Synthesis of 1,2,3,4,6-Penta-*O*-acetyl-5-deoxy-5-*C*-[(*RS*)-ethylphosphinyl]-α- and -β-D-glucopyranoses and Their Structural Analysis by 400-MHz Proton Nuclear Magnetic Resonance

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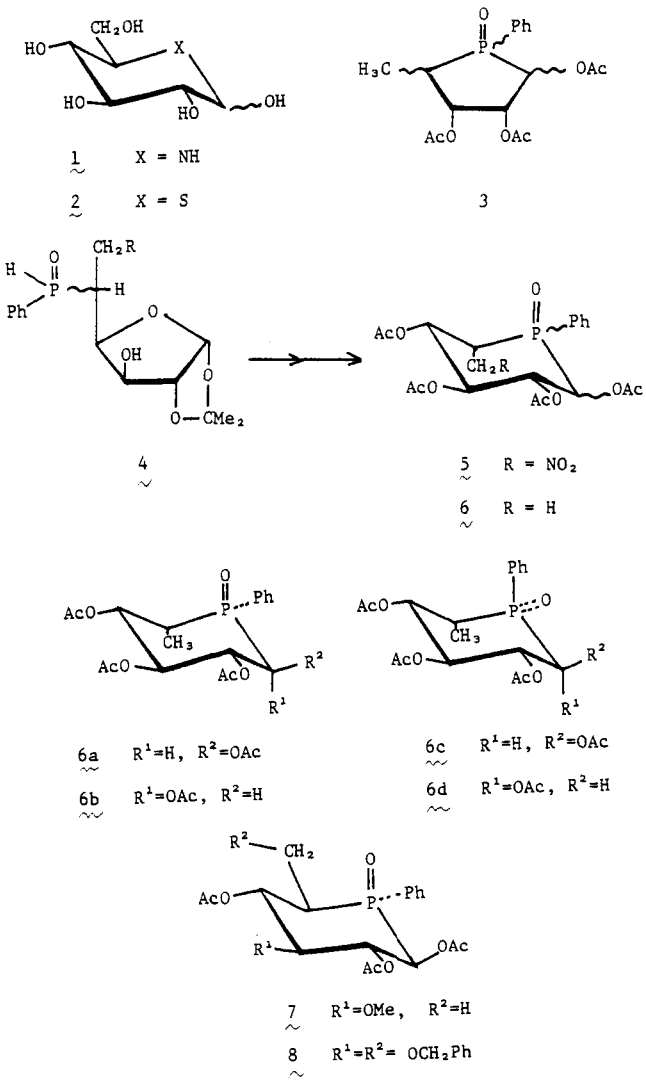
Debenzylation of (5*RS*)-3,6-di-*O*-benzyl-5-deoxy-5-*C*-[ethylmethoxyphosphinyl]-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranose (**13**) over 10% Pd/C afforded the tricyclic compound **14**, which, on treatment with chlorotriphenylmethane in pyridine, provided a 1:1 mixture of (5*R*)-5-deoxy-5-*C*-[(*R*)-*O*-*cyclo*-ethylphosphinyl]-1,2-*O*-isopropylidene-6-*O*-(triphenylmethyl)-α-D-*xylo*-hexofuranose (**15a**) and its (5*S*)-5-*C*-[(*S*)-ethylphosphinyl] diastereomer (**15b**). Treatment of **15a,b** with sodium dihydrobis(2-methoxyethoxy)aluminate, followed by the action of mineral acid and acetic anhydride, yielded the title compounds (**18a–d**), the structures of which were established on the basis of mass and 400-MHz ^{1}H NMR spectra. A possible reaction pathway for the exclusive formation of these unsubstituted 5-deoxy-5-*C*-phosphinyl-D-glucopyranoses is discussed.

5-Amino-5-deoxy-D-glucose (**1**), a naturally occurring antibiotic (nojirimycin), is well-known to show various antibacterial activities.[2] 5-Deoxy-5-thio-D-glucose (**2**) has been shown to be a potent, competitive inhibitor of cellular D-glucose transport[3] and also selectively toxic to hypoxic radioresistant tumor cells.[4] Both compounds have already been synthesized.[2,3] Thus, sugar analogues, having a phosphorus atom in the hemiacetal ring, are interesting not only from the viewpoint of their physicochemical properties but also from that of the potential utility of their biological activities. As part of our effort to prepare such hexopyranoses, along with pentofuranoses[5,6] (e.g., **3**), we reported tetra-*O*-acetyl derivatives of 5,6-dideoxy-5-*C*-[(*RS*)-phenylphosphinyl]-α,β-L-idopyranoses (**5**[7,8] and **6**[9-12]) and a tri-*O*-acetyl derivative of 5,6-dideoxy-3-*O*-methyl-5-*C*-[(*S*)-phenylphosphinyl]-β-D-glucopyranose[13,14] (**7**). All of these P sugars were 6-deoxyhexopyranoses, because of various difficulties encountered in the preparation of the precursors for 6-O-substituted 5-deoxy-5-*C*-phosphinyl-hexopyranoses.

However, protection of the HO-3 and -6 groups with benzyl groups furnished compound **8** with the complete glucose structure, 1,2,4-tri-*O*-acetyl-3,6-di-*O*-benzyl-5-



(1) (a) Okayama University. (b) Shizuoka University. (c) The University of Alberta.

