Force Field Calculations on the Structures of Transition Metal Complexes. 1. Application to Copper(II) Complexes in Square-Planar Coordination

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The molecular modeling methods have found wide acceptance in the fields of organic chemistry and biochemistry. This study introduces a new algorithm to overcome the special problems encountered when extending standard force fields to metal–organic and inorganic complexes. The extension can easily be incorporated in common modeling programs. The application to the complexes of Cu(II) in square-planar coordination validates the approach. A general parametrization for Cu(II) consistent with the TRIPOS 5.2 force field is developed on the basis of the X-ray structures of 27 complexes with nitrogen- and oxygen-coordinated copper. The metal environment can be calculated to better than 2 pm for the bond lengths and 2° for the bond angles. Some larger deviations for the torsion angles can be attributed to the intermolecular interactions in the crystal.

Introduction

The synthetic work on transition metal complexes has been intensified since they were recognized as model systems to study the structural and electronic properties of the active sites in metalloproteins.[1] Copper atoms play an important role in enzymes where they are responsible for redox processes or for the coordination and activation of oxygen molecules.[2] The studies of copper model systems have revealed the impact of the properties of the ligand molecules on the structure and reactivity of the complexes.[3] The coordination symmetry of Cu(II) complexes depends strongly on the nature and size of the ligands. Nearly every symmetry intermediate between the tetrahedral and square-planar environments has been verified by an appropriate choice of the ligands.[4] Thus, the prediction of the structures of copper complexes would be the first step to a rational design of copper catalysts.

Force field methods have been successfully applied to the determination and prediction of the structures of organic molecules.[5] Special force fields have been developed for biochemical species like proteins and enzymes also.[6] But only little work has been spent to extend the force fields to metal complexes and metal centers in metalloproteins.[7] The flexibility of the coordination sphere and the resultant large variety of possible metal environments due to the broad range of bond angles at the metal atom is the main reason for the lack of the force field parametrization. Only recently Allured et al.[8] have proposed an interesting algorithm to deal with this flexibility by introducing a Fourier expansion instead of the harmonic bond angle term in common force fields.

We describe here a new method to handle the metal coordination by retaining the standard bond angle terms but solving the "unique labeling" problem[8] encountered when dealing with the high-symmetry coordinations like square-planar or trigonal-bipyramidal. The method can be easily implemented with every force field because it does not need new potential functions and will therefore be available for protein force fields also.

We validate the approach by a novel parametrization of Cu(II) complexes with a square-planar coordination that is consistent with the TRIPOS 5.2 force field.[5b] The equilibrium values for the bond lengths and bond angles are derived from the X-ray data for 27 representative copper complexes with various types of ligands coordinated via nitrogen or oxygen atoms. The force constants are chosen to reproduce the important features of the vibrational spectra of these copper complexes. The parameter set is refined by a fit of the optimized geometries to the X-ray structures.

Implementation of the TRIPOS 5.2 Force Field

In a former approach to a limited set of Cu(II) complexes[9] the standard TRIPOS force field[5b] of the SYBYL modeling program[10] was applied. We wanted to extend this preliminary study to a more rigorous treatment for general Cu(II) compounds. The multiple reference problem described below made it necessary to add some code in the setup of the parameter list for the energy and gradient calculations. Therefore, we employed the molecular

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modeling program MOBY 1.5[11] for the actual calculations because its source code was available for the necessary modifications.

MOBY 1.5 uses the mathematical expressions for the valence and nonvalence terms of the AMBER force field.[12] According to the AMBER force field the valence contributions V_{val} to the force field energy V_{tot} consist of harmonic terms for bond lengths and bond angles and Fourier terms for the torsional and improper torsional potentials:

$$V_{tot} = V_{val} + V_{nonval} \tag{1}$$

$$V_{val} = V_b + V_\theta + V_\phi + V_{imp} \tag{2}$$

$$V_b = \sum_b k_b(b - b_0)^2 \tag{3}$$

$$V_\theta = \sum_\theta k_\theta(\theta - \theta_0)^2 \tag{4}$$

$$V_\phi = \sum_\phi V_0(1 - \cos(n\phi - \phi_0)) \tag{5}$$

The harmonic potentials are defined by the force constants k_b and k_θ for the bond lengths and bond angle functions, respectively, and their corresponding reference values b_0 and θ_0. These parameters are determined to reproduce experimental data for the corresponding geometry parameters. The V_0 amplitudes of the torsion terms are chosen to reproduce the height of the experimental torsional barrier for the bond, while the multiplicity n reflects the periodicity of the torsional potential and the shift ϕ_0 determines the minimum energy torsion angle. This Fourier term is also applied to the improper torsions (out-of-plane potentials) where the torsion angle is defined by a central atom and the three neighbors bonded to it.

