Carbohydrate Research, 70 (1979) 247–261

SYNTHESIS OF 5,6-DIDEOXY-3-*O*-METHYL-5-*C*-(PHENYLPHOSPHINYL)-D-GLUCOPYRANOSE AND ITS 1,2,4-TRIACETATE*

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(Received April 24th, 1978; accepted for publication in revised form, July 28th, 1978)

ABSTRACT

Methyl phenylphosphonite or dimethyl phosphite underwent acid-catalyzed addition reactions with some hexofuranos-5-ulose 5-(*p*-tolylsulfonylhydrazones) (**7**, **9**, and **16**), to give the corresponding adducts, **17**, **18**, **19**, and **21**. The isomer ratios of the adducts were affected by a 3-substituent in the hydrazones. Treatment of adduct **21** with sodium borohydride and sodium dihydrobis(2-methoxyethoxy)-aluminate (SDMA), followed by acid hydrolysis, gave 5,6-dideoxy-3-*O*-methyl-5-*C*-(phenylphosphinyl)-D-glucopyranose (**26**), which was acetylated to give the 1,2,4-tri-*O*-acetyl derivatives **27a** and **27b**. Conformational analysis of compound **27a** by X-ray crystallography revealed that the compound was 1,2,4-tri-*O*-acetyl-5,6-dideoxy-3-*O*-methyl-5-*C*-[(*S*)-phenylphosphinyl]-β-D-glucopyranose in the $^4C_1$(D) form having all substituents equatorial.

INTRODUCTION

In the chemical modification of sugar derivatives, there have been synthesized many heteroatom-containing sugars, such as amino[1,2] and thio sugars[1,3]. Only a few phosphorus analogs have been synthesized, because of procedural difficulties. Syntheses of phosphorus analogs of xylopyranose[4] and ribopyranose[5], having phosphorus as the ring heteroatom, have been reported. The synthesis of a phosphorus analog of 6-deoxy-D-glucose through addition of phosphine to 3-*O*-acetyl-5,6-dideoxy-1,2-*O*-isopropylidene-6-*C*-nitro-α-D-*xylo*-hex-5-enofuranose has recently been described[6]. This paper deals with the synthesis of 5,6-dideoxy-3-*O*-methyl-5-*C*-

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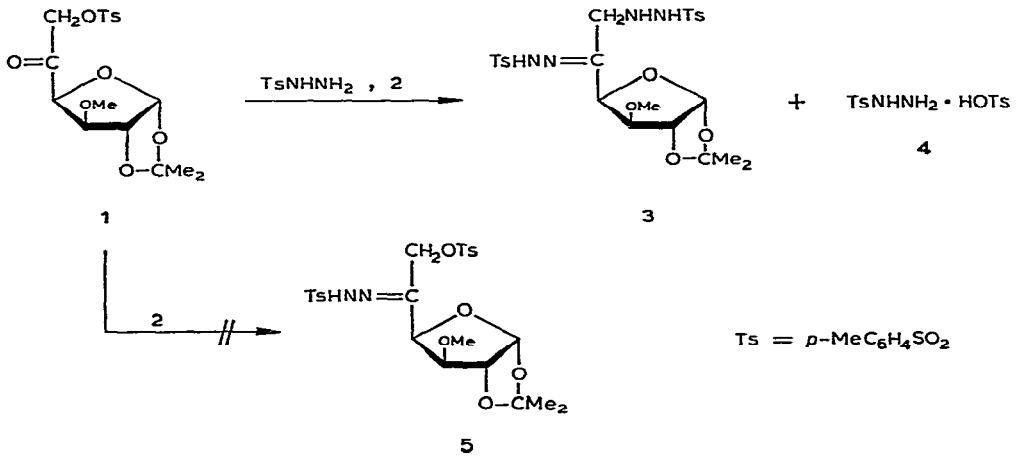
(phenylphosphinyl)-D-glucopyranose via a hydrazone intermediate[7], and with the conformational analysis of the 1,2,4-triacetate.

RESULTS AND DISCUSSION

The reaction of 1,2-*O*-isopropylidene-3-*O*-methyl-6-*O*-*p*-tolylsulfonyl-α-D-*xylo*-hexofuranos-5-ulose (**1**) with 1–3 equivs. of *p*-toluenesulfonylhydrazide (**2**) in methanol for 27 h at room temperature gave the hydrazone **3** and hydrazonium salt **4**, but no hydrazone **5**. The production of compound **3** shows that formation of the hydrazone and substitution of a *p*-toluenesulfonate group[8] occur at the same time.



6-Deoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-5-ulose (**6**) was prepared from 6-deoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hex-5-enofuranose according to the method of Ohle *et al.*[9]. Compound **6** was converted into the corresponding hydrazone **7** in 80% yield by the action of hydrazide **2** in methanol.

The hydroxyl group of compound **6** was methylated by methyl iodide and silver oxide to give 6-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-*xylo*-hexofuranos-5-ulose (**8**) in 60% yield. The reaction of glycosulose **8** with hydrazide **2** gave the corresponding hydrazone **9** in 70% yield.

1,2:5,6-Di-*O*-isopropylidene-α-D-allofuranose (**10**) was converted into 3-*O*-benzyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (**11**) in 75% yield by Whistler's method[10]. Compound **11** was hydrolyzed to afford 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-allofuranose[10] (**12**), which was treated with sodium metaperiodate to give 3-*O*-benzyl-1,2-*O*-isopropylidene-5-*aldehydo*-α-D-*ribo*-pentodialdo-1,4-furanose (**13**) in 80% yield from compound **11**. Treatment of compound **13** with methylmagnesium iodide afforded 3-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hexofuranose (**14**, 89% crude yield)[11], which was oxidized to afford the glyculose **15**. 3-*O*-Benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hexofuranos-5-ulose 5-(*p*-tolylsulfonylhydrazone) (**16**) was synthesized by treatment of the glycosulose **15** with the hydrazide **2**