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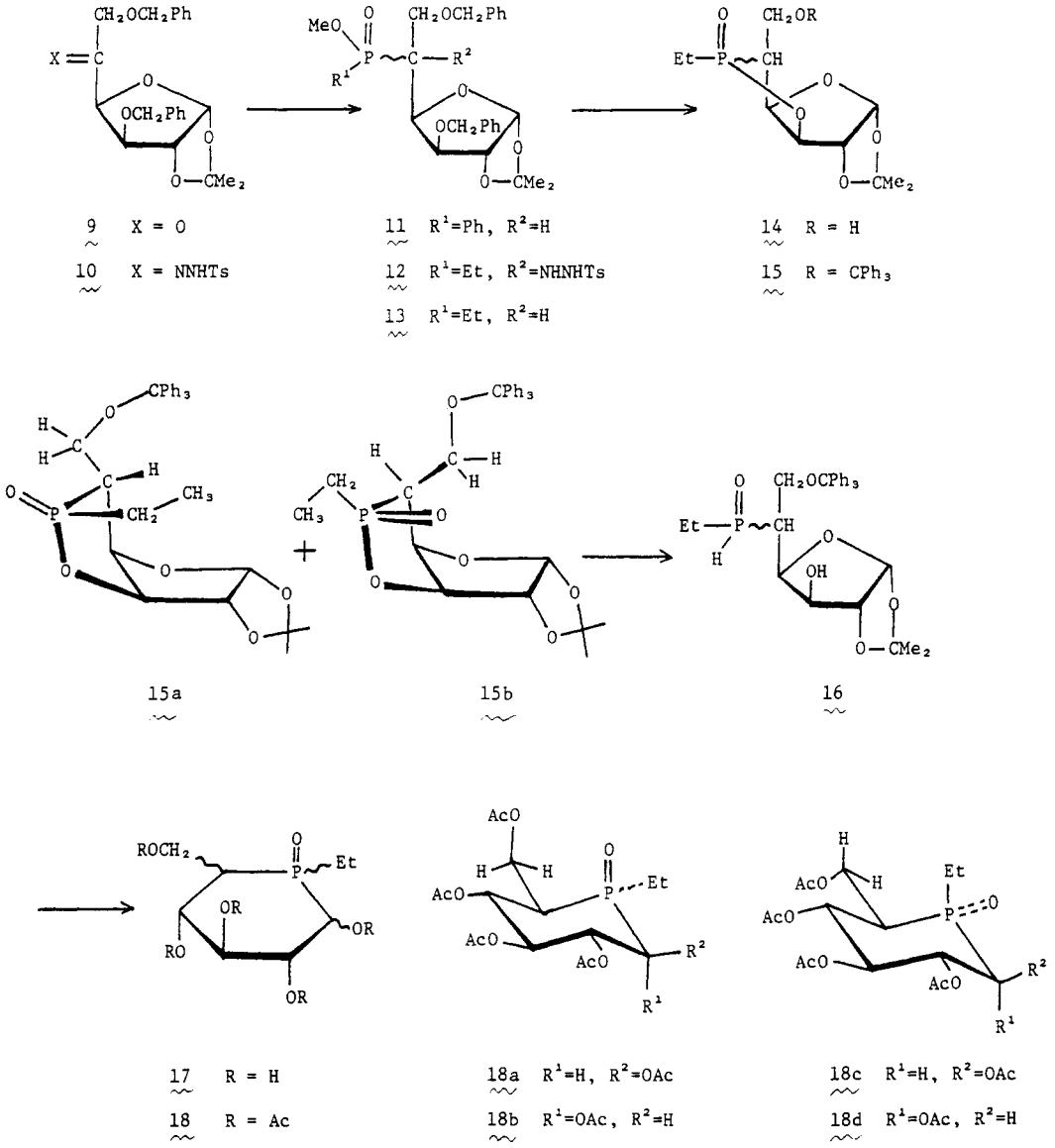
Scheme I. Preparation of 5-Deoxy-5-*C*-(ethylphosphinyl)-D-glucopyranoses



deoxy-5-*C*-[(*S*)-phenylphosphinyl]-β-D-glucopyranose, by the sequence of **9** → **10** → **11** → **8**, although the yield of the three-step conversion of **11** into **8** was very low (2% overall) because of the appreciable decomposition of **11** during the preparation[15] (Scheme I). Moreover, the unexpected difficulties in deprotecting the benzyl groups from **8** prompted us to search an alternative, effective route for preparation of the hitherto unreported, unsubstituted 5-deoxy-5-*C*-phosphinyl-D-glucopyranoses, which we now describe herein.[16]

Our strategy for obtaining a higher yield of such D-gluco-type P sugars is to reverse the relative size of the substituents at P-5 and C-6 of the key intermediate before the ring transposition (i.e., **16** → **17**, Scheme I). This is based on the fact that the precursors **4** (R = H, NO_2), which bear a relatively large substituent at P-5 compared with that at C-6, solely produced the L-iodopyranoses **5** and **6**.[9-12]

The addition of methyl ethylphosphinate to the hydrazone[15] **10** (a mixture of the *E* and *Z* isomers) in the presence of trifluoromethanesulfonic acid gave compound **12**, which, on reduction with sodium borohydride in oxolane (THF), yielded the 5-deoxy-5-*C*-phosphinyl compound **13** as a mixture of diastereomers (with respect to C-5 and phosphorus) in a 58% overall yield from **10**. Debenzylation of **13** was found to be sluggish but was effected by repeated hydrogenolysis over 10% Pd/C in ethanol at 40 °C. The product proved to be the tricyclic compound **14**, which, on treatment with chlorotriphenylmethane in pyridine, followed by purification on a column of silica gel with 1:1 (v/v) ethyl acetate–benzene as the eluant, mainly yielded an inseparable mixture (1:1) of only two diastereomers of **15** (by 400-MHz ^1H NMR, 17% overall yield from **13**). The most likely structures, (5*R*)-5-deoxy-5-*C*-[(*R*)-*O*-*cyclo*-ethylphosphinyl]-1,2-*O*-isopropylidene-6-*O*-(triphenylmethyl)-α-D-*xylo*-hexofuranose (**15a**) and its (5*S*)-5-*C*-[(*S*)-ethylphosphinyl] diastereomer **15b**, for these products were derived from their spectral analysis (high-resolution mass and 400-MHz NMR spectra); the chemical shift of each proton signal and the dependence of the $^2J_{HP}$, $^3J_{HP}$, and $^3J_{HH}$ values on their dihedral angles (see below for discussion) were carefully taken into consideration.

