# Crystal and Molecular Structure of Bis[copper(II) D-penicillamine disulfide] Nonahydrate, a Derivative of Copper(II) Cystinate

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**Abstract:** The crystal structure of the title compound, $[(H_2O)Cu(O_2CCH(NH_2)C(CH_3)_2SSC(CH_3)_2CH(NH_2)CO_2)_2Cu(H_2O)]\cdot 7H_2O$, has been determined using single-crystal three-dimensional X-ray data collected by counter methods with an automated diffractometer. The structure consists of dimeric [copper(II) D-penicillamine disulfide]$_2$ units in which nonequivalent copper atoms are bridged by two penicillamine disulfide ligands. The dimeric units are linked by a three-dimensional hydrogen bonded network formed by water molecules, carboxylate oxygen atoms, and amino acid nitrogen atoms. Two nitrogen and two oxygen atoms from the terminal amino acid moieties are attached to each copper atom in an approximately trans square-planar fashion. Copper atoms are displaced from the best least-squares planes of these atoms (0.06, 0.11 Å) in the direction of water molecules which occupy a fifth coordination site. Disulfide units are located in the interior of the dimer. Apical O–Cu–S angles (169.6 (7), 166.5 (7)°) and Cu–S distances (3.057 (10), 3.138 (9) Å) suggest that the sulfur atoms are weakly bound to copper and occupy a sixth coordination site. The copper coordination environment is best described as tetragonal. The complex crystallizes in the monoclinic space group $C_2$ ($C_2^3$, no. 5) and has unit cell dimensions of $a = 12.266$ (5), $b = 19.769$ (5), $c = 15.698$ (5) Å, and $\beta = 92.14$ (5)°. A density of 1.534 g/cm$^3$ was calculated for four formula units in the unit cell and this agreed well with that of 1.54 (1) g/cm$^3$ measured by the density gradient method. A total of 1229 unique reflections with $F^2 \geqslant 2\sigma$, collected using graphite monochromated Mo K$\alpha$ radiation, was used for the solution and refinement of the structure. The structure was solved by the heavy-atom method and refined using full-matrix least-squares techniques to conventional agreement indices of $R_F = 0.077$ and $R_{wF} = 0.09$.

The preferred chemotherapeutic treatment for Wilson's disease (hepatolenticular degeneration) is the oral administration of D-penicillamine, which promotes the urinary excretion of excess body copper.[2] Since both penicillamine disulfide (PDS) and penicillaminecysteine disulfide (PCDS) have been detected in the urine of patients undergoing penicillamine therapy,[3] excess body copper may be excreted as the PDS complex[4] and/or the PCDS complex. In contrast to $[Cu^{II}PDS]_2\cdot 9H_2O$, which is highly water soluble, copper(II) cystinate complexes are water insoluble, possibly reflecting the clinical observation that oral cysteine therapy does not promote copper removal.[5,6] Copper removal in the form of a mixed valence Cu$^I$,Cu$^{II}$-penicillamine complex has also been proposed.[7] In view of the importance of these copper amino acid derivatives, an examination of their structural and spectroscopic properties appeared worthwhile. Of the above complexes, single crystals suitable for X-ray diffraction analysis could be grown only for $[Cu^{II}PDS]_2\cdot 9H_2O$; the structure of this complex is reported below.

## Experimental Section

D-Penicillamine was kindly donated by Merck and Co., Inc., Rahway, N. J. CuCl$_2\cdot 2H_2O$ was obtained from Matheson Coleman and Bell. Both chemicals were used as received. D-PDS was prepared from D-penicillamine by the method of Butenandt, *et al.*,[8] and melted in the range 204–205° (lit.[8] 204–205°). Crystals of $[Cu^{II}\text{-D-PDS}]_2\cdot 9H_2O$ were grown from cold isopropyl alcohol–water mixtures containing equimolar amounts of copper(II) chloride and D-PDS. In a typical preparation, 1.2 mmol of PDS was dissolved in 40 ml of distilled water to which 1.2 mmol of CuCl$_2\cdot 2H_2O$ in 10 ml of water was added. Next, PDS was neutralized by the addition of 2.4 mmol of NaHCO$_3$ in 10 ml of H$_2O$. After removal of CO$_2$ under vacuum, the solution was filtered using a membrane filter (0.2-μm pores) and diluted to 100 ml with water and then to 200 ml with isopropyl alcohol. When placed in a refrigerator and allowed to stand for several days, the solution yielded well-formed blue prisms of $[Cu^{II}\text{-D-PDS}]_2\cdot 9H_2O$. The crystals were quite efflorescent; upon standing in air, they rapidly lost weight, cracked, and ultimately formed a blue powder. As a result, elemental analysis was not attempted and the empirical formula was determined by X-ray analysis.

A crystal approximately 0.25 × 0.12 × 0.12 mm was coated with vaseline and mounted along its long dimension ($c$ axis) in a sealed capillary. Precession and Weissenberg photographs revealed a monoclinic space group with systematic absences of $hkl$, $h + k = 2n + 1$ and $0k0$, $k = 2n + 1$. Although three space groups, $C_2$ ($C_2^3$, no. 5), $Cm$ ($C_s^3$, no. 8) and $C_{2/m}$ ($C_{2h}^3$, no. 12), are consistent with these extinctions, the centrosymmetric space group $C_{2/m}$ was rejected initially because the complex was expected to be optically active. Subsequent solution and refinement of the structure eliminated $Cm$ and confirmed the space group as $C_2$.

Unit cell constants were determined at 22 ± 1° from a least-squares fit of ten moderately intense reflections centered on an Enraf-Nonius CAD-3 computer-controlled diffractometer. Values of the cell parameters and their estimated standard deviations are given in Table I.

Attempts to measure the density by conventional flotation methods gave inconsistent results, presumably due to loss of water. Better results were obtained by the density gradient method[9] using a mixture of carbon tetrabromide and carbon tetrachloride as the high-density medium and bromobenzene as the low-density me-

(1) Alfred P. Sloan Foundation Fellow, 1971–1973.

(2) H. V. Aposhian, *Ann. N. Y. Acad. Sci.*, 179, 481 (1971); *Brit. Med. J.*, 1, 270 (1971).

(3) B. S. Hartley and J. M. Walshe, *Lancet*, 434 (1963).

