Carbohydrate Research, 193 (1989) 9–21
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

AN IMPROVED SYNTHESIS OF THE 5-DEOXY-5-(HYDROXYPHOSPHINYL)-D-GLUCOPYRANOSES, AND CRYSTAL STRUCTURES OF 1,2,3,4,6-PENTA-*O*-ACETYL-5-DEOXY-5-[(*R*)-METHOXYPHOSPHINYL]-β-D-GLUCOPYRANOSE AND ITS 5-[(*R*)-ETHYLPHOSPHINYL] CONGENER

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(Received August 17th, 1988; accepted for publication, in revised form, March 8th, 1989)

ABSTRACT

Treatment of 3-*O*-acetyl-5-deoxy-5-(dimethoxyphosphinyl)-1,2-*O*-isopropylidene-α-D-glucofuranose (**7**) with dihydropyran in the presence of pyridinium *p*-toluenesulfonate gave the 6-*O*-(tetrahydropyran-2-yl) derivative in 91% yield. Ring-enlargement of this compound by the known, 2-step procedure gave 5-deoxy-5-(hydroxyphosphinyl)-D-glucopyranoses in an overall yield from **7** twice as high as that obtained by the previous, alternative route via the corresponding 6-*O*-(triphenylmethyl)-α-D-glucofuranose precursor. X-Ray crystallographic analyses were performed on the two title compounds, penta-*O*-acetyl-5-deoxy-5-(methoxyphosphinyl)- (**12b**) and -5-(ethylphosphinyl)-β-D-glucopyranose (**13b**). The results show that both have the $^4C_1$ conformation and the substituents on C-1 to C-5 are quasi-equatorial (nomenclature of Jeffrey and Yates). The methoxy group of **12b** is in a quasi-equatorial position, whereas the ethyl group of **13b** is attached bisectionally to P-5.

INTRODUCTION

We recently reported[1] that 3-*O*-acetyl-5-deoxy-5-[ethyl(methoxy)phosphinyl]-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranose gave a high yield of its 6-*O*-(tetrahydropyran-2-yl) derivative **1**, which in turn provided exclusively 5-deoxy-5-(ethylphosphinyl)-L-idopyranoses (**3**) by the usual two-step ring-transposition procedure. This differs strikingly from previous observation[2] of the exclusive conversion of the 6-*O*-(triphenylmethyl) compound **2** into the D-glucopyranose analogs **4**. Our interest in further investigation of the physicochemical properties, as well as

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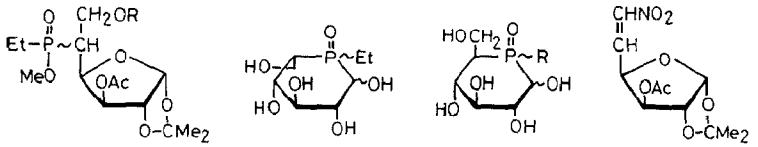


1 R = THP
2 R = CPh_3
THP = tetrahydropyran-2-yl

3

4 R = Et
5 R = OH

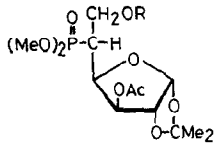
6

the potential biological activity, of various ring-phosphorus-containing sugar analogs[3–5] led us to seek a more efficient procedure for the preparation of these compounds. We now describe an improved synthesis of 5-deoxy-5-(hydroxyphosphinyl)-D-glucopyranoses (**5**) from 3-*O*-acetyl-5,6-dideoxy-1,2-*O*-isopropylidene-6-nitro-α-D-*xylo*-hex-5-enofuranose[6] (**6**) by further modification of the previous procedures and the use of a different protecting group on an intermediate. We also describe the X-ray crystallographic analysis of two of these D-glucopyranose analogs to confirm their structures and conformations.

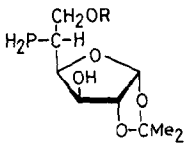
RESULTS AND DISCUSSION

Synthesis. — By slight modification of the previous method[7,8], 3-*O*-acetyl-5-deoxy-5-(dimethoxyphosphinyl)-1,2-*O*-isopropylidene-α-D-glucofuranose (**7**) was prepared from **6** with some improvements in yield. Treatment of **7** with dihydropyran in dichloromethane in the presence of pyridinium *p*-toluenesulfonate[9] afforded the 6-*O*-(tetrahydropyran-2-yl) derivative **8** in 91% yield.