Since reliable charge distributions for the molecules in this study are not available and the additional parameters are essentially of a valence force field type, we omitted the Coulomb term of the force field. Thus, the nonvalence contribution V_{nonval} is given by the van der Waals term and the hydrogen-bonding term only. The van der Waals term is calculated by a Lennard-Jones 12–6 potential

$$V_{vdW} = \sum_{i,j} \epsilon_{ij}((\sigma_{ij}/r_{ij})^{12} - 2(\sigma_{ij}/r_{ij})^6) \tag{6}$$

with the usual definition of the mixed-atom parameters:

$$\epsilon_{ij} = \sqrt{\epsilon_{ii} + \epsilon_{jj}} \tag{7}$$

$$\sigma_{ij} = (\sigma_{ii} + \sigma_{jj})/2 \tag{8}$$

The centers i and j must be separated by more than two bonds.

The formulas for the TRIPOS force field differ only in the form of the out-of-plane potential, which is calculated via an improper torsion term

$$V_{imp} = V_0(1 + \cos(n\phi_{imp} - 180)) \tag{9}$$

in the AMBER force field while a harmonic potential for the distance of the central atom to the plane of its bonded neighbors

$$V_{oop} = k_{oop}(d - d_0)^2 \qquad d_0 = 0 \tag{10}$$

is used in the TRIPOS force field. This different out-of-plane term was coded for MOBY.

A second difference is found for the treatment of the formal bond orders. While a pair of AMBER center types carries the information about the order of the connecting bond, the TRIPOS force field needs this bond order to distinguish between different types of bonds. The MOBY 1.5 parameter set was extended to account for bond orders when bond length and torsion parameters are selected.

The AMBER force field contains a specific term

$$V_{Hbo} = \sum_{H,HA} (C_{H,HA}/r_{H,HA}^{12}) - (D_{H,HA}/r_{H,HA}^{10}) \tag{11}$$

to fine tune the hydrogen-bonding interactions between the acidic hydrogen H and a hydrogen bond acceptor HA, while the TRIPOS force field simply ignores the van der Waals radius of the acidic hydrogen atom in the expression for the σ_{ij}

$$\sigma_{H,HA} \equiv \sigma_{HA}/2 \tag{12}$$

of the Lennard-Jones 12–6 potential for these pairs of centers. A flag was implemented in MOBY to indicate the treatment of the hydrogen bond potential according to the TRIPOS force field.

These extensions to the MOBY program were also added to the code of MAXIMOBY,[13] which was employed to run the optimizations and normal coordinate analyses for the full set of reference compounds.

The parameters needed for the potential functions of the organic ligands were taken from the paper by Clark et al.,[5b] and the appropriate center types and parameters for the copper environment were developed in this study. The resultant force field data were stored in a MOBY parameter file for easy reference by the two programs.

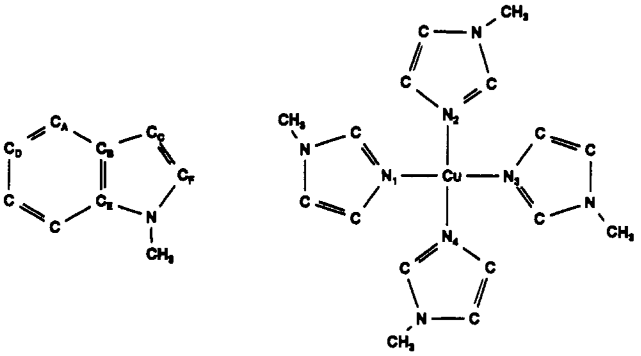

Figure 1. Sample structures for the "unique labeling" problem.

Multiple Reference Problem

The high symmetry of the coordination shell in metal complexes leads to a new problem in their force field treatment that is usually not encountered in organic compounds. This problem was called the "unique labeling" problem by Allured et al.[8] The substituents X at an atom C with a tetrahedral, trigonal, or linear environment in an organic molecule can be treated as symmetrically equivalent with identical bond angles (X–C–X = 109.47, 120, or 180°). The three chemically nonequivalent carbon atoms A, B, and C in the indene molecule (Figure 1) can be described by the same center type for a sp²-hybridized carbon atom. But this generalization will introduce large strain energy contributions. The assignment of different center types to A, B, and C can be used to fine tune the specific bond angle patterns (D–A–B = 120°, A–B–C = 132°, A–B–E = 120°, E–B–C = B–C–F = 108°) and to remove the strain in the annelated ring system.

The situation is different in a coordinative environment. A central copper atom in a square-planar coordination that carries

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four chemically equivalent ligands N exhibits bond angles of 90 and 180° for the same triple of center types N–CU–N (Figure 1). It would be necessary to assign different center types N′ and N″ to the equivalent ligand atoms to account for the two bond angles (N′–CU–N′ = 90°, N′–CU–N″ = 180°, N″–CU–N″ = 90°). Similarly, in a trigonal-pyramidal symmetry the bond angles of 90, 120, and 180° are needed, while an octahedral symmetry can again be handled with the 90 and 180° reference values only. Thus, an artificial assignment of different center types to chemically equivalent centers is needed to handle these coordination spheres in a standard force field.

Allured et al.[8] introduced a continuous Fourier potential to allow for potential energy minima at various angle values.

