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Structures of 2-Amino-6-methyldipyrido[1,2-*a*:3′,2′-d]imidazole (Glu-P-1) and Its Hydrobromide Dihydrate: a Potent Mutagenic Product from the Dry Distillation of Glutamic Acid

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Abstract. $C_{11}H_{10}N_4$: monoclinic, $C2/c$, $a = 16{\cdot}579$ (7), $b = 9{\cdot}080$ (5), $c = 15{\cdot}137$ (7) Å, $\beta = 119{\cdot}02$ (2)°, $Z = 8$. $C_{11}H_{11}N_4^+.Br^-.2H_2O$: triclinic, $P\bar{1}$, $a = 10{\cdot}659$ (5), $b = 9{\cdot}342$ (5), $c = 7{\cdot}440$ (4) Å, $\alpha = 105{\cdot}43$ (2), $\beta = 75{\cdot}59$ (2), $\gamma = 108{\cdot}66$ (2)°, $Z = 2$. The final R values including H atoms were 0·04 and 0·05 respectively. The present study established the chemical and molecular structure of Glu-P-1, a small amount of which had been produced artificially.

Introduction. It was found that a charry material which is produced at the surface of broiled fish and meats exhibits a high mutagenic activity (Nagao, Honda, Seino, Yahagi, Kawachi & Sugimura, 1977; Sugimura *et al.*, 1977). Since then a certain mutagenic principle has been extracted from the pyrolysis products of DL-tryptophan, DL-phenylalanine and L-glutamic acid.

To obtain the precise structural information necessary for studying the mechanism of induction of mutation and to determine the protonation site for the hydrobromide, we have undertaken the present X-ray crystallographic analysis. A preliminary paper describing the extraction, purification and structure of the principle has been published (Yamamoto *et al.*, 1978).

The lattice constants and intensity data for both crystals were obtained with a Philips PW 1100 diffractometer using Cu $K\alpha$ radiation monochromated by a graphite plate. The θ–2θ scan technique was employed for the whole angular range up to $2\theta = 140°$.

Background was measured at each end of the scan range for half the total scan time. 955 and 1694 reflexions were measured, respectively, for the free and hydrobromide crystals as being above the $2\sigma(I)$ level. Lorentz and polarization corrections were applied to the intensities to obtain the structure amplitudes.

The crystal structure of the free molecule was determined by the direct method and that of the hydrobromide by the heavy-atom method. Both structures were refined by the block-diagonal least-squares method using the program *HBLS* IV (Okaya & Ashida, 1967).

The assignment of the atomic species, especially the location of the N atoms, was determined by inspection of a difference electron density map. Later, this was confirmed by elucidating the location of the H atoms and also by consideration of the chemical structure based on the refined bond lengths and angles. The composition of the molecule was in complete agreement with that found by mass spectrography. The final R values were 0·042 and 0·049, respectively, for the free and hydrobromide crystals including H atoms. Positional parameters are listed in Table 1.*

Discussion. The present determination elucidated the structure of Glu-P-1 as 2-amino-6-methyldipyrido[1,2-*a*:3′,2′-*d*]imidazole, as shown in Fig. 1. The bond lengths and valency angles for the two crystals are compared in Fig. 2. The standard deviations are estimated as σ(C–C) = 0·01 and 0·01, σ(C–H) = 0·08 and 0·08 Å, σ(C–C–C) = 0·7 and 0·6, σ(C–C–H) = 3·6 and 3·8 and σ(H–C–H) = 5·1 and 5·3° for the free molecule and hydrobromide respectively. As in Trp-P-1 (Itai & Iitaka, 1978), the present molecule consists of three conjugated fused rings. The planarities of the molecules are compared in Table 2.

The C···C and C···N bond lengths range from 1·343 to 1·426 Å and 1·329 to 1·405 Å, respectively, in the free molecule while they range from 1·340 to 1·426 Å and from 1·322 to 1·405 Å in the hydrobromide. The greatest differences in bond lengths between the free and hydrobromide molecules are 0·032 and 0·024 Å for the C(2)–C(3) and C(9)–N(4)

* Lists of structure factors and temperature factors for both compounds have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 34487 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

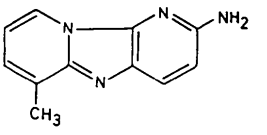

Fig. 1. Chemical structure of Glu-P-1.