Reduction of **8** with sodium dihydridobis(2-methoxyethoxy)aluminate (SDMA) gave an unstable, colorless syrup, for which the 5-deoxy-5-phosphino structure **10** was confirmed, for the first time, on the basis of high-resolution mass and ^{1}H-n.m.r. spectral data. A noteworthy feature of the n.m.r. spectra is the large magnitude (200 Hz) of $^1J_{P\text{-}5,H}$. Intermediate **10** was hydrolyzed in ethanolic 0.5M hydrochloric acid and then oxidized with hydrogen peroxide, providing exclusively the 5-deoxy-5-(hydroxyphosphinyl)-D-glucopyranoses[7] **5** as a mixture. This product on derivatization gave the expected four separable, per-*O*-acetyl 5-deoxy-5-(methoxyphosphinyl) compounds[7] **12a–d**. The configuration and yield of each isomer is given in the Experimental section. The conversion[7] of **7** into **5** via 6-*O*-(triphenylmethyl) compound **9** was also reexamined. While the formation of the unstable 5-deoxy-5-phosphino-6-*O*-(triphenylmethyl) intermediate **11** (upon reduction with SDMA) was established spectroscopically by this study, no appreciable improvement was shown in the yield of **12** from **9**. Indeed, the yield of 5-deoxy-5-(hydroxyphosphinyl)-D-glucopyranoses (**5**) from **7** via **8** was nearly twice that from **7** via **9**. Most interesting is the fact that, in the absence of a *P*-substituent, the stereochemical course of the ring-transposition step (**10** or **11** → **5**) was not affected by the change in the 6-*O*-protecting group from trityl to THP. This is in sharp contrast to the behavior of the reduction products of **1** and **2**, just cited.



7 R = H
8 R = THP
9 R = CPh_3



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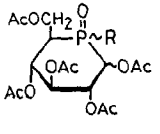
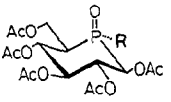
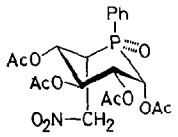
11 R = CPh_3



12 a–d R = OMe
13 a–d R = Et



12 b R = OMe
13 b R = Et



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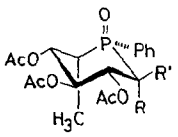
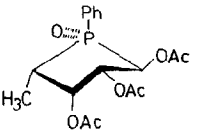


15 R = H, R′ = OAc
16 R = OAc, R′ = H
17 R = R′ = H



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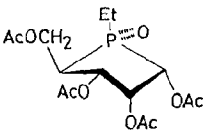

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X-Ray structural analysis. — Among the per-*O*-acetyl-5-deoxy-5-(methoxyphosphinyl)-D-glucopyranoses (**12a–d**) and the corresponding four 5-(ethylphosphinyl) derivatives **13a–d**, products having m.p. 167–168° (**12b**) and 233° (**13b**) were obtained in crystalline form, and characterized as penta-*O*-acetyl-5-deoxy-5-[(*R*)-methoxyphosphinyl]-β-D-glucopyranose and its 5-[(*R*)-ethylphosphinyl] analog, both approximately in the $^4C_1$(D) conformation in solution, on the basis of 400-MHz, ^{1}H-n.m.r. spectral data[2,7]. These tentative stereochemical conclusions prompted us to carry out X-ray crystallographic analyses of **12b** and **13b**, which we thought would confirm our assignments (made from n.m.r. spectroscopy) of configurations and conformations to the remaining per-*O*-acetyl compounds **12a, c, d** and **13a, c, d**. Moreover, as no crystallographic analyses of D-glucopyranose analogs having phosphorus in the hemiacetal ring had been reported, such an X-ray analysis would provide valuable information for our comparative X-ray crystallographic study of a series of P-in-the-ring aldohexopyranoses and aldopentofuranoses [*e.g.*, the L-idopyranoses **14** (ref. 10), **15, 16** (ref. 11), and **17** (ref. 12), L-lyxofuranose **18** (ref. 13), and D-ribofuranose **19** (ref. 14)]. The results should also be of value from the view point of molecular biology[3].

Rod-shaped crystals of **12b** and **13b** were grown from ethyl acetate–hexane. Inspection of a number of reflection profiles showed some irregularities, especially for **13b**, indicating moderate to poor crystal qualities. Attempts to find crystals more suitable for X-ray measurements failed. Precise lattice constants and the intensity data for one octant ($-h$ $+k$ $+l$) (**12b**) and two octants ($\pm h$ $+k$ $+l$) (**13b**) were then measured on a Stoe four-circle diffractometer with Ni-filtered Cu$K\alpha$ radiation with the ω–2θ-scan technique.

Both structures were solved with MITHRIL[15]. Subsequent least-squares refinements were done with the XTAL program system[16]. A Lorentz and polarization correction and an analytical absorption correction were applied. Anomalous

scattering coefficients of phosphorus and oxygen were included in the structure factor calculation during refinement. The heavy atoms were refined with anisotropic temperature factors. For both compounds, an isotropic extinction correction was included in the refinement. A few hydrogen atoms could be located from difference syntheses, but as these could not be refined we decided to fix all hydrogens at calculated positions 110 pm apart from the parent atom. Because the hydrogen positions in the acetyl-methyl groups were ambiguous (they could be staggered with respect to the carbonyl oxygen atom or the ether oxygen atom), both possible positions, half occupied, were used. This type of disorder had previously been observed in several acetylated sugars[17,18].

After convergence of all parameters, final R values of 5.9% for **12b** and 8.3% for **13b** were obtained. A summary of crystallographic and refinement data is given in Table I. The final atomic coordinates of **12b** and **13b** are given in Tables II and III*, respectively.