We will here use a different approach based on a set of harmonic potentials for bond angles common to standard force fields like AMBER,[6a] DISCOVER,[6b] CHARMM,[6c] and TRIPOS.[10]

The algorithm is implemented in MOBY 1.5 as follows: (i) For every triple of center types constituting a bond angle several reference values and their corresponding force constants can be provided. (ii) Prior to a single energy calculation, an optimization, or a MD simulation the program chooses the reference value closest to the actual bond angle in the current geometry. (iii) This reference value and the force constant is retained throughout the energy and gradient calculations. Thus, only one harmonic term is calculated for every bond angle but the reference values and force constants are assigned such as to minimize the potential energy in the starting geometry.

For the copper complex in Figure 1 the reference values for the bond angle N–CU–N are 90 and 180° with the force constants $k_\theta(90°)$ and $k_\theta(180°)$. The algorithm will then assign the potential

$$V_\theta(90°) = k_\theta(90°)(\theta - 90)^2 \qquad (13)$$

to the angles N_1–CU–N_2, N_1–CU–N_4, N_2–CU–N_3, and N_3–CU–N_4, while the potential

$$V_\theta(180°) = k_\theta(180°)(\theta - 180)^2 \qquad (14)$$

will be used for the two trans angles N_1–CU–N_3 and N_2–CU–N_4.

The advantages of this approach are as follows: (i) It solves the unique labeling problem because no artificial assignment of different center types to chemically equivalent atoms is necessary. (ii) No changes to the routines for the calculation of the energy and its first and second derivatives are necessary. (ii) Different force constants k_θ for different reference values (e.g. $k_\theta(90°) \neq k_\theta(180°)$) can be applied to mimic harder or softer potentials for specific bond angles. (iii) A zero potential energy is calculated for ideal geometries. (iv) Only a single set of bond angle parameters is needed to study various coordination symmetries. So the four reference values 90, 109.5, 120, and 180° for a bond angle L–CU–L allow one to handle tetrahedral, square-planar, trigonal, trigonal-bipyramidal, and octahedral coordinations of copper atoms in one molecule simultaneously. (v) Different coordination spheres can be studied by simply changing the starting geometry and thus forcing the program to select different reference values.

If different force constants are assigned to the various reference values, the selection of the appropriate reference value can be based on geometric or energetic arguments. Either the reference value that differs least from the current value of the bond angle can be chosen or that reference value is used for which the potential energy is lowest. Thus, for reference values of 90 and 180° and the corresponding force constants of 40 kcal/(mol rad) and 20 kcal/(mol rad), respectively, a starting bond angle of 130° would lead to a reference value of 90° according to the geometric choice (line G in Figure 2), while the reference value of 180° is used if the selection by energy is applied (line E in Figure 2).

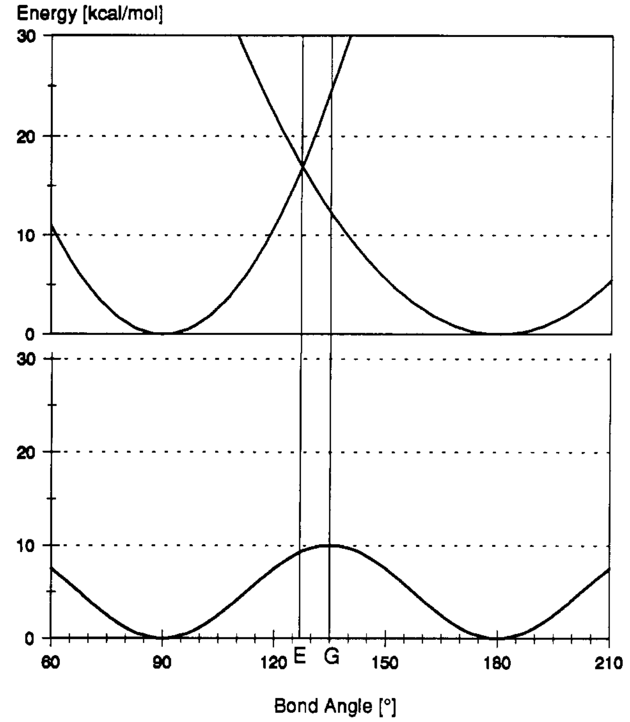

Figure 2. Potential energy curves for the two models for the bond angle term. Top: Superposition of the two potentials given in eqs 13 and 14. Bottom: Fourier term $V_\theta = V_0{}^*\ (1 + \cos(4\theta + 180))$.[8] The amplitude V_0 is set to 5 kcal/mol in accordance with the harmonic force constant of 40 kcal/mol for the 90° reference in eq 13. G denotes the borderline between the 90 and 180° references for a selection of the reference value by geometry, while E denotes the borderline for a selection by energy (see text).

