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Crystal and Molecular Structure of (5,5,8,8,13,13,16,16-Octamethyl-1,4,9,12-tetraazacyclohexadeca-1,3,9,11-tetraene)copper(I) Perchlorate. A Model for the Entatic State in Blue Copper Proteins

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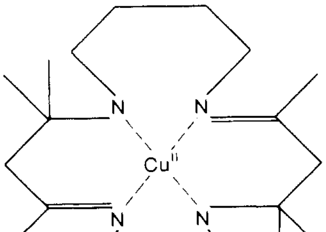
Received October 2, 1987

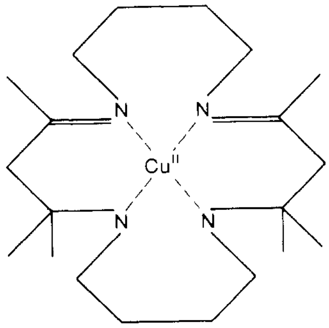
This paper presents the first simple Cu(I) model of the entatic state of blue copper proteins, with extensive distortion from the preferred 90° dihedral angle between the donor atoms around the metal center. The synthesis and structure of the macrocyclic complex (5,5,8,8,13,13,16,16-octamethyl-1,4,9,12-tetraazacyclohexadeca-1,3,9,11-tetraene)copper(I) perchlorate, [Cu(Me$_8$[16]-teteneN$_4$)]ClO$_4$, are described. The complex, M_r = 495.53, crystallizes in the space group $P2_1/n$ with a = 10.912 (2) Å, b = 16.876 (3) Å, c = 13.149 (2) Å, β = 97.92 (2)°, and V = 2398 (1) Å^3. The dihedral angle between the N1-Cu-N2 and N3-Cu-N4 planes is 56.7°. The macrocyclic ligand is insufficiently flexible to permit the preferred tetrahedral angle between the coordinate bonds of Cu(I) and the preferred 90° dihedral angles between the N-Cu-N planes. The Cu(I) complex was oxidized to the corresponding Cu(II) complex, [Cu(Me$_8$[16]teteneN$_4$)](ClO$_4$)$_2$.

Introduction

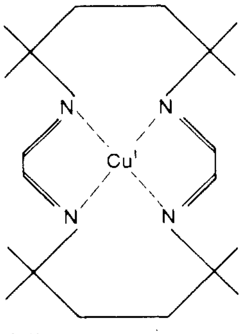
The synthesis of macrocyclic complexes containing two seven-membered chelate rings has previously been reported by this group.[1] A compound (**1**) having trans double bonds exhibits an essentially square-planar structure, with a dihedral angle between the N1-Cu-N2 and N1′-Cu-N2′ planes of 11.5°. A second complex having cis double bonds (**2**) exhibits significant distortion toward a tetrahedral structure. The dihedral angle between N1-Cu-N2 and N3-Cu-N4 in this compound is 36.6°. This evidence suggests that the distortion is due to the cis placement of the double bonds. It is noteworthy that two other copper(II) compounds with significant distortions toward tetrahedral structures have cis double-bond placement analogous to that in **2**. These compounds are [*N*,*N*′-biphenyl-2,2′-diylbis(salicylaldiminato)]copper(II)[2] and [bis(2-hydroxyacetophenone) trimethylenediiminoato]copper(II)[3] with dihedral angles between the O-Cu-N planes of 34.4 and 37.0°, respectively. Other attempts to produce tetrahedral distortion through the introduction of seven-membered chelate rings have resulted in the formation of distorted-square-pyramidal complexes.[4,5] Tetrahedral distortion has of course been observed in a number of copper(II) complexes[6-12] where steric interactions prevent the adoption of a square-planar geometry, as in the essentially tetrahedral isosparteine complex of Streib et al.[6] or the bis(*N*-*tert*-butylsalicylaldiminato)copper(II) complex of Cheeseman et al.[7]



1 [Cu^{II}-(trans-[18]-dieneN$_4$)]$^{2+}$



2 [Cu^{II}-(cis-[18]-dieneN$_4$)]$^{2+}$



3 [Cu-(Me$_8$-[16]-tetene$_4$)]$^+$

In a sense, all tetrahedrally distorted copper(II) complexes serve as simple models of blue copper proteins such as plastocyanin. Single-crystal X-ray diffraction studies of the blue copper protein plastocyanin by Freeman et al.[13] show that the copper environment is highly distorted from tetrahedral. This "entatic-state" geometry, which is not highly favorable for either copper(I) or copper(II), presumably facilitates the redox transition between Cu(I) and Cu(II) forms of the protein by eliminating, or greatly reducing, the reorganization steps in the familiar Marcus mechanism for outer-sphere electron transfer.

