L'enchaînement intermoléculaire s'effectue de façon analogue dans les deux composés par deux types de liaisons hydrogènes décrites sur la Fig. 5 et correspondant pour chaque composé à deux bandes d'absorption infrarouge à 3350 et 3180 cm^{-1}.

Analogie structurale avec les dérivés du DPA

La conformation d'une partie de ces molécules peut être comparée à celle observée dans les amides dérivés du DPA. Les atomes C(2), C(3), C(5), C(7) de la DEPM forment un plan moyen P_1 équivalent à un des groupements propyles de la *N*-méthyl dipropylacétamide (Grand & Cohen-Addad, 1973), comme le montrent les Figs. 3 et 4. Ainsi les distances C(2)–C(7) valent 3,85 Å pour la DEPM et 3,88 Å pour la *N*-méthyl dipropylacétamide, les distances O–C(7) correspondantes étant de 4,69 et 4,68 Å respectivement.

Cette analogie se retrouve pour les autres amides du DPA qui ont des conformations identiques. De même, la DPPM peut être comparée à la dibutylacétamide (Cohen-Addad & Grand, 1974), les distances C(2)–C(9) valant 4,97 et 5,08 Å et les distances O–C(9), 5,64 et 5,65 Å, respectivement pour les deux composés.

En conclusion, à l'état cristallin, la diéthylpropionamide et la dipropylpropionamide sont des racémates de conformations semblables mais non isomorphes, qui présentent, en partie, une analogie structurale avec les amides dérivés du DPA. Contrairement à celles-ci, la symétrie de la chaîne dialkyle par rapport au plan du groupement amide n'est pas conservée pour la DEPM et la DPPM. Par ailleurs, d'après les comparaisons ci-dessus, la même analogie structurale que pour ces dérivés du DPA existe entre la DEPM, la DPPM et la conformation repliée de l'acide γ-aminobutyrique (Ferrandes *et al.*, 1974). Ceci justifie le phénomène d'inhibition compétitive de la GABA transaminase vis-à-vis du GABA présenté par les acides dialkylpropioniques. En relation avec ces résultats, d'autres composés de cette série seront étudiés.

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The Crystal and Molecular Structure of Bis-(L-asparaginato)copper(II), $[Cu(OOCCHNH_2CH_2CONH_2)_2]_n$

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The structure of bis-(L-asparaginato)copper(II) has been determined by photographic methods and refined to R 0·107 for 636 unique reflexions by least-squares procedures. The monoclinic unit cell, space group $P2_1$, has $a=5{\cdot}028$ (1), $b=18{\cdot}928$ (4), $c=6{\cdot}174$ (1) Å, $\beta=96{\cdot}4$ (1)°, $Z=2$. The Cu atom is in a tetragonally distorted octahedral environment. A carboxyl oxygen and the α-amino nitrogen atom from each ligand bond to Cu in a *trans* square-planar configuration (Cu–O 1·95, Cu–N 2·02 Å). The octahedron is completed by bridging amide oxygen atoms from adjacent molecules (Cu–O 2·53, 2·77 Å) separated by **c** translations. This arrangement produces infinite chains parallel to **c**. A three-dimensional hydrogen-bonding network between the chains is evident.

Introduction

Much interest has centred on the role of metal complexes of amino acids in cancer chemotherapy and the subject has been reviewed by Williams (1972*a*). The use of a mixed-ligand complex involving asparagine in combination with various metal ions has been suggested (Williams, 1972*b*) as a possible antimetabolite

in tumour cells. Charlson (1973) outlined work carried out which aimed at poisoning tumours with metal ions administered as the complexes of 1-aminocyclopentanecarboxylic acid, L-asparagine and L-glutamine. Biological testing and other related work on these compounds performed in this institution has been reported recently (Charlson, Trainor & Watton, 1974). The structure of L-asparagine is known (Kartha & de Vries, 1961), as is that of its complex with Cd (Flook, Freeman, Moore & Scudder, 1973). Here we present the results of the crystal-structure analysis of bis-(L-asparaginato)copper(II), $Cu(L\text{-}asn)_2$.

