Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

[1-Hydroxy-1-phosphono-2-(trimethylphosphonium-1-yl)ethyl]phosphonate monohydrate

Rong Cao,[a] Michael P. Hudock,[a] Yonghui Zhang,[b] Scott R. Wilson[c] and Eric Oldfield[b]*

[a]Center for Biophysics and Computational Biology, University of Illinois at Urbana-Champaign, 607 South Mathews Avenue, Urbana, Illinois 61801, USA, [b]Department of Chemistry, University of Illinois at Urbana-Champaign, 600 South Mathews Avenue, Urbana, Illinois 61801, USA, and [c]School of Chemical Sciences, Box 59-1, University of Illinois at Urbana-Champaign, 505 South Mathews Avenue, Urbana, Illinois 61801, USA

Correspondence e-mail: eo@chad.scs.uiuc.edu

Key indicators

Single-crystal X-ray study
T = 193 K
Mean σ(C–C) = 0.003 Å
R factor = 0.035
wR factor = 0.092
Data-to-parameter ratio = 17.8

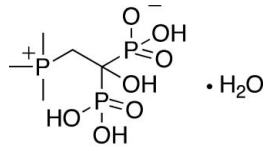
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 9 January 2006
Accepted 10 February 2006

The title compound, $C_5H_{15}O_7P_3{\cdot}H_2O$, crystallizes as a zwitterionic monohydrate and forms a layer structure with water molecules hydrogen bonded to the phosphonate groups.

Comment

Bisphosphonates are used extensively to treat a variety of bone resorption diseases and also have activity against a variety of pathogenic protozoa (Yardley, 2002) in addition to being immunomodulators (Sato *et al.*, 2005). Most bisphosphonates contain a positively charged nitrogen-containing side chain and are inhibitors of the enzyme farnesyl diphosphate synthase (EC 2.5.1.10). However, other side-chain motifs are also possible and here we report the structure of a novel bisphosphonate containing a trimethylphosphonium side chain, *viz*. (I).



(I)

The title compound crystallizes as the zwitterionic monohydrate. Inspection of the P—O distances (Table 1) reveals the presence of two protonated O atoms (O1 and O2) in one phosphonate group but only one protonated O atom (O4) in the other, consistent with a zwitterionic phosphonium–monoanionic bisphosphonate structure and the presence of water molecules (as opposed to hydronium ions) (Fig. 1).

The PCP backbone of the bisphosphonate group has a similar conformation to those reported previously (Van Brussel *et al.*, 2003; Gossman *et al.*, 2002, 2003). The trimethylphosphonium group has, as expected, a close to tetrahedral geometry (Table 1).

The bisphosphonate molecules in the crystal structure form sheet structures stabilized by an extensive hydrogen-bond network, with the water molecules forming intermolecular hydrogen bonds with the unprotonated atoms (O3 and O6) of the phosphonate group of the adjacent molecule (Fig. 2).

Experimental

Bromoacetic acid (2 mmol) was added to a solution of trimethylphosphine (2 mmol) in acetone (6 ml) and the reaction mixture was stirred for 6 h. The white precipitate was filtered, washed with diethyl ether and dried *in vacuo*. The resulting precipitate was added to a mixture of H_3PO_3 (5 equivalents) and toluene (5 ml) and heated to 353 K until the mixture melted. $POCl_3$ (5 equivalents) was added

dropwise and the mixture stirred at 353 K for 5 h. Upon cooling, the supernatant was decanted, 5 ml water added and the mixture refluxed for 1 h. Solvent was removed *in vacuo*, acetone added and the resulting white powder collected and crystallized from 2-propanol–water (2:1) to afford the anhydrous compound. Analysis calculated for $C_5H_{15}O_7P_3$: C 21.44, H 5.40%; found: C 21.12, H 5.37%. ^{1}H NMR (400 MHz, D_2O): δ 2.72 (*q*, J = 13.3 Hz, 2H), 1.75 (*d*, J = 14.4 Hz, 9H). ^{31}P NMR (162 MHz, D_2O): δ 25.3 (*t*, J = 23 Hz, 1P), 16.6 (*d*, J = 23 Hz, 1P). Crystals of the monohydrate were grown by vapor diffusion of ethanol into an aqueous solution of the bisphosphonate.

Crystal data

$C_5H_{15}O_7P_3\cdot H_2O$
M_r = 298.10
Monoclinic, $P2_1/c$
a = 7.165 (2) Å
b = 10.545 (4) Å
c = 16.613 (6) Å
β = 98.475 (5)°
V = 1241.6 (7) Å^3
Z = 4
D_x = 1.595 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 938 reflections
θ = 3.5–28.1°
μ = 0.50 mm^{-1}
T = 193 (2) K
Plate, colorless
0.70 × 0.24 × 0.03 mm

Data collection

Siemens Platform/SMART CCD diffractometer
ω scans
Absorption correction: integration (*SHELXTL*/*XPREP*; Bruker, 2001)
T_{min} = 0.814, T_{max} = 0.985
12219 measured reflections
3055 independent reflections
2379 reflections with $I > 2\sigma(I)$
R_{int} = 0.037
θ_{max} = 28.3°
$h = -9 \rightarrow 9$
$k = -14 \rightarrow 14$
$l = -22 \rightarrow 22$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.035
$wR(F^2)$ = 0.092
S = 1.02
3055 reflections
172 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0487P)^2 + 0.4585P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.41 e Å^{-3}
$\Delta\rho_{min}$ = −0.31 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O1—P2	1.5551 (15)	O4—P1	1.5509 (14)
O2—P2	1.5443 (15)	O5—P1	1.5029 (14)
O3—P2	1.4928 (15)	O6—P1	1.5113 (15)
C4—P3—C5	110.58 (13)	C4—P3—C2	110.84 (10)
C4—P3—C3	108.53 (13)	C5—P3—C2	114.41 (11)
C5—P3—C3	107.52 (12)	C3—P3—C2	104.59 (10)