The atomic numbering scheme and bond lengths are given in Figs. 1 and 2. Selected torsion angles are listed in Table IV. The two compounds have very similar molecular structures, as can be seen from their ORTEP[16,19] representations in Fig. 3.

As indicated by the ring torsion angles (Table IV) and the Cremer–Pople

TABLE I

CRYSTAL AND REFINEMENT DATA FOR **12b** AND **13b**

	12b[a]	**13b**[a]
Formula	$C_{17}H_{25}O_{12}P$	$C_{18}H_{27}O_{11}P$
Space group	$P3_2$	$P3_2$
Lattice constants	$a = 1.1212(8)$	$a = 1.1690(6)$
(nm)	$c = 1.5241(4)$	$c = 1.4477(5)$
Cell volume (nm^3)	1.6593	1.7133
Crystal size (mm)	$0.32 \times 0.12 \times 0.12$	$0.6 \times 0.15 \times 0.15$
ρ_X (g/cm^3)	1.354	1.309
μ (CuK_α, cm^{-1})	16.36	15.47
Reflections	1649	2800
after merging	1507	1773
unobserved ($I < 2\sigma$)	165	88
R_F	5.9%	8.3%
wR_F	4.6%	7.3%
S	2.92	6.21
Function minimized	$\Sigma_h[1/\sigma_F(\|F\|_o - \|F\|_c)^2]$	$\Sigma_h[1/\sigma_F(\|F\|_o - \|F\|_c)^2]$

[a]Numbers in parentheses are e.s.d. values.

*A complete atom list, with the hydrogen atom parameters and the temperature parameters included, and the list of observed and calculated structure factors, as well as the list of bond angles for **12b** and **13b**, 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/415/*Carbohydr. Res.*, 193 (1989) 9–21.

TABLE II

ATOMIC PARAMETERS AND U_{eq} AND U VALUES FOR **12b**

Atom	x[a]	y[a]	z[a]	U_{eq}, U(Å^2)
P-5	0.0272(3)	0.0194(3)	0.69020(−)	6.6(1) × 10^{-2}
O-50	0.0445(7)	0.0531(7)	0.7847(4)	8.6(3)
O-51	0.0756(8)	−0.0860(8)	0.6693(5)	9.4(3)
C-51	0.072(1)	−0.149(1)	0.5912(8)	12.4(7)
C-1	−0.150(1)	−0.046(1)	0.6541(6)	6.8(4)
O-1	−0.2438(7)	−0.1619(7)	0.7058(4)	7.1(3)
C-11	−0.316(1)	−0.285(1)	0.6717(9)	9.5(6)
C-12	−0.420(1)	−0.385(1)	0.7276(8)	9.2(5)
O-11	−0.293(1)	−0.307(1)	0.5960(7)	16.6(6)
C-2	−0.184(1)	0.065(1)	0.6632(6)	7.6(5)
O-2	−0.3261(8)	0.0126(8)	0.6378(5)	9.0(3)
C-21	−0.417(1)	−0.002(1)	0.6996(9)	10.9(6)
C-22	−0.552(1)	−0.035(2)	0.6633(8)	12.6(7)
O-21	−0.3884(9)	0.015(1)	0.7768(6)	14.7(5)
C-3	−0.094(1)	0.189(1)	0.6057(6)	6.6(4)
O-3	−0.1428(7)	0.2833(7)	0.6139(4)	8.8(3)
C-31	−0.216(1)	0.302(1)	0.5482(9)	10.3(6)
C-32	−0.267(2)	0.391(2)	0.569(1)	15.7(8)
O-31	−0.227(1)	0.247(1)	0.4789(6)	15.4(5)
C-4	0.054(1)	0.261(1)	0.6308(6)	6.8(4)
O-4	0.1226(7)	0.3750(7)	0.5701(4)	8.0(3)
C-41	0.208(1)	0.502(1)	0.601(1)	9.7(6)
C-42	0.277(1)	0.607(1)	0.5302(9)	12.1(7)
O-41	0.226(1)	0.5237(9)	0.6803(6)	12.2(4)
C-5	0.121(1)	0.1732(9)	0.6241(5)	6.0(4)
C-6	0.270(1)	0.244(1)	0.6499(6)	6.8(4)
O-6	0.3555(7)	0.3501(7)	0.5879(5)	8.0(3)
C-61	0.387(1)	0.305(2)	0.5149(8)	9.5(6)
C-62	0.470(1)	0.431(1)	0.4547(8)	13.0(7)
O-61	0.358(1)	0.194(1)	0.4998(6)	13.6(5)

[a]Numbers in parentheses are e.s.d. values.

puckering parameters[20–22] given in Table V, the pyranoid rings of **12b** and **13b** have a rather regular $^4C_1$ conformation. In both molecules, the acetoxyl groups on C-1 to C-4, as well as the substituent at C-5, are in quasi-equatorial positions (nomenclature of Jeffrey and Yates[23], see substituent diagrams in Fig. 4). The acetoxyl groups on C-1 to C-4 have the usual, *syn*-parallel arrangement of the C=O bond with the C–H bond of the adjacent ring-atom, as their torsion angles C-*i*1–O-*i*–C-*i*–H-*i* (i = 1–4) are all close to zero. The phosphinyl oxygen atom O-50 is attached axially in both compounds. A characteristic difference exists between the methoxy group of **12b** and ethyl group of **13b** in that the methoxy group is in a quasi-equatorial position, with the O–C bond nearly *anti*-parallel to the P=O bond (torsion angle O-50–P-5–O-51–C-51 ≈ 177°), whereas the ethyl group is attached bisectionally and the corresponding torsion angle O-50–P-5–C-51–C-52 is 30°.

