonds and also through intermolecular Cu−O interactions, completing an elongated octahedral coordination around copper. The distances between the copper atom and the carboxyl oxygens of the neighboring molecules are much longer in bis(α-aminoisobutyrato)copper(II) and bis(1-aminocyclopentanecarboxylato)copper(II) (3.045 and 3.116 Å, respectively) than in the other four molecules (from 2.629 Å in bis(L-leucinato)copper(II) to 2.848 Å in the complex with L-alanine).

The diastereoselectivity (or, more specifically, enantioselectivity) effect of the system copper(II)/*N,N*-dimethylvaline was determined experimentally through polarimetric titration in chloroform solution.[12a] The prevailing structures are the MDL meso-complexes and the effect is (3.45 ± 0.55) kJ mol^{-1}.

Results and Discussion

Calculation. All calculations were performed with the Consistent Force Field (CFF) program for conformational analysis,[20-22] which was further modified to cope with the electrostatic models. The minimization of conformational potential energy has been done by a very fast variable metric algorithm[23] which starts out as steepest descent and ends up being quadratically convergent. The set of potential energy

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(19) Oliva, G.; Castellano, E. E.; Zukerman-Schpector, J. *Acta Crystallogr.* **1986**, *C42*, 19.

(20) Niketić, S. R.; Rasmussen, Kj. *The Consistent Force Field: A Documentation, Lecture Notes in Chemistry*; Springer: Berlin, 1977; Vol. 3.

(21) Rasmussen, Kj. *Potential Energy Functions in Conformational Analysis*; Lecture Notes in Chemistry; Springer: Berlin, 1985; Vol. 37.

(22) Rasmussen, Kj.; Engelsen, S. B.; Fabricius, J.; Rasmussen, B. In *Recent Experimental and Computational Advances in Molecular Spectroscopy*; Fausto, R., Ed.; NATO ASI Series C: Mathematical and Physical Sciences; Kluwer Academic Publisher: Dordrecht, The Netherlands, 1993; Vol. 406, p 381.

(23) (a) Dennis, J. E.; More, J. J. *SIAM Rev.* **1977**, *19*, 46. (b) Engelsen, S. B. Ph.D. Thesis, Technical University of Denmark, Lyngby, 1991.

Table 1. Potential Energy Parameter Set for Model 7[a,b]

bond	k_b	b_0	bond	k_b	b_0
M−N	251.650	2.000	K−Q	1200.000	1.240
N−C	862.800	1.471	K−O	330.000	1.280
C−C	719.000	1.540	K−C	370.000	1.510
C−H	719.000	1.093	M−O	270.000	1.950
N−H	805.280	1.011	M−X	9.198	0.000

angle	k_ϑ	ϑ_0	angle	k_ϑ	ϑ_0
M−N−H	28.760	1.911	C−N−C	143.800	1.911
M−N−C	57.520	1.911	K−C−H	93.470	1.911
N−C−C	143.800	1.911	N−C−K	143.800	1.911
N−C−H	93.470	1.911	C−C−K	143.800	1.911
H−N−H	76.214	1.911	O−K−Q	80.000	2.138
H−C−H	74.776	1.911	C−K−Q	80.000	2.138
C−N−H	93.470	1.911	C−K−O	80.000	2.007
H−C−C	93.470	1.911	K−O−M	60.000	1.920
C−C−C	143.800	1.911			

torsion	V_φ	n	torsion	V_φ	n
−C−N−	3.000	3.000	−K−C−	0.500	6.000
−C−C−	3.000	3.000	−O−M−	4.000	−4.000
−O−K−	5.000	−2.000	−M−N−	0.001	12.000

out-of-plane torsion	k_χ
Q(K−O−C)	100.000

nonbonding[d]	a	b	c
H- - -H	0.660	4.080	49.200
C- - -C	23.700	4.320	297.800
Q- - -Q	18.640	4.550	200.000
K- - -K	23.700	4.320	297.800
H- - -N	2.810	4.320	99.200
H- - -C	3.140	4.200	121.100
H- - -K	3.140	4.200	121.100
H- - -O	2.810	4.320	99.200
H- - -Q	3.140	4.200	121.100
H- - -M	3.140	4.200	121.100
C- - -N	21.210	4.440	244.000
C- - -K	23.700	4.320	297.800
C- - -Q	21.218	4.440	244.000
C- - -O	21.210	4.440	244.000
C- - -M	23.700	4.320	297.800
N- - -K	21.210	4.440	244.000
N- - -Q	18.640	4.550	200.000
O- - -K	21.210	4.440	244.000
O- - -Q	18.640	4.550	200.000
K- - -M	23.700	4.320	297.800
K- - -Q	21.210	4.440	244.000
Q- - -M	21.210	4.440	244.000

charge[c]	q	charge[c]	q
N	−0.375	X	−0.750
O	−0.375		

[a] Uncommon symbols: K, planar carbon atom; Q, double-bonded oxygen atom; M, copper(II); X, "dummy" atom. [b] Units are as follows: k_b, kcal mol^{-1} Å^{-2}; b_0, Å; k_ϑ, kcal mol^{-1} rad^{-2}; ϑ_0, rad; V_φ, kcal mol^{-1}; k_χ, kcal mol^{-1} rad^{-2}; a kcal mol^{-1} [10^{-4}]; b, Å^{-1}; c, kcal mol^{-1} Å^6. [c] q is in electron units; the expression for electrostatic interaction (see eq 1) has to be multiplied by 332.091 kcal mol^{-1} Å in order to be in kcal mol^{-1}; the dielectric constant $\epsilon_r = 2$. [d] Buckingham function, eq 2.

functions of model 8 has been parametrized by first exercising initial trial and error guesses and then using the optimization algorithm, which is a variant of the general least-squares method (the Levenberg−Marquardt algorithm).[21,22] Crystal simulations were carried out using the Williams variant of the Ewald lattice summation method[21,24] with a spherical and abrupt cutoff limit as large as 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.

Potential Energy Parameter Sets. The potential energy parameter set of model 7 is given in Table 1.

Table 2. Potential Energy Parameter Sets for Model 8[a]

	M8-P0		M8-P7a		M8-kr47	
bond	k_b	b_0	k_b	b_0	k_b	b_0
M−N	251.650	2.000	284.188	1.908	284.188	1.910
N−C	862.800	1.471	754.366	1.475	754.366	1.462
C−C	719.000	1.540	1179.101	1.540	1179.101	1.525
C−H	676.000	1.093	674.590	1.093	674.590	1.093
N−H	805.280	1.011	805.280	1.011	805.280	1.011
K−Q	1354.000	1.240	1349.806	1.213	1349.806	1.216
K−O	330.000	1.280	504.542	1.280	504.542	1.294
K−C	370.000	1.510	352.678	1.509	352.678	1.544
M−O	270.000	1.950	323.371	1.826	323.371	1.831
M−X	20.000	0.000	18.199	0.000	20.011	0.000

	M8-P0		M8-P7a		M8-kr47	
angle	k_ϑ	ϑ_0	k_ϑ	ϑ_0	k_ϑ	ϑ_0
M−N−H	28.760	1.911	28.760	1.911	28.760	1.911
M−N−C	57.520	1.911	75.273	1.911	75.273	1.911
N−C−C	143.800	1.911	188.330	1.911	188.330	1.911
N−C−H	93.470	1.911	103.594	1.911	103.594	1.911
H−N−H	76.214	1.911	76.214	1.911	76.214	1.911
H−C−H	74.776	1.911	93.482	1.911	93.482	1.911
C−N−H	93.470	1.911	93.437	1.911	93.437	1.911
H−C−C	93.470	1.911	50.000	1.911	50.000	1.911
C−C−C	143.800	1.911	208.988	1.911	208.988	1.911
C−N−C	143.800	1.911	215.853	1.911	215.853	1.911
K−C−H	93.470	1.911	106.476	1.911	106.476	1.911
N−C−K	143.800	1.911	240.340	1.911	240.340	1.911
C−C−K	143.800	1.911	139.942	1.911	139.942	1.911
O−K−Q	80.000	2.138	50.000	2.138	50.000	2.138
C−K−Q	80.000	2.138	59.791	2.138	59.791	2.138
C−K−O	80.000	2.007	124.447	2.007	124.447	2.007
K−O−M	60.000	1.920	9.546	1.920	9.546	1.920

