steric factors must be of minor importance. In Table 3 there are four complexes $[Pt(DMSO)Cl_3]^-$, for which both the *cis* and the *trans* influence is constant. The distribution of 0·006 Å for the Pt—S distance in these complexes, calculated as $\sigma = [\Sigma(d_n - \bar{d})/(n-1)]^{1/2}$, indicates that experimental errors and packing forces are of minor importance as compared to other factors. If complexes [Pt(DMSO)-Cl*XY*], with Cl *trans* to S (15 distances, constant *trans* influence), are included in the calculation the distribution is increased to 0·022 Å, which thus emphasizes the importance of the *cis* influence of *X*/*Y* on S. If, on the other hand, the distribution is calculated for complexes $[Pt(DMSO)Cl_2X]$, with the two Cl atoms in the *cis* position (eight distances, constant *cis* influence), it is only slightly smaller, 0·017 Å. Hence it may be concluded that both *cis* and *trans* influences are important for the distribution of the Pt—S distance and that they are significantly larger than the effect of packing forces.

Financial support from the Swedish Natural Science Research Council is gratefully acknowledged.

References

ABRAHAMS, S. C. & KEVE, E. T. (1971). *Acta Cryst.* A**27**, 157–165.

BUGARCIC, Z., NORÉN, B., OSKARSSON, Å., STÅLHANDSKE, C. & ELDING, L. I. (1991). *Acta Chem. Scand.* **45**, 361–366.

Checklist for Authors (1985). *Acta Cryst.* B**41**, 1–4.

COTTON, F. A. & FRANCIS, R. (1960). *J. Am. Chem. Soc.* **82**, 2986–2991.

DAVIES, J. A. (1981). *Adv. Inorg. Chem. Radiochem.* **24**, 115–187.

ELDING, L. I. & OSKARSSON, Å. (1987). *Inorg. Chim Acta*, **130**, 209–213.

LANGS, D. A., HARE, C. R. & LITTLE, R. G. (1967). *Chem. Commun.* pp. 1080–1081.

LUNDGREN, J. O. (1982). Crystallographic computer programs. Report No. UUIC-B13-4-05. Univ. of Uppsala, Sweden.

UGOZZOLI, F. (1987). *Comput. Chem.* **11**, 109–120.

WALKER, N. & STUART, D. (1983). *Acta Cryst.* A**39**, 158–166.

Acta Cryst. (1991). C**47**, 2104–2107

Structure of 1-(*S*)-(3-Hydroxy-2-phosphonylmethoxypropyl)cytosine; an Antiviral Agent

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(*Received* 3 *July* 1990; *accepted* 22 *November* 1990)

Abstract. 4-Amino-1-(*S*)-{2-[(dihydroxyphosphoryl)-methoxy]-3-hydroxypropyl}-2(1*H*)-pyrimidinone, $C_8H_{14}N_3O_6P$, $M_r = 279{\cdot}19$, orthorhombic, $P2_12_12_1$, $a = 6{\cdot}926$ (1), $b = 9{\cdot}084$ (2), $c = 18{\cdot}602$ (3) Å, $V = 1170{\cdot}4$ (4) Å^3, $Z = 4$, $D_x = 1{\cdot}58$ (1) Mg m^{-3}, λ(Cu $K\alpha$) = 1·54178 Å, $\mu = 2{\cdot}4$ mm^{-1}, $F(000) = 584$, $T = 168$ K, final $R = 0{\cdot}024$ for 1393 unique observed reflections. The molecule has been found to exist in a folded zwitterionic form where the negatively charged phosphonyl group and the positively charged cytosine ring are in proximity. The crystal packing involves significant intermolecular hydrogen-bond contacts.

