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Structure of Iproniazid Phosphate

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Abstract

All hydrogen positions in the structure of a potent monoamine oxidase inhibitor, iproniazid phosphate, 1-isonicotinoyl-2-isopropylhydrazinium phosphate, $C_9H_{14}N_3O^+.H_2PO_4^-$, have been determined and refined. The isopropylhydrazine side chain is protonated and extended. N and O atoms of the iproniazid cation and O atoms of the $H_2PO_4^-$ anion are held together by a hydrogen-bond network.

Comment

Iproniazid perfectly inhibits the activity of monoamine oxidase (MAO), which is important for drug metabolism (Masuda, Nakamura & Shimomura, 1990). It also has carcinogenic potency (Parodi *et al.*, 1981). The crystal structure of iproniazid phosphate has been determined previously with a final value of $R = 0.089$ by using Cu $K\alpha$ radiation (Chieh & Palenik, 1971). Since the H atoms in both the isopropyl and phosphate groups could not be determined, the structure including all H atoms was determined and refined in this study. The two structures resemble each other in their protonation and hydrogen-bond schemes.

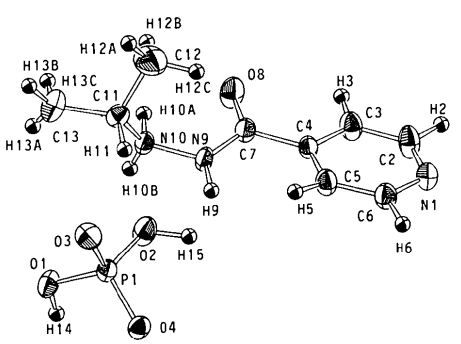

Fig. 1. Perspective view of iproniazid phosphate with the atomic numbering scheme.

Experimental

Crystal data

$C_9H_{14}N_3O^+.H_2O_4P^-$
$M_r = 277.22$
Triclinic
$P\bar{1}$
$a = 9.036$ (1) Å
$b = 10.094$ (1) Å
$c = 7.8868$ (9) Å
$\alpha = 94.11$ (1)°
$\beta = 98.84$ (1)°
$\gamma = 116.556$ (8)°
$V = 627.7$ (1) Å^3
$Z = 2$
$D_x = 1.467$ Mg m^{-3}
Mo $K\alpha$ radiation
$\lambda = 0.71069$ Å
Cell parameters from 25 reflections
$\theta = 18.6$–$20.75°$
$\mu = 0.229$ mm^{-1}
$T = 296$ K
Plate
0.4 × 0.3 × 0.3 mm
Colorless
Crystal source: Tokyo Kasei Kogyo Ltd, lot AZ01

Data collection

Rigaku AFC-5*R* diffractometer
ω-2θ scans
Absorption correction: *DIFABS* (Walker & Stuart, 1983)
$T_{min} = 0.92$, $T_{max} = 1.10$
3050 measured reflections
2869 independent reflections
2088 observed reflections $[I > 3\sigma(I)]$
$R_{int} = 0.016$
$\theta_{max} = 27.5°$
$h = 0 \rightarrow 11$
$k = -12 \rightarrow 11$
$l = -9 \rightarrow 9$
3 standard reflections monitored every 150 reflections
intensity variation: 2.02%

Refinement

Refinement on F
Final $R = 0.039$
$wR = 0.046$
$S = 1.55$
2088 reflections
227 parameters
All H-atom parameters refined
$w = 4F_o^2/[\sigma^2(F_o^2)]$
$(\Delta/\sigma)_{max} = 0.02$
$\Delta\rho_{max} = 0.22$ e Å^{-3}
$\Delta\rho_{min} = -0.39$ e Å^{-3}
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV, Table 2.2A)

The scan rate was 32° min^{-1} in ω and the scan width was $(1.52 + 0.30 \tan\theta)°$. The ratio of peak counting time to background counting time was 2:1. Refinement was by full-matrix least squares. H atoms were revealed on a difference Fourier map and were included in further refinement with isotropic thermal parameters. Data collection: *Rigaku MSC/AFC Data Collection and Refinement Software* (Rigaku Corporation, 1988). Cell refinement: *Rigaku MSC/AFC Data Collection and Refinement Software*. Programs used to solve structure: *MITHRIL* (Gilmore, 1984); *DIRDIF* (Beurskens, 1984). All calculations including data reduction: *TEXSAN* (Molecular Structure Corporation, 1985).