In Figure 2 the graphs for the potentials of a square-planar coordination sphere according to the model by Allured et al.[8] and by our approach are given. The Fourier potential has the interesting feature of continuity. But this continuity does not have any physical justification in the "real" world. It makes no sense in a square-planar environment to allow for a continuous change of the bond angle from 90 to 180°, because this would lead to a second bond angle that decreases to 0°. In molecular dynamics simulations at high temperatures during a search for new conformations of the molecule the high-energy region of the transition state may be sampled. Thus, the possible transitions into the 180° minimum will lead to unreasonable structures. The preservation of the starting reference value in our model prevents the occurrence of these unreasonable structures.

The slower increase of the potential energy on deviation from the idealized bond angle as described by a cosine term instead of the parabolic potential can be recognized for deviations of 20° and more (see Figure 2). In none of the compounds in this study were deviations larger than 15° found. Thus, the softer potential would not make any difference in the results. On the other hand, the flexibility of our model to allow for different force constants for the different reference values offers a simple way to fine tune the bond angle potential.

Reference Structures

A survey of the Cambridge Crystallographic Data Bank[14] revealed 4527 compounds containing copper. But only 296 compounds were found that contain exactly one copper atom with four ligands coordinated via nitrogen or oxygen that were solved to an *R*-value of less than 5%. The combination of ligands in these complexes cover the range from four nitrogens to one nitrogen and three oxygens. We selected 41 representative

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(14) Cambridge Structural Data Bank, Version 4. Cambridge Crystallographic Data Centre, University Chemical Laboratory, Cambridge, 1989.

structures in which the most frequent ligands alkyl-nitrogen, imidazole, amino acids, pyrimidine, and α,β-unsaturated carbonyl groups are found. Single bonded as well as chelating ligands are included.

A total of 14 of these compounds showed a heavily distorted square-planar Cu(II) coordination that would better be called a less distorted tetrahedral environment (trans bond angles L–CU–L of less than 150°), and they were omitted from the current investigation leaving 27 test structures for this study.

Figure 3 gives a simple graphical representation for the molecules in this study. Besides some open structures with four isolated ligands (e.g. **6** and **17**), chelating ligands with five- or six-membered ring systems including the copper atom (e.g. **4** and **19**) and highly crowded structures like **2** are investigated.

New Center Types and Force Field Parameters

The ligands in the complexes used for our parametrization coordinate via nitrogen or oxygen atoms to the copper atom. The TRIPOS force field has seven nitrogen center types and two oxygen center types. These center types differ in the hybridization and their coordination geometry. The sp^2 nitrogens differentiate to N.2 in isolated or conjugated double bonds, N.ar in aromatic systems and N.am for the special treatment of amidic nitrogens with partial double-bond character in the bond to the adjacent carbonyl group. The sp^3 nitrogens are cast into aliphatic N.3 and planar N.pl3. The two oxygen center types differ in their hybridization only.

While N.3 and N.am do not cause problems in their assignment, the remaining center types may lead to ambiguities. So, the aromatic nitrogen N.ar of a pyridine will find a third bond when coordinated to a metal atom. This bond exhibits a coordinative bond formed by an empty orbital at the metal center and the in-plane electron pair. The azaadenyl ligand in **3** may coordinate by substitution of the acidic hydrogen at an N.pl3 center or by the electron pair of the "aromatic" nitrogen. Thus, the character of the nitrogen atoms may change with the pH value of the solution.

An oxygen atom of a carbonyl group that coordinates to the metal atom via the lone pair may preserve the sp^2-hybridized character or it may switch to a sp^3- hybridization. From the statistical analysis of the X-ray structures of the reference compounds the effect of the coordination on the bonds from the coordinated atom to its neighbor in the organic ligand could be derived. For the oxygen-bonded ligands significant changes in the bond lengths to the coordinated atom have been determined, while for the nitrogen atoms the bond lengths are only slightly changed. To account for this observation we introduced new center types for the oxygen O.2 and O.3 types. The new types U.2 and U.3 have the same properties as O.2 and O.3, respectively, but their bond lengths to the neighboring carbon atoms are increased to mimic the transfer of bonding character to the Cu–O bond.

In this study the center types of the coordinating atoms were determined for the isolated ligand. These center types were then used for the coordinated ligand also. Any ambiguities in the center type assignments were resolved by analyzing further experimental data (like hydrogen positions) and spectroscopic data.

In the treatment of the copper complexes new parameters were needed for the valence contributions of the copper–ligand unit. The reference values for the bond length term were determined from the average bond lengths found in the X-ray structures of unstrained complexes. The idealized values of 90 and 180° were taken as the references for the bond angles at the copper atom. The reference values for the bond angles of the type X–L–Cu were derived according to the hybridization of the uncoordinated ligand. Thus, 109.5° angles were used for sp^3-hybridized oxygens (U.3) and nitrogens (N.3) while 120° angles were applied for the carbonyl oxygen (U.2) and the sp^2-hybridized nitrogens (N.2, N.ar, etc.).

