A NEW ROUTE FOR PREPARATION OF 5-DEOXY-5-HYDROXYPHOSPHINYL-D-GLUCO- AND L-IDOPYRANOSE DERIVATIVES

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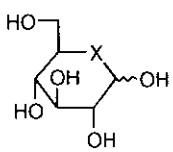
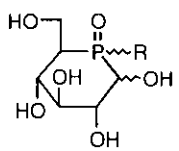
Abstract - By starting with known 3,6-di-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-5-ulose (**5**), the 3,6-di-*O*-benzyl derivatives (**8** and **10**) of the title phospho-sugar analogs were prepared in six steps through the key intermediates, 5-deoxy-5-dimethoxyphosphinyl-1,2-*O*-isopropylidene-α-D-gluco- and -L-idofuranoses (**7a** and **7b**), respectively. These products (**8** and **10**) were respectively converted into the corresponding 1,2,4-tri-*O*-acetyl-5-methoxyphosphinyl derivatives (**9** and **11**), whose structures and conformations (mostly in $^4C_1$) were established by spectroscopy.

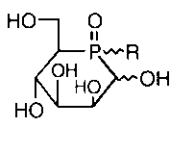
Various sugar analogs (pseudo-sugars) containing a heteroatom, instead of oxygen, in the ring have been prepared due to a wide variety of interest in their chemical and biochemical properties,[1,2] representative examples being 5-amino-5-deoxy-D-glucopyranose (**1**) (nojirimycin)[3] and 5-thio-D-glucopyranose (**2**).[4] In view of such a chemical modification, we have prepared various sugar analogs having a phosphorus atom in the ring (phospho-sugar),[5] such as D-glucopyranose (**3**)[6-8] and D-mannopyranose analogs (**4**).[9,10] We describe herein a new route for an improved, unambiguous preparation of hitherto unknown analogs of D-gluco- and L-idopyranose having a hydroxyphosphinyl group in the ring.



1 X = NH
2 X = S



3 R = OH, Ph, Et

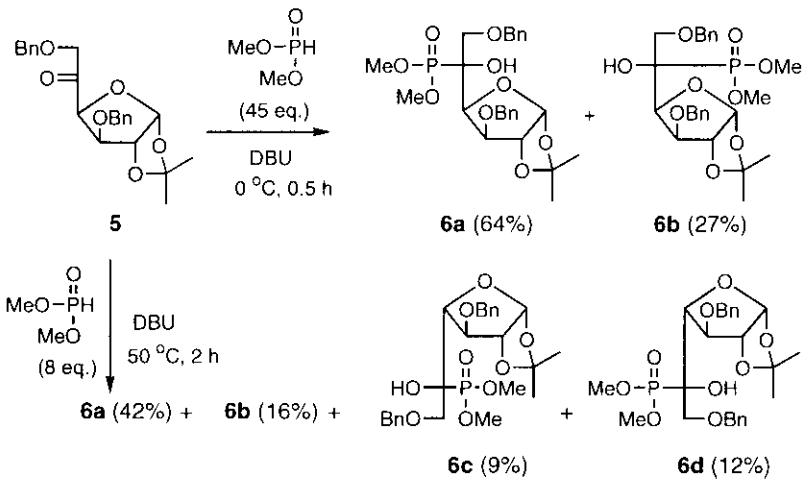


4 R = OH, Me

In most cases, a key step in the synthesis of phospho-sugars of a hexopyranose type has been a stereoselective introduction of a phosphinyl group into the C-5 position of an appropriate hexofuranose precursor.[5-11] Indeed, in the synthesis of 5-deoxy-5-phosphinyl-D-glucopyranoses (**3**), the addition reaction of an appropriate phosphonate (or phosphinate) reagent to 3-*O*-acetyl-5,6-dideoxy-1,2-*O*-isopropylidene-6-nitro-α-D-*xylo*-hex-5-enofuranose in the presence of triethylamine took place in such a way as to give the

D-glucofuranose type preferentially over the L-idofuranose type in a ratio of approximately 9:1.[11] However, the conversion of their 6-nitro group of the resulting intermediates into its 6-hydroxyl derivatives and the subsequent protection of this 6-OH required multi-step procedures, thus causing the overall yield of **3** rather low.[6-8]

In the mean time, it has become apparent in this series of synthesis that protection of 3- and 6-hydroxyl groups with a suitable group is essential to perform effective functional transformations. After examining several protecting groups, we found that a hydrophobic group such as benzyl facilitated the isolation of reaction intermediates and products, most of which are highly water-soluble. We therefore devised a new route for preparation of 5-deoxy-5-dimethoxyphosphinyl-1,2-*O*-isopropylidene-α-D-glucofuranose (**7a**) by starting with 3,6-di-*O*-benzyl-protected 5-ulose (**5**).[12]



