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SYNTHESIS OF 1,2,4-TRI-*O*-ACETYL-3,6-DI-*O*-BENZYL-5-DEOXY-5-*C*-[(*S*)-PHENYLPHOSPHINYL]-β-D-GLUCOPYRANOSE: THE FIRST *gluco* TYPE OF HEXOPYRANOSE DERIVATIVE HAVING PHOSPHORUS IN THE HEMIACETAL RING

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ABSTRACT

Oxidation of 3,6-di-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose with pyridinium chlorochromate in the presence of molecular sieves, followed by conversion into the *p*-tolylsulfonylhydrazone, addition of methyl phenylphosphinate, and reduction with sodium borohydride, provided the key intermediate, namely, 5(*R*,*S*)-3,6-di-*O*-benzyl-5-deoxy-1,2-*O*-isopropylidene-5-*C*-[(methoxy)phenylphosphinyl]-α-D-*xylo*-hexofuranose, in 23% overall yield. Treatment of this compound with sodium dihydrobis(2-methoxyethoxy)aluminate, followed by the action of mineral acid and acetic anhydride, yielded the crystalline title compound, the structure of which was established on the basis of mass and 400-MHz, ^{1}H-n.m.r. spectra. A general dependence of $^2J_{PH}$ values on the O=P–C–H dihedral angles effectively served for assigning the configuration of C-1, C-5, and the ring-phosphorus atom of the present product and other such 5-*C*-phosphinylhexopyranoses.

INTRODUCTION

In our effort, because of their physicochemical and biological interest, to prepare hexopyranoses, along with pentopyranoses[1], having phosphorus in the hemiacetal ring, we reported a tri-*O*-acetyl derivative of 5,6-dideoxy-3-*O*-methyl-5-*C*-[(*S*)-phenylphosphinyl]-β-D-glucopyranose[2] (**12**), the tetra-*O*-acetyl derivatives of 5,6-dideoxy-5-*C*-[(*R*,*S*)-phenylphosphinyl]-α,β-L-idopyranoses[3] (*e.g.*, **14**), and the 6-deoxy-6-nitro derivatives[1,4] (*e.g.*, **13**). Because of various difficulties in preparing

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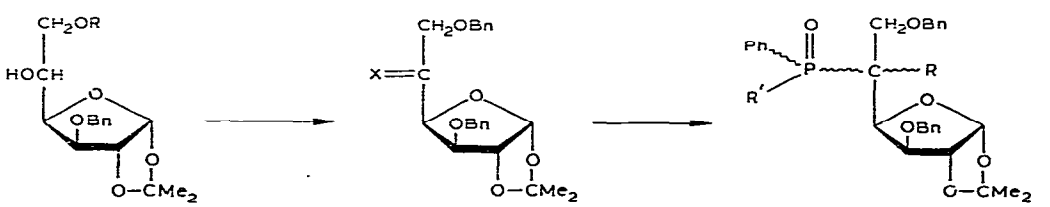
the precursors for 6-*O*-substituted 5-deoxy-5-*C*-(phosphinyl)hexopyranoses; all of these sugars are 6-deoxyhexopyranoses. The fact that the *gluco* type (sugar **12**) was obtained when a methoxyl group was present on C-3 prompted us to protect the HO-3 group with a suitable group, and we now report a convenient route for the preparation of a 5-*C*-phosphinylglucopyranose derivative which is the first example of the complete glucose structure having phosphorus in the hemiacetal ring.

