Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: PA1184). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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(*S*)-[1-(Benzyloxycarbonylamino)ethyl]-phosphonic Acid

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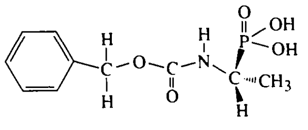
Abstract

The title compound, $C_{10}H_{14}NO_5P$, is one of a series of novel carbonic anhydrase inhibitors [Ösapay & Csiba (1993). *Eur. J. Med. Chem.* **28**, 355–361]. In an initial approach to structure–activity relationship studies, the molecular structure of the title compound was determined by X-ray crystallography. The molecule is fully extended with a *trans* urethane moiety. The phosphonate group emerges from the plane of the backbone with a 92.3° torsion angle. The orientation of phosphonate groups facilitates the formation of two intermolecular hydrogen bridges (1.812 and 2.253 Å) between adjacent phosphonate moieties.

Comment

A series of phosphonic analogs of amino acids and peptides showed significant inhibitory potency for the esterase activity of the human carbonic anhydrase (HCA). The title compound, (*S*)-[1-(benzyloxycarbonylamino)-ethyl]phosphonic acid, (1), possesses the strongest inhibitory activity toward both HCA isoenzymes I and II. The structure determination of (1) was undertaken within the context of investigations on a hypothetical inhibitor–enzyme complex by computer directed analysis (Ösapay & Csiba, 1993).



(1)

Intramolecular bond distances and angles, listed in Table 2, do not deviate significantly from the expected values (*Chemistry Data Book*, 1982). The molecule has a fully extended structure with *trans* backbone torsion angles: C(8)—O(1)—C(7)—C(6) −166.6, C(7)—O(1)—C(8)—N(1) −179.1 and C(9)—N(1)—C(8)—O(1) −179.2°. The aromatic ring is planar within experimental error and it is in a *gauche*$^-$ position relative to the CH_2—O bond; the torsion angle C(1)—C(6)—C(7)—O(1) is −67.8°. The chain O(5)—P(1)—C(9)—N(1) is close to planar with a torsion angle of 167.7°, and the torsion angle C(8)—N(1)—C(9)—P(1) of −92.3° indicates that the phosphonate group emerges from the plane of the backbone. The P atom has an approximate tetrahedral environment of one C and three O atoms. The P(1)—C(9) distance has a value of 1.834 (5) Å, which is close to that of 1.82 Å in aminomethylphosphonic acid (Darriet, Darriet, Cassaigne & Neuzil, 1975). There are two types of P—O bonds, which are affected by their participation in intermolecular hydrogen-bridge formation. The two HO—P bonds have lengths of 1.552 (4) [P(1)—O(5)] and 1.529 (4) Å [P(1)—O(4)] (P—OH bonds are found in the range 1.56–1.57 Å in the literature), while the P═O bond is

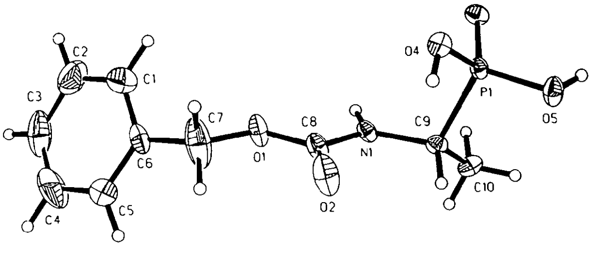


Fig. 1. *ORTEP* (Johnson, 1965) view of the title compound. The atoms are drawn with 30% probability ellipsoids.

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1.474 (4) Å, compared with 1.44 Å found for the non-hydrogen-bonded structure of trimethylphosphine oxide (Wang, 1965). In the crystals, the molecules pack by forming chains *via* intermolecular hydrogen bonds of the type P═O···H—O—P, between two phosphonate groups along the **x** direction (Fig. 2), and of the type N—H···O, between an amide N atom and an adjacent O atom. Of these interactions (Table 2), N(1)—H(1*A*)···O(2^{i}) is the weakest and O(5)···H(5*A*)—O(3^{iii}) is the most distorted.

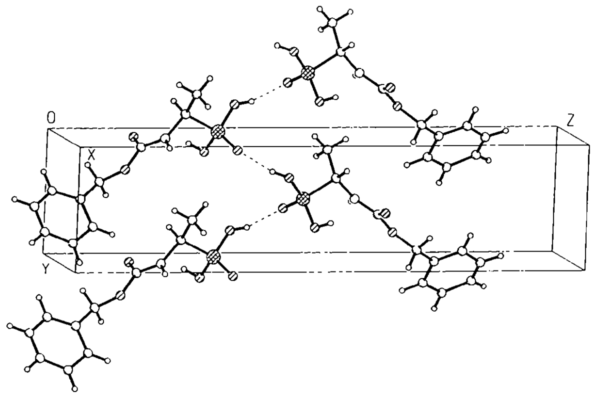

Fig. 2. Unit-cell packing diagram of the title compound.