In the present work, the synthesis and structure determination of a blue copper protein model that mimics the entatic state are described. The tetradentate ligand in **3** has been designed such that it may not adopt either a square-planar configuration about copper(II) or a tetrahedral configuration about copper(I). This

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0020-1669/88/1327-1638$01.50/0

was achieved by introducing steric hindrance in the form of *gem*-dimethyl groups into a macrocyclic ligand that must form two seven-membered chelate rings. The copper macrocyclic complex formed from this ligand is described in this report.

Experimental Section

$[Cu(Me_8[16]teteneN_4)]ClO_4$ (3). To 9.3 g of 2,5-diamino-2,5-dimethylhexane (from Aldrich Chemical Co., purified by repeated recrystallization from aqueous ethanol as the hydrochloride) in 50 mL of methanol was added slowly with stirring a solution of 11.2 g of cupric perchlorate hexahydrate in 20 mL of methanol. A small amount of 2-propanol was then added, and the blue-purple crystals of bis(2,5-diamino-2,5-dimethylhexane)copper(II) perchlorate were filtered off and dried.

A solution of 6 mL of 40% glyoxal was added to 20 mL of methanol, and this solution was in turn added dropwise to a stirred mixture of bis(2,5-diamino-2,5-dimethylhexane)copper(II) perchlorate in 200 mL of methanol. The reaction mixture was stirred for 3 days at room temperature. It was then filtered, and the deep green filtrate was evaporated to about one-fourth of its original volume. A few drops of water were added, and the solution was refrigerated. The cold solution yielded a crop of almost black crystals, which were separated by filtration and air-dried. The product was recrystallized from an ethanol–water solution by slow evaporation at 5 °C. The yield was ca. 1 g. Anal. Found (calcd) for $C_{20}H_{36}ClCuN_4O_4$: C, 48.5 (48.6); H, 7.32 (6.96); N, 11.3 (10.9). IR data: ν(Cl–O) of ClO_4^-, vs, s, 1100 cm^{-1}; conjugated ν(C=N) vibrations, m, 1622, 1670 cm^{-1}.

Attempted Reactions of Other Diamines with Glyoxal in the Presence of Copper(II). The following bis(diamine)copper(II) complexes were reacted with glyoxal in a manner similar to that described for 2,5-diamino-2,5-dimethylhexane: 1,4-butanediamine, 1,6-hexanediamine, and 1,8-octanediamine. In each case the reaction yielded brown polymeric materials and no macrocyclic products were isolated even following purification with activated charcoal. The reaction of bis(2,5-diamino-2,5-dimethylhexane)nickel(II) perchlorate with glyoxal, under conditions similar to those used for the analogous copper(II) complex, yielded large quantities of polymeric material and no macrocyclic complexes.

$Cu(Me_8[16]teteneN_4)(ClO_4)_2$ (4). When two drops of Br_2 were added to a solution of 0.5 g of the complex dissolved in methanol, the solution turned yellow-green and a green crystalline solid slowly formed upon cooling. The product was filtered and air-dried. Anal. Found (calcd) for $C_{20}H_{36}Cl_2CuN_4O_8$: C, 40.4 (40.2); H, 6.10 (6.30); N, 9.42 (9.57). IR data: ν(Cl–O) of ClO_4^-, vs, br, $\simeq$1100 cm^{-1}; ν(C=N) complex, 1661, 1617 cm^{-1}.

X-ray Data Collection

Single crystals of the Cu(I) complex **3** were grown from an ethanol-water solution at 5 °C. A crystal of approximate dimensions 0.35 × 0.25 × 0.2 mm was mounted with the glass fiber perpendicular to the long axis. A CAD-4 automated diffractometer with graphite-monochromated Mo Kα radiation (λ = 0.71073 Å) was used to obtain intensity data. Unit cell parameters were determined from least-squares treatment of 25 reflections obtained at medium and high angles: a = 10.912 (2) Å, b = 16.876 (3) Å, c = 13.149 (2) Å, β = 97.92 (2)°, V = 2398 (1) Å^3. Systematic absences of the type $h0l$ with $h + l = 2n + 1$ and $0k0$ with $k = 2n + 1$ fixed the space group as $P2_1/n$ (No. 14) with Z = 4.