Since the force constants of the TRIPOS 5.2 force field for organic molecules are not determined by a fit to vibrational spectra, no unique procedure is available to determine new force constants. Additionally, the vibrational spectra of the copper compounds are not analyzed in detail and only ranges of frequencies are reported for the Cu–ligand bonds.[16] Tables 1–4 list the characteristics of the new center types and the valence force field parameters derived in this study (see eqs 3–6). The force constants listed in Table 2 lead to vibrational frequencies for the symmetric and asymmetric L–Cu–L stretches within the ranges of the experimental data but may not reproduce the vibrational spectrum of a specific compound very well.

The force constants for the bond angle potentials cannot be determined by reference to experimental data because no accurate assignments are available. We ran the optimizations with various sets of force constants and found the overall best agreement between the X-ray and optimized structures for the force constants given in Table 3. The lower force constants for the trans angles are justified by the fact that the range of these angles in the X-ray geometries is broader than for the 90° bond angles indicating a softer potential.

We introduced no torsion potentials for the Cu–ligand bonds because no specific orientations for the ligands about this bond were found in the experimental data. Nevertheless, the ring systems formed by chelating ligands like α,β-unsaturated carbonyl compounds showed a tendency to be planar despite the strain introduced in the ring due to long copper–ligand bonds. This observation had to be regarded by adding a small torsion potential about the CU–U.2 and CU–U.3 bonds that preserves the planarity (see Figure 7).

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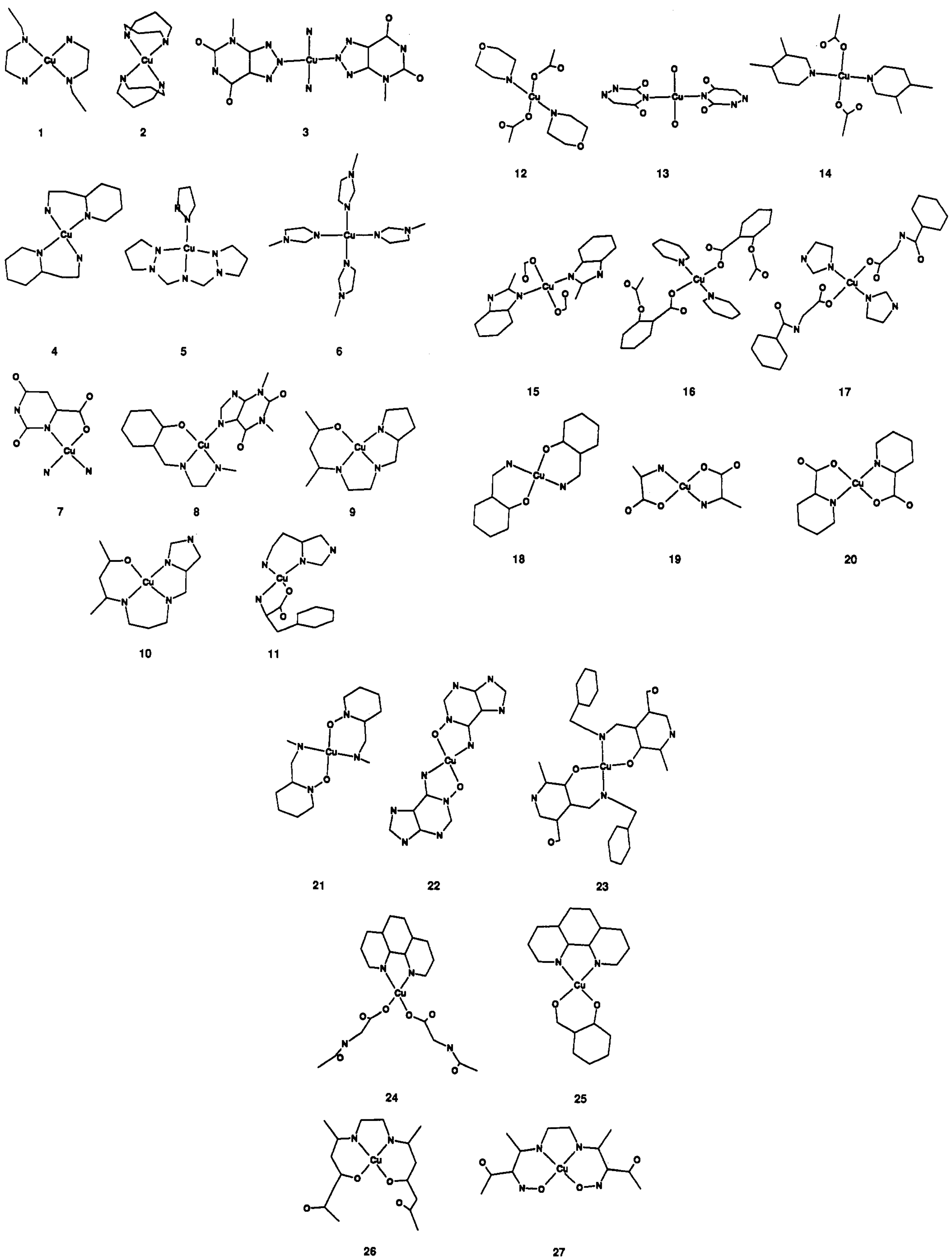

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27

Figure 3. Reference structures for the parametrization.[15]

Procedures

We employed the PC-based molecular modeling program MOBY 1.5[11] extended for use of the TRIPOS force field[17] for the preparation of the starting structures and the visualization and analysis of the optimized geometries. The geometry optimizations and vibrational analyses were

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(17) β-Version of MOBY 1.6, to be released in spring 1994.