Introduction. The recent discovery of the potent antiviral activity of several (*S*)-*N*-(3-hydroxy-2-phosphonylmethoxypropyl) derivatives of heterocyclic bases (DeClercq, Holý, Rosenberg, Sakuma, Balzarini & Maudgal, 1986) has attracted considerable attention to this novel group of nucleotide analogues. The chemical structure of these compounds is characterized by a replacement of the nucleotide carbohydrate moiety with a 2,3-dihydroxypropyl chain linked to the heterocyclic base by the stable C—N linkage and by regiospecific substitution of the phosphonylmethyl ether group for the phosphoric acid ester residue. It is assumed (Holý, 1986) that these compounds might adopt conformations resembling those of their natural nucleotide counterparts and, consequently, might replace nucleotides in enzyme–substrate/product complexes. The biological

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0108-2701/91/102104-04$03.00

activity in the series is limited to the (2*S*)-enantiomers; it was only encountered with compounds derived from explicitly basic heterocyclic systems bearing amino groups, *e.g.* adenine, 2,6-diaminopurine, 2-aminopurine, guanine and cytosine (DeClercq, Sakuma, Baba, Pauwels, Balzarini, Rosenberg & Holý, 1987). All these facts suggest the involvement of intramolecular stabilization forces in determining the preferred conformation(s) of these compounds – most probably an interaction of the base and the phosphonate group of the side chain. This paper describes the structure of the cytosine derivative.

Experimental. The title compound (HPMPC) was synthesized, according to the procedure of Holý, Rosenberg & Dvořáková (1989), as a monohydrate of its free-acid form. A small sample was recrystallized by slow evaporation from water and a colourless single crystal, 0·2 × 0·2 × 0·2 mm, was used for diffraction measurements on a CAD-4 diffractometer at low temperature with Ni-filtered Cu $K\alpha$ radiation. The unit-cell parameters were determined by least-squares fit of 48 reflections in the range $41 < 2\theta < 56°$. The space group was determined from systematic absences. 1417 reflections were measured with $0 \le h \le 8$, $0 \le k \le 11$, $0 \le l \le 23$, $2\theta_{max} = 150°$ and the ω–2θ scan mode. Three standard reflections were monitored every 2 h and showed a 2% variation. 1393 reflections with $I > 1{\cdot}96\sigma_I$ were considered observed. The net intensities were corrected for Lorentz and polarization factors, but not for absorption. The structure was solved with the *MULTAN*87 direct-methods package (Debaerdemaeker, Germain, Main, Tate & Woolfson, 1987) and refined by the full-matrix least-squares procedure of *SHELX*76 (Sheldrick, 1976). The hydrogen atoms were easily found on a difference Fourier map. All atoms of HPMPC were refined with fixed site-occupation factors of 1·0 and with no other constraints. The function minimized was $\sum w(|F_o| - |F_c|)^2$. Final R and wR values for the (*S*)-enantiomorph (known from the synthesis) are 0·0236 and 0·0323 and the corresponding values for the (*R*)-enantiomorph, calculated with inverted coordinates, are 0·0324 and 0·0463. The goodnees of fit $S = 1{\cdot}461$. 219 parameters were refined, $(\Delta/\sigma)_{max} = 0{\cdot}018$. The weighting function used was $w = 1{\cdot}0/(\sigma_F^2 + 0{\cdot}0003F^2)$ with σ_F from counting statistics. Maximum and minimum values of the final $\Delta\rho$ map were 0·20 and −0·31 e Å^{-3}, respectively. Atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1974, Vol. IV). All atoms were considered neutral. The final structural parameters were calculated with *PARST*88 (Nardelli, 1988).

HPMPC

Discussion. An *ORTEP* view (Johnson, 1975) of the molecule is shown in Fig. 1. The fractional atomic coordinates and equivalent displacement parameters U_{eq} are given in Table 1, selected bond lengths, bond angles and torsion angles are in Table 2.* The crystal packing is shown in Fig. 2.