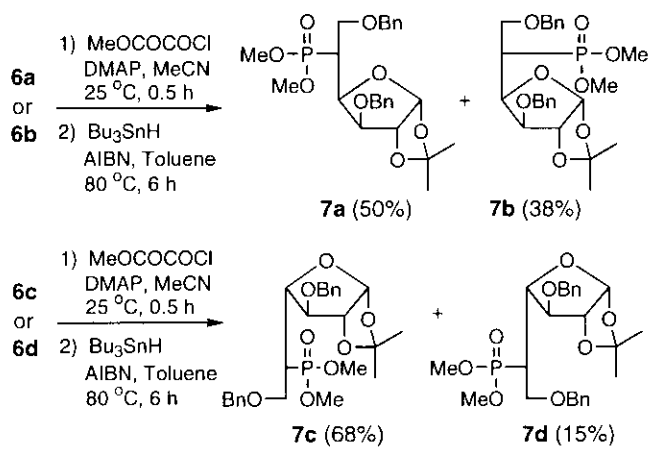
Scheme 1

First, the addition reaction of dimethyl phosphonate (45 equiv.) to **5** was examined in the presence of DBU (1.2 equiv.) at 0 °C for 0.5 h and the reactants were concentrated at 45—50 °C *in vacuo*. The products thus isolated were the anticipated (5*R*)-5-phosphinyl-D-*xylo*-hexofuranose (**6a**) and its (5*S*)-epimer (**6b**), as well as two other minor, unexpected isomers (Scheme 1). The structures of these minor products were proved by spectroscopy to be the C-4-inverted (5*R*)-L-*arabino*-hexofuranose (**6c**) and its (5*S*)-epimer (**6d**). This led us to modify the base-catalyzed addition reaction conditions as follows: **5** was treated with dimethyl phosphonate and DBU under the same conditions as above but the reactants were quenched with saturated aqueous ammonium chloride before evaporation of the excess phosphonate *in vacuo*. Then, we obtained only **6a** (64%) and its (5*S*)-epimer (**6b**) (27%) and no C-4 inversion of **5** was observed.

On the other hand, we also took investigation on the optimum conditions to cause above C-4 inversion and found that the addition reaction at 50 °C for 2 h with a higher concentration of DBU gave all four products (**6a**—**d**) in the yields shown in Scheme 1. Furthermore, treatment of **6a** with DBU in dimethyl phosphonate at 45 °C for 2 h was also found to give all four compounds (**6a**) (37% recovery), (**6b**) (12%), (**6c**) (7%) and (**6d**) (9%). This suggests that the reverse reaction of **6a** to regenerate **5** is presumed to take

place partly, causing the base-catalyzed C-4 inversion of **5**.

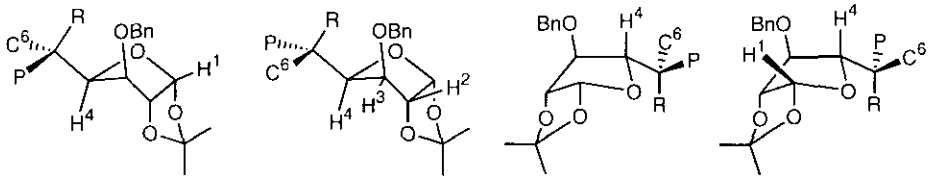
The deoxygenation of 5-hydroxyl group of **6a** and **6b** was best achieved by application of the Dolan and MacMilan's procedure:[13] Namely, the (5*R*)-epimer (**6a**) was first converted into methyl oxalyl ester and then reduced with tributylstannan, affording the 5-phosphinyl-D-glucofuranose derivative (**7a**) (50%) and the L-ido isomer (**7b**) (38%) (Scheme 2). Similarly, (5*S*)-epimer (**6b**) yielded **7a** and **7b** in almost the same ratio and yields as those from **6a**. On the other hand, the conversion of either of D-*arabino*-hexofuranoses (**6c** or **6d**) similarly provided D-galactofuranose (**7c**) (68%) and L-altrofuranose (**7d**) (15%). The former product (**7c**) is anticipated to be an important precursor for a convenient synthesis of a phospho-sugar analog of hitherto unprepared D-galactose.[14]



