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Sodium 3-ammonio-1-hydroxypropylidene-1,1-bisphosphonate monohydrate

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Key indicators

Single-crystal X-ray study
T = 120 K
Mean σ(C–C) = 0.003 Å
R factor = 0.045
wR factor = 0.111
Data-to-parameter ratio = 17.6

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

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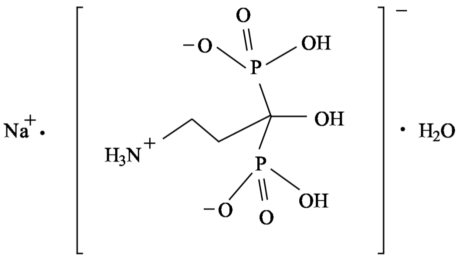
The title compound, sodium pamidronate monohydrate, $Na^+\cdot C_3H_{10}NO_7P_2^-\cdot H_2O$, crystallizes in sheets in the *ab* plane through Na—O coordination and hydrogen bonding to the pamidronate zwitterion. The neutral sheets are connected through hydrogen bonding, including the water molecule in the *c* direction.

Comment

Many bisphosphonates are effective drugs for a number of bone disorders, such as osteoporosis (Rodan & Martin, 2000). In addition, bisphosphonates have shown promising anti-parasitic activity (Martin *et al.*, 2001). In a search for stable salts suitable for pharmaceutical preparations, the title compound was synthesized.



(I)

The geometric features of the pamidronate zwitterion agree well with previous studies (see below) of pamidronates. The P—O distances show the same bimodal distribution as found by Gossman *et al.*, 2003), *viz.* 1.491–1.522 Å for unprotonated and 1.579–1.592 Å for protonated O atoms. The C1—C2—C3—N1 torsion angle [163.9 (2)°] indicates a *trans* conformation, as found in hydrogen pamidronate (Shkol'nikova *et al.*, 1990) and disodium pamidronate (Vega *et al.*, 2002), but contrary to the *gauche* configuration found in calcium pamidronate (Fernández *et al.*, 2002).

The crystal structure is formed by Na—O coordination and hydrogen bonding. The Na—O_6 coordination polyhedra each connect three pamidronate zwitterions, forming neutral sheets in the *ab* plane, while the water molecule reinforces the hydrogen bonding in the *c* direction only. All available O—H and N—H H atoms are involved in hydrogen bonds.

Experimental

Sodium pamidronate monohydrate (1 g) was dissolved in sterilized water (15 ml) and heated under reflux until dissolved. Slow cooling yielded small crystals which were used to nucleate a repeated recrystallization. The resulting crystals were dried in vacuum at 313 K for 24 h.

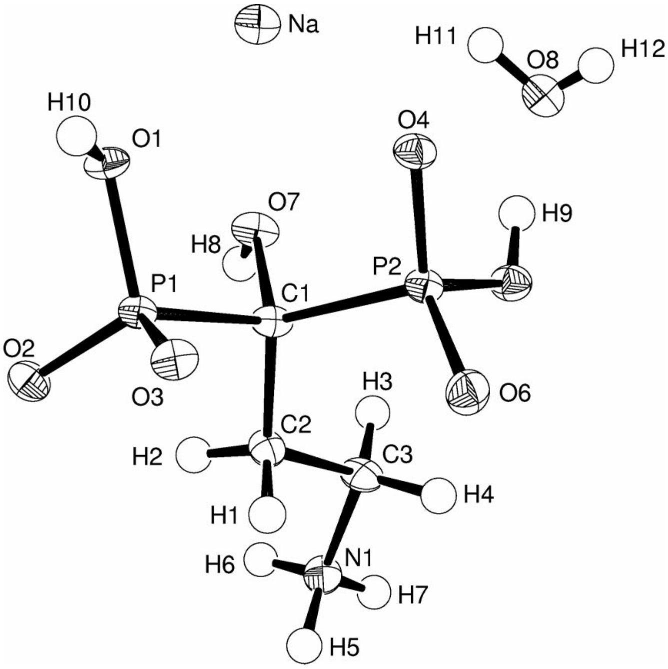


Figure 1

A view of sodium pamidronate monohydrate, showing 75% probability displacement ellipsoids and the atomic numbering. H atoms are represented by circles of arbitrary size.

