SYNTHESIS AND STRUCTURE OF 1,2-O-ISOPROPYLIDENE-α-D-

GLUCOFURANOSE 3,5-PHENYLCYCLOPHOSPHONATE

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The molecular and crystal structure of glucofuranose 3,5-phenylcyclophosphonate, containing a six-membered 1,3,2-dioxaphosphorinane fragment, was determined by x-ray crystallography. The structural and stereochemical characteristics of the compound are compared with those of our previously investigated 0, S, and Se derivatives of the cyclic phosphonates of furanoses with a seven-membered 1,3,2-dioxaphosphenane fragment.

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Earlier [1, 2], during the treatment of 1,2-0-propylidene- α -D-glucopyranose 3,5,6-bicyclophosphate and its sulfur and selenium analogs with water, we obtained the corresponding 1,2-0-isopropylidene- α -D-glucofuranose 3,6-cyclophosphates (I-III).



The 3,6-cyclophosphate (I) can also be obtained by the reaction of 1,2-0-isopropylidene- α -glucofuranose 3,5,6-bicyclophosphite with 30% aqueous hydrogen peroxide. When the reaction was extended to benzoyl peroxide, the process was stereospecific, and the monocyclic derivative of 1,2-0-isopropylidene- α -D-glucofuranose (IV) was obtained. The reaction was conducted in boiling dioxane for 2 h. According to NMR spectroscopy, the product had a different structure in the phosphocyclic fragment.



To determine the molecular and crystal structure of (IV) we carried out an x-ray crystallographic analysis. As a result it was shown that ring A in compound (IV) was a phenylphosphonic acid derivative, attached to the sugar skeleton through the hydroxyls at positions 3 and 5. Thus, compound (IV) (1,2-O-isopropylidene- α -D-glucofuranose 3,5-phenylcyclophosphonate) contains a six-membered 1,3,2-dioxaphosphorinane ring.

EXPERIMENTAL

The x-ray experiment was conducted with colorless crystals measuring 0.1 × 0.25 × 0.45 mm on a Nicolet P3 automatic diffractometer (λ Mo, β filter). We measured 915 reflections

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Atom	x	y y	z	U ^{eq} iso
Р	1320(1)	3053(1)	5000	48(1)
0(1)	5044(2)	3609(3)	2024(7)	100(2)
O(2)	4446(2)	1788(3)	4314(5)	65(1)
O(3)	2364(2)	2927(3)	5640(4)	55(1)
O(4)	3438(2)	3669(2)	1640(5)	61(1)
O(5)	1180(2)		2319(8)	83(1)
O(6)	1257(2)	2900(3)	2438(5)	60(1)
0(7)	523(2)	2115(4)	6225(7)	65(1)
C(1)	4244(3)	3865(5)	3101(11)	61(2)
C(2)	3940(3)	2763(5)	4864(10)	51(2)
C(3)	2861(3)	2104(5)	4446(8)	47(2)
C(4)	2785(4)	2297(5)	1998(9)	48(2)
C(5)	1797(3)	2208(4)	1064(6)	52(1)
C(6)	1182(3)	764(4)	541(9)	75(2)
C(7)	5263(3)	2446(5)	2968(10)	69(2)
C(8)	5330(4)	1454(7)	1167(13)	120(4)
C(9)	6193(3)	2978(5)	4304(10)	100(3)
C(10)	1401(3)	4818(4)	5463(7)	48(2)
C(11)	1024(2)	5182(4)	7405(7)	59(2)
C(12)	1064(3)	6563(6)	7746(10)	74(2)
C(13)	1471(4)	7562(6)	6203(11)	82(3)
C(14)	1838(3)	7193(5)	4299(9)	80(2)
C(15)	1820(3)	5833(5)	3953(9)	62(2)
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TABLE 1. Atomic Coordinates (×10⁴) and Temperature Factors (Å 2 × 10 3)

with I $\geq 3\sigma(I)$ to $2\theta_{max} = 45^{\circ}$. The crystals were monoclinic; a = 14.262(3), b = 10.073(2), c = 6.087(1) Å, $\gamma = 107.30(2)^{\circ}$, V = 834.9(3) Å³, M = 342, C₁₅H₁₀O₇P, Z = 2, P2₁, R = 0.023, R_w = 0.026. The structure was solved by the direct method and refined by least-squares treatment using the SHELXTL package with anisotropic (P, C, O) and isotropic (H) parameters and the $\omega = 1/\sigma^2 |F|$ weighting scheme [3]. The hydrogen atoms were localized in difference syntheses, and their position and temperature parameters were included in the final refinement. The atomic coordinates are given in Table 1.