Attempts to determine the absolute configuration by refining the Rogers (1981) η parameter, using *SHELXTL* (Sheldrick, 1990*b*), were inconclusive. However, refining the Flack (1983) parameter [$x = 0.14\,(5)$] using F^2 data indicated that the determined structure represents the correct enantiomer, which is confirmed by physiochemical evidence, such as the optical rotation value which is identical to the literature data.

Experimental

The synthesis and resolution of (*R*,*S*)-[1-(benzyloxycarbonylamino)ethyl]phosphonic acid for preparation of (1) have been described previously (Ösapay, Szilágyi & Seres, 1987). Crystals for this study were grown from ethyl acetate by slow evaporation over a period of six months.

Crystal data

$C_{10}H_{14}NO_5P$
$M_r = 259.2$
Monoclinic
$P2_1$
$a = 4.845\,(1)$ Å
$b = 5.517\,(1)$ Å
$c = 23.033\,(3)$ Å
$\beta = 93.62\,(1)°$
$V = 614.4\,(2)$ Å^3
$Z = 2$
$D_x = 1.402$ Mg m^{-3}

Cu $K\alpha$ radiation
$\lambda = 1.54178$ Å
Cell parameters from 25 reflections
$\theta = 25–40°$
$\mu = 2.103$ mm^{-1}
$T = 296$ K
Plate
0.33 × 0.16 × 0.08 mm
Colourless

Data collection

Rigaku AFC-6*R* diffractometer
$2\theta–\theta$ scans
Absorption correction:
ψ scan
$T_{\min} = 0.91$, $T_{\max} = 0.99$
1196 measured reflections
1031 independent reflections
933 observed reflections
[$F > 4\sigma(F)$]

$R_{\rm int} = 0.0145$
$\theta_{\max} = 60.0°$
$h = 0 \rightarrow 5$
$k = 0 \rightarrow 6$
$l = -25 \rightarrow 25$
3 standard reflections
monitored every 100 reflections
intensity decay: not significant

Refinement

Refinement on *F*
$R = 0.045$
$wR = 0.061$
$S = 1.68$
933 reflections
153 parameters
$w = 1/[\sigma^2(F) + 0.001F^2]$

$(\Delta/\sigma)_{\max} = 0.012$
$\Delta\rho_{\max} = 0.37$ e Å^{-3}
$\Delta\rho_{\min} = -0.22$ e Å^{-3}
Extinction correction: none
Atomic scattering factors from Cromer & Waber (1974)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2)

$$U_{\rm eq} = (1/3)\Sigma_i\Sigma_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$$

	x	*y*	*z*	$U_{\rm eq}$
P(1)	0.1266 (2)	0.3614	0.9225 (1)	0.036 (1)
O(1)	0.0129 (7)	0.0843 (11)	0.7373 (2)	0.067 (2)
O(2)	0.3823 (7)	0.2891 (13)	0.7756 (2)	0.086 (2)
O(3)	−0.1247 (7)	0.2545 (8)	0.9448 (2)	0.045 (1)
O(4)	0.3467 (7)	0.1709 (9)	0.9115 (2)	0.050 (1)
O(5)	0.2731 (7)	0.5568 (9)	0.9619 (2)	0.057 (1)
N(1)	−0.0410 (7)	0.3397 (12)	0.8094 (2)	0.042 (1)
C(1)	−0.1506 (21)	−0.3452 (20)	0.6634 (4)	0.101 (4)
C(2)	−0.3073 (25)	−0.4540 (22)	0.6185 (6)	0.136 (6)
C(3)	−0.2975 (23)	−0.3643 (32)	0.5636 (5)	0.137 (7)
C(4)	−0.1363 (26)	−0.1867 (32)	0.5530 (4)	0.133 (6)
C(5)	0.0079 (20)	−0.0794 (19)	0.5961 (3)	0.102 (4)
C(6)	0.0147 (13)	−0.1538 (19)	0.6519 (3)	0.068 (2)
C(7)	0.1891 (15)	−0.0373 (27)	0.6981 (4)	0.124 (5)
C(8)	0.1413 (11)	0.2399 (14)	0.7746 (2)	0.056 (2)
C(9)	0.0418 (9)	0.5163 (11)	0.8532 (2)	0.040 (2)
C(10)	−0.1760 (12)	0.7112 (12)	0.8593 (3)	0.055 (2)

Table 2. *Selected geometric parameters* (Å, °)