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Moreover, an inspection of the CPK models for **15** shows the presence of considerable steric congestion between the methylene group of C-6 and PCH_2CH_3 when both substituents become cis on the *cyclo*-phosphonate ring, supporting structures **15a** and **15b**, in which these substituents are in trans configuration.

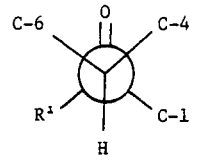
Since reduction with sodium dihydrobis(2-methoxyethoxy)aluminate (SDMA) was known[5,12,15] to cause partial epimerization at C-5 in a similar system, mixture **15** was directly subjected to reduction with SDMA. Because of its facile air oxidation, the product **16** was, without isolation, refluxed with ethanolic 0.5 M hydrochloric acid, affording the 5-deoxy-5-*C*-(ethylphosphinyl)hexopyranoses **17**, which were characterized by conversion into the peracetates **18** with acetic anhydride in pyridine on a manner similar to that described previously.[5,12,15] Purification on a column of silica gel with 1:19 (v/v) methanol–dichloromethane as the eluant gave **18** (in a 30% overall yield from **15**) as a colorless oil, which was found to consist of almost equal amounts of four components referred to as **18a–d** according to the TLC R_f values (R_f 0.47, 0.45, 0.40, and 0.37, respectively, with the same eluant).

On dilution of the mixture with ethyl acetate–hexane, the fraction **18a** crystallized as colorless prisms, mp 233 °C dec. The molecular composition of this crystalline compound was confirmed by the EI high-resolution mass spectrum, which clearly gave the M + 1 ion at m/z 451, corresponding to $C_{18}H_{28}O_{11}P$. The precise structure, 1,2,3,4,6-penta-*O*-acetyl-5-deoxy-5-*C*-[(*R*)-ethylphosphinyl]-β-D-glucopyranose (**18a**), for this product was established on the evidence of the 400-MHz ^1H NMR spectrum, which closely resembled those[15] of structurally similar analogues **7** and **8**. The H-1 signal of **18a** consisted of a triple doublet at δ 5.38 with large $J_{1,2}$ (11.0 Hz), small $J_{1,P}$ (3.6 Hz), and extremely small $J_{1,5}$ (0.2 Hz, long-range coupling) values. On the other hand, the $J_{4,5}$ value was significantly large (11.5 Hz), whereas $J_{5,P}$ was small (3.5 Hz). As both $J_{2,3}$ and $J_{3,4}$ were large (10.0 Hz), these values led to the (*R*)-phosphinyl-D-gluco-type structure with the $^4C_1$ (D) conformation of the rigid pyranoid ring for this crystalline compound **18a**;[17] assignments of all signals, along with those of **8** for comparison, are summarized in Table I.

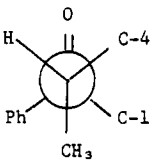
Concentration of the above filtrate, followed by careful separation of the residue by low-pressured liquid chromatography with methanol–dichloromethane as the eluant, mainly gave three fractions, A–C (R_f 0.45, 0.40, 0.37). The fastest eluting fraction (A) yielded a colorless oil, which was found by the analysis of its 400-MHz NMR to be the α anomer (**18b**) of **18a**; the parameters of the NMR signals are recorded in Table I. The magnitudes of the $J_{1,2}$ and $J_{1,P}$ values (3.2 and 11.7 Hz, respectively) were reversed from those of the β anomer **18a**, and no 1,5 W coupling was observed. Those splitting patterns of the H-1 signals in the NMR spectra of **18a** and **18b** closely resembled those of the 5-deoxy-5-*C*-[(*S*)-phenylphosphinyl]-α-idopyranoses **6a** and **6b**.[11] The rest of the NMR signals of **18b** were similar to those of **18a**.

The slowest eluting fraction (C) was a colorless oil, which consisted of a major component, **18d**, contaminated by a small amount of minor products. An appreciable upfield shift (0.4–0.7 ppm) was observed for the H-2 and H-4 signals of **18d** compared with those of **18a** and **18b**. Such a remarkable shift was observed in the case of the iodopyranoses **6c** and **6d**.[11] The remaining absorptions of **18d** were similar to those of **18b**. These spectral data led to the structure 1,2,3,4,6-penta-*O*-acetyl-5-deoxy-5-*C*-[(*S*)-ethylphosphinyl]-α-D-glucopyranose for compound **18d**; the assignments for the NMR signals are also listed in Table I.