RESULTS AND DISCUSSION

The general appearance of the molecule of (IV) and the bond lengths are given in Fig. 1. The bond angles, the coordinates of the hydrogen atoms, and the temperature factors are given in Tables 2 and 3. The packing of the molecules in a projection onto the (010) plane is shown in Fig. 2.

In cyclic phosphorus esters the internal angles at the oxygen atoms depend strongly on the number of atoms and on the strain of the ring. In [4] during comparison of the structure of the six- and seven-membered rings of organophosphorus molecules with similar structure it was noticed that the internal angles were smaller in the six-membered rings (~116°) than in the seven-membered rings (~119°). Further "contraction" of the rings to five-membered reduced the angles to ~110°C [5], whereas an increase to ~124°C was naturally observed in the eight-membered heterocycles [6]. Thus, for example, in the structure in [7], the molecules of which of which contain five- and seven-membered organophosphorus ring simultaneously, the P-O-C angles are 116 and 123°C respectively.

In six-membered dioxaphosphorinane rings the endocyclic angles at the oxygen atoms usually vary in the range of 115-120° [8]. The increase of the angles at the O3 and O6 atoms in the structure of compound (IV) (av. 125.4°) can therefore be considered extremely significant. [In the structures (I-III) the average value of the P-O-V angles is smaller and amounts to 121.5°.]

In [9] it was noticed that the P-O-C angle in the esters of tetracoordinated phosphorus is a more sensitive parameter of the strain in the ring than the O-P-O angle. In fact, although ring A in the structure of (IV) has an extended chair conformation for this fragment [the P and C4 atoms deivate from the "best" plane of the four atoms (± 0.038 Å) by -0.362 and

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Angle	ω	Angle	ω
O(3)-P-O(6)	105,4(1)	O(3)-P-O(7)	113,3(2)
O(6) - P - O(7)	115,9(2)	O(3) - P - C(10)	105,0(2)
O(6) - P - C(10)	104,0(2)	O(7) - P - C(10)	112,2(2)
C(1) - O(1) - C(7)	110,6(4)	C(2) - O(2) - C(7)	109,2(3)
P - O(3) - C(3)	124,0(2)	C(1) - O(4) - C(4)	107,8(3)
P - O(6) - C(5)	126,8(3)	O(1) - C(1) - O(4)	110,5(5)
O(1) - C(1) - C(2)	105,6(4)	O(4) - C(1) - C(2)	107,4(3)
O(2) - C(2) - C(1)	104,3(4)	O(2) - C(2) - C(3)	108,6(4)
C(1) - C(2) - C(3)	103,7(4)	O(3) - C(3) - C(2)	106,0(4)
O(3) - C(3) - C(4)	111,0(4)	C(2) - C(3) - C(4)	102,3(4)
O(4) - C(4) - C(3)	102,9(4)	O(4) - C(4) - C(5)	109,3(4)
C(3) - C(4) - C(5)	117,9(4)	O(6) - C(5) - C(4)	112,2(3)
O(6) - C(5) - C(6)	110,5(3)	C(4) - C(5) - C(6)	114,1(4)
O(5) - C(6) - C(5)	110,3(4)	O(1) - C(7) - O(2)	105,6(4)
O(1)-C(7)-C(8)	109,0(5)	O(2) - C(7) - C(8)	108,4(4)
O(1)-C(7)-C(9)	108,1(4)	O(2) - C(7) - C(9)	111,5(5)
C(8) - C(7) - C(9)	113,8(5)	P - C(10) - C(11)	119,0(3)
P-C(10)-C(15)	121,7(4)	C(11) - C(10) - C(15)	119,3(4)
C(10) - C(11) - C(12)	119,1(4)	C(11)-C(12)-C(13)	120,9(6)
C(12) - C(13) - C(14)	119,6(5)	C(13) - C(14) - C(15)	120,2(5)
C(10)-C(15)-C(14)	120,9(5)		

TABLE 2. Bond Angles ω (deg) in the Molecule of (IV)



Fig. 1. General appearance and the bond lengths of the molecule of (IV).

0.503 Å on different sides], the "chair" is largely flattened. [The phosphorus atoms is deflected from the plane of the three oxygen atoms significantly less (0.453 Å) than in the structures of (I-III) (av. 0.579 Å).] The angles of inflection between the central plane and the planes of the O-P-O and carbon atoms are 22.4 and 40.5°, whereas these angles are usually in the range of 40-60° [10, 11]. Analogous flattering of the six-membered ring, accompanied by an increase in the P-O-C angles, was observed in [12] for cyclic monophosphates.

