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CARBOHYDRATE RESEARCH

Note

X-ray single crystal structure analyses of 5-deoxy-5-*C*-(alkylphosphinyl)-glucopyranose

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Abstract

X-ray crystallographic analyses were performed on single crystals of 1,2,3,4-tetra-*O*-acetyl-5-deoxy-5-*C*-(isopropylphosphinyl)-D-ribopyranoses, 1,2,3,4-tetra-*O*-acetyl-5-deoxy-5-*C*-(isopropylphosphinyl)-D-xylopyranoses, and 1,2,4-tri-*O*-acetyl-5-deoxy-3-*O*-methyl-5-C-(phenylphosphinyl)-D-ribopyranoses. These compounds have the (R_P) configuration at the phosphorus atom with the $^4C_1$ conformation of the pyranose ring, and the conformation supported by NMR studies.

Keywords: Phospha sugar; NMR; X-ray; Configuration; Conformation

In previous papers [1–4], we reported the syntheses of phospha sugars which were assigned as 1,2,3,4-tetra-*O*-acetyl-5-deoxy-5-*C*-(isopropylphosphinyl)-β,α-D-ribopyranoses **5a** and **5b**, 1,2,3,4-tetra-*O*-acetyl-5-deoxy-5-*C*-(isopropylphosphinyl))-β,α-D-xylopyranoses **7a** and **7b**, and 1,2,4-tri-*O*-acetyl-5-deoxy-3-*O*-methyl-5-C-[(R, S)-(phenylphosphinyl)-β-D-ribopyranoses **9a** and **9b**, however, the conformations of these compounds were not determined. Yamamoto et al had previously reported [5–9] the syntheses of phospha sugars, determination of the configuration at phosphorus in the six membered pyranoid rings, and the conformation of the heterocycles by ^{1}H NMR. The X-ray analyses of phospha sugar analogs have also been reported by Luger et al [10–14]. We herein report the analyses of 5-deoxy-5-(alkylphosphinyl)-glucopyranoses **5**, **7**, and **9** by ^{1}H NMR (270 MHz) and X-ray crystallography.

1. Results and discussion

Methyl 5-deoxy-5-*C*-(ethoxyisopropylphosphinyl)-2,3-*O*-isopropylidene-β-D-ribopyranoside **4**, 3-*O*-acetyl-5-deoxy-5-*C*-(ethoxyisopropylphosphinyl)-1,2-*O*-isopropylidene-α-D-xylofuranose **6**, and 5-deoxy-1,2-*O*-isopropylidene-5-*C*-(methoxyphenylphosphinyl)-3-*O*-methyl-α-D-ribofuranose **8** were synthesized from methyl 5-deoxy-5-iodo-2,3-*O*-isopropylidene-β-D-ribofuranose **1**, 3-*O*-acetyl-5-