Experimental

The complex was prepared by adding a stoichiometric amount of cupric acetate in aqueous solution to a dilute aqueous solution of L-asparagine. Slow evaporation yielded royal-blue elongated prisms of $Cu(L\text{-}asn)_2$.

Analysis: calculated for $C_8H_{14}N_4O_6Cu$, C=29·5%, H=4·3%, N=17·2%; found C=29·8%, H=4·4%, N=17·1%.

Crystal data

$C_8H_{14}N_4O_6Cu$, $M=325{\cdot}8$, monoclinic, $a=5{\cdot}028$ (1), $b=18{\cdot}928$ (4), $c=6{\cdot}174$ (1) Å, $\beta=96{\cdot}4$ (1)°, $V=583{\cdot}9$ Å^3, $D_m=1{\cdot}84$ g cm^{-3} (by flotation), $Z=2$, $D_c=1{\cdot}85$ g cm^{-3}; $F(000)=334$, μ(Mo $K\alpha$)=20·2 cm^{-1}. Systematic absences $0k0$ if $k=2n+1$, space group $P2_1(C_2^2$, No. 4) or $P2_1/m$ (C_{2h}^2, No. 11).

Cell parameters were determined from precession photographs taken with Mo $K\alpha$ radiation. The crystal used for the collection of intensities had approximate dimensions 0·5×0·3×0·2 mm. Intensities were estimated visually from precession photographs for the layers 0–3 about **a**, **c** and [$\bar{1}$01]. Each reflexion was corrected for Lorentz and polarization effects but not for absorption or extinction. The observed structure-factor amplitudes were placed on a common scale by internal correlation and 636 non-zero unique reflexions were obtained.

Scattering factors were taken from *International Tables for X-ray Crystallography* (1962). All calculations were carried out with the X-RAY package (Stewart, Kruger, Ammon, Dickinson & Hall, 1972) on a UNIVAC 1108 computer.

Structure determination

For the centrosymmetric space group $P2_1/m$ with $Z=2$ the molecules must possess either a centre of symmetry or a mirror plane, neither of which is feasible for the molecule unless racemization has occurred. Thus the space group is $P2_1$, which imposes no symmetry constraints on the molecule and is confirmed by the successful refinement of the structure.

The positions of the Cu atom and the atoms forming the two five-membered coordination rings, O(11), N(11), C(11), C(12), O(21), N(21), C(21), C(22), were obtained from a Patterson synthesis. The complete solution of the structure for the non-hydrogen atoms was obtained from a series of Fourier syntheses each

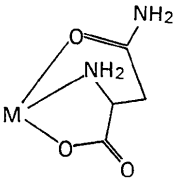

Fig. 1. Possible tridentate coordination of L-asparagine.

Table 1. *Atomic coordinates (fractional) and thermal parameters with estimated standard deviations in parentheses*

The anisotropic thermal parameters are in the form $\exp[-(h^2a^{*2}U_{11}+k^2b^{*2}U_{22}+l^2c^{*2}U_{33}+2hka^*b^*U_{12}+2hla^*c^*U_{13}+2klb^*c^*U_{23})]$.