	M8-P0		M8-P7a		M8-kr47	
torsion	V_φ	n	V_φ	n	V_φ	n
−C−N−	3.000	3.000	3.000	3.000	3.000	3.000
−C−C−	3.000	3.000	3.000	3.000	3.000	3.000
−O−K−	5.000	−2.000	5.000	−2.000	5.000	−2.000
−K−C−	0.500	6.000	0.500	6.000	0.500	6.000
−O−M−	4.000	−4.000	4.000	−4.000	4.000	−4.000
−M−N−	0.001	12.000	0.001	12.000	0.001	12.000

	k_χ		
out-of-plane torsion	M8-P0	M8-P7a	M8-kr47
Q(K−O−C)	100.000	100.000	100.000

	M8-P0		M8-P7a		M8-kr47	
nonbonding[b]	A	B	A	B	A	B
H- -	132.000	7.000	59.088	10.420	89.581	10.308
C- -	576.000	19.000	971.397	8.328	1014.431	7.400
N- -	378.000	15.000	418.191	5.284	409.873	5.000
O- -	378.000	15.000	1175.000	21.636	1196.580	21.000
Q- -	378.000	15.000	108.638	20.882	136.736	19.800
M- -	576.000	19.000	291.660	26.786	302.366	26.500
K- -	576.000	19.000	871.762	6.653	849.835	6.000
X- -	132.000	7.000	13.535	4.250	9.650	3.928

	q		
charge	M8-P0	M8-P7a	M8-kr47
H	0.100	0.036	−0.027
C	−0.233	−0.202	−0.257
K	0.100	0.007	0.089
Q	−0.100	0.183	0.225
M	1.500	0.918	0.908
N	−0.375	−0.467	−0.580
O	−0.375	−0.499	−0.539
X	−0.750	−1.010	−1.093

[a] The units are the same as in Table 1, except as follows: A, (kcal mol^{-1} Å^{12})$^{1/2}$; B, (kcal mol^{-1} Å^6)$^{1/2}$. [b] Lennard−Jones function, eq 3.

The potential energy parameter sets of model 8 are given in Table 2. There are three force fields here: M8-P0, M8-P7a, and M8-kr47.

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(24) Pietilä, L.-O.; Rasmussen, Kj. *J. Comput. Chem.* **1984**, *5*(3), 252.

M8-P0 was an initial parameter set for parameter optimization. It was the same as the model 7 parameter set in the valence-angle bending, torsional and out-of-plane parts and almost identical in the bonding part (the new k_b were chosen such that C—H and C═O bond-stretching would fit the IR spectra[25] of group I molecules). In order to perform crystal simulations by the CFF,[24] the nonbonded potential had to be modeled by the Lennard-Jones instead of the Buckingham function, and electrostatic nonbonded interactions had to be introduced as well. The one-atom empirical parameters, A_i and B_i, of V_{NB} (eq 3) were calculated by means of the van der Waals well depth, E_i, and the equilibrium van der Waals distance, r^*, derived from the Buckingham potential (eq 2) $[A_i = (E_{ii}r_{ii}^{*12})^{1/2}$, $B_i = (2E_{ii}r_{ii}^{*6})^{1/2}]$. For the metal atom, M, and the "dummy" atom, X, A_i and B_i were set equal to the values for carbon and hydrogen, respectively. After these parameters had been selected, the initial $k_{b,MX}$ and the charge parameters were chosen so as to reproduce the geometries of the molecules on which the parameters would be optimized as closely as possible to their experimental structures.

The experimental data that the empirical parameters were optimized on were internal coordinates (bond lengths and valence and torsional angles) determined from the crystal structures[9-11] and a few IR frequencies (for C═O and C—H bond-stretching)[25] of group I molecules.

The optimization was carried out until an equilibrium fit was obtained such that a small change of any of the parameters caused its disturbance. The resulting force field, M8-P7a, was computed as if the molecules were isolated *in vacuo*.

M8-P7a is an initial parameter set for a further parameter optimization cycle. This time intermolecular interactions were taken into account, so as the molecules in the crystal lattice are surrounded by other molecules. The experimental data were the same internal coordinates as before, plus the lattice constants of the group I compounds. In the last stage of the optimization process the fourth molecule, bis(1-aminocyclopentanecarboxylato)copper(II),[17] was included in order to get a better parametrized charge parameter for hydrogens bonded to nitrogen. M8-kr47 is the final force field.

While model 7 keeps the values of the partial charges equal to the charge parameters, model 8 allows the partial charge assignment and neutralization to be done by a special charge redistribution algorithms that is part of the CFF program.[22] In this algorithm the X is treated as a highly electronegative halogen, in accordance with the assumption that the "dummy" atoms represent the electron pair. The partial charge assignments inside the nine molecules due to the charge parameters given in Table 2 are found in Table 3.

Initial Positions of the "Dummy" Atoms. An inherent property of model 8 is that final results depend mostly on the initial positions of the X atoms. Different positions can lead to different copper(II) configurations, especially for molecules of group II.

In order to get consistent results the following "dummy" atoms orientation was chosen: X and X′ perpendicular to the ⟨NMO⟩ and the ⟨N′MO′⟩ plane, respectively. Given the orientation, the M—X distance was varied in an attempt to find an answer to the question of how to choose an M—X initial, such as to be sure that it will lead to a correct minimum. A correct minimum is a minimum that gives the best agreement with experimental structure through the rms deviations and the comparison of the unit cell volumes (only the correct minima are discussed in Tables 4—6 and Figure 4).

Table 3. Assignment of Charges for Nine Copper(II) Bis(amino acidates) Due to the Charge Redistribution Algorithm, Using the Charge Parameters Given in Table 2[a]

