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X-RAY CRYSTAL, AND MOLECULAR, STRUCTURE OF 1,2,3-TRI-*O*-ACETYL-4,5-DIDEOXY-4-*C*-[(*R*)-PHENYLPHOSPHINYL]-α-L-LYXOFURANOSE: THE FIRST X-RAY ANALYSIS OF A PENTOFURANOSE HAVING PHOSPHORUS IN THE HEMIACETAL RING

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ABSTRACT

X-Ray crystallographic analysis was performed on the compound to which had been assigned the structure of 1,2,3-tri-*O*-acetyl-4,5-dideoxy-4-*C*-[(*R*)-phenylphosphinyl]-α-L-lyxofuranose. The results showed that the compound has the proposed configuration, the five-membered ring is in the E_3 conformation, with a tendency towards the $^3T_2$ form, the substituents at P-5 and C-5 are linked bisectionally, the acetoxyl group at C-2 and the methyl group at C-4 are linked quasiequatorially, and the acetoxyl group at C-3 is linked axially.

INTRODUCTION

We reported in a previous paper[1] the synthesis of seven kinds of 1,2,3-tri-*O*-acetyl-4,5-dideoxy-4-*C*-(phenylphosphinyl)pentofuranose (**5**), starting from D-glucose, and employing the relevant processes for **1**→**5** (see Scheme 1). The structures of the 4-*C*-[(*R,S*)-phenylphosphinyl]-D-*ribo*- and L-*lyxo*-furanoses (**6**–**9**), together with their probable conformations, were assigned to these products (**5**) by careful analysis of the 400-MHz, ^{1}H-n.m.r. spectra, particularly by examining the δ values of the protons on the five-membered ring and H-5, and by using a general dependence of the $^2J_{PH}$ and $^3J_{PH}$ values on the O=P–C–H and P–C–C–H dihedral angles.

Compound **9a** was obtained as crystals (m.p. 155–156°), and its yield was the highest among these products (**5**). It was proposed[1] that **9a** was likely to exist in the E_3 conformation, and that the orientation of the phenyl ring was almost *syn*-parallel to H-3. These tentative assignments necessitated a precise, X-ray crystallographic analysis of **9a**, which, in turn, was considered to justify the validity of the assignments

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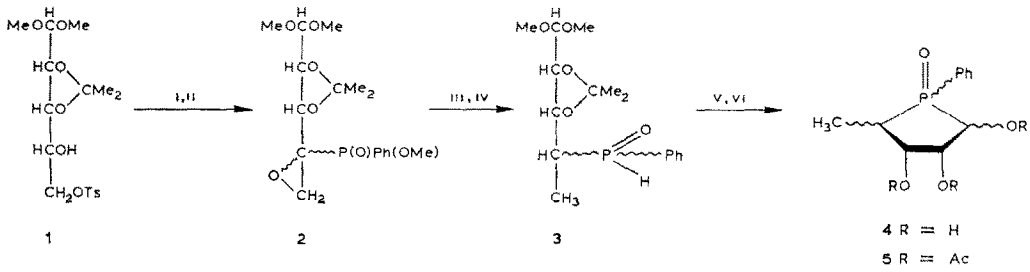
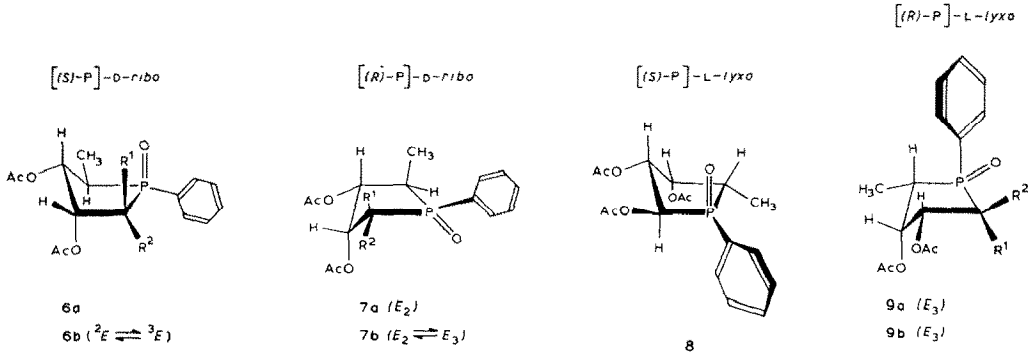