RESULTS AND DISCUSSION

5,6-Anhydro-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose[5], prepared from 3-*O*-benzyl-1,2-*O*-isopropylidene-6-*O*-*p*-tolylsulfonyl-α-D-glucofuranose (**1**), served as the starting material for this synthesis. The epoxide was treated with sodium phenylmethoxide to give the 3,6-di-*O*-benzyl-D-glucofuranose (**2**) in 70% yield. Oxidation of **2** was then performed by each of the following methods, all of which gave satisfactory results: (*i*) pyridinium chlorochromate (PCC) with molecular sieves in dichloromethane[6] at room temp. (90% yield), (*ii*) PCC with sodium acetate[7] at 5° (>90%), (*iii*) oxalyl chloride–dimethyl sulfoxide–triethylamine in dichloromethane[8] at −70° (>90%), and (*iv*) trifluoroacetic anhydride–dimethyl sulfoxide–triethylamine[9] at −70° to room temp. (>90%). Because of its simplicity in preparative work on a large scale, we normally employed method (*i*).

The product, ketone **3**, shows a sharp, i.r. absorption-band at 1745 cm^{-1}, and may be distilled under high vacuum. According to the method developed[10] for conversion of a carbonyl function into a C–P bond reductively, ketone **3** was treated with *p*-tolylsulfonylhydrazine in the presence of molecular sieves, to afford a quantitative yield of a mixture of two hydrazones (**4** and **5**), isomeric with respect to the N=C-5 bond, in the ratio of 7:3. Taking into account the deshielding effect, on the proximate protons, of the *p*-tolylsulfonylamido group, the slightly downfield shift of the H_2-6 signal of the major product **4** and that of the H-1, 2, 3, and 4 signals of **5**, compared with the other counterparts, led to assignment as the *E* and *Z* isomer, respectively, for the products, the *E*-isomer **4** being considered to be favored (in view of its stereochemistry).

Although **4** and **5** were separable by chromatography on silica gel, the two isomers gave the same product (**6**) in the next step. Thus, without separation, hydra-



