

Enzyme-mimetic model compounds: conformational analysis and far-IR study of $\text{Cu}(\text{TAAB})^{2+}$

P. Weinberger^{a,*}, R. Schamschule^b, A.B.J. Parusel^b, G. Köhler^b, W. Linert^a

^a Institute for Inorganic Chemistry, Vienna University of Technology, Getreidemarkt 9/153, A-1060 Vienna, Austria

^b Institute for Theoretical Chemistry and Radiation Chemistry, University of Vienna, Althanstraße 14, A-1090 Vienna, Austria

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Abstract

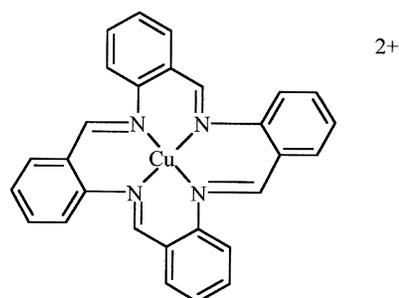
Many enzymes occurring in nature like superoxide dismutase are systems rather too big to be accessible for vibrational and quantum chemical investigations. Thus, enzyme-mimetic model compounds consisting of a biological active metal centre surrounded by a macrocyclic ligand are used to shed light on binding properties of the active metal centre. Far- and mid-range IR spectroscopic investigations and a conformational analysis with the semi-empirical ZINDO/1 method of superoxide dismutase-mimetic complex $\text{Cu}[\text{TAAB}]^{2+}$ are performed (TAAB = [*b,f,j,n*][1,5,9,13]tetra-aza-cyclohexadecine (tetra-anhydroamino benzaldehyde)). A distorted tetrahedral copper(II) centre with slightly twisted phenyl subunits is determined as the most stable conformation. Calculated mid- and far-IR spectra are in good agreement with the experimental data and confirm the proposed structure. A harmonic normal-coordinate analysis is used to assign the vibrational modes of the observed spectra. ©2000 Elsevier Science Inc. All rights reserved.

Keywords: Conformational analysis; $\text{Cu}[\text{TAAB}]^{2+}$; Far-infrared; Normal-coordinate analysis; Semi-empirical calculations

1. Introduction

Many biologically important molecules—for instance the metalloporphyrines—consist of a metal centre and a conjugated macrocyclic ligand. The chelation by four nitrogen-donors is thermodynamically and kinetically very stable. The biological activity of metalloporphyrines is due to changes in the oxidation state of the central metal, to substitution reactions of more labile extraplanar ligands and to substituent exchanges at the ring system. However, the elucidation of many of these reactions in physiologically relevant surroundings is often tedious. Therefore, it is important to elucidate the behaviour and role of metals in macrocyclic surroundings by investigating systems less complicated than those of the entire enzyme. An enzyme-mimetic model compound for the copper-containing enzyme superoxide dismutase [1] is the copper(II) complex of the tetrameric Schiff base [*b,f,j,n*][1,5,9,13]tetra-aza-cyclohexadecine (tetra-anhydroamino benzaldehyde), $\text{Cu}(\text{TAAB})^{2+}$ (see Scheme 1) [2–4].

The structure and electrochemistry [5–8], DNase like activity [9,10], as well as the reaction kinetics in physiolog-



Scheme 1. Chemical structure of $[\text{Cu}(\text{TAAB})]^{2+}$.

ically relevant surroundings, are well investigated, but a vibrational characterisation—especially regarding the copper coordination site—has not been performed so far. Our aim was to elucidate the bond strengths and vibrational features especially with respect to the copper(II) coordination site. The present study sheds light on these properties by vibrational investigations performed in the far- and mid-range IR. The observed data are correlated to a complete normal-coordinate analysis based on semi-empirical calculations.