There are several possible reasons for the flattering of the phosphate ring observed in (IV). It may be the effect of crystal packing or the result of steric interaction with the bulky substitutent at the phosphorus atom by analogy with [13], where the dioxaphosphor-



Fig. 2. Packing of the molecules in a projection onto the (010) plane.

inane ring adopts the half-chair conformation in the molecule with the triphenyl substituent. The distortion of the tetrahedral environment of the phosphorus atom may arise as a result of the "hinge" effect of the oxygen atom, which arises in the transition from sp^3 to sp^2 hybridization and gives rise to an increase in the negative charge at the phosphorus atom owing to the increase in the π -bonding character of the P-O bond [9].

In ring A of (IV) not only is there an increase in the endocyclic P-O-C angles but the angles at the carbon atoms are also inequal - the angle at C⁴ is increased (117.9°) compared with the internal angles at the C3 and C5 atoms (111.0 and 112.2°). This clearly results from condensation of ring A with the furanose ring B, since the angles at the carbon atoms in phosphate rings without substituents are equal and amount to 110-112° [8]. A similar increase in the angle at the C4 atom was observed in the structures of (I-III) (av. 120.6°), where addition of the furanose ring also takes place at the C3-C4 bond. The chemically equivalent bond lengths also differ somewhat from each other, but their values are close to those described for 1,3,2-dioxaphosphorinane 2-oxide systems [8].

In the seven-membered (I-III) and six-membered (IV) phosphorus rings it is important to establish the position of the substituents at the phosphorus atom in relation to the "best" planes of fragments A. For this purpose we used the torsion angles of the P-X and P-07 bonds and the 03-C3 bond, which lie in the best plane. In the molecules of (I-III) the X=P-03-C3 angles are -172.3, -170.8, and -170.5°, i.e., the 08=P, S=P, and Se=P bonds and the 03-C3 bond are almost coplanar, and the 08, S, and Se atoms are consequently in the equatorial position. The 07-P-03-C3 angles are 59.1, 59.0, and 59.5°, i.e., the oxygen atoms of the hydroxyl groups in the molecules of (I-III) are in the pseudoaxial position.

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Atom	x	y	z ·	Ueq iso
H(5)O	551(28)	-804(41)	2302(87)	129(13)
H(1)	4416(23)	4756(36)	3698(78)	70(11)
H(2)	4097(22)	3057(34)	6362(66)	52(11)
H(3)	2623(19)	1234(28)	4836(59)	48(8)
H(4)	3009(21)	1616(31)	1215(58)	57(10)
H(5)	1917(21)	2715(33)	-371(69)	46(10)
H(61)	1429(31)	104(46)	-278(88)	63(18)
H(62)	501(26)	792(39)	211(91)	91(13)
H(81)	5826(37)	1963(58)	200(117)	147(18)
H(82)	4650(37)	1178(53)	279(124)	153(19)
H(83)	5444(36)	748(53)	1726(108)	171(19)
H(91)	6311(34)	2149(54)	4875(101)	125(16)
H(92)	6086(32)	3569(49)	5580(107)	138(16)
H(93)	6682(32)	3363(52)	3374(98)	133(16)
H(11)	699(23)	4435(35)	8583(75)	63(11)
H(12)	813(26)	6808(40)	8983(80)	97(13)
H(13)	1471(25)	8528(40)	6335(74)	97(13)
H(14)	2097(25)	7882(37)	3176(76)	108(13)
H(15)	2074(24)	5553(33)	2711(68)	73(11)
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TABLE 3. Coordinates of the Hydrogen Atoms (×10⁴) and the Temperature Factors (Å × 10³)

The C10-P-03-C3 angle in the molecule of (IV) is -140.6°, i.e., the C10 atom of the phenyl ring is in the pseudoequatorial position to ring A. The O7 oxygen atom of the phosphoryl P=07 bond in turn is axial to the O3-C3-C5-C6 plane, since the O7=P-O3-C3 angle is 96.7°.

In the structure of (IV) the phenyl ring D does not eclipse the phosphoryl bond, since the torsion angle 07=P-C10-C11 is 24.5°, and the 07 atom is deflected from the plane D by -0.636 Å (Fig. 2). The angle between the average plane of the fragment D and the 03, C3, C5, C6 plane of ring A is 68.1°.