	x/a	y/b	z/c	U (Å^2)
Cu	0·1906 (7)	0	0·2504 (6)	
O(11)	0·3961 (41)	−0·0874 (11)	0·2574 (40)	0·040 (5)
O(12)	0·4224(48)	−0·1944 (13)	0·3962 (39)	0·053 (6)
O(13)	−0·1484 (51)	−0·0500 (14)	0·8985 (43)	0·055 (7)
O(21)	−0·0112 (42)	0·0884 (12)	0·2234 (38)	0·041 (6)
O(22)	−0·0358 (46)	0·1937 (13)	0·0580 (40)	0·048 (6)
O(23)	0·4849 (42)	0·0537 (11)	−0·4330 (32)	0·035 (5)
N(11)	−0·0513 (51)	−0·0493 (13)	0·4387 (44)	0·034 (6)
N(12)	−0·1839 (54)	−0·1637 (15)	0·9867 (47)	0·043 (7)
N(21)	0·4119 (49)	0·0494 (14)	0·0389 (40)	0·032 (6)
N(22)	0·6493 (69)	0·1640 (20)	−0·5016 (63)	0·068 (9)
C(11)	0·2916 (70)	−0·1370 (19)	0·3611 (63)	0·046 (9)
C(12)	0·0605 (66)	−0·1202 (18)	0·5049 (58)	0·045 (8)
C(13)	0·1519 (63)	−0·1309 (17)	0·7449 (60)	0·044 (8)
C(14)	−0·0659 (65)	−0·1080 (18)	0·8742 (57)	0·041 (8)
C(21)	0·0520 (56)	0·1349 (14)	0·0769 (50)	0·029 (7)
C(22)	0·2185 (59)	0·0995 (15)	−0·0931 (51)	0·034 (7)
C(23)	0·3480 (63)	0·1528 (18)	−0·2112 (55)	0·045 (9)
C(24)	0·5134 (59)	0·1183 (14)	−0·3964 (50)	0·027 (6)

	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
Cu	0·0362 (15)	0·0297 (13)	0.0352 (16)	−0·0044 (27)	0·0086 (13)	0·0095 (23)

phased by an increasing number of atoms. A structure-factor calculation based on these 19 atoms gave an R of 0·22.

Refinement of the structure was carried out by full-matrix least-squares calculations in which the function minimized was $\sum w\Delta^2$. The weight for each reflexion was unity. Initially the refinement included positional and isotropic thermal parameters for each atom with an overall scale factor. In the latter stages anisotropic thermal parameters for Cu were used. Refinement was terminated when the shift in any parameter was less than $0{\cdot}05\sigma$. The final values for R and R' $[=(\sum w\Delta^2/\sum w|F_o|^2)^{1/2}]$ were 0·107 and 0·108, respectively. A final difference synthesis showed no peaks higher than 1·0 e Å^{-3}.

The final atomic coordinates and thermal parameters are given in Table 1.*

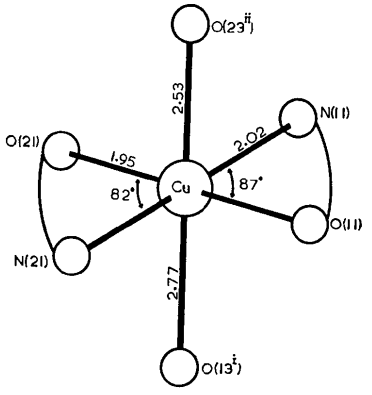

Fig. 2. Coordination about the copper atom.

Discussion

The bond lengths and angles are given in Table 2. Although at first hexa-coordination to the metal atom might be expected to occur *via* tridentate behaviour of two L-asparagine ligands (Fig. 1), molecular models suggest that such an arrangement would be severely strained. This appears to be the case as demonstrated by the present structure determination.

The coordination sphere about the copper atom is shown diagramatically in Fig. 2. A carboxyl oxygen and the α-amino nitrogen atom from each ligand coordinate to Cu in a *trans* square-planar configuration, the Cu–O and Cu–N distances being 1·95 and 2·02 Å, respectively.

The octahedral environment about Cu is completed

* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 30753 (6pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1 NZ, England.