2. Experimental

The complex was synthesised according to well-known procedures [11]. The powder sample was measured on a

* Corresponding author. Fax: +431-58801, ext. 15399; e-mail: weinberg@mail.zserv.tuwien.ac.at

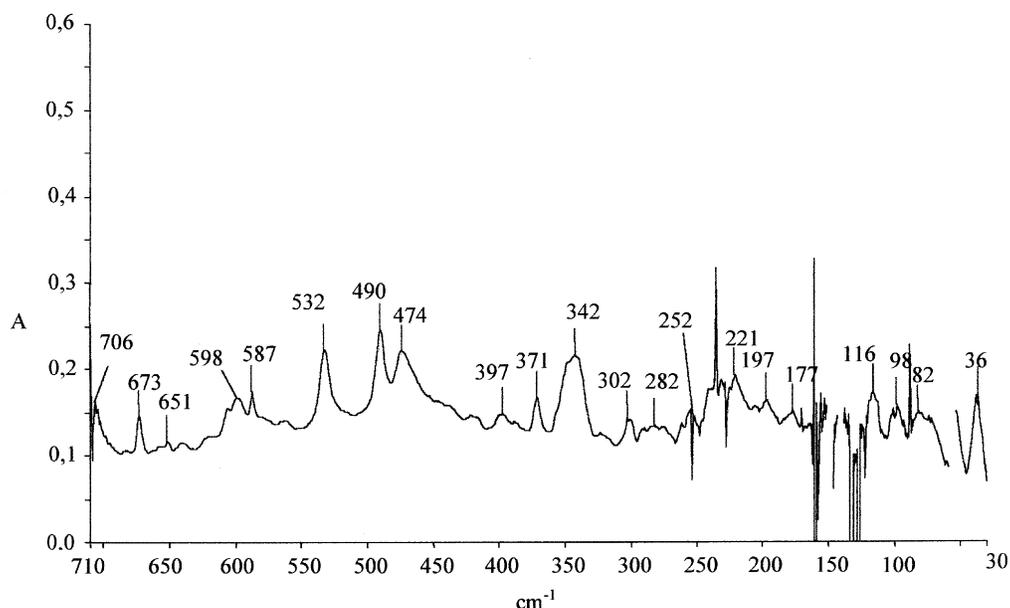


Fig. 1. Far-FT-IR spectrum (in absorbance units A) of $\text{Cu}(\text{TAAB})^{2+}$ in polyethylene matrix.

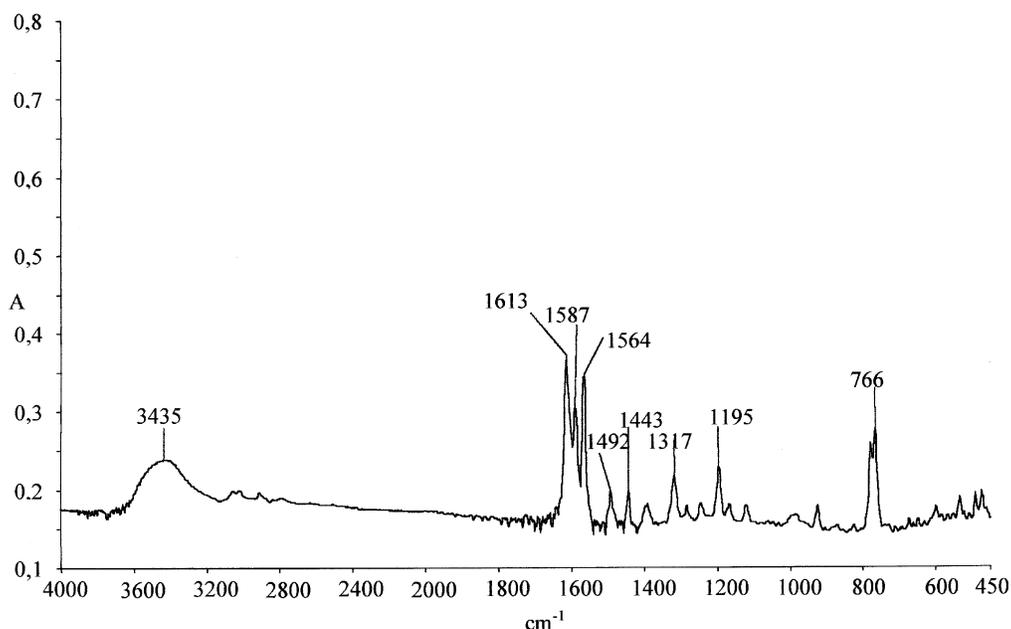


Fig. 2. Mid-FT-IR spectrum (in % transmittance) of $\text{Cu}(\text{TAAB})^{2+}$ in KBr matrix.