	partial charges/*e*				partial charges/*e*		
atom	M8-P0	M8-P7a	M8-kr47	atom	M8-P0	M8-P7a	M8-kr47
Bis(L-*N*,*N*-dimethylvalinato)copper(II)							
M	2.084	1.681	1.740	$C^{1,2}(H_3)$	−0.355	−0.105	0.073
X	−0.666	−0.921	−0.990	$C^{\alpha}(H)$	−0.155	−0.033	0.018
N	−0.291	−0.378	−0.477	$C^{\beta}(H)$	−0.249	−0.149	−0.127
O	−0.291	−0.409	−0.436	$C^{\gamma,\delta}(H_3)$	−0.449	−0.222	−0.072
K	0.403	0.134	0.212	H(C)	0.184	0.125	0.076
Q	−0.766	−0.187	−0.127				
Bis(L-*N*,*N*-dimethylisoleucinato)copper(II)							
M	2.084	1.678	1.738	$C^{1,2}(H_3)$	−0.356	−0.107	0.071
X	−0.666	−0.923	−0.992	$C^{\alpha}(H)$	−0.156	−0.035	0.016
N	−0.291	−0.380	−0.479	$C^{\beta}(H)$	−0.250	−0.152	−0.128
O	−0.291	−0.412	−0.438	$C^{\gamma,\epsilon}(H_3)$	−0.449	−0.224	−0.074
K	0.402	0.132	0.210	$C^{\delta}(H_2)$	−0.349	−0.188	−0.101
Q	−0.766	−0.189	−0.128	H(C)	0.184	0.123	0.074
Bis(D,L-*N*,*N*-diethylalaninato)copper(II)							
M	2.084	1.681	1.740	$C^{1,3}(H_3)$	−0.255	−0.069	0.045
X	−0.666	−0.921	−0.990	$C^{2,4}(H_3)$	−0.449	−0.222	−0.072
N	−0.291	−0.378	−0.477	$C^{\alpha}(H)$	−0.155	−0.033	0.018
O	−0.291	−0.409	−0.436	$C^{\beta}(H_3)$	−0.449	−0.222	−0.072
K	0.403	0.134	0.212	H(C)	0.184	0.125	0.076
Q	−0.766	−0.187	−0.127				
Bis(L-leucinato)copper(II)							
M	2.082	1.679	1.737	$C^{\alpha}(H)$	−0.157	−0.034	0.015
X	−0.668	−0.922	−0.993	$C^{\beta}(H_2)$	−0.351	−0.187	−0.102
N	−0.293	−0.379	−0.480	$C^{\gamma}(H)$	−0.251	−0.151	−0.130
O	−0.293	−0.411	−0.439	$C^{\delta,\epsilon}(H_3)$	−0.451	−0.233	−0.075
K	0.401	0.133	0.209	H(C)	0.182	0.124	0.073
Q	−0.768	−0.188	−0.130	H(N)	0.213	0.252	0.303
Bis(L-alaninato)copper(II)							
M	2.085	1.693	1.746	Q	−0.765	−0.174	−0.120
X	−0.665	−0.909	−0.983	$C^{\alpha}(H)$	−0.155	−0.020	0.025
N	−0.290	−0.366	−0.471	$C^{\beta}(H_3)$	−0.448	−0.209	−0.066
O	−0.290	−0.397	−0.430	H(C)	0.185	0.138	0.082
K	0.403	0.147	0.219	H(N)	0.216	0.265	0.312
Bis(2-aminobutyrato)copper(II)							
M	2.083	1.687	1.742	$C^{\alpha}(H)$	−0.156	−0.026	0.021
X	−0.667	−0.915	−0.988	$C^{\beta}(H_2)$	−0.350	−0.179	−0.097
N	−0.292	−0.372	−0.475	$C^{\gamma}(H_3)$	−0.450	−0.216	−0.070
O	−0.292	−0.403	−0.434	H(C)	0.183	0.131	0.078
K	0.402	0.140	0.214	H(N)	0.215	0.259	0.308
Q	−0.767	−0.180	−0.125				
Bis(α-aminoisobutyrato)copper(II)							
M	2.083	1.687	1.742	Q	−0.767	−0.180	−0.125
X	−0.667	−0.915	−0.988	C^{α}	−0.056	0.010	−0.007
N	−0.292	−0.372	−0.475	$C^{\beta,\gamma}(H_3)$	−0.450	−0.216	−0.070
O	−0.292	−0.403	−0.434	H(C)	0.183	0.132	0.078
K	0.402	0.140	0.214	H(N)	0.292	0.259	0.308
Bis(1-aminocyclopentanecarboxylato)copper(II)							
M	2.090	1.688	1.746	C^{α}	−0.049	0.011	−0.002
X	−0.660	−0.914	−0.983	$C^{\beta,\gamma}(H_2)$	−0.343	−0.178	−0.093
N	−0.285	−0.371	−0.471	$C^{\delta,\epsilon}(H_2)$	−0.343	−0.178	−0.093
O	−0.285	−0.402	−0.430	H(C)	0.190	0.133	0.082
K	0.409	0.142	0.219	H(N)	0.221	0.260	0.313
Q	−0.760	−0.179	−0.120				

[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.

For each molecule the dependence of initial energy on the initial M—X distance had been checked, *in crystal* and *in vacuo*, for the M8-kr47 force field (Figures 2 and 3). It can be noticed that for group I molecules (Figure 2) the energy dependence is different from that for group II (Figure 3) molecules. For group I it is similar in both cases, when a molecule is treated as *in vacuo* and *in crystal*. Therefore it can be concluded that the

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(25) Sabolović, J.; Rasmussen, Kj. Unpublished results. Vibrational bond-stretching frequencies: bis(L-*N*,*N*-dimethylvalinato)copper(II), C—H at 2969, 2936, and 2883 cm^{-1} and C═O at 1662 cm^{-1}; bis(L-*N*,*N*-dimethylisoleucinato)copper(II), C—H at 2965, 2940, and 2880 cm^{-1} and C═O at 1660 and 1645 cm^{-1}; bis(D,L-*N*,*N*-diethylalaninato)copper(II), C—H at 2973, 2963, 2938, 2896, and 2876 cm^{-1} and C═O at 1671 and 1648 cm^{-1}.