The molecule assumes a folded conformation where the phosphonyl group and the cytosine ring

* Lists of structure factors and atomic displacement parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 53776 (11 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

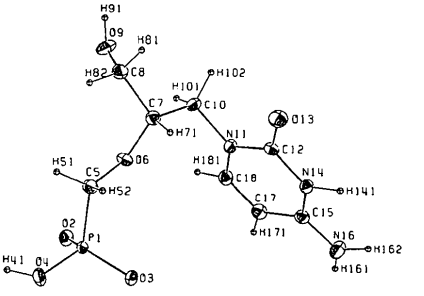

Fig. 1. *ORTEP* view of the molecule.

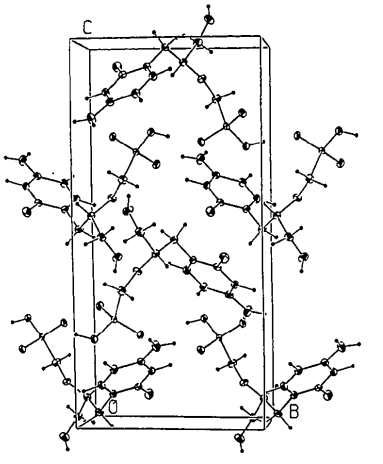

Fig. 2. Crystal packing.

Table 1. *Fractional atomic coordinates and U_{eq} values (Å^2) with e.s.d.'s in parentheses*

$U_{eq} = \frac{1}{3}(U_{11} + U_{22} + U_{33})$

	x	y	z	U_{eq}
P1	0·4415 (1)	0·2936 (0)	0·7180 (0)	0·0118 (1)
O2	0·2807 (2)	0·3864 (1)	0·6871 (1)	0·0170 (3)
O3	0·3783 (2)	0·1599 (1)	0·7594 (1)	0·0164 (3)
O4	0·5765 (2)	0·3872 (2)	0·7679 (1)	0·0191 (4)
C5	0·5948 (3)	0·2330 (2)	0·6446 (1)	0·0169 (5)
O6	0·4705 (2)	0·1609 (1)	0·5949 (1)	0·0152 (3)
C7	0·5623 (3)	0·0553 (2)	0·5491 (1)	0·0149 (4)
C8	0·6931 (3)	0·1247 (2)	0·4931 (1)	0·0179 (5)
O9	0·5793 (2)	0·1945 (2)	0·4387 (1)	0·0225 (4)
C10	0·3983 (3)	−0·0302 (2)	0·5142 (1)	0·0174 (5)
N11	0·2924 (2)	−0·1202 (2)	0·5669 (1)	0·0149 (4)
C12	0·3706 (3)	−0·2553 (2)	0·5843 (1)	0·0155 (5)
O13	0·5223 (2)	−0·3006 (2)	0·5601 (1)	0·0228 (4)
N14	0·2586 (2)	−0·3388 (2)	0·6309 (1)	0·0142 (4)
C15	0·0882 (3)	−0·2970 (2)	0·6596 (1)	0·0154 (4)
N16	−0·0005 (3)	−0·3888 (2)	0·7030 (1)	0·0217 (4)
C17	0·0160 (3)	−0·1558 (2)	0·6405 (1)	0·0172 (5)
C18	0·1212 (3)	−0·0734 (2)	0·5946 (1)	0·0171 (5)
H41	0·590 (5)	0·482 (4)	0·756 (2)	0·047 (8)
H51	0·662 (4)	0·315 (3)	0·626 (1)	0·021 (6)
H52	0·707 (4)	0·172 (3)	0·664 (1)	0·030 (6)
H71	0·638 (4)	−0·009 (2)	0·581 (1)	0·020 (6)
H81	0·770 (4)	0·045 (3)	0·474 (1)	0·024 (6)
H82	0·782 (3)	0·193 (2)	0·517 (1)	0·014 (5)
H91	0·641 (5)	0·184 (3)	0·402 (2)	0·040 (8)
H101	0·311 (4)	0·041 (3)	0·493 (1)	0·022 (6)
H102	0·450 (4)	−0·096 (3)	0·475 (1)	0·027 (6)
H141	0·306 (4)	−0·442 (3)	0·647 (1)	0·037 (7)
H161	−0·106 (5)	−0·365 (3)	0·720 (1)	0·037 (8)
H162	0·058 (3)	−0·482 (3)	0·710 (1)	0·017 (5)
H171	−0·097 (4)	−0·119 (3)	0·659 (1)	0·028 (6)
H181	0·082 (4)	0·023 (3)	0·579 (1)	0·024 (6)