1 2 3 4 R = H 5 R = Ac

Scheme 1. i, Me_2SO—$(COCl)_2$—Et_3N; ii, PhPH(O)OMe, iii, H_2-Raney Ni; iv, $NaAlH_2(OCH_2CH_2OMe)_2$, v, H_3O^+, vi, Ac_2O—C_5H_5N

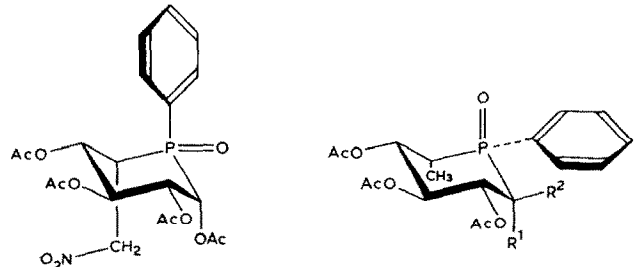


6a 6b ($^2E \rightleftharpoons {}^3E$) 7a ($E_2$) 7b ($E_2 \rightleftharpoons E_3$) 8 9a ($E_3$) 9b ($E_3$)

a, R^1 = H, R^2 = OAc, b, R^1 = OAc, R^2 = H (conformations in $CDCl_3$)

of the configurations and conformations to the rest of the pentofuranoses (**6–8**, **9b**) made by use of ^{1}H-n.m.r.-spectral analysis[1].

Moreover, such an X-ray analysis would be of value, not only from the viewpoint of comparative, X-ray crystallographic study of hexopyranoses having phosphorus in the hemiacetal ring [**10** (ref. 2), **11**, **12** (ref. 3), and **13** (refs. 4 and 5)], but also from that of molecular biology.



10

	R^1	R^2
11	H	OAc
12	OAc	H
13	H	H

TABLE I

CRYSTAL DATA[a] FOR **9a**

Formula	$C_{17}H_{21}O_7P$
Lattice constants	a = 1.5298(5)
(nm, degrees)	b = 0.5718(4)
	c = 2.2839(6)
	β = 106.04(3)
Cell volume (nm^3)	V = 1.9200
Formula units/cell	Z = 4
Space group	monoclinic C2
Linear absorption coefficient	μ = 15.67
(CuKα, cm^{-1})	
X-Ray density ($Mg.m^{-3}$)	ρ_x = 1.266
Total number of reflections ($\theta < 64°$)	1750
Unobserved ($I < 2\sigma$)	282

[a]Values of e.s.d. in parentheses.

EXPERIMENTAL

Very thin, needle-shaped crystals of the title compound **9a** (grown from ethyl acetate–hexane) were available. A specimen having a size of $\sim 0.05 \times 0.03 \times 0.6$ mm was used for the X-ray measurements. Precise lattice-constants and the intensity data for two octands (h, k, l, and $\bar{h}$, k, l) were measured on a DEC PDP 15/40 controlled Stoe, four-circle diffractometer with Ni-filtered, CuKα radiation (λ = 154.18 pm). A summary of the crystallographic data is given in Table I.

A few attempts at phase determination with MULTAN[6] failed. As the space-group C2 is known to be unsuitable for direct methods, no further MULTAN calculations were made, and Patterson methods were applied. The phosphorus position was readily located from the Harker plane (u, 0, w). Several other atomic positions were determined by searching systematically for pairs of intermolecular, Patterson vectors having equal v, for which the sums of u and w were equal to the phosphorus Harker peak. The complete structure was then obtained from difference syntheses.

The refinement with least-squares methods was executed with the corresponding programs of the X RAY 76 program[7] system. The intensity data were corrected for the anomalous scattering of phosphorus. Because of the very small crystal size, an absorption correction was not applied. The heavy atoms were refined with anisotropic temperature-factors, and the hydrogen positions, which were all located from difference syntheses, were refined with isotropic, thermal parameters. The distribution of ΔF was found to be almost independent of |F|, and we therefore decided to use unit weights. After convergence of all parameters, a final R-value of 3.7% was obtained. The final atomic coordinates are given in Table II*.

*A complete atom list, with the temperature parameters included, and the list of observed and calculated structure factors, can be obtained on request from Elsevier Scientific Publishing Company, BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/230/*Carbohydr. Res.*, 110 (1982) 187–194.