Table 2
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O8—H17···O3	0.836 (17)	1.936 (18)	2.753 (2)	165 (3)
O8—H16···O6^{i}	0.829 (17)	1.926 (18)	2.748 (2)	170 (3)
O7—H15···O3^{ii}	0.807 (16)	2.014 (18)	2.768 (2)	155 (2)
O1—H12···O5^{i}	0.835 (17)	1.646 (17)	2.477 (2)	174 (3)
O2—H13···O6^{iii}	0.796 (17)	1.707 (18)	2.488 (2)	166 (3)
O4—H14···O8^{iv}	0.830 (16)	1.694 (17)	2.509 (2)	167 (3)

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

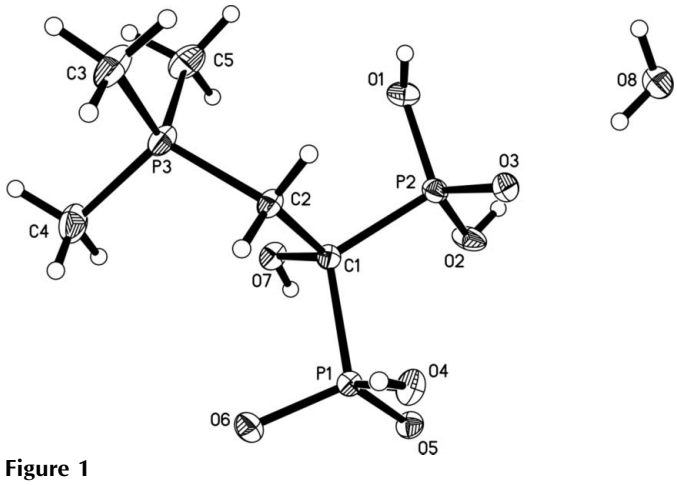


Figure 1
SHELXTL (Bruker, 2001) plot, showing 35% probability displacement ellipsoids for non-H atoms and circles of arbitrary size for H atoms.

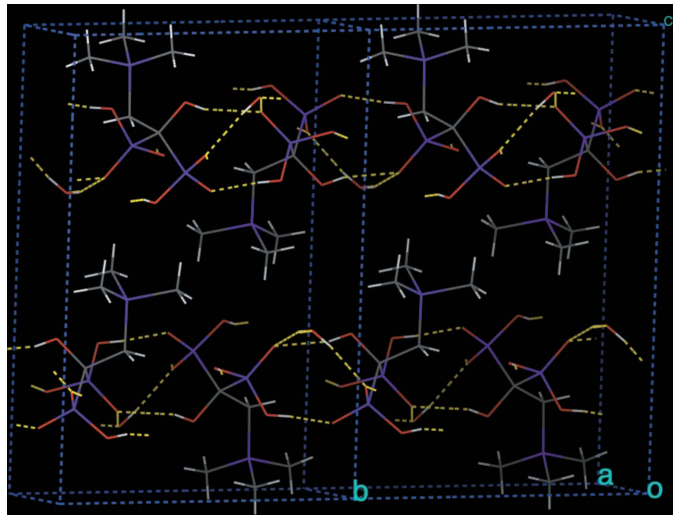


Figure 2
CERIUS^2 (Accelrys, 2005) view looking down the *a* axis, showing the proposed hydrogen-bond interactions between neighboring molecules. Sheets of hydrogen-bonded phosphonate groups can be seen stabilized by bridging water molecules. Hydrogen bonds are represented by dashed yellow lines.

Methyl H-atom positions were optimized by rotation about R—C bonds with idealized C—H distances [C—H = 0.96 Å (AFIX 137)]. Methylene and hydroxyl H atoms 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. Methyl and hydroxyl H-atom U_{iso} values were assigned as 1.5 times U_{eq} of the carrier atom; the remaining H-atom U_{iso} values were assigned as 1.2 times the carrier U_{eq}.

Data collection: *SMART* (Bruker, 2001); 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 GM-65307 to EO). YZ is an American Heart Association, Midwest Affiliate, Postdoctoral Fellow. The Materials Chemistry Laboratory at the University of

Illinois was supported in part by grants NSF CHE 95–03145 and NSF CHE 03–43032 from the National Science Foundation.

References

Accelrys (2005). *CERIUS*^{2}. Accelrys Inc., San Diego, CA, USA.
Bruker (2001). *SAINT* (Version 6.22), *SHELXTL* (Version 6.10), *SMART* (Version 5.625) and *XCIF* (Version 6.12). Bruker AXS Inc., Madison, Wisconsin, USA.
Gossman, W. L., Wilson, S. R. & Oldfield, E. (2002). *Acta Cryst.* C**58**, m599–m600.
Gossman, W. L., Wilson, S. R. & Oldfield, E. (2003). *Acta Cryst.* C**59**, m33–m36.
Sato, K., Kimura, S., Segawa, H., Yokota, A., Matsumoto, S., Kuroda, J., Nogawa, M., Yuasa, T., Kiyono, Y., Wada, H. & Maekawa, T. (2005). *Int. J. Cancer*, **116**, 94–99.
Van Brussel, E. M., Gossman, W. L., Wilson, S. R. & Oldfield, E. (2003). *Acta Cryst.* C**59**, o93–o94.
Yardley, V., Khan, A. A., Martin, M. B., Slifer, T. R., Araujo, F. G., Moreno, S. N., Docampo, R., Croft, S. L. & Oldfield, E. (2002). *Antimicrob. Agents Chemother.* **46**, 929–931.