Table 2. *Selected bond lengths* (Å), *bond angles* (°) *and torsion angles* (°) *with e.s.d.'s in parentheses*

P1—O2	1·510 (1)	C10—N11	1·472 (3)
P1—O3	1·503 (1)	N11—C12	1·380 (3)
P1—O4	1·568 (2)	N11—C18	1·361 (2)
P1—C5	1·815 (2)	C12—O13	1·215 (2)
C5—O6	1·423 (2)	C12—N14	1·389 (3)
O6—C7	1·432 (2)	N14—C15	1·350 (2)
C7—C8	1·518 (3)	C15—N16	1·313 (3)
C7—C10	1·522 (3)	C15—C17	1·422 (3)
C8—O9	1·431 (3)	C17—C18	1·349 (3)

O4—P1—C5	105·1 (1)	C10—N11—C18	120·8 (2)
O3—P1—C5	108·1 (1)	C10—N11—C12	117·0 (2)
O3—P1—O4	108·0 (1)	C12—N11—C18	122·1 (2)
O2—P1—C5	108·3 (1)	N11—C12—N14	114·4 (2)
O2—P1—O4	111·2 (1)	N11—C12—O13	123·6 (2)
O2—P1—O3	115·5 (1)	O13—C12—N14	122·0 (2)
P1—C5—O6	105·9 (1)	C12—N14—C15	125·6 (2)
C5—O6—C7	115·2 (2)	N14—C15—C17	117·5 (2)
O6—C7—C10	105·3 (2)	N14—C15—N16	118·3 (2)
O6—C7—C8	113·3 (2)	N16—C15—C17	124·2 (2)
C8—C7—C10	111·4 (2)	C15—C17—C18	118·0 (2)
C7—C8—O9	109·9 (2)	N11—C18—C17	122·5 (2)
C7—C10—N11	111·8 (2)		

P1—C5—O6—C7	−155·8 (1)	C12—N14—C15—C17	0·3 (3)
C5—O6—C7—C10	167·3 (2)	N14—C15—C17—C18	0·6 (3)
O6—C7—C10—N11	−67·4 (2)	C15—C17—C18—N11	−0·5 (3)
O6—C7—C8—O9	−72·8 (2)	C17—C18—N11—C12	−0·4 (3)
C7—C10—N11—C12	−82·5 (2)	C18—N11—C12—N14	1·1 (3)
N11—C12—N14—C15	−1·1 (3)		

are in proximity. The shortest interatomic distances within the molecule between the phosphonyl group and the cytosine ring are O3···C18 = 4·130 (3) and O2···H181 = 4·11 (3) Å, respectively. These distances are rather longer than the corresponding van der Waals distances.