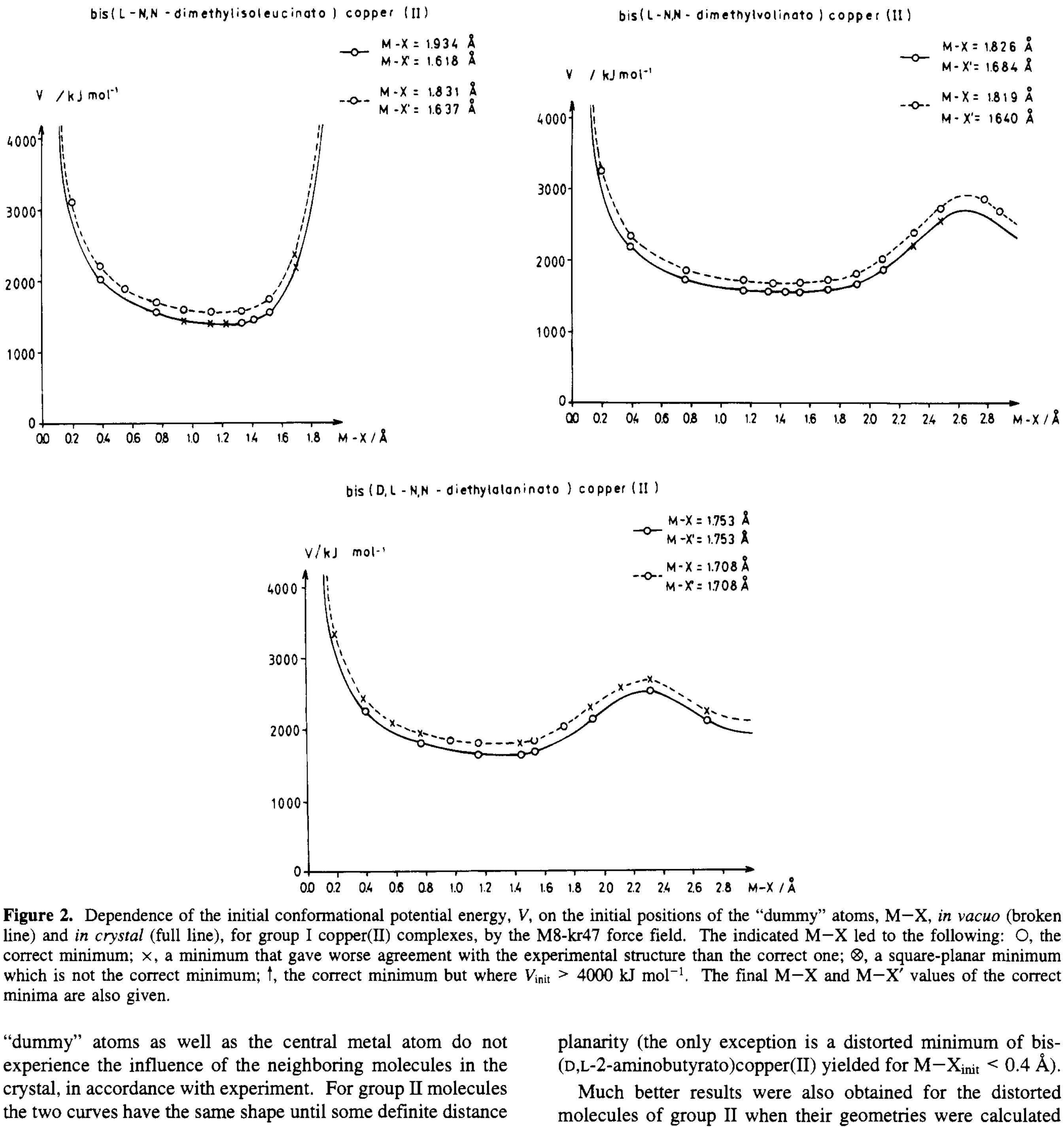

Figure 2. Dependence of the initial conformational potential energy, *V*, on the initial positions of the "dummy" atoms, M−X, *in vacuo* (broken line) and *in crystal* (full line), for group I copper(II) complexes, by the M8-kr47 force field. The indicated M−X led to the following: ○, the correct minimum; ×, a minimum that gave worse agreement with the experimental structure than the correct one; ⊗, a square-planar minimum which is not the correct minimum; †, the correct minimum but where $V_{\text{init}} > 4000$ kJ mol^{-1}. The final M−X and M−X′ values of the correct minima are also given.

"dummy" atoms as well as the central metal atom do not experience the influence of the neighboring molecules in the crystal, in accordance with experiment. For group II molecules the two curves have the same shape until some definite distance is reached. After that distance, the energy *in crystal* suddenly increases while for an isolated molecule it retains its steady, approximately constant value. The sudden energy rise is caused by increased repulsive nonbonded interactions as the "dummy" atoms approach the carboxyl oxygens of the neighboring molecules, apically coordinated to the copper atom in the crystal lattice.

Model 8 prefers distorted over planar copper(II) coordination for the molecules *in vacuo*. That means that if the initial coordination is planar, during energy minimization it can distort depending on the "dummy" atom positions, as for bis(D,L-*N,N*-diethylalaninato)copper(II) and bis(1-aminocyclopentanecarboxylato)copper(II), with the energy difference between the planar and the distorted conformation of 0.69 and 5.93 kJ mol^{-1}, respectively, or remain planar, as for bis(α-aminoisobutyrato)copper(II) and bis(D,L-2-aminobutyrato)copper(II). If it is distorted at the beginning, it will remain distorted. In the crystal simulation, on the contrary, planar molecules retain their planarity (the only exception is a distorted minimum of bis(D,L-2-aminobutyrato)copper(II) yielded for $\text{M}-\text{X}_{\text{init}} < 0.4$ Å).

Much better results were also obtained for the distorted molecules of group II when their geometries were calculated *in crystal* rather than as isolated molecules. *In vacuo* they are much more distorted (a severe distorted tetrahedron) than as *in crystal*. This fact may lead us to the conclusion that model 8 describes relatively well a true physical situation, that the intermolecular interactions maintain the planarity of the copper(II) coordination polyhedron. It might be concluded also that these molecules in liquid phase could have more distorted copper(II) coordination than in the crystal lattice.

From data in Figures 2 and 3, it is obvious that a rule for choosing the initial "dummy" atom positions cannot be established because each molecule is a case of its own. The only noticed regularity is that *in crystal* the correct minima for bis(L-alaninato)copper(II), bis(D,L-2-aminobutyrato)copper(II), bis(α-aminoisobutyrato)copper(II), and bis(1-aminocyclopentanecarboxylato)copper(II) have similar orientation of X and X′ with respect to N, O, N′, and O′ (N−M−X=N′−M−X′ = 109°, N−M−X′=N′−M−X = 71°, X−M−O=X′−M−O′ = 84°, X′−M−O=X−M−O = 96°). Starting with similar orientation

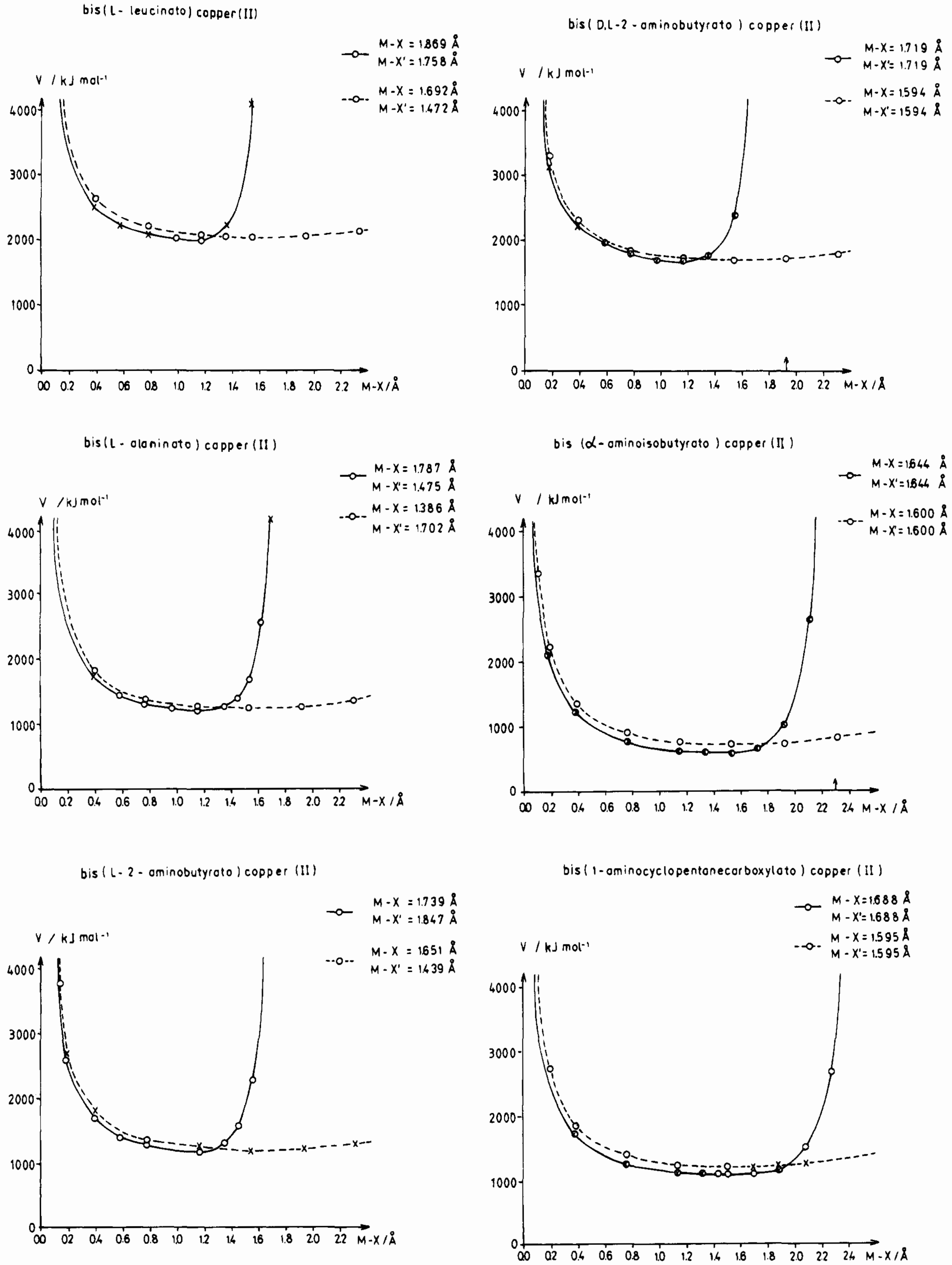

Figure 3. Dependence of the initial conformational potential energy, *V*, as in Figure 2, but for the group II copper(II) complexes.

of the "dummy" atoms in the same complexes and in bis(L-2-aminobutyrato)copper(II) too, the correct minima were obtained except for bis(D,L-2-aminobutyrato)copper(II), where it led to another planar minimum found before. For bis(L-2-aminobutyrato)copper(II), the complex that had the worst disagreement with the experimental data, although the "dummy" atoms orientation had changed during the geometry optimization, a new and better minimum was obtained (denoted as part B in Table 4 and Figure 4, with the final M−X = 1.727 Å and M−X' = 1.763 Å).