P(1)—O(3)	1.474 (4)	P(1)—O(4)	1.529 (4)
P(1)—O(5)	1.552 (4)	P(1)—C(9)	1.834 (5)
O(1)—C(7)	1.45 (1)	O(1)—C(8)	1.339 (8)
O(2)—C(8)	1.197 (7)	N(1)—C(8)	1.347 (7)
N(1)—C(9)	1.441 (7)	C(1)—C(2)	1.38 (2)
C(1)—C(6)	1.36 (1)	C(2)—C(3)	1.36 (2)
C(3)—C(4)	1.29 (2)	C(4)—C(5)	1.32 (2)
C(5)—C(6)	1.35 (1)	C(6)—C(7)	1.47 (1)
C(9)—C(10)	1.519 (8)		
O(3)—P(1)—O(4)	112.5 (2)	O(3)—P(1)—O(5)	115.5 (2)
O(4)—P(1)—O(5)	106.0 (2)	O(3)—P(1)—C(9)	110.2 (2)
O(4)—P(1)—C(9)	107.3 (2)	O(5)—P(1)—C(9)	104.8 (2)
C(7)—O(1)—C(8)	115.4 (5)	C(8)—N(1)—C(9)	122.0 (4)
C(2)—C(1)—C(6)	119.6 (9)	C(1)—C(2)—C(3)	119 (1)
C(2)—C(3)—C(4)	121 (1)	C(3)—C(4)—C(5)	119.8 (10)
C(4)—C(5)—C(6)	124 (1)	C(1)—C(6)—C(5)	116.2 (8)
C(1)—C(6)—C(7)	121.2 (7)	C(5)—C(6)—C(7)	122.6 (9)
O(1)—C(7)—C(6)	108.7 (6)	O(1)—C(8)—O(2)	124.8 (6)
O(1)—C(8)—N(1)	110.4 (5)	O(2)—C(8)—N(1)	124.8 (6)
P(1)—C(9)—N(1)	109.4 (4)	P(1)—C(9)—C(10)	111.6 (4)
N(1)—C(9)—C(10)	112.3 (4)		

C(8)—O(1)—C(7)—C(6)	−166.6	O(4)—P(1)—C(9)—N(1)	55.3
C(7)—O(1)—C(8)—O(2)	3.1	O(4)—P(1)—C(9)—C(10)	−179.8
C(7)—O(1)—C(8)—N(1)	−179.1	O(5)—P(1)—C(9)—N(1)	167.7
C(9)—N(1)—C(8)—O(1)	−179.2	O(5)—P(1)—C(9)—C(10)	−67.4
C(9)—N(1)—C(8)—O(2)	−1.4	C(8)—N(1)—C(9)—P(1)	−92.3
O(3)—P(1)—C(9)—N(1)	−67.4	C(8)—N(1)—C(9)—C(10)	143.2
O(3)—P(1)—C(9)—C(10)	57.5		

D—H···*A*	H···*A*	*D*—H···*A*
N(1)—H(1*A*)···O(2^{i})	1.963	155.8
O(4)—H(4*A*)···O(3^{ii})	2.253	111.5
O(5)—H(5*A*)···O(3^{iii})	1.812	149.3

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

The crystal was mounted along the largest dimension and data were collected with a diffractometer equipped with a copper rotating anode and a highly oriented graphite monochromator using a constant scan speed of 8° min^{-1} in ω. Weak reflections [$I < 5\sigma(I)$] were rescanned a maximum of four times and the counts accumulated to assure good counting statistics. The data were corrected for Lorentz and polarization effects.

The systematic absences ($0k0$, $k = 2n + 1$) indicated a choice between the $P2_1$ and $P2_1/m$ space groups. Since the molecule is chiral, the former space group was chosen. All non-H atoms were refined anisotropically by the full-matrix least-squares method. H atoms were included in ideal positions with a fixed isotropic $U = 0.08$ Å^2. The final difference map was devoid of significant features.

All calculations were performed on a Silicon Graphics Personal Iris 4D/35 IBM-compatible PC. *TEXSAN* (Molecular Structure Corporation, 1990) was used for data reduction, *SHELXS*86 (Sheldrick, 1990*a*) for structure solution and *SHELXTL* (Sheldrick, 1990*b*) for structure refinement.

We are grateful to Professor Richard E. Marsh at California Institute of Technology, USA, for his helpful comments on the manuscript.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: MD1002). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Redetermination of 4-Hydroxy-3-nitrobenzenearsonic Acid

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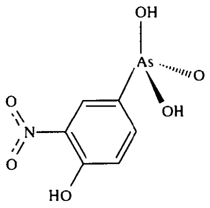
Abstract

The structure of the title compound, $C_6H_6AsNO_6$, has been redetermined to provide a more accurate molecular model. The molecule contains a pentavalent As atom coordinated in an approximately tetrahedral configuration to three O atoms and a benzene ring C atom. The molecules are linked by a network of hydrogen bonds between the O atoms of the arsonic group, around centres of inversion.

Comment

Organo-arsenic compounds have attracted interest because of their possible biomedical uses (Dhubhghaill & Sadler, 1991) and numerous structural studies have been carried out by obsolete photographic methods. One such example is the title compound, (I) (Chatterjee & Sen Gupta, 1977), where oscillation and Weissenberg photographs were taken along three crystallographic axes with Cu $K\alpha$ radiation, and the intensities were measured visually using the multiple-film technique. The structure was refined to $R = 0.12$ for 1271 observed reflections and no absorption correction was applied. This redetermination, using modern diffraction apparatus and computational methods, is in good agreement with the model determined by Chatterjee & Sen Gupta (1977) but improves the accuracy quite significantly. For example, the R factor is reduced to 0.058 and uncertainties in bond lengths and angles are reduced by a factor of two or more.



(I)

H atoms on the benzene ring were generated in their most logical positions and included in the structure-factor calculations but not refined. Attempts were made to locate the H atoms associated with the arsonic and