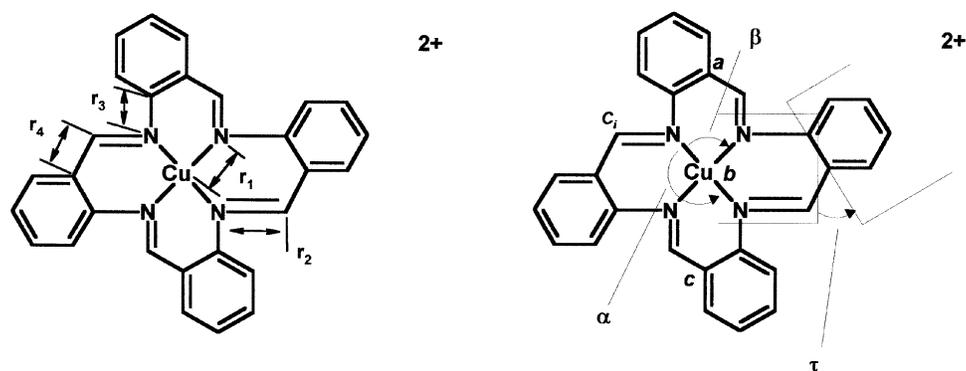
Perkin-Elmer system 2000 far-FT-IR spectrometer within the range $710\text{--}30\text{ cm}^{-1}$ in a reference-sample shuttle mode using polyethylene as matrix. To accomplish a reasonable signal-to-noise ratio, 1000 cycles, each consisting of one polyethylene reference pellet scan, followed by four sample scans and another reference scan, were summed. The sample compartment was constantly purged with nitrogen of highest available purity (99.99%). The far-FT-IR spectrum of $\text{Cu}(\text{TAAB})^{2+}$ is depicted in Fig. 1 (see above).

For acquisition of the mid-range IR the powder sample was measured on a Perkin-Elmer 16 PC FT-IR spectrometer within the range $4000\text{--}600\text{ cm}^{-1}$. Sixty-four scans of the sample pellets using KBr as matrix were added up. The sam-

ple compartment was constantly purged with nitrogen of highest available purity (99.99%). The mid FT-IR spectrum of $\text{Cu}(\text{TAAB})^{2+}$ is given in Fig. 2 (see above).

3. Theoretical

The heat of formation of several conformations corresponding to minima of the potential energy surface was compared to determine the geometric structure around the active copper site in $\text{Cu}(\text{TAAB})^{2+}$. The geometries of these conformations were derived by full geometry optimisations with varying starting geometries. Several copper(II) sphere con-



Scheme 2. Characteristic structural parameters of $[\text{Cu}(\text{TAAB})]^{2+}$: Definition of important bond lengths (left) and angles (right). The torsional angle τ is defined as the angle between the plane of a phenyl ring and the plane containing the copper centre and two neighbouring nitrogen atoms.

formations were selected, ranging from an undistorted tetrahedral to a perfect planar conformation. Several distorted starting geometries were added to ensure a sufficient exploration of the relevant subsection of the potential energy surface. The heat of formation was compared for the conformations yielded by scanning of the energy hypersurface to determine the most stable conformation. Important geometric parameters were compared to characterise the yielded conformations (see Scheme 2).

Additional to several important bond lengths (see Scheme 2, left), the copper–nitrogen angles α and β , describing the Jahn–Teller distortion of the copper inner sphere, are presented for all conformations. The torsional angle τ is presented as another relevant structural parameter. It describes the twisting of the phenyl subunits out of the plane defined by its two neighbouring nitrogen atoms and the copper centre. The carbon–copper–carbon angle γ is introduced to characterise the change from the tetrahedral to planar conformations.

For the ground state equilibrium geometry yielded by the geometry optimisation procedure described above, the far- and mid-range IR spectra were calculated. A harmonic normal-coordinate analysis was performed to assign prominent peaks in the experimental spectra to vibrational modes of the model compound. Due to the size of the model compound, the fast semi-empirical ZINDO/1 [12] method implemented in the software package HYPERCHEM [13] was chosen for these theoretical investigations.