(4) D. D. Perrin, *Suom. Kemistilehti A.*, 42, 205 (1969); *Chem. Abstr.*, 72, 51030 (1970).

(5) Another plausible explanation proposed by Aposhian is that cysteine is metabolized more rapidly in the body than penicillamine. See ref 2 and H. V. Aposhian in "Metal Binding in Medicine," M. J. Seven, Ed., J. B. Lippincott Co., Philadelphia, Pa., 1960, Chapter 39.

(6) Oral administration of PDS does not promote copper removal, for reasons as yet unknown: J. M. Walshe, *Brit. Med. Bull.*, 13, 132 (1957).

(7) Y. Sugiura and H. Tanaka, *Mol. Pharmacol.*, 8, 249 (1972). This complex also appears to be a promising electronic structural model for the copper blue proteins. We are attempting to characterize its molecular and electronic structure.

(8) A. Butenandt, H. Jatzkewitz, and U. Schiedt, *Z. Physiol. Chem.*, 285, 238 (1950); *Chem. Abstr.*, 45, 5624g (1951).

(9) B. W. Low and F. M. Richards, *J. Amer. Chem. Soc.*, 74, 1660 (1952).

**Table I**

| Space group $C_2$ ($C_2{}^3$, no. 5) |
| --- |
| $Z = 4$ |
| $a = 12.266\,(5), b = 19.769\,(5), c = 15.698\,(5)$ Å |
| $\beta = 92.14\,(5)°$ |
| $d_{\text{obsd}} = 1.54\,(1)$ g/cm³ |
| $d_{\text{calcd}} = 1.534$ g/cm³ |
| $V = 3804$ Å³ |
| $\lambda = 0.71069$ Å |
| $\mu = 14.50$ cm⁻¹ |
| Temp $22 \pm 1°$ |

dium. Sodium acetate ($d = 1.528$ g/cm³)[10] and sucrose ($d = 1.588$ g/cm³)[10] were added to the solvent mixture as standards, and the resulting mixture was centrifuged. Several single crystals of the complex were isolated from their mother liquor, blotted, and added to the gradient. The mixture was again centrifuged and the density of the complex was determined by interpolation. This procedure led to an observed density of $1.54 \pm 0.01$ g/cm³, in good agreement with that calculated.

Data were collected at $22 \pm 1°$ with the Enraf-Nonius diffractometer. Graphite monochromated Mo K$\alpha$ radiation was detected with a scintillation counter and a pulse height analyser set to admit approximately 90% of the K$\alpha$ peak. Molybdenum radiation was chosen to minimize the need for absorption corrections. A number of crystals of varying size were mounted and examined photographically; however, all except that used for data collection decomposed within several days, presumably because of loss of water. For the crystal used to collect data, calculated transmission factors[11] for representative high and low order reflections showed them to be in the range 0.84–0.85 for Mo K$\alpha$ radiation and 0.48–0.66 for Cu K$\alpha$ radiation. In view of the small range with Mo K$\alpha$ radiation, absorption corrections were not applied. A $\theta$–$2\theta$ scan was used to collect a unique data set to a maximum of $2\theta = 40°$. Reflections with $2\theta < 4°$ were shielded by the beam-stop and were not recorded. The scan range $S$ was a function of $\theta$ chosen according to $S = (1.80 + 0.1 \tan \theta)°$. Each reflection was scanned before being recorded, and zirconium foil attenuators were automatically inserted if the intensity of the diffracted beam exceeded 6000 counts/sec. A circular aperture 1.3 mm in diameter was placed 4.1 cm from the crystal. Background measurements were made at the beginning and end of each scan with the counter stationary; the total time for background counts equalled the scan time. The scan rate was $^1/_6$ deg sec⁻¹ and each reflection was scanned repeatedly to a maximum of six scans or until 6000 total counts were obtained. Intensities were placed on a common scale by dividing by the number of scans. The intensity of a standard reflection, measured at 50 reflection intervals, was consistent to $\pm 3\%$ and showed no significant trend.

A total of 1982 reflections were collected and corrected for Lorentz and polarization effects. Standard deviations were assigned to $F^2$ values according to

$$\sigma(F^2) = \frac{1}{(\text{Lp})}(N_t + (0.02N_n)^2)^{1/2}$$

where $N_t$ is the total count (scan plus background) and $N_n$ is the net count (scan minus background). An estimate of the overall scale factor was obtained using Wilson's method and subsequently refined. Of the 1982 measured reflections, 1229 with $F^2 \geq 2\sigma$ were used in the subsequent refinement of the structure.

**Structure Determination.** The structure was solved by the heavy-atom method and refined using least-squares techniques. Space group $C_2$ has four general positions, and the presence of four dimers per unit cell requires one dimer per asymmetric unit. Approximate coordinates for the two unique copper atoms were obtained from a normal sharpened Patterson map; no set of copper coordinates consistent with the largest vectors on the map could be obtained for either space group $Cm$ or $C_{2/m}$. A series of structure factor, difference Fourier calculations revealed the coordinates of the remaining nonhydrogen atoms. As might be expected, ligand carbon, nitrogen, and oxygen atoms were somewhat easier to locate than water oxygen atoms, one of which was later found to be on a site of fractional occupancy. With all non-hydrogen scattering matter present and the water site fully occupied, the initial agreement factor $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ was 0.20.

Isotropic refinement was initiated using atomic scattering factors from the international tables[12] for Cu, S, O, N, and C. All atoms were treated as neutral species. Both real and imaginary parts of the anomalous dispersion corrections were applied to copper and sulfur.[12] Initial refinement was based on $F^2$ and weights were set according to $w = 1/\sigma^2$. Three refinement cycles of all atomic positional and isotropic thermal parameters, followed by one cycle with anisotropic thermal parameters for copper and sulfur reduced $R_F$ to 0.091. At this point, one lattice water oxygen atom [O(17)] showed an abnormally high isotropic temperature factor ($ca.$ 15). For further refinement, this atom was included with a multiplicity of 0.5 (the accuracy of the observed density is not sufficient to determine the empirical formula to within one-half of a water molecule).