Intensity data were collected by the θ–2θ scan method. Scan speeds ranged from 20°/min for the most intense reflections to 2°/min for the weakest. The angular scan width was $A + 0.347 \tan \theta_{\lambda_{\alpha2}}$ where $\theta_{\lambda_{\alpha2}}$ is determined by the formula

$$\theta_{\lambda_{\alpha2}} = \theta_{\lambda_{\alpha1}} + \left(\frac{360}{2}\,\frac{\lambda_{\alpha2} - \lambda_{\alpha1}}{\lambda_{\alpha1}}\right)\tan\theta_{\alpha1}$$

and A depends on the crystal mosaic spread and on the divergence of the primary beam. A for this structue was 0.7. The scan was extended on each side of the peak by 25% for background measurement. Unique data were collected up to 2θ = 50°. Three standard reflections scanned approximately every 150 reflections were used to place the intensity data on a common scale. Systematic variation in these standards was not observed. Reflection intensities were calculated from peak and background measurements as $I = S(C - RB)$, where S = scan rate, C = total integrated peak count, B = total background count, and R = the ratio of the scan time for the peak to the scan time for the background. The estimated error was calculated as $\sigma(I) = [S^2(C + R^2B) + (pI)^2]^{1/2}$; p is dependent on the diffractometer used and had a value of 0.05 in the present instance. Of 4352 reflections originally collected, 751 were considered unobserved and a total of 3078 unique data with $I > 3\sigma(I)$ were used in the refinement.

Table I. Positional and Equivalent Isotropic Thermal Parameters for Non-Hydrogen Atoms in $[Cu(Me_8[16]teteneN_4)]ClO_4$

atom	x	y	z	B(eqv), Å^2
Cu	0.15858 (5)	0.10184 (4)	0.23815 (4)	2.83
Cl	0.6928 (2)	0.4154 (1)	0.2172 (1)	5.35
O1	0.7645 (9)	0.4056 (4)	0.3105 (5)	13.16
O2	0.6509 (9)	0.4856 (4)	0.1839 (6)	16.58
O3	0.6578 (9)	0.3508 (5)	0.1585 (7)	14.67
O4	0.8055 (11)	0.4220 (10)	0.1674 (14)	25.71
N1	0.3089 (4)	0.1151 (2)	0.1609 (3)	2.74
N2	0.0663 (4)	0.1268 (2)	0.0951 (3)	2.77
N3	0.0658 (4)	0.1484 (2)	0.3498 (3)	2.69
N4	0.1933 (4)	0.0131 (2)	0.3456 (3)	2.67
C1	0.2730 (5)	0.1216 (3)	0.0649 (4)	3.42
C2	0.1420 (5)	0.1377 (4)	0.0310 (4)	3.70
C3	−0.0678 (5)	0.1465 (3)	0.0653 (4)	3.24
C4	−0.0868 (5)	0.2170 (4)	−0.0086 (4)	4.59
C5	−0.1334 (6)	0.0725 (4)	0.0189 (4)	4.65
C6	−0.1157 (4)	0.1665 (3)	0.1659 (4)	3.43
C7	−0.0492 (5)	0.2347 (3)	0.2269 (4)	3.29
C8	−0.0176 (5)	0.2187 (3)	0.3411 (4)	3.11
C9	0.0569 (6)	0.2879 (3)	0.3933 (4)	4.05
C10	−0.1376 (5)	0.2058 (4)	0.3897 (4)	4.09
C11	0.0670 (5)	0.1003 (3)	0.4240 (4)	3.53
C12	0.1489 (5)	0.0322 (3)	0.4266 (4)	3.48
C13	0.2792 (5)	−0.0551 (3)	0.3464 (4)	3.08
C14	0.3524 (6)	−0.0718 (4)	0.4528 (5)	4.65
C15	0.2025 (6)	−0.1257 (3)	0.3081 (5)	4.31
C16	0.3670 (5)	−0.0329 (3)	0.2702 (4)	3.34
C17	0.4388 (4)	0.0445 (3)	0.2940 (4)	3.18
C18	0.4407 (4)	0.0987 (3)	0.2012 (4)	3.08
C19	0.5120 (5)	0.0600 (4)	0.1220 (4)	4.34
C20	0.4974 (5)	0.1782 (4)	0.2343 (5)	4.79

Table II. Least-Squares Planes through Selected Atoms in $[Cu(Me_8[16]teteneN_4)]ClO_4$ and Dihedral Angles between These Planes

Equations of the Planes[a]

plane, no.	atoms included	A	B	C	D
1	Cu/N1/N2	−0.0014	−0.9755	−0.2198	−2.3604
2	Cu/N2/N3	0.5263	0.8501	−0.0194	2.0845
3	Cu/N3/N4	−0.7852	−0.4718	−0.4012	−3.0749
4	Cu/N1/N4	−0.2990	−0.6711	−0.6784	−3.6459

dihedral angles between planes: 1–3, 56.7°; 2–4, 135.6°

[a] Equations of the planes are of the form $Ax + By + Cz - D = 0$.