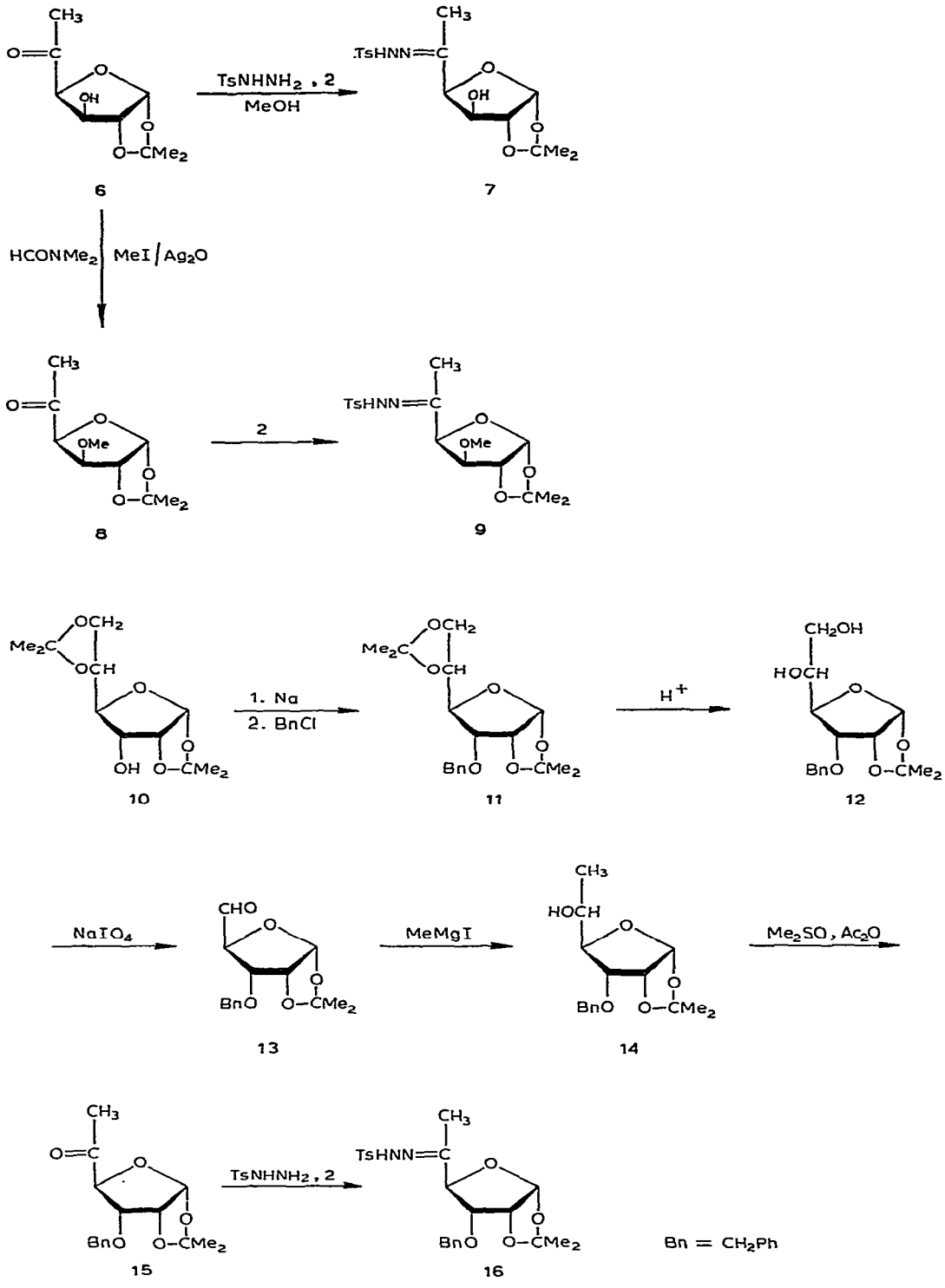

CH3
O=C
OH
O–CMe2
TsNHNH2 , 2
MeOH
TsHNN=C
6
7
HCONMe2
MeI / Ag2O
OMe
8
9
Me2C
OCH2
OCH
OH
1. Na
2. BnCl
BnO
H+
CH2OH
HOCH
10
11
12
NaIO4
CHO
MeMgI
HOCH
Me2SO , Ac2O
13
14
15
16
Bn = CH2Ph

TABLE I

THE RESULTS OF THE REACTION OF HYDRAZONES **7** AND **9** WITH PHOSPHORUS COMPOUNDS

Hydrazone	*Phosphorus compound*	*Solvent*	*Catalyst*	*Reaction temperature (°)*	*Reaction time (h)*	*Results*[a]
7	$(MeO)_2POH$	None	None	10	24	No reaction
		None	None	25	216	4 Components
		None	M.s.[b]	25	72	No reaction
	PhP(O)(OMe)H	None	None	10	72	No reaction
		None	Et_3N	25	48	Decomposition
		None	NaOMe	60	48	Decomposition
	$PhPH_2$	EtOH	None	60	48	3–6 Components
9	$(MeO)_2POH$	None	M.s.[b]	60	72	No reaction
		None	NaOMe	R.t.[e]	288	No reaction
		THF[c]	BPO[d]	95	5	4–6 Components
	$PhPH_2$	EtOH	None	R.t.[e]	72	Decomposition
	$PhP(O)H_2$	THF[c]	None	R.t.[e]	20	Decomposition

[a]The reactions were followed by means of t.l.c. on silica gel. [b]Molecular sieve 5A (ref. 12). [c]Oxolane. [d]Benzoyl peroxide. [e]Room temperature.