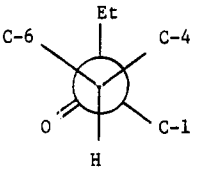
Chart I. Newman Projection Along the C(5)-P(5) Bond and the $J_{4,5}$ and $J_{5,P}$ Values



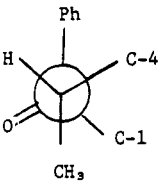
	$J_{4,5}$	$J_{5,P}$
8[a]	11.5	4.0
18a	11.5	3.5
18b	14.5	4.5



	$J_{4,5}$	$J_{5,P}$
6a[b]	4.6	21.7
6b[b]	4.7	21.6



	$J_{4,5}$	$J_{5,P}$
18d	12.0	18.0



	$J_{4,5}$	$J_{5,P}$
6c[b]	4.3	15.6
6d[b]	4.6	15.5

[a] Reference 15. [b] Reference 11.

Fraction B was found to consist mainly of a major product (**18c**, R_f 0.40) but contained a considerable amount of **18d** and other minor products. Although the NMR signals of the major product were not completely clear, the probable structure **18c** (β anomer of **18d**) was assigned to this product on the basis of its clearly recognizable signals (Table I), which closely resembled those of **18d**. Moreover, the order of the R_f values of compounds **18a–d** on silica gel TLC completely coincides with those of structurally analogous compounds **6a–d** with a similar solvent system.[12]

When hexopyranoses having a phosphorus atom in the ring exist in the $^4C_1$ (D) conformation (as judged by the large values of $J_{2,3}$ and $J_{3,4}$), it is now generally established that the combination of the $J_{4,5}$ value and the geminal P–C–H coupling constants ($J_{5,P}$) provides a quick method for the assignment of the C-5 configuration, because those values obviously depend upon the magnitude of the approximate H—C(5)—C(4)—H and O=P—C(5)—H dihedral angles,[5,11,15,18] as illustrated in the "Newman" projections (Chart I). Thus the large values of $J_{4,5}$ (12–14 Hz) indicate the D-gluco configuration (e.g., **7**, **8**, **18a–d**), whereas the small values ($J_{4,5}$ = 4–5 Hz) are compatible with the L-ido configuration[11,15] (e.g., **6a–d**).

When the $J_{5,P}$ values are small (3–5 Hz), an anti conformation for O=P—C(5)—H can be assigned, which indicates the phosphinyl oxygen atom linked axially to the ring P atom (**7**, **8**, **18a,b**). On the other hand, the large values of the H—C(5)—P geminal coupling constants ($J_{5,P}$ = 15–22 Hz) are in conformity with the gauche coupling

(17) An X-ray crystallographic analysis of **18a** is to be resumed.

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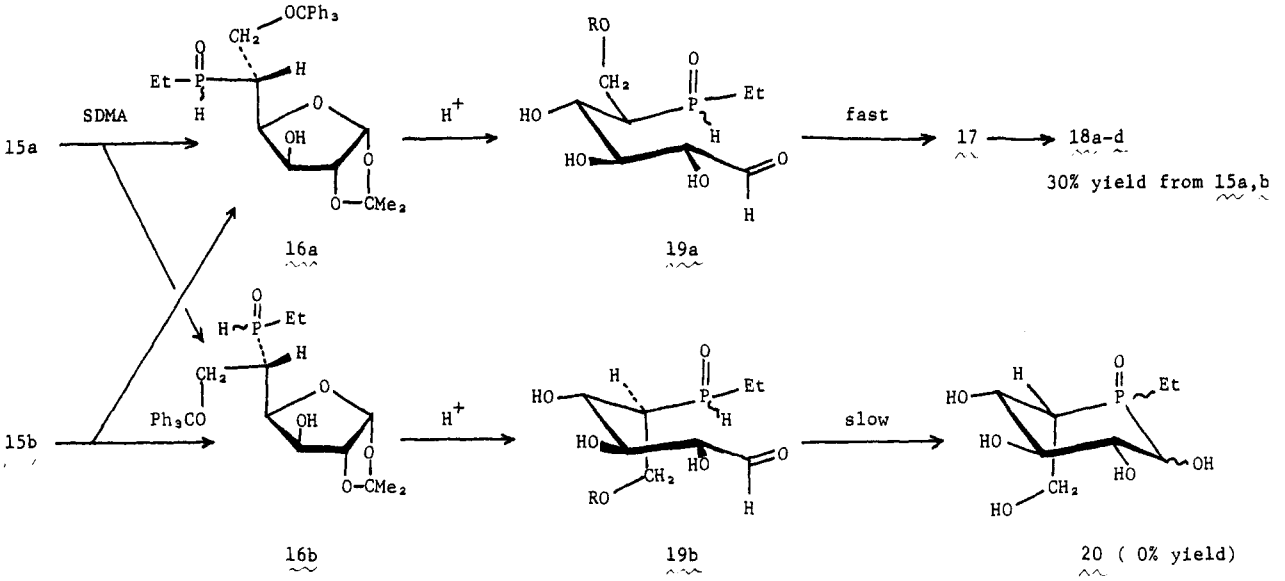
Table I. ^{1}H NMR (400 MHz) Parameters for 5-Deoxy-5-*C*-(ethylphosphinyl)-D-*xylo*-hexofuranoses and -D-glucopyranoses in $CDCl_3$[a]