The bond lengths around the phosphorus atom agree well with those

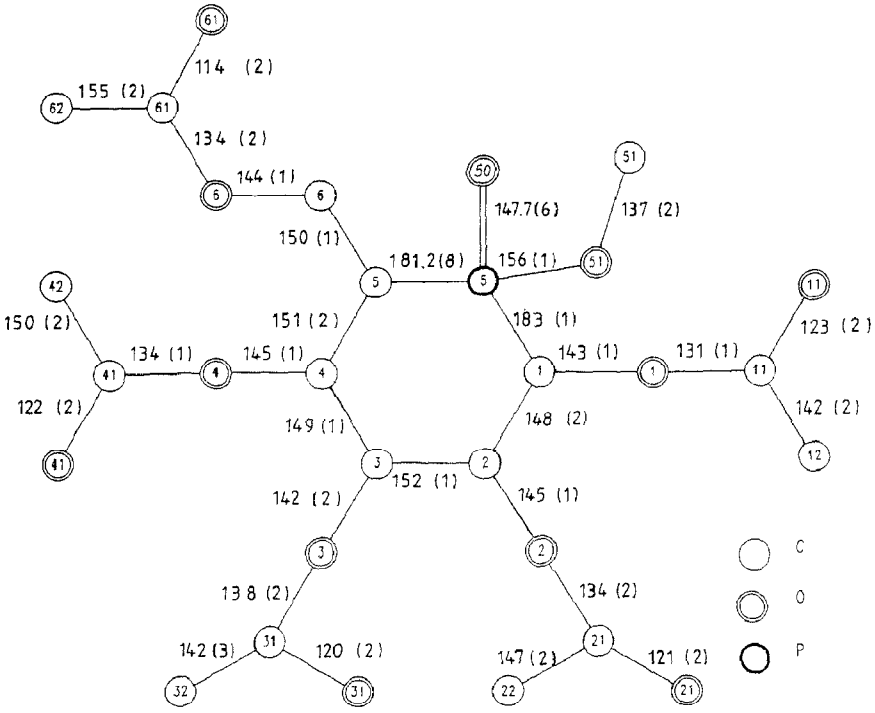

Fig. 1. Atom-numbering scheme with bond lengths (in pm; e.s.d. values in parentheses) for **12b**.

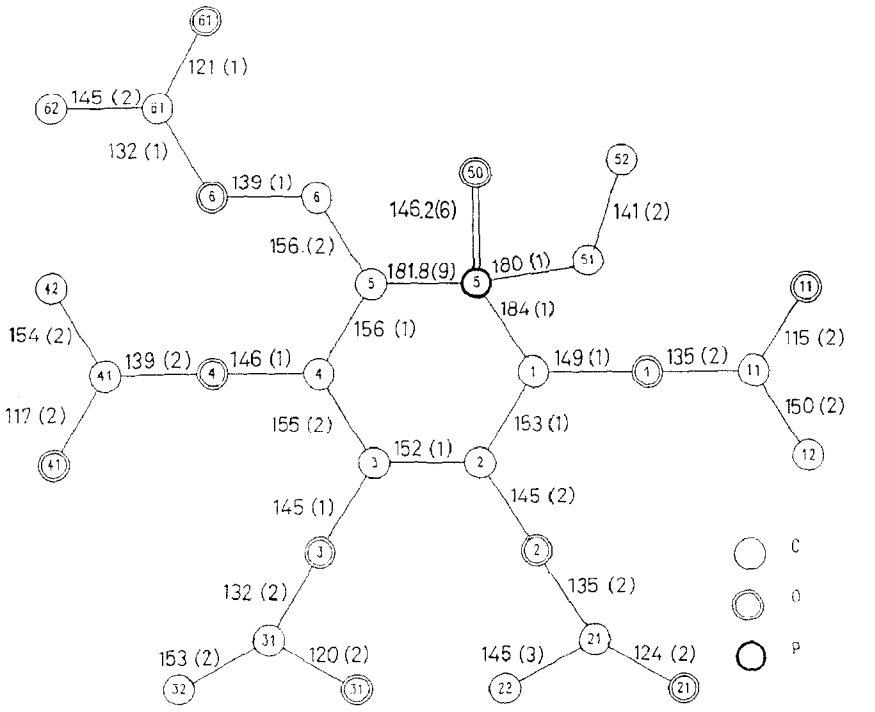

Fig. 2. Atom-numbering scheme with bond lengths (in pm; e.s.d. values in parentheses) for **13b**.

