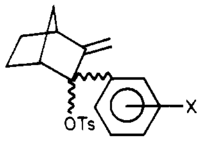
fit ($r = 0.999$) similar to the plot in Figure 1 is also observed.

Brown and his co-workers in a recent paper[20] questioned the previous ^{13}C NMR spectroscopic conclusions[12,13] on the onset of nonclassical σ delocalization in 2-phenyl-2-norbornyl cations **3**-R with electron-withdrawing substituents. They argued that they have observed high exo/endo rate ratios in most tertiary derivatives including systems such as **10** and **11**[21] with a wide variety of substituents on the aryl ring. We reiterate our view that the "tool of increasing electron demand" as applied to solvolytic studies is too coarse to fully detect changes in the electron demand of a system unless the magnitude of such a demand is indeed large. Even negatively substituted phenyl rings are 6π systems capable of significant charge delocalization; thus, the residual σ-bond delocalization effect should be small in 2-phenyl-2-norbornyl cations. Moreover, the observation of high exo/endo rate ratios in tertiary norbornyl systems does not provide any diagnostic test for the presence or absence of nonclassical σ delocalization. As pointed out by Brown in many of his works,[11b,21] such an effect may be of steric origin. Our present ^{13}C NMR spectroscopic study demonstrates the regular phenylcarbenium ion nature of 2,5-diphenyl-2,5-norbornyl dications **1**-R, even with strong electron-withdrawing substituents, in contrast to 2-phenyl-2-norbornyl cations **3**-R, where the onset of σ delocalization is observed with electron-withdrawing substituents. This study is in accord with the structure and stability of the parent 2-norbornyl cation based on a variety of spectroscopic[11,22] and calorimetric studies[23] in the condensed phase.



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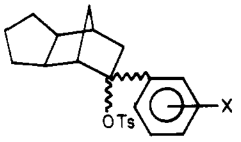

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Experimental Section

The exo,exo diols **4**-R were prepared by the addition of organomagnesium or organolithium reagents to the diketone **2**.[14] exo,exo-2,5-Norbornanediol (**4**-H) was prepared by the reported "hydroboration-oxidation" of norbornadiene.[14] The diols **5**-R (mixture of cis and trans) were prepared from the commercially available cyclohexane-1,4-dione.[15] All the new diols showed satisfactory spectroscopic and analytical data.

Preparation of Dications. Freshly distilled SbF_5 and FSO_3H were used. To the appropriate superacid dissolved in about a twofold amount of SO_2ClF at dry ice-acetone (ca. -78 °C) or petroleum ether-liquid nitrogen slush temperature (-140 °C) was slowly added, with vigorous stirring, a cooled slurry or solution of the corresponding diol precursor in SO_2ClF, resulting in an approximately 10-15% solution of the ion.

^{13}C NMR Spectra were obtained by using a Varian Associates Model FT-80 spectrometer, equipped with a multinuclei broad band variable temperature probe. The chemical shifts were referenced from external capillary tetramethylsilane.

Acknowledgments. Support of our work by the National Science Foundation is gratefully acknowledged.

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Crystal Structure and Spectroscopic Properties of Violet Glutathione-Copper(II) Complex with Axial Sulfur Coordination and Two Copper Sites via a Disulfide Bridge

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Abstract: The violet glutathione-Cu(II) complex, $[Cu^{II}GSSGCu^{II}]Na_4 \cdot 6H_2O$, was firstly isolated as a single crystal. The X-ray crystallographic analysis of the binuclear complex showed that each Cu(II) atom is in a distorted square-pyramidal configuration and the Cu(II)-Cu(II) distance is 5.21 Å. The coordination of Cu(1) involved the two deprotonated peptide nitrogens, N(1) and N(2), the glutamic amine nitrogen, N(3), and the glycinyl terminal carboxylate oxygen, O(1), in an approximate planar coordination while the cysteinyl sulfur, S(1), is bonded apically to form a square pyramid. The Cu(51) ion is similarly coordinated to N(51), N(52), N(53), O(51), and S(51). The apical Cu(II)-S mean distance is 3.22 Å and a direction of this bond is bent by 22° from the perpendicular C_{4v} axis of the square-planar basal plane. Of special interest is the Cu(II) coordination by the sulfur atoms of the disulfide bridge. The Cu(II) complex was also characterized by magnetic susceptibility and electron spin resonance (ESR), electronic, circular dichroism, and X-ray photoelectron spectra (X-ray PES). The magnetic susceptibility and ESR spectra showed that the internuclear Cu(II)-Cu(II) interaction is negligibly small. The ESR parameters and X-ray PES binding energies determined were as follows: $g_{zz} = 2.251$, $g_{xx} = 2.047$, $g_{yy} = 2.038$, $A_{zz} = 177.2$, $A_{xx} = 43.8$, and $A_{yy} = 36.0$ G (ESR); Cu $2p_{3/2} = 933.1$ and 943.9, S 2p = 163.4 and 167.5, N 1s = 399.4, O 1s = 531.2, and Na 1s = 1071.1 eV (X-ray PES). The present results provide valuable information for biologically significant glutathione-Cu(II) complexes.

Introduction

Glutathione-Cu(II) complexes are of biological and chemical interest. Marzullo and Friedhoff[2a] identified an inhibitor of opiate receptor binding as a glutathione-Cu(II) complex from human red blood cells and from rabbit brain. It has been reported that the Cu(II) complex is involved in rheumatoid arthritis and that the inhibitory activity is due to a complex of oxidized glutathione

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(1) (a) Niihama Technical College. (b) Kyoto University. (c) Ehime University. (d) University of Tokyo.