	chemical shift								
compd	AcO-1,[b] H-1	AcO-2,[b] H-2	AcO-3,[b] H-3	AcO-4,[b] H-4	H-5	AcO-6,[b] H^a-6	H^b-6	P-CH_2-C	P-C-CH_3
15a	1.31,[c] 5.80 (d, $J_{1,2}$ 3.5)	1.48,[c] 4.68 (dd, $J_{2,3}$ 0.4)	4.55 (ddd, $J_{3,P}$ 22.9, $J_{3,4}$ 2.4)	4.73 (d)	2.36 (dd, $J_{5,P}$ 6.5, $J_{5,6b}$ 4.5)	7.18–7.52[d] (m), 3.94 (dd, $J_{6a,6b}$ 10.3, $J_{6a,P}$ 3.2)	3.52 (ddd, $J_{6b,P}$ 15.0)	1.81 (dq, $^2J_{H,P}$ 15.0)	1.19 (dt, $^3J_{H,P}$ 19.2, $^3J_{H,H}$ 7.6)
15b	1.33,[c] 6.05 (d, $J_{1,2}$ 3.2)	1.48,[c] 4.73 (dd, $J_{2,3}$ 0.5)	4.29 (ddd, $J_{3,P}$ 21.0, $J_{3,4}$ 3.0)	4.80 (dd, $J_{4,5}$ 7.2)	1.95 (dt, $J_{5,P}$ 11.0, $J_{5,6a}$ 7.0)	7.18–7.52[d] (m), 3.61 (dt, $J_{6a,6b}$ 10.0, $J_{6a,P}$ 7.0)	3.45 (ddd, $J_{6b,P}$ 18.0)	2.02 (dq, $^2J_{H,P}$ 15.0)	1.26 (dt, $^3J_{H,P}$ 17.9, $^3J_{H,H}$ 7.6)
8[e]	1.88,[b] 5.57 (ddd, $J_{1,2}$ 11.2, $J_{1,P}$ 2.8, $J_{1,5}$ 0.3)	1.87,[b] 5.83 (ddd, $J_{2,3}$ 9.5, $J_{2,P}$ 3.0)	4.70,[f] 7.32[h] (m), 3.88 (dd, $J_{3,4}$ 9.8)	1.86,[b] 5.70 (ddd, $J_{4,5}$ 11.5, $J_{4,P}$ 2.8)	2.65 (dddddd, $J_{5,6a}$ 7.0, $J_{5,6b}$ 6.0, $J_{5,P}$ 4.0)	4.19[g] (d), 3.89 (ddd, $J_{6a,P}$ 10.0, $J_{6a,6b}$ 9.8)	4.21[g] (d), 3.79 (ddd, $J_{6b,P}$ 14.5)	7.27[h] (m)	7.75[i] (m, ortho), 7.47[i] (m, meta), 7.56[i] (m, para)
18a	2.16,[b] 5.38 (ddd, $J_{1,2}$ 11.0, $J_{1,P}$ 3.6, $J_{1,5}$ 0.2)	2.07,[b] 5.72 (ddd, $J_{2,3}$ 10.0, $J_{2,P}$ 3.0)	2.01,[b] 5.22 (t, $J_{3,4}$ 10.0)	2.06,[b] 5.58 (ddd, $J_{4,5}$ 11.5, $J_{4,P}$ 2.7)	2.37 (ddddd, $J_{5,6a}$ 7.4, $J_{5,6b}$ 5.0, $J_{5,P}$ 3.5)	1.99,[b] 4.49 (td, $J_{6a,P}$ 11.5, $J_{6a,6b}$ 11.5)	4.45 (ddd, $J_{6b,P}$ 15.0)	2.04 (dq, $^2J_{H,P}$ 15)	1.19 (dt, $^3J_{H,P}$ 19.3, $^3J_{H,H}$ 7.6)
18b	2.21,[b] 5.84 (dd, $J_{1,P}$ 11.7, $J_{1,2}$ 3.2)	2.09,[b] 5.55 (ddd, $J_{2,3}$ 12.5, $J_{2,P}$ 0.3)	2.03,[b] 5.45 (dd, $J_{3,4}$ 11.8)	2.07,[b] 5.58 (ddd, $J_{4,5}$ 14.5, $J_{4,P}$ 3.0)	2.50 (dddd, $J_{5,6a}$ 8.3, $J_{5,6b}$ 6.3, $J_{5,P}$ 4.5)	1.98,[b] 4.45 (ddd, $J_{6a,P}$ 16.2, $J_{6a,6b}$ 14.5)	4.41 (ddd, $J_{6b,P}$ 18.5)	1.72 (dq, $^2J_{H,P}$ 15)	1.21 (dt, $^3J_{H,P}$ 18.3, $^3J_{H,H}$ 7.5)
18c	2.14,[b] 5.70 (dd, $J_{1,P}$ 11, $J_{1,2}$ 10.5)	2.07,[b] 5.25 (t, $J_{2,3}$ 11)	2.05,[b] 5.65 (t, $J_{3,4}$ 11)	2.00,[b] 5.23[j]	2.58[j]	2.00,[b] 4.75 (ddd, $J_{6a,P}$ 23, $J_{6a,6b}$ 12)	4.29 (ddd, $J_{6b,P}$ 9)	2.1[j]	1.40 (dt, $^3J_{H,P}$ 18, $^3J_{H,H}$ 7.5)
18d	2.09,[b] 5.53 (dd, $J_{1,P}$ 11.0, $J_{1,2}$ 2.0)	2.07,[b] 5.19 (ddd, $J_{2,3}$ 9.2, $J_{2,P}$ 0.5)	2.06,[b] 5.23 (dd, $J_{3,4}$ 10.0)	2.08,[b] 4.87 (ddd, $J_{4,5}$ 12.0, $J_{4,P}$ 4.0)	2.53 (dddd, $J_{5,P}$ 18.0, $J_{5,6a}$ 3.8, $J_{5,6b}$ 2.0)	2.04,[b] 4.68 (ddd, $J_{6a,P}$ 23.1, $J_{6a,6b}$ 11.8)	4.29 (ddd, $J_{6b,P}$ 8.7)	1.84 (dq, $^2J_{H,P}$ 15.2)	1.37 (dt, $^3J_{H,P}$ 17.6, $^3J_{H,H}$ 7.6)

[a] Abbreviations: d, doublet; t, triplet; q, quartet. Coupling constants (J, Hz) were confirmed by double resonance. Chemical shifts (δ values) are in parts per million from Me_4Si. [b] Acetoxyl (assignments may have to be interchanged). [c] Methyl group of 1,2-*O*-isopropylidene. [d] $(C_6H_5)_3C$-O(6). [e] Reference 11. [f] $C_6H_5CH_2O(3)$. [g] $C_6H_5CH_2O(6)$; J = 11.8 Hz. [h] $C_6H_5CH_2O(3,6)$. [i] P-C_6H_5. [j] The splitting patterns of the signals closely resemble those of **18d**, although exact coupling constants remain undetermined.