1 R = Ts
2 R = Bn

3 X = O
4 X = NNHTs (*E*)
5 X = NNHTs (*Z*)

6 R = NHNHTs, R′ = OMe
7 R = H, R′ = OMe
8 R = R′ = H

TABLE I

400-MHz, ^{1}H-N.M.R. PARAMETERS FOR 5-DEOXY-5-*C*-(PHENYLPHOSPHINYL)HEXOPYRANOSES IN $CDCl_3$

Compound	*AcO-1*[a] *H-1*	*AcO-2*[a] *H-2*	*AcO-3*[a] *H-3*	*AcO-4*[a] *H-4*	*H-5*	*R-6* *H-6*	P-C_6H_5 {o m p
11	1.88[a] s 5.57 ddd $J_{1,2}$ 11.2 $J_{1,P}$ 2.8 $J_{1,5}$ 0.3	1.87[a] s 5.83 ddd $J_{1,2}$ 11.2 $J_{2,3}$ 9.5 $J_{2,P}$ 3.0	4.70[b] s 7.32[d] m 7.27[d] m 3.88 dd $J_{3,4}$ 9.8 $J_{2,3}$ 9.5	1.86[a] s 5.70 ddd $J_{4,5}$ 11.5 $J_{3,4}$ 9.8 $J_{4,P}$ 2.8	2.65 ddddd $J_{4,5}$ 11.5 $J_{5,6a}$ 7.0 $J_{5,6b}$ 6.0 $J_{5,P}$ 4.0 $J_{1,5}$ 0.3	4.19[c] d 4.21[c] d 7.27[e] m 3.89 ddd (H-*a*) $J_{6,P}$ 10.0 $J_{6,6}$ 9.8 $J_{5,6}$ 7.0 3.70 ddd (H-*b*) $J_{6,P}$ 14.5 $J_{6,6}$ 9.8 $J_{5,6}$ 6.0	7.75 m 7.47 m 7.56 m
12	2.14[a] s 5.60 ddd $J_{1,2}$ 11.0 $J_{1,P}$ 2.7 $J_{1,5}$ 0.3	2.05[a] s 5.78 ddd $J_{1,2}$ 11.0 $J_{2,3}$ 9.6 $J_{2,P}$ 2.8	3.49[f] s 3.58 dd $J_{3,4}$ 9.8 $J_{2,3}$ 9.6	1.90[a] s 5.52 ddd $J_{4,5}$ 12.0 $J_{3,4}$ 9.8 $J_{4,P}$ 2.7	2.15 dqdd $J_{4,5}$ 12.0 $J_{5,6}$ 7.0 $J_{5,P}$ 3.5 $J_{1,5}$ 0.3	1.06[g] dd $J_{6,P}$ 15.0 $J_{5,6}$ 7.0	7.74 m 7.54 m 7.61 m
13	2.04[a] s 5.94 dd $J_{1,2}$ 10.5 $J_{1,P}$ 2.2	1.98[a] s 5.87 ddd $J_{1,2}$ 10.5 $J_{2,3}$ 9.5 $J_{2,P}$ 3.5	2.02[a] s 5.54 dd $J_{3,4}$ 9.8 $J_{2,3}$ 9.5	1.93[a] s 5.88 ddd $J_{3,4}$ 9.8 $J_{4,5}$ 6.5 $J_{4,P}$ 3.2	3.57 dqdd $J_{5,P}$ 11.5 $J_{5,6a}$ 8.5 $J_{4,5}$ 6.5 $J_{5,6b}$ 2.0	4.58 dd (H-*a*) $J_{6,6}$ 14.0 $J_{5,6}$ 8.5 $J_{6,P}$ 3.5 4.34 dd (H-*b*) $J_{6,6}$ 14.0 $J_{6,P}$ 11.4 $J_{5,6}$ 2.0	7.92 m 7.62 m 7.71 m
14[h]	2.06[a] s 6.11 dd $J_{1,2}$ 10.75 $J_{1,P}$ 2.75	2.01[a] s 5.80 ddd $J_{1,2}$ 10.75 $J_{2,3}$ 9.5 $J_{2,P}$ 2.4	2.056[a] s 5.55 ddd $J_{3,4}$ 10.1 $J_{2,3}$ 9.5	1.95[a] s 5.76 ddd $J_{3,4}$ 10.1 $J_{4,5}$ 4.6 $J_{4,P}$ 3.4	2.79 dqd $J_{5,P}$ 21.7 $J_{5,6}$ 7.6 $J_{4,5}$ 4.6	1.10[g] dd $J_{6,P}$ 16.8 $J_{5,6}$ 7.6	7.80 m 7.54 m 7.60 m

[a]Acetoxyl assignments are interconvertible; *J* values (in Hz) confirmed by double resonance. [b]$C_6H_5CH_2O$-3. [c]$C_6H_5CH_2O$-6, *J* 11.8. [d]$C_6H_5CH_2O$-3. [e]$C_6H_5CH_2O$-6. [f]CH_3O-3. [g]H_3-6. [h]Ref. 3. Chemical shifts (δ values) are in p.p.m. from Me_4Si.

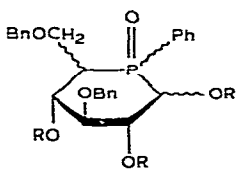
zones **4** and **5** were treated with three equivalents of methyl phenylphosphinate in the presence of trifluoromethanesulfonic acid, to give the adduct **6** in 75% yield; weaker acids, such as *p*-toluenesulfonic acid, gave a less satisfactory yield. Product **6** consisted of a mixture of four diastereoisomers (as concerned the C-5 and P atom) in the ratios of ~1:2:10:10, but the last two (major) isomers could not be completely separated by chromatography in a column of silica gel, and the configuration of each diastereoisomer could not be decided by 60-MHz n.m.r. spectroscopy. The *p*-tolylsulfonylhydrazino group of **6** was removed by reduction with sodium borohydride

in oxolane, providing the intermediate **7** in 34% yield (again as a mixture of four diastereoisomers).