Table 1. *Atomic coordinates and isotropic or equivalent isotropic thermal parameters* (Å^2)

B_{iso} for H atoms; $B_{eq} = (8\pi^2/3)\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$ for other atoms.

	x	y	z	B_{iso}/B_{eq}
P(1)	0.92340 (7)	0.35902 (6)	0.26902 (8)	1.93 (2)
O(1)	0.8137 (2)	0.3128 (2)	0.4107 (2)	2.70 (5)
O(2)	1.0536 (2)	0.2981 (2)	0.3095 (3)	3.32 (7)
O(3)	0.8048 (2)	0.2794 (2)	0.0972 (2)	2.79 (6)
O(4)	1.0153 (2)	0.5275 (2)	0.2844 (2)	2.23 (5)
O(8)	1.1627 (3)	0.1033 (2)	−0.0787 (3)	3.49 (7)
N(1)	1.6383 (3)	0.5302 (2)	−0.2533 (3)	2.68 (6)
N(9)	1.0403 (2)	0.2456 (2)	−0.1605 (3)	2.27 (6)
N(10)	0.8852 (2)	0.1410 (2)	−0.1236 (2)	1.98 (6)

C(2)	1.6264 (3)	0.4175 (3)	−0.1684 (4)	3.14 (9)
C(3)	1.4778 (3)	0.3147 (3)	−0.1301 (3)	2.80 (8)
C(4)	1.3317 (3)	0.3277 (3)	−0.1816 (3)	2.03 (7)
C(5)	1.3420 (3)	0.4429 (3)	−0.2724 (3)	2.54 (8)
C(6)	1.4966 (3)	0.5413 (3)	−0.3035 (3)	2.62 (8)
C(7)	1.1718 (3)	0.2158 (2)	−0.1361 (3)	2.18 (7)
C(11)	0.7470 (3)	0.0672 (3)	−0.2840 (3)	2.40 (7)
C(12)	0.7931 (5)	−0.0167 (4)	−0.4154 (5)	4.5 (1)
C(13)	0.5861 (4)	−0.0298 (4)	−0.2263 (4)	3.7 (1)
H(2)	1.731 (4)	0.4111 (3)	−0.133 (3)	3.9 (6)
H(3)	1.480 (4)	0.232 (3)	−0.066 (4)	4.3 (7)
H(5)	1.246 (3)	0.456 (3)	−0.314 (3)	2.9 (5)
H(6)	1.507 (3)	0.622 (3)	−0.364 (4)	3.7 (6)
H(9)	1.038 (3)	0.321 (3)	−0.192 (3)	3.5 (6)
H(10*A*)	0.907 (3)	0.073 (3)	−0.073 (3)	2.7 (5)
H(10*B*)	0.850 (4)	0.204 (4)	−0.008 (4)	6.5 (9)
H(11)	0.738 (3)	0.151 (3)	−0.330 (3)	3.1 (6)
H(12*A*)	0.706 (4)	−0.063 (4)	−0.519 (5)	5.8 (8)
H(12*B*)	0.813 (4)	−0.083 (4)	−0.358 (4)	4.3 (8)
H(12C)	0.898 (4)	0.046 (4)	−0.445 (4)	5.3 (8)
H(13*A*)	0.556 (4)	0.023 (4)	−0.136 (5)	5.6 (8)
H(13*B*)	0.491 (4)	−0.064 (4)	−0.323 (5)	6.0 (8)
H(13C)	0.592 (5)	−0.106 (4)	−0.184 (5)	7.0 (1)
H(14)	0.870 (4)	0.370 (4)	0.501 (4)	5.6 (9)
H(15)	1.151 (5)	0.354 (4)	0.281 (5)	7.0 (1)

Table 2. *Bond lengths* (Å), *bond angles* (°) *and hydrogen-bond lengths* (Å)

