Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

[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

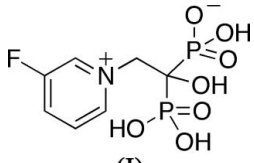
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 17 January 2006
Accepted 6 February 2006

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}.

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).

This work was supported in part by the United States Public Health Service (grant No. GM-073216 to EO). YZ is an American Heart Association, Midwest Affiliate, Posdoctoral Fellow. The Materials Chemistry Laboratory at the University of Illinois was supported in part by grants NSF CHE 95–03145

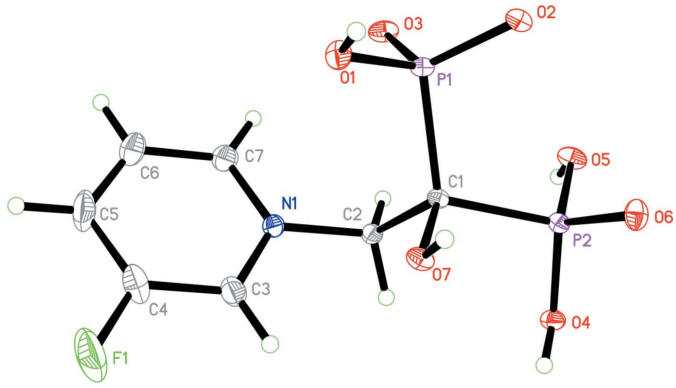


Figure 1
SHELXTL (Bruker, 2001) plot showing 35% probability ellipsoids for non-H atoms and circles of arbitrary size for H atoms.

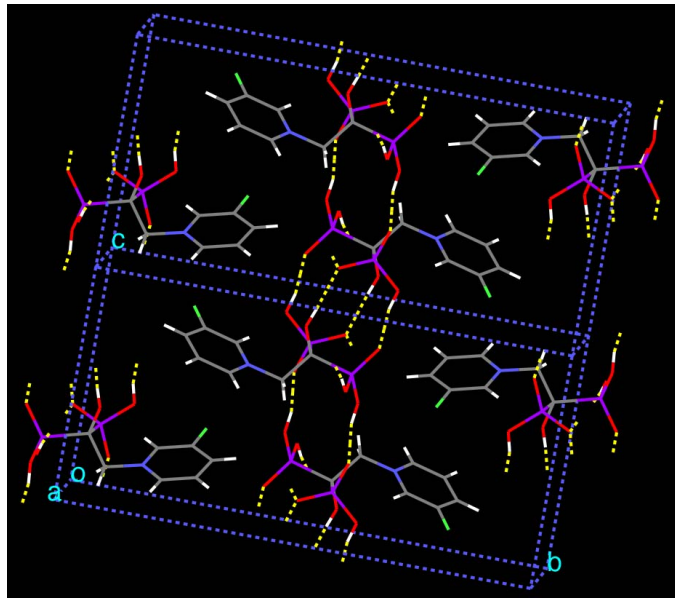


Figure 2
CERIUS^2 (Accelrys, 2005) view of the crystal structure, showing the hydrogen-bonded network between the bisphosphonates. Hydrogen bonds are shown as dashed yellow lines.

and NSF CHE 03–43032 from the National Science Foundation.

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