Scheme 2

The C-5 configurations of these 5-phosphinyl compounds (**6a—d** and **7a—d**) were assigned on the basis of the large magnitudes of $J_{4,5}$ values (*i.e.*, the *anti* relationship of H-4/H-5 for **7a—d**) and the presence of the long-range couplings ($^5J_{1,P}$, $^5J_{2,P}$ and $^4J_{3,P}$) (see Table 1 and Figure 1). It is known that (5*RS*)-1,2-*O*-isopropylidene-α-D-*xylo*- and β-L-*arabino*-hexofuranose derivatives have the E_4 and $^1T_0$ conformational preference, respectively.[15] Although compounds (**6a—d**) have a hydroxyl group at C-5 position, they seem to have almost the same conformation and configuration as those of the corresponding 5-deoxy compounds (**7a—d**), because of a similar characteristic tendency of the corresponding coupling constants between **6a—d** and **7a—d**. Thus, α-D-*gluco* configurations for **7a** and **6a** were confirmed by the presence of $^5J_{1,P}$, whereas the β-L-*ido* configurations for **7b** and **6b** were derived from the presence of $^5J_{2,P}$ and $^4J_{3,P}$. Similarly, the β-L-*altro* configurations for **7d** and **6d** were derived from the presence of $^5J_{1,5}$. Therefore, the conformations of their C-5 epimers (**7c** and **6c**) were assigned to be the α-D-*galacto* form.

The major product (**7a**) was then reduced with sodium dihydrobis(2-methoxyethoxy)aluminate (SDMA) to give the 5-phosphino derivative, which, by the action of hydrochloric acid and then by the hydrogen peroxide oxidation, afforded 3,6-di-*O*-benzyl-5-deoxy-5-hydroxyphosphinyl-D-glucopyranoses (**8**), the separation and structural assignment of which were made by converting it into the 5-methoxyphosphinyl-



6a R = OH **6b** R = OH **6c** R = OH **6d** R = OH
7a R = H **7b** R = H **7c** R = H **7d** R = H

Figure 1. The most favorable conformations for **6a**—**d** and **7a**—**d**

Table 1. ^{1}H and ^{31}P NMR Parameters for Compounds **6a**—**d** and **7a**—**d** in $CDCl_3$

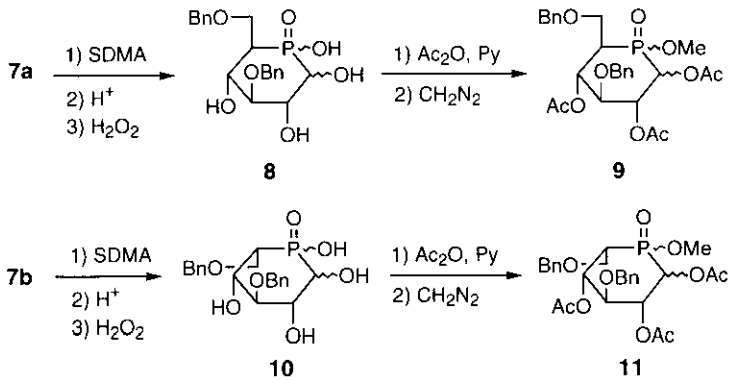
Compound	Chemical shifts / δ											
	H-1	H-2	H-3	H-4	H-5	H-6	H-6'	$P(OMe)_2$[b]	CMe_2	CH_2O-3[c,d]	CH_2O-6[c,d]	^{31}P
6a	5.99	4.59	4.43	4.54	(4.93)[a]	3.88	3.82	3.76, 3.74	1.49, 1.33	4.63, 4.60[e]	4.69, 4.64[e]	26.3
6b	6.01	4.50	4.25	4.475	(4.58)[a]	3.92	3.79	3.84, 3.80	1.52, 1.32	4.36, 4.15[e]	4.58, 4.47[f]	23.6
6c	5.91	4.64	4.31	4.69	(3.51)[a]	3.83	3.58	3.78, 3.775	1.57, 1.34	4.56, 4.46[f]	4.52, 4.52	25.7
6d	5.87	5.62	4.60	5.62	(3.50)[a]	3.80	3.80	3.77, 3.76	1.53, 1.34	4.66, 4.625[f]	4.60, 4.60	25.8
7a	5.87	4.60	4.08	4.52	2.82	4.00	3.91	3.67, 3.64	1.51, 1.33	4.63, 4.55[e]	4.59, 4.56[e]	31.9
7b	5.93	4.53	3.81	4.48	2.67	3.74	3.46	3.755, 3.74	1.52, 1.31	4.50, 4.18[f]	4.49, 4.31[f]	32.1
7c	5.87	4.61	4.32	4.46	2.61	3.795	3.78	3.75, 3.73	1.55, 1.33	4.47, 4.45[f]	4.51, 4.51	30.5
7d	5.94	4.64	4.43	4.58	2.61	3.99	3.93	3.67, 3.64	1.44, 1.30	4.59, 4.55[f]	4.63, 4.59[f]	31.6