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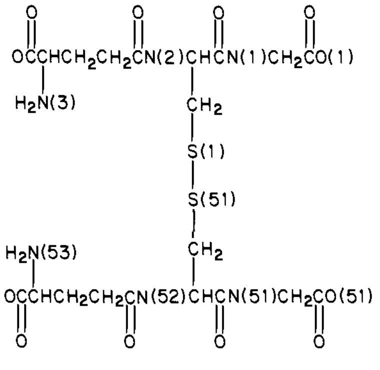
with Cu(II).[2b] On the other hand, the interaction of glutathione with Cu(II) and other transition metals has been investigated using different physicochemical methods. Earlier potentiometric and polarographic studies suggested that glutathione combines with metal ions by chelation either through the amino and carboxyl groups of the glutamyl residue or through the thiol group of the cysteinyl residue.[3] Perrin and Watt[4] proposed that a copper analogous Zn(II) complex of reduced glutathione has two five-membered chelate rings. Using the ^{13}C nuclear magnetic resonance (NMR) method, on the contrary, Rabenstein and his collaborator[5] reached the conclusion that not only five-membered chelate rings but also seven-membered rings may be involved in the Zn(II) complex at pD >10.5. It was assumed from the ESR results that for 1:2 reduced glutathione–Cu(II) complex one copper ion Cu(A) is coordinated by the cysteinyl residue and the other Cu(B) by the terminal functional groups of the glutamyl residue.[6] Recently, Kroneck[7] stated that a binuclear Cu(II) complex with oxidized glutathione consists of the six-coordinated Cu(II) in different body compartments and that this complex is a model for ESR-nondetectable copper in blue oxidases. The discrepancies in these experimental data and conclusions result from (1) the multiplicity of metal-binding sites by glutathione ligand, (2) pH dependence of ionization of the various coordination groups, (3) redox reaction between thiol group and Cu(II) ion, and (4) formation of precipitate in the complex formation. Despite the biological and chemical significance of the glutathione–Cu(II) complexes, the complex as a single crystal has apparently not been isolated.

We succeeded in isolating the binuclear oxidized glutathione–Cu(II) complex as a needle-like single crystal from a 1:1 reduced glutathione–Cu(II) reaction mixture. X-ray crystallographic analysis of the violet Cu(II) complex clarified the presence of two Cu(II) sites via a disulfide bridge (copper–copper distance = 5.21 Å) and of apical S–Cu(II) bonding (3.22 Å). In addition, this complex was also characterized by magnetic susceptibility and electron spin resonance (ESR), electronic, circular dichroism (CD), and X-ray photoelectron spectra (X-ray PES). One of the most important features of the isolated Cu(II) complex is the unique sulfur apical coordination largely deviating from the C_{4v} axis in the distorted square-pyramidal geometry. In this paper, the donor atoms of oxidized glutathione are numbered in the same manner as used in reporting the crystal structure as follows:



$$\mathrm{O\overset{O}{\overset{\|}{C}}\underset{H_2N(3)}{CH}CH_2CH_2\overset{O}{\overset{\|}{C}}N(2)\underset{CH_2S(1)}{CH}\overset{O}{\overset{\|}{C}}N(1)CH_2\overset{O}{\overset{\|}{C}}O(1)}$$

$$\mathrm{O\underset{O}{\underset{\|}{C}}\overset{H_2N(53)}{CH}CH_2CH_2\underset{O}{\underset{\|}{C}}N(52)\overset{S(51)CH_2}{CH}\underset{O}{\underset{\|}{C}}N(51)CH_2\underset{O}{\underset{\|}{C}}O(51)}$$

Experimental Section

Preparation of Crystal. An aqueous solution (1 mL) of 1 mM $CuCl_2 \cdot 2H_2O$ was added to an aqueous solution (5 mL) of 1 mM reduced glutathione keeping the pH value at neutral range with addition of carbonate-free sodium hydroxide under a nitrogen atmosphere. The pH value of the resulting solution was finally adjusted to 11.3 at room temperature. Purified ethanol (10 mL) was added to the reaction mixture and the precipitate filtered off. Additional ethanol (50 mL) was added to the filtrate to give a red-violet precipitate, which was crystallized as a needle-like crystal from water–ethanol (1:3) solution. The yield was approximately 60%. The microanalysis satisfied the molecular formula $[Cu_2(C_{20}H_{24}N_6O_{12}S_2)]Na_4 \cdot 6H_2O$. Anal. Calcd: C, 25.78; H, 3.89; N, 9.02; Cu, 13.64. Found: C, 25.51; H, 3.90; N, 8.77; Cu, 13.71. Mp 240 °C dec. The presence of four Na atoms per molecule of this complex was also detected by both atomic absorption and flame emission spectrophotometries, using a Nippon Jarrell Ash AA-782. The infrared spectrum of the isolated Cu(II) complex showed a disappearance of ν(SH), $\nu(NH_3^+)$, and ν(COOH) bands at 2500, 3100, and 1700 cm^{-1}, respectively, as observed in the glutathione ligand.

Table I. Crystal Data for Glutathione-Copper(II) Sodium Salt Hexahydrate, $[Cu_2(C_{20}H_{24}N_6O_{12}S_2)] \cdot Na_4 \cdot 6H_2O$

crystal system	monoclinic	$a = 27.876$ (19) Å
space group	C2	$b = 12.338$ (9) Å
$Z = 4$		$c = 13.414$ (9) Å
$d_X = 1.460$ g cm^{-3}		$\beta = 107.28$ (7)°
		$V = 4405.2$ Å^3

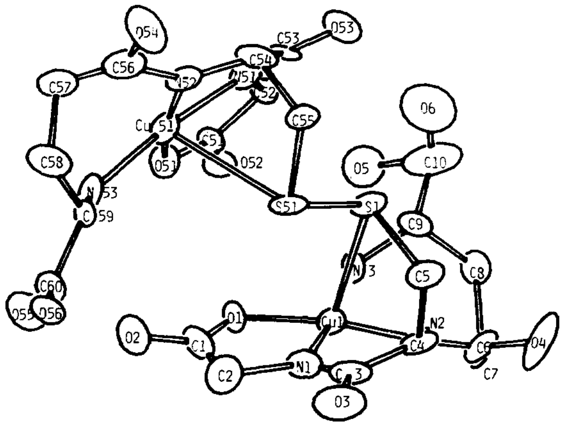


Figure 1. Molecular structure of the complex. The atoms in the second half of the molecule have 50 added to the number of the corresponding atoms in the first half.