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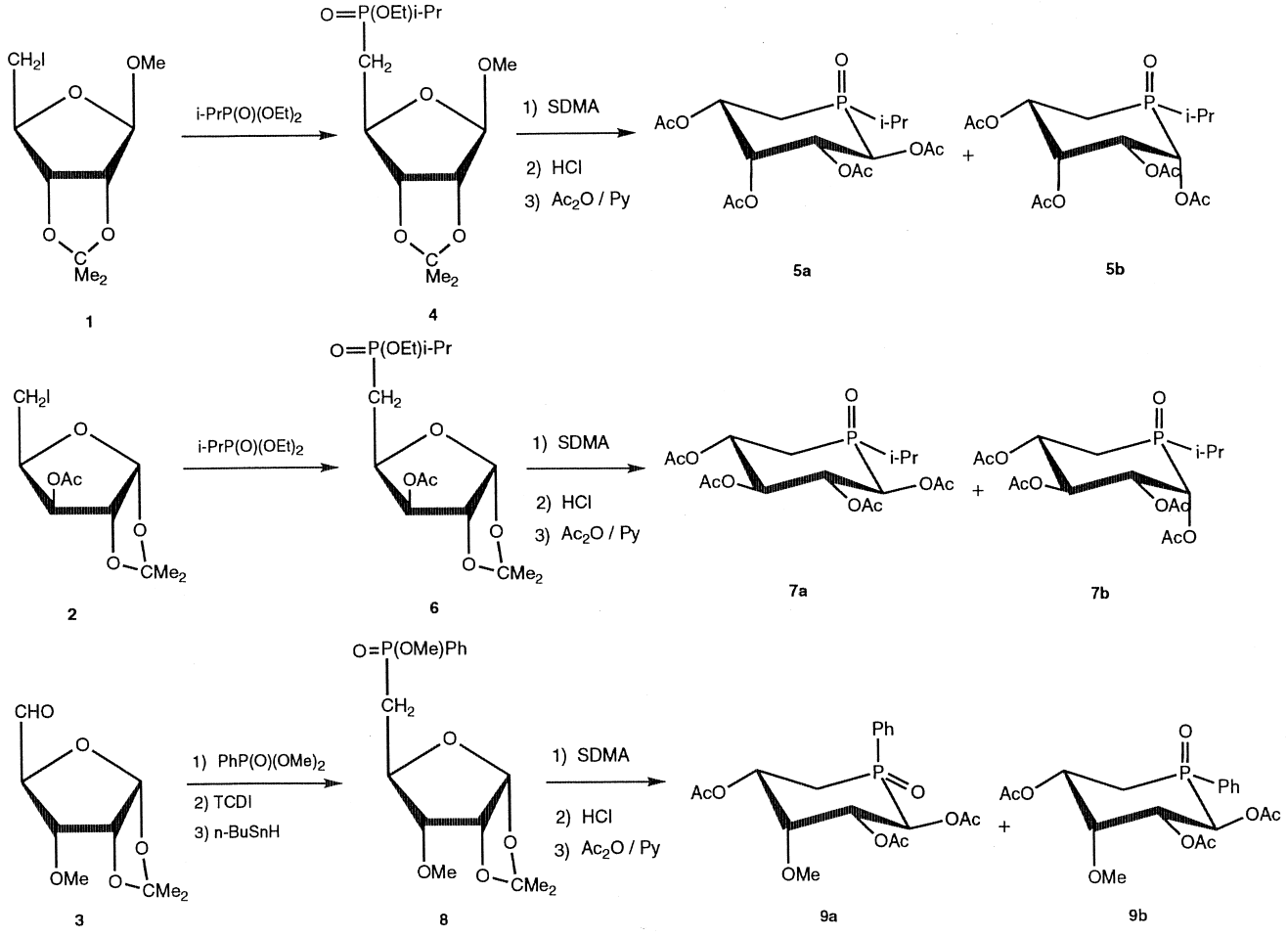
deoxy-5-iodo-1,2-*O*-isopropylidene-α-D-xylofuranose **2** and 1,2-*O*-isopropylidene-3-*O*-methyl-α-D-ribo-pentadialdo-1,4-furanose **3**, respectively, in good yield. Treatment of compounds **4**, **6**, and **8** with sodium dihydrobis(2-methoxyethoxy)aluminate (SDMA) giving 5-deoxy-5-alkyl- or 5-deoxy-5-phenyl-phosphino derivatives followed by ring-enlargement of these derivatives by the ring opening and closing two steps known procedure gave pyranose type phospha sugars **5**, **7**, and **9** in good yields (Scheme 1).

Determination of the absolute configuration at the phosphorus atom and the conformational analysis of the pyranoid ring were carried out for phospha sugars **5a**, **5b**, **7a**, **7b**, **9a**, and **9b** prepared previously [1–4]. The precise structures of these compounds were determined on the basis of the 270 MHz ^{1}H NMR spectra. The assignments of all signals were readily made employing first-order analysis with the aid of a decoupling technique. The results are summarized in Table 1. $^4C_1$ (D) conformation for all pyranose type phospha sugar derivatives was established. In the case of sugar analogs **5a**, **5b**, **7a**, and **7b** the assignments were difficult, because the signals of Ha-5 and He-5 overlapped with acetyl groups, and H-1, H-2, and H-4 overlapped each other on the ^{1}H NMR spectra in $CDCl_3$. When the ^{1}H NMR measurements of **5a**, **5b**, **7a**, and **7b** were carried out in benzene-d_6, the signals of H-1, H-2, H-4, H-5a, H-5e, and acetyl protons were separated from each other due to anisotropy of the solvent. In order to assign the ^{1}H NMR signals of phospha sugars **5a**, **5b**, **7a**, and **7b**, the chemical shift differences of each proton signal and the dependence of various J values reflecting the dihedral angles on solvents used were carefully taken into consideration. The ^{1}H NMR spectral data of **5a**, **5b**, **7a**, and **7b** generally agree with the characteristic features of δ and J values for pyranose type phospha sugars occurring in an approximate $^4C_1$ (D) conformation (see Table 1). Namely, the quasi-axial orientation of the P=O