Solution and Refinement of the Structure

The copper atom position was determined from a three-dimensional Patterson map. All non-hydrogen atoms were determined by subsequent difference Fourier methods and were refined positionally and isotropically to convergence, after which they were refined anisotropically. The hydrogen atom positions were then calculated and included as a fixed contribution in the final cycles of least-squares refinement. Recalculation of their positions followed by refinement was continued until the largest σ/Δ = 0.7.

Residuals were calculated[14] as $R_F = [\sum(||F_o| - |F_c||)/\sum|F_o|]$ and $R_{wF} = [\sum w(|F_o| - |F_c|)^2/\sum wF_o^2]^{1/2}$. Reflections were weighted as $w = 1/\sigma^2(F_o) = 4F_o^2/[\sigma(F_o)^2]^2$ where $\sigma(F_o)^2 = [\sigma^2(I) + (pI)^2]^{1/2}/Lp$. The function minimized was $\sum w(|F_o| - |F_c|)^2$. Final residuals were calculated as R_F = 0.056 and R_{wF} = 0.081, and the error in an observation of unit weight, S, was 2.34. Neutral-atom scattering factors[15] were used, and anomalous dispersion terms were applied. Corrections for absorption were unnecessary because of the low absorption coefficient (μ = 10.9) of the complex.

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(14) All calculations were performed on a PDP11/60 computer using programs from: "Enraf-Nonius Structure Determination Package (SDP)"; Enraf-Nonius: Delft, Holland, 1975; revised, 1980.

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Table III. Important Bond Distances (Å) and Bond Angles (deg) in $[Cu(Me_8[16]teteneN_4)]ClO_4$

Cu–N1	2.057 (3)	Cu–N3	2.052 (3)
Cu–N2	2.051 (3)	Cu–N4	2.058 (3)
N1–C1	1.278 (4)	N3–C11	1.267 (4)
C1–C2	1.462 (5)	C11–C12	1.453 (5)
C2–N2	1.273 (4)	C12–N4	1.270 (4)
N2–C3	1.499 (4)	N4–C13	1.484 (4)
C3–C4	1.533 (5)	C13–C14	1.539 (5)
C3–C5	1.524 (5)	C13–C15	1.502 (5)
C3–C6	1.526 (5)	C13–C16	1.525 (5)
C6–C7	1.528 (5)	C16–C17	1.534 (5)
C7–C8	1.519 (5)	C17–C18	1.528 (5)
C8–C9	1.531 (5)	C18–C19	1.529 (5)
C8–C10	1.549 (5)	C18–C20	1.517 (5)
C8–N3	1.490 (4)	C18–N1	1.489 (4)
Cl–O1	1.371 (5)	Cl–O3	1.359 (5)
Cl–O2	1.324 (4)	Cl–O4	1.475 (9)
N1–Cu–N2	81.3 (1)	N2–Cu–N3	110.4 (1)
N1–Cu–N3	144.8 (1)	N2–Cu–N4	143.1 (1)
N1–Cu–N4	109.5 (1)	N3–Cu–N4	81.3 (1)
Cu–N1–C1	110.0 (2)	Cu–N3–C8	127.3 (2)
Cu–N1–C18	126.9 (2)	Cu–N3–C11	110.6 (2)
Cu–N2–C2	110.8 (2)	Cu–N4–C12	109.6 (2)
Cu–N2–C3	128.6 (2)	Cu–N4–C13	128.7 (2)
N1–C1–C2	117.9 (3)	N3–C11–C12	117.7 (3)
C1–C2–N2	118.0 (3)	C11–C12–N4	119.1 (3)
C2–N2–C3	119.6 (3)	C12–N4–C13	120.4 (3)
N2–C3–C4	112.3 (3)	N4–C13–C14	113.3 (3)
N2–C3–C5	108.1 (3)	N4–C13–C15	106.9 (3)
N2–C3–C6	105.1 (3)	N4–C13–C16	105.0 (3)
C4–C3–C5	111.6 (3)	C14–C13–C15	110.8 (3)
C4–C3–C6	110.2 (3)	C14–C13–C16	110.3 (3)
C5–C3–C6	109.3 (3)	C15–C13–C16	110.3 (3)
C3–C6–C7	115.3 (3)	C13–C16–C17	115.1 (3)
C6–C7–C8	114.3 (3)	C16–C17–C18	114.2 (3)
C7–C8–N3	105.7 (3)	C17–C18–N1	106.1 (3)
C7–C8–C9	110.0 (3)	C17–C18–C19	110.7 (3)
C7–C8–C10	110.1 (3)	C17–C18–C20	110.5 (3)
C9–C8–N3	107.0 (3)	C19–C18–N1	113.2 (3)
C9–C8–C10	110.4 (3)	C19–C18–C20	110.3 (3)
C10–C8–N3	113.5 (3)	C20–C18–N1	105.9 (3)
C8–N3–C11	120.7 (3)	C18–N1–C1	121.2 (3)
O1–Cl–O2	122.2 (4)	O2–Cl–O3	118.2 (4)
O1–Cl–O3	119.5 (3)	O2–Cl–O4	93.2 (6)
O1–Cl–O4	90.0 (6)	O3–Cl–O4	89.8 (6)