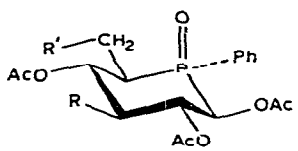
As reduction with sodium dihydrobis(2-methoxyethoxy)aluminate (SDMA) was known to cause partial epimerization at C-5 in a similar system[3], mixture **7** was directly subjected to reduction with SDMA, to give phosphinyl compound **8**. This was hydrolyzed best with 1:1 0.2M HCl–ethanol at 80°, affording the phosphinylhexopyranoses **9**: because of the apparent decomposition of **8** at elevated temperature in acid, optimization of the conditions required intensive studies concerning the acid strength, concentration, solvent, and temperature. As **9** was expected to be a mixture of the eight diastereoisomers theoretically possible (with respect to C-1, C-5, and the ring-phosphorus atom), structural assignment was made by converting **7** into the peracetates **10** by treatment with acetic anhydride in pyridine. Purification of the crude mixture of products by t.l.c. gave crystalline compound **11** of melting point 210° (dec.) as the only isolable product, in 2% overall yield from **7**; the rest was a mixture practically inseparable by a variety of methods.

Compound **11** clearly exhibited the molecular-ion peak at *m/z* 595, corresponding to $C_{32}H_{35}O_9P$, in both the high-resolution and field-desorption mass spectra. The precise structure of **11** was determined by comparing its 400-MHz, ^{1}H-n.m.r. spectrum with those of structurally similar analogs[2–4]. The assignment of all signals was readily made by employing first-order analysis with the aid of a decoupling technique, and the results are summarized in Table I.

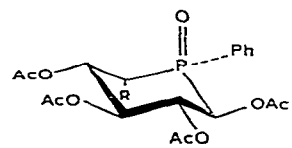
The H-1 signal of **11** consists of a triple doublet with large $J_{1,2}$ (11.2 Hz), small $J_{1,P}$ (2.8 Hz), and extremely small $J_{1,5}$ (0.3 Hz; W-coupling) values. On the other hand, the $J_{4,5}$ value is significantly large (11.5 Hz), whereas $J_{5,P}$ is small (4.0 Hz); the magnitudes of these are the reverse of those[3,4] of the L-idopyranoses (*e.g.*, **13** and **14**). It seems now to have been generally observed[3,11,12] that $^2J_{PH}$ is much larger when the coupled proton lies close to the phosphoryl oxygen atom, and is small when remote, exactly as was noted for the lone pair in P(III) compounds[12]. As both $J_{2,3}$ and $J_{3,4}$ of **11** were large (9.5 and 9.8 Hz), these J values led to the 5-deoxy-5-*C*-[(*S*)-phenylphosphinyl]-β-D-glucopyranose structure [with the $^4C_1$(D) conformation of the rigid pyranoid ring] for **11**. The splitting patterns of the n.m.r.



9 R = H
10 R = Ac



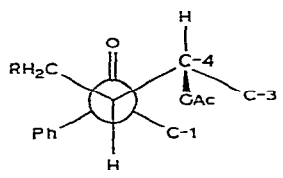
11 R = R' = OBn
12 R = OMe, R' = H

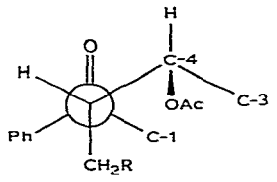


13 R = CH_2NO_2
14 R = CH_3

Ph = C_6H_5
Bn = $CH_2C_6H_5$
Ts = $SO_2C_6H_4Me$-*p*

spectrum of **11** closely resembled that of the 6-deoxy-3-*O*-methyl-β-D-glucopyranose **12**, but differed markedly from those of the L-*ido* compounds **13** and **14**, particularly with regard to the $J_{4,5}$ and $J_{5,P}$ values; the spectra of **12** and **13** were previously[2,4] recorded at 60 MHz, but are now available at 400 MHz, as shown in Table I. It now becomes apparent that, when the ring-phosphorus atom has the (*S*) configuration, as in compounds **11–14**, combination of the values of the geminal, P-C-H coupling-constants $J_{5,P}$ and those of $J_{4,5}$ provides a quick method for assignment of the configuration of C-5, because those values obviously depend upon the magnitude of the approximate O=P–C-5-H and H-C-5–C-4-H dihedral angles, as illustrated in the "Newman" projections depicted.