Further refinement was based on $F$ and a weighting scheme was chosen by an analysis of variance[11] to make $\Delta F/\sigma$ independent of $F_o$. This procedure led to the following assignments for $\sigma(F_o)$: $\sigma(F_o) = 1.56 - 0.095|F_o|, 0 < |F_o| < 8.6$; $\sigma(F_o) = 0.74, 8.6 < |F_o| < 15.1$; $\sigma(F_o) = -0.49 + 0.08|F_o|, |F_o| \geq 15.1$. One cycle of refinement, again with anisotropic copper and sulfur temperature factors, reduced $R_F$ to 0.086 and $R_{wF} = [\Sigma w(F_o - F_c)^2/\Sigma wF_o^2]^{1/2}$, the function minimized, to 0.101. Ligand hydrogen atom coordinates were calculated and these atoms were added as a fixed atom contribution to the overall structure factor calculation with isotropic temperature factors equal to those of the carbon atom to which they are bound. Hydrogen atom parameters were not refined. Coordinates of the methylene, methyne, and nitrogen hydrogen atoms were calculated readily from the coordinates of their surrounding heavier atoms and the expected geometry about carbon or nitrogen. Typically, these coordinates were located in positive regions of a difference map calculated at this point. Methyl group hydrogen coordinates were fixed to give the expected C–H bond lengths and tetrahedral angles. The methyl groups were then rotated at 10° intervals until at least two of the three hydrogen atoms were in positive regions of the map. No attempt was made to locate water hydrogen atoms. Two additional cycles of refinement reduced $R_F$ to 0.080.

At this point, an attempt was made to deduce the absolute configuration of the complex using Hamilton's $R$ factor ratio test.[13] The coordinates of all atoms were inverted to give the L enantiamorph and both enantiamorphs were refined equivalently (two cycles). The L form converged to $R_F = 0.0783$ while the D form gave $R_F = 0.0774$. For this refinement, 1229 reflections were used and 219 parameters were varied. The one-dimensional hypothesis that the L configuration is correct can be rejected at better than the 0.005 level and the D enantiamorph assumed correct. A D configuration is consistent with circular dichroism spectra[14] and the known configuration of D-penicillamine.

One additional cycle of refinement using the D configuration gave final values of $R_F = 0.077$ and $R_{wF} = 0.091$. All positional and thermal parameter changes were within their estimated standard deviation for the last cycle of refinement. The final error in an observation of unit weight was 1.23. A final difference Fourier showed a general background of approximately 0.5 e/Å³ and no peaks larger than 0.9 e/Å³. Of those peaks above background, only two were not residuals of known atoms. Both were 0.9 e/Å³ in height and were approximately 0.8 Å from O(14). These peaks could be due to hydrogen atoms, to uncompensated anisotropic thermal vibrations, to additional water sites (which would cause the O(14) site to be partially occupied), or to a combination of these factors. Since the isotropic temperature factor for O(14) was not abnormally large compared with the remaining lattice water molecules, the third possibility was deemed unlikely. In view of the essential correctness of the structure and of the cost in-

(10) R. C. Weast, Ed., "Handbook of Chemistry and Physics," 46th ed, Chemical Rubber Co., Cleveland, Ohio, 1965.

(11) In addition to local programs for the IBM 360/67 computer, local modifications of the following programs were employed: Coppen's ABSORB absorption program; Zalkin's FORDAP Fourier program; Johnson's ORTEP II thermal ellipsoid plotting program; Busing, Martin, and Levy's ORFFE error function, and ORFLS least-squares programs. The analysis of variance was carried out using program NANOVA obtained from Dr. I. Bernal; see J. S. Ricci, Jr., C. A. Eggers, and I. Bernal, *Inorg. Chim. Acta*, 6, 97 (1972).

(12) "International Tables for X-Ray Crystallography," Vol. III, Kynoch Press, Birmingham, England, 1962, pp 201–213.

(13) W. C. Hamilton, *Acta Crystallogr.*, 18, 502 (1965).

(14) T. Yasui, J. Hidaka, and Y. Shimura, *J. Amer. Chem. Soc.*, 87, 2762 (1965).

**Table II.** Fractional Atomic Coordinates[a] and Thermal Parameters[b] for $[Cu^{II}\text{-D-PDS}]_2 \cdot 9H_2O$

| Atom | $x$ | $y$ | $z$ | $\beta_{11}$ | $\beta_{22}$ | $\beta_{33}$ | $\beta_{12}$ | $\beta_{13}$ | $\beta_{23}$ |
|---|---|---|---|---|---|---|---|---|---|
| Cu(1) | −463.2 (2) | −787.9 (2) | −661.4 (2) | 23 (2) | 15 (1) | 31 (2) | −5 (2) | 3 (1) | 4 (1) |
| Cu(2) | −383.6 (2) | $-1/2^c$ | −834.7 (2) | 24 (3) | 19 (1) | 28 (2) | 0 (2) | 6 (2) | −1 (1) |
| S(1) | −242.2 (5) | −609.4 (4) | −679.1 (4) | 33 (5) | 16 (2) | 18 (4) | 2 (3) | 1 (3) | 1 (2) |
| S(2) | −273.4 (6) | −641.4 (4) | −800.9 (5) | 31 (6) | 21 (2) | 23 (4) | −7 (3) | 0 (4) | 5 (2) |
| S(3) | −583.4 (6) | −675.2 (4) | −759.4 (5) | 42 (6) | 21 (3) | 39 (5) | −1 (3) | 8 (4) | 4 (3) |
| S(4) | −600.6 (6) | −619.0 (4) | −651.0 (5) | 43 (6) | 19 (3) | 31 (4) | −5 (3) | −5 (4) | 3 (3) |

