Communications to the Editor

Simple Models for "Blue" Copper Proteins. The Copper-Thiaether Complexes

Sir:

The "blue" copper proteins have generated exceptional interest because of the characteristic intense absorption band observed for these species in the 600-nm region.[1,2] The complexity of these proteins has thus far made it impossible to establish the exact ligand environment of the copper(II) ion which gives rise to this intense band. The apparent absence of any low molecular weight models exhibiting similar spectral characteristics earlier led to the hypothesis that the 600-nm band arises from a highly distorted ligand environment around the copper ion which is imposed by the protein superstructure[3,4] with the specific proposal that a five-coordinate copper site is involved.[5-7] Recent Raman and x-ray photoelectron studies on plastocyanin, ceruloplasmin, and related blue copper proteins have indicated the presence of a coordinated sulfur donor atom in the copper(II) inner-coordination sphere[6-8] which has been linked to the 600-nm band.

We wish to report the first known examples of low molecular weight complexes which not only mimic the spectral characteristics of the "blue" copper proteins but also exhibit similar redox potentials. In ongoing kinetic and thermodynamic studies in this laboratory on the copper(II) complexes of low molecular weight macrocyclic and open-chain polythiaethers,[9] we have noted the appearance of an intense absorption band in the 600-nm region (see Figure 1) as well as an additional intense band near 400 nm. Although the thiaether complexes of copper(II) are relatively weak ($K < 10^4$), it has been possible to establish quantitatively the stability constants of these complexes[9] and thereby determine the molar absorptivity values. The resolved data, as presented in Table I, yield molar absorptivities for the 600-nm band which are at least tenfold larger than would be anticipated for a normal d–d transition, in agreement with recent suggestions that the 600-nm transition in "blue" copper proteins represents a S → Cu(II) charge transfer band.[7,8,10]

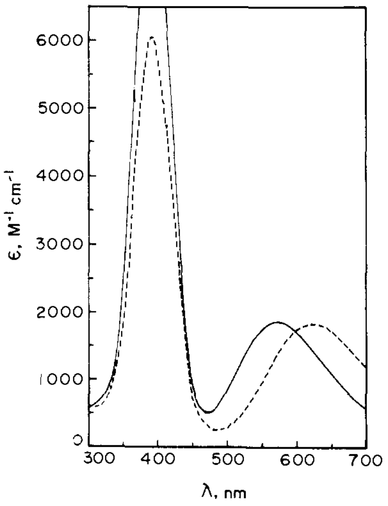


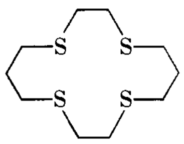
Figure 1. Visible spectra of the copper(II) complexes of 13-ane-S_4 (- - -) and 14-ane-S_4 (—) showing the intense absorption bands in the vicinity of 400 and 600 nm. Although the spectra shown here were obtained at 25° in 80% methanol-20% water containing 0.1 *M* $HClO_4$, these spectra have been found to be virtually independent of solvent composition and acid strength.

Table I. Spectral Data for Copper(II)–Thiaether Complexes in 80% Methanol–20% Water (by wt) at 25°, $\mu = 0.1\ M$ ($HClO_4$)

Ligand[a]	K_{CuL}	λ_{max} (~400-nm band)	ϵ_{400}	λ_{max} (~600-nm band)	ϵ_{600}
12-ane-S_4	2.4×10^2	387	6.0×10^3	675	2.0×10^3
13-ane-S_4	2.7×10^2	390	6.0×10^3	625	1.8×10^3
14-ane-S_4	3.1×10^3	390	8.2×10^3	570	1.9×10^3
15-ane-S_4	2.3×10^2	414	8.0×10^3	565	1.14×10^3
16-ane-S_4	9	440	6.1×10^3	603	0.8×10^3
15-ane-S_5[b]	9.8×10^2	414	$\sim 7 \times 10^3$	565	$\sim 2 \times 10^3$
20-ane-S_6[c]	—	420	$\sim 7.1 \times 10^3$	545	$\sim 1.4 \times 10^3$
Et_2-TTU	14	410	6.8×10^3	612	1.1×10^3

[a] For identification of ligands, see ref 9. [b] 15-ane-S_5 represents 1,4,7,10,13-pentathiocyclopentadecane. [c] 20-ane-S_6 represents 1,4,7,10,14,17-hexathiacycloeicosane.

An x-ray crystallographic study of the most stable copper(II)-polythiaether complex involving the 14-ane-S_4 ligand shows the Cu(II) to be symmetrically centered within the plane of the four sulfur atoms (Cu–S bond lengths, 2.30 Å) with perchlorates bonded in the axial positions (Cu–O bond lengths, 2.65 Å).[11] The single-crystal spectrum for this complex[12] is essentially identical with the solution spectrum (see Table I) with the 570-nm band exhibiting a polarization which establishes that it arises from the Cu(II)–S bonds. This unequivocally demonstrates that (i) *thiaether sulfurs bonded to Cu(II) are capable of generating intense absorption bands in the 600-nm region* and (ii) *distortion from tetragonal symmetry is not a prime requirement for producing these intense bands.*



All evidence to date[13] indicates that the 14-ane-S_4 complex maintains the same basic structure in the solution state with the four sulfur donor atoms coordinated to the copper(II) in a planar array while the perchlorate ions compete with solvent molecules as the ligating species at the axial sites. By contrast, the 12-ane-S_4 and 13-ane-S_4 ligands appear to be too small to permit planar coordination to copper(II).[14,15] Yet the latter complexes exhibit virtually identical molar absorptivity values in the 600-nm band to that of the 14-ane-S_4 complex (see Table I and Figure 1) suggesting that *no specific coordination geometry to Cu(II) is required for the generation of this band.* Furthermore, the spectral similarity of the complexes with the open-chain ligand, Et_2-TTU, as well as with the 15-ane-S_5 and 20-ane-S_6 compounds establishes that neither a cyclic ligand nor four sulfur donor atoms are required.