Scheme 1.

Table 1
^{1}H NMR chemical shifts and coupling constants for phospha sugars **5**, **7**[a], and **9**[b]

Diastereomer	Chemical shift (δ, ppm)														
	H-1	H-2	H-3	H-4	H-5e	H-5a	AcO-1,2,3,4[c]				P-CH	P-C-Me	P-C-Me′		
5a	5.23	5.72	5.43	5.50	2.56	1.79	1.69	1.68	1.67	1.65	1.26	0.74	0.89		
5b	5.67	5.64	5.44	5.38	1.79	1.64	1.50	1.45	1.42	1.39	1.26	0.71	0.65		
7a	5.50	5.66	5.74	5.37	1.85	1.61	1.48	1.46	1.41	1.37	1.42[d)]	0.75	0.67		
7b	5.75	5.59	5.41	5.46	2.14	1.33[c)]	1.50	1.47	1.45	1.36	1.10	0.58	0.65		
	H-1	H-2	H-3	H-4	He-5	Ha-5	MeO	AcO-1,2,4[d]			Ph(o)	Ph(m)	Ph(p)		
9a	6.27	4.83	3.83	4.96	2.87	2.82	3.63	2.06	2.12	2.13	7.75	7.51	7.60		
9b	5.96	5.54	4.06	5.60	2.62	2.41	3.64	1.95	2.08	2.09	7.89	7.57	7.64		
	$J_{1,2}$	$J_{1,P}$	$J_{2,3}$	$J_{2,P}$	$J_{3,4}$	$J_{4,5e}$	$J_{4,5a}$	$J_{4,P}$	$J_{5a,5a}$	$J_{5e,P}$	$J_{5a,P}$	$J_{5e,1}$	$J_{P\text{-}CH}$	$J_{CH\text{-}Me}$	$J_{P\text{-}C\text{-}Me}$
5a	10.5	10.0	4.5	2.5	2.2	4.5	10.3	4.8	14.0	22.9	11.8	0	15.6	7.3	17.8
5b	2.7	14.0	3.1	0.5	3.0	4.5	12.0	2.2	14.0	23.4	13.6	2.5	14.0	7.0	12.4
7a	11.1	5.0	9.2	2.2	9.5	4.6	11.5	4.8	14.6	22.9	11.8	0	14.1	7.0	17.0
7b	2.7	14.4	10.5	0.5	10.1	4.6	12.6	2.2	14.3	23.4	13.6	2.2	14.3	7.3	14.6
	$J_{1,2}$	$J_{1,P}$	$J_{2,3}$	$J_{2,P}$	$J_{3,4}$	$J_{4,5e}$	$J_{4,5a}$	$J_{4,P}$	$J_{5e,5a}$	$J_{5e,P}$	$J_{5a,P}$	$J_{P,o}$	$J_{P,m}$	$J_{P,p}$	$J_{o,m}$	$J_{m,p}$	$J_{o,p}$
9a	11.6	11.9	3.2	5.8	2.4	3.8	10.5	5.4	15.1	18.4	17.5	11.8	3.3	1.7	7.7	7.7	1.5
9b	11.4	11.6	3.6	3.5	2.4	3.8	13.8	2.2	14.0	15.2	5.4	12.5	3.3	1.7	7.5	7.5	1.5

[a] Determined in C_6D_6.
[b] Determined in $CDCl_3$.
[c] The assignments of acetoxyl groups may be interconvertible.
[d] Approximation or uncertainty caused by overlapping of acetoxyl signals by may be included.