| Atom | $x$ | $y$ | $z$ | $B$ | Atom | $x$ | $y$ | $z$ | $B$ |
|---|---|---|---|---|---|---|---|---|---|
| O(1) | −339 (1) | −801 (1) | −732 (1) | 1.8 (4) | O(13) | −900 (2) | −486 (1) | −903 (2) | 4.9 (6) |
| O(2) | −157 (2) | −806 (1) | −720 (1) | 4.0 (5) | O(14) | −456 (2) | −357 (1) | −667 (2) | 6.0 (7) |
| O(3) | −248 (1) | −469 (1) | −777 (1) | 2.3 (4) | O(15) | −427 (2) | −387 (1) | −873 (2) | 6.5 (7) |
| O(4) | −70 (2) | −479 (1) | −782 (1) | 3.2 (5) | O(16) | −397 (2) | −882 (2) | −568 (2) | 6.2 (7) |
| O(5) | −591 (1) | −781 (1) | −589 (1) | 2.1 (4) | O(17) | −326 (4) | −888 (3) | −996 (3) | 4 (1) |
| O(6) | −768 (2) | −796 (1) | −592 (1) | 3.0 (4) | O(18) | $-1/2$ | −647 (2) | −1 | 4.6 (8) |
| O(7) | −518 (2) | −537 (1) | −886 (1) | 3.4 (5) | N(1) | −365 (2) | −731 (1) | −590 (1) | 1.3 (4) |
| O(8) | −697 (2) | −544 (1) | −872 (1) | 3.3 (5) | N(2) | −288 (2) | −515 (1) | −929 (1) | 2.2 (5) |
| O(9) | −18 (3) | −498 (2) | −599 (2) | 10 (1) | N(3) | −568 (2) | −832 (1) | −746 (1) | 1.8 (5) |
| O(10) | −361 (3) | −344 (2) | −108 (3) | 11 (1) | N(4) | −471 (2) | −497 (1) | −727 (1) | 2.6 (5) |
| O(11) | −241 (3) | −450 (2) | −591 (3) | 10 (1) | C(1) | −248 (3) | −787 (2) | −696 (2) | 3.0 (7) |
| O(12) | −424 (2) | −775 (2) | −914 (2) | 7.3 (8) | C(2) | −249 (2) | −744 (2) | −612 (2) | 1.3 (6) |
| C(3) | −181 (2) | −679 (2) | −610 (2) | 1.3 (6) | C(12) | −681 (2) | −801 (1) | −727 (2) | 1.1 (6) |
| C(4) | −184 (2) | −645 (2) | −520 (2) | 1.7 (6) | C(13) | −701 (3) | −734 (2) | −776 (2) | 2.9 (8) |
| C(5) | −62 (2) | −689 (2) | −627 (2) | 1.7 (6) | C(14) | −700 (3) | −747 (2) | −874 (2) | 3.9 (9) |
| C(6) | −167 (2) | −608 (2) | −873 (2) | 1.3 (6) | C(15) | −811 (3) | −708 (2) | −759 (2) | 3.5 (8) |
| C(7) | −51 (2) | −626 (2) | −840 (2) | 2.2 (7) | C(16) | −652 (2) | −532 (1) | −681 (2) | 1.1 (6) |
| C(8) | −188 (3) | −652 (2) | −955 (2) | 3.6 (9) | C(17) | −631 (2) | −491 (2) | −598 (2) | 2.3 (6) |
| C(9) | −179 (3) | −534 (2) | −891 (2) | 2.4 (7) | C(18) | −780 (3) | −533 (2) | −701 (2) | 4.0 (9) |
| C(10) | −164 (2) | −492 (2) | −811 (2) | 1.2 (6) | C(19) | −590 (2) | −499 (2) | −752 (2) | 1.2 (6) |
| C(11) | −681 (2) | −791 (2) | −630 (2) | 1.8 (6) | C(20) | −602 (2) | −526 (1) | −844 (2) | 0.9 (6) |

Hydrogen Coordinates ×10³

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| HC2 | −209 | −776 | −560 | 1.3 | HC7-1 | −7 | −609 | −883 | 2.0 |
| HN1-1 | −383 | −681 | −600 | 1.4 | HC7-2 | −44 | −685 | −837 | 2.0 |
| HN1-2 | −375 | −747 | −523 | 1.4 | HC7-3 | −37 | −609 | −776 | 2.0 |
| HC4-1 | −237 | −604 | −527 | 1.9 | HC8-1 | −274 | −665 | −966 | 4.0 |
| HC4-2 | −102 | −632 | −501 | 1.9 | HC8-2 | −158 | −627 | −1010 | 4.0 |
| HC4-3 | −215 | −683 | −475 | 1.9 | HC8-3 | −144 | −703 | −950 | 4.0 |
| HC5-1 | −14 | −646 | −610 | 1.9 | HC9 | −120 | −525 | −941 | 2.4 |
| HC5-2 | −53 | −704 | −693 | 1.9 | HN2-1 | −315 | −560 | −974 | 2.4 |
| HC5-3 | −26 | −734 | −588 | 1.9 | HN2-2 | −275 | −474 | −974 | 2.4 |
| HC12 | −749 | −836 | −744 | 1.0 | HC17-1 | −550 | −468 | −595 | 2.2 |
| HN3-1 | −552 | −825 | −813 | 1.7 | HC17-2 | −633 | −527 | −541 | 2.2 |
| HN3-2 | −573 | −890 | −737 | 1.7 | HC17-3 | −693 | −454 | −591 | 2.2 |
| HC14-1 | −782 | −758 | −899 | 4.0 | HC18-1 | −805 | −569 | −754 | 5.1 |
| HC14-2 | −646 | −789 | −893 | 4.0 | HC18-2 | −813 | −484 | −716 | 5.1 |
| HC14-3 | −671 | −701 | −90ᵢ | 4.0 | HC18-3 | −824 | −553 | −644 | 5.1 |
| HC15-1 | −798 | −671 | −706 | 4.2 | HC19 | −637 | −395 | −590 | 1.2 |
| HC15-2 | −863 | −748 | −735 | 4.2 | HN4-1 | −448 | −544 | −688 | 2.7 |
| HC15-3 | −845 | −685 | −813 | 4.2 | HN4-2 | −452 | −454 | −689 | 2.7 |

[a] Atomic coordinates are ×10³. [b] The form of the anisotropic thermal ellipsoid is $\exp[-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{13}hl + 2\beta_{23}kl)]$. [c] The $y$ coordinate of Cu(2) fixes the origin.
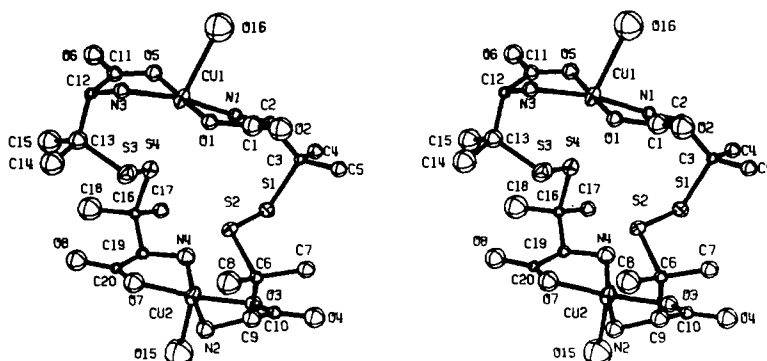


**Figure 1.** Stereoscopic view of $[Cu^{11})\text{-D-PDS}]_2 \cdot 9H_2O$. For clarity, the lattice water molecules are not shown.

volved for additional refinement, this problem was not examined further.