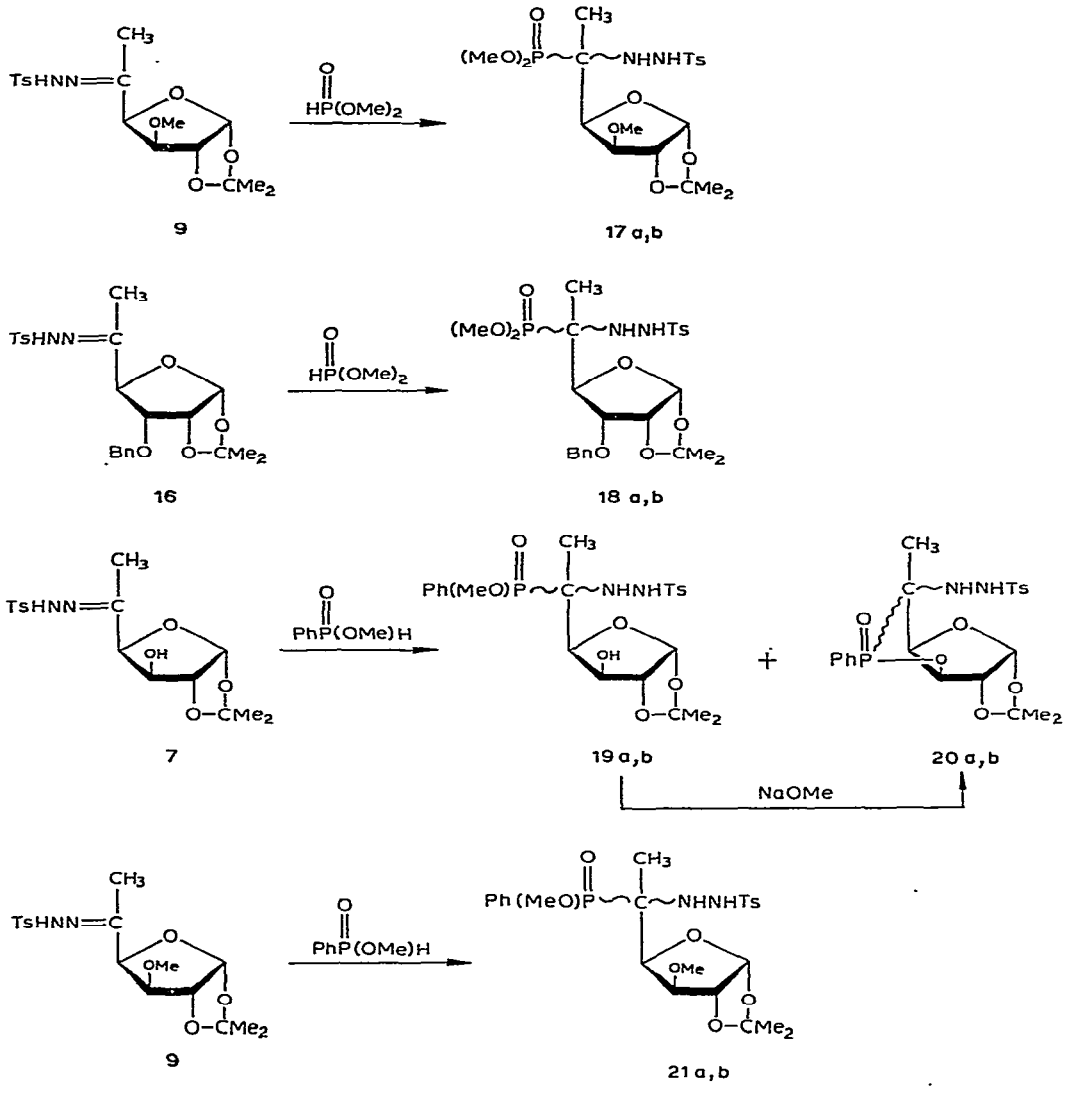
in methanol (35% yield from compound **13**). Compound **16** consisted of *syn* and *anti* isomers from consideration of its ^{1}H-n.m.r. spectrum (methyl signals of the CH_3-C_6H_4 group appeared at δ 2.27 and 2.30 in $CDCl_3$ solution).

The reactions of hydrazones **7** and **9** with dimethyl phosphite, methyl phenylphosphonite, phenylphosphine, and phenylphosphinous acid were examined under various conditions, namely, no catalyst, basic, and radical conditions, as shown in Table I.

Table I shows that the reactions did not lead to adducts of hydrazones and phosphorus compounds under the conditions employed.

Acid-catalyzed addition-reactions were also attempted. The reaction of hydrazone **9** with a 5–12 fold excess of dimethyl phosphite in the presence of anhydrous *p*-toluenesulfonic acid (0.15–0.45 mol equivalent) under nitrogen for 24–50 h afforded (5*RS*)-5,6-dideoxy-5-*C*-(dimethoxyphosphinyl)-1,2-*O*-isopropylidene-3-*O*-methyl-5-*C*-(2-*p*-tolylsulfonylhydrazino)-α-D-*xylo*-hexofuranoses (**17a** and **b**) in 70% yield, which were separated into crystalline and syrupy components (**17a** and **17b**, respectively) from hot ethanol (the ratio of **17a** to **17b** was 6:1). Compounds **17a** and **17b** were 5-epimers, as deduced from their ^{1}H-n.m.r. spectra. When a weaker acid, namely, trifluoroacetic acid, was used as the catalyst, the addition reaction was so slow that the starting hydrazone **9** was detected, even after 142 h at 40°.

The reaction of hydrazone **16** with dimethyl phosphite in the presence of 0.27 mol-equiv. of *p*-toluenesulfonic acid for 40–50 h at room temperature afforded syrupy adducts (97% yield), (5*RS*)-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-5-*C*-(dimethoxyphosphinyl)-5-*C*-(2-*p*-tolylsulfonylhydrazino)-α-D-*ribo*-hexofuranoses(**18a**



and **b**), which consisted of D-allose and L-altrose derivatives in 1:1 ratio, based on the ^{1}H-n.m.r. spectrum. The substituent at C-3 seems not to exert a steric effect on the rate of the addition reaction, but it does influence the isomer ratio.

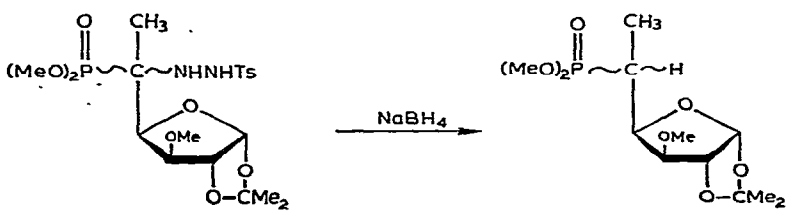
The reaction of hydrazone 7 with methyl phenylphosphonite for 30–45 h in the presence of *p*-toluenesulfonic acid gave four products, namely, two isomers of (5*RS*)-5,6-dideoxy-1,2-*O*-isopropylidene-5-*C*-[(methoxy)phenylphosphinyl]-5-*C*-(2-*p*-tolylsulfonylhydrazino)-α-D-*xylo*-hexofuranoses (**19a** and **b**, 15%), and two isomers of (5*RS*)-5,6-dideoxy-5-*C*-(3-*O*-*cyclo*-phenylphosphinate)-1,2-*O*-isopropylidene-5-*C*-(2-*p*-tolylsulfonylhydrazino)-α-D-*xylo*-hexofuranoses (**20a** and **20b**, 51 and 26%, respectively). The last two compounds showed no methoxyl or hydroxyl absorp-

tion in their ^{1}H-n.m.r. and/or i.r. spectra. Compounds **19a** and **19b** readily afforded compounds **20a** and **20b** by treatment with sodium methoxide. Hence, compounds **19a** and **19b** were expected to be converted into compounds **20a** and **20b** during isolation employing sodium hydrogencarbonate (see Experimental section).

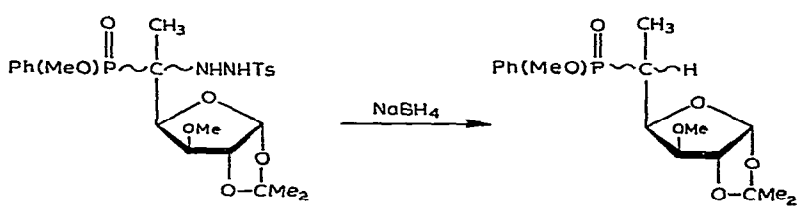
When compound **9** was treated with methyl phenylphosphonite in the presence of 0.2–0.25 mol-equiv. of *p*-toluenesulfonic acid for 16–20 h, (5*RS*)-5,6-dideoxy-1,2-*O*-isopropylidene-5-*C*-[(methoxy)phenylphosphinyl]-3-*O*-methyl-5-*C*-(2-*p*-tolylsulfonylhydrazino)-α-D-*xylo*-hexofuranoses (**21a** and **b**) were obtained as a syrup. The reaction of compound **9** with methyl phenylphosphonite in the presence of 2.5 mol-equivs. of trifluoroacetic acid afforded compounds **21a** and **21b** after 65 h.