Table 2
Crystal and structure refinement for **5b**, **7b**, and **9b**

Molecular formula	**5b**	**7b**	**9b**
	$C_{16}H_{25}O_9P$	$C_{16}H_{25}O_9P$	$C_{18}H_{23}O_8P$
Molecular weight	392.34	392.34	398.35
Temperature (**K**)	293	293	293
Crystal system	Monoclinic	Orthorhombic	Orthorhombic
Space group	$P2_1$	$P2_12_12_1$	$P2_12_12_1$
Unit cell dimentions (Å)			
a	8.8359	12.435	10.022
b	9.180	16.412	22.337
c	12.6117	10.105	8.796
β(°)	94.473		
Volume (Å^3)	1019.8	2062.2	1969.0
Z (molecules/cell)	4	4	4
Density (calculated, g cm^{-3})	1.555	1.264	1.344
Absorption coefficient (mm^{-1})			
F (000)	832.0	832.0	840.0
Crystal size (mm)	0.2×0.2×0.3	0.2×0.2×0.3	0.2×0.2×0.3
θ range for data collection (°)	51.1–57.0	48.5–55.0	42.3–54.1
Index ranges for data collection			
Reflections collected	1750	1784	1720
Independent reflections	1633(Rint = 0.059)		
Refinement method	Full-matrix least-squares on F^2		
Goodness of fit indicator	2.77	1.54	2.07
Final *R* indices [$I > 2\sigma(I)$]			
*R*1	0.043	0.035	0.047
*wR*2	0.036	0.031	0.038
Largest diff. peak and hole (e Å^{-3})	0.15 and −0.29	0.12 and −0.11	0.25 and −0.20

group in all of these phospha sugar derivatives are established by the downfield chemical shifts of the H-2 and H-4 signals compared with previous reports [9]. The α-orientation of C-1 is derived by considering the small magnitudes of $J_{1,2}$(2.7–3.8 Hz) and $J_{1,5e}$ (2.2–2.5 Hz) values of **5b** and **7b**, whereas the β-anomers **5a** and **7a** show large $J_{1,2}$ (10.0–11.1 Hz) and negligible $J_{1,5e}$ values. The coupling constants of $J_{2,3}$ and $J_{3,4}$ of compounds **5** and **9** showed small Hz (2.2–4.5 Hz), and $J_{2,3}$ and $J_{3,4}$ of compounds **7** showed large Hz (9.2–10.5 Hz).

Table 3
Selected torsion angles for **5b**, **7b**, and **9b**

Sequence	**5b**	**7b**	**9b**
	Angle (degrees)	Angle (degrees)	Angle (degrees)
C-1–C-2–C-3–C-4	−58.0	−58.1	−68.4
C-2–C-3–C-4–C-5	−57.5	59.2	64.1
P-1–C-5–C-4–C-3	−60.8	−62.8	−61.6
C-1–P-1–C-5–C-4	57.1	57.0	55.4
P-1–C-1–C-2–C-3	59.7	57.9	66.6
O-1–P-1–C-6–C-7	−60.7	−57.9	−31.8
O-1–P-1–C-5–C-4	−60.8	−60.2	−65.7
O-1–P-1–C-6–C-8	−58.4	65.2	146.6[a]
O-4–C-3–C-4–O-5	−68.0	61.3	62.3
O-5–C-4–C-3–C-2	175.6	−179.1	−177.4
O-3–C-2–C-3–O-4	63.3	−63.8	−64.0
O-2–C-1–C-2–O-3	60.6	62.9	−56.4
O-2–C-1–P-1–C-6	49.8	−46.8	74.3

[a] The torsion angle 146.6 degree is that of O-1–P-1–C-6–C-11.