Table 2. *Bond lengths* (Å) *and angles* (°), *with estimated standard deviations in parentheses*

Cu—O(11)	1·947 (21)	Cu—O(21)	1·954 (22)
Cu—N(11)	2·004 (28)	Cu—N(21)	2·035 (26)
Cu—O(13^{i})	2·774 (25)	Cu—O(23^{ii})	2·529 (20)
C(11)–O(11)	1·282 (44)	C(21)–O(21)	1·326 (38)
C(11)–O(12)	1·277 (43)	C(21)–O(22)	1·198 (36)
C(12)–N(11)	1·526 (38)	C(22)–N(21)	1·493 (42)
C(11)–C(12)	1·571 (53)	C(21)–C(22)	1·565 (44)
C(12)–C(13)	1·516 (50)	C(22)–C(23)	1·435 (46)
C(13)–C(14)	1·489 (50)	C(23)–C(24)	1·621 (47)
C(14)–O(13)	1·190 (43)	C(24)–O(23)	1·248 (34)
C(14)–N(12)	1·318 (48)	C(24)–N(22)	1·428 (45)
O(11)–Cu—N(11)	86·9 (10)	O(21)—Cu—N(21)	82·4 (9)
O(11)–Cu—O(13^{i})	90·3 (8)	O(21)—Cu—O(23^{ii})	88·6 (7)
N(11)–Cu—O(13^{i})	86·3 (9)	N(21)—Cu—O(23^{ii})	89·8 (8)
O(11)–Cu—O(21)	176·2 (10)	N(11)—Cu—N(21)	175·3 (10)
O(13^{i})–Cu—O(23^{ii})	176·1 (7)		
O(11)–Cu—N(21)	94·5 (10)	O(21)—Cu—N(11)	96·1 (10)
O(13^{i})–Cu—N(21)	89·2 (9)	O(23^{ii})–Cu—N(11)	94·6 (9)
O(13^{i})–Cu—O(21)	87·6 (8)	O(23^{ii})–Cu—O(11)	93·5 (8)
Cu—O(11)–C(11)	112·8 (21)	Cu—O(21)—C(21)	117·7 (19)
Cu—O(13^{i})–C(14^{i})	102·8 (20)	Cu—O(23^{ii})–C(24^{ii})	125·4 (17)
Cu—N(11)–C(12)	110·1 (20)	Cu—N(21)—C(22)	105·5 (17)
O(11)–C(11)–O(12)	118·5 (32)	O(21)—C(21)—O(22)	124·7 (29)
O(11)–C(11)–C(12)	120·3 (29)	O(21)—C(21)—C(22)	111·1 (23)
O(12)–C(11)–C(12)	118·4 (31)	O(22)—C(21)—C(22)	123·5 (27)
C(11)–C(12)–C(13)	111·3 (26)	C(21)—C(22)—C(23)	110·4 (24)
C(11)–C(12)–N(11)	107·9 (27)	C(21)—C(22)—N(21)	105·3 (23)
C(13)–C(12)–N(11)	116·9 (27)	C(23)—C(22)—N(21)	113·9 (24)
C(12)–C(13)–C(14)	108·9 (26)	C(22)—C(23)—C(24)	112·3 (26)
C(13)–C(14)–O(13)	128·6 (32)	C(23)—C(24)—O(23)	117·3 (26)
C(13)–C(14)–N(12)	114·6 (27)	C(23)—C(24)—N(22)	114·9 (27)
O(13)–C(14)–N(12)	116·8 (32)	O(23)—C(24)—N(22)	127·6 (31)

Roman numerals as superscripts refer to the following equivalent positions relative to the atoms at x,y,z: i $x,y,z-1$; ii $x,y,1+z$.

via amide oxygen atoms from neighbouring molecules. The two Cu to amide oxygen atom distances are not equivalent (2·53 and 2·77 Å) but their values are typical of those found in Cu(II) complexes with tetragonally elongated octahedral environments (Hathaway & Billing, 1970; Hathaway & Hodgson, 1973). The directions of these bonds are almost collinear with the normal to the least-squares plane through the atoms in the coordination square-plane (Table 3), the distortion angles being 2·1° [Cu–O(13^{i})] and 3·2° [Cu–O(23^{ii})]. The amide oxygen coordination links adjacent Cu environments and gives rise to infinite chains parallel to **c** (Fig. 3). This contrasts with the three-dimensional networks formed in other known metal complexes of amino acids (Flook *et al.*, 1973; Takenaka, Oshima, Yamada & Watanabé, 1973; Gramaccioli & Marsh, 1966). The chains are held in the crystal lattice by a hydrogen-bond network (Fig. 3).