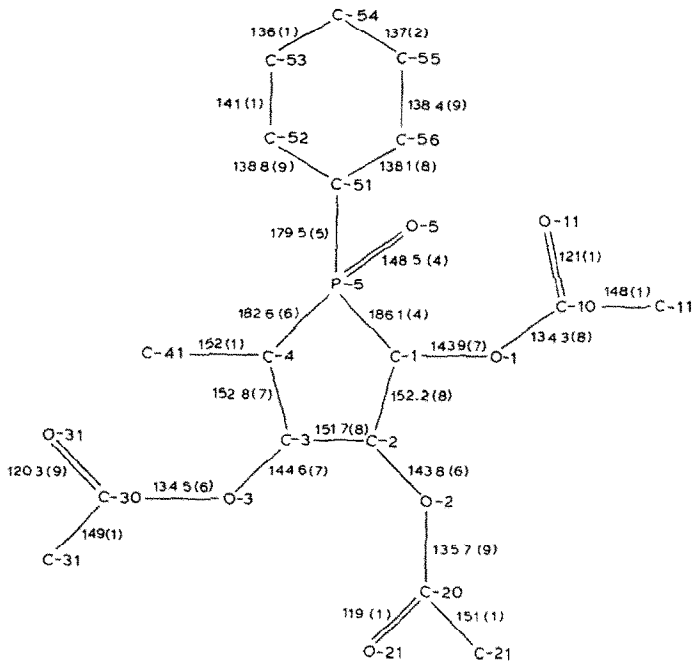


Fig. 1. Atom-numbering scheme and bond lengths (pm; e.s.d. values in parentheses) for **9a**.

RESULTS AND DISCUSSION

The atomic-numbering scheme and bond lengths are given in Fig. 1. An ORTEP[8] representation of the molecular structure of **9a** is shown in Fig. 2. Bond angles and a choice of torsion angles are listed in Tables III and IV.

The five-membered ring has the E_3 conformation, with a tendency towards the $^3T_2$ form. The Cremer–Pople puckering parameters are $q_2 = 42.2$ pm and $\varphi_2 = 102.98°$ (refs. 9 and 10). The asymmetry parameters after Duax, Weeks, and Rohrer[11] are $\Delta c_s = 8.4°$ for the E_3 conformation and $\Delta c_2 = 12.9°$ for the $^3T_2$ conformation.

The exocyclic bonds are in positions that are in agreement with the found geometry for the five-membered ring. The substituents at P-5 and C-1 are linked bisectionally (with the exception of H-1, which is in the quasiaxial range, see Fig. 3), so that an eclipsed arrangement is present along the P-5–C-1 bond.

The acetoxyl group on C-2 and the methyl group on C-4 are linked quasi-equatorially, whereas the *O*-acetyl group on O-3 is linked axially. C-3 is the out-of-plane atom in the E_3 conformation, and its distance from the mean plane through the other four ring atoms is 61 pm.

The bond lengths around the hetero atom show a distribution already observed in our previous investigations on **10–13** (refs. 2–5). The endocyclic lengths P-5–C-4 and P-5–C-1 are 182.6 and 186.1 pm, respectively. The corresponding values (averages) for **10** are 183.1 and 184.6 pm, and 181.4 and 183.5 pm for **11/12**. Hence, these bond

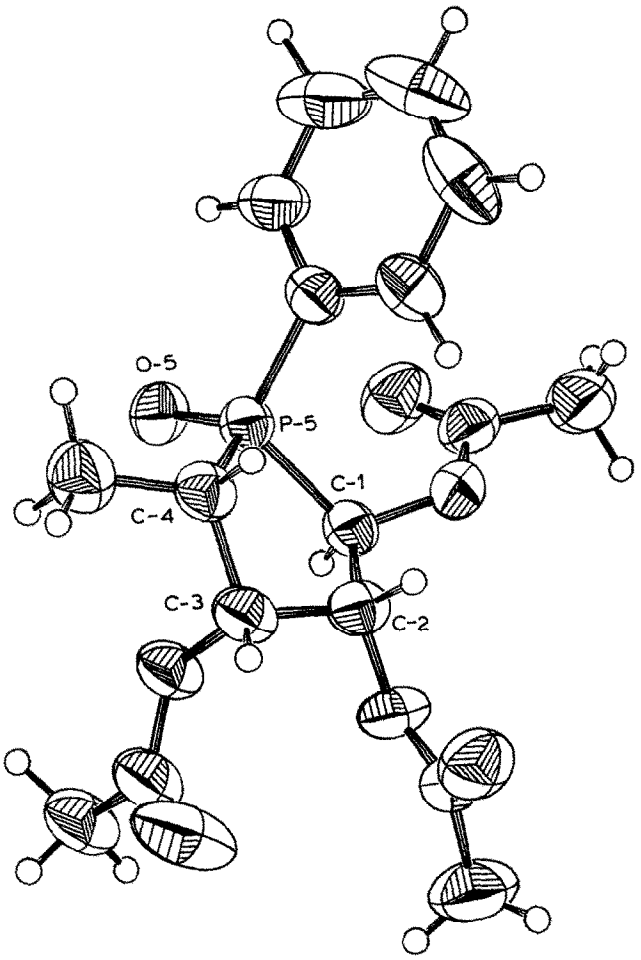


Fig. 2. ORTEP[8] representation of the molecular model of **9a**. [The thermal ellipsoids are drawn at the 50% level.]