Spectroscopic Measurements. The pH of all solutions was measured using a glass electrode, Radiometer Type PHM 62. Electronic and CD spectra of the Cu(II) complex were recorded on a Hitachi recording spectrometer (Model 200-20) and a JASCO J-20 spectropolarimeter, respectively. X-ray photoelectron spectra of the crystalline glutathione–Cu(II) complex were recorded at −100 °C on a Varian V-IEE 15 spectrometer. The spectra were standardized on the C 1s line at 284 eV which results from the aliphatic hydrocarbons. The standard deviation of the energy values was 0.1 eV. Magnetic susceptibility was measured in the continuous temperature range from 55 to 293 K using a Shimadzu Type MB-2 magnetic torsion balance, equipped with a low-temperature cryostat. Manganese Tutton salt was used for the calibrations of the thermometers and field gradient. The temperature-independent paramagnetism per g-ion of Cu(II) was taken to be 60 × 10^{-6} cgs emu.[8] The ESR measurements were carried out at 77 K under a true glass of 25% ethylene glycol aqueous solution using a JES-ME-3X spectrometer operating with 100-kHz magnetic field modulation. The ESR operating frequency (X-band) was measured with a Takeda-Riken microwave frequency counter and g values were determined taking Li–TCNQ (g = 2.0026) as a standard. The magnetic field was calibrated by the splitting of Mn(II) in MgO (ΔH_{3-4} = 86.9 G).

Crystallographic Data. The crystal grown in water–ethanol solution was used for the X-ray diffraction measurement. The specimen of approximate dimensions 0.70 × 0.24 × 0.12 mm was sealed in a thin-walled glass capillary to prevent loss of the solvent of crystallization. The diffraction angles and the intensities were measured on a Philips PW 1100 four-circle diffractometer using Cu Kα radiation monochromated by a graphite plate. Crystal data are listed in Table I. Of the total of 4574 reflections within the 2θ range from 6 to 156°, 3533 were measured as above the $2\sigma(I)$ level and these reflections were used for the structure determination.

Structure Determination by X-ray Diffraction. The crystal structure was determined by the heavy-atom method initially phased by the contributions of the two copper atoms. Repeated cycles of Fourier and

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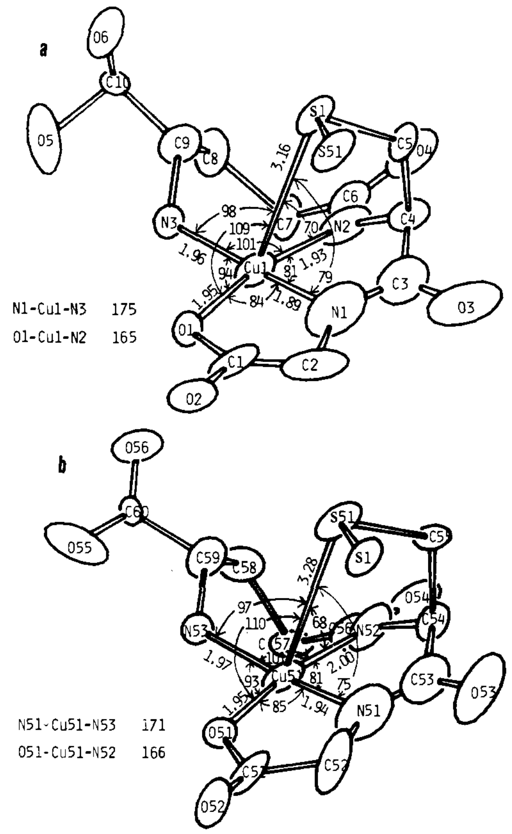

Figure 2. Coordination geometry around (a) Cu(1) and (b) Cu(51).

Table II. Bond Lengths[a] (Å)

Cu1		Cu51	
	Metal-Ligand Bonds		
Cu1-S1	3.16 (1)	Cu51-S51	3.28 (1)
Cu1-N1	1.89 (3)	Cu51-N51	1.94 (2)
Cu1-N2	1.93 (2)	Cu51-N52	2.00 (3)
Cu1-N3	1.96 (2)	Cu51-N53	1.97 (2)
Cu1-O1	1.95 (2)	Cu51-O51	1.95 (2)
	Ligand Molecules		
S1-S51	2.06 (1)		
S1-C5	1.84 (3)	S51-C55	1.85 (4)
C1-C2	1.23 (7)	C51-C52	1.59 (4)
C1-O1	1.55 (4)	C51-O51	1.32 (3)
C1-O2	1.46 (5)	C51-O52	1.11 (4)
C2-N1	1.52 (3)	C52-N51	1.52 (4)
C3-C4	1.40 (4)	C53-C54	1.45 (4)
C3-N1	1.38 (4)	C53-N51	1.38 (4)
C3-O3	1.33 (5)	C53-O53	1.21 (3)
C4-C5	1.48 (4)	C54-C55	1.62 (5)
C4-N2	1.45 (3)	C54-N52	1.49 (3)
C6-C7	1.42 (4)	C56-C57	1.65 (6)
C6-N2	1.32 (3)	C56-N52	1.25 (5)
C6-O4	1.37 (3)	C56-O54	1.05 (7)
C7-C8	1.61 (4)	C57-C58	1.53 (6)
C8-C9	1.52 (4)	C58-C59	1.50 (5)
C9-C10	1.48 (5)	C59-C60	1.58 (3)
C9-N3	1.43 (3)	C59-N53	1.44 (4)
C10-O5	1.24 (5)	C60-O55	1.18 (5)
C10-O6	1.10 (6)	C60-O56	1.25 (4)

[a] Standard deviations are given in parentheses.

