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# Pyridoxal, $C_8H_9NO_3$, and Pyridoxamine Dihydrate, $C_8H_{12}N_2O_2.2H_2O$

By Cindy L. MacLaurin and Mary Frances Richardson

*Department of Chemistry, Brock University, St Catharines, Ontario, Canada L2S 3A1*

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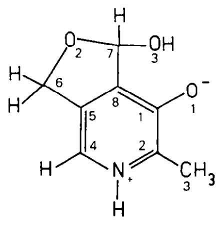
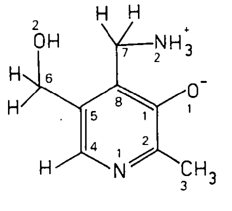
**Abstract.** Pyridoxal (PL): $M_r = 167\cdot16$, monoclinic, *Cc*, $a = 12\cdot093$ (1), $b = 9\cdot1067$ (7), $c = 7\cdot317$ (1) Å, $\beta = 113\cdot99$ (1)°, $V = 736\cdot19$ Å$^3$, $Z = 4$, $D_m = 1\cdot52$, $D_x = 1\cdot51$ g cm$^{-3}$, Mo $K\alpha$, $\lambda = 0\cdot71073$ Å, $\mu = 1\cdot25$ cm$^{-1}$, $F(000) = 352$, $T = 295$ K, $R = 0\cdot034$ for 1693 data with $F > 6\sigma(F)$. Pyridoxamine dihydrate ($PM.2H_2O$): $M_r = 204\cdot23$, monoclinic, $P2_1/c$, $a = 10\cdot8819$ (8), $b = 4\cdot6033$ (5), $c = 20\cdot9791$ (3) Å, $\beta = 96\cdot563$ (8)°, $V = 1043\cdot95$ Å$^3$, $Z = 4$, $D_m = 1\cdot35$, $D_x = 1\cdot30$ g cm$^{-3}$, Mo $K\alpha$, $\lambda = 0\cdot71073$ Å, $\mu = 1\cdot16$ cm$^{-1}$, $F(000) = 440$, $T = 295$ K, $R = 0\cdot039$ for 1394 data with $F > 6\sigma(F)$. PL exists as the hemiacetal in the zwitterionic form in which the pyridine ring is protonated. PM is also in a zwitterionic form with the aminomethyl group protonated. There is extensive hydrogen bonding in both structures.

**Introduction.** The $B_6$ vitamers contain a phenolic group and one or more basic sites thus allowing the possibility of several tautomeric forms for each vitamer. Infrared spectral data (T. A. Franklin & Richardson, 1980) suggested that pyridoxine (PN) existed in the solid in the nondipolar form, but that PL and $PM.2H_2O$ were dipolar, with the pyridine N and aminomethyl N protonated, respectively. The crystal structure of PN confirmed that it crystallizes in the nondipolar form (Longo, Franklin & Richardson, 1982) and the present work shows that PL and PM are in the predicted tautomeric forms. The structure of PL was solved previously by Rao, Poojary & Manohar (1982), but the coordinates were neither published nor deposited with the Cambridge Data Centre. Since our structure is the same as theirs, we have deposited all of the structural information for this compound.



**PL**



**PM**

**Experimental.** PL by neutralization of PL.HCl and recrystallization from water, crystal 0·57 × 0·23 × 0·15 mm; $PM.2H_2O$ by neutralization of PM.2HCl and recrystallization from water, crystal 0·45 × 0·06 × 0·03 mm; $D_m$ by flotation; CAD-4 diffractometer, graphite-monochromatized Mo $K\alpha$ radiation; lattice parameters from 25 reflections with $10° < \theta < 28°$ (PL) or $10° < \theta < 25°$ ($PM.2H_2O$); 3713 $\pm h$, $\pm k$, $\pm l$ reflections with $\theta < 30°$ for PL, 1743 unique; 3778 $h$, $\pm k$, $\pm l$ reflections with $\theta < 25°$ for $PM.2H_2O$, 1828 unique; $\omega$–$2\theta$ scans, $\omega$-scan width $(0\cdot8 + 0\cdot35\tan\theta)°$, extended 25% on each side for background measurement; Lp corrections, no absorption correction; one standard measured for each crystal, variation ±2%; structure solved by direct methods; full-matrix least squares refinement, $\sum w(|F_o| - |F_c|)^2$ minimized; H-atom positions calculated except $-CH_3$, $-OH$ and $-NH$; 125 parameters consisting of 49 positional parameters, 72 anisotropic temperature factors, two isotropic temperature factors for H atoms, an overall scale factor and an extinction parameter for PL; 173 parameters consisting of 84 positional parameters, 84 anisotropic temperature factors, two isotropic temperature factors for H atoms, an extinction coefficient, an overall scale factor, and an occupancy factor for the disordered methyl group for $PM.2H_2O$; $R_w = 0\cdot039$ for PL, 0·046 for $PM.2H_2O$; $w = [\sigma^2(F) + pF^2]^{-1}$, $p = 0\cdot0005$ for PL, 0·0006 for $PM.2H_2O$; $(\Delta/\sigma)_{\max}$ (non-H atoms) = 0·2 for PL, 0·4 for $PM.2H_2O$; final difference map with no features greater than 0·6 e Å$^{-3}$ or less than −0·4 e Å$^{-3}$ for PL, 0·2 and −0·2 e Å$^{-3}$ for $PM.2H_2O$; extinction coefficients 0·003 for PL, 0·01 for $PM.2H_2O$; scattering factors from *International Tables for X-ray Crystallography* (1974); computer programs *MULTAN*80 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980), *SHELX*76 (Sheldrick, 1976), and *ORTEP*II (Johnson, 1976).

