X-Ray Crystal Structure of the Copper(II) Complex of Mugineic Acid, a Naturally Occurring Metal Chelator of Graminaceous Plants

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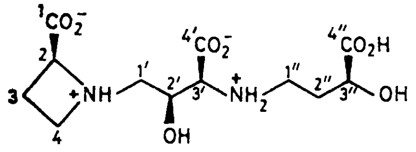
Summary The *X*-ray crystal structure of the copper complex of mugineic acid shows that the ligand molecule co-ordinates with the copper ion in a hexadentate fashion, forming a distorted octahedral geometry.

MUGINEIC acid {(2*S*,2′*S*,3′*S*,3″*S*)-*N*-[3-carboxy-3-(3-carboxy-3-hydroxypropylamino)-2-hydroxypropyl]-azetidine-2-carboxylic acid} (**1**), an amino-acid isolated as an exudate from the roots of water-cultured barley (*Hordeum vulgare* L. var. Minorimugi), is the first compound to be shown to play a role in the uptake and transport of iron in higher plants.[1,2] It is capable of effectively solubilizing $Fe(OH)_3$ within the pH range 4—9, and its addition to the medium of water-cultured rice at pH 7 increases the plants content of chlorophyll.[2] However, the iron-solubilizing action is strongly inhibited by the presence of divalent metals, the order of inhibition being $Cu > Co \geqslant Zn > Mn$.[1,3] It is assumed that mugineic acid preferentially chelates with divalent metal ions, forming a more stable complex than that with Fe^{3+}. Elucidation of the structure of the mugineic acid–copper(II) complex should help to clarify the still obscure biological function of mugineic acid.



(1)

The mugineic acid–Cu^{II} complex was formed upon leaving an equimolar mixture of mugineic acid and $CuSO_4{\cdot}5H_2O$ in water for 10 min at room temperature, and crystals of the complex were obtained as blue plates by recrystallization from EtOH–Pr^iOH. This complex, m.p. 261—282 °C (decomp.), shows the following spectral data: u.v. $\lambda_{max}(H_2O)$ 248 (ϵ 4480) and 685 nm (54); c.d. $\lambda_{max}(H_2O)$ 204 ($\Delta\epsilon$ −10·70), 247 (+7·90), 583 (+0·08), and 755 nm (−0·27); i.r. ν_{max}(KBr) 3350, 3300, 3250, and 1638 cm^{-1}.

Crystal data: $C_{12}H_{18}CuN_2O_8$, $M = 381{\cdot}83$, monoclinic, space group $P2_1$, $a = 6{\cdot}069(1)$, $b = 13{\cdot}617(1)$, $c = 9{\cdot}005(1)$ Å, $\beta = 106{\cdot}4(1)°$, $U = 714{\cdot}1(1)$ Å^3, $D_m = 1{\cdot}768$ g cm^{-3}, $D_c = 1{\cdot}776$ g cm^{-3}, $Z = 2$. The structure was solved by the heavy-atom method, and refined by least-squares to $R = 0{\cdot}052$ using 1384 independent reflections. The molecular structure is illustrated in the Figure.†

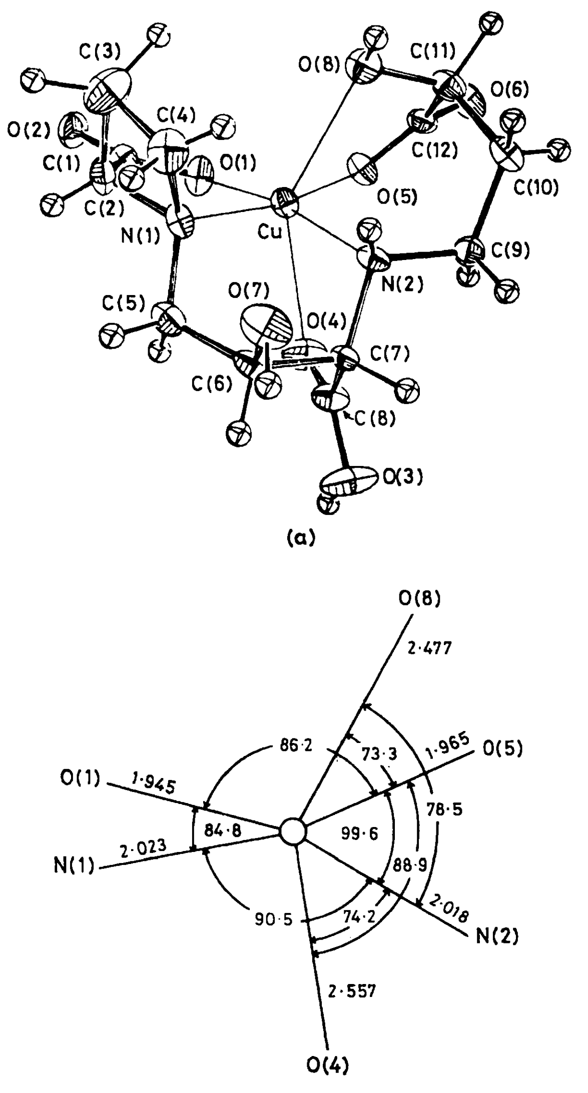


FIGURE. (a) A perspective drawing of the mugineic acid–Cu^{II} complex. (b) Co-ordination about the copper ion in the complex, with bond lengths (Å) and angles (°). E.s.d.s of the bond lengths and angles are 0·003—0·004 Å and 0·2°, respectively.

In view of the biological importance of copper complexes of amino-acids and peptides, numerous studies have been carried out to determine the modes of amino-acid and peptide chelation of copper. In many cases the co-ordinated copper atom adopts the tetragonally distorted octahedral

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† The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

geometry, and the two weaker apical bonds are linked either to other groups of an adjacent ligand molecule or to solvent molecules such as water.[4] As shown in the Figure, however, the central hexadentate copper ion of the title complex is co-ordinated solely to the oxygen and nitrogen functionalities of one ligand molecule, and the two axial bonds to the copper are weaker than the four equatorial bonds. Note also that C(3) and C(4) of the azetidine ring are not involved in the complexation. Mugineic acid is probably the lowest molecular weight natural product found so far which is capable of forming an intramolecular hexadentate copper complex.

(*Received, 2nd December* 1980; *Com.* 1285.)

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[1] S. Takagi, *Soil Sci. Plant Nutr.* (*Tokyo*), 1976, **22**, 423.

[2] T. Takemoto, K. Nomoto, S. Fushiya, R. Ouchi, G. Kusano, H. Hikino, S. Takagi, Y. Matsuura, and M. Kakudo, *Proc. Jpn. Acad., Ser. B.*, 1978, **54**, 469.

[3] J. G. Hunter and O. Vergano, *Ann. Appl. Biol.*, 1953, **40**, 761.

[4] H. C. Freeman in 'The Biochemistry of Copper,' eds. J. Peisach, P. Aisen, and W. E. Blumberg, Academic Press, New York, 1966, p. 77; N. Camerman, J. K. Fawcett, T. P. A. Kruck, B. Sarkar, and A. Camerman, *J. Am. Chem. Soc.*, 1978, **100**, 2690.