The reaction of compound **17a** with sodium borohydride in oxolane afforded (5*RS*)-5,6-dideoxy-5-*C*-(dimethoxyphosphinyl)-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-*xylo*-hexofuranose (**22a**) in 22% yield.

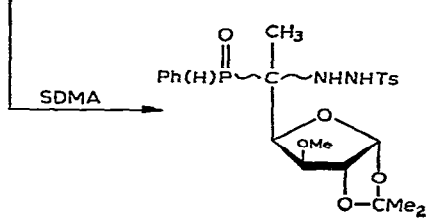
The reaction of compounds **21a** and **21b** with an excess amount of sodium borohydride at room temperature showed two products (70% yield) by t.l.c. analysis. The ^{1}H-n.m.r. spectrum of the product showed that it was a mixture of the isomers of (5*RS*)-5,6-dideoxy-1,2-*O*-isopropylidene-5-*C*-[(methoxy)phenylphosphinyl]-3-*O*-methyl-α-D-*xylo*-hexofuranose (**23a, b**).



17a 22a



21a,b 23a,b



24 a,b

TABLE II

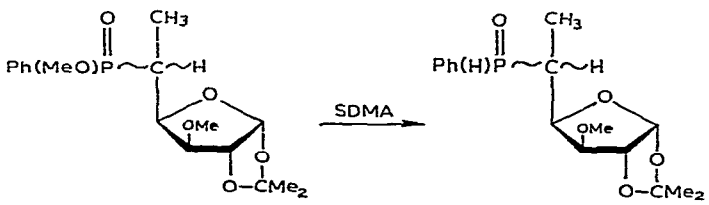
THE DEHYDRAZINATION OF COMPOUNDS **21a,b**

Reagents	*Mol ratio*	*Solvents*	*Reaction temperature (°)*	*Reaction time (h)*	*Additive*	*Product (yield, %)*
$NaBH_4$	15–20	THF[a]	R.t.[b]	72–96	None	**23a, b** (70)
	6	DMF[c]	R.t.[b]	16	None	No reaction
	5	DMF[c]	70–80	3.5	None	**23a, b** (Trace) **9** (53%)
$NaBH_3CN$	5	THF[a]	Reflux	7	TsOH[d]	No reaction
None	—	DMF[c]	Reflux	7 (min)	Na_2CO_3	**9**[e]

[a]Oxolane. [b]Room temperature. [c]*N,N*-Dimethylformamide. [d]*p*-Toluenesulfonic acid. [e]The reaction was checked by t.l.c. analysis.

Attempts to obtain compound **23** from compound **21** were made; the results are summarized in Table II.

The phosphinate **23a** was reduced with an excess of sodium dihydrobis(2-methoxyethoxy)aluminate (SDMA)[13] in oxolane at 0°. Addition of a solution of hydrochloric acid in oxolane afforded a syrup after processing. Resolution of the products by preparative t.l.c. gave (5*RS*)-5,6-dideoxy-1,2-*O*-isopropylidene-5-*C*-(phenylphosphinyl)-3-*O*-methyl-α-D-*xylo*-hexofuranoses (**25a** and **b**, 41% yield), which showed P–H absorption at 2350 cm^{-1} in the infrared[14].



23 a 25 a,b

Reduction of compound **21** with SDMA afforded (5*RS*)-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-5-*C*-(phenylphosphinyl)-5-*C*-(2-*p*-tolylsulfonylhydrazino)-α-D-*xylo*-hexofuranoses (**24a** and **b**), but no compound **25**. Another possible method to prepare **25**, by reduction of compound **23a** with lithium aluminum hydride followed by air oxidation[15], was not attempted, because this reaction sometimes affords complex results[5,16].

An attempt to prepare a sugar derivative having a phosphorus atom as the ring heteroatom was achieved by acid-catalyzed hydrolysis of compound **25**, where an addition reaction of a P–H group to the formyl group was expected. Compound **25** was hydrolyzed in aqueous oxolane containing 0.5M hydrochloric acid at 90–100°. Neutralization of the acid by an ion-exchange resin, followed by product isolation, afforded a syrup in 75% crude yield. The syrup no longer showed P–H absorption

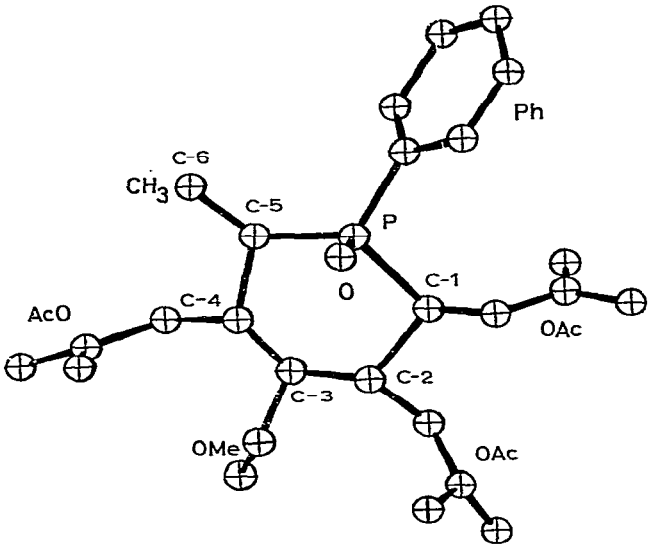
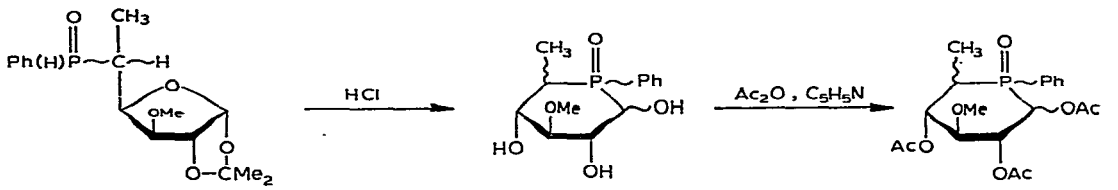


Fig. 1. Computer-generated drawing of compound **27a**.

