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Ethyl (2-pyridylmethyl)phosphonate

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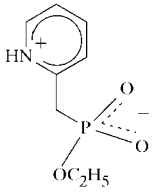
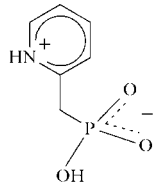
Molecules of the title compound, $C_8H_{12}NO_3P$, exist as zwitterions. The positive charge formally located on the N atom is spread over the pyridyl ring. A partial delocalization of negative charge within the O⋯P⋯O system is observed. The conformational features and hydrogen-bonding network of the title compound are compared with the structure of (2-pyridylmethyl)phosphonic acid.

Comment

Coordination compounds of Pt^{II} (cisplatin, carboplatin and oxaliplatin) are widely use in antitumor therapy (Reedijk, 2003; Judson & Kelland, 2000), and platinum–aminophosphonate complexes show particular activity against bone malignancies (Bloemink *et al.*, 1999; Galanski *et al.*, 1999), since phosphonic acid derivatives display a high affinity to bone tissue (Klenner *et al.*, 1990). Platinum(II) complexes containing diethyl pyridylmethylphosphonate, which are analogs of cisplatin, have shown antitumor activity against sarcoma Sa 180 in mice (Aranowska *et al.*, 2005), and are also capable of activating *in vivo* mast cells (Brzezińska-Błaszczyk *et al.*, 1996) and affecting *in vitro* blood platelet aggregation (Kostka & Ochocki, 1996).



(I)



(II)

Following our work on the synthesis and structure determination of pyridylmethylphosphonate derivatives as novel ligands (Chęcińska *et al.*, 2002) for antineoplastic platinum(II) complexes (Chęcińska *et al.*, 2003), the title compound, (I) (Fig. 1), was synthesized and an X-ray diffraction study was undertaken. We compare the results with the crystal structure of (2-pyridylmethyl)phosphonic acid, (II) (Gałdecki & Wolf, 1990). The Cambridge Structural Database (CSD; Version 5.25; Allen, 2002) contains many structures involving diethyl pyridylmethylphosphonates (especially as ligands in metal complexes) but no structure of a monoester of pyridylmethylphosphonate.

Molecules of aminophosphonic acids usually exists as zwitterions, as does (I). The N atom is protonated, and the positive charge formally located on this N atom is spread over the pyridyl ring. The significant difference between the P1—O1 and P1—O3 bond distances (Table 1) may indicate a partial delocalization of negative charge within the O⋯P⋯O system. These P—O bond lengths differ significantly from the corresponding values observed for (II) [1.507 (3) and 1.500 (4) Å; Gałdecki & Wolf, 1990] and (4-pyridylmethyl)-phosphonic acid [1.506 (2) and 1.5039 (14) Å; Gałdecki & Wolf, 1996]. On the other hand, the P1—O1 and P1—O3 distances are similar to those found in the structure of 3-pyridylmethylphosphonic acid [1.4860 (18) and 1.515 (17) Å; Chęcińska *et al.*, 2002]. It is interesting to compare the overall orientations of the molecules of (I) and (II). While the two molecules have essentially similar conformations, they differ in the positioning of the N atom with regard to the phosphonate group (Fig. 2). The orientation of the linking C atom causes a 'reversed' conformation (Table 3). In both structures, the P atom has tetrahedral geometry (distorted towards trigonal pyramidal), with an elongated P1—C1 apical bond. It seems that two effects may influence the angular deformation of these PO_3C tetrahedra, *viz*. their molecular structural differences and/or intermolecular interactions.

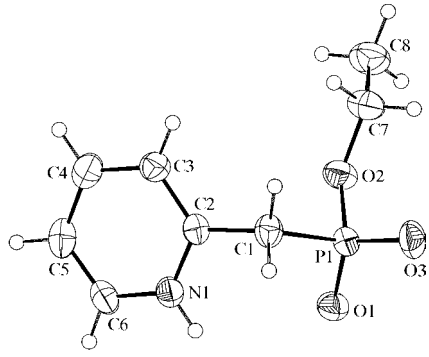


Figure 1
The structure of the title compound, showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 40% probability level and H atoms are shown as small spheres of arbitrary radii.

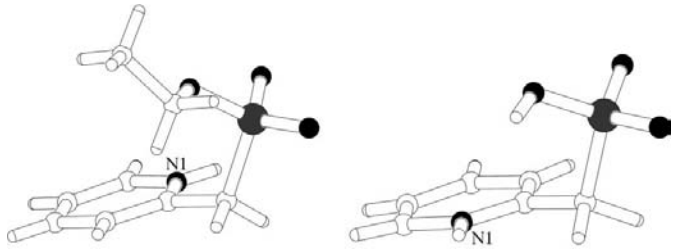


Figure 2
A comparison of the molecular conformations of (I) and (II).