11: $J_{5,P}$ 4.0, $J_{4,5}$ 11.5 Hz
12: $J_{5,P}$ 3.5, $J_{4,5}$ 12.0 Hz

13: $J_{5,P}$ 11.5, $J_{4,5}$ 6.5 Hz
14: $J_{5,P}$ 21.7, $J_{4,5}$ 4.6 Hz

"Newman" projection along C-5–P-5 bond, and $^2J_{PH}$ and $J_{4,5}$ values.

As was observed in the formation of **11** and **12**, only phosphinyl sugars of the *gluco* type were isolated when the hydroxyl groups at C-3 of the precursors (*e.g.*, **8**) were protected, for example, with a benzyl or a methyl group. It is not yet certain how this protection affects the course of the ring transposition of the *xylo*-hexofuranoses to phosphinyl-gluco- or -ido-pyranoses from the viewpoint of stereochemical and electronic requirements. Nevertheless, the present work demonstrates an effective way of preparing a *gluco* type of 5-*C*-phosphinyl sugar from a *xylo*-hexofuranose, and further establishes the effective use of ^{1}H-n.m.r. spectra for determining the configuration and conformation of 5-*C*-phosphinylhexopyranoses.

EXPERIMENTAL

General methods. — Melting points are uncorrected. Silica gel B-5F (Wako Pure Chemical Industries, Ltd., Japan) was used for t.l.c. Products in t.l.c. were detected with sulfuric acid–ethanol or cobalt(II) chloride–acetone as the indicator. All reactions were monitored by t.l.c. Optical rotations were determined with a Yanagimoto OR-10 polarimeter. I.r. spectra were recorded with IR-S and IR-A-1 (Japan Optical Laboratory) spectrophotometers. ^{1}H-N.m.r. spectra were recorded with a Hitachi–Perkin–Elmer R-20A (60 MHz) or Bruker WH-400 cryospectrometer (400 MHz; for compounds **11**, **12**, and **13**) at 27°. Chemical shifts are reported as values in parts per million relative to tetramethylsilane (δ 0.0) as the internal standard.

To confirm the coupling constants, spin decoupling was performed for each proton signal. For all compounds whose n.m.r. spectra were recorded at 400 MHz, the spectra were completely interpretable by first-order analysis.

5,6-Anhydro-3-O-benzyl-1,2-O-isopropylidene-α-D-glucofuranose. — This compound was prepared from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose in four steps, according to Meyer and Reichstein[5], and was used without purification.

Synthesis of 3,6-di-O-benzyl-1,2-O-isopropylidene-α-D-glucofuranose (**2**). — The method of Whistler *et al.*[13] was applied. To a cold solution of sodium phenylmethoxide, prepared by dissolving sodium (0.47 g) in benzyl alcohol (48 mL), was added the 5,6-anhydro-D-glucofuranose derivative (5.99 g), the mixture was stirred for 4 days at room temperature, the base neutralized with 0.5M sulfuric acid, the suspension filtered, and the aqueous layer extracted with chloroform. The organic layers were combined, successively washed with saturated, aqueous sodium hydrogencarbonate and brine, dried (sodium sulfate), and evaporated *in vacuo*, giving a colorless oil from which traces of benzyl alcohol were removed by pump; the residue was chromatographed in a column of silica gel with 1:8 (v/v) ethyl acetate–benzene as the eluant, giving **2** as a syrup (5.8 g, 70%): $[\alpha]_D^{25}$ −25.9° (*c* 1.06, $CHCl_3$); ^{1}H-n.m.r. data ($CDCl_3$): δ 1.26, 1.43 (s, 6 H, CMe_2), 2.64 (s, 1 H, OH-5), 3.66 (m, 1 H, H-5), 4.07–4.11 (m, 3 H, H-2,3,4), 4.51, 4.57 (m, 6 H, H_2-6, O-CH_2Ph-3,6), 5.85 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), and 7.31 (s, 10 H, O-C-C_6H_5-3,6); *m/z* 400 (M^+).