Scheme II. Possible Pathway for the Formation of 5-Deoxy-5-C-phosphinyl-D-glucopyranoses 18a-d from Precursors 15a,b



(as were observed in the cases of **6c,d** and **18d**). A similar dependence of $J_{1,P}$ and $J_{1,2}$ upon the O=P—C(1)—H and H—C(1)—C(2)—H dihedral angles can be applied to the assignment of the C-1 configurations of hexopyranoses **18a–d** in a similar manner as those of **6**[11] and **8**.[15]

As were observed in the formation of **18a–d**, the phosphinyl sugars of only gluco type were isolated when the 1:1 mixture of the precursors **15a** and **15b** was reduced with SDMA, followed by the action of mineral acid to effect the ring transpostion of the *xylo*-hexofuranoses **16** to the phosphinylglucopyranoses **17**. No peracetyl derivatives of 5-deoxy-5-*C*-[(*RS*)-ethylphosphinyl]-L-idopyranose (**20**) appeared to be present among the reaction products. Such a predominant formation of the gluco-type P sugars is in striking contrast to the result of the previous, similar ring transformation of **4** to the L-idopyranoses **6** solely.[11,12]

A possible explanation for these results is that the ring-closure of the open-chain phosphinyl intermediate **19a** is much faster than that of the counterpart **19b**, because both precursors **16a** and **16b** are expected to be almost equally derived from **15a** and **15b** by reduction with SDMA as illustrated in Scheme II. The combined yields of the four diastereomers **18a–d** were approximately 30%, and a large amount of polar substances remained uneluted by the initial chromatographic purification. Thus, instead of the sluggish intramolecular cyclization to give L-idopyranoses **20**, most of the epimer **19b** presumably yielded intermolecularly condensed, polar products to a considerable extent.

In contrast, the exclusive formation of the L-idopyranoses **5** and **6** from the precursors **4** may be rationalized in terms of the thermodynamically controlled production of a 5*S* epimer of **4** (corresponding to formula **16b**) after an equilibration by the strongly basic SDMA during the reduction, since there exists apparently less steric congestion between the bulky *P*-phenyl and the 3-hydroxyl group in **4**. This 5*S* epimer in turn readily affords **5** and **6** despite the presence of a slightly less favorable steric requirement for the intermediate similar to **19b** in Scheme II.

The formation of the glucopyranoses **7** and **8**, both of which were isolated only in a few percent yield, is presumably due to the facile crystallization of these compounds from the crude reaction mixture.[7,8,15] As the rest of the products were not examined in detail, an appreciable amount of the corresponding L-iodopyranoses could have actually been produced.

Although more precise mechanistic study with regard to this intricate ring transposition, as well as the improvement of the yield, remains to be done, the present work clearly demonstrates a novel way for preparation of the unsubstituted 5-deoxy-5-*C*-phosphinyl-D-glucopyranoses from D-*xylo*-hexofuranoses and further establishes the effective use of ^{1}H NMR for determining the configuration and conformation of sugars containing phosphorus in the ring.

Experimental Section

Melting points were measured with a Yanagimoto MP-S3 instrument and are uncorrected. ^{1}H NMR spectra were recorded with a Hitachi Perkin-Elmer R-20A (60 MHz) or a Bruker WH-400 cryospectrometer (400 MHz, for **15a,b** and **18a–d**) at 27 °C. Chemical shifts are reported as δ values in parts per million relative to tetramethylsilane (δ 0.0) as an internal standard. Spin decoupling was performed for each proton signal to confirm the coupling constants. Mass spectra were measured with an AEI MS 50 ultrahigh-resolution instrument (for the accurate mass measurement) and an AEI MS 12 apparatus (for chemical ionization with NH_3) and are given in terms of m/z (relative intensity) compared with the base peak and possible assignments. Optical rotation was determined with a Nihonbunko DIP-4 polarimeter. Microanalyses were performed in Sankyo Research Laboratories, Sankyo Co. Ltd. Column chromatography was performed with Wako C-200 silica gel. TLC was carried out on silica gel 60F precoated plates (0.25 mm, Merck).

(5*RS*)-3,6-Di-*O*-benzyl-5-deoxy-1,2-*O*-isopropylidene-5-*C*-(ethylmethoxyphosphinyl)-5-*C*-[(*p*-tolylsulfonyl)-hydrazino]-α-D-*xylo*-hexofuranose (12). Methyl ethylphosphinate[19] (7.0 g, 64.8 mmol) was added to a solution of 3,6-di-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-5-ulose (*E,Z*)-5-(*p*-tolylsulfonyl)hydrazone[15] (**10**; 6.16 g, 10.9 mmol) in dry benzene (2 mL). The mixture was stirred under argon at 20 °C for 35 h and then diluted with CH_2Cl_2 (40 mL) and saturated aqueous $NaHCO_3$ (50 mL). After separation, the organic layer was washed with water, dried (Na_2SO_4), and evaporated in vacuo. The residue was chromatographed on a silica gel column with ethyl acetate–benzene (1:1) as the eluant. The hexofuranose **12**, which was a mixture of four diastereomers with respect to C-5 and phosphorus, was obtained as a colorless syrup: 6.41 g (88%); ^{1}H NMR ($CDCl_3$) δ 0.72–2.20 (10 H, m, CMe_2, P-CCH_3, NH), 2.36

(19) Petrov, K. A.; Bliznyuk, N. K.; Studnev, Yu. N.; Kolomiets, A. F. *Zh. Obshch. Khim.* **1961**, *31*, 179.

