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Benzamidinium dihydrogenphosphate

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Key indicators

Single-crystal X-ray study
T = 294 K
Mean σ(C–C) = 0.008 Å
R factor = 0.067
wR factor = 0.172
Data-to-parameter ratio = 13.6

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

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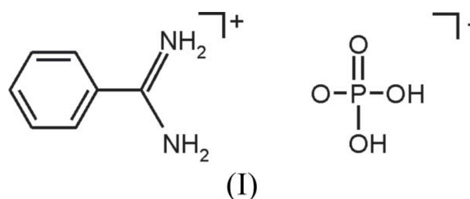
Cations and anions of benzamidinium dihydrogenphosphate, $C_7H_9N_2^+\cdot H_2PO_4$, are connected by $NH_2\cdots O{=}P$ and $NH_2\cdots O(H){-}P$ hydrogen bonds between benzamidinium NH_2 groups and dihydrogenphosphate O atoms into an infinite three-dimensional network. The anions are connected through $P{-}OH\cdots O{=}P$ interactions.

Comment

The structure of benzamidinium dihydrogenphosphate, (I), has been determined as a part of our continuing synthetic, spectroscopic and structural investigations of dihydrogenphosphates (Kolev *et al.*, 2007) and hydrogensquarates (Kolev *et al.*, 2005; Kolev, Spiteller, *et al.*, 2006; Kolev, Yancheva *et al.*, 2006) of biologically active amines and various substituted amidines. It is known that factor Xa (FXa) is a key enzyme for the intervention of the blood coagulation cascade and for the development of new antithrombotic agents (Willardsen *et al.*, 2004). Many drugs developed as potential inhibitors of coagulation enzymes contain the benzamidine functionality (Koshio *et al.*, 2005). Commonly, compounds of this class are reversible inhibitors of trypsin and other peptidases that show a selectivity for arginine, or possibly lysine. The cationic amidino group of the inhibitor interacts with a carboxylate located at the bottom of the S1 subsite, and there are also hydrophobic interactions with the sides of the S1 pocket. Benzamidine is, therefore, a common component of mixtures of inhibitors designed to suppress peptidase activity in biological samples (Bode *et al.*, 1983; Krieger *et al.*, 1974, Powers & Harper, 1986). Its cation has also been included in a number of protein structure determinations (Bode *et al.*, 1990; Marquart *et al.*, 1983; Sprang *et al.*, 1987).



(I)

Phosphates are an essential nutrient for all organisms, which have, therefore, evolved regulatory mechanisms for its acquisition, storage and release (Torriani-Gorini *et al.*, 1994). The evidence, to date, indicates that regulation of the overall rhenal tubular phosphate transfer occurs at the level of the proximal tubular border membrane Na/phosphate cotransport system (Dousa, 1996; Kempson, 1996). Hyperphosphatemia and increased calcium phosphate production are important

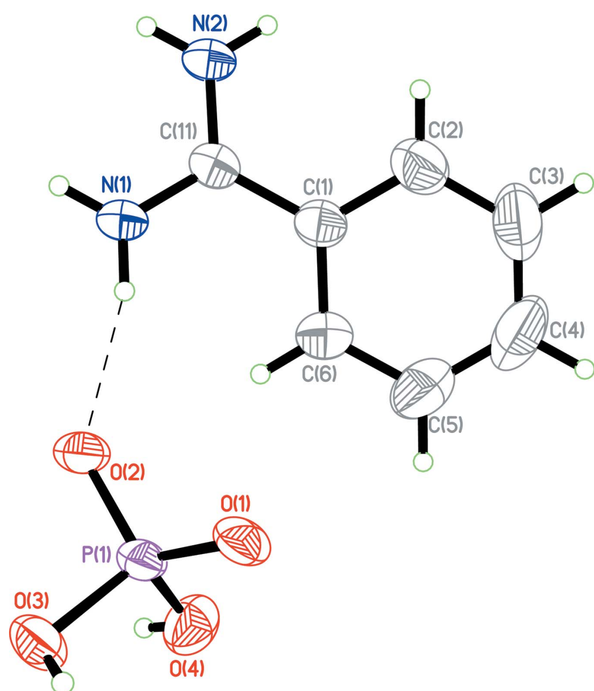


Figure 1
The asymmetric unit of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probality level. The dashed line indicates a hydrogen bond.