Table 1. Center Types

center type	ϵ_{ii} (kcal/mol)	σ_{ii} (Å)	atomic no.	max valency	atomic wt
CU	0.100	1.30	29	4	63.5
U2	0.116	1.55	8	2	16.0
U3	0.116	1.55	8	2	16.0

Table 2. Bond Lengths

atom 1	atom 2	k_b (kcal/(mol Å))	b_0 (Å)
CU	N.2	60.00	1.99
CU	N.3	90.00	1.98
CU	N.am	75.00	1.89
CU	N.ar	40.00	2.01
CU	N.pl3	60.00	1.99
CU	U.2	160.00	1.91
CU	U.3	105.00	1.96
U2	C.2	777.60	1.28
U2	C.ar	350.00	1.31
U2	N.2	600.00	1.32
U3	C.2	777.60	1.27
U3	H	503.75	0.95
U3	N.pl3	310.00	1.36

Table 3. Bond Angles

atom 1	atom 2	atom 3	k_θ (kcal/(mol rad))	θ_0 (deg)
a	CU	*a*	40.0000	90.0
a	CU	*a*	20.0000	180.0
CU	N.2	*a*	65.7227	120.0
CU	N.3	*a*	65.7227	109.5
CU	N.am	*a*	32.8613	120.0
CU	N.ar	*a*	32.8613	120.0
CU	N.pl3	*a*	65.7227	120.0
CU	O.2	*a*	32.8613	120.0
CU	U.2	C.2	65.7227	120.0
CU	U.2	C.ar	32.8613	120.0
CU	U.2	N.2	32.8613	120.0
CU	U.3	C.2	32.8613	109.5
CU	U.3	H	32.8613	109.5
CU	U.3	N.pl3	32.8613	109.5

[a] Any atom.

Table 4. Torsion Angles

atom 1	atom 2	atom 3	atom 4	V_0 (kcal/mol)	ϕ_0 (deg)	*n*
a	CU	N.2	*a*	0.1	180	2
a	CU	N.3	*a*	0.1	180	2
a	CU	N.am	*a*	0.1	180	2
a	CU	N.ar	*a*	0.1	180	2
a	CU	N.pl3	*a*	0.1	180	2
a	CU	U.2	*a*	0.1	180	2
N.2	CU	U.2	C.2	2.0	180	2
N.2	CU	U.2	C.ar	2.0	180	2
N.2	CU	U.2	N.2	2.0	180	2
U.2	CU	U.2	C.2	1.0	180	2
U.2	CU	U.2	C.ar	1.0	180	2
a	CU	U.3	*a*	0.1	180	2
a	U.2	C.2	*a*	0.5	180	2
a	U.2	C.ar	*a*	0.5	180	2
a	U.2	N.2	*a*	0.5	180	2
a	U.3	C.2	*a*	2.9	180	2
a	U.3	N.pl3	*a*	0.5	0	2
a	O.2	N.2	*a*	0.5	180	2

[a] Any atom.

Table 5. Comparison of the Internal Coordinates of the X-ray Structures and Optimized Structures[a]

	CU	HEAVY	ALL
	Bond Lengths (pm)		
no. of terms	112	607	1220
dev[b]	0.1	−0.1	−0.1
mean dev	2.3	2.5	1.5
rms	1.9	2.2	2.0
	Bond Angles (deg)		
no. of terms	168	910	2165
dev	−0.3	0.4	−0.1
mean dev	1.2	2.5	1.6
rms	1.5	2.3	1.9
	Torsion Angles (deg)		
no. of terms	334	1075	3006
dev	−2.7	0.2	−0.2
mean dev	12.1	5.7	6.8
rms	21.2	13.6	13.3
	Torsion Angles in Ring Systems (deg)		
no. of terms	227	933	2298
dev	−0.6	0.1	−0.1
mean dev	6.5	3.7	3.8
rms	6.0	4.8	4.8

[a] For the definition of CU, HEAVY, and ALL, see text. [b] Dev = deviation.

carried out with MAXIMOBY 3.0[13] run as well on a PC as on an IBM RS6000-32H workstation.

The following procedure was used to obtain the minimum energy structures for all 27 complexes.

(1) The suite of 27 structures were extracted from the Cambridge Crystallographic Data Bank.[14] The bonding framework was generated, and center types and bond orders and the hydrogen atoms were added. The structures were written to a MOBY library file for subsequent optimizations with MAXIMOBY.