(3 H, s, S–C_6–CH_3), 3.84–4.70 (12 H, m, H-2,3,4,6,6′, OCH_2Ph-3,6, POMe), 5.80–6.0 (1 H, m, H-1), 6.35–6.60 (1 H, m, NH), 7.09–7.58 (14 H, m, O–C–C_6H_5-3,6, S–C_6H_4–C). Anal. Calcd for $C_{33}H_{43}N_2O_9SP$: C, 58.74; H, 6.42; N, 4.15. Found: C, 58.66; H, 6.47; N, 3.96.

(5*RS*)-3,6-Di-*O*-benzyl-5-deoxy-1,2-*O*-isopropylidene-5-*C*-(ethylmethoxyphosphinyl)-α-D-*xylo*-hexofuranose (13). Sodium borohydride (5.2 g, 13.7 mmol) was added to a solution of **12** (4.2 g, 6.23 mmol) in dry THF (120 mL). The mixture was stirred at 20 °C for 23 h and then brought to pH 4 with 1.7 M acetic acid at 0 °C. After solvent evaporation in vacuo, the residue was diluted with CH_2Cl_2, washed with saturated aqueous $NaHCO_3$ and then with water, dried over anhydrous Na_2SO_4, and evaporated in vacuo. The residue was chromatographed on a silica gel column with ethyl acetate–benzene (1:1) as the eluant, thus giving **13** as a mixture of diastereomers: 2.02 g (66%, a colorless syrup); ^{1}H NMR 0.72–1.80 (9 H, m, CMe_2, P–CCH_3), 2.35 (1 H, m, H-5), 3.40–3.75 (12 H, m, H-2,3,4,6,6′, OCH_2Ph-3,6, POMe), 5.85, 5.93 (1 H, 2 d, $J_{1,2}$ = 4 Hz), 7.33, 7.36 (10 H, 2 s, O–C–C_6H_5-3,6).

(5*R*)-5-Deoxy-5-*C*-[(*R*)-*O*-*cyclo*-ethylphosphinyl]-1,2-*O*-isopropylidene-6-*O*-(triphenylmethyl)-α-D-*xylo*-hexofuranose (15a) and Its (5*S*)-5-*C*-[(*S*)-ethylphosphinyl] Diastereomer 15b. To a solution of **13** (1.70 g, 3.47 mmol) in absolute ethanol (8 mL) was added 10% Pd/C (1.0 g). The mixture was hydrogenated at 40 °C until the absorbtion of hydrogen ceased. After filtration of the catalyst, the filtrate was evaporated to dryness. The residue, which was found (by TLC) still to contain the starting material **13**, was repeatedly hydrogenated until **13** disappeared, thus giving **(5*RS*)-5-deoxy-5-*C*-[(*RS*)-3-*O*-*cyclo*-ethylphosphinyl]-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranose (14)** as a colorless syrup (0.99 g). This was directly used in the next step without purification.

A mixture of the above crude product **14** (0.99 g) and triphenylmethyl chloride (2.00 g, 7.17 mmol) in dry pyridine (12 mL) was heated at 35–40 °C for 84 h. After addition of a small amount of water, the solvent was evaporated at 15 °C in vacuo (pump). The residue was diluted with CH_2Cl_2, washed with saturated aqueous $NaHCO_3$ and then with water, dried (Na_2SO_4), and evaporated in vacuo. Chromatography of the residue on a silica gel column with ethyl acetate–benzene (1:1) as the eluant gave a mixture of **15a** and **15b** (1:1) as a colorless syrup: 0.53 g (17% yield from **13**); ^{1}H NMR (400 MHz, $CDCl_3$), see Table I; CI (NH_3) MS, *m/z* (relative intensity) 521 (0.4, M + 1), 520 (0.2, M), 519 (0.7, M – 1), 279 (41, M – CPh_3 + 2), 243 (100, CPh_3); EI MS, *m/z* (relative intensity) 505 (0.34, M – CH_3), 277 (12.5, M – CPh_3), 244 (23, Ph_3CH), 243 (100, Ph_3C); exact mass calcd for $C_{29}H_{30}O_6P$ [(M – CH_3)$^+$] 505.1780, found 505.1751, calcd for $C_{11}H_{18}O_6P$ [(M – CPh_3)$^+$] 277.0841, found 277.0835.

1,2,3,4,6-Penta-*O*-acetyl-5-deoxy-5-*C*-[(*R*)-ethylphosphinyl]-β-D-glucopyranose (18a), Its α Anomer 18b, and the 5-*C*-(*S*)-Phosphinyl-α,β-D-glucopyranoses 18c,d. A solution of SDMA (70% in toluene, 0.4 mL) in dry benzene (5 mL) was slowly added at 0 °C to a stirred solution of **15a,b** (0.33 g) in dry benzene (7 mL) under argon, followed by stirring at 5 °C for ca. 1 h (until the starting material disappeared). Then, water (0.5 mL) was added at 0 °C 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 **(5*RS*)-5-deoxy-5-*C*-[(*RS*)-ethylphosphinyl]-1,2-*O*-isopropylidene-6-*O*-(triphenylmethyl)-α-D-*xylo*-hexofuranose (16)** as a syrup.