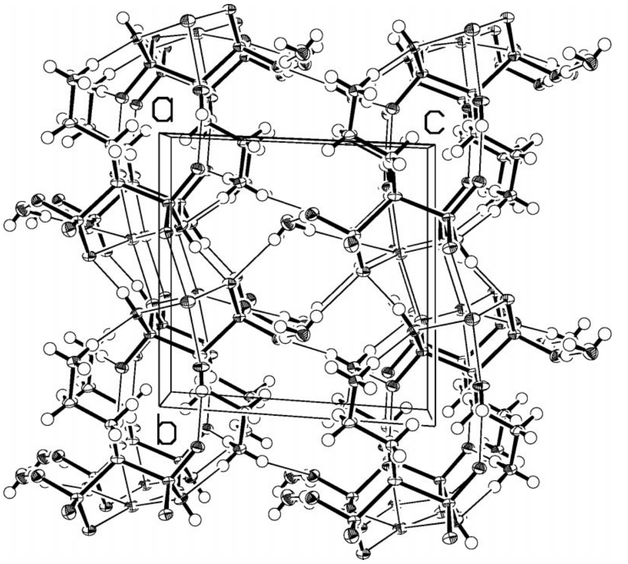


Figure 2

The crystal packing of sodium pamidronate monohydrate viewed along the *a* axis. Hydrogen bonds and sodium coordination are indicated by thin lines.

Crystal data

$Na^+ \cdot C_3H_{10}NO_7P_2^- \cdot H_2O$
$M_r = 275.07$
Triclinic, $P\overline{1}$
$a = 5.8699$ (5) Å
$b = 9.1235$ (8) Å
$c = 9.3113$ (8) Å
$\alpha = 86.746$ (2)°
$\beta = 77.125$ (2)°
$\gamma = 87.728$ (2)°
$V = 485.15$ (7) $Å^3$

$Z = 2$
$D_x = 1.883$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 3147 reflections
$\theta = 3.1–30.7°$
$\mu = 0.52$ mm^{-1}
$T = 120$ (2) K
Lath, colorless
0.35 × 0.08 × 0.02 mm

Data collection

Bruker SMART APEX diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2002)
$T_{min} = 0.8$, $T_{max} = 1.0$
6525 measured reflections

2811 independent reflections
2543 reflections with $I > 2\sigma(I)$
$R_{int} = 0.027$
$\theta_{max} = 30.8°$
$h = -8 \rightarrow 8$
$k = -13 \rightarrow 13$
$l = -13 \rightarrow 13$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.045$
$wR(F^2) = 0.111$
$S = 1.10$
2811 reflections
160 parameters
H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.056P)^2 + 0.4254P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.96$ e $Å^{-3}$
$\Delta\rho_{min} = -0.44$ e $Å^{-3}$

Table 1

Selected geometric parameters (Å, °).

Na—O6^i	2.2611 (17)	P1—C1	1.858 (2)
Na—O3^i	2.3174 (16)	P2—O6	1.4902 (15)
Na—O3^{ii}	2.3394 (16)	P2—O4	1.5185 (15)
Na—O1	2.3987 (17)	P2—O5	1.5751 (15)
Na—O4	2.4382 (17)	P2—C1	1.843 (2)
Na—O7	2.5371 (17)	O7—C1	1.436 (2)
P1—O3	1.4956 (15)	C1—C2	1.534 (3)
P1—O2	1.5108 (14)	C2—C3	1.523 (3)
P1—O1	1.5913 (15)	C3—N1	1.496 (2)
O3—P1—O2	114.45 (8)	O4—P2—C1	106.46 (8)
O3—P1—O1	111.03 (8)	O5—P2—C1	104.85 (8)
O2—P1—O1	108.83 (8)	O7—C1—C2	113.34 (15)
O3—P1—C1	110.64 (8)	O7—C1—P2	104.80 (12)
O2—P1—C1	108.74 (8)	C2—C1—P2	112.75 (13)
O1—P1—C1	102.45 (8)	O7—C1—P1	108.29 (13)
O6—P2—O4	117.49 (9)	C2—C1—P1	106.06 (13)
O6—P2—O5	108.37 (9)	P2—C1—P1	111.64 (10)
O4—P2—O5	108.96 (8)	C3—C2—C1	116.35 (16)
O6—P2—C1	109.99 (9)	N1—C3—C2	108.03 (16)

Symmetry codes: (i) $x-1, y, z$; (ii) $-x, -y+1, -z$.