Synthesis of 3,6-di-O-benzyl-1,2-O-isopropylidene-α-D-xylo-hexofuranos-5-ulose (**3**). — To a stirred suspension of finely powdered molecular sieves 3A (4.0 g) and PPC (1.57 g) in dry dichloromethane (10 mL) was carefully added a solution of **2** (1.07 g) in dry dichloromethane (10 mL) at 0°. The mixture was stirred for 4 h at 20°, isopropyl alcohol (0.36 mL) was added at 0° (to stop the oxidation), the mixture was triturated with ether (300 mL) for 24 h at 20°, and the precipitate was filtered off through active carbon. The filtrate was evaporated *in vacuo*, to give **3** (0.96 g, 90%) as a colorless syrup; b.p. 110°/0.05 Torr; $[\alpha]_D^{25}$ −51.0° (*c* 1.07, $CHCl_3$); ^{1}H-n.m.r. data ($CDCl_3$): δ 1.30, 1.44 (s, 6 H, CMe_2), 4.31–4.60 (m, 8 H, H-3,4,6,6', O-CH_2-Ph-3,6), 4.78 (d, 1 H, $J_{2,1}$ 3.6 Hz, H-2), 6.02 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), and 7.33 (s, 10 H, O-C-C_6H_5-3,6).

Synthesis of 3,6-di-O-benzyl-1,2-O-isopropylidene-α-D-xylo-hexofuranos-5-ulose (E *and* Z) *5-p-tolylsulfonylhydrazone* (**4** and **5**). — A solution of **3** (8.84 g) in absolute methanol (40 mL) and then *p*-tolylsulfonylhydrazine (6.39 g) were added to a stirred suspension of molecular sieves 3A (30 g) in absolute methanol (80 mL). The mixture was heated for 20 h at 40°, with stirring, diluted with chloroform, the precipitate filtered off, and the filtrate successively washed with cold dilute hydrochloric acid and saturated, aqueous sodium hydrogencarbonate, dried (sodium sulfate), and evaporated *in vacuo*, to give a syrup (13.0 g, 100%) which was a 7:3 mixture of **4** and **5**, separable by chromatography in a column of silica gel with ethyl acetate–benzene as the eluant; **4**: $[\alpha]_D^{25}$ −95.4° (*c* 0.93, $CHCl_3$), **5**: −41.1° (*c* 1.14, $CHCl_3$); ^{1}H-n.m.r. data ($CDCl_3$) for **4**: δ 1.27, 1.46 (s, 6 H, CMe_2), 2.37 (s, 3 H, S-C_6-CH_3), 4.01 (d, 1 H, $J_{3,4}$ 3.0 Hz, H-3), 4.25–4.36 (m, 6 H, H-6,6', O-CH_2-Ph-3,6), 4.53 (d, 1 H, $J_{2,1}$ 3.6 Hz, H-2),

4.78 (d, 1 H, $J_{4,3}$ 3.0 Hz, H-4), 5.91 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), and 7.03–7.72 (m, 14 H, O-C-C_6H_5-3,6, S-C_6H_4-C); for **5**: 1.30, 1.43 (s, 6 H, CMe_2), 2.33 (s, 3 H, S-C_6-CH_3), 3.87 (d, 2 H, $J_{6,6'}$ 6.0 Hz, H-6,6'), 4.06 (d, 1 H, $J_{3,4}$ 3.0 Hz, H-3), 4.16 (s, 2 H, O-CH_2-Ph-3), 4.38 (m, 2 H, O-CH_2-Ph-6), 4.52 (d, 1 H, $J_{2,1}$ 3.6 Hz, H-2), 4.83 (d, 1 H, $J_{4,3}$ 3.0 Hz, H-4), 6.05 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 7.08–7.83 (m, 14 H, O-C-C_6H_5-3,6, S-C_6H_4-C), and 9.94 (m, 1 H, NH).