To a solution of the above product **16** in ethanol (2 mL) was added oxygen-free 0.5 M HCl (20 mL), and the mixture was refluxed under argon for 5 h. The mixture was cooled, the acid neutralized by passing the mixture through a column of Amberlite IRA-45 anion-exchange resin (weakly basic), the eluant was filtered, and the filtrate was evaporated in vacuo to give **(5*RS*)-5-deoxy-5-*C*-[(*RS*)-ethylphosphinyl]-α,β-D-gluco- and/or -L-idopyranoses (17)** as a colorless syrup.

To a solution of **17** in dry pyridine (3.5 mL) was added acetic anhydride (2.2 mL) at 0 °C, and the mixture was stirred at 20 °C for 22 h. A small amount of water was added, and most of the pyridine was evaporated in vacuo. The residue was diluted with CH_2Cl_2 and successively washed with 0.3 M HCl, saturated aqueous $NaHCO_3$, and water. The organic layer was dried (Na_2SO_4) and evaporated in vacuo. The residue was chromatographed on a silica gel column with MeOH–CH_2Cl_2 (1:99) as the eluant. The fraction having R_f 0.5–0.3 (in 1:19 MeOH–CH_2Cl_2) was collected and concentrated in vacuo, giving the peracetates **18** as a diastereomeric mixture: colorless oil; 85.6 mg (30% overall yield from **15a,b**).

The product was diluted with ethyl acetate (3 mL) and allowed to stand at 5 °C overnight, thus depositing **18a** (11 mg, 4% yield from **15**) as colorless needles (from ethanol–ethyl acetate): mp 233 °C dec; R_f 0.47 (MeOH–$CHCl_3$, 1:19); $[\alpha]^{28}_D$ +3.64° (*c* 0.66, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$), see Table I; EI MS, *m/z* (relative intensity) 451 (2.7, M + 1), 408 (1.1, M – CH_2CO), 349 (66, M – AcO – CH_2CO), 307 (100; M – AcO – $2CH_2CO$), 306 (72), 289 (33, M – 2AcO – Ac), 265 (20, M – AcO – $3CH_2CO$), 247 (93.6, M – 2AcO – Ac – CH_2CO), 246 (20), 205 (73, M – 2AcO – Ac – $2CH_2CO$), 204 (23), 203 (17, 2AcO – 3Ac), 187 (70, M – 3AcO – 2Ac), 186 (67); exact mass calcd for $C_{18}H_{28}O_{11}P$ [(M + 1)$^+$] 451.1369, found 451.1362.

The above filtrate was then separated by chromatography on a silica gel column (Merck Lobar prepacked, Size A) with MeOH–CH_2Cl_2 (1:99) as the eluant into three fractions, A–C.

Fraction A (R_f 0.45) gave **18b** as a colorless oil: 18.5 mg (7% from **15**); ^{1}H NMR (400 MHz, $CDCl_3$), see Table I; EI MS, *m/z* (relative intensity) 451 (5.6, M + 1), 408 (4.7, M – CH_2O), 391 (10, M – AcO), 349 (77, M – AcO – CH_2CO), 307 (99), 306 (100, M – AcO – Ac – CH_2CO), 289 (44, M – 2AcO – CH_2CO), 247 (75, M – 2AcO – Ac – CH_2CO), 205 (42, M – 2AcO – Ac – $2CH_2CO$), 187 (41, M – 3AcO – 2Ac),186 (51); exact mass calcd for $C_{18}H_{28}O_{11}P$ [(M+1)$^+$] 451.1369, found 451.1376.

Fraction B (R_f 0.40) gave a colorless oil (5 mg, 2% from **15**) which was mostly **18c** but contained a small amount of **18d** and some impurities; ^{1}H NMR ($CDCl_3$), see Table I.

Fraction C (R_f 0.37) gave a colorless oil (5 mg, 2% from **15**) which consisted mainly of **18d**; ^{1}H NMR (400 MHz, $CDCl_3$), see Table I.

Besides these separated products, an unseparated mixture of **18a–d** (26 mg) was recovered from the intermediate fractions.

Registry No. (*E*)-**10**, 81823-13-4; (*Z*)-**10**, 81823-14-5; **12** (isomer 1), 84175-56-4; **12** (isomer 2), 84175-57-5; **12** (isomer 3), 84175-58-6; **12** (isomer 4), 84175-59-7; **13** (isomer 1), 84175-60-0; **13** (isomer 2), 84175-61-1; **13** (isomer 3), 84175-62-2; **13** (isomer 4), 84175-63-3; **14** (isomer 1), 84175-64-4; **14** (isomer 2), 84175-65-5; **14** (isomer 3), 84175-66-6; **14** (isomer 4), 84175-67-7; **15a**, 84175-68-8; **15b**, 84175-69-9; **16** (isomer 1), 84175-69-9; **16** (isomer 2), 84175-71-3; **16** (isomer 3), 84192-61-0; **16** (isomer 4), 84192-62-1; **17** (isomer 1), 84175-72-4; **17** (isomer 2), 84175-73-5; **17** (isomer 3), 84175-74-6; **17** (isomer 4), 84175-75-7; **18a**, 84175-76-8; **18b**, 84175-77-9; **18c**, 84175-78-0; **18d**, 84175-79-1; methyl ethylphosphinate, 27852-48-8.