	Coupling constants / Hz												
	$J_{1,2}$	$J_{1,P}$	$J_{2,3}$	$J_{2,P}$	$J_{3,4}$	$J_{3,P}$	$J_{4,5}$	$J_{4,P}$	$J_{5,6}$	$J_{5,6'}$	$J_{5,P}$	$J_{6,6'}$	$J_{6,P}$	$J_{6',P}$
6a	3.7	1.5	0	0	2.8	0		0.5				9.2	25.6	13.4
6b	3.7	0	0	1.8	3.0	1.0		4.0				9.8	7.9	14.5
6c	4.0	0	1.2	0	4.3	0		2.5				9.8	9.8	21.4
6d	3.7	0.8	g	0	g	0		g				–	17.1	17.1
7a	3.7	1.2	0	0	3.0	0	10.8	5.2	2.8	5.2	19.8	9.2	16.5	28.7
7b	4.0	0	0	2.1	3.1	1.0	10.1	7.0	4.3	4.0	18.6	9.5	10.9	26.2
7c	4.0	0	1.0	0	3.1	0	9.2	11.3	5.5	4.0	20.4	9.2	13.1	16.6
7d	4.0	1.5	0.8	0	1.8	0	10.1	3.7	3.7	3.4	20.5	7.5	28.7	11.9

[a] HO-5. [b] J_{POMe} = 10.7—11.0 Hz. [c] The assignment of CH_2O-3 or -6 signals may have to be interchanged. [d] Ph: δ = 7.24—7.36 (10H, m) except for **6b** [δ = 7.12 (2H, dd), 7.27—7.33 (8H, m)] and **7b** [δ = 7.18 (2H, dd), 7.26—7.32 (8H, m)]. [e] ^{2}J = 10.7—11.0 Hz. [f] ^{2}J = 11.6—11.9 Hz. [g] Uncertain because of overlapping with other signals.

1,2,4-tri-*O*-acetates (**9**): after chromatographic purification, the 5-deoxy-5-[(*R*)-methoxyphosphinyl]-α-D-glucopyranose (**9a**) (5.2% overall yield from **8**), its β-anomer (**9b**) (5.9%), 5-[(*S*)-methoxyphosphinyl]-α-D-glucopyranose (**9c**) (10.8%), and its β-anomer (**9d**) (11.3%) were obtained (Scheme 3). The yield of each product from **7a** turned out to be substantially better than that of penta-*O*-acetyl derivatives of D-glucopyranose (**3**) from the 3-*O*-acetyl-6-*O*-(tetrahydropyran-2-yl)-α-D-glucofuranose precursor.[6]

Any of L-idopyranose type phospho-sugars having hydoxyphosphinyl-in-the-ring has been synthesized so far. In this regard, compound (**7b**) was subjected to the same, three-step ring-transposition reaction to give 3,6-di-*O*-benzyl-5-deoxy-5-hydroxyphosphinyl-L-idopyranose (**10**). This was led to **11** for isolation and structural assignment; after purification by column chromatography, 1,2,4-tri-*O*-acetyl-3,6-di-*O*-benzyl-5-deoxy-5-[(*R*)-methoxyphosphinyl]-β-L-idopyranose (**11a**) (10.0% from **7b**), its α-anomer (**11b**) (4.4%), 5-[(*S*)-methoxyphosphinyl]-β-D-idopyranose (**11c**) (13.2%), and its α-anomer (**11d**) (9.3%) were obtained in much better yields compared with the case of 5-deoxy-5-ethylphosphinyl congeners.[8]

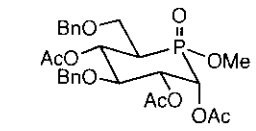


Scheme 3

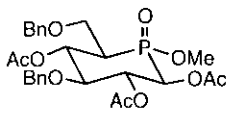
The structural assignments of **9a—d** and **11a—d** were made by the analysis of the ^{1}H-NMR spectra (see Table 2). The D-glucopyranose configuration is assignable to **9a—d** on the basis of their large values of $J_{4,5}$ (11—12 Hz). In contrast, the small values of $J_{4,5}$ (4—6 Hz) for **11a—d** indicate the L-idopyranose structure. The $^4C_1$ conformation of **9a—d** and **11b,d** are derived from the large magnitudes of $J_{2,3}$ and $J_{3,4}$ (9—10 Hz) and the small magnitudes of $J_{2,P}$ and $J_{4,P}$ (0.5—7 Hz). Compound (**11c**), which has the relatively small $J_{3,4}$ value (7.0 Hz) and the relatively large $J_{4,P}$ value (14.4 Hz), also seems to prefer the $^4C_1$ conformation, although a local flattering of the pyranose ring is caused by 1,3-diaxial repulsion between $BnOCH_2$ group and AcO-1. Compound (**11a**) is considered to exist as an equilibrium mixture (*ca.* 2:3) of the $^4C_1$ and $^1C_4$ conformers, taking into consideration the relatively large magnitudes of $J_{2,P}$ and $J_{4,P}$ (17—23 Hz).