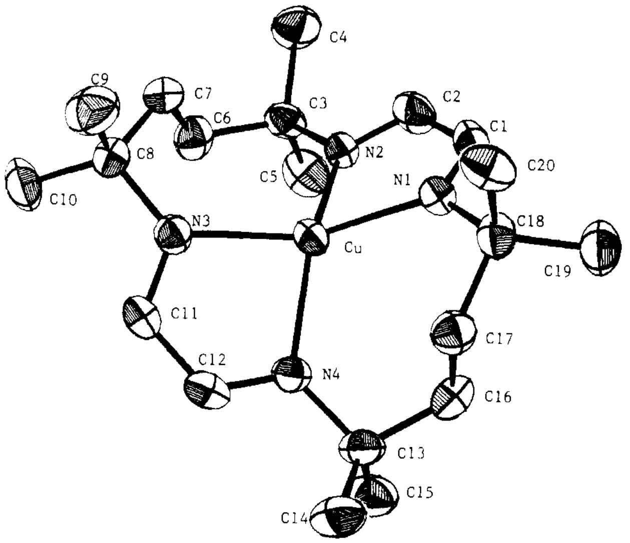

Figure 1. Molecular representation of the 50% probability level of $[Cu(Me_8[16]teteneN_4)]ClO_4$. The numbering scheme for the complex ion is indicated.

Results and Discussion

The structure of the $[Cu^I(Me_8[16]teteneN_4)]ClO_4$ complex ion is shown in Figure 1 together with the numbering scheme used in the tables. Positional and thermal parameters are listed in Table I. Dihedral angles were calculated from the least-squares-plane equations for the N–Cu–N plane as shown in Table II. Table III lists the important bond distances and angles for the complex ion. Final structure factors and anisotropic temperature factors are available as supplementary material. $[Cu^I(Me_8[16]teteneN_4)]$ is probably best viewed as a highly distorted tetrahedral cuprous complex. The dihedral angles between N–Cu–N planes (Table I) deviate significantly from the 90° angles seen in a tetrahedral structure or the 0° angles expected for square-planar geometry. The similarity between these distortions and those observed by Freeman et al.[13] for plastocyanin is noted. Figure 1 demonstrates the distorted-tetrahedral geometry in the complex.

The use of macrocyclic ligands incorporating large chelate rings and sterically hindered groups should make possible a variety of models for the entatic state of copper-containing proteins. It should be possible, through modification of ligand bulk, to obtain almost any desired dihedral angle about Cu, within the range 0–90°. These compounds should then be ideal for studying the intrinsic spectral and electrochemical properties of distorted-tetrahedral Cu(I) and distorted-planar Cu(II). Electron-transfer rate studies of a series of such complexes differing in the degree of tetrahedral–planar distortions would provide valuable insights into the relationship between structure and electron-transfer functions of blue copper proteins.

Work planned for the immediate future on these systems consists of synthesis of the Cu(II) analogue of the complex described here and measurement of electronic absorption spectra and redox potentials of the Cu(I) and Cu(II) complexes.

Acknowledgment. This work was supported by The Robert A. Welch Foundation under Research Grant A-259 (A.E.M., J.H.T., J.W.L.) and Research Grant A-673 (A.C., P.R.R.).

Registry No. **3**, 113584-67-1; **4**, 113584-69-3; 2,5-diamino-2,5-dimethylhexane, 23578-35-0; glyoxal, 107-22-2; 1,4-butanediamine, 110-60-1; 1,6-hexanediamine, 124-09-4; 1,8-octanediamine, 373-44-4; bis(2,5-diamino-2,5-dimethylhexane)nickel(II) perchlorate, 113646-59-6.

Supplementary Material Available: For $[Cu(Me_8[16]teteneN_4)]ClO_4$, tables listing thermal and positional parameters, derived hydrogen positions, and general temperature factor expressions (7 pages); tables of calculated and observed structure factors (14 pages). Ordering information is given on any current masthead page.