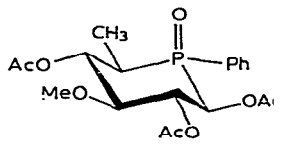
in the i.r. indicating that the product must have been 5,6-dideoxy-3-*O*-methyl-5-*C*-(phenylphosphinyl)-D-gluco- or -L-ido-furanose. The syrup was acetylated with acetic anhydride–pyridine and the totally acetylated crude product (70%) was crystallized from hot ethanol to give a high-melting component [**27a**, m.p., 304–306° (sealed tube), subliming at ~280°], and a low-melting isomer (**27b**, m.p. 164–165°). The ^{1}H-n.m.r. spectrum of compound **27a** in chloroform-*d* showed no P–H signal, but it showed three acetyl peaks, one phenyl signal, and one methoxyl peak (see Experimental section). The spectrum clearly shows that the phosphorus atom is situated in the hemiacetal ring. Elemental analysis supported the molecular formula $C_{19}H_{25}O_8P$, and the mass spectrum showed a molecular-ion peak at *m/e* 412 and a base peak at *m/e* 85. The ^{1}H-n.m.r. coupling-constants between H-1, H-2, H-3, and H-4 could not be determined, because their signals were not well resolved (δ 3.46–6.10). X-Ray analysis (Fig. 1) of a well prepared crystal established that the compound was 1,2,4-tri-*O*-acetyl-5,6-dideoxy-3-*O*-methyl-5-*C*-[(*S*)-phenylphosphinyl]-β-D-glucopyranose-$^4C_1$(D), having the acetoxyl, methoxyl, and phenyl groups equatorially disposed[17].

The mass spectrum of compound **27b** showed a molecular-ion peak at *m/e* 412 and a base peak at *m/e* 85. The peak at *m/e* 353 (M^+ — OAc) showed a major intensity-difference from that of compound **27a**. Compound **27b** ($[\alpha]_D^{15}$ +37.3°) may be the α anomer of compound **27a** ($[\alpha]_D^{15}$ +23.2°), because a single acetoxyl signal, which appeared at highest field (δ 1.90) in **27a** was shifted to lower field (δ 2.07) in **27b**.

This work thus establishes synthesis of 5,6-dideoxy-3-*O*-methyl-5-*C*-(phenylphosphinyl)-D-glucopyranose (**26**) from the hydrazone **9**.



25 a,b 26 27 a,b



27 a

EXPERIMENTAL

General methods. — Melting and boiling points are uncorrected. Solvents were removed *in vacuo*. I.r. spectra were recorded with a Hitachi–Perkin–Elmer 337 spectrophotometer. The ^{1}H-n.m.r. spectra were recorded with Hitachi–Perkin–Elmer R-20 (60 MHz) and Hitachi R-24 (60 MHz) spectrometers, with tetramethylsilane (Me_4Si) as the internal standard. Optical rotations were determined with a DIP-4 digital polarimeter (Japan Optics Laboratory). Silica gel G-10 (Nakarai Chemicals Ltd., Japan) was used for analytical and preparative t.l.c. Products were detected by t.l.c. with sulfuric acid–ethanol and/or cobalt(II) chloride–acetone as indicator. All reactions were monitored by t.l.c.

Materials. — 1,2-*O*-Isopropylidene-3-*O*-methyl-6-*O*-(*p*-tolylsulfonyl)-α-D-*xylo*-hexofuranos-5-ulose (**1**) was prepared by Stevens' method[18]. 6-Deoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-5-ulose (**6**, m.p. 96.5–99.5°) was synthesized by the method of Ohle and Deplangue from 6-deoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hex-5-enofuranose[9]. 1,2:5,6-Di-*O*-isopropylidene-α-D-allofuranose (**10**, m.p. 76–78°) was prepared from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose according to Stevens' method[18]. Methyl phenylphosphonite (b.p. 89°/0.2 mmHg) was prepared from phenylphosphonous dichloride[19]. Phenylphosphine (b.p. 159°) was synthesized by the method of Mann and Millar[20]. Sodium dihydrobis(2-methoxyethoxy)aluminate (SDMA) was a 70% solution in benzene (supplied by Wako Pure Chemical Industries, Ltd., Japan).

Reaction of compound **1** *with* p-*toluenesulfonylhydrazide* (**2**). — Treatment of compound **1** with 3 equivs. of hydrazide **2** for 27 h at room temperature afforded 6-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-6-*C*-(2-*p*-tolylsulfonylhydrazino)-α-D-*xylo*-hexofuranos-5-ulose 5-(*p*-tolylsulfonylhydrazone) (**3**) and *p*-tolylsulfonylhydrazinium *p*-toluenesulfonate (**4**).

Compound **3** had m.p. 180–181° (dec.), and showed ν_{max}^{KBr} 3400 and 3170 cm^{-1} (NH), but no C=O absorption.

Anal. Calc. for $C_{24}H_{32}N_4O_8S_2$: C, 50.69; H, 5.67; N, 9.85. Found: C, 49.63; H, 5.93; N, 9.18.

Compound **4** melted at 180–183°.

Anal. Calc. for $C_{14}H_{18}N_2O_3S_2$: C, 46.91; H, 5.06; N, 7.85. Found: C, 46.43; H, 5.02; N, 7.75.

When other conditions were employed, for example, treatment of **1** with the hydrazide **2** in methanol for 2–4 days at room temperature, 3–5 products were detected by t.l.c.

*Synthesis of 6-deoxy-1,2-*O*-isopropylidene-α-*D*-xylo-hexofuranos-5-ulose 5-(p-tolylsulfonylhydrazone)* (**7**). — A mixture of 6-deoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-5-ulose (**6**, 1.0 g) and hydrazide **2** (1.0 g) in methanol (15 mL) was kept at room temperature until no carbonyl absorption was observed in the i.r. spectrum (25 h). Evaporation of methanol *in vacuo* followed by recrystallization of the product from chloroform–petroleum ether afforded 1.4 g (80%) of compound **7**; m.p. 165–166° (dec.), $[\alpha]_D^{15.5}$ −76.9° (*c* 1.0, chloroform); ν_{max}^{MeOH} 1600 cm^{-1} (C=N); ^{1}H-n.m.r. ($CDCl_3$): δ 1.29, 1.45 (6H, s, CMe_2), 1.92 (3H, s, 5-Me), 2.41 (3H, s, Ar-Me), 1.95–3.67 (1H, OH), 4.30–4.75 (3H, H-2, H-3, H-4), 5.94 (1H, d, $J_{1,2}$ 3.8 Hz, H-1), 7.58 (4H, q, C_6H_4), and 8.00–8.65 (1H, NH).

Anal. Calc. for $C_{16}H_{22}N_2O_6S$: C, 51.88; H, 5.99; N, 7.56. Found: C, 51.70; H, 6.26; N, 7.50.