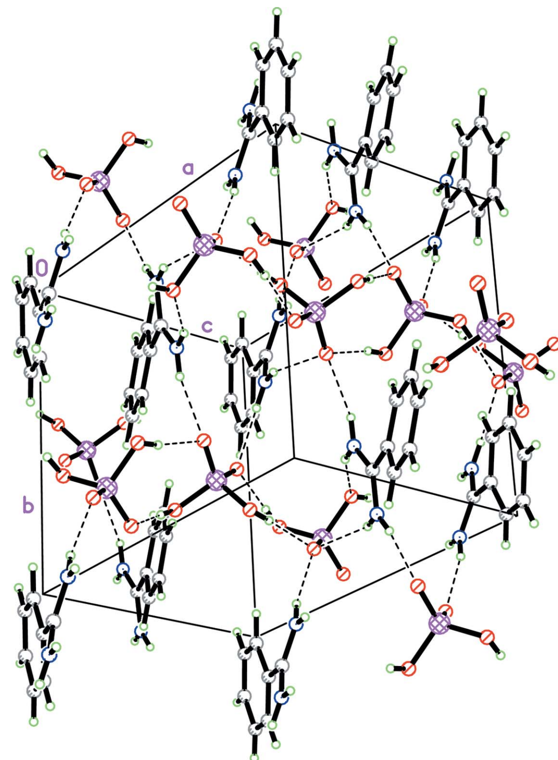


Figure 2
Linkage of the anions and cations of (I) into a three-dimensional network through hydrogen bonds (dashed lines).

contributors to vascular calcifications in patients with uremia (Block *et al.*, 1998).

A detailed knowledge of the structure and spectroscopic properties of the benzamidinium cation is a prerequisite for understanding its binding properties and (I) contains this cation in the presence of the biologically important dihydrogenphosphate anion. The crystal structure of benzamidine has already been reported (Barker *et al.*, 1996).

The asymmetric unit of (I) is depicted in Fig. 1 and a packing diagram in Fig. 2. N—H···O hydrogen bonds between the benzamidinium amino groups and the dihydrogenphosphate counter-ions link the cations and anions of (I) into a three-dimensional network. The anions are connected into infinite double chains through O—H···O interactions running along the *c* axis.

Experimental

The starting compound benzamidine was received as a white powder from Bachem (Switzerland) and recrystallized from methanol. A high yield and suitable crystals of (I) for X-ray analysis were obtained by mixing a 20 ml methanol solution of benzamidine (6 mmol, 776 mg) with an equimolar amount of 50% phosphorous acid. The reaction mixture was stirred for 10 h at room temperature and product formation monitored by thin-layer chromatography. After completion of the reaction, the resulting solution was filtered off and the filtrate set aside, affording crystals of (I) after 24 h. The product was separated by filtration, dried in air and characterized by elemental analysis, mass spectrometry and IR, Raman and NMR spectroscopy. The IR spectrum of (I) exhibits ν N^+H_2 stretching modes between 3400 and 3000 cm^{-1}, with the highest frequency peak at 3353 cm^{-1}. This region overlaps with the ν OH bands of hydrogen-bonded dihydrogenphosphate anions. The intense peaks at 1231 and 1088 cm^{-1} can be assigned to ν P=ON and ν PO(H), respectively, and the peaks at 1700 and 1680 cm^{-1} to bending δ N^+H_2 modes. A full theoretical vibrational analysis and experimental assignment by means of solid-state linear polarized IR spectroscopy is now in progress for (I) and will be published at a later date.

Crystal data

$C_7H_9N_2^+\cdot H_2O_4P^-$
$M_r = 218.15$
Monoclinic, $P2_1/c$
$a = 12.259$ (3) Å
$b = 10.067$ (2) Å
$c = 8.0578$ (16) Å
$\beta = 91.28$ (3)°
$V = 994.2$ (3) Å^3
$Z = 4$
$D_x = 1.457$ Mg m^{-3}
Mo $K\alpha$ radiation
$\mu = 0.27$ mm^{-1}
$T = 294$ (2) K
Broken prism, colourless
0.49 × 0.30 × 0.23 mm

Data collection

Siemens P4 four-circle diffractometer
ω scans
Absorption correction: ψ scan (*XPREP*; Sheldrick, 1995)
$T_{min} = 0.877$, $T_{max} = 0.939$
1875 measured reflections
1739 independent reflections
1071 reflections with $I > 2\sigma(I)$
$R_{int} = 0.055$
$\theta_{max} = 25.0$°
3 standard reflections every 100 reflections intensity decay: 2%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.067$
$wR(F^2) = 0.172$
$S = 1.07$
1739 reflections
128 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0866P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.40$ e Å^{-3}
$\Delta\rho_{min} = -0.38$ e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.007 (2)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H12···O2^{i}	0.86	2.06	2.891 (5)	161
N1—H11···O3^{ii}	0.86	2.22	3.028 (5)	157
N2—H22···O1^{iii}	0.86	2.01	2.833 (5)	160
N2—H21···O2^{ii}	0.86	2.12	2.892 (5)	149
O3—H3′···O2^{iv}	0.82	1.83	2.643 (4)	171
O4—H4′···O1^{v}	0.82	1.80	2.616 (4)	178

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

H atoms were treated as riding, with C—H = 0.93, N—H = 0.86 and O—H = 0.82 Å and with U_{iso}(H) = 1.2U_{eq}(C,N) and 1.4U_{eq}(O).

Data collection: *R3m/V* (Siemens, 1989); cell refinement: *R3m/V*; data reduction: *XDISK* (Siemens, 1989); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL-Plus* (Sheldrick, 1995); software used to prepare material for publication: *SHELXL97*.

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