**Discussion.** Final atomic coordinates for $PM.2H_2O$ are in Table 1; bond distances and bond angles are in Table 2.*

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* Lists of structure factors, anisotropic temperature factors, H atom positions, hydrogen-bonding parameters, and least-squares planes for $PM.2H_2O$ and atomic parameters, bond distances, bond angles, hydrogen-bonding parameters, and least-squares planes for PL have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39721 (31 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Table 1. *Atomic parameters for pyridoxamine dihydrate*

$$U_{\mathrm{eq}} = \tfrac{1}{3}\textstyle\sum_i\sum_j U_{ij}a^*_i a^*_j \mathbf{a}_i.\mathbf{a}_j.$$

| | $x$ | $y$ | $z$ | $U_{\mathrm{eq}}$(Å$^2$) |
|---|---|---|---|---|
| O(1) | 0·3357 (1) | 0·3539 (3) | 0·32327 (9) | 0·0317 |
| O(2) | 0·3427 (1) | 0·8296 (3) | 0·55507 (7) | 0·0399 |
| O(3) | 0·2999 (1) | 0·4287 (4) | 0·19545 (7) | 0·0405 |
| O(4) | −0·1988 (1) | 0·4318 (4) | 0·36333 (8) | 0·0426 |
| N(1) | 0·0550 (1) | 0·4689 (4) | 0·39689 (8) | 0·0325 |
| N(2) | 0·4624 (2) | 0·8547 (4) | 0·35311 (9) | 0·0327 |
| C(1) | 0·2591 (2) | 0·4529 (4) | 0·36310 (9) | 0·0249 |
| C(2) | 0·1337 (2) | 0·3661 (4) | 0·35783 (9) | 0·0277 |
| C(3) | 0·0846 (2) | 0·1512 (5) | 0·30742 (11) | 0·0377 |
| C(4) | 0·0968 (2) | 0·6585 (4) | 0·44326 (10) | 0·0321 |
| C(5) | 0·2175 (2) | 0·7560 (4) | 0·45271 (9) | 0·0270 |
| C(6) | 0·2566 (2) | 0·9617 (5) | 0·50735 (10) | 0·0360 |
| C(7) | 0·4329 (2) | 0·7496 (5) | 0·41688 (10) | 0·0337 |
| C(8) | 0·3000 (2) | 0·6530 (5) | 0·41146 (9) | 0·0249 |

Table 2. *Principal bond distances* (Å) *and angles* (°) *in pyridoxamine dihydrate*

| | | | |
|---|---|---|---|
| C(1)—O(1) | 1·327 (2) | C(5)—C(6) | 1·510 (3) |
| C(1)—C(2) | 1·414 (3) | C(6)—O(2) | 1·427 (2) |
| C(2)—C(3) | 1·501 (3) | C(5)—C(8) | 1·399 (3) |
| C(2)—N(1) | 1·338 (2) | C(7)—C(8) | 1·505 (3) |
| N(1)—C(4) | 1·347 (2) | C(7)—N(2) | 1·492 (2) |
| C(4)—C(5) | 1·381 (3) | C(8)—C(1) | 1·404 (3) |