lengths are longer for **10** and **9a** in comparison with **11** and **12**, although the differences are only in the range of the double or threefold standard deviation (*cf.*, for **13**, P-5–C-5 = 181.6 pm, and P-5–C-1 = 180.3 pm). The exocyclic bonds, P-5–O-5 (148.5 pm) and P-5–C-51 (179.5 pm) agree well with all previously determined bond-lengths of that type.

The plane of the phenyl ring has an orientation parallel to the P-5–O-5 bond, indicated by the almost-zero, torsion angle C-56–C-51–P-5–O-5 = 4.0(6)°. In this orientation, steric collisions with the adjacent acetoxyl group on C-1 are avoided. The acetoxyl group on C-1 differs remarkably from the usual, *syn*-parallel arrangement of the C=O bond with the C–H bond of the corresponding ring-atom. The torsion angle C-10–O-1–C-1–H-1 is 57(4)°, and hence, greatly different from zero.

TABLE II

ATOMIC PARAMETERS

Atom	*x*	*y*	*z*
C 1	.3493(4)	.062(1)	.2502(2)
O 1	.4045(2)	.1285(8)	.2112(2)
C 10	.4168(3)	−.029(1)	.1706(3)
O 11	.3804(3)	−.218(1)	.1645(2)
C 11	.4796(5)	.062(2)	.1372(3)
C 2	.3508(4)	.265(1)	.2935(2)
O 2	.4342(3)	.2464(8)	.3415(2)
C 20	.4678(4)	.449(1)	.3701(3)
O 21	.4344(3)	.6351(9)	.3566(2)
C 21	.5515(8)	.396(3)	.4211(4)
C 3	.2667(4)	.252(1)	.3163(2)
O 3	.2747(2)	.0504(7)	.3556(1)
C 30	.3031(4)	.085(1)	.4162(3)
O 31	.3171(5)	.277(1)	.4381(2)
C 31	.3164(7)	−.142(2)	.4498(3)
C 4	.1864(4)	.211(1)	.2602(2)
C 41	.0975(5)	.145(2)	.2733(3)
P 5	.22691(8)	0.0000(—)	.21365(6)
O 5	.1986(3)	−.2458(7)	.2189(2)
C 51	.1982(3)	.104(1)	.1365(2)
C 52	.2268(4)	.321(1)	.1217(3)
C 53	.2044(7)	.384(2)	.0594(4)
C 54	.1554(7)	.238(2)	.0153(3)
C 55	.1271(5)	.025(2)	.0307(3)
C 56	.1491(4)	−.043(1)	.0912(3)
H 1	.370(3)	−.07(1)	.272(2)
H 111	.452(5)	.20(2)	.109(4)
H 112	.482(4)	.00(2)	.109(3)
H 113	.541(4)	.10(1)	.166(3)
H 2	.352(3)	.401(8)	.273(2)
H 211	.581(7)	.27(2)	.418(5)
H 212	.582(9)	.54(3)	.426(6)
H 213	.536(5)	.36(2)	.457(4)
H 3	.261(3)	.388(9)	.339(2)
H 311	.254(5)	−.23(2)	.429(4)
H 312	.297(5)	−.14(2)	.484(3)
H 313	.377(6)	−.15(2)	.468(4)
H 4	.179(3)	.35(1)	.240(2)
H 411	.080(4)	.26(1)	.302(3)
H 412	.102(4)	−.02(1)	.299(3)
H 413	.046(4)	.14(1)	.234(3)
H 52	.262(4)	.45(2)	.153(3)
H 53	.227(4)	.53(1)	.051(3)
H 54	.141(4)	.29(1)	−.024(3)
H 55	.080(5)	−.09(2)	−.002(3)
H 56	.129(5)	−.20(2)	.102(3)

TABLE III

BOND ANGLES[a]