The α-orientation of C-1 for **9a,c** and the β-orientation for **11a,c** are derived by considering the small magnitudes of $J_{1,2}$ (3—4 Hz) , whereas the β-D-anomers (**9b,d**) and α-L-anomers (**11b,d**) show large $J_{1,2}$ values (10—11 Hz). A slight down field shift (0.2—0.3 ppm) of H-2 signals of **9a,b** and **11a,b**, compared with those of **9c,d** and **11c,d**, indicates an axial P=O orientation of the formers and an equatorial

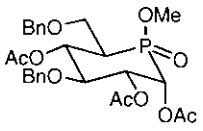
P=O orientation of the latters.



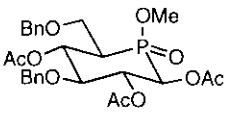
9a



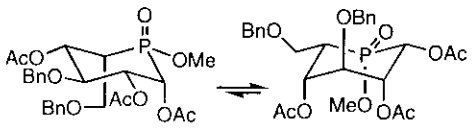
9b



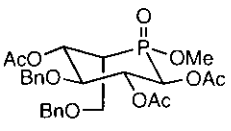
9c



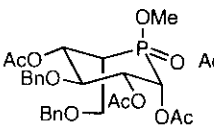
9d



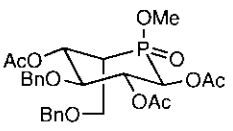
11a



11b



11c



11d

Table 2. ^{1}H and ^{31}P NMR Parameters for Compounds **9a—d** and **11a—d** in $CDCl_3$

Compound	Chemical shifts / δ												
	H-1	H-2	H-3	H-4	H-5	H-6	H-6'	POMe	AcO-1,2,4[a]	CH_2O-3,6[b,c]			^{31}P
9a	5.63	5.45	3.91	5.41	2.65	3.915	3.68	3.67	2.19, 1.93, 1.81	4.68, 4.61; 4.49, 4.43			39.4
9b	5.28	5.55	3.68	5.36	2.40	3.96	3.66	3.68	2.11, 1.90, 1.85	4.64, 4.62; 4.54, 4.48			39.3
9c	5.64	5.19	3.82	5.43	2.64	3.85	3.73	3.76	2.20, 1.93, 1.82	4.68, 4.59; 4.47, 4.415			38.3
9d	5.39	5.38	3.64	5.44	2.31	3.85	3.76	3.81	2.11, 1.89, 1.80	4.60, 4.60; 4.46, 4.41			36.2
11a	5.66	5.56	3.97	5.45	2.99	3.87	3.72	3.81	2.09, 2.00, 1.92	4.53, 4.42; 4.71, 4.71			37.1
11b	5.60	5.51	4.18	5.45	2.78	d	d	3.71	2.12, 1.93, 1.88	4.63, 4.60; 4.61, 4.61			38.7
11c	5.60	5.22	4.02	5.22	2.92	3.90	3.86	3.83	2.08, 1.955, 1.95	4.75, 4.68; 4.58, 4.50			38.7
11d	5.76	5.28	4.28	5.17	2.61	3.82	3.75	3.92	2.11, 1.91, 1.875	4.80, 4.56; 4.65, 4.59			39.2

	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_{POMe}
9a	2.9	14.7	10.2	0.5	9.3	12.2	1.5	5.9	6.8	13.7	9.8	10.2	14.7	11.2
9b	10.3	6.3	9.3	3.9	9.3	10.8	5.4	7.6	5.4	13.2	9.3	12.2	15.5	11.2
9c	3.0	15.6	10.1	0.5	9.5	11.6	2.1	4.9	3.1	14.3	9.5	7.0	19.8	10.7
9d	11.0	2.2	9.3	1.5	9.5	11.6	2.4	4.9	3.4	12.5	9.8	8.0	18.0	10.7
11a[e]	3.7	9.2	6.1	16.8	5.5	4.0	23.2	4.0	8.4	19.3	9.8	7.9	6.5	10.7
11b	10.7	6.1	8.6	3.4	8.8	5.5	6.8	3.3	3.3	25.6	d	d	d	11.0
11c[f]	3.4	13.7	8.6	4.9	7.0	4.8	14.4	4.3	7.0	21.1	9.8	12.2	9.2	10.7
11d	10.7	5.5	9.5	1.8	10.0	6.1	1.0	2.6	2.6	25.3	9.6	7.5	28.4	10.4