Table 3. *Equations of the planes of best fit in the form* $lX'+mY'+nZ'-p=0$ *where the orthogonalized coordinates* X', Y', Z' *are derived from the atomic coordinates* X, Y, Z *by:* $X'=X+Z\cos\beta$, $Y'=Y$, $Z'=Z\sin\beta$

Deviations (Å) of the most relevant atoms from the planes are given in square brackets.

	l	*m*	*n*	*p*
Plane (1): Cu, N(11), N(21), O(11), O(21)	0·4957	0·3516	0·7941	1·5637

[Cu 0·046, N(11) −0·032, N(21) −0·032, O(11) 0·008, O(21) 0·009]

Plane (2): Cu, N(11), O(11), C(11), C(12)	0·5106	0·3294	0·7942	1·6037

[Cu 0·018, N(11) −0·059, O(11) 0·032, C(11) 0·085, C(12) −0·076, O(12) 0·060]

Plane (3): Cu, N(21), O(21), C(21)	0·5047	0·4245	0·7517	1·5847

[Cu −0·033, N(21) 0·023, O(21) 0·050, C(21) −0·041, C(22) −0·63, O(22) 0·13]

The two L-asparagine ligands are not equivalent and in particular show differences in the five-membered coordination rings. The ring formed by Cu, N(11), O(11), C(11), C(12) may be considered as planar whereas that formed for the corresponding atoms in the other ligand shows significant distortion from planarity (Table 3). Molecular models show that if the two ligands are of the same optical isomeric form and in a *trans* configuration then, to permit the amido-groups to bridge adjacent molecules, strain is enforced in one of the five-membered coordination rings. It is of interest that *cis*-coordination of the ligands would not enforce distortion for a similar bridging arrangement.

The bidentate behaviour of the α-amino acid group of the asparagine ligands in this structure is similar to that found in the corresponding cadmium (Flook *et al.*, 1973) and zinc (Stephens, Vagg & Williams, 1974) complexes. However in the latter compounds the amido groups remain uncoordinated and the bridging is *via* carbonyl oxygen atoms of the acid groups of neighbouring units.