TABLE III

ATOMIC PARAMETERS AND U_{eq} AND U VALUES FOR **13b**

Atom	x[a]	y[a]	z[a]	U_{eq}, U(Å^2)
P-5	0.6514(2)	0.3614(2)	0.02331(−)	6.02(8) × 10^{-2}
O-50	0.6381(6)	0.3627(6)	−0.0770(4)	7.1(2)
C-51	0.500(1)	0.260(1)	0.0843(8)	8.6(4)
C-52	0.402(1)	0.147(2)	0.037(1)	20.0(1)
C-1	0.7674(9)	0.3053(9)	0.0573(6)	7.2(4)
O-1	0.7359(7)	0.1881(7)	−0.0011(5)	8.6(3)
C-11	0.695(1)	0.073(1)	0.045(1)	11.9(6)
C-12	0.695(1)	−0.019(1)	−0.027(1)	13.7(7)
O-11	0.683(1)	0.066(1)	0.1239(7)	21.4(8)
C-2	0.910(1)	0.411(1)	0.0365(7)	7.6(4)
O-2	0.9947(7)	0.3614(7)	0.0692(6)	10.4(3)
C-21	1.064(2)	0.338(2)	0.005(1)	14.6(8)
C-22	1.157(2)	0.305(2)	0.046(1)	19.0(1)
O-21	1.052(1)	0.348(1)	−0.0790(9)	17.0(6)
C-3	0.9466(9)	0.5328(9)	0.0945(7)	7.4(4)
O-3	1.0868(6)	0.6202(6)	0.0793(6)	8.6(3)
C-31	1.166(1)	0.642(1)	0.1503(9)	9.7(5)
C-32	1.308(1)	0.725(1)	0.117(1)	14.4(7)
O-31	1.1329(8)	0.6010(9)	0.2276(7)	12.1(4)
C-4	0.8739(8)	0.6062(8)	0.0616(6)	5.5(3)
O-4	0.9261(6)	0.7203(7)	0.1227(5)	8.5(3)
C-41	0.963(1)	0.841(1)	0.081(1)	10.7(6)
C-42	1.013(1)	0.947(1)	0.157(1)	16.6(9)
O-41	0.962(1)	0.858(1)	0.0014(8)	15.9(6)
C-5	0.7224(9)	0.5218(9)	0.0792(6)	6.7(3)
C-6	0.6563(8)	0.5982(8)	0.0376(7)	6.6(3)
O-6	0.6714(6)	0.6994(6)	0.0962(5)	7.9(3)
C-61	0.598(1)	0.674(1)	0.1707(8)	8.9(5)
C-62	0.634(1)	0.784(1)	0.233(1)	14.0(7)
O-61	0.5068(8)	0.5638(8)	0.1835(7)	11.7(4)

[a]Numbers in parentheses are e.s.d. values.

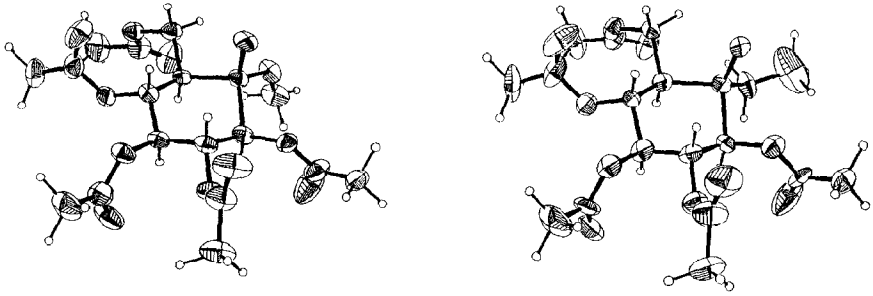

Fig. 3. ORTEP representations of molecular models of **12b** (left) and **13b** (right). Thermal ellipsoids are plotted at the 30% probability level.

TABLE IV

SELECTED TORSION ANGLES IN **12b** AND **13b**

Sequence	**12b** *Angle*[a] *(degrees)*	**13b** *Angle*[a] *(degrees)*
C-1–C-2–C-3–C-4	−65(1)	−70(1)
C-2–C-3–C-4–C-5	61(1)	67(1)
C-3–C-4–C-5–P-5	−56.4(8)	−56.9(9)
C-4–C-5–P-5–C-1	50.3(7)	47.5(7)
C-5–P-5–C-1–C-2	−54(7)	−51.1(7)
P-5–C-1–C-2–C-3	62.5(9)	64(1)
H-1–C-1–O-1–C-11	7(2)	3(1)
H-2–C-2–O-2–C-21	−8(2)	−6(1)
H-3–C-3–O-3–C-31	13(1)	8(2)
H-4–C-4–O-4–C-41	12(2)	12(1)
P-5–C-5–C-6–O-6	167.9(8)	160.1(5)
C-4–C-5–C-6–O-6	−68(1)	−79(9)
C-5–C-6–O-6–C-61	−80(1)	−77(1)
C-6–O-6–C-61–C-62	177(1)	172(1)
O-50–P-5–O-51–C-51	176.9(8)	
O-50–P-5–C-51–C-52		30(2)

[a]Numbers in parentheses are e.s.d. values.