Anal. (for **4**) Calc. for $C_{30}H_{34}N_2O_7S$: C, 63.59; H, 6.05; N, 4.94. Found: C, 63.31; H, 6.31; N, 4.98.

Synthesis of 5(R,S)-*3,6-di*-O-*benzyl-5-deoxy-1,2*-O-*isopropylidene-5*-C-[(*methoxy*)*phenylphosphinyl*]-*5*-C-(p-*tolylsulfonylhydrazino*)-α-D-xylo-*hexofuranose* (**6**). — The tosylhydrazone mixture **4** (0.78 g) was dissolved in methyl phenylphosphinate (0.70 g) with stirring. The solution was degassed, and then filled with argon, and a few drops of trifluoromethanesulfonic acid were added at 0°. The mixture was stirred for 20 h at 20°, diluted with chloroform and aqueous sodium hydrogencarbonate (to decompose the excess of phosphinate), the layers separated, and the aqueous layer extracted with chloroform. The organic layers were combined, dried (sodium sulfate), and evaporated. The product **6** was a colorless syrup (0.86 g, 75%) separable by chromatography in a column of silica gel, with ethyl acetate–benzene as the eluant, into three fractions: **6a**, **6b**, and **6c** (ratios 1:2:20); $[\alpha]_D^{21}$: **6a**, −3.18°; **6b**, −6.36°; and **6c**, −17.6° (*c* 1.01, 1.89, and 1.00, respectively; $CHCl_3$); ^{1}H-n.m.r. data ($CDCl_3$) for **6a**: 1.33, 1.52 (s, 6 H, CMe_3), 2.41 (s, 3 H, S-C_6-CH_3), 3.35–5.15 (m, 13 H, O-CH_2-Ph-3,6, P-OCH_3, H-2,3,4,5,6,6'), 5.92 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), and 7.14–7.85 (m, 19 H, O-C-C_6H_5-3,6, S-C_6H_4-C, P-C_6H_5); for **6b**: 1.28, 1.40 (s, 6 H, CMe_2), 2.38 (s, 3 H, S-C_6-CH_3), 3.34–5.46 (m, 13 H, O-CH_2-Ph-3,6, P-OCH_3, H-2,3,4,5,6,6'), 5.91 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), and 7.26–8.05 (m, 19 H, O-C-C_6H_5-3,6, S-C_6H_4-C, P-C_6-H_5); for **6c** (a 1:1 diastereoisomeric mixture): 1.12, 1.20, 1.27, 1.46 (s, 6 H, CMe_2), 2.38 (s, 3 H, S-C_6-CH_3), 3.48–4.80 (m, 13 H, O-CH_2-Ph-3,6, P-OCH_3, H-2,3,4,5,6,6'), 5.80, 5.77 (d, 1 H, $J_{1,2}$ 4.8 Hz, H-1), and 7.05–8.07 (m, 19 H, O-C-C_6H_5-3,6, S-C_6H_4-C, P-C_6H_5).

Synthesis of 5-(R,S)-*3,6-di*-O-*benzyl-5-deoxy-1,2*-O-*isopropylidene-5*-C-[(*methoxy*)*phenylphosphinyl*]-α-D-xylo-*hexofuranose* (**7**). — To a stirred solution of **6c** (1.00 g) in anhydrous oxolane (70 mL) was added, under argon, sodium borohydride (0.64 g) at 0°. The mixture was stirred for 30 h at room temperature, carefully quenched at 0° by the addition of enough 5M acetic acid to give pH 4, the pH brought to 7 with saturated, aqueous sodium hydrogencarbonate, and the mixture extracted with chloroform. The extracts were combined, dried (sodium sulfate), and evaporated *in vacuo*. Chromatography of the residue in a column of silica gel, with ethyl acetate–benzene as the eluant, gave **7c** (0.25 g, 34%) as a colorless syrup which was an ~4:1 mixture of two distereoisomers; $[\alpha]_D^{22}$ −1.7° (*c* 1.08, CH_3OH); ^{1}H-n.m.r. data ($CDCl_3$): δ 1.10, 1.20, 1.29*, 1.40* (s, 6 H, CMe_2), 3.1* (m, 1 H, H-5), 3.90* (d, 3 H, $^3J_{PH}$ 10 Hz, P-OCH_3), 3.55–4.68 (m, 9 H, O-CH_2-Ph-3,6, H-2,3,4,6,6'), 5.91, 5.98* (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), and 7.2–8.0 (m, 15 H, O-C-C_6H_5-3,6, P-C_6H_5) (*: due to the major diastereoisomer).