Table 4
Bond lengths (Å) for compound **5b**, **7b**, and **9b**

5b		**7b**		**9b**	
Atoms	Bond lengths	Atoms	Bond lengths	Atoms	Bond lengths
P-1–O-1	1.499(4)	P-1–O-1	1.479(4)	P-1–O-1	1.486(5)
P-1–C-5	1.813(7)	P-1–C-5	1.801(6)	P-1–C-5	1.815(7)
O-2–C-1	1.444(7)	O-2–C-1	1.437(6)	O-2–C-1	1.443(7)
O-3–C-2	1.449(8)	O-3–C-2	1.443(6)	O-3–C-2	1.454(8)
O-4–C-3	1.455(7)	O-4–C-3	1.435(6)	O-4–C-3	1.416(8)
O-5–C-4	1.429(7)	O-5–C-4	1.443(5)	O-5–C-4	1.430(8)
O-6–C-11	1.211(8)	O-6–C-9	1.187(6)	O-6–C-12	1.19(1)
O-10–C-9	1.173(9)	O-8–C-12	1.175(6)	O-27–C-15	1.204(9)
C-1–C-2	1.504(9)	C-1–C-2	1.512(6)	C-6–C-7	1.381(1)
C-2–C-3	1.510(8)	C-2–C-3	1.514(6)	C-7–C-8	1.37(1)
C-3–C-4	1.524(9)	C-3–C-4	1.523(7)	C-8–C-9	1.41(1)
C-4–C-5	1.523(9)	C-4–C-5	1.509(8)	C-9–C-10	1.37(1)
C-6–C-7	1.51(1)	C-6–C-7	1.516(1)	C-10–C-11	1.40(1)
P-1–C-1	1.849(7)	C-10–C-11	1.483(8)	C-15–C-16	1.49(1)
P-1–C-6	1.806(7)	C-12–C-16	1.507(9)	C-17–C-18	1.51(1)
O-2–C-9	1.389(8)	P-1–C-1	1.828(5)	P-1–C-1	1.834(7)
O-3–C-11	1.334(8)	P-1–C-6	1.816(7)	P-1–C-6	1.808(7)
O-4–C-13	1.349(8)	O-2–C-9	1.355(6)	O-2–C-17	1.365(8)
O-5–C-15	1.321(7)	O-3–C-12	1.337(6)	O-3–C-15	1.349(8)
O-9–C-15	1.207(7)	O-4–C-10	1.355(6)	O-4–C-14	1.424(1)
O-11–C-13	1.207(9)	O-5–C-13	1.324(7)	O-5–C-12	1.350(9)
C-6–C-8	1.53(1)	O-7–C-10	1.185(6)	O-7–C-17	1.189(8)
C-9–C-10	1.52(1)	O-9–C-13	1.188(7)	C-1–C-2	1.527(8)
C-11–C-12	1.48(1)	C-6–C-8	1.509(1)	C-2–C-3	1.527(9)
C-13–C-14	1.50(1)	C-9–C-15	1.493(9)	C-3–C-4	1.498(1)
C-15–C-16	1.46(1)	C-13–C-14	1.486(9)	C-4–C-5	1.574(1)
C6–C11	1.395(9)				
C12–C13	1.48(1)				

These tentative stereochemical conclusions promoted us to carry out X-ray crystallographic analyses of **5a**, **7b**, and **9b**. Rod-shaped crystals of **5a**, **7b**, and **9b** were grown from ethyl acetate-hexane. Precise lattice constants and three dimensional intensity data were obtained by a RIGAKU AFC7R controlled Stoe four-circle diffractometer with Ni-filtered CuK_α radiation. A summary of the crystallographic data, selected torsion angles, and bond lengths are shown in Tables 2–4, respectively. Phase determination was made by a direct method (SHELXS) [15] and expanded using Fourier techniques [16]. ORTEP plots for compounds **5a**, **7b**, and **9b** are shown by Figs 1–3, respectively. As indicated by the ring torsion angles given in Table 3, the pyranoid rings of **5a**, **7b**, and **9b** have a