Final atomic parameters, together with estimated standard deviations derived from the inverse matrix, are given in Table II, while Figure 1 shows a stereoscopic view of the molecule and gives the numbering scheme. A list of observed and calculated structure factors is available.[15]

(15) See paragraph at end of paper regarding supplementary material.

**Table III.** Bond Distances (Å), Angles (deg) and Deviations from Least-Square Planes for [Cu$^{II}$-D-PDS]$_2$·9H$_2$O$^a$

| Copper Coordination Environment | | | |
|---|---|---|---|
| Atoms | Distance | Atoms | Distance |
| Cu(1)-N(1) | 1.97 (2) | Cu(2)-N(2) | 1.95 (2) |
| Cu(1)-N(3) | 2.01 (2) | Cu(2)-N(4) | 2.05 (2) |
| Cu(1)-O(1) | 1.97 (2) | Cu(2)-O(3) | 1.97 (2) |
| Cu(1)-O(5) | 1.97 (2) | Cu(2)-O(7) | 1.94 (2) |
| Cu(1)-O(6) | 2.48 (3) | Cu(2)-O(15) | 2.38 (3) |
| Cu(1)···S(3) | 3.057 (10) | Cu(2)···S(2) | 3.138 (9) |
| Cu(1)····Cu(2) | 6.399 (5) | | |

| Ligand 1 | | Ligand 2 | |
|---|---|---|---|
| N(1)-C(2) | 1.49 (3) | N(3)-C(12) | 1.56 (3) |
| C(2)-C(1) | 1.57 (4) | C(12)-C(11) | 1.53 (4) |
| C(1)-O(1) | 1.27 (3) | C(11)-O(5) | 1.26 (3) |
| C(1)-O(2) | 1.24 (4) | C(11)-O(6) | 1.26 (3) |
| C(2)-C(3) | 1.53 (4) | C(12)-C(13) | 1.55 (4) |
| C(3)-C(4) | 1.56 (4) | C(13)-C(14) | 1.56 (5) |
| C(3)-C(5) | 1.50 (4) | C(13)-C(15) | 1.45 (5) |
| C(3)-S(1) | 1.91 (3) | C(13)-S(3) | 1.86 (3) |
| S(1)-S(2) | 2.03 (1) | S(3)-S(4) | 2.05 (1) |
| S(2)-C(6) | 1.88 (3) | S(4)-C(16) | 1.87 (3) |
| C(6)-C(7) | 1.54 (4) | C(16)-C(17) | 1.56 (4) |
| C(6)-C(8) | 1.54 (5) | C(16)-C(18) | 1.61 (4) |
| C(6)-C(9) | 1.50 (4) | C(16)-C(19) | 1.51 (4) |
| C(9)-C(10) | 1.52 (4) | C(19)-C(20) | 1.54 (4) |
| C(10)-O(3) | 1.26 (3) | C(20)-O(7) | 1.26 (3) |
| C(10)-O(4) | 1.25 (3) | C(20)-O(8) | 1.29 (3) |
| N(2)-C(9) | 1.49 (4) | N(4)-C(19) | 1.50 (3) |

| Copper Coordination Environment | | | |
|---|---|---|---|
| Atoms | Angle | Atoms | Angle |
| N(1)-Cu(1)-O(1) | 85.4 (8) | N(2)-Cu(2)-O(3) | 83.0 (9) |
| N(1)-Cu(1)-O(5) | 96.8 (8) | N(2)-Cu(2)-O(7) | 99.1 (9) |
| N(1)-Cu(1)-N(3) | 171 (1) | N(2)-Cu(2)-N(4) | 171 (1) |
| N(3)-Cu(1)-O(1) | 93.5 (8) | N(4)-Cu(2)-O(3) | 93.7 (8) |
| N(3)-Cu(1)-O(5) | 84.8 (8) | N(4)-Cu(2)-O(7) | 83.5 (9) |
| O(1)-Cu(1)-O(5) | 176.1 (9) | O(3)-Cu(2)-O(7) | 175.0 (9) |
| O(16)-Cu(1)-S(3) | 169.6 (7) | O(15)-Cu(2)-S(2) | 166.5 (7) |
| O(16)-Cu(1)-N(1) | 84.6 (9) | O(15)-Cu(2)-N(2) | 95 (1) |
| O(16)-Cu(1)-N(3) | 105 (1) | O(15)-Cu(2)-N(4) | 94 (1) |
| O(16)-Cu(1)-O(1) | 89.7 (8) | O(15)-Cu(2)-O(3) | 89.7 (9) |
| O(16)-Cu(1)-O(5) | 87.4 (8) | O(15)-Cu(2)-O(7) | 95 (1) |

| Ligand 1 | | Ligand 2 | |
|---|---|---|---|
| Cu(1)-N(1)-C(2) | 110 (2) | Cu(1)-N(3)-C(12) | 104 (2) |
| Cu(1)-O(1)-C(1) | 115 (2) | Cu(1)-O(5)-C(11) | 113 (2) |