When a mixture of **6a** and **6b** was similarly reduced, a mixture of **7a** and **7b** was obtained; by ^{1}H-n.m.r. spectroscopy, these were found to be diastereoisomers of **7c**.

Synthesis of 1,2,4-tri-O-acetyl-3,6-di-O-benzyl-5-deoxy-5-C-(phenylphosphinyl)-β-D-glucopyranose (**11**). — SDMA (70% in toluene, 0.4 mL) was slowly added at 0° to a stirred solution of **7** (0.30 g) in dry toluene (7 mL) under argon, followed by stirring for 20 min. Then, water (0.5 mL) was added at 0° to decompose the excess of SDMA. The mixture was stirred for 30 min, and centrifuged to remove aluminum hydroxide. The precipitate was extracted with several portions of benzene. The organic layers were combined, and evaporated *in vacuo*, giving a quantitative yield of *5*(R,S)-*3,6-di-O-benzyl-5-deoxy-1,2-O-isopropylidene-5-C-(phenylphosphinyl)-α-D-xylo-hexofuranose* (**8**) as a syrup; R_F 0.25 and 0.30 in 1:2 ethyl acetate–benzene.

To a solution of **8** (0.28 g) in ethanol (10 mL) was added oxygen-free, 0.24M hydrochloric acid (10 mL), and the mixture (pH 1) was heated under argon for 2 h at 80° (bath), and then overnight at 40–50°. The mixture was cooled, the acid neutralized by passing through a column of Amberlite IRA-45 anion-exchange resin (weakly basic), the eluate filtered, and the filtrate evaporated *in vacuo*, to give *5*(R,S)-*3,6-di-O-benzyl-5-deoxy-5-C-(phenylphosphinyl)-α,β-D-gluco-* or *-L-ido-pyranose*, or both (**9**) as an oil; R_F: 0.1 in 1:1 ethyl acetate–benzene.

To a solution of **9** in dry pyridine (10 mL) was added acetic anhydride (1 mL) at 0°, and the mixture was stirred for 20 h at room temperature. A small amount of water was added, most of the pyridine was evaporated *in vacuo*, the residue was dissolved in chloroform, and the solution washed successively with cold, dilute hydrochloric acid, water, and saturated, aqueous sodium hydrogencarbonate, dried (sodium sulfate), and evaporated *in vacuo*. The residue was purified by t.l.c. on silica gel with 1:2 ethyl acetate–benzene as the eluant. The band having R_F 0.3–0.4 was separated, eluted with ethanol, and the eluant removed *in vacuo*, giving **11** (6.5 mg, 2% overall yield from **7**) as colorless prisms (from ethyl acetate–hexane), m.p. 210° (dec.); ^{1}H-n.m.r. data (400 MHz; $CDCl_3$): see Table I; high-resolution, e.i. mass spectrum*, *m/z* (relative intensity): 595 (0.5; M^+), 535 (4), 493 (7), 429 (24), 323 (21), 279 (7), 237 (7), 125 (7), 91 (100), and 43 (28); ^{23}Na-f.d. mass spectrum* *m/z* (relative intensity): 618 (16; M + Na), 595 (100; M), and 279 (52); calc. for $C_{23}H_{26}O_6P$ ($M - CH_2CO_2 - C_7H_7O$): 429.1466, found: 429.1428.

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