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The crystal-packing arrangements in (I) and (II) are as follows. The hydrogen-bonding network in (I) is different from that in (II) (Figs. 3 and 4), resulting in part from the absence of aromatic π–π interactions between the pyridyl rings in (I). Moreover, an N1—H1···O1($1-x$, $1-y$, $1-z$) hydrogen bond is responsible for the formation of a cyclic dimer about a centre of symmetry; an $R_2^2(12)$ graph-set descriptor (Bernstein *et al.*, 1995) is generated. Additionally, the crystal structure is dominated by a network of weak intermolecular C—H···O interactions. These three interactions (Table 2) produce patterns whose first-level descriptors are *C*(7), *C*(4) and *C*(6), respectively. This combination of N—H···O and C—H···O hydrogen bonds links the molecules into a three-dimensional network. In the structure of (I), a weak intermolecular C—H···π interaction is also observed, whereas this type of interaction is not found in (II).

In (II), atom N1 is involved in an almost linear intermolecular N1—H2···O3 interaction (Table 4). Propagation of this contact produces a chain running along [001], which can be described by the *C*(6) motif (Bernstein *et al.*, 1995). A short intermolecular contact of 2.559 (5) Å between atoms O1 and O2($1-x$, $-y$, $1-z$) is also observed. The packing of (II) involves two weak C—H···O interactions (Table 4), which link the molecules to form infinite chains running parallel to the [001] direction; for both chains, the first-level graph-set descriptor is *C*(7). All three chains are organized into closely packed layers perpendicular to the *a* axis. Neighbouring layers are further connected *via* π–π stacking interactions between the pyridyl rings, with an interplanar spacing of 3.49 Å [the centroid–centroid separation is 3.623 (3) Å].

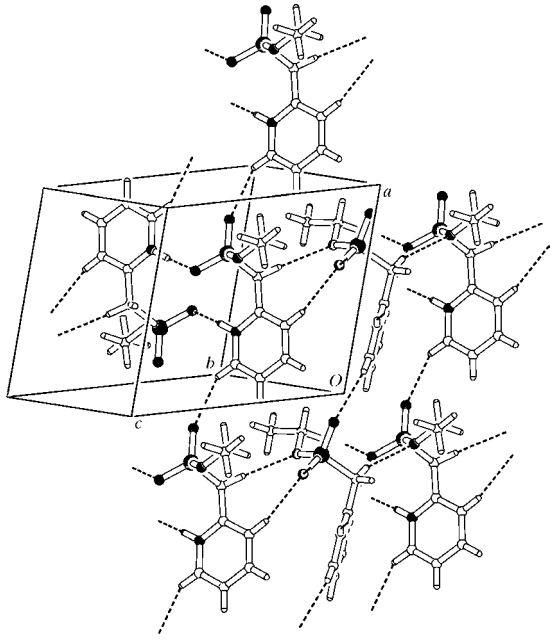

Figure 3
The hydrogen-bonding network in (I). P, O and N atoms are shaded. Dashed lines indicate hydrogen bonds and weak interactions.

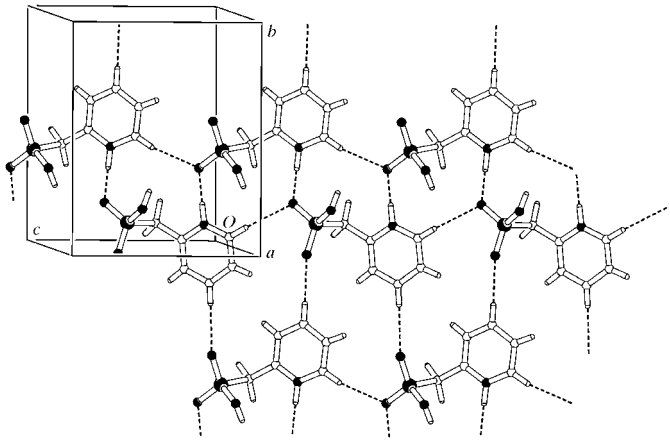

Figure 4
The hydrogen-bonding network in (II), using the same conventions as in Fig. 3.

Experimental

The title compound was prepared by dealkylation of one of the ester groups in diethyl (2-pyridylmethyl)phosphonate using hydrobromic acid in glacial acetic acid. Diethyl (2-pyridylmethyl)phosphonate was prepared according to the procedures described by Kostka & Ochocki (1983). To diethyl (2-pyridylmethyl)phosphonate (1.50 g, 6.60 mmol) was added 33% hydrobromic acid in glacial acetic acid and the mixture was stirred at room temperature for 2 h. The reaction was carried out under dry conditions. Excess HBr and CH_3COOH were then evaporated under reduced pressure, the residue was dissolved in water (8 ml), and $NaHCO_3$ was added until the pH of the mixture became neutral. The solution was evaporated to dryness and ethanol (10 ml) was added. After filtration, the ethanol was evaporated. The oily residue was dissolved in water (20 ml) and extracted with chloroform (3 × 20 ml). The aqueous solution was evaporated to a volume of 5 ml and applied to a column of Dowex 50 W × 4 (H^+ form; 20 ml). Fractions were checked *via* thin-layer chromatography [eluant: isopropanol/NH_3(aq)/H_2O, 8:1:1]. Collected fractions were evaporated to dryness, dry ethanol (10 ml) was added to the residue, the precipitate was filtered off and the solvent was evaporated to dryness (yield 62%). Diffraction-quality crystals of (I) were obtained from ethanol by slow evaporation of the solvent at room temperature (m.p. 451–452 K).