P(1)—O(1)	1.565 (2)	O(1)—H(14)	0.82 (3)
P(1)—O(2)	1.557 (2)	O(2)—H(15)	0.89 (4)
P(1)—O(3)	1.502 (2)	N(9)—H(9)	0.83 (3)
P(1)—O(4)	1.508 (2)	N(10)—H(10*A*)	0.89 (3)
O(8)—C(7)	1.226 (3)	N(10)—H(10*B*)	1.24 (4)
N(1)—C(2)	1.333 (3)	C(2)—H(2)	0.98 (3)
N(1)—C(6)	1.337 (3)	C(3)—H(3)	1.01 (3)
N(9)—N(10)	1.418 (2)	C(5)—H(5)	0.95 (3)
N(9)—C(7)	1.341 (3)	C(6)—H(6)	0.95 (3)
N(10)—C(11)	1.504 (3)	C(11)—H(11)	0.98 (3)
C(2)—C(3)	1.377 (3)	C(12)—H(12*A*)	0.96 (3)
C(3)—C(4)	1.386 (3)	C(12)—H(12*B*)	0.90 (3)
C(4)—C(5)	1.385 (3)	C(12)—H(12*C*)	0.95 (3)
C(4)—C(7)	1.500 (3)	C(13)—H(13*A*)	1.00 (4)
C(5)—C(6)	1.378 (3)	C(13)—H(13*B*)	0.97 (4)
C(11)—C(12)	1.512 (4)	C(13)—H(13*C*)	0.88 (4)
C(11)—C(13)	1.508 (4)		
O(1)—P(1)—O(2)	105.3 (1)	C(3)—C(4)—C(5)	118.0 (2)
O(1)—P(1)—O(3)	106.3 (1)	C(3)—C(4)—C(7)	118.1 (2)
O(1)—P(1)—O(4)	110.1 (1)	C(5)—C(4)—C(7)	123.9 (2)
O(2)—P(1)—O(3)	110.4 (1)	C(4)—C(5)—C(6)	118.9 (2)
O(2)—P(1)—O(4)	109.74 (9)	N(1)—C(6)—C(5)	123.4 (2)
O(3)—P(1)—O(4)	114.6 (1)	O(8)—C(7)—N(9)	121.9 (2)
C(2)—N(1)—C(6)	117.4 (2)	O(8)—C(7)—C(4)	121.5 (2)
N(10)—N(9)—C(7)	118.6 (2)	N(9)—C(7)—C(4)	116.7 (2)
N(9)—N(10)—C(11)	112.5 (2)	N(10)—C(11)—C(12)	111.6 (2)
N(1)—C(2)—C(3)	123.5 (2)	N(10)—C(11)—C(13)	107.4 (2)
C(2)—C(3)—C(4)	119.0 (2)	C(12)—C(11)—C(13)	113.8 (3)

D (at *x*, *y*, *z*)	*A*	*D*···*A*	Symmetry code
O(2)	N(1)	2.670 (3)	i
N(10)	O(3)	2.553 (3)	ii
N(9)	O(4)	2.761 (3)	iii
O(1)	O(4)	2.615 (3)	iv
N(10)	O(8)	2.939 (3)	v

Symmetry code: (i) $3-x, 1-y, -z$; (ii) x, y, z; (iii) $2-x, 1-y, -z$; (iv) $2-x, 1-y, 1-z$; (v) $-2-x, -y, -z$.

Lists of structure factors, anisotropic thermal parameters and complete geometry have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 71205 (24 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: OH1009]

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Structure of 2,4-Dinitrophenylhydrazine

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Abstract

The crystal structure of a potential DNA damaging and mutagenic agent, 2,4-dinitrophenylhydrazine, has been determined. The four nitro O atoms and the amino N atom of the hydrazine side chain are almost in the same plane as the phenyl ring. The three-dimensional arrangement of the molecules is held together by hydrogen bonds between nitro O atoms and the imino and amino groups of the hydrazine side chain.

Comment

A number of hydrazine derivatives have been widely used in the medical and industrial fields. They have been shown to be potentially carcinogenic in animals having DNA damaging activity or mutagenicity (Toth, 1975; Parodi *et al.*, 1981; Mori *et al.*, 1988; Morpurgo *et al.*, 1988). However, the modes of action of hydrazine derivatives have not yet been clarified. In order to investigate their biological activity, it is important to determine their precise structures. In this study, as one of structural determinations of hydrazine derivatives, the structure of 2,4-dinitrophenylhydrazine has been determined.