Bond	*Angle*	*Bond*	*Angle*
O-1–C-1–C-2	107.0(5)	O-1–C-1–P-5	117.5(3)
C-2–C-1–P-5	105.6(4)	C-1–O-1–C-10	117.8(5)
O-1–C-10–O-11	122.2(6)	O-1–C-10–C-11	110.8(7)
O-11–C-10–C-11	127.1(8)	C-1–C-2–O-2	106.8(4)
C-1–C-2–C-3	108.8(5)	O-2–C-2–C-3	113.1(4)
C-2–O-2–C-20	116.3(5)	O-2–C-20–O-21	124.2(5)
O-2–C-20–C-21	109.3(8)	O-21–C-20–C-21	126.5(8)
C-2–C-3–O-3	108.5(5)	C-2–C-3–C-4	106.4(4)
O-3–C-3–C-4	108.0(5)	C-3–O-3–C-30	118.1(5)
O-3–C-30–O-31	122.0(6)	O-3–C-30–C-31	111.3(6)
O-31–C-30–C-31	126.7(6)	C-3–C-4–C-41	115.5(5)
C-3–C-4–P-5	105.4(4)	C-41–C-4–P-5	114.6(5)
C-1–P-5–C-4	94.3(2)	C-1–P-5–O-5	115.0(2)
C-1–P-5–C-51	108.8(2)	C-4–P-5–O-5	115.2(3)
C-4–P-5–C-51	108.8(3)	O-5–P-5–C-51	113.2(2)
P-5–C-51–C-52	121.7(4)	P-5–C-51–C-56	118.1(5)
C-52–C-51–C-56	120.1(5)	C-51–C-52–C-53	117.9(6)
C-52–C-53–C-54	121.2(9)	C-53–C-54–C-55	120.2(8)
C-54–C-55–C-56	119.9(8)	C-51–C-56–C-55	120.7(8)

[a]In degrees; e.s.d. values in parentheses.

TABLE IV

A CHOICE OF TORSION ANGLES[a] FOR **9a**

Sequence	*Angle (degrees)*
C-1–C-2–C-3–C-4	−47.2(6)
C-2–C-3–C-4–P-5	40.9(5)
C-3–C-4–P-5–C-1	−20.3(4)
C-4–P-5–C-1–C-2	−5.4(4)
P-5–C-1–C-2–C-3	30.5(5)
O-1–C-1–C-2–C-3	156.4(4)
O-2–C-2–C-3–C-4	−165.8(5)
O-3–C-3–C-4–P-5	−75.4(5)
C-41–C-4–P-5–C-1	−148.5(4)
O-5–P-5–C-1–C-2	−125.8(4)
C-51–P-5–C-1–C-2	106.2(4)
O-11–C-10–O-1–C-1	3.0(7)
O-21–C-20–O-2–C-2	−2.5(9)
O-31–C-30–O-3–C-3	4(1)
C-52–C-51–P-5–O-5	−173.6(5)
C-56–C-51–P-5–O-5	4.0(6)
C-10–O-1–C-1–H-1	57(4)
C-20–O-2–C-2–H-2	37(3)
C-30–O-3–C-3–H-3	−21(3)

[a]Values of e.s.d. in parentheses.

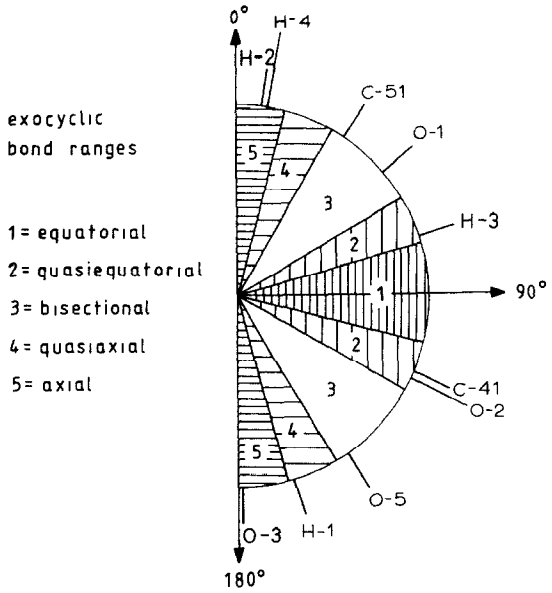


Fig. 3. Illustration of the bond types of the five-membered-ring substituents. [For each substituent, the angle between its exocyclic bond and the normal of the five-membered ring is plotted.]

For the two other acetoxyl groups, on C-2 and C-3, this angle is $+37(3)°$ and $-21(3)°$, respectively.

These findings have led to the precise structure, for the first time, of a pentofuranose having phosphorus in the hemiacetal ring, and they also demonstrate the effectiveness and correctness of the results derived from the 400-MHz, ^{1}H-n.m.r. analysis.

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