Table III. Bond Angles[a] (Deg)

Cu1		Cu51	
	Metal-Ligand Bonds		
S1-Cu1-N1	79 (1)	S51-Cu51-N51	75 (1)
S1-Cu1-N2	70 (1)	S51-Cu51-N52	68 (1)
S1-Cu1-N3	98 (1)	S51-Cu51-N53	97 (1)
S1-Cu1-O1	109 (1)	S51-Cu51-O51	110 (1)
N1-Cu1-N2	81 (1)	N51-Cu51-N52	81 (1)
N1-Cu1-N3	175 (1)	N51-Cu51-N53	171 (1)
N1-Cu1-O1	84 (1)	N51-Cu51-O51	85 (1)
N2-Cu1-N3	101 (1)	N52-Cu51-N53	101 (1)
N2-Cu1-O1	165 (1)	N52-Cu51-O51	166 (1)
N3-Cu1-O1	94 (1)	N53-Cu51-O51	93 (1)
	Ligand Molecules		
S51-S1-Cu1	105 (0)	S1-S51-Cu51	104 (0)
S51-S1-C5	104 (1)	S1-S51-C55	103 (1)
Cu1-S1-C5	85 (1)	Cu51-S51-C55	87 (1)
C2-C1-O1	136 (4)	C52-C51-O51	108 (2)
C2-C1-O2	125 (4)	C52-C51-O52	123 (3)
O1-C1-O2	99 (3)	O51-C51-O52	129 (3)
N1-C2-C1	97 (3)	N51-C52-C51	114 (2)
C4-C3-N1	115 (3)	C54-C53-N51	113 (2)
C4-C3-O3	129 (3)	C54-C53-O53	129 (3)
N1-C3-O3	115 (3)	N51-C53-O53	118 (2)
C5-C4-C3	113 (2)	C55-C54-C53	105 (3)
C5-C4-N2	113 (2)	C55-C54-N52	108 (3)
C3-C4-N2	107 (2)	C53-C54-N52	113 (3)
C7-C6-N2	121 (2)	C57-C56-N52	118 (4)
C7-C6-O4	120 (3)	C57-C56-O54	118 (5)
N2-C6-O4	119 (2)	N52-C56-O54	123 (5)
C8-C7-C6	118 (2)	C58-C57-C56	109 (4)
C9-C8-C7	113 (2)	C59-C58-C57	116 (3)
C10-C9-C8	107 (2)	C60-C59-C58	107 (2)
C10-C9-N3	114 (2)	C60-C59-N53	115 (2)
C8-C9-N3	112 (2)	C58-C59-N53	111 (2)
O5-C10-C9	117 (3)	O55-C60-C59	114 (3)
O5-C10-O6	120 (4)	O55-C60-O56	129 (3)
C9-C10-O6	122 (4)	C59-C60-O56	117 (2)
Cu1-N1-C2	122 (2)	Cu51-N51-C52	111 (2)
Cu1-N1-C3	115 (2)	Cu51-N51-C53	118 (2)
C2-N1-C3	123 (3)	C52-N51-C53	129 (2)
Cu1-N2-C4	111 (1)	Cu51-N52-C54	110 (2)
Cu1-N2-C6	128 (2)	Cu51-N52-C56	126 (3)
C4-N2-C6	121 (2)	C54-N52-C56	123 (3)
Cu1-N3-C9	120 (2)	Cu51-N53-C59	119 (2)
Cu1-O1-C1	100 (2)	Cu51-O51-C51	122 (2)
S1-C5-C4	112 (2)	S51-C55-C54	110 (2)

[a] Standard deviations are given in parentheses.

difference Fourier syntheses coupled with structure-factor calculations revealed the disposition of 52 nonhydrogen atoms. The refinement of the coordinates and anisotropic thermal parameters of the 52 atoms by the block diagonal matrix least-squares method yielded an R factor of 0.17 for 3533 reflections. The intensities were scaled to the initial state by using those of the three reference reflections monitored every 2 h. Only a slight decrease (3% during the whole process of measurement) was noted. Some superlattice reflections of hkl with l = half-integer were measured as being slightly above the $2\sigma(I)$ level, but the number of reflections was so small that the present unit cell was chosen for the structure determination.

Results and Discussion

Description of the Structure. As shown in Figure 1, the glutathione molecule coordinates with the two copper ions with the symmetrical two peptide groups forming a binuclear complex anion. The coordination of each Cu(II) ion is illustrated in Figure 2a,b. The two five-coordinated groups are connected through a disulfide bridge formed between the two cysteinyl side chains. The coordination of Cu(1) involved the two deprotonated peptide nitrogens, N(1) and N(2), the glutamic amine nitrogen, N(3), and the glycinyl terminal carboxylate oxygen, O(1), in an approximate planar coordination while the cysteinyl sulfur, S(1), is bonded apically to form a square pyramid. The Cu(51) ion is similarly coordinated to N(51), N(52), N(53), O(51), and S(51). The α-carboxyl group of glutamic acid does not participate in the Cu(II) coordination. Except that he assumed the coordination of the glutamic acid carboxylate O(5) and reversed the assignment of the Cu-S bonding (i.e., Cu(1)-S(51) and Cu(51)-S(1)), Kroneck's proposed structure is similar.[7] As clearly shown by the difference in the torsional angles about the S-S bond, Cu(1)-S(1)-S(51)-Cu(51) = -73.1° and C(5)-S(1)-S(51)-C(55) = 108.5°, the operation which relates the two nuclei is not a rotational translation along the disulfide bond but rather is a simple rotation about the pseudodiad axis running perpendicular

Table IV. Deviations of Atoms from the Least-Squares Plane (Å)[a]

Deviations from the Basal Plane of the Coordination Pyramid			
N1	-0.059	N51	-0.087
N2	0.051	N52	0.075
N3	-0.043	N53	-0.067
O1	0.051	O51	0.079
Cu1*	0.026	Cu51*	0.072
S1*	-2.917	S51*	-2.934
C1*	-0.099	C51*	-0.069
O2*	-0.197	O52*	-0.220
C2*	-0.029	C52*	-0.135
C3*	-0.359	C53*	-0.519
O3*	-0.510	O53*	-0.740
C4*	-0.649	C54*	-0.534
C6*	0.486	C56*	0.628
C9*	-0.660	C59*	-0.612
Deviations from Chelate Ring			
Glycyl Residue			
Cu1	-0.004	Cu51	-0.011
O1	0.032	O51	0.021
C1	-0.059	C51	-0.020
C2	0.047	C52	0.008
N1	-0.016	N51	0.002
O2*	-0.151	O52*	-0.148
Cysteinyl Residue			
Cu1	-0.140	Cu51	-0.133
N1	0.073	N51	0.125
C3	0.056	C53	-0.035
C4	-0.215	C54	-0.116
N2	0.225	N52	0.158
O3*	0.117	O53*	0.002
Carboxyl and Amide Group			
C1	-0.037	C51	0.026
C2	0.016	C52	-0.006
O1	0.011	O51	-0.008
O2	0.010	O52	-0.011
N1	-0.015	N51	0.008
C3	0.050	C53	-0.027
O3	-0.018	O53	0.011
C4	-0.017	C54	0.008
N2	-0.014	N52	-0.019
C6	0.040	C56	0.055
O4	-0.013	O54	-0.023
C7	-0.013	C57	-0.013
C10	-0.047	C60	-0.022
C9	0.013	C59	0.006
O5	0.015	O55	0.008
O6	0.019	O56	0.008