Crystal data

$C_8H_{12}NO_3P$
M_r = 201.16
Monoclinic, $P2_1/c$
a = 8.7169 (5) Å
b = 11.2997 (5) Å
c = 9.7940 (5) Å
β = 104.534 (4)°
V = 933.82 (8) Å^3
Z = 4
D_x = 1.431 Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 33.1–37.2°
μ = 2.44 mm^{-1}
T = 293 (2) K
Prism, colourless
0.30 × 0.30 × 0.15 mm

Data collection

Rigaku AFC-5*S* diffractometer
ω scans
Absorption correction: analytical (de Meulenaer & Tompa, 1965)
T_{min} = 0.535, T_{max} = 0.702
1849 measured reflections
1743 independent reflections
1268 reflections with $I > 2\sigma(I)$
R_{int} = 0.018
θ_{max} = 70.0°
$h = -8 \rightarrow 10$
$k = -2 \rightarrow 13$
$l = -11 \rightarrow 11$
3 standard reflections
every 150 reflections
intensity decay: 1.9%

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0819P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.046$	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2) = 0.134$	$\Delta\rho_{max} = 0.36$ e Å^{-3}
$S = 1.02$	$\Delta\rho_{min} = -0.41$ e Å^{-3}
1743 reflections	Extinction correction: *SHELXL*97
119 parameters	Extinction coefficient: 0.025 (2)
H-atom parameters constrained	

Table 1
Selected geometric parameters (Å, °) for (I).

P1—O3	1.4702 (19)	P1—C1	1.822 (3)
P1—O1	1.4925 (19)	C1—C2	1.498 (4)
P1—O2	1.601 (2)		
O3—P1—O1	118.85 (13)	O1—P1—C1	108.12 (12)
O3—P1—O2	113.22 (12)	O2—P1—C1	104.58 (12)
O1—P1—O2	103.37 (11)	C2—C1—P1	115.16 (19)
O3—P1—C1	107.73 (13)		

Table 2
Hydrogen-bonding geometry (Å, °) for (I).

Cg is the centroid of the pyridyl ring.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1···O1^{i}	0.86	1.77	2.612 (3)	168
C6—H6···O3^{ii}	0.93	2.44	3.183 (3)	137
C3—H3···O1^{iii}	0.93	2.49	3.384 (3)	161
C1—H12···O2^{iii}	0.97	2.52	3.430 (3)	156
C8—H8*B*···*Cg*^{iv}	0.96	2.96	3.663 (3)	131

Symmetry codes: (i) $1-x, 1-y, 1-z$; (ii) $x-1, y, z$; (iii) $x, \frac{1}{2}-y, z-\frac{1}{2}$; (iv) $1-x, y-\frac{1}{2}, \frac{1}{2}-z$.

Table 3
Relevant torsion angles (°) describing the overall orientations of molecules of (I) and (II).

Torsion angle	(I)†	(II)‡
N1—C2—C1—P1	74.7 (3)	−97.2 (4)
C3—C2—C1—P1	−106.6 (3)	81.5 (5)
C2—C1—P1—O1	−52.1 (2)	−61.0 (4)
C2—C1—P1—O2	57.5 (2)	57.9 (4)
C2—C1—P1—O3	178.3 (2)	173.3 (3)

† This work. ‡ Gałdecki & Wolf (1990).

All H atoms were placed in idealized positions (C—H = 0.93–0.97 Å and N—H = 0.86 Å) and constrained to ride on their parent atoms, with U_{iso}(H) values of $1.2U_{eq}$(C,N) [or $1.5U_{eq}(C_{methyl})$].

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1989); cell refinement: *MSC/AFC Diffractometer Control Software*; data reduction: *CrystalStructure* (Rigaku/MSC, 2002); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2001); software used to prepare material for publication: *PLATON*.

Table 4
Hydrogen-bonding geometry (Å, °) for (II).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H2···O3^{v}	0.96 (7)	1.67 (7)	2.627 (5)	176 (7)
C4—H6—O1^{vi}	0.95 (7)	2.44 (7)	3.375 (6)	167 (5)
C6—H8—O3^{vii}	0.97 (6)	2.59 (6)	3.348 (6)	135 (5)

Symmetry codes: (v) $x, \frac{1}{2}-y, z-\frac{1}{2}$; (vi) $x, -\frac{1}{2}-y, z-\frac{1}{2}$; (vii) $x, y, z-1$.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: GA1090). Services for accessing these data are described at the back of the journal.

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