*Synthesis of 5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-*D*-xylo-hexofuranos-5-ulose 5-(p-tolylsulfonylhydrazone)* (**9**). — Compound **6** was treated with silver oxide and methyl iodide in *N*,*N*-dimethylformamide[21] to give 6-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-*xylo*-hexofuranos-5-ulose (**8**) in 66% yield, b.p. 63–67°/0.07 mmHg. Glyculose **8** was then treated with *p*-toluenesulfonylhydrazide (**2**) with subsequent recrystallization from methanol to give the corresponding hydrazone **9** in 70% yield; m.p. 166–167° (dec.), $[\alpha]_D^{15.5}$ −97.9° (*c* 0.95, chloroform); ν_{max}^{KBr} 3280 (NH), 1600 cm^{-1} (C=N); ^{1}H-n.m.r. ($CDCl_3$); δ 1.33, 1.50 (6H, s, CMe_2), 1.83 (3H, s, 5-Me), 2.45 (3H, s, Ar-Me), 3.13 (3H, s, OMe), 3.69 (1H, d, $J_{3,4}$ 4.1 Hz, H-3), 4.61 (1H, d, $J_{3,4}$ 4.1 Hz, H-4), 4.82 (1H, d, $J_{1,2}$ 3.8 Hz, H-2), 5.96 (1H, d, $J_{1,2}$ 3.8 Hz, H-1), 7.58 (4H, q, C_6H_4), and 8.26 (1H, s, NH).

Anal. Calc. for $C_{17}H_{24}N_2O_6S$: C, 53.11; H, 6.29; N, 7.28. Found: C, 53.02; H, 6.29; N, 7.03.

*Synthesis of 3-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-α-*D*-ribo-hexofuranose* (**14**).—Treatment of compound **10** with sodium metal followed by addition of α-chlorotoluene in dry ether[10] afforded 3-*O*-benzyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (**11**), m.p. 64.5–65.5°, in 75% yield. Hydrolysis of compound **11** in aqueous acetic acid[10] for 6 h at 40° gave 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-allofuranose (**12**) quantitatively. Reaction of compound **12** with sodium metaperiodate afforded 3-*O*-benzyl-1,2-*O*-isopropylidene-5-*aldehydo*-α-D-*ribo*-pentodialdo-1,4-furanose (**13**) in 80% yield[22], ν_{max}^{neat} 1730 cm^{-1} (C=O). Treatment of compound **13** with methyl-

magnesium iodide in boiling dry ether[11] for 2 h under reflux, followed by conventional processing, afforded compound **14** in 89% yield; ^{1}H-n.m.r. (CCl_4): δ 1.40, 1.60 (6H, s, CMe_2), 1.0–1.5 (3H, m, 5-Me), 3.10–3.30 (1H, OH), 3.1–3.3, 3.6–4.2 (6H, m, H-2,3,4,5,O-CH_2), 5.90 (1H, d H-1), and 7.5 (5H, Ph).

*Synthesis of 3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene-α-D-*ribo*-hexofuranos-5-ulose 5-(p-tolylsulfonylhydrazone)* (**16**). — Compound **14** was oxidized[18] to give mainly 3-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hexofuranos-5-ulose (**15**), R_F 0.61 [t.l.c., silica gel, 1:1 (v/v) ethyl acetate–petroleum ether], which was treated with a slight excess of *p*-toluenesulfonylhydrazide in methanol without further purification to afford the hydrazone. Recrystallization from methanol–water gave pure compound **16**; m.p. 167–169° (dec.), $[\alpha]_D^{16.5}$ −6.25° (*c* 5.2, chloroform), yield 35% from compound **13**; ^{1}H-n.m.r. ($CDCl_3$); δ 1.27, 1.46 (6H, s, CMe_2), 1.52, 1.78 (3H, s, 5-Me), 2.27, 2.30 (3H, s, Ar-Me), 3.53–3.85, 4.07–5.08 (3H, H-2,3,4), 4.78 (2H, s, OCH_2), 5.5–5.8 (1H, H-1), and 6.88–7.95 (9H, Ph, C_6H_4).

Anal. Calc. for $C_{23}H_{28}N_2O_6S$: C, 59.98; H, 6.13; N, 6.08. Found: C, 59.72; H, 6.18; N, 6.19.

Reaction of hydrazone **9** *with dimethyl phosphite.* — *p*-Toluenesulfonic acid (0.5 g) was added to a solution of hydrazone **9** (3.0 g) in dimethyl phosphite. The mixture was kept for 60 h at room temperature with subsequent addition of aqueous sodium hydrogencarbonate and extraction by chloroform, which was then evaporated off. Unreacted dimethyl phosphite was removed under diminished pressure, and then a chloroform solution of the residue was further extracted with aqueous sodium hydrogencarbonate and water. Evaporation of the chloroform afforded a syrup (2.8 g), which was dissolved in hot ethanol, giving 1.2 g of crystalline (5*RS*)-5,6-dideoxy-5-*C*-(dimethoxyphosphinyl)-1,2-*O*-isopropylidene-3-*O*-methyl-5-*C*-(2-*p*-tolylsulfonylhydrazino)-α-D-*xylo*-hexofuranose (**17a**, yield 32%). The mother liquor contained compound **17a** and its diastereoisomer (**17b**) in a ratio of 5:2. Compound **17a** had m.p. 153–155° (dec.), $[\alpha]_D^{16.5}$ −29.8° (*c* 7.1, chloroform), ν_{max}^{KBr} 3310, 3170 (NH), 1235 (P=O), 670 cm^{-1} (P–C); ^{1}H-n.m.r. ($CDCl_3$); δ 1.22, 1.36 (6H, s, CMe_2), 1.33 (3H, d, $J_{PC,CH}$ 16.5 Hz, 5-Me), 2.35 (3H, s, Ar-Me), 3.24 (3H, s, OMe), 3.67, 3.78 (6H, d, $J_{PO,CH}$ 10.5 Hz, POMe), 3.6–4.0 (2H, m, H-3,4), 4.45 (1H, d, $J_{1,2}$ 4.0 Hz, H-2), 5.0–5.4 (1H, NH), 5.78 (1H, d, $J_{1,2}$ 4.0 Hz, H-1), 6.40 (1H, s, NH), and 7.40 (4H, q, C_6H_4).

Anal. Calc. for $C_{19}H_{31}N_2O_9PS$: C, 46.15; H, 6.32; N, 5.67. Found: C, 46.13; H, 6.33; N, 5.61.

Reaction of compound **9** with dimethyl phosphite in the presence of 2.5 mol-equivs. of trifluoroacetic acid at room temperature proceeded very slowly; starting material was still detected (t.l.c.), even after 90 h.