[a] Atoms marked with an asterisk are not included in the least-squares claculations.

to the disulfide bond. The equatorial planes of the two coordinated groups form an angle of 122.5° with each other. The distance between the Cu(II) ions is rather short (5.21 Å) but the metal ions are separated by the disulfide bridge adopting the conformations described above. This situation presumably accounts for the lack of magnetic interaction between the two Cu(II) ions (see the subsequent sections). The bond lengths and valency angles calculated for each coordinated group are shown in Figure 2a,b and Tables II and III. The values are normal and in good overall agreement if large standard deviations are permitted (0.04 Å for C–C and 3° for C–C–C). However, some comments should be made on the distortions of the coordination geometry. The present complex showed no significant deviation of Cu(II) from the basal plane formed by the four equatorial ligand atoms. As seen in Table IV, which lists the deviations of atoms from the basal plane (root mean square deviations are 0.051 and 0.077 Å for Cu(1) and Cu(51) coordination planes, respectively), the planarity of the chelate atoms is poor and the deviation of Cu(II) is in the same order of magnitude as that of the other ligand atoms (0.026 and 0.072 Å for Cu(1) and Cu(51), respectively). On the other hand, the axial Cu–S bond markedly deviates from the normal of the basal plane. The inclination angles are found to be as much as 21° for Cu(1) and 23° for the Cu(51) coordination pyramid. These distortions can probably be accounted for by the formation of the unique five-membered chelate ring, Cu–N–C–C–S, utilizing the axial coordination site. The average Cu–S distance (3.22 Å, range 3.16–3.28 Å) is seen as the sum of the square dsp^2 radius for Cu(II) of ca. 1.30 Å and the van der Waals radius of 1.85 Å.[9] A somewhat longer value is consistent with a weak bonding interaction.[10] The distortion of the equatorial rings should also be noted. If one looks at the angles subtended by the ligand atoms at the central Cu(II) ion, it is evident that small angles of about 83° are found for the five-membered chelate rings while for the seven-membered rings large angles of about 100° are observed. The conformation of each chelate ring is illustrated by denoting the endocyclic torsion angles (see Table V). The terminal five-membered ring (C–O–Cu–N–C) adopts a nearly planar conformation while the second ring (C–N–Cu–N–C) takes an envelope form with a flap atom N(2) or Cu(51) (the conformation is slightly different for the two coordinated groups). Both seven-membered rings adopt a boat conformation with flagpoles at C(9), N(2)–C(6) and C(59), N(52)–C(56), respectively.

The elemental analysis indicated that the present crystal contains four sodium atoms and six water molecules per molecule

Table V. Endocyclic Torsion Angles (Deg) Calculated for Various Chelate Rings

Cu1-O1-C1-C2	-12	Cu51-O51-C51-C52	-4
O1-C1-C2-N1	13	O51-C51-C52-N51	3
C1-C2-N1-Cu1	-7	C51-C52-N51-Cu51	-1
C2-N1-Cu1-O1	2	C52-N51-Cu51-O51	-1
N1-Cu1-O1-C1	3	N51-Cu51-O51-C51	3
Cu1-N1-C3-C4	5	Cu51-N51-C53-C54	-12
N1-C3-C4-N2	-27	N51-C53-C54-N52	-7
C3-C4-N2-Cu1	38	C53-C54-N52-Cu51	21
C4-N2-Cu1-N1	-29	C54-N52-Cu51-N51	-21
N2-Cu1-N1-C3	14	N52-Cu51-N51-N53	19
Cu1-N2-C6-C7	-9	Cu51-N52-C56-C57	0
N2-C6-C7-C8	81	N52-C56-C57-C58	83
C6-C7-C8-C9	-53	C56-C57-C58-C59	-63
C7-C8-C9-N3	-46	C57-C58-C59-N53	-38
C8-C9-N3-Cu1	87	C58-C59-N53-Cu51	83
C9-N3-Cu1-N2	-29	C59-N53-Cu51-N52	-23
N3-Cu1-N2-C6	-26	N53-Cu51-N52-N56	-37
Cu1-N2-C4-C5	-88	Cu51-N52-N54-C55	-94
N2-C4-C5-S1	53	N52-C54-C55-S51	57
C4-C5-S1-Cu1	-10	C54-C55-S51-Cu51	-12
C5-S1-Cu1-N2	-22	C55-S51-Cu51-N52	-22
S1-Cu1-N2-C4	52	S51-Cu51-N52-C54	57

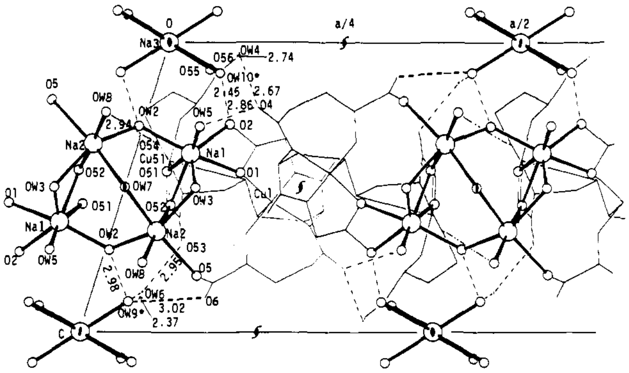

Figure 3. Projection of the crystal structure along the *b* axis showing the arrangement of the sodium ion hydration polyhedra. Hydrogen bonds are shown by broken lines. Because of the disorder of the water molecules, W(9) and W(10) were assigned the occupancy factor of $^1/_2$. Some hydrogen bond distances involving W(9) and W(10) have abnormal values.