Table 3. *Hydrogen bonds* (Å, °) *with e.s.d.'s in parentheses*

O4—H41	O4···O3^{i}	H41···O3^{i}	O4—H41···O3^{i}
0·90 (3)	2·548 (2)	1·65 (3)	176 (3)
O9—H91	O9···O2^{ii}	H91···O2^{ii}	O9—H91···O2^{ii}
0·80 (3)	2·822 (2)	2·03 (3)	168 (3)
N16—H162	N16···O2^{iii}	H162···O2^{iii}	N16—H162···O2^{iii}
0·94 (2)	2·837 (2)	2·00 (2)	147 (2)
N14—H141	N14···O2^{iii}	H141···O2^{iii}	N14—H141···O2^{iii}
1·03 (3)	2·711 (2)	1·744 (3)	154 (2)
N16—H161	N16···O3^{iv}	H161···O3^{iv}	N16—H161···O3^{iv}
0·83 (3)	2·744 (3)	1·94 (3)	166 (3)

Symmetry codes: (i) $-x+1, y+0·5, -z+1·5$; (ii) $x+0·5, -y+0·5, -z+1$; (iii) $x, y-1, z$; (iv) $-x, y-0·5, -z+1·5$.

Only one hydrogen atom has been found in the phosphonyl group and this indicates that the group is negatively charged. The fact that the P1—O2 and P1—O3 distances are almost equal supports this idea. The hydrogen atom H141 is bound to N14 in the cytosine ring, which indicates that this part of the molecule is positively charged. The cytosine ring is almost planar which can be seen from the corresponding torsion angles in Table 2.

The structure of HPMPC can be compared with the crystal structure of 1-β-D-arabinofuranosylcytosine 5′-monophosphate trihydrate, which was also found to be zwitterionic, and its conformation also falls within one of the most preferred confomational states for the arabinose nucleotides and ribonucleotides (Sherfinski, Marsh, Chwang & Sundaralingam, 1979). The spatial relationship between the phosphonyl group and the cytosine ring is similar, but the cytosine ring approaches the phosphonyl group more closely and, pronouncedly, by its C—C edge, whereas in HPMPC the ring face approaches the phosphonyl group. Corresponding bond lengths and bond angles of the two structures agree within 0·020 (5) Å and 2·0 (3)°, respectively.

The zwitterionic molecules of HPMPC in the crystal are connected by a number of hydrogen bonds (Table 3). The donor–acceptor distance of the hydrogen bond O4···O3 can be compared with the corresponding one in the structure of phosphoric acid (Furberg, 1955), where it was found to be 2·53 (1) Å. The distances corresponding to O4···O3, N14···O2 and N16···O2/N16···O3 were found by Sherfinski *et al.* (1979) to be 2·617 (5), 2·923 (5) and 2·790 (5) Å, respectively. The rather short hydrogen bonds of HPMPC are evidence of strong intermolecular interactions among the molecules in the crystal.

This work was supported in part by grant CA17562 from the National Cancer Institute, USA. The authors thank Dr Vratislav Langer, Chalmers University and University of Göteborg, Sweden, for kindly providing comparative data from the Cambridge Structural Database.

References

DEBAERDEMAEKER, T., GERMAIN, G., MAIN, P., TATE, C. & WOOLFSON, M. M. (1987). *MULTAN87. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data.* Univ. of York, England.

DECLERCQ, E., HOLÝ, A., ROSENBERG, I., SAKUMA, T., BALZARINI, J. & MAUDGAL, P. C. (1986). *Nature (London)*, **323**, 464–467.

DECLERCQ, E., SAKUMA, T., BABA, M., PAUWELS, R., BALZARINI, J., ROSENBERG, I. & HOLÝ, A. (1987). *Antiviral Res.* **8**, 261–272.

FURBERG, S. (1955). *Acta Chem. Scand.* **9**, 1557–1566.

HOLÝ, A. (1986). *Chem. Scr.* **26**, 83–89.

HOLÝ, A., ROSENBERG, I. & DVOŘÁKOVÁ, H. (1989). *Collect. Czech. Chem. Commun.* **54**, 2470–2501.

JOHNSON, C. K. (1975). *ORTEP.* Oak Ridge National Laboratory, Tennessee, USA.

NARDELLI, M. (1988). *PARST88. A System of Computer Routines for Calculating Molecular Parameters from the Results of Crystal Structure Analysis.* Univ. of Parma, Italy.

