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[2-(3-Fluoropyridinium-1-yl)-1-hydroxy-1-phosphonoethyl]phosphonate

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Key indicators

Single-crystal X-ray study
T = 193 K
Mean σ(C–C) = 0.003 Å
R factor = 0.032
wR factor = 0.088
Data-to-parameter ratio = 18.2

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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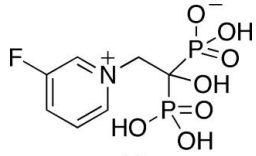
The title compound, $C_7H_{10}FNO_7P_2$, crystallizes in the zwitterionic form. In the crystal structure, molecules are linked *via* intermolecular O—H···O hydrogen bonds involving phosphonate groups, forming a two-dimensional framework. In addition, weak intermolecular C—H···O hydrogen bonds involving the pyridinium groups further connect molecules, forming a three-dimensional framework.

Comment

Nitrogen-containing geminal bisphosphonates are used clinically to treat a variety of bone resorption diseases such as osteoporosis (Sambrook *et al.*, 2004) and Paget's disease (Vasireddy *et al.*, 2003) and more recently they have been found to have antiparasitic (Yardley *et al.*, 2002), anticancer (Clezardin, 2005) and immunomodulatory activity (Sanders *et al.*, 2004). It is believed that they act by inhibiting the isoprenoid biosynthesis pathway enzyme farnesyl diphosphate synthase (FPPS) (EC 2.5.1.10) (Martin *et al.*, 1999; Hosfield *et al.*, 2004; van Beek *et al.*, 1999) with the charged (ammonium, imidazolium) side chains acting as carbocation transition state reactive intermediates. Another class of bisphosphonates are the pyridinium-1-yl species, which contain a fixed (+1) side-chain charge (Sanders *et al.*, 2005). We report here the first structure of one such active compound, *viz*. (I).



(I)

The molecule of (I) crystallizes in the zwitterionic form and there are no solvent molecules present (unlike the monohydrates found with the sulfonium, phosphonium and arsonium bisphosphonates; Zhang *et al.*, 2006; Cao *et al.*, 2006; Hudock *et al.*, 2006). Consequently, there must be three protonated phosphonate O atoms (found to be O1, O4 and O5) and three non-protonated phosphonate O atoms (found to be O2, O3 and O6), as shown in Fig. 1.

The P1···N1 distance [3.2469 (13) Å] is considerably shorter than the P2···N1 distance [4.1195 (14) Å], consistent with a strong intramolecular interaction between the pyridinium N atom and the anionic phosphonate group, and the overall structure closely resembles that found for the monohydrate form of risedronate (Gossman *et al.*, 2003) which contains a pyridinium N atom (at a position equivalent to that found here for C4). In the crystal structure, molecules are

linked *via* intermolecular O—H···O hydrogen bonds involving phosphonate groups, forming a two-dimensional framework (Fig. 2 and Table 1). In addition, weak intermolecular C—H···O hydrogen bonds involving the pyridinium groups further connect molecules, forming a three-dimensional framework (Table 1).

Experimental

The title compound was prepared as described previously (Sanders *et al.*, 2005). Crystals were grown by vapor diffusion of ethanol into an aqueous solution of the bisphosphonate at room temperature using the sitting-drop method.

Crystal data

$C_7H_{10}FNO_7P_2$
M_r = 301.10
Monoclinic, $P2_1/c$
a = 6.1892 (10) Å
b = 19.1693 (4) Å
c = 9.3312 (10) Å
β = 93.667 (10)°
V = 1104.8 (3) Å^3
Z = 4
D_x = 1.810 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 4398 reflections
θ = 3.1–29.9°
μ = 0.44 mm^{-1}
T = 193 (2) K
Block (acircular), colourless
0.10 × 0.10 × 0.06 mm

Data collection

Bruker Kappa-APEXII CCD diffractometer
φ and ω scans
Absorption correction: integration (*SHELXTL/XPREP*; Bruker, 2001)
T_{min} = 0.967, T_{max} = 0.981
15680 measured reflections
3201 independent reflections
2665 reflections with $I > 2\sigma(I)$
R_{int} = 0.032
θ_{max} = 30.0°
$h = -8 \rightarrow 8$
$k = -26 \rightarrow 26$
$l = -13 \rightarrow 13$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.033
$wR(F^2)$ = 0.088
S = 1.03
3201 reflections
176 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0429P)^2 + 0.6018P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.002
$\Delta\rho_{max}$ = 0.50 e Å^{-3}
$\Delta\rho_{min}$ = −0.32 e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O5—H3···O3^{i}	0.867 (15)	1.577 (16)	2.4209 (15)	163 (2)
O1—H1···O6^{ii}	0.834 (15)	1.679 (16)	2.4950 (15)	165 (2)
O4—H2···O2^{iii}	0.840 (15)	1.749 (15)	2.5846 (15)	173 (2)
O7—H4···O2^{ii}	0.827 (15)	1.880 (15)	2.7056 (15)	177 (2)
C2—H5···O5^{i}	0.99	2.40	3.3326 (17)	156
C2—H6···O3^{iii}	0.99	2.26	3.2216 (16)	163
C3—H7···O1^{iii}	0.95	2.51	3.430 (2)	164
C5—H8···O4^{iv}	0.95	2.59	3.312 (2)	133
C6—H9···O6^{v}	0.95	2.45	3.260 (2)	143