Table 2

Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N1—H5···O2^{iii}	0.94 (3)	1.85 (3)	2.782 (2)	167 (3)
N1—H6···O1^{iv}	0.91 (3)	2.16 (3)	3.060 (2)	171 (3)
N1—H7···O5^v	0.87 (3)	2.09 (3)	2.895 (2)	155 (3)
O7—H8···O2^{iv}	0.807 (17)	1.837 (18)	2.641 (2)	174 (3)
O5—H9···O8^{vi}	0.837 (17)	1.703 (18)	2.532 (2)	171 (3)
O1—H10···O4^{ii}	0.817 (17)	1.726 (18)	2.544 (2)	179 (3)
O8—H11···O6^i	0.852 (17)	1.794 (18)	2.644 (2)	175 (3)
O8—H12···O4^{vii}	0.818 (17)	1.999 (18)	2.815 (2)	176 (3)

Symmetry codes: (i) $x-1, y, z$; (ii) $-x, -y+1, -z$; (iii) $-x+1, -y, -z$; (iv) $-x, -y, -z$; (v) $-x+1, -y, -z-1$; (vi) x, y, z; (vii) $-x, -y+1, -z-1$.

All H parameters were initially refined freely. In the final cycles, the H atoms of CH_2 groups were placed in calculated positions with C—H = 0.93 Å and refined as riding atoms. For OH and water H atoms, the distances were restrained to 0.84 (2) Å. Coordinates of the NH_3 H atoms were refined freely. The displacement parameters were set to 1.2 (CH_2) or 1.5 (OH and NH_3) times U_{eq} of the corresponding C, O or N atoms.

Acta Cryst. (2005). E**61**, m132–m134 Stahl *et al.* • $Na^+ \cdot C_3H_{10}NO_7P_2^- \cdot H_2O$ **m133**

Data collection: *SMART* (Bruker, 1999); cell refinement: *SAINT-Plus* (Bruker, 1999); data reduction: *SAINT-Plus*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 2000); program(s) used to refine structure: *SHELXTL*; molecular graphics: *ORTEP-3* (Farrugia, 1997); software used to prepare material for publication: *SHELXTL*.

References

Bruker (1999) *SMART* and *SAINT-Plus*. Bruker AXS Inc., Madison, Wisconsin, USA.

Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.

Fernández, D., Vega, D. & Goeta, A. (2002). *Acta Cryst.* C**58**, m494–m497.

Gossman, W. L., Wilson, S. R. & Oldfield, E. (2003). *Acta Cryst.* C**59**, m33–m36.

Martin, M. B., Grimly, J. S., Lewis, J. C., Heath, H. T. III, Baily, B. N., Kendrick, H., Yardley, V., Caldera, A., Lira, R., Urbina, J. A., Moreno, S. N. J., Docampo, R., Croft, S. L. & Oldfield, E. (2001). *J. Med. Chem.* **44**, 909–916.

Rodan, G. A. & Martin, T. J. (2000). *Science*, **289**, 1508–1514.

Sheldrick, G. M. (2000). *SHELXTL*. Version 6.10. Bruker AXS Inc., Madison, Wisconsin, USA.

Sheldrick, G. M. (2002). *SADABS*. Version 2.03. University of Göttingen, Germany.

Shkol'nikova, L. M., Sotman, S. S. & Afonin, E. G. (1990). *Krystallografiya*, **35**, 1442–1449. [English version: *Sov. Phys. Crystallogr.* **35**, 850–854.].

Vega, D., Fernandez, D. & Ellena, J. A. (2002). *Acta Cryst.* C**58**, m77–m80.

m134 Stahl *et al.* • $Na^+ \cdot C_3H_{10}NO_7P_2^- \cdot H_2O$ *Acta Cryst.* (2005). E**61**, m132–m134