TABLE V

CREMER-POPLE PUCKERING PARAMETERS

Parameter	**12b**[a]	**13b**[a]	*Ideal* $^4C_1$
q_2,q_3	6(1), 63(1) pm	6(1), 65(1) pm	0, Q
ϕ	47(11)°	141(10)°	free
Q	63(1) pm	65(1) pm	$\sqrt{1/6}$ × bond length
θ	5(1)°	5(1)°	0°

[a]Numbers in parentheses are e.s.d. values.

previously observed in investigations of the phosphorus-containing sugar analogs **14–19** (refs. 10–14), with the exception of the P=O bond in **13b**, which is slightly shorter [146.2(6) pm] than those [148.3(2)–149.2(4) pm][12] of compounds **15–19**.

These findings establish the precise structures of the P-in-the-ring D-gluco-pyranoses for the first time and also strongly support the validity of the proposed structures and conformations (derived by ^{1}H-n.m.r. spectroscopy) of the aldohexo-pyranose analogs **12a, c, d** and **13a, c, d**. Although most of the ^{1}H-n.m.r. spectral data for **12a–d** had been reported previously[7], more accurate, completely resolved parameters for these compounds have now been obtained at 500 MHz. These data, together with those for **13b**, are summarized in Table VI. The values are completely compatible with the $^4C_1$ conformations of the compounds in $CDCl_3$ solution.

TABLE VI

^{1}H-N.M.R. PARAMETERS[a] (500 MHz, $CDCl_3$) FOR THE DIASTEREOISOMERIC PENTA-*O*-ACETYL-5-DEOXY-5-(METHOXYPHOSPHINYL)-D-GLUCOPYRANOSES COMPARED WITH THE VALUES FOR **13b**

Compound	*Chemical shifts (δ)*												
	H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*	CH_3CO-*1,2,3,4,6*[b]					$POCH_3$
12a	5.65	5.48	5.46	5.49	2.67	4.42	4.36	2.21, 2.07, 2.05, 2.01, 2.00					3.77
12b	5.31	5.54	5.22	5.44	2.45	4.43	4.40	2.15, 2.08, 2.05, 2.01, 2.00					3.84
12c	5.48	5.35	5.20	5.33	2.45	4.60	4.26	2.13, 2.05, 2.03, 1.99, 1.99					3.97
12d	5.70	5.19	5.42	5.31	2.75	4.63	4.25	2.22, 2.04, 2.04, 2.01, 1.98					3.93
13b[c]	5.37	5.74	5.22	5.58	2.36	4.47	4.42	2.16, 2.07, 2.06, 2.01, 1.99					[d]
	Coupling constants (Hz)												
	$J_{1,2}$	$J_{1,P}$	$J_{2,3}$	$J_{2,P}$	$J_{3,4}$	$J_{4,5}$	$J_{4,P}$	$J_{5,6}$	$J_{5,6'}$	$J_{5,P}$	$J_{6,6'}$	$J_{6,P}$	$J_{6',P}$	J_{P,CH_3}
12a	2.5	14.7	10.0	0.2	9.0	12.0	3.0	5.7	4.5	13.3	11.8	16.7	13.1	11.2
12b	10.5	5.6	9.4	3.6	9.6	11.0	4.3	5.1	6.1	13.0	11.6	14.5	16.1	11.3
12c	10.8	2.8	9.9	1.8	9.6	11.8	2.2	4.9	3.6	12.0	11.8	20.1	11.4	10.5
12d	2.9	15.6	10.5	2.8	9.8	12.0	2.0	4.5	3.0	13.5	12.0	22.5	10.0	10.7
13b[c]	11.0	3.6	9.9	3.0	9.8	11.7	2.9	7.4	5.2	3.1	11.8	11.8	15.2	[d]

[a]Close examination (including simulation analysis) of the parameters has resulted in slight corrections of some of the previously reported values[7]. [b]Acetylmethyl assignments may have to be interchanged. [c]From ref. 4. [d]Parameters for the P-Et group are not quoted here.

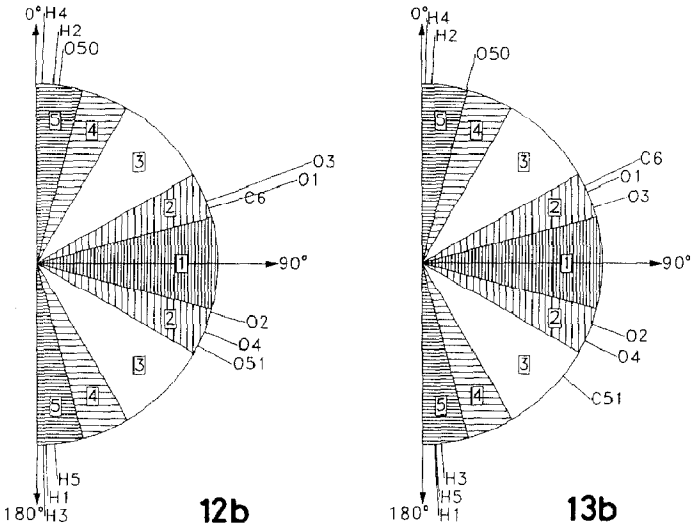

Fig. 4. Substituent diagrams for **12b** and **13b**. For each substituent, the angle between its exocyclic bond and the normal to the mean plane of the ring is plotted. According to the notation used in the program PUCK distributed by Jeffrey and Yates[23], the bond-groupings are: 1, equatorial; 2, quasi-equatorial; 3, bisectional; 4, quasi-axial; and 5, axial.