Symmetry codes: (i) $-x+1, -y+1, -z+1$; (ii) $-x+1, -y+1, -z+2$; (iii) $x+1, y, z$; (iv) $-x+2, y-\frac{1}{2}, -z+\frac{3}{2}$; (v) $-x+1, y-\frac{1}{2}, -z+\frac{3}{2}$.

Methyl H-atom positions, R—CH_3, were optimized by rotation about R—C bonds with idealized C—H, R—H and H···H distances (methyl C—H = 0.96 Å with AFIX). Hydroxyl H-atom positions were located in late difference Fourier maps and restrained to ideal bond lengths (O—H = 0.84 Å) using an effective standard deviation of 0.02 Å. The remaining H atoms were included as idealized riding atoms (methylene C—H = 0.97 Å and ring C—H = 0.93 Å). Methyl and hydroxyl H-atom U_{iso}(H) values were assigned as 1.5 times U_{eq} of the carrier atom; remaining H-atom U_{iso}(H) values were assigned as 1.2 times carrier U_{eq}.

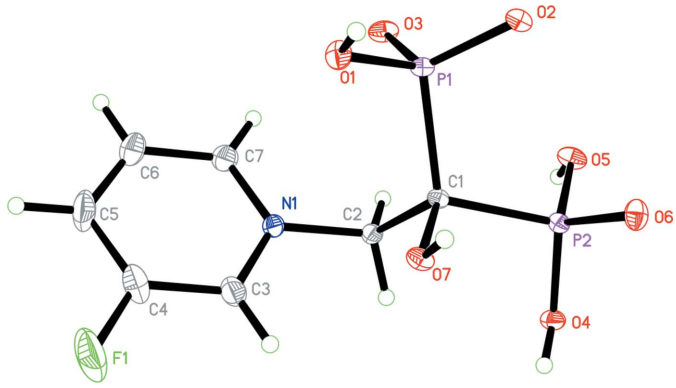


Figure 1
SHELXTL (Bruker, 2001) plot showing 35% probability ellipsoids for non-H atoms and circles of arbitrary size for H atoms.

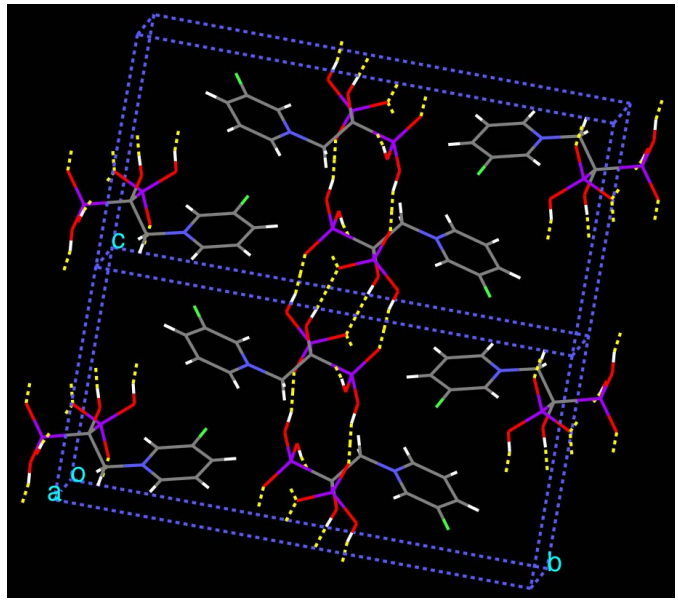


Figure 2
CERIUS^2 (Accelrys, 2005) view of the crystal structure, showing the hydrogen-bonded network between the bisphosphonates. Hydrogen bonds are shown as dashed yellow lines.

Data collection: *APEX2* (Bruker, 2004); cell refinement: *SAINT* (Bruker, 2001); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Bruker, 2001); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *XCIF* (Bruker, 2001).

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