| | | | |
|---|---|---|---|
| C(4)—N(1)—C(2) | 119·0 (2) | C(6)—C(5)—C(4) | 119·6 (2) |
| C(2)—C(1)—O(1) | 121·6 (2) | C(8)—C(5)—C(4) | 117·9 (2) |
| C(8)—C(1)—O(1) | 120·7 (2) | C(8)—C(5)—C(6) | 122·5 (2) |
| C(8)—C(1)—C(2) | 117·7 (2) | C(5)—C(6)—O(2) | 111·8 (2) |
| C(1)—C(2)—N(1) | 122·1 (2) | C(8)—C(7)—N(2) | 109·4 (1) |
| C(3)—C(2)—N(1) | 117·6 (2) | C(5)—C(8)—C(1) | 119·8 (2) |
| C(3)—C(2)—C(1) | 120·2 (2) | C(7)—C(8)—C(1) | 118·1 (2) |
| C(5)—C(4)—N(1) | 123·5 (2) | C(7)—C(8)—C(5) | 122·2 (2) |

The PM molecule is shown in Fig. 1. PM is a zwitterion in the crystal, where a proton has been transferred from the phenolic group to the aminomethyl group. Bond distances and angles are similar to those in other vitamin $B_6$ derivatives (Bacon & Plant, 1980; K. J. Franklin & Richardson, 1980; Longo & Richardson, 1980; Longo, Franklin & Richardson, 1982; Rao, Poojary & Manohar, 1982). The differences which do occur are characteristic of the particular zwitterion; *e.g.* the C(1)—O(1) distance is shorter in structures containing an ionized phenolic group than in derivatives having an un-ionized phenolic group. The C(1)—O(1) distances in PL and PM.$2H_2O$ are 1·290 (1) and 1·327 (2) Å, respectively, whereas this distance in nondipolar pyridoxine is 1·374 (4) Å (Longo, Franklin & Richardson, 1982).

The pyridine ring is essentially planar in PM.$2H_2O$, but the non-ring atoms C(3), C(6), C(7), and O(1) deviate from the ring plane by −0·027 (2) to 0·054 (2) Å. This is common for vitamin $B_6$ structures but there are no obvious patterns in the deviations from planarity.

The packing diagram for PM.$2H_2O$ is shown in Fig. 2. Each of the eight potential hydrogen-bond donors is involved in hydrogen bonding. Surprisingly, the phenolate oxygen O(1) acts as an acceptor in three hydrogen bonds: an intramolecular one [N(2)—N(N2*A*)···O(1)], an intermolecular one [N(2)—H(N2*C*)···O(1)($x$, $y$+1,$z$)], and one from a water molecule [O(3)—H(O3*B*)···O(1)]. The pyridine nitrogen N(1) is hydrogen bonded to the water molecule O(4). Additional hydrogen bonds link the water molecules to each other and to the $-CH_2OH$ and $-CH_2NH_3^+$ substituents on the ring. The N···O and O···O distances range from 2·7 to 2·9 Å, and the angles at H vary from 135 to 180°.

There are two basic packing arrangements in vitamin $B_6$ structures. In the first, translationally related molecules are stacked and the $b$ axis is about 4·6 Å long. In the second, glide-related molecules are stacked along the $b$ axis, and the $b$ axis is about 9·1 Å long. PM.$2H_2O$ adopts the first arrangement, as does pyridoxine (Longo, Franklin & Richardson, 1982). PL and PM.HCl adopt the second packing (Rao, Poojary & Manohar, 1982; Longo & Richardson, 1980). It is tempting to relate the differences in stacking to the protonation sites: both PL and PM.HCl are protonated at the pyridine-ring N atom, whereas pyridoxine and PM.$2H_2O$ are not. Stacking glide-related molecules

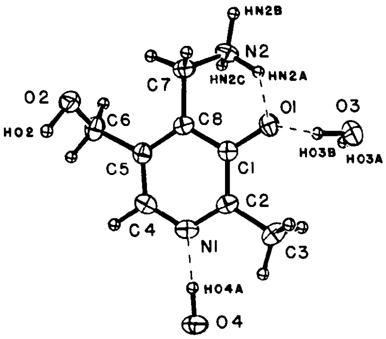

Fig. 1. Molecular structure and numbering scheme for PM.$2H_2O$. Dotted lines indicate hydrogen bonds. The small spheres are H atoms; H(O4*B*) is not shown as it lies directly under O(4). Thermal ellipsoids are shown at the 50% probability level.