[a] The assignment of acetyl signals may have to be interchanged. [b] ^{2}J = 11.3—11.9 Hz: the assignment of CH_2O-3 or -6 may have to be interchanged. [c] Ph: δ = 7.20—7.36 (10H, m). [d] Uncertain because of overlapping with other signals. [e] $J_{1,5}$ = 0.8, $J_{2,4}$ = 1.0 Hz. [f] $J_{1,5}$ = 1.2 Hz.

Although improvement in yields of some steps has to be made, the work described so far demonstrates an effective way for preparation of 5-deoxy-5-hydroxyphosphinyl-D-gluco- and L-idopyranoses. Their yields were much higher and reaction steps are fewer than the previously employed methods. Also, debezylation of the phospho-sugars (**8—11**) has remained to be performed. This, however, is expected to undergo smoothly, upon taking into account our previous deprotection experiments with other phospho-sugars: Debenzylation of 1,2,4-tri-*O*-acetyl-3-*O*-benzyl-5-deoxy-5-methoxyphosphinyl-D-xylopyranose[6] and 1,4-anhydro-5-*O*-benzyl-4-deoxy-4-methoxyphosphinyl-D-ribitol[16] was readily achieved by catalytic hydrogenation over 10% Pd/C in methanol in the presence of formic acid.

EXPERIMENTAL SECTION

All reactions were monitored by TLC (Merck silica gel 60F, 0.25 mm) with AcOEt as the solvent system. Column chromatography was performed by Katayama Silica Gel 60K070. The NMR spectra were measured in $CDCl_3$ with Varian VXR-500 (500 MHz for ^1H) and VXR-200 (81 MHz for ^{31}P) spectrometers at 22 °C. Chemical shifts are reported as δ values relative to tetramethylsilane (internal standard for ^1H) and 85% phosphoric acid (external standard for ^{31}P). The MS spectra were taken on a VG-70SE instrument and are given in terms of *m/z* (relative intensity) compared with the base peak.

*(5R)- and (5S)-3,6-Di-O-benzyl-5-deoxy-5-dimethoxyphosphinyl-1,2-O-isopropylidene-α-D-*xylo-*hexofuranoses (**6a,b**) and -β-L-*arabino-*hexofuranoses (**6c,d**).* *A.* DBU (4.50 mL, 30.1 mmol) was dropwise added to a solution of **5**[12] (10.0 g, 25.1 mmol) in dimethyl phosphonate (102 mL, 1.11 mol) at 0 °C and the solution was stirred at this temperature for 30 min under argon. The excess phosphonate was distilled off under reduced pressure (0.3 Torr) at 50 °C. The residue was separated by column chromatography with a gradient eluent of 1:1 AcOEt–hexane → AcOEt into four fractions.

Fraction A (R_f = 0.58) gave the (5*R*)-α-D-*xylo*-hexofuranose (**6a**) as a colorless syrup (5.49 g, 43%): ^1H and ^{31}P NMR, see Table 1; FAB MS *m/z* 509 (M+1; 34), 419 (5), 181 (15), 91 (100). Found: *m/z* 509.1949. Calcd for $C_{25}H_{34}O_9P$: M+1, 509.1941.

Fraction B (R_f = 0.53) gave the (5*S*)-β-L-*arabino*-hexofuranose (**6d**) as a colorless syrup (1.79 g, 14%): ^1H and ^{31}P NMR, see Table 1.

Fraction C (R_f = 0.38) gave the (5*R*)-β-L-*arabino*-hexofuranose (**6c**) as colorless prisms (1.17 g, 9.2%): mp 94—95 °C (from 2:1 AcOEt-hexane); ^1H and ^{31}P NMR, see Table 1; FAB MS *m/z* 509 (M+1; 14), 451 (11), 419 (5), 361 (7), 181 (22), 91 (100). Found: *m/z* 509.1951. Calcd for $C_{25}H_{34}O_9P$: M+1, 509.1941.

Fraction D (R_f = 0.30) gave the (5*S*)-α-D-*xylo*-hexofuranose (**6b**) as a colorless syrup (1.66 g, 13%): ^1H and ^{31}P NMR, see Table 1.