4. Results and discussion

The conformational analysis performed with the semi-empirical ZINDO/1 method resulted in three stationary points of the potential energy surface of $\text{Cu}(\text{TAAB})^{2+}$. One stationary point corresponds to a tetrahedral conformation, where the four nitrogen atoms form a slightly distorted tetrahedron around the central copper(II) ion (labelled tetrahedral in Tables 1 and 2). Additionally, two conformations with quadratic-planar copper–nitrogen arrangement (referred to as planar and twisted) were found (see Table 1).

Table 1
Characteristic geometric parameters of $\text{Cu}[\text{TAAB}]^{2+}$ for the ground state equilibrium geometry (tetrahedral), a twisted planar (twisted) and a planar (planar) conformation

	Tetrahedral	Twisted planar	Planar
r_1 (pm)	191	194	199
r_2 (pm)	132	133	133
r_3 (pm)	141	141	142
r_4 (pm)	144	143	142
α (°)	93	90	90
β (°)	154	180	180
γ (°)	130	180	180
τ (°)	8	20	0

Table 2
The heats of formation ΔH (kJ mol^{-1}) and the energy gaps $\Delta(\Delta H)$ to the most stable conformation (kJ mol^{-1}) for $\text{Cu}[\text{TAAB}]^{2+}$. The ground state equilibrium geometry (tetrahedral) is compared with a twisted planar (twisted) and a planar (planar) conformation

	Tetrahedral	Twisted planar	Planar
ΔH	–51847.2	–51689.2	–51524.1
$\Delta(\Delta H)$		158.0	323.1

For the tetrahedral conformation, the ligand is folded into a saddle-like arrangement ($\beta = 154^\circ$, $\gamma = 130^\circ$, see Table 1) with slightly twisted phenyl subunits ($\tau = 8^\circ$). Except for the twisting angle τ , the two conformations with planar arrangement show similar geometries around the copper(II) centre. One is found with untwisted phenyl moieties ($\tau = 0^\circ$, referred to as planar), and the other with a propeller-like twisted arrangement of the phenyl subunits ($\tau = 20^\circ$, referred to as twisted).

The comparison of the heat of formation of these three conformations yielded the tetrahedral conformation as the most stable one. The energy gap between the tetrahedral and the twisted conformation is calculated to be $158.0 \text{ kJ mol}^{-1}$, whereas the energy gap between tetrahedral and the planar conformation is calculated to be $323.1 \text{ kJ mol}^{-1}$ (see Table 2). There is no high energy barrier for a conformational change between the two possible tetrahedral-like conforma-

tions (with the carbon bridges bent up or down). The vibrational modes corresponding to such a conformational change can be assigned to far-IR absorption bands below 92 cm^{-1} , consisting of a vibrational mode from a tetrahedral towards the planar conformation, and symmetric and asymmetric phenyl twist modes between 60 and 92 cm^{-1} (see Table 3). We want to emphasise that the vibrational transition from one to the other conformation has no planar transition state. The molecule always keeps its bent structure of the carbon bridges, involving a pathway via the twisted conformation. The geometric arrangement of the ligand, in combination with the found flexibility of the inner sphere geometry with low barriers against conformational changes, makes this system easily accessible to even large reactants and for stabilisation involving direct copper–solvent interactions.

The prominent absorption feature at 474 and 490 cm^{-1} can be assigned to vibrational modes corresponding to a distortion of the copper–nitrogen tetrahedron. Other vibrational modes which can be—according to the results of the normal-coordinate analysis—described by specific motions of parts of the molecule are the vibration involving a linear displacement of the copper atom relative to the nitrogen tetrahedron at 98 cm^{-1} , the 180° -symmetric copper–nitrogen bending mode (200 cm^{-1}), and the copper–nitrogen stretch vibrations ($640\text{--}680\text{ cm}^{-1}$). The weak additional modes between 80 and 200 cm^{-1} do have contributions from general motions of nearly all atoms of the molecule and are therefore characterising the far-IR spectrum of $\text{Cu}(\text{TAAB})^{2+}$.