Reaction of hydrazone **16** *with dimethyl phosphite.* — Treatment of the hydrazone **16** with dimethyl phosphite was performed essentially as just described to afford (5*RS*)-3-*O*-benzyl-5,6-dideoxy-5-*C*-(dimethoxyphosphinyl)-1,2-*O*-isopropylidene-5-*C*-(2-*p*-tolylsulfonylhydrazino)-α-D-*ribo*-hexofuranoses (**18a** and **b**) in 97% yield, ^{1}H-n.m.r. ($CDCl_3$): δ 1.27, 1.47 (6H, s, CMe_2), 1.19, 1.22 (3H, d, $J_{PC,CH}$ 15.3 Hz, 5-Me),

2.27, 2.32 (3H, s, Ar-Me), 3.50–3.88 (6H, m, POMe), 4.00–4.83 (6H, m, O-CH_2, H-2,3,4, NH), 5.52, 5.66 (1H, d, H-1), 6.40–6.72 (1H, NH), and 7.26 (9H, m, Ph, C_6H_4).

Reaction of hydrazone **7** *with methyl phenylphosphonite.* — *p*-Toluenesulfonic acid (0.2 g) was added to a mixture of hydrazone **7** (2.05 g) and methyl phenylphosphonite (4.2 g). After the hydrazone **7** had reacted completely, sodium hydrogencarbonate and water were added to hydrolyze the excess of methyl phenylphosphonite, and then the mixture was extracted with chloroform. The chloroform layer was washed, dried, and evaporated to a syrup (quantitative yield), that crystallized from methanol to afford (5*RS*)-5,6-dideoxy-1,2-*O*-isopropylidene-5-(3-*O*-*cyclo*-phenylphosphinate)-5-*C*-(2-*p*-tolylsulfonylhydrazino)-α-D-*xylo*-hexofuranose (**20b**) in 26% yield; m.p. 188° (dec.). The mother liquor gave (5*RS*)-5,6-dideoxy-1,2-*O*-isopropylidene-5-*C*-[(methoxy)phenylphosphinyl]-5-*C*-(2-*p*-tolylsulfonylhydrazino)-α-D-*xylo*-hexofuranoses (**19a** and **b**, 15% yield) and the diastereoisomer of compound **20b** (**20a**, 51% yield) after separation by column chromatography on silica gel. Spectral and analytical data for compounds **19** and **20** are as follows:

Compounds **19a, b**: ^{1}H-n.m.r. ($CDCl_3$): δ 1.33, 1.55 (9H, CMe_2, 5-Me), 2.33 (3H, s, Ar-Me), 2.60–2.90 (1H, OH), 3.66 (3H, d, $J_{PO,CH}$ 10.9 Hz, POMe), 4.25–5.35 (4H, m, H-2,3,4, NH), 5.97 (1H, d, $J_{1,2}$ 3.9 Hz, H-1), and 6.9–7.9 (10H, m, Ph, C_6H_4, NH).

Compound **20a**: ^{1}H-n.m.r. ($CDCl_3$): δ 1.03 (3H, dd, $J_{PC,CH}$ 16 Hz, 5-Me), 1.31, 1.50 (6H, s, CMe_2), 2.32 (3H, s, Ar-Me), 4.17–5.35 (4H, m, H-2,3,4, NH), 5.95 (1H, d, $J_{1,2}$ 3.8 Hz, H-1), and 6.85–7.93 (10H, m, Ph, C_6H_4, NH).

Compound **20b**: ν_{max}^{KBr} 3300, 3110 (NH), 690 cm^{-1} (P-C); ^{1}H-n.m.r. (Me_2SO-d_6): δ 1.30, 1.47 (6H, s, CMe_2), 1.50 (3H, d, $J_{PC,CH}$ 13.5 Hz, 5-Me), 2.38 (3H, s, Ar-Me), 4.42 (1H, dd, $J_{PC,CH}$ 24 Hz, $J_{3,4}$ 2.6 Hz, H-4), 4.82–5.10 (2H, m, H-2,3), 5.95 (1H, d, $J_{1,2}$ 3.8 Hz, H-1), 7.05–7.80 (10H, m, Ph, C_6H_4, NH), and 8.40 (1H, NH); mass-spectral data, (*m/e*) 494 (M^+), 479, 353, and 278 (base peak).

Anal. Calc. for $C_{22}H_{27}N_2O_7PS$: C, 53.44; H, 5.50; N, 5.67. Found: C, 52.95; H, 5.50; N, 5.51.

Reaction of hydrazone **9** *with methyl phenylphosphonite.* — *p*-Toluenesulfonic acid (0.02 g) was added to a solution of hydrazone **9** in methyl phenylphosphonite. Consumption of the hydrazone was completed within 16–20 h at room temperature. Processing as already described afforded (5*RS*)-5,6-dideoxy-1,2-*O*-isopropylidene-5-*C*-[(methoxy)phenylphosphinyl]-3-*O*-methyl-5-*C*-(2-*p*-tolylsulfonylhydrazino)-α-D-*xylo*-hexofuranoses (**21a** and **b**) in quantitative yield; ^{1}H-n.m.r. ($CDCl_3$): δ 0.65–1.58 (9H, m, CMe_2, 5-Me), 2.33 (3H, s, Ar-Me), 3.12–4.70 (9H, m, H-2,3,4, OMe, POMe), 5.3–5.65 (1H, m, NH), 5.84 (1H, d, $J_{1,2}$ 3.8 Hz, H-1), 6.30–6.55 (1H, m, NH), and 6.88–8.05 (9H, m, Ph, C_6H_4).

The reaction of hydrazone **9** with methyl phenylphosphonite in the presence of trifluoroacetic acid also proceeded within 65 h to afford compounds **21a** and **b**.

Dehydrazination of compound **17a**. — Treatment of compound **17a** (0.58 g) with an excess of sodium borohydride (0.3 g) in boiling (reflux) oxolane (20 mL) for

4 h, followed by addition of aqueous acetic acid, neutralization with sodium hydrogencarbonate, and extraction with chloroform, afforded a syrup. Resolution by t.l.c. gave the glycosulose **9** (26% yield) and (5*RS*)-5,6-dideoxy-1,2-*O*-isopropylidene-5-*C*-(dimethoxyphosphinyl)-3-*O*-methyl-α-D-*xylo*-hexofuranose (**22a**, 22% yield), $[\alpha]_D^{15.5}$ −37.8° (*c* 1.0, $CHCl_3$), ν_{max}^{neat} 1240 (P=O), 740 cm^{-1} (P-C); ^{1}H-n.m.r. ($CDCl_3$): δ 1.31 (3H, dd, $J_{5,6}$ 7.2 Hz, $J_{PC,CH}$ 18.0 Hz, 5-Me), 1.33, 1.51 (6H, s, CMe_2), 2.0–3.0 (1H, m, H-5), 3.41 (3H, s, OMe), 3.75 (6H, d, $J_{PO,CH}$ 10.6 Hz, POMe), 3.25–4.33 (2H, m, H-3,4), 4.55 (1H, d, $J_{1,2}$ 4.1 Hz, H-2), and 5.79 (1H, d, $J_{1,2}$ 4.1 Hz, H-1).