B. Compound (**5**) (990 mg, 2.48 mmol) was stirred with dimethyl phosphonate (9.9 mL, 108 mmol) and DBU (0.445 mL, 2.98 mmol) at 0 °C for 30 min. The mixture was treated with saturated NH_4Cl (10 mL) at rt overnight and extracted with CH_3Cl three times. The combined organic layers were washed with water, dried (Na_2SO_4), and evaporated *in vacuo* (50 °C, 0.3 Torr). The residue was chromatographed to give **6a** (810 mg, 64%) and **6b** (347 mg, 27%).

C. Compound (**5**) (146 mg, 0.366 mmol) was treated with dimethyl phosphonate (0.270 mL, 2.94 mmol) and DBU (0.066 mL, 0.44 mmol) at 50 °C for 2 h and worked up with the same procedure described above, to give **6a** (78.3 mg, 42%), **6b** (29.6 mg, 16%), **6c** (16.9 mg, 9%), and **6d** (22.7 mg, 12%).

D. Compound (**6a**) (186 mg, 0.366 mmol) was treated with dimethyl phosphonate (0.270 mL, 2.94 mmol) and DBU (0.066 mL, 0.44 mmol) at 50 °C for 2 h and worked up with the same procedure described above, to give **6a** (69.6 mg, 37%), **6b** (22.9 mg, 12%), **6c** (13.0 mg, 7%), and **6d** (17.3 mg, 9%).

*3,6-Di-*O*-benzyl-5-deoxy-5-dimethoxyphosphinyl-1,2-*O*-isopropylidene-α-D-gluco-* and *β-L-idofuranose (7a,b).* Monomethyl oxalyl chloride (5.47 mL, 59.5 mmol) was added to a solution of **6a** (6.05 g, 11.9 mmol) and DMAP (7.27 g, 59.5 mmol) in dry MeCN (100 mL) at 0 °C. The mixture was stirred at 0 °C for 30 min under argon, poured into water and extracted with $CHCl_3$. The organic layer was washed with saturated $NaHCO_3$ and brine, dried (Na_2SO_4) and evaporated *in vacuo*. The residue was coevaporated with dry toluene and dissolved in the same solvent (100 mL). Bu_3SnH (4.80 mL, 17.8 mmol) and AIBN (293 mg, 1.78 mmol) were added under argon. The mixture was stirred at 80 °C for 6 h and then concentrated *in vacuo*. The residue was separated by column chromatography to give **7a** and **7b**.

7a: Colorless syrup (2.94 g, 50%); R_f = 0.60; ^1H and ^{31}P NMR, see Table 1; FAB MS *m/z* 493 (M + 1, 20), 435 (18), 237 (12), 185 (21), 91 (100). Found: *m/z* 493.1998. Calcd for $C_{25}H_{34}O_8P$: M + 1, 493.1992.

7b: Colorless syrup (2.24 g, 38%); R_f = 0.38; ^1H and ^{31}P NMR, see Table 1; FAB MS *m/z* 493 (M + 1, 11), 435 (12), 237 (8), 185 (16), (100). Found: *m/z* 493.1981. Calcd for $C_{25}H_{34}O_8P$: M + 1, 493.1992.

*3,6-Di-*O*-benzyl-5-deoxy-5-dimethoxyphosphinyl-1,2-*O*-isopropylidene-α-D-galacto- and β-L-arbino-furanose (7c,d).* By use of the same procedures as described for **7a**,**b**, compound (**6c**) (145 mg, 0.285 mmol) was converted into **7c** and **7d**.

7c: Colorless needles (95.5 mg, 68%); mp 68—69 °C (from 2:1 AcOEt–hexane); ^1H and ^{31}P NMR, see Table 1; FAB MS *m/z* 493 (M+1; 10), 435 (12), 345 (6), 237 (9), 185 (16), 91 (100). Found: *m/z* 493.2001. Calcd for $C_{25}H_{34}O_8P$: M+1, 493.1992. *Anal.* Calcd for $C_{25}H_{33}O_8P$: C, 60.97; H, 6.75. Found: C, 60.68; H, 6.85.

7d: Colorless syrup (21.4 mg, 15%): ^1H and ^{31}P NMR, see Table 1.