SHELDRICK, G. M. (1976). *SHELX76.* Program for crystal structure determination. Univ. of Cambridge, England.

SHERFINSKI, J. S., MARSH, R. E., CHWANG, A. K. & SUNDARALINGAM, M. (1979). *Acta Cryst.* B**35**, 2141–2144.

Acta Cryst. (1991). C**47**, 2107–2109

Structure of 10-*tert*-Butyl-7β-ethynyl-7α-hydroxyspiro[5.5]undec-1-en-3-one*

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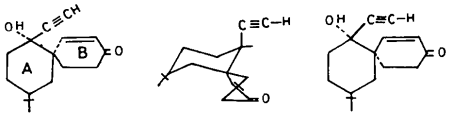
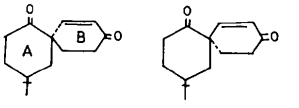
(*Received* 10 *September* 1990; *accepted* 6 *March* 1991)

Abstract. $C_{17}H_{24}O_2$, $M_r = 260{\cdot}36$, monoclinic, $P2_1/c$, $a = 10{\cdot}712\ (3)$, $b = 11{\cdot}817\ (3)$, $c = 12{\cdot}318\ (3)$ Å, $\beta = 107{\cdot}75\ (2)°$, $V = 1485{\cdot}0\ (4)$ Å^3, $Z = 4$, $D_m = 1{\cdot}16\ (2)$, $D_x = 1{\cdot}168$ g cm^{-3}, graphite-monochromatized Cu $K\alpha$ radiation, $\lambda = 1{\cdot}5418$ Å, $\mu = 5{\cdot}47$ cm^{-1}, $F(000) = 568$, $T = 298$ K, final $R = 0{\cdot}040$, $wR = 0{\cdot}037$ for 2087 reflections with $I > 2\sigma(I)$. One of the cyclohexane rings is in the chair conformation and the other is in the half-chair conformation. Molecules are stabilized by O—H···O intermolecular hydrogen bonds.

Introduction. The title compound was studied mainly to learn the geometry of the spiro carbinol (1). In particular the relative orientation of the unsaturated rings is of unusual importance in understanding the mechanism of base-catalyzed rearrangements of oxy-Cope systems (Seshu Sekhara Rao, Kumar, Rajagopalan & Swaminathan, 1982; Swaminathan, 1984). This carbinol (m.p. 405–406 K) was obtained (Ravikumar, 1985) by the ethynylation of the spiro diketone (4) and assigned the stereochemistry indicated in structure (1), also represented conformationally in structure (2). This assignment was tentative based on the assumptions (i) that the sp^2 C atom at the spiro junction is more likely to have an axial orientation with respect to ring *A* in the diketone (4) and (ii) that the attack of the acetylide ion occurs axially as has been established for 2,2-disubstituted cyclohexanones (Milas, Macdonald & Black, 1948; Attenburrow, Cameron, Chapman, Evans, Hems, Jansen & Walker, 1952). It was of interest therefore to determine unequivocally the structure of (1) by X-ray analysis.



(1) (2) (3)



(4) (5)

Experimental. The title compound was synthesised in the Department of Organic Chemistry, University of Madras, and its density was measured by flotation. White needle-shaped crystals from benzene, 0·40 × 0·20 × 0·50 mm, Enraf–Nonius CAD-4 single-crystal diffractometer, $\omega/2\theta$ scan, cell parameters from 20 accurately centred reflections, $30 \le 2\theta \le 60°$. Lp correction but no absorption correction, three check reflections measured every 100 reflections showed a 3% change in the intensity of standard reflections, $0 \le h \le 11$, $0 \le k \le 14$, $-14 \le l \le 14$, 2251 unique reflections, $R_{int} = 0{\cdot}067$, 2087 reflections with $I > 2\sigma(I)$ used in the least-squares refinement. Structure

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0108-2701/91/102107-03$03.00