| Ligand 1 | | Ligand 2 | |
|---|---|---|---|
| O(1)-C(1)-C(2) | 116 (3) | O(5)-C(11)-C(12) | 120 (2) |
| O(1)-C(1)-O(2) | 126 (3) | O(5)-C(11)-O(6) | 121 (2) |
| O(2)-C(1)-C(2) | 117 (3) | O(6)-C(11)-C(12) | 119 (2) |
| N(1)-C(2)-C(1) | 110 (2) | N(3)-C(12)-C(11) | 105 (2) |
| N(1)-C(2)-C(3) | 113 (2) | N(3)-C(12)-C(13) | 112 (2) |
| C(1)-C(2)-C(3) | 117 (2) | C(11)-C(12)-C(13) | 112 (2) |
| C(2)-C(3)-C(4) | 111 (2) | C(12)-C(13)-C(14) | 110 (3) |
| C(2)-C(3)-C(5) | 115 (2) | C(12)-C(13)-C(15) | 109 (3) |
| C(2)-C(3)-S(1) | 112 (2) | C(12)-C(13)-S(3) | 111 (2) |
| C(4)-C(3)-C(5) | 107 (2) | C(14)-C(13)-C(15) | 106 (3) |
| C(4)-C(3)-S(1) | 100 (2) | C(14)-C(13)-S(3) | 102 (2) |
| C(5)-C(3)-S(1) | 110 (2) | C(15)-C(13)-S(3) | 118 (3) |
| C(3)-S(1)-S(2) | 110 (1) | C(13)-S(3)-S(4) | 110 (1) |
| S(1)-S(2)-C(6) | 110.3 (9) | S(3)-S(4)-C(16) | 109 (1) |
| S(2)-C(6)-C(7) | 112 (2) | S(4)-C(16)-C(17) | 104 (2) |
| S(2)-C(6)-C(8) | 102 (2) | S(4)-C(16)-C(18) | 111 (2) |
| S(2)-C(6)-C(9) | 113 (2) | S(4)-C(16)-C(19) | 114 (2) |
| C(7)-C(6)-C(8) | 106 (2) | C(17)-C(16)-C(18) | 107 (2) |
| C(7)-C(6)-C(9) | 112 (2) | C(17)-C(16)-C(19) | 109 (2) |
| C(8)-C(6)-C(9) | 112 (3) | C(18)-C(16)-C(19) | 112 (2) |
| C(6)-C(9)-C(10) | 112 (3) | C(16)-C(19)-C(20) | 121 (2) |
| C(6)-C(9)-N(2) | 114 (2) | C(16)-C(19)-N(4) | 109 (2) |
| N(2)-C(9)-C(10) | 105 (2) | N(4)-C(19)-C(20) | 108 (2) |
| C(9)-C(10)-O(3) | 119 (2) | C(19)-C(20)-O(7) | 120 (2) |
| C(9)-C(10)-O(4) | 120 (2) | C(19)-C(20)-O(8) | 118 (2) |
| O(3)-C(10)-O(4) | 121 (2) | O(7)-C(20)-O(8) | 121 (2) |
| Cu(2)-O(3)-C(10) | 112 (2) | Cu(2)-O(7)-C(20) | 115 (2) |
| Cu(2)-N(2)-C(9) | 107 (2) | Cu(2)-N(4)-C(19) | 108 (2) |

Dihedral Angles

| C(3)-S(1)-S(2)/ | | C(13)-S(3)-S(4)/ | |
|---|---|---|---|
| S(1)-S(2)-C(6) | 103 (1) | S(3)-S(4)-C(16) | 101 (1) |

Least-Squares Planes

(1) Plane defined by O(1), O(5), N(1), N(3)
Distance to plane (Å)

| O(1) | 0.11 | N(3) | -0.11 |
|---|---|---|---|
| O(5) | 0.11 | Cu(1) | 0.06 |
| N(1) | -0.11 | | |

(2) Plane defined by O(5), O(7), N(2), N(4)
Distance to plane (Å)

| O(3) | -0.03 | N(4) | 0.04 |
|---|---|---|---|
| O(7) | -0.05 | Cu(2) | -0.11 |
| N(2) | 0.04 | | |

$^a$ Unit weights were employed in the calculation of all planes.

## Results and Discussion

The structure consists of dimeric [Cu$^{II}$-D-PDS]$_2$ units in which crystallographically nonequivalent copper atoms are bridged by two PDS ligands. Interatomic bond distances and angles of interest are given in Table III. Coordination of the amino acid moieties is approximately trans planar for Cu(2) and trans puckered for Cu(1). Cu-O(equatorial) distances are equivalent within experimental error and average to 1.96 ± 0.02 Å. However, Cu-N distances for nitrogen atoms on ligand 1 (2.05 (2), 2.01 (2)) are significantly longer than those for ligand 2 (1.97 (2), 1.95 (2)). Atoms Cu(1) and Cu(2) are displaced 0.06 and 0.11 Å, respectively, from the best least-squares planes defined by the coordinating amino acid oxygen and nitogen atoms (Table III) in the direction of water oxygen atoms O(15) and O(16), which occupy a fifth coordination site. The distances Cu(1)-O(16) and Cu(2)-O(15), although not equivalent, lie within the range expected[16] for Cu$^{II}$-O(axial) bonds.

The temperature factors of the amino acid oxygen atoms are low compared with those of the lattice water molecules. This is consistent with the ease with which crystals of this complex dehydrate in air.

The disulfide units exhibit typical S-S bond lengths[17] and are located in the interior of the dimer, while the methyl groups point toward lattice water molecules. Thus, sulfur atoms could occupy a sixth coordination site. Disulfide complexation with first row d$^n$ ions is rare and, to our knowledge, has not been substantiated previously for Cu(II). Table IV lists a number of M-S (thioether or disulfide) distances which have been reported. The equatorial distances are indicative of strong M-S interaction and suggest that an equatorial Cu$^{II}$-S(disulfide) distance would lie in the range 2.4-2.5 Å. Since apical Cu$^{II}$-O distances are typically 0.3-0.5 Å longer than the corresponding equatorial distances,[16] an apical Cu$^{II}$-S(disulfide) distance might be expected to lie in the range 2.7-3.0 Å, as do the axial Cu$^{II}$-S(thioether) distances in Table IV. How-

(16) H. C. Freeman in "Advances in Protein Chemistry," C. B. Anfinsen, Jr., M. L. Anson, J. T. Edsall, F. M. Richards, Ed., Academic Press, New York, N. Y., 1967, pp 257-424.

(17) J. D. Lee and M. W. R. Bryant, *Acta Crystallogr., Sect. B,* **25,** 2094 (1969).