Dehydrazination of compounds **21a** *and* **b**. — Treatment of compounds **21a** and **b** (3.3 g) with an excess of sodium borohydride (4.8 g) in dry oxolane for 80–90 h (no NH absorption was observed in the i.r. spectrum at this time) at room temperature, followed by isolation as already described, afforded a syrup (70% yield). The syrup was separated into two isomers, (5*RS*)-5,6-dideoxy-1,2-*O*-isopropylidene-5-*C*-[(methoxy)phenylphosphinyl]-3-*O*-methyl-α-D-*xylo*-hexofuranoses (**23a** and **23b**). The yields and the R_F values of compound **23a** and **23b** were 45 and 11%, and 0.46 and 0.55 (eluent: 2:1 ethyl acetate–benzene), respectively.

The ^{1}H-n.m.r. data ($CDCl_3$) for compound **23a** were: δ 0.91–1.58 (3H, m, 5-Me), 1.31, 1.48 (6H, s, CMe_2), 2.0–3.0 (1H, m, H-5), 3.15, 3.45 (3H, s, OMe), 3.2–4.6 (6H, m, H-2,3,4, POMe), 5.61–5.83 (1H, H-1), and 7.1–7.95 (5H, m, Ph).

Reduction of (5RS)-*5,6-dideoxy-1,2*-O-*isopropylidene-5*-C-[(*methoxy*)*phenylphosphinyl*]-*3*-O-*methyl*-α-D-xylo-*hexofuranose* (**23a**). — Compound **23a** (0.48 g) was treated with a 7-fold excess of sodium dihydrobis(2-methoxyethoxy)aluminate (SDMA) in oxolane (35 mL) under nitrogen for 2 h at 0°. The mixture was neutralized with dilute hydrochloric acid in oxolane, and then filtered. Chloroform was added to the filtrate, and the organic layer was washed and dried. Evaporation of the chloroform afforded a syrup, which was purified by preparative t.l.c. to give (5*RS*)-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-5-*C*-(phenylphosphinyl)-α-D-*xylo*-hexofuranoses (**25a** and **b**) in 41% yield; ν_{max}^{neat} 2350 cm^{-1} (PH); ^{1}H-n.m.r. ($CDCl_3$): δ 0.97–1.60 (9H, m, CMe_2, 5-Me), 2.0–3.0 (1H, m, H-5), 3.11, 3.48 (3H, s, OMe), 3.75, 3.96 (1H, d, $J_{3,4}$ 3.5 Hz, H-3), 4.1–4.5 (1H, m, H-4), 4.55, 4.66 (1H, d, $J_{1,2}$ 4.1 Hz, H-2), 5.75–5.94 (1H, m, H-1), 7.35–7.95 (5H, m, Ph), and 11.14–11.49 (0.5H, PH, the other 0.5H of the PH group was presumably overlapped by other signals).

Reduction of compounds **21a** *and* **b** *with SDMA*. — Compounds **21a** and **b** (0.43 g) were treated with 2.7 mol-equivs. of SDMA in oxolane (15 mL) under nitrogen for 3 h at room temperature. The same isolation as already described gave mainly (5*RS*)-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-5-*C*-(phenylphosphinyl)-5-*C*-(2-*p*-tolylsulfonylhydrazino)-α-D-*xylo*-hexofuranoses (**24a** and **b**), in 25% yield; ν_{max}^{neat} 3310 (NH), 2350 cm^{-1} (PH); ^{1}H-n.m.r. ($CHCl_3$): δ 0.8–1.60 (9H, m, CMe_2, 5-Me), 2.32, 2.38 (3H, s, Ar-Me), 2.90–4.65 (6H, H-2,3,4, OMe), 4.93–5.15 (1H, NH), 5.73–5.95 (1H, m, H-1), 6.53–6.80 (1H, NH), 6.9–8.0 (9H, m, Ph, C_6H_4), 11.17 and 11.55 (0.5H, s, PH, the remaining 0.5H signal of PH apparently was superposed upon other signals).

Hydrolysis of compounds **25a, b.** — A solution of compounds **25a** and **b** (0.279 g) in oxolane (3 mL) was treated with 0.5M hydrochloric acid (10 mL) under nitrogen for 5 h at 90–100°. The solution was neutralized with IR-410 resin, and then water was evaporated to afford syrupy 5,6-dideoxy-3-*O*-methyl-5-*C*-(phenylphosphinyl)-D-gluco- or L-ido-pyranose (**26**) in 75% yield.

Acetylation of compound **26.** — Compound **26** (0.183 g) was treated with acetic anhydride (2 mL) in pyridine (10 mL) for 15 h at room temperature. After removal of volatile materials, chloroform was added to the residue, and then the solution was washed with aqueous sodium hydrogencarbonate and water, and dried. Evaporation of the solvent gave a syrup (0.185 g), which gave crystalline 1,2,4-tri-*O*-acetyl-5,6-dideoxy-3-*O*-methyl-5-*C*-[(*S*)-phenylphosphinyl]-β-D-glucopyranose (**27a**, 43 mg), in 16% yield; m.p. 304–306° (from ethanol, sealed tube), $[\alpha]_D^{15}$ +23.2° (*c* 0.35, $CHCl_3$); ^{1}H-n.m.r. ($CDCl_3$): δ 1.09 (3H, dd, $J_{PC,CH}$ 14.2 Hz, $J_{5,6}$ 6.7 Hz, 5-Me), 1.90, 2.07, 2.16 (9H, s, OAc), 1.8–3.0 (1H, m, H-5), 3.55 (3H, s, OMe), 3.46–3.86 (1H, H-3), 5.33–6.10 (3H, m, H-1,2,4), and 7.43–8.10 (5H, m, Ph), mass-spectral data, (*m/e*) 412 (M^+, assumed to be 100%), 353 (M^+ — OAc, 91%), and 85 (base peak).

Anal. Calc. for $C_{19}H_{25}O_8P$: C, 55.34; H, 6.11. Found: C, 55.47; H, 6.09.

The ethanolic mother-liquor gave another crystalline product (**27b**), which was an isomer of compound **27a**, m.p. 164–165°, $[\alpha]_D^{15}$ +37.3° ($CHCl_3$), mass-spectral data, (*m/e*) 412 (M^+, assumed to be 100%), 353 (M^+ — OAc, 1550%), 85 (base peak).

Anal. Calc. for $C_{19}H_{25}O_8P$: C, 55.34; H, 6.11. Found: C, 55.18; H, 6.11.

X-Ray analysis of compound **27a.** — The sample for X-ray analysis was prepared from an ethanolic solution of compound **27a** by very slow evaporation of the solvent. A computer-generated drawing was made, based on the X-ray analysis (Fig. 1).

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