Three prominent peaks at 766 cm^{-1} are assigned to a copper–nitrogen stretching. The medium–strong bands at 1176 and 1195 cm^{-1} are assigned to inner-sphere vibrational modes, the out-of-plane bending of the C_i carbon (see Scheme 2), and the inner-sphere carbon–carbon and carbon–nitrogen bending vibrations, respectively (see Table 4). Phenyl carbon–carbon vibrations are found at 1443 and 1492

Table 3

Normal-coordinate analysis of the far-IR spectra of $\text{Cu}[\text{TAAB}]^{2+}$. Harmonic frequencies (cm^{-1}) and assignment of important vibrational modes of the far-IR spectra of $\text{Cu}[\text{TAAB}]^{2+}$ calculated with the semi-empirical ZINDO/1 method ^a

Harmonic frequency	Mode
36	bending: tetrahedral \rightarrow planar
61–82	sym. bending \rightarrow twisted phenyl subunits
92	asym. bending \rightarrow twisted phenyl subunits
98	Cu out of N-tetrahedron motion
116	C–C out-of-plane bending (inner-sphere)
180–200	sym. Cu–N bending
221–342	C–C bending
371–430	C–N out-of-plane bending
474–490	Cu–N tetrahedral distortion
532–548	C–C out-of-plane bending (phenyl)
570–587	C–C bending (phenyl)
598	structural stretching vibration
640–680	Cu–N stretching (sym)
706	structural stretching and bending, phenyl twisting

^a vw, very weak; w, weak; m, medium; s, strong; vs, very strong.

Table 4

Normal-coordinate analysis of the mid-range IR spectra of $\text{Cu}[\text{TAAB}]^{2+}$. Harmonic frequencies (cm^{-1}) and assignment of important vibrational modes of the mid-range IR spectra of $\text{Cu}[\text{TAAB}]^{2+}$ calculated with the semi-empirical ZINDO/1 method ^a

Harmonic frequency		Mode
3435	vs	aqueous O–H stretching
1613	vs	C–C bend vibrations (phenyl)
1587	vs	C–C bend vibrations (phenyl)
1564	vs	C=N vibration
1508	w	C–H bending (H at C_i)
1492	m	C–C stretch vibrations (phenyl)
1443	m	C–C stretch vibrations (phenyl)
1327	s	sym. C–H bending (in-plane, phenyl)
1275	w	asym. C–C bending (in-plane, phenyl)
1243	w	sym. C–C bending (in-plane, phenyl)
1195	s	inner-sphere C–C and C–N bending
1176	w	C out-of-plane bending (C_i)
1170–800	w	out-of-plane vibrations
766	s	sym. Cu–N stretching

^a vw, very weak; w, weak; m, medium; s, strong; vs, very strong; sym, symmetric; asym, asymmetric. Note: asym(A) corresponds to a mode with partial symmetry, asym(B) to the totally asymmetric mode.

cm^{-1} (stretching modes) and at 1587 and 1613 cm^{-1} (bending modes). The very broad absorption feature around 3435 cm^{-1} (see Fig. 2) is attributed to an aqueous O–H stretching vibration of the $\text{Cu}(\text{TAAB})(\text{NO}_2)_2 \cdot \text{aq}$.

5. Conclusions

Far- and mid-range FT-IR spectra of $\text{Cu}[\text{TAAB}]^{2+}$ revealed absorption features characteristic for a four-fold coordinated copper(II). A conformational analysis of $\text{Cu}[\text{TAAB}]^{2+}$ resulted in a ground state equilibrium geometry confirming a slightly distorted tetrahedral arrangement of the nitrogen atoms with the copper in the centre. The slightly twisted phenyl subunits further stabilise this conformation. Due to the flexibility of the folded ligand system, the copper(II) active site is easily accessible even for relatively bulky reactants. A possible inversion pathway is found to involve a planar conformation with strongly twisted phenyl substituents rather than a totally planar one. A normal-coordinate analysis of the far-IR region confirms the possibility of this conformational change for $\text{Cu}[\text{TAAB}]^{2+}$.

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