**Table IV.** Metal–Sulfur Bond Distances

| Compound | Bond type | | Distance (Å) | Ref |
|---|---|---|---|---|
| Ni$^{II}$(C$_{16}$H$_{22}$N$_4$S$_2$)Cl(ClO$_4$) | Equatorial | Ni$^{II}$–S(disulfide) | 2.472 (5) | a |
| Cu$^{II}$(C$_6$H$_{16}$N$_2$O$_2$S)Cl$_2$ | Equatorial | Cu$^{II}$–S(thioether) | 2.410 (1) | b |
| Cu$^{I}$(C$_4$H$_{10}$S$_2$)Cl | | Cu$^{I}$–S(disulfide) | 2.34 (1), 2.40 (1) | c |
| Cu$^{II}$(C$_5$H$_4$NCO$_2$)$_2$[SC(NH$_2$)$_2$]$_2$ | Axial | Cu$^{II}$–S(thioether) | 2.943 (1) | d |
| Cu$^{II}$(C$_5$H$_4$NCO$_2$)$_2$[SC(NH$_2$)NHCH$_2$CH=CH$_2$]$_2$ | Axial | Cu$^{II}$–S(thioether) | 2.927 (1) | d |
| [Cu$^{II}$-D-PDS]$_2$·9H$_2$O | Axial | Cu$^{II}$–S(disulfide) | 3.057 (10), 3.138 (9) | This work |

$^a$ P. E. Riley and K. Seff, *Inorg. Chem.*, **11**, 2993 (1972). $^b$ J. Coetzer, *Acta Crystallogr., Sect. B*, **26**, 1414 (1970). $^c$ C. I. Branden, *Acta Chem. Scand.*, **21**, 1000 (1967). $^d$ M. B. Ferrari, L. C. Capacchi, G. G. Fava, A. Montenero, and M. Nardelli, *Sov. Phys.-Crystallogr.*, **17**, 16 (1972).
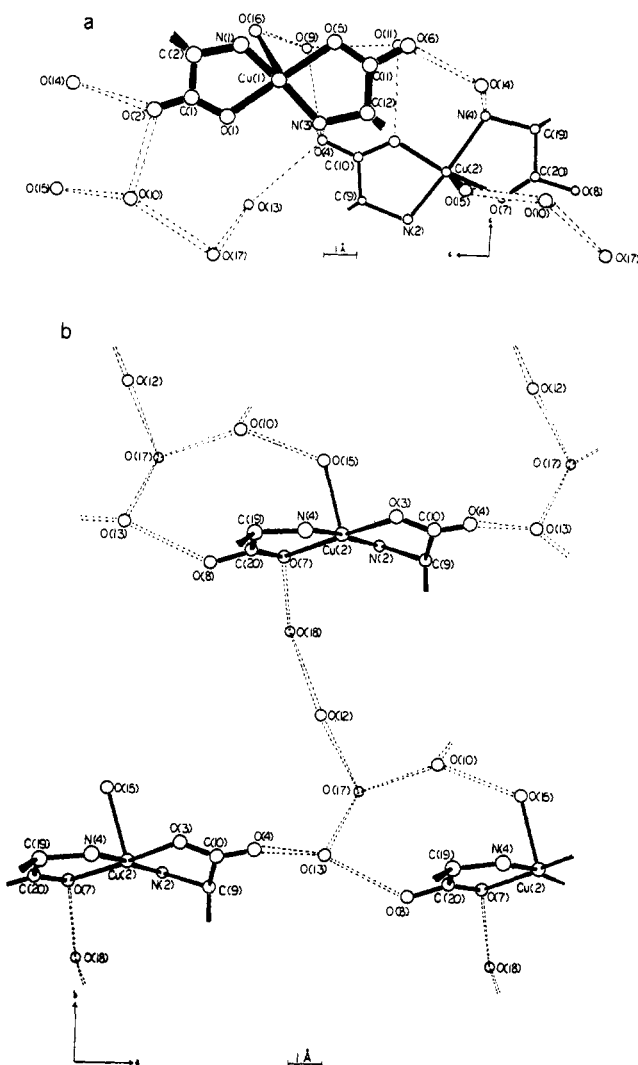


**Figure 2.** Portions of the unit cell contents showing the hydrogen bonding network: (a) view along $b$, (b) view along $d_{001}$.

ever, an additional lengthening of the Cu(II)–S bond is expected when a relatively poor ligand such as disulfide is trans coordinated to a water molecule. Thus, the observed Cu–S distances (3.057 (10), 3.138 (9) Å) in the present structure are consistent with a weak bonding interaction. Interestingly, S(2), with the longer Cu–S distance, shows the short Cu–O(axial) distance, again in accord with a weak interaction. The disulfide dihedral angles C(3)–S(1)–S(2)/S(1)–S(2)–C(6) and C(13)–S(3)–S(4)/S(3)–S(4)–C(16) are equivalent experimentally, as are the S–S bond lengths, and do not reflect the difference in Cu–S bond lengths. This is further evidence that the interaction is weak and suggests that it

might not be detected readily by spectroscopic techniques. Lastly, the trans S–Cu–O angles are similar to O(apical)–Cu$^{II}$–O(apical) angles found for several Cu(II) amino acid dihydrate derivatives.[16] Accordingly, the coordination geometry in [Cu$^{II}$-D-PDS]$_2$·9H$_2$O is best described as tetragonal rather than distorted square pyramidal.

Average bond distances and angles for the remainder of the dimer are as expected and show no unusual trends. For example, C(sp$^3$)–C(sp$^3$) distances average to 1.54 ± 0.04 Å, while the average of the C–C–C angles is 111 ± 2°. Thus, there appears to be little strain associated with the formation of the weak Cu$^{II}$–S(disulfide) bonds, possibly because of the flexibility provided by the disulfide dihedral angles.