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Table VI. Coordination Distances around the Sodium Ions[a]

atom	coordinate to	distance, Å
Na1	O1	2.25 (2)
	O2	2.46 (4)
	O51	2.51 (3)
	O52	2.57 (3)
	OW2	2.33 (2)
	OW3	2.21 (4)
	OW5	2.67 (5)
Na2	O5	2.73 (3)
	O52	2.09 (3)
	OW2	2.32 (3)
	OW3	2.45 (5)
	OW7	2.65 (3)
	OW8	2.34 (4)
Na3	O55 × 2[c]	2.29 (3)
	OW9[b] × 2	2.67 (4)
	OW10[b] × 2	2.53 (6)

[a] Standard deviations are given in parentheses. [b] A reduced occupancy factor of $^1/_2$ was assumed. [c] Since Na3 lies on the diad axis, equivalent bond lengths appear twice.

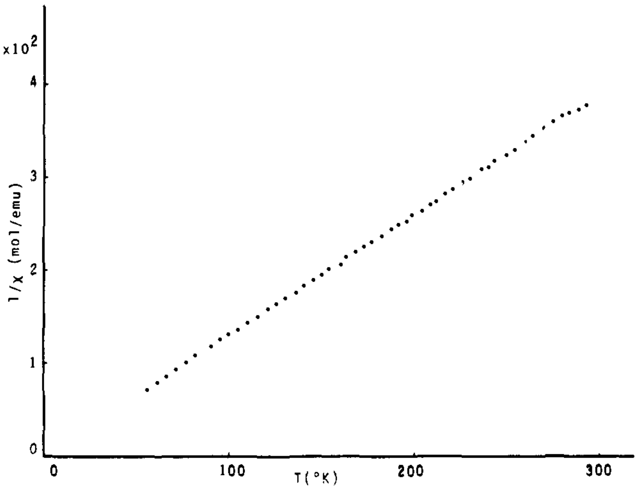

Figure 4. Inverse molar susceptibilities of $[\mathrm{Cu^{II}GSSGCu^{II}}]\mathrm{Na_4{\cdot}6H_2O}$ complex vs. temperature.

of the complex. However, the result of the X-ray structure determination showed that there are 2.5 sodium ions and 7.5 water molecules contained in an asymmetric unit (0.5 comes from the atoms lying on the diad axis) together with one molecule of the complex and that no further sodium ions and water molecules can be located on the difference electron density map. The arrangement of the hydrated sodium ions is shown in Figure 3 and coordination geometries around the sodium ions are summarized in Table VI. As seen in Figure 3 and Table VI, Na(1), Na(2), and Na(3) coordinate to four, two, and two carboxyl oxygens and three, four, and four water oxygen atoms, respectively forming seven-, six-, and six-coordinated groups. The coordination polyhedra of Na(1) and Na(2) are connected by sharing their edges and the combined polyhedra are further connected with symmetry-related polyhedra by sharing corners to form a ring of polyhedra. The rings are separated in the *b* and *c* directions by another polyhedra formed by Na(3) and in the *a* direction of the complex anions. Between the polyhedra and complex anions, there are several hydrogen bonds stabilizing the crystal structure.

Magnetic Susceptibility. Magnetic susceptibility of the isolated Cu(II) complex showed an excellent accordance with the Curie–Weiss law, with a Curie constant of 0.77 (K·emu)/mol and a Weiss constant of 0.5 ± 2 K. The correction for the diamagnetic contribution ($\chi_{\mathrm{dia}} = -0.276 \times 10^{-3}$ emu/mol) was calculated both by Pascal's method on the basis of determined structure and by measuring the diamagnetic contribution of the reduced glutathione. No particular deviation from the straight lines was detected on the $1/\chi$–T plot throughout the present temperature (see Figure 4). The effective magnetic moment $\mu_{\mathrm{eff}} = 1.75\ \mu_{\mathrm{B}}$/copper justifies the conclusion that the respective binding copper atoms exist in a divalent state. Furthermore, the small θ value indicates that the interatomic magnetic interaction between two copper nuclei is actually negligible. An intermolecular spin exchange or antiferromagnetic interaction ($J < 0$) has been reported for the coplanar dimer, in which the interatomic Cu(II)–Cu(II) distance is ca. 6 Å,[11] and effective overlap between the two unpaired orbitals ($d_{x^2-y^2}$) can thus be expected. In the stacked square-planar structure, as demonstrated by X-ray analysis, the interaction through the axial ligand should be weak in comparison with the case of a coplanar dimer, since the weak axial interaction is most likely in the $d_{x^2-y^2}$ ground state doublet. The same theoretical conclusion is applied to axial bridged Cu(II) dimer with a five-coordinated metal center (C_{4v} symmetry).[12]

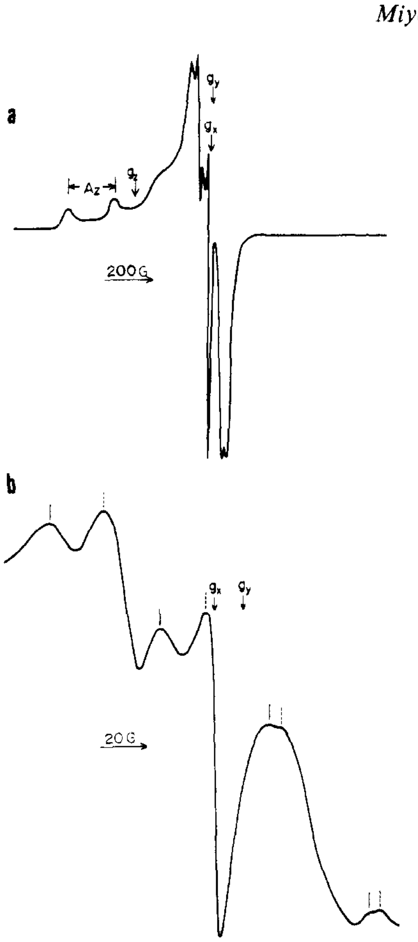

Figure 5. ESR spectra of the isolated glutathione–Cu(II) complex in 1:4 ethylene glycol–water solution at pH 11.3 (77 K). Spectrum (b) shows the perpendicular region.