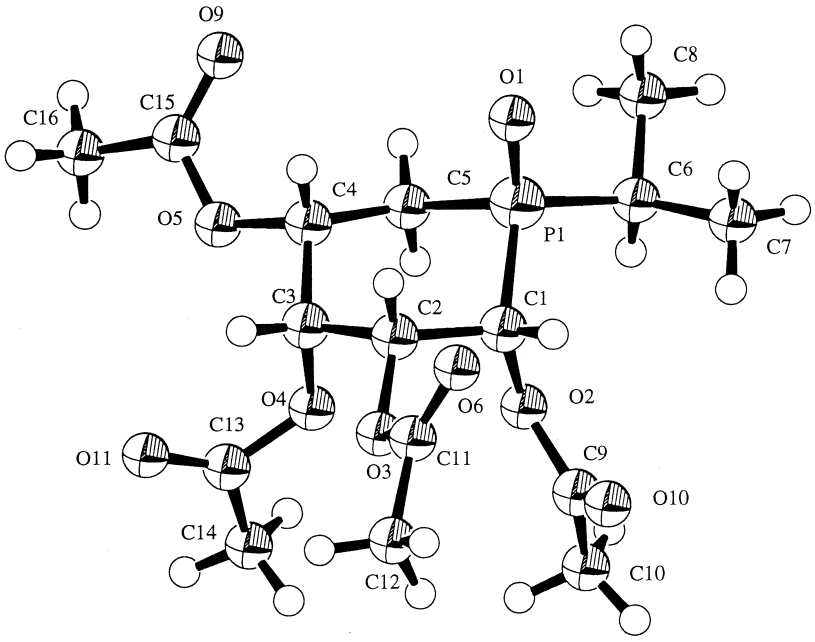


Fig. 1. ORTEP plot for compound **5b**.

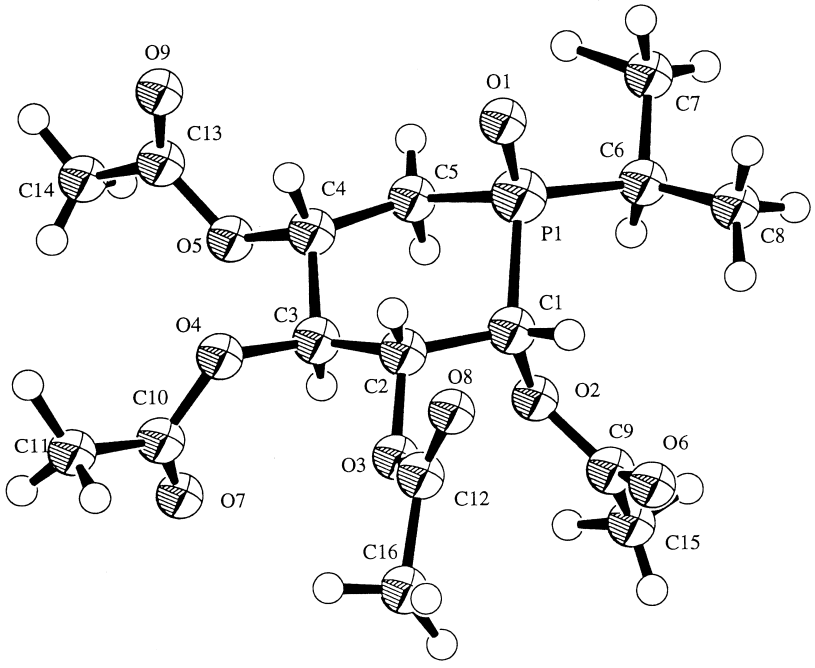


Fig. 2. ORTEP plot for compound **7b**.