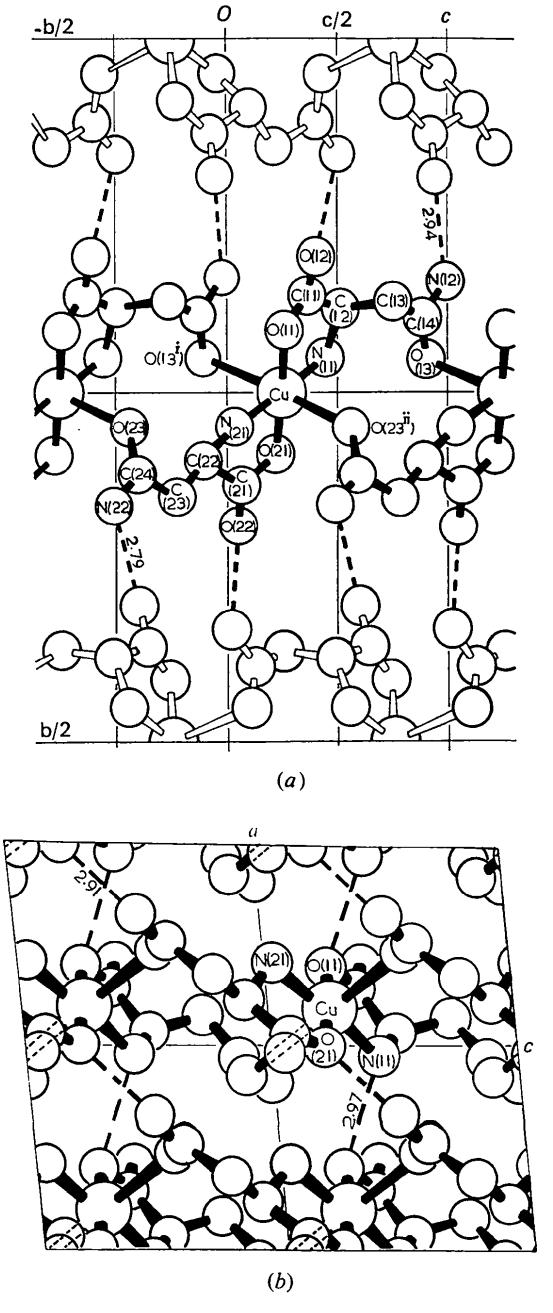

Fig. 3. Molecular packing in the crystal and the labelling of the atoms. Proposed hydrogen bonds are represented by broken lines. (*a*) Projection of the contents of the cell on the (100) plane. (*b*) Projection of the primary molecular unit on the (010) plane; those related to this by the screw axes are omitted for clarity.

We thank Mr K. E. Trainor, Dr A. J. Charlson and Professor E. C. Watton for suggesting the problem and for their many helpful discussions.

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The Crystal Structure of 8-Aza-2,6-diaminopurine Sulfate Monohydrate

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The crystal and molecular structure of 8-aza-2,6-diaminopurine sulfate monohydrate, $(C_4N_7H_6)_2SO_4.H_2O$, has been determined from three-dimensional diffractometer X-ray data. The material crystallizes in space group $P\bar{1}$ of the triclinic system with two formula units in a cell of dimensions $a=6{\cdot}813$ (5), $b=15{\cdot}117$ (11), $c=8{\cdot}182$ (5) Å, $\alpha=91{\cdot}71$ (1), $\beta=106{\cdot}21$ (1), and $\gamma=93{\cdot}57$ (1)°. The observed and calculated densities are 1·71 and 1·72 g cm^{-3}, respectively. The structure has been refined by full-matrix least-squares techniques to a final value of the conventional R value (on F) of 0·039 for 2706 independent intensities. The two independent 8-aza-2,6-diaminopurine cations (ADPH) are very similar, and the sites of protonation are at N(3) and N(8); this result is similar to that observed in the 8-azaguaninium cation (AGH) but different from that found in the protonated form of natural purines. The hydrogen bonding in the crystal is extremely complicated, with all hydrogen atoms and all acceptor atoms except N(1) of one ADPH cation participating. The bond lengths and angles in the cations are normal, showing the anticipated effects of the protonation at N(3) and N(8).

Introduction

8-Aza-2,6-diaminopurine and other 8-azapurines are extremely important analogs of the nucleic acid constituents because of their anti-neoplastic properties; the carcinostatic activities of these compounds vary greatly, however (Montgomery, Johnston & Shealy, 1970), with 8-azaguanine showing a broad range of activity while 8-aza-2,6-diaminopurine is only moderately effective against Adenocarcinoma 755 (Montgomery, 1959). In an attempt to obtain a rational correlation between the molecular structures of these compounds and their biological activities, we have undertaken a series of crystallographic investigations of the aza analogs of nucleic acid constituents. We report here the results of our three-dimensional X-ray determination of the crystal and molecular structure of 8-aza-2,6-diaminopurine sulfate monohydrate. A preliminary account of this structure has appeared elsewhere (Singh, Lewis, & Hodgson, 1974).

Experimental

8-Aza-2,6-diaminopurine sulfate was obtained from Sigma Chemical Co., St. Louis, Missouri, and plate-like crystals were grown by slow evaporation of a solution of the compound in 1 M sulfuric acid. The cell data are reported in Table 1. The space group was obtained from Weissenberg and precession photography, and the cell constants by least-squares refinement of the locations of 12 reflections on a diffractometer. The crystal used for the data collection had approximate dimensions 0·60 × 0·30 × 0·15 mm and was mounted along the long axis; this direction corresponds to the crystallographic a axis. Intensity data (see Table 1) were collected using a Picker FACS-I automatic

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