Electron Spin Resonance Spectra. The ESR spectra of the isolated Cu(II) complex at 77 K and pH 11.3 are shown in Figure 5. Figure 5b clearly shows that the ESR splitting of the perpendicular region is not due to nitrogen (^{14}N, $I = 1$) superhyperfine splitting, but to the anisotropy in the *x* and *y* directions. The spin Hamiltonian parameters determined were as follows: $g_{zz} = 2.251$, $g_{xx} = 2.047$, $g_{yy} = 2.038$, $A_{zz} = 177.2$, $A_{xx} = 43.8$, and $A_{yy} = 36.0$ G. Kroneck reported that the 1:2 oxidized glutathione–Cu(II) complex at 110 K and pH 11.0 shows a weak ESR signal at $g = 4$ resulting from the spin-forbidden $\Delta_m = 2$ transition in a spin-coupled Cu(II) dimer which has metal–metal interactions via the disulfide bridge.[7] In the present isolated glutathione–Cu(II) complex, however, the ESR absorptions at half-field ($g = 4$) have never been observed. The lower A_{zz} value by approximately 20 G as compared with the square-planar complex is indicative of a reduced electron density along the perpendicular axis of the

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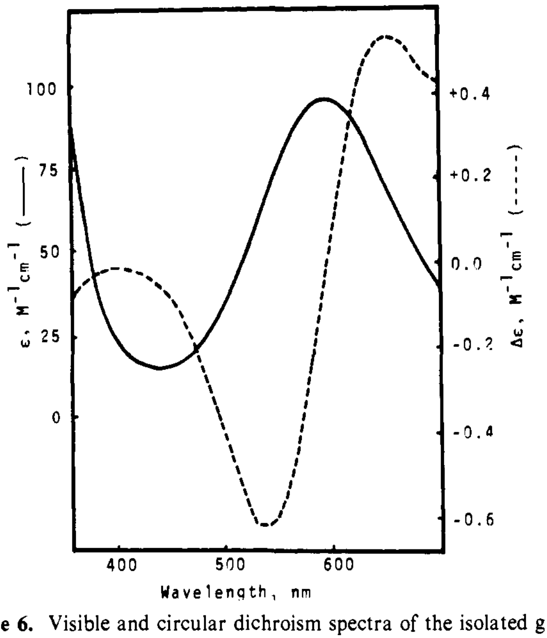

Figure 6. Visible and circular dichroism spectra of the isolated glutathione–Cu(II) complex in aqueous solution at pH 11.3.

Table VII. Electron Binding Energies (eV) and Satellite Splittings

	Cu $2p_{3/2}$					
compd	satellite	main peak	S 2p	N 1s	O 1s	Na 1s
glutathione–Cu(II) crystal	943.9	933.1	163.4 167.5	399.4	531.2	1071.1
N-mercaptoacetylglycyl-L-histidine	943.5	932.1	163.0 167.4	399.2	530.8	
Cu(II)–(glycine)$_2$	942.8	934.8		399.9	531.6	
$K_2[Cu^{II}(NHCONHCONH)_2]\cdot 4H_2O$	943.3	934.8		398.9	531.5	
Cu(I)–SCN		933.1	164.3	399.1		

copper site.[13]

Electronic and Circular Dichroism Spectra. The violet glutathione–Cu(II) complex gave an absorption maximum at 16 860 cm^{-1} (ϵ 95/copper) and CD extrema at 25 000 ($\Delta\epsilon$ −0.02), 18 700 (−0.63), and 15 300 cm^{-1} (+0.53), respectively (see Figure 6). A band in the ultraviolet region displayed a shoulder at 40 800 cm^{-1} (ϵ 8000) which is assigned to a $N(\sigma) \rightarrow Cu(II)$ charge transfer (CT) transition.[14] The visible absorption is similar to that of the tetraglycine–Cu(II) complex which has a five-coordinated geometry at pH 8.[15] It is well known that the d–d transitions for Cu(II) complexes with a square-pyramidal geometry (C_{4v}) occur with slightly lower energy (<19 000 cm^{-1}) than those of the square-planar complex.[16] The visible bands at 18 700 ($d_{xz,yz} \rightarrow d_{x^2-y^2}$) and 15 300 cm^{-1} ($d_{xy} \rightarrow d_{x^2-y^2}$) seen in the present complex suggest the Cu(II) complex of a square-pyramidal type. As for the sulfur donor, the sulfur coordination in equatorial position has been demonstrated to show a CT transition at ca. 25 000 cm^{-1} with a strong intensity (ϵ >1000).[17] The CD extremum at near 25 000 cm^{-1} in the present Cu(II) complex is assigned to $S(\sigma) \rightarrow Cu(II)$ CT transition. In contrast with the equatorial sulfur binding, the considerably weak intensity of the axial sulfur binding is related to the poor overlap between the axially disposed cysteinyl sulfur and the ground-state orbital ($d_{x^2-y^2}$) of the color center. The same point has been made by Amundsen et al., who in electronic absorption studies found that a new band at 27 500 cm^{-1} appeared by apical coordination of RS$^-$.[14]

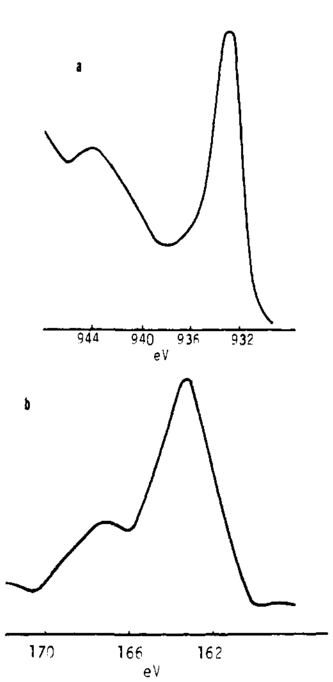

Figure 7. X-ray photoelectron spectra of the crystalline $[Cu^{II}GSSGCu^{II}]Na_4\cdot 6H_2O$: (a) Cu $2p_{3/2}$ and (b) S 2p region.