The dimeric [Cu$^{II}$-D-PDS]$_2$ units are linked in the crystal by an extensive hydrogen bonding network involving water molecules, carboxylate oxygen atoms, and amino acid nitrogen atoms. Table V shows O···O

**Table V.** Probable Hydrogen Bonding Contacts in [Cu$^{II}$-D-PDS]$_2$·9H$_2$O

| Atoms | Distance (Å) | Atoms | Distance (Å) |
|---|---|---|---|
| O(2)···O(10) | 2.82 (5) | O(9)···O(16) | 2.76 (5) |
| O(2)···O(14) | 2.75 (3) | O(10)···O(15) | 2.77 (5) |
| O(3)···O(11) | 2.95 (4) | O(10)···O(17) | 2.90 (6) |
| O(4)···O(9) | 2.94 (4) | O(12)···O(17) | 2.85 (6) |
| O(4)···O(13) | 2.89 (3) | O(12)···O(18) | 3.01 (4) |
| O(6)···O(14) | 2.83 (3) | O(13)···O(17) | 2.62 (6) |
| O(7)···O(18) | 2.82 (3) | O(14)···N(4) | 2.93 (4) |
| O(8)···O(13) | 2.77 (3) | N(3)···O(4) | 2.94 (3) |
| O(9)···O(11) | 2.92 (5) | | |

and N···O distances in the range expected for hydrogen bonding, while Figure 2 shows representative portions of the unit cell contents and serves to illustrate the network character. In Figure 2a, for example, arrays of atoms held together by hydrogen, dative, and covalent bonds can be traced roughly along [100]. One such array is given by O(17)···O(10)···O(15)–Cu(2)–O(3)–C(10)–O(4)···O(13)···O(17)'. Similar linkages can be observed roughly along [010] in Figure 2b. In addition to this network, there also appears to be a weak interaction directly between the dimers as evidenced by the N(3)···O(4) distance of 2.94 (3) Å.

The present study supports an earlier proposal by Hawkins and Perrin[18] that a ligand bridged dimer is a major component of aqueous Cu(II) cystinate solution. Noting that steric restraints prevent both ends of cystinate from attaching to a single Cu(II) ion, they

(18) C. J. Hawkins and D. D. Perrin, *Inorg. Chem.*, **2**, 843 (1963).

postulated that the solution dimer and the solid complexes isolated from approximately neutral solutions share a di-μ-cystinato-dicopper(II) structural feature. The present structure supports their suggestion, although polymeric[19] Cu(II) cystinate complexes cannot definitely be excluded. Both cis and trans copper(II) L-cystinate complexes have been isolated and characterized in our laboratories. These studies will be published elsewhere.[20]

**Supplementary Material Available.** A listing of structure factor amplitudes will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D. C. 20036. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche, referring to code number JACS-74-726.

(19) D. Otto, G. Ferenc, and M. Tamas, *Magy. Kem. Foly.*, **68**, 1 (1962); *Chem. Abstr.*, **57**, 172*f* (1962).

(20) J. A. Thich, D. Mastropaolo, J. Potenza, and H. J. Schugar, to be submitted for publication.

# Porphyrin–Annulene Redox-Related Ligand Pair. Electrochemical Synthesis and Characterization of the Reduction Products of the Cobalt, Copper, and Nickel Complexes of a Tetraaza[16]annulene

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**Abstract:** $Co^{II}(TAAB)^{2+}$, $Ni^{II}(TAAB)^{2+}$, and $Cu^{II}(TAAB)^{2+}$ undergo successive one-electron electrochemical reductions to form stable complexes which have been formulated as derivatives of the dianionic ligand $TAAB^{2-}$, a porphyrin analog. The reactants contain the well-characterized annulene-like ligand tetrabenzo[*b,f,j,n*][1,5,9,13]-tetraazacyclohexadecine. The reduction products, which are tentatively assigned the formulations [$Co^{III}$-$(TAAB^{2-})$]$ClO_4$, [$Co^{II}(TAAB^{2-})$]$CH_3CN$, [$Ni^{III}(TAAB^{2-})$]$ClO_4$, [$Ni^{II}(TAAB^{2-})$]$^0$, and [$Cu^{III}(TAAB^{2-})$]$ClO_4$, have been synthesized by controlled potential electrolysis and, in some cases, by chemical means and characterized by the usual chemical and physical measurements. Voltammetric studies at dme and rpe and cyclic voltammetric studies have been carried out on all these compounds in methanol and acetonitrile. The reduced complexes of cobalt have a unique electrochemistry which considerably strengthens the suggestion that they possess electronic and structural characteristics which differ significantly from that of the parent $Co^{II}(TAAB)^{2+}$ complex and that they should be formulated as complexes of the dianion ligand, $TAAB^{2-}$. The dramatic rearrangement to $Co^{III}$-$(TAAB^{2-})^+$ is thought to proceed relatively slowly *via* a $Co^{I}(TAAB)^+$ intermediate. The lifetime of this intermediate is sufficiently long to facilitate its detection and characterization by electrochemical and spectral measurements. The $Co^{III}(TAAB^{2-})^+$ complex can be reoxidized to the original $Co^{II}(TAAB)^{2+}$ using cyclic voltammetry. The relationship between the annulene TAAB and the two-electron oxidation product of the porphyrin dianion is clarified.

M etalloporphyrins exhibit a rich oxidation–reduction chemistry and a number of studies[1–5] have revealed their general tendency to undergo multiple one-electron oxidation processes. A point of particular interest to us at this time is the conclusion that the ligand in various metalloporphyrins undergoes a total of two one-electron oxidations. We assert that the 16-membered great ring of the two-electron oxidation product is essentially an analog of [16]annulene, *i.e.*, a tetraaza[16]annulene (I). It follows that the chemistry of the product chelates should be that of tetraazaannulene complexes.

Similarly, the two-electron reduction product of the related pure organic chemical system, [16]annulene,[6] should provide an analog for the parent porphyrin. Oth and coworkers[7] found that [16]annulene itself

(1) A. Wolberg and J. Manassen, *J. Amer. Chem. Soc.*, **92**, 2982 (1970).

(2) A. Stanienda and G. Biehl, *Z. Phys. Chem. (Frankfurt am Main)*, **52**, 254 (1967).

(3) J. Fajer, D. C. Borg, A. Forman, D. Dolphin, and R. H. Felton, *J. Amer. Chem. Soc.*, **92**, 3451 (1970).

(4) D. Dolphin, R. H. Felton, D. C. Borg, and J. Fajer, *J. Amer. Chem. Soc.*, **92**, 743 (1970).

(5) R. H. Felton, D. Dolphin, D. C. Borg, and J. Fajer, *J. Amer. Chem. Soc.*, **91**, 196 (1969).

(6) F. Sondheimer and Y. Gaoni, *J. Amer. Chem. Soc.*, **83**, 4863 (1961).

(7) J. F. M. Oth, G. Anthoine, and J. M. Gilles, *Tetrahedron Lett.*, **60**, 6265 (1968); J. F. Oth, H. Baumann, J. M. Gilles, and G. Schröder, *J. Amer. Chem. Soc.*, **94**, 3498 (1972).