Table 4. Experimental and Theoretical Crystal Data (Lattice Constants, Unit Cell Volumes, and Comparison of the Volumes)[a]

Bis(L-*N*,*N*-dimethylvalinato)copper(II) (Orthorhombic, $P2_12_12_1$, $Z = 4$)

	exp	M8-P7a	M8-kr47		exp	M8-P7a	M8-kr47
a	6.698	6.210	6.571	β	90.00	90.00	90.00
b	21.631	22.041	22.298	γ	90.00	90.00	90.00
c	12.011	10.541	11.199	V	1740.2	1442.8	1640.9
α	90.00	90.00	90.00	$100(V - V_{exp})/V_{exp}$		−17.1	−5.7

Bis(L-*N*,*N*-dimethylisoleucinato)copper(II) (Monoclinic, $P2_1$, $Z = 2$)

	exp	M8-P7a	M8-kr47		exp	M8-P7a	M8-kr47
a	11.882	9.454	10.251	β	113.62	115.40	113.96
b	6.830	7.179	7.328	γ	90.0	90.0	90.0
c	12.867	12.902	13.036	V	956.7	791.0	894.9
α	90.00	90.00	90.00	$100(V - V_{exp})/V_{exp}$		−17.3	−6.5

Bis(D,L-*N*,*N*-diethylalaninato)copper(II) (Triclinic, $P1$, $Z = 1$)

	exp	M8-P7a	M8-kr47		exp	M8-P7a	M8-kr47
a	7.454	7.037	7.327	β	93.78	90.98	95.50
b	8.092	7.791	7.914	γ	100.46	100.71	98.62
c	8.210	8.068	8.332	V	420.5	343.5	385.2
α	118.69	126.76	124.24	$100(V - V_{exp})/V_{exp}$		−18.3	−8.4

Bis(L-leucinato)copper(II) (Monoclinic, $P2_1$, $Z = 2$)

	exp	M8-P7a	M8-kr47		exp	M8-P7a	M8-kr47
a	9.725	10.396	10.865	β	105.79	81.75	122.67
b	5.127	4.761	4.979	γ	90.00	90.00	90.00
c	14.689	13.259	15.873	V	704.8	649.5	722.9
α	90.00	90.00	90.00	$100(V - V_{exp})/V_{exp}$		−7.8	−2.6

Bis(L-Alaninato)copper(II) (Monoclinic, $P2_1$, $Z = 2$)

	exp	M8-P7a	M8-kr47		exp	M8-P7a	M8-kr47
a	9.166	9.316	9.643	β	94.60	70.58	70.38
b	5.045	4.666	4.755	γ	90.00	90.00	90.00
c	9.521	9.821	10.448	V	438.9	402.6	451.2
α	90.00	90.00	90.00	$100(V - V_{exp})/V_{exp}$		−8.3	2.8

Bis(L-2-aminobutyrato)copper(II) (Monoclinic, $P2_1$, $Z = 2$)

			M8-kr47					M8-kr47	
	exp	M8-P7a	A	B		exp	M8-P7a	A	B
a	9.464	9.762	8.002	11.633	β	90.60	84.36	88.31	62.05
b	5.060	6.541	5.838	4.921	γ	90.00	90.00	90.00	90.00
c	11.189	8.030	11.172	10.720	V	535.8	510.3	521.7	542.0
α	90.00	90.00	90.00	90.00	$100(V - V_{exp})/V_{exp}$		−4.8	−2.6	1.2

Bis(D,L-2-aminobutyrato)copper(II) (Monoclinic, $P2_1/c$, $Z = 2$)

	exp	M8-P7a	M8-kr47		exp	M8-P7a	M8-kr47
a	11.138	10.841	10.921	β	92.15	110.84	92.93
b	5.066	6.239	5.782	γ	90.00	90.00	90.00
c	9.487	6.875	8.253	V	534.9	434.6	520.5
α	90.00	90.00	90.00	$100(V - V_{exp})/V_{exp}$		−18.8	−2.7

Bis(α-aminoisobutyrato)copper(II) (Monoclinic, $P2_1/c$, $Z = 2$)

	exp	M8-P7a	M8-kr47		exp	M8-P7a	M8-kr47
a	10.470	13.396	10.505	β	115.6	140.0	125.6
b	5.335	5.035	5.802	γ	90.0	90.0	90.0
c	10.201	10.379	10.552	V	515.9	450.0	522.9
α	90.0	90.0	90.0	$100(V - V_{exp})/V_{exp}$		−12.8	1.4

Bis(1-aminocyclopentanecarboxylato)copper(II) (Monoclinic, $P2_1/a$, $Z = 2$)

	exp	M8-P7a	M8-kr47		exp	M8-P7a	M8-kr47
a	10.838	11.181	11.593	β	94.38	93.10	91.14
b	5.504	5.896	5.965	γ	90.00	90.00	90.00
c	10.839	9.278	9.692	V	644.7	610.7	670.1
α	90.00	90.00	90.00	$100(V - V_{exp})/V_{exp}$		−5.3	3.9

[a] Lattice constants *a*, *b*, and *c* are expressed in Å, α, β, and γ are expressed in degrees, and volume V is expressed in Å^3. Crystal system, space group, and Z are given in parentheses.

Comparison of Experimental and Theoretical Structures. In order to provide a test of the general efficacy of model 8, both force fields, M8-P7a and M8-kr47, are used to predict the structures of nine copper(II) complexes with amino acids, *in vacuo* and *in crystal* simulation.

Coordination polyhedron geometry of copper(II), errors in reproduction of internal coordinates and overall similarity yielded by model 8 are also compared with the corresponding results of model 7 (Tables 5 and 6).

When we compare experimental and theoretical structures, we try to answer the following questions:

(1) How well does model 8 reproduce the unit cell constants and the unit cell volumes? Which force field, M8-P7a or M8-kr47, is better?

(2) How do the models simulate the shapes of copper(II) coordination polyhedra?

(3) Does model 8 give lower root-mean-square deviations of the internal coordinates and the overall similarities *in vacuo* or *in crystal* simulation? Is there any difference in the simulation of group I and group II geometries? Which force field is better?

(4) How do the results of model 8 stand in a comparison with model 7? Which model is better?

(5) How do the models reproduce the Cu−N and Cu−O bond lengths?

Crystal Simulations by Model 8. The experimental lattice constants and the unit cell volumes of the nine copper(II) complexes are compared with the values calculated by the two model 8 force fields (Table 4).

The latest force field, M8-kr47, gives much better reproduction than M8-P7a, not only for the four molecules on which it has been optimized but also for the other five complexes. The error in the unit cell constants is about 35% higher with M8-P7a than with M8-kr47 (up from 1.276 to 0.764 Å rms for a, b, and c constants and 14.89 rather than 10.12° rms for α, β, and γ unit cell angles). Consequently, the rms of the unit cell volumes is 42.8 Å^3 by M8-kr47 (70.5 for group I molecules and 16.2 Å^3 for the copper(II) amino acidates of group II) in comparison with 125.8 Å^3 by M8-P7a (201.5 and 70.5 Å^3 for groups I and II, respectively). In other words, the volumes are 66% better reproduced with the M8-kr47 than with the M8-P7a force field.

Simulation of Copper(II) Coordination Polyhedra Distortion. A comparison of experimental and theoretical values of the eight angles that describe the shape of copper(II) coordination polyhedron by means of root-mean-square deviations is given in Table 5.