EXPERIMENTAL

General methods. — Procedures similar to those described in previous papers (*e.g.*, refs. 1, 2) were employed. N.m.r. spectra were determined on solutions in $CDCl_3$; values are referenced to tetramethylsilane.

Materials. — The following compounds were prepared by slight modifications of literature methods, resulting in some improvement of yields: 3-*O*-acetyl-5,6-dideoxy-1,2-*O*-isopropylidene-6-nitro-α-D-*xylo*-hex-5-enofuranose[6,7] (**6**, 63% overall from 1,2-*O*-isopropylidene-α-D-glucofuranose); 3-*O*-acetyl-5-deoxy-5-(dimethoxyphosphinyl)-1,2-*O*-isopropylidene-α-D-glucofuranose[7,8] (**7**, 42% overall from **6**); and 3-*O*-acetyl-5-deoxy-5-(dimethoxyphosphinyl)-1,2-*O*-isopropylidene-6-*O*-(triphenylmethyl)-α-D-glucofuranose[7] (**9**, 50% from **7**).

3-O-*Acetyl-5-deoxy-5-(dimethoxyphosphinyl)-1,2-*O*-isopropylidene-6-*O*-(tetrahydropyran-2-yl)-α-D-glucofuranose* (**8**). — A solution of **7** (560 mg, 1.58 mmol) and dihydropyran (400 mg, 4.76 mmol) in dry dichloromethane (10 mL) containing pyridinium *p*-toluenesulfonate (120 mg, 0.477 mmol) was stirred for 6 h at room temperature. Then the solution was diluted with ether, washed once with half-saturated brine to remove the catalyst, dried (Na_2SO_4), and concentrated *in vacuo*. The residue was purified in a short column of silica gel with EtOAc–hexane as eluant, giving **8** as a colorless syrup (631 mg, 91%); R_F 0.42, 0.39 [EtOAc, two diastereoisomers with regard to the tetrahydropyranyl (THP) group]; ^{1}H-n.m.r.

(500 MHz): δ 1.29, 1.29*, 1.475, 1.48* (4 s, 6 H, CCH_3), 1.45–1.80 (m, 6 H, CH_2 of THP), 2.055, 2.06* (2 s, 3 H, CH_3CO), 2.49, 2.52* (2 dddd, 1 H, $J_{5,P}$ 20.4, 20.8*, $J_{4,5}$ 10.8, 11.0*, $J_{5,6'}$ 4.4, 2.2*, $J_{5,6}$ 2.2, 3.7* Hz, H-5), 3.49, 3.66*, 3.75, 3.77* (4 d, 6 H, $^3J_{P,H}$ all 10.8 Hz, $POCH_3$), 3.50, 3.52*, 3.93, 3.97* (4 m, 2 H, H-6 of THP), 3.75, 3.77* (2 ddd, 1 H, $J_{6,6'}$ 10.0, 9.2*, $J_{6',P}$ 8.7, 10.6* Hz, H-6'), 4.25, 4.18* (2 ddd, 1 H, $J_{6,P}$ 13.7, 35.0* Hz, H-6), 4.45, 4.46* (2 d, 1 H, $J_{1,2}$ 4.3, 3.9* Hz, H-2), 4.49, 4.58* (2 ddd, 1 H, $J_{4,P}$ 4.0, 3.5*, $J_{3,4}$ both 2.5 Hz, H-4), 4.69, 4.78* (2 m, 1 H, H-2 of THP), 5.20, 5.21* (2 d, 1 H, H-3), and 5.81, 5.83* (2 d, 1 H, H-1); *m/z* 438 (1.4, M^+), 423 (14), 355 (74), 339 (100), 279 (46), 267 (25), 249 (35), 237 (82), 219 (72), 207 (51), 191 (33), 183 (73), 165 (45), 153 (65), 137 (94), 109 (43), 85 (82), and 43 (79).

Anal. Calc. for $C_{18}H_{31}O_{10}P$: C, 49.31; H, 7.13; mol. wt., 438.1655. Found: C, 49.03; H, 6.97; mol. wt., 438.1636.