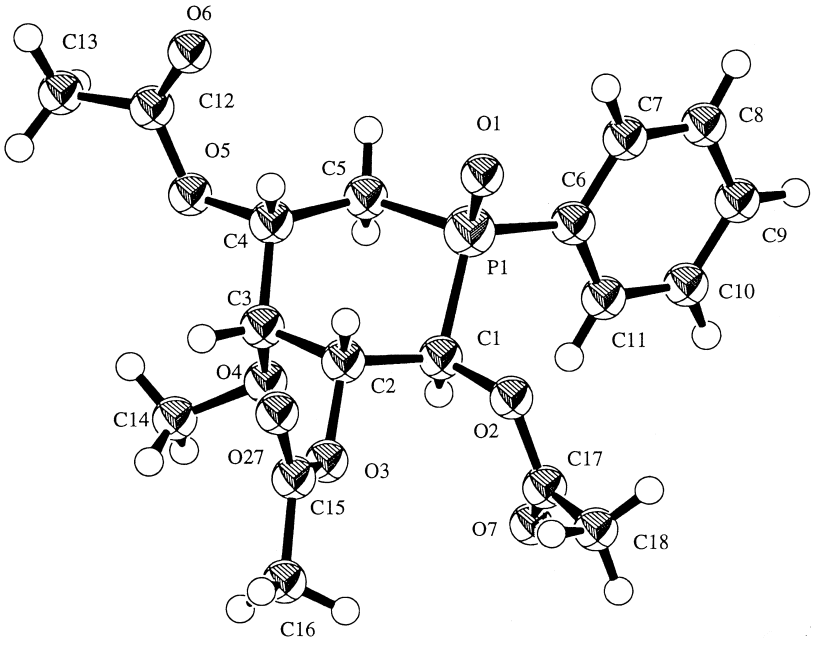


Fig. 3. ORTEP plot for compound **9b**.

rather regular $^4C_1$ conformation. As Figs 1–3 show, compounds **5b** and **7b** are 1,2,3,4-tetra-*O*-acetyl-5-deoxy-5-*C*-[(*R*)-isopropylphosphinyl]-β-D-ribopyranose and 1,2,3,4-tetra-*O*-acetyl-5-deoxy-5-*C*-[(*R*)-isopropylphosphinyl]-β-D-xylopyranose. These two pyranoses are in $^4C_1$ (D) conformation. In compound **7b**, the substitutents at C2, C3, C4, and P link equatorially, while that at C-1 links axially. In compounds **5b** and **9b**, the substituents at C-2, C-4, and P link equatorially, and that at C-3 links axially. In these molecules, the acetoxy groups on C-1 to C-4 are in quasi-equatorial positions. The acetoxy groups on C-1 to C-4 have usual syn-parallel arrangement of the C=O bond with the C–H bond of the adjacent ring atom, and anti-parallel arrangement of the P=O bond with the C–H bond of isopropyl group. On comparison of the present internal torsion angles of six membered ring of the sugar analogs **5a**, **7b**, and **9b** observed by the X-ray crystallographic analyses with those of previous X-ray data for 5-deoxy-5-phosphinyl-D-glucopyranose derivatives, the present torsion angles of C-1–C-2–C-3–C-4 and P-1–C-1–C-2–C-3 are smaller than those of previous structures by ca. 2–7°, and the present torsion angles of P-1–C-5–C-4–C-3 and C-1–P-1–C-5–C-4 are larger than those of previous structures by ca. 2–3° [11–14]. The Cremer–Pople [17] puckering parameters of Q=0.646Å, θ=9.778°, Ψ=161.6° for **5b**, Q=0.634Å, θ=10.6°, Ψ=10.0° for **7b**, and Q=0.693Å, θ=5.00°, Ψ=27.9° for **9b**, respectively. The deviation of C-1 and C-4 from the plane defined by C-2, C-3, C-5 and P are 0.769 and −0.689Å for **5b**, 0.783 and −0.656Å for **7b** and 0.732 and −0.718Å for **9b**, respectively.

2. Experimental

Synthetic procedures employed in the present paper for all phosphorus containing sugar analogs were similar to those described in the previous papers [1–4]. ^{1}H NMR Spectra were measured in $CDCl_3$ (TMS as the internal standard) on a JASCO EX270 (270 MHz) spectrometer. X-Ray single crystallographic measurements were conducted on a RIGAKU AFC7R using cut crystals of size (0.2×0.2×0.3 mm). Phase determination was made by a direct method (SHELXS) [15] and expanded using Fourier techniques [16]. After convergence of all parameters, final *R* values of 3.8% for **5b**, 4.3% for **7b**, and 4.7% for **9a** were obtained, respectively. In the final stage, refinement was made with anisotropic temperature-factors for all non-hydrogen atoms. The methyl hydrogen atoms were left unrefined.

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