(2) The optimizations consist of three steps: (i) steepest descent optimization to relax the starting geometry (SD, maximum 2000 steps, $\Delta E < 10^{-5}$); (ii) conjugate gradient steps for a preliminary optimization (CG, maximum 2000 steps, $\Delta E < 10^{-7}$); (iii) final BFGS[18] steps to reach the minimum (BFGS, maximum 2000 steps, $\Delta E < 10^{-12}$). The final RMS of the gradient was always below 0.005 kcal/(mol Å).

(3) Then the minimum finder option of MAXIMOBY was envoked to ensure convergence to an energy minimum. The minimum finder consists of an optimization according to the criteria last set and a subsequent normal coordinate analysis. Whenever a nontrivial vibration with an imaginary frequency is determined, the geometry is changed according to the corresponding normal coordinate until a decrease of the energy is found. Then the optimization is restarted at this geometry.

(4) The resultant geometries are stored in a MOBY library for later analysis of the results and the comparison of the internal coordinates between the starting structures and optimized structures.

Results for the 27 Cu(II) Complexes

Table 5 summarizes the statistics of the comparison of the starting structures and the optimized structures for the internal coordinates (bond lengths, bond angles, torsion angles). Three different groups of geometry parameters are compared: (i) only those internal coordinates that contain the copper atom but no hydrogen atoms (CU); (ii) the coordinates that contain no Cu and no hydrogen atoms (HEAVY); (iii) all internal geometry parameters (ALL). The deviations for all coordinates are smaller than for the two other groups because here the hydrogen atoms are included and these hydrogen atoms have been added automatically to the structures with bonds lengths and bond angles consistent with the force field parameters.

The deviations for the bond lengths and bond angles agree with the findings of Clark et al.[5b] in their analysis of purely organic compounds and reflect the reliability of the TRIPOS 5.2 force field. The torsion angles show a larger deviation between the X-ray and optimized structures. We will discuss some of the complexes that cause these larger deviations below.

The center type assignment of the TRIPOS force field is not sensitive enough to account e.g. for the special bonding schemes in the ligands with aza-substituted π-systems. The electron delocalization in these ligands is underestimated by the pattern of alternating single and double bonds as it is introduced by the center types of the TRIPOS force field. This fact causes additional strain especially in those complexes where these ligands are connected to each other (e.g. **3** and **5**). We have tried a different

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(18) (a) Broyden, C. G. *Math. Comput.* **1967**, *21*, 368–370. (b) Fletcher, R. *Comput. J.* **1970**, *13*, 317–320. (c) Goldfarb, D. *Math. Comput.* **1970**, *24*, 23–27. (d) Shanno, D. F. *Math. Comput.* **1970**, *24*, 647–649.

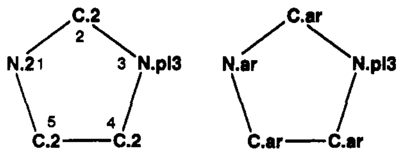

Figure 4. Different assignments of center types for the imidazole system: Left, original TRIPOS force field; right, modified TRIPOS assignment that better accounts for the electron delocalization in the ring.

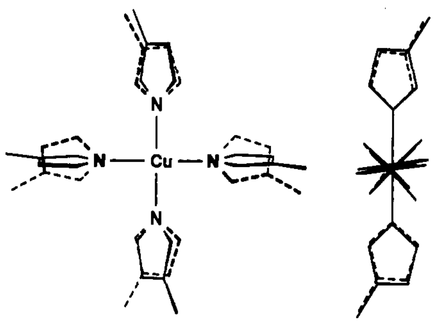

Figure 5. Superposition of the X-ray (full lines) and optimized structures (dashed lines) of **6**: Left, viewed from the top; right, viewed from the right-hand side.

Table 6. Comparison of the Bond Lengths and Bond Angles of the X-ray Structure of the Imidazole Ring (XRAY) and the Optimized Structures as Calculated with the Original (TRIPOS 5.2) and Modified Center Types (mod TRIPOS)

	TRIPOS 5.2	XRAY	mod TRIPOS
	Bond Lengths (pm)		
1-2	125.4	131.0	134.9
2-3	129.9	134.5	135.1
3-4	131.7	136.7	134.8
4-5	134.6	135.1	139.3
5-1	143.6	137.3	134.8
mean dev/rms	4.4/2.3		2.6/1.5
	Bond Angles (deg)		
1-2-3	107.2	111.0	106.4
2-3-4	110.5	107.3	109.3
3-4-5	110.1	106.2	107.9
4-5-1	100.0	109.3	105.2
5-1-2	112.2	106.1	111.1
mean dev/rms	5.2/2.5		3.5/1.5

scheme by using the aromatic nitrogen and carbon center types for the imidazole rings in compound **6**. The agreement between experimental and optimized structures is significantly better than with the original center types (see Table 6 and Figure 4). Thus, some of the deviations between X-ray and optimized structures are caused by inconsistencies in the TRIPOS 5.2 center type assignments within the organic part of the molecules.