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Table 1. *Fractional atomic coordinates* ($\times 10^4$, *for* H $\times 10^3$) *of Glu-P-1*

	x	*y*	*z*
(*a*) Free molecule			
C(1)	3075 (2)	−783 (4)	2059 (2)
C(2)	2452 (2)	−943 (4)	2450 (3)
C(3)	2615 (2)	−264 (4)	3328 (2)
C(4)	3424 (2)	556 (4)	3839 (2)
C(5)	4565 (2)	1958 (4)	4806 (2)
C(6)	5212 (2)	2925 (4)	5543 (2)
C(7)	5959 (2)	3318 (4)	5453 (3)
C(8)	6117 (2)	2770 (4)	4677 (3)
C(9)	5515 (2)	1851 (4)	3974 (2)
C(10)	3992 (2)	591 (3)	3404 (2)
C(11)	5035 (3)	3449 (5)	6375 (3)
N(1)	3862 (2)	−16 (3)	2543 (2)
N(2)	2862 (2)	−1387 (4)	1143 (2)
N(3)	3781 (2)	1417 (3)	4712 (2)
N(4)	4731 (2)	1475 (3)	4027 (2)
H(C2)	185 (2)	−143 (4)	204 (2)
H(C3)	217 (2)	−33 (3)	357 (2)
H(C7)	644 (2)	399 (3)	597 (2)
H(C8)	665 (2)	310 (3)	460 (2)
H(C9)	558 (2)	145 (3)	342 (2)
H(C11)	555 (3)	405 (4)	688 (3)
H′(C11)	485 (3)	254 (4)	664 (3)
H″(C11)	447 (2)	392 (4)	612 (3)
H(N2)	320 (2)	−133 (4)	86 (2)
H′(N2)	217 (2)	−194 (3)	68 (2)
(*b*) Hydrobromide dihydrate			
C(1)	3197 (6)	−84 (7)	3998 (8)
C(2)	1850 (6)	−261 (8)	3531 (9)
C(3)	1758 (6)	364 (8)	2055 (9)
C(4)	3007 (6)	1165 (7)	1171 (8)
C(5)	4693 (6)	2598 (7)	−582 (8)
C(6)	5553 (6)	3539 (7)	−1823 (8)
C(7)	6884 (7)	3999 (8)	−1762 (9)
C(8)	7405 (6)	3557 (9)	−466 (10)
C(9)	6578 (6)	2635 (7)	714 (9)
C(10)	4172 (5)	1292 (7)	1756 (8)
C(11)	4967 (7)	3991 (8)	−3187 (9)
N(1)	4290 (5)	680 (6)	3136 (6)
N(2)	3124 (5)	−714 (7)	5453 (8)
N(3)	3374 (5)	1999 (6)	−284 (7)
N(4)	5238 (4)	2182 (5)	671 (6)
Br	345 (1)	−2976 (1)	7704 (1)
O(1)	1426 (5)	2163 (6)	−1887 (7)
O(2)	1528 (6)	3967 (7)	−4327 (8)
H(N2)	390 (6)	−60 (7)	563 (7)
H′(N2)	230 (6)	−12 (7)	607 (7)
H(C2)	94 (5)	−89 (7)	410 (7)
H(C3)	88 (6)	25 (7)	176 (7)
H(N3)	270 (6)	204 (7)	−17 (8)
H(C11)	458 (6)	300 (7)	−248 (8)
H′(C11)	585 (6)	427 (7)	−248 (8)
H″(C11)	585 (6)	492 (7)	−367 (8)
H(C7)	752 (6)	460 (7)	−252 (8)
H(C8)	838 (6)	393 (7)	−56 (7)
H(C9)	688 (6)	208 (7)	160 (8)

bonds respectively, and for bond angles are 8·1 and 4·7°, respectively, for C(8)–C(9)–N(4) and C(4)–N(3)–C(5). The widening of C(4)–N(3)–C(5) in the protonated form has been commonly observed in

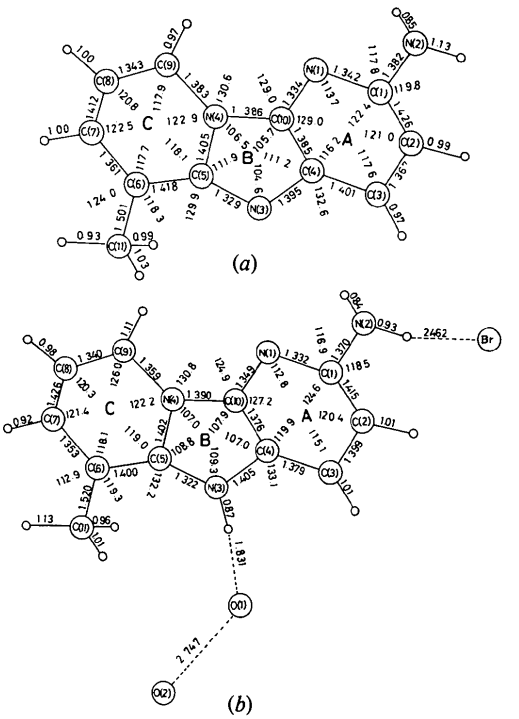

Fig. 2. Bond lengths (Å) and valency angles (°) of Glu-P-1 found in the crystals of (*a*) the free molecule, and (*b*) the hydrobromide dihydrate.