Group I N-alkylated copper(II) amino acidates have the lowest rms($\Delta\vartheta$) and rms($\Delta\vartheta$, $\Delta\varphi$, $\Delta\beta$) values yielded by M8-P7a, *in vacuo*, and by M8-kr47, *in crystal*. This is not a surprise because the force fields were optimized on these molecules, in corresponding environments.

In crystal simulation by M8-P7a produces, however, a great distortion of the bis(L-*N*,*N*-dimethylvalinato)copper(II) coordination polyhedron ($\Delta(\mathrm{N{-}M{-}N'}) = 10.6°$, $\Delta(\mathrm{N'{-}M{-}O}) = -8.9°$, $\Delta(\mathrm{O'{-}N'{-}N{-}O}) = 8.7°$). The copper(II) coordination of the other two N-alkylated complexes is also worse reproduced but not so pronouncedly as for the first molecule. Therefore, M8-P7a is suitable only if the molecules are treated as isolated while it reproduces their geometry worse when calculated as *in crystal*. This fact is a reason why further parameter optimization or intramolecular as well on intermolecular properties of the same molecules has been carried out.

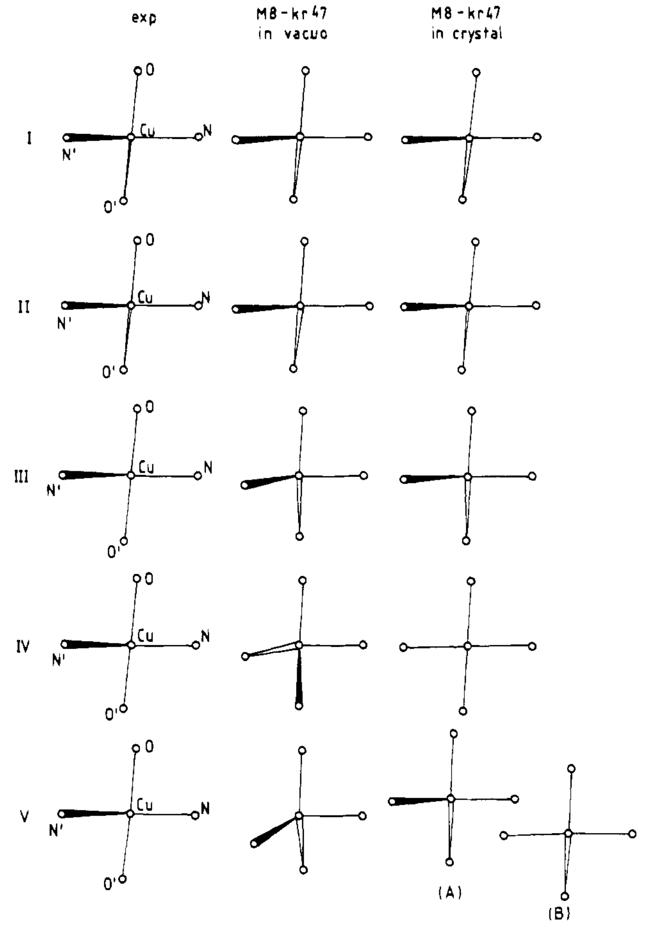

Figure 4. Copper coordination polyhedra obtained by the M8-kr47 force field, *in vacuo* and *in crystal*, compared with their experimental structures: I, bis(L-*N*,*N*-dimethylvalinato)copper(II); II, bis(L-*N*,*N*-dimethylisoleucinato)copper(II); III, bis(L-leucinato)copper(II); IV, bis(L-alaninato)copper(II); V, bis(L-2-aminobutyrato)copper(II).

The resulting force field, M8-kr47, predicts the geometry of bis(D,L-*N*,*N*-diethylalaninato)copper(II) and bis(L-*N*,*N*-dimethylvalinato)copper(II) (Figure 4) reasonably well if they are calculated as isolated molecules as well as *in crystal*. The difference in the two structures, however, is substantial for bis(L-*N*,*N*-dimethylisoleucinato)copper(II) (Figure 4), where the most critical angles are O−M−O′ and O′−N′−N−O, where deviations from the experimental values are greater *in vacuo* than *in crystal* (up from 9.0 to 1.4° for $\Delta(\mathrm{O{-}M{-}O'})$, and 13.3 rather than 4.8° for $\Delta(\mathrm{O'{-}N'{-}N{-}O})$). Anyway, the distinction between *in vacuo* and *in crystal* rms for group I molecules is smaller with M8-kr47 than with M8-P7a (Table 5). This proves that the parameter optimization on the internal coordinates as well as on the lattice constants, *i.e.* a comparison of the experimental data with the calculated internal coordinates and crystal unit cell organization is needed in order to get suitable parameters for nonbonded interactions.

Both force fields, M8-P7a and M8-kr47, give comparable results for group II molecules (Table 5). Simulation *in crystal* is a necessity because the intermolecular interactions stabilize the planarity of copper(II) coordination. For molecules with irregular square-planar central metal coordination the planarity is preserved not depending on the initial positions of the "dummy" atoms, unlike for the isolated molecules. For complexes whose coordination polyhedra in real crystal states are described as flattened tetrahedra, the intermolecular interactions suppress the severe distortion towards a tetrahedron present in the vacuum simulation and keep them closer to planarity (Figure 4).

The models appear to be capable of reproducing the correct shape of the coordination polyhedron. In comparison with model 7, model 8 is better in reproducing the angles of the copper(II) polyhedron for group I but worse for group II molecules (Table 5).

Errors in Internal Coordinates Calculations. For each molecule the average error, the rms error and the maximum error for each quantity (bond length, b, valence angle, ϑ, and torsional angle, φ) as well as the overall similarity measured

Table 5. Total Errors in Calculating the Structures of Nine Copper(II) Complexes (Group I and Group II Molecules)[a]