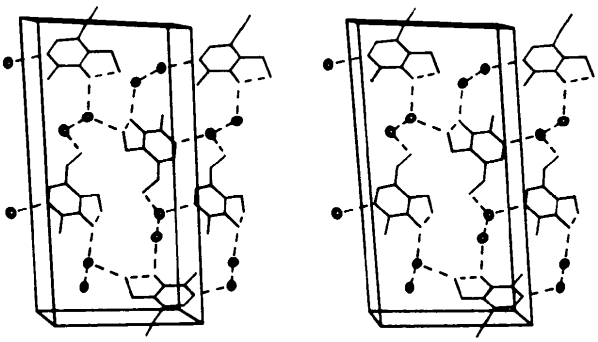

Fig. 2. Packing diagram for PM.$2H_2O$. The $x$ axis is horizontal; $z$ is vertical. Dotted lines indicate hydrogen bonds.

places the centres of positive charge as far apart as possible. Translational stacking is not surprising for pyridoxine since it is nondipolar in the crystal. However, minimizing electrostatic repulsions is not the sole determinant of packing behaviour, as PM.$2H_2O$ contains translational stacks of PM molecules in spite of the fact that PM is a zwitterion.

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# *N*-Isobutyrylbenzamide, $C_{11}H_{13}NO_2$

By Robert B. Bates,* Kim D. Janda and Michael E. Wright

*Department of Chemistry, University of Arizona, Tucson, Arizona* 85721, *USA*

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**Abstract.** $M_r = 191{\cdot}2$, orthorhombic, $Pca2_1$, $a = 8{\cdot}878\,(2)$, $b = 13{\cdot}464\,(4)$, $c = 9{\cdot}009\,(2)$ Å, $U = 1077\,(1)$ Å$^3$, $Z = 4$, $D_x = 1{\cdot}179$ Mg m$^{-3}$, $\lambda$(Mo $K\alpha$) $= 0{\cdot}71073$ Å, $\mu = 0{\cdot}088$ mm$^{-1}$, $F(000) = 408$, $T = 293$ K. Final $R = 0{\cdot}048$ for 385 observed reflections. A product of an unusual oxidation reaction is shown to be the title compound, apparently the first acyclic imide to be studied by X-ray crystallography. Unlike cyclic imides, this imide has O atoms in a 'U' conformation. Electrostatic repulsions between O atoms are relieved by twisting the $\pi$ system and by opening the O—C—N and C—N—C angles. Bifurcated hydrogen bonds from HN to the O atoms of an adjacent molecule join adjacent molecules in the crystal.

**Introduction.** During efforts to synthesize the antitumor agent deoxybouvardin, we hydrogenated the azlactone prepared by condensing acetone with hippuric acid and obtained, among other products (Bates & Janda, 1984), a highly crystalline substance in 2% yield whose $^1$H NMR spectrum indicated the presence of an isopropyl group and a phenyl group. A crystal-structure analysis was performed on this substance when it appeared to be the best method of establishing the arrangement of atoms between the isopropyl group and phenyl group.

**Experimental.** Crystal dimensions $0{\cdot}4 \times 0{\cdot}1 \times 0{\cdot}1$ mm. Syntex $P2_1$ four-circle diffractometer. Cell constants from 25 reflections with $7 \leq 2\theta \leq 14°$. No absorption correction. $2\theta_{\max} = 45°$. Range of *hkl*: 0–9, 0–14, 0–9. Three check reflections collected after every 200 data points showed no appreciable crystal decay. 385 of 764 reflections with $I > 3\sigma(I)$ used in $F^2$ refinement, $R_{\text{int}} = 0{\cdot}048$. Structure solved by *MULTAN*80 (Main *et al.*, 1980) using 180 highest *E* values; 11 non-H atoms found in first *E* map; other three non-H atoms put in calculated positions. Refinement of non-H atoms with isotropic temperature factors gave $R = 0{\cdot}102$, final refinement (126 parameters) was of non-H atoms with anisotropic temperature factors after adding H atoms in calculated positions with isotropic temperature factors; $R = 0{\cdot}048$, $wR = 0{\cdot}054$, $S = 2{\cdot}0$, weighting scheme of Corfield, Doedens & Ibers (1967), with $p = 0{\cdot}04$. $(\Delta/\sigma)_{\max} = 0{\cdot}007$. $\Delta\rho = -0{\cdot}3$–$0{\cdot}3$ e Å$^{-3}$. Atomic scattering factors from *International Tables for X-ray Crystallography* (1962). Least-squares-refinement program *NUCLS* (Doedens & Ibers, 1967), plotter program *ORTEP* (Johnson, 1965).

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* To whom correspondence should be addressed.

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