*5-Deoxy-1,2-O-isopropylidene-5-phosphino-6-O-(tetrahydropyran-2-yl)-α-*D*-glucofuranose* (**10**). — To a solution of **8** (630 mg, 1.44 mmol) in dry benzene (7 mL), was added, in small portions with stirring, a solution of sodium dihydridobis-(2-methoxyethoxy)aluminate (70% in toluene, 1.10 mL, 3.1 equiv.) in dry benzene (3 mL) over a period of 15 min at 0° under nitrogen. The stirring was continued for 1 h at this temperature. Then water (1 mL) was added at 0°, and the mixture was stirred for 30 min and centrifuged to remove aluminum hydroxide; the precipitate was extracted with several portions of benzene. The organic layer was combined and evaporated in vacuo, giving **10** as a colorless syrup; R_F 0.73 (3:1 EtOAc–hexane); ^{1}H-n.m.r. (60 MHz): δ 1.31, 1.41 (2 s, 3 H each, CCH_3), 1.4–1.8 (m, 6 H, CH_2 of THP), 2.3–2.8 (m, 1 H, D_2O exchangeable, *H*O-3), 2.45 (m, 1 H, H-5), 2.82 (dd, 2 H, $^1J_{P,H}$ 200, $^3J_{5,PH}$ 6.8 Hz, H_2P), 3.5–4.4 (m, 6 H, H-3,4,6,6', and H-6 of THP), 4.52 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-2), 4.68 (m, 1 H, H-2 of THP), and 5.90 (d, 1 H, H-1); *m/z* 321 (50, M + 1), 305 (10), 237 (28), 221 (10), 161 (50), 129 (38), 100 (52), 85 (100), 67 (95), and 43 (95); high-resolution m.s.: calc. for $C_{14}H_{26}O_6P$ (M + 1), *m/z* 321.1467, found 321.1447. The compound was not stable enough for elemental analysis.

*1,2,3,4,6-Penta-O-acetyl-5-deoxy-5-[(R)-methoxyphosphinyl]-α-*D*-gluco-pyranose* (**12a**), *the β-anomer* (**12b**), *the* [(S)-*methoxyphosphinyl*]-*β-*D*-gluco-pyranose* (**12c**), *and its α-anomer* (**12d**). — The above syrup **10** was immediately subjected to the four-step procedure similar to that employed previously[7] for **9**, first giving **5** as an amorphous solid (255 mg, 78% from **8**); R_F 0.23 (5:3:1 2-propanol–EtOAc–water).

Methylation of **5** with diazomethane, followed by acetylation with acetic anhydride–pyridine, gave a mixture of peracetates **12** (240 mg, 37% overall from **8**). This crude product was twice purified in a column of silica gel with EtOAc–hexane, thus giving **12a** [colorless syrup, 7.4% overall yield from **8**, R_F 0.59

*Values without asterisk are for one diastereoisomer, those with asterisks for the other. Some assignments may have to be interchanged.

(EtOAc)], **12d** (colorless syrup, 1.8%, R_F 0.54), **12c** (colorless syrup, 0.8%, R_F 0.52), and **12b** (colorless prisms, m.p. 167–168°, 4.1%, R_F 0.49); ^{1}H-n.m.r. data for each product are recorded in Table VI.

5-Deoxy-1,2-O-isopropylidene-5-phosphino-6-O-(triphenylmethyl)-α-D-glucofuranose (**11**). — The procedure described for **10** was applied to **9**, giving **11** as a colorless syrup; R_F 0.73 (3:1 EtOAc–hexane); ^{1}H-n.m.r. (60 MHz): δ 1.32, 1.50 (2 s, each 3 H, CCH_3), 2.0–2.5 (m, 1 H, D_2O exchangeable, *H*O-3), 2.28 (m, 1 H, H-5), 2.80 (dd, 2 H, $^1J_{P,H}$ 200, $^3J_{5,PH}$ 6.8 Hz, H_2P), 3.2–3.6 (m, 2 H, H-6,6′), 4.26 (br. d, 1 H, $J_{3,4}$ 2.3 Hz, H-3), 4.45 (m, 1 H, H-4), 4.52 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-2), 5.88 (d, 1 H, H-1), and 7.2–7.5 (m, 15 H, Ph–H); *m/z* 479 (0.9, M + 1), 478 (2.6, M^+), 461 (0.8), 296 (7), 243 (100), 235 (11), 187 (17), 177 (20), 165 (31), 129 (7), and 3 (6); high-resolution.

Anal. m.s.: calc. for $C_{28}H_{31}O_5P$, *m/z* 478.1909, found 478.1895. The compound was not stable enough for elemental analysis.

Compound **11** was immediately converted into **5** and then to **12a–d** by the procedure just described, giving **12a** (7.5% overall yield from **9**), **12b** (4.8%), **12c** (0.9%), and **12d** (1.6%).

ACKNOWLEDGMENTS

We are grateful to Professor (Emeritus) Saburo Inokawa for helpful discussion and to Mr. Shin-ichi Takekuma (Kinki Univ., Osaka) for the measurement of mass spectra. The present work was partially supported by Grant-in-Aid for Scientific Research No. 63540500 from the Ministry of Education, Science, and Culture (Japan) and the Fonds der Chemischen Industrie (F.R.G.).

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