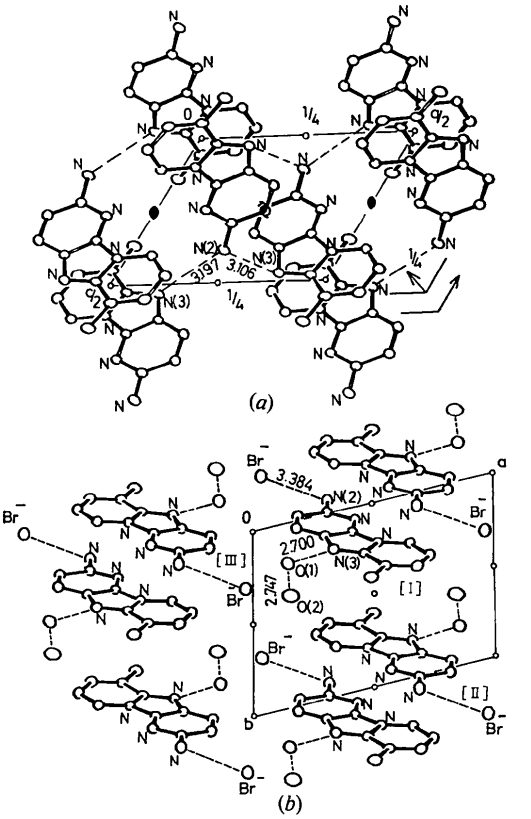

Fig. 3. Projections of the crystal structures of (*a*) the free molecule and (*b*) the hydrobromide dihydrate. Hydrogen bonds are shown by broken lines.

Table 2. *Deviations of the atoms from the least-squares planes*

		Free molecule	Hydrobromide molecule
Ring *A*	C(1)	0·012 Å	0·001 Å
	C(2)	−0·014	−0·009
	C(3)	0·003	0·008
	C(4)	0·010	0·002
	C(10)	−0·013	−0·010
	N(1)	0·002	0·009
	N(2)*	0·091	0·008
Ring *B*	N(3)	0·001	−0·001
	C(4)	−0·004	0·001
	C(10)	0·006	−0·001
	N(4)	−0·005	0·000
	N(5)	0·003	0·000
Ring *C*	N(4)	0·018	−0·003
	C(5)	−0·009	0·002
	C(6)	−0·007	−0·002
	C(7)	0·014	0·003
	C(8)	−0·005	0·003
	C(9)	−0·011	0·003
	C(11)*	−0·029	0·020

* Atoms not included in the least-squares calculation.

pyrimidines and purines (Sundaralingam & Jensen, 1965; Singh, 1965; Rao & Sundaralingam, 1970; Prusiner, Brennan & Sundaralingam, 1973; Koyama, Nakamura, Umezawa & Iitaka, 1976).

Comparison of the corresponding bond lengths and angles in the hydrobromide with those in Trp-P-1 acetic acid solvate (Itai & Iitaka, 1978) indicates that the most significant deviations are found in the five-membered ring. This may be the effect of the substitution of the C atom by N(4). As can be seen in Fig. 3(*b*), the protonated N(3) forms a strong hydrogen bond to the water O(1) with an N(3)···O(1) distance of 2·700 Å.

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The Structure of (*Z*)-2-Ethynyl-5-phenyl-2-adamantanol*

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Abstract. $C_{18}H_{20}O$, orthorhombic, $P2_12_12$, a = 20·743 (6), b = 13·286 (3), c = 10·243 (3) Å, Z = 8. R = 0·050 for 2700 reflections collected on a diffractometer using Cu $K\alpha$ radiation. There are two crystallographically independent molecules in the asymmetric unit which have the same Z configuration, but their phenyl groups are oriented differently with respect to the mirror planes of the adamantane moieties. The dihedral angles between these planes are 44·5 and 10·4°, the latter being the normal contact angle. The molecule with the larger angle exhibits strong thermal motion by fitting loosely in the structure. Effects of overcrowding on the shape of the phenyl groups are observed. A network of O—H···O hydrogen bonds holds the polar parts of the molecules with a disordered arrangement of the hydroxyl H atoms.

Introduction. This report is the second in our series of investigations on 2-substituted adamantanes (for the previous report see Okaya, Małuszyńska, Chiou & le Noble, 1978). The present structure has been chosen in order to establish its configuration; it is expected that

* Crystallographic Studies on Adamantanes. II.

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