		model 8			
		M8-P7a		M8-kr47	
	model 7	*in vacuo*	*in crystal*	*in vacuo*	*in crystal*
		Coordination Polyhedron Angles[b]			
total					
rms($\Delta\vartheta$)	1.9	7.9	4.4	8.5	3.7
rms($\Delta\vartheta$, $\Delta\varphi$, $\Delta\beta$)	2.4	11.2	5.4	12.3	4.2
group I					
rms($\Delta\vartheta$)	2.3	1.0	4.3	2.9	1.5
rms($\Delta\vartheta$, $\Delta\varphi$, $\Delta\beta$)	2.6	1.4	4.8	4.1	1.9
group II					
rms($\Delta\vartheta$)	1.6	9.7	4.5	10.2	4.5
rms($\Delta\vartheta$, $\Delta\varphi$, $\Delta\beta$)	2.3	13.7	5.7	14.8	5.6
		Bonds[c]			
total ($N_b = 171$)					
$\langle\Delta b\rangle$	−0.018	0.010	0.013	0.004	0.007
rms(Δb)	0.036	0.036	0.038	0.029	0.031
$\Delta b_{\max}$	−0.121 (MO)	0.108 (MN)	0.113 (MN)	0.089 (MN)	0.094 (MN)
group I ($N_b = 67$)					
$\langle\Delta b\rangle$	−0.018	−0.005	−0.003	−0.008	−0.006
rms(Δb)	0.039	0.021	0.022	0.022	0.021
$\Delta b_{\max}$	−0.110 (MO)	−0.073 (NC)	−0.067 (NC)	−0.072 (NC)	−0.069 (NC)
group II ($N_b = 104$)					
$\langle\Delta b\rangle$	−0.019	0.019	0.023	0.012	0.016
rms(Δb)	0.033	0.043	0.045	0.033	0.036
$\Delta b_{\max}$	−0.075 (MO)	0.108 (MN)	0.113 (MN)	0.089 (MN)	0.094 (MN)
		Valence Angles			
total ($N_\vartheta = 278$)					
$\langle\Delta\vartheta\rangle$	0.4		0.4		0.1
rms($\Delta\vartheta$)	2.3		2.8		2.4
$\Delta\vartheta_{\max}$	5.9 (MNC)		17.6 (NMN)		19.9 (NMN)
group I ($N_\vartheta = 114$)					
$\langle\Delta\vartheta\rangle$	0.4	0.0	0.0	0.0	−0.2
rms($\Delta\vartheta$)	2.5	1.8	2.7	1.9	2.7
$\Delta\vartheta_{\max}$	5.9 (MNC)	6.0 (CCC)	10.5 (NMN)	9.0 (OMO)	−5.3 (CNC)
group II ($N_\vartheta = 164$)					
$\langle\Delta\vartheta\rangle$	0.5		0.7		0.4
rms($\Delta\vartheta$)	1.6		4.5		4.5
$\Delta\vartheta_{\max}$	−5.6 (CKQ)		17.6 (NMN)		19.9 (NMN)
		Torsions			
total ($N_\varphi = 127$)					
$\langle\Delta\varphi\rangle$	−0.4		0.3		0.1
rms($\Delta\varphi$)	12.0		8.4		8.4
$\Delta\varphi_{\max}$	43.7 (CCCC)		25.1 (CCCC)		27.1 (CCCC)
group I ($N_\varphi = 43$)					
$\langle\Delta\varphi\rangle$	−0.1	−0.1	0.5	0.5	−0.1
rms($\Delta\varphi$)	4.0	2.7	5.7	2.7	3.2
$\Delta\varphi_{\max}$	−11.2 (CCNM)	6.9 (CCCN)	10.3 (OKCN)	13.3 (ONNO)	9.9 (CCNM)
group II ($N_\varphi = 84$)					
$\langle\Delta\varphi\rangle$	−0.6		0.3		0.0
rms($\Delta\varphi$)	14.4		9.5		10.1
$\Delta\varphi_{\max}$	43.7 (CCCC)		25.1 (CCCC)		27.1 (CCCC)
		Overall Similarity			
total ($N = 1408$)					
rms(Δr)	0.163		0.195		0.163
group I ($N = 673$)					
rms(Δr)	0.091	0.079	0.126	0.082	0.120
group II ($N = 735$)					
rms(Δr)	0.207		0.241		0.194

[a] Errors for bond lengths (b) and interatomic distances (r) are in Å, and those for valence (ϑ), distortion (β), and torsional (φ) angles are in degrees. The hydrogens and the "dummy" atoms are not taken into account. The A conformer of bis(L-2-aminobutyrato)copper(II) is considered. [b] The coordination polyhedron angles are as follows: six valence angles ϑ (N−Cu−N′, N−Cu−O, N−Cu−O′, N′−Cu−O, N′−Cu−O′, and O−Cu−O′), the "torsional" angle φ (O′−N′−N−O), and the distortion angle β. The distortion coordinate β is defined as the angle between the bisectors of the two N−Cu−O angles in opposite chelate rings. [c] $\langle\Delta Y\rangle$ denotes the average error, rms(ΔY) the root-mean-square deviation, and N_Y number of terms, where Y stands for the internal coordinate. $Y_{\max}$ is the maximum error (the corresponding internal coordinate is given in parentheses).

by the rms deviations of the interatomic distances (r) were calculated. The total errors over the whole set of nine molecules and for each group of complexes are listed in Table 5.

Because the copper(II) coordination of group II complexes is greatly tetrahedrally distorted by *in vacuo* calculations in comparison to their experimental structures, the total errors in

Table 6. Statistical Analysis (Mean and Standard Deviation) of Cu–N and Cu–O Bond Lengths in Copper(II) Chelates with Amino Acids (Group II) and Their N-Alkylated Derivatives (Group I)[a]

	exp	model 7	model 8[b]
		Group I	
Cu–N	2.022 (0.012)	2.045 (0.004)	2.020 (0.007)
Cu–O	1.903 (0.010)	2.006 (0.001)	1.905 (0.003)
		Group II	
Cu–N	1.984 (0.008)	2.026 (0.001)	1.909 (0.008)
Cu–O	1.947 (0.012)	2.004 (0.001)	1.891 (0.010)

[a] All values are given in Å. [b] M8-kr47 (*in crystal*); the bond lengths of the A conformer of bis(L-2-aminobutyrato)copper(II) are considered.

valence angles, torsion angles, and overall similarities are considered only for *in crystal* calculations.

Bond Lengths. M8-kr47 shows a better agreement between the experimental and the predicted bond lengths than M8-P7a and model 7 (0.031 Å rms rather than 0.038 and 0.036 Å, respectively, Table 5).

Valence Angles. The total error in the valence angles is the lowest with model 7 (2.3° rms) but about the same with M8-kr47 (2.4° rms). M8-kr47 is better than model 7 for group I molecules while the opposite is valid for group II compounds (Table 5).

Torsional Angles. Both M8 force fields give the same error in the torsions (8.4° rms) and better reproduction than model 7 for all the molecules (Table 5).

Overall Similarity. The rms(Δr) over the nine molecules is the same with M8-kr47 and model 7 (0.163 Å), but higher with M8-P7a (Table 5). For group I molecules *in vacuo* calculations by both models yield a better agreement with the experimental structures than the crystal simulations (Table 5). For group II complexes the lowest rms(Δr) is obtained with M8-kr47, the highest again with M8-P7a (Table 5).

Average Errors. The total average error with the M8-kr47 force field is 0.007 Å (−0.018 Å with model 7) in the bonds (out of 171), 0.1° (0.4° with model 7) in the valence angles (out of 278), and 0.1° (−0.4° with model 7) in the torsions (out of 127), indicating that the general scales for these quantities are appropriate (Table 5).

Reproduction of the Cu–N and Cu–O Bond Lengths. The experimental Cu–N and Cu–O bond lengths of the nine copper(II) amino acidates are compared with their model 7 and model 8 values (Table 6).

The Cu–N bonds are longer than the Cu–O ones for all the molecules and this relationship has been preserved theoretically. The experimental bond lengths are different for groups I and II copper(II) chelates: the Cu–N bonds of group I are longer than those of group II while the Cu–O bonds of group I are shorter than those of group II (the differences of the means are +0.038 and −0.044 Å, respectively). The latter relation is not fulfilled with the models: the difference is higher with model 8 (the mean Cu–O bond of group I is greater than that of group II by 0.018 Å) than with model 7 (essentially the same bond lengths). Although the M8-kr47 force field reproduces the Cu–N and Cu–O bonds for N-alkylated copper(II) amino acidates within experimental errors, the reproduction of the group II bond lengths is not so good: the mean Cu–N and Cu–O bonds of model 8 are shorter than the experimental ones (by 0.075 Å, Cu–N, and by 0.056 Å, Cu–O). With model 7 the bond lengths of group II are overestimated by 0.052 Å, Cu–N, and 0.057 Å, Cu–O.

Therefore, a wish to reproduce the Cu–N and Cu–O bond lengths equally well for both classes of copper(II) amino acidates, with and without axial copper(II) coordination, still remains a challenge.