Compound **6** exhibits an interesting geometry change upon optimization. While the *trans*-imidazole systems form pairwise a plane in the X-ray structure with opposite dihedral angles between the plane of coordination and the ligand planes, they obtain a "propeller"-like conformation in the optimized geometry (see Figure 5). Thus, the symmetry of the ligand sphere is increased from C_2 in the solid state to C_4 in the isolated molecule. This difference introduces a deviation of 43° for the torsion angles at the copper atom. Similarly, in **13** the O–CU–O unit is rotated by about 30° about the N–CU–N direction (see Figure 6). Here the positon of the water molecules in the solid state is stabilized by hydrogen bonds to the ring systems in the neighboring complexes. In the absence of these intermolecular interactions the optimized structure is energetically more favorable by about 2 kcal/mol than the crystal structure.

The effect of the crystal packing can also be seen for **24**. The crystal structure is characterized by intermolecular interactions between three species. This interaction stabilizes the elongated conformation of the side chain. The optimized structure of the isolated molecule exhibits a significant van der Waals interaction between the two side chains and causes the nearly parallel orientation (see Figure 7).

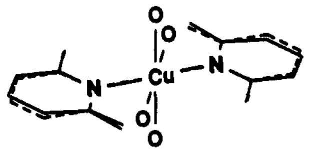

Figure 6. Superposition of the X-ray (full lines) and optimized structures (dashed lines) of **13**.

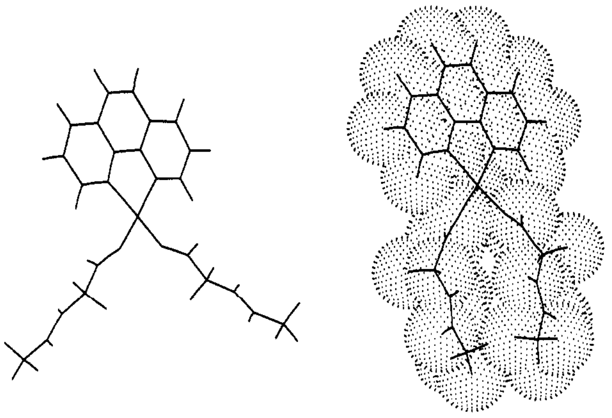

Figure 7. Comparison of the X-ray (left) structure and the optimized structure (van der Waals surface, right) of **24** showing the dominating interaction between the ligands.

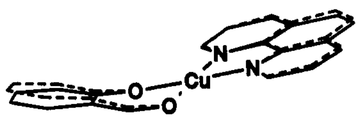

Figure 8. Superposition of the X-ray (full lines) and optimized structures (dashed lines) of **25**.

An interesting effect is found for the compounds **8** and **25**. Here a six-membered ring is formed by the copper atom and a conjugated α,β-unsaturated carbonyl group that binds back to the metal atom by an amino and hydroxy group, respectively. The six-membered ring is slightly tilted out of planarity indicating the strain introduced by the long Cu–O and Cu–N bonds (see Figure 8). This structural feature is well reproduced in the optimized geometries although the tilt is slightly overestimated (optimized structure = 15°, X-ray structure = 10°).

Conclusion

In this study molecular modeling methods have been applied to a large variety of square-planar Cu(II) complexes for the first time. Single bonded and chelating ligands are investigated that coordinate to the metal atom via oxygen and nitrogen. The standard valence terms used in the TRIPOS 5.2 force field are suitable to account for the rather flexible coordination sphere of Cu(II). The parameters developed give a very satisfactory description of the geometries of the complexes. The limited scope of our parametrization allows us to reproduce the bonding environment at the copper atom even slightly better than for organic molecules using the same force field. The larger deviations for the torsion angles can be attributed to the specific environment in the crystal because the energy differences between the final optimized structures and the conformations in the solid state are always less than 2 kcal/mol.

Allured et al. have discussed the necessity to derive new algebraic formulas for the valence force field terms of metal atoms[8] due to the broader range of bond angles (i.e. softer potentials) at the metal atoms. In the X-ray structures of the test molecules of this study the maximum deviations from the idealized 90° bond angles are less than 10°, while for the 180° bond angles maximum deviations of 15° were found. The force field reproduces these deviations satisfactorily as can be seen from the statistics of the bond angles at the Cu atom (see Table 5). Thus, no new force field terms are needed to determine bond angle changes of up to 20° if the force constants for the 180° angles are set to a lower value than for the 90° angles.

The algorithm to solve the multiple reference problem is very well applicable to the copper complexes as it was for the force field calculations on metallocenes.[19] This algorithm does not need any new force field terms and parameters but can be implemented in a very straightforward manner by only a minor recoding for the assignment of the force field parameters to a given bond angle potential. The parameters derived can easily be transferred to other force field implementations that use harmonic potentials for the bond lengths and bond angles.

Further investigations of Cu(II) complexes in a square-pyramidal coordination and extensions to other metal complexes with platinum and zinc are under way.

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Supplementary Material Available: The Cartesian coordinates of the X-ray and optimized structures and the complete parameter file are available by sending an empty PC-diskette to the author (U.H.).

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(19) Höweler, U.; Mohr, R.; Knickmeier, M.; Erker, G. *Organometallics*, in press.