The phosphorus atom is deflected very little (-0.055 Å) from the plane of the phenyl ring $C10-C15(\pm 0.013 \text{ \AA})$. In this case it can be supposed that the phosphorus atoms and the phenyl rings have some mutual effect similar to the inductive effect of d_{π} -p_{π} conjugation, since the P-Ph bond is slightly shortened to 1.770 Å compared with the standard value of

1.801 Å for the $P=(0)-C_{Ar}$, bond [14]. However, this interaction does not affect the geometric characteristics of the phenyl ring. [The average values of the bond angles (120.0°) and the interatomic distances (1.379 Å) are standard [14].]

As in (I-III), the furanose ring in the molecule of (IV) has the envelope conformation at C4, and its geometric characteristics are similar to those found in the structures of (I-III). The deflection of the C4 atom from the plane of the four atoms (± 0.050 Å) amounts to -0.569 Å [in (I-III) av. -0.636 Å]; the angles between the O4, C3, C4 and O4, C1, C2, C3 planes are 141.8° in (IV) [in (I-III) av. 136.8°]. The endocyclic angles and interatomic C-O and C-C distances differ little from each other and are close to the standard values [14].

To answer the question as to whether inversion of the original α -D-glucofuranose occurs in compounds (IV) and (I-III) it is necessary to determine the mutual positions of the C5-O and C4-O4 bonds in these structures, starting from the values of the torsion angles. The O4-C4-C5-O5 torsion angles in (I-III) are equal (av. 51.3°), while the O4-C4-C5-O6 angle in (IV) is -75.8°. Consequently, although the configuration of the monosaccharide skeleton is preserved in (I-IV), the C5-O5(H) bond in compounds (I-III) is turned to the right from the C4-O2 bond by 51.3°, while in (IV) it is turned to the left by 75.8°. (The O6 atom is included in ring A).

In compound (IV) the hydroxymethylene group >C6O5 (H5O) is, as it were, withdrawn

"under" the plane of the phosphate ring, forming an angle of 72.1° with the plane of the 03-C3-C5-C6 atoms. Here, the torsion angle 04-C4-C5-C6 amounts to 157.6° , i.e., the 04-C2 and C5-C6 bonds are almost parallel but with the <u>trans</u> orientation. Being arranged in this way, the hydroxyl group -05H50 enters into intermolecular interaction with the 07 oxygen atom of the phosphoryl group of another molecule, related by symmetry to the first by a 2_1 axis (Fig. 2). As a result of the formation of a weak 05 ... 07' hydrogen bond (2.731 Å, 05-H50...07' angle 159°, H50...07' 1.82 Å) some elongation of the C5-C6 bond (1.580 Å) and shortening of the C6-05 bond (1.405 Å in comparison with the published values of $C(sp^3)-C(sp^2)$ 1.530 Å and $C(sp^3)-OH$ 1.432 Å [14] are observed.

In the molecule of (IV), like (I), the O2 oxygen atom of the 1,2,0-dioxolane fragment C is deflected from the average plane of the four atoms (± 0.001 Å) by 0.309 Å [by 0.300 Å in (1)] with the envelope conformation; the angle between the C1, C2, C7, O1 and C2, O2, C7 planes is 157.9° [in (I) 158.6°]. The bond angles of the fragments C in (I-IV) are close to each other, but small differences are observed in the values of the chemically equivalent bonds. In the molecule of (IV) the C1-O1 bond corresponds in value (1.404 Å) to the exocyclic bond in furanose [14], while the elongation of the analogous C2-O2 bond to 1.421 Å is due to the deflection of the O2 atom from the plane of the four atoms [1.427 Å in (I)].

In all the structures the BC fragment has a distorted "butterfly" conformation with a dihedral angle of 122.5° [121.4° in (I-III)].

Thus, during investigation of 1,2-O-isopropylidene- α -D-glucofuranose 3,5-phenylcyclophosphonate (IV) we established that the six-membered phosphate ring has the conformation of a strongly flattened chair. The O7 atom of the phosphoryl bond is in the axial position to the central plane of the ring A, while the C10 atom of the phenyl substituent is in the pseudoaxial position. The furanose-dioxolane bicycle has a distorted "butterfly" conformation. The oxygen atom of the hydroxymethylene group, situated "under" the phosphate ring A of one molecule, forms a hydrogen bond with the oxygen atom of the O7(=P) phosphoryl group of another molecule, related to the first by a 2_1 screw axis. The conformation of the initial monosaccharide skeleton is preserved in the molecule.

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