Table 7. Estimates of Potential Energy, Gibbs Free Energy, Statistical Weights (eq 5) and the Enantioselectivity Effect of the Two Isomers of Bis(*N,N*-dimethylvalinato)copper(II) at 298.16 K[a]

	conformational potential			Gibbs free energy		
no.	MLL	MDL	$\Delta\langle V\rangle$	MLL	MDL	$\Delta\langle G\rangle$
			Model 7			
1–6	13.812 (0.0036)	13.284 (0.0006)		10.891 (0.0105)	10.736 (0.0016)	
3–6	14.456 (0.0028)	13.198 (0.0006)		10.918 (0.0104)	12.158 (0.0009)	
4–4	19.353 (0.0004)	21.983 (0.0000)		14.917 (0.0021)	15.434 (0.0002)	
4–6	8.183 (0.0352)	8.269 (0.0045)		4.700 (0.1272)	5.248 (0.0145)	
5–6	14.182 (0.0031)	9.710 (0.0025)		14.555 (0.0024)	9.922 (0.0022)	
6–6	0.000 (0.9547)	−5.125 (0.9918)		0.000 (0.8469)	−5.197 (0.9805)	
enantioselectivity			5.439			5.869
			M8-P7a			
1–1	7.340 (0.0185)	18.576 (0.0002)		4.641 (0.0435)	−5.648 (0.1980)	
1–3	8.916 (0.0098)	15.238 (0.0008)		7.067 (0.0164)	14.371 (0.0001)	
1–5	12.034 (0.0028)	14.759 (0.0102)		12.921 (0.0015)	14.034 (0.0001)	
1–6	0.396 (0.3044)	3.979 (0.0792)		−1.674 (0.5561)	1.340 (0.0118)	
2–6	11.989 (0.0028)	15.132 (0.0009)		14.950 (0.0007)	17.022 (0.0000)	
3–3	9.013 (0.0094)	19.710 (0.0001)		10.746 (0.0037)	−9.000 (0.7655)	
3–5	12.307 (0.0025)	14.693 (0.0011)		17.224 (0.0003)	18.594 (0.0000)	
3–6	0.530 (0.2883)	3.803 (0.0851)		2.741 (0.0937)	5.087 (0.0026)	
5–6	11.095 (0.0041)	11.619 (0.0036)		14.519 (0.0008)	13.521 (0.0001)	
6–6	0.000 (0.3571)	−1.834 (0.8268)		0.000 (0.2830)	−0.174 (0.0218)	
enantioselectivity			1.484			7.714
			M8-kr47			
1–1	18.847 (0.0004)	28.603 (0.0000)		10.321 (0.0087)	−3.741 (0.7636)	
1–3	21.541 (0.0001)	27.281 (0.0000)		13.782 (0.0022)	21.563 (0.0000)	
1–6	5.294 (0.1010)	9.988 (0.0410)		1.052 (0.3668)	5.232 (0.0205)	
2–6	17.168 (0.0008)	21.076 (0.0005)		15.889 (0.0009)	19.808 (0.0001)	
3–3	22.575 (0.0001)	33.293 (0.0000)		15.130 (0.0013)	28.167 (0.0000)	
3–6	7.592 (0.0400)	12.172 (0.0170)		5.613 (0.0583)	10.180 (0.0028)	
5–6	14.115 (0.0029)	15.352 (0.0047)		16.231 (0.0008)	16.681 (0.0002)	
6–6	0.000 (0.8544)	2.236 (0.9362)		0.000 (0.5607)	−0.573 (0.2127)	
enantioselectivity			−1.894			3.724

[a] Only the minima with substantial (>0.0005) statistical weights are listed. Energy values are in kJ mol^{-1}. Statistical weights are given in parentheses. The minima of the conformational energy are denoted as in ref 26. Zero points: V = 1011.280 kJ mol^{-1}, G = 2065.890 kJ mol^{-1} (model 7); V = 1274.484 kJ mol^{-1}, G = 2334.016 kJ mol^{-1} (M8-P7a); V = 1274.002 kJ mol^{-1}, G = 2354.522 kJ mol^{-1} (M8-kr47).

Calculation of the Diastereoselectivity Effect. In order to determine the effect theoretically, the strain energy, V, and the Gibbs free energy, G, of each of 21 MLL and 21 MDL isomers were calculated along with their statistical weights (Table 7). For the "dummy" atom the relative atomic mass was taken to be 0.0005, to assure that the X's vibrational contributions to

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(26) Raos, N.; Simeon, Vl. *Croat. Chem. Acta* **1983**, *56*, 79.

the Gibbs free energy would be negligible in comparison to the vibrations of the real atoms. However, six vibrational contributions that correspond to the Xs, appeared to be different for each conformer. Therefore, they were subtracted from the total Gibbs free energies.

Among MLL conformers, the 6-6 has the lowest strain and the Gibbs free energy by model 7 and M8-kr47. With M8-P7a it has the lowest strain energy, but the 1-6 has the lowest Gibbs free energy. The 6-6 MLL isomer corresponds to the conformer determined in the crystal state.[9]

The MDL isomers show a quite different distribution. The 6-6 has the highest statistical weight when the strain energies are calculated and the lowest Gibbs free energy by model 7. The Gibbs free energy calculations of M8-P7a and M8-kr47 give the 3-3 and 1-1 MDL as the most stable conformer, respectively.

Model 7 and M8-P7a overestimate the enantioselectivity effect when it is calculated as a difference of the MLL and the MDL average Gibbs free energies. When it is determined with respect to the strain energies, model 7 gives too high a value and model 8 too low a value. The effect is reproduced within the experimental error only with the M8-kr47 force field ($\Delta\langle G\rangle = 3.72$ kJ mol^{-1}), by taking the vibrational energies into account.

Conclusions

The M8-kr47 force field simulates the structural and thermodynamical properties of the checked copper(II) amino acidates better than the M8-P7a force field. This fact reveals that the force field optimization should be done with respect to the internal coordinates (intramolecular properties) as well as to the unit cell constants (intermolecular properties) in order to get a suitable redistribution of the properties among the empirical parameters of the proposed potential energy function set.

Although the new electrostatic model, model 8, simulates well the geometries of the copper(II) complexes with N-alkylated amino acids (group I molecules) *in vacuo* like *in crystal* simulation, group II molecules have to be treated as *in crystal* in order to get a better agreement with their experimental structures.

The active role of the "dummy" atoms in the nonbonded interactions is somehow a disadvantage of the new electrostatic model because the equilibrium conformation of a molecule depends on their initial positions. The problem is more stressed in the complexes of group II, with the distorted copper(II) coordination, which are linked to each other by hydrogen bonds and with apical coordination to the metal atom in the crystal lattice. The apically coordinated oxygens from the neighboring molecules are also, to some degree, part of the copper(II) coordination sphere and the initial relation between them and the "dummy" atoms influences the geometry optimization process. Therefore, the model cannot be recommended for predictive purposes for complexes with similar nonbonded interactions in the crystal state. It would be interesting to examine, for instance, how a more sophisticated potential energy function for the description of the hydrogen bonds instead of the simple nonbonded potentials might influence the results.

In comparison to the results yielded by model 7, model 8 reproduces the geometries of the nine molecules in a similar manner but gives the value of the enantioselectivity effect in the copper(II)/*N*,*N*-dimethylvaline system within the very limits of experimental error. The latter is not fulfilled by model 7.

The fact that *in crystal* simulations by model 8 alleviate the *in vacuo* severe distortion of the copper(II) coordination polyhedron and stabilize its planarity observed experimentally in the crystal state and that the model yields a good reproduction of the enantioselectivity effect, which is based on *in vacuo* calculations encourages us to continue with the further force field development of the electrostatic models.

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Supplementary Material Available: For each of the nine molecules the experimental and theoretical values of the copper(II) coordination polyhedron angles and also the corresponding rms($\Delta\vartheta$) and rms($\Delta\vartheta$, $\Delta\varphi$, $\Delta\beta$) deviations are presented in Table S1 and the number of bond, angle, and torsional terms, the average error, the rms error, and the maximum error for each quantity (bond lengths, valence angles, and torsional angles) and the overall similarity rms(Δr) are given in Table S2, and energy values for the bis(*N*,*N*-dimethylvalinato)copper(II) isomers which are not listed in Table 7 are given in Table S3 (8 pages). Ordering information is available on any current masthead page.

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