*1,2,4-Tri-*O*-acetyl-3,6-di-*O*-benzyl-5-deoxy-5-methoxyphosphinyl-D-glucopyranose (9a—d).* To a solution of **7a** (228 mg, 0.463 mmol) in dry toluene (2.5 mL) was added, with stirring, a solution of 0.34 M SDMA in toluene (3.5 mL, 1. 2 mmol) in small portions during 30 min at 0 °C under argon. The stirring was continued at 0 °C for 1 h. Then, water (0.10 mL) was added to decompose excess SDMA and the mixture was centrifuged. The precipitate was extracted with several portions of toluene. The organic layers were combined and evaporated *in vacuo* and the remaining syrup was immediately treated with 1:1 2-propanol–0.5 M hydrochloric acid (5.0 mL) at 90 °C for 2 h under argon. After cooling, the reactants were neutralized with Amberlite IRA-93ZU. The resin was filtered off and washed with aqueous ethanol. The filtrate was evaporated *in vacuo*. The residue was dissolved in 2-propanol (2.6 mL), treated with 30% hydrogen peroxide (0.6 mL) at rt for 12 h and then concentrated *in vacuo* to give crude 3,6-di-*O*-benzyl-5-deoxy-5-hydroxyphosphinyl-α,β-D-glucopyranoses (**8**) as a colorless syrup. This was dissolved in dry pyridine (2.0 mL), and acetic anhydride (1.0 mL) was added at 0 °C. The mixture was stirred at rt

for 18 h, diluted with a small amount of cold water, and concentrated *in vacuo*. The residue was dissolved in ethanol and passed through a column of Amberlite IR-120(H^+) (20 mL). The eluent was evaporated *in vacuo* and the residue was methylated with ethereal diazomethane in dry CH_2Cl_2 (2.0 mL) at 0 °C. After evaporation of the solvent, the residue was separated by column chromatography with a gradient eluent of 2:1 AcOEt-hexane → AcOEt into three fractions A—C.

Fraction A (R_f = 0.50) gave the 5-[(*R*)-methoxyphosphinyl]-α-D-glucopyranose (**9a**) as a colorless syrup (13.2 mg, 5.2% from **7a**): ^1H and ^{31}P NMR, see Table 2; FAB MS *m/z* 549 (M+1; 15), 507 (5), 459 (6), 181 (8), 93 (100). Found: *m/z* 549.1883. Calcd for $C_{27}H_{34}O_{10}P$: M+1, 549.1890.

Fraction B (R_f = 0.46) gave 5-[(*R*)-P]-β-isomer (**9b**) as colorless needles (15.0 mg, 5.9% from **7a**): mp 222—223 °C (from MeOH); ^1H and ^{31}P NMR, see Table 2; FAB MS *m/z* 549 (M+1; 12), 507 (4), 491 (4), 461 (6), 369 (12), 277 (18), 185 (89), 93 (100). Found: *m/z* 549.1903. Calcd for $C_{27}H_{34}O_{10}P$: M+1, 549.1890. *Anal.* Calcd for $C_{27}H_{33}O_{10}P$: C, 59.12; H, 6.06. Found: C, 58.88; H, 6.15.

Fraction C (R_f = 0.42—0.39) gave a colorless syrup (56.3 mg) which consisted of 5-[(*S*)-P]-α-isomer **9c** (10.9% from **7a**) and its β-isomer (**9d**) (11.3%): ^1H and ^{31}P NMR, see Table 2.

*1,2,4-Tri-O-acetyl-3,6-di-O-benzyl-5-deoxy-5-methoxyphosphinyl-L-idopyranose (**11a—d**).* The procedures similar to those for the preparation of compounds (**9**) from **7a** were employed. Thus, compound (**7b**) (229 mg, 0.465 mmol) were converted into the diastereomeric L-idopyranoses (**11**) *via* intermediate (**10**). The crude product (**11**) was separated by column chromatography into three fractions A—C.

Fraction A (R_f = 0.48) gave the 5-[(*R*)-methoxyphosphinyl]-β-L-idopyranose (**11a**) as a colorless syrup (25.5 mg, 10.0% from **7b**): ^1H and ^{31}P NMR, see Table 2; FAB MS *m/z* 549 (M+1; 18), 507 (2), 459 (5), 181 (9), 91 (100). Found: *m/z* 549.1898. Calcd for $C_{27}H_{34}O_{10}P$: M+1, 549.1890.

Fraction B (R_f = 0.43) gave a colorless syrup (34.9 mg) which consisted of 5-[(*R*)-P]-α-isomer (**11b**) (4.4% from **7b**) and its 5-[(*S*)-P]-α-isomer (**11d**) (9.3%): ^1H and ^{31}P NMR, see Table 2.

Fraction C (R_f = 0.39) gave 5-[(*S*)-P]-β-isomer (**11c**) as a colorless syrup (33.6 mg, 13.2% from **7b**): ^1H and ^{31}P NMR, see Table 2; FAB MS *m/z* 549 (M+1; 12), 507 (4), 459 (8), 441 (5), 181 (10), 91 (100). Found: *m/z* 549.1879. Calcd for $C_{27}H_{33}O_{10}P$: M+1, 549.1890.

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