X-ray Photoelectron Spectra. Figure 7 shows the X-ray PES of the present Cu(II) complex in (a) Cu $2p_{3/2}$ and (b) S 2p regions, respectively. The binding energy obtained was as follows: Cu $2p_{3/2}$ = 933.1 (main peak) and 943.9 (satellite), S 2p = 163.4 (main peak) and 167.5 (minor peak), N 1s = 399.4, O 1s = 531.2, and Na 1s = 1071.1 eV. Table VII summarizes the X-ray PES data of the present glutathione–Cu(II) complex and its related peptide–Cu(II) complexes.[13,18] The Cu(II) complexes of nitrogenous ligands such as glycine and biuret exhibit the Cu $2p_{3/2}$ main signal at approximately 935 eV with a satellite peak. On the contrary, Cu(I) complexes always display the homogeneous Cu $2p_{3/2}$ signal near 933 eV and lack the satellite peak.[18] The Cu $2p_{3/2}$ binding energy (933.1 eV) of the crystalline glutathione–Cu(II) complex appears to indicate that copper is present in the oxidation state near 1+. In general, the N 1s binding energies of Cu–N(amino group) and Cu–N(deprotonated amide group) are 400.0 and 398.9 eV, respectively.[18] The N 1s binding energy (399.4 eV) of the complex we demonstrated is consistent with the value of $^1/_6 \times 2$ [N 1s(amino) + 2 × N 1s(amide)], supporting the structure of a Cu(II) complex coordinated by one amino and two deprotonated nitrogen donors. In fact, the violet bis(biuret)–Cu(II) complex, in which copper is coordinated to four deprotonated amide nitrogen atoms, has the low binding energy (398.9 eV) of N 1s. The O 1s binding energy (531.2 eV) of the Cu(II) complex suggests the presence of a coordinated oxygen atom, because the O 1s values of various amino acid–Cu(II) complexes and free amino acids are in the ranges of 531.1–532.2 and 530.5–531.0 eV, respectively.[18] Our product has been also identified as a Na salt (Na 1s = 1071.1 eV) of $[Cu^{II}GSSGCu^{II}]^{4-}$ on the basis of its composition. The sulfur 2p value is detectable at 163.4 and 167.5 eV. The minor sulfur signal at 167.5 eV is presumably due to some oxidized sulfur (RSO_3^-)[18] or to a satellite of the S 2p signal based on a $S \rightarrow Cu(II)$ charge transfer (LMCT) transition.[19] It is known that the sulfur 2p region X-ray PES of plastocyanin[20] and several sulfur-containing peptide–Cu(II)

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complexes[13,19] consist of two signals separated by approximately 5 eV. For this assignment, however, there are different opinions.[20,21] Gray and co-workers reinterpreted that the S 2p high binding energy (HBE) signal of plastocyanin resulted from the oxidation of sulfur as a result of bombardment by the X-rays.[22] Larsson proposed the possibility of LMCT transition for the HBE line.[23] Probably, the photoredox behavior of the Cu(II)-S complexes accounts for the decrease of the Cu $2p_{3/2}$ binding energy and for the induction of the S 2p HBE line.

In conclusion, this study clarified the unique structure of the binuclear Cu(II) complex of glutathione, a typical ligand of biological origin. The essential characteristics of the present Cu(II) complex are unique axial sulfur coordination in a distorted square-pyramidal geometry and the presence of two copper sites via a disulfide bridge. The bond distance and direction of the apical S-Cu(II) are 3.22 Å and bent by 22° from the basal plane, respectively. The internuclear dipolar interaction between two Cu(II) ions is negligibly small, though the Cu(II)-Cu(II) distance via the disulfide bridge is 5.21 Å. The magnetic susceptibility and ESR features of the Cu(II) complex also support the result. Our crystallographic and spectroscopic results provide valuable information for biologically significant glutathione-Cu(II) complexes.

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Generalized Molecular Orbital Theory. Application to Borane and Diborane

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Abstract: The effect of electron correlation on the electron distribution and bonding of diborane is examined in several basis sets. The generalized molecular orbital method is used to define optimized orbitals for the configuration interaction calculations. The results indicate that at least double-ζ (two functions per atomic orbital) and polarization functions (*d* functions on B and *p* functions on H) are needed to adequately describe the electron density of diborane. Electron correlation shifts electron density away from the hydrogens, both terminal and bridging, and into the interior of the cluster and increases the direct B-B contribution to the bonding. We have also calculated the dissociation energy of diborane ($B_2H_6 \rightarrow 2BH_3$). The experimental value is 35 kcal/mol, while without electron correlation the theoretical value is only about 20 kcal/mol. Thus, electron correlation increases the stability of the cluster by about 15 kcal/mol. Our results suggest that the substantial effect of electron correlation on the bonding of diborane is a general result and will apply to other cluster systems.

There has been considerable interest in the electronic structure of the electron-deficient borane clusters.[1] Because these clusters are electron deficient, there are one or more low-lying nonbonding orbitals which are unoccupied in the single-determinant approximation. We speculated that this might give rise to important near-degenerate correlation effects in these systems. Furthermore, the B-H bond distance for bridging for boron-hydrogen bonds is longer and closer to dissociation than the terminal boron-hydrogen bonds. Therefore, electron correlation might be more important for these bridging bonds than for the terminal ones.

Table I. Total Energies and Number of Spin Configurations for BH_3 Calculations[a]

	MIN	DZ	DZP
HF	-26.077	-26.376	-26.390
GMO	-26.095 [13]	-26.393 [13]	-26.410 [13]
GMO CI	-26.125 [61]	-26.423 [61]	-26.429 [61]
GMO PL	-26.125 [61]	-26.429 [280]	-26.463 [595]
GMO SD	-26.125 [61]	-26.438 [517]	-26.495 [1942]
GMO SD(Q)[b]	-26.126	-26.440	-26.500

[a] Atomic units (hartrees); number of spin configurations in brackets. [b] Quadruples estimated from Davidson's formula.

Diborane, the simplest cluster in this series, was chosen for study by the generalized molecular orbital (GMO) technique.[2] This technique is a simple means of obtaining a set of primary orbitals for use in a configuration interaction (CI) calculation. It is particularly well suited for systems with a large number of electrons in the same region of space as one finds in clusters. In addition to the general question of the importance of electron correlation in the bonding of diborane, the value of the dissociation energy of diborane into two borane fragments has been a matter of controversy. The experimental values cluster around 60 kcal/mol from mass spectral studies[3] and around 35 kcal/mol from kinetic measurements.[4] Previous theoretical works[5] suggest that

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