An ESR spectrum of the Cu(II)-(14-ane-S_4) complex in frozen methanol could not be readily interpreted due to the presence of both free and complexed Cu(II) (as a result of the low complex stability constant). However, the ESR spectrum does rule out the presence of a ligand free-radical system as the source of the 600-nm band. Moreover, extensive kinetic studies on this and other thiaether complexes[9,13] rule out the presence of dimeric copper species, and the identical kinetic behavior observed by monitoring either at 600 or 400 nm provides strong evidence that a single species gives rise to both absorption bands.

In agreement with the relatively high affinity of Cu(I) for thiaether sulfur donors,[16] Cu(II) in the thiaether complexes has been found to be readily reduced to Cu(I) in a reversible manner. Preliminary cyclic voltammetric measurements on the 13-ane-S_4 and 14-ane-S_4 complexes (presumed to represent nonplanar and planar sulfur coordination, respectively) indicate a reduction potential in the vicinity of +0.7 V (vs. SHE in 80% methanol) which is strikingly similar to the Cu(II)-Cu(I) potentials which have been observed in the blue copper proteins.[7]

In the recent studies identifying the presence of one or more Cu(II)-S bonds in the blue copper proteins,[6-8] the reporting investigators have suggested that the sulfhydryl moiety of a cysteine residue is involved, presumably because thiaether sulfurs have generally been assumed to have little affinity for Cu(II).[16-18] However, the present work strongly suggests that *the thiaether sulfurs of methionine groups* (which generally equal or exceed the number of cysteine residues)[19] *represent the ligating S-donor atom(s) in blue copper proteins.* This would then account for the observation that Cu(II) is not automatically reduced to Cu(I) as would be anticipated if sulfhydryl coordination were involved.

Although the thiaether complexes lack the nitrogen- and/or oxygen-donor atoms which are presumed to comprise part of copper's inner coordination sphere in the blue copper proteins, the existence of both the intense 600-nm absorption band and the positive reduction potentials characteristic of blue copper proteins should make them promising models for further studies on the importance of copper-sulfur interactions in these and other copper-containing proteins.

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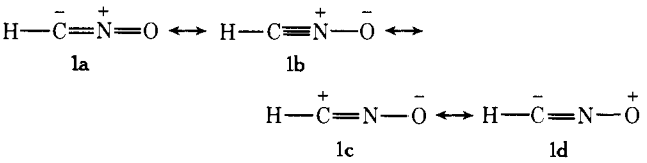
Concerted 1,3-Dipolar Addition of Fulminic Acid to Acetylene and Ethylene. An ab Initio Molecular Orbital Study

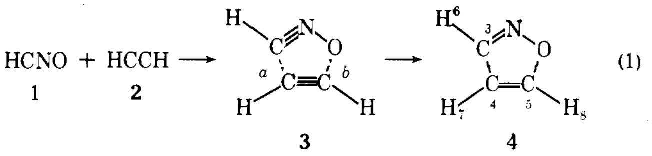
Sir:

The thermal addition of 1,3-dipoles to unsaturated molecules[1] is one of the textbook examples for the application of orbital symmetry rules.[2] In valence bond terms, 1,3-dipoles are written as a superposition of dipolar structures such as **1a–d.** The molecular orbital description of 1,3-dipoles[3] reveals that these compounds are isoconjugate with the allyl anion, i.e., possess 4π electrons which are delocalized over three atoms. In some 1,3-dipoles, e.g., in fulminic acid (**1**) and in nitrile oxides RCNO there is a second, orthogonal π system, also containing four electrons. The addition of a 1,3-dipole to an unsaturated molecule (the dipolarophile) can then be formulated as a $({}_{\pi}4_s + {}_{\pi}2_s)$ process and is therefore expected to proceed in a concerted, stereospecific manner.[2] In accordance with this prediction, the experimental data are generally interpreted as being fully compatible only with a transition state, **3**, in which both new σ bonds *a* and *b* between dipole (e.g., fulminic acid) and dipolarophile (e.g., acetylene **2**) are formed to a similar extent.[3]



$$\mathrm{H{-}\overset{-}{C}{=}\overset{+}{N}{=}O \longleftrightarrow H{-}C{\equiv}\overset{+}{N}{-}\overset{-}{O} \longleftrightarrow H{-}\overset{+}{C}{=}N{-}\overset{-}{O} \longleftrightarrow H{-}\overset{-}{C}{=}N{-}\overset{+}{O}}$$

1a **1b** **1c** **1d**



(1)

There have been numerous attempts to rationalize relative reactivities of different dipoles and dipolarophiles, and the direction of addition in unsymmetrically substituted systems, on the basis of simple molecular orbital theory.[4] These calculations usually involve rather drastic assumptions concerning the geometry of the transition state. Since transition states are